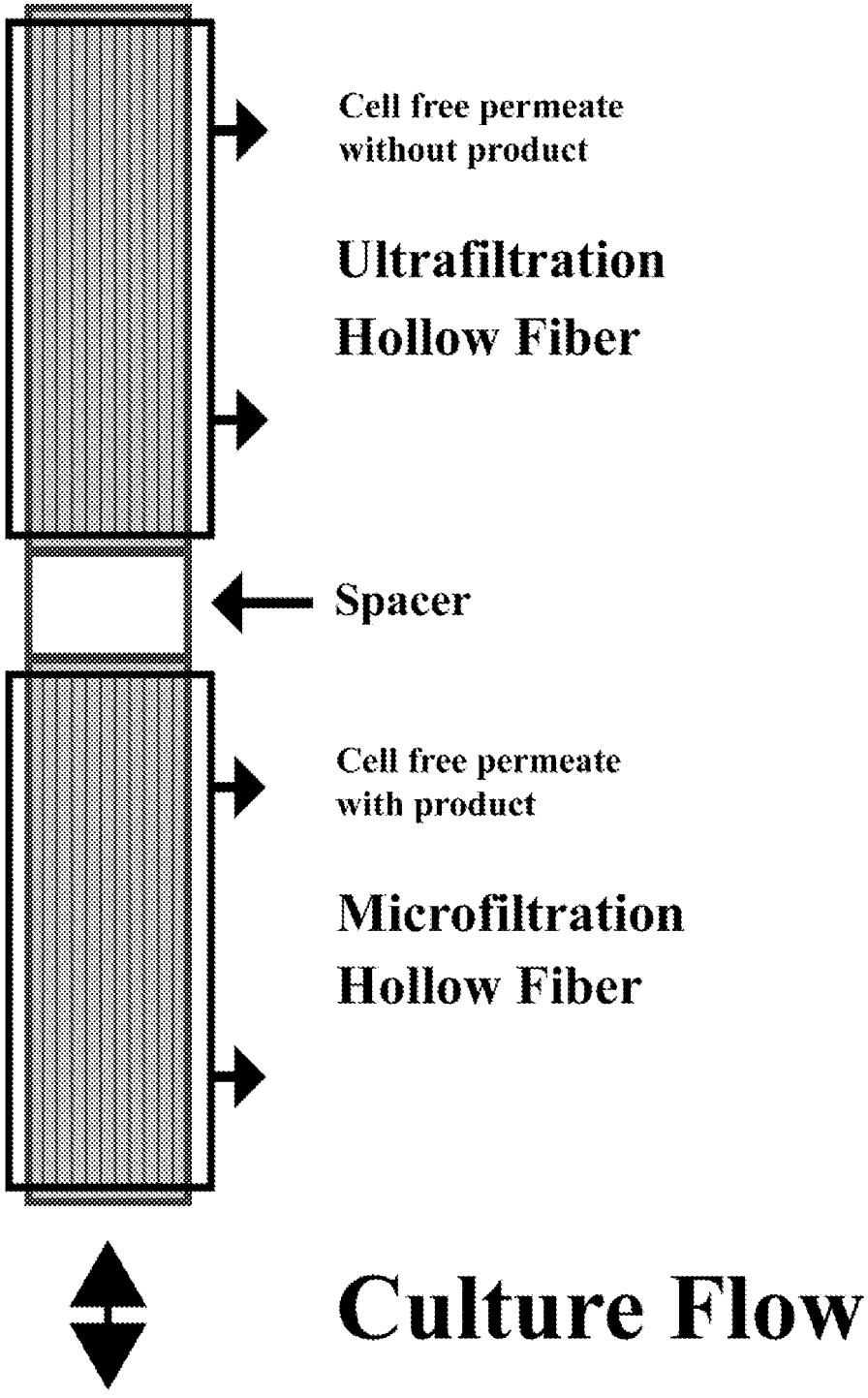

Cell free permeate
without product
Ultrafiltration
Hollow Fiber
Spacer
Cell free permeate
with product
Microfiltration
Hollow Fiber
Culture Flow

Figure 1

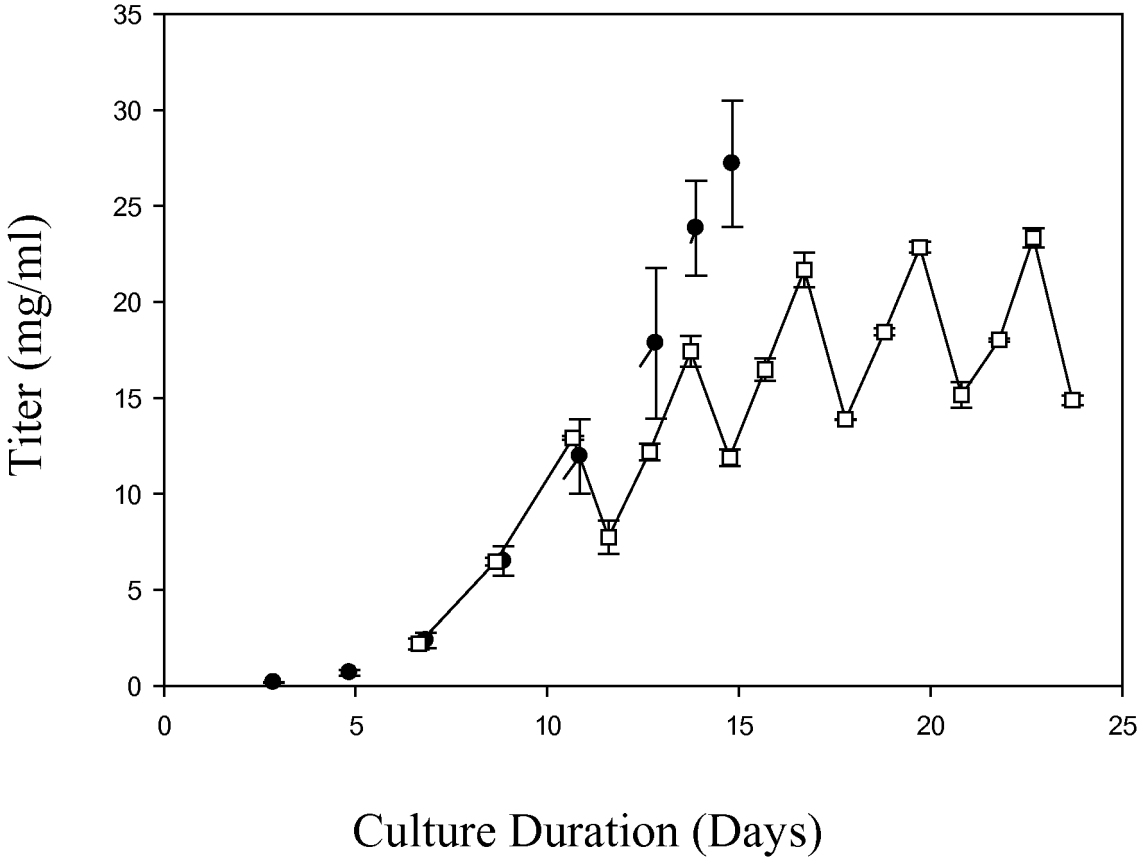

Titer (mg/ml)
35
30
25
20
15
10
5
0
0
5
10
15
20
25
Culture Duration (Days)

Figure 2

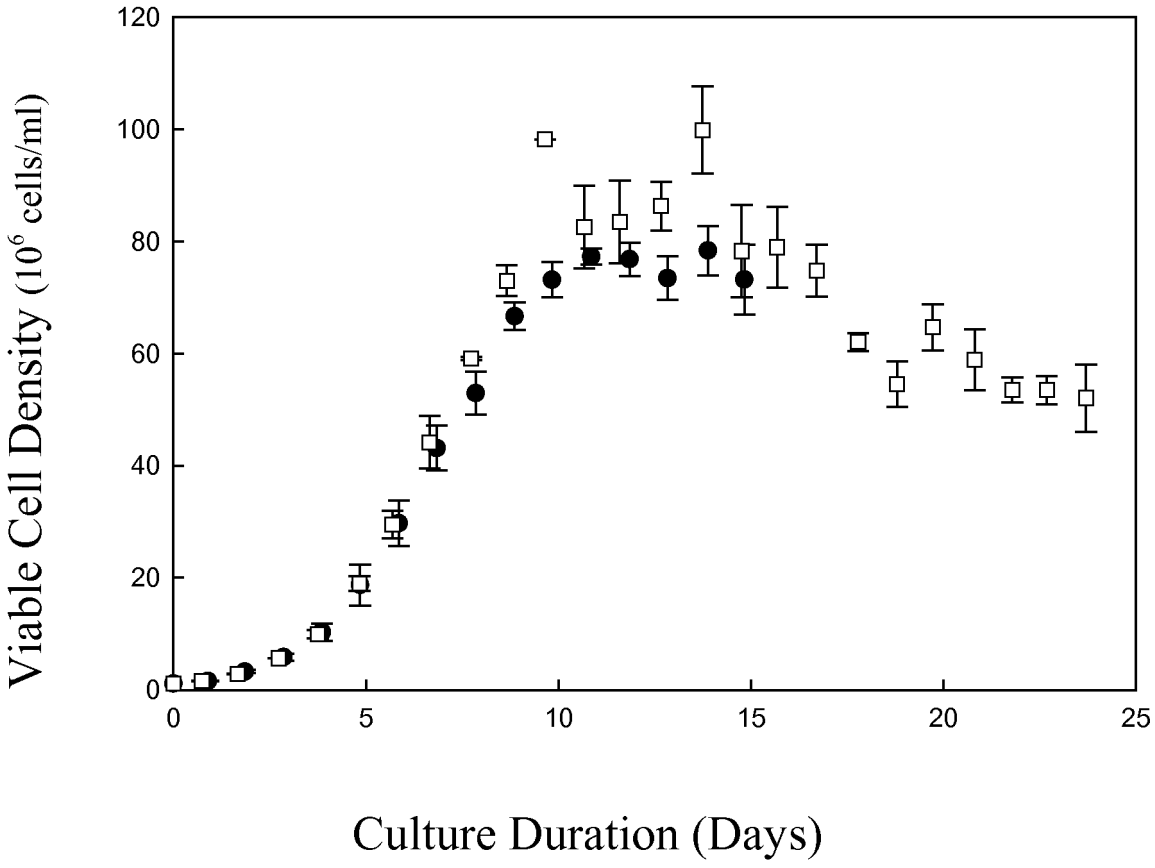

Viable Cell Density (10^6 cells/ml)
120
100
80
60
40
20
0
0
5
10
15
20
25
Culture Duration (Days)

Figure 3

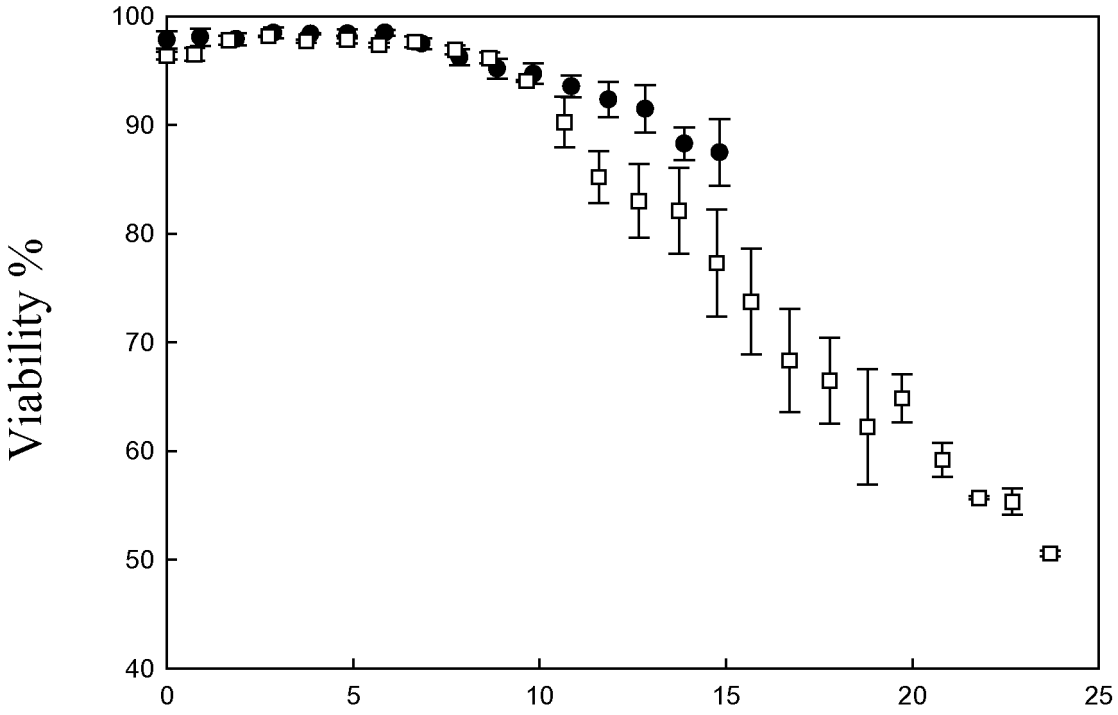

Viability %
100
90
80
70
60
50
40
0
5
10
15
20
25
Culture Duration (Days)

Figure 4

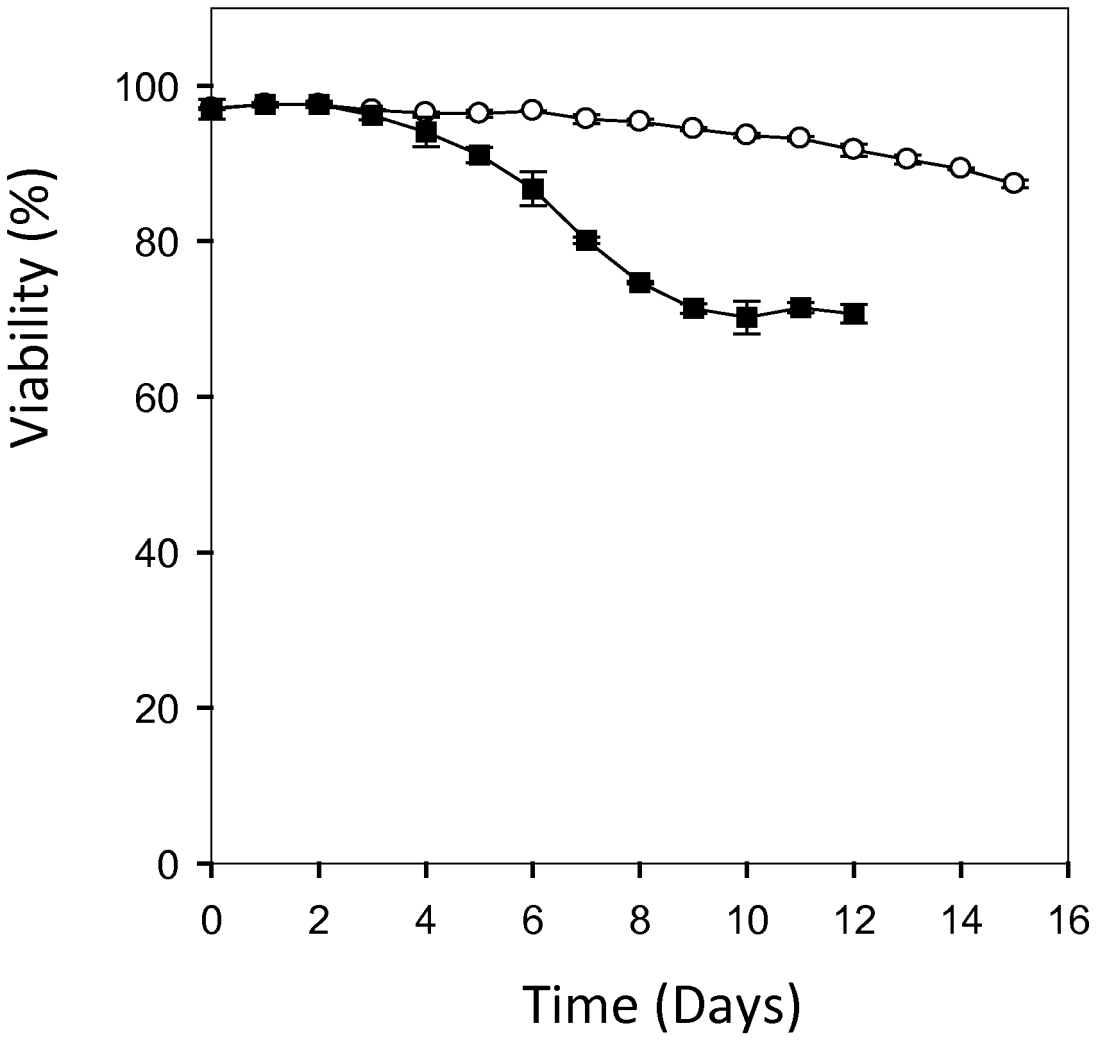
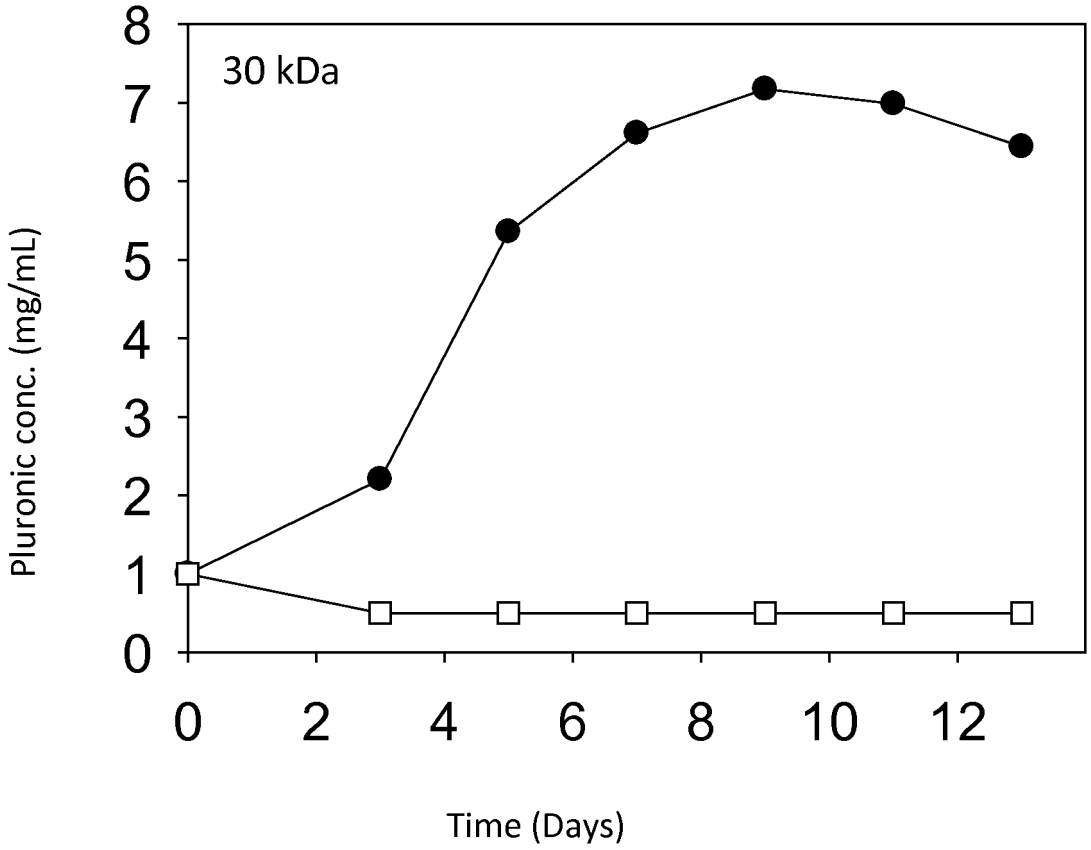


Figure 5


30 kDa
Pluronic conc. (mg/mL)
0
1
2
3
4
5
6
7
8
0
2
4
6
8
10
12
Time (Days)

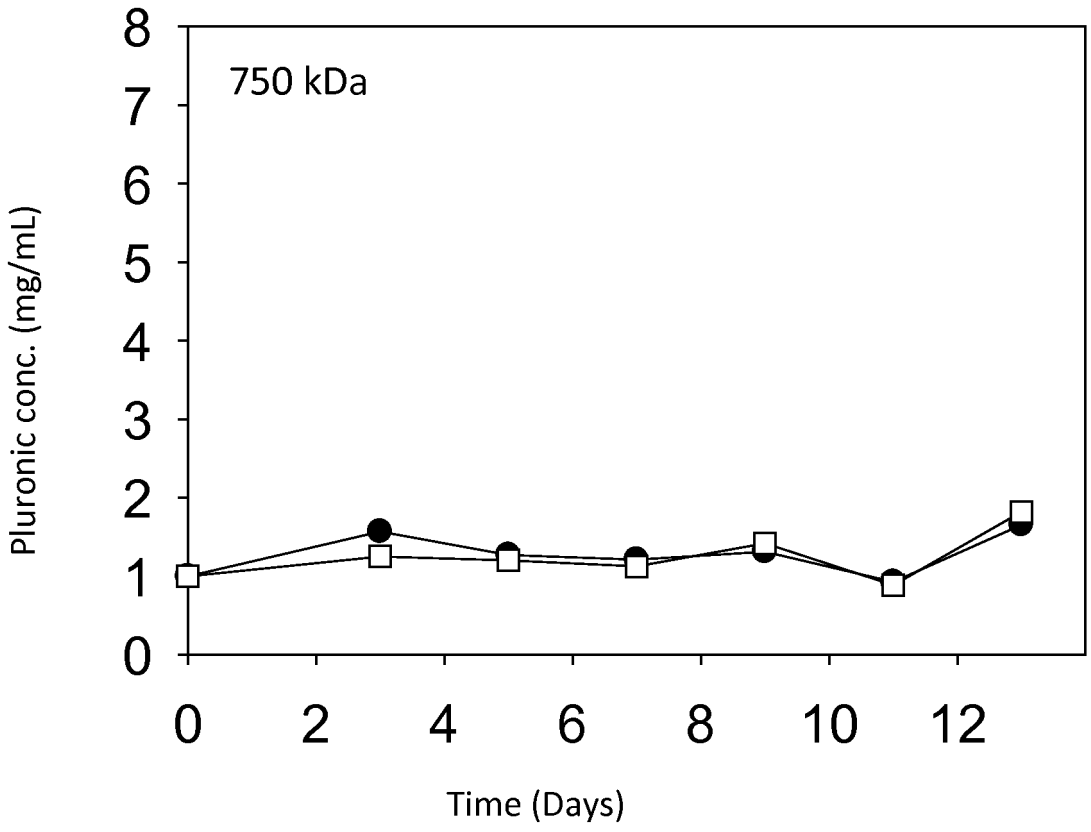
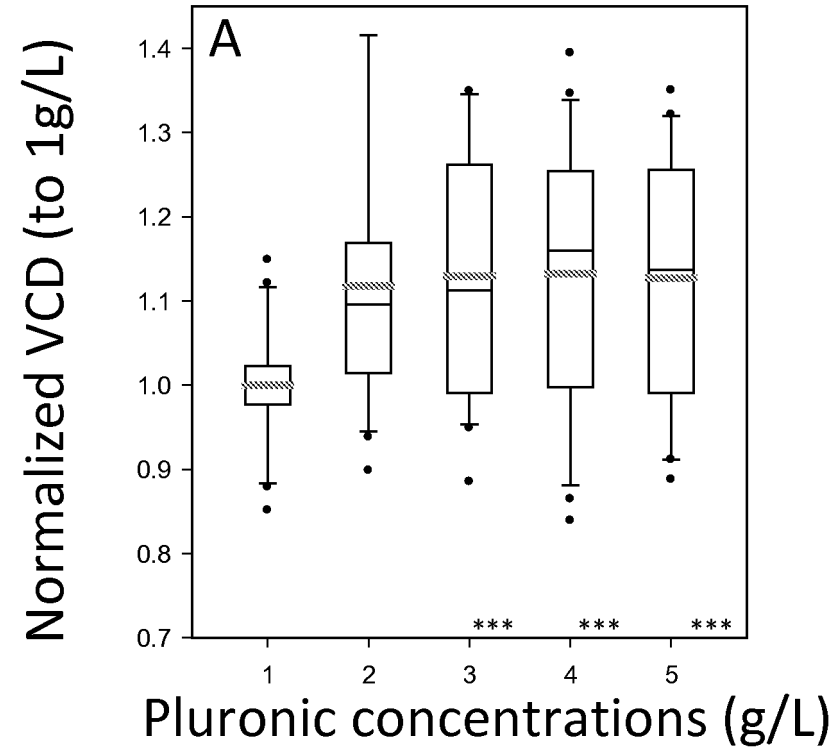

750 kDa
Pluronic conc. (mg/mL)
0
1
2
3
4
5
6
7
8
0
2
4
6
8
10
12
Time (Days)

Figure 6


A
Normalized VCD (to 1g/L)
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
***
***
***
1
2
3
4
5
Pluronic concentrations (g/L)

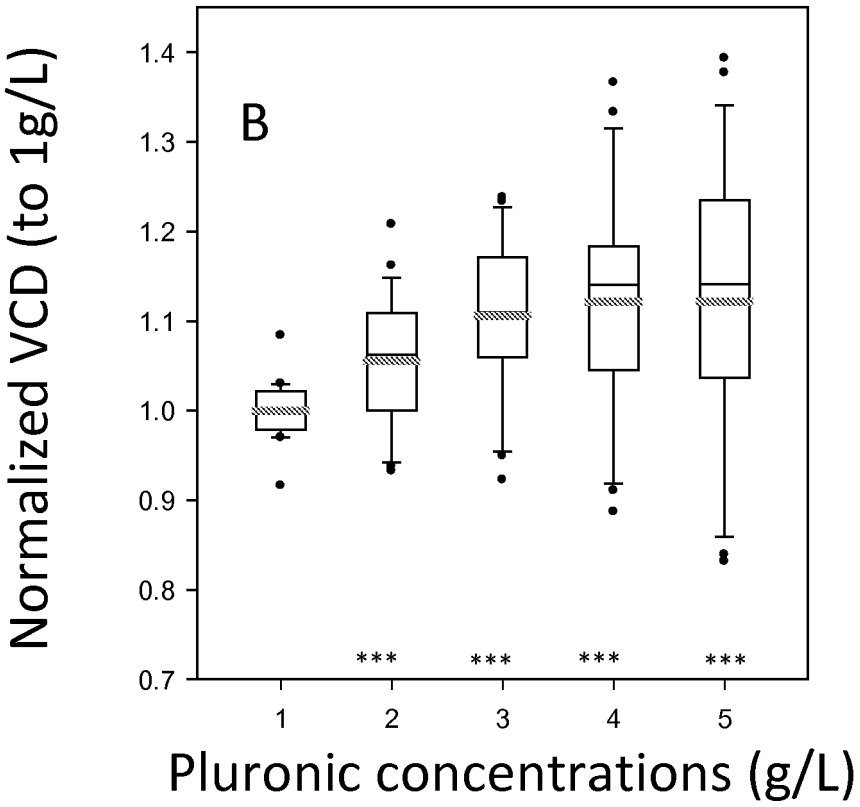
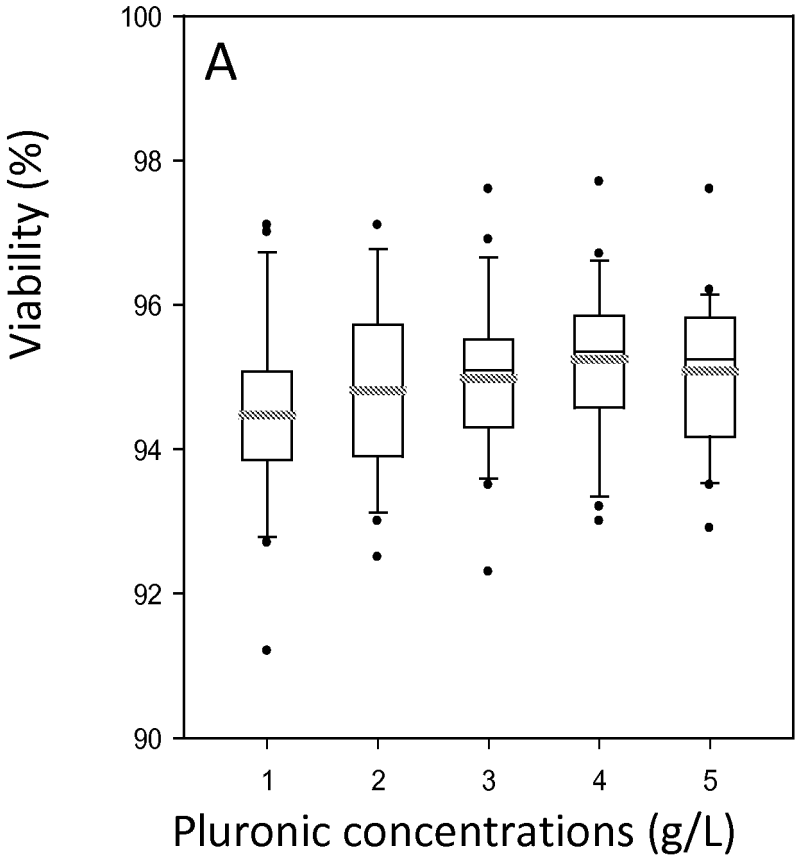

B
Normalized VCD (to 1g/L)
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
***
***
***
***
1
2
3
4
5
Pluronic concentrations (g/L)

Figure 7A


A
Viability (%)
100
98
96
94
92
90
1
2
3
4
5
Pluronic concentrations (g/L)

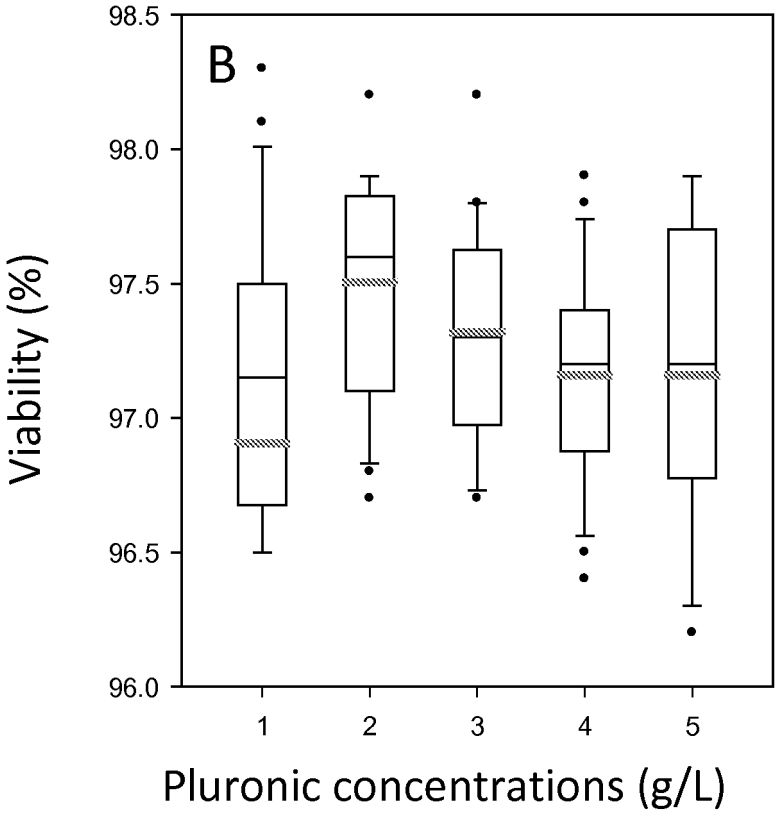
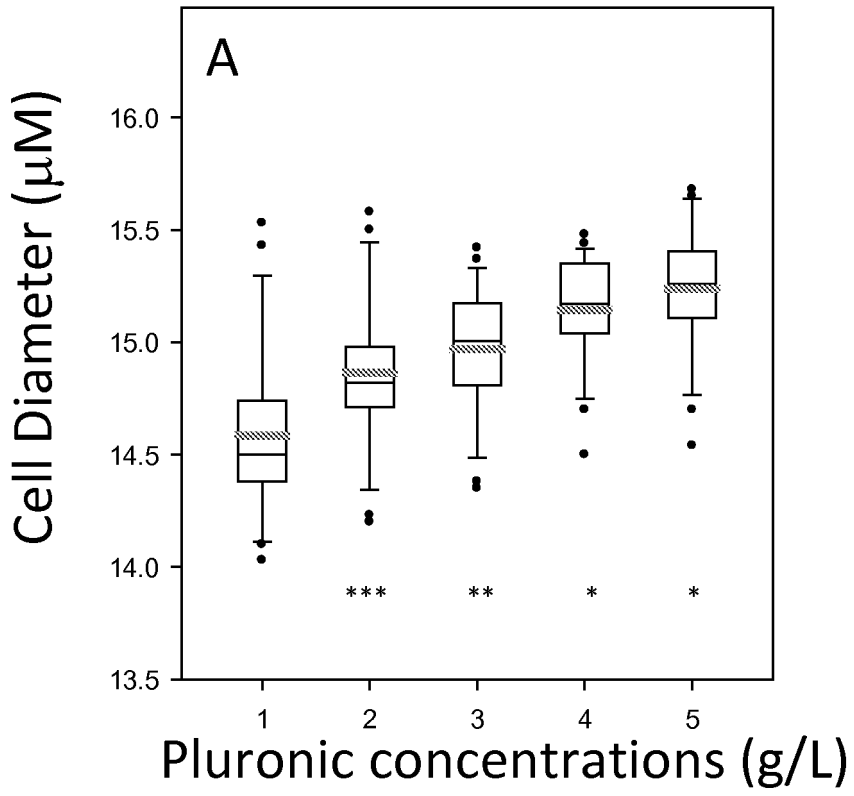

B
Viability (%)
98.5
98.0
97.5
97.0
96.5
96.0
1
2
3
4
5
Pluronic concentrations (g/L)

Figure 7B


A
Cell Diameter (µM)
16.0
15.5
15.0
14.5
14.0
13.5
***
**
*
*
1
2
3
4
5
Pluronic concentrations (g/L)

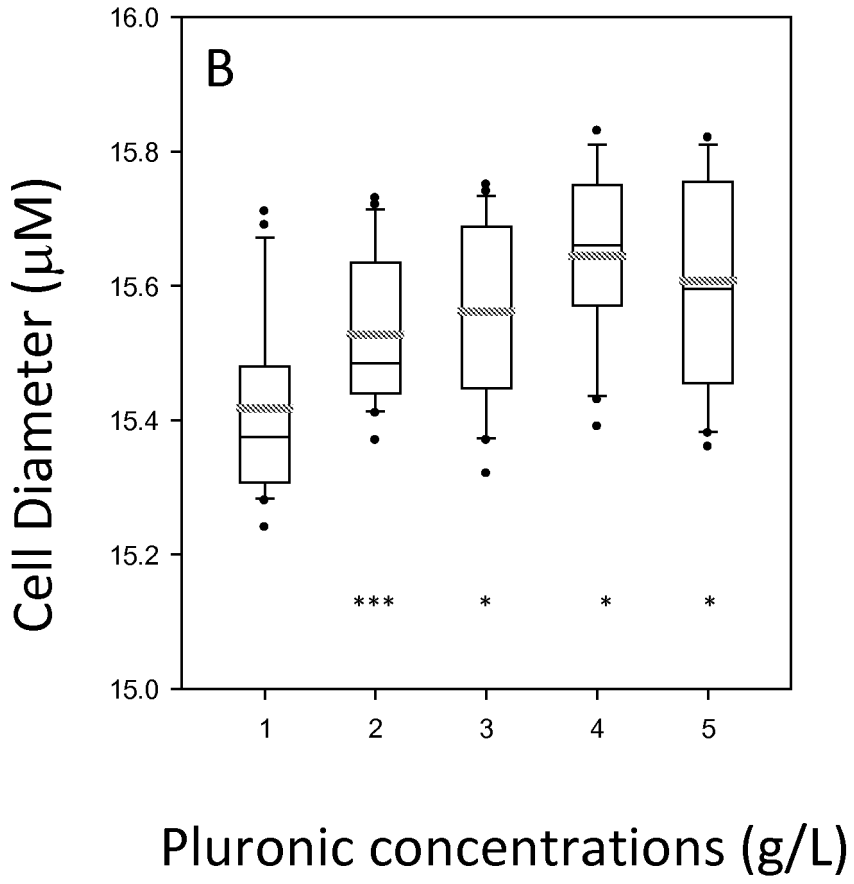

B
Cell Diameter (µM)
16.0
15.8
15.6
15.4
15.2
15.0
***
*
*
*
1
2
3
4
5
Pluronic concentrations (g/L)

Figure 7C

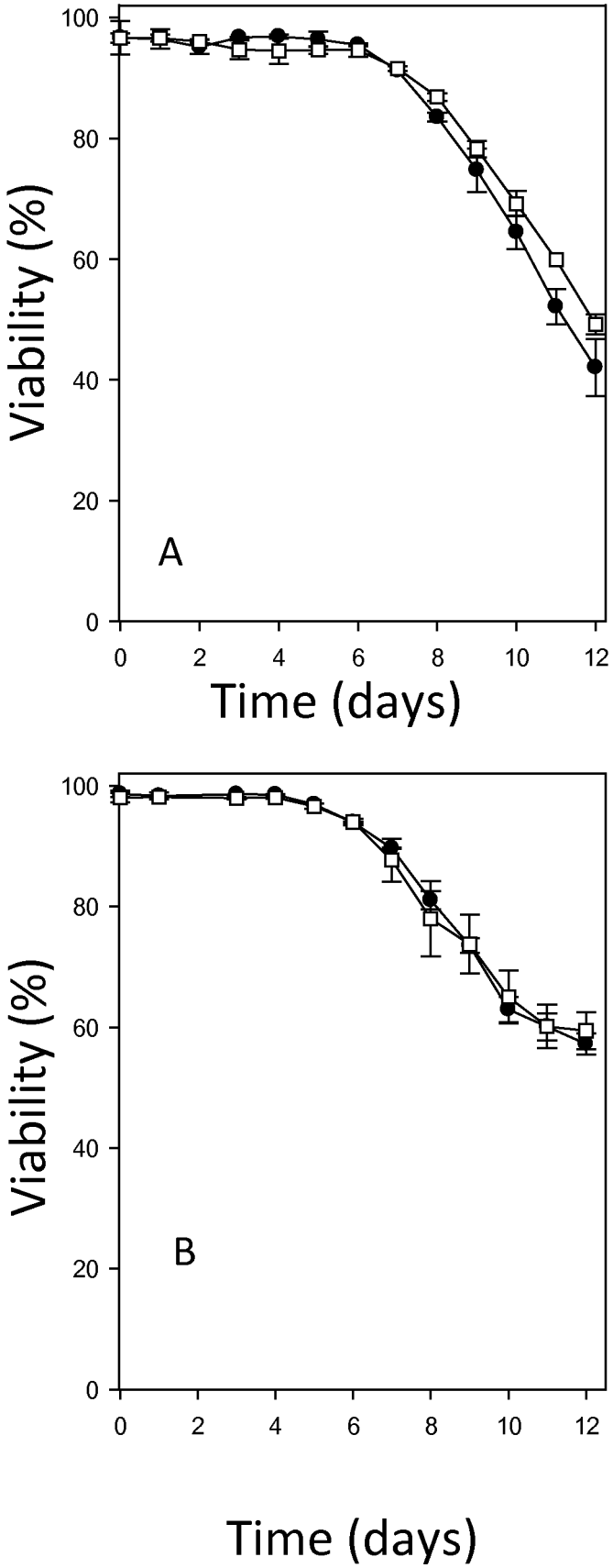

100
80
60
40
20
0
Viability (%)
A
0
2
4
6
8
10
12
Time (days)
100
80
60
40
20
0
Viability (%)
B
0
2
4
6
8
10
12
Time (days)

Figure 8

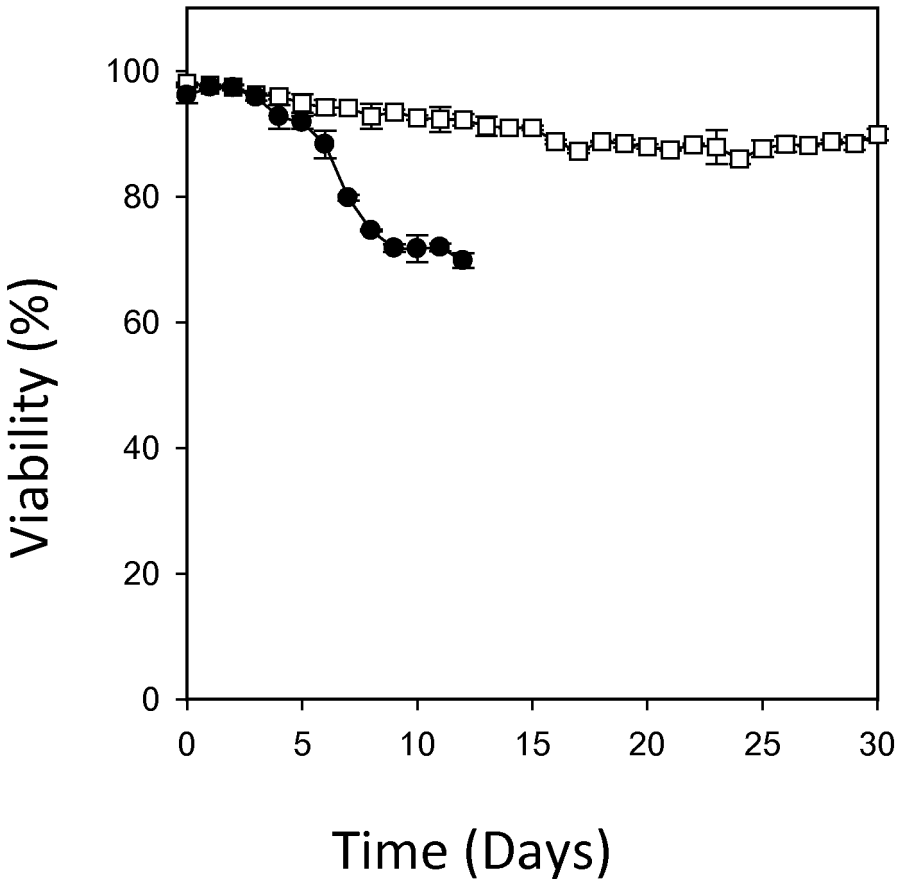


Figure 9

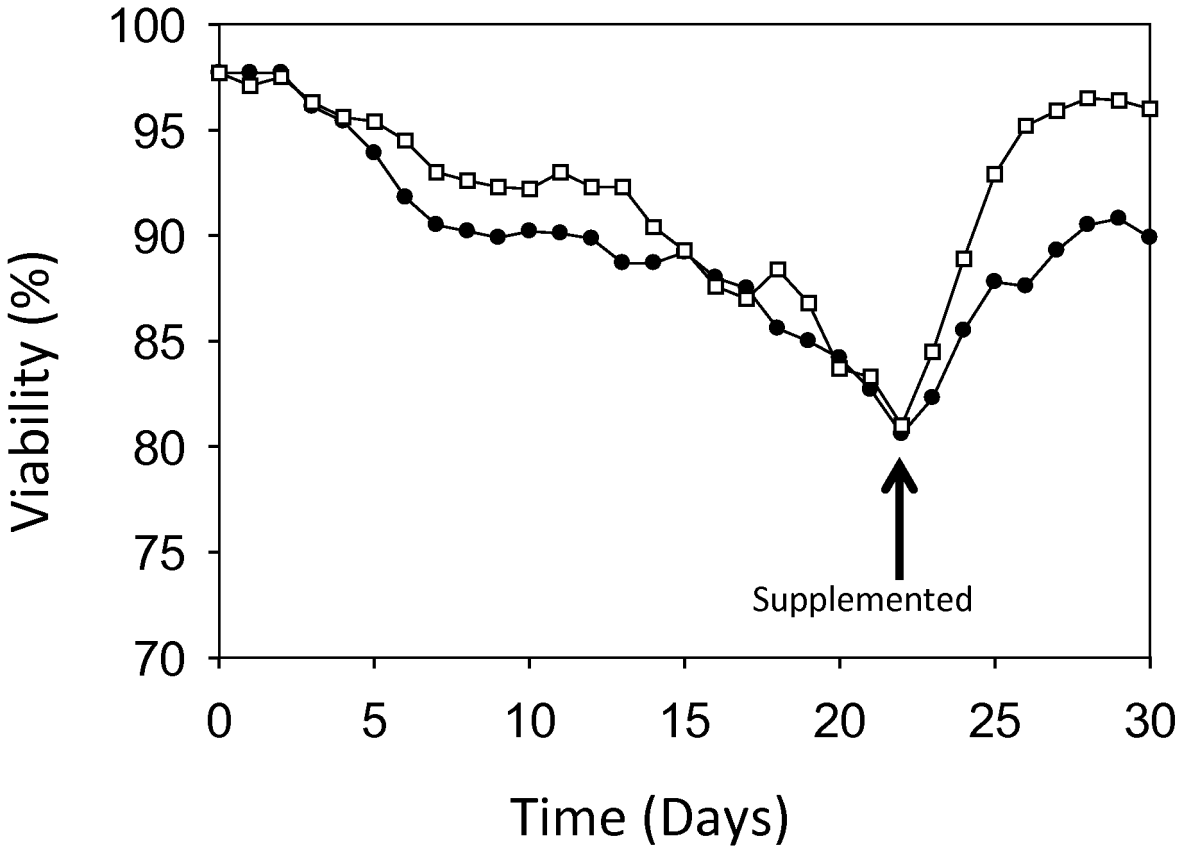

100
95
90
85
80
75
70
Viability (%)
0
5
10
15
20
25
30
Time (Days)
Supplemented

Figure 10

FIG.11A

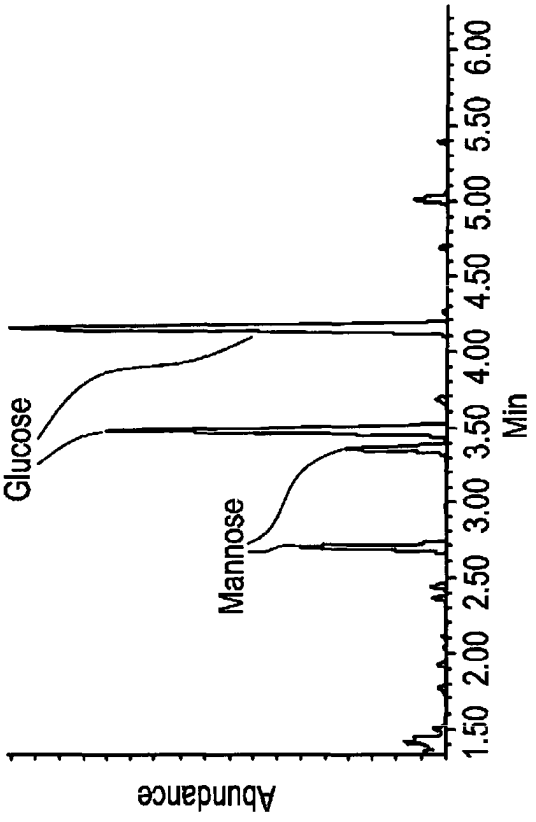


FIG.11B

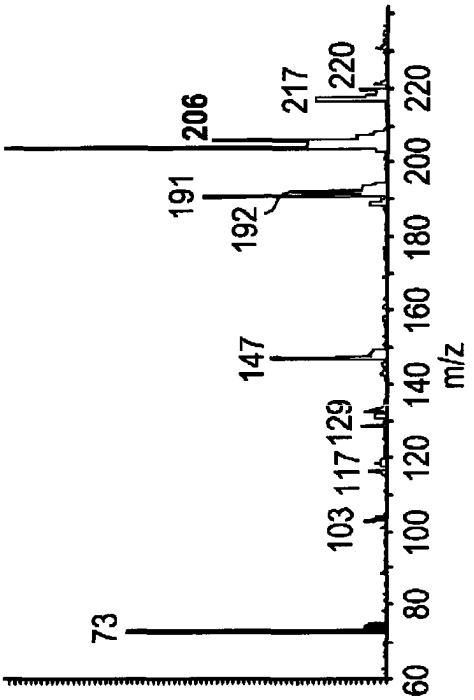


FIG.11C

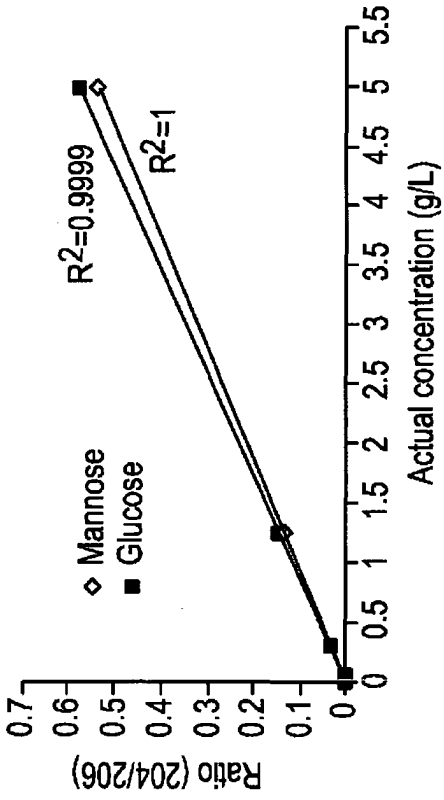


FIG. 12A

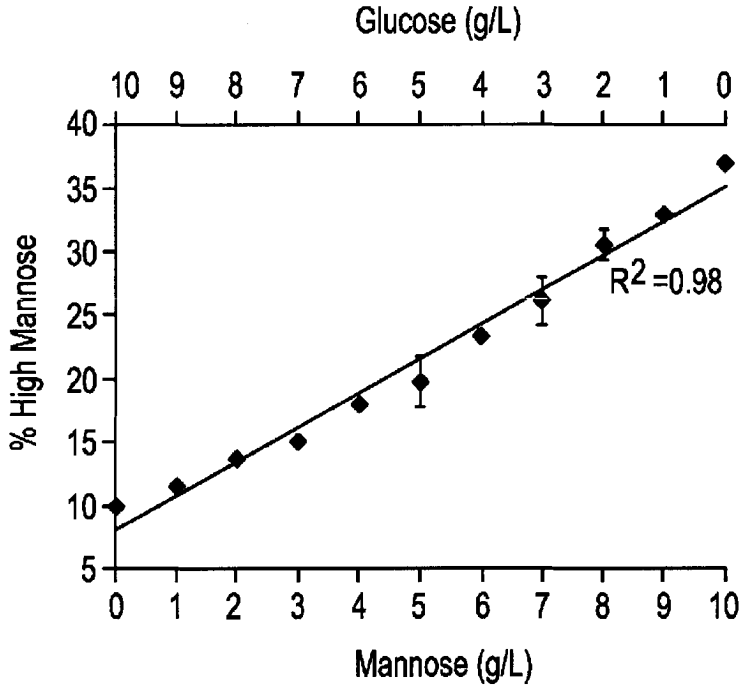


FIG. 12B

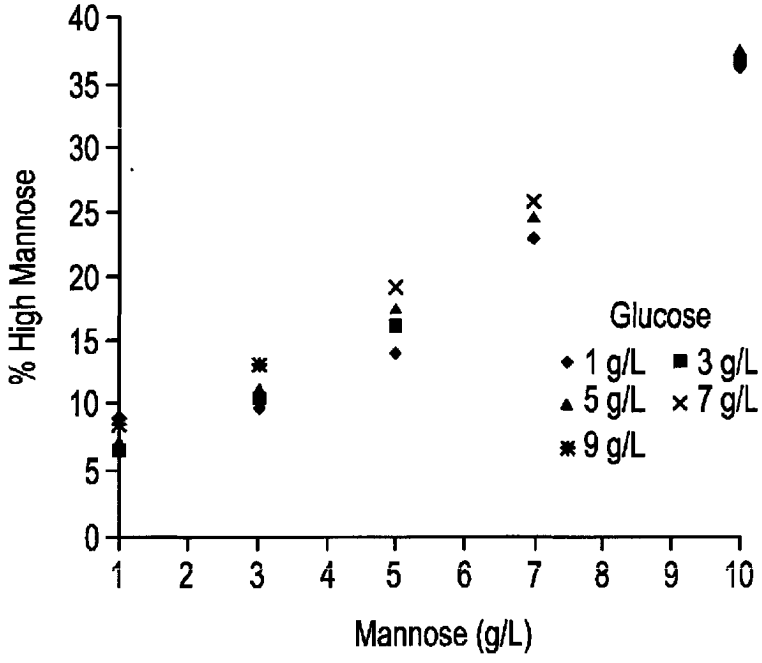


FIG. 13

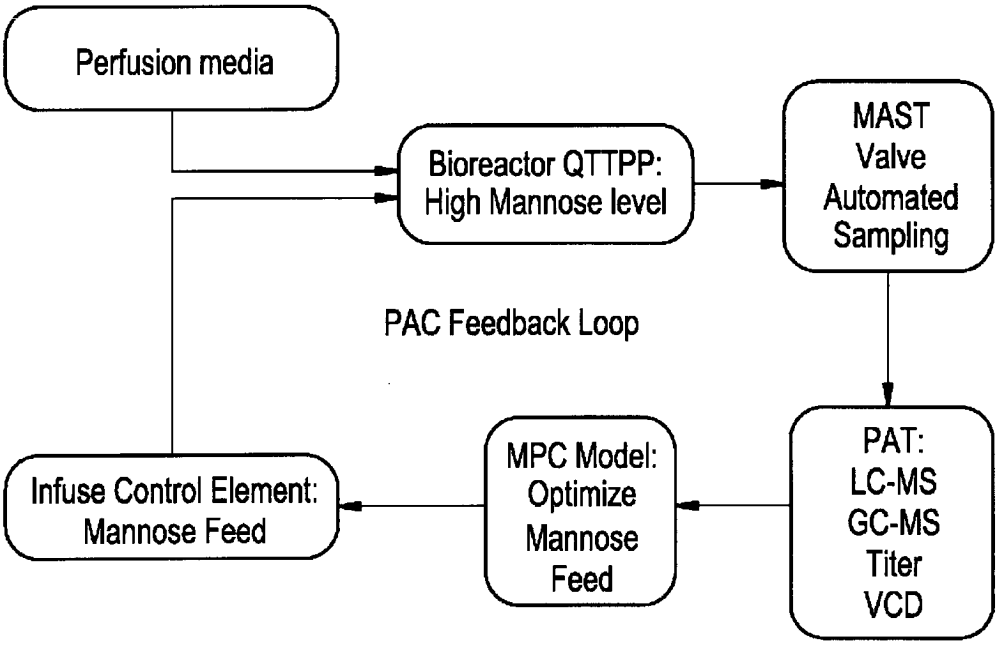

Perfusion media
Bioreactor QTTPP:
High Mannose level
MAST
Valve
Automated
Sampling
PAC Feedback Loop
PAT:
LC-MS
GC-MS
Titer
VCD
MPC Model:
Optimize
Mannose
Feed
Infuse Control Element:
Mannose Feed

FIG. 14A

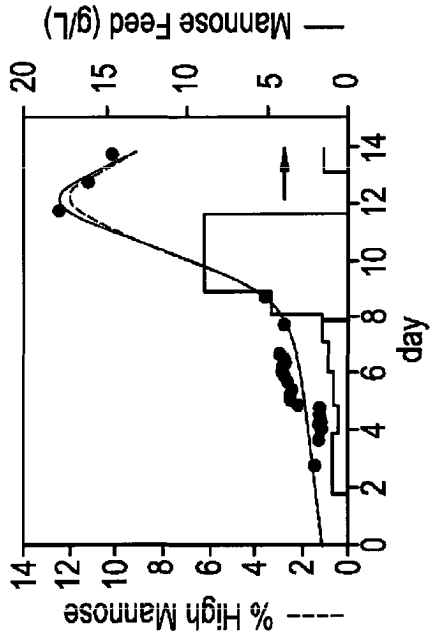


FIG. 14B

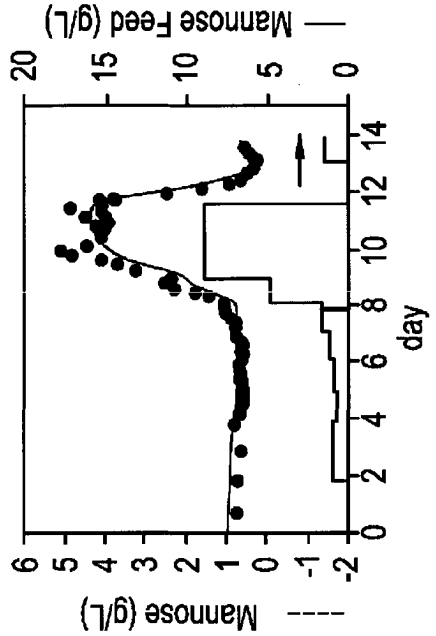


FIG. 14C

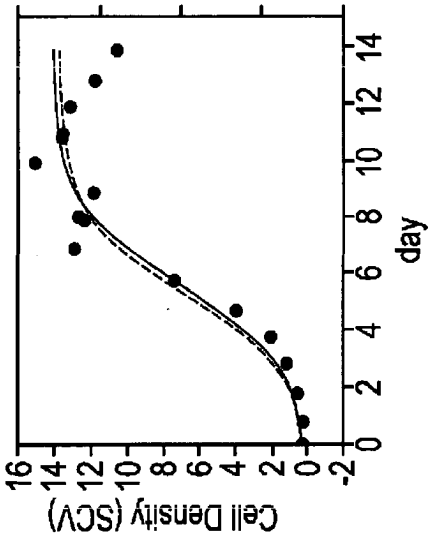


FIG. 14D

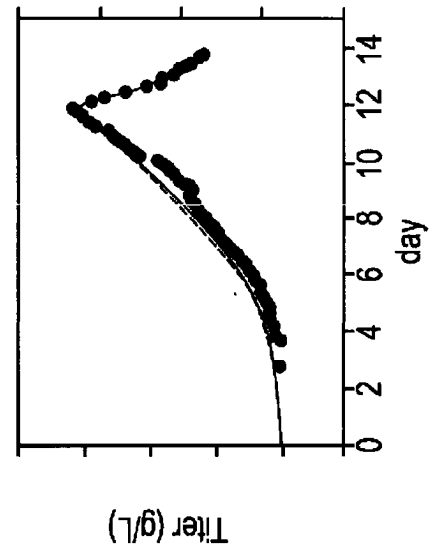


FIG. 15A

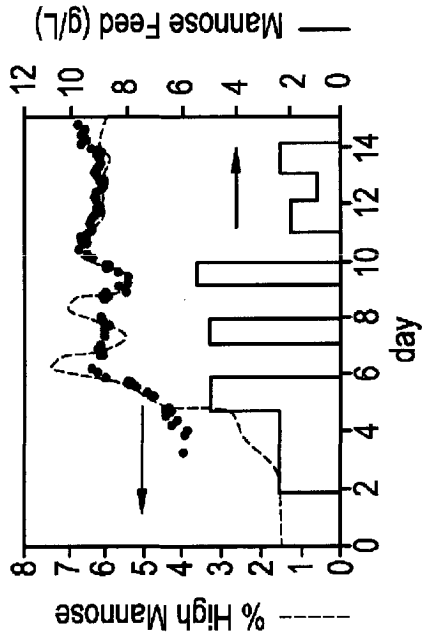


FIG. 15B

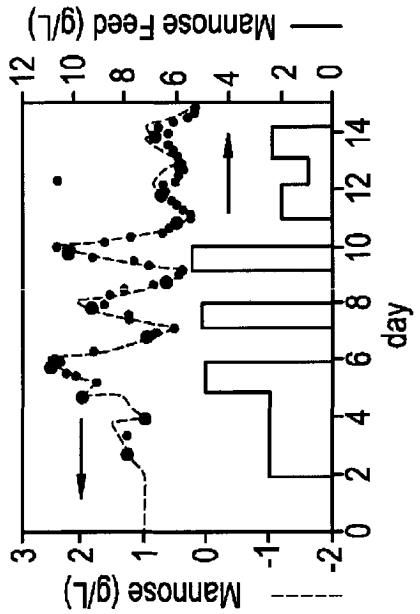


FIG. 15C

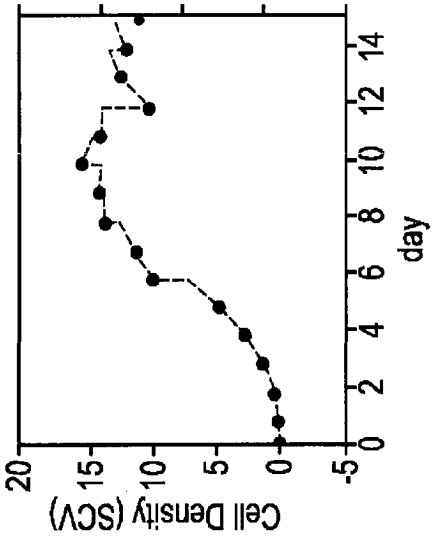


FIG. 15D

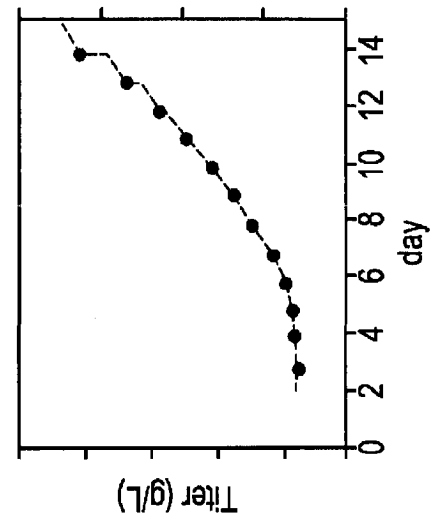
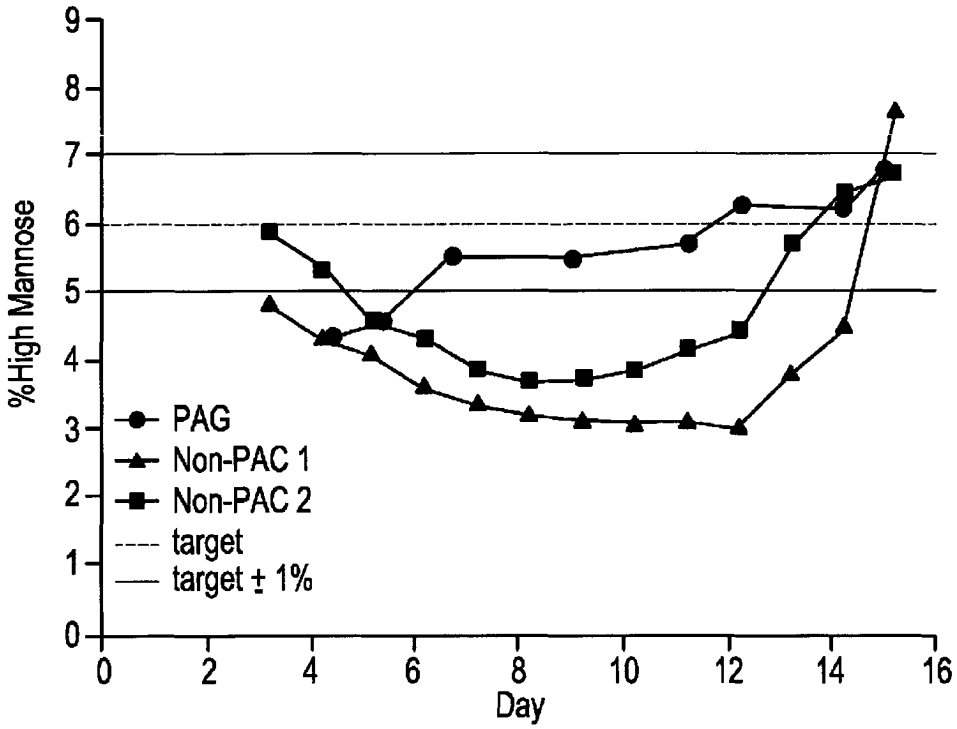


FIG. 16


%High Mannose
Day
PAG
Non-PAC 1
Non-PAC 2
target
target ± 1%
0
1
2
3
4
5
6
7
8
9
0
2
4
6
8
10
12
14
16