Evolving Evolvable Networks

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Term Project, Signals and Systems in Biology

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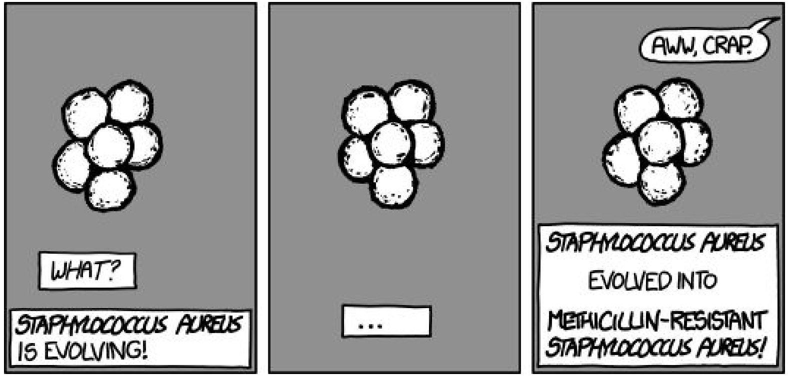
Motivation

- ➢ Why do biological networks showcase characteristic properties**?**
  - Modularity
  - Scale freeness
  - Robustness
- ➢ How does the structure of the biological network evolve**?**
- ➢ What are biological networks trying to optimize**?**
  - Evolvability
  - Robustness
  - ER Tradeoff
  - Cost of Complexity



Source: XKCD

Fitness Factors

- *Evolvability*: ability of the network to cope with the changing surrounding by taking up new functions **[Valiant 2009]**
- *Robustness*: degree to which the network can withstand perturbations, continuing to carry out vital functions
- *Complexity*: measure of the resource load of putting together and running of the network

Prior Art

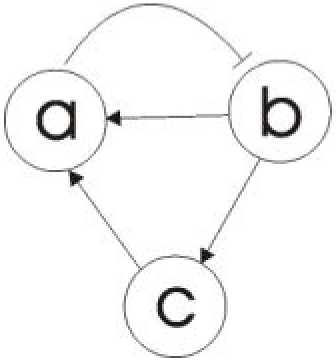
1. Evolution of network properties: evolution under modular objective functions Spontaneous evolution of modularity and network motifs, **[Nadav Kashtan and Uri Alon, 2005]**
2. Quantifying evolvability in small biological networks: optimise signal processing ability, change in functions from change in parameters **[A. Mugler, E. Ziv, I. Nemenman, and C.H. Wiggins, 2009]**
3. Robustness and evolvability in genetic regulatory networks **[Maximino Aldana, Enrique Balleza, Stuart Kauffman, Osbaldo Resendiz, 2006]**

Problem Statement

“To study the evolution of directed biological networks (and their properties) using a generalised objective function capturing **evolvability**, **robustness**, and constraints of **complexity** (resource load).”

Problem Representation

➢ Characterising evolvability and robustness: periodic attractors in Random Boolean Networks **[Kauffman, 1969]**, with gene duplication and divergence



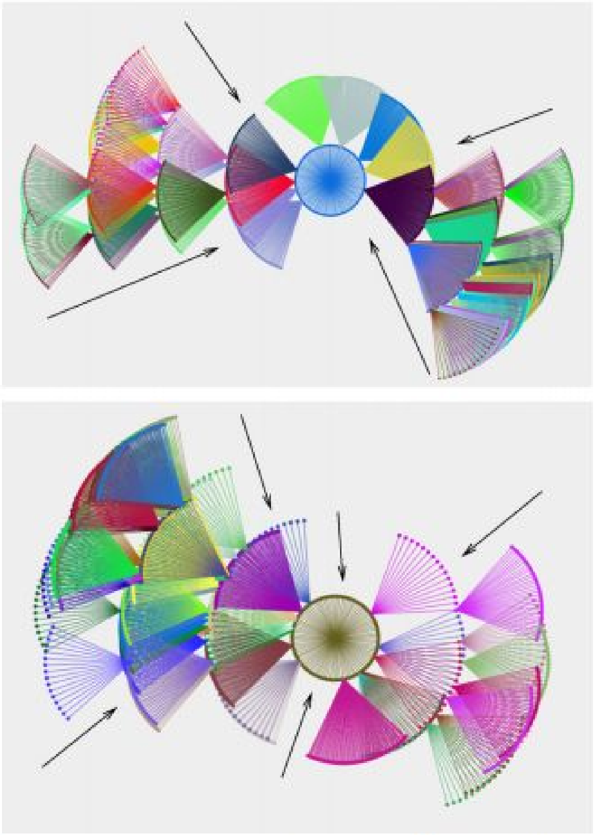
		0;0	0;1	1;0	1;1
a	b;c	0	1	1	0
b	a;a	1	0	0	1
c	b;b	0	1	1	1

Source: University of Tubingen

➢ Complexity: measure of adjusted average distance, taking in account, the accessibility of the network defined as the count of finite length paths

Fitness Function - Evolvability and Robustness

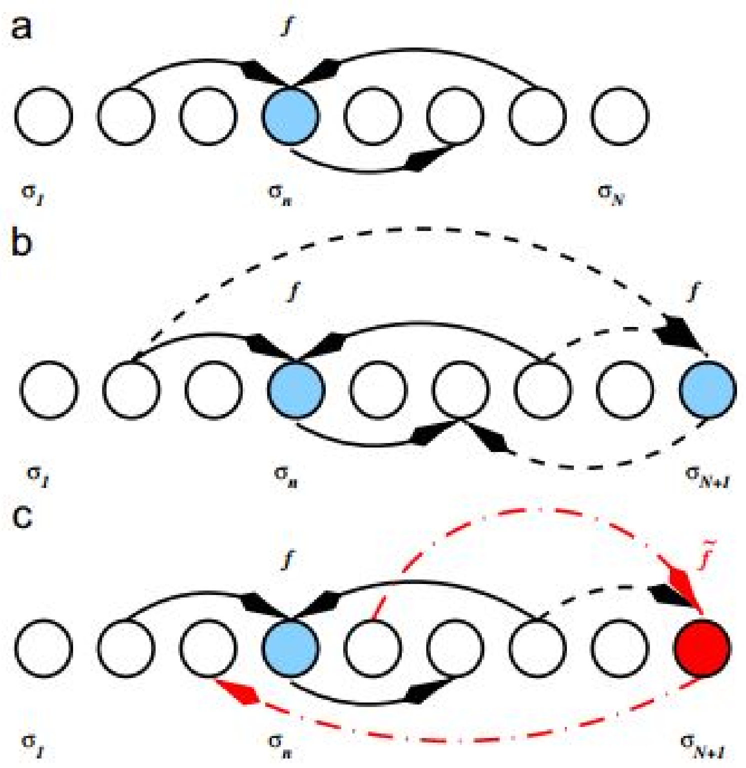
- Perturbations: permanent genetic changes
- Dynamic attractors: cell fates
    - Genotype → Phenotype mappings
    - Study attractor landscape!
- Evolvability: under perturbation, introduction of new attractors/attractor states
- Robustness: under perturbation, retention of attractors/attractor states



Source: Aldana et al. 2006

Fitness Function - Evolvability and Robustness

- Gene Duplication and Divergence
- Neofunctionalisation
  - Expansion
  - Contraction
  - Innovation
  - Elimination



Source: Aldana et al. 2006

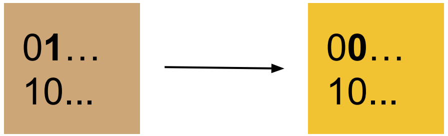
Fitness Function - Complexity

- ➢ Accessibility - fraction of finite value paths in the networks
- ➢ Adjusted average distance - average shortest path length calculated by taking finite length paths only
- ➢ Complexity - ratio of accessibility and adjusted average distance. The value is high for highly connected as well as sparse networks, thus, regarding both the extremes as complex

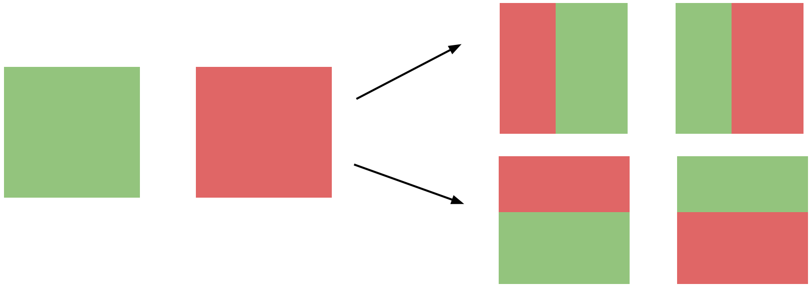
Genetic Algorithm

- ➢ Individual - adjacency matrix of the network (0 or 1)

- ➢ Mutation - flipping of the value in the matrix



- ➢ Crossover - overlapping of matrices along a random row or column



Experiments and Analysis

- Robustness - knocking out nodes based on betweenness centrality and measuring the change in shortest path lengths and connectivity
- Scale free - analysis of degree distribution
- Modularity - Clustering Coefficient for small world network

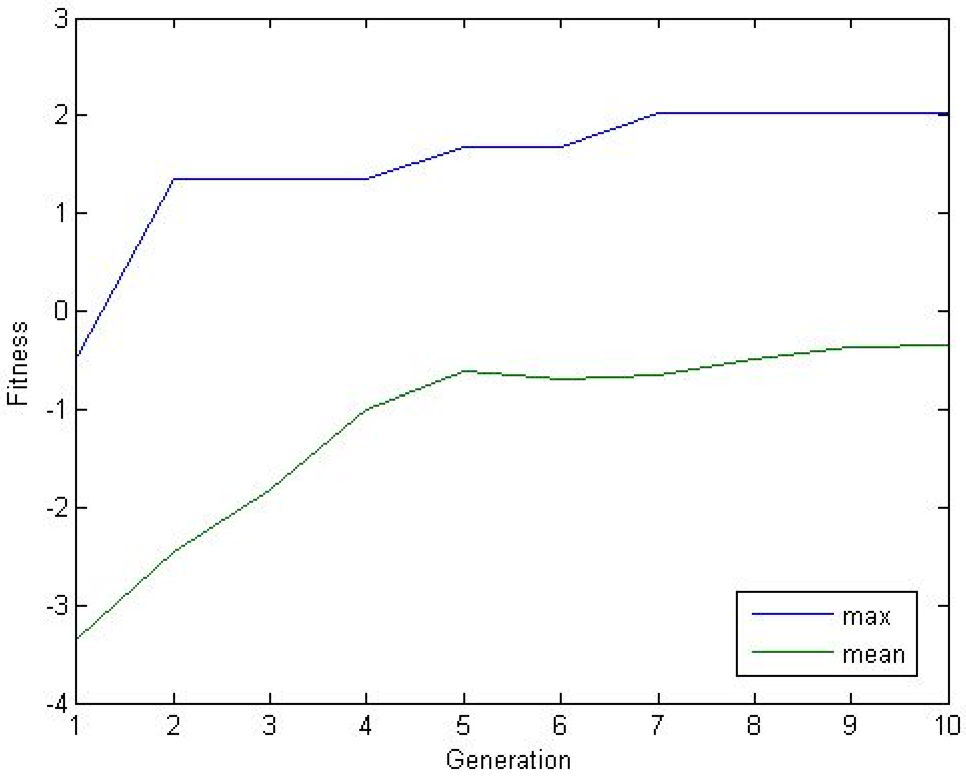
N = 10 (Number of attractor states?)

For ER: 10 runs, full mutations

For GA: 6, 8, 10 nodes. Multiple configs.

Experiments and Analysis

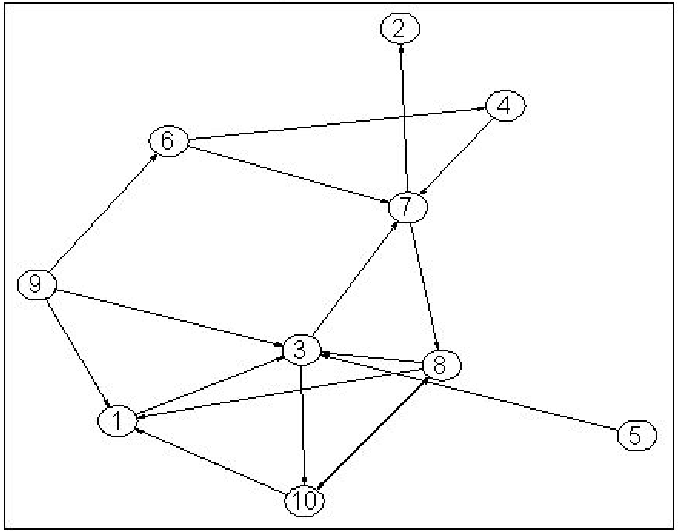
Increase in maximum and mean fitness values of the population while executing Genetic Algorithm for 10 generations



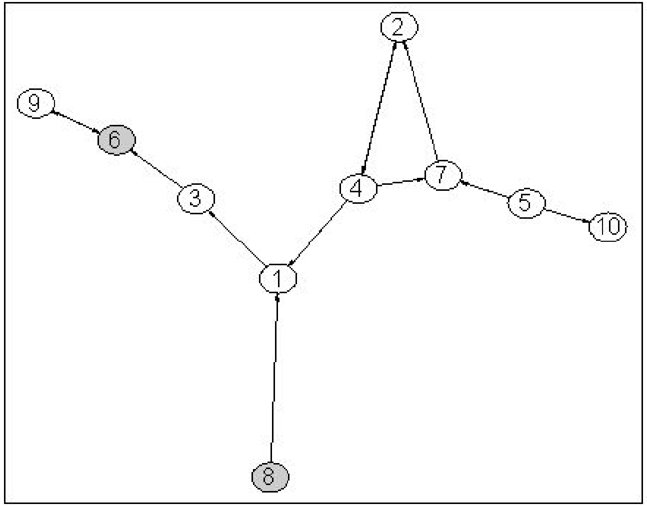
Results

Evolved Networks

N = 10, 10 generations, 20 individuals



Low Penalty



High Penalty

Results

Modularity

A graph is considered small-world, if its average local **clustering coefficient** is significantly higher than a random graph constructed on the same vertex set.

Evolved Network (Total degree 17)	Random Graph p = 0.2 (Total degree 19)
0.2146	0.0385

Results

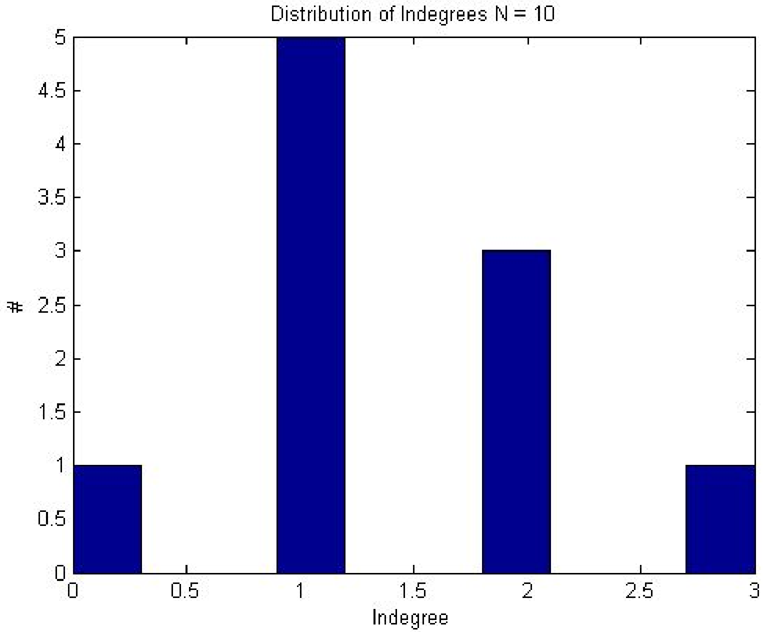
Robustness

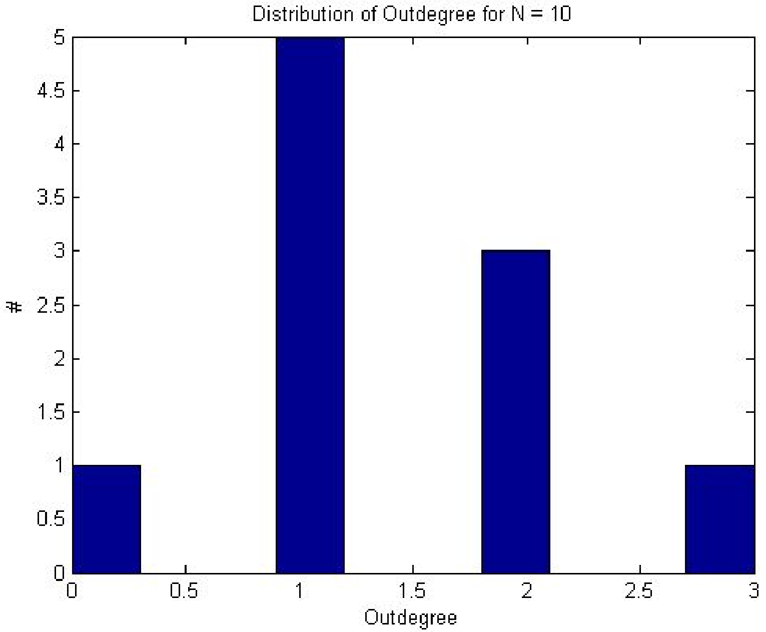
1. Identify node with highest betweenness centrality (node number 7, here).
2. Estimate loss in reachability in the network, using adjusted average distance (AAD) and number of pairs of disconnected nodes.

	Original Network	**Network after KO of node#7**
AAD	0.5700	0.3827
# disconnected pairs	43/100	50/100

Results

Scale freeness





In Conclusion

- ➢ Evolvability, robustness and complexity are naturally important factors of biological evolution, and hence a good notion to define the idea of ***fitness*.**
- ➢ Some key network properties are observed in the so-evolved networks
- ➢ Future work:
  - learning weights of the fitness function attributes:

    $$f = w_e*evolvability + w_r*robustness + w_c*complexity$$

  - Further GA parallelisation
  - Simulations for larger networks, to a large number of generations, to better support our hypothesis

Key References

- **Nadav Kashtan and Uri Alon**, *Spontaneous evolution of modularity and network motifs*, PNAS, September 27 2005, vol. 102, no. 39, 13773–13778, www.pnas.org/cgi/doi/10.1073/pnas.0503610102
- **A. Mugler, E. Ziv, I. Nemenman, and C.H. Wiggins**, *Quantifying evolvability in small biological networks,* IET Syst Biol. 2009 September, 3(5): 379–387. doi:10.1049/iet-syb.2008.0165
- **Maximino Aldana, Enrique Balleza, Stuart Kauffman and Osbaldo Resendiz**, *Robustness and evolvability in genetic regulatory networks*, Journal of Theoretical Biology 245 (2007) 433–448

Thank You
Questions?