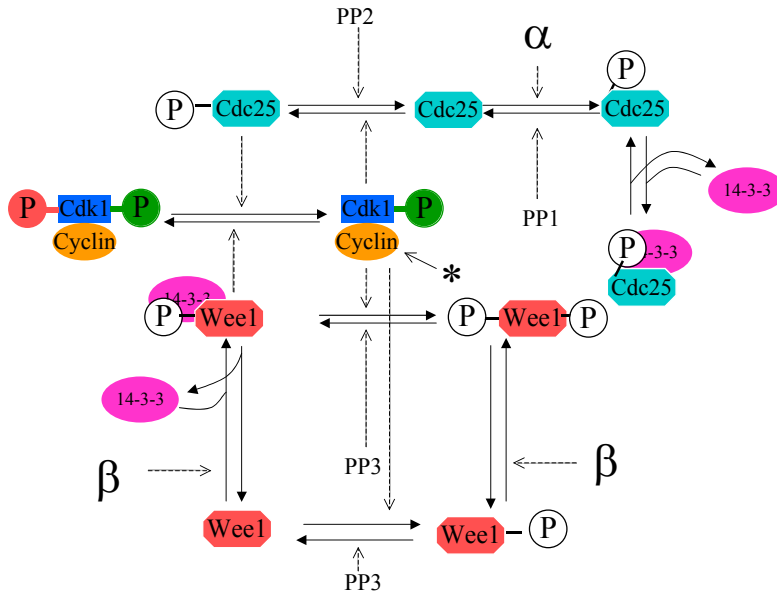


Where do the data come from?

Exercise A - Mining useful data from the literature: When comparing simulations from our preliminary model of the DNA replication checkpoint (see wiring diagram below) to data from Lee et al. (Figure 5B), major discrepancies were discovered. The simulations show that immunodepletion of Wee1 accelerated entry into mitosis, whereas the experimental data show no effect and only a partial bypass of a DNA replication checkpoint. In 1995, Mueller et al. discovered Myt, a second MPF kinase.



Using information from these two papers,

- 1) wire Myt1 into the above diagram. How does this wiring differ from that of Wee1? How is it similar?
- 2) ascribe relative activity to Wee1 and Myt1 as MPF (cyclin B/Cdk1) kinases.
- 3) predict how the changes you made will affect: a) the rate of entry into mitosis, b) the effect of Wee1 immunodepletions, and c) the effect of unreplicated DNA on entry into mitosis.

Exercise B - Designing new experiments for mathematical modeling: Your rewired diagram containing Myt1 and the differential equations and kinetic parameters you would have added/modified in the model generate a set of hypotheses to be tested experimentally.

1. What are the main hypothesis and/or assumptions of your rewired model that should be tested experimentally?

2. Outline a series of experiments to test these hypotheses. Be sure to consider methodologies, reagents needed (e.g. recombinant proteins), controls. Do these experiments require a highly quantitative approach or will a qualitative (yes or no) answer suffice? Estimate the time and money that these experiments would require?