Analysis of Complex Systems

Lecture 5: Network changes over time: development and deconstruction

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Objectives

Network development

- preferential attachment (-> scale-free)
- gene duplication (-> hierarchy)
- accelerated growth (-> hubs)

Network growth in space

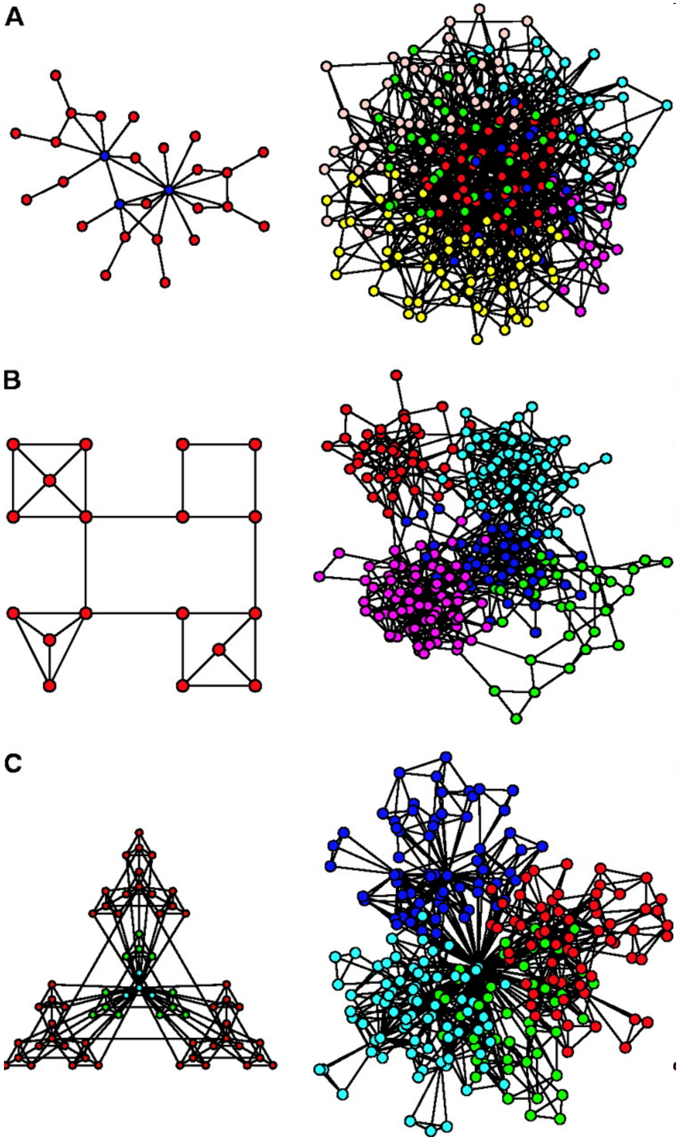
- distance dependence

Network decay

- measures of network integrity
- functional performance

Network development

Developmental goals



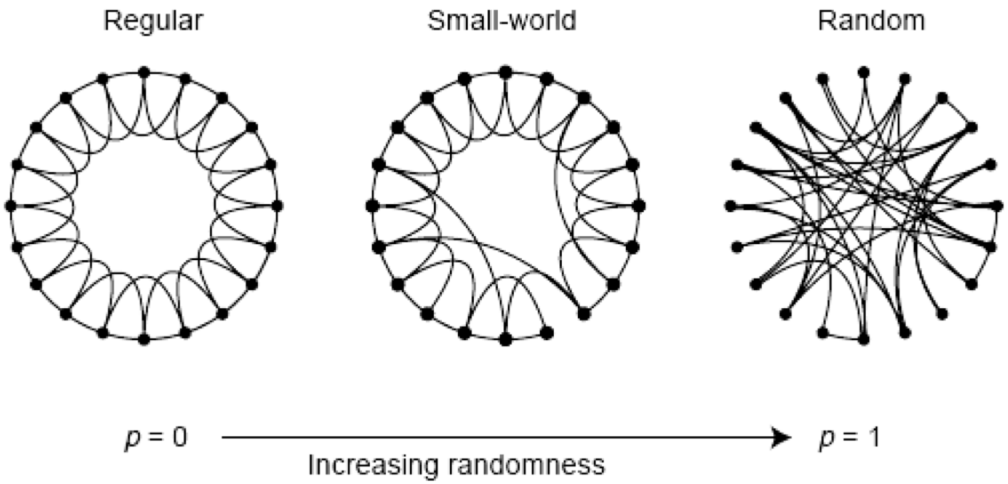
Target-based: generate a specific type of graph

Types could be:

A: scale-free
B: modular (multiple clusters)
C: hierarchical (scale-free topology
with embedded modularity)
D: small-world (not shown)

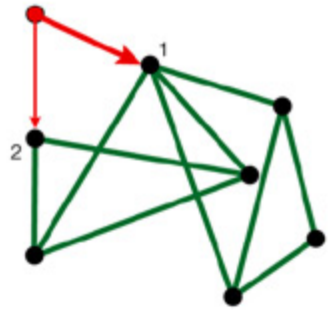
Process-based: generate a network in the same way as natural networks evolve (and see what type of graph emerges)

Generation of small-world networks



Watts & Strogatz, Nature, 1998

Preferential attachment (scale-free)



Start with small core network

Add new node at each time step

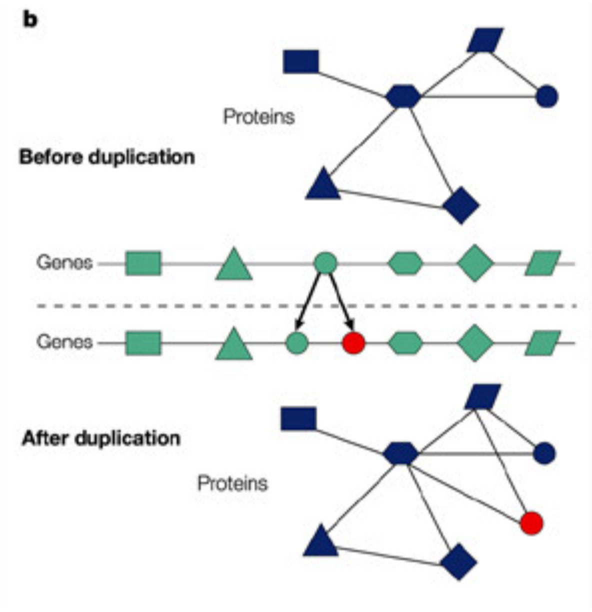
New node establishes connections with existing nodes

Probability for establishing a connection with existing node *i* depends on the relative degree of that node: $\Pi(k_i) = k_i / \Sigma_j k_j$

(‘Rich gets richer’, ‘Matthews effect’)

Barabasi & Albert, Science, 1999

Gene duplication (scale-free)



Gene duplication

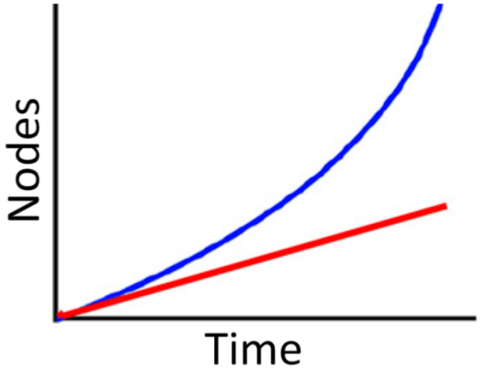
Extra protein -> growth in the protein interaction network

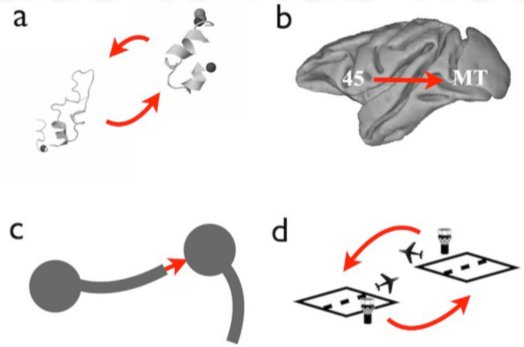
Proteins that interacted with the original duplicated protein will each gain a new interaction to the new protein

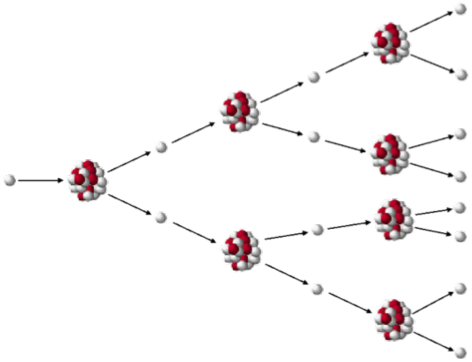
Therefore proteins with a large number of interactions (hubs) tend to gain links more often, as it is more likely that they interact with the protein that has been duplicated.

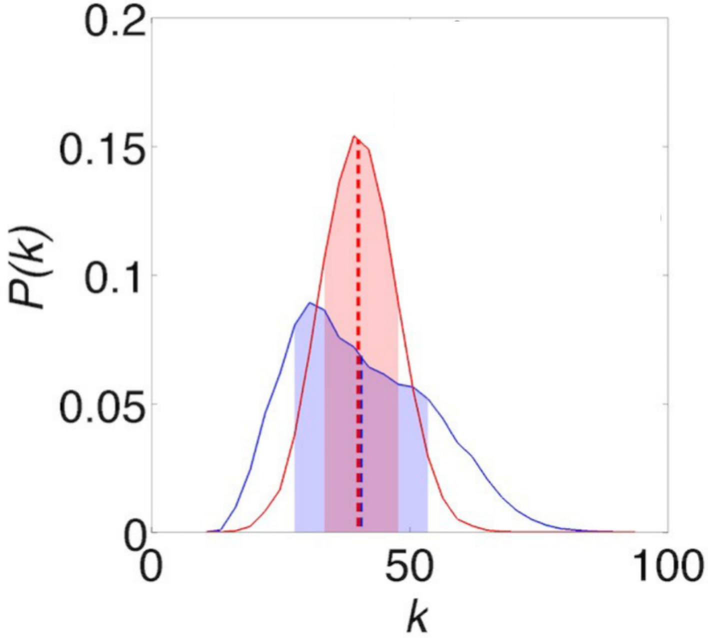
Barabási & Oltvai (2004). Nature Reviews Genetics 5, 101-113

Accelerated growth leads to hub nodes



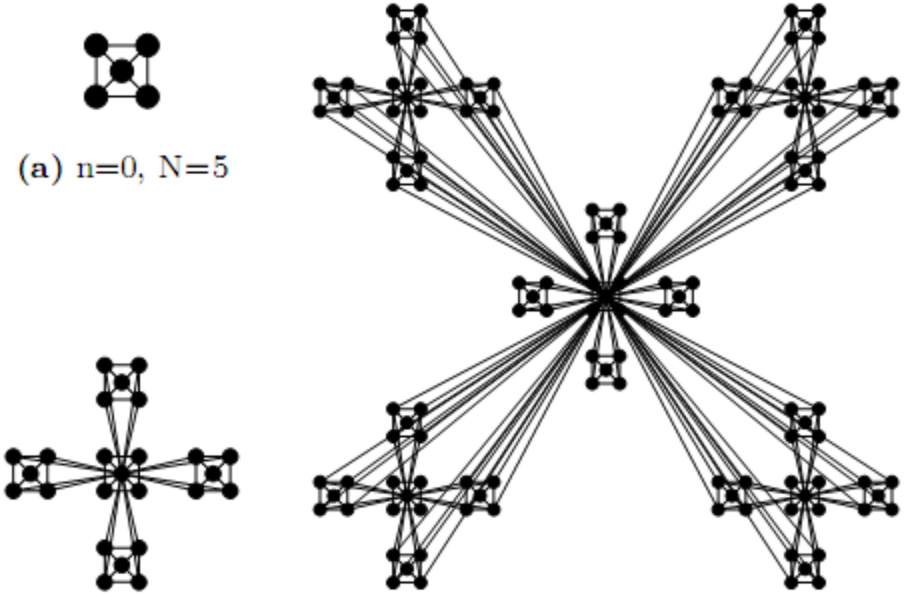






Kaiser (2017) *Trends in Cognitive Sciences*
Bauer & Kaiser (2017) *Royal Society Open Science*

Hierarchical scale-free networks



(a) n=0, N=5

(b) n=1, N=25

(c) n=2, N=125

Starting from a fully connected cluster of five nodes shown in (a), we create four identical replicas, connecting the peripheral nodes of each cluster to the central node of the original cluster (b). In the next step we create four replicas and connect the peripheral nodes again, as shown in (c), to the central node of the original module, obtaining a N = 125 node network.

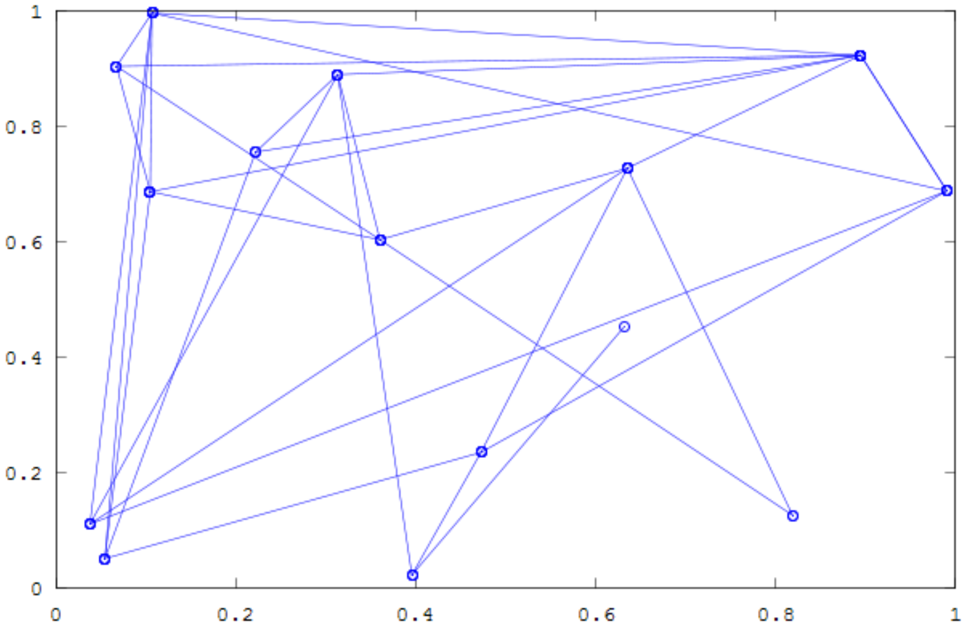
Ravasz & Barabasi (2003). *Phys. Rev. E* **67**, 026112.
Ravasz et al. (2002) *Science* **297**, 1551-1555.

Spatial Network Growth

Spatial Graphs

Spatial graph:

Each node has a spatial coordinate (usually 2D or 3D)



Matlab (random spatial graph with 16 nodes):

```
xy = rand(16, 2);       % random 2D coordinates
A = rand(16)<0.1        % random graph with 10% edge density
gplot(A, xy);           % visualize the network
```

Modeling of spatial network growth

Motivation:

- biological networks (neurons, proteins, animal populations) have a spatial position
- nodes can only interact over a short distance (no complete knowledge of the network!)

Problem with existing growth models:

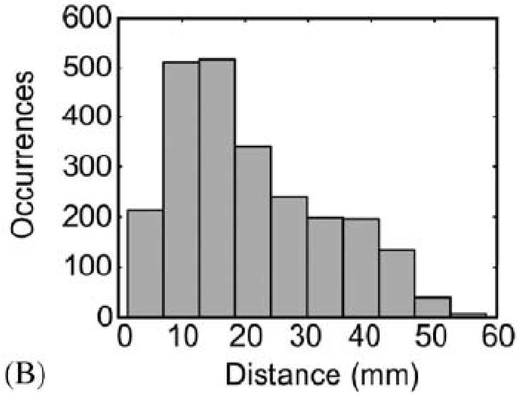
- algorithms are independent of spatial position
- preferential attachment is unlikely due to the spatial distance between nodes

Distance dependence: neural networks

Global connectivity (between areas)

Kaiser & Hilgetag, 2004

Macaque
(one hemisphere)

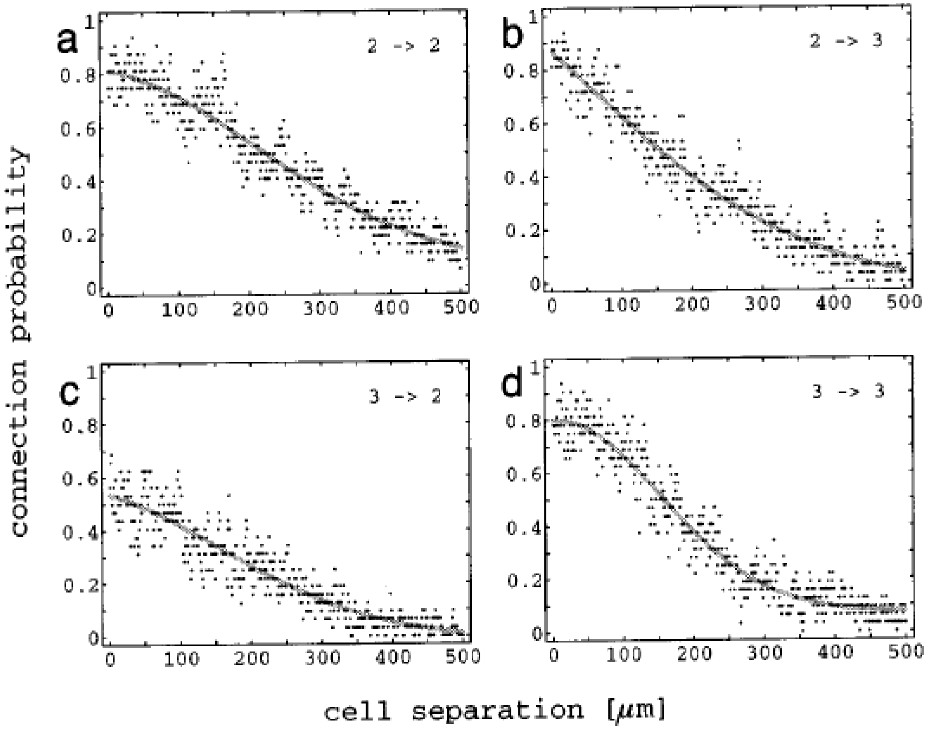


Local connectivity

Braitenberg & Schuez, 1998

Hellwig, 2000

Rat visual cortex
(layers 2, 3)



Distance dependence: protein interaction networks

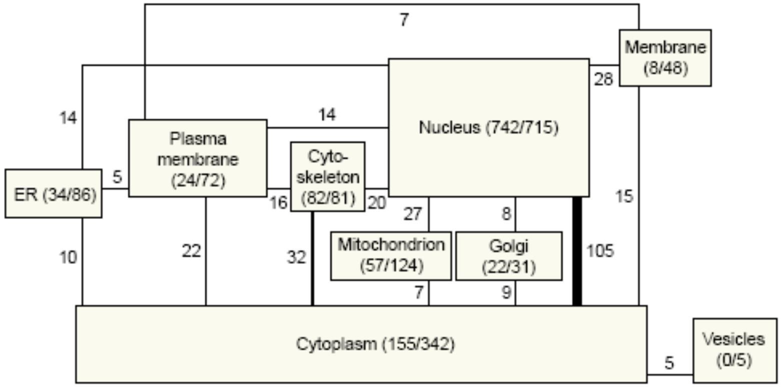
Non-metric distance (ordinal values):

0: same compartment

1: adjacent compartment

2: next-but-one neighbouring compartment

…



Protein-protein interactions occur more often between proteins in same or adjacent reaction compartments

Distance-dependent spatial growth

Models:

- Growth of the Internet* : $P(u,v) = \beta\ e^{\frac{-d(u,v)}{L\ \alpha}}$

Biological reasons for protein interaction distance dependence: physical interaction

Biological reasons for neural distance dependence: Growth factors guide axons over long distances picking up this trace depends on the distance to the source of the growth factor (chemical gradient)

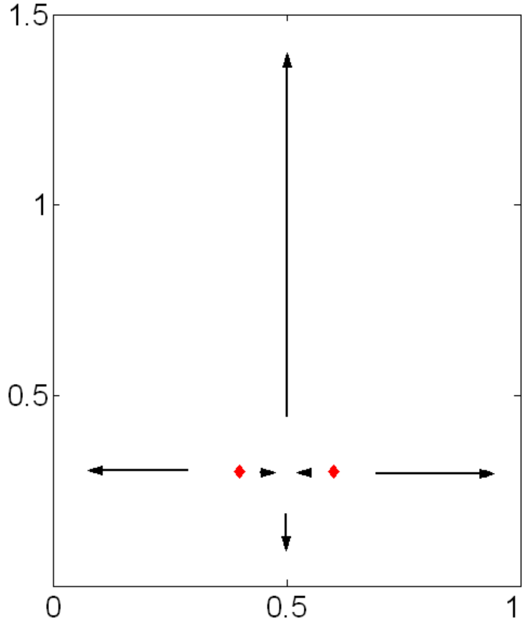
$$c(x,t) = \frac{Q}{2\ \sqrt{\pi}\ D\ t}\ e^{\frac{-x^2}{4\ D\ t}}$$

*** Waxman, IEEE J. Sel. Areas Commun., 6(9):1617–1622**

Spatial Network Growth

- Generate one node after another
- Each new node established links to the existing network
- Edge formation probability depends on spatial distance *d* between nodes *u* and *v*

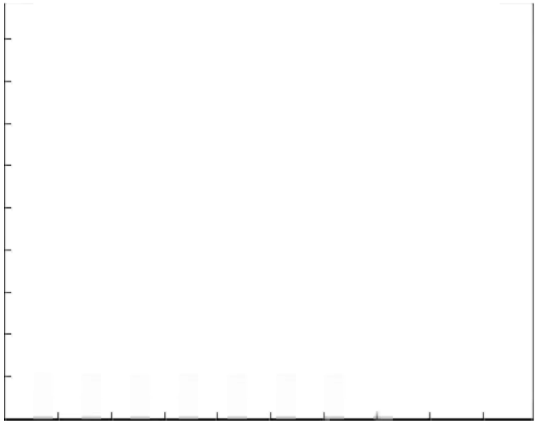
$$P(u,v) = \beta\, e^{-\alpha\ d(u,v)}$$

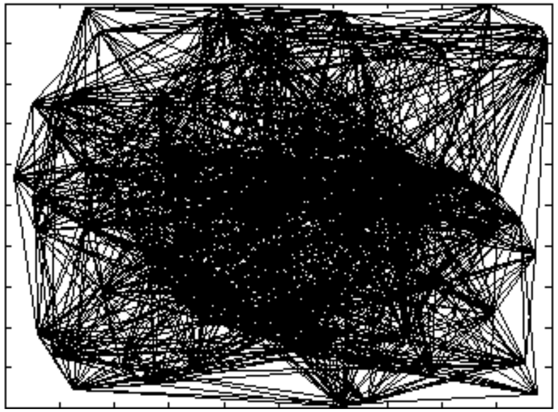


Kaiser & Hilgetag (2004). Spatial Growth of Real-world Networks. *Phys. Rev. E* 69:036103

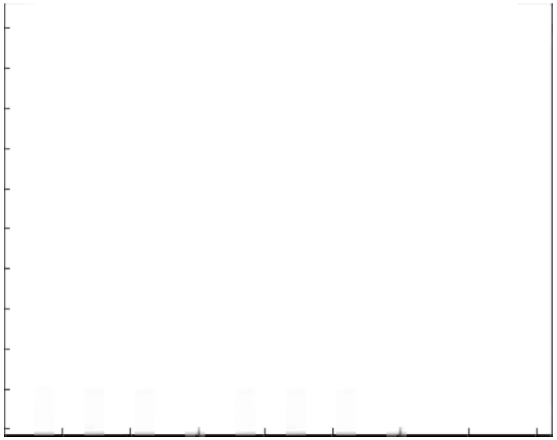
Role of borders

Borders (limited)

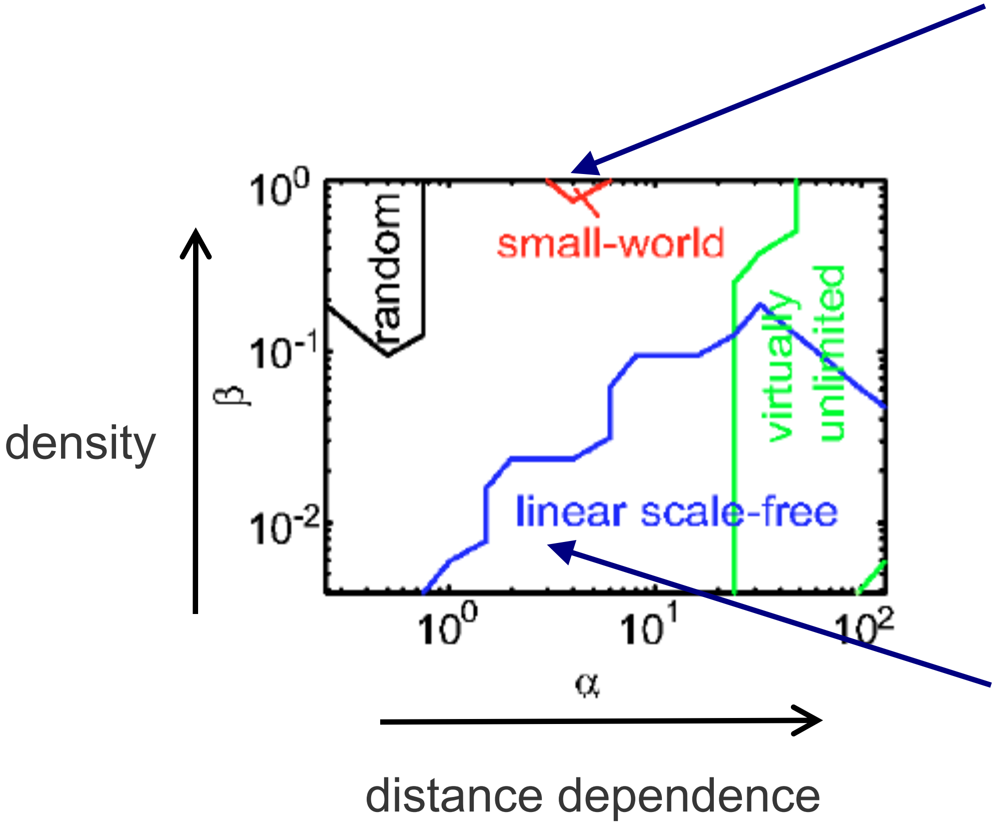




Unlimited growth



Resulting network topology



Cortical Networks

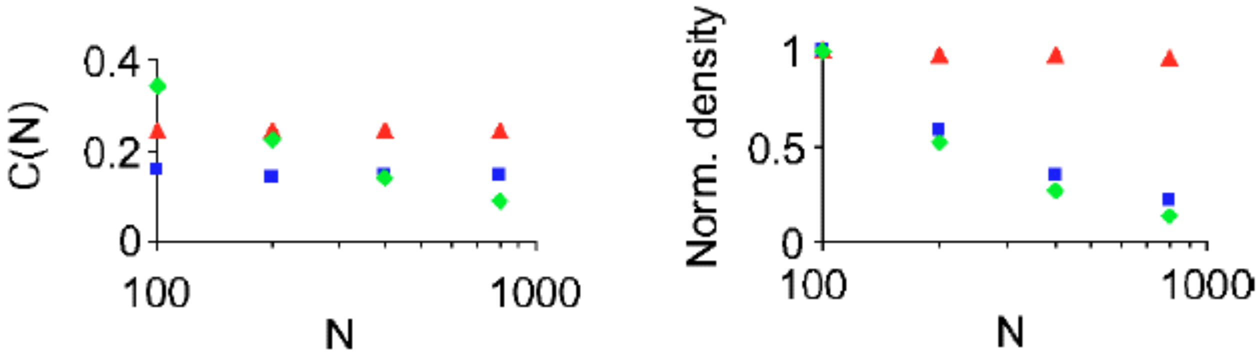
density

distance dependence

Yeast Protein-Protein Interaction Network

Kaiser & Hilgetag (2004). Spatial Growth of Real-world Networks. *Phys. Rev. E* 69:036103

Distinguishing growth types by network evolution

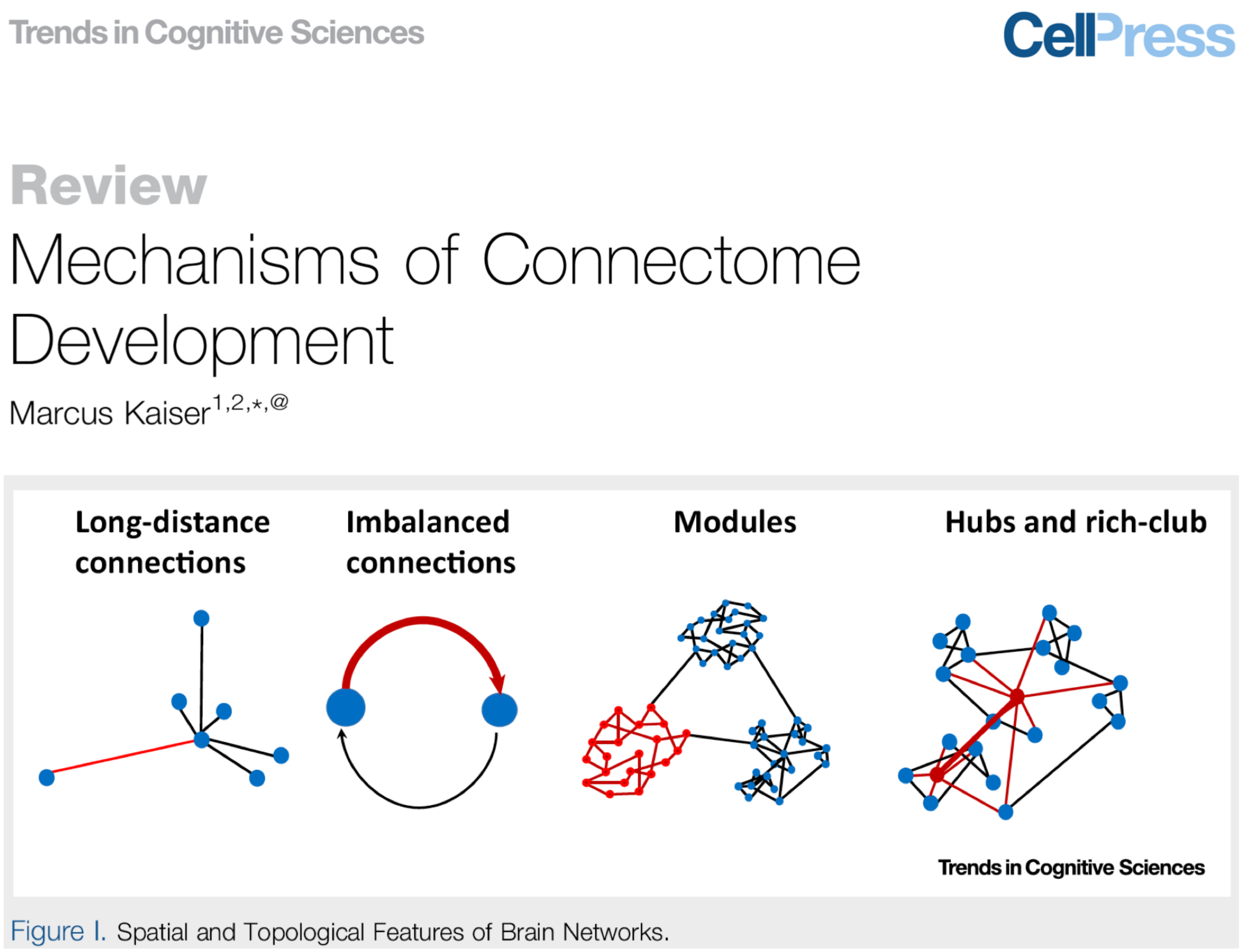


Limited spatial growth

Unlimited spatial growth

Preferential attachment (BA-Model)

Kaiser & Hilgetag (2004). Spatial Growth of Real-world Networks. *Phys. Rev. E* 69:036103



Trends in Cognitive Sciences

CellPress

Review

Mechanisms of Connectome Development

Marcus Kaiser[1,2,*,@]

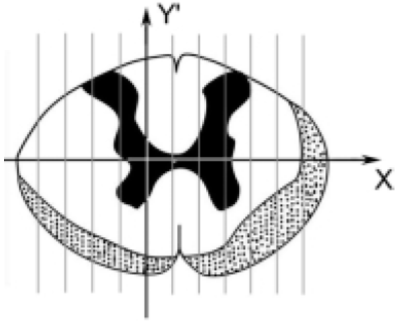
Figure I. Spatial and Topological Features of Brain Networks.

Kaiser (2017) *Trends in Cognitive Sciences*

Network changes (Robustness)

Neural robustness against network damage (lesions)

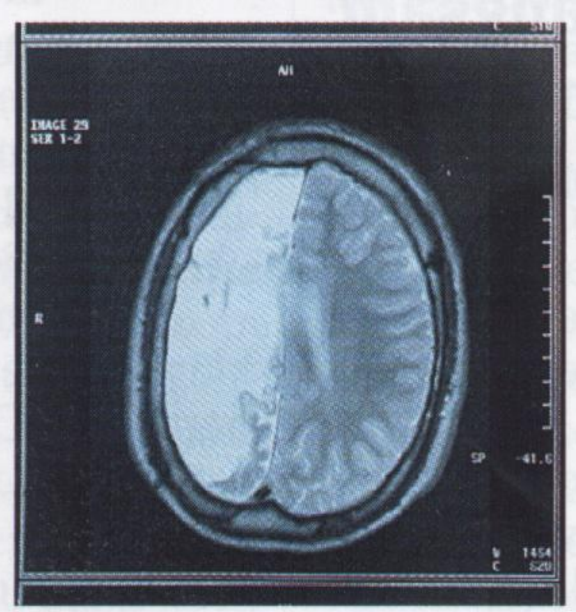
Rats: Spinal chord injury



large recovery possible with as few as 5% of remaining intact fibers

You et al., 2003

Human: Compensation for loss of one hemisphere at age 11

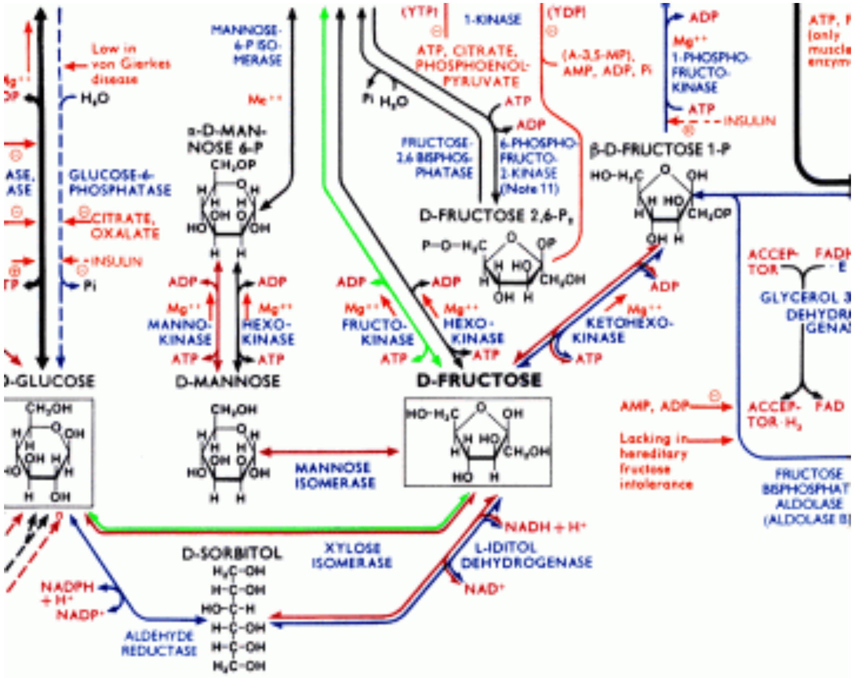


Cellular robustness against damage (gene knockouts)

- Mutations can be compensated by gene copies or alternative pathways*:

  ~70% of single-gene knockouts are non-lethal

- The metabolism can adjust to changes in the environment (e.g. switch between aerob and anaerob metabolism)



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[*] **A. Wagner. Robustness against mutations in genetic networks of yeast. *Nature Genetics*, 24, 355-361 (2000).**

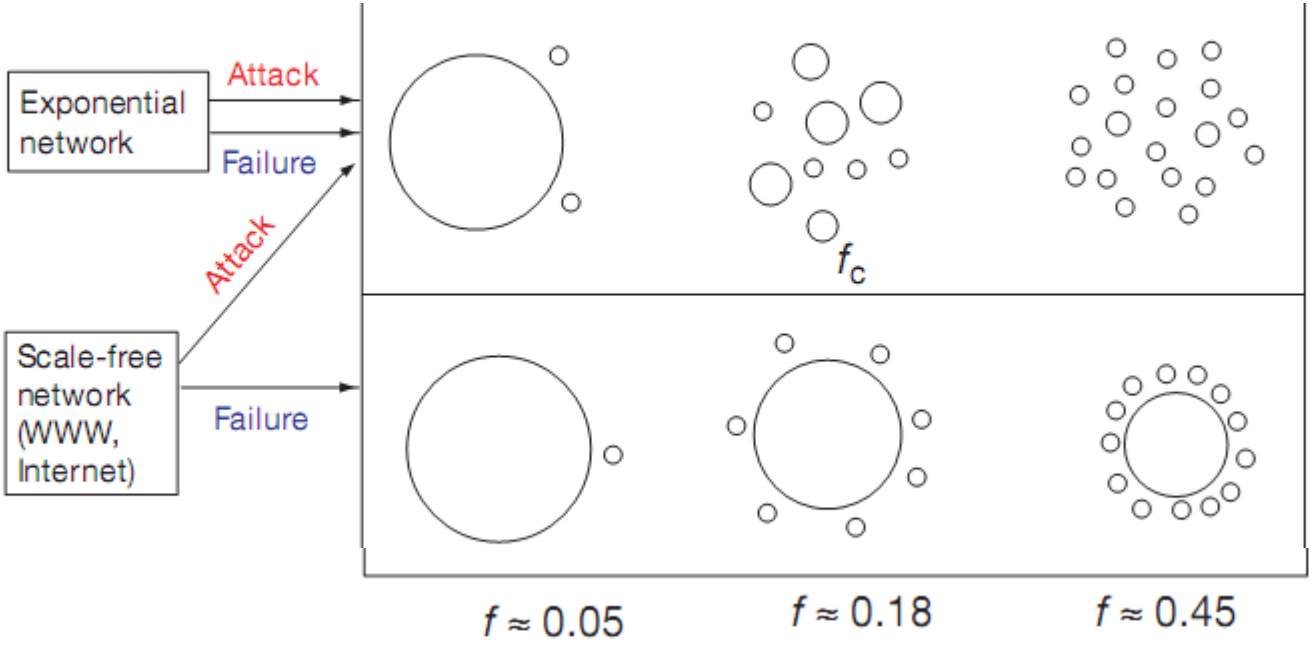
Measures of structural integrity

How is the global topology of the network affected?

Idea: Changes in *structural* properties might indicate *functional* changes (like lower performance of the system)

	Structural measure	Potential functional impact	
⬆	All-pairs shortest path	longer transmission time	Alzheimer
⬇	Reachability ⬆ Fragmentation	occurrence of isolated parts (components)	
⬇	Clustering coefficient	less interaction within modules	Schizophrenia

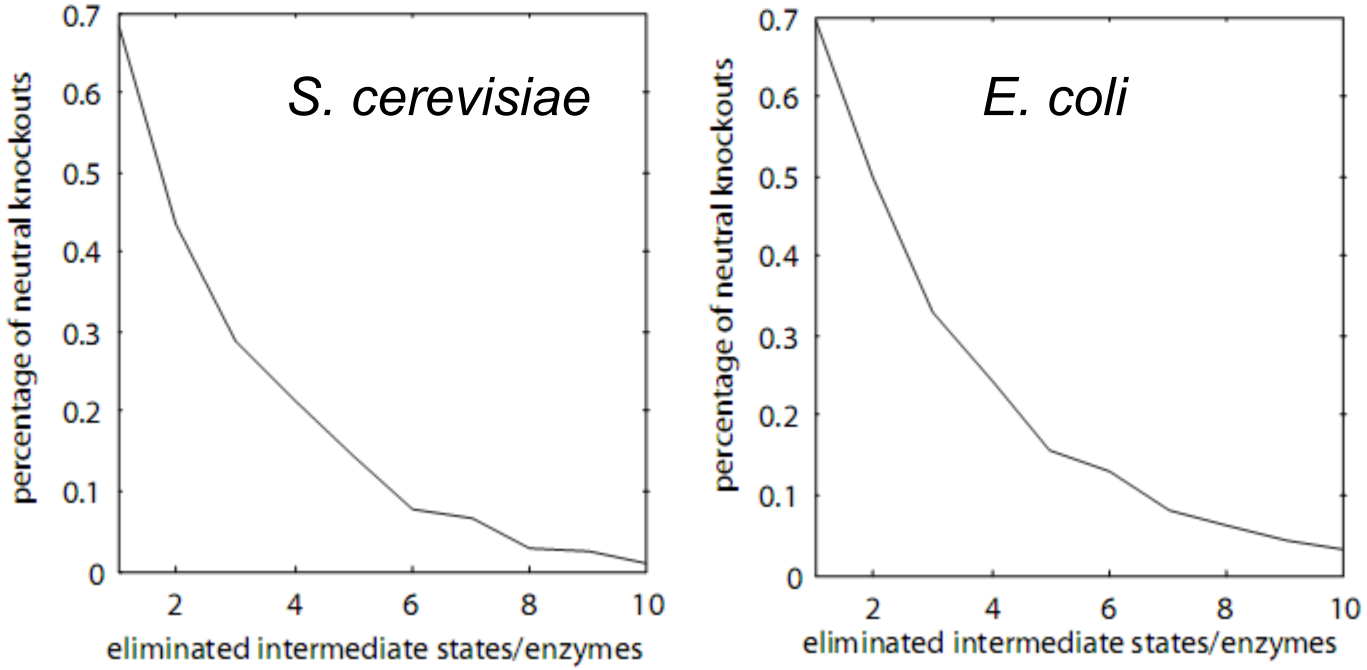
Example: fragmentation



f: fraction of removed nodes
f_c: fraction where the network breaks into small fragments

Albert R, Jeong H, Barabasi AL (2000) Nature 406: 378–382

Example: shortest paths after gene knockouts



Neutral knockout: no reduction of shortest path lengths (alternative pathway of the same length was available)

One removed enzyme can correspond to several removed links in the metabolic network!

Neutral single-enzyme (“single-gene”) knockout in 70% of the cases as for experimental knockout studies!

Measures of functional performance

After deletion of nodes or edges, measures for functional performance could decrease (or increase!)

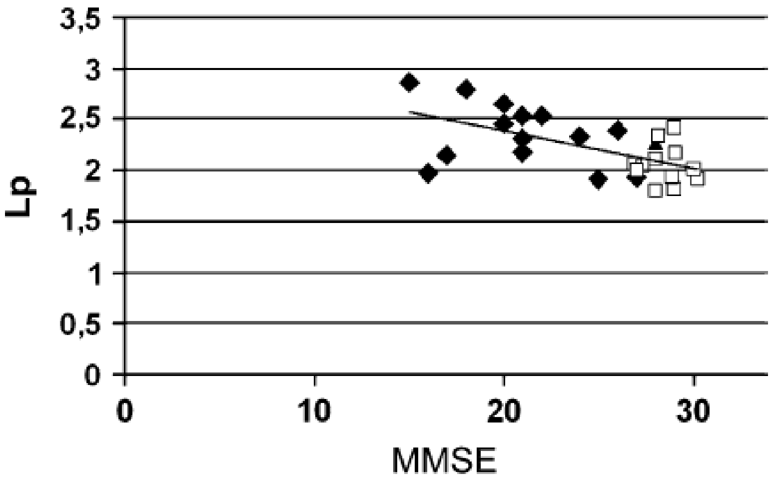
Response time (patients) or processing time (computers)

Substrate consumption in gene knockout experiments

Etc.

Example: cognitive deficits

Alzheimer



MMSE: Mini Mental State Examination

Diamonds: Alzheimer patients

Empty squares: Control

Lp: Characteristic Path Length

Stam et al. (2007) Cerebral Cortex, 17:92

Summary

- How can small-world, scale-free, or hierarchical networks be generated?
- What is a spatial graph? What does distance dependence mean?
- What are measures of network integrity and how do they indicate functional performance?

Q&A – 1

1. Preferential attachment to highly-connected nodes results in scale-free networks. Can you think of other preferences and their effect on the resulting network?

2. What models for generating spatial graphs do you know?

3. What nodes or edges would you assume to have the largest impact on network integrity (see previous lecture)?