

Bioinformatics: Network Analysis

Networks as a Guiding Tool

COMP 572 (BIOS 572 / BIOE 564) - Fall 2013

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- ❖ Networks have been used to

- ❖ guide GWAS

- ❖ predict protein function

- ❖ model epidemics

- ❖ ...

Efficient network-guided multi-locus association mapping with graph cuts

Chloé-Agathe Azencott^{1,*}, Dominik Grimm¹, Mahito Sugiyama¹, Yoshinobu Kawahara² and Karsten M. Borgwardt^{1,3}

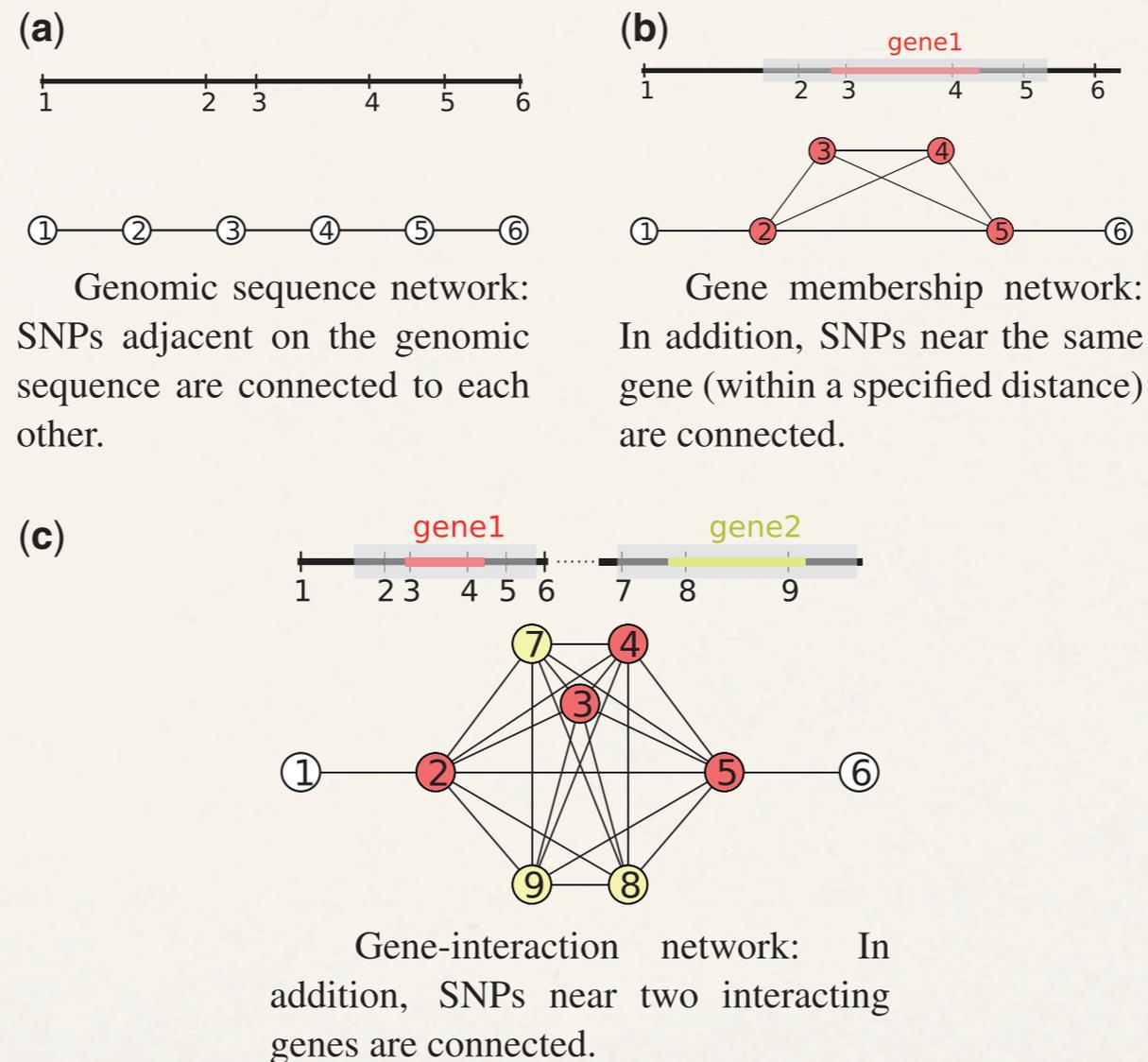
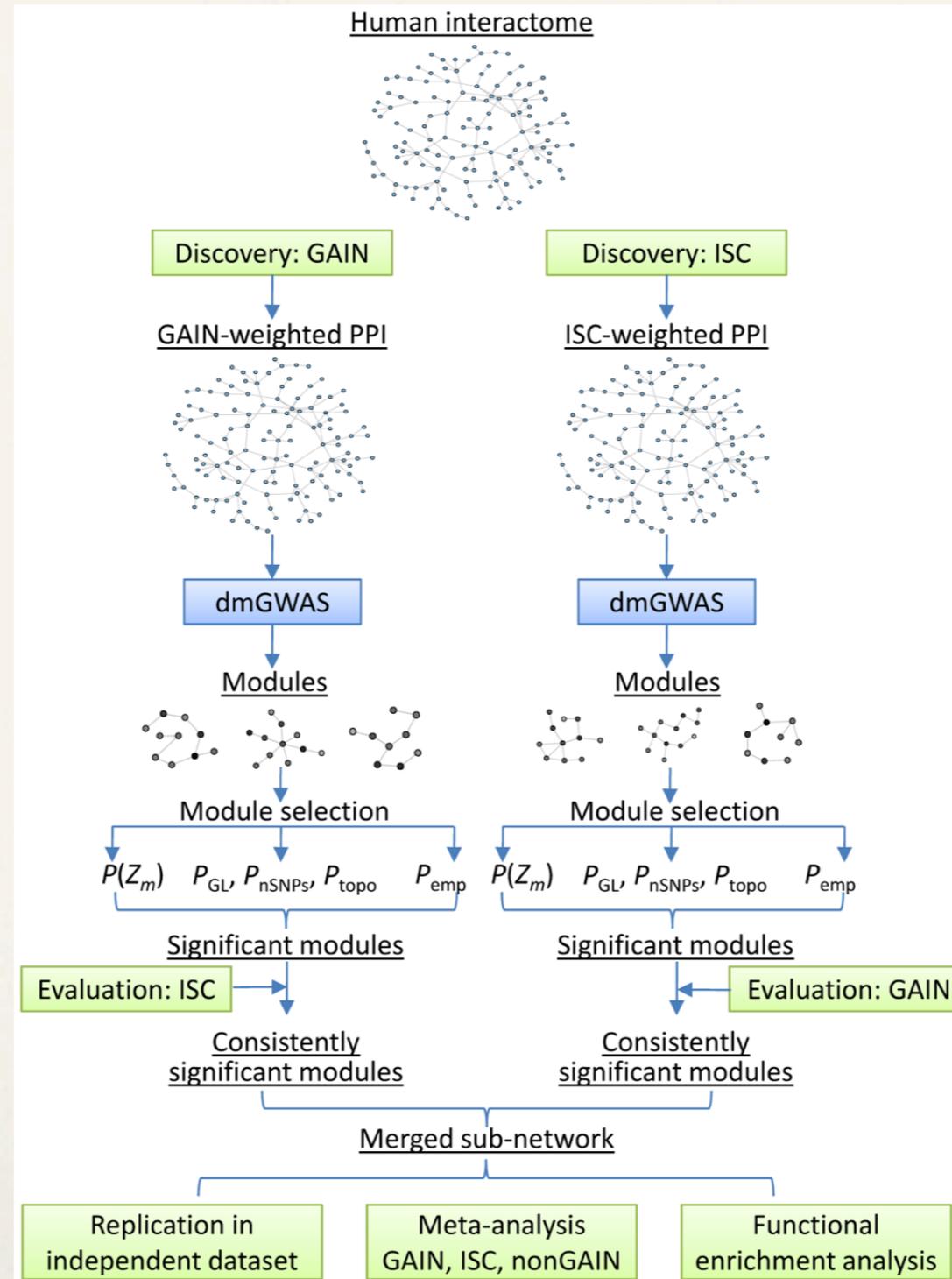


Fig. 1. Small examples of the three types of networks considered

Network-Assisted Investigation of Combined Causal Signals from Genome-Wide Association Studies in Schizophrenia

Peilin Jia^{1,2}, Lily Wang³, Ayman H. Fanous^{4,5,6,7}, Carlos N. Pato⁷, Todd L. Edwards^{8,9}, The International Schizophrenia Consortium¹, Zhongming Zhao^{1,2,10*}



Network-based prediction of protein function

Roded Sharan¹, Igor Ulitsky¹ and Ron Shamir*

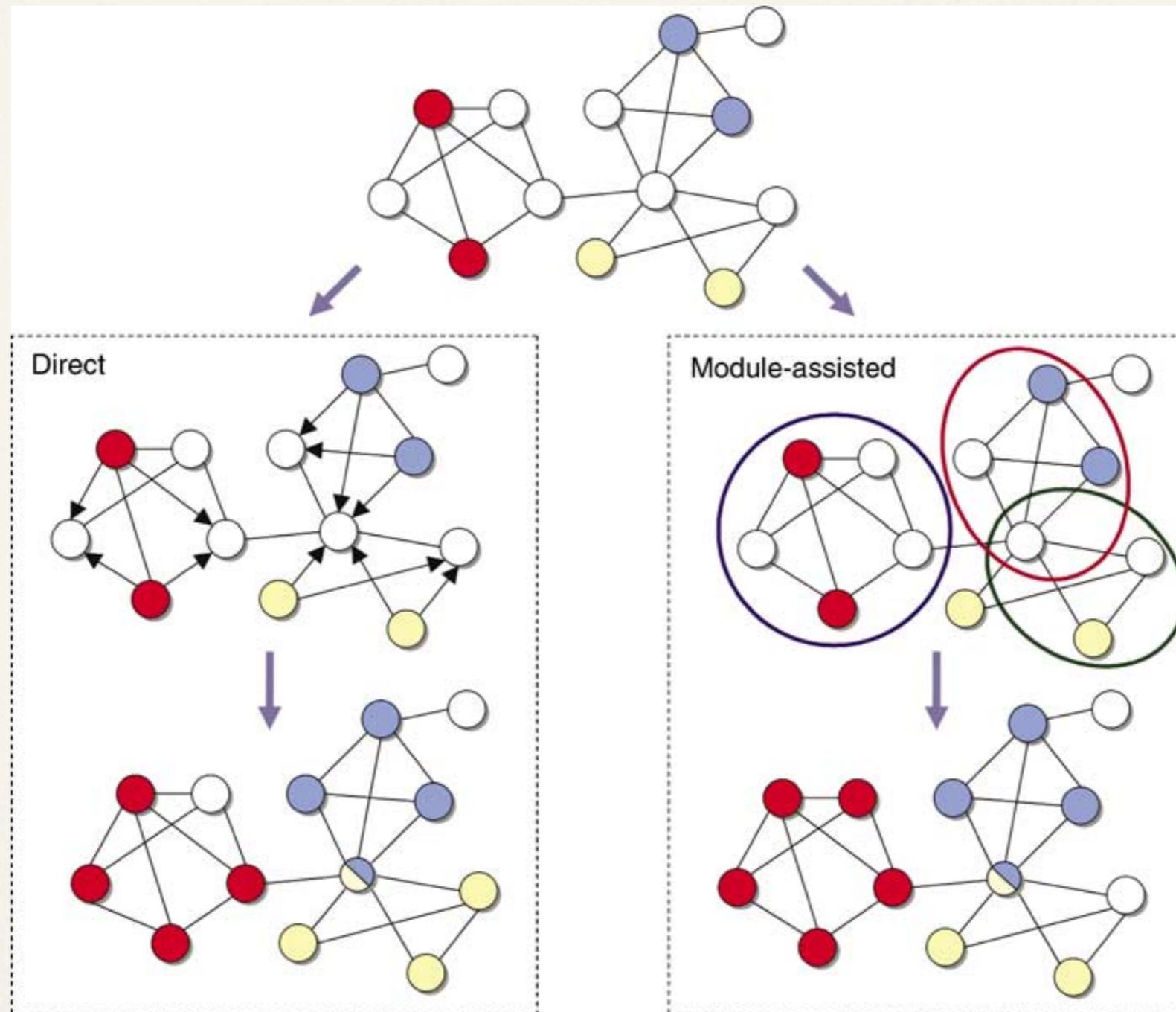


Figure 2 Direct versus module-assisted approaches for functional annotation. The scheme shows a network in which the functions of some proteins are known (top), where each function is indicated by a different color. Unannotated proteins are in white. In the direct methods (left), these proteins are assigned a color that is unusually prevalent among their neighbors. The direction of the edges indicates the influence of the annotated proteins on the unannotated ones. In the module-assisted methods (right), modules are first identified based on their density. Then, within each module, unannotated proteins are assigned a function that is unusually prevalent in the module. In both methods, proteins may be assigned with several functions.

Epidemics and Networks

Diseases and the Networks that Transmit Them

- ❖ The patterns by which epidemics spread through a population is determined not just by the properties of the pathogen carrying it (contagiousness, the length of the infection period, severity, etc.), but also by network structures within the population it is affecting.
- ❖ The opportunities for a disease to spread are given by a contact network: there is a node for each person, and an edge if two people come into contact with each other in a way that makes it possible for the disease to spread from one to the other.

Diseases and the Networks that Transmit Them

- ❖ Accurately modeling the underlying network is crucial to understanding the spread of an epidemic.

...how travel patterns within a city affect the spread of disease

.....

Modelling disease outbreaks in realistic urban social networks

**Stephen Eubank¹, Hasan Guclu², V. S. Anil Kumar¹, Madhav V. Marathe¹,
Aravind Srinivasan³, Zoltán Toroczkai⁴ & Nan Wang⁵**

Network theory and SARS: predicting outbreak diversity

Lauren Ancel Meyers^{a,b,*,1}, Babak Pourbohloul^{c,1,2}, M.E.J. Newman^{b,d},
Danuta M. Skowronski^{c,2}, Robert C. Brunham^{c,2}

..how travel patterns via the worldwide airline network affect the spread of
disease

The role of the airline transportation network in the prediction and predictability of global epidemics

Vittoria Colizza*, Alain Barrat[†], Marc Barthélemy*[‡], and Alessandro Vespignani*[§]

Diseases and the Networks that Transmit Them

- ❖ Contact networks are also important in understanding how diseases spread through animal populations (e.g., the 2001 foot-and-mouth outbreak in the UK) and plant populations.
- ❖ Similar models have been employed for studying the spread of computer viruses...

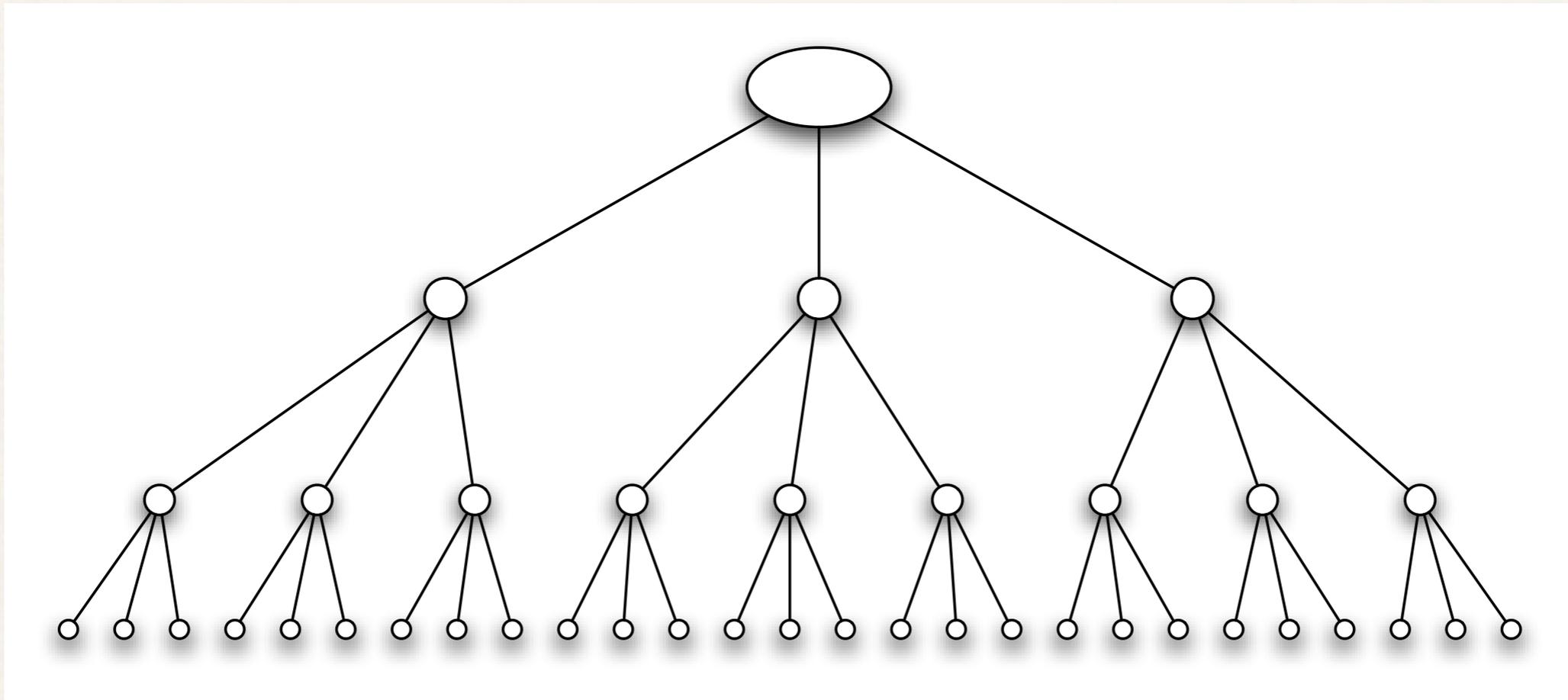
Diseases and the Networks that Transmit Them

- ❖ The pathogen and the network are closely intertwined: even within the same population, the contact networks for two different diseases can have very different structures, depending on the diseases' respective modes of transmission.
- ❖ (Think of airborne transmission based on coughs and sneezes, compared to a sexually transmitted disease, and think of the density of the contact networks!)

Branching Processes

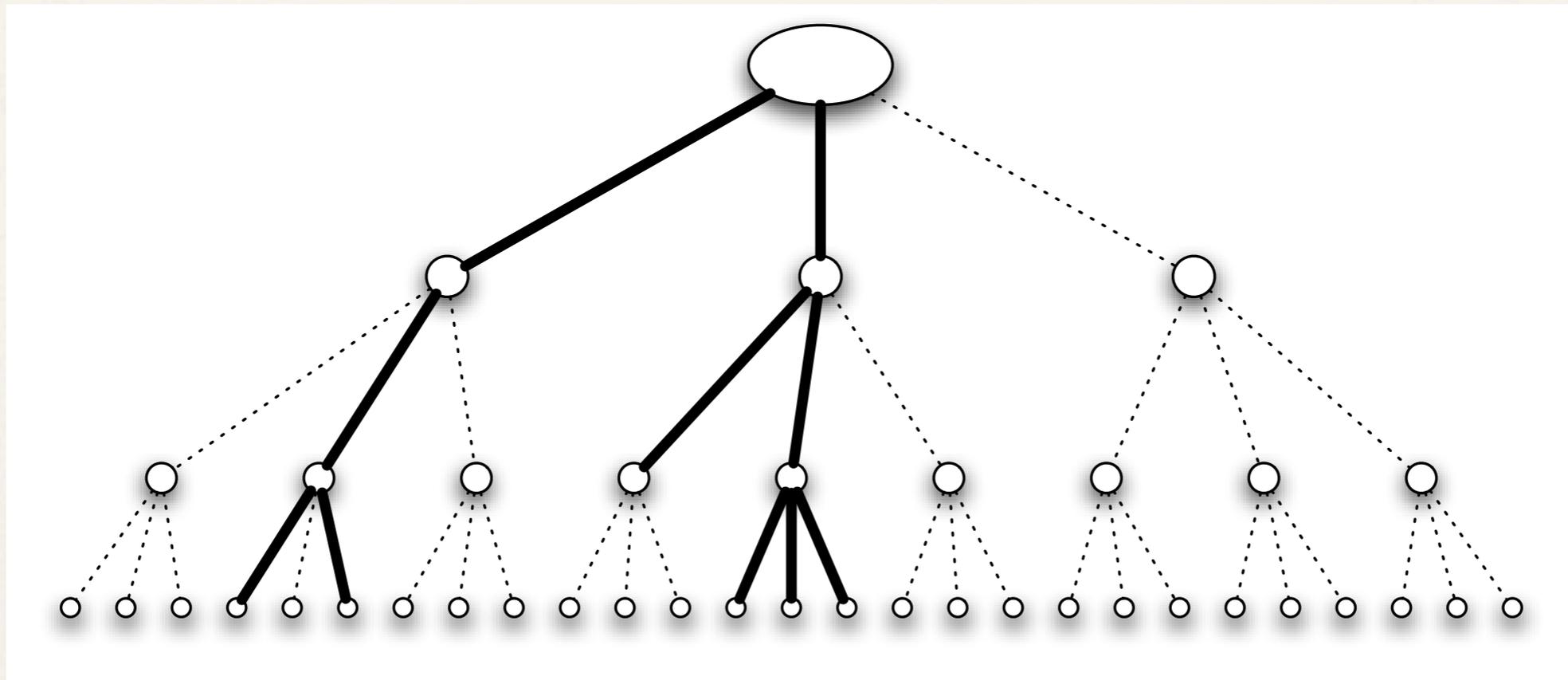
- ❖ The simplest model of contagion: every person is in contact with k people
 - ❖ First wave: a person carrying a new disease enters a population and transmits it to each of his contacts independently with probability p .
 - ❖ Second wave: each person in the first wave transmits to each of his contacts independently with probability p (the contacts of people are mutually exclusive)
 - ❖ and so on..

Branching Processes



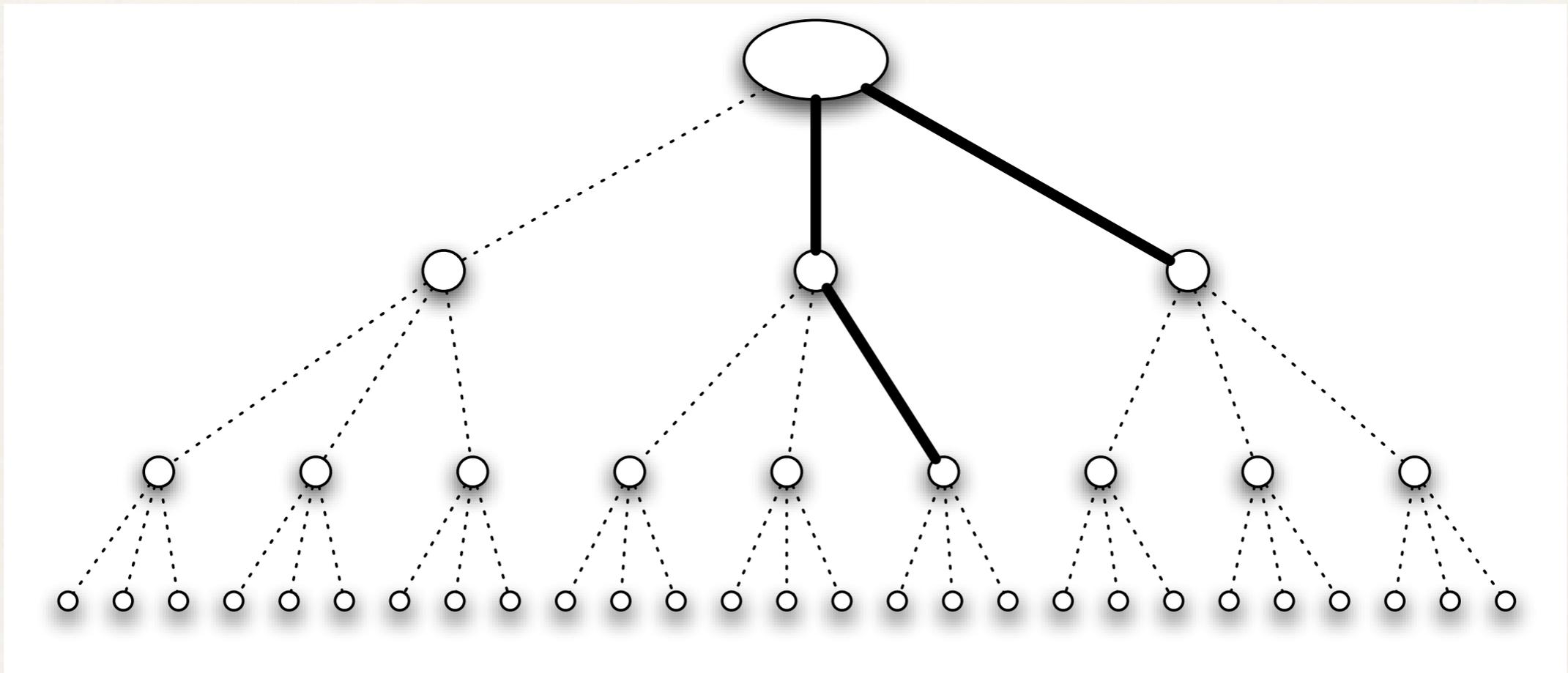
(a) *The contact network for a branching process*

Branching Processes



(b) *With high contagion probability, the infection spreads widely*

Branching Processes



(c) *With low contagion probability, the infection is likely to die out quickly*

The Basic Reproductive Number R_0

- ❖ The basic reproductive number, denote R_0 , is the expected number of new cases of the disease caused by a single individual.
- ❖ For the simple branching process we saw, we have $R_0=kp$.

The Basic Reproductive Number R_0

Claim: If $R_0 < 1$, then with probability 1, the disease dies out after a finite number of waves. If $R_0 > 1$, then with probability greater than 0 the disease persists by infecting at least one person in each wave.

The Basic Reproductive Number R_0

- ❖ Implication: It's always good to reduce the value of R_0 !
- ❖ Quarantining people reduces k and encouraging behavioral measures such as sanitary practices reduces p .

- ❖ Clearly, the branching process is too simplistic!

The SIR Epidemic Model

- ❖ An individual node goes through three potential stages during the course of the epidemic:
 - ❖ Susceptible: Before the node has caught the disease, it is susceptible to infection from its neighbors.
 - ❖ Infectious: Once the node has caught the disease, it is infectious and has some probability of infecting each of its susceptible neighbors.
 - ❖ Removed: After a particular node has experienced the full infectious period, this node is removed from consideration.

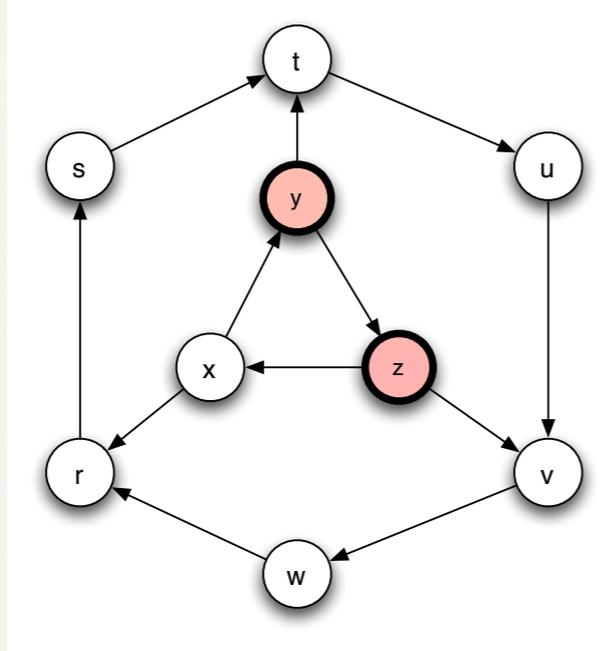
The SIR Epidemic Model

- ❖ Given this three-stage “life cycle” for the disease at each node, a model for epidemics on networks can be defined.
- ❖ The network structure: a directed graph representing the contact network (edge u to v means that if u becomes infected, the disease has the potential to spread to v).
- ❖ Two other quantities: p (the probability of contagion) and t_I (the length of infection)

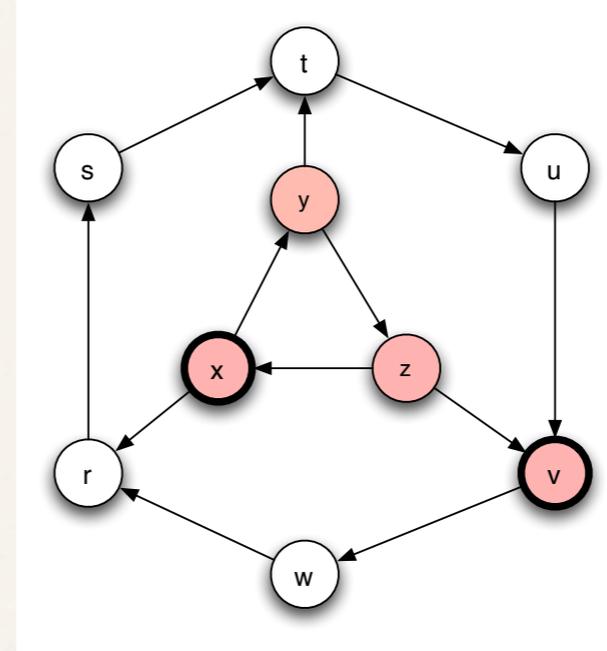
The SIR Epidemic Model

- Initially, some nodes are in the I state and all others are in the S state.
- Each node v that enters the I state remains infectious for a fixed number of steps t_I .
- During each of these t_I steps, v has a probability p of passing the disease to each of its susceptible neighbors.
- After t_I steps, node v is no longer infectious or susceptible to further bouts of the disease; we describe it as *removed* (R), since it is now an inert node in the contact network that can no longer either catch or transmit the disease.

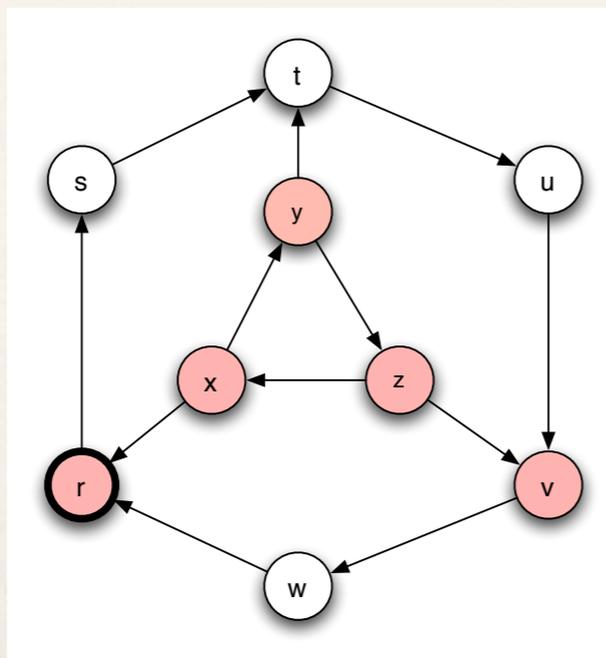
The SIR Epidemic Model



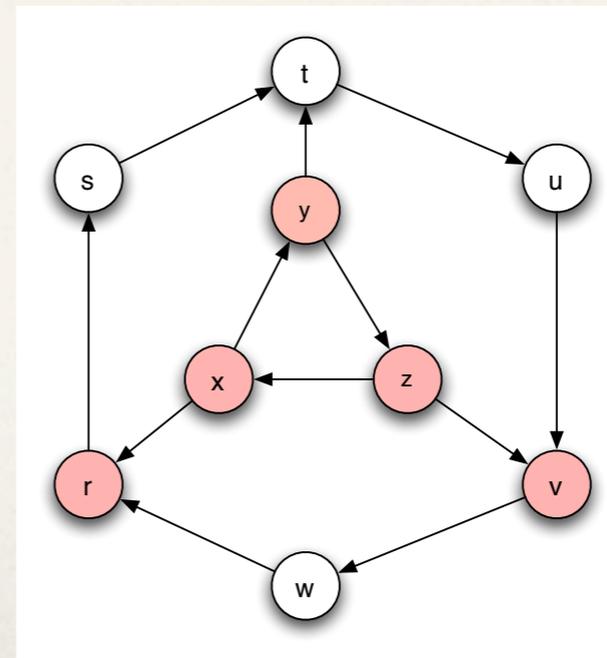
(a)



(b)



(c)



(d)

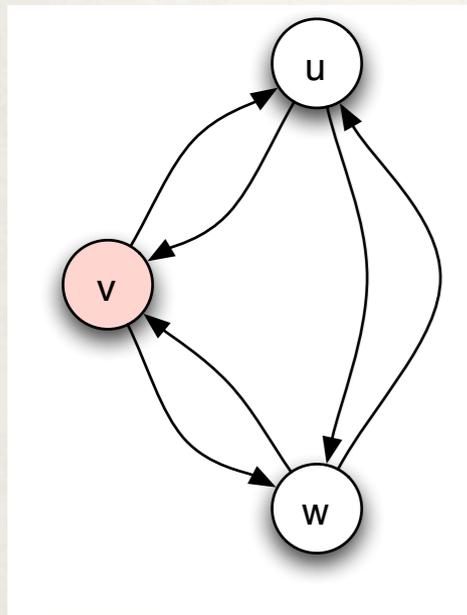
The SIS Epidemic Model

- ❖ The SIR epidemic model is appropriate for epidemics in which each individual contracts the disease at most once.
- ❖ To allow for nodes that can be reinfected multiple times, a model can have only the S and I, but not R, states.

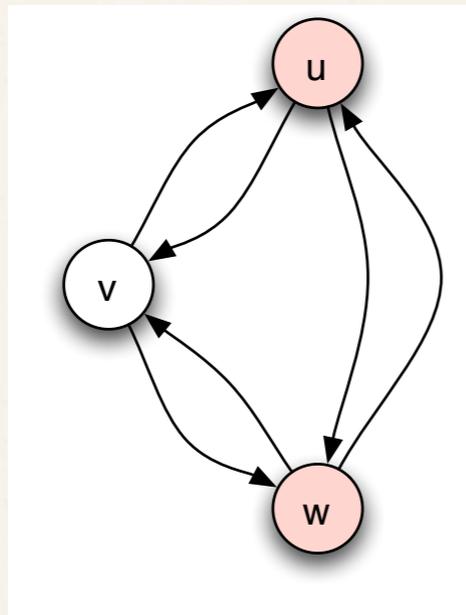
The SIS Epidemic Model

- Initially, some nodes are in the I state and all others are in the S state.
- Each node v that enters the I state remains infectious for a fixed number of steps t_I .
- During each of these t_I steps, v has a probability p of passing the disease to each of its susceptible neighbors.
- After t_I steps, node v is no longer infectious, and it returns to the S state.

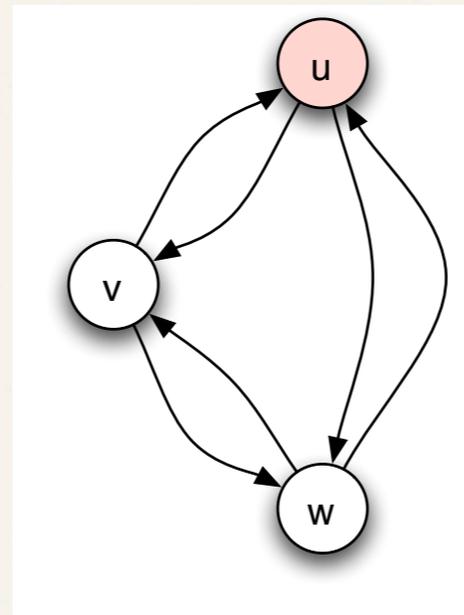
The SIS Epidemic Model



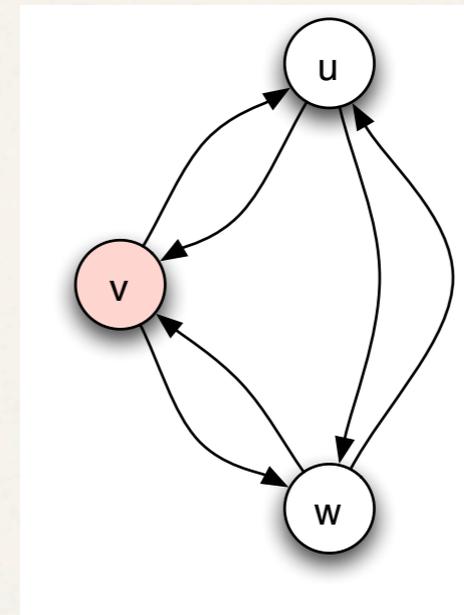
(a)



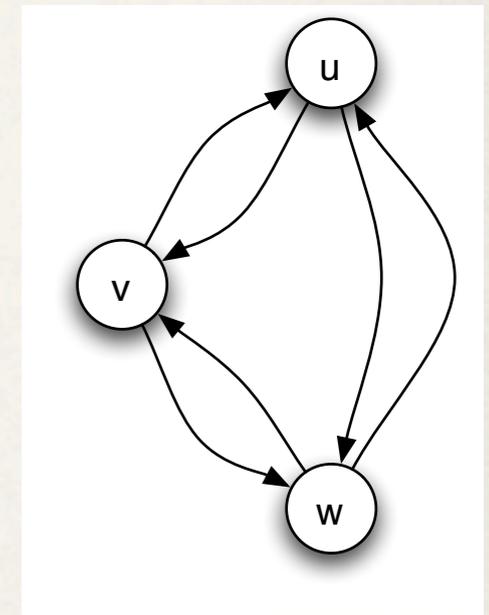
(b)



(c)

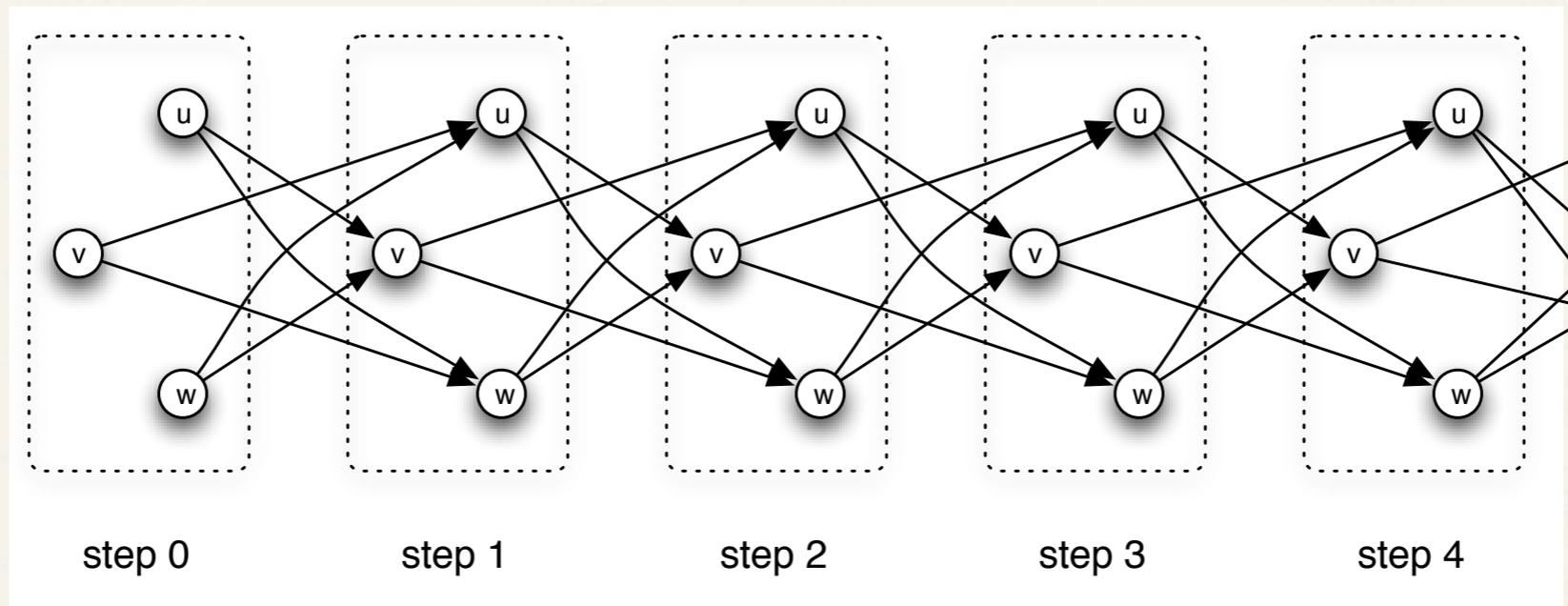


(d)

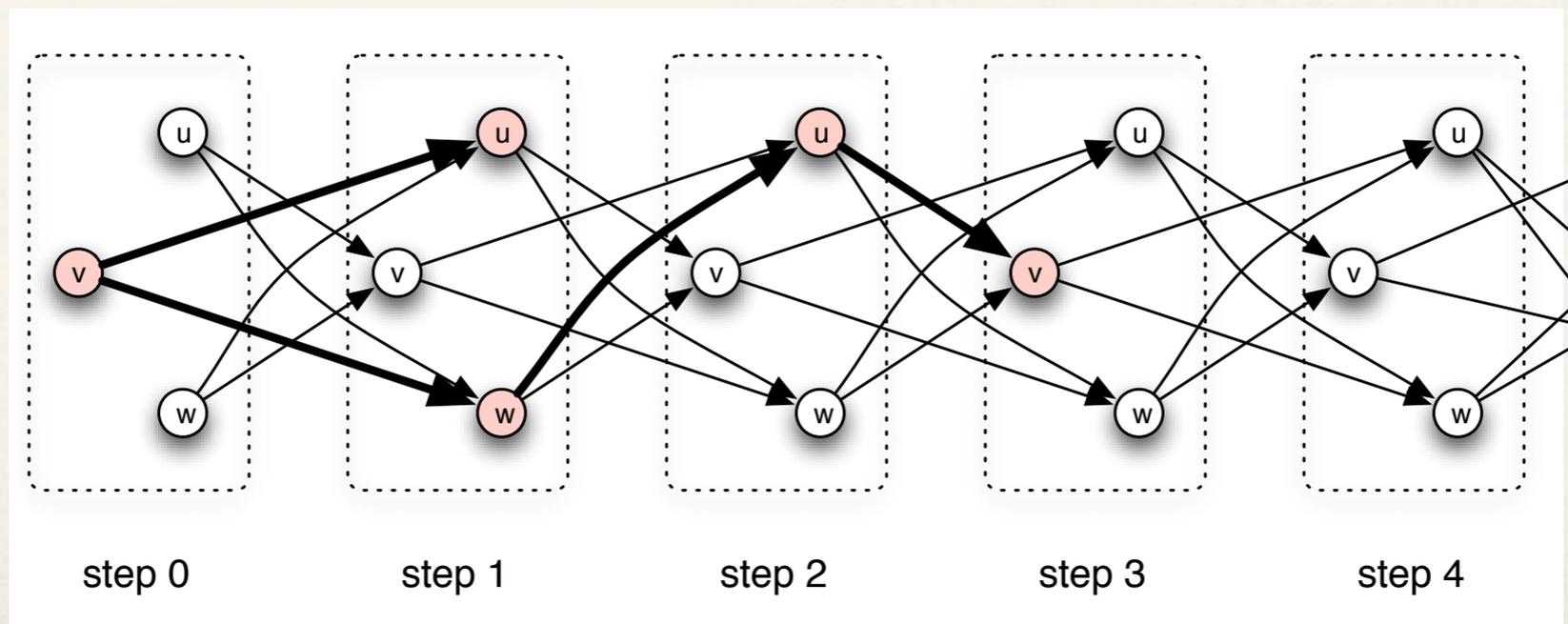


(e)

A Connection Between SIR and SIS



(a) To represent the SIS epidemic using the SIR model, we use a “time-expanded” contact network



(b) The SIS epidemic can then be represented as an SIR epidemic on this time-expanded network.

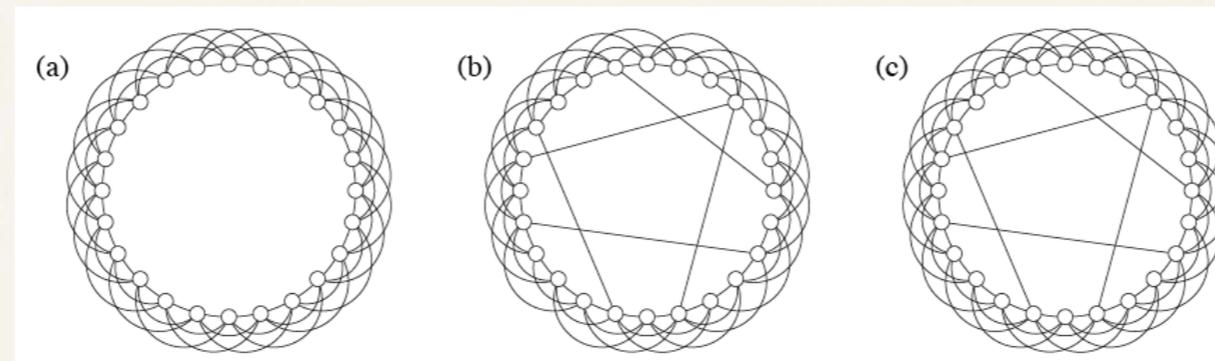
The SIRS Epidemic Model

- ❖ Combines SIR and SIS:
 - ❖ After an infected node recovers, it passes briefly through the R state on its way back to the S state.

Small World Effect in an Epidemiological Model

Marcelo Kuperman^{1,*} and Guillermo Abramson^{1,2,†}

Recall: the small-world model (p : probability of rewiring an edge)



The number of infected people ($n_{\text{inf}}(t)$) by SIRS epidemic:

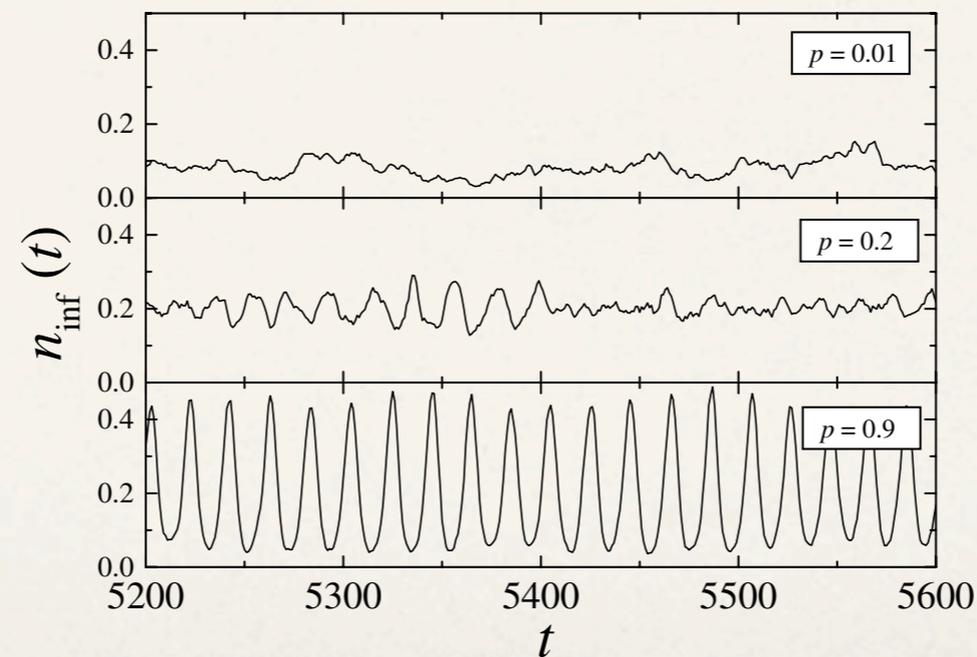


FIG. 1. Fraction of infected elements as a function of time. Three time series are shown, corresponding to different values of the disorder parameter p , as shown in the legends. Other parameters are $N = 10^4$, $K = 3$, $\tau_I = 4$, $\tau_R = 9$, $N_{\text{inf}}(0) = 0.1$.

Acknowledgments

- ❖ Slides on epidemics and networks are based on the book “Networks, Crowds, and Markets” by Easley and Kleinberg.