

Questions

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1 Landscape of epithelial–mesenchymal plasticity as an emergent property of coordinated teams in regulatory networks

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2 Low dimensionality of phenotypic space as an emergent property of coordinated teams in biological regulatory networks

- It remains elusive whether teams can drive low dimensional dynamics of such networks? What does this mean really? How can teams drive the low dimensional phenotypic
- Recently, tripathy et al showed most of the variance in phenotypic switching is often what regulatory networks underlying binary cell fate decision systems including those of EMT operate along.
- Are number of edges and nodes a factor in this? Are the networks which were looked into all biological? Can we create hypothetical networks which satisfy the teams model of mutual activation and large scale inhibition and see if number of edges and nodes are a factor?
- Dimension reduction by teams
It is very intuitive that teams makes the landscape bimodal but it also reduces the dimension of it? What does it mean? Can a bimodal landscape be of a higher dimension?
- How is team strength defined?
- What does it mean to change the kinetic parameters.
- How is a network defined? You consider n number of edges and nodes and connect them in a certain manner taking care of the fact if they're activating or deactivating. Now to randomize this network we change one edge at a time and perform RACIPE on it and measure stable states. Therefore in this method, the identity of network is changed by changing connections one edge at a time.
Alternatively if RACIPE conserves activating/deactivating nature of the network which it probably should then the number of activating and deactivating nodes are an identity of the network
What does boolean perturbations conserve and change?
- What causes hybrid states to cluster and not cluster? What dictates if there is a continuum of possible hybrid states between the extremes. If there isn't a continuum then how could we possibly determine the number of hybrid states possible?
- Teams try to maintain one phenotype. How does EMT occur? Also consider a stem cell, teams explains how we have just two phenotypes but how is team set into action? I.e we know that once we have teams we'll have two phenotypes but how do we form teams in the first place?
- “In developmental contexts, the property of canalization is frequently observed, where cellular phenotypes are sensitive only to a small set of specific perturbations”
What does this mean?

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- Network randomization: Edge type is swapped between two nodes (activation to inhibition and vice versa) Why? Could swapping be considered between two nodes which aren't connected

3 Landscape of epithelial-mesenchymal plasticity as an emergent property of coordinated teams in regulatory networks

- The goal is to predict phenotypes based on team strength and not relying on simulations. Team strength seems to take care of only the boolean connections so does this mean the rates and stuff doesn't matter? And it's only the network topology which gives the network its characteristics
- **Def: Steady State Frequency (SSF)** Fraction of initial conditions that converge to this given steady state.
- **Def: Coherence** This is about local stability of steady state. Can be estimated by fraction of "neighbouring" states that converge to the steady state. The calculation follows perturbation procedure. One node is perturbed at a time -> active -> inactive and vice versa. Is the node flipped back?. The number of times the original steady state is returned after such perturbations gives coherence .
- Minimum SSF is not consistent the same way as maximum SSF (wild type networks >)
- **Def: Frustration:** When two nodes are connected via two contradictory edges. Eg A and B have an activating and one inhibiting link in between them. This paper defines frustration to be the case where the network's stable state has a different configuration than the connection which might mean the previous thing that is overall the network makes the connection as per steady state but there are inhibitory links which destabilize the steady state configuration.
- Bimodality coefficient of frustration?
- Coming up with algorithms to test network stability in a certain direction.
- The paper defines something called strength on page 8. What is it really? and following that there's some analysis about team strength and some correlation matrices. I do not understand that part.

4 Emergent Properties of coupled bistable switches

- Preliminary reading indicates that this paper investigates how can elementary network motifs be joined together and result in larger motifs. What I now wonder is could this joining of motifs resulting in bigger motifs result in a bigger network. Assume an undifferentiated cell clearly it doesn't have a bistable network motif as of them but eventually it gets one and assuming it is due to a network like what we're studying then it must've been set into action and come into existence. How? could it be possibly due to a cascade of joining of networks?