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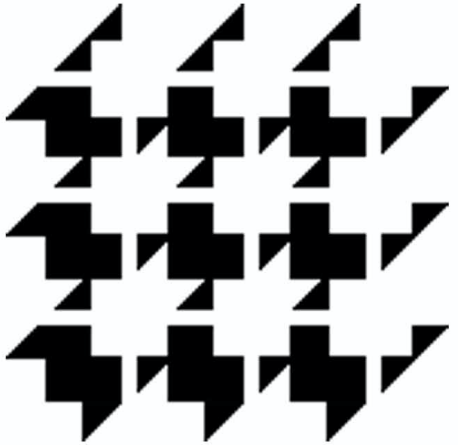

Analyzing gene regulatory networks by comparing the dynamics obtained via DSGRN (Dynamic Signatures Generated by Regulatory Networks) and RACIPE (Random Circuit Perturbation)

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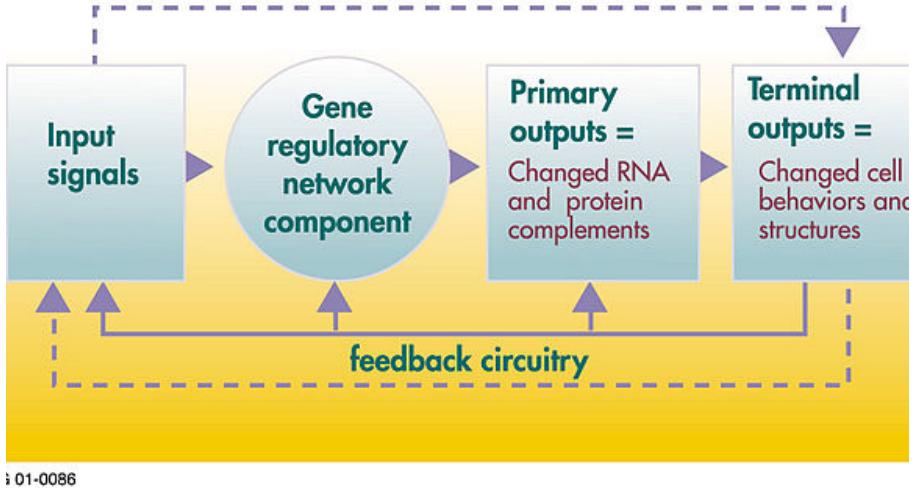
Abstract/Project Description

In this research project, we are studying the analyses generated by Huang et al. using random circuit perturbation (RACIPE). After gaining a comprehensive understanding of Huang's paper, we will attempt to use RACIPE to reproduce these results. We will move from there to produce analogous results in DSGRN. After both sets of results have been generated, we will compare our RACIPE results to our DSGRN results.

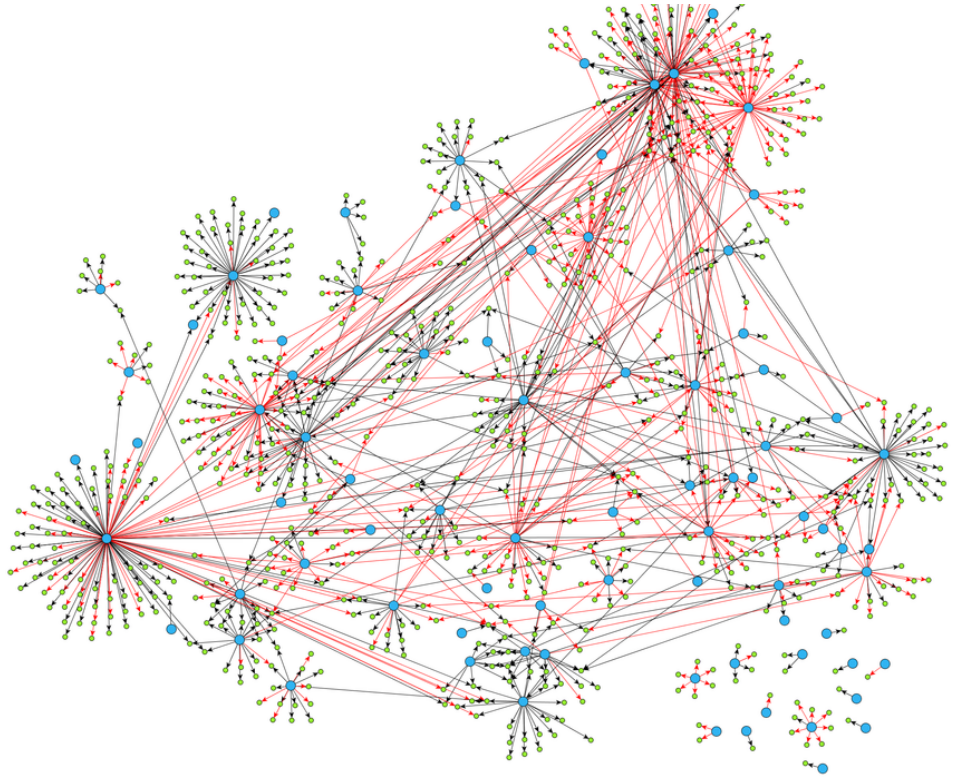
Gene Regulatory Networks



Gene Regulatory Networks (GRNs) are collections of molecular regulators that interact with each other and other substances in the cell to govern gene expression levels of mRNA and proteins.

They are often assembled into pathways and networks to be studied under the umbrellas of systems and computational biology.

Entirely understanding these networks would allow us to target diseases, namely cancer, accurately without the devastating side effects on healthy cells that mark today's drugs.



DSGRN (Dynamic Signatures Generated by Regulatory Networks)

- The current state of modeling GRNs
- Difficulty in knowing the many kinetic parameters required in popular ODE models
- People turn to Boolean models, which have serious flaws for studying GRNs
- DSGRN: computing coarse information without solving the ODE system
- ”Coarse” and invariant sets
- Gives information about the dynamics for all possible parameter values

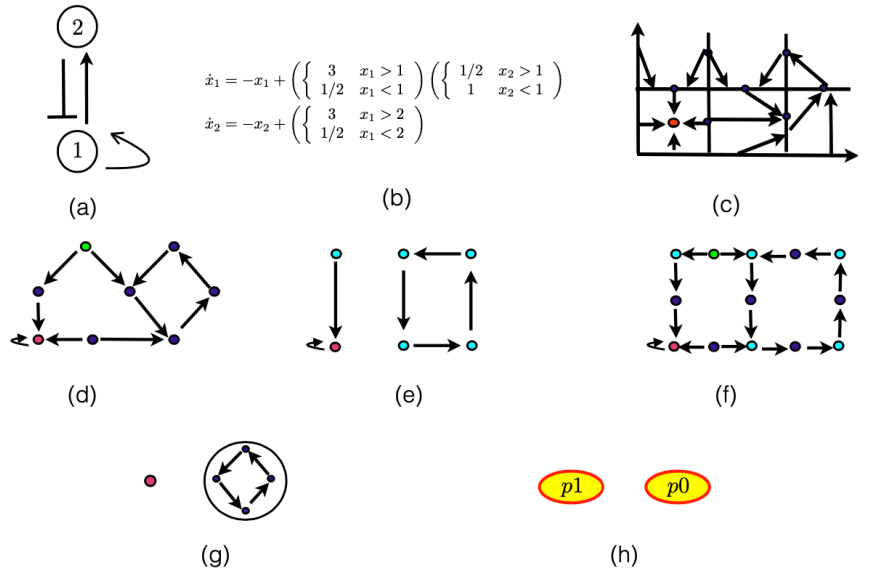
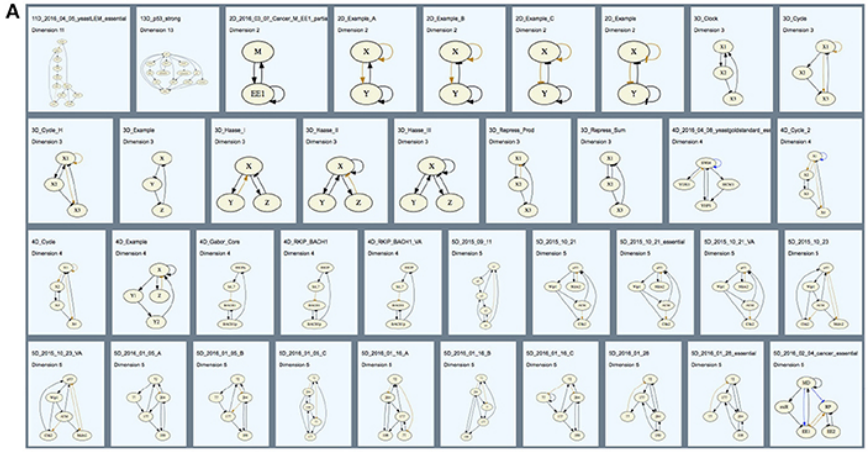
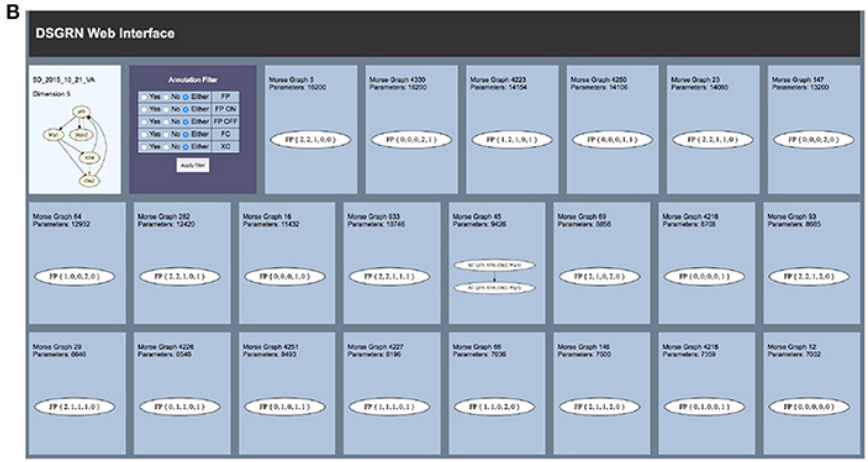
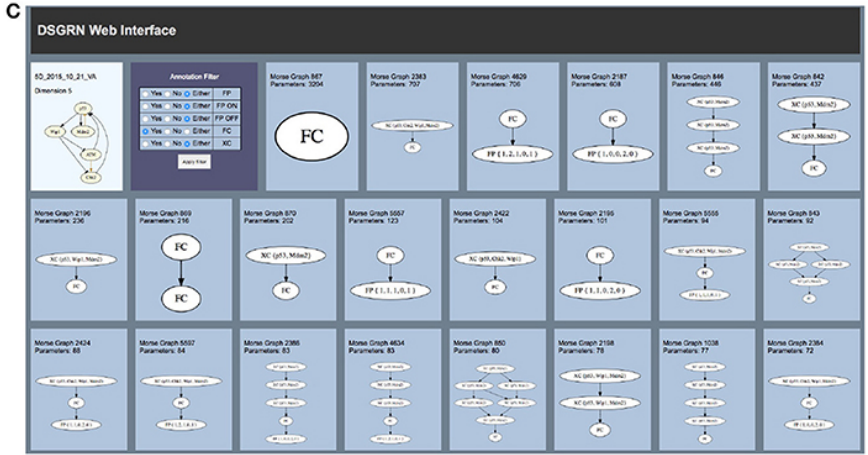


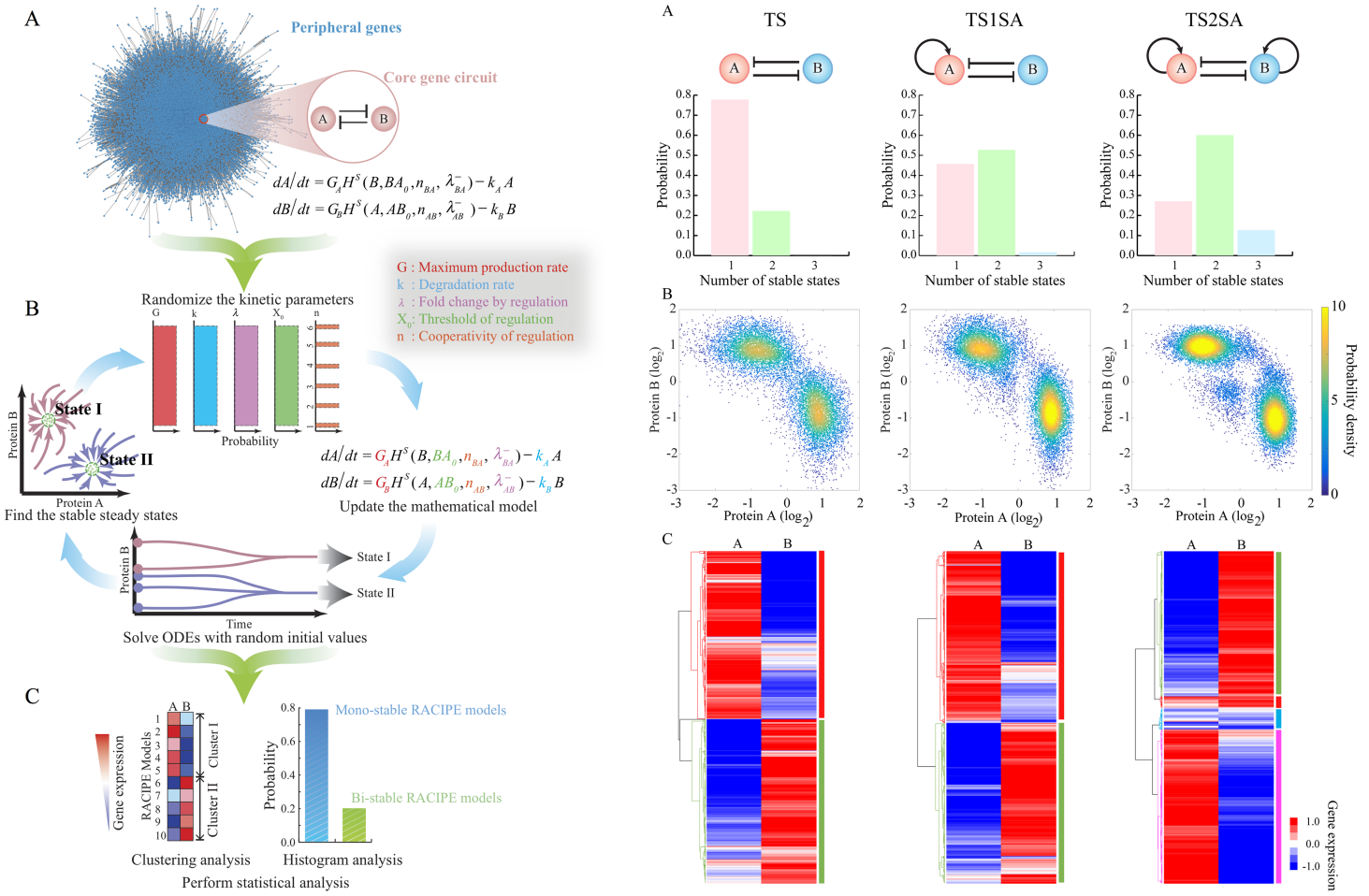
Figure 1. (a) *Regulatory network* **RN**; (b) *a set of equations with a particular choice of parameters for* **RN**; (c) *phase space;* (d) *wall graph;* (e) *domain graph;* (f) *wall-domain graph;* (g) *a set of strongly connected components of the wall, domain, or wall-domain graph;* (h) *Morse graph representing strongly connected components.*







RACIPE (*ra*ndom *ci*rcuit *pe*rturbation)



- Core gene regulatory circuitry
- Without detailed kinetic parameters
- Many random kinetic models all from a fixed circuit topology
- Statistical analysis employed to determine robust dynamical properties
- Topology, not parameters

Huang, B., Lu, M., Jia, D., Ben-Jacob, E., Levine, H., & Onuchic, J. N. (2017). Interrogating the topological robustness of gene regulatory circuits by randomization. PLOS Comput Biol, 13(3), e1005456–21. http://doi.org/10.1371/journal.pcbi.1005456

Future Work

The results of the comparisons between our RACIPE and DSGRN results could potentially lead to a paper describing the results and could also lead to additional problems that could be studied during the research project or afterwards, such as applying these ideas to networks of biological interest, understanding how to sample for large networks, understanding how to apply these ideas to a broader range of dynamics, computing volumes of the DSGRN regions of parameter space, or understanding how the regions change as a function of more realistic parameters.

Thank You for Listening!

and

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