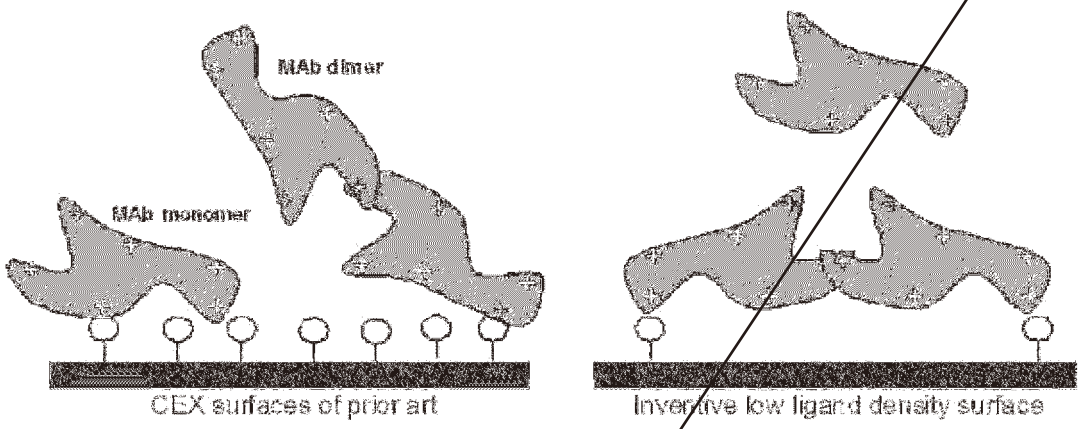

MAb dimer
MAb monomer
CEX surfaces of prior art
Inventive low ligand density surface

Figure 1

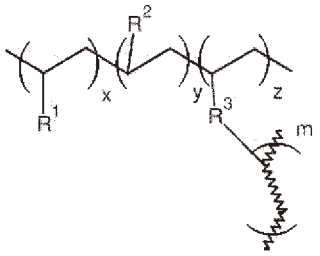


Figure 2A

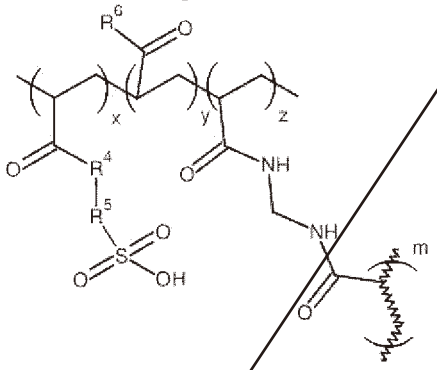


Figure 2B

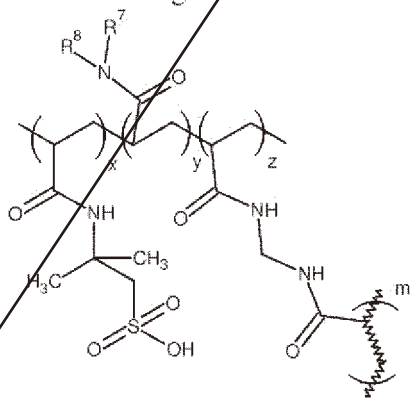


Figure 2C

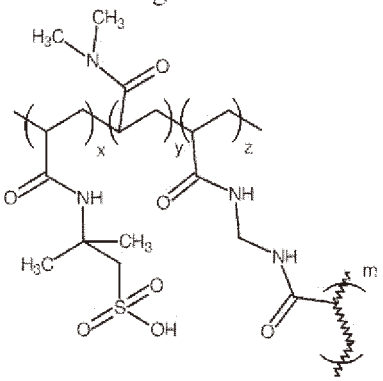


Figure 2D

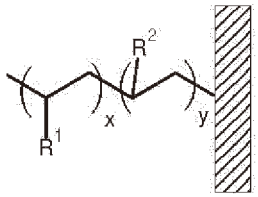


Figure 2E

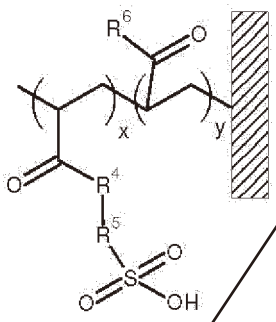


Figure 2F

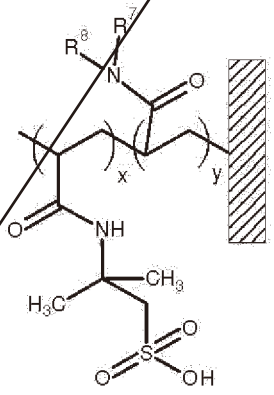


Figure 2G

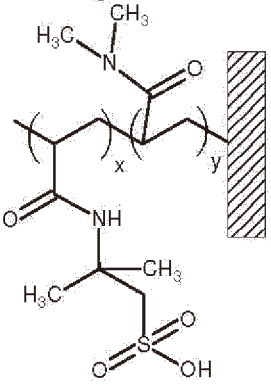


Figure 2H

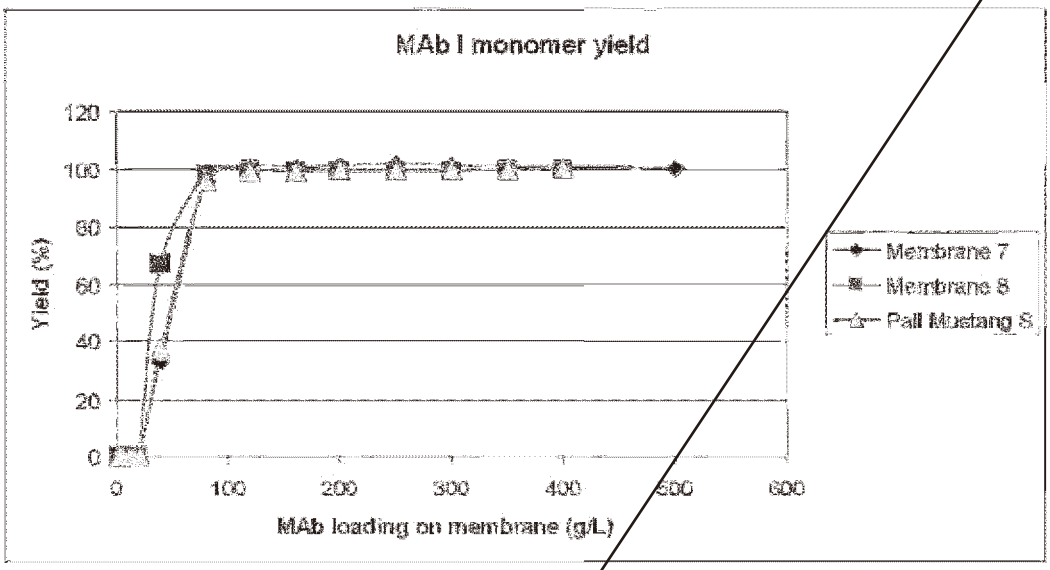

MAb I monomer yield
120
100
80
60
40
20
0
Yield (%)
0
100
200
300
400
500
600
MAb loading on membrane (g/L)
Membrane 7
Membrane 8
Pall Mustang S

Figure 3A

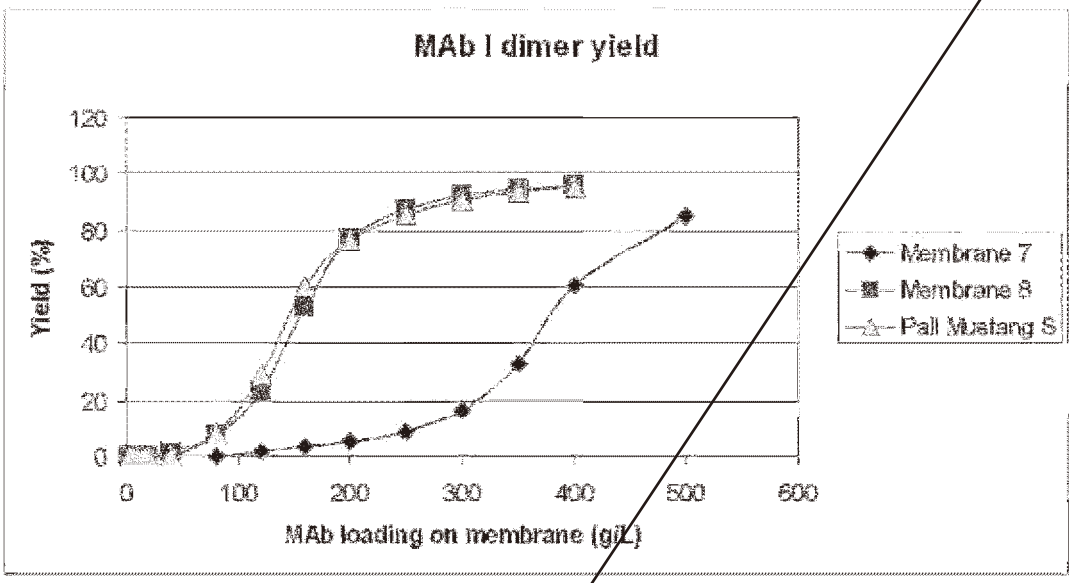

MAb I dimer yield
Yield (%)
120
100
80
60
40
20
0
0
100
200
300
400
500
600
MAb loading on membrane (g/L)
Membrane 7
Membrane 8
Pall Mustang S

Figure 3B

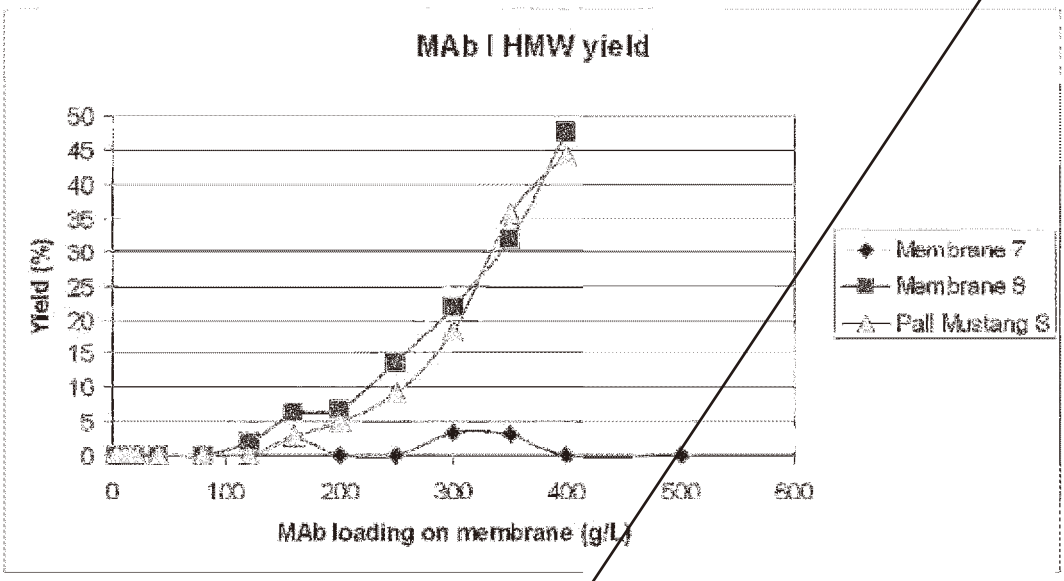

MAb I HMW yield
Yield (%)
50
45
40
35
30
25
20
15
10
5
0
0
100
200
300
400
500
600
MAb loading on membrane (g/L)
Membrane 7
Membrane S
Pall Mustang S

Figure 3C

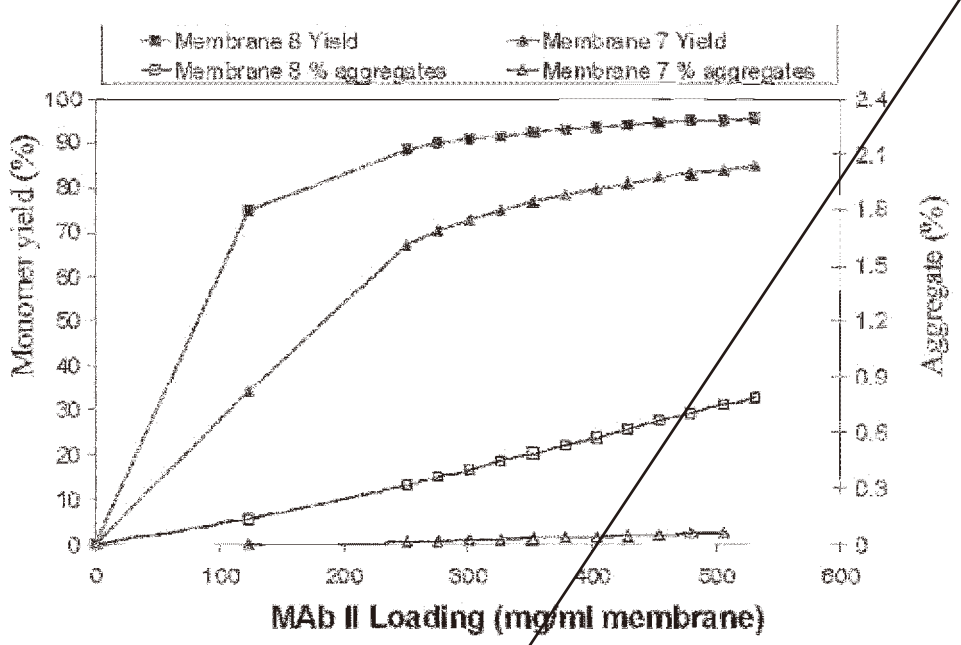

Membrane 8 Yield
Membrane 7 Yield
Membrane 8 % aggregates
Membrane 7 % aggregates
Monomer yield (%)
Aggregate (%)
MAb II Loading (mg/ml membrane)
0
10
20
30
40
50
60
70
80
90
100
0.3
0.6
0.9
1.2
1.5
1.8
2.1
2.4
0
100
200
300
400
500
600

Figure 4A

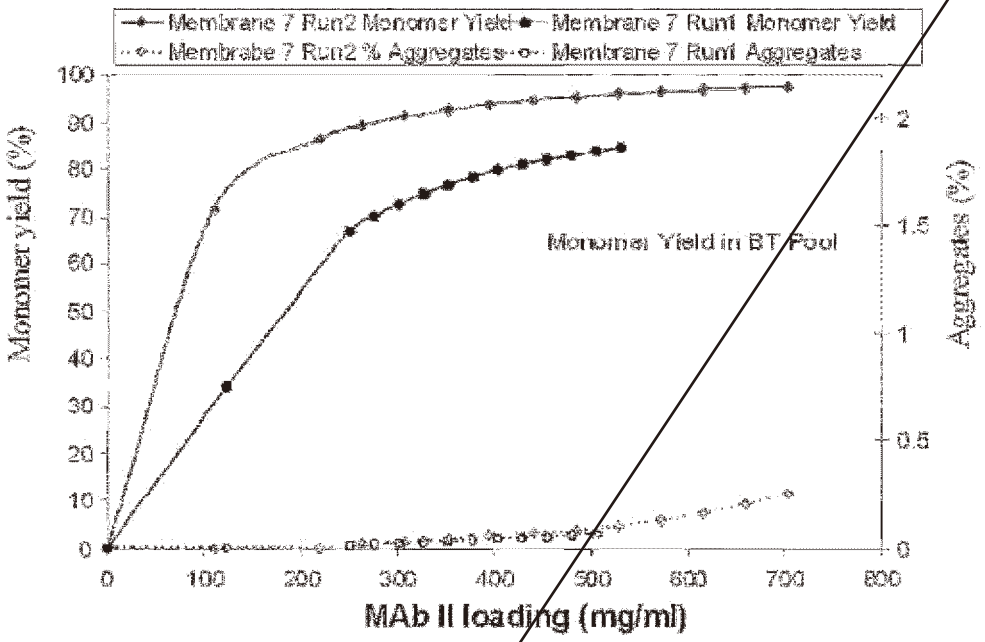

Membrane 7 Run2 Monomer Yield
Membrane 7 Run1 Monomer Yield
Membrabe 7 Run2 % Aggregates
Membrane 7 Run1 Aggregates
Monomer yield (%)
Aggregates (%)
Monomer Yield in BT Pool
MAb II loading (mg/ml)
0
10
20
30
40
50
60
70
80
90
100
0
0.5
1
1.5
2
0
100
200
300
400
500
600
700
800

Figure 4B

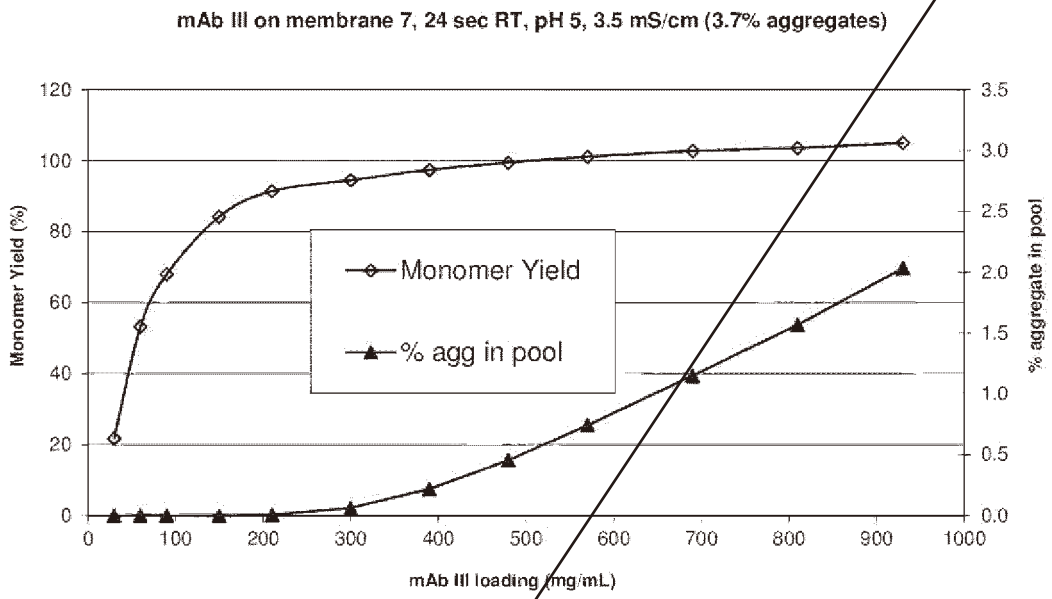

mAb III on membrane 7, 24 sec RT, pH 5, 3.5 mS/cm (3.7% aggregates)
Monomer Yield (%)
% aggregate in pool
mAb III loading (mg/mL)
Monomer Yield
% agg in pool
0
20
40
60
80
100
120
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
0
100
200
300
400
500
600
700
800
900
1000

Figure 5

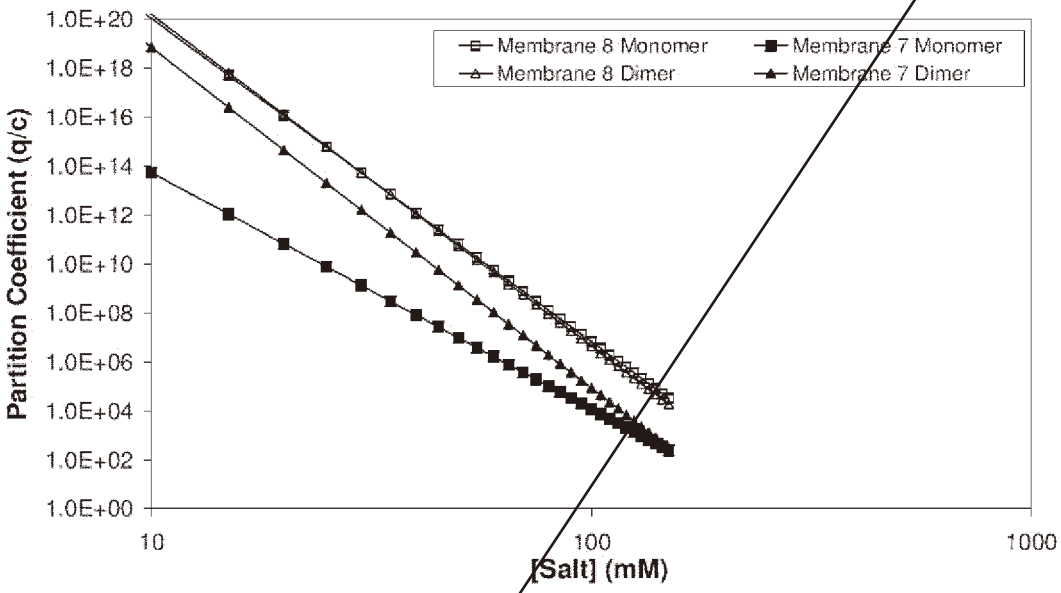

Membrane 8 Monomer
Membrane 7 Monomer
Membrane 8 Dimer
Membrane 7 Dimer
Partition Coefficient (q/c)
1.0E+20
1.0E+18
1.0E+16
1.0E+14
1.0E+12
1.0E+10
1.0E+08
1.0E+06
1.0E+04
1.0E+02
1.0E+00
10
100
1000
[Salt] (mM)

Figure 6A

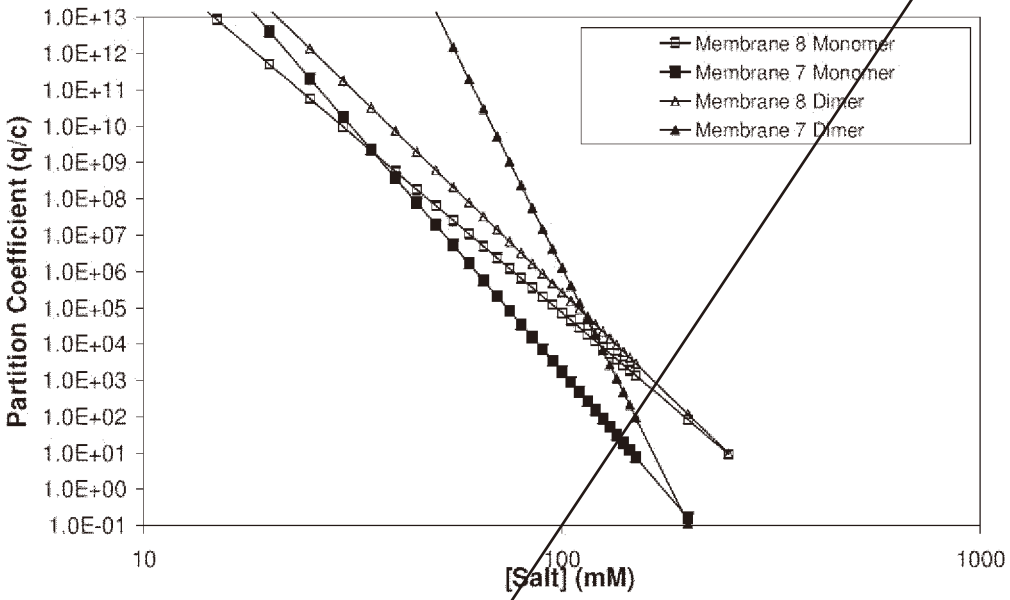

Membrane 8 Monomer
Membrane 7 Monomer
Membrane 8 Dimer
Membrane 7 Dimer
Partition Coefficient (q/c)
1.0E+13
1.0E+12
1.0E+11
1.0E+10
1.0E+09
1.0E+08
1.0E+07
1.0E+06
1.0E+05
1.0E+04
1.0E+03
1.0E+02
1.0E+01
1.0E+00
1.0E-01
10
100
1000
[Salt] (mM)

Figure 6B

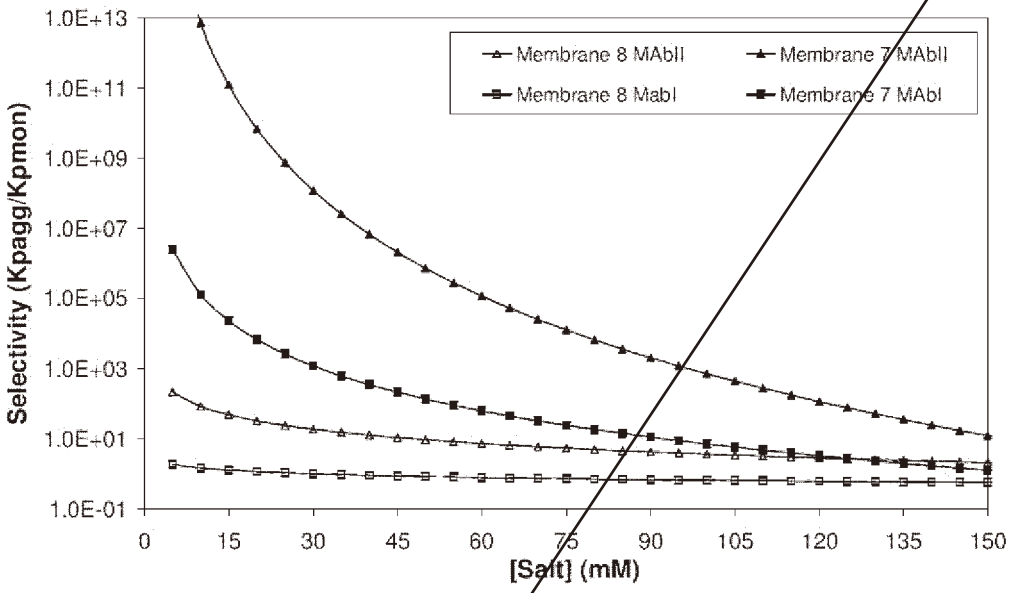

Membrane 8 MAbII
Membrane 7 MAbII
Membrane 8 MabI
Membrane 7 MAbI
Selectivity (Kpagg/Kpmon)
1.0E+13
1.0E+11
1.0E+09
1.0E+07
1.0E+05
1.0E+03
1.0E+01
1.0E-01
0
15
30
45
60
75
90
105
120
135
150
[Salt] (mM)

Figure 7

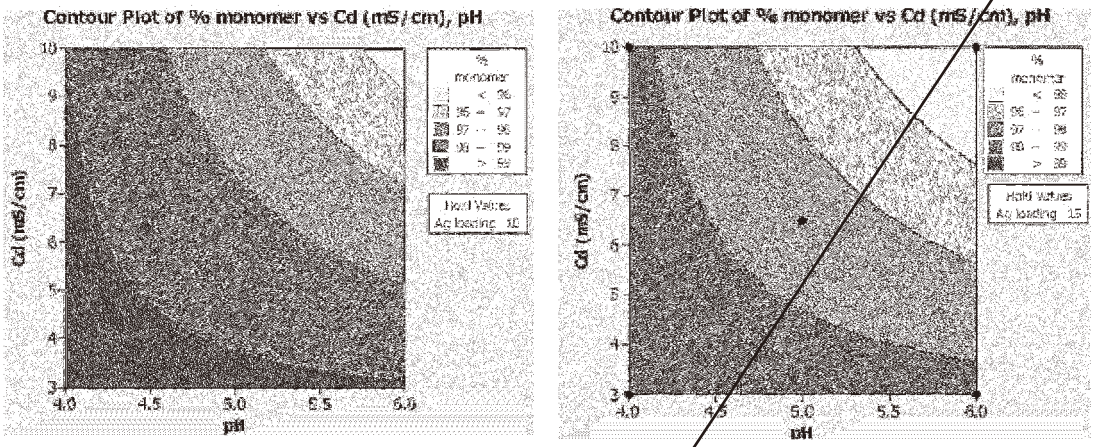

Contour Plot of % monomer vs Cd (mS/cm), pH
Cd (mS/cm)
pH
% monomer
Hold Values
Ag loading 1.0
Contour Plot of % monomer vs Cd (mS/cm), pH
Cd (mS/cm)
pH
% monomer
Hold Values
Ag loading 1.5

Figure 8

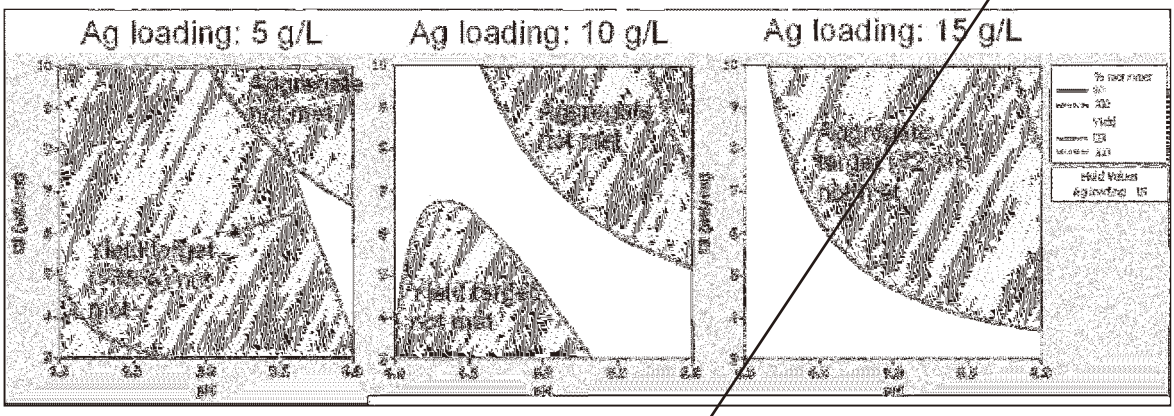


Figure 9

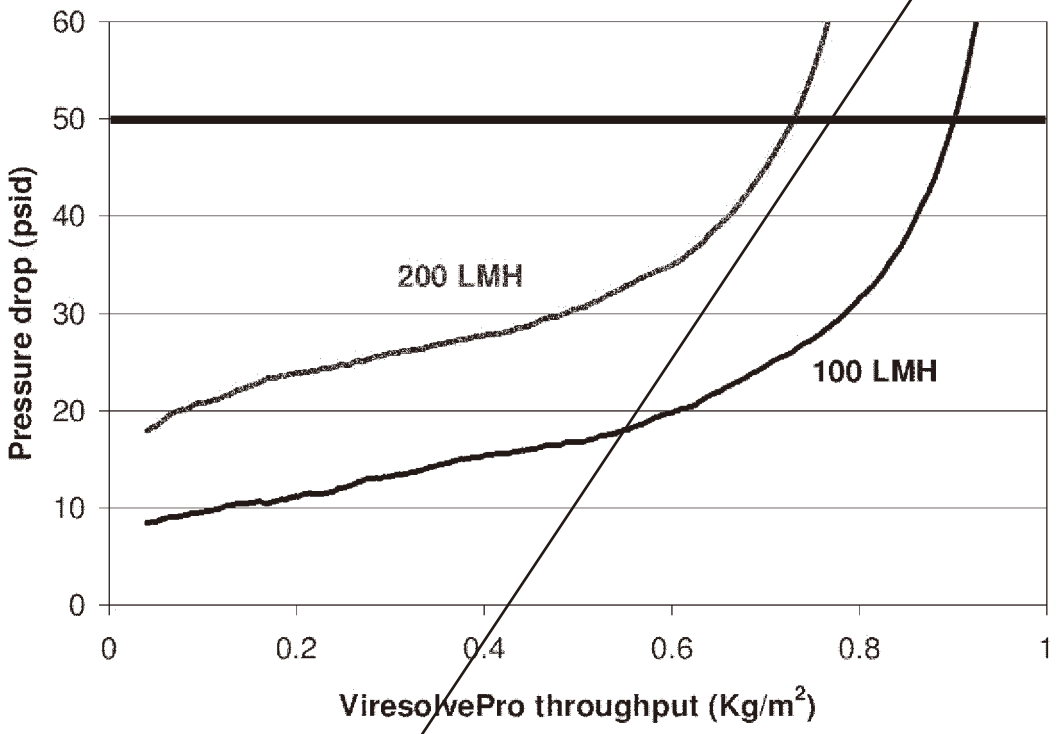

60
50
40
30
20
10
0
Pressure drop (psid)
200 LMH
100 LMH
0
0.2
0.4
0.6
0.8
1
ViresolvePro throughput (Kg/m2)

Fig. 10

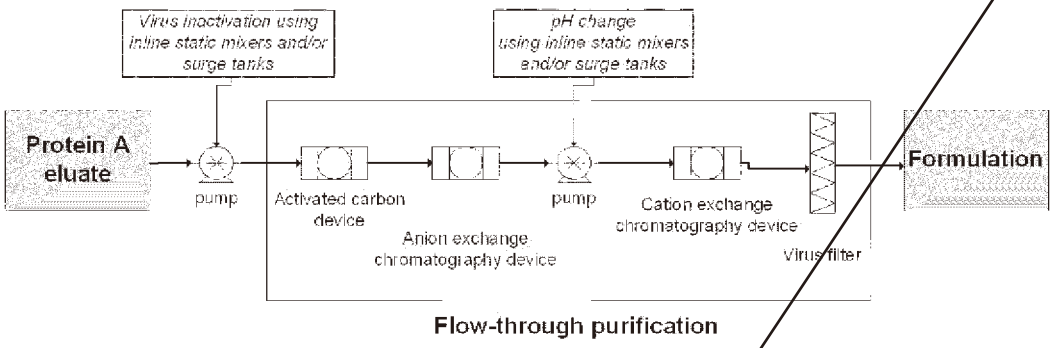

Virus inactivation using inline static mixers and/or surge tanks
pH change using inline static mixers and/or surge tanks
Protein A eluate
pump
Activated carbon device
Anion exchange chromatography device
pump
Cation exchange chromatography device
Virus filter
Formulation
Flow-through purification

Fig. 11.

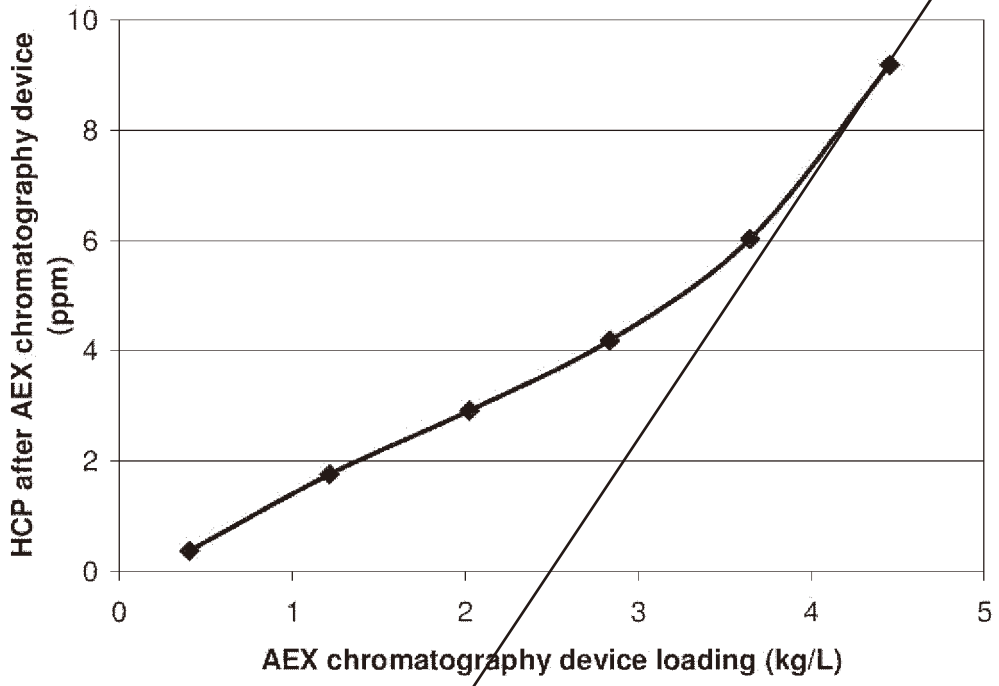

HCP after AEX chromatography device (ppm)
10
8
6
4
2
0
0
1
2
3
4
5
AEX chromatography device loading (kg/L)

Fig. 12

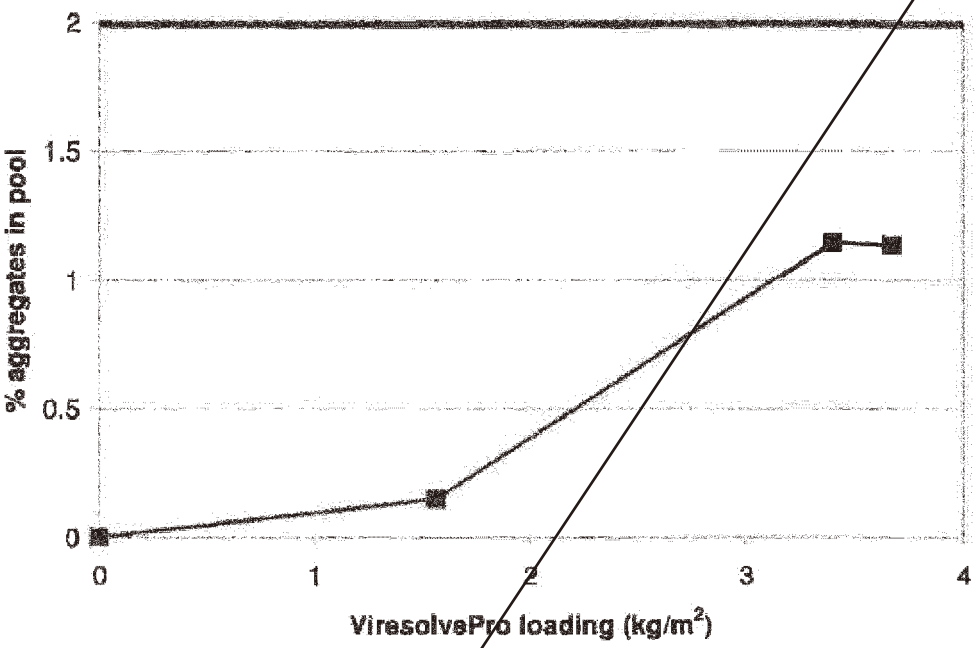

2
1.5
1
0.5
0
% aggregates in pool
0
1
2
3
4
ViresolvePro loading (kg/m2)

Figure 13.

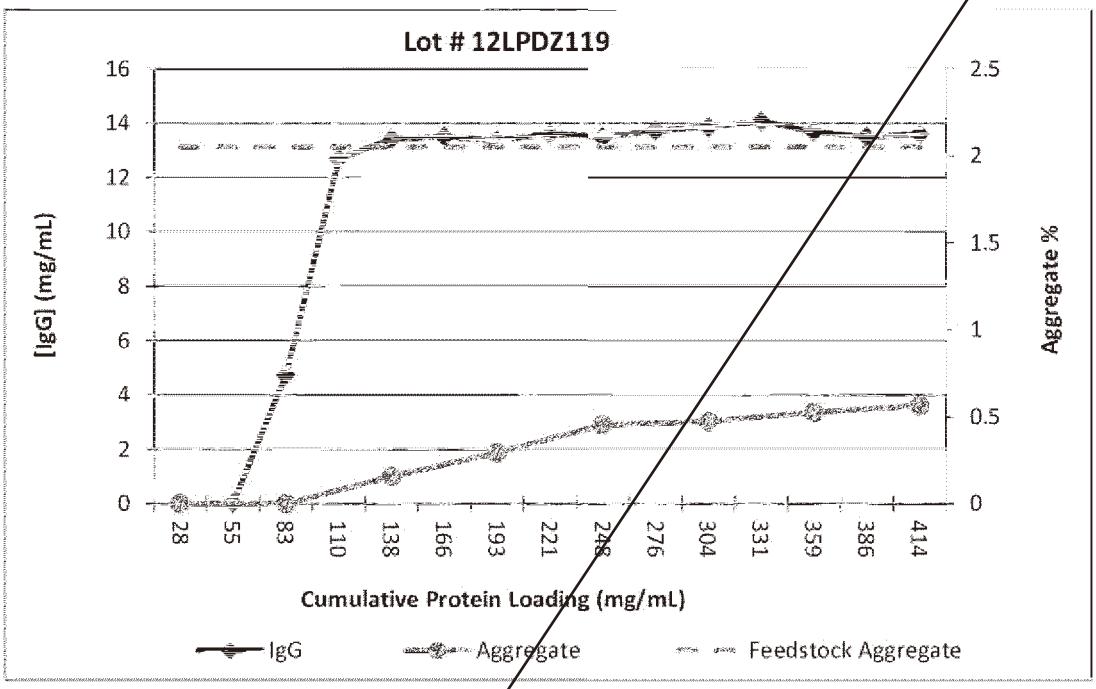

Lot # 12LPDZ119
[IgG] (mg/mL)
Aggregate %
Cumulative Protein Loading (mg/mL)
IgG
Aggregate
Feedstock Aggregate

Figure 14

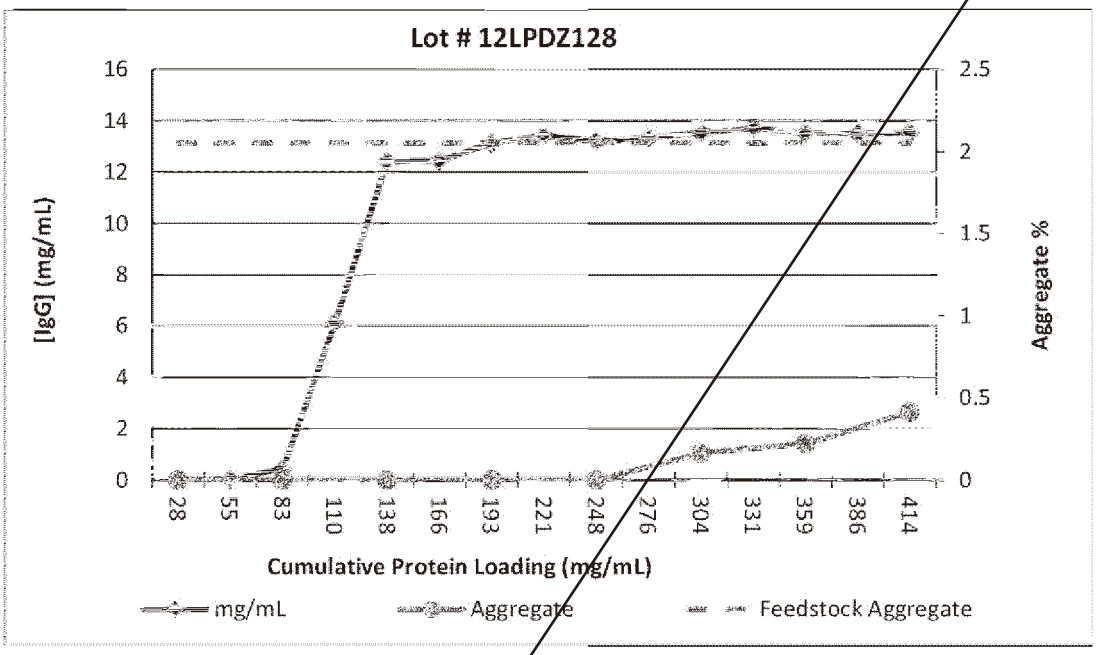

Lot # 12LPDZ128
[IgG] (mg/mL)
Aggregate %
Cumulative Protein Loading (mg/mL)
mg/mL
Aggregate
Feedstock Aggregate

Figure 15

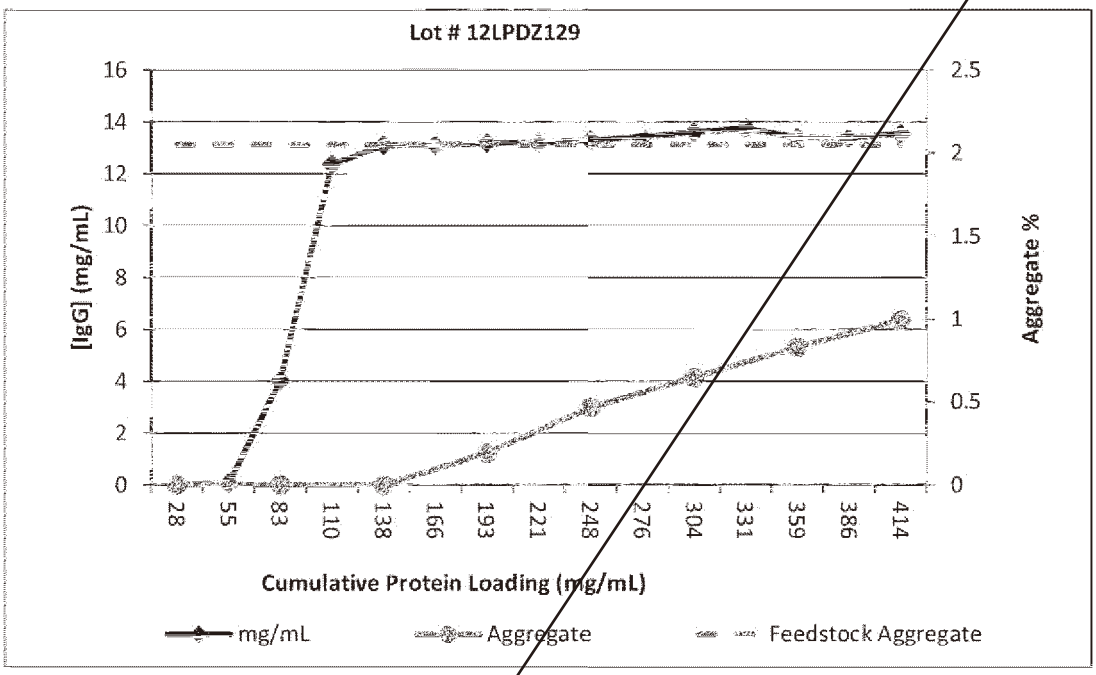

Lot # 12LPDZ129
[IgG] (mg/mL)
Aggregate %
Cumulative Protein Loading (mg/mL)
mg/mL
Aggregate
Feedstock Aggregate
0
2
4
6
8
10
12
14
16
0
0.5
1
1.5
2
2.5
28
55
83
110
138
166
193
221
248
276
304
331
359
386
414

Figure 16

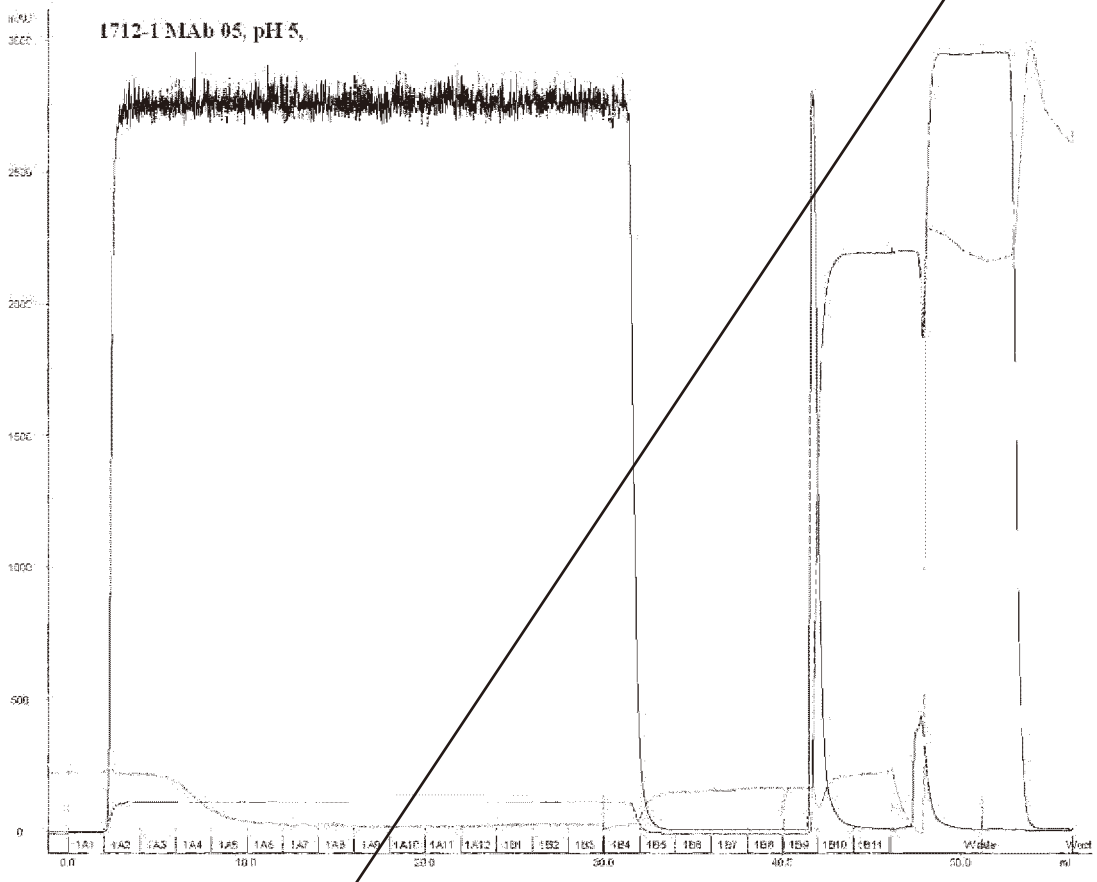

1712-1 MAb 05, pH 5,
mAU
3000
2500
2000
1500
1000
500
0
1A1
1A2
1A3
1A4
1A5
1A6
1A7
1A8
1A9
1A10
1A11
1A12
1B1
1B2
1B3
1B4
1B5
1B6
1B7
1B8
1B9
1B10
1B11
Waste
Pool
0.0
10.0
20.0
30.0
40.0
50.0
ml

Figure 17

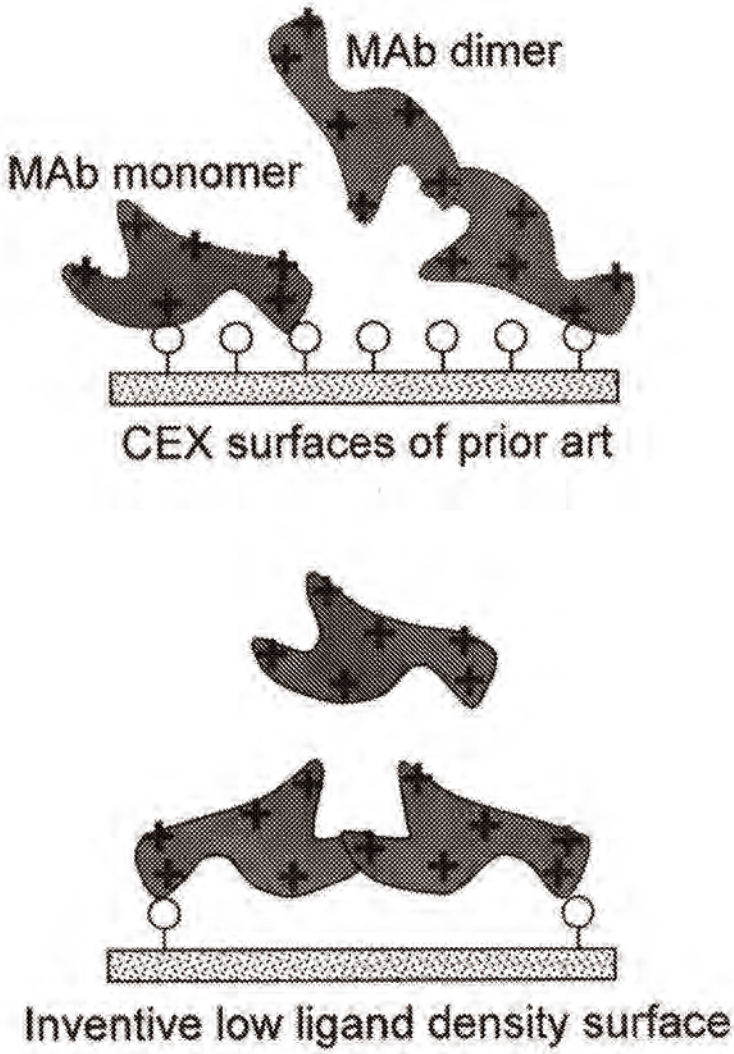

MAb dimer
MAb monomer
CEX surfaces of prior art
Inventive low ligand density surface

Figure 1

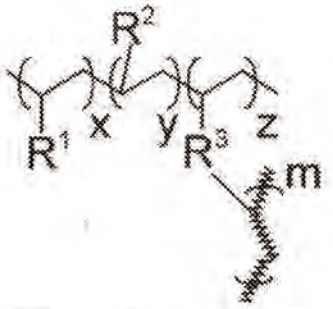


Figure 2A

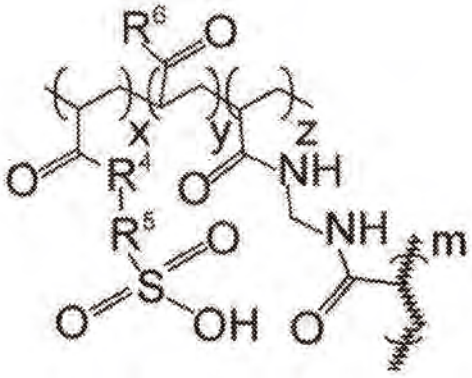


Figure 2B

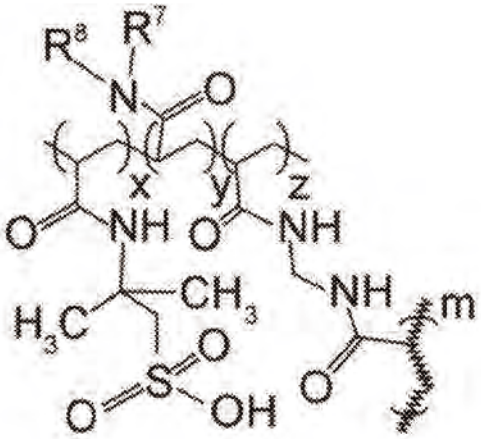


Figure 2C

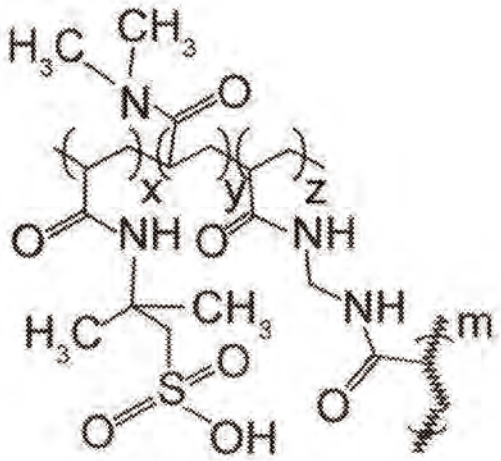


Figure 2D

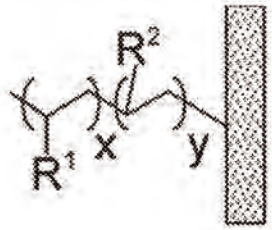


Figure 2E

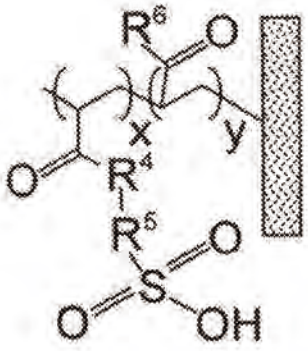


Figure 2F

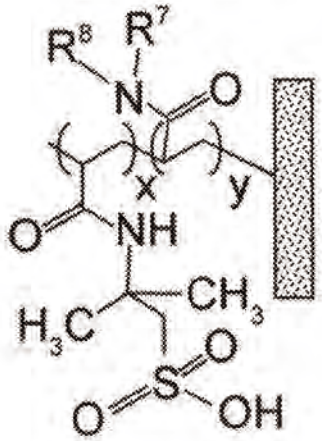


Figure 2G

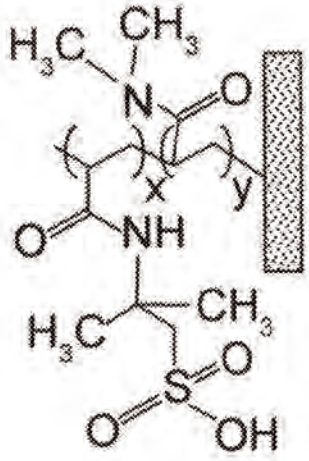


Figure 2H

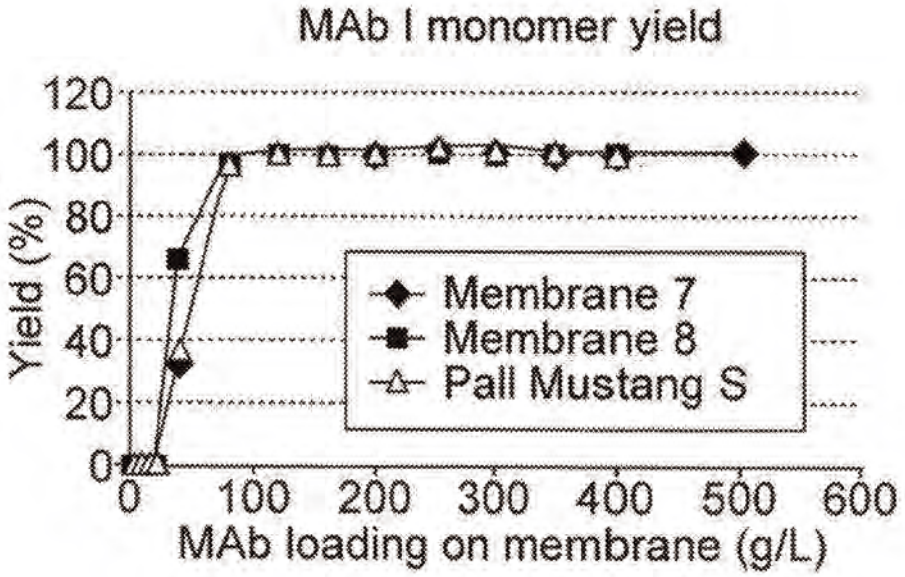

MAb I monomer yield
120
100
80
60
40
20
0
Yield (%)
0
100
200
300
400
500
600
MAb loading on membrane (g/L)
Membrane 7
Membrane 8
Pall Mustang S

Figure 3A

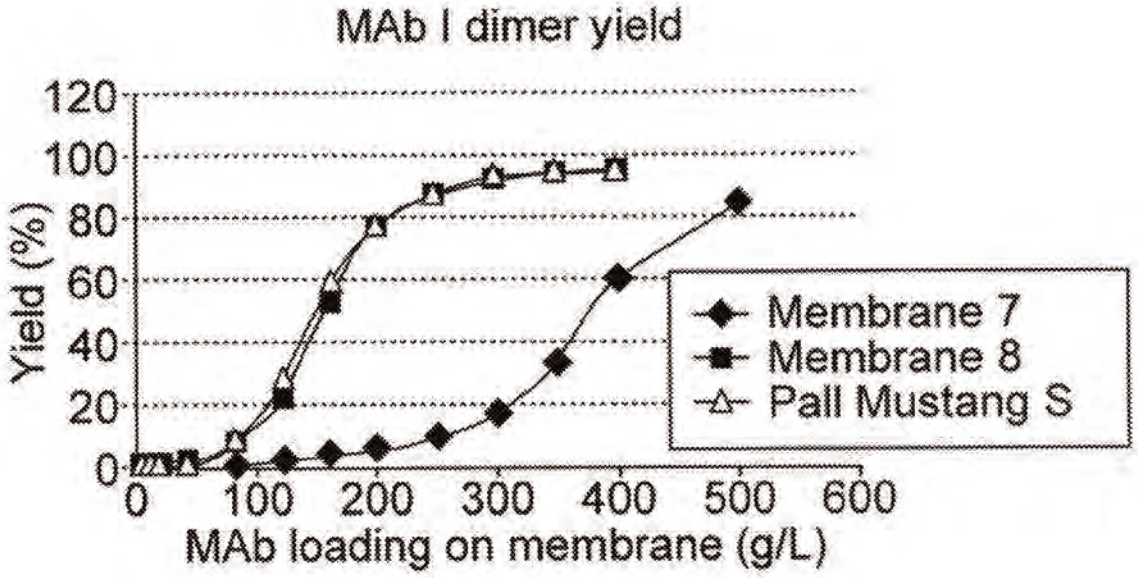

MAb I dimer yield
120
100
80
60
40
20
0
Yield (%)
0
100
200
300
400
500
600
MAb loading on membrane (g/L)
Membrane 7
Membrane 8
Pall Mustang S

Figure 3B

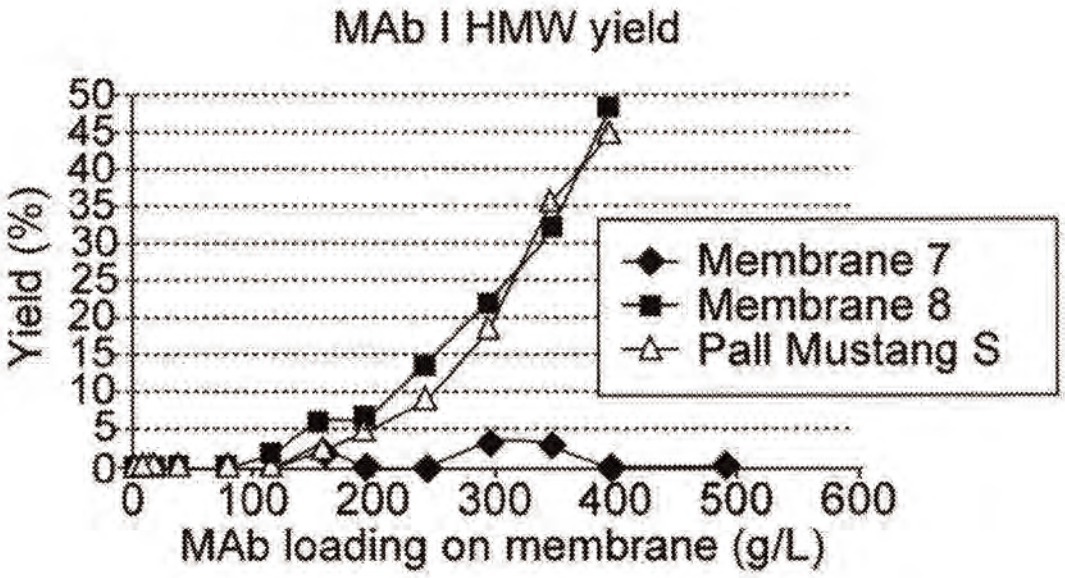

MAb I HMW yield
Yield (%)
50
45
40
35
30
25
20
15
10
5
0
0
100
200
300
400
500
600
MAb loading on membrane (g/L)
Membrane 7
Membrane 8
Pall Mustang S

Figure 3C

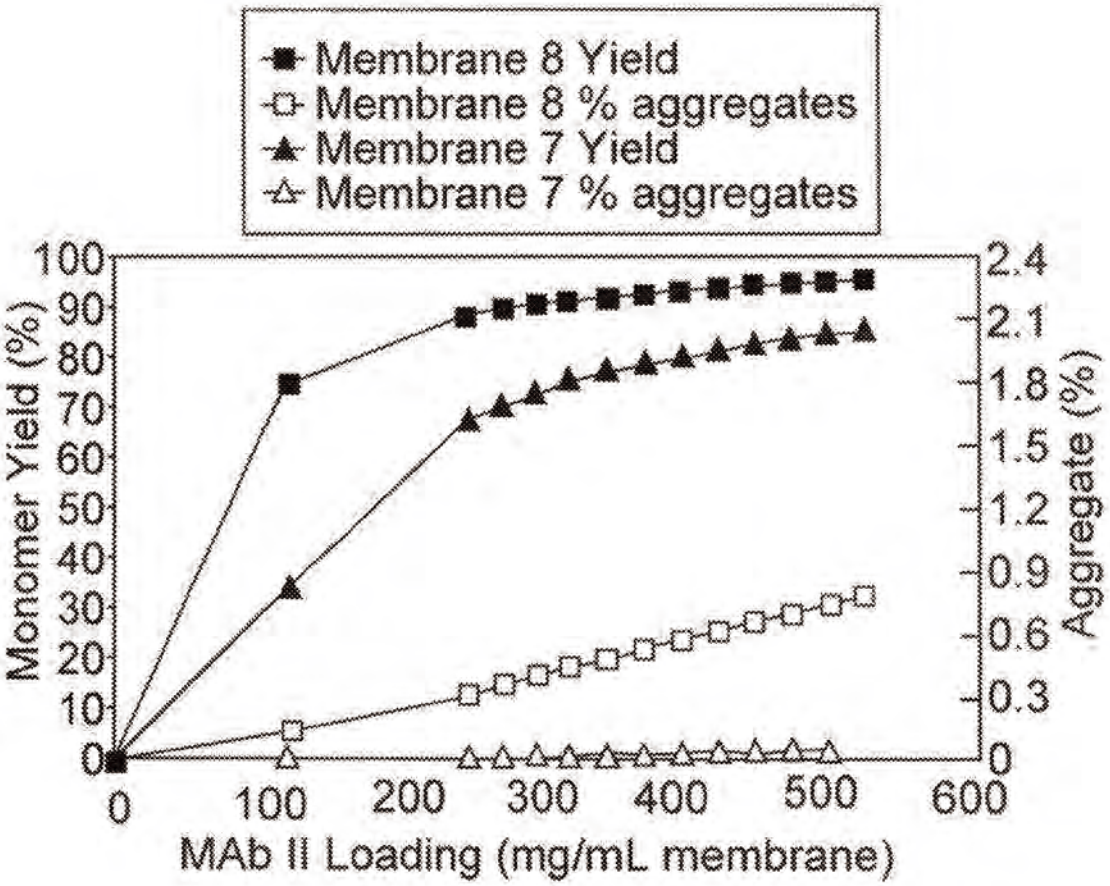

Membrane 8 Yield
Membrane 8 % aggregates
Membrane 7 Yield
Membrane 7 % aggregates
Monomer Yield (%)
Aggregate (%)
MAb II Loading (mg/mL membrane)
0
10
20
30
40
50
60
70
80
90
100
0.3
0.6
0.9
1.2
1.5
1.8
2.1
2.4
0
100
200
300
400
500
600

Figure 4A

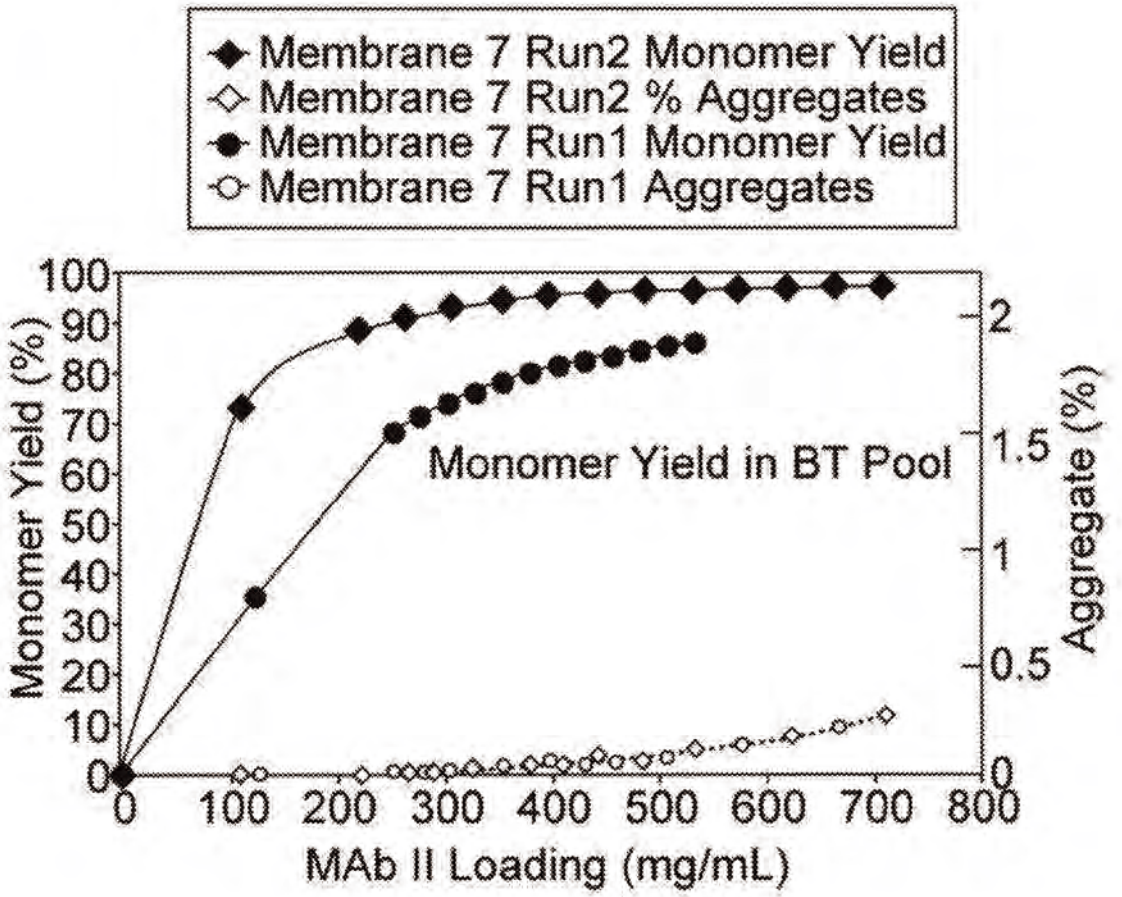

Membrane 7 Run2 Monomer Yield
Membrane 7 Run2 % Aggregates
Membrane 7 Run1 Monomer Yield
Membrane 7 Run1 Aggregates
Monomer Yield (%)
Aggregate (%)
Monomer Yield in BT Pool
MAb II Loading (mg/mL)
0
10
20
30
40
50
60
70
80
90
100
0.5
1
1.5
2
100
200
300
400
500
600
700
800

Figure 4B

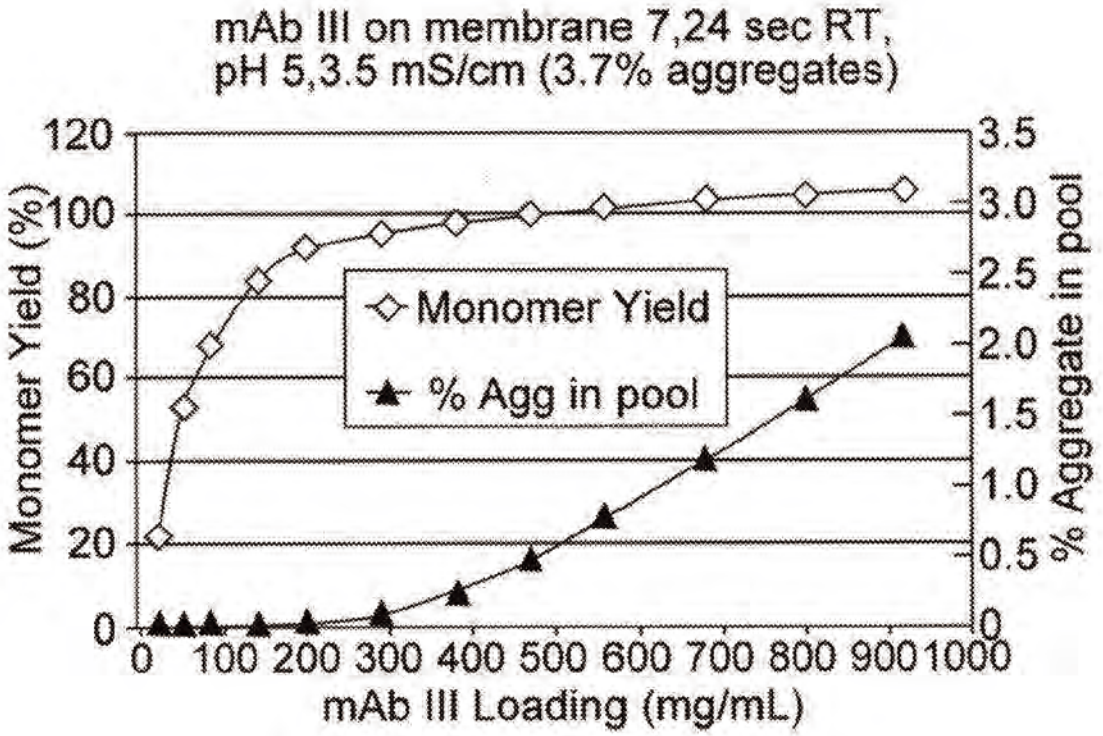

mAb III on membrane 7,24 sec RT,
pH 5,3.5 mS/cm (3.7% aggregates)
Monomer Yield (%)
% Aggregate in pool
Monomer Yield
% Agg in pool
mAb III Loading (mg/mL)
0
20
40
60
80
100
120
0.5
1.0
1.5
2.0
2.5
3.0
3.5
0 100 200 300 400 500 600 700 800 900 1000

Figure 5

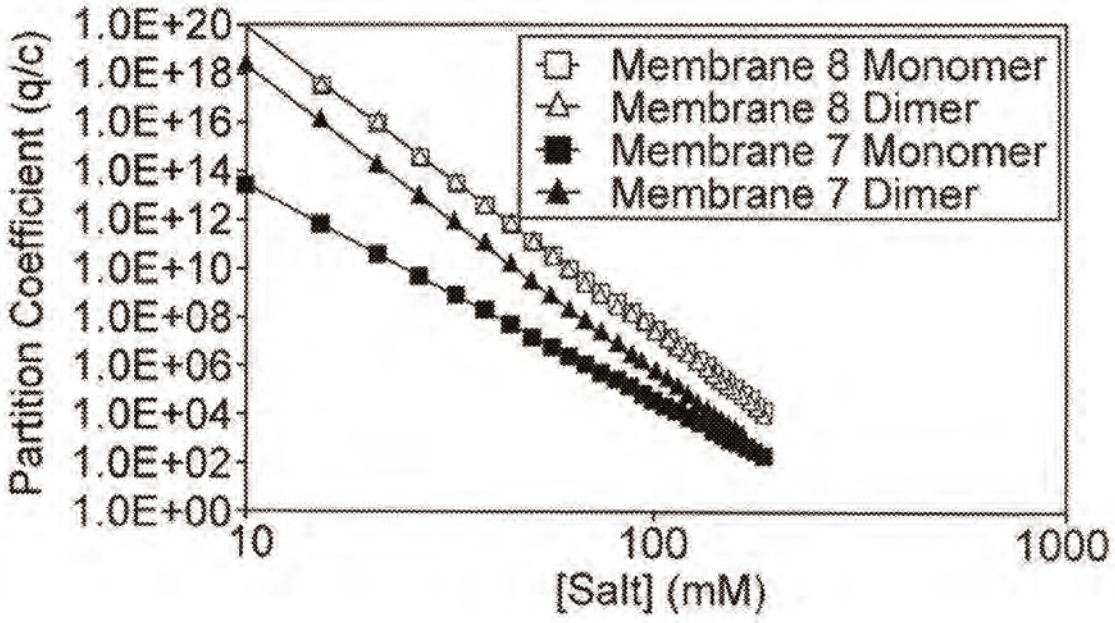

Partition Coefficient (q/c)
1.0E+20
1.0E+18
1.0E+16
1.0E+14
1.0E+12
1.0E+10
1.0E+08
1.0E+06
1.0E+04
1.0E+02
1.0E+00
10
100
1000
[Salt] (mM)
Membrane 8 Monomer
Membrane 8 Dimer
Membrane 7 Monomer
Membrane 7 Dimer

Figure 6A

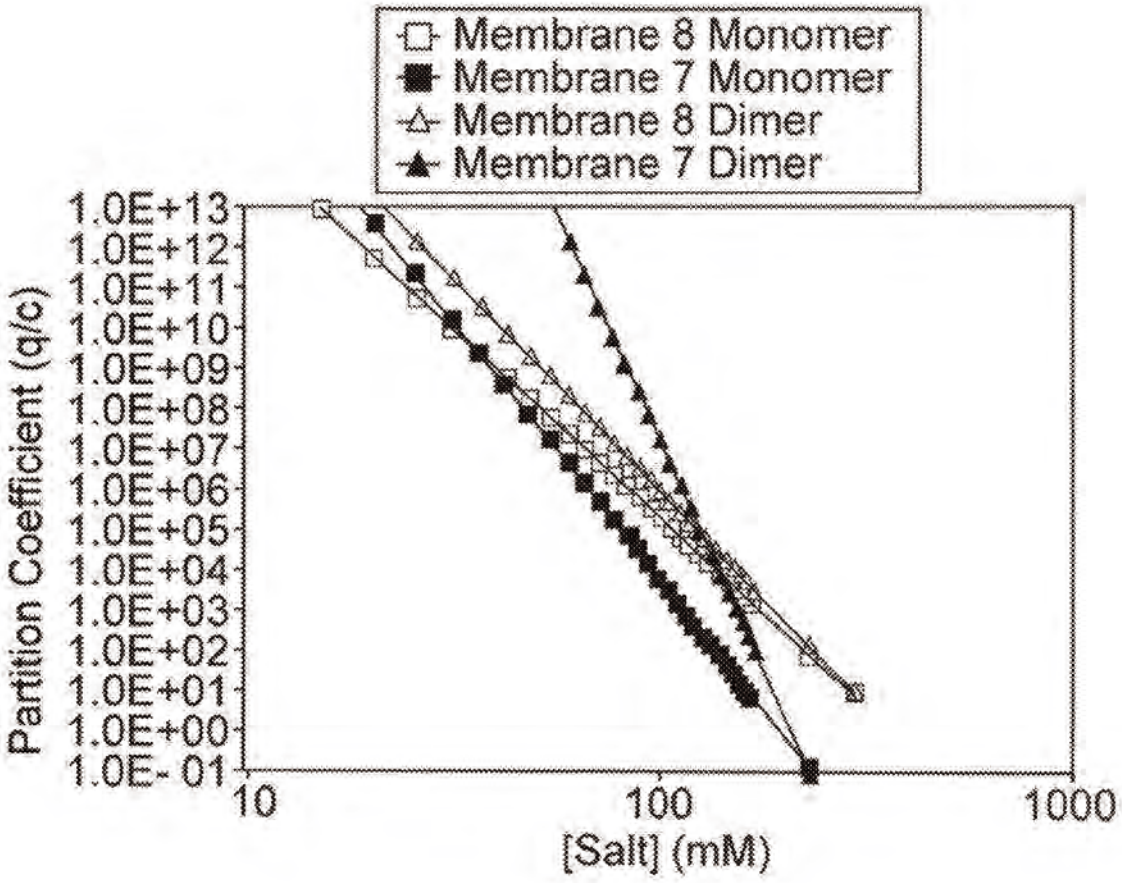

Membrane 8 Monomer
Membrane 7 Monomer
Membrane 8 Dimer
Membrane 7 Dimer
Partition Coefficient (q/c)
1.0E+13
1.0E+12
1.0E+11
1.0E+10
1.0E+09
1.0E+08
1.0E+07
1.0E+06
1.0E+05
1.0E+04
1.0E+03
1.0E+02
1.0E+01
1.0E+00
1.0E- 01
10
100
1000
[Salt] (mM)

Figure 6B

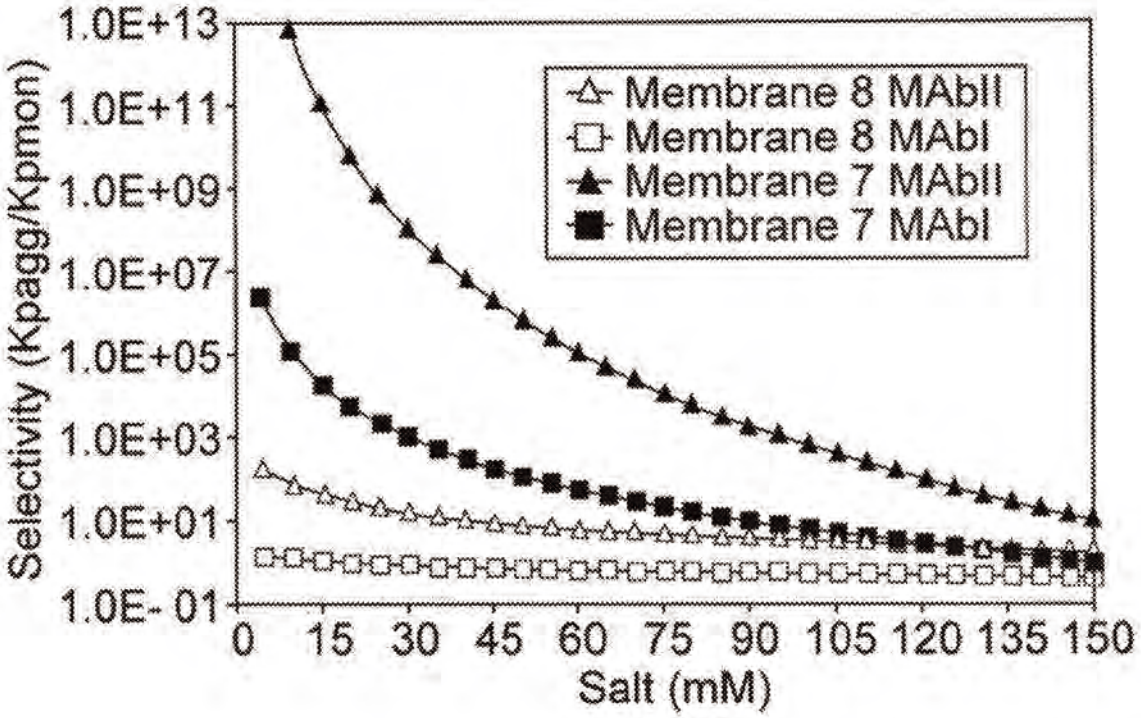
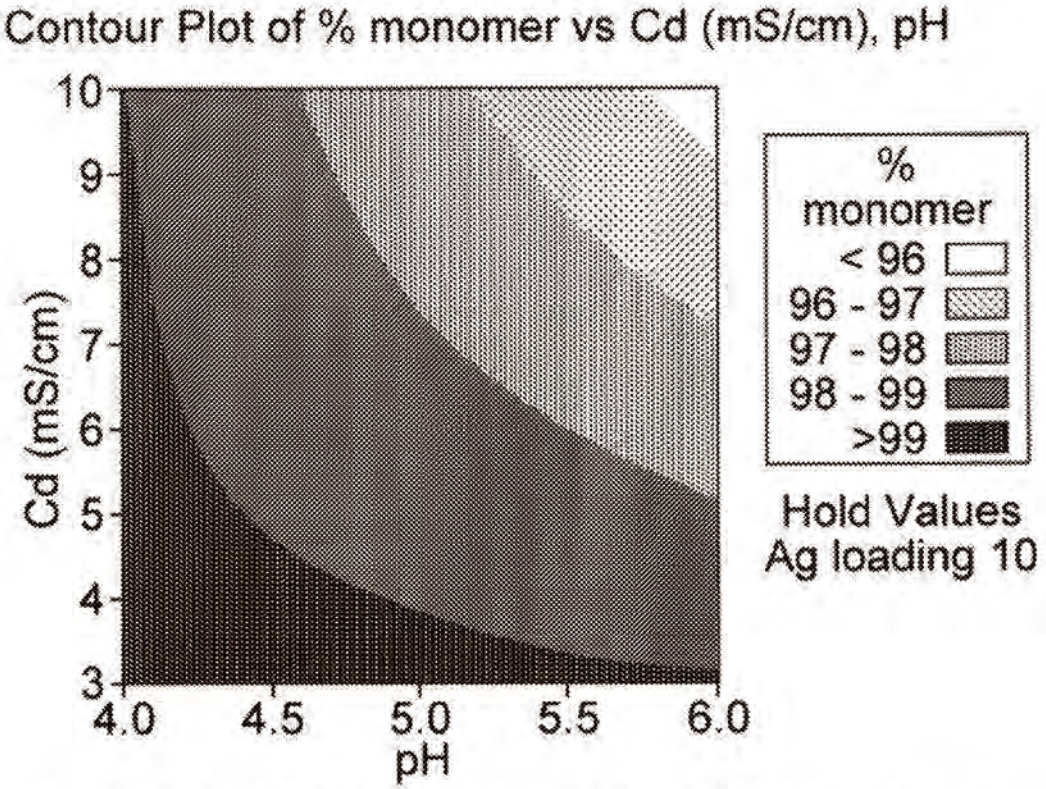

1.0E+13
1.0E+11
1.0E+09
1.0E+07
1.0E+05
1.0E+03
1.0E+01
1.0E- 01
Selectivity (Kpagg/Kpmon)
0 15 30 45 60 75 90 105 120 135 150
Salt (mM)
Membrane 8 MAbII
Membrane 8 MAbI
Membrane 7 MAbII
Membrane 7 MAbI

Figure 7


Contour Plot of % monomer vs Cd (mS/cm), pH
Cd (mS/cm)
10
9
8
7
6
5
4
3
4.0
4.5
5.0
5.5
6.0
pH
% monomer
< 96
96 - 97
97 - 98
98 - 99
>99
Hold Values
Ag loading 10

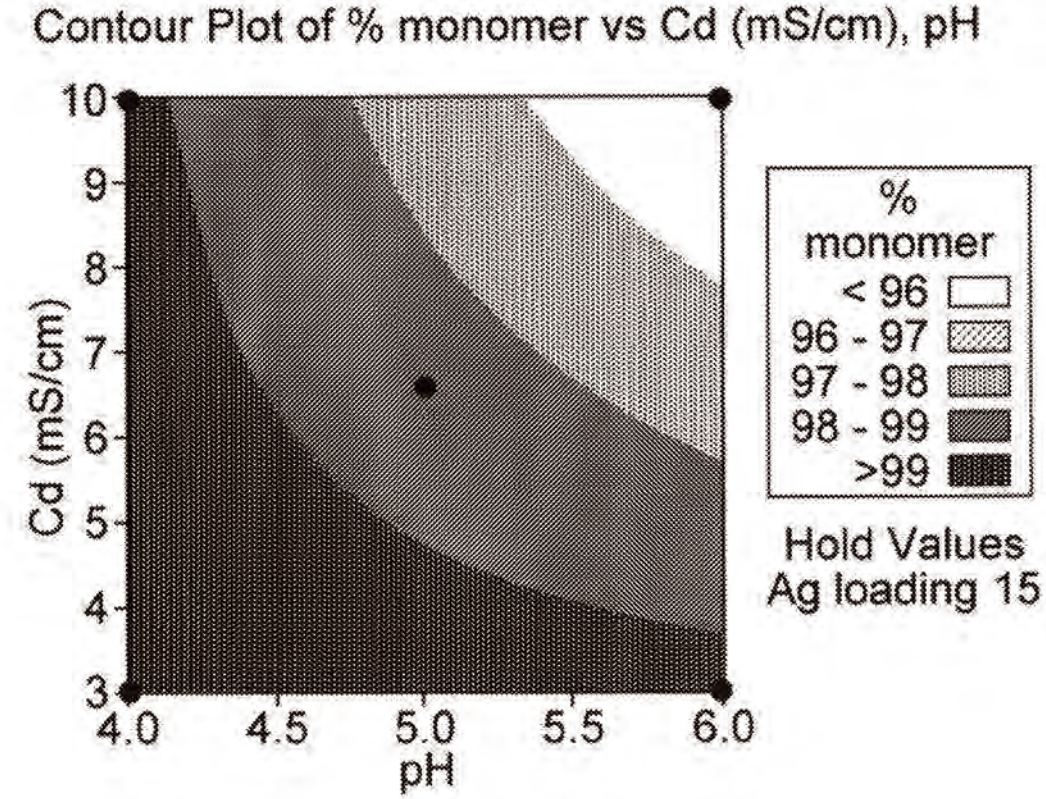

Contour Plot of % monomer vs Cd (mS/cm), pH
Cd (mS/cm)
10
9
8
7
6
5
4
3
4.0
4.5
5.0
5.5
6.0
pH
% monomer
< 96
96 - 97
97 - 98
98 - 99
>99
Hold Values
Ag loading 15

Figure 8

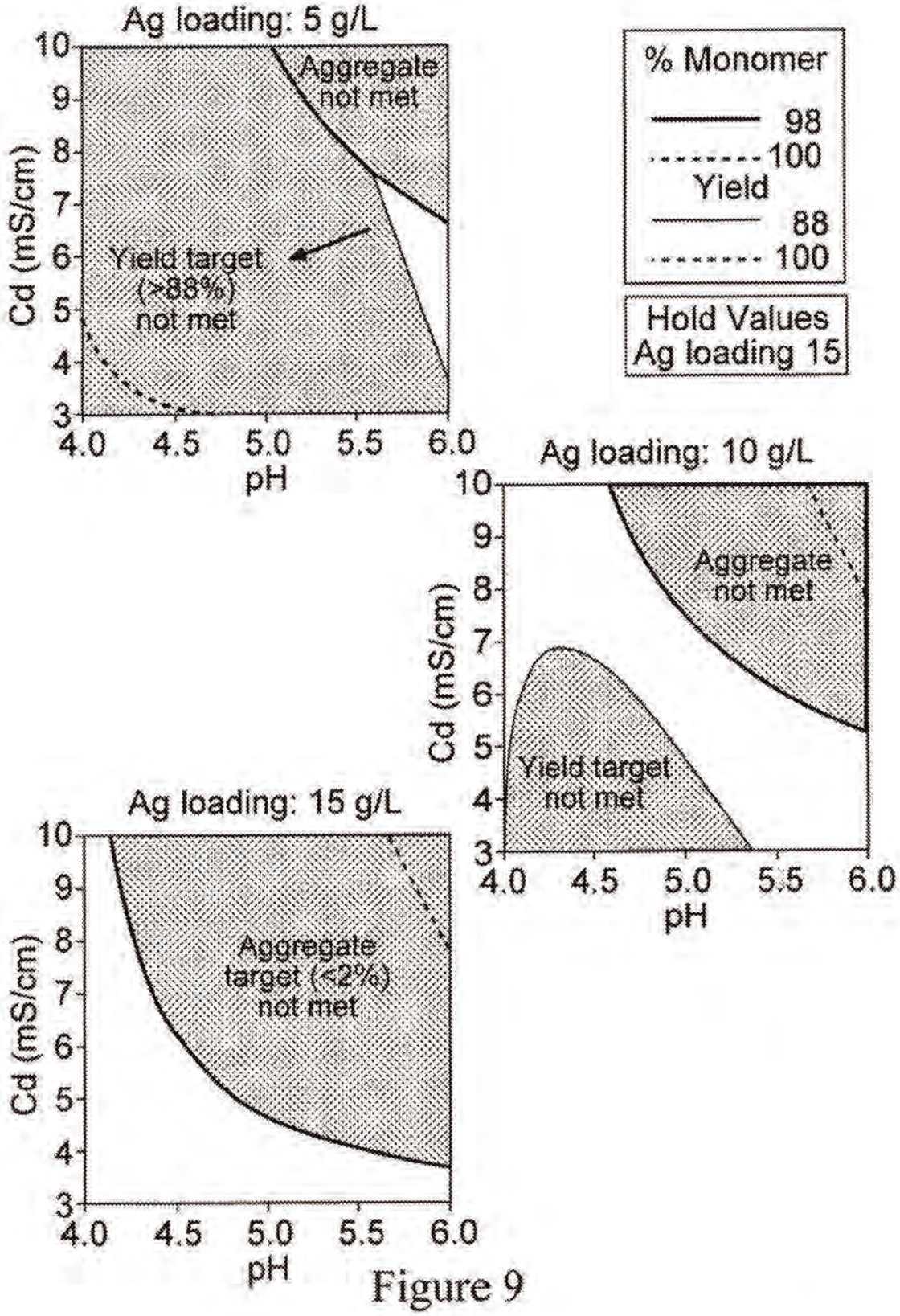

Ag loading: 5 g/L
Aggregate not met
Yield target (>88%) not met
Cd (mS/cm)
pH
% Monomer
98
100
Yield
88
100
Hold Values Ag loading 15
Ag loading: 10 g/L
Aggregate not met
Yield target not met
Ag loading: 15 g/L
Aggregate target (≤2%) not met

Figure 9

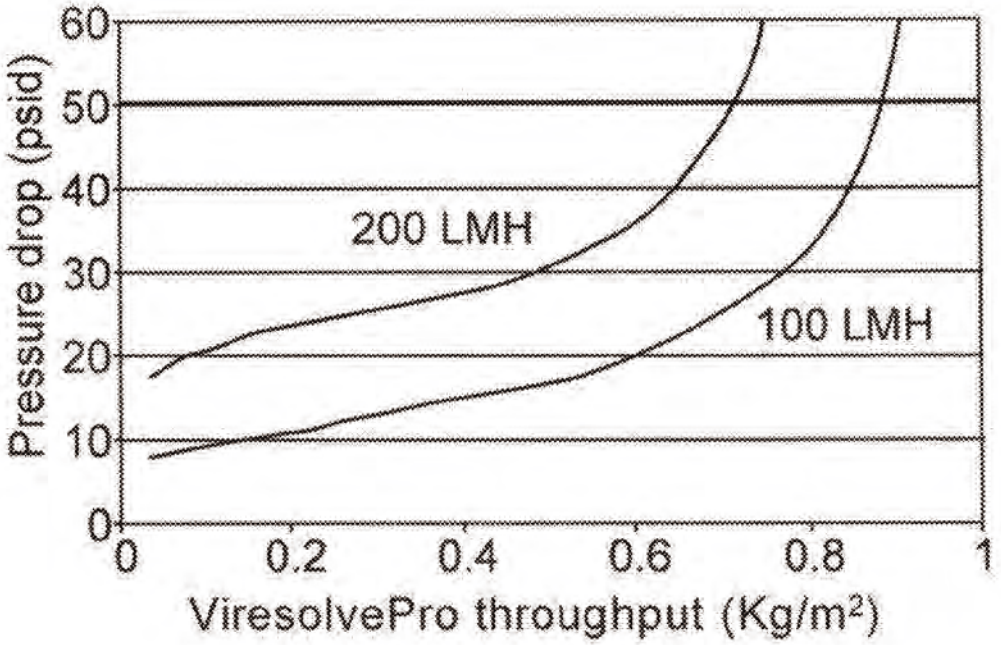

Pressure drop (psid)
60
50
40
30
20
10
0
200 LMH
100 LMH
0
0.2
0.4
0.6
0.8
1
ViresolvePro throughput (Kg/m²)

Figure 10

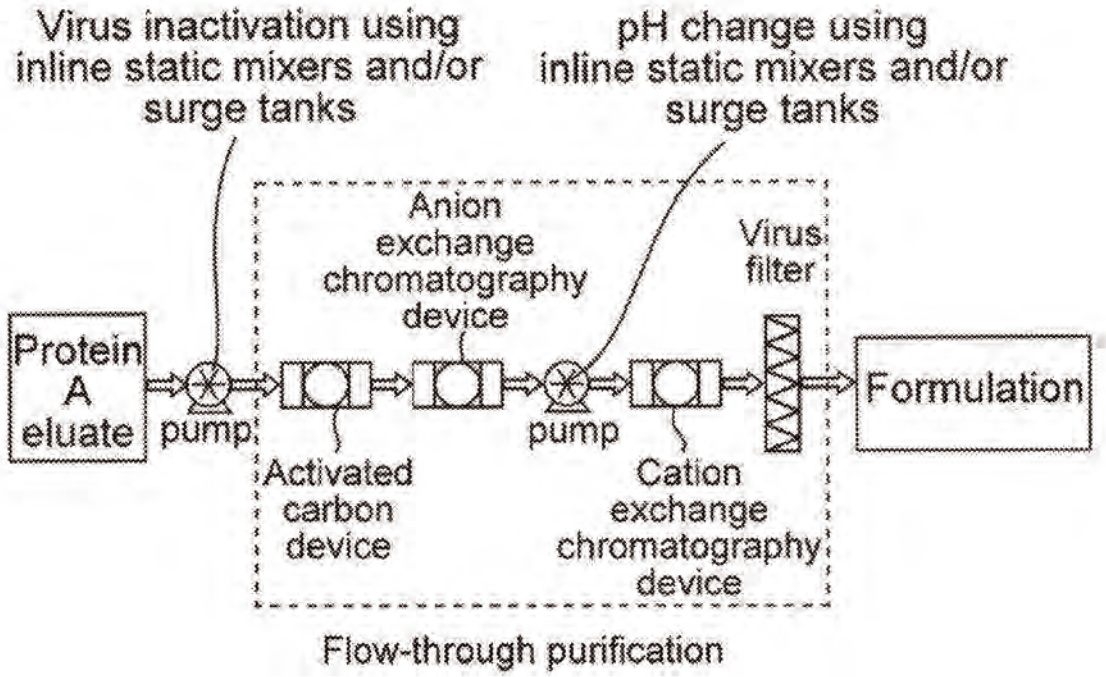

Virus inactivation using inline static mixers and/or surge tanks
pH change using inline static mixers and/or surge tanks
Anion exchange chromatography device
Virus filter
Protein A eluate
pump
Activated carbon device
pump
Cation exchange chromatography device
Formulation
Flow-through purification

Figure 11

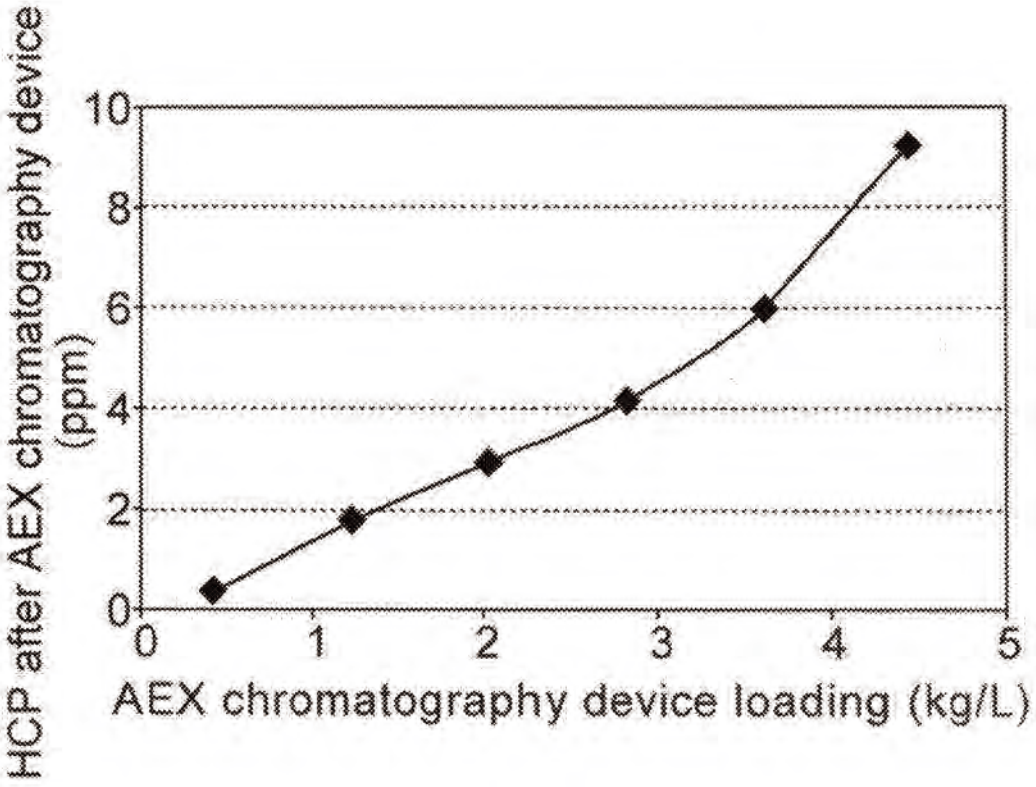

HCP after AEX chromatography device (ppm)
10
8
6
4
2
0
0
1
2
3
4
5
AEX chromatography device loading (kg/L)

Figure 12

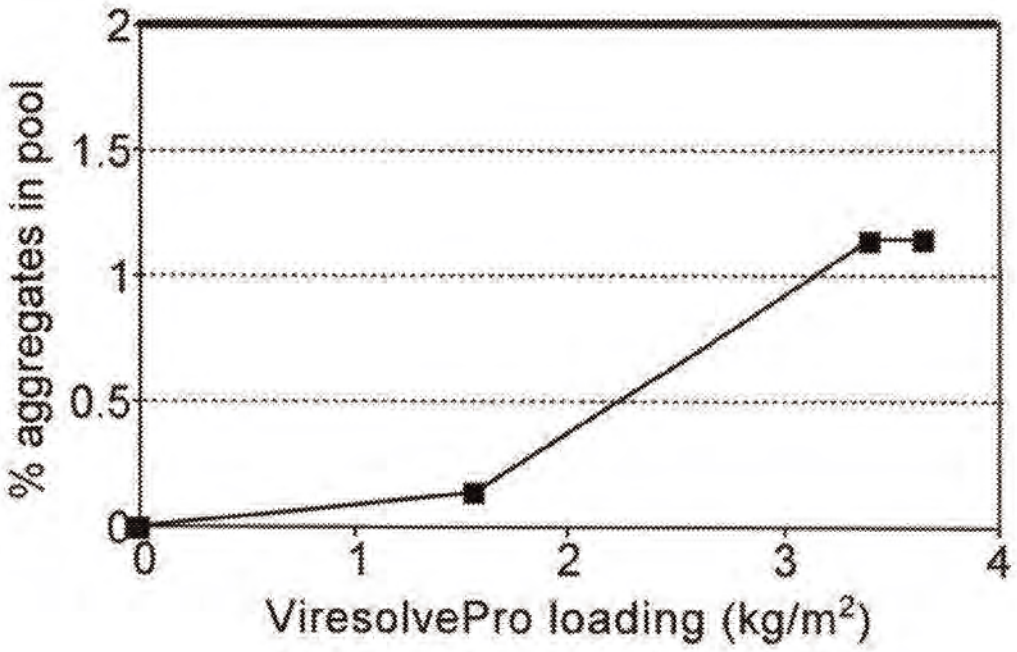

% aggregates in pool
2
1.5
1
0.5
0
0
1
2
3
4
ViresolvePro loading (kg/m²)

Figure 13

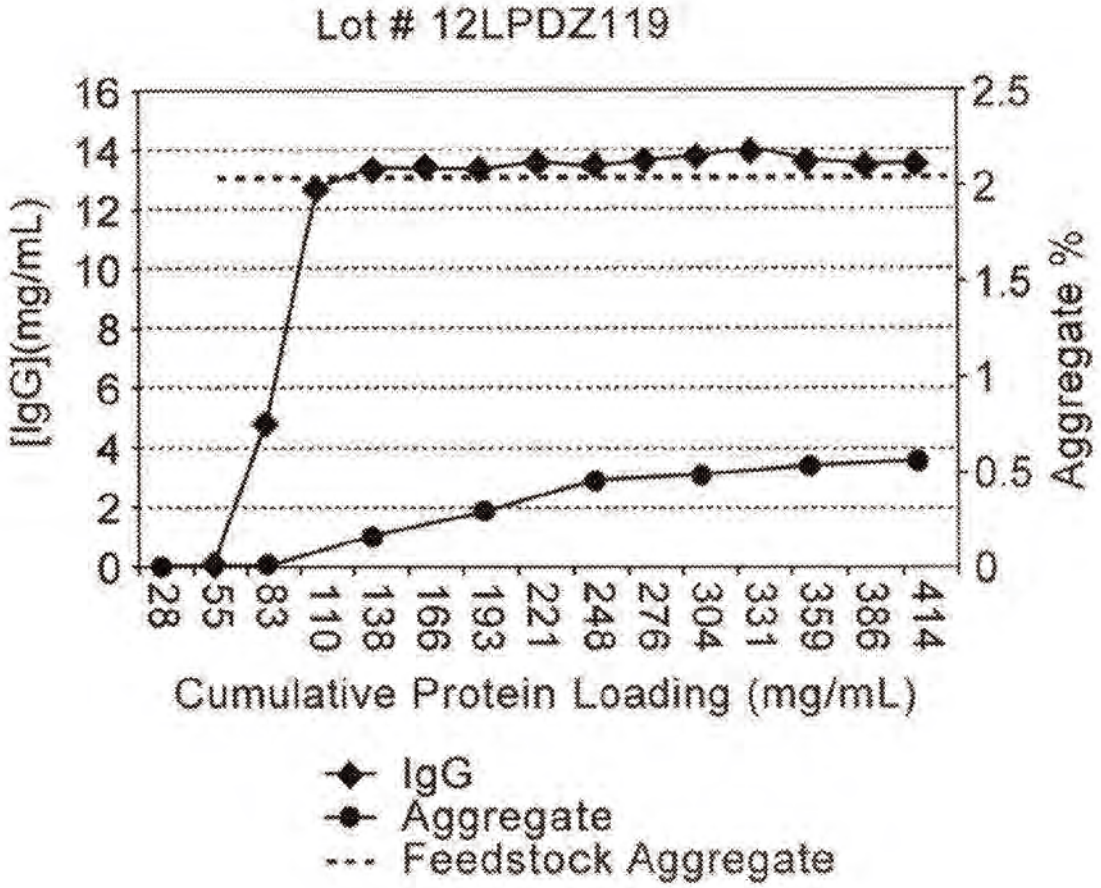

Lot # 12LPDZ119
[IgG](mg/mL)
Aggregate %
16
14
12
10
8
6
4
2
0
2.5
2
1.5
1
0.5
0
28
55
83
110
138
166
193
221
248
276
304
331
359
386
414
Cumulative Protein Loading (mg/mL)
IgG
Aggregate
Feedstock Aggregate

Figure 14

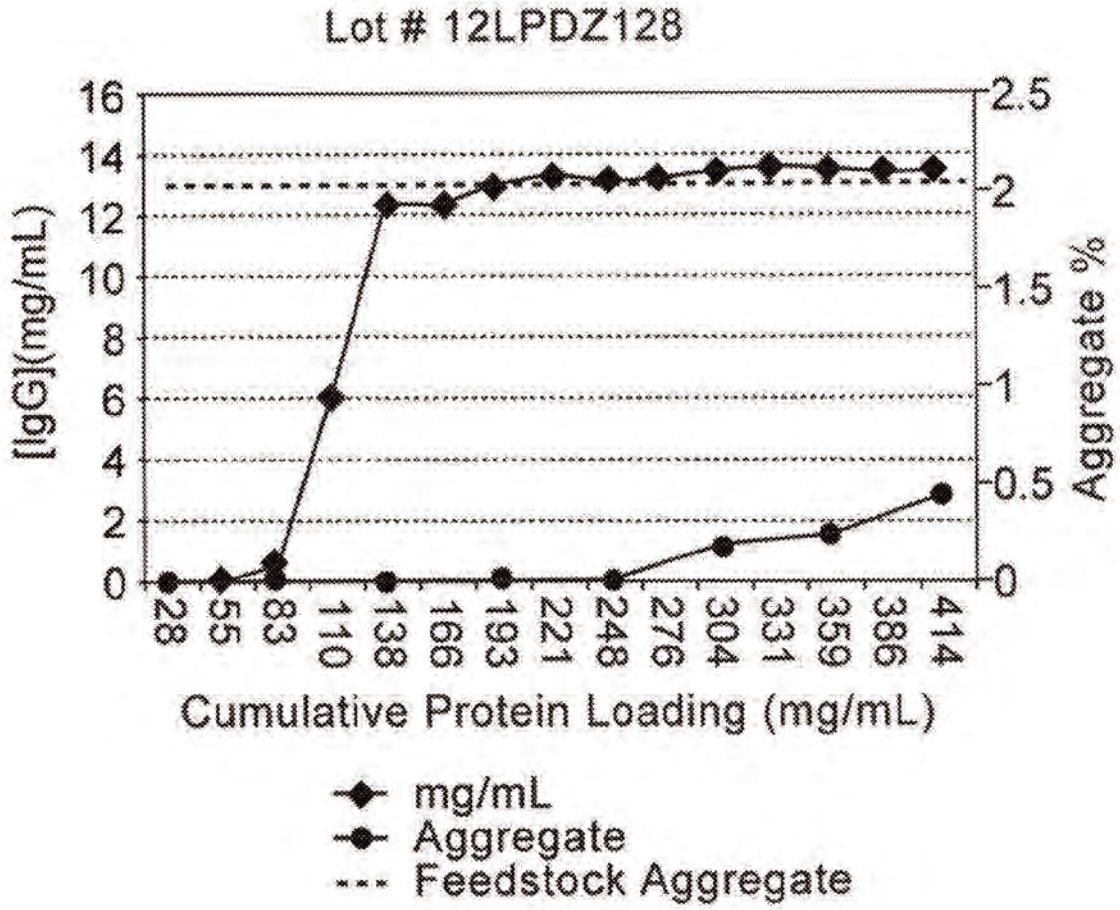

Lot # 12LPDZ128
[IgG](mg/mL)
Aggregate %
16
14
12
10
8
6
4
2
0
2.5
2
1.5
1
0.5
0
28
55
83
110
138
166
193
221
248
276
304
331
359
386
414
Cumulative Protein Loading (mg/mL)
mg/mL
Aggregate
Feedstock Aggregate

Figure 15

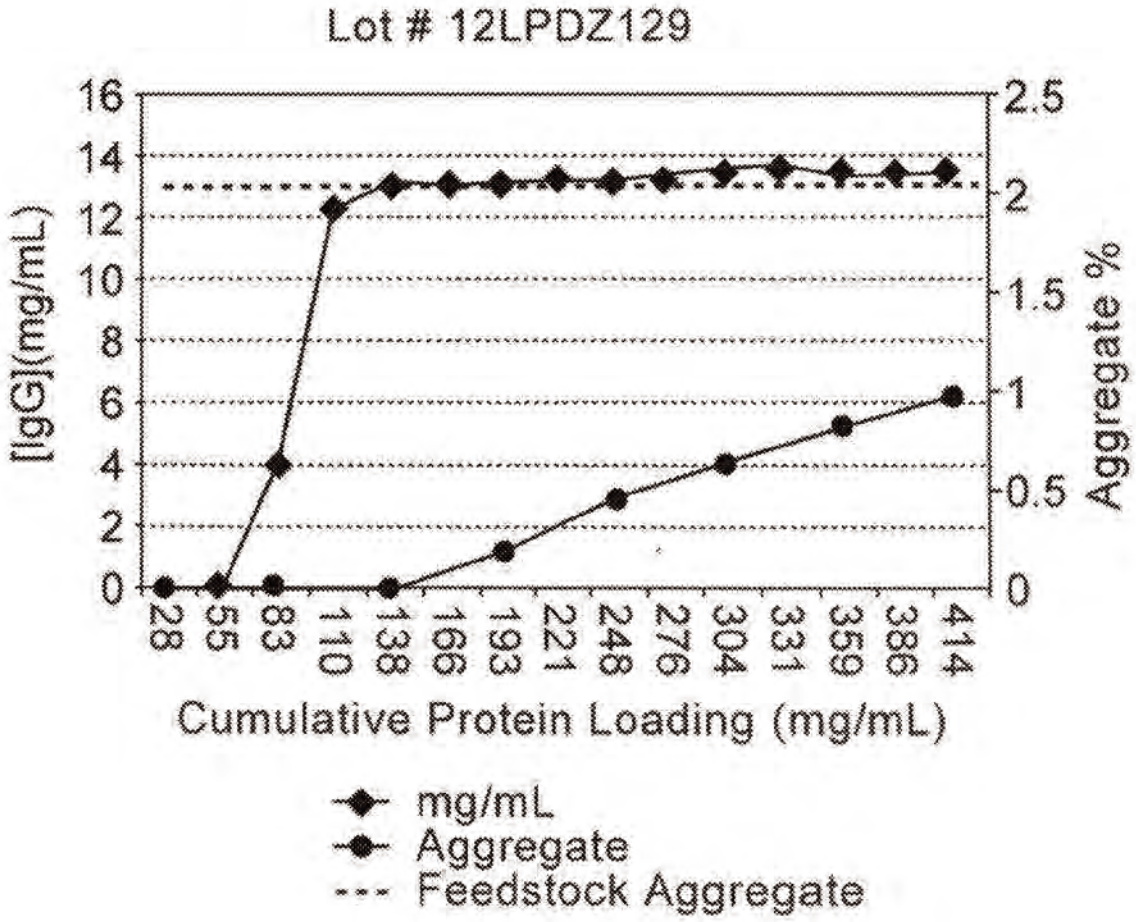

Lot # 12LPDZ129
[IgG](mg/mL)
Aggregate %
16
14
12
10
8
6
4
2
0
2.5
2
1.5
1
0.5
0
28
55
83
110
138
166
193
221
248
276
304
331
359
386
414
Cumulative Protein Loading (mg/mL)
mg/mL
Aggregate
Feedstock Aggregate

Figure 16

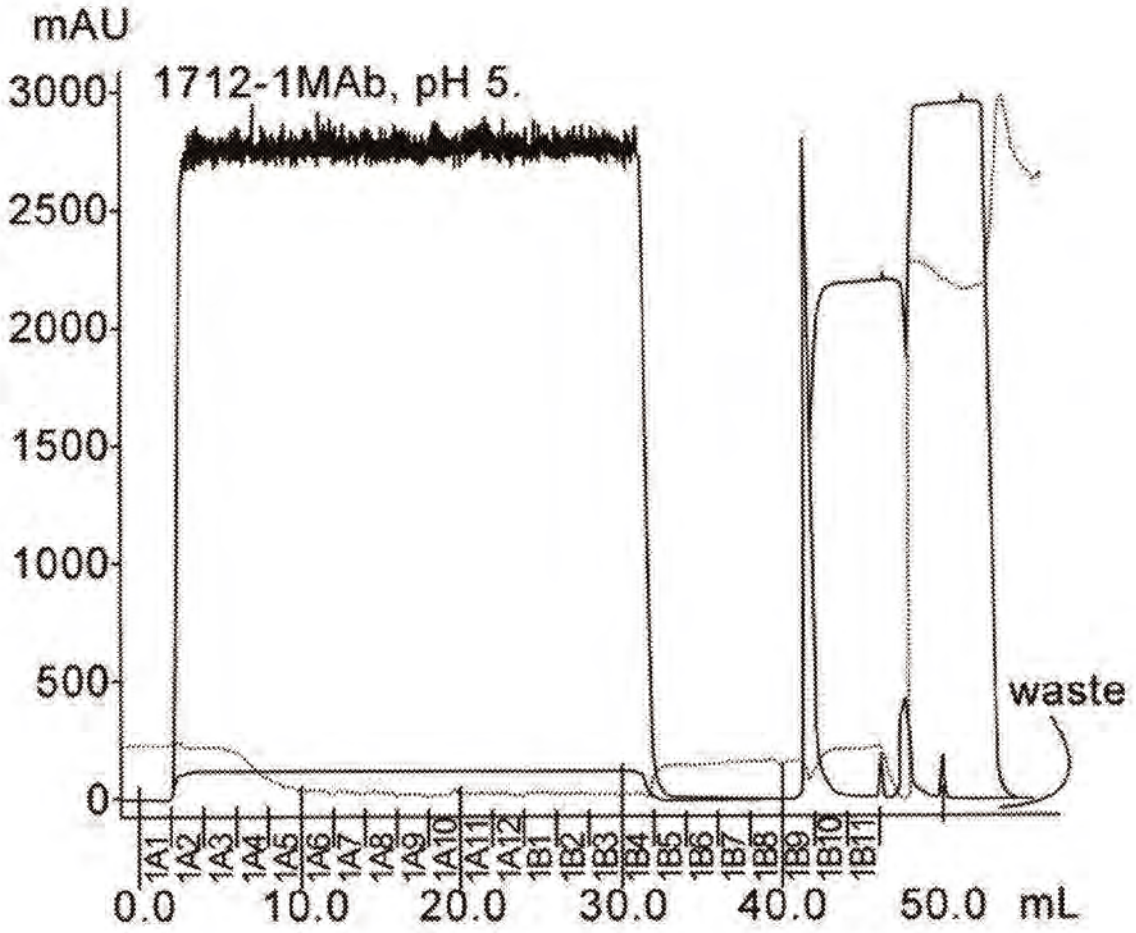

mAU
1712-1MAb, pH 5.
3000
2500
2000
1500
1000
500
0
waste
1A1
1A2
1A3
1A4
1A5
1A6
1A7
1A8
1A9
1A10
1A11
1A12
1B1
1B2
1B3
1B4
1B5
1B6
1B7
1B8
1B9
1B10
1B11
0.0
10.0
20.0
30.0
40.0
50.0
mL

Figure 17