A Bayesian Workflow for Metabolic Pathways

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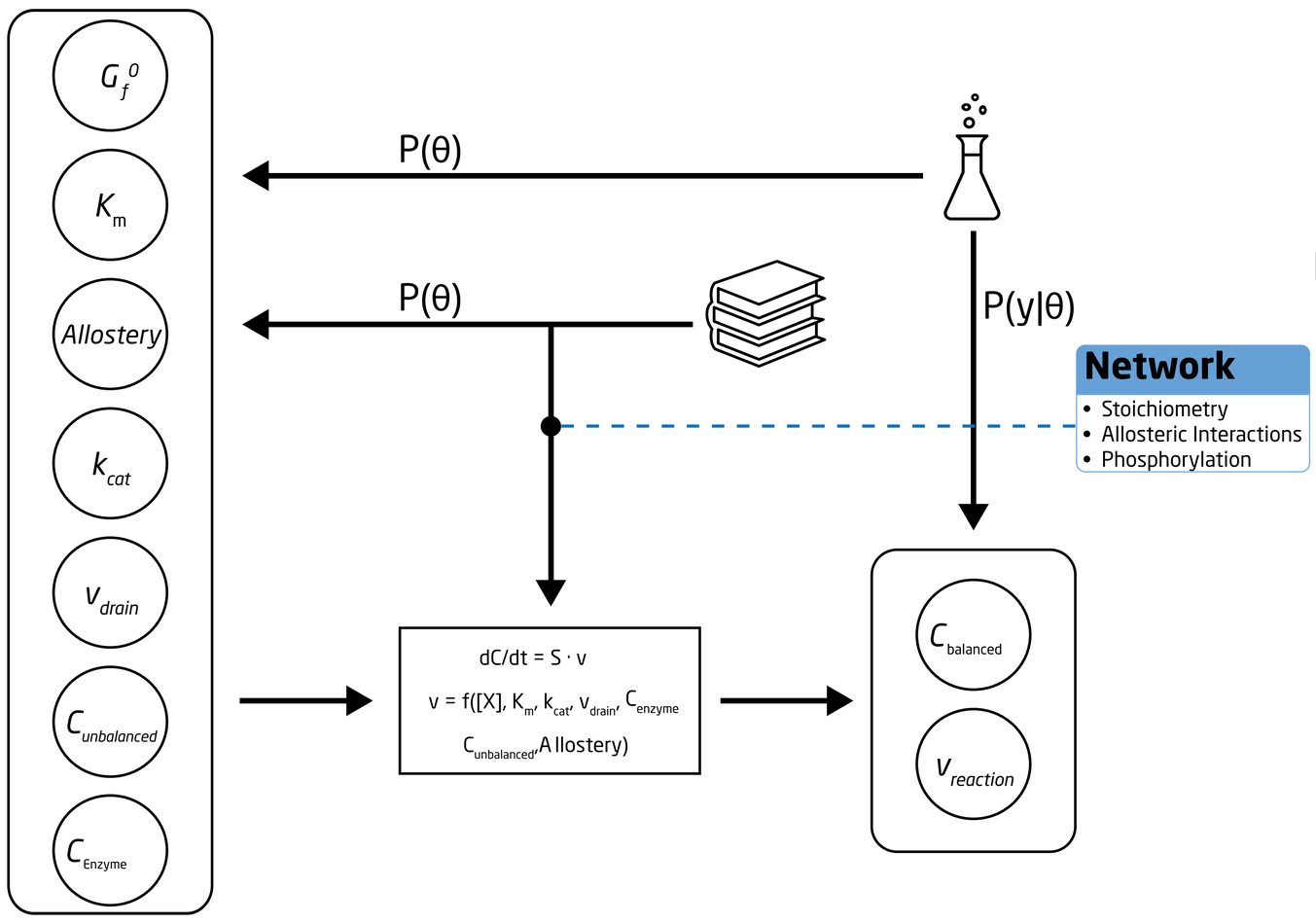
Summary

The proposed workflow is a summary of our kinetic modelling framework: Maud. I highlight the best practices for model development in a Bayesian workflow; the difficulties associated with sloppy parameter models[1]; and briefly highlight their use in the DBTL cycle.

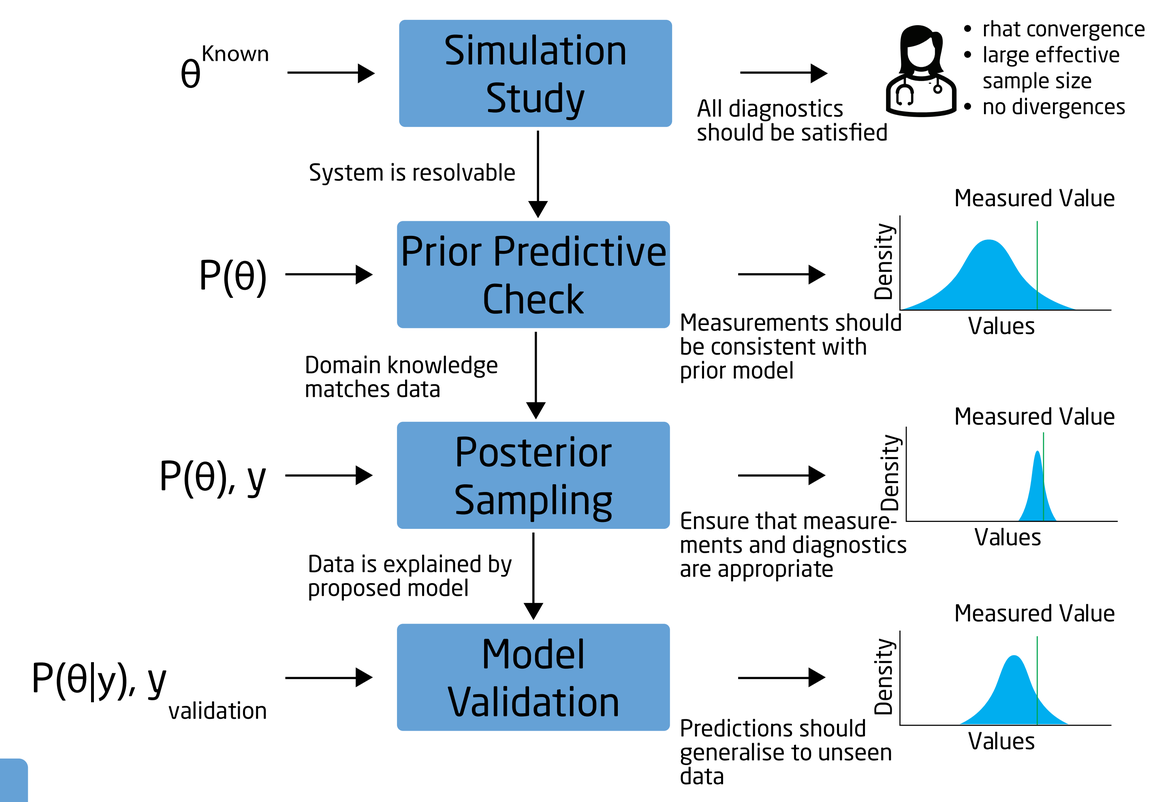
Maud Workflow

Our framework is implemented in Python with parameter inference conducted by Hamiltonian Monte Carlo in Stan[2]. The current implementation is limited to steady-state metabolism.



Model Development Workflow

Constructing kinetic models is tedious, prone to errors, and has a long feedback time. This workflow is a foundation for model development and approaches Bayesian inference in a principled way.



Conclusions

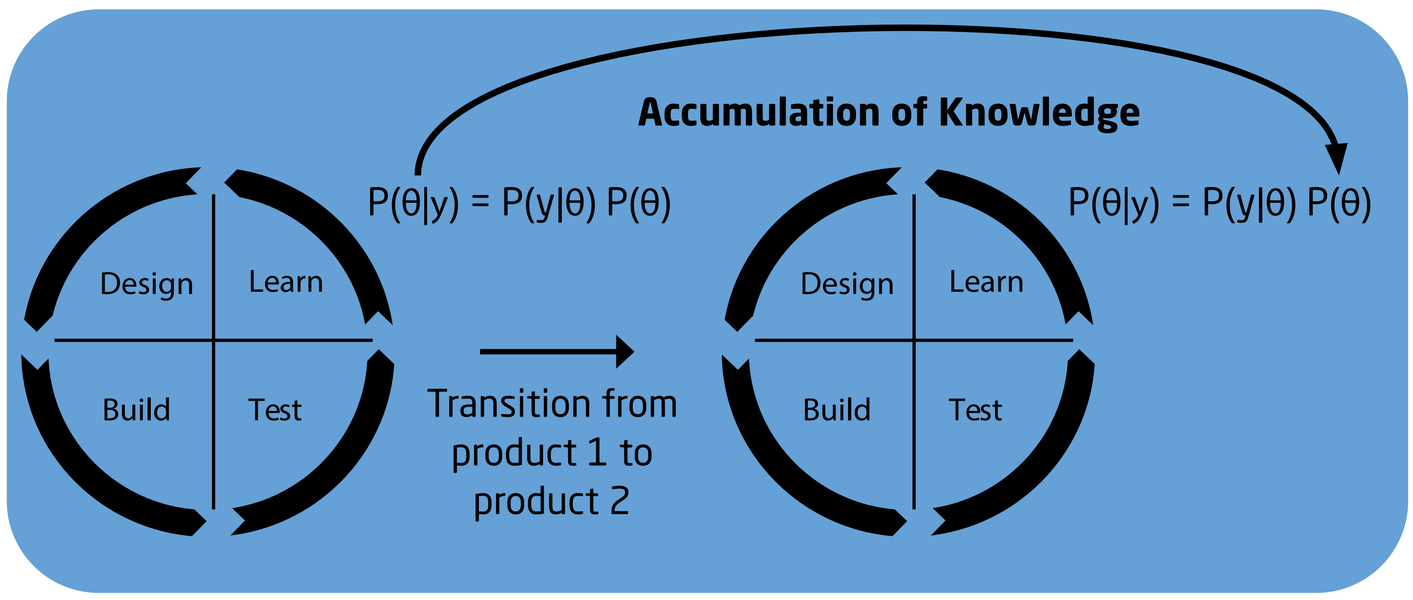
1. Our framework provides an option for construction and sampling of kinetic models
2. The joint posterior distribution is highly correlated between parameters

Limitations

- Solving steady-state is a bottleneck
- Experimental noise + homeostasis + mechanistic parametersation = Difficult geomtry

Bayesian Inference and Mechanistic Models

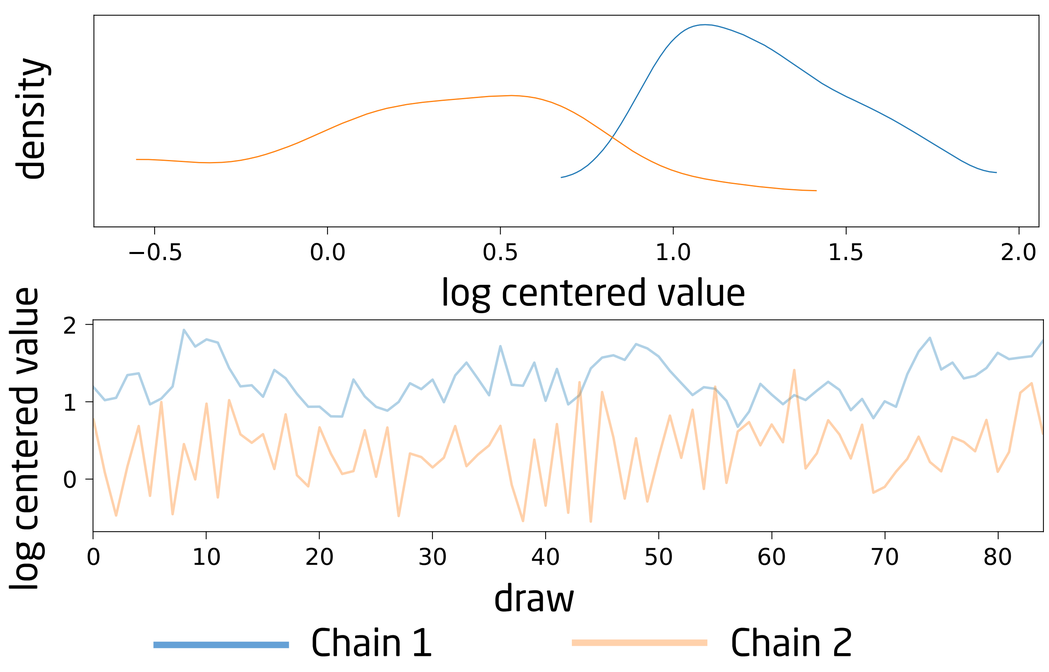
- The realisation of the posterior distribution synthesises the available information about the mechanistic parameters.
- Using posterior distributions as future priors has the potential to reduce compute time by constraining the parameter space.



Example of Difficult Posterior Distribution

- Simulation study of methionine cycle
- Chains have difficulty converging despite HMC algorithm

Trace plot of log-scaled allosteric eq. constant



References | Poster Summary | Useful Links | Additional Plots

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Acknowledgements: