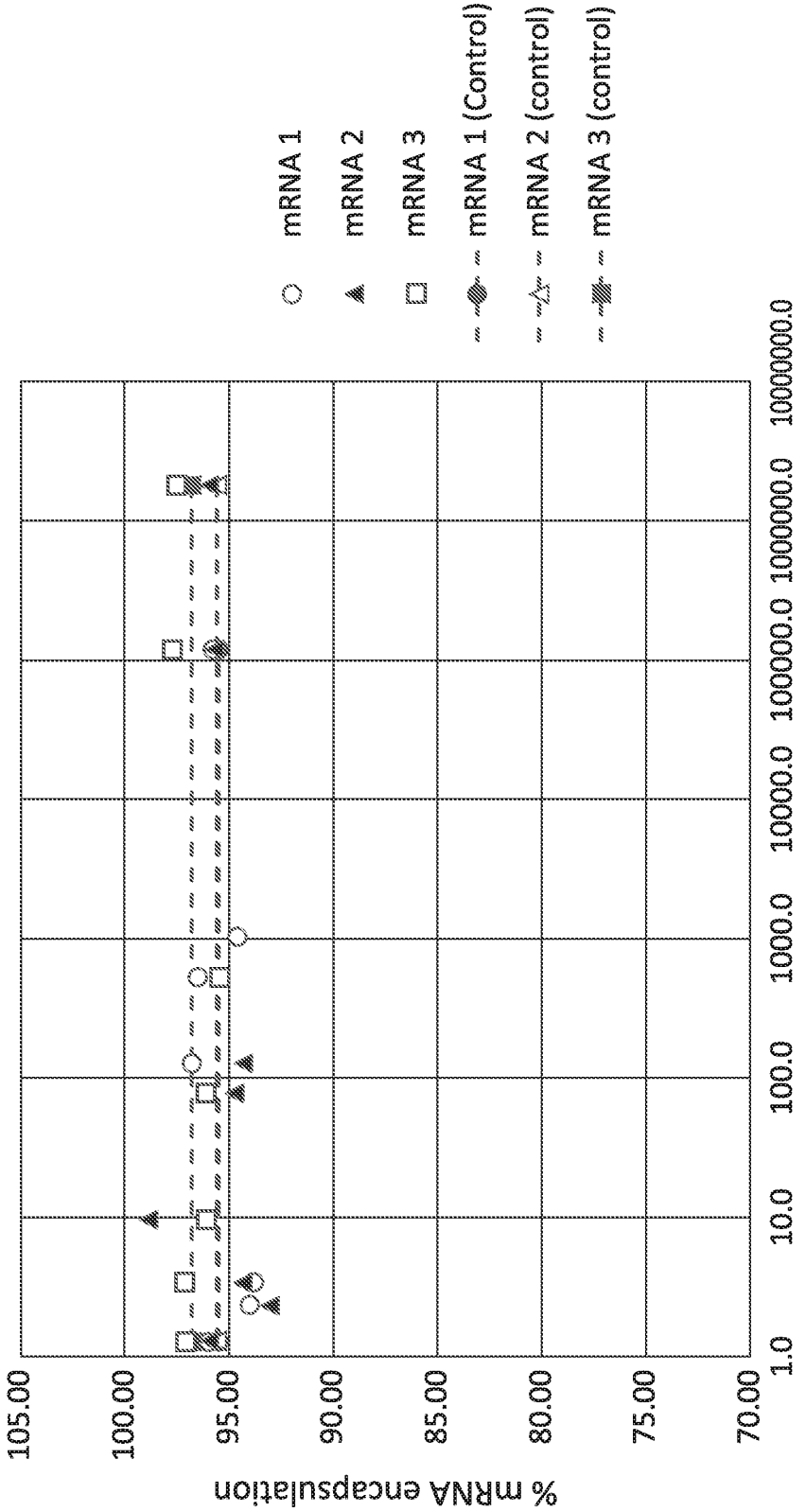

mRNA 1
mRNA 2
mRNA 3
mRNA 1 (Control)
mRNA 2 (control)
mRNA 3 (control)
% mRNA encapsulation
105.00
100.00
95.00
90.00
85.00
80.00
75.00
70.00
1.0
10.0
100.0
1000.0
10000.0
100000.0
1000000.0
10000000.0
Residence Time (ms)

Fig. 1

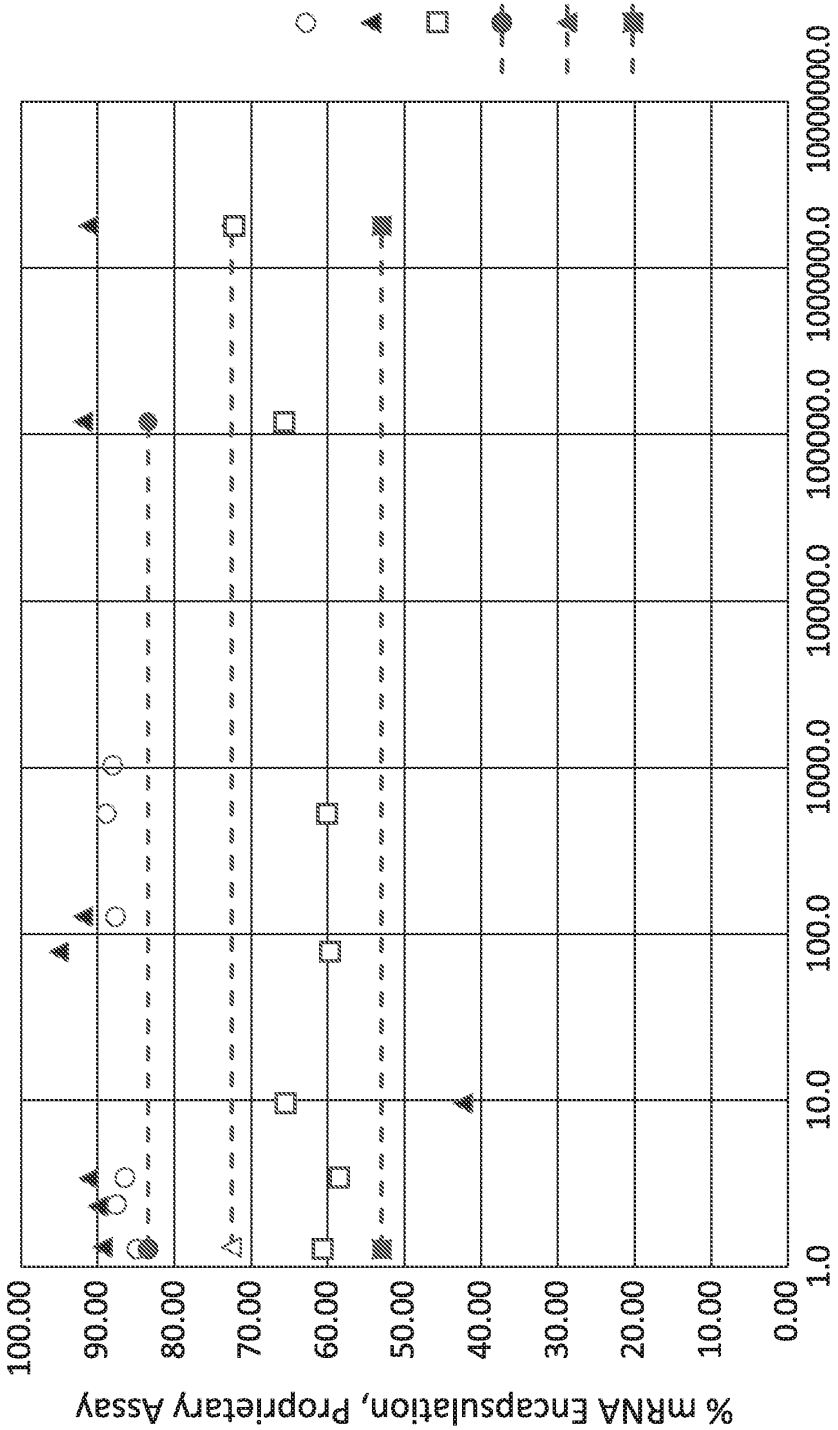

% mRNA Encapsulation, Proprietary Assay
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
1.0
10.0
100.0
1000.0
10000.0
100000.0
1000000.0
10000000.0
Residence Time (ms)
mRNA 1
mRNA 2
mRNA 3
mRNA 1
mRNA 2
mRNA 3

Fig. 2

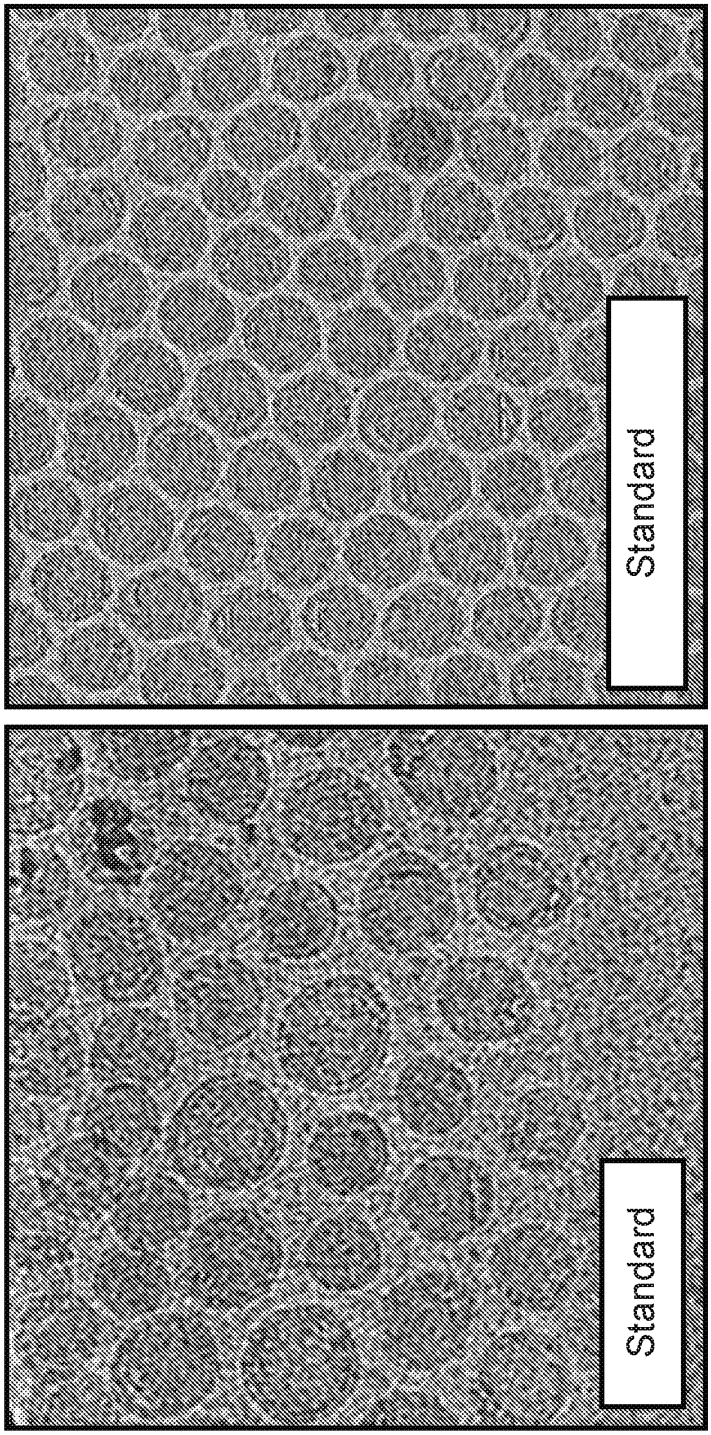


Fig. 3

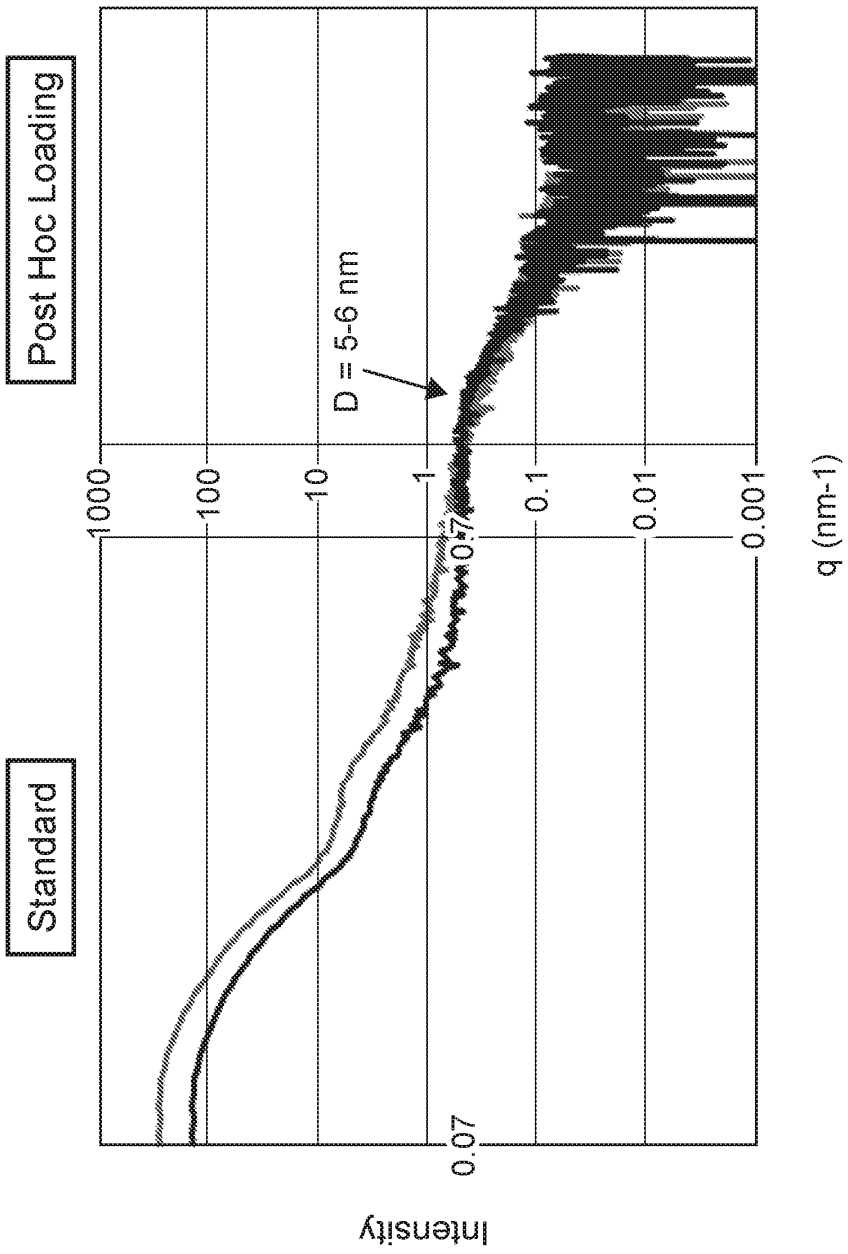

Post Hoc Loading
Standard
D = 5-6 nm
1000
100
10
1
0.7
0.1
0.01
0.001
q (nm-1)
0.07
Intensity

Fig. 4

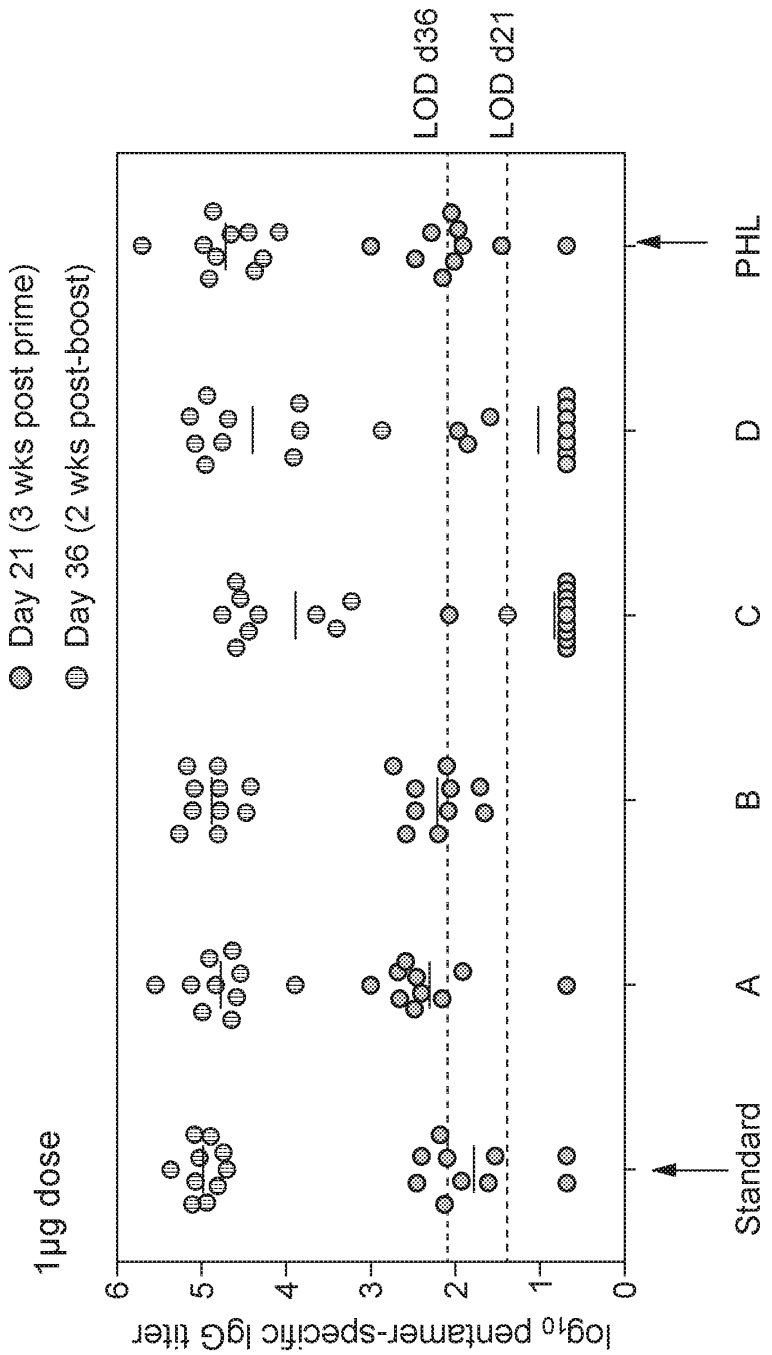

Day 21 (3 wks post prime)
Day 36 (2 wks post-boost)
1µg dose
LOD d36
LOD d21
log10 pentamer-specific IgG titer
0
1
2
3
4
5
6
Standard
A
B
C
D
PHL

Fig. 5

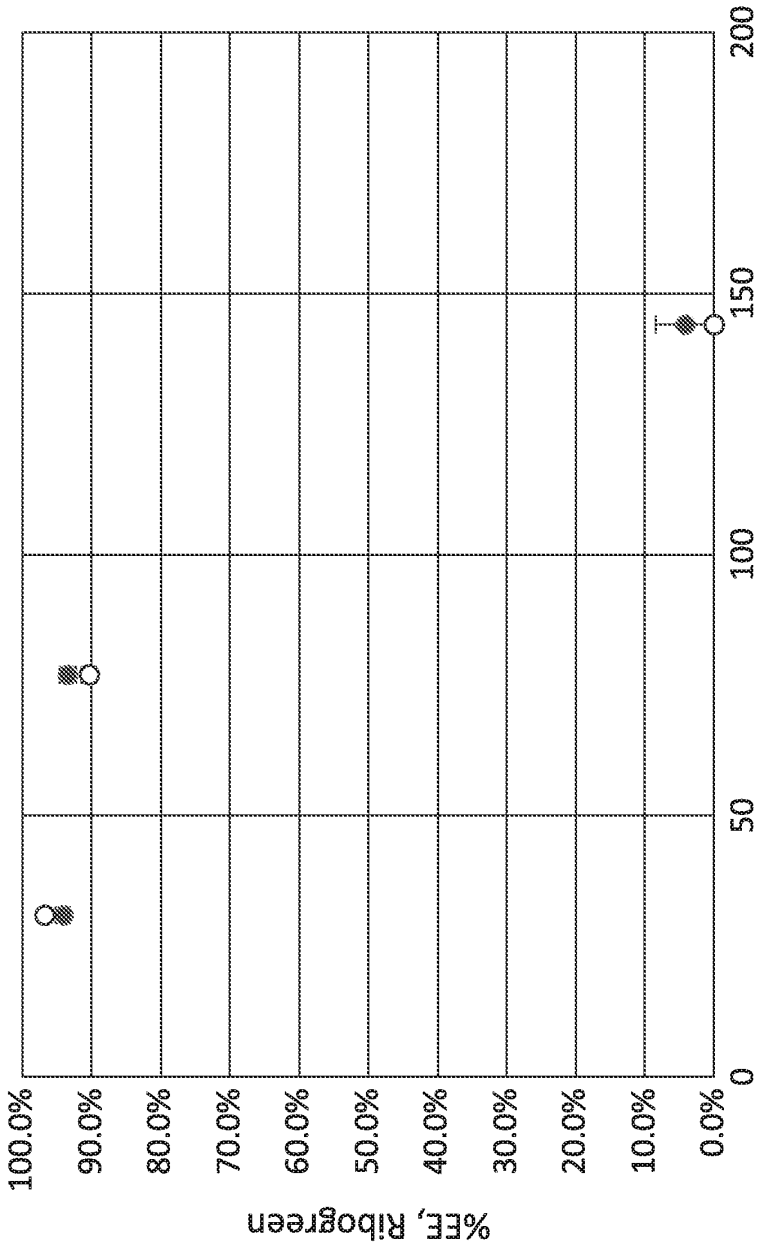

%EE, Ribogreen
100.0%
90.0%
80.0%
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
0.0%
0
50
100
150
200
Initial Empty LNP Diameter (nm)
0.5 mg/mL, 18 degC
0.5 mg/mL, 55 degC

Fig. 6

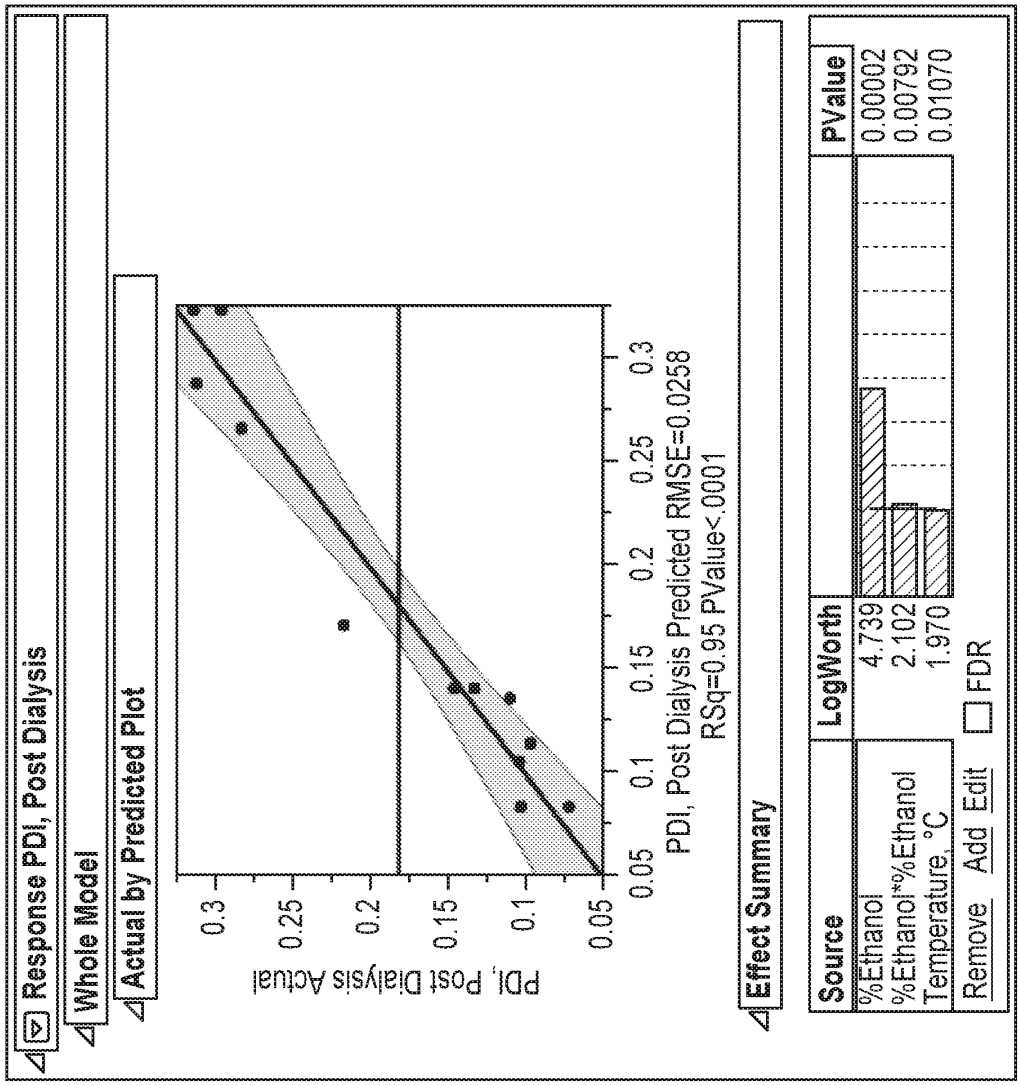

Response PDI, Post Dialysis
Whole Model
Actual by Predicted Plot
PDI, Post Dialysis Actual
0.3
0.25
0.2
0.15
0.1
0.05
0.05 0.1 0.15 0.2 0.25 0.3
PDI, Post Dialysis Predicted RMSE=0.0258
RSq=0.95 PValue<.0001
Effect Summary
Source
LogWorth
PValue
%Ethanol
%Ethanol*%Ethanol
Temperature, °C
4.739
2.102
1.970
0.00002
0.00792
0.01070
Remove Add Edit
FDR

Fig. 7

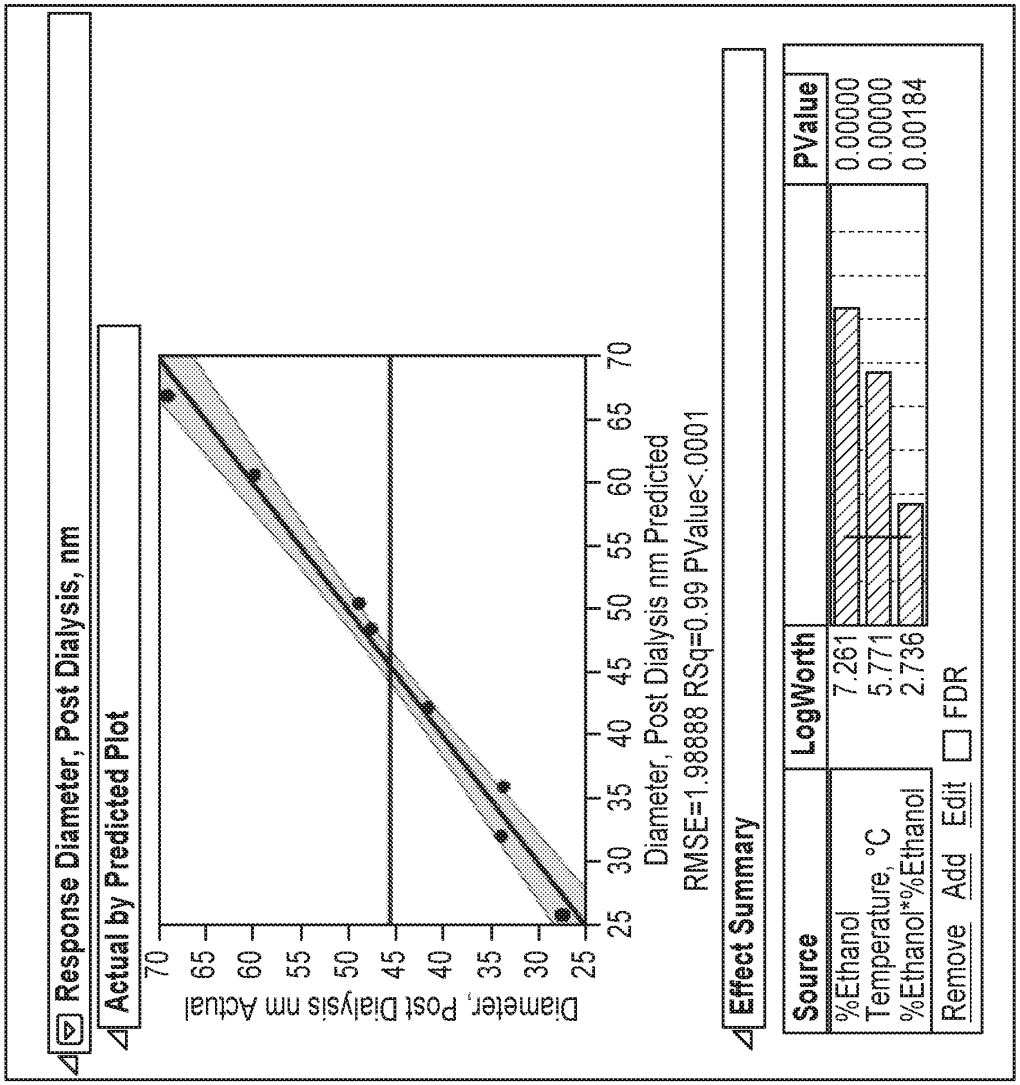

Response Diameter, Post Dialysis, nm
Actual by Predicted Plot
Diameter, Post Dialysis nm Actual
Diameter, Post Dialysis nm Predicted
RMSE=1.98888 RSq=0.99 PValue<.0001
Effect Summary
Source
LogWorth
PValue
%Ethanol
7.261
0.00000
Temperature, °C
5.771
0.00000
%Ethanol*%Ethanol
2.736
0.00184
Remove Add Edit FDR

Fig. 8

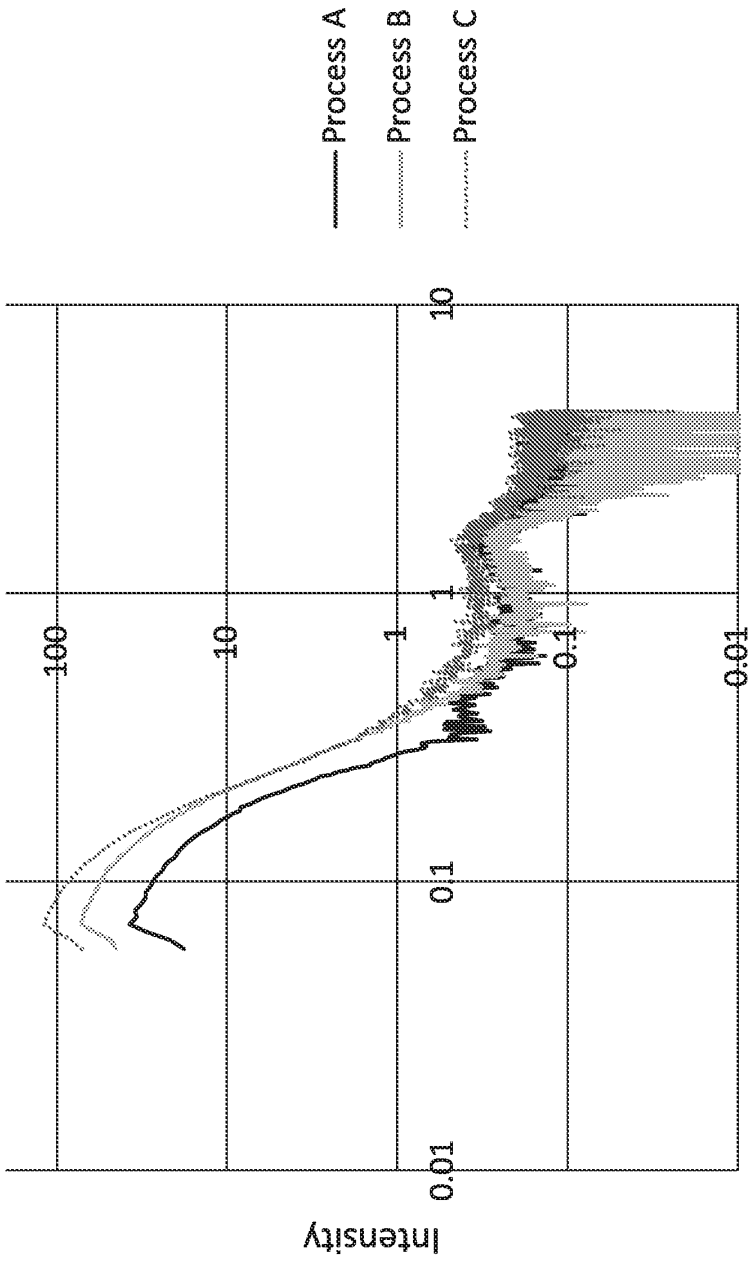

Process A
Process B
Process C
Intensity
0.01
0.1
1
10
100
0.01
0.1
1
10
q (nm-1)

Fig. 9

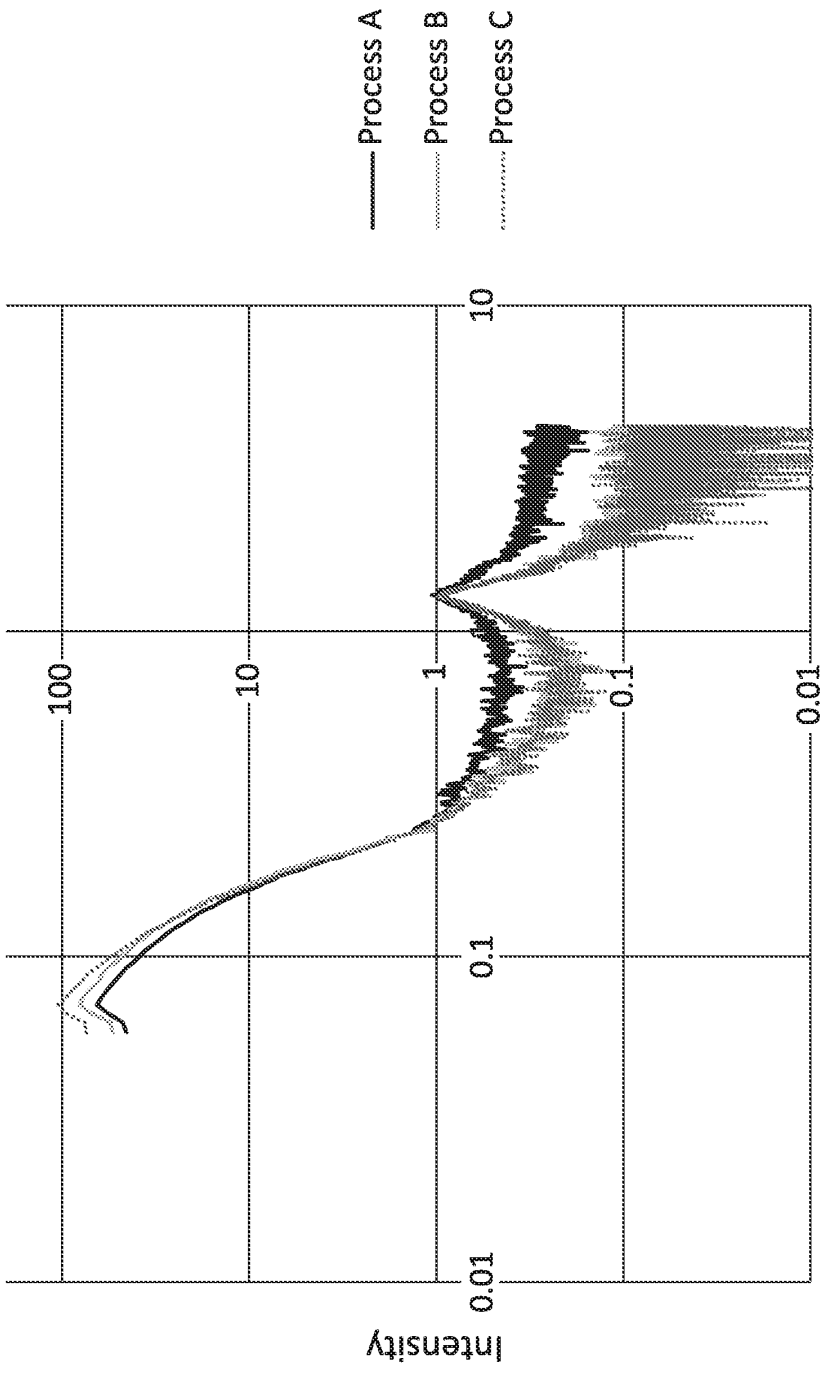

Process A
Process B
Process C
Intensity
100
10
1
0.1
0.01
10
0.1
0.01
q (nm-1)

Fig. 10

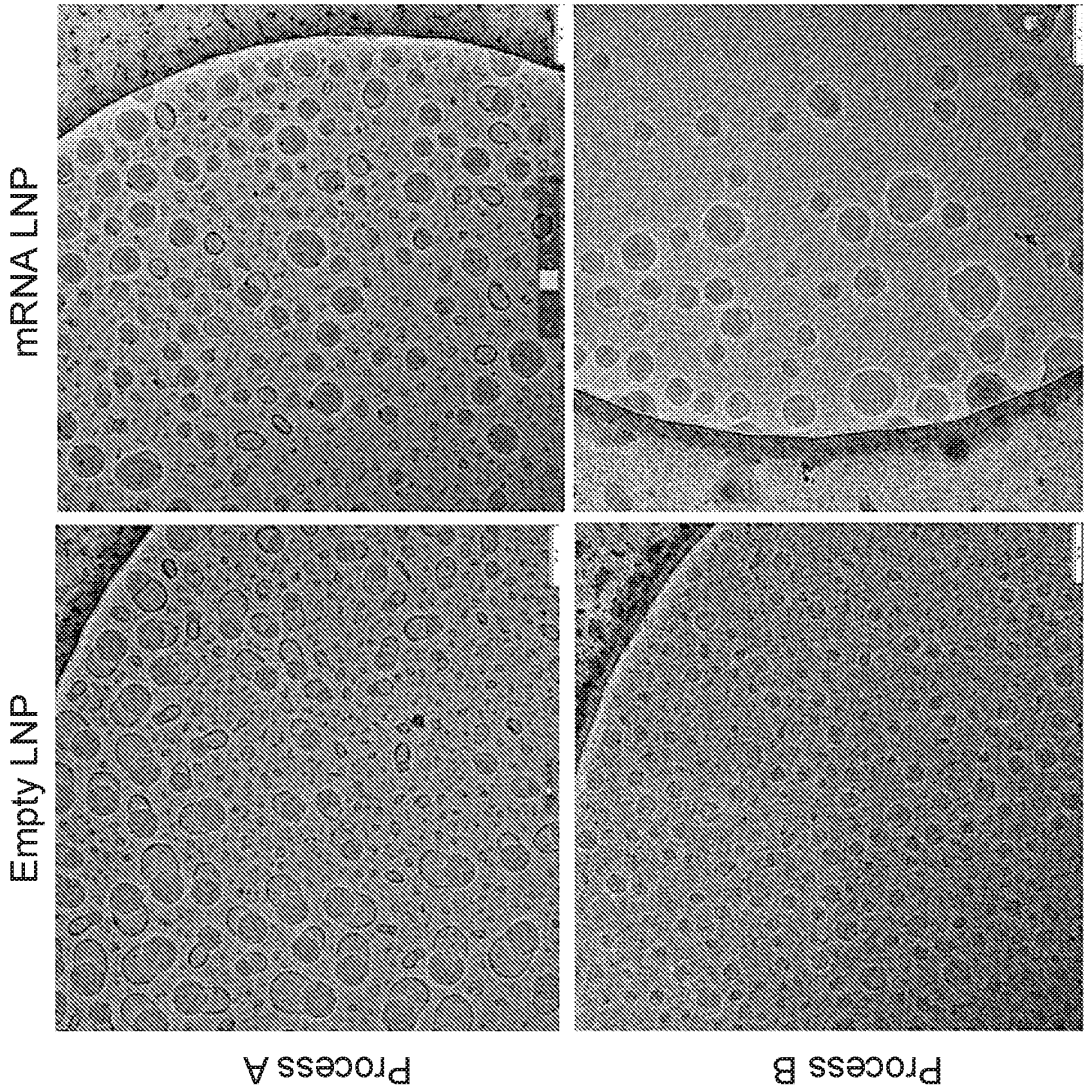


Fig. 11

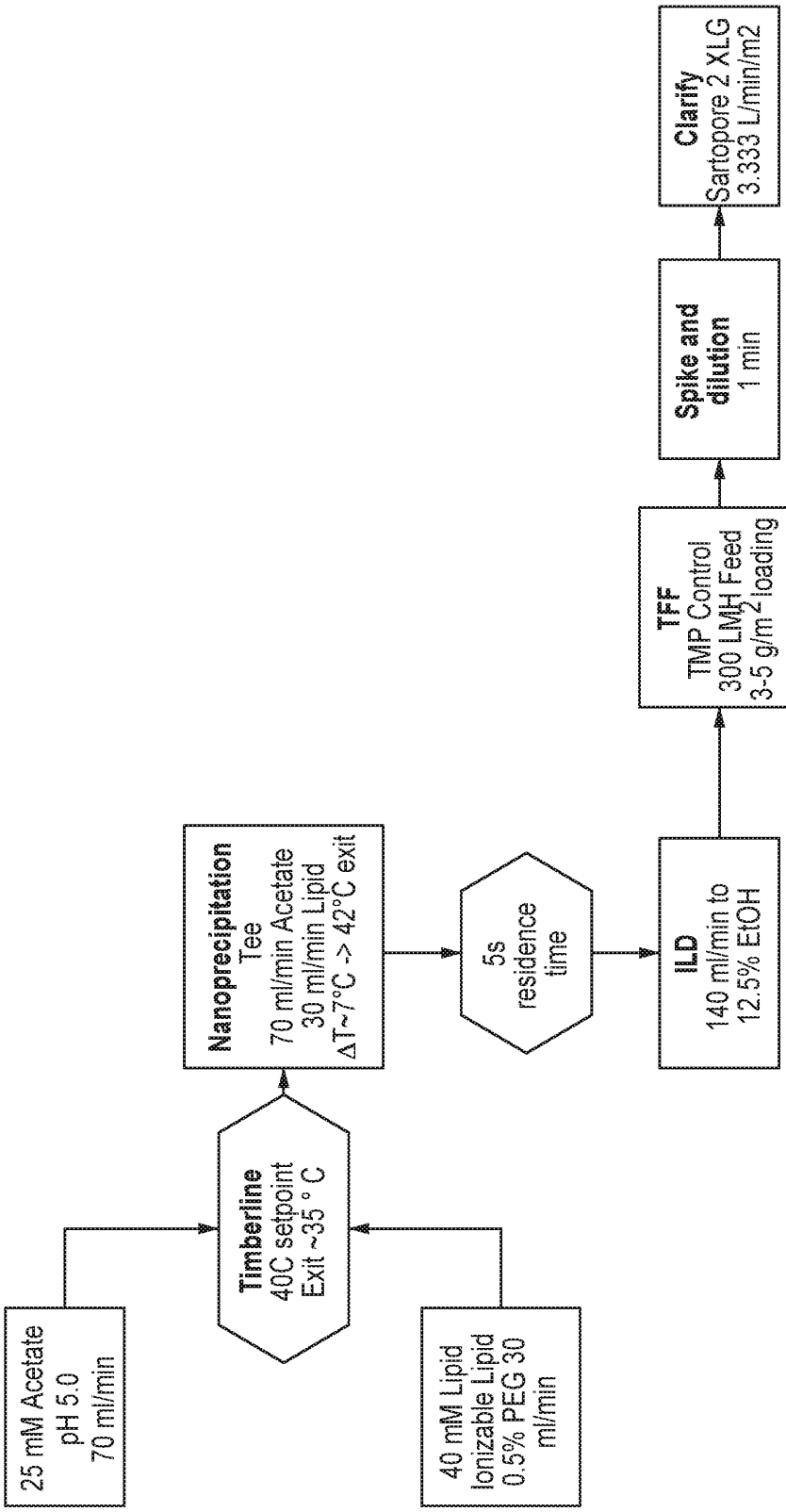

25 mM Acetate
pH 5.0
70 ml/min
40 mM Lipid
Ionizable Lipid
0.5% PEG 30
ml/min
Timberline
40C setpoint
Exit ~35 ° C
Nanoprecipitation
Tee
70 ml/min Acetate
30 ml/min Lipid
ΔT~7°C -> 42°C exit
5s
residence
time
ILD
140 ml/min to
12.5% EtOH
TFF
TMP Control
300 LMH Feed
3-5 g/m2 loading
Spike and
dilution
1 min
Clarify
Sartopore 2 XLG
3.333 L/min/m2

Fig. 12

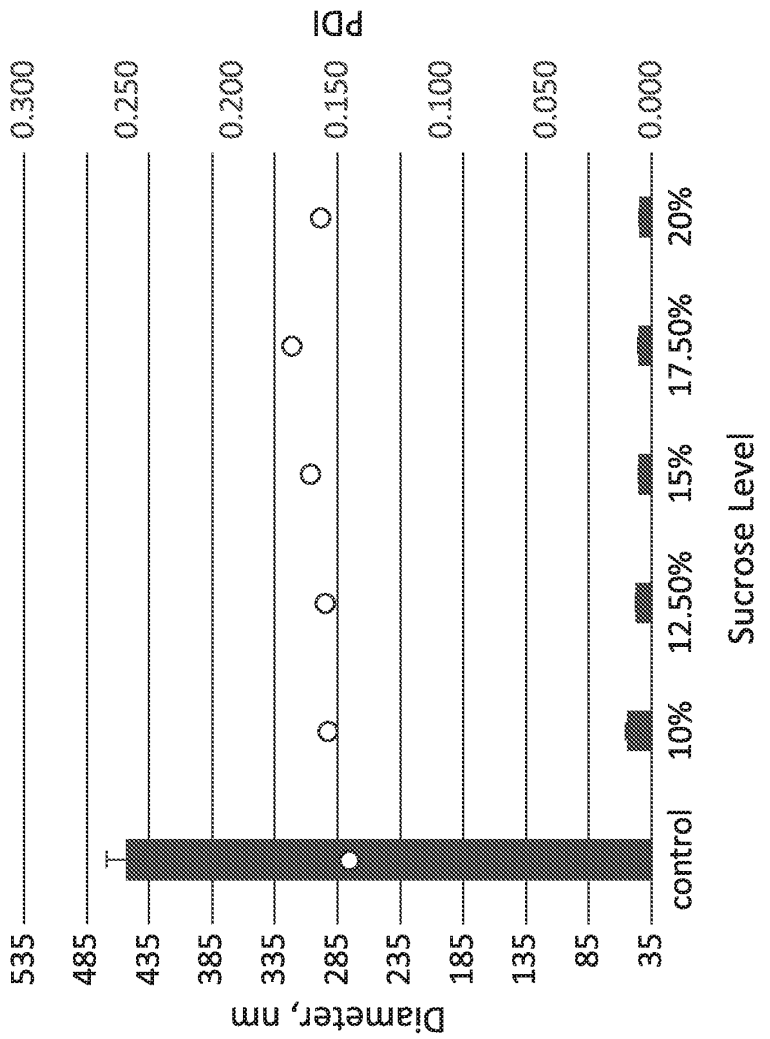

PDI
0.300
0.250
0.200
0.150
0.100
0.050
0.000
Diameter, nm
535
485
435
385
335
285
235
185
135
85
35
control
10%
12.50%
15%
17.50%
20%
Sucrose Level

Fig. 13

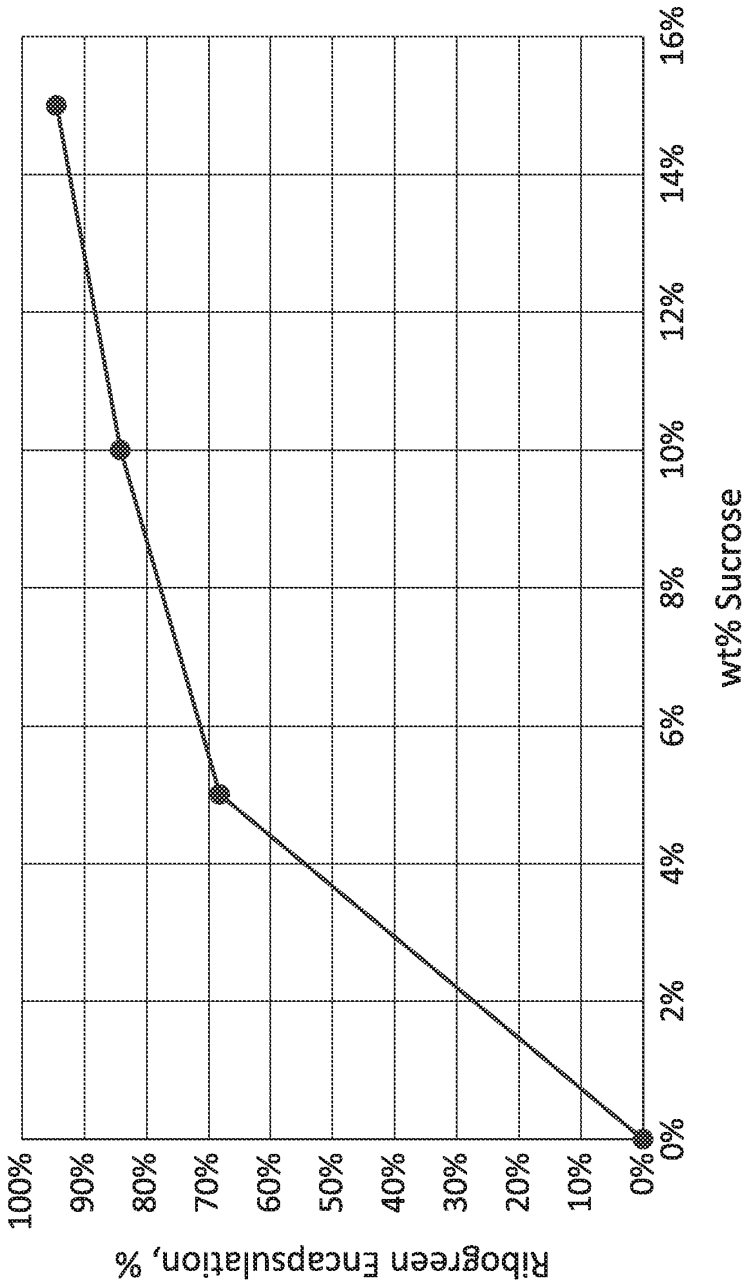

Ribogreen Encapsulation, %
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0%
2%
4%
6%
8%
10%
12%
14%
16%
wt% Sucrose

Fig. 14

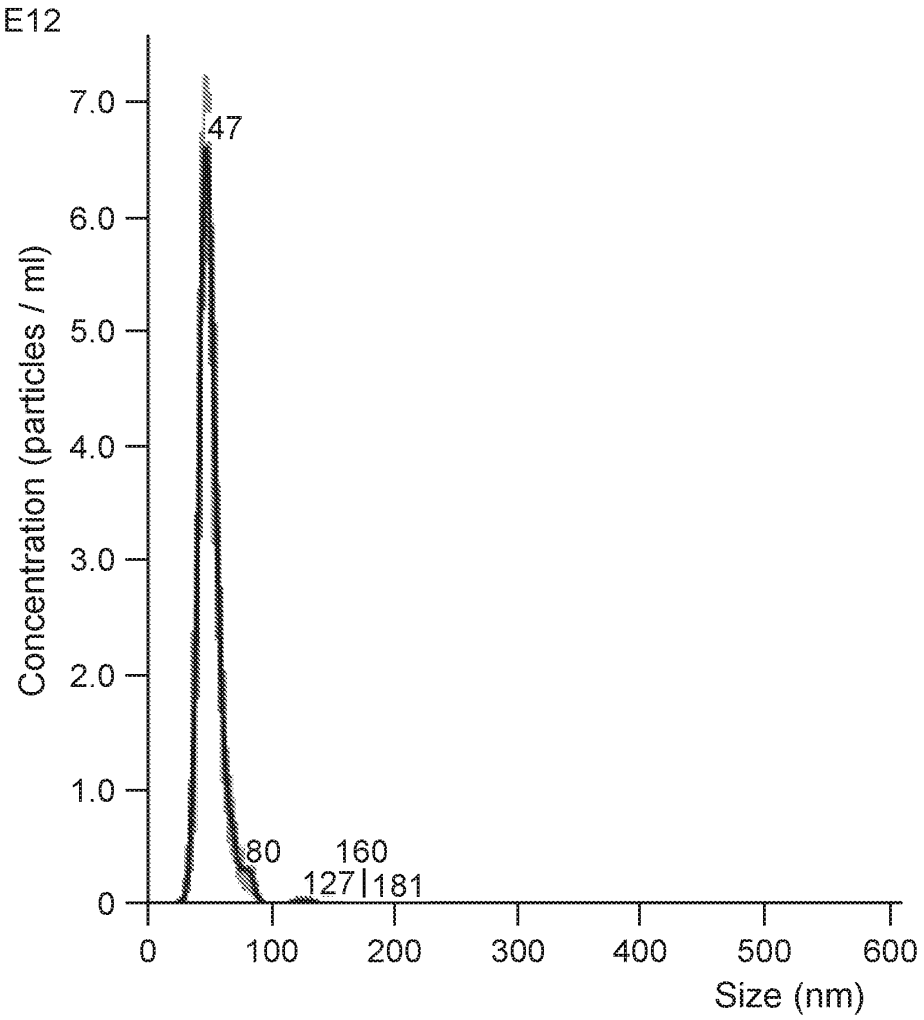

E12
Concentration (particles / ml)
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
47
80
160
127
181
0
100
200
300
400
500
600
Size (nm)

Fig. 15A

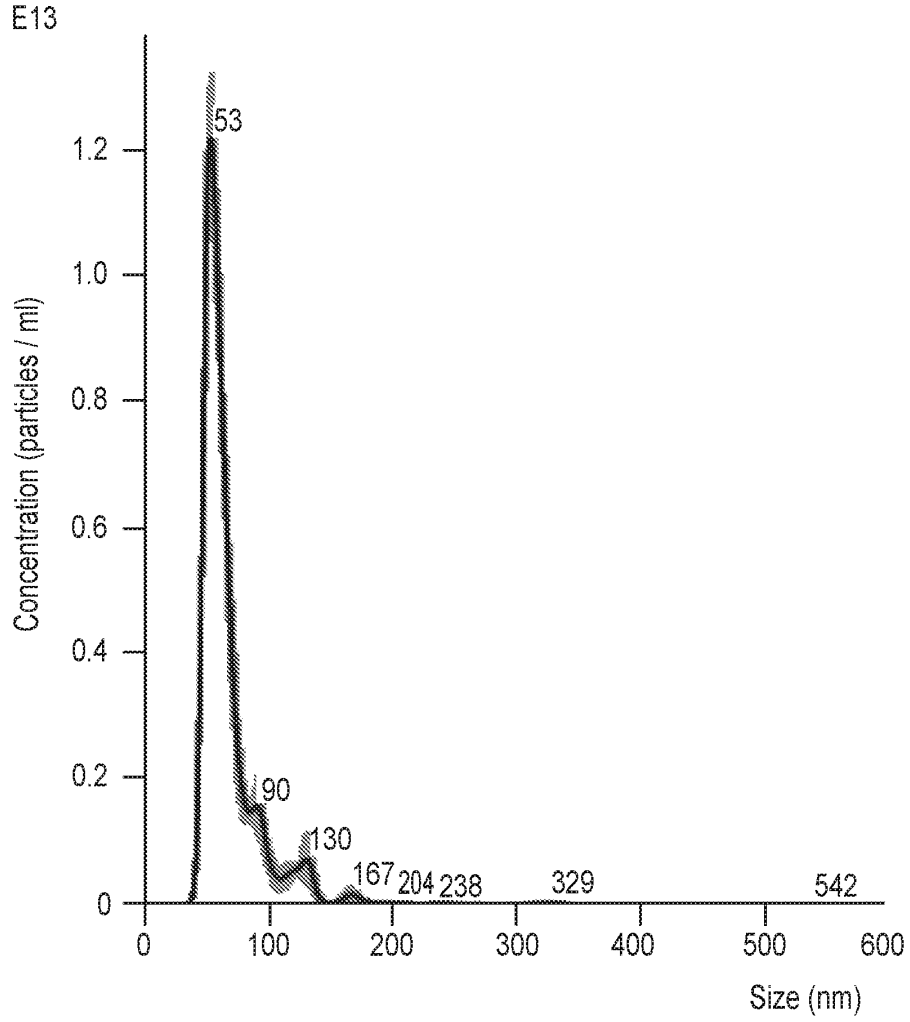

E13
Concentration (particles / ml)
1.2
1.0
0.8
0.6
0.4
0.2
0
53
90
130
167
204
238
329
542
0
100
200
300
400
500
600
Size (nm)

Fig. 15B

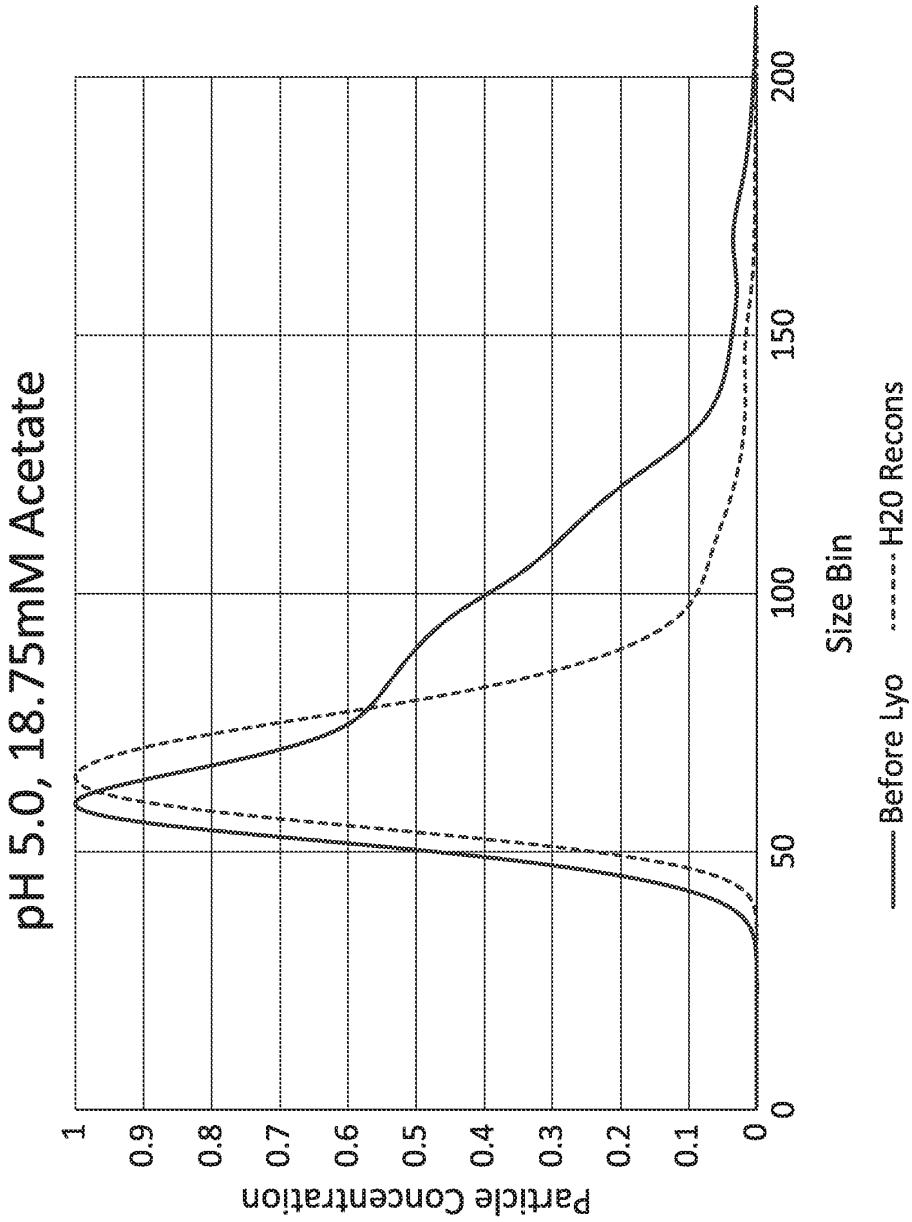

pH 5.0, 18.75mM Acetate
Particle Concentration
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0
50
100
150
200
Size Bin
Before Lyo
H20 Recons

Fig. 16

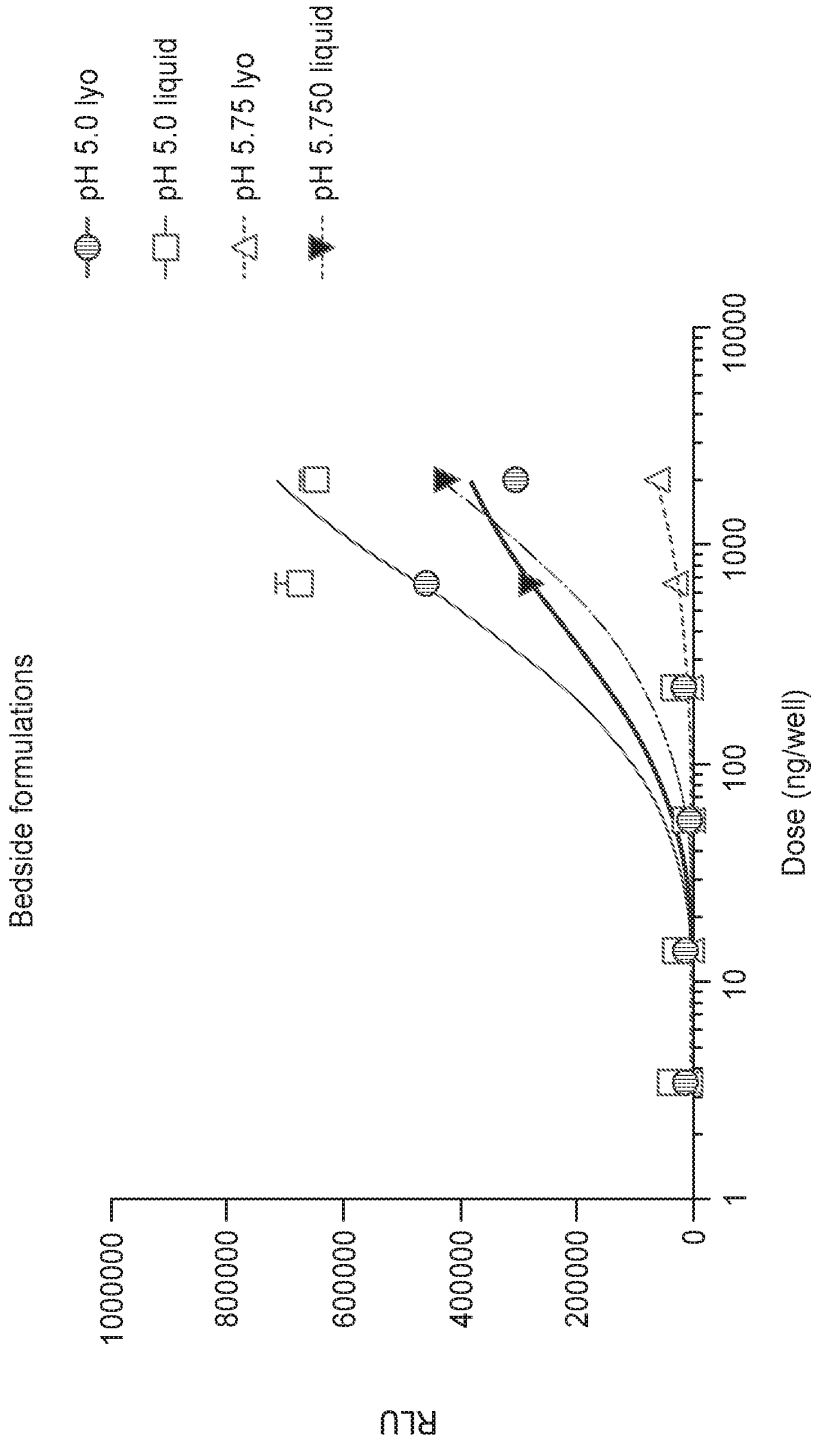

Bedside formulations
pH 5.0 lyo
pH 5.0 liquid
pH 5.75 lyo
pH 5.750 liquid
RLU
1000000
800000
600000
400000
200000
0
1
10
100
1000
10000
Dose (ng/well)

Fig. 17

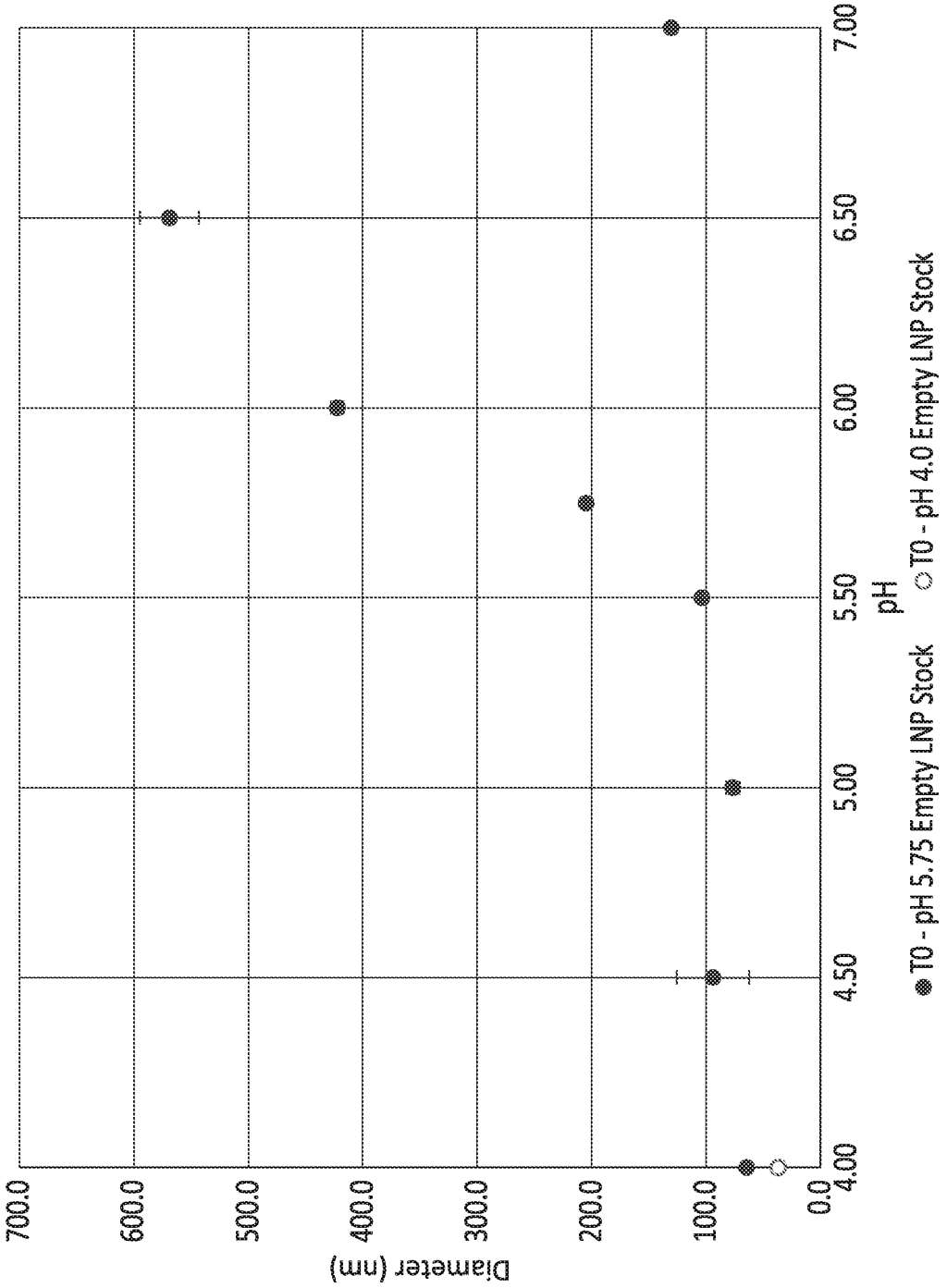

Diameter (nm)
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0.0
4.00
4.50
5.00
5.50
6.00
6.50
7.00
pH
T0 - pH 5.75 Empty LNP Stock
T0 - pH 4.0 Empty LNP Stock

Fig. 18

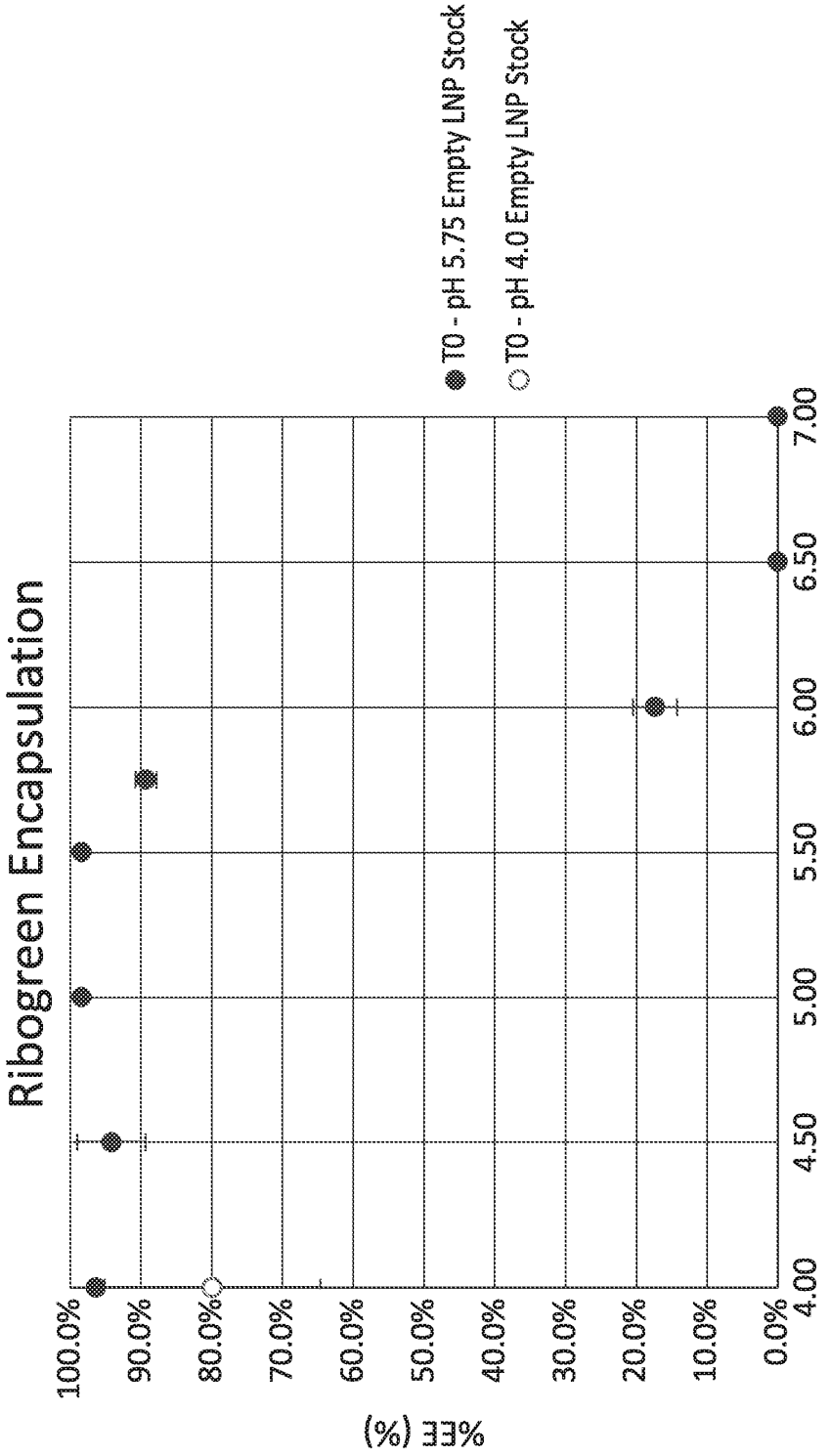

Ribogreen Encapsulation
T0 - pH 5.75 Empty LNP Stock
T0 - pH 4.0 Empty LNP Stock
%EE (%)
100.0%
90.0%
80.0%
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
0.0%
4.00
4.50
5.00
5.50
6.00
6.50
7.00
pH

Fig. 19

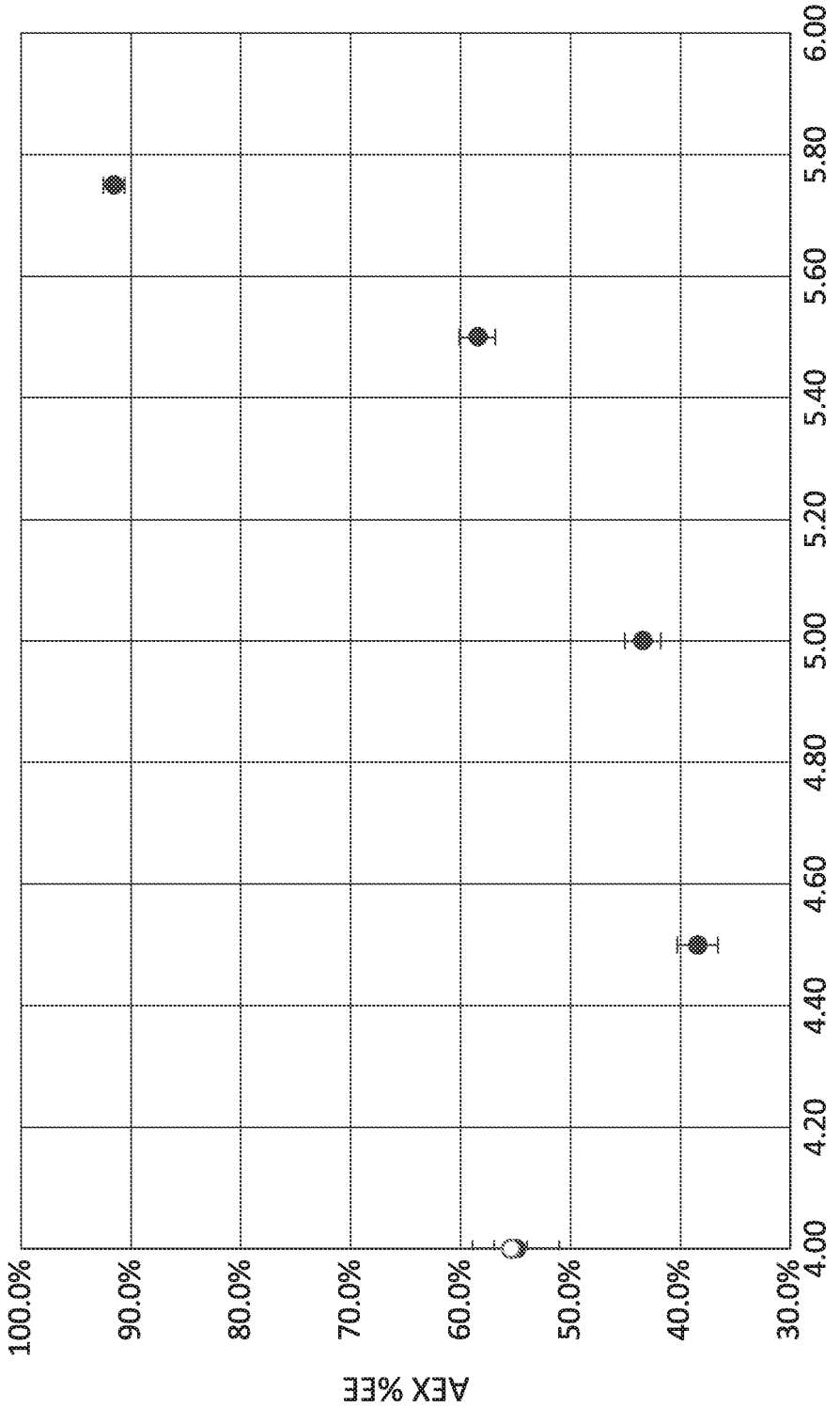

AEX %EE
100.0%
90.0%
80.0%
70.0%
60.0%
50.0%
40.0%
30.0%
4.00
4.20
4.40
4.60
4.80
5.00
5.20
5.40
5.60
5.80
6.00
pH

Fig. 20

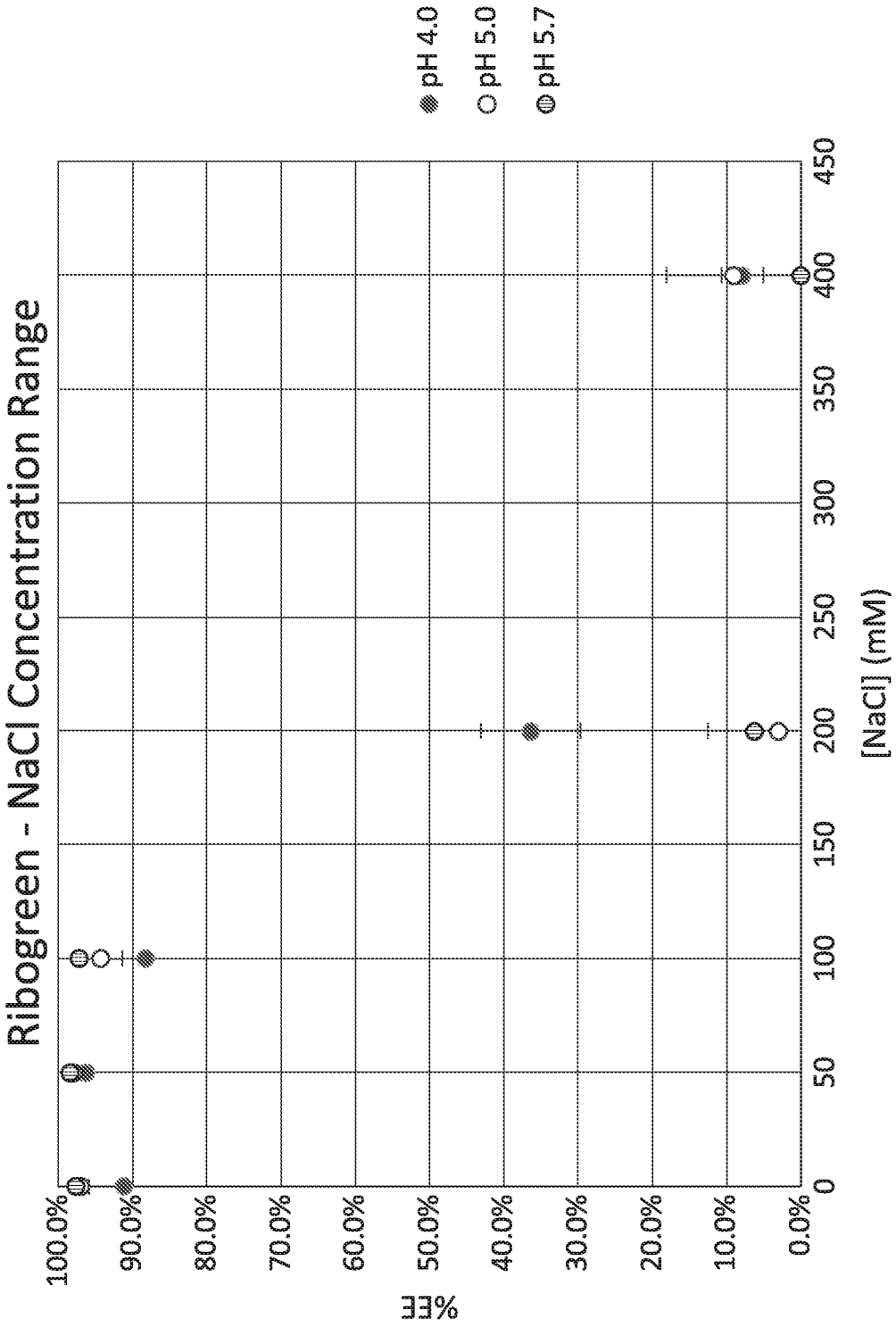

Ribogreen - NaCl Concentration Range
pH 4.0
pH 5.0
pH 5.7
%EE
100.0%
90.0%
80.0%
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
0.0%
0
50
100
150
200
250
300
350
400
450
[NaCl] (mM)

Fig. 21

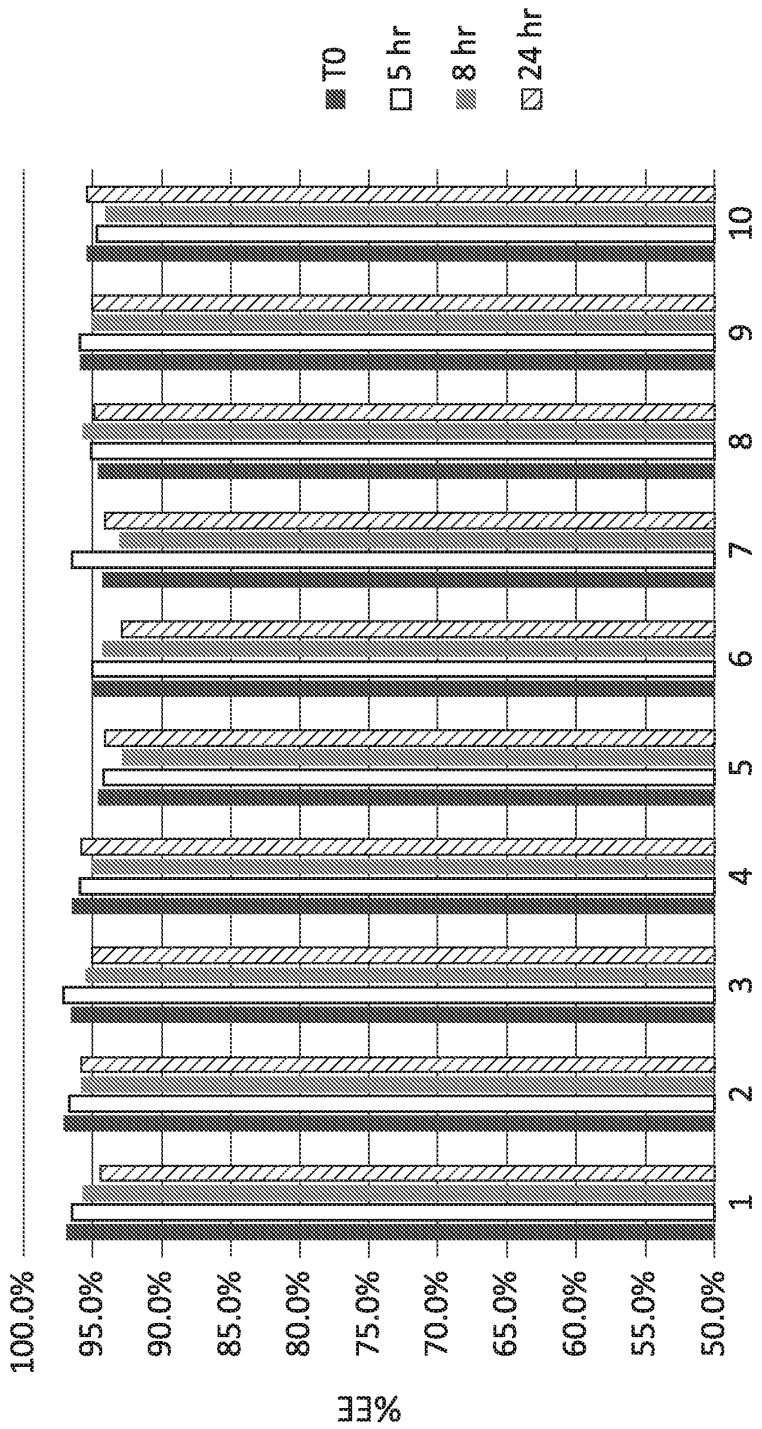

T0
5 hr
8 hr
24 hr
%EE
100.0%
95.0%
90.0%
85.0%
80.0%
75.0%
70.0%
65.0%
60.0%
55.0%
50.0%
1
2
3
4
5
6
7
8
9
10
Batch No.

Fig. 22

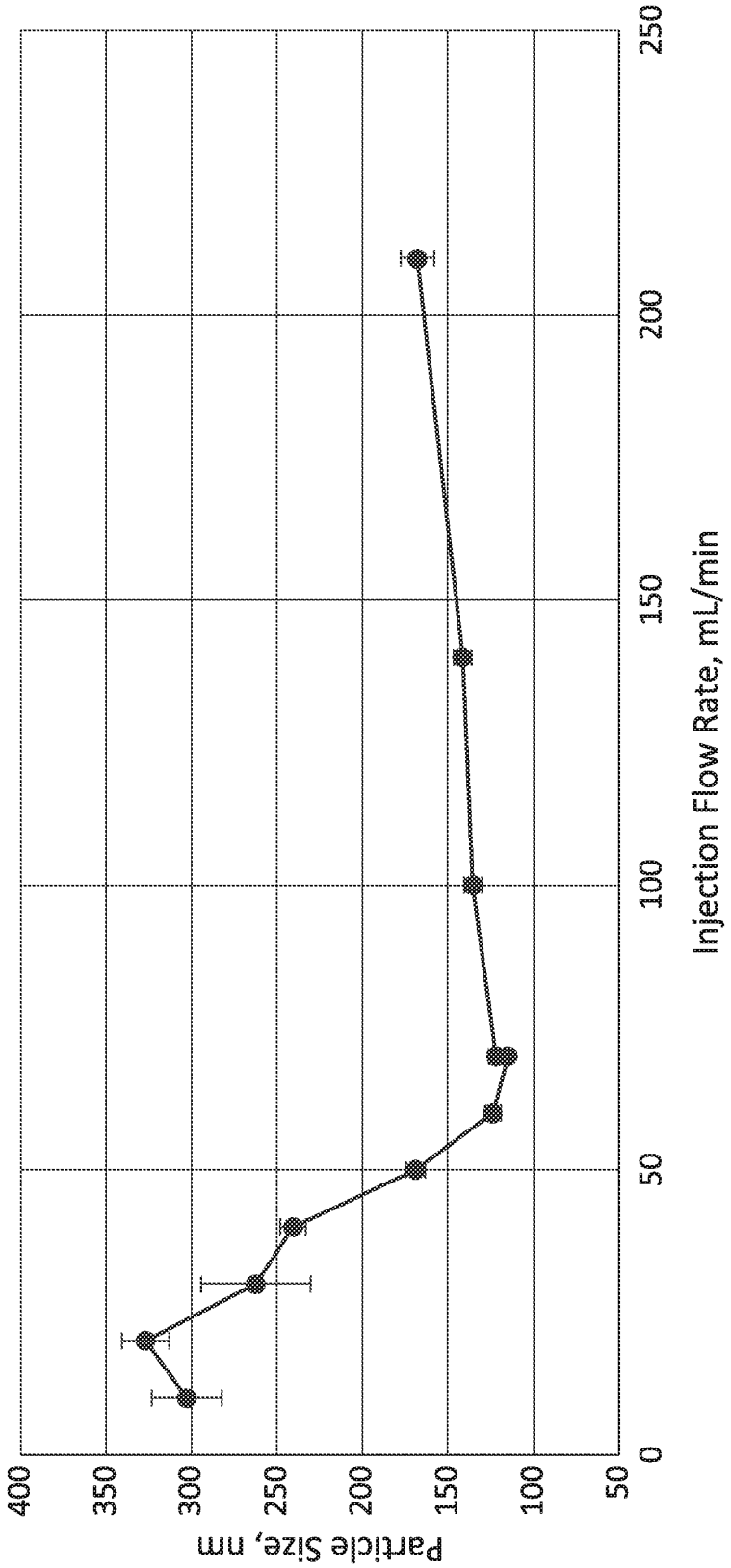

Particle Size, nm
400
350
300
250
200
150
100
50
0
50
100
150
200
250
Injection Flow Rate, mL/min

Fig. 23

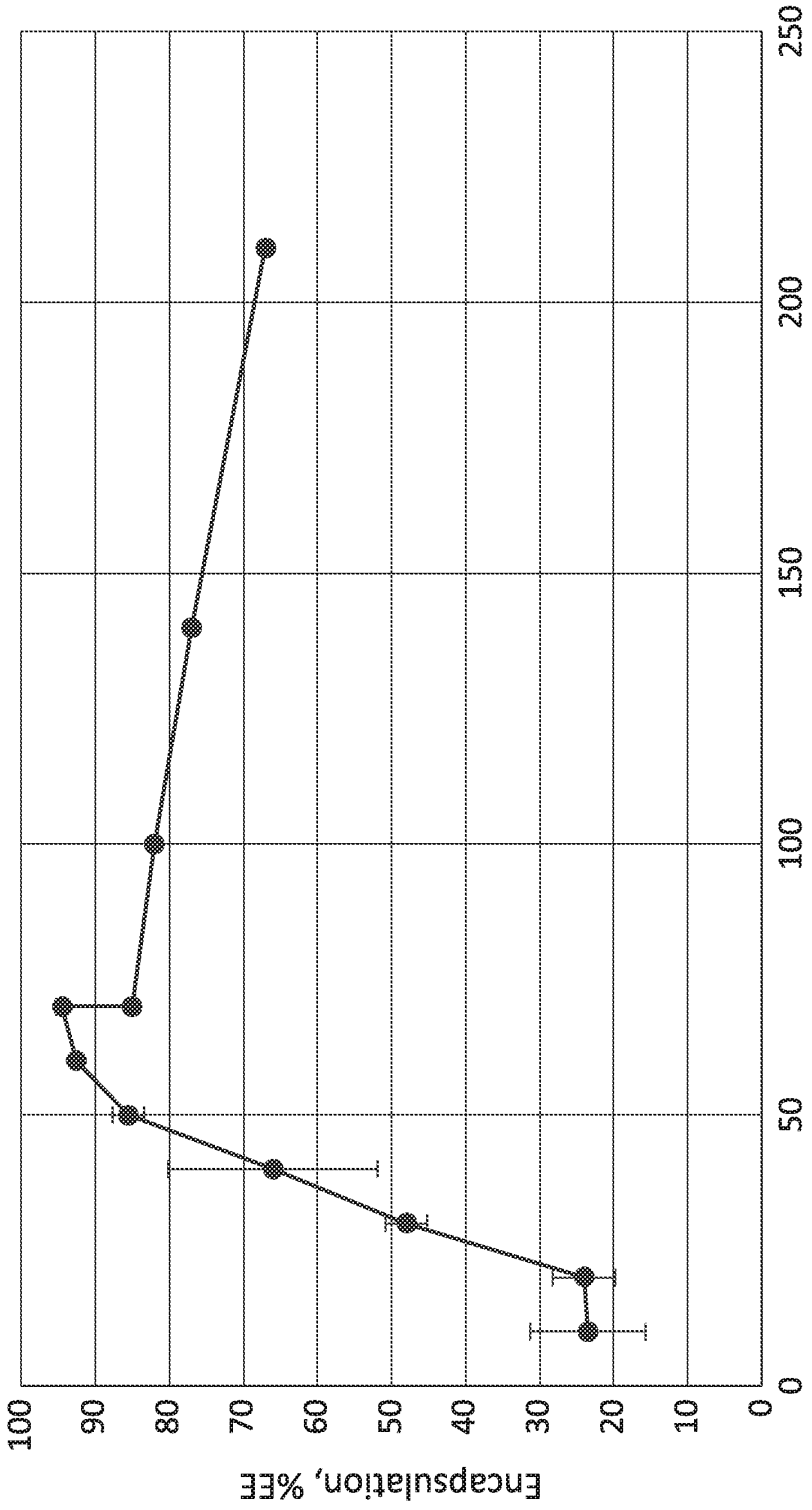

Encapsulation, %EE
100
90
80
70
60
50
40
30
20
10
0
0
50
100
150
200
250
Injection Flow Rate, mL/min

Fig. 24

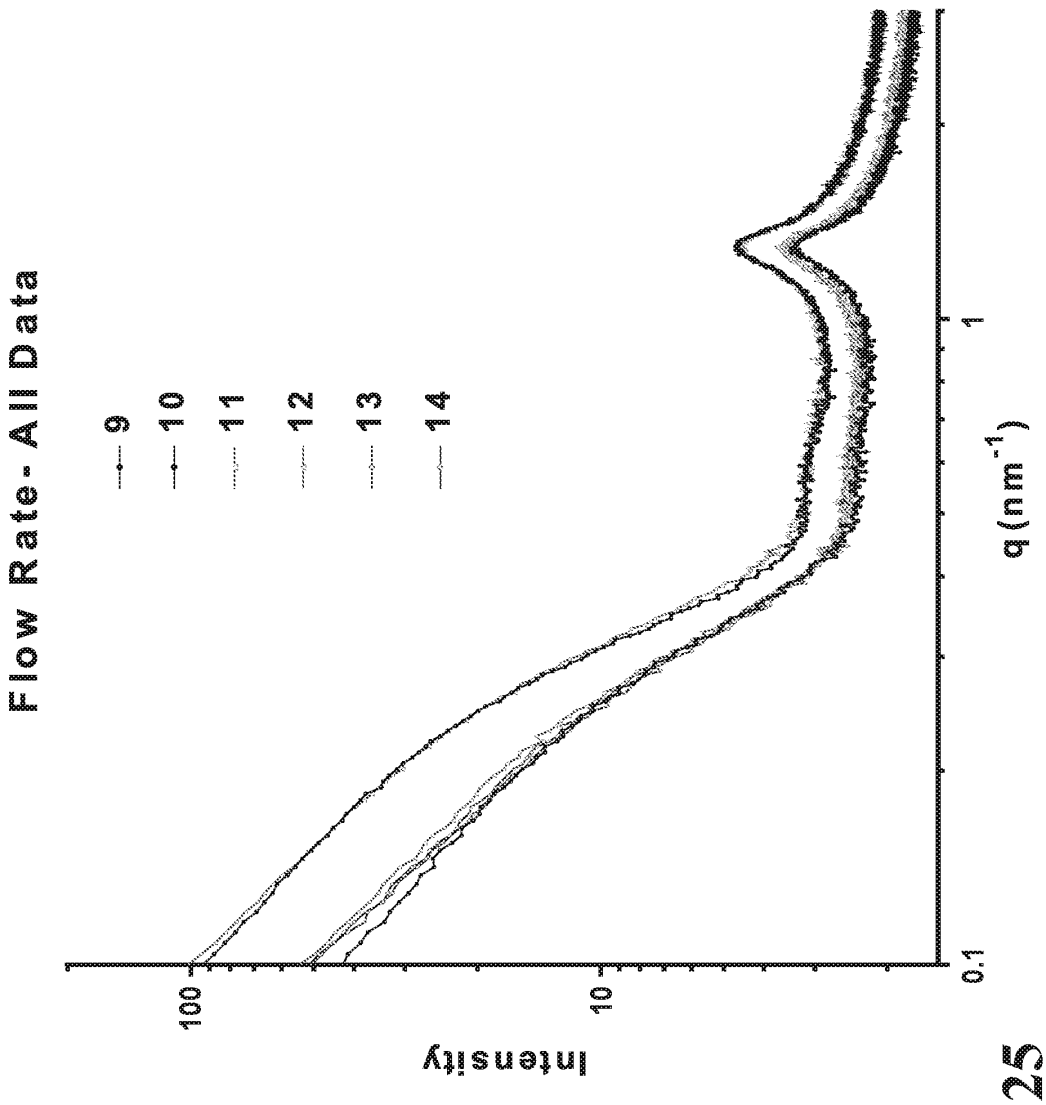


Fig. 25

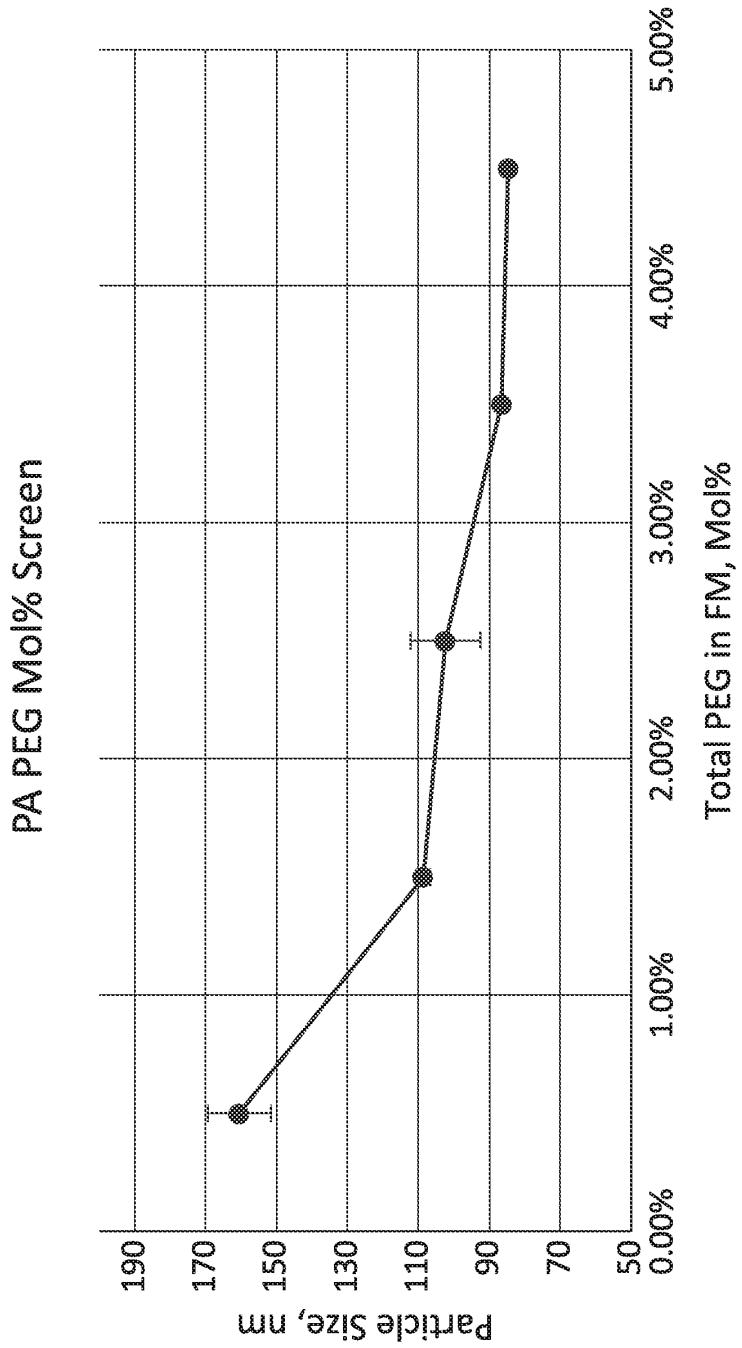

PA PEG Mol% Screen
Particle Size, nm
190
170
150
130
110
90
70
50
0.00%
1.00%
2.00%
3.00%
4.00%
5.00%
Total PEG in FM, Mol%

Fig. 26

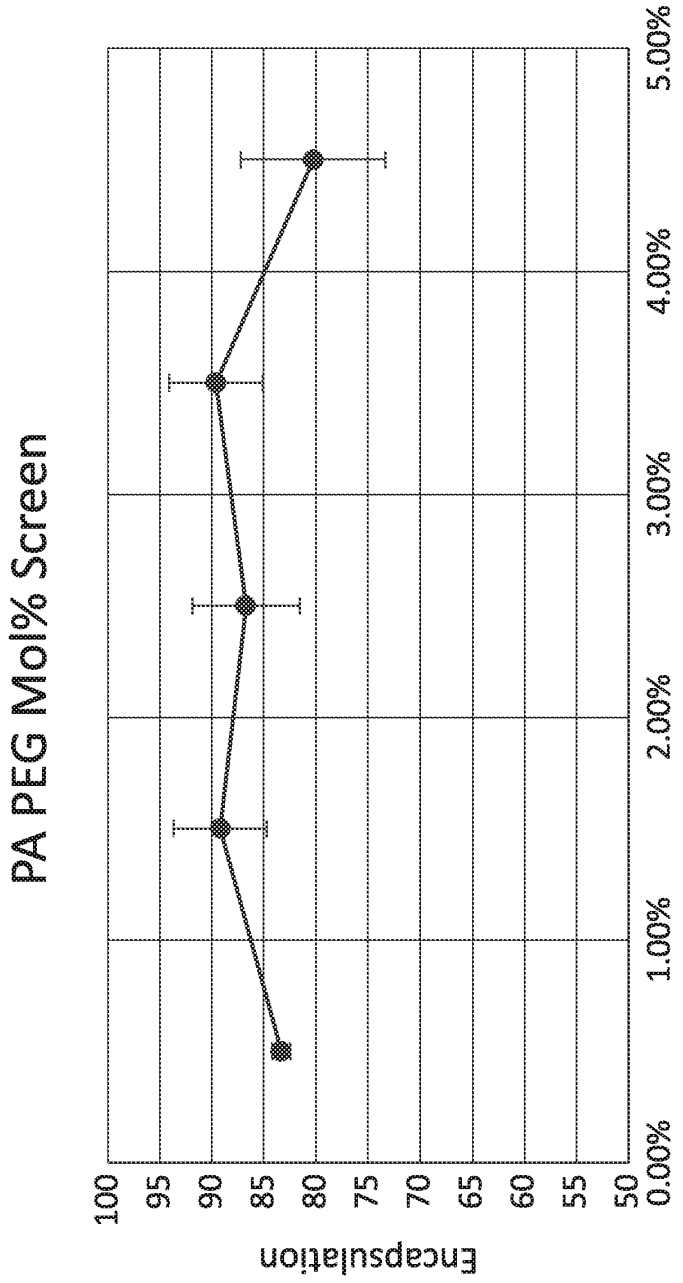

PA PEG Mol% Screen
Encapsulation
100
95
90
85
80
75
70
65
60
55
50
0.00%
1.00%
2.00%
3.00%
4.00%
5.00%
Total PEG in FM, Mol%

Fig. 27

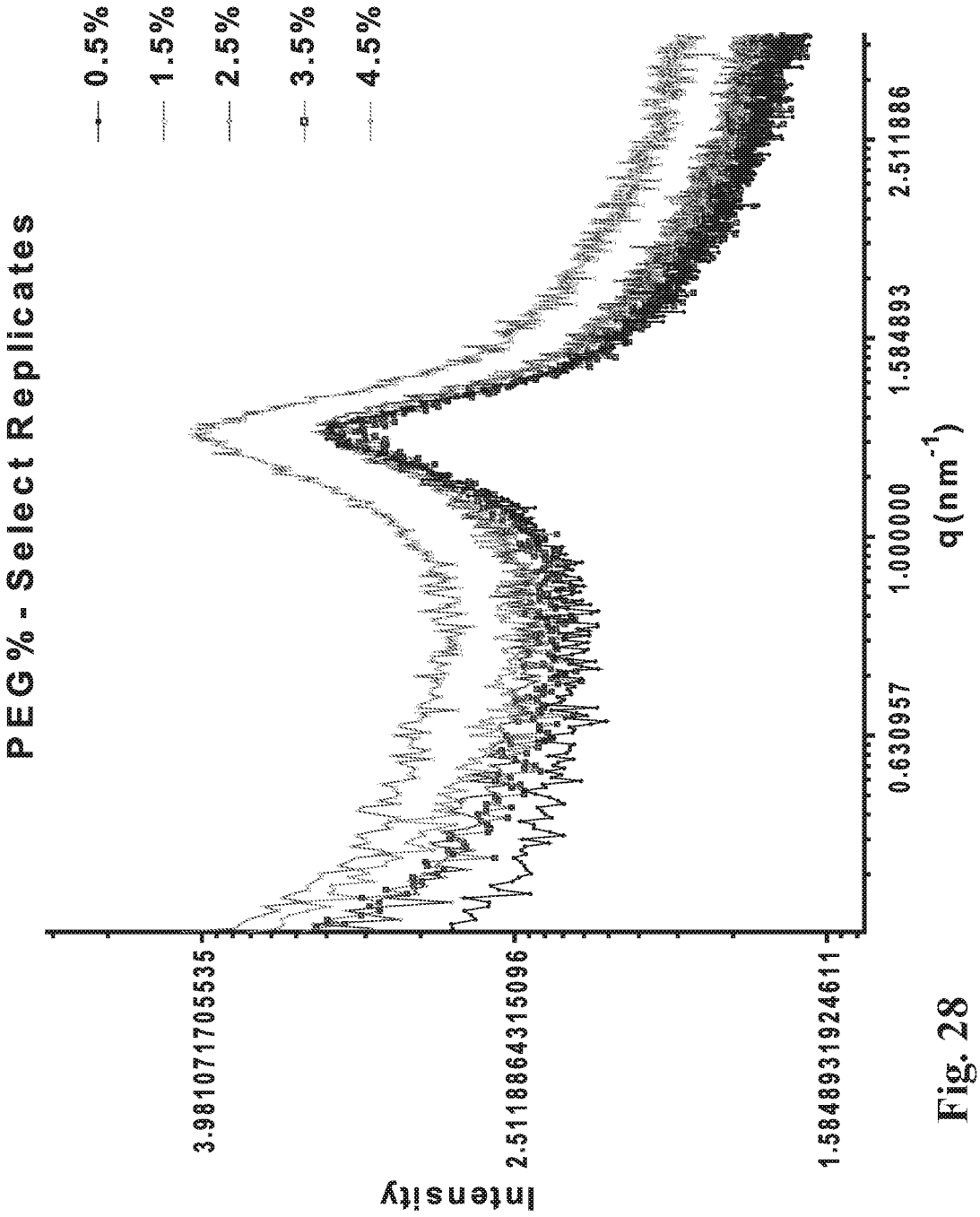

PEG% - Select Replicates
0.5%
1.5%
2.5%
3.5%
4.5%
Intensity
3.981071705535
2.511886431509 6
1.584893192461 1
0.630957
1.000000
1.584893
2.511886
q(nm-1)

Fig. 28

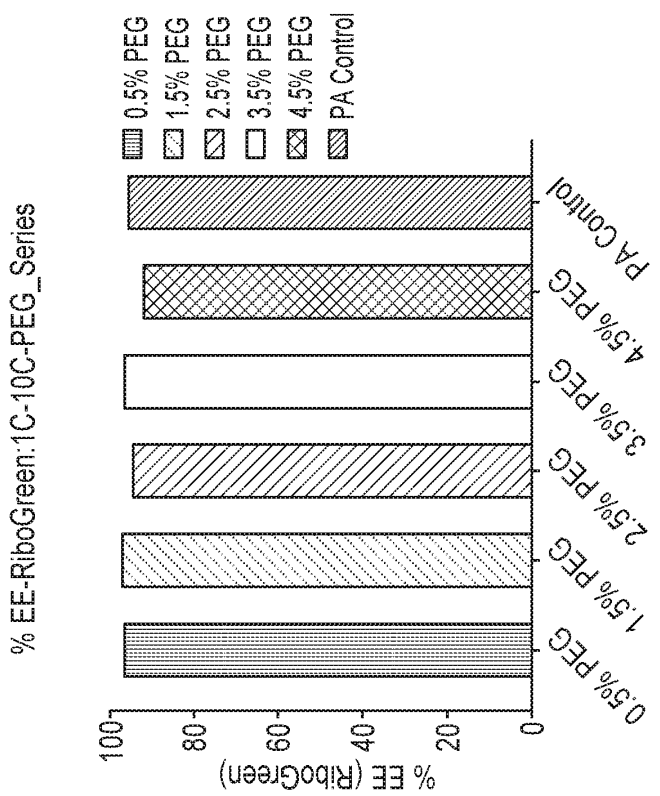


Fig. 29B

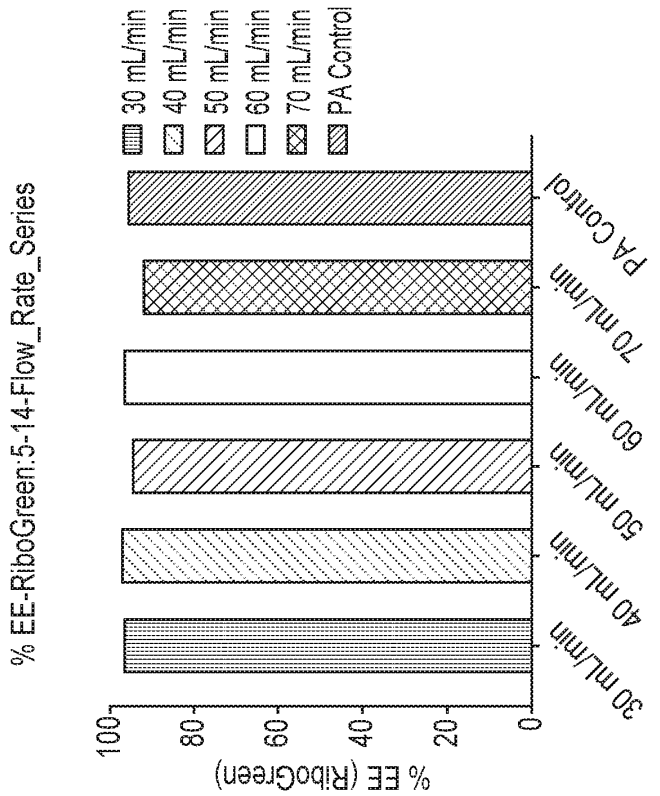


Fig. 29A

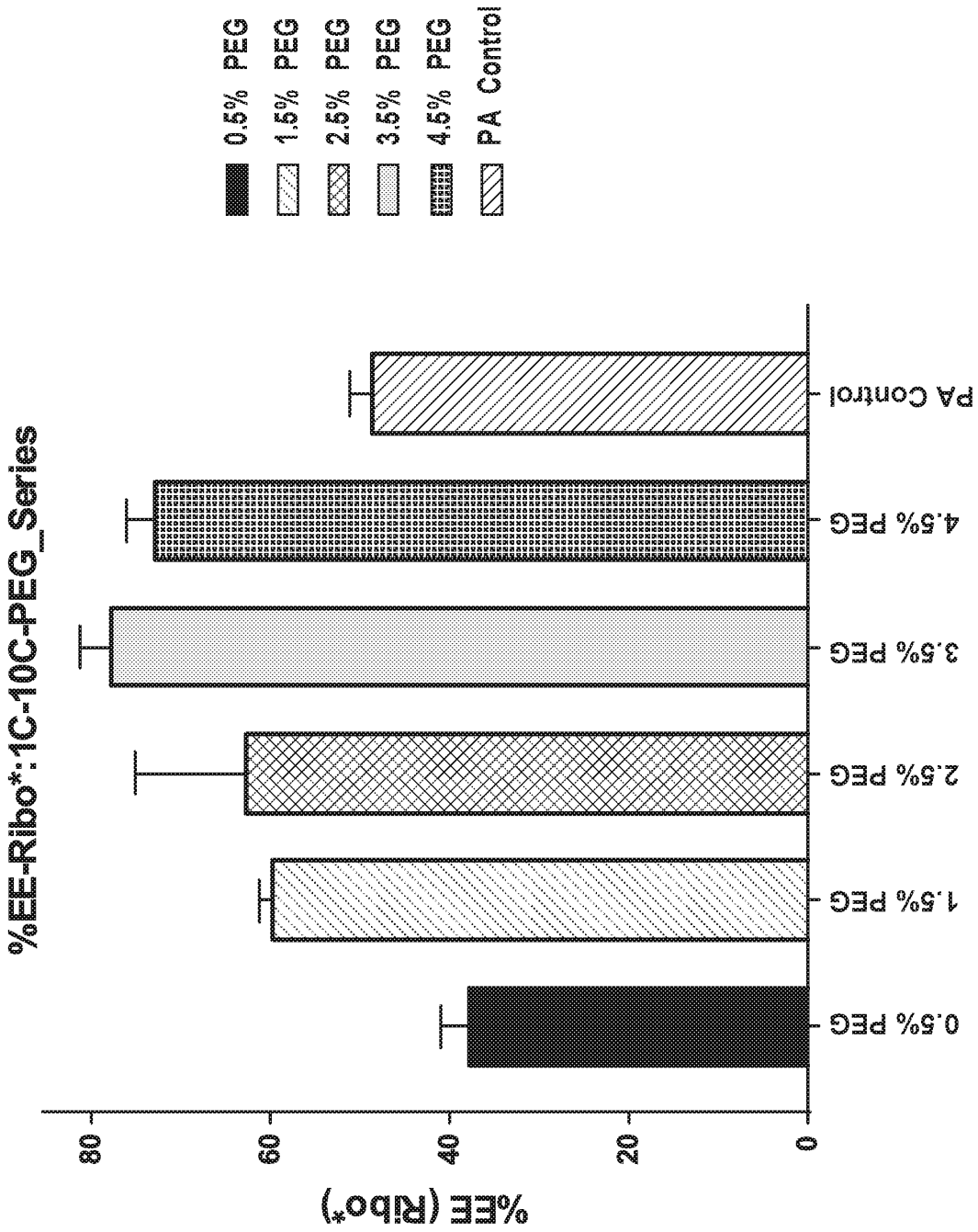

%EE-Ribo*:1C-10C-PEG_Series
0.5% PEG
1.5% PEG
2.5% PEG
3.5% PEG
4.5% PEG
PA Control
%EE (Ribo*)
0
20
40
60
80
0.5% PEG
1.5% PEG
2.5% PEG
3.5% PEG
4.5% PEG
PA Control

Fig. 30

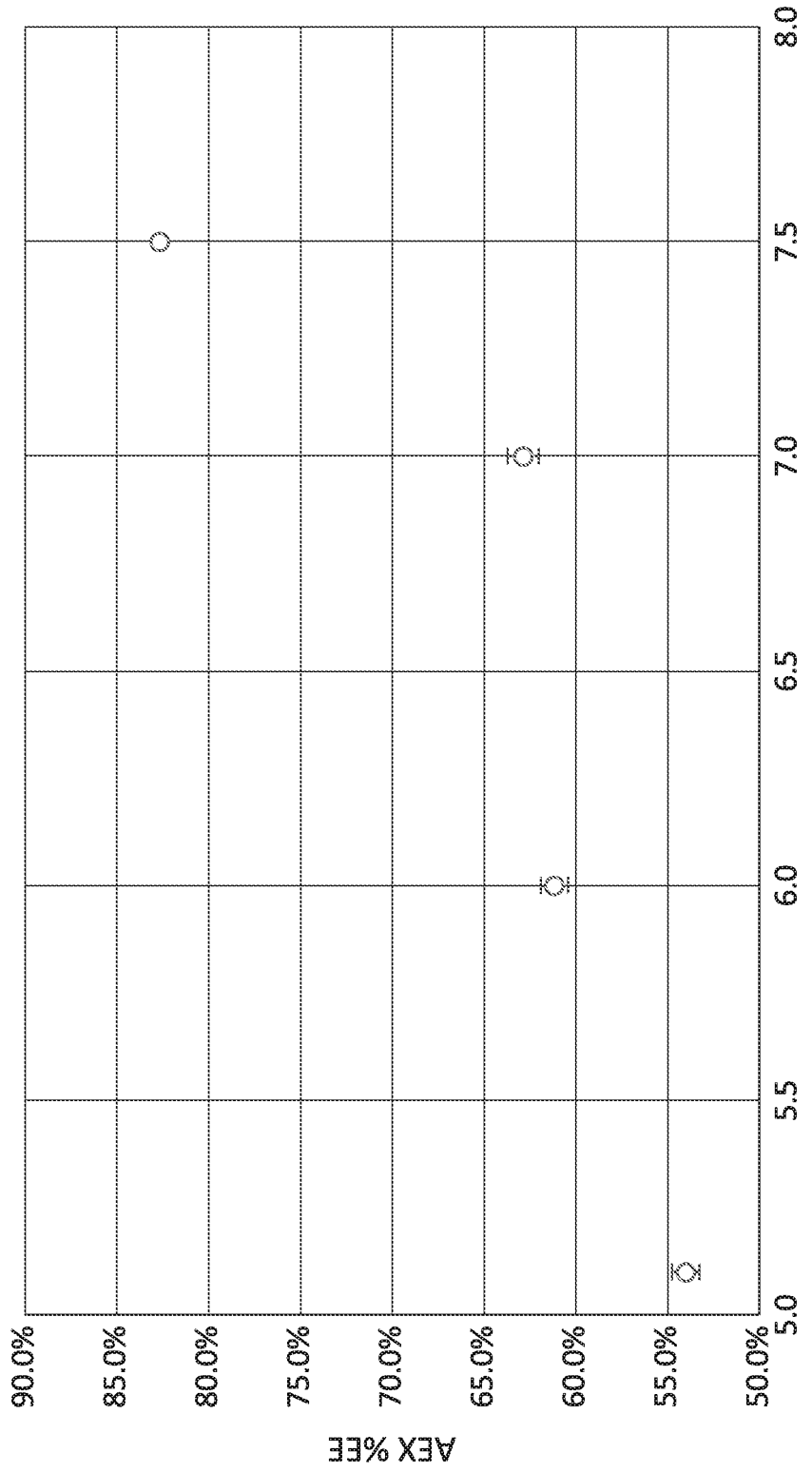

AEX %EE
90.0%
85.0%
80.0%
75.0%
70.0%
65.0%
60.0%
55.0%
50.0%
5.0
5.5
6.0
6.5
7.0
7.5
8.0
Final pH

Fig. 31

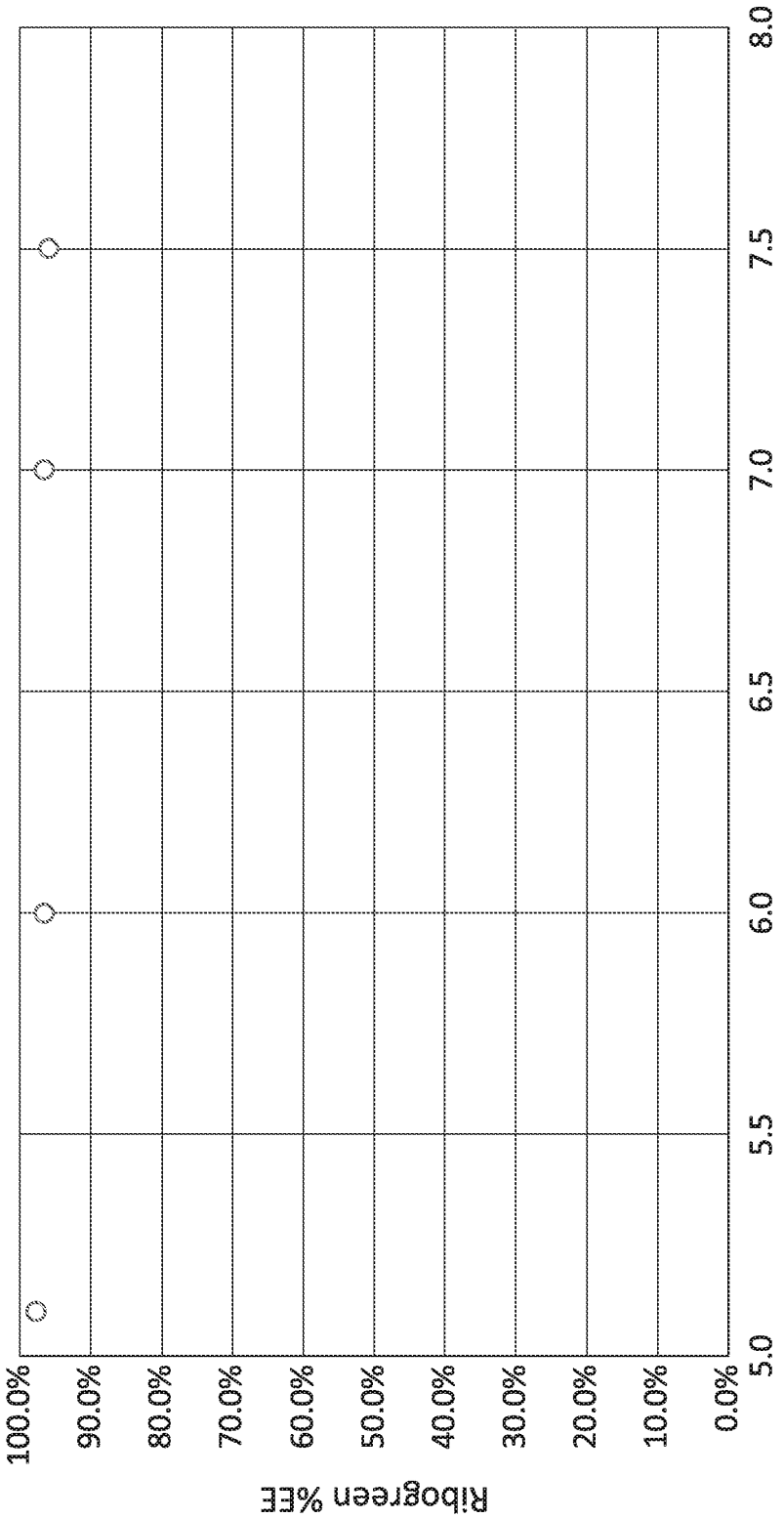

Ribogreen %EE
100.0%
90.0%
80.0%
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
0.0%
5.0
5.5
6.0
6.5
7.0
7.5
8.0
Final pH

Fig. 32

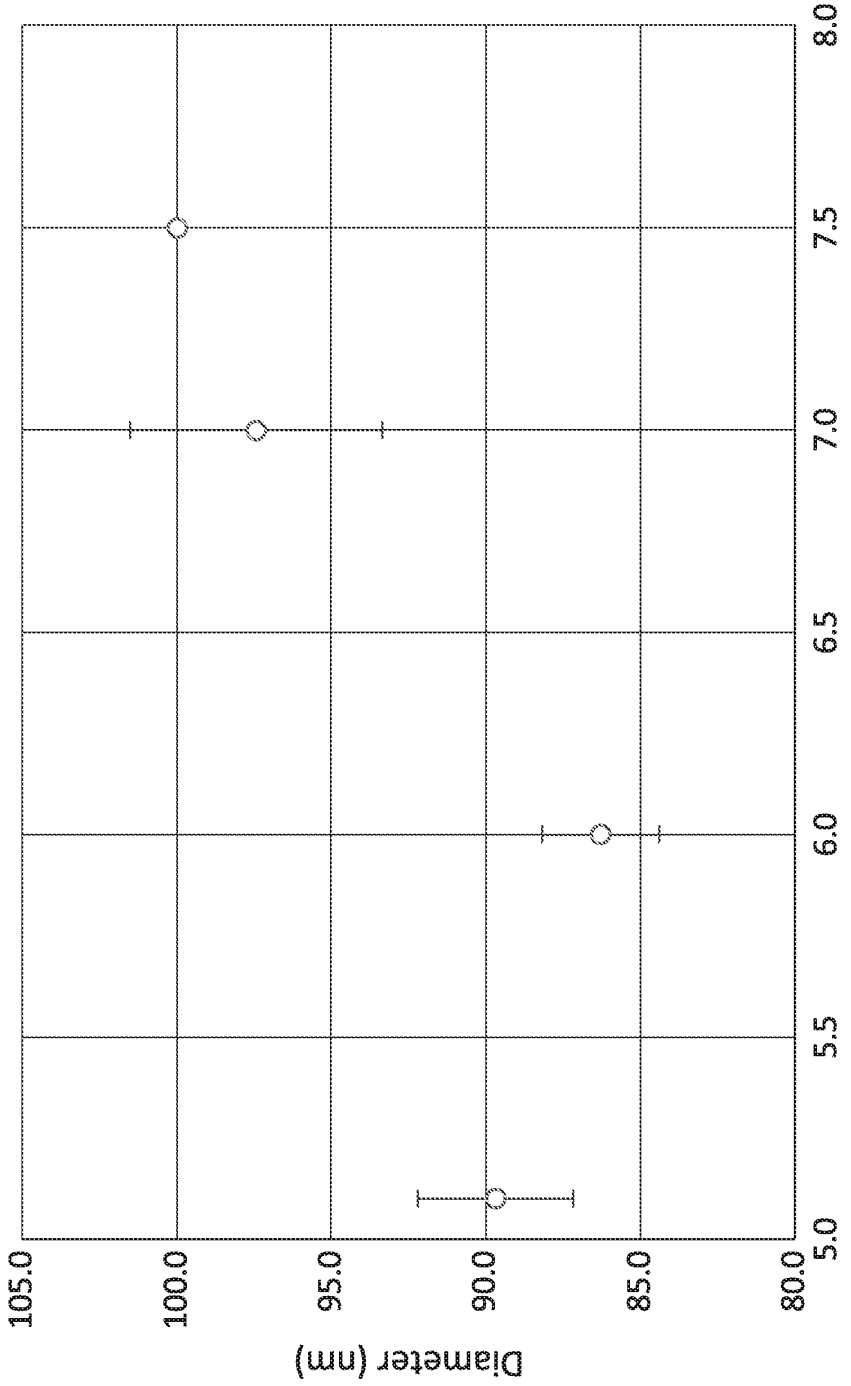

105.0
100.0
95.0
90.0
85.0
80.0
Diameter (nm)
5.0
5.5
6.0
6.5
7.0
7.5
8.0
Final pH

Fig. 33

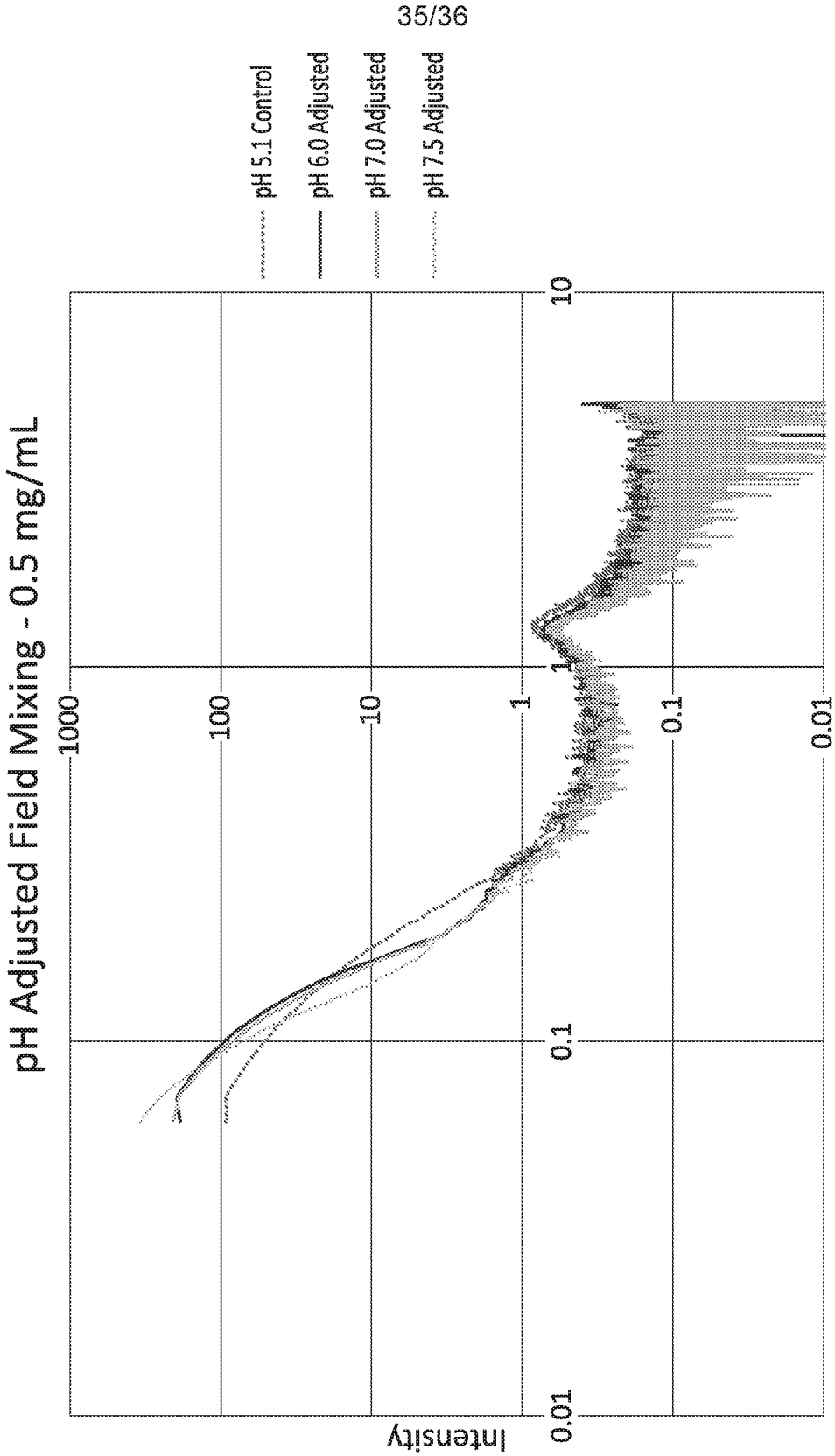

pH Adjusted Field Mixing - 0.5 mg/mL
pH 5.1 Control
pH 6.0 Adjusted
pH 7.0 Adjusted
pH 7.5 Adjusted
Intensity
1000
100
10
1
0.1
0.01
10
1
0.1
0.01
q (nm-1)

Fig. 34

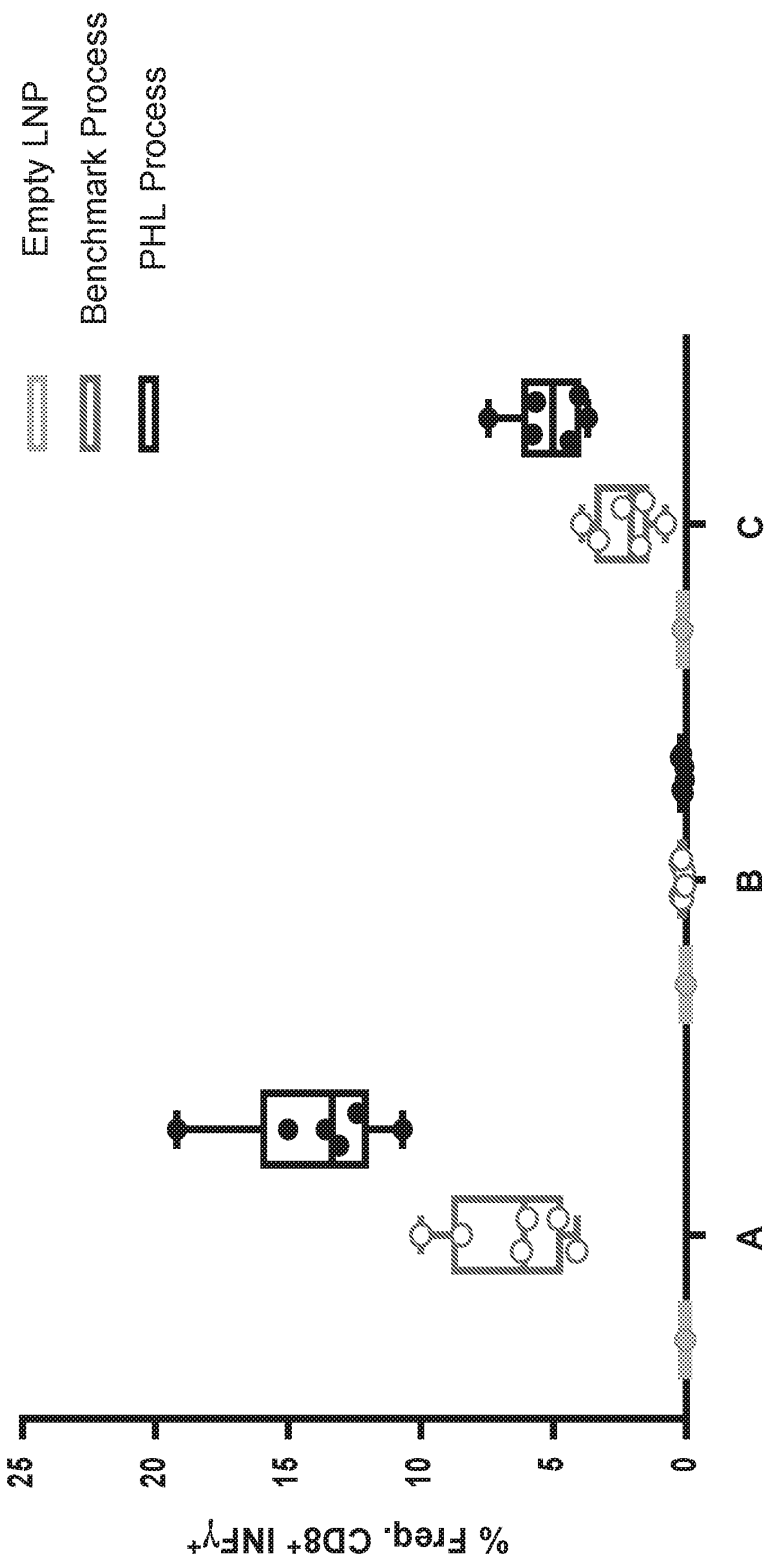

Empty LNP
Benchmark Process
PHL Process
% Freq. CD8+ INFγ+
25
20
15
10
5
0
A
B
C

Fig. 35