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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RACIPE and the Half-Functional Rule

Project Progress

Over the past week, we worked on understanding the random circuit perturbation method developed by Huang et al. We did so by reading the second paper on RACIPE and the additional files for both papers. We also learned the inner workings of the half-functional rule, which is necessary for understanding how they randomly sample the thresholds. Lastly, we started reading the RACIPE code and source files (in progress).
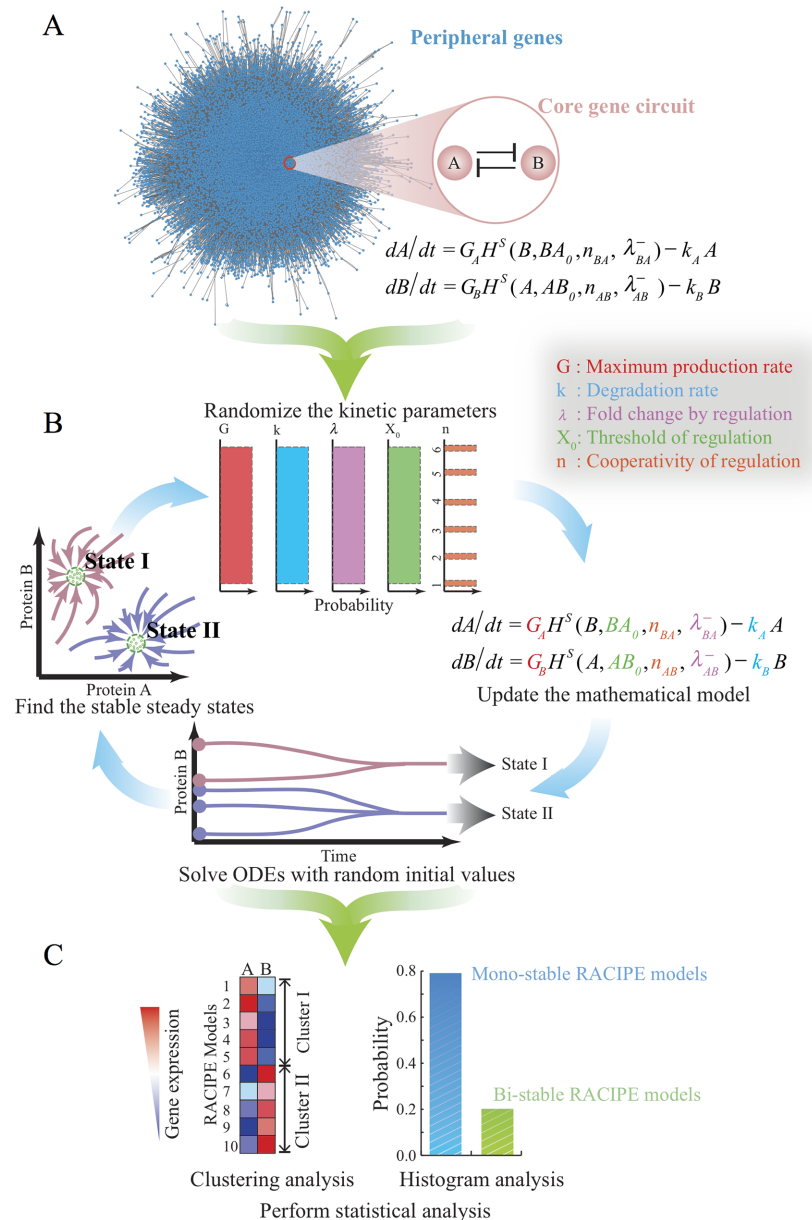
The application does the following:

- Randomizes all key parameters in set ranges, except the threshold values.

- Solve the rate equations, which are comprised of Hill functions and the parameters.

- Steady states are found, and the process is repeated.

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

A

1. An isolated gene
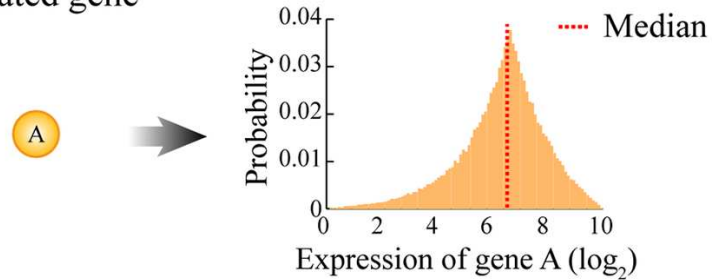
2. To find the thresholds for ourward regulations from gene A

Only consider inward regulations on A

Median of thresholds for gene A
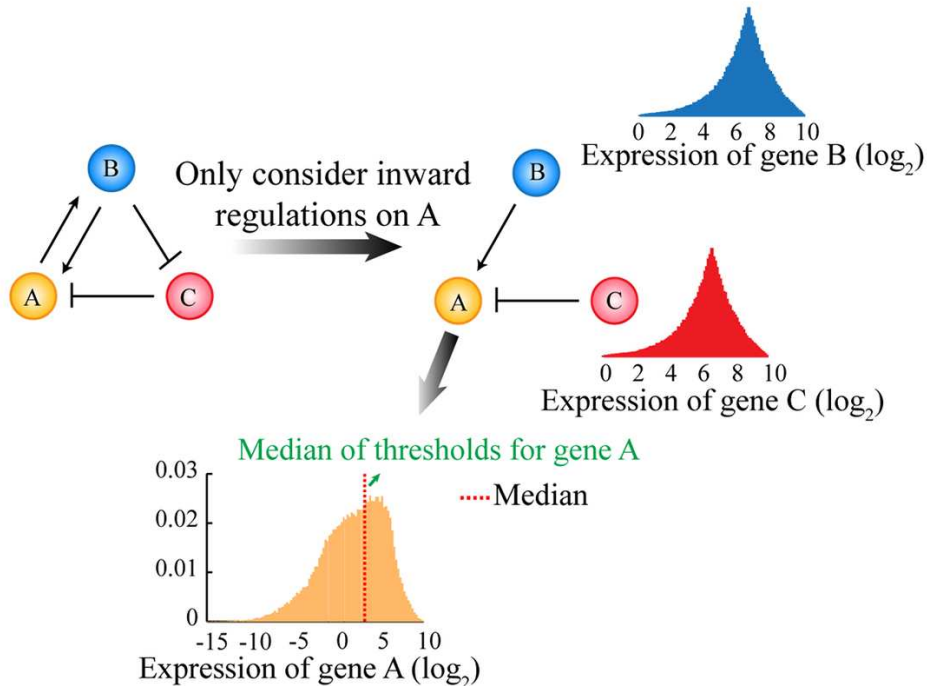
The method used to find range for the randomization of thresholds:
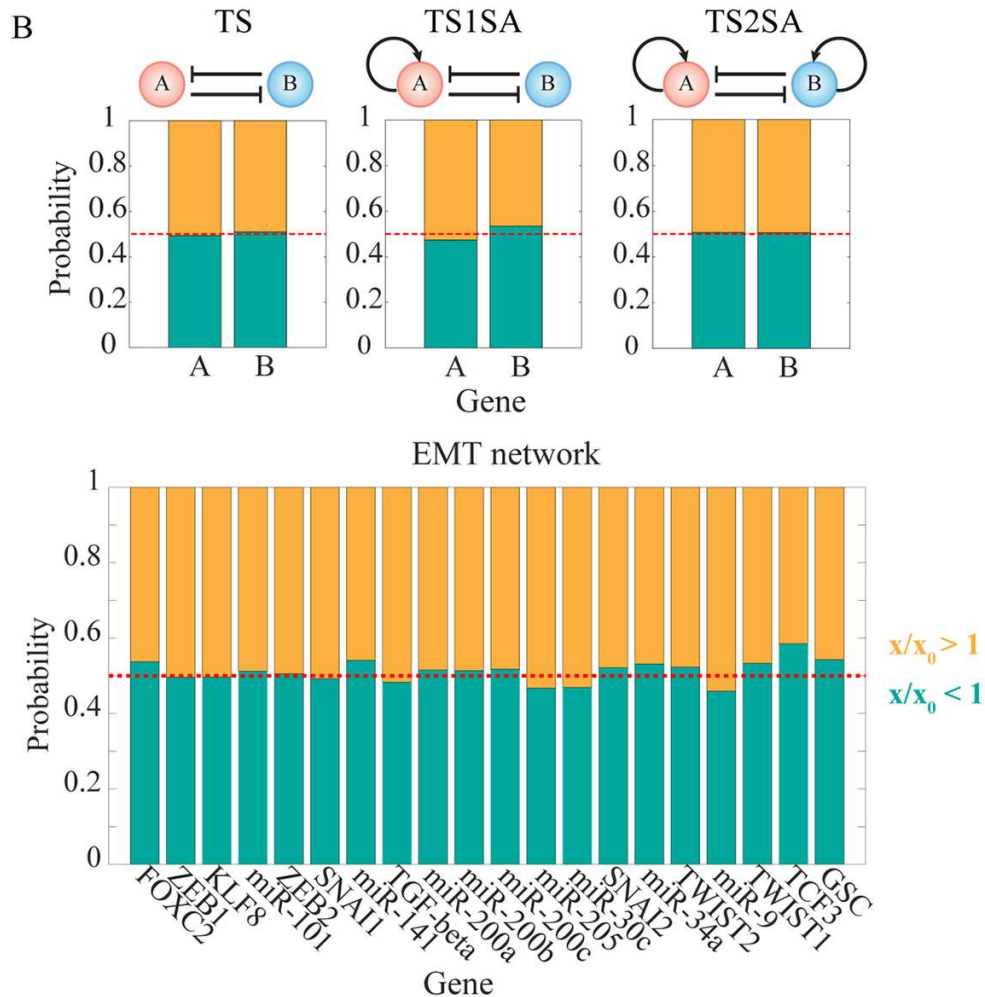
- Model the rate equation for a gene A without regulation. Then choose the median value for the threshold of that gene's expression (M).

- Now consider all the inward regulations on a gene A. Model their sources as isolated genes and multiply those results by the Hill functions for these genes, where the thresholds are chosen randomly between 0.02*M to 1.98*M.

- Find the median of these Hill-shifted distributions. The range of 0.02*M to 1.98*M is passed out of the function in which the half-functional rule is performed.

- Repeat for all other genes.

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The method used in random sampling for thresholds:

- The half-functional rule is used such that the median value chosen results in 50 of the values being below the threshold and 50% being above it. This ensures that the link is active half of the time, which allows for a good understanding of each link in the circuit.

- Here are some tests that were done by Huang et al. which show the half-functional rule being satisfied in their method. This can be inferred from the pictures where yellow region shows threshold being less than the gene expression while the opposite is true for the green region. The dotted red lines are where the gene expressions equal their thresholds.

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Next Steps

Our next steps include understanding the code of RACIPE and studying parts of the RACIPE papers that were previously less relevant to our work. This will help with reproducing their results, our next focus.

Once we are confident about RACIPE and have reproduced their toggle switch results, we will move on to DSGRN. After solving the same toggle switch problems in DSGRN, we will compare the results generated by both applications.

Thank You for Listening!

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