NASA Astrobiology Institute

Director's Seminar Series

4/28/2008 - Steven Benner

Experimental Paleogenetics

Philosophical challenge: Most scientists view historical hypotheses inherently non-scientific.
Response: Create a new field, experimental paleogenetics, which tests historical hypotheses by resurrecting parts of the historical past for laboratory study.
Task: Infer structure of ancestral life forms from structure of their descendents.
Lessons: RNA world existed, and was complex. Bacteria lived three billion years ago at 65°C. Aromatase in pigs manages large litters; alcohol fermentation in yeast response to Cretaceous environment changes.
Current limits: Always can use more sequences (but EF reconstructions not greatly changed by the Sargasso Sea); extinctions have eliminated the deepest record; could use a new branch of life.

The protogenome, separated from origins by a complex RNA world, is not near the origins of life. Not much simpler.

1
00:00:09,200 --> 00:00:06,980
good morning everyone welcome to a nai

2
00:00:11,299 --> 00:00:09,210
director seminar I just heard an open

3
00:00:12,830 --> 00:00:11,309
mic which i'm pretty sure wasn't Steve

4
00:00:16,099 --> 00:00:12,840
so you might just want to check your

5
00:00:19,700 --> 00:00:16,109
mics I am very very pleased that Steve

6
00:00:21,349 --> 00:00:19,710
Benner is here to give the NAI director

7
00:00:24,380 --> 00:00:21,359
seminar this morning or this afternoon

8
00:00:26,630 --> 00:00:24,390
depending on where you are Steve's group

9
00:00:29,480 --> 00:00:26,640
at the foundation for applied molecular

10
00:00:32,810 --> 00:00:29,490
evolution which is a foundation that he

11
00:00:35,810 --> 00:00:32,820
began is addressing some of the most

12
00:00:37,970 --> 00:00:35,820
profound questions in understanding our

13
00:00:39,619 --> 00:00:37,980

nature of life and in particular the

14
00:00:43,910 --> 00:00:39,629
question that Steve's group is

15
00:00:46,100 --> 00:00:43,920
addressing is what's required of life in

16
00:00:48,500 --> 00:00:46,110
that it couldn't have been any other way

17
00:00:50,090 --> 00:00:48,510
and what's contingent and that it could

18
00:00:53,090 --> 00:00:50,100
have been lots of other ways and Steve

19
00:00:55,340 --> 00:00:53,100
as a chemist is approaching this through

20
00:00:57,290 --> 00:00:55,350
synthetic biology which is a field which

21
00:01:00,319 --> 00:00:57,300
steve has and his colleagues have been a

22
00:01:02,479 --> 00:01:00,329
pioneer in developing in particular what

23
00:01:05,539 --> 00:01:02,489
they have done is to use organic

24
00:01:07,160 --> 00:01:05,549
chemical synthesis to prepare artificial

25
00:01:09,440 --> 00:01:07,170
genetic systems and then actually

26
00:01:12,530 --> 00:01:09,450
operate those systems to produce

27
00:01:14,570 --> 00:01:12,540
proteins that have amino acids other

28
00:01:17,270 --> 00:01:14,580
than the amino acids that are normally

29
00:01:18,920 --> 00:01:17,280
used by proteins and they're applying

30
00:01:24,760 --> 00:01:18,930
these in a wide variety of areas

31
00:01:27,020 --> 00:01:24,770
including dressing haha y ok Steve

32
00:01:30,200 --> 00:01:27,030
including addressing the big questions

33
00:01:32,830 --> 00:01:30,210
and also in areas such as personalized

34
00:01:35,359 --> 00:01:32,840
medicine where they are working on

35
00:01:38,450 --> 00:01:35,369
developing ways of treating individuals

36
00:01:40,940 --> 00:01:38,460
based on the individual's own genetic

37
00:01:43,370 --> 00:01:40,950
makeup so we are really really

38
00:01:45,800 --> 00:01:43,380

privileged to have Steve with us today

39
00:01:48,200 --> 00:01:45,810
to give the talk steve has both a

40
00:01:50,389 --> 00:01:48,210
bachelor's and a master's in molecular

41
00:01:53,410 --> 00:01:50,399
biophysics and biochemistry from Yale

42
00:01:59,709 --> 00:01:53,420
and a PhD in chemistry from Harvard and

43
00:02:02,780 --> 00:01:59,719
he will be speaking with us today on for

44
00:02:05,060 --> 00:02:02,790
general approaches I forget the exact

45
00:02:08,240 --> 00:02:05,070
title here I know I have it for general

46
00:02:10,729 --> 00:02:08,250
approaches to the nature of life is

47
00:02:14,120 --> 00:02:10,739
probably close enough Steve I will just

48
00:02:16,490 --> 00:02:14,130
turn it over to you ok thanks very much

49
00:02:19,160 --> 00:02:16,500
Karl Hoffmann feel free I'm not sure how

50
00:02:22,160 --> 00:02:19,170
these conferencing systems work but if

51
00:02:24,800 --> 00:02:22,170
you have an opportunity to interrupt me

52
00:02:27,860 --> 00:02:24,810
and ask the question as we go through

53
00:02:30,020 --> 00:02:27,870
this talk will feel free to do so well I

54
00:02:31,730 --> 00:02:30,030
guess you are looking at my first slide

55
00:02:34,720 --> 00:02:31,740
what is like would that be correct is

56
00:02:37,970 --> 00:02:34,730
that some place in front you yes it is

57
00:02:41,360 --> 00:02:37,980
okay excellent and this is of course is

58
00:02:44,890 --> 00:02:41,370
a question that is both provocative and

59
00:02:47,720 --> 00:02:44,900
central is the part of the problem just

60
00:02:51,710 --> 00:02:47,730
so that I now have advanced the slides

61
00:02:54,590 --> 00:02:51,720
the next one correct all it's working

62
00:02:58,010 --> 00:02:54,600
okay excellent so yeah keep in mind that

63
00:03:00,590 --> 00:02:58,020

about five years ago John Burris and I

64
00:03:03,110 --> 00:03:00,600
about John bearish persuaded me to join

65
00:03:05,000 --> 00:03:03,120
this committee that was put together by

66
00:03:06,680 --> 00:03:05,010
the National Research Council to talk

67
00:03:08,720 --> 00:03:06,690
about the limits of organic life and

68
00:03:11,030 --> 00:03:08,730
planetary systems was actually

69
00:03:13,640 --> 00:03:11,040
commissioned by NASA and the National

70
00:03:15,260 --> 00:03:13,650
Research Council put various people

71
00:03:16,430 --> 00:03:15,270
together some of whom I guess are in

72
00:03:18,620 --> 00:03:16,440
attendance here and you can see your

73
00:03:20,960 --> 00:03:18,630
names listed one of the things that the

74
00:03:23,990 --> 00:03:20,970
committee decided not to do at the

75
00:03:26,960 --> 00:03:24,000
outset was to decide not to try to

76
00:03:30,080 --> 00:03:26,970
define life I thought that was a bit

77
00:03:32,180 --> 00:03:30,090
cowardly myself because if you're going

78
00:03:35,630 --> 00:03:32,190
to argue about the limits of life you at

79
00:03:38,960 --> 00:03:35,640
least have to have some criteria for

80
00:03:41,120 --> 00:03:38,970
what a definition of life would be but

81
00:03:43,580 --> 00:03:41,130
then Carol Cleland got involved in the

82
00:03:45,610 --> 00:03:43,590
organization periphery and her point of

83
00:03:48,980 --> 00:03:45,620
course was it in order to define life

84
00:03:50,570 --> 00:03:48,990
you actually have to have a theory of

85
00:03:52,850 --> 00:03:50,580
light and in fact if you talk to any of

86
00:03:54,590 --> 00:03:52,860
these philosophers long enough you can

87
00:03:57,590 --> 00:03:54,600
see the comment which i think is on the

88
00:04:00,350 --> 00:03:57,600

bottom of the of the first slide which

89
00:04:02,600 --> 00:04:00,360
is that please go make sure i have this

90
00:04:04,310 --> 00:04:02,610
zoom to fit on my screen which is

91
00:04:07,730 --> 00:04:04,320
actually when you talk to a philosopher

92
00:04:08,960 --> 00:04:07,740
long enough they will persuade you that

93
00:04:11,210 --> 00:04:08,970
you don't even know how to define

94
00:04:12,800 --> 00:04:11,220
definition and you don't even know how

95
00:04:14,750 --> 00:04:12,810
to define water and that's one of the

96
00:04:17,270 --> 00:04:14,760
things that philosopher has i've done to

97
00:04:19,400 --> 00:04:17,280
us so very much what you talk about is

98
00:04:20,630 --> 00:04:19,410
very much connected to what you think is

99
00:04:23,719 --> 00:04:20,640
possible and what you might think

100
00:04:25,670 --> 00:04:23,729
actually exists and that of course is

101
00:04:26,150 --> 00:04:25,680
himself as driven by theory and the

102
00:04:28,160 --> 00:04:26,160
theory

103
00:04:29,600 --> 00:04:28,170
may or may not be complete in fact we

104
00:04:31,070 --> 00:04:29,610
know from the history of science that

105
00:04:33,320 --> 00:04:31,080
many times with the theories that we

106
00:04:35,630 --> 00:04:33,330
thought were quite reliable on which we

107
00:04:37,910 --> 00:04:35,640
were making constructive actions turned

108
00:04:38,930 --> 00:04:37,920
out to be not true at all so one of the

109
00:04:41,450 --> 00:04:38,940
things that we would like to do is not

110
00:04:43,610 --> 00:04:41,460
have a definition that is just a laundry

111
00:04:46,940 --> 00:04:43,620
list of the attributes of known living

112
00:04:48,980 --> 00:04:46,950
systems and I pulled the list here out

113
00:04:51,410 --> 00:04:48,990

of a textbook you know the ability to

114
00:04:54,560 --> 00:04:51,420
reproduce the ability to utilize energy

115
00:04:56,030 --> 00:04:54,570
that you excrete waste that you move or

116
00:04:57,740 --> 00:04:56,040
you have the ability to respond to

117
00:04:59,510 --> 00:04:57,750
external stimuli as all a laundry list

118
00:05:02,240 --> 00:04:59,520
of attributes it's not really much of a

119
00:05:04,070 --> 00:05:02,250
definition um that's not because biology

120
00:05:05,300 --> 00:05:04,080
doesn't have definitions and some of

121
00:05:07,700 --> 00:05:05,310
them are now listed on this particular

122
00:05:09,050 --> 00:05:07,710
slide so many of you for example

123
00:05:10,760 --> 00:05:09,060
especially if you're coming from the

124
00:05:12,530 --> 00:05:10,770
background of cell biology know about

125
00:05:14,240 --> 00:05:12,540
the cell theory of life there's

126
00:05:16,160 --> 00:05:14,250
obviously the evolutionary theory of

127
00:05:17,360 --> 00:05:16,170
life their various information the

128
00:05:19,490 --> 00:05:17,370
reason life and there's various

129
00:05:21,200 --> 00:05:19,500
molecular theories of life and these

130
00:05:22,910 --> 00:05:21,210
have operated over the last several

131
00:05:25,010 --> 00:05:22,920
hundred years certainly the cell theory

132
00:05:27,530 --> 00:05:25,020
of life has emerged after the microscope

133
00:05:29,660 --> 00:05:27,540
came along and therefore was able to

134
00:05:31,570 --> 00:05:29,670
identify a whole world of cellular life

135
00:05:34,880 --> 00:05:31,580
that was not visible to the naked eye

136
00:05:36,380 --> 00:05:34,890
well so so like theory of life is you

137
00:05:38,090 --> 00:05:36,390
know certainly one that's quite popular

138
00:05:40,820 --> 00:05:38,100

it's actually used for example when

139
00:05:43,940 --> 00:05:40,830
people look for life in the cosmos

140
00:05:46,909 --> 00:05:43,950
certainly NASA missions so Eve this is

141
00:05:50,120 --> 00:05:46,919
actually a older slide this is actually

142
00:05:52,100 --> 00:05:50,130
from book who is looking at cork cells

143
00:05:53,930 --> 00:05:52,110
and in fact he is the individual who

144
00:05:55,580 --> 00:05:53,940
came up with the word cell in English

145
00:05:57,260 --> 00:05:55,590
language because he was looking at what

146
00:06:01,490 --> 00:05:57,270
looked to him like small rooms or

147
00:06:04,760 --> 00:06:01,500
chambers mostly implants schwann of

148
00:06:09,740 --> 00:06:04,770
course and schleiden were the people who

149
00:06:14,090 --> 00:06:09,750
actually looked at the unification of

150
00:06:15,740 --> 00:06:14,100
life in 1847 exit was in 1840 this this

151
00:06:16,790 --> 00:06:15,750
is actually an english translation of

152
00:06:19,190 --> 00:06:16,800
their book which you can actually

153
00:06:22,850 --> 00:06:19,200
download from the history of science

154
00:06:24,920 --> 00:06:22,860
foundation in berlin and it's in just in

155
00:06:26,420 --> 00:06:24,930
case you think that we put in the modern

156
00:06:29,240 --> 00:06:26,430
world a gloss on what ancient people

157
00:06:31,400 --> 00:06:29,250
were thinking 150 years ago it's

158
00:06:34,310 --> 00:06:31,410
actually quite clear that these folks

159
00:06:35,600 --> 00:06:34,320
were actually trying to unify life and a

160
00:06:36,860 --> 00:06:35,610
theoretical sense in fact their whole

161
00:06:39,500 --> 00:06:36,870
introduction to this

162
00:06:41,750 --> 00:06:39,510
it's a discussion about how deplorable

163
00:06:44,030 --> 00:06:41,760

it is that people who study plants and

164
00:06:45,890 --> 00:06:44,040
people who said the animals don't talk

165
00:06:47,780 --> 00:06:45,900
to each other and what he's going to use

166
00:06:49,460 --> 00:06:47,790
is try to use the cell structure of both

167
00:06:52,460 --> 00:06:49,470
of these as a way of trying to unify

168
00:06:56,270 --> 00:06:52,470
life in some sort of theory now the fact

169
00:06:58,010 --> 00:06:56,280
that this is driving and our idea of

170
00:06:59,540 --> 00:06:58,020
what constitutes life at a very

171
00:07:02,000 --> 00:06:59,550
fundamental level is the fact that a

172
00:07:05,000 --> 00:07:02,010
couple months ago proto light announced

173
00:07:07,280 --> 00:07:05,010
its plans this was last August to create

174
00:07:11,440 --> 00:07:07,290
artificial life in three to five years

175
00:07:13,460 --> 00:07:11,450
this caused quite a flurry in the press

176
00:07:14,840 --> 00:07:13,470
not the least of which was because

177
00:07:16,430 --> 00:07:14,850
people thought it was dangerous but what

178
00:07:18,590 --> 00:07:16,440
did they consider will they put this

179
00:07:21,050 --> 00:07:18,600
picture out there's a cell structure and

180
00:07:23,600 --> 00:07:21,060
indeed when we go look for life in the

181
00:07:25,280 --> 00:07:23,610
cosmos we also look for cell structures

182
00:07:27,230 --> 00:07:25,290
very frequently and this is of course on

183
00:07:28,880 --> 00:07:27,240
the right the famous picture from the

184
00:07:30,560 --> 00:07:28,890
island hills meteorite which is looking

185
00:07:33,200 --> 00:07:30,570
at structures it looks sort of cell like

186
00:07:35,030 --> 00:07:33,210
him from that a large amount of

187
00:07:37,130 --> 00:07:35,040
speculation was started as to whether

188
00:07:39,050 --> 00:07:37,140

there might have been life that formed

189
00:07:41,450 --> 00:07:39,060
those so the cell theory of life is fine

190
00:07:43,880 --> 00:07:41,460
but really the as the debate over the

191
00:07:44,960 --> 00:07:43,890
island Hills meteorite illustrates cell

192
00:07:47,300 --> 00:07:44,970
like structures are really not

193
00:07:49,580 --> 00:07:47,310
definitive biosignatures and they can be

194
00:07:52,130 --> 00:07:49,590
generated by many non light living

195
00:07:53,720 --> 00:07:52,140
processes as well well I'm not going to

196
00:07:55,610 --> 00:07:53,730
dwell on the second theory it's one of

197
00:07:58,100 --> 00:07:55,620
my favorites sort of the evolutionary

198
00:08:00,020 --> 00:07:58,110
theory of life this is the animal room

199
00:08:01,610 --> 00:08:00,030
at the natural history museum in Paris

200
00:08:04,130 --> 00:08:01,620
where you can see people trying to

201
00:08:07,070 --> 00:08:04,140
classify all forms of life that they

202
00:08:08,600 --> 00:08:07,080
could find on earth upstairs from this

203
00:08:11,150 --> 00:08:08,610
room you can actually find the original

204
00:08:13,370 --> 00:08:11,160
fossils that Cuvier was actually looking

205
00:08:15,500 --> 00:08:13,380
at when he came up with his first

206
00:08:17,020 --> 00:08:15,510
concepts of evolution of course Lamarck

207
00:08:19,310 --> 00:08:17,030
statue is out in front of this guy

208
00:08:20,660 --> 00:08:19,320
what's quite clear is that the

209
00:08:23,090 --> 00:08:20,670
evolutionary theory of life is

210
00:08:25,400 --> 00:08:23,100
classically defined has really not been

211
00:08:27,860 --> 00:08:25,410
as successful as it could be in

212
00:08:29,900 --> 00:08:27,870
particular it really did not identify

213
00:08:31,960 --> 00:08:29,910

the central fact that life on Earth is

214
00:08:36,850 --> 00:08:31,970
monophyletic so it doesn't actually

215
00:08:39,380 --> 00:08:36,860
transparently make obvious that

216
00:08:41,450 --> 00:08:39,390
microbial life and macroscopic light

217
00:08:43,070 --> 00:08:41,460
were actually related by common ancestor

218
00:08:44,990 --> 00:08:43,080
even though they have cells because of

219
00:08:48,130 --> 00:08:45,000
course at some point he decided life as

220
00:08:49,490 --> 00:08:48,140
a natural state and that cells are

221
00:08:51,290 --> 00:08:49,500
necessary for

222
00:08:53,510 --> 00:08:51,300
I hear force of this conclusion that you

223
00:08:55,040 --> 00:08:53,520
have plants based on cells and animals

224
00:08:57,020 --> 00:08:55,050
based themselves it could just as easily

225
00:08:59,180 --> 00:08:57,030
be the fact that those arose

226
00:09:01,700 --> 00:08:59,190
independently by conversions rather than

227
00:09:04,580 --> 00:09:01,710
by common ancestry and so it really

228
00:09:06,950 --> 00:09:04,590
turned to molecular theories of life to

229
00:09:09,470 --> 00:09:06,960
come up with the essential understanding

230
00:09:11,990 --> 00:09:09,480
of monophyletic system you're looking

231
00:09:13,820 --> 00:09:12,000
just at three structures the structure

232
00:09:15,890 --> 00:09:13,830
in the middle upper part of the slide of

233
00:09:18,560 --> 00:09:15,900
urea this is the compound that was made

234
00:09:21,190 --> 00:09:18,570
in 1828 by bowler which is what

235
00:09:24,100 --> 00:09:21,200
discarded anti-white to listen or

236
00:09:26,660 --> 00:09:24,110
discarded vitalism as a theory of light

237
00:09:28,100 --> 00:09:26,670
the metabolism in the lower left of

238
00:09:30,230 --> 00:09:28,110

people are arguing that this is

239
00:09:31,880 --> 00:09:30,240
essential feature of life and in fact if

240
00:09:33,560 --> 00:09:31,890
you go through the laundry lists if you

241
00:09:36,470 --> 00:09:33,570
learn in high school biology about what

242
00:09:38,540 --> 00:09:36,480
like this the ability to take in energy

243
00:09:41,450 --> 00:09:38,550
and just secrete waste is all part of

244
00:09:43,580 --> 00:09:41,460
the metabolism definition tab metabolism

245
00:09:45,680 --> 00:09:43,590
the concept of life then of course in

246
00:09:47,300 --> 00:09:45,690
the right isn't one of my favorite

247
00:09:49,010 --> 00:09:47,310
theories of life which is the so-called

248
00:09:50,690 --> 00:09:49,020
gene theory of life which is the

249
00:09:52,300 --> 00:09:50,700
argument that in order to have life you

250
00:09:54,560 --> 00:09:52,310
have to have a molecule that contains

251
00:09:57,079 --> 00:09:54,570
information that can be passed from

252
00:09:59,420 --> 00:09:57,089
generation to generation perhaps with

253
00:10:03,170 --> 00:09:59,430
some errors that allow the first steps

254
00:10:05,870 --> 00:10:03,180
of a Darwinian evolution to proceed so

255
00:10:07,579 --> 00:10:05,880
that's cool the question today and it's

256
00:10:09,200 --> 00:10:07,589
a little ambitious but the question is

257
00:10:12,620 --> 00:10:09,210
whether we can bring these together I

258
00:10:16,490 --> 00:10:12,630
actually gave a talk on the top wedge of

259
00:10:19,670 --> 00:10:16,500
this four-part diagram a couple days ago

260
00:10:21,950 --> 00:10:19,680
at the nest apps icon so I won't go into

261
00:10:23,690 --> 00:10:21,960
great detail of this but one of our

262
00:10:25,670 --> 00:10:23,700
goals is to whether we can take the

263
00:10:28,160 --> 00:10:25,680

bottom wedge which is really the Natural

264
00:10:30,410 --> 00:10:28,170
History view may be supported by

265
00:10:32,780 --> 00:10:30,420
molecular evolution to work backwards in

266
00:10:34,610 --> 00:10:32,790
time so that we can go to a simpler form

267
00:10:37,040 --> 00:10:34,620
of life now the theory here is really

268
00:10:38,600 --> 00:10:37,050
very very very krups naive but that is

269
00:10:40,970 --> 00:10:38,610
that if you go backwards in time to a

270
00:10:43,400 --> 00:10:40,980
simpler form of life what will remain as

271
00:10:46,790 --> 00:10:43,410
you examine more and more ancient life

272
00:10:51,020 --> 00:10:46,800
is is life that is more essential that

273
00:10:53,540 --> 00:10:51,030
is a simpler form of life is more

274
00:10:56,150 --> 00:10:53,550
reflective of what is necessary for life

275
00:10:58,630 --> 00:10:56,160
in general and that more derived forms

276
00:11:01,880 --> 00:10:58,640
of life have all the baggage of history

277
00:11:02,920 --> 00:11:01,890
super impose upon what is essential for

278
00:11:04,720 --> 00:11:02,930
light and therefore make it

279
00:11:06,610 --> 00:11:04,730
typical are more difficult to see what

280
00:11:08,380 --> 00:11:06,620
is the Center for life so one of the

281
00:11:13,090 --> 00:11:08,390
ideas that maybe is we can look at the

282
00:11:14,740 --> 00:11:13,100
tree at the bottom of the four-part

283
00:11:16,740 --> 00:11:14,750
diagram you can see how you can look at

284
00:11:19,480 --> 00:11:16,750
the three kingdoms and maybe in for

285
00:11:21,550 --> 00:11:19,490
ancestral life-forms and from those

286
00:11:23,889 --> 00:11:21,560
resurrect them maybe even for laboratory

287
00:11:24,820 --> 00:11:23,899
study combine them with the fossils on

288
00:11:26,019 --> 00:11:24,830

the right to try to come up with

289
00:11:29,139 --> 00:11:26,029
something more essential to life

290
00:11:31,510 --> 00:11:29,149
something essential here meaning in the

291
00:11:33,280 --> 00:11:31,520
essence is something more basic and

292
00:11:35,050 --> 00:11:33,290
we've tried this I mean certainly

293
00:11:36,699 --> 00:11:35,060
molecular evolution is what has brought

294
00:11:38,320 --> 00:11:36,709
together sort of the classical

295
00:11:40,269 --> 00:11:38,330
evolutionary with the molecular

296
00:11:42,010 --> 00:11:40,279
evolution right theory for those of you

297
00:11:43,870 --> 00:11:42,020
who are not familiar with this I really

298
00:11:45,820 --> 00:11:43,880
three components of a molecular

299
00:11:48,280 --> 00:11:45,830
evolution analysis especially when you

300
00:11:49,389 --> 00:11:48,290
deal with proteins and I've drawn them

301
00:11:51,460 --> 00:11:49,399
here in the upper left-hand corner

302
00:11:53,800 --> 00:11:51,470
you're looking at amino acid sequences

303
00:11:55,960 --> 00:11:53,810
or at least the first 20 amino acids of

304
00:11:59,320 --> 00:11:55,970
proteins from box from sheep and from

305
00:12:00,880 --> 00:11:59,330
camel um it's transparently obvious on

306
00:12:03,310 --> 00:12:00,890
the similarities between those three

307
00:12:06,490 --> 00:12:03,320
sequences that they are related by

308
00:12:08,680 --> 00:12:06,500
common ancestry if you have any kind of

309
00:12:10,810 --> 00:12:08,690
statistical model where you propose that

310
00:12:12,460 --> 00:12:10,820
those sequences arose and their

311
00:12:14,140 --> 00:12:12,470
similarities by random chance the

312
00:12:17,800 --> 00:12:14,150
chances of that happening are quite

313
00:12:19,660 --> 00:12:17,810

small you can notice of course that the

314
00:12:21,940 --> 00:12:19,670
camel sequence is more different from

315
00:12:23,949 --> 00:12:21,950
the ox and the sheep and the options of

316
00:12:25,449 --> 00:12:23,959
sheep differ from each other and from

317
00:12:27,100 --> 00:12:25,459
that comes the second part of the

318
00:12:29,230 --> 00:12:27,110
phylogenetic analysis which you see on

319
00:12:31,510 --> 00:12:29,240
the right which is the evolutionary tree

320
00:12:34,269 --> 00:12:31,520
which shows the familial relationships

321
00:12:36,220 --> 00:12:34,279
of these species that oxen sheep diverge

322
00:12:38,740 --> 00:12:36,230
from each other after they both diverse

323
00:12:42,760 --> 00:12:38,750
as an ancestral form from camel and of

324
00:12:44,410 --> 00:12:42,770
course the whole set divers long after

325
00:12:46,420 --> 00:12:44,420
Megan's split off from that lineage

326
00:12:49,300 --> 00:12:46,430
leading the modern ruminants so that's

327
00:12:51,100 --> 00:12:49,310
an important component the third thing

328
00:12:53,380 --> 00:12:51,110
which is not as often discussed bits

329
00:12:54,650 --> 00:12:53,390
than known from I guess ever since Linus

330
00:12:58,340 --> 00:12:54,660
Pauling and meals

331
00:13:00,259 --> 00:12:58,350
candolyn the 1960s proposed it was if

332
00:13:03,319 --> 00:13:00,269
you have the sequences of the descendant

333
00:13:06,230 --> 00:13:03,329
proteins you can infer the sequences of

334
00:13:08,749 --> 00:13:06,240
the ancestral proteins and I'm just at

335
00:13:14,389 --> 00:13:08,759
the bottom left of this slide pointing

336
00:13:15,410 --> 00:13:14,399
to a an evolutionary reconstruction you

337
00:13:17,840 --> 00:13:15,420
know if you want to know what is a

338
00:13:20,269 --> 00:13:17,850

position one of this protein from oxen

339
00:13:23,119 --> 00:13:20,279
we need the ancestor of oxen sheep will

340
00:13:25,819 --> 00:13:23,129
the Ox has AK it's a lysine at position

341
00:13:28,699 --> 00:13:25,829
1 the Sheep also has AK that's a lie

342
00:13:31,220 --> 00:13:28,709
seen also in position one therefore it

343
00:13:33,590 --> 00:13:31,230
is most parsimonious that it requires

344
00:13:36,319 --> 00:13:33,600
the fewest number of amino acid

345
00:13:38,389 --> 00:13:36,329
replacements to assume that the ancestor

346
00:13:41,420 --> 00:13:38,399
also had a keg or a lysine in position

347
00:13:44,509 --> 00:13:41,430
one and so the ancestral sequence which

348
00:13:46,869 --> 00:13:44,519
has a lysine in position one a k is in

349
00:13:50,059 --> 00:13:46,879
black at the bottom of that alignment e

350
00:13:51,379 --> 00:13:50,069
is the second amino acid but you know

351
00:13:52,610 --> 00:13:51,389
when you get to the position three in

352
00:13:55,220 --> 00:13:52,620
the alignment you got a problem because

353
00:13:57,530 --> 00:13:55,230
ox has a tee that's a three inning and

354
00:13:59,769 --> 00:13:57,540
cheap have a nest that's a searing what

355
00:14:02,870 --> 00:13:59,779
do you do because if you go to the tree

356
00:14:05,540 --> 00:14:02,880
reconstruction of the lower left if you

357
00:14:08,540 --> 00:14:05,550
infer that the ancestor had a tea or a

358
00:14:10,819 --> 00:14:08,550
threonine in position three then there

359
00:14:13,280 --> 00:14:10,829
was one change which produce the Syrian

360
00:14:15,230 --> 00:14:13,290
the modern sheep in contrast that you

361
00:14:17,660 --> 00:14:15,240
assume that the ancestor has a searing

362
00:14:19,730 --> 00:14:17,670
at position 3 then there's one change in

363
00:14:21,980 --> 00:14:19,740

the lineage leading the modern ox that

364
00:14:24,639 --> 00:14:21,990
put a three inning there those two

365
00:14:26,960 --> 00:14:24,649
inferences about the ancestral state

366
00:14:29,629 --> 00:14:26,970
reconstructed at position 3 are equally

367
00:14:32,600 --> 00:14:29,639
parsimonious that is they both require

368
00:14:35,540 --> 00:14:32,610
one change in the tree and therefore in

369
00:14:38,150 --> 00:14:35,550
classical analysis one would not know

370
00:14:40,639 --> 00:14:38,160
whether to put a 39 or Siri at position

371
00:14:42,110 --> 00:14:40,649
3 and the ancestral sequence and by the

372
00:14:45,049 --> 00:14:42,120
way that's true even if you're a fan of

373
00:14:46,639 --> 00:14:45,059
maximum likelihood the analyses you

374
00:14:48,980 --> 00:14:46,649
still have about a forty-eight percent

375
00:14:50,449 --> 00:14:48,990
chance that they're being a threonine at

376
00:14:52,160 --> 00:14:50,459
the MSS or at that site may have

377
00:14:54,499 --> 00:14:52,170
forty-seven percent chance that it's a

378
00:14:56,059 --> 00:14:54,509
Syrian and the remaining five percent of

379
00:15:00,230 --> 00:14:56,069
the probability is distributed over all

380
00:15:02,329 --> 00:15:00,240
the other amino acids so never mind we

381
00:15:03,490 --> 00:15:02,339
live in the age of the genome everybody

382
00:15:05,500 --> 00:15:03,500
and his brother has have

383
00:15:08,020 --> 00:15:05,510
his genome sequence and so if you

384
00:15:09,820 --> 00:15:08,030
actually look at the database you're

385
00:15:13,210 --> 00:15:09,830
likely to find an out-group in this case

386
00:15:15,130 --> 00:15:13,220
camel which conveniently has a 39 in

387
00:15:17,740 --> 00:15:15,140
position three and that resolves the

388
00:15:20,050 --> 00:15:17,750

ambiguity and imprints of the ancestral

389
00:15:21,490 --> 00:15:20,060
sequence and so these are the you know

390
00:15:25,810 --> 00:15:21,500
the ways in which you can bring together

391
00:15:27,790 --> 00:15:25,820
sort of a historical theory our sixth

392
00:15:29,950 --> 00:15:27,800
oracle model for life based of

393
00:15:32,610 --> 00:15:29,960
paleontology and the mullet molecular

394
00:15:36,010 --> 00:15:32,620
structure of life in a productive way

395
00:15:37,420 --> 00:15:36,020
well now um now we can try to go

396
00:15:39,730 --> 00:15:37,430
backwards in time we can try to

397
00:15:42,070 --> 00:15:39,740
understand the details of interactions

398
00:15:44,890 --> 00:15:42,080
between chemistry and homology using

399
00:15:48,450 --> 00:15:44,900
this and our real goal of course was to

400
00:15:51,070 --> 00:15:48,460
try to get an experimental carlet here

401
00:15:52,900 --> 00:15:51,080
for what we do in silico with the

402
00:15:55,300 --> 00:15:52,910
sequences which you saw in the previous

403
00:15:57,010 --> 00:15:55,310
slide one of your problems is that most

404
00:16:02,100 --> 00:15:57,020
people think that because evolution

405
00:16:06,010 --> 00:16:02,110
occurred in the past its hypotheses are

406
00:16:08,590 --> 00:16:06,020
intrinsically untestable and therefore

407
00:16:10,540 --> 00:16:08,600
essentially an unscientific and any of

408
00:16:12,310 --> 00:16:10,550
you talk to creationists or intelligent

409
00:16:15,220 --> 00:16:12,320
design people they will remind you of

410
00:16:17,530 --> 00:16:15,230
this at the at the time but it's not

411
00:16:19,810 --> 00:16:17,540
true there are clearly predictions that

412
00:16:22,630 --> 00:16:19,820
can be made about future discoveries and

413
00:16:25,090 --> 00:16:22,640

future analyses that can be made with

414
00:16:26,920 --> 00:16:25,100
evolutionary theory but one of the major

415
00:16:29,140 --> 00:16:26,930
questions is whether we could ever get

416
00:16:31,960 --> 00:16:29,150
an experimental Carla in the laboratory

417
00:16:34,300 --> 00:16:31,970
to test or these just so stories that

418
00:16:37,420 --> 00:16:34,310
molecular evolutionists as well as their

419
00:16:41,140 --> 00:16:37,430
their compatriots in classical evolution

420
00:16:42,730 --> 00:16:41,150
are constantly created and that actually

421
00:16:44,740 --> 00:16:42,740
is an idea that actually goes back to

422
00:16:46,780 --> 00:16:44,750
the line is polynomials of can lure

423
00:16:49,480 --> 00:16:46,790
about 4000 actually closer to 50 years

424
00:16:51,970 --> 00:16:49,490
ago now which was it if you can infer

425
00:16:55,090 --> 00:16:51,980
the sequences of ancient proteins using

426
00:16:57,610 --> 00:16:55,100
the process I just described you to the

427
00:16:59,170 --> 00:16:57,620
magic of recombinant DNA technology you

428
00:17:01,390 --> 00:16:59,180
could resurrect them you can bring them

429
00:17:03,579 --> 00:17:01,400
back to light in the laboratory where

430
00:17:05,860 --> 00:17:03,589
you can study them and therefore bring

431
00:17:08,760 --> 00:17:05,870
the power of experimental method to bear

432
00:17:10,300 --> 00:17:08,770
on the questions that relate history

433
00:17:12,550 --> 00:17:10,310
function in the

434
00:17:15,430 --> 00:17:12,560
ancient world in particular to molecular

435
00:17:18,190 --> 00:17:15,440
structure and of course one thing is

436
00:17:19,450 --> 00:17:18,200
quite clear is that as a set of the

437
00:17:21,040 --> 00:17:19,460
bottom of this slide what these

438
00:17:23,320 --> 00:17:21,050

experiments are going to show is

439
00:17:25,600 --> 00:17:23,330
something that perhaps a few people in

440
00:17:28,030 --> 00:17:25,610
this conference need to have shown to

441
00:17:30,160 --> 00:17:28,040
them and that is that evolution is

442
00:17:32,530 --> 00:17:30,170
extremely powerful as a way at least in

443
00:17:35,320 --> 00:17:32,540
modern Terran life of getting function

444
00:17:37,240 --> 00:17:35,330
out of molecules and of course that is

445
00:17:39,970 --> 00:17:37,250
one of the things that supports our view

446
00:17:41,890 --> 00:17:39,980
that evolution if not the defining

447
00:17:44,560 --> 00:17:41,900
feature of living system system you're

448
00:17:47,530 --> 00:17:44,570
going to be a defining feature of living

449
00:17:51,310 --> 00:17:47,540
systems well let me just take a look at

450
00:17:53,740 --> 00:17:51,320
the the major problem in the planet over

451
00:17:55,780 --> 00:17:53,750
the last 40 million years Al Gore

452
00:17:57,880 --> 00:17:55,790
notwithstanding it is not global warming

453
00:18:00,790 --> 00:17:57,890
it has been global cooling you're

454
00:18:03,180 --> 00:18:00,800
looking on this plot to the left the

455
00:18:06,010 --> 00:18:03,190
isotope ratio data that shows that

456
00:18:08,440 --> 00:18:06,020
decomposition of the D the decline of

457
00:18:10,990 --> 00:18:08,450
global temperature of tens of degrees

458
00:18:12,490 --> 00:18:11,000
centigrade since the eocene let me see

459
00:18:14,830 --> 00:18:12,500
if this pointer actually we're some of

460
00:18:16,360 --> 00:18:14,840
this work there's the eocene here so

461
00:18:17,950 --> 00:18:16,370
that's this so that's the eocene there's

462
00:18:20,590 --> 00:18:17,960
the legacy and there's the myosin

463
00:18:23,380 --> 00:18:20,600

there's the pliocene the line going up

464
00:18:27,010 --> 00:18:23,390
indicates a ratio of isotopes and co

465
00:18:29,620 --> 00:18:27,020
precipitated shirts which is showing the

466
00:18:32,680 --> 00:18:29,630
cooling of the water in which they are

467
00:18:35,020 --> 00:18:32,690
precipitating as well as the ice ages

468
00:18:37,300 --> 00:18:35,030
which appears here but there's actually

469
00:18:38,890 --> 00:18:37,310
a couple of global cooling from a time

470
00:18:41,500 --> 00:18:38,900
when the planet was much much warmer

471
00:18:43,390 --> 00:18:41,510
where they were tropical rainforest

472
00:18:45,520 --> 00:18:43,400
pretty much everywhere in Nebraska

473
00:18:49,000 --> 00:18:45,530
weather is now an open savanna or

474
00:18:50,740 --> 00:18:49,010
Prairie cooling in the legacy and

475
00:18:53,230 --> 00:18:50,750
romantically then cooling again the

476
00:18:57,280 --> 00:18:53,240
myosin of course cooling in the modern

477
00:18:59,140 --> 00:18:57,290
ages with the ice ages and we have on

478
00:19:02,110 --> 00:18:59,150
the right and artist rendition of sort

479
00:19:05,350 --> 00:19:02,120
of how this had an impact on you you as

480
00:19:07,180 --> 00:19:05,360
a primate grew up evolutionarily in

481
00:19:10,390 --> 00:19:07,190
tropical rainforests where you had a

482
00:19:13,570 --> 00:19:10,400
bunch of vitamin C coming from fruits

483
00:19:14,860 --> 00:19:13,580
and vegetables you lost your ability as

484
00:19:17,290 --> 00:19:14,870
a result or at least without

485
00:19:20,530 --> 00:19:17,300
evolutionary consequences to make

486
00:19:22,870 --> 00:19:20,540
vitamin C when the planet cooled and

487
00:19:24,640 --> 00:19:22,880
dried the rainforest 10

488
00:19:27,400 --> 00:19:24,650

the primates who are making quite a good

489
00:19:29,380 --> 00:19:27,410
living in the trees even as far north of

490
00:19:32,080 --> 00:19:29,390
Scandinavia all of a sudden had their

491
00:19:34,510 --> 00:19:32,090
source of vitamin C as well as other

492
00:19:36,820 --> 00:19:34,520
things removed and so what happened of

493
00:19:40,030 --> 00:19:36,830
course was a extinction of primates over

494
00:19:43,360 --> 00:19:40,040
a large range part of their range and so

495
00:19:45,220 --> 00:19:43,370
you can't belong as a toolmaker unable

496
00:19:47,740 --> 00:19:45,230
to sort of take over the fun and despite

497
00:19:49,390 --> 00:19:47,750
the global cooling the global climate

498
00:19:51,730 --> 00:19:49,400
change should actually drive many things

499
00:19:53,830 --> 00:19:51,740
and this is work from lynn margulis

500
00:19:55,410 --> 00:19:53,840
referring to penetrate biology you're

501
00:19:58,870 --> 00:19:55,420
talking about the interaction between

502
00:20:01,000 --> 00:19:58,880
the planets and the life form and one of

503
00:20:02,650 --> 00:20:01,010
the things it drove was what you could

504
00:20:04,380 --> 00:20:02,660
sort of see in the back of this Savannah

505
00:20:08,440 --> 00:20:04,390
which is the emergence of grasses

506
00:20:10,960 --> 00:20:08,450
grasses really were not present more

507
00:20:13,840 --> 00:20:10,970
than in any large abundance more than 40

508
00:20:15,400 --> 00:20:13,850
million years ago in fact when they shot

509
00:20:17,410 --> 00:20:15,410
Jurassic Park they had a hard time

510
00:20:19,360 --> 00:20:17,420
getting an authentic background without

511
00:20:21,280 --> 00:20:19,370
grasses which have taken over the place

512
00:20:23,710 --> 00:20:21,290
but for those of you who have never

513
00:20:26,050 --> 00:20:23,720

eaten grass you can should know that the

514
00:20:28,740 --> 00:20:26,060
grass is about twenty-five percent

515
00:20:31,990 --> 00:20:28,750
silica it's a low nutrition source and

516
00:20:33,850 --> 00:20:32,000
one of the impacts of grasses taking

517
00:20:36,790 --> 00:20:33,860
over large parts of what had previously

518
00:20:39,430 --> 00:20:36,800
been tropical or semi-tropical forest

519
00:20:41,350 --> 00:20:39,440
was it it drove the emergence of a new

520
00:20:43,930 --> 00:20:41,360
kind of animal and I've already

521
00:20:46,900 --> 00:20:43,940
mentioned them there the sheep's are the

522
00:20:50,290 --> 00:20:46,910
Sheep the oxen and the camels these are

523
00:20:52,090 --> 00:20:50,300
animals that pen actually eat grass and

524
00:20:54,550 --> 00:20:52,100
make a living at well they don't

525
00:20:57,100 --> 00:20:54,560
actually eat grass what the oxen do is

526
00:20:59,740 --> 00:20:57,110
they collect the grass that's a low

527
00:21:01,630 --> 00:20:59,750
nutrition food arising because of the

528
00:21:03,250 --> 00:21:01,640
cooling and prairies about 40 million

529
00:21:06,340 --> 00:21:03,260
years ago and then of course really in

530
00:21:08,740 --> 00:21:06,350
the minus scene after the rooming

531
00:21:12,430 --> 00:21:08,750
collects the grass they feed the grass

532
00:21:14,260 --> 00:21:12,440
to bacteria that are growing in their

533
00:21:16,060 --> 00:21:14,270
first stomach and then they of course

534
00:21:18,160 --> 00:21:16,070
cough up the bacteria from time to time

535
00:21:20,980 --> 00:21:18,170
and shoe it which gives the classical

536
00:21:22,960 --> 00:21:20,990
ruminants physiology and then what the

537
00:21:25,510 --> 00:21:22,970
rumen does is they eat fresh bacteria

538
00:21:27,460 --> 00:21:25,520

they feed the bacteria to digestive

539
00:21:30,160 --> 00:21:27,470
enzymes and the subsequent chambers of

540
00:21:33,670 --> 00:21:30,170
their stomachs and in the small and

541
00:21:35,680 --> 00:21:33,680
large intestines and the key point is

542
00:21:36,280 --> 00:21:35,690
that this is a new lifestyle it's

543
00:21:38,230 --> 00:21:36,290
something that I

544
00:21:40,900 --> 00:21:38,240
the only emerged in the pan is a logical

545
00:21:43,180 --> 00:21:40,910
record about 40 million years ago its

546
00:21:45,100 --> 00:21:43,190
emerging at the time or shortly before

547
00:21:47,740 --> 00:21:45,110
the time the grass has become important

548
00:21:50,410 --> 00:21:47,750
and it requires a new kind of digested

549
00:21:51,580 --> 00:21:50,420
entomology to support and that's because

550
00:21:53,440 --> 00:21:51,590
as many of you know who are

551
00:21:55,900 --> 00:21:53,450
microbiologist is a bacteria are

552
00:22:00,700 --> 00:21:55,910
terribly rich in ribonucleic acid that

553
00:22:03,880 --> 00:22:00,710
is RNA the ribonucleic acid is really

554
00:22:05,590 --> 00:22:03,890
not present in the enemies and an

555
00:22:08,590 --> 00:22:05,600
abundance and the food of other animals

556
00:22:12,160 --> 00:22:08,600
and so the ox takes in about seventeen

557
00:22:14,200 --> 00:22:12,170
percent of its nitrogen in one of our

558
00:22:16,090 --> 00:22:14,210
and and therefore they need to digestive

559
00:22:18,070 --> 00:22:16,100
ribonuclease than unions I'm in the

560
00:22:20,110 --> 00:22:18,080
digestive tract that will break down the

561
00:22:21,580 --> 00:22:20,120
RNA that's coming from their new

562
00:22:23,500 --> 00:22:21,590
lifestyle that is eating freshly

563
00:22:26,020 --> 00:22:23,510

fermenting bacteria which is coming from

564
00:22:28,180 --> 00:22:26,030
a new lifestyle of eating grass which

565
00:22:30,190 --> 00:22:28,190
requires bacteria and the cellulases

566
00:22:32,770 --> 00:22:30,200
that are in the bacteria to convert the

567
00:22:36,910 --> 00:22:32,780
low nutrition something a reasonable

568
00:22:38,830 --> 00:22:36,920
refreshing so all of a sudden you have

569
00:22:40,840 --> 00:22:38,840
ribonuclease which is shown in three

570
00:22:42,370 --> 00:22:40,850
ways on this slide on the right hand

571
00:22:44,770 --> 00:22:42,380
side you compute see a three-dimensional

572
00:22:47,110 --> 00:22:44,780
structure of this protein below you see

573
00:22:49,060 --> 00:22:47,120
the one amino acid sequence of these

574
00:22:50,680 --> 00:22:49,070
proteins or whose sequence you've

575
00:22:52,270 --> 00:22:50,690
already seen at least in the first 20

576
00:22:54,670 --> 00:22:52,280
letters when I was describing the trees

577
00:22:56,950 --> 00:22:54,680
then you can see the chemical mechanism

578
00:23:00,130 --> 00:22:56,960
which shows how ribonuclease goes about

579
00:23:04,210 --> 00:23:00,140
its business of breaking RNA into small

580
00:23:06,130 --> 00:23:04,220
pieces yes ma'am cool well that's a just

581
00:23:08,230 --> 00:23:06,140
so story okay that's a story that says

582
00:23:10,330 --> 00:23:08,240
well planet cooled the grasslands

583
00:23:12,780 --> 00:23:10,340
emerged animals that have room in a

584
00:23:16,180 --> 00:23:12,790
digestion emerge they seem to have

585
00:23:19,240 --> 00:23:16,190
enzymes that digest the grasses and they

586
00:23:22,660 --> 00:23:19,250
have these ruins which contain bacteria

587
00:23:25,260 --> 00:23:22,670
that that's just the RNA the coming it's

588
00:23:27,880 --> 00:23:25,270

coming out of the which is which is

589
00:23:30,340 --> 00:23:27,890
contained Vic Terry wit that have RNA

590
00:23:33,310 --> 00:23:30,350
that need ribonuclease to tie Jess how's

591
00:23:36,130 --> 00:23:33,320
that and the question is whether you can

592
00:23:38,830 --> 00:23:36,140
now make that correlation very classical

593
00:23:41,320 --> 00:23:38,840
physiology to actual intellectual or

594
00:23:44,620 --> 00:23:41,330
chemistry and the answer as you can by

595
00:23:46,950 --> 00:23:44,630
resurrecting ancient ribonucleases and I

596
00:23:49,350 --> 00:23:46,960
just put down here some species

597
00:23:52,919 --> 00:23:49,360
which look at the last four million

598
00:23:54,539 --> 00:23:52,929
years of ribonuclease divergence so we

599
00:23:56,549 --> 00:23:54,549
have a swamp Buffalo and the river

600
00:23:57,990 --> 00:23:56,559
buffalo and the ox and then the Elon

601
00:24:00,690 --> 00:23:58,000
does the out-group this is a non

602
00:24:03,600 --> 00:24:00,700
domesticated remit the ancient species

603
00:24:05,789 --> 00:24:03,610
called portex whose outline is

604
00:24:08,850 --> 00:24:05,799
representative in that little black box

605
00:24:11,460 --> 00:24:08,860
at the top is the ancestor now remember

606
00:24:14,130 --> 00:24:11,470
no fossil corresponds exactly to a tree

607
00:24:16,470 --> 00:24:14,140
determined by molecular data but it's

608
00:24:18,600 --> 00:24:16,480
close enough and so you can resurrect an

609
00:24:21,360 --> 00:24:18,610
ancient ribonuclease from this guy who

610
00:24:23,070 --> 00:24:21,370
didn't live hasn't lived for four

611
00:24:25,500 --> 00:24:23,080
million years and that's how the protein

612
00:24:28,230 --> 00:24:25,510
behaves and the answer is well pretty

613
00:24:30,419 --> 00:24:28,240

much like the modern proteins behave now

614
00:24:32,760 --> 00:24:30,429
we have a couple of criteria to decide

615
00:24:36,389 --> 00:24:32,770
whether or not a modern protein has a

616
00:24:39,180 --> 00:24:36,399
digestive role in fact whenever you

617
00:24:40,680 --> 00:24:39,190
resurrect an ancient protein since you

618
00:24:43,380 --> 00:24:40,690
are not resurrecting the ancient

619
00:24:47,250 --> 00:24:43,390
organism at the same time you have to do

620
00:24:49,889 --> 00:24:47,260
something in vitro that sheds light on a

621
00:24:52,350 --> 00:24:49,899
historical hypothesis here we're going

622
00:24:55,350 --> 00:24:52,360
to be asking when this ribonucleic

623
00:24:57,750 --> 00:24:55,360
became a knight chested ensign and to do

624
00:24:59,789 --> 00:24:57,760
so we use much the same logic the

625
00:25:02,100 --> 00:24:59,799
classical evolutionary people use which

626
00:25:05,159 --> 00:25:02,110
is the statement that well if the

627
00:25:08,130 --> 00:25:05,169
Tyrannosaurus Rex tooth looks like it is

628
00:25:10,440 --> 00:25:08,140
optimum for tearing flesh then it's a

629
00:25:13,710 --> 00:25:10,450
flesh eater here we're going to look at

630
00:25:17,100 --> 00:25:13,720
kinetic properties of ribonucleases

631
00:25:18,590 --> 00:25:17,110
modern and resurrected we're going to

632
00:25:21,299 --> 00:25:18,600
look for example at their stability

633
00:25:23,190 --> 00:25:21,309
against digestion but remember these are

634
00:25:25,200 --> 00:25:23,200
proteins that are in the digestive tract

635
00:25:27,899 --> 00:25:25,210
there are enzymes that hydrolyze

636
00:25:29,490 --> 00:25:27,909
proteins also in the digestive tract so

637
00:25:31,980 --> 00:25:29,500
one of our goals is going to be to make

638
00:25:34,980 --> 00:25:31,990

sure that the ancient protein as well as

639
00:25:39,019 --> 00:25:34,990
the modern protein is itself stable

640
00:25:41,010 --> 00:25:39,029
advanced digestion which is of course a

641
00:25:43,769 --> 00:25:41,020
requirement for approaching to be

642
00:25:46,049 --> 00:25:43,779
digested we also look at its ability to

643
00:25:48,000 --> 00:25:46,059
look at many different substrates and

644
00:25:51,419 --> 00:25:48,010
digestive tract you have to take almost

645
00:25:53,279 --> 00:25:51,429
all RNA sequences there are certain

646
00:25:54,720 --> 00:25:53,289
things that a digestive enzyme does not

647
00:25:56,909 --> 00:25:54,730
have to do and that's listed at the

648
00:25:59,360 --> 00:25:56,919
bottom of this slide does not need to

649
00:26:01,280 --> 00:25:59,370
digest double strand RNA the snow

650
00:26:04,280 --> 00:26:01,290
to bind in double-stranded nucleic acids

651
00:26:06,200 --> 00:26:04,290
of any types kind but we're going to

652
00:26:08,270 --> 00:26:06,210
look at the ancient protein say if it

653
00:26:10,280 --> 00:26:08,280
behaves like a digestive enzyme being

654
00:26:13,040 --> 00:26:10,290
stable itself against a session and

655
00:26:14,720 --> 00:26:13,050
having broad substrate specificity but

656
00:26:17,120 --> 00:26:14,730
no interacting with double strand

657
00:26:19,190 --> 00:26:17,130
nucleic acids then it was a digestive

658
00:26:21,799 --> 00:26:19,200
enzyme and that's sort of where we go on

659
00:26:24,650 --> 00:26:21,809
this well what's kind of amusing is that

660
00:26:27,470 --> 00:26:24,660
digestive behavior in ribonuclease is in

661
00:26:29,780 --> 00:26:27,480
fact found back to our humerus which is

662
00:26:31,640 --> 00:26:29,790
this fellow over here on the left right

663
00:26:33,110 --> 00:26:31,650

and overall this tree in fact if you

664
00:26:35,120 --> 00:26:33,120
look at on the right hand side of this

665
00:26:37,730 --> 00:26:35,130
tree you'll see all sorts of animals all

666
00:26:40,549 --> 00:26:37,740
of which are ruminants all which chew

667
00:26:43,160 --> 00:26:40,559
their cud all of them are descended from

668
00:26:45,320 --> 00:26:43,170
ancestors ruminant which is represented

669
00:26:48,410 --> 00:26:45,330
by the lower case number g in this tree

670
00:26:50,240 --> 00:26:48,420
lived about 35 million years ago he was

671
00:26:52,840 --> 00:26:50,250
probably a room in it as well but the

672
00:26:55,340 --> 00:26:52,850
point was it his ribonuclease as

673
00:26:58,160 --> 00:26:55,350
resurrected in the laboratory extinct

674
00:26:59,960 --> 00:26:58,170
now for 35 million years behaves in the

675
00:27:02,870 --> 00:26:59,970
laboratory like a digestive enzyme

676
00:27:04,970 --> 00:27:02,880
should its table itself to digestion

677
00:27:07,940 --> 00:27:04,980
attacks on digestive subjects and does

678
00:27:09,440 --> 00:27:07,950
not act on non by chester substrate is

679
00:27:11,650 --> 00:27:09,450
that clear so what we're doing here is

680
00:27:14,630 --> 00:27:11,660
just you know making sort of the

681
00:27:17,060 --> 00:27:14,640
groundwork it turns out that what I've

682
00:27:20,000 --> 00:27:17,070
just said you is different the minute

683
00:27:22,970 --> 00:27:20,010
you go farther back in time that is if

684
00:27:25,010 --> 00:27:22,980
you go back to the acadec sis which is

685
00:27:30,110 --> 00:27:25,020
this little fellow with a fossil here on

686
00:27:31,640 --> 00:27:30,120
the left of the slide this guy is not a

687
00:27:34,480 --> 00:27:31,650
room and as far as we can tell he's

688
00:27:37,400 --> 00:27:34,490

actually coming up in the eocene he's a

689
00:27:40,870 --> 00:27:37,410
ancestor of presumably not only the

690
00:27:44,450 --> 00:27:40,880
classical ruminants but also the camels

691
00:27:46,610 --> 00:27:44,460
and then maybe even the pig of the

692
00:27:49,760 --> 00:27:46,620
hippopotamus the point is that the

693
00:27:52,910 --> 00:27:49,770
resurrected ancestral protein is not a

694
00:27:54,799 --> 00:27:52,920
digestive enzyme it does not act on non

695
00:27:56,419 --> 00:27:54,809
digestive that's right it does not act

696
00:27:58,640 --> 00:27:56,429
LM digestive subjects it's not itself

697
00:28:00,410 --> 00:27:58,650
particularly stable the digestion but it

698
00:28:03,080 --> 00:28:00,420
is actually curious enough about 10

699
00:28:04,970 --> 00:28:03,090
times more active on non digestive

700
00:28:07,040 --> 00:28:04,980
substrates that's a whole story about

701
00:28:09,530 --> 00:28:07,050
what that enzyme was doing back in that

702
00:28:11,510 --> 00:28:09,540
organism but it was not been Chesham so

703
00:28:12,789 --> 00:28:11,520
okay so fair enough that's a way in

704
00:28:16,940 --> 00:28:12,799
which we play

705
00:28:20,210 --> 00:28:16,950
to show how effective evolution is to

706
00:28:22,369 --> 00:28:20,220
manage in this case global cooling you

707
00:28:24,889 --> 00:28:22,379
know it's not getting us all that far

708
00:28:27,470 --> 00:28:24,899
back in time doing more essential or a

709
00:28:29,210 --> 00:28:27,480
life one that is more representative of

710
00:28:31,549 --> 00:28:29,220
the essence of life in fact that I

711
00:28:34,190 --> 00:28:31,559
acadec sis doesn't look well he looks

712
00:28:36,649 --> 00:28:34,200
like half sheep and half pig but he's

713
00:28:38,090 --> 00:28:36,659

not in any sense permanent to get

714
00:28:39,680 --> 00:28:38,100
something primitive by the strategy of

715
00:28:42,169 --> 00:28:39,690
going backwards in time you got to go

716
00:28:44,840 --> 00:28:42,179
back a lot farther and for this we have

717
00:28:46,899 --> 00:28:44,850
had a marvelous collaboration with Aaron

718
00:28:50,060 --> 00:28:46,909
Bouchet he's also here at the foundation

719
00:28:52,549 --> 00:28:50,070
we looked at elongation factors and it's

720
00:28:54,980 --> 00:28:52,559
a it's a great protein because as many

721
00:28:57,440 --> 00:28:54,990
of you know there's a structure but it

722
00:28:59,570 --> 00:28:57,450
happens to be present all over and all

723
00:29:03,950 --> 00:28:59,580
sorts of life forms all three kingdoms

724
00:29:07,430 --> 00:29:03,960
of life it was a present the last common

725
00:29:09,889 --> 00:29:07,440
ancestor it is used to assist delivering

726
00:29:12,230 --> 00:29:09,899
of charge transfer RNA to the ribosome

727
00:29:13,639 --> 00:29:12,240
and we can therefore because it's

728
00:29:15,649 --> 00:29:13,649
everywhere and because it's highly

729
00:29:17,930 --> 00:29:15,659
concerned we can infer the sequences of

730
00:29:20,480 --> 00:29:17,940
the ancient elongation factors from its

731
00:29:22,609 --> 00:29:20,490
descendants we also have an in vitro

732
00:29:24,049 --> 00:29:22,619
assay as i mentioned in order to when

733
00:29:25,700 --> 00:29:24,059
you resurrect something ancient you're

734
00:29:28,549 --> 00:29:25,710
not going to have the ancient organism

735
00:29:31,129 --> 00:29:28,559
as a context but at least following the

736
00:29:34,310 --> 00:29:31,139
idea the president is the key to the

737
00:29:37,310 --> 00:29:34,320
past is true that the temperature that

738
00:29:40,489 --> 00:29:37,320

the elongation factors work optimally in

739
00:29:42,799 --> 00:29:40,499
modern bacteria are the temperatures at

740
00:29:44,810 --> 00:29:42,809
which those bacteria live I mean just to

741
00:29:48,649 --> 00:29:44,820
show you an example of that this isn't a

742
00:29:50,840 --> 00:29:48,659
gtp-binding essay for the elongation

743
00:29:53,090 --> 00:29:50,850
factor isolated from ecoli which is

744
00:29:56,419 --> 00:29:53,100
living in your gut comfortably at 37

745
00:29:59,180 --> 00:29:56,429
degrees centigrade the enzyme the

746
00:30:01,970 --> 00:29:59,190
elongation factor works best at 37

747
00:30:05,299 --> 00:30:01,980
degrees that's what the maximum of this

748
00:30:07,190 --> 00:30:05,309
plot means that's the temperature where

749
00:30:09,409 --> 00:30:07,200
it lives and of course if you go to

750
00:30:11,330 --> 00:30:09,419
thermos which is living up 65 degrees

751
00:30:13,039 --> 00:30:11,340
nice light the elongation factor from

752
00:30:15,649 --> 00:30:13,049
that it has a max actually did the

753
00:30:17,930 --> 00:30:15,659
maximum binding temperatures about 65

754
00:30:20,720 --> 00:30:17,940
degrees as well so that means that if

755
00:30:23,890 --> 00:30:20,730
you have a the ability to get into your

756
00:30:26,140 --> 00:30:23,900
hands the elongation factor from any age

757
00:30:27,730 --> 00:30:26,150
bacteria that you're interested in you

758
00:30:28,960 --> 00:30:27,740
have the ability to infer the

759
00:30:34,210 --> 00:30:28,970
temperature at which that ancient

760
00:30:35,920 --> 00:30:34,220
bacteria lived and eric and mike and a

761
00:30:38,470 --> 00:30:35,930
few other people working in the lab went

762
00:30:41,350 --> 00:30:38,480
back and did that keep in mind is an

763
00:30:44,320 --> 00:30:41,360

enormous amount of ambiguity in the

764
00:30:46,000 --> 00:30:44,330
trees that you infer for in this

765
00:30:48,520 --> 00:30:46,010
particular case we only were able to go

766
00:30:49,750 --> 00:30:48,530
back as far as deep into the eubacterial

767
00:30:52,120 --> 00:30:49,760
tree and then there's all sorts of

768
00:30:54,550 --> 00:30:52,130
questions about where aquafx trees and

769
00:30:55,990 --> 00:30:54,560
there's all sorts of issues but we've

770
00:30:57,790 --> 00:30:56,000
looked at a couple of trees and we

771
00:31:00,550 --> 00:30:57,800
sampled a couple of sequences to

772
00:31:03,510 --> 00:31:00,560
represent the ambiguity the idea here is

773
00:31:05,440 --> 00:31:03,520
to try to determine whether the

774
00:31:09,580 --> 00:31:05,450
interpretation of the result that as the

775
00:31:12,850 --> 00:31:09,590
temperature optimum is ambiguous with

776
00:31:15,730 --> 00:31:12,860
respect to the ambiguity in the

777
00:31:17,350 --> 00:31:15,740
evolutionary model or conversely to try

778
00:31:19,240 --> 00:31:17,360
to determine whether or not the

779
00:31:21,760 --> 00:31:19,250
inference in this particular case that

780
00:31:24,610 --> 00:31:21,770
the ancestral bacterium lifted 65

781
00:31:26,950 --> 00:31:24,620
degrees is robust with respect to

782
00:31:29,080 --> 00:31:26,960
ambiguities in the trees inferred

783
00:31:30,910 --> 00:31:29,090
ancestral sequences in the light and so

784
00:31:34,750 --> 00:31:30,920
the green line was with one tree you can

785
00:31:37,680 --> 00:31:34,760
read the paper which we call PSA the

786
00:31:43,030 --> 00:31:37,690
blue line was a different tree MLS a and

787
00:31:45,280 --> 00:31:43,040
the the result was real quite the same

788
00:31:47,910 --> 00:31:45,290

the ancestral protein had a temperature

789
00:31:50,200 --> 00:31:47,920
optimum also 65 degrees centigrade

790
00:31:53,230 --> 00:31:50,210
indicating a bit at least with a part of

791
00:31:56,530 --> 00:31:53,240
the tree that we have sampled sorry more

792
00:31:58,360 --> 00:31:56,540
precise at least for the tree space that

793
00:32:00,490 --> 00:31:58,370
we have sampled and the ancestral

794
00:32:02,230 --> 00:32:00,500
sequences that we have simply the

795
00:32:04,360 --> 00:32:02,240
conclusion that the ancestor it was a

796
00:32:09,220 --> 00:32:04,370
thermo file but not a hyperthermic file

797
00:32:12,270 --> 00:32:09,230
is reasonably robust well since that

798
00:32:14,620 --> 00:32:12,280
time eric has gone back and looked at

799
00:32:16,720 --> 00:32:14,630
resurrected elongation factors

800
00:32:19,030 --> 00:32:16,730
throughout the tree this is just

801
00:32:21,450 --> 00:32:19,040
extracted from a recent paper that just

802
00:32:24,070 --> 00:32:21,460
came out a couple weeks ago in nature

803
00:32:26,020 --> 00:32:24,080
you're looking at temperatures

804
00:32:28,240 --> 00:32:26,030
everywhere and if you're interested for

805
00:32:30,780 --> 00:32:28,250
example as I mentioned at the bottom the

806
00:32:32,620 --> 00:32:30,790
temperature when the plants acquired

807
00:32:35,740 --> 00:32:32,630
chloroplasts it's around here somewhere

808
00:32:36,820 --> 00:32:35,750
it's over here someplace or when the

809
00:32:38,860 --> 00:32:36,830
mitochondria became

810
00:32:41,139 --> 00:32:38,870
in this severe you look at this tree get

811
00:32:43,090 --> 00:32:41,149
an idea of the temperature history at

812
00:32:47,230 --> 00:32:43,100
least in new bacterial images for which

813
00:32:48,460 --> 00:32:47,240

we have descendants well alright there's

814
00:32:50,289 --> 00:32:48,470
a big disappointment here I mean

815
00:32:52,570 --> 00:32:50,299
obviously I think it don't get me wrong

816
00:32:54,190 --> 00:32:52,580
I'm delighted to know something about

817
00:32:57,389 --> 00:32:54,200
the temperature history of life on Earth

818
00:33:00,789 --> 00:32:57,399
and to the extent to which this record

819
00:33:02,649 --> 00:33:00,799
made by inferring the sequences of

820
00:33:04,779 --> 00:33:02,659
ancient proteins and bringing them back

821
00:33:07,269 --> 00:33:04,789
to life in the lab correlates the

822
00:33:09,460 --> 00:33:07,279
geological records it's delightful and

823
00:33:11,769 --> 00:33:09,470
Don low and Paul canal have come up with

824
00:33:14,110 --> 00:33:11,779
geological statements as well about this

825
00:33:16,870 --> 00:33:14,120
temperature history but of course we're

826
00:33:19,330 --> 00:33:16,880
still not back to essence as far as we

827
00:33:21,220 --> 00:33:19,340
can tell in metabolism the agent you

828
00:33:23,889 --> 00:33:21,230
bacterium is I think it's probably

829
00:33:26,409 --> 00:33:23,899
simpler than the modern diversity of

830
00:33:28,269 --> 00:33:26,419
bacterial modern world but it's still

831
00:33:30,490 --> 00:33:28,279
reasonably complicated it still is a

832
00:33:33,279 --> 00:33:30,500
fellow who is able to make proteins by

833
00:33:35,889 --> 00:33:33,289
translation it's still is able to you

834
00:33:37,840 --> 00:33:35,899
don't do wide range of metabolisms is in

835
00:33:40,629 --> 00:33:37,850
no sense primitive and it no sense

836
00:33:42,490 --> 00:33:40,639
origins so so while we going back in

837
00:33:47,860 --> 00:33:42,500
time we and gotten a lot of interesting

838
00:33:50,019 --> 00:33:47,870

data and you can review a lot of this we

839
00:33:51,970 --> 00:33:50,029
aren't yet to origins we're showing up

840
00:33:53,259 --> 00:33:51,980
to essence but never in a mine we've

841
00:33:54,509 --> 00:33:53,269
managed to make some progress we

842
00:33:56,470 --> 00:33:54,519
certainly have dealt with this so-called

843
00:33:58,180 --> 00:33:56,480
philosophical challenge that I mentioned

844
00:34:00,279 --> 00:33:58,190
a few moments ago that most scientists

845
00:34:02,620 --> 00:34:00,289
really don't view historical hypotheses

846
00:34:04,600 --> 00:34:02,630
as being inherently not a scientific

847
00:34:06,610 --> 00:34:04,610
effect you talk to most molecular

848
00:34:08,349 --> 00:34:06,620
biologists you don't really get the

849
00:34:10,419 --> 00:34:08,359
impression that they have a constructive

850
00:34:11,770 --> 00:34:10,429
belief in evolution right they they

851
00:34:12,730 --> 00:34:11,780
they'll tell you they believe in

852
00:34:14,409 --> 00:34:12,740
evolution but it doesn't really

853
00:34:17,320 --> 00:34:14,419
influence how they carry out their

854
00:34:19,210 --> 00:34:17,330
professional lives and so certainly if

855
00:34:20,500 --> 00:34:19,220
you can go back and in first structures

856
00:34:22,000 --> 00:34:20,510
of ancient life-forms from the

857
00:34:24,339 --> 00:34:22,010
structures of their descendants we can

858
00:34:26,320 --> 00:34:24,349
come up with some of these stories one

859
00:34:28,030 --> 00:34:26,330
of which I mentioned to you I haven't

860
00:34:31,780 --> 00:34:28,040
mentioned me some of the others that you

861
00:34:35,109 --> 00:34:31,790
see cool well alright not much simpler

862
00:34:36,879 --> 00:34:35,119
not much in essence and so um we

863
00:34:39,460 --> 00:34:36,889

certainly are prepared to go in the

864
00:34:41,619 --> 00:34:39,470
direction that Jerry Joyce was one of

865
00:34:44,020 --> 00:34:41,629
many authors of this so-called NASA

866
00:34:46,570 --> 00:34:44,030
definition of life as a chemical system

867
00:34:48,460 --> 00:34:46,580
capable of Darwinian evolution we've now

868
00:34:50,290 --> 00:34:48,470
gotten kept it straight and evolution

869
00:34:53,200 --> 00:34:50,300
together into our

870
00:34:55,750 --> 00:34:53,210
area of life by the way we don't have

871
00:34:57,520 --> 00:34:55,760
cells there and then it's interesting

872
00:34:59,410 --> 00:34:57,530
question mr. whether they belong there

873
00:35:01,750 --> 00:34:59,420
but of course you can ask the question

874
00:35:03,490 --> 00:35:01,760
is if it's that simple I the essence of

875
00:35:05,740 --> 00:35:03,500
life is a chemical system that can do

876
00:35:08,950 --> 00:35:05,750
this Darwinian game how would you

877
00:35:11,080 --> 00:35:08,960
establish this given intelligence really

878
00:35:13,720 --> 00:35:11,090
cannot take us back to a truly essential

879
00:35:15,310 --> 00:35:13,730
life form and that we're also by the way

880
00:35:17,530 --> 00:35:15,320
having difficulty with this top wage

881
00:35:20,470 --> 00:35:17,540
which I discussed a week ago at the apps

882
00:35:22,270 --> 00:35:20,480
icon which is that we're still flailing

883
00:35:24,580 --> 00:35:22,280
around trying to get the pieces of

884
00:35:26,560 --> 00:35:24,590
origins together in a way that ties

885
00:35:28,270 --> 00:35:26,570
origins with what NASA is telling us

886
00:35:30,730 --> 00:35:28,280
about what's out here in the left wedge

887
00:35:32,500 --> 00:35:30,740
and so this gets to this the right-hand

888
00:35:34,360 --> 00:35:32,510

wedge this is sort of the remaining game

889
00:35:36,190 --> 00:35:34,370
in town which which Carl mentioned

890
00:35:38,770 --> 00:35:36,200
already which is this idea of synthetic

891
00:35:41,470 --> 00:35:38,780
biology it's actually a very old

892
00:35:42,610 --> 00:35:41,480
tradition and I mean right now people

893
00:35:44,260 --> 00:35:42,620
are talking about this as being a new

894
00:35:46,090 --> 00:35:44,270
field and pacsun think college is not

895
00:35:48,850 --> 00:35:46,100
really a field it's a sweet search

896
00:35:51,190 --> 00:35:48,860
strategy that complements other research

897
00:35:53,670 --> 00:35:51,200
strategies that we understand the world

898
00:35:55,960 --> 00:35:53,680
around us so people obviously use

899
00:35:58,360 --> 00:35:55,970
observation and something biology has

900
00:36:01,930 --> 00:35:58,370
used observation from the origin of the

901
00:36:04,180 --> 00:36:01,940
species another approach is analysis

902
00:36:05,680 --> 00:36:04,190
which is in some sense reductionist it's

903
00:36:07,570 --> 00:36:05,690
your first thing you do with the living

904
00:36:10,570 --> 00:36:07,580
species kill it and then you take it

905
00:36:12,550 --> 00:36:10,580
apart and that's certainly been done

906
00:36:14,920 --> 00:36:12,560
since the Enlightenment it's been done

907
00:36:18,070 --> 00:36:14,930
the molecular sentence for the last 150

908
00:36:23,350 --> 00:36:18,080
200 years very very very very productive

909
00:36:25,510 --> 00:36:23,360
but one of the things is that without a

910
00:36:28,060 --> 00:36:25,520
third will approach the third research

911
00:36:31,420 --> 00:36:28,070
strategy is synthesis which is to create

912
00:36:33,010 --> 00:36:31,430
life and it sort of goes by you know the

913
00:36:35,920 --> 00:36:33,020

philosophy if you're so smart why don't

914
00:36:38,530 --> 00:36:35,930
you rich right i mean synthesis says

915
00:36:39,880 --> 00:36:38,540
that if you really understand life or

916
00:36:43,120 --> 00:36:39,890
anything else for that matter you i'd be

917
00:36:45,580 --> 00:36:43,130
from making if you understand why and

918
00:36:47,470 --> 00:36:45,590
you know certain organic compounds our

919
00:36:49,570 --> 00:36:47,480
red dyes you ought to be able to make a

920
00:36:52,180 --> 00:36:49,580
red dye or if you under think that you

921
00:36:53,590 --> 00:36:52,190
understand why particular compound has

922
00:36:54,080 --> 00:36:53,600
pharmaceutical value out of they would

923
00:36:54,920 --> 00:36:54,090
make it

924
00:36:57,890 --> 00:36:54,930
compound which have the same

925
00:37:00,650 --> 00:36:57,900
pharmaceutical value so synthesis

926
00:37:03,830 --> 00:37:00,660
Android chemistry in particular as a way

927
00:37:07,400 --> 00:37:03,840
of testing understanding by constructing

928
00:37:10,880 --> 00:37:07,410
new forms of matter it is a special

929
00:37:12,980 --> 00:37:10,890
value and it is a way and enforcing

930
00:37:14,990 --> 00:37:12,990
discipline upon scientists in

931
00:37:17,480 --> 00:37:15,000
contradiction to their human instincts

932
00:37:19,790 --> 00:37:17,490
right the human instinct is that when

933
00:37:22,490 --> 00:37:19,800
data are emerging that contradict your

934
00:37:25,550 --> 00:37:22,500
theory you discard the data you don't

935
00:37:27,440 --> 00:37:25,560
discard the theory it's a very common in

936
00:37:29,120 --> 00:37:27,450
some sense it's necessary because most

937
00:37:30,530 --> 00:37:29,130
of the data you collected doesn't agree

938
00:37:33,170 --> 00:37:30,540

with your theory as an artifact is

939
00:37:35,030 --> 00:37:33,180
arising because the instrument is broken

940
00:37:37,370 --> 00:37:35,040
or because you haven't done right of the

941
00:37:39,530 --> 00:37:37,380
experiment correctly but when synthesis

942
00:37:42,620 --> 00:37:39,540
does is celexa put them on the moon goal

943
00:37:44,120 --> 00:37:42,630
that forces scientists across uncharted

944
00:37:46,460 --> 00:37:44,130
grounds where they're forced to

945
00:37:49,700 --> 00:37:46,470
encounter and solve unscripted problems

946
00:37:51,380 --> 00:37:49,710
in ways and do not allow self-deceptions

947
00:37:52,970 --> 00:37:51,390
and my favorite example for this is

948
00:37:54,620 --> 00:37:52,980
always the Mars climate orbiter that is

949
00:37:58,100 --> 00:37:54,630
if the guidance software is metric in

950
00:37:59,840 --> 00:37:58,110
the heart where it's English the rocket

951
00:38:01,460 --> 00:37:59,850
crashes now all the way out if you look

952
00:38:03,710 --> 00:38:01,470
at the mission reports you know they

953
00:38:05,390 --> 00:38:03,720
were evidence there's reason to believe

954
00:38:08,000 --> 00:38:05,400
if something was wrong it was put aside

955
00:38:10,310 --> 00:38:08,010
what synthesis does by setting this

956
00:38:11,780 --> 00:38:10,320
ambitious goal is to force you not to

957
00:38:13,970 --> 00:38:11,790
follow your instinct you've got to

958
00:38:16,760 --> 00:38:13,980
eventually have things work and for that

959
00:38:18,980 --> 00:38:16,770
synthesis guys discovery innovation in

960
00:38:20,450 --> 00:38:18,990
ways that analysis cannot and my

961
00:38:22,400 --> 00:38:20,460
favorite quote from Paul wonder actually

962
00:38:25,250 --> 00:38:22,410
from almost 30 years ago is it actually

963
00:38:27,380 --> 00:38:25,260

just to show you that synthesis is not a

964
00:38:30,590 --> 00:38:27,390
field it's the chemistry is almost a

965
00:38:32,960 --> 00:38:30,600
subfield within synthesis now chemistry

966
00:38:34,760 --> 00:38:32,970
has taken a tremendous advantage about

967
00:38:37,400 --> 00:38:34,770
it because we are able to make new forms

968
00:38:39,200 --> 00:38:37,410
of matter through synthesis as well and

969
00:38:41,570 --> 00:38:39,210
imagine how much easier it would be to

970
00:38:44,330 --> 00:38:41,580
do geology and to test a theory of plate

971
00:38:46,520 --> 00:38:44,340
tectonics if you could you know like

972
00:38:48,320 --> 00:38:46,530
Hitchhiker's Guide go to Magrathea and

973
00:38:50,000 --> 00:38:48,330
have them make you a new planet with a

974
00:38:52,190 --> 00:38:50,010
slightly different tweak that you could

975
00:38:56,090 --> 00:38:52,200
then study to see whether your theory

976
00:38:57,500 --> 00:38:56,100
help out how true here you're looking at

977
00:38:59,960 --> 00:38:57,510
four structures there are four different

978
00:39:01,400 --> 00:38:59,970
molecules to an organic chemist everyone

979
00:39:01,809 --> 00:39:01,410
has meaning I've already mentioned the

980
00:39:04,209 --> 00:39:01,819
one

981
00:39:06,999 --> 00:39:04,219
I'm left-hand corner the synthesis of

982
00:39:10,239 --> 00:39:07,009
urea was what led to the downfall of

983
00:39:12,430 --> 00:39:10,249
vitalism this molecule here psycho

984
00:39:15,939 --> 00:39:12,440
locket Etrian brand new synthesis by

985
00:39:18,069 --> 00:39:15,949
Bill cetera that it it forms the

986
00:39:21,279 --> 00:39:18,079
underpinnings of modern understanding of

987
00:39:22,479 --> 00:39:21,289
a run aromaticity a feature of benzene

988
00:39:24,519 --> 00:39:22,489

that you were forced to learn when you

989
00:39:25,719 --> 00:39:24,529
took organic chemistry I mean this

990
00:39:28,239 --> 00:39:25,729
structure all the way over here is

991
00:39:30,130 --> 00:39:28,249
vitamin b12 it was to the attempted

992
00:39:32,319 --> 00:39:30,140
synthesis of baton and you might imagine

993
00:39:33,819 --> 00:39:32,329
that making that molecule was indeed

994
00:39:36,279 --> 00:39:33,829
putting a man on the moon it was a

995
00:39:38,170 --> 00:39:36,289
difficult molecule to make but the

996
00:39:39,729 --> 00:39:38,180
principles of orbital symmetry emerged

997
00:39:41,439 --> 00:39:39,739
from that synthesis as scientists were

998
00:39:43,180 --> 00:39:41,449
dragged kicking and screaming across

999
00:39:44,949 --> 00:39:43,190
uncharted territory they encountered

1000
00:39:47,739 --> 00:39:44,959
problems they tried to make that

1001
00:39:49,569 --> 00:39:47,749
molecule and their failure to solve them

1002
00:39:52,239 --> 00:39:49,579
with existing Theory force them to come

1003
00:39:54,880 --> 00:39:52,249
up with new theory well the same thing

1004
00:39:56,499 --> 00:39:54,890
is for life okay and certainly when we

1005
00:39:59,319 --> 00:39:56,509
started going back and trying to

1006
00:40:00,579 --> 00:39:59,329
understand the gene theory of life one

1007
00:40:02,949 --> 00:40:00,589
of the questions you have to ask

1008
00:40:05,529 --> 00:40:02,959
yourself is what is the chemical

1009
00:40:07,120 --> 00:40:05,539
structures necessary to support a gene

1010
00:40:08,739 --> 00:40:07,130
that will then support Darwinian

1011
00:40:11,620 --> 00:40:08,749
evolution which will then support life

1012
00:40:14,170 --> 00:40:11,630
and one of the things that we may was

1013
00:40:16,599 --> 00:40:14,180

the compound not the left-hand compound

1014
00:40:18,699 --> 00:40:16,609
but the next one in the left compound of

1015
00:40:20,859 --> 00:40:18,709
quarters natural DNA what we may was

1016
00:40:23,859 --> 00:40:20,869
natural DNA with a repeating negative

1017
00:40:26,380 --> 00:40:23,869
charge has an replace replaced by a

1018
00:40:28,239 --> 00:40:26,390
structural unit these s double bond o s

1019
00:40:31,029 --> 00:40:28,249
double bond o which is very similar in

1020
00:40:33,609 --> 00:40:31,039
structure to the phosphates that join

1021
00:40:36,430 --> 00:40:33,619
natural DNA but which lack the repeating

1022
00:40:38,410 --> 00:40:36,440
charge and if you go back and read this

1023
00:40:40,989 --> 00:40:38,420
article as well as articles of follow

1024
00:40:43,779 --> 00:40:40,999
that when you replace the repeating

1025
00:40:45,219 --> 00:40:43,789
charge in a backbone of DNA by a

1026
00:40:48,759 --> 00:40:45,229
non-repeating unit that is otherwise

1027
00:40:51,489 --> 00:40:48,769
hydrophilic the molecule ceases to

1028
00:40:53,890 --> 00:40:51,499
support molecular recognition rule-based

1029
00:40:56,380 --> 00:40:53,900
molecular recognition after a point

1030
00:40:58,839 --> 00:40:56,390
these molecules here actually will work

1031
00:41:00,729 --> 00:40:58,849
as small fragments but when you to

1032
00:41:02,499 --> 00:41:00,739
longer fragment be things start to fall

1033
00:41:05,289 --> 00:41:02,509
and you start to have non-genetic

1034
00:41:07,150 --> 00:41:05,299
behavior and so from this came what we

1035
00:41:10,749 --> 00:41:07,160
call the polyelectrolyte theory of a

1036
00:41:13,180 --> 00:41:10,759
gene the attempt to make a DNA molecule

1037
00:41:15,220 --> 00:41:13,190
that doesn't have a repeating charge in

1038
00:41:17,560 --> 00:41:15,230

the backbone led to a failure

1039
00:41:22,270 --> 00:41:17,570
we can't we couldn't and of course that

1040
00:41:24,700 --> 00:41:22,280
forced us to rethink what was missing in

1041
00:41:26,800 --> 00:41:24,710
our existing theories and from that what

1042
00:41:29,349 --> 00:41:26,810
was missing in our existing theory was a

1043
00:41:31,750 --> 00:41:29,359
full understanding of why that DNA

1044
00:41:33,550 --> 00:41:31,760
molecule or RNA has these repeating

1045
00:41:35,410 --> 00:41:33,560
charges in the benefit they turn out to

1046
00:41:38,590 --> 00:41:35,420
be very important for the rule-based

1047
00:41:40,780 --> 00:41:38,600
molecular recognition properties that

1048
00:41:42,970 --> 00:41:40,790
are essential for inheritance that are

1049
00:41:44,440 --> 00:41:42,980
also essential for evolution and that's

1050
00:41:46,210 --> 00:41:44,450
captured under this idea of a

1051
00:41:48,849 --> 00:41:46,220
second-generation model for DNA

1052
00:41:50,680 --> 00:41:48,859
structure it also provides a way for

1053
00:41:52,510 --> 00:41:50,690
which you might look for the universal

1054
00:41:55,090 --> 00:41:52,520
gene not just the gene on earth by

1055
00:41:57,180 --> 00:41:55,100
looking for not the basis which we have

1056
00:41:59,859 --> 00:41:57,190
shown and we'll show you in a minute our

1057
00:42:02,859 --> 00:41:59,869
variable but by looking for the backbone

1058
00:42:04,720 --> 00:42:02,869
repeating charge that under at least a

1059
00:42:08,500 --> 00:42:04,730
polyelectrolyte theory of a gene is

1060
00:42:10,810 --> 00:42:08,510
required for all genes to work well cool

1061
00:42:12,640 --> 00:42:10,820
it's clear that other things don't

1062
00:42:13,900 --> 00:42:12,650
require it as as Carl mentioned in the

1063
00:42:17,020 --> 00:42:13,910

introduction I mean there you are

1064
00:42:18,849 --> 00:42:17,030
there's your for basis the base is under

1065
00:42:21,940 --> 00:42:18,859
the Watson and Crick theory of a gene

1066
00:42:24,220 --> 00:42:21,950
were central the backbone phosphates

1067
00:42:26,380 --> 00:42:24,230
were peripheral well we now know that

1068
00:42:28,720 --> 00:42:26,390
the back of phosphates are quite central

1069
00:42:31,030 --> 00:42:28,730
the bases are actually although not

1070
00:42:32,950 --> 00:42:31,040
peripheral are certainly less central in

1071
00:42:35,890 --> 00:42:32,960
the sense that they can certainly be

1072
00:42:37,690 --> 00:42:35,900
changed a lot easier actually the good

1073
00:42:40,240 --> 00:42:37,700
test for the students in the audience to

1074
00:42:42,340 --> 00:42:40,250
look at those four structures I have cgt

1075
00:42:44,500 --> 00:42:42,350
and a which you'll notice I only have a

1076
00:42:46,540 --> 00:42:44,510
in quotation marks the others are not in

1077
00:42:49,150 --> 00:42:46,550
quotation marks that's because the

1078
00:42:51,099 --> 00:42:49,160
structure of a is actually already been

1079
00:42:55,330 --> 00:42:51,109
changed from what is present in your DNA

1080
00:42:56,680 --> 00:42:55,340
and all the students should now mention

1081
00:43:00,060 --> 00:42:56,690
that the person sitting next to them in

1082
00:43:03,370 --> 00:43:00,070
authority why that structures wrong or

1083
00:43:05,830 --> 00:43:03,380
different it actually is better I'll

1084
00:43:07,900 --> 00:43:05,840
pause for two seconds that's enough

1085
00:43:09,280 --> 00:43:07,910
pause and then direct your attention for

1086
00:43:10,660 --> 00:43:09,290
those of you didn't know the answer to

1087
00:43:13,030 --> 00:43:10,670
this amino group down here at the bottom

1088
00:43:14,920 --> 00:43:13,040

that's actually not President add name

1089
00:43:17,290 --> 00:43:14,930
God made a mistake when she made this

1090
00:43:19,720 --> 00:43:17,300
come how she left at all and that's why

1091
00:43:21,880 --> 00:43:19,730
adenine and thymine forms only two

1092
00:43:23,490 --> 00:43:21,890
hydrogen bonds not the three hydrogen

1093
00:43:26,520 --> 00:43:23,500
bonds that hold the other GCC

1094
00:43:28,230 --> 00:43:26,530
spare one of the questions of course is

1095
00:43:30,000 --> 00:43:28,240
again you know if you're so smart why

1096
00:43:32,160 --> 00:43:30,010
don't you just design a new genetic

1097
00:43:34,080 --> 00:43:32,170
molecule and I've already told you that

1098
00:43:35,460 --> 00:43:34,090
we failed once we're not smart enough to

1099
00:43:36,960 --> 00:43:35,470
design a genetic molecule where the

1100
00:43:40,290 --> 00:43:36,970
repeating negative charge has been

1101
00:43:44,580 --> 00:43:40,300
removed but we turned out to be able to

1102
00:43:46,980 --> 00:43:44,590
design a new genetic system where we

1103
00:43:48,660 --> 00:43:46,990
shuffled around the hydrogen bond donors

1104
00:43:50,760 --> 00:43:48,670
and accepted groups let me just point

1105
00:43:53,370 --> 00:43:50,770
out the watson-crick rules for those of

1106
00:43:54,870 --> 00:43:53,380
you who are students right the

1107
00:43:56,790 --> 00:43:54,880
watson-crick base pairing rule is

1108
00:43:59,030 --> 00:43:56,800
following this two rules of

1109
00:44:00,870 --> 00:43:59,040
complementarity one is a size

1110
00:44:03,180 --> 00:44:00,880
complementarity principle that is at

1111
00:44:05,180 --> 00:44:03,190
large things pair with small things of

1112
00:44:07,740 --> 00:44:05,190
big purine pairs of a small perimeter

1113
00:44:09,840 --> 00:44:07,750

the other rule is in hydrogen bond

1114
00:44:11,940 --> 00:44:09,850
donors which I have here is these red

1115
00:44:13,770 --> 00:44:11,950
hydrogen's pair with hydrogen bond

1116
00:44:17,190 --> 00:44:13,780
acceptor which I have us the blue

1117
00:44:19,170 --> 00:44:17,200
nitrogen to oxygen so see as a small

1118
00:44:21,060 --> 00:44:19,180
thing presenting a hydrogen bond red

1119
00:44:23,970 --> 00:44:21,070
blue-blue that's a hydrogen bond donor

1120
00:44:25,410 --> 00:44:23,980
acceptor acceptor pairs with G a big

1121
00:44:29,490 --> 00:44:25,420
thing having a hydrogen bond acceptor

1122
00:44:32,610 --> 00:44:29,500
donor donor blue red red and that is how

1123
00:44:34,740 --> 00:44:32,620
you get to base pairs obviously a and T

1124
00:44:37,040 --> 00:44:34,750
even with you know deep down here at the

1125
00:44:38,820 --> 00:44:37,050
bottom have the same size

1126
00:44:41,490 --> 00:44:38,830
complementarity just as the hydrogen

1127
00:44:43,590 --> 00:44:41,500
bond patterns are different with T it's

1128
00:44:46,410 --> 00:44:43,600
blue red blue and with a in this

1129
00:44:48,900 --> 00:44:46,420
modified varmis red blue red and so that

1130
00:44:51,840 --> 00:44:48,910
means if this big thing a does not pair

1131
00:44:55,170 --> 00:44:51,850
with C and this big thing G does not

1132
00:44:59,610 --> 00:44:55,180
pair with see well by switching around

1133
00:45:01,170 --> 00:44:59,620
by shuffling by moving the red things

1134
00:45:03,240 --> 00:45:01,180
and the blue things a hydrogen bond

1135
00:45:06,540 --> 00:45:03,250
donors and acceptors back and forth you

1136
00:45:07,890 --> 00:45:06,550
can conjecture Lee create a new form of

1137
00:45:09,360 --> 00:45:07,900
genetic substance but of course

1138
00:45:11,400 --> 00:45:09,370

synthesis is how you test that

1139
00:45:13,620 --> 00:45:11,410
conjecture and so you make all these

1140
00:45:16,440 --> 00:45:13,630
compounds and you discover the yes

1141
00:45:19,860 --> 00:45:16,450
indeed you can make many of them and you

1142
00:45:21,660 --> 00:45:19,870
can do what we do in DNA synthesis is we

1143
00:45:24,420 --> 00:45:21,670
measure melting temperatures of DNA

1144
00:45:26,040 --> 00:45:24,430
strands that contain funny things I just

1145
00:45:28,920 --> 00:45:26,050
put up a whole bunch of stuff here which

1146
00:45:31,290 --> 00:45:28,930
includes all of the base pairs that we

1147
00:45:34,110 --> 00:45:31,300
made which contain three hydrogen bonds

1148
00:45:35,250 --> 00:45:34,120
between the big thing down here the

1149
00:45:38,430 --> 00:45:35,260
small thing the big

1150
00:45:40,530 --> 00:45:38,440
small thing this row contains base pairs

1151
00:45:42,000 --> 00:45:40,540
between big and small but there are two

1152
00:45:43,740 --> 00:45:42,010
hydrogen bonds because we leave

1153
00:45:45,090 --> 00:45:43,750
something off at the bottom or here we

1154
00:45:46,290 --> 00:45:45,100
leave something off at the top or there

1155
00:45:48,480 --> 00:45:46,300
will be something off at the bottom

1156
00:45:50,460 --> 00:45:48,490
another thing off at the bottom here's

1157
00:45:53,490 --> 00:45:50,470
something joined by exactly one hydrogen

1158
00:45:55,230 --> 00:45:53,500
bond and we have all sorts of other

1159
00:45:57,210 --> 00:45:55,240
structural parameters I won't go into

1160
00:46:00,060 --> 00:45:57,220
discussing but you can read about in

1161
00:46:02,310 --> 00:46:00,070
this paper that we wrote about five

1162
00:46:04,410 --> 00:46:02,320
years ago with Ron guard that creates

1163
00:46:06,450 --> 00:46:04,420

rules so if you want to go back and

1164
00:46:09,600 --> 00:46:06,460
design your own artificial genetic

1165
00:46:12,390 --> 00:46:09,610
system if these rules are correct again

1166
00:46:14,850 --> 00:46:12,400
this is a synthesis proposition or

1167
00:46:16,260 --> 00:46:14,860
synthesis testable proposition you ought

1168
00:46:18,600 --> 00:46:16,270
to be able to make anything following

1169
00:46:21,060 --> 00:46:18,610
rules but one of the rules is that yep

1170
00:46:22,980 --> 00:46:21,070
three hydrogen bonds is better than two

1171
00:46:24,780 --> 00:46:22,990
and two hydrogen bonds is better than

1172
00:46:26,310 --> 00:46:24,790
one that's what's shown in this

1173
00:46:28,020 --> 00:46:26,320
particular diagram where you're looking

1174
00:46:30,330 --> 00:46:28,030
on the left at melting temperatures of

1175
00:46:33,030 --> 00:46:30,340
some representative samples the red dots

1176
00:46:34,290 --> 00:46:33,040
are melting temperatures of species we

1177
00:46:37,530 --> 00:46:34,300
have a base in the middle which is

1178
00:46:40,200 --> 00:46:37,540
joined by three hydrogen bonds yellow

1179
00:46:42,690 --> 00:46:40,210
dots and that diagram or measuring

1180
00:46:44,490 --> 00:46:42,700
melling temperatures of species which

1181
00:46:46,680 --> 00:46:44,500
would contain base courage chillin by

1182
00:46:49,290 --> 00:46:46,690
two hydrogen bonds and the black are

1183
00:46:51,270 --> 00:46:49,300
either mismatches or one hydrogen bond

1184
00:46:53,760 --> 00:46:51,280
and you'll discover that three hydrogen

1185
00:46:55,470 --> 00:46:53,770
bonds is better than two which is better

1186
00:46:57,530 --> 00:46:55,480
than one that is red dots are better

1187
00:46:59,730 --> 00:46:57,540
than yellow dots there than black dots

1188
00:47:01,800 --> 00:46:59,740

even when when you have size

1189
00:47:04,500 --> 00:47:01,810
complementarity that is a purine pairs

1190
00:47:07,050 --> 00:47:04,510
of the primitive as big pairs with small

1191
00:47:10,230 --> 00:47:07,060
it's also true to some extent win big

1192
00:47:12,270 --> 00:47:10,240
pairs with big and small pairs are small

1193
00:47:16,380 --> 00:47:12,280
so we have some relatively stable

1194
00:47:18,270 --> 00:47:16,390
permanent criminal even when you have a

1195
00:47:20,970 --> 00:47:18,280
small thing paired with small thing

1196
00:47:22,470 --> 00:47:20,980
letters not sighs complimentary but if

1197
00:47:24,750 --> 00:47:22,480
you have three hydrogen bonds joining

1198
00:47:26,580 --> 00:47:24,760
them they still look pretty well well

1199
00:47:27,900 --> 00:47:26,590
that's kind of cool now I know I sure

1200
00:47:29,970 --> 00:47:27,910
how many cameras there on the audience

1201
00:47:31,560 --> 00:47:29,980
and I put these two slides up just in

1202
00:47:34,470 --> 00:47:31,570
case people are interested in how you go

1203
00:47:37,770 --> 00:47:34,480
back and do this right we don't get the

1204
00:47:40,290 --> 00:47:37,780
right answers right the first time we

1205
00:47:43,170 --> 00:47:40,300
identify trends we rationalize

1206
00:47:45,180 --> 00:47:43,180
exceptions we test hypotheses so as I

1207
00:47:46,390 --> 00:47:45,190
mentioned we have a small thing pair

1208
00:47:50,260 --> 00:47:46,400
with a small thing in

1209
00:47:52,990 --> 00:47:50,270
non sighs complementary fashion joined

1210
00:47:54,970 --> 00:47:53,000
by three hydrogen bonds but you know

1211
00:47:57,910 --> 00:47:54,980
this is actually more stable than we

1212
00:47:59,230 --> 00:47:57,920
expected to be based on trends and part

1213
00:48:01,329 --> 00:47:59,240

of the reason we think that's the case

1214
00:48:03,700 --> 00:48:01,339
is because this base has a positive

1215
00:48:06,370 --> 00:48:03,710
charge on the nitrogen as being

1216
00:48:08,650 --> 00:48:06,380
indicated here next but the positive

1217
00:48:11,620 --> 00:48:08,660
charge seems to be good in the stacking

1218
00:48:14,349 --> 00:48:11,630
of a base pair it turns out that if you

1219
00:48:17,349 --> 00:48:14,359
put a negative charge as we have here on

1220
00:48:20,079 --> 00:48:17,359
this red blue red thing it's less stable

1221
00:48:23,170 --> 00:48:20,089
and um come out you come up with this

1222
00:48:24,970 --> 00:48:23,180
rule that you're not allowed to have an

1223
00:48:26,620 --> 00:48:24,980
aniline or negative charge in the

1224
00:48:28,690 --> 00:48:26,630
nucleobase stack even though you can't

1225
00:48:30,519 --> 00:48:28,700
have a positive charge and there are all

1226
00:48:34,329 --> 00:48:30,529
sorts of other rules that we can go back

1227
00:48:36,190 --> 00:48:34,339
and test by making new forms of matter

1228
00:48:38,260 --> 00:48:36,200
this is the synthesis strategy right

1229
00:48:40,720 --> 00:48:38,270
complement analysis complements

1230
00:48:42,789 --> 00:48:40,730
observation we couldn't go back and make

1231
00:48:46,480 --> 00:48:42,799
these new forms of matter we would have

1232
00:48:49,329 --> 00:48:46,490
some problems actually trying to to get

1233
00:48:51,579 --> 00:48:49,339
this theory to be well grounded in our

1234
00:48:52,990 --> 00:48:51,589
heads there's a whole story which I

1235
00:48:55,120 --> 00:48:53,000
won't tell which you can read about in

1236
00:48:56,680 --> 00:48:55,130
this paper by Daniel hooter where it

1237
00:48:59,079 --> 00:48:56,690
turns out that some of these things this

1238
00:49:01,269 --> 00:48:59,089

is a donor donor acceptor hydrogen

1239
00:49:03,279 --> 00:49:01,279
bonding pattern on a small heterocycle

1240
00:49:05,710 --> 00:49:03,289
it turns out that some of those don't

1241
00:49:07,630 --> 00:49:05,720
work very well because of chemical

1242
00:49:10,210 --> 00:49:07,640
instability not not a hydrogen bonding

1243
00:49:12,430 --> 00:49:10,220
instability and so we fixed that by

1244
00:49:14,289 --> 00:49:12,440
doing chemical changes and we also had

1245
00:49:17,049 --> 00:49:14,299
problems which you find in modern bases

1246
00:49:20,049 --> 00:49:17,059
call tautomerization this is where

1247
00:49:21,579 --> 00:49:20,059
hydrogen's move around spontaneously you

1248
00:49:23,319 --> 00:49:21,589
don't want to have hydrogen moving

1249
00:49:25,269 --> 00:49:23,329
around in the molecule that you're using

1250
00:49:27,250 --> 00:49:25,279
to have kids especially if you're using

1251
00:49:29,500 --> 00:49:27,260
those hydrogen bonds tell what

1252
00:49:31,329 --> 00:49:29,510
information goes into the kids because

1253
00:49:33,579 --> 00:49:31,339
moving hydrogen's around changes the

1254
00:49:35,500 --> 00:49:33,589
information that's a mutation we had one

1255
00:49:38,620 --> 00:49:35,510
of these base pairs was extremely new

1256
00:49:40,569 --> 00:49:38,630
tunic ten percent of the time it was

1257
00:49:43,240 --> 00:49:40,579
causing a mutation and ninety percent of

1258
00:49:45,579 --> 00:49:43,250
the time only was it complementing the

1259
00:49:48,130 --> 00:49:45,589
correct compliment and so we had to fix

1260
00:49:50,200 --> 00:49:48,140
that so you can see all sorts of ways in

1261
00:49:52,029 --> 00:49:50,210
which Simmons synthesis is demonstrating

1262
00:49:54,190 --> 00:49:52,039
this predictive manipulative control

1263
00:49:56,680 --> 00:49:54,200

over base pairing using this sort of

1264
00:49:58,809 --> 00:49:56,690
metal language of organic chemistry this

1265
00:49:59,549 --> 00:49:58,819
is just a way of saying that our theory

1266
00:50:04,799 --> 00:49:59,559
is good

1267
00:50:07,319 --> 00:50:04,809
enough to create a DNA system with now

1268
00:50:09,509 --> 00:50:07,329
on additional eight letters that

1269
00:50:11,309 --> 00:50:09,519
watson-crick base brain really is pretty

1270
00:50:13,799 --> 00:50:11,319
much as simple as shuffling hydrogen

1271
00:50:15,420 --> 00:50:13,809
bond donors and acceptors back and forth

1272
00:50:17,519 --> 00:50:15,430
within the context of size

1273
00:50:19,799 --> 00:50:17,529
complementarity and that was not the

1274
00:50:22,049 --> 00:50:19,809
case as I mentioned a moment ago for the

1275
00:50:24,449 --> 00:50:22,059
backbone so our theory is good enough to

1276
00:50:27,120 --> 00:50:24,459
understand basis but Arthur is not good

1277
00:50:28,920 --> 00:50:27,130
tough to understand the backbone um and

1278
00:50:30,179 --> 00:50:28,930
this has been terribly useful I won't go

1279
00:50:32,400 --> 00:50:30,189
through all the studies if some of you

1280
00:50:35,370 --> 00:50:32,410
have had HIV hepatitis b your hepatitis

1281
00:50:38,279 --> 00:50:35,380
c you would be one of the four hundred

1282
00:50:40,709 --> 00:50:38,289
thousand patients last year that use

1283
00:50:44,969 --> 00:50:40,719
this non-standard genetic information to

1284
00:50:47,059 --> 00:50:44,979
help personalized healthcare no I'm the

1285
00:50:49,979 --> 00:50:47,069
time has gone to sleep on the frame

1286
00:50:53,519 --> 00:50:49,989
clock but so let's see how we're doing

1287
00:50:55,349 --> 00:50:53,529
with respect to time ok good well one of

1288
00:50:57,299 --> 00:50:55,359

the questions you can ask is okay great

1289
00:51:00,329 --> 00:50:57,309
that's the polyelectrolyte theory of the

1290
00:51:03,390 --> 00:51:00,339
gene but now the question is well can

1291
00:51:06,029 --> 00:51:03,400
you get this artificial genic system to

1292
00:51:08,160 --> 00:51:06,039
support Darwinian evolution of course at

1293
00:51:09,509 --> 00:51:08,170
some point you're going to say well you

1294
00:51:11,339 --> 00:51:09,519
can get it to support Darwinian

1295
00:51:14,519 --> 00:51:11,349
evolution can you get it to support life

1296
00:51:17,189 --> 00:51:14,529
um one of our problems of course was

1297
00:51:20,279 --> 00:51:17,199
that we did not have the stomach to

1298
00:51:23,179 --> 00:51:20,289
create a brand-new enzyme that would

1299
00:51:25,919 --> 00:51:23,189
accept a genetic alphabet with 12

1300
00:51:27,509 --> 00:51:25,929
nucleotides different before that we

1301
00:51:30,449 --> 00:51:27,519
already have plus the eight that we

1302
00:51:34,529 --> 00:51:30,459
invented and furthermore the natural

1303
00:51:37,140 --> 00:51:34,539
polymerizes I think God or evolution has

1304
00:51:39,390 --> 00:51:37,150
given us are well adapted for the four

1305
00:51:41,640 --> 00:51:39,400
bases that we already have and so we

1306
00:51:43,169 --> 00:51:41,650
spent a lot of time trying to get DNA

1307
00:51:45,120 --> 00:51:43,179
polymerases that would work with the

1308
00:51:47,669 --> 00:51:45,130
expenditure natick alphabet with 12

1309
00:51:49,769 --> 00:51:47,679
letters in addition to the four and it

1310
00:51:53,400 --> 00:51:49,779
all came down to a focus on this green

1311
00:51:55,140 --> 00:51:53,410
pair of electrons so this is done shared

1312
00:51:58,259 --> 00:51:55,150
pair of electrons is presented to the

1313
00:52:02,299 --> 00:51:58,269

minor groove by both C and G which are

1314
00:52:06,449 --> 00:52:02,309
shown here they're also presented by T

1315
00:52:09,059 --> 00:52:06,459
or just case uracil and a in this case

1316
00:52:10,030 --> 00:52:09,069
amino a and these unshared pair of

1317
00:52:14,200 --> 00:52:10,040
electrons in the minor

1318
00:52:16,450 --> 00:52:14,210
groove is a recognition spot for polymer

1319
00:52:18,670 --> 00:52:16,460
ases and we had really only two choices

1320
00:52:20,530 --> 00:52:18,680
one was to change the amino acids that

1321
00:52:23,050 --> 00:52:20,540
we're looking for those green electrons

1322
00:52:25,570 --> 00:52:23,060
in the minor groove or to go to one of

1323
00:52:27,790 --> 00:52:25,580
the synthetic pairs which is this donor

1324
00:52:30,910 --> 00:52:27,800
donor acceptor hydrogen bonding pattern

1325
00:52:33,280 --> 00:52:30,920
which has a green pair of electrons on

1326
00:52:35,290 --> 00:52:33,290
both the big component here and the

1327
00:52:38,310 --> 00:52:35,300
small component there now we've done

1328
00:52:41,950 --> 00:52:38,320
both of these at this point and and and

1329
00:52:43,510 --> 00:52:41,960
that that's the same slide so so and

1330
00:52:45,670 --> 00:52:43,520
there's the recognition element that's

1331
00:52:47,200 --> 00:52:45,680
where most polymerizes are looking for

1332
00:52:48,730 --> 00:52:47,210
that unshared pair of electrons and

1333
00:52:51,430 --> 00:52:48,740
those are the amino acid residues and

1334
00:52:53,230 --> 00:52:51,440
family a plume races on the left and

1335
00:52:55,450 --> 00:52:53,240
family be Clem races on the right that

1336
00:52:58,990 --> 00:52:55,460
are actually looking for that green pair

1337
00:53:00,970 --> 00:52:59,000
of electrons some of which some of the

1338
00:53:02,890 --> 00:53:00,980

extra letters in the genetic opera that

1339
00:53:06,190 --> 00:53:02,900
we have made don't have them here's one

1340
00:53:07,810 --> 00:53:06,200
that does not and some of them of the

1341
00:53:09,640 --> 00:53:07,820
extra letters in the genetic alphabet

1342
00:53:12,070 --> 00:53:09,650
that we may do have that green pair of

1343
00:53:14,740 --> 00:53:12,080
electrons so both strategies were

1344
00:53:17,160 --> 00:53:14,750
followed and I won't go to the detail

1345
00:53:20,110 --> 00:53:17,170
this is a case where we're doing a

1346
00:53:24,670 --> 00:53:20,120
Darwinian evolution actually an

1347
00:53:27,100 --> 00:53:24,680
artificial six-letter genetic system

1348
00:53:29,020 --> 00:53:27,110
those are the six letters four of them

1349
00:53:32,290 --> 00:53:29,030
are natural cytosine is natural gwanny

1350
00:53:34,570 --> 00:53:32,300
is natural timing is natural and Adnan

1351
00:53:36,880 --> 00:53:34,580
is natural this pair is a pair of

1352
00:53:38,560 --> 00:53:36,890
hydrogen bonding species that are a

1353
00:53:41,020 --> 00:53:38,570
fifth and six letter the genetic

1354
00:53:42,690 --> 00:53:41,030
alphabet if you look closely the red and

1355
00:53:45,280 --> 00:53:42,700
blue hydrogen bond donor and acceptor

1356
00:53:47,530 --> 00:53:45,290
things are not at the same spots as they

1357
00:53:49,510 --> 00:53:47,540
are here there's not a green pair of

1358
00:53:52,030 --> 00:53:49,520
electrons down where my laser pointer is

1359
00:53:56,620 --> 00:53:52,040
but we have engineered the reverse

1360
00:53:58,990 --> 00:53:56,630
transcriptase that is doing this PCR

1361
00:54:00,820 --> 00:53:59,000
type of amplification by replacing the

1362
00:54:04,030 --> 00:54:00,830
amino acid at position 1 88 in a

1363
00:54:07,150 --> 00:54:04,040

position amino acid at position 4 78 to

1364
00:54:09,400 --> 00:54:07,160
try to let the natural enzyme take these

1365
00:54:11,530 --> 00:54:09,410
unnatural substrates and it was from

1366
00:54:14,430 --> 00:54:11,540
this that Phillip ball gave us this

1367
00:54:17,170 --> 00:54:14,440
wonderful headline article enzyme stitch

1368
00:54:21,010 --> 00:54:17,180
non-natural DNA guided evolution

1369
00:54:23,799 --> 00:54:21,020
man-made stuff of life all right um

1370
00:54:25,210 --> 00:54:23,809
there were problems with this system as

1371
00:54:27,700 --> 00:54:25,220
well I've already mentioned about

1372
00:54:31,480 --> 00:54:27,710
tautomerism there's a work that we've

1373
00:54:34,690 --> 00:54:31,490
done to allow six-letter pcr to manage

1374
00:54:36,339 --> 00:54:34,700
that and there's now a six-letter pcr

1375
00:54:44,140 --> 00:54:36,349
that we have with a six letters being

1376
00:54:46,329 --> 00:54:44,150
Phi of T instead of comedy and I so see

1377
00:54:48,069 --> 00:54:46,339
Isis see and icg which are two

1378
00:54:50,380 --> 00:54:48,079
additional letters so there's this

1379
00:54:52,569 --> 00:54:50,390
second example of a six letter based

1380
00:54:55,599 --> 00:54:52,579
there and that's what got me called an

1381
00:54:58,240 --> 00:54:55,609
old school synthetic biologist meaning

1382
00:55:02,140 --> 00:54:58,250
somebody who tries to come up with new

1383
00:55:04,299 --> 00:55:02,150
genetic systems that work as a way of

1384
00:55:06,400 --> 00:55:04,309
testing these basic questions like how

1385
00:55:09,280 --> 00:55:06,410
life got started or whether forms in my

1386
00:55:11,980 --> 00:55:09,290
in my tank this sale for those of you

1387
00:55:16,480 --> 00:55:11,990
interested the just to close the circle

1388
00:55:18,490 --> 00:55:16,490

we do have now a case where we actually

1389
00:55:20,589 --> 00:55:18,500
have done a six letter P Sierra this is

1390
00:55:22,420 --> 00:55:20,599
just published last year where there's

1391
00:55:24,520 --> 00:55:22,430
an unshared pair of electrons the green

1392
00:55:25,750 --> 00:55:24,530
electrons in the minor groove which is

1393
00:55:28,059 --> 00:55:25,760
where the laser pointer is pointing

1394
00:55:30,609 --> 00:55:28,069
right now the other green pair of

1395
00:55:32,470 --> 00:55:30,619
electrons is over here now you can

1396
00:55:35,950 --> 00:55:32,480
decide for yourself whether or not the

1397
00:55:37,599 --> 00:55:35,960
system can undergo Darwinian evolution

1398
00:55:40,359 --> 00:55:37,609
we have in this paper and you can look

1399
00:55:42,160 --> 00:55:40,369
at this the fact that we have

1400
00:55:44,589 --> 00:55:42,170
polymerizes that will amplify a

1401
00:55:46,539 --> 00:55:44,599
six-letter genetic system where the

1402
00:55:49,450 --> 00:55:46,549
fifth and six letters are these two

1403
00:55:52,150 --> 00:55:49,460
bases we have mutations impact on

1404
00:55:53,829 --> 00:55:52,160
surveys this base over here and this

1405
00:55:55,750 --> 00:55:53,839
space over here what i've shown you here

1406
00:55:58,089 --> 00:55:55,760
is the possibility of this system doing

1407
00:56:01,299 --> 00:55:58,099
mutation about one percent of the time

1408
00:56:03,940 --> 00:56:01,309
this guy the funny small thing will not

1409
00:56:07,150 --> 00:56:03,950
find it's appropriate partner the funny

1410
00:56:09,010 --> 00:56:07,160
big thing but it will deprotonate and it

1411
00:56:11,440 --> 00:56:09,020
deprotonate it changes the hydrogen

1412
00:56:14,380 --> 00:56:11,450
bonding pattern so that the compliment /

1413
00:56:17,799 --> 00:56:14,390

here is not the funny big thing but

1414
00:56:19,359 --> 00:56:17,809
rather natural g and there's a mutation

1415
00:56:23,349 --> 00:56:19,369
process that we can look in this system

1416
00:56:25,420 --> 00:56:23,359
where g is replaced instead of that and

1417
00:56:27,970 --> 00:56:25,430
likewise this guy every now and then

1418
00:56:29,860 --> 00:56:27,980
we'll hair template opposite protonated

1419
00:56:33,160 --> 00:56:29,870
see these are mechanism

1420
00:56:36,940 --> 00:56:33,170
by which you've all this system and not

1421
00:56:38,740 --> 00:56:36,950
only replace the two additional bases by

1422
00:56:40,180 --> 00:56:38,750
the two standard basis but also convert

1423
00:56:42,220 --> 00:56:40,190
the two standard basis into the two

1424
00:56:45,310 --> 00:56:42,230
additional basis and you can see a

1425
00:56:48,340 --> 00:56:45,320
system which can undergo the basis of

1426
00:56:49,540 --> 00:56:48,350
point mutation and well keep in mind

1427
00:56:51,760 --> 00:56:49,550
that Jerry Joyce did not talk about

1428
00:56:54,010 --> 00:56:51,770
chemical system capable Darwinian

1429
00:56:55,660 --> 00:56:54,020
evolution which is certainly is when you

1430
00:56:57,370 --> 00:56:55,670
talk about with a self-sustaining

1431
00:56:59,410 --> 00:56:57,380
chemical system paper with Darwin

1432
00:57:00,850 --> 00:56:59,420
evolution what's absolutely clear right

1433
00:57:03,160 --> 00:57:00,860
now is in order for this is undergo

1434
00:57:05,020 --> 00:57:03,170
Darwinian evolution you have to have a

1435
00:57:07,030 --> 00:57:05,030
graduate student or postdoc sitting

1436
00:57:09,700 --> 00:57:07,040
there at every cycle and adding reagents

1437
00:57:12,550 --> 00:57:09,710
removing waste products some supporting

1438
00:57:14,560 --> 00:57:12,560

the metabolism and so the evolution of

1439
00:57:17,500 --> 00:57:14,570
this particular system is slow on two

1440
00:57:19,120 --> 00:57:17,510
surgeries so that's basically what we

1441
00:57:20,740 --> 00:57:19,130
have to say I mean there's are the four

1442
00:57:22,240 --> 00:57:20,750
paths I've obviously talked about the

1443
00:57:23,800 --> 00:57:22,250
bottom and the right triangle in large

1444
00:57:25,540 --> 00:57:23,810
part because I spent a lot of time on

1445
00:57:27,430 --> 00:57:25,550
the other two triangles just a week ago

1446
00:57:31,360 --> 00:57:27,440
for a conference that many of you were

1447
00:57:33,520 --> 00:57:31,370
at but with that let me stop them really

1448
00:57:35,890 --> 00:57:33,530
summarize just by saying that yes you

1449
00:57:39,100 --> 00:57:35,900
can go backwards in time to simpler life

1450
00:57:40,840 --> 00:57:39,110
but not to essentially it's really not

1451
00:57:44,410 --> 00:57:40,850
all that clear that it's all about

1452
00:57:46,000 --> 00:57:44,420
informative about what we think is

1453
00:57:47,380 --> 00:57:46,010
necessary for the essence of life

1454
00:57:48,940 --> 00:57:47,390
although it's quite clear the Darwinian

1455
00:57:50,650 --> 00:57:48,950
evolution is a very effective way of

1456
00:57:53,680 --> 00:57:50,660
doing things it may not be the only way

1457
00:57:55,540 --> 00:57:53,690
um but certainly this is what drives us

1458
00:57:57,670 --> 00:57:55,550
to construct artificial light in the

1459
00:58:01,450 --> 00:57:57,680
laboratory with a target on chemistry

1460
00:58:03,790 --> 00:58:01,460
and Darwin and not other things that we

1461
00:58:05,500 --> 00:58:03,800
may not what we thought of and certainly

1462
00:58:06,910 --> 00:58:05,510
reject like vitalism that certainly

1463
00:58:09,160 --> 00:58:06,920

other things that we haven't necessary

1464
00:58:10,840 --> 00:58:09,170
thought but by saying this ambitious

1465
00:58:12,370 --> 00:58:10,850
goal the thought is that we're being

1466
00:58:14,920 --> 00:58:12,380
dragged kicking and screaming across

1467
00:58:17,890 --> 00:58:14,930
uncharted territory where if we are

1468
00:58:19,870 --> 00:58:17,900
unable to get emergent properties out of

1469
00:58:20,980 --> 00:58:19,880
sight in vitro selection experiments

1470
00:58:23,350 --> 00:58:20,990
with a six letter or eight letter

1471
00:58:24,910 --> 00:58:23,360
genetic alphabet we're going to be

1472
00:58:26,830 --> 00:58:24,920
missing something in our theory of life

1473
00:58:29,140 --> 00:58:26,840
and that's of course what this emphasis

1474
00:58:32,230 --> 00:58:29,150
activity centers a strategy is supposed

1475
00:58:33,550 --> 00:58:32,240
to produce so let me stop oh thank you

1476
00:58:37,420 --> 00:58:33,560
for your attention I'll be happy to

1477
00:58:39,070 --> 00:58:37,430
answer any questions I can receive okay

1478
00:58:41,150 --> 00:58:39,080
thank you Steve I call the back right

1479
00:58:45,210 --> 00:58:41,160
speaker

1480
00:58:47,640 --> 00:58:45,220
okay if you have a question would you

1481
00:58:49,740 --> 00:58:47,650
please raise your hand on WebEx and I'll

1482
00:58:51,630 --> 00:58:49,750
also give folks an opportunity to just

1483
00:58:53,849 --> 00:58:51,640
jump in with questions but while I've

1484
00:58:57,120 --> 00:58:53,859
got the open mic here let me just put in

1485
00:58:59,450 --> 00:58:57,130
a plug first of all for the archives if

1486
00:59:02,069 --> 00:58:59,460
you would like to tell somebody about

1487
00:59:04,170 --> 00:59:02,079
Steve's talk and they weren't able to

1488
00:59:06,750 --> 00:59:04,180

hear it it's going to be archived within

1489
00:59:09,299 --> 00:59:06,760
a few days on the NAI website you'll be

1490
00:59:11,579 --> 00:59:09,309
able to see Steve's face and actually

1491
00:59:13,829 --> 00:59:11,589
see everything except the laser pointer

1492
00:59:15,750 --> 00:59:13,839
which he used excellently I must say and

1493
00:59:17,730 --> 00:59:15,760
unfortunately that's the one thing that

1494
00:59:20,010 --> 00:59:17,740
isn't present in the archive but I think

1495
00:59:23,039 --> 00:59:20,020
anybody who didn't see the talk and

1496
00:59:24,510 --> 00:59:23,049
would like to will enjoy being able to

1497
00:59:27,089 --> 00:59:24,520
do it on the archive and of course all

1498
00:59:31,200 --> 00:59:27,099
the other talks from this year are

1499
00:59:33,270 --> 00:59:31,210
archived there as well and let me also

1500
00:59:35,700 --> 00:59:33,280
while I have the open mic just put in a

1501
00:59:38,010 --> 00:59:35,710
plug for the next director seminar which

1502
00:59:40,500 --> 00:59:38,020
is going to be giovanna tinetti on jun

1503
00:59:43,890 --> 00:59:40,510
2nd and she's going to be talking about

1504
00:59:46,079 --> 00:59:43,900
her work on understanding the

1505
00:59:48,750 --> 00:59:46,089
characteristics of extrasolar planets

1506
00:59:50,579 --> 00:59:48,760
and with that marco do we have any hands

1507
00:59:57,630 --> 00:59:50,589
raised on WebEx we have a question from

1508
00:59:59,520 --> 00:59:57,640
Goddard God please go ahead when you

1509
01:00:02,520 --> 00:59:59,530
talk about the bases you are just say

1510
01:00:05,190 --> 01:00:02,530
you use a basis and then try to see if

1511
01:00:08,069 --> 01:00:05,200
they work with their four ways we took

1512
01:00:10,410 --> 01:00:08,079
up supernatural why do we don't you have

1513
01:00:12,750 --> 01:00:10,420

a system completely sign tip synthetic

1514
01:00:14,609 --> 01:00:12,760
and with the eight basis you know

1515
01:00:19,020 --> 01:00:14,619
interacting between them without their

1516
01:00:21,180 --> 01:00:19,030
for that we know well yeah that's a good

1517
01:00:24,390 --> 01:00:21,190
question the answer is because that's a

1518
01:00:26,039 --> 01:00:24,400
lot more work right adding two plus four

1519
01:00:27,690 --> 01:00:26,049
that are natural that can be purchased

1520
01:00:29,640 --> 01:00:27,700
from sigma-aldrich and where the

1521
01:00:32,460 --> 01:00:29,650
triphosphates are available from tri

1522
01:00:34,680 --> 01:00:32,470
link is a lot easier for anyone graduate

1523
01:00:36,210 --> 01:00:34,690
student or postdoc to do them to have

1524
01:00:39,000 --> 01:00:36,220
the poor graduate student wrote o'clock

1525
01:00:40,559 --> 01:00:39,010
have to make six triphosphates which is

1526
01:00:42,690 --> 01:00:40,569
actually the difficult synthesis of

1527
01:00:44,819 --> 01:00:42,700
making the nucleus size one thing making

1528
01:00:47,220 --> 01:00:44,829
the triphosphate is more difficult so

1529
01:00:50,099 --> 01:00:47,230
that's so we have not for example done

1530
01:00:51,680 --> 01:00:50,109
the pie EAD that is the permitting with

1531
01:00:56,329 --> 01:00:51,690
a donor acceptor donor and is

1532
01:00:59,870 --> 01:00:56,339
then the piña ad and I a dee da which is

1533
01:01:02,540 --> 01:00:59,880
the but that's only because what happens

1534
01:01:05,030 --> 01:01:02,550
is one of these base pairs gets assigned

1535
01:01:08,540 --> 01:01:05,040
to one individual who has to make both

1536
01:01:10,099 --> 01:01:08,550
components right and that's also enough

1537
01:01:11,809 --> 01:01:10,109
work the last thing that they want to do

1538
01:01:14,240 --> 01:01:11,819

before i let them graduate is to make

1539
01:01:16,579 --> 01:01:14,250
another pair of tripods and another pair

1540
01:01:18,319 --> 01:01:16,589
of tripod sites so that's the that's the

1541
01:01:19,760 --> 01:01:18,329
correct answer to your question the

1542
01:01:21,950 --> 01:01:19,770
question of course is whether or not it

1543
01:01:23,750 --> 01:01:21,960
would be easier to come up with an

1544
01:01:25,940 --> 01:01:23,760
artificial genexus and their reasons I

1545
01:01:28,010 --> 01:01:25,950
believe that it would if we hitched

1546
01:01:29,960 --> 01:01:28,020
aside the natural basis and part of that

1547
01:01:32,240 --> 01:01:29,970
reason is because way in which the

1548
01:01:34,579 --> 01:01:32,250
heterocycle is joined the sugar that

1549
01:01:36,950 --> 01:01:34,589
there are three base pairs where the

1550
01:01:39,970 --> 01:01:36,960
heterocycle is joined to the sugar by

1551
01:01:42,890 --> 01:01:39,980
carbon-nitrogen bond and those are the

1552
01:01:44,630 --> 01:01:42,900
forces standard the two standard base

1553
01:01:47,109 --> 01:01:44,640
pairs plus one of the unnatural ones and

1554
01:01:49,640 --> 01:01:47,119
there are three that are joined by

1555
01:01:51,559 --> 01:01:49,650
carbon-carbon bonds there's reason to

1556
01:01:53,540 --> 01:01:51,569
believe that uniformity would be easier

1557
01:01:57,109 --> 01:01:53,550
to achieve in a high fidelity genetic

1558
01:01:58,760 --> 01:01:57,119
system unfortunately all of the systems

1559
01:02:00,140 --> 01:01:58,770
that are enjoying by carbon carbon or

1560
01:02:01,880 --> 01:02:00,150
the non centered basis which would

1561
01:02:04,220 --> 01:02:01,890
require somebody to actually make them

1562
01:02:05,990 --> 01:02:04,230
all at the same time but the but that

1563
01:02:07,490 --> 01:02:06,000

might very well be an easier system to

1564
01:02:09,650 --> 01:02:07,500
implement so there are reason to think

1565
01:02:11,780 --> 01:02:09,660
that the chemical properties which are

1566
01:02:14,780 --> 01:02:11,790
distributed unevenly across these 12

1567
01:02:17,300 --> 01:02:14,790
letters in the genetic alphabet would we

1568
01:02:19,280 --> 01:02:17,310
be find it easier if we were to pick and

1569
01:02:22,069 --> 01:02:19,290
choose in a way that does not include

1570
01:02:23,480 --> 01:02:22,079
for standard into non center but just

1571
01:02:25,329 --> 01:02:23,490
from the point of view of beating a poor

1572
01:02:27,970 --> 01:02:25,339
graduate student into making them or a

1573
01:02:32,420 --> 01:02:27,980
postdoc the same and that's why we do it

1574
01:02:38,900 --> 01:02:32,430
okay thanks we have a question from

1575
01:02:41,300 --> 01:02:38,910
Colorado hi can you hear me safe I can

1576
01:02:44,630 --> 01:02:41,310
oh good just stealing I enjoyed your

1577
01:02:48,200 --> 01:02:44,640
talk like it though hi I have a question

1578
01:02:50,030 --> 01:02:48,210
about using microbial paler genetics to

1579
01:02:51,380 --> 01:02:50,040
infer things about the earliest forms of

1580
01:02:54,109 --> 01:02:51,390
life I noticed you didn't talk about

1581
01:02:55,760 --> 01:02:54,119
lateral gene transfer which makes it I

1582
01:02:58,609 --> 01:02:55,770
understand and perhaps I'm wrong about

1583
01:03:00,880 --> 01:02:58,619
this difficult to infer what the very

1584
01:03:03,410 --> 01:03:00,890
earliest forms of life were like

1585
01:03:04,770 --> 01:03:03,420
microbial life and even more importantly

1586
01:03:08,790 --> 01:03:04,780
up

1587
01:03:11,070 --> 01:03:08,800
complex cooperative arrangement among

1588
01:03:13,560 --> 01:03:11,080

proteins and nucleic acids and it's

1589
01:03:16,800 --> 01:03:13,570
achieved and legs nor through ribosomes

1590
01:03:18,840 --> 01:03:16,810
and so carlo's and others have argued

1591
01:03:20,910 --> 01:03:18,850
that you know whatever life came early

1592
01:03:22,530 --> 01:03:20,920
or couldn't have been able to do

1593
01:03:23,820 --> 01:03:22,540
Darwinian evolution there must be some

1594
01:03:25,710 --> 01:03:23,830
kind of approach unit which he

1595
01:03:28,050 --> 01:03:25,720
speculates might have done something

1596
01:03:29,780 --> 01:03:28,060
like Lamarckian evolution so I just

1597
01:03:33,840 --> 01:03:29,790
wondered whether you view these as

1598
01:03:37,410 --> 01:03:33,850
problems for the idea of microbial

1599
01:03:40,920 --> 01:03:37,420
phylogenetics I've microbial paleo

1600
01:03:43,440 --> 01:03:40,930
genetics yeah I do in their big problems

1601
01:03:45,480 --> 01:03:43,450
first I I don't think it I'm trying to

1602
01:03:46,860 --> 01:03:45,490
avoid saying I hope I did say that all

1603
01:03:48,720 --> 01:03:46,870
that we were really doing was going back

1604
01:03:49,920 --> 01:03:48,730
deep into the eubacterial tree which is

1605
01:03:52,020 --> 01:03:49,930
really all that we've done with the

1606
01:03:54,030 --> 01:03:52,030
elongation factors we actually are

1607
01:03:56,970 --> 01:03:54,040
nowhere well I know how close we are

1608
01:03:59,790 --> 01:03:56,980
we're we're not at the last common

1609
01:04:03,720 --> 01:03:59,800
ancestor of archaia a new bacteria for

1610
01:04:05,070 --> 01:04:03,730
example the the cat to that of course is

1611
01:04:08,280 --> 01:04:05,080
that as I mentioned we haven't gotten

1612
01:04:12,090 --> 01:04:08,290
into any sense a essential form of life

1613
01:04:13,410 --> 01:04:12,100

we still do rely on the autumn two

1614
01:04:15,090 --> 01:04:13,420
things actually we rely on the

1615
01:04:17,220 --> 01:04:15,100
definition of the tree in here that tree

1616
01:04:19,170 --> 01:04:17,230
is being really defined as the ribosomal

1617
01:04:20,970 --> 01:04:19,180
tree but it's like the elongation factor

1618
01:04:23,910 --> 01:04:20,980
tree right which happens to have very

1619
01:04:25,380 --> 01:04:23,920
nice congruence so the ribosomal trace

1620
01:04:29,250 --> 01:04:25,390
that we're not looking at least lateral

1621
01:04:30,930 --> 01:04:29,260
transfer elongation factors in there and

1622
01:04:33,300 --> 01:04:30,940
their immediate coach substrates or

1623
01:04:36,330 --> 01:04:33,310
coenzymes but what what is quite clear

1624
01:04:39,810 --> 01:04:36,340
is that we do not necessarily have a

1625
01:04:42,000 --> 01:04:39,820
speciation concepts we have defined

1626
01:04:44,880 --> 01:04:42,010
basically the species tree as the

1627
01:04:47,040 --> 01:04:44,890
elongation factor tree / ribosomal RNA

1628
01:04:49,110 --> 01:04:47,050
tree but look one of the big questions

1629
01:04:51,720 --> 01:04:49,120
about Darwinian evolution frankly and

1630
01:04:53,940 --> 01:04:51,730
what we have not addressed and i guess i

1631
01:04:55,290 --> 01:04:53,950
was trying to say this but I didn't say

1632
01:04:57,570 --> 01:04:55,300
it effectively in the talks let me try

1633
01:04:59,700 --> 01:04:57,580
to say it effectively now and that is

1634
01:05:02,010 --> 01:04:59,710
one of the big questions about whether

1635
01:05:04,110 --> 01:05:02,020
or not life can be simply a chemical

1636
01:05:06,030 --> 01:05:04,120
system capable of Darwinian evolution is

1637
01:05:08,490 --> 01:05:06,040
whether you do need to have both

1638
01:05:11,370 --> 01:05:08,500

proteins and nucleic acids to have to

1639
01:05:13,640 --> 01:05:11,380
our way in evolution so about seven

1640
01:05:15,890 --> 01:05:13,650
years ago we wrote a paper for a NASA

1641
01:05:18,019 --> 01:05:15,900
book white paper where

1642
01:05:20,809 --> 01:05:18,029
the argument was made that we didn't

1643
01:05:22,069 --> 01:05:20,819
have well that a genetic molecule is how

1644
01:05:24,289 --> 01:05:22,079
going to have a hard time being a

1645
01:05:25,400 --> 01:05:24,299
catalytic molecule catalytic molecule is

1646
01:05:27,109 --> 01:05:25,410
going to have a hard time being a

1647
01:05:28,730 --> 01:05:27,119
genetic molecule why well because of

1648
01:05:31,430 --> 01:05:28,740
genetic molecule templates where are

1649
01:05:33,279 --> 01:05:31,440
Catholic molecule fold genetic molecule

1650
01:05:36,319 --> 01:05:33,289
tries have the same physical properties

1651
01:05:38,539 --> 01:05:36,329
regardless of building block

1652
01:05:40,130 --> 01:05:38,549
substitution whereas a catalytic you'll

1653
01:05:42,140 --> 01:05:40,140
need to have different properties as a

1654
01:05:44,750 --> 01:05:42,150
function of building block substitution

1655
01:05:46,460 --> 01:05:44,760
and so all these things were because you

1656
01:05:49,549 --> 01:05:46,470
had to have a property a for a genetic

1657
01:05:51,710 --> 01:05:49,559
marker property not a for a catalytic

1658
01:05:53,569 --> 01:05:51,720
molecule and vice versa it was actually

1659
01:05:55,700 --> 01:05:53,579
very hard to conceive of molecular

1660
01:05:59,539 --> 01:05:55,710
systems that could do both catalysis and

1661
01:06:01,670 --> 01:05:59,549
genetics at RNA which has certainly the

1662
01:06:03,349 --> 01:06:01,680
ability demonstrated a Duke boat was

1663
01:06:05,029 --> 01:06:03,359

actually quite special in the world of

1664
01:06:06,799 --> 01:06:05,039
biopolymers it really is hard to find

1665
01:06:08,539 --> 01:06:06,809
any other biopolymer that does a good

1666
01:06:10,160 --> 01:06:08,549
job of both folding when it wants to and

1667
01:06:12,440 --> 01:06:10,170
not folding when it doesn't want to or

1668
01:06:14,960 --> 01:06:12,450
changing the physical property went once

1669
01:06:17,890 --> 01:06:14,970
and not change physical property when it

1670
01:06:20,150 --> 01:06:17,900
wants to and so the one essence of

1671
01:06:22,760 --> 01:06:20,160
Darwinian evolution that is really

1672
01:06:25,099 --> 01:06:22,770
missed right now and it is missed for

1673
01:06:28,309 --> 01:06:25,109
sure in this going backwards in time is

1674
01:06:32,960 --> 01:06:28,319
whether a single biopolymer can support

1675
01:06:35,059 --> 01:06:32,970
during evolution and so help me God the

1676
01:06:37,549 --> 01:06:35,069
answer that question which we found

1677
01:06:41,630 --> 01:06:37,559
entirely satisfactory 20 years ago was

1678
01:06:45,289 --> 01:06:41,640
that yes that molecule is RNA it did so

1679
01:06:47,599 --> 01:06:45,299
an early Earth problem solved okay it's

1680
01:06:50,240 --> 01:06:47,609
unfortunately not an acceptable answer

1681
01:06:52,549 --> 01:06:50,250
20 years later right now we have had the

1682
01:06:54,049 --> 01:06:52,559
most miserable time getting well let me

1683
01:06:56,210 --> 01:06:54,059
obviously gone Burke and various people

1684
01:06:58,190 --> 01:06:56,220
there's a large number of people Jack

1685
01:07:00,200 --> 01:06:58,200
szostak Jerry Joyce has gotten catalysis

1686
01:07:02,660 --> 01:07:00,210
out of nucleic acids but it's been

1687
01:07:04,670 --> 01:07:02,670
extremely difficult to get an RNA

1688
01:07:07,400 --> 01:07:04,680

molecule that catalyzes a great length

1689
01:07:09,260 --> 01:07:07,410
template directed synthesis of RNA p 10

1690
01:07:10,910 --> 01:07:09,270
round his student Hannah's a or have

1691
01:07:13,970 --> 01:07:10,920
come close to sort they've done the best

1692
01:07:16,460 --> 01:07:13,980
job today um and it's been extremely

1693
01:07:18,380 --> 01:07:16,470
difficult to find evidence out of the

1694
01:07:21,160 --> 01:07:18,390
paradox of the genetic molecule must do

1695
01:07:24,170 --> 01:07:21,170
x and a cowlick molecule must do not x

1696
01:07:26,420 --> 01:07:24,180
further when RNA wanders into a region

1697
01:07:29,029 --> 01:07:26,430
of highly G rich sequence pace it tends

1698
01:07:29,450 --> 01:07:29,039
to fold it doesn't tend the display rule

1699
01:07:31,670 --> 01:07:29,460
base

1700
01:07:33,770 --> 01:07:31,680
molecular evolution anymore so your

1701
01:07:35,570 --> 01:07:33,780
question is spot-on we wear the big

1702
01:07:37,790 --> 01:07:35,580
puzzle right now is between the

1703
01:07:39,800 --> 01:07:37,800
molecular description of evolution the

1704
01:07:41,120 --> 01:07:39,810
essence of light and then evolution as

1705
01:07:42,530 --> 01:07:41,130
we know in the modern world is whether

1706
01:07:45,460 --> 01:07:42,540
or not what we get in the modern world

1707
01:07:48,200 --> 01:07:45,470
can be gotten with a single biopolymer

1708
01:07:50,570 --> 01:07:48,210
I'd be a lot happier if a we could make

1709
01:07:53,660 --> 01:07:50,580
RNA from prebiotic precursors in

1710
01:07:57,440 --> 01:07:53,670
high-yield we can make it half-baked I

1711
01:07:59,780 --> 01:07:57,450
would be a lot happier if we can had an

1712
01:08:01,430 --> 01:07:59,790
RNA molecule that with facility

1713
01:08:04,040 --> 01:08:01,440

catalyzes the synthesis of RNA

1714
01:08:06,940 --> 01:08:04,050
especially it had a complete cycle I'd

1715
01:08:09,320 --> 01:08:06,950
be a lot better happier if we have a

1716
01:08:11,540 --> 01:08:09,330
reasonable Mathematica or theoretical

1717
01:08:14,920 --> 01:08:11,550
description of how catalytic power is

1718
01:08:20,840 --> 01:08:14,930
distributed within RNA sequence things I

1719
01:08:22,579 --> 01:08:20,850
many of you have this go ahead okay

1720
01:08:24,440 --> 01:08:22,589
there aren't any more hands raised so if

1721
01:08:29,709 --> 01:08:24,450
anybody would like to just jump in with

1722
01:08:38,479 --> 01:08:34,400
isteve it's Lisa Pratt I'm particularly

1723
01:08:41,599 --> 01:08:38,489
interested in this this sulfur anchored

1724
01:08:42,920 --> 01:08:41,609
backbone and wondering if you can can

1725
01:08:45,890 --> 01:08:42,930
say anything about what happens if you

1726
01:08:48,610 --> 01:08:45,900
get away from from circum neutral pH

1727
01:08:51,530 --> 01:08:48,620
conditions if we were to think about

1728
01:08:53,809 --> 01:08:51,540
early evolution in a very acidic

1729
01:08:57,229 --> 01:08:53,819
environment can we uncouple ourselves

1730
01:09:00,200 --> 01:08:57,239
from phosphate backbones yeah yeah but

1731
01:09:02,030 --> 01:09:00,210
that's a very good question i'm there's

1732
01:09:04,670 --> 01:09:02,040
a paper that we wrote for again one of

1733
01:09:06,910 --> 01:09:04,680
these NASA things which discuss life at

1734
01:09:10,070 --> 01:09:06,920
very low pH in life at very high pH and

1735
01:09:12,620 --> 01:09:10,080
it's it's absolutely certain that you

1736
01:09:14,930 --> 01:09:12,630
must get away from certain features of

1737
01:09:17,660 --> 01:09:14,940
natural nucleic acid standard nucleic

1738
01:09:19,940 --> 01:09:17,670

acids standard Terran nucleic acids if

1739
01:09:23,720 --> 01:09:19,950
you want to go to higher acidity for

1740
01:09:26,180 --> 01:09:23,730
example certainly DNA doesn't do a very

1741
01:09:29,180 --> 01:09:26,190
good job at high at high acidity a low

1742
01:09:31,640 --> 01:09:29,190
pH the bases fall off of DNA and this

1743
01:09:34,729 --> 01:09:31,650
becomes a horrible mess of deep

1744
01:09:36,740 --> 01:09:34,739
urination and deeper imagination um it's

1745
01:09:38,930 --> 01:09:36,750
an interesting question in fact what was

1746
01:09:41,140 --> 01:09:38,940
the talk of that I gave I guess with

1747
01:09:42,579 --> 01:09:41,150
with Andrew poriyal session at the

1748
01:09:44,740 --> 01:09:42,589
site conference as to whether you could

1749
01:09:47,220 --> 01:09:44,750
get away with the repeating negative

1750
01:09:49,809 --> 01:09:47,230
charge by having a repeating dipole

1751
01:09:51,820 --> 01:09:49,819
where the positive ends of the dipole

1752
01:09:53,530 --> 01:09:51,830
we're all tucked inside the molecule on

1753
01:09:55,720 --> 01:09:53,540
the negative ends or outside these sort

1754
01:09:57,640 --> 01:09:55,730
of effective charge that without having

1755
01:09:59,530 --> 01:09:57,650
a net charge and we were actually

1756
01:10:00,970 --> 01:09:59,540
focused more on Titan as the place

1757
01:10:02,500 --> 01:10:00,980
because there you have to go to high pH

1758
01:10:05,500 --> 01:10:02,510
you have to go to a more hydrophobic

1759
01:10:09,070 --> 01:10:05,510
solvent and you have to go to lower

1760
01:10:10,660 --> 01:10:09,080
temperatures and so the idea is the

1761
01:10:13,270 --> 01:10:10,670
shortage of the question is but we don't

1762
01:10:14,550 --> 01:10:13,280
know but the speculation was that you

1763
01:10:17,470 --> 01:10:14,560

could get away from this pole

1764
01:10:19,810 --> 01:10:17,480
electrolyte model for the backbone at

1765
01:10:21,700 --> 01:10:19,820
low temperatures in hydrophobic solvents

1766
01:10:23,620 --> 01:10:21,710
where you just couldn't tolerate you

1767
01:10:26,729 --> 01:10:23,630
can't dissolve a repeating charge and

1768
01:10:29,080 --> 01:10:26,739
solvent like methane at any temperature

1769
01:10:31,060 --> 01:10:29,090
but the idea was yes you might be able

1770
01:10:33,939 --> 01:10:31,070
to get away from it that way the higher

1771
01:10:36,100 --> 01:10:33,949
acidity conditions that you find in the

1772
01:10:37,540 --> 01:10:36,110
solar system like Venus for example or

1773
01:10:40,360 --> 01:10:37,550
of course also very polar so you

1774
01:10:43,180 --> 01:10:40,370
wouldn't need to get away from the

1775
01:10:44,649 --> 01:10:43,190
higher acidity the me for repeating

1776
01:10:46,959 --> 01:10:44,659
sulfuric acid will dissolve a

1777
01:10:49,000 --> 01:10:46,969
polyelectrolyte just fine like it was

1778
01:10:50,140 --> 01:10:49,010
dissolved most things but then of course

1779
01:10:51,880 --> 01:10:50,150
you really have to worry about the

1780
01:10:54,100 --> 01:10:51,890
acid-base properties in the acid

1781
01:10:56,910 --> 01:10:54,110
stability of the of that of the

1782
01:10:59,520 --> 01:10:56,920
acid-base properties of the bases

1783
01:11:03,010 --> 01:10:59,530
paradoxically to find the nucleobases

1784
01:11:05,439 --> 01:11:03,020
and yeah we had proposed a whole number

1785
01:11:07,330 --> 01:11:05,449
of CGI ko Sai's carbon glycosides which

1786
01:11:10,270 --> 01:11:07,340
would be stable under Venusian

1787
01:11:11,770 --> 01:11:10,280
atmosphere type ph's what they would

1788
01:11:13,600 --> 01:11:11,780

still have the repeating negative charge

1789
01:11:16,930 --> 01:11:13,610
in the back row you will really need to

1790
01:11:18,790 --> 01:11:16,940
get away from that repeating charge if

1791
01:11:20,470 --> 01:11:18,800
you go to a hydrophobic solvent like

1792
01:11:24,070 --> 01:11:20,480
what you see on the surface notions of

1793
01:11:26,050 --> 01:11:24,080
Titan and then your problem is frankly

1794
01:11:28,870 --> 01:11:26,060
that nothing dissolves the temperatures

1795
01:11:30,790 --> 01:11:28,880
of the surface oceans of Titan that was

1796
01:11:32,439 --> 01:11:30,800
the point that William Baines made in

1797
01:11:35,290 --> 01:11:32,449
his talk at the absite conference last

1798
01:11:36,729 --> 01:11:35,300
week that anything cold is a bad solvent

1799
01:11:41,200 --> 01:11:36,739
not because it's a bad solvent just

1800
01:11:43,840 --> 01:11:41,210
because it's cold and and so managing

1801
01:11:48,990 --> 01:11:43,850
surface genetics genetics and the ocean

1802
01:11:54,640 --> 01:11:52,740
Steve this discussion reminds me of a

1803
01:11:56,229 --> 01:11:54,650
talk at the lab

1804
01:11:58,899 --> 01:11:56,239
sturgeon of life Gordon research

1805
01:12:01,450 --> 01:11:58,909
conference in Ventura that was given by

1806
01:12:03,669 --> 01:12:01,460
felisa wolf Simon I think I real Anbar

1807
01:12:07,180 --> 01:12:03,679
and somebody else who may very well be

1808
01:12:09,880 --> 01:12:07,190
on this net we're co-authors in which

1809
01:12:12,160 --> 01:12:09,890
she was talking about the possibility of

1810
01:12:14,919 --> 01:12:12,170
arsenic substituting for phosphorus and

1811
01:12:18,640 --> 01:12:14,929
I'm just wondering if these approaches

1812
01:12:20,919 --> 01:12:18,650
of synthetic biology enable you to

1813
01:12:23,050 --> 01:12:20,929

investigate the theoretical possibility

1814
01:12:24,850 --> 01:12:23,060
of a system which is fundamentally

1815
01:12:26,919 --> 01:12:24,860
different in this other way or some

1816
01:12:30,189 --> 01:12:26,929
other ways for example with artesunate

1817
01:12:32,020 --> 01:12:30,199
substituting for phosphate well I mean I

1818
01:12:34,840 --> 01:12:32,030
is a good organic chemist I would say

1819
01:12:37,120 --> 01:12:34,850
not only is this strategy of synthesis a

1820
01:12:39,189 --> 01:12:37,130
way of investigating that question it's

1821
01:12:41,890 --> 01:12:39,199
a necessary way of investigating that

1822
01:12:44,350 --> 01:12:41,900
question that is there is no proposal

1823
01:12:46,390 --> 01:12:44,360
for that hypothesis in the chemical

1824
01:12:47,770 --> 01:12:46,400
community they will meet the chemists

1825
01:12:50,500 --> 01:12:47,780
standard of proof that will be

1826
01:12:53,919 --> 01:12:50,510
acceptable to the chemical community all

1827
01:12:56,020 --> 01:12:53,929
that is absent of an experiment where

1828
01:12:58,330 --> 01:12:56,030
you try to make the DNA that contains

1829
01:12:59,860 --> 01:12:58,340
arsenic in the background and and of

1830
01:13:02,380 --> 01:12:59,870
course when police your first mentioned

1831
01:13:04,419 --> 01:13:02,390
that to us and Paul Paul Davies also and

1832
01:13:06,160 --> 01:13:04,429
we went out and tried in trying to make

1833
01:13:07,810 --> 01:13:06,170
something and what we encountered

1834
01:13:09,550 --> 01:13:07,820
products this is the example is was

1835
01:13:11,520 --> 01:13:09,560
actually chemistry of arsenate that's

1836
01:13:14,740 --> 01:13:11,530
well known and that is at the arsenate

1837
01:13:16,870 --> 01:13:14,750
ester unlike the phosphate ester falls

1838
01:13:18,720 --> 01:13:16,880

apart with half-lives of minutes and

1839
01:13:21,550 --> 01:13:18,730
water at room temperature the phosphate

1840
01:13:23,770 --> 01:13:21,560
esters and DNA have half-lives on the

1841
01:13:26,110 --> 01:13:23,780
winter walks 10 to the 15 seconds is

1842
01:13:28,870 --> 01:13:26,120
what we are talking about that is 10 to

1843
01:13:32,290 --> 01:13:28,880
the 13th minutes not one to five minutes

1844
01:13:34,870 --> 01:13:32,300
so so the arsenate esters are orders of

1845
01:13:36,880 --> 01:13:34,880
magnitudes 10 to the 13th as Carl Sagan

1846
01:13:38,709 --> 01:13:36,890
was a billions and billions and billions

1847
01:13:41,169 --> 01:13:38,719
of times less stable than phosphate

1848
01:13:43,060 --> 01:13:41,179
esters meaning it is really unlikely she

1849
01:13:45,160 --> 01:13:43,070
would have arsenide based DNA in aqueous

1850
01:13:47,080 --> 01:13:45,170
mini at room temperature earth room

1851
01:13:49,300 --> 01:13:47,090
temperature but yeah I mean the point

1852
01:13:51,070 --> 01:13:49,310
here is that you can't you're not

1853
01:13:52,870 --> 01:13:51,080
allowed in the chemistry community I

1854
01:13:55,060 --> 01:13:52,880
mean you're allowed in the planetary

1855
01:13:56,979 --> 01:13:55,070
community right to propose a super-earth

1856
01:13:59,410 --> 01:13:56,989
a very large rocky earth without then

1857
01:14:01,030 --> 01:13:59,420
going out making one but no one will

1858
01:14:03,350 --> 01:14:01,040
complain to you and reject your paper

1859
01:14:05,540 --> 01:14:03,360
because you did not make an earth with a

1860
01:14:07,850 --> 01:14:05,550
the five times the current earth and

1861
01:14:09,620 --> 01:14:07,860
test your theory on it but in chemistry

1862
01:14:11,510 --> 01:14:09,630
if you propose a structure that you

1863
01:14:13,700 --> 01:14:11,520

control on a sheet of paper you have an

1864
01:14:16,430 --> 01:14:13,710
obligation or you have to give up your

1865
01:14:18,050 --> 01:14:16,440
union card to try to make it I in fact

1866
01:14:20,300 --> 01:14:18,060
it's worse than that you almost have an

1867
01:14:21,530 --> 01:14:20,310
obligation to make it you always have an

1868
01:14:24,170 --> 01:14:21,540
obligation to make it in the chemistry

1869
01:14:26,180 --> 01:14:24,180
community before you publish the privet

1870
01:14:27,470 --> 01:14:26,190
limit so in this sense the chemists have

1871
01:14:29,930 --> 01:14:27,480
a very different way of approaching

1872
01:14:31,430 --> 01:14:29,940
science than the planetary scientists or

1873
01:14:32,930 --> 01:14:31,440
the astrophysicists who don't have to

1874
01:14:40,990 --> 01:14:32,940
make a new star before they can publish

1875
01:14:50,240 --> 01:14:43,730
thanks Steve any further questions

1876
01:14:52,250 --> 01:14:50,250
please just jump in if you have one okay