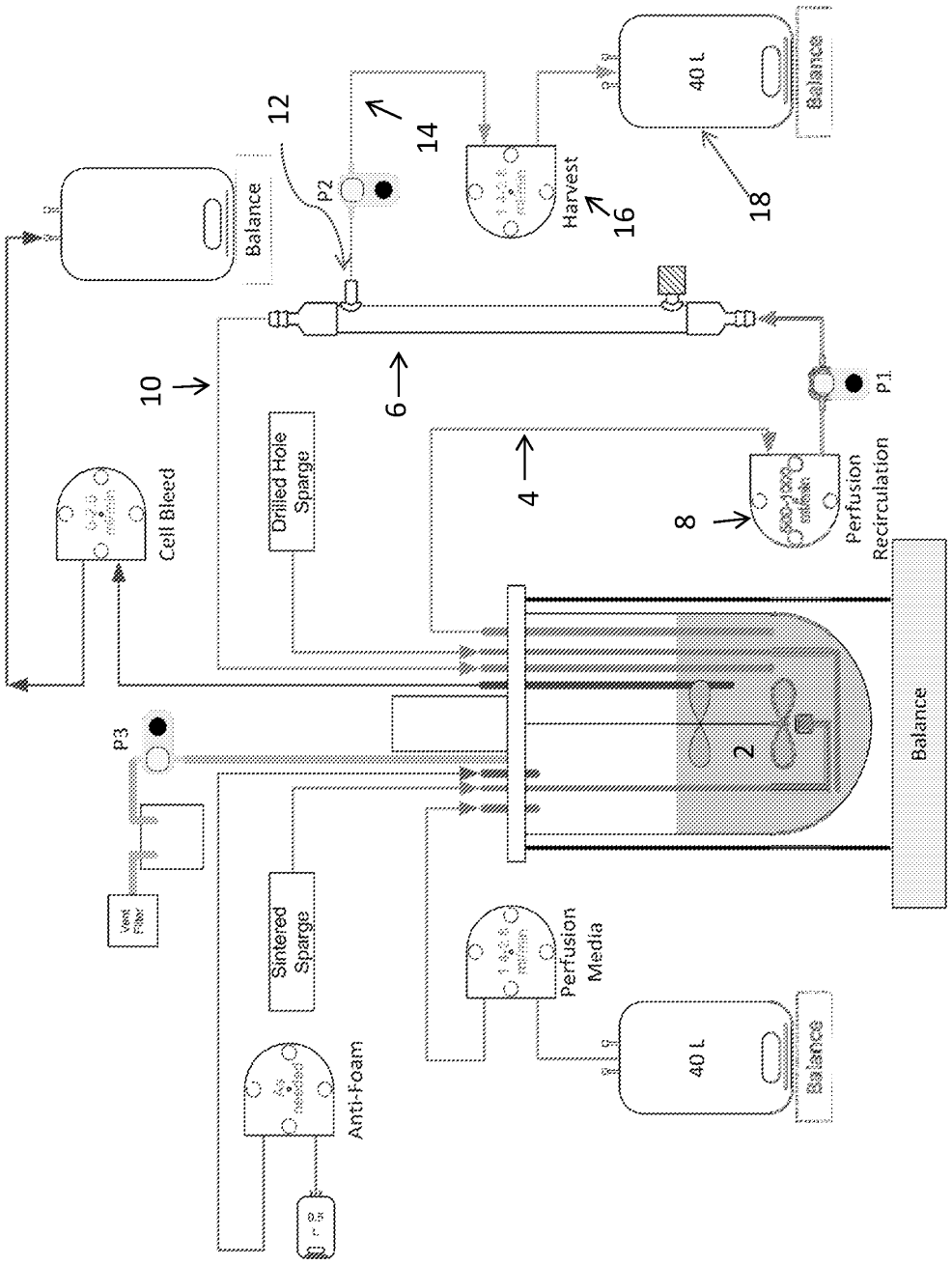
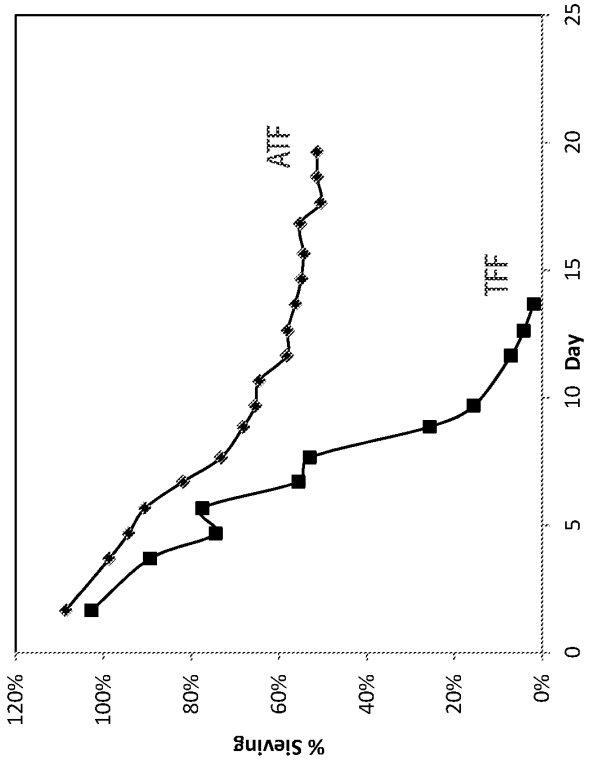

40 L
Balance
12
14
P2
Harvest
16
18
Balance
10
6
P1
Drilled Hole Sparge
4
8
Cell Bleed
Perfusion Recirculation
P3
2
Balance
Vent Filter
Sintered Sparge
Perfusion Media
Anti-Foam
40 L
Balance

FIG. 1


% Sieving
120%
100%
80%
60%
40%
20%
0%
0
5
10
15
20
25
Day
ATF
TFF

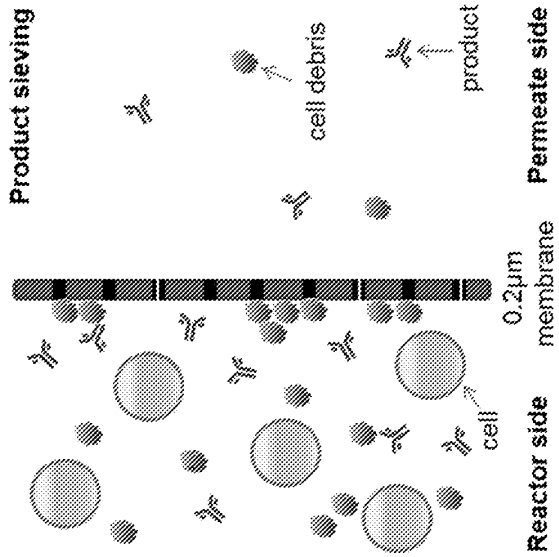

Product sieving
cell debris
product
Permeate side
0.2µm
membrane
cell
Reactor side

FIG. 2

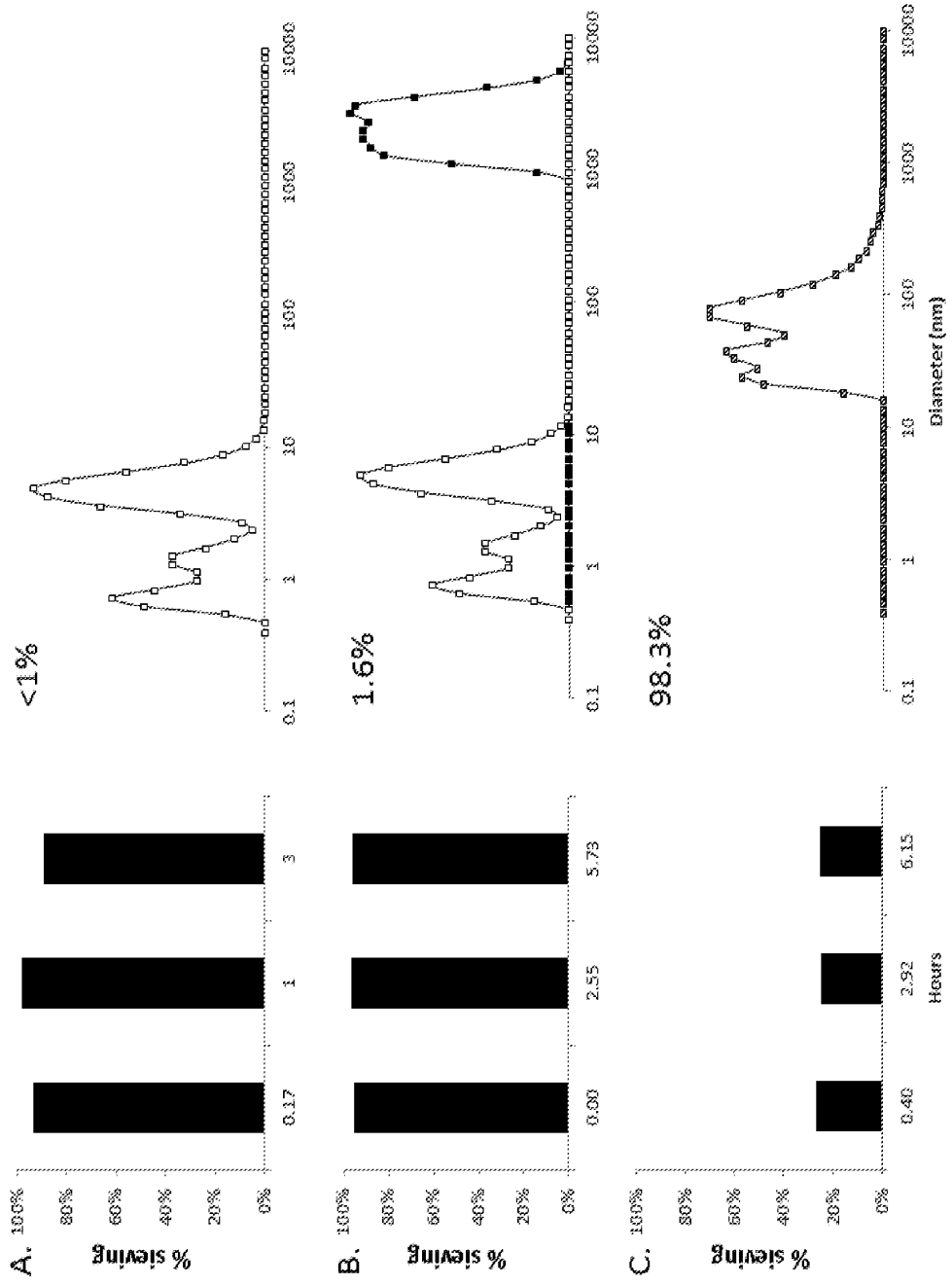

A.
% sieving
100%
80%
60%
40%
20%
0%
0.17
1
3
Hours
<1%
0.1
1
10
100
1000
10000
B.
% sieving
100%
80%
60%
40%
20%
0%
0.00
2.55
5.73
Hours
1.6%
0.1
1
10
100
1000
10000
C.
% sieving
100%
80%
60%
40%
20%
0%
0.40
2.92
6.15
Hours
98.3%
0.1
1
10
100
1000
10000
Diameter (nm)

FIG. 3

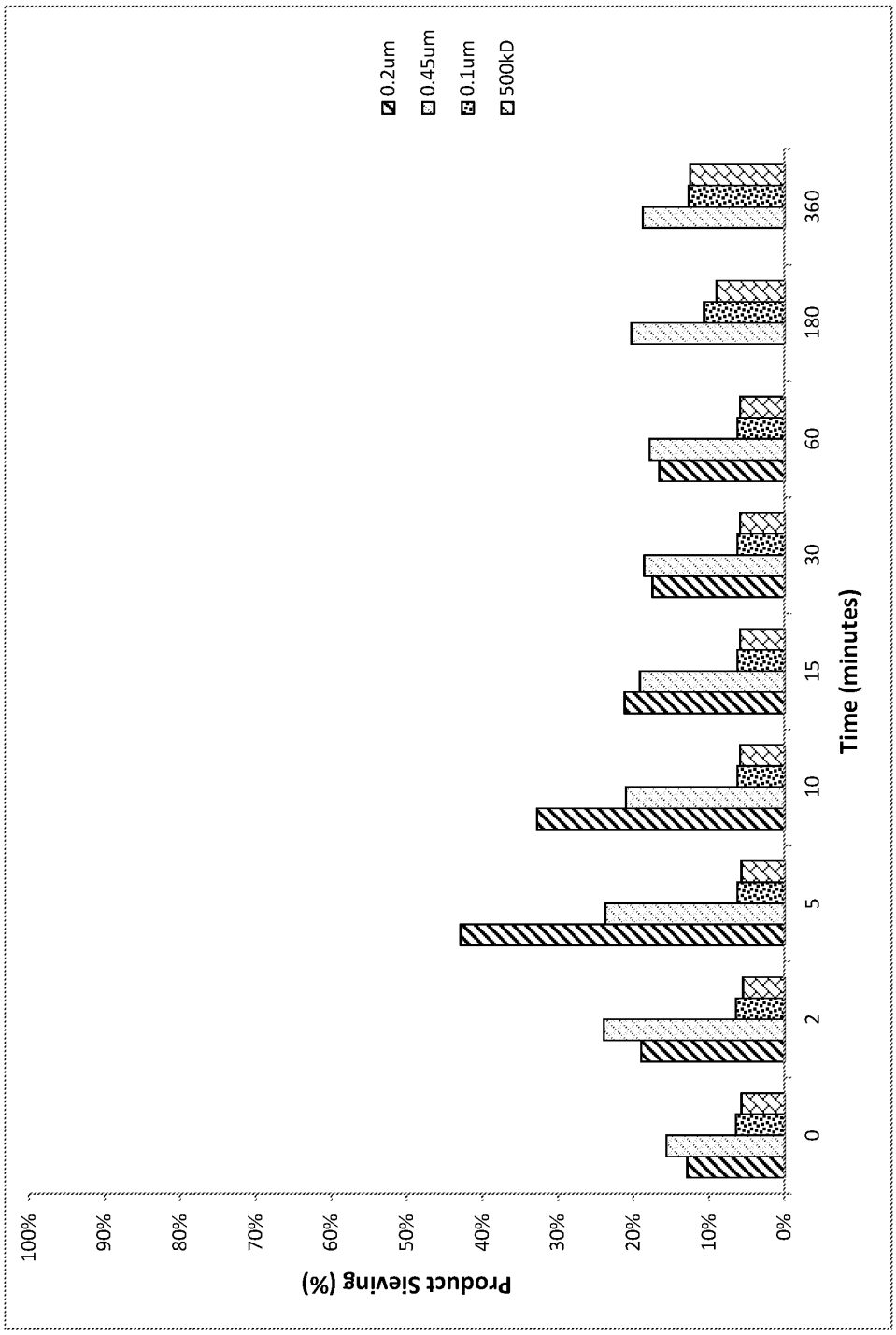

0.2um
0.45um
0.1um
500kD
Product Sieving (%)
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
2
5
10
15
30
60
180
360
Time (minutes)

FIG. 4

A)

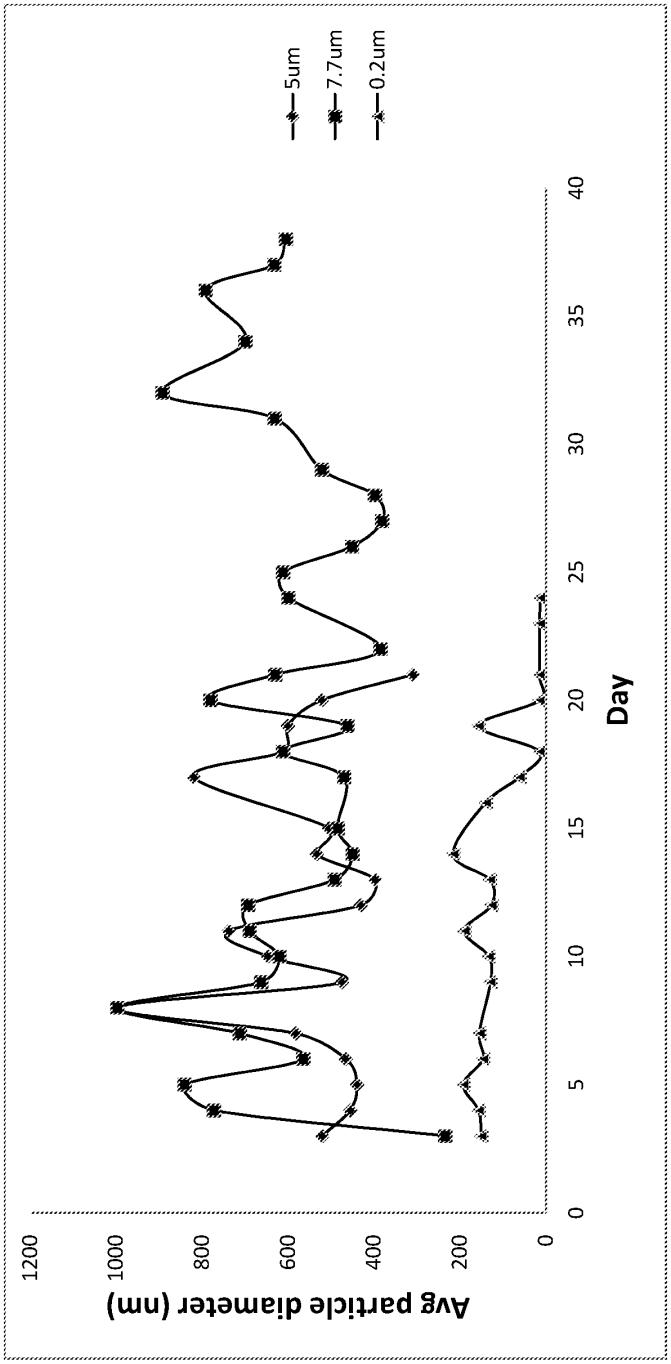

Avg particle diameter (nm)
1200
1000
800
600
400
200
0
0
5
10
15
20
25
30
35
40
Day
5um
7.7um
0.2um

FIG. 5

B)

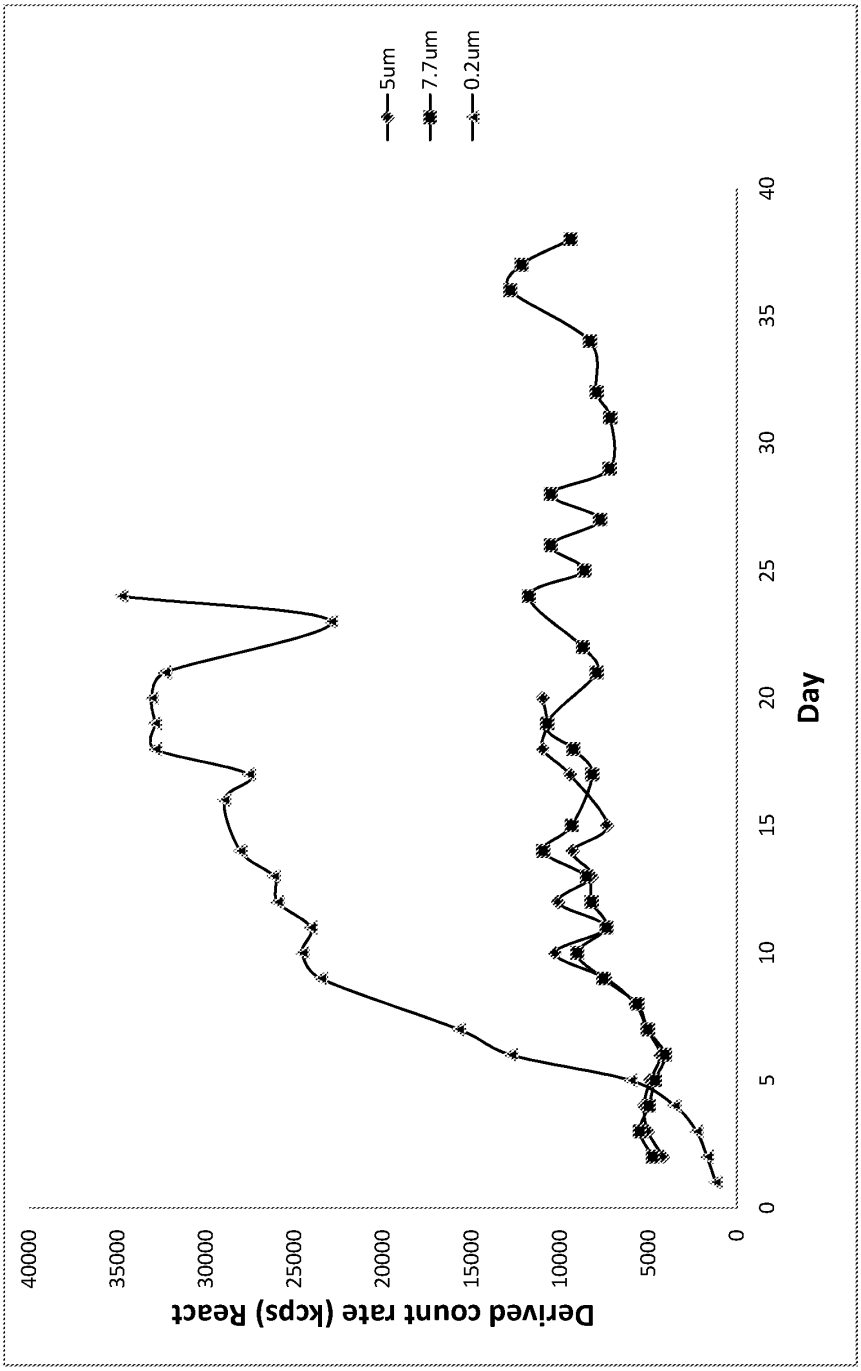

5um
7.7um
0.2um
Derived count rate (kcps) React
40000
35000
30000
25000
20000
15000
10000
5000
0
0
5
10
15
20
25
30
35
40
Day

FIG. 5

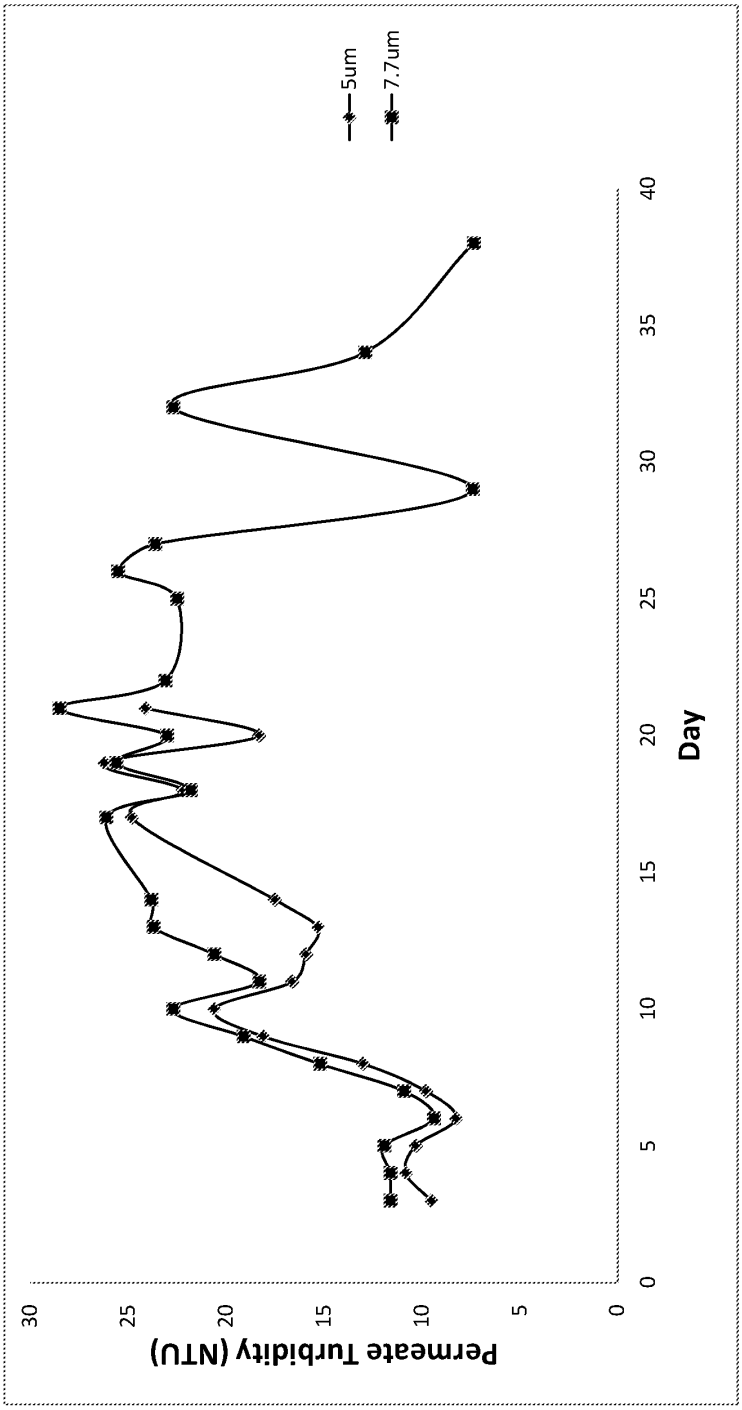


FIG. 6

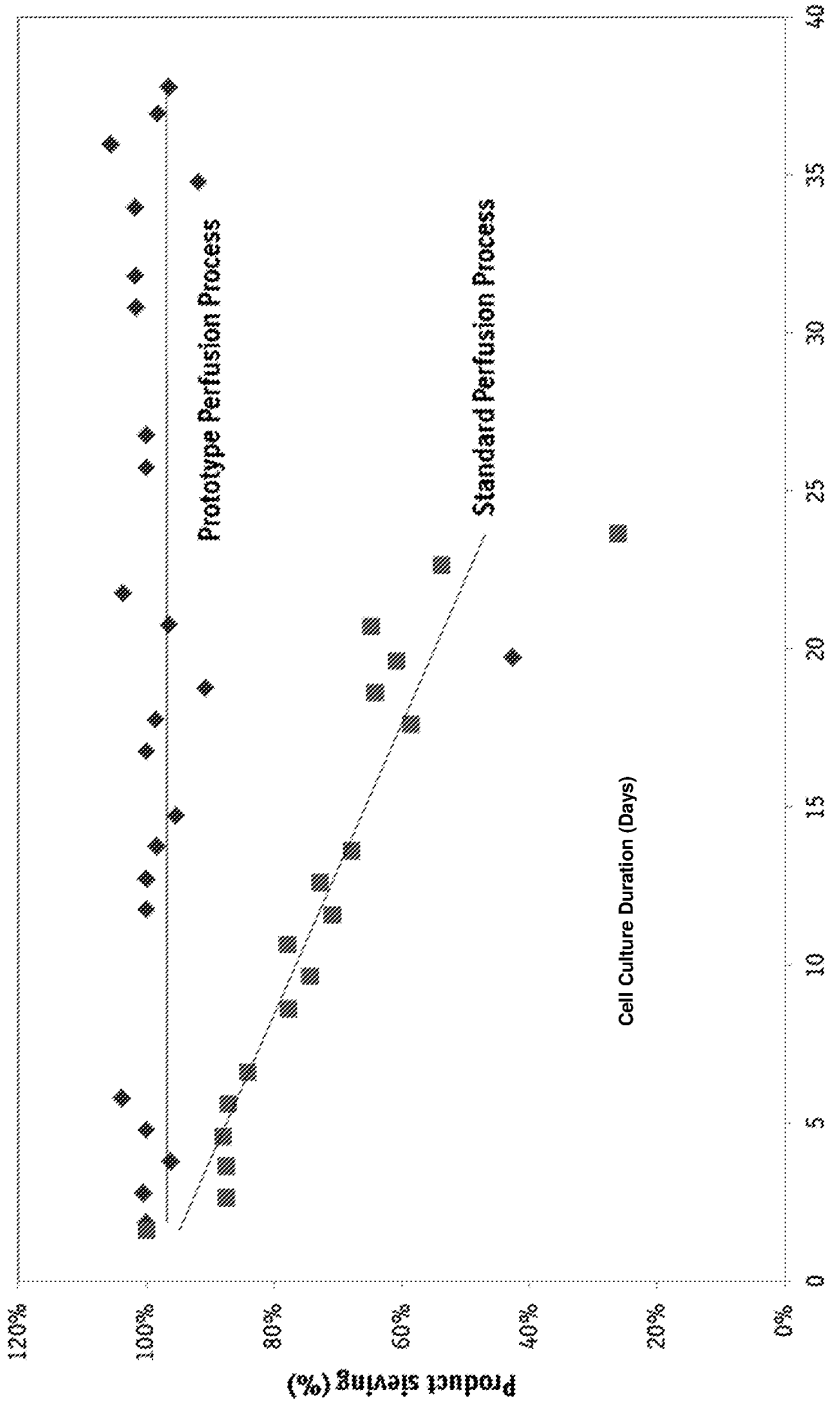

Prototype Perfusion Process
Standard Perfusion Process
Cell Culture Duration (Days)
Product sieving (%)
120%
100%
80%
60%
40%
20%
0%
0
5
10
15
20
25
30
35
40

FIG. 7

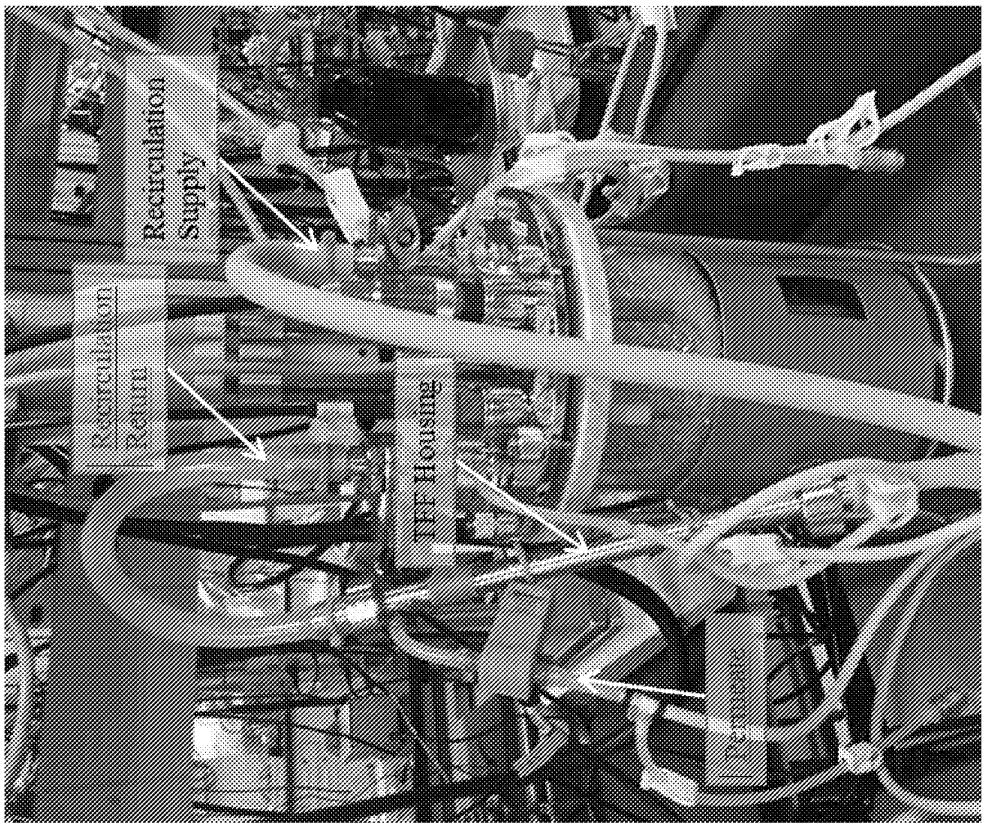


FIG. 8

A)

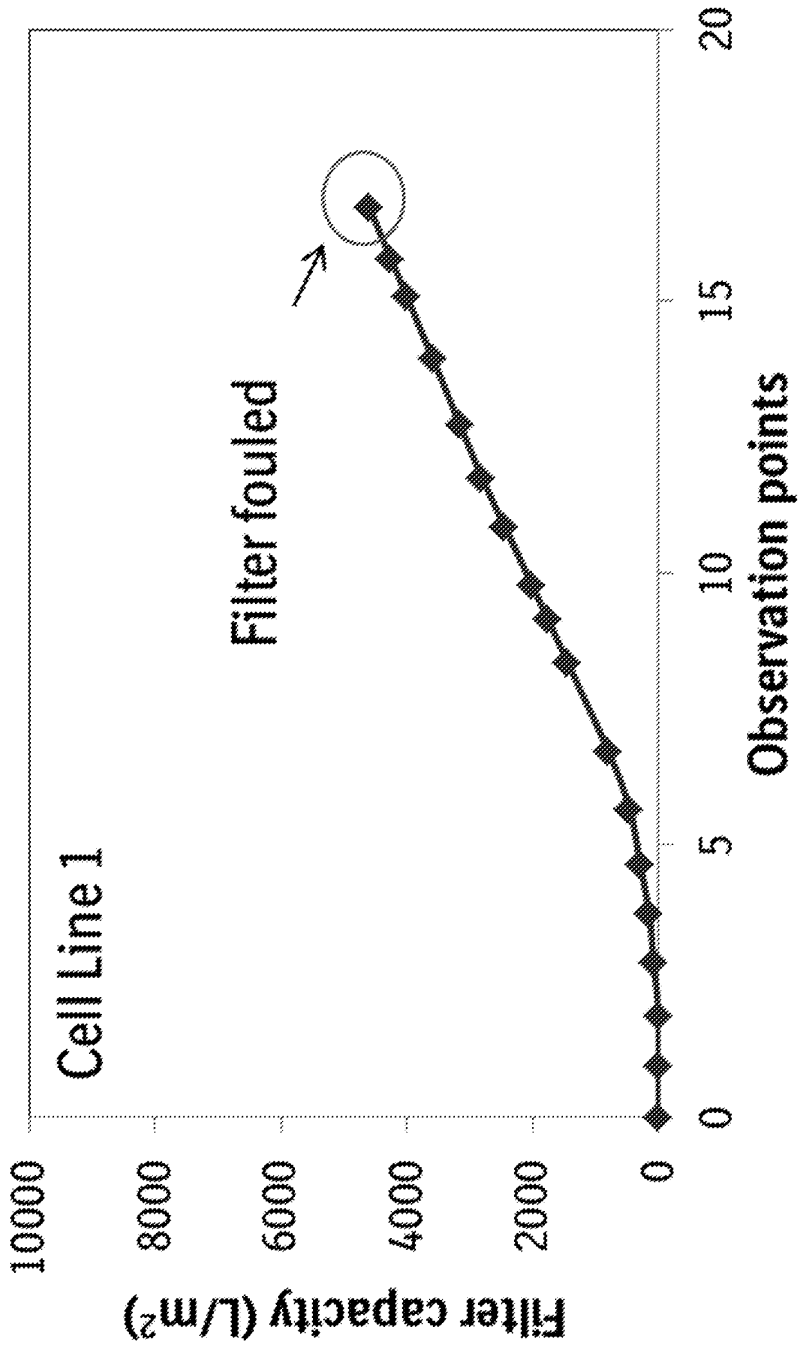

Filter capacity (L/m²)
10000
8000
6000
4000
2000
0
0
5
10
15
20
Observation points
Cell Line 1
Filter fouled

FIG. 9

B)

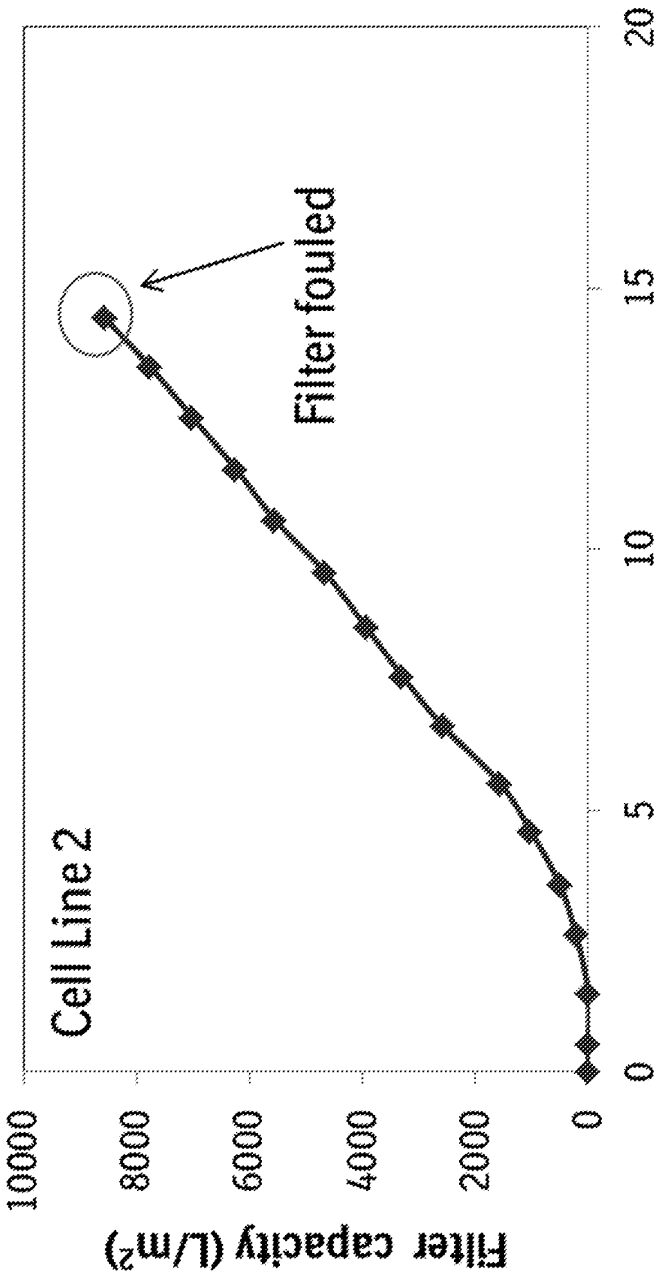

Cell Line 2
Filter fouled
Filter capacity (L/m²)
Observation points
10000
8000
6000
4000
2000
0
0
5
10
15
20

FIG. 9

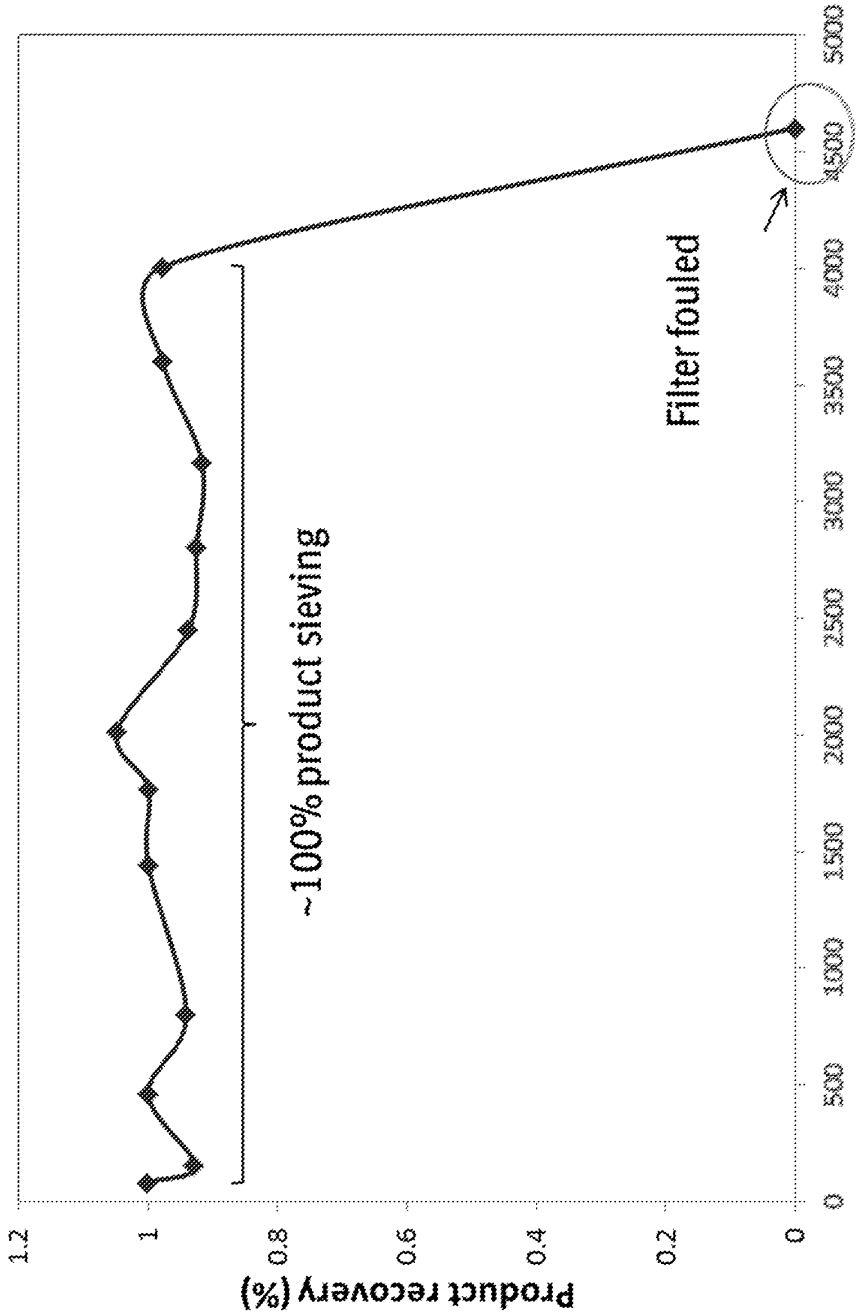

Product recovery (%)
1.2
1
0.8
0.6
0.4
0.2
0
0
500
1000
1500
2000
2500
3000
3500
4000
4500
5000
Total volume filtrate/filter area (L/m²)
~100% product sieving
Filter fouled

FIG. 10