
AbSciCon
2019

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

2
00:00:11,610 --> 00:00:09,079
[Applause]

3
00:00:13,439 --> 00:00:11,620
my name is Vincent Richie and as the

4
00:00:15,600 --> 00:00:13,449
slide says I'm going to be talking about

5
00:00:16,890 --> 00:00:15,610
investigation of embittered individual

6
00:00:19,409 --> 00:00:16,900
and combined effects of blah blah blah

7
00:00:21,510 --> 00:00:19,419
blah blah that's boring so we're gonna

8
00:00:24,479 --> 00:00:21,520
get rid of it I think a better title for

9
00:00:26,790 --> 00:00:24,489
this talk would be what works and what

10
00:00:28,710 --> 00:00:26,800
works on earth and I'm going to be

11
00:00:31,529 --> 00:00:28,720
talking specifically specifically about

12
00:00:34,979 --> 00:00:31,539
RNAi oligomerization but this can really

13
00:00:36,210 --> 00:00:34,989

be applied to any sort of biological or

14
00:00:40,380 --> 00:00:36,220
prebiotic product that we're interested

15
00:00:41,969 --> 00:00:40,390
in so I want to start out by talking

16
00:00:44,759 --> 00:00:41,979
about two different approaches to

17
00:00:46,109 --> 00:00:44,769
prebiotic chemical experiments the first

18
00:00:48,899 --> 00:00:46,119
of which is a more traditional approach

19
00:00:52,200 --> 00:00:48,909
and we start out by looking at modern

20
00:00:53,280 --> 00:00:52,210
life we take these cells we look at

21
00:00:55,469 --> 00:00:53,290
what's inside of them we break them down

22
00:00:58,170 --> 00:00:55,479
into these simpler components we sort of

23
00:01:01,490 --> 00:00:58,180
pick our favorite component and then try

24
00:01:04,920 --> 00:01:01,500
to replicate it in the lab abiotic ly

25
00:01:08,270 --> 00:01:04,930
then we try to take the parameters that

26
00:01:10,920 --> 00:01:08,280
work and apply them to the early Earth

27
00:01:12,320 --> 00:01:10,930
so we look at this and we say where

28
00:01:14,930 --> 00:01:12,330
could this have happened

29
00:01:17,160 --> 00:01:14,940
but the problem is more often than not

30
00:01:19,430 --> 00:01:17,170
we get a system that doesn't look like

31
00:01:22,890 --> 00:01:19,440
anywhere on the early Earth or very

32
00:01:24,990 --> 00:01:22,900
dissimilar to the early Earth so an

33
00:01:30,200 --> 00:01:25,000
alternative approach would be to start

34
00:01:32,190 --> 00:01:30,210
with the earth we can take the earth and

35
00:01:34,020 --> 00:01:32,200
take different parameters that describe

36
00:01:37,920 --> 00:01:34,030
the different environments that we think

37
00:01:41,399 --> 00:01:37,930
were around before life and replicate

38
00:01:44,340 --> 00:01:41,409

those conditions in the lab and see what

39
00:01:45,930 --> 00:01:44,350
comes out of it so as I said we're going

40
00:01:48,450 --> 00:01:45,940
to be talking about I'm going to be

41
00:01:50,190 --> 00:01:48,460
talking about RNA here but this can be

42
00:01:51,980 --> 00:01:50,200
proteins or amino acids or whatever you

43
00:01:54,090 --> 00:01:51,990
like

44
00:01:56,850 --> 00:01:54,100
so we have conditions that foster

45
00:01:58,649 --> 00:01:56,860
prebiotic chemical reactions and we have

46
00:02:01,800 --> 00:01:58,659
conditions that were present on the

47
00:02:04,170 --> 00:02:01,810
early earth the key to finding that the

48
00:02:06,539 --> 00:02:04,180
pathways that are feasible for prebiotic

49
00:02:10,710 --> 00:02:06,549
chemistry is to look in the overlap

50
00:02:12,300 --> 00:02:10,720
between these two sets of conditions so

51
00:02:14,160 --> 00:02:12,310
if we're applying this to RNA

52
00:02:17,179 --> 00:02:14,170
oligomerization we might be interested

53
00:02:21,839 --> 00:02:17,189
in several variables and

54
00:02:24,449 --> 00:02:21,849
temperature pressure and any catalysts

55
00:02:25,949 --> 00:02:24,459
and for the sake of this talk we're

56
00:02:26,970 --> 00:02:25,959
gonna stick with these three and we're

57
00:02:31,589 --> 00:02:26,980
going to be talking about aqueous

58
00:02:33,629 --> 00:02:31,599
catalysts so this figure shows all of

59
00:02:35,910 --> 00:02:33,639
the conditions at least prior to this

60
00:02:38,250 --> 00:02:35,920
week that have been explored in the

61
00:02:41,670 --> 00:02:38,260
laboratory setting relating to RNA

62
00:02:46,009 --> 00:02:41,680
polymerization and we can compare that

63
00:02:48,899 --> 00:02:46,019

to the PT space that we think represents

64
00:02:50,970 --> 00:02:48,909
early Earth's surface environments and

65
00:02:52,710 --> 00:02:50,980
we see immediately that the majority of

66
00:02:56,429 --> 00:02:52,720
this PT space has not been filled out

67
00:02:59,250 --> 00:02:56,439
yet we're sort of stuck at one bar and a

68
00:03:00,929 --> 00:02:59,260
sort of moderate temperatures we did a

69
00:03:03,899 --> 00:03:00,939
decent job with temperatures as a

70
00:03:07,920 --> 00:03:03,909
community and we could do a similar

71
00:03:10,679 --> 00:03:07,930
comparison for our catalysts so we have

72
00:03:12,209 --> 00:03:10,689
several sets of metal catalysts

73
00:03:16,530 --> 00:03:12,219
including uranium and the lanthanides

74
00:03:20,819 --> 00:03:16,540
that have been investigated as effective

75
00:03:21,839 --> 00:03:20,829
catalysts for oligomers ation and some

76
00:03:24,659 --> 00:03:21,849
of these work and some of them don't

77
00:03:26,789 --> 00:03:24,669
work so well but we can compare that to

78
00:03:29,159 --> 00:03:26,799
the elements that we would expect to

79
00:03:31,289 --> 00:03:29,169
find in a prebiotic early Earth

80
00:03:33,349 --> 00:03:31,299
environment such as the open ocean so in

81
00:03:38,849 --> 00:03:33,359
that case the major cations would be

82
00:03:40,890 --> 00:03:38,859
sodium magnesium calcium and iron so

83
00:03:42,539 --> 00:03:40,900
there's not a lot of overlap but there

84
00:03:44,849 --> 00:03:42,549
is some overlap we have magnesium and

85
00:03:48,390 --> 00:03:44,859
calcium we're still missing sodium and

86
00:03:50,490 --> 00:03:48,400
iron well let's take magnesium and

87
00:03:52,589 --> 00:03:50,500
calcium for a second

88
00:03:54,689 --> 00:03:52,599

those have only been explored at one

89
00:03:57,110 --> 00:03:54,699
specific concentration by the sawai

90
00:03:59,369 --> 00:03:57,120
group in the in the 70s and 80s and that

91
00:04:00,780 --> 00:03:59,379
was only at 12 and a half million more

92
00:04:01,979 --> 00:04:00,790
so we don't know what increasing or

93
00:04:06,030 --> 00:04:01,989
decreasing the concentration would

94
00:04:11,460 --> 00:04:06,040
really do so we have this large empty

95
00:04:12,449 --> 00:04:11,470
plot with one data point on it so we

96
00:04:14,399 --> 00:04:12,459
don't know what the rest of this looks

97
00:04:16,560 --> 00:04:14,409
like so what do we do well we do

98
00:04:18,149 --> 00:04:16,570
experiments in our lab these are

99
00:04:19,649 --> 00:04:18,159
relatively simple experiments they're

100
00:04:22,140 --> 00:04:19,659
done in micro centrifuge tubes they're

101
00:04:23,790 --> 00:04:22,150
100 microliters experiments and all we

102
00:04:24,810 --> 00:04:23,800
do is add our aqueous metal solution at

103
00:04:27,570 --> 00:04:24,820
the concentration that we're interested

104
00:04:29,640 --> 00:04:27,580
in and we add our nucleotide now in this

105
00:04:30,180 --> 00:04:29,650
case we're using a phosphor emitters of

106
00:04:31,770 --> 00:04:30,190
light

107
00:04:33,960 --> 00:04:31,780
inactivated nucleotide is not

108
00:04:36,810 --> 00:04:33,970
particularly realistic in its own right

109
00:04:39,270 --> 00:04:36,820
necessarily but it is useful in the lab

110
00:04:40,970 --> 00:04:39,280
for probing these reactions and seeing

111
00:04:42,720 --> 00:04:40,980
how they'll behave and respond to

112
00:04:47,730 --> 00:04:42,730
different variables like temperature

113
00:04:50,700 --> 00:04:47,740

pressure and different catalysts so we

114
00:04:53,940 --> 00:04:50,710
take that solution we wait three days

115
00:04:57,120 --> 00:04:53,950
and then we extract our products and we

116
00:04:58,320 --> 00:04:57,130
measure them with maldi-tof m/s and we

117
00:05:00,330 --> 00:04:58,330
get a mass spec that looks something

118
00:05:03,510 --> 00:05:00,340
like this where each peak corresponds to

119
00:05:05,640 --> 00:05:03,520
the addition of a single nucleotide and

120
00:05:16,550 --> 00:05:05,650
again this could be a polypeptide or

121
00:05:23,970 --> 00:05:21,750
hmm here we have a max length of six so

122
00:05:26,730 --> 00:05:23,980
this is how we're going to denote the

123
00:05:31,560 --> 00:05:26,740
success or assess the extent of the this

124
00:05:33,630 --> 00:05:31,570
reaction going forward so you got a

125
00:05:35,460 --> 00:05:33,640
preview of these results but these are

126
00:05:37,740 --> 00:05:35,470
those max lengths for different

127
00:05:40,230 --> 00:05:37,750
concentrations of calcium chloride and

128
00:05:42,330 --> 00:05:40,240
we see that there's a sort of optimal

129
00:05:45,240 --> 00:05:42,340
concentration right around one molar but

130
00:05:47,120 --> 00:05:45,250
this is a relatively broad profile here

131
00:05:49,710 --> 00:05:47,130
and and it works over a range of

132
00:05:51,210 --> 00:05:49,720
concentrations we can also compare that

133
00:05:54,450 --> 00:05:51,220
to our negative controls which are

134
00:05:56,490 --> 00:05:54,460
represented by the orange line this is

135
00:06:01,650 --> 00:05:56,500
containing no metal catalyst it's just

136
00:06:03,600 --> 00:06:01,660
water and imp a but again we don't want

137
00:06:05,130 --> 00:06:03,610
to be stuck at 1 PT point we want to

138
00:06:07,230 --> 00:06:05,140

expand this and look at a range of

139
00:06:09,200 --> 00:06:07,240
temperatures and also a range of

140
00:06:12,870 --> 00:06:09,210
pressures and if we do experiments at

141
00:06:14,159 --> 00:06:12,880
one kil bar for example perhaps we can

142
00:06:18,420 --> 00:06:14,169
then extrapolate and then fill out a

143
00:06:19,800 --> 00:06:18,430
large chunk of this PT space we can do

144
00:06:21,330 --> 00:06:19,810
our high-pressure experiments in a

145
00:06:24,120 --> 00:06:21,340
static pressure vessel by loading our

146
00:06:25,440 --> 00:06:24,130
experiments into syringes and these

147
00:06:27,900 --> 00:06:25,450
syringes contain our experiments and

148
00:06:29,820 --> 00:06:27,910
when we apply pressure with water we use

149
00:06:35,360 --> 00:06:29,830
this group on that pressure is

150
00:06:38,070 --> 00:06:35,370
redirected to the sample so we have our

151
00:06:41,040 --> 00:06:38,080
concentration profile we need to pick

152
00:06:42,489 --> 00:06:41,050
one or two or however many

153
00:06:43,809 --> 00:06:42,499
concentration points that we're

154
00:06:44,859 --> 00:06:43,819
interested in to do our other

155
00:06:50,260 --> 00:06:44,869
experiments so we're gonna pick one

156
00:06:52,659 --> 00:06:50,270
molar and this is what we get we have

157
00:06:55,239 --> 00:06:52,669
our 1 bar our atmospheric experiments in

158
00:06:56,499 --> 00:06:55,249
orange and our one kill bar experiments

159
00:06:58,389 --> 00:06:56,509
in white and we see that there really

160
00:07:00,760 --> 00:06:58,399
isn't a large difference between these

161
00:07:03,309 --> 00:07:00,770
two so we can say in this particular

162
00:07:07,959 --> 00:07:03,319
system not all systems that pressure

163
00:07:11,350 --> 00:07:07,969

isn't particularly significant we also

164
00:07:12,790 --> 00:07:11,360
see that there is a moderate decrease in

165
00:07:18,399 --> 00:07:12,800
oligomers lengths as you increase

166
00:07:21,489 --> 00:07:18,409
temperature so we can do this with the

167
00:07:24,189 --> 00:07:21,499
other metals as well we have calcium we

168
00:07:25,509 --> 00:07:24,199
did this with sodium and magnesium but

169
00:07:28,649 --> 00:07:25,519
what about iron we've heard a lot about

170
00:07:31,629 --> 00:07:28,659
iron today and throughout the conference

171
00:07:34,029 --> 00:07:31,639
what can I do for RNA we know it it's

172
00:07:36,339 --> 00:07:34,039
good for amino and acid synthesis and a

173
00:07:38,619 --> 00:07:36,349
variety of other reactions what about

174
00:07:40,269 --> 00:07:38,629
RNA oligomerization but this is a little

175
00:07:42,249 --> 00:07:40,279
bit more complicated but because we have

176
00:07:46,449 --> 00:07:42,259
to keep our systems and oxic otherwise

177
00:07:48,279 --> 00:07:46,459
we'll just end up with a rusty tube so

178
00:07:50,739 --> 00:07:48,289
instead of using microcentrifuge tube we

179
00:07:53,199 --> 00:07:50,749
use gas tight exit a nerve isles we load

180
00:07:55,059 --> 00:07:53,209
our nucleotide into these vials and we

181
00:07:58,959 --> 00:07:55,069
flush the headspace with pure nitrogen

182
00:08:02,980 --> 00:07:58,969
to expel any oxygen then we inject our

183
00:08:07,809 --> 00:08:02,990
anoxic iron solution again we wait three

184
00:08:11,829 --> 00:08:07,819
days extract our products and we end up

185
00:08:14,049 --> 00:08:11,839
with the mass spec so these are the

186
00:08:16,359 --> 00:08:14,059
results of our iron experiments and

187
00:08:17,679 --> 00:08:16,369
again well note first that we're on a

188
00:08:22,109 --> 00:08:17,689

log scale now just to make everything

189
00:08:25,509 --> 00:08:22,119
easier to see but again we end up with a

190
00:08:30,159 --> 00:08:25,519
local optimum concentration right around

191
00:08:33,730 --> 00:08:30,169
100 millimolar and again we have our

192
00:08:38,889 --> 00:08:33,740
negative control down here at 2 but we

193
00:08:43,329 --> 00:08:38,899
get up to about about 6 we don't want to

194
00:08:45,400 --> 00:08:43,339
be stuck so we explored this optimal

195
00:08:48,819 --> 00:08:45,410
concentration over temperature as well

196
00:08:50,530 --> 00:08:48,829
just like we did for calcium and we get

197
00:08:53,710 --> 00:08:50,540
a nice linear relationship with

198
00:09:00,800 --> 00:08:58,400
but this time all of these experiments

199
00:09:02,510 --> 00:09:00,810
are above our baseline our negative

200
00:09:03,980 --> 00:09:02,520
control here so even at our highest

201
00:09:09,890 --> 00:09:03,990
temperatures we're still seeing an

202
00:09:12,740 --> 00:09:09,900
enhancement of oligomerization however

203
00:09:15,320 --> 00:09:12,750
this concentration is outside the

204
00:09:21,860 --> 00:09:15,330
feasible limits for prebiotic iron in

205
00:09:23,570 --> 00:09:21,870
the early ocean so we have our optimal

206
00:09:25,250 --> 00:09:23,580
concentration and then this is sort of

207
00:09:29,750 --> 00:09:25,260
the range of estimates in the literature

208
00:09:33,230 --> 00:09:29,760
for prebiotic ocean iron so we have this

209
00:09:36,200 --> 00:09:33,240
other point up here this is sort of the

210
00:09:38,030 --> 00:09:36,210
maximum feasible concentration so let's

211
00:09:40,820 --> 00:09:38,040
take that instead and ask us the

212
00:09:43,160 --> 00:09:40,830
ourselves the same question well this is

213
00:09:46,250 --> 00:09:43,170

what it looks like in blue and we don't

214
00:09:48,440 --> 00:09:46,260
see that decrease in oligomerization

215
00:09:50,330 --> 00:09:48,450
with temperature in fact we beat out the

216
00:09:57,110 --> 00:09:50,340
higher concentration when we get out to

217
00:10:00,980 --> 00:09:57,120
80 or 90 so we've added some of these

218
00:10:06,260 --> 00:10:00,990
missing elements to our table we have

219
00:10:08,570 --> 00:10:06,270
our four primary metal cations in the

220
00:10:10,730 --> 00:10:08,580
early ocean what can we do with that

221
00:10:13,610 --> 00:10:10,740
well we we can start to ask ourselves

222
00:10:15,170 --> 00:10:13,620
what a more complex environment might

223
00:10:16,760 --> 00:10:15,180
look like but we're still going to keep

224
00:10:22,070 --> 00:10:16,770
it relatively simple we're going to look

225
00:10:23,680 --> 00:10:22,080
at the open ocean we have our controls

226
00:10:26,870 --> 00:10:23,690
are negative in our positive control so

227
00:10:28,640 --> 00:10:26,880
2 for no catalysts and with 1 molar

228
00:10:30,380 --> 00:10:28,650
calcium chloride which is what we use as

229
00:10:33,770 --> 00:10:30,390
our positive positive we get Penta MERS

230
00:10:35,810 --> 00:10:33,780
and then before we put everything in one

231
00:10:37,850 --> 00:10:35,820
pot let's just make sure we know what

232
00:10:40,430 --> 00:10:37,860
each thing does individually so if we

233
00:10:43,010 --> 00:10:40,440
look at calcium at modern ocean

234
00:10:47,440 --> 00:10:43,020
concentrations we see that we get

235
00:10:51,560 --> 00:10:47,450
trimers sodium sulfate we get dimers

236
00:10:54,560 --> 00:10:51,570
magnesium chloride trimers and sodium

237
00:10:56,300 --> 00:10:54,570
chloride dimers so when we put these

238
00:10:57,680 --> 00:10:56,310

together we can ask ourselves okay are

239
00:10:59,270 --> 00:10:57,690
we going to get trimers or ever again

240
00:11:01,910 --> 00:10:59,280
get timers or are we going to get three

241
00:11:03,740 --> 00:11:01,920
plus two plus three plus two turns out

242
00:11:05,300 --> 00:11:03,750
that we just get three so these aren't

243
00:11:05,879 --> 00:11:05,310
additive at least in terms of the

244
00:11:07,559 --> 00:11:05,889
lengths that

245
00:11:11,099 --> 00:11:07,569
we get we can't really say anything

246
00:11:15,629 --> 00:11:11,109
about yields because we're using multi

247
00:11:17,249 --> 00:11:15,639
and it's not quantifiable but we're

248
00:11:20,729 --> 00:11:17,259
interested in the early ocean so we add

249
00:11:23,780 --> 00:11:20,739
in iron and when we mix that with our

250
00:11:27,329 --> 00:11:23,790
other components at our other salts at

251
00:11:29,629 --> 00:11:27,339
modern concentrations and take out the

252
00:11:31,949 --> 00:11:29,639
sulfate because there wasn't any sulfate

253
00:11:34,019 --> 00:11:31,959
we can run similar experiments and we

254
00:11:36,599 --> 00:11:34,029
see that again the biggest sort of wins

255
00:11:39,359 --> 00:11:36,609
so iron which is up here at five is

256
00:11:44,999 --> 00:11:39,369
pretty close to what we get for our iron

257
00:11:47,849 --> 00:11:45,009
rich synthetic seawater let's push it a

258
00:11:49,319 --> 00:11:47,859
little bit farther because we don't know

259
00:11:51,059 --> 00:11:49,329
exactly what the Hadean look like as

260
00:11:54,720 --> 00:11:51,069
we've discussed throughout this

261
00:11:59,059 --> 00:11:54,730
conference so let's test a range of

262
00:12:04,169 --> 00:12:01,979
so here we have twice modern salinity

263
00:12:07,739 --> 00:12:04,179

half modern solidity and modern salinity

264
00:12:10,850 --> 00:12:07,749
in green and we see that as we would

265
00:12:13,949 --> 00:12:10,860
probably expect slightly higher salinity

266
00:12:15,629 --> 00:12:13,959
produces slightly longer oligomers all

267
00:12:20,400 --> 00:12:15,639
of these are above our negative control

268
00:12:22,069 --> 00:12:20,410
and as I showed before there's no

269
00:12:25,409 --> 00:12:22,079
relationship with temperature because

270
00:12:33,749 --> 00:12:25,419
we're sort of below that 10 millimolar

271
00:12:35,400 --> 00:12:33,759
level for iron so our takeaway points

272
00:12:38,280 --> 00:12:35,410
from this is that iron is very

273
00:12:40,699 --> 00:12:38,290
significant not only for RNA synthesis

274
00:12:42,769 --> 00:12:40,709
but for a variety of prebiotic reactions

275
00:12:45,109 --> 00:12:42,779
but more than that I want to emphasize

276
00:12:47,909 --> 00:12:45,119
the importance of starting with

277
00:12:50,999 --> 00:12:47,919
environmental considerations and working

278
00:12:52,679 --> 00:12:51,009
our way up from there and it doesn't

279
00:12:54,960 --> 00:12:52,689
have to be earth it can be Europa

280
00:12:56,939 --> 00:12:54,970
Enceladus or Titan or whatever we're

281
00:12:58,889 --> 00:12:56,949
interested in but we have to interpret

282
00:13:00,239 --> 00:12:58,899
our data and design our experiments with

283
00:13:02,970 --> 00:13:00,249
our environment in mind that way we're

284
00:13:08,549 --> 00:13:02,980
not shoehorning an environment on to the

285
00:13:10,829 --> 00:13:08,559
early Earth so with that I'll thank our

286
00:13:13,070 --> 00:13:10,839
funding agencies and I'll take any