Novel network centrality and community measures

and their changes in crisis and adaptation

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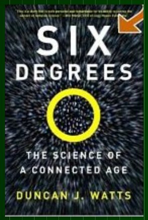
Advantages of network multi-disciplinarity

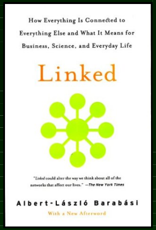
Networks have general properties

- small-worldness
- hubs (scale-free degree distribution)
- nested hierarchy
- stabilization by weak links

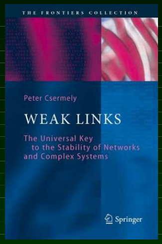
Karinthy, 1929



Watts & Strogatz, 1998



Barabasi & Albert, 1999



Csermely, 2004; 2009

Generality of network properties offers

- judgment of importance
- innovation-transfer across different layers of complexity

Example to break conceptual barriers

Early-warning signals for critical transitions

Marten Scheffer[1], Jordi Bascompte[2], William A. Brock[3], Victor Brovkin[5], Stephen R. Carpenter[4], Vasilis Dakos[1], Hermann Held[6], Egbert H. van Nes[1], Max Rietkerk[7] & George Sugihara[8]

ecosystem, market, climate
- slower recovery from perturbations
- increased self-similarity of behaviour
- increased variance of fluctuation-patterns

Nature 461:53

Aging is an early warning signal of a critical transition: death

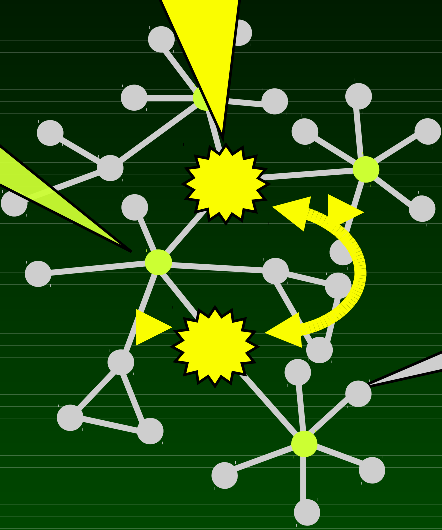
Prevention: elements with less predictable behaviour
- omnivores, top-predators
- market gurus
- stem cells

Csermely et al., Science Signaling 4:pt3

Creative nodes: central, but unpredictable

Creative: few links to hubs, unexpected re-routing, flexible, **unpredictable**

Distributor: hub, specialized to signal distribution, **predictable**



Problem solver: specialized to a task, **predictable**

change of roles

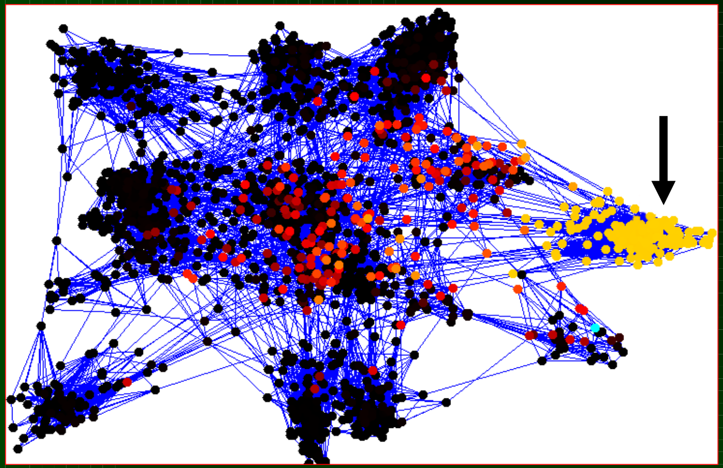
Csermely,
Nature 454:5
TiBS 33:569
TiBS 35:539

3 novel types of dynamic centrality

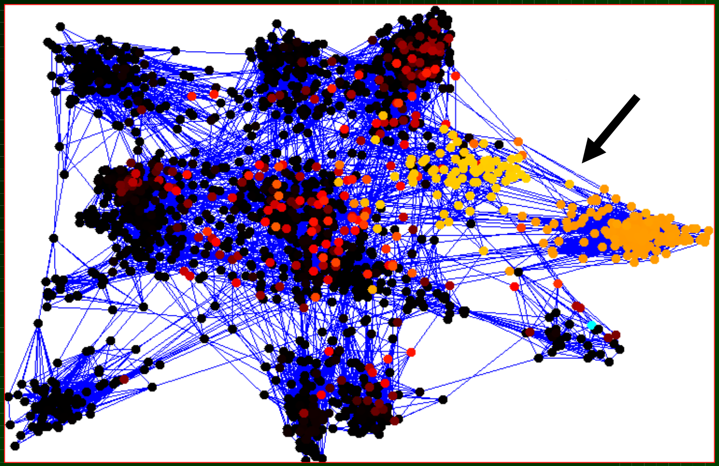
- topological centrality is key for perturbation dissipation
  (Turbine: www.linkgroup.hu/Turbine.php)
- game-centrality: prediction of biological regulators
  (NetworGame: www.linkgroup.hu/NetworGame.php)
- community centrality: prediction of survival importance
  (ModuLand: www.linkgroup.hu/modules.php)

Hubs + inter-modular nodes are top transmitters of network perturbations

Start: module-centre hub



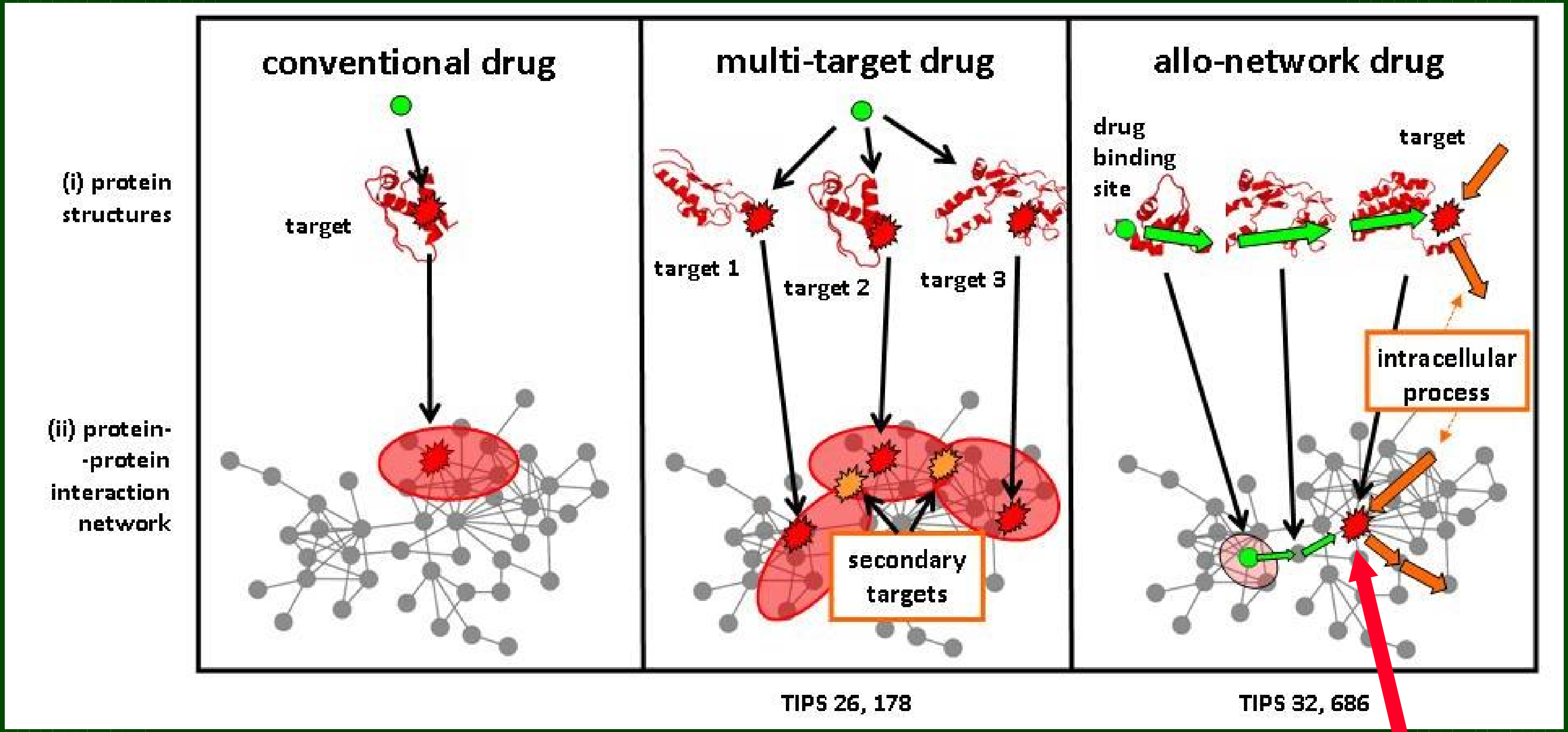
Starting node: bridge

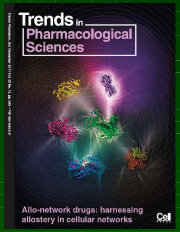


Szalay & Csermely, Science Signaling 4:pt3

www.linkgroup.hu/Turbine.php

Use of network perturbations: allo-network drugs





Nussinov *et al*, Trends Pharmacol Sci 32:686

+ hit of intra-cellular paths

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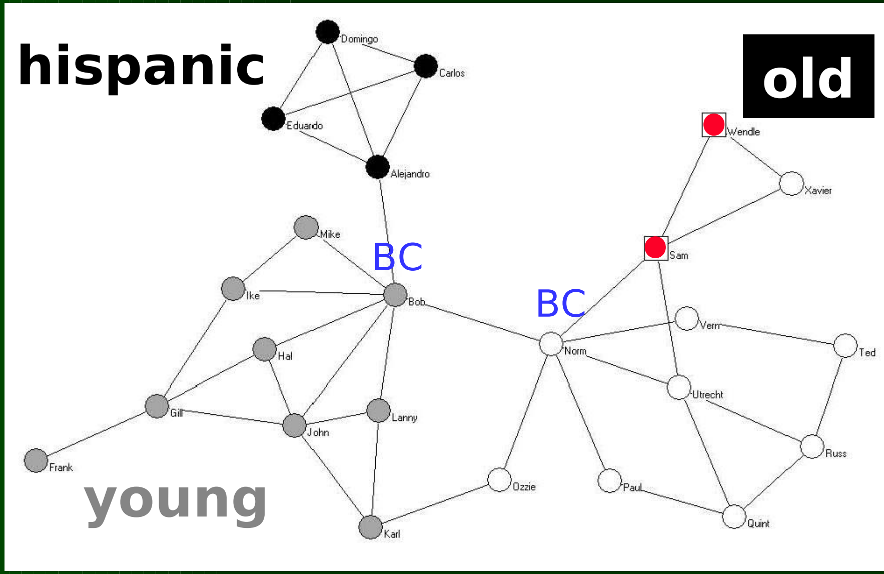
Game-centrality: prediction of key nodes to break cooperation



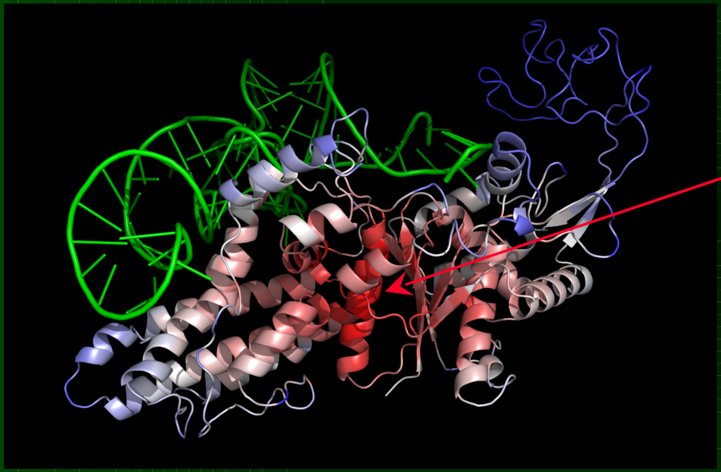
● union leaders: strike

BC sociogram leaders: work

Hawk-dove game *(PD game: same)*
Start: all-cooperation = strike
Strike-breaker: defects
BC-s are the best strike-breakers

Wang, Szalay, Zhang & Csermely, PLoS ONE 3:e1917;
Simko & Csermely, Science Signaling 4:pt3
www.linkgroup.hu/NetworGame.php
Michael's strike network; Michael, Forest Prod. J. 47:41

Bridges are crucial for cooperation



- Met-tRNA-synthase protein structure network signaling amino acids *(Ghosh, PNAS 104:15711)*: largest game-centrality
- yeast protein-protein interaction network amino acids regulating evolution *(Levy, PLoS Biol 6:e264)*: large game centrality

Simko & Csermely, in preparation
www.linkgroup.hu/NetworGame.php

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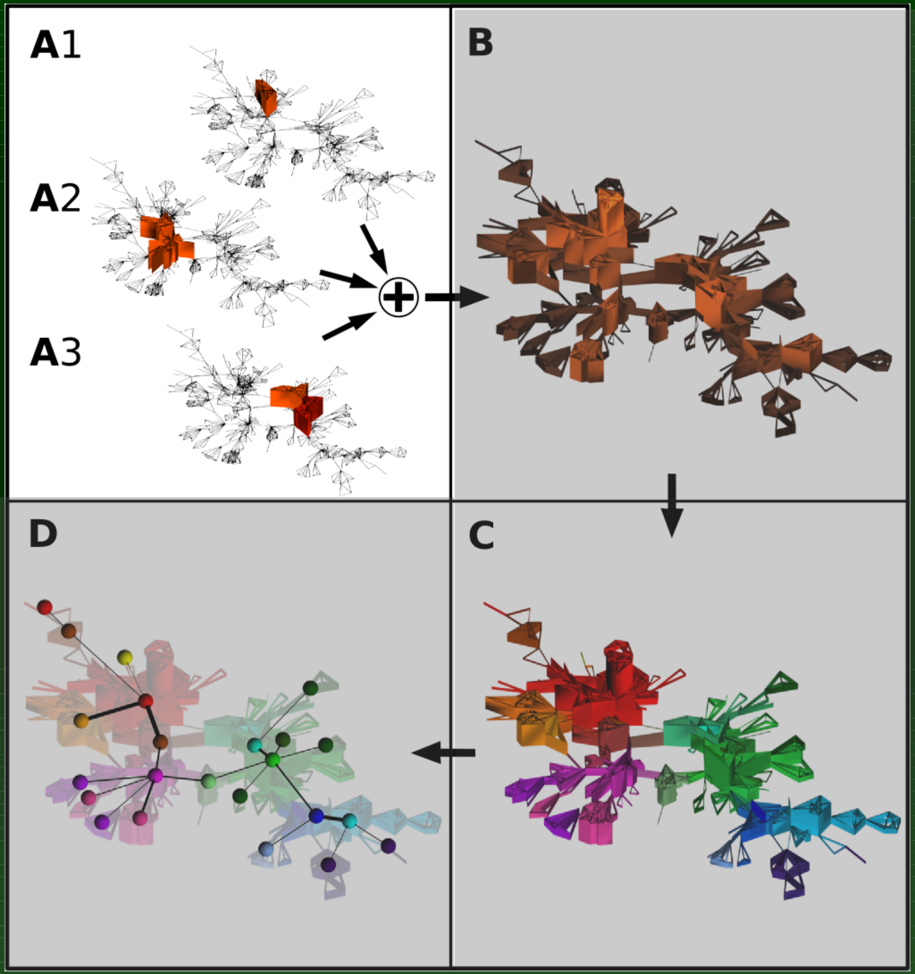
The ModuLand method family detects overlapping network communities

influence zones of all nodes/links

community landscape

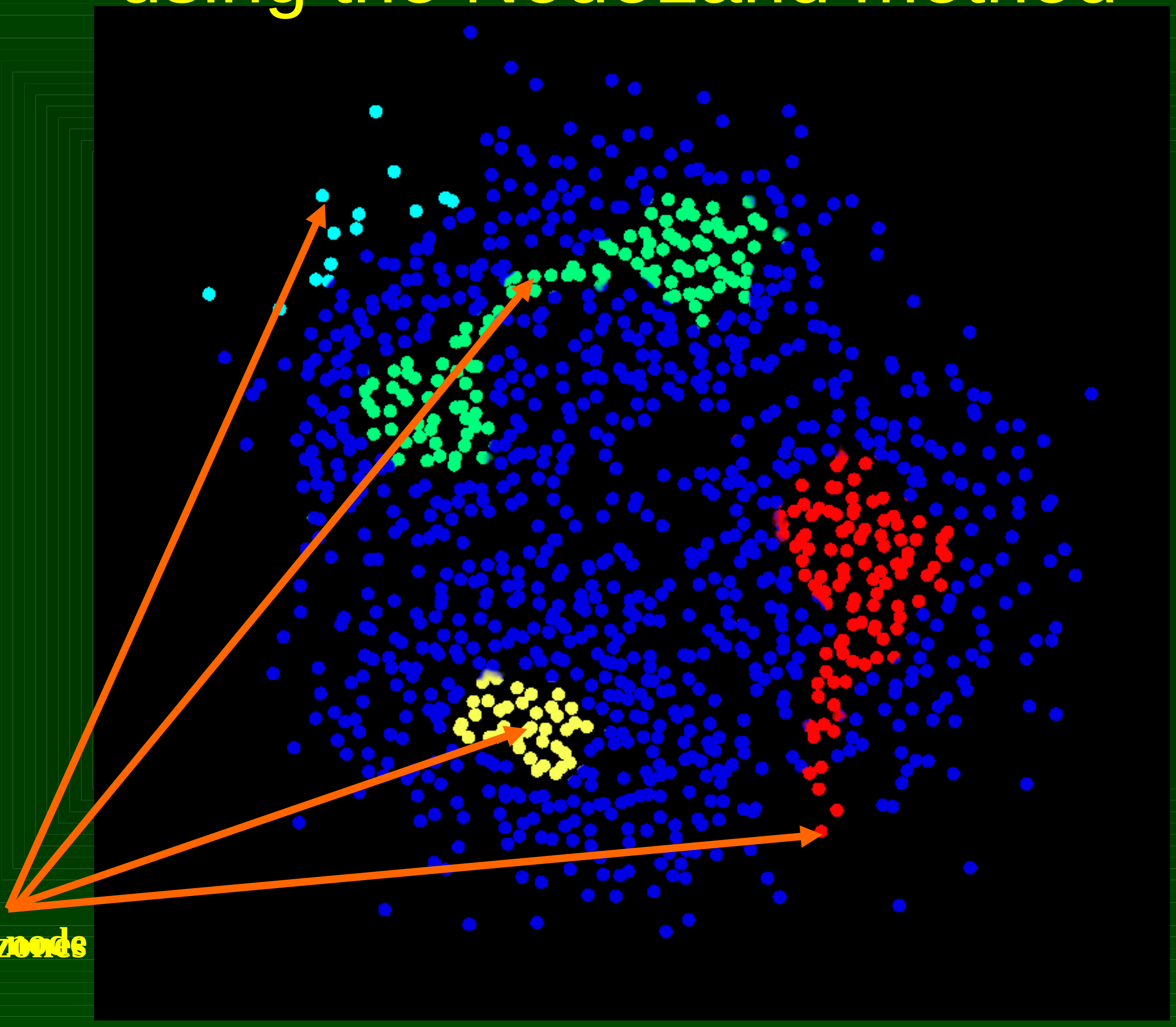


network hierachy

communities as landscape hills

Kovacs *et al*, PLoS ONE 5:e12528
www.linkgroup.hu/modules.php
network of network scientists; Newman PRE 74:036104

Influence zones
using the NodeLand method



community-44: 1127 schoolchildren, 5096 friendships; Add-Health

The ModuLand method family detects overlapping network communities

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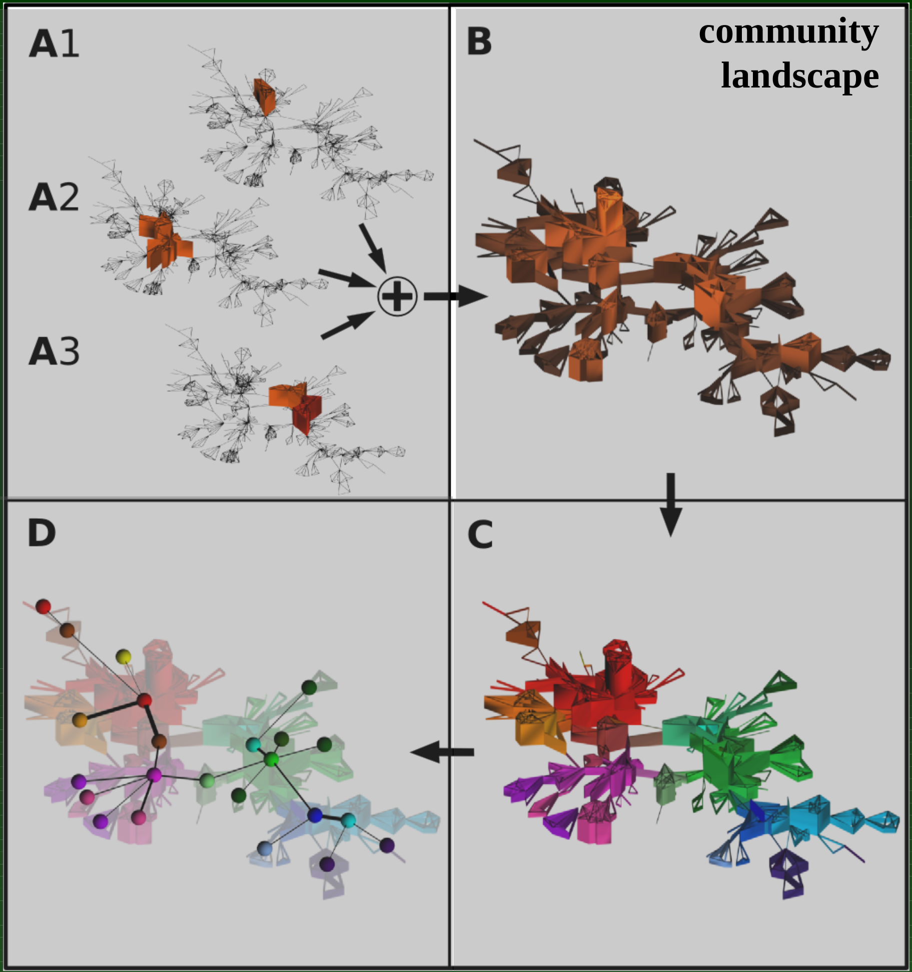


community centrality: a measure of the influence of all other nodes

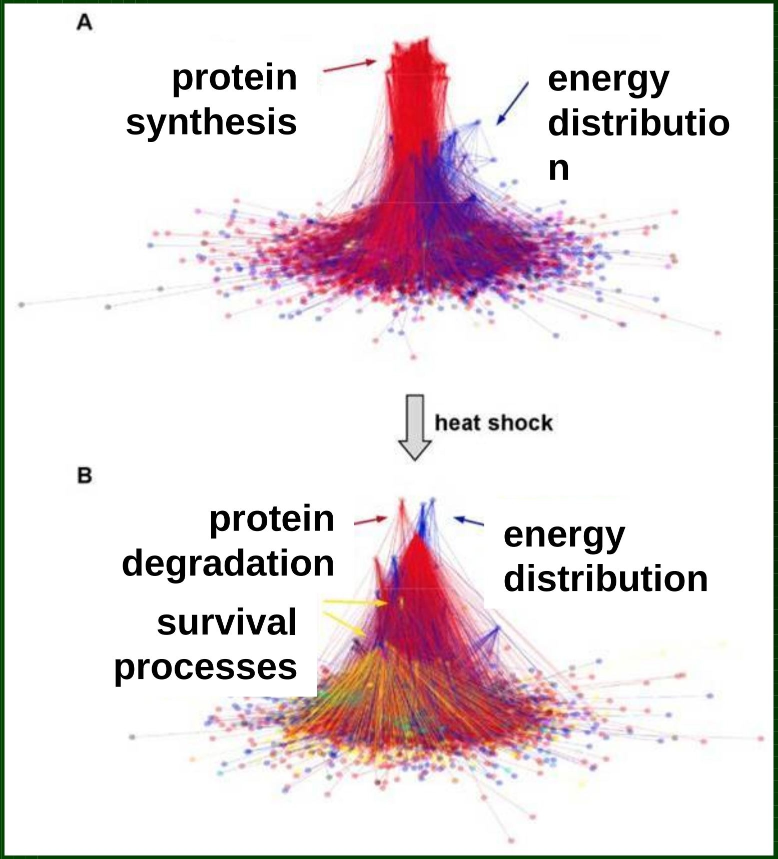
communities as landscape hills

available as a Cytoscape plug-in

Kovacs *et al*, PLoS ONE 5:e12528
www.linkgroup.hu/modules.php
network of network scientists; Newman PRE 74:036104

shows the centre of modules too!

Community centrality reflects the importance in stress-survival

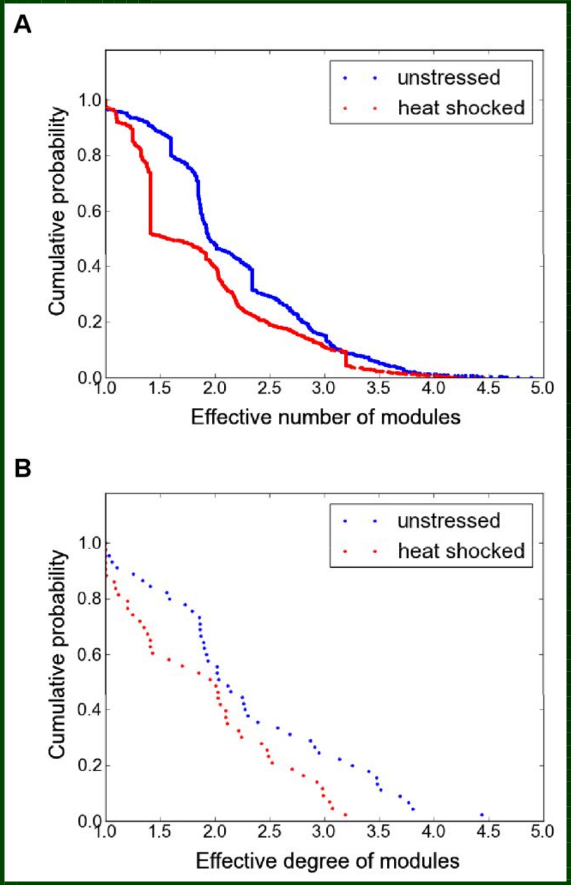


community centrality

- yeast protein-protein interaction network: 5223 nodes, 44314 links
- stress: 15 min 37°C heat shock
- link-weight changes: mRNA expression level changes

Csermely & Mihalik
PLoS Comput. Biol. 7:e1002187

Changes of yeast interactome in crisis: a model of systems level adaptation



- *BioGrid yeast interactome: 5223 nodes, 44314 links*
- *stress: 15 min 37°C heat shock*
- *link-weight changes: mRNA expression level changes*
- *ModuLand program, PLoS ONE 5:e12528*

Stressed yeast cell:

- nodes belong to less modules
- modules have less intensive contacts

smaller overlaps between modules

Csermely & Mihalik
PLoS Comput. Biol. 7:e1002187

Consequences of network crisis-adaptation

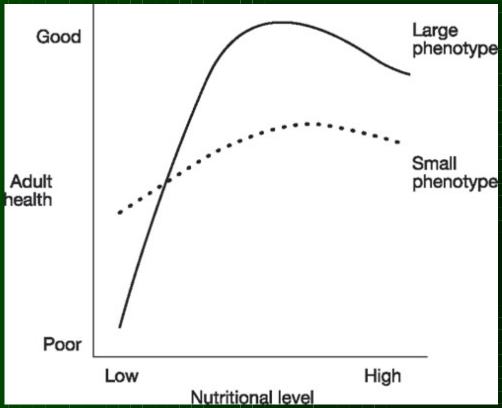
more cohesive and separated network communities

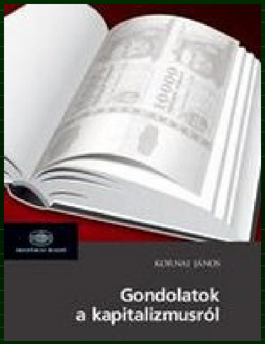
- spared links
- noise and damage localization
- modular independence: larger response-space, conflict-management

Generality: emergence of two phenotypes

- robust in yeast: many PPI-s, many types of stresses
- ecosystems: food limitation see otters, patchiness in drought
- brain: modular reorganization in learning
- social networks: Uzzi: broker stress, Estrada: model system
- economy: Schumpeterian creative destruction
  Haldane & May: US Volcker Rule separates bank system modules

Many resources: large phenotype
few resources: small phenotype





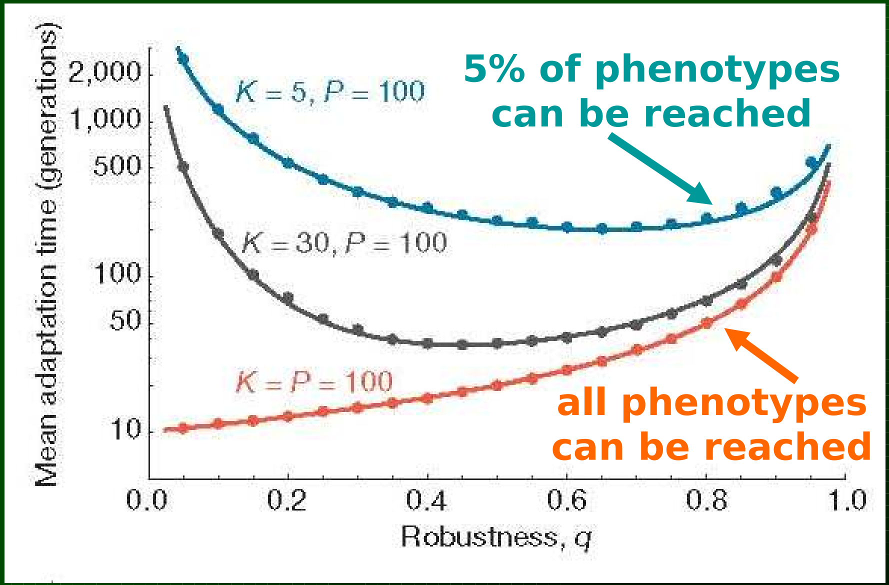
Bateson et al.
Nature 430:419

Janos Kornai: Thoughts about capitalism
(*in Hungarian, in preparation in English*)

Metabolism:
large: rapid, overspending
small: slow, 'thrifty'
'overeating' society: diabetes

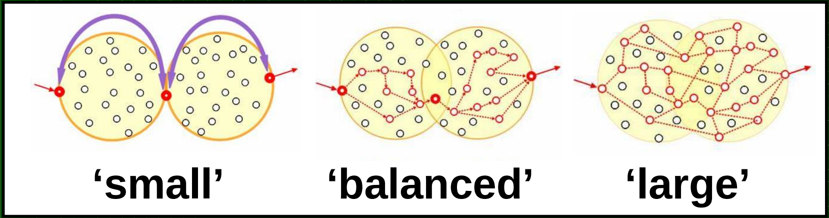
Society:
large: capitalism
small: socialism
surplus and shortage economies

Low adaptation potential of ‘small’ and large’ phenotypes



Draghi, Parsons, Wagner & Plotkin, Nature 463:353

stress, crisis

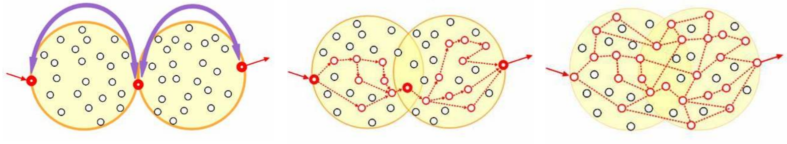


−	+	+	**possibility of adaptation**
+	+	−	**effect of adaptation**

Take-home messages

1. Perturbation, game and community centralities are useful to reveal functionally important nodes

2. Community rearrangements may be a general mechanism of system level adaptation



'small' 'balanced' 'large'

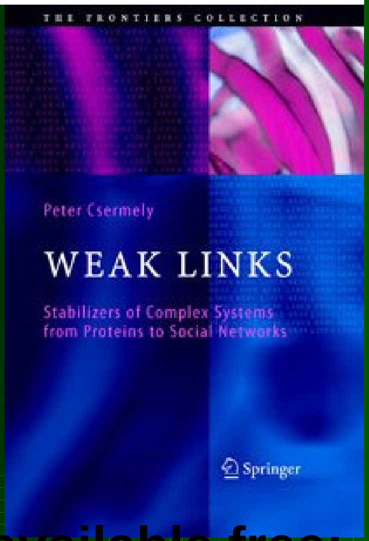
A network component of evolvability?

−	+	+	possibility of adaptation
+	+	−	effect of adaptation

stress, crisis

Acknowledgments

Peter Csermely:
Weak Links
Springer, 2009



available free:

Google-books

www.linkgroup.hu
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Turbine algorithm: perturbation model

$$\frac{dE}{dt} = -\sum_{i=0} l\left(\frac{E - E_e}{2} w_i\right) - D_0$$

dissipation of perturbations

$$\frac{dw_l}{dt} = C_s\left((E_s - E_e)w_l\right)^2 - (A_s + A_e)t^2$$

'learning' – 'aging': changes of link weights

$$\frac{dw_c}{dt} = -C_w \frac{dw_l}{dt}\frac{1}{l}$$

attenuation of other links, if a link gains weight

E_s, free energy of starting node; E_e, free energy of the other node on the link; *l*, degree; *w*, link weight; D_0, dissipation constant; C_s, amplification constant; *A*, aging sensitivity; C_w, attenuation constant

if perturbation exceeds a limit: links are exchanged to half as many random links

Farkas *et al.*, Science Signaling 4:pt3

www.linkgroup.hu/Turbine.php

Importance of modular overlaps

of protein-protein interaction networks in stress

networks:
- STRING 7 (**5329**/190018)
- BioGRID (**5329**/91749)
- Ekman (**2444**/6271)

weights:
- equal units
- proteins (Nature 441:840)
- mRNA-s (Cell 95:717)

resting protein weight

multiplication

average

resting link-weight

mRNA expression

continuous weights | **discrete weights**

unique stress | **average stress**

stressed protein weight

multiplication

average

stressed link-weight

13 stress conditions, 65 experiments
(Gasch et al, Mol. Biol. Cell 11:4241)

6 stress conditions, 32 experiments
(Causton et al, Mol. Biol. Cell 12:323)

Mihalik & Csermely
PLoS Comput. Biol. 7:e1002187

analysis of overlapping network modules:
ModuLand method