70 Homework 1
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1.  Historically, what two factors have held back scientists from constructing high-quality whole-cell models? (10 pts)

    Firstly, there was not enough information for constructing high-quality whole-cell models. With the advent of next-gen sequencing and genomics now people are capable of generating comprehensive data which can be used to construct high-quality whole-cell models.

    Secondly, it is hard to model the very complex interactions in a cell a with a single computational model. Thus, researchers tried to make simpler models with underlying assumptions but these simpler models were based on assumptions which do not apply to all cellular processes.

2.  What general strategy was used to construct the model in this paper? (10 pts)

    The strategy discussed in the paper was to divide the whole system into smaller independent modules. Each of these modules was modeled independently and then integrated together. They defined 28 modules and independently built, parameterized and tested a sub-model for each of these modules. Each module was modeled using appropriate mathematical model.

3.  After it was constructed, how was the model validated experimentally? Is there enough data to validate all the parameters defined in the model? (10 pts)

    The authors didn't perform any experiments themselves, but they used a number of independent experimental data sets to validate their model. They found that the model is agreement with the previously published data e.g. they found that the mRNA and protein level distributions predicted by the model were consistent with the reported single cell measurements.

    No, there was not enough data to validate all the parameters involved in the model. A more comprehensive validation of the model will require more experimental data about *M. genitalium.*

4.  Give an example of how this model was used to for the purposes of predictive biology and explain and interpret the results. (10 pts)

    The authors used the model to predict novel gene function and kinetic parameters. They first experimentally measured growth rates of 12 single-gene disruption strains and compared results with the model. They found IpdA gene, which was determined as non-essential, had a severe impact on cell growth. They found a gene Nox with similar gene sequence as IpdA and found strong evidence that the products of IpdA and Nox are functionally related. Thus, in absence of IpdA gene product, Nox gene product can help sustain the growth. They used the model to do simulation and found that in absence of IpdA, to reproduce the growth rates as previously reported Nox dependent reaction would require a rate constant, $k=50$ $s^{-1}$.