Investigating Intrinsic Fluctuations in Biochemical Systems

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Project Details

PhD Supervisor: Prof. Alan McKane
Project Collaborators: Prof. Pedro Mendes & Dr. Jürgen Pahle (M.I.B.)

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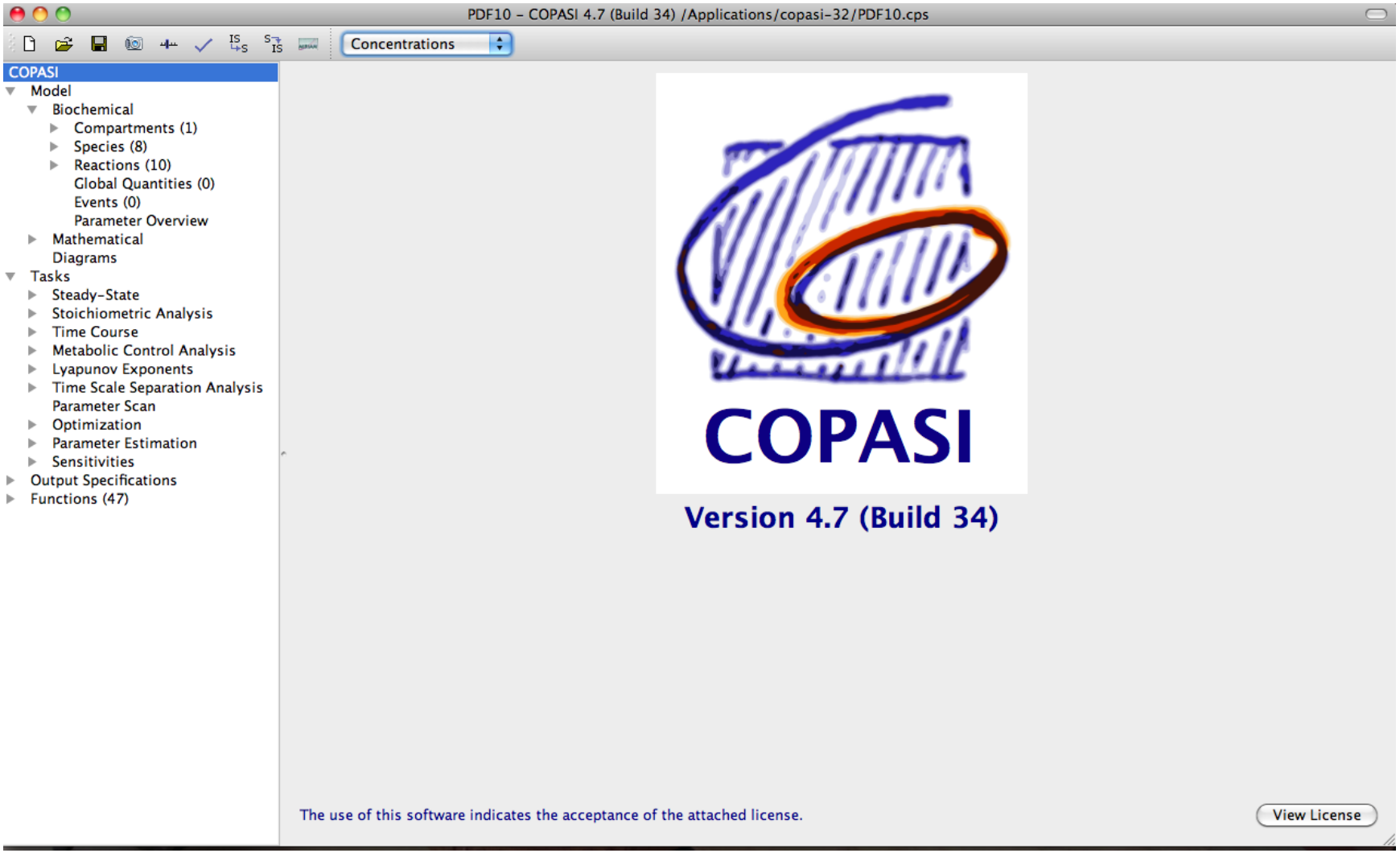
Project Aim: We are interested in describing stochastic fluctuations in biochemical systems. We want to automate fluctuation analysis from statistical physics, so it can be incorporated into a software package

COPASI



Software available from: www.copasi.org

Deterministic Modelling of Biochemical Systems

For a biochemical model with M species

$$\begin{aligned}
\frac{dx_1}{dt} &= f_1(\mathbf{x}) \\
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&\vdots \\
\frac{dx_M}{dt} &= f_M(\mathbf{x})
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When is this approach not appropriate?

The Master Equation: A Stochastic Approach

State space is discrete: the number of molecules of each species.
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$$\frac{dP(n,t)}{dt} = \sum_{n' \neq n} T(n|n')P(n',t) - \sum_{n' \neq n} T(n'|n)P(n,t).$$

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In general, the master equation can't be solve exactly.

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$$\frac{\partial \Pi}{\partial t} = -\sum_{i,j}^{M} A_{ij} \frac{\partial y_j \Pi}{\partial y_i} + \frac{1}{2} \sum_{i,j}^{M} B_{ij} \frac{\partial^2 \Pi}{\partial y_i \partial y_j}.$$

Fluctuations described by matrices A and B. We want to describe the fluctuations around the steady state in terms of covariances $\Xi_{ij} = \langle y_i y_j \rangle - \langle y_j \rangle \langle y_i \rangle$. This satisfies the Lyapunov equation

$$A\Xi + \Xi A^T + B = 0.$$

Procedure for quantifying fluctuations in COPASI

- Describe biochemical model in COPASI
- Find a fixed point and check stability
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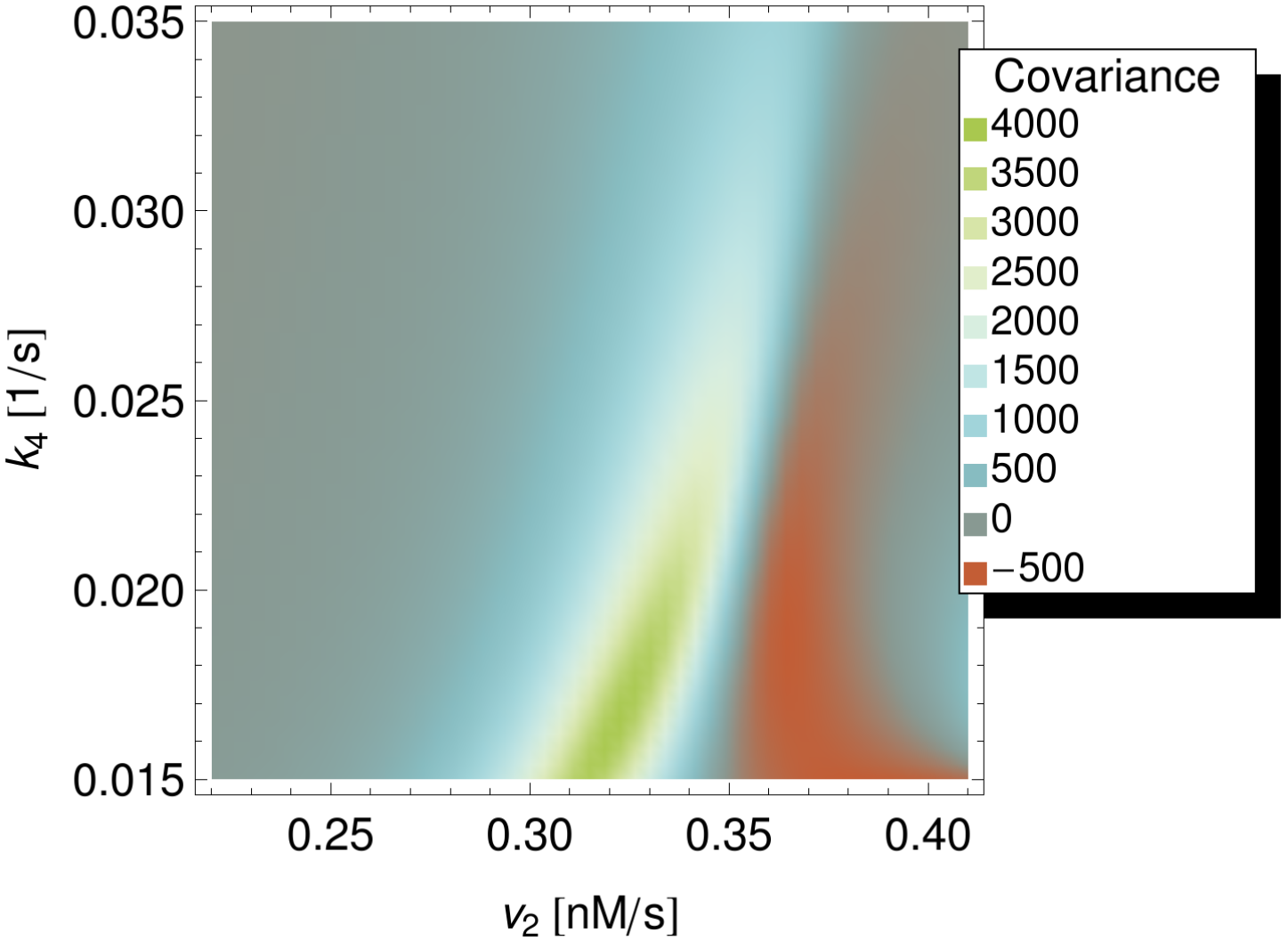
LNA with the Parameter Scan Task



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  This can be a problem if the system is close to a boundary
- Multi-stable systems

Our Work

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Biochemical Fluctuations, Optimisation and the Linear Noise Approximation
Jürgen Pahle, Joseph D. Challenger, Pedro Mendes and Alan J. McKane
Accepted for publication by BMC Systems Biology

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The technique has been extended so that it can be applied to multi-comparment systems
Multi-Compartment Linear Noise Approximation
Joseph D. Challenger, Jürgen Pahle and Alan J. McKane
Submitted to Phys. Rev. E (available on Arxiv)

Thanks for listening

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