Overall goal: Reproduce Figure 1 from main paper:

Figure 1A:

Shows that:

1. The characteristics of period and dampness are not coupled.
2. The proportion of damped cells does not affect FRP in constant darkness.

Figure 1B:

Shows that:

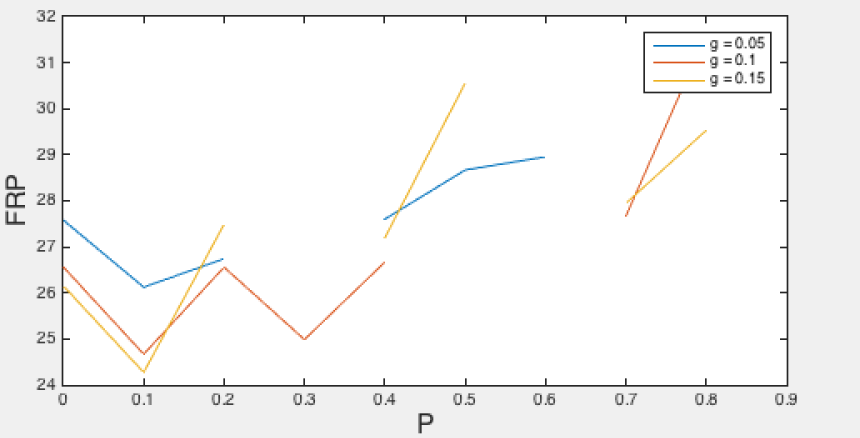
1. Independent of light intensity when you have a higher proportion of damped cells, the system is more easily entrained.
2. When you adjust the intensity, higher intensities further boost the entrainment ability of the model.

Milestone 2:

Victoria: I have a working code base for my model here: https://github.com/victoriachistolini/Goodwin_Model . The model shows evidence of syncrony when run with several cells whose parameter sets have been randomly generated (https://github.com/victoriachistolini/Goodwin_Model/blob/master/goodwin_model/figures/syncrony_10_Random_Cells.png). I have also made progress with a library of cells. I have 40 total parameter sets that have been hand classified as either damped or sustained. I have kept track of the ratio of dampening for each of the parameter sets so that we may be able to update the definition of dampedness at any time during the experiment. I have tried to replicate figure 1a from the main paper with my parameter sets, but I am getting some bizarre results. Perhaps there is evidcence of correlation: https://github.com/victoriachistolini/Goodwin_Model/blob/master/goodwin_model/figures/fig1a/fig1a2.jpg or unexplained dips in period: https://github.com/victoriachistolini/Goodwin_Model/blob/master/goodwin_model/figures/fig1a/fig1a3.jpg .

Douglas: I have a working code base for my model from Stephanie that shows clear signs of synchrony. It shows synchrony both when tested with a population of cells with identical initial conditions and wildly different initial conditions. I have replicated a number of the figures from the LG16 paper. I had made a library of about ~50 parameter sets split between sustained and damped with relatively similar periods between the damped and sustained parameter sets. I generated all the parameter sets by running the simulation with 1 cell and looking at the oscillations of PER mRNA to see how it compared to the oscillation produced by the original parameter set. I have also tried to figure out a way to quantitatively measure dampness.

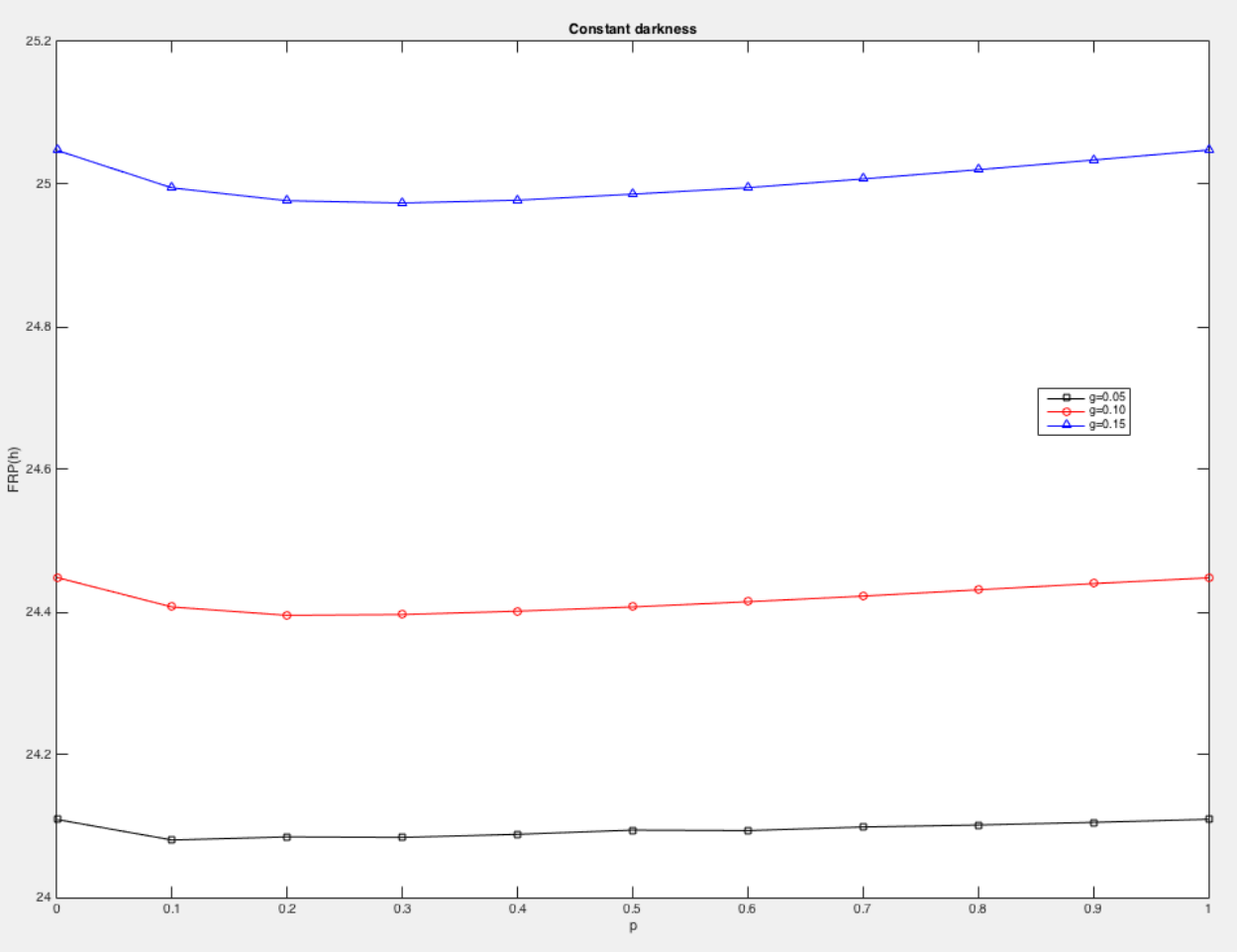
Although I have relied more on by-eye comparisons to default oscillations, I am also calculating a “dampedness ratio,” which is the difference of the starting and ending PER mRNA amplitude divided by the average amplitude over all oscillations. The most significant challenge I have run into so far is related to determining a method to perturb the original parameters to get the damped and sustained parameter sets. I am having difficulties balancing the high levels of perturbation needed to produce damped oscillations with the low levels of perturbations needed to maintain high-levels of intracellular synchrony. I spent a while trying to figure out how much to perturb which parameters, and have settled on perturbing *k1, k2, k3, k4, k5, k6, k7* and *k8* and with a Gaussian Distribution that has □ set to the original parameter value divided by 20. When I used the library I made to reproduce figure 1A from Gu et al. I got very bizarre results:



I have decided to remake my library more carefully using the perturbation method described above.

Fan

I implemented the model in the paper directly, following their model of producing damped and self-sustained cells, and recording the period of the cells by analyzing the periods of the states. Currently I have produced some similar result as in Fig1.(a), and is running code to simulate Fig1.(b). The result for Fig1.(a) is:



The data points locate at roughly the same range as in the paper, though the pattern is not exactly the same.

As for Fig1.(b), my previous model had problems such as incorrect light-dark cycle periods that might have rendered my results incorrect -- those models showed a tendency of a rising LLE instead of a dropping one as p increases (even to the point that when p is 1, the LLE went to 24h for high Kf value). Sadly, after fixing the LD cycle issue, this is still what one of the simulations that took over n21 resulted into.

Jay:

I am using code from Taylor & Wang's Phase-amplitude paper. The simulation code returns the periods for each run, which we can take the mean of to determine the average period of the oscillators at each point, to remake figure 1 a from the main paper. Taylor & Wang also generated 83 self-sustaining parameter sets. I haven't found an effective way to perturb these parameter sets for the non-self sustaining parameters.

I also replicated Figure 3B from Taylor & Wang, where TTX blocks intercellular signalling between the network. The time where the network is silenced is qualitatively visable, but the level o

Planning for Milestone 3

Steps:

For both figures:

Step 0 – Make sure the model with multiple cells is able to synchronize:
1. Plot the trajectory of one of the proteins for each of the cells in the model
2. Calculate the order parameter.

Step 1 – determine a library of dampened and sustained oscillators:
1. Douglas create a library of ~100 parameter sets
2. Jay adjust lambda and a_0 -> you will need to determine the threshold that makes the oscillators damped and sustained for you model.
3. Fan part of the model, use Gaussian to adjust parameters
4. Victoria create a library 75 damped, 75 sustained.

Step 2 – determine a scalar on the mean field coupling that creates weak, moderate and strong coupling intensity

Step 3 – determine a scalar for the light pulse function that creates weak, moderate and strong coupling intensity.

For Figure 1A:

In order to calculate the FRP you will want to find the mean period of all of the cells for a single model protein and get the period, report this for:
1. varying coupling strengths: weak, moderate and strong.
2. In constant darkness
3. varying proportions of damped cells: 0-100%

For Figure 1B:

In order to calculate the LLE find the mean period of all of the cells for a single model protein and get the period. For each data point you need to find the lower level of entrainment, which will require multiple runs. For each run adjust the t-cycle to find the lowest that the cells can entrain to. In order to adjust the t-cycle, adjust the mod on the light pulse function. Report this for:

1. varying light intensities: weak, moderate and strong.
2. a coupling strength of moderate, weak and strong.