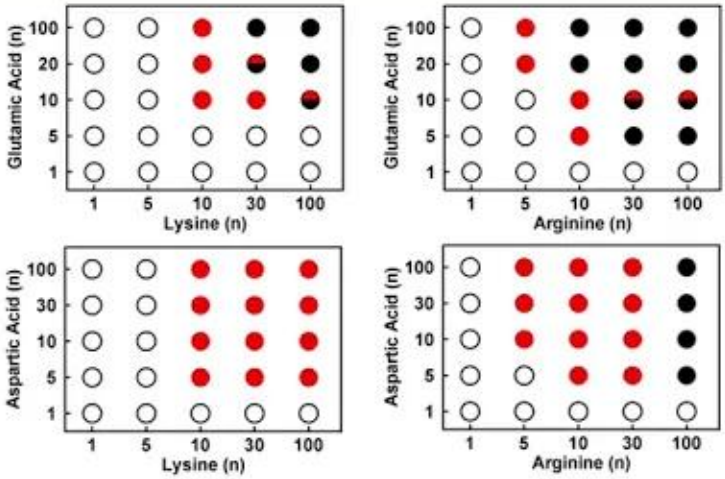
Glutamic acid tends to form more aggregates compared to aspartic acid



Low buffer concentrations: 15 mM KCl, 0.5 mM Mg^{2+} and 10 mM Tris pH 8

1
00:00:04,309 --> 00:00:02,389
hello everyone welcome

2
00:00:06,710 --> 00:00:04,319
uh today i'm going to talk about our

3
00:00:08,870 --> 00:00:06,720
recently published study

4
00:00:11,669 --> 00:00:08,880
uh some of the interesting questions i

5
00:00:13,990 --> 00:00:11,679
was motivated for this study includes

6
00:00:16,790 --> 00:00:14,000
how did first cells assemble from

7
00:00:19,510 --> 00:00:16,800
periodic components and what fundamental

8
00:00:20,470 --> 00:00:19,520
physical chemistry underlies living

9
00:00:22,070 --> 00:00:20,480
cells

10
00:00:24,790 --> 00:00:22,080
and so

11
00:00:26,470 --> 00:00:24,800
this study is going to be about

12
00:00:30,950 --> 00:00:26,480
periodically

13
00:00:37,350 --> 00:00:30,960

relevant compartments and how their

14
00:00:42,830 --> 00:00:40,229
why do i care about compartments

15
00:00:46,069 --> 00:00:42,840
because all cells are

16
00:00:48,709 --> 00:00:46,079
compartments and cell use both

17
00:00:51,029 --> 00:00:48,719
membranous and non-membranous organelles

18
00:00:53,590 --> 00:00:51,039
to compartmentalize biomolecules and

19
00:00:55,430 --> 00:00:53,600
regulate reactions which is important

20
00:00:57,189 --> 00:00:55,440
for controlling cellular activity

21
00:01:00,950 --> 00:00:57,199
necessary for life

22
00:01:02,229 --> 00:01:00,960
and the here are um

23
00:01:04,549 --> 00:01:02,239
listed

24
00:01:05,590 --> 00:01:04,559
advantages of compartmentalization for

25
00:01:07,270 --> 00:01:05,600
instance

26
00:01:09,990 --> 00:01:07,280
you can maintain high local

27
00:01:13,510 --> 00:01:10,000
concentrations you can have selective

28
00:01:16,310 --> 00:01:13,520
entry and of solutes and you can provide

29
00:01:18,230 --> 00:01:16,320
favorable conditions such as ph

30
00:01:20,550 --> 00:01:18,240
and a different

31
00:01:22,390 --> 00:01:20,560
concentration for crowding agents

32
00:01:25,670 --> 00:01:22,400
and you can protect

33
00:01:28,149 --> 00:01:25,680
insights from the damaging contact

34
00:01:31,429 --> 00:01:28,159
conditions

35
00:01:33,270 --> 00:01:31,439
there are two ways of um possible

36
00:01:35,270 --> 00:01:33,280
probability compartments

37
00:01:36,390 --> 00:01:35,280
including membrane base and liquid

38
00:01:39,990 --> 00:01:36,400

droplets

39
00:01:42,870 --> 00:01:40,000
um you can have uh your liquid uh

40
00:01:45,749 --> 00:01:42,880
droplet assemble into this compartment

41
00:01:46,710 --> 00:01:45,759
and use your biomolecules

42
00:01:48,389 --> 00:01:46,720
uh

43
00:01:50,230 --> 00:01:48,399
you can have your biomolecules

44
00:01:52,469 --> 00:01:50,240
compartmentalized in these

45
00:01:54,630 --> 00:01:52,479
little droplets or you can have your

46
00:01:56,789 --> 00:01:54,640
lipid

47
00:01:58,230 --> 00:01:56,799
vesicle and you can actually

48
00:02:00,950 --> 00:01:58,240
load these lipid vesicles with

49
00:02:03,109 --> 00:02:00,960
biomolecules as you can see here with

50
00:02:06,630 --> 00:02:03,119
primordial earlier

51
00:02:09,029 --> 00:02:06,640
soup you have some pre

52
00:02:11,910 --> 00:02:09,039
some molecules and they can actually

53
00:02:14,790 --> 00:02:11,920
form both of these compartments

54
00:02:16,790 --> 00:02:14,800
i'm going to focus on phase separation

55
00:02:19,190 --> 00:02:16,800
specifically for this talk

56
00:02:21,510 --> 00:02:19,200
i'm going to focus on specifically

57
00:02:23,190 --> 00:02:21,520
associated face separation

58
00:02:26,150 --> 00:02:23,200
and

59
00:02:28,869 --> 00:02:26,160
as a complex conservation

60
00:02:30,869 --> 00:02:28,879
and then you have negatively impulsively

61
00:02:34,070 --> 00:02:30,879
charged molecules and then you mix

62
00:02:37,750 --> 00:02:34,080
damage certain ratios you will have

63
00:02:39,990 --> 00:02:37,760

causary droplets condensed causatopas

64
00:02:42,630 --> 00:02:40,000
and you will have most of your molecules

65
00:02:45,670 --> 00:02:42,640
condensed in this droplet phase

66
00:02:48,309 --> 00:02:45,680
and you will have polymer deficient

67
00:02:51,830 --> 00:02:48,319
continuous waste these two phases exist

68
00:02:55,030 --> 00:02:51,840
in equilibrium and even though

69
00:02:58,309 --> 00:02:55,040
pace separation and condensation has

70
00:03:00,309 --> 00:02:58,319
been recently gained attention the first

71
00:03:05,990 --> 00:03:00,319
this term coined in

72
00:03:11,750 --> 00:03:09,430
um let's say you have this um

73
00:03:14,309 --> 00:03:11,760
periodically relevant molecules they are

74
00:03:16,309 --> 00:03:14,319
charged and they are negatively imposed

75
00:03:18,630 --> 00:03:16,319
to each other and you mix them what you

76
00:03:19,509 --> 00:03:18,640
will observe is either

77
00:03:22,070 --> 00:03:19,519
this

78
00:03:23,990 --> 00:03:22,080
clear solution or

79
00:03:25,990 --> 00:03:24,000
here on the right you will see as a

80
00:03:29,110 --> 00:03:26,000
turbid solution

81
00:03:30,789 --> 00:03:29,120
you can basically differentiate by eye

82
00:03:33,430 --> 00:03:30,799
but you can also use

83
00:03:35,830 --> 00:03:33,440
uh your visible spectroscopy

84
00:03:36,869 --> 00:03:35,840
differentiate between these solutions

85
00:03:40,070 --> 00:03:36,879
so

86
00:03:41,750 --> 00:03:40,080
if you have low curvedity you will have

87
00:03:45,110 --> 00:03:41,760
high transmittance

88
00:03:47,990 --> 00:03:45,120

and the light will pass through easily

89
00:03:50,070 --> 00:03:48,000
and if you have high privacy you will

90
00:03:52,710 --> 00:03:50,080
have low transmittance

91
00:03:53,589 --> 00:03:52,720
and light will not be able to pass

92
00:03:57,270 --> 00:03:53,599
through

93
00:04:01,670 --> 00:03:59,589
of course when you mix them and they

94
00:04:03,429 --> 00:04:01,680
will look like this but

95
00:04:04,869 --> 00:04:03,439
you don't know actually what you have in

96
00:04:07,429 --> 00:04:04,879
your solution

97
00:04:10,070 --> 00:04:07,439
if you have this color solution and

98
00:04:12,390 --> 00:04:10,080
lotor with solution it will look like

99
00:04:14,390 --> 00:04:12,400
this under the microscope as your

100
00:04:17,349 --> 00:04:14,400
solution you're not going to absorb any

101
00:04:19,990 --> 00:04:17,359
formation however when you have the high

102
00:04:22,150 --> 00:04:20,000
turbidity you can either have causal

103
00:04:24,230 --> 00:04:22,160
rates um look at

104
00:04:26,150 --> 00:04:24,240
causal rates if you're appearing as

105
00:04:29,030 --> 00:04:26,160
spherical fluid droplets

106
00:04:30,950 --> 00:04:29,040
while precipitates form these amorphous

107
00:04:32,710 --> 00:04:30,960
salt clusters and you will need

108
00:04:34,870 --> 00:04:32,720
microscopes to differentiate between

109
00:04:40,790 --> 00:04:34,880
this

110
00:04:43,590 --> 00:04:40,800
how

111
00:04:46,629 --> 00:04:43,600
face separation can be affected by just

112
00:04:49,830 --> 00:04:46,639
simply changing the salt concentration

113
00:04:52,790 --> 00:04:49,840

as uh the title says polymer land and

114
00:04:56,950 --> 00:04:52,800
salt effective phase separation here you

115
00:05:00,150 --> 00:04:56,960
can see the uh x um

116
00:05:02,710 --> 00:05:00,160
axis the salt concentration as you

117
00:05:04,950 --> 00:05:02,720
increase the salt concentration

118
00:05:07,350 --> 00:05:04,960
uh you can change the aggregate

119
00:05:10,629 --> 00:05:07,360
formation you see here like big chunk

120
00:05:13,350 --> 00:05:10,639
to cause a rate and you can change the

121
00:05:15,830 --> 00:05:13,360
cause of it to uniform solution even

122
00:05:18,790 --> 00:05:15,840
more increasing this will increasing the

123
00:05:21,510 --> 00:05:18,800
salt concentration to higher values

124
00:05:22,790 --> 00:05:21,520
so other important factors also include

125
00:05:24,710 --> 00:05:22,800
that

126
00:05:27,990 --> 00:05:24,720
affected phase separation includes total

127
00:05:32,150 --> 00:05:28,000
polymer concentration polymer length

128
00:05:36,550 --> 00:05:33,909
it is quite

129
00:05:41,590 --> 00:05:36,560
an interesting phenomenon that like can

130
00:05:46,629 --> 00:05:45,110
and recently people discovered that

131
00:05:51,189 --> 00:05:46,639
activities in cell can be

132
00:05:57,029 --> 00:05:54,230
number of cytoplasmic nucleoplasmic

133
00:05:59,510 --> 00:05:57,039
cellular condensate composed of rna and

134
00:06:01,830 --> 00:05:59,520
protein have been reported to have

135
00:06:03,749 --> 00:06:01,840
liquid phase characteristic

136
00:06:06,550 --> 00:06:03,759
non-barminous organelles within the

137
00:06:08,950 --> 00:06:06,560
cells such as nucleoli and p cornelius

138
00:06:10,790 --> 00:06:08,960

have recently been found to exhibit

139
00:06:12,870 --> 00:06:10,800
liquid-like behavior

140
00:06:15,270 --> 00:06:12,880
including spherical shape

141
00:06:18,150 --> 00:06:15,280
fusion and dripping

142
00:06:20,150 --> 00:06:18,160
there are many consequence of this such

143
00:06:22,870 --> 00:06:20,160
as biomolecule partitioning

144
00:06:27,909 --> 00:06:22,880
colocalization sequestration and

145
00:06:31,270 --> 00:06:29,590
so

146
00:06:33,189 --> 00:06:31,280
my motivation

147
00:06:35,029 --> 00:06:33,199
was for this study just to answer a

148
00:06:37,510 --> 00:06:35,039
couple questions as i

149
00:06:39,670 --> 00:06:37,520
mentioned at the beginning how to talk

150
00:06:41,590 --> 00:06:39,680
how did first cell assemble from

151
00:06:42,550 --> 00:06:41,600
priority components

152
00:06:45,590 --> 00:06:42,560
um

153
00:06:47,270 --> 00:06:45,600
there are multiple questions under lies

154
00:06:48,390 --> 00:06:47,280
between this question you can actually

155
00:06:50,309 --> 00:06:48,400
ask

156
00:06:53,189 --> 00:06:50,319
further

157
00:06:55,749 --> 00:06:53,199
such as can we form compartments with

158
00:06:58,870 --> 00:06:55,759
low multivalency components

159
00:07:00,469 --> 00:06:58,880
how low we can go

160
00:07:03,749 --> 00:07:00,479
and another big

161
00:07:04,950 --> 00:07:03,759
question that motivated this day is what

162
00:07:09,990 --> 00:07:04,960
physical

163
00:07:11,749 --> 00:07:10,000

underlies living cell and protocell

164
00:07:16,150 --> 00:07:11,759
models and

165
00:07:22,309 --> 00:07:19,589
here are the molecules i have employed

166
00:07:23,990 --> 00:07:22,319
i have used positively charged lysine

167
00:07:25,110 --> 00:07:24,000
and arginine

168
00:07:28,469 --> 00:07:25,120
and

169
00:07:31,270 --> 00:07:28,479
acid

170
00:07:33,270 --> 00:07:31,280
um number of charge per molecule and

171
00:07:34,629 --> 00:07:33,280
length play a crucial role in phase

172
00:07:36,390 --> 00:07:34,639
separation

173
00:07:39,189 --> 00:07:36,400
longer the molecule

174
00:07:41,589 --> 00:07:39,199
or higher the charge density there is

175
00:07:44,390 --> 00:07:41,599
higher propensity to phase separate

176
00:07:49,589 --> 00:07:44,400
we were curious how short we can go and

177
00:07:52,070 --> 00:07:50,309
so

178
00:07:56,309 --> 00:07:52,080
we change

179
00:08:01,029 --> 00:07:56,319
hundred mer

180
00:08:02,309 --> 00:08:01,039
and i also included nucleotides amp adp

181
00:08:03,189 --> 00:08:02,319
and atp

182
00:08:06,390 --> 00:08:03,199
which

183
00:08:09,189 --> 00:08:06,400
has different charges amp has

184
00:08:12,629 --> 00:08:09,199
two charges adp has

185
00:08:20,309 --> 00:08:12,639
three charges and atp has

186
00:08:25,589 --> 00:08:23,909
then i examined all this combination

187
00:08:26,790 --> 00:08:25,599
between the negatively and positively

188
00:08:29,430 --> 00:08:26,800

charged

189
00:08:32,550 --> 00:08:29,440
molecules and as

190
00:08:34,389 --> 00:08:32,560
of course with different lengths and i

191
00:08:35,829 --> 00:08:34,399
just classified them into three

192
00:08:37,269 --> 00:08:35,839
categories

193
00:08:39,350 --> 00:08:37,279
first one

194
00:08:40,949 --> 00:08:39,360
if i didn't observe anything under the

195
00:08:42,709 --> 00:08:40,959
microscope also

196
00:08:46,310 --> 00:08:42,719
supported by the

197
00:08:49,030 --> 00:08:46,320
uvs uh studies uh i will call them no

198
00:08:50,070 --> 00:08:49,040
formation and with this little empty

199
00:08:52,829 --> 00:08:50,080
square

200
00:08:55,990 --> 00:08:52,839
and if they then i combine

201
00:08:57,269 --> 00:08:56,000
them and they form compartments and

202
00:08:58,550 --> 00:08:57,279
cause rates

203
00:09:01,269 --> 00:08:58,560
specifically

204
00:09:03,670 --> 00:09:01,279
uh i will call them causarate if they

205
00:09:08,470 --> 00:09:03,680
just force amorphous solid structures

206
00:09:12,949 --> 00:09:11,110
and uh colors above the pictures

207
00:09:15,430 --> 00:09:12,959
represents the condition

208
00:09:18,230 --> 00:09:15,440
observed for polluter light mixtures

209
00:09:19,670 --> 00:09:18,240
liquid causers appear as small spherical

210
00:09:21,670 --> 00:09:19,680
fluid droplets

211
00:09:23,509 --> 00:09:21,680
while precipitates form amorphous

212
00:09:25,990 --> 00:09:23,519
certain clusters

213
00:09:28,949 --> 00:09:26,000

both lysine and arginine formed causal

214
00:09:31,430 --> 00:09:28,959
rates with adp and atp as you can see

215
00:09:32,710 --> 00:09:31,440
from the phase diagrams just under the

216
00:09:35,670 --> 00:09:32,720
pictures

217
00:09:38,389 --> 00:09:35,680
only however arginine was able to form

218
00:09:39,990 --> 00:09:38,399
conservation aamp with the lowest

219
00:09:41,910 --> 00:09:40,000
charged nucleotide

220
00:09:47,829 --> 00:09:41,920
arginine seems to have stronger

221
00:09:52,870 --> 00:09:51,269
then i look at the possible combinations

222
00:09:55,269 --> 00:09:52,880
for uh

223
00:09:58,389 --> 00:09:55,279
amino acid combinations

224
00:10:00,710 --> 00:09:58,399
and observe some trends such as glutamic

225
00:10:01,750 --> 00:10:00,720
acid tends to form more aggregates

226
00:10:07,190 --> 00:10:01,760
compared

227
00:10:10,389 --> 00:10:07,200
contained composition called face

228
00:10:11,910 --> 00:10:10,399
separated shorter lens but aspartic

229
00:10:17,350 --> 00:10:11,920
leads to more face separated

230
00:10:22,710 --> 00:10:20,550
so i had the quality library to explore

231
00:10:24,949 --> 00:10:22,720
physical chemical properties

232
00:10:26,870 --> 00:10:24,959
of these compartments right i'm not

233
00:10:27,990 --> 00:10:26,880
going to talk about all the things we

234
00:10:30,150 --> 00:10:28,000
have done

235
00:10:31,350 --> 00:10:30,160
but if you are curious uh you are

236
00:10:34,150 --> 00:10:31,360
welcome to

237
00:10:37,269 --> 00:10:34,160
reference for the paper here

238
00:10:38,949 --> 00:10:37,279

and explore all the partitioning studies

239
00:10:40,949 --> 00:10:38,959
and

240
00:10:42,949 --> 00:10:40,959
ph studies we have done

241
00:10:44,870 --> 00:10:42,959
so

242
00:10:46,710 --> 00:10:44,880
basically

243
00:10:51,030 --> 00:10:46,720
i'm going to talk about

244
00:10:57,030 --> 00:10:54,150
nucleotides and their structures

245
00:10:59,670 --> 00:10:57,040
and the rest of the talk evaluated

246
00:11:01,430 --> 00:10:59,680
labeled nucleotide they do partition in

247
00:11:02,710 --> 00:11:01,440
the causart

248
00:11:04,710 --> 00:11:02,720
phase

249
00:11:06,790 --> 00:11:04,720
selectively and you can actually

250
00:11:08,790 --> 00:11:06,800
calculate this concentration by

251
00:11:10,790 --> 00:11:08,800
basically using

252
00:11:12,550 --> 00:11:10,800
calibration curves

253
00:11:15,030 --> 00:11:12,560
and it will

254
00:11:18,550 --> 00:11:15,040
give you it will give you the value

255
00:11:24,870 --> 00:11:21,990
of course i had many systems

256
00:11:28,389 --> 00:11:24,880
so i just have selected

257
00:11:32,389 --> 00:11:28,399
certain ones to further study

258
00:11:35,430 --> 00:11:32,399
and they are selected here um it's

259
00:11:37,190 --> 00:11:35,440
you can see it has a different length

260
00:11:38,470 --> 00:11:37,200
and i just increase the length and i

261
00:11:41,509 --> 00:11:38,480
also choose

262
00:11:42,710 --> 00:11:41,519
one system with a different identity

263
00:11:45,590 --> 00:11:42,720

including

264
00:11:51,910 --> 00:11:49,269
in order to understand the structure of

265
00:11:55,430 --> 00:11:51,920
nucleotides within the droplets i used

266
00:11:58,550 --> 00:11:55,440
double-stranded rna

267
00:12:01,670 --> 00:11:58,560
use two labels one of them is doner and

268
00:12:03,750 --> 00:12:01,680
other one is acceptor fluorescent labels

269
00:12:05,750 --> 00:12:03,760
and if they are close enough you will

270
00:12:07,910 --> 00:12:05,760
observe a

271
00:12:10,389 --> 00:12:07,920
energy transfer and you will observe

272
00:12:11,750 --> 00:12:10,399
higher threat efficiency but when they

273
00:12:14,310 --> 00:12:11,760
are separate

274
00:12:15,350 --> 00:12:14,320
uh there is going to be no energy

275
00:12:17,910 --> 00:12:15,360
transfer

276
00:12:19,990 --> 00:12:17,920
and you will observe lower threat

277
00:12:24,310 --> 00:12:20,000
efficiency depends on the distance

278
00:12:31,350 --> 00:12:28,629
if you uh look at uh the fret efficiency

279
00:12:33,910 --> 00:12:31,360
uh graph here um this is

280
00:12:36,389 --> 00:12:33,920
uh for different system in

281
00:12:39,110 --> 00:12:36,399
x the x axis you will see the different

282
00:12:42,230 --> 00:12:39,120
system corresponding and you will have

283
00:12:43,190 --> 00:12:42,240
the um corrected fret values for each

284
00:12:45,430 --> 00:12:43,200
system

285
00:12:47,350 --> 00:12:45,440
as a as a

286
00:12:48,790 --> 00:12:47,360
control i have done

287
00:12:51,910 --> 00:12:48,800
single stranded

288
00:12:54,870 --> 00:12:51,920

systems uh which actually basically same

289
00:12:58,069 --> 00:12:54,880
strand with two different labels in a

290
00:12:59,670 --> 00:12:58,079
buffer and as i expected i observed zero

291
00:13:01,509 --> 00:12:59,680
fret efficiency

292
00:13:05,269 --> 00:13:01,519
in the buffer

293
00:13:07,670 --> 00:13:05,279
however when i had

294
00:13:10,230 --> 00:13:07,680
double double-stranded system within the

295
00:13:11,829 --> 00:13:10,240
buffer this is going to be our base

296
00:13:13,750 --> 00:13:11,839
and it's going to be the highest wall if

297
00:13:16,470 --> 00:13:13,760
you observe and

298
00:13:19,670 --> 00:13:16,480
it was around 0.6

299
00:13:23,350 --> 00:13:19,680
and what i observed is the very

300
00:13:25,430 --> 00:13:23,360
interesting as i increase the length

301
00:13:26,870 --> 00:13:25,440
the thread efficiency

302
00:13:28,470 --> 00:13:26,880
went to

303
00:13:29,430 --> 00:13:28,480
uh lower

304
00:13:30,710 --> 00:13:29,440
which

305
00:13:33,350 --> 00:13:30,720
means that

306
00:13:34,710 --> 00:13:33,360
my double-stranded structures was

307
00:13:38,870 --> 00:13:34,720
melting

308
00:13:43,990 --> 00:13:38,880
as i increase the length of the

309
00:13:49,030 --> 00:13:46,829
so just to summarize

310
00:13:51,829 --> 00:13:49,040
um i

311
00:13:55,829 --> 00:13:51,839
have shown with this study that

312
00:13:59,910 --> 00:13:58,230
be used as rna concentrating

313
00:14:01,430 --> 00:13:59,920

microvolumes

314
00:14:04,949 --> 00:14:01,440
and

315
00:14:06,069 --> 00:14:04,959
actually when you think about the

316
00:14:07,110 --> 00:14:06,079
shorter

317
00:14:08,470 --> 00:14:07,120
length

318
00:14:10,790 --> 00:14:08,480
components

319
00:14:13,430 --> 00:14:10,800
they actually more effective than their

320
00:14:14,470 --> 00:14:13,440
higher multivalency counterparts doing

321
00:14:17,990 --> 00:14:14,480
that

322
00:14:19,030 --> 00:14:18,000
and um the compartments

323
00:14:22,069 --> 00:14:19,040
can

324
00:14:25,189 --> 00:14:22,079
accumulate functional arrays

325
00:14:27,829 --> 00:14:25,199
while largely preserving the structures

326
00:14:31,269 --> 00:14:27,839
which is very important to function so

327
00:14:34,550 --> 00:14:31,279
when you have this shorter

328
00:14:36,710 --> 00:14:34,560
components they will actually

329
00:14:38,069 --> 00:14:36,720
preserve the structure

330
00:14:41,269 --> 00:14:38,079
which

331
00:14:45,110 --> 00:14:41,279
can help the improve the functionality

332
00:14:52,389 --> 00:14:47,269
i just want to acknowledge the funding

333
00:14:55,509 --> 00:14:52,399
from nasa and nsf and my previous uh