The fraction of activating and inhibiting connections controls the dynamics of biological networks

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Background

- Theory of complex networks has been applied in many seemingly unrelated fields
  - Sociology
  - Neuroscience
  - The Internet
  - Biology
- Networks are patterns of molecular interactions within cells, which can be analyzed in the same manner as other complex networks
  - For instance, the model we use is nearly identical to a neuroscience model that has been extensively studied
  - Data collected from other fields of study has direct potential to be relevant
  - Analysis techniques from other fields of study are also potentially relevant

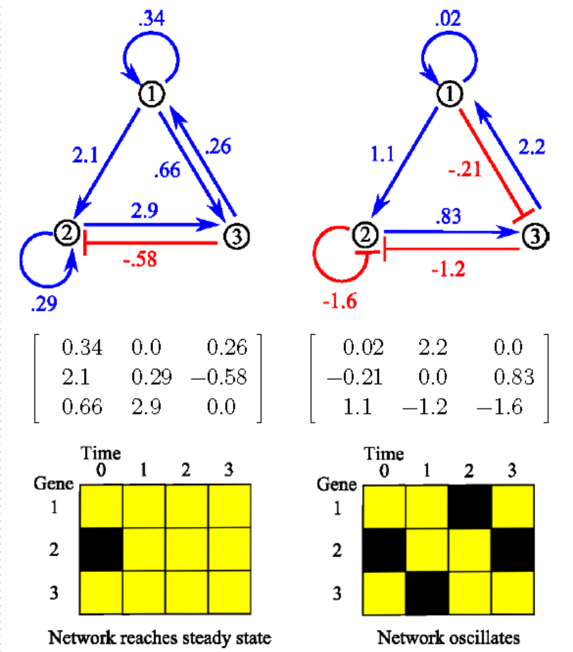
M. E. J. Newman & S. H. Strogatz & D. J. Watts,. Working Papers 00-07-042, Santa Fe Institute. (2000)

Watts DJ, Strogatz SH. Nature. 393(6684):440-2 (1998)

Model

- Mathematical realization of our model:
  - *W* is a *n x n* matrix
    - Element *ij* is the strength of the effect of gene *j* on gene *I*
  - *S* is a vector
    - Element *i* is the expression level of gene *i*
  - *F* is a nonlinear function (i.e. hyperbolic tangent)
- We define two types of dynamics:
  - Steady-state
    - The state vectors become equal after some number of iterations.
  - Oscillatory
    - The network oscillates between two states with the number of iterations between cycles as the period length.

$$s_i(t+1) = f\left(\sum_{j=1}^{N} W_{ij}\, s_j(t)\right)$$

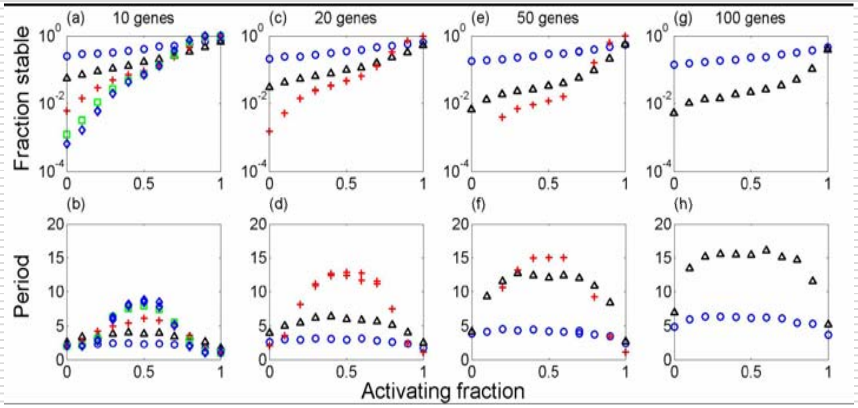


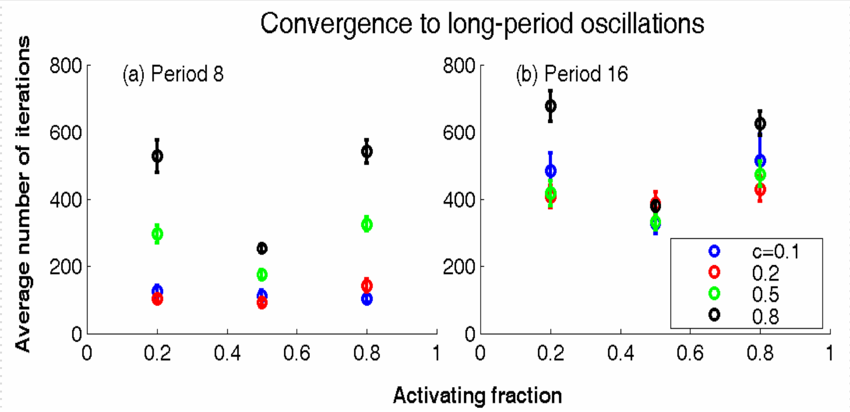
M. Siegal and A. Bergman, Proc Natl Acad Sci U S A. 99(16): 10528–10532 (2002)

Wagner, G. P. Am. Zool. 36: 36-43 (1996)

Random Networks

- Generated using Erdos-Renyi random graph model
  - Constant probability *c* of a connection between any two nodes
- Activating fraction controls the dynamics of the network
  - Small activating fraction: oscillatory dynamics
  - Large activating fraction: steady-state dynamics
- Random graphs evolved using the Great Deluge Algorithm
- Graphs converge faster with an activating fraction near 0.5





Biological Topologies

- Five topologies studied:
  - WNT signaling pathway
  - Notch signaling pathway
  - Nerve Growth Factor network signaling pathway
  - Arabidopsis circadian oscillator (see figure)
  - Drosophila circadian oscillator

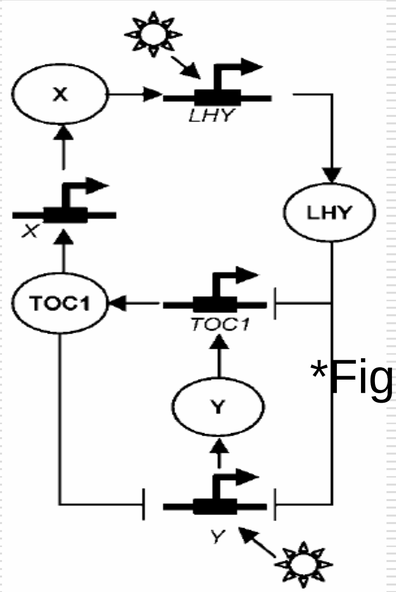
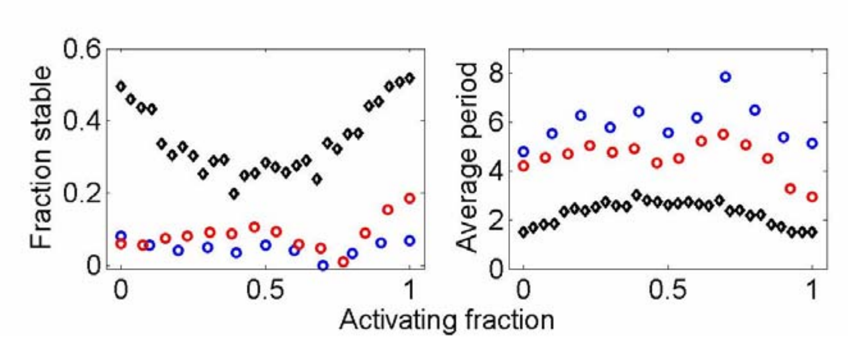


*Figure from…

- Supports our model
- Oscillatory and steady state networks function as expected.



Discussion

- Activating fraction plays a major role in the overall dynamics of networks
  - Randomly generated networks
    - Large *a*: networks tend to reach steady state
    - Small *a*: networks tend to oscillate with period 2
    - Intermediate *a*: networks tend to oscillate with a longer period
  - Network optimization
    - Most rapid convergence to steady-state seen with large *a*
    - Most rapid convergence to long-period oscillations seen with a=0.5
  - Biological network topologies
    - Signalign networks tend to reach steady-state
    - Circadian oscillators tend to oscillate