Application of Formal Methods to Biological System Modelling

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Objectives

- Model Transformation
  - System abstraction
  - Add perturbing components

- New Biological Model
  - Reaction Network modelling
  - Parametrized ODE system
  - Uncertain parameters

- Experiments or Hypothesis
  - Experimental results
  - Constraint between parameters

Set Based Verification

- Check if model can reproduce experimental results
- Constraint & hypothesis verified
- Find all valid parameter sets

Motivating Examples: Cadmidia project, Iron Homeostasis model.

Reachability Analysis ...

- Replace a large number of simulations by exhaustive analysis
- Can deal with uncertain parameter sets
- Ensure the model validation
- Can deal with complex temporal constraints (STL)

... using Bernstein Coefficients

Motivations

- Reaction networks → Polynomials
- Low degree & sparse
- Parametrized

Properties

\[
\rho(x) = \sum_{b} \lambda^b, \quad \forall x \in B, \quad \rho(x) \in \mathbb{R}^n
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Model Reduction with Time-Scales Decomposition

- Reduce stiffness
- Reduce computational cost
- Understand slow/fast mechanisms

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Approach

1. Time-scale identification
2. Slow/Fast separation
3. Subsystem separation
4. Subsystem computation

Bernstein Enclosure

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Challenges and Methods

1. Uncertain parameters
2. Complex constraints between parameters
3. Complex behaviours
4. Uncertain initial states
5. Stiff ODE
6. Non-linear dynamics
7. Large dimension

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