

## Generating a biologically plausible ensemble

- A. Network structure  
(with signs of interactions)
- B. Expression states in cell types  
(fixed point attractors)

Constrain the truth tables with desired biological fixed points

Constrain the truth tables with biologically meaningful Boolean functions that conform to the signs of the interactions

Generate the lists of allowed Boolean functions at each node

## Modeling choices

1. 

Is a Boolean model available?

Yes → Does the model satisfy all expected hierarchies?

No → Model selection algorithm

Relative stability measures

BOA, MFPT, SSP, BTR, SIND

Exact, Stochastic (set noise intensity to 5%, set trajectories to 2500)

Model selection approach

Exhaustive search, Greedy search

4. Partial or complete information about the expected biological landscape as inequalities

5. Set threshold : Minimum fraction of state space to be occupied by the basins of biological attractors (In this work, threshold = 0.87)

## Model selection algorithm

Initialize with the given Boolean model or a random model from the ensemble that does not satisfy all expected hierarchies

Apply greedy search

A new Boolean model is obtained

Is the fraction of basin sizes occupied by all biological attractors  $\geq$  threshold?

Does the model satisfy all expected hierarchies?

Terminate search

An alternative model is obtained which satisfies the expected landscape