



Sijbren Otto

*Emergence & evolution of self-replicating
molecules from dynamic molecular networks*

1
00:00:00,160 --> 00:00:13,690

[Music]

2
00:00:19,460 --> 00:00:16,849
thank you for the introduction and thank

3
00:00:24,890 --> 00:00:19,470
you very much for the kind invitation to

4
00:00:26,779 --> 00:00:24,900
visit LC and and talk about what we've

5
00:00:30,349 --> 00:00:26,789
been up to in the in the recent few

6
00:00:34,100 --> 00:00:30,359
years and that is really have I made it

7
00:00:35,870 --> 00:00:34,110
a rather rather protracted title but

8
00:00:37,910 --> 00:00:35,880
really the basic question is can we make

9
00:00:41,720 --> 00:00:37,920
life in the lab this is what keeps us

10
00:00:43,610 --> 00:00:41,730
occupied at the moment and this comes

11
00:00:45,889 --> 00:00:43,620
from our work on self-replicating

12
00:00:48,860 --> 00:00:45,899
molecules that pop up out of dynamic

13
00:00:51,350 --> 00:00:48,870

like here networks and really all is an

14

00:00:53,750 --> 00:00:51,360

adventure in systems chemistry so we're

15

00:00:56,330 --> 00:00:53,760

in the business of looking at complex

16

00:00:58,340 --> 00:00:56,340

molecular systems and see look for

17

00:01:00,950 --> 00:00:58,350

emergent properties that commodities and

18

00:01:03,529 --> 00:01:00,960

life is probably the most exciting of

19

00:01:07,640 --> 00:01:03,539

all of those of all the emergent

20

00:01:10,730 --> 00:01:07,650

properties you can think of so we're not

21

00:01:15,499 --> 00:01:10,740

so much directly interested in this

22

00:01:16,640 --> 00:01:15,509

question here how did life start in to

23

00:01:20,120 --> 00:01:16,650

the point that it doesn't really know it

24

00:01:21,830 --> 00:01:20,130

doesn't impact directly in what we do

25

00:01:24,670 --> 00:01:21,840

we're very intrigued by the question

26
00:01:27,109 --> 00:01:24,680
nevertheless but our philosophy is more

27
00:01:30,140 --> 00:01:27,119
let's see if we can make something that

28
00:01:33,230 --> 00:01:30,150
looks like life in a lab and not be

29
00:01:38,719 --> 00:01:33,240
constrained by anything prebiotic

30
00:01:40,940 --> 00:01:38,729
irrelevant or not just make life in in

31
00:01:43,880 --> 00:01:40,950
as easy way as we can

32
00:01:46,310 --> 00:01:43,890
helping it in any way that we feel is

33
00:01:49,520 --> 00:01:46,320
necessary and in the process we hope of

34
00:01:51,560 --> 00:01:49,530
course to learn a lot about what it

35
00:01:53,569 --> 00:01:51,570
takes to become a life which then

36
00:01:57,050 --> 00:01:53,579
directly informs on this question here

37
00:02:00,050 --> 00:01:57,060
how did life start so even though we're

38
00:02:04,609 --> 00:02:00,060

not directly targeting it I hope was to

39

00:02:08,529 --> 00:02:04,619

learn a lot so when you want to make

40

00:02:11,839 --> 00:02:08,539

life it's a little bit like trying to

41

00:02:13,760 --> 00:02:11,849

find a lost key in a dark Street so this

42

00:02:18,980 --> 00:02:13,770

is more or less the guidance you have

43

00:02:20,810 --> 00:02:18,990

start now it's not as bad as this

44

00:02:24,800 --> 00:02:20,820

because there are some lampposts in the

45

00:02:28,010 --> 00:02:24,810

street and we know we've heard already

46

00:02:29,600 --> 00:02:28,020

about life probably requiring requiring

47

00:02:34,610 --> 00:02:29,610

a compartment so you can start looking

48

00:02:38,000 --> 00:02:34,620

at things that have compared Monsanto

49

00:02:41,510 --> 00:02:38,010

become a life somehow you can look at

50

00:02:43,100 --> 00:02:41,520

metabolism in the same way you can hope

51
00:02:47,090 --> 00:02:43,110
to find the key and there the lamppost

52
00:02:50,720 --> 00:02:47,100
it says replication and there's the for

53
00:02:52,070 --> 00:02:50,730
so this is usually the three modes three

54
00:02:55,010 --> 00:02:52,080
are identified as the three most

55
00:02:57,680 --> 00:02:55,020
important elements of life but there's a

56
00:03:00,380 --> 00:02:57,690
force that I'd like to emphasize here

57
00:03:01,760 --> 00:03:00,390
that's the the aspect and we all noticed

58
00:03:04,910 --> 00:03:01,770
the aspect that life is far from

59
00:03:10,220 --> 00:03:04,920
equilibrium we usually factored into the

60
00:03:14,840 --> 00:03:10,230
metabolism one but I took it out because

61
00:03:16,880 --> 00:03:14,850
I think there is something really rather

62
00:03:19,520 --> 00:03:16,890
important in the a difficulty reom

63
00:03:23,990 --> 00:03:19,530

aspect of life and rather important to

64

00:03:25,850 --> 00:03:24,000

also develop molecular systems that are

65

00:03:28,220 --> 00:03:25,860

in this similar amic regime here and

66

00:03:29,720 --> 00:03:28,230

that's not trivial this is not at least

67

00:03:33,100 --> 00:03:29,730

for a chemist this is not what your

68

00:03:35,900 --> 00:03:33,110

being being claimed to start off with oh

69

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

perhaps already because we're not

70

00:03:41,210 --> 00:03:37,920

trained as chemists to do anything that

71

00:03:43,520 --> 00:03:41,220

is far from equilibrium if you are a

72

00:03:46,280 --> 00:03:43,530

chemist you're trained to make stable

73

00:03:48,230 --> 00:03:46,290

molecules if you're Procter and Gamble

74

00:03:49,580 --> 00:03:48,240

or Unilever and you sell laundry

75

00:03:51,199 --> 00:03:49,590

detergent you don't want lonely

76
00:03:53,150 --> 00:03:51,209
detergent to change it to something else

77
00:03:56,270 --> 00:03:53,160
after the customer bought it and then

78
00:03:59,780 --> 00:03:56,280
there's on his way home so stable is

79
00:04:02,000 --> 00:03:59,790
good for most of chemistry but not when

80
00:04:05,180 --> 00:04:02,010
you want to make something that is a

81
00:04:07,790 --> 00:04:05,190
life because a life is not life is not

82
00:04:11,949 --> 00:04:07,800
at equilibrium is far from it and I'll

83
00:04:18,039 --> 00:04:11,959
come back to that at the end of my talk

84
00:04:23,780 --> 00:04:18,049
so these so where we had like

85
00:04:25,850 --> 00:04:23,790
isolated lampposts and for quite a while

86
00:04:27,650 --> 00:04:25,860
research quite intense research has been

87
00:04:30,260 --> 00:04:27,660
done in East these areas

88
00:04:32,780 --> 00:04:30,270

so more in some areas more than others I

89

00:04:34,430 --> 00:04:32,790

guess making things metabolize and

90

00:04:37,430 --> 00:04:34,440

taking that as a starting point for

91

00:04:39,200 --> 00:04:37,440

making life is still very hurt and also

92

00:04:41,510 --> 00:04:39,210

far from equilibrium systems haven't

93

00:04:44,570 --> 00:04:41,520

received a lot of attention but these

94

00:04:47,330 --> 00:04:44,580

other two have and so the light the

95

00:04:49,310 --> 00:04:47,340

light intensity is increased to the

96

00:04:51,260 --> 00:04:49,320

point ever now you can start thinking

97

00:04:53,630 --> 00:04:51,270

about merging these and have already

98

00:04:56,000 --> 00:04:53,640

alluded to this so maybe the pro best

99

00:04:57,950 --> 00:04:56,010

approach to life is not to focus on any

100

00:05:01,730 --> 00:04:57,960

of these ones individually but try to

101
00:05:05,560 --> 00:05:01,740
look at systems but share two maybe more

102
00:05:09,290 --> 00:05:05,570
but that's got heart of these essential

103
00:05:12,490 --> 00:05:09,300
characteristics of life so what am I

104
00:05:15,740 --> 00:05:12,500
going to talk about today then so I

105
00:05:17,300 --> 00:05:15,750
summarized the main findings on this

106
00:05:19,370 --> 00:05:17,310
slide here so that you know what's

107
00:05:21,290 --> 00:05:19,380
coming your way I'll show you how

108
00:05:23,410 --> 00:05:21,300
self-replicating molecules can emerge

109
00:05:25,790 --> 00:05:23,420
spontaneously from a superfund

110
00:05:27,650 --> 00:05:25,800
interconverting molecules so that's

111
00:05:29,750 --> 00:05:27,660
starting off under the lamppost it says

112
00:05:32,480 --> 00:05:29,760
replication and we do this not because

113
00:05:35,150 --> 00:05:32,490

we think that's the best lamppost but

114

00:05:39,110 --> 00:05:35,160

rather because that was the one we found

115

00:05:41,960 --> 00:05:39,120

ourselves under so whether that's the

116

00:05:44,510 --> 00:05:41,970

best spot to find the key no idea but

117

00:05:47,390 --> 00:05:44,520

that's the best spot for us to look it's

118

00:05:49,760 --> 00:05:47,400

the best place we can actually start get

119

00:05:53,240 --> 00:05:49,770

started and I'll show you that these

120

00:05:54,710 --> 00:05:53,250

replicators can acquire information very

121

00:05:57,880 --> 00:05:54,720

very trivial information that this

122

00:06:01,370 --> 00:05:57,890

states but nevertheless and complexify

123

00:06:02,900 --> 00:06:01,380

spontaneously in rather small steps I'll

124

00:06:04,760 --> 00:06:02,910

show you that at least the basic

125

00:06:06,860 --> 00:06:04,770

ingredients of the FIR Darwinian

126

00:06:09,620 --> 00:06:06,870

evolution are there this replication

127

00:06:12,290 --> 00:06:09,630

mutation and selection I'll show you an

128

00:06:14,300 --> 00:06:12,300

example where replicators spontaneously

129

00:06:16,460 --> 00:06:14,310

diversify we start with one we end up

130

00:06:19,210 --> 00:06:16,470

with more and I'll show you an example

131

00:06:21,560 --> 00:06:19,220

where again trivial but where

132

00:06:23,390 --> 00:06:21,570

replication the replicators adapt their

133

00:06:28,280 --> 00:06:23,400

structure to change in the environments

134

00:06:30,830 --> 00:06:28,290

and I'll show you at the end how you can

135

00:06:34,010 --> 00:06:30,840

make dissipative systems and actually I

136

00:06:36,140 --> 00:06:34,020

think this is at least the bit I'm most

137

00:06:37,820 --> 00:06:36,150

excited about right now where you can

138

00:06:39,620 --> 00:06:37,830

start populating thermodynamically

139

00:06:41,240 --> 00:06:39,630

disfavored state so that's what life is

140

00:06:43,340 --> 00:06:41,250

right it's not a kinetic

141

00:06:44,480 --> 00:06:43,350

it's not a thermodynamic product it's

142

00:06:46,460 --> 00:06:44,490

not the kinetic practical in the sense

143

00:06:47,860 --> 00:06:46,470

is the first one you make it's not the

144

00:06:50,690 --> 00:06:47,870

stoma dynamic products something else

145

00:06:52,160 --> 00:06:50,700

how do you populate states that it's not

146

00:06:53,990 --> 00:06:52,170

the first you make it's also not the one

147

00:06:57,770 --> 00:06:54,000

you make when you when you wait a bit

148

00:07:00,980 --> 00:06:57,780

and so I'll come back to that and now if

149

00:07:02,540 --> 00:07:00,990

I have time towards the end I also say

150

00:07:04,370 --> 00:07:02,550

something about compartments is not

151
00:07:06,530 --> 00:07:04,380
necessarily very connected to any of the

152
00:07:09,950 --> 00:07:06,540
the above but we'd like it to become

153
00:07:13,700 --> 00:07:09,960
eventually at one point so what's our

154
00:07:15,830 --> 00:07:13,710
recipe done for life so we start off

155
00:07:17,690 --> 00:07:15,840
with replicators as I said and

156
00:07:20,030 --> 00:07:17,700
exponential replicators allowed them to

157
00:07:23,360 --> 00:07:20,040
mutate then operate the system far from

158
00:07:25,190 --> 00:07:23,370
equilibrium and then that should allow

159
00:07:27,110 --> 00:07:25,200
Darwinian evolution of the replicators

160
00:07:29,420 --> 00:07:27,120
to occur and for a while we thought if

161
00:07:31,520 --> 00:07:29,430
we were there then the Iranian evolution

162
00:07:35,210 --> 00:07:31,530
would this take over and will lead us

163
00:07:38,210 --> 00:07:35,220

places and that was I think now looking

164

00:07:41,570 --> 00:07:38,220

back at it now is probably a bit naive

165

00:07:43,130 --> 00:07:41,580

and there's more required in order for

166

00:07:46,550 --> 00:07:43,140

Darwinian evolution to actually go

167

00:07:49,480 --> 00:07:46,560

places and do things other than make

168

00:07:52,220 --> 00:07:49,490

trivial changes to the system and that's

169

00:07:54,590 --> 00:07:52,230

that go places means invention of new

170

00:07:57,409 --> 00:07:54,600

traits and how that might work is

171

00:07:59,570 --> 00:07:57,419

something where we're trying to find out

172

00:08:02,270 --> 00:07:59,580

but we still haven't got much of a clue

173

00:08:03,680 --> 00:08:02,280

about so where oh I'll probably need to

174

00:08:06,350 --> 00:08:03,690

leave you somewhere between four and

175

00:08:11,240 --> 00:08:06,360

five - it's the end by the end of the

176

00:08:13,400 --> 00:08:11,250

tool so self-replication auto catalysis

177

00:08:15,820 --> 00:08:13,410

we're by no means the first people to

178

00:08:18,880 --> 00:08:15,830

work on this so let me

179

00:08:22,060 --> 00:08:18,890

introduced the topic briefly so this is

180

00:08:24,430 --> 00:08:22,070

the blueprint by which 90 99 percent of

181

00:08:27,340 --> 00:08:24,440

self-replicating molecules work and be

182

00:08:29,650 --> 00:08:27,350

that self replicators based on RNA that

183

00:08:31,420 --> 00:08:29,660

tides completely synthetic molecules it

184

00:08:33,700 --> 00:08:31,430

doesn't matter this they all weigh the

185

00:08:36,339 --> 00:08:33,710

same principle there is a template

186

00:08:38,770 --> 00:08:36,349

molecule with two binding sites there's

187

00:08:41,020 --> 00:08:38,780

food molecules with complimentary

188

00:08:43,180 --> 00:08:41,030

binding motives you make a ternary

189

00:08:45,250 --> 00:08:43,190

complex so the template with the two

190

00:08:47,110 --> 00:08:45,260

food molecules that brings the two

191

00:08:49,360 --> 00:08:47,120

reactive ends of those two food

192

00:08:50,980 --> 00:08:49,370

molecules in close proximity reaction

193

00:08:52,900 --> 00:08:50,990

goes faster if those ends are in close

194

00:08:55,000 --> 00:08:52,910

proximity then they go then the reaction

195

00:08:57,610 --> 00:08:55,010

goes when they're not so you accelerate

196

00:09:00,220 --> 00:08:57,620

the the ligation here you make the

197

00:09:02,500 --> 00:09:00,230

duplex the duplex you dissociates make

198

00:09:04,990 --> 00:09:02,510

two replicators that can eats undergo

199

00:09:06,700 --> 00:09:05,000

their own replication cycle so the idea

200

00:09:08,920 --> 00:09:06,710

is you start with one then after one

201
00:09:10,690 --> 00:09:08,930
round you have two to make four four

202
00:09:12,910 --> 00:09:10,700
make eight eight make sixteen so

203
00:09:14,710 --> 00:09:12,920
exponential replication but as we

204
00:09:16,930 --> 00:09:14,720
already heard yesterday there's a

205
00:09:19,660 --> 00:09:16,940
problem with this template dissociation

206
00:09:21,310 --> 00:09:19,670
step it's actually quite hard to make

207
00:09:23,680 --> 00:09:21,320
this dissociate this is by molecular

208
00:09:25,330 --> 00:09:23,690
complex and their conditions were done

209
00:09:26,950 --> 00:09:25,340
associates this is their molecular

210
00:09:31,000 --> 00:09:26,960
complex but the interactions are the

211
00:09:33,910 --> 00:09:31,010
same so entropy is it's your enemy here

212
00:09:36,970 --> 00:09:33,920
it would really much prefer to make this

213
00:09:38,770 --> 00:09:36,980

over that so if you once you've made it

214

00:09:40,960 --> 00:09:38,780

it's kind of hard to dissociate if this

215

00:09:43,180 --> 00:09:40,970

association doesn't happen then the

216

00:09:45,280 --> 00:09:43,190

exponential growth doesn't happen now

217

00:09:47,020 --> 00:09:45,290

it's that bad well it depends on what

218

00:09:48,880 --> 00:09:47,030

you want to do but if you want to do

219

00:09:50,950 --> 00:09:48,890

that we need evolution it turns out to

220

00:09:53,530 --> 00:09:50,960

be bad for most systems in the most

221

00:09:55,450 --> 00:09:53,540

circumstances because for Darwinian

222

00:09:57,280 --> 00:09:55,460

evolution universe an area like this two

223

00:10:00,550 --> 00:09:57,290

replicators competing for a common food

224

00:10:06,430 --> 00:10:00,560

source and if replicators also die in

225

00:10:08,590 --> 00:10:06,440

some way then for Darwinian evolution

226

00:10:10,300 --> 00:10:08,600

the desired outcome is that only one of

227

00:10:13,300 --> 00:10:10,310

those two replicators survives and the

228

00:10:15,940 --> 00:10:13,310

other one goes extinct and that you can

229

00:10:17,650 --> 00:10:15,950

show mathematically and assess Marius as

230

00:10:19,990 --> 00:10:17,660

describe this and if a for some time ago

231

00:10:22,680 --> 00:10:20,000

and that will only work if the

232

00:10:24,550 --> 00:10:22,690

Replicators are exponential for most

233

00:10:26,670 --> 00:10:24,560

depends a little bit on how your

234

00:10:28,990 --> 00:10:26,680

destruction process works but for most

235

00:10:31,600 --> 00:10:29,000

destruction processes that

236

00:10:33,160 --> 00:10:31,610

what is the situation so exponential

237

00:10:35,350 --> 00:10:33,170

replicators gives the fievel of the

238

00:10:37,510 --> 00:10:35,360

fittest but some exponential ones if you

239

00:10:39,810 --> 00:10:37,520

have product inhibition exponential

240

00:10:43,030 --> 00:10:39,820

growth doesn't doesn't occur completely

241

00:10:44,800 --> 00:10:43,040

you like the growth may still happen

242

00:10:47,260 --> 00:10:44,810

replication may still happen but it be

243

00:10:50,520 --> 00:10:47,270

so exponential and then that leads to

244

00:10:52,960 --> 00:10:50,530

indefinite go existence of a and B and

245

00:10:54,670 --> 00:10:52,970

therefore no Darwinian evolution the

246

00:10:58,780 --> 00:10:54,680

Iranian evolution needs to burn its

247

00:11:02,560 --> 00:10:58,790

bridges so how can you get around this

248

00:11:04,480 --> 00:11:02,570

problem there are some but only very

249

00:11:07,720 --> 00:11:04,490

there are only two or three replicators

250

00:11:09,370 --> 00:11:07,730

in the literature where that actually

251
00:11:12,190 --> 00:11:09,380
has been shown to replicate

252
00:11:13,780 --> 00:11:12,200
exponentially but it's not clear what

253
00:11:15,400 --> 00:11:13,790
makes them replicate exponentially in

254
00:11:17,170 --> 00:11:15,410
these systems we were lucky enough to

255
00:11:19,960 --> 00:11:17,180
run into the system it also does

256
00:11:24,960 --> 00:11:19,970
exponential replication and we we now

257
00:11:30,810 --> 00:11:24,970
and do know why that that works and I'll

258
00:11:34,810 --> 00:11:30,820
show that in an animation biscuits

259
00:11:36,250 --> 00:11:34,820
running of how the system had a

260
00:11:38,950 --> 00:11:36,260
replicator emerged in the first place

261
00:11:40,720 --> 00:11:38,960
and also how they become exponential so

262
00:11:42,520 --> 00:11:40,730
we started off as very simple molecules

263
00:11:46,090 --> 00:11:42,530

which have two reactive ends they can

264

00:11:48,130 --> 00:11:46,100

make with which they can arrange

265

00:11:50,160 --> 00:11:48,140

themselves into rings rings of different

266

00:11:53,230 --> 00:11:50,170

sizes you have large rings small rings

267

00:11:55,720 --> 00:11:53,240

the ligation between the building blocks

268

00:11:57,700 --> 00:11:55,730

here is a chemical reaction that is

269

00:11:59,800 --> 00:11:57,710

reversible so it's a covalent bond but

270

00:12:01,510 --> 00:11:59,810

one that can you can also break again so

271

00:12:05,020 --> 00:12:01,520

you see the exchange for building blocks

272

00:12:07,210 --> 00:12:05,030

between different rings so you have

273

00:12:08,920 --> 00:12:07,220

initially a ring a super rings different

274

00:12:12,250 --> 00:12:08,930

ring sizes that are own equilibrium was

275

00:12:14,100 --> 00:12:12,260

one another after a while and actually

276

00:12:16,750 --> 00:12:14,110

it does take a little while you see the

277

00:12:18,880 --> 00:12:16,760

stacking of rings of one particular ring

278

00:12:21,340 --> 00:12:18,890

size occurring and once you have a

279

00:12:24,340 --> 00:12:21,350

nucleus it grows relatively fast but

280

00:12:26,320 --> 00:12:24,350

initially in a linear fashion and it

281

00:12:28,570 --> 00:12:26,330

actually pulls the equilibrium over to

282

00:12:30,430 --> 00:12:28,580

the ring size that makes the stack but

283

00:12:33,300 --> 00:12:30,440

disks the growth of the stack is still

284

00:12:35,860 --> 00:12:33,310

linear it's not exponential and it's

285

00:12:37,690 --> 00:12:35,870

that it becomes exponential the moment

286

00:12:41,050 --> 00:12:37,700

you start agitating this mixture here

287

00:12:43,210 --> 00:12:41,060

then these stacks start to break and now

288

00:12:46,330 --> 00:12:43,220

you have if you break a stack it

289

00:12:48,430 --> 00:12:46,340

the number of ends so gross process

290

00:12:49,690 --> 00:12:48,440

accelerates so it grows is directly

291

00:12:51,160 --> 00:12:49,700

proportional the rate of growth

292

00:12:53,740 --> 00:12:51,170

proportional the number of ends you have

293

00:12:55,900 --> 00:12:53,750

so you saw one stack become two to

294

00:12:59,530 --> 00:12:55,910

become four four become eight eight

295

00:13:03,160 --> 00:12:59,540

becomes 16 and so on until at the end of

296

00:13:05,350 --> 00:13:03,170

the the animation here all the building

297

00:13:07,810 --> 00:13:05,360

blocks that you have have all been

298

00:13:10,900 --> 00:13:07,820

converted into this one ring size that

299

00:13:12,790 --> 00:13:10,910

make the stacks so in this way the

300

00:13:15,160 --> 00:13:12,800

assembly process of rings into stacks

301

00:13:17,440 --> 00:13:15,170

drives the synthesis of the ring that

302

00:13:19,840 --> 00:13:17,450

makes the stacks in the mixture of

303

00:13:22,270 --> 00:13:19,850

different ring sizes so it's an assembly

304

00:13:25,750 --> 00:13:22,280

driven self-replication process where

305

00:13:27,780 --> 00:13:25,760

mechanical energy allows you to achieve

306

00:13:30,400 --> 00:13:27,790

exponential growth of these systems

307

00:13:34,390 --> 00:13:30,410

mechanical energy it's kind of the trick

308

00:13:37,420 --> 00:13:34,400

that allows you to liberate replicators

309

00:13:40,510 --> 00:13:37,430

from the stacks or at least create more

310

00:13:41,800 --> 00:13:40,520

stack ends so because it's very

311

00:13:44,590 --> 00:13:41,810

important for the rest of the tool cup

312

00:13:46,840 --> 00:13:44,600

summarize what you just seen on the in

313

00:13:48,100 --> 00:13:46,850

the animation in one slide so you see

314

00:13:51,400 --> 00:13:48,110

here a little building block it's

315

00:13:53,140 --> 00:13:51,410

somewhat different to transition to the

316

00:13:54,840 --> 00:13:53,150

actual molecular structure that makes

317

00:13:57,640 --> 00:13:54,850

this all happen

318

00:13:59,110 --> 00:13:57,650

so we have a simple building block that

319

00:14:00,400 --> 00:13:59,120

makes ring that can make rings of

320

00:14:02,020 --> 00:14:00,410

different sizes that they can all

321

00:14:04,510 --> 00:14:02,030

exchange with one another and there's a

322

00:14:06,190 --> 00:14:04,520

slow nucleation phase where you find

323

00:14:08,560 --> 00:14:06,200

where you start forming a short stack

324

00:14:10,630 --> 00:14:08,570

that then grows and at the point it

325

00:14:13,030 --> 00:14:10,640

grows long enough that mechanical energy

326

00:14:16,390 --> 00:14:13,040

can do something with it it will start

327

00:14:18,760 --> 00:14:16,400

entering this gross breakage cycle here

328

00:14:21,010 --> 00:14:18,770

so where long things break into smaller

329

00:14:23,520 --> 00:14:21,020

ones that then in each grow again and

330

00:14:27,610 --> 00:14:23,530

break again and this is how you end up

331

00:14:28,750 --> 00:14:27,620

with this exponential growth process so

332

00:14:31,540 --> 00:14:28,760

this is the building block that does

333

00:14:34,060 --> 00:14:31,550

this so it's a die file that make that

334

00:14:36,300 --> 00:14:34,070

from allowing it to react with oxygen

335

00:14:38,710 --> 00:14:36,310

from the air and just water neutral

336

00:14:42,730 --> 00:14:38,720

ambient conditions

337

00:14:44,520 --> 00:14:42,740

it makes rings of disulfides and the

338

00:14:47,050 --> 00:14:44,530

blue bit here is a peptide sequence

339

00:14:50,260 --> 00:14:47,060

fairly short peptide five amino acids

340

00:14:51,900 --> 00:14:50,270

long designed to have alternating

341

00:14:55,540 --> 00:14:51,910

hydrophobic hydrophilic hydrophobic

342

00:14:56,800 --> 00:14:55,550

amino acids which predisposes it to form

343

00:14:58,840 --> 00:14:56,810

beta sheets

344

00:15:01,030 --> 00:14:58,850

but it's too sure to do this by itself

345

00:15:04,269 --> 00:15:01,040

so it needs quite a few of these

346

00:15:05,860 --> 00:15:04,279

peptides displayed in one ring before

347

00:15:08,620 --> 00:15:05,870

there's enough interaction energy

348

00:15:12,250 --> 00:15:08,630

between the peptides to stack them up

349

00:15:13,780 --> 00:15:12,260

into a beta sheet so in this particular

350

00:15:16,150 --> 00:15:13,790

for this particular sequence this

351

00:15:19,690 --> 00:15:16,160

happens with with ring size six so you

352

00:15:22,210 --> 00:15:19,700

see that stacking and then growing so

353

00:15:25,500 --> 00:15:22,220

chemically this is the again the same

354

00:15:28,000 --> 00:15:25,510

building block Dicer the dithiol

355

00:15:31,060 --> 00:15:28,010

oxidized to disulfide so you make these

356

00:15:35,680 --> 00:15:31,070

disulfide rings that initially arrow in

357

00:15:37,450 --> 00:15:35,690

equilibrium with one another now as I

358

00:15:38,829 --> 00:15:37,460

said mechanical energy and also it was

359

00:15:40,570 --> 00:15:38,839

also apparent from the from the

360

00:15:43,960 --> 00:15:40,580

animation mechanical energy is crucial

361

00:15:45,760 --> 00:15:43,970

here so if we don't provide it if we

362

00:15:47,710 --> 00:15:45,770

don't stir in the system would just have

363

00:15:50,890 --> 00:15:47,720

a homogeneous solution of these building

364

00:15:54,220 --> 00:15:50,900

blocks in water and what happens you do

365

00:15:56,170 --> 00:15:54,230

form rings but the rings don't then you

366

00:15:57,940 --> 00:15:56,180

may even form a few nuclei but the

367

00:16:00,280 --> 00:15:57,950

process of converting primary nuclei

368

00:16:03,370 --> 00:16:00,290

into secondary and making long stacks is

369

00:16:04,630 --> 00:16:03,380

very very slow so you you get stuck at

370

00:16:06,490 --> 00:16:04,640

the states where there's only super

371

00:16:10,360 --> 00:16:06,500

there are only small rings Reimer and

372

00:16:13,690 --> 00:16:10,370

tetra mer if you do stir the system the

373

00:16:15,640 --> 00:16:13,700

outcome is quite different in this case

374

00:16:17,560 --> 00:16:15,650

you make a cyclic heptamer so a seven

375

00:16:21,520 --> 00:16:17,570

membered ring with this building block

376

00:16:23,380 --> 00:16:21,530

when you stir it but if you ask this guy

377

00:16:26,380 --> 00:16:23,390

here how you should prepare a cocktail

378

00:16:28,480 --> 00:16:26,390

he says shaken not stirred so what

379

00:16:31,360 --> 00:16:28,490

happens if you do that you actually end

380

00:16:33,790 --> 00:16:31,370

up with a different replicator so the in

381

00:16:38,470 --> 00:16:33,800

this for this particular peptide the

382

00:16:40,199 --> 00:16:38,480

exact way of agitation decides the

383

00:16:42,400 --> 00:16:40,209

outcome between two competing

384

00:16:45,160 --> 00:16:42,410

replicators a six membered and the seven

385

00:16:48,520 --> 00:16:45,170

membered ring and we understand why this

386

00:16:50,790 --> 00:16:48,530

why this works why this difference is if

387

00:16:54,690 --> 00:16:50,800

you want to know you can ask me later

388

00:16:57,610 --> 00:16:54,700

but bottom line is agitation allows

389

00:16:59,170 --> 00:16:57,620

replication and this is just some

390

00:17:02,290 --> 00:16:59,180

electron microscopy to show you that

391

00:17:03,940 --> 00:17:02,300

there are really stacks of rings that

392

00:17:05,980 --> 00:17:03,950

have a diameter that corresponds to the

393

00:17:07,960 --> 00:17:05,990

diameter of the ring for both the hexa

394

00:17:10,630 --> 00:17:07,970

mirandy and the and the epimer but if

395

00:17:12,880 --> 00:17:10,640

you look at try and find any of these

396

00:17:18,100 --> 00:17:12,890

thanks in the Trimurti tumor sample you

397

00:17:19,990 --> 00:17:18,110

see nothing it's also catalytic and the

398

00:17:23,110 --> 00:17:20,000

kinetics of this it's also slow as she

399

00:17:26,800 --> 00:17:23,120

dad the kinetics of this already hints

400

00:17:29,320 --> 00:17:26,810

at it so this is the distribution of

401

00:17:31,120 --> 00:17:29,330

ring sizes with time if you start off as

402

00:17:33,430 --> 00:17:31,130

monomer it oxidizes initially you make

403

00:17:36,460 --> 00:17:33,440

trimaran tetramer rings and then after

404

00:17:38,200 --> 00:17:36,470

about three weeks you see after my rings

405

00:17:40,870 --> 00:17:38,210

growing so there's a slow process and a

406

00:17:43,300 --> 00:17:40,880

lot of credit to d2 jackie the pc

407

00:17:46,240 --> 00:17:43,310

student to discover this for not

408

00:17:47,680 --> 00:17:46,250

stopping after a week and just keep

409

00:17:49,420 --> 00:17:47,690

monitoring and seeing of anything

410

00:17:53,370 --> 00:17:49,430

changes actually not done that we would

411

00:17:56,170 --> 00:17:53,380

have missed an awful lot of fun so this

412

00:17:57,490 --> 00:17:56,180

sigmoid I growth curve suggests thoughts

413

00:17:58,720 --> 00:17:57,500

of catalysis if you want to prove it

414

00:18:00,580 --> 00:17:58,730

what you do is you take some of this

415

00:18:01,870 --> 00:18:00,590

material at the end you introduce it in

416

00:18:03,790 --> 00:18:01,880

the beginning you see the moment you

417

00:18:08,410 --> 00:18:03,800

introduce it immediately shoots off so

418

00:18:10,000 --> 00:18:08,420

it's all the catalytic definitely so we

419

00:18:12,460 --> 00:18:10,010

have an exponential replicator

420

00:18:14,920 --> 00:18:12,470

how about mutations well if you want to

421

00:18:17,800 --> 00:18:14,930

mutate allowed us to mutate and the

422

00:18:20,530 --> 00:18:17,810

simplest thing is simplest thing to do

423

00:18:22,330 --> 00:18:20,540

is to offer it a set of different

424

00:18:23,560 --> 00:18:22,340

building blocks not only one but

425

00:18:25,660 --> 00:18:23,570

offering the choice and then he can

426

00:18:28,000 --> 00:18:25,670

decide to change the structure but

427

00:18:29,980 --> 00:18:28,010

before we offered it any choice we first

428

00:18:31,540 --> 00:18:29,990

made those building blocks and looked at

429

00:18:33,640 --> 00:18:31,550

what they did individually to get a bit

430

00:18:35,050 --> 00:18:33,650

of a feel for what the system I do so

431

00:18:36,790 --> 00:18:35,060

this was the original building block

432

00:18:38,530 --> 00:18:36,800

that has this peptide sequence here we

433

00:18:41,560 --> 00:18:38,540

played around with that physician there

434

00:18:44,380 --> 00:18:41,570

made it and then initially less

435

00:18:46,030 --> 00:18:44,390

hydrophobic and we found we lose now the

436

00:18:47,470 --> 00:18:46,040

seven membered ring we only make six

437

00:18:49,690 --> 00:18:47,480

membered rings if we change this to a

438

00:18:51,760 --> 00:18:49,700

phenyl alanine in that position make it

439

00:18:54,130 --> 00:18:51,770

less hydrophobic still we go to even

440

00:18:56,410 --> 00:18:54,140

smaller rings like pentamer and for a

441

00:18:58,540 --> 00:18:56,420

nafta lien trimer and tetramer rings

442

00:19:00,070 --> 00:18:58,550

already start stacking so there seems to

443

00:19:01,870 --> 00:19:00,080

be a correlation between hydrophobicity

444

00:19:03,790 --> 00:19:01,880

of the peptides stickiness of the

445

00:19:05,740 --> 00:19:03,800

peptide if you like and ring size of the

446

00:19:07,180 --> 00:19:05,750

replicator that we're making also goes

447

00:19:09,550 --> 00:19:07,190

the other direction if you make it more

448

00:19:11,860 --> 00:19:09,560

hydrophilic with a serine or an alanine

449

00:19:16,540 --> 00:19:11,870

in that position there we make octomorg

450

00:19:18,330 --> 00:19:16,550

rings so there appears to be a kind of

451

00:19:20,710 --> 00:19:18,340

selection rule for the emergence of

452

00:19:23,110 --> 00:19:20,720

replicators and selection rules when it

453

00:19:24,430 --> 00:19:23,120

comes to ring size the stronger we make

454

00:19:25,660 --> 00:19:24,440

the peptide peptide interaction

455

00:19:27,970 --> 00:19:25,670

so the more hydrophobic we make the

456

00:19:29,740 --> 00:19:27,980

peptides and the smaller the ring is

457

00:19:31,450 --> 00:19:29,750

that can already stack and that makes

458

00:19:33,850 --> 00:19:31,460

sense if you regard this from the

459

00:19:35,140 --> 00:19:33,860

perspective of multi valency that sides

460

00:19:37,600 --> 00:19:35,150

already glued that hold the Rings

461

00:19:39,730 --> 00:19:37,610

together if you make the glue stronger

462

00:19:43,810 --> 00:19:39,740

you need less of it so already smaller

463

00:19:46,120 --> 00:19:43,820

rings can start stacking so this is a

464

00:19:48,490 --> 00:19:46,130

structure of the drawing laid out of the

465

00:19:51,250 --> 00:19:48,500

octo marygreen to suit impress upon you

466

00:19:52,900 --> 00:19:51,260

that we're really making maybe not such

467

00:19:54,730 --> 00:19:52,910

complex structures because a time the

468

00:19:58,210 --> 00:19:54,740

same building block but certainly large

469

00:19:59,800 --> 00:19:58,220

structures well we are making the

470

00:20:02,260 --> 00:19:59,810

molecules are making them we only make

471

00:20:04,000 --> 00:20:02,270

the building blocks so this you see the

472

00:20:09,460 --> 00:20:04,010

autonomous emergence of these types of

473

00:20:13,510 --> 00:20:09,470

of complex molecules from from really

474

00:20:15,640 --> 00:20:13,520

rather simple experiments so now going

475

00:20:17,230 --> 00:20:15,650

back to our mutation so we've now looked

476

00:20:18,970 --> 00:20:17,240

at the individual building blocks what

477

00:20:20,560 --> 00:20:18,980

do they do when we mix them well what

478

00:20:22,360 --> 00:20:20,570

happens when we offer in a system a

479

00:20:25,180 --> 00:20:22,370

choice as to which building block and

480

00:20:26,470 --> 00:20:25,190

incorporates so we started off mixing

481

00:20:27,970 --> 00:20:26,480

the serine in the phenyl alanine

482

00:20:30,070 --> 00:20:27,980

building blocks the serine by itself

483

00:20:31,750 --> 00:20:30,080

wants to make eight membered rings the

484

00:20:34,090 --> 00:20:31,760

phenyl alanine wants to make six

485

00:20:35,800 --> 00:20:34,100

membered rings so this question then was

486

00:20:37,690 --> 00:20:35,810

what would happen if we mixed them and

487

00:20:40,990 --> 00:20:37,700

it we didn't really have a clue so we

488

00:20:43,270 --> 00:20:41,000

destroyed it and this is the outcome you

489

00:20:45,010 --> 00:20:43,280

so again if you look at the at what

490

00:20:45,940 --> 00:20:45,020

emerges with time and he started off

491

00:20:47,950 --> 00:20:45,950

with the building blocks that I'm

492

00:20:50,140 --> 00:20:47,960

oxidized you first see the emergence

493

00:20:53,370 --> 00:20:50,150

after about three four days of her first

494

00:20:56,050 --> 00:20:53,380

set of replicators in blue and those are

495

00:20:57,520 --> 00:20:56,060

six membered rings rich in the phenyl

496

00:20:59,140 --> 00:20:57,530

alanine building block which by itself

497

00:21:03,010 --> 00:20:59,150

wants to make six membered rings so this

498

00:21:08,320 --> 00:21:03,020

is f6 and here's F 5 s 1 F 4 s 2 and F 3

499

00:21:12,220 --> 00:21:08,330

s 3 so he makes these one-to-one but as

500

00:21:15,210 --> 00:21:12,230

you see the one to the the the 3 plus 3

501
00:21:20,050 --> 00:21:15,220
macro cycle is not the most abundant

502
00:21:24,270 --> 00:21:20,060
then after about 10 days after about 10

503
00:21:28,900 --> 00:21:24,280
days and we see the emergent of set B

504
00:21:30,220 --> 00:21:28,910
which consists of also hexamers and this

505
00:21:32,560 --> 00:21:30,230
was a bit of a surprise because you

506
00:21:34,750 --> 00:21:32,570
would expect the left over building

507
00:21:37,360 --> 00:21:34,760
block the serine by itself forms octamer

508
00:21:38,140 --> 00:21:37,370
but in this system with phenyl alanine

509
00:21:42,240 --> 00:21:38,150
present

510
00:21:48,100 --> 00:21:42,250
does 4x immerse and even foams the six

511
00:21:50,640 --> 00:21:48,110
hexamer there so what happens here is

512
00:21:53,740 --> 00:21:50,650
that you first see the emergence of a

513
00:21:55,810 --> 00:21:53,750

set of replicators that are six membered

514

00:21:57,430 --> 00:21:55,820

rings rich in phenyl alanine and then

515

00:21:58,870 --> 00:21:57,440

after a little while nothing happens and

516

00:22:01,030 --> 00:21:58,880

the ECD merges of a second set of

517

00:22:03,670 --> 00:22:01,040

replicators and it turns out the second

518

00:22:05,680 --> 00:22:03,680

set there's an ancestral relationship

519

00:22:07,630 --> 00:22:05,690

between the first and the second set so

520

00:22:11,530 --> 00:22:07,640

the second set is promoted by the

521

00:22:13,900 --> 00:22:11,540

presence of the first and we could even

522

00:22:18,130 --> 00:22:13,910

test weights of the mutants within the

523

00:22:19,870 --> 00:22:18,140

first set of of if you call it quasi

524

00:22:21,640 --> 00:22:19,880

species I don't know whether that term

525

00:22:23,800 --> 00:22:21,650

is quite appropriate here but it's

526

00:22:25,810 --> 00:22:23,810

shares a lot of similarities to quasi

527

00:22:27,850 --> 00:22:25,820

species which within the first set of

528

00:22:29,650 --> 00:22:27,860

replicators is most responsible for

529

00:22:32,050 --> 00:22:29,660

giving rise to the second and it's those

530

00:22:36,790 --> 00:22:32,060

that are most structurally similar to

531

00:22:39,070 --> 00:22:36,800

the second set of replicators so this

532

00:22:41,770 --> 00:22:39,080

starts to have some similarity to how I

533

00:22:44,140 --> 00:22:41,780

guess speciation occurs and in in

534

00:22:46,180 --> 00:22:44,150

biology but it's with completely

535

00:22:49,390 --> 00:22:46,190

inanimate system of self-replicating

536

00:22:53,200 --> 00:22:49,400

molecules okay then

537

00:22:56,530 --> 00:22:53,210

back to our recipe so we have a

538

00:22:58,930 --> 00:22:56,540

replicator that commute AIDS now let's

539

00:23:00,520 --> 00:22:58,940

see what happens if we start operating

540

00:23:03,280 --> 00:23:00,530

this far from equilibrium so anything

541

00:23:05,020 --> 00:23:03,290

I've showed you so far was only looking

542

00:23:06,400 --> 00:23:05,030

for a system that went so it was only

543

00:23:08,200 --> 00:23:06,410

looking at systems that went to

544

00:23:10,150 --> 00:23:08,210

inanimate feet downhill we started with

545

00:23:12,670 --> 00:23:10,160

building blocks tiles they oxidize give

546

00:23:15,310 --> 00:23:12,680

dye so fights also an anomaly downhill

547

00:23:16,960 --> 00:23:15,320

so the only thing we the only difference

548

00:23:19,200 --> 00:23:16,970

there is we end up with one product or

549

00:23:21,970 --> 00:23:19,210

another is the kinetics and the

550

00:23:25,440 --> 00:23:21,980

thermodynamics of formation of those

551

00:23:28,540 --> 00:23:25,450

products but we're not necessarily

552

00:23:30,850 --> 00:23:28,550

having we're not making systems that are

553

00:23:35,350 --> 00:23:30,860

dissipating energy or in a continuous

554

00:23:38,890 --> 00:23:35,360

way yet life of course is far from

555

00:23:41,140 --> 00:23:38,900

equilibrium and and it does exhibit a

556

00:23:43,720 --> 00:23:41,150

continuous turnover of pretty much all

557

00:23:46,690 --> 00:23:43,730

its constituents add a quite stunning

558

00:23:49,510 --> 00:23:46,700

rate so if you look at the half-lives

559

00:23:52,090 --> 00:23:49,520

for instance of mammalian messenger RNA

560

00:23:52,480 --> 00:23:52,100

it's about nine hours if you look at

561

00:23:54,700 --> 00:23:52,490

protein

562

00:23:58,799 --> 00:23:54,710

half less on average sterve there are

563

00:24:01,990 --> 00:23:58,809

two days so every protein on average is

564

00:24:04,470 --> 00:24:02,000

broken down and resynthesized every

565

00:24:07,390 --> 00:24:04,480

second day

566

00:24:12,160 --> 00:24:07,400

so also Darwinian evolution requires is

567

00:24:16,000 --> 00:24:12,170

making an degradation or burst and death

568

00:24:18,910 --> 00:24:16,010

so if you have if you start with some

569

00:24:21,040 --> 00:24:18,920

species makes mutant it replicates and

570

00:24:23,290 --> 00:24:21,050

does this in a sloppy way so you have

571

00:24:25,570 --> 00:24:23,300

different mutants some survive some

572

00:24:27,760 --> 00:24:25,580

survive others die the ones that survive

573

00:24:28,840 --> 00:24:27,770

can mutate again and and and so on so

574

00:24:31,450 --> 00:24:28,850

that's the idea of Darwinian evolution

575

00:24:35,950 --> 00:24:31,460

only works or a virtue of there also

576

00:24:37,930 --> 00:24:35,960

being deaths in the system so if you

577

00:24:39,669 --> 00:24:37,940

want to move in this direction what you

578

00:24:42,730 --> 00:24:39,679

learn really should do is read our

579

00:24:44,410 --> 00:24:42,740

replicators is also make them die that's

580

00:24:45,730 --> 00:24:44,420

kind of tough on you when you're sorry

581

00:24:46,930 --> 00:24:45,740

when you're a chemist you make stuff

582

00:24:48,940 --> 00:24:46,940

you're not in the business of destroying

583

00:24:51,540 --> 00:24:48,950

it again the least you usually try to

584

00:24:53,860 --> 00:24:51,550

avoid this but now we we have to do it

585

00:24:56,200 --> 00:24:53,870

so what I've showed you so far was only

586

00:24:58,120 --> 00:24:56,210

this we have food making replicator and

587

00:25:00,660 --> 00:24:58,130

once we've made a replicator it was

588

00:25:03,250 --> 00:25:00,670

there there wasn't really any way if

589

00:25:05,710 --> 00:25:03,260

that any process that let it that lets

590

00:25:07,600 --> 00:25:05,720

do its destruction but that's what we

591

00:25:10,060 --> 00:25:07,610

now want to introduce some way some way

592

00:25:13,000 --> 00:25:10,070

of making replicators go to save some

593

00:25:15,910 --> 00:25:13,010

waste product and the easiest and

594

00:25:19,060 --> 00:25:15,920

perhaps trivial way of doing this is to

595

00:25:22,540 --> 00:25:19,070

convert is to do this in a flow system

596

00:25:25,270 --> 00:25:22,550

you keep adding food and you remove the

597

00:25:30,640 --> 00:25:25,280

food you remove some of this the system

598

00:25:32,680 --> 00:25:30,650

and the same flow rate again so that you

599

00:25:34,450 --> 00:25:32,690

your urine basically a continuously

600

00:25:36,820 --> 00:25:34,460

stirred tank reactor you start off with

601
00:25:39,070 --> 00:25:36,830
a replicator in here and as long as it

602
00:25:42,730 --> 00:25:39,080
replicates faster then it's being flown

603
00:25:46,930 --> 00:25:42,740
out it persists the nice thing about

604
00:25:48,310 --> 00:25:46,940
this system is you can still do you can

605
00:25:51,340 --> 00:25:48,320
change the environment while it's

606
00:25:53,799 --> 00:25:51,350
replicating and we did this in one

607
00:25:56,410 --> 00:25:53,809
particular way we added a bit of trifler

608
00:25:58,990 --> 00:25:56,420
ethanol so kind of a useful solvent

609
00:26:01,630 --> 00:25:59,000
known from biochemistry and from protein

610
00:26:03,280 --> 00:26:01,640
peptide chemistry to make the

611
00:26:05,080 --> 00:26:03,290
interactions between peptides stronger

612
00:26:05,830 --> 00:26:05,090
so if you increase the amount of tyrel

613
00:26:07,570 --> 00:26:05,840

fluorescent

614

00:26:09,909 --> 00:26:07,580

should start making replicators that

615

00:26:11,169 --> 00:26:09,919

have a smaller ring size if our

616

00:26:15,190 --> 00:26:11,179

understanding of the replicator is

617

00:26:16,630 --> 00:26:15,200

correct so this is what we then done in

618

00:26:18,039 --> 00:26:16,640

the experiment we started with octamer

619

00:26:19,600 --> 00:26:18,049

replicator so what you see in the

620

00:26:22,060 --> 00:26:19,610

background here is the concentration of

621

00:26:24,970 --> 00:26:22,070

try fluorescent oh we start off in 50%

622

00:26:26,740 --> 00:26:24,980

fry fluorescent oh we're probably the

623

00:26:28,690 --> 00:26:26,750

octamer is not the idea the best

624

00:26:30,549 --> 00:26:28,700

replicator indeed it withers away and

625

00:26:33,820 --> 00:26:30,559

you see the hexamer replicator taking

626

00:26:38,049 --> 00:26:33,830

over to the point here where it's almost

627

00:26:41,830 --> 00:26:38,059

completely but certainly dominance then

628

00:26:43,690 --> 00:26:41,840

we flowed out the we didn't add more try

629

00:26:46,299 --> 00:26:43,700

for ethanol with the food we just flown

630

00:26:48,159 --> 00:26:46,309

in the food with in in pure water so we

631

00:26:51,519 --> 00:26:48,169

see the try for ethanol content go down

632

00:26:53,769 --> 00:26:51,529

and you see that the that the hexamer

633

00:26:57,130 --> 00:26:53,779

replicator Goes Down and the octamer

634

00:26:58,389 --> 00:26:57,140

replicator comes back up so we see that

635

00:27:02,769 --> 00:26:58,399

the nature of the environment dictates

636

00:27:06,220 --> 00:27:02,779

what replicator we have and also what we

637

00:27:07,899 --> 00:27:06,230

showed was previously already the

638

00:27:10,149 --> 00:27:07,909

October and hexamer replicator also

639

00:27:12,250 --> 00:27:10,159

cross catalytic to some extent so you

640

00:27:15,580 --> 00:27:12,260

can consider October and hexamer to be

641

00:27:17,950 --> 00:27:15,590

mutants of one replicator set so this

642

00:27:19,720 --> 00:27:17,960

experiment here then shows that by

643

00:27:20,380 --> 00:27:19,730

changing the environment we favor one

644

00:27:23,529 --> 00:27:20,390

mutants

645

00:27:26,470 --> 00:27:23,539

over another selectively and reversibly

646

00:27:28,600 --> 00:27:26,480

as well so it's having this now has all

647

00:27:30,659 --> 00:27:28,610

the ingredients and all the essential

648

00:27:35,289 --> 00:27:30,669

characteristics of Darwinian evolution

649

00:27:36,669 --> 00:27:35,299

replication mutation selection but in a

650

00:27:38,169 --> 00:27:36,679

very trivial way the only thing we

651

00:27:43,330 --> 00:27:38,179

change is macrocycle size if our

652

00:27:44,710 --> 00:27:43,340

replicator so we did a similar type of

653

00:27:45,669 --> 00:27:44,720

experiments with guanidinium chloride

654

00:27:48,539 --> 00:27:45,679

now I don't

655

00:27:50,740 --> 00:27:48,549

that doesn't really per se add anything

656

00:27:52,389 --> 00:27:50,750

but I still want to show it because it

657

00:27:54,250 --> 00:27:52,399

leads home to the next point which is

658

00:27:57,029 --> 00:27:54,260

doing the same as I showed you before

659

00:27:59,799 --> 00:27:57,039

and the flow but then in in dissipative

660

00:28:01,899 --> 00:27:59,809

conditions and chemically fuelled so

661

00:28:03,639 --> 00:28:01,909

with this system is the phenyl alanine

662

00:28:05,440 --> 00:28:03,649

lan's if you put this in water it wants

663

00:28:07,029 --> 00:28:05,450

to make the hexamer replicator if you

664

00:28:08,350 --> 00:28:07,039

put it in wanted indium chloride for

665

00:28:11,529 --> 00:28:08,360

reason we don't quite fully understand

666

00:28:12,940 --> 00:28:11,539

yet it makes drawing a replicator so the

667

00:28:15,279 --> 00:28:12,950

timer replicator is the most stable

668

00:28:17,740 --> 00:28:15,289

compound in guanidinium chloride so it's

669

00:28:19,190 --> 00:28:17,750

also the first one that forms so if you

670

00:28:21,170 --> 00:28:19,200

start off with food

671

00:28:22,730 --> 00:28:21,180

the lowest barrier is to make destroy a

672

00:28:26,020 --> 00:28:22,740

replicator and it's also destined when

673

00:28:28,580 --> 00:28:26,030

I'm with the most stable structure now

674

00:28:30,020 --> 00:28:28,590

why do I show this here you think okay

675

00:28:32,570 --> 00:28:30,030

I've seen you know these replicators now

676

00:28:35,270 --> 00:28:32,580

I think this is may we here now we have

677

00:28:36,980 --> 00:28:35,280

a nice opportunity to try and see if we

678

00:28:38,630 --> 00:28:36,990

can push the system away from what it

679

00:28:39,860 --> 00:28:38,640

wants to make kinetically away from what

680

00:28:41,810 --> 00:28:39,870

it meant to make them more dynamically

681

00:28:44,060 --> 00:28:41,820

because there's this hexamer replicator

682

00:28:46,820 --> 00:28:44,070

also it's so many that mcclee disfavor

683

00:28:49,270 --> 00:28:46,830

did we start here it actually goes there

684

00:28:51,800 --> 00:28:49,280

we just don't if we don't do anything

685

00:28:53,360 --> 00:28:51,810

it's also not the kinetic product if we

686

00:28:54,620 --> 00:28:53,370

start here it doesn't make any of this

687

00:28:58,580 --> 00:28:54,630

it actually makes the trimer

688

00:29:00,320 --> 00:28:58,590

so we have a system which is making a

689

00:29:02,360 --> 00:29:00,330

kinetic lien thermodynamically favored

690

00:29:05,090 --> 00:29:02,370

replicator can we do something to this

691

00:29:05,990 --> 00:29:05,100

system to populate the hexamer and why

692

00:29:07,850 --> 00:29:06,000

is that important

693

00:29:09,800 --> 00:29:07,860

because I guess this is where life's

694

00:29:13,580 --> 00:29:09,810

it's not here here's thermodynamic

695

00:29:15,710 --> 00:29:13,590

equilibrium here's death here is your

696

00:29:19,010 --> 00:29:15,720

out of equilibrium at least by some by

697

00:29:20,810 --> 00:29:19,020

by a little bit can we populate it so

698

00:29:26,570 --> 00:29:20,820

anybody has any idea how you could do

699

00:29:29,030 --> 00:29:26,580

this how could you get here so you need

700

00:29:32,060 --> 00:29:29,040

to do something to the the barrier and

701

00:29:34,390 --> 00:29:32,070

you need to do this in and also in a in

702

00:29:37,100 --> 00:29:34,400

a if you if you only do catalysis then

703

00:29:39,170 --> 00:29:37,110

you might just you need to do this in a

704

00:29:41,060 --> 00:29:39,180

way that breaks microscopic

705

00:29:43,970 --> 00:29:41,070

reversibility as well so you need to

706

00:29:45,350 --> 00:29:43,980

lower the barrier in one direction but

707

00:29:46,010 --> 00:29:45,360

not on the other so I'll come back to

708

00:29:50,620 --> 00:29:46,020

that in a minute

709

00:29:53,210 --> 00:29:50,630

so the way to do this is to start

710

00:29:56,930 --> 00:29:53,220

linking the system up with an energy

711

00:30:00,080 --> 00:29:56,940

source fuel it chemically somehow and so

712

00:30:05,420 --> 00:30:00,090

we have to make replicators dying go

713

00:30:07,340 --> 00:30:05,430

back to food and in that regime not

714

00:30:09,740 --> 00:30:07,350

someone anomic stability rules but as

715

00:30:13,130 --> 00:30:09,750

adi process calls its dynamic kinetic

716

00:30:15,110 --> 00:30:13,140

stability so here's how to do it

717

00:30:17,900 --> 00:30:15,120

chemically so we start off with our

718

00:30:20,900 --> 00:30:17,910

building block a file makes bor and we

719

00:30:23,240 --> 00:30:20,910

add oxidants makes the disulfides we add

720

00:30:25,100 --> 00:30:23,250

reductants at the same time she'd make

721

00:30:27,320 --> 00:30:25,110

the disulfide go back to style so we go

722

00:30:30,080 --> 00:30:27,330

around in a circle but it's fueled now

723

00:30:33,110 --> 00:30:30,090

by having oxidants and reductants in the

724

00:30:36,340 --> 00:30:33,120

system so experimentally this is

725

00:30:38,570 --> 00:30:36,350

looks now so we have they now we have a

726
00:30:41,150 --> 00:30:38,580
system where we don't fly anything out

727
00:30:42,920 --> 00:30:41,160
again the only thing we flow we only

728
00:30:45,050 --> 00:30:42,930
fell in and we flow in oxidant and

729
00:30:47,510 --> 00:30:45,060
reductant at the slow flow rate so

730
00:30:50,390 --> 00:30:47,520
there's not mature circuiting and we do

731
00:30:52,790 --> 00:30:50,400
continues oxidation and reduction and

732
00:30:55,010 --> 00:30:52,800
then and on this regime if you start out

733
00:30:57,530 --> 00:30:55,020
with the one-to-one or derivatives mixture

734
00:31:00,380 --> 00:30:57,540
of timer and extra my replicator you see

735
00:31:02,780 --> 00:31:00,390
the hexamer it's the one that wins if

736
00:31:04,220 --> 00:31:02,790
you do to control we just allow things

737
00:31:06,440 --> 00:31:04,230
to go through equilibrium was the same

738
00:31:11,630 --> 00:31:06,450

starting point you see the timer is the

739

00:31:13,310 --> 00:31:11,640

one that wins so why does it work we're

740

00:31:16,820 --> 00:31:13,320

playing around with the various we have

741

00:31:19,040 --> 00:31:16,830

now a reduction process and an oxidation

742

00:31:21,680 --> 00:31:19,050

process so we may convert thiols to dye

743

00:31:25,040 --> 00:31:21,690

sulfites and disulfide spectra styles in

744

00:31:27,800 --> 00:31:25,050

separate pathways this is shown here so

745

00:31:30,440 --> 00:31:27,810

the oxidation is the solid line and the

746

00:31:32,840 --> 00:31:30,450

reduction is the dotted line and the way

747

00:31:36,590 --> 00:31:32,850

the system works out is that the

748

00:31:39,140 --> 00:31:36,600

reduction of the trimer the most similar

749

00:31:41,840 --> 00:31:39,150

maquis table replicators faster than the

750

00:31:43,640 --> 00:31:41,850

reduction of the thermodynamically less

751
00:31:46,070 --> 00:31:43,650
stable hexamer replicator so this

752
00:31:48,770 --> 00:31:46,080
barrier is smaller than that barrier so

753
00:31:51,740 --> 00:31:48,780
that if the system runs it will go very

754
00:31:53,510 --> 00:31:51,750
fast to here but very fast

755
00:31:56,810 --> 00:31:53,520
out of there again it can go uphill

756
00:31:59,570 --> 00:31:56,820
because it's linked to another reaction

757
00:32:03,830 --> 00:31:59,580
this basically the oxidation of the

758
00:32:06,770 --> 00:32:03,840
reductants that drives that and you then

759
00:32:09,050 --> 00:32:06,780
go if you're here once every while

760
00:32:11,210 --> 00:32:09,060
you're able to jump that barrier and

761
00:32:13,580 --> 00:32:11,220
well and once you're end up here you're

762
00:32:17,810 --> 00:32:13,590
very slow to return so it's now

763
00:32:22,160 --> 00:32:17,820

selection is now by basically resistance

764

00:32:24,020 --> 00:32:22,170

to us and reduction that now populates

765

00:32:26,540 --> 00:32:24,030

the thermodynamically least stable

766

00:32:30,230 --> 00:32:26,550

replicator okay I've already gone over

767

00:32:33,650 --> 00:32:30,240

time so I think I should skip sorry cap

768

00:32:36,560 --> 00:32:33,660

out the vid on compartmentalization and

769

00:32:38,690 --> 00:32:36,570

leave you with some thoughts and I'll

770

00:32:45,370 --> 00:32:38,700

leave up here while the discussion is

771

00:32:50,139 --> 00:32:47,009

[Applause]

772

00:32:59,499 --> 00:32:50,149

thank you for that lovely talk we'll

773

00:33:01,299 --> 00:32:59,509

take questions start with to think about

774

00:33:04,869 --> 00:33:01,309

emergence of self replicators is not

775

00:33:06,609 --> 00:33:04,879

uncommon so we're in the on earth can I

776

00:33:20,529 --> 00:33:06,619

look at such a system that is not

777

00:33:22,269 --> 00:33:20,539

biological well maybe I should should

778

00:33:24,549 --> 00:33:22,279

have said it's less common than I would

779

00:33:27,129 --> 00:33:24,559

than I expected it's less uncommon than

780

00:33:30,190 --> 00:33:27,139

I expected so the reason the motivation

781

00:33:32,980 --> 00:33:30,200

I say that is that we actually never we

782

00:33:34,840 --> 00:33:32,990

never designed any of this and we ran

783

00:33:37,029 --> 00:33:34,850

into one and then knowing there was one

784

00:33:38,590 --> 00:33:37,039

we looked at all the data other systems

785

00:33:40,690 --> 00:33:38,600

other molecules and we had similar we

786

00:33:42,879 --> 00:33:40,700

had also self-replicating molecules in

787

00:33:45,669 --> 00:33:42,889

there so the moment you have a system I

788

00:33:47,279 --> 00:33:45,679

guess if I kind of generalize our system

789

00:33:52,090 --> 00:33:47,289

in the moment you have a system where

790

00:33:54,249 --> 00:33:52,100

molecules interconvert and assemble the

791

00:33:55,930 --> 00:33:54,259

assembly process then drives the

792

00:33:58,600 --> 00:33:55,940

replication the moment you have a system

793

00:34:01,509 --> 00:33:58,610

like that you stand the pretty good

794

00:34:05,169 --> 00:34:01,519

chance of finding self replicators there

795

00:34:06,730 --> 00:34:05,179

no geological environments that would

796

00:34:09,220 --> 00:34:06,740

work in AI

797

00:34:11,049 --> 00:34:09,230

I'm insufficient of a geochemist

798

00:34:12,549 --> 00:34:11,059

Darwin's answer to this was as soon as

799

00:34:14,799 --> 00:34:12,559

some molecule becomes interesting you'll

800

00:34:17,079 --> 00:34:14,809

be gobbled up by existing life yeah

801
00:34:19,089 --> 00:34:17,089
but presumably you can go a little bit

802
00:34:20,889 --> 00:34:19,099
down this path without becoming too

803
00:34:22,809 --> 00:34:20,899
interesting to extant life and therefore

804
00:34:27,280 --> 00:34:22,819
you would see some of these things

805
00:34:29,379 --> 00:34:27,290
maybe I doubt it because I think I think

806
00:34:31,299 --> 00:34:29,389
the problem with life now I mean where

807
00:34:32,740 --> 00:34:31,309
would you find with I think the relevant

808
00:34:36,639 --> 00:34:32,750
question is where we do have found it

809
00:34:37,960 --> 00:34:36,649
before life became competitive to the

810
00:34:40,659 --> 00:34:37,970
building blocks that it needs because

811
00:34:42,700 --> 00:34:40,669
it's still I mean this just works but in

812
00:34:45,190 --> 00:34:42,710
and they're rather specified conditions

813
00:34:48,820 --> 00:34:45,200

and it takes three weeks right first

814

00:34:52,690 --> 00:34:48,830

emergent one says there is faster but

815

00:34:53,680 --> 00:34:52,700

yeah I said finding it now I wouldn't

816

00:34:55,480 --> 00:34:53,690

know where to start looking

817

00:35:05,920 --> 00:34:55,490

I wouldn't know what it would be

818

00:35:06,580 --> 00:35:05,930

worthwhile effort even thank you very

819

00:35:08,230 --> 00:35:06,590

nice talk

820

00:35:10,150 --> 00:35:08,240

I just wanted to push back a little bit

821

00:35:11,680 --> 00:35:10,160

against your statement towards the

822

00:35:13,300 --> 00:35:11,690

beginning where you said that you have

823

00:35:15,730 --> 00:35:13,310

to have exponential replication so that

824

00:35:18,010 --> 00:35:15,740

you can have a single winner to have

825

00:35:19,900 --> 00:35:18,020

evolution because then later you showed

826

00:35:22,260 --> 00:35:19,910

that there was benefit to keeping

827

00:35:25,360 --> 00:35:22,270

diversity in the system to have the

828

00:35:27,450 --> 00:35:25,370

octamer in local amounts as well as a

829

00:35:29,440 --> 00:35:27,460

hexamer when the environment changed

830

00:35:31,590 --> 00:35:29,450

yeah but there you need to be careful

831

00:35:34,600 --> 00:35:31,600

because they're they're cross catalytic

832

00:35:38,020 --> 00:35:34,610

so they're not competing with one

833

00:35:39,670 --> 00:35:38,030

another they're competing for the same

834

00:35:42,160 --> 00:35:39,680

resource yeah but they're also making

835

00:35:45,130 --> 00:35:42,170

each other so then you come to regard

836

00:35:47,020 --> 00:35:45,140

those as two separate replicator they're

837

00:35:49,930 --> 00:35:47,030

part of one speed there are two mutants

838

00:35:52,450 --> 00:35:49,940

of the same replicator that's view does

839

00:35:54,040 --> 00:35:52,460

but but is there any particular reason

840

00:35:58,300 --> 00:35:54,050

why you also wouldn't want to have some

841

00:36:00,580 --> 00:35:58,310

other species that say was not part of

842

00:36:03,420 --> 00:36:00,590

the same quasi species because it might

843

00:36:05,500 --> 00:36:03,430

also be more fit later to generate

844

00:36:08,470 --> 00:36:05,510

metabolic networks or for their

845

00:36:10,540 --> 00:36:08,480

complexity I think I'm all in favor of

846

00:36:12,430 --> 00:36:10,550

having a system that where you have more

847

00:36:17,260 --> 00:36:12,440

than just one molecular species there I

848

00:36:20,140 --> 00:36:17,270

mean we have the ecology already we seen

849

00:36:22,840 --> 00:36:20,150

some arguments for for that but those

850

00:36:25,810 --> 00:36:22,850

the coexistence of different replicators

851

00:36:28,330 --> 00:36:25,820

usually requires there them to have

852

00:36:29,920 --> 00:36:28,340

different say food niches so if there's

853

00:36:31,930 --> 00:36:29,930

only that one single food niche they

854

00:36:33,400 --> 00:36:31,940

should only be and there will only be if

855

00:36:36,880 --> 00:36:33,410

you have exponential replicators one

856

00:36:39,010 --> 00:36:36,890

single occupant of it maybe instead of

857

00:36:43,180 --> 00:36:39,020

mutants of the same species but still

858

00:36:48,220 --> 00:36:43,190

one single species so in order to have

859

00:36:50,230 --> 00:36:48,230

diversity you need to and I think we've

860

00:36:53,710 --> 00:36:50,240

seen this in the the system where we

861

00:36:55,930 --> 00:36:53,720

have the the two sets of replicators one

862

00:36:59,020 --> 00:36:55,940

emerges first the other one later where

863

00:37:01,329 --> 00:36:59,030

it actually one prefers to be one built

864

00:37:03,190 --> 00:37:01,339

itself mostly from one of

865

00:37:05,529 --> 00:37:03,200

Locsin the other mostly from the other

866

00:37:06,729 --> 00:37:05,539

but they they share a little bit of each

867

00:37:08,140 --> 00:37:06,739

other's building blocks so this is

868

00:37:11,219 --> 00:37:08,150

somewhere in between where you can argue

869

00:37:13,809 --> 00:37:11,229

is this there's now two species or not

870

00:37:16,559 --> 00:37:13,819

it's not two species yet because they

871

00:37:19,089 --> 00:37:16,569

there are some intermediates but and the

872

00:37:21,190 --> 00:37:19,099

we've looked at cross catalysis between

873

00:37:24,849 --> 00:37:21,200

these two the the f6 doesn't cause

874

00:37:29,400 --> 00:37:24,859

catalyzed s6 and vice-versa but the f-4s

875

00:37:31,959 --> 00:37:29,410

2 and the s4 f2 are cross catalytic so

876

00:37:33,940 --> 00:37:31,969

so that's all fine but do we really do

877

00:37:35,229 --> 00:37:33,950

we really have to have exponential

878

00:37:37,930 --> 00:37:35,239

replication you know could we have

879

00:37:41,289 --> 00:37:37,940

something that's sub-exponential and

880

00:37:42,729 --> 00:37:41,299

still have system with evolvability I

881

00:37:45,700 --> 00:37:42,739

guess offensive what you want to do but

882

00:37:47,529 --> 00:37:45,710

if you if you're after extinction of and

883

00:37:49,029 --> 00:37:47,539

I guess the Iranian Revolution does do

884

00:37:51,849 --> 00:37:49,039

that right and if you want to if you

885

00:37:54,309 --> 00:37:51,859

want that to happen then that's that is

886

00:37:56,469 --> 00:37:54,319

what you need or to be more precise you

887

00:38:00,640 --> 00:37:56,479

need a growth order and replicator that

888

00:38:01,870 --> 00:38:00,650

is at least equal to do the order of the

889

00:38:04,239 --> 00:38:01,880

replicator in the destruction process

890

00:38:06,009 --> 00:38:04,249

which is usually first so that's why the

891

00:38:21,230 --> 00:38:06,019

growth order also needs to be first and

892

00:38:28,970 --> 00:38:25,160

this is my thing so the my question is

893

00:38:33,049 --> 00:38:28,980

your system do not include the metallic

894

00:38:39,440 --> 00:38:33,059

proteins know and just you camp patoot

895

00:38:41,750 --> 00:38:39,450

right so the therefore it's a I have a

896

00:38:44,420 --> 00:38:41,760

benefiting with with him

897

00:38:48,920 --> 00:38:44,430

it's a still it's quite different from

898

00:38:51,920 --> 00:38:48,930

the analog of what is life in your

899

00:38:55,579 --> 00:38:51,930

experiment so what do you feel the role

900

00:38:58,910 --> 00:38:55,589

of metric proteins and also electron

901
00:39:01,700 --> 00:38:58,920
transfer in your system well we have V

902
00:39:04,480 --> 00:39:01,710
Docs processes right so we're changing

903
00:39:06,740 --> 00:39:04,490
oxidation states not necessarily through

904
00:39:08,990 --> 00:39:06,750
reaction that involves electrons but we

905
00:39:11,150 --> 00:39:09,000
do redox chemistry in this particular

906
00:39:13,910 --> 00:39:11,160
system the chemical fuel in order to

907
00:39:16,160 --> 00:39:13,920
populated it a disfavored replicator

908
00:39:17,539 --> 00:39:16,170
that happens because we linked the

909
00:39:21,190 --> 00:39:17,549
system up with oxidation and reduction

910
00:39:25,430 --> 00:39:21,200
and it continues in a continuous fashion

911
00:39:26,630 --> 00:39:25,440
so in that regard our system also relies

912
00:39:30,559 --> 00:39:26,640
on redox care

913
00:39:33,259 --> 00:39:30,569

redox processes for sure whether it l

914

00:39:38,420 --> 00:39:33,269

could imagine doing the same thing also

915

00:39:44,799 --> 00:39:38,430

is maybe coupling just was it hydration

916

00:39:48,499 --> 00:39:44,809

the dehydration type within metal absent

917

00:39:49,870 --> 00:39:48,509

proteins just but still probably the

918

00:39:54,349 --> 00:39:49,880

redox state

919

00:39:56,839 --> 00:39:54,359

okay changing but I think well in order

920

00:39:59,960 --> 00:39:56,849

to make something so your your questions

921

00:40:01,999 --> 00:39:59,970

more can I imagine life without redox

922

00:40:04,160 --> 00:40:02,009

chemistry yeah metallic proteins it's a

923

00:40:07,789 --> 00:40:04,170

flu before exam three electron like like

924

00:40:13,450 --> 00:40:07,799

Fe or Fe s and the Morrigan a demo as

925

00:40:19,460 --> 00:40:13,460

well so that that is a key a wildlife

926

00:40:22,400 --> 00:40:19,470

can you know continuously yeah I I'm I

927

00:40:24,890 --> 00:40:22,410

would argue I would my gut feeling is

928

00:40:26,870 --> 00:40:24,900

there's nothing that you could probably

929

00:40:28,220 --> 00:40:26,880

think of a life-form if you probably

930

00:40:29,900 --> 00:40:28,230

couldn't make it

931

00:40:32,090 --> 00:40:29,910

our current life we could probably think

932

00:40:34,160 --> 00:40:32,100

of a life form that doesn't do that sort

933

00:40:35,300 --> 00:40:34,170

of chemistry yeah yeah okay let's

934

00:40:40,260 --> 00:40:35,310

continue today after birth

935

00:40:55,260 --> 00:40:42,680

[Applause]