



**217: THINKING BEYOND LUCA: STEM LIFE  
AND PRIMORDIAL DIVERSITY I**

1  
00:00:04,470 --> 00:00:03,669  
hi everyone

2  
00:00:06,470 --> 00:00:04,480  
uh

3  
00:00:08,710 --> 00:00:06,480  
thanks for coming to our session today

4  
00:00:10,790 --> 00:00:08,720  
thinking beyond luca stem life and

5  
00:00:14,150 --> 00:00:10,800  
primordial diversity

6  
00:00:17,029 --> 00:00:14,160  
uh so we are going to begin our session

7  
00:00:19,269 --> 00:00:17,039  
uh today with a remote lecture

8  
00:00:21,269 --> 00:00:19,279  
uh by antonio loscano

9  
00:00:24,710 --> 00:00:21,279  
the last universal common ancestor

10  
00:00:27,910 --> 00:00:26,550  
thanks antonio

11  
00:00:29,509 --> 00:00:27,920  
my pleasure

12  
00:00:31,509 --> 00:00:29,519  
i think you can hear me without any

13  
00:00:33,350 --> 00:00:31,519

problem right

14

00:00:35,190 --> 00:00:33,360

yes we can hear you loud and clear

15

00:00:37,190 --> 00:00:35,200

lovely thank you so much well first of

16

00:00:40,150 --> 00:00:37,200

all i want to thank the organizers of

17

00:00:43,110 --> 00:00:40,160

this session anton greg aaron for

18

00:00:45,750 --> 00:00:43,120

inviting me and i have to apologize for

19

00:00:47,350 --> 00:00:45,760

being unable to be there i had a small

20

00:00:48,950 --> 00:00:47,360

health issue so

21

00:00:51,510 --> 00:00:48,960

i wasn't able to

22

00:00:54,069 --> 00:00:51,520

to travel to to atlanta which is a place

23

00:00:55,510 --> 00:00:54,079

i feel very much at home and let me

24

00:00:57,670 --> 00:00:55,520

start by

25

00:01:00,470 --> 00:00:57,680

recalling what i think was an is an

26

00:01:03,830 --> 00:01:00,480

extraordinary example of scientific

27

00:01:06,469 --> 00:01:03,840

insight in 1969 when he

28

00:01:11,350 --> 00:01:06,479

got the position of associate professor

29

00:01:14,630 --> 00:01:11,360

of microbiology in illinois um

30

00:01:18,230 --> 00:01:14,640

carlos sent a letter to francis creek

31

00:01:21,590 --> 00:01:18,240

expressing his idea of using a different

32

00:01:24,070 --> 00:01:21,600

molecular markers in order to study the

33

00:01:26,789 --> 00:01:24,080

very early stages of a

34

00:01:29,590 --> 00:01:26,799

biological evolution of cell evolution

35

00:01:31,990 --> 00:01:29,600

and if you go uh down the first page of

36

00:01:34,390 --> 00:01:32,000

his lecture he says something that is

37

00:01:37,350 --> 00:01:34,400

extraordinary in his in terms of his

38

00:01:40,310 --> 00:01:37,360

understanding of the basic biological

39

00:01:42,950 --> 00:01:40,320

processes of contemporary cells and he

40

00:01:45,190 --> 00:01:42,960

says well if i want to

41

00:01:47,429 --> 00:01:45,200

study from a molecular perspective

42

00:01:49,670 --> 00:01:47,439

molecules the obvious choice of molecule

43

00:01:51,910 --> 00:01:49,680

here lies in the components of the

44

00:01:54,310 --> 00:01:51,920

translational apparatus and he was very

45

00:01:55,830 --> 00:01:54,320

right and then afterwards after a few

46

00:01:58,230 --> 00:01:55,840

years with the extraordinary

47

00:02:00,630 --> 00:01:58,240

collaboration of

48

00:02:03,109 --> 00:02:00,640

george fox and mitch sorghing and others

49

00:02:05,910 --> 00:02:03,119

they came out in a classical paper

50

00:02:08,469 --> 00:02:05,920

published in 1977 in the journal of

51  
00:02:12,229 --> 00:02:08,479  
molecular evolution they came up with

52  
00:02:14,229 --> 00:02:12,239  
the idea that in fact in terms of a very

53  
00:02:17,270 --> 00:02:14,239  
early divergence

54  
00:02:20,309 --> 00:02:17,280  
cells could be classified or could be

55  
00:02:24,070 --> 00:02:20,319  
located into one or three major groups

56  
00:02:26,869 --> 00:02:24,080  
the archaea that until then not first

57  
00:02:28,470 --> 00:02:26,879  
recognizes a monophyletic group the

58  
00:02:29,830 --> 00:02:28,480  
bacteria which

59  
00:02:32,630 --> 00:02:29,840  
includes all the

60  
00:02:35,589 --> 00:02:32,640  
prokaryotes we are familiar with and the

61  
00:02:38,150 --> 00:02:35,599  
nuclear cytoplasm of the eukaryotes and

62  
00:02:40,309 --> 00:02:38,160  
because of the differences in

63  
00:02:42,390 --> 00:02:40,319

translation and replication between

64

00:02:44,470 --> 00:02:42,400

these different groups they came to the

65

00:02:46,309 --> 00:02:44,480

conclusion that these three lines were

66

00:02:48,470 --> 00:02:46,319

derived from what they called the

67

00:02:51,190 --> 00:02:48,480

progeny and they gave a very precise

68

00:02:54,550 --> 00:02:51,200

definition of the progeny it was defined

69

00:02:57,430 --> 00:02:54,560

originally as a hypothetical biological

70

00:02:59,670 --> 00:02:57,440

entity ancestral to the tracial lineages

71

00:03:01,350 --> 00:02:59,680

and that with they say are the

72

00:03:04,149 --> 00:03:01,360

rudimentary

73

00:03:06,710 --> 00:03:04,159

imprecise linkage between the genotype

74

00:03:08,390 --> 00:03:06,720

and phenotype it is it was a system in

75

00:03:10,630 --> 00:03:08,400

which the separation between genotype

76

00:03:12,550 --> 00:03:10,640

and phenotype was not complete

77

00:03:14,790 --> 00:03:12,560

at the time i was traveling quite

78

00:03:16,869 --> 00:03:14,800

frequently to houston to collaborate

79

00:03:19,509 --> 00:03:16,879

with john o'rourke in some issues

80

00:03:23,350 --> 00:03:19,519

related to prebiotic chemistry i had the

81

00:03:26,309 --> 00:03:23,360

chance to meet and prepare and befriend

82

00:03:29,350 --> 00:03:26,319

george fox and we actually published uh

83

00:03:30,949 --> 00:03:29,360

in a book in 1992 what we thought was

84

00:03:33,350 --> 00:03:30,959

the first

85

00:03:35,190 --> 00:03:33,360

and most complete with the information

86

00:03:37,910 --> 00:03:35,200

available of the

87

00:03:40,550 --> 00:03:37,920

genomic traits of the genetic traits of

88

00:03:43,030 --> 00:03:40,560

the progeny we actually made a very very

89

00:03:45,190 --> 00:03:43,040  
detailed analysis of the available

90

00:03:47,270 --> 00:03:45,200  
character and we came to the conclusion

91

00:03:49,270 --> 00:03:47,280  
that in fact the

92

00:03:51,509 --> 00:03:49,280  
homology between the different

93

00:03:53,910 --> 00:03:51,519  
components of the rna polymerase of the

94

00:03:56,949 --> 00:03:53,920  
three groups of the elongation factors

95

00:03:59,670 --> 00:03:56,959  
of the ribosomal rna and so on indicated

96

00:04:02,869 --> 00:03:59,680  
that translation was of a modern type we

97

00:04:04,390 --> 00:04:02,879  
found evidence in the three groups of uh

98

00:04:06,710 --> 00:04:04,400  
because of the reports that had been

99

00:04:08,789 --> 00:04:06,720  
published of dna topoisomers two of

100

00:04:10,710 --> 00:04:08,799  
current node biosynthesis and this led

101  
00:04:13,030 --> 00:04:10,720  
us to conclude that it was already

102  
00:04:16,469 --> 00:04:13,040  
endowed with a dna genome there was

103  
00:04:19,349 --> 00:04:16,479  
clearly an epsilon distributed atpase

104  
00:04:20,469 --> 00:04:19,359  
found in the three lines and a number of

105  
00:04:24,150 --> 00:04:20,479  
um

106  
00:04:27,030 --> 00:04:24,160  
of enzymes associated with very basic

107  
00:04:29,830 --> 00:04:27,040  
metabolic processes so our conclusion

108  
00:04:32,070 --> 00:04:29,840  
was that in fact the project note was

109  
00:04:34,070 --> 00:04:32,080  
not sash it was already

110  
00:04:37,590 --> 00:04:34,080  
sell very much like the ones that we see

111  
00:04:40,629 --> 00:04:37,600  
today now with the explosion of a

112  
00:04:44,550 --> 00:04:40,639  
genomic instrument with the

113  
00:04:46,710 --> 00:04:44,560

capability of sequencing very rapidly uh

114

00:04:49,510 --> 00:04:46,720

genes and genomes and with the

115

00:04:52,710 --> 00:04:49,520

availability of more rapid

116

00:04:55,670 --> 00:04:52,720

computers uh in fact the

117

00:04:57,830 --> 00:04:55,680

attempts to define the so-called project

118

00:05:00,390 --> 00:04:57,840

or the ancestor of the treatment cell

119

00:05:02,550 --> 00:05:00,400

domains multiplied and exploded in an

120

00:05:04,710 --> 00:05:02,560

extraordinary way and you can see in

121

00:05:06,870 --> 00:05:04,720

this list how the

122

00:05:09,350 --> 00:05:06,880

ideas the descriptions of the nature of

123

00:05:11,670 --> 00:05:09,360

the protein are diverse and rose and fox

124

00:05:13,830 --> 00:05:11,680

had proposed that it was a entity in

125

00:05:15,430 --> 00:05:13,840

which phenotype and genotype had not yet

126

00:05:17,350 --> 00:05:15,440

occurred uh

127

00:05:19,670 --> 00:05:17,360

myself together with george fox and

128

00:05:22,150 --> 00:05:19,680

general proposed that it was a bacteria

129

00:05:24,790 --> 00:05:22,160

like cellular entity mushakian and

130

00:05:27,830 --> 00:05:24,800

kerning proposed that it was a

131

00:05:29,830 --> 00:05:27,840

cell and dog with an rna genome an idea

132

00:05:32,070 --> 00:05:29,840

that has impact in fact has been

133

00:05:34,469 --> 00:05:32,080

repeated by others like patrick for tear

134

00:05:36,150 --> 00:05:34,479

and so on but what is very surprising is

135

00:05:38,469 --> 00:05:36,160

the strong differences in our

136

00:05:40,870 --> 00:05:38,479

descriptions of the progeny some say

137

00:05:43,749 --> 00:05:40,880

that it was it had like membranes some

138

00:05:46,230 --> 00:05:43,759

say that it was a network of inorganic

139

00:05:48,870 --> 00:05:46,240

compartments harboring and leaks of

140

00:05:52,070 --> 00:05:48,880

virus like genetic elements some say

141

00:05:54,310 --> 00:05:52,080

that like patrick forte that it was uh

142

00:05:56,309 --> 00:05:54,320

say i was formed by rna cells that

143

00:05:59,029 --> 00:05:56,319

acquired dna genomes through

144

00:06:01,270 --> 00:05:59,039

polyphylactic viral infections and so on

145

00:06:03,430 --> 00:06:01,280

well when one looks at the methodologies

146

00:06:05,670 --> 00:06:03,440

behind these descriptions the first

147

00:06:08,390 --> 00:06:05,680

thing that is surprising is to realize

148

00:06:11,749 --> 00:06:08,400

that uh there is a confusion between

149

00:06:14,469 --> 00:06:11,759

cellular sen ancestors and organismal

150

00:06:17,189 --> 00:06:14,479

sentences which are not quite the same

151  
00:06:18,629 --> 00:06:17,199  
every contemporary biomolecule has its

152  
00:06:20,629 --> 00:06:18,639  
own history

153  
00:06:22,550 --> 00:06:20,639  
that traces back to an individual

154  
00:06:26,230 --> 00:06:22,560  
moleculars and ancestor and this

155  
00:06:29,430 --> 00:06:26,240  
confusion of course leads to as very uh

156  
00:06:31,990 --> 00:06:29,440  
complicated antagonistic definitions of

157  
00:06:34,790 --> 00:06:32,000  
what the progenitor means or what the

158  
00:06:37,110 --> 00:06:34,800  
less common ancestor means and

159  
00:06:39,430 --> 00:06:37,120  
clearly something that has to be kept in

160  
00:06:41,830 --> 00:06:39,440  
mind is the reconstruction of the thin

161  
00:06:44,150 --> 00:06:41,840  
complement of this look our less common

162  
00:06:46,390 --> 00:06:44,160  
ancestor must include traits that

163  
00:06:48,469 --> 00:06:46,400

originated in different evolutionary

164

00:06:52,710 --> 00:06:48,479

stages in different cells

165

00:06:54,870 --> 00:06:52,720

now clearly the biases that we have when

166

00:06:56,950 --> 00:06:54,880

trying to describe the nature of the

167

00:06:59,189 --> 00:06:56,960

less common ancestor have to do with

168

00:07:00,950 --> 00:06:59,199

unjustified theoretical assumptions for

169

00:07:03,749 --> 00:07:00,960

instance the idea that you can

170

00:07:06,150 --> 00:07:03,759

extrapolate molecular phylogenys back

171

00:07:08,070 --> 00:07:06,160

into the waters of the primitive soup

172

00:07:11,830 --> 00:07:08,080

the confusion between ancient and

173

00:07:13,510 --> 00:07:11,840

primitive people that deny the with some

174

00:07:15,110 --> 00:07:13,520

people say with very good reasons i

175

00:07:17,830 --> 00:07:15,120

don't think this is the case the

176

00:07:20,550 --> 00:07:17,840

existence of an rna protein world

177

00:07:22,550 --> 00:07:20,560

with very unrealistic definitions of

178

00:07:24,950 --> 00:07:22,560

primitive environments that include some

179

00:07:27,430 --> 00:07:24,960

misunderstandings of prebiotic chemistry

180

00:07:29,749 --> 00:07:27,440

and then we have methodological issues

181

00:07:32,870 --> 00:07:29,759

like the definitions of sequence ability

182

00:07:35,830 --> 00:07:32,880

biased sample size primary structure

183

00:07:38,150 --> 00:07:35,840

based searches undetected gene gain and

184

00:07:40,150 --> 00:07:38,160

loss including of words and recognized

185

00:07:41,830 --> 00:07:40,160

lateral gene transfer

186

00:07:43,909 --> 00:07:41,840

but perhaps the most important thing

187

00:07:45,990 --> 00:07:43,919

that we have to keep in mind is that

188

00:07:49,029 --> 00:07:46,000

nowadays the natural the less common

189

00:07:52,230 --> 00:07:49,039

ancestor should be defined as the nature

190

00:07:54,710 --> 00:07:52,240

of the ancestor the less common ancestor

191

00:07:57,510 --> 00:07:54,720

of prokaryotes of bacteria on the one

192

00:08:00,629 --> 00:07:57,520

hand and the archaea with the nuclear

193

00:08:01,430 --> 00:08:00,639

cytoplasm as a sister group of bacteria

194

00:08:03,510 --> 00:08:01,440

and

195

00:08:04,950 --> 00:08:03,520

we have been trying to in my group in

196

00:08:08,070 --> 00:08:04,960

mexico we have been trying to

197

00:08:10,950 --> 00:08:08,080

characterize the traits of this and less

198

00:08:13,430 --> 00:08:10,960

common ancestor and so far what we have

199

00:08:16,550 --> 00:08:13,440

is that there is a significant numbers

200

00:08:18,869 --> 00:08:16,560

of rna-related protein architectures of

201

00:08:20,710 --> 00:08:18,879

course the obvious are proteins

202

00:08:23,029 --> 00:08:20,720

associated with

203

00:08:24,869 --> 00:08:23,039

the ribosome and so on but also many

204

00:08:28,469 --> 00:08:24,879

many proteins associated with the

205

00:08:30,469 --> 00:08:28,479

metabolism of rna there are apparent it

206

00:08:33,750 --> 00:08:30,479

was a modern type of transcription and

207

00:08:35,670 --> 00:08:33,760

translation a dna genome encoding a wide

208

00:08:38,070 --> 00:08:35,680

array of repair and recombination

209

00:08:39,990 --> 00:08:38,080

mechanisms reverse gi rays which in the

210

00:08:43,029 --> 00:08:40,000

opinion of some colleagues implies a

211

00:08:44,790 --> 00:08:43,039

thermophilic lifestyle lipid membranes

212

00:08:45,750 --> 00:08:44,800

although the actual nature of those

213

00:08:49,030 --> 00:08:45,760

membranes

214

00:08:51,110 --> 00:08:49,040

remains an open problem for chemic

215

00:08:54,790 --> 00:08:51,120

chemiosmotic coupling

216

00:08:58,070 --> 00:08:54,800

a number of um

217

00:09:00,070 --> 00:08:58,080

enzymes that indicate metabolic pathways

218

00:09:02,389 --> 00:09:00,080

and so on but

219

00:09:05,030 --> 00:09:02,399

what is fascinating is to realize that

220

00:09:07,269 --> 00:09:05,040

when you look at the enzymes of some

221

00:09:10,070 --> 00:09:07,279

metabolic pathways

222

00:09:12,550 --> 00:09:10,080

you actually see that we fail to

223

00:09:15,990 --> 00:09:12,560

recognize and this is a very common

224

00:09:18,070 --> 00:09:16,000

problem we fail to recognize in when you

225

00:09:21,269 --> 00:09:18,080

are comparing sequences many

226

00:09:23,350 --> 00:09:21,279

biosynthetic enzymes and some police

227

00:09:26,310 --> 00:09:23,360

have attempted to explain this absence

228

00:09:29,110 --> 00:09:26,320

by assuming that the metabolic pathway

229

00:09:32,030 --> 00:09:29,120

intermediates were provided by a biotic

230

00:09:34,949 --> 00:09:32,040

or geochemical processes by

231

00:09:36,949 --> 00:09:34,959

biosynthesis a prebiotic synthesis that

232

00:09:38,630 --> 00:09:36,959

took place in the in the primitive

233

00:09:40,710 --> 00:09:38,640

oceans that

234

00:09:43,269 --> 00:09:40,720

or perhaps that early metabolic roots

235

00:09:45,990 --> 00:09:43,279

depended on a spontaneous reaction that

236

00:09:48,310 --> 00:09:46,000

we know cannot cure in some cases or

237

00:09:50,430 --> 00:09:48,320

that different organisms were encoding

238

00:09:53,190 --> 00:09:50,440

different catalysts that were shared by

239

00:09:54,949 --> 00:09:53,200

multi-directional that protein transfer

240

00:09:57,190 --> 00:09:54,959

well the problem with some of these

241

00:09:59,750 --> 00:09:57,200

hypotheses is that if you look at the

242

00:10:02,790 --> 00:09:59,760

biosynthesis let us say of nucleotides

243

00:10:05,430 --> 00:10:02,800

what you find is a number of molecules

244

00:10:07,430 --> 00:10:05,440

are extremely unstable and it's very

245

00:10:09,750 --> 00:10:07,440

difficult to account for their presence

246

00:10:11,590 --> 00:10:09,760

in the primitive oceans of the earth or

247

00:10:13,030 --> 00:10:11,600

the primitive soup or the primitive

248

00:10:16,150 --> 00:10:13,040

environment whatever you want to

249

00:10:19,150 --> 00:10:16,160

describe it and i think that one can say

250

00:10:21,670 --> 00:10:19,160

that yes very likely there were some uh

251  
00:10:23,990 --> 00:10:21,680  
semi-enzymatic rules that existed during

252  
00:10:28,389 --> 00:10:24,000  
the early stages of cell evolution this

253  
00:10:30,470 --> 00:10:28,399  
is an argument that stanley miller and i

254  
00:10:32,949 --> 00:10:30,480  
insisted on but

255  
00:10:35,269 --> 00:10:32,959  
more in addition one has to say that we

256  
00:10:38,230 --> 00:10:35,279  
don't have any good prebiotic synthesis

257  
00:10:40,310 --> 00:10:38,240  
of most metabolic intermediates most of

258  
00:10:42,949 --> 00:10:40,320  
them are actually quite unstable

259  
00:10:45,110 --> 00:10:42,959  
chemically and have very very small have

260  
00:10:47,430 --> 00:10:45,120  
life and the bottleneck effects will

261  
00:10:50,069 --> 00:10:47,440  
hinder the efficiency of these semi

262  
00:10:52,630 --> 00:10:50,079  
enzymatic biosynthetic roots so the

263  
00:10:55,590 --> 00:10:52,640

conclusion is that most likely we don't

264

00:10:58,710 --> 00:10:55,600

have to appeal to these mechanisms they

265

00:11:01,590 --> 00:10:58,720

are very very unrealistic biochemically

266

00:11:02,630 --> 00:11:01,600

chemically geochemically and most likely

267

00:11:05,590 --> 00:11:02,640

we have been

268

00:11:07,670 --> 00:11:05,600

failing so far to identify the missing

269

00:11:10,710 --> 00:11:07,680

enzymes now

270

00:11:13,750 --> 00:11:10,720

if we go to the issue of the nature of

271

00:11:16,550 --> 00:11:13,760

the genome of the less common ancestor

272

00:11:18,790 --> 00:11:16,560

all the evidences that we have collected

273

00:11:21,110 --> 00:11:18,800

suggests that there was a dna genome

274

00:11:23,590 --> 00:11:21,120

that was including a wide array of

275

00:11:26,550 --> 00:11:23,600

repair and recombination mechanisms and

276

00:11:28,630 --> 00:11:26,560

let me just summarize this and at the

277

00:11:31,829 --> 00:11:28,640

least the inventory that we have been

278

00:11:34,310 --> 00:11:31,839

able to complete we have evidence of dna

279

00:11:36,870 --> 00:11:34,320

repair by reversal of damage we found

280

00:11:40,790 --> 00:11:36,880

very good evidence for the conservation

281

00:11:43,110 --> 00:11:40,800

of photolysis for uh photoproliasis

282

00:11:46,230 --> 00:11:43,120

we found very very good evidence of

283

00:11:47,750 --> 00:11:46,240

oxygen repair like uracil dna because he

284

00:11:50,389 --> 00:11:47,760

lays

285

00:11:52,710 --> 00:11:50,399

a number of glycosylases excision repair

286

00:11:54,949 --> 00:11:52,720

and so on and we found evidence of

287

00:11:57,110 --> 00:11:54,959

endonucleases associated with uv damage

288

00:11:58,069 --> 00:11:57,120

repair now of course this

289

00:12:01,190 --> 00:11:58,079

is a

290

00:12:03,910 --> 00:12:01,200

not considering the issue of the

291

00:12:06,150 --> 00:12:03,920

possibility of electrical gene transfer

292

00:12:08,389 --> 00:12:06,160

but the question is what was the nature

293

00:12:10,470 --> 00:12:08,399

of the left common ancestor uh we

294

00:12:13,509 --> 00:12:10,480

sincerely believe that the conservation

295

00:12:16,389 --> 00:12:13,519

of so many sequences related to dna

296

00:12:18,470 --> 00:12:16,399

metabolisms and the sequence similarity

297

00:12:20,710 --> 00:12:18,480

served by many ancient proteins suggest

298

00:12:22,790 --> 00:12:20,720

that there was considerable fidelity

299

00:12:25,509 --> 00:12:22,800

already in the genetic system of the

300

00:12:27,750 --> 00:12:25,519

less common ancestor but this similarity

301  
00:12:30,710 --> 00:12:27,760  
is rarely seen we know that very clearly

302  
00:12:33,030 --> 00:12:30,720  
from rna genomes such as viral genomes

303  
00:12:34,470 --> 00:12:33,040  
is rarely conserved

304  
00:12:37,590 --> 00:12:34,480  
in the case of

305  
00:12:39,269 --> 00:12:37,600  
sequences encoded by rna and well the

306  
00:12:41,590 --> 00:12:39,279  
question has been

307  
00:12:44,470 --> 00:12:41,600  
being raised back and forth a number of

308  
00:12:47,590 --> 00:12:44,480  
times and in a very interesting paper uh

309  
00:12:49,430 --> 00:12:47,600  
published uh some 15 years ago pool and

310  
00:12:51,910 --> 00:12:49,440  
logan raised the possibility that the

311  
00:12:54,150 --> 00:12:51,920  
less human ancestor was impacted out

312  
00:12:55,430 --> 00:12:54,160  
with an rna genome

313  
00:12:59,030 --> 00:12:55,440

since there was for instance

314

00:13:00,310 --> 00:12:59,040

experimental data demonstrating

315

00:13:03,269 --> 00:13:00,320

that

316

00:13:04,069 --> 00:13:03,279

viral rna genomes can undergo repair by

317

00:13:09,990 --> 00:13:04,079

the

318

00:13:12,069 --> 00:13:10,000

an uh leicester meniscus where an rna

319

00:13:15,110 --> 00:13:12,079

genome is consistent with

320

00:13:17,030 --> 00:13:15,120

uh uh roses proposals that claim that

321

00:13:19,509 --> 00:13:17,040

the less common ancestor was in fact a

322

00:13:22,310 --> 00:13:19,519

highly diverse population of metabolic

323

00:13:25,910 --> 00:13:22,320

complementary cellular progenys with our

324

00:13:28,550 --> 00:13:25,920

small linear rna genomes so is the first

325

00:13:31,590 --> 00:13:28,560

possibility this one suggested uh

326

00:13:34,069 --> 00:13:31,600

mentioned by boolean logan correct well

327

00:13:36,629 --> 00:13:34,079

we do know that in fact dna can be

328

00:13:40,069 --> 00:13:36,639

damaged by alkylation and the bases can

329

00:13:43,430 --> 00:13:40,079

undergo methylation these are very well

330

00:13:45,910 --> 00:13:43,440

described very well understood and we

331

00:13:47,829 --> 00:13:45,920

know of several mechanisms that are

332

00:13:50,310 --> 00:13:47,839

present in

333

00:13:52,710 --> 00:13:50,320

dna

334

00:13:55,509 --> 00:13:52,720

repair of methylation which include the

335

00:13:57,990 --> 00:13:55,519

cutting off the nucleotide

336

00:14:00,069 --> 00:13:58,000

that has been methylated just cutting

337

00:14:03,030 --> 00:14:00,079

off the base that has been methylated

338

00:14:05,430 --> 00:14:03,040

all we know the direct repair mechanisms

339

00:14:07,430 --> 00:14:05,440

that recognize recognize the alkylated

340

00:14:10,550 --> 00:14:07,440

bases which exactly is exactly the

341

00:14:13,430 --> 00:14:10,560

mechanism that was proposed by pull and

342

00:14:14,230 --> 00:14:13,440

logan well let us take a brief look at

343

00:14:17,189 --> 00:14:14,240

these

344

00:14:19,829 --> 00:14:17,199

dna repair mechanisms that recognize the

345

00:14:23,590 --> 00:14:19,839

alkylated bases and yes indeed we have

346

00:14:25,590 --> 00:14:23,600

an enzyme that's a um alfb which is a

347

00:14:28,470 --> 00:14:25,600

monomeric behind the

348

00:14:32,310 --> 00:14:28,480

diode oxygenase the enzyme is very well

349

00:14:35,269 --> 00:14:32,320

characterized it requires iron but the

350

00:14:38,310 --> 00:14:35,279

problem is that the enzymes very

351

00:14:42,069 --> 00:14:38,320

absolutely depends strongly on free

352

00:14:44,310 --> 00:14:42,079

oxygen and clearly

353

00:14:45,910 --> 00:14:44,320

this oxygen was unavailable in the

354

00:14:47,350 --> 00:14:45,920

prebiotic and in the primitive

355

00:14:50,389 --> 00:14:47,360

environment when the less common

356

00:14:53,030 --> 00:14:50,399

ancestor population was floating around

357

00:14:56,230 --> 00:14:53,040

and although it is true that rna can be

358

00:14:58,550 --> 00:14:56,240

methylated rna can be repaired by rb

359

00:15:04,870 --> 00:14:58,560

most likely what we are seeing is a lack

360

00:15:10,829 --> 00:15:08,389

dna and rna associated proteins as was

361

00:15:13,829 --> 00:15:10,839

described in the

362

00:15:15,990 --> 00:15:13,839

1970s by emily super candle and others

363

00:15:18,310 --> 00:15:16,000

so what are our conclusions and our

364

00:15:20,389 --> 00:15:18,320

questions well what we call the

365

00:15:23,030 --> 00:15:20,399

leicester answer was most likely a

366

00:15:25,509 --> 00:15:23,040

population of complex bacterial-like

367

00:15:28,230 --> 00:15:25,519

cells and that with many of the traits

368

00:15:30,790 --> 00:15:28,240

of extreme protect x and prokaryotes it

369

00:15:33,110 --> 00:15:30,800

was neither approaching nor a direct

370

00:15:36,150 --> 00:15:33,120

medium descendant of the rna world if

371

00:15:38,550 --> 00:15:36,160

there was an rna world as soft today

372

00:15:40,550 --> 00:15:38,560

comparative genomics is an essential

373

00:15:43,430 --> 00:15:40,560

tool but it doesn't provide that with

374

00:15:46,069 --> 00:15:43,440

any direct evidence of the rna world

375

00:15:47,590 --> 00:15:46,079

pre-rna world or much less on the origin

376

00:15:49,590 --> 00:15:47,600

of life itself

377

00:15:51,670 --> 00:15:49,600

that i sincerely believe the

378

00:15:54,310 --> 00:15:51,680

reconstruction of the trace of the less

379

00:15:56,470 --> 00:15:54,320

common ancestor requires a clear

380

00:15:59,269 --> 00:15:56,480

understanding of primitive environment

381

00:16:01,269 --> 00:15:59,279

and of chemical realities at that the

382

00:16:03,829 --> 00:16:01,279

origin and early diversification of

383

00:16:05,990 --> 00:16:03,839

light proceeded at a surprisingly rapid

384

00:16:07,749 --> 00:16:06,000

pace and that after what is very

385

00:16:10,230 --> 00:16:07,759

surprising is this is something that

386

00:16:12,310 --> 00:16:10,240

assange miller and i pointed out many

387

00:16:14,310 --> 00:16:12,320

many years ago after the rapid

388

00:16:16,710 --> 00:16:14,320

biological evolution that took place

389

00:16:18,949 --> 00:16:16,720

following the origins of life the basic

390

00:16:21,430 --> 00:16:18,959

genetic traits and major molecular

391

00:16:23,990 --> 00:16:21,440

processes have persisted essentially

392

00:16:26,310 --> 00:16:24,000

unchained for more than 3.5 10 to the

393

00:16:28,470 --> 00:16:26,320

nine years which i think is quite an

394

00:16:30,710 --> 00:16:28,480

extraordinary feat of

395

00:16:39,350 --> 00:16:30,720

biological conservation thank you so

396

00:16:43,189 --> 00:16:41,590

thanks antonio and we have a lot of time

397

00:16:44,710 --> 00:16:43,199

for questions

398

00:16:47,189 --> 00:16:44,720

so um

399

00:16:50,389 --> 00:16:47,199

i don't see any in the chat right now

400

00:16:52,230 --> 00:16:50,399

uh but please come up to the mics and

401  
00:16:57,030 --> 00:16:52,240  
um ask your questions we have about 15

402  
00:16:57,040 --> 00:17:03,189  
did i speak so rapidly i'm surprised

403  
00:17:03,199 --> 00:17:09,829  
maybe i can start with a question

404  
00:17:14,150 --> 00:17:12,150  
hi nice talk thanks this is jen glass

405  
00:17:15,990 --> 00:17:14,160  
from georgia tech i'm sorry i missed it

406  
00:17:18,309 --> 00:17:16,000  
um could you go

407  
00:17:20,549 --> 00:17:18,319  
could you go back and um i was wondering

408  
00:17:22,630 --> 00:17:20,559  
about your oxygen story could you just

409  
00:17:24,390 --> 00:17:22,640  
explain okay

410  
00:17:26,710 --> 00:17:24,400  
okay so how did it

411  
00:17:28,230 --> 00:17:26,720  
repair without oxygen can you just go

412  
00:17:29,909 --> 00:17:28,240  
through that one more time for me if you

413  
00:17:32,549 --> 00:17:29,919

wouldn't mind and are there any

414

00:17:36,390 --> 00:17:32,559

alternative theories yeah thanks yeah no

415

00:17:38,710 --> 00:17:36,400

i'll be absolutely delighted well uh dna

416

00:17:41,990 --> 00:17:38,720

the basis and the same is true of rna

417

00:17:43,750 --> 00:17:42,000

bases can be methylated and

418

00:17:46,070 --> 00:17:43,760

you don't want your bases to be

419

00:17:49,430 --> 00:17:46,080

methylated because of you're altering

420

00:17:51,590 --> 00:17:49,440

your genetic information so cells have

421

00:17:53,909 --> 00:17:51,600

the ball

422

00:17:57,110 --> 00:17:53,919

mechanisms to actually

423

00:18:00,070 --> 00:17:57,120

cut off the alkyl groups that can affect

424

00:18:02,470 --> 00:18:00,080

the bases and these mechanisms include

425

00:18:04,870 --> 00:18:02,480

the nucleotide excision repair i mean

426

00:18:09,029 --> 00:18:04,880

you cut off the entire nucleotide and

427

00:18:11,990 --> 00:18:09,039

then um comp er repair it with a a

428

00:18:14,230 --> 00:18:12,000

complementary strand you can just cut

429

00:18:15,830 --> 00:18:14,240

off the base and then that has been

430

00:18:17,990 --> 00:18:15,840

methylated and then the same thing

431

00:18:20,789 --> 00:18:18,000

happens or you can actually have

432

00:18:23,669 --> 00:18:20,799

mechanisms that recognize directly the

433

00:18:25,750 --> 00:18:23,679

alkylated bases which is the mechanisms

434

00:18:26,789 --> 00:18:25,760

that poole and logan were suggesting

435

00:18:28,870 --> 00:18:26,799

could have

436

00:18:30,230 --> 00:18:28,880

play a role in the

437

00:18:33,590 --> 00:18:30,240

in the in

438

00:18:35,830 --> 00:18:33,600

in rna genomes uh well the problem is

439

00:18:38,470 --> 00:18:35,840

that the the enzyme is extremely well

440

00:18:41,590 --> 00:18:38,480

known the domain has been the active

441

00:18:43,990 --> 00:18:41,600

domain of this the dio

442

00:18:46,470 --> 00:18:44,000

has been very very well characterized

443

00:18:49,590 --> 00:18:46,480

the biochemistry is known in exclusive

444

00:18:51,909 --> 00:18:49,600

detail and you require an iron iron two

445

00:18:56,470 --> 00:18:51,919

you require actually this is better you

446

00:18:59,669 --> 00:18:56,480

require um also glutamate which is then

447

00:19:02,549 --> 00:18:59,679

reduced to succinate and

448

00:19:05,430 --> 00:19:02,559

but the problem is that this enzyme

449

00:19:09,029 --> 00:19:05,440

necessarily cannot work in the absence

450

00:19:11,190 --> 00:19:09,039

of free oxygen it is a must there have

451  
00:19:14,870 --> 00:19:11,200  
been attempts to actually substitute it

452  
00:19:18,310 --> 00:19:14,880  
by nitrogen two or other components it

453  
00:19:22,390 --> 00:19:18,320  
simply doesn't work so i think yes this

454  
00:19:25,110 --> 00:19:22,400  
enzyme can repair methylated rna but

455  
00:19:28,470 --> 00:19:25,120  
only under oxygen rich conditions which

456  
00:19:30,070 --> 00:19:28,480  
are extremely unlikely in the very early

457  
00:19:32,549 --> 00:19:30,080  
stages when

458  
00:19:38,549 --> 00:19:32,559  
prior to the separation of the archaea

459  
00:19:43,029 --> 00:19:41,270  
in other words this is a mechanism one

460  
00:19:44,230 --> 00:19:43,039  
question in chat

461  
00:19:47,190 --> 00:19:44,240  
so

462  
00:19:50,830 --> 00:19:47,200  
and then we will go back to

463  
00:19:53,029 --> 00:19:50,840

people here so a question from chad

464

00:19:54,789 --> 00:19:53,039

hello louder

465

00:19:57,270 --> 00:19:54,799

closer to the

466

00:19:57,280 --> 00:20:00,870

sorry okay this mic's a little better

467

00:20:05,909 --> 00:20:03,430

uh so we have one question from the chat

468

00:20:08,630 --> 00:20:05,919

uh how do the two types of membrane

469

00:20:10,789 --> 00:20:08,640

lipids fit into the luca problem were

470

00:20:13,270 --> 00:20:10,799

both archaeal and bacterial eukarya

471

00:20:16,470 --> 00:20:13,280

types present from the beginning

472

00:20:19,510 --> 00:20:16,480

it's a major major unresolved issue

473

00:20:21,750 --> 00:20:19,520

people like julie peretto and others

474

00:20:22,630 --> 00:20:21,760

have argued that perhaps the two types

475

00:20:24,630 --> 00:20:22,640

of

476

00:20:26,950 --> 00:20:24,640

ellipses were already present in the

477

00:20:28,870 --> 00:20:26,960

less common ancestor we really do not

478

00:20:31,110 --> 00:20:28,880

know we don't have a good answer for

479

00:20:34,470 --> 00:20:31,120

that question and that

480

00:20:37,430 --> 00:20:34,480

is argued by pedeto and others it could

481

00:20:38,310 --> 00:20:37,440

be that a different uh

482

00:20:40,710 --> 00:20:38,320

uh

483

00:20:43,190 --> 00:20:40,720

evolutionary trait selected for the

484

00:20:44,870 --> 00:20:43,200

separation between the two but i i would

485

00:20:47,510 --> 00:20:44,880

say that that's one of the most

486

00:20:49,669 --> 00:20:47,520

troubling issues that we actually have

487

00:20:51,430 --> 00:20:49,679

when trying to reconstruct the

488

00:20:54,470 --> 00:20:51,440

gene complement of the last common

489

00:20:56,390 --> 00:20:54,480

ancestor uh which is exactly what i have

490

00:20:59,029 --> 00:20:56,400

been concentrating together with my

491

00:21:05,750 --> 00:20:59,039

group on different on different traits

492

00:21:11,590 --> 00:21:07,669

hello tony burnett here from georgia

493

00:21:13,430 --> 00:21:11,600

tech and i was wondering um so we have

494

00:21:15,430 --> 00:21:13,440

this uh

495

00:21:17,590 --> 00:21:15,440

we developed now this notion that the

496

00:21:19,350 --> 00:21:17,600

last universal common ancestor

497

00:21:21,430 --> 00:21:19,360

has lots of

498

00:21:23,110 --> 00:21:21,440

complicated things just like a lot of

499

00:21:26,070 --> 00:21:23,120

modern cells um

500

00:21:28,470 --> 00:21:26,080

i'm wondering what you think of the

501  
00:21:29,510 --> 00:21:28,480  
relative merits of sort of two different

502  
00:21:32,149 --> 00:21:29,520  
models

503  
00:21:34,710 --> 00:21:32,159  
of why luca is

504  
00:21:37,669 --> 00:21:34,720  
who and when it is like you can have a

505  
00:21:40,549 --> 00:21:37,679  
model where just attrition over time you

506  
00:21:42,549 --> 00:21:40,559  
accidentally kill off lineages versus a

507  
00:21:46,070 --> 00:21:42,559  
model in which shortly before it you

508  
00:21:47,909 --> 00:21:46,080  
have some kind of an explosive advantage

509  
00:21:50,630 --> 00:21:47,919  
and uh that's and that could be the

510  
00:21:52,549 --> 00:21:50,640  
reason that the node is where it is what

511  
00:21:54,870 --> 00:21:52,559  
do you think of the relative merits of

512  
00:21:56,870 --> 00:21:54,880  
these two ideas or maybe something else

513  
00:22:01,430 --> 00:21:56,880

i haven't thought of

514

00:22:02,789 --> 00:22:01,440

well no what i really think is that

515

00:22:09,029 --> 00:22:02,799

so far

516

00:22:11,909 --> 00:22:09,039

ancestor are are by necessity based on

517

00:22:14,789 --> 00:22:11,919

sequence comparisons which is fine but

518

00:22:17,430 --> 00:22:14,799

the problem is that a sequence by itself

519

00:22:19,350 --> 00:22:17,440

is well a set of sequences is not

520

00:22:22,149 --> 00:22:19,360

telling you the whole story the whole

521

00:22:23,029 --> 00:22:22,159

biology of the system what i think is

522

00:22:25,029 --> 00:22:23,039

that

523

00:22:28,390 --> 00:22:25,039

and i may be completely wrong in this

524

00:22:32,549 --> 00:22:28,400

but i think is that we had uh

525

00:22:35,789 --> 00:22:32,559

uh sales populations that were uh

526

00:22:38,549 --> 00:22:35,799

by accretion of genes by uh gene

527

00:22:41,190 --> 00:22:38,559

duplications and so on were undergoing

528

00:22:42,549 --> 00:22:41,200

very very rapid uh

529

00:22:45,909 --> 00:22:42,559

evolution

530

00:22:48,470 --> 00:22:45,919

and rapid relative to geological times

531

00:22:50,070 --> 00:22:48,480

not necessarily rapidly to the rates of

532

00:22:52,870 --> 00:22:50,080

evolution of

533

00:22:56,549 --> 00:22:52,880

microbes or prokaryotes and then one

534

00:22:58,630 --> 00:22:56,559

line by still unknown reasons uh was the

535

00:23:01,270 --> 00:22:58,640

one that became more successful than the

536

00:23:03,029 --> 00:23:01,280

others but clearly

537

00:23:05,110 --> 00:23:03,039

uh since

538

00:23:07,510 --> 00:23:05,120

lateral gene transfer is a phenomenon

539

00:23:10,070 --> 00:23:07,520

that you cannot completely cut off some

540

00:23:12,070 --> 00:23:10,080

of the genes of those other existing

541

00:23:15,830 --> 00:23:12,080

populations may have survived and may

542

00:23:18,390 --> 00:23:15,840

have made it to the the lca

543

00:23:21,270 --> 00:23:18,400

i don't know if i'm answering properly

544

00:23:23,909 --> 00:23:21,280

your your question but

545

00:23:27,590 --> 00:23:23,919

but i think that one simply has to

546

00:23:31,110 --> 00:23:27,600

realize how quickly uh prokaryotes adapt

547

00:23:34,149 --> 00:23:31,120

to environmental insults to consider

548

00:23:36,870 --> 00:23:34,159

that something equivalent was taking uh

549

00:23:39,029 --> 00:23:36,880

place very very early on

550

00:23:40,549 --> 00:23:39,039

thanks you've answered my question by

551  
00:23:42,789 --> 00:23:40,559  
saying it is that it's the wrong

552  
00:23:45,029 --> 00:23:42,799  
question which is a good answer thanks

553  
00:23:46,710 --> 00:23:45,039  
thank you look it's a stimulating

554  
00:23:48,870 --> 00:23:46,720  
question

555  
00:23:50,630 --> 00:23:48,880  
um hello my name is sausan from the

556  
00:23:53,029 --> 00:23:50,640  
university of arizona

557  
00:23:55,029 --> 00:23:53,039  
and i was wondering how we can use all

558  
00:23:56,870 --> 00:23:55,039  
this information about lucas nature to

559  
00:23:58,390 --> 00:23:56,880  
infer the environment it was in

560  
00:24:00,710 --> 00:23:58,400  
specifically that in the introduction

561  
00:24:02,710 --> 00:24:00,720  
you mentioned about how people i think

562  
00:24:05,269 --> 00:24:02,720  
it was wasted all the inferred reverse

563  
00:24:07,430 --> 00:24:05,279

guy rays being traced back to luca and

564

00:24:09,510 --> 00:24:07,440

then a couple of years later catchphole

565

00:24:11,430 --> 00:24:09,520

and four terror were like no

566

00:24:13,669 --> 00:24:11,440

it was a probably horizontal gene

567

00:24:16,470 --> 00:24:13,679

transferred from an archaeal

568

00:24:18,390 --> 00:24:16,480

domain to the bacterial domain and that

569

00:24:20,789 --> 00:24:18,400

just put the whole thermophilic luca

570

00:24:22,470 --> 00:24:20,799

debate even on more

571

00:24:23,909 --> 00:24:22,480

high stance um

572

00:24:27,909 --> 00:24:23,919

and then you mentioned that it might

573

00:24:29,590 --> 00:24:27,919

have a uv radiation repair mechanism

574

00:24:30,950 --> 00:24:29,600

so that means it could have been closer

575

00:24:33,110 --> 00:24:30,960

to the surface and maybe away from

576  
00:24:35,590 --> 00:24:33,120  
hydrothermal vents as a lot of people do

577  
00:24:38,149 --> 00:24:35,600  
suggest and i would like your opinion on

578  
00:24:40,230 --> 00:24:38,159  
how we can reconcile all of this

579  
00:24:42,390 --> 00:24:40,240  
into where luca or the population of

580  
00:24:45,029 --> 00:24:42,400  
luca might have existed

581  
00:24:47,029 --> 00:24:45,039  
well the problem is that to reconcile

582  
00:24:49,909 --> 00:24:47,039  
the descriptions of the

583  
00:24:51,269 --> 00:24:49,919  
luca or lca whatever you want to call it

584  
00:24:53,510 --> 00:24:51,279  
with

585  
00:24:55,909 --> 00:24:53,520  
our reconstructions of the primitive

586  
00:24:57,510 --> 00:24:55,919  
environment we will need more detailed

587  
00:24:59,909 --> 00:24:57,520  
reconstructions of the primitive

588  
00:25:02,549 --> 00:24:59,919

environment which we absolutely like i

589

00:25:05,830 --> 00:25:02,559

mean even today we have an argument of

590

00:25:08,549 --> 00:25:05,840

how abundant was co2 in the primitive

591

00:25:11,110 --> 00:25:08,559

atmosphere i think we know for sure that

592

00:25:13,990 --> 00:25:11,120

there was uh the flux of uv light was

593

00:25:16,549 --> 00:25:14,000

higher and then than it is today and

594

00:25:19,909 --> 00:25:16,559

hence one can understand that way the

595

00:25:22,630 --> 00:25:19,919

ability to repair the presence the

596

00:25:25,269 --> 00:25:22,640

universal presence of uv

597

00:25:28,070 --> 00:25:25,279

light damage repair but

598

00:25:30,470 --> 00:25:28,080

i think that the main problem there is

599

00:25:32,710 --> 00:25:30,480

that we don't have a

600

00:25:34,070 --> 00:25:32,720

precise description of the last human

601  
00:25:35,510 --> 00:25:34,080  
ancestor

602  
00:25:38,950 --> 00:25:35,520  
there are some things that we know for

603  
00:25:41,590 --> 00:25:38,960  
sure for instance a higher

604  
00:25:43,510 --> 00:25:41,600  
flux of uv light

605  
00:25:46,950 --> 00:25:43,520  
i think that the same would be true for

606  
00:25:48,630 --> 00:25:46,960  
the absence of oxygen uh especially

607  
00:25:50,470 --> 00:25:48,640  
prior to the

608  
00:25:53,669 --> 00:25:50,480  
divergence of the

609  
00:25:56,070 --> 00:25:53,679  
into archaea and bacteria but other than

610  
00:25:57,590 --> 00:25:56,080  
that i will be

611  
00:25:59,750 --> 00:25:57,600  
very very

612  
00:26:03,029 --> 00:25:59,760  
skeptical of making very strong

613  
00:26:06,470 --> 00:26:03,039

statements although i have to say that i

614

00:26:11,350 --> 00:26:06,480

do like the idea of

615

00:26:14,710 --> 00:26:11,360

lca or luca living in lukewarm waters

616

00:26:17,190 --> 00:26:14,720

is this contradictory with the idea of

617

00:26:18,230 --> 00:26:17,200

a hot origin of life no

618

00:26:20,470 --> 00:26:18,240

because

619

00:26:23,190 --> 00:26:20,480

luca is very far removed from the

620

00:26:27,350 --> 00:26:23,200

origins of life if not in time at least

621

00:26:30,950 --> 00:26:28,870

so we have

622

00:26:31,750 --> 00:26:30,960

we have a couple of short questions from

623

00:26:36,390 --> 00:26:31,760

chad

624

00:26:40,070 --> 00:26:39,110

the first one is from fabia or sula by

625

00:26:42,630 --> 00:26:40,080

tutti

626

00:26:45,110 --> 00:26:42,640

how wide spread is the gene i'll be in

627

00:26:47,510 --> 00:26:45,120

prokaryotes today are there any

628

00:26:49,510 --> 00:26:47,520

alternatives to perform the same

629

00:26:51,990 --> 00:26:49,520

same type of repair

630

00:26:53,990 --> 00:26:52,000

it's a very good question the the gene

631

00:26:56,870 --> 00:26:54,000

is extremely extremely widely

632

00:26:59,510 --> 00:26:56,880

distributed it's found also

633

00:27:01,990 --> 00:26:59,520

of course it's present in

634

00:27:05,269 --> 00:27:02,000

a aerobic uh

635

00:27:07,350 --> 00:27:05,279

prokaryote it's extremely abundant in

636

00:27:09,510 --> 00:27:07,360

albi there are

637

00:27:13,430 --> 00:27:09,520

it's absent and that's easy to

638

00:27:16,950 --> 00:27:13,440

understand in a number of parasitic

639

00:27:21,029 --> 00:27:16,960

uh eukaryotes uh that live in in the

640

00:27:23,750 --> 00:27:21,039

guts for instance and the hormone the

641

00:27:27,029 --> 00:27:23,760

homologues of the alpha domain have a

642

00:27:29,990 --> 00:27:27,039

very very wide distribution

643

00:27:31,350 --> 00:27:30,000

a brief question

644

00:27:33,430 --> 00:27:31,360

thank you very much

645

00:27:37,909 --> 00:27:33,440

for your presentation my name is

646

00:27:40,470 --> 00:27:37,919

vladimir sobotin university of wisconsin

647

00:27:42,470 --> 00:27:40,480

you already partially uh

648

00:27:44,070 --> 00:27:42,480

answered my questions that it's the

649

00:27:49,190 --> 00:27:44,080

greatest mystery

650

00:27:55,190 --> 00:27:52,149

appeared in a form bacteria like

651  
00:27:56,710 --> 00:27:55,200  
ancestral structure already surrounded

652  
00:27:59,750 --> 00:27:56,720  
by a membrane

653  
00:28:02,310 --> 00:27:59,760  
and how membranes simultaneously occur

654  
00:28:05,029 --> 00:28:02,320  
together with information molecules is a

655  
00:28:07,830 --> 00:28:05,039  
great mystery you said it

656  
00:28:10,230 --> 00:28:07,840  
but could you imagine uh

657  
00:28:13,990 --> 00:28:10,240  
evolution of a

658  
00:28:16,470 --> 00:28:14,000  
membrane compartment themselves like in

659  
00:28:18,070 --> 00:28:16,480  
a lipid world hypothesis

660  
00:28:21,669 --> 00:28:18,080  
but as a

661  
00:28:24,789 --> 00:28:21,679  
sphere or in a form of liposuction

662  
00:28:26,789 --> 00:28:24,799  
that we know that liposomes can

663  
00:28:28,070 --> 00:28:26,799

divide they can fuse

664

00:28:30,789 --> 00:28:28,080

and they can

665

00:28:34,789 --> 00:28:30,799

be in a different level

666

00:28:37,510 --> 00:28:34,799

of a waterproof on a bottom on a top and

667

00:28:40,950 --> 00:28:37,520

they can actually evolve themselves

668

00:28:44,230 --> 00:28:40,960

without any information modules

669

00:28:47,350 --> 00:28:44,240

have you ever considered this hypothesis

670

00:28:50,310 --> 00:28:47,360

and not it itself you're raising up but

671

00:28:52,549 --> 00:28:50,320

i think it's a fascinating issue um i

672

00:28:54,950 --> 00:28:52,559

don't think that mechanism will apply

673

00:28:58,549 --> 00:28:54,960

for the less common ancestor for the

674

00:29:00,870 --> 00:28:58,559

luca but certainly certainly one thing

675

00:29:03,430 --> 00:29:00,880

that biologists have not considered

676

00:29:06,950 --> 00:29:03,440

sufficiently is what is called a

677

00:29:10,230 --> 00:29:06,960

structural heredity which they clearly

678

00:29:13,110 --> 00:29:10,240

is involved in the multiplication of

679

00:29:15,430 --> 00:29:13,120

structures in the absence of a genetic

680

00:29:18,310 --> 00:29:15,440

material a good case will be the

681

00:29:24,470 --> 00:29:18,320

centromeres or centrioles another case

682

00:29:29,350 --> 00:29:26,789

replication with no transmission of

683

00:29:31,909 --> 00:29:29,360

hereditary information which will be

684

00:29:34,950 --> 00:29:31,919

exactly the case of the liposomes i

685

00:29:37,990 --> 00:29:34,960

think this is not denying the key role

686

00:29:39,350 --> 00:29:38,000

that genetic material has in in

687

00:29:42,389 --> 00:29:39,360

evolution in

688

00:29:44,549 --> 00:29:42,399

in continuity in time and you know

689

00:29:46,789 --> 00:29:44,559

opening the possibility of divergence

690

00:29:49,590 --> 00:29:46,799

and adaptation and evolution and

691

00:29:52,789 --> 00:29:49,600

adaptation but clearly it's a mechanism

692

00:29:55,590 --> 00:29:52,799

that i would certainly not uh put away

693

00:29:57,590 --> 00:29:55,600

when thinking of pre-cellular systems

694

00:29:59,909 --> 00:29:57,600

yeah and the next question

695

00:30:02,149 --> 00:29:59,919

uh do you think that heredity of

696

00:30:05,430 --> 00:30:02,159

liposuction would be

697

00:30:08,710 --> 00:30:05,440

present as a quantum of our liposuction

698

00:30:10,870 --> 00:30:08,720

so we are running out of time uh so we

699

00:30:12,950 --> 00:30:10,880

just had time for one question so i

700

00:30:15,510 --> 00:30:12,960

would just want to thank professor

701  
00:30:16,710 --> 00:30:15,520  
alaskana for his wonderful presentation

702  
00:30:19,830 --> 00:30:16,720  
and

703  
00:30:21,830 --> 00:30:19,840  
uh his uh answers to to all these many

704  
00:30:24,070 --> 00:30:21,840  
questions but we have to move to the

705  
00:30:25,510 --> 00:30:24,080  
next uh presenter who is timothy

706  
00:30:27,909 --> 00:30:25,520  
zakowiczky

707  
00:30:30,389 --> 00:30:27,919  
and who is going to present a talk on

708  
00:30:32,549 --> 00:30:30,399  
origins of the modern reductive

709  
00:30:36,310 --> 00:30:32,559  
carboxylic acid cycle in the evolution

710  
00:30:36,320 --> 00:30:48,830  
thank

711  
00:30:59,909 --> 00:30:51,909  
you of questions

712  
00:31:03,190 --> 00:31:01,269  
hello everyone

713  
00:31:04,149 --> 00:31:03,200

my name is tim i'm a first year phd

714

00:31:05,909 --> 00:31:04,159

student at the university of

715

00:31:06,870 --> 00:31:05,919

wisconsin-madison

716

00:31:08,549 --> 00:31:06,880

although this work was actually

717

00:31:10,230 --> 00:31:08,559

conducted last summer

718

00:31:13,110 --> 00:31:10,240

during the blue marble space institute

719

00:31:14,630 --> 00:31:13,120

of science young science program

720

00:31:16,389 --> 00:31:14,640

um so the topic of my presentation is

721

00:31:18,710 --> 00:31:16,399

the origins of the modern reductive tca

722

00:31:20,230 --> 00:31:18,720

cycle and the evolution of life

723

00:31:22,870 --> 00:31:20,240

carbon fixation is one of the most

724

00:31:24,230 --> 00:31:22,880

fundamental processes in life today

725

00:31:26,310 --> 00:31:24,240

in simple terms it just involves

726

00:31:29,110 --> 00:31:26,320

incorporation of carbon dioxide from the

727

00:31:31,190 --> 00:31:29,120

atmosphere into biological molecules and

728

00:31:34,630 --> 00:31:31,200

is present in all three domains of life

729

00:31:35,830 --> 00:31:34,640

in archaea bacteria and eukaryotes

730

00:31:37,830 --> 00:31:35,840

and there are actually many different

731

00:31:39,029 --> 00:31:37,840

biochemical pathways with which life can

732

00:31:40,710 --> 00:31:39,039

fix carbon

733

00:31:43,350 --> 00:31:40,720

some of which you might have heard more

734

00:31:46,389 --> 00:31:43,360

about such as the calvin cycle which is

735

00:31:48,230 --> 00:31:46,399

common in cyanobacteria and plants or

736

00:31:50,230 --> 00:31:48,240

the reductive acetyl quay pathway also

737

00:31:51,909 --> 00:31:50,240

known as woodland dial pathway

738

00:31:54,789 --> 00:31:51,919

which is this ancient carbon fixation

739

00:31:57,350 --> 00:31:54,799

pathway present in some mesanogens

740

00:31:59,669 --> 00:31:57,360

but of the main interest to our study

741

00:32:01,750 --> 00:31:59,679

was the reductive tca cycle reductive

742

00:32:03,509 --> 00:32:01,760

tricarboxylic acid cycle which is

743

00:32:05,909 --> 00:32:03,519

basically krebs cycle that runs in

744

00:32:07,750 --> 00:32:05,919

reverse so krebs cycle is oxidative tca

745

00:32:10,950 --> 00:32:07,760

cycle it runs the oxidative direction

746

00:32:13,590 --> 00:32:10,960

and releases co2 and reductive tca

747

00:32:16,470 --> 00:32:13,600

fixates co2 instead

748

00:32:19,029 --> 00:32:16,480

so rtca is a very important biochemical

749

00:32:21,110 --> 00:32:19,039

pathway for the field of origins of life

750

00:32:22,230 --> 00:32:21,120

and astrobiology in general for a few

751  
00:32:24,549 --> 00:32:22,240  
reasons

752  
00:32:26,070 --> 00:32:24,559  
first of all our tca is autocatalytic

753  
00:32:27,509 --> 00:32:26,080  
and autocatalytic pathways are

754  
00:32:29,909 --> 00:32:27,519  
particularly interesting because they

755  
00:32:31,430 --> 00:32:29,919  
present a really unique way to rapidly

756  
00:32:32,870 --> 00:32:31,440  
increase complexity in the prebiotic

757  
00:32:35,110 --> 00:32:32,880  
setting

758  
00:32:37,350 --> 00:32:35,120  
and also rtca involves biologically

759  
00:32:39,190 --> 00:32:37,360  
common metabolites so tricarboxylic

760  
00:32:40,870 --> 00:32:39,200  
acids that are present in basically all

761  
00:32:42,470 --> 00:32:40,880  
organisms

762  
00:32:44,310 --> 00:32:42,480  
and there were studies that have shown

763  
00:32:45,750 --> 00:32:44,320

that some reactions of rtc can be

764

00:32:48,630 --> 00:32:45,760

catalyzed without the presence of

765

00:32:50,710 --> 00:32:48,640

enzymes for example using minerals

766

00:32:53,909 --> 00:32:50,720

but of the main interest to our study

767

00:32:56,470 --> 00:32:53,919

was that rtca has a really strange and

768

00:32:58,149 --> 00:32:56,480

patchy phylogenetic distribution it is

769

00:33:01,110 --> 00:32:58,159

present only in a few rare groups of

770

00:33:03,190 --> 00:33:01,120

bacteria and that's it no archaea no

771

00:33:06,070 --> 00:33:03,200

eukaryotes only a few rare groups of

772

00:33:08,310 --> 00:33:06,080

archaea oh bacteria which is not exactly

773

00:33:09,750 --> 00:33:08,320

very consistent with the idea of it

774

00:33:12,149 --> 00:33:09,760

being this really ancient carbon

775

00:33:13,669 --> 00:33:12,159

fixation pathway

776

00:33:14,710 --> 00:33:13,679

so here's what the actual cycle looks

777

00:33:16,310 --> 00:33:14,720

like

778

00:33:18,070 --> 00:33:16,320

first of all you can see that two axle

779

00:33:20,470 --> 00:33:18,080

acetates are produced per one round of

780

00:33:21,509 --> 00:33:20,480

the cycle and this is a catalytic part

781

00:33:23,590 --> 00:33:21,519

of it

782

00:33:25,430 --> 00:33:23,600

um and so one excel acetate is coming

783

00:33:27,110 --> 00:33:25,440

from pyruvate carboxylation

784

00:33:29,750 --> 00:33:27,120

and the other one from the cleavage of

785

00:33:33,269 --> 00:33:31,430

and also you can see the three

786

00:33:34,630 --> 00:33:33,279

irreversible steps of the cycle that are

787

00:33:37,110 --> 00:33:34,640

catalyzed differently from their

788

00:33:39,590 --> 00:33:37,120

counterparts in oxidative tca so two of

789

00:33:41,350 --> 00:33:39,600

them are marked in red here

790

00:33:43,350 --> 00:33:41,360

and the third one is actually this

791

00:33:45,350 --> 00:33:43,360

reaction which is the reaction of

792

00:33:46,710 --> 00:33:45,360

citrate cleavage to oxaloacetate and

793

00:33:50,310 --> 00:33:46,720

acetyl-coa

794

00:33:52,310 --> 00:33:50,320

um which is also key because it enables

795

00:33:55,110 --> 00:33:52,320

the auto-catalytic part of the rtca

796

00:33:59,430 --> 00:33:56,870

and there are actually two distinct ways

797

00:34:01,669 --> 00:33:59,440

citrate can be citrate can be cleaved

798

00:34:04,149 --> 00:34:01,679

um the first way is just a simple one

799

00:34:06,710 --> 00:34:04,159

enzyme reaction using the enzyme aco or

800

00:34:08,310 --> 00:34:06,720

atp citrate lyase which just cleaves

801  
00:34:09,430 --> 00:34:08,320  
citrate into acetyl-coa and excel

802  
00:34:11,270 --> 00:34:09,440  
acetate

803  
00:34:12,710 --> 00:34:11,280  
uh and the second way is actually when

804  
00:34:15,510 --> 00:34:12,720  
citrate is first converted into

805  
00:34:18,310 --> 00:34:15,520  
acetyl-coa intermediate using ccs or

806  
00:34:20,710 --> 00:34:18,320  
citric acintase and then cedric way is

807  
00:34:23,109 --> 00:34:20,720  
cleaved by citral coil ias into

808  
00:34:24,550 --> 00:34:23,119  
acetyl-coa and oxaloacetate

809  
00:34:27,669 --> 00:34:24,560  
and here you can also see the reverse

810  
00:34:30,389 --> 00:34:27,679  
reaction of cs or citrate syntase that

811  
00:34:34,629 --> 00:34:30,399  
catalyzes while the synthesis of citrate

812  
00:34:37,669 --> 00:34:34,639  
which is just a simple one-step process

813  
00:34:39,669 --> 00:34:37,679

so here is a pattern of how all the

814

00:34:41,829 --> 00:34:39,679

enzymes that i just mentioned with a lot

815

00:34:43,669 --> 00:34:41,839

of abbreviations are related to each

816

00:34:45,829 --> 00:34:43,679

other um some of this is from the

817

00:34:47,669 --> 00:34:45,839

literature and we've also our findings

818

00:34:48,550 --> 00:34:47,679

also confirmed the scheme

819

00:34:51,190 --> 00:34:48,560

so

820

00:34:52,950 --> 00:34:51,200

first of all you can see the two enzyme

821

00:34:55,510 --> 00:34:52,960

system which is often proposed to be

822

00:34:58,550 --> 00:34:55,520

ancestral so you have the enzyme ccs

823

00:35:00,829 --> 00:34:58,560

that produces citrul coa citrocynthase

824

00:35:02,390 --> 00:35:00,839

and ccl which leaves citrul

825

00:35:04,870 --> 00:35:02,400

citracle

826

00:35:06,790 --> 00:35:04,880

and is present in only a few rare groups

827

00:35:08,069 --> 00:35:06,800

of bacteria

828

00:35:11,109 --> 00:35:08,079

also

829

00:35:14,310 --> 00:35:11,119

these two enzymes ccs and ccl have

830

00:35:18,069 --> 00:35:14,320

homologs among other gca enzymes for

831

00:35:20,430 --> 00:35:18,079

example ccs is homologous to scs or

832

00:35:24,390 --> 00:35:20,440

suknokoisentase which catalyzes

833

00:35:27,349 --> 00:35:24,400

succincoasynthesis or breakdown in

834

00:35:29,829 --> 00:35:27,359

both oxidative and reductive tca

835

00:35:31,910 --> 00:35:29,839

and then ccl is homologous to citrate

836

00:35:34,150 --> 00:35:31,920

synthase which is an enzyme exclusively

837

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

unique to oxidative tca that catalyzes

838

00:35:38,310 --> 00:35:35,920

citrate synthesis

839

00:35:40,390 --> 00:35:38,320

and subsequently so also looking at

840

00:35:42,230 --> 00:35:40,400

homologs here is especially important

841

00:35:43,910 --> 00:35:42,240

because they're much more common than

842

00:35:45,750 --> 00:35:43,920

the actual citric cleavage enzymes and

843

00:35:47,349 --> 00:35:45,760

did not experience as many losses in

844

00:35:48,950 --> 00:35:47,359

their evolutionary history so we can

845

00:35:51,030 --> 00:35:48,960

infer a lot more from looking at their

846

00:35:53,670 --> 00:35:51,040

evolution

847

00:35:56,390 --> 00:35:53,680

and the last citric cleavage system is

848

00:35:58,470 --> 00:35:56,400

the more derived one enzyme system that

849

00:36:00,550 --> 00:35:58,480

is just acl that first started out as a

850

00:36:02,390 --> 00:36:00,560

two subunit enzyme uh that still

851  
00:36:04,310 --> 00:36:02,400  
catalyzed the one step reaction without

852  
00:36:07,349 --> 00:36:04,320  
the citroclase intermediate

853  
00:36:10,470 --> 00:36:07,359  
and this resulted from fusion of cc one

854  
00:36:12,710 --> 00:36:10,480  
of the subunits of ccs and ccl so this

855  
00:36:14,790 --> 00:36:12,720  
is the intermediary step basically

856  
00:36:17,349 --> 00:36:14,800  
and then the two subunits of icl fused

857  
00:36:20,950 --> 00:36:17,359  
again in eukaryotes and you get just one

858  
00:36:22,950 --> 00:36:20,960  
subunit enzyme that does the same thing

859  
00:36:24,870 --> 00:36:22,960  
so in order to investigate the rarity of

860  
00:36:26,390 --> 00:36:24,880  
this key reaction we try to do a survey

861  
00:36:27,670 --> 00:36:26,400  
of is as distribution

862  
00:36:29,510 --> 00:36:27,680  
and

863  
00:36:31,430 --> 00:36:29,520

flow genetic analysis using various

864

00:36:35,109 --> 00:36:31,440

databases such as keg

865

00:36:36,870 --> 00:36:35,119

and cbi genbank or syntax

866

00:36:38,710 --> 00:36:36,880

so first of all what we found is that

867

00:36:40,790 --> 00:36:38,720

the distribution so here are some of our

868

00:36:42,550 --> 00:36:40,800

findings regarding the distribution of

869

00:36:43,910 --> 00:36:42,560

acidic cleavage reaction overlaid on the

870

00:36:46,069 --> 00:36:43,920

tree of life

871

00:36:49,190 --> 00:36:46,079

and you can see a few things here

872

00:36:51,109 --> 00:36:49,200

so first of all we identified a few

873

00:36:52,870 --> 00:36:51,119

taxa in which complete rtc is

874

00:36:55,270 --> 00:36:52,880

theoretically possible at least they

875

00:36:57,589 --> 00:36:55,280

have all the necessary enzymes for that

876

00:36:59,990 --> 00:36:57,599

and note that there is only one archaeon

877

00:37:01,750 --> 00:37:00,000

the microarchite

878

00:37:03,510 --> 00:37:01,760

and it's basically the only archaeon we

879

00:37:06,390 --> 00:37:03,520

found we found that could even

880

00:37:08,630 --> 00:37:06,400

theoretically have our tca

881

00:37:10,310 --> 00:37:08,640

but the main finding is that it's from

882

00:37:12,870 --> 00:37:10,320

this it's really unclear which of the

883

00:37:16,230 --> 00:37:12,880

ancestors had which enzyme and how this

884

00:37:18,390 --> 00:37:16,240

whole system evolved as a whole

885

00:37:20,310 --> 00:37:18,400

but what is interesting is that most

886

00:37:22,790 --> 00:37:20,320

taxa that had the two enzyme systems so

887

00:37:24,550 --> 00:37:22,800

ccs and ccl actually were oxygen

888

00:37:26,790 --> 00:37:24,560

tolerant thermophiles with incomplete

889

00:37:29,190 --> 00:37:26,800

tca so incomplete

890

00:37:30,710 --> 00:37:29,200

either oxidative or reductive tca

891

00:37:32,550 --> 00:37:30,720

and it what's particularly interesting

892

00:37:35,510 --> 00:37:32,560

is oxygen tolerance defined here is both

893

00:37:37,030 --> 00:37:35,520

aerobes and microarea files because it's

894

00:37:39,109 --> 00:37:37,040

really strange that the ancestral form

895

00:37:40,230 --> 00:37:39,119

of the supposedly ancient reaction is

896

00:37:43,910 --> 00:37:40,240

actually mostly present in

897

00:37:47,190 --> 00:37:45,910

um then we looked at the phalagenese and

898

00:37:49,430 --> 00:37:47,200

i believe i don't have enough time to

899

00:37:52,069 --> 00:37:49,440

get into too much detail with these but

900

00:37:53,670 --> 00:37:52,079

the main takeaway is that as you can see

901  
00:37:56,230 --> 00:37:53,680  
there are very few monophyletic groups

902  
00:37:57,670 --> 00:37:56,240  
when athletic taxonomic groups here

903  
00:37:59,270 --> 00:37:57,680  
which indicates there were likely

904  
00:38:00,630 --> 00:37:59,280  
abundant horizontal gene transfers in

905  
00:38:03,109 --> 00:38:00,640  
the evolutionary history of these

906  
00:38:05,270 --> 00:38:03,119  
enzymes so this is the phylogeny of acl

907  
00:38:09,109 --> 00:38:05,280  
the one enzyme system and this is a

908  
00:38:12,150 --> 00:38:09,119  
phylogeny of ccl partici and is homolog

909  
00:38:14,710 --> 00:38:13,030  
with

910  
00:38:16,230 --> 00:38:14,720  
succinyl quasantes though it's a little

911  
00:38:18,470 --> 00:38:16,240  
bit more interesting

912  
00:38:21,109 --> 00:38:18,480  
because what we see is that multiple

913  
00:38:23,910 --> 00:38:21,119

distantly related citric cleaving clades

914

00:38:24,950 --> 00:38:23,920

actually have monophyletic scs

915

00:38:27,430 --> 00:38:24,960

so

916

00:38:29,750 --> 00:38:27,440

this implies either that succinoque

917

00:38:31,190 --> 00:38:29,760

synthase is capable of central coe

918

00:38:32,870 --> 00:38:31,200

synthesis as well

919

00:38:34,390 --> 00:38:32,880

which was empirically demonstrated to

920

00:38:36,310 --> 00:38:34,400

not be the case

921

00:38:39,109 --> 00:38:36,320

uh at least with a few central quay

922

00:38:41,109 --> 00:38:39,119

synthases that we know of empirically

923

00:38:42,390 --> 00:38:41,119

um and therefore the likely conclusion

924

00:38:44,150 --> 00:38:42,400

is that it was due to horizontal gene

925

00:38:46,630 --> 00:38:44,160

transfer event or a sequence of events

926  
00:38:48,870 --> 00:38:46,640  
from a similar source organism

927  
00:38:50,390 --> 00:38:48,880  
and also adding to that

928  
00:38:52,710 --> 00:38:50,400  
as we found by looking at synteny for

929  
00:38:54,310 --> 00:38:52,720  
all these organisms tca related genes

930  
00:38:55,990 --> 00:38:54,320  
are often located in close proximity to

931  
00:38:58,069 --> 00:38:56,000  
each other in the genomes

932  
00:38:59,990 --> 00:38:58,079  
which increases the likelihood of some

933  
00:39:02,550 --> 00:39:00,000  
kinds of linked transfers linked

934  
00:39:04,550 --> 00:39:02,560  
horizontal gene transfer events

935  
00:39:06,630 --> 00:39:04,560  
which in general implies that civic

936  
00:39:09,030 --> 00:39:06,640  
cleavage was might have been also

937  
00:39:10,790 --> 00:39:09,040  
obtained horizontally linked to scs in

938  
00:39:12,630 --> 00:39:10,800

these organisms in these bacteria

939

00:39:14,150 --> 00:39:12,640

specifically again we don't see this

940

00:39:17,190 --> 00:39:14,160

pattern in archaea that have citric

941

00:39:18,710 --> 00:39:17,200

cleavage but don't have complete rtca

942

00:39:20,550 --> 00:39:18,720

albeit it is important to mention that

943

00:39:22,150 --> 00:39:20,560

deep time horizontal gene transfers are

944

00:39:24,150 --> 00:39:22,160

next to impossible to definitively

945

00:39:26,390 --> 00:39:24,160

resolve particularly since parametric

946

00:39:29,109 --> 00:39:26,400

methods of inferno agts such as

947

00:39:30,870 --> 00:39:29,119

comparing gc content or cotton bias just

948

00:39:32,230 --> 00:39:30,880

don't work here because we're talking

949

00:39:34,550 --> 00:39:32,240

about events that could have happened

950

00:39:37,829 --> 00:39:34,560

billions of years ago

951

00:39:39,349 --> 00:39:37,839

so this is basically all we have

952

00:39:42,069 --> 00:39:39,359

another interesting implication of our

953

00:39:44,390 --> 00:39:42,079

findings are in regards to the evolution

954

00:39:46,630 --> 00:39:44,400

of metabolic mutualism or syntrophy uh

955

00:39:48,470 --> 00:39:46,640

especially in the case of rtca so let's

956

00:39:50,069 --> 00:39:48,480

look at this example first and establish

957

00:39:52,550 --> 00:39:50,079

the ectosymbiotic relationship between

958

00:39:54,710 --> 00:39:52,560

nanohalarkia and halarkia both groups of

959

00:39:58,150 --> 00:39:54,720

archaea that inhabit highly saline

960

00:40:00,470 --> 00:39:58,160

environments and what we see is really

961

00:40:03,030 --> 00:40:00,480

interesting so halorequia a really

962

00:40:05,750 --> 00:40:03,040

well-known and well-established group

963

00:40:08,550 --> 00:40:05,760

have basically all rtca enzymes with

964

00:40:10,630 --> 00:40:08,560

exceptional one or one enzyme system uh

965

00:40:12,950 --> 00:40:10,640

the system for citric cleavage

966

00:40:15,589 --> 00:40:12,960

while nanohilarchia which are frequently

967

00:40:17,270 --> 00:40:15,599

known to be their ectosymbians

968

00:40:19,430 --> 00:40:17,280

are known to only have citric cleavage

969

00:40:22,470 --> 00:40:19,440

enzymes particularly of the two enzymes

970

00:40:24,150 --> 00:40:22,480

the two enzyme system of ccs and ccl

971

00:40:25,750 --> 00:40:24,160

which implies of course a possibility

972

00:40:27,990 --> 00:40:25,760

that there could have been could be some

973

00:40:29,589 --> 00:40:28,000

kind of centrifuge going on with citrate

974

00:40:31,990 --> 00:40:29,599

being transferred from one archaean to

975

00:40:33,510 --> 00:40:32,000

another and the product like excellent

976

00:40:35,430 --> 00:40:33,520

state or acetyl-coa being transferred

977

00:40:37,829 --> 00:40:35,440

back and there are actually multiple

978

00:40:39,670 --> 00:40:37,839

suitable transporters in both organisms

979

00:40:41,829 --> 00:40:39,680

and this is obviously speculative and

980

00:40:43,990 --> 00:40:41,839

requires empirical validation but we see

981

00:40:46,309 --> 00:40:44,000

a very similar pattern for a lot of

982

00:40:48,870 --> 00:40:46,319

other groups of syntrophic partners in

983

00:40:51,510 --> 00:40:48,880

our study such as asgar kian misanogens

984

00:40:53,829 --> 00:40:51,520

or microarchites and certain plasmas and

985

00:40:56,150 --> 00:40:53,839

a few other groups as well um so this is

986

00:40:59,510 --> 00:40:56,160

not just unique to halo or kia although

987

00:41:01,109 --> 00:40:59,520

yes it does require empirical validation

988

00:41:03,190 --> 00:41:01,119

but why is interesting specifically with

989

00:41:05,349 --> 00:41:03,200

scalar kia is because it actually adds

990

00:41:08,069 --> 00:41:05,359

more context to one previously proposed

991

00:41:09,510 --> 00:41:08,079

idea or the purple earth hypothesis

992

00:41:11,430 --> 00:41:09,520

which basically states that due to

993

00:41:14,390 --> 00:41:11,440

spectral complementarity of halo kill

994

00:41:16,870 --> 00:41:14,400

bacteriodopsins so mark here

995

00:41:18,230 --> 00:41:16,880

and chlorophylls

996

00:41:19,589 --> 00:41:18,240

the evolution of the latter could have

997

00:41:21,750 --> 00:41:19,599

happened due to the competition for

998

00:41:23,109 --> 00:41:21,760

wavelengths with retinal phototrophs so

999

00:41:25,109 --> 00:41:23,119

like halo archaea again that use

1000

00:41:26,950 --> 00:41:25,119

bacteriodopsins which have a retinal

1001  
00:41:28,390 --> 00:41:26,960  
pigment

1002  
00:41:29,990 --> 00:41:28,400  
but this is complicated by the fact that

1003  
00:41:31,270 --> 00:41:30,000  
there is no carbon fixation in modern

1004  
00:41:33,430 --> 00:41:31,280  
halo archaea

1005  
00:41:34,950 --> 00:41:33,440  
so there's no coupling of a process that

1006  
00:41:36,550 --> 00:41:34,960  
produces a lot of reducing equivalents

1007  
00:41:38,950 --> 00:41:36,560  
like photosynthesis the process that

1008  
00:41:39,910 --> 00:41:38,960  
requires them like carbon fixation

1009  
00:41:41,109 --> 00:41:39,920  
and

1010  
00:41:42,630 --> 00:41:41,119  
our findings provide a possible

1011  
00:41:45,589 --> 00:41:42,640  
explanation for that either so possible

1012  
00:41:47,349 --> 00:41:45,599  
rtc in the past or and therefore serious

1013  
00:41:49,270 --> 00:41:47,359

cleavage enzymes in nanohero kia being

1014

00:41:50,790 --> 00:41:49,280

acquired horizontally

1015

00:41:52,390 --> 00:41:50,800

or just through rtc operating

1016

00:41:54,230 --> 00:41:52,400

syntrophically

1017

00:41:55,750 --> 00:41:54,240

and we also discussed a little bit about

1018

00:41:57,030 --> 00:41:55,760

how syntrophy could be in general

1019

00:41:57,829 --> 00:41:57,040

important for the field of origins of

1020

00:41:59,109 --> 00:41:57,839

life

1021

00:42:01,270 --> 00:41:59,119

because it's significantly more common

1022

00:42:03,109 --> 00:42:01,280

than expected and was shown to be

1023

00:42:04,230 --> 00:42:03,119

product of selection rather than random

1024

00:42:06,150 --> 00:42:04,240

losses

1025

00:42:07,990 --> 00:42:06,160

um and there are even a few lines of

1026

00:42:09,190 --> 00:42:08,000

evidence for the prevalence of syntropic

1027

00:42:11,030 --> 00:42:09,200

interactions early in the evolution of

1028

00:42:12,550 --> 00:42:11,040

life as well

1029

00:42:14,470 --> 00:42:12,560

so basically our main conclusions are

1030

00:42:16,790 --> 00:42:14,480

that citric leavage in modern bacteria

1031

00:42:18,470 --> 00:42:16,800

possessing rtca is likely a consequence

1032

00:42:20,069 --> 00:42:18,480

of deep time horizontal gene transfers

1033

00:42:22,790 --> 00:42:20,079

and therefore modern distribution of

1034

00:42:24,230 --> 00:42:22,800

rtca might not reflect its origins

1035

00:42:25,430 --> 00:42:24,240

and that syntropic interactions might

1036

00:42:27,190 --> 00:42:25,440

have played a role in the evolution of

1037

00:42:28,390 --> 00:42:27,200

our dca origins of life as a whole as

1038

00:42:30,390 --> 00:42:28,400

well

1039

00:42:32,309 --> 00:42:30,400

and as i mentioned this project was

1040

00:42:33,829 --> 00:42:32,319

started doing the the msi asean

1041

00:42:37,670 --> 00:42:33,839

scientist program and i would like to

1042

00:42:38,870 --> 00:42:37,680

thank the whole um the sarma lab for

1043

00:42:39,750 --> 00:42:38,880

all the help and feedback on this

1044

00:42:46,470 --> 00:42:39,760

project

1045

00:42:53,910 --> 00:42:48,630

thank you we have a time for one short

1046

00:42:59,109 --> 00:42:56,710

hi oh god that was a great talk uh julie

1047

00:43:00,390 --> 00:42:59,119

huber from woodsault oceanographic and i

1048

00:43:02,550 --> 00:43:00,400

just want to say this is why i like

1049

00:43:04,309 --> 00:43:02,560

coming to these meetings because

1050

00:43:06,390 --> 00:43:04,319

your rare

1051  
00:43:08,710 --> 00:43:06,400  
you know organisms are the most abundant

1052  
00:43:10,950 --> 00:43:08,720  
organisms at deepsea hydrothermal vents

1053  
00:43:12,870 --> 00:43:10,960  
and i was curious you know when we

1054  
00:43:14,309 --> 00:43:12,880  
sequence these environments over half of

1055  
00:43:15,750 --> 00:43:14,319  
half of them are epsilons and

1056  
00:43:17,750 --> 00:43:15,760  
aquificailys

1057  
00:43:19,670 --> 00:43:17,760  
and i was wondering if any of the

1058  
00:43:22,390 --> 00:43:19,680  
metagenome assembled genomes that we're

1059  
00:43:23,990 --> 00:43:22,400  
pulling out of these natural ecosystems

1060  
00:43:25,910 --> 00:43:24,000  
that represent way more than the culture

1061  
00:43:28,230 --> 00:43:25,920  
diversity if they can be incorporated

1062  
00:43:30,230 --> 00:43:28,240  
into your work

1063  
00:43:33,349 --> 00:43:30,240

thank you for your question uh yes i was

1064

00:43:35,349 --> 00:43:33,359

trying to largely avoid uh environmental

1065

00:43:37,349 --> 00:43:35,359

assemblies just because a lot of it is

1066

00:43:39,349 --> 00:43:37,359

uncultured and it really pains me every

1067

00:43:40,790 --> 00:43:39,359

time i see a good enzyme that is just

1068

00:43:43,030 --> 00:43:40,800

from something that's

1069

00:43:44,630 --> 00:43:43,040

not very well known um

1070

00:43:46,069 --> 00:43:44,640

but yeah i think i only incorporated a

1071

00:43:50,069 --> 00:43:46,079

few

1072

00:43:51,910 --> 00:43:50,079

from a more well-known taxa uh at least

1073

00:43:53,430 --> 00:43:51,920

from a literature perspective but yeah

1074

00:43:55,589 --> 00:43:53,440

they're definitely rtc could definitely

1075

00:43:56,790 --> 00:43:55,599

be significantly more distributed and

1076  
00:43:58,630 --> 00:43:56,800  
actually one of the ideas that was

1077  
00:44:00,150 --> 00:43:58,640  
previously proposed as well was that it

1078  
00:44:02,309 --> 00:44:00,160  
originated in archaea instead of

1079  
00:44:04,069 --> 00:44:02,319  
bacteria even though it's now entirely

1080  
00:44:05,349 --> 00:44:04,079  
absent in archaea which could

1081  
00:44:07,030 --> 00:44:05,359  
potentially suggest that there could

1082  
00:44:09,190 --> 00:44:07,040  
have been some kind of lineage that we

1083  
00:44:11,750 --> 00:44:09,200  
either don't know about or that just

1084  
00:44:13,829 --> 00:44:11,760  
died out at some point

1085  
00:44:16,630 --> 00:44:13,839  
that possessed the cycle and then

1086  
00:44:18,309 --> 00:44:16,640  
transferred it to modern bacteria

1087  
00:44:20,630 --> 00:44:18,319  
so yeah looking at environmental

1088  
00:44:22,790 --> 00:44:20,640

metagenomes is definitely really

1089

00:44:26,069 --> 00:44:22,800

interesting especially for for this kind

1090

00:44:29,190 --> 00:44:28,150

do you have more questions

1091

00:44:30,550 --> 00:44:29,200

okay

1092

00:44:32,630 --> 00:44:30,560

thank you kim

1093

00:44:36,150 --> 00:44:32,640

and we'd like to move into the next

1094

00:44:38,309 --> 00:44:36,160

speaker uh who is uh veronica merizewski

1095

00:44:41,510 --> 00:44:38,319

and she is going to be talking about

1096

00:44:43,910 --> 00:44:41,520

scaling patterns in enzyme diversity and

1097

00:45:02,950 --> 00:44:43,920

the universality of life

1098

00:45:07,510 --> 00:45:05,670

all right hello my name is veronica and

1099

00:45:10,950 --> 00:45:07,520

i am going to talk to you all about a

1100

00:45:12,470 --> 00:45:10,960

new way of finding universality in life

1101

00:45:14,790 --> 00:45:12,480

to start we're all familiar with the

1102

00:45:16,550 --> 00:45:14,800

fact that life is very diverse on earth

1103

00:45:18,550 --> 00:45:16,560

and apart from a shared genetic code we

1104

00:45:20,550 --> 00:45:18,560

don't actually know what is common to

1105

00:45:21,829 --> 00:45:20,560

all instances of life

1106

00:45:23,670 --> 00:45:21,839

so that's a question i'm really

1107

00:45:27,430 --> 00:45:23,680

interested in what unites all life in

1108

00:45:29,270 --> 00:45:27,440

the universe regardless of environment

1109

00:45:31,030 --> 00:45:29,280

this is a useful question just because

1110

00:45:32,710 --> 00:45:31,040

it's interesting in itself but also

1111

00:45:34,230 --> 00:45:32,720

uncovering universal features of life

1112

00:45:36,230 --> 00:45:34,240

will help us in endeavors such as

1113

00:45:38,390 --> 00:45:36,240

constructing minimal life

1114

00:45:40,550 --> 00:45:38,400

constraining early models of or the

1115

00:45:43,829 --> 00:45:40,560

earliest life and searching for life

1116

00:45:46,150 --> 00:45:43,839

agnostically or weird life

1117

00:45:48,069 --> 00:45:46,160

so one way to find this universality is

1118

00:45:49,109 --> 00:45:48,079

to look at scaling patterns and if

1119

00:45:51,430 --> 00:45:49,119

you're not familiar with scaling

1120

00:45:53,750 --> 00:45:51,440

patterns all they are are how some

1121

00:45:55,430 --> 00:45:53,760

attribute changes as the system size

1122

00:45:57,589 --> 00:45:55,440

increases so you can have a linear

1123

00:45:59,349 --> 00:45:57,599

relationship but you can also have other

1124

00:46:01,670 --> 00:45:59,359

interesting ones such as sublinear or

1125

00:46:03,270 --> 00:46:01,680

super linear behavior

1126  
00:46:05,030 --> 00:46:03,280  
and throughout this presentation i will

1127  
00:46:07,109 --> 00:46:05,040  
demonstrate scaling relationships in the

1128  
00:46:08,230 --> 00:46:07,119  
way i just showed you as well as in log

1129  
00:46:09,990 --> 00:46:08,240  
space

1130  
00:46:12,870 --> 00:46:10,000  
where the slope denotes what scaling

1131  
00:46:14,390 --> 00:46:12,880  
behavior is so above one is super linear

1132  
00:46:18,230 --> 00:46:14,400  
below one is sub

1133  
00:46:21,990 --> 00:46:19,510  
the good news is that we've found

1134  
00:46:24,390 --> 00:46:22,000  
scaling in biology already so a very

1135  
00:46:26,870 --> 00:46:24,400  
common example is the metabolic rate of

1136  
00:46:28,470 --> 00:46:26,880  
animals where on this plot in the x-axis

1137  
00:46:30,790 --> 00:46:28,480  
you see body mass

1138  
00:46:32,870 --> 00:46:30,800

and on the yc metabolic rate

1139

00:46:35,510 --> 00:46:32,880

and i wanted to

1140

00:46:37,670 --> 00:46:35,520

stress that it's very very strange that

1141

00:46:39,270 --> 00:46:37,680

so many of these diverse organisms fall

1142

00:46:41,190 --> 00:46:39,280

within this line

1143

00:46:42,710 --> 00:46:41,200

and what it's showing us is that with

1144

00:46:45,109 --> 00:46:42,720

all these organisms despite their

1145

00:46:47,109 --> 00:46:45,119

differences are all experiencing the

1146

00:46:49,270 --> 00:46:47,119

same universal constraints

1147

00:46:51,589 --> 00:46:49,280

so the reason we see this we learned

1148

00:46:53,190 --> 00:46:51,599

decades after this observation is that

1149

00:46:55,190 --> 00:46:53,200

there is a universality in

1150

00:46:57,829 --> 00:46:55,200

cardiovascular branching patterns that's

1151

00:46:59,109 --> 00:46:57,839

optimized for energy transport

1152

00:47:00,870 --> 00:46:59,119

in case you're not convinced that

1153

00:47:03,190 --> 00:47:00,880

scaling is very useful especially in the

1154

00:47:04,630 --> 00:47:03,200

purposes of astrobiology a quote from

1155

00:47:07,670 --> 00:47:04,640

jeffrey west who does research in this

1156

00:47:09,510 --> 00:47:07,680

work has a wonderful quote laid out if

1157

00:47:11,109 --> 00:47:09,520

you tell me the size of a mammal i can

1158

00:47:12,710 --> 00:47:11,119

use the scaling loss to tell you almost

1159

00:47:14,630 --> 00:47:12,720

everything about the average values of

1160

00:47:16,790 --> 00:47:14,640

its measurable characteristics so just

1161

00:47:18,470 --> 00:47:16,800

how much food it needs to eat each day

1162

00:47:20,549 --> 00:47:18,480

what its heart rate is

1163

00:47:22,870 --> 00:47:20,559

how long it will take to mature

1164

00:47:25,030 --> 00:47:22,880

the length and radius of its aorta

1165

00:47:27,430 --> 00:47:25,040

how many offspring you'll have

1166

00:47:29,430 --> 00:47:27,440

and so on and this is just knowing one

1167

00:47:31,670 --> 00:47:29,440

piece of information which is the size

1168

00:47:35,349 --> 00:47:31,680

and no other details so scaling laws

1169

00:47:36,950 --> 00:47:35,359

have immense predictive power

1170

00:47:39,349 --> 00:47:36,960

now what i want to do is find hidden

1171

00:47:41,190 --> 00:47:39,359

universality from biochemistry because

1172

00:47:42,630 --> 00:47:41,200

fewer studies have looked at that so

1173

00:47:44,309 --> 00:47:42,640

when we talk about size here what i'm

1174

00:47:46,790 --> 00:47:44,319

referring to is the size of an organism

1175

00:47:49,430 --> 00:47:46,800

or community's biochemical space or what

1176

00:47:51,270 --> 00:47:49,440

an organism is capable of biochemically

1177

00:47:53,190 --> 00:47:51,280

and an attribute what i'm interested is

1178

00:47:55,829 --> 00:47:53,200

is in the diversity of biochemical

1179

00:47:59,990 --> 00:47:57,270

and so what i'm showing here is pretty

1180

00:48:01,589 --> 00:48:00,000

abstract and one way to get about this

1181

00:48:03,349 --> 00:48:01,599

to make it more concrete is to look at

1182

00:48:05,349 --> 00:48:03,359

enzymes because they're a great proxy

1183

00:48:06,470 --> 00:48:05,359

for biochemical function they catalyze

1184

00:48:08,549 --> 00:48:06,480

most reactions

1185

00:48:10,630 --> 00:48:08,559

and along with that conveniently for us

1186

00:48:13,670 --> 00:48:10,640

they're classified by a four-digit ec

1187

00:48:15,510 --> 00:48:13,680

code that is related to its function

1188

00:48:17,190 --> 00:48:15,520

to break that down at the first digit we

1189

00:48:19,750 --> 00:48:17,200

have the broadest function for example

1190

00:48:21,190 --> 00:48:19,760

ec1 are the exceeda reductase enzymes

1191

00:48:24,390 --> 00:48:21,200

and there are any enzymes that transfer

1192

00:48:25,829 --> 00:48:24,400

electrons from one molecule to another

1193

00:48:27,510 --> 00:48:25,839

when we get to the second digit we're

1194

00:48:29,270 --> 00:48:27,520

adding more specificity we're saying

1195

00:48:32,069 --> 00:48:29,280

that these are oxidoreductases that use

1196

00:48:33,190 --> 00:48:32,079

choh groups as electron donors by the

1197

00:48:34,470 --> 00:48:33,200

third digit we're adding more

1198

00:48:36,630 --> 00:48:34,480

information we're specifying the

1199

00:48:38,230 --> 00:48:36,640

electron acceptor and by the time we get

1200

00:48:40,710 --> 00:48:38,240

to the fourth digit we're specifying the

1201

00:48:42,549 --> 00:48:40,720

exact enzyme so this is useful for us

1202

00:48:45,990 --> 00:48:42,559

because we can look at different

1203

00:48:47,430 --> 00:48:46,000

specificity levels of function

1204

00:48:49,030 --> 00:48:47,440

to give you a bird's eye view of all of

1205

00:48:51,510 --> 00:48:49,040

the broad functions all of the first

1206

00:48:52,870 --> 00:48:51,520

digit ecs we have the oxidoreductases as

1207

00:48:54,309 --> 00:48:52,880

we just mentioned

1208

00:48:55,829 --> 00:48:54,319

transferases which are enzymes that

1209

00:48:57,670 --> 00:48:55,839

transfer molecular groups from one

1210

00:48:59,829 --> 00:48:57,680

molecule to another

1211

00:49:01,430 --> 00:48:59,839

hydrolases which cleave molecular bonds

1212

00:49:03,750 --> 00:49:01,440

using hydrolysis

1213

00:49:05,670 --> 00:49:03,760

lyses which cleave bonds using any other

1214

00:49:08,710 --> 00:49:05,680

method besides hydrolysis

1215

00:49:13,109 --> 00:49:08,720

isomerases which shuffle molecules

1216

00:49:16,950 --> 00:49:15,030

so going back to this rather than saying

1217

00:49:18,470 --> 00:49:16,960

the size of biochemical space like what

1218

00:49:19,829 --> 00:49:18,480

does that actually mean

1219

00:49:21,750 --> 00:49:19,839

we can look at the total enzymes that

1220

00:49:23,109 --> 00:49:21,760

are encoded in a genome or metagenome

1221

00:49:24,230 --> 00:49:23,119

because that data is actually available

1222

00:49:25,910 --> 00:49:24,240

to us

1223

00:49:27,589 --> 00:49:25,920

and instead of saying diversity

1224

00:49:29,349 --> 00:49:27,599

biochemical functions we can talk about

1225

00:49:32,790 --> 00:49:29,359

the number of unique enzymes within a

1226

00:49:37,349 --> 00:49:34,870

so in the past we asked if enzyme

1227

00:49:39,589 --> 00:49:37,359

diversity scales across the domains and

1228

00:49:41,589 --> 00:49:39,599

across levels of biological organization

1229

00:49:43,750 --> 00:49:41,599

aka on the organism scale versus

1230

00:49:45,589 --> 00:49:43,760

ecosystem scale and we looked only at

1231

00:49:47,430 --> 00:49:45,599

the broad first digit ecs for this

1232

00:49:49,430 --> 00:49:47,440

question and we also want to know is

1233

00:49:51,270 --> 00:49:49,440

there universal behavior for all of

1234

00:49:52,710 --> 00:49:51,280

these biological groups because there's

1235

00:49:54,549 --> 00:49:52,720

no reason to suppose that there would be

1236

00:49:56,069 --> 00:49:54,559

such a relationship

1237

00:49:58,230 --> 00:49:56,079

the way we did this is we use the joint

1238

00:50:00,549 --> 00:49:58,240

genome institute or jgi which contains

1239

00:50:02,549 --> 00:50:00,559

thousands of genos and metagenomes

1240

00:50:04,790 --> 00:50:02,559

and they're lovely because they have a

1241

00:50:06,870 --> 00:50:04,800

pipeline to annotate these genomes and

1242

00:50:09,349 --> 00:50:06,880

infer what enzymes are present and from

1243

00:50:11,510 --> 00:50:09,359

there they have ec codes tacked onto it

1244

00:50:13,430 --> 00:50:11,520

nice way to organize our data

1245

00:50:15,270 --> 00:50:13,440

and with our data set post filtering to

1246

00:50:17,829 --> 00:50:15,280

make sure we have high quality data we

1247

00:50:19,190 --> 00:50:17,839

have hundreds of thousands of samples

1248

00:50:22,150 --> 00:50:19,200

which is enough for us to make some

1249

00:50:24,309 --> 00:50:22,160

statistical generalizations

1250

00:50:26,470 --> 00:50:24,319

so good news scaling does exist at the

1251

00:50:28,870 --> 00:50:26,480

broadest first digit ec function and we

1252

00:50:31,030 --> 00:50:28,880

showed that in our most recent paper so

1253

00:50:32,549 --> 00:50:31,040

what you're looking at here is

1254

00:50:34,309 --> 00:50:32,559

all of the scaling relationships for the

1255

00:50:36,150 --> 00:50:34,319

first digit and if we're looking

1256

00:50:38,630 --> 00:50:36,160

specifically at one data point that

1257

00:50:40,950 --> 00:50:38,640

represents a genome and on the x-axis

1258

00:50:42,950 --> 00:50:40,960

that's the total biochemical toolkit and

1259

00:50:45,990 --> 00:50:42,960

on the y-axis we have how many unique

1260

00:50:48,150 --> 00:50:46,000

enzymes are within that particular class

1261

00:50:50,069 --> 00:50:48,160

and also there is universality for a lot

1262

00:50:52,150 --> 00:50:50,079

of these ecs so for example with the

1263

00:50:53,990 --> 00:50:52,160

axial reductases it's super linear

1264

00:50:55,750 --> 00:50:54,000

whether you're talking about bacteria

1265

00:50:59,829 --> 00:50:55,760

archaea or the metagenome which

1266

00:51:01,910 --> 00:50:59,839

represents a large scale ecosystem

1267

00:51:03,270 --> 00:51:01,920

and here what i'm showing are the slopes

1268

00:51:04,870 --> 00:51:03,280

of the trend lines that i just showed

1269

00:51:06,470 --> 00:51:04,880

you in the previous plot and the

1270

00:51:08,630 --> 00:51:06,480

universality comes from the fact that

1271

00:51:10,710 --> 00:51:08,640

within a given row we have the same

1272

00:51:12,870 --> 00:51:10,720

color across the board now you'll notice

1273

00:51:14,390 --> 00:51:12,880

that with the lyses and the asom races

1274

00:51:17,589 --> 00:51:14,400

they're not demonstrating that universal

1275

00:51:19,990 --> 00:51:17,599

behavior and i have some ideas as to why

1276

00:51:21,670 --> 00:51:20,000

so with the ec system that was made for

1277

00:51:24,230 --> 00:51:21,680

biochemists to do traditional

1278

00:51:25,910 --> 00:51:24,240

biochemistry but what we're after is to

1279

00:51:28,230 --> 00:51:25,920

look at a more abstract sense of

1280

00:51:30,710 --> 00:51:28,240

function so if we combine hydrolases and

1281

00:51:32,710 --> 00:51:30,720

lyses which are enzymes that both cleave

1282

00:51:34,390 --> 00:51:32,720

molecular bonds then we see that

1283

00:51:36,870 --> 00:51:34,400

universal behavior and happens to be

1284

00:51:38,790 --> 00:51:36,880

super linear isomerase is still not

1285

00:51:41,349 --> 00:51:38,800

universal but i suspect that's because

1286

00:51:42,710 --> 00:51:41,359

those enzymes act out on one molecule

1287

00:51:44,870 --> 00:51:42,720

and typically you'll have things like

1288

00:51:46,230 --> 00:51:44,880

intramolecular oxide reductase reactions

1289

00:51:49,030 --> 00:51:46,240

in them which i think makes that more of

1290

00:51:51,270 --> 00:51:49,040

a mixed bag category

1291

00:51:52,870 --> 00:51:51,280

so currently what i'm after is i want to

1292

00:51:55,190 --> 00:51:52,880

see if there's scaling behavior for the

1293

00:51:57,190 --> 00:51:55,200

more specific ecs the second and third

1294

00:51:59,270 --> 00:51:57,200

digits i also want to know if that

1295

00:52:01,670 --> 00:51:59,280

scaling is universal as you look down at

1296

00:52:03,349 --> 00:52:01,680

levels of specificity

1297

00:52:05,510 --> 00:52:03,359

and finally i want to see to what extent

1298

00:52:07,270 --> 00:52:05,520

scaling laws hold in deep time and i

1299

00:52:09,030 --> 00:52:07,280

want to see if the scaling coefficients

1300

00:52:11,190 --> 00:52:09,040

or the slopes are correlated with

1301  
00:52:12,630 --> 00:52:11,200  
phylogenetic distances the idea being

1302  
00:52:15,510 --> 00:52:12,640  
that if you're more closely related to

1303  
00:52:17,589 --> 00:52:15,520  
one organism you'd have a similar slope

1304  
00:52:19,510 --> 00:52:17,599  
to that organism

1305  
00:52:21,750 --> 00:52:19,520  
so looking at this first question uh

1306  
00:52:24,309 --> 00:52:21,760  
good news again scaling does exist at

1307  
00:52:26,470 --> 00:52:24,319  
the second and third digit level so what

1308  
00:52:28,390 --> 00:52:26,480  
you're seeing here are oxy reductases

1309  
00:52:29,910 --> 00:52:28,400  
across levels of specificity and these

1310  
00:52:30,950 --> 00:52:29,920  
all happen to demonstrate super linear

1311  
00:52:32,870 --> 00:52:30,960  
behavior

1312  
00:52:34,870 --> 00:52:32,880  
interesting

1313  
00:52:36,870 --> 00:52:34,880

the same is true for ligases these

1314

00:52:39,190 --> 00:52:36,880

ligases all demonstrate sublinear

1315

00:52:41,030 --> 00:52:39,200

behavior

1316

00:52:43,109 --> 00:52:41,040

now is it the case that it's universal

1317

00:52:45,109 --> 00:52:43,119

across levels of specificity all of the

1318

00:52:47,589 --> 00:52:45,119

time

1319

00:52:49,430 --> 00:52:47,599

not really so that is not always the

1320

00:52:52,230 --> 00:52:49,440

case for example with the transferases

1321

00:52:53,670 --> 00:52:52,240

ec2 that demonstrates sublinear behavior

1322

00:52:55,430 --> 00:52:53,680

but when we look at the second digit

1323

00:52:57,430 --> 00:52:55,440

then we see more of a mixed bag of

1324

00:53:00,230 --> 00:52:57,440

different sublinear linear and super

1325

00:53:01,670 --> 00:53:00,240

linear behavior

1326

00:53:03,109 --> 00:53:01,680

now finally is there a correlation

1327

00:53:05,030 --> 00:53:03,119

between scaling coefficients and

1328

00:53:07,670 --> 00:53:05,040

phylogenetic distance

1329

00:53:09,750 --> 00:53:07,680

what we found when we examined these

1330

00:53:11,670 --> 00:53:09,760

slopes at the phylum level is that there

1331

00:53:13,349 --> 00:53:11,680

are differences in these scaling slopes

1332

00:53:15,270 --> 00:53:13,359

so what you're looking at here are

1333

00:53:17,910 --> 00:53:15,280

different phyla bacteria

1334

00:53:19,510 --> 00:53:17,920

across these different ecs and plotted

1335

00:53:21,190 --> 00:53:19,520

here on the lines are the slopes and

1336

00:53:22,390 --> 00:53:21,200

their confidence intervals so you can

1337

00:53:24,630 --> 00:53:22,400

see there are differences and not

1338

00:53:26,790 --> 00:53:24,640

surprisingly the oxial reductases have

1339

00:53:29,190 --> 00:53:26,800

slopes above one the transferases

1340

00:53:31,829 --> 00:53:29,200

typically are slopes below one

1341

00:53:33,750 --> 00:53:31,839

but the point is that they're different

1342

00:53:35,670 --> 00:53:33,760

but they're not necessarily correlated

1343

00:53:38,470 --> 00:53:35,680

with phylogenetic distance so this is a

1344

00:53:40,870 --> 00:53:38,480

tree representing bacterial orders

1345

00:53:42,790 --> 00:53:40,880

and these colors on the grid plot

1346

00:53:45,270 --> 00:53:42,800

represent the scaling slope so you'd

1347

00:53:46,950 --> 00:53:45,280

expect there to be more similar colors

1348

00:53:49,270 --> 00:53:46,960

uh clustered together if there was a

1349

00:53:50,630 --> 00:53:49,280

correlation but that's not looking like

1350

00:53:51,990 --> 00:53:50,640

that's the case

1351  
00:53:53,430 --> 00:53:52,000  
we're going to perform more statistical

1352  
00:53:55,750 --> 00:53:53,440  
analyses to

1353  
00:53:57,750 --> 00:53:55,760  
make that result more robust so if it's

1354  
00:53:59,190 --> 00:53:57,760  
not correlated but there are differences

1355  
00:54:01,750 --> 00:53:59,200  
then could it be the case that the

1356  
00:54:04,710 --> 00:54:01,760  
random partitioning of taxa into

1357  
00:54:06,309 --> 00:54:04,720  
different groups is you know what leads

1358  
00:54:08,630 --> 00:54:06,319  
to these scaling slopes in other words

1359  
00:54:11,510 --> 00:54:08,640  
if we randomize what taxon is in which

1360  
00:54:12,390 --> 00:54:11,520  
group will we still see the same thing

1361  
00:54:14,390 --> 00:54:12,400  
uh

1362  
00:54:16,150 --> 00:54:14,400  
the answer is we don't quite know yet

1363  
00:54:17,990 --> 00:54:16,160

but i do want to illustrate what i mean

1364

00:54:19,670 --> 00:54:18,000

by this idea

1365

00:54:22,069 --> 00:54:19,680

currently i'm running these permutation

1366

00:54:24,309 --> 00:54:22,079

tests basically mixing up which taxon

1367

00:54:26,230 --> 00:54:24,319

goes where and the idea is if the

1368

00:54:28,950 --> 00:54:26,240

standard deviation of our true data

1369

00:54:30,870 --> 00:54:28,960

happens to lie outside of the permuted

1370

00:54:32,790 --> 00:54:30,880

standard deviations then we can say with

1371

00:54:35,670 --> 00:54:32,800

some degree of confidence that it's not

1372

00:54:37,349 --> 00:54:35,680

the result of just random partitioning

1373

00:54:38,630 --> 00:54:37,359

and if that's true then that makes it

1374

00:54:40,309 --> 00:54:38,640

more interesting because there might be

1375

00:54:42,710 --> 00:54:40,319

some physical reason at play that we

1376

00:54:44,710 --> 00:54:42,720

just don't know about

1377

00:54:46,230 --> 00:54:44,720

okay so summary of all the questions

1378

00:54:48,069 --> 00:54:46,240

answers so far

1379

00:54:49,190 --> 00:54:48,079

and my future goals are to investigate

1380

00:54:51,109 --> 00:54:49,200

why there are differences in these

1381

00:54:52,309 --> 00:54:51,119

scaling slopes

1382

00:54:54,150 --> 00:54:52,319

i also want to know what specific

1383

00:54:55,829 --> 00:54:54,160

biochemical functions drive the first

1384

00:54:57,589 --> 00:54:55,839

digit scaling because i think that'll

1385

00:54:58,230 --> 00:54:57,599

give some hint as to what the mechanism

1386

00:55:02,390 --> 00:54:58,240

is

1387

00:55:03,829 --> 00:55:02,400

universality in the first place

1388

00:55:06,069 --> 00:55:03,839

and i also want to control for sampling

1389

00:55:07,910 --> 00:55:06,079

bias in the phyla so it's not uncommon

1390

00:55:09,510 --> 00:55:07,920

for a given phylum to have thousands of

1391

00:55:11,910 --> 00:55:09,520

samples whereas another one might have

1392

00:55:14,069 --> 00:55:11,920

50. so in order to make this more robust

1393

00:55:16,150 --> 00:55:14,079

i want to make sure that all phyla are

1394

00:55:17,750 --> 00:55:16,160

evenly sampled

1395

00:55:19,190 --> 00:55:17,760

so going back to these goals that i

1396

00:55:21,109 --> 00:55:19,200

mentioned earlier

1397

00:55:23,270 --> 00:55:21,119

i believe that universal scaling and

1398

00:55:26,549 --> 00:55:23,280

function can aid in these endeavors and

1399

00:55:28,309 --> 00:55:26,559

particularly with luca we can infer how

1400

00:55:30,710 --> 00:55:28,319

many enzymes might have been present in

1401

00:55:32,549 --> 00:55:30,720

this system and using these scaling laws

1402

00:55:34,710 --> 00:55:32,559

we can actually determine what ratios of

1403

00:55:37,270 --> 00:55:34,720

functions we would expect and along with

1404

00:55:39,109 --> 00:55:37,280

that for searching for life agnostically

1405

00:55:40,789 --> 00:55:39,119

we're talking about function here and

1406

00:55:42,470 --> 00:55:40,799

that means that we can substitute

1407

00:55:44,150 --> 00:55:42,480

compounds and we can think about

1408

00:55:45,750 --> 00:55:44,160

alternative biochemistries to make our

1409

00:55:48,150 --> 00:55:45,760

search for life

1410

00:55:50,230 --> 00:55:48,160

elsewhere in the universe a little more

1411

00:55:52,390 --> 00:55:50,240

open-minded

1412

00:55:54,230 --> 00:55:52,400

so big thank you to the e-life team and

1413

00:55:56,150 --> 00:55:54,240

for our collaborators and thank you all

1414

00:56:05,270 --> 00:55:56,160

for being here and listening

1415

00:56:08,789 --> 00:56:07,589

hi i'm vladimir subotin university of

1416

00:56:11,270 --> 00:56:08,799

this country

1417

00:56:12,470 --> 00:56:11,280

now when you showed this graph

1418

00:56:18,309 --> 00:56:12,480

that uh

1419

00:56:22,390 --> 00:56:20,230

oh yes

1420

00:56:24,910 --> 00:56:22,400

uh i wonder uh

1421

00:56:26,789 --> 00:56:24,920

that you restricted this uh

1422

00:56:27,990 --> 00:56:26,799

representation

1423

00:56:35,589 --> 00:56:28,000

only

1424

00:56:37,190 --> 00:56:35,599

mammals but particular to placental

1425

00:56:40,069 --> 00:56:37,200

mammals

1426

00:56:41,349 --> 00:56:40,079

and what about other tax for example

1427

00:56:44,390 --> 00:56:41,359

what

1428

00:56:46,309 --> 00:56:44,400

jellyfish or octopus yeah for sure yeah

1429

00:56:47,670 --> 00:56:46,319

so fortunately other scholars have

1430

00:56:50,630 --> 00:56:47,680

investigated this question and have

1431

00:56:52,470 --> 00:56:50,640

looked at all life so there is a plot

1432

00:56:55,430 --> 00:56:52,480

that exists that includes things like

1433

00:56:57,670 --> 00:56:55,440

prokaryotes and non-placental mammals

1434

00:56:59,589 --> 00:56:57,680

i just chose this plot for simplicity to

1435

00:57:01,589 --> 00:56:59,599

illustrate this idea that you can have

1436

00:57:03,589 --> 00:57:01,599

really despair organisms that fall

1437

00:57:06,549 --> 00:57:03,599

within this universal line

1438

00:57:06,559 --> 00:57:09,750

hi oh love it

1439

00:57:12,630 --> 00:57:11,349

we just have some questions in the chat

1440

00:57:14,150 --> 00:57:12,640

oh

1441

00:57:17,910 --> 00:57:14,160

um

1442

00:57:18,710 --> 00:57:17,920

a question from joanna monte meisel

1443

00:57:20,710 --> 00:57:18,720

how

1444

00:57:24,710 --> 00:57:20,720

does this compare to the scaling laws

1445

00:57:29,750 --> 00:57:27,109

subscribing yeah

1446

00:57:32,789 --> 00:57:29,760

the chat keeps moving uh

1447

00:57:34,549 --> 00:57:32,799

by molina and why one minute

1448

00:57:36,710 --> 00:57:34,559

do i have this correct that you are

1449

00:57:39,270 --> 00:57:36,720

getting differences among phyla in

1450

00:57:41,510 --> 00:57:39,280

enzymes whereas they fail to find them

1451  
00:57:44,309 --> 00:57:41,520  
in other gene types such as

1452  
00:57:48,580 --> 00:57:44,319  
transcriptional regulators

1453  
00:58:05,190 --> 00:57:57,210  
[Music]

1454  
00:58:05,200 --> 00:58:13,349  
i don't think this is working anymore

1455  
00:58:17,430 --> 00:58:15,270  
yeah that's a really great question i'm

1456  
00:58:19,990 --> 00:58:17,440  
actually not familiar with that

1457  
00:58:21,990 --> 00:58:20,000  
particular study uh but i will look into

1458  
00:58:23,910 --> 00:58:22,000  
that and get back to you if possible

1459  
00:58:25,510 --> 00:58:23,920  
that's really interesting uh because so

1460  
00:58:27,750 --> 00:58:25,520  
far we've only looked at genomes and we

1461  
00:58:29,190 --> 00:58:27,760  
haven't looked at um transcription data

1462  
00:58:30,789 --> 00:58:29,200  
yet

1463  
00:58:32,870 --> 00:58:30,799

and uh really quick one more question

1464

00:58:35,030 --> 00:58:32,880

from the audience

1465

00:58:36,549 --> 00:58:35,040

so great talk just have a

1466

00:58:37,829 --> 00:58:36,559

kind of a quick question related to

1467

00:58:39,990 --> 00:58:37,839

transcription i know i haven't looked at

1468

00:58:42,549 --> 00:58:40,000

it yet but you can kind of do a census

1469

00:58:44,230 --> 00:58:42,559

of enzymes and presence but they not may

1470

00:58:46,390 --> 00:58:44,240

not necessarily be part of functional

1471

00:58:48,309 --> 00:58:46,400

pathways particularly in some archaean

1472

00:58:49,990 --> 00:58:48,319

bacteria so i'm wondering if you've

1473

00:58:51,430 --> 00:58:50,000

looked at complete pathways and if the

1474

00:58:52,710 --> 00:58:51,440

scaling patterns

1475

00:58:55,030 --> 00:58:52,720

remain in some of those complete

1476

00:58:57,430 --> 00:58:55,040

pathways rather than just in individual

1477

00:58:59,190 --> 00:58:57,440

ec classified numbers

1478

00:59:03,270 --> 00:58:59,200

okay it was a little bit hard to hear

1479

00:59:07,349 --> 00:59:04,390

we don't necessarily

1480

00:59:08,789 --> 00:59:07,359

know if those enzymes are expressed um

1481

00:59:10,549 --> 00:59:08,799

and that that is a shortcoming of the

1482

00:59:12,309 --> 00:59:10,559

study right so there is far more

1483

00:59:14,630 --> 00:59:12,319

metagenomes and genomes available than

1484

00:59:17,270 --> 00:59:14,640

transcriptomic data uh and the

1485

00:59:18,630 --> 00:59:17,280

transcriptomic data that does exist is

1486

00:59:21,349 --> 00:59:18,640

at least in jgi is usually the

1487

00:59:22,549 --> 00:59:21,359

metagenomic data whereas for this study

1488

00:59:23,910 --> 00:59:22,559

that i'm currently working on i'm

1489

00:59:26,230 --> 00:59:23,920

interested in the more individual

1490

00:59:28,230 --> 00:59:26,240

organisms like archaea and bacteria

1491

00:59:30,829 --> 00:59:28,240

but if you know of data sources that

1492

00:59:33,510 --> 00:59:30,839

have such data please let me

1493

00:59:35,600 --> 00:59:33,520

know thank you

1494

00:59:41,750 --> 00:59:35,610

all right thank you okay thanks

1495

00:59:47,190 --> 00:59:43,270

so next we have

1496

00:59:51,589 --> 00:59:49,190

for an evolutionary perspective on

1497

00:59:53,510 --> 00:59:51,599

prions trends and function of prion

1498

01:00:13,190 --> 00:59:53,520

candidates across all three domains of

1499

01:00:17,349 --> 01:00:15,829

so at 12 minutes i'll just like

1500

01:00:18,630 --> 01:00:17,359

gesture and i'll give you three minutes

1501

01:00:20,230 --> 01:00:18,640

for questions

1502

01:00:22,309 --> 01:00:20,240

but i'll let you wrap up your thoughts

1503

01:00:25,190 --> 01:00:22,319

and go into that time

1504

01:00:28,789 --> 01:00:27,190

thank you so much for coming my name is

1505

01:00:31,349 --> 01:00:28,799

thomas zaykovsky

1506

01:00:32,950 --> 01:00:31,359

i'm a neurobiologist fascinated with the

1507

01:00:35,510 --> 01:00:32,960

early evolution

1508

01:00:37,349 --> 01:00:35,520

and i'm working at nasa ames with lynn

1509

01:00:39,430 --> 01:00:37,359

rothschild

1510

01:00:42,150 --> 01:00:39,440

today i'd like to share with you a

1511

01:00:44,069 --> 01:00:42,160

radical idea that i that came to my mind

1512

01:00:46,789 --> 01:00:44,079

during my phd

1513

01:00:49,190 --> 01:00:46,799

an idea that an aggregate discovered in

1514

01:00:50,710 --> 01:00:49,200

human brain could be a relic of early

1515

01:00:53,510 --> 01:00:50,720

evolution

1516

01:00:55,190 --> 01:00:53,520

so in my research i focus on pre-ends

1517

01:00:56,870 --> 01:00:55,200

preamps are fascinating because they're

1518

01:00:58,710 --> 01:00:56,880

so controversial

1519

01:01:01,430 --> 01:00:58,720

let me give you an example

1520

01:01:04,309 --> 01:01:01,440

prions were first discovered as a

1521

01:01:08,230 --> 01:01:04,319

protein aggregates in patients suffering

1522

01:01:09,430 --> 01:01:08,240

from infectious brain disorders

1523

01:01:11,430 --> 01:01:09,440

but first

1524

01:01:13,670 --> 01:01:11,440

koreans were thought to be viruses i

1525

01:01:16,390 --> 01:01:13,680

mean those disorders were thought to be

1526

01:01:17,670 --> 01:01:16,400

caused by viruses it took decades to

1527

01:01:20,309 --> 01:01:17,680

accept the

1528

01:01:21,910 --> 01:01:20,319

controversial idea that the protein

1529

01:01:23,510 --> 01:01:21,920

itself could carry biological

1530

01:01:26,549 --> 01:01:23,520

information

1531

01:01:27,589 --> 01:01:26,559

from an organism to another eventually

1532

01:01:29,990 --> 01:01:27,599

causing

1533

01:01:33,109 --> 01:01:30,000

a disease

1534

01:01:35,950 --> 01:01:33,119

so for the first 20 maybe 30 years

1535

01:01:38,549 --> 01:01:35,960

springs were widely

1536

01:01:40,870 --> 01:01:38,559

recognizable as

1537

01:01:42,309 --> 01:01:40,880

infectious proteins but recently we have

1538

01:01:44,630 --> 01:01:42,319

experienced dramatic shift in

1539

01:01:46,630 --> 01:01:44,640

perspective on prunes

1540

01:01:48,870 --> 01:01:46,640

maybe even to the extent that the name

1541

01:01:50,549 --> 01:01:48,880

itself no longer gives the justice to

1542

01:01:53,349 --> 01:01:50,559

the phenomenon

1543

01:01:56,309 --> 01:01:53,359

the name prion was invented to reflect

1544

01:01:59,829 --> 01:01:56,319

infectious nature of proteins it is an

1545

01:02:00,870 --> 01:01:59,839

acronym for protein nauseous infectious

1546

01:02:04,150 --> 01:02:00,880

particle

1547

01:02:07,430 --> 01:02:04,160

but in recent years we have found

1548

01:02:09,589 --> 01:02:07,440

uh not only prions in mammals but many

1549

01:02:12,390 --> 01:02:09,599

other organisms including bacteria

1550

01:02:15,270 --> 01:02:12,400

archaea and even viruses

1551

01:02:17,910 --> 01:02:15,280

so and since the term infection is

1552

01:02:20,309 --> 01:02:17,920

reserved for invasion and growth of

1553

01:02:24,069 --> 01:02:20,319

germs in a body the name itself no

1554

01:02:25,910 --> 01:02:24,079

longer properly describes the phenomena

1555

01:02:28,069 --> 01:02:25,920

so it was

1556

01:02:29,829 --> 01:02:28,079

if that wasn't enough prions uh were

1557

01:02:30,870 --> 01:02:29,839

recently found to play beneficial

1558

01:02:33,910 --> 01:02:30,880

functions

1559

01:02:35,029 --> 01:02:33,920

both in human and microorganisms

1560

01:02:37,270 --> 01:02:35,039

in yeast

1561

01:02:39,029 --> 01:02:37,280

prunes can facilitate rapid adaptation

1562

01:02:41,990 --> 01:02:39,039

to changing environment

1563

01:02:43,990 --> 01:02:42,000

and there are a powerful epigenetic

1564

01:02:46,309 --> 01:02:44,000

mechanism of adaptation

1565

01:02:49,910 --> 01:02:46,319

that likely existed more than one

1566

01:02:51,990 --> 01:02:49,920

billion years ago when these two species

1567

01:02:53,750 --> 01:02:52,000

diverged

1568

01:02:55,750 --> 01:02:53,760

in fact some

1569

01:02:57,029 --> 01:02:55,760

researchers are so impressed by the new

1570

01:02:59,109 --> 01:02:57,039

perspective

1571

01:03:00,829 --> 01:02:59,119

that they call it the largest paradigm

1572

01:03:03,510 --> 01:03:00,839

shifts

1573

01:03:06,309 --> 01:03:03,520

since identification of dna is a

1574

01:03:08,710 --> 01:03:06,319

molecule of heredity pretty bold

1575

01:03:10,630 --> 01:03:08,720

uh in a paper that we published last

1576

01:03:12,789 --> 01:03:10,640

year we have found

1577

01:03:13,990 --> 01:03:12,799

uh that candidate prion proteins from

1578

01:03:15,670 --> 01:03:14,000

archaea

1579

01:03:18,630 --> 01:03:15,680

can uh transmit

1580

01:03:20,870 --> 01:03:18,640

phenotypes for many generations when

1581

01:03:23,349 --> 01:03:20,880

expressed in modal organisms

1582

01:03:25,430 --> 01:03:23,359

the motivation for this paper was to

1583

01:03:27,670 --> 01:03:25,440

search for pre and specifically in the

1584

01:03:29,349 --> 01:03:27,680

domain archaea because it was the last

1585

01:03:31,910 --> 01:03:29,359

domain of life

1586

01:03:33,430 --> 01:03:31,920

not studied in regards to prince at the

1587

01:03:34,390 --> 01:03:33,440

time

1588

01:03:37,750 --> 01:03:34,400

and

1589

01:03:39,910 --> 01:03:37,760

with this work

1590

01:03:42,230 --> 01:03:39,920

uh we have helped to close the gap in

1591

01:03:44,230 --> 01:03:42,240

understanding how widespread

1592

01:03:46,390 --> 01:03:44,240

the prion phenomenon is on the

1593

01:03:48,710 --> 01:03:46,400

evolutionary tree of life

1594

01:03:50,789 --> 01:03:48,720

and it was the first step to start

1595

01:03:53,990 --> 01:03:50,799

asking questions about the origin of

1596

01:03:58,150 --> 01:03:54,000

prions so climbing the evolutionary tree

1597

01:03:59,349 --> 01:03:58,160

uh of life downward

1598

01:04:02,549 --> 01:03:59,359

uh

1599

01:04:04,870 --> 01:04:02,559

so could it be that prion aggregation

1600

01:04:07,349 --> 01:04:04,880

or protein

1601  
01:04:11,190 --> 01:04:07,359  
aggregates capable of storing biological

1602  
01:04:14,150 --> 01:04:11,200  
information exists on early earth

1603  
01:04:16,470 --> 01:04:14,160  
could they be forming abiotically

1604  
01:04:18,630 --> 01:04:16,480  
what roles could these aggregates have

1605  
01:04:20,710 --> 01:04:18,640  
in early life or maybe could they even

1606  
01:04:24,829 --> 01:04:20,720  
facilitate the origin of life these are

1607  
01:04:27,510 --> 01:04:24,839  
the major questions that motivate my

1608  
01:04:29,670 --> 01:04:27,520  
research uh to understand the potential

1609  
01:04:31,589 --> 01:04:29,680  
functions of the oldest prions on earth

1610  
01:04:33,270 --> 01:04:31,599  
let's spend a little bit of time looking

1611  
01:04:37,670 --> 01:04:33,280  
at how they work in contemporary

1612  
01:04:40,230 --> 01:04:37,680  
organisms so on this animation

1613  
01:04:43,109 --> 01:04:40,240

you can see a pre and protein in its

1614

01:04:45,829 --> 01:04:43,119

native soluble state and like all pre

1615

01:04:47,270 --> 01:04:45,839

and proteins it can misfold another term

1616

01:04:49,910 --> 01:04:47,280

from medicine

1617

01:04:52,710 --> 01:04:49,920

actually more adequately we should say

1618

01:04:55,109 --> 01:04:52,720

it obtains an alternative fold it

1619

01:04:57,029 --> 01:04:55,119

changes its confirmation increasing its

1620

01:05:00,470 --> 01:04:57,039

beta sheet content

1621

01:05:03,430 --> 01:05:00,480

in this form it can start force other

1622

01:05:04,710 --> 01:05:03,440

copies of itself to do the same

1623

01:05:07,029 --> 01:05:04,720

and

1624

01:05:08,630 --> 01:05:07,039

in this stage these proteins can adhere

1625

01:05:11,349 --> 01:05:08,640

to each other

1626

01:05:14,470 --> 01:05:11,359

forming a very tight interactions

1627

01:05:16,230 --> 01:05:14,480

and in consequence forming an insoluble

1628

01:05:21,109 --> 01:05:16,240

amyloid fiber

1629

01:05:22,630 --> 01:05:21,119

is very rigid it

1630

01:05:25,510 --> 01:05:22,640

is resistant to high range of

1631

01:05:27,829 --> 01:05:25,520

temperatures ph and even degradation and

1632

01:05:30,309 --> 01:05:27,839

importantly amyloids can be made out of

1633

01:05:31,510 --> 01:05:30,319

very short peptides even prebiotically

1634

01:05:33,990 --> 01:05:31,520

possible

1635

01:05:36,630 --> 01:05:34,000

so it's likely that amyloids existed on

1636

01:05:39,270 --> 01:05:36,640

early earth

1637

01:05:41,430 --> 01:05:39,280

importantly amyloid

1638

01:05:43,750 --> 01:05:41,440

grows exponentially fast

1639

01:05:46,390 --> 01:05:43,760

at first there is a lag phase but then

1640

01:05:48,710 --> 01:05:46,400

it grows exponentially quick

1641

01:05:50,870 --> 01:05:48,720

and it quickly leads to depletion of

1642

01:05:53,430 --> 01:05:50,880

native natively folded versions of the

1643

01:05:55,670 --> 01:05:53,440

protein that builds it so

1644

01:05:57,589 --> 01:05:55,680

pre-owned proteins that have amyloid

1645

01:05:58,549 --> 01:05:57,599

fold in it

1646

01:06:01,029 --> 01:05:58,559

these

1647

01:06:03,670 --> 01:06:01,039

prion proteins aggregates in the form of

1648

01:06:05,349 --> 01:06:03,680

amyloid are often unable to perform

1649

01:06:06,950 --> 01:06:05,359

their functions that they had before

1650

01:06:09,990 --> 01:06:06,960

they aggregated

1651  
01:06:12,390 --> 01:06:10,000  
so if that happens in a microorganism

1652  
01:06:13,430 --> 01:06:12,400  
phenotypically it looks like the gene

1653  
01:06:16,309 --> 01:06:13,440  
deletion

1654  
01:06:19,430 --> 01:06:16,319  
but in fact the gene is not affected

1655  
01:06:21,589 --> 01:06:19,440  
therefore the change in the phenotype

1656  
01:06:23,270 --> 01:06:21,599  
uh yeah it depends on the protein

1657  
01:06:28,390 --> 01:06:23,280  
aggregation and it's shared

1658  
01:06:31,589 --> 01:06:30,230  
and just like in case of chromatin

1659  
01:06:34,069 --> 01:06:31,599  
epigenetics

1660  
01:06:37,430 --> 01:06:34,079  
the trait can be heritable because the

1661  
01:06:39,190 --> 01:06:37,440  
aggregate can be passed to daughter cell

1662  
01:06:41,589 --> 01:06:39,200  
and continue recruiting freshly

1663  
01:06:44,230 --> 01:06:41,599

synthesized copies of the same protein

1664

01:06:46,630 --> 01:06:44,240

to the growing amyloid rendering the

1665

01:06:48,390 --> 01:06:46,640

protein unable to perform its functions

1666

01:06:50,470 --> 01:06:48,400

for many generations

1667

01:06:52,710 --> 01:06:50,480

if the amyloid aggregate can be passed

1668

01:06:55,990 --> 01:06:52,720

to another generation of cells this is

1669

01:06:58,829 --> 01:06:56,000

what we call prion so in this

1670

01:07:01,270 --> 01:06:58,839

sense prion is a heritable aggregate or

1671

01:07:03,750 --> 01:07:01,280

condensate that can change cellular

1672

01:07:07,349 --> 01:07:03,760

phenotypes for generations in case of

1673

01:07:09,430 --> 01:07:07,359

classical east prion protein sup 35

1674

01:07:12,150 --> 01:07:09,440

the switch to amyloid promoting state

1675

01:07:14,069 --> 01:07:12,160

happens every 1 million divisions and is

1676

01:07:15,910 --> 01:07:14,079

stable for a thousand generations for

1677

01:07:18,150 --> 01:07:15,920

ten thousand generations

1678

01:07:19,349 --> 01:07:18,160

in other words prion behave as molecular

1679

01:07:20,549 --> 01:07:19,359

switches

1680

01:07:23,750 --> 01:07:20,559

uh

1681

01:07:26,789 --> 01:07:23,760

they can broaden phenotypic diversity

1682

01:07:29,990 --> 01:07:26,799

and paraphrasing adriana guzi having a

1683

01:07:32,150 --> 01:07:30,000

protein that can exist an on and off

1684

01:07:34,870 --> 01:07:32,160

state where one of the states is

1685

01:07:36,870 --> 01:07:34,880

heritable is a wonderful way to transmit

1686

01:07:39,029 --> 01:07:36,880

information and it would be surprising

1687

01:07:41,589 --> 01:07:39,039

if nature didn't utilize it for

1688

01:07:43,829 --> 01:07:41,599

the system in order to solve specific

1689

01:07:45,829 --> 01:07:43,839

problems during evolution

1690

01:07:49,029 --> 01:07:45,839

and here are some examples how yeast can

1691

01:07:51,670 --> 01:07:49,039

benefit from prions on the top left part

1692

01:07:53,670 --> 01:07:51,680

you can see the prion gar plus

1693

01:07:56,069 --> 01:07:53,680

the rate of garplast formation can be

1694

01:07:58,309 --> 01:07:56,079

influenced by lactic acid and in

1695

01:08:00,870 --> 01:07:58,319

consequence enabling yeast to use

1696

01:08:03,430 --> 01:08:00,880

various carbon sources

1697

01:08:04,870 --> 01:08:03,440

switching from metabolic specialists to

1698

01:08:07,190 --> 01:08:04,880

generalists

1699

01:08:09,829 --> 01:08:07,200

other consequences of pre-information

1700

01:08:12,230 --> 01:08:09,839

include switching to

1701

01:08:14,870 --> 01:08:12,240

increasing sporulation or even

1702

01:08:17,829 --> 01:08:14,880

expressing subtelomeric regions which is

1703

01:08:21,189 --> 01:08:17,839

an example how prion mechanism regulates

1704

01:08:23,669 --> 01:08:21,199

another epigenetic mechanism

1705

01:08:26,229 --> 01:08:23,679

my personally favorite

1706

01:08:29,590 --> 01:08:26,239

example is prion

1707

01:08:30,470 --> 01:08:29,600

psi plus made of scp-35 protein that i

1708

01:08:32,229 --> 01:08:30,480

mentioned

1709

01:08:34,630 --> 01:08:32,239

on the previous slide it's

1710

01:08:35,990 --> 01:08:34,640

formation allows to read through

1711

01:08:39,829 --> 01:08:36,000

stop codons

1712

01:08:41,669 --> 01:08:39,839

it uncovers hidden genetic traits so

1713

01:08:44,149 --> 01:08:41,679

this can be a wonderful mechanism

1714

01:08:46,550 --> 01:08:44,159

facilitating evolution because anything

1715

01:08:49,349 --> 01:08:46,560

after a stop codon is not experiencing

1716

01:08:51,910 --> 01:08:49,359

selection pressure and can mutate freely

1717

01:08:57,349 --> 01:08:51,920

but after the prion is formed it

1718

01:09:00,870 --> 01:08:59,030

as i mentioned i'm very interested in

1719

01:09:03,349 --> 01:09:00,880

finding out what are the oldest pregnant

1720

01:09:04,550 --> 01:09:03,359

functions so recently machine learning

1721

01:09:05,990 --> 01:09:04,560

tools

1722

01:09:07,590 --> 01:09:06,000

were developed that allowed the

1723

01:09:10,709 --> 01:09:07,600

prediction

1724

01:09:12,870 --> 01:09:10,719

of prion behavior bioinformatically

1725

01:09:14,789 --> 01:09:12,880

based on amino acid sequences

1726

01:09:17,269 --> 01:09:14,799

so our recent work focused on

1727

01:09:19,829 --> 01:09:17,279

computational on computation on

1728

01:09:21,510 --> 01:09:19,839

bioinformatics and the future work will

1729

01:09:24,550 --> 01:09:21,520

again be

1730

01:09:26,709 --> 01:09:24,560

lab based prion confirmation of the

1731

01:09:28,630 --> 01:09:26,719

behavior of the protease

1732

01:09:30,630 --> 01:09:28,640

uh so the problem with prions is that

1733

01:09:32,630 --> 01:09:30,640

unfortunately their sequence of the

1734

01:09:35,110 --> 01:09:32,640

prion domain the fragment of the protein

1735

01:09:37,829 --> 01:09:35,120

that is responsible for aggregation

1736

01:09:40,470 --> 01:09:37,839

those prion domains are very homogeneous

1737

01:09:43,349 --> 01:09:40,480

and in many cases consist of just long

1738

01:09:46,149 --> 01:09:43,359

stretches of glutamine asparagine

1739

01:09:48,709 --> 01:09:46,159

this composition of preon domains

1740

01:09:51,110 --> 01:09:48,719

challenges the con the conventional

1741

01:09:52,070 --> 01:09:51,120

phylogenetic approach it's really hard

1742

01:09:55,030 --> 01:09:52,080

to say

1743

01:09:57,430 --> 01:09:55,040

if they are conserved based on sequence

1744

01:09:59,990 --> 01:09:57,440

uh pre and domains are modular that's

1745

01:10:01,110 --> 01:10:00,000

another characteristic of pre of prion

1746

01:10:02,790 --> 01:10:01,120

domains

1747

01:10:05,430 --> 01:10:02,800

that means that you can attach it to

1748

01:10:07,910 --> 01:10:05,440

another non-prion protein and convey the

1749

01:10:08,790 --> 01:10:07,920

ability to form a heritable aggregate to

1750

01:10:13,750 --> 01:10:08,800

it

1751  
01:10:16,630 --> 01:10:13,760  
identify candidate prion domains in all

1752  
01:10:19,030 --> 01:10:16,640  
proteomes of unipro from uniprot

1753  
01:10:20,870 --> 01:10:19,040  
uh proteomes of organisms representing

1754  
01:10:23,590 --> 01:10:20,880  
all three domains of life

1755  
01:10:25,270 --> 01:10:23,600  
and then we annotate functional domains

1756  
01:10:27,510 --> 01:10:25,280  
of the candidate

1757  
01:10:29,030 --> 01:10:27,520  
uh using gene ontology and keg

1758  
01:10:31,430 --> 01:10:29,040  
description so the

1759  
01:10:33,750 --> 01:10:31,440  
the other domain except the prion domain

1760  
01:10:36,950 --> 01:10:33,760  
that exists in this polypeptide

1761  
01:10:39,590 --> 01:10:36,960  
uh so we analyze the functional domain

1762  
01:10:42,950 --> 01:10:39,600  
that coexists with prion domain and the

1763  
01:10:45,110 --> 01:10:42,960

in the same polypeptide chain

1764

01:10:48,550 --> 01:10:45,120

uh so first we generated phallogenetic

1765

01:10:49,750 --> 01:10:48,560

trees marking the predicted preons in

1766

01:10:52,709 --> 01:10:49,760

all

1767

01:10:55,350 --> 01:10:52,719

uh available high quality proteomes the

1768

01:10:57,830 --> 01:10:55,360

blue lines on the tree indicate proteome

1769

01:10:59,990 --> 01:10:57,840

with uh at least one per pre on

1770

01:11:01,990 --> 01:11:00,000

candidate in it the bars around the

1771

01:11:04,630 --> 01:11:02,000

three indicate how many prion candidates

1772

01:11:06,390 --> 01:11:04,640

per proteom we have found so blue is

1773

01:11:09,270 --> 01:11:06,400

more than five green is more than ten

1774

01:11:10,070 --> 01:11:09,280

and fif and red is more than fifteen

1775

01:11:12,950 --> 01:11:10,080

uh

1776

01:11:14,790 --> 01:11:12,960

pre and candidates per thousand proteins

1777

01:11:16,630 --> 01:11:14,800

the take-home message is that eukarya

1778

01:11:18,709 --> 01:11:16,640

have much more prion candidates per

1779

01:11:21,350 --> 01:11:18,719

protein than other domains and it could

1780

01:11:23,910 --> 01:11:21,360

be that better protein aggregation

1781

01:11:26,390 --> 01:11:23,920

handling systems in eukaryotes allow

1782

01:11:29,910 --> 01:11:26,400

them to use prunes for more widely

1783

01:11:31,669 --> 01:11:29,920

avoiding lethal aggregations but

1784

01:11:33,350 --> 01:11:31,679

it could also just be a bias of a

1785

01:11:35,910 --> 01:11:33,360

prediction system that is trained on

1786

01:11:37,990 --> 01:11:35,920

eukaryotic proteins

1787

01:11:40,149 --> 01:11:38,000

so next we looked at enriched functions

1788

01:11:42,390 --> 01:11:40,159

of preon candidates in different domains

1789

01:11:44,470 --> 01:11:42,400

enriched means that these specific geo

1790

01:11:47,030 --> 01:11:44,480

terms were more likely to be found in

1791

01:11:53,510 --> 01:11:47,040

prion

1792

01:11:55,750 --> 01:11:53,520

domain and we found two enriched

1793

01:11:57,750 --> 01:11:55,760

functions coexisting with prion domains

1794

01:12:00,070 --> 01:11:57,760

that are conserved across all three

1795

01:12:03,669 --> 01:12:00,080

domains of life calcium ion binding and

1796

01:12:06,550 --> 01:12:03,679

helicases calcium ion biting is a common

1797

01:12:08,630 --> 01:12:06,560

for proteins engage in signaling and

1798

01:12:10,790 --> 01:12:08,640

this observation goes well

1799

01:12:13,510 --> 01:12:10,800

uh in line with the hypothesis that

1800

01:12:15,830 --> 01:12:13,520

prions can work as hubs that integrate

1801

01:12:18,070 --> 01:12:15,840

diverse inputs and actuate diverse

1802

01:12:20,310 --> 01:12:18,080

outputs as molecular switches

1803

01:12:22,709 --> 01:12:20,320

just like in signaling should do and

1804

01:12:25,590 --> 01:12:22,719

helicases can influence activity of many

1805

01:12:27,910 --> 01:12:25,600

genes at the same time and this can

1806

01:12:30,630 --> 01:12:27,920

provide immediate access to genetically

1807

01:12:33,669 --> 01:12:30,640

complex traits uh this role of prions

1808

01:12:35,830 --> 01:12:33,679

was already suggested in east and our

1809

01:12:38,390 --> 01:12:35,840

data shows that it could actually be a

1810

01:12:40,950 --> 01:12:38,400

concert function of prions and all

1811

01:12:43,830 --> 01:12:40,960

domains of life and potentially the most

1812

01:12:45,990 --> 01:12:43,840

ancient prion functions as well

1813

01:12:48,310 --> 01:12:46,000

so looking at keg annotations of

1814

01:12:50,470 --> 01:12:48,320

proteins annotated with geo as calcium

1815

01:12:52,470 --> 01:12:50,480

ion binding because consistently we

1816

01:12:55,030 --> 01:12:52,480

found the same description

1817

01:12:57,510 --> 01:12:55,040

uh in all domains of life but none of

1818

01:12:59,189 --> 01:12:57,520

them was yet shown to behave as a prion

1819

01:13:00,790 --> 01:12:59,199

an experiment so these are all very

1820

01:13:03,350 --> 01:13:00,800

interesting candidates to study in the

1821

01:13:06,070 --> 01:13:03,360

lab looking at keg annotations of

1822

01:13:08,709 --> 01:13:06,080

another they did as helicases we found

1823

01:13:11,030 --> 01:13:08,719

several confirmed prions in bacteria the

1824

01:13:13,350 --> 01:13:11,040

most common ko annotation was

1825

01:13:15,189 --> 01:13:13,360

transcription termination factor rho and

1826

01:13:17,669 --> 01:13:15,199

the rho protein was the first pre and

1827

01:13:20,630 --> 01:13:17,679

confirmed in bacteria specifically uh

1828

01:13:23,430 --> 01:13:20,640

clostridium botulinum so in eukaryotes

1829

01:13:26,709 --> 01:13:23,440

multiple different helicases showed up

1830

01:13:28,709 --> 01:13:26,719

in the data set including ddx 3 5 and 6.

1831

01:13:30,630 --> 01:13:28,719

in a very recent publication our

1832

01:13:32,229 --> 01:13:30,640

collaborators from stanford they showed

1833

01:13:35,030 --> 01:13:32,239

the ddx-5

1834

01:13:37,030 --> 01:13:35,040

uh forms cytoplasmic aggregates in old

1835

01:13:38,630 --> 01:13:37,040

fish and mice

1836

01:13:40,950 --> 01:13:38,640

and all they when they express it in

1837

01:13:43,270 --> 01:13:40,960

yeast that form heritable aggregates so

1838

01:13:46,070 --> 01:13:43,280

these experiments strength strengthens

1839

01:13:47,910 --> 01:13:46,080

our confidence in the prediction model

1840

01:13:49,270 --> 01:13:47,920

uh so let's go beyond the enriched

1841

01:13:51,590 --> 01:13:49,280

functions now

1842

01:13:54,550 --> 01:13:51,600

on the and we have to finish

1843

01:13:56,630 --> 01:13:54,560

all right so that's a conclusion

1844

01:13:59,030 --> 01:13:56,640

on the left side there is there are

1845

01:14:00,870 --> 01:13:59,040

numbers of overlapping

1846

01:14:02,709 --> 01:14:00,880

functions so there is many more if we're

1847

01:14:05,350 --> 01:14:02,719

not looking at the

1848

01:14:07,430 --> 01:14:05,360

enriched ones so i'd like to finish the

1849

01:14:10,229 --> 01:14:07,440

presentation with the hypothesis that we

1850

01:14:12,630 --> 01:14:10,239

came up uh during uh looking analyzing

1851

01:14:15,189 --> 01:14:12,640

this data that prion regulation

1852

01:14:17,510 --> 01:14:15,199

of the fundamental sub-processes could

1853

01:14:19,270 --> 01:14:17,520

be an evolutionary ancient one even if

1854

01:14:20,229 --> 01:14:19,280

the sequence of the individual pre and

1855

01:14:22,709 --> 01:14:20,239

domain

1856

01:14:24,709 --> 01:14:22,719

are not evolutionary conserved and thank

1857

01:14:26,390 --> 01:14:24,719

you so much for your attention and to my

1858

01:14:31,590 --> 01:14:26,400

co-workers

1859

01:14:34,709 --> 01:14:33,030

so

1860

01:14:36,550 --> 01:14:34,719

unfortunately we don't have time for

1861

01:14:39,270 --> 01:14:36,560

questions um

1862

01:14:40,950 --> 01:14:39,280

uh but uh moving along to our final uh

1863

01:14:42,870 --> 01:14:40,960

speaker of the session

1864

01:14:45,430 --> 01:14:42,880

uh foreign

1865

01:14:47,110 --> 01:14:45,440

will be uh

1866

01:14:49,189 --> 01:14:47,120

uh presenting work entitled the

1867

01:14:50,790 --> 01:14:49,199

phenotype of the last common

1868

01:14:55,110 --> 01:14:50,800

of the last universal common ancestor

1869

01:14:55,120 --> 01:14:59,750

and then three minutes

1870

01:15:18,550 --> 01:15:01,910

okay should they just close this and

1871

01:15:25,110 --> 01:15:21,669

uh hello everyone um

1872

01:15:27,990 --> 01:15:25,120

great to be here um most of the main

1873

01:15:31,189 --> 01:15:28,000

message let's say from today can be

1874

01:15:33,189 --> 01:15:31,199

summarized in the first conclusion of

1875

01:15:36,470 --> 01:15:33,199

antonio lascano talk

1876

01:15:39,590 --> 01:15:36,480

that is uh luca is probably a complex

1877

01:15:41,750 --> 01:15:39,600

population of cells that resembles

1878

01:15:44,070 --> 01:15:41,760

modern prokaryotes

1879

01:15:46,229 --> 01:15:44,080

uh i'm currently a research associate

1880

01:15:48,390 --> 01:15:46,239

working on malaria at harvard university

1881

01:15:50,310 --> 01:15:48,400

and broad institute but

1882

01:15:52,470 --> 01:15:50,320

let's talk about luca

1883

01:15:55,350 --> 01:15:52,480

so though

1884

01:15:57,510 --> 01:15:55,360

as laskano also has mentioned it uh luca

1885

01:15:58,310 --> 01:15:57,520

is is is way

1886

01:16:04,070 --> 01:15:58,320

uh

1887

01:16:08,470 --> 01:16:04,080

after life originated that is to say if

1888

01:16:11,270 --> 01:16:08,480

we consider the darwinian threshold

1889

01:16:15,030 --> 01:16:11,280

hypothesis suggested by ways that is

1890

01:16:18,630 --> 01:16:15,040

there is an rna world there is then

1891

01:16:20,550 --> 01:16:18,640

progeny note like up to lucas so when

1892

01:16:23,110 --> 01:16:20,560

talking about luca we are talking about

1893

01:16:24,630 --> 01:16:23,120

this common ancestor of our living

1894

01:16:27,350 --> 01:16:24,640

organism today

1895

01:16:31,030 --> 01:16:27,360

anything related to luca uh

1896

01:16:32,310 --> 01:16:31,040

reconstruction is subject to debate uh

1897

01:16:35,189 --> 01:16:32,320

obviously

1898

01:16:37,669 --> 01:16:35,199

so we all know this uh image and we grow

1899

01:16:39,750 --> 01:16:37,679

up with this with having a three domain

1900

01:16:43,110 --> 01:16:39,760

of life trees with bacteria arcane

1901

01:16:44,229 --> 01:16:43,120

eukarya and as you know the discovery of

1902

01:16:46,310 --> 01:16:44,239

asgard

1903

01:16:47,750 --> 01:16:46,320

archaea

1904

01:16:49,350 --> 01:16:47,760

and other

1905

01:16:51,590 --> 01:16:49,360

arcane

1906

01:16:53,030 --> 01:16:51,600

cells that share many characteristics

1907

01:16:53,830 --> 01:16:53,040

with eukaryotes

1908

01:16:56,070 --> 01:16:53,840

uh

1909

01:16:58,070 --> 01:16:56,080

lead us to think that there is probably

1910

01:17:00,390 --> 01:16:58,080

just two domains of life bacteria and

1911

01:17:03,430 --> 01:17:00,400

archaea with eukaryotes uh

1912

01:17:07,430 --> 01:17:03,440

is a group that emerged much later

1913

01:17:09,510 --> 01:17:07,440

uh during evolution with luca and its

1914

01:17:12,310 --> 01:17:09,520

derived um

1915

01:17:14,630 --> 01:17:12,320

and its distance like the last bacterial

1916

01:17:17,430 --> 01:17:14,640

common ancestor and the last rkl common

1917

01:17:20,390 --> 01:17:17,440

ancestor for which also

1918

01:17:22,630 --> 01:17:20,400

i will show some more constructions

1919

01:17:24,950 --> 01:17:22,640

so obviously when we come to the

1920

01:17:27,990 --> 01:17:24,960

reconstruction of ancestral states and

1921

01:17:30,390 --> 01:17:28,000

go back in time we usually use fossils

1922

01:17:33,990 --> 01:17:30,400

and fortunately for microbes

1923

01:17:35,189 --> 01:17:34,000

this is not possible and we therefore

1924

01:17:38,470 --> 01:17:35,199

rely on

1925

01:17:39,590 --> 01:17:38,480

mainly on the gene genomes or genetic

1926

01:17:42,830 --> 01:17:39,600

sequences

1927

01:17:46,310 --> 01:17:42,840

or uh other any other statistical

1928

01:17:48,149 --> 01:17:46,320

inference in order to reconstruct past

1929

01:17:49,189 --> 01:17:48,159

characters

1930

01:17:50,229 --> 01:17:49,199

so

1931

01:17:52,709 --> 01:17:50,239

uh

1932

01:17:56,310 --> 01:17:52,719

we for a long time luca has been taught

1933

01:17:58,229 --> 01:17:56,320

as a minimal or primitive cell like

1934

01:18:01,669 --> 01:17:58,239

maybe half a life and recent

1935

01:18:03,750 --> 01:18:01,679

reconstructions by ways it all have uh

1936

01:18:05,350 --> 01:18:03,760

concluded that luca must have been like

1937

01:18:06,990 --> 01:18:05,360

a very simple

1938

01:18:10,390 --> 01:18:07,000

cell with about

1939

01:18:13,510 --> 01:18:10,400

350 proteins this is the just to give

1940

01:18:16,630 --> 01:18:13,520

you an idea is about the size of on the

1941

01:18:19,669 --> 01:18:16,640

obligates on the symbiotic bacteria that

1942

01:18:21,030 --> 01:18:19,679

we found we find today so all of the

1943

01:18:23,510 --> 01:18:21,040

reconstructions

1944

01:18:25,830 --> 01:18:23,520

that we know of are based on the absence

1945

01:18:29,350 --> 01:18:25,840

or presence of genes

1946

01:18:30,149 --> 01:18:29,360

and based on genome genomic data here i

1947

01:18:30,950 --> 01:18:30,159

will

1948

01:18:33,830 --> 01:18:30,960

uh

1949

01:18:36,390 --> 01:18:33,840

talk about a different approach that is

1950

01:18:39,910 --> 01:18:36,400

based on on on on

1951

01:18:41,590 --> 01:18:39,920

a phenotype and not genomes so we know

1952

01:18:44,070 --> 01:18:41,600

that it is still

1953

01:18:47,350 --> 01:18:44,080

inherently difficult to predict

1954

01:18:49,030 --> 01:18:47,360

phenotype simply by a presence or

1955

01:18:51,750 --> 01:18:49,040

absence of genes although we can do it

1956

01:18:53,189 --> 01:18:51,760

in some cases and here we will use so if

1957

01:18:55,510 --> 01:18:53,199

we consider

1958

01:18:57,750 --> 01:18:55,520

observing traits that we have today

1959

01:18:59,350 --> 01:18:57,760

let's say mortality or shape or whatever

1960

01:19:01,430 --> 01:18:59,360

so you we can use

1961

01:19:04,229 --> 01:19:01,440

in this example by asian

1962

01:19:08,310 --> 01:19:04,239

inferences and using a

1963

01:19:10,870 --> 01:19:08,320

markov models and we can infer

1964

01:19:13,110 --> 01:19:10,880

ancestral states and obtain some

1965

01:19:15,590 --> 01:19:13,120

posterior probabilities

1966

01:19:17,189 --> 01:19:15,600

for for those states

1967

01:19:19,350 --> 01:19:17,199

so

1968

01:19:22,790 --> 01:19:19,360

those ancestral state reconstruction

1969

01:19:26,310 --> 01:19:22,800

methods has been used to for like

1970

01:19:28,630 --> 01:19:26,320

diatoms that has been done also on other

1971

01:19:31,669 --> 01:19:28,640

eukaryotes and more recently we we used

1972

01:19:34,830 --> 01:19:31,679

this method to reconstruct uh ancestral

1973

01:19:36,870 --> 01:19:34,840

states for fermicutes uh bacteria

1974

01:19:39,030 --> 01:19:36,880

so to

1975

01:19:41,270 --> 01:19:39,040

reconstruct the character the ancient

1976

01:19:44,630 --> 01:19:41,280

character of lucca i have collected more

1977

01:19:47,030 --> 01:19:44,640

than 3 000 phenotypic characters and i

1978

01:19:47,750 --> 01:19:47,040

went during three years and a half over

1979

01:19:50,550 --> 01:19:47,760

the

1980

01:19:53,510 --> 01:19:50,560

berges manual of systematic bacteriology

1981

01:19:54,310 --> 01:19:53,520

and we collected data on shape motility

1982

01:19:57,110 --> 01:19:54,320

uh

1983

01:19:58,790 --> 01:19:57,120

environmental data spar formation

1984

01:19:59,990 --> 01:19:58,800

membrane etc

1985

01:20:02,709 --> 01:20:00,000

and

1986

01:20:06,310 --> 01:20:02,719

obviously when we reconstruct ancestral

1987

01:20:08,709 --> 01:20:06,320

states uh there is the problem of uh or

1988

01:20:11,510 --> 01:20:08,719

horizontal gene transfer in our case

1989

01:20:15,110 --> 01:20:11,520

what we did is we did some simulations

1990

01:20:16,950 --> 01:20:15,120

on a horizontal trade transfer that is

1991

01:20:19,110 --> 01:20:16,960

considering a trait

1992

01:20:20,229 --> 01:20:19,120

uh and how it can be transferred and how

1993

01:20:23,030 --> 01:20:20,239

this

1994

01:20:25,270 --> 01:20:23,040

transfer might impact our constructions

1995

01:20:28,149 --> 01:20:25,280

and just to summarize here what i want

1996

01:20:30,310 --> 01:20:28,159

to see to show you we did two

1997

01:20:32,310 --> 01:20:30,320

different simulations one that is a

1998

01:20:35,750 --> 01:20:32,320

local transfer approach and the second

1999

01:20:38,470 --> 01:20:35,760

one is a global transfer approach and

2000

01:20:41,350 --> 01:20:38,480

we expect that using a bromanian motion

2001  
01:20:44,390 --> 01:20:41,360  
model and we and we expect that the the

2002  
01:20:46,310 --> 01:20:44,400  
slot will in any case and

2003  
01:20:47,669 --> 01:20:46,320  
that it doesn't impact our construction

2004  
01:20:50,550 --> 01:20:47,679  
it will be one

2005  
01:20:53,430 --> 01:20:50,560  
and as you can see the more we increase

2006  
01:20:56,950 --> 01:20:53,440  
the number of simulation up to 1000

2007  
01:20:58,950 --> 01:20:56,960  
for the local uh inference for local

2008  
01:21:01,030 --> 01:20:58,960  
transfer it does not impact

2009  
01:21:03,830 --> 01:21:01,040  
significantly our inference but for the

2010  
01:21:07,030 --> 01:21:03,840  
global transfer when we simulate this up

2011  
01:21:10,229 --> 01:21:07,040  
to 1000 event there is a huge

2012  
01:21:12,629 --> 01:21:10,239  
variance and obviously it does impact

2013  
01:21:16,390 --> 01:21:12,639

the the the inferences

2014

01:21:19,510 --> 01:21:16,400

so what's we have reconstructed so based

2015

01:21:21,910 --> 01:21:19,520

on uh this method uh and the biasing

2016

01:21:24,790 --> 01:21:21,920

framework we reconstructed luca as a

2017

01:21:27,590 --> 01:21:24,800

halo tolerant hyperthermophile or

2018

01:21:30,470 --> 01:21:27,600

although it is still there is debate

2019

01:21:32,950 --> 01:21:30,480

about the hyperthermophilia fluca it was

2020

01:21:34,790 --> 01:21:32,960

uh it has evolved in neutral ph and in

2021

01:21:38,070 --> 01:21:34,800

aquatic environments

2022

01:21:40,709 --> 01:21:38,080

uh it was anaerobic uh chemologotrophic

2023

01:21:43,830 --> 01:21:40,719

and uh curiously it has catalase and

2024

01:21:46,149 --> 01:21:43,840

oxidase which exists that it might uh

2025

01:21:48,149 --> 01:21:46,159

it was probably able to resist oxidative

2026

01:21:50,870 --> 01:21:48,159

stress uh

2027

01:21:53,110 --> 01:21:50,880

but we know that concentration of oxygen

2028

01:21:54,830 --> 01:21:53,120

at that time might have been like

2029

01:21:57,750 --> 01:21:54,840

less than

2030

01:21:59,590 --> 01:21:57,760

0.001 uh so

2031

01:22:01,910 --> 01:21:59,600

this the presence of catalyst and

2032

01:22:03,990 --> 01:22:01,920

oxidase may be also due to the fact of

2033

01:22:05,350 --> 01:22:04,000

possible horizontal ancient horizontal

2034

01:22:08,950 --> 01:22:05,360

gene transfer

2035

01:22:11,189 --> 01:22:08,960

so the the the distance of

2036

01:22:13,430 --> 01:22:11,199

other distance of luca the last rkl

2037

01:22:15,990 --> 01:22:13,440

common ancestor has also similar

2038

01:22:17,750 --> 01:22:16,000

characteristics as luca has been halo

2039

01:22:20,390 --> 01:22:17,760

turreted hollow tolerant

2040

01:22:23,270 --> 01:22:20,400

hyperthermophile we were not sure if it

2041

01:22:25,430 --> 01:22:23,280

was aerobic or anaerobic

2042

01:22:27,750 --> 01:22:25,440

for the last bacterial common ancestor

2043

01:22:30,470 --> 01:22:27,760

it was also anaerobic hemolytrophic it

2044

01:22:33,350 --> 01:22:30,480

has also catalyzed and

2045

01:22:35,669 --> 01:22:33,360

it was halo tolerance and thermophile it

2046

01:22:37,669 --> 01:22:35,679

was not hyperthermophile but thermophile

2047

01:22:38,550 --> 01:22:37,679

and evolving neutral ph

2048

01:22:39,669 --> 01:22:38,560

so

2049

01:22:41,750 --> 01:22:39,679

for now

2050

01:22:44,629 --> 01:22:41,760

anything that we think about luca like

2051  
01:22:46,790 --> 01:22:44,639  
for example it's a morphology it's based

2052  
01:22:49,990 --> 01:22:46,800  
on intuition so we think that it might

2053  
01:22:51,830 --> 01:22:50,000  
have looked like a prokaryote but it's

2054  
01:22:54,709 --> 01:22:51,840  
we never when

2055  
01:22:56,229 --> 01:22:54,719  
it has never been reconstructed so

2056  
01:22:58,470 --> 01:22:56,239  
here we

2057  
01:23:01,590 --> 01:22:58,480  
the variety of bacterial shape or

2058  
01:23:03,590 --> 01:23:01,600  
archaeal shape is huge but we we summer

2059  
01:23:05,510 --> 01:23:03,600  
we simplify this into three main

2060  
01:23:07,990 --> 01:23:05,520  
categories like cocoid that is just

2061  
01:23:10,629 --> 01:23:08,000  
divide and the road that it has a known

2062  
01:23:13,270 --> 01:23:10,639  
elongation machinery and avoid

2063  
01:23:14,390 --> 01:23:13,280

that has like a septal growth and then

2064

01:23:17,030 --> 01:23:14,400

division

2065

01:23:19,189 --> 01:23:17,040

so when we and feared uh reconstructed

2066

01:23:23,110 --> 01:23:19,199

the ancestral state we found that luca

2067

01:23:25,350 --> 01:23:23,120

was probably an avoid motile cell that

2068

01:23:27,350 --> 01:23:25,360

has a monodermic uh

2069

01:23:29,910 --> 01:23:27,360

it was monoderm like having a

2070

01:23:32,709 --> 01:23:29,920

once a single membrane and we were not

2071

01:23:36,149 --> 01:23:32,719

sure it was performing or not and it has

2072

01:23:37,669 --> 01:23:36,159

a genome size of approximately 2.5 which

2073

01:23:39,430 --> 01:23:37,679

is close to

2074

01:23:41,189 --> 01:23:39,440

current

2075

01:23:44,070 --> 01:23:41,199

genome size in some

2076

01:23:46,790 --> 01:23:44,080

bacteria and archaea so the rkl common

2077

01:23:49,590 --> 01:23:46,800

ancestor was also avoid motile has a

2078

01:23:52,149 --> 01:23:49,600

cell wall and was monodermic

2079

01:23:55,590 --> 01:23:52,159

and the last bacterial common ancestor

2080

01:23:57,910 --> 01:23:55,600

was likely a rod shaped uh

2081

01:24:00,229 --> 01:23:57,920

like bacterium it has a cell wall we

2082

01:24:02,390 --> 01:24:00,239

were not sure it was monodermic and it

2083

01:24:04,709 --> 01:24:02,400

had it was probably spore

2084

01:24:07,750 --> 01:24:04,719

non-sport-forming this reconstruction of

2085

01:24:10,709 --> 01:24:07,760

the last bacterial common ancestor is uh

2086

01:24:12,790 --> 01:24:10,719

similar to what has just been done

2087

01:24:15,189 --> 01:24:12,800

recently by coleman using a genomic

2088

01:24:16,550 --> 01:24:15,199

approach except that they found it was a

2089

01:24:18,870 --> 01:24:16,560

dynamic

2090

01:24:19,910 --> 01:24:18,880

cell

2091

01:24:22,149 --> 01:24:19,920

so

2092

01:24:26,550 --> 01:24:22,159

given this complexity of

2093

01:24:29,189 --> 01:24:26,560

luca shape and size and genome it's

2094

01:24:32,550 --> 01:24:29,199

given the also the the earth formation

2095

01:24:35,270 --> 01:24:32,560

timeline and given uh when

2096

01:24:37,910 --> 01:24:35,280

the luca had appeared on earth at the

2097

01:24:42,390 --> 01:24:37,920

first time life must have been evolved

2098

01:24:45,110 --> 01:24:42,400

very quickly uh cellular into complex

2099

01:24:49,030 --> 01:24:45,120

cells and it was probably as much

2100

01:24:51,270 --> 01:24:49,040

complex as many uh modern uh

2101  
01:24:52,070 --> 01:24:51,280  
bacteria and archaea

2102  
01:24:53,590 --> 01:24:52,080  
so

2103  
01:24:55,750 --> 01:24:53,600  
this is one of the

2104  
01:24:58,470 --> 01:24:55,760  
message the second message i want to

2105  
01:25:00,709 --> 01:24:58,480  
tell you and that is for me very

2106  
01:25:01,910 --> 01:25:00,719  
important since i've i've

2107  
01:25:04,870 --> 01:25:01,920  
worked with

2108  
01:25:07,990 --> 01:25:04,880  
many biophysicists and mathematicians is

2109  
01:25:12,390 --> 01:25:08,000  
the scale at which we are uh observing

2110  
01:25:14,870 --> 01:25:12,400  
or studying uh luca or microbes so

2111  
01:25:16,350 --> 01:25:14,880  
at the small scale at the micro scale

2112  
01:25:18,790 --> 01:25:16,360  
the physics became

2113  
01:25:21,510 --> 01:25:18,800

counterintuitive it's not the physics we

2114

01:25:23,189 --> 01:25:21,520

are experiencing daily gravity has not

2115

01:25:25,990 --> 01:25:23,199

the same importance that it has on

2116

01:25:28,470 --> 01:25:26,000

macroscopic organisms and by studying

2117

01:25:31,430 --> 01:25:28,480

microbes and by reconstructing ancestral

2118

01:25:33,189 --> 01:25:31,440

environment or ancestral uh selective

2119

01:25:34,950 --> 01:25:33,199

pressure uh

2120

01:25:38,310 --> 01:25:34,960

even at the time of luca we have to

2121

01:25:40,709 --> 01:25:38,320

consider the micro scale biophysics like

2122

01:25:43,270 --> 01:25:40,719

for example the low reynold numbers in

2123

01:25:45,430 --> 01:25:43,280

which it evolves brownian motion

2124

01:25:49,270 --> 01:25:45,440

kinematic reversibility and molecular

2125

01:25:52,149 --> 01:25:49,280

diffusion just to cite a few

2126

01:25:54,950 --> 01:25:52,159

so this is very important elements in

2127

01:25:56,629 --> 01:25:54,960

when studying microbes we tend generally

2128

01:25:59,189 --> 01:25:56,639

i i highlight this because we tend

2129

01:26:01,430 --> 01:25:59,199

generally as microbiologists to think

2130

01:26:03,990 --> 01:26:01,440

with our intuitive

2131

01:26:05,590 --> 01:26:04,000

physics uh when observing microbes while

2132

01:26:07,830 --> 01:26:05,600

we should not

2133

01:26:09,510 --> 01:26:07,840

finally if we look at

2134

01:26:10,470 --> 01:26:09,520

life in in space

2135

01:26:16,550 --> 01:26:10,480

i will

2136

01:26:20,790 --> 01:26:16,560

probably it will be microbial first

2137

01:26:23,270 --> 01:26:20,800

before it can be in if if we find

2138

01:26:26,229 --> 01:26:23,280

life in at least our solar system i will

2139

01:26:28,550 --> 01:26:26,239

look for microbials and i will look for

2140

01:26:32,950 --> 01:26:28,560

motility i will look for dna i will look

2141

01:26:36,229 --> 01:26:32,960

for any sign that is uh that is that is

2142

01:26:38,790 --> 01:26:36,239

uh that is similar to what we observe on

2143

01:26:41,110 --> 01:26:38,800

on microbes on earth

2144

01:26:43,350 --> 01:26:41,120

and with this i would like to thank my

2145

01:26:46,709 --> 01:26:43,360

colleagues and collaborators stewards

2146

01:26:55,990 --> 01:26:46,719

say chris and andrew and thanks if you

2147

01:27:03,990 --> 01:26:57,669

great thank you so we have time for a

2148

01:27:07,990 --> 01:27:05,510

on the left

2149

01:27:11,669 --> 01:27:08,000

thank you very much for watching again

2150

01:27:15,910 --> 01:27:13,189

and you mentioned that there is no

2151  
01:27:16,830 --> 01:27:15,920  
participation of gravity due to small

2152  
01:27:20,070 --> 01:27:16,840  
size

2153  
01:27:23,189 --> 01:27:20,080  
right i said it's negligible it's very

2154  
01:27:27,270 --> 01:27:23,199  
negligible in comparison to to our scale

2155  
01:27:29,270 --> 01:27:27,280  
yeah so on a scale of a sphere of a one

2156  
01:27:32,790 --> 01:27:29,280  
micron

2157  
01:27:34,950 --> 01:27:32,800  
considering different uh in a

2158  
01:27:37,830 --> 01:27:34,960  
in a density 10 percent

2159  
01:27:41,110 --> 01:27:37,840  
is going to descend in a water with a

2160  
01:27:44,149 --> 01:27:41,120  
speed uh one millimeter per hour

2161  
01:27:47,350 --> 01:27:44,159  
if it's a five micron it's a

2162  
01:27:51,270 --> 01:27:47,360  
one millimeter uh no sorry

2163  
01:27:52,950 --> 01:27:51,280

one micron is about 24 hours and five

2164

01:27:55,590 --> 01:27:52,960

microns uh

2165

01:27:57,350 --> 01:27:55,600

radius is about uh

2166

01:27:59,270 --> 01:27:57,360

one hour

2167

01:28:01,830 --> 01:27:59,280

yes approximately

2168

01:28:02,950 --> 01:28:01,840

so it's a it's still

2169

01:28:04,470 --> 01:28:02,960

sizeable

2170

01:28:06,790 --> 01:28:04,480

moving

2171

01:28:09,990 --> 01:28:06,800

it does what i mean by that it's it's it

2172

01:28:12,310 --> 01:28:10,000

will not have really the same impact as

2173

01:28:13,830 --> 01:28:12,320

it at of course it has

2174

01:28:16,709 --> 01:28:13,840

there is there is gravity that's

2175

01:28:17,590 --> 01:28:16,719

mosquito gravity at all scales but it is

2176

01:28:20,149 --> 01:28:17,600

not

2177

01:28:22,390 --> 01:28:20,159

in term of evolutionary impact or

2178

01:28:25,270 --> 01:28:22,400

selective pressures i don't think it

2179

01:28:28,229 --> 01:28:25,280

will be comparable to what we observe uh

2180

01:28:29,910 --> 01:28:28,239

on on macro scale organisms that's just

2181

01:28:33,030 --> 01:28:29,920

what i mean yeah unless selective

2182

01:28:35,750 --> 01:28:33,040

pressure is uv

2183

01:28:37,830 --> 01:28:35,760

yeah so thank you next question

2184

01:28:38,790 --> 01:28:37,840

all right that was a great thought thank

2185

01:28:40,629 --> 01:28:38,800

you thank you

2186

01:28:43,350 --> 01:28:40,639

can you tell us about

2187

01:28:46,390 --> 01:28:43,360

what you think that happened between the

2188

01:28:48,070 --> 01:28:46,400

in terms of the the genomic genomic

2189

01:28:50,390 --> 01:28:48,080

increase between the last universal

2190

01:28:51,270 --> 01:28:50,400

common ancestor and to the last

2191

01:28:53,750 --> 01:28:51,280

uh

2192

01:28:55,590 --> 01:28:53,760

bacterial common ancestor because it

2193

01:28:57,430 --> 01:28:55,600

seems that you found like

2194

01:28:59,430 --> 01:28:57,440

some increase in the genome right but

2195

01:29:02,070 --> 01:28:59,440

not in the last uh

2196

01:29:05,590 --> 01:29:02,080

archaea common ancestor

2197

01:29:08,950 --> 01:29:05,600

you mean here yeah from

2198

01:29:11,750 --> 01:29:08,960

2.5 to do you think that was like a new

2199

01:29:12,950 --> 01:29:11,760

genome new genes evolving like or gene

2200

01:29:14,709 --> 01:29:12,960

transfer

2201

01:29:16,709 --> 01:29:14,719

or doubling of

2202

01:29:17,830 --> 01:29:16,719

like genomic duplication something like

2203

01:29:21,430 --> 01:29:17,840

this

2204

01:29:23,669 --> 01:29:21,440

that's a good question i i personally uh

2205

01:29:25,270 --> 01:29:23,679

i i i don't have like a clear

2206

01:29:26,310 --> 01:29:25,280

explanation for that

2207

01:29:28,229 --> 01:29:26,320

uh

2208

01:29:30,950 --> 01:29:28,239

all what i can say that there is the

2209

01:29:33,430 --> 01:29:30,960

constructions were done independently so

2210

01:29:35,830 --> 01:29:33,440

we didn't we we tested for trends if

2211

01:29:38,870 --> 01:29:35,840

there is increase or decrease uh in

2212

01:29:40,149 --> 01:29:38,880

genome through time uh using different

2213

01:29:41,750 --> 01:29:40,159

phylogenies

2214

01:29:45,270 --> 01:29:41,760

but we

2215

01:29:47,830 --> 01:29:45,280

we i didn't specifically test for like

2216

01:29:50,229 --> 01:29:47,840

the the increase or decrease for from

2217

01:29:52,470 --> 01:29:50,239

luca to laca for example

2218

01:29:54,629 --> 01:29:52,480

but thanks that's a good question yeah

2219

01:29:56,709 --> 01:29:54,639

so unfortunately we're out of time yes

2220

01:30:02,229 --> 01:29:56,719

sure uh but let's thank our speakers

2221

01:30:05,830 --> 01:30:04,070

and yeah and thank you everyone for your