Evolutionary Dynamics Project: Evolution of Protein-Protein Interaction Network

Michał Sanocki

Protein–Protein Interaction (PPI) networks

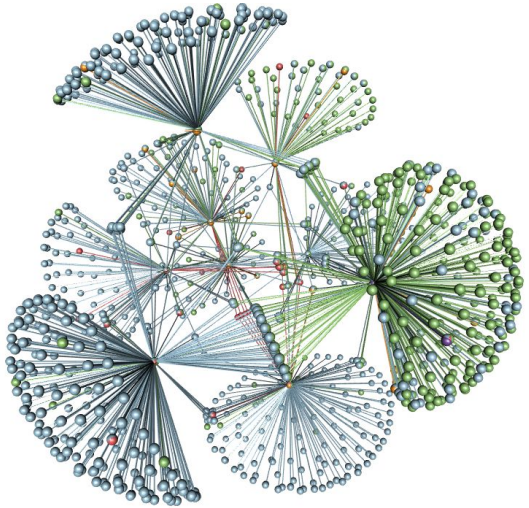
Architecture:

Nodes - proteins

Edges - connections between

interactive proteins

Reflect the cell’s machinery and signaling pathways



Human HIV-1 protein-protein interaction network

https://commons.wikimedia.org/wiki/File:Multiplex_Human_HIV-1_protein-protein_interaction_network_%28edge-colored_visualization%29.png

Mutation Mechanism

Previous literature mutation mechanism:

Mutant - new node with k - new edges

Mutant edges selected randomly - uniformly or weighted by degree or gene expression

Proposed mutation mechanism:

Mutant has a “parent” node

Mutant deletes Kd - edges of parent and adds Ka new edges

By default Ka=Kd >=1

Mutation rate - percentage of parent edges that will be changed

K = Parent_degree*mutation_rate

Note: Actual mutation rate varies because we have to round up the numbers and Ka,Kd have to be at least one

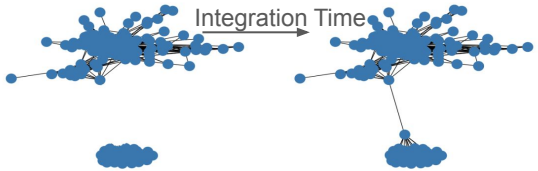
Properties:

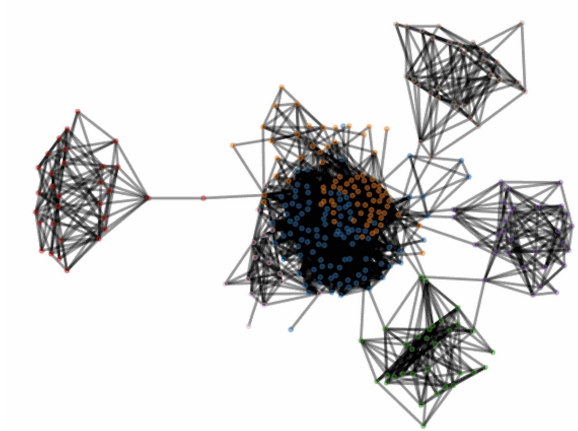
1. Better Structure preservation
2. Varied mutant degree
3. Parent degree is equal to mutant degree

Klein, B., Holmér, L., Smith, K.M. *et al.* A computational exploration of resilience and evolvability of protein–protein interaction networks. *Commun Biol* 4, 1352 (2021). https://doi.org/10.1038/s42003-021-02867-8

Investigated Properties

1. Resilience
2. Integration time
3. Number of Communities
4. Modularity
5. Structure preservation





Properties

Resilience

$$H_{msh}(G) = -\frac{1}{\log(N)} \sum_{x=1}^{X} p_x \log p_x$$

$$R(G) = 1 - \sum_{f=0}^{1} \frac{H_{msh}(G_f)}{r_f}$$

Communities

Greedy Algorithm - Find Partition to maximize modularity

Modularity

$$Q = \frac{1}{2m} \sum_{i,j} \left[A_{ij} - \frac{k_i k_j}{2m} \right] \delta(c_i, c_j),$$

Simulations

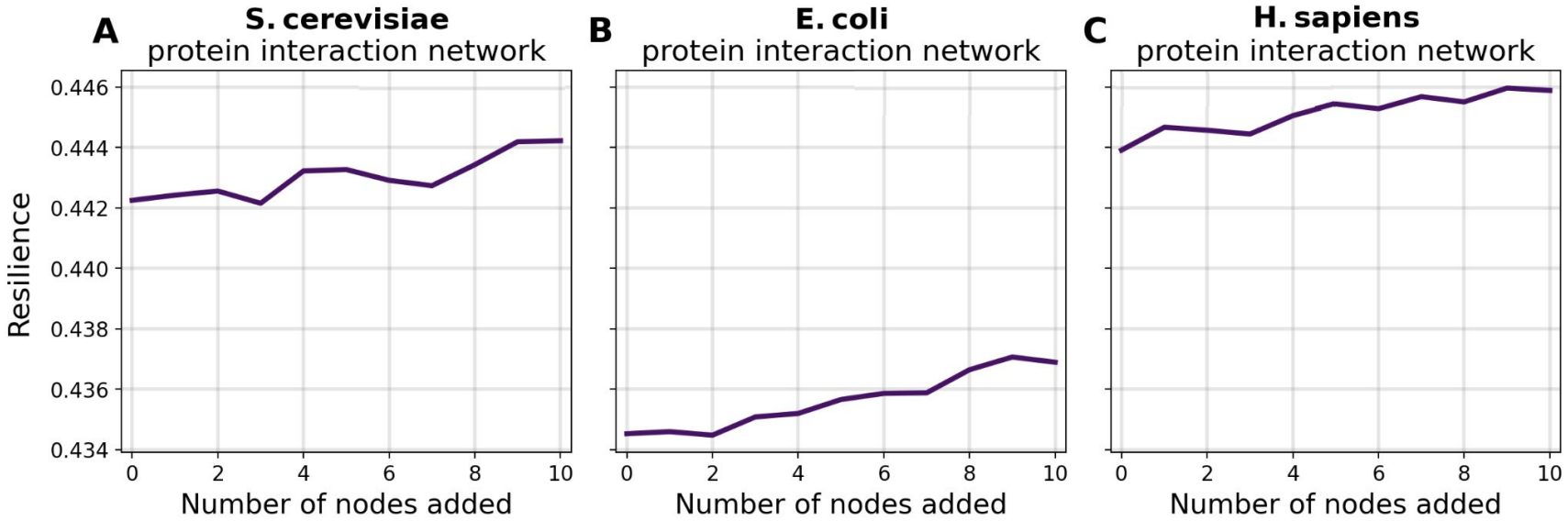
1. Addition of 10 nodes to 3 different networks - Comparison to previous mechanism

2. Influence of Mutation rate: integration time, resilience, number of communities and modularity x 100 to achieve statistical significance

3. Long simulations (300 added nodes) to investigate changes in network structure

Experiment#1 Comparison to Literature Mechanism

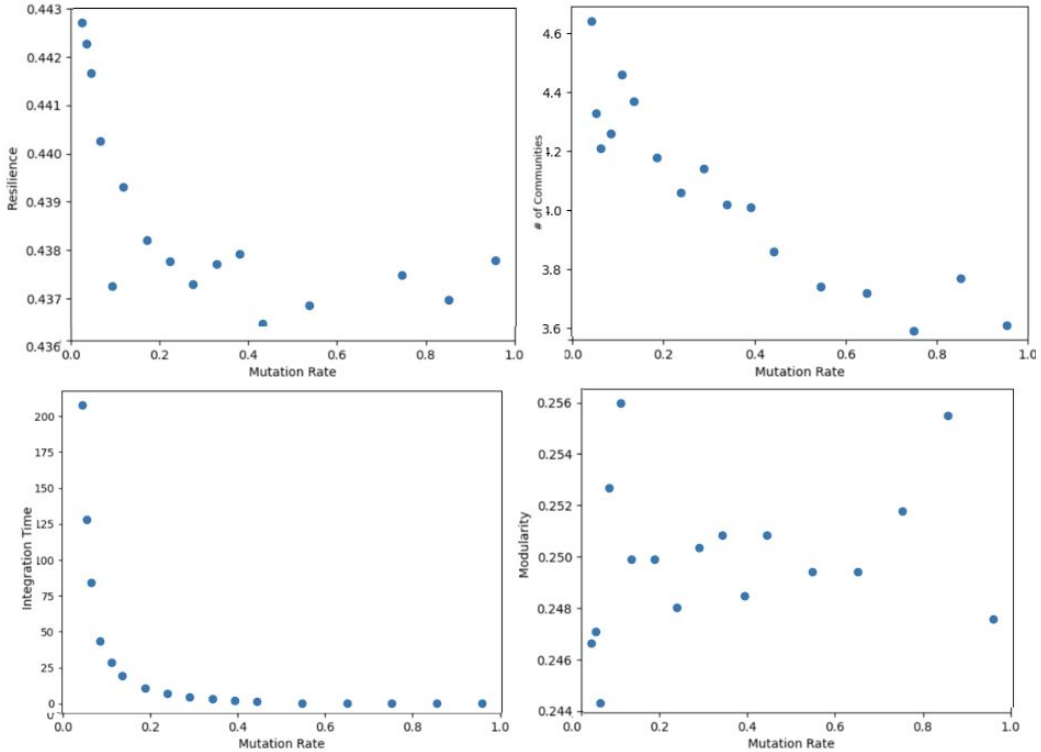
Higher resilience compared to previous mechanism



Benchmarked model:	0.438	0.432	0.440

Experiment#2: Mutation Rates and Network Parameters

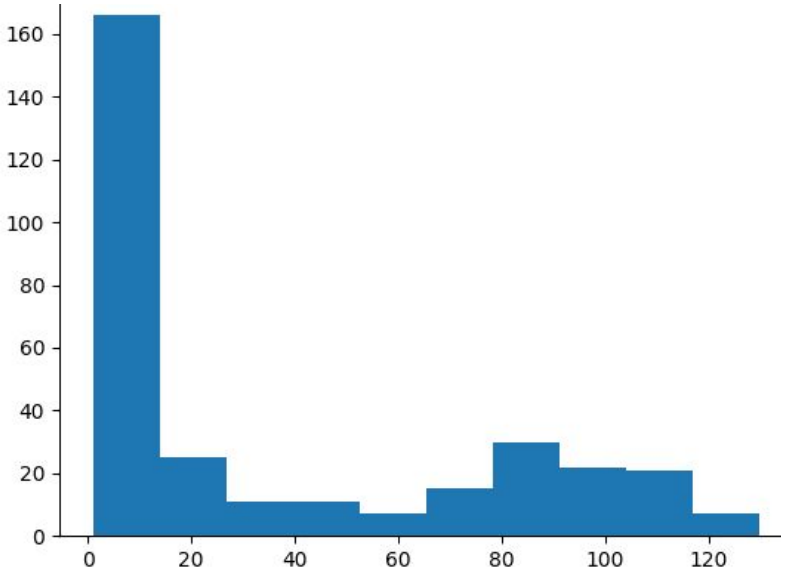
Trade-off between integration time and number of communities and resilience



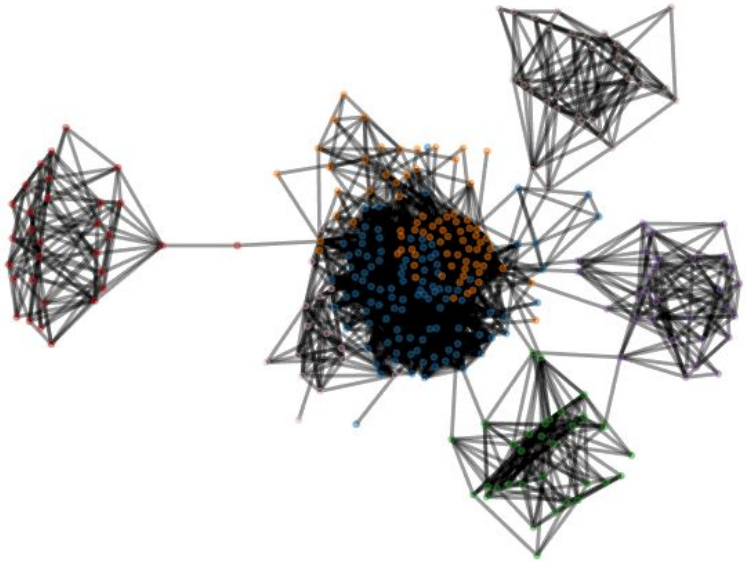
Experiment#3: Evolution of networks structure

Structural diversity loss ->need for better modeling scheme

Degree Histogram



Network



Conclusions

1. **Proposed mechanism can be used to model evolutionary changes in PPIs**
   Achieved higher resilience changes than benchmarked literature models

2. **Mutation Rates Impact Key Network parameters**
   Trade off between integration time and resilience and number of communities

3. **Decreased Network Diversity Over Time:**
   For sufficiently long simulations network becomes homogeneous