Peptide Supply

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1 150401 ASN SSL IFN none

1.1 Attempt 1

Parameters	
Time	10 days
Self Peptide Supply	$0 molecules/s$
bP_T	3.177334×10^{-11} /molecules/s
bP_C	3.177334×10^{-11} /molecules/s

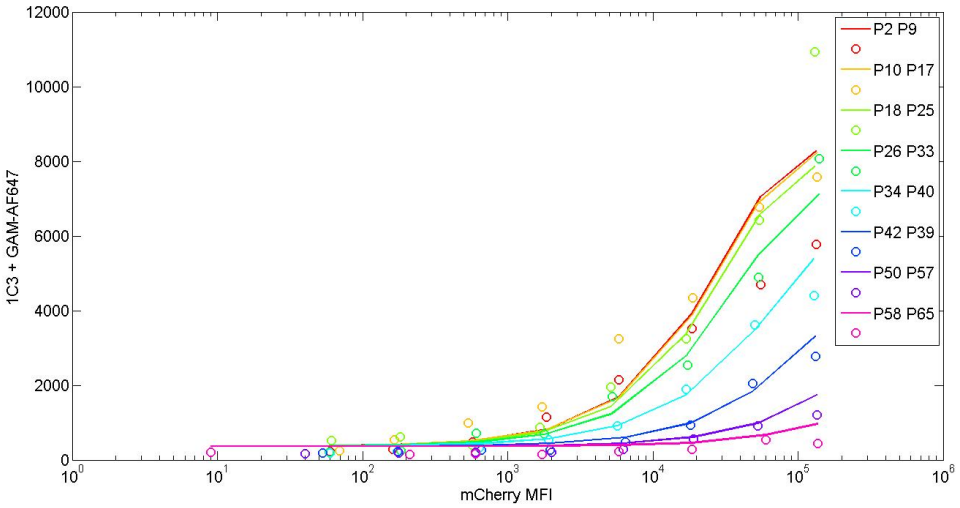
- Fitting Method 1: Scale target and competitor concentration by sf1 and sf2 resp. to fit for supply, then scale output cell surface data using polyfit ie p1*MeP1 + p2 to get best fit to data. sf0=[1,100]

Best Fit Scale Factors	
sf1	0.0230
sf2	0.5702
p1	0.0009
p2	364.3225
err	$5.4132 \times 10^{+03}$

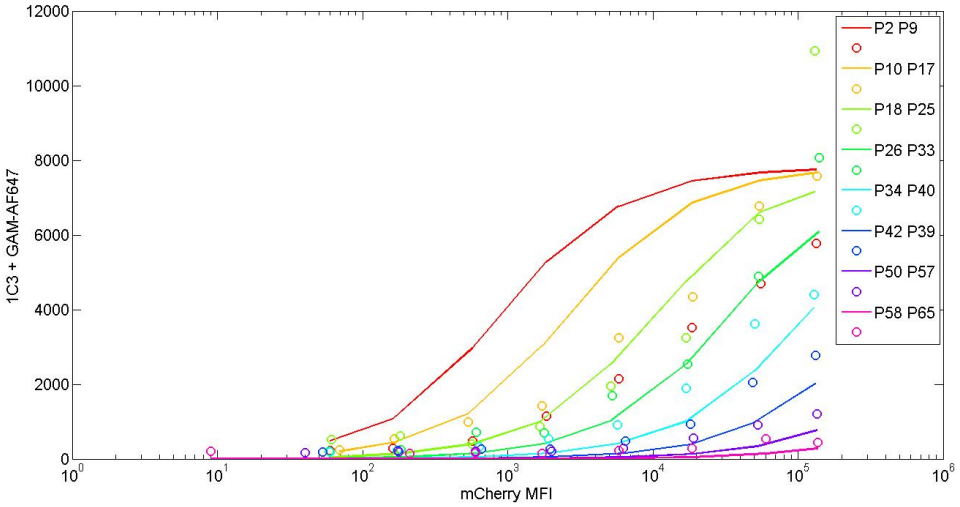
- Fitting Method 2: Scale target and competitor concentration by sf1 and sf2 resp. to fit for supply, then scale output cell surface data by sf3 to get best fit to data. sf0=[1,100,1]

Best Fit Scale Factors	
sf1	2.2079
sf2	79.1768
sf3	0.0009
resid	$4.3045 \times 10^{+07}$

- Evaluation: The first fitting method performs much better than the second however both fits are quite poor. The data for P2 P9, P10 P17, P18 P25 and P26 P33 are not in the order you would expect. Ie you would expect P2 P9 to have the largest cell surface presentation because it has the lowest competitor concentration, however P18 P25 suddenly jumps up at the end. This may explain the bad fit for both the methods used above. The data for the lowest four lines are in the order you would expect. All lines (with the exception of the top 2) seem to be in order of concentration up until the 6th data point. Perhaps ignoring the final two data points would give a better fit and treat the strange behaviour at the end as outliers? However, because of the strange order of the top 4 lines, and because we are fitting for the same set of scale factors for each line, it does not seem possible to get a good fit to this data, unless we used different scale factors for each line.



(a)



(b)

Figure 1: Best fit to the data for a) Fitting method 1, b) Fitting method 2, where the best fit scale factors are given in tables 2 and 3 respectively

2 150422-ASN-SSL-IFN-none

2.1 Attempt 1

Parameters	
Time	10 days
Self Peptide Supply	0 molecules/s
bP_T	3.177334×10^{-11} /molecules/s
bP_C	3.177334×10^{-11} /molecules/s

- Fitting Method 1: Scale target and competitor concentration by sf1 and sf2 resp. to fit for supply, then scale output cell surface data using polyfit ie p1*MeP1 + p2 to get best fit to data. sf0=[1,100]

Best Fit Scale Factors	
sf1	0.0669
sf2	1.1652
p1	0.0011
p2	361.8626
err	$6.6111e+03$

- Evaluation: Fitting method 1 does not produce a very good fit to the data. I would have expected a better fit to this data than the 150401 data in section 1, because with the exception of the top two lines from data points 7-8, the lines are in order of the competitor concentration. Perhaps we should ignore the final 2 data points for the top two lines and just fit to the others? The data for both 150401 and 150422 suggests that the small changes in competitor concentration between the P2 P9 and P10 P17 should produce a noticeable difference in cell surface abundance. However in both figures 1a and 2 the simulated trajectories for these two lines are very similar. There is a large difference between them in figure 1b, however the over all fit is much worse. Perhaps the two predicted lines are so similar because the simulation takes the cell surface levels after t=10 days and so after such a long time the off-rate is more influential on the cell surface abundance than supply or competition? Perhaps reducing the time at which the simulated 'measurement' is taken will give a better fit?

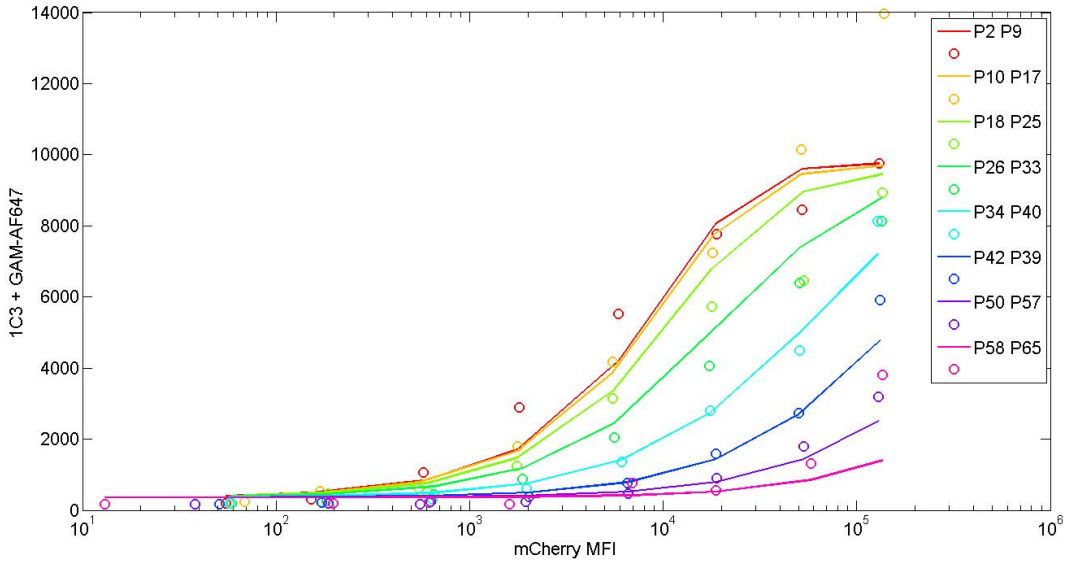


Figure 2: Best fit to the data for Fitting method 1 to data 150422-ASN-SSL-IFN-none, where the best fit scale factors are given in table 5

2.2 Attempt 2

Parameters	
Time	$10 days$
Self Peptide Supply	0 molecules/s
bP_T	$3.177334e-11$ /molecules/s
bP_C	$3.177334e-11$ /molecules/s

- Fitting Method 1: Scale target and competitor concentration by sf1 and sf2 resp. to fit for supply, then scale output cell surface data using polyfit ie p1*MeP1 + p2 to get best fit to data. Resid calculated for all points except data points 7 and 8 for lines V-ASN P2 and V-ASN P10. sf0=[1,100]

Best Fit Scale Factors	
sf1	0.0999
sf2	1.0934
p1	0.0010
p2	156.4038
err	$3.3296e+07$

- Evaluation: Fitting method 1 does not produce a very good fit to the data. I would have expected a better fit to this data than the 150401 data in section 1, because with the exception of the top two lines from data points 7-8, the lines are in order of the competitor concentration. Perhaps we should ignore the final 2 data points for the top two lines and just fit to the others? The data for both 150401 and 150422 suggests that the small changes in competitor concentration between the P2 P9 and P10 P17 should produce a noticeable difference in cell surface abundance. However in both figures 1a and 2 the simulated trajectories for these two lines are very similar. There is a large difference between them in figure 1b, however the over all fit is much worse. Perhaps the two predicted lines are so similar because the simulation takes the cell surface levels after t=10 days and so after such a long time the off-rate is more influential on the cell surface abundance than supply or competition? Perhaps reducing the time at which the simulated 'measurement' is taken will give a better fit?

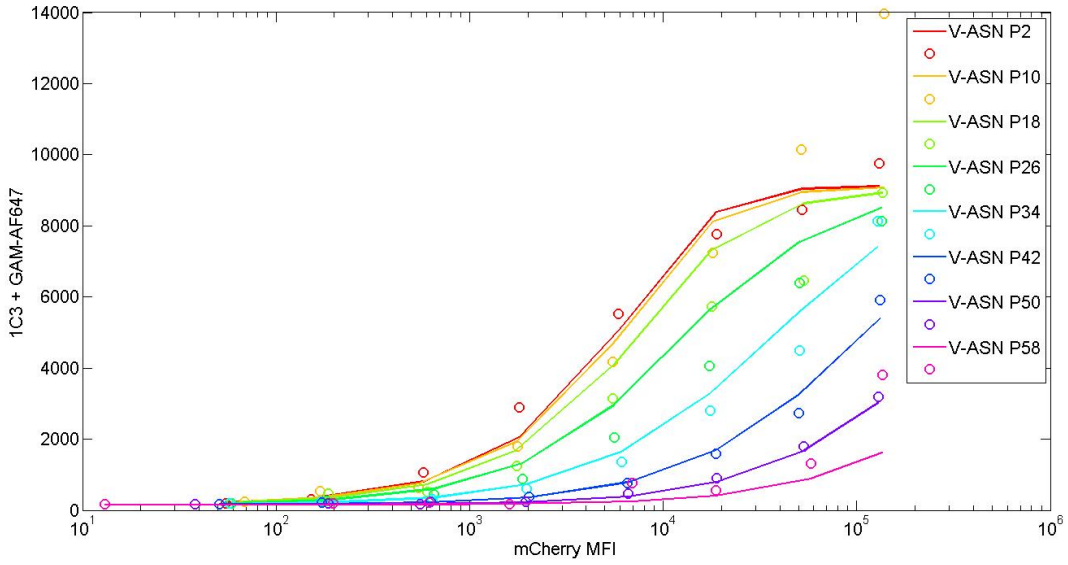


Figure 3: t=10days, sf1= 0.0999, sf2 = 1.0934, p1 = 0.0010, p2 = 156.4038, err = $3.3296e+07$

2.3 Attempt 3

Parameters	
Time	1 day
Self Peptide Supply	$0 molecules/s$
bP_T	$3.177334e-11$ /molecules/s
bP_C	$3.177334e-11$ /molecules/s

- Fitting Method 1: Scale target and competitor concentration by sf1 and sf2 resp. to fit for supply, then scale output cell surface data using polyfit ie p1*MeP1 + p2 to get best fit to data. Error calculated for all points. sf0=[1,100]

Best Fit Scale Factors	
sf1	0.8804
sf2	14.8020
p1	0.0015
p2	343.9527
err	$6.3597e+03$

- Evaluation: Reducing time improves fit.

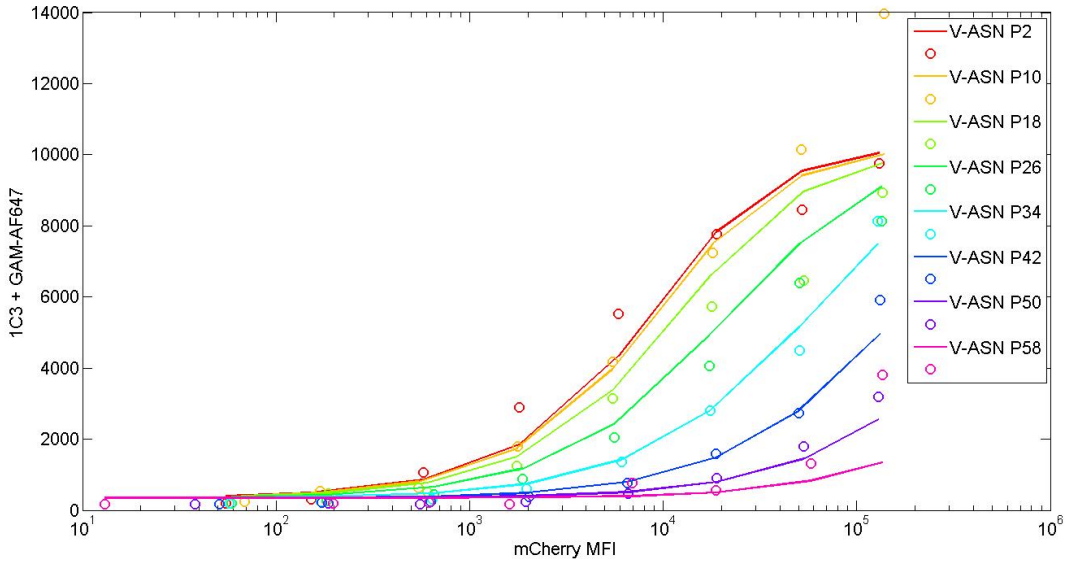


Figure 4: t=1 day, sf1 =0.8804, sf2=14.8020, p1 =0.0015, p2 =343.9527, err= $6.3597e+03$

2.4 Attempt 4

Parameters	
Time	1 day
Self Peptide Supply	35000 molecules/s
u_{self}	$1e-3s^{-1}$
bP_{self}	$3.177334e-11$ /molecules/s
bP_T	$3.177334e-11$ /molecules/s
bP_C	$3.177334e-11$ /molecules/s

- Fitting Method 1: Scale target and competitor concentration by sf1 and sf2 resp. to fit for supply, then scale output cell surface data using polyfit ie p1*MeP1 + p2 to get best fit to data. Resid calculated for all points except data points 7 and 8 for lines V-ASN P2 and V-ASN P10. sf0=[1,100]

Best Fit Scale Factors	
sf1	0.9214
sf2	15.4831
p1	0.0015
p2	341.8633
err	$6.3319e+03$

- Evaluation: Reducing time does not improve fit and including self peptides does not really improve fit for fitting method 1.

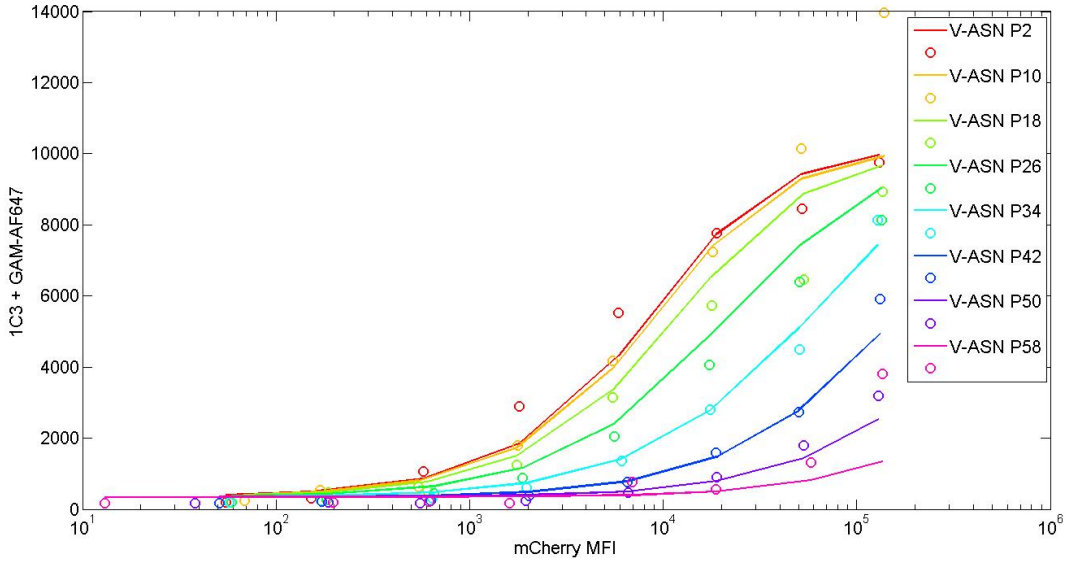


Figure 5: t=1 day, sf1 =0.9214, sf2=15.4831, p1 =0.0015, p2 =341.8633, err = $6.3319e+03$

2.5 Attempt 5

Parameters	
Time	10 days
Self Peptide Supply	$0 molecules/s$
bP_T	$3.177334e-9$ /molecules/s
bP_C	$3.177334e-11$ /molecules/s

- Fitting Method 1: Scale target and competitor concentration by sf1 and sf2 resp. to fit for supply, then scale output cell surface data by sf3 to get best fit to data. sf0=[1,1000]

Best Fit Scale Factors	
sf1	2.1745
sf2	$1.3297e+03$
p1	0.0012
p2	341.5584
err	$5.0349e+03$

- Evaluation: Increasing the binding rate of the target peptide compared to the competitor peptide improves the fit slightly (and ignoring the first line when doing the fit).

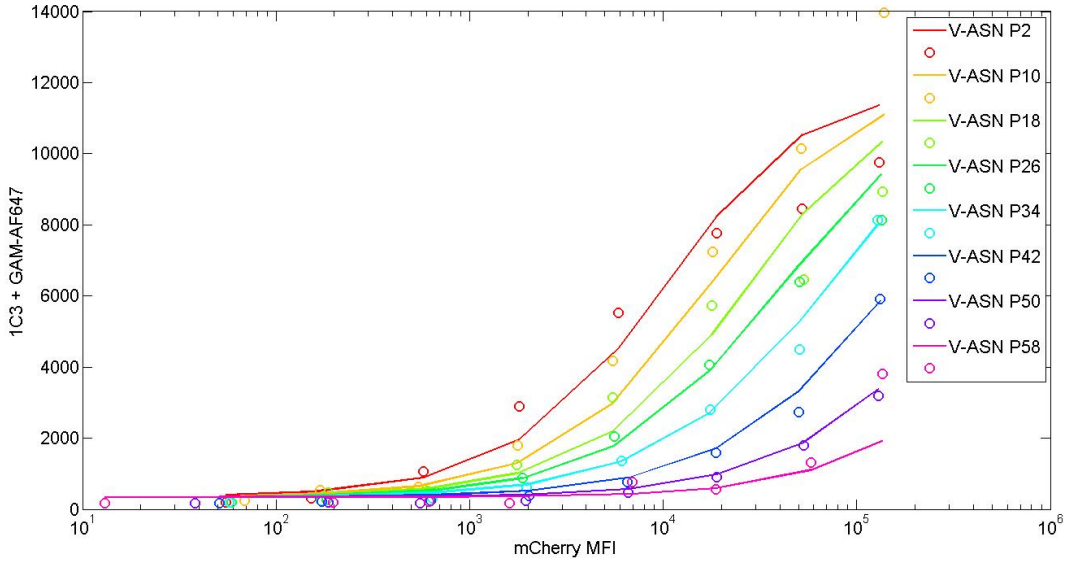


Figure 6: t=10days, sf1 = 2.1745, sf2 =$1.3297e+03$, p1 = 0.0012, p2 =341.5584, err =$5.0349e+03$

2.6 Attempt 6

Parameters	
Time	10 days
Self Peptide Supply	0 molecules/s
bP_T	$3.177334e-9$ /molecules/s
bP_C	$3.177334e-11$ /molecules/s

- Fitting Method 1: Scale target and competitor concentration by sf1 and sf2 resp. to fit for supply, then scale output cell surface data by sf3 to get best fit to data. sf0=[1,1]

Best Fit Scale Factors	
sf1	0.0905
sf2	2.3538
p1	0.0011
p2	284.6238
err	$5.9197e+03$

- Evaluation: Increasing the binding rate of the target peptide compared to the competitor peptide and including the first line produces similar fit to attempt 5.

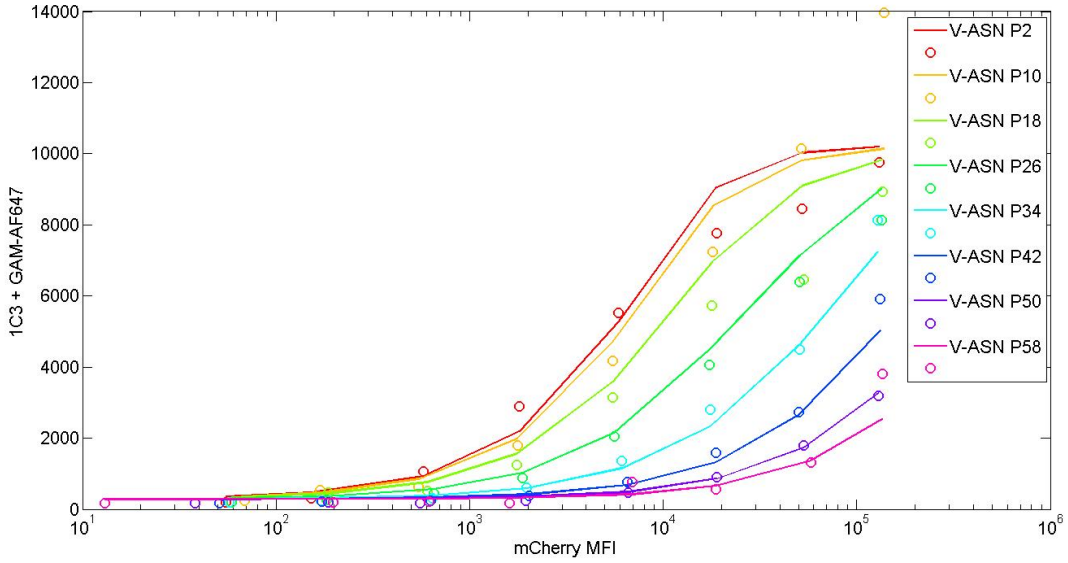


Figure 7: t=10days, sf1= 0.0905, sf2 = 2.3538, p1 =0.0011, p2 =284.6238, err = $5.9197e+03$

2.7 Attempt 7

Parameters	
Time	1 hour
Self Peptide Supply	0 molecules/s
bP_T	$3.177334e-11$ /molecules/s
bP_C	$3.177334e-11$ /molecules/s

- Fitting Method 1: Scale target and competitor concentration by sf1 and sf2 resp. to fit for supply, then scale output cell surface data by sf3 to get best fit to data. sf0=[1,1]

Best Fit Scale Factors	
sf1	50.0718
sf2	565.9833
p1	0.0253
p2	272.0332
err	$5.8382e+03$

- Evaluation: Reducing the simulation time to 1 hour produces the best fit when fitting for all lines.

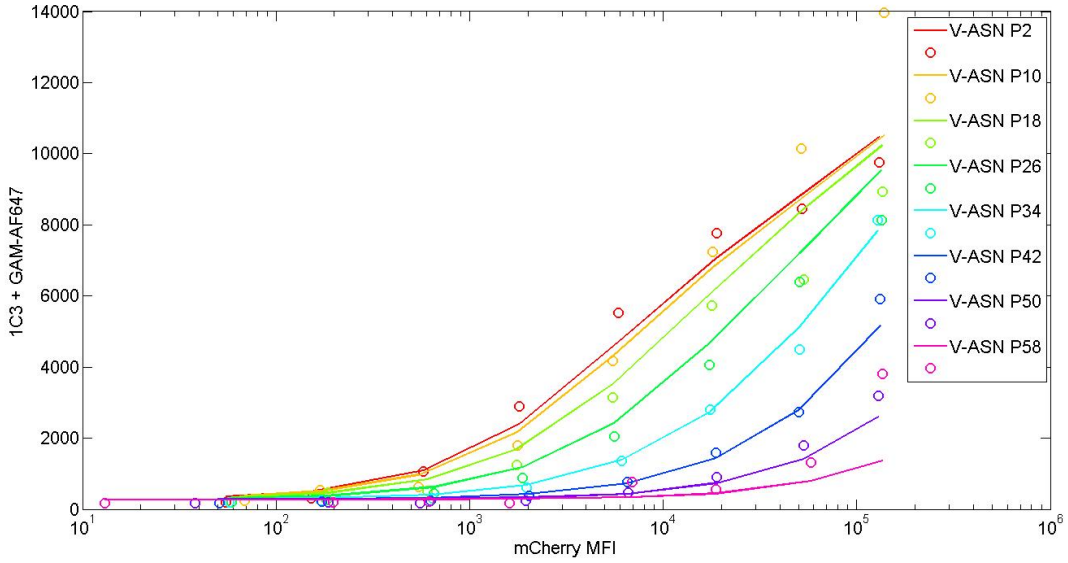


Figure 8: t=1hr, sf1 = 50.0718, sf2 =565.9833, p1 = 0.0253, p2 = 272.0332, err =$5.8382e+03$

2.8 Attempt 8

Parameters	
Time	1 hour
Self Peptide Supply	10000 molecules/s
u_{self}	$1e-3s^{-1}$
bP_{self}	$3.177334e-11$ /molecules/s
bP_T	$3.177334e-11$ /molecules/s
bP_C	$3.177334e-11$ /molecules/s

- Fitting Method 1: Scale target and competitor concentration by sf1 and sf2 resp. to fit for supply, then scale output cell surface data by sf3 to get best fit to data. sf0=[1,1]

Best Fit Scale Factors	
sf1	50.2073
sf2	567.5229
p1	0.0253
p2	272.0222
err	$5.8375e+03$

- Evaluation: Reducing the simulation time to 1 hour and including 10000 self peptides produces a slightly better fit than without self peptides for similar scale factor values.

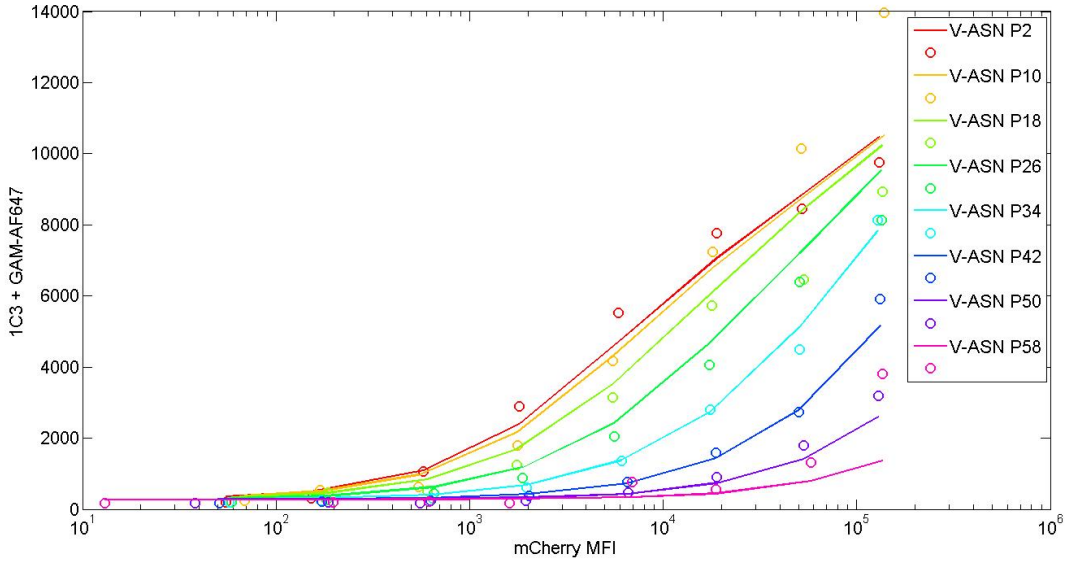


Figure 9: t=1hr, sf1 = 50.0718, sf2 =565.9833, p1 = 0.0253, p2 = 272.0332, err =$5.8382e+03$, self peps= 10000 molecules/s

2.9 Overview

- Err decreases as decrease time up to 1 hour, then any lower than that err begins to increase again
- As err decreases with time, the parameters p and sf increase - it would be useful to know if we expect the MFI measurements to be higher or lower than the actual concentrations!

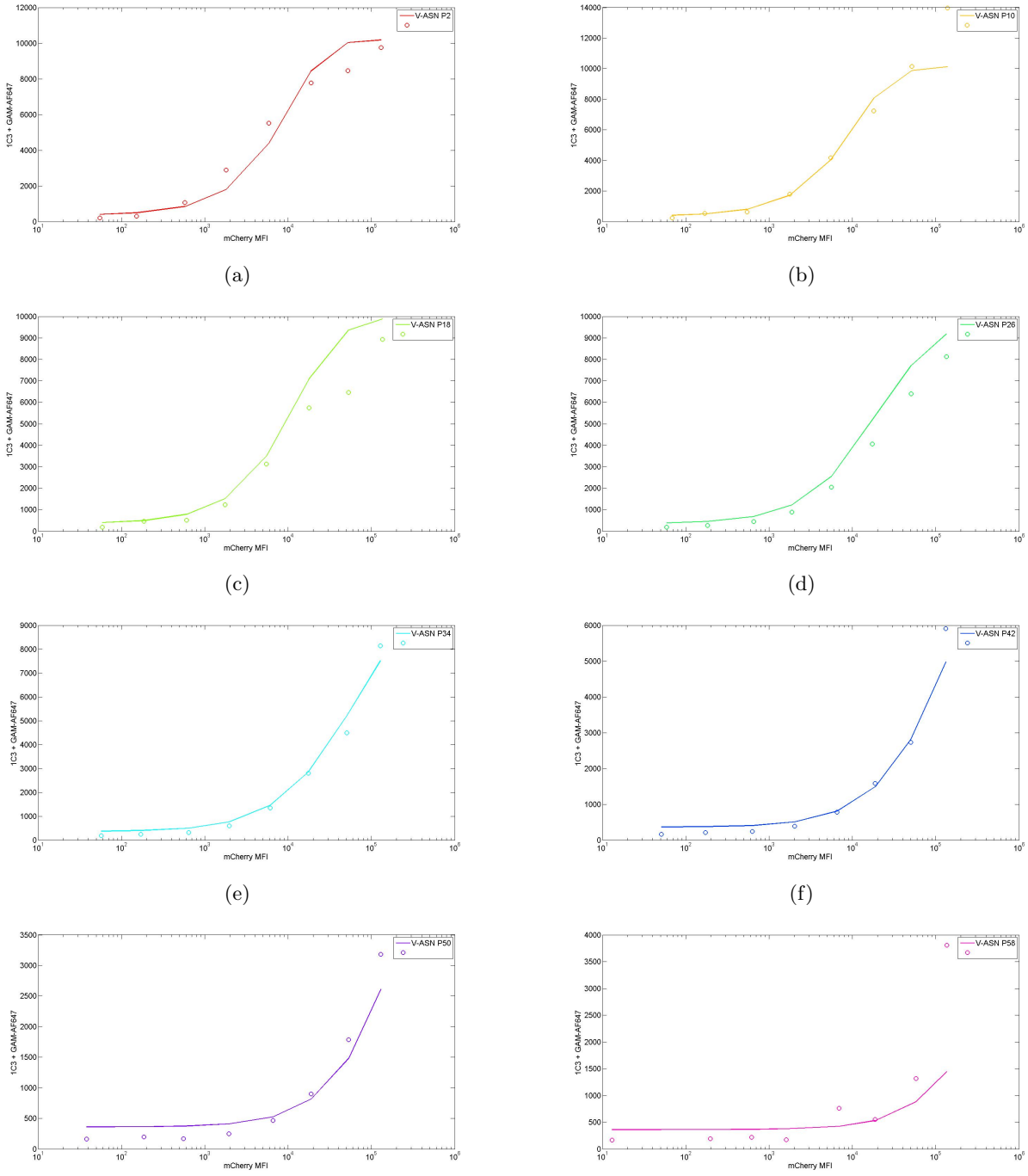
t(hrs)	err	p	sf
24	6.3597×10^3	[0.0015, 343.9527]	[0.8804, 14.802]
10	6.3378×10^3	[0.0026, 341.9502]	[2.3725, 38.1307]
5	6.3308×10^3	[0.0048, 338.7170]	[5.0715, 76.9844]
2	6.1591×10^3	[0.0122, 308.6003]	[15.6758, 209.8721]
1	5.8382×10^3	[0.0253, 272.0332]	[50.0718, 565.9833]
0.5	5.9245×10^3	[0.0425, 258.0930]	[322.1, 2.7757×10^3]

3 154022-ASN-SSL-IFN-none: Attempt 1

Parameters	
Time	10 days
Self Peptide Supply	0 molecules/s
bP_T	$3.177334e-11$ /molecules/s
bP_C	$3.177334e-11$ /molecules/s

- Fitting Method 1: Scale target and competitor concentration by sf1 and sf2 resp. to fit for supply, then scale output cell surface data using polyfit ie p1*MeP1 + p2 to get best fit to data. sf0=[1,100]

Best Fit Scale Factors	
sf1	0.0669
sf2	1.1652
p1	0.0011
p2	361.8626
err	$6.6111e+03$



(a) (b) (c) (d) (e) (f) (g) (h)

Figure 10: t=10days, sf1 =0.0669, sf2 = 1.1652, p1 =0.0011, p2 =361.8626, err = $6.6111e+03$

4 154022-ASN-SSL-IFN-none: Attempt 3

Parameters	
Time	1 day
Self Peptide Supply	0 molecules/s
bP_T	$3.177334e-11$ /molecules/s
bP_C	$3.177334e-11$ /molecules/s

- Fitting Method 1: Scale target and competitor concentration by sf1 and sf2 resp. to fit for supply, then scale output cell surface data using polyfit ie p1*MeP1 + p2 to get best fit to data. Error calculated for all points. sf0=[1,100]

Best Fit Scale Factors	
sf1	0.8804
sf2	14.8020
p1	0.0015
p2	343.9527
err	$6.3597e+03$

- Attempt 1 vs Attempt 3: Reducing the time from 10 days to 1 decreases the error between the fit and the data, but comparing the individual fits the difference is not too noticeable.

5 154022-ASN-SSL-IFN-none: Attempt 7

Parameters	
Time	1 hour
Self Peptide Supply	0 molecules/s
bP_T	$3.177334e-11$ /molecules/s
bP_C	$3.177334e-11$ /molecules/s

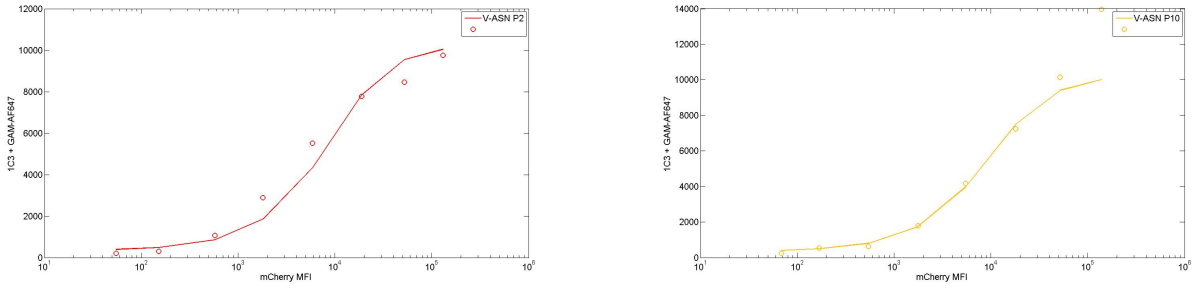
- upreg applied to synthesis of M, T, binding of M-T, and binding of peptide to M-T
- Fitting Method 1: Scale target and competitor concentration by sf1 and sf2 resp. to fit for supply, then scale output cell surface data by sf3 to get best fit to data. sf0=[1,1]

Best Fit Scale Factors	
sf1	50.0718
sf2	565.9833
p1	0.0253
p2	272.0332
err	$5.8382e+03$

6 154022-ASN-SSL-IFN-1: Attempt 1

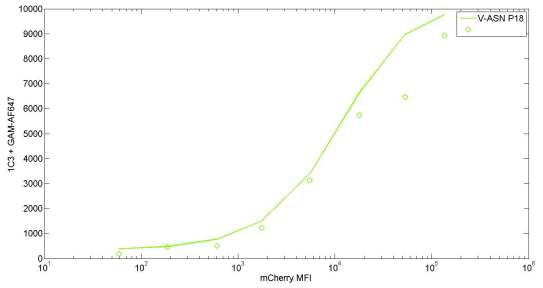
Parameters	
Time	1 hr
Self Peptide Supply	0 molecules/s
bP_T	$3.177334e-11$ /molecules/s
bP_C	$3.177334e-11$ /molecules/s

- upreg applied to synthesis of M, T, binding of M-T, and binding of peptide to M-T
- Fitting Method 1: Scale target and competitor concentration by sf1 and sf2 resp. to fit for supply, whilst also including up regulation factor, then scale output cell surface data using polyfit ie p1*MeP1 + p2 to get best fit to data. sf0=[1,1,1]

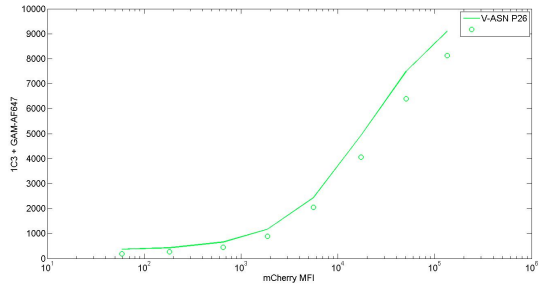


(a)

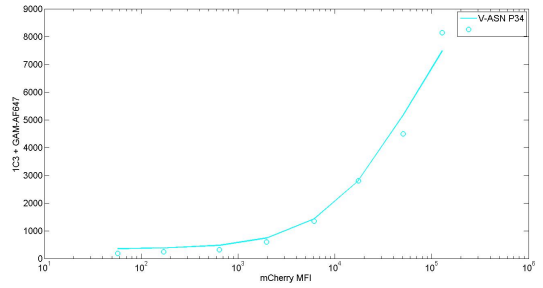
(b)



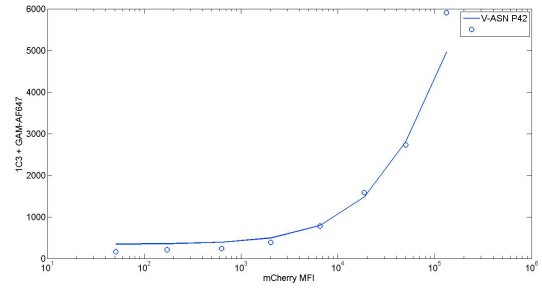
(c)



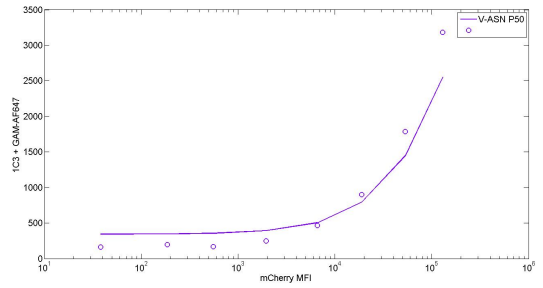
(d)



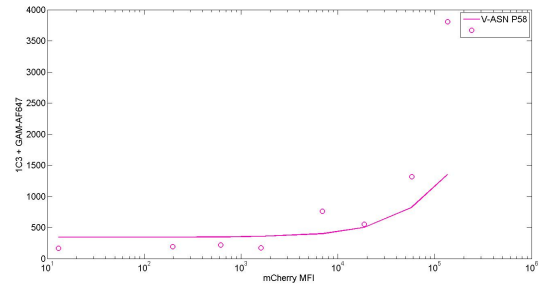
(e)



(f)

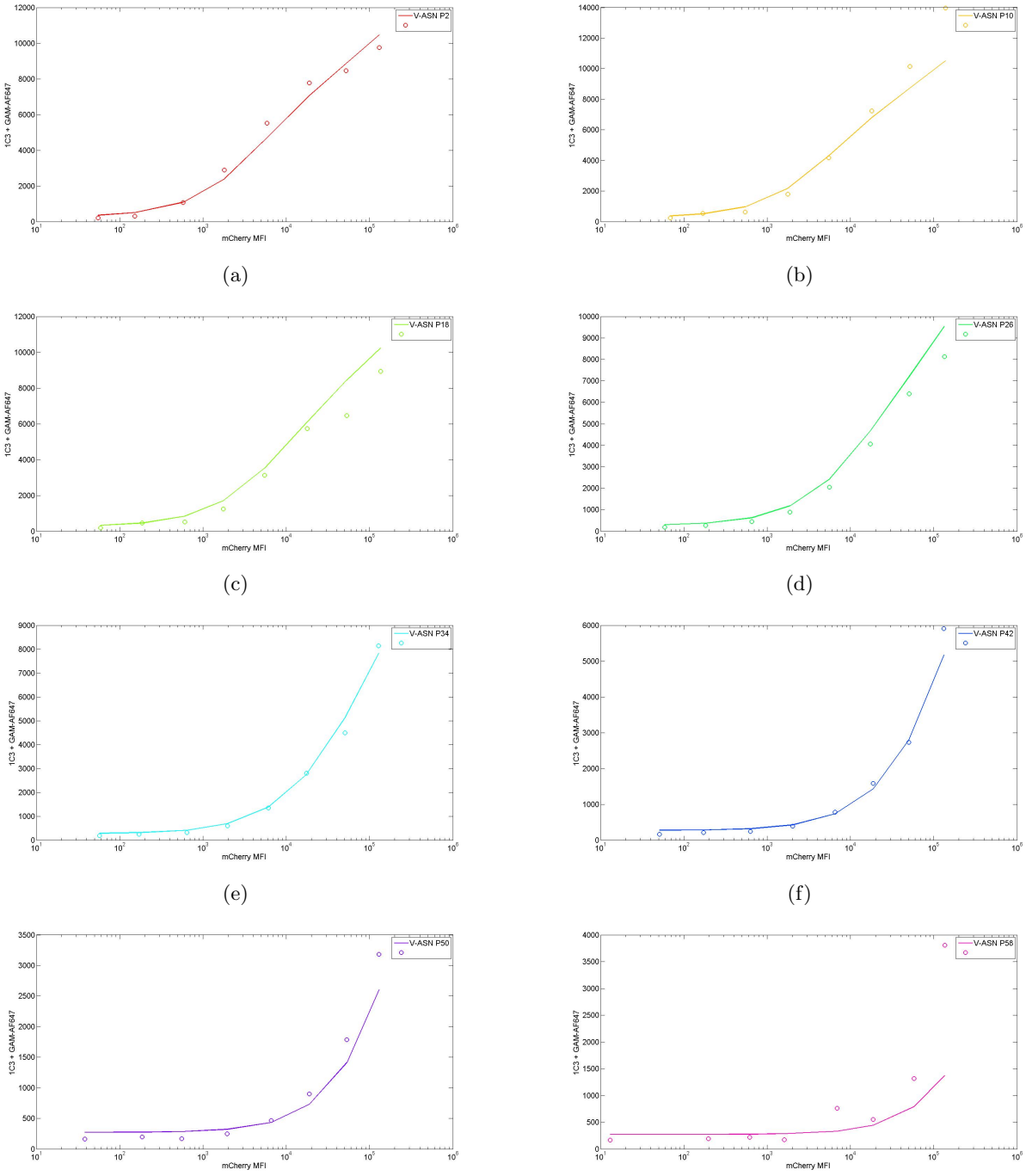


(g)



(h)

Figure 11: t=24 hours, sf1 = 0.8804, sf2= 14.8020, p1 =0.0015, p2 =343.9527, err =$6.3597e+03$



(a) (b) (c) (d) (e) (f) (g) (h)

Figure 12: t=1hr, sf1 = 50.0718, sf2 =565.9833, p1 = 0.0253, p2 = 272.0332, err =$5.8382e+03$

Best Fit Scale Factors	
sf1	1.8445
sf2	8.4180
upreg	15.3862
p1	0.0109
p2	$1.8628e+03$
err	$3.1155e+04$

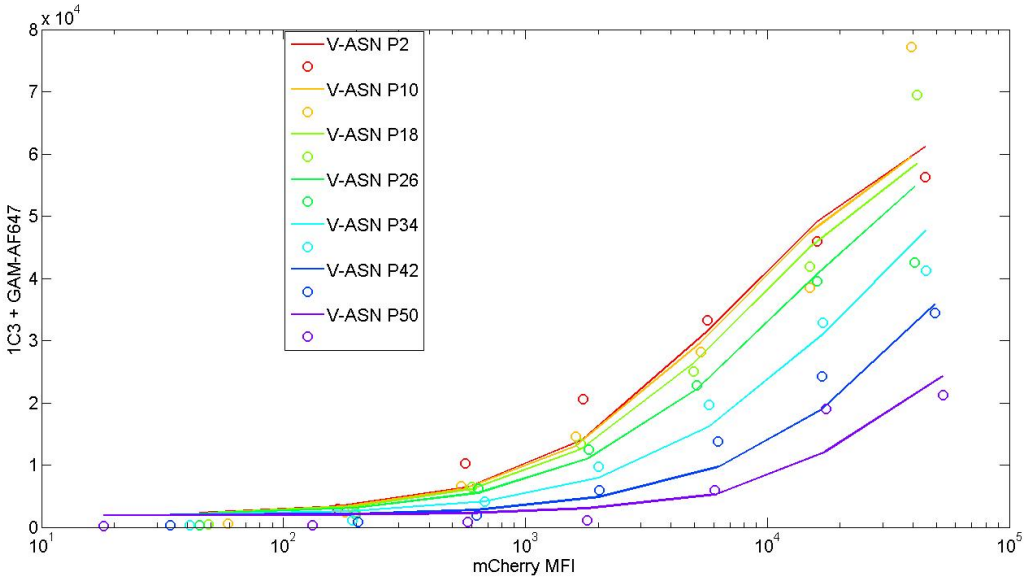


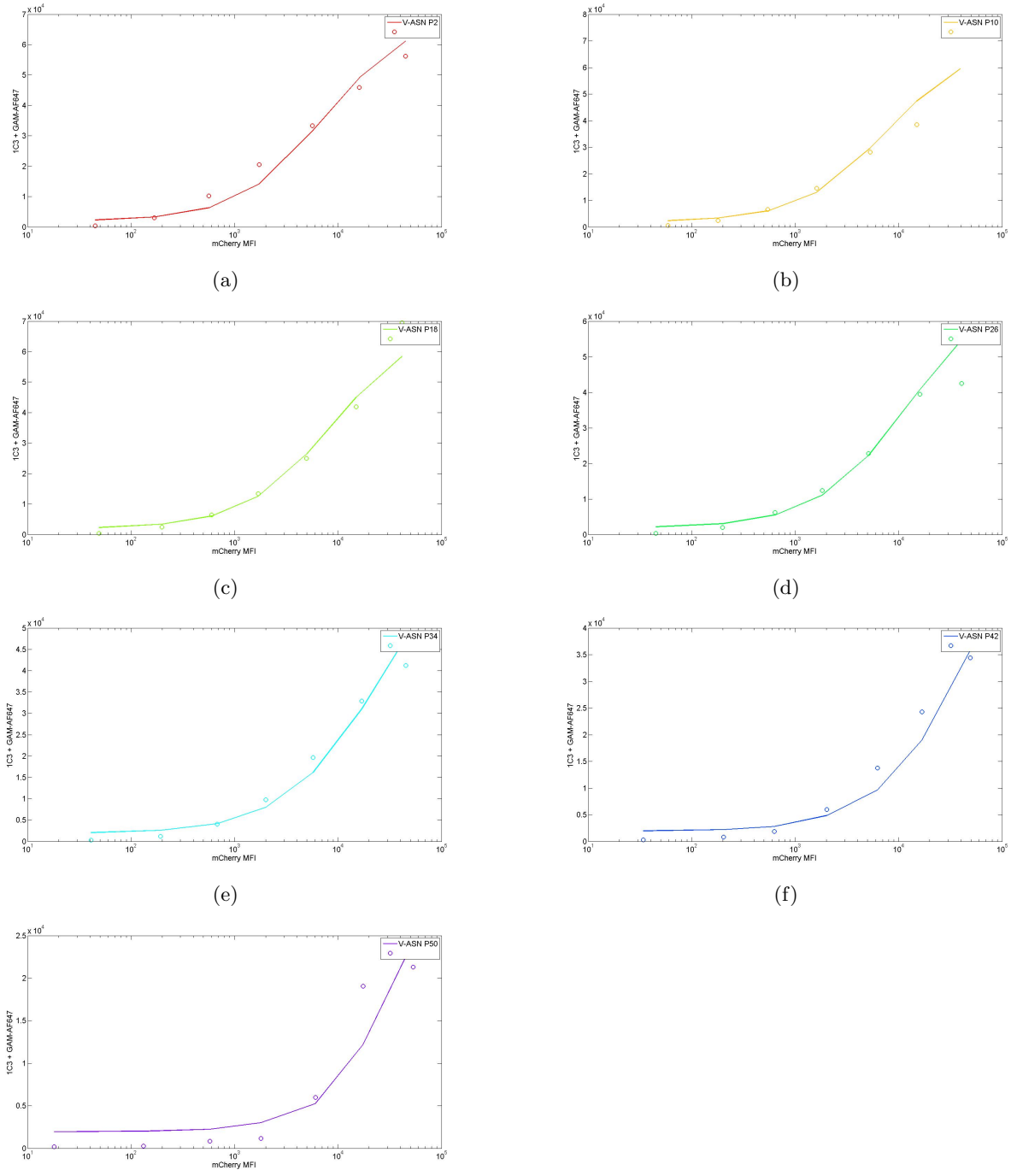
Figure 13: time = 1hr, sf1 =1.8445, sf2 =8.4180, upreg =15.3862, p1 = 0.0109, p2 = $1.8628e+03$, err =$3.1155e+04$

7 154022-ASN-SSL-IFN-1: Attempt 2

Parameters	
Time	10 days
Self Peptide Supply	0 molecules/s
bP_T	$3.177334e-11$ /molecules/s
bP_C	$3.177334e-11$ /molecules/s

- Fitting Method 1: Scale target and competitor concentration by sf1 and sf2 resp. to fit for supply, whilst also including up regulation factor, then scale output cell surface data using polyfit ie p1*MeP1 + p2 to get best fit to data. sf0=[1,1,1]

Best Fit Scale Factors	
sf1	1.5598
sf2	8.7253
upreg	0.0815
p1	0.6790
p2	$1.9391+03$
err	$3.1397e+04$



(a) (b) (c) (d) (e) (f) (g)

Figure 14: time = 1hr, sf1 =1.8445, sf2 =8.4180, upreg =15.3862, p1 = 0.0109, p2 = $1.8628e+03$, err =$3.1155e+04$

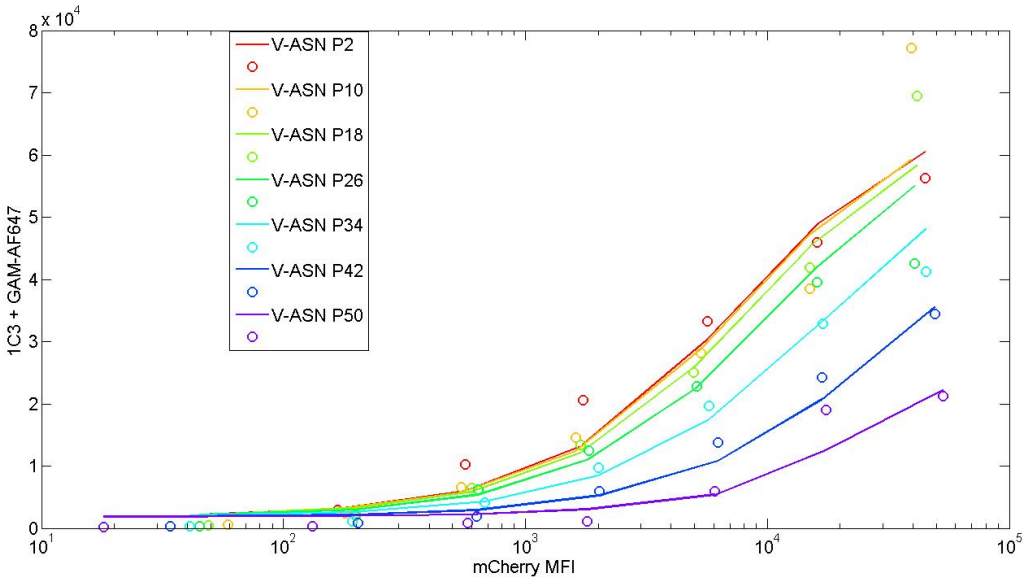


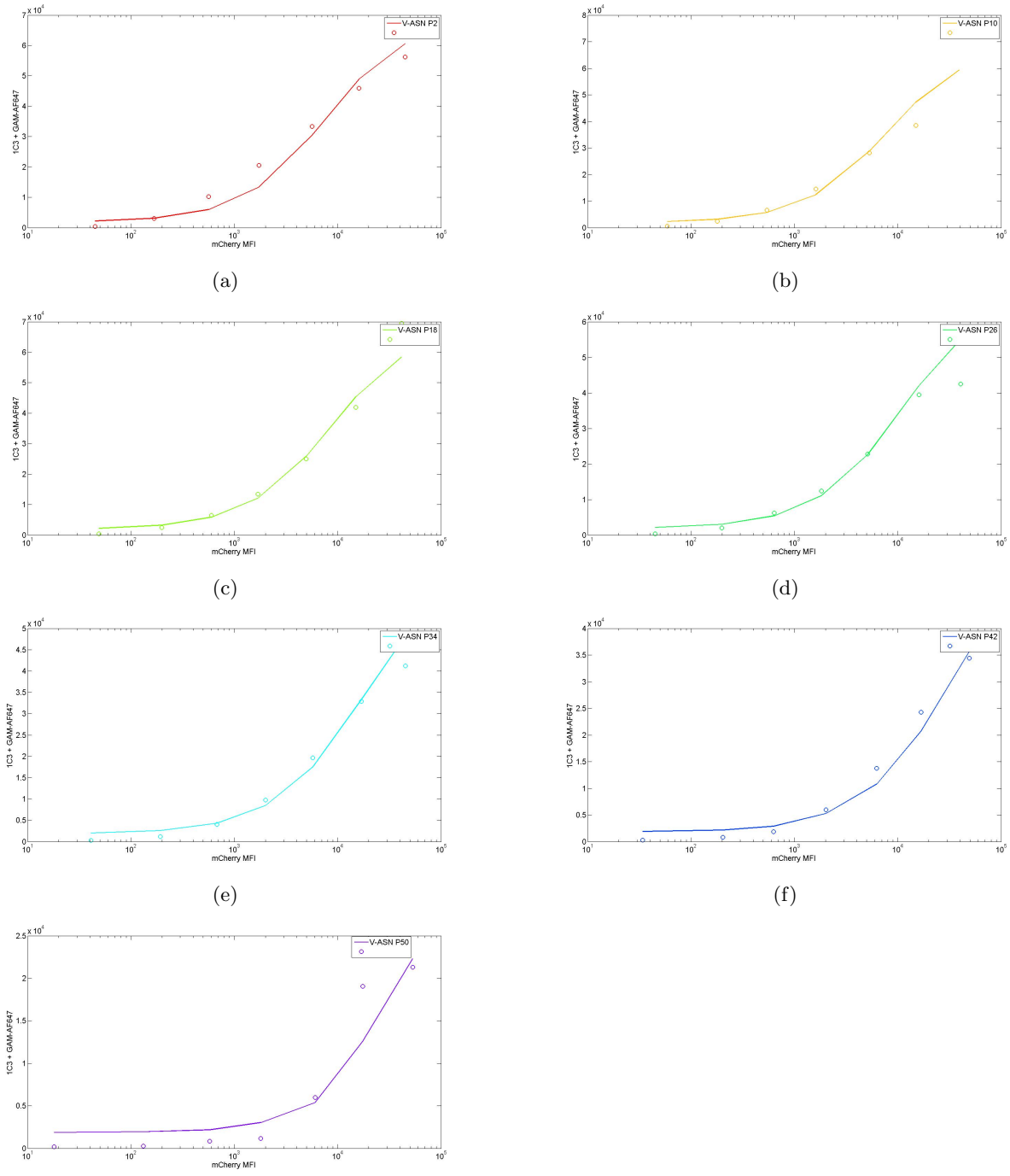
Figure 15: t=10 days sf1= 1.5598, sf2 =8.7253, upreg = 0.0815, p1 = 0.6790, p2 = 1.9391 + 03, err = $3.1397e+04$

8 154022-ASN-SSL-IFN-1: Attempt 3

Parameters	
Time	1 hour
Self Peptide Supply	0 molecules/s
bP_T	$3.177334e-11$ /molecules/s
bP_C	$3.177334e-11$ /molecules/s

- Fitting Method 1: Scale target and competitor concentration by sf1=50.0718 and sf2=565.9833 resp. to fit for supply, whilst also including up regulation factor, then scale output cell surface data using polyfit ie p1*MeP1 + p2, where p1=0.0253 and p2=272.0332 to get best fit to data.
- Using sf1, sf2, p1 and p2 determined in attempt 7 above, and upregulating only the synthesis of M and T, and fitting for upreg, does not provide a very good fit.

Best Fit Scale Factors	
upreg	6.9721
err	$2.1091e+09$



(a) (b) (c) (d) (e) (f) (g)

Figure 16: t=10 days sf1= 1.5598, sf2 =8.7253, upreg = 0.0815, p1 = 0.6790, p2 = 1.9391 + 03, err = $3.1397e + 04$

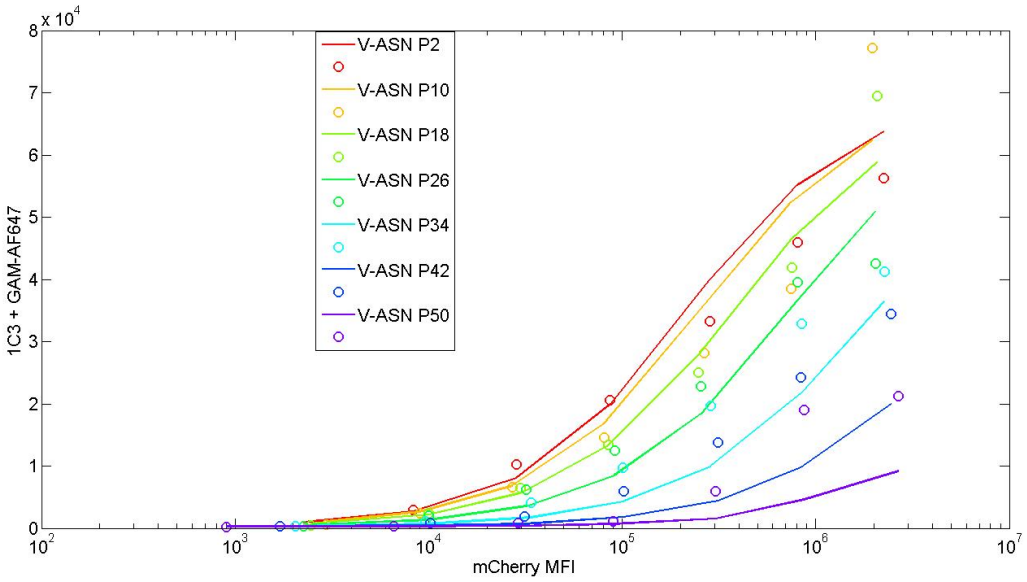


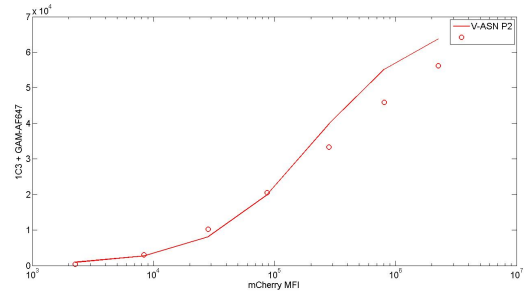
Figure 17: time = 1hr, sf1=50.0718 and sf2=565.9833, p1=0.0253 and p2=272.0332, upreg = 6.9721 and resid = $2.1091e+09$

9 154022-ASN-SSL-IFN-1: Attempt 4

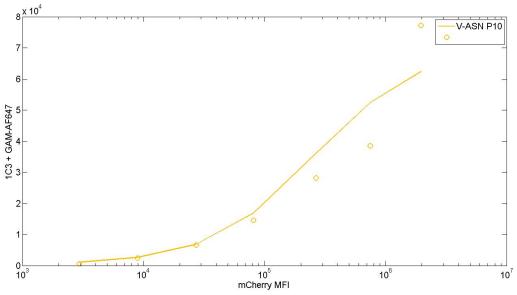
Parameters	
Time	1 hour
Self Peptide Supply	0 molecules/s
bP_T	$3.177334e-11$ /molecules/s
bP_C	$3.177334e-11$ /molecules/s

Best Fit Scale Factors	
sf1	0.9968
sf2	4.6958
upreg	24.6905
p1	0.0095
p2	$2.1224e+03$
err	$3.1755e+04$

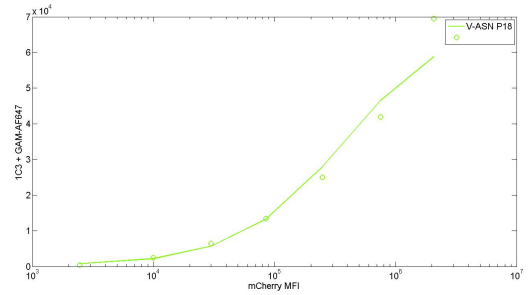
- Fitting Method 1: Scale target and competitor concentration by sf1 and sf2 resp. to fit for supply, whilst also including up regulation factor, then scale output cell surface data using polyfit ie p1*MeP1 + p2, to get best fit to data. sf0=[1,1,1]
- Upregulating only the synthesis of M and T, and fitting for upreg.



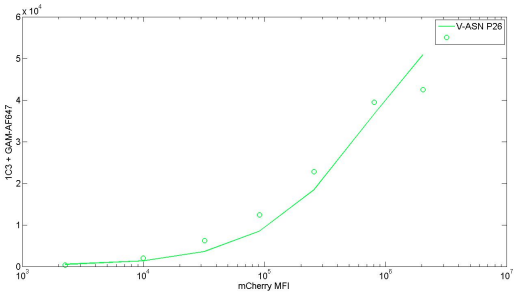
(a)



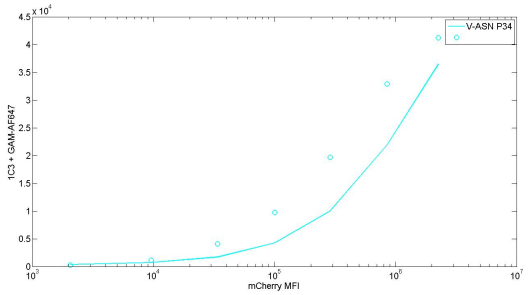
(b)



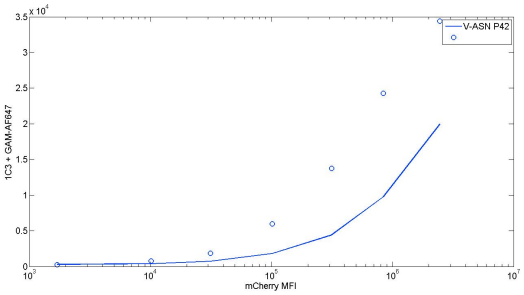
(c)



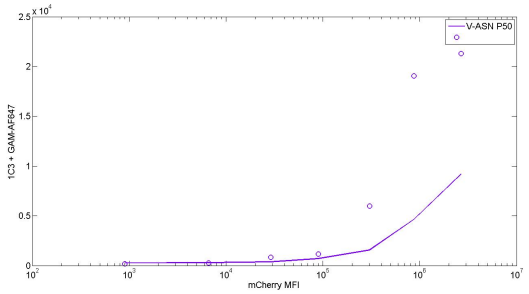
(d)



(e)



(f)



(g)

Figure 18: time = 1hr, sf1=50.0718 and sf2=565.9833, p1=0.0253 and p2=272.0332, upreg = 6.9721 and resid = $2.1091e+09$

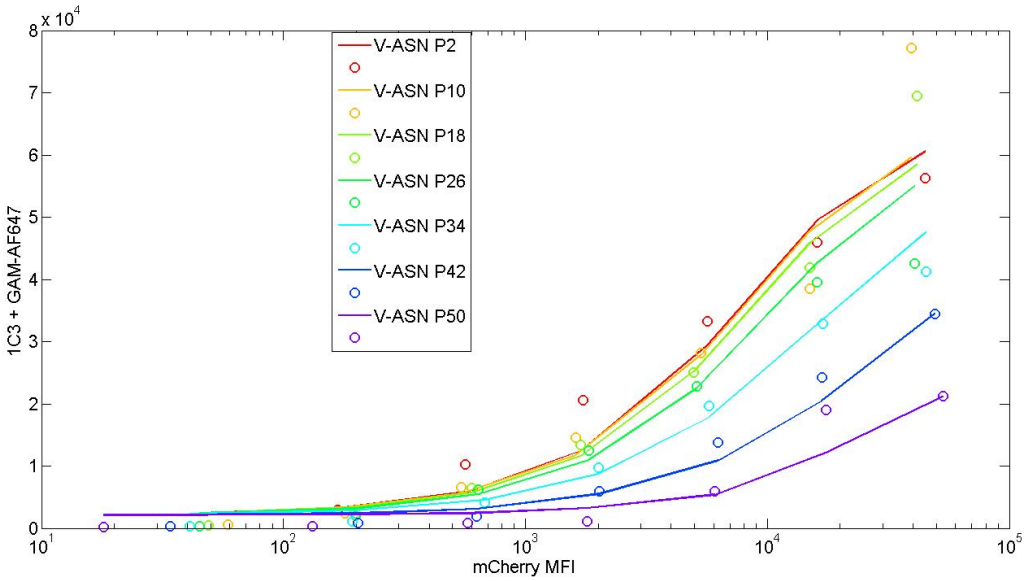
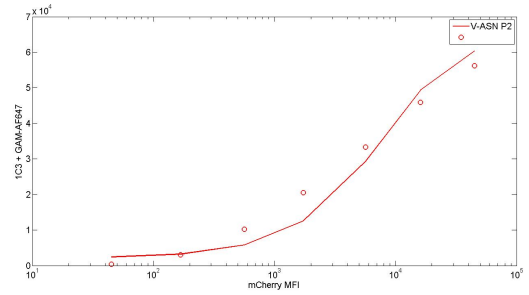
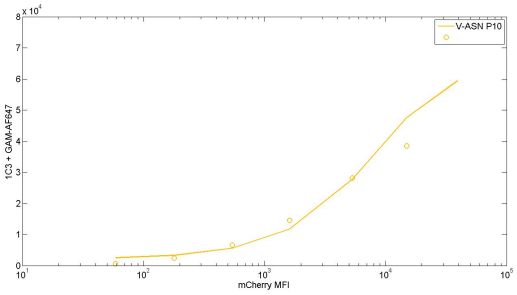


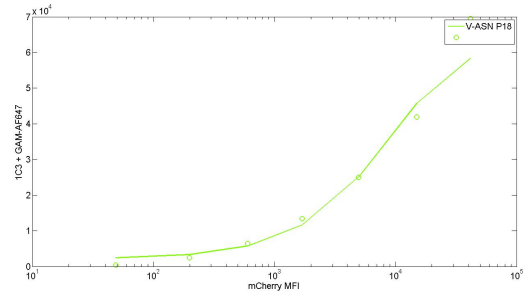
Figure 19: time = 1hr, sf1=0.9968 and sf2=4.6958, p1=0.0095 and p2=$2.1224e+03$, upreg = 24.6905 and resid = $3.1755e+04$



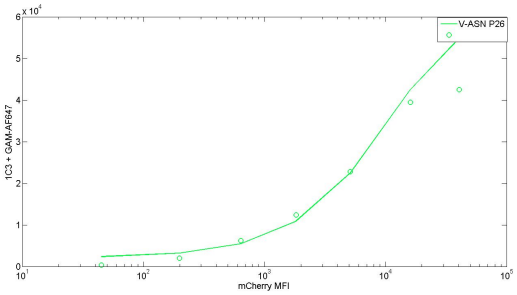
(a)



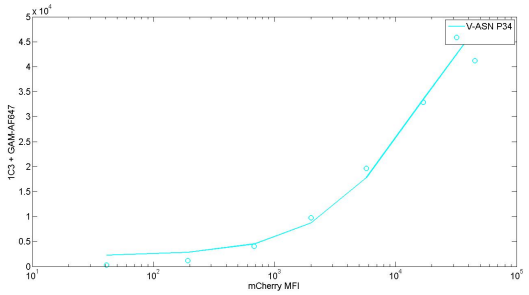
(b)



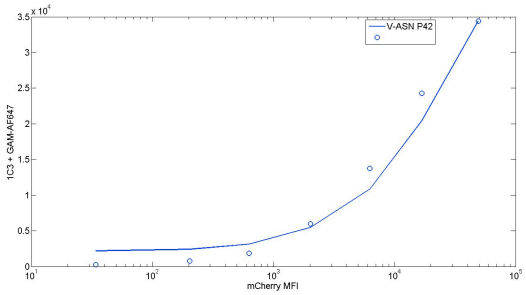
(c)



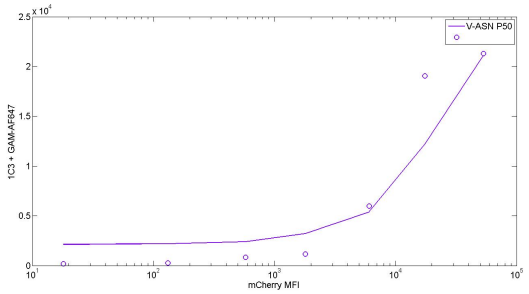
(d)



(e)



(f)



(g)

Figure 20: time = 1hr, sf1=0.9968 and sf2=4.6958, p1=0.0095 and p2=2.1224$e+03$, upreg = 24.6905 and resid = 3.1755$e+04$