EARTH-LIFE
SCIENCE
INSTITUTE

Martha Grover

A system-level viewpoint on the chemical origins of life

1
00:00:00,160 --> 00:00:14,169
[Music]

2
00:00:17,450 --> 00:00:15,499
thank you

3
00:00:20,300 --> 00:00:17,460
I appreciate the opportunity to talk to

4
00:00:22,790 --> 00:00:20,310
you all today I'm from Georgia Tech it

5
00:00:24,410 --> 00:00:22,800
which is in Atlanta Georgia and I'm

6
00:00:26,839 --> 00:00:24,420
gonna be talking to you today about a

7
00:00:29,089 --> 00:00:26,849
research that I've been involved in in

8
00:00:31,519 --> 00:00:29,099
the Center for chemical evolution the

9
00:00:33,410 --> 00:00:31,529
title is a system-level viewpoint on the

10
00:00:34,790 --> 00:00:33,420
chemical origins of life probably the

11
00:00:36,560 --> 00:00:34,800
word polymer should appear somewhere in

12
00:00:38,780 --> 00:00:36,570
this title because it's very a polymer

13
00:00:41,240 --> 00:00:38,790

focused in terms of the research we've

14
00:00:42,229 --> 00:00:41,250
been doing and by system-level there are

15
00:00:44,990 --> 00:00:42,239
a lot of different things that could

16
00:00:46,910 --> 00:00:45,000
that could mean but I'm coming from a

17
00:00:47,840 --> 00:00:46,920
background in engineering I'm in the

18
00:00:50,510 --> 00:00:47,850
school of chemical and biomolecular

19
00:00:52,580 --> 00:00:50,520
engineering at Georgia Tech and I'm in

20
00:00:54,770 --> 00:00:52,590
the the field subfield called process

21
00:00:56,360 --> 00:00:54,780
systems engineering usually what that

22
00:00:58,700 --> 00:00:56,370
means is that we use mathematical models

23
00:01:00,560 --> 00:00:58,710
to help encode our understanding and

24
00:01:03,950 --> 00:01:00,570
then make predictions and design systems

25
00:01:05,600 --> 00:01:03,960
my particular original area of research

26
00:01:06,530 --> 00:01:05,610
is in feedback control although I'm not

27
00:01:08,660 --> 00:01:06,540
actually going to talk to you about

28
00:01:12,140 --> 00:01:08,670
feedback control today but certainly I

29
00:01:13,340 --> 00:01:12,150
think that's relevant to the research

30
00:01:16,700 --> 00:01:13,350
we're all talking about this meeting as

31
00:01:18,560 --> 00:01:16,710
well and so I'm gonna I'm gonna try to

32
00:01:20,570 --> 00:01:18,570
talk about some of the research that

33
00:01:22,999 --> 00:01:20,580
we've been doing and some of the

34
00:01:27,499 --> 00:01:23,009
insights that we've learned from this

35
00:01:33,690 --> 00:01:31,590
so the research goal is to design and

36
00:01:36,029 --> 00:01:33,700
demonstrate prebiotic ly plausible

37
00:01:37,770 --> 00:01:36,039
minimal systems that can first of all

38
00:01:40,260 --> 00:01:37,780

polymerize so we're not assuming that we

39
00:01:42,779 --> 00:01:40,270
start with the polymers but we are we do

40
00:01:45,419 --> 00:01:42,789
have a polymer focused a research

41
00:01:47,399 --> 00:01:45,429
program we want to store information in

42
00:01:49,649 --> 00:01:47,409
those polymers transfer the information

43
00:01:50,969 --> 00:01:49,659
through replication catalyzed reactions

44
00:01:54,319 --> 00:01:50,979
or perform other functions and

45
00:01:56,789 --> 00:01:54,329
ultimately undergo chemical evolution

46
00:01:58,559 --> 00:01:56,799
now ideally it would be nice to find a

47
00:02:02,010 --> 00:01:58,569
common environment in which all of these

48
00:02:05,100 --> 00:02:02,020
steps could occur for nucleic acid

49
00:02:07,169 --> 00:02:05,110
polymers peptides other biopolymers

50
00:02:08,460 --> 00:02:07,179
maybe polysaccharides we don't

51
00:02:10,199 --> 00:02:08,470
necessarily have to find a common

52
00:02:12,809 --> 00:02:10,209
environment but if we do start to find

53
00:02:14,940 --> 00:02:12,819
key features common features in the

54
00:02:21,150 --> 00:02:14,950
environment that might might be helpful

55
00:02:22,650 --> 00:02:21,160
going forward and in order to design and

56
00:02:24,569 --> 00:02:22,660
demonstrate these systems we need to not

57
00:02:26,220 --> 00:02:24,579
necessarily solve but address what are

58
00:02:29,520 --> 00:02:26,230
some long-standing problems in the field

59
00:02:32,670 --> 00:02:29,530
many of which were articulated in Shaw

60
00:02:34,199 --> 00:02:32,680
stacks a list of eight problems that was

61
00:02:35,819 --> 00:02:34,209
referenced in the in the past talk one

62
00:02:38,309 --> 00:02:35,829
is the the water problem if we're trying

63
00:02:39,720 --> 00:02:38,319

to make biopolymers or proto biopolymers

64
00:02:42,180 --> 00:02:39,730
through condensation reactions that's

65
00:02:43,979 --> 00:02:42,190
just not favored in water the hydrolysis

66
00:02:44,849 --> 00:02:43,989
is driving us backwards so that's

67
00:02:46,979 --> 00:02:44,859
something that we need to deal with

68
00:02:49,740 --> 00:02:46,989
another one is the Strand inhibition

69
00:02:53,009 --> 00:02:49,750
problem in order to have copying we

70
00:02:55,680 --> 00:02:53,019
could use thermal cycling in order to

71
00:02:57,030 --> 00:02:55,690
drive strand separation but upon cooling

72
00:02:59,039 --> 00:02:57,040
then the strands might just come back

73
00:03:00,089 --> 00:02:59,049
together so that's another another

74
00:03:02,759 --> 00:03:00,099
problem that we've been trying to

75
00:03:05,970 --> 00:03:02,769
address and a third is the single winter

76
00:03:08,039 --> 00:03:05,980
scenario survival of the fittest so many

77
00:03:11,159 --> 00:03:08,049
especially theoretical models especially

78
00:03:13,470 --> 00:03:11,169
particularly eigen have selection based

79
00:03:14,789 --> 00:03:13,480
on replication and that doesn't

80
00:03:17,629 --> 00:03:14,799
necessarily need to lead to a productive

81
00:03:20,190 --> 00:03:17,639
outcome in terms of designing minimal

82
00:03:21,330 --> 00:03:20,200
evolutionary systems so really we need

83
00:03:25,500 --> 00:03:21,340
to select for function not just

84
00:03:27,509 --> 00:03:25,510
replication and we also need to generate

85
00:03:28,949 --> 00:03:27,519
and sustain diversity in our system so

86
00:03:34,320 --> 00:03:28,959
that we can continue to have evolution

87
00:03:41,160 --> 00:03:37,560
and we're as a systems engineer I'm very

88
00:03:43,470 --> 00:03:41,170

focused on designing an entire system

89
00:03:45,120 --> 00:03:43,480
out of parts ideally these are parts

90
00:03:47,460 --> 00:03:45,130
that we understand well we may that may

91
00:03:49,080 --> 00:03:47,470
or may not be true in the system and the

92
00:03:50,850 --> 00:03:49,090
research I will be talking to you about

93
00:03:52,260 --> 00:03:50,860
going forward but we look at parts and

94
00:03:54,600 --> 00:03:52,270
how they interact with each other so

95
00:03:56,490 --> 00:03:54,610
it's the interactions between the parts

96
00:03:58,740 --> 00:03:56,500
that ultimately lead to this system

97
00:04:00,030 --> 00:03:58,750
level or emergent behavior and so we

98
00:04:02,100 --> 00:04:00,040
really want to understand not only the

99
00:04:05,040 --> 00:04:02,110
chemistry but also the environment and

100
00:04:06,780 --> 00:04:05,050
the coupling between them and the main

101
00:04:09,390 --> 00:04:06,790
concept that we have been looking at in

102
00:04:12,000 --> 00:04:09,400
this research is the environmental cycle

103
00:04:14,400 --> 00:04:12,010
so here maybe we have the Sun that's

104
00:04:17,009 --> 00:04:14,410
driving water evaporation and then that

105
00:04:20,009 --> 00:04:17,019
gives us maybe this viscous layer here

106
00:04:23,040 --> 00:04:20,019
that has low water activity then we have

107
00:04:24,810 --> 00:04:23,050
rehydration at night maybe cooling and

108
00:04:27,180 --> 00:04:24,820
then we have this cycle that goes on so

109
00:04:29,220 --> 00:04:27,190
you know we all we are we all know we're

110
00:04:31,500 --> 00:04:29,230
all driven by cycles those of us who

111
00:04:33,780 --> 00:04:31,510
came from abroad very aware of it

112
00:04:36,300 --> 00:04:33,790
through the jet lag that we're now out

113
00:04:38,130 --> 00:04:36,310

of sync but we do want to look at

114
00:04:39,750 --> 00:04:38,140
environmental cycles they're not only

115
00:04:41,880 --> 00:04:39,760
prebiotic ly possible but probably

116
00:04:44,940 --> 00:04:41,890
prebiotic ly necessary that could be

117
00:04:48,240 --> 00:04:44,950
daily or tidal or seasonal cycles these

118
00:04:50,790 --> 00:04:48,250
could be hot cold wet dry pH swings all

119
00:04:52,380 --> 00:04:50,800
of the above the hot cold could really

120
00:04:55,250 --> 00:04:52,390
drive the wet and dry and that could

121
00:04:57,570 --> 00:04:55,260
then drive the pH swings in fact so

122
00:04:59,970 --> 00:04:57,580
having this sort of cycle driven by the

123
00:05:02,820 --> 00:04:59,980
influx of solar energy gives us non

124
00:05:06,510 --> 00:05:02,830
equilibrium behavior and it induces

125
00:05:08,040 --> 00:05:06,520
reversible phenomenon that are lifelike

126
00:05:11,940 --> 00:05:08,050
in some ways I'm not going to define

127
00:05:13,200 --> 00:05:11,950
life for you but but over the course of

128
00:05:14,940 --> 00:05:13,210
the cycle we want to sometimes have

129
00:05:16,680 --> 00:05:14,950
polymerization and then sometimes have

130
00:05:18,690 --> 00:05:16,690
hydrolysis and we don't want to just

131
00:05:20,280 --> 00:05:18,700
drive ourselves into a thermodynamic

132
00:05:23,000 --> 00:05:20,290
dead-end we might want to have duplex

133
00:05:25,260 --> 00:05:23,010
formation but then separate then

134
00:05:27,210 --> 00:05:25,270
separation later on in the cycle and

135
00:05:31,130 --> 00:05:27,220
that these sorts of dynamic reversible

136
00:05:33,390 --> 00:05:31,140
systems are lifelike in some sense and

137
00:05:34,770 --> 00:05:33,400
then the other feature in addition to

138
00:05:36,360 --> 00:05:34,780

the environmental cycles that we have

139
00:05:40,290 --> 00:05:36,370
really been focusing on are non aqueous

140
00:05:42,420 --> 00:05:40,300
solvents so we are water-based or not

141
00:05:44,909 --> 00:05:42,430
trying to argue that life the origins of

142
00:05:46,770 --> 00:05:44,919
life did not involve water but that

143
00:05:47,250 --> 00:05:46,780
might not be the whole story in terms of

144
00:05:49,320 --> 00:05:47,260
this

145
00:05:51,660 --> 00:05:49,330
either the solvent being an

146
00:05:53,490 --> 00:05:51,670
environmental condition so there were

147
00:05:55,950 --> 00:05:53,500
many organics present in the prebiotic

148
00:05:58,830 --> 00:05:55,960
inventory and some of these non aqueous

149
00:06:00,900 --> 00:05:58,840
solvents could have been created from

150
00:06:04,650 --> 00:06:00,910
non volatile organics after water

151
00:06:07,080 --> 00:06:04,660
evaporation and some of the desirable

152
00:06:08,280 --> 00:06:07,090
features of non aqueous solvents in this

153
00:06:10,350 --> 00:06:08,290
context are that we can drive

154
00:06:12,180 --> 00:06:10,360
condensation polymerization forward if

155
00:06:16,290 --> 00:06:12,190
we remove the water that's off the water

156
00:06:17,640 --> 00:06:16,300
problem for us we can also these

157
00:06:19,590 --> 00:06:17,650
solvents might be more viscous than

158
00:06:21,570 --> 00:06:19,600
water and that can give us differential

159
00:06:24,660 --> 00:06:21,580
mobility between different species in

160
00:06:27,150 --> 00:06:24,670
these solvents and also it can promote

161
00:06:29,430 --> 00:06:27,160
intermolecular folding by suppressing

162
00:06:31,890 --> 00:06:29,440
intermolecular reactions so if we have a

163
00:06:33,090 --> 00:06:31,900

viscous solvent then the species might

164
00:06:35,130 --> 00:06:33,100
not be very mobile and they might have

165
00:06:37,530 --> 00:06:35,140
more time to fold before they undergo

166
00:06:42,890 --> 00:06:37,540
intermolecular interactions or the

167
00:06:47,220 --> 00:06:45,660
so in order to understand the system

168
00:06:49,110 --> 00:06:47,230
level behavior one of the tools that we

169
00:06:52,340 --> 00:06:49,120
have available to us is mathematical

170
00:06:54,540 --> 00:06:52,350
modeling and this allows us to evaluate

171
00:06:56,310 --> 00:06:54,550
interactions between the environment and

172
00:06:58,800 --> 00:06:56,320
the chemistry in order to predict

173
00:07:01,080 --> 00:06:58,810
overall system level performance this

174
00:07:02,610 --> 00:07:01,090
can be helpful because there are so many

175
00:07:04,260 --> 00:07:02,620
different parameters that we might be

176
00:07:06,960 --> 00:07:04,270
able to vary and a model can help us

177
00:07:08,460 --> 00:07:06,970
clarify what some of the minimal

178
00:07:11,010 --> 00:07:08,470
interactions in our system need to be

179
00:07:13,710 --> 00:07:11,020
and what is the window of performance

180
00:07:18,720 --> 00:07:13,720
that we can get with maybe a minimal

181
00:07:21,060 --> 00:07:18,730
type of experimental system so this

182
00:07:22,860 --> 00:07:21,070
model also can help us or a model can

183
00:07:24,780 --> 00:07:22,870
help to predict trade-offs between

184
00:07:26,250 --> 00:07:24,790
simultaneously occurring phenomena in

185
00:07:30,570 --> 00:07:26,260
our system which is hard to do with a

186
00:07:32,790 --> 00:07:30,580
more reductionist approach and we

187
00:07:34,050 --> 00:07:32,800
considered a particular case study that

188
00:07:36,750 --> 00:07:34,060

I'm going to talk to you about today

189
00:07:38,610 --> 00:07:36,760
which is the idea that the first

190
00:07:40,170 --> 00:07:38,620
functional biopolymer could have been

191
00:07:41,720 --> 00:07:40,180
the monomer synthetase this is an idea

192
00:07:44,490 --> 00:07:41,730
that Naqada has talked about before and

193
00:07:47,070 --> 00:07:44,500
Nick is a really collaborator on all of

194
00:07:52,980 --> 00:07:47,080
this work so appreciate his little setup

195
00:07:54,420 --> 00:07:52,990
in the back but the idea is that if we

196
00:07:55,950 --> 00:07:54,430
want to select for function a simpler

197
00:07:57,900 --> 00:07:55,960
function than say a polymerase would be

198
00:07:58,680 --> 00:07:57,910
to make more monomer so that's what

199
00:08:00,780 --> 00:07:58,690
we're looking at in this particular

200
00:08:02,850 --> 00:08:00,790
study and looking for reactor

201
00:08:04,860 --> 00:08:02,860
and diffusivities in our system that

202
00:08:07,920 --> 00:08:04,870
would allow us to have functional

203
00:08:10,140 --> 00:08:07,930
evolution and we also looked at this

204
00:08:12,570 --> 00:08:10,150
made this assumption of Universal

205
00:08:13,710 --> 00:08:12,580
sequence replication in which all of our

206
00:08:15,180 --> 00:08:13,720
different sequences had the same

207
00:08:16,980 --> 00:08:15,190
replication rate so we weren't going to

208
00:08:18,690 --> 00:08:16,990
get selection based on that inherent

209
00:08:20,730 --> 00:08:18,700
replication rate and so we were going to

210
00:08:26,790 --> 00:08:20,740
look for selection based on other

211
00:08:27,990 --> 00:08:26,800
properties of the system so and in this

212
00:08:30,840 --> 00:08:28,000
particular study that I going to talk

213
00:08:33,170 --> 00:08:30,850

about was led by Sarah Walker who was a

214
00:08:35,370 --> 00:08:33,180
postdoc in the Center at the time and

215
00:08:38,850 --> 00:08:35,380
did this work collaboratively with Nick

216
00:08:42,060 --> 00:08:38,860
and myself so we defined this relatively

217
00:08:44,280 --> 00:08:42,070
minimal a chemical system in which we

218
00:08:46,400 --> 00:08:44,290
had a de phase that was dehydrated in a

219
00:08:49,890 --> 00:08:46,410
night phase which was hydrated and

220
00:08:51,780 --> 00:08:49,900
during the dehydrated day phase we had

221
00:08:53,850 --> 00:08:51,790
different monomers of type A and B so

222
00:08:56,610 --> 00:08:53,860
instead of four nucleobases you could

223
00:08:59,400 --> 00:08:56,620
just think of a two called a and B and

224
00:09:02,460 --> 00:08:59,410
they could form through a spontaneous

225
00:09:03,960 --> 00:09:02,470
polymerization random sequences so

226
00:09:07,130 --> 00:09:03,970
that's one of the parameters in our

227
00:09:09,600 --> 00:09:07,140
model is a rate constant for spontaneous

228
00:09:11,010 --> 00:09:09,610
formation of new sequences we also could

229
00:09:13,020 --> 00:09:11,020
have copying of those sequences the

230
00:09:15,630 --> 00:09:13,030
replication rate so those are two of the

231
00:09:17,100 --> 00:09:15,640
five parameters in our model and during

232
00:09:19,080 --> 00:09:17,110
the night phase we could break down

233
00:09:21,450 --> 00:09:19,090
those sequences through hydrolysis and

234
00:09:23,610 --> 00:09:21,460
also during that hydrated phase we would

235
00:09:27,630 --> 00:09:23,620
have diffusion the monomers and polymers

236
00:09:29,370 --> 00:09:27,640
could both diffuse these these monomers

237
00:09:30,660 --> 00:09:29,380
are all assumed to be the same length we

238
00:09:34,050 --> 00:09:30,670

have a lot of simplifications in this

239
00:09:35,790 --> 00:09:34,060
model they're all xx MERS and they form

240
00:09:37,830 --> 00:09:35,800
based on second-order reaction kinetics

241
00:09:39,360 --> 00:09:37,840
from the monomers so the rates of

242
00:09:40,830 --> 00:09:39,370
polymer formation are dependent on the

243
00:09:42,270 --> 00:09:40,840
local resources in the system and that

244
00:09:44,130 --> 00:09:42,280
was that was another property that we

245
00:09:46,220 --> 00:09:44,140
want to bring in so really depending on

246
00:09:48,510 --> 00:09:46,230
where these sequences nucleated

247
00:09:51,180 --> 00:09:48,520
spatially they would be more or less fit

248
00:09:53,310 --> 00:09:51,190
based on the local resources not based

249
00:09:54,780 --> 00:09:53,320
on their inherent sequence because all

250
00:09:57,660 --> 00:09:54,790
sequences have the same rate constants

251
00:10:00,690 --> 00:09:57,670
for replication so this slide just shows

252
00:10:02,190 --> 00:10:00,700
an example of one particular set of five

253
00:10:06,510 --> 00:10:02,200
parameters that are shown there on the

254
00:10:09,120 --> 00:10:06,520
right and what we saw was over time on

255
00:10:14,880 --> 00:10:09,130
the top right the total population in

256
00:10:19,990 --> 00:10:17,850
the total polymer population grew from

257
00:10:21,310 --> 00:10:20,000
monomers and then stabilized but we had

258
00:10:22,900 --> 00:10:21,320
a lot of dynamics in terms of our

259
00:10:36,240 --> 00:10:22,910
individual sequences and I'm just going

260
00:10:40,240 --> 00:10:38,650
okay so early on in the system we didn't

261
00:10:42,340 --> 00:10:40,250
have any sequences and then we had many

262
00:10:43,870 --> 00:10:42,350
random sequences form some of them took

263
00:10:45,970 --> 00:10:43,880

hold in the population like that upper

264
00:10:48,670 --> 00:10:45,980
blue one others went extinct these are

265
00:10:50,230 --> 00:10:48,680
stochastic simulations so we can have

266
00:10:51,819 --> 00:10:50,240
zero one behavior or we can have

267
00:10:53,460 --> 00:10:51,829
actually a large number of species in

268
00:10:55,930 --> 00:10:53,470
our system like 800 for that blue one

269
00:10:57,490 --> 00:10:55,940
and we looked at not only the temporal

270
00:10:59,769 --> 00:10:57,500
evolution but also spatial distribution

271
00:11:01,389 --> 00:10:59,779
because we have these diffusivities so

272
00:11:03,280 --> 00:11:01,399
the polymers are shown in that upper set

273
00:11:04,630 --> 00:11:03,290
of panels and the monomers in the lower

274
00:11:06,699 --> 00:11:04,640
set of panels but you can see these

275
00:11:10,440 --> 00:11:06,709
clusters emerging which actually we did

276
00:11:12,850 --> 00:11:10,450
not expect but it actually came through

277
00:11:15,130 --> 00:11:12,860
recycling of monomers so that when we

278
00:11:17,050 --> 00:11:15,140
had hydrolysis and freed monomers from

279
00:11:18,970 --> 00:11:17,060
polymers they would be more likely to be

280
00:11:20,889 --> 00:11:18,980
taken up by nearby polymers and that

281
00:11:22,569 --> 00:11:20,899
stabilized the cluster even though we

282
00:11:27,460 --> 00:11:22,579
did not build in any inherent

283
00:11:30,160 --> 00:11:27,470
interaction between the polymers so as

284
00:11:32,319 --> 00:11:30,170
we varied the monomer diffusion rate

285
00:11:34,870 --> 00:11:32,329
across the top and the polymer diffusion

286
00:11:36,639 --> 00:11:34,880
rate down the bottom we saw differences

287
00:11:38,889 --> 00:11:36,649
in terms of the spatial patterning so we

288
00:11:40,509 --> 00:11:38,899

could have larger clusters if we had

289
00:11:41,860 --> 00:11:40,519
more polymer diffusion the monomer

290
00:11:43,930 --> 00:11:41,870
diffusion was actually important in

291
00:11:44,980 --> 00:11:43,940
order to have good resource allocations

292
00:11:52,090 --> 00:11:44,990
so that the mountain would be available

293
00:11:53,410 --> 00:11:52,100
to all of these replicating polymers ok

294
00:11:55,090 --> 00:11:53,420
so I talked about the importance of

295
00:11:56,350 --> 00:11:55,100
functional selection but up until this

296
00:11:58,840 --> 00:11:56,360
point we had all these replicating

297
00:12:01,000 --> 00:11:58,850
polymers that had no function so in this

298
00:12:03,540 --> 00:12:01,010
particular case study we then introduced

299
00:12:05,590 --> 00:12:03,550
at a later time the appearance of

300
00:12:10,360 --> 00:12:05,600
functional polymer that could make more

301
00:12:12,189 --> 00:12:10,370
a and what we saw was that compared to

302
00:12:14,439 --> 00:12:12,199
the green curve with no functional

303
00:12:16,689 --> 00:12:14,449
sequence once this functional polymer

304
00:12:18,220 --> 00:12:16,699
was introduced we had this this red

305
00:12:20,050 --> 00:12:18,230
curve that really bootstrapped up the

306
00:12:24,310 --> 00:12:20,060
entire population so by making more

307
00:12:26,650 --> 00:12:24,320
monomer it not only was it amplified in

308
00:12:29,079 --> 00:12:26,660
the population but also everybody

309
00:12:32,110 --> 00:12:29,089
benefited but not as much okay so this

310
00:12:34,480 --> 00:12:32,120
Illustrated that really there was a

311
00:12:37,090 --> 00:12:34,490
balance needed between competition and

312
00:12:40,030 --> 00:12:37,100
cooperation to achieve higher system

313
00:12:42,939 --> 00:12:40,040

level performance and and this was

314
00:12:45,190 --> 00:12:42,949
enabled by limited diffusing furthermore

315
00:12:47,170 --> 00:12:45,200
if at a later time and added

316
00:12:50,010 --> 00:12:47,180
different location we introduced the B

317
00:12:52,180 --> 00:12:50,020
synthetase to a different sequence now

318
00:12:53,950 --> 00:12:52,190
we could really bootstrap up the

319
00:12:55,780 --> 00:12:53,960
population with that blue curve up to a

320
00:12:59,320 --> 00:12:55,790
much higher level because we could

321
00:13:02,680 --> 00:12:59,330
better utilize both RA and RB polymer

322
00:13:04,960 --> 00:13:02,690
and so this is a way that we could build

323
00:13:07,030 --> 00:13:04,970
out something like a hyper cycle in

324
00:13:08,440 --> 00:13:07,040
which we did not need to have both of

325
00:13:09,280 --> 00:13:08,450
these functions appearing at the same

326
00:13:11,980 --> 00:13:09,290
time they could appear at different

327
00:13:14,800 --> 00:13:11,990
times in different locations stepwise

328
00:13:21,910 --> 00:13:14,810
building up a cooperative chemical

329
00:13:23,590 --> 00:13:21,920
Network okay so what were some of the

330
00:13:25,510 --> 00:13:23,600
insights that we gained from this one

331
00:13:28,560 --> 00:13:25,520
was that the optimal system behavior in

332
00:13:30,790 --> 00:13:28,570
order to generate and sustain diversity

333
00:13:32,170 --> 00:13:30,800
occurred at sweet spot so it wasn't

334
00:13:33,400 --> 00:13:32,180
always more is better and so this is

335
00:13:36,040 --> 00:13:33,410
something that without a mathematical

336
00:13:37,690 --> 00:13:36,050
model would be difficult to predict that

337
00:13:39,070 --> 00:13:37,700
we wanted to have some reversibility in

338
00:13:41,290 --> 00:13:39,080

our polymerization so that we could

339
00:13:42,430 --> 00:13:41,300
generate new sequences and continue to

340
00:13:44,320 --> 00:13:42,440
look through sequence space for these

341
00:13:46,510 --> 00:13:44,330
probably small fraction of sequences

342
00:13:48,100 --> 00:13:46,520
that would be functional but if you have

343
00:13:49,960 --> 00:13:48,110
to traverse ability then all have reddit

344
00:13:51,640 --> 00:13:49,970
a would be lost right so we need a

345
00:13:53,320 --> 00:13:51,650
middle ground there we also needed a

346
00:13:57,220 --> 00:13:53,330
middle ground in terms of diffusion of

347
00:13:58,510 --> 00:13:57,230
polymer and and monomer in order to have

348
00:14:01,270 --> 00:13:58,520
some diffusion to efficiently use

349
00:14:03,430 --> 00:14:01,280
utilize all of our resources but by

350
00:14:04,900 --> 00:14:03,440
having limited diffusion we were able to

351
00:14:06,550 --> 00:14:04,910
then generate different functional

352
00:14:08,620 --> 00:14:06,560
sequences and not have a single winner

353
00:14:11,380 --> 00:14:08,630
scenario but to generate and sustain

354
00:14:13,060 --> 00:14:11,390
diversity and have the ability to

355
00:14:14,970 --> 00:14:13,070
continue to explore sequence space so

356
00:14:18,580 --> 00:14:14,980
that we could have this cooperative

357
00:14:20,920 --> 00:14:18,590
catalytic Network evolve our develop

358
00:14:22,180 --> 00:14:20,930
over time and so that's the second

359
00:14:24,400 --> 00:14:22,190
bullet point that these cooperative

360
00:14:25,780 --> 00:14:24,410
networks could emerge stepwise we don't

361
00:14:29,920 --> 00:14:25,790
have to have the hyper cycle if you're

362
00:14:31,240 --> 00:14:29,930
all at one time and the third insight

363
00:14:33,220 --> 00:14:31,250

that we gained was that this clustering

364
00:14:35,650 --> 00:14:33,230
emerged through our recycling dynamic

365
00:14:39,220 --> 00:14:35,660
through breaking down and reusing these

366
00:14:41,140 --> 00:14:39,230
monomers and that was just not something

367
00:14:44,470 --> 00:14:41,150
that we anticipated when we started

368
00:14:46,330 --> 00:14:44,480
running these simulations and and also

369
00:14:48,460 --> 00:14:46,340
that this limited diffusion on surfaces

370
00:14:50,710 --> 00:14:48,470
could provide an early sort of

371
00:14:56,270 --> 00:14:50,720
compartmentalization prior to

372
00:15:02,360 --> 00:14:59,900
so in designing our experiments we took

373
00:15:04,130 --> 00:15:02,370
forward some of these ideas and that

374
00:15:06,350 --> 00:15:04,140
backbone reversibility and monomers

375
00:15:09,680 --> 00:15:06,360
recycling was going to be important to

376
00:15:11,300 --> 00:15:09,690
explore sequence space the environmental

377
00:15:13,580 --> 00:15:11,310
cycling was helpful for driving

378
00:15:15,650 --> 00:15:13,590
condensation and hydrolysis driving

379
00:15:19,040 --> 00:15:15,660
duplex separation and ultimately

380
00:15:20,930 --> 00:15:19,050
replication that we wanted to build in

381
00:15:23,930 --> 00:15:20,940
limited diffusion to bias our mobility

382
00:15:25,610 --> 00:15:23,940
and that we wanted to continue to look

383
00:15:30,530 --> 00:15:25,620
for selection based not only on

384
00:15:31,700 --> 00:15:30,540
replication but really unfunctional so

385
00:15:33,470 --> 00:15:31,710
next I want to talk to you about a

386
00:15:35,840 --> 00:15:33,480
candidate that we have for reversible

387
00:15:37,280 --> 00:15:35,850
linkages and this is a work that Shang

388
00:15:38,480 --> 00:15:37,290

Shang you talked about yesterday and his

389
00:15:39,980 --> 00:15:38,490
poster and we'll talk about again

390
00:15:41,750 --> 00:15:39,990
tomorrow if you want more details so

391
00:15:44,150 --> 00:15:41,760
I'll give some of the highlights the

392
00:15:46,250 --> 00:15:44,160
hypothesis was that polyesters could be

393
00:15:48,170 --> 00:15:46,260
a prebiotic precursor to peptides so

394
00:15:49,880 --> 00:15:48,180
instead of looking at amino acids look

395
00:15:52,670 --> 00:15:49,890
at alpha hydroxy acids which are also

396
00:15:54,740 --> 00:15:52,680
present in miller-urey type experiments

397
00:15:57,560 --> 00:15:54,750
and there are a number of indications

398
00:16:00,790 --> 00:15:57,570
that polyesters and alpha hydroxy yeah

399
00:16:04,610 --> 00:16:00,800
play this role one is that the ribozyme

400
00:16:07,040 --> 00:16:04,620
that the ribosome catalyzes alpha

401
00:16:09,170 --> 00:16:07,050
hydroxy acid coupling that the

402
00:16:10,460 --> 00:16:09,180
polyesters could also have similar side

403
00:16:11,960 --> 00:16:10,470
chain interactions although they would

404
00:16:14,450 --> 00:16:11,970
not have the backbone hydrogen bonds of

405
00:16:15,770 --> 00:16:14,460
peptides and that the ester bond just

406
00:16:18,710 --> 00:16:15,780
simply polymerize is more readily than

407
00:16:21,290 --> 00:16:18,720
the amide bond and so this could really

408
00:16:22,850 --> 00:16:21,300
help us in generating significant yield

409
00:16:26,600 --> 00:16:22,860
and length in terms of our polymers

410
00:16:28,310 --> 00:16:26,610
through non enzymatic reactions and so

411
00:16:30,290 --> 00:16:28,320
this this idea was put forward by Leslie

412
00:16:32,030 --> 00:16:30,300
Orgel and has been out there for a while

413
00:16:33,680 --> 00:16:32,040

but people thought well maybe polyesters

414
00:16:35,780 --> 00:16:33,690
are just not stable enough but actually

415
00:16:37,670 --> 00:16:35,790
our simulations and actually maybe we

416
00:16:41,170 --> 00:16:37,680
want them to we don't want them to be

417
00:16:43,400 --> 00:16:41,180
too stable if we want to evolve so this

418
00:16:46,280 --> 00:16:43,410
slide shows kind of a comparison between

419
00:16:48,350 --> 00:16:46,290
amino and alpha and amino and hydroxy

420
00:16:51,050 --> 00:16:48,360
acids if you're trying to do non

421
00:16:52,640 --> 00:16:51,060
enzymatic peptide polymerization you

422
00:16:54,950 --> 00:16:52,650
have a couple of problems one is that

423
00:16:58,280 --> 00:16:54,960
it's thermodynamically unfavorable in

424
00:17:00,350 --> 00:16:58,290
terms of drying reactions or or in

425
00:17:02,650 --> 00:17:00,360
solvent and then we also have the dakedo

426
00:17:06,260 --> 00:17:02,660
Pipper zine sink in which we form this

427
00:17:08,360 --> 00:17:06,270
cyclic dimer so the ester solution has a

428
00:17:10,130 --> 00:17:08,370
more favorable bond formation free

429
00:17:12,880 --> 00:17:10,140
energy and although it does form cycle

430
00:17:15,140 --> 00:17:12,890
they're reversible so we've been looking

431
00:17:17,150 --> 00:17:15,150
for the last five years or so and

432
00:17:20,300 --> 00:17:17,160
reactions of these polyesters and this

433
00:17:22,000 --> 00:17:20,310
shows one of our early papers led by

434
00:17:24,350 --> 00:17:22,010
arena Mamedov and

435
00:17:26,660 --> 00:17:24,360
malic acid cycling and we built a

436
00:17:29,930 --> 00:17:26,670
kinetic model to predict the effect

437
00:17:31,790 --> 00:17:29,940
under wet/dry cycles under different

438
00:17:33,770 --> 00:17:31,800

temperatures and we did the experiments

439
00:17:36,680 --> 00:17:33,780
and they agreed pretty well in terms of

440
00:17:38,180 --> 00:17:36,690
the monomer dimer and trimer

441
00:17:40,100 --> 00:17:38,190
concentrations and it showed kind of a

442
00:17:42,680 --> 00:17:40,110
ratcheting behavior in which we could

443
00:17:44,300 --> 00:17:42,690
form the poly malic acid over time and

444
00:17:46,850 --> 00:17:44,310
then achieve kind of a cyclic steady

445
00:17:49,270 --> 00:17:46,860
state in terms of polymerizing forward

446
00:17:55,310 --> 00:17:49,280
and then hydrolyzing somewhat during the

447
00:17:59,000 --> 00:17:55,320
wet period so the idea here was that the

448
00:18:01,940 --> 00:17:59,010
polyesters could be a proto peptide but

449
00:18:03,260 --> 00:18:01,950
then along the way our team member

450
00:18:07,280 --> 00:18:03,270
around christian murphy said well what

451
00:18:09,380 --> 00:18:07,290
about Esther amid exchange so we all

452
00:18:11,630 --> 00:18:09,390
said what and then you know did some of

453
00:18:13,670 --> 00:18:11,640
the initial experiments to try this out

454
00:18:16,790 --> 00:18:13,680
we published a paper last year at on

455
00:18:18,770 --> 00:18:16,800
Covanta cami on this topic in which by

456
00:18:20,420 --> 00:18:18,780
first making polyesters and then adding

457
00:18:24,500 --> 00:18:20,430
amino acids into the system they

458
00:18:26,780 --> 00:18:24,510
exchanged and if we dry and cycle

459
00:18:29,810 --> 00:18:26,790
glycine only we really make nothing with

460
00:18:31,850 --> 00:18:29,820
lactic acid we do make polymers but when

461
00:18:33,250 --> 00:18:31,860
we mix them together we form all of

462
00:18:36,710 --> 00:18:33,260
these different copolymers

463
00:18:38,240 --> 00:18:36,720

moreover over time because the amadon is

464
00:18:44,540 --> 00:18:38,250
more stable we move further and farther

465
00:18:46,250 --> 00:18:44,550
toward peptides and then Shan Shan is

466
00:18:49,040 --> 00:18:46,260
posters talking about a system level

467
00:18:51,920 --> 00:18:49,050
model in which we consider the wet dry

468
00:18:53,990 --> 00:18:51,930
cycling of this mixture of hydroxy and

469
00:18:55,460 --> 00:18:54,000
amino acids and we look at the different

470
00:18:57,590 --> 00:18:55,470
species that are formed there all Quan

471
00:18:59,690 --> 00:18:57,600
nine different species quantitated here

472
00:19:02,420 --> 00:18:59,700
over time at four different temperatures

473
00:19:05,960 --> 00:19:02,430
and he built a kinetic model to describe

474
00:19:08,750 --> 00:19:05,970
based on five parameters a forward

475
00:19:11,240 --> 00:19:08,760
polymerization rate for the polyester is

476
00:19:13,580 --> 00:19:11,250
a hydrolysis rate a strand exchange mass

477
00:19:17,450 --> 00:19:13,590
transfer coefficient we also have

478
00:19:18,920 --> 00:19:17,460
hydrolysis and we're able to get really

479
00:19:21,020 --> 00:19:18,930
remarkable achievement I think between

480
00:19:22,220 --> 00:19:21,030
for all nine of these species and helped

481
00:19:23,869 --> 00:19:22,230
us to understand that this reaction

482
00:19:25,699 --> 00:19:23,879
could be understood in terms of element

483
00:19:27,979 --> 00:19:25,709
tree mass action kinetics and

484
00:19:29,509 --> 00:19:27,989
diffusional mass transfer and from the

485
00:19:32,059 --> 00:19:29,519
model we were able to gain some insights

486
00:19:33,769 --> 00:19:32,069
that it for different temperatures our

487
00:19:35,269 --> 00:19:33,779
rate constants and mass transfer

488
00:19:36,859 --> 00:19:35,279

coefficient really are very Arrhenius

489
00:19:38,749 --> 00:19:36,869
like now this would never be expected

490
00:19:40,969 --> 00:19:38,759
because we're drying the system it's

491
00:19:43,609 --> 00:19:40,979
really not ideal but we can still see

492
00:19:44,809 --> 00:19:43,619
this same Arenas type of behavior and we

493
00:19:47,479 --> 00:19:44,819
were also able to look at the reaction

494
00:19:50,299 --> 00:19:47,489
pathway and to show that compared to

495
00:19:52,609 --> 00:19:50,309
just drying and cycling the amino acids

496
00:19:56,869 --> 00:19:52,619
we were really able to lower the barrier

497
00:19:59,149 --> 00:19:56,879
towards making the peptide bond by

498
00:20:01,789 --> 00:19:59,159
having this two-step reaction using the

499
00:20:04,609 --> 00:20:01,799
hydroxy acids and also that it was

500
00:20:06,439 --> 00:20:04,619
really based on the analysis of the

501
00:20:09,049 --> 00:20:06,449
model that it's an engine of the

502
00:20:10,609 --> 00:20:09,059
entropic barrier and not the enthalpic

503
00:20:15,960 --> 00:20:10,619
barrier may be similar to something that

504
00:20:21,000 --> 00:20:19,570
so some of the insights that we gained

505
00:20:24,610 --> 00:20:21,010
from this particular study is that

506
00:20:27,180 --> 00:20:24,620
hydroxy acids could potentially play the

507
00:20:29,620 --> 00:20:27,190
role of amino acids in a prototype tide

508
00:20:31,990 --> 00:20:29,630
that was the original idea then we had

509
00:20:33,519 --> 00:20:32,000
this kind of turn in the road where now

510
00:20:35,440 --> 00:20:33,529
it turns out the hydroxy acids might be

511
00:20:37,539 --> 00:20:35,450
the catalyst for the amino acid

512
00:20:41,019 --> 00:20:37,549
polymerization through ester and

513
00:20:42,850 --> 00:20:41,029

exchange over time we go from having

514
00:20:45,700 --> 00:20:42,860
these copolymers between hydroxy and

515
00:20:47,500 --> 00:20:45,710
amino acid to peptides but it also may

516
00:20:49,600 --> 00:20:47,510
be that these copolymers also called FC

517
00:20:51,279 --> 00:20:49,610
peptides could actually be important

518
00:20:53,139 --> 00:20:51,289
evolutionary intermediates because they

519
00:20:57,340 --> 00:20:53,149
have greater reversibility through the

520
00:21:04,210 --> 00:20:57,350
ester bond than do the amino acids and

521
00:21:06,970 --> 00:21:04,220
peptides and moreover we had kind of a

522
00:21:08,590 --> 00:21:06,980
new view on the water problem which is

523
00:21:11,110 --> 00:21:08,600
that perhaps it's not a problem at all

524
00:21:13,480 --> 00:21:11,120
so our simulation study had indicated

525
00:21:15,820 --> 00:21:13,490
that we really needed this recycling and

526
00:21:18,840 --> 00:21:15,830
reversibility in order to evolve to

527
00:21:21,010 --> 00:21:18,850
generate and sustain diversity and so

528
00:21:23,080 --> 00:21:21,020
perhaps that is why life uses

529
00:21:24,970 --> 00:21:23,090
condensation polymers is that because it

530
00:21:26,620 --> 00:21:24,980
needs to have these bonds that are

531
00:21:29,260 --> 00:21:26,630
reversible that could be broken by water

532
00:21:33,789 --> 00:21:29,270
in order to search sequence base and

533
00:21:35,799 --> 00:21:33,799
evolve and now I'd like to move on to

534
00:21:38,799 --> 00:21:35,809
kind of the third of the three topics

535
00:21:40,389 --> 00:21:38,809
that I wanted to discuss today which is

536
00:21:44,019 --> 00:21:40,399
some recent work of ours on the Strand

537
00:21:45,880 --> 00:21:44,029
inhibition problem and so now this is

538
00:21:47,110 --> 00:21:45,890

more of a nucleic acid viewpoint as

539
00:21:52,360 --> 00:21:47,120
opposed to the previous study that's

540
00:21:55,330 --> 00:21:52,370
more that's a focusing on peptides the

541
00:21:58,120 --> 00:21:55,340
Strand inhibition problem is about

542
00:22:01,210 --> 00:21:58,130
replication really of a generally of a

543
00:22:03,549 --> 00:22:01,220
duplex sort of structure and let's say

544
00:22:06,669 --> 00:22:03,559
you want to make a copy of that red-blue

545
00:22:09,130 --> 00:22:06,679
say maybe DNA or RNA sequence you can

546
00:22:11,470 --> 00:22:09,140
heat not enzymatically or snow enzymes

547
00:22:13,930 --> 00:22:11,480
so you can heat the system and separate

548
00:22:15,549 --> 00:22:13,940
the strands but when you cool the system

549
00:22:18,100 --> 00:22:15,559
instead of making a copy instead of

550
00:22:19,810 --> 00:22:18,110
coding and and doubling the number of

551
00:22:22,570 --> 00:22:19,820
strands in the system when you cool down

552
00:22:24,909 --> 00:22:22,580
you really just go back to because the

553
00:22:28,360 --> 00:22:24,919
duplex reforms that's the thermodynamic

554
00:22:31,480 --> 00:22:28,370
product and so you and

555
00:22:34,000 --> 00:22:31,490
and this was a problem articulated by

556
00:22:35,320 --> 00:22:34,010
Jack szostak in his paper that was

557
00:22:37,360 --> 00:22:35,330
mentioned earlier and they've also

558
00:22:38,560 --> 00:22:37,370
recently published an approach to

559
00:22:40,270 --> 00:22:38,570
solving stranded admission using

560
00:22:41,830 --> 00:22:40,280
arginine and so we have a different

561
00:22:44,770 --> 00:22:41,840
approach that we have been looking at

562
00:22:46,810 --> 00:22:44,780
which is to use viscosity so the

563
00:22:48,730 --> 00:22:46,820

hypothesis is that through Mars through

564
00:22:50,610 --> 00:22:48,740
thermal cycling in a viscous environment

565
00:22:53,440 --> 00:22:50,620
you can overcome strand inhibition and

566
00:22:55,840 --> 00:22:53,450
promote template directed nucleic acid

567
00:22:57,880 --> 00:22:55,850
synthesis so now if we have a viscous

568
00:23:00,100 --> 00:22:57,890
environment we can heat the system and

569
00:23:04,680 --> 00:23:00,110
separate the strands same as the same as

570
00:23:08,230 --> 00:23:04,690
in aqueous buffer but now when we cool

571
00:23:10,780 --> 00:23:08,240
what we thought what our hypothesis the

572
00:23:12,160 --> 00:23:10,790
hypothesis was that when we would cool

573
00:23:14,650 --> 00:23:12,170
the long strands would not move very

574
00:23:16,060 --> 00:23:14,660
fast in the viscous solution the short

575
00:23:18,460 --> 00:23:16,070
strands would move faster and they would

576
00:23:21,430 --> 00:23:18,470
be able to coat this but actually when

577
00:23:22,030 --> 00:23:21,440
we kind of did some numbers work some

578
00:23:23,350 --> 00:23:22,040
numbers

579
00:23:24,850 --> 00:23:23,360
it didn't seem like maybe we were going

580
00:23:26,049 --> 00:23:24,860
to get that much differential mobility

581
00:23:28,630 --> 00:23:26,059
because they're probably going square

582
00:23:31,380 --> 00:23:28,640
root of the length and so but anyway it

583
00:23:33,460 --> 00:23:31,390
was you know something that we want that

584
00:23:36,880 --> 00:23:33,470
hypothesis the Nick had and that we we

585
00:23:38,230 --> 00:23:36,890
tried out and what we found actually was

586
00:23:42,760 --> 00:23:38,240
that we were getting intermolecular

587
00:23:44,710 --> 00:23:42,770
folding and of the long strands and that

588
00:23:46,540 --> 00:23:44,720

was probably also playing a role along

589
00:23:47,799 --> 00:23:46,550
with the differential mobility in order

590
00:23:50,799 --> 00:23:47,809
to keep the long strands from coming

591
00:23:53,620 --> 00:23:50,809
back apart and that would give us a

592
00:23:55,060 --> 00:23:53,630
window of time a kinetic solution to

593
00:23:57,400 --> 00:23:55,070
this thermodynamic problem of strand

594
00:23:59,440 --> 00:23:57,410
inhibition in which we could coat the

595
00:24:01,510 --> 00:23:59,450
long strands maybe using kind of a

596
00:24:03,669 --> 00:24:01,520
toehold mechanism to open up the strands

597
00:24:05,680 --> 00:24:03,679
with these short oligomers coat them

598
00:24:08,850 --> 00:24:05,690
ligate them before we actually got to

599
00:24:13,180 --> 00:24:08,860
the thermodynamic duplex Reformation and

600
00:24:15,760 --> 00:24:13,190
then we could go around again so this

601
00:24:17,440 --> 00:24:15,770
was a paper that was published this year

602
00:24:20,650 --> 00:24:17,450
is online in Nature Chemistry and should

603
00:24:22,660 --> 00:24:20,660
come out 2017 at some point in a in an

604
00:24:24,669 --> 00:24:22,670
actual issue so a one thing that we

605
00:24:27,040 --> 00:24:24,679
needed to do is to choose the viscous

606
00:24:28,750 --> 00:24:27,050
solvent the work I'll show you today is

607
00:24:31,120 --> 00:24:28,760
using like choline which is a mixture of

608
00:24:33,190 --> 00:24:31,130
glycerol and choline chloride also known

609
00:24:37,630 --> 00:24:33,200
as a eutectic solvent or a deep eutectic

610
00:24:39,850 --> 00:24:37,640
solvent and this is a system that also

611
00:24:41,860 --> 00:24:39,860
arena had been looking at previously for

612
00:24:44,760 --> 00:24:41,870
a nucleic acid

613
00:24:48,400 --> 00:24:44,770

Assembly G quadruplex in particular and

614
00:24:50,260 --> 00:24:48,410
what they have found in a group in the

615
00:24:52,240 --> 00:24:50,270
past is that within this particular

616
00:24:55,840 --> 00:24:52,250
mixture of glycol E and the B form of

617
00:24:57,640 --> 00:24:55,850
DNA was retained and so that's kind of I

618
00:24:59,380 --> 00:24:57,650
don't know interesting and and notable I

619
00:25:02,770 --> 00:24:59,390
think that DNA would take its native

620
00:25:04,510 --> 00:25:02,780
form and these solvents are also

621
00:25:06,910 --> 00:25:04,520
miscible with water and so we could have

622
00:25:09,040 --> 00:25:06,920
a cycle with these non aqueous solvents

623
00:25:13,420 --> 00:25:09,050
with water some periods of time and then

624
00:25:15,820 --> 00:25:13,430
dehydrated other periods of time and the

625
00:25:18,160 --> 00:25:15,830
the melting temperature of DNA is also

626
00:25:19,270 --> 00:25:18,170
it's suppressed it's lowered in these

627
00:25:21,340 --> 00:25:19,280
solvents and that turned out to be just

628
00:25:23,020 --> 00:25:21,350
helpful from a practical point of view

629
00:25:24,760 --> 00:25:23,030
in the experiment that we could we could

630
00:25:29,799 --> 00:25:24,770
separate our straight and long very long

631
00:25:32,240 --> 00:25:29,809
strands under reasonable temperatures

632
00:25:34,580 --> 00:25:32,250
and so these are just going to show you

633
00:25:38,930 --> 00:25:34,590
a few of the results this slide shows

634
00:25:40,910 --> 00:25:38,940
how we were able to just look at do that

635
00:25:42,680 --> 00:25:40,920
separating the duplex and then cooling

636
00:25:45,140 --> 00:25:42,690
it back down and we had a window of time

637
00:25:46,850 --> 00:25:45,150
and this glyco leaned in which we could

638
00:25:47,930 --> 00:25:46,860

get the single-stranded DNA so you can

639
00:25:49,730 --> 00:25:47,940
look you look at the gel at the top

640
00:25:52,340 --> 00:25:49,740
there's the top bands is the double

641
00:25:53,990 --> 00:25:52,350
double duplex DNA and the lower one is a

642
00:25:56,960 --> 00:25:54,000
single strand so and glyco lean we would

643
00:25:59,030 --> 00:25:56,970
have a period of time in which we would

644
00:26:01,190 --> 00:25:59,040
have single strand before it really old

645
00:26:04,669 --> 00:26:01,200
where as an aqueous buffer it would

646
00:26:06,560 --> 00:26:04,679
really pretty much immediately Rhea Neil

647
00:26:08,450 --> 00:26:06,570
unless we had an extremely high cooling

648
00:26:10,130 --> 00:26:08,460
rate something like 40 degrees C per

649
00:26:13,810 --> 00:26:10,140
minute which probably is not prebiotic

650
00:26:17,419 --> 00:26:13,820
ly plausible and then we were able to

651
00:26:20,210 --> 00:26:17,429
show that we could lie date assemble

652
00:26:22,100 --> 00:26:20,220
nucleotides on those long pieces during

653
00:26:24,470 --> 00:26:22,110
that window of time and so that's really

654
00:26:27,260 --> 00:26:24,480
what this particular slide shows we

655
00:26:31,010 --> 00:26:27,270
looked at eleven-thirty tumors adjacent

656
00:26:34,640 --> 00:26:31,020
along a three Killa base template and we

657
00:26:36,440 --> 00:26:34,650
could make the full-length product in

658
00:26:41,180 --> 00:26:36,450
glycol in whereas we would not be able

659
00:26:43,340 --> 00:26:41,190
to make it in aqueous buffer and so

660
00:26:45,740 --> 00:26:43,350
again I wanted to describe the

661
00:26:48,590 --> 00:26:45,750
progression of ideas that got us to this

662
00:26:52,820 --> 00:26:48,600
point there's actually this earlier idea

663
00:26:54,049 --> 00:26:52,830

notice again image on/off 2010 on using

664
00:26:57,380 --> 00:26:54,059
non aqueous solvents to drive

665
00:26:58,490 --> 00:26:57,390
condensation polymerization and so

666
00:27:00,980 --> 00:26:58,500
there's the kind of history of that

667
00:27:02,750 --> 00:27:00,990
within the center research and the HUD

668
00:27:04,520 --> 00:27:02,760
lab the original idea for this project

669
00:27:07,580 --> 00:27:04,530
was to add visca jhin's to aqueous

670
00:27:09,230 --> 00:27:07,590
buffer B polysaccharides to slow the REO

671
00:27:10,850 --> 00:27:09,240
kneeling of the duplex to get that

672
00:27:12,169 --> 00:27:10,860
differential mobility that turned out

673
00:27:13,520 --> 00:27:12,179
from a practical point of view to be

674
00:27:14,570 --> 00:27:13,530
sort of difficult we had these sugars

675
00:27:16,430 --> 00:27:14,580
and we were trying to separate our

676
00:27:20,900 --> 00:27:16,440
duplex and we were caramelizing the

677
00:27:22,610 --> 00:27:20,910
sugars and and so so we decided to try

678
00:27:25,450 --> 00:27:22,620
to use it the small molecule non aqueous

679
00:27:27,740 --> 00:27:25,460
viscous solvents instead as a visca j'en

680
00:27:29,450 --> 00:27:27,750
we really didn't need the fact that they

681
00:27:33,350 --> 00:27:29,460
were non aqueous so much but we wanted

682
00:27:35,030 --> 00:27:33,360
the viscous part then we were able to

683
00:27:36,230 --> 00:27:35,040
observe the desired behavior but it

684
00:27:37,669 --> 00:27:36,240
wasn't really for the reason that we

685
00:27:39,740 --> 00:27:37,679
thought it wasn't necessarily so much of

686
00:27:41,450 --> 00:27:39,750
viscosity maybe partly but the

687
00:27:43,110 --> 00:27:41,460
intramolecular folding that happened

688
00:27:45,210 --> 00:27:43,120

while we had this window of time

689
00:27:47,549 --> 00:27:45,220
Stram separation more than the

690
00:27:49,200 --> 00:27:47,559
preferential diffusion but ultimately

691
00:27:50,549 --> 00:27:49,210
this gave us a new insight which is that

692
00:27:54,030 --> 00:27:50,559
viscous environments could help us

693
00:27:56,430 --> 00:27:54,040
select for long strands and folded

694
00:27:58,530 --> 00:27:56,440
structures for function for

695
00:28:00,420 --> 00:27:58,540
catalytically functional nucleic acid

696
00:28:03,480 --> 00:28:00,430
polymers under may be more typical

697
00:28:04,680 --> 00:28:03,490
aqueous buffer conditions the unfolded

698
00:28:07,170 --> 00:28:04,690
structures are actually easier to

699
00:28:09,450 --> 00:28:07,180
replicate and so you're selecting for

700
00:28:10,590 --> 00:28:09,460
lack of function and set up our function

701
00:28:14,310 --> 00:28:10,600
so we think this can actually be a

702
00:28:15,810 --> 00:28:14,320
pretty important idea going forward so

703
00:28:18,180 --> 00:28:15,820
I'll just make a few closing remarks

704
00:28:20,460 --> 00:28:18,190
while the light is still yellow orange

705
00:28:22,110 --> 00:28:20,470
one is that through this estimate

706
00:28:23,730 --> 00:28:22,120
exchange mechanism the peptide World may

707
00:28:25,919 --> 00:28:23,740
actually be more accessible than has

708
00:28:28,110 --> 00:28:25,929
previously been thought challenging the

709
00:28:32,070 --> 00:28:28,120
single dominance of the RNA world

710
00:28:34,020 --> 00:28:32,080
hypothesis perhaps there were multiple

711
00:28:36,200 --> 00:28:34,030
things going on at once that are all

712
00:28:38,310 --> 00:28:36,210
important as well as their interactions

713
00:28:40,290 --> 00:28:38,320

another insight is that in an aqueous

714
00:28:42,240 --> 00:28:40,300
environment condensation polymers may

715
00:28:46,830 --> 00:28:42,250
have been selected in life because they

716
00:28:48,510 --> 00:28:46,840
could evolve we also think that viscous

717
00:28:51,260 --> 00:28:48,520
environments can drive selection for

718
00:28:53,510 --> 00:28:51,270
folding and functions function and that

719
00:28:55,350 --> 00:28:53,520
furthermore that this research

720
00:28:58,740 --> 00:28:55,360
serendipity that we're having these

721
00:29:01,100 --> 00:28:58,750
surprises that are helpful may or may

722
00:29:04,080 --> 00:29:01,110
not suggest that some of these

723
00:29:05,880 --> 00:29:04,090
environments and chemistry's together as

724
00:29:10,740 --> 00:29:05,890
a system could mimic some key features

725
00:29:13,590 --> 00:29:10,750
of the prebiotic world so with that I

726
00:29:15,540 --> 00:29:13,600
just like to acknowledge all the members

727
00:29:18,900 --> 00:29:15,550
of the Center for chemical evolution and

728
00:29:20,010 --> 00:29:18,910
our funding from NSF and NASA also like

729
00:29:22,820 --> 00:29:20,020
to acknowledge some of the key players

730
00:29:24,810 --> 00:29:22,830
in the work I presented today NIC hood

731
00:29:26,669 --> 00:29:24,820
first and foremost and thank him for

732
00:29:28,860 --> 00:29:26,679
inviting me into the center to work on

733
00:29:31,290 --> 00:29:28,870
this exciting area Sarah Walker

734
00:29:33,540 --> 00:29:31,300
qianxiang you Kristine he and arena

735
00:29:34,710 --> 00:29:33,550
ma'am Adama and I believe Chris butch

736
00:29:36,240 --> 00:29:34,720
I did not talk about Chris's work I

737
00:29:40,500 --> 00:29:36,250
think I believe he's the tall one

738
00:29:42,690 --> 00:29:40,510

standing in the back right there in this

739
00:29:45,330 --> 00:29:42,700
picture from the center so anyway of

740
00:29:48,120 --> 00:29:45,340
many many Center members to acknowledge

741
00:29:50,250 --> 00:29:48,130
here and I also just listed three of the

742
00:29:52,320 --> 00:29:50,260
key publications from this work and with

743
00:29:55,340 --> 00:29:52,330
that I'd like to conclude and welcome

744
00:29:55,350 --> 00:30:01,520
[Applause]

745
00:30:10,140 --> 00:30:03,240
hey-ya so we have some time for

746
00:30:12,030 --> 00:30:10,150
questions and discussion hi um I was

747
00:30:15,330 --> 00:30:12,040
very interested by your work at the

748
00:30:18,420 --> 00:30:15,340
beginning with the the polymers and

749
00:30:21,480 --> 00:30:18,430
wondered are you aware of Dave Demers

750
00:30:23,340 --> 00:30:21,490
work on polymerization like around

751
00:30:25,770 --> 00:30:23,350
thermal vents because that also gets rid

752
00:30:28,830 --> 00:30:25,780
of your problem of actually dropping 40

753
00:30:31,380 --> 00:30:28,840
degrees in a minute so you're talking

754
00:30:40,560 --> 00:30:31,390
about the Strand inhibition problem with

755
00:30:44,010 --> 00:30:40,570
the 40 degrees yeah so so you don't well

756
00:30:46,830 --> 00:30:44,020
or even polymerizing or even naturing

757
00:30:48,840 --> 00:30:46,840
and sort of along those lines it seems

758
00:30:51,290 --> 00:30:48,850
to me that your results are going to

759
00:30:54,420 --> 00:30:51,300
depend a lot on the concentration of

760
00:30:56,100 --> 00:30:54,430
your solutes and so presumably you would

761
00:30:57,270 --> 00:30:56,110
not have very much of your double strand

762
00:30:59,760 --> 00:30:57,280
you have much more short

763
00:31:01,560 --> 00:30:59,770

eligos or single nucleotides and

764
00:31:03,990 --> 00:31:01,570
therefore I question whether that

765
00:31:06,090 --> 00:31:04,000
actually is a terrific way to get

766
00:31:09,390 --> 00:31:06,100
variability and you don't actually have

767
00:31:10,740 --> 00:31:09,400
a strand inhibition problem so so

768
00:31:13,020 --> 00:31:10,750
because there's so much more monomer

769
00:31:20,070 --> 00:31:13,030
than polymer that that would help with

770
00:31:22,710 --> 00:31:20,080
strand inhibition so so that would be a

771
00:31:25,290 --> 00:31:22,720
helpful direction I agree with that when

772
00:31:27,420 --> 00:31:25,300
many of our initial experiments in this

773
00:31:30,180 --> 00:31:27,430
case here we have four to one monomer to

774
00:31:31,860 --> 00:31:30,190
polymer or ligament a polymer although

775
00:31:33,720 --> 00:31:31,870
early on we did experiments more with

776
00:31:39,780 --> 00:31:33,730
twenty to one something like that

777
00:31:41,880 --> 00:31:39,790
DNA is remarkably good associating well

778
00:31:43,800 --> 00:31:41,890
you know where I I guess one thing that

779
00:31:47,420 --> 00:31:43,810
I would say is that that we're trying to

780
00:31:51,470 --> 00:31:47,430
design and demonstrate minimal chemical

781
00:31:53,940 --> 00:31:51,480
systems that can evolve and so we're not

782
00:31:55,620 --> 00:31:53,950
saying that this environment is right

783
00:31:57,300 --> 00:31:55,630
and this environment is wrong but we're

784
00:32:01,850 --> 00:31:57,310
focusing on this particular environment

785
00:32:04,820 --> 00:32:01,860
of drawing and rewedding but you know we

786
00:32:07,350 --> 00:32:04,830
look forward to seeing evolving systems

787
00:32:08,460 --> 00:32:07,360
from other environments as well this is

788
00:32:14,279 --> 00:32:08,470

the particular advice

789
00:32:16,620 --> 00:32:14,289
that were that we're considering okay

790
00:32:19,529 --> 00:32:16,630
great thank you very exciting work and

791
00:32:22,080 --> 00:32:19,539
as a planetary scientists have been

792
00:32:24,510 --> 00:32:22,090
always wondering what the environment

793
00:32:26,549 --> 00:32:24,520
was during a time of origin of life and

794
00:32:31,799 --> 00:32:26,559
the artwork is quite interesting in that

795
00:32:35,970 --> 00:32:31,809
science but exactly how viscous that

796
00:32:40,320 --> 00:32:35,980
environment you require you give as an

797
00:32:44,909 --> 00:32:40,330
example an auto code and how frequent

798
00:32:49,440 --> 00:32:44,919
were your environment change some

799
00:32:52,980 --> 00:32:49,450
examples well choline is about a hundred

800
00:32:56,220 --> 00:32:52,990
centipoise viscosity which is about a

801
00:32:59,159 --> 00:32:56,230
similar to motor oil so not as viscous

802
00:33:01,470 --> 00:32:59,169
as honey but significantly more viscous

803
00:33:03,750 --> 00:33:01,480
than water now we've also demonstrated

804
00:33:06,060 --> 00:33:03,760
this approach with this is work for DNA

805
00:33:08,250 --> 00:33:06,070
but we've also done it in RNA and we've

806
00:33:12,990 --> 00:33:08,260
also demonstrated the phenomenon and

807
00:33:18,960 --> 00:33:13,000
glycerol and in raylene a urea choline

808
00:33:21,390 --> 00:33:18,970
chloride so if we also have diluted the

809
00:33:23,340 --> 00:33:21,400
glycol in with water and so we can also

810
00:33:26,940 --> 00:33:23,350
see the effective viscosity just simply

811
00:33:29,490 --> 00:33:26,950
through dilution so you know this seems

812
00:33:32,600 --> 00:33:29,500
to be a general physical principle and

813
00:33:35,490 --> 00:33:32,610

phenomenon that's not specific only to

814
00:33:40,470 --> 00:33:35,500
glycol Ian in this particular viscosity

815
00:33:43,620 --> 00:33:40,480
but you do need to have enough slowing

816
00:33:45,210 --> 00:33:43,630
of a movement so that you can get this

817
00:33:47,730 --> 00:33:45,220
intramolecular folding but it seems to

818
00:33:52,760 --> 00:33:47,740
have a pretty broad window but these are

819
00:33:58,260 --> 00:33:52,770
for motor oil the the temperature here

820
00:34:00,630 --> 00:33:58,270
so we needed to separate the two strands

821
00:34:03,149 --> 00:34:00,640
and so in order to do that we needed to

822
00:34:05,299 --> 00:34:03,159
get above the melting temperature so in

823
00:34:08,520 --> 00:34:05,309
glycol eeen that's about fifty degrees

824
00:34:11,820 --> 00:34:08,530
and so so we needed to separate the

825
00:34:14,159 --> 00:34:11,830
strands and then we cool down to ambient

826
00:34:16,829 --> 00:34:14,169
temperature room temperature at a

827
00:34:19,349 --> 00:34:16,839
variety of different rates so I went

828
00:34:20,909 --> 00:34:19,359
through this fairly quickly but you can

829
00:34:22,120 --> 00:34:20,919
see here we tried a number of different

830
00:34:24,820 --> 00:34:22,130
rates from four degrees

831
00:34:26,620 --> 00:34:24,830
see per minute up to 40 degrees c per

832
00:34:30,850 --> 00:34:26,630
minute and and then compared the aqueous

833
00:34:35,830 --> 00:34:30,860
buffer to the glycol een so really this

834
00:34:37,450 --> 00:34:35,840
is a proof of principle so exactly what

835
00:34:40,270 --> 00:34:37,460
these numbers would be would depend on

836
00:34:43,090 --> 00:34:40,280
your viscosity would depend on the

837
00:34:45,250 --> 00:34:43,100
particular nucleic acid polymer that

838
00:34:47,470 --> 00:34:45,260

you're looking at so the we're looking

839
00:34:49,000 --> 00:34:47,480
at glycol één which is glycerol and

840
00:34:51,010 --> 00:34:49,010
choline chloride so glycerol would be

841
00:34:53,950 --> 00:34:51,020
considered prebiotic lea plausible the

842
00:34:55,990 --> 00:34:53,960
core choline chloride is the choline is

843
00:34:57,910 --> 00:34:56,000
questionable you know maybe you could

844
00:35:00,160 --> 00:34:57,920
argue and it's been mentioned in

845
00:35:02,320 --> 00:35:00,170
prebiotic literature but we're really

846
00:35:04,510 --> 00:35:02,330
using this as a proof of principle more

847
00:35:13,630 --> 00:35:04,520
than that this particular solvent would

848
00:35:18,359 --> 00:35:16,210
and thank you very much I've got

849
00:35:23,829 --> 00:35:18,369
interested in earning enough your

850
00:35:27,700 --> 00:35:23,839
hypothesis that their hydroxy acid can

851
00:35:29,609 --> 00:35:27,710
work as a catalyst for amino acid for

852
00:35:33,999 --> 00:35:29,619
meditation

853
00:35:39,849 --> 00:35:34,009
why did you conclude in that way I just

854
00:35:44,140 --> 00:35:39,859
asking the hydroxy acid has some

855
00:35:47,920 --> 00:35:44,150
specificity for selective amino acid

856
00:35:50,620 --> 00:35:47,930
sequence or you have the general

857
00:35:56,859 --> 00:35:50,630
catalyst reaction for any types of I

858
00:35:58,450 --> 00:35:56,869
mean so so if we look at the the figures

859
00:36:00,579 --> 00:35:58,460
on the right there you can see that the

860
00:36:03,759 --> 00:36:00,589
amino acids and the hydroxy acids have

861
00:36:07,269 --> 00:36:03,769
their analog so glycine and glycolic

862
00:36:09,370 --> 00:36:07,279
acid alanine and lactic acid so they

863
00:36:11,680 --> 00:36:09,380

differ only by the amine group versus

864
00:36:13,720 --> 00:36:11,690
the O H group so so they're very similar

865
00:36:15,579 --> 00:36:13,730
to amino acids and that was what led

866
00:36:17,259 --> 00:36:15,589
Nick I don't know eight years ago to

867
00:36:18,999 --> 00:36:17,269
come to my office and say look you got

868
00:36:22,749 --> 00:36:19,009
to read this paper about glycolic acid

869
00:36:25,239 --> 00:36:22,759
and an or gal had had talked about its

870
00:36:27,249 --> 00:36:25,249
importance but this ester Hammad

871
00:36:29,499 --> 00:36:27,259
exchange is not so much about the

872
00:36:32,940 --> 00:36:29,509
similarity between these molecules it's

873
00:36:35,620 --> 00:36:32,950
a stramit exchange is a well known

874
00:36:38,680 --> 00:36:35,630
chemical reaction and in elementary

875
00:36:41,650 --> 00:36:38,690
textbooks but it just had not been

876
00:36:43,479 --> 00:36:41,660
applied to these polymers or in an

877
00:36:45,479 --> 00:36:43,489
origins context actually these deficits

878
00:36:47,769 --> 00:36:45,489
peptides are documented in terms of

879
00:36:52,180 --> 00:36:47,779
biomedical applications in the

880
00:36:55,769 --> 00:36:52,190
literature and so it was sort of right

881
00:36:59,079 --> 00:36:55,779
there hiding in plain sight I think

882
00:37:05,170 --> 00:36:59,089
couldn't find it any selectivity for

883
00:37:06,940 --> 00:37:05,180
each or so we tried we have tried this

884
00:37:09,430 --> 00:37:06,950
reaction for many different hydroxy

885
00:37:11,859 --> 00:37:09,440
acids and many different amino acids and

886
00:37:13,839 --> 00:37:11,869
some have more reactivity than others

887
00:37:16,299 --> 00:37:13,849
but it is a general phenomenon it's not

888
00:37:21,130 --> 00:37:16,309

specific to particular amino acid and we

889
00:37:22,660 --> 00:37:21,140
have made sequences copolymer sequences

890
00:37:24,880 --> 00:37:22,670
with different amino acids different

891
00:37:27,249 --> 00:37:24,890
hydroxy acids so it's a it's a it's a

892
00:37:27,640 --> 00:37:27,259
just a general reaction that just has no

893
00:37:30,690 --> 00:37:27,650
differ

894
00:37:34,690 --> 00:37:30,700
so rates depending on the particular

895
00:37:40,360 --> 00:37:34,700
hydroxy acid or amino acid but it seems

896
00:37:43,360 --> 00:37:40,370
to be very robust so I'm just wondering

897
00:37:45,610 --> 00:37:43,370
about the geochemical settings of the

898
00:37:51,040 --> 00:37:45,620
dry/wet cycles or any kind of cycles

899
00:37:53,590 --> 00:37:51,050
like that so it is really interesting to

900
00:37:55,120 --> 00:37:53,600
have like these polymers clusters and

901
00:37:57,400 --> 00:37:55,130
everything but these kind of settings

902
00:37:59,980 --> 00:37:57,410
should don't you like also take it to

903
00:38:03,910 --> 00:37:59,990
account the fact that well you will have

904
00:38:05,950 --> 00:38:03,920
salts in the in the water and since you

905
00:38:07,960 --> 00:38:05,960
have salt it will be like a evaporite

906
00:38:09,220 --> 00:38:07,970
basin or whatever so you will have to

907
00:38:12,250 --> 00:38:09,230
take into account the fact that you have

908
00:38:15,310 --> 00:38:12,260
at least one more of any salt the salt

909
00:38:18,070 --> 00:38:15,320
there so after you have your brine is it

910
00:38:22,360 --> 00:38:18,080
reversible do you expect that you will

911
00:38:26,650 --> 00:38:22,370
have the same kind of result yes

912
00:38:28,630 --> 00:38:26,660
certainly adding other species will add

913
00:38:29,950 --> 00:38:28,640

complexity to the reactions and

914
00:38:33,550 --> 00:38:29,960
potentially change the events we have

915
00:38:35,380 --> 00:38:33,560
been focusing more on pH dependence one

916
00:38:37,690 --> 00:38:35,390
point that I did not make here but that

917
00:38:39,100 --> 00:38:37,700
is important for the estimated exchange

918
00:38:43,990 --> 00:38:39,110
reactions is that because we have

919
00:38:46,180 --> 00:38:44,000
hydroxy acids they're acidic so that

920
00:38:50,200 --> 00:38:46,190
drives forward and acid catalyzed

921
00:38:52,390 --> 00:38:50,210
polymerization of the polyesters and

922
00:38:53,800 --> 00:38:52,400
then when we dry its might start out not

923
00:38:55,690 --> 00:38:53,810
as acidic then we dry down then it

924
00:38:56,920 --> 00:38:55,700
becomes acidic so there's a lot going on

925
00:38:58,810 --> 00:38:56,930
that we've been looking at in terms of

926
00:39:00,460 --> 00:38:58,820
the pH dynamics of the system not that

927
00:39:02,410 --> 00:39:00,470
we're imposing but that just sort of

928
00:39:05,860 --> 00:39:02,420
naturally emerge from the lactic acid

929
00:39:08,170 --> 00:39:05,870
presence of the the hydroxy acid so we

930
00:39:09,580 --> 00:39:08,180
also have talked about the presence of

931
00:39:11,650 --> 00:39:09,590
salt and the addition of salt and that's

932
00:39:13,330 --> 00:39:11,660
something that you know of course will

933
00:39:17,220 --> 00:39:13,340
have impact on the system but I don't

934
00:39:19,480 --> 00:39:17,230
think it's a show stopper in any way

935
00:39:21,700 --> 00:39:19,490
we've we've talked about it actually in

936
00:39:23,740 --> 00:39:21,710
some of the other projects and kind of

937
00:39:26,020 --> 00:39:23,750
the micro environments direction that I

938
00:39:28,180 --> 00:39:26,030

did not talk about today but certainly

939
00:39:34,390 --> 00:39:28,190
I'm salt we would be present and we play

940
00:39:36,970 --> 00:39:34,400
a role when you refer to the monomers in

941
00:39:39,220 --> 00:39:36,980
taste are you assuming that these thin

942
00:39:41,170 --> 00:39:39,230
stages are actually like short polymers

943
00:39:43,359 --> 00:39:41,180
of either peptide

944
00:39:46,569 --> 00:39:43,369
you know lactic has always worried it

945
00:39:49,030 --> 00:39:46,579
can actually drive the chemical reaction

946
00:39:51,220 --> 00:39:49,040
and throughout the metabolic yes so the

947
00:39:53,020 --> 00:39:51,230
idea in those simulations is that we

948
00:39:55,240 --> 00:39:53,030
have a fixed amount of mass in the

949
00:39:57,370 --> 00:39:55,250
system the simulation is closed to mass

950
00:39:59,049 --> 00:39:57,380
and that it's a scarce resource and the

951
00:40:01,930 --> 00:39:59,059
different polymers are competing for it

952
00:40:04,780 --> 00:40:01,940
and so that if a polymer could make more

953
00:40:05,890 --> 00:40:04,790
than especially that's co-localize you

954
00:40:08,559 --> 00:40:05,900
know then it would have a great

955
00:40:09,910 --> 00:40:08,569
advantage in terms of replication but

956
00:40:12,640 --> 00:40:09,920
yeah the assumption is that there would

957
00:40:14,380 --> 00:40:12,650
be a similar small molecule present in

958
00:40:16,480 --> 00:40:14,390
the environment that's similar to the

959
00:40:19,030 --> 00:40:16,490
monomer and this would you know perhaps

960
00:40:20,349 --> 00:40:19,040
you know truncate off some piece or

961
00:40:22,720 --> 00:40:20,359
perform some sort of chemical

962
00:40:24,960 --> 00:40:22,730
modification that would turn it into say

963
00:40:27,220 --> 00:40:24,970

the amino acid and then if you

964
00:40:28,750 --> 00:40:27,230
incorporate the recycling cycle I really

965
00:40:32,109 --> 00:40:28,760
loved that recycling cycle concept

966
00:40:35,079 --> 00:40:32,119
because actually because the sequence of

967
00:40:37,809 --> 00:40:35,089
those polymers in the environment will

968
00:40:40,240 --> 00:40:37,819
be governed by the composition of those

969
00:40:42,160 --> 00:40:40,250
each polymers so actually if they're if

970
00:40:45,099 --> 00:40:42,170
you introduce these monomers in taste

971
00:40:48,280 --> 00:40:45,109
into the system then that will probably

972
00:40:50,049 --> 00:40:48,290
change the composition of the in the

973
00:40:51,549 --> 00:40:50,059
environment which will change the

974
00:40:54,250 --> 00:40:51,559
sequence based kind of kind of shape the

975
00:40:55,390 --> 00:40:54,260
sequence space of the those randomly

976
00:40:56,620 --> 00:40:55,400
yeah that's right and that's what you

977
00:40:59,079 --> 00:40:56,630
can see actually in this middle panel

978
00:41:01,380 --> 00:40:59,089
here where we have a nays I'm we have an

979
00:41:03,730 --> 00:41:01,390
enrichment of the a monomer and then

980
00:41:06,039 --> 00:41:03,740
depletion of the B monomer in this case

981
00:41:07,690 --> 00:41:06,049
though we had all of our polymers we're

982
00:41:09,490 --> 00:41:07,700
assumed to have equal amounts of a and B

983
00:41:10,480 --> 00:41:09,500
different sequences but same composition

984
00:41:12,069 --> 00:41:10,490
so we just didn't introduce that

985
00:41:13,450 --> 00:41:12,079
additional complexity into the

986
00:41:15,430 --> 00:41:13,460
simulation but you're absolutely right

987
00:41:17,799 --> 00:41:15,440
that if we have more a than that would

988
00:41:19,599 --> 00:41:17,809

it be easier for polymers rich in a to

989
00:41:21,069 --> 00:41:19,609
replicate and that would be an

990
00:41:25,290 --> 00:41:21,079
additional effect to include that we did

991
00:41:30,390 --> 00:41:28,920
I can use this one okay so towards the

992
00:41:33,150 --> 00:41:30,400
end you had this very brief comment that

993
00:41:35,670 --> 00:41:33,160
perhaps the biological polymers evolved

994
00:41:37,710 --> 00:41:35,680
because they are good at evolution which

995
00:41:38,700 --> 00:41:37,720
I think sounds very interesting so I was

996
00:41:42,690 --> 00:41:38,710
wondering if you could say a little tiny

997
00:41:48,180 --> 00:41:42,700
bit more about that I think I don't know

998
00:41:49,520 --> 00:41:48,190
I mean I do I like that idea as well and

999
00:41:53,280 --> 00:41:49,530
that's something that Nick and I have

1000
00:41:58,380 --> 00:41:53,290
discussing and that he perhaps really

1001
00:41:59,760 --> 00:41:58,390
articulated but but but I think we think

1002
00:42:05,190 --> 00:41:59,770
was kind of present in this earlier

1003
00:42:07,170 --> 00:42:05,200
modeling study that yeah I guess I guess

1004
00:42:10,620 --> 00:42:07,180
I would like to hear people who disagree

1005
00:42:12,180 --> 00:42:10,630
and for what reasons I think it it makes

1006
00:42:14,610 --> 00:42:12,190
a lot of sense but that we just don't

1007
00:42:16,140 --> 00:42:14,620
want we don't want a system that is too

1008
00:42:18,750 --> 00:42:16,150
stable that's something that we saw very

1009
00:42:20,760 --> 00:42:18,760
clearly in that simulation study was

1010
00:42:24,120 --> 00:42:20,770
that if you have a limited monomer

1011
00:42:25,680 --> 00:42:24,130
resource and you want to explore so many

1012
00:42:27,680 --> 00:42:25,690
sequences you have this combinatorial

1013
00:42:30,900 --> 00:42:27,690

explosion of sequences you just can't

1014
00:42:32,880 --> 00:42:30,910
lock up all of your resources in

1015
00:42:34,860 --> 00:42:32,890
sequences that are probably not

1016
00:42:36,390 --> 00:42:34,870
functional and so this turnover is so

1017
00:42:39,090 --> 00:42:36,400
important so that's what that recycling

1018
00:42:40,860 --> 00:42:39,100
recycling idea is is about is that you

1019
00:42:43,350 --> 00:42:40,870
you need to have that recycling and so

1020
00:42:45,480 --> 00:42:43,360
you know these probably esters that orgo

1021
00:42:49,110 --> 00:42:45,490
had talked about them as being a

1022
00:42:51,030 --> 00:42:49,120
potential proto peptide but they were

1023
00:42:53,220 --> 00:42:51,040
maybe just dismissed because they're

1024
00:42:56,130 --> 00:42:53,230
just not stable enough and that that but

1025
00:43:00,000 --> 00:42:56,140
actually you just can't be too stable

1026
00:43:04,370 --> 00:43:00,010
or you're just not going to get em okay

1027
00:43:08,390 --> 00:43:04,380
well thank you very much for for that

1028
00:43:20,740 --> 00:43:08,400
[Applause]