Canalising strength of a node in emt networks

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Canalizing strength of a node

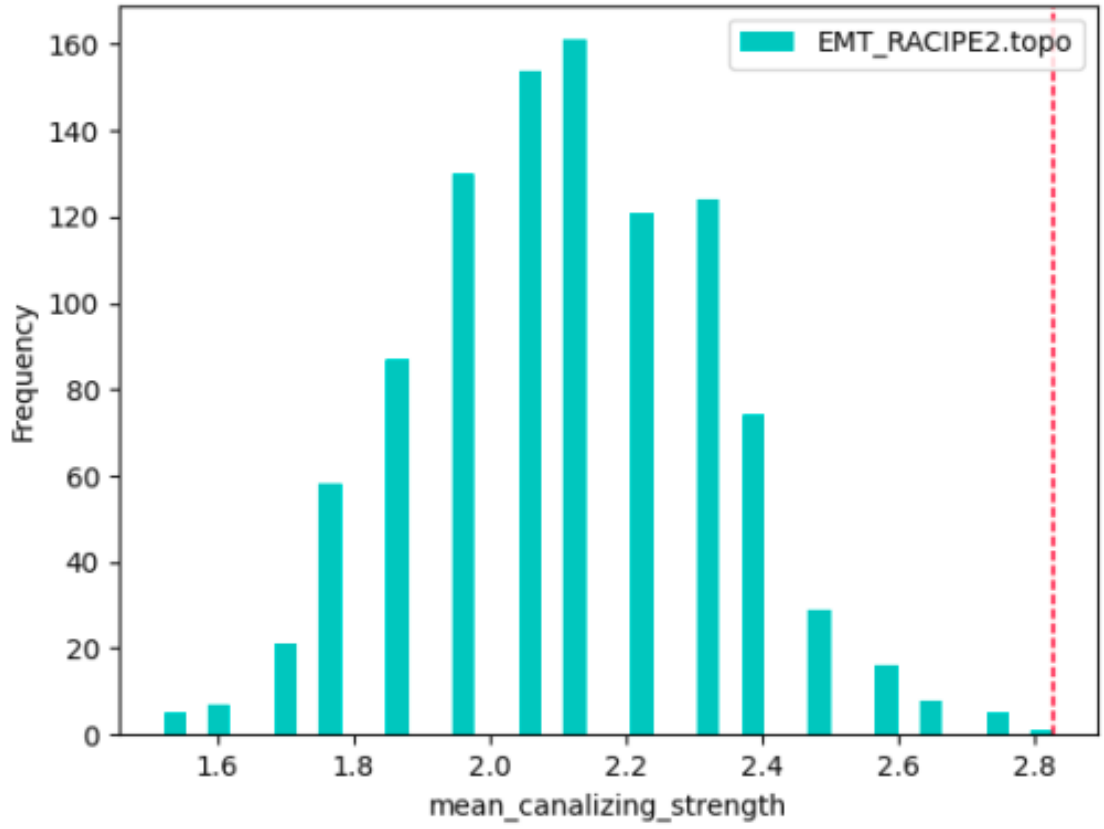
We define a metric called canalizing strength of a node as

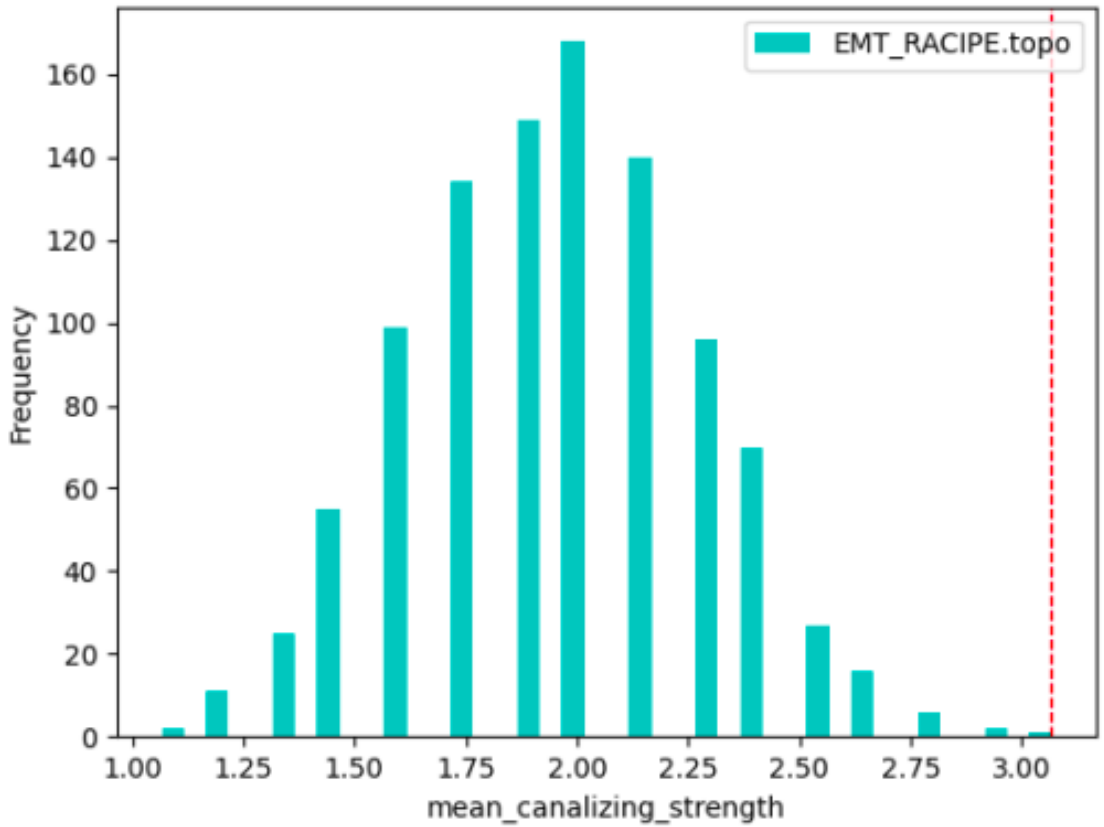
$$|\mu_{excitatory} - \mu_{inhibitory}|$$

It is the absolute difference in the number of excitatory and inhibitory outgoing connections of a node. Nodes which have more outgoing edges of a similar nature acts uniformly on other nodes compared to nodes having edges of different natures, such nodes can have more number of outcomes for an input.

EMT networks have high mean canalizing value

Upon random swapping of edges (10 at a time) so that the in and out degree of a node is constant, it was found that the wild type network has higher mean than most random networks.


EMT_RACIPE2.topo
Frequency
0
20
40
60
80
100
120
140
160
1.6
1.8
2.0
2.2
2.4
2.6
2.8
mean_canalizing_strength


EMT_RACIPE.topo
Frequency
0
20
40
60
80
100
120
140
160
1.00
1.25
1.50
1.75
2.00
2.25
2.50
2.75
3.00
mean_canalizing_strength

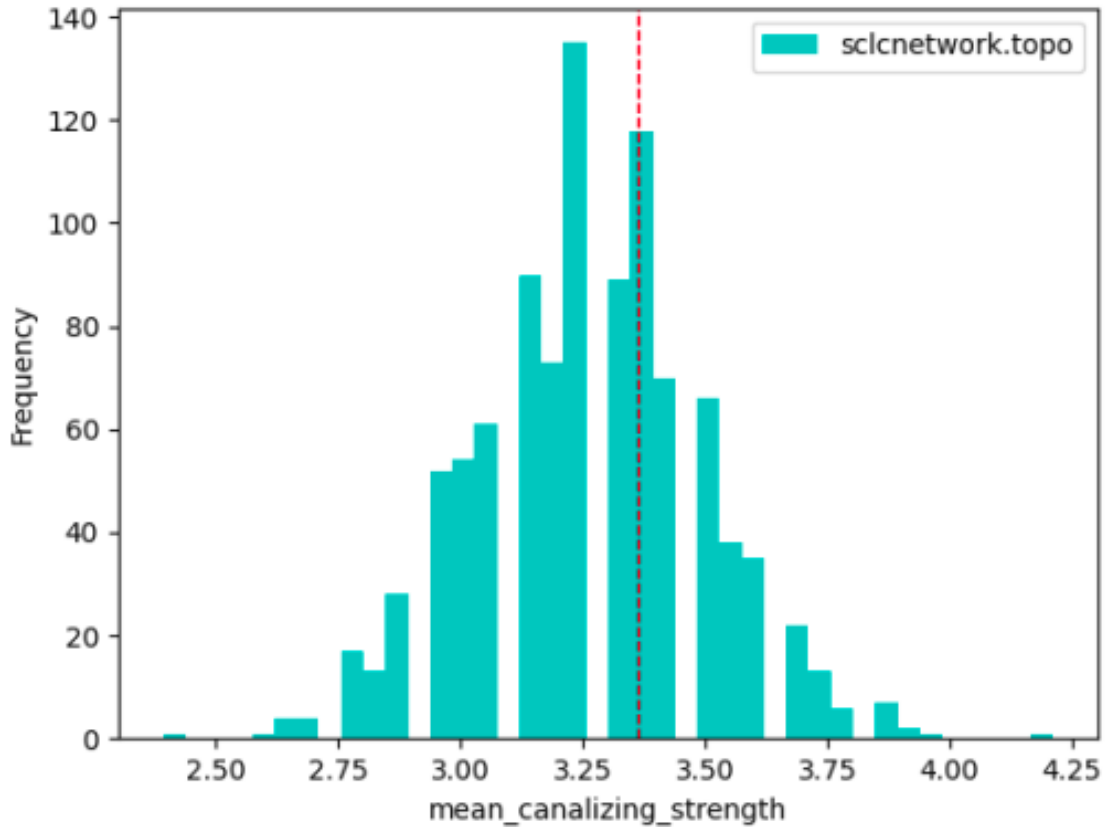
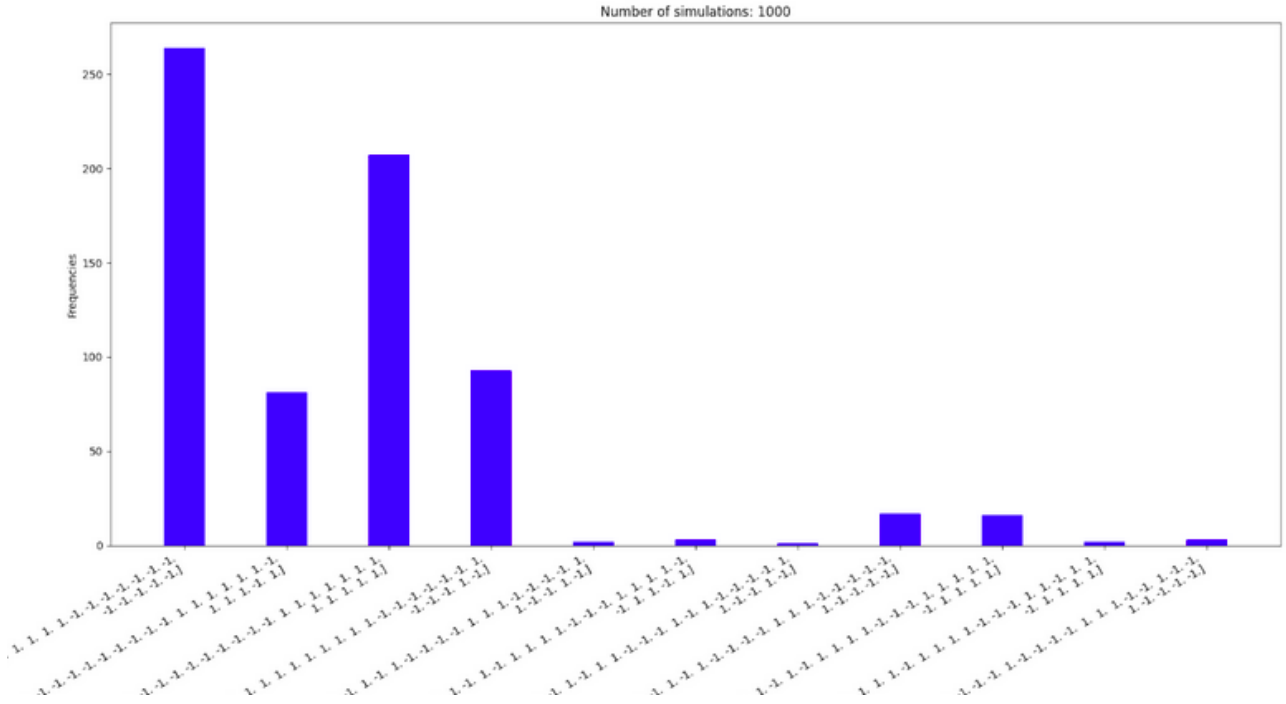


Figure: sclcnetwork

Knockout Of Nodes

Since in the networks concerned there aren't many nodes, node knockout analysis did not allow for elimination of several confounding factors like high indegree etc. No consistent results were obtained on node knockout

Steady states without any node knockout



Steady states after knockout of a node with canalising value 3

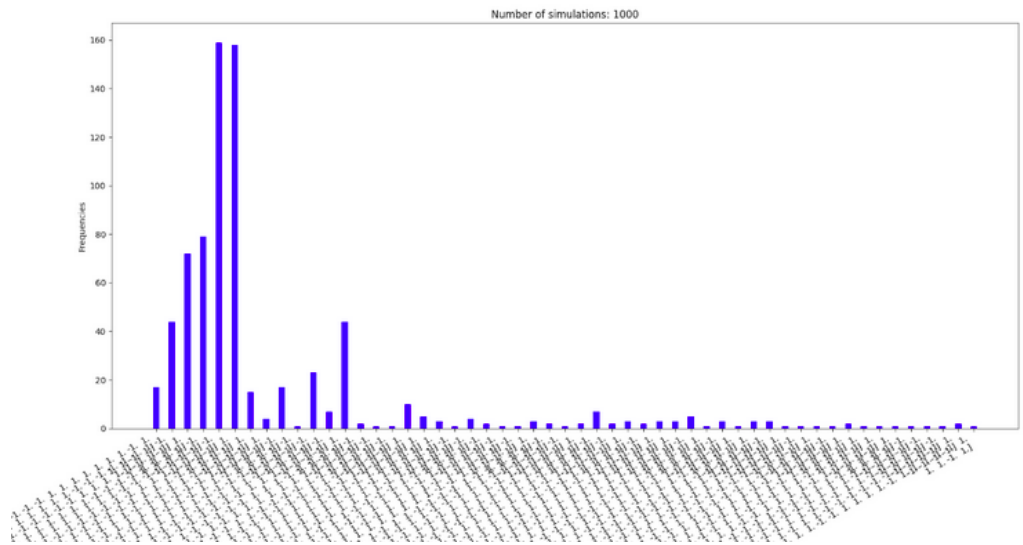


Figure: Destabilizing

Steady states after knockout of a different node with canalising value 3

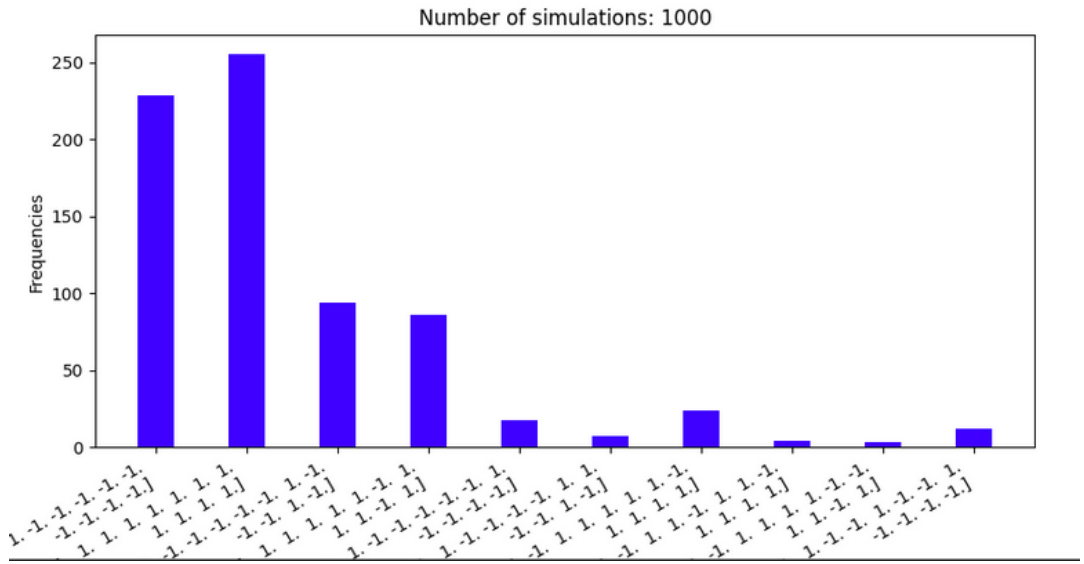


Figure: Stabilizing

Boolean Formalism

The rules of boolean formalims are as follows.

$S_j = 1$ if $\sum_i adj[i][j] * S_i > 0$

$S_j = -1$ if $\sum_i adj[i][j] * S_i < 0$

$S_j = S_j$ if $\sum_i adj[i][j] * S_i = 0$

In the case where the above sum is 0 we let the node have whatever state it had before and be somewhat 'unregulated'

Steady states using boolean formalism

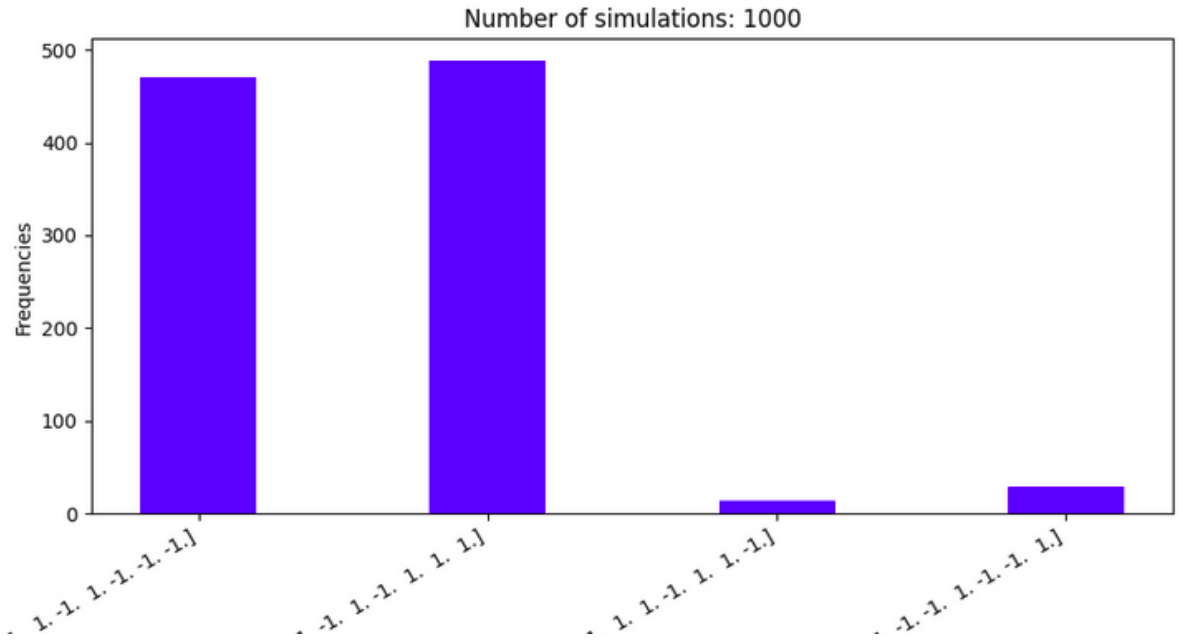


Figure: EMT Network 15 nodes

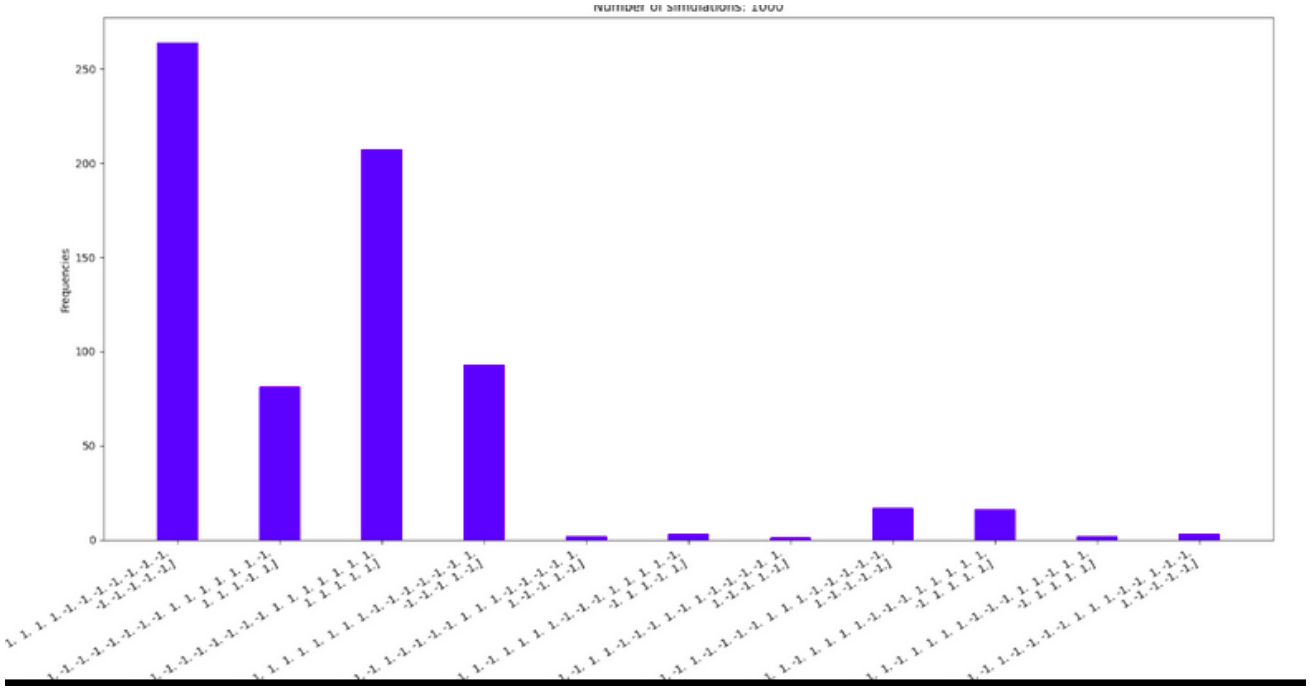


Figure: EMT Network 23 nodes

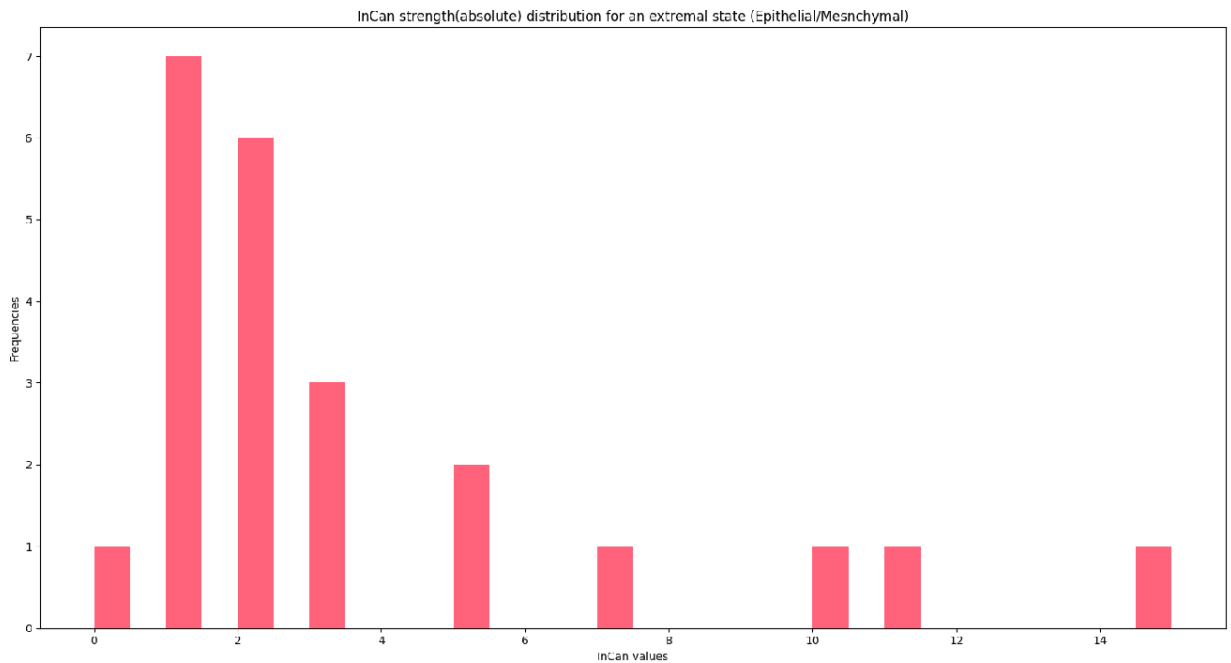
Dynamic InCanalising Strength

It quantifies how much activating or inhibhiting regulation and node is under at a certain time step. It is defined as follows for the J'th node

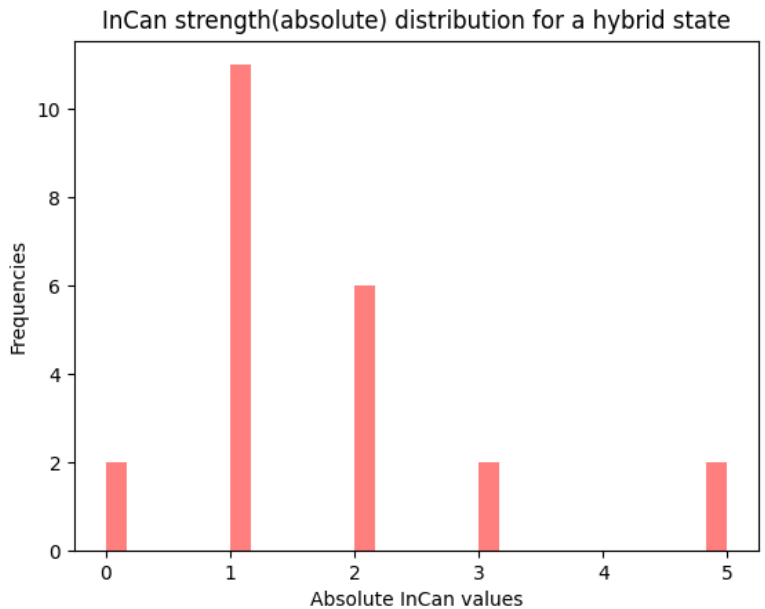
$$\sum_i adj[i][j] * S_i$$

Here, S_i denotes the state of I'th node and adj refers to the adjacency matrix of the network

Distribution of absolute InCan value for an extremal state(epithelial or mesenchymal



Hybrid States have more nodes with lesser InCan value indicating "lesser regulation"



Three State Formalism

The three state formalism with the following rules renders the node with canalising strength 0 incapable of any forward regulation and affecting the state of other nodes at each time step.

$S_j = 1$ if $\sum_i adj[i][j] * S_i > 0$

$S_j = -1$ if $\sum_i adj[i][j] * S_i < 0$

$S_j = 0$ if $\sum_i adj[i][j] * S_i = 0$

Results using three state formalism

Upon using the three state formalism which dynamically sets the expression level of the the nodes having incan strength 0 and renders them incapable of any forward regulation. We find that upon using this formalism all hybrid states dissapear in all the biological networks considered.

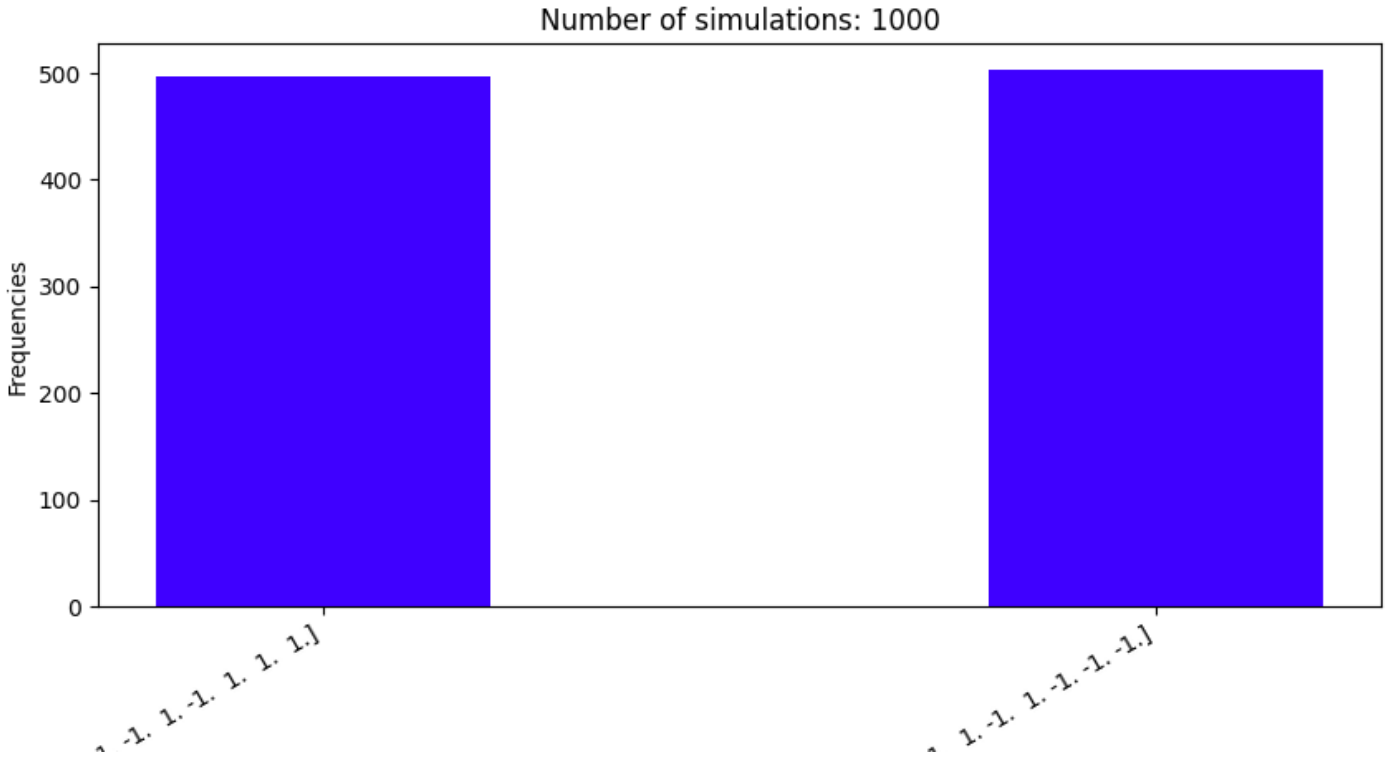


Figure: EMT network 15 nodes

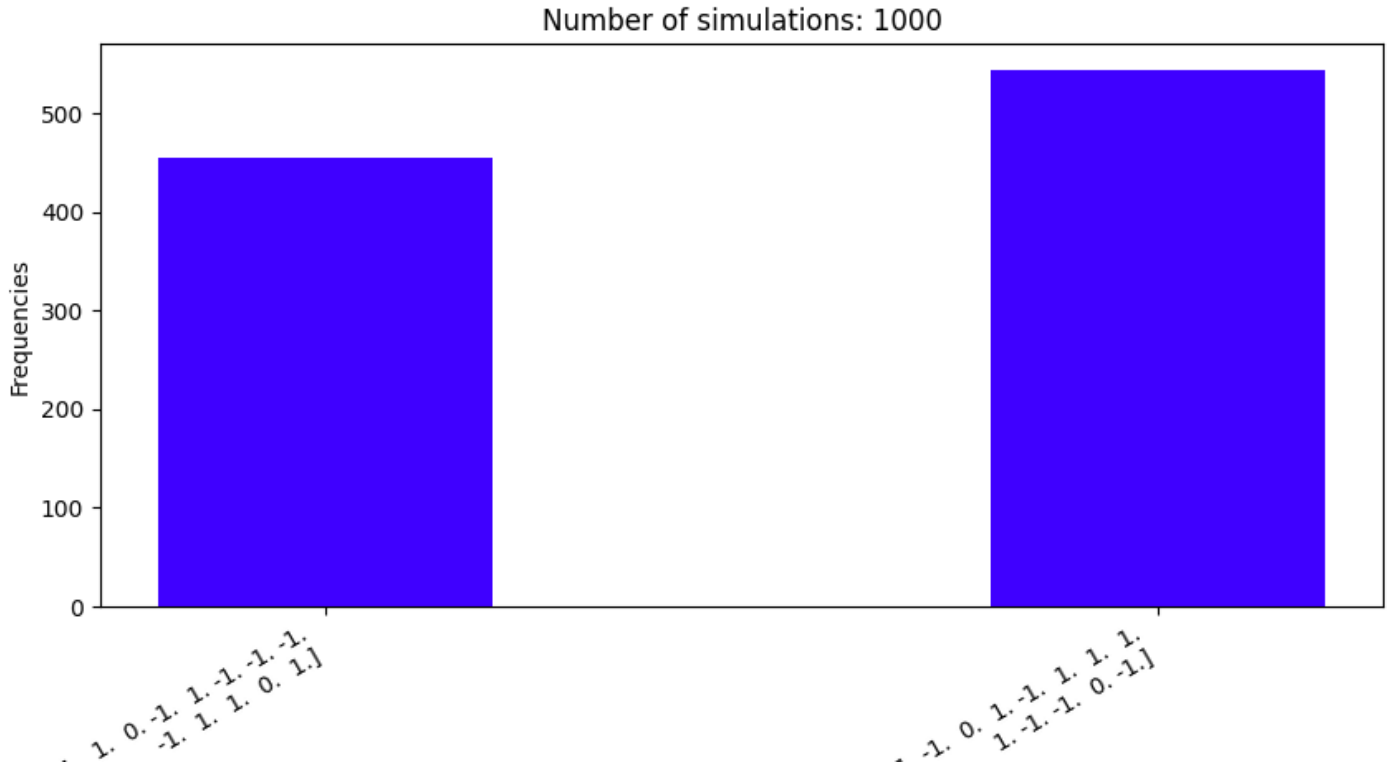


Figure: EMT network 23 nodes