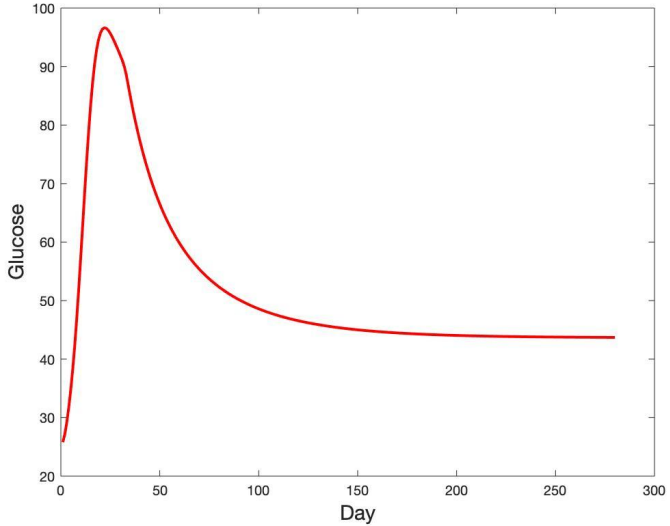
Kalman Filters
Week 6

Subteam 2

Last Week's Problem

- Parametrization happening, but biologically inaccurate results and bad glucose fits



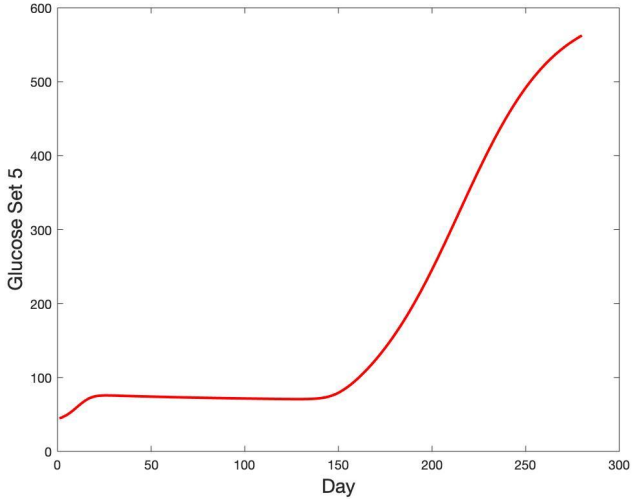
Estimating All Parameters

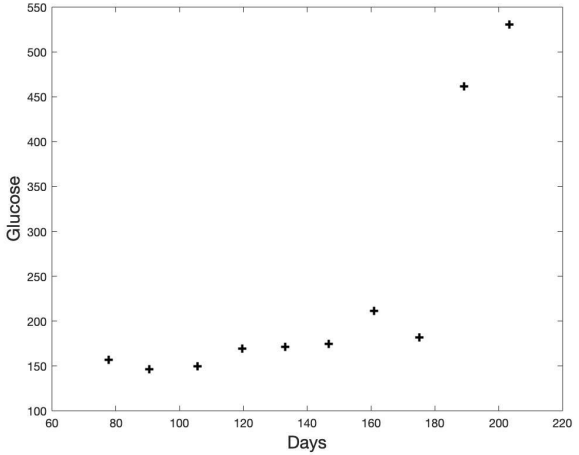
- Shift to allowing all parameters to move during parametrization instead of being held constant
- Parameters are related → need to allow for these relationships
- Try to keep movement somewhat limited (more on this later)

Defining Success

- Concerned with:
  - Glucose fits to real data
  - Behavior of immune cells
- Glucose fits: Least Squares Error
- Immune cells: Eyeball Test

Glucose Fits Attempt 1 (Mouse 6) - Dual





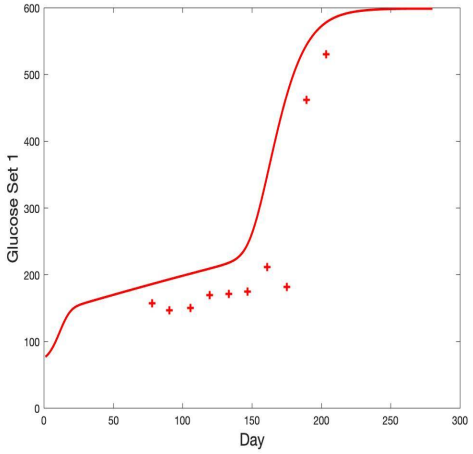
Two Issues: glucose level during steady state and time of onset

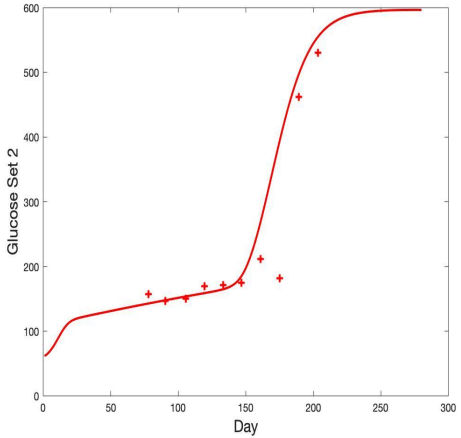
Identifying Critical Parameters

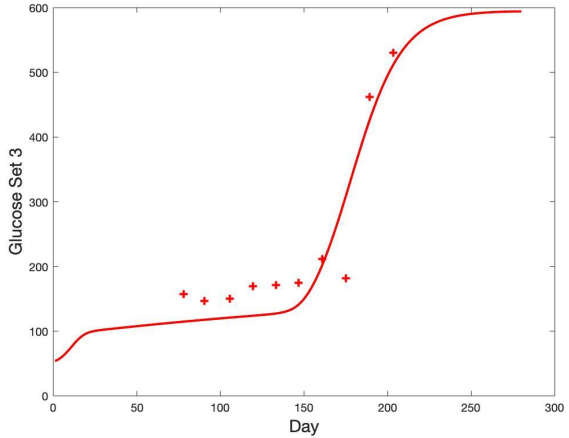
- Eta, Alpha_eta, Beta_eta
  - Control time of onset and steepness of curve
- To begin with, only allowing movement in alpha_eta and beta_eta, later in week freed up eta as well

$$eta_{vary} = eta + 2 * eta * (1 + tanh(alpha_{eta} * (t - beta_{eta} * 7)))$$

Glucose Fits Attempt 2 (Mouse 6) - Dual



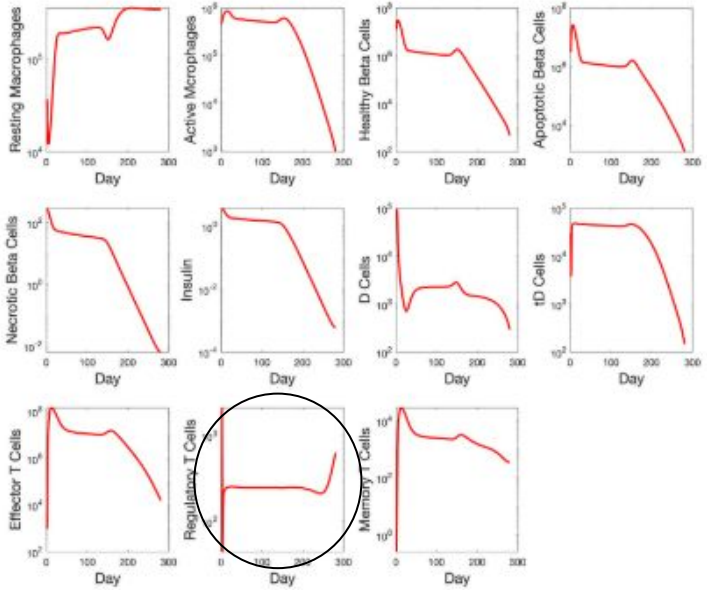




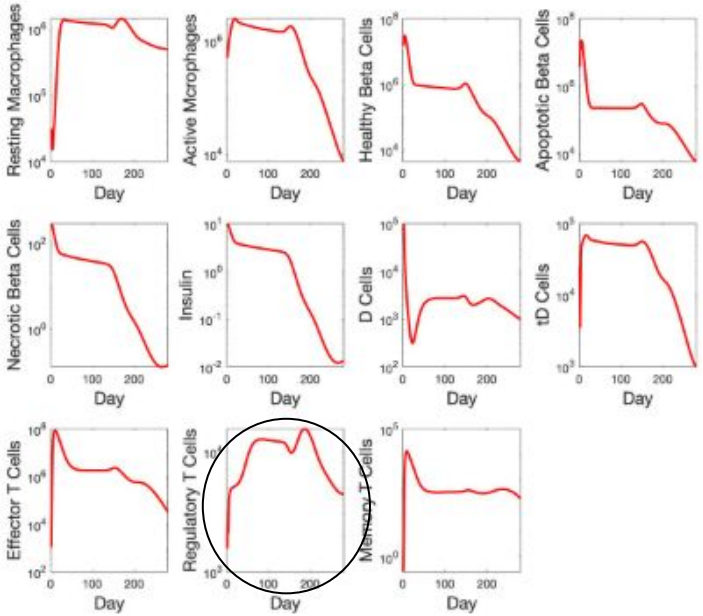
Run	Error
1	354.363
2	226.119
3	163.88

Immune Cells - Dual

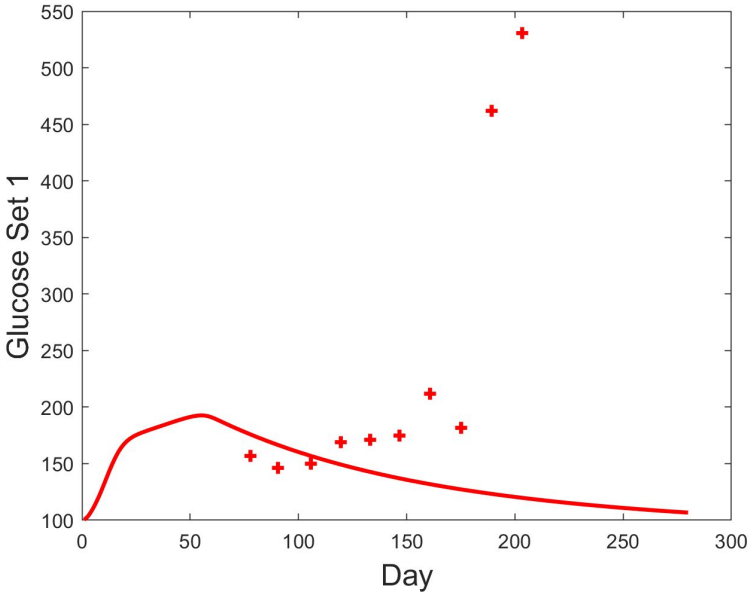
Using Parameter Estimates

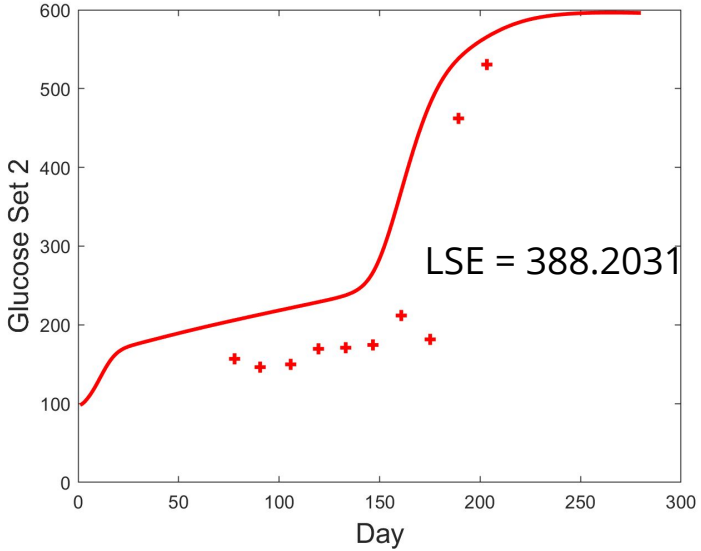


Using Baseline Parameters



Glucose Fit Attempt with Joint

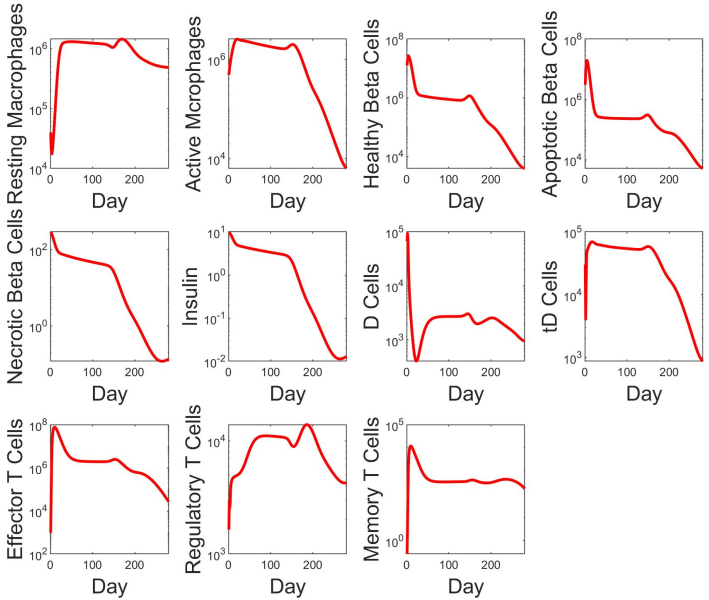




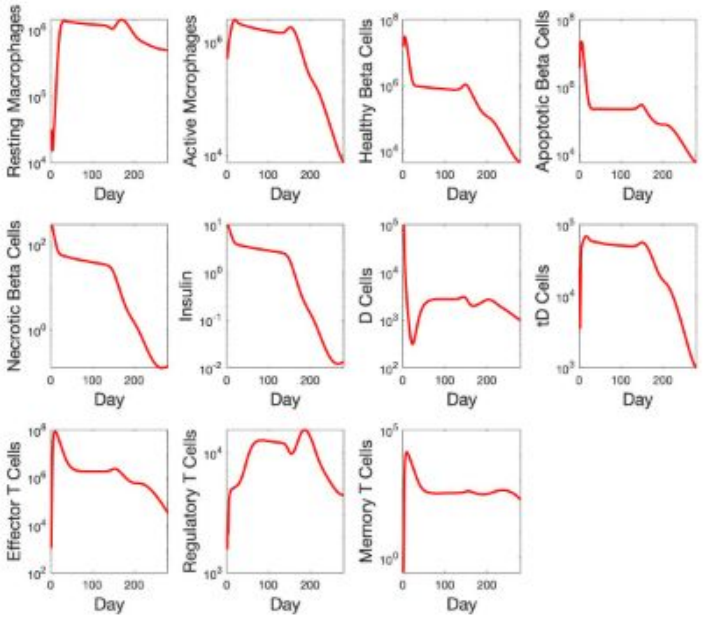
*The fits never got any better after the second iteration

Looking at All States - Joint

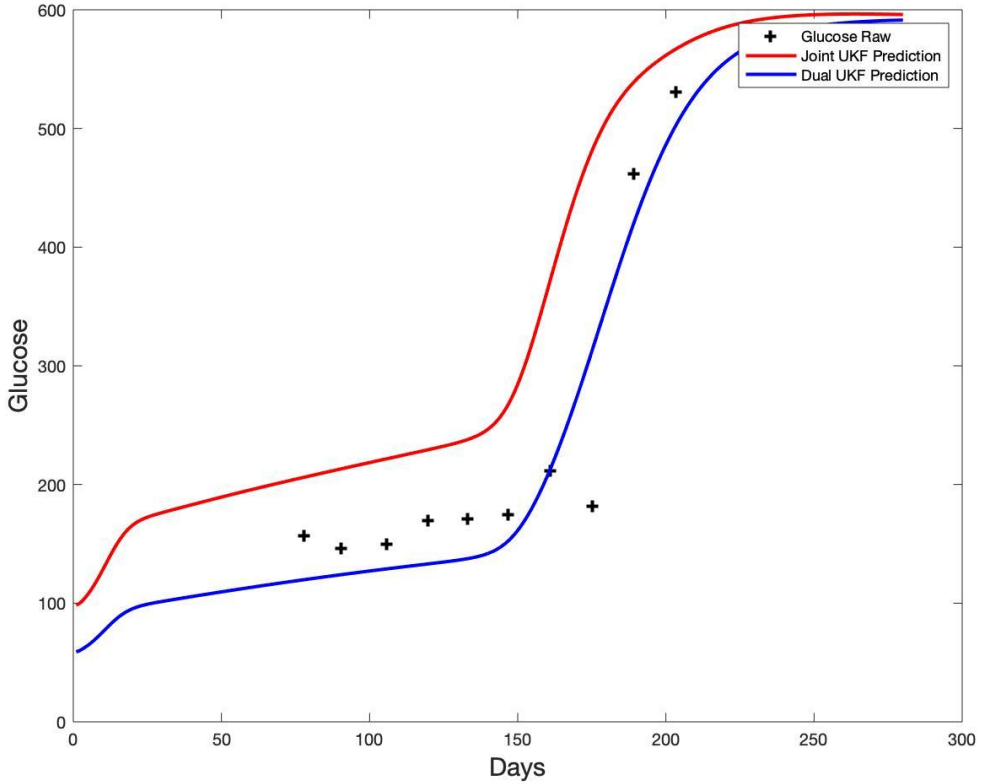
Parameter Estimates



Baseline Parameters

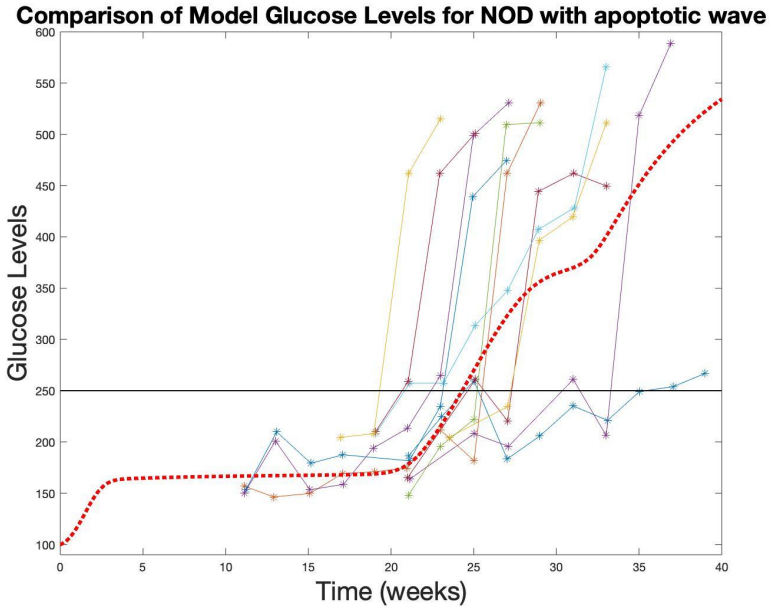


Comparison of Dual and Joint

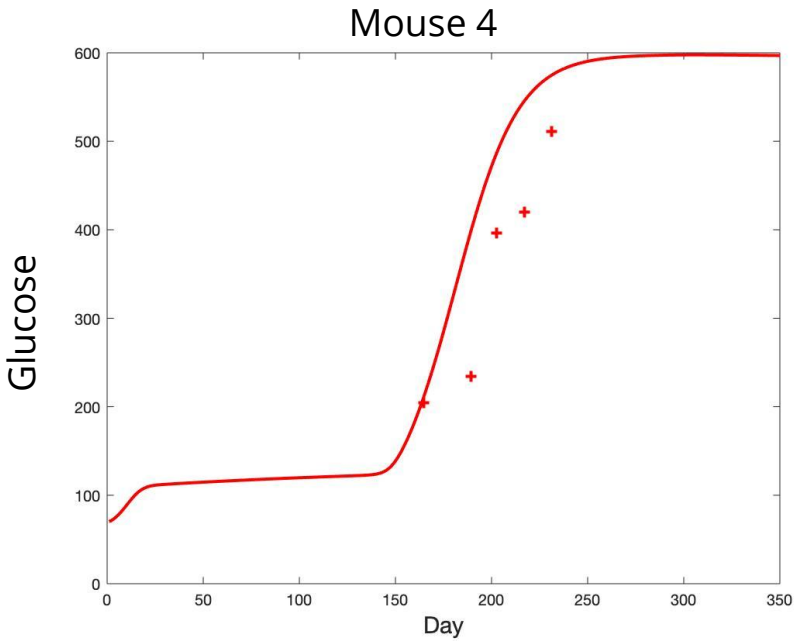


Applying Code to Other Mice

- Mouse 6 is a “good” mouse, need to see how performance changes when more obscure behavior
- Testing acute vs progressive mice
- How can we use fits to multiple mice effectively?

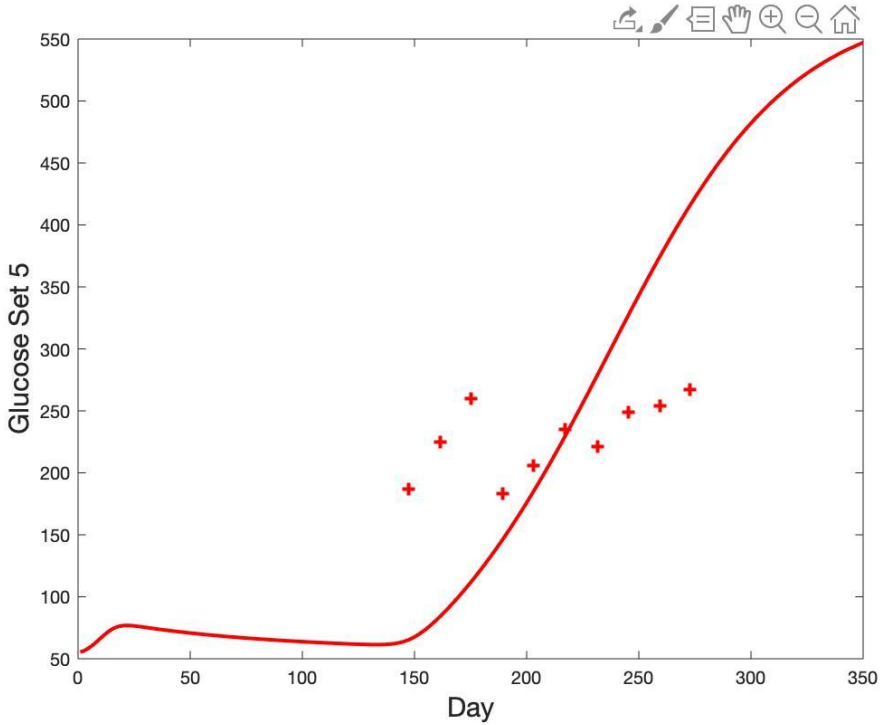


Mice 4 and 7 (Acute) - Dual

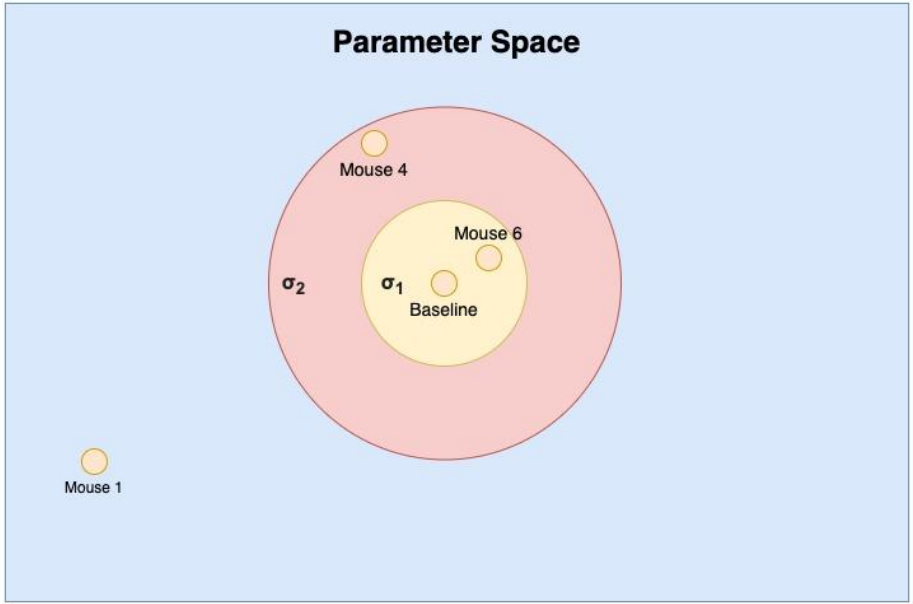


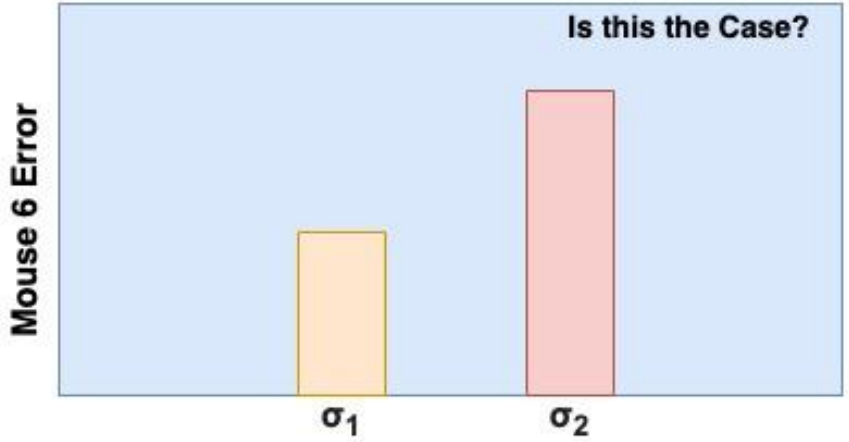
In order to get these results, we needed to raise the variances from our Mouse 6 fits!

Mouse 1 (Progressive) - Dual



- Very irregular raw data
- Algorithm still expects a sudden jump in glucose
- Not enough parameter movement

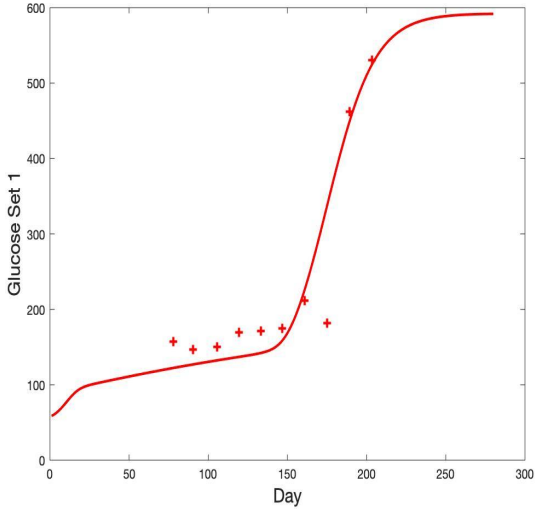

Parameter Space
Mouse 4
Mouse 6
σ_2
σ_1
Baseline
Mouse 1

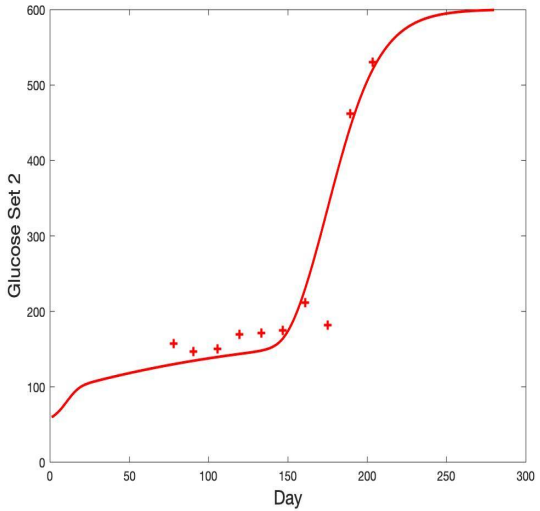

Is this the Case?
Mouse 6 Error
σ_1
σ_2

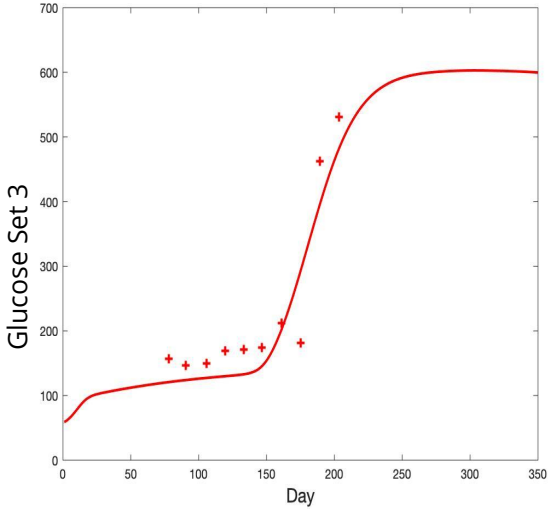
Example that it Might Not Be - Dual

With increased variance on mouse 6 data:

Run	Error
1	170.48
2	165.77
3	160.34



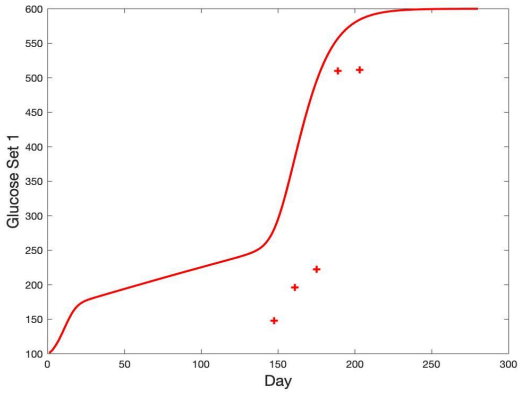


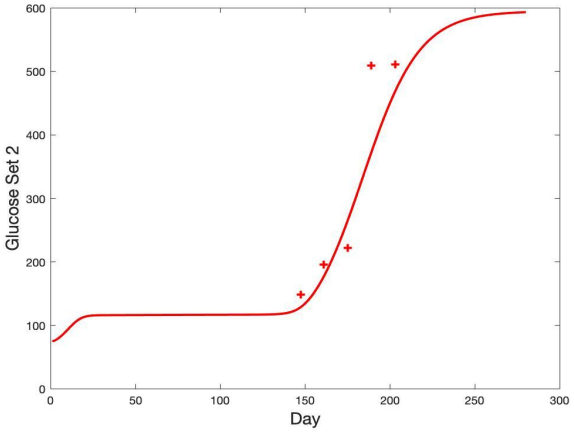


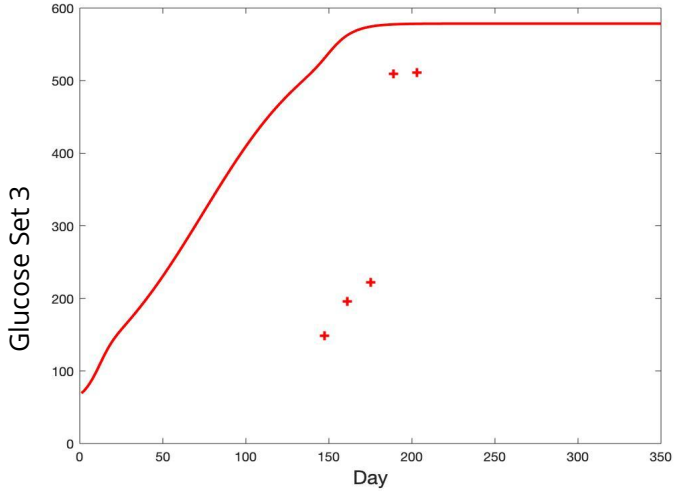
***At this point eta is now moving too**

Example that it Could Be (Mouse 7)

Run	Error
1	368.184
2	153.78
3	643.52







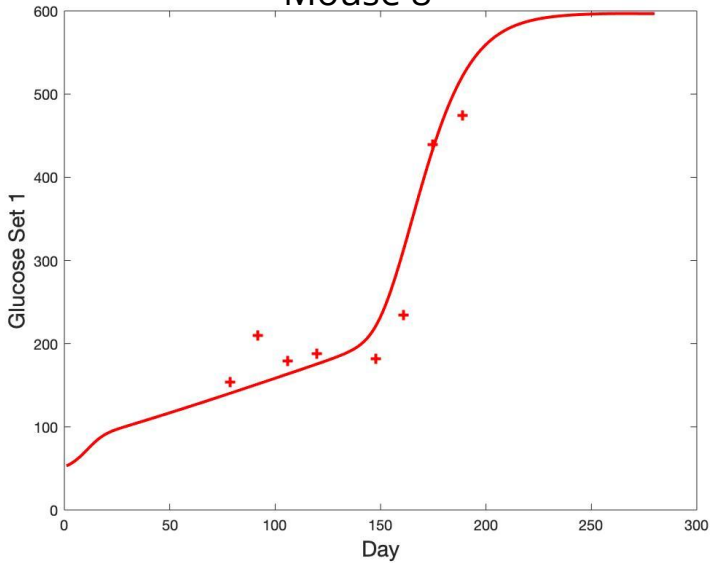
What is Causing This Issue

- For some mice, it appears that the algorithm finds a good fit in, for example, iteration *t*, but then drastically deviates from it in *t+1*
  - Example of this is on previous slide and additional example in weekly report
- Hypothesis: larger variance drives parameters outside of the optimal search area
  - Possible solution: introduce check at end of iteration: is the error of this iteration less than the previous? If no, then terminate with previous iteration as final estimate

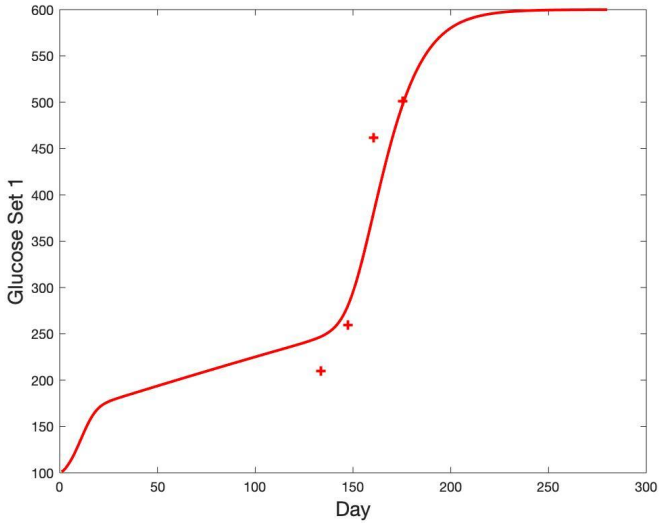
One Iteration May Now Be Enough

Allowing eta to vary with alpha_eta and beta_eta results in:

Mouse 8



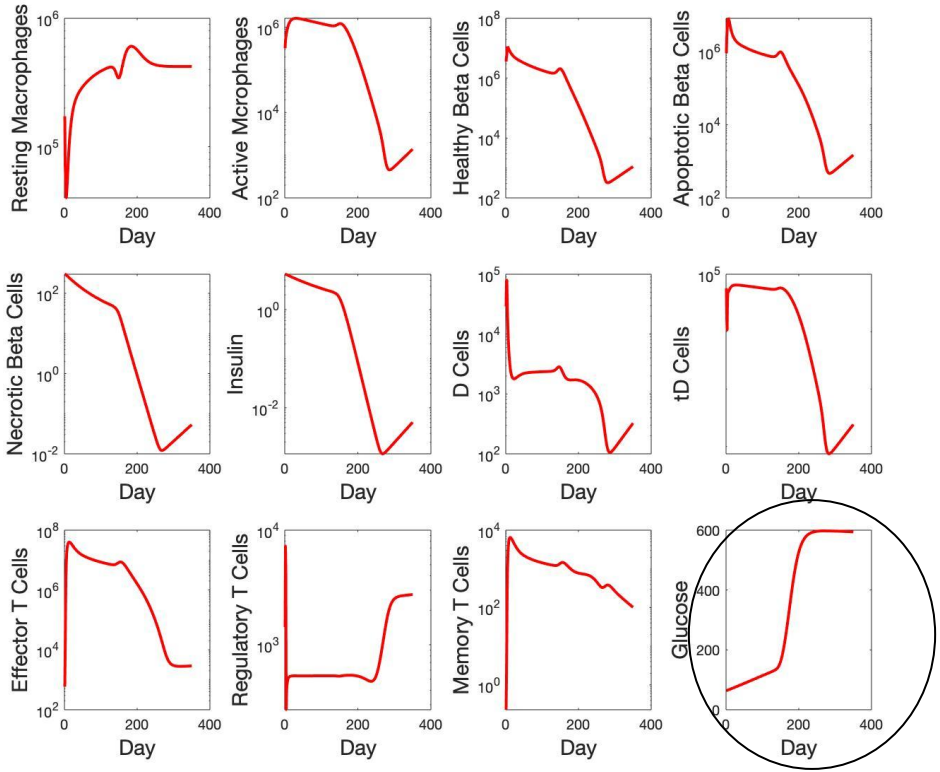
Mouse 10



A Second Biological Check

- These parameters are meant to “live on the edge”
  - If no wave, mouse should get healthy
  - If wave, mouse should get sick
- To check this, can plot the whole system with final parameter estimates + NO wave

A Second Biological Check



Why is Mouse Still Getting Sick?

- Relationship between parameter eta and macrophage clearance rates is very sensitive
- Eta is moving, clearance rates held constant currently
- Need clearance rates to move, but this must be done very carefully

Big Picture

- Maximize number of datasets
  - Possibility of combining Li and Matthews
  - Deterministic nature of UKF limits possibilities on Li alone
- Create distributions of key parameters
  - Use as prior distributions for MCMC (informative prior)

Overall Workflow