

# 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.)

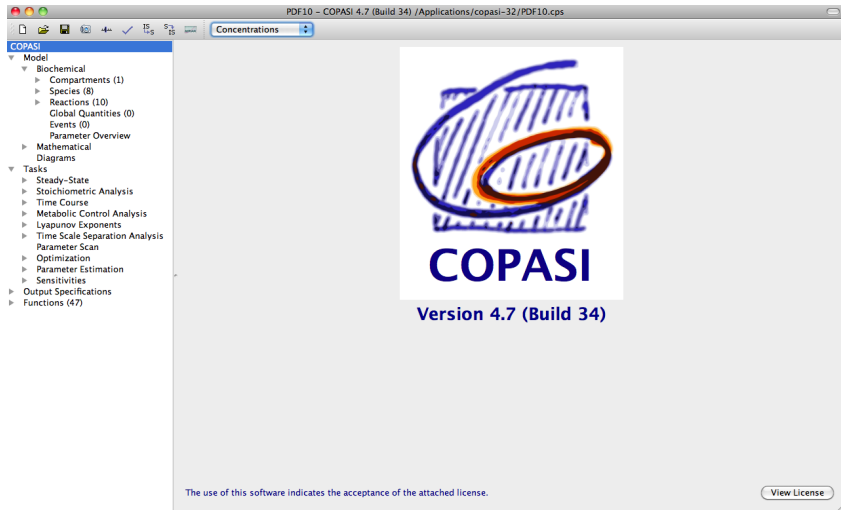
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Project Aim: We are interested in describing stochastic fluctuations in biochemical systems. We want to automate fluctuation analysis from statistical physics, so it can be incorporated into a software package

# COPASI



The screenshot shows the COPASI software interface. The title bar reads "PDF10 - COPASI 4.7 (Build 34) / Applications/copasi-32/PDF10.cps". The main window displays the COPASI logo, which consists of a stylized blue and orange shape above the text "COPASI" in blue, and "Version 4.7 (Build 34)" below it. On the left side, there is a tree view menu with the following items:

- Model
  - Biochemical
    - Compartments (1)
    - Species (8)
    - Reactions (10)
    - Global Quantities (0)
    - Events (0)
    - Parameter Overview
  - Mathematical Diagrams
- Tasks
  - Steady-State
  - Stoichiometric Analysis
  - Time Course
  - Metabolic Control Analysis
  - Lyapunov Exponents
  - Time Scale Separation Analysis
  - Parameter Scan
  - Optimization
  - Parameter Estimation
  - Sensitivities
  - Output Specifications
  - Functions (47)

At the bottom of the window, there is a text box that says "The use of this software indicates the acceptance of the attached license." and a button labeled "View License".

Software available from: [www.copasi.org](http://www.copasi.org)

# Deterministic Modelling of Biochemical Systems

For a biochemical model with  $M$  species

$$\frac{dx_1}{dt} = f_1(\mathbf{x})$$

$$\frac{dx_2}{dt} = f_2(\mathbf{x})$$

$\vdots$

$$\frac{dx_M}{dt} = f_M(\mathbf{x})$$

where  $\mathbf{x} = (x_1, x_2, \dots, x_M)$  are the chemical concentrations.

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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.  
The system 'jumps' from state to state when a reaction occurs.



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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

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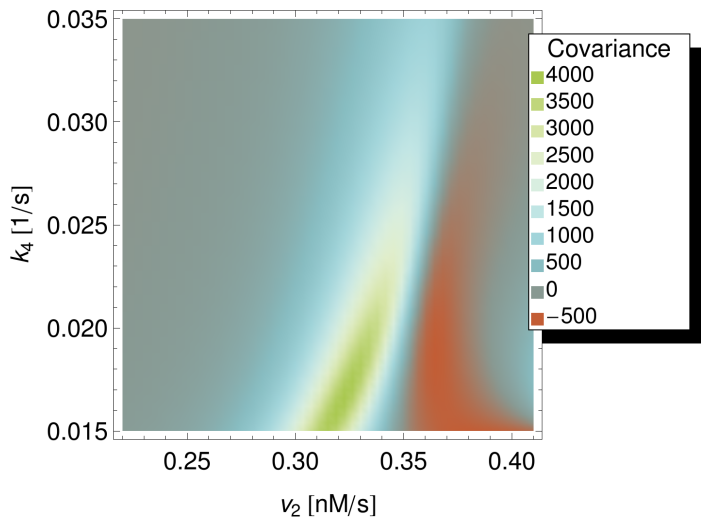
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# LNA with the Parameter Scan Task



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- 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



# Our Work

Biochemical Fluctuations, Optimisation and the Linear Noise Approximation

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The technique has been extended so that it can be applied to multi-compartment 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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