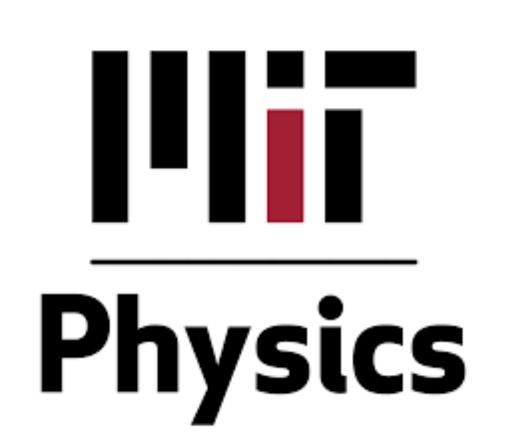


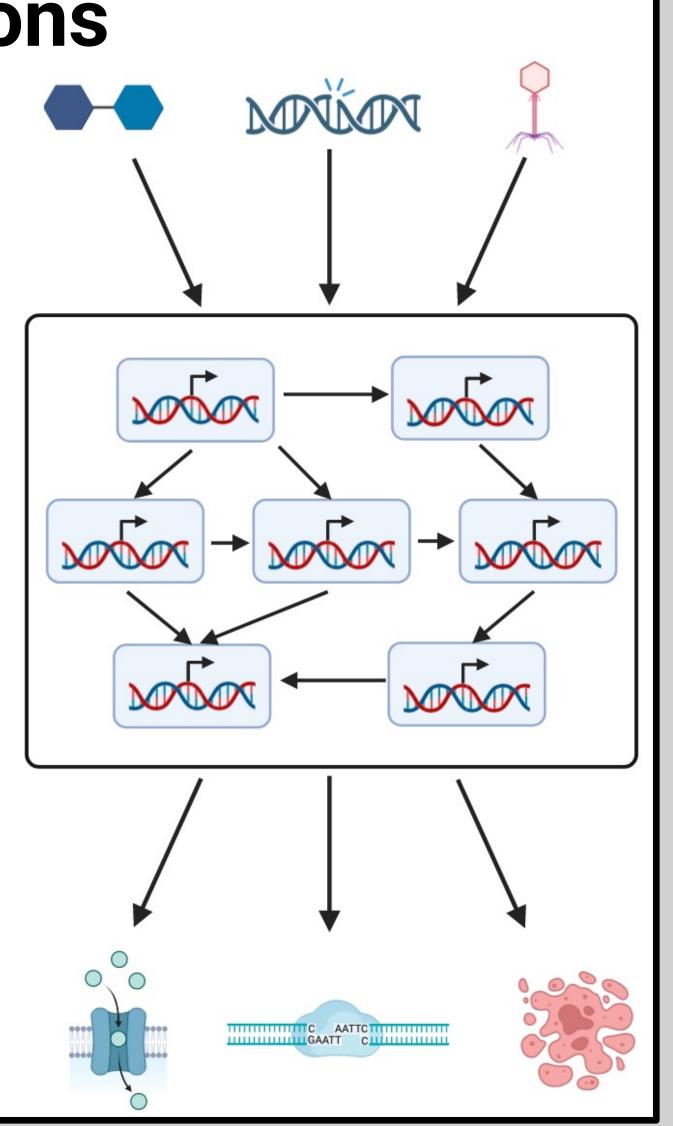
Clusters and Loops are Overly Abundant in Oscillatory Gene Regulatory Networks



Chris Viets, Hamza Çoban, Ron Weiss

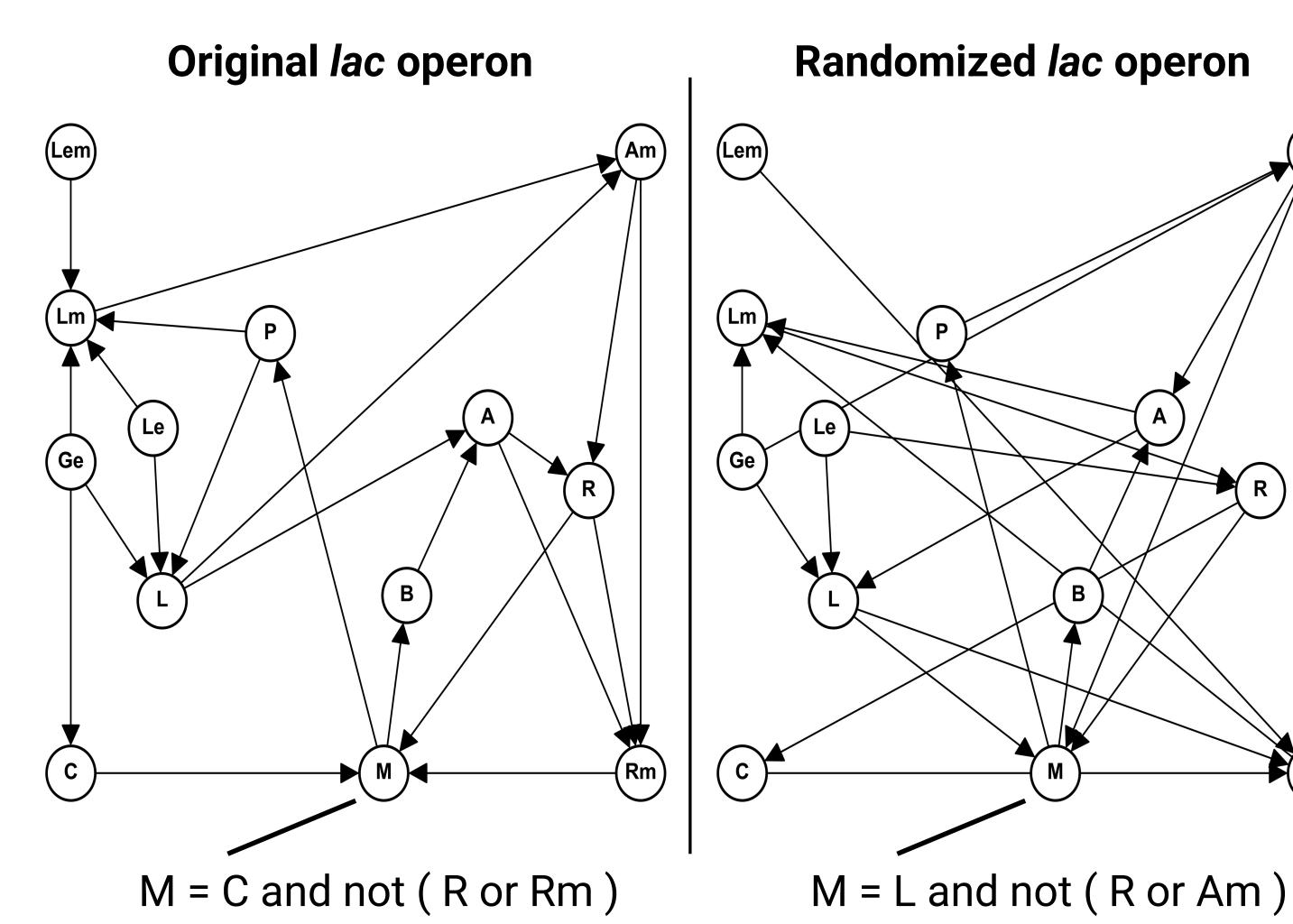
Motivation and Questions

- Gene regulatory networks (GRNs) allow cells to respond to environmental signals.
- GRNs can be modeled as Boolean networks with a logic function governing each node.
- Simplistic model makes complex systems computationally tractable.
- Objective: compare Boolean GRN models to null models with equivalent properties.
- To what extent does topology contribute to network stability?
- Which topological features best account for network stability?

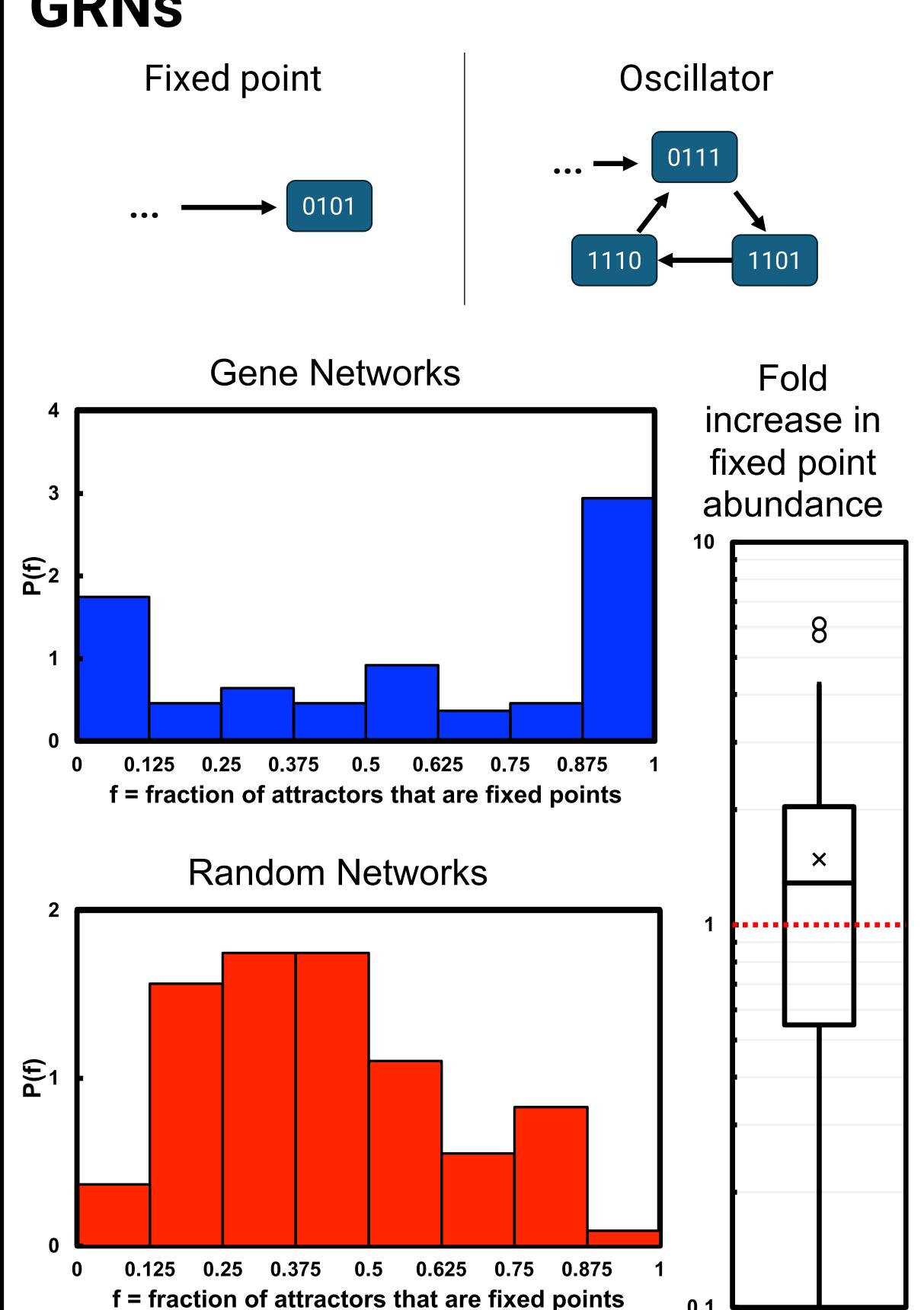


Methods

- 87 GRN models were obtained from CellCollective database [1].
- Random networks were generated such that indegrees, out-degrees, and logic functions were preserved at each node.
- Stability analysis averaged results from 100 random networks with 1000 initial conditions on each. Cluster and loop analyses averaged results over 1000 random networks.

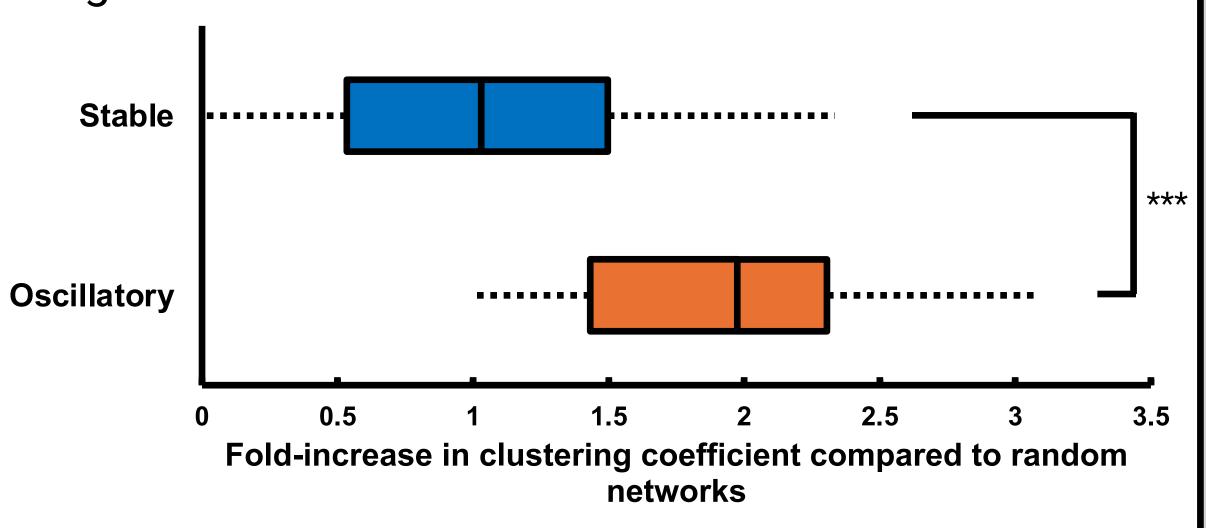


Fixed points are abundant in **GRNs**

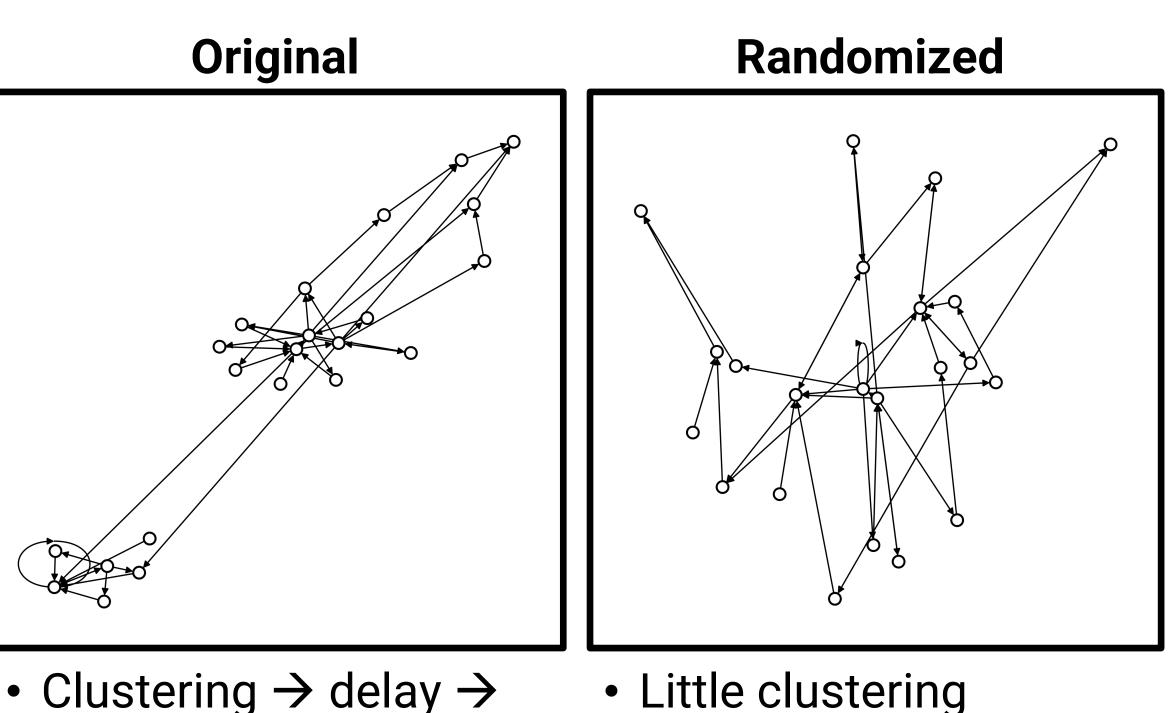


Clusters are overrepresented in oscillatory GRNs

Local clustering coefficient = cliquishness of node's neighbors



Example: fungus iron acquisition GRN uses clustering to maintain cell survival

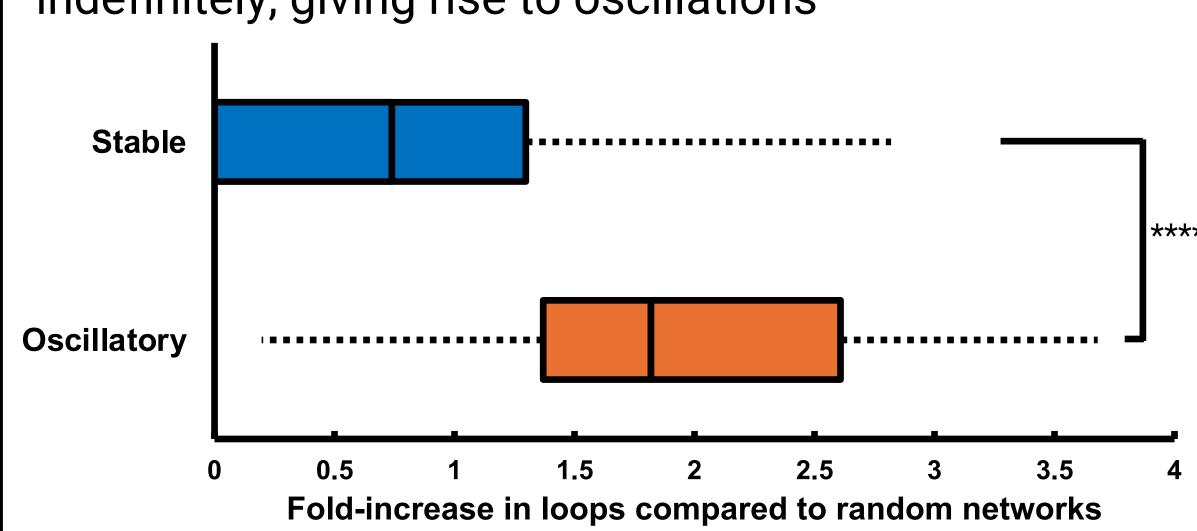


- oscillation
- Pulsatile response
- Cell survival in host

- Little clustering
- Static response
- Cell death by reactive oxygen species

Loop frequency decreases in stable GRNs

Loops allow signal to continue propagating indefinitely, giving rise to oscillations



Potential Applications

- Systems Biology: Predict cell behaviors from GRNs without needing to know the nature of any genegene interactions.
- Synthetic biology: Use network topology to design cell circuits with pulsatile or static responses.
- **Biomedicine:** GRN topologies reveal potential genetic targets for effective disease therapies.

[1] Helikar, T., Kowal, B., McClenathan, S. *et al*. The Cell Collective: Toward an open and collaborative approach to systems biology. BMC Syst Biol 6, 96 (2012).