503: From Autocatalysis to Evolution III

1
00:00:04,630 --> 00:00:02,470
hello everyone it's a great pleasure to

2
00:00:06,789 --> 00:00:04,640
have you here all we had a very exciting

3
00:00:08,710 --> 00:00:06,799
session i think uh online on auto

4
00:00:11,430 --> 00:00:08,720
catalysis from motocades to evolution

5
00:00:13,350 --> 00:00:11,440
and today is the hybrid session we will

6
00:00:19,269 --> 00:00:13,360
have three talks

7
00:00:19,279 --> 00:00:25,910
yeah and so

8
00:00:32,150 --> 00:00:28,790
so it's a pleasure to to welcome dieter

9
00:00:34,150 --> 00:00:32,160
brown from ludwig maximilian universitat

10
00:00:35,590 --> 00:00:34,160
in munich

11
00:00:37,910 --> 00:00:35,600
and he's going to tell us about

12
00:00:40,790 --> 00:00:37,920
recreating the first steps of life using

13
00:00:42,869 --> 00:00:40,800

non-equilibrium settings

14
00:00:45,350 --> 00:00:42,879
thanks for having me

15
00:00:46,950 --> 00:00:45,360
and thanks for allowing the optimistic

16
00:00:49,190 --> 00:00:46,960
title let's see

17
00:00:51,270 --> 00:00:49,200
uh how we see life and the origins of

18
00:00:53,830 --> 00:00:51,280
life trying to figure out the emergence

19
00:00:55,910 --> 00:00:53,840
of life is i think a twofold into mixed

20
00:00:58,229 --> 00:00:55,920
axis chemicals

21
00:00:59,590 --> 00:00:58,239
physics has to come together that's what

22
00:01:02,069 --> 00:00:59,600
we try to do

23
00:01:04,390 --> 00:01:02,079
and it's like a maze we try to you know

24
00:01:06,310 --> 00:01:04,400
hop around do experiments figure out

25
00:01:08,469 --> 00:01:06,320
what are good conditions for this and we

26
00:01:11,270 --> 00:01:08,479
started the whole story by saying okay

27
00:01:12,789 --> 00:01:11,280
let's put the psi chemistry for a second

28
00:01:14,789 --> 00:01:12,799
and we use a protein to do the

29
00:01:15,990 --> 00:01:14,799
replication for our first evolutionary

30
00:01:17,990 --> 00:01:16,000
cycles

31
00:01:19,749 --> 00:01:18,000
we looked for convection traps where you

32
00:01:21,910 --> 00:01:19,759
have thermocycling

33
00:01:24,230 --> 00:01:21,920
but recently figured out that air water

34
00:01:26,310 --> 00:01:24,240
interfaces can help them if you combine

35
00:01:28,149 --> 00:01:26,320
them and you'll see an example of that

36
00:01:31,429 --> 00:01:28,159
but towards the end of the talk what i

37
00:01:34,469 --> 00:01:31,439
try to show you is that as we go more

38
00:01:36,630 --> 00:01:34,479

more towards chemistry rna ribozymes

39
00:01:37,510 --> 00:01:36,640
two three prime cyclic nucleotides we

40
00:01:39,910 --> 00:01:37,520
might

41
00:01:41,590 --> 00:01:39,920
lead to a real balance between chemistry

42
00:01:44,310 --> 00:01:41,600
and physics

43
00:01:46,550 --> 00:01:44,320
and examples of what we did is you know

44
00:01:48,469 --> 00:01:46,560
thermal gradients some phrases in a

45
00:01:51,109 --> 00:01:48,479
flow-through system running for a

46
00:01:52,870 --> 00:01:51,119
selection for the longer sequences but

47
00:01:55,030 --> 00:01:52,880
you can also have a look on sequence

48
00:01:57,109 --> 00:01:55,040
space evolution focusing yourself in

49
00:02:00,310 --> 00:01:57,119
sequence base or configure

50
00:02:02,870 --> 00:02:00,320
a convection cell which is basically

51
00:02:04,310 --> 00:02:02,880
able to run delicate rna molecules and

52
00:02:05,510 --> 00:02:04,320
still thermally cycle them without

53
00:02:08,469 --> 00:02:05,520
destroying and actually also

54
00:02:11,990 --> 00:02:08,479
accumulating or have a replicator made

55
00:02:14,470 --> 00:02:12,000
out of trna like molecules what i'll

56
00:02:17,430 --> 00:02:14,480
talk today about is is a system here

57
00:02:20,550 --> 00:02:17,440
it's it's air water interface basically

58
00:02:22,710 --> 00:02:20,560
a piece of of a of a cleft in a rock

59
00:02:25,510 --> 00:02:22,720
where you have some water at the bottom

60
00:02:27,270 --> 00:02:25,520
a larger volume on top as you heat and

61
00:02:29,750 --> 00:02:27,280
cool them at the same

62
00:02:32,949 --> 00:02:29,760
continuously you'll you'll see at the

63
00:02:34,869 --> 00:02:32,959

interface this dynamics so bubbles are

64
00:02:36,949 --> 00:02:34,879
forming on the cold side because they

65
00:02:38,550 --> 00:02:36,959
evaporate on the warm side

66
00:02:40,949 --> 00:02:38,560
it grows so large that they touch the

67
00:02:43,270 --> 00:02:40,959
warm side jump onto the warm side

68
00:02:45,190 --> 00:02:43,280
evaporate and you see these coffee ring

69
00:02:47,270 --> 00:02:45,200
effects here

70
00:02:49,190 --> 00:02:47,280
while at the interface molecules are

71
00:02:51,750 --> 00:02:49,200
also accumulating what you see here is a

72
00:02:53,990 --> 00:02:51,760
fluorescence of of dna molecule and you

73
00:02:56,470 --> 00:02:54,000
can actually simulate these conditions

74
00:02:58,229 --> 00:02:56,480
on a computer finite element methods and

75
00:03:00,390 --> 00:02:58,239
figure out that these

76
00:03:03,910 --> 00:03:00,400
settings are actually accumulating

77
00:03:06,229 --> 00:03:03,920
larger molecules always better so it has

78
00:03:08,550 --> 00:03:06,239
a selection physical selection pressure

79
00:03:10,149 --> 00:03:08,560
for length which we think is important

80
00:03:12,309 --> 00:03:10,159
for any replicating system because

81
00:03:14,149 --> 00:03:12,319
otherwise you get for the fast short

82
00:03:15,190 --> 00:03:14,159
replicating molecules and the test

83
00:03:17,350 --> 00:03:15,200
system

84
00:03:20,229 --> 00:03:17,360
was here to use a polymerase chain

85
00:03:21,830 --> 00:03:20,239
reaction a pcr but the interesting point

86
00:03:24,309 --> 00:03:21,840
here was that we used it at a

87
00:03:27,030 --> 00:03:24,319
temperature but actually the template

88
00:03:30,070 --> 00:03:27,040

which we wanted to replicate by you know

89
00:03:31,509 --> 00:03:30,080
those cycles of strand separation

90
00:03:33,670 --> 00:03:31,519
and have then

91
00:03:36,710 --> 00:03:33,680
the polymerase do the job

92
00:03:38,390 --> 00:03:36,720
was lower than the 51

93
00:03:39,350 --> 00:03:38,400
base target

94
00:03:42,149 --> 00:03:39,360
still

95
00:03:44,630 --> 00:03:42,159
we got an amplification and we'll show

96
00:03:46,789 --> 00:03:44,640
you later this amplification actually

97
00:03:48,789 --> 00:03:46,799
created molecules up a thousand bases

98
00:03:50,949 --> 00:03:48,799
long and we understand how this is

99
00:03:52,869 --> 00:03:50,959
possible and i'll go through the story

100
00:03:55,750 --> 00:03:52,879
here you see how at the interface the

101
00:03:57,190 --> 00:03:55,760
replication is triggered and this is

102
00:04:01,030 --> 00:03:57,200
really running

103
00:04:03,750 --> 00:04:01,040
uh and being created at the interface

104
00:04:06,229 --> 00:04:03,760
so what happens here is that the

105
00:04:08,550 --> 00:04:06,239
molecules as they are replicated in this

106
00:04:11,750 --> 00:04:08,560
interplay between the dry side on top

107
00:04:15,509 --> 00:04:11,760
and the wet side at the bottom

108
00:04:17,110 --> 00:04:15,519
is is doing the job and you see actually

109
00:04:19,590 --> 00:04:17,120
if you have a thermocycler where you do

110
00:04:21,189 --> 00:04:19,600
the pcr you see the usual that if you

111
00:04:23,350 --> 00:04:21,199
have competition between the long and

112
00:04:25,670 --> 00:04:23,360
the short strength the long strain is

113
00:04:28,150 --> 00:04:25,680

losing the short frame is making the

114
00:04:29,590 --> 00:04:28,160
show but the funny part is that if you

115
00:04:31,430 --> 00:04:29,600
put this on

116
00:04:32,950 --> 00:04:31,440
such a

117
00:04:35,350 --> 00:04:32,960
temperature gradient with these air

118
00:04:37,430 --> 00:04:35,360
water interface you see that both are

119
00:04:39,430 --> 00:04:37,440
you know equally well

120
00:04:41,189 --> 00:04:39,440
and you see these very large strands on

121
00:04:42,629 --> 00:04:41,199
top and you might wonder oh that's some

122
00:04:44,870 --> 00:04:42,639
dirt effect and we don't fully

123
00:04:45,749 --> 00:04:44,880
understand so we went for sequencing

124
00:04:48,870 --> 00:04:45,759
these

125
00:04:51,270 --> 00:04:48,880
and figure out what might be happening

126
00:04:53,670 --> 00:04:51,280
and the story is now the following we

127
00:04:57,110 --> 00:04:53,680
only saw those long strands if we added

128
00:04:59,030 --> 00:04:57,120
co2 into the mixture now we add the co2

129
00:05:01,189 --> 00:04:59,040
and this fluorescence signal

130
00:05:04,070 --> 00:05:01,199
you see here in the fret you see that if

131
00:05:06,870 --> 00:05:04,080
you add the co2 the chambers that the uh

132
00:05:09,110 --> 00:05:06,880
is that in these bubbles the strands are

133
00:05:11,590 --> 00:05:09,120
separating you get single-stranded rna

134
00:05:14,310 --> 00:05:11,600
or dna and you also see at the same time

135
00:05:16,230 --> 00:05:14,320
that the ph drops so what's to be

136
00:05:18,870 --> 00:05:16,240
expected here is that

137
00:05:21,029 --> 00:05:18,880
as the water evaporates from the bottom

138
00:05:23,909 --> 00:05:21,039

even if this is very salty you'll get

139
00:05:26,230 --> 00:05:23,919
pure water on the side this bubble grows

140
00:05:28,870 --> 00:05:26,240
then jumps on the other side where you

141
00:05:30,230 --> 00:05:28,880
have previously dried the dna then you

142
00:05:33,830 --> 00:05:30,240
have a very low

143
00:05:34,870 --> 00:05:33,840
salt environment for this dna

144
00:05:37,189 --> 00:05:34,880
and

145
00:05:39,430 --> 00:05:37,199
if you add the co2 on top of it because

146
00:05:41,430 --> 00:05:39,440
this is low salt it's not buffering

147
00:05:42,550 --> 00:05:41,440
anymore you also get a low ph because of

148
00:05:44,790 --> 00:05:42,560
co2

149
00:05:47,189 --> 00:05:44,800
and it turns out we can now

150
00:05:49,189 --> 00:05:47,199
calculate and figure out what is the

151
00:05:51,510 --> 00:05:49,199
salt concentration by these optical

152
00:05:53,670 --> 00:05:51,520
measurements you find it's a very low

153
00:05:56,550 --> 00:05:53,680
magnesium chloride concentration about

154
00:05:57,830 --> 00:05:56,560
40 volts lower than the bulk

155
00:06:02,790 --> 00:05:57,840
and

156
00:06:05,430 --> 00:06:02,800
the situation in this setting is now

157
00:06:06,870 --> 00:06:05,440
that as you change the ph with these two

158
00:06:08,870 --> 00:06:06,880
droplets

159
00:06:11,670 --> 00:06:08,880
and you change the salt within these two

160
00:06:15,430 --> 00:06:11,680
droplets you enable a

161
00:06:17,430 --> 00:06:15,440
cycling at this setting for your bulk

162
00:06:19,590 --> 00:06:17,440
and in the dual down here

163
00:06:22,629 --> 00:06:19,600

and you see already in this

164
00:06:25,110 --> 00:06:22,639
fret calibration here that in the blue

165
00:06:27,510 --> 00:06:25,120
you separate the strands

166
00:06:29,870 --> 00:06:27,520
by not only going for low salt that

167
00:06:32,710 --> 00:06:29,880
would not have been enough but by

168
00:06:34,629 --> 00:06:32,720
acidification by the co2 please note

169
00:06:37,590 --> 00:06:34,639
that co2 on early earth would be a

170
00:06:40,309 --> 00:06:37,600
common gas a common atmosphere so you

171
00:06:42,629 --> 00:06:40,319
would actually expect to have co2 around

172
00:06:44,550 --> 00:06:42,639
and the control experiments clearly show

173
00:06:47,110 --> 00:06:44,560
you only get this effect if you have co2

174
00:06:48,950 --> 00:06:47,120
if you just use normal atmosphere you're

175
00:06:51,670 --> 00:06:48,960
not getting it

176
00:06:53,830 --> 00:06:51,680
now back to the sequencing i told you we

177
00:06:55,830 --> 00:06:53,840
got these very long strands and the gel

178
00:06:59,670 --> 00:06:55,840
it was hard to quantify by sequencing

179
00:07:01,510 --> 00:06:59,680
you found up to 1300 bases

180
00:07:02,390 --> 00:07:01,520
and we looked at the sequences and we

181
00:07:05,350 --> 00:07:02,400
looked

182
00:07:07,510 --> 00:07:05,360
on which part of that phase space which

183
00:07:10,150 --> 00:07:07,520
we explored the shorter strands thread

184
00:07:11,350 --> 00:07:10,160
probes to figure out when these strands

185
00:07:14,070 --> 00:07:11,360
are melting

186
00:07:16,870 --> 00:07:14,080
we find that these sequences all pile up

187
00:07:20,070 --> 00:07:16,880
along this melting line

188
00:07:22,390 --> 00:07:20,080

so here are our starting strands

189
00:07:24,309 --> 00:07:22,400
remember that we have about 50 50 gc

190
00:07:26,870 --> 00:07:24,319
content at a 50 mirror

191
00:07:29,510 --> 00:07:26,880
then we also see some aggregated parts

192
00:07:31,189 --> 00:07:29,520
where you make those templates next to

193
00:07:34,150 --> 00:07:31,199
each other and you make longer strands

194
00:07:37,510 --> 00:07:34,160
of it but then you see these

195
00:07:39,589 --> 00:07:37,520
strands here which in this case got a

196
00:07:42,230 --> 00:07:39,599
higher a t than gc

197
00:07:45,029 --> 00:07:42,240
content indicating that you had a

198
00:07:47,990 --> 00:07:45,039
selection pressure which was kind of

199
00:07:49,830 --> 00:07:48,000
driven by two forces and i just give you

200
00:07:51,110 --> 00:07:49,840
the full picture here this is only the

201
00:07:53,029 --> 00:07:51,120
small picture

202
00:07:57,110 --> 00:07:53,039
down here so

203
00:07:59,189 --> 00:07:57,120
these white sequences up here apparently

204
00:08:01,510 --> 00:07:59,199
really were selected for being at that

205
00:08:03,270 --> 00:08:01,520
melting transition now it makes sense to

206
00:08:05,270 --> 00:08:03,280
push it for a system where it can

207
00:08:07,430 --> 00:08:05,280
actually separate the strands

208
00:08:11,270 --> 00:08:07,440
and in this case it actually had to

209
00:08:14,230 --> 00:08:11,280
change the at gc content to do that

210
00:08:16,309 --> 00:08:14,240
please keep in mind that still in this

211
00:08:18,469 --> 00:08:16,319
setting the system seems to be pushed

212
00:08:20,390 --> 00:08:18,479
for longer strands so this

213
00:08:22,309 --> 00:08:20,400

it was not enough to keep those short

214
00:08:24,230 --> 00:08:22,319
sequences those were not the sequences

215
00:08:26,950 --> 00:08:24,240
we are seeing in the majority

216
00:08:29,350 --> 00:08:26,960
but those accumulation effects at these

217
00:08:31,589 --> 00:08:29,360
interfaces most probably were driving

218
00:08:33,509 --> 00:08:31,599
the system also for long australians so

219
00:08:35,190 --> 00:08:33,519
what you can see here is that the simple

220
00:08:38,550 --> 00:08:35,200
air water interface

221
00:08:40,230 --> 00:08:38,560
is enabling with co2 to give you low

222
00:08:43,589 --> 00:08:40,240
salt conditions while you have a high

223
00:08:46,949 --> 00:08:44,470
and

224
00:08:49,190 --> 00:08:46,959
the co2 the acidification of that allows

225
00:08:50,230 --> 00:08:49,200
you to really fully separate really long

226
00:08:51,990 --> 00:08:50,240
strands

227
00:08:54,310 --> 00:08:52,000
now the same thing should actually be

228
00:08:58,870 --> 00:08:54,320
possible also for rna and we'll get to

229
00:09:03,430 --> 00:09:01,110
there's some modeling you can do

230
00:09:05,430 --> 00:09:03,440
and the modeling confirms the

231
00:09:07,910 --> 00:09:05,440
replication simple replication model

232
00:09:09,910 --> 00:09:07,920
confirms the dynamics and the sequence

233
00:09:11,670 --> 00:09:09,920
selection you have in there

234
00:09:14,070 --> 00:09:11,680
so as we want to go for

235
00:09:18,150 --> 00:09:14,080
origin of life figuring out processes

236
00:09:20,630 --> 00:09:18,160
how to start replication how to start

237
00:09:22,389 --> 00:09:20,640
the first cycles of darwin evolution we

238
00:09:23,829 --> 00:09:22,399

went through a number of molecules and

239
00:09:26,230 --> 00:09:23,839
we could go through the advantages

240
00:09:28,070 --> 00:09:26,240
disadvantages of these systems

241
00:09:30,389 --> 00:09:28,080
as they are more aggressive making more

242
00:09:32,949 --> 00:09:30,399
side products more mild but then often

243
00:09:35,509 --> 00:09:32,959
not really covering all the bases or

244
00:09:37,430 --> 00:09:35,519
difficult to achieve with simple

245
00:09:39,750 --> 00:09:37,440
probiotic chemistry and we just looked

246
00:09:41,910 --> 00:09:39,760
back again into chemistries from the

247
00:09:44,150 --> 00:09:41,920
1970s to the two three cyclic

248
00:09:46,070 --> 00:09:44,160
nucleotides and we figured out that at

249
00:09:48,470 --> 00:09:46,080
high ph

250
00:09:51,750 --> 00:09:48,480
with including the g base

251
00:09:54,310 --> 00:09:51,760
these are uh giving us a nice setting

252
00:09:56,389 --> 00:09:54,320
and the 70s analytical techniques were

253
00:09:57,430 --> 00:09:56,399
not yet ready and most experiments were

254
00:09:59,269 --> 00:09:57,440
tried

255
00:10:02,069 --> 00:09:59,279
or published experimentally try this

256
00:10:04,470 --> 00:10:02,079
with a and with g people

257
00:10:06,230 --> 00:10:04,480
had a hard time to separate molecules so

258
00:10:07,829 --> 00:10:06,240
also these systems actually behave quite

259
00:10:11,350 --> 00:10:07,839
nicely in these

260
00:10:13,750 --> 00:10:11,360
water interfaces where we've seen before

261
00:10:16,470 --> 00:10:13,760
phosphorylation encapsulation and

262
00:10:18,470 --> 00:10:16,480
vesicle for tricycling crystallization

263
00:10:20,150 --> 00:10:18,480

and and that enrichment of that coffee

264
00:10:22,230 --> 00:10:20,160
ring effect

265
00:10:25,509 --> 00:10:22,240
so let's see what the system can do for

266
00:10:27,509 --> 00:10:25,519
us and we go for about ph 9 to 11

267
00:10:30,310 --> 00:10:27,519
with quite right a

268
00:10:31,990 --> 00:10:30,320
large range of temperatures and can for

269
00:10:34,350 --> 00:10:32,000
example in such a system run the

270
00:10:36,630 --> 00:10:34,360
phosphorylation to make these with

271
00:10:38,230 --> 00:10:36,640
trimetaphosphate quite specifically we

272
00:10:41,110 --> 00:10:38,240
don't get

273
00:10:43,590 --> 00:10:41,120
much if all detectable 5-prime

274
00:10:46,949 --> 00:10:43,600
phosphorylation but then also in the dry

275
00:10:49,670 --> 00:10:46,959
state with the initial ph you find a

276
00:10:53,190 --> 00:10:49,680
quite efficient polymerization

277
00:10:55,829 --> 00:10:53,200
so between ph 8 and 12 you get these

278
00:10:58,870 --> 00:10:55,839
oligomer lengths it goes up to 15

279
00:11:00,790 --> 00:10:58,880
roughly we're still improving here

280
00:11:02,389 --> 00:11:00,800
and this is a polymerization

281
00:11:03,590 --> 00:11:02,399
which is driven

282
00:11:05,110 --> 00:11:03,600
which is shown

283
00:11:07,110 --> 00:11:05,120
for g

284
00:11:09,590 --> 00:11:07,120
it is a bit more difficult to get all

285
00:11:11,670 --> 00:11:09,600
the bases involved again work in

286
00:11:15,269 --> 00:11:11,680
progress so this is the best we could

287
00:11:17,110 --> 00:11:15,279
achieve so far where we have mixed

288
00:11:18,470 --> 00:11:17,120

four bases at five millimolar

289
00:11:20,949 --> 00:11:18,480
concentration

290
00:11:23,030 --> 00:11:20,959
and this experiment in blue was now

291
00:11:23,910 --> 00:11:23,040
again running these water interfaces so

292
00:11:26,150 --> 00:11:23,920
they

293
00:11:28,150 --> 00:11:26,160
a water cycling

294
00:11:29,509 --> 00:11:28,160
dry wet cycling you are implementing

295
00:11:32,790 --> 00:11:29,519
here

296
00:11:34,389 --> 00:11:32,800
is also effective and gives you

297
00:11:37,590 --> 00:11:34,399
quite an efficient

298
00:11:39,750 --> 00:11:37,600
polymerization dynamics

299
00:11:42,150 --> 00:11:39,760
so how do we detect this that's a longer

300
00:11:44,389 --> 00:11:42,160
story and i think it's also an important

301
00:11:45,670 --> 00:11:44,399
story to discuss that we are sure what

302
00:11:49,110 --> 00:11:45,680
we are seeing

303
00:11:51,269 --> 00:11:49,120
it has a safety precipitation step first

304
00:11:52,550 --> 00:11:51,279
we could omit it but it also reduced a

305
00:11:54,710 --> 00:11:52,560
little bit the construction of the

306
00:11:56,389 --> 00:11:54,720
monomers in the mix and we are really

307
00:11:59,110 --> 00:11:56,399
sure that we get

308
00:12:01,670 --> 00:11:59,120
a clean ionization this is then run

309
00:12:04,790 --> 00:12:01,680
through hplc at 60 degrees high

310
00:12:08,310 --> 00:12:04,800
temperature special oligonucleotide

311
00:12:11,110 --> 00:12:08,320
column which even poly g can separate

312
00:12:13,670 --> 00:12:11,120
nicely without binding effects we can

313
00:12:14,870 --> 00:12:13,680

detect over three orders of magnitude

314
00:12:17,110 --> 00:12:14,880
have a

315
00:12:18,310 --> 00:12:17,120
please note the logarithmic scale here a

316
00:12:20,389 --> 00:12:18,320
raw

317
00:12:22,949 --> 00:12:20,399
mass spectrum which we then fit with the

318
00:12:24,190 --> 00:12:22,959
isotope pattern for all the molecules we

319
00:12:27,190 --> 00:12:24,200
want to check out

320
00:12:28,870 --> 00:12:27,200
[Applause]

321
00:12:29,750 --> 00:12:28,880
questions i'm happy to address these

322
00:12:31,910 --> 00:12:29,760
here

323
00:12:33,829 --> 00:12:31,920
so by that we could see for the

324
00:12:36,550 --> 00:12:33,839
polymerization what is interesting i

325
00:12:40,230 --> 00:12:36,560
think is that under very similar

326
00:12:42,629 --> 00:12:40,240
actually best running at ph 10 is also a

327
00:12:43,350 --> 00:12:42,639
templated ligation

328
00:12:44,710 --> 00:12:43,360
of

329
00:12:52,629 --> 00:12:44,720
a

330
00:12:54,790 --> 00:12:52,639
prime cyclic

331
00:12:56,069 --> 00:12:54,800
ending we get efficient

332
00:12:58,790 --> 00:12:56,079
um

333
00:13:01,110 --> 00:12:58,800
uh ligation that's ph nine actually at

334
00:13:03,190 --> 00:13:01,120
ph 10 or 11 this is boosted almost by

335
00:13:05,509 --> 00:13:03,200
factor of 10 so it seems to confirm that

336
00:13:07,190 --> 00:13:05,519
these are interesting conditions

337
00:13:09,030 --> 00:13:07,200
and of course it would be interesting to

338
00:13:11,030 --> 00:13:09,040

see that these polymerizations would be

339
00:13:13,829 --> 00:13:11,040
good enough to make that next step

340
00:13:15,590 --> 00:13:13,839
that's the major goal for the next years

341
00:13:18,389 --> 00:13:15,600
what we're doing

342
00:13:20,550 --> 00:13:18,399
if you then either actually try to do

343
00:13:22,470 --> 00:13:20,560
this in a dry state

344
00:13:25,590 --> 00:13:22,480
and you see the template ligation in the

345
00:13:28,069 --> 00:13:25,600
dry step which is still humid

346
00:13:30,310 --> 00:13:28,079
and then you could go just by wet

347
00:13:31,829 --> 00:13:30,320
low salt to separate the strains please

348
00:13:33,829 --> 00:13:31,839
note that all that chemistry doesn't

349
00:13:35,990 --> 00:13:33,839
need any magnesium doesn't need any salt

350
00:13:37,670 --> 00:13:36,000
to go so you could really make a fresh

351
00:13:39,590 --> 00:13:37,680
water cycle here

352
00:13:42,470 --> 00:13:39,600
but you could also think about that air

353
00:13:44,150 --> 00:13:42,480
water interface we saw before where you

354
00:13:47,189 --> 00:13:44,160
have a little bit magnesium in the mix

355
00:13:49,509 --> 00:13:47,199
but the wet in the hue with the co2

356
00:13:50,470 --> 00:13:49,519
gives you also efficient separation and

357
00:13:51,509 --> 00:13:50,480
that's

358
00:13:53,590 --> 00:13:51,519
something

359
00:13:54,629 --> 00:13:53,600
we are trying right now that we have a

360
00:13:58,550 --> 00:13:54,639
template

361
00:14:00,629 --> 00:13:58,560
have a ligating ribozyme have three

362
00:14:03,189 --> 00:14:00,639
parts which make a hammerhead

363
00:14:05,430 --> 00:14:03,199

ribozyme now if you normally do that in

364
00:14:06,949 --> 00:14:05,440
a in a normal vial you need high enough

365
00:14:07,990 --> 00:14:06,959
magnesium concentration that you'll

366
00:14:10,550 --> 00:14:08,000
never give

367
00:14:12,870 --> 00:14:10,560
uh get these ligated templates

368
00:14:15,350 --> 00:14:12,880
ligated strands off the template

369
00:14:18,069 --> 00:14:15,360
so you never have this configuration and

370
00:14:20,069 --> 00:14:18,079
the hammerhead folded replicated

371
00:14:21,990 --> 00:14:20,079
configuration at the same time

372
00:14:24,629 --> 00:14:22,000
interestingly enough in this chamber you

373
00:14:27,509 --> 00:14:24,639
can go down to five millimolar magnesium

374
00:14:29,189 --> 00:14:27,519
which is uh then cycling in here and we

375
00:14:31,990 --> 00:14:29,199
see at the same time this ligation

376
00:14:34,230 --> 00:14:32,000
affinity activity and actually the

377
00:14:37,509 --> 00:14:34,240
activity of the hammerhead ribozyme so

378
00:14:39,350 --> 00:14:37,519
it seems that we can go for rna-based

379
00:14:41,590 --> 00:14:39,360
ligating systems which

380
00:14:44,389 --> 00:14:41,600
have both at the same time templating

381
00:14:46,949 --> 00:14:44,399
ligation and actually unfolding from the

382
00:14:50,230 --> 00:14:46,959
template and being functional

383
00:14:54,069 --> 00:14:50,240
okay so with that i want to leave it we

384
00:14:56,870 --> 00:14:54,079
try to balance out this physical side of

385
00:14:59,110 --> 00:14:56,880
of making non-equilibrium condition to

386
00:15:01,110 --> 00:14:59,120
to drive the replication system

387
00:15:04,069 --> 00:15:01,120
and the same time also get more and more

388
00:15:05,910 --> 00:15:04,079

to a setting of chemistries which is

389
00:15:07,750 --> 00:15:05,920
simple that uh you know the

390
00:15:10,550 --> 00:15:07,760
phosphorylation is a

391
00:15:13,030 --> 00:15:10,560
simple mode which you get reasonably

392
00:15:14,710 --> 00:15:13,040
reliable without much more molecules so

393
00:15:15,990 --> 00:15:14,720
the idea you would start this

394
00:15:18,949 --> 00:15:16,000
evolutionary process with three

395
00:15:20,069 --> 00:15:18,959
molecules a jeep a c and a trimethyl

396
00:15:20,949 --> 00:15:20,079
phosphate

397
00:15:27,990 --> 00:15:20,959
and

398
00:15:29,749 --> 00:15:28,000
make a non-experienced setting where you

399
00:15:32,310 --> 00:15:29,759
can run it here through

400
00:15:34,389 --> 00:15:32,320
these evolutionary cycles

401
00:15:36,389 --> 00:15:34,399
if you break and hydrolyze the strands

402
00:15:39,030 --> 00:15:36,399
it's very likely that you end up with

403
00:15:41,430 --> 00:15:39,040
these cyclic two three prime again it's

404
00:15:43,189 --> 00:15:41,440
a major product of the hydrolysis here

405
00:15:44,710 --> 00:15:43,199
even if you lose one phosphate or you

406
00:15:47,430 --> 00:15:44,720
lose both

407
00:15:49,030 --> 00:15:47,440
the idea is that very similar conditions

408
00:15:51,749 --> 00:15:49,040
same condition bring you back to the

409
00:15:55,350 --> 00:15:51,759
trinity phosphate and that should be

410
00:15:59,110 --> 00:15:55,360
then able to explore

411
00:16:01,189 --> 00:15:59,120
sequences which are able to boost this

412
00:16:03,030 --> 00:16:01,199
ligation reaction here so that would be

413
00:16:04,230 --> 00:16:03,040

then the onset of a darwinian evolution

414
00:16:07,189 --> 00:16:04,240
where you would

415
00:16:09,350 --> 00:16:07,199
enhance the perhaps not so strong

416
00:16:10,389 --> 00:16:09,360
ligation activity in the beginning

417
00:16:12,710 --> 00:16:10,399
with

418
00:16:15,670 --> 00:16:12,720
strands and i think running that even in

419
00:16:17,670 --> 00:16:15,680
a dry state would be very interesting

420
00:16:20,310 --> 00:16:17,680
so that's where we are funding is below

421
00:16:22,310 --> 00:16:20,320
we look out for postdoc as short

422
00:16:24,550 --> 00:16:22,320
advertisement for hours of life meeting

423
00:16:27,110 --> 00:16:24,560
munich in about three weeks

424
00:16:29,090 --> 00:16:27,120
and i'm happy to take questions thanks

425
00:16:33,990 --> 00:16:29,100
very much

426
00:16:36,150 --> 00:16:34,000
[Applause]

427
00:16:38,069 --> 00:16:36,160
thank you very much for this impressive

428
00:16:39,749 --> 00:16:38,079
work so questions

429
00:16:42,069 --> 00:16:39,759
very nice

430
00:16:43,670 --> 00:16:42,079
uh bryce clifton from georgia tech um

431
00:16:46,150 --> 00:16:43,680
can you speak more about the

432
00:16:48,150 --> 00:16:46,160
environments that this sort of um

433
00:16:50,949 --> 00:16:48,160
like dew cycling and capillaries might

434
00:16:53,430 --> 00:16:50,959
be found

435
00:16:56,870 --> 00:16:53,440
uh the idea where you would get these

436
00:16:57,910 --> 00:16:56,880
low salt conditions uh would be rather

437
00:16:59,990 --> 00:16:57,920
you know

438
00:17:01,350 --> 00:17:00,000

not deep in the ocean

439
00:17:05,510 --> 00:17:01,360
you need some

440
00:17:07,829 --> 00:17:05,520
so you have to high pressures will

441
00:17:09,990 --> 00:17:07,839
prevent any bubbles

442
00:17:12,710 --> 00:17:10,000
in the rocks so you would say i would

443
00:17:15,110 --> 00:17:12,720
say you know anything

444
00:17:17,990 --> 00:17:15,120
20 30 degrees uh

445
00:17:20,309 --> 00:17:18,000
30 meters in the water you know or above

446
00:17:22,470 --> 00:17:20,319
so the idea would be rather go above for

447
00:17:23,510 --> 00:17:22,480
volcanic island where you have fresh

448
00:17:26,110 --> 00:17:23,520
water

449
00:17:28,630 --> 00:17:26,120
where the volcano might provide you

450
00:17:30,070 --> 00:17:28,640
trimetaphosphate source and

451
00:17:31,990 --> 00:17:30,080
and

452
00:17:34,549 --> 00:17:32,000
also we will kind of providing you

453
00:17:36,150 --> 00:17:34,559
naturally very polished rock samples

454
00:17:37,909 --> 00:17:36,160
you'd rather want to hide a little bit

455
00:17:38,870 --> 00:17:37,919
in a pore that you're not burned by the

456
00:17:39,750 --> 00:17:38,880
uv

457
00:17:42,390 --> 00:17:39,760
um

458
00:17:44,310 --> 00:17:42,400
but that you know some centimeters of

459
00:17:45,669 --> 00:17:44,320
rock could give you that

460
00:17:50,310 --> 00:17:45,679
um

461
00:17:51,909 --> 00:17:50,320
we

462
00:17:53,510 --> 00:17:51,919
there's

463
00:17:57,110 --> 00:17:53,520

more more evidence that you can get for

464
00:17:58,070 --> 00:17:57,120
high ph conditions uh in

465
00:18:01,029 --> 00:17:58,080
in

466
00:18:03,990 --> 00:18:01,039
and

467
00:18:06,310 --> 00:18:04,000
geoscience

468
00:18:08,150 --> 00:18:06,320
can be provided which is matching the

469
00:18:09,510 --> 00:18:08,160
condition

470
00:18:12,230 --> 00:18:09,520
thank you um

471
00:18:14,390 --> 00:18:12,240
one more question also please um

472
00:18:17,909 --> 00:18:14,400
with the cyclic phosphate

473
00:18:20,710 --> 00:18:17,919
ligation uh it tends to form at least

474
00:18:23,190 --> 00:18:20,720
when templated uh vast majority of the

475
00:18:25,110 --> 00:18:23,200
two prime five prime linkage are you

476
00:18:27,590 --> 00:18:25,120
seeing that or are you seeing different

477
00:18:29,590 --> 00:18:27,600
results with no magnesium

478
00:18:32,390 --> 00:18:29,600
and um

479
00:18:33,830 --> 00:18:32,400
you know it's degrades pretty fast um

480
00:18:36,150 --> 00:18:33,840
compared to the

481
00:18:37,669 --> 00:18:36,160
uh you know canonical linkage can you

482
00:18:39,029 --> 00:18:37,679
say anything about that

483
00:18:41,110 --> 00:18:39,039
yes i mean that's also in the

484
00:18:42,549 --> 00:18:41,120
polarization while for the three five

485
00:18:45,029 --> 00:18:42,559
prime it's quite established that it

486
00:18:48,230 --> 00:18:45,039
makes the right one we're not sure here

487
00:18:50,470 --> 00:18:48,240
actually also already uh it's it's quite

488
00:18:52,230 --> 00:18:50,480

tricky to get the digest and the mass

489
00:18:54,150 --> 00:18:52,240
spec all together we

490
00:18:57,510 --> 00:18:54,160
we kind of would estimate right now it's

491
00:19:00,310 --> 00:18:57,520
50 50 hard to say you know still you get

492
00:19:02,150 --> 00:19:00,320
base pairing but it's more fragile now

493
00:19:05,510 --> 00:19:02,160
since you have that feedback loop down

494
00:19:07,350 --> 00:19:05,520
here i wouldn't be too concerned because

495
00:19:08,789 --> 00:19:07,360
you have a fast way to recycle your

496
00:19:10,870 --> 00:19:08,799
molecules if you go through that

497
00:19:12,710 --> 00:19:10,880
hydrolysis

498
00:19:15,430 --> 00:19:12,720
and then you would you know slowly

499
00:19:17,830 --> 00:19:15,440
select out the more stable ones

500
00:19:22,150 --> 00:19:20,150
we also hope that you know some rock

501
00:19:24,789 --> 00:19:22,160
interactions might have helped there

502
00:19:26,950 --> 00:19:24,799
that we might find you know

503
00:19:29,190 --> 00:19:26,960
peptides helping there we might find you

504
00:19:31,510 --> 00:19:29,200
know ribozymes helping there you know

505
00:19:34,070 --> 00:19:31,520
the point i want to make is that the the

506
00:19:36,549 --> 00:19:34,080
core process seems to be here under one

507
00:19:38,310 --> 00:19:36,559
pot condition so we have the steps here

508
00:19:40,230 --> 00:19:38,320
they are inefficient they have problems

509
00:19:41,590 --> 00:19:40,240
but that's nice because

510
00:19:44,710 --> 00:19:41,600
upon that

511
00:19:48,390 --> 00:19:44,720
evolutionary dynamics could kick in and

512
00:19:50,150 --> 00:19:48,400
help it by evolutionary process

513
00:19:52,230 --> 00:19:50,160

so if you know if you would not get

514
00:19:55,270 --> 00:19:52,240
anything then you could say okay it's a

515
00:19:56,870 --> 00:19:55,280
hard game right because you there's no

516
00:20:00,470 --> 00:19:56,880
there's no base

517
00:20:02,710 --> 00:20:00,480
reactivity but you have that

518
00:20:04,830 --> 00:20:02,720
thank you

519
00:20:07,909 --> 00:20:04,840
john ian of university of

520
00:20:09,990 --> 00:20:07,919
wisconsin-madison thanks for a very uh

521
00:20:13,750 --> 00:20:10,000
interesting talk i had a question about

522
00:20:17,029 --> 00:20:13,760
the pcr study where if i understand you

523
00:20:18,149 --> 00:20:17,039
had uh initial populations of templates

524
00:20:21,510 --> 00:20:18,159
that got

525
00:20:23,909 --> 00:20:21,520
longer over time is it necessary to have

526
00:20:25,190 --> 00:20:23,919
a seed template or is it possible that

527
00:20:27,270 --> 00:20:25,200
you could be

528
00:20:28,789 --> 00:20:27,280
um could you start a could you have an

529
00:20:32,950 --> 00:20:28,799
initial condition with just the

530
00:20:34,470 --> 00:20:32,960
nucleotides triphosphates and the enzyme

531
00:20:36,710 --> 00:20:34,480
i mean this polarization you saw here

532
00:20:39,029 --> 00:20:36,720
had no template it just starts from

533
00:20:40,710 --> 00:20:39,039
itself in the dry state so you basically

534
00:20:42,789 --> 00:20:40,720
all you have for that reaction is the g

535
00:20:45,430 --> 00:20:42,799
molecule nothing else no salt no

536
00:20:47,430 --> 00:20:45,440
catalyzer catalyzer you need to shift

537
00:20:50,390 --> 00:20:47,440
the ph wait for a day

538
00:20:53,029 --> 00:20:50,400

and you get those ten words

539
00:20:55,029 --> 00:20:53,039
you know having said that if

540
00:20:58,390 --> 00:20:55,039
by evolutionary dynamics you would have

541
00:20:59,990 --> 00:20:58,400
already some old rna hanging around it's

542
00:21:01,909 --> 00:21:00,000
of course the hope that already the

543
00:21:04,390 --> 00:21:01,919
polymerization is a bit biased and it's

544
00:21:06,630 --> 00:21:04,400
a little bit faster and better but we've

545
00:21:08,310 --> 00:21:06,640
not yet explored polymerization of that

546
00:21:10,230 --> 00:21:08,320
all we know is that the

547
00:21:12,789 --> 00:21:10,240
templated ligation of course would then

548
00:21:15,270 --> 00:21:12,799
pick it up you know it's it's

549
00:21:18,310 --> 00:21:15,280
the history of the sequence could either

550
00:21:20,470 --> 00:21:18,320
come in here perhaps already here but

551
00:21:22,230 --> 00:21:20,480
those would be

552
00:21:24,630 --> 00:21:22,240
the ways how the evolutionary cycles

553
00:21:26,789 --> 00:21:24,640
could pick up sequence information out

554
00:21:28,310 --> 00:21:26,799
there i guess i was referring to the

555
00:21:30,870 --> 00:21:28,320
first part of your talk where you were

556
00:21:32,789 --> 00:21:30,880
doing the pcr cycling and i was

557
00:21:33,909 --> 00:21:32,799
initiating with templates and getting

558
00:21:36,149 --> 00:21:33,919
much

559
00:21:39,750 --> 00:21:36,159
very long uh templates is it necessary

560
00:21:42,950 --> 00:21:39,760
to have a seed template in this system

561
00:21:45,110 --> 00:21:42,960
um i mean the the controls we run were

562
00:21:47,830 --> 00:21:45,120
you know without seed we got nothing

563
00:21:49,830 --> 00:21:47,840

it's a bit important point here because

564
00:21:52,470 --> 00:21:49,840
you want to be sure that your primers of

565
00:21:55,510 --> 00:21:52,480
the pcr is not you know priming the

566
00:21:58,070 --> 00:21:55,520
system and doing it but my guess gut

567
00:22:00,149 --> 00:21:58,080
feeling but we have not done it is if

568
00:22:02,070 --> 00:22:00,159
you would be a bit sloppy in your in

569
00:22:04,230 --> 00:22:02,080
your primer design you know you make

570
00:22:06,070 --> 00:22:04,240
primer dimers and then i would say in

571
00:22:07,750 --> 00:22:06,080
such a setting it would be very likely

572
00:22:09,909 --> 00:22:07,760
that if you have a primer diameter down

573
00:22:13,990 --> 00:22:09,919
there it will also start the evolution

574
00:22:18,630 --> 00:22:16,149
also if you would start with a longer

575
00:22:20,390 --> 00:22:18,640
template here because the pcr is quite

576
00:22:22,630 --> 00:22:20,400
precise

577
00:22:24,870 --> 00:22:22,640
i would also give a good chance that

578
00:22:26,390 --> 00:22:24,880
some of these sequences are still you

579
00:22:28,789 --> 00:22:26,400
know then retained

580
00:22:30,870 --> 00:22:28,799
here we push the system for

581
00:22:32,870 --> 00:22:30,880
you know starting here and apparently it

582
00:22:33,750 --> 00:22:32,880
wants to replicate up here so there was

583
00:22:36,950 --> 00:22:33,760
no

584
00:22:39,430 --> 00:22:36,960
way to to keep on the sequences other

585
00:22:41,510 --> 00:22:39,440
than you know duplicating them up to

586
00:22:43,350 --> 00:22:41,520
here and then the system had to give up

587
00:22:44,789 --> 00:22:43,360
because this is too far away from the

588
00:22:46,870 --> 00:22:44,799

melting temperature and then really

589
00:22:48,630 --> 00:22:46,880
evolve its own sequence

590
00:22:50,870 --> 00:22:48,640
but i would guess if you would give it a

591
00:22:53,350 --> 00:22:50,880
more proper template

592
00:22:56,230 --> 00:22:53,360
you would be able to tune it

593
00:22:58,310 --> 00:22:56,240
and make it start from the right place

594
00:23:00,710 --> 00:22:58,320
very elegant work thank you thank you

595
00:23:06,950 --> 00:23:00,720
very much let's approach victor again

596
00:23:11,909 --> 00:23:09,430
so lena is from the university of

597
00:23:14,789 --> 00:23:11,919
wisconsin-madison and he's going to tell

598
00:23:17,110 --> 00:23:14,799
us about a chemical ecosystem selection

599
00:23:25,350 --> 00:23:17,120
framework for studying the origins of

600
00:23:28,310 --> 00:23:27,029
i just don't want to jingle while i'm up

601
00:23:30,950 --> 00:23:28,320
here

602
00:23:32,950 --> 00:23:30,960
uh hi yeah so i want to tell you about

603
00:23:34,630 --> 00:23:32,960
some of the work that our research group

604
00:23:35,590 --> 00:23:34,640
has been doing over the last several

605
00:23:38,390 --> 00:23:35,600
years

606
00:23:40,390 --> 00:23:38,400
trying to resolve or at least contribute

607
00:23:42,070 --> 00:23:40,400
to the resolution of

608
00:23:44,149 --> 00:23:42,080
i think what is still the biggest

609
00:23:45,510 --> 00:23:44,159
mystery to me about the origin of life

610
00:23:48,070 --> 00:23:45,520
which is how

611
00:23:51,909 --> 00:23:48,080
non-living stuff non-living components

612
00:23:53,990 --> 00:23:51,919
can give rise to life to living systems

613
00:23:55,750 --> 00:23:54,000

in the complete absence of a prior

614
00:23:58,470 --> 00:23:55,760
living process

615
00:24:00,149 --> 00:23:58,480
namely evolution so our group has been

616
00:24:02,149 --> 00:24:00,159
using both theory and wet lab

617
00:24:03,990 --> 00:24:02,159
experiments to try to

618
00:24:06,710 --> 00:24:04,000
generate lifelike systems in a

619
00:24:08,390 --> 00:24:06,720
laboratory setting to try to answer this

620
00:24:12,710 --> 00:24:08,400
question

621
00:24:15,029 --> 00:24:12,720
what were the first evolvers

622
00:24:17,190 --> 00:24:15,039
what are the simplest chemical systems

623
00:24:19,430 --> 00:24:17,200
that we can imagine that are capable of

624
00:24:22,230 --> 00:24:19,440
adaptive evolution that themselves don't

625
00:24:23,750 --> 00:24:22,240
require evolution to appear

626
00:24:26,390 --> 00:24:23,760
now there have been many suggestions as

627
00:24:29,430 --> 00:24:26,400
to what the first evolvers might be how

628
00:24:32,310 --> 00:24:29,440
ranging from individual nucleic acid

629
00:24:33,750 --> 00:24:32,320
molecules to protocells to metabolic

630
00:24:35,590 --> 00:24:33,760
cycles

631
00:24:37,110 --> 00:24:35,600
and the scenario we find most plausible

632
00:24:38,549 --> 00:24:37,120
in our exploring

633
00:24:41,430 --> 00:24:38,559
is that the first evolvers were

634
00:24:43,909 --> 00:24:41,440
ecosystems of interacting auto catalytic

635
00:24:45,430 --> 00:24:43,919
cycles and one particular appeal of this

636
00:24:47,590 --> 00:24:45,440
model is that it could explain how

637
00:24:50,149 --> 00:24:47,600
evolution might be possible in the

638
00:24:51,750 --> 00:24:50,159

absence of genetic polymers as opposed

639
00:24:54,870 --> 00:24:51,760
to assuming that those genetic polymers

640
00:24:56,950 --> 00:24:54,880
were required for evolution to initiate

641
00:24:58,470 --> 00:24:56,960
but what would evolution look like in

642
00:25:00,390 --> 00:24:58,480
these systems that's been the primary

643
00:25:01,909 --> 00:25:00,400
challenge with these models

644
00:25:03,909 --> 00:25:01,919
and there have been a few ideas

645
00:25:06,070 --> 00:25:03,919
including auto catalytic core models

646
00:25:07,990 --> 00:25:06,080
like the one shown here that attributes

647
00:25:10,230 --> 00:25:08,000
the potential for evolvability to the

648
00:25:12,789 --> 00:25:10,240
presence of nested auto catalytic cores

649
00:25:14,390 --> 00:25:12,799
within larger auto catalytic networks

650
00:25:16,470 --> 00:25:14,400
but still these models have not

651
00:25:18,549 --> 00:25:16,480
comprehensively explained how evolution

652
00:25:20,390 --> 00:25:18,559
might initiate in these systems which is

653
00:25:22,070 --> 00:25:20,400
what our lab has been trying to tackle

654
00:25:24,149 --> 00:25:22,080
so we've really built on these models

655
00:25:27,110 --> 00:25:24,159
this is work led by our theoretical

656
00:25:29,029 --> 00:25:27,120
group primarily by postdoc zhang pang

657
00:25:31,269 --> 00:25:29,039
who have developed a chemical ecology

658
00:25:33,029 --> 00:25:31,279
paradigm to describe the behavior of

659
00:25:35,190 --> 00:25:33,039
sets of interacting auto catalytic

660
00:25:38,070 --> 00:25:35,200
cycles we refer to these as chemical

661
00:25:40,149 --> 00:25:38,080
ecosystems and the reason for this name

662
00:25:42,630 --> 00:25:40,159
is that they found that the behavior of

663
00:25:44,950 --> 00:25:42,640

even the simplest auto catalytic systems

664
00:25:47,350 --> 00:25:44,960
can be approximated or modeled using

665
00:25:48,870 --> 00:25:47,360
ecological principles and the growth of

666
00:25:51,430 --> 00:25:48,880
these systems can actually be

667
00:25:53,510 --> 00:25:51,440
approximated using logistic growth which

668
00:25:55,830 --> 00:25:53,520
essentially means that the behavior of

669
00:25:58,549 --> 00:25:55,840
these systems is essentially similar to

670
00:26:00,230 --> 00:25:58,559
populations of biological species

671
00:26:02,789 --> 00:26:00,240
and even more interestingly when you

672
00:26:05,830 --> 00:26:02,799
have pairs of interacting auto catalytic

673
00:26:08,230 --> 00:26:05,840
cycles that behave either as competitors

674
00:26:10,070 --> 00:26:08,240
mutualists or even predator and prey

675
00:26:12,390 --> 00:26:10,080
then they start to display dynamic

676
00:26:13,990 --> 00:26:12,400
behaviors that are very reminiscent of

677
00:26:16,230 --> 00:26:14,000
what you'd see in ecological

678
00:26:18,070 --> 00:26:16,240
interactions observed in biological

679
00:26:20,230 --> 00:26:18,080
populations

680
00:26:22,950 --> 00:26:20,240
now the big consequence of this chemical

681
00:26:25,110 --> 00:26:22,960
ecology model so far is that it suggests

682
00:26:27,669 --> 00:26:25,120
that chemical ecosystems might be able

683
00:26:29,669 --> 00:26:27,679
to evolve as a result of the sum total

684
00:26:32,070 --> 00:26:29,679
or at least a combination of different

685
00:26:34,710 --> 00:26:32,080
ecological interactions

686
00:26:36,950 --> 00:26:34,720
so we've actually been trying to explain

687
00:26:39,269 --> 00:26:36,960
how natural selection among such

688
00:26:41,029 --> 00:26:39,279

ecosystems could happen in natural

689
00:26:43,190 --> 00:26:41,039
settings so going beyond these models

690
00:26:45,110 --> 00:26:43,200
this abstract world and actually trying

691
00:26:46,870 --> 00:26:45,120
to conceive of how this might look like

692
00:26:49,110 --> 00:26:46,880
right how might this have happened at

693
00:26:50,950 --> 00:26:49,120
the origin of life by considering

694
00:26:53,430 --> 00:26:50,960
natural environments and the one we like

695
00:26:55,350 --> 00:26:53,440
to imagine is a sea floor

696
00:26:57,190 --> 00:26:55,360
recognizing that an important component

697
00:26:59,430 --> 00:26:57,200
of these environments is mineral

698
00:27:01,510 --> 00:26:59,440
surfaces now minerals have long been

699
00:27:03,590 --> 00:27:01,520
implicated in the origin of life for

700
00:27:05,990 --> 00:27:03,600
various reasons they do really cool

701
00:27:07,669 --> 00:27:06,000
things like absorb or stick to different

702
00:27:09,430 --> 00:27:07,679
organic components including some of the

703
00:27:12,149 --> 00:27:09,440
building blocks of life and they can

704
00:27:14,310 --> 00:27:12,159
also impart catalytic activities and in

705
00:27:16,230 --> 00:27:14,320
essence in essence replacing or

706
00:27:18,470 --> 00:27:16,240
preceding the function of biological

707
00:27:20,230 --> 00:27:18,480
enzymes

708
00:27:22,549 --> 00:27:20,240
and so we like to imagine that

709
00:27:24,470 --> 00:27:22,559
ecosystems uh chemical ecosystems that

710
00:27:26,950 --> 00:27:24,480
absorbed on mineral surfaces which we

711
00:27:29,590 --> 00:27:26,960
endearingly refer to as slimes for

712
00:27:31,590 --> 00:27:29,600
surface limited molecular ecosystems

713
00:27:34,310 --> 00:27:31,600

once they're absorbed to mineral

714
00:27:36,630 --> 00:27:34,320
surfaces if there's continual turnover

715
00:27:39,909 --> 00:27:36,640
of these surfaces with the exposure of

716
00:27:41,669 --> 00:27:39,919
new mineral faces removal of old ones

717
00:27:43,430 --> 00:27:41,679
this would effectively enrich for

718
00:27:46,070 --> 00:27:43,440
variants of these ecosystems that are

719
00:27:48,149 --> 00:27:46,080
better at getting from grain to grain

720
00:27:50,630 --> 00:27:48,159
so in principle this chemical ecosystem

721
00:27:53,029 --> 00:27:50,640
model could explain how you can get

722
00:27:55,110 --> 00:27:53,039
evolution and complexification

723
00:27:57,269 --> 00:27:55,120
without implicating compartments or even

724
00:27:59,269 --> 00:27:57,279
genetic polymers

725
00:28:01,350 --> 00:27:59,279
now of course a really important part of

726
00:28:04,070 --> 00:28:01,360
our work and what i've been focusing on

727
00:28:05,830 --> 00:28:04,080
in my phd is to try to validate and test

728
00:28:07,510 --> 00:28:05,840
this model empirically

729
00:28:09,190 --> 00:28:07,520
and to do this we've been developing an

730
00:28:11,350 --> 00:28:09,200
experimental framework

731
00:28:13,510 --> 00:28:11,360
that is designed to generate and study

732
00:28:15,269 --> 00:28:13,520
these slimes in a laboratory setting

733
00:28:17,350 --> 00:28:15,279
we've called it chemical ecosystem

734
00:28:19,510 --> 00:28:17,360
selection it's directly inspired by

735
00:28:21,590 --> 00:28:19,520
microbial ecosystem selection which you

736
00:28:23,269 --> 00:28:21,600
can think of as experimental evolution

737
00:28:25,269 --> 00:28:23,279
that allows you to select for community

738
00:28:26,310 --> 00:28:25,279

level traits as opposed to individual

739
00:28:28,310 --> 00:28:26,320
traits

740
00:28:30,950 --> 00:28:28,320
and the basic principle is very very

741
00:28:32,789 --> 00:28:30,960
simple it just involves combining some

742
00:28:35,269 --> 00:28:32,799
kind of food rich solution with a

743
00:28:37,750 --> 00:28:35,279
mineral phase so mineral grains and

744
00:28:40,470 --> 00:28:37,760
deploying an analog of experimental

745
00:28:42,950 --> 00:28:40,480
evolution with repeated dilution

746
00:28:45,510 --> 00:28:42,960
so to do this we incubate ingredients

747
00:28:47,750 --> 00:28:45,520
allow for slimes to establish themselves

748
00:28:50,389 --> 00:28:47,760
and then we go in and transfer a small

749
00:28:53,110 --> 00:28:50,399
subset from one generation usually about

750
00:28:55,029 --> 00:28:53,120
10 to 20 percent to a new reaction

751
00:28:57,510 --> 00:28:55,039
vessel containing fresh ingredients so

752
00:28:59,909 --> 00:28:57,520
fresh food inputs fresh uncolonized

753
00:29:02,070 --> 00:28:59,919
mineral surface and we do this over and

754
00:29:04,710 --> 00:29:02,080
over again with the hopes of selectively

755
00:29:06,149 --> 00:29:04,720
enriching for variance the variants here

756
00:29:07,510 --> 00:29:06,159
in this diagram are depicted by

757
00:29:09,190 --> 00:29:07,520
different colors

758
00:29:11,110 --> 00:29:09,200
that are better at getting from grain to

759
00:29:12,870 --> 00:29:11,120
grain so in effect imposing a form of

760
00:29:15,029 --> 00:29:12,880
natural selection

761
00:29:17,669 --> 00:29:15,039
and of course we routinely sample both

762
00:29:20,149 --> 00:29:17,679
the bulk solution the mineral grains and

763
00:29:22,310 --> 00:29:20,159

deploy a suite of different analytical

764
00:29:25,590 --> 00:29:22,320
techniques to track what's happening in

765
00:29:27,190 --> 00:29:25,600
response to the selection procedure

766
00:29:29,190 --> 00:29:27,200
now the really nice thing about this

767
00:29:30,789 --> 00:29:29,200
approach is that it isn't specific to a

768
00:29:32,950 --> 00:29:30,799
particular set of conditions so it's

769
00:29:34,870 --> 00:29:32,960
fairly agnostic in that regard

770
00:29:37,350 --> 00:29:34,880
it can be deployed basically on any

771
00:29:39,350 --> 00:29:37,360
combination of inputs and you can tailor

772
00:29:40,470 --> 00:29:39,360
it to test various hypotheses about what

773
00:29:42,950 --> 00:29:40,480
might be necessary

774
00:29:44,710 --> 00:29:42,960
for the origins of these processes

775
00:29:47,029 --> 00:29:44,720
now we've tested quite a few different

776
00:29:49,510 --> 00:29:47,039
combinations in our laboratory in this

777
00:29:51,830 --> 00:29:49,520
table i'm showing an example of a recipe

778
00:29:53,510 --> 00:29:51,840
that we've been exploring we've also

779
00:29:54,870 --> 00:29:53,520
played with different variations of this

780
00:29:57,269 --> 00:29:54,880
recipe

781
00:29:58,870 --> 00:29:57,279
it was inspired by the outputs of spark

782
00:30:00,549 --> 00:29:58,880
discharge experiments like the miller

783
00:30:02,630 --> 00:30:00,559
yuri experiment although we've made

784
00:30:03,909 --> 00:30:02,640
quite a few other additions

785
00:30:06,310 --> 00:30:03,919
the point here is that there's an

786
00:30:08,230 --> 00:30:06,320
infinite number of recipes you could try

787
00:30:10,630 --> 00:30:08,240
we actually recently published a sort of

788
00:30:12,870 --> 00:30:10,640

guide for what one might consider when

789
00:30:16,630 --> 00:30:12,880
putting together such a recipe uh what

790
00:30:18,389 --> 00:30:16,640
kinds of parameters you might consider

791
00:30:19,830 --> 00:30:18,399
and then and that's regardless of

792
00:30:21,510 --> 00:30:19,840
whether you're synthesizing it by

793
00:30:23,029 --> 00:30:21,520
simulating a particular process or

794
00:30:24,070 --> 00:30:23,039
assembling them from off-the-shelf

795
00:30:25,590 --> 00:30:24,080
reagents

796
00:30:27,909 --> 00:30:25,600
on the mineral side we've also tried

797
00:30:29,430 --> 00:30:27,919
quite a few we've targeted kind of crowd

798
00:30:32,070 --> 00:30:29,440
favorites among the origin of life

799
00:30:33,269 --> 00:30:32,080
community so things like iron sulfides

800
00:30:35,510 --> 00:30:33,279
clayman rolls we've tried

801
00:30:37,110 --> 00:30:35,520
montmorillonite and chloride i believe

802
00:30:39,750 --> 00:30:37,120
uh different phosphates but of course

803
00:30:41,269 --> 00:30:39,760
the list is goes on

804
00:30:43,110 --> 00:30:41,279
and then there are also a bunch of other

805
00:30:45,669 --> 00:30:43,120
parameters to consider like what the

806
00:30:47,350 --> 00:30:45,679
headspace is like is this an anoxic

807
00:30:48,470 --> 00:30:47,360
experiment do we include molecular

808
00:30:50,149 --> 00:30:48,480
oxygen

809
00:30:52,950 --> 00:30:50,159
uh what kind of incubation temperature

810
00:30:55,590 --> 00:30:52,960
are we talking about light no light

811
00:30:57,669 --> 00:30:55,600
the list goes on but some important ones

812
00:30:59,909 --> 00:30:57,679
are time between transfers so how long

813
00:31:01,830 --> 00:30:59,919

do we let these samples incubate before

814
00:31:03,669 --> 00:31:01,840
doing our serial dilution and then what

815
00:31:05,269 --> 00:31:03,679
is that dilution strength how strong is

816
00:31:06,630 --> 00:31:05,279
that selection

817
00:31:08,149 --> 00:31:06,640
and that is determined by how much is

818
00:31:09,750 --> 00:31:08,159
carried over from one generation to

819
00:31:11,590 --> 00:31:09,760
another so as you can see when you

820
00:31:13,029 --> 00:31:11,600
factor all these things in there's an

821
00:31:14,950 --> 00:31:13,039
infinite parameter space one might

822
00:31:17,190 --> 00:31:14,960
consider

823
00:31:18,789 --> 00:31:17,200
so one combination of conditions though

824
00:31:21,110 --> 00:31:18,799
that has been producing interesting

825
00:31:22,950 --> 00:31:21,120
patterns for us we published the results

826
00:31:24,789 --> 00:31:22,960
a few years ago

827
00:31:27,110 --> 00:31:24,799
we used a recipe that was quite similar

828
00:31:30,070 --> 00:31:27,120
to the one i just showed in that table

829
00:31:31,590 --> 00:31:30,080
we combined it with pyrite under anoxic

830
00:31:33,269 --> 00:31:31,600
conditions

831
00:31:34,789 --> 00:31:33,279
and in this case we tracked the

832
00:31:36,230 --> 00:31:34,799
concentration of free inorganic

833
00:31:37,590 --> 00:31:36,240
phosphate remaining at the end of a

834
00:31:39,669 --> 00:31:37,600
generation

835
00:31:41,269 --> 00:31:39,679
in 10 independently replicated lineages

836
00:31:42,950 --> 00:31:41,279
which is what you're seeing here and

837
00:31:45,029 --> 00:31:42,960
when we looked at the inorganic

838
00:31:46,389 --> 00:31:45,039

phosphate across generations we saw a

839
00:31:48,070 --> 00:31:46,399
really interesting pattern

840
00:31:50,149 --> 00:31:48,080
the reason by the way we tracked this

841
00:31:51,990 --> 00:31:50,159
particular proxy is because in that

842
00:31:54,310 --> 00:31:52,000
experiment we actually included atp as a

843
00:31:56,230 --> 00:31:54,320
phosphate source and we wanted a proxy

844
00:31:57,909 --> 00:31:56,240
for how much atp hydrolysis had been

845
00:31:59,909 --> 00:31:57,919
happening and when we looked at that you

846
00:32:01,029 --> 00:31:59,919
can see this really neat oscillatory

847
00:32:02,630 --> 00:32:01,039
pattern

848
00:32:03,750 --> 00:32:02,640
now there are lots of ways to interpret

849
00:32:05,190 --> 00:32:03,760
this pattern

850
00:32:07,909 --> 00:32:05,200
one of the simplest

851
00:32:09,350 --> 00:32:07,919
observations is that it is consistent

852
00:32:11,509 --> 00:32:09,360
with the presence of some kind of

853
00:32:13,909 --> 00:32:11,519
non-linear feedback loop which is

854
00:32:15,430 --> 00:32:13,919
consistent also with autocatalysis now

855
00:32:17,509 --> 00:32:15,440
of course we don't know for sure that

856
00:32:19,190 --> 00:32:17,519
that's what it is at the time we were

857
00:32:21,029 --> 00:32:19,200
not really equipped to do any in-depth

858
00:32:22,870 --> 00:32:21,039
chemical analysis we only had these very

859
00:32:23,990 --> 00:32:22,880
high level traits to track

860
00:32:25,350 --> 00:32:24,000
and we also

861
00:32:27,110 --> 00:32:25,360
were not able to carry out this

862
00:32:29,590 --> 00:32:27,120
experiment for longer you can see that

863
00:32:31,590 --> 00:32:29,600

once we saw these data we wish we had

864
00:32:33,029 --> 00:32:31,600
budgeted our materials to carry it out

865
00:32:34,470 --> 00:32:33,039
farther past 40 generations

866
00:32:36,470 --> 00:32:34,480
unfortunately we couldn't

867
00:32:39,110 --> 00:32:36,480
but all of this motivated the work i'm

868
00:32:40,950 --> 00:32:39,120
about to show you

869
00:32:42,710 --> 00:32:40,960
so

870
00:32:44,870 --> 00:32:42,720
naturally we wanted to repeat this

871
00:32:46,230 --> 00:32:44,880
experiment and do a few things carry out

872
00:32:49,029 --> 00:32:46,240
for longer

873
00:32:50,630 --> 00:32:49,039
but also couple it to more informative

874
00:32:53,190 --> 00:32:50,640
analytical techniques in particular

875
00:32:54,470 --> 00:32:53,200
chromatography mass spectrometry

876
00:32:57,190 --> 00:32:54,480
so

877
00:32:59,110 --> 00:32:57,200
the pandemic and supply chain issues hit

878
00:33:01,590 --> 00:32:59,120
us pretty hard however as i'm sure it

879
00:33:03,029 --> 00:33:01,600
did many of us in this room and we had

880
00:33:04,549 --> 00:33:03,039
to go back to the drawing board a little

881
00:33:06,310 --> 00:33:04,559
bit because a lot of the materials we

882
00:33:08,870 --> 00:33:06,320
were using to do the experiments

883
00:33:11,029 --> 00:33:08,880
previously were not easily available so

884
00:33:12,070 --> 00:33:11,039
plastic shortages rubber shortages were

885
00:33:14,070 --> 00:33:12,080
all

886
00:33:15,830 --> 00:33:14,080
kind of problematic for us but this

887
00:33:17,029 --> 00:33:15,840
forced us to adapt our format to

888
00:33:17,990 --> 00:33:17,039

actually something that was a little bit

889
00:33:19,750 --> 00:33:18,000
easier

890
00:33:21,430 --> 00:33:19,760
so we carried out an experiment in

891
00:33:23,029 --> 00:33:21,440
microtiter plates

892
00:33:25,350 --> 00:33:23,039
one advantage to this is that we could

893
00:33:27,110 --> 00:33:25,360
use uh better liquid handling techniques

894
00:33:29,190 --> 00:33:27,120
so we could use multi-channel pipettes

895
00:33:31,909 --> 00:33:29,200
and increase the throughput a little bit

896
00:33:33,990 --> 00:33:31,919
we could also look at multiple replicate

897
00:33:35,750 --> 00:33:34,000
lineages many more than we were able to

898
00:33:38,950 --> 00:33:35,760
before so we went from being able to

899
00:33:41,350 --> 00:33:38,960
handle maybe 10 20 at once to 96

900
00:33:42,070 --> 00:33:41,360
which was really helpful

901
00:33:45,350 --> 00:33:42,080
so

902
00:33:46,630 --> 00:33:45,360
using this format we used inputs that

903
00:33:49,110 --> 00:33:46,640
were similar to the ones i just showed

904
00:33:51,750 --> 00:33:49,120
you with a few key differences one is we

905
00:33:54,710 --> 00:33:51,760
replaced atp with chlorapatite as a

906
00:33:56,630 --> 00:33:54,720
mineral we also included pyrite and with

907
00:33:58,470 --> 00:33:56,640
a team of very talented undergraduate

908
00:34:00,470 --> 00:33:58,480
students and master's students we were

909
00:34:02,389 --> 00:34:00,480
able to carry out a long-term experiment

910
00:34:04,389 --> 00:34:02,399
for 70 generations

911
00:34:06,389 --> 00:34:04,399
which is the world record for longest

912
00:34:07,909 --> 00:34:06,399
ecosystem selection experiment so far

913
00:34:10,069 --> 00:34:07,919

maybe not experimental evolution but

914
00:34:12,869 --> 00:34:10,079
certainly this particular protocol

915
00:34:14,550 --> 00:34:12,879
we did that in about seven months so

916
00:34:16,149 --> 00:34:14,560
we learned a lot as we did this there

917
00:34:17,829 --> 00:34:16,159
were a lot of challenges but i think

918
00:34:19,430 --> 00:34:17,839
overall we kind of convinced ourselves

919
00:34:21,270 --> 00:34:19,440
that it was possible to do these high

920
00:34:23,190 --> 00:34:21,280
throughput experiments over long periods

921
00:34:25,030 --> 00:34:23,200
of time which will probably be very

922
00:34:26,710 --> 00:34:25,040
helpful in the future

923
00:34:28,310 --> 00:34:26,720
and of course as i mentioned our plan

924
00:34:29,750 --> 00:34:28,320
all along was to do this so we could

925
00:34:31,669 --> 00:34:29,760
couple it to more sophisticated

926
00:34:33,510 --> 00:34:31,679
analytical techniques which i'll tell

927
00:34:35,030 --> 00:34:33,520
you about now so really the gold

928
00:34:36,950 --> 00:34:35,040
standard for at least for the kind of

929
00:34:39,190 --> 00:34:36,960
analysis we were trying to do

930
00:34:41,669 --> 00:34:39,200
with these very complex mixtures

931
00:34:43,909 --> 00:34:41,679
is lcm sms so

932
00:34:45,829 --> 00:34:43,919
this is actually just a snapshot of our

933
00:34:47,990 --> 00:34:45,839
mixture that i just talked to you about

934
00:34:49,750 --> 00:34:48,000
after one generation and with quite

935
00:34:51,430 --> 00:34:49,760
stringent filtering we're still dealing

936
00:34:52,629 --> 00:34:51,440
with tens of thousands of unique

937
00:34:55,109 --> 00:34:52,639
features

938
00:34:57,109 --> 00:34:55,119

which is a big mess and making sense of

939
00:34:58,470 --> 00:34:57,119
this data is really difficult

940
00:35:00,790 --> 00:34:58,480
just for those who are curious this is a

941
00:35:02,630 --> 00:35:00,800
uplc msms system

942
00:35:05,670 --> 00:35:02,640
we're doing all of this acquisition in

943
00:35:07,990 --> 00:35:05,680
data dependent mode and this is really

944
00:35:10,230 --> 00:35:08,000
going to enable us to do untargeted

945
00:35:11,750 --> 00:35:10,240
screenings of products and the reason

946
00:35:14,390 --> 00:35:11,760
we're doing this ultimately is we'd like

947
00:35:17,030 --> 00:35:14,400
to be able to track distribution changes

948
00:35:18,550 --> 00:35:17,040
in our products across generations

949
00:35:20,470 --> 00:35:18,560
we're really lucky to benefit from the

950
00:35:21,589 --> 00:35:20,480
expertise of a postdoc stephanie colon

951
00:35:23,270 --> 00:35:21,599
santos

952
00:35:25,270 --> 00:35:23,280
who is an expert in this kind of

953
00:35:27,990 --> 00:35:25,280
analysis of making sense of really

954
00:35:30,310 --> 00:35:28,000
complex mixtures by lcm sms

955
00:35:32,470 --> 00:35:30,320
in mixtures that are relevant to origin

956
00:35:34,230 --> 00:35:32,480
of life questions so things like the

957
00:35:36,470 --> 00:35:34,240
combinatorial explosions you get out of

958
00:35:38,150 --> 00:35:36,480
foremost formamide reactions

959
00:35:39,670 --> 00:35:38,160
so our plan is to apply these methods

960
00:35:41,829 --> 00:35:39,680
that she's been developing to make sense

961
00:35:43,829 --> 00:35:41,839
of our own mixtures and we're really

962
00:35:46,950 --> 00:35:43,839
just starting to do that in this

963
00:35:48,470 --> 00:35:46,960

long-term ecosystem selection experiment

964
00:35:49,910 --> 00:35:48,480
but the other thing that we're trying to

965
00:35:51,990 --> 00:35:49,920
do is

966
00:35:53,750 --> 00:35:52,000
validate or confirm that there is

967
00:35:56,829 --> 00:35:53,760
autocatalysis occurring in these

968
00:35:58,950 --> 00:35:56,839
reactions and also possibly signs of

969
00:36:01,990 --> 00:35:58,960
evolvability and one way we hope to do

970
00:36:03,349 --> 00:36:02,000
this is to identify new products

971
00:36:05,430 --> 00:36:03,359
make standards for them make this

972
00:36:07,589 --> 00:36:05,440
quantitative and track the concentration

973
00:36:09,430 --> 00:36:07,599
and how it's changing across generations

974
00:36:11,190 --> 00:36:09,440
and seeing if we find evidence of super

975
00:36:13,030 --> 00:36:11,200
linear growth which would be indicative

976
00:36:15,109 --> 00:36:13,040
of auto catalytic growth

977
00:36:17,109 --> 00:36:15,119
we'd also can do

978
00:36:19,430 --> 00:36:17,119
things like pca and other data

979
00:36:21,430 --> 00:36:19,440
dimensionality reduction procedures to

980
00:36:24,470 --> 00:36:21,440
get a broad sense of how our different

981
00:36:25,990 --> 00:36:24,480
lineages are behaving across generations

982
00:36:28,150 --> 00:36:26,000
and these are actually just snapshots

983
00:36:30,870 --> 00:36:28,160
from that experiment i just showed you

984
00:36:33,750 --> 00:36:30,880
uh generation 69 and 70. what we're

985
00:36:35,190 --> 00:36:33,760
comparing here are our 24 experimental

986
00:36:37,829 --> 00:36:35,200
lineages

987
00:36:40,069 --> 00:36:37,839
compared to controls that are set up

988
00:36:41,750 --> 00:36:40,079

identically to those lineages with the

989
00:36:43,990 --> 00:36:41,760
same materials but don't have any

990
00:36:45,750 --> 00:36:44,000
history of transfer so we're comparing

991
00:36:48,390 --> 00:36:45,760
samples that have zero transfers versus

992
00:36:50,069 --> 00:36:48,400
ones that have 69 or 70.

993
00:36:52,150 --> 00:36:50,079
and when we do that we see interesting

994
00:36:54,390 --> 00:36:52,160
clustering we see these different

995
00:36:56,069 --> 00:36:54,400
groups we're not entirely sure what the

996
00:36:57,750 --> 00:36:56,079
significance significance of those

997
00:36:59,030 --> 00:36:57,760
groups are yet um we don't see any

998
00:37:00,790 --> 00:36:59,040
evidence of any kind of positional

999
00:37:02,230 --> 00:37:00,800
effects although we recognize there are

1000
00:37:03,670 --> 00:37:02,240
lots of different experimental

1001
00:37:05,430 --> 00:37:03,680
parameters that might explain this

1002
00:37:06,390 --> 00:37:05,440
clustering and we're working on figuring

1003
00:37:07,670 --> 00:37:06,400
that out

1004
00:37:09,670 --> 00:37:07,680
but we also see these interesting

1005
00:37:11,430 --> 00:37:09,680
outliers now the really cool thing would

1006
00:37:13,910 --> 00:37:11,440
have been if those outliers were the

1007
00:37:15,349 --> 00:37:13,920
same in different generations uh that

1008
00:37:17,030 --> 00:37:15,359
would indicate some kind of lineage

1009
00:37:19,990 --> 00:37:17,040
effect which would be a really excellent

1010
00:37:21,190 --> 00:37:20,000
crude level uh or crude way to

1011
00:37:23,430 --> 00:37:21,200
establish whether or not there's any

1012
00:37:25,270 --> 00:37:23,440
kind of history or memory happening here

1013
00:37:27,910 --> 00:37:25,280

that is not happening here at least not

1014
00:37:29,430 --> 00:37:27,920
um in this particular data set um these

1015
00:37:31,190 --> 00:37:29,440
are different lineages the two orange

1016
00:37:33,589 --> 00:37:31,200
dots you see kind of floating off on by

1017
00:37:35,430 --> 00:37:33,599
themselves or not the simulink lineage

1018
00:37:37,349 --> 00:37:35,440
okay

1019
00:37:39,589 --> 00:37:37,359
um so of course more work is needed to

1020
00:37:41,190 --> 00:37:39,599
understand these methods like i said we

1021
00:37:43,190 --> 00:37:41,200
are just in the beginning of making

1022
00:37:45,030 --> 00:37:43,200
sense of these data um here are some

1023
00:37:45,829 --> 00:37:45,040
examples of what we might be looking for

1024
00:37:47,910 --> 00:37:45,839
so

1025
00:37:50,390 --> 00:37:47,920
heritability plots where that allowed us

1026
00:37:52,390 --> 00:37:50,400
to try to plot trait values in one

1027
00:37:53,990 --> 00:37:52,400
generation versus another if we see any

1028
00:37:55,910 --> 00:37:54,000
kind of significant correlation that

1029
00:37:57,829 --> 00:37:55,920
might again be indicative of lineage

1030
00:37:59,829 --> 00:37:57,839
effects we also have a sense of what

1031
00:38:02,550 --> 00:37:59,839
things should look like with respect to

1032
00:38:05,270 --> 00:38:02,560
rate of propagation changes over time if

1033
00:38:07,270 --> 00:38:05,280
there is evolution operating or not

1034
00:38:09,990 --> 00:38:07,280
and so we'll ask you to stay tuned for

1035
00:38:11,750 --> 00:38:10,000
all of that and i will just end by

1036
00:38:13,510 --> 00:38:11,760
saying that we think that the chemical

1037
00:38:14,550 --> 00:38:13,520
ecology model in this experimental

1038
00:38:16,550 --> 00:38:14,560

framework

1039
00:38:19,270 --> 00:38:16,560
can help us resolve some key questions

1040
00:38:21,109 --> 00:38:19,280
about the origins of lifelike processes

1041
00:38:22,550 --> 00:38:21,119
in the absence of prior living processes

1042
00:38:24,550 --> 00:38:22,560
like evolution

1043
00:38:25,990 --> 00:38:24,560
and as a bonus we've also identified

1044
00:38:27,510 --> 00:38:26,000
conditions that provide really

1045
00:38:28,710 --> 00:38:27,520
interesting results

1046
00:38:30,630 --> 00:38:28,720
and so with that i'm just going to

1047
00:38:32,870 --> 00:38:30,640
finish by acknowledging the really large

1048
00:38:34,230 --> 00:38:32,880
group of people that make this possible

1049
00:38:35,750 --> 00:38:34,240
including the baum lab and other

1050
00:38:38,300 --> 00:38:35,760
collaborators both at university

1051
00:38:45,430 --> 00:38:38,310
wisconsin and beyond thank you

1052
00:38:45,440 --> 00:38:50,390
okay thank you so questions for lena

1053
00:38:55,910 --> 00:38:54,390
maybe are there questions online marco

1054
00:38:59,030 --> 00:38:55,920
no no tips

1055
00:39:01,829 --> 00:38:59,040
so i have a question uh so did you try

1056
00:39:03,670 --> 00:39:01,839
to split some lineages and also do you

1057
00:39:05,190 --> 00:39:03,680
see some contingencies in the

1058
00:39:08,150 --> 00:39:05,200
trajectories because when you talk about

1059
00:39:10,710 --> 00:39:08,160
lineages you you mean linear successions

1060
00:39:12,310 --> 00:39:10,720
but did you try to split sound

1061
00:39:13,750 --> 00:39:12,320
uh we have not tried to split any of the

1062
00:39:16,230 --> 00:39:13,760
lineages but that would be a really

1063
00:39:17,190 --> 00:39:16,240

interesting experiment to do um but no

1064
00:39:19,270 --> 00:39:17,200
we haven't tried that we just

1065
00:39:21,510 --> 00:39:19,280
independently propagated these lineages

1066
00:39:24,069 --> 00:39:21,520
vertically and are making sense of those

1067
00:39:27,750 --> 00:39:25,430
we have a question

1068
00:39:30,150 --> 00:39:27,760
a lovely talk so i saw in your slides

1069
00:39:32,069 --> 00:39:30,160
you flashed a little cartoon of an

1070
00:39:33,829 --> 00:39:32,079
orbeez mass spectrometer and i was just

1071
00:39:35,990 --> 00:39:33,839
wondering if you've taken

1072
00:39:37,829 --> 00:39:36,000
a sort of proteomics type of data

1073
00:39:40,390 --> 00:39:37,839
analysis approach to see if you have any

1074
00:39:41,670 --> 00:39:40,400
peptides growing in these slimes no we

1075
00:39:44,310 --> 00:39:41,680
have not but that would be really

1076
00:39:45,990 --> 00:39:44,320
interesting to do um yeah we're just in

1077
00:39:47,910 --> 00:39:46,000
the infancy like i'm not an analytical

1078
00:39:49,190 --> 00:39:47,920
chemist by training uh we actually just

1079
00:39:50,230 --> 00:39:49,200
gained access to this instrument

1080
00:39:51,510 --> 00:39:50,240
recently

1081
00:39:52,710 --> 00:39:51,520
um but yeah that would be really

1082
00:39:56,790 --> 00:39:52,720
interesting to do so i'd love to talk to

1083
00:40:07,030 --> 00:39:58,230
okay okay

1084
00:40:12,390 --> 00:40:10,069
we now welcome philippe reneger

1085
00:40:14,069 --> 00:40:12,400
from the harvard medical school and

1086
00:40:15,910 --> 00:40:14,079
philip is going to tell us about

1087
00:40:18,230 --> 00:40:15,920
efficient identification of auto

1088
00:40:22,950 --> 00:40:18,240

catalysis in chemical and biological

1089
00:40:27,910 --> 00:40:25,270
all right thank you for attending my

1090
00:40:31,190 --> 00:40:27,920
talk at the last day of the conference

1091
00:40:32,870 --> 00:40:31,200
i'll tell you a bit how we identify

1092
00:40:35,990 --> 00:40:32,880
auto catalysis in chemical and

1093
00:40:37,750 --> 00:40:36,000
biological networks with our efficient

1094
00:40:39,990 --> 00:40:37,760
sort of algorithm

1095
00:40:41,550 --> 00:40:40,000
so first i will

1096
00:40:44,470 --> 00:40:41,560
introduce the importance of

1097
00:40:46,710 --> 00:40:44,480
autocatalysis so autocatalysis as i'm

1098
00:40:48,790 --> 00:40:46,720
sure most of you are aware means that

1099
00:40:50,790 --> 00:40:48,800
there are chemical reactions where the

1100
00:40:53,510 --> 00:40:50,800
product is also the catalyst for the

1101
00:40:56,630 --> 00:40:53,520
reaction or where differently the

1102
00:40:58,950 --> 00:40:56,640
catalyst makes copies of itself which is

1103
00:41:01,990 --> 00:40:58,960
of course an important concept in the

1104
00:41:04,069 --> 00:41:02,000
field of abiogenesis because this type

1105
00:41:05,750 --> 00:41:04,079
of reaction is very stable against

1106
00:41:08,309 --> 00:41:05,760
environmental shocks and molecular

1107
00:41:11,349 --> 00:41:08,319
degradation and it also plays a major

1108
00:41:13,910 --> 00:41:11,359
role in many models how abiogenesis

1109
00:41:16,069 --> 00:41:13,920
could work because this is a chemical

1110
00:41:18,550 --> 00:41:16,079
analog of a system that is able to feed

1111
00:41:21,349 --> 00:41:18,560
on input and grow and reproduce

1112
00:41:23,990 --> 00:41:21,359
and in a way even life as it exists

1113
00:41:26,309 --> 00:41:24,000

today could be seen like that because

1114
00:41:30,470 --> 00:41:26,319
living organisms eat

1115
00:41:34,069 --> 00:41:30,480
sustain themselves grow and reproduce

1116
00:41:35,270 --> 00:41:34,079
so here are some favorite autocality

1117
00:41:37,750 --> 00:41:35,280
cycles

1118
00:41:40,390 --> 00:41:37,760
in the biological fields on the left

1119
00:41:42,230 --> 00:41:40,400
hand side you see the reductive citric

1120
00:41:44,790 --> 00:41:42,240
acid cycle which

1121
00:41:45,829 --> 00:41:44,800
absorbs carbon dioxide to make more of

1122
00:41:47,510 --> 00:41:45,839
itself

1123
00:41:50,390 --> 00:41:47,520
and on the right hand side you see the

1124
00:41:51,510 --> 00:41:50,400
glyoxylate cycle which is also based on

1125
00:41:55,030 --> 00:41:51,520
the

1126
00:41:58,150 --> 00:41:55,040
citric acid cycle but instead of

1127
00:41:59,190 --> 00:41:58,160
producing two equivalents of formal

1128
00:42:02,550 --> 00:41:59,200
for

1129
00:42:05,750 --> 00:42:02,560
carbon dioxide it makes dioxide and does

1130
00:42:07,270 --> 00:42:05,760
add it copies the catalytic species

1131
00:42:09,750 --> 00:42:07,280
itself

1132
00:42:12,390 --> 00:42:09,760
and there are also chemical analogs i

1133
00:42:14,470 --> 00:42:12,400
decided to use as an example the formos

1134
00:42:16,710 --> 00:42:14,480
reaction which is probably most familiar

1135
00:42:18,470 --> 00:42:16,720
to this community

1136
00:42:21,349 --> 00:42:18,480
in essence

1137
00:42:23,589 --> 00:42:21,359
form aldehyde polymerizes to

1138
00:42:25,670 --> 00:42:23,599

carbohydrates carbohydrate-like

1139
00:42:28,230 --> 00:42:25,680
structures and here are two of the

1140
00:42:30,550 --> 00:42:28,240
cycles because the form hosa system is

1141
00:42:32,790 --> 00:42:30,560
an actually rather complicated

1142
00:42:35,270 --> 00:42:32,800
convolution of auto catalytic cycles of

1143
00:42:37,030 --> 00:42:35,280
which a few are very active and most are

1144
00:42:40,069 --> 00:42:37,040
not

1145
00:42:42,309 --> 00:42:40,079
so when we look at all of these cycles

1146
00:42:44,790 --> 00:42:42,319
can we find commonalities

1147
00:42:47,829 --> 00:42:44,800
well the first and really obvious one

1148
00:42:49,750 --> 00:42:47,839
they're all of a cyclic structure

1149
00:42:51,829 --> 00:42:49,760
the second one is that in all of those

1150
00:42:53,910 --> 00:42:51,839
cycles you will see there is some

1151
00:42:57,030 --> 00:42:53,920
species some molecular species that

1152
00:42:59,670 --> 00:42:57,040
splits into two parts that are still in

1153
00:43:02,630 --> 00:42:59,680
the cycle i call this a quasi-dimer it

1154
00:43:04,069 --> 00:43:02,640
doesn't need to be dimeric but it is

1155
00:43:06,470 --> 00:43:04,079
able to break

1156
00:43:08,470 --> 00:43:06,480
and what you will also always see is

1157
00:43:11,670 --> 00:43:08,480
that there is some molecular species

1158
00:43:14,150 --> 00:43:11,680
these two fragments are united into

1159
00:43:16,790 --> 00:43:14,160
and it is not a coincidence that you see

1160
00:43:18,710 --> 00:43:16,800
these motives in all of these cycles i

1161
00:43:19,990 --> 00:43:18,720
presented before those are necessary

1162
00:43:22,309 --> 00:43:20,000
conditions

1163
00:43:25,030 --> 00:43:22,319

a catalytic cycle must fulfill in order

1164
00:43:27,349 --> 00:43:25,040
to be auto catalytic

1165
00:43:29,829 --> 00:43:27,359
so but if you look at this from a graph

1166
00:43:32,309 --> 00:43:29,839
algorithmic perspective this suggests a

1167
00:43:34,230 --> 00:43:32,319
detection algorithm doesn't it

1168
00:43:36,790 --> 00:43:34,240
let's pretend this grey blob on the

1169
00:43:38,790 --> 00:43:36,800
right hand side is some reaction network

1170
00:43:42,630 --> 00:43:38,800
you're interested in whether biological

1171
00:43:44,950 --> 00:43:42,640
or primordial or strictly chemical

1172
00:43:47,349 --> 00:43:44,960
how could you now find autocatalytic

1173
00:43:48,470 --> 00:43:47,359
cycles with what you have seen

1174
00:43:50,790 --> 00:43:48,480
first

1175
00:43:53,190 --> 00:43:50,800
go through all the reactions and find

1176
00:43:55,270 --> 00:43:53,200
those that have more than one product

1177
00:43:57,270 --> 00:43:55,280
this would be the dimer splitting

1178
00:43:59,829 --> 00:43:57,280
reactions

1179
00:44:01,910 --> 00:43:59,839
then find all of the molecules that can

1180
00:44:04,230 --> 00:44:01,920
be produced by at least two different

1181
00:44:07,270 --> 00:44:04,240
ways or at least with a coefficient

1182
00:44:09,349 --> 00:44:07,280
greater than one

1183
00:44:11,190 --> 00:44:09,359
then look for all the paths in the

1184
00:44:14,069 --> 00:44:11,200
network that combine the

1185
00:44:16,710 --> 00:44:14,079
lead from the reaction to the molecule

1186
00:44:18,069 --> 00:44:16,720
and here is one of the problems of the

1187
00:44:20,790 --> 00:44:18,079
algorithm

1188
00:44:22,550 --> 00:44:20,800

while finding the shortest path

1189
00:44:25,510 --> 00:44:22,560
is efficient

1190
00:44:26,630 --> 00:44:25,520
finding all paths is a combinatorial

1191
00:44:28,950 --> 00:44:26,640
problem

1192
00:44:31,990 --> 00:44:28,960
so we often need to regularize for

1193
00:44:35,270 --> 00:44:32,000
example by deciding we only want paths

1194
00:44:39,670 --> 00:44:37,750
and the fourth part of the algorithm

1195
00:44:41,510 --> 00:44:39,680
would be then to find all paths that

1196
00:44:43,109 --> 00:44:41,520
lead from the molecule back to the

1197
00:44:45,349 --> 00:44:43,119
reaction

1198
00:44:47,589 --> 00:44:45,359
and if you have more than two of the

1199
00:44:49,430 --> 00:44:47,599
paths from reaction to molecule and at

1200
00:44:50,710 --> 00:44:49,440
least one from the molecule to the

1201
00:44:53,910 --> 00:44:50,720
reaction

1202
00:44:57,349 --> 00:44:53,920
then as this pseudo code shows you have

1203
00:44:58,550 --> 00:44:57,359
found a possible auto catalytic cycle

1204
00:45:02,790 --> 00:44:58,560
basic

1205
00:45:06,150 --> 00:45:02,800
just based on the graph topology alone

1206
00:45:09,270 --> 00:45:06,160
so we looked for use cases of this

1207
00:45:11,109 --> 00:45:09,280
and we used terrestrial biological

1208
00:45:13,349 --> 00:45:11,119
networks because those are the largest

1209
00:45:15,670 --> 00:45:13,359
and most challenging ones

1210
00:45:17,829 --> 00:45:15,680
and so we went through the big database

1211
00:45:20,870 --> 00:45:17,839
which is openly accessible and went

1212
00:45:25,270 --> 00:45:20,880
through all of these different organisms

1213
00:45:26,230 --> 00:45:25,280

and ran our algorithm so this

1214
00:45:28,390 --> 00:45:26,240
this

1215
00:45:30,150 --> 00:45:28,400
column here shows the metabolites that

1216
00:45:32,550 --> 00:45:30,160
are not in the

1217
00:45:34,630 --> 00:45:32,560
energy currency system these are the

1218
00:45:36,390 --> 00:45:34,640
metabolites that are in the energy

1219
00:45:40,470 --> 00:45:36,400
currency system

1220
00:45:43,030 --> 00:45:40,480
atp adp amp and so on

1221
00:45:45,910 --> 00:45:43,040
and you see that we find up to dozens of

1222
00:45:47,190 --> 00:45:45,920
different auto catalytic cycles for each

1223
00:45:49,589 --> 00:45:47,200
of those

1224
00:45:51,750 --> 00:45:49,599
metabolic networks

1225
00:45:53,589 --> 00:45:51,760
the bracketed number here means we have

1226
00:45:56,470 --> 00:45:53,599
organized the

1227
00:45:59,109 --> 00:45:56,480
raw number of autocatalytic cycles into

1228
00:46:01,550 --> 00:45:59,119
sets where all the metabolites are equal

1229
00:46:04,790 --> 00:46:01,560
for example you see here are normal

1230
00:46:07,030 --> 00:46:04,800
anomalously large amounts

1231
00:46:09,349 --> 00:46:07,040
like 800 different cycles that's because

1232
00:46:13,349 --> 00:46:09,359
they include some enzyme that performs a

1233
00:46:15,109 --> 00:46:13,359
very common reaction like atp to adp

1234
00:46:17,270 --> 00:46:15,119
which can be implemented by a whole

1235
00:46:19,589 --> 00:46:17,280
plethora of different enzymes but it's

1236
00:46:22,150 --> 00:46:19,599
basically the same auto catalytic cycles

1237
00:46:26,150 --> 00:46:22,160
so the bracketed number here shows the

1238
00:46:32,069 --> 00:46:29,349

so as i said we had to regula regularize

1239
00:46:34,309 --> 00:46:32,079
the number of path lengths

1240
00:46:35,750 --> 00:46:34,319
because otherwise this combinatorial

1241
00:46:37,990 --> 00:46:35,760
algorithm

1242
00:46:39,430 --> 00:46:38,000
calculates for an indeterminable amount

1243
00:46:41,510 --> 00:46:39,440
of time

1244
00:46:43,190 --> 00:46:41,520
and maybe you have noticed this

1245
00:46:45,910 --> 00:46:43,200
little anomaly here in the field

1246
00:46:49,349 --> 00:46:45,920
dactylum where we suddenly find almost 8

1247
00:46:51,589 --> 00:46:49,359
000 different autocatalytic cycles

1248
00:46:54,550 --> 00:46:51,599
and upon closer inspection we found that

1249
00:46:57,270 --> 00:46:54,560
the network entry in the big database

1250
00:46:59,270 --> 00:46:57,280
has some very important errors in the

1251
00:47:01,109 --> 00:46:59,280
iron ii iron three

1252
00:47:02,710 --> 00:47:01,119
assignments which is adduct and which is

1253
00:47:05,190 --> 00:47:02,720
product and this in

1254
00:47:07,510 --> 00:47:05,200
induce this huge number of

1255
00:47:10,309 --> 00:47:07,520
fake cycles and below here you see the

1256
00:47:13,109 --> 00:47:10,319
corrected network which has an

1257
00:47:14,630 --> 00:47:13,119
expectedly low number of auto catalytic

1258
00:47:19,829 --> 00:47:14,640
cycles

1259
00:47:20,549 --> 00:47:19,839
like if jerry picked a few examples for

1260
00:47:23,030 --> 00:47:20,559
you

1261
00:47:25,670 --> 00:47:23,040
and i must stress that we do not know if

1262
00:47:28,069 --> 00:47:25,680
these auto catalytic cycles actually run

1263
00:47:30,549 --> 00:47:28,079

like that in the metabolism all we are

1264
00:47:33,109 --> 00:47:30,559
saying is that the topological features

1265
00:47:36,790 --> 00:47:33,119
of autocatalysis are there

1266
00:47:38,710 --> 00:47:36,800
but of course enzyme control

1267
00:47:41,510 --> 00:47:38,720
adds a whole new dimension we do not

1268
00:47:43,349 --> 00:47:41,520
consider at this stage for example here

1269
00:47:47,670 --> 00:47:43,359
are some carbohydrate-based

1270
00:47:50,390 --> 00:47:47,680
auto-catalytic cycles in homo sapiens

1271
00:47:52,950 --> 00:47:50,400
this one i found as a chemist kind of

1272
00:47:56,790 --> 00:47:52,960
curious because this is a terpenoid auto

1273
00:47:57,990 --> 00:47:56,800
catalytic cycle we found in homo sapiens

1274
00:47:59,990 --> 00:47:58,000
where

1275
00:48:02,069 --> 00:48:00,000
farnell

1276
00:48:03,990 --> 00:48:02,079
pure phosphate

1277
00:48:05,349 --> 00:48:04,000
assembles c5

1278
00:48:08,390 --> 00:48:05,359
bodies into

1279
00:48:10,710 --> 00:48:08,400
into more of itself

1280
00:48:14,950 --> 00:48:10,720
and here is one we found in the energy

1281
00:48:16,549 --> 00:48:14,960
currency metabolism where amp adp atp as

1282
00:48:18,390 --> 00:48:16,559
a set

1283
00:48:20,630 --> 00:48:18,400
catalyze the

1284
00:48:23,510 --> 00:48:20,640
absorption of adenosine

1285
00:48:26,710 --> 00:48:23,520
and of pep to make more

1286
00:48:28,470 --> 00:48:26,720
of adp to fuse basically those

1287
00:48:31,430 --> 00:48:28,480
and those

1288
00:48:33,990 --> 00:48:31,440

and pay special attention here we also

1289
00:48:35,589 --> 00:48:34,000
take one phosphate unit from gtp and

1290
00:48:37,829 --> 00:48:35,599
make gdp

1291
00:48:40,390 --> 00:48:37,839
because we found another system that has

1292
00:48:43,349 --> 00:48:40,400
this as a subsystem

1293
00:48:46,549 --> 00:48:43,359
and here is interesting because gdp is

1294
00:48:49,510 --> 00:48:46,559
recycled back to gtp

1295
00:48:51,270 --> 00:48:49,520
and so here gtp is necessary in a

1296
00:48:52,870 --> 00:48:51,280
stoichiometric amount to run

1297
00:48:55,670 --> 00:48:52,880
autocatalytically

1298
00:48:57,670 --> 00:48:55,680
but here it is only a catalytic amount

1299
00:48:59,990 --> 00:48:57,680
and the interesting thing here is the

1300
00:49:01,670 --> 00:49:00,000
number of auto catalytic cycles that run

1301
00:49:04,069 --> 00:49:01,680
simultaneously

1302
00:49:06,710 --> 00:49:04,079
will be controlled by the number of gdp

1303
00:49:12,549 --> 00:49:06,720
plus gdp that is available so this is

1304
00:49:17,750 --> 00:49:15,670
so here we also correlated the

1305
00:49:19,510 --> 00:49:17,760
autotrophic

1306
00:49:21,910 --> 00:49:19,520
property of

1307
00:49:24,069 --> 00:49:21,920
these organisms as determined by various

1308
00:49:26,790 --> 00:49:24,079
publications we found

1309
00:49:29,750 --> 00:49:26,800
to the number of auto catalytic cycles

1310
00:49:31,349 --> 00:49:29,760
divided by metabolic by

1311
00:49:34,309 --> 00:49:31,359
size to have a

1312
00:49:37,990 --> 00:49:34,319
entity of metabolic density and what we

1313
00:49:40,630 --> 00:49:38,000

find that the autotrophic

1314
00:49:42,549 --> 00:49:40,640
organisms have a higher density of auto

1315
00:49:44,870 --> 00:49:42,559
catalytic cycles

1316
00:49:46,870 --> 00:49:44,880
so

1317
00:49:49,750 --> 00:49:46,880
not sure if this has a

1318
00:49:50,950 --> 00:49:49,760
importance but it is there

1319
00:49:53,829 --> 00:49:50,960
and

1320
00:49:56,950 --> 00:49:53,839
what i want to say in the last part of

1321
00:49:59,430 --> 00:49:56,960
my talk is pattern auto catalysis

1322
00:50:02,150 --> 00:49:59,440
because so far in the

1323
00:50:03,910 --> 00:50:02,160
most in the most communities

1324
00:50:05,670 --> 00:50:03,920
autocatalysis is treated like a

1325
00:50:07,829 --> 00:50:05,680
molecular property but you need to

1326
00:50:08,790 --> 00:50:07,839
realize that chemistry does not happen

1327
00:50:11,030 --> 00:50:08,800
on the

1328
00:50:13,349 --> 00:50:11,040
level of entire molecules it happens on

1329
00:50:15,430 --> 00:50:13,359
the level of functional groups

1330
00:50:17,750 --> 00:50:15,440
so if you look at this autocatalytic

1331
00:50:20,390 --> 00:50:17,760
cycle i constructed it it is not

1332
00:50:22,470 --> 00:50:20,400
empirical but it is based on theoretical

1333
00:50:25,349 --> 00:50:22,480
predictions

1334
00:50:27,589 --> 00:50:25,359
where a primary amide catalyzes the

1335
00:50:31,349 --> 00:50:27,599
hydrolysis of

1336
00:50:33,190 --> 00:50:31,359
hydrogen cyanide to formamide

1337
00:50:35,109 --> 00:50:33,200
but if you really look under the hood

1338
00:50:37,030 --> 00:50:35,119

and you look at the involved functional

1339
00:50:38,309 --> 00:50:37,040
groups you will see what actually

1340
00:50:41,030 --> 00:50:38,319
happens

1341
00:50:42,790 --> 00:50:41,040
is that a primary amide catalyzes the

1342
00:50:44,549 --> 00:50:42,800
hydrolysis

1343
00:50:46,870 --> 00:50:44,559
of a nitrile

1344
00:50:49,510 --> 00:50:46,880
to another

1345
00:50:51,829 --> 00:50:49,520
primary amide so in the end the

1346
00:50:54,150 --> 00:50:51,839
concentration of the active functional

1347
00:50:56,950 --> 00:50:54,160
group does increase even if the

1348
00:50:59,109 --> 00:50:56,960
molecular auto catalytic cycle does not

1349
00:51:02,069 --> 00:50:59,119
directly show you this

1350
00:51:03,990 --> 00:51:02,079
so we suspect that even below all of

1351
00:51:06,630 --> 00:51:04,000
these auto catalytic cycles that we

1352
00:51:09,349 --> 00:51:06,640
found so far there is another layer of

1353
00:51:11,750 --> 00:51:09,359
shadow metabolism where auto catalytic

1354
00:51:14,150 --> 00:51:11,760
cycles might exist that we are not even

1355
00:51:15,990 --> 00:51:14,160
aware of yet

1356
00:51:26,710 --> 00:51:16,000
so with that i come to the end of my

1357
00:51:32,870 --> 00:51:29,990
okay some questions for philip

1358
00:51:34,710 --> 00:51:32,880
i can yeah

1359
00:51:37,430 --> 00:51:34,720
hi anthony burnett here from georgia

1360
00:51:40,069 --> 00:51:37,440
tech and i was wondering so when you

1361
00:51:42,230 --> 00:51:40,079
were looking through networks for

1362
00:51:43,670 --> 00:51:42,240
auto catalytic loops sorry

1363
00:51:44,870 --> 00:51:43,680

it was like you were looking at species

1364
00:51:46,390 --> 00:51:44,880
whether they were

1365
00:51:48,870 --> 00:51:46,400
autotrophic heterotrophic all these

1366
00:51:51,910 --> 00:51:48,880
things any thought of extending this

1367
00:51:54,470 --> 00:51:51,920
kind of analysis to metagenomes or

1368
00:51:57,589 --> 00:51:54,480
ecosystems of microbes

1369
00:51:59,510 --> 00:51:57,599
oh no we didn't do any of that we kept

1370
00:52:01,430 --> 00:51:59,520
it to the level of metabolic networks

1371
00:52:03,910 --> 00:52:01,440
and the reason is simply that i don't

1372
00:52:06,549 --> 00:52:03,920
know anything about that i'm a chemist

1373
00:52:08,390 --> 00:52:06,559
and a programmer by training so

1374
00:52:09,990 --> 00:52:08,400
we kept it at the level of pure

1375
00:52:11,990 --> 00:52:10,000
metabolites so far but it's an

1376
00:52:15,670 --> 00:52:12,000
interesting suggestion

1377
00:52:19,829 --> 00:52:17,750
hello uh first of all thank you for your

1378
00:52:21,990 --> 00:52:19,839
talk it was great um my name is tim i'm

1379
00:52:23,670 --> 00:52:22,000
from the university of wisconsin-madison

1380
00:52:26,710 --> 00:52:23,680
uh and i was wondering about your

1381
00:52:29,270 --> 00:52:26,720
finding with um the greater abundance of

1382
00:52:30,950 --> 00:52:29,280
autocatalysis in autotrophs

1383
00:52:33,190 --> 00:52:30,960
do you know which

1384
00:52:34,710 --> 00:52:33,200
categories of pathways could that be

1385
00:52:36,870 --> 00:52:34,720
responsible for and could it be an

1386
00:52:39,109 --> 00:52:36,880
artifact of coupling between carbon

1387
00:52:41,650 --> 00:52:39,119
fixation and some other

1388
00:52:42,870 --> 00:52:41,660

pathways like respiration

1389
00:52:45,190 --> 00:52:42,880
[Music]

1390
00:52:46,470 --> 00:52:45,200
we haven't even thought about that yet

1391
00:52:49,109 --> 00:52:46,480
but it

1392
00:52:50,710 --> 00:52:49,119
sounds interesting so no i cannot answer

1393
00:52:55,349 --> 00:52:50,720
that sorry

1394
00:53:00,470 --> 00:52:58,069
georgia tech so my question is you uh

1395
00:53:03,589 --> 00:53:00,480
you've done analysis on

1396
00:53:04,390 --> 00:53:03,599
networks using modern metabolic networks

1397
00:53:07,829 --> 00:53:04,400
yes

1398
00:53:10,309 --> 00:53:07,839
there was a paper a few years ago by

1399
00:53:12,069 --> 00:53:10,319
hyman hartmann and segre from boston

1400
00:53:14,470 --> 00:53:12,079
university

1401
00:53:17,270 --> 00:53:14,480
who attempted to show some

1402
00:53:20,870 --> 00:53:17,280
uh remnants of uh

1403
00:53:23,270 --> 00:53:20,880
catalytic networks without phosphates

1404
00:53:26,790 --> 00:53:23,280
uh so can you have you thought about

1405
00:53:31,670 --> 00:53:26,800
exploring going that level and exploring

1406
00:53:36,069 --> 00:53:34,870
your networks in at a much simpler

1407
00:53:37,190 --> 00:53:36,079
metabolic

1408
00:53:39,270 --> 00:53:37,200
level

1409
00:53:41,910 --> 00:53:39,280
oh absolutely we are planning on working

1410
00:53:43,829 --> 00:53:41,920
with daniel secret on similar questions

1411
00:53:45,910 --> 00:53:43,839
and using smaller networks would be

1412
00:53:48,309 --> 00:53:45,920
especially useful for us because then we

1413
00:53:49,510 --> 00:53:48,319

don't have to restrict our algorithm so

1414
00:53:50,309 --> 00:53:49,520
strictly

1415
00:53:52,790 --> 00:53:50,319
so

1416
00:53:56,549 --> 00:53:52,800
yes that is what we plan next

1417
00:53:56,559 --> 00:54:00,870
online questions maybe

1418
00:54:05,510 --> 00:54:04,309
and well i have a question so you um

1419
00:54:07,030 --> 00:54:05,520
you say the

1420
00:54:08,710 --> 00:54:07,040
rightly so that it's a necessary

1421
00:54:11,750 --> 00:54:08,720
condition only so

1422
00:54:14,150 --> 00:54:11,760
how could we focus as experimentalists

1423
00:54:17,030 --> 00:54:14,160
our attention on more specific cycles

1424
00:54:19,270 --> 00:54:17,040
that could be sufficiently

1425
00:54:21,109 --> 00:54:19,280
sufficient conditions for the catalyst

1426
00:54:23,270 --> 00:54:21,119
well for that we would have to do more

1427
00:54:24,390 --> 00:54:23,280
refinement because as you pointed out

1428
00:54:27,190 --> 00:54:24,400
correctly

1429
00:54:30,069 --> 00:54:27,200
our graph topological search

1430
00:54:32,069 --> 00:54:30,079
is just the

1431
00:54:35,349 --> 00:54:32,079
it's just a pre-screening because it is

1432
00:54:36,390 --> 00:54:35,359
a necessary but not sufficient condition

1433
00:54:38,710 --> 00:54:36,400
so

1434
00:54:41,030 --> 00:54:38,720
with regards to the experiment

1435
00:54:43,190 --> 00:54:41,040
what this detection can just do is point

1436
00:54:45,270 --> 00:54:43,200
out the auto catalytic cycles that could

1437
00:54:47,190 --> 00:54:45,280
be there you need to

1438
00:54:49,910 --> 00:54:47,200

you include additional data in

1439
00:54:52,309 --> 00:54:49,920
subsequent analysis

1440
00:54:54,390 --> 00:54:52,319
to make that distinction which ones are

1441
00:54:57,109 --> 00:54:54,400
interesting for example by

1442
00:55:00,789 --> 00:54:57,119
using consistent thermodynamic and or

1443
00:55:10,549 --> 00:55:02,549
thank you

1444
00:55:15,270 --> 00:55:13,530
so now we have an online talk

1445
00:55:17,510 --> 00:55:15,280
[Music]

1446
00:55:19,670 --> 00:55:17,520
by armin kiyani

1447
00:55:21,030 --> 00:55:19,680
so let's sign

1448
00:55:22,870 --> 00:55:21,040
display uh

1449
00:55:23,910 --> 00:55:22,880
i mean

1450
00:55:26,230 --> 00:55:23,920
yes

1451
00:55:28,150 --> 00:55:26,240
so uh armin from the university of

1452
00:55:30,069 --> 00:55:28,160
renningen is going to tell us about

1453
00:55:32,549 --> 00:55:30,079
integrating compartmentalization

1454
00:55:35,349 --> 00:55:32,559
metabolism and self-replication

1455
00:55:37,430 --> 00:55:35,359
the world de novo life

1456
00:55:39,109 --> 00:55:37,440
uh hi everyone my name is armin i'm

1457
00:55:41,030 --> 00:55:39,119
doing my phd at the university of

1458
00:55:42,470 --> 00:55:41,040
toronto again in the netherlands today

1459
00:55:45,270 --> 00:55:42,480
i'm going to talk to you about some of

1460
00:55:46,309 --> 00:55:45,280
the work i've been doing on integration

1461
00:55:49,990 --> 00:55:46,319
of

1462
00:55:50,950 --> 00:55:50,000
system

1463
00:55:54,230 --> 00:55:50,960

so

1464
00:55:55,910 --> 00:55:54,240
life has been known as

1465
00:55:59,510 --> 00:55:55,920
life as we know it is composed of

1466
00:56:02,549 --> 00:55:59,520
non-living methods like dna protein or

1467
00:56:07,510 --> 00:56:02,559
lipids however when these molecules are

1468
00:56:12,870 --> 00:56:10,549
in these two states is complex of

1469
00:56:14,950 --> 00:56:12,880
chemical reactions that can give rise to

1470
00:56:18,150 --> 00:56:14,960
some emergent behavior that we know it

1471
00:56:20,789 --> 00:56:18,160
as live so if we change the initial

1472
00:56:22,390 --> 00:56:20,799
condition or the initial molecules

1473
00:56:23,349 --> 00:56:22,400
probably we have different kinds of

1474
00:56:25,510 --> 00:56:23,359
chemical

1475
00:56:28,390 --> 00:56:25,520
reaction network and also different

1476
00:56:30,470 --> 00:56:28,400
emergent properties so the question is

1477
00:56:31,990 --> 00:56:30,480
is it possible to have life based on

1478
00:56:33,190 --> 00:56:32,000
different chemistry

1479
00:56:34,870 --> 00:56:33,200
um

1480
00:56:38,789 --> 00:56:34,880
we don't know because we have only one

1481
00:56:40,470 --> 00:56:38,799
example of life in there so we uh in our

1482
00:56:41,750 --> 00:56:40,480
group as well as many other gurus we are

1483
00:56:43,990 --> 00:56:41,760
trying to

1484
00:56:45,510 --> 00:56:44,000
make kind of fully synthetic life or de

1485
00:56:47,430 --> 00:56:45,520
novo life

1486
00:56:49,109 --> 00:56:47,440
add another example of

1487
00:56:51,109 --> 00:56:49,119
life indeed so

1488
00:56:53,990 --> 00:56:51,119

in order to make innova life we need to

1489
00:56:56,630 --> 00:56:54,000
focus on phenomena of life instead of

1490
00:56:59,109 --> 00:56:56,640
the example of life that we have so what

1491
00:57:00,870 --> 00:56:59,119
is what life is is a very uh

1492
00:57:03,190 --> 00:57:00,880
long-standing unanswered question

1493
00:57:04,789 --> 00:57:03,200
however we can describe life with its

1494
00:57:07,190 --> 00:57:04,799
features like metabolism

1495
00:57:09,510 --> 00:57:07,200
self-replication compartmentalization in

1496
00:57:11,589 --> 00:57:09,520
a regime for from equilibrium and also

1497
00:57:12,390 --> 00:57:11,599
capable of undergoing darwinian

1498
00:57:14,870 --> 00:57:12,400
evolution

1499
00:57:16,150 --> 00:57:14,880
so it is believed that if we can make

1500
00:57:17,750 --> 00:57:16,160
each of these

1501
00:57:19,829 --> 00:57:17,760
features synthetically and then

1502
00:57:23,190 --> 00:57:19,839
integrate all of them in one single

1503
00:57:27,030 --> 00:57:23,200
system what we can get uh one we get can

1504
00:57:29,430 --> 00:57:27,040
be called life probably so

1505
00:57:32,549 --> 00:57:29,440
that many different groups have tried to

1506
00:57:35,030 --> 00:57:32,559
make each of these properties separately

1507
00:57:37,030 --> 00:57:35,040
or integration of some of them among

1508
00:57:39,670 --> 00:57:37,040
them it seems that a server application

1509
00:57:42,069 --> 00:57:39,680
is a very good candidate because uh

1510
00:57:43,750 --> 00:57:42,079
living system need to make copy of

1511
00:57:45,430 --> 00:57:43,760
itself

1512
00:57:46,870 --> 00:57:45,440
so a few uh fully synthetic

1513
00:57:49,510 --> 00:57:46,880

self-replicating molecules have been

1514
00:57:52,150 --> 00:57:49,520
reported so far one of them by our group

1515
00:57:53,750 --> 00:57:52,160
a decade ago in which is work based on

1516
00:57:57,349 --> 00:57:53,760
dynamic combination or chemistry

1517
00:57:59,589 --> 00:57:57,359
approach uh the main molecule is this

1518
00:58:03,510 --> 00:57:59,599
molecule

1519
00:58:05,510 --> 00:58:03,520
with two tiles which is decorated with

1520
00:58:08,230 --> 00:58:05,520
endopeptide which are alternating

1521
00:58:10,870 --> 00:58:08,240
hydrophobic hydrophilic uh mine acid

1522
00:58:12,870 --> 00:58:10,880
open oxidation this tile group will be

1523
00:58:15,829 --> 00:58:12,880
oxidized to

1524
00:58:17,589 --> 00:58:15,839
disulfide bonds and make different micro

1525
00:58:19,990 --> 00:58:17,599
cycles and all of them are input in

1526
00:58:21,750 --> 00:58:20,000
equilibrium together however when one of

1527
00:58:24,230 --> 00:58:21,760
this micro cycle for example hexamer

1528
00:58:25,990 --> 00:58:24,240
here can stack on top of each other so

1529
00:58:28,150 --> 00:58:26,000
it draws all equilibrium towards

1530
00:58:31,670 --> 00:58:28,160
formation of itself in a autocatalytic

1531
00:58:34,069 --> 00:58:31,680
process and this fiber will grow

1532
00:58:35,990 --> 00:58:34,079
elongate and if we

1533
00:58:38,309 --> 00:58:36,000
mechanically agitate the system this

1534
00:58:40,549 --> 00:58:38,319
fiber will break and each of them can

1535
00:58:41,349 --> 00:58:40,559
grow again so the whole process is kind

1536
00:58:43,510 --> 00:58:41,359
of

1537
00:58:46,150 --> 00:58:43,520
autocatholic

1538
00:58:49,430 --> 00:58:46,160

or exponential step replication so

1539
00:58:51,349 --> 00:58:49,440
another feature of life is metabolism

1540
00:58:54,309 --> 00:58:51,359
a few system in which

1541
00:58:56,470 --> 00:58:54,319
replicator and metabolism are integrated

1542
00:58:57,990 --> 00:58:56,480
have been reported a few of them in our

1543
00:59:01,190 --> 00:58:58,000
group i am going to show one of them

1544
00:59:03,750 --> 00:59:01,200
that i'm going to come back to later so

1545
00:59:06,069 --> 00:59:03,760
we showed that our replicators are able

1546
00:59:07,910 --> 00:59:06,079
to recruit um

1547
00:59:10,150 --> 00:59:07,920
cofactor which is performing here which

1548
00:59:13,270 --> 00:59:10,160
is not active in the solution but as

1549
00:59:15,430 --> 00:59:13,280
soon as it incorporates inside the

1550
00:59:17,750 --> 00:59:15,440
replicator it would be activated and by

1551
00:59:20,630 --> 00:59:17,760
shining light it converts triple oxygen

1552
00:59:23,030 --> 00:59:20,640
to single oxygen then single oxygen is

1553
00:59:25,270 --> 00:59:23,040
very active oxidizing agent it can

1554
00:59:27,430 --> 00:59:25,280
accelerate oxidation of monomer to

1555
00:59:29,829 --> 00:59:27,440
trimer testomer or

1556
00:59:32,390 --> 00:59:29,839
other microcycle and accelerate the

1557
00:59:33,190 --> 00:59:32,400
replication so indeed in this system we

1558
00:59:36,549 --> 00:59:33,200
have

1559
00:59:38,549 --> 00:59:36,559
our replicators are able to make our own

1560
00:59:40,710 --> 00:59:38,559
uh their own food

1561
00:59:42,789 --> 00:59:40,720
so it's the second feature the first

1562
00:59:44,710 --> 00:59:42,799
feature of life is compartmentalization

1563
00:59:47,990 --> 00:59:44,720

life is compartmentalized nerves to

1564
00:59:50,150 --> 00:59:48,000
protect itself from the environment so

1565
00:59:51,670 --> 00:59:50,160
it is the main topic of my research and

1566
00:59:52,870 --> 00:59:51,680
also the main topic that i'm going to

1567
00:59:54,069 --> 00:59:52,880
talk to you

1568
00:59:56,230 --> 00:59:54,079
today

1569
00:59:58,069 --> 00:59:56,240
so in order to make

1570
01:00:01,510 --> 00:59:58,079
integrate compartmentalization with

1571
01:00:03,510 --> 01:00:01,520
replication and metabolism we need a

1572
01:00:05,910 --> 01:00:03,520
compartment with some very special

1573
01:00:08,230 --> 01:00:05,920
features first of all our replicators

1574
01:00:10,390 --> 01:00:08,240
should be able to have positive feedback

1575
01:00:11,589 --> 01:00:10,400
on formation of compartment compartment

1576
01:00:13,109 --> 01:00:11,599
material

1577
01:00:15,190 --> 01:00:13,119
and also

1578
01:00:17,109 --> 01:00:15,200
the compartment material itself should

1579
01:00:20,630 --> 01:00:17,119
be able to form from building block and

1580
01:00:22,230 --> 01:00:20,640
then assemble as a compartment however

1581
01:00:25,829 --> 01:00:22,240
the building block shouldn't be able to

1582
01:00:28,069 --> 01:00:25,839
form compartments so then we can

1583
01:00:31,349 --> 01:00:28,079
make a positive feedback on formation of

1584
01:00:33,990 --> 01:00:31,359
compartment and the last thing

1585
01:00:34,710 --> 01:00:34,000
last but not least is partitioning so

1586
01:00:37,430 --> 01:00:34,720
our

1587
01:00:39,349 --> 01:00:37,440
lung positive sharp fiber should be able

1588
01:00:41,750 --> 01:00:39,359

to be accommodated inside compartment

1589
01:00:44,150 --> 01:00:41,760
because we need compartments for our

1590
01:00:45,750 --> 01:00:44,160
replicators so among different

1591
01:00:47,750 --> 01:00:45,760
compartments that have been studied over

1592
01:00:50,150 --> 01:00:47,760
the last years like i showed a few of

1593
01:00:52,789 --> 01:00:50,160
them here uh classification is very a

1594
01:00:54,470 --> 01:00:52,799
promising candidate because they are

1595
01:00:57,190 --> 01:00:54,480
boundary layers they don't have any

1596
01:01:00,549 --> 01:00:57,200
membrane so our positively charged fiber

1597
01:01:02,150 --> 01:01:00,559
are able to be partitioned inside so

1598
01:01:05,270 --> 01:01:02,160
class surveys are liquid liquid phase

1599
01:01:07,510 --> 01:01:05,280
separated drop that usually when the

1600
01:01:10,069 --> 01:01:07,520
affinity of some special molecules

1601
01:01:12,309 --> 01:01:10,079
together is higher than their affinity

1602
01:01:14,710 --> 01:01:12,319
to environment they form

1603
01:01:18,549 --> 01:01:14,720
this droplets and other molecules based

1604
01:01:20,710 --> 01:01:18,559
on the interactions can now may have a

1605
01:01:22,950 --> 01:01:20,720
tendency in order to be partitioned

1606
01:01:25,349 --> 01:01:22,960
inside this compartment however most of

1607
01:01:27,750 --> 01:01:25,359
compartment material or

1608
01:01:29,990 --> 01:01:27,760
sorry most of compartment droplets are

1609
01:01:32,309 --> 01:01:30,000
formed from compartment material

1610
01:01:34,870 --> 01:01:32,319
a system in which the compartment

1611
01:01:37,109 --> 01:01:34,880
material itself can be formed from its

1612
01:01:38,789 --> 01:01:37,119
own building block is very rare so in

1613
01:01:41,349 --> 01:01:38,799

order to address this problem that we

1614
01:01:43,750 --> 01:01:41,359
need for our uh system

1615
01:01:47,270 --> 01:01:43,760
uh i actually designed this villain

1616
01:01:49,910 --> 01:01:47,280
block so i use the same approach like

1617
01:01:52,230 --> 01:01:49,920
dynamical military chemistry i use the

1618
01:01:54,630 --> 01:01:52,240
benzene with two tiles but i changed the

1619
01:01:57,190 --> 01:01:54,640
step by chain to a block of positive and

1620
01:01:59,190 --> 01:01:57,200
block of negative charge so

1621
01:02:01,670 --> 01:01:59,200
number of lysine and a number of

1622
01:02:03,910 --> 01:02:01,680
glutamic acids is shown with m

1623
01:02:05,990 --> 01:02:03,920
the open oxidation as we expected they

1624
01:02:08,390 --> 01:02:06,000
form different microcycles then i

1625
01:02:10,230 --> 01:02:08,400
hypothesize that probably for one of

1626
01:02:12,630 --> 01:02:10,240
these microcycles the interaction should

1627
01:02:15,029 --> 01:02:12,640
be enough to go under phase separation

1628
01:02:16,950 --> 01:02:15,039
and in autocatalytic process draw all

1629
01:02:18,309 --> 01:02:16,960
equilibrium towards formation of the

1630
01:02:19,990 --> 01:02:18,319
cell based on that

1631
01:02:22,150 --> 01:02:20,000
we played around with the number of

1632
01:02:24,470 --> 01:02:22,160
different number of lysine and glutamic

1633
01:02:26,470 --> 01:02:24,480
acid and made different uh millenballer

1634
01:02:28,789 --> 01:02:26,480
that i'm showing you a few of them here

1635
01:02:31,190 --> 01:02:28,799
so as you see in this table it's based

1636
01:02:32,710 --> 01:02:31,200
on the concentration and the number of

1637
01:02:35,270 --> 01:02:32,720
n and m

1638
01:02:37,270 --> 01:02:35,280

by increasing the peptide lengths

1639
01:02:39,990 --> 01:02:37,280
the concentration in viscosity which

1640
01:02:42,710 --> 01:02:40,000
form uh would be higher would be wider

1641
01:02:45,349 --> 01:02:42,720
indeed so indeed in this system coaster

1642
01:02:47,109 --> 01:02:45,359
rate uh emerged from building blocks so

1643
01:02:49,510 --> 01:02:47,119
this concentration is concentration of

1644
01:02:52,710 --> 01:02:49,520
building block and for some people like

1645
01:02:55,670 --> 01:02:52,720
like k2 e2e as you see uh coaster of it

1646
01:02:57,750 --> 01:02:55,680
emerge only in one consonant in very

1647
01:03:00,789 --> 01:02:57,760
narrow concentration which is 12 around

1648
01:03:02,950 --> 01:03:00,799
12 millimolar however we could find some

1649
01:03:04,789 --> 01:03:02,960
building blocks in which and these three

1650
01:03:06,710 --> 01:03:04,799
that can form uh

1651
01:03:08,390 --> 01:03:06,720
classified can emerge from them in a

1652
01:03:11,349 --> 01:03:08,400
wider range

1653
01:03:12,870 --> 01:03:11,359
so with that um i'm going to show one of

1654
01:03:14,549 --> 01:03:12,880
them kinetic of one of them to you which

1655
01:03:16,470 --> 01:03:14,559
is k5b5

1656
01:03:18,870 --> 01:03:16,480
as you see at the beginning you have

1657
01:03:21,670 --> 01:03:18,880
lots of monomer then monomer decreasing

1658
01:03:23,349 --> 01:03:21,680
and the amount of tetramer is increasing

1659
01:03:26,069 --> 01:03:23,359
uh at the beginning the solution is

1660
01:03:27,589 --> 01:03:26,079
completely clear however after around

1661
01:03:29,910 --> 01:03:27,599
one day it would be turbid the

1662
01:03:32,150 --> 01:03:29,920
terribility emerged when

1663
01:03:34,470 --> 01:03:32,160

the tetramer image so tetramer is our

1664
01:03:36,870 --> 01:03:34,480
probably coaster rating material so

1665
01:03:39,510 --> 01:03:36,880
characterizing this assistant the

1666
01:03:40,309 --> 01:03:39,520
therapeutic one by uh electromicroscopy

1667
01:03:42,870 --> 01:03:40,319
show

1668
01:03:48,309 --> 01:03:42,880
very small droplets and however

1669
01:03:52,870 --> 01:03:50,789
from very small to very big

1670
01:03:55,750 --> 01:03:52,880
which is shown in the next video as you

1671
01:03:57,910 --> 01:03:55,760
see there are very small aggregates at

1672
01:03:59,029 --> 01:03:57,920
the beginning uh we use fluorescent dye

1673
01:04:01,510 --> 01:03:59,039
in order to

1674
01:04:03,750 --> 01:04:01,520
monitor the emergence but then the the

1675
01:04:05,510 --> 01:04:03,760
quads that emerge and they get bigger

1676
01:04:08,470 --> 01:04:05,520
and bigger and some of them coalesce

1677
01:04:11,190 --> 01:04:08,480
together to make even bigger clusters so

1678
01:04:13,029 --> 01:04:11,200
with that we have uh each of these

1679
01:04:15,190 --> 01:04:13,039
features separately

1680
01:04:17,510 --> 01:04:15,200
many other groups have tried to make

1681
01:04:19,510 --> 01:04:17,520
each of these features or system

1682
01:04:21,349 --> 01:04:19,520
capturing one or

1683
01:04:23,829 --> 01:04:21,359
a binary combination of two of these

1684
01:04:25,190 --> 01:04:23,839
features however a system in which all

1685
01:04:27,510 --> 01:04:25,200
three

1686
01:04:29,990 --> 01:04:27,520
features are combined or integrated

1687
01:04:32,150 --> 01:04:30,000
functionally together uh is not achieved

1688
01:04:34,630 --> 01:04:32,160

yet so it is something that i'm going to

1689
01:04:36,150 --> 01:04:34,640
talk a little bit in the rest of my talk

1690
01:04:38,470 --> 01:04:36,160
so the first

1691
01:04:41,190 --> 01:04:38,480
requirement was formation from building

1692
01:04:42,950 --> 01:04:41,200
block the second one is partitioning so

1693
01:04:45,270 --> 01:04:42,960
we um

1694
01:04:46,230 --> 01:04:45,280
labeled our fibers with cyan dye and

1695
01:04:47,109 --> 01:04:46,240
then

1696
01:04:49,029 --> 01:04:47,119
we

1697
01:04:50,789 --> 01:04:49,039
studied this with three of this

1698
01:04:52,390 --> 01:04:50,799
conservative form

1699
01:04:56,710 --> 01:04:52,400
building like a phone cast everything

1700
01:04:59,430 --> 01:04:56,720
wide range as you see for k5 e5

1701
01:05:01,430 --> 01:04:59,440
the partitioning is the highest

1702
01:05:03,510 --> 01:05:01,440
so the next thing is positive feedback

1703
01:05:05,990 --> 01:05:03,520
of replicator as i showed before our

1704
01:05:06,789 --> 01:05:06,000
replicators are able to harness light to

1705
01:05:09,829 --> 01:05:06,799
make

1706
01:05:13,510 --> 01:05:09,839
singlet oxygen so we can use this system

1707
01:05:16,150 --> 01:05:13,520
indeed what we did uh was we used the k5

1708
01:05:17,589 --> 01:05:16,160
e5 monomer which is which has two tiles

1709
01:05:21,109 --> 01:05:17,599
and then studied this in different

1710
01:05:23,430 --> 01:05:21,119
conditions so it is a tetramer

1711
01:05:26,069 --> 01:05:23,440
a survey material so i'm going i'm going

1712
01:05:28,870 --> 01:05:26,079
just to show test from our tracks so

1713
01:05:30,309 --> 01:05:28,880

then we add fiber and cofactor uh

1714
01:05:32,150 --> 01:05:30,319
without shining light you see the

1715
01:05:34,789 --> 01:05:32,160
profile is more or less the same it's

1716
01:05:37,270 --> 01:05:34,799
not very different however as soon as we

1717
01:05:39,029 --> 01:05:37,280
shine light to the system uh the kinetic

1718
01:05:41,670 --> 01:05:39,039
would be very different and all of the

1719
01:05:44,309 --> 01:05:41,680
monomer will be converted to tetramer in

1720
01:05:47,270 --> 01:05:44,319
couple of hours instead of two days so

1721
01:05:49,990 --> 01:05:47,280
it shows that um the fibers and the

1722
01:05:52,309 --> 01:05:50,000
fiber activity has positive feedback on

1723
01:05:54,549 --> 01:05:52,319
formation of plaster with what we

1724
01:05:55,430 --> 01:05:54,559
were looking for so in this video you

1725
01:05:57,990 --> 01:05:55,440
see

1726
01:05:59,589 --> 01:05:58,000
in this box there is no glass array

1727
01:06:02,230 --> 01:05:59,599
but also there are some

1728
01:06:04,870 --> 01:06:02,240
aggregates of fiber the red spots are

1729
01:06:07,990 --> 01:06:04,880
excited for frame so what you see uh

1730
01:06:11,510 --> 01:06:08,000
over time uh the quad survey emerge from

1731
01:06:14,069 --> 01:06:11,520
bunch of fibers and then they uh grow

1732
01:06:16,309 --> 01:06:14,079
and also some of them attach together

1733
01:06:18,069 --> 01:06:16,319
and make even bigger ones so with that

1734
01:06:20,950 --> 01:06:18,079
system actually we have positive

1735
01:06:22,630 --> 01:06:20,960
feedback based on only synthetic

1736
01:06:25,430 --> 01:06:22,640
chemistry

1737
01:06:27,910 --> 01:06:25,440
so the next one is to have some function

1738
01:06:28,630 --> 01:06:27,920

out of this system so in this system you

1739
01:06:30,069 --> 01:06:28,640
see

1740
01:06:31,349 --> 01:06:30,079
first we

1741
01:06:33,829 --> 01:06:31,359
can find

1742
01:06:35,029 --> 01:06:33,839
fibers with cofactor inside uh

1743
01:06:37,910 --> 01:06:35,039
cholesterol

1744
01:06:39,670 --> 01:06:37,920
and then we add food nutrition it's uh

1745
01:06:42,549 --> 01:06:39,680
the starting the building block of

1746
01:06:44,390 --> 01:06:42,559
cholesterol so we did it and we monitor

1747
01:06:47,109 --> 01:06:44,400
it over time as you see

1748
01:06:49,510 --> 01:06:47,119
in the left hand side without shining

1749
01:06:52,390 --> 01:06:49,520
light indeed we didn't excite buffering

1750
01:06:55,829 --> 01:06:52,400
so i call it dark so in the dark one you

1751
01:06:58,470 --> 01:06:55,839
see the monomer uh converted to tetramer

1752
01:07:00,710 --> 01:06:58,480
in around one day however in the right

1753
01:07:04,390 --> 01:07:00,720
hand side we shine it we excite full

1754
01:07:06,150 --> 01:07:04,400
frame as you see only in two or three

1755
01:07:07,910 --> 01:07:06,160
hours all of the monomer will be

1756
01:07:10,549 --> 01:07:07,920
converted to

1757
01:07:13,349 --> 01:07:10,559
test somewhere so it is shown in the

1758
01:07:15,430 --> 01:07:13,359
video as well as you can see in the same

1759
01:07:17,109 --> 01:07:15,440
time time scale

1760
01:07:19,829 --> 01:07:17,119
the one in the dark doesn't give that

1761
01:07:21,990 --> 01:07:19,839
much but the one in the light grow even

1762
01:07:24,230 --> 01:07:22,000
in the course of 10 minutes

1763
01:07:25,589 --> 01:07:24,240

so with that i would like to conclude

1764
01:07:27,349 --> 01:07:25,599
first of all we could make a

1765
01:07:29,670 --> 01:07:27,359
self-synthesizing class survey that they

1766
01:07:31,670 --> 01:07:29,680
form from the classified material and

1767
01:07:33,750 --> 01:07:31,680
custom materials from the building block

1768
01:07:35,670 --> 01:07:33,760
and also we showed that our

1769
01:07:36,789 --> 01:07:35,680
fibers are able to harness light in

1770
01:07:39,589 --> 01:07:36,799
order to

1771
01:07:41,349 --> 01:07:39,599
make their own compartment also they can

1772
01:07:44,390 --> 01:07:41,359
have positive feedback on growth of

1773
01:07:46,470 --> 01:07:44,400
their own compartment with that

1774
01:07:48,630 --> 01:07:46,480
i'm going to acknowledge some people

1775
01:07:51,029 --> 01:07:48,640
first of all steven motor my supervisor

1776
01:07:52,950 --> 01:07:51,039
and also my students uh jan and emino

1777
01:07:55,980 --> 01:07:52,960
and thank you for your attention i'm

1778
01:08:02,710 --> 01:07:55,990
happy to take any questions

1779
01:08:08,470 --> 01:08:04,230
thank you armin

1780
01:08:08,480 --> 01:08:13,750
we have one here

1781
01:08:17,590 --> 01:08:16,470
i i mean um really exciting interesting

1782
01:08:18,470 --> 01:08:17,600
talk

1783
01:08:20,470 --> 01:08:18,480
um

1784
01:08:22,390 --> 01:08:20,480
i was just trying to reconcile in my

1785
01:08:24,950 --> 01:08:22,400
head i mean the cartoons that you were

1786
01:08:26,950 --> 01:08:24,960
generally showing for the structure

1787
01:08:29,189 --> 01:08:26,960
of these entities had a very strong sort

1788
01:08:31,030 --> 01:08:29,199

of like fibril morphology

1789
01:08:32,229 --> 01:08:31,040
and then yet the images that you were

1790
01:08:34,149 --> 01:08:32,239
showing us have these kind of like

1791
01:08:35,269 --> 01:08:34,159
droplets and it's not

1792
01:08:37,110 --> 01:08:35,279
i mean generally at least in the

1793
01:08:38,870 --> 01:08:37,120
biophysics world we would normally think

1794
01:08:41,189 --> 01:08:38,880
of fibrils and droplets as you know

1795
01:08:43,669 --> 01:08:41,199
having distinct epitopes to associate

1796
01:08:46,309 --> 01:08:43,679
with them so i'm curious if you have any

1797
01:08:48,070 --> 01:08:46,319
hypothesis or model as to why

1798
01:08:49,749 --> 01:08:48,080
something that you think is forming kind

1799
01:08:52,309 --> 01:08:49,759
of like fibrils would form these

1800
01:08:54,630 --> 01:08:52,319
droplets

1801
01:08:57,110 --> 01:08:54,640
yeah that's very good question actually

1802
01:09:00,870 --> 01:08:57,120
uh because fiber as i mentioned from a

1803
01:09:03,669 --> 01:09:00,880
single oxygen so it's kind of

1804
01:09:04,950 --> 01:09:03,679
difficult to figure it out why

1805
01:09:07,990 --> 01:09:04,960
become

1806
01:09:09,829 --> 01:09:08,000
these fibers are not inside the password

1807
01:09:13,829 --> 01:09:09,839
at the beginning but what we have seen

1808
01:09:16,070 --> 01:09:13,839
is that over time by uh monitoring the

1809
01:09:17,430 --> 01:09:16,080
with another prop which is under

1810
01:09:19,910 --> 01:09:17,440
development

1811
01:09:21,749 --> 01:09:19,920
is the kind of fingerprint prop we can

1812
01:09:24,149 --> 01:09:21,759
say that fibers

1813
01:09:26,070 --> 01:09:24,159

later they can go inside but at the

1814
01:09:29,030 --> 01:09:26,080
beginning besides the fiber

1815
01:09:31,349 --> 01:09:29,040
are in micro meter range however the

1816
01:09:35,349 --> 01:09:31,359
droplets are very small so am i

1817
01:09:40,070 --> 01:09:37,430
yes

1818
01:09:44,309 --> 01:09:42,229
hi thank you for your talk becca guth

1819
01:09:46,789 --> 01:09:44,319
metzler from georgia tech

1820
01:09:48,870 --> 01:09:46,799
so if we take what we were seeing from

1821
01:09:51,749 --> 01:09:48,880
your videos and extend it these

1822
01:09:53,749 --> 01:09:51,759
coastervates would eventually merge and

1823
01:09:55,750 --> 01:09:53,759
form a single phase in which they're no

1824
01:09:59,110 --> 01:09:55,760
longer acting as compartments in the

1825
01:10:01,590 --> 01:09:59,120
same way so do you have any ideas of how

1826
01:10:04,630 --> 01:10:01,600
these coastervates could maybe split or

1827
01:10:07,510 --> 01:10:04,640
keep from merging into a single phase

1828
01:10:09,430 --> 01:10:07,520
actually another um yeah that's true it

1829
01:10:12,310 --> 01:10:09,440
takes around a couple of days and for

1830
01:10:15,669 --> 01:10:12,320
some of the life like the longer one or

1831
01:10:19,110 --> 01:10:15,679
k5b5 or even longer it takes around two

1832
01:10:20,870 --> 01:10:19,120
weeks to be uh one phase so around two

1833
01:10:23,990 --> 01:10:20,880
weeks they are stable so we have a still

1834
01:10:26,630 --> 01:10:24,000
two phases liquid liquid phase operation

1835
01:10:28,550 --> 01:10:26,640
and uh however four is fleeting this

1836
01:10:30,950 --> 01:10:28,560
passage is something that we are

1837
01:10:32,470 --> 01:10:30,960
hardly trying to figure it out and then

1838
01:10:34,709 --> 01:10:32,480

we're working on that so it's something

1839
01:10:35,669 --> 01:10:34,719
that is i think very uh

1840
01:10:38,229 --> 01:10:35,679
kind of

1841
01:10:40,630 --> 01:10:38,239
difficult to do because we we want to do

1842
01:10:43,270 --> 01:10:40,640
it with some chemical reaction not

1843
01:10:45,750 --> 01:10:43,280
mechanical agitation so for that you

1844
01:10:47,510 --> 01:10:45,760
haven't achieved yet but you're working

1845
01:10:48,550 --> 01:10:47,520
on

1846
01:10:50,550 --> 01:10:48,560
thank you

1847
01:10:51,910 --> 01:10:50,560
we have an online question

1848
01:10:53,430 --> 01:10:51,920
um it's from j

1849
01:10:55,750 --> 01:10:53,440
forsythe

1850
01:10:58,390 --> 01:10:55,760
um it says if the peptide sequence has

1851
01:11:01,189 --> 01:10:58,400
changed from blocks of k and e to random

1852
01:11:02,270 --> 01:11:01,199
or alternating ke sequences

1853
01:11:03,830 --> 01:11:02,280
is a

1854
01:11:06,470 --> 01:11:03,840
co-acer

1855
01:11:08,790 --> 01:11:06,480
formation reduced or loss

1856
01:11:11,990 --> 01:11:08,800
yeah we haven't tried that but i

1857
01:11:14,310 --> 01:11:12,000
i guess that with the uh we have

1858
01:11:17,430 --> 01:11:14,320
alternating positive and negative charge

1859
01:11:20,950 --> 01:11:17,440
because the the charge density on the

1860
01:11:23,030 --> 01:11:20,960
chain then is very very low i guess

1861
01:11:23,990 --> 01:11:23,040
we couldn't get class of it honestly and

1862
01:11:27,430 --> 01:11:24,000
even for

1863
01:11:29,270 --> 01:11:27,440

for a shorter one like k3

1864
01:11:31,750 --> 01:11:29,280
classified emerge only in very very

1865
01:11:34,229 --> 01:11:31,760
narrow range like just 12 from the molar

1866
01:11:38,229 --> 01:11:34,239
or a little bit different so i guess if

1867
01:11:40,550 --> 01:11:38,239
we uh have k e k e k something like this

1868
01:11:42,149 --> 01:11:40,560
uh we can't get it so however if you

1869
01:11:43,830 --> 01:11:42,159
haven't tried that and i think it will

1870
01:11:48,070 --> 01:11:43,840
be very interesting to see the behavior

1871
01:11:56,870 --> 01:11:50,149
okay thank you very much thank you again

1872
01:12:01,910 --> 01:12:00,149
and now we have veiter opu from the max

1873
01:12:03,189 --> 01:12:01,920
planck institute for mathematics in

1874
01:12:05,189 --> 01:12:03,199
sciences

1875
01:12:06,870 --> 01:12:05,199
and he's going to tell us about the

1876
01:12:09,030 --> 01:12:06,880
discovery of rna-based surface

1877
01:12:14,070 --> 01:12:09,040
self-reproducers from an experimental

1878
01:12:20,950 --> 01:12:17,990
thank you let me just share my screen

1879
01:12:22,870 --> 01:12:20,960
so okay so now we will be talking about

1880
01:12:25,189 --> 01:12:22,880
an ongoing project

1881
01:12:27,110 --> 01:12:25,199
where we try to design rna-based cycle

1882
01:12:28,709 --> 01:12:27,120
producers using a combination of

1883
01:12:31,830 --> 01:12:28,719
experiments and

1884
01:12:34,149 --> 01:12:31,840
computations basically

1885
01:12:36,390 --> 01:12:34,159
let me start by the context we are

1886
01:12:38,630 --> 01:12:36,400
talking about

1887
01:12:39,669 --> 01:12:38,640
supporting one scenario of the origin of

1888
01:12:42,229 --> 01:12:39,679

life

1889
01:12:44,470 --> 01:12:42,239
so not the whole story but some

1890
01:12:46,070 --> 01:12:44,480
specific windows where we already assume

1891
01:12:49,030 --> 01:12:46,080
that you already have some kind of

1892
01:12:51,270 --> 01:12:49,040
complex molecules such as nucleotides

1893
01:12:53,990 --> 01:12:51,280
and at some point in the history

1894
01:12:56,070 --> 01:12:54,000
um you reach a kind of complexity in

1895
01:12:57,510 --> 01:12:56,080
which you can

1896
01:12:59,750 --> 01:12:57,520
have the first

1897
01:13:02,149 --> 01:12:59,760
complex enough molecule that can

1898
01:13:04,870 --> 01:13:02,159
self-replicate so from itself produce

1899
01:13:07,430 --> 01:13:04,880
again other copies of itself so the

1900
01:13:10,149 --> 01:13:07,440
question we are trying to assess

1901
01:13:12,709 --> 01:13:10,159
is um how lucky are that kind of

1902
01:13:15,350 --> 01:13:12,719
molecules is that rare or is it possible

1903
01:13:19,270 --> 01:13:15,360
to have this kind of scenario

1904
01:13:21,910 --> 01:13:19,280
in the context of the theory work right

1905
01:13:25,510 --> 01:13:21,920
so to assess this question we try to

1906
01:13:28,790 --> 01:13:25,520
look in existing rna molecules so modern

1907
01:13:31,510 --> 01:13:28,800
rna natural ones and we know one example

1908
01:13:32,950 --> 01:13:31,520
of a self-reproducer that is based on

1909
01:13:35,270 --> 01:13:32,960
eric

1910
01:13:39,350 --> 01:13:35,280
so it's the group one entrant from the

1911
01:13:41,430 --> 01:13:39,360
other piece so this type family of rna

1912
01:13:43,750 --> 01:13:41,440
is known to be able to set flights from

1913
01:13:45,990 --> 01:13:43,760

the genome so you have the whole genome

1914
01:13:48,550 --> 01:13:46,000
and the sequences encoded in it and this

1915
01:13:50,790 --> 01:13:48,560
molecule is able to cut itself from the

1916
01:13:52,630 --> 01:13:50,800
genome and glue together the remaining

1917
01:13:54,790 --> 01:13:52,640
two strains

1918
01:13:56,950 --> 01:13:54,800
so from the

1919
01:13:58,070 --> 01:13:56,960
databases we have online we know only

1920
01:14:02,550 --> 01:13:58,080
about

1921
01:14:05,910 --> 01:14:02,560
3000 homologs of this family

1922
01:14:07,910 --> 01:14:05,920
i'm showing here below a tree of the sub

1923
01:14:08,950 --> 01:14:07,920
plus it's just to show that in the

1924
01:14:11,750 --> 01:14:08,960
family

1925
01:14:13,990 --> 01:14:11,760
you have a very diverse set of sequences

1926
01:14:15,750 --> 01:14:14,000
but also a very diverse set of

1927
01:14:17,669 --> 01:14:15,760
structures i'm talking about molecular

1928
01:14:19,510 --> 01:14:17,679
structures in this case

1929
01:14:21,750 --> 01:14:19,520
so

1930
01:14:24,070 --> 01:14:21,760
it performs self-application

1931
01:14:25,830 --> 01:14:24,080
in a specific manner so you start with

1932
01:14:27,350 --> 01:14:25,840
four different

1933
01:14:30,709 --> 01:14:27,360
fragments

1934
01:14:33,270 --> 01:14:30,719
first a non-covalent complex is formed

1935
01:14:35,110 --> 01:14:33,280
by self-assembly and this

1936
01:14:37,030 --> 01:14:35,120
non-covalent complex is able to

1937
01:14:38,709 --> 01:14:37,040
characterize the formation

1938
01:14:43,910 --> 01:14:38,719

of

1939
01:14:46,390 --> 01:14:43,920
violent gains between the fragments

1940
01:14:48,070 --> 01:14:46,400
so the question we are trying to assess

1941
01:14:50,709 --> 01:14:48,080
here is

1942
01:14:53,189 --> 01:14:50,719
whether those rnas are

1943
01:14:56,390 --> 01:14:53,199
very likely in the sql space and to

1944
01:14:59,910 --> 01:14:56,400
answer this question we look at all the

1945
01:15:02,310 --> 01:14:59,920
formulas in resounding sequences from

1946
01:15:05,990 --> 01:15:02,320
databases

1947
01:15:11,990 --> 01:15:08,830
we do an active exploration of the sql

1948
01:15:14,390 --> 01:15:12,000
space of groupon entries so we start by

1949
01:15:17,110 --> 01:15:14,400
building a generative model that will be

1950
01:15:18,070 --> 01:15:17,120
trained on natural sequences found

1951
01:15:20,149 --> 01:15:18,080
in

1952
01:15:21,270 --> 01:15:20,159
databases

1953
01:15:23,430 --> 01:15:21,280
and from

1954
01:15:26,070 --> 01:15:23,440
the model we have a sequence phase from

1955
01:15:28,709 --> 01:15:26,080
which we sample

1956
01:15:29,750 --> 01:15:28,719
possible values and in the end we test

1957
01:15:32,390 --> 01:15:29,760
them for

1958
01:15:34,550 --> 01:15:32,400
self-reproduction so in the end we take

1959
01:15:36,310 --> 01:15:34,560
the output of the experimental testing

1960
01:15:38,630 --> 01:15:36,320
of self-reproduction to correct the

1961
01:15:42,790 --> 01:15:38,640
model if necessary and will go forward

1962
01:15:45,030 --> 01:15:42,800
and explore all sequences what is that

1963
01:15:46,390 --> 01:15:45,040

at this point there are two main and

1964
01:15:47,430 --> 01:15:46,400
nodes

1965
01:15:49,189 --> 01:15:47,440
uh

1966
01:15:50,070 --> 01:15:49,199
what kind of generative model should we

1967
01:15:52,390 --> 01:15:50,080
use

1968
01:15:53,990 --> 01:15:52,400
to model such a complicated space as the

1969
01:15:57,030 --> 01:15:54,000
sequence space

1970
01:15:58,709 --> 01:15:57,040
and how can we uh

1971
01:16:01,030 --> 01:15:58,719
test for

1972
01:16:03,030 --> 01:16:01,040
that many sequences because in this case

1973
01:16:14,870 --> 01:16:03,040
if one wants to explore the sequence

1974
01:16:17,910 --> 01:16:15,750
the

1975
01:16:20,870 --> 01:16:17,920
experimental style developed first

1976
01:16:22,390 --> 01:16:20,880
starting a catholic asia that is divided

1977
01:16:23,430 --> 01:16:22,400
into steps

1978
01:16:25,110 --> 01:16:23,440
so

1979
01:16:27,590 --> 01:16:25,120
those two steps represent the two type

1980
01:16:29,350 --> 01:16:27,600
of catalytic activity group one engines

1981
01:16:31,189 --> 01:16:29,360
are able to perform

1982
01:16:33,030 --> 01:16:31,199
so you have as i said earlier the

1983
01:16:34,630 --> 01:16:33,040
cutting

1984
01:16:36,229 --> 01:16:34,640
reaction where

1985
01:16:38,630 --> 01:16:36,239
the

1986
01:16:40,390 --> 01:16:38,640
sequence is tested for

1987
01:16:43,430 --> 01:16:40,400
being able to cut

1988
01:16:46,229 --> 01:16:43,440

one part of itself so the splicing part

1989
01:16:49,910 --> 01:16:46,239
and the second phase is the testing

1990
01:16:51,910 --> 01:16:49,920
whether the rna is able to attach

1991
01:16:54,870 --> 01:16:51,920
a different fragment

1992
01:16:56,870 --> 01:16:54,880
so in the end of this essay you have

1993
01:16:57,990 --> 01:16:56,880
if the evidence is active when you're

1994
01:17:00,390 --> 01:16:58,000
testing

1995
01:17:02,630 --> 01:17:00,400
the area itself attached to a fragment

1996
01:17:04,070 --> 01:17:02,640
that you know the sequence

1997
01:17:06,070 --> 01:17:04,080
and then you can

1998
01:17:08,149 --> 01:17:06,080
use the output of the essay

1999
01:17:10,709 --> 01:17:08,159
send that to deep sequencing and then

2000
01:17:13,510 --> 01:17:10,719
have a bunch of reads on which we have

2001
01:17:16,470 --> 01:17:13,520
copies of you every name which

2002
01:17:18,630 --> 01:17:16,480
the if it's active some coffees of some

2003
01:17:20,470 --> 01:17:18,640
copies of them will have the substrate

2004
01:17:22,950 --> 01:17:20,480
attached to it so then in the end you

2005
01:17:25,669 --> 01:17:22,960
can complete the weight and estimate

2006
01:17:27,510 --> 01:17:25,679
kind of proxy of activity for this s

2007
01:17:30,550 --> 01:17:27,520
right

2008
01:17:33,510 --> 01:17:30,560
but still in the end of this you only

2009
01:17:34,709 --> 01:17:33,520
have a proxy for the self-reproduction

2010
01:17:37,830 --> 01:17:34,719
we know that

2011
01:17:40,390 --> 01:17:37,840
the modern cyber producers are able to

2012
01:17:42,390 --> 01:17:40,400
perform this but it's only a necessary

2013
01:17:48,070 --> 01:17:42,400

condition

2014
01:17:50,070 --> 01:17:48,080
to be the coupon engine but not um

2015
01:17:53,030 --> 01:17:50,080
surely to be a self-reproducer so in the

2016
01:17:55,110 --> 01:17:53,040
end we take a couple of them

2017
01:17:57,030 --> 01:17:55,120
in a long throughput manner in this

2018
01:17:59,590 --> 01:17:57,040
situation where we

2019
01:18:00,630 --> 01:17:59,600
cut them cut those sequences into two

2020
01:18:05,110 --> 01:18:00,640
parts

2021
01:18:10,630 --> 01:18:07,910
do them together in here so if they are

2022
01:18:12,790 --> 01:18:10,640
capable of reproducing themselves after

2023
01:18:15,750 --> 01:18:12,800
being cut we assume that they are able

2024
01:18:19,910 --> 01:18:17,430
so on the other side for the

2025
01:18:22,790 --> 01:18:19,920
computational part we started by

2026
01:18:24,790 --> 01:18:22,800
statistical exploration we use in this

2027
01:18:26,550 --> 01:18:24,800
case a model that is called black

2028
01:18:29,110 --> 01:18:26,560
protein analysis

2029
01:18:31,910 --> 01:18:29,120
the basic idea is that you take the

2030
01:18:35,110 --> 01:18:31,920
sequence of your target every name

2031
01:18:37,590 --> 01:18:35,120
you look for homologs in databases and

2032
01:18:40,790 --> 01:18:37,600
then you use low order statistics what i

2033
01:18:42,790 --> 01:18:40,800
mean here is frequencies of nucleotides

2034
01:18:45,750 --> 01:18:42,800
positions and the pair

2035
01:18:49,030 --> 01:18:45,760
of positions so using those kind of

2036
01:18:51,669 --> 01:18:49,040
frequencies one can parameterize a model

2037
01:18:53,990 --> 01:18:51,679
that will extract the statistical

2038
01:18:56,310 --> 01:18:54,000

signature of pairwise and single-side

2039
01:18:57,830 --> 01:18:56,320
frequencies and be able to

2040
01:18:59,270 --> 01:18:57,840
sample

2041
01:19:02,149 --> 01:18:59,280
new sequences

2042
01:19:04,630 --> 01:19:02,159
so with this we first tested our model

2043
01:19:06,550 --> 01:19:04,640
on a completely and untrained task which

2044
01:19:09,030 --> 01:19:06,560
is the contact prediction

2045
01:19:11,270 --> 01:19:09,040
and the model performed really well at

2046
01:19:13,430 --> 01:19:11,280
recovering contacts in the actual

2047
01:19:15,910 --> 01:19:13,440
structure of the

2048
01:19:18,630 --> 01:19:15,920
of the groupon engine targeted here

2049
01:19:21,189 --> 01:19:18,640
so we use that model to sample first a

2050
01:19:23,430 --> 01:19:21,199
small batch of white sequences that we

2051
01:19:25,110 --> 01:19:23,440
tested for the essay and one has been

2052
01:19:27,110 --> 01:19:25,120
found to be active for the

2053
01:19:29,669 --> 01:19:27,120
self-reproduction in this time

2054
01:19:32,149 --> 01:19:29,679
so we cut one of them into two pieces

2055
01:19:34,149 --> 01:19:32,159
and it was able to recover itself

2056
01:19:36,630 --> 01:19:34,159
and this variant was found at 44

2057
01:19:39,110 --> 01:19:36,640
mutation from absorption

2058
01:19:40,390 --> 01:19:39,120
however we saw one shortcoming

2059
01:19:43,110 --> 01:19:40,400
uh

2060
01:19:45,110 --> 01:19:43,120
for this approach which is if we look at

2061
01:19:47,669 --> 01:19:45,120
the sequence space like this and we have

2062
01:19:50,390 --> 01:19:47,679
our natural sequences here if the

2063
01:19:52,709 --> 01:19:50,400

underlying distribution is

2064
01:19:53,510 --> 01:19:52,719
following the natural one is fine but if

2065
01:19:56,709 --> 01:19:53,520
it's

2066
01:19:57,590 --> 01:19:56,719
only one subset of the natural of the

2067
01:19:59,590 --> 01:19:57,600
real

2068
01:20:00,630 --> 01:19:59,600
sephora producer then

2069
01:20:03,350 --> 01:20:00,640
you would have

2070
01:20:05,189 --> 01:20:03,360
kind of a limited exploration

2071
01:20:07,590 --> 01:20:05,199
so we thought maybe we can go for

2072
01:20:10,390 --> 01:20:07,600
something that is less vertical based on

2073
01:20:12,550 --> 01:20:10,400
the secondary structure of rnas so we

2074
01:20:15,910 --> 01:20:12,560
can compute second structure based on

2075
01:20:18,790 --> 01:20:15,920
sequences quite efficiently and use that

2076
01:20:21,430 --> 01:20:18,800
as we know this construction of existing

2077
01:20:24,149 --> 01:20:21,440
group one engine we can use that to

2078
01:20:26,070 --> 01:20:24,159
uh sample new sequences so we tested it

2079
01:20:28,629 --> 01:20:26,080
on deep conditional scan

2080
01:20:29,510 --> 01:20:28,639
data and we found correct trend in the

2081
01:20:33,270 --> 01:20:29,520
data

2082
01:20:35,590 --> 01:20:33,280
so we use this um this score to sample

2083
01:20:38,229 --> 01:20:35,600
new sequences using some genetic

2084
01:20:39,910 --> 01:20:38,239
algorithm and multicam exploration

2085
01:20:42,550 --> 01:20:39,920
however in the end

2086
01:20:46,149 --> 01:20:42,560
the few sequences we tested were not

2087
01:20:47,910 --> 01:20:46,159
active for the ac needed for the cipher

2088
01:20:50,470 --> 01:20:47,920

prediction test

2089
01:20:52,390 --> 01:20:50,480
so at this point uh we have a method

2090
01:20:54,149 --> 01:20:52,400
that is able to find active uh

2091
01:20:56,870 --> 01:20:54,159
environment but stay quite close to

2092
01:20:58,629 --> 01:20:56,880
giving observation and on the other side

2093
01:21:03,189 --> 01:20:58,639
we have the physics phase kind of

2094
01:21:06,470 --> 01:21:03,199
approach but uh is not very successful

2095
01:21:08,149 --> 01:21:06,480
at finding active sequences but then we

2096
01:21:09,189 --> 01:21:08,159
thought maybe we can combine both of

2097
01:21:10,149 --> 01:21:09,199
them

2098
01:21:13,189 --> 01:21:10,159
to

2099
01:21:15,510 --> 01:21:13,199
have both capabilities and then we

2100
01:21:17,510 --> 01:21:15,520
perform a high throughput screening in

2101
01:21:18,629 --> 01:21:17,520
which we test it for thousands of

2102
01:21:22,070 --> 01:21:18,639
parents

2103
01:21:24,470 --> 01:21:22,080
three main hypotheses whether uh first

2104
01:21:26,709 --> 01:21:24,480
whether the statistical model combined

2105
01:21:27,960 --> 01:21:26,719
with the structure is able to

2106
01:21:29,189 --> 01:21:27,970
enlarge the

2107
01:21:32,550 --> 01:21:29,199
[Music]

2108
01:21:34,629 --> 01:21:32,560
spectrum of possible designs

2109
01:21:37,750 --> 01:21:34,639
actively designed i mean the second

2110
01:21:40,830 --> 01:21:37,760
hypothesis is whether we need to model

2111
01:21:43,669 --> 01:21:40,840
interaction between position engineering

2112
01:21:46,629 --> 01:21:43,679
um so for this one we sampled sequences

2113
01:21:48,950 --> 01:21:46,639

according only on prof and third

2114
01:21:51,189 --> 01:21:48,960
we tested the hypothesis of the

2115
01:21:52,390 --> 01:21:51,199
secondary structure but now at the level

2116
01:21:56,149 --> 01:21:52,400
of thousand

2117
01:21:58,310 --> 01:21:56,159
values so you can see here the results

2118
01:22:01,830 --> 01:21:58,320
of this experiment where we have here

2119
01:22:03,830 --> 01:22:01,840
represented a bit more than 2 000

2120
01:22:05,830 --> 01:22:03,840
sequences that have been found at least

2121
01:22:07,669 --> 01:22:05,840
once attached to the substrate we were

2122
01:22:11,030 --> 01:22:07,679
looking for

2123
01:22:13,270 --> 01:22:11,040
so you can see here three main points

2124
01:22:15,669 --> 01:22:13,280
three main results first of all the more

2125
01:22:17,669 --> 01:22:15,679
you do mutation so you see here it's the

2126
01:22:19,990 --> 01:22:17,679
number of mutations from the reference

2127
01:22:23,110 --> 01:22:20,000
sequence right right in this case

2128
01:22:26,070 --> 01:22:23,120
and on the y-axis you have the activity

2129
01:22:28,070 --> 01:22:26,080
rate so the main

2130
01:22:31,350 --> 01:22:28,080
the first point here is that the more

2131
01:22:34,629 --> 01:22:31,360
you limitation the more you lose

2132
01:22:38,149 --> 01:22:34,639
activity and as it is in uh log scale

2133
01:22:40,550 --> 01:22:38,159
you use it exponentially quick quickly

2134
01:22:42,629 --> 01:22:40,560
the second point is that this problem is

2135
01:22:44,790 --> 01:22:42,639
actually quite difficult so we perform

2136
01:22:45,669 --> 01:22:44,800
some some random mutation and when you

2137
01:22:49,110 --> 01:22:45,679
do

2138
01:22:52,229 --> 01:22:49,120

only like 12 to 20 mutation completely

2139
01:22:55,270 --> 01:22:52,239
kill the activity

2140
01:22:57,990 --> 01:22:55,280
however if you combined this statistic

2141
01:23:00,629 --> 01:22:58,000
and structure we were able to explore

2142
01:23:04,950 --> 01:23:00,639
mutation space from plane mutation to

2143
01:23:07,430 --> 01:23:04,960
other obviously quite enhanced mutations

2144
01:23:09,990 --> 01:23:07,440
so in the end we took a few of them

2145
01:23:13,030 --> 01:23:10,000
tested them for the self prediction

2146
01:23:15,590 --> 01:23:13,040
and we found five active out of six

2147
01:23:18,149 --> 01:23:15,600
using this uh the pool of sequences we

2148
01:23:20,870 --> 01:23:18,159
have with the statistical structure

2149
01:23:22,950 --> 01:23:20,880
however we found on zero acting when we

2150
01:23:25,030 --> 01:23:22,960
considered the ones that were found for

2151
01:23:26,629 --> 01:23:25,040
the structure base so we're not

2152
01:23:28,390 --> 01:23:26,639
completely sure because it's still an

2153
01:23:29,270 --> 01:23:28,400
ongoing project but

2154
01:23:31,030 --> 01:23:29,280
uh

2155
01:23:33,590 --> 01:23:31,040
maybe for some of them there are some

2156
01:23:34,629 --> 01:23:33,600
kind of patterns that were that

2157
01:23:35,830 --> 01:23:34,639
enhance

2158
01:23:38,950 --> 01:23:35,840
cause

2159
01:23:42,550 --> 01:23:38,960
cross catalysis

2160
01:23:45,189 --> 01:23:42,560
uh here you can see a projection into

2161
01:23:47,270 --> 01:23:45,199
the first and second principal component

2162
01:23:51,189 --> 01:23:47,280
of these natural sequences and

2163
01:23:52,070 --> 01:23:51,199

projection of our designs here in color

2164
01:23:55,270 --> 01:23:52,080
and

2165
01:23:58,149 --> 01:23:55,280
the in the orange dots you can see the

2166
01:23:59,030 --> 01:23:58,159
sequences that were found with at least

2167
01:24:01,030 --> 01:23:59,040
one

2168
01:24:03,750 --> 01:24:01,040
suture so they were found at least

2169
01:24:05,669 --> 01:24:03,760
active so it's our pool of potentially

2170
01:24:09,430 --> 01:24:05,679
active variants which is

2171
01:24:11,590 --> 01:24:09,440
roughly more than 2 000 in these states

2172
01:24:12,870 --> 01:24:11,600
so to finish my presentation would like

2173
01:24:15,030 --> 01:24:12,880
to thank

2174
01:24:17,750 --> 01:24:15,040
uh collaborators so especially can you

2175
01:24:19,590 --> 01:24:17,760
know better did incredible work to for

2176
01:24:22,070 --> 01:24:19,600
the experience you could vlog yes here

2177
01:24:23,669 --> 01:24:22,080
we perform simulate all the

2178
01:24:25,750 --> 01:24:23,679
the experience site

2179
01:24:28,629 --> 01:24:25,760
and collaborative and computational

2180
01:24:30,550 --> 01:24:28,639
performance simulations and designs

2181
01:24:51,510 --> 01:24:30,560
thank you for your attention so i'm

2182
01:24:57,030 --> 01:24:54,709
online questions no

2183
01:24:59,189 --> 01:24:57,040
okay so we'll be able to discuss with

2184
01:25:01,110 --> 01:24:59,199
you later

2185
01:25:03,110 --> 01:25:01,120
i'll take the opportunity to

2186
01:25:06,470 --> 01:25:03,120
start the the next talk which is our

2187
01:25:09,270 --> 01:25:06,480
last talk is a short talk

2188
01:25:12,629 --> 01:25:10,470

sorry

2189
01:25:14,149 --> 01:25:12,639
the hub

2190
01:25:15,669 --> 01:25:14,159
and he's going to tell us about

2191
01:25:16,870 --> 01:25:15,679
combinatorial explosion versus

2192
01:25:18,790 --> 01:25:16,880
compression

2193
01:25:29,830 --> 01:25:18,800
what can we learn from multi-component

2194
01:25:29,840 --> 01:25:34,870
hello everyone take this off

2195
01:25:38,390 --> 01:25:36,870
hello everyone my name is vahab i'm a

2196
01:25:40,470 --> 01:25:38,400
graduate student here in the williams

2197
01:25:41,990 --> 01:25:40,480
lab at georgia tech and today i want to

2198
01:25:43,590 --> 01:25:42,000
talk to you about combinatorial

2199
01:25:45,750 --> 01:25:43,600
compression and explosion and what we're

2200
01:25:47,270 --> 01:25:45,760
doing in the laboratory to tip this

2201
01:25:50,229 --> 01:25:47,280
balance

2202
01:25:52,790 --> 01:25:50,239
so one obstacle in studying prebiotic

2203
01:25:54,790 --> 01:25:52,800
chemical reactions is this that they're

2204
01:25:56,950 --> 01:25:54,800
very heterogeneous and messy and as a

2205
01:25:58,950 --> 01:25:56,960
result we get this combinatorial

2206
01:26:00,790 --> 01:25:58,960
explosion where we get a lot of products

2207
01:26:03,110 --> 01:26:00,800
out and this has been uh

2208
01:26:04,709 --> 01:26:03,120
this was uh mentioned by some of the

2209
01:26:11,590 --> 01:26:04,719
earlier speakers in this session here

2210
01:26:16,070 --> 01:26:13,669
and what we're doing in the lab is using

2211
01:26:18,950 --> 01:26:16,080
a multi-component system we have nine

2212
01:26:20,550 --> 01:26:18,960
components shown here on the screen

2213
01:26:23,430 --> 01:26:20,560

eight of these are capable of

2214
01:26:25,350 --> 01:26:23,440
polymerization and through dehydration

2215
01:26:28,550 --> 01:26:25,360
so we call these building blocks and

2216
01:26:29,990 --> 01:26:28,560
what we do is dry out these samples for

2217
01:26:31,830 --> 01:26:30,000
72 hours

2218
01:26:33,910 --> 01:26:31,840
at a constant temperature of about 45

2219
01:26:36,709 --> 01:26:33,920
degrees celsius and at this mild

2220
01:26:38,950 --> 01:26:36,719
temperature under anoxic conditions

2221
01:26:41,189 --> 01:26:38,960
we're able to observe some novel trends

2222
01:26:42,310 --> 01:26:41,199
and particularly i want to focus on

2223
01:26:45,590 --> 01:26:42,320
combinatorial what we're calling

2224
01:26:50,870 --> 01:26:49,510
and so looking at some hplc data we can

2225
01:26:52,870 --> 01:26:50,880
see

2226
01:26:54,149 --> 01:26:52,880
we can separate by hydrophobicity and so

2227
01:26:56,629 --> 01:26:54,159
each of these peaks is going to

2228
01:26:57,590 --> 01:26:56,639
correspond to a specific chemical

2229
01:26:59,910 --> 01:26:57,600
product

2230
01:27:01,030 --> 01:26:59,920
and in the case of two building block

2231
01:27:03,430 --> 01:27:01,040
dry downs where we have just two

2232
01:27:07,350 --> 01:27:03,440
components here at the top in the blue

2233
01:27:08,390 --> 01:27:07,360
trace we get seven unique products out

2234
01:27:09,990 --> 01:27:08,400
and when we look at another two

2235
01:27:12,229 --> 01:27:10,000
component system or two building block

2236
01:27:15,510 --> 01:27:12,239
system uh then the red trace we have

2237
01:27:17,750 --> 01:27:15,520
eight distinct chemical species

2238
01:27:19,830 --> 01:27:17,760

now taking those two systems and

2239
01:27:21,669 --> 01:27:19,840
comparing them to a

2240
01:27:23,830 --> 01:27:21,679
that a building block system that i

2241
01:27:26,149 --> 01:27:23,840
showed you earlier in that system we

2242
01:27:28,310 --> 01:27:26,159
only see 11 and what's happening is

2243
01:27:29,669 --> 01:27:28,320
we're getting kind of a difference in

2244
01:27:31,510 --> 01:27:29,679
the way this

2245
01:27:32,870 --> 01:27:31,520
system is sampling the potential product

2246
01:27:35,270 --> 01:27:32,880
space

2247
01:27:36,070 --> 01:27:35,280
so we can visualize this using a fractal

2248
01:27:37,910 --> 01:27:36,080
tree

2249
01:27:39,430 --> 01:27:37,920
if we are looking at a two building

2250
01:27:41,110 --> 01:27:39,440
block system the

2251
01:27:42,310 --> 01:27:41,120
we're making a couple assumptions here

2252
01:27:44,149 --> 01:27:42,320
one of those is that we're not getting

2253
01:27:46,310 --> 01:27:44,159
anything longer than a trimer and that

2254
01:27:47,669 --> 01:27:46,320
we are only able to polymerize at two

2255
01:27:49,189 --> 01:27:47,679
sites on each

2256
01:27:50,470 --> 01:27:49,199
which is true for some but in some cases

2257
01:27:53,350 --> 01:27:50,480
our molecules can polymerize at more

2258
01:27:55,990 --> 01:27:53,360
locations some in just one

2259
01:27:57,350 --> 01:27:56,000
but there are 12 possibilities here

2260
01:27:59,990 --> 01:27:57,360
however when we

2261
01:28:01,510 --> 01:28:00,000
do this experimentally we are sampling

2262
01:28:03,910 --> 01:28:01,520
about two-thirds of the space we get

2263
01:28:05,270 --> 01:28:03,920

eight products out in um one of our

2264
01:28:07,110 --> 01:28:05,280
cases

2265
01:28:08,709 --> 01:28:07,120
seven in the other that i showed

2266
01:28:10,149 --> 01:28:08,719
when we compare this to the eight

2267
01:28:11,990 --> 01:28:10,159
building block system there's a much

2268
01:28:13,350 --> 01:28:12,000
larger theoretical combinatorial space

2269
01:28:15,030 --> 01:28:13,360
available

2270
01:28:16,709 --> 01:28:15,040
there's about 600 potential products

2271
01:28:19,669 --> 01:28:16,719
here again up to length trimer and

2272
01:28:22,149 --> 01:28:19,679
assuming just linkages at two locations

2273
01:28:23,590 --> 01:28:22,159
but in the experiments that we are doing

2274
01:28:25,510 --> 01:28:23,600
we only see

2275
01:28:26,950 --> 01:28:25,520
11 products and so we're sampling a much

2276
01:28:30,229 --> 01:28:26,960
smaller

2277
01:28:31,669 --> 01:28:30,239
proportion of this combinatorial space

2278
01:28:34,629 --> 01:28:31,679
and this is this is the effect that

2279
01:28:37,030 --> 01:28:34,639
we're calling combinatorial compression

2280
01:28:38,390 --> 01:28:37,040
and this is interesting for us because

2281
01:28:40,470 --> 01:28:38,400
it seems to indicate that certain

2282
01:28:41,669 --> 01:28:40,480
pathways are being selected for over

2283
01:28:42,629 --> 01:28:41,679
others

2284
01:28:44,229 --> 01:28:42,639
and

2285
01:28:46,629 --> 01:28:44,239
i'm going to wrap up by

2286
01:28:48,070 --> 01:28:46,639
saying that the takeaway i hope that you

2287
01:28:49,590 --> 01:28:48,080
are able to get from this is that adding

2288
01:28:51,030 --> 01:28:49,600

more components to your system isn't

2289
01:28:53,510 --> 01:28:51,040
necessarily going to cause a

2290
01:28:56,070 --> 01:28:53,520
combinatorial explosion and so maybe

2291
01:28:58,149 --> 01:28:56,080
don't be intimidated by it

2292
01:28:59,590 --> 01:28:58,159
that all being said we are doing other

2293
01:29:01,510 --> 01:28:59,600
work with this system and i would

2294
01:29:05,590 --> 01:29:01,520
encourage you to

2295
01:29:07,830 --> 01:29:05,600
attend kevita matanye's talk later today

2296
01:29:09,110 --> 01:29:07,840
and we also have a pre-print available

2297
01:29:10,229 --> 01:29:09,120
that just came out earlier this week if

2298
01:29:11,430 --> 01:29:10,239
you're interested in learning more about

2299
01:29:13,110 --> 01:29:11,440
some of the work we're doing with this

2300
01:29:14,709 --> 01:29:13,120
system

2301
01:29:16,149 --> 01:29:14,719
with that i'd like to acknowledge the

2302
01:29:18,149 --> 01:29:16,159
grants that supported this work from the

2303
01:29:19,510 --> 01:29:18,159
nsf and nasa as well as my advisor

2304
01:29:21,590 --> 01:29:19,520
lauren williams

2305
01:29:24,310 --> 01:29:21,600
miranda franco pinter and kavita matanya

2306
01:29:26,820 --> 01:29:24,320
as well as the entire williams lab and

2307
01:29:50,950 --> 01:29:26,830
that's all i have today thank you

2308
01:29:54,310 --> 01:29:53,189
from uh

2309
01:29:56,070 --> 01:29:54,320
very interesting result and i'm just

2310
01:29:57,510 --> 01:29:56,080
wondering um

2311
01:29:58,950 --> 01:29:57,520
you showed the eighth component the two

2312
01:30:00,790 --> 01:29:58,960
come on what if you have the a component

2313
01:30:02,709 --> 01:30:00,800

you start leaving out one of each one of

2314
01:30:04,629 --> 01:30:02,719
them how much does that affect the

2315
01:30:06,950 --> 01:30:04,639
landscape you see because it seems like

2316
01:30:08,310 --> 01:30:06,960
some of them might be dominating the

2317
01:30:09,669 --> 01:30:08,320
reaction pathways

2318
01:30:11,750 --> 01:30:09,679
i struggle to hear your question a

2319
01:30:14,149 --> 01:30:11,760
little bit but um you're asking if

2320
01:30:16,629 --> 01:30:14,159
certain uh molecules are dominating that

2321
01:30:21,189 --> 01:30:16,639
reaction space if you leave out one of

2322
01:30:25,350 --> 01:30:22,790
yeah so we're we're setting up these

2323
01:30:26,390 --> 01:30:25,360
binary dry downs of uh subsets of the

2324
01:30:27,990 --> 01:30:26,400
eight component system to figure out

2325
01:30:29,590 --> 01:30:28,000
which are the most reactive species we

2326
01:30:31,189 --> 01:30:29,600
are seeing that um some are more

2327
01:30:41,350 --> 01:30:31,199
reactive than others so yes that's

2328
01:30:46,709 --> 01:30:44,229
we'll talk um this may be somewhat

2329
01:30:49,350 --> 01:30:46,719
simple-minded question but

2330
01:30:50,470 --> 01:30:49,360
when you show the hplc with the peaks

2331
01:30:52,310 --> 01:30:50,480
and you say

2332
01:30:54,550 --> 01:30:52,320
these are like we have like 11 products

2333
01:30:56,229 --> 01:30:54,560
does that include the eight starting

2334
01:30:58,950 --> 01:30:56,239
materials so are there only only three

2335
01:31:01,270 --> 01:30:58,960
products or have you subtracted out the

2336
01:31:03,030 --> 01:31:01,280
the starting materials

2337
01:31:06,070 --> 01:31:03,040
uh so

2338
01:31:07,669 --> 01:31:06,080

the ones that were labeled are the

2339
01:31:09,990 --> 01:31:07,679
products so i don't think that they

2340
01:31:13,830 --> 01:31:10,000
include the starting materials they i

2341
01:31:15,430 --> 01:31:13,840
believe they elude out much earlier on

2342
01:31:16,709 --> 01:31:15,440
but i

2343
01:31:17,910 --> 01:31:16,719
don't know as much about the hplc that

2344
01:31:19,430 --> 01:31:17,920
was carried by somebody else so i i

2345
01:31:20,470 --> 01:31:19,440
could uh refer you to one of my

2346
01:31:26,229 --> 01:31:20,480
colleagues who might be able to better

2347
01:31:31,910 --> 01:31:29,750
hi uh lou chao from nasa goddard um

2348
01:31:32,790 --> 01:31:31,920
sorry if this is another hplc question

2349
01:31:34,870 --> 01:31:32,800
but

2350
01:31:37,350 --> 01:31:34,880
what solvent did you use and do you

2351
01:31:40,550 --> 01:31:37,360
expect that there are potentially other

2352
01:31:42,149 --> 01:31:40,560
targets that may be

2353
01:31:43,830 --> 01:31:42,159
not soluble in the solvent that you use

2354
01:31:46,870 --> 01:31:43,840
for the hplc

2355
01:31:48,229 --> 01:31:46,880
yeah so um yeah again i'm not i wasn't

2356
01:31:49,189 --> 01:31:48,239
the one working with hplc and i'm not as

2357
01:31:51,590 --> 01:31:49,199
familiar with it but i believe we're

2358
01:31:52,470 --> 01:31:51,600
using an acetonitrile water solvent

2359
01:31:54,550 --> 01:31:52,480
system

2360
01:31:56,310 --> 01:31:54,560
um and as far as whether there are

2361
01:31:57,590 --> 01:31:56,320
things that we're not seeing uh yes i

2362
01:31:58,950 --> 01:31:57,600
think that's possible and we're going to

2363
01:32:01,350 --> 01:31:58,960

be explaining other methods to see if we

2364
01:32:04,390 --> 01:32:01,360
see other products there

2365
01:32:14,390 --> 01:32:06,709
okay so let's thank all our speakers