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No Predictive Power without Knowing Parameter Uncertainty

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Parameter uncertainty is a prevalent aspect of systems biology modeling. It is therefore important to understand how this aspect relates to one of the most important properties of any model, namely predictive power. When a model is calibrated under normal circumstances, some parameters are insensitive and therefore uncertain. When the model is applied to predict dynamics under different circumstances, e.g., after a mutation or adding a chemical, these uncertainties might cause large uncertainties in the predicted dynamics. In this presentation a general framework is presented to study this relationship quantitatively. For this, a quantifier for prediction uncertainty within a Bayesian framework via Markov Chain Monte Carlo sampling is employed. The prediction uncertainties for six highly diverse systems biology models are computed, using realistic data and a set of systematically generated predictions. It turns out that the models are not only sloppy in terms of parameter uncertainty but also in terms of prediction uncertainty. The effect of parameter uncertainty on prediction uncertainty strongly depends on the type of prediction. Prediction uncertainty has therefore to be determined for each application separately. For this to be feasible in practice, each model should be supplemented with a sample of the posterior distribution of the parameters.