SBvar: Varying Parameter Analysis for Systems Biology

BIOEN 537 Software Project

Rachel Ng

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Background

- Biochemical systems can be modelled mathematically and simulated based on reaction networks that convert reactants to products
- Tellurium & Roadrunner are existing packages that handle SBML models, ODEs, simulations, and steady state calculations.
- Understanding the effect of changing parameters on the dynamical system is important for experimentalists and theorists
  - What if reaction rates are incorrect?
  - What range of concentrations can I use to maximize production of this species?
  - What combinations of concentrations would activate the synthetic switch?
- Important aspect of varying parameter analysis (robustness analysis)
  - Data structures: high dimensional, efficiency, organization conditions and simulations
  - Simulations: timeseries, steady states, peaks, clusters
  - Visualization: 1D line plot, 2D Contour maps, 3D surfaces

Use case 1: Assessing robustness of steady state to varying parameters.

1. Load antimony model
2. Create experiment (1D or 2D)
   - model
   - parameter(s) and range(s)
3. Calculate steady states for each condition
4. Plot relationship of steady state with parameter(s)

Use case 2: Assessing robustness of time course to varying parameters.

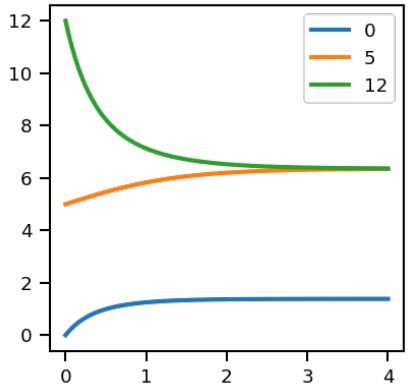
1. Load antimony model
2. Create experiment (1D or 2D)
   - model
   - parameter(s) and range(s)
3. Simulate full time course for each condition
4. Analyze time course (maximum, shape, oscillations, etc.)
5. Plot relationship of time course metrics with parameter(s)

Demo – Bistability System

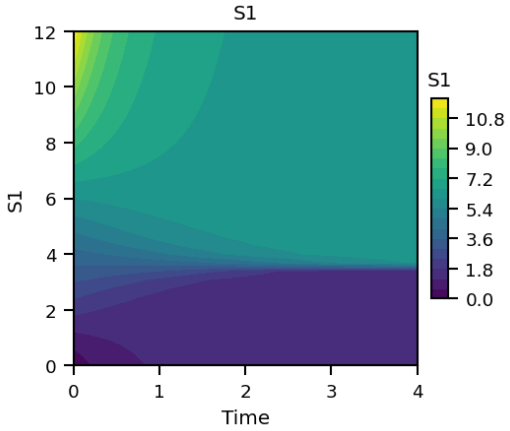
- https://github.com/racng/SBvar/blob/main/notebook/bistable_system.ipynb
- Model: Try S1 = [0, 5, 12]
  - high or low steady state depending on initial value of S1

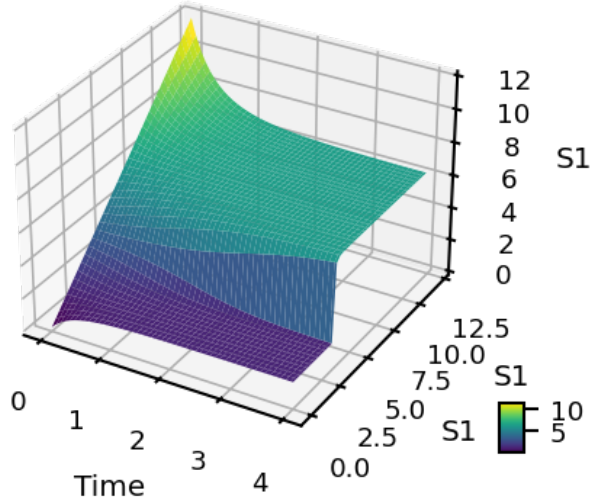
```
$Xo -> S1; 1 + Xo*(32+(S1/0.75)^3.2)/(1 +(S1/4.3)^3.2);
S1 -> $X1; k1*S1;

Xo = 0.09; X1 = 0.0;
S1 = 0.5; k1 = 3.2;
```



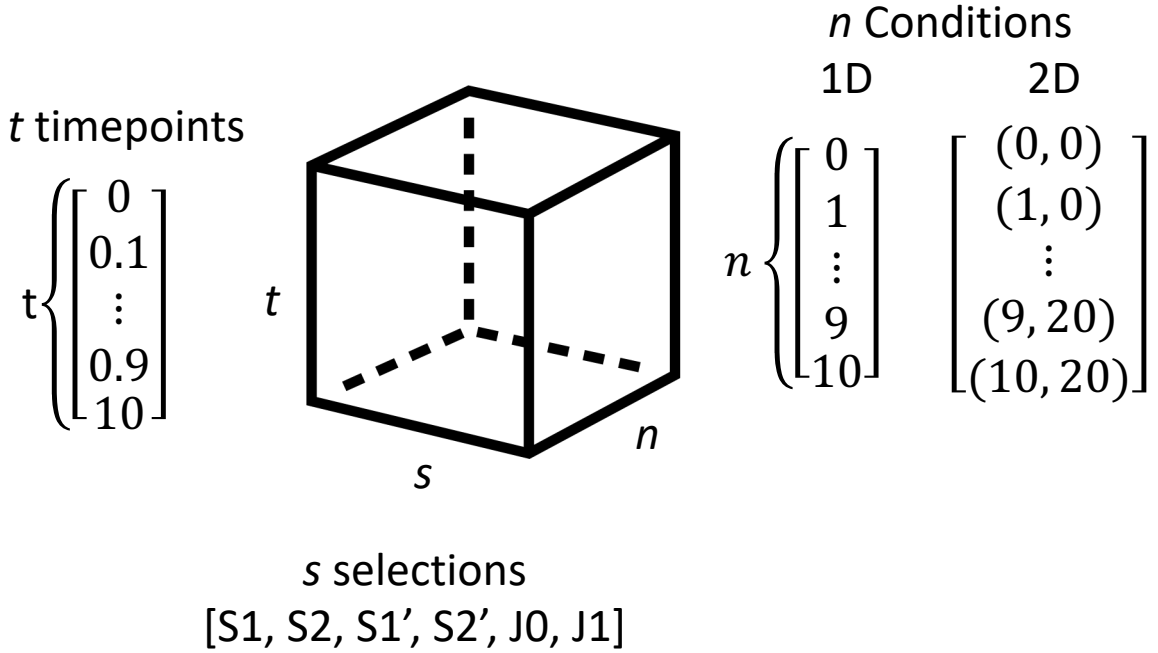
- One-way experiment
  - Vary S1 from 0 to 12, 40 points
  - Simulate from t=0 to t=4, 100 points
- Visualize time course across all S1 conditions





Design – Experiment Object

- roadrunner object – model specification
- selections: concentrations, derivatives (exclude for s.s.), reaction rates
- timepoints: start, end, number of points
- simulations: 3D matrix (t x s x n)
- steady states: 2D matrix (n x s)
- conditions: 1D (n x 1) or 2D (n x 2)
- iterator:
  - simulate
  - steady state
  - …
- vector ↔ mesh grid



Design – Plotting

- Extracting data from 1D or 2D Experiment
  - time series
  - steady state
  - time point
- plot_mesh
  - surface (3D)
  - contour (2D/3D)
  - filled contour (2D/3D)
- plot_line

Design – Time Course Analysis

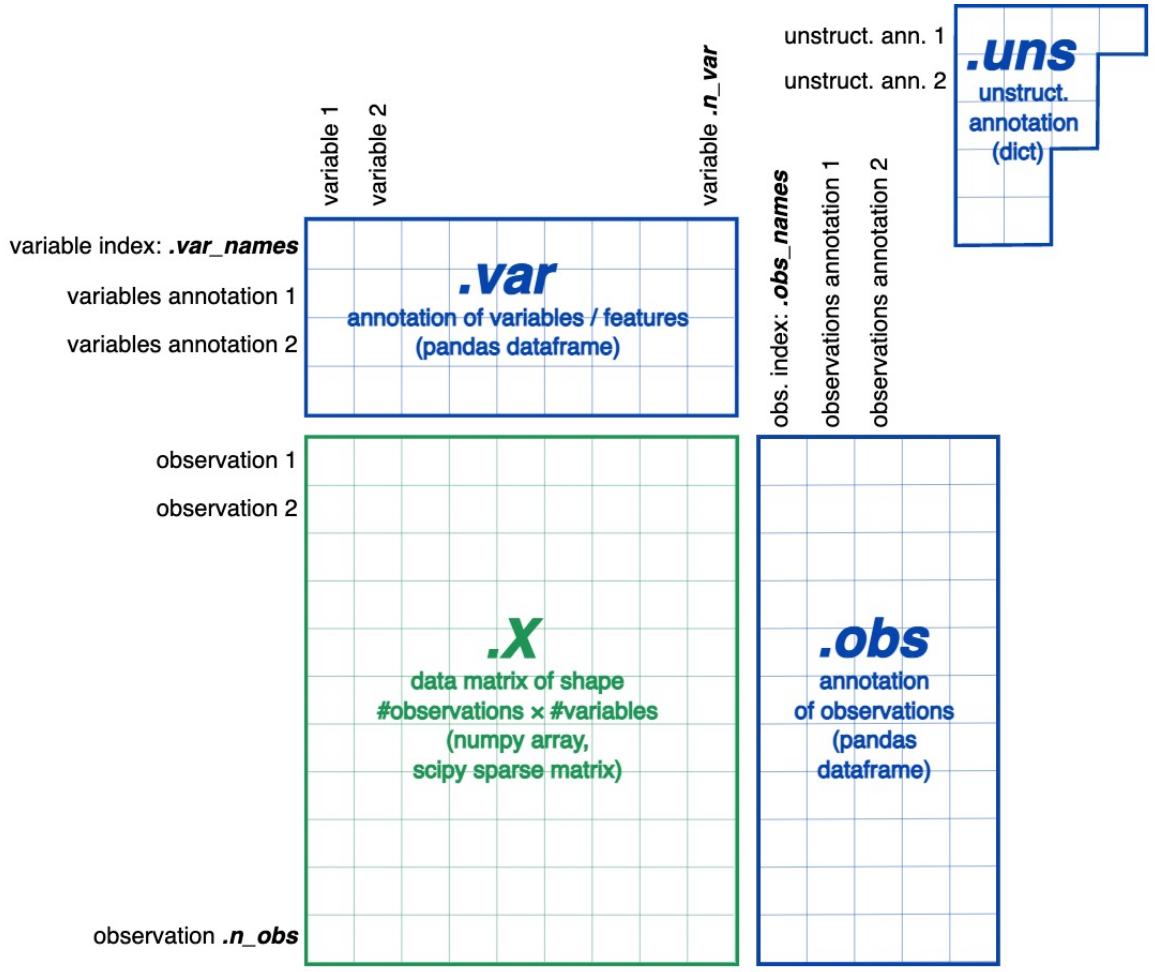
Characterizing simulated time courses for each condition

→ Condition-level annotations.

- kmeans_cluster
- kshape_cluster
- time_to_max
- max
- fit_sinusoid

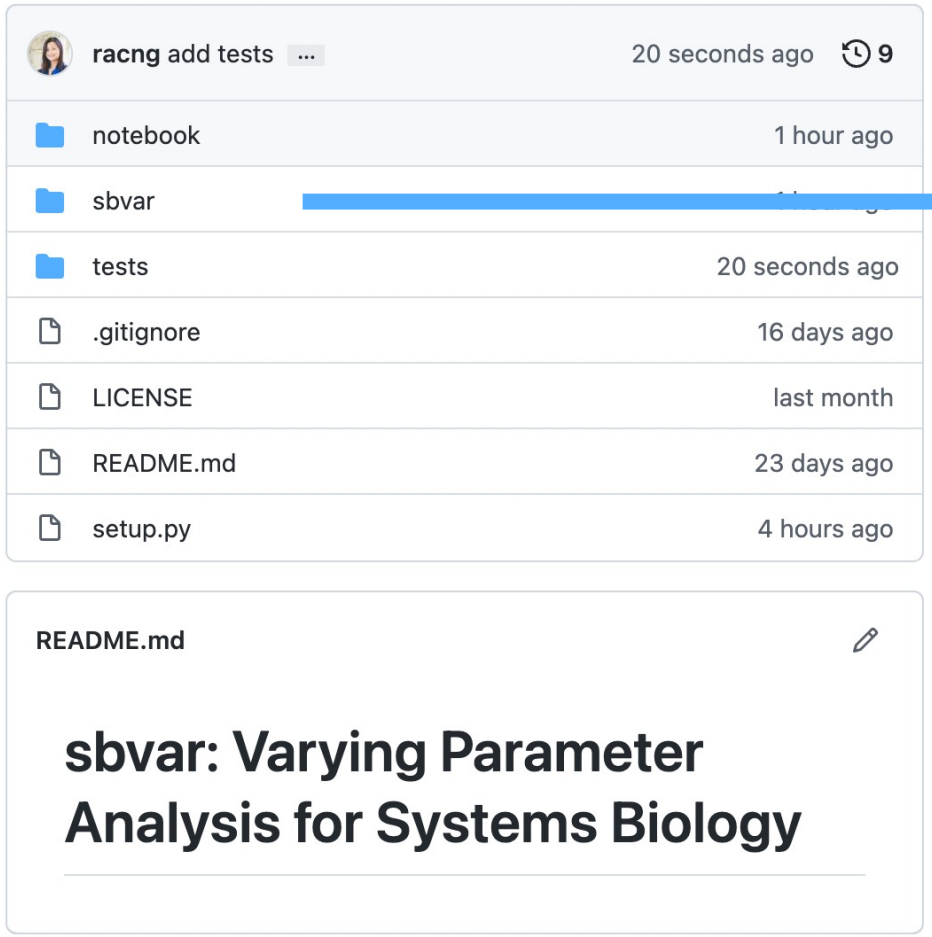
Design - IO

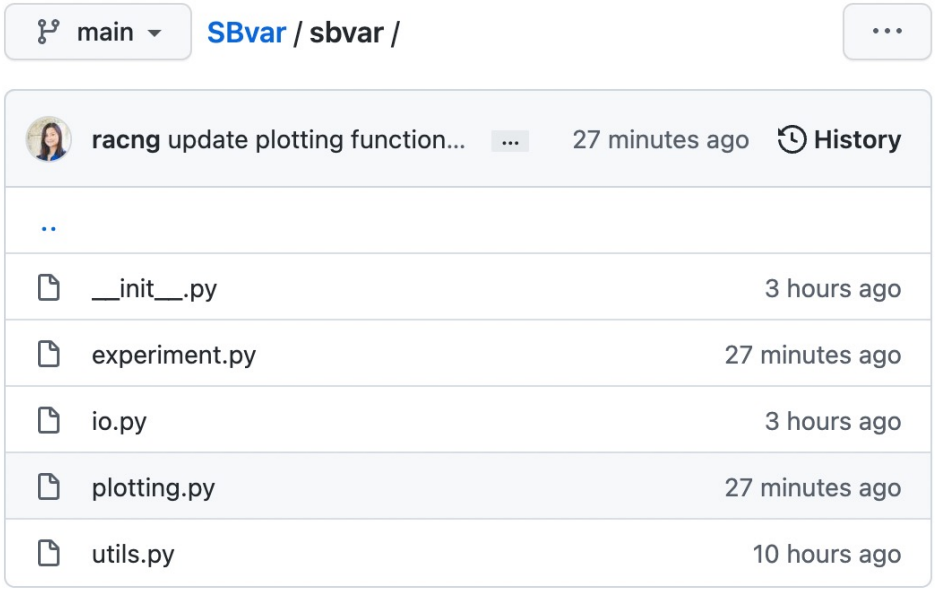
- AnnData – Annotated Data
  - observations → conditions
  - variables → selections
  - obs → annotation of conditions
    - steady states
    - maximum
    - clusters
  - var → annotation of selections
    - type (reaction/species/derivative)
  - uns → dictionary of attributes
    - experiment dimension
    - antimony model



Project Structure

- github repository: https://github.com/racng/SBvar





Lessons learned and future work

- searching through roadrunner attributes and methods
- Slicing and reshaping high dimension arrays to match meshgrid is tricky
- Moving child class methods to parent class
- Future work:
  - tests
  - lineplot
  - timeseries clustering
  - find maximum
  - oscillation magnitude/frequency