
AbSciCon
2019

1
00:00:00,790 --> 00:00:07,320
[Music]

2
00:00:12,210 --> 00:00:09,560
[Applause]

3
00:00:14,070 --> 00:00:12,220
so we are interested in the first

4
00:00:15,960 --> 00:00:14,080
replicating molecules which could well

5
00:00:19,859 --> 00:00:15,970
have been RNA or something very similar

6
00:00:23,960 --> 00:00:19,869
and we're imagining there was something

7
00:00:33,570 --> 00:00:23,970
like a polymerase ribozyme which in our

8
00:00:35,970 --> 00:00:33,580
we have a pointer okay so in our in our

9
00:00:37,710 --> 00:00:35,980
cartoonist the red blob is a polymerase

10
00:00:39,990 --> 00:00:37,720
ribozyme which is functioning as a

11
00:00:42,630 --> 00:00:40,000
catalyst and it's binding to another

12
00:00:44,100 --> 00:00:42,640
strand which is the template and we're

13
00:00:46,350 --> 00:00:44,110

supposing the template is the same

14
00:00:49,040 --> 00:00:46,360
sequences itself and it's making the

15
00:00:51,510 --> 00:00:49,050
complementary strand to the template and

16
00:00:53,729 --> 00:00:51,520
there are ribosomes that work like this

17
00:00:56,400 --> 00:00:53,739
in the lab so this is a real one that

18
00:00:58,680 --> 00:00:56,410
came from the 2001 paper here and the

19
00:01:01,619 --> 00:00:58,690
best ones of this type now go up to 200

20
00:01:03,930 --> 00:01:01,629
nucleotides so this is good except that

21
00:01:05,730 --> 00:01:03,940
this one won't work with its own

22
00:01:08,130 --> 00:01:05,740
sequence as a template so it doesn't yet

23
00:01:10,680 --> 00:01:08,140
replicate itself so if we think about

24
00:01:12,710 --> 00:01:10,690
there's three requirements that are that

25
00:01:15,539 --> 00:01:12,720
a sequence must have in order to sustain

26
00:01:16,770 --> 00:01:15,549
replication in the RNA world it would

27
00:01:18,719 --> 00:01:16,780
have to be able to work on its own

28
00:01:20,520 --> 00:01:18,729
sequence it would have to be able to

29
00:01:22,740 --> 00:01:20,530
replicate faster than the breakdown rate

30
00:01:24,179 --> 00:01:22,750
of the same sequence by by hydrolysis

31
00:01:26,490 --> 00:01:24,189
and it would have to be accurate enough

32
00:01:28,170 --> 00:01:26,500
to maintain the sequence and roughly

33
00:01:30,330 --> 00:01:28,180
speaking that means that the numbers of

34
00:01:33,690 --> 00:01:30,340
the average numbers of errors per whole

35
00:01:37,039 --> 00:01:33,700
sequence replication is 1 or less so

36
00:01:39,359 --> 00:01:37,049
that's the error threshold into criteria

37
00:01:41,640 --> 00:01:39,369
the basic theory of the error threshold

38
00:01:45,300 --> 00:01:41,650

goes back to I'd encircled ecce de go

39
00:01:48,270 --> 00:01:45,310
and I'm going to explain it on one slide

40
00:01:50,460 --> 00:01:48,280
so P is going to be the concentration of

41
00:01:54,030 --> 00:01:50,470
my functional molecule which is a red a

42
00:01:57,480 --> 00:01:54,040
red a red square there it can replicate

43
00:02:00,480 --> 00:01:57,490
at a rate which is R naught and then X

44
00:02:02,100 --> 00:02:00,490
is the concentration of mutant sequences

45
00:02:04,410 --> 00:02:02,110
which are black circles on here and they

46
00:02:07,050 --> 00:02:04,420
replicate at a slow rate R 1 which is

47
00:02:09,150 --> 00:02:07,060
less than R naught there's a breakdown

48
00:02:10,979 --> 00:02:09,160
rate which I'll call V and I'm assuming

49
00:02:13,199 --> 00:02:10,989
for the simple case it's the same for

50
00:02:15,420 --> 00:02:13,209
all kinds of sequencers so in order to

51
00:02:18,330 --> 00:02:15,430
survive the good ones must replicate

52
00:02:20,650 --> 00:02:18,340
faster than V so the red ones have a

53
00:02:23,710 --> 00:02:20,660
fast replicate faster than V

54
00:02:25,780 --> 00:02:23,720
and then there's a mutation probability

55
00:02:27,580 --> 00:02:25,790
M which is the probability of a

56
00:02:31,540 --> 00:02:27,590
deleterious mutations somewhere in the

57
00:02:33,550 --> 00:02:31,550
sequence per replication and it turns

58
00:02:35,800 --> 00:02:33,560
out then that there is a maximum error

59
00:02:37,570 --> 00:02:35,810
rate that can be sustained that's called

60
00:02:40,420 --> 00:02:37,580
the error threshold so the red ones

61
00:02:42,880 --> 00:02:40,430
survive if the error rate is less than

62
00:02:45,100 --> 00:02:42,890
the maximum M which is called the error

63
00:02:46,900 --> 00:02:45,110

threshold so this is a very simplest is

64
00:02:49,000 --> 00:02:46,910
a very simple theory it's a 5-minute

65
00:02:51,880 --> 00:02:49,010
theory and what comes out of it is this

66
00:02:54,640 --> 00:02:51,890
if there's no if the error is put if the

67
00:02:57,010 --> 00:02:54,650
replication is perfect so M is zero then

68
00:02:59,320 --> 00:02:57,020
I get all red ones as I turn up the

69
00:03:01,000 --> 00:02:59,330
mutation rate the red ones go down and

70
00:03:02,410 --> 00:03:01,010
down and there's an as an error

71
00:03:05,230 --> 00:03:02,420
threshold here which is the maximum

72
00:03:08,470 --> 00:03:05,240
sustainable error rate and since the in

73
00:03:11,700 --> 00:03:08,480
this case the this is the case where the

74
00:03:14,680 --> 00:03:11,710
the black ones the X's cannot replicate

75
00:03:17,830 --> 00:03:14,690
by themselves the replication rate of

76
00:03:19,540 --> 00:03:17,840
the the r1 and the replication rate of

77
00:03:21,940 --> 00:03:19,550
the black ones is less than V so the I

78
00:03:24,910 --> 00:03:21,950
ones don't die when there's no red ones

79
00:03:27,070 --> 00:03:24,920
left okay so everything dies when

80
00:03:29,980 --> 00:03:27,080
mutation is high so that's the basic

81
00:03:33,840 --> 00:03:29,990
error threshold theory but we we're not

82
00:03:35,950 --> 00:03:33,850
interested well I'll go back on the this

83
00:03:38,470 --> 00:03:35,960
this would apply to something like a

84
00:03:40,840 --> 00:03:38,480
virus that is multiplying inside a cell

85
00:03:42,640 --> 00:03:40,850
and the cell provides the magical

86
00:03:45,220 --> 00:03:42,650
ingredients that are necessary for the

87
00:03:47,230 --> 00:03:45,230
virus to replicate itself but in the RNA

88
00:03:50,199 --> 00:03:47,240

world there's no magical cell there

89
00:03:53,020 --> 00:03:50,209
so the what that the RNA ribozyme asked

90
00:03:55,240 --> 00:03:53,030
to copy itself so now our a reaction

91
00:03:57,580 --> 00:03:55,250
scheme looks like this a red one meets a

92
00:03:59,740 --> 00:03:57,590
red one and it makes an orange one the

93
00:04:02,500 --> 00:03:59,750
orange one is the complementary sequence

94
00:04:02,920 --> 00:04:02,510
to the red if a red one meets an orange

95
00:04:10,170 --> 00:04:02,930
one

96
00:04:12,850 --> 00:04:10,180
replicate but if a mutation happens

97
00:04:14,530 --> 00:04:12,860
instead of a red a red plus a red should

98
00:04:16,810 --> 00:04:14,540
make an orange but it makes a black one

99
00:04:18,370 --> 00:04:16,820
by mistake and a red plus an orange

100
00:04:21,849 --> 00:04:18,380
should make a red but it makes a black

101
00:04:23,500 --> 00:04:21,859
one by mistake and if a red meets the

102
00:04:25,600 --> 00:04:23,510
black it makes another rat another black

103
00:04:27,370 --> 00:04:25,610
so we're always assuming that mutation

104
00:04:28,900 --> 00:04:27,380
takes you from the functional ones to

105
00:04:30,940 --> 00:04:28,910
the non-functional ones because it's

106
00:04:32,770 --> 00:04:30,950
much easier to go wrong than it is to

107
00:04:34,030 --> 00:04:32,780
put your mistake right so we just assume

108
00:04:38,350 --> 00:04:34,040
Mew

109
00:04:40,060 --> 00:04:38,360
makes the bad ones all the time and so

110
00:04:42,610 --> 00:04:40,070
now we can do a 5-minute theory of that

111
00:04:44,710 --> 00:04:42,620
so these these equations are the well

112
00:04:46,060 --> 00:04:44,720
mixed theory they just tell you what

113
00:04:47,860 --> 00:04:46,070

would the concentrations of these

114
00:04:50,200 --> 00:04:47,870
molecules be in a well mixed reaction

115
00:04:52,350 --> 00:04:50,210
system that's a five minute theory and

116
00:04:57,400 --> 00:04:52,360
the five minute theory of this says

117
00:05:00,190 --> 00:04:57,410
everything dies because because the

118
00:05:02,260 --> 00:05:00,200
parasites take over in this in this case

119
00:05:06,010 --> 00:05:02,270
the parasites always take over and this

120
00:05:08,950 --> 00:05:06,020
is accomplice is a a cooperative system

121
00:05:10,540 --> 00:05:08,960
right one red one can do it by itself

122
00:05:12,580 --> 00:05:10,550
you need a group of red ones they have

123
00:05:14,380 --> 00:05:12,590
to cooperate and cooperative systems are

124
00:05:17,020 --> 00:05:14,390
taken over by parasites in the well

125
00:05:18,910 --> 00:05:17,030
mixed in the well mixed case so now we

126
00:05:20,530 --> 00:05:18,920
already know because this is this this

127
00:05:23,200 --> 00:05:20,540
kind of problem has been studied many

128
00:05:25,810 --> 00:05:23,210
times before we already know there's two

129
00:05:28,659 --> 00:05:25,820
ways of saving you from the parasites

130
00:05:33,580 --> 00:05:28,669
either you have spatial clustering or

131
00:05:35,860 --> 00:05:33,590
you have protocells so so in a spatial

132
00:05:37,390 --> 00:05:35,870
clustering model we have they have

133
00:05:39,220 --> 00:05:37,400
positions now the molecules have

134
00:05:41,650 --> 00:05:39,230
positions there's still three types of

135
00:05:44,080 --> 00:05:41,660
strand and what what happens is when you

136
00:05:45,670 --> 00:05:44,090
have slow diffusion in a spatial model

137
00:05:48,070 --> 00:05:45,680
you get clusters of functional ones

138
00:05:50,170 --> 00:05:48,080

together so the functional ones meet the

139
00:05:52,840 --> 00:05:50,180
other functional ones more more often

140
00:05:55,630 --> 00:05:52,850
than by chance and therefore they have a

141
00:05:58,510 --> 00:05:55,640
benefit which is counteracting the

142
00:06:00,969 --> 00:05:58,520
mutational benefit of the parasites so

143
00:06:06,390 --> 00:06:00,979
clusters of red ones can survive whereas

144
00:06:11,710 --> 00:06:09,070
similar bit different argument explains

145
00:06:14,200 --> 00:06:11,720
why replicators in protocells survive

146
00:06:16,690 --> 00:06:14,210
it's because when we have finite numbers

147
00:06:18,040 --> 00:06:16,700
of strands in protocells some cells are

148
00:06:19,900 --> 00:06:18,050
good here's a good one it has only

149
00:06:21,670 --> 00:06:19,910
functional molecules this one is going

150
00:06:23,530 --> 00:06:21,680
to multiply fast and divide and produce

151
00:06:25,930 --> 00:06:23,540
others other prone to cells which will

152
00:06:28,540 --> 00:06:25,940
also have functional molecules whereas

153
00:06:30,550 --> 00:06:28,550
something like this is being taken over

154
00:06:33,580 --> 00:06:30,560
by the black parasites but this one is

155
00:06:35,530 --> 00:06:33,590
not going to grow and divide so cell

156
00:06:37,659 --> 00:06:35,540
some cells that are destroyed by

157
00:06:39,430 --> 00:06:37,669
parasites but not all of them and the

158
00:06:41,110 --> 00:06:39,440
whole system survives because there are

159
00:06:43,270 --> 00:06:41,120
some good cells which are not taken over

160
00:06:44,980 --> 00:06:43,280
by parasites so that's group selection

161
00:06:46,310 --> 00:06:44,990
right so this is this is group selection

162
00:06:47,990 --> 00:06:46,320
saying selection works

163
00:06:50,450 --> 00:06:48,000

the level of cells as well as at the

164
00:06:51,980 --> 00:06:50,460
level of molecules and it's the group

165
00:06:54,650 --> 00:06:51,990
selection at the level of the cells that

166
00:06:58,160 --> 00:06:54,660
favors the survival of the polymer ages

167
00:06:59,990 --> 00:06:58,170
so all that has been fairly well studied

168
00:07:02,300 --> 00:07:00,000
but the problem is it's apples and

169
00:07:04,520 --> 00:07:02,310
oranges right what I what I want to know

170
00:07:07,040 --> 00:07:04,530
then that the question for this talk is

171
00:07:10,610 --> 00:07:07,050
which of these two mechanisms is better

172
00:07:13,760 --> 00:07:10,620
and by better I mean which makes it

173
00:07:17,360 --> 00:07:13,770
easier for polymerases to survive so

174
00:07:19,520 --> 00:07:17,370
that means a lower minimum replication

175
00:07:21,800 --> 00:07:19,530
rate is required in a better model a

176
00:07:23,210 --> 00:07:21,810
lower replication rate is required so

177
00:07:25,310 --> 00:07:23,220
it's easier to find a functional

178
00:07:28,250 --> 00:07:25,320
catalyst that works and in a better

179
00:07:30,170 --> 00:07:28,260
model the error rate that is tolerated

180
00:07:33,860 --> 00:07:30,180
is higher that's a higher mutation rate

181
00:07:36,110 --> 00:07:33,870
a higher error session okay so I want to

182
00:07:38,990 --> 00:07:36,120
be able to compare spatial models and

183
00:07:42,620 --> 00:07:39,000
protocell models in a quantitative way

184
00:07:43,880 --> 00:07:42,630
and then we then we hit this apples and

185
00:07:47,300 --> 00:07:43,890
oranges problem because they have

186
00:07:48,590 --> 00:07:47,310
different parameters so then we have to

187
00:07:51,470 --> 00:07:48,600
do a bit of thinking about what does a

188
00:07:53,540 --> 00:07:51,480

spatial model mean so in in the simplest

189
00:07:55,730 --> 00:07:53,550
spatial models we put things on Latin we

190
00:07:56,750 --> 00:07:55,740
put one strand on each lattice site and

191
00:07:59,240 --> 00:07:56,760
we say they interact with their

192
00:08:01,190 --> 00:07:59,250
neighbors and so well maybe that means

193
00:08:02,630 --> 00:08:01,200
something like a surface and molecules

194
00:08:04,060 --> 00:08:02,640
are stuck on their surface and two

195
00:08:07,130 --> 00:08:04,070
molecules next to each other can

196
00:08:09,380 --> 00:08:07,140
interact with each other but I find that

197
00:08:11,750 --> 00:08:09,390
hard to believe

198
00:08:12,950 --> 00:08:11,760
I can't imagine real molecules doing

199
00:08:14,750 --> 00:08:12,960
this if they're actually stuck to a

200
00:08:19,370 --> 00:08:14,760
surface right if you know if this is

201
00:08:21,230 --> 00:08:19,380
going to wrap ups if this is gonna if

202
00:08:22,580 --> 00:08:21,240
this is going to replicate its neighbor

203
00:08:24,830 --> 00:08:22,590
well maybe the neighbor needs to move

204
00:08:26,630 --> 00:08:24,840
somehow so it can't be stuck and if it

205
00:08:28,430 --> 00:08:26,640
is if it's not stuck then why does it

206
00:08:31,370 --> 00:08:28,440
not diffuse off into the third dimension

207
00:08:34,510 --> 00:08:31,380
away from the surface so I can't really

208
00:08:36,830 --> 00:08:34,520
see these spatial models representing

209
00:08:39,740 --> 00:08:36,840
really ribosomes that are permanently

210
00:08:41,930 --> 00:08:39,750
stuck to a surface but what what makes a

211
00:08:44,890 --> 00:08:41,940
little bit more sense is to think about

212
00:08:46,970 --> 00:08:44,900
the spatial models representing

213
00:08:48,980 --> 00:08:46,980

molecules which are in a constrained

214
00:08:52,280 --> 00:08:48,990
environment so that the diffusion is

215
00:08:55,040 --> 00:08:52,290
slow so what you what what matters in

216
00:08:57,200 --> 00:08:55,050
these surface in that in the spatial

217
00:08:59,540 --> 00:08:57,210
models is diffusion is slow so clusters

218
00:09:02,810 --> 00:08:59,550
arise and diffusion in

219
00:09:04,940 --> 00:09:02,820
a 3d open pool is going to be fast so

220
00:09:06,860 --> 00:09:04,950
you get well mixed and things die right

221
00:09:08,540 --> 00:09:06,870
so we have to have an advice if the

222
00:09:09,920 --> 00:09:08,550
spatial model is to be relevant we need

223
00:09:12,710 --> 00:09:09,930
an environment where diffusion is slow

224
00:09:15,530 --> 00:09:12,720
and once such might be pause interrupts

225
00:09:17,300 --> 00:09:15,540
so this is a paper proposed while back

226
00:09:18,920 --> 00:09:17,310
by cooling and Martin they're imagining

227
00:09:22,130 --> 00:09:18,930
reactions going on in little pools in

228
00:09:23,840 --> 00:09:22,140
Iraq little pores in Iraq and each of

229
00:09:26,240 --> 00:09:23,850
these little pores or crevasses

230
00:09:27,560 --> 00:09:26,250
molecules in one in one place can

231
00:09:29,690 --> 00:09:27,570
interact with each other and then they

232
00:09:33,889 --> 00:09:29,700
move very slowly across the whole

233
00:09:35,900 --> 00:09:33,899
structure so we so we now study a model

234
00:09:38,329 --> 00:09:35,910
like this a lattice model where there

235
00:09:41,840 --> 00:09:38,339
can be many molecules per site and

236
00:09:43,579 --> 00:09:41,850
things on one site can interact with one

237
00:09:46,400 --> 00:09:43,589
another and there's some very slow

238
00:09:49,220 --> 00:09:46,410

hopping from one to the next so this

239
00:09:52,009 --> 00:09:49,230
this this lattice model is representing

240
00:09:56,120 --> 00:09:52,019
something like that and the nice thing

241
00:09:58,670 --> 00:09:56,130
now is that this is this is apples and

242
00:10:00,590 --> 00:09:58,680
apples right because I can compare this

243
00:10:02,780 --> 00:10:00,600
lattice model with multiple strands per

244
00:10:05,060 --> 00:10:02,790
site with a protocell model with

245
00:10:08,300 --> 00:10:05,070
multiple strands per site and the rules

246
00:10:10,310 --> 00:10:08,310
of replication inside one cell are the

247
00:10:13,069 --> 00:10:10,320
same as the rules for replication inside

248
00:10:15,260 --> 00:10:13,079
one site on the lattice and so those two

249
00:10:17,389 --> 00:10:15,270
are directly comparable what's different

250
00:10:20,150 --> 00:10:17,399
is the fact that in the cell model we

251
00:10:22,730 --> 00:10:20,160
have growth and division of cells in the

252
00:10:24,470 --> 00:10:22,740
lattice model we have no growth and

253
00:10:28,670 --> 00:10:24,480
division but we have diffusion between

254
00:10:30,470 --> 00:10:28,680
neighboring sites so well we do

255
00:10:32,030 --> 00:10:30,480
simulations of these things we get

256
00:10:35,210 --> 00:10:32,040
different shapes of the error threshold

257
00:10:36,949 --> 00:10:35,220
curves but qualitatively similar you

258
00:10:38,750 --> 00:10:36,959
know if there's no mutation the red ones

259
00:10:41,569 --> 00:10:38,760
do well you come to a point where

260
00:10:44,210 --> 00:10:41,579
mutation kills you and this is the error

261
00:10:45,949 --> 00:10:44,220
threshold and we want to know how do the

262
00:10:52,400 --> 00:10:45,959
error thresholds compare in these

263
00:10:53,750 --> 00:10:52,410

different models right I got three

264
00:10:55,280 --> 00:10:53,760
curves here because there are three

265
00:10:57,680 --> 00:10:55,290
slightly different proto cell models

266
00:10:59,150 --> 00:10:57,690
which I'm not going to explain we there

267
00:11:01,280 --> 00:10:59,160
are different ways of formulating these

268
00:11:03,130 --> 00:11:01,290
models but all of these three are very

269
00:11:05,329 --> 00:11:03,140
similar and they're proto cell models

270
00:11:07,160 --> 00:11:05,339
there's three curves here which are

271
00:11:09,949 --> 00:11:07,170
slightly different spatial models and

272
00:11:11,070 --> 00:11:09,959
they're all much worse than the proto

273
00:11:13,139 --> 00:11:11,080
cell models

274
00:11:15,360 --> 00:11:13,149
and there's one in the middle which is

275
00:11:16,889 --> 00:11:15,370
the old our old version of one per site

276
00:11:18,540 --> 00:11:16,899
on the lattice so this is the this is

277
00:11:20,790 --> 00:11:18,550
the oranges which we can't really

278
00:11:23,550 --> 00:11:20,800
compare but these are two lots of apples

279
00:11:25,460 --> 00:11:23,560
and what we say is protocells are much

280
00:11:28,470 --> 00:11:25,470
better than spatial models for two

281
00:11:30,329 --> 00:11:28,480
reasons because the error threshold

282
00:11:32,220 --> 00:11:30,339
where I should say this is the error

283
00:11:35,069 --> 00:11:32,230
threshold this is the maximum tolerated

284
00:11:36,990 --> 00:11:35,079
value of the of the error and the error

285
00:11:40,199 --> 00:11:37,000
threshold is much higher for protocells

286
00:11:42,900 --> 00:11:40,209
and spatial models and then this point

287
00:11:45,900 --> 00:11:42,910
here is the minimum replication rate

288
00:11:47,699 --> 00:11:45,910

necessary for survival and the minimum

289
00:11:51,050 --> 00:11:47,709
replication rate for the protocells is

290
00:11:53,639 --> 00:11:51,060
less than it is for the spatial models

291
00:11:55,470 --> 00:11:53,649
meaning that for both of those reasons

292
00:12:00,600 --> 00:11:55,480
it's easier for replicators to survive

293
00:12:04,530 --> 00:12:00,610
in protocells so why do protocells work

294
00:12:07,259 --> 00:12:04,540
better because group selection works in

295
00:12:09,000 --> 00:12:07,269
protocells cells with good teams of

296
00:12:11,180 --> 00:12:09,010
molecules grow and divide and they

297
00:12:14,100 --> 00:12:11,190
replace the slow-growing cells and

298
00:12:16,530 --> 00:12:14,110
either we keep the cell constant and

299
00:12:19,019 --> 00:12:16,540
when one cell multiplies another one is

300
00:12:21,600 --> 00:12:19,029
removed or we keep the number of strands

301
00:12:23,400 --> 00:12:21,610
limited which then leads to an effective

302
00:12:26,910 --> 00:12:23,410
amudha love the cells with no strands so

303
00:12:29,310 --> 00:12:26,920
so so one way or another there's group

304
00:12:31,079 --> 00:12:29,320
selection in proto cells which is not

305
00:12:32,490 --> 00:12:31,089
really happening spatial models because

306
00:12:34,860 --> 00:12:32,500
in spatial models when we have good

307
00:12:36,600 --> 00:12:34,870
combination of when we have a good team

308
00:12:38,670 --> 00:12:36,610
of molecules on one side it fills up

309
00:12:41,970 --> 00:12:38,680
that site and stops itself replicating

310
00:12:43,860 --> 00:12:41,980
it can only continue by sending by

311
00:12:45,900 --> 00:12:43,870
diffusing molecules out of that site to

312
00:12:47,880 --> 00:12:45,910
its neighbors so that mechanism works

313
00:12:55,350 --> 00:12:47,890

but it works less whoops but it's less

314
00:13:03,720 --> 00:12:55,360
well than the proto salt this is Madhu

315
00:13:05,340 --> 00:13:03,730
this is this is just to say so far I've

316
00:13:07,079 --> 00:13:05,350
been assuming that the rate of

317
00:13:08,819 --> 00:13:07,089
replication of the parasites was the

318
00:13:11,460 --> 00:13:08,829
same as the replication of the of the

319
00:13:13,050 --> 00:13:11,470
functional molecules so the parasites

320
00:13:15,150 --> 00:13:13,060
were not adapted they were just

321
00:13:16,769 --> 00:13:15,160
non-functional now I want to say what if

322
00:13:19,670 --> 00:13:16,779
the parasites were adapted they're

323
00:13:23,680 --> 00:13:19,680
adapted to be good templates and they

324
00:13:26,350 --> 00:13:23,690
and they multiply faster than they

325
00:13:28,900 --> 00:13:26,360
than the functional molecules so the

326
00:13:31,360 --> 00:13:28,910
blue curves are my old protocell and

327
00:13:33,130 --> 00:13:31,370
spacial case where the replication rate

328
00:13:36,970 --> 00:13:33,140
of the parasite is the same as the as

329
00:13:39,610 --> 00:13:36,980
the polymerase okay those two and now I

330
00:13:41,650 --> 00:13:39,620
have a new version the red and the pink

331
00:13:43,450 --> 00:13:41,660
where the replication rate of the

332
00:13:45,220 --> 00:13:43,460
parasite is now twice as much as the

333
00:13:49,120 --> 00:13:45,230
replication rate of the polymerase and

334
00:13:50,710 --> 00:13:49,130
so the answer is both of these Mollett a

335
00:13:52,600 --> 00:13:50,720
protocell and spatial models still

336
00:13:55,450 --> 00:13:52,610
survive even when you have adapted

337
00:13:57,310 --> 00:13:55,460
parasites okay so the parasites can

338
00:13:59,290 --> 00:13:57,320

adapt to be better than the protein the

339
00:14:02,590 --> 00:13:59,300
polymerizes themselves and this

340
00:14:05,140 --> 00:14:02,600
mechanism of protocells or spatial

341
00:14:07,450 --> 00:14:05,150
models both save you from being killed

342
00:14:10,710 --> 00:14:07,460
by the parasites but what happens then

343
00:14:13,180 --> 00:14:10,720
is that the error thresholds come down

344
00:14:16,240 --> 00:14:13,190
relative to the red curve is below the

345
00:14:17,710 --> 00:14:16,250
blue curve in both cases right but the

346
00:14:19,720 --> 00:14:17,720
difference between the red and the pink

347
00:14:21,640 --> 00:14:19,730
is actually larger than the difference

348
00:14:24,700 --> 00:14:21,650
between the blue and there than the blue

349
00:14:25,810 --> 00:14:24,710
and the two blues okay so the when

350
00:14:28,030 --> 00:14:25,820
parasites are better

351
00:14:29,650 --> 00:14:28,040
the advantage of Perl to cells is larger

352
00:14:32,380 --> 00:14:29,660
than it was when they weren't then we

353
00:14:33,760 --> 00:14:32,390
were neutral parasites so so I'm arguing

354
00:14:36,010 --> 00:14:33,770
that this advantage that we see for

355
00:14:38,080 --> 00:14:36,020
protocells is robust to different ways

356
00:14:40,110 --> 00:14:38,090
of formulating the model and to the and

357
00:14:42,550 --> 00:14:40,120
to different rates of parasite

358
00:14:46,840 --> 00:14:42,560
multiplication so what what does all

359
00:14:49,150 --> 00:14:46,850
this mean it probably means that

360
00:14:52,450 --> 00:14:49,160
compartments like protocells came very

361
00:14:56,860 --> 00:14:52,460
early in evolution so so Damon diamond

362
00:14:58,870 --> 00:14:56,870
is a Jing replicating sequences inside

363
00:15:00,790 --> 00:14:58,880

visa calls that are formed when we

364
00:15:04,960 --> 00:15:00,800
fought when we have ripped wetting and

365
00:15:09,040 --> 00:15:04,970
drying of of shallow pools in the

366
00:15:11,020 --> 00:15:09,050
presence of lipids okay so there so the

367
00:15:12,850 --> 00:15:11,030
environment provided by the lipids is

368
00:15:17,170 --> 00:15:12,860
good for polymerization maybe we get

369
00:15:20,440 --> 00:15:17,180
sandwich RNAs inside inside membranes

370
00:15:22,090 --> 00:15:20,450
and it also creates visa calls okay so

371
00:15:24,010 --> 00:15:22,100
maybe they were present all along maybe

372
00:15:25,300 --> 00:15:24,020
that maybe the lipid membranes and the

373
00:15:28,240 --> 00:15:25,310
reason fuels were present all along

374
00:15:31,260 --> 00:15:28,250
maybe the first replicators involved

375
00:15:41,860 --> 00:15:39,120
inside cells okay was that time okay so

376
00:15:47,020 --> 00:15:41,870
the other thing I just want to say half

377
00:15:48,370 --> 00:15:47,030
a minute about is what we really need is

378
00:15:51,580 --> 00:15:48,380
something like this we need multiple

379
00:15:53,680 --> 00:15:51,590
genes so we don't just want one kind of

380
00:15:55,600 --> 00:15:53,690
replicator that replicates itself we

381
00:15:58,210 --> 00:15:55,610
want that replicator then to be able to

382
00:16:02,740 --> 00:15:58,220
replicate other genes with different

383
00:16:05,140 --> 00:16:02,750
functions so cells also have an

384
00:16:07,060 --> 00:16:05,150
advantage in that if you have molecules

385
00:16:09,130 --> 00:16:07,070
with different functions inside a cell

386
00:16:11,410 --> 00:16:09,140
then group selection and light enables

387
00:16:15,480 --> 00:16:11,420
the survival of unlinked molecules with

388
00:16:20,990 --> 00:16:15,490

different functions finished

389
00:16:25,490 --> 00:16:22,879
all right so it looks like we have time

390
00:17:03,710 --> 00:16:25,500
for a few quick questions just so we'll

391
00:17:04,370 --> 00:17:03,720
start with Dave and back right so I see

392
00:17:06,439 --> 00:17:04,380
what you're saying

393
00:17:09,260 --> 00:17:06,449
what what you what you mean in these

394
00:17:13,370 --> 00:17:09,270
molecules is very slow diffusion like

395
00:17:15,500 --> 00:17:13,380
you need you need the desk the basically

396
00:17:18,620 --> 00:17:15,510
they move by an amount of order their

397
00:17:20,510 --> 00:17:18,630
own size in their own lifetime right so

398
00:17:23,090 --> 00:17:20,520
in terms of a lattice they can hop once

399
00:17:25,250 --> 00:17:23,100
to a neighboring lattice site in their

400
00:17:28,580 --> 00:17:25,260
own lifetime and if they go faster than

401
00:17:30,289 --> 00:17:28,590
that they end up being mixed and then

402
00:17:37,940 --> 00:17:30,299
you lose the advantage of the clustering

403
00:17:50,100 --> 00:17:47,940
yes right really what I'm trying to say

404
00:17:51,919 --> 00:17:50,110
is you need to have very slow diffusion

405
00:17:54,299 --> 00:17:51,929
so you need to have strong binding and

406
00:17:56,159 --> 00:17:54,309
if you have strong binding you mess

407
00:18:03,390 --> 00:17:56,169
things up right you messed you mess up

408
00:18:27,779 --> 00:18:03,400
the template okay I maybe we can quickly

409
00:18:31,720 --> 00:18:30,669
okay I know that policing comes up when

410
00:18:35,710 --> 00:18:31,730
you're talking about evolution of

411
00:18:37,570 --> 00:18:35,720
cooperation in Pilar in organisms what

412
00:18:39,970 --> 00:18:37,580
does a policing molecule tell me what's

413
00:19:03,580 --> 00:18:39,980

a police molecule is and I don't know

414
00:19:05,409 --> 00:19:03,590
what it is something that comes to mind

415
00:19:07,510 --> 00:19:05,419
there is this idea that you can have

416
00:19:09,789 --> 00:19:07,520
tags on molecules which indicate that

417
00:19:11,710 --> 00:19:09,799
this is a functional molecule and it

418
00:19:13,810 --> 00:19:11,720
must must be present in order for the

419
00:19:16,029 --> 00:19:13,820
polymerase to replicate this this

420
00:19:18,669 --> 00:19:16,039
sequence right so that can that can

421
00:19:22,779 --> 00:19:18,679
eliminate parasites which don't have the

422
00:19:24,639 --> 00:19:22,789
tag but doesn't eliminate mutations

423
00:19:26,230 --> 00:19:24,649
occurring in the functional molecule

424
00:19:27,580 --> 00:19:26,240
such that the functional bit is no

425
00:19:30,639 --> 00:19:27,590
longer functional and the tag is still

426
00:19:32,110 --> 00:19:30,649
present so there's a little bit along

427
00:19:33,519 --> 00:19:32,120
the lines that you're talking about but

428
00:19:36,220 --> 00:19:33,529
I don't think it saves you from the

429
00:19:37,720 --> 00:19:36,230
probe so it's basically there's a there

430
00:19:41,500 --> 00:19:37,730
is a problem here of parasites which