

Full-Stack Modeling of Biological Circuits: From Specifications to Implementation using Python



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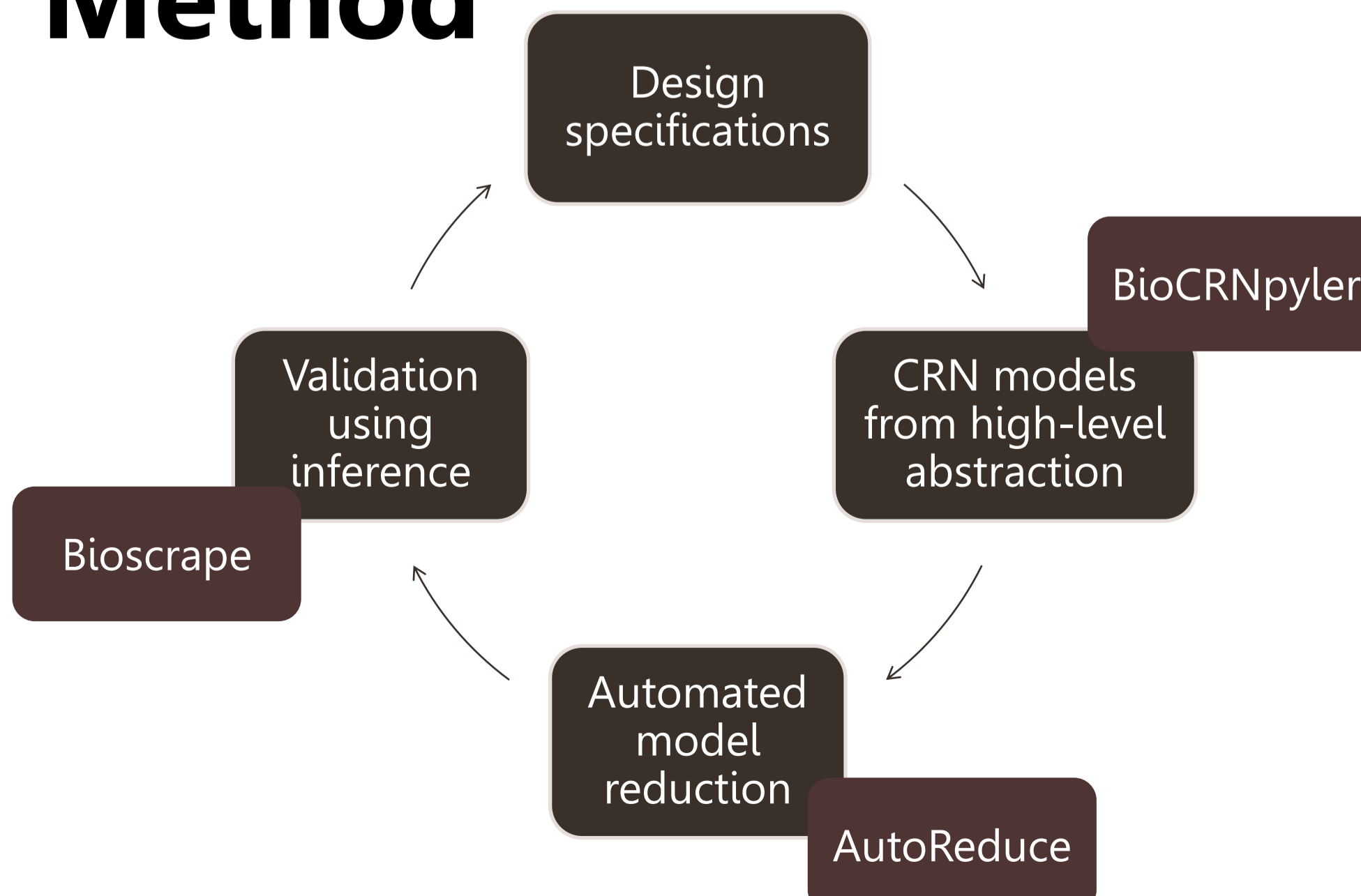
The Problem

- Abstractions of engineered biological circuit models are often arbitrarily chosen.
- Design specifications and implementation models are not always consistent.
- An automated, easy-to-use pipeline to explore biological circuit designs starting from high-level abstractions - to appropriate ODEs for parameter inference does not exist.

Objective

Develop an iterative Python pipeline to model, analyze, and validate a biological circuit design.

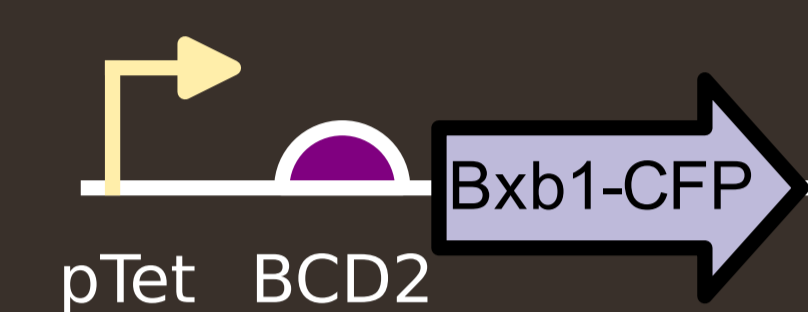
Method



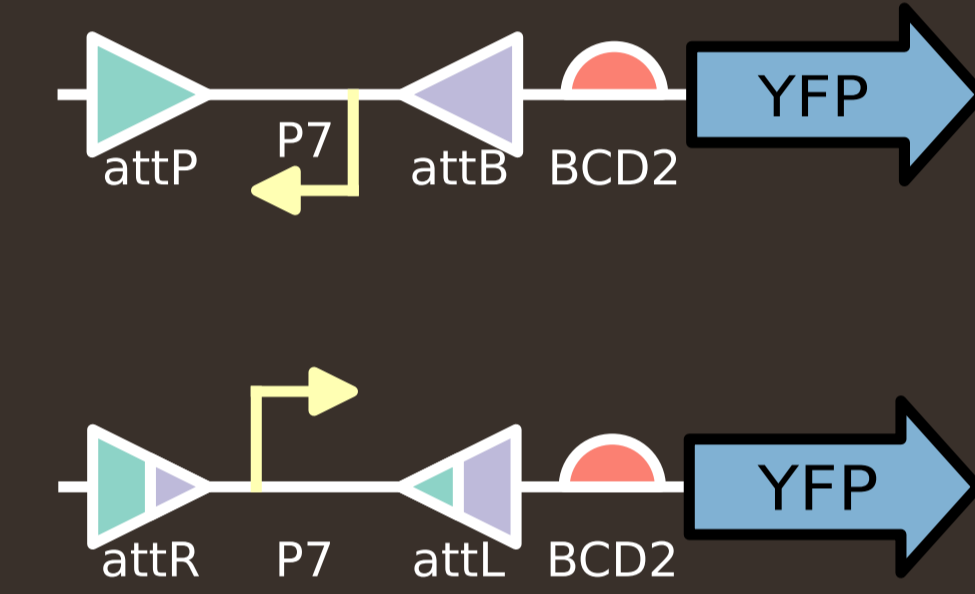
Illustrating the Python pipeline for Integrases in TX-TL

1 Circuit Design

Integrase expression in TX-TL activates YFP expression but shows loading effects.

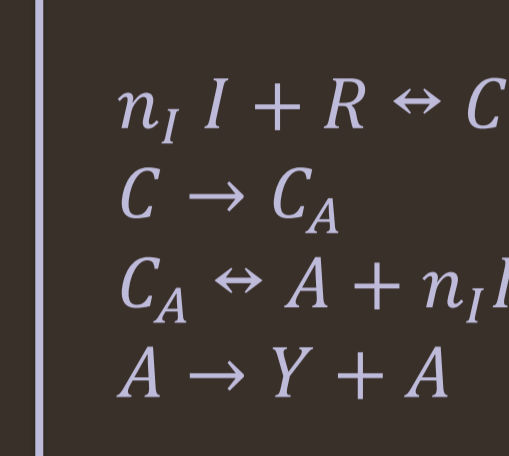


Our iterative Python pipeline elucidates these effects.



2 Mathematical Modeling

Context-Free (Iteration 1)

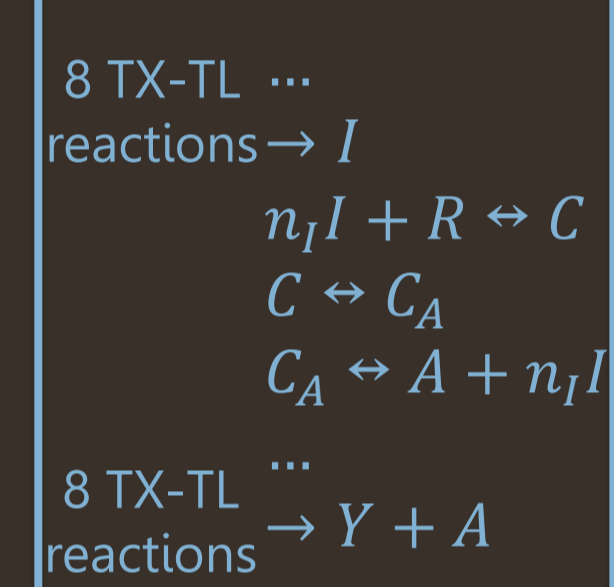


Simplified ODE

$$\begin{aligned}
 \frac{dCFP}{dt} &= k \frac{I^n}{I^n + K^n} \\
 \frac{dYFP}{dt} &= k_Y A
 \end{aligned}$$

Parameter Inference

TX-TL Resources (Iteration 2)



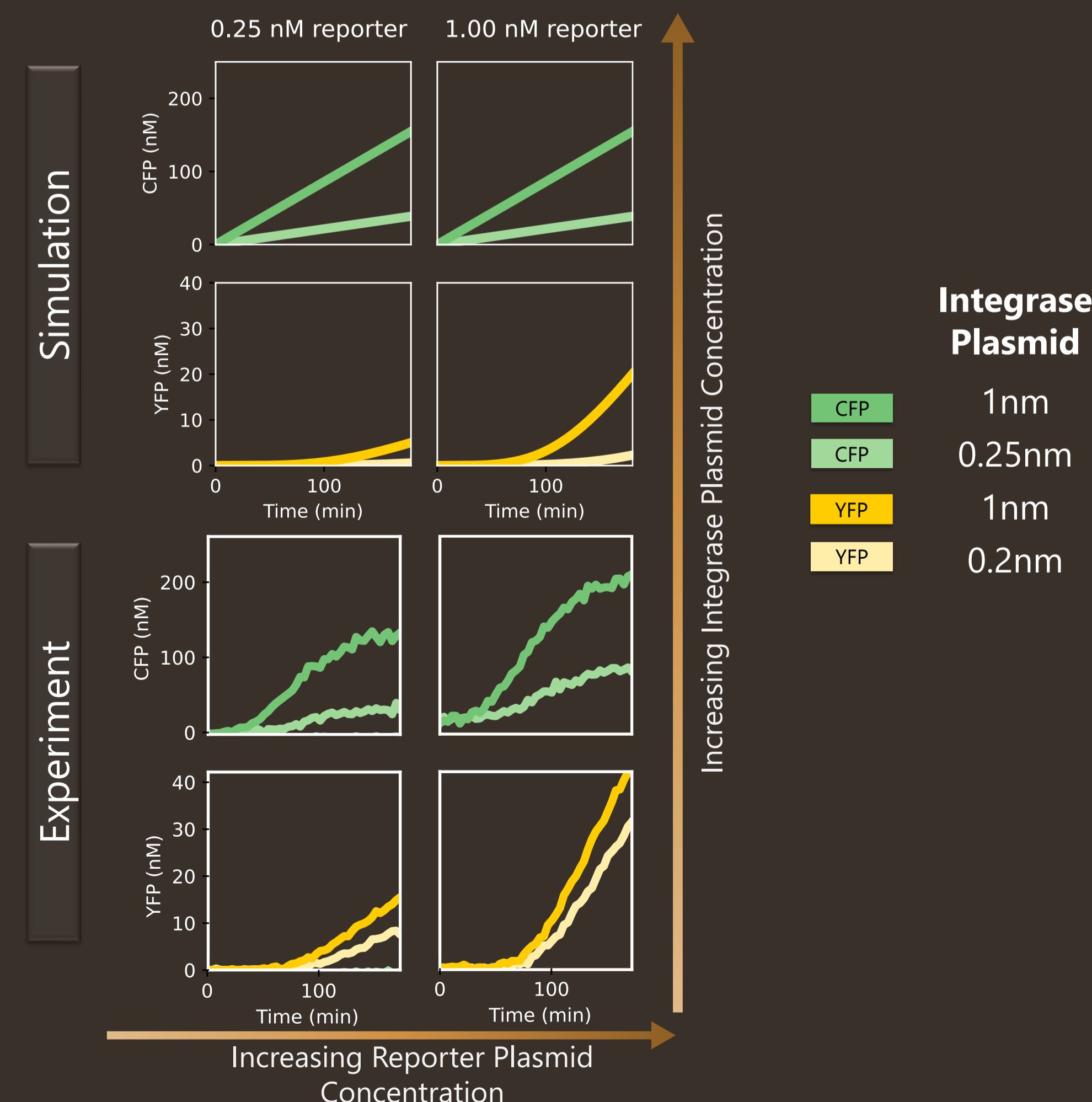
Reduced ODE

8 variable nonlinear ODE

mRNA₁, Ribosome, Integrase-CFP, DNA, mRNA₂, YFP, C_{P1}, C_{R1}

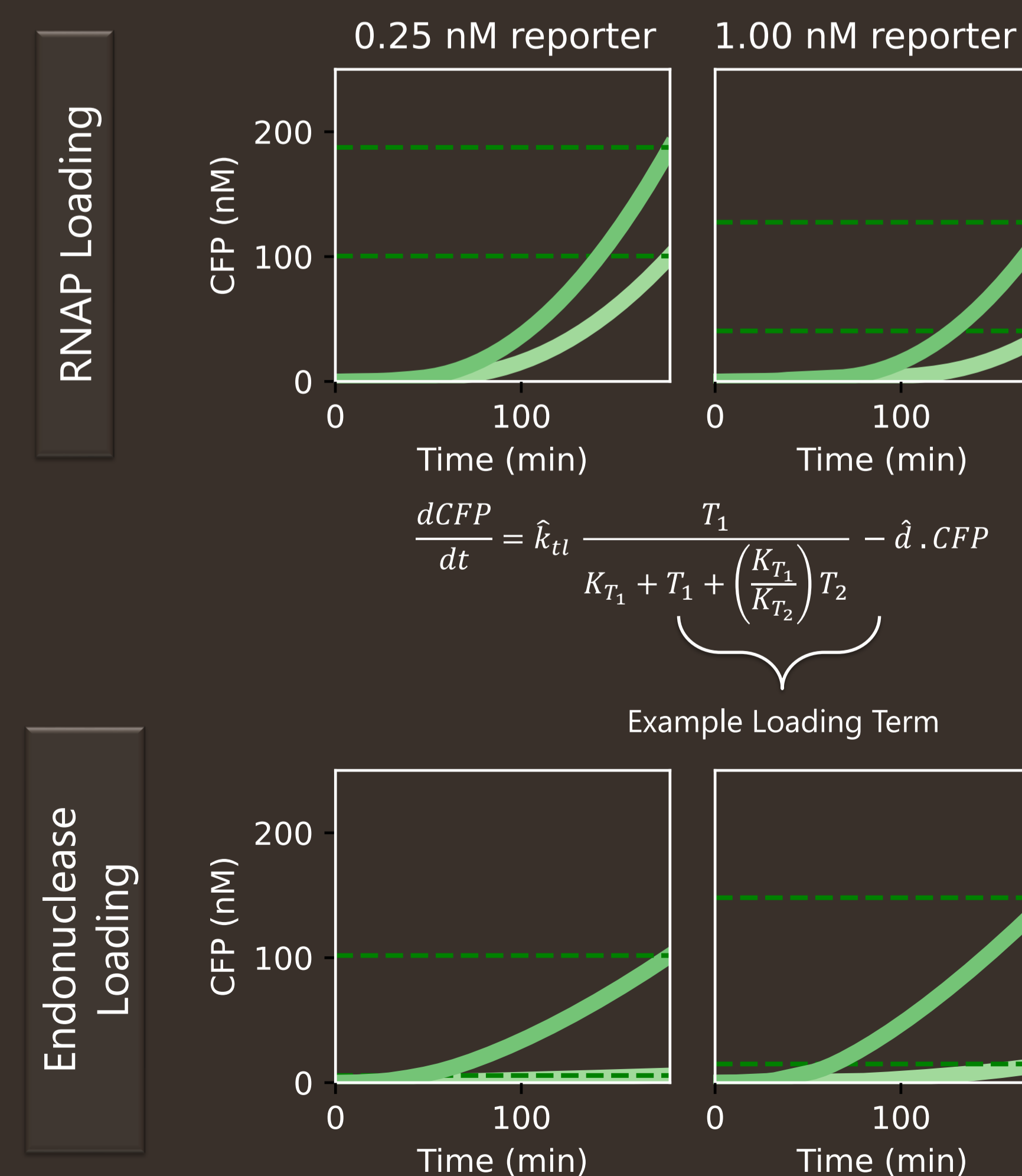
3 Parameter Inference

Iteration 1: Simplified model and experimental data



4 Design Space Exploration

Iteration 2: With RNA polymerase, ribosome, and endonucleases



Conclusion

We present a Python pipeline for the design, analysis, and validation of biological circuits using three open-source software tools:

- **BioCRNpyler**: Build CRN models in diverse contexts.
- **AutoReduce**: Automated dimensionality reduction.
- **Bioscrape**: Simulate and validate.

Further Info



BuildACell:
 BioCRNpyler AutoReduce
 Bioscrape



BioCRNpyler: Compiling Chemical Reaction Networks from Biomolecular Parts in Diverse Contexts
 William Poole, Ayush Pandey, Andrey Shur, Zoltan A. Tuza, Richard M. Murray
 PLoS Computational Biology, 2022

Robustness guarantees for structured model reduction of dynamical systems with applications to biomolecular models
 Ayush Pandey and Richard M. Murray
 International Journal of Robust and Nonlinear Control, 2022

Acknowledgments

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