



ASTROVIROLOGY



WORKSHOP
WITHOUT
WALLS

1
00:00:05,269 --> 00:00:02,310
good morning everybody thank you so much

2
00:00:07,349 --> 00:00:05,279
for agreeing to participate

3
00:00:09,030 --> 00:00:07,359
in this effort

4
00:00:10,870 --> 00:00:09,040
we are

5
00:00:13,030 --> 00:00:10,880
doing this as one of our workshops

6
00:00:15,509 --> 00:00:13,040
without walls which is a

7
00:00:18,390 --> 00:00:15,519
tradition here at nai we think we

8
00:00:21,590 --> 00:00:18,400
invented it and we have done it for a

9
00:00:23,670 --> 00:00:21,600
huge variety of topics and with great

10
00:00:25,429 --> 00:00:23,680
results so

11
00:00:28,950 --> 00:00:25,439
let me give you my own personal

12
00:00:31,429 --> 00:00:28,960
perspective on why astrobiology why now

13
00:00:33,830 --> 00:00:31,439

i am not a virologist although i

14

00:00:36,870 --> 00:00:33,840

appreciate viruses and i think i'm

15

00:00:39,910 --> 00:00:36,880

seeing them everywhere in my own work um

16

00:00:41,670 --> 00:00:39,920

but uh i hold the position that uh the

17

00:00:43,990 --> 00:00:41,680

late dr barry

18

00:00:47,910 --> 00:00:44,000

blumberg held and of course he was a

19

00:00:51,110 --> 00:00:47,920

nobel uh laureate uh winning uh

20

00:00:54,869 --> 00:00:51,120

virologist and chemist and uh who worked

21

00:00:56,869 --> 00:00:54,879

extensively of course with um hepatitis

22

00:01:00,229 --> 00:00:56,879

and various other

23

00:01:02,869 --> 00:01:00,239

uh aspects of medical virology but who

24

00:01:04,149 --> 00:01:02,879

was of course extremely passionate about

25

00:01:11,109 --> 00:01:04,159

astro

26

00:01:14,070 --> 00:01:11,119

director of the institute i now had

27

00:01:17,429 --> 00:01:14,080

we are in our 20th year and nai is going

28

00:01:20,550 --> 00:01:17,439

away as an entity and being replaced by

29

00:01:22,710 --> 00:01:20,560

a new way of organizing astrobiology

30

00:01:24,550 --> 00:01:22,720

within nasa

31

00:01:27,270 --> 00:01:24,560

but i have always felt since barry

32

00:01:28,789 --> 00:01:27,280

passed away and he was a good friend of

33

00:01:30,950 --> 00:01:28,799

astrobiology

34

00:01:33,109 --> 00:01:30,960

and a good friend of mine

35

00:01:34,390 --> 00:01:33,119

and at the time he passed away

36

00:01:37,590 --> 00:01:34,400

we were

37

00:01:39,109 --> 00:01:37,600

in the process of sort of pre-organizing

38

00:01:41,270 --> 00:01:39,119

an effort

39

00:01:44,630 --> 00:01:41,280

to do a field trip for the

40

00:01:47,910 --> 00:01:44,640

uh astrovirology focus group uh into

41

00:01:50,710 --> 00:01:47,920

caves to actually look at what the uh

42

00:01:52,870 --> 00:01:50,720

vyram situation might be in cave

43

00:01:55,630 --> 00:01:52,880

environments which is where i typically

44

00:01:58,149 --> 00:01:55,640

work and do primarily

45

00:02:01,990 --> 00:01:58,159

bacteriological and archaeal

46

00:02:05,350 --> 00:02:02,000

studies so when barry passed away

47

00:02:06,789 --> 00:02:05,360

of course the plans for that halted

48

00:02:10,150 --> 00:02:06,799

and so

49

00:02:12,470 --> 00:02:10,160

before we sunset the institute i would

50

00:02:15,030 --> 00:02:12,480

like to uh you know do something to

51
00:02:18,309 --> 00:02:15,040
honor his great work in that field and

52
00:02:21,589 --> 00:02:18,319
his passionate devotion to astrobiology

53
00:02:24,869 --> 00:02:21,599
and his faith in uh pursuing the

54
00:02:26,869 --> 00:02:24,879
astrovirological aspects of astrobiology

55
00:02:28,869 --> 00:02:26,879
which i think are extremely important

56
00:02:32,309 --> 00:02:28,879
and have not received the attention that

57
00:02:35,270 --> 00:02:32,319
many other areas of astrobiology have

58
00:02:39,030 --> 00:02:35,280
on top of that of course why now

59
00:02:41,509 --> 00:02:39,040
part of the reason is because

60
00:02:43,670 --> 00:02:41,519
for those of you not familiar with the

61
00:02:46,390 --> 00:02:43,680
nasa and its processes

62
00:02:49,270 --> 00:02:46,400
one of the things that governs what we

63
00:02:51,670 --> 00:02:49,280

choose to do in science and missions

64

00:02:54,070 --> 00:02:51,680

is a every 10-year

65

00:02:56,630 --> 00:02:54,080

so-called decadal study that happens

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00:03:00,229 --> 00:02:56,640

within all of the four major science

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00:03:00,949 --> 00:03:00,239

branches of nasa so nasa is comprised of

68

00:03:23,270 --> 00:03:00,959

a

69

00:03:25,990 --> 00:03:23,280

um

70

00:03:27,910 --> 00:03:26,000

advisory and assessment activity by the

71

00:03:30,309 --> 00:03:27,920

national academy of sciences

72

00:03:33,750 --> 00:03:30,319

so the nrc or whatever it's calling us

73

00:03:35,670 --> 00:03:33,760

itself this week the academies are the

74

00:03:38,550 --> 00:03:35,680

entity that actually does this

75

00:03:41,750 --> 00:03:38,560

assessment and produces a

76

00:03:43,750 --> 00:03:41,760

large and um very uh

77

00:03:46,630 --> 00:03:43,760

attention-getting document

78

00:03:49,430 --> 00:03:46,640

and by attention-getting i mean that uh

79

00:03:51,830 --> 00:03:49,440

congress pays attention to what

80

00:03:54,309 --> 00:03:51,840

the guidance is that we receive from the

81

00:03:56,390 --> 00:03:54,319

national academies and so

82

00:03:58,630 --> 00:03:56,400

one of the ways uh in fact one of the

83

00:04:02,470 --> 00:03:58,640

main ways to get attention for a

84

00:04:05,429 --> 00:04:02,480

particular field or a particular type of

85

00:04:07,670 --> 00:04:05,439

mission concept or whatever it might be

86

00:04:09,270 --> 00:04:07,680

that one is pitching is to produce a

87

00:04:11,509 --> 00:04:09,280

white paper for

88

00:04:14,710 --> 00:04:11,519

uh that process

89

00:04:17,270 --> 00:04:14,720

now the latest intel i have about this

90

00:04:19,830 --> 00:04:17,280

is that the letter of authorization from

91

00:04:20,710 --> 00:04:19,840

nasa has not yet been received

92

00:04:22,710 --> 00:04:20,720

by

93

00:04:25,909 --> 00:04:22,720

the national academy so we don't know

94

00:04:27,270 --> 00:04:25,919

exactly the um

95

00:04:29,990 --> 00:04:27,280

precise

96

00:04:32,070 --> 00:04:30,000

timing but word on the street has it

97

00:04:34,390 --> 00:04:32,080

that the

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00:04:37,030 --> 00:04:34,400

white paper submission process will be

99

00:04:39,670 --> 00:04:37,040

opening in february and that it will

100

00:04:42,870 --> 00:04:39,680

close probably in the

101
00:04:44,550 --> 00:04:42,880
april to may time frame and then of

102
00:04:46,790 --> 00:04:44,560
course the

103
00:04:49,909 --> 00:04:46,800
panels that are constituted as part of

104
00:04:52,150 --> 00:04:49,919
the decadal process will then deliberate

105
00:04:54,790 --> 00:04:52,160
and so uh it is

106
00:04:57,030 --> 00:04:54,800
very timely for us to engage in this now

107
00:04:59,030 --> 00:04:57,040
this the middle of september

108
00:05:01,350 --> 00:04:59,040
uh that gives us october november

109
00:05:03,990 --> 00:05:01,360
december january february to about the

110
00:05:05,909 --> 00:05:04,000
middle of february so that's five months

111
00:05:09,029 --> 00:05:05,919
to really try to

112
00:05:10,950 --> 00:05:09,039
see whether we can produce a

113
00:05:12,870 --> 00:05:10,960

consensus white paper

114

00:05:14,629 --> 00:05:12,880

the good thing about the white papers is

115

00:05:16,150 --> 00:05:14,639

that they're very short the bad thing

116

00:05:18,710 --> 00:05:16,160

about the white papers is that they're

117

00:05:20,390 --> 00:05:18,720

very short and so it's very challenging

118

00:05:21,749 --> 00:05:20,400

to write them

119

00:05:25,990 --> 00:05:21,759

one of the things that is really

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00:05:28,469 --> 00:05:26,000

important about white papers is that

121

00:05:31,270 --> 00:05:28,479

instead of a particular field or mission

122

00:05:32,150 --> 00:05:31,280

concept idea or planetary body for that

123

00:05:34,950 --> 00:05:32,160

matter

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00:05:37,430 --> 00:05:34,960

having a zillion different papers

125

00:05:41,189 --> 00:05:37,440

all with a few authors on them what

126
00:05:43,670 --> 00:05:41,199
really has the most impact is a limited

127
00:05:46,469 --> 00:05:43,680
number of papers with a very large

128
00:05:48,230 --> 00:05:46,479
number of co-authors and co-signers or

129
00:05:51,510 --> 00:05:48,240
we make everybody a co-signer we do

130
00:05:54,550 --> 00:05:51,520
whatever we want there's there's no

131
00:05:57,110 --> 00:05:54,560
good template for writing these so they

132
00:05:58,790 --> 00:05:57,120
are all over the map the astrophysics

133
00:06:01,270 --> 00:05:58,800
ones that just came in because

134
00:06:03,990 --> 00:06:01,280
astrophysics is is about a year in

135
00:06:07,029 --> 00:06:04,000
advance of the planetary

136
00:06:09,990 --> 00:06:07,039
and so that's already well underway uh

137
00:06:11,909 --> 00:06:10,000
there were 940 white papers

138
00:06:14,150 --> 00:06:11,919

which is probably not a good thing that

139

00:06:16,629 --> 00:06:14,160

there were that many um

140

00:06:19,189 --> 00:06:16,639

and many of them had you know one or two

141

00:06:21,029 --> 00:06:19,199

authors not very ideal and of course

142

00:06:23,189 --> 00:06:21,039

their their formats were all over the

143

00:06:24,150 --> 00:06:23,199

place and so um

144

00:06:29,189 --> 00:06:24,160

that

145

00:06:31,350 --> 00:06:29,199

i think with the you know relatively

146

00:06:34,309 --> 00:06:31,360

small and intimate nature

147

00:06:37,670 --> 00:06:34,319

of the astrovirology community which i

148

00:06:40,230 --> 00:06:37,680

am not part exactly but i'm a fan girl

149

00:06:42,469 --> 00:06:40,240

and trying to promote

150

00:06:43,749 --> 00:06:42,479

that i think that we ought to be able to

151

00:06:44,550 --> 00:06:43,759

come up with

152

00:06:47,189 --> 00:06:44,560

uh

153

00:06:48,790 --> 00:06:47,199

one or at worst two documents that

154

00:06:51,270 --> 00:06:48,800

really promote

155

00:06:53,510 --> 00:06:51,280

aspects of astrovirology that we believe

156

00:06:55,350 --> 00:06:53,520

are germane to

157

00:06:57,350 --> 00:06:55,360

nasa's mission

158

00:07:00,070 --> 00:06:57,360

to

159

00:07:01,670 --> 00:07:00,080

understand the origins and evolution of

160

00:07:04,469 --> 00:07:01,680

life on earth

161

00:07:05,350 --> 00:07:04,479

and to extend that to other planets and

162

00:07:09,029 --> 00:07:05,360

to

163

00:07:11,670 --> 00:07:09,039

seek evidence of life elsewhere and then

164

00:07:13,990 --> 00:07:11,680

uh one of the third components that is

165

00:07:16,950 --> 00:07:14,000

often left out of the picture is the

166

00:07:19,909 --> 00:07:16,960

aspect of what is the future destination

167

00:07:22,230 --> 00:07:19,919

of life on our planet and beyond so

168

00:07:24,629 --> 00:07:22,240

really the big questions that nasa has

169

00:07:27,990 --> 00:07:24,639

scoped out are really all across this

170

00:07:30,870 --> 00:07:28,000

time spectrum and broadly across

171

00:07:33,270 --> 00:07:30,880

the life sciences as they apply to space

172

00:07:35,749 --> 00:07:33,280

and earth's deep time history

173

00:07:38,790 --> 00:07:35,759

so one of the things that i have

174

00:07:41,749 --> 00:07:38,800

suggested for the two other

175

00:07:45,830 --> 00:07:41,759

white paper groups that i'm working with

176
00:07:47,350 --> 00:07:45,840
is that a robust big review journal

177
00:07:48,950 --> 00:07:47,360
article

178
00:07:52,150 --> 00:07:48,960
to be submitted to the journal

179
00:07:54,550 --> 00:07:52,160
astrobiology be prepared

180
00:07:57,510 --> 00:07:54,560
previously to the white paper so what

181
00:08:01,350 --> 00:07:57,520
this allows us to do as a group is to

182
00:08:02,550 --> 00:08:01,360
really dig in and fully flesh out our

183
00:08:05,230 --> 00:08:02,560
current

184
00:08:07,990 --> 00:08:05,240
group thinking about the scope of

185
00:08:11,270 --> 00:08:08,000
astrobiology its

186
00:08:13,510 --> 00:08:11,280
its impact on the field of astrobiology

187
00:08:15,710 --> 00:08:13,520
what are the potentials for

188
00:08:17,670 --> 00:08:15,720

astrobiological

189

00:08:19,909 --> 00:08:17,680

observations

190

00:08:22,710 --> 00:08:19,919

or theorizing even

191

00:08:25,110 --> 00:08:22,720

as they apply to upcoming

192

00:08:26,790 --> 00:08:25,120

mission opportunities and of course i

193

00:08:30,790 --> 00:08:26,800

would not even though this is in the

194

00:08:32,870 --> 00:08:30,800

planetary decadal um some of you may not

195

00:08:35,750 --> 00:08:32,880

be aware that there are plans afoot to

196

00:08:37,990 --> 00:08:35,760

move space biology into the science

197

00:08:39,829 --> 00:08:38,000

mission directorate well if you're not a

198

00:08:42,070 --> 00:08:39,839

bureaucrat then you probably think who

199

00:08:44,389 --> 00:08:42,080

cares but it makes a big difference in

200

00:08:47,030 --> 00:08:44,399

terms of how money flows and how things

201
00:08:49,470 --> 00:08:47,040
get managed and so in terms of the

202
00:08:52,230 --> 00:08:49,480
impact on

203
00:08:54,870 --> 00:08:52,240
astrobiology and where it overlaps with

204
00:08:56,949 --> 00:08:54,880
space biology there is a big overlap

205
00:08:59,350 --> 00:08:56,959
that has been artificially separated for

206
00:09:02,630 --> 00:08:59,360
many decades within the way nasa does

207
00:09:04,710 --> 00:09:02,640
business and so clearly viruses

208
00:09:08,870 --> 00:09:04,720
because we know they play such a major

209
00:09:11,350 --> 00:09:08,880
role in us as entities us as astronauts

210
00:09:14,230 --> 00:09:11,360
um the environment the microbial

211
00:09:17,110 --> 00:09:14,240
environment of spacecraft and

212
00:09:19,750 --> 00:09:17,120
potentially human habitats on the moon

213
00:09:23,030 --> 00:09:19,760

and mars there is significant crossover

214

00:09:24,070 --> 00:09:23,040

as it applies i think to the

215

00:09:27,350 --> 00:09:24,080

virus

216

00:09:30,550 --> 00:09:27,360

concerns that we have about earth

217

00:09:32,550 --> 00:09:30,560

biology in the space context so i just

218

00:09:33,829 --> 00:09:32,560

want to set the scene for that i'm

219

00:09:35,509 --> 00:09:33,839

hoping that

220

00:09:37,509 --> 00:09:35,519

you guys will be enthusiastic about

221

00:09:39,269 --> 00:09:37,519

putting together a paper i'll do

222

00:09:41,990 --> 00:09:39,279

everything i can to facilitate it

223

00:09:43,030 --> 00:09:42,000

obviously since it's not my field i have

224

00:09:46,870 --> 00:09:43,040

little

225

00:09:49,910 --> 00:09:46,880

specific intellectual content to

226

00:09:51,670 --> 00:09:49,920

donate but i do have my understanding of

227

00:09:54,550 --> 00:09:51,680

the way nasa works and the way

228

00:09:56,710 --> 00:09:54,560

astrobiology works and i think i can

229

00:09:59,590 --> 00:09:56,720

help with how we can make the biggest

230

00:10:01,829 --> 00:09:59,600

impact with this and then my uh

231

00:10:03,910 --> 00:10:01,839

envisionment and the the the core group

232

00:10:06,790 --> 00:10:03,920

that i've been working with

233

00:10:13,269 --> 00:10:09,750

we're envisioning a distillation of the

234

00:10:15,269 --> 00:10:13,279

very high level messages from that

235

00:10:18,389 --> 00:10:15,279

paper construction

236

00:10:21,030 --> 00:10:18,399

process making it into the white paper

237

00:10:23,350 --> 00:10:21,040

and we're on a very short timeline as i

238

00:10:24,470 --> 00:10:23,360

said it would be nice if we had

239

00:10:26,630 --> 00:10:24,480

essentially

240

00:10:28,949 --> 00:10:26,640

the paper already completed and

241

00:10:30,389 --> 00:10:28,959

submitted to astrobiology

242

00:10:33,030 --> 00:10:30,399

the journal

243

00:10:35,430 --> 00:10:33,040

well in advance of february so that we

244

00:10:38,710 --> 00:10:35,440

can at least cite ourselves uh in the

245

00:10:41,430 --> 00:10:38,720

white paper if not anything more and

246

00:10:43,269 --> 00:10:41,440

also um i've been in talks with sherry

247

00:10:47,430 --> 00:10:43,279

katy who is the

248

00:10:50,470 --> 00:10:47,440

executive editor of astrobiology i

249

00:10:53,110 --> 00:10:50,480

have served forever on the as a senior

250

00:10:55,269 --> 00:10:53,120

editor for astrobiology so she knows

251
00:10:56,949 --> 00:10:55,279
that this and other relevant white

252
00:10:59,110 --> 00:10:56,959
papers are coming and is very

253
00:11:01,269 --> 00:10:59,120
enthusiastic about finding way to

254
00:11:03,910 --> 00:11:01,279
publish them in as timely a fashion as

255
00:11:06,550 --> 00:11:03,920
possible so that is the

256
00:11:09,910 --> 00:11:06,560
bureaucratic and political framework

257
00:11:12,389 --> 00:11:09,920
and uh and my personal interest

258
00:11:13,430 --> 00:11:12,399
the other folks on the core team that

259
00:11:15,990 --> 00:11:13,440
have been

260
00:11:19,110 --> 00:11:16,000
trying to put this together of course uh

261
00:11:20,310 --> 00:11:19,120
ken stedman who is on the screen and ken

262
00:11:22,030 --> 00:11:20,320
has been

263
00:11:24,949 --> 00:11:22,040

the fearless leader keeping

264

00:11:27,430 --> 00:11:24,959

astrovirology alive within

265

00:11:31,110 --> 00:11:27,440

the astrobiology realm uh through

266

00:11:33,190 --> 00:11:31,120

tireless and often unrewarded efforts

267

00:11:34,630 --> 00:11:33,200

over the years and hopefully we can

268

00:11:36,389 --> 00:11:34,640

change that

269

00:11:38,790 --> 00:11:36,399

and then my lovely young colleagues who

270

00:11:40,710 --> 00:11:38,800

are here in the room uh gary trouball

271

00:11:42,949 --> 00:11:40,720

and lawrence

272

00:11:43,750 --> 00:11:42,959

livermore sorry we have two lawrences

273

00:11:49,030 --> 00:11:43,760

here

274

00:11:51,190 --> 00:11:49,040

a wonderful virologist and kathy

275

00:11:54,310 --> 00:11:51,200

bywaters who has many talents in

276

00:11:56,629 --> 00:11:54,320

astrobiology and who is here at nasa

277

00:11:58,389 --> 00:11:56,639

ames as a scientist so with that let me

278

00:12:00,150 --> 00:11:58,399

turn it over to ken who has prepared

279

00:12:01,990 --> 00:12:00,160

some initial remarks

280

00:12:04,150 --> 00:12:02,000

welcome everybody and i'm delighted to

281

00:12:07,269 --> 00:12:04,160

see you and i plan to learn a whole lot

282

00:12:11,829 --> 00:12:09,590

hey thanks penny and welcome to

283

00:12:15,750 --> 00:12:11,839

everybody uh

284

00:12:18,150 --> 00:12:15,760

particular thanks again to gary um

285

00:12:20,310 --> 00:12:18,160

huge thanks to him in terms of really

286

00:12:23,030 --> 00:12:20,320

getting all of this together thanks to

287

00:12:25,190 --> 00:12:23,040

everybody else particularly the speakers

288

00:12:26,470 --> 00:12:25,200

i'm not sure how many of you are online

289

00:12:28,150 --> 00:12:26,480

already

290

00:12:31,030 --> 00:12:28,160

for

291

00:12:33,750 --> 00:12:31,040

agreeing to work with us on this a lot

292

00:12:36,790 --> 00:12:33,760

of this was really kind of last minute

293

00:12:38,550 --> 00:12:36,800

so again hugely appreciated

294

00:12:41,590 --> 00:12:38,560

to all of those people who are going to

295

00:12:44,310 --> 00:12:41,600

be participating later on today i think

296

00:12:47,430 --> 00:12:44,320

pretty much everybody knows that this is

297

00:12:50,230 --> 00:12:47,440

going to be recorded a couple of things

298

00:12:52,629 --> 00:12:50,240

about zoom and just generally how we're

299

00:12:55,269 --> 00:12:52,639

going to be organizing this some of you

300

00:12:57,670 --> 00:12:55,279

have already found the chat window

301
00:12:59,190 --> 00:12:57,680
which i have just opened up here on the

302
00:13:01,829 --> 00:12:59,200
side

303
00:13:03,030 --> 00:13:01,839
if anybody wants to go ahead and tweet

304
00:13:05,110 --> 00:13:03,040
this

305
00:13:07,350 --> 00:13:05,120
hashtag astrovirology let's see if we

306
00:13:10,629 --> 00:13:07,360
can get it trending or maybe get it to

307
00:13:12,870 --> 00:13:10,639
go viral as the case may be

308
00:13:16,150 --> 00:13:12,880
over the next couple of days that would

309
00:13:17,829 --> 00:13:16,160
be absolutely awesome um we shall see

310
00:13:19,030 --> 00:13:17,839
i'm not going to make any guarantees

311
00:13:21,030 --> 00:13:19,040
about that

312
00:13:22,790 --> 00:13:21,040
and i didn't pay them to support it

313
00:13:25,110 --> 00:13:22,800

either so

314

00:13:26,310 --> 00:13:25,120

um a couple of other things um given

315

00:13:28,870 --> 00:13:26,320

hopefully all of you have seen the

316

00:13:31,990 --> 00:13:28,880

schedule um we've scheduled a half hour

317

00:13:34,150 --> 00:13:32,000

for each speaker actually scheduled 20

318

00:13:35,910 --> 00:13:34,160

minutes for each speaker and then 10

319

00:13:38,870 --> 00:13:35,920

minutes for questions and there are a

320

00:13:41,030 --> 00:13:38,880

couple of reasons for that one is we

321

00:13:42,629 --> 00:13:41,040

want to give people lots of chances to

322

00:13:43,750 --> 00:13:42,639

ask questions

323

00:13:45,829 --> 00:13:43,760

number two

324

00:13:48,550 --> 00:13:45,839

um speaking for myself i know i have a

325

00:13:49,990 --> 00:13:48,560

nasty tendency to go over my time limit

326

00:13:51,509 --> 00:13:50,000

so that gives us a little bit of

327

00:13:53,269 --> 00:13:51,519

flexibility but only a little bit of

328

00:13:55,509 --> 00:13:53,279

flexibility

329

00:13:57,629 --> 00:13:55,519

the other thing is since we are trying

330

00:13:59,590 --> 00:13:57,639

to do this um as

331

00:14:01,430 --> 00:13:59,600

multinationally as possible that's

332

00:14:04,310 --> 00:14:01,440

partly why we're doing

333

00:14:06,550 --> 00:14:04,320

a half day this morning and a half day

334

00:14:08,949 --> 00:14:06,560

tomorrow afternoon is to allow people in

335

00:14:11,189 --> 00:14:08,959

different time zones to be able to get

336

00:14:13,189 --> 00:14:11,199

into this but part of that also means we

337

00:14:15,670 --> 00:14:13,199

really have to try and keep the time and

338

00:14:17,430 --> 00:14:15,680

so if people actually do end up

339

00:14:18,870 --> 00:14:17,440

finishing early

340

00:14:19,670 --> 00:14:18,880

shock horror

341

00:14:21,670 --> 00:14:19,680

or

342

00:14:24,230 --> 00:14:21,680

the question period doesn't go quite as

343

00:14:26,470 --> 00:14:24,240

long that gives everybody a

344

00:14:28,069 --> 00:14:26,480

physiology break for a couple of minutes

345

00:14:30,790 --> 00:14:28,079

you can go and grab some coffee you know

346

00:14:33,189 --> 00:14:30,800

whatever it is so we can start in each

347

00:14:36,629 --> 00:14:33,199

of the half hour windows to make sure

348

00:14:39,910 --> 00:14:36,639

that everything starts on time and then

349

00:14:42,870 --> 00:14:39,920

hopefully ends on time and the ending on

350

00:14:44,710 --> 00:14:42,880

time thing um hopefully marco will just

351
00:14:46,710 --> 00:14:44,720
you know completely cut everybody off

352
00:14:48,870 --> 00:14:46,720
after half an hour and switches over to

353
00:14:51,350 --> 00:14:48,880
whoever the next person is i will um

354
00:14:53,910 --> 00:14:51,360
i'll defer to him and say it's all the

355
00:14:56,629 --> 00:14:53,920
technical people's fault um rather than

356
00:14:59,269 --> 00:14:56,639
me being mr nasty and coming in and

357
00:15:02,150 --> 00:14:59,279
saying no um this is it we've got to cut

358
00:15:03,990 --> 00:15:02,160
everything off and so that's sort of i

359
00:15:05,990 --> 00:15:04,000
feel my role

360
00:15:08,710 --> 00:15:06,000
in terms of the

361
00:15:11,430 --> 00:15:08,720
questions anybody who's on zoom should

362
00:15:14,150 --> 00:15:11,440
be able to ask questions directly there

363
00:15:15,990 --> 00:15:14,160

but also you can type in a question into

364

00:15:17,990 --> 00:15:16,000

the chat and then

365

00:15:20,550 --> 00:15:18,000

one or other of us will then actually

366

00:15:22,949 --> 00:15:20,560

read it to whoever the speaker is and so

367

00:15:25,110 --> 00:15:22,959

they can answer those questions and so

368

00:15:26,870 --> 00:15:25,120

those are the kinds of ways that we'd

369

00:15:28,870 --> 00:15:26,880

like to try and

370

00:15:30,310 --> 00:15:28,880

keep this thing

371

00:15:32,470 --> 00:15:30,320

running

372

00:15:34,790 --> 00:15:32,480

bear with us particularly with me this

373

00:15:36,710 --> 00:15:34,800

is my first workshop without walls first

374

00:15:37,990 --> 00:15:36,720

sort of virtual meeting

375

00:15:40,949 --> 00:15:38,000

so

376

00:15:41,910 --> 00:15:40,959

let us know if stuff is working or not

377

00:15:44,150 --> 00:15:41,920

working

378

00:15:46,150 --> 00:15:44,160

etc if it's a technical thing maybe you

379

00:15:47,590 --> 00:15:46,160

could pop something into the chat

380

00:15:48,470 --> 00:15:47,600

hopefully somebody can help you with

381

00:15:49,590 --> 00:15:48,480

that

382

00:15:51,509 --> 00:15:49,600

if it's a

383

00:15:53,990 --> 00:15:51,519

non-technical thing things you like

384

00:15:56,710 --> 00:15:54,000

about this process you don't like about

385

00:15:58,790 --> 00:15:56,720

it please give us some feedback and so

386

00:16:01,910 --> 00:15:58,800

that we can think about how we can do

387

00:16:04,629 --> 00:16:01,920

this better in future and one of our

388

00:16:07,030 --> 00:16:04,639

presenters later on said that this is a

389

00:16:08,389 --> 00:16:07,040

really great way to

390

00:16:10,710 --> 00:16:08,399

lower our

391

00:16:12,230 --> 00:16:10,720

carbon footprint in terms of putting

392

00:16:14,790 --> 00:16:12,240

together meetings

393

00:16:17,110 --> 00:16:14,800

and again hopefully widen the audience

394

00:16:19,269 --> 00:16:17,120

make this a lot more accessible to lots

395

00:16:20,550 --> 00:16:19,279

of different people so any

396

00:16:23,590 --> 00:16:20,560

comments

397

00:16:26,069 --> 00:16:23,600

thoughts um etc along those lines we'd

398

00:16:29,430 --> 00:16:26,079

really greatly appreciate and as penny

399

00:16:32,470 --> 00:16:29,440

mentioned um hopefully we'll be able to

400

00:16:34,389 --> 00:16:32,480

lean on as many of you as possible in

401
00:16:37,829 --> 00:16:34,399
terms of trying to put together a review

402
00:16:40,069 --> 00:16:37,839
article putting together a white paper

403
00:16:43,829 --> 00:16:40,079
so that we can really kind of

404
00:16:46,629 --> 00:16:43,839
advance the field of astrovirology um

405
00:16:48,389 --> 00:16:46,639
beyond the four walls that you can see

406
00:16:51,189 --> 00:16:48,399
behind me right here

407
00:16:53,990 --> 00:16:51,199
and a few of my colleagues as far as

408
00:16:55,829 --> 00:16:54,000
that's concerned so before i have a

409
00:16:57,670 --> 00:16:55,839
little presentation i just wanted to

410
00:17:00,629 --> 00:16:57,680
open things up for

411
00:17:03,110 --> 00:17:00,639
any sort of technical general questions

412
00:17:05,429 --> 00:17:03,120
before we sort of move into the

413
00:17:07,189 --> 00:17:05,439

formal parts of the presentation so does

414

00:17:09,510 --> 00:17:07,199

anybody have anything

415

00:17:11,510 --> 00:17:09,520

uh that we want to try and clarify

416

00:17:14,309 --> 00:17:11,520

before we move into that otherwise i've

417

00:17:20,870 --> 00:17:14,319

got a couple of slides on the

418

00:17:24,230 --> 00:17:22,549

so i got a quick question on the chat

419

00:17:26,230 --> 00:17:24,240

group can we share the workshop link via

420

00:17:32,070 --> 00:17:26,240

twitter i think absolutely

421

00:17:35,270 --> 00:17:33,750

someone else on the chatroom says it's

422

00:17:35,830 --> 00:17:35,280

too late they've already done it so

423

00:17:39,190 --> 00:17:35,840

thank you

424

00:17:41,029 --> 00:17:39,200

[Laughter]

425

00:17:43,270 --> 00:17:41,039

yeah no the idea is to make this as as

426

00:17:45,990 --> 00:17:43,280

widespread as absolutely possible uh

427

00:17:49,110 --> 00:17:46,000

that's uh sort of proselytizing as much

428

00:17:51,830 --> 00:17:49,120

as as we possibly can

429

00:17:53,830 --> 00:17:51,840

okay any other sort of question kinds of

430

00:17:57,029 --> 00:17:53,840

things along these lines

431

00:17:57,990 --> 00:17:57,039

okay let me see if i can share my screen

432

00:18:00,950 --> 00:17:58,000

and

433

00:18:03,990 --> 00:18:00,960

give you a couple of slides on

434

00:18:08,310 --> 00:18:04,000

what we've thought about astrobiology

435

00:18:13,110 --> 00:18:08,320

in the past so let me see

436

00:18:16,310 --> 00:18:13,120

which one we've got here okay hopefully

437

00:18:19,430 --> 00:18:16,320

you see my screen here okay good so

438

00:18:21,669 --> 00:18:19,440

um this is um speaking of articles in

439

00:18:24,710 --> 00:18:21,679

astrobiology hopefully some of you have

440

00:18:26,390 --> 00:18:24,720

seen this i suspect very few of you have

441

00:18:27,190 --> 00:18:26,400

actually seen

442

00:18:29,190 --> 00:18:27,200

the

443

00:18:31,669 --> 00:18:29,200

cover picture because it seems that

444

00:18:34,630 --> 00:18:31,679

nobody looks at covers anymore

445

00:18:38,230 --> 00:18:34,640

but this is the article that aaron

446

00:18:39,430 --> 00:18:38,240

berliner um tomohiro mochizuki and i put

447

00:18:40,950 --> 00:18:39,440

together

448

00:18:42,710 --> 00:18:40,960

um basically a couple of years ago and

449

00:18:44,070 --> 00:18:42,720

it came out right at the beginning of

450

00:18:47,029 --> 00:18:44,080

2018

451

00:18:48,150 --> 00:18:47,039

and really sort of a

452

00:18:50,870 --> 00:18:48,160

i'd like to think of a sort of a

453

00:18:53,669 --> 00:18:50,880

backbone to think about astrovirology

454

00:18:54,870 --> 00:18:53,679

and how it could be fitting into

455

00:19:08,470 --> 00:18:54,880

a

456

00:19:12,710 --> 00:19:08,480

move

457

00:19:14,430 --> 00:19:12,720

slides forward there we go uh most of

458

00:19:17,270 --> 00:19:14,440

the press actually thought this is what

459

00:19:18,310 --> 00:19:17,280

astrovirology is

460

00:19:21,669 --> 00:19:18,320

so

461

00:19:24,390 --> 00:19:21,679

um i think this is one thing that we do

462

00:19:26,750 --> 00:19:24,400

need to be careful about whenever i talk

463

00:19:29,510 --> 00:19:26,760

to the general public about

464

00:19:32,549 --> 00:19:29,520

astrobiology the immediate thing is oh

465

00:19:34,070 --> 00:19:32,559

should we be scared now this particular

466

00:19:35,350 --> 00:19:34,080

one unfortunately

467

00:19:38,950 --> 00:19:35,360

in the original it's actually an

468

00:19:40,950 --> 00:19:38,960

animated gif where you have the uh

469

00:19:43,270 --> 00:19:40,960

quote viruses which actually look to me

470

00:19:45,350 --> 00:19:43,280

a lot more like macrophages bouncing

471

00:19:47,510 --> 00:19:45,360

back and forth against this background

472

00:19:49,190 --> 00:19:47,520

it's really um

473

00:19:51,510 --> 00:19:49,200

frightening i guess is

474

00:19:54,549 --> 00:19:51,520

one way in lots of different ways of

475

00:19:56,710 --> 00:19:54,559

thinking about the term so um

476

00:19:59,110 --> 00:19:56,720

i'd like to think much more about this

477

00:20:01,510 --> 00:19:59,120

in terms of astrobiology

478

00:20:03,110 --> 00:20:01,520

astrovirology excuse me rather than

479

00:20:05,750 --> 00:20:03,120

this um

480

00:20:07,750 --> 00:20:05,760

in terms of the killer alien viruses and

481

00:20:09,350 --> 00:20:07,760

thanks to penny for sort of bringing up

482

00:20:11,830 --> 00:20:09,360

the

483

00:20:15,750 --> 00:20:11,840

origins of sort of thinking about

484

00:20:19,110 --> 00:20:15,760

viruses in an astrobiology context this

485

00:20:21,350 --> 00:20:19,120

was really the brainchild of

486

00:20:23,909 --> 00:20:21,360

barry blumberg the late barry blumberg

487

00:20:27,110 --> 00:20:23,919

and it he actually founded

488

00:20:29,190 --> 00:20:27,120

the virus focus group um i believe

489

00:20:32,950 --> 00:20:29,200

remember correctly it was in 2002 so

490

00:20:37,830 --> 00:20:32,960

about 17 years ago now and the basic

491

00:20:39,669 --> 00:20:37,840

take home of the virus focus group was

492

00:20:42,390 --> 00:20:39,679

barry wanted people to think about

493

00:20:44,549 --> 00:20:42,400

viruses because he was really

494

00:20:45,990 --> 00:20:44,559

excited about viruses and

495

00:20:46,870 --> 00:20:46,000

so was i

496

00:20:49,990 --> 00:20:46,880

and

497

00:20:54,149 --> 00:20:50,000

then when barry actually asked me to be

498

00:20:55,029 --> 00:20:54,159

co-chair of the virus focus group um as

499

00:21:52,029 --> 00:20:55,039

a

500

00:21:54,230 --> 00:21:52,039

in the bigger picture of

501
00:21:55,510 --> 00:21:54,240
astrobiology but

502
00:21:57,110 --> 00:21:55,520
this also gets to the point of you what

503
00:21:59,110 --> 00:21:57,120
is astrobiology and you can sort of

504
00:22:01,590 --> 00:21:59,120
think about astrobiology i think also in

505
00:22:04,230 --> 00:22:01,600
the larger context is astrobiology is

506
00:22:06,630 --> 00:22:04,240
really kind of biology as well

507
00:22:08,710 --> 00:22:06,640
just with a little bit of an astro

508
00:22:12,630 --> 00:22:08,720
context that goes with it

509
00:22:15,190 --> 00:22:12,640
so until now the virus focus group has

510
00:22:18,390 --> 00:22:15,200
basically been putting together

511
00:22:21,110 --> 00:22:18,400
workshops symposia field trips and as i

512
00:22:23,750 --> 00:22:21,120
say unfortunately as penny mentioned

513
00:22:26,669 --> 00:22:23,760

we didn't get to do the

514

00:22:28,630 --> 00:22:26,679

underground workshop field trip in

515

00:22:31,110 --> 00:22:28,640

astrovirology which would have been i

516

00:22:34,310 --> 00:22:31,120

think absolutely fascinating

517

00:22:36,390 --> 00:22:34,320

but we really concentrated on sort of

518

00:22:39,750 --> 00:22:36,400

the things that we knew a little bit

519

00:22:42,710 --> 00:22:39,760

about and also trying to get people

520

00:22:44,950 --> 00:22:42,720

from different fields of virology

521

00:22:45,909 --> 00:22:44,960

to start thinking together

522

00:22:47,750 --> 00:22:45,919

about

523

00:22:50,149 --> 00:22:47,760

you know the bigger picture again

524

00:22:52,710 --> 00:22:50,159

astrovirology so this again completely

525

00:22:54,950 --> 00:22:52,720

ties into the idea of a white paper

526

00:22:57,750 --> 00:22:54,960

ties into the idea of putting together a

527

00:23:00,070 --> 00:22:57,760

review paper to try and start to tie

528

00:23:03,510 --> 00:23:00,080

together some of these strings

529

00:23:05,110 --> 00:23:03,520

which have been really very independent

530

00:23:06,110 --> 00:23:05,120

in terms of

531

00:23:08,549 --> 00:23:06,120

different

532

00:23:10,470 --> 00:23:08,559

virologists thinking about these things

533

00:23:13,110 --> 00:23:10,480

as yeah barry always used to say he

534

00:23:15,510 --> 00:23:13,120

wasn't really a virologist i always say

535

00:23:17,750 --> 00:23:15,520

i'm not really a virologist but i think

536

00:23:20,630 --> 00:23:17,760

most virologists would say well i'm a

537

00:23:21,510 --> 00:23:20,640

this or a that or whatever so

538

00:23:24,390 --> 00:23:21,520

you know

539

00:23:25,669 --> 00:23:24,400

actually what what is astrovirology and

540

00:23:27,669 --> 00:23:25,679

tying that together i think is a really

541

00:23:29,510 --> 00:23:27,679

important aspect about

542

00:23:32,549 --> 00:23:29,520

this whole point of a white paper and

543

00:23:34,070 --> 00:23:32,559

putting together a a review article so

544

00:23:35,110 --> 00:23:34,080

what we've mostly talked about before

545

00:23:37,750 --> 00:23:35,120

and again a lot of this is going to be

546

00:23:39,029 --> 00:23:37,760

coming back up today um evolution of

547

00:23:43,350 --> 00:23:39,039

viruses

548

00:23:44,710 --> 00:23:43,360

very few people even a lot of scientists

549

00:23:47,269 --> 00:23:44,720

even a lot of

550

00:23:49,350 --> 00:23:47,279

real virologists don't have a good

551
00:23:51,590 --> 00:23:49,360
handle on how absolutely ubiquitous

552
00:23:53,909 --> 00:23:51,600
viruses are

553
00:23:55,269 --> 00:23:53,919
the whole area of virus ecology is

554
00:23:57,510 --> 00:23:55,279
really taking off we're going to hear

555
00:24:01,029 --> 00:23:57,520
from a couple of speakers about what's

556
00:24:02,470 --> 00:24:01,039
going on in terms of viruses roles in

557
00:24:04,950 --> 00:24:02,480
ecology

558
00:24:06,630 --> 00:24:04,960
virus diversity particularly in terms of

559
00:24:08,870 --> 00:24:06,640
structure i'll talk a little bit about

560
00:24:10,230 --> 00:24:08,880
this in my talk at the very end

561
00:24:11,669 --> 00:24:10,240
and

562
00:24:13,350 --> 00:24:11,679
one of my favorite lines again

563
00:24:14,950 --> 00:24:13,360

particularly in terms of an outreach

564

00:24:19,110 --> 00:24:14,960

point of view is that viruses have a bad

565

00:24:22,549 --> 00:24:19,120

rap um i think there are lots of

566

00:24:23,909 --> 00:24:22,559

viruses that do good things so far all

567

00:24:25,830 --> 00:24:23,919

of the work in virology has been

568

00:24:29,190 --> 00:24:25,840

thinking about pathogenic viruses and

569

00:24:31,590 --> 00:24:29,200

the roles that those have vast majority

570

00:24:34,789 --> 00:24:31,600

and then finally the only sort of real

571

00:24:36,390 --> 00:24:34,799

direct connection to astro and space and

572

00:24:38,310 --> 00:24:36,400

again thanks to penny for bringing this

573

00:24:42,070 --> 00:24:38,320

up has been

574

00:24:43,750 --> 00:24:42,080

um the idea of how could viruses and

575

00:24:47,190 --> 00:24:43,760

very specifically actually the

576

00:24:50,549 --> 00:24:47,200

extracellular form of viruses or virions

577

00:24:52,950 --> 00:24:50,559

survive in a space environment

578

00:24:55,990 --> 00:24:52,960

and this brings all kinds of ideas about

579

00:24:57,990 --> 00:24:56,000

panspermia but also space environment in

580

00:25:00,070 --> 00:24:58,000

a much broader picture you know other

581

00:25:02,710 --> 00:25:00,080

extraterrestrial environments as well

582

00:25:04,390 --> 00:25:02,720

and this i think is an area and we can

583

00:25:05,750 --> 00:25:04,400

talk more about it in the next couple of

584

00:25:08,630 --> 00:25:05,760

half days

585

00:25:10,470 --> 00:25:08,640

is really i think a very open area for

586

00:25:12,950 --> 00:25:10,480

research and something that

587

00:25:16,230 --> 00:25:12,960

personally i think that the field should

588

00:25:18,470 --> 00:25:16,240

be doing a lot of more work on

589

00:25:21,190 --> 00:25:18,480

so i've got a couple more just really

590

00:25:22,310 --> 00:25:21,200

quick so fun things of what we have been

591

00:25:25,110 --> 00:25:22,320

able to do

592

00:25:27,510 --> 00:25:25,120

in the past um again a couple of

593

00:25:30,870 --> 00:25:27,520

workshops first workshop we had was here

594

00:25:33,190 --> 00:25:30,880

in portland um and hopefully you can see

595

00:25:35,029 --> 00:25:33,200

barry those of you who remember a

596

00:25:37,830 --> 00:25:35,039

newberry right here in the middle

597

00:25:40,390 --> 00:25:37,840

again very much the focus of this whole

598

00:25:42,310 --> 00:25:40,400

project some of you may recognize some

599

00:25:44,710 --> 00:25:42,320

of the other people here forced rower

600

00:25:47,669 --> 00:25:44,720

has been a real leader in virus ecology

601
00:25:50,149 --> 00:25:47,679
um when he um first came up and asked me

602
00:25:51,750 --> 00:25:50,159
where to find the nasa meeting i wasn't

603
00:25:54,070 --> 00:25:51,760
sure if he was supposed to be here or a

604
00:25:55,510 --> 00:25:54,080
lost guy at some rock concert um those

605
00:25:56,549 --> 00:25:55,520
of you know forrest would appreciate

606
00:25:59,510 --> 00:25:56,559
that

607
00:26:00,390 --> 00:25:59,520
and paul turner greek stewards a lot of

608
00:26:02,070 --> 00:26:00,400
the real

609
00:26:03,430 --> 00:26:02,080
leading people and then right here

610
00:26:06,070 --> 00:26:03,440
hiding at the back are not completely

611
00:26:07,750 --> 00:26:06,080
hiding of course is sherry cady

612
00:26:09,909 --> 00:26:07,760
we had an app cycon meeting this is one

613
00:26:11,510 --> 00:26:09,919

of my favorite astrovirology slides

614

00:26:14,230 --> 00:26:11,520

roger hendricks came up with this you

615

00:26:17,029 --> 00:26:14,240

know lining up all of the viruses end to

616

00:26:18,870 --> 00:26:17,039

end ends up being the viruses on earth

617

00:26:21,669 --> 00:26:18,880

ends up being something like

618

00:26:24,630 --> 00:26:21,679

a few million light years so a

619

00:26:26,470 --> 00:26:24,640

ridiculously large number of viruses

620

00:26:29,669 --> 00:26:26,480

we also had a really

621

00:26:31,110 --> 00:26:29,679

fun trip and workshop to mono lake um

622

00:26:32,870 --> 00:26:31,120

where the

623

00:26:35,190 --> 00:26:32,880

we were actually able to go out on mono

624

00:26:38,070 --> 00:26:35,200

lake itself visit pahoia island which has

625

00:26:40,870 --> 00:26:38,080

a number of very interesting hot springs

626

00:26:42,630 --> 00:26:40,880

very near there mammoth lakes the long

627

00:26:44,549 --> 00:26:42,640

valley caldera also has some really

628

00:26:46,950 --> 00:26:44,559

interesting hot springs so we were able

629

00:26:48,630 --> 00:26:46,960

to sample there again

630

00:26:50,549 --> 00:26:48,640

barry even though he said he was getting

631

00:26:53,110 --> 00:26:50,559

seasick seems to have really enjoyed

632

00:26:55,990 --> 00:26:53,120

this particular trip and mona lake is

633

00:26:58,549 --> 00:26:56,000

really flat very few waves and then our

634

00:26:59,990 --> 00:26:58,559

last field trip was to lassen volcanic

635

00:27:02,710 --> 00:27:00,000

national park which is one of the main

636

00:27:04,950 --> 00:27:02,720

field sites that i work in

637

00:27:07,190 --> 00:27:04,960

and also had the opportunity to go to

638

00:27:09,110 --> 00:27:07,200

the hat creek observatory

639

00:27:11,029 --> 00:27:09,120

and with jill tarter and talk a little

640

00:27:13,350 --> 00:27:11,039

bit about seti so it's really been a

641

00:27:14,789 --> 00:27:13,360

whole combination of

642

00:27:17,190 --> 00:27:14,799

different

643

00:27:19,350 --> 00:27:17,200

aspects of thinking about

644

00:27:20,630 --> 00:27:19,360

viruses in a bigger sense and the last

645

00:27:23,350 --> 00:27:20,640

thing i wanted to mention is that we've

646

00:27:24,870 --> 00:27:23,360

also been very involved in outreach and

647

00:27:26,870 --> 00:27:24,880

trying to reach a lot of other people

648

00:27:28,710 --> 00:27:26,880

and i'm noticing that it is now

649

00:27:30,950 --> 00:27:28,720

8 30 so

650

00:27:32,549 --> 00:27:30,960

in terms of keeping on time let's see if

651
00:27:34,630 --> 00:27:32,559
we can switch over to steve benner

652
00:27:36,470 --> 00:27:34,640
assuming that he is actually

653
00:27:38,710 --> 00:27:36,480
online here and i'll actually let steve

654
00:27:39,990 --> 00:27:38,720
introduce himself because i keep

655
00:27:42,789 --> 00:27:40,000
forgetting which institute he's

656
00:27:47,990 --> 00:27:42,799
associated with

657
00:27:52,549 --> 00:27:50,389
so steve is steve around

658
00:27:54,310 --> 00:27:52,559
yes yes he is

659
00:27:56,310 --> 00:27:54,320
good online

660
00:27:57,350 --> 00:27:56,320
you cannot all unmute your microphone

661
00:27:58,789 --> 00:27:57,360
there

662
00:28:02,870 --> 00:27:58,799
so steve we should be able to hear you

663
00:28:06,230 --> 00:28:02,880

now oh i was unmuted by the host okay um

664

00:28:08,710 --> 00:28:06,240

yeah i am unable to drop my s

665

00:28:10,870 --> 00:28:08,720

power presentation presentation onto the

666

00:28:13,190 --> 00:28:10,880

screen that i'm able to share in

667

00:28:15,669 --> 00:28:13,200

in zoom actually i'm not quite clear why

668

00:28:18,630 --> 00:28:15,679

that's the case but uh

669

00:28:21,190 --> 00:28:18,640

um can and then for some reason

670

00:28:23,669 --> 00:28:21,200

zoom has blocked out on the control

671

00:28:27,430 --> 00:28:23,679

panel i think so can you actually for me

672

00:28:31,269 --> 00:28:28,789

sure i will do that let me bring those

673

00:28:32,549 --> 00:28:31,279

up really quickly okay

674

00:28:35,029 --> 00:28:32,559

excellent

675

00:28:37,510 --> 00:28:35,039

i i don't i don't fit my talk that

676

00:28:40,070 --> 00:28:37,520

really does not fit into this uh

677

00:28:42,070 --> 00:28:40,080

session as i looked at all the other

678

00:28:43,909 --> 00:28:42,080

ways in which people were talking about

679

00:28:46,630 --> 00:28:43,919

things as i think has nothing to do with

680

00:28:49,350 --> 00:28:46,640

viruses unless you wanted to detect them

681

00:28:50,710 --> 00:28:49,360

on uh um unless you wanted to detect

682

00:28:52,789 --> 00:28:50,720

them on that

683

00:28:54,950 --> 00:28:52,799

on earth so um now am i going to say to

684

00:28:56,070 --> 00:28:54,960

you please change slide

685

00:29:00,149 --> 00:28:56,080

or why

686

00:29:05,350 --> 00:29:02,549

all right don't go back one slide um

687

00:29:07,669 --> 00:29:05,360

that first slide okay so uh keep in mind

688

00:29:09,510 --> 00:29:07,679

that nasa is very much interested in i

689

00:29:13,830 --> 00:29:09,520

mean well the public is interested in

690

00:29:16,389 --> 00:29:13,840

and the public is nasa's customer um

691

00:29:18,630 --> 00:29:16,399

is i mean obviously nasa provides to the

692

00:29:20,470 --> 00:29:18,640

educated elite the

693

00:29:23,190 --> 00:29:20,480

you know if you're not

694

00:29:24,630 --> 00:29:23,200

a high brow you watch world wrestling

695

00:29:26,950 --> 00:29:24,640

federation for your

696

00:29:28,870 --> 00:29:26,960

entertainment nasa provides a sense of

697

00:29:31,110 --> 00:29:28,880

mission a sense of entertainment and a

698

00:29:32,549 --> 00:29:31,120

sense of purpose to the general public

699

00:29:33,830 --> 00:29:32,559

those who are familiar with this kind of

700

00:29:35,990 --> 00:29:33,840

things and those are people who

701

00:29:38,070 --> 00:29:36,000

particularly knew carl sagan is

702

00:29:40,070 --> 00:29:38,080

the one question that is at the top of

703

00:29:42,310 --> 00:29:40,080

everybody's mind in the public when you

704

00:29:43,269 --> 00:29:42,320

do surveys is whether or not life is out

705

00:29:45,110 --> 00:29:43,279

there

706

00:29:46,389 --> 00:29:45,120

we don't know quite what life is but

707

00:29:48,549 --> 00:29:46,399

there's this concept of a

708

00:29:50,310 --> 00:29:48,559

self-sustaining chemical system capable

709

00:29:52,149 --> 00:29:50,320

of darwinian evolution

710

00:29:54,389 --> 00:29:52,159

and that is

711

00:29:56,149 --> 00:29:54,399

a theory definition of life that carl

712

00:29:58,870 --> 00:29:56,159

sagan was very much instrumental in

713

00:30:00,710 --> 00:29:58,880

pushing um and it's a theory definition

714

00:30:02,549 --> 00:30:00,720

i'm using the formulation of carol

715

00:30:04,789 --> 00:30:02,559

cleveland here who's was the

716

00:30:08,070 --> 00:30:04,799

astrobiology resident philosopher

717

00:30:09,830 --> 00:30:08,080

because it is a statement not only about

718

00:30:11,990 --> 00:30:09,840

sort of definitional terms which are

719

00:30:13,590 --> 00:30:12,000

very hard to pin down but it really is a

720

00:30:15,430 --> 00:30:13,600

statement that when we adopt this theory

721

00:30:17,590 --> 00:30:15,440

definition we are saying what we think

722

00:30:19,669 --> 00:30:17,600

is the only way to generate matter as

723

00:30:21,909 --> 00:30:19,679

organic matter or whatever and the

724

00:30:23,909 --> 00:30:21,919

properties of value in life and that

725

00:30:26,230 --> 00:30:23,919

only way to do it is by this darwinian

726
00:30:28,710 --> 00:30:26,240
process of replication with errors where

727
00:30:31,669 --> 00:30:28,720
the errors are themselves replicable and

728
00:30:34,149 --> 00:30:31,679
then natural selection does the rest so

729
00:30:37,110 --> 00:30:34,159
your goal right now is to go out and

730
00:30:38,310 --> 00:30:37,120
find systems capable of darwinian

731
00:30:40,950 --> 00:30:38,320
evolution

732
00:30:42,710 --> 00:30:40,960
chris chiba and various other people

733
00:30:45,029 --> 00:30:42,720
made the comment that this was not an

734
00:30:48,310 --> 00:30:45,039
operational definition because what were

735
00:30:50,070 --> 00:30:48,320
you going to do fly to you know mars

736
00:30:52,870 --> 00:30:50,080
land and then sit around and wait for

737
00:30:54,789 --> 00:30:52,880
something to evolve well that's not a

738
00:30:57,590 --> 00:30:54,799

correct way of looking at this right

739

00:30:59,669 --> 00:30:57,600

what you you don't have to wait for a

740

00:31:02,070 --> 00:30:59,679

rabbit to evolve when you have a rabbit

741

00:31:04,149 --> 00:31:02,080

in your possession to make or a pair of

742

00:31:05,590 --> 00:31:04,159

rabbits in any case

743

00:31:07,190 --> 00:31:05,600

to make the statement that they have the

744

00:31:09,350 --> 00:31:07,200

capability of evolution so what you're

745

00:31:10,950 --> 00:31:09,360

looking for is molecular structures that

746

00:31:12,149 --> 00:31:10,960

have that capability you're not looking

747

00:31:14,310 --> 00:31:12,159

for the actual

748

00:31:17,830 --> 00:31:14,320

evolution itself all right so the next

749

00:31:19,509 --> 00:31:17,840

um slide is going to say what darwinism

750

00:31:21,990 --> 00:31:19,519

needs

751
00:31:23,909 --> 00:31:22,000
as a by way of informational polymer and

752
00:31:25,590 --> 00:31:23,919
there are two criteria that are both

753
00:31:28,070 --> 00:31:25,600
extremely important one of them is the

754
00:31:29,110 --> 00:31:28,080
so-called schrodinger aperiodic crystal

755
00:31:31,830 --> 00:31:29,120
structure

756
00:31:34,630 --> 00:31:31,840
and that means that the genetic polymer

757
00:31:37,350 --> 00:31:34,640
must be able to change its information

758
00:31:38,950 --> 00:31:37,360
content without changing its structure

759
00:31:42,549 --> 00:31:38,960
because all the building blocks have got

760
00:31:44,070 --> 00:31:42,559
to fit into the same packed form

761
00:31:45,430 --> 00:31:44,080
there's a second

762
00:31:47,029 --> 00:31:45,440
requirement that is that the genetic

763
00:31:48,950 --> 00:31:47,039

biopolymers be able to keep its

764

00:31:50,149 --> 00:31:48,960

properties constant with changing

765

00:31:52,789 --> 00:31:50,159

information

766

00:31:54,789 --> 00:31:52,799

and so the next slide

767

00:31:57,110 --> 00:31:54,799

shows you the picture of erwin schweiner

768

00:31:59,269 --> 00:31:57,120

he wrote this book in 1943 what's

769

00:32:01,509 --> 00:31:59,279

remarkable about this book is that he

770

00:32:02,549 --> 00:32:01,519

did not know the structure of dna it was

771

00:32:04,870 --> 00:32:02,559

not to be

772

00:32:07,190 --> 00:32:04,880

a watson crick double helix only came

773

00:32:08,470 --> 00:32:07,200

out 10 years later but schrodinger was a

774

00:32:10,149 --> 00:32:08,480

physicist

775

00:32:13,669 --> 00:32:10,159

he was famous for the schrodinger

776

00:32:15,990 --> 00:32:13,679

equation in quantum mechanics by 1943 he

777

00:32:18,070 --> 00:32:16,000

was slumming by doing biology that's

778

00:32:19,110 --> 00:32:18,080

sort of what many physicists did at that

779

00:32:21,110 --> 00:32:19,120

time

780

00:32:23,750 --> 00:32:21,120

but and what he knew was that simple

781

00:32:25,669 --> 00:32:23,760

binding cannot guarantee

782

00:32:28,230 --> 00:32:25,679

faithful information transfer at least

783

00:32:30,389 --> 00:32:28,240

not the level that's needed for biology

784

00:32:32,630 --> 00:32:30,399

because a simple binding gives you a

785

00:32:34,630 --> 00:32:32,640

titration curve which has a classical

786

00:32:37,669 --> 00:32:34,640

sigmoidal shape which if you ever did

787

00:32:40,149 --> 00:32:37,679

any work like this in your biochemistry

788

00:32:42,230 --> 00:32:40,159

laboratory you're familiar with and what

789

00:32:45,029 --> 00:32:42,240

you need to do to get faith for

790

00:32:47,509 --> 00:32:45,039

replication is sharp phase transitions

791

00:32:49,669 --> 00:32:47,519

between a correct pairing and an

792

00:32:51,669 --> 00:32:49,679

incorrect pairing and

793

00:32:53,430 --> 00:32:51,679

for that schrodinger said we have to

794

00:32:55,990 --> 00:32:53,440

rely on what's called the physics of

795

00:32:58,070 --> 00:32:56,000

phase transition now i won't go into the

796

00:33:00,310 --> 00:32:58,080

physics of phase translations but the

797

00:33:02,230 --> 00:33:00,320

melting of a crystal is an example of

798

00:33:05,870 --> 00:33:02,240

this which everybody's familiar with so

799

00:33:08,950 --> 00:33:05,880

if you take ice at minus

800

00:33:11,830 --> 00:33:08,960

0.0001 degrees centigrade and then move

801
00:33:14,470 --> 00:33:11,840
it to plus a 0.00 or one degree celsius

802
00:33:16,870 --> 00:33:14,480
the entire ice cube goes from a solid to

803
00:33:19,509 --> 00:33:16,880
a liquid in a phase transition and by

804
00:33:21,830 --> 00:33:19,519
the way impurities in that ice crystal

805
00:33:24,789 --> 00:33:21,840
will cause that melting point to be

806
00:33:26,630 --> 00:33:24,799
lower and broader and so the physics of

807
00:33:29,909 --> 00:33:26,640
phase transition

808
00:33:32,389 --> 00:33:29,919
is what allows very precise exclusion of

809
00:33:34,710 --> 00:33:32,399
impurities from a crystal it also is

810
00:33:36,630 --> 00:33:34,720
what you're relying on in dna to exclude

811
00:33:38,549 --> 00:33:36,640
impurities as mismatches when you're

812
00:33:40,870 --> 00:33:38,559
doing dna replication

813
00:33:42,950 --> 00:33:40,880

and for that and this is the key point

814

00:33:45,830 --> 00:33:42,960

the exchangeable informational building

815

00:33:46,789 --> 00:33:45,840

blocks must all have the same size and

816

00:33:48,870 --> 00:33:46,799

shape

817

00:33:50,950 --> 00:33:48,880

they must all fit into

818

00:33:52,710 --> 00:33:50,960

obviously a crystal of ice all the water

819

00:33:54,389 --> 00:33:52,720

molecules are identical and so there's

820

00:33:56,310 --> 00:33:54,399

really no information in the crystal

821

00:33:58,470 --> 00:33:56,320

structure of ice but

822

00:34:00,789 --> 00:33:58,480

um what schrodinger said okay great what

823

00:34:03,909 --> 00:34:00,799

we can do is make the molecules that are

824

00:34:06,389 --> 00:34:03,919

in that crystal a little different

825

00:34:09,270 --> 00:34:06,399

therefore it's a periodic in terms of

826

00:34:11,829 --> 00:34:09,280

its placement of these building blocks

827

00:34:14,550 --> 00:34:11,839

the a periodicity is what contains the

828

00:34:16,470 --> 00:34:14,560

information the genetic information but

829

00:34:18,869 --> 00:34:16,480

in order for this to work at all all the

830

00:34:20,389 --> 00:34:18,879

building blocks have to fit into exactly

831

00:34:25,510 --> 00:34:20,399

the same structure

832

00:34:28,710 --> 00:34:26,710

um

833

00:34:31,270 --> 00:34:28,720

this is of course actually uh i wish i

834

00:34:33,589 --> 00:34:31,280

had control this i'm going to go to the

835

00:34:36,069 --> 00:34:33,599

next slide for me so i should put a put

836

00:34:37,750 --> 00:34:36,079

in here somewhere structure of dna

837

00:34:39,829 --> 00:34:37,760

um that's a perfectly good structure of

838

00:34:42,869 --> 00:34:39,839

dna on the left let's go to the next

839

00:34:42,879 --> 00:34:46,149

the next slide

840

00:34:51,669 --> 00:34:49,190

yeah there you go so i you know i've put

841

00:34:53,589 --> 00:34:51,679

here the gc

842

00:34:56,629 --> 00:34:53,599

a cg base pair in the upper left hand

843

00:34:58,870 --> 00:34:56,639

corner and the t a base pair the next

844

00:35:01,750 --> 00:34:58,880

one down as you can see these are

845

00:35:04,550 --> 00:35:01,760

essentially the same size and shape i've

846

00:35:06,390 --> 00:35:04,560

actually fixed for those of you who are

847

00:35:08,790 --> 00:35:06,400

going to take a test on this subject i

848

00:35:10,630 --> 00:35:08,800

have actually fixed the structure of a

849

00:35:13,030 --> 00:35:10,640

to put an amino group

850

00:35:15,030 --> 00:35:13,040

down to form a third hydrogen bond with

851
00:36:06,150 --> 00:35:15,040
t

852
00:36:07,829 --> 00:36:06,160
assembling and he was building a

853
00:36:09,990 --> 00:36:07,839
structure for dna which had three

854
00:36:13,589 --> 00:36:10,000
strands of

855
00:36:15,510 --> 00:36:13,599
dna not two strands and watson

856
00:36:17,030 --> 00:36:15,520
writes in his book how any biologist

857
00:36:19,430 --> 00:36:17,040
would know that the important thing

858
00:36:21,829 --> 00:36:19,440
number was two not three

859
00:36:25,750 --> 00:36:21,839
but when watson and crick finally got

860
00:36:26,550 --> 00:36:25,760
the structures of the gc pair correct

861
00:36:27,990 --> 00:36:26,560
which

862
00:36:29,910 --> 00:36:28,000
they were they were trying to build a

863
00:36:31,510 --> 00:36:29,920

model with an incorrect structure of g

864

00:36:33,430 --> 00:36:31,520

the first thing that they said when they

865

00:36:35,910 --> 00:36:33,440

looked at those base pairs was aha this

866

00:36:37,430 --> 00:36:35,920

fits um

867

00:36:39,109 --> 00:36:37,440

schrodinger's a periodic crystal

868

00:36:43,109 --> 00:36:39,119

structure that is we can exchange

869

00:36:46,230 --> 00:36:43,119

g pairs for a t pairs or c g pairs for t

870

00:36:48,310 --> 00:36:46,240

a pairs or c g pairs for gc pairs and

871

00:36:49,349 --> 00:36:48,320

not change the overall structure so

872

00:36:51,109 --> 00:36:49,359

that's the first thing that they

873

00:36:51,910 --> 00:36:51,119

recognize about their model was that it

874

00:36:54,470 --> 00:36:51,920

fits

875

00:36:56,790 --> 00:36:54,480

schrodinger's criteria for

876

00:36:58,630 --> 00:36:56,800

aperiodic crystal structures now the

877

00:37:00,630 --> 00:36:58,640

other structures on this pair are all

878

00:37:02,390 --> 00:37:00,640

synthetic biology structures these are

879

00:37:04,870 --> 00:37:02,400

molecules that we have made

880

00:37:07,030 --> 00:37:04,880

and you can see we are changing the

881

00:37:08,390 --> 00:37:07,040

hydrogen bond donor and acceptor

882

00:37:09,990 --> 00:37:08,400

patterns we've

883

00:37:12,550 --> 00:37:10,000

written on these structures blue

884

00:37:15,109 --> 00:37:12,560

hydrogens as hydrogen bond donors

885

00:37:17,670 --> 00:37:15,119

so c is a hydrogen bond donor acceptor

886

00:37:18,630 --> 00:37:17,680

acceptor pattern blue red red

887

00:37:23,589 --> 00:37:18,640

which

888

00:37:24,630 --> 00:37:23,599

acceptor donor donor hydrogen bonding

889

00:37:25,910 --> 00:37:24,640

pattern

890

00:37:28,230 --> 00:37:25,920

and

891

00:37:30,230 --> 00:37:28,240

t is a small thing with a

892

00:37:32,069 --> 00:37:30,240

red blue red hydrogen bond acceptor

893

00:37:33,109 --> 00:37:32,079

donor acceptor pattern which pairs with

894

00:37:35,430 --> 00:37:33,119

a big

895

00:37:37,349 --> 00:37:35,440

amino adenine blue red blue donor

896

00:37:38,710 --> 00:37:37,359

acceptor donor and the rest of the

897

00:37:40,710 --> 00:37:38,720

structures here is there eight more

898

00:37:42,550 --> 00:37:40,720

nucleotides none of them are actually

899

00:37:44,870 --> 00:37:42,560

natural as far as we know

900

00:37:48,069 --> 00:37:44,880

they shuffle the hydrogen bond donor and

901
00:37:49,430 --> 00:37:48,079
acceptor pairs but they keep the

902
00:37:50,870 --> 00:37:49,440
size

903
00:37:53,670 --> 00:37:50,880
of the hair

904
00:37:56,630 --> 00:37:53,680
uniform so that you can replace anything

905
00:37:59,990 --> 00:37:56,640
any pair any of the six pairs on that

906
00:38:02,150 --> 00:38:00,000
slide by any of the other

907
00:38:03,910 --> 00:38:02,160
five pairs or the six pairs in the

908
00:38:04,950 --> 00:38:03,920
reverse direction and not change the

909
00:38:06,710 --> 00:38:04,960
structure

910
00:38:09,589 --> 00:38:06,720
and this artificially expanded genetic

911
00:38:11,109 --> 00:38:09,599
information system is in fact perfectly

912
00:38:13,270 --> 00:38:11,119
capable of meeting the schrodinger

913
00:38:16,829 --> 00:38:13,280

aperiodic crystal structure

914

00:38:20,069 --> 00:38:16,839

so the next slide i think maybe

915

00:38:22,310 --> 00:38:20,079

has yeah there you go so these are

916

00:38:25,670 --> 00:38:22,320

crystal structures at the bottom

917

00:38:26,950 --> 00:38:25,680

you're seeing um uh

918

00:38:30,310 --> 00:38:26,960

b c

919

00:38:33,270 --> 00:38:30,320

d e plus c d and e are three different

920

00:38:35,910 --> 00:38:33,280

structures of three different

921

00:38:38,069 --> 00:38:35,920

dna duplexes built from

922

00:38:41,349 --> 00:38:38,079

in this particular case eight letters of

923

00:38:43,430 --> 00:38:41,359

genetic alphabet but all still fitting

924

00:38:46,069 --> 00:38:43,440

the schrodinger aperiodic crystal

925

00:38:47,109 --> 00:38:46,079

structure and the structures are all the

926
00:38:49,510 --> 00:38:47,119
same

927
00:38:51,589 --> 00:38:49,520
uh c d and e and if that doesn't it

928
00:38:53,510 --> 00:38:51,599
doesn't seem so for you the structure b

929
00:38:55,349 --> 00:38:53,520
has all of them placed on top of each

930
00:38:56,710 --> 00:38:55,359
other so let me just pause there and

931
00:38:58,630 --> 00:38:56,720
make sure everybody understands the

932
00:39:00,710 --> 00:38:58,640
schrodinger a periodic crystal structure

933
00:39:02,230 --> 00:39:00,720
that is to have a darwinian molecule you

934
00:39:05,109 --> 00:39:02,240
got to be able to replace the

935
00:39:06,230 --> 00:39:05,119
informational units without disrupting a

936
00:39:10,310 --> 00:39:06,240
crystal

937
00:39:15,670 --> 00:39:12,710
is anybody there

938
00:39:17,670 --> 00:39:15,680

you're good okay so that's the that's

939

00:39:22,470 --> 00:39:17,680

the first requirement okay next slide

940

00:39:26,870 --> 00:39:24,950

yeah and so there you go so the first

941

00:39:29,270 --> 00:39:26,880

thing is that darwinism needs is a

942

00:39:30,790 --> 00:39:29,280

genetic system able to change encoded

943

00:39:31,990 --> 00:39:30,800

information without changing its

944

00:39:33,829 --> 00:39:32,000

structure

945

00:39:35,670 --> 00:39:33,839

that's schrodinger and by the way

946

00:39:37,349 --> 00:39:35,680

homochirality

947

00:39:39,430 --> 00:39:37,359

which is sought by many of the

948

00:39:41,510 --> 00:39:39,440

life-detection missions that nasa is

949

00:39:44,150 --> 00:39:41,520

contemplating including for example the

950

00:39:45,670 --> 00:39:44,160

mission to europa is actually not a

951
00:39:47,990 --> 00:39:45,680
primary

952
00:39:48,790 --> 00:39:48,000
attribute of living systems

953
00:39:50,630 --> 00:39:48,800
it's

954
00:39:52,550 --> 00:39:50,640
it is a derivative

955
00:39:55,430 --> 00:39:52,560
of the schrodinger a periodic crystal

956
00:39:59,030 --> 00:39:55,440
structure and is absolutely required for

957
00:40:01,510 --> 00:39:59,040
the informational biopolymers but uh

958
00:40:03,430 --> 00:40:01,520
biological systems actually mix d and l

959
00:40:04,870 --> 00:40:03,440
amino acids all the time in fact

960
00:40:07,670 --> 00:40:04,880
gramocide and there's lots of

961
00:40:09,670 --> 00:40:07,680
antibiotics that do this um what you

962
00:40:12,470 --> 00:40:09,680
can't do is have that system be the

963
00:40:14,950 --> 00:40:12,480

evolvable system as an in an information

964

00:40:15,990 --> 00:40:14,960

sense of the term so if you went looking

965

00:40:18,390 --> 00:40:16,000

for

966

00:40:20,550 --> 00:40:18,400

homochirality on europa and you managed

967

00:40:22,950 --> 00:40:20,560

to land yourself in a pile of gramocidin

968

00:40:25,829 --> 00:40:22,960

you would not see that

969

00:40:27,349 --> 00:40:25,839

as a you would not see homochirality as

970

00:40:28,069 --> 00:40:27,359

a life detection

971

00:40:32,550 --> 00:40:28,079

uh

972

00:40:34,069 --> 00:40:32,560

gramocided as being the product of a

973

00:40:37,510 --> 00:40:34,079

biological

974

00:40:39,349 --> 00:40:37,520

processes but homochirona is what you're

975

00:40:41,190 --> 00:40:39,359

going to see in the informational

976

00:40:43,829 --> 00:40:41,200

biopolymer and so your problem when you

977

00:40:45,829 --> 00:40:43,839

do life detection in space or for that

978

00:40:48,069 --> 00:40:45,839

matter in antarctica

979

00:40:50,150 --> 00:40:48,079

you do need to know that you're looking

980

00:40:52,550 --> 00:40:50,160

at an informational

981

00:40:54,390 --> 00:40:52,560

biopolymer before you start looking for

982

00:40:55,990 --> 00:40:54,400

homochirality

983

00:40:58,150 --> 00:40:56,000

so that actually brings us the next

984

00:40:59,750 --> 00:40:58,160

system which is the genetic system

985

00:41:02,550 --> 00:40:59,760

not the the

986

00:41:04,870 --> 00:41:02,560

structures of the building blocks must

987

00:41:07,670 --> 00:41:04,880

not only be robust with respect to

988

00:41:10,230 --> 00:41:07,680

replacement so as to not disrupt a

989

00:41:12,470 --> 00:41:10,240

periodic crystal structure but changing

990

00:41:14,870 --> 00:41:12,480

encoded information also has to be

991

00:41:17,349 --> 00:41:14,880

possible without changing the physical

992

00:41:19,829 --> 00:41:17,359

chemical behavior of the informational

993

00:41:22,309 --> 00:41:19,839

polymer such as its solubility it's

994

00:41:23,829 --> 00:41:22,319

molecular recognition it's reactivity

995

00:41:26,230 --> 00:41:23,839

and one thing we know from terran

996

00:41:28,870 --> 00:41:26,240

biochemistry is that these systems are

997

00:41:31,910 --> 00:41:28,880

actually hard to find so in proteins for

998

00:41:34,390 --> 00:41:31,920

example and i've used sickle cell anemia

999

00:41:36,630 --> 00:41:34,400

here as an example

1000

00:41:38,870 --> 00:41:36,640

a single amino acid change in a protein

1001
00:41:40,870 --> 00:41:38,880
of 500 amino acids can cause that

1002
00:41:42,950 --> 00:41:40,880
protein to precipitate and that's in

1003
00:41:44,870 --> 00:41:42,960
fact what's forming sickle cells and

1004
00:41:47,030 --> 00:41:44,880
biological systems

1005
00:41:49,430 --> 00:41:47,040
so hey you know if you had your genetic

1006
00:41:51,910 --> 00:41:49,440
polymer where you changed a g to an a or

1007
00:41:54,710 --> 00:41:51,920
t to a c to try to get more fitness and

1008
00:41:55,589 --> 00:41:54,720
then the dna precipitated it would be a

1009
00:41:58,150 --> 00:41:55,599
really

1010
00:42:00,630 --> 00:41:58,160
difficult to evolve system so you've got

1011
00:42:03,990 --> 00:42:00,640
to be able to keep the reactivity more

1012
00:42:05,670 --> 00:42:04,000
or less constant so the next slide maybe

1013
00:42:07,430 --> 00:42:05,680

let's just see what i got here

1014

00:42:09,829 --> 00:42:07,440

yeah um so

1015

00:42:12,470 --> 00:42:09,839

the polyelectrolyte theory of the gene

1016

00:42:13,430 --> 00:42:12,480

says that what you need to have to give

1017

00:42:14,870 --> 00:42:13,440

that

1018

00:42:16,470 --> 00:42:14,880

stable

1019

00:42:18,470 --> 00:42:16,480

physical properties with respect to

1020

00:42:20,710 --> 00:42:18,480

information change that has had this

1021

00:42:24,309 --> 00:42:20,720

repeating charge in the backbone

1022

00:42:25,670 --> 00:42:24,319

and the reason for that is because

1023

00:42:27,910 --> 00:42:25,680

that

1024

00:42:29,270 --> 00:42:27,920

the same molecule is charged as the most

1025

00:42:30,390 --> 00:42:29,280

important thing you can say about a

1026
00:42:32,230 --> 00:42:30,400
molecule

1027
00:42:34,230 --> 00:42:32,240
right not only does it

1028
00:42:36,710 --> 00:42:34,240
describe its solubility in water which

1029
00:42:38,390 --> 00:42:36,720
of course is night and day or charge

1030
00:42:41,349 --> 00:42:38,400
versus not charged

1031
00:42:43,109 --> 00:42:41,359
it also dominates all other electronic

1032
00:42:45,670 --> 00:42:43,119
properties of a molecule so a molecule

1033
00:42:47,910 --> 00:42:45,680
can have a charge that is a monopole

1034
00:42:49,190 --> 00:42:47,920
and if it doesn't have a charge then you

1035
00:42:50,790 --> 00:42:49,200
can start saying well it doesn't have a

1036
00:42:53,990 --> 00:42:50,800
dipole

1037
00:42:56,069 --> 00:42:54,000
important thing you can say about a

1038
00:42:58,150 --> 00:42:56,079

molecule if you're like benzene and you

1039

00:42:59,510 --> 00:42:58,160

don't have a dipole or a charge then you

1040

00:43:01,430 --> 00:42:59,520

can go down and ask well does it have a

1041

00:43:03,670 --> 00:43:01,440

quadrupole which benzene actually has

1042

00:43:05,349 --> 00:43:03,680

and that becomes the most important

1043

00:43:06,710 --> 00:43:05,359

feature of the molecule that dominates

1044

00:43:08,950 --> 00:43:06,720

its behavior

1045

00:43:10,630 --> 00:43:08,960

how are we doing

1046

00:43:11,910 --> 00:43:10,640

so a charge is big

1047

00:43:14,550 --> 00:43:11,920

if you don't have a charge you can worry

1048

00:43:16,150 --> 00:43:14,560

about charge separation that is a dipole

1049

00:43:17,510 --> 00:43:16,160

if you don't have a dipole you can start

1050

00:43:19,589 --> 00:43:17,520

worrying about what higher order

1051

00:43:22,069 --> 00:43:19,599

structures but the point about a

1052

00:43:25,030 --> 00:43:22,079

polyelectrolyte is it lets you change

1053

00:43:26,950 --> 00:43:25,040

the bases without changing the behavior

1054

00:43:29,349 --> 00:43:26,960

of the molecule and so if you go to the

1055

00:43:31,190 --> 00:43:29,359

next slide i just show you

1056

00:43:33,750 --> 00:43:31,200

one of the empirical tests of this from

1057

00:43:35,510 --> 00:43:33,760

our laboratory we we tried to make

1058

00:43:37,910 --> 00:43:35,520

dna without

1059

00:43:39,910 --> 00:43:37,920

repeating charges and and i'm not going

1060

00:43:41,750 --> 00:43:39,920

to go into great detail but there's dna

1061

00:43:43,589 --> 00:43:41,760

on your left and there is a molecule

1062

00:43:46,069 --> 00:43:43,599

that we made at great expense and effort

1063

00:43:48,950 --> 00:43:46,079

on the right you'll see i've added a

1064

00:43:51,430 --> 00:43:48,960

proton to the phosphorus to make sulfur

1065

00:43:53,270 --> 00:43:51,440

that removes the backbone charges

1066

00:43:54,950 --> 00:43:53,280

and what you'll discover about this

1067

00:43:57,910 --> 00:43:54,960

molecule is that when you get rid of the

1068

00:44:02,470 --> 00:43:59,829

what now happens is this molecule has a

1069

00:44:04,790 --> 00:44:02,480

repeating dipole and instead of

1070

00:44:06,710 --> 00:44:04,800

behaving like a respectable

1071

00:44:09,829 --> 00:44:06,720

genetic biopolymer it starts behaving

1072

00:44:11,670 --> 00:44:09,839

like sickle cell hemoglobin right it

1073

00:44:13,109 --> 00:44:11,680

folds and actually the next slide shows

1074

00:44:15,589 --> 00:44:13,119

you just for fun

1075

00:44:17,190 --> 00:44:15,599

a folding unfolding thermodynamic

1076

00:44:18,870 --> 00:44:17,200

property right you have

1077

00:44:21,589 --> 00:44:18,880

you have i've got an eight

1078

00:44:23,910 --> 00:44:21,599

letter oligonucleotide a cell phone you

1079

00:44:26,710 --> 00:44:23,920

cell phone g cell phone g so phone use

1080

00:44:29,510 --> 00:44:26,720

cell phone c seven asophone u

1081

00:44:31,750 --> 00:44:29,520

and you're looking at here a plot of the

1082

00:44:34,069 --> 00:44:31,760

um ultraviolet

1083

00:44:35,910 --> 00:44:34,079

spectrum as a function of temperature

1084

00:44:38,069 --> 00:44:35,920

and you're looking at the unfolding of

1085

00:44:40,870 --> 00:44:38,079

this particular molecule because these

1086

00:44:43,349 --> 00:44:40,880

molecules fold like proteins well why

1087

00:44:45,670 --> 00:44:43,359

because unlike dna they do not have a

1088

00:44:48,069 --> 00:44:45,680

repeating negative charge and like

1089

00:44:50,150 --> 00:44:48,079

proteins they have a repeating dipole

1090

00:44:51,670 --> 00:44:50,160

and so they behave like proteins making

1091

00:44:53,670 --> 00:44:51,680

a single change

1092

00:44:54,870 --> 00:44:53,680

in the sequence of bases in that

1093

00:44:56,950 --> 00:44:54,880

molecule

1094

00:44:59,109 --> 00:44:56,960

will change his physical properties

1095

00:45:01,030 --> 00:44:59,119

including its solubility dramatically

1096

00:45:03,109 --> 00:45:01,040

and this therefore is not an adequate

1097

00:45:05,030 --> 00:45:03,119

molecule for

1098

00:45:07,750 --> 00:45:05,040

or darwinism

1099

00:45:12,470 --> 00:45:08,710

good

1100

00:45:16,309 --> 00:45:14,309

yeah and so i mean i just sort of

1101

00:45:18,150 --> 00:45:16,319

schematically put this out here so

1102

00:45:20,790 --> 00:45:18,160

you're looking at the repeating dipole

1103

00:45:22,790 --> 00:45:20,800

in peptides or in cell phones it's like

1104

00:45:23,589 --> 00:45:22,800

putting a bunch of magnets on a string

1105

00:45:25,270 --> 00:45:23,599

right

1106

00:45:26,710 --> 00:45:25,280

north poles in the south pole if you let

1107

00:45:29,030 --> 00:45:26,720

go of the ends of the string the whole

1108

00:45:30,470 --> 00:45:29,040

thing will collapse upon itself

1109

00:45:32,630 --> 00:45:30,480

but in contrast if you have a

1110

00:45:34,710 --> 00:45:32,640

polyelectrolyte that is a molecule with

1111

00:45:37,349 --> 00:45:34,720

a repeating charge here a repeating

1112

00:45:39,270 --> 00:45:37,359

negative charge but this also works

1113

00:45:41,829 --> 00:45:39,280

if the molecule has a repeating positive

1114

00:45:44,470 --> 00:45:41,839

charge that molecule doesn't fold and

1115

00:45:46,150 --> 00:45:44,480

therefore it can template and

1116

00:45:48,390 --> 00:45:46,160

the next thing i should mention is on

1117

00:45:50,390 --> 00:45:48,400

the next slide which is that

1118

00:45:52,790 --> 00:45:50,400

this if you get rid of that repeating

1119

00:45:55,270 --> 00:45:52,800

backbone charge you also lose

1120

00:45:56,950 --> 00:45:55,280

blocks and qrik rules so here's just a

1121

00:45:59,829 --> 00:45:56,960

structure of one of those cell phone

1122

00:46:00,950 --> 00:45:59,839

molecules which i've shown we have a uu

1123

00:46:04,309 --> 00:46:00,960

pair

1124

00:46:05,829 --> 00:46:04,319

um the next slide uh shows you a little

1125

00:46:08,470 --> 00:46:05,839

bit more graphically what's going on

1126
00:46:11,670 --> 00:46:08,480
here you've got two kinds of repulsion

1127
00:46:13,109 --> 00:46:11,680
right you have the repulsion at the top

1128
00:46:15,670 --> 00:46:13,119
of that structure where the

1129
00:46:18,230 --> 00:46:15,680
double-headed arrows are showing

1130
00:46:19,670 --> 00:46:18,240
repulsion between backbone phosphates of

1131
00:46:21,030 --> 00:46:19,680
a single strand

1132
00:46:23,750 --> 00:46:21,040
and that's of course what keeps the

1133
00:46:25,750 --> 00:46:23,760
molecule unfolded and then you'll notice

1134
00:46:28,710 --> 00:46:25,760
that the coulombic charge repulsion

1135
00:46:31,510 --> 00:46:28,720
between strands what that does is lets

1136
00:46:34,870 --> 00:46:31,520
the molecules

1137
00:46:36,630 --> 00:46:34,880
law

1138
00:46:38,390 --> 00:46:36,640

predicts of course that the backbones

1139

00:46:40,309 --> 00:46:38,400

repel in fact

1140

00:46:42,390 --> 00:46:40,319

as an experimental piece of evidence to

1141

00:46:45,030 --> 00:46:42,400

support that dna duplexes are more

1142

00:46:47,109 --> 00:46:45,040

stable in high salt where the backbone

1143

00:46:48,309 --> 00:46:47,119

charges are shielded from each other by

1144

00:46:50,870 --> 00:46:48,319

salt

1145

00:46:53,589 --> 00:46:50,880

um but what this backbone repeating

1146

00:46:55,589 --> 00:46:53,599

charge does is drives strand strand

1147

00:46:57,829 --> 00:46:55,599

interactions as far as possible from the

1148

00:47:00,390 --> 00:46:57,839

backbone and that's what gives watson

1149

00:47:02,390 --> 00:47:00,400

qrik rules get rid of the repeating

1150

00:47:04,309 --> 00:47:02,400

backbone charges is now many synthetic

1151

00:47:07,270 --> 00:47:04,319

biologists have done

1152

00:47:09,190 --> 00:47:07,280

that that those rules go away

1153

00:47:11,750 --> 00:47:09,200

okay so go to the next slide for me

1154

00:47:14,069 --> 00:47:11,760

please

1155

00:47:16,150 --> 00:47:14,079

yeah so the darwinian informational

1156

00:47:18,069 --> 00:47:16,160

biopolymers must be charged because

1157

00:47:20,790 --> 00:47:18,079

among uh in water at least because it

1158

00:47:22,630 --> 00:47:20,800

keeps the polymer dissolved tomorrow

1159

00:47:25,270 --> 00:47:22,640

these backbone backbone coulomb

1160

00:47:26,950 --> 00:47:25,280

repulsions force strand strand contacts

1161

00:47:29,270 --> 00:47:26,960

are the watson crick edges of the

1162

00:47:31,190 --> 00:47:29,280

nuclear bases that's what gives you the

1163

00:47:33,030 --> 00:47:31,200

rules that you memorize in middle school

1164

00:47:35,670 --> 00:47:33,040

a pairs with t and g

1165

00:47:37,510 --> 00:47:35,680

c and of course polyanionic structure

1166

00:47:39,829 --> 00:47:37,520

discourages folding and that's what lets

1167

00:47:41,030 --> 00:47:39,839

you do template

1168

00:47:45,109 --> 00:47:41,040

all right

1169

00:47:49,990 --> 00:47:47,990

and by the way synthesis

1170

00:47:52,470 --> 00:47:50,000

again tests as i did not mention this

1171

00:47:53,750 --> 00:47:52,480

when i put up all these slides of all

1172

00:47:55,990 --> 00:47:53,760

these structures that fit the

1173

00:47:57,270 --> 00:47:56,000

schrodinger aperiodic crystal structure

1174

00:47:59,910 --> 00:47:57,280

but everything that we do in this

1175

00:48:01,990 --> 00:47:59,920

molecule also

1176

00:48:04,549 --> 00:48:02,000

has that repeating charge phosphate in

1177

00:48:07,030 --> 00:48:04,559

the backbone so this is a perfectly good

1178

00:48:09,750 --> 00:48:07,040

evolvable genetic system with 12 letters

1179

00:48:13,030 --> 00:48:09,760

instead of four i'm not saying necessary

1180

00:48:15,990 --> 00:48:13,040

that life on europa or enceladus

1181

00:48:18,710 --> 00:48:16,000

or sub i know in the water ammonia ocean

1182

00:48:20,710 --> 00:48:18,720

beneath titan will have a 12 letter off

1183

00:48:23,430 --> 00:48:20,720

of it but they could because they meet

1184

00:48:25,670 --> 00:48:23,440

the two criteria of required for

1185

00:48:27,910 --> 00:48:25,680

darwinism and by the way these are

1186

00:48:29,750 --> 00:48:27,920

sufficient criteria we actually don't

1187

00:48:32,390 --> 00:48:29,760

have to have any other features of that

1188

00:48:34,230 --> 00:48:32,400

biopolymer it has to be a repeating

1189

00:48:35,109 --> 00:48:34,240

backbone charge that can be a positive

1190

00:48:36,549 --> 00:48:35,119

charge

1191

00:48:38,950 --> 00:48:36,559

and the building blocks must be

1192

00:48:41,430 --> 00:48:38,960

exchangeable without changing their

1193

00:48:42,710 --> 00:48:41,440

overall size and packing

1194

00:48:46,150 --> 00:48:42,720

all right

1195

00:48:49,109 --> 00:48:46,950

great

1196

00:48:51,829 --> 00:48:49,119

okay no one's either i've either killed

1197

00:48:53,990 --> 00:48:51,839

you all or

1198

00:48:56,710 --> 00:48:54,000

all right so the next slide says all

1199

00:48:57,750 --> 00:48:56,720

right great so this by the way just for

1200

00:48:59,349 --> 00:48:57,760

fun

1201

00:49:02,390 --> 00:48:59,359

i just put some stuff in here just to

1202

00:49:04,230 --> 00:49:02,400

show you how good a 12 genetic system is

1203

00:49:07,270 --> 00:49:04,240

as long as it keeps the schrodinger it

1204

00:49:08,630 --> 00:49:07,280

periodic crystal structure

1205

00:49:10,390 --> 00:49:08,640

in tow and

1206

00:49:12,230 --> 00:49:10,400

the repeating

1207

00:49:14,309 --> 00:49:12,240

bonding patterns we just published this

1208

00:49:17,030 --> 00:49:14,319

paper with an eight letter genetic

1209

00:49:19,030 --> 00:49:17,040

system where we measured hundreds of

1210

00:49:22,630 --> 00:49:19,040

melting temperatures of thermodynamic

1211

00:49:26,790 --> 00:49:22,640

properties of the formation of atgc sb

1212

00:49:29,589 --> 00:49:26,800

and zp pairs the sb and zp pairs you've

1213

00:49:32,390 --> 00:49:29,599

never seen in your middle school classes

1214

00:49:33,829 --> 00:49:32,400

but there they are structurally and

1215

00:49:36,390 --> 00:49:33,839

if you want to look at the predicted

1216

00:49:38,150 --> 00:49:36,400

melting temperatures on the right side

1217

00:49:40,549 --> 00:49:38,160

on the

1218

00:49:43,349 --> 00:49:40,559

x-axis and the experimental temperatures

1219

00:49:46,069 --> 00:49:43,359

on the y-axis

1220

00:49:48,150 --> 00:49:46,079

the correlation coefficient is uh r

1221

00:49:50,470 --> 00:49:48,160

square is about 0.87

1222

00:49:53,829 --> 00:49:50,480

this is just as good as with natural dna

1223

00:49:55,750 --> 00:49:53,839

and by the way the depends from this are

1224

00:49:58,630 --> 00:49:55,760

not the funny bases not the funny

1225

00:50:00,710 --> 00:49:58,640

nucleotides they outlier is a t

1226

00:50:03,589 --> 00:50:00,720

okay which as you know is joined by only

1227

00:50:05,270 --> 00:50:03,599

two hydrogen bonds and that creates no

1228

00:50:07,670 --> 00:50:05,280

ends of problems when you're trying to

1229

00:50:10,950 --> 00:50:07,680

design primers and probes

1230

00:50:13,349 --> 00:50:10,960

do biotechnology but the point is that

1231

00:50:15,510 --> 00:50:13,359

this is an evolvable system which is

1232

00:50:16,870 --> 00:50:15,520

just meeting two requirements

1233

00:50:19,829 --> 00:50:16,880

scrotinger's requirement and the

1234

00:50:21,990 --> 00:50:19,839

polyelectrolyte requirement and other

1235

00:50:23,990 --> 00:50:22,000

everything else can be changed in the

1236

00:50:25,910 --> 00:50:24,000

system including the hydrogen bonding

1237

00:50:27,430 --> 00:50:25,920

patterns the number of bases the side

1238

00:50:29,349 --> 00:50:27,440

chains depends on the basis the

1239

00:50:31,030 --> 00:50:29,359

functionality of the bases any of a

1240

00:50:32,950 --> 00:50:31,040

number of things so again i'm not

1241

00:50:34,470 --> 00:50:32,960

necessarily expecting to see this on

1242

00:50:37,109 --> 00:50:34,480

enceladus but

1243

00:50:38,710 --> 00:50:37,119

um you can see that the rules are

1244

00:50:40,470 --> 00:50:38,720

predictive in the sense that we can go

1245

00:50:42,870 --> 00:50:40,480

into the laboratory and make our own

1246

00:50:44,790 --> 00:50:42,880

darwinian systems just by following

1247

00:50:45,829 --> 00:50:44,800

these two rules

1248

00:50:49,430 --> 00:50:45,839

okay

1249

00:50:55,430 --> 00:50:51,750

yeah and i just am beating a dead horse

1250

00:51:00,790 --> 00:50:58,790

okay so okay now we want to use these

1251

00:51:03,510 --> 00:51:00,800

features to build a life detection

1252

00:51:05,190 --> 00:51:03,520

device and um

1253

00:51:06,390 --> 00:51:05,200

one of the things that's very important

1254

00:51:08,950 --> 00:51:06,400

to know is that if i have a

1255

00:51:11,270 --> 00:51:08,960

polyelectrolyte if i have it in dilute

1256

00:51:14,230 --> 00:51:11,280

solution it's very easy to concentrate

1257

00:51:15,990 --> 00:51:14,240

that from a dilute solution well how all

1258

00:51:17,829 --> 00:51:16,000

i have to well all i have to do is put

1259

00:51:20,150 --> 00:51:17,839

down a detector which is at the bottom

1260

00:51:21,589 --> 00:51:20,160

of the slide with a bunch of positive

1261

00:51:23,349 --> 00:51:21,599

charges on it

1262

00:51:25,430 --> 00:51:23,359

and that of course will absorb a

1263

00:51:27,910 --> 00:51:25,440

biopolymer from solution with a bunch of

1264

00:51:30,790 --> 00:51:27,920

negative charges on it and because of

1265

00:51:33,190 --> 00:51:30,800

what we call polyvalency

1266

00:51:36,950 --> 00:51:33,200

um the repeating negatively charged

1267

00:51:39,030 --> 00:51:36,960

backbone will displace

1268

00:51:41,190 --> 00:51:39,040

inorganic ions like bromide with a

1269

00:51:44,549 --> 00:51:41,200

single negative charge or sulfate with

1270

00:51:46,309 --> 00:51:44,559

two negative charges or perchlorate

1271

00:51:48,470 --> 00:51:46,319

which unfortunately has one negative

1272

00:51:49,430 --> 00:51:48,480

charge but never mind

1273

00:51:51,829 --> 00:51:49,440

that's

1274

00:51:53,430 --> 00:51:51,839

but so it's very easy if i take a dilute

1275

00:51:55,109 --> 00:51:53,440

solution

1276
00:51:56,309 --> 00:51:55,119
to concentrate

1277
00:52:05,190 --> 00:51:56,319
a

1278
00:52:08,710 --> 00:52:05,200
loop solution

1279
00:52:13,430 --> 00:52:11,510
and so you can imagine a device in fact

1280
00:52:15,190 --> 00:52:13,440
we wrote a paper about this two years

1281
00:52:15,990 --> 00:52:15,200
ago which you can read

1282
00:52:19,030 --> 00:52:16,000
where

1283
00:52:21,030 --> 00:52:19,040
you could put two plates okay

1284
00:52:22,710 --> 00:52:21,040
in and the two plates one of them has a

1285
00:52:24,549 --> 00:52:22,720
bunch of negative charges on it one of

1286
00:52:27,270 --> 00:52:24,559
them has a bunch of positive charges on

1287
00:52:29,030 --> 00:52:27,280
it the first one is supposed to capture

1288
00:52:31,430 --> 00:52:29,040

martian genetic polymers if the

1289

00:52:32,390 --> 00:52:31,440

repeating backbone charge happens have

1290

00:52:33,430 --> 00:52:32,400

the

1291

00:52:34,309 --> 00:52:33,440

positive

1292

00:52:36,150 --> 00:52:34,319

the

1293

00:52:38,549 --> 00:52:36,160

positively charged plate captures

1294

00:52:41,670 --> 00:52:38,559

martian dna if it's repeating backbone

1295

00:52:44,069 --> 00:52:41,680

unit charge is negative and so they will

1296

00:52:45,589 --> 00:52:44,079

concentrate this from dilute solution

1297

00:52:49,030 --> 00:52:45,599

and then the next point we should make

1298

00:52:51,270 --> 00:52:49,040

is that you want to be able to

1299

00:52:53,910 --> 00:52:51,280

then asks or query what is absorbed to

1300

00:52:56,230 --> 00:52:53,920

see whether it is fitting

1301
00:52:58,870 --> 00:52:56,240
schrodinger's requirement that's kind of

1302
00:53:01,109 --> 00:52:58,880
interesting because

1303
00:53:03,510 --> 00:53:01,119
if i take dna and its building blocks

1304
00:53:05,750 --> 00:53:03,520
each of the building blocks is chiral

1305
00:53:06,870 --> 00:53:05,760
and so they will rotate plain polarized

1306
00:53:09,589 --> 00:53:06,880
light

1307
00:53:11,910 --> 00:53:09,599
um but if i hook them all together the

1308
00:53:14,069 --> 00:53:11,920
chirality is bigger you have a super

1309
00:53:15,750 --> 00:53:14,079
chirality and that's because each of the

1310
00:53:19,190 --> 00:53:15,760
little building blocks was the same

1311
00:53:22,069 --> 00:53:19,200
chirality that is homochiron induces a

1312
00:53:24,630 --> 00:53:22,079
bigger chirality in this particular case

1313
00:53:27,349 --> 00:53:24,640

for example in your dna a right-handed

1314

00:53:29,829 --> 00:53:27,359

not a left-handed double helix and that

1315

00:53:31,030 --> 00:53:29,839

right-handed double helix has more

1316

00:53:33,190 --> 00:53:31,040

rotation

1317

00:53:35,670 --> 00:53:33,200

of the polarized light

1318

00:53:38,549 --> 00:53:35,680

it's more optically active

1319

00:53:40,829 --> 00:53:38,559

if you will it's super chiral because it

1320

00:53:42,710 --> 00:53:40,839

has amplified the

1321

00:53:44,470 --> 00:53:42,720

microscopic chirality of each of its

1322

00:53:46,710 --> 00:53:44,480

building blocks and that's actually

1323

00:53:49,030 --> 00:53:46,720

something that can be detected

1324

00:53:50,950 --> 00:53:49,040

by in this particular case making the

1325

00:53:53,270 --> 00:53:50,960

mole this thing that's absorbing the

1326
00:53:55,670 --> 00:53:53,280
molecules um

1327
00:53:57,270 --> 00:53:55,680
a waveguide and putting plane polarized

1328
00:53:58,390 --> 00:53:57,280
light through it

1329
00:54:00,549 --> 00:53:58,400
um so

1330
00:54:02,790 --> 00:54:00,559
if there is in fact a homochiropolymer

1331
00:54:05,510 --> 00:54:02,800
absorbed that well plain polarized light

1332
00:54:08,309 --> 00:54:05,520
will be much more rotating

1333
00:54:10,150 --> 00:54:08,319
rotated than if it's not

1334
00:54:14,309 --> 00:54:10,160
um

1335
00:54:18,230 --> 00:54:16,390
yeah and so you know then there's only

1336
00:54:20,470 --> 00:54:18,240
questions about sensitivity which i

1337
00:54:22,870 --> 00:54:20,480
won't go through here but obviously you

1338
00:54:24,549 --> 00:54:22,880

can just do a biacore surface plasma

1339

00:54:26,230 --> 00:54:24,559

resonance absorption to detect the

1340

00:54:28,710 --> 00:54:26,240

absorption of these things the

1341

00:54:30,150 --> 00:54:28,720

sensitivity is low the long path length

1342

00:54:31,829 --> 00:54:30,160

is required

1343

00:54:34,549 --> 00:54:31,839

and we don't actually know what the

1344

00:54:36,789 --> 00:54:34,559

refractive index is of martian dna so

1345

00:54:40,230 --> 00:54:36,799

you have a problem managing that so the

1346

00:54:43,109 --> 00:54:41,430

is of course you can look for the

1347

00:54:45,750 --> 00:54:43,119

ultraviolet absorption of the side

1348

00:54:47,589 --> 00:54:45,760

chains onto that waveguide

1349

00:54:49,829 --> 00:54:47,599

that's a more sensitive test but again

1350

00:54:51,109 --> 00:54:49,839

we don't know that martian dna absorbs

1351

00:54:53,510 --> 00:54:51,119

uv light

1352

00:54:55,270 --> 00:54:53,520

the next slide

1353

00:54:58,069 --> 00:54:55,280

is what i just mentioned this sort of

1354

00:55:00,470 --> 00:54:58,079

macro chirality we can look for rotation

1355

00:55:01,910 --> 00:55:00,480

of plane polarized light which will be

1356

00:55:04,309 --> 00:55:01,920

greater

1357

00:55:06,630 --> 00:55:04,319

for my polymer of homocurrent building

1358

00:55:07,829 --> 00:55:06,640

blocks than rotation of the monomers

1359

00:55:11,270 --> 00:55:07,839

collectively

1360

00:55:14,470 --> 00:55:12,789

and by the way none of this precludes

1361

00:55:16,470 --> 00:55:14,480

downstream analysis if you're building

1362

00:55:19,109 --> 00:55:16,480

your life detection instrument so you

1363

00:55:21,270 --> 00:55:19,119

know we can obviously collect the

1364

00:55:23,829 --> 00:55:21,280

allegedly darwinian polyelectrolyte

1365

00:55:26,230 --> 00:55:23,839

polymer and then displace it later to do

1366

00:55:28,950 --> 00:55:26,240

multi-mass effect or some information to

1367

00:55:31,030 --> 00:55:28,960

get some information about the detailed

1368

00:55:34,390 --> 00:55:31,040

structure of the polyelectrolyte next

1369

00:55:38,549 --> 00:55:36,230

yeah so i mean this is a complete

1370

00:55:41,109 --> 00:55:38,559

architecture it's a wonderful concept

1371

00:55:43,109 --> 00:55:41,119

you go to the martian polar ice cap or

1372

00:55:45,270 --> 00:55:43,119

for that matter you can go to antarctica

1373

00:55:46,549 --> 00:55:45,280

you dump ice in the top

1374

00:55:48,710 --> 00:55:46,559

um

1375

00:55:51,510 --> 00:55:48,720

you know the mars cap is nice because it

1376

00:55:53,750 --> 00:55:51,520

surveys the entire accessible surface by

1377

00:55:55,829 --> 00:55:53,760

dust storms so you don't have to do

1378

00:55:58,470 --> 00:55:55,839

caching or make correct guesses about

1379

00:56:00,549 --> 00:55:58,480

locales to sample you got to stall the

1380

00:56:03,190 --> 00:56:00,559

sample but you got to keep in mind that

1381

00:56:05,270 --> 00:56:03,200

as all the other steps that i'm doing

1382

00:56:07,910 --> 00:56:05,280

are using energy but that can all be

1383

00:56:09,910 --> 00:56:07,920

added to the budget for the thawing

1384

00:56:11,750 --> 00:56:09,920

budget for the energy of falling of the

1385

00:56:13,750 --> 00:56:11,760

material you got to disrupt cell

1386

00:56:15,910 --> 00:56:13,760

compartments now remember i'm going to

1387

00:56:18,630 --> 00:56:15,920

put this into a cyclonic sharpless

1388

00:56:20,150 --> 00:56:18,640

centrifuge and if i've got dust in there

1389

00:56:21,990 --> 00:56:20,160

in cells thus

1390

00:56:24,710 --> 00:56:22,000

the abrasive dust will

1391

00:56:26,710 --> 00:56:24,720

disrupt cells pretty much for free

1392

00:56:29,430 --> 00:56:26,720

this sharpless centrifuge

1393

00:56:32,789 --> 00:56:29,440

that central tube is spinning and so all

1394

00:56:34,710 --> 00:56:32,799

the minerals go to the outside surface

1395

00:56:35,910 --> 00:56:34,720

and some of those minerals maybe a lot

1396

00:56:37,670 --> 00:56:35,920

of them are chiral and they would

1397

00:56:39,430 --> 00:56:37,680

interfere with the optical activity

1398

00:56:40,870 --> 00:56:39,440

measurement so they're being

1399

00:56:42,789 --> 00:56:40,880

set out to the side you can actually

1400

00:56:45,510 --> 00:56:42,799

withdraw them for

1401
00:56:46,789 --> 00:56:45,520
if you want to to and analyze them and

1402
00:56:49,349 --> 00:56:46,799
then you pass the liquid through your

1403
00:56:51,030 --> 00:56:49,359
polyelectric like capture things and you

1404
00:56:52,710 --> 00:56:51,040
can sample any of these things

1405
00:56:54,950 --> 00:56:52,720
microscopically

1406
00:56:56,870 --> 00:56:54,960
or you can do mineralogical samples i'm

1407
00:56:58,230 --> 00:56:56,880
delighted to look at that cyclonic

1408
00:57:00,470 --> 00:56:58,240
filtrated minerals and see whether

1409
00:57:02,470 --> 00:57:00,480
there's orate there you can see

1410
00:57:04,710 --> 00:57:02,480
metabolites in the evaporated waste and

1411
00:57:06,789 --> 00:57:04,720
you can look at downstream analysis of

1412
00:57:08,950 --> 00:57:06,799
polyelectrolytes with there's really no

1413
00:57:10,150 --> 00:57:08,960

possibility here for false positives

1414

00:57:12,230 --> 00:57:10,160

because

1415

00:57:15,349 --> 00:57:12,240

there's no other way of getting a

1416

00:57:17,750 --> 00:57:15,359

polyelectrolyte building block uh

1417

00:57:19,430 --> 00:57:17,760

assembled assembly with a set of

1418

00:57:21,589 --> 00:57:19,440

building blocks that are homochiral

1419

00:57:22,870 --> 00:57:21,599

except by the influence of darwinism i

1420

00:57:23,829 --> 00:57:22,880

think

1421

00:57:25,589 --> 00:57:23,839

of course

1422

00:57:28,630 --> 00:57:25,599

false negatives are a matter of

1423

00:57:31,589 --> 00:57:28,640

sensitivity of the device

1424

00:57:34,950 --> 00:57:31,599

all right that's all i have right now um

1425

00:57:37,109 --> 00:57:34,960

i think there's no slide to follow right

1426
00:57:39,030 --> 00:57:37,119
yeah there you go so let me stop and

1427
00:57:40,309 --> 00:57:39,040
answer any questions you have

1428
00:57:43,750 --> 00:57:40,319
steve unfortunately we're running a

1429
00:57:46,789 --> 00:57:43,760
little short on time so maybe if people

1430
00:57:48,549 --> 00:57:46,799
um have a chance to ask you questions

1431
00:57:50,789 --> 00:57:48,559
maybe they can do that offline or maybe

1432
00:57:52,950 --> 00:57:50,799
in a chat window a little bit later on

1433
00:57:56,890 --> 00:57:52,960
if that would work for you no problem

1434
00:57:56,900 --> 00:58:01,750
[Applause]

1435
00:58:01,760 --> 00:58:06,829
okay we got arvind

1436
00:58:13,190 --> 00:58:09,670
online all right can everyone see the

1437
00:58:16,710 --> 00:58:14,150
either

1438
00:58:19,190 --> 00:58:16,720

uh thanks uh gary kathy

1439

00:58:20,710 --> 00:58:19,200

ken and penny for organizing this uh

1440

00:58:22,150 --> 00:58:20,720

virtual conference it's awesome to

1441

00:58:24,390 --> 00:58:22,160

listen to a variety of different things

1442

00:58:25,510 --> 00:58:24,400

already and some of the concepts put

1443

00:58:27,990 --> 00:58:25,520

forward

1444

00:58:30,150 --> 00:58:28,000

so today i'm kind of going to be talking

1445

00:58:32,390 --> 00:58:30,160

about some weird stuff that we've been

1446

00:58:33,829 --> 00:58:32,400

noticing with single-stranded dna

1447

00:58:36,150 --> 00:58:33,839

viruses and i'm going to take you into

1448

00:58:39,349 --> 00:58:36,160

the world of single-stranded dna viruses

1449

00:58:43,829 --> 00:58:39,359

in quite a complex system

1450

00:58:49,030 --> 00:58:46,470

all right so before i go into

1451

00:58:50,309 --> 00:58:49,040

the whole field of signals with dna

1452

00:58:52,309 --> 00:58:50,319

viruses i want to actually start

1453

00:58:54,549 --> 00:58:52,319

tackling a couple of things which i

1454

00:58:56,309 --> 00:58:54,559

think are very important and these are

1455

00:58:58,950 --> 00:58:56,319

concepts of evolution

1456

00:59:00,630 --> 00:58:58,960

and we all know that viruses evolved by

1457

00:59:02,470 --> 00:59:00,640

three main mechanisms

1458

00:59:04,789 --> 00:59:02,480

and one is basically nucleotide

1459

00:59:07,349 --> 00:59:04,799

substitutions where you basically get

1460

00:59:10,230 --> 00:59:07,359

mutations occurring or some of which are

1461

00:59:12,390 --> 00:59:10,240

identifiers some of which are beneficial

1462

00:59:15,030 --> 00:59:12,400

others are pretty much

1463

00:59:16,630 --> 00:59:15,040

neutral and then to repair mutations

1464

00:59:17,750 --> 00:59:16,640

that are deleterious

1465

00:59:18,950 --> 00:59:17,760

by

1466

00:59:20,630 --> 00:59:18,960

again

1467

00:59:22,870 --> 00:59:20,640

mutating those sites is actually very

1468

00:59:24,230 --> 00:59:22,880

complex and to fix them is a very very

1469

00:59:26,309 --> 00:59:24,240

slow process

1470

00:59:28,870 --> 00:59:26,319

however there are viruses that are very

1471

00:59:31,109 --> 00:59:28,880

good at fixing a variety of mutations by

1472

00:59:33,030 --> 00:59:31,119

a mechanism called recombination

1473

00:59:35,190 --> 00:59:33,040

and this usually happens when you have

1474

00:59:36,870 --> 00:59:35,200

two viral templates within

1475

00:59:38,630 --> 00:59:36,880

a cell

1476
00:59:40,069 --> 00:59:38,640
and what happens is there is template

1477
00:59:41,270 --> 00:59:40,079
swapping that takes place during

1478
00:59:43,270 --> 00:59:41,280
reputation

1479
00:59:46,309 --> 00:59:43,280
and in this mechanism you can generate

1480
00:59:48,390 --> 00:59:46,319
chimeric viruses numeric genomes and as

1481
00:59:50,950 --> 00:59:48,400
a consequence of that to repair a

1482
00:59:53,670 --> 00:59:50,960
deleterious mutation is actually very

1483
00:59:55,910 --> 00:59:53,680
very beneficial it's very efficient in

1484
00:59:56,870 --> 00:59:55,920
this kind of mechanism but at the same

1485
00:59:59,030 --> 00:59:56,880
time

1486
01:00:01,510 --> 00:59:59,040
if a virus is trying to explore sequence

1487
01:00:03,190 --> 01:00:01,520
landscapes then it is able to do this

1488
01:00:05,190 --> 01:00:03,200

very efficiently using these kind of

1489

01:00:06,950 --> 01:00:05,200

mechanisms

1490

01:00:08,870 --> 01:00:06,960

um and then

1491

01:00:11,190 --> 01:00:08,880

we have something that is very very

1492

01:00:13,349 --> 01:00:11,200

unusual but unique in the sense that we

1493

01:00:15,349 --> 01:00:13,359

have reassortment which takes place

1494

01:00:17,510 --> 01:00:15,359

which we commonly know in the field of

1495

01:00:19,910 --> 01:00:17,520

influenza where you have eight segments

1496

01:00:21,829 --> 01:00:19,920

that they can reassort over time and as

1497

01:00:23,990 --> 01:00:21,839

a result of that you get different

1498

01:00:26,789 --> 01:00:24,000

variations of at least the hemoglobin

1499

01:00:30,069 --> 01:00:26,799

and neuraminidase and as a consequence

1500

01:00:31,589 --> 01:00:30,079

we have immunizations every year to try

1501

01:00:33,030 --> 01:00:31,599

and combat the different variants that

1502

01:00:34,549 --> 01:00:33,040

come through through

1503

01:00:36,870 --> 01:00:34,559

reassortment

1504

01:00:39,030 --> 01:00:36,880

but what is less known is that there are

1505

01:00:41,670 --> 01:00:39,040

viruses which are segmented and

1506

01:00:42,789 --> 01:00:41,680

multipatient viruses as well where each

1507

01:00:45,109 --> 01:00:42,799

segment

1508

01:00:47,750 --> 01:00:45,119

or each genomic element that constitute

1509

01:00:50,230 --> 01:00:47,760

the entire genome is packaged into an

1510

01:00:52,150 --> 01:00:50,240

individual capsid and there as well you

1511

01:00:54,549 --> 01:00:52,160

get reassortment taking place so it's

1512

01:00:57,190 --> 01:00:54,559

almost like each chromosome is patched

1513

01:01:00,150 --> 01:00:57,200

into an individual virion and those all

1514

01:01:02,549 --> 01:01:00,160

have to act together within a system

1515

01:01:04,470 --> 01:01:02,559

um to actually create an active

1516

01:01:06,789 --> 01:01:04,480

infection

1517

01:01:08,870 --> 01:01:06,799

so if we kind of unpack all of this and

1518

01:01:11,750 --> 01:01:08,880

start looking at viruses in a general

1519

01:01:14,390 --> 01:01:11,760

context viruses are very unusual in the

1520

01:01:17,750 --> 01:01:14,400

sense that the genomic material can vary

1521

01:01:19,829 --> 01:01:17,760

from dna to rna and also in terms of

1522

01:01:22,150 --> 01:01:19,839

polarity and also whether they're

1523

01:01:24,069 --> 01:01:22,160

double-stranded or not there also is

1524

01:01:26,470 --> 01:01:24,079

topological differences whether they can

1525

01:01:28,390 --> 01:01:26,480

be circular or linear

1526

01:01:30,950 --> 01:01:28,400

the things that is really unique about

1527

01:01:33,589 --> 01:01:30,960

single-stranded dna viruses is

1528

01:01:35,349 --> 01:01:33,599

majority of their muscular viruses

1529

01:01:37,190 --> 01:01:35,359

however

1530

01:01:39,670 --> 01:01:37,200

there is something that is very amazing

1531

01:01:41,750 --> 01:01:39,680

is that they actually are able to infect

1532

01:01:43,510 --> 01:01:41,760

all donald trump

1533

01:01:45,750 --> 01:01:43,520

and you're able to infect archaea

1534

01:01:48,710 --> 01:01:45,760

bacteria we know viruses that infect

1535

01:01:50,950 --> 01:01:48,720

diatoms fungi a variety of invertebrates

1536

01:01:53,030 --> 01:01:50,960

plants and obviously

1537

01:01:55,670 --> 01:01:53,040

through metagenomic approaches we're

1538

01:01:57,109 --> 01:01:55,680

discovering viruses that we have no idea

1539

01:01:59,109 --> 01:01:57,119

what they infect

1540

01:02:00,789 --> 01:01:59,119

but within these single stranded dna

1541

01:02:02,150 --> 01:02:00,799

viruses they're different conformations

1542

01:02:04,789 --> 01:02:02,160

of genomic

1543

01:02:07,029 --> 01:02:04,799

systems where you could have monopod

1544

01:02:09,029 --> 01:02:07,039

site or multipartite

1545

01:02:10,789 --> 01:02:09,039

molecules so basically you could have

1546

01:02:13,829 --> 01:02:10,799

one single chromosome into which all the

1547

01:02:16,390 --> 01:02:13,839

genetic material is packaged or you have

1548

01:02:18,069 --> 01:02:16,400

multiple chromosomes that then carry

1549

01:02:20,549 --> 01:02:18,079

different genetic information and

1550

01:02:23,430 --> 01:02:20,559

they're all unique in that context

1551
01:02:25,510 --> 01:02:23,440
but one thing that we've really

1552
01:02:26,950 --> 01:02:25,520
focused on these viruses primarily is

1553
01:02:29,190 --> 01:02:26,960
because we're under keen on

1554
01:02:31,029 --> 01:02:29,200
understanding evolution of these viruses

1555
01:02:32,710 --> 01:02:31,039
and these viral genomes are relatively

1556
01:02:35,029 --> 01:02:32,720
small so we can actually sequence them

1557
01:02:37,109 --> 01:02:35,039
to completion and we can look at coding

1558
01:02:39,430 --> 01:02:37,119
and non-coding regions to figure out

1559
01:02:41,349 --> 01:02:39,440
what the variations are

1560
01:02:43,029 --> 01:02:41,359
now one of the unique thing about some

1561
01:02:46,069 --> 01:02:43,039
of these viruses single-stranded dna

1562
01:02:48,549 --> 01:02:46,079
viruses not all but a vast number of

1563
01:02:51,190 --> 01:02:48,559

them is that they have certain very very

1564

01:02:53,190 --> 01:02:51,200

unique properties and one of them is a

1565

01:02:55,750 --> 01:02:53,200

enzyme called replication initiator

1566

01:02:57,430 --> 01:02:55,760

protein which actually has two domains

1567

01:03:00,309 --> 01:02:57,440

it's got an endonuclease domain and a

1568

01:03:01,750 --> 01:03:00,319

helicase domain which initiate the whole

1569

01:03:03,589 --> 01:03:01,760

mechanism of replication of these

1570

01:03:04,390 --> 01:03:03,599

circular molecules

1571

01:03:06,470 --> 01:03:04,400

and

1572

01:03:09,109 --> 01:03:06,480

very very unique motifs which are very

1573

01:03:12,390 --> 01:03:09,119

recognizable across the system

1574

01:03:15,029 --> 01:03:12,400

but if we were to break those two motifs

1575

01:03:17,109 --> 01:03:15,039

and draw some phylogeny infer phylogeny

1576

01:03:19,190 --> 01:03:17,119

based on that based on all the single

1577

01:03:22,150 --> 01:03:19,200

stranded dna viruses that encode these

1578

01:03:24,549 --> 01:03:22,160

kind of proteins we notice that the

1579

01:03:26,710 --> 01:03:24,559

phylogeny is not congruent and that kind

1580

01:03:29,670 --> 01:03:26,720

of suggests to us that these viruses

1581

01:03:32,069 --> 01:03:29,680

have at some point exchanged material or

1582

01:03:33,990 --> 01:03:32,079

are recombinant even at a protein level

1583

01:03:35,589 --> 01:03:34,000

so some of this obviously we can't

1584

01:03:37,349 --> 01:03:35,599

detect at the nucleotide level we can

1585

01:03:39,829 --> 01:03:37,359

see it at a protein level because of

1586

01:03:41,510 --> 01:03:39,839

these variations

1587

01:03:43,510 --> 01:03:41,520

but the other thing that is staggering

1588

01:03:45,510 --> 01:03:43,520

about these viruses and these are

1589

01:03:48,069 --> 01:03:45,520

nucleotide substitution rates that we've

1590

01:03:49,510 --> 01:03:48,079

calculated other people have calculated

1591

01:03:51,670 --> 01:03:49,520

we've calculated based on lab

1592

01:03:53,270 --> 01:03:51,680

experiments we've made infectious clones

1593

01:03:56,870 --> 01:03:53,280

put them into a system

1594

01:03:59,349 --> 01:03:56,880

measured mutation rates over 15 years

1595

01:04:01,829 --> 01:03:59,359

in some cases see what's been going on

1596

01:04:04,230 --> 01:04:01,839

and if you look at them that all across

1597

01:04:06,309 --> 01:04:04,240

the theme of single-stranded dna viruses

1598

01:04:08,309 --> 01:04:06,319

it appears to be a theme that the

1599

01:04:10,309 --> 01:04:08,319

mutation rates are really high or the

1600

01:04:13,029 --> 01:04:10,319

substitution rates are really high and

1601
01:04:15,990 --> 01:04:13,039
in some cases they're as high as those

1602
01:04:18,309 --> 01:04:16,000
of rna viruses and this general

1603
01:04:20,950 --> 01:04:18,319
hypothesis has always been that rna

1604
01:04:23,349 --> 01:04:20,960
viruses are actually error prone because

1605
01:04:25,829 --> 01:04:23,359
they use low fidelity enzymes

1606
01:04:28,950 --> 01:04:25,839
whereas here you've got dna viruses

1607
01:04:31,190 --> 01:04:28,960
which are using host dna polymerases yet

1608
01:04:33,109 --> 01:04:31,200
they have such high mutation rates or

1609
01:04:34,870 --> 01:04:33,119
substitution rates so that's kind of

1610
01:04:37,270 --> 01:04:34,880
something that's really been

1611
01:04:39,750 --> 01:04:37,280
hugging a whole group of us

1612
01:04:41,510 --> 01:04:39,760
so now let's start dwelling into small

1613
01:04:43,829 --> 01:04:41,520

groups of viruses and take you through a

1614

01:04:46,150 --> 01:04:43,839

journey of what we've been discovering

1615

01:04:47,670 --> 01:04:46,160

in the single-stranded dna virus field

1616

01:04:49,510 --> 01:04:47,680

and so there are these viruses called

1617

01:04:51,589 --> 01:04:49,520

gemini viruses that infect plants and

1618

01:04:53,829 --> 01:04:51,599

they're unique in the sense that if you

1619

01:04:55,349 --> 01:04:53,839

look at the topology of the genomes even

1620

01:04:57,750 --> 01:04:55,359

though they're single stranded they

1621

01:04:59,510 --> 01:04:57,760

bi-directionally transcribe so that

1622

01:05:02,470 --> 01:04:59,520

means the complementary sense is

1623

01:05:04,870 --> 01:05:02,480

required to transcribe some of

1624

01:05:07,190 --> 01:05:04,880

the open reading frames but at the most

1625

01:05:09,430 --> 01:05:07,200

they encode about five

1626

01:05:11,910 --> 01:05:09,440

to six uh proteins

1627

01:05:13,829 --> 01:05:11,920

but within this group at the top right

1628

01:05:16,069 --> 01:05:13,839

and uh left-hand side you can see there

1629

01:05:17,990 --> 01:05:16,079

are some things called bengoma viruses

1630

01:05:19,670 --> 01:05:18,000

and they can assume two conformations in

1631

01:05:21,270 --> 01:05:19,680

the sense they can be monopartite or

1632

01:05:23,510 --> 01:05:21,280

both bioptych but they have two

1633

01:05:26,309 --> 01:05:23,520

different molecules which are roughly

1634

01:05:28,150 --> 01:05:26,319

the same size about 2.7 kb get packaged

1635

01:05:29,990 --> 01:05:28,160

into individual variants and they have

1636

01:05:31,829 --> 01:05:30,000

to work together

1637

01:05:33,430 --> 01:05:31,839

but when we start unpacking these things

1638

01:05:34,870 --> 01:05:33,440

and we look at the two main prominent

1639

01:05:37,029 --> 01:05:34,880

proteins that they encode which is the

1640

01:05:39,190 --> 01:05:37,039

replicationist initiative protein and

1641

01:05:41,670 --> 01:05:39,200

the capsid protein and we in further

1642

01:05:44,069 --> 01:05:41,680

phylogenies we notice that in a vast

1643

01:05:46,309 --> 01:05:44,079

number of cases those phylogenys are not

1644

01:05:48,630 --> 01:05:46,319

congruent and that straightaway tells us

1645

01:05:51,029 --> 01:05:48,640

that these viruses are very recombinant

1646

01:05:53,349 --> 01:05:51,039

in nature they recombine very

1647

01:05:55,270 --> 01:05:53,359

commonly and evolve through mechanisms

1648

01:05:56,950 --> 01:05:55,280

of recombination

1649

01:05:59,109 --> 01:05:56,960

so at one point we thought okay let's

1650

01:06:01,670 --> 01:05:59,119

study mechanisms of recombination in

1651
01:06:03,270 --> 01:06:01,680
these viruses so if you start looking at

1652
01:06:04,789 --> 01:06:03,280
viruses in general and you want to study

1653
01:06:07,430 --> 01:06:04,799
recombination

1654
01:06:09,270 --> 01:06:07,440
there are basic hypothetical things that

1655
01:06:11,190 --> 01:06:09,280
you can put forward you take two genomes

1656
01:06:13,670 --> 01:06:11,200
that are say ten percent batteries from

1657
01:06:16,390 --> 01:06:13,680
each other at a nucleotide level chop

1658
01:06:18,789 --> 01:06:16,400
them in half make reciprocal chimeras

1659
01:06:20,470 --> 01:06:18,799
and put them into a system into host

1660
01:06:22,150 --> 01:06:20,480
and your outcomes can be a simple

1661
01:06:24,549 --> 01:06:22,160
recombinant which is a two breakpoint

1662
01:06:26,069 --> 01:06:24,559
recombinant where a small piece inserts

1663
01:06:27,349 --> 01:06:26,079

or you can have complex recombinants

1664

01:06:29,190 --> 01:06:27,359

where you have lots and lots of

1665

01:06:30,150 --> 01:06:29,200

recombination events so you get a mosaic

1666

01:06:32,870 --> 01:06:30,160

pattern

1667

01:06:34,789 --> 01:06:32,880

across the genome on the other side you

1668

01:06:36,710 --> 01:06:34,799

can also have unique sub genomic

1669

01:06:39,349 --> 01:06:36,720

elements where you get deletion and

1670

01:06:41,670 --> 01:06:39,359

insertion of unknown sequences in most

1671

01:06:43,670 --> 01:06:41,680

cases could be even host nucleic acid

1672

01:06:45,190 --> 01:06:43,680

that gets integrated

1673

01:06:46,950 --> 01:06:45,200

and when you analyze all of these

1674

01:06:48,870 --> 01:06:46,960

genomes there are going to be fitness

1675

01:06:51,589 --> 01:06:48,880

tradeoffs and you can measure fitness

1676

01:06:54,470 --> 01:06:51,599

tradeoffs which genomes are

1677

01:06:56,069 --> 01:06:54,480

beneficial which ones are not so we set

1678

01:06:58,230 --> 01:06:56,079

an experiment together where we thought

1679

01:07:00,630 --> 01:06:58,240

okay let's take two viruses these are

1680

01:07:01,589 --> 01:07:00,640

two brass infecting viruses and mazes

1681

01:07:03,349 --> 01:07:01,599

across

1682

01:07:05,670 --> 01:07:03,359

and we found these in africa there were

1683

01:07:07,349 --> 01:07:05,680

a problem with within the industry so we

1684

01:07:09,750 --> 01:07:07,359

were working with this

1685

01:07:10,870 --> 01:07:09,760

and we took two viruses that were 10

1686

01:07:13,190 --> 01:07:10,880

different from each other at the

1687

01:07:14,710 --> 01:07:13,200

nucleotide level we chopped them in half

1688

01:07:16,630 --> 01:07:14,720

give the other half to the other

1689

01:07:17,829 --> 01:07:16,640

individual make right make reciprocal

1690

01:07:19,349 --> 01:07:17,839

primeras

1691

01:07:20,870 --> 01:07:19,359

and then we put them back into a maze

1692

01:07:23,029 --> 01:07:20,880

genotype

1693

01:07:25,990 --> 01:07:23,039

and the viruses were able to recombine

1694

01:07:28,710 --> 01:07:26,000

and find an optimal solution

1695

01:07:30,710 --> 01:07:28,720

which is found in nature today

1696

01:07:33,190 --> 01:07:30,720

within 30 days

1697

01:07:36,630 --> 01:07:33,200

so they were able to explore 10 sequence

1698

01:07:38,390 --> 01:07:36,640

diversity in 30 days and get to

1699

01:07:40,390 --> 01:07:38,400

where they needed to be and what is

1700

01:07:42,870 --> 01:07:40,400

present in nature today

1701

01:07:45,190 --> 01:07:42,880

as an optimal solution in 10 days

1702

01:07:46,069 --> 01:07:45,200

and if you change the variety of main so

1703

01:07:47,670 --> 01:07:46,079

basically

1704

01:07:49,750 --> 01:07:47,680

you've got some sort of genetic traits

1705

01:07:51,910 --> 01:07:49,760

that we embed into this selective

1706

01:07:54,789 --> 01:07:51,920

breeding what you notice is that the

1707

01:07:56,470 --> 01:07:54,799

maize plants are very very sensitive to

1708

01:07:59,190 --> 01:07:56,480

these kind of things so they have low

1709

01:08:01,029 --> 01:07:59,200

tolerance to the virus very susceptible

1710

01:08:03,510 --> 01:08:01,039

the viruses seem to be exploring a bit

1711

01:08:05,990 --> 01:08:03,520

of sequence space but still aggregating

1712

01:08:08,549 --> 01:08:06,000

to an area which is very very common

1713

01:08:09,990 --> 01:08:08,559

down here which is immediate solution

1714

01:08:11,910 --> 01:08:10,000

but if you put it into a resistant

1715

01:08:13,510 --> 01:08:11,920

variety pretty much everything goes to

1716

01:08:16,550 --> 01:08:13,520

that one solution that is required in

1717

01:08:18,390 --> 01:08:16,560

nature so this is very staggering that

1718

01:08:20,870 --> 01:08:18,400

in nature this evolution experiment has

1719

01:08:23,590 --> 01:08:20,880

taken place over 250 years

1720

01:08:24,950 --> 01:08:23,600

we've done it in 30 days in latin

1721

01:08:27,189 --> 01:08:24,960

experiment

1722

01:08:28,709 --> 01:08:27,199

but also we noticed there is some level

1723

01:08:31,030 --> 01:08:28,719

of genome plasticity within these

1724

01:08:33,590 --> 01:08:31,040

molecules these viruses so here is an

1725

01:08:34,870 --> 01:08:33,600

example of a gemini viruses myopathic

1726

01:08:36,470 --> 01:08:34,880

and you will notice that we've been

1727

01:08:38,550 --> 01:08:36,480

discovering these groups of viruses

1728

01:08:40,789 --> 01:08:38,560

where this entire segment has been

1729

01:08:43,110 --> 01:08:40,799

incorporated into this molecule to

1730

01:08:45,669 --> 01:08:43,120

generate a larger molecule and still in

1731

01:08:47,430 --> 01:08:45,679

expanse so one thing that we can't

1732

01:08:48,630 --> 01:08:47,440

figure out is whether this is an

1733

01:08:49,510 --> 01:08:48,640

acquisition

1734

01:08:51,269 --> 01:08:49,520

or

1735

01:08:53,749 --> 01:08:51,279

these molecules have been derived from a

1736

01:08:56,149 --> 01:08:53,759

deletion of assignment and that's how

1737

01:08:58,229 --> 01:08:56,159

these viruses evolve so there is a

1738

01:09:00,149 --> 01:08:58,239

variety of different things

1739

01:09:02,470 --> 01:09:00,159

and so within this context how do you

1740

01:09:03,590 --> 01:09:02,480

start pairing these molecules together

1741

01:09:06,229 --> 01:09:03,600

like

1742

01:09:07,669 --> 01:09:06,239

is this and this totally related we can

1743

01:09:09,910 --> 01:09:07,679

do that by there are these common

1744

01:09:11,910 --> 01:09:09,920

regions we can look at them and because

1745

01:09:13,829 --> 01:09:11,920

one is required to replicate the other

1746

01:09:15,829 --> 01:09:13,839

we're able to do this

1747

01:09:17,349 --> 01:09:15,839

but it's also very complicated so we're

1748

01:09:19,749 --> 01:09:17,359

trying to come up with new methods to

1749

01:09:21,430 --> 01:09:19,759

understand how we can put these pairings

1750

01:09:22,950 --> 01:09:21,440

together and some of them are based on

1751

01:09:24,630 --> 01:09:22,960

network analysis

1752

01:09:27,110 --> 01:09:24,640

but when we even start looking at

1753

01:09:28,630 --> 01:09:27,120

phylogenies of these spared molecules

1754

01:09:30,550 --> 01:09:28,640

there isn't any congruence they're

1755

01:09:32,630 --> 01:09:30,560

pretty much exchanging

1756

01:09:33,749 --> 01:09:32,640

uh or trading with each other very

1757

01:09:35,269 --> 01:09:33,759

openly

1758

01:09:36,789 --> 01:09:35,279

so that leads me to another group of

1759

01:09:39,030 --> 01:09:36,799

viruses which i think are very very

1760

01:09:41,349 --> 01:09:39,040

important because these are the

1761

01:09:43,269 --> 01:09:41,359

multi-component viruses again infecting

1762

01:09:45,990 --> 01:09:43,279

plants but we're discovering similar

1763

01:09:48,630 --> 01:09:46,000

viruses in eukaryotic systems

1764

01:09:50,870 --> 01:09:48,640

and these molecules are six to eight

1765

01:09:53,669 --> 01:09:50,880

molecules each one gets packaged into an

1766

01:09:56,470 --> 01:09:53,679

individual variant and each one encodes

1767

01:09:57,910 --> 01:09:56,480

one single protein so in this case here

1768

01:10:00,149 --> 01:09:57,920

at the top there is a protein that

1769

01:10:02,149 --> 01:10:00,159

initiates replication replicates all

1770

01:10:03,669 --> 01:10:02,159

these molecules here is the molecule

1771

01:10:05,590 --> 01:10:03,679

that encodes the capsid protein that

1772

01:10:07,830 --> 01:10:05,600

needs to encapsulate all of these so you

1773

01:10:09,430 --> 01:10:07,840

can imagine the shear dynamics of these

1774

01:10:10,790 --> 01:10:09,440

molecules having to interact with each

1775

01:10:12,870 --> 01:10:10,800

other other

1776

01:10:14,630 --> 01:10:12,880

and inside a cell system also the

1777

01:10:16,790 --> 01:10:14,640

delivery is also important because at

1778

01:10:18,870 --> 01:10:16,800

some point within a host you need to get

1779

01:10:20,709 --> 01:10:18,880

all of these into a

1780

01:10:22,790 --> 01:10:20,719

system so they can all cooperate and

1781

01:10:24,550 --> 01:10:22,800

produce progeny

1782

01:10:26,470 --> 01:10:24,560

so we started studying them in greater

1783

01:10:28,070 --> 01:10:26,480

detail and we started noticing that they

1784

01:10:29,910 --> 01:10:28,080

were reassuring

1785

01:10:31,510 --> 01:10:29,920

very much like influenza viruses they're

1786

01:10:34,550 --> 01:10:31,520

able to trade

1787

01:10:37,110 --> 01:10:34,560

molecules between each other very openly

1788

01:10:38,950 --> 01:10:37,120

and what was really staggering is that

1789

01:10:41,270 --> 01:10:38,960

when we look at individual molecules

1790

01:10:42,550 --> 01:10:41,280

between themselves they were recombining

1791

01:10:44,070 --> 01:10:42,560

very rapidly

1792

01:10:45,350 --> 01:10:44,080

we take these molecules they're all

1793

01:10:47,189 --> 01:10:45,360

different

1794

01:10:49,270 --> 01:10:47,199

we analyze them for recombination and

1795

01:10:50,709 --> 01:10:49,280

they're also recombining

1796

01:10:52,630 --> 01:10:50,719

in these common regions so they're

1797

01:10:54,630 --> 01:10:52,640

actually exploring sequence space at a

1798

01:10:56,310 --> 01:10:54,640

completely different league which is

1799

01:10:59,590 --> 01:10:56,320

really fascinating in the sense that

1800

01:11:01,590 --> 01:10:59,600

these viruses are just like

1801

01:11:03,590 --> 01:11:01,600

viruses around red bull and acid and

1802

01:11:04,630 --> 01:11:03,600

they just stop there to explore sequence

1803

01:11:06,390 --> 01:11:04,640

space and they're going to do it no

1804

01:11:08,390 --> 01:11:06,400

matter what

1805

01:11:11,270 --> 01:11:08,400

so the other thing that we were always

1806

01:11:13,830 --> 01:11:11,280

fascinated by is why are these viruses

1807

01:11:16,070 --> 01:11:13,840

single stranded because single-stranded

1808

01:11:17,830 --> 01:11:16,080

nucleic acid is not stable double-strand

1809

01:11:19,590 --> 01:11:17,840

and nucleic acid is stable

1810

01:11:21,350 --> 01:11:19,600

so we assumed that they would be forming

1811

01:11:23,350 --> 01:11:21,360

complex secondary structures within the

1812

01:11:24,630 --> 01:11:23,360

genomic elements when they're packaged

1813

01:11:27,590 --> 01:11:24,640

into genomes

1814

01:11:29,510 --> 01:11:27,600

so we took all we analyzed all the

1815

01:11:32,630 --> 01:11:29,520

sequences of single-stranded dna viruses

1816

01:11:34,709 --> 01:11:32,640

that were available in public databases

1817

01:11:36,790 --> 01:11:34,719

did folding analysis so basically in

1818

01:11:38,830 --> 01:11:36,800

sync analysis of folding and tried to

1819

01:11:41,189 --> 01:11:38,840

look for paired sites that we saw very

1820

01:11:43,030 --> 01:11:41,199

commonly and when we start looking at

1821

01:11:45,430 --> 01:11:43,040

these paired sites in

1822

01:11:47,510 --> 01:11:45,440

our in silico folding experiments what

1823

01:11:49,189 --> 01:11:47,520

we noticed is that purifying selection

1824

01:11:51,669 --> 01:11:49,199

is strongest at websites which is not

1825

01:11:53,590 --> 01:11:51,679

surprising we also notice synonymous

1826

01:11:56,470 --> 01:11:53,600

substitution rates are low at paid

1827

01:11:58,630 --> 01:11:56,480

genomic size not surprisingly

1828

01:12:00,790 --> 01:11:58,640

in our evolution experiments we notice

1829

01:12:03,350 --> 01:12:00,800

that mutations tend to accumulate in

1830

01:12:05,750 --> 01:12:03,360

unpaid sites makes sense now

1831

01:12:09,910 --> 01:12:05,760

but what was staggering is that we saw

1832

01:12:12,870 --> 01:12:09,920

evidence of complementarity of uh to

1833

01:12:13,470 --> 01:12:12,880

evolve base pairs so there is some sort

1834

01:12:15,510 --> 01:12:13,480

of

1835

01:12:18,229 --> 01:12:15,520

complementarity involved in it that if

1836

01:12:19,590 --> 01:12:18,239

one with one nucleotide here in a base

1837

01:12:21,910 --> 01:12:19,600

paired region

1838

01:12:23,669 --> 01:12:21,920

uh it mutates there is a compensatory

1839

01:12:25,189 --> 01:12:23,679

mutation that takes place to retain that

1840

01:12:27,350 --> 01:12:25,199

particular structure

1841

01:12:29,510 --> 01:12:27,360

so we started noticing that

1842

01:12:31,350 --> 01:12:29,520

these single-stranded genomes fall into

1843

01:12:33,189 --> 01:12:31,360

complex sacrifice structures those

1844

01:12:35,189 --> 01:12:33,199

complex secondary structures

1845

01:12:37,430 --> 01:12:35,199

are very unique that there is some sort

1846

01:12:38,709 --> 01:12:37,440

of co-evolution taking place of paid

1847

01:12:40,149 --> 01:12:38,719

sites

1848

01:12:41,910 --> 01:12:40,159

and so this had never been shown and

1849

01:12:43,990 --> 01:12:41,920

this was kind of really interesting and

1850

01:12:45,510 --> 01:12:44,000

this also suggests that the secondary

1851

01:12:46,709 --> 01:12:45,520

structure is highly likely very

1852

01:12:49,189 --> 01:12:46,719

important

1853

01:12:51,189 --> 01:12:49,199

for either regulatory mechanisms or

1854

01:12:54,870 --> 01:12:51,199

maintaining some sort of genomic

1855

01:12:56,310 --> 01:12:54,880

integrity within capsid proteins

1856

01:12:58,550 --> 01:12:56,320

and now i'm going to take you away from

1857

01:13:00,390 --> 01:12:58,560

the plant side of things and go into

1858

01:13:03,590 --> 01:13:00,400

area which i think is interesting

1859

01:13:06,149 --> 01:13:03,600

because it involves human activities

1860

01:13:08,470 --> 01:13:06,159

and here is a virus that i've worked

1861

01:13:09,430 --> 01:13:08,480

extensively with it's virus that infects

1862

01:13:13,669 --> 01:13:09,440

parrots

1863

01:13:15,990 --> 01:13:13,679

again a single-spreaded dna virus and

1864

01:13:19,350 --> 01:13:16,000

puts only two proteins it's about two

1865

01:13:21,350 --> 01:13:19,360

kilobase in size but it actually

1866

01:13:23,590 --> 01:13:21,360

induces physiological changes in an

1867

01:13:25,750 --> 01:13:23,600

animal it suppresses its immune system

1868

01:13:29,030 --> 01:13:25,760

the animal's response in a lot of ways

1869

01:13:31,189 --> 01:13:29,040

is feather loss anemia in severe cases

1870

01:13:33,270 --> 01:13:31,199

like this one here there's a sulphur

1871

01:13:35,990 --> 01:13:33,280

crested cockatoo that has pretty much

1872

01:13:38,310 --> 01:13:36,000

lost most of its feathers as well as its

1873

01:13:39,910 --> 01:13:38,320

beak and you know you have to give it to

1874

01:13:41,990 --> 01:13:39,920

the australians for writing beautiful

1875

01:13:43,590 --> 01:13:42,000

obituaries about the birds and this is

1876

01:13:46,310 --> 01:13:43,600

cocky bennett that traveled around the

1877

01:13:49,590 --> 01:13:46,320

world died at the age of roughly 120

1878

01:13:52,070 --> 01:13:49,600

years so parents do live that long

1879

01:13:54,149 --> 01:13:52,080

and spent the last 20 years in a pub and

1880

01:13:56,870 --> 01:13:54,159

that's what it looked like

1881

01:13:58,790 --> 01:13:56,880

and so the phylogenetic tree on the

1882

01:14:00,470 --> 01:13:58,800

right hand side kind of suggests some

1883

01:14:02,870 --> 01:14:00,480

very very unique things

1884

01:14:05,270 --> 01:14:02,880

that here what you have is some sort of

1885

01:14:08,149 --> 01:14:05,280

a pet trade system taking place that are

1886

01:14:10,870 --> 01:14:08,159

breeding facilities from which there are

1887

01:14:12,950 --> 01:14:10,880

pushing some of the

1888

01:14:14,950 --> 01:14:12,960

legal and illegal trafficking of animals

1889

01:14:17,350 --> 01:14:14,960

to different zones and then what you're

1890

01:14:19,590 --> 01:14:17,360

getting is establishment of new viruses

1891

01:14:20,630 --> 01:14:19,600

and new ecosystems that haven't been

1892

01:14:21,990 --> 01:14:20,640

before

1893

01:14:24,070 --> 01:14:22,000

and we've analyzed some of the

1894

01:14:25,990 --> 01:14:24,080

facilities in poland for example we've

1895

01:14:27,910 --> 01:14:26,000

worked with veterinarians there to look

1896

01:14:29,830 --> 01:14:27,920

at recombination beds in some of these

1897

01:14:31,590 --> 01:14:29,840

facilities and a variety of different

1898

01:14:33,270 --> 01:14:31,600

carrots they come in from different

1899

01:14:35,750 --> 01:14:33,280

parts of the world they're brought into

1900

01:14:37,750 --> 01:14:35,760

these aviaries the animals are stressed

1901

01:14:39,510 --> 01:14:37,760

and before unite

1902

01:14:41,750 --> 01:14:39,520

the virus is just circulating and being

1903

01:14:43,910 --> 01:14:41,760

exchanged and here we've got a genome of

1904

01:14:45,990 --> 01:14:43,920

the virus that is more than two-thirds

1905

01:14:48,630 --> 01:14:46,000

of recombinant that we identify in these

1906

01:14:50,390 --> 01:14:48,640

kind of systems so these legal and

1907

01:14:52,790 --> 01:14:50,400

illegal trade systems are also

1908

01:14:55,270 --> 01:14:52,800

facilitating the spread of these viruses

1909

01:14:56,550 --> 01:14:55,280

and evolution of these viruses at a much

1910

01:14:58,229 --> 01:14:56,560

rapid rate than people have thought

1911

01:14:59,990 --> 01:14:58,239

before

1912

01:15:01,590 --> 01:15:00,000

and now we go into genomics kind of

1913

01:15:03,270 --> 01:15:01,600

systems and we start realizing that

1914

01:15:05,350 --> 01:15:03,280

actually we know very little about

1915

01:15:07,030 --> 01:15:05,360

cellular standard dna viruses because

1916

01:15:09,430 --> 01:15:07,040

through metagenomic approaches we just

1917

01:15:11,510 --> 01:15:09,440

keep finding viruses a lot of which we

1918

01:15:13,110 --> 01:15:11,520

don't even know the hosts for and here's

1919

01:15:15,110 --> 01:15:13,120

a big group of viruses that we've

1920

01:15:17,030 --> 01:15:15,120

recently established as a family level

1921

01:15:19,270 --> 01:15:17,040

structure however

1922

01:15:21,669 --> 01:15:19,280

these viruses the first group of them

1923

01:15:24,070 --> 01:15:21,679

were found to infect fungi induce

1924

01:15:26,390 --> 01:15:24,080

hypovirulence but we find them in pretty

1925

01:15:28,070 --> 01:15:26,400

much all different systems you can see

1926

01:15:30,149 --> 01:15:28,080

all the different kind of

1927

01:15:32,390 --> 01:15:30,159

sample types that have been identified

1928

01:15:33,990 --> 01:15:32,400

and they've got a huge diversity and so

1929

01:15:35,430 --> 01:15:34,000

these things are really abundant in

1930

01:15:37,350 --> 01:15:35,440

nature

1931

01:15:39,669 --> 01:15:37,360

but what is staggering again about them

1932

01:15:41,990 --> 01:15:39,679

is that they encourage two proteins and

1933

01:15:43,350 --> 01:15:42,000

we try to draw the phylogenesis of the

1934

01:15:45,750 --> 01:15:43,360

capsid protein and the replication

1935

01:15:48,310 --> 01:15:45,760

initiated proteins and not congruent at

1936

01:15:50,070 --> 01:15:48,320

all these are highly recombinant viruses

1937

01:15:51,030 --> 01:15:50,080

that are present

1938

01:15:53,510 --> 01:15:51,040

but

1939

01:15:55,110 --> 01:15:53,520

we find related viruses in nature and

1940

01:15:57,990 --> 01:15:55,120

here is something we found in an ice

1941

01:16:00,790 --> 01:15:58,000

core this is kind of work from uh terry

1942

01:16:03,430 --> 01:16:00,800

young and eric kellwood's group that i

1943

01:16:05,669 --> 01:16:03,440

was involved with and it might roughly

1944

01:16:08,709 --> 01:16:05,679

just short of 200 meters left in an ice

1945

01:16:09,990 --> 01:16:08,719

core they identified the virus and

1946

01:16:12,470 --> 01:16:10,000

we kind of worked together to try and

1947

01:16:13,990 --> 01:16:12,480

figure out what the virus was and then

1948

01:16:15,270 --> 01:16:14,000

we looked at it and thought wow this

1949

01:16:17,030 --> 01:16:15,280

looks very very similar to a

1950

01:16:18,630 --> 01:16:17,040

plant-infected virus in terms of its

1951

01:16:21,910 --> 01:16:18,640

genomic elements

1952

01:16:23,990 --> 01:16:21,920

so with bob gilbertson at uc davis we

1953

01:16:25,270 --> 01:16:24,000

generated an infectious clone put it

1954

01:16:27,350 --> 01:16:25,280

into plants

1955

01:16:29,990 --> 01:16:27,360

and lo and behold this virus was able to

1956

01:16:32,310 --> 01:16:30,000

replicate and spread but we dated this

1957

01:16:34,870 --> 01:16:32,320

layer and was dated at about 700 years

1958

01:16:37,189 --> 01:16:34,880

old so we resurrected a virus that was

1959

01:16:39,189 --> 01:16:37,199

700 years old through reverse genetics

1960

01:16:41,270 --> 01:16:39,199

so this also suggests and should be a

1961

01:16:43,590 --> 01:16:41,280

quotient for us that

1962

01:16:45,189 --> 01:16:43,600

the climate change impacts are real in

1963

01:16:47,510 --> 01:16:45,199

the sense that we're melting permafrost

1964

01:16:49,350 --> 01:16:47,520

at a very very rapid rate and so there

1965

01:16:50,470 --> 01:16:49,360

are pathogens and organisms that are

1966

01:16:53,030 --> 01:16:50,480

trapped

1967

01:16:55,510 --> 01:16:53,040

in these ecosystems that are now being

1968

01:16:57,350 --> 01:16:55,520

uh released into environments and some

1969

01:16:59,030 --> 01:16:57,360

of these environments haven't dealt with

1970

01:17:00,390 --> 01:16:59,040

these these

1971

01:17:03,030 --> 01:17:00,400

organisms and so what are the

1972

01:17:05,590 --> 01:17:03,040

consequences going to be in future for

1973

01:17:08,310 --> 01:17:05,600

either uh displacing certain organisms

1974

01:17:09,830 --> 01:17:08,320

out of these ecosystems as these uh

1975

01:17:11,030 --> 01:17:09,840

permafrost layers

1976

01:17:13,350 --> 01:17:11,040

go

1977

01:17:15,350 --> 01:17:13,360

so if we take back a bigger picture and

1978

01:17:17,189 --> 01:17:15,360

go back a few steps and look right riots

1979

01:17:19,030 --> 01:17:17,199

we know all of these viruses

1980

01:17:21,189 --> 01:17:19,040

single-splinted viruses that encode the

1981

01:17:23,270 --> 01:17:21,199

replication initiative protein have

1982

01:17:25,830 --> 01:17:23,280

these two motifs but some of these

1983

01:17:28,630 --> 01:17:25,840

motifs we also identify in fungal

1984

01:17:29,430 --> 01:17:28,640

elements sorry in plasmids

1985

01:17:31,430 --> 01:17:29,440

and

1986

01:17:33,110 --> 01:17:31,440

so we can start building network like

1987

01:17:34,870 --> 01:17:33,120

analysis and if you just take the

1988

01:17:36,630 --> 01:17:34,880

helicase domain and we know helicase

1989

01:17:38,390 --> 01:17:36,640

domains are present in a lot of

1990

01:17:40,630 --> 01:17:38,400

different systems including replication

1991

01:17:42,950 --> 01:17:40,640

machinery and repair machinery we can

1992

01:17:44,630 --> 01:17:42,960

start building networks of similarity

1993

01:17:47,189 --> 01:17:44,640

and we start noticing that some of these

1994

01:17:48,950 --> 01:17:47,199

helicase domains are also found in other

1995

01:17:51,510 --> 01:17:48,960

groups of viruses which are

1996

01:17:53,750 --> 01:17:51,520

circular double-stranded dna viruses but

1997

01:17:55,189 --> 01:17:53,760

a variety of different plasmids as well

1998

01:17:57,350 --> 01:17:55,199

and from there we can start then

1999

01:17:59,430 --> 01:17:57,360

inferring concepts of where these

2000

01:18:01,990 --> 01:17:59,440

viruses have evolved from and you start

2001

01:18:03,510 --> 01:18:02,000

noticing that it's not just one system

2002

01:18:05,990 --> 01:18:03,520

there is multiple acquisition and

2003

01:18:08,310 --> 01:18:06,000

multiple events that have led to these

2004

01:18:09,910 --> 01:18:08,320

viruses evolving from each other and if

2005

01:18:12,229 --> 01:18:09,920

you look at it at a much more broader

2006

01:18:13,910 --> 01:18:12,239

perspective we start noticing that some

2007

01:18:15,669 --> 01:18:13,920

of these viruses

2008

01:18:18,550 --> 01:18:15,679

haven't just evolved in a one clear

2009

01:18:20,470 --> 01:18:18,560

lineage process there have been multiple

2010

01:18:23,110 --> 01:18:20,480

evolution processes from plasmids and

2011

01:18:26,070 --> 01:18:23,120

plasmid like ancestral sequences that

2012

01:18:29,189 --> 01:18:26,080

have led to emergence or evolution of

2013

01:18:31,350 --> 01:18:29,199

these viruses in nature

2014

01:18:32,630 --> 01:18:31,360

and then what you can start doing is

2015

01:18:34,790 --> 01:18:32,640

this is something that i've been

2016

01:18:36,870 --> 01:18:34,800

fascinated with is that viruses all have

2017

01:18:38,390 --> 01:18:36,880

capsule proteins the capsid proteins are

2018

01:18:40,550 --> 01:18:38,400

very important because they recognize

2019

01:18:41,430 --> 01:18:40,560

certain particular receptors to get into

2020

01:18:43,590 --> 01:18:41,440

cells

2021

01:18:45,350 --> 01:18:43,600

now

2022

01:18:47,110 --> 01:18:45,360

can and a variety of other people have

2023

01:18:48,630 --> 01:18:47,120

found that there are certain viruses

2024

01:18:51,110 --> 01:18:48,640

single-stranded hernia viruses that

2025

01:18:53,510 --> 01:18:51,120

encode capsid proteins that are much

2026

01:18:55,590 --> 01:18:53,520

more closely related to viruses

2027

01:18:58,550 --> 01:18:55,600

which are rna viruses that have similar

2028

01:19:00,870 --> 01:18:58,560

capsid proteins so here is an example is

2029

01:19:03,030 --> 01:19:00,880

chongus viruses are rna viruses their

2030

01:19:04,229 --> 01:19:03,040

capsid proteins are very similar to some

2031

01:19:06,390 --> 01:19:04,239

of the capsular proteins that are

2032

01:19:08,310 --> 01:19:06,400

encoded by single-stranded dna viruses

2033

01:19:10,470 --> 01:19:08,320

so where has this chimeric acquisition

2034

01:19:12,390 --> 01:19:10,480

taken place at a cdna level at some

2035

01:19:14,149 --> 01:19:12,400

point so these viruses

2036

01:19:16,790 --> 01:19:14,159

have some sort of a

2037

01:19:19,110 --> 01:19:16,800

proxy in terms of capsid fault space and

2038

01:19:21,430 --> 01:19:19,120

i think capsid fault space and mark

2039

01:19:23,590 --> 01:19:21,440

cuprof is a big proponent of this is

2040

01:19:25,830 --> 01:19:23,600

that capsid false space is limited and

2041

01:19:27,590 --> 01:19:25,840

as a consequence of it

2042

01:19:29,990 --> 01:19:27,600

is that there's only so much fault space

2043

01:19:32,310 --> 01:19:30,000

you can have at a protein capsid level

2044

01:19:33,910 --> 01:19:32,320

and some of these viruses are then

2045

01:19:35,430 --> 01:19:33,920

acquiring these

2046

01:19:37,590 --> 01:19:35,440

capsid like molecules from different

2047

01:19:39,270 --> 01:19:37,600

areas and so here are all the gemini

2048

01:19:41,110 --> 01:19:39,280

virus captured proteins that we know

2049

01:19:44,149 --> 01:19:41,120

about and what is interesting about

2050

01:19:46,070 --> 01:19:44,159

these is they actually have

2051

01:19:48,550 --> 01:19:46,080

a capsid fold

2052

01:19:49,990 --> 01:19:48,560

which is very similar to that of an rna

2053

01:19:52,310 --> 01:19:50,000

virus which is satellite tobacco

2054

01:19:53,350 --> 01:19:52,320

necrotic virus and you can see the vast

2055

01:19:55,669 --> 01:19:53,360

number of

2056

01:19:57,990 --> 01:19:55,679

unclassified circular dna viruses that

2057

01:19:59,910 --> 01:19:58,000

have this fold as well when you start

2058

01:20:01,750 --> 01:19:59,920

looking at network analysis so these

2059

01:20:04,310 --> 01:20:01,760

network analysis are becoming very very

2060

01:20:06,709 --> 01:20:04,320

important in the way we understand and

2061

01:20:09,189 --> 01:20:06,719

so yes complemented with phylogenetic

2062

01:20:11,270 --> 01:20:09,199

trees these are very very good ways of

2063

01:20:14,229 --> 01:20:11,280

pulling down

2064

01:20:16,830 --> 01:20:14,239

related sequences and understanding

2065

01:20:19,270 --> 01:20:16,840

more broader concepts of viral

2066

01:20:22,149 --> 01:20:19,280

evolution and so i want to kind of start

2067

01:20:23,990 --> 01:20:22,159

ending this with a bigger concept and

2068

01:20:25,590 --> 01:20:24,000

this is that if you look at

2069

01:20:27,510 --> 01:20:25,600

phallogenetic tree on the right hand

2070

01:20:29,430 --> 01:20:27,520

side you notice these are all single

2071

01:20:31,350 --> 01:20:29,440

stranded dna viruses and called

2072

01:20:33,590 --> 01:20:31,360

replication associated or initiative

2073

01:20:36,550 --> 01:20:33,600

proteins and the ones that are well

2074

01:20:39,510 --> 01:20:36,560

classified are in these little triangles

2075

01:20:41,110 --> 01:20:39,520

lapse branches uh labeled here

2076

01:20:43,669 --> 01:20:41,120

everything else that's on this

2077

01:20:46,229 --> 01:20:43,679

illustration here are texture that we've

2078

01:20:48,550 --> 01:20:46,239

identified in our research group now

2079

01:20:50,149 --> 01:20:48,560

everything that is in red is what we

2080

01:20:52,709 --> 01:20:50,159

have identified

2081

01:20:54,229 --> 01:20:52,719

right uh in the entire ecosystems

2082

01:20:57,030 --> 01:20:54,239

so to me

2083

01:20:58,950 --> 01:20:57,040

if i were to draw a plot of viruses that

2084

01:21:00,790 --> 01:20:58,960

exist on this planet in terms of what we

2085

01:21:02,950 --> 01:21:00,800

know about them today they would be

2086

01:21:05,430 --> 01:21:02,960

scattered on this plot on a 10 by 10

2087

01:21:07,270 --> 01:21:05,440

grid in various different places and if

2088

01:21:09,189 --> 01:21:07,280

i was to sum that up in terms of where

2089

01:21:11,830 --> 01:21:09,199

our current knowledge is it would be

2090

01:21:14,149 --> 01:21:11,840

less than one percent of all the viruses

2091

01:21:15,189 --> 01:21:14,159

we know on the planet so that means we

2092

01:21:17,270 --> 01:21:15,199

have

2093

01:21:19,510 --> 01:21:17,280

a lot of work to do in terms of if we

2094

01:21:22,709 --> 01:21:19,520

really want to understand virology

2095

01:21:25,510 --> 01:21:22,719

we're far from it we've only had a huge

2096

01:21:27,830 --> 01:21:25,520

bias to viruses that cause disease and

2097

01:21:30,470 --> 01:21:27,840

viruses that cause disease in organisms

2098

01:21:32,390 --> 01:21:30,480

that we dearly care about like plants

2099

01:21:34,709 --> 01:21:32,400

animals humans

2100

01:21:36,629 --> 01:21:34,719

everything else we've just neglected

2101
01:21:38,470 --> 01:21:36,639
and also as ken mentioned we've

2102
01:21:41,110 --> 01:21:38,480
completely looked at it from a disease

2103
01:21:42,629 --> 01:21:41,120
angle never from a beneficial angle and

2104
01:21:45,270 --> 01:21:42,639
we do know that viruses are most

2105
01:21:47,350 --> 01:21:45,280
abundant entity on the planet if they're

2106
01:21:48,870 --> 01:21:47,360
so abundant

2107
01:21:50,870 --> 01:21:48,880
they should be having beneficial roles

2108
01:21:52,470 --> 01:21:50,880
in ecosystems and we do know that in

2109
01:21:54,470 --> 01:21:52,480
marine ecosystems there are very very

2110
01:21:57,830 --> 01:21:54,480
important

2111
01:21:59,430 --> 01:21:57,840
for carbon sink and at the bottom here

2112
01:22:01,189 --> 01:21:59,440
is a very very unique paper which i

2113
01:22:03,350 --> 01:22:01,199

think is great and this is part of the

2114

01:22:05,750 --> 01:22:03,360

efforts of the tara oceans project and

2115

01:22:07,430 --> 01:22:05,760

if you look at in the uh epipelagic

2116

01:22:08,709 --> 01:22:07,440

samples that the water columns that

2117

01:22:10,390 --> 01:22:08,719

they've looked at

2118

01:22:12,950 --> 01:22:10,400

they've saturated

2119

01:22:14,950 --> 01:22:12,960

the amount of viruses they can find so

2120

01:22:17,030 --> 01:22:14,960

they've got to a level that doesn't

2121

01:22:17,990 --> 01:22:17,040

matter how much at that layer they

2122

01:22:19,510 --> 01:22:18,000

sample

2123

01:22:21,669 --> 01:22:19,520

they have got

2124

01:22:23,669 --> 01:22:21,679

a very good handle of sequence space in

2125

01:22:25,830 --> 01:22:23,679

the regions they've sampled but when you

2126

01:22:28,550 --> 01:22:25,840

go into different areas they're still

2127

01:22:30,550 --> 01:22:28,560

not close to it and i think with single

2128

01:22:32,470 --> 01:22:30,560

stranded dna viruses i think we're in

2129

01:22:35,189 --> 01:22:32,480

this stage that we're not even at all

2130

01:22:36,709 --> 01:22:35,199

close to having figured out everything

2131

01:22:38,390 --> 01:22:36,719

so with that i'd like to thank all of

2132

01:22:39,990 --> 01:22:38,400

the who have been involved in a lot of

2133

01:22:42,629 --> 01:22:40,000

the work that i do that have spent for

2134

01:22:45,430 --> 01:22:42,639

the last 15 20 years and there are

2135

01:22:48,229 --> 01:22:45,440

groups of people all around the world as

2136

01:22:50,229 --> 01:22:48,239

well as a whole lot of crew that have

2137

01:22:51,189 --> 01:22:50,239

you know students in my lab and are

2138

01:22:52,629 --> 01:22:51,199

still

2139

01:23:08,790 --> 01:22:52,639

staffing my research group thank you

2140

01:23:14,310 --> 01:23:10,790

questions anyone

2141

01:23:18,070 --> 01:23:14,320

hey arvin siobhan here hi siobhan

2142

01:23:20,310 --> 01:23:18,080

so i posted this to the chat but

2143

01:23:22,149 --> 01:23:20,320

what's the real risk of these viruses

2144

01:23:24,790 --> 01:23:22,159

being in infectious capsids as the

2145

01:23:26,550 --> 01:23:24,800

permafrost thaws i would worry about

2146

01:23:29,270 --> 01:23:26,560

things like the tabama viruses because

2147

01:23:30,870 --> 01:23:29,280

those things can withstand incineration

2148

01:23:33,430 --> 01:23:30,880

and all kinds of environmental

2149

01:23:35,030 --> 01:23:33,440

challenges but should we actually worry

2150

01:23:36,229 --> 01:23:35,040

about intact

2151

01:23:37,430 --> 01:23:36,239

virions

2152

01:23:38,790 --> 01:23:37,440

that could actually be infectious from

2153

01:23:40,390 --> 01:23:38,800

permafrost are we just going to keep

2154

01:23:42,950 --> 01:23:40,400

learning about

2155

01:23:44,229 --> 01:23:42,960

what was there hundreds of years ago and

2156

01:23:46,470 --> 01:23:44,239

we could resurrect these things with

2157

01:23:47,590 --> 01:23:46,480

reverse genetics that's very very cool

2158

01:23:49,030 --> 01:23:47,600

but they're not actually going to infect

2159

01:23:51,030 --> 01:23:49,040

our plants tomorrow

2160

01:23:52,470 --> 01:23:51,040

well they could in fact so

2161

01:23:54,470 --> 01:23:52,480

look at our pollution levels on the

2162

01:23:56,070 --> 01:23:54,480

planet microplastics are pretty much

2163

01:23:58,390 --> 01:23:56,080

everywhere a lot of these viruses will

2164

01:24:00,229 --> 01:23:58,400

bind to microplastics microflaxes

2165

01:24:01,510 --> 01:24:00,239

uh they seem to get into systems we've

2166

01:24:02,790 --> 01:24:01,520

got a lot of detergents in our

2167

01:24:04,870 --> 01:24:02,800

ecosystems

2168

01:24:07,270 --> 01:24:04,880

and so detergents mean you've got

2169

01:24:09,910 --> 01:24:07,280

actually a beautiful surfactant that can

2170

01:24:11,830 --> 01:24:09,920

deliver things straight into a variety

2171

01:24:14,390 --> 01:24:11,840

of different organisms especially single

2172

01:24:16,149 --> 01:24:14,400

cell organisms and we've got vectors

2173

01:24:17,910 --> 01:24:16,159

insects that are pretty much picking up

2174

01:24:19,590 --> 01:24:17,920

a lot of this material through the

2175

01:24:21,750 --> 01:24:19,600

foraging behavior and they will be

2176

01:24:25,110 --> 01:24:21,760

taking in and injecting it so the

2177

01:24:26,070 --> 01:24:25,120

plausibility of a scenario like this is

2178

01:24:29,510 --> 01:24:26,080

there

2179

01:24:31,910 --> 01:24:29,520

the frequency or how viable they are i

2180

01:24:32,790 --> 01:24:31,920

cannot kind of speak on that

2181

01:24:45,990 --> 01:24:32,800

but

2182

01:24:48,950 --> 01:24:47,590

arvind ken here

2183

01:24:51,510 --> 01:24:48,960

yes hi ken

2184

01:24:53,350 --> 01:24:51,520

uh just a quick question in terms of the

2185

01:24:55,590 --> 01:24:53,360

astrovirology and also put this in the

2186

01:24:57,030 --> 01:24:55,600

chat is and maybe mark's the right

2187

01:24:59,110 --> 01:24:57,040

person to ask this question of but do

2188

01:25:01,430 --> 01:24:59,120

you think that if there are limited

2189

01:25:04,550 --> 01:25:01,440

numbers of folds that you can use for

2190

01:25:07,270 --> 01:25:04,560

capsids um would that potentially be a

2191

01:25:09,750 --> 01:25:07,280

way that one could think about

2192

01:25:11,189 --> 01:25:09,760

virion detection techniques that maybe

2193

01:25:13,030 --> 01:25:11,199

you could put on a spacecraft or

2194

01:25:18,070 --> 01:25:13,040

something like that

2195

01:25:22,550 --> 01:25:19,510

don't forget

2196

01:25:23,590 --> 01:25:22,560

that protein sequence space is great all

2197

01:25:25,350 --> 01:25:23,600

right

2198

01:25:27,350 --> 01:25:25,360

sorry nucleotide sequence space is very

2199

01:25:29,189 --> 01:25:27,360

great then you get into protein sequence

2200

01:25:31,270 --> 01:25:29,199

space and you get into four space so you

2201

01:25:33,830 --> 01:25:31,280

can have the same fold

2202

01:25:35,669 --> 01:25:33,840

yet you could have 30 percent diversity

2203

01:25:37,910 --> 01:25:35,679

at a nucleotide level

2204

01:25:39,830 --> 01:25:37,920

so i think our detection in this kind of

2205

01:25:41,110 --> 01:25:39,840

system is unless we have initial

2206

01:25:47,669 --> 01:25:41,120

approaches

2207

01:25:49,590 --> 01:25:47,679

detecting fault are very poor even today

2208

01:25:52,550 --> 01:25:49,600

so i think one thing that we really need

2209

01:25:55,110 --> 01:25:52,560

to do is accelerate our crystal uh

2210

01:25:57,270 --> 01:25:55,120

structure solving programs all around

2211

01:26:00,310 --> 01:25:57,280

the world to solve structures of

2212

01:26:02,550 --> 01:26:00,320

proteins and once better databases we

2213

01:26:04,470 --> 01:26:02,560

can start threading through homology

2214

01:26:06,790 --> 01:26:04,480

modeling a variety of these protein

2215

01:26:09,430 --> 01:26:06,800

structures so that is one way but there

2216

01:26:11,830 --> 01:26:09,440

is a likelihood we might be able to come

2217

01:26:13,030 --> 01:26:11,840

up with ways of using ai based

2218

01:26:15,270 --> 01:26:13,040

techniques

2219

01:26:26,149 --> 01:26:15,280

to detect certain folds that we haven't

2220

01:26:26,159 --> 01:26:31,890

anyone else

2221

01:26:34,629 --> 01:26:33,189

[Music]

2222

01:26:36,950 --> 01:26:34,639

so i think we're gonna have to shift

2223

01:26:39,510 --> 01:26:36,960

over here quickly to brit so let's thank

2224

01:26:42,790 --> 01:26:39,520

arvind for um

2225

01:26:46,310 --> 01:26:42,800

whirlwind of single-stranded dna viruses

2226

01:26:46,320 --> 01:26:50,709

okay can everybody hear me

2227

01:26:56,390 --> 01:26:53,830

yes we can hear you great all right

2228

01:27:00,950 --> 01:26:56,400

and once i get this started let me know

2229

01:27:06,310 --> 01:27:03,590

is the powerpoint up for everyone else

2230

01:27:08,149 --> 01:27:06,320

it is we can see it all right terrific

2231

01:27:09,990 --> 01:27:08,159

i must admit this is my first virtual

2232

01:27:11,270 --> 01:27:10,000

workshop like this i like it a lot and i

2233

01:27:13,189 --> 01:27:11,280

imagine that there's going to be many

2234

01:27:14,950 --> 01:27:13,199

many more of these in the future

2235

01:27:16,310 --> 01:27:14,960

as we start decreasing our carbon

2236

01:27:17,270 --> 01:27:16,320

footprint so thanks for getting this

2237

01:27:18,470 --> 01:27:17,280

going

2238

01:27:20,470 --> 01:27:18,480

um

2239

01:27:22,790 --> 01:27:20,480

so that was i'm very pleased actually to

2240

01:27:24,709 --> 01:27:22,800

be talking just after arvin because

2241

01:27:27,669 --> 01:27:24,719

i don't actually spend much time on

2242

01:27:29,750 --> 01:27:27,679

viral evolution but it's hopefully now

2243

01:27:32,470 --> 01:27:29,760

you've been suitably convinced that it

2244

01:27:34,229 --> 01:27:32,480

happens rapidly and is important and

2245

01:27:36,629 --> 01:27:34,239

over longer time skills and so what

2246

01:27:38,550 --> 01:27:36,639

instead i'm going to talk about today is

2247

01:27:40,070 --> 01:27:38,560

co-evolution and why

2248

01:27:42,709 --> 01:27:40,080

interactions between

2249

01:27:44,390 --> 01:27:42,719

viruses and in particular bacteriophages

2250

01:27:47,350 --> 01:27:44,400

are important in shaping bacterial

2251

01:27:49,669 --> 01:27:47,360

populations and communities

2252

01:27:50,870 --> 01:27:49,679

and so just to bring everybody up to the

2253

01:27:53,189 --> 01:27:50,880

same page when we're talking about

2254

01:27:54,870 --> 01:27:53,199

coevolution of course the first question

2255

01:27:57,669 --> 01:27:54,880

is co-evolution between what type of

2256

01:27:59,510 --> 01:27:57,679

phage and there are generally speaking

2257

01:28:01,669 --> 01:27:59,520

three types of phages lytic phage

2258

01:28:03,270 --> 01:28:01,679

temperate phage or filamentous phage

2259

01:28:04,470 --> 01:28:03,280

here and see i'm going to ignore the

2260

01:28:06,149 --> 01:28:04,480

filamentous phage although i think

2261

01:28:07,350 --> 01:28:06,159

they're incredibly neat

2262

01:28:09,270 --> 01:28:07,360

um

2263

01:28:11,430 --> 01:28:09,280

and focus primarily on lytic phage for

2264

01:28:12,950 --> 01:28:11,440

this talk but i don't want to ignore all

2265

01:28:15,350 --> 01:28:12,960

of the incredible diversity that

2266

01:28:16,870 --> 01:28:15,360

temperate phage introduce and so i'm

2267

01:28:18,950 --> 01:28:16,880

just going to spend a second here before

2268

01:28:21,189 --> 01:28:18,960

shifting to my own work

2269

01:28:23,910 --> 01:28:21,199

and so for thinking about the impact

2270

01:28:26,070 --> 01:28:23,920

that bacteriophages have on bacterial

2271

01:28:28,149 --> 01:28:26,080

communities and populations one of the

2272

01:28:30,070 --> 01:28:28,159

obvious ones is through direct

2273

01:28:32,390 --> 01:28:30,080

horizontal gene transfer and the genes

2274

01:28:35,350 --> 01:28:32,400

that they introduce as they themselves

2275

01:28:37,270 --> 01:28:35,360

integrate into a bacterial genome and so

2276

01:28:39,750 --> 01:28:37,280

these temperate phages when they form

2277

01:28:42,149 --> 01:28:39,760

lysogens in bacteria can completely

2278

01:28:43,910 --> 01:28:42,159

change the bacterial phenotype and one

2279

01:28:45,830 --> 01:28:43,920

of the ways that we care about this is

2280

01:28:47,990 --> 01:28:45,840

if that happens to change bacterial

2281

01:28:50,070 --> 01:28:48,000

pathogenicity for example

2282

01:28:51,990 --> 01:28:50,080

but this is just an example and of

2283

01:28:54,310 --> 01:28:52,000

course there are many different axes

2284

01:28:56,470 --> 01:28:54,320

across which phenotype can change

2285

01:28:59,110 --> 01:28:56,480

potentially including colonization of

2286

01:29:00,629 --> 01:28:59,120

spaceships for example but here this is

2287

01:29:02,310 --> 01:29:00,639

a really nice study not from my group

2288

01:29:04,709 --> 01:29:02,320

but they looked specifically at this

2289

01:29:08,390 --> 01:29:04,719

emerging opportunistic pathogen they

2290

01:29:11,830 --> 01:29:08,400

compared 795 genomes of this pathogen

2291

01:29:14,709 --> 01:29:11,840

and found over 4 000 prophages

2292

01:29:16,310 --> 01:29:14,719

let me just move this here and so

2293

01:29:18,470 --> 01:29:16,320

of those prophages and i'm just showing

2294

01:29:21,430 --> 01:29:18,480

this beautiful phylogeny they created

2295

01:29:23,910 --> 01:29:21,440

they did it with the proteome as well

2296

01:29:25,430 --> 01:29:23,920

this diversity is important in part

2297

01:29:27,590 --> 01:29:25,440

because as i already said this is

2298

01:29:29,669 --> 01:29:27,600

generating diversity in the bacterial

2299

01:29:33,430 --> 01:29:29,679

population and community as well

2300

01:29:35,350 --> 01:29:33,440

they found that 78 of the genomes had uh

2301

01:29:37,830 --> 01:29:35,360

i'm sorry of the intact prophages so

2302

01:29:39,510 --> 01:29:37,840

these are prophages that are remain

2303

01:29:41,430 --> 01:29:39,520

capable of exercising again and

2304

01:29:44,709 --> 01:29:41,440

infecting a new host

2305

01:29:46,390 --> 01:29:44,719

70 78 of them encoded potential

2306

01:29:47,590 --> 01:29:46,400

virulence genes

2307

01:29:49,270 --> 01:29:47,600

and so

2308

01:29:50,709 --> 01:29:49,280

if you want to understand pathogenicity

2309

01:29:53,669 --> 01:29:50,719

and bacterial virulence this sort of

2310

01:29:55,110 --> 01:29:53,679

argues that ignoring prophages which

2311

01:29:59,990 --> 01:29:55,120

we quite often do especially in

2312

01:30:03,830 --> 01:30:02,229

let's see here there we go

2313

01:30:05,590 --> 01:30:03,840

so if we go back here for a moment as i

2314

01:30:07,830 --> 01:30:05,600

already said most of what i'm going to

2315

01:30:09,990 --> 01:30:07,840

be discussing today is lytic phages here

2316

01:30:11,910 --> 01:30:10,000

in a and these are phages that are

2317

01:30:13,830 --> 01:30:11,920

obligate killers of their host so they

2318

01:30:16,149 --> 01:30:13,840

inject their own dna or rna hijack the

2319

01:30:18,950 --> 01:30:16,159

machinery birth must burst the cell in

2320

01:30:20,470 --> 01:30:18,960

order to reproduce and infect new hosts

2321

01:30:22,550 --> 01:30:20,480

and of course this has obvious

2322

01:30:24,790 --> 01:30:22,560

ecological ramifications it's killing

2323

01:30:25,830 --> 01:30:24,800

bacteria this was why people got excited

2324

01:30:27,990 --> 01:30:25,840

about lytic phage when they were

2325

01:30:30,310 --> 01:30:28,000

discovered in the 20s because

2326

01:30:32,070 --> 01:30:30,320

this was before antibiotics a way to

2327

01:30:34,390 --> 01:30:32,080

kill bacteria

2328

01:30:37,110 --> 01:30:34,400

but they do far more than that and so if

2329

01:30:39,350 --> 01:30:37,120

we want to understand bacteriophage oh

2330

01:30:41,990 --> 01:30:39,360

i'm sorry here we go if we want to

2331

01:30:43,830 --> 01:30:42,000

understand bacteria phage co-evolution

2332

01:30:46,070 --> 01:30:43,840

one of the first parts of this is to

2333

01:30:47,750 --> 01:30:46,080

understand how bacteria evolve resistant

2334

01:30:49,270 --> 01:30:47,760

so these phages are there they're

2335

01:30:50,550 --> 01:30:49,280

obligate killers that already said so

2336

01:30:53,110 --> 01:30:50,560

they're putting a strong selection

2337

01:30:55,110 --> 01:30:53,120

pressure on their bacterial hosts and

2338

01:30:56,950 --> 01:30:55,120

this is just three very simple uh the

2339

01:30:59,350 --> 01:30:56,960

most simple examples and the potentially

2340

01:31:01,590 --> 01:30:59,360

the most common but bacterial resistance

2341

01:31:03,030 --> 01:31:01,600

mechanisms are constantly

2342

01:31:05,990 --> 01:31:03,040

being

2343

01:31:08,310 --> 01:31:06,000

discovered and so here on in a you have

2344

01:31:09,750 --> 01:31:08,320

a simple change in the receptor so

2345

01:31:11,270 --> 01:31:09,760

phages must bind to recognize a

2346

01:31:13,030 --> 01:31:11,280

bacterial cell and so of course the

2347

01:31:15,270 --> 01:31:13,040

bacteria can change that receptor and

2348

01:31:17,590 --> 01:31:15,280

instantly be resistant to that phage it

2349

01:31:18,390 --> 01:31:17,600

can no longer detect the bacterial cell

2350

01:31:19,990 --> 01:31:18,400

or

2351

01:31:22,470 --> 01:31:20,000

it could use these crispr cast

2352

01:31:24,870 --> 01:31:22,480

mechanisms so this is a mechanism by

2353

01:31:27,189 --> 01:31:24,880

which bacteria can recognize specific

2354

01:31:28,950 --> 01:31:27,199

sections of phage the phage genome and

2355

01:31:31,189 --> 01:31:28,960

block translation of that transcription

2356

01:31:34,229 --> 01:31:31,199

of that phage and then the last one here

2357

01:31:36,550 --> 01:31:34,239

in c is apoptosis or cell suicide the

2358

01:31:38,790 --> 01:31:36,560

idea that once a bacterial cell detects

2359

01:31:40,870 --> 01:31:38,800

phage infection it actually kills itself

2360

01:31:43,189 --> 01:31:40,880

before the phage can do that protecting

2361

01:31:46,229 --> 01:31:43,199

neighboring cells and likely in any

2362

01:31:47,830 --> 01:31:46,239

given microbiome or bacterial community

2363

01:31:50,950 --> 01:31:47,840

all of these mechanisms are happening

2364

01:31:54,470 --> 01:31:52,870

of course you wouldn't have co-evolution

2365

01:31:55,990 --> 01:31:54,480

without the flip side and you again you

2366

01:31:57,030 --> 01:31:56,000

already heard a nice talk about viral

2367

01:31:58,790 --> 01:31:57,040

evolution

2368

01:32:01,030 --> 01:31:58,800

in the case of phages here's just one

2369

01:32:02,790 --> 01:32:01,040

very nice example of how phages can

2370

01:32:05,830 --> 01:32:02,800

counter adapt against crispr cast

2371

01:32:08,149 --> 01:32:05,840

resistance crispr resistance and so here

2372

01:32:11,270 --> 01:32:08,159

what you're looking at is at low density

2373

01:32:13,189 --> 01:32:11,280

this crispr resistance is actually quite

2374

01:32:15,270 --> 01:32:13,199

effective and so this is not work from

2375

01:32:17,270 --> 01:32:15,280

my lab this is a work that was done in

2376

01:32:19,270 --> 01:32:17,280

two separate labs they find the same

2377

01:32:21,350 --> 01:32:19,280

result but actually if you get enough

2378

01:32:22,950 --> 01:32:21,360

phages infecting the same cell the

2379

01:32:25,590 --> 01:32:22,960

phages can essentially work together to

2380

01:32:27,030 --> 01:32:25,600

overcome crispr resistance and so this

2381

01:32:29,990 --> 01:32:27,040

is one

2382

01:32:31,110 --> 01:32:30,000

example of how phages counter adapt

2383

01:32:33,110 --> 01:32:31,120

of course if it's a receptor

2384

01:32:34,550 --> 01:32:33,120

modification a counter modification

2385

01:32:37,430 --> 01:32:34,560

would do the trick a change in the tail

2386

01:32:39,030 --> 01:32:37,440

fiber and so forth and so what i tend to

2387

01:32:41,669 --> 01:32:39,040

think about when i think about bacteria

2388

01:32:44,310 --> 01:32:41,679

and phage interacting is the constant

2389

01:32:46,870 --> 01:32:44,320

arms race as bacteria evolve resistance

2390

01:32:49,350 --> 01:32:46,880

and phage counter adapt and this in

2391

01:32:51,270 --> 01:32:49,360

theory can go on indefinitely now in

2392

01:32:53,270 --> 01:32:51,280

practice it's not clear phage genomes

2393

01:32:55,110 --> 01:32:53,280

are small and so there's probably our

2394

01:32:56,390 --> 01:32:55,120

cycles and there's going to be some sort

2395

01:32:57,990 --> 01:32:56,400

of finite

2396

01:32:59,350 --> 01:32:58,000

amount of evolution that can happen

2397

01:33:00,390 --> 01:32:59,360

before you're almost back where you

2398

01:33:02,709 --> 01:33:00,400

started

2399

01:33:04,790 --> 01:33:02,719

potentially

2400

01:33:07,270 --> 01:33:04,800

and so just to give you a few examples

2401
01:33:08,870 --> 01:33:07,280
of why we should care about coevolution

2402
01:33:09,910 --> 01:33:08,880
um this is beautiful work from steve

2403
01:33:10,790 --> 01:33:09,920
patterson

2404
01:33:13,510 --> 01:33:10,800
showing

2405
01:33:15,990 --> 01:33:13,520
that um co-evolution as opposed to just

2406
01:33:18,149 --> 01:33:16,000
evolution really speeds up the molecular

2407
01:33:20,470 --> 01:33:18,159
evolution and so this is a sort of in

2408
01:33:22,950 --> 01:33:20,480
vitro test tube experiment here where

2409
01:33:25,510 --> 01:33:22,960
they either allowed bacteria and phage

2410
01:33:29,030 --> 01:33:25,520
to co-evolve so these are the c one

2411
01:33:31,030 --> 01:33:29,040
through six or just evolve

2412
01:33:33,750 --> 01:33:31,040
okay in this case they keep one player

2413
01:33:35,350 --> 01:33:33,760

fixed and they allow the other to evolve

2414

01:33:36,870 --> 01:33:35,360

and what you can see here is that this

2415

01:33:39,030 --> 01:33:36,880

is just a phylogeny you can see that

2416

01:33:41,270 --> 01:33:39,040

there's far less or slower molecular

2417

01:33:42,709 --> 01:33:41,280

evolution when evolution happens when

2418

01:33:44,709 --> 01:33:42,719

you fix one of the players and don't

2419

01:33:46,790 --> 01:33:44,719

allow them to counter-adapt than if you

2420

01:33:48,470 --> 01:33:46,800

allow for co-evolution and the other

2421

01:33:50,470 --> 01:33:48,480

thing they were able to show here is

2422

01:33:53,270 --> 01:33:50,480

that this leads to rapid diversification

2423

01:33:55,189 --> 01:33:53,280

so rapid specificity and diversification

2424

01:33:56,310 --> 01:33:55,199

so here along the top and b you're

2425

01:33:58,470 --> 01:33:56,320

looking at

2426

01:34:00,709 --> 01:33:58,480

the different co-evolution lines and who

2427

01:34:03,189 --> 01:34:00,719

those phages can infect and you can see

2428

01:34:06,149 --> 01:34:03,199

that for example c4 is capable of

2429

01:34:07,430 --> 01:34:06,159

infecting a different set of hosts than

2430

01:34:09,430 --> 01:34:07,440

c6

2431

01:34:11,910 --> 01:34:09,440

and so this happened within a very short

2432

01:34:13,750 --> 01:34:11,920

period of time in the lab and really to

2433

01:34:15,669 --> 01:34:13,760

me emphasizes how

2434

01:34:17,270 --> 01:34:15,679

important co-evolution is both at the

2435

01:34:18,950 --> 01:34:17,280

molecular level and then at the

2436

01:34:21,350 --> 01:34:18,960

phenotypic level and this is work from

2437

01:34:22,950 --> 01:34:21,360

angus buckling now uh older work where

2438

01:34:27,110 --> 01:34:22,960

they just simply looked at bacterial

2439

01:34:29,030 --> 01:34:27,120

phenotype these different more

2440

01:34:31,350 --> 01:34:29,040

and they could show that if you look in

2441

01:34:33,270 --> 01:34:31,360

this sort of test tube experiment if you

2442

01:34:34,550 --> 01:34:33,280

allow phage co-evolution in a test tube

2443

01:34:36,709 --> 01:34:34,560

versus if you allow the bacteria to

2444

01:34:39,030 --> 01:34:36,719

evolve alone when the phages are present

2445

01:34:40,870 --> 01:34:39,040

the diversity the allopatric diversity

2446

01:34:43,189 --> 01:34:40,880

so how different two test tubes to

2447

01:34:45,910 --> 01:34:43,199

populate populations end up being from

2448

01:34:48,550 --> 01:34:45,920

one another is far higher when phages

2449

01:34:50,629 --> 01:34:48,560

are present than when they're absent

2450

01:34:52,709 --> 01:34:50,639

so rapid and molecular evolution rapid

2451

01:34:54,790 --> 01:34:52,719

phenotypic diversification hopefully

2452

01:34:56,870 --> 01:34:54,800

i've convinced you by this moment that

2453

01:34:58,070 --> 01:34:56,880

coevolution matters if you want to be

2454

01:35:00,070 --> 01:34:58,080

understanding

2455

01:35:01,830 --> 01:35:00,080

bacteria

2456

01:35:03,189 --> 01:35:01,840

and one of the ways that you can measure

2457

01:35:05,750 --> 01:35:03,199

coevolution and i would say the gold

2458

01:35:07,430 --> 01:35:05,760

standard way if you can do it is using a

2459

01:35:08,709 --> 01:35:07,440

time shift experiment so i'm just going

2460

01:35:10,470 --> 01:35:08,719

to spend a moment here because i'll show

2461

01:35:11,590 --> 01:35:10,480

you some data

2462

01:35:13,750 --> 01:35:11,600

using this but this is just a

2463

01:35:15,990 --> 01:35:13,760

theoretical model from a paper that

2464

01:35:17,510 --> 01:35:16,000

dieter ever put out a few years back

2465

01:35:19,669 --> 01:35:17,520

which is a great primer for anyone

2466

01:35:21,750 --> 01:35:19,679

interested in time shift experiments the

2467

01:35:24,470 --> 01:35:21,760

idea here is simply you would co-evolve

2468

01:35:25,750 --> 01:35:24,480

your populations and then freeze through

2469

01:35:27,510 --> 01:35:25,760

time or if you happen to have a

2470

01:35:29,030 --> 01:35:27,520

permafrost sample you know you can thaw

2471

01:35:31,430 --> 01:35:29,040

through time

2472

01:35:32,390 --> 01:35:31,440

and do a cross inoculation where you're

2473

01:35:34,390 --> 01:35:32,400

taking

2474

01:35:35,830 --> 01:35:34,400

bacteria let's say from one time point

2475

01:35:37,830 --> 01:35:35,840

and you're challenging that bacteria

2476

01:35:39,910 --> 01:35:37,840

with phages from the past

2477

01:35:41,750 --> 01:35:39,920

or phages from the future and you have a

2478

01:35:43,590 --> 01:35:41,760

clear prediction that they should be

2479

01:35:45,750 --> 01:35:43,600

more resistant

2480

01:35:48,149 --> 01:35:45,760

to phages from the past and less

2481

01:35:50,550 --> 01:35:48,159

resistant to phages from the future

2482

01:35:52,629 --> 01:35:50,560

as those phages have counter adapted to

2483

01:35:55,030 --> 01:35:52,639

any resistance mechanisms and this sort

2484

01:35:57,669 --> 01:35:55,040

of directionality is indicative of this

2485

01:36:00,149 --> 01:35:57,679

these arms race dynamics in a

2486

01:36:01,669 --> 01:36:00,159

co-evolving system

2487

01:36:03,189 --> 01:36:01,679

and you can do this in test tube

2488

01:36:05,350 --> 01:36:03,199

populations and this is a really nice

2489

01:36:07,590 --> 01:36:05,360

one from pauline scanlon

2490

01:36:09,270 --> 01:36:07,600

where you again take your bacteria in

2491

01:36:11,510 --> 01:36:09,280

this case pseudomonas fluorescens and a

2492

01:36:13,830 --> 01:36:11,520

phage allow them to co-evolve over time

2493

01:36:15,669 --> 01:36:13,840

and do a huge matrix cross where you

2494

01:36:17,189 --> 01:36:15,679

take bacteria here from different time

2495

01:36:18,709 --> 01:36:17,199

points and you cross them with phages

2496

01:36:20,790 --> 01:36:18,719

from different time points

2497

01:36:23,189 --> 01:36:20,800

and what this allows you to do is

2498

01:36:25,510 --> 01:36:23,199

actually measure you can show that over

2499

01:36:26,629 --> 01:36:25,520

time bacteria increase their resistance

2500

01:36:27,910 --> 01:36:26,639

to phage

2501
01:36:29,590 --> 01:36:27,920
through those mechanisms i already

2502
01:36:31,990 --> 01:36:29,600
described but that phages are

2503
01:36:33,750 --> 01:36:32,000
continually counter adapting to that and

2504
01:36:35,270 --> 01:36:33,760
in this particular case this is a true

2505
01:36:37,510 --> 01:36:35,280
arms race because

2506
01:36:39,830 --> 01:36:37,520
the bacteria are never in the course of

2507
01:36:41,109 --> 01:36:39,840
this experiment once again susceptible

2508
01:36:42,149 --> 01:36:41,119
to phages from the start of the

2509
01:36:44,310 --> 01:36:42,159
experiment

2510
01:36:46,470 --> 01:36:44,320
resistance continues to increase and

2511
01:36:47,990 --> 01:36:46,480
phage infectivity continues to increase

2512
01:36:49,910 --> 01:36:48,000
so they're chasing one another through

2513
01:36:51,350 --> 01:36:49,920

space

2514

01:36:53,510 --> 01:36:51,360

and again we know this happens very

2515

01:36:55,510 --> 01:36:53,520

rapidly in a test tube but what my lab

2516

01:36:57,590 --> 01:36:55,520

specifically focuses on is whether this

2517

01:36:58,790 --> 01:36:57,600

happens in the real world and whether

2518

01:37:00,629 --> 01:36:58,800

that matters

2519

01:37:02,390 --> 01:37:00,639

and we do that in in two different ways

2520

01:37:05,270 --> 01:37:02,400

we do that in terms of looking at

2521

01:37:07,350 --> 01:37:05,280

pairwise interactions between phages and

2522

01:37:08,950 --> 01:37:07,360

bacteria we focus on the plant pathogens

2523

01:37:10,870 --> 01:37:08,960

pseudomonas ring a

2524

01:37:12,070 --> 01:37:10,880

we have some new work as well on erwinia

2525

01:37:14,229 --> 01:37:12,080

and lavora

2526
01:37:16,070 --> 01:37:14,239
called the causal agent of fireblade and

2527
01:37:17,669 --> 01:37:16,080
then also just the role that phages play

2528
01:37:20,149 --> 01:37:17,679
in the broader microbiome in these

2529
01:37:22,629 --> 01:37:20,159
microbial communities and the system we

2530
01:37:24,790 --> 01:37:22,639
use is the phylosphere above ground

2531
01:37:26,629 --> 01:37:24,800
tissue of plants this is an incredibly

2532
01:37:29,750 --> 01:37:26,639
convenient system because the spatial

2533
01:37:31,830 --> 01:37:29,760
scale is very clear

2534
01:37:34,550 --> 01:37:31,840
and so i'm going to start by showing you

2535
01:37:37,109 --> 01:37:34,560
some work on the sort of more black boxy

2536
01:37:41,750 --> 01:37:37,119
community level and follow and finish

2537
01:37:46,229 --> 01:37:43,910
the first experiment i ever did when i

2538
01:37:47,990 --> 01:37:46,239

started to try to get a hold of what was

2539

01:37:50,070 --> 01:37:48,000

happening in a natural system the

2540

01:37:51,109 --> 01:37:50,080

phylosphere of a horse chestnut tree in

2541

01:37:53,590 --> 01:37:51,119

this case

2542

01:37:55,750 --> 01:37:53,600

is i went out and i just simply asked

2543

01:37:57,590 --> 01:37:55,760

what bacteriophages are in these leaves

2544

01:37:59,669 --> 01:37:57,600

and who are they infecting

2545

01:38:02,390 --> 01:37:59,679

and this is only focused on culturable

2546

01:38:03,990 --> 01:38:02,400

components of the microbial community

2547

01:38:06,390 --> 01:38:04,000

but nonetheless if you do that if you

2548

01:38:08,870 --> 01:38:06,400

culture bacteria from a given leaf and

2549

01:38:11,030 --> 01:38:08,880

then you filter that leaf juice and see

2550

01:38:12,709 --> 01:38:11,040

whatever viruses are in there and ask

2551

01:38:15,270 --> 01:38:12,719

who can they infect

2552

01:38:17,270 --> 01:38:15,280

you find that phages are far more

2553

01:38:19,350 --> 01:38:17,280

infective so this is a sympatric phage

2554

01:38:21,750 --> 01:38:19,360

from the same tree they're far more

2555

01:38:23,750 --> 01:38:21,760

infective to bacteria from that same

2556

01:38:25,109 --> 01:38:23,760

tree than they are to bacteria from a

2557

01:38:26,950 --> 01:38:25,119

neighboring tree

2558

01:38:28,550 --> 01:38:26,960

and this just is a nice starting place

2559

01:38:30,310 --> 01:38:28,560

it's an old paper now but it's a nice

2560

01:38:32,070 --> 01:38:30,320

starting place because it tells us that

2561

01:38:34,149 --> 01:38:32,080

in a natural system like the tree

2562

01:38:35,270 --> 01:38:34,159

phylosphere that phages are there

2563

01:38:37,189 --> 01:38:35,280

they're in high abundance they're

2564

01:38:40,550 --> 01:38:37,199

infecting about 15

2565

01:38:42,550 --> 01:38:40,560

of the bacteria in their local community

2566

01:38:44,070 --> 01:38:42,560

and that they're well adapted

2567

01:38:46,070 --> 01:38:44,080

and as soon as you have that evidence

2568

01:38:47,270 --> 01:38:46,080

for adaptation

2569

01:38:48,709 --> 01:38:47,280

that suggests that they should be

2570

01:38:51,669 --> 01:38:48,719

putting strong selection pressure on

2571

01:38:53,430 --> 01:38:51,679

their bacterial hosts for resistance

2572

01:38:55,189 --> 01:38:53,440

so how do we test that well i already

2573

01:38:57,590 --> 01:38:55,199

told you the gold standard way to test

2574

01:38:59,430 --> 01:38:57,600

it is with the time shift experiment

2575

01:39:01,109 --> 01:38:59,440

the downside of a black box approach

2576

01:39:04,550 --> 01:39:01,119

like this is you can't follow a single

2577

01:39:06,390 --> 01:39:04,560

lineage through time so we're sort of

2578

01:39:08,310 --> 01:39:06,400

glossing over we're making a broader

2579

01:39:10,070 --> 01:39:08,320

statement about evolution here as a

2580

01:39:11,990 --> 01:39:10,080

function of turnover between species

2581

01:39:14,229 --> 01:39:12,000

turnovers between strain as well as

2582

01:39:15,669 --> 01:39:14,239

mutation but nonetheless we can take a

2583

01:39:18,070 --> 01:39:15,679

similar approach

2584

01:39:19,270 --> 01:39:18,080

and we can ask again we take our leaves

2585

01:39:21,270 --> 01:39:19,280

from these trees and we put them into

2586

01:39:23,510 --> 01:39:21,280

the freezer you can then resurrect the

2587

01:39:25,430 --> 01:39:23,520

bacteria and the phage and say for a

2588

01:39:28,070 --> 01:39:25,440

given bacterial host let's say here's

2589

01:39:30,550 --> 01:39:28,080

just an illustrative example

2590

01:39:32,149 --> 01:39:30,560

a bacterium from july from tree number

2591

01:39:34,470 --> 01:39:32,159

two

2592

01:39:35,189 --> 01:39:34,480

and you can then challenge that bacteria

2593

01:39:37,590 --> 01:39:35,199

with

2594

01:39:38,790 --> 01:39:37,600

potential phage so this filtered leaf

2595

01:39:40,550 --> 01:39:38,800

juice

2596

01:39:43,270 --> 01:39:40,560

from earlier time points for example

2597

01:39:45,669 --> 01:39:43,280

june here uh the contemporary time point

2598

01:39:47,510 --> 01:39:45,679

july or later time points august and

2599

01:39:49,590 --> 01:39:47,520

september for example

2600

01:39:51,109 --> 01:39:49,600

so if we do that and we lump across our

2601

01:39:54,310 --> 01:39:51,119

the eight trees that i used in this

2602

01:39:59,189 --> 01:39:56,709

what we find is a similar result to what

2603

01:40:01,750 --> 01:39:59,199

Pauline Scanlan and others often find in

2604

01:40:02,709 --> 01:40:01,760

test tubes which is to say a directional

2605

01:40:04,470 --> 01:40:02,719

pattern

2606

01:40:06,870 --> 01:40:04,480

where in this case if we look at

2607

01:40:08,390 --> 01:40:06,880

bacterial resistance oh sorry about the

2608

01:40:10,229 --> 01:40:08,400

y-axis there something funny is going on

2609

01:40:11,669 --> 01:40:10,239

but the bacterial resistance on the

2610

01:40:14,149 --> 01:40:11,679

y-axis

2611

01:40:15,830 --> 01:40:14,159

we can say that bacteria are more

2612

01:40:17,750 --> 01:40:15,840

resistant to phages that they've

2613

01:40:19,510 --> 01:40:17,760

experienced previously in the season so

2614

01:40:22,070 --> 01:40:19,520

this is the past phage

2615

01:40:23,510 --> 01:40:22,080

okay so if they've been under selection

2616

01:40:25,270 --> 01:40:23,520

from that phage

2617

01:40:26,310 --> 01:40:25,280

they are more likely to be resistant to

2618

01:40:27,910 --> 01:40:26,320

it

2619

01:40:30,550 --> 01:40:27,920

the contemporary time point somewhere in

2620

01:40:32,310 --> 01:40:30,560

the middle and then future phages tend

2621

01:40:34,950 --> 01:40:32,320

to have counter-adapted and overcome

2622

01:40:36,470 --> 01:40:34,960

that resistance and so another way of

2623

01:40:38,149 --> 01:40:36,480

saying that is bacteria are least

2624

01:40:40,149 --> 01:40:38,159

resistant to phages that they have not

2625

01:40:42,149 --> 01:40:40,159

yet encountered phages that have likely

2626
01:40:43,750 --> 01:40:42,159
counter-adapted to that contemporary

2627
01:40:45,590 --> 01:40:43,760
resistance

2628
01:40:47,109 --> 01:40:45,600
i should say that the solid bar here is

2629
01:40:48,950 --> 01:40:47,119
just the average across the trees and

2630
01:40:51,109 --> 01:40:48,960
there is a lot of variation not every

2631
01:40:52,709 --> 01:40:51,119
tree is behaving in the same way but the

2632
01:40:54,790 --> 01:40:52,719
pattern is highly statistically

2633
01:40:56,950 --> 01:40:54,800
significant even if you pull out this

2634
01:41:00,310 --> 01:40:56,960
sort of super co-evolving population

2635
01:41:04,229 --> 01:41:01,590
okay

2636
01:41:06,790 --> 01:41:04,239
so so far i've told it told you that in

2637
01:41:08,629 --> 01:41:06,800
a natural system phages are present

2638
01:41:10,229 --> 01:41:08,639

they're highly prevalent

2639

01:41:11,510 --> 01:41:10,239

they should be they're obligate killers

2640

01:41:13,430 --> 01:41:11,520

so they should be putting selection on

2641

01:41:15,350 --> 01:41:13,440

their hosts and indeed it looks like

2642

01:41:16,950 --> 01:41:15,360

bacteria are becoming more resistant

2643

01:41:18,950 --> 01:41:16,960

through the season as they're

2644

01:41:21,189 --> 01:41:18,960

encountering these phages in a natural

2645

01:41:23,830 --> 01:41:21,199

system

2646

01:41:25,350 --> 01:41:23,840

what does that mean for diversity so

2647

01:41:27,189 --> 01:41:25,360

i've again given you some nice examples

2648

01:41:28,790 --> 01:41:27,199

from a test tube that we have clear and

2649

01:41:30,629 --> 01:41:28,800

we have clear theory the kill the winter

2650

01:41:33,189 --> 01:41:30,639

theory is a good example of that where

2651

01:41:36,070 --> 01:41:33,199

we expect that phages should as they

2652

01:41:37,590 --> 01:41:36,080

adapt to common bacterial types

2653

01:41:39,590 --> 01:41:37,600

they actually take

2654

01:41:41,750 --> 01:41:39,600

the fitness of common types down and

2655

01:41:44,070 --> 01:41:41,760

they should be increasing diversity of

2656

01:41:46,310 --> 01:41:44,080

the microbial population or community

2657

01:41:48,070 --> 01:41:46,320

but can we actually show that to be true

2658

01:41:49,910 --> 01:41:48,080

uh which is it's a bit of a challenge

2659

01:41:52,229 --> 01:41:49,920

and again as a first pass we took a

2660

01:41:53,990 --> 01:41:52,239

black box approach and by we here this

2661

01:41:55,750 --> 01:41:54,000

work was led by norma marella who's a

2662

01:41:56,709 --> 01:41:55,760

phd student in the lab who just recently

2663

01:41:58,629 --> 01:41:56,719

finished

2664

01:41:59,669 --> 01:41:58,639

um and so what she did was went out to

2665

01:42:01,990 --> 01:41:59,679

the field

2666

01:42:03,430 --> 01:42:02,000

sampled a whole microbiome so in this

2667

01:42:05,189 --> 01:42:03,440

case we used tomato it's a very

2668

01:42:07,430 --> 01:42:05,199

convenient model system

2669

01:42:09,270 --> 01:42:07,440

she was able to go out to fields sample

2670

01:42:11,669 --> 01:42:09,280

the whole tomato plant

2671

01:42:12,870 --> 01:42:11,679

wash off all of the bacteria and the

2672

01:42:15,990 --> 01:42:12,880

viruses

2673

01:42:17,750 --> 01:42:16,000

from the surface of leaves and then

2674

01:42:20,070 --> 01:42:17,760

through a series of filtration steps

2675

01:42:22,070 --> 01:42:20,080

separate that microbiome into two

2676

01:42:24,950 --> 01:42:22,080

components the microbial community the

2677

01:42:26,390 --> 01:42:24,960

bacteria and then the viral component

2678

01:42:29,350 --> 01:42:26,400

and the nice thing about that is then we

2679

01:42:31,590 --> 01:42:29,360

can either inoculate sterile plants with

2680

01:42:32,950 --> 01:42:31,600

either the bacterial community alone or

2681

01:42:34,950 --> 01:42:32,960

that bacterial community where the

2682

01:42:36,950 --> 01:42:34,960

phages have been recombined

2683

01:42:38,790 --> 01:42:36,960

and again a very black box approach but

2684

01:42:41,750 --> 01:42:38,800

it allows us to get a really nice

2685

01:42:43,830 --> 01:42:41,760

average of whether phages are generally

2686

01:42:46,550 --> 01:42:43,840

making a difference during initial

2687

01:42:48,950 --> 01:42:46,560

microbiome colonization in this case

2688

01:42:52,149 --> 01:42:48,960

and we use digital droplet pcr as a way

2689

01:42:54,950 --> 01:42:52,159

of quantifying absolute abundance

2690

01:42:56,790 --> 01:42:54,960

of our bacteria using 16s probe

2691

01:42:57,910 --> 01:42:56,800

and also for future studies that i'll

2692

01:43:00,629 --> 01:42:57,920

show you

2693

01:43:03,750 --> 01:43:00,639

specific bacteria as well

2694

01:43:05,270 --> 01:43:03,760

okay so she sprayed plants and replicate

2695

01:43:07,750 --> 01:43:05,280

with either the bacterial component

2696

01:43:10,629 --> 01:43:07,760

alone or the bacteria with it sympatric

2697

01:43:11,910 --> 01:43:10,639

the same phage from that

2698

01:43:13,669 --> 01:43:11,920

community

2699

01:43:16,390 --> 01:43:13,679

and the first thing to say is when we

2700

01:43:17,750 --> 01:43:16,400

look at the plants a day later so a day

2701

01:43:20,390 --> 01:43:17,760

after they're inoculated with this

2702

01:43:22,790 --> 01:43:20,400

diverse microbial community we can show

2703

01:43:25,669 --> 01:43:22,800

that the when you recombine with the

2704

01:43:28,709 --> 01:43:25,679

phage this orange bar here that overall

2705

01:43:30,550 --> 01:43:28,719

abundance so the ddpcr copy number

2706

01:43:32,149 --> 01:43:30,560

per leaf is lower

2707

01:43:34,790 --> 01:43:32,159

and this shouldn't surprise you these

2708

01:43:36,550 --> 01:43:34,800

phages are obligate killers but it is at

2709

01:43:38,790 --> 01:43:36,560

least suggesting that they really are

2710

01:43:40,950 --> 01:43:38,800

finding hosts and knocking them out in

2711

01:43:43,030 --> 01:43:40,960

this community

2712

01:43:45,189 --> 01:43:43,040

that effect on density goes away after

2713

01:43:47,189 --> 01:43:45,199

day seven although a lot changes on the

2714

01:43:48,310 --> 01:43:47,199

leaves carrying capacity is reached so

2715

01:43:50,149 --> 01:43:48,320

probably there's a lot of strain

2716

01:43:53,270 --> 01:43:50,159

switching here as the community is

2717

01:43:54,870 --> 01:43:53,280

establishing and stabilizing

2718

01:43:56,870 --> 01:43:54,880

the second thing we can do then is

2719

01:43:59,189 --> 01:43:56,880

sequence our microbial community and ask

2720

01:44:00,790 --> 01:43:59,199

what effect phages had on the whole

2721

01:44:02,149 --> 01:44:00,800

community composition

2722

01:44:03,510 --> 01:44:02,159

and i'll just show you one example of

2723

01:44:05,910 --> 01:44:03,520

that here

2724

01:44:08,390 --> 01:44:05,920

to say that again when you have phages

2725

01:44:11,350 --> 01:44:08,400

present there's a clear compositional

2726

01:44:12,790 --> 01:44:11,360

shift so this is a pcoa plot where we're

2727

01:44:14,870 --> 01:44:12,800

just looking at

2728

01:44:17,189 --> 01:44:14,880

community composition and beta

2729

01:44:19,270 --> 01:44:17,199

dissimilarity among them so all you need

2730

01:44:20,390 --> 01:44:19,280

to know here is if two points are

2731

01:44:22,229 --> 01:44:20,400

further apart

2732

01:44:23,990 --> 01:44:22,239

that means the community members have

2733

01:44:26,310 --> 01:44:24,000

less in common so the community is more

2734

01:44:27,750 --> 01:44:26,320

different

2735

01:44:29,910 --> 01:44:27,760

and so

2736

01:44:31,669 --> 01:44:29,920

again you can see that the bacteria and

2737

01:44:33,750 --> 01:44:31,679

phage replicates cluster out whether it

2738

01:44:35,750 --> 01:44:33,760

be day one or seven and the bacteria

2739

01:44:37,590 --> 01:44:35,760

only cluster out and the treatment

2740

01:44:39,910 --> 01:44:37,600

whether or not phage or that is there or

2741

01:44:42,070 --> 01:44:39,920

not explains 13 of the variation in

2742

01:44:43,270 --> 01:44:42,080

community composition and so again this

2743

01:44:45,270 --> 01:44:43,280

just suggests that if you're trying to

2744

01:44:47,350 --> 01:44:45,280

explain microbial microbiome diversity

2745

01:44:48,709 --> 01:44:47,360

whether it be a microbiome in a human

2746

01:44:51,430 --> 01:44:48,719

gut or in a

2747

01:44:53,430 --> 01:44:51,440

lake um ignoring the phages you're going

2748

01:44:56,629 --> 01:44:53,440

to miss this sort of explanatory power

2749

01:44:58,149 --> 01:44:56,639

of at least 13

2750

01:45:00,950 --> 01:44:58,159

and then the final thing she was able to

2751
01:45:02,390 --> 01:45:00,960
do using this same data set here the 16s

2752
01:45:04,950 --> 01:45:02,400
amplicon dataset

2753
01:45:06,790 --> 01:45:04,960
is ask what impacts phages had overall

2754
01:45:08,629 --> 01:45:06,800
on diversity and i've already given you

2755
01:45:10,390 --> 01:45:08,639
a theoretical reason why we expect

2756
01:45:11,750 --> 01:45:10,400
phages to maintain diversity i've

2757
01:45:13,750 --> 01:45:11,760
already shown you that this happens in a

2758
01:45:15,830 --> 01:45:13,760
test tube so hopefully this won't come

2759
01:45:17,910 --> 01:45:15,840
as a surprise although to me science is

2760
01:45:19,430 --> 01:45:17,920
always surprising when it

2761
01:45:21,109 --> 01:45:19,440
meets expectation

2762
01:45:22,310 --> 01:45:21,119
and so what you're looking at here is on

2763
01:45:24,550 --> 01:45:22,320

the left

2764

01:45:25,910 --> 01:45:24,560

alpha diversity so you can think about

2765

01:45:26,790 --> 01:45:25,920

this as

2766

01:45:28,950 --> 01:45:26,800

how many

2767

01:45:31,510 --> 01:45:28,960

otu or what the richness of species are

2768

01:45:33,189 --> 01:45:31,520

there and at day seven so we don't

2769

01:45:35,270 --> 01:45:33,199

really see an impact at day one which is

2770

01:45:36,629 --> 01:45:35,280

not particularly surprising but at day

2771

01:45:39,590 --> 01:45:36,639

seven once these communities have

2772

01:45:41,910 --> 01:45:39,600

established we find that indeed when

2773

01:45:44,229 --> 01:45:41,920

phages are present there are there's a

2774

01:45:46,070 --> 01:45:44,239

higher diversity of bacteria in these

2775

01:45:47,350 --> 01:45:46,080

microbiomes

2776

01:45:49,669 --> 01:45:47,360

and so

2777

01:45:51,590 --> 01:45:49,679

that fits beautifully with theory the

2778

01:45:53,350 --> 01:45:51,600

more surprising result for us although

2779

01:45:55,189 --> 01:45:53,360

again does fit with theory is on the

2780

01:45:57,430 --> 01:45:55,199

right here and what you're looking at is

2781

01:45:59,270 --> 01:45:57,440

the average ray curtis distances among

2782

01:46:01,990 --> 01:45:59,280

replicates and so another way of saying

2783

01:46:04,470 --> 01:46:02,000

that is how different is the microbiome

2784

01:46:06,709 --> 01:46:04,480

of two plants that received only

2785

01:46:08,629 --> 01:46:06,719

bacteria from one another or two plants

2786

01:46:11,990 --> 01:46:08,639

that received bacteria and phage from

2787

01:46:14,470 --> 01:46:12,000

one another so within treatment

2788

01:46:16,070 --> 01:46:14,480

but differences among individual plants

2789

01:46:17,830 --> 01:46:16,080

and what you can see here is no

2790

01:46:20,149 --> 01:46:17,840

significant differences at day one but

2791

01:46:22,550 --> 01:46:20,159

at day seven we actually have decreased

2792

01:46:24,149 --> 01:46:22,560

beta diversity in the presence of phage

2793

01:46:26,470 --> 01:46:24,159

and i think this is really neat because

2794

01:46:28,229 --> 01:46:26,480

it's suggesting that phages are really

2795

01:46:29,669 --> 01:46:28,239

moving the microbiome in this in the

2796

01:46:31,510 --> 01:46:29,679

same direction so they're sort of

2797

01:46:34,390 --> 01:46:31,520

raining in the microbiome in a similar

2798

01:46:37,669 --> 01:46:35,910

okay so i'm just going to finish up here

2799

01:46:40,390 --> 01:46:37,679

in the last

2800

01:46:41,270 --> 01:46:40,400

seven minutes or so by zooming in a bit

2801

01:46:51,270 --> 01:46:41,280

on

2802

01:46:54,550 --> 01:46:51,280

plant pathogen of broad host range and

2803

01:46:56,550 --> 01:46:54,560

we focus on tomato plants

2804

01:46:58,870 --> 01:46:56,560

and this work here is a recent paper

2805

01:47:01,189 --> 01:46:58,880

that's come out from kathy hernandez

2806

01:47:03,430 --> 01:47:01,199

and so the citations down there if

2807

01:47:05,990 --> 01:47:03,440

you're interested in the full story but

2808

01:47:08,310 --> 01:47:06,000

we became very interested in

2809

01:47:10,629 --> 01:47:08,320

the idea that co-evolution is likely to

2810

01:47:12,310 --> 01:47:10,639

be very different in a test tube from in

2811

01:47:14,709 --> 01:47:12,320

a plant and i've already shown you some

2812

01:47:17,109 --> 01:47:14,719

evidence that that's true but we wanted

2813

01:47:19,750 --> 01:47:17,119

a very specific test of this and so

2814

01:47:21,590 --> 01:47:19,760

because we know that we can grow our

2815

01:47:23,030 --> 01:47:21,600

strains on a tomato plant in very

2816

01:47:24,709 --> 01:47:23,040

controlled conditions

2817

01:47:26,870 --> 01:47:24,719

we thought this is a nice comparison to

2818

01:47:28,709 --> 01:47:26,880

a test tube so what i'm showing you here

2819

01:47:30,950 --> 01:47:28,719

is in our in vitro lines this is a

2820

01:47:33,350 --> 01:47:30,960

typical experimental evolution

2821

01:47:34,950 --> 01:47:33,360

setup where on the far left on the

2822

01:47:37,430 --> 01:47:34,960

bottom here the treatments we have

2823

01:47:39,109 --> 01:47:37,440

bacteria alone and the passage three is

2824

01:47:40,629 --> 01:47:39,119

the midpoint passage six is the end of

2825

01:47:42,629 --> 01:47:40,639

the experiment and you just look at

2826
01:47:44,629 --> 01:47:42,639
whether they evolved resistance or not

2827
01:47:46,470 --> 01:47:44,639
and the bacteria alone lines do not

2828
01:47:48,149 --> 01:47:46,480
involve resistance

2829
01:47:50,950 --> 01:47:48,159
and the um

2830
01:47:53,750 --> 01:47:50,960
the co-evolved or if you allow either of

2831
01:47:55,270 --> 01:47:53,760
them to evolve as a fixed against the

2832
01:47:57,590 --> 01:47:55,280
other one

2833
01:47:59,510 --> 01:47:57,600
so in other words phage can evolve to

2834
01:48:00,629 --> 01:47:59,520
fix bacteria or bacteria can evolve to

2835
01:48:03,109 --> 01:48:00,639
fix phage

2836
01:48:05,830 --> 01:48:03,119
in either of those cases we see

2837
01:48:07,189 --> 01:48:05,840
that resistance spreads and the two

2838
01:48:09,109 --> 01:48:07,199

different colored dots it's not really

2839

01:48:10,470 --> 01:48:09,119

important but that's ancestral phage or

2840

01:48:12,870 --> 01:48:10,480

the contemporary phage during

2841

01:48:13,590 --> 01:48:12,880

co-evolution or evolution

2842

01:48:15,189 --> 01:48:13,600

so

2843

01:48:16,950 --> 01:48:15,199

in a test tube

2844

01:48:19,590 --> 01:48:16,960

resistance evolves very quickly is the

2845

01:48:21,590 --> 01:48:19,600

take-home message from this slide

2846

01:48:23,750 --> 01:48:21,600

and that's not surprising what you can

2847

01:48:25,750 --> 01:48:23,760

then do is take resistant mutants and

2848

01:48:27,590 --> 01:48:25,760

susceptible mutants put them back in a

2849

01:48:30,870 --> 01:48:27,600

plant in the presence or absence of

2850

01:48:31,669 --> 01:48:30,880

phage and measure selection for that

2851

01:48:33,590 --> 01:48:31,679

type

2852

01:48:35,189 --> 01:48:33,600

and i'm just focusing here on the 24

2853

01:48:37,030 --> 01:48:35,199

hours so this is you inoculate the

2854

01:48:38,550 --> 01:48:37,040

plants and 24 hours later you can use

2855

01:48:40,709 --> 01:48:38,560

droplet digital pcr to measure

2856

01:48:42,229 --> 01:48:40,719

pseudomonas ring a and what i want you

2857

01:48:43,590 --> 01:48:42,239

to take away again this is in a test

2858

01:48:45,830 --> 01:48:43,600

tube is

2859

01:48:47,669 --> 01:48:45,840

when there are phage present in that

2860

01:48:49,830 --> 01:48:47,679

tube the bacterial density of

2861

01:48:51,669 --> 01:48:49,840

pseudomonas serine is lower for

2862

01:48:53,910 --> 01:48:51,679

susceptible mutants than resistant

2863

01:48:56,629 --> 01:48:53,920

mutants in other words selection should

2864

01:48:58,390 --> 01:48:56,639

favor resistance mutants and indeed

2865

01:49:00,550 --> 01:48:58,400

that's what we see resistance spreads in

2866

01:49:02,310 --> 01:49:00,560

a test tube very quickly

2867

01:49:04,629 --> 01:49:02,320

in most cases we see it happening in

2868

01:49:05,590 --> 01:49:04,639

under 48 hours

2869

01:49:07,510 --> 01:49:05,600

okay

2870

01:49:09,590 --> 01:49:07,520

so what happens in a plant

2871

01:49:11,590 --> 01:49:09,600

in this case she took the same strains

2872

01:49:13,669 --> 01:49:11,600

in the same experimental setup but now

2873

01:49:15,350 --> 01:49:13,679

put these bacteria in phage in a plant

2874

01:49:16,870 --> 01:49:15,360

and i'm showing you one example here but

2875

01:49:19,270 --> 01:49:16,880

she re-ran the experiment in many

2876

01:49:21,750 --> 01:49:19,280

different ways and many different mois

2877

01:49:24,470 --> 01:49:21,760

and what we found was that we did not

2878

01:49:26,550 --> 01:49:24,480

see the evolution of resistance and this

2879

01:49:28,390 --> 01:49:26,560

importantly and in contrast to what i've

2880

01:49:30,950 --> 01:49:28,400

just shown you from a whole microbe a

2881

01:49:33,109 --> 01:49:30,960

natural microbial community this is

2882

01:49:35,030 --> 01:49:33,119

resistance by mutation whereas

2883

01:49:37,270 --> 01:49:35,040

previously those resistance mechanisms

2884

01:49:39,910 --> 01:49:37,280

were open to strain replacement species

2885

01:49:42,470 --> 01:49:39,920

sorting etc if you're looking at

2886

01:49:45,270 --> 01:49:42,480

evolution by by mutation in this

2887

01:49:47,589 --> 01:49:45,280

particular system it seems like

2888

01:49:50,629 --> 01:49:47,599

we don't see the evolution of resistance

2889

01:49:53,270 --> 01:49:50,639

whereas we did rapidly in a test tube

2890

01:49:54,870 --> 01:49:53,280

okay so this blank figure should be

2891

01:49:56,550 --> 01:49:54,880

pretty convincing that it does not

2892

01:49:57,589 --> 01:49:56,560

happen rapidly

2893

01:49:59,350 --> 01:49:57,599

but why

2894

01:50:00,550 --> 01:49:59,360

and so we took that same approach that i

2895

01:50:02,390 --> 01:50:00,560

just showed you where we took our

2896

01:50:04,870 --> 01:50:02,400

resistant mutants and importantly these

2897

01:50:06,950 --> 01:50:04,880

are resistant mutants that were evolved

2898

01:50:07,990 --> 01:50:06,960

in vitro because we don't find them in

2899

01:50:11,669 --> 01:50:08,000

planta

2900

01:50:13,189 --> 01:50:11,679

ask how they grow in the presence or

2901

01:50:15,830 --> 01:50:13,199

absence of phage

2902

01:50:17,990 --> 01:50:15,840

and in total contrast to the figure i

2903

01:50:21,270 --> 01:50:18,000

showed you previously from in vitro in

2904

01:50:23,510 --> 01:50:21,280

this case in the presence of phage

2905

01:50:25,430 --> 01:50:23,520

there is no selective advantage to

2906

01:50:26,310 --> 01:50:25,440

resistance

2907

01:50:28,070 --> 01:50:26,320

okay

2908

01:50:29,750 --> 01:50:28,080

so that's not to say that phages aren't

2909

01:50:31,830 --> 01:50:29,760

doing anything because you can see if

2910

01:50:35,109 --> 01:50:31,840

you just look at the susceptible mutants

2911

01:50:36,790 --> 01:50:35,119

that their growth rate is is decreased

2912

01:50:38,310 --> 01:50:36,800

in the presence of phage relative to the

2913

01:50:41,510 --> 01:50:38,320

absence if you compare the blue and the

2914

01:50:43,430 --> 01:50:41,520

green bars there so phages are killing

2915

01:50:44,709 --> 01:50:43,440

their hosts in this environment and

2916

01:50:46,870 --> 01:50:44,719

they're not killing the resistant

2917

01:50:49,270 --> 01:50:46,880

mutants but the difference here is that

2918

01:50:50,870 --> 01:50:49,280

that strength of selection is not strong

2919

01:50:52,870 --> 01:50:50,880

enough to overcome the cost of

2920

01:50:54,790 --> 01:50:52,880

resistance and we've previously

2921

01:50:55,830 --> 01:50:54,800

demonstrated costs of resistance in this

2922

01:50:57,750 --> 01:50:55,840

system

2923

01:51:01,109 --> 01:50:57,760

the majority of resistance mutations

2924

01:51:03,830 --> 01:51:01,119

happen by via changes in the lps pathway

2925

01:51:06,390 --> 01:51:03,840

and we know that lps the lps receptor

2926

01:51:08,470 --> 01:51:06,400

that these phages use to bind changes in

2927

01:51:10,229 --> 01:51:08,480

that receptor can come at huge fitness

2928

01:51:12,310 --> 01:51:10,239

costs especially in the plant

2929

01:51:16,070 --> 01:51:12,320

environment and that was work previously

2930

01:51:20,550 --> 01:51:18,470

so the takeaway from this section is

2931

01:51:23,189 --> 01:51:20,560

that bacteriophage coevolution does

2932

01:51:25,350 --> 01:51:23,199

matter but the impact of it is going to

2933

01:51:27,189 --> 01:51:25,360

vary depending on the environment and we

2934

01:51:28,950 --> 01:51:27,199

need to be a little bit cautious moving

2935

01:51:31,430 --> 01:51:28,960

from test tube experiments to making

2936

01:51:33,270 --> 01:51:31,440

predictions about the real world

2937

01:51:35,109 --> 01:51:33,280

but you will notice that there's this

2938

01:51:37,270 --> 01:51:35,119

potential juxtaposition between what

2939

01:51:39,109 --> 01:51:37,280

i've shown happens rapidly in a natural

2940

01:51:40,709 --> 01:51:39,119

system and what's happening in this more

2941

01:51:43,350 --> 01:51:40,719

controlled system and i think there

2942

01:51:45,430 --> 01:51:43,360

remains a lot of work to be done as to

2943

01:51:47,589 --> 01:51:45,440

how much of what we see in terms of

2944

01:51:49,510 --> 01:51:47,599

phage mediated selection in nature is

2945

01:51:51,990 --> 01:51:49,520

the result of mutational change within a

2946

01:51:54,550 --> 01:51:52,000

lineage versus larger ecological

2947

01:51:56,790 --> 01:51:54,560

processes

2948

01:51:58,390 --> 01:51:56,800

and so to summarize um hopefully what

2949

01:52:00,310 --> 01:51:58,400

i've been able to convince you of is if

2950

01:52:03,270 --> 01:52:00,320

we're trying to understand microbial

2951
01:52:05,030 --> 01:52:03,280
communities which as a field we are very

2952
01:52:06,310 --> 01:52:05,040
interested in at the moment

2953
01:52:09,430 --> 01:52:06,320
we know that these communities are

2954
01:52:11,350 --> 01:52:09,440
complex um in terms of diversity and

2955
01:52:13,350 --> 01:52:11,360
across space they're very highly

2956
01:52:15,189 --> 01:52:13,360
variable so individuals host different

2957
01:52:17,189 --> 01:52:15,199
microbiomes different lakes etc have

2958
01:52:19,189 --> 01:52:17,199
different microbiomes they're dynamic

2959
01:52:21,109 --> 01:52:19,199
across time and if you're thinking about

2960
01:52:23,990 --> 01:52:21,119
a host associated microbiome they're

2961
01:52:25,510 --> 01:52:24,000
critical to shaping host phenotype and

2962
01:52:26,709 --> 01:52:25,520
through the series of

2963
01:52:28,310 --> 01:52:26,719

experiments i've just shown you

2964

01:52:30,390 --> 01:52:28,320

hopefully i've made a convincing

2965

01:52:32,550 --> 01:52:30,400

argument that phages are likely to be

2966

01:52:34,629 --> 01:52:32,560

important in all of these and through

2967

01:52:37,109 --> 01:52:34,639

this coevolutionary process they're

2968

01:52:39,109 --> 01:52:37,119

likely to shape composition

2969

01:52:40,550 --> 01:52:39,119

chain by adapting to local bacteria

2970

01:52:42,870 --> 01:52:40,560

potentially driving different

2971

01:52:44,390 --> 01:52:42,880

populations apart or in some cases

2972

01:52:46,870 --> 01:52:44,400

moving them together as i showed you

2973

01:52:49,109 --> 01:52:46,880

from the tomato plants

2974

01:52:49,990 --> 01:52:49,119

drive changes in composition over time

2975

01:52:51,750 --> 01:52:50,000

and

2976
01:52:54,550 --> 01:52:51,760
as i showed you in terms of prophages in

2977
01:52:56,390 --> 01:52:54,560
particular be important in shaping

2978
01:52:58,550 --> 01:52:56,400
their bacterial host phenotype which

2979
01:53:01,109 --> 01:52:58,560
could have important implications for

2980
01:53:03,510 --> 01:53:01,119
the eukaryotic host again if it's a host

2981
01:53:05,910 --> 01:53:03,520
associated microbe

2982
01:53:08,870 --> 01:53:05,920
and with that i will thank my my group

2983
01:53:15,900 --> 01:53:08,880
the organizers of today's and tomorrow's

2984
01:53:15,910 --> 01:53:19,990
[Applause]

2985
01:53:23,750 --> 01:53:22,149
thanks for that brett that was great uh

2986
01:53:29,270 --> 01:53:23,760
i just wanted to open up if anyone had a

2987
01:53:31,910 --> 01:53:30,070
i'll

2988
01:53:33,109 --> 01:53:31,920

ask the first question again uh hybrid

2989

01:53:35,270 --> 01:53:33,119

this guy

2990

01:53:37,109 --> 01:53:35,280

uh how much

2991

01:53:39,910 --> 01:53:37,119

uh how quickly are the bacteria

2992

01:53:43,430 --> 01:53:39,920

multiplying in planta because you've got

2993

01:53:45,589 --> 01:53:43,440

a difference in speed per unit of human

2994

01:53:47,910 --> 01:53:45,599

measured time can we adjust it at all to

2995

01:53:50,229 --> 01:53:47,920

bacterial generation time oh i would

2996

01:53:51,910 --> 01:53:50,239

love to know that answer um well we we

2997

01:53:54,790 --> 01:53:51,920

can get it a little bit with our droplet

2998

01:53:56,310 --> 01:53:54,800

digital pcr now we can look at

2999

01:53:58,790 --> 01:53:56,320

growth rates

3000

01:53:59,750 --> 01:53:58,800

and it's a good question

3001

01:54:01,430 --> 01:53:59,760

you know

3002

01:54:03,589 --> 01:54:01,440

i wonder

3003

01:54:05,350 --> 01:54:03,599

we could probably mine kathy's data set

3004

01:54:06,950 --> 01:54:05,360

a bit better to get an idea of that but

3005

01:54:08,870 --> 01:54:06,960

we're still measuring generally our

3006

01:54:11,990 --> 01:54:08,880

droplet digital pcr we're measuring

3007

01:54:13,510 --> 01:54:12,000

after 24 hours 48 hours 72 hours i think

3008

01:54:14,870 --> 01:54:13,520

we need a much more fine scale

3009

01:54:17,270 --> 01:54:14,880

resolution to

3010

01:54:19,589 --> 01:54:17,280

to not also then be averaging over death

3011

01:54:21,510 --> 01:54:19,599

and so forth um

3012

01:54:24,310 --> 01:54:21,520

but it's a it's a it's a good question

3013

01:54:29,990 --> 01:54:24,320

and i think we could potentially do it

3014

01:54:35,669 --> 01:54:32,470

perfect i'll ask the next question

3015

01:54:37,990 --> 01:54:35,679

um i was going back to the tomato plants

3016

01:54:39,750 --> 01:54:38,000

and viruses on them versus viruses added

3017

01:54:41,669 --> 01:54:39,760

to them this kind of a lock thinners

3018

01:54:43,910 --> 01:54:41,679

versus a toxinous approach you know in

3019

01:54:46,149 --> 01:54:43,920

california you can go several months

3020

01:54:48,550 --> 01:54:46,159

with no rain and this idea of watering

3021

01:54:50,310 --> 01:54:48,560

and this we're watering plants so

3022

01:54:52,310 --> 01:54:50,320

if you think we're watering plants for

3023

01:54:53,910 --> 01:54:52,320

the whole summer and we're adding a a

3024

01:54:55,189 --> 01:54:53,920

certain water source

3025

01:54:57,109 --> 01:54:55,199

and then

3026

01:54:58,790 --> 01:54:57,119

they maybe get used to those phages or

3027

01:55:01,109 --> 01:54:58,800

those viruses in the water source but

3028

01:55:03,109 --> 01:55:01,119

then we'll get rainfall

3029

01:55:04,470 --> 01:55:03,119

probably from the ocean that comes in

3030

01:55:07,030 --> 01:55:04,480

and we're adding these new types of

3031

01:55:08,470 --> 01:55:07,040

viruses so do you see impacts maybe or

3032

01:55:10,790 --> 01:55:08,480

have if you thought about that maybe

3033

01:55:12,629 --> 01:55:10,800

different water sources and this idea of

3034

01:55:14,229 --> 01:55:12,639

the community switches with the season

3035

01:55:17,430 --> 01:55:14,239

because of this

3036

01:55:18,709 --> 01:55:17,440

i think it's a great question um

3037

01:55:20,310 --> 01:55:18,719

i haven't thought about it within an

3038

01:55:21,669 --> 01:55:20,320

agricultural setting to be honest

3039

01:55:23,990 --> 01:55:21,679

especially irrigation water but i think

3040

01:55:26,470 --> 01:55:24,000

that's a really nice place to look where

3041

01:55:28,709 --> 01:55:26,480

we are doing that is i mentioned briefly

3042

01:55:31,030 --> 01:55:28,719

fire blight disease we've been sampling

3043

01:55:33,350 --> 01:55:31,040

pear trees for three years now monthly

3044

01:55:35,990 --> 01:55:33,360

in berkeley and

3045

01:55:38,470 --> 01:55:36,000

we we should be able to have once we do

3046

01:55:40,149 --> 01:55:38,480

the the metaviromics of that

3047

01:55:42,470 --> 01:55:40,159

we should be able to get an idea of

3048

01:55:44,870 --> 01:55:42,480

whether we see wholesale changes in the

3049

01:55:46,950 --> 01:55:44,880

the virum that's there

3050

01:55:48,390 --> 01:55:46,960

depending on rainfall and i think that

3051

01:55:50,070 --> 01:55:48,400

would be really neat but unfortunately

3052

01:55:51,270 --> 01:55:50,080

we're probably at least a year from that

3053

01:55:52,470 --> 01:55:51,280

answer

3054

01:55:53,669 --> 01:55:52,480

but i haven't thought about it doing it

3055

01:56:05,270 --> 01:55:53,679

in an agricultural field and i think

3056

01:56:09,109 --> 01:56:06,950

um i've actually got a follow-up

3057

01:56:11,189 --> 01:56:09,119

question on that so brits um just

3058

01:56:12,950 --> 01:56:11,199

thinking about it from generalists and

3059

01:56:14,470 --> 01:56:12,960

specialist viruses

3060

01:56:16,310 --> 01:56:14,480

and so leading on from the previous

3061

01:56:18,470 --> 01:56:16,320

question to me if you've got different

3062

01:56:20,709 --> 01:56:18,480

sources

3063

01:56:23,589 --> 01:56:20,719

that the hosts

3064

01:56:25,510 --> 01:56:23,599

are susceptible to different

3065

01:56:27,830 --> 01:56:25,520

varieties of viruses they're not very

3066

01:56:29,510 --> 01:56:27,840

unique so so that means the viruses the

3067

01:56:32,870 --> 01:56:29,520

phages that are infecting them are not

3068

01:56:34,790 --> 01:56:32,880

specialists but they're more generalists

3069

01:56:37,030 --> 01:56:34,800

so again that's a huge goal of our pair

3070

01:56:38,550 --> 01:56:37,040

project is to see whether that host

3071

01:56:40,149 --> 01:56:38,560

range changes over the course of the

3072

01:56:41,430 --> 01:56:40,159

season

3073

01:56:43,109 --> 01:56:41,440

but something just occurred to me that's

3074

01:56:44,470 --> 01:56:43,119

relevant to both of these questions

3075

01:56:46,149 --> 01:56:44,480

which is that if we're thinking about

3076

01:56:47,910 --> 01:56:46,159

this dispersal in immigration and

3077

01:56:50,229 --> 01:56:47,920

turnover as a function of rain for

3078

01:56:51,669 --> 01:56:50,239

example one of the critical and i think

3079

01:56:53,109 --> 01:56:51,679

unanswered questions that i would love

3080

01:56:54,870 --> 01:56:53,119

to hear from this community if there's

3081

01:56:57,430 --> 01:56:54,880

data out there that i don't know about

3082

01:56:59,430 --> 01:56:57,440

is the relative dispersal rates in the

3083

01:57:01,109 --> 01:56:59,440

environment of phage versus bacteria

3084

01:57:03,510 --> 01:57:01,119

because i think that's critical if we're

3085

01:57:05,270 --> 01:57:03,520

looking in rain you know how much of

3086

01:57:06,790 --> 01:57:05,280

course we know pseudomonas ring a our

3087

01:57:09,750 --> 01:57:06,800

focal pathogen moves through the water

3088

01:57:11,189 --> 01:57:09,760

cycle but we know much less about

3089

01:57:12,709 --> 01:57:11,199

phage movement

3090

01:57:15,109 --> 01:57:12,719

through the water cycle and so i would

3091

01:57:18,070 --> 01:57:15,119

be very keen to if anyone knows of good

3092

01:57:19,430 --> 01:57:18,080

data sets contrasting movement of phage

3093

01:57:21,430 --> 01:57:19,440

and bacteria

3094

01:57:22,950 --> 01:57:21,440

um we might not have time now but please

3095

01:57:24,709 --> 01:57:22,960

email me if you do have that i would

3096

01:57:27,350 --> 01:57:24,719

love to have that conversation a bit

3097

01:57:31,589 --> 01:57:29,830

or in marine systems for that matter

3098

01:57:33,189 --> 01:57:31,599

let's thank brit again i think this

3099

01:57:40,790 --> 01:57:33,199

might be a great transition to rachel so

3100

01:57:45,109 --> 01:57:44,149

um hi this is rachel did you want me to

3101

01:57:47,830 --> 01:57:45,119

just

3102

01:57:49,350 --> 01:57:47,840

start and share my screen or how does

3103

01:57:51,189 --> 01:57:49,360

that go

3104

01:57:53,589 --> 01:57:51,199

yeah can you start your

3105

01:57:55,510 --> 01:57:53,599

camera first

3106

01:57:57,750 --> 01:57:55,520

um so we can see you

3107

01:57:59,589 --> 01:57:57,760

there you go

3108

01:58:01,189 --> 01:57:59,599

yeah and then um click the share on the

3109

01:58:03,350 --> 01:58:01,199

button and share your screen and we

3110

01:58:06,709 --> 01:58:03,360

should be good to go so i should have my

3111

01:58:08,629 --> 01:58:06,719

um slides in like um view mode or

3112

01:58:10,229 --> 01:58:08,639

whatever

3113

01:58:13,109 --> 01:58:10,239

okay we're not seeing your screen share

3114

01:58:14,390 --> 01:58:13,119

yet but yeah you can go to the slideshow

3115

01:58:27,750 --> 01:58:14,400

mode

3116

01:58:32,629 --> 01:58:29,830

um

3117

01:58:36,470 --> 01:58:32,639

yeah we're seeing your desktop now

3118

01:58:38,310 --> 01:58:36,480

yeah so now i have to switch to

3119

01:58:46,790 --> 01:58:38,320

yeah on top

3120

01:58:46,800 --> 01:58:51,910

i don't know why i can't um i'm sorry

3121

01:58:55,750 --> 01:58:53,510

there

3122

01:59:00,830 --> 01:58:55,760

yep

3123

01:59:05,270 --> 01:59:03,030

um um

3124

01:59:07,109 --> 01:59:05,280

okay so um i

3125

01:59:08,870 --> 01:59:07,119

sorry i haven't gotten to participate in

3126

01:59:11,270 --> 01:59:08,880

the whole thing of this workshop it

3127

01:59:13,669 --> 01:59:11,280

seems really cool and i and it's very

3128

01:59:16,070 --> 01:59:13,679

awkward for me to be presenting without

3129

01:59:17,990 --> 01:59:16,080

having anybody to talk to i assume

3130

01:59:19,990 --> 01:59:18,000

there's people out there and i'm happy

3131

01:59:22,470 --> 01:59:20,000

to take questions whenever but i know

3132

01:59:25,669 --> 01:59:22,480

that's kind of awkward in this scenario

3133

01:59:27,830 --> 01:59:25,679

so um i guess i'll just talk through

3134

01:59:30,229 --> 01:59:27,840

um the way we're looking at viruses now

3135

01:59:32,149 --> 01:59:30,239

which is a little bit different than i

3136

01:59:34,790 --> 01:59:32,159

think probably i know at least the way

3137

01:59:37,990 --> 01:59:34,800

brit was was describing the ecology and

3138

01:59:39,189 --> 01:59:38,000

evolution um and i think that it's a

3139

01:59:41,830 --> 01:59:39,199

little bit different than the way people

3140

01:59:43,350 --> 01:59:41,840

think about it in microbes normally so

3141

01:59:45,189 --> 01:59:43,360

we're thinking about

3142

01:59:47,189 --> 01:59:45,199

viral symbiosis

3143

01:59:49,750 --> 01:59:47,199

and i wanted to kind of go back all the

3144

01:59:52,149 --> 01:59:49,760

way to the beginning because i'm really

3145

01:59:54,070 --> 01:59:52,159

interested in the origin of life

3146

01:59:55,910 --> 01:59:54,080

and we were in this

3147

01:59:58,149 --> 01:59:55,920

nasa astrobiology institute that was

3148

02:00:00,550 --> 01:59:58,159

looking at the processes of the origin

3149

02:00:02,790 --> 02:00:00,560

of life so i just want to remind you a

3150

02:00:04,950 --> 02:00:02,800

couple of things about that and then put

3151
02:00:05,750 --> 02:00:04,960
viruses in that context

3152
02:00:08,310 --> 02:00:05,760
so

3153
02:00:11,350 --> 02:00:08,320
of course you know this three domain

3154
02:00:14,790 --> 02:00:11,360
tree of life that was published

3155
02:00:17,030 --> 02:00:14,800
by carl rose in 1977

3156
02:00:19,589 --> 02:00:17,040
and i'm almost you know embarrassed to

3157
02:00:23,109 --> 02:00:19,599
put it up there um again because i hope

3158
02:00:25,430 --> 02:00:23,119
we all take this um now as a as a true

3159
02:00:27,430 --> 02:00:25,440
understanding of the way

3160
02:00:29,669 --> 02:00:27,440
life emerged even if we're not sure

3161
02:00:33,430 --> 02:00:29,679
exactly how the archaean eukaryotes are

3162
02:00:35,510 --> 02:00:33,440
related um as the trees are changing but

3163
02:00:37,669 --> 02:00:35,520

uh the same year

3164

02:00:40,149 --> 02:00:37,679

he also published a second paper which

3165

02:00:42,790 --> 02:00:40,159

was on the concept of cellular evolution

3166

02:00:45,109 --> 02:00:42,800

and people know less about that work but

3167

02:00:46,950 --> 02:00:45,119

i think it's really really important it

3168

02:00:48,950 --> 02:00:46,960

was less about the

3169

02:00:51,270 --> 02:00:48,960

relationships between the organisms and

3170

02:00:53,990 --> 02:00:51,280

more about the process of evolution and

3171

02:00:57,189 --> 02:00:54,000

how that changed in tempo and mode over

3172

02:00:59,350 --> 02:00:57,199

the um course of evolution so very

3173

02:01:02,390 --> 02:00:59,360

quickly what he said was that we know

3174

02:01:04,470 --> 02:01:02,400

that there's fossils of cyanobacteria

3175

02:01:07,189 --> 02:01:04,480

and i know these dates change around but

3176

02:01:08,550 --> 02:01:07,199

it's something like 3.5 billion years

3177

02:01:11,510 --> 02:01:08,560

ago

3178

02:01:13,350 --> 02:01:11,520

and by that time then if we believe

3179

02:01:15,750 --> 02:01:13,360

those fossils and those dates we would

3180

02:01:17,910 --> 02:01:15,760

have had an entire cell that was

3181

02:01:21,270 --> 02:01:17,920

functioning and doing oxygenic

3182

02:01:23,709 --> 02:01:21,280

photosynthesis which is a long way to go

3183

02:01:27,189 --> 02:01:23,719

if the earth started in

3184

02:01:30,550 --> 02:01:27,199

4.4.5 billion years ago so in that first

3185

02:01:34,229 --> 02:01:30,560

billion years we went all the way from

3186

02:01:36,950 --> 02:01:34,239

chemistry to full cell

3187

02:01:39,910 --> 02:01:36,960

biology and oxygenic photosynthesis

3188

02:01:42,149 --> 02:01:39,920

um whereas since then really in

3189

02:01:44,629 --> 02:01:42,159

comparison we've done very little we've

3190

02:01:47,189 --> 02:01:44,639

just kind of articulated on these things

3191

02:01:49,270 --> 02:01:47,199

and we still kind of function basically

3192

02:01:52,070 --> 02:01:49,280

as cells in the same way

3193

02:01:54,229 --> 02:01:52,080

so his question here is what changed and

3194

02:01:56,470 --> 02:01:54,239

what was different about

3195

02:01:58,790 --> 02:01:56,480

the pre-cellular

3196

02:02:02,390 --> 02:01:58,800

part of life and

3197

02:02:03,830 --> 02:02:02,400

the last 3.5 billion years and his idea

3198

02:02:05,830 --> 02:02:03,840

was that there was a change in

3199

02:02:07,270 --> 02:02:05,840

evolutionary mode and he called this

3200

02:02:10,310 --> 02:02:07,280

change in evolutionary mode the

3201
02:02:11,750 --> 02:02:10,320
darwinian transition because he thought

3202
02:02:15,750 --> 02:02:11,760
one of the things that made this

3203
02:02:19,189 --> 02:02:15,760
transition happen was that um we

3204
02:02:22,070 --> 02:02:19,199
the life changed from uh the form of

3205
02:02:26,070 --> 02:02:22,080
life he calls a progenote which is

3206
02:02:28,950 --> 02:02:26,080
not a cell um to a cellular form of life

3207
02:02:33,030 --> 02:02:28,960
and this mode of um

3208
02:02:36,470 --> 02:02:33,040
of of evolution that changes from this

3209
02:02:38,870 --> 02:02:36,480
progenode state to a cellular state is

3210
02:02:41,189 --> 02:02:38,880
what he called the darwinian transition

3211
02:02:43,109 --> 02:02:41,199
so let's think about what evolution is

3212
02:02:44,629 --> 02:02:43,119
like in a prognote state where there

3213
02:02:46,709 --> 02:02:44,639

aren't cells that are defining an

3214

02:02:49,189 --> 02:02:46,719

individual

3215

02:02:51,109 --> 02:02:49,199

and the cost of that or how that changed

3216

02:02:52,870 --> 02:02:51,119

the evolutionary mode he obviously

3217

02:02:54,629 --> 02:02:52,880

thought that it slowed things down and

3218

02:02:55,589 --> 02:02:54,639

that kind of makes sense when you think

3219

02:02:58,950 --> 02:02:55,599

about

3220

02:03:02,070 --> 02:02:58,960

the way horizontal gene transfer and

3221

02:03:04,709 --> 02:03:02,080

recombination shapes um the

3222

02:03:06,790 --> 02:03:04,719

way cells evolve today so the the

3223

02:03:09,189 --> 02:03:06,800

evolutionary mode of the progenote is

3224

02:03:11,510 --> 02:03:09,199

one that he thought was was getting the

3225

02:03:12,950 --> 02:03:11,520

relationship was just trying to put

3226

02:03:15,510 --> 02:03:12,960

together the relationship between

3227

02:03:17,510 --> 02:03:15,520

genotype and phenotype so there were no

3228

02:03:20,709 --> 02:03:17,520

cells it was this kind of super

3229

02:03:22,390 --> 02:03:20,719

molecular aggregate that kind of was

3230

02:03:24,390 --> 02:03:22,400

evolving as a pool

3231

02:03:26,310 --> 02:03:24,400

and that actually in classical

3232

02:03:28,870 --> 02:03:26,320

population genetics

3233

02:03:31,030 --> 02:03:28,880

allows selection to work more quickly

3234

02:03:34,390 --> 02:03:31,040

because it can work independently on

3235

02:03:37,830 --> 02:03:34,400

single pieces of keep single components

3236

02:03:40,070 --> 02:03:37,840

and optimize them specifically for the

3237

02:03:43,430 --> 02:03:40,080

specific conditions that the

3238

02:03:45,589 --> 02:03:43,440

uh protein is evolving um in

3239

02:03:47,669 --> 02:03:45,599

but and it also allows new components to

3240

02:03:49,830 --> 02:03:47,679

come together rather freely without the

3241

02:03:52,550 --> 02:03:49,840

constraints of having to interact or be

3242

02:03:57,750 --> 02:03:52,560

linked together but it comes at a cost

3243

02:04:02,629 --> 02:04:00,629

the way selection acts and you lose

3244

02:04:03,589 --> 02:04:02,639

diversity in that process

3245

02:04:07,189 --> 02:04:03,599

and so

3246

02:04:11,350 --> 02:04:07,199

um this kind of prevents the uh specific

3247

02:04:14,629 --> 02:04:11,360

evolution of a single context specific

3248

02:04:15,990 --> 02:04:14,639

um interaction between these molecules

3249

02:04:16,870 --> 02:04:16,000

so

3250

02:04:18,870 --> 02:04:16,880

um

3251

02:04:21,430 --> 02:04:18,880

he kind of i think based some of these

3252

02:04:24,310 --> 02:04:21,440

ideas on sol spiegelman um who was

3253

02:04:27,270 --> 02:04:24,320

thinking about the origin of cells as

3254

02:04:30,470 --> 02:04:27,280

well and thinking about why chromosomes

3255

02:04:33,030 --> 02:04:30,480

kind of consolidated at this darwinian

3256

02:04:35,189 --> 02:04:33,040

um threshold and so

3257

02:04:38,550 --> 02:04:35,199

he thinks that you know these com this

3258

02:04:40,709 --> 02:04:38,560

complexity and the size of the genome

3259

02:04:43,830 --> 02:04:40,719

was increasing

3260

02:04:47,030 --> 02:04:43,840

and possibly changing into a dna genome

3261

02:04:49,030 --> 02:04:47,040

for this reason to be able to have a

3262

02:04:51,430 --> 02:04:49,040

more complexity

3263

02:04:52,790 --> 02:04:51,440

and be able to solve more complicated

3264

02:04:55,589 --> 02:04:52,800

problems

3265

02:04:57,189 --> 02:04:55,599

but putting it together again has this

3266

02:04:59,270 --> 02:04:57,199

trade-off because now you have

3267

02:05:02,229 --> 02:04:59,280

everything linked together into one

3268

02:05:04,870 --> 02:05:02,239

chromosome inside one cell and all of

3269

02:05:07,270 --> 02:05:04,880

those things being linked prevents

3270

02:05:08,629 --> 02:05:07,280

selection from independently acting on

3271

02:05:10,950 --> 02:05:08,639

anyone

3272

02:05:12,790 --> 02:05:10,960

so this may be going a little far but

3273

02:05:14,950 --> 02:05:12,800

i'm just reminding you population

3274

02:05:16,310 --> 02:05:14,960

genetics that i hope you had a long time

3275

02:05:18,950 --> 02:05:16,320

ago

3276

02:05:22,069 --> 02:05:18,960

where if you have high linkage and the

3277

02:05:24,229 --> 02:05:22,079

selection acts on a particular gene it's

3278

02:05:26,790 --> 02:05:24,239

going to act on the whole region of that

3279

02:05:27,990 --> 02:05:26,800

and in clonal organisms that's the whole

3280

02:05:30,229 --> 02:05:28,000

chromosome

3281

02:05:32,709 --> 02:05:30,239

whereas if there's little pieces and

3282

02:05:34,950 --> 02:05:32,719

aggregates that are independent

3283

02:05:37,910 --> 02:05:34,960

selection can hack act on each one of

3284

02:05:40,950 --> 02:05:37,920

them independently so it decreases the

3285

02:05:43,189 --> 02:05:40,960

efficiency of selection

3286

02:05:47,189 --> 02:05:43,199

but increases the specificity of

3287

02:05:50,709 --> 02:05:47,199

selection to put to consolidate genomes

3288

02:05:54,390 --> 02:05:50,719

in through this darwinian

3289

02:05:56,629 --> 02:05:54,400

transition okay so in that context now

3290

02:05:58,550 --> 02:05:56,639

we can start to think about viruses and

3291

02:06:01,350 --> 02:05:58,560

how what we know about the way these

3292

02:06:03,910 --> 02:06:01,360

consolidated chromosomes all together

3293

02:06:05,910 --> 02:06:03,920

are evolving and i think that we all

3294

02:06:08,390 --> 02:06:05,920

know that um

3295

02:06:09,830 --> 02:06:08,400

by by comparative genomics with many

3296

02:06:11,750 --> 02:06:09,840

different strains and population

3297

02:06:13,910 --> 02:06:11,760

genomics that

3298

02:06:16,069 --> 02:06:13,920

there are still a lot of mobile genes

3299

02:06:18,550 --> 02:06:16,079

that are moving around so we haven't

3300

02:06:21,350 --> 02:06:18,560

fully crossed this threshold into

3301

02:06:23,270 --> 02:06:21,360

completely vertical transmission

3302

02:06:25,830 --> 02:06:23,280

instead there's components of every

3303

02:06:28,870 --> 02:06:25,840

genome that are coming and going

3304

02:06:32,790 --> 02:06:28,880

that have not passed this threshold and

3305

02:06:34,709 --> 02:06:32,800

they allow selection to act efficiently

3306

02:06:37,669 --> 02:06:34,719

and more specifically on those

3307

02:06:39,830 --> 02:06:37,679

components than otherwise

3308

02:06:42,550 --> 02:06:39,840

might happen

3309

02:06:45,669 --> 02:06:42,560

now the difference here is that these

3310

02:06:48,069 --> 02:06:45,679

are independent genetic units

3311

02:06:50,310 --> 02:06:48,079

most of the time i think they're viruses

3312

02:06:52,709 --> 02:06:50,320

and other mobile elements

3313

02:06:53,750 --> 02:06:52,719

that then get kind of co-opted by their

3314

02:06:55,750 --> 02:06:53,760

host

3315

02:06:57,750 --> 02:06:55,760

and so this is where the pangenome

3316

02:06:59,430 --> 02:06:57,760

concept comes in

3317

02:07:01,109 --> 02:06:59,440

which comes from looking at many

3318

02:07:03,030 --> 02:07:01,119

different microbial

3319

02:07:05,510 --> 02:07:03,040

genomes and seeing that there's a core

3320

02:07:08,149 --> 02:07:05,520

genome that evolves as you would think

3321

02:07:10,310 --> 02:07:08,159

it does by the rules of of population

3322

02:07:12,069 --> 02:07:10,320

genetics and the modern synthesis and

3323

02:07:14,149 --> 02:07:12,079

then there's this variable genome which

3324

02:07:15,510 --> 02:07:14,159

is a set of genes that come and go that

3325

02:07:16,709 --> 02:07:15,520

we're still trying to figure out the

3326

02:07:18,709 --> 02:07:16,719

rules on

3327

02:07:21,350 --> 02:07:18,719

and those are important genes that

3328

02:07:23,830 --> 02:07:21,360

encode really important traits we know

3329

02:07:25,910 --> 02:07:23,840

this mostly in pathogens where we've

3330

02:07:28,310 --> 02:07:25,920

seen toxins virulence factors and

3331

02:07:30,310 --> 02:07:28,320

antibiotic resistance moving around and

3332

02:07:32,550 --> 02:07:30,320

spreading on these

3333

02:07:34,310 --> 02:07:32,560

highly mobile genes

3334

02:07:35,750 --> 02:07:34,320

that makes sense in the context of

3335

02:07:38,069 --> 02:07:35,760

selection these things are more

3336

02:07:39,510 --> 02:07:38,079

efficiently under selection if they're

3337

02:07:43,109 --> 02:07:39,520

highly mobile

3338

02:07:45,830 --> 02:07:43,119

so um but if they're their own lifestyle

3339

02:07:48,149 --> 02:07:45,840

their own fitness viruses then we have

3340

02:07:50,790 --> 02:07:48,159

to start thinking about the interaction

3341

02:07:52,950 --> 02:07:50,800

between the chromosome and viruses as a

3342

02:07:56,950 --> 02:07:52,960

symbiosis and how they evolve

3343

02:07:57,669 --> 02:07:56,960

independently and separately um to um

3344

02:08:00,229 --> 02:07:57,679

to

3345

02:08:03,030 --> 02:08:00,239

in this mode of evolution that i think

3346

02:08:04,229 --> 02:08:03,040

is kind of beyond the darwinian

3347

02:08:06,310 --> 02:08:04,239

transition

3348

02:08:08,390 --> 02:08:06,320

that brings us into this more mobile

3349

02:08:10,149 --> 02:08:08,400

world

3350

02:08:12,310 --> 02:08:10,159

so what are the evolutionary rules we

3351

02:08:14,149 --> 02:08:12,320

need to start looking at um

3352

02:08:16,790 --> 02:08:14,159

at the different types of viruses there

3353

02:08:19,669 --> 02:08:16,800

are and i know that viruses are very

3354

02:08:20,950 --> 02:08:19,679

famous for their antagonistic

3355

02:08:24,629 --> 02:08:20,960

effects on

3356

02:08:27,189 --> 02:08:24,639

on communities and populations and

3357

02:08:29,189 --> 02:08:27,199

they certainly are changing dynamics and

3358

02:08:31,350 --> 02:08:29,199

microbiomes and and

3359

02:08:34,149 --> 02:08:31,360

um are really

3360

02:08:36,149 --> 02:08:34,159

important in that way but i think what's

3361

02:08:38,550 --> 02:08:36,159

often missed is the other forms of

3362

02:08:41,270 --> 02:08:38,560

viruses the ones that are latent that

3363

02:08:43,430 --> 02:08:41,280

are in the chromosome as pro viruses and

3364

02:08:45,990 --> 02:08:43,440

are being transmitted from generation

3365

02:08:48,310 --> 02:08:46,000

disgeneration vertically and co-evolving

3366

02:08:50,229 --> 02:08:48,320

with their host chromosome background

3367

02:08:53,189 --> 02:08:50,239

and then chronic viruses like the one

3368

02:08:55,589 --> 02:08:53,199

i'm going to talk about which like ssv

3369

02:08:59,350 --> 02:08:55,599

which doesn't kill its host and kill its

3370

02:09:01,589 --> 02:08:59,360

host as it um as it is transmitted but

3371

02:09:04,470 --> 02:09:01,599

buds from the host and so that allows

3372

02:09:06,709 --> 02:09:04,480

the symbiosis to possibly evolve towards

3373

02:09:09,589 --> 02:09:06,719

more of a mutualism between the virus

3374

02:09:11,830 --> 02:09:09,599

and the host chromosome

3375

02:09:13,830 --> 02:09:11,840

so i think we know very little about

3376

02:09:15,589 --> 02:09:13,840

viruses in general and their different

3377

02:09:18,629 --> 02:09:15,599

lifestyles because they're really hard

3378

02:09:20,550 --> 02:09:18,639

to study on a kind of a population level

3379

02:09:22,629 --> 02:09:20,560

and one of the breakthroughs that is

3380

02:09:25,589 --> 02:09:22,639

allowing us to do that is crispr cast

3381

02:09:27,910 --> 02:09:25,599

immunity so i don't need to talk about

3382

02:09:30,709 --> 02:09:27,920

the specifics of crispr cast immunity

3383

02:09:32,790 --> 02:09:30,719

and the elegant immune system that that

3384

02:09:34,550 --> 02:09:32,800

has evolved because i'm sure you all

3385

02:09:36,790 --> 02:09:34,560

know about that but i just want to

3386

02:09:38,870 --> 02:09:36,800

remind you that this also provides a

3387

02:09:41,109 --> 02:09:38,880

tool for evolutionary biologists to keep

3388

02:09:43,109 --> 02:09:41,119

track of virus host interactions over

3389

02:09:47,109 --> 02:09:43,119

time so the

3390

02:09:49,589 --> 02:09:47,119

in the process of acquiring immunity to

3391

02:09:53,189 --> 02:09:49,599

viruses through crisprs

3392

02:09:55,270 --> 02:09:53,199

um bacterial and archaeal cells add new

3393

02:09:57,910 --> 02:09:55,280

spacers onto their

3394

02:10:00,790 --> 02:09:57,920

on into their genome add a new component

3395

02:10:03,270 --> 02:10:00,800

a small component sequence piece of the

3396

02:10:05,830 --> 02:10:03,280

genome of the virus into their own

3397

02:10:07,430 --> 02:10:05,840

chromosome they record a memory of that

3398

02:10:10,310 --> 02:10:07,440

interaction

3399

02:10:12,629 --> 02:10:10,320

in the crispr cast immunity and that

3400

02:10:14,229 --> 02:10:12,639

allows us to look back at populations

3401

02:10:15,990 --> 02:10:14,239

and try to figure out what kind of

3402

02:10:18,470 --> 02:10:16,000

interactions are happening between

3403

02:10:20,790 --> 02:10:18,480

viruses and hosts and how this might be

3404

02:10:22,709 --> 02:10:20,800

impacting their evolution over time

3405

02:10:24,790 --> 02:10:22,719

because of the population signatures

3406

02:10:27,030 --> 02:10:24,800

that are in the crispr arrays or in the

3407

02:10:28,390 --> 02:10:27,040

immune diversity so we've been using

3408

02:10:30,149 --> 02:10:28,400

immune diversity

3409

02:10:32,149 --> 02:10:30,159

to link um

3410

02:10:34,550 --> 02:10:32,159

microbial cells to

3411

02:10:36,390 --> 02:10:34,560

their viruses and also to try to

3412

02:10:38,790 --> 02:10:36,400

understand how their interactions are

3413

02:10:41,669 --> 02:10:38,800

happening in natural populations

3414

02:10:44,069 --> 02:10:41,679

because this is really hard to do

3415

02:10:46,470 --> 02:10:44,079

so now i was just going to give a little

3416

02:10:49,109 --> 02:10:46,480

example of what we've learned by doing

3417

02:10:51,750 --> 02:10:49,119

this and how this uncovers aspects of

3418

02:10:53,350 --> 02:10:51,760

symbiosis that you might not um have

3419

02:10:55,109 --> 02:10:53,360

thought about

3420

02:10:57,350 --> 02:10:55,119

or that we that one might not think

3421

02:11:00,229 --> 02:10:57,360

about in any system

3422

02:11:03,430 --> 02:11:00,239

and that is to look at this population

3423

02:11:06,470 --> 02:11:03,440

of cell pholubus icelandicus um cell

3424

02:11:10,790 --> 02:11:06,480

pholipus is a g is a lives in geothermal

3425

02:11:11,830 --> 02:11:10,800

hot springs in meta populations and it

3426

02:11:15,510 --> 02:11:11,840

um

3427

02:11:17,750 --> 02:11:15,520

is a hyperthermophilic chronarchia

3428

02:11:18,950 --> 02:11:17,760

and acetophile

3429

02:11:20,629 --> 02:11:18,960

um and

3430

02:11:22,870 --> 02:11:20,639

because it evolves in these meta

3431

02:11:25,830 --> 02:11:22,880

populations we're looking at dynamics

3432

02:11:28,790 --> 02:11:25,840

across this like nested scale which is

3433

02:11:31,510 --> 02:11:28,800

how the virus interacts with the host

3434

02:11:33,430 --> 02:11:31,520

with its host with sulfolobis how that

3435

02:11:36,149 --> 02:11:33,440

interaction changes interactions with

3436

02:11:38,229 --> 02:11:36,159

other organisms in the hot spring and i

3437

02:11:40,229 --> 02:11:38,239

call this an island because it's very

3438

02:11:42,069 --> 02:11:40,239

clearly defined and so we can link

3439

02:11:44,790 --> 02:11:42,079

dynamics that are happening between

3440

02:11:48,550 --> 02:11:44,800

virus and host to this one relatively

3441

02:11:50,950 --> 02:11:48,560

well-defined ecosystem and compare the

3442

02:11:52,629 --> 02:11:50,960

different ecosystems to each other and

3443

02:11:54,950 --> 02:11:52,639

to understand the dynamics that are

3444

02:11:56,310 --> 02:11:54,960

specific within and between them and

3445

02:11:58,629 --> 02:11:56,320

then we're putting that into kind of a

3446

02:12:01,030 --> 02:11:58,639

whole big global context

3447

02:12:02,790 --> 02:12:01,040

although we don't see migration between

3448

02:12:05,990 --> 02:12:02,800

these different locations that we've

3449

02:12:07,510 --> 02:12:06,000

sampled for viruses or for hosts so

3450

02:12:09,830 --> 02:12:07,520

we've looked really closely at two

3451

02:12:11,669 --> 02:12:09,840

populations of sofolobis

3452

02:12:14,069 --> 02:12:11,679

one from yellowstone national park and

3453

02:12:15,830 --> 02:12:14,079

one from kamchatka russia

3454

02:12:18,149 --> 02:12:15,840

and

3455

02:12:19,990 --> 02:12:18,159

kind of looked at the dynamics that are

3456

02:12:23,030 --> 02:12:20,000

happening in those populations in their

3457

02:12:25,189 --> 02:12:23,040

genomes and what it told us was that the

3458

02:12:28,629 --> 02:12:25,199

dynamics are basically

3459

02:12:29,510 --> 02:12:28,639

driven by viruses and mobile elements um

3460

02:12:40,470 --> 02:12:29,520

the

3461

02:12:42,390 --> 02:12:40,480

factors like crisprs that

3462

02:12:45,030 --> 02:12:42,400

caught that mediate the interaction

3463

02:12:46,390 --> 02:12:45,040

between viruses and their hosts so we've

3464

02:12:49,669 --> 02:12:46,400

isolated

3465

02:12:51,669 --> 02:12:49,679

a 10 year time series of hosts and

3466

02:12:56,149 --> 02:12:51,679

viruses from these two independent

3467

02:12:57,990 --> 02:12:56,159

populations um and you can see here that

3468

02:12:59,830 --> 02:12:58,000

they're different between the different

3469

02:13:03,030 --> 02:12:59,840

populations so

3470

02:13:05,430 --> 02:13:03,040

in yellowstone we find mostly sirvs

3471

02:13:07,350 --> 02:13:05,440

which are lytic viruses while we also

3472

02:13:09,910 --> 02:13:07,360

find chronic

3473

02:13:11,669 --> 02:13:09,920

ssvs as well but we don't find them

3474

02:13:13,669 --> 02:13:11,679

plaquing as much and we find them

3475

02:13:16,870 --> 02:13:13,679

integrated into the chromosome in

3476

02:13:19,990 --> 02:13:16,880

kamtaka we find ssvs that that cause

3477

02:13:21,830 --> 02:13:20,000

plaques and no sirvs but we find a

3478

02:13:23,990 --> 02:13:21,840

couple other lytic viruses that we're

3479

02:13:27,589 --> 02:13:24,000

working on characterizing so we have the

3480

02:13:31,750 --> 02:13:27,599

same interaction between a single um

3481

02:13:34,229 --> 02:13:31,760

host type so the lubus type and

3482

02:13:36,629 --> 02:13:34,239

the same virus and two kind of different

3483

02:13:38,870 --> 02:13:36,639

ecosystems with other viruses around

3484

02:13:40,550 --> 02:13:38,880

them so we're trying to understand how

3485

02:13:44,550 --> 02:13:40,560

the co-evolution between the chronic

3486

02:13:46,229 --> 02:13:44,560

virus and its um sofalopus host is

3487

02:13:47,669 --> 02:13:46,239

changing in these different viral

3488

02:13:51,990 --> 02:13:47,679

contexts

3489

02:13:53,990 --> 02:13:52,000

okay so um lots of years of work by um

3490

02:13:55,990 --> 02:13:54,000

but mostly not done by me have

3491

02:13:59,189 --> 02:13:56,000

characterized the interactions between

3492

02:14:01,910 --> 02:13:59,199

sulfolobis and sirv

3493

02:14:03,270 --> 02:14:01,920

and also between cell pholubus endostate

3494

02:14:07,189 --> 02:14:03,280

virus and

3495

02:14:10,310 --> 02:14:07,199

um and sulfolubus and um

3496

02:14:12,629 --> 02:14:10,320

we know that this sirv is lytic it has

3497

02:14:15,910 --> 02:14:12,639

this amazing pyramids that cause that

3498

02:14:19,589 --> 02:14:15,920

cause the cells to lyse whereas uh so

3499

02:14:21,830 --> 02:14:19,599

ssv is a budding virus that is chronic

3500

02:14:23,669 --> 02:14:21,840

um we know that there are globally that

3501

02:14:25,990 --> 02:14:23,679

both the host and the viruses are

3502

02:14:27,910 --> 02:14:26,000

globally isolated so there's specific

3503

02:14:29,350 --> 02:14:27,920

genotypes income chaka that are

3504

02:14:31,669 --> 02:14:29,360

different from the ones that are in

3505

02:14:33,910 --> 02:14:31,679

yellowstone suggesting there might be

3506

02:14:36,310 --> 02:14:33,920

local adaptation between hosts and

3507

02:14:39,830 --> 02:14:36,320

viruses in these contexts and we've

3508

02:14:42,069 --> 02:14:39,840

looked most closely at the ssv and

3509

02:14:44,069 --> 02:14:42,079

islandic sulfur libous icelandicus

3510

02:14:46,950 --> 02:14:44,079

interaction in

3511

02:14:49,910 --> 02:14:46,960

kanchaka russia which is a large

3512

02:14:52,310 --> 02:14:49,920

population that's well mixed and pretty

3513

02:14:56,149 --> 02:14:52,320

stable over time meaning we've gone

3514

02:14:59,189 --> 02:14:56,159

there in 2000 and 2010 and seen the same

3515

02:15:01,990 --> 02:14:59,199

level of crispr diversity

3516

02:15:03,910 --> 02:15:02,000

main and virus diversity maintained over

3517

02:15:07,430 --> 02:15:03,920

time

3518

02:15:10,149 --> 02:15:07,440

and the maintenance of that large

3519

02:15:12,149 --> 02:15:10,159

large diversity of crispr alleles tells

3520

02:15:14,470 --> 02:15:12,159

us that there's some kind there's not

3521

02:15:17,109 --> 02:15:14,480

like selective sweeps of viruses that

3522

02:15:19,189 --> 02:15:17,119

are happening in these populations that

3523

02:15:20,790 --> 02:15:19,199

are clearing diversity at least immune

3524

02:15:23,990 --> 02:15:20,800

diversity out

3525

02:15:25,830 --> 02:15:24,000

so that's an interesting dynamic that is

3526

02:15:28,550 --> 02:15:25,840

i think we think is conferred by

3527

02:15:31,990 --> 02:15:28,560

crispers so the crispers kind of

3528

02:15:35,030 --> 02:15:32,000

influence allow this stable diversity in

3529

02:15:36,870 --> 02:15:35,040

crispr and the hosts um to evolve and

3530

02:15:38,870 --> 02:15:36,880

we've looked very

3531

02:15:40,629 --> 02:15:38,880

closely at this using modeling

3532

02:15:45,030 --> 02:15:40,639

approaches

3533

02:15:47,189 --> 02:15:45,040

to identify what aspects of the system

3534

02:15:50,069 --> 02:15:47,199

might allow it to

3535

02:15:51,589 --> 02:15:50,079

evolve this diversity and where if we

3536

02:15:54,390 --> 02:15:51,599

don't have this diversity what the

3537

02:15:55,510 --> 02:15:54,400

impact on the host and virus population

3538

02:15:56,709 --> 02:15:55,520

are

3539

02:15:59,109 --> 02:15:56,719

and so

3540

02:16:00,790 --> 02:15:59,119

this is an example an old example now we

3541

02:16:02,709 --> 02:16:00,800

have many more

3542

02:16:05,270 --> 02:16:02,719

complex examples that we've looked at

3543

02:16:08,149 --> 02:16:05,280

more closely now but

3544

02:16:10,470 --> 02:16:08,159

it's a simulation showing that this kind

3545

02:16:12,950 --> 02:16:10,480

of diversity can persist you can see

3546

02:16:15,350 --> 02:16:12,960

there's many colors of host in some of

3547

02:16:18,470 --> 02:16:15,360

these peaks and those colors mean that

3548

02:16:20,950 --> 02:16:18,480

you have many different crispr alleles

3549

02:16:23,830 --> 02:16:20,960

coexisting in a single population and

3550

02:16:26,629 --> 02:16:23,840

they all match the same virus but in

3551

02:16:29,270 --> 02:16:26,639

different ways so it's this the idea

3552

02:16:30,470 --> 02:16:29,280

that you can have a one to many one

3553

02:16:33,349 --> 02:16:30,480

viruses

3554

02:16:35,429 --> 02:16:33,359

virus matches many different immune

3555

02:16:38,950 --> 02:16:35,439

alleles that

3556

02:16:40,150 --> 02:16:38,960

controls the dynamics of this system

3557

02:16:41,910 --> 02:16:40,160

and so we've looked at what those

3558

02:16:43,910 --> 02:16:41,920

dynamics are and we see that when

3559

02:16:46,790 --> 02:16:43,920

there's a high diversity or what we call

3560

02:16:47,589 --> 02:16:46,800

distributed immunity the viruses are

3561

02:16:50,389 --> 02:16:47,599

have

3562

02:16:52,309 --> 02:16:50,399

difficulty persisting and

3563

02:16:54,950 --> 02:16:52,319

go extinct in the population probably

3564

02:16:57,830 --> 02:16:54,960

because they're at very low numbers

3565

02:17:00,389 --> 02:16:57,840

because they have to find a host and so

3566

02:17:01,990 --> 02:17:00,399

we see this in kamchatka

3567

02:17:04,629 --> 02:17:02,000

we see that there's

3568

02:17:07,349 --> 02:17:04,639

these ssvs that are persisting and yet

3569

02:17:10,950 --> 02:17:07,359

we see high distributed immunity to this

3570

02:17:13,190 --> 02:17:10,960

virus in this population and we don't

3571

02:17:14,389 --> 02:17:13,200

really were asked and we were asking how

3572

02:17:16,389 --> 02:17:14,399

this could be

3573

02:17:18,629 --> 02:17:16,399

because the virus shouldn't be able to

3574

02:17:20,309 --> 02:17:18,639

survive and persist in an environment

3575

02:17:23,190 --> 02:17:20,319

where there's this

3576

02:17:25,270 --> 02:17:23,200

really diversified crispr cast immunity

3577

02:17:27,429 --> 02:17:25,280

so we've calculated population

3578

02:17:28,870 --> 02:17:27,439

distributed immunity in the different

3579

02:17:31,270 --> 02:17:28,880

populations that we've looked at

3580

02:17:33,750 --> 02:17:31,280

relative to ssv and seen that it's

3581

02:17:36,070 --> 02:17:33,760

pretty high and that if you use these

3582

02:17:38,709 --> 02:17:36,080

calculations to try to predict whether

3583

02:17:41,349 --> 02:17:38,719

the virus should persist it's very

3584

02:17:44,790 --> 02:17:41,359

unlikely to invade and persist in this

3585

02:17:49,750 --> 02:17:44,800

ecosystem it's just really hard for any

3586

02:17:51,669 --> 02:17:49,760

ssv to find a host it can infect

3587

02:17:56,309 --> 02:17:51,679

so we tried to look at this in the lab

3588

02:17:57,349 --> 02:17:56,319

we took ssv the ssv9 which can isolated

3589

02:18:06,709 --> 02:17:57,359

and

3590

02:18:09,509 --> 02:18:06,719

establish a chronic infection in the lab

3591

02:18:11,270 --> 02:18:09,519

and we can see that the infected cells

3592

02:18:14,309 --> 02:18:11,280

grow as you would predict with a chronic

3593

02:18:16,309 --> 02:18:14,319

virus and produce viruses over time but

3594

02:18:18,549 --> 02:18:16,319

also we've been able to show that crispr

3595

02:18:20,469 --> 02:18:18,559

immunity works against this virus by

3596

02:18:22,870 --> 02:18:20,479

genetically engineering the system to

3597

02:18:26,070 --> 02:18:22,880

knock out crispers and so that only in

3598

02:18:28,549 --> 02:18:26,080

the crispr knockouts can this virus

3599

02:18:30,549 --> 02:18:28,559

persist so there is this dynamic where

3600

02:18:33,190 --> 02:18:30,559

crispers recognize

3601

02:18:35,750 --> 02:18:33,200

ssv and yet ssv persists in the

3602

02:18:37,589 --> 02:18:35,760

population so we had this question of

3603

02:18:39,669 --> 02:18:37,599

how this can happen and we tested this

3604

02:18:42,469 --> 02:18:39,679

question by

3605

02:18:45,429 --> 02:18:42,479

competing an infected strain against an

3606

02:18:46,870 --> 02:18:45,439

immune strain in the lab and this is

3607

02:18:49,349 --> 02:18:46,880

where we uncovered something that we

3608

02:18:52,709 --> 02:18:49,359

were kind of surprised to find

3609

02:18:55,110 --> 02:18:52,719

the ssv infection has a small cost to

3610

02:18:57,190 --> 02:18:55,120

the host so the persistent chronic

3611

02:18:59,509 --> 02:18:57,200

infection has a small cost to the host

3612

02:19:02,549 --> 02:18:59,519

we haven't been able to measure a cost

3613

02:19:04,709 --> 02:19:02,559

in the um of the immunity

3614

02:19:06,389 --> 02:19:04,719

but when we put the two cells together

3615

02:19:09,030 --> 02:19:06,399

the infected strain

3616

02:19:10,870 --> 02:19:09,040

wins every time so the top graph here

3617

02:19:14,230 --> 02:19:10,880

you see the competition between an

3618

02:19:15,750 --> 02:19:14,240

immune strain and an uninfected um

3619

02:19:18,070 --> 02:19:15,760

strain of

3620

02:19:20,629 --> 02:19:18,080

sulfolopus and you can see that they

3621

02:19:23,030 --> 02:19:20,639

they persist over the time scale that we

3622

02:19:25,750 --> 02:19:23,040

were looking at whereas if you put the

3623

02:19:27,990 --> 02:19:25,760

same background infected strain and

3624

02:19:30,870 --> 02:19:28,000

compete it with an immune strain the

3625

02:19:33,429 --> 02:19:30,880

infected strain wins and actually kills

3626

02:19:34,709 --> 02:19:33,439

off the rest of the

3627

02:19:37,669 --> 02:19:34,719

immune

3628

02:19:39,990 --> 02:19:37,679

and uninfected cells

3629

02:19:42,709 --> 02:19:40,000

so we've looked at this as

3630

02:19:45,750 --> 02:19:42,719

we think this is a mutualism it allows a

3631

02:19:48,070 --> 02:19:45,760

host to invade even when rare the host

3632

02:19:50,389 --> 02:19:48,080

cell if it's carrying a virus it can

3633

02:19:52,070 --> 02:19:50,399

invade a new population by killing off

3634

02:19:55,030 --> 02:19:52,080

competitors whether or not they're

3635

02:19:57,110 --> 02:19:55,040

immune and that helps the host and it

3636

02:19:58,790 --> 02:19:57,120

helps the virus because the virus

3637

02:20:00,790 --> 02:19:58,800

probably wouldn't be able to find any

3638

02:20:03,990 --> 02:20:00,800

hosts in that

3639

02:20:07,990 --> 02:20:04,000

very diverse crispr population

3640

02:20:10,550 --> 02:20:08,000

so we have this um idea that the chronic

3641

02:20:14,230 --> 02:20:10,560

virus has turned into this mutualist

3642

02:20:17,030 --> 02:20:14,240

conferring a very adaptive trait in a

3643

02:20:19,349 --> 02:20:17,040

competitive trait to the host which is

3644

02:20:22,230 --> 02:20:19,359

killing its competitors and in the

3645

02:20:26,469 --> 02:20:22,240

meanwhile also um

3646

02:20:28,790 --> 02:20:26,479

establishing its its own fitness um in a

3647

02:20:30,389 --> 02:20:28,800

a population that has very few

3648

02:20:34,230 --> 02:20:30,399

susceptible hosts

3649

02:20:37,510 --> 02:20:34,240

um so this is just an example i i it's

3650

02:20:39,670 --> 02:20:37,520

you know an idiosyncrasy perhaps but i

3651
02:20:42,309 --> 02:20:39,680
think it shows how

3652
02:20:44,710 --> 02:20:42,319
the virus host interaction can evolve

3653
02:20:47,429 --> 02:20:44,720
new traits for the host

3654
02:20:50,870 --> 02:20:47,439
that change its fitness in the in a

3655
02:20:52,790 --> 02:20:50,880
population and that is the kind of

3656
02:20:54,389 --> 02:20:52,800
selection we're talking about when we're

3657
02:20:56,950 --> 02:20:54,399
talking about

3658
02:20:58,630 --> 02:20:56,960
moving genes around and sometimes virus

3659
02:20:59,670 --> 02:20:58,640
infection really changes the traits of

3660
02:21:01,590 --> 02:20:59,680
the host

3661
02:21:03,590 --> 02:21:01,600
as it's evolving through

3662
02:21:06,389 --> 02:21:03,600
evolutionary time

3663
02:21:08,469 --> 02:21:06,399

so just don't forget i guess it's not it

3664

02:21:10,630 --> 02:21:08,479

goes without saying here that this these

3665

02:21:12,870 --> 02:21:10,640

types of interactions are happening

3666

02:21:16,870 --> 02:21:12,880

everywhere all the time

3667

02:21:20,550 --> 02:21:16,880

and maybe they're compensating for this

3668

02:21:23,990 --> 02:21:20,560

loss of flexibility that came

3669

02:21:26,630 --> 02:21:24,000

with the darwinian transition where we

3670

02:21:29,050 --> 02:21:26,640

transitioned to an individual cellular

3671

02:21:30,150 --> 02:21:29,060

vertical mode of evolution

3672

02:21:32,389 --> 02:21:30,160

[Music]

3673

02:21:33,270 --> 02:21:32,399

um so this is my

3674

02:21:35,990 --> 02:21:33,280

uh

3675

02:21:37,750 --> 02:21:36,000

lab the i chose two

3676

02:21:40,870 --> 02:21:37,760

different pictures that are actually out

3677

02:21:43,349 --> 02:21:40,880

of date now but because the work has has

3678

02:21:44,950 --> 02:21:43,359

been going forward through time

3679

02:21:46,790 --> 02:21:44,960

to highlight the people that actually

3680

02:21:48,790 --> 02:21:46,800

did the work

3681

02:21:52,550 --> 02:21:48,800

in the top picture

3682

02:21:54,550 --> 02:21:52,560

maria bautista really isolated the ssv

3683

02:21:55,910 --> 02:21:54,560

and made it tractable to work with in

3684

02:21:59,510 --> 02:21:55,920

the lab

3685

02:22:00,870 --> 02:21:59,520

in our model system changing did all the

3686

02:22:04,309 --> 02:22:00,880

genetics

3687

02:22:08,070 --> 02:22:04,319

that we needed to test crispr function

3688

02:22:10,469 --> 02:22:08,080

and the and samantha dwarf is has been

3689

02:22:13,110 --> 02:22:10,479

working on the interaction between

3690

02:22:14,710 --> 02:22:13,120

infected and uninfected cells

3691

02:22:17,670 --> 02:22:14,720

and we are

3692

02:22:19,750 --> 02:22:17,680

very collaborative with lots of labs all

3693

02:22:22,389 --> 02:22:19,760

around the world and that's really

3694

02:22:23,670 --> 02:22:22,399

important to note especially on this

3695

02:22:29,030 --> 02:22:23,680

work

3696

02:22:31,670 --> 02:22:29,040

the modeling and mark young

3697

02:22:34,230 --> 02:22:31,680

to do the virus isolation

3698

02:22:36,630 --> 02:22:34,240

and we're now working on new models with

3699

02:22:38,150 --> 02:22:36,640

mercedes pascal at the university of

3700

02:22:40,309 --> 02:22:38,160

chicago

3701

02:22:45,290 --> 02:22:40,319

and so i'd love to have any questions if

3702

02:22:45,300 --> 02:22:50,469

[Applause]

3703

02:22:56,070 --> 02:22:52,070

i guess let's open it up for questions

3704

02:22:56,080 --> 02:23:04,950

i have far too many but i'll wait

3705

02:23:10,469 --> 02:23:06,790

well maybe i'll start with one just uh

3706

02:23:12,710 --> 02:23:10,479

to fire things off um i do the killer

3707

02:23:14,070 --> 02:23:12,720

killer archaeas or the sharkayas i saw

3708

02:23:14,950 --> 02:23:14,080

your nice little image there in the

3709

02:23:18,389 --> 02:23:14,960

corner

3710

02:23:20,790 --> 02:23:18,399

um do you think that the

3711

02:23:23,030 --> 02:23:20,800

um this killer effect might also have

3712

02:23:25,670 --> 02:23:23,040

something to do with what maria found

3713

02:23:27,510 --> 02:23:25,680

again with the ssv9

3714

02:23:29,830 --> 02:23:27,520

and the

3715

02:23:31,349 --> 02:23:29,840

um dormancy effect do you think there

3716

02:23:34,790 --> 02:23:31,359

might be something there do you have any

3717

02:23:37,670 --> 02:23:34,800

ideas what might be going on there

3718

02:23:40,550 --> 02:23:37,680

yes and we're working on this um it is

3719

02:23:42,389 --> 02:23:40,560

the same we've identified the killer as

3720

02:23:44,870 --> 02:23:42,399

a toxin

3721

02:23:48,710 --> 02:23:44,880

it's a protein that's

3722

02:23:50,309 --> 02:23:48,720

produced by the cells exogenous

3723

02:23:54,630 --> 02:23:50,319

it

3724

02:23:59,190 --> 02:23:54,640

washed away

3725

02:24:00,550 --> 02:23:59,200

and persists in the environment then the

3726

02:24:04,230 --> 02:24:00,560

cells die

3727

02:24:06,710 --> 02:24:04,240

so i think um what the fact that she was

3728

02:24:07,830 --> 02:24:06,720

seeing with dormancy was that she would

3729

02:24:09,670 --> 02:24:07,840

um

3730

02:24:12,230 --> 02:24:09,680

she would challenge the cells with the

3731

02:24:13,190 --> 02:24:12,240

supernatant presumably with the toxin in

3732

02:24:18,070 --> 02:24:13,200

it

3733

02:24:21,030 --> 02:24:18,080

and so the dormancy was a reaction to

3734

02:24:22,870 --> 02:24:21,040

that um to seeing that toxin and then

3735

02:24:25,670 --> 02:24:22,880

being released from whatever effect it

3736

02:24:28,469 --> 02:24:25,680

was we're working on what happens in the

3737

02:24:31,190 --> 02:24:28,479

cell in response to this toxin and why

3738

02:24:33,270 --> 02:24:31,200

the infected cells don't get killed by

3739

02:24:34,870 --> 02:24:33,280

the toxin themselves and are resistant

3740

02:24:47,990 --> 02:24:34,880

to it

3741

02:24:51,750 --> 02:24:49,590

so if no one else will i'll keep going

3742

02:24:53,270 --> 02:24:51,760

on this too so um there as you well know

3743

02:24:55,349 --> 02:24:53,280

there are you know toxin antitoxin

3744

02:24:56,630 --> 02:24:55,359

systems also in in sulphur lowest but

3745

02:24:58,550 --> 02:24:56,640

many other organisms you think this is a

3746

02:25:00,870 --> 02:24:58,560

more generalizable thing you can start

3747

02:25:01,990 --> 02:25:00,880

thinking about toxin eddy toxins

3748

02:25:03,429 --> 02:25:02,000

as well

3749

02:25:05,190 --> 02:25:03,439

in these sort of you know not

3750

02:25:06,950 --> 02:25:05,200

necessarily killer archaea but you know

3751

02:25:07,830 --> 02:25:06,960

killer bacteria killer other kinds of

3752

02:25:10,469 --> 02:25:07,840

things

3753

02:25:12,950 --> 02:25:10,479

sure and i also think that um it's

3754

02:25:15,510 --> 02:25:12,960

actually good so one of the puzzling

3755

02:25:16,710 --> 02:25:15,520

pieces for a long time press was why

3756

02:25:18,630 --> 02:25:16,720

would uh

3757

02:25:21,670 --> 02:25:18,640

a virus want to kill

3758

02:25:24,150 --> 02:25:21,680

possible susceptible new hosts

3759

02:25:26,630 --> 02:25:24,160

and i think that the ant we think now

3760

02:25:27,830 --> 02:25:26,640

that the anti-toxin must be encoded on

3761

02:25:33,190 --> 02:25:27,840

the virus

3762

02:25:34,790 --> 02:25:33,200

n is not recognized by immunity then

3763

02:25:36,950 --> 02:25:34,800

those hosts live

3764

02:25:38,710 --> 02:25:36,960

so it's kind of a way of the virus

3765

02:25:41,349 --> 02:25:38,720

screening through

3766

02:25:44,389 --> 02:25:41,359

immune cells because you have to it's

3767

02:25:46,469 --> 02:25:44,399

like a addiction system but exogenous

3768

02:25:48,710 --> 02:25:46,479

right so you have to get infected in

3769

02:25:50,870 --> 02:25:48,720

order to resist the toxin

3770

02:25:53,510 --> 02:25:50,880

um which i think is really interesting

3771

02:25:55,270 --> 02:25:53,520

and seems pretty powerful so i would be

3772

02:25:57,349 --> 02:25:55,280

surprised if it hadn't

3773

02:26:07,590 --> 02:25:57,359

evolved elsewhere

3774

02:26:12,389 --> 02:26:09,510

i could keep asking questions about this

3775

02:26:15,590 --> 02:26:12,399

for ages as you know i'm a bit of a

3776

02:26:19,990 --> 02:26:17,270

um

3777

02:26:21,910 --> 02:26:20,000

in in the interests of everyone you know

3778

02:26:23,429 --> 02:26:21,920

needing physiology breaks and so on and

3779

02:26:25,110 --> 02:26:23,439

so forth and this is i think a great

3780

02:26:27,110 --> 02:26:25,120

lead-in to joshua vites who's actually

3781

02:26:29,910 --> 02:26:27,120

talking right after the break oh great

3782

02:26:31,270 --> 02:26:29,920

unless somebody else has any other

3783

02:26:32,870 --> 02:26:31,280

thoughts should we just go ahead and go

3784

02:26:35,270 --> 02:26:32,880

on break until

3785

02:26:36,870 --> 02:26:35,280

10 40 pacific

3786

02:26:38,389 --> 02:26:36,880

that work for everyone

3787

02:26:40,710 --> 02:26:38,399

i think that's a great idea i also

3788

02:26:42,469 --> 02:26:40,720

wanted to highlight if everyone has time

3789

02:26:44,389 --> 02:26:42,479

actually look at the comments that are

3790

02:26:46,790 --> 02:26:44,399

in zoom they're actually some great

3791

02:26:49,510 --> 02:26:46,800

engaging conversations and be great to

3792

02:26:51,349 --> 02:26:49,520

get more feedback from people or just

3793

02:26:53,590 --> 02:26:51,359

really think about it i really love the

3794

02:26:54,389 --> 02:26:53,600

discussion that's going on there also we

3795

02:26:56,950 --> 02:26:54,399

will

3796

02:26:58,950 --> 02:26:56,960

have that transcript available uh takes

3797

02:27:00,389 --> 02:26:58,960

maybe a couple days for us to figure out

3798

02:27:01,990 --> 02:27:00,399

how to do that

3799

02:27:03,590 --> 02:27:02,000

but we are recording everybody's

3800

02:27:05,429 --> 02:27:03,600

comments so

3801

02:27:07,990 --> 02:27:05,439

a lot of these topics

3802

02:27:09,190 --> 02:27:08,000

uh can be folded into our follow-on

3803

02:27:10,630 --> 02:27:09,200

discussions

3804

02:27:13,830 --> 02:27:10,640

you know in the process of putting

3805

02:27:16,389 --> 02:27:13,840

together a paper in the white paper

3806

02:27:17,670 --> 02:27:16,399

all right great time thank you

3807

02:27:19,910 --> 02:27:17,680

we're good to go

3808

02:27:21,830 --> 02:27:19,920

okay great thank you

3809

02:27:24,389 --> 02:27:21,840

thanks for having me here today this

3810

02:27:25,510 --> 02:27:24,399

virtual workshop my name is joshua weitz

3811

02:27:27,830 --> 02:27:25,520

and i'll be talking about viral

3812

02:27:30,469 --> 02:27:27,840

infection modes invasion fitness

3813

02:27:32,070 --> 02:27:30,479

across a continuum from lysis to latency

3814

02:27:33,830 --> 02:27:32,080

and i've hidden myself so i assume you

3815

02:27:35,190 --> 02:27:33,840

can see me and you can see these slides

3816

02:27:36,790 --> 02:27:35,200

is that right and you can hear my voice

3817

02:27:38,950 --> 02:27:36,800

someone get great

3818

02:27:41,030 --> 02:27:38,960

okay and let's see as long as i can

3819

02:27:42,870 --> 02:27:41,040

get it to advance that would be good so

3820

02:27:44,550 --> 02:27:42,880

we've heard a lot about viruses already

3821

02:27:47,110 --> 02:27:44,560

today i'm sure tomorrow is well and

3822

02:27:48,389 --> 02:27:47,120

usually when one thinks about viruses at

3823

02:27:50,230 --> 02:27:48,399

least in

3824

02:27:51,990 --> 02:27:50,240

a public setting it's often because one

3825

02:27:53,910 --> 02:27:52,000

is thinking about

3826

02:27:56,469 --> 02:27:53,920

see again if my buttons are clicking

3827

02:28:04,150 --> 02:27:59,270

sorry for the

3828

02:28:10,150 --> 02:28:06,469

let me see if we've

3829

02:28:12,469 --> 02:28:11,510

there we go

3830

02:28:14,550 --> 02:28:12,479

uh

3831

02:28:16,469 --> 02:28:14,560

we usually talk about viruses in public

3832

02:28:19,349 --> 02:28:16,479

context in terms of those viruses that

3833

02:28:21,429 --> 02:28:19,359

might cause uh mortality and morbidity

3834

02:28:22,790 --> 02:28:21,439

uh with respect to humans human diseases

3835

02:28:25,429 --> 02:28:22,800

like ebola

3836

02:28:27,429 --> 02:28:25,439

zika or influenza and i think it's fair

3837

02:28:29,349 --> 02:28:27,439

to say that this audience knows that

3838

02:28:31,270 --> 02:28:29,359

viruses infect organisms really across

3839

02:28:34,070 --> 02:28:31,280

the span of diversity of life from

3840

02:28:36,070 --> 02:28:34,080

humans mammals birds insects also plants

3841

02:28:38,710 --> 02:28:36,080

but crucially also microbes in other

3842

02:28:40,790 --> 02:28:38,720

words microbes get sick too and i've

3843

02:28:43,429 --> 02:28:40,800

given some examples and the prior talk

3844

02:28:45,349 --> 02:28:43,439

uh touched on one of those uh the sulfur

3845

02:28:47,190 --> 02:28:45,359

spindle viruses and other archaeal

3846

02:28:49,830 --> 02:28:47,200

viruses and also of course there are

3847

02:28:51,270 --> 02:28:49,840

viruses of bacteria amoeba and so on and

3848

02:28:52,550 --> 02:28:51,280

so i'm going to spend some time today

3849

02:28:54,469 --> 02:28:52,560

using these

3850

02:28:57,510 --> 02:28:54,479

virus and microbes particularly viruses

3851
02:28:59,510 --> 02:28:57,520
of bacteria as a means to think about

3852
02:29:02,550 --> 02:28:59,520
the ways in which infection mode might

3853
02:29:04,790 --> 02:29:02,560
differ and not necessarily

3854
02:29:06,790 --> 02:29:04,800
always be antagonistic to hosts so just

3855
02:29:07,830 --> 02:29:06,800
to get everyone on the same page

3856
02:29:10,790 --> 02:29:07,840
you're probably aware that when

3857
02:29:12,309 --> 02:29:10,800
bacterial viruses phage bacteria phage

3858
02:29:14,550 --> 02:29:12,319
or in the environment they might diffuse

3859
02:29:17,190 --> 02:29:14,560
until they're in contact with a target

3860
02:29:19,670 --> 02:29:17,200
cell inject their genetic material into

3861
02:29:21,190 --> 02:29:19,680
the host redirect cellular machinery in

3862
02:29:23,190 --> 02:29:21,200
order to make more

3863
02:29:25,830 --> 02:29:23,200

genetic material viral genetic material

3864

02:29:27,830 --> 02:29:25,840

which can self-assembles uh and into

3865

02:29:30,389 --> 02:29:27,840

these mature virions and through a time

3866

02:29:32,469 --> 02:29:30,399

process uh often there's a hole that's

3867

02:29:34,070 --> 02:29:32,479

made in the inner membrane

3868

02:29:36,309 --> 02:29:34,080

some cleavage in the cell wall and then

3869

02:29:37,750 --> 02:29:36,319

through a time process releases these

3870

02:29:39,750 --> 02:29:37,760

virus particles back into the

3871

02:29:41,349 --> 02:29:39,760

environment and so clearly for that

3872

02:29:44,230 --> 02:29:41,359

particular cell

3873

02:29:46,150 --> 02:29:44,240

that's the end of its uh its life but

3874

02:29:47,830 --> 02:29:46,160

that doesn't necessarily mean that the

3875

02:29:49,110 --> 02:29:47,840

death of one cell is the death of a

3876

02:29:50,630 --> 02:29:49,120

population

3877

02:29:52,870 --> 02:29:50,640

so because of this antagonistic

3878

02:29:54,309 --> 02:29:52,880

relationship the fact that this virus in

3879

02:29:57,110 --> 02:29:54,319

some ways

3880

02:29:58,550 --> 02:29:57,120

consumes or eats the hosts fajros from

3881

02:30:00,070 --> 02:29:58,560

to devour

3882

02:30:01,670 --> 02:30:00,080

the predator prey model has been the

3883

02:30:03,990 --> 02:30:01,680

basis for quite a lot of studies of

3884

02:30:06,630 --> 02:30:04,000

virus micro population dynamics how we

3885

02:30:09,190 --> 02:30:06,640

move from cellular level models up to

3886

02:30:11,270 --> 02:30:09,200

population level models and so here on

3887

02:30:13,110 --> 02:30:11,280

the left i've just given one variant of

3888

02:30:15,110 --> 02:30:13,120

a classic example and again my

3889

02:30:17,349 --> 02:30:15,120

background is theory and modeling and

3890

02:30:19,190 --> 02:30:17,359

here you have interaction between some

3891

02:30:21,670 --> 02:30:19,200

resources that are being flowed into the

3892

02:30:23,750 --> 02:30:21,680

system cells that take up those

3893

02:30:25,990 --> 02:30:23,760

resources and viruses that infect

3894

02:30:27,910 --> 02:30:26,000

reproduce and kill those cells and the

3895

02:30:29,750 --> 02:30:27,920

left-hand side denotes a non-linear

3896

02:30:31,510 --> 02:30:29,760

dynamical system where you have

3897

02:30:33,830 --> 02:30:31,520

resources are

3898

02:30:35,349 --> 02:30:33,840

bacteria and viruses v

3899

02:30:37,590 --> 02:30:35,359

and again the process of nutrient

3900

02:30:40,790 --> 02:30:37,600

consumption turns resources into cells

3901
02:30:43,270 --> 02:30:40,800
infection turns cells into more viruses

3902
02:30:45,750 --> 02:30:43,280
and with these simple ingredients

3903
02:30:48,870 --> 02:30:45,760
one can track the expected dynamics in

3904
02:30:51,030 --> 02:30:48,880
time and here on the right i've shown

3905
02:30:53,270 --> 02:30:51,040
time implicitly where prey is on the

3906
02:30:55,270 --> 02:30:53,280
x-axis and prey on the y-axis and

3907
02:30:57,190 --> 02:30:55,280
what you see are these counterclockwise

3908
02:30:59,030 --> 02:30:57,200
cycles in other words when there are a

3909
02:31:00,950 --> 02:30:59,040
lot of prey around the viruses do well

3910
02:31:03,510 --> 02:31:00,960
increasing in abundance when there are a

3911
02:31:05,429 --> 02:31:03,520
lot of viruses they drive the prey down

3912
02:31:07,030 --> 02:31:05,439
when there are few prey then viruses go

3913
02:31:09,270 --> 02:31:07,040

down and because there are a few viruses

3914

02:31:11,429 --> 02:31:09,280

then bacteria can recover and these are

3915

02:31:12,870 --> 02:31:11,439

really lockable terror like dynamics so

3916

02:31:15,270 --> 02:31:12,880

for the same reasons you see these

3917

02:31:16,630 --> 02:31:15,280

oscillations within lynx hair systems

3918

02:31:18,230 --> 02:31:16,640

it's presumably the same reason you

3919

02:31:19,429 --> 02:31:18,240

might see them within virus microbe

3920

02:31:21,110 --> 02:31:19,439

systems

3921

02:31:23,349 --> 02:31:21,120

and there's experimental evidence that

3922

02:31:25,030 --> 02:31:23,359

these kinds of population cycles can be

3923

02:31:26,790 --> 02:31:25,040

observed in the laboratory these are

3924

02:31:28,950 --> 02:31:26,800

classic work brendan bohan and rich

3925

02:31:32,469 --> 02:31:28,960

lenski and their predator prey-like

3926

02:31:34,150 --> 02:31:32,479

cycles between phage t4 and e coli b

3927

02:31:35,830 --> 02:31:34,160

it's about a seven to eight day

3928

02:31:37,830 --> 02:31:35,840

experiment here

3929

02:31:39,910 --> 02:31:37,840

and you can see with time

3930

02:31:41,990 --> 02:31:39,920

oscillations of large magnitude and the

3931

02:31:44,550 --> 02:31:42,000

population densities of viruses and

3932

02:31:47,349 --> 02:31:44,560

hosts you can see at times virus to host

3933

02:31:49,429 --> 02:31:47,359

ratios don't just get to be one or ten

3934

02:31:50,309 --> 02:31:49,439

to one but can be a hundred to one or

3935

02:31:52,230 --> 02:31:50,319

more

3936

02:31:54,710 --> 02:31:52,240

and the oscillations are not because of

3937

02:31:56,469 --> 02:31:54,720

some exogenous driving of the system

3938

02:31:58,150 --> 02:31:56,479

it's not as if the system is being

3939

02:32:00,309 --> 02:31:58,160

driven by some oscillatory resource

3940

02:32:03,270 --> 02:32:00,319

input this is in a chemostat

3941

02:32:05,910 --> 02:32:03,280

with steady flow of minimal media and

3942

02:32:07,990 --> 02:32:05,920

nonetheless the feedback between virus

3943

02:32:10,230 --> 02:32:08,000

and microbes at the cellular level

3944

02:32:12,070 --> 02:32:10,240

translates into endogenous large scale

3945

02:32:14,389 --> 02:32:12,080

oscillations and they're shifted if you

3946

02:32:16,309 --> 02:32:14,399

notice the peaks of the virals

3947

02:32:18,950 --> 02:32:16,319

abundances are slightly shifted forward

3948

02:32:19,750 --> 02:32:18,960

in time with respect to bacterial peaks

3949

02:32:22,469 --> 02:32:19,760

okay

3950

02:32:23,590 --> 02:32:22,479

and so with that in mind

3951

02:32:25,670 --> 02:32:23,600

and i'm sorry that there's some

3952

02:32:27,830 --> 02:32:25,680

technical issues here

3953

02:32:31,030 --> 02:32:27,840

the sharing screen seems to forget that

3954

02:32:33,590 --> 02:32:31,040

i am here with a computer

3955

02:32:35,270 --> 02:32:33,600

so maybe

3956

02:32:37,670 --> 02:32:35,280

let me

3957

02:32:39,030 --> 02:32:37,680

go back is there any way i can do this

3958

02:32:40,469 --> 02:32:39,040

just by

3959

02:32:45,110 --> 02:32:40,479

zooming in it's the sharing of the

3960

02:32:51,270 --> 02:32:47,910

let's see if i go into that view

3961

02:32:54,950 --> 02:32:53,349

okay sorry about that delay this way at

3962

02:32:57,590 --> 02:32:54,960

least i can click on the new slide if i

3963

02:33:02,710 --> 02:32:59,590

and so these virus host interactions

3964

02:33:03,910 --> 02:33:02,720

modify the fit of cells on short time

3965

02:33:08,070 --> 02:33:03,920

scales

3966

02:33:09,830 --> 02:33:08,080

accept there to be oscillatory dynamics

3967

02:33:12,070 --> 02:33:09,840

and then once you start scaling this up

3968

02:33:14,389 --> 02:33:12,080

to ecosystems this effect of killing

3969

02:33:15,190 --> 02:33:14,399

individual cells and populations can

3970

02:33:16,790 --> 02:33:15,200

have

3971

02:33:18,230 --> 02:33:16,800

large ecosystem level effects

3972

02:33:20,309 --> 02:33:18,240

particularly we're insured often in

3973

02:33:22,389 --> 02:33:20,319

global oceans and part of the reason for

3974

02:33:24,950 --> 02:33:22,399

that is that the number of viruses

3975

02:33:27,030 --> 02:33:24,960

outnumber those of microbes largely

3976

02:33:29,510 --> 02:33:27,040

bacteria but some archaea anywhere from

3977

02:33:30,870 --> 02:33:29,520

about one to one to a hundred to one and

3978

02:33:33,349 --> 02:33:30,880

if you look on the axis here we're

3979

02:33:35,910 --> 02:33:33,359

talking about typical densities of 50

3980

02:33:37,830 --> 02:33:35,920

million 50 million uh viruses or

3981

02:33:39,990 --> 02:33:37,840

virus-like particles per milliliter

3982

02:33:41,349 --> 02:33:40,000

again in excess of those of bacteria so

3983

02:33:43,429 --> 02:33:41,359

all that lysis

3984

02:33:46,550 --> 02:33:43,439

presumably leads to big

3985

02:33:48,710 --> 02:33:46,560

changes in microbial densities

3986

02:33:50,389 --> 02:33:48,720

effects on microbial mortality as well

3987

02:33:52,469 --> 02:33:50,399

as the regeneration of carbon and other

3988

02:33:54,230 --> 02:33:52,479

nutrients back into the environment

3989

02:33:56,070 --> 02:33:54,240

but all the examples i've given thus far

3990

02:33:58,550 --> 02:33:56,080

really focuses on the effective viruses

3991

02:34:01,349 --> 02:33:58,560

as killing agents antagonistic

3992

02:34:02,710 --> 02:34:01,359

uh obligate intracellular parasites that

3993

02:34:04,710 --> 02:34:02,720

end up just killing the host in order to

3994

02:34:06,710 --> 02:34:04,720

make more of themselves so the question

3995

02:34:08,150 --> 02:34:06,720

i want to ask and really focus on

3996

02:34:10,150 --> 02:34:08,160

in my time today is do viruses and

3997

02:34:12,150 --> 02:34:10,160

microbes do more than kill

3998

02:34:14,230 --> 02:34:12,160

or prepare to kill

3999

02:34:16,790 --> 02:34:14,240

and the answer is yes and has been known

4000

02:34:19,670 --> 02:34:16,800

to be yes for quite a long time

4001

02:34:21,349 --> 02:34:19,680

and lysogeny and tempered phage

4002

02:34:23,030 --> 02:34:21,359

really provide a number of lessons from

4003

02:34:25,830 --> 02:34:23,040

a simple system going all the way back

4004

02:34:28,550 --> 02:34:25,840

to andre loff and others of

4005

02:34:30,469 --> 02:34:28,560

the pantheon of those who understood

4006

02:34:32,389 --> 02:34:30,479

viruses and tried to understand

4007

02:34:35,190 --> 02:34:32,399

the viral impacts on gene regulation and

4008

02:34:37,590 --> 02:34:35,200

molecular biology and the key idea

4009

02:34:39,349 --> 02:34:37,600

within tempered phage is that you have

4010

02:34:41,990 --> 02:34:39,359

the injection of the genetic material

4011

02:34:44,469 --> 02:34:42,000

into the host but then a genetic switch

4012

02:34:46,550 --> 02:34:44,479

really a decision between two

4013

02:34:49,030 --> 02:34:46,560

pathways one which is lysis which i've

4014

02:34:51,830 --> 02:34:49,040

already described and the other which is

4015

02:34:53,429 --> 02:34:51,840

integration of the viral genome into the

4016

02:34:55,910 --> 02:34:53,439

cellular genome

4017

02:34:58,389 --> 02:34:55,920

where it is termed a prophage and that

4018

02:35:00,870 --> 02:34:58,399

prophage that viral genome can then

4019

02:35:03,590 --> 02:35:00,880

terribly be passed on from mother to

4020

02:35:06,389 --> 02:35:03,600

daughter cell across the replication and

4021

02:35:09,270 --> 02:35:06,399

at some later point can be induced and

4022

02:35:12,710 --> 02:35:09,280

by induced i mean that the prophage

4023

02:35:14,630 --> 02:35:12,720

excises itself from the cellular genome

4024

02:35:16,150 --> 02:35:14,640

reinitiating the lytic cycle and then

4025

02:35:17,910 --> 02:35:16,160

heads out again

4026

02:35:19,750 --> 02:35:17,920

and although this is classic work

4027

02:35:22,070 --> 02:35:19,760

there's still quite a lot of activity

4028

02:35:25,190 --> 02:35:22,080

trying to understand these switches both

4029

02:35:28,070 --> 02:35:25,200

that switch in how to be temperate how

4030

02:35:30,150 --> 02:35:28,080

to make this decision after the virus

4031

02:35:32,150 --> 02:35:30,160

injects this genetic material and then

4032

02:35:33,830 --> 02:35:32,160

how the process of induction works this

4033

02:35:34,950 --> 02:35:33,840

is one example from the work of edo

4034

02:35:37,110 --> 02:35:34,960

golding

4035

02:35:38,870 --> 02:35:37,120

who is soon to be i believe at uiuc he's

4036

02:35:40,790 --> 02:35:38,880

been at baylor college of medicine for a

4037

02:35:43,429 --> 02:35:40,800

number of years and using a labeling

4038

02:35:46,710 --> 02:35:43,439

system is able you see in panel b

4039

02:35:49,030 --> 02:35:46,720

identify when i phage because the capsid

4040

02:35:52,150 --> 02:35:49,040

has been marked with this yfp has

4041

02:35:54,550 --> 02:35:52,160

attached excuse me to a cell and then

4042

02:35:57,030 --> 02:35:54,560

depending on the fate there's a reporter

4043

02:35:59,750 --> 02:35:57,040

system that those cells that have been

4044

02:36:01,270 --> 02:35:59,760

faded to lysogyny turn red so they're

4045

02:36:03,190 --> 02:36:01,280

normally growing and you can see them

4046

02:36:05,910 --> 02:36:03,200

actually divide and that red color pass

4047

02:36:08,070 --> 02:36:05,920

terribly between the two cells and those

4048

02:36:09,510 --> 02:36:08,080

cells that then produce new phages

4049

02:36:11,270 --> 02:36:09,520

produce these

4050

02:36:12,389 --> 02:36:11,280

again labeled phage

4051
02:36:15,270 --> 02:36:12,399
and the point i want to make here

4052
02:36:17,830 --> 02:36:15,280
although these are dichotomous outcomes

4053
02:36:18,710 --> 02:36:17,840
these decisions are probabilistic

4054
02:36:21,030 --> 02:36:18,720
meaning

4055
02:36:23,510 --> 02:36:21,040
it's not as if a particular

4056
02:36:24,790 --> 02:36:23,520
cell or particular virus encodes yes 100

4057
02:36:27,030 --> 02:36:24,800
of the time going this way and then

4058
02:36:29,030 --> 02:36:27,040
deterministically depending on the state

4059
02:36:30,950 --> 02:36:29,040
of the host it'll pop out

4060
02:36:32,150 --> 02:36:30,960
there is a relationship between cell

4061
02:36:34,230 --> 02:36:32,160
state

4062
02:36:36,550 --> 02:36:34,240
particularly if the cell is not in a

4063
02:36:38,309 --> 02:36:36,560

good state maybe a phage can detect that

4064

02:36:40,150 --> 02:36:38,319

and get out there's also a relationship

4065

02:36:41,910 --> 02:36:40,160

between multiplicity of infection other

4066

02:36:44,469 --> 02:36:41,920

factors and that is a long and

4067

02:36:45,990 --> 02:36:44,479

interesting topic maybe for another day

4068

02:36:49,270 --> 02:36:46,000

and all that revolves on how to be

4069

02:36:51,830 --> 02:36:49,280

tempered how does a virus regulate

4070

02:36:53,670 --> 02:36:51,840

detect what's going on in a cell in a

4071

02:36:55,190 --> 02:36:53,680

way that can change these probabilities

4072

02:36:56,950 --> 02:36:55,200

this initial decision switch and this

4073

02:36:58,630 --> 02:36:56,960

induction switch

4074

02:37:00,630 --> 02:36:58,640

but there's another question which is an

4075

02:37:02,870 --> 02:37:00,640

evolutionary question which is why to be

4076

02:37:04,550 --> 02:37:02,880

tempered in the first place

4077

02:37:06,710 --> 02:37:04,560

and frank stewart and bruce levin in the

4078

02:37:08,950 --> 02:37:06,720

mid 80s asked this question and they

4079

02:37:10,550 --> 02:37:08,960

proposed one of many uh a feast or

4080

02:37:12,309 --> 02:37:10,560

famine hypothesis

4081

02:37:13,349 --> 02:37:12,319

the idea that tempered phage do better

4082

02:37:15,030 --> 02:37:13,359

when there are a few hosts that are

4083

02:37:16,950 --> 02:37:15,040

available and the extracellular

4084

02:37:19,190 --> 02:37:16,960

mortality rate is high but but they did

4085

02:37:21,270 --> 02:37:19,200

offer a caveat and they said in spite of

4086

02:37:23,190 --> 02:37:21,280

the intuitive appeal of this low-density

4087

02:37:25,670 --> 02:37:23,200

hypothesis they're unable to find

4088

02:37:27,270 --> 02:37:25,680

solutions meaning they could impose

4089

02:37:29,429 --> 02:37:27,280

those conditions and that seemed to

4090

02:37:31,190 --> 02:37:29,439

favor the temperate phage

4091

02:37:33,030 --> 02:37:31,200

but it wasn't as if they understood the

4092

02:37:34,550 --> 02:37:33,040

principles by which that might happen so

4093

02:37:36,389 --> 02:37:34,560

the idea is that maybe when there are

4094

02:37:38,710 --> 02:37:36,399

fewer phages around it's better not to

4095

02:37:41,110 --> 02:37:38,720

kill off the last hosts but that has a

4096

02:37:43,990 --> 02:37:41,120

bit of a group selection or aspirational

4097

02:37:45,349 --> 02:37:44,000

level to the argument

4098

02:37:47,030 --> 02:37:45,359

though there is some evidence that this

4099

02:37:48,790 --> 02:37:47,040

is really what happens or at least that

4100

02:37:50,870 --> 02:37:48,800

had been the paradigm

4101
02:37:53,349 --> 02:37:50,880
in marine systems there was a notion of

4102
02:37:55,270 --> 02:37:53,359
seasonal time bombs the idea that in low

4103
02:37:57,349 --> 02:37:55,280
productivity low density environments

4104
02:37:58,630 --> 02:37:57,359
this is work by jennifer brum

4105
02:38:01,670 --> 02:37:58,640
and colleagues there are other similar

4106
02:38:03,830 --> 02:38:01,680
studies that when you look and use an

4107
02:38:05,750 --> 02:38:03,840
induction assay to try to pull out the

4108
02:38:08,710 --> 02:38:05,760
number of lysogens pull phage out that

4109
02:38:10,550 --> 02:38:08,720
are lysogens when over the winter or

4110
02:38:12,469 --> 02:38:10,560
spring there are less productivity and

4111
02:38:13,910 --> 02:38:12,479
fewer cells then in fact you see a lot

4112
02:38:15,910 --> 02:38:13,920
of lysogens and in the summer when

4113
02:38:18,309 --> 02:38:15,920

things are productive in a lot of cells

4114

02:38:19,590 --> 02:38:18,319

then you don't see many lysogens in

4115

02:38:21,990 --> 02:38:19,600

contrast when you look under the

4116

02:38:23,830 --> 02:38:22,000

microscope there's a higher fraction of

4117

02:38:24,790 --> 02:38:23,840

lytically infected cells

4118

02:38:26,469 --> 02:38:24,800

okay

4119

02:38:28,630 --> 02:38:26,479

and so that's the contrast here between

4120

02:38:30,230 --> 02:38:28,640

the top and the bottom panel and this

4121

02:38:32,870 --> 02:38:30,240

had been the paradigm until i would say

4122

02:38:35,030 --> 02:38:32,880

just a few years ago when an alternative

4123

02:38:36,710 --> 02:38:35,040

hypothesis was presented it's turned

4124

02:38:38,469 --> 02:38:36,720

piggy back the winner some of you may be

4125

02:38:40,469 --> 02:38:38,479

familiar with it the idea is really

4126

02:38:42,710 --> 02:38:40,479

quite the opposite the claim is that

4127

02:38:44,230 --> 02:38:42,720

misogyny is positively correlated with

4128

02:38:46,070 --> 02:38:44,240

increases in host density and

4129

02:38:47,990 --> 02:38:46,080

productivity in other words lytic

4130

02:38:49,429 --> 02:38:48,000

activity goes down as there's more

4131

02:38:51,429 --> 02:38:49,439

productive or

4132

02:38:52,950 --> 02:38:51,439

denser environments and there's a

4133

02:38:55,750 --> 02:38:52,960

background to why

4134

02:38:57,110 --> 02:38:55,760

this was of interest to the authors

4135

02:38:59,190 --> 02:38:57,120

and also

4136

02:39:01,270 --> 02:38:59,200

some additional context on density

4137

02:39:03,590 --> 02:39:01,280

relationships but there's some direct

4138

02:39:05,590 --> 02:39:03,600

evidence that they presented by looking

4139

02:39:08,150 --> 02:39:05,600

at a range of microbial densities and on

4140

02:39:10,950 --> 02:39:08,160

the y-axis here evidence from

4141

02:39:12,790 --> 02:39:10,960

metagenomics that there was some

4142

02:39:15,030 --> 02:39:12,800

increase in lysogen we have to use

4143

02:39:16,630 --> 02:39:15,040

proxies here by looking environments

4144

02:39:19,030 --> 02:39:16,640

they look for things like the percent of

4145

02:39:20,230 --> 02:39:19,040

pro virus like reeds things that might

4146

02:39:23,110 --> 02:39:20,240

indicate

4147

02:39:25,270 --> 02:39:23,120

the potential for latency

4148

02:39:27,750 --> 02:39:25,280

and despite claims in the paper i would

4149

02:39:29,830 --> 02:39:27,760

argue as you see here that there's not a

4150

02:39:33,590 --> 02:39:29,840

really strong relationship between the y

4151
02:39:35,590 --> 02:39:33,600
and the x-axis for pro-virus-like reads

4152
02:39:38,710 --> 02:39:35,600
there's not a strong relation between

4153
02:39:40,870 --> 02:39:38,720
the y and x-axis for integrases

4154
02:39:43,670 --> 02:39:40,880
nor for excision agents and these are

4155
02:39:45,190 --> 02:39:43,680
all indicators of things that look like

4156
02:39:46,790 --> 02:39:45,200
they have the potential getting in and

4157
02:39:48,389 --> 02:39:46,800
getting out

4158
02:39:49,750 --> 02:39:48,399
so the takeaway at least from my

4159
02:39:51,349 --> 02:39:49,760
perspective is that at the moment

4160
02:39:53,429 --> 02:39:51,359
there's an absence of evidence for a

4161
02:39:55,510 --> 02:39:53,439
positive correlation between lysogenic

4162
02:39:57,590 --> 02:39:55,520
proxies and cell density

4163
02:39:59,750 --> 02:39:57,600

and what can be more about that there's

4164

02:40:02,070 --> 02:39:59,760

other ways to look for these proxies by

4165

02:40:03,510 --> 02:40:02,080

looking directly at ratios of viruses to

4166

02:40:06,150 --> 02:40:03,520

microbes as a proxy i think there are

4167

02:40:08,230 --> 02:40:06,160

other issues there but nonetheless i do

4168

02:40:10,150 --> 02:40:08,240

think that this paper and to some of

4169

02:40:12,389 --> 02:40:10,160

this you know debate and back and forth

4170

02:40:14,070 --> 02:40:12,399

has raised perhaps even a more important

4171

02:40:15,510 --> 02:40:14,080

question which is what are the

4172

02:40:17,190 --> 02:40:15,520

environmental conditions that should

4173

02:40:19,349 --> 02:40:17,200

favor lysogeny

4174

02:40:21,830 --> 02:40:19,359

over lysis i don't think that question

4175

02:40:24,710 --> 02:40:21,840

has been resolved and i'm going to try

4176
02:40:26,790 --> 02:40:24,720
to begin to address that question today

4177
02:40:29,190 --> 02:40:26,800
by turning to an old lesson that some of

4178
02:40:30,550 --> 02:40:29,200
you probably know and it turns out that

4179
02:40:31,670 --> 02:40:30,560
there are different

4180
02:40:33,030 --> 02:40:31,680
ways of saying this in different

4181
02:40:34,710 --> 02:40:33,040
languages and cultures the one i'm

4182
02:40:36,710 --> 02:40:34,720
familiar with is a bird in the hand is

4183
02:40:39,190 --> 02:40:36,720
worth two in the bush

4184
02:40:41,429 --> 02:40:39,200
the idea you have something now

4185
02:40:43,429 --> 02:40:41,439
and you might trade it for something in

4186
02:40:44,790 --> 02:40:43,439
the future but you better trade up

4187
02:40:46,309 --> 02:40:44,800
because you're not certain of how much

4188
02:40:48,389 --> 02:40:46,319

you're going to get

4189

02:40:50,469 --> 02:40:48,399

and so i claim that this relates to a

4190

02:40:52,469 --> 02:40:50,479

puzzle that we should be asking

4191

02:40:54,070 --> 02:40:52,479

which is a virus in the cell's worth and

4192

02:40:55,910 --> 02:40:54,080

in the bloom

4193

02:40:58,630 --> 02:40:55,920

but what is n

4194

02:41:01,030 --> 02:40:58,640

right the virus has the cell right now

4195

02:41:03,990 --> 02:41:01,040

sure it could put out a whole bunch of

4196

02:41:06,790 --> 02:41:04,000

virus or virus particles back into the

4197

02:41:09,269 --> 02:41:06,800

environment but how many is worth

4198

02:41:11,269 --> 02:41:09,279

sending back out versus the one cell

4199

02:41:13,510 --> 02:41:11,279

that you have right now

4200

02:41:16,150 --> 02:41:13,520

and so i want to make this comparison

4201
02:41:18,070 --> 02:41:16,160
more direct by talking about the notion

4202
02:41:20,309 --> 02:41:18,080
of viral proliferation

4203
02:41:21,910 --> 02:41:20,319
and thinking about what really is the

4204
02:41:23,349 --> 02:41:21,920
fitness of these different viral

4205
02:41:24,870 --> 02:41:23,359
strategies when we view them at the

4206
02:41:26,950 --> 02:41:24,880
individual level

4207
02:41:28,870 --> 02:41:26,960
and i'll start with the typical idea of

4208
02:41:30,630 --> 02:41:28,880
lytic viruses where you have this virus

4209
02:41:32,950 --> 02:41:30,640
it encounters

4210
02:41:36,389 --> 02:41:32,960
a cell infects the cell i'm going to

4211
02:41:38,550 --> 02:41:36,399
call that the mother virus as opposed to

4212
02:41:40,389 --> 02:41:38,560
the mother cell

4213
02:41:42,469 --> 02:41:40,399

and it eventually will lyse and produce

4214

02:41:44,710 --> 02:41:42,479

100 virus particles i'm going to make

4215

02:41:47,670 --> 02:41:44,720

the claim that that is not its fitness

4216

02:41:49,590 --> 02:41:47,680

a hundred is not how many uh

4217

02:41:52,550 --> 02:41:49,600

the offspring that particular mother

4218

02:41:54,309 --> 02:41:52,560

virus has because 97 of those virus

4219

02:41:55,830 --> 02:41:54,319

particles might never find a new

4220

02:41:58,309 --> 02:41:55,840

susceptible cell

4221

02:41:59,910 --> 02:41:58,319

they might decay be unstable or so on

4222

02:42:01,429 --> 02:41:59,920

and in this particular example only

4223

02:42:04,550 --> 02:42:01,439

three

4224

02:42:06,870 --> 02:42:04,560

find encounter and successfully infect

4225

02:42:08,790 --> 02:42:06,880

into a new cell and we'll call those

4226
02:42:10,710 --> 02:42:08,800
daughter viruses and so therefore i

4227
02:42:12,469 --> 02:42:10,720
would claim that in this case the

4228
02:42:13,910 --> 02:42:12,479
fitness at the individual level the

4229
02:42:15,590 --> 02:42:13,920
number of offspring over the course of

4230
02:42:16,630 --> 02:42:15,600
the lifetime of this mother virus is

4231
02:42:17,750 --> 02:42:16,640
three

4232
02:42:19,990 --> 02:42:17,760
and they've

4233
02:42:22,230 --> 02:42:20,000
been obtained horizontally

4234
02:42:25,269 --> 02:42:22,240
via horizontal transmission from one

4235
02:42:27,830 --> 02:42:25,279
cell to other cells in the environment

4236
02:42:30,469 --> 02:42:27,840
on the other hand latent viruses also

4237
02:42:33,269 --> 02:42:30,479
have a way of reproducing

4238
02:42:36,389 --> 02:42:33,279

the mother virus might divide

4239

02:42:38,150 --> 02:42:36,399

and therefore produce progeny daughters

4240

02:42:40,070 --> 02:42:38,160

and daughter viruses that they will

4241

02:42:41,990 --> 02:42:40,080

count their own fitness on their own and

4242

02:42:43,349 --> 02:42:42,000

if the mother cell divides three times

4243

02:42:44,870 --> 02:42:43,359

before it dies whether because it's

4244

02:42:47,030 --> 02:42:44,880

grazed or

4245

02:42:49,349 --> 02:42:47,040

sticks to something or lyses for some

4246

02:42:51,269 --> 02:42:49,359

other reason now just in vertical

4247

02:42:52,550 --> 02:42:51,279

transmission alone it's also possible to

4248

02:42:54,389 --> 02:42:52,560

have the same

4249

02:42:56,150 --> 02:42:54,399

fitness okay

4250

02:42:58,150 --> 02:42:56,160

so the point i'm trying to make here is

4251
02:42:59,910 --> 02:42:58,160
that two vastly different strategies can

4252
02:43:02,070 --> 02:42:59,920
lead to the same notion or calculation

4253
02:43:04,309 --> 02:43:02,080
of fitness at the individual level

4254
02:43:05,750 --> 02:43:04,319
and from an ecological perspective it

4255
02:43:08,389 --> 02:43:05,760
would be good to know how this depends

4256
02:43:09,750 --> 02:43:08,399
on cell densities and other factors if

4257
02:43:11,349 --> 02:43:09,760
we're beginning to understand which of

4258
02:43:13,670 --> 02:43:11,359
these particular strategies might be

4259
02:43:16,150 --> 02:43:13,680
favored or continuum of these strategies

4260
02:43:18,870 --> 02:43:16,160
might be favored in the environment

4261
02:43:20,389 --> 02:43:18,880
so to do that what my group has done in

4262
02:43:23,349 --> 02:43:20,399
collaboration with

4263
02:43:25,349 --> 02:43:23,359

rachel whitaker with some folks uh uh

4264

02:43:28,150 --> 02:43:25,359

in my group juan lin lia student and

4265

02:43:29,910 --> 02:43:28,160

mike cortez uh a former postdoc now

4266

02:43:33,030 --> 02:43:29,920

faculty and hire a google deck also

4267

02:43:35,269 --> 02:43:33,040

former osaka now faculty is take this

4268

02:43:37,670 --> 02:43:35,279

individual perspective and translate it

4269

02:43:38,950 --> 02:43:37,680

into a population perspective

4270

02:43:40,870 --> 02:43:38,960

so i've given you the example on the

4271

02:43:41,990 --> 02:43:40,880

bottom left of what happens for the

4272

02:43:44,710 --> 02:43:42,000

individual

4273

02:43:46,630 --> 02:43:44,720

the top is meant to be a box model

4274

02:43:49,910 --> 02:43:46,640

describing susceptible cells that can

4275

02:43:52,389 --> 02:43:49,920

become infected that generate offspring

4276

02:43:54,710 --> 02:43:52,399

various virus particles these viruses

4277

02:43:56,950 --> 02:43:54,720

then re-effect and start the cycle and

4278

02:43:59,269 --> 02:43:56,960

the right-hand side is the translation

4279

02:44:00,870 --> 02:43:59,279

of those into a dynamical system

4280

02:44:02,389 --> 02:44:00,880

and i just want to point out here that

4281

02:44:04,389 --> 02:44:02,399

this last equation the change in the

4282

02:44:06,950 --> 02:44:04,399

number of virus particles goes up

4283

02:44:09,110 --> 02:44:06,960

because of lysis so every time at a rate

4284

02:44:10,710 --> 02:44:09,120

ada that the cell is lysed it produces

4285

02:44:13,429 --> 02:44:10,720

beta offspring

4286

02:44:15,990 --> 02:44:13,439

and virus particles are lost because

4287

02:44:17,190 --> 02:44:16,000

they're removed due to infection or due

4288

02:44:18,469 --> 02:44:17,200

to decay

4289

02:44:20,309 --> 02:44:18,479

and i'm not going to go into all the

4290

02:44:22,550 --> 02:44:20,319

details today

4291

02:44:24,230 --> 02:44:22,560

other than to say that one can calculate

4292

02:44:25,830 --> 02:44:24,240

instead of that number three a generic

4293

02:44:28,469 --> 02:44:25,840

description of how

4294

02:44:30,150 --> 02:44:28,479

many offspring

4295

02:44:31,910 --> 02:44:30,160

the virus might have in terms of this

4296

02:44:34,070 --> 02:44:31,920

complete cell cycle from an infected

4297

02:44:36,150 --> 02:44:34,080

cell to new infected cells

4298

02:44:37,670 --> 02:44:36,160

in terms of these details here but i'll

4299

02:44:38,630 --> 02:44:37,680

just translate them

4300

02:44:40,389 --> 02:44:38,640

which is

4301
02:44:42,710 --> 02:44:40,399
the number of virus particles produce

4302
02:44:44,710 --> 02:44:42,720
you start with 100

4303
02:44:46,710 --> 02:44:44,720
a fraction of those

4304
02:44:49,190 --> 02:44:46,720
reach a new uh

4305
02:44:50,710 --> 02:44:49,200
cell before they decay and only a

4306
02:44:52,389 --> 02:44:50,720
certain fraction of them are going to

4307
02:44:54,150 --> 02:44:52,399
lyse before they wash out so that's the

4308
02:44:56,710 --> 02:44:54,160
complete cycle the virus gets into a

4309
02:44:58,870 --> 02:44:56,720
cell it has a probability of releasing

4310
02:45:00,870 --> 02:44:58,880
beta particles and only a fraction of

4311
02:45:03,429 --> 02:45:00,880
those make it to the new cell and that

4312
02:45:05,190 --> 02:45:03,439
then becomes the horizontal fitness

4313
02:45:07,269 --> 02:45:05,200

and when one looks then at the relation

4314

02:45:09,590 --> 02:45:07,279

between susceptible population some

4315

02:45:11,110 --> 02:45:09,600

ecological trait and a viral trait one

4316

02:45:13,190 --> 02:45:11,120

finds that it's not inevitable that

4317

02:45:15,269 --> 02:45:13,200

viruses can invade if there aren't

4318

02:45:17,510 --> 02:45:15,279

enough hoes or if their traits are not

4319

02:45:19,670 --> 02:45:17,520

sufficiently favorable for that host and

4320

02:45:22,550 --> 02:45:19,680

there's a lot of examples of viruses uh

4321

02:45:25,030 --> 02:45:22,560

infecting hosts that may not be uh the

4322

02:45:26,710 --> 02:45:25,040

optimal host in the environment then you

4323

02:45:28,230 --> 02:45:26,720

get the extinction or decay of that

4324

02:45:29,590 --> 02:45:28,240

particular phage on that one host

4325

02:45:31,510 --> 02:45:29,600

whereas the better the virus is that

4326
02:45:33,510 --> 02:45:31,520
exploiting the host the more susceptible

4327
02:45:35,670 --> 02:45:33,520
hosts there are the easier it is for the

4328
02:45:37,269 --> 02:45:35,680
virus to spread

4329
02:45:39,269 --> 02:45:37,279
and the takeaway here is that ecological

4330
02:45:40,870 --> 02:45:39,279
conditions with more susceptible cells

4331
02:45:43,030 --> 02:45:40,880
and viral traits that are more efficient

4332
02:45:47,750 --> 02:45:43,040
infection and also can survive longer in

4333
02:45:52,790 --> 02:45:49,590
now in contrast we can do the same thing

4334
02:45:55,349 --> 02:45:52,800
with the latent virus case but here

4335
02:45:57,429 --> 02:45:55,359
rather than necessarily looking at the

4336
02:46:00,710 --> 02:45:57,439
horizontal transmission i'm going to

4337
02:46:02,070 --> 02:46:00,720
focus on just the case where fitness is

4338
02:46:03,590 --> 02:46:02,080

passed vertically

4339

02:46:05,590 --> 02:46:03,600

and again i won't go through some of the

4340

02:46:08,630 --> 02:46:05,600

mathematics here other than to say that

4341

02:46:10,309 --> 02:46:08,640

one can calculate this vertical fitness

4342

02:46:13,269 --> 02:46:10,319

and reduce it down to this simple

4343

02:46:15,349 --> 02:46:13,279

equation which is how long the cell

4344

02:46:16,870 --> 02:46:15,359

lives for multiply by its division rate

4345

02:46:19,590 --> 02:46:16,880

which gives you the average number of

4346

02:46:21,269 --> 02:46:19,600

offspring and if that's greater than one

4347

02:46:22,950 --> 02:46:21,279

then there are more daughter virus than

4348

02:46:26,230 --> 02:46:22,960

there are mother viruses and therefore

4349

02:46:28,790 --> 02:46:26,240

they are going to proliferate etc etc

4350

02:46:31,510 --> 02:46:28,800

so again here this is an example as we

4351
02:46:33,590 --> 02:46:31,520
increase susceptible populations the red

4352
02:46:35,750 --> 02:46:33,600
line is the horizontal fitness and i've

4353
02:46:38,630 --> 02:46:35,760
shown three blue lines

4354
02:46:40,950 --> 02:46:38,640
which shows how this vertical fitness

4355
02:46:42,950 --> 02:46:40,960
changes with susceptible cell density

4356
02:46:45,269 --> 02:46:42,960
notably it goes down

4357
02:46:47,110 --> 02:46:45,279
because if you infect a susceptible cell

4358
02:46:49,990 --> 02:46:47,120
and there are many other competitors you

4359
02:46:51,750 --> 02:46:50,000
have to face all those competitors

4360
02:46:53,670 --> 02:46:51,760
in the same niche so essentially there's

4361
02:46:55,190 --> 02:46:53,680
increasing niche competition

4362
02:46:57,110 --> 02:46:55,200
nonetheless if there are benefits of

4363
02:46:59,190 --> 02:46:57,120

lysogen in other words if the fitness of

4364

02:47:00,950 --> 02:46:59,200

the infected cell is better than that of

4365

02:47:04,070 --> 02:47:00,960

the uninfected cell then there's a

4366

02:47:06,790 --> 02:47:04,080

larger domain in which as you see to

4367

02:47:08,389 --> 02:47:06,800

presumably very high densities of cells

4368

02:47:10,790 --> 02:47:08,399

it actually might be better to be a

4369

02:47:12,150 --> 02:47:10,800

lysogen than to kill the cell and try to

4370

02:47:13,830 --> 02:47:12,160

find others

4371

02:47:15,110 --> 02:47:13,840

so the takeaway here is that ecological

4372

02:47:17,510 --> 02:47:15,120

conditions with reduced niche

4373

02:47:19,750 --> 02:47:17,520

competition direct cell benefits or low

4374

02:47:23,110 --> 02:47:19,760

variant survivorship all favor latent

4375

02:47:27,190 --> 02:47:25,349

and there's also

4376

02:47:29,750 --> 02:47:27,200

things in between these dichotomous

4377

02:47:31,269 --> 02:47:29,760

outcomes so here's an example in which a

4378

02:47:33,429 --> 02:47:31,279

cell is infected

4379

02:47:34,550 --> 02:47:33,439

and it can both

4380

02:47:36,389 --> 02:47:34,560

divide

4381

02:47:38,710 --> 02:47:36,399

generating progeny that are themselves

4382

02:47:41,269 --> 02:47:38,720

infected but through a budding process

4383

02:47:43,910 --> 02:47:41,279

rather than a lytic process release

4384

02:47:46,389 --> 02:47:43,920

progeny and therefore the chronic viral

4385

02:47:48,630 --> 02:47:46,399

fitness is a combination between the

4386

02:47:50,630 --> 02:47:48,640

horizontal fitness and the vertical

4387

02:47:52,630 --> 02:47:50,640

fitness and here in this particular

4388

02:47:54,950 --> 02:47:52,640

example in the lower left

4389

02:47:57,349 --> 02:47:54,960

there's one division event and two of

4390

02:47:59,510 --> 02:47:57,359

the uh butted off viruses that find new

4391

02:48:02,870 --> 02:47:59,520

cells so the total fitness remains three

4392

02:48:04,309 --> 02:48:02,880

even though it's through distinct modes

4393

02:48:06,630 --> 02:48:04,319

and so the point i'm making here is that

4394

02:48:08,230 --> 02:48:06,640

then when we think about chronic viruses

4395

02:48:10,469 --> 02:48:08,240

and their fitness it becomes an

4396

02:48:12,150 --> 02:48:10,479

aggregation of both the horizontal and

4397

02:48:13,590 --> 02:48:12,160

the vertical components

4398

02:48:15,030 --> 02:48:13,600

and

4399

02:48:17,030 --> 02:48:15,040

the point i'll make here i've already

4400

02:48:19,349 --> 02:48:17,040

told you what those are based on is that

4401

02:48:22,070 --> 02:48:19,359

we increase uh susceptible densities we

4402

02:48:24,230 --> 02:48:22,080

can compare all three strategies finding

4403

02:48:26,070 --> 02:48:24,240

that maybe at lower cell densities the

4404

02:48:27,590 --> 02:48:26,080

vertical mode is dominant at very high

4405

02:48:29,110 --> 02:48:27,600

cell densities the horizontal mode and

4406

02:48:30,469 --> 02:48:29,120

there can be a mix mode that can be

4407

02:48:32,230 --> 02:48:30,479

dominating between

4408

02:48:34,710 --> 02:48:32,240

though the precise position of these can

4409

02:48:36,950 --> 02:48:34,720

change the more that the cell is

4410

02:48:38,710 --> 02:48:36,960

benefited by the viral infection that

4411

02:48:41,110 --> 02:48:38,720

blue line can go up and start to move

4412

02:48:43,190 --> 02:48:41,120

over to the right in cell densities

4413

02:48:45,030 --> 02:48:43,200

so again the takeaway here is that

4414

02:48:46,469 --> 02:48:45,040

temperate and chronic modes are favored

4415

02:48:47,910 --> 02:48:46,479

when susceptible populations are

4416

02:48:49,349 --> 02:48:47,920

relatively low

4417

02:48:51,590 --> 02:48:49,359

lysosomes have a relative growth

4418

02:48:54,230 --> 02:48:51,600

advantage or extracellular decay rates

4419

02:48:55,910 --> 02:48:54,240

are high so in fact some of these early

4420

02:48:58,550 --> 02:48:55,920

predictions by steward 11 really are

4421

02:49:00,309 --> 02:48:58,560

recapitulated but here rather than

4422

02:49:02,550 --> 02:49:00,319

trying to figure out how to balance

4423

02:49:04,550 --> 02:49:02,560

virus particles with inspected cells

4424

02:49:06,950 --> 02:49:04,560

answering that question of how many

4425

02:49:08,630 --> 02:49:06,960

uh in the bloom we should count by

4426

02:49:10,790 --> 02:49:08,640

calculating fitness

4427

02:49:13,990 --> 02:49:10,800

in terms of these viral life cycles we

4428

02:49:15,269 --> 02:49:14,000

get a direct answer to this question

4429

02:49:17,429 --> 02:49:15,279

and you can read more in this virus

4430

02:49:19,030 --> 02:49:17,439

evolution paper it came out

4431

02:49:20,950 --> 02:49:19,040

earlier this year

4432

02:49:22,469 --> 02:49:20,960

so to answer this question i think that

4433

02:49:23,670 --> 02:49:22,479

we should be thinking about unified

4434

02:49:24,710 --> 02:49:23,680

metrics

4435

02:49:27,110 --> 02:49:24,720

and thinking

4436

02:49:29,990 --> 02:49:27,120

maybe alternatively to the predator prey

4437

02:49:31,269 --> 02:49:30,000

paradigm to use an epidemiological

4438

02:49:32,550 --> 02:49:31,279

paradigm

4439

02:49:33,910 --> 02:49:32,560

which is the

4440

02:49:35,429 --> 02:49:33,920

something referred to as the basic

4441

02:49:37,429 --> 02:49:35,439

reproduction number

4442

02:49:39,429 --> 02:49:37,439

the average number of new infected cells

4443

02:49:41,990 --> 02:49:39,439

produced by a single typical infected

4444

02:49:44,469 --> 02:49:42,000

cell and its progeny varies in an

4445

02:49:46,469 --> 02:49:44,479

otherwise susceptible population right

4446

02:49:48,710 --> 02:49:46,479

and using this perspective we can in an

4447

02:49:51,269 --> 02:49:48,720

apples to apples way compare both the

4448

02:49:53,429 --> 02:49:51,279

horizontal mode which produces various

4449

02:49:55,349 --> 02:49:53,439

but doesn't necessarily go vertically

4450

02:49:57,750 --> 02:49:55,359

and the latent mode even if it doesn't

4451
02:49:59,750 --> 02:49:57,760
make a virus particle it still can have

4452
02:50:01,830 --> 02:49:59,760
fitness in the sense of having newly

4453
02:50:04,230 --> 02:50:01,840
infected cells

4454
02:50:05,750 --> 02:50:04,240
and the last thing i want to do here

4455
02:50:07,990 --> 02:50:05,760
i've probably moved a little bit too

4456
02:50:09,990 --> 02:50:08,000
quickly as others have noted it's hard

4457
02:50:12,230 --> 02:50:10,000
to know what the feedback is but i'm

4458
02:50:14,710 --> 02:50:12,240
happy to take questions which is in

4459
02:50:15,990 --> 02:50:14,720
calculating

4460
02:50:18,389 --> 02:50:16,000
these

4461
02:50:20,550 --> 02:50:18,399
values of are not i've assumed

4462
02:50:21,670 --> 02:50:20,560
dichotomous outcomes

4463
02:50:24,469 --> 02:50:21,680

either

4464

02:50:26,230 --> 02:50:24,479

lysis or latency it turns out

4465

02:50:28,550 --> 02:50:26,240

technically it gets much harder i'd say

4466

02:50:31,830 --> 02:50:28,560

conceptually gets much harder when there

4467

02:50:32,790 --> 02:50:31,840

can be a mix between modes and we know

4468

02:50:34,230 --> 02:50:32,800

that

4469

02:50:36,870 --> 02:50:34,240

phage lambda

4470

02:50:38,870 --> 02:50:36,880

temperphage in general latent viruses

4471

02:50:41,030 --> 02:50:38,880

can go out of the latent mode and then

4472

02:50:42,230 --> 02:50:41,040

initiate uh lysis and it's been quite

4473

02:50:44,469 --> 02:50:42,240

hard for us to figure out how to do

4474

02:50:47,030 --> 02:50:44,479

these calculations until recently

4475

02:50:48,150 --> 02:50:47,040

so i'm gonna now just in one slide

4476
02:50:49,670 --> 02:50:48,160
highlight something that's on the

4477
02:50:51,750 --> 02:50:49,680
bioarchive

4478
02:50:54,790 --> 02:50:51,760
which is we've been able to come up this

4479
02:50:56,870 --> 02:50:54,800
is a graphical way of depicting what we

4480
02:50:58,550 --> 02:50:56,880
think the right way to think about

4481
02:51:00,630 --> 02:50:58,560
fitness is

4482
02:51:03,030 --> 02:51:00,640
and there's a lot of diagrams here we

4483
02:51:06,630 --> 02:51:03,040
actually use these diagrams to calculate

4484
02:51:08,550 --> 02:51:06,640
the idea of the top line

4485
02:51:10,710 --> 02:51:08,560
is that this is a model in which e

4486
02:51:13,269 --> 02:51:10,720
stands for exposed the virus i is

4487
02:51:16,309 --> 02:51:13,279
actively infected via the virion and s

4488
02:51:19,190 --> 02:51:16,319

is a susceptible cell I is a lysogen

4489

02:51:21,510 --> 02:51:19,200

so p1 that first diagram says the cell

4490

02:51:23,269 --> 02:51:21,520

is exposed it goes infected makes a

4491

02:51:25,670 --> 02:51:23,279

virus that viruses

4492

02:51:27,910 --> 02:51:25,680

contacts a new susceptible cell and

4493

02:51:30,469 --> 02:51:27,920

makes a cycle the black to black says a

4494

02:51:33,269 --> 02:51:30,479

cycle is created horizontally we call

4495

02:51:34,870 --> 02:51:33,279

that a lytic loop but we also have a

4496

02:51:37,670 --> 02:51:34,880

lysogenic loop which is there's a

4497

02:51:40,150 --> 02:51:37,680

lysogen it doubles so the offspring is

4498

02:51:42,070 --> 02:51:40,160

the lysogen stills the virus that's

4499

02:51:44,469 --> 02:51:42,080

a lysogenic loop

4500

02:51:48,230 --> 02:51:44,479

but we can have something which is a

4501
02:51:50,630 --> 02:51:48,240
lysolytic loop which is the exposed cell

4502
02:51:53,429 --> 02:51:50,640
integrates the prophage comes out into

4503
02:51:56,790 --> 02:51:53,439
an active infection produces viruses and

4504
02:51:59,110 --> 02:51:56,800
goes back to e but passes through the

4505
02:52:01,110 --> 02:51:59,120
lysogenic loop

4506
02:52:02,550 --> 02:52:01,120
those numbers then we can calculate the

4507
02:52:03,830 --> 02:52:02,560
fitness associated with each we have to

4508
02:52:05,190 --> 02:52:03,840
add them up

4509
02:52:06,950 --> 02:52:05,200
but it turns out when we do the

4510
02:52:09,190 --> 02:52:06,960
calculations and to really understand

4511
02:52:11,590 --> 02:52:09,200
them once you start to mix loop we have

4512
02:52:13,110 --> 02:52:11,600
to think through two generations

4513
02:52:15,590 --> 02:52:13,120

but because we have to think through two

4514

02:52:17,670 --> 02:52:15,600

generations you can mix these modes and

4515

02:52:19,190 --> 02:52:17,680

they're all these diagrams here and also

4516

02:52:21,190 --> 02:52:19,200

explains why there's the power of one

4517

02:52:23,110 --> 02:52:21,200

half at the end we have to discount the

4518

02:52:24,790 --> 02:52:23,120

fact that we've looked over two

4519

02:52:25,750 --> 02:52:24,800

generations and we have to compare that

4520

02:52:28,630 --> 02:52:25,760

back

4521

02:52:30,309 --> 02:52:28,640

to the one generation case this might

4522

02:52:32,710 --> 02:52:30,319

seem a little complicated though it's

4523

02:52:35,349 --> 02:52:32,720

kind of appealing in certain ways

4524

02:52:37,349 --> 02:52:35,359

the advantage of it has been is that

4525

02:52:39,030 --> 02:52:37,359

irrespective of the population dynamic

4526

02:52:41,590 --> 02:52:39,040

model you write down

4527

02:52:43,590 --> 02:52:41,600

whether this exposed infected virus

4528

02:52:45,750 --> 02:52:43,600

model there's work by thomas byrne

4529

02:52:47,670 --> 02:52:45,760

gruber recently on a resource implicit

4530

02:52:49,429 --> 02:52:47,680

model with implicit infections and the

4531

02:52:51,110 --> 02:52:49,439

steward 11 model which is resource

4532

02:52:53,030 --> 02:52:51,120

explicit

4533

02:52:55,429 --> 02:52:53,040

all of these models it turns out have

4534

02:52:57,429 --> 02:52:55,439

the exact same formula but the

4535

02:52:59,590 --> 02:52:57,439

quantitative values differ depending on

4536

02:53:01,670 --> 02:52:59,600

particular details but these are the

4537

02:53:03,590 --> 02:53:01,680

combinations of ways in which you can

4538

02:53:05,030 --> 02:53:03,600

have these life cycles

4539

02:53:06,710 --> 02:53:05,040

and it turns out you can make

4540

02:53:08,950 --> 02:53:06,720

predictions they look more or less the

4541

02:53:10,790 --> 02:53:08,960

same when viewed in this way

4542

02:53:12,389 --> 02:53:10,800

so the takeaway here is

4543

02:53:13,590 --> 02:53:12,399

um if you're interested in having talked

4544

02:53:14,550 --> 02:53:13,600

more and you can read more on the

4545

02:53:16,389 --> 02:53:14,560

archive

4546

02:53:18,469 --> 02:53:16,399

that a loop-based approach decomposes

4547

02:53:19,990 --> 02:53:18,479

viral fitness into lytic lysogenic and

4548

02:53:21,510 --> 02:53:20,000

lysolytic loops so we really have

4549

02:53:23,830 --> 02:53:21,520

mechanisms that we can think about

4550

02:53:25,429 --> 02:53:23,840

rather than just a long algebraic mess

4551
02:53:27,349 --> 02:53:25,439
we can think about ways in which these

4552
02:53:29,429 --> 02:53:27,359
loops are contributing to viral fitness

4553
02:53:31,429 --> 02:53:29,439
which transcends model details and i

4554
02:53:33,990 --> 02:53:31,439
hope reveals some generic mechanisms for

4555
02:53:35,910 --> 02:53:34,000
the benefits of latency

4556
02:53:38,309 --> 02:53:35,920
and then the last thing i'll ask is what

4557
02:53:39,830 --> 02:53:38,319
is a virus i think the this project

4558
02:53:42,309 --> 02:53:39,840
collaboration previously with rachel

4559
02:53:44,550 --> 02:53:42,319
wood or mark young and the ongoing work

4560
02:53:46,230 --> 02:53:44,560
has has for me at least raised some new

4561
02:53:48,710 --> 02:53:46,240
questions which is i used to think of a

4562
02:53:50,630 --> 02:53:48,720
virus as a capsid

4563
02:53:52,550 --> 02:53:50,640

containing genetic material and

4564

02:53:54,150 --> 02:53:52,560

obligated intracellular parasite

4565

02:53:55,910 --> 02:53:54,160

but then you might think well maybe it's

4566

02:53:57,750 --> 02:53:55,920

the virus cell right a little infected

4567

02:53:59,190 --> 02:53:57,760

cell or maybe it's a lysosome

4568

02:54:00,870 --> 02:53:59,200

and i would actually say now that it's

4569

02:54:02,309 --> 02:54:00,880

really all of the above

4570

02:54:04,150 --> 02:54:02,319

that viral fitness in the environment

4571

02:54:06,309 --> 02:54:04,160

depends on measuring the present and

4572

02:54:08,070 --> 02:54:06,319

long-term value of infection but we have

4573

02:54:10,150 --> 02:54:08,080

to start thinking i think about the

4574

02:54:12,309 --> 02:54:10,160

entire viral life cycle whether it's

4575

02:54:14,230 --> 02:54:12,319

inside or outside hosts and i think

4576

02:54:16,389 --> 02:54:14,240

it'll take some time to figure this out

4577

02:54:17,750 --> 02:54:16,399

whether through theory experiments as

4578

02:54:19,830 --> 02:54:17,760

well as field work

4579

02:54:21,590 --> 02:54:19,840

and so with that i'll wrap up i think i

4580

02:54:23,030 --> 02:54:21,600

just have a few minutes left

4581

02:54:24,790 --> 02:54:23,040

again acknowledging some of the folks

4582

02:54:26,469 --> 02:54:24,800

here georgia tech

4583

02:54:28,230 --> 02:54:26,479

collaborators former postdocs michael

4584

02:54:30,230 --> 02:54:28,240

cortez and haria gulbadak who have their

4585

02:54:33,349 --> 02:54:30,240

own groups and mathematics at florida

4586

02:54:36,150 --> 02:54:33,359

state and you all lafayette uh

4587

02:54:38,309 --> 02:54:36,160

also at montana uh state university mark

4588

02:54:39,910 --> 02:54:38,319

young and ui you see rachel whitaker if

4589

02:54:41,910 --> 02:54:39,920

you want to read about the latest work

4590

02:54:44,070 --> 02:54:41,920

it's on the archive and there's probably

4591

02:54:45,910 --> 02:54:44,080

a lot more to see we have a

4592

02:54:47,830 --> 02:54:45,920

website twitter and also code data

4593

02:54:50,290 --> 02:54:47,840

information on the github site so thank

4594

02:55:03,830 --> 02:54:50,300

you for your attention

4595

02:55:06,309 --> 02:55:05,110

okay i don't know if there's time left

4596

02:55:07,429 --> 02:55:06,319

there's probably very little time left

4597

02:55:09,269 --> 02:55:07,439

for questions maybe just one or two

4598

02:55:13,590 --> 02:55:09,279

minutes

4599

02:55:17,190 --> 02:55:15,830

hey

4600

02:55:18,630 --> 02:55:17,200

go for it

4601
02:55:20,550 --> 02:55:18,640
all right thanks

4602
02:55:23,269 --> 02:55:20,560
josh i was just wondering about

4603
02:55:25,670 --> 02:55:23,279
situations where the lysogen becomes

4604
02:55:27,429 --> 02:55:25,680
inactivated during sort of one of these

4605
02:55:28,950 --> 02:55:27,439
infection loops and how you might

4606
02:55:30,950 --> 02:55:28,960
account for its fitness in that

4607
02:55:33,030 --> 02:55:30,960
situation like is it still a virus is it

4608
02:55:34,630 --> 02:55:33,040
no longer a virus

4609
02:55:36,710 --> 02:55:34,640
yeah so i mean there's lots of examples

4610
02:55:39,030 --> 02:55:36,720
of these defunct prophage and that's one

4611
02:55:41,670 --> 02:55:39,040
of the risks of staying in too long

4612
02:55:43,030 --> 02:55:41,680
and that certainly decreases if even

4613
02:55:44,550 --> 02:55:43,040

though we are counting fitness

4614

02:55:46,150 --> 02:55:44,560

vertically

4615

02:55:47,910 --> 02:55:46,160

there is a presumption here that at some

4616

02:55:50,150 --> 02:55:47,920

point the virus could still

4617

02:55:52,389 --> 02:55:50,160

get out and disentangle its fate and

4618

02:55:53,910 --> 02:55:52,399

when that stops happening we can have

4619

02:55:54,950 --> 02:55:53,920

that argument at what point that is and

4620

02:55:56,950 --> 02:55:54,960

maybe other people here are going to

4621

02:55:58,630 --> 02:55:56,960

talk about it that it stops being a

4622

02:56:00,790 --> 02:55:58,640

virus and maybe becomes some other kind

4623

02:56:03,190 --> 02:56:00,800

of genetic element but at least in our

4624

02:56:07,269 --> 02:56:03,200

case that would be a loss

4625

02:56:09,269 --> 02:56:07,279

because it's another way of losing the

4626

02:56:11,269 --> 02:56:09,279

viral genome and its ability to have

4627

02:56:13,190 --> 02:56:11,279

both routes at that point and then the

4628

02:56:14,870 --> 02:56:13,200

calculations we could modify but that i

4629

02:56:16,309 --> 02:56:14,880

would view not as positive for viral

4630

02:56:17,750 --> 02:56:16,319

fitness and siobhan might have something

4631

02:56:19,990 --> 02:56:17,760

to say about that

4632

02:56:21,910 --> 02:56:20,000

uh i i think there's a great pairing of

4633

02:56:24,950 --> 02:56:21,920

uh talks but i was actually thinking the

4634

02:56:27,510 --> 02:56:24,960

same thing that uh lewis was um

4635

02:56:29,510 --> 02:56:27,520

do you need to model the loss of uh

4636

02:56:31,110 --> 02:56:29,520

intact viruses due to

4637

02:56:33,110 --> 02:56:31,120

you know defunct prophages or is that

4638

02:56:35,030 --> 02:56:33,120

not uh important because you're not

4639

02:56:37,349 --> 02:56:35,040

modeling uh

4640

02:56:39,510 --> 02:56:37,359

inactive variants you know defunct

4641

02:56:40,630 --> 02:56:39,520

defective variants in the model yeah so

4642

02:56:42,550 --> 02:56:40,640

i mean at least at this point there

4643

02:56:43,349 --> 02:56:42,560

would be probably another level to do

4644

02:56:44,630 --> 02:56:43,359

but

4645

02:56:47,510 --> 02:56:44,640

within the

4646

02:56:49,990 --> 02:56:47,520

the lysogenic the lysogenic phase there

4647

02:56:52,230 --> 02:56:50,000

is a loss term so i view that as an

4648

02:56:54,230 --> 02:56:52,240

additional loss term whether or not that

4649

02:56:56,710 --> 02:56:54,240

still confers immunity is that cell now

4650

02:56:59,510 --> 02:56:56,720

susceptible is it you know maybe it's

4651
02:57:01,670 --> 02:56:59,520
immune but it can't transmit we haven't

4652
02:57:03,510 --> 02:57:01,680
gone into that level of detail and i

4653
02:57:05,750 --> 02:57:03,520
agree that that is a nice challenge to

4654
02:57:07,190 --> 02:57:05,760
think about but at least we i think we

4655
02:57:09,830 --> 02:57:07,200
should think of that as a loss in terms

4656
02:57:16,469 --> 02:57:09,840
of the the average fitness that it's

4657
02:57:16,479 --> 02:57:27,910
okay i think what a time thank you

4658
02:57:32,230 --> 02:57:30,469
i guess we'll move on to you siobhan now

4659
02:57:34,070 --> 02:57:32,240
okay i've got zoom open i'm trying to

4660
02:57:45,510 --> 02:57:34,080
share screen

4661
02:57:48,469 --> 02:57:46,710
am i sharing the screen and i don't

4662
02:57:50,790 --> 02:57:48,479
think i am

4663
02:57:52,790 --> 02:57:50,800

now if you

4664

02:57:54,630 --> 02:57:52,800

mouse over the bottom of the screen

4665

02:57:57,510 --> 02:57:54,640

there should be a share button that's

4666

02:57:59,670 --> 02:57:57,520

green and you click on that oh sorry i

4667

02:58:11,269 --> 02:57:59,680

was doing it from my zoom app that was

4668

02:58:15,429 --> 02:58:12,710

all right

4669

02:58:16,630 --> 02:58:15,439

do you guys see a screen

4670

02:58:19,429 --> 02:58:16,640

yes we do

4671

02:58:21,349 --> 02:58:19,439

okay

4672

02:58:23,750 --> 02:58:21,359

all right so i do think that uh

4673

02:58:25,429 --> 02:58:23,760

thematically it works very well uh to go

4674

02:58:26,870 --> 02:58:25,439

from josh's talk to this one because

4675

02:58:31,030 --> 02:58:26,880

it's about

4676

02:58:33,030 --> 02:58:31,040

what a virus chooses to do not in a um

4677

02:58:35,269 --> 02:58:33,040

you know philosophical

4678

02:58:38,710 --> 02:58:35,279

uh human choice way but genetically what

4679

02:58:41,670 --> 02:58:40,710

and a virus need not

4680

02:58:50,150 --> 02:58:41,680

uh

4681

02:58:55,510 --> 02:58:52,710

a virus if it's replicating in a host is

4682

02:58:57,190 --> 02:58:55,520

already doing a pretty good job

4683

02:58:58,870 --> 02:58:57,200

it's making children it can have a

4684

02:59:00,950 --> 02:58:58,880

pretty good life if there are a lot of

4685

02:59:02,469 --> 02:59:00,960

uh hosts around

4686

02:59:05,110 --> 02:59:02,479

there's no need for a virus to think

4687

02:59:08,309 --> 02:59:05,120

about having an expanded host range it

4688

02:59:11,190 --> 02:59:08,319

wouldn't be relevant in its life

4689

02:59:12,870 --> 02:59:11,200

however um when viruses do think of

4690

02:59:14,710 --> 02:59:12,880

changing their host range sometimes they

4691

02:59:16,389 --> 02:59:14,720

spill over into humans

4692

02:59:18,630 --> 02:59:16,399

and then they become headline grabbing

4693

02:59:20,230 --> 02:59:18,640

viruses

4694

02:59:21,990 --> 02:59:20,240

a lot of what we know about host range

4695

02:59:23,349 --> 02:59:22,000

evolution comes from human infecting

4696

02:59:24,790 --> 02:59:23,359

viruses because we've studied them

4697

02:59:27,510 --> 02:59:24,800

intensively

4698

02:59:29,590 --> 02:59:27,520

intriguingly most emergent viruses in

4699

02:59:31,990 --> 02:59:29,600

humans need a host range mutation but

4700

02:59:33,670 --> 02:59:32,000

generally only about one point mutation

4701
02:59:35,349 --> 02:59:33,680
to be able a new host to infect new

4702
02:59:36,550 --> 02:59:35,359
hosts

4703
02:59:38,550 --> 02:59:36,560
uh the

4704
02:59:42,389 --> 02:59:38,560
human infecting viruses i'm showing here

4705
02:59:44,309 --> 02:59:42,399
are rna-based this is not a fluke rna

4706
02:59:46,950 --> 02:59:44,319
viruses are the most emergent

4707
02:59:49,429 --> 02:59:46,960
pathogens in humans in part because rna

4708
02:59:51,670 --> 02:59:49,439
viruses have high mutation rates

4709
02:59:53,510 --> 02:59:51,680
and sometimes those mutations will have

4710
02:59:55,269 --> 02:59:53,520
an effect on host range

4711
02:59:57,590 --> 02:59:55,279
so i'm showing you a figure here

4712
02:59:59,269 --> 02:59:57,600
that has on the y-axis mutation rate in

4713
03:00:00,469 --> 02:59:59,279

per site in the genome per genomic

4714

03:00:03,349 --> 03:00:00,479

replication

4715

03:00:05,110 --> 03:00:03,359

and along the x-axis genome size in log

4716

03:00:06,309 --> 03:00:05,120

of kilobases

4717

03:00:08,389 --> 03:00:06,319

and i have

4718

03:00:10,710 --> 03:00:08,399

a stock art representing different kinds

4719

03:00:13,030 --> 03:00:10,720

of organisms a mouse for mammals

4720

03:00:15,190 --> 03:00:13,040

bacteria a phage for big double-stranded

4721

03:00:17,910 --> 03:00:15,200

dna viruses some

4722

03:00:20,389 --> 03:00:17,920

of arvin's uh presented beautifully on

4723

03:00:22,790 --> 03:00:20,399

the small single-stranded dna viruses

4724

03:00:24,710 --> 03:00:22,800

here rna viruses do have a range that's

4725

03:00:26,950 --> 03:00:24,720

why we have a lengthy ebola showing a

4726
03:00:28,630 --> 03:00:26,960
range of rna virus mutation rates and up

4727
03:00:29,830 --> 03:00:28,640
here we have a viroid which is not viral

4728
03:00:31,910 --> 03:00:29,840
so we're not going to talk about it

4729
03:00:33,750 --> 03:00:31,920
today

4730
03:00:35,590 --> 03:00:33,760
rna viruses have high mutation rates

4731
03:00:38,309 --> 03:00:35,600
sometimes those mutations are going to

4732
03:00:41,269 --> 03:00:38,319
infect host range

4733
03:00:42,710 --> 03:00:41,279
what are the advantages of having

4734
03:00:44,469 --> 03:00:42,720
mutations that affect host range in your

4735
03:00:47,030 --> 03:00:44,479
population what are the constraints of

4736
03:00:49,830 --> 03:00:47,040
having a host range mutation i've been

4737
03:00:52,070 --> 03:00:49,840
studying this in a model rna virus

4738
03:00:53,750 --> 03:00:52,080

system but there are a number of groups

4739

03:00:56,870 --> 03:00:53,760

have studied this even in some human

4740

03:00:58,870 --> 03:00:56,880

infecting systems generally host range

4741

03:01:03,110 --> 03:00:58,880

has been studied in the modern era in

4742

03:01:06,230 --> 03:01:03,120

rna viruses more than in dna viruses

4743

03:01:09,190 --> 03:01:06,240

there's an obvious relationship between

4744

03:01:11,510 --> 03:01:09,200

uh host range in viruses which is a a

4745

03:01:14,870 --> 03:01:11,520

good proxy for the resource niche breath

4746

03:01:18,309 --> 03:01:14,880

of viruses and how many virus

4747

03:01:20,790 --> 03:01:18,319

progeny that we expect viruses to make

4748

03:01:22,550 --> 03:01:20,800

uh in each given host i'm not going

4749

03:01:24,550 --> 03:01:22,560

quite as detailed back into the

4750

03:01:26,070 --> 03:01:24,560

mathematical literature as josh but this

4751
03:01:27,910 --> 03:01:26,080
model that a jack of all trades is a

4752
03:01:29,670 --> 03:01:27,920
master of none has been articulated in

4753
03:01:31,910 --> 03:01:29,680
the ecological literature including

4754
03:01:35,190 --> 03:01:31,920
mathematically since the 60s that

4755
03:01:37,269 --> 03:01:35,200
basically if you are a a virus whose

4756
03:01:39,670 --> 03:01:37,279
niche is being illustrated by the red

4757
03:01:42,070 --> 03:01:39,680
line you're necessarily we're going to

4758
03:01:43,830 --> 03:01:42,080
call you a specialist because you infect

4759
03:01:46,230 --> 03:01:43,840
a narrow range of hosts and you're

4760
03:01:47,990 --> 03:01:46,240
better at infecting those hosts than the

4761
03:01:49,990 --> 03:01:48,000
pink virus whose we're calling the

4762
03:01:51,429 --> 03:01:50,000
generalist these are relative terms you

4763
03:01:52,550 --> 03:01:51,439

can't possibly

4764

03:01:54,070 --> 03:01:52,560

call something a specialist or

4765

03:01:56,070 --> 03:01:54,080

generalist without having another one to

4766

03:01:59,750 --> 03:01:56,080

compare it to there's no objective

4767

03:02:00,710 --> 03:01:59,760

definition for specialism or journalism

4768

03:02:11,349 --> 03:02:00,720

i

4769

03:02:13,030 --> 03:02:11,359

there's a

4770

03:02:15,510 --> 03:02:13,040

similar amount of fitness under each

4771

03:02:18,710 --> 03:02:15,520

curve in total

4772

03:02:20,389 --> 03:02:18,720

my pop culture metaphor for our uh the

4773

03:02:22,630 --> 03:02:20,399

jack of all trades is the master of none

4774

03:02:25,030 --> 03:02:22,640

is aging if anyone has suggestions uh

4775

03:02:27,269 --> 03:02:25,040

for a more updated 2000 and teens or

4776
03:02:28,389 --> 03:02:27,279
beyond uh metaphor please put them in

4777
03:02:29,910 --> 03:02:28,399
chat

4778
03:02:32,550 --> 03:02:29,920
what i tend to think about it is if you

4779
03:02:34,710 --> 03:02:32,560
are specializing on a very specific uh

4780
03:02:36,790 --> 03:02:34,720
kind of prey you can be very very good

4781
03:02:38,309 --> 03:02:36,800
at catching it and uh keeping your

4782
03:02:40,070 --> 03:02:38,319
narrow focus in the short time period

4783
03:02:42,469 --> 03:02:40,080
that that prey may be around

4784
03:02:44,630 --> 03:02:42,479
but a generalist isn't necessarily

4785
03:02:46,469 --> 03:02:44,640
tracking down one particular way of

4786
03:02:48,070 --> 03:02:46,479
getting points the generalist is aware

4787
03:02:49,670 --> 03:02:48,080
that there are lots of ways to get

4788
03:02:51,110 --> 03:02:49,680

points in the pac-man game and so

4789

03:02:52,630 --> 03:02:51,120

they're not uh

4790

03:02:54,309 --> 03:02:52,640

going to necessarily catch as many

4791

03:02:55,429 --> 03:02:54,319

ghosts but they're going to get perhaps

4792

03:02:56,710 --> 03:02:55,439

more points

4793

03:03:01,349 --> 03:02:56,720

by

4794

03:03:07,269 --> 03:03:04,630

in viruses as i uh had said verbally

4795

03:03:08,950 --> 03:03:07,279

before the specialist we expect has more

4796

03:03:10,309 --> 03:03:08,960

offspring from each infected host when

4797

03:03:12,469 --> 03:03:10,319

they get into a host they're more

4798

03:03:13,429 --> 03:03:12,479

productive they get more fitness out of

4799

03:03:14,550 --> 03:03:13,439

it

4800

03:03:16,870 --> 03:03:14,560

uh the

4801

03:03:18,950 --> 03:03:16,880

pink generalist we say

4802

03:03:20,870 --> 03:03:18,960

has a different set of advantages it

4803

03:03:22,630 --> 03:03:20,880

doesn't have to wait until it finds a

4804

03:03:24,150 --> 03:03:22,640

suitable host and have reduced search

4805

03:03:25,750 --> 03:03:24,160

time it can come across lots of

4806

03:03:28,150 --> 03:03:25,760

different hosts and have offspring in

4807

03:03:29,190 --> 03:03:28,160

them but we expect it not to have as

4808

03:03:30,710 --> 03:03:29,200

many

4809

03:03:32,309 --> 03:03:30,720

offspring in each host

4810

03:03:34,550 --> 03:03:32,319

i'm going to talk about three stories

4811

03:03:36,150 --> 03:03:34,560

today the first is a blast from the past

4812

03:03:37,349 --> 03:03:36,160

part of my thesis work which actually

4813

03:03:38,550 --> 03:03:37,359

looked at this

4814

03:03:40,950 --> 03:03:38,560

in

4815

03:03:43,030 --> 03:03:40,960

an rna experimental system does a larger

4816

03:03:45,030 --> 03:03:43,040

host range in and of itself reduce the

4817

03:03:46,469 --> 03:03:45,040

fitness on the usual host do we see that

4818

03:03:48,710 --> 03:03:46,479

just the acquisition of a host range

4819

03:03:50,070 --> 03:03:48,720

mutation brings your fitness down and

4820

03:03:53,030 --> 03:03:50,080

puts you on the generalist curve

4821

03:03:54,950 --> 03:03:53,040

compared to the specialist curve

4822

03:03:57,349 --> 03:03:54,960

so the system i work with is the rna

4823

03:03:59,269 --> 03:03:57,359

phage 56 which is a fantastic

4824

03:04:00,870 --> 03:03:59,279

model system in experimental evolution

4825

03:04:02,870 --> 03:04:00,880

it's incredibly popular because even

4826

03:04:05,349 --> 03:04:02,880

though it is a bacteriophage

4827

03:04:08,469 --> 03:04:05,359

it looks like a eukaryotic virus it has

4828

03:04:10,550 --> 03:04:08,479

a lipid coat very only physics and its

4829

03:04:13,670 --> 03:04:10,560

relatives and family sister verde have a

4830

03:04:16,870 --> 03:04:13,680

lipid code only cystiviruses have a

4831

03:04:18,389 --> 03:04:16,880

segmented genome there is a three

4832

03:04:20,150 --> 03:04:18,399

tripartite

4833

03:04:21,670 --> 03:04:20,160

segmented genome

4834

03:04:24,070 --> 03:04:21,680

segmentation was thought to evolve to

4835

03:04:25,750 --> 03:04:24,080

deal with eukaryotic cellular machinery

4836

03:04:27,670 --> 03:04:25,760

and their preferences so it doesn't make

4837

03:04:29,030 --> 03:04:27,680

a lot of sense that a tripartite genome

4838

03:04:31,750 --> 03:04:29,040

would have evolved in prokaryotic

4839

03:04:34,870 --> 03:04:31,760

viruses and in terms of phylogenetic

4840

03:04:37,269 --> 03:04:34,880

evidence uh the rna-dependent rna

4841

03:04:39,590 --> 03:04:37,279

polymerase which is the only shared gene

4842

03:04:41,670 --> 03:04:39,600

across all rna viruses when you do the

4843

03:04:43,670 --> 03:04:41,680

phylogenetics of that gene five six

4844

03:04:46,389 --> 03:04:43,680

groups with eukaryote infecting rio

4845

03:04:48,389 --> 03:04:46,399

viruses and not with other rna phages

4846

03:04:50,630 --> 03:04:48,399

it's got a pretty small genome

4847

03:04:53,910 --> 03:04:50,640

and it has a high mutation rate compared

4848

03:04:56,469 --> 03:04:53,920

to the double-stranded dna viruses that

4849

03:04:58,630 --> 03:04:56,479

uh were being envisioned in josh's talk

4850

03:05:00,870 --> 03:04:58,640

but because it's a double-stranded rna

4851
03:05:05,990 --> 03:05:00,880
virus perhaps it has the lowest measured

4852
03:05:09,750 --> 03:05:07,510
physics is a phage it infects

4853
03:05:12,389 --> 03:05:09,760
pseudomonas bacteria i have a phylogeny

4854
03:05:14,790 --> 03:05:12,399
here of the very broad pseudomonas

4855
03:05:17,670 --> 03:05:14,800
phylogeny outgroup rooted with e coli

4856
03:05:19,670 --> 03:05:17,680
there are roughly uh five fairly

4857
03:05:22,150 --> 03:05:19,680
distinct groups that and i've given you

4858
03:05:23,670 --> 03:05:22,160
a uh characteristic species name to

4859
03:05:25,910 --> 03:05:23,680
represent each of them

4860
03:05:28,309 --> 03:05:25,920
five sixes normal hosts are found in the

4861
03:05:30,790 --> 03:05:28,319
serengeti clay it was isolated as a

4862
03:05:32,950 --> 03:05:30,800
potential bio-control agent or agent for

4863
03:05:34,710 --> 03:05:32,960

piecing pathomorphasiocola the cause

4864

03:05:37,750 --> 03:05:34,720

of halo bean blight

4865

03:05:38,870 --> 03:05:37,760

uh you can easily get physics to infect

4866

03:05:41,269 --> 03:05:38,880

other

4867

03:05:43,190 --> 03:05:41,279

uh cp's ringy pathobars

4868

03:05:45,349 --> 03:05:43,200

when they have host range mutations and

4869

03:05:48,710 --> 03:05:45,359

there's one other known alternative host

4870

03:05:51,190 --> 03:05:48,720

you can use for 56 it is called

4871

03:05:53,670 --> 03:05:51,200

pseudomonas pseudoalkalogenesis era that

4872

03:05:55,349 --> 03:05:53,680

stands for east river isolate a it was

4873

03:05:57,830 --> 03:05:55,359

dredged up from the east river in the

4874

03:05:59,349 --> 03:05:57,840

1970s by molecular biologists working on

4875

03:06:02,230 --> 03:05:59,359

physics and we don't know much about its

4876

03:06:07,910 --> 03:06:05,030

so a long time ago i isolated host range

4877

03:06:10,950 --> 03:06:07,920

mutants uh on two piece ring pathobars

4878

03:06:14,150 --> 03:06:10,960

um atrophosians and tomato and on era

4879

03:06:16,550 --> 03:06:14,160

and i sequenced using sanger sequencing

4880

03:06:18,150 --> 03:06:16,560

to find that each one of my mutants had

4881

03:06:20,630 --> 03:06:18,160

one of nine different mutations in the

4882

03:06:23,750 --> 03:06:20,640

same protein in 5 6 this

4883

03:06:25,510 --> 03:06:23,760

p3 host attachment protein so it was

4884

03:06:28,710 --> 03:06:25,520

already a target that we would have

4885

03:06:29,830 --> 03:06:28,720

expected and had been known for 30 years

4886

03:06:32,710 --> 03:06:29,840

was a place where you could get host

4887

03:06:35,590 --> 03:06:32,720

range mutants for 5 secs

4888

03:06:37,590 --> 03:06:35,600

of the 9 distinct mutations i found

4889

03:06:39,830 --> 03:06:37,600

three of them enabled physics to infect

4890

03:06:42,150 --> 03:06:39,840

atrophasians and dra

4891

03:06:45,269 --> 03:06:42,160

five allowed it to infect tomato and dra

4892

03:06:46,870 --> 03:06:45,279

and one allowed it to infect era alone

4893

03:06:49,269 --> 03:06:46,880

i then measured their fitness on the

4894

03:06:51,110 --> 03:06:49,279

original host p serinki patho aphasia

4895

03:06:52,870 --> 03:06:51,120

licola to see if carrying these

4896

03:06:54,710 --> 03:06:52,880

mutations already

4897

03:06:57,269 --> 03:06:54,720

led to a fitness cost

4898

03:06:59,990 --> 03:06:57,279

and i measured fitnesses as a 24-hour

4899

03:07:01,830 --> 03:07:00,000

paired growth assay where the wild-type

4900

03:07:02,790 --> 03:07:01,840

virus and the host range mutant could

4901
03:07:05,030 --> 03:07:02,800
grow

4902
03:07:06,550 --> 03:07:05,040
side by side and we could see which one

4903
03:07:08,790 --> 03:07:06,560
of them left more descendants after that

4904
03:07:10,950 --> 03:07:08,800
much time

4905
03:07:12,630 --> 03:07:10,960
and in this figure the y-axis is the

4906
03:07:14,870 --> 03:07:12,640
fitness on the original host pseudomonas

4907
03:07:16,469 --> 03:07:14,880
serenity path of our phaseolicula the

4908
03:07:18,950 --> 03:07:16,479
fitness of the wild type ancestor is

4909
03:07:20,790 --> 03:07:18,960
shown by the dotted line at one

4910
03:07:22,150 --> 03:07:20,800
across the x-axis you have the nine

4911
03:07:24,309 --> 03:07:22,160
different mutations

4912
03:07:25,990 --> 03:07:24,319
in p3 that i found in that study the

4913
03:07:29,750 --> 03:07:26,000

color coding tells you what the host

4914

03:07:32,230 --> 03:07:29,760

range of the descendant of viruses are

4915

03:07:35,429 --> 03:07:32,240

red for infecting tomato and era blue

4916

03:07:37,269 --> 03:07:35,439

for atrophos black for era

4917

03:07:39,910 --> 03:07:37,279

what should be clear from here is that

4918

03:07:41,750 --> 03:07:39,920

most of the time but not all of the time

4919

03:07:43,750 --> 03:07:41,760

we see that there is an immediate loss

4920

03:07:45,670 --> 03:07:43,760

in fitness on the original host just for

4921

03:07:47,429 --> 03:07:45,680

carrying a host range mutation there's

4922

03:07:49,429 --> 03:07:47,439

been no ecological history there's been

4923

03:07:51,910 --> 03:07:49,439

no time for a lot of natural selection

4924

03:07:54,389 --> 03:07:51,920

to occur in a novel host but just having

4925

03:07:56,309 --> 03:07:54,399

that flexibility in being able to attach

4926

03:07:58,710 --> 03:07:56,319

and infect a couple of different hosts

4927

03:08:00,950 --> 03:07:58,720

already is giving you an immeasurable

4928

03:08:03,030 --> 03:08:00,960

fitness cost on your original host two

4929

03:08:06,469 --> 03:08:03,040

of our nine mutations did not have a

4930

03:08:09,110 --> 03:08:06,479

statistically detectable uh cost in

4931

03:08:11,349 --> 03:08:09,120

on the original host as other people

4932

03:08:13,269 --> 03:08:11,359

have done similar studies in other

4933

03:08:15,590 --> 03:08:13,279

systems including human viruses we see

4934

03:08:17,429 --> 03:08:15,600

the same pattern most of the time we see

4935

03:08:19,990 --> 03:08:17,439

a cost an explicit antagonistic

4936

03:08:22,309 --> 03:08:20,000

clitropy but there seem to be a couple

4937

03:08:24,150 --> 03:08:22,319

of ways that viruses can do this

4938

03:08:26,710 --> 03:08:24,160

where we don't detect a cost in the lab

4939

03:08:29,110 --> 03:08:26,720

of having carrying around an extra

4940

03:08:30,469 --> 03:08:29,120

ability to have a wider host range

4941

03:08:32,550 --> 03:08:30,479

i'm going to take two of these

4942

03:08:35,030 --> 03:08:32,560

particular host range mutations further

4943

03:08:37,750 --> 03:08:35,040

into the next study uh one from the

4944

03:08:40,710 --> 03:08:37,760

n-terminal end of uh the p3 protein one

4945

03:08:43,510 --> 03:08:40,720

from closer to the c-terminal end

4946

03:08:46,309 --> 03:08:43,520

ehe and g515s is what i won't refer to

4947

03:08:49,830 --> 03:08:48,070

so now we know that having a host range

4948

03:08:51,670 --> 03:08:49,840

mutation in and of itself can cause a

4949

03:08:54,550 --> 03:08:51,680

fitness effect but how does having a

4950

03:08:56,550 --> 03:08:54,560

host stream mutation affect a virus's

4951
03:08:58,950 --> 03:08:56,560
ability to jump into another novel host

4952
03:09:00,309 --> 03:08:58,960
how does it affect serial host shifting

4953
03:09:02,710 --> 03:09:00,319
so we have two

4954
03:09:06,150 --> 03:09:02,720
mutants that infect uh

4955
03:09:07,670 --> 03:09:06,160
are phaseolicula tomato and era a wild

4956
03:09:09,670 --> 03:09:07,680
type that only infects the original host

4957
03:09:11,830 --> 03:09:09,680
phaseolicula and we studied them in a

4958
03:09:14,230 --> 03:09:11,840
couple of different ways to measure the

4959
03:09:16,469 --> 03:09:14,240
mutational spectrum of how each of these

4960
03:09:18,150 --> 03:09:16,479
three strains can get into a third host

4961
03:09:19,590 --> 03:09:18,160
atrophasians

4962
03:09:21,990 --> 03:09:19,600
uh the way i'm going to show you results

4963
03:09:24,710 --> 03:09:22,000

from is from illumina sequencing we grew

4964

03:09:26,870 --> 03:09:24,720

up a high titer lysate of the virus on

4965

03:09:29,030 --> 03:09:26,880

the last host it had experienced so

4966

03:09:30,550 --> 03:09:29,040

either the original host or

4967

03:09:31,510 --> 03:09:30,560

in this case host tomato and those two

4968

03:09:32,389 --> 03:09:31,520

strains

4969

03:09:34,550 --> 03:09:32,399

uh

4970

03:09:36,630 --> 03:09:34,560

that was our before population we then

4971

03:09:39,750 --> 03:09:36,640

took a sample of that put the rest of it

4972

03:09:41,750 --> 03:09:39,760

onto a plate of atrophasians and uh let

4973

03:09:43,349 --> 03:09:41,760

it grow and whatever plaques grew up we

4974

03:09:45,910 --> 03:09:43,359

harvested them and isolated their

4975

03:09:47,830 --> 03:09:45,920

genomes we now had two uh populations of

4976

03:09:49,910 --> 03:09:47,840

viruses before and after exposure to

4977

03:09:52,309 --> 03:09:49,920

atrophasians and we threw that onto

4978

03:09:54,790 --> 03:09:52,319

aluminum i seek

4979

03:09:56,950 --> 03:09:54,800

and the results we got are shown here on

4980

03:09:59,670 --> 03:09:56,960

the y-axis i'm showing you the change in

4981

03:10:02,150 --> 03:09:59,680

shannon entropy so what i'm showing you

4982

03:10:04,229 --> 03:10:02,160

is the amount of polymorphism at the

4983

03:10:06,870 --> 03:10:04,239

different sites in this case in the m

4984

03:10:09,750 --> 03:10:06,880

segment this is representing 4 000 ish

4985

03:10:10,630 --> 03:10:09,760

bases in the m segment

4986

03:10:13,910 --> 03:10:10,640

the

4987

03:10:15,670 --> 03:10:13,920

after exposure atrophasians minus uh

4988

03:10:17,429 --> 03:10:15,680

prior to exposure to atrophos so

4989

03:10:19,670 --> 03:10:17,439

anything you're seeing above the zero

4990

03:10:21,429 --> 03:10:19,680

line which is represented by most of the

4991

03:10:23,910 --> 03:10:21,439

genome that those are mutations that

4992

03:10:26,790 --> 03:10:23,920

were over represented in the after

4993

03:10:28,389 --> 03:10:26,800

atrophasians exposure rather than before

4994

03:10:30,790 --> 03:10:28,399

i've given you a bit of shading to show

4995

03:10:33,110 --> 03:10:30,800

you where the p3 host attachment protein

4996

03:10:34,870 --> 03:10:33,120

is on the medium segment

4997

03:10:37,110 --> 03:10:34,880

the first thing you should see is that

4998

03:10:40,070 --> 03:10:37,120

we're not seeing a lot of

4999

03:10:43,030 --> 03:10:40,080

positive changes in shannon entropy

5000

03:10:44,389 --> 03:10:43,040

outside of the p3 region we're seeing a

5001
03:10:45,990 --> 03:10:44,399
lot of the host range mutations are

5002
03:10:47,670 --> 03:10:46,000
really happening there

5003
03:10:50,710 --> 03:10:47,680
also you should be able to tell that

5004
03:10:52,550 --> 03:10:50,720
there's more diverse sites associated

5005
03:10:54,469 --> 03:10:52,560
with enrichment for the wild type

5006
03:10:57,990 --> 03:10:54,479
population on the top rather than the

5007
03:10:59,830 --> 03:10:58,000
ehg or the g515s populations below the

5008
03:11:02,229 --> 03:10:59,840
wild type had more different ways to

5009
03:11:04,070 --> 03:11:02,239
infect atrophasians than the two strains

5010
03:11:06,790 --> 03:11:04,080
that already had a host range mutation

5011
03:11:08,070 --> 03:11:06,800
in their p3 gene

5012
03:11:09,990 --> 03:11:08,080
i'm showing you just the results from

5013
03:11:11,750 --> 03:11:10,000

illumina we also did this with

5014

03:11:13,830 --> 03:11:11,760

painstaking cloning

5015

03:11:15,830 --> 03:11:13,840

and sanger sequencing and when we did

5016

03:11:18,150 --> 03:11:15,840

that approach with groups of 50

5017

03:11:21,030 --> 03:11:18,160

individual mutants we found that

5018

03:11:23,030 --> 03:11:21,040

about 20 of the clones we pulled up from

5019

03:11:25,670 --> 03:11:23,040

phi 6 wild-type didn't have any

5020

03:11:27,590 --> 03:11:25,680

mutations in their p3 gene

5021

03:11:29,269 --> 03:11:27,600

we were surprised by this that was a

5022

03:11:31,030 --> 03:11:29,279

really high result occasionally that's

5023

03:11:33,030 --> 03:11:31,040

happened in five six studies in the past

5024

03:11:35,590 --> 03:11:33,040

but it's been one out of forty two out

5025

03:11:37,670 --> 03:11:35,600

of a hundred but it was closer to one

5026

03:11:39,429 --> 03:11:37,680

out of five in this study

5027

03:11:40,950 --> 03:11:39,439

and the illumina sequencing results gave

5028

03:11:42,070 --> 03:11:40,960

us some perspective of what was

5029

03:11:43,429 --> 03:11:42,080

happening there

5030

03:11:45,429 --> 03:11:43,439

because we got to see that there was

5031

03:11:48,070 --> 03:11:45,439

similar enrichment uh in the small

5032

03:11:52,469 --> 03:11:48,080

segment in uh for five six wild type but

5033

03:11:54,790 --> 03:11:52,479

not for five six ehg or 5 6 g515s

5034

03:11:56,229 --> 03:11:54,800

no part none of the genes on the small

5035

03:11:58,950 --> 03:11:56,239

segment have ever been associated with

5036

03:12:00,710 --> 03:11:58,960

host range and very intriguingly the

5037

03:12:03,349 --> 03:12:00,720

gene that has the most

5038

03:12:04,870 --> 03:12:03,359

over-represented sites both in

5039

03:12:06,309 --> 03:12:04,880

our luminous sequencing and once we got

5040

03:12:08,070 --> 03:12:06,319

these results we went back and we did

5041

03:12:10,389 --> 03:12:08,080

sanger sequencing on our clones we

5042

03:12:12,229 --> 03:12:10,399

confirmed that they had

5043

03:12:15,590 --> 03:12:12,239

single mutations or in some cases double

5044

03:12:16,550 --> 03:12:15,600

mutations in the p12 gene on the small

5045

03:12:19,670 --> 03:12:16,560

segment

5046

03:12:23,030 --> 03:12:19,680

p12 is a protein that's not even in the

5047

03:12:25,190 --> 03:12:23,040

fully assembled and articulated uh five

5048

03:12:27,269 --> 03:12:25,200

six variant it's not part of the

5049

03:12:28,710 --> 03:12:27,279

structure of the of the variant so this

5050

03:12:31,349 --> 03:12:28,720

is a really interesting

5051
03:12:33,110 --> 03:12:31,359
result that there is this way that so

5052
03:12:35,990 --> 03:12:33,120
the 5 6 wild type can enhance its host

5053
03:12:37,910 --> 03:12:36,000
range possibly in helping it get out of

5054
03:12:39,990 --> 03:12:37,920
that first p uh first infected

5055
03:12:41,910 --> 03:12:40,000
atrophoscene cell we don't have any

5056
03:12:44,309 --> 03:12:41,920
we're just speculating at this point but

5057
03:12:45,510 --> 03:12:44,319
those pathways appear to be closed off

5058
03:12:47,349 --> 03:12:45,520
to

5059
03:12:52,469 --> 03:12:47,359
the five six strings that already have a

5060
03:12:56,550 --> 03:12:54,870
all in all wild type just has a lot of

5061
03:12:58,710 --> 03:12:56,560
different ways to get into atrophasians

5062
03:13:01,429 --> 03:12:58,720
having a host range mutation is limiting

5063
03:13:03,030 --> 03:13:01,439

you already and this is clearly due to

5064

03:13:04,630 --> 03:13:03,040

epistasis and interaction amongst

5065

03:13:06,389 --> 03:13:04,640

mutations the mutations that are

5066

03:13:08,630 --> 03:13:06,399

conferring um the ability to infect

5067

03:13:10,309 --> 03:13:08,640

atrophasians for the wild type aren't

5068

03:13:13,510 --> 03:13:10,319

necessarily working for those that

5069

03:13:15,830 --> 03:13:13,520

already have a mutation in their p3 gene

5070

03:13:18,070 --> 03:13:15,840

we assume that this is a problem of p3

5071

03:13:19,269 --> 03:13:18,080

structural stability that if you have a

5072

03:13:21,269 --> 03:13:19,279

tweak that

5073

03:13:24,150 --> 03:13:21,279

allows you to expand your host range and

5074

03:13:26,150 --> 03:13:24,160

get into host tomato another tweak not

5075

03:13:27,910 --> 03:13:26,160

as many of those secondary tweaks can

5076
03:13:29,510 --> 03:13:27,920
are tolerated even though they would

5077
03:13:31,349 --> 03:13:29,520
allow you to maybe get into another host

5078
03:13:33,349 --> 03:13:31,359
it may be reducing very instability in

5079
03:13:35,590 --> 03:13:33,359
some way shape or form

5080
03:13:38,630 --> 03:13:35,600
this is potentially a more generalizable

5081
03:13:40,550 --> 03:13:38,640
thing beyond phi 6 while we see zoonotic

5082
03:13:43,110 --> 03:13:40,560
uh spillover from

5083
03:13:45,429 --> 03:13:43,120
a common source population into

5084
03:13:48,229 --> 03:13:45,439
other hosts a lot serial host shifting

5085
03:13:50,630 --> 03:13:48,239
of a bird flu going into

5086
03:13:52,389 --> 03:13:50,640
a horse and then going into a dog from

5087
03:13:54,550 --> 03:13:52,399
the horse which has happened for

5088
03:13:56,950 --> 03:13:54,560

influenza those kinds of sequential host

5089

03:13:58,229 --> 03:13:56,960

shiftings are rarer so

5090

03:13:59,510 --> 03:13:58,239

epistatic interactions amongst

5091

03:14:02,870 --> 03:13:59,520

two-string mutations might be a

5092

03:14:03,750 --> 03:14:02,880

generalizable problem for viruses

5093

03:14:05,830 --> 03:14:03,760

again

5094

03:14:07,830 --> 03:14:05,840

this is a fairly short-term scale that

5095

03:14:10,870 --> 03:14:07,840

we're examining the costs and benefits

5096

03:14:14,070 --> 03:14:10,880

of host change mutations on i this is

5097

03:14:16,309 --> 03:14:14,080

only a few generations 10 15 generations

5098

03:14:19,190 --> 03:14:16,319

from the spontaneous host range mutation

5099

03:14:21,110 --> 03:14:19,200

itself we also have been giving our

5100

03:14:22,950 --> 03:14:21,120

viral strain some time to evolve in

5101
03:14:24,950 --> 03:14:22,960
their uh in different environments to

5102
03:14:26,870 --> 03:14:24,960
see what the effects are on the

5103
03:14:28,630 --> 03:14:26,880
evolutionary trajectory if you carry

5104
03:14:31,269 --> 03:14:28,640
host range mutations

5105
03:14:33,750 --> 03:14:31,279
so this is a study that went for 30

5106
03:14:35,910 --> 03:14:33,760
overnight passages so roughly 150 viral

5107
03:14:38,469 --> 03:14:35,920
generations with four treatments the

5108
03:14:40,309 --> 03:14:38,479
wild type 56 virus shown in teal

5109
03:14:43,030 --> 03:14:40,319
and the eag virus

5110
03:14:44,790 --> 03:14:43,040
shown in a pale beige color if it

5111
03:14:46,870 --> 03:14:44,800
evolved just on the original host

5112
03:14:48,870 --> 03:14:46,880
phaseolicolla wildtype of course can

5113
03:14:50,790 --> 03:14:48,880

only infect phaseoliculus so we have

5114

03:14:53,190 --> 03:14:50,800

wild-type infecting phaseolicula for 30

5115

03:14:56,229 --> 03:14:53,200

passages ehg infecting phaseolicola for

5116

03:14:58,309 --> 03:14:56,239

30 passages or ehg alternating daily

5117

03:15:01,590 --> 03:14:58,319

passage on the original host and a novel

5118

03:15:03,670 --> 03:15:01,600

host either tomato and red or era in

5119

03:15:06,229 --> 03:15:03,680

black so four different treatments that

5120

03:15:08,790 --> 03:15:06,239

would allow us to to compare the effects

5121

03:15:10,550 --> 03:15:08,800

of genetic generalism by looking at the

5122

03:15:12,150 --> 03:15:10,560

wild type evolving on phasing likelihood

5123

03:15:14,389 --> 03:15:12,160

compared to eag evolving on facing

5124

03:15:17,110 --> 03:15:14,399

allicula or the effect of ecological

5125

03:15:18,550 --> 03:15:17,120

generalism eag it has a host strange

5126

03:15:20,150 --> 03:15:18,560

mutation but it's still seeing that

5127

03:15:22,790 --> 03:15:20,160

original host a constant host

5128

03:15:25,349 --> 03:15:22,800

environment compared to uh forcing it to

5129

03:15:28,389 --> 03:15:25,359

see multiple hosts either two in the

5130

03:15:31,349 --> 03:15:28,399

pisaringi species or a pisaringi and a

5131

03:15:32,630 --> 03:15:31,359

pietra uh pcoral colligence alternating

5132

03:15:35,190 --> 03:15:32,640

days

5133

03:15:36,229 --> 03:15:35,200

the fitness results are shown on this

5134

03:15:38,150 --> 03:15:36,239

slide

5135

03:15:40,389 --> 03:15:38,160

on the y-axis we have relative fitness

5136

03:15:42,469 --> 03:15:40,399

on the original host phaseolicula in

5137

03:15:43,670 --> 03:15:42,479

this case one does not mean the fitness

5138

03:15:45,429 --> 03:15:43,680

of the

5139

03:15:47,910 --> 03:15:45,439

wild-type virus it means the fitness of

5140

03:15:48,950 --> 03:15:47,920

the common competitor we used to compare

5141

03:15:51,429 --> 03:15:48,960

all these

5142

03:15:53,269 --> 03:15:51,439

strains to the black box is the wild

5143

03:15:54,229 --> 03:15:53,279

type

5144

03:15:56,070 --> 03:15:54,239

fitness

5145

03:15:58,309 --> 03:15:56,080

those teal are the four descended

5146

03:16:00,550 --> 03:15:58,319

populations uh wild type evolved on the

5147

03:16:03,590 --> 03:16:00,560

original host for 30 days it's about the

5148

03:16:06,070 --> 03:16:03,600

same fitness as it had when it started

5149

03:16:09,750 --> 03:16:06,080

the gray box is the original fitness of

5150

03:16:11,510 --> 03:16:09,760

the ehe ancestor the pale dots are

5151
03:16:13,910 --> 03:16:11,520
after 30 days of evolution on phase

5152
03:16:16,070 --> 03:16:13,920
aligala again it was pretty decent

5153
03:16:16,950 --> 03:16:16,080
infecting vasolicola we don't see a big

5154
03:16:19,590 --> 03:16:16,960
change

5155
03:16:22,309 --> 03:16:19,600
in orange we see the eag populations

5156
03:16:24,389 --> 03:16:22,319
that alternated with host tomato in

5157
03:16:25,910 --> 03:16:24,399
burgundy the population is alternated

5158
03:16:27,910 --> 03:16:25,920
with host era

5159
03:16:29,190 --> 03:16:27,920
there are more data points for these

5160
03:16:30,870 --> 03:16:29,200
latter two groups because we measure

5161
03:16:33,429 --> 03:16:30,880
their fitness coming off of phase

5162
03:16:35,670 --> 03:16:33,439
allicola and coming off of tomato or era

5163
03:16:39,110 --> 03:16:35,680

so day 29 and day 30 to make sure there

5164

03:16:41,030 --> 03:16:39,120

wasn't a maternal host effect

5165

03:16:43,030 --> 03:16:41,040

when you compare between wild type and

5166

03:16:44,710 --> 03:16:43,040

eag grown on the same host you don't see

5167

03:16:48,469 --> 03:16:44,720

a lot of difference there's not a big

5168

03:16:50,389 --> 03:16:48,479

cost of carrying ehe longer term on the

5169

03:16:53,190 --> 03:16:50,399

host physiolicola they're both doing

5170

03:16:54,950 --> 03:16:53,200

just fine when you compare the different

5171

03:16:57,269 --> 03:16:54,960

kinds of generalist environments that

5172

03:16:59,990 --> 03:16:57,279

eag could be in we saw something pretty

5173

03:17:01,670 --> 03:17:00,000

surprising which is even though the ehe

5174

03:17:04,229 --> 03:17:01,680

that was exposed to both phaseolic and

5175

03:17:06,309 --> 03:17:04,239

tomato was seeing phaseolicola every

5176
03:17:08,550 --> 03:17:06,319
other day some of the populations were

5177
03:17:10,870 --> 03:17:08,560
losing fitness on the original host

5178
03:17:12,710 --> 03:17:10,880
there was so much selection on the novel

5179
03:17:15,349 --> 03:17:12,720
host that this was

5180
03:17:17,110 --> 03:17:15,359
apparently more important to the uh the

5181
03:17:18,710 --> 03:17:17,120
fitness of the overall

5182
03:17:20,710 --> 03:17:18,720
uh multiple day fitness of these

5183
03:17:22,309 --> 03:17:20,720
organisms that we still are seeing

5184
03:17:25,750 --> 03:17:22,319
fitness declining on the original host

5185
03:17:27,190 --> 03:17:25,760
despite exposure to the original host

5186
03:17:28,550 --> 03:17:27,200
and i can show you some molecular

5187
03:17:29,670 --> 03:17:28,560
evidence for that strong selection in

5188
03:17:32,550 --> 03:17:29,680

this figure

5189

03:17:34,710 --> 03:17:32,560

now i'm showing you the top ten snips

5190

03:17:36,550 --> 03:17:34,720

from each of four replicate populations

5191

03:17:39,349 --> 03:17:36,560

that were evolved from the wild type on

5192

03:17:40,790 --> 03:17:39,359

phaseolicola ehe and phaseolicula ehg

5193

03:17:42,630 --> 03:17:40,800

alternating between phase glycol and

5194

03:17:45,030 --> 03:17:42,640

tomato ehg alternating between

5195

03:17:47,830 --> 03:17:45,040

phaseolicola and era

5196

03:17:50,150 --> 03:17:47,840

light color pink indicates a low

5197

03:17:52,469 --> 03:17:50,160

frequency closer to zero dark purple

5198

03:17:54,550 --> 03:17:52,479

indicates a high frequency

5199

03:17:56,389 --> 03:17:54,560

and darkest purple would be one and what

5200

03:17:58,950 --> 03:17:56,399

you can see here is that

5201
03:18:00,630 --> 03:17:58,960
the of the top ten snips we don't see a

5202
03:18:02,790 --> 03:18:00,640
lot of snips going to particularly high

5203
03:18:04,070 --> 03:18:02,800
frequency in the populations evolving on

5204
03:18:07,269 --> 03:18:04,080
phaseolic

5205
03:18:09,830 --> 03:18:07,279
wild type and its isagenic uh

5206
03:18:11,990 --> 03:18:09,840
eag immediate offspring host range

5207
03:18:13,670 --> 03:18:12,000
mutant we're already pretty good at

5208
03:18:15,910 --> 03:18:13,680
infecting phase gallicola we don't see a

5209
03:18:17,349 --> 03:18:15,920
lot of change happening in 30 days but

5210
03:18:18,710 --> 03:18:17,359
the ehe populations that we're

5211
03:18:21,190 --> 03:18:18,720
experiencing a more generalist

5212
03:18:23,349 --> 03:18:21,200
environment we see some significant

5213
03:18:24,870 --> 03:18:23,359

selection uh some mutations are even

5214

03:18:27,910 --> 03:18:24,880

being fixed because

5215

03:18:29,349 --> 03:18:27,920

in the novel host genetic diversity uh

5216

03:18:30,710 --> 03:18:29,359

apparently

5217

03:18:33,030 --> 03:18:30,720

uh is

5218

03:18:34,870 --> 03:18:33,040

helping out these uh these viruses get

5219

03:18:36,469 --> 03:18:34,880

to a better fitness level and so we see

5220

03:18:38,550 --> 03:18:36,479

that there's a very different

5221

03:18:39,990 --> 03:18:38,560

evolutionary scenario for the generalist

5222

03:18:41,910 --> 03:18:40,000

viruses when they're in the different

5223

03:18:43,269 --> 03:18:41,920

hosts they are experiencing a selection

5224

03:18:44,309 --> 03:18:43,279

that they weren't experiencing when they

5225

03:18:48,630 --> 03:18:44,319

were just

5226

03:18:49,429 --> 03:18:48,640

cruising along in their usual uh host

5227

03:18:52,070 --> 03:18:49,439

so

5228

03:18:55,269 --> 03:18:52,080

perhaps unsatisfyingly the answer to

5229

03:18:57,110 --> 03:18:55,279

what are the benefits and uh

5230

03:18:59,429 --> 03:18:57,120

detractions of having an expanded host

5231

03:19:01,990 --> 03:18:59,439

range is well it there's pluses and

5232

03:19:03,830 --> 03:19:02,000

minuses there absolutely are fitness

5233

03:19:05,030 --> 03:19:03,840

costs and episodic costs of hosting

5234

03:19:07,910 --> 03:19:05,040

mutations that can influence

5235

03:19:10,070 --> 03:19:07,920

evolutionary trajectories but

5236

03:19:11,830 --> 03:19:10,080

whether or not these things are good or

5237

03:19:14,070 --> 03:19:11,840

bad are going to depend on what kind of

5238

03:19:16,790 --> 03:19:14,080

environment the virus lives in if you're

5239

03:19:19,190 --> 03:19:16,800

in an extremely homogenous environment

5240

03:19:21,830 --> 03:19:19,200

let's imagine an industrial fermenter

5241

03:19:23,110 --> 03:19:21,840

there's no reason to have a lot of host

5242

03:19:25,429 --> 03:19:23,120

refutations

5243

03:19:27,110 --> 03:19:25,439

you want to kill the dominant bacteria

5244

03:19:29,110 --> 03:19:27,120

the only bacteria that they put in there

5245

03:19:30,870 --> 03:19:29,120

to ferment the

5246

03:19:32,389 --> 03:19:30,880

food substance they're interested in if

5247

03:19:34,710 --> 03:19:32,399

you're out in a more natural community

5248

03:19:37,030 --> 03:19:34,720

with many many different hosts around

5249

03:19:39,349 --> 03:19:37,040

you that may make it would make a lot

5250

03:19:42,070 --> 03:19:39,359

more sense to have some expanded hosting

5251
03:19:43,510 --> 03:19:42,080
mutations in your standing population

5252
03:19:47,590 --> 03:19:43,520
genetic variation

5253
03:19:50,150 --> 03:19:47,600
even if they confer small

5254
03:19:52,630 --> 03:19:50,160
levels of fitness effects on your the

5255
03:19:54,309 --> 03:19:52,640
host you more typically encounter

5256
03:19:56,070 --> 03:19:54,319
most of the work i presented today was

5257
03:19:58,309 --> 03:19:56,080
the thesis work of lola jiao who's now a

5258
03:20:00,389 --> 03:19:58,319
post-doc at oxford big data institute

5259
03:20:02,070 --> 03:20:00,399
she was helped by uh two undergrads

5260
03:20:03,750 --> 03:20:02,080
drago stomate and alvin crespo and

5261
03:20:05,269 --> 03:20:03,760
manchester pastricia a postdoc in my

5262
03:20:07,429 --> 03:20:05,279
group was also contributed to the

5263
03:20:08,550 --> 03:20:07,439

mutational spectrum project thank you so

5264

03:20:10,469 --> 03:20:08,560

much for listening thank you for the

5265

03:20:21,110 --> 03:20:10,479

invitation organizers and i'm happy to

5266

03:20:25,510 --> 03:20:23,429

i actually have a question to start off

5267

03:20:26,389 --> 03:20:25,520

sure so

5268

03:20:29,110 --> 03:20:26,399

if we're

5269

03:20:32,309 --> 03:20:29,120

thinking about culturing viruses for the

5270

03:20:34,309 --> 03:20:32,319

future this idea that

5271

03:20:37,190 --> 03:20:34,319

maybe to increase our ability to culture

5272

03:20:38,630 --> 03:20:37,200

viruses we want viruses that can infect

5273

03:20:40,790 --> 03:20:38,640

many different types of hosts with a

5274

03:20:43,030 --> 03:20:40,800

broad host range right so you're saying

5275

03:20:45,190 --> 03:20:43,040

if we go along this line that if we have

5276
03:20:47,190 --> 03:20:45,200
a more simple environment which selects

5277
03:20:50,150 --> 03:20:47,200
for a certain type of

5278
03:20:51,830 --> 03:20:50,160
metabolism maybe that it will be harder

5279
03:20:54,150 --> 03:20:51,840
to culture viruses from those type of

5280
03:20:55,670 --> 03:20:54,160
environments

5281
03:20:58,630 --> 03:20:55,680
i don't know if we know enough to answer

5282
03:21:00,389 --> 03:20:58,640
one way or the other at this point um

5283
03:21:02,309 --> 03:21:00,399
even though we didn't see

5284
03:21:04,950 --> 03:21:02,319
many high frequency snips in our

5285
03:21:07,190 --> 03:21:04,960
population survived on just the original

5286
03:21:09,670 --> 03:21:07,200
host physiolicula they did have a higher

5287
03:21:11,190 --> 03:21:09,680
diversity overall than our populations

5288
03:21:13,990 --> 03:21:11,200

that we're seeing a wider number of

5289

03:21:16,150 --> 03:21:14,000

hosts because selection purges diversity

5290

03:21:17,830 --> 03:21:16,160

at linked sites you know we always

5291

03:21:20,070 --> 03:21:17,840

forget this you know evolution's great

5292

03:21:21,750 --> 03:21:20,080

it natural election is great except it's

5293

03:21:23,750 --> 03:21:21,760

getting rid of that lovely diversity

5294

03:21:26,389 --> 03:21:23,760

that helps the next step that

5295

03:21:30,790 --> 03:21:28,070

i'm not sure we have a science-based

5296

03:21:37,590 --> 03:21:30,800

answer to that question yet

5297

03:21:41,429 --> 03:21:39,429

i had you question sort of a more

5298

03:21:44,630 --> 03:21:41,439

general one

5299

03:21:47,030 --> 03:21:44,640

have you or anyone else looked at some

5300

03:21:48,469 --> 03:21:47,040

of the more you know broad host range

5301
03:21:49,990 --> 03:21:48,479
viruses

5302
03:21:52,070 --> 03:21:50,000
um because in this case you're looking

5303
03:21:54,070 --> 03:21:52,080
at these individual mutations in a nice

5304
03:21:56,070 --> 03:21:54,080
well-defined system but if you think

5305
03:21:57,910 --> 03:21:56,080
about it from some of the the cucumber

5306
03:22:00,870 --> 03:21:57,920
mosaic viruses or those that have you

5307
03:22:02,870 --> 03:22:00,880
know much broader host ranges do you see

5308
03:22:04,469 --> 03:22:02,880
the same kinds of trade-offs you know

5309
03:22:06,469 --> 03:22:04,479
fitness or otherwise or has anybody

5310
03:22:09,110 --> 03:22:06,479
really done good experiments that i

5311
03:22:11,670 --> 03:22:09,120
imagine that's hard to do

5312
03:22:14,389 --> 03:22:11,680
we know that broad host range plant

5313
03:22:16,309 --> 03:22:14,399

viruses see different uh plant hosts

5314

03:22:18,630 --> 03:22:16,319

differently and a lot of that's the work

5315

03:22:20,790 --> 03:22:18,640

of marilyn bruce nick's group santiago

5316

03:22:22,389 --> 03:22:20,800

lane has some work too but marilyn uh

5317

03:22:23,910 --> 03:22:22,399

really characterized that the kinds of

5318

03:22:26,229 --> 03:22:23,920

mutations that are favored in the

5319

03:22:28,309 --> 03:22:26,239

different environments uh are it's

5320

03:22:31,030 --> 03:22:28,319

clearly different in uh different plant

5321

03:22:32,229 --> 03:22:31,040

hosts but we don't in plant viruses we

5322

03:22:34,229 --> 03:22:32,239

don't see a lot of host specific

5323

03:22:36,229 --> 03:22:34,239

adaptation so you see this when you're

5324

03:22:38,710 --> 03:22:36,239

infecting a plant but it doesn't seem to

5325

03:22:40,950 --> 03:22:38,720

persist when you're looking at the

5326

03:22:42,630 --> 03:22:40,960

between host

5327

03:22:44,630 --> 03:22:42,640

evolution even if you're keeping them in

5328

03:22:45,990 --> 03:22:44,640

the same host for long periods of time

5329

03:22:47,269 --> 03:22:46,000

it's been

5330

03:22:48,469 --> 03:22:47,279

a frustrating difference between the

5331

03:22:49,750 --> 03:22:48,479

phage literature and the plant

5332

03:22:51,830 --> 03:22:49,760

literature is that there's much more

5333

03:22:54,229 --> 03:22:51,840

host specific adaptation that you can

5334

03:22:55,590 --> 03:22:54,239

measure in the phage literature

5335

03:22:59,990 --> 03:22:55,600

is that possibly because of how they're

5336

03:23:04,469 --> 03:23:01,670

and my postdoc also was whispering the

5337

03:23:06,550 --> 03:23:04,479

exact same thing i vectors

5338

03:23:09,590 --> 03:23:06,560

plant viruses are often uh vector

5339

03:23:11,269 --> 03:23:09,600

specific and host generalist but this is

5340

03:23:13,910 --> 03:23:11,279

these sorts of patterns occur even in

5341

03:23:15,510 --> 03:23:13,920

wind transmitted plants viruses so this

5342

03:23:16,950 --> 03:23:15,520

isn't something that's restricted

5343

03:23:18,710 --> 03:23:16,960

because you have to be you don't have to

5344

03:23:20,710 --> 03:23:18,720

look a certain way to go

5345

03:23:22,710 --> 03:23:20,720

with a vector between hosts

5346

03:23:25,110 --> 03:23:22,720

on a population level even with the same

5347

03:23:26,790 --> 03:23:25,120

host we don't see as much host specific

5348

03:23:28,150 --> 03:23:26,800

adaptation

5349

03:23:30,870 --> 03:23:28,160

when people look at this question of

5350

03:23:34,070 --> 03:23:30,880

broader host range in animals the they

5351
03:23:35,590 --> 03:23:34,080
do shorthand it to arbor viruses versus

5352
03:23:37,349 --> 03:23:35,600
something that's mammal specific and

5353
03:23:39,670 --> 03:23:37,359
that's not a great comparison either

5354
03:23:52,309 --> 03:23:39,680
because yeah

5355
03:23:52,319 --> 03:23:58,389
any other questions

5356
03:24:01,030 --> 03:23:59,670
i'm curious if you've done similar

5357
03:24:02,870 --> 03:24:01,040
experiments with single-stranded dna

5358
03:24:05,670 --> 03:24:02,880
viruses

5359
03:24:09,750 --> 03:24:05,680
we so singles uh our single-stranded dna

5360
03:24:12,389 --> 03:24:09,760
um phage in the lab is 5x174 and it is

5361
03:24:14,710 --> 03:24:12,399
pretty difficult to get onto alternative

5362
03:24:16,870 --> 03:24:14,720
hosts there's a very short list of

5363
03:24:18,790 --> 03:24:16,880

alternative hosts for that particular

5364

03:24:20,469 --> 03:24:18,800

virus it doesn't have

5365

03:24:21,910 --> 03:24:20,479

a massive host range

5366

03:24:26,950 --> 03:24:21,920

mutation generation ability it's

5367

03:24:30,550 --> 03:24:28,950

and i i work with many uh people who

5368

03:24:31,830 --> 03:24:30,560

work on the gemini viruses the the

5369

03:24:33,510 --> 03:24:31,840

biggest group of plant-infecting

5370

03:24:35,750 --> 03:24:33,520

single-stranded dna viruses and the lack

5371

03:24:40,389 --> 03:24:35,760

of host-specific adaptation is just

5372

03:24:43,910 --> 03:24:42,150

thanks yeah we're of course we're

5373

03:24:46,309 --> 03:24:43,920

looking at some of these strange

5374

03:24:50,309 --> 03:24:46,319

single-stranded dna viruses as well and

5375

03:24:52,070 --> 03:24:50,319

you know love to have some handles on it

5376
03:24:54,070 --> 03:24:52,080
they're everywhere and someone should

5377
03:24:56,790 --> 03:24:54,080
develop one of the ones that infects

5378
03:24:59,590 --> 03:24:56,800
fungi or you know some protists into a

5379
03:25:01,830 --> 03:24:59,600
good working experimental system

5380
03:25:03,349 --> 03:25:01,840
i agree

5381
03:25:04,550 --> 03:25:03,359
i'll take an archaeal system if you can

5382
03:25:08,550 --> 03:25:04,560
get that thing

5383
03:25:13,670 --> 03:25:08,560
the 25 kb one to grow well

5384
03:25:17,750 --> 03:25:15,590
arvin had a nice notice in the chat

5385
03:25:20,150 --> 03:25:17,760
group about um that plan virus evolution

5386
03:25:21,590 --> 03:25:20,160
and ecology that was their recent arvind

5387
03:25:23,830 --> 03:25:21,600
are you still around

5388
03:25:24,870 --> 03:25:23,840

um online here that was a recent review

5389

03:25:29,429 --> 03:25:24,880

correct

5390

03:25:30,790 --> 03:25:29,439

covers a lot of work from ecology to

5391

03:25:33,030 --> 03:25:30,800

evolution

5392

03:25:35,269 --> 03:25:33,040

also looks at tradeoff hypothesis in

5393

03:25:37,750 --> 03:25:35,279

there talks about insects playing a

5394

03:25:40,710 --> 03:25:37,760

major role and how insects and plant

5395

03:25:44,710 --> 03:25:40,720

viruses have potentially co-evolved

5396

03:25:48,229 --> 03:25:46,950

yeah thanks it's um i can say this

5397

03:25:57,190 --> 03:25:48,239

because i'm not one of the authors it's

5398

03:26:00,870 --> 03:25:58,550

we're still at the point where they have

5399

03:26:02,790 --> 03:26:00,880

to have special mixer sessions at asv

5400

03:26:04,389 --> 03:26:02,800

for the animal and plant virus people to

5401
03:26:06,550 --> 03:26:04,399
talk to each other and try to figure out

5402
03:26:08,550 --> 03:26:06,560
what's similar across our disciplines

5403
03:26:13,429 --> 03:26:08,560
and those rooms don't include the phage

5404
03:26:18,389 --> 03:26:16,469
the vast numbers of us

5405
03:26:20,790 --> 03:26:18,399
i i think if we have take hands on this

5406
03:26:23,510 --> 03:26:20,800
call we'll be fine

5407
03:26:26,469 --> 03:26:23,520
no um which i think is a great

5408
03:26:29,590 --> 03:26:26,479
transition so in theory in the schedule

5409
03:26:31,910 --> 03:26:29,600
um i'm supposed to say something about

5410
03:26:34,710 --> 03:26:31,920
closing remarks um i'd actually much

5411
03:26:36,710 --> 03:26:34,720
prefer to open this up to

5412
03:26:38,389 --> 03:26:36,720
really everyone

5413
03:26:40,790 --> 03:26:38,399

uh to

5414

03:26:42,070 --> 03:26:40,800

make comments and unfortunately i snuck

5415

03:26:44,309 --> 03:26:42,080

out at the break but it seems that there

5416

03:26:46,389 --> 03:26:44,319

were some issues with seeing yourself

5417

03:26:48,469 --> 03:26:46,399

and not seeing yourself

5418

03:26:49,910 --> 03:26:48,479

as far as being bizarre for presentation

5419

03:26:51,269 --> 03:26:49,920

wise

5420

03:26:52,950 --> 03:26:51,279

do we have any

5421

03:26:56,070 --> 03:26:52,960

more feedback on that or any other

5422

03:26:58,229 --> 03:26:56,080

questions for other people um before we

5423

03:27:06,309 --> 03:26:58,239

sort of wrap up for today and then pick

5424

03:27:11,830 --> 03:27:09,269

anybody at ni central have some uh

5425

03:27:13,349 --> 03:27:11,840

comments thoughts um i completely agree

5426
03:27:15,510 --> 03:27:13,359
with the the chats we need to try and

5427
03:27:16,950 --> 03:27:15,520
get a transcript for that um i think

5428
03:27:18,150 --> 03:27:16,960
there's a lot of really cool stuff going

5429
03:27:19,670 --> 03:27:18,160
on there i just haven't been able to

5430
03:27:22,309 --> 03:27:19,680
split my

5431
03:27:24,630 --> 03:27:22,319
attention i'm really bad at multitasking

5432
03:27:27,349 --> 03:27:25,990
uh well

5433
03:27:29,349 --> 03:27:27,359
you know i've been paying attention to

5434
03:27:31,269 --> 03:27:29,359
the chats and answering a few things and

5435
03:27:34,469 --> 03:27:31,279
asking a few things so we will have

5436
03:27:37,269 --> 03:27:34,479
those captured um we also

5437
03:27:40,309 --> 03:27:37,279
uh would like to make sure that everyone

5438
03:27:43,269 --> 03:27:40,319

from whom we have slides uh is willing

5439

03:27:46,150 --> 03:27:43,279

to have us post them on the nai website

5440

03:27:48,150 --> 03:27:46,160

under this workshop

5441

03:27:50,870 --> 03:27:48,160

so i guess we'll

5442

03:27:52,630 --> 03:27:50,880

you know ask anyone who presented who

5443

03:27:54,309 --> 03:27:52,640

doesn't want that to happen to certainly

5444

03:27:57,269 --> 03:27:54,319

email us right away

5445

03:27:58,790 --> 03:27:57,279

if not we'll certainly confirm with you

5446

03:28:01,190 --> 03:27:58,800

before we post them

5447

03:28:01,910 --> 03:28:01,200

uh if you need to take any proprietary

5448

03:28:06,790 --> 03:28:01,920

or

5449

03:28:09,030 --> 03:28:06,800

what uh if you need to do a clean up on

5450

03:28:11,190 --> 03:28:09,040

them and after that uh within a couple

5451

03:28:13,110 --> 03:28:11,200

of days we'll have those posted also

5452

03:28:16,309 --> 03:28:13,120

we've recorded this so for any of you

5453

03:28:17,830 --> 03:28:16,319

who joined us uh late or intermittently

5454

03:28:19,910 --> 03:28:17,840

uh you'll be able to catch the parts

5455

03:28:22,229 --> 03:28:19,920

that you didn't

5456

03:28:24,389 --> 03:28:22,239

you weren't able to join us for

5457

03:28:26,710 --> 03:28:24,399

and then for anybody who wasn't

5458

03:28:29,030 --> 03:28:26,720

present right at the beginning

5459

03:28:32,309 --> 03:28:29,040

one of the aspirations of this effort is

5460

03:28:33,830 --> 03:28:32,319

to produce tangible product and one is a

5461

03:28:35,830 --> 03:28:33,840

journal article

5462

03:28:38,550 --> 03:28:35,840

produced by you folks

5463

03:28:41,750 --> 03:28:38,560

i'll facilitate it as much as i can

5464

03:28:44,070 --> 03:28:41,760

for the journal astrobiology and then a

5465

03:28:46,790 --> 03:28:44,080

distillation of that for the upcoming

5466

03:28:48,550 --> 03:28:46,800

planetary decadal white paper so that's

5467

03:28:49,830 --> 03:28:48,560

just to recap what i said in the

5468

03:28:50,870 --> 03:28:49,840

beginning for those of you who weren't

5469

03:28:52,710 --> 03:28:50,880

on

5470

03:28:54,469 --> 03:28:52,720

and with that i think uh that's all i

5471

03:28:56,870 --> 03:28:54,479

need to say

5472

03:29:00,229 --> 03:28:56,880

except i had a great time and a lot of

5473

03:29:03,590 --> 03:29:01,830

yeah thanks and any comments if you

5474

03:29:06,550 --> 03:29:03,600

don't feel like um sharing them in a

5475

03:29:09,190 --> 03:29:06,560

general chat feel free to do a direct

5476

03:29:10,630 --> 03:29:09,200

chat to any of us um as far as that's

5477

03:29:13,110 --> 03:29:10,640

concerned you can also find our email

5478

03:29:14,790 --> 03:29:13,120

addresses etc i haven't been watching on

5479

03:29:18,790 --> 03:29:14,800

twitter i'm sure we've completely blown

5480

03:29:23,110 --> 03:29:21,590

and uh yeah let's see and thanks again

5481

03:29:24,790 --> 03:29:23,120

penny for pointing out the the article

5482

03:29:27,190 --> 03:29:24,800

and white papers we will be reaching out

5483

03:29:29,910 --> 03:29:27,200

to you i guarantee that um that will

5484

03:29:32,229 --> 03:29:29,920

happen keep an eye on your your inboxes

5485

03:29:35,830 --> 03:29:32,239

and we will we'll let you know about

5486

03:29:37,750 --> 03:29:35,840

that um i will try and synthesize a

5487

03:29:41,030 --> 03:29:37,760

little bit more of what i've heard today

5488

03:29:42,229 --> 03:29:41,040

um as i was uh personally chatting with

5489

03:29:43,990 --> 03:29:42,239

someone

5490

03:29:45,910 --> 03:29:44,000

even i'm a little overwhelmed at this

5491

03:29:47,990 --> 03:29:45,920

point so i need to sit back and

5492

03:29:49,349 --> 03:29:48,000

synthesize some of these things maybe

5493

03:29:51,990 --> 03:29:49,359

re-listen to a couple of the

5494

03:29:55,349 --> 03:29:52,000

presentations and i'll try and fit some

5495

03:29:57,269 --> 03:29:55,359

of that into my closing talk tomorrow as

5496

03:29:59,190 --> 03:29:57,279

well

5497

03:30:01,269 --> 03:29:59,200

one other point that i want to make

5498

03:30:03,750 --> 03:30:01,279

we've had a great turnout for this the

5499

03:30:05,990 --> 03:30:03,760

highest number of participants on at any

5500

03:30:08,070 --> 03:30:06,000

one time was 87

5501
03:30:10,150 --> 03:30:08,080
and we probably have a few more of that

5502
03:30:11,910 --> 03:30:10,160
in terms of you know total coming and

5503
03:30:13,910 --> 03:30:11,920
going so

5504
03:30:15,110 --> 03:30:13,920
that exceeds my expectations for how

5505
03:30:17,190 --> 03:30:15,120
many people we could pull out of the

5506
03:30:19,030 --> 03:30:17,200
woodwork who are interested in this

5507
03:30:20,550 --> 03:30:19,040
whether or not they happen to be experts

5508
03:30:22,630 --> 03:30:20,560
so i think that there's a lot of

5509
03:30:24,950 --> 03:30:22,640
interest in the community and

5510
03:30:27,190 --> 03:30:24,960
that makes it worth having gone to the

5511
03:30:29,670 --> 03:30:27,200
trouble of doing this to try to get

5512
03:30:31,990 --> 03:30:29,680
everybody to be talking to each other

5513
03:30:34,150 --> 03:30:32,000

including folks that may not consider

5514

03:30:35,750 --> 03:30:34,160

themselves virologists we discussed this

5515

03:30:37,510 --> 03:30:35,760

at the beginning uh there are many

5516

03:30:39,190 --> 03:30:37,520

people who are not virologists but who

5517

03:30:42,150 --> 03:30:39,200

have uh

5518

03:30:43,910 --> 03:30:42,160

uh probably things to contribute and uh

5519

03:30:47,349 --> 03:30:43,920

getting them also thinking along the

5520

03:30:48,710 --> 03:30:47,359

lines of the role of viruses and other

5521

03:30:50,950 --> 03:30:48,720

mobile

5522

03:30:53,670 --> 03:30:50,960

genetic entities that are moving things

5523

03:30:55,590 --> 03:30:53,680

around i think is really worthwhile

5524

03:30:57,750 --> 03:30:55,600

for the effort and so i look forward to

5525

03:30:59,349 --> 03:30:57,760

seeing everybody tomorrow afternoon and

5526
03:31:00,309 --> 03:30:59,359
maybe a few additional people that we

5527
03:31:01,990 --> 03:31:00,319
didn't have

5528
03:31:03,990 --> 03:31:02,000
who couldn't make it today so thanks

5529
03:31:06,070 --> 03:31:04,000
everybody for attending i wanted to

5530
03:31:07,590 --> 03:31:06,080
throw one last bit in there if you're

5531
03:31:09,110 --> 03:31:07,600
not a virus specialist or even if you

5532
03:31:11,190 --> 03:31:09,120
are you may have not understood some of

5533
03:31:12,950 --> 03:31:11,200
the jargon that was discussed today on

5534
03:31:15,510 --> 03:31:12,960
our website we have some helpful

5535
03:31:17,110 --> 03:31:15,520
resources but also feel free to email us

5536
03:31:19,349 --> 03:31:17,120
with any questions there's no bad

5537
03:31:21,510 --> 03:31:19,359
question if you want to know what is a

5538
03:31:23,510 --> 03:31:21,520

lytic virus or something please email us

5539

03:31:24,630 --> 03:31:23,520

so we can help you out that way if you

5540

03:31:26,389 --> 03:31:24,640

feel like it might help you be more

5541

03:31:30,389 --> 03:31:26,399

engaging tomorrow and might be useful

5542

03:31:36,150 --> 03:31:33,670

yeah all i can say is is thank you um to

5543

03:31:39,429 --> 03:31:36,160

everybody has participated this has been

5544

03:31:42,710 --> 03:31:39,439

um really really wonderful at least from

5545

03:31:45,750 --> 03:31:42,720

from my highly biased point of view

5546

03:31:47,830 --> 03:31:45,760

so um thanks to everybody and hopefully

5547

03:31:49,750 --> 03:31:47,840

we'll see all of you or at least hear

5548

03:31:50,550 --> 03:31:49,760

from some of you tomorrow

5549

03:31:52,830 --> 03:31:50,560

great