

Experiment planning, Chip 14

Hypothesis testing-Dose calculation

Proposed Doses

- **Dose 1:** 2500 mU/L
- **Dose 2:** 3500 mU/L

- For H1 we restrict the insulin independent glucose uptake to be less than 40% of the total uptake. Otherwise we would get many solutions where the majority of glucose uptake is insulin independent.
- The glucose measurements have very low uncertainty. The data points with $SEM < 5\%$ of the mean value are corrected with 9% of the mean value, which is the highest value found in the data.
- The data corresponding to normoglycemia in days 1-3 was not used in the parameter estimation. To reproduce these data, one would need to have very different insulin sensitivity values for hyper-and hypoglycemia. Therefore, the model can not account for this and was not used in the estimation.
- To calculate the insulin dose:
 - The first dose gives approximately the minimal difference that would be detectable given the SEM in the data. The maximal SEM in the data is used for this, to account for possible systematic errors.
 - The higher dose gives a larger difference between the hypotheses, and is still in the range of insulin values that we have seen in the experiments. This dose could possibly be larger.

Experimental Measurements: Glucose

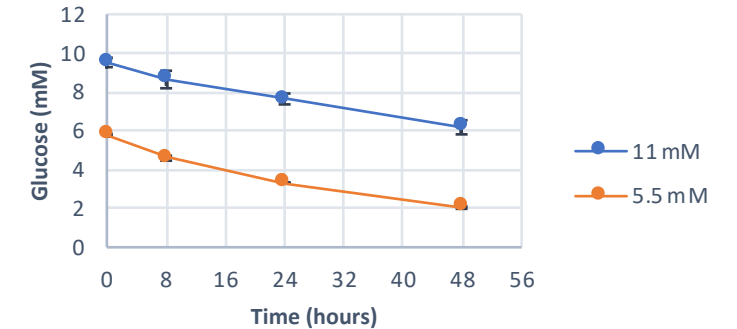
Glucose

Correct below 5%

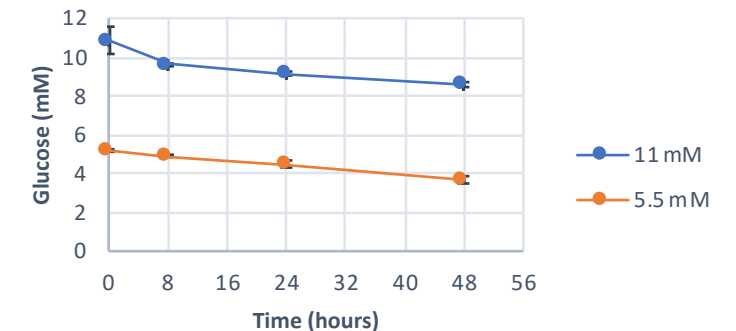
day	time	mean	SD	SEM	Co-Culture Medium	SEM/mean(%)	SEM (corrected)
1	0	5.7695	0.093338	0.066	Normoglycemic (5.5 mM), 50 μ M Hydrocortisone	1.143946616	0.5346
	8	4.588	0.119943	0.059972		1.307034654	0.42516
	24	3.311	0.318668	0.183983		5.556720493	0.18398
	47.9	2.042	0.327808	0.18926		9.266853388	0.18926
7.000	144	5.185	0.115	0.066178	Normoglycemic (11 mM), 50 μ M Hydrocortisone	1.276417655	0.48041
	152	4.909	0.255	0.127463		2.596645202	0.45484
	168	4.489	0.070	0.034957		0.778655027	0.41599
	191.9	3.674	0.126	0.06315		1.718842779	0.34043
1	0	9.519	0.482	0.240908	Hyperglycemic (11 mM), 50 μ M Hydrocortisone	2.530775582	0.882042123
	8	8.641	0.902	0.451056		5.220252194	0.451055891
	24	7.640	0.563	0.281532		3.685209762	0.70787607
	47.9	6.179	0.728	0.363815		5.887689561	0.363815057
7.000	144	10.860	1.406	0.702955	Hyperglycemic (11 mM), 50 μ M Hydrocortisone	6.473035222	0.702955443
	152	9.593	0.145	0.072285		0.753484126	0.888922128
	168	9.151	0.209	0.104461		1.141570036	0.847896913
	191.9	8.579	0.256	0.127954		1.491542395	0.794895393
mean						0.541508064	

Data with initial SD

Glucose, Days 1-3



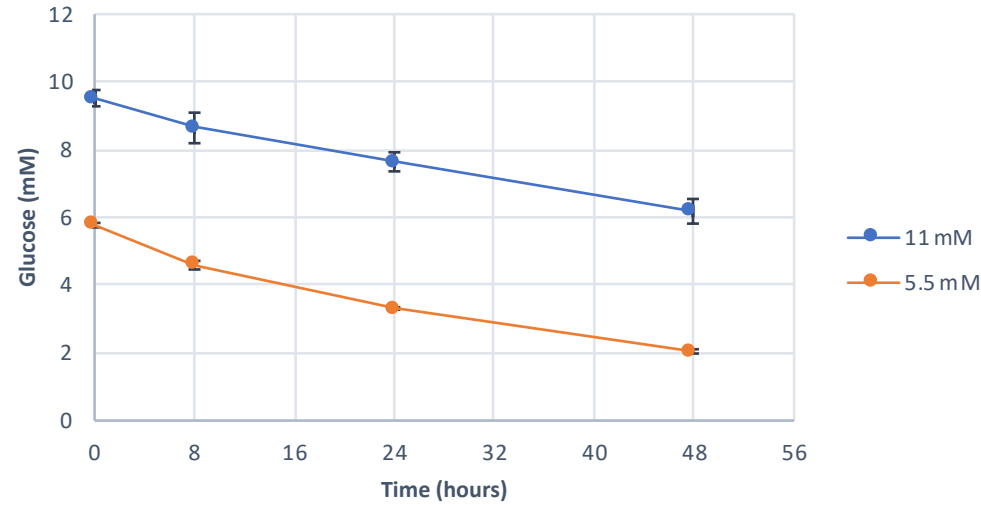
Glucose, Days 7-9



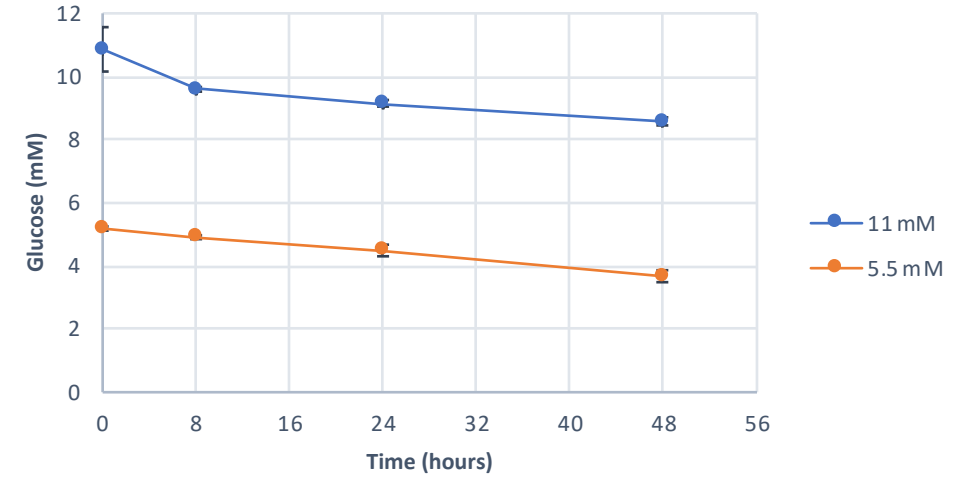
- Correction in the data:** If the initial SEM was below 5% of the mean value, the SEM was set to 9% of the mean value instead. This avoids data points with too low standard deviation.

Experimental Measurements: Insulin

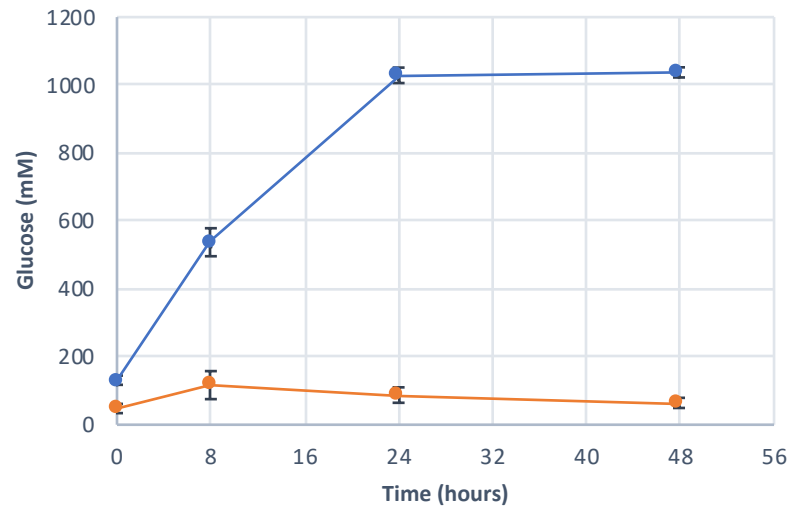
Glucose, Days 1-3



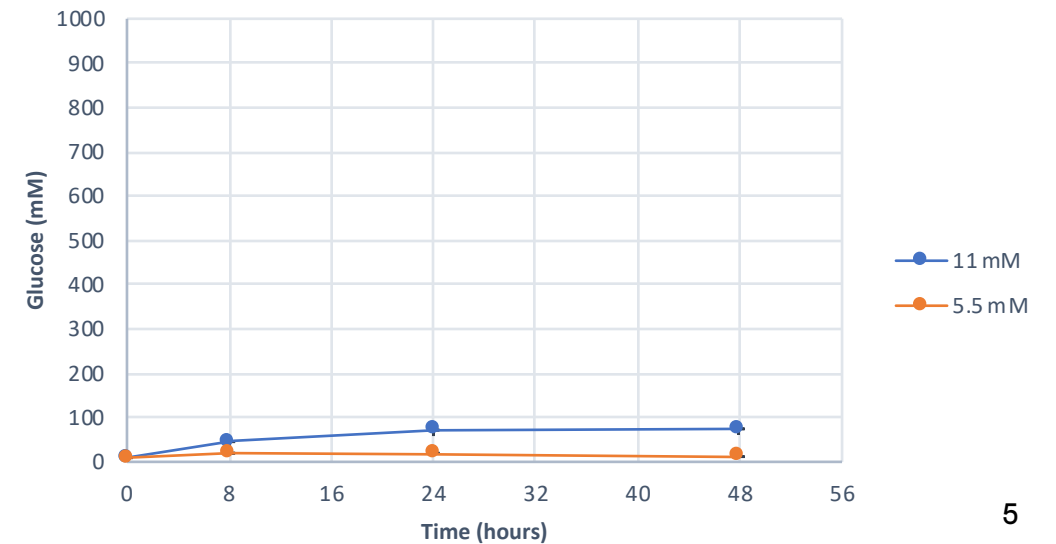
Glucose, Days 7-9



Insulin, Days 1-3

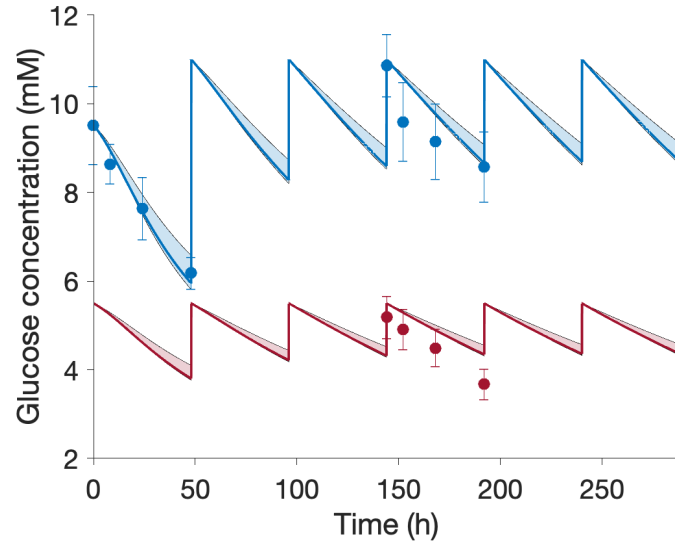


Insulin, Days 7-9

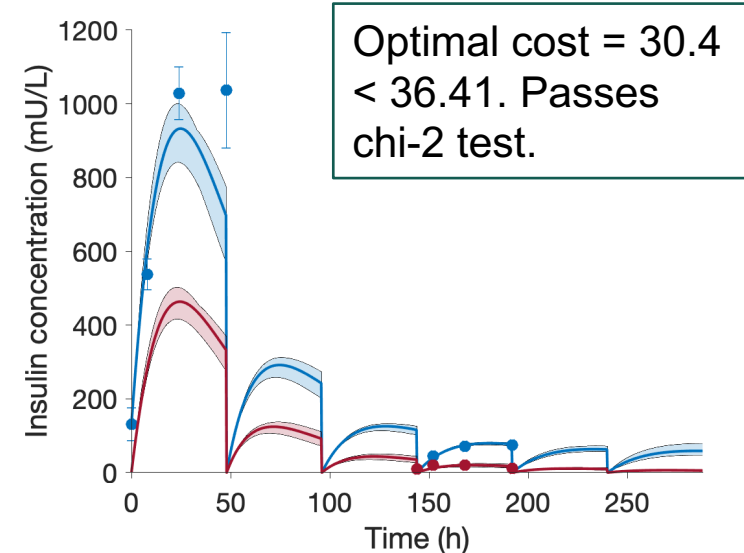
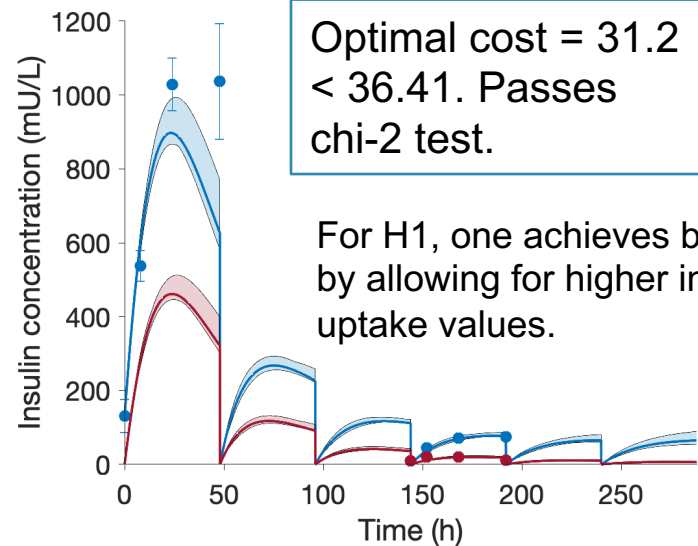
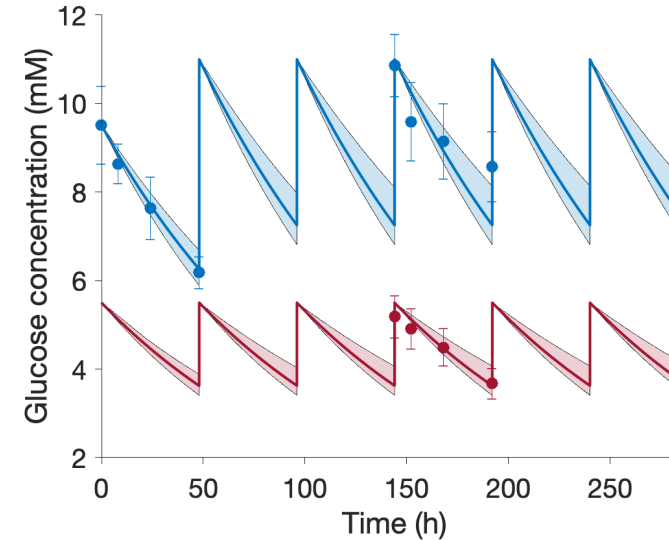


Hypothesis: Fitting to Experimental Data

Hypothesis 1

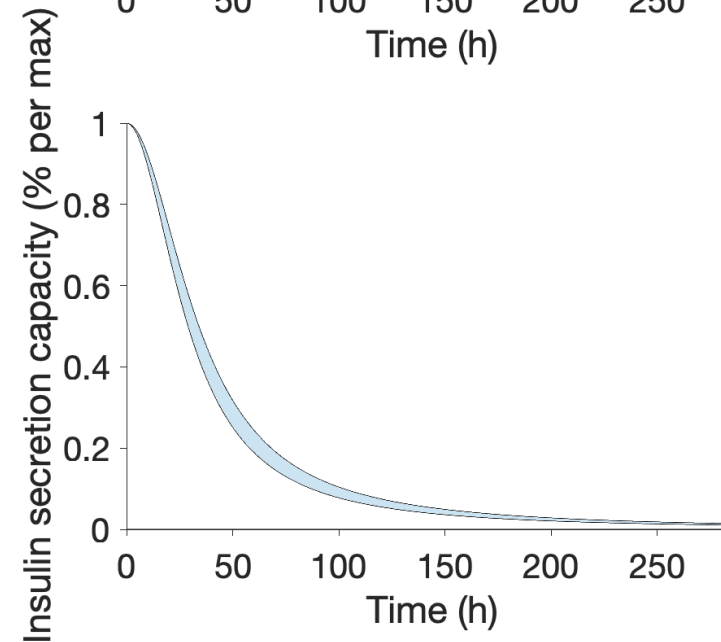
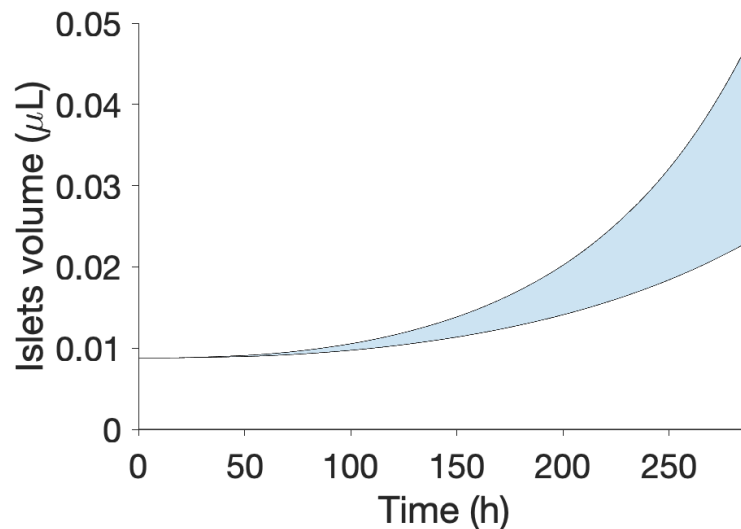
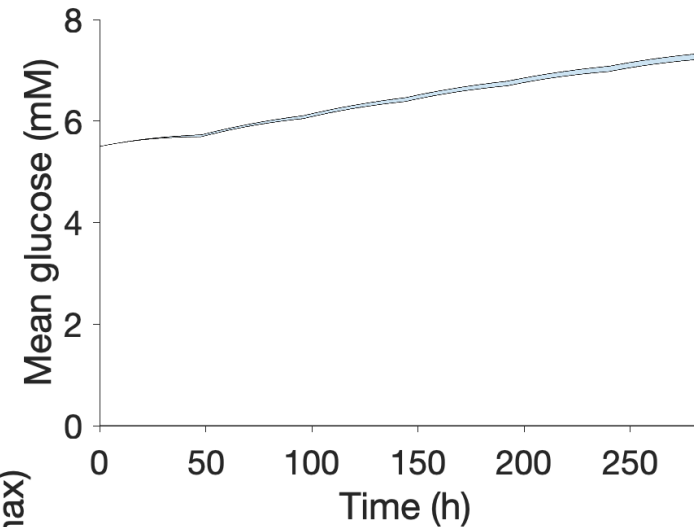
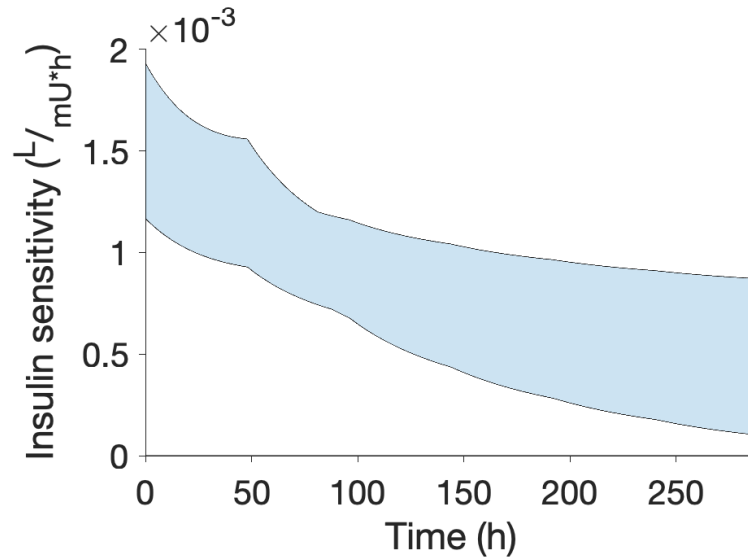


Hypothesis 2



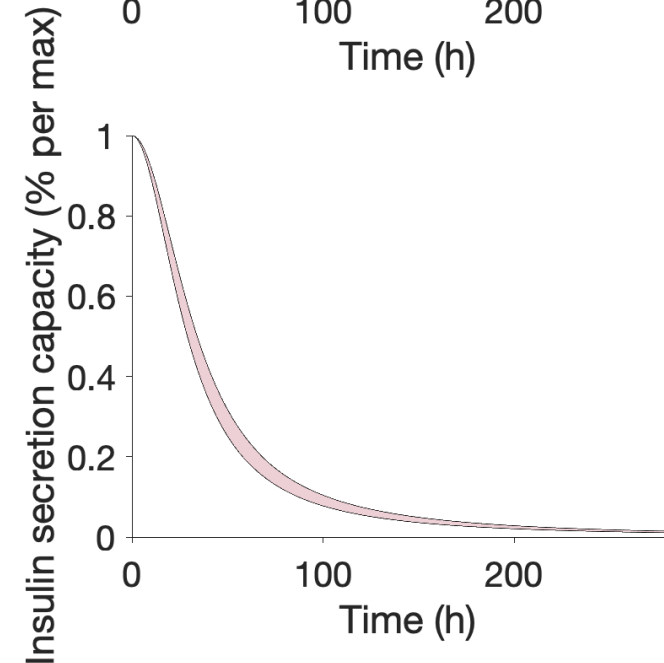
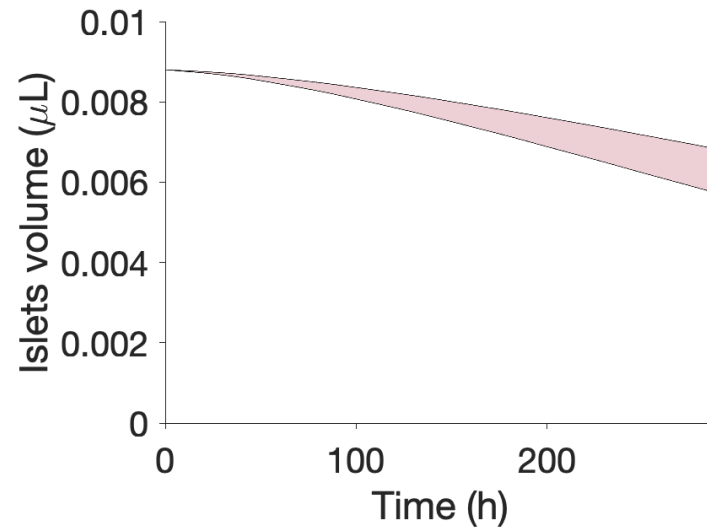
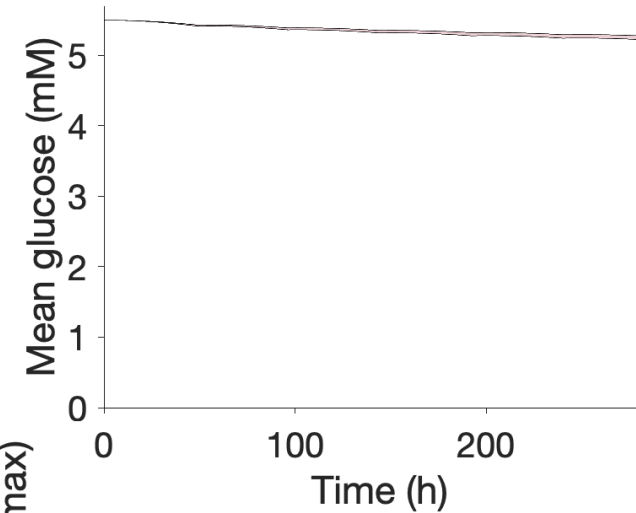
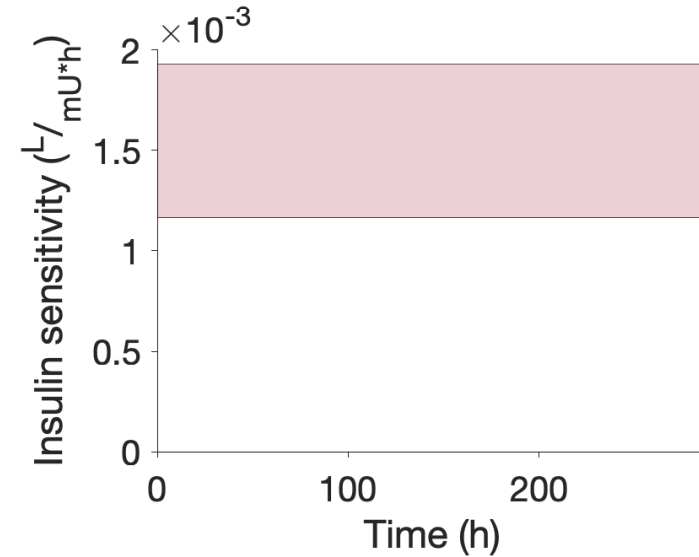
Hypothesis 1: Disease Progression Variables

- Hyperglycemia**



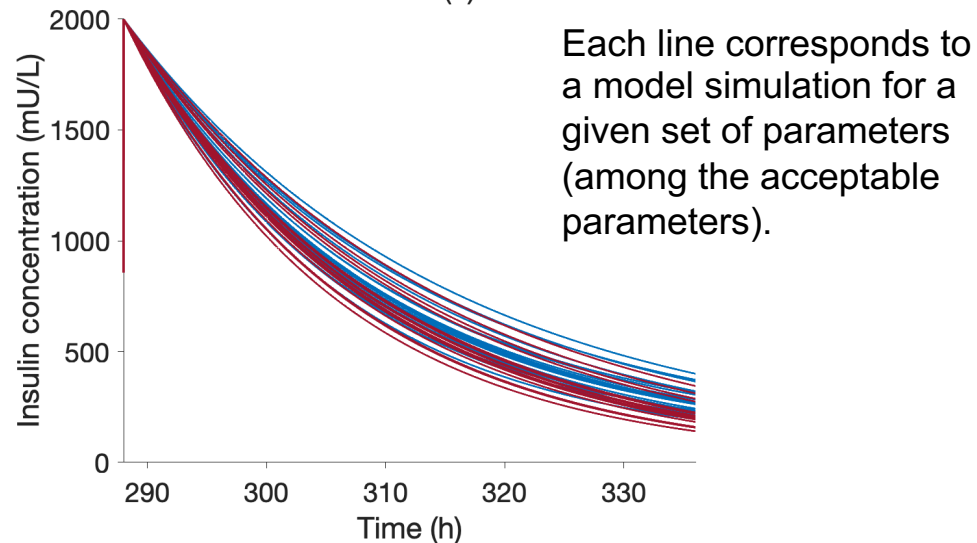
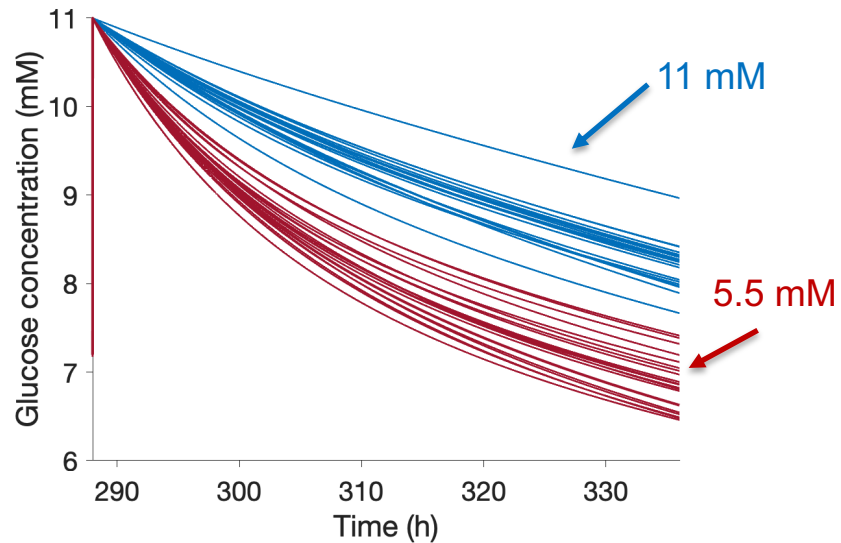
Hypothesis 1: Disease Progression Variables

- Normoglycemia**

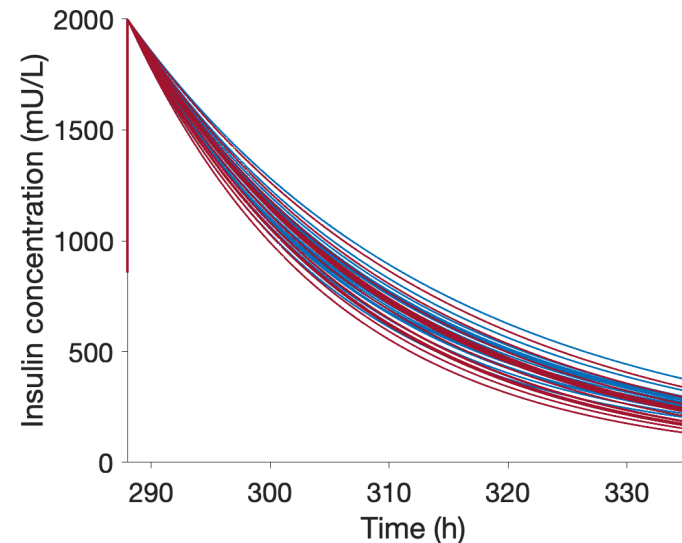
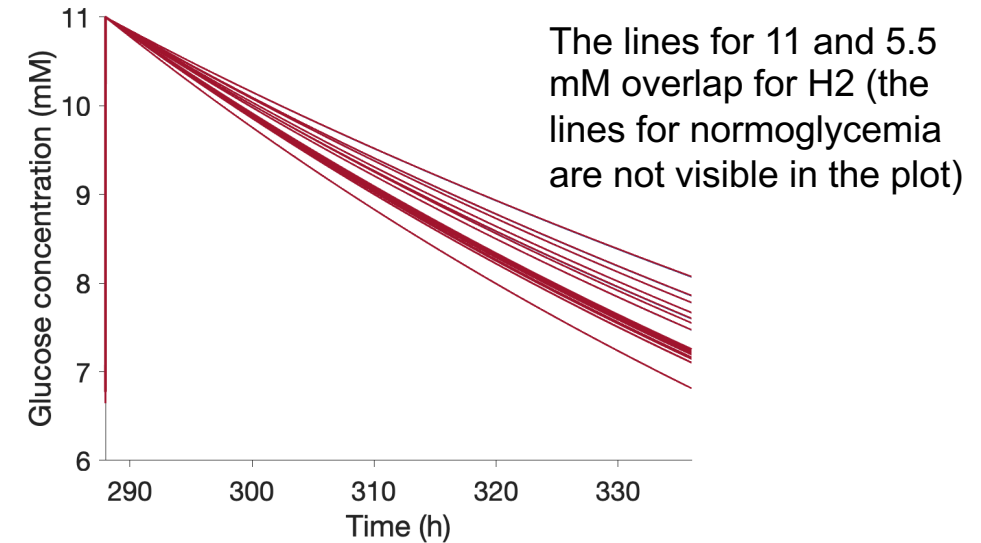


Example of Insulin Experiment

Hypothesis 1



Hypothesis 2

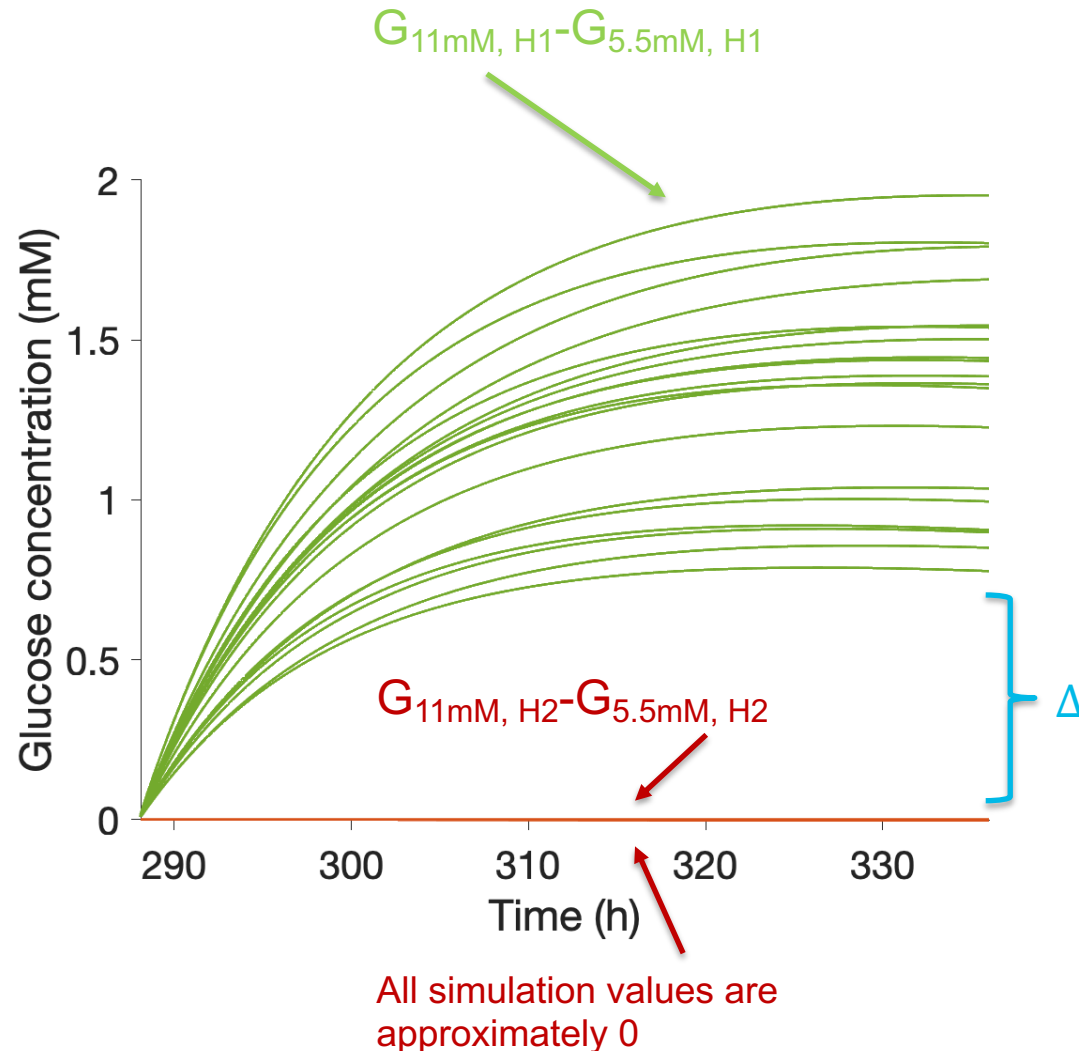


- Dose: 2000 mU/L at day 13

Calculation of Insulin Doses

- Dose: 2000 mU/L at day 13

- Maximum SEM in the data: 0.88 mM



Insulin Dose (mU/L)	Delta (mM)
1500	0.59
1600	0.64
1700	0.67
1900	0.74
2000	0.78
2200	0.85
2400	0.9
2500	0.94
2700	0.99
2900	1.05
3000	1.09
3200	1.13
3400	1.18
3500	1.209
3600	1.23
3800	1.3
4000	1.35
4500	1.4

Higher than SEM

3500 mU/L is among the
highest
levels in the experiments

Proposed doses

Δ (difference between H1 and H2) should be larger than the variability (SEM) in the experimental data