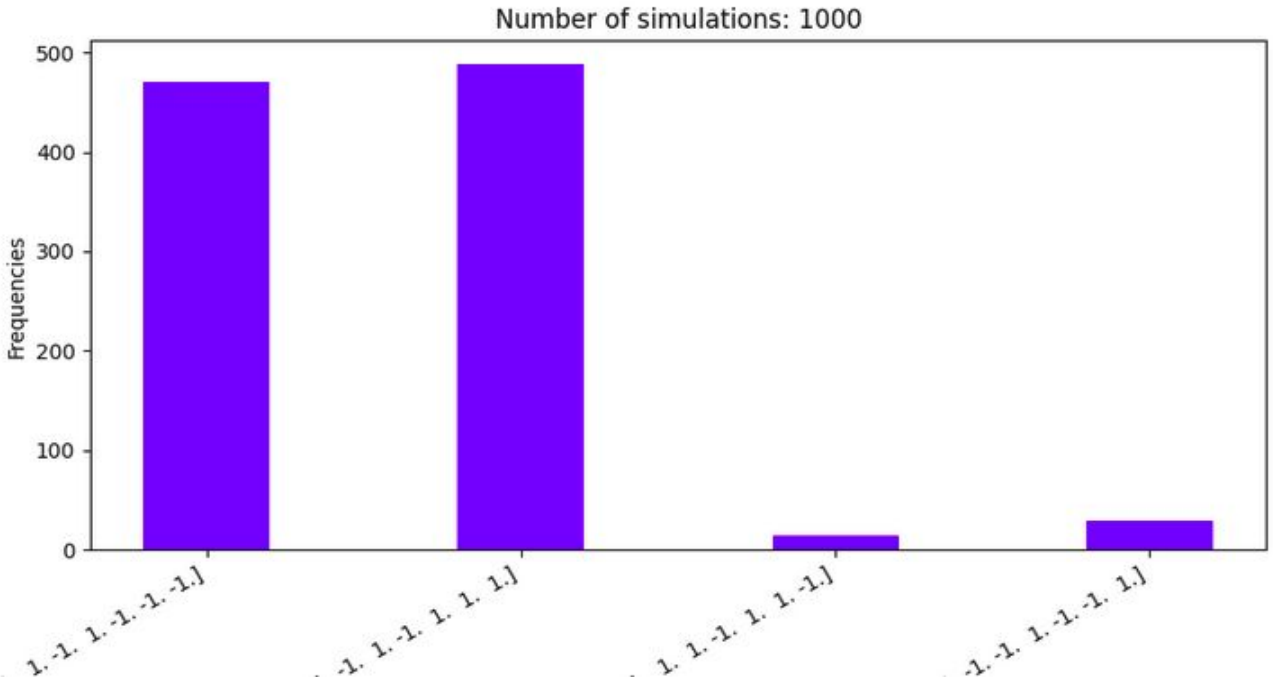
Turn-off formalism

Ising Formalism

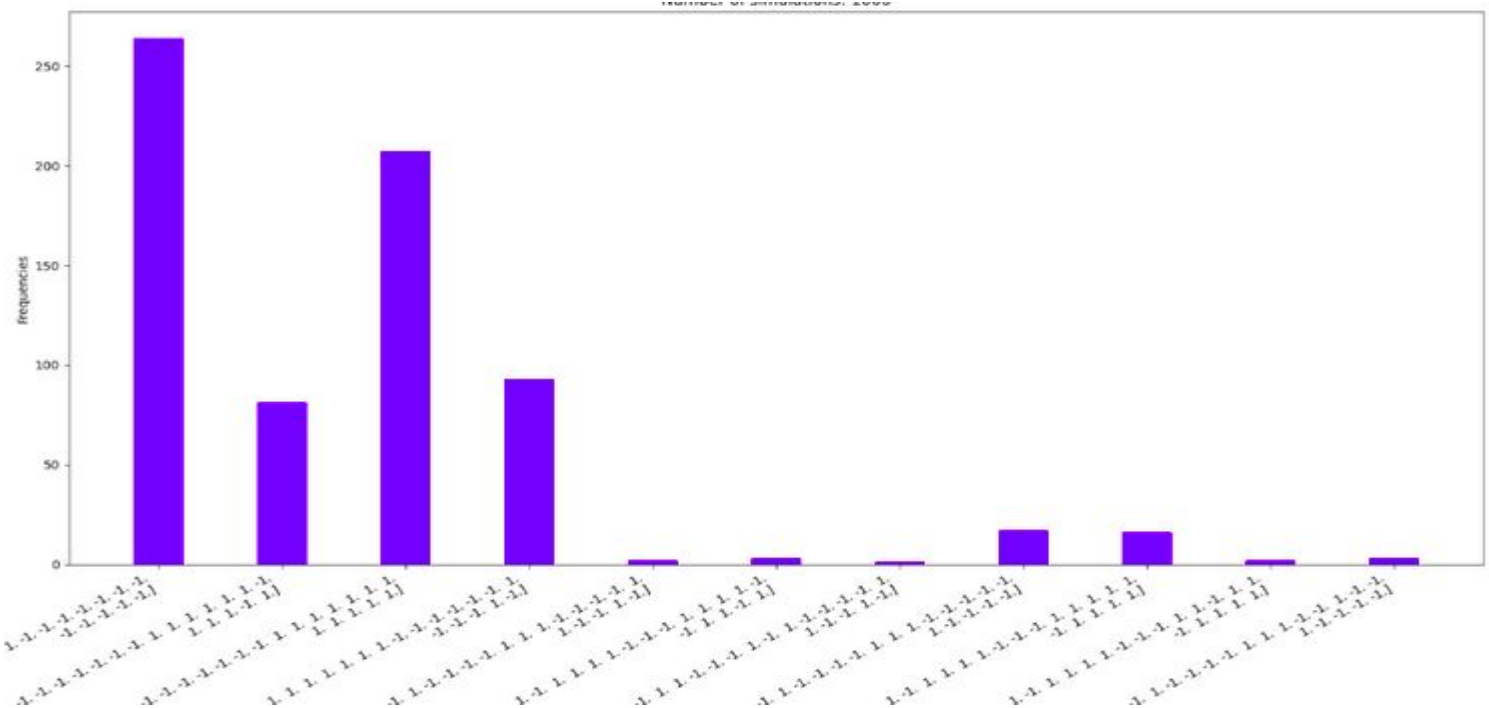
$$S_j = 1 \text{ if } \sum_i adj[i][j] * S_i > 0$$
$$S_j = -1 \text{ if } \sum_i adj[i][j] * S_i < 0$$
$$S_j = S_j \text{ if } \sum_i adj[i][j] * S_i = 0$$

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

The steady state distribution obtained with ising formalism for a 15 node emt network



The steady state distribution obtained with ising formalism for a 23 node emt network (1000 simulations)



Turn-off formalism (Three states)

When the sum is 0, we update the state of the node to be 0 instead of letting it be whatever it was.

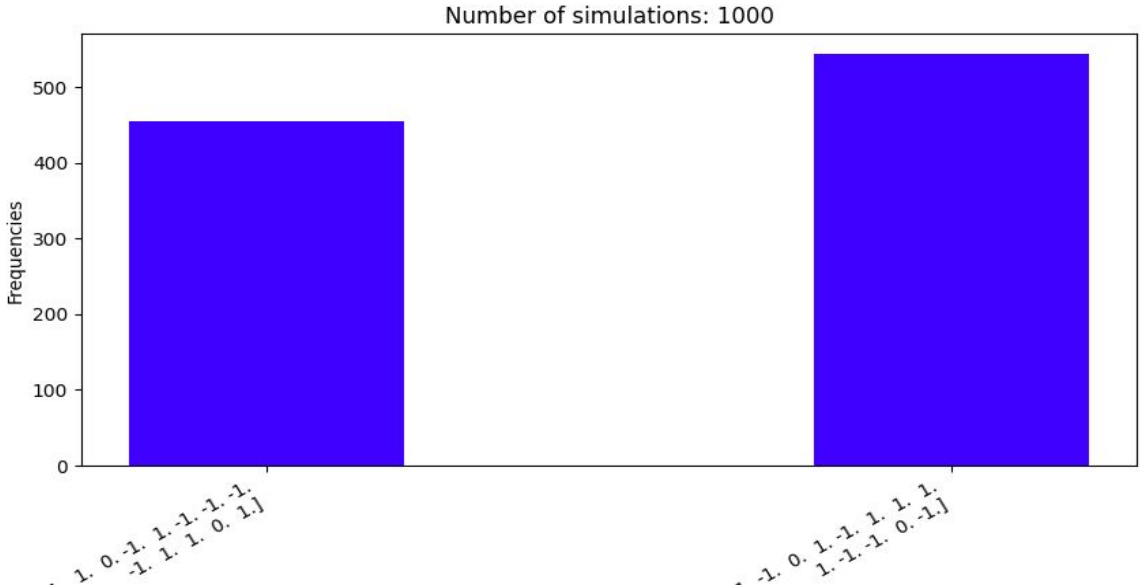
$$S_j = 1 \text{ if } \sum_i adj[i][j] * S_i > 0$$
$$S_j = -1 \text{ if } \sum_i adj[i][j] * S_i < 0$$
$$S_j = 0 \text{ if } \sum_i adj[i][j] * S_i = 0$$

What does it do?

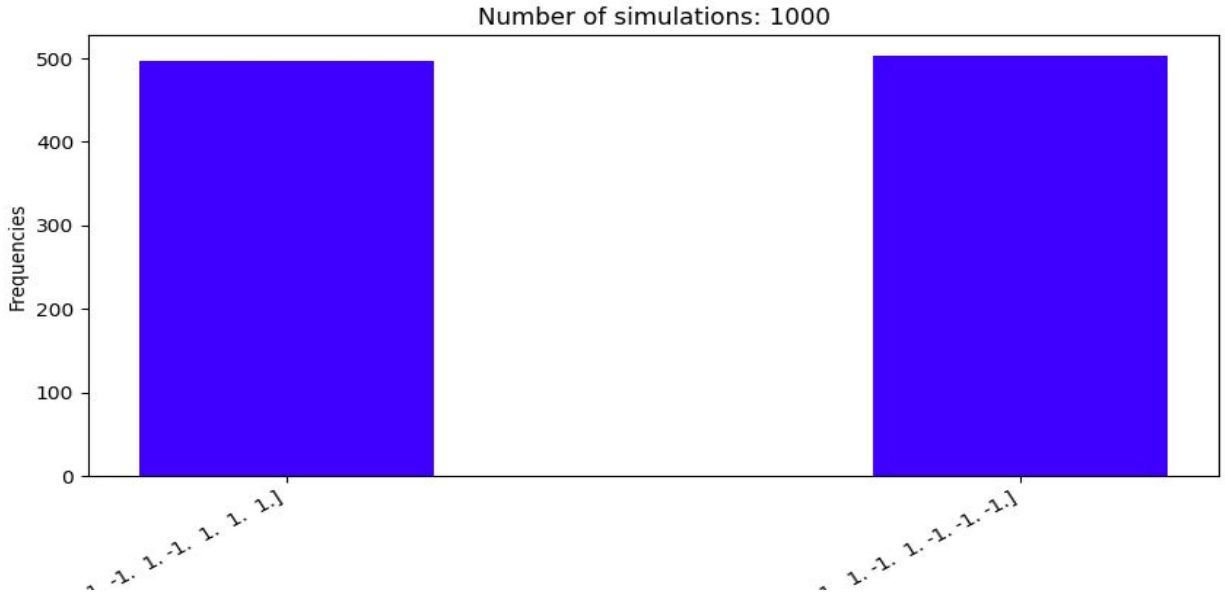
The turn off formalism effectively “silences” the nodes which have sum=0, in other words it disallows “unregulated/noisy nodes” to affect other nodes.

What we see after implementing this formalism is that hybrid states completely disappear in all the biological networks.

The steady state distribution obtained with turn-off formalism for a 23 node emt network



The steady state distribution obtained with turn-off formalism for a 15 node emt network

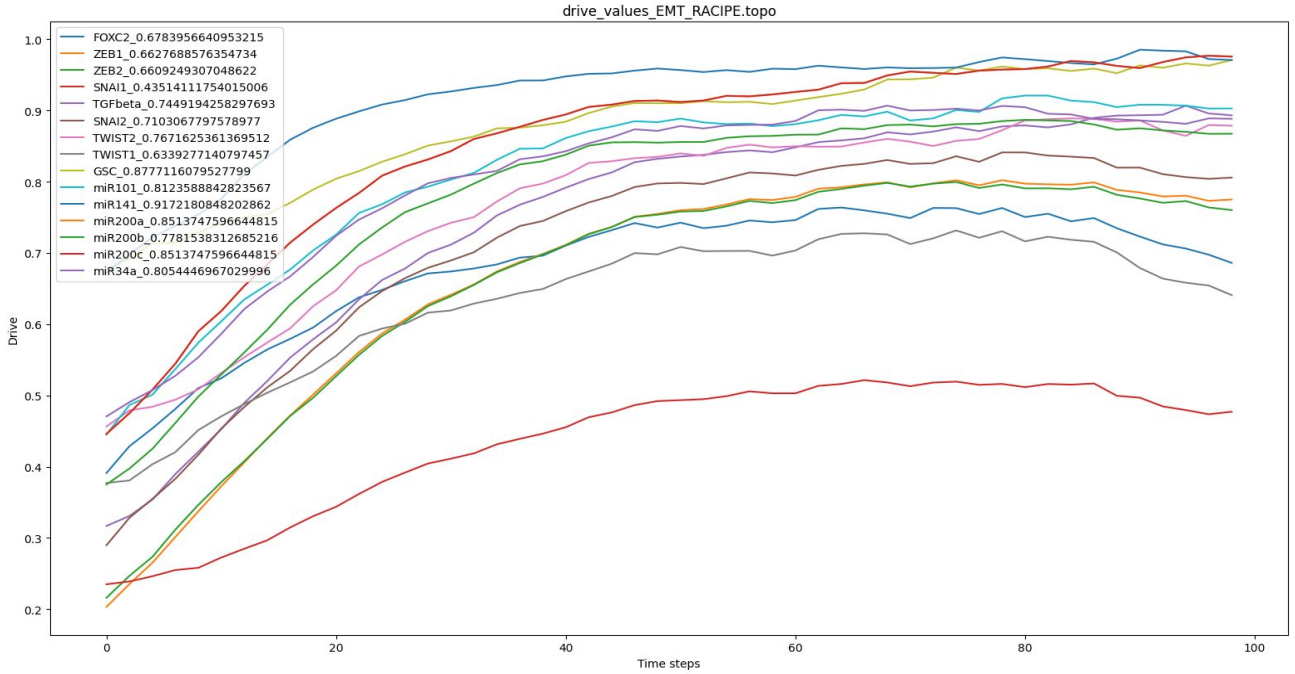


A new metric: Drive

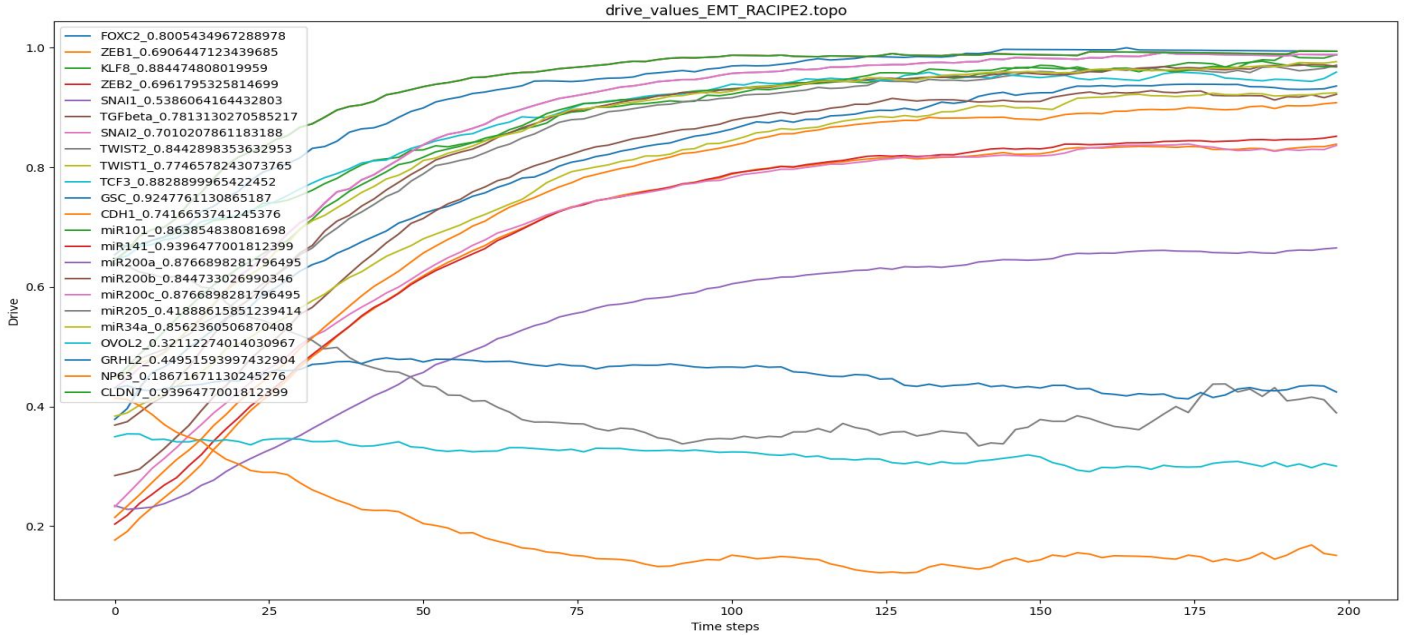
Since the three state formalism silences “noisy” nodes, we study a metric called drive which attempts at explaining how “noisy” a node is at a given time step during simulation. A node having 0 drive would be noisy and hence would be silenced. S_i is the state of the i’th node at the given time step of simulation and I_j is the indegree of j’th node

$$\frac{\left| \sum_i adj[i][j] * S_i \right|}{I_j}$$

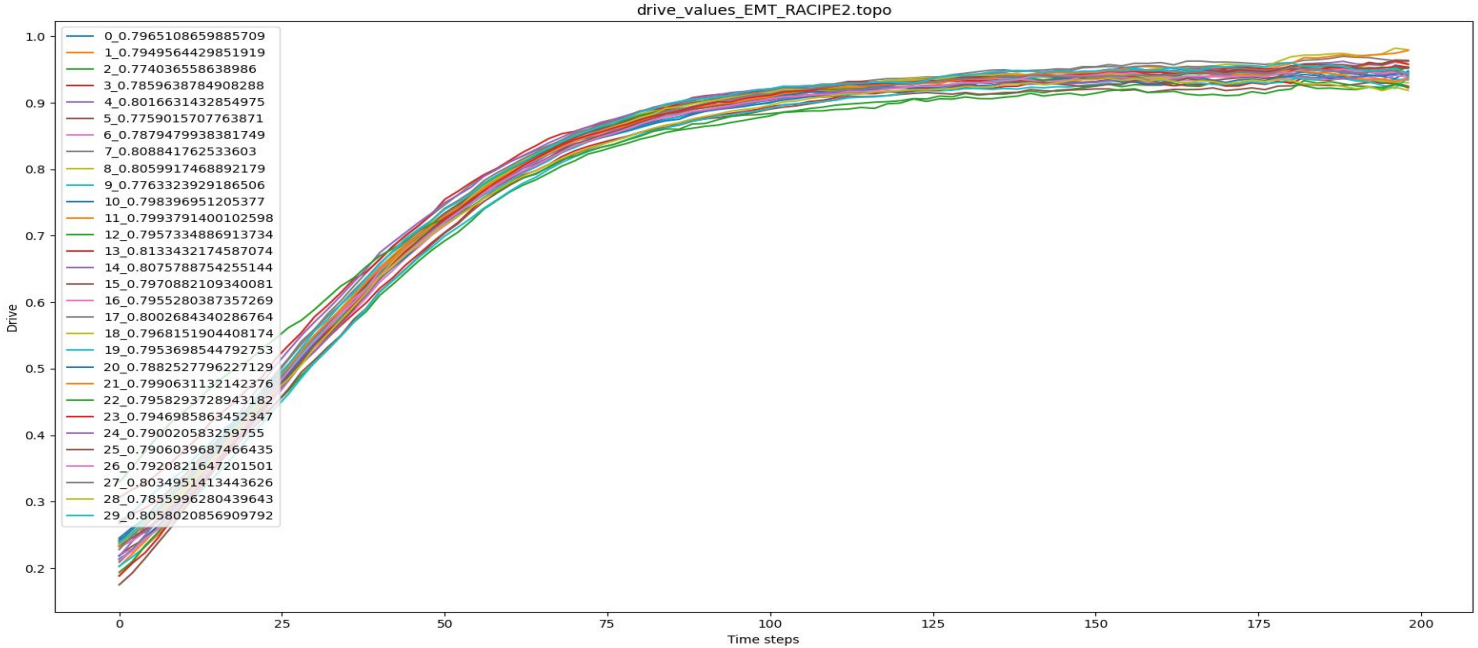
Presence of noisy nodes in biological networks (SNAI1)



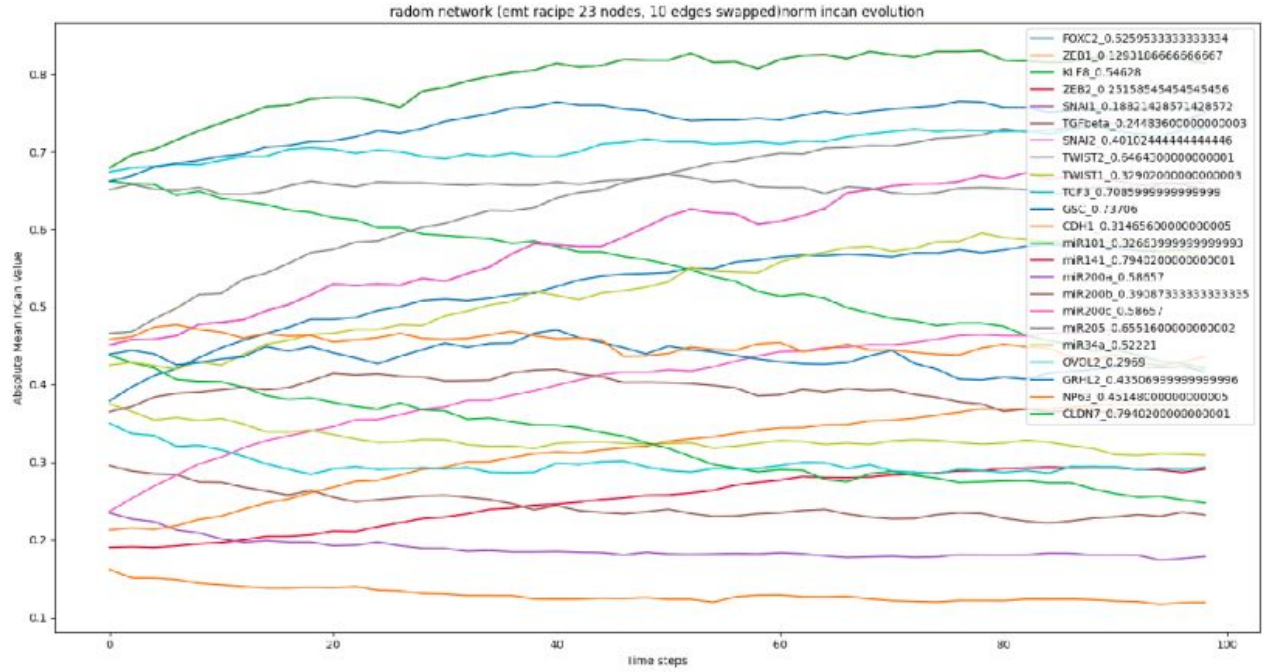
23 node EMT network (NP63,OVOL2,miR205, GRHL2)



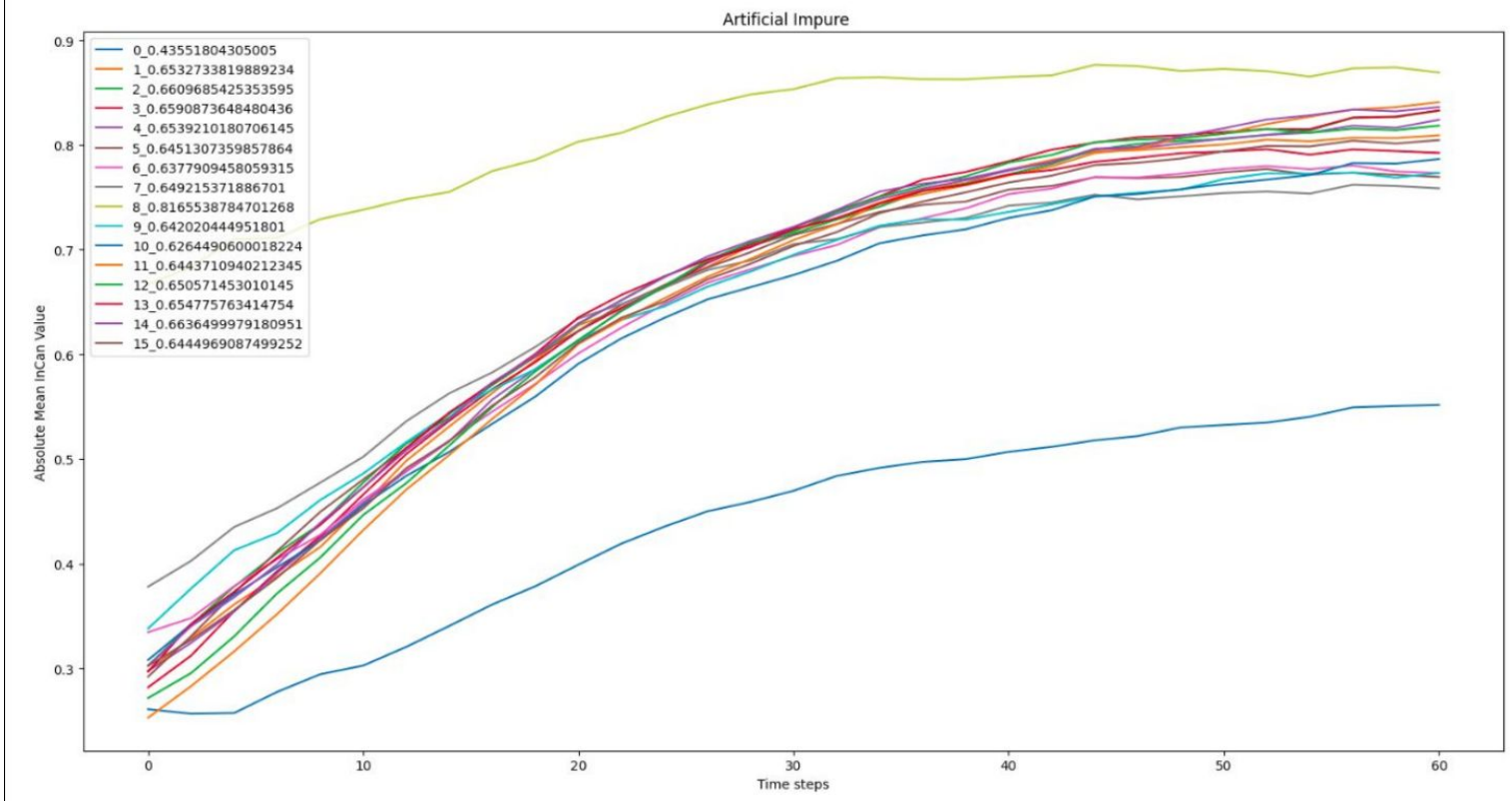
Drive plots for pure artificial networks (density =0.3)



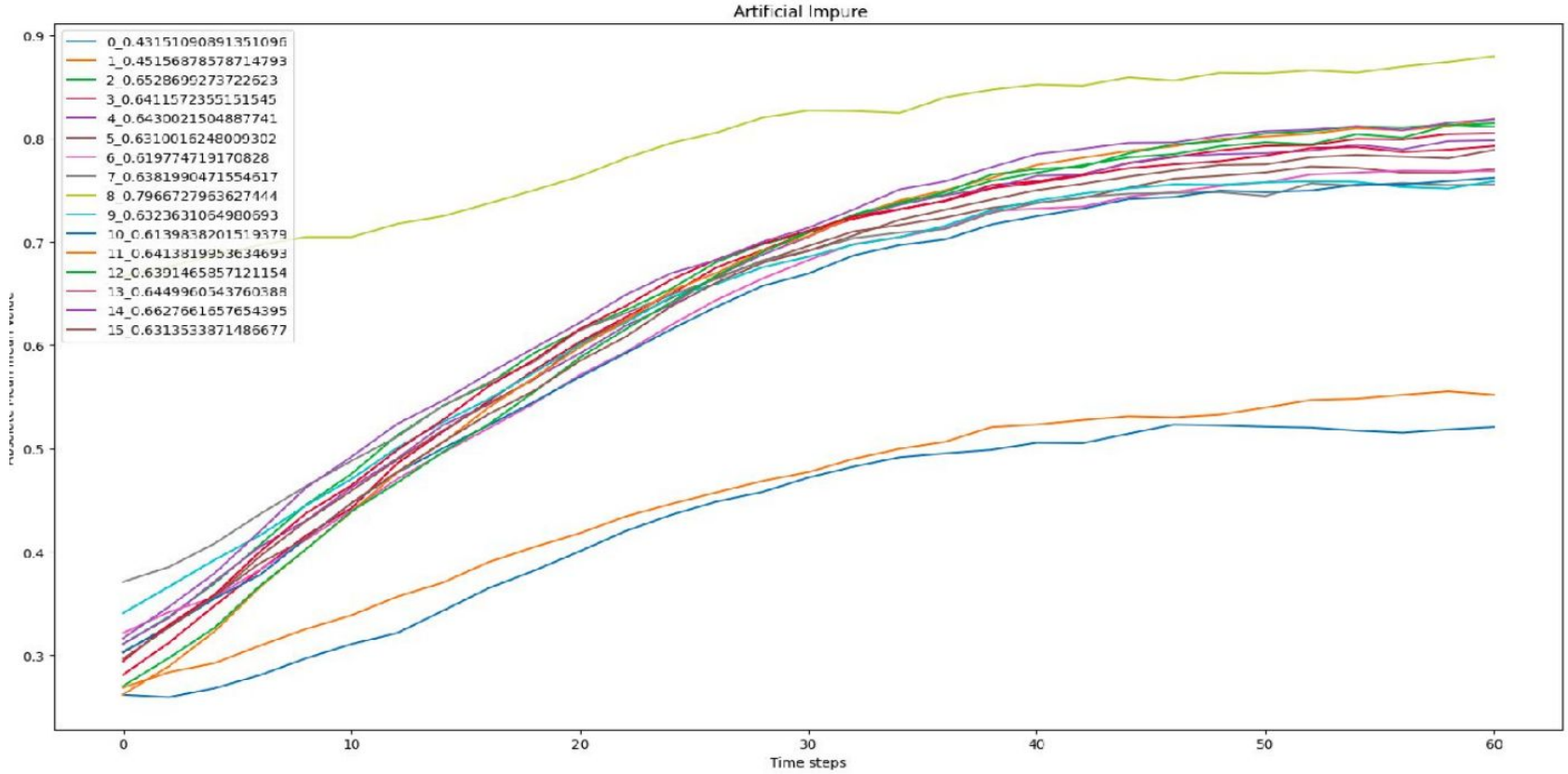
Random networks have more consistently unregulated nodes



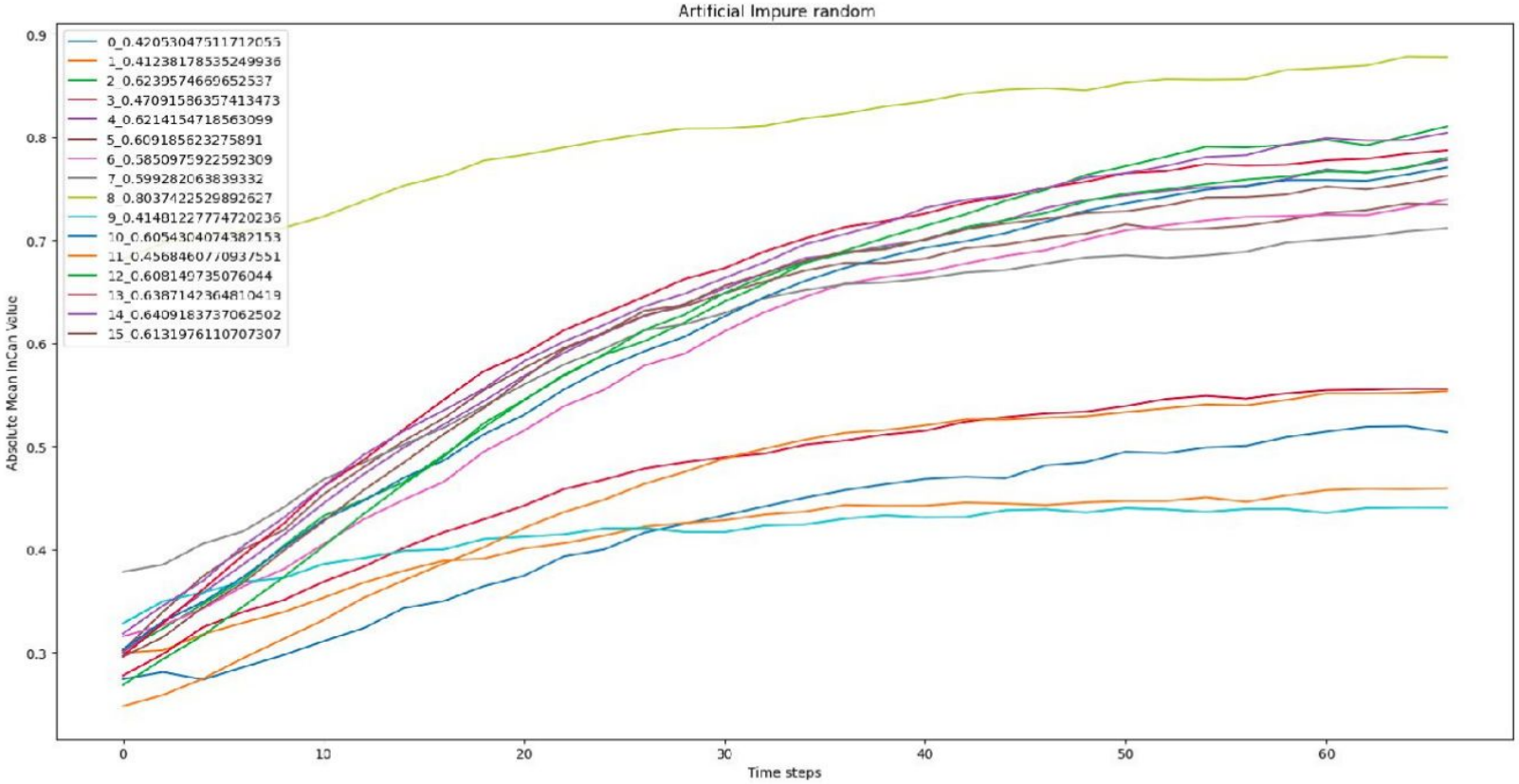
Impure artificial networks have noisy nodes.



2 impure edges

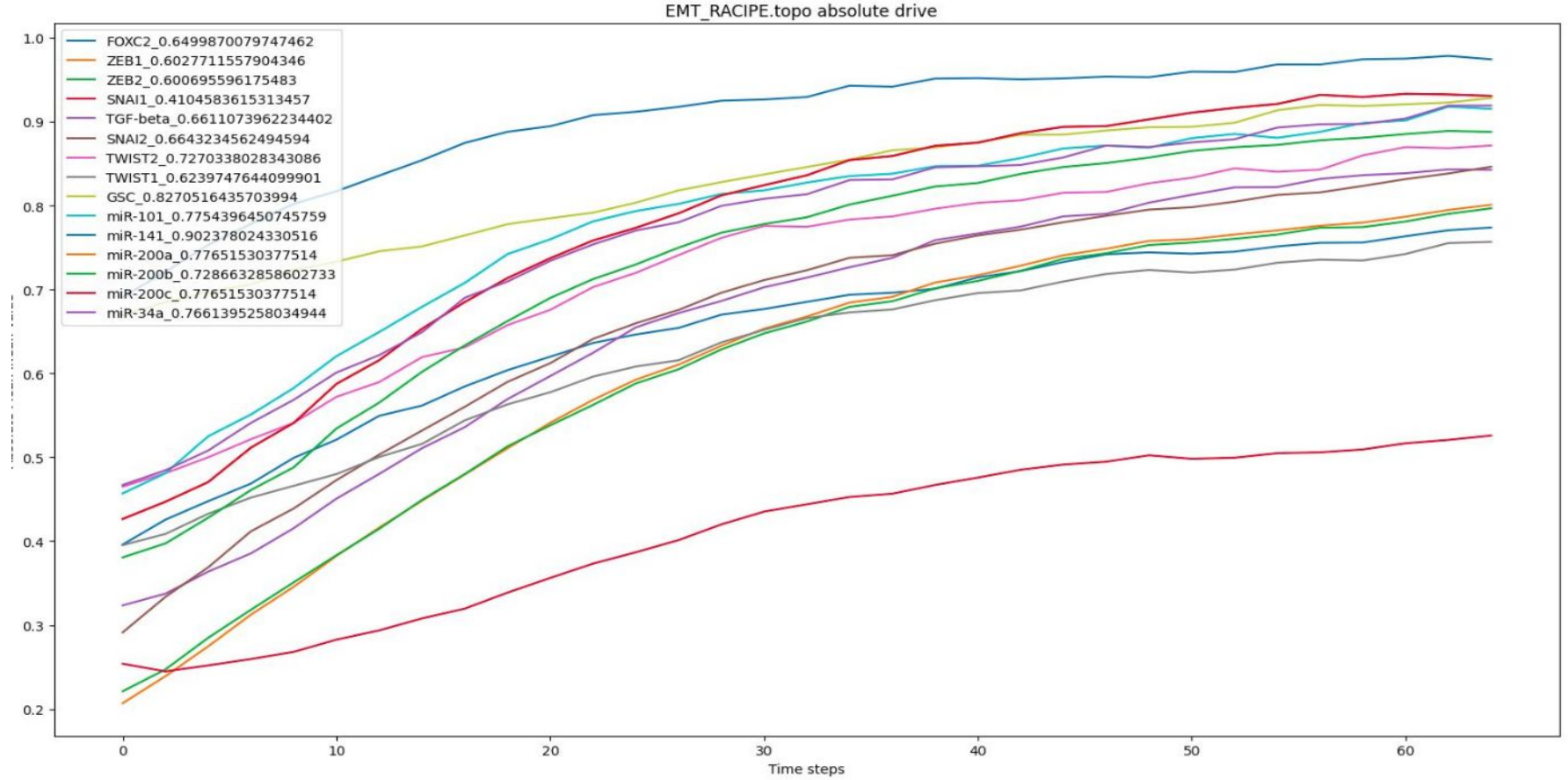


Multiple impurities added to artificial network

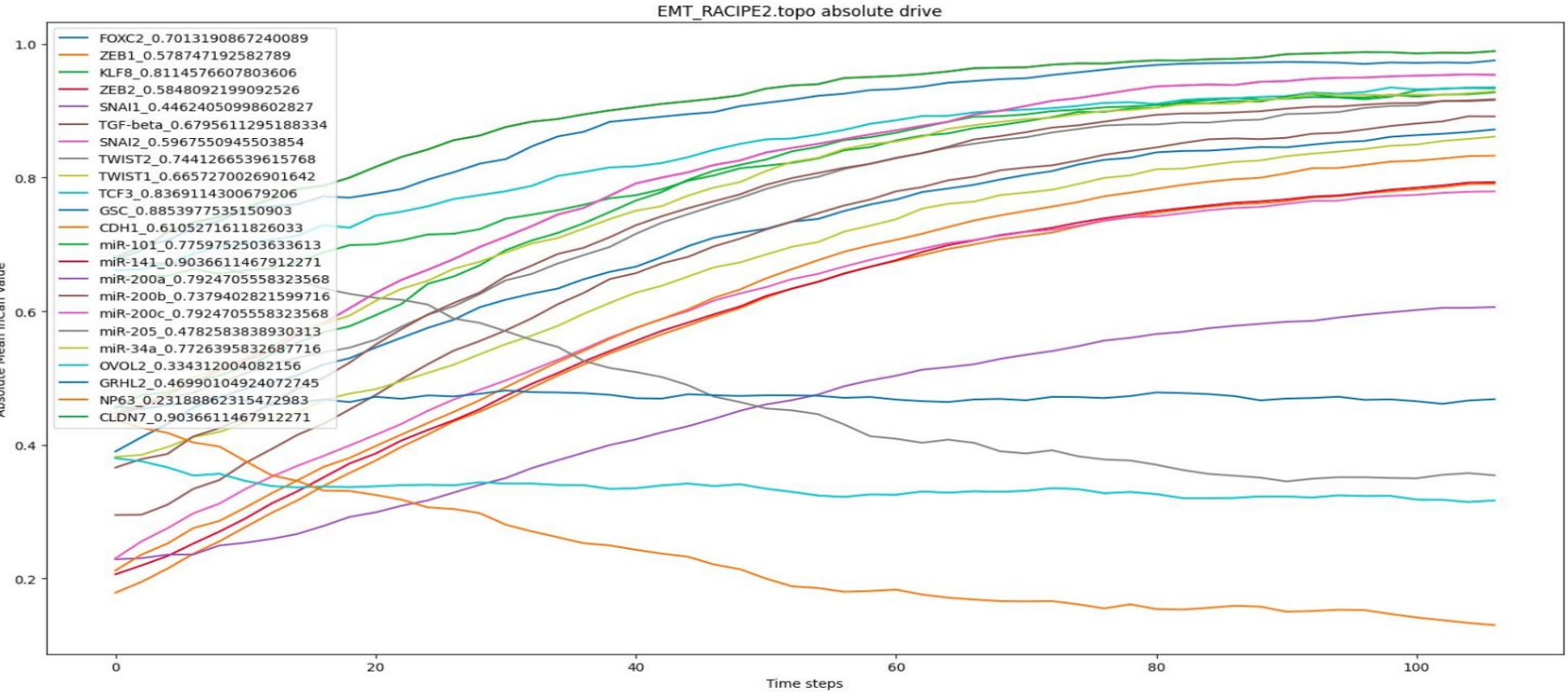


If we change impure edges to pure edges, noisy nodes disappear in biological networks

Wild type


EMT_RACIPE.topo absolute drive
FOXC2_0.6499870079747462
ZEB1_0.6027711557904346
ZEB2_0.600695596175483
SNAI1_0.4104583615313457
TGF-beta_0.6611073962234402
SNAI2_0.6643234562494594
TWIST2_0.7270338028343086
TWIST1_0.6239747644099901
GSC_0.8270516435703994
miR-101_0.7754396450745759
miR-141_0.902378024330516
miR-200a_0.77651530377514
miR-200b_0.7286632858602733
miR-200c_0.77651530377514
miR-34a_0.7661395258034944
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0
10
20
30
40
50
60
Time steps

Wild type


EMT_RACIPE2.topo absolute drive
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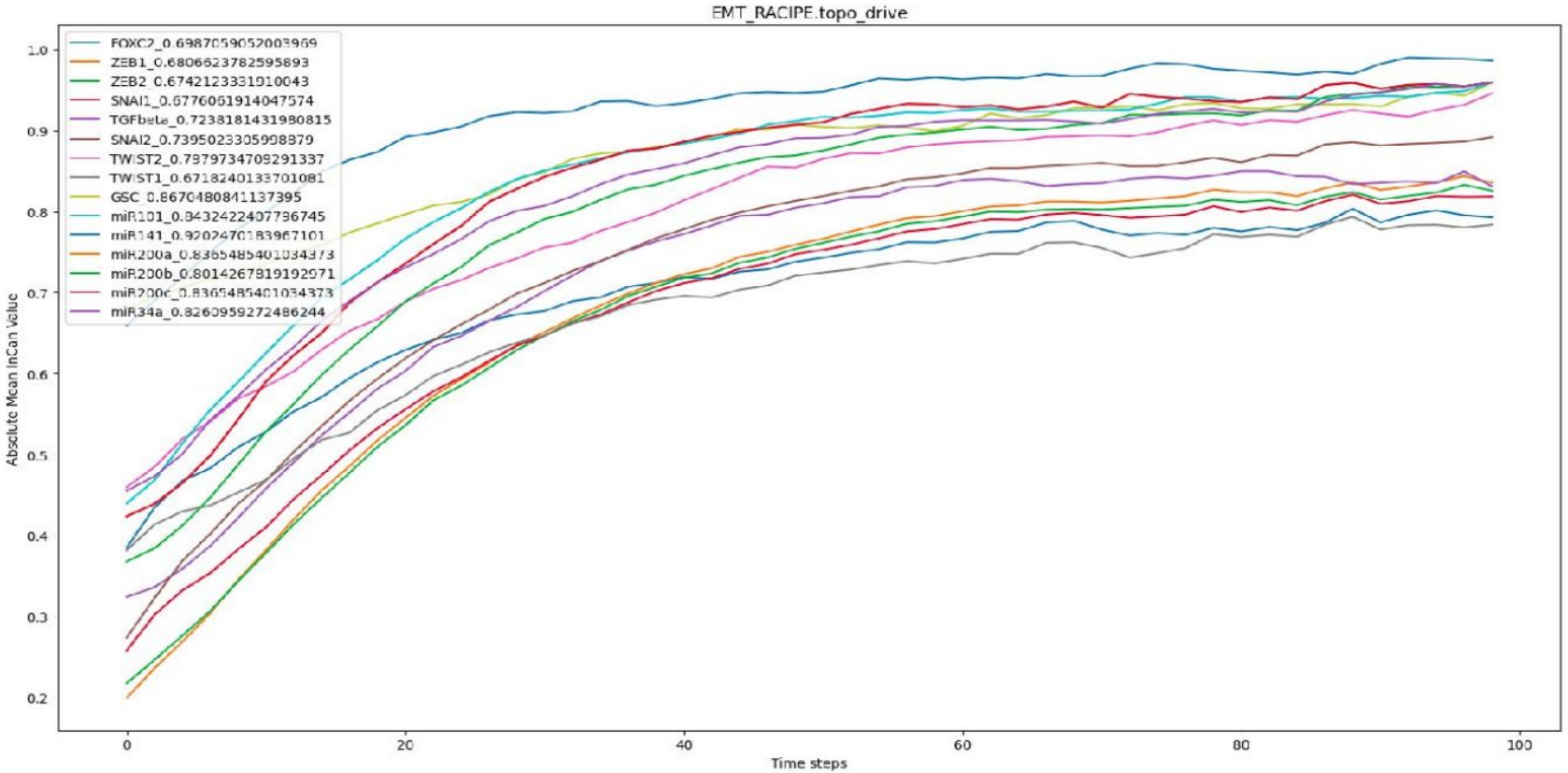
ZEB1_0.578747192582789
KLF8_0.8114576607803606
ZEB2_0.5848092199092526
SNAI1_0.44624050998602827
TGF-beta_0.6795611295188334
SNAI2_0.5967550945503854
TWIST2_0.7441266539615768
TWIST1_0.6657270026901642
TCF3_0.8369114300679206
GSC_0.8853977535150903
CDH1_0.6105271611826033
miR-101_0.7759752503633613
miR-141_0.9036611467912271
miR-200a_0.7924705558323568
miR-200b_0.7379402821599716
miR-200c_0.7924705558323568
miR-205_0.4782583838930313
miR-34a_0.7726395832687716
OVOL2_0.334312004082156
GRHL2_0.46990104924072745
NP63_0.23188862315472983
CLDN7_0.9036611467912271
Absolute Mean HCan Value
1.0
0.8
0.6
0.4
0.2
0
20
40
60
80
100
Time steps

“Purified”


EMT_RACIPE.topo_drive
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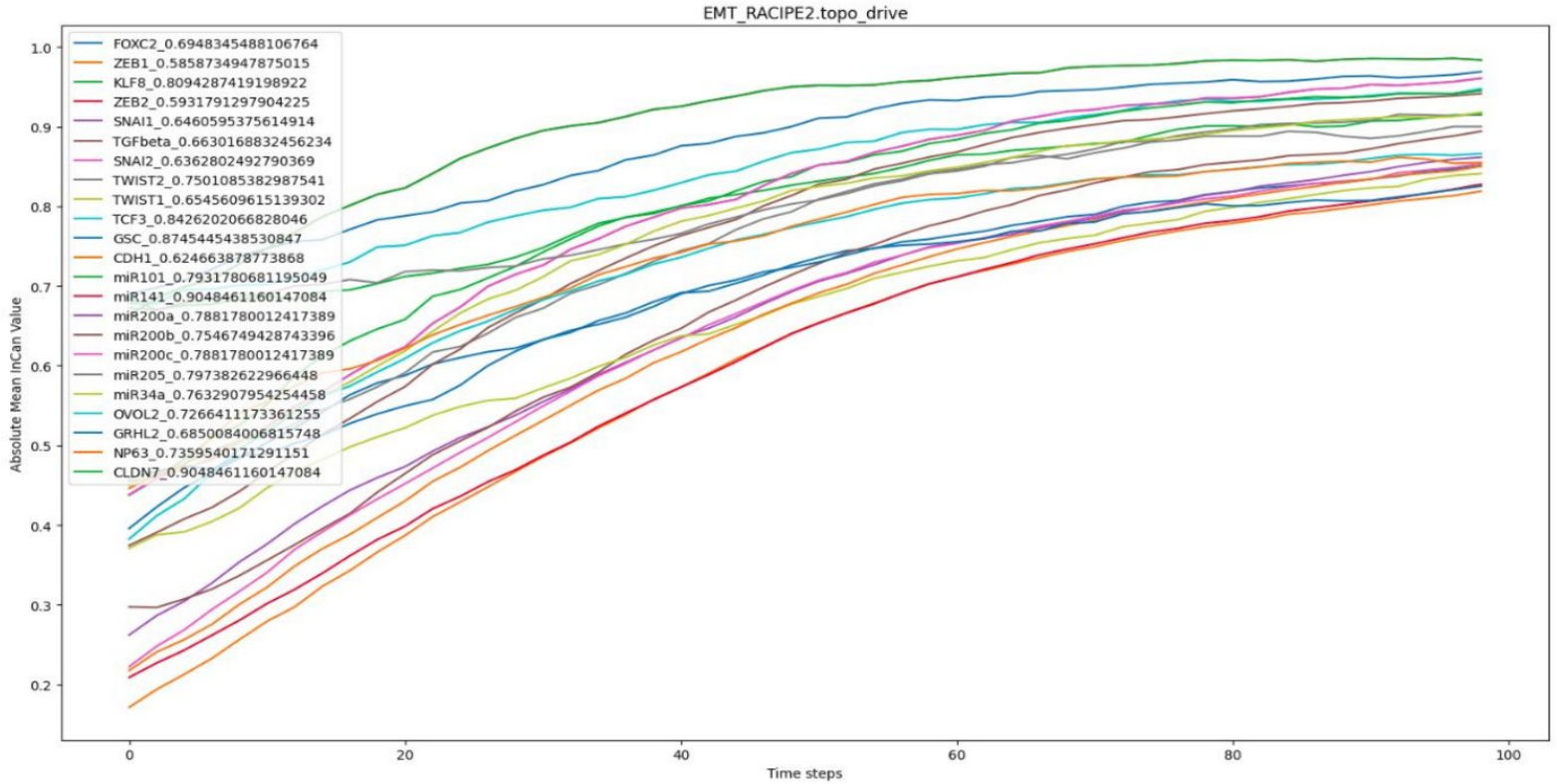
ZEB1_0.6806623782595893
ZEB2_0.6742123331910043
SNAI1_0.6776061914047574
TGFbeta_0.7238181431980815
SNAI2_0.7395023305998879
TWIST2_0.7979734709291337
TWIST1_0.6718240133701081
GSC_0.8670480841137395
miR101_0.8432422407796745
miR141_0.9202470183967101
miR200a_0.8365485401034373
miR200b_0.8014267819192971
miR200c_0.8365485401034373
miR34a_0.8260959272486244
Absolute Mean InCan Value
Time steps
0
20
40
60
80
100
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0

“Purified”


EMT_RACIPE2.topo_drive
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ZEB1_0.5858734947875015
KLF8_0.8094287419198922
ZEB2_0.5931791297904225
SNAI1_0.6460595375614914
TGFbeta_0.6630168832456234
SNAI2_0.6362802492790369
TWIST2_0.7501085382987541
TWIST1_0.6545609615139302
TCF3_0.8426202066828046
GSC_0.8745445438530847
CDH1_0.624663878773868
miR101_0.7931780681195049
miR141_0.9048461160147084
miR200a_0.7881780012417389
miR200b_0.7546749428743396
miR200c_0.7881780012417389
miR205_0.797382622966448
miR34a_0.7632907954254458
OVOL2_0.7266411173361255
GRHL2_0.685008400681574 8
NP63_0.7359540171291151
CLDN7_0.9048461160147084
Absolute Mean inCan Value
Time steps
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0
20
40
60
80
100