Strong community organization of populations can promote long-term recurrence of epidemic diseases

Sitabhra Sinha

in collaboration with

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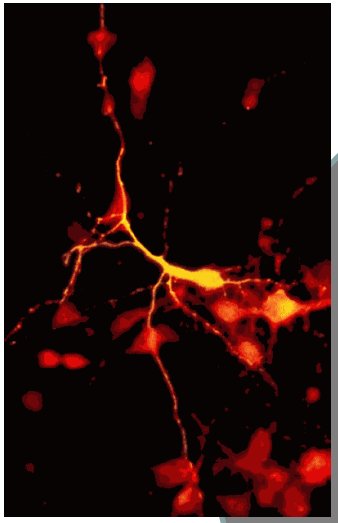
K Chandrashekar (IMSc)

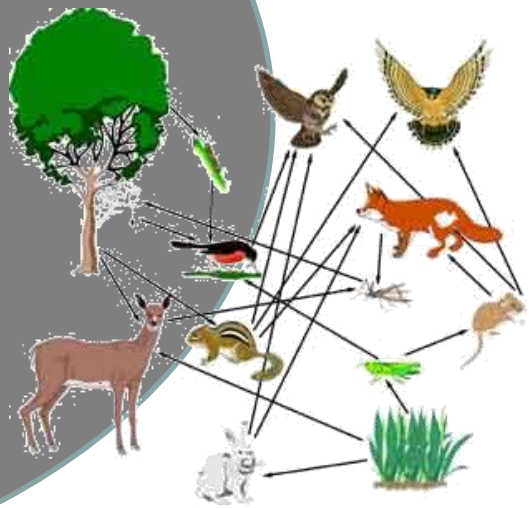
Brain cortical organization

Epidemics in society

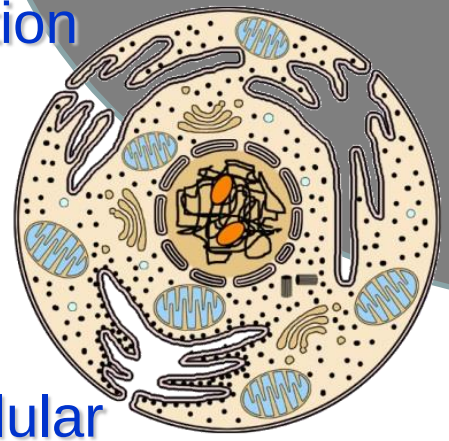


Neuronal communication

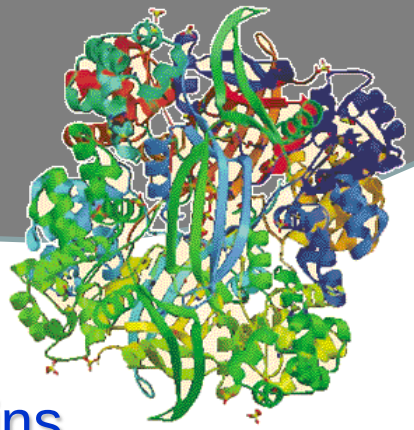
Complex Networks Research in our group



Food webs

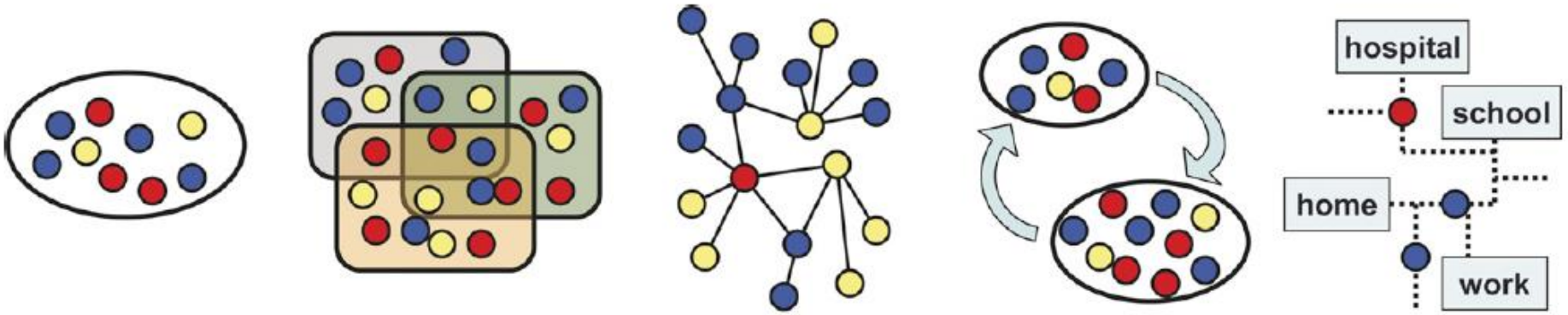


Intra-cellular signalling



Proteins

Multiple Scales of Epidemic Models

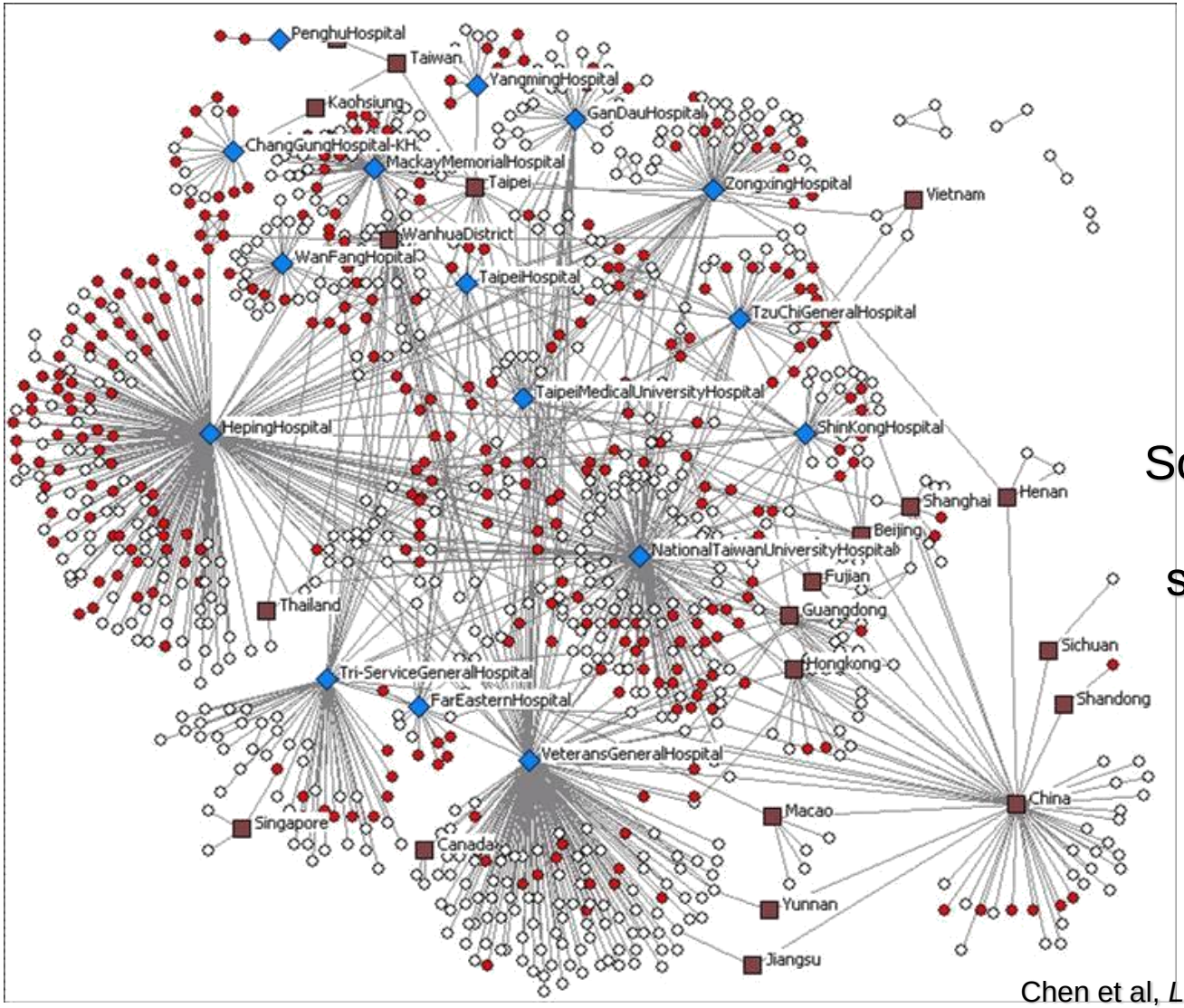


Homogeneous mixing	Social structure	Contact network models	Multi-scale models	Agent Based models
No consideration of spatial or social structure in a community	Individuals grouped according to demographic properties: age, gender,…	Agents affect those who are in direct contact with them	Spreading between communities in different spatial locations	Detailed consideration of spatial movements & interpersonal contact

V Colizza,,M Barthelemy,A Barrat and A Vespignani, *Comptes Rendus Biologies* **330**: 364-74 (2007)

Importance of contact network structure

Contagion propagation in society through contact



Spread of SARS from Taiwan, 2003

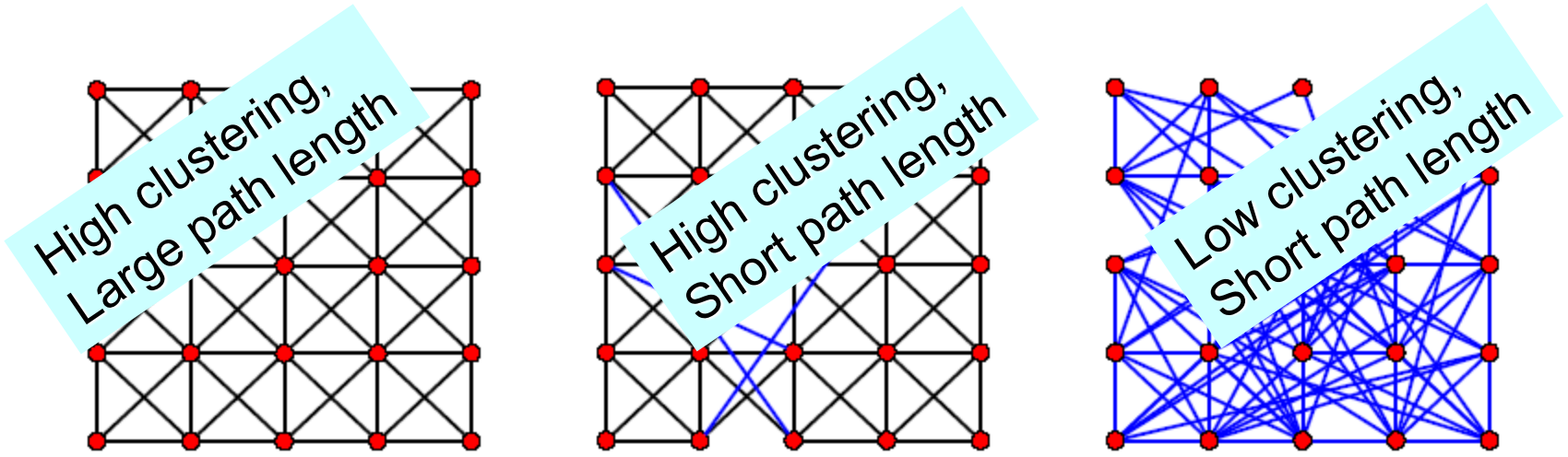
"The small-worlds of public health" (CDC director)

Social contact networks over which epidemics spread have "modular" character

Chen et al, *Lect Notes Comp Sci* 4506 (2009) 23

"Small-world" networks

Watts and Strogatz (1998): Many biological, technological and social networks have connection topologies that lie between the two extremes of completely regular and completely random.



Regular Network
p = 0

"Small-world" Network
0 < p < 1

Random Network
p = 1

Increasing Randomness

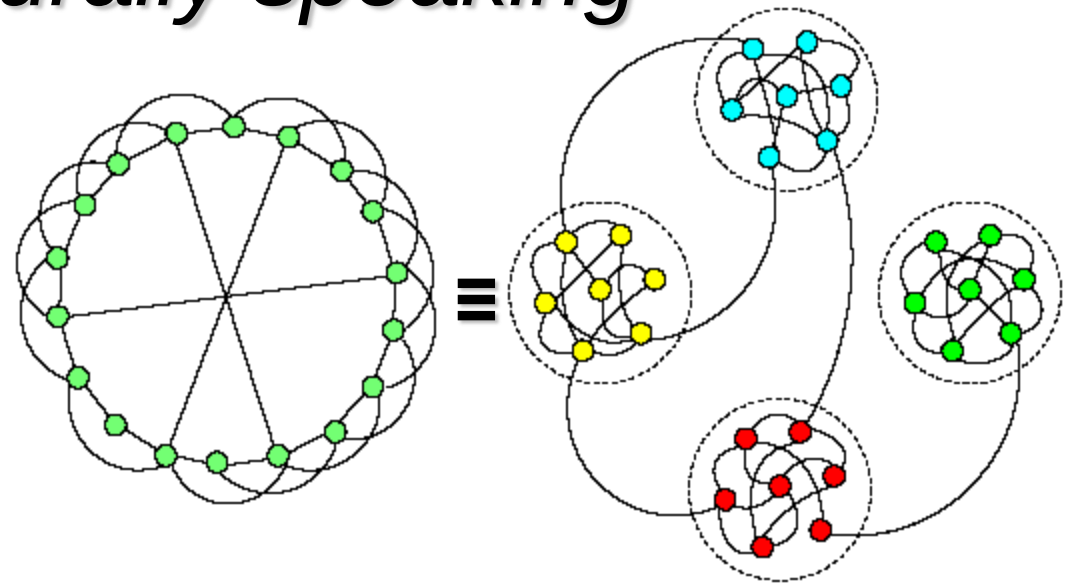
p: fraction of random, long-range connections

Why small-world pattern in complex networks?

R K Pan and S Sinha, *EPL* **85** 68006 (2009)

Structurally speaking

Watts-Strogatz network



Modular network

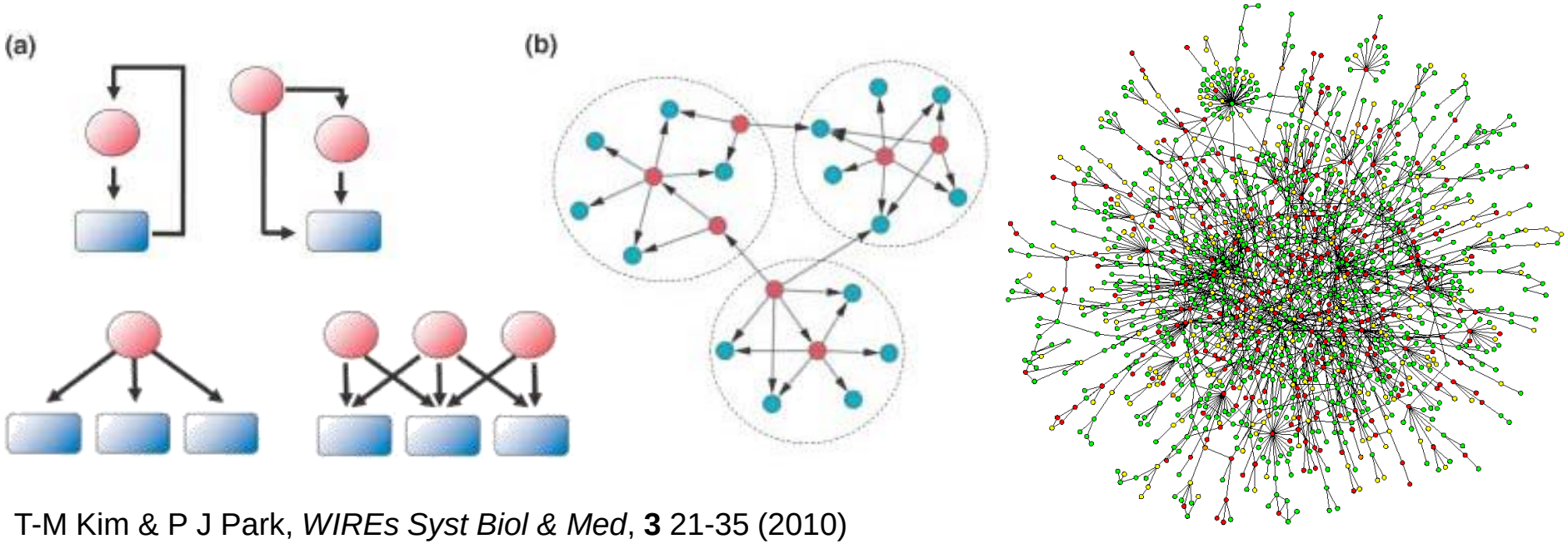
All the classic “small-world” structural properties of Watts-Strogatz small world networks e.g., high clustering, short average distance, etc. are *also seen* in modular networks

Networks have **community** organizations or **modular** structure: dense connections *within* certain sub-networks (modules) & relatively few connections *between* modules

Modules: A *mesoscopic* organizational principle of networks

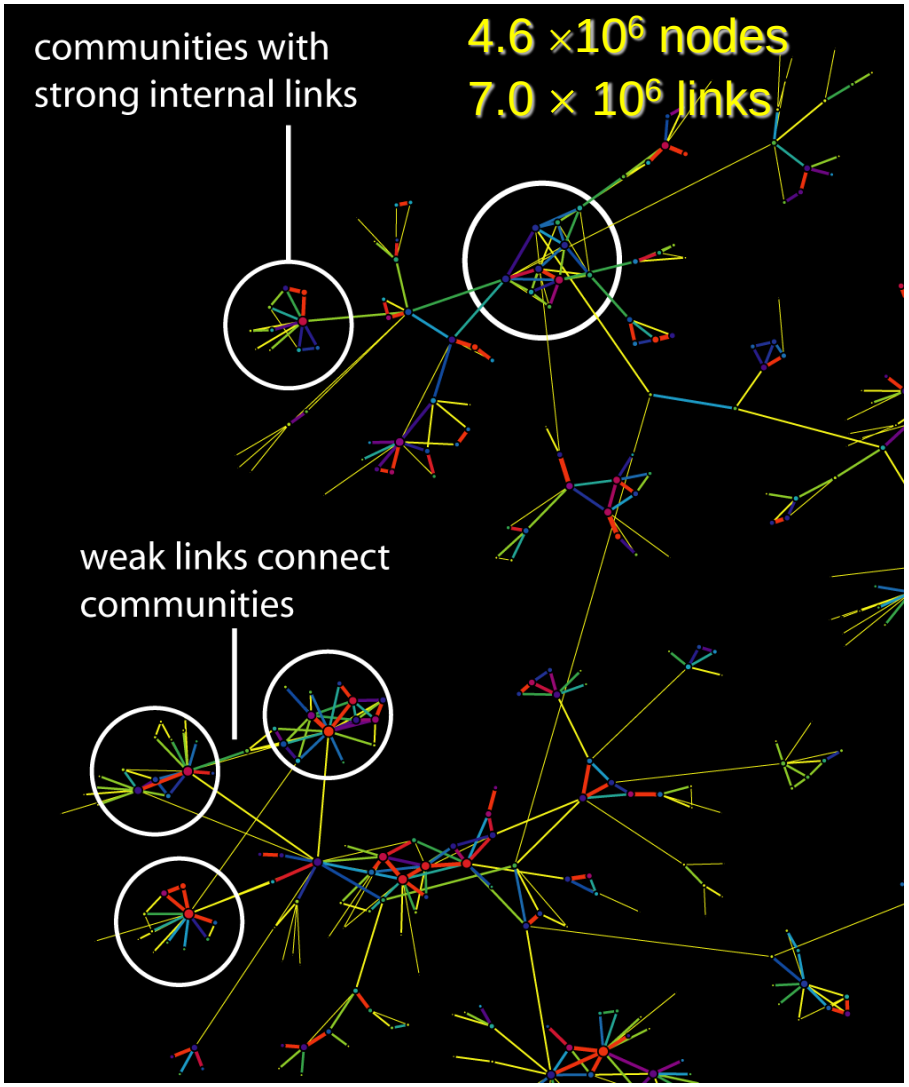
Going beyond *motifs* but more detailed than *global* description (*L*, *C* etc.)

Micro *Meso* *Macro*



T-M Kim & P J Park, *WIREs Syst Biol & Med*, **3** 21-35 (2010)

Modularity of social networks



J P Onnela et al. *PNAS*,**104**,7332 (2007)

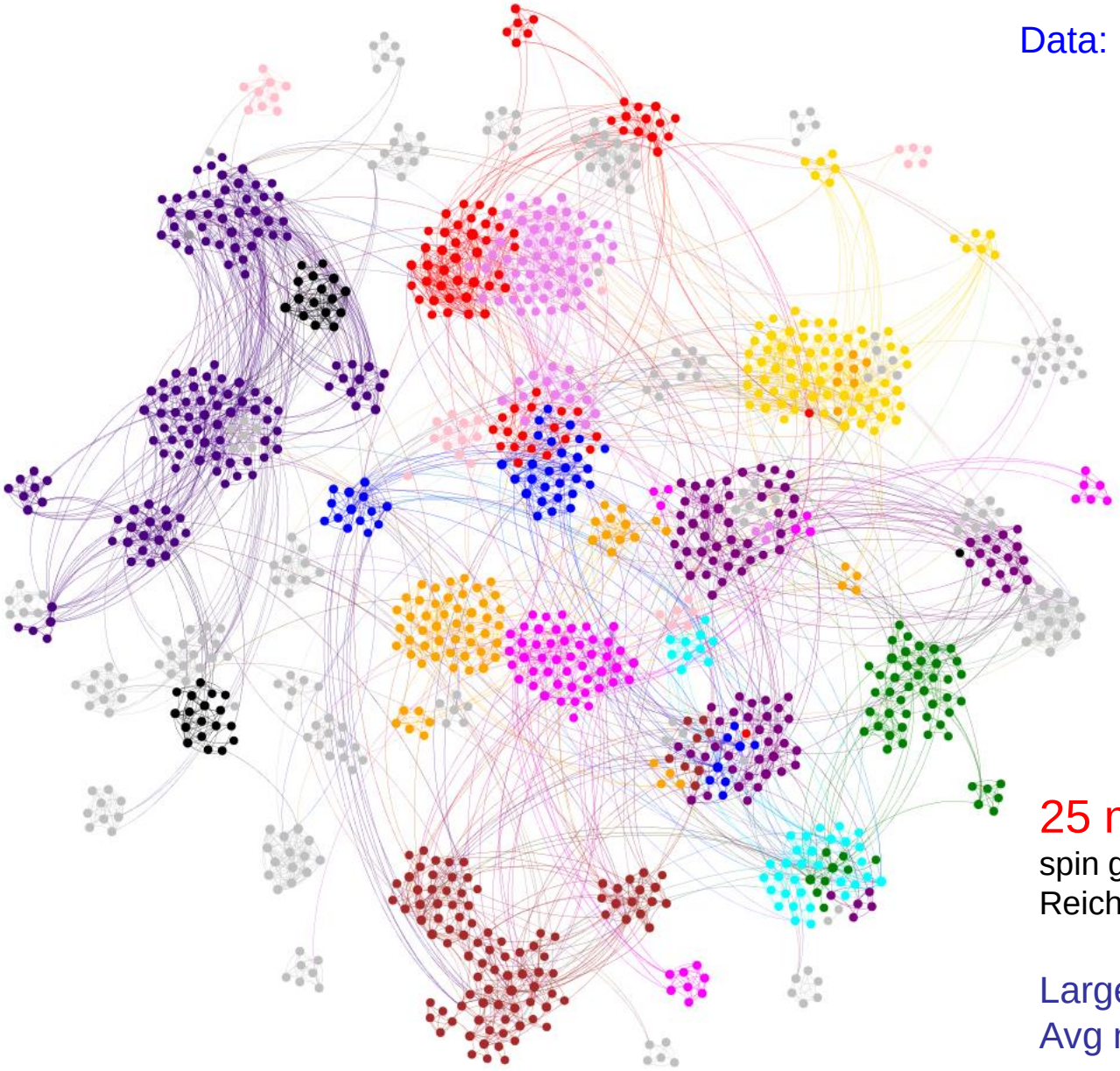
Modules: Cohesive groups

communities with dense internal & sparse external connections

Examples of modular social networks

- Cell phone communication
- Scientific collaborators
- e-mail communication
- PGP encryption ”web-of-trust”
- non-human animals

Modularity in Social Network of a Karnataka Village



Data: Bharatha Swamukti Samsthe microfinance institution
Nodes: Individuals
Links: Social relations

Described in Banerjee et al, *Science* (2013)

Village “55”

Population:1180 individuals
Largest connected component: 1151 individuals

25 modules

spin glass simulated annealing method
Reichardt & Bornholdt, PRE (2006)

Largest module: 127 nodes
Avg module size: 47 nodes

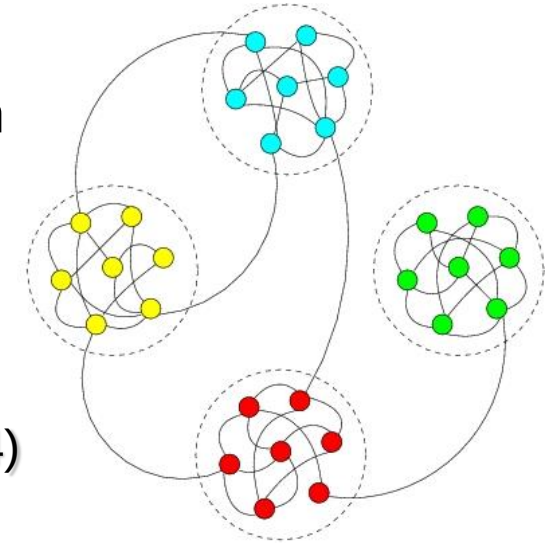
Node colors represent the community to which they belong

Community detection

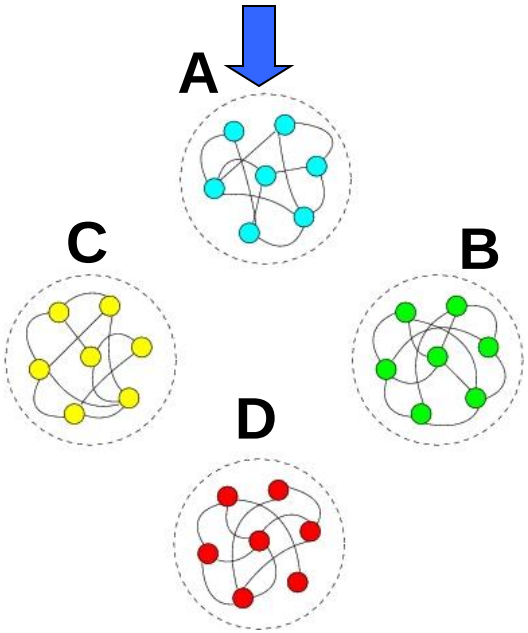
How to quantify the degree of modularity for a given partitioning of a network into communities ?

A suggested measure

$$Q \equiv \frac{1}{2L} \sum_{i,j} \left[A_{ij} - \frac{k_i k_j}{2L} \right] \delta_{c_i c_j}$$ (Newman, EPJB, 2004)

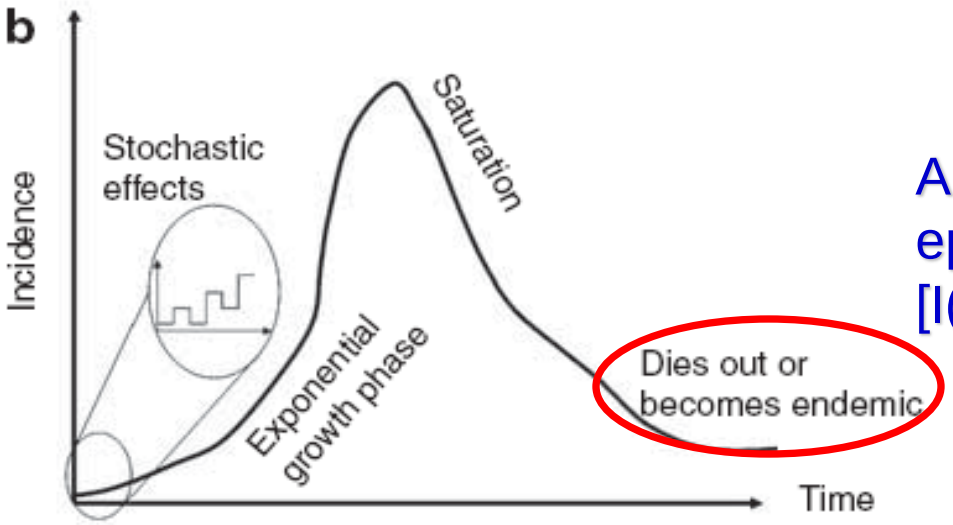


A: Adjacency matrix
L : Total number of links
k_i : degree of *i*-th node
c_i : label of module to which *i*-th node belongs



Modules determined through maximization of Q
by using various optimization techniques

We investigate the long-term transmission of epidemics in modular contact networks



A disease that starts out as an epidemic, eventually either *dies out* [I(t)=0] or becomes *endemic*

T D Hollingsworth, *J Pub Health Policy* **30** 328-341 (2009)

In particular, we focus on the possibility of

Persistence

i.e., existence (circulation) of the disease in the population for an indefinite period, i.e., $I(t) > 0$ as $t \to \infty$

To model the transmission of contagion on the network we use

SIRS dynamics

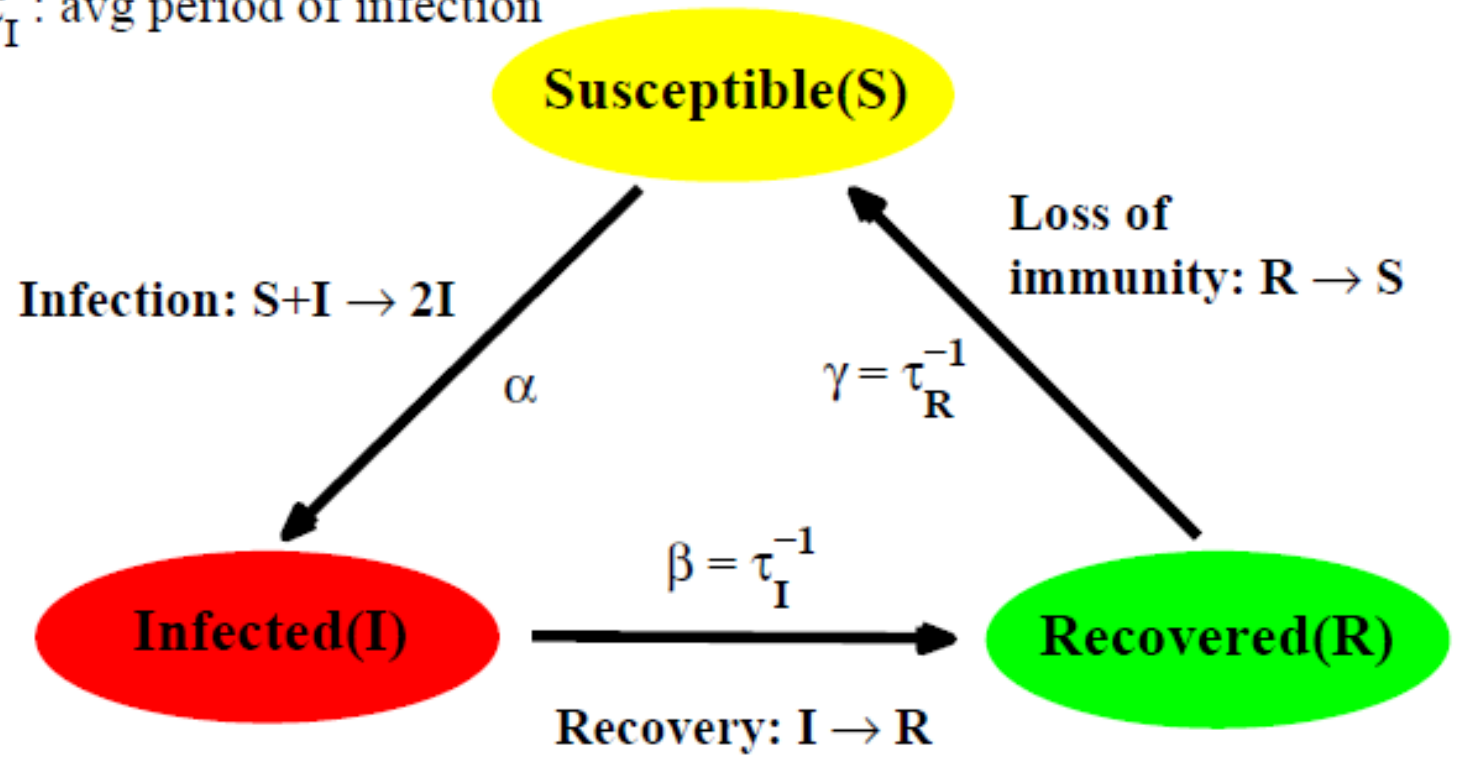
α : rate of infection

β: rate of recovery

τ_I : avg period of infection

γ : rate of immunity loss

τ_R : avg period of immunity

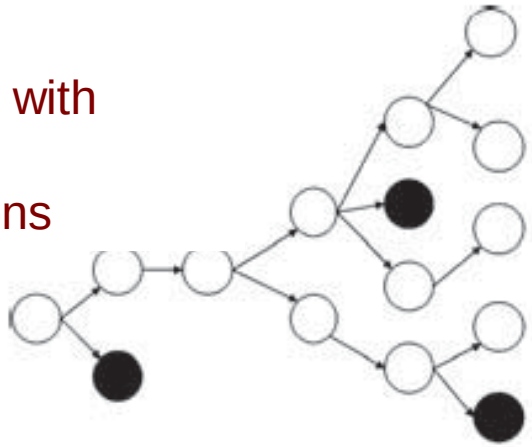


The intensity of an epidemic quantified by the

Basic reproduction number R_0

Mean number of new infections caused by a single infectious individual in a wholly susceptible population (as in the beginning of an epidemic): If each infected person on average infects more than one other individual, $R_0 > 1 \Rightarrow$ Epidemic

Epidemic if *basic reproduction number* $R_0 \approx N \alpha \tau_I > 1$



R = 1.75

Initially the epidemic may die out due to stochastic fluctuations, but once established it grows exponentially until pool of susceptible individuals is exhausted

T D Hollingsworth, *J Pub Health Policy* **30** 328-341 (2009)

Stochastic simulation of contagion propagation

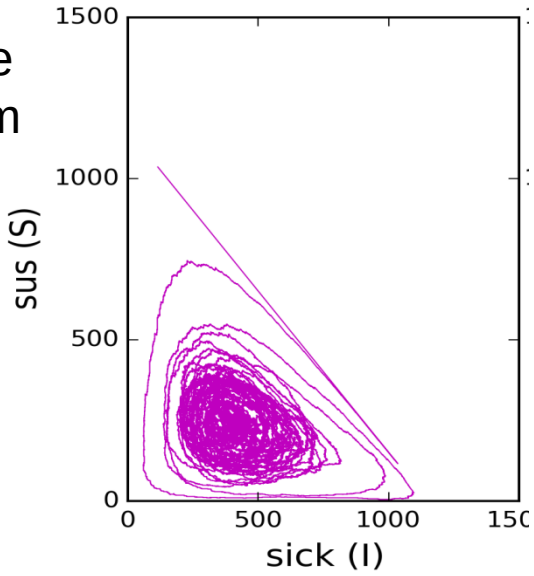
Modified version of **Gillespie algorithm**, an exact procedure for numerically simulating time evolution of a reaction system

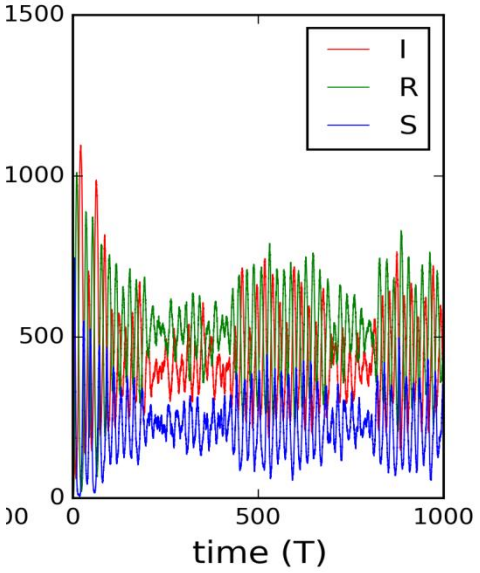
Algorithm

1. ***Initialization****:* Initialize the number of agents in the system, rates of infection/ recovery/loss of recovery, and random number generators.
2. ***Monte Carlo step****:* Generate random numbers to determine the next stochastic event to occur as well as the time interval.

- If *P* is the rate of a stochastic event and a number *r* is obtained from uniform random number generator , then time to next event is (1/ *P*)ln(1/*r*).
- The probability of a particular event (infection/recovery/loss of recovery) to happen is proportional to the ratio of its rate to the sum of the rates of all reactions.

3. ***Update****:* Increase the time step by the randomly generated time in Step 2. Update the number of agents in different states (S/I/R) based on the event that occurred.
4. ***Iterate****:* Go back to Step 2 unless the number of infected agents is zero or the simulation time has been exceeded.

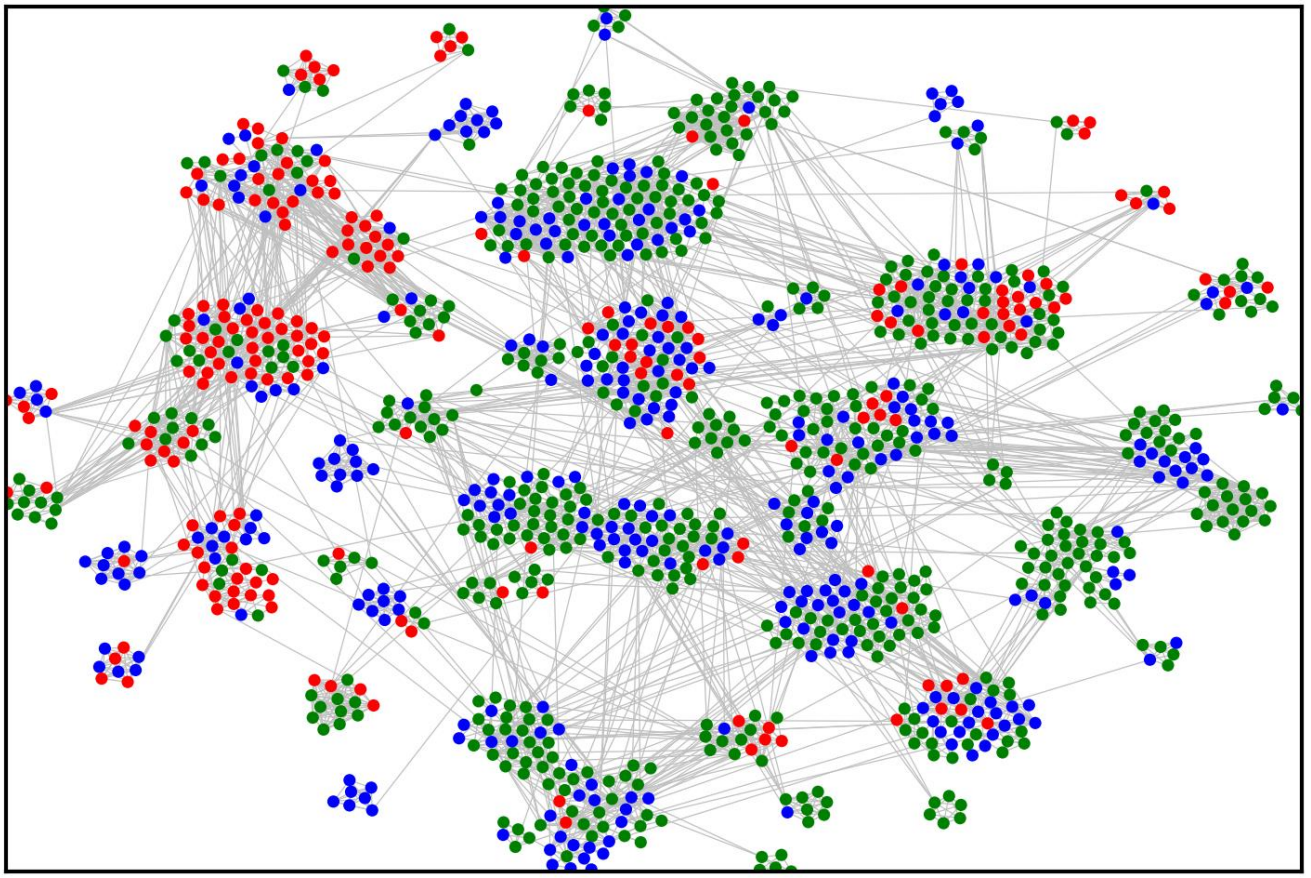




Note: The rates of I→R and R→S events are $\beta_i = exp(\eta(\Delta t_I - \langle \tau_I \rangle))$ & $\gamma_i = exp(\eta(\Delta t_R - \langle \tau_R \rangle))$

η governs the nature of the distribution of τ_I and τ_R (low values give exponential, higher give Gaussian)

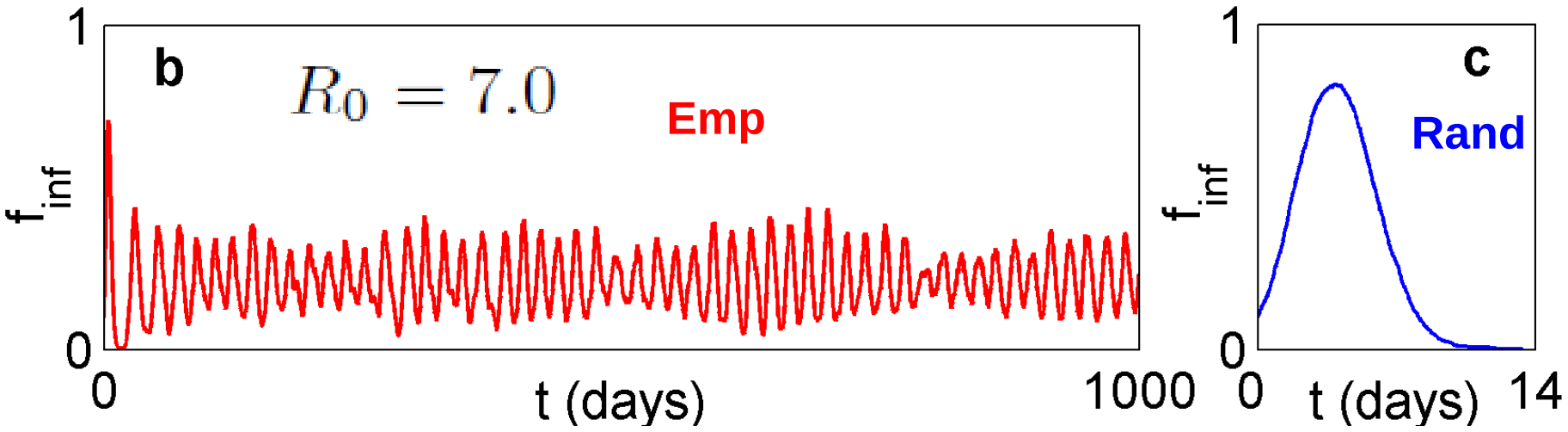
Progress of an epidemic in a Karnataka Village



Susceptible Infected Recovered

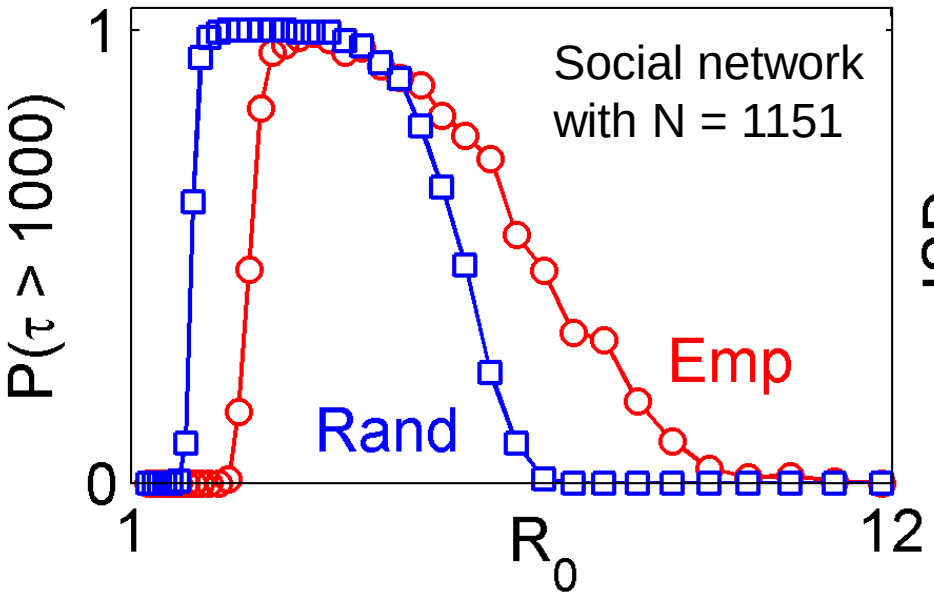
Modularity promotes disease persistence

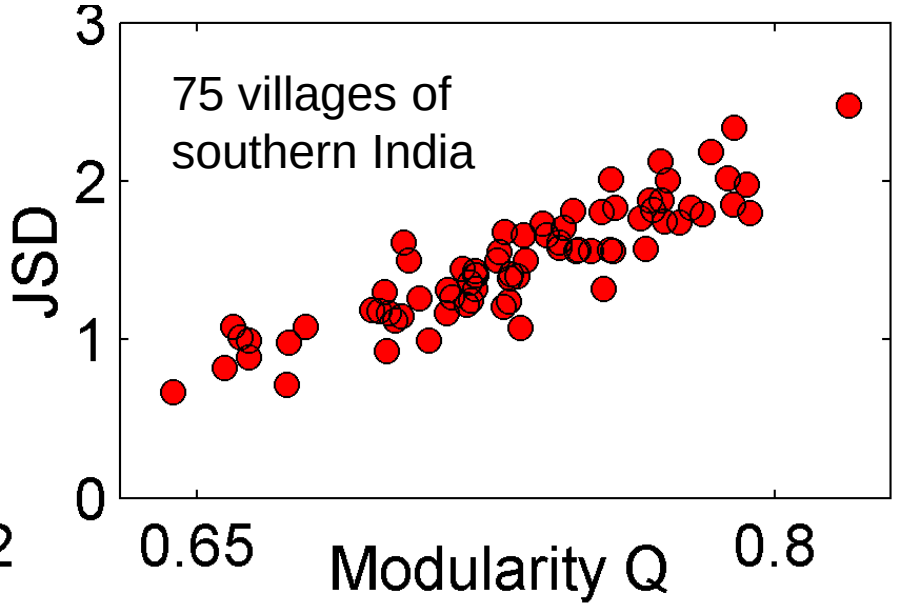
Contagia in empirical **modular** social contact network are **surprisingly persistent** compared to degree-preserved **randomized** networks which do not have community organization



Difference even more pronounced if modularity is enhanced by selectively decreasing inter-modular connectivity

Quantifying relation between persistence & modularity





The ***difference*** in the persistence probability distributions for empirical and randomized networks can be measured by the Jensen-Shannon divergence, defined for a pair of discrete probability distributions P and Q as:

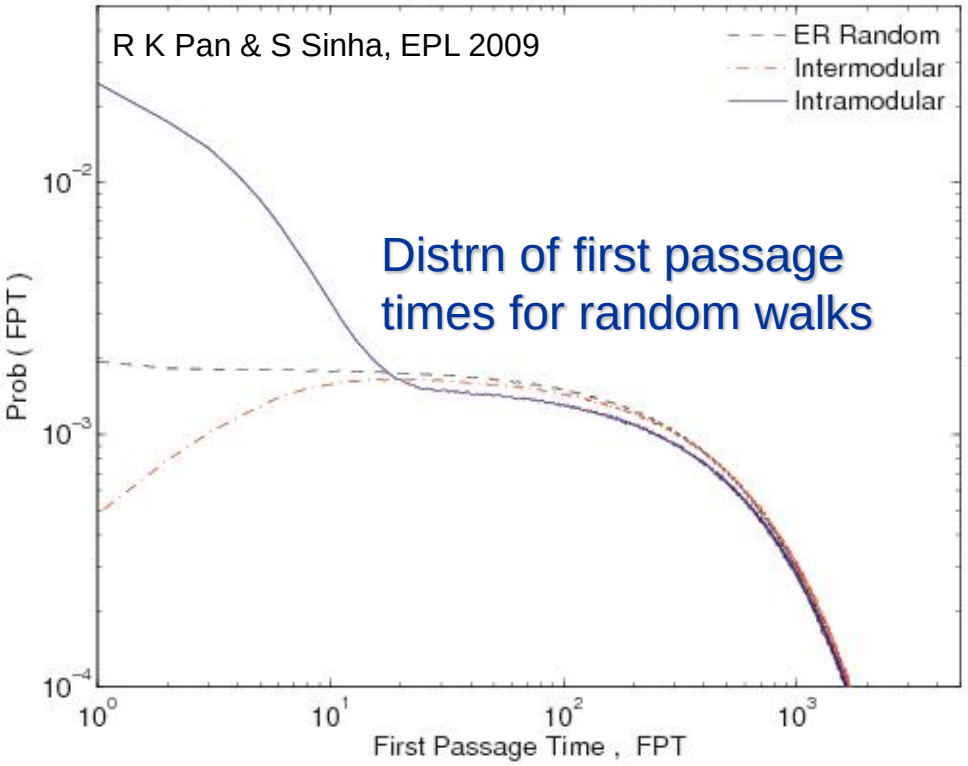
$$JSD(P,Q) = \frac{1}{2}\Sigma_i(P_i \ln \frac{P_i}{M_i} + Q_i \ln \frac{Q_i}{M_i}), \text{ where } M = 1/2(P+Q)$$

As modularity Q of empirical contact network increases, JSD increases almost linearly (linear corr coeff is 0.89 with p=0).

The presence of disease persistence in contact networks with community organization can be understood by analyzing

Diffusion process on modular networks

E.g., Random walker moving from one node to randomly chosen neighboring node



Shows the existence of two *distinct* time scales:

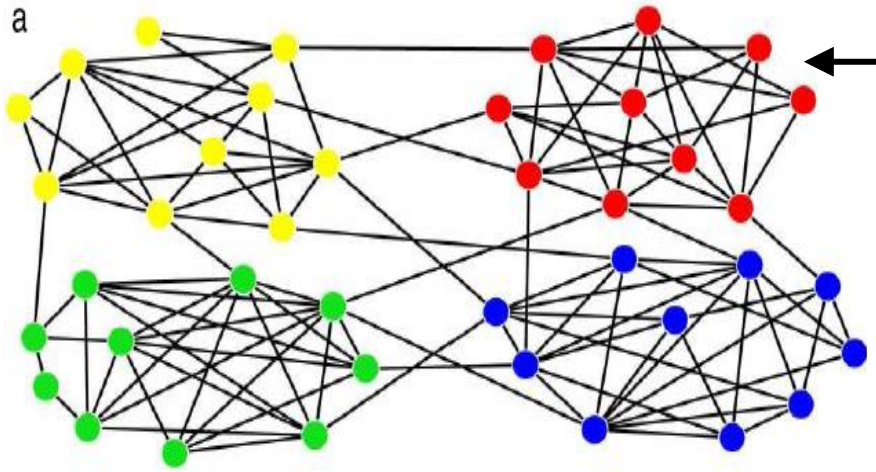
- fast intra-modular diffusion
- slower inter-modular diffusion

while random networks show a continuous range of time scales

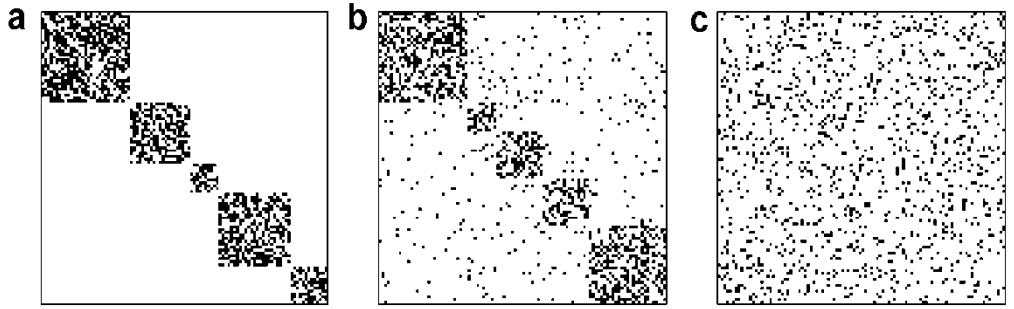
In modular networks, the disease spreads slowly from module to module, allowing parts of the network to recover before spreading !

A simple model of modular networks

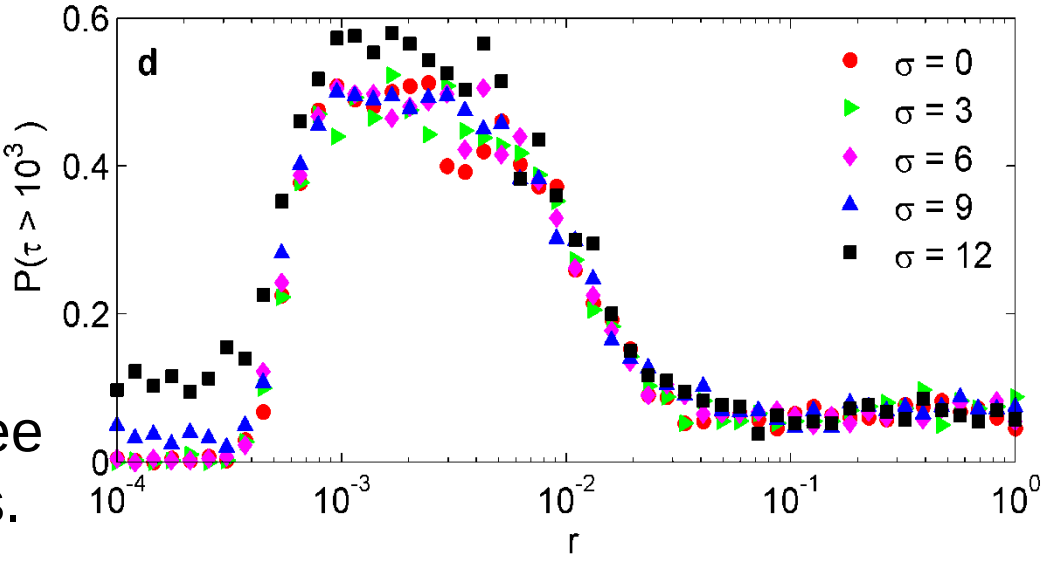
Model parameter *r* : Ratio of inter- to intra-modular connection density



Module ≡ random network



Modules can be of different sizes → heterogeneity measured by standard deviation of module size σ.



Very similar behavior w.r.t. degree of heterogeneity in module sizes.

Random modular networks are Small-World: Comparison with Watts-Strogatz model

Communication efficiency

$E = [\text{avg path length}, \ell\,]^{-1} = 2/N(N-1) \sum_{i>j} d_{ij}$

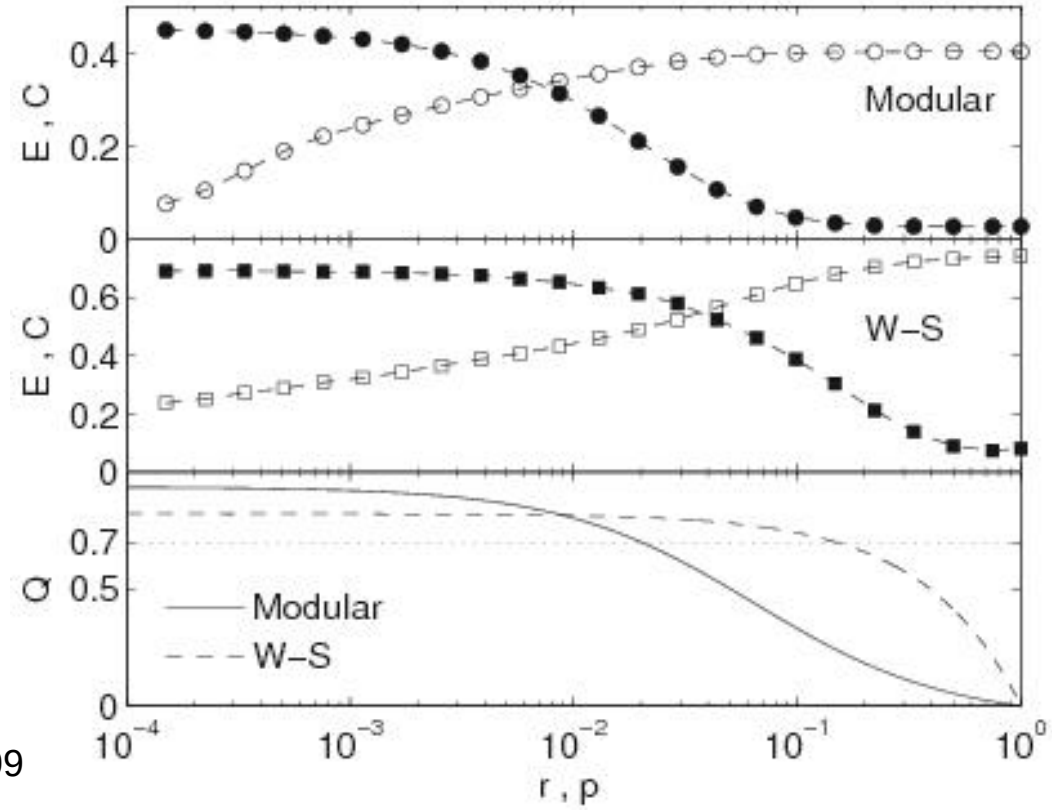
Clustering coefficient

C = fraction of observed to potential triads

$= (1/N) \sum_i 2n_i / k_i (k_i - 1)$

WS and Modular networks behave similarly as function of *p* or *r* (Also for between-ness centrality, edge clustering, etc)

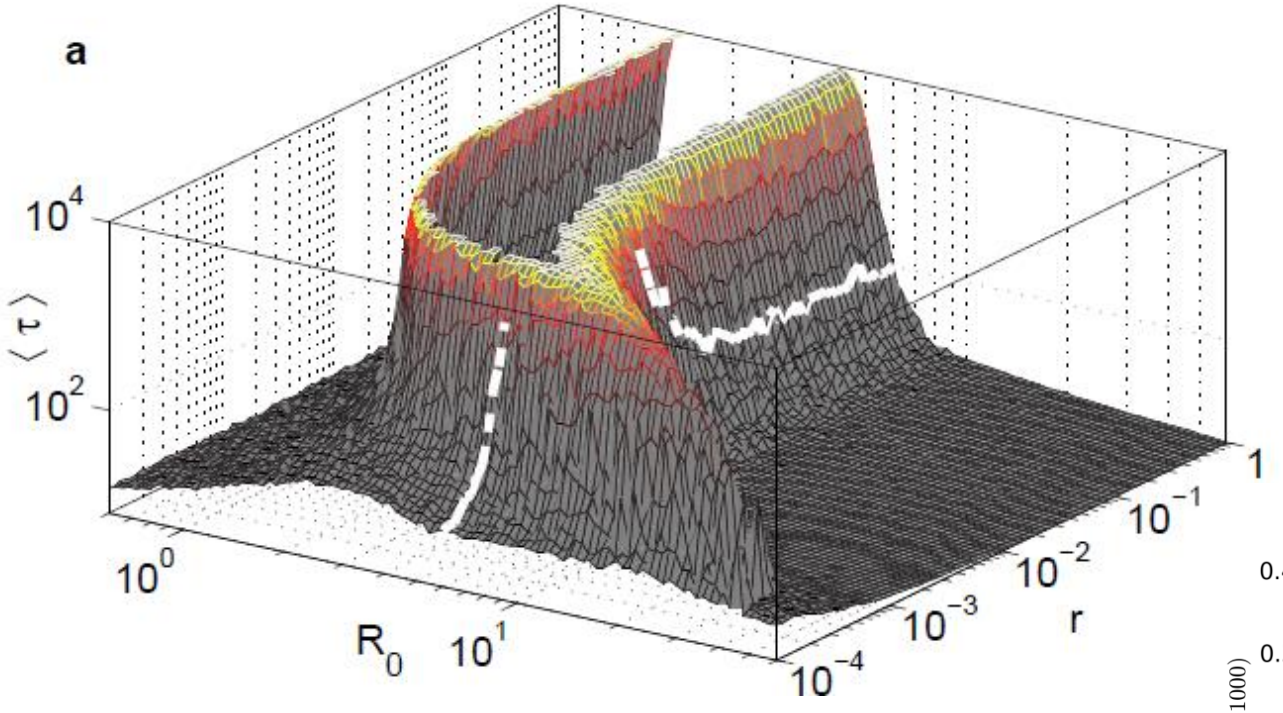
In fact, for same N and <k>, we can find *p* and *r* such that the WS and Modular networks have the same *"modularity"* Q



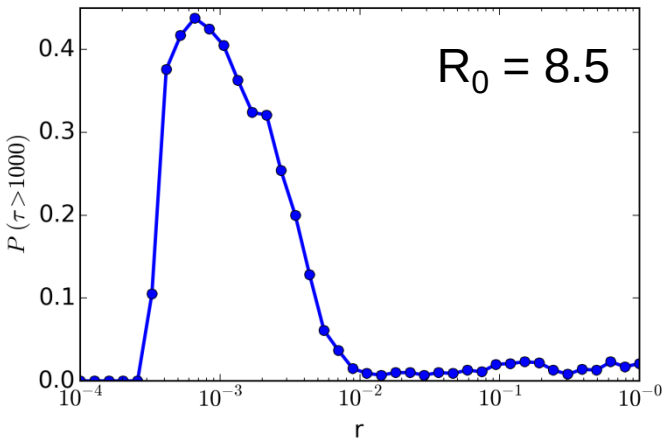
R K Pan and S Sinha EPL 2009

Existence of communities can make highly infectious diseases persistent

For isolated modules (r=0) and homogeneous networks (r=1) epidemic with high infection rate (R_0) dies out quickly…



…but for intermediate modularity highly infectious contagia are persistent.



m=64 modules of size n=16 avg degree <k> = 12
Avgd over 100 rlzns

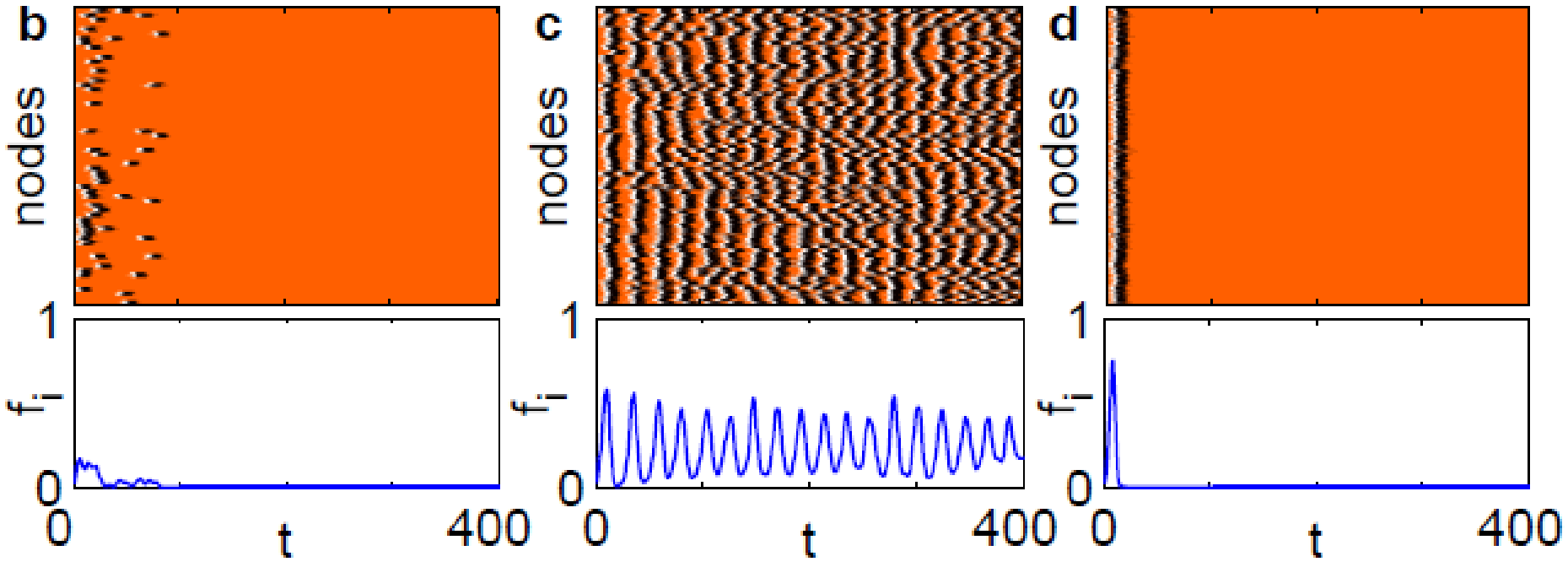
Persistence in a critical range of *r*

For a critical range of modularity for contact network ($r \sim 10^{-3}$), highly infectious contagia are persistent.

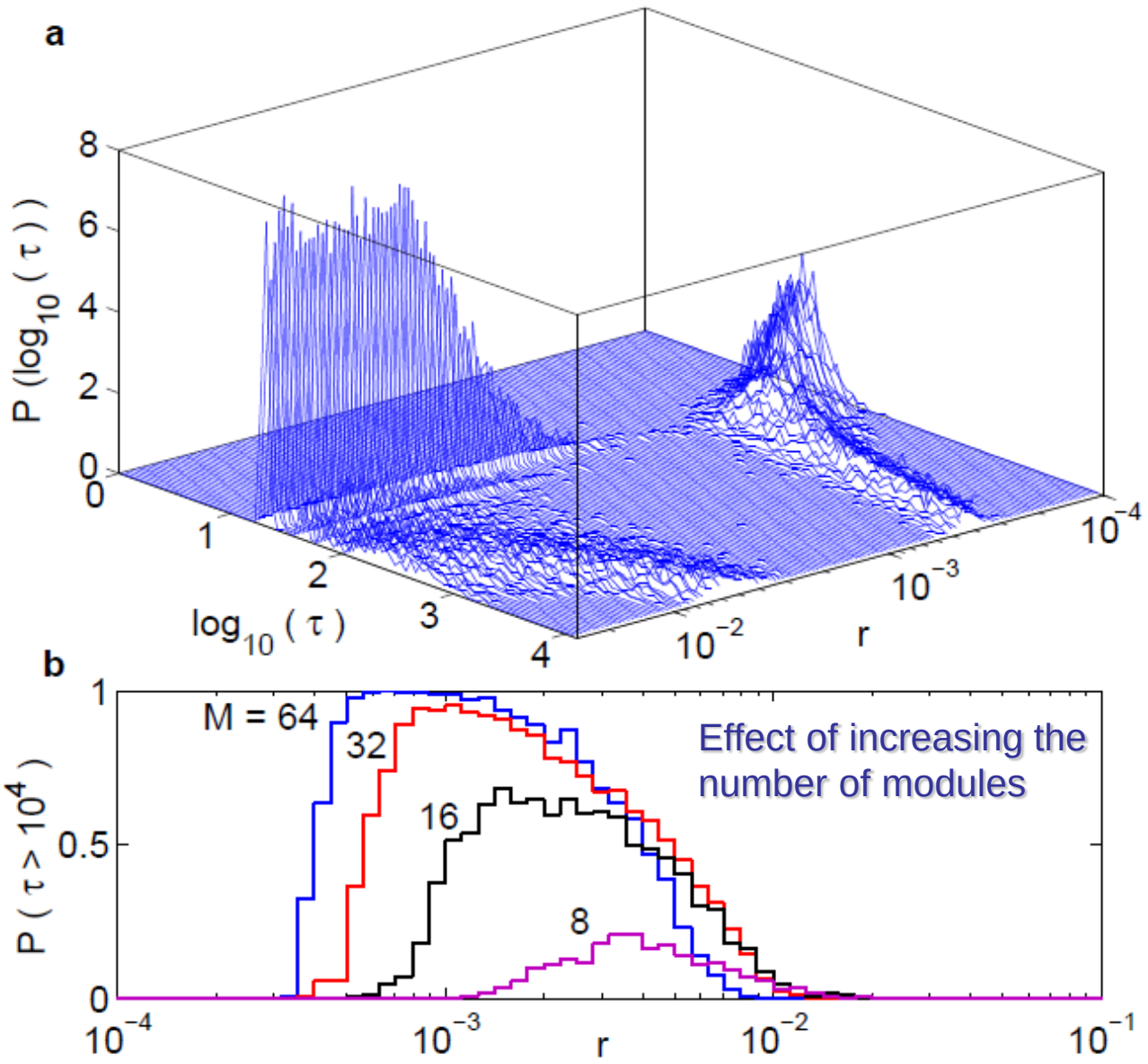
r = 0.0002: rapid extinction

r = 0.002: persistence

r = 0.02: rapid extinction



Persistence in a critical range of modularity



Distribution of persistence time τ shows bimodal character for large r – with the upper branch diverging for a critical range of modularity…

…while for lower r the distribution is unimodal with avg τ decreasing rapidly as the modules are effectively isolated ($R_0 = 6$)

Mechanism: Existence of distinct time-scales in Modular networks

(R K Pan and S Sinha, EPL 2009)

Consider set of random walkers moving on a network s.t. $\Sigma_i \rho_i(t) = 1 \ \forall t$ (*number conservation*)

ρ_i: fraction of random walkers at node i in time t

Walker on node i moves with equal probability to any node directly linked to i $\Rightarrow$ *Local continuity eqn*: $\rho_i(t+1) - \rho_i(t) = \sum_j A_{ij} \rho_j(t)/k_j - \sum_j A_{ji} \rho_i(t)/k_i$

in-flow out-flow

Master eqn: $\rho(t+1) - \rho(t) = D\rho$, D: diffusion matrix = $(A/k) - I$

i.e., $D_{ij} = A_{ij}/k_j - \delta_{ij} = -L_{ij}/k_j \Rightarrow$ D related to Laplacian matrix

Evolution of walker distrn: $\rho(t+1) = T\rho(t)$, where $T = D+I$

T: transition matrix for Markov chain defined on network

$\Rightarrow \rho(t+1) = T^t \rho(t)$, T acting as time-propagator for the random walk

In general, T is not symmetric but…

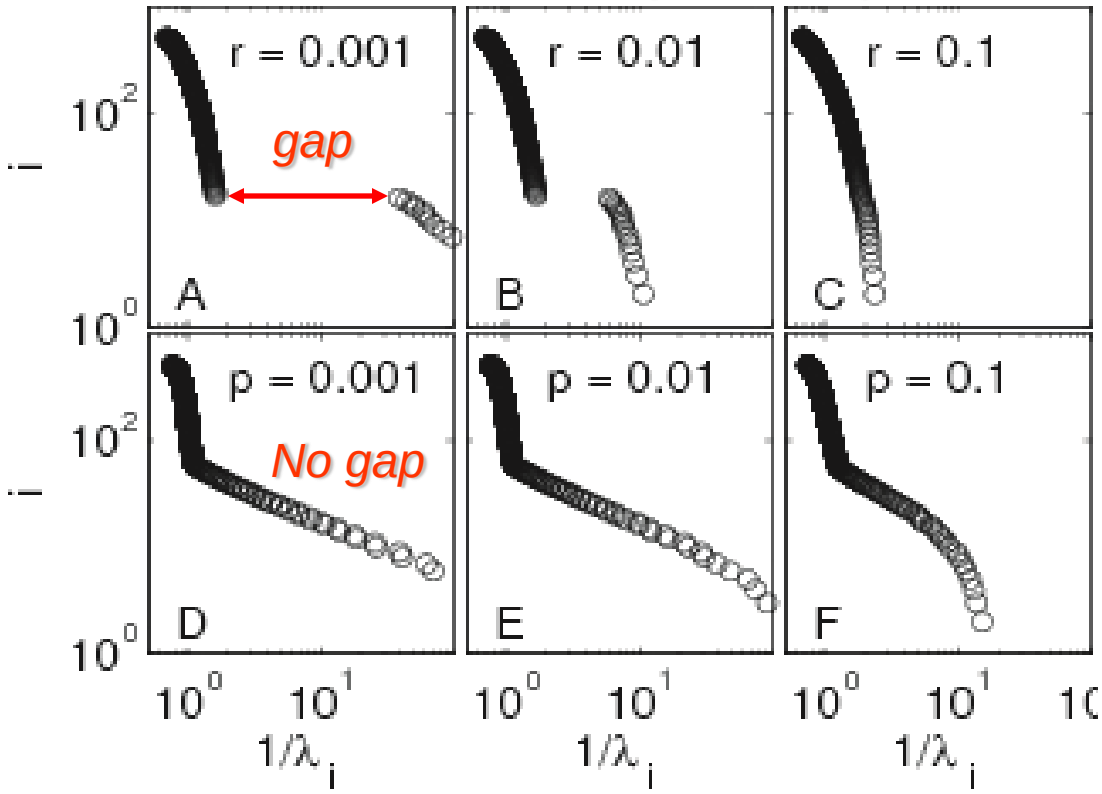
I–T related to symmetric normalized Laplacian L(= k – A) by similarity transformation: same eigenvalues!

Differences in time-scales of modes $\Rightarrow$ gap in spectrum of L

Eigenvalue spectra of the Laplacian

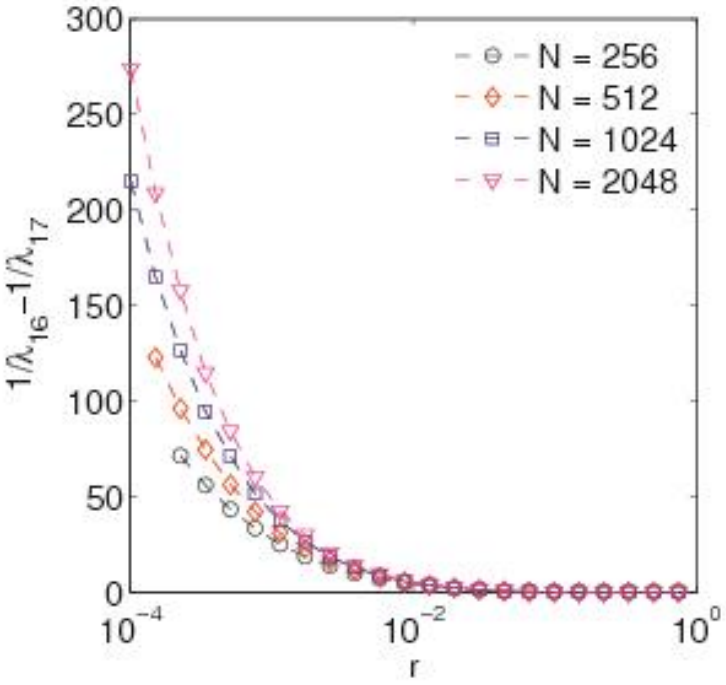
Shows the existence of spectral gap ⇒ distinct time scales

Modular network Laplacian spectra



WS network Laplacian spectra

Spectral gap in modular networks diverges with decreasing r



Existence of distinct time-scales in Modular networks

No such distinction in Watts-Strogatz small-world networks

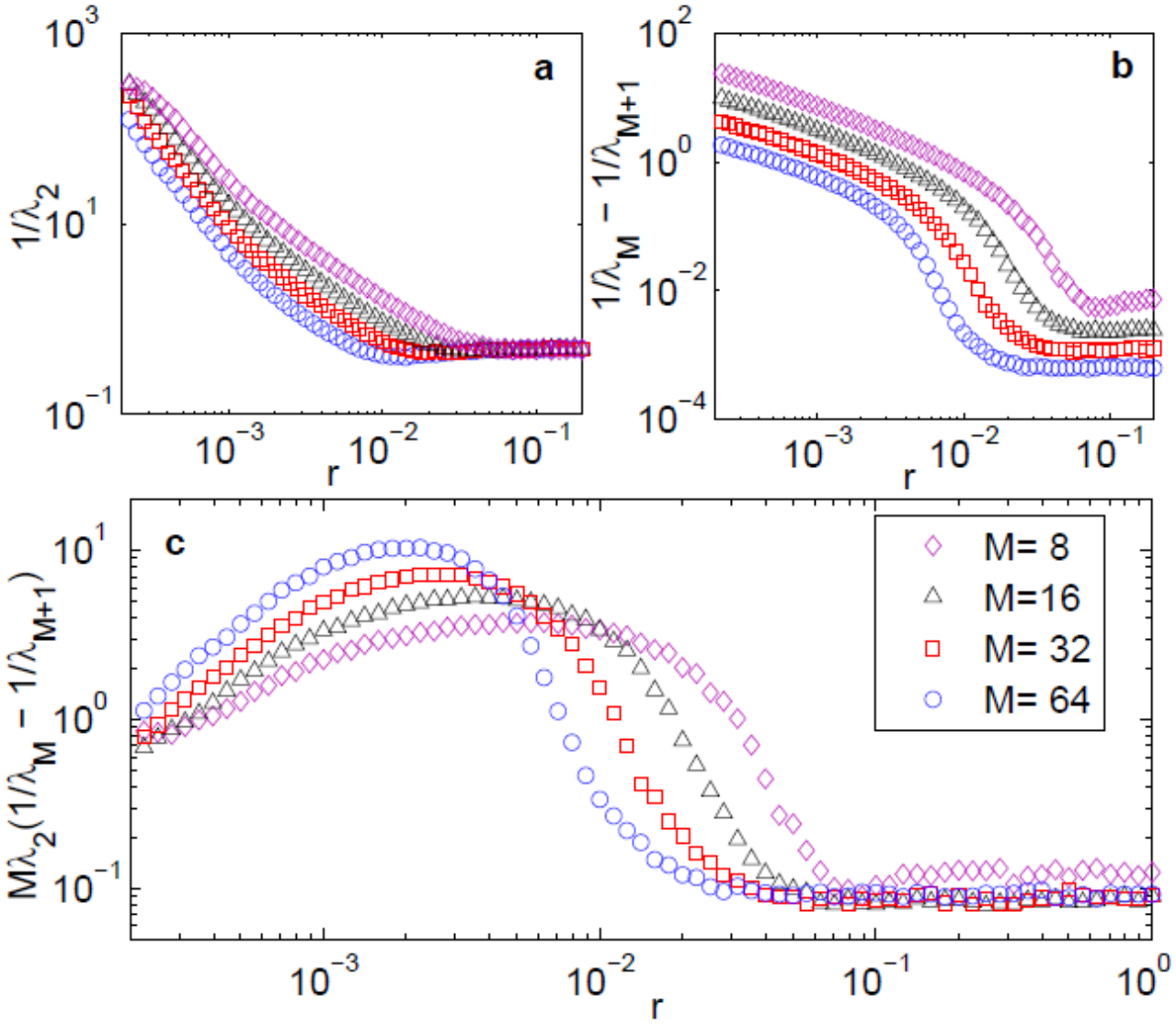
R K Pan and S Sinha, EPL 2009

The mechanism of enhanced persistence

Time-scale for global diffusion (inverse of smallest finite Laplacian eigenvalue) decreases with increasing r…

…. so does the time-scale separation between inter- and intra-modular diffusion events (the Laplacian spectral gap)

However – the ratio of the two show non-monotonic dependence on modularity



contagion spreads slowly from module to module, allowing parts of the network to recover before return of infection!

Implications

- Diseases with low R_0 may be terminated by effective quarantine procedure to isolate communities from each other.
- Specific groups may be targeted (e.g., school children, certain “high-risk-of-infection” professions, long-distance commuters, etc) depending on their role in connecting the different modules
- Isolating communities may **not** be particularly effective in preventing highly contagious (high R_0) diseases from becoming persistent.
- However a more effective immunization strategy of identifying individuals who connect otherwise isolated communities and making them high-priority targets for vaccination

Thanks

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PhD program in Computational Biology @ IMSc

http://www.imsc.res.in/biology_imsc

The Institute of Mathematical Sciences has started a PhD program in Computational Biology from 2014 (degree awarded under HBNI)

Students from Basic Sciences/Engineering/Medicine encouraged to apply with scores from a national-level research eligibility exam (GATE, NET, JEST, JGEEBLS, BINC, etc.) – shortlisted candidates will be called for interview in June/July

Selected candidates will do 1 year coursework followed by a comprehensive exam before commencement of PhD research

Summer Internships http://www.imsc.res.in/biology_summer_research_programme

NNMCB Internships & Visiting Program

http://www.iiserpune.ac.in/~nnmcb
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National Network for Mathematical & Computational Biology

Coordination by Department of Mathematics, IISc Bangalore

Chennai node: IMSc Chennai (responsible for TN, Kerala and Andhra Pradesh)

Internships available at various Institutes (application process starts in October)

Visiting Program allows scientists to spend time at different institutes

Details in NNMCB website or write to node coordinators