Introduction to Epidemic Spreading Theory

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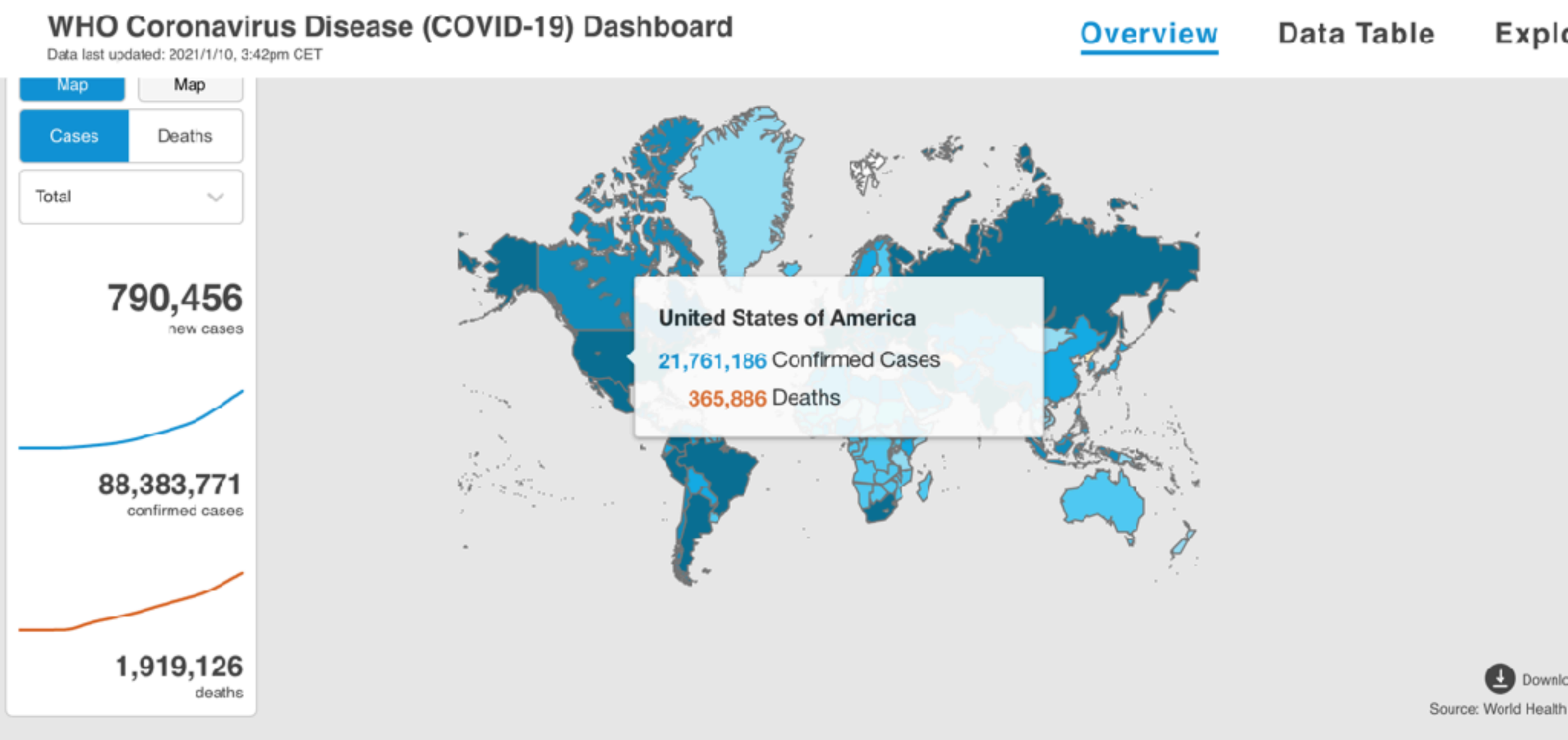
Ver. 3

Overview

- Prologue: some history
- Basics: Infections and Epidemic Models
- Deterministic Epidemic Models
- Stochastic Epidemic Models (Branching process)
- Epidemic processes on Complex Networks
- Numerical Methods
- Spreading in Other Domains
- Summary

References (Books & Review Papers)

- R. Anderson and R. May, Infectious Diseases of Humans, Oxford Univ. Press (1992).
- M. J. Keeling and P. Rohani, Modeling Infectious Diseases in Humans and Animals, Princeton Univ. Press (2011).
- D. J. Daley and J. Gani, Epidemic Modelling, Cambridge Univ. Press (2007).
- R. Sole and S. F. Elena, Viruses as Complex Adaptive Systems, Princeton Univ. Press (2019).
- M. E. J. Newman, Networks, Oxford Univ. Press (2018) [Chap. 17. Epidemics on Networks]
- R. Pastor-Satorras, C. Castellano, P. Van Mieghem, and A. Vespignani, Epidemic processes in complex networks, Rev. Mod. Phys., 87, 925 (2015); https://arxiv.org/abs/1408.2701
- J. C. Miller, A primer on the use of probability generating functions in infectious disease modeling, Infectious Disease Modeling, 3, 192 (2018).



Globally, as of **3:42pm CET, 10 January 2021**, there have been **88,383,771 confirmed cases** of COVID-19, including **1,919,126 deaths**, reported to WHO.

The earliest human

- Small Group:

  chronic vs acute diseases

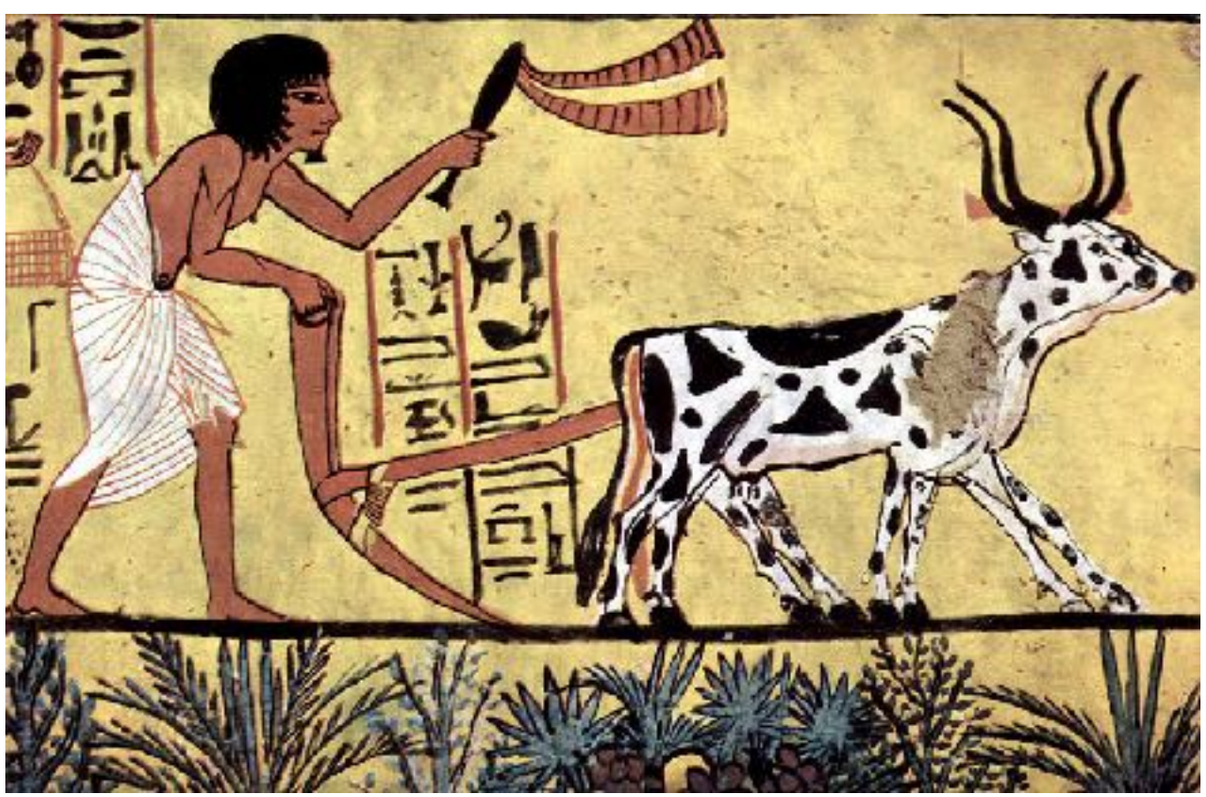
- Frequent migration

- Vector-borne diseases:

  아프리카 수면병 (tsetse fly),

  Malaria (mosquito)

The neolithic revolution

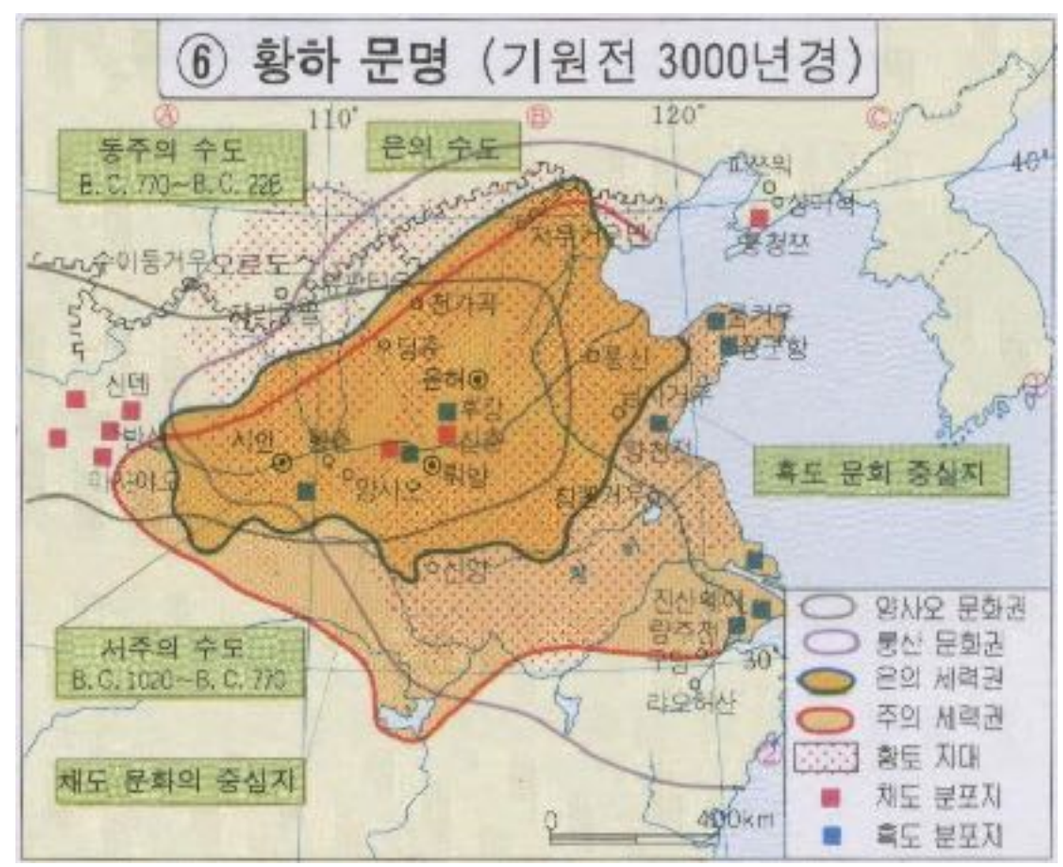


- Sedentary lifestyle
- More population
- Domestication of animals

Measles (홍역)	Dog
Smallpox (천연두)	Cow
Influenza	Bird
Covid-19	Manidae (천산갑)

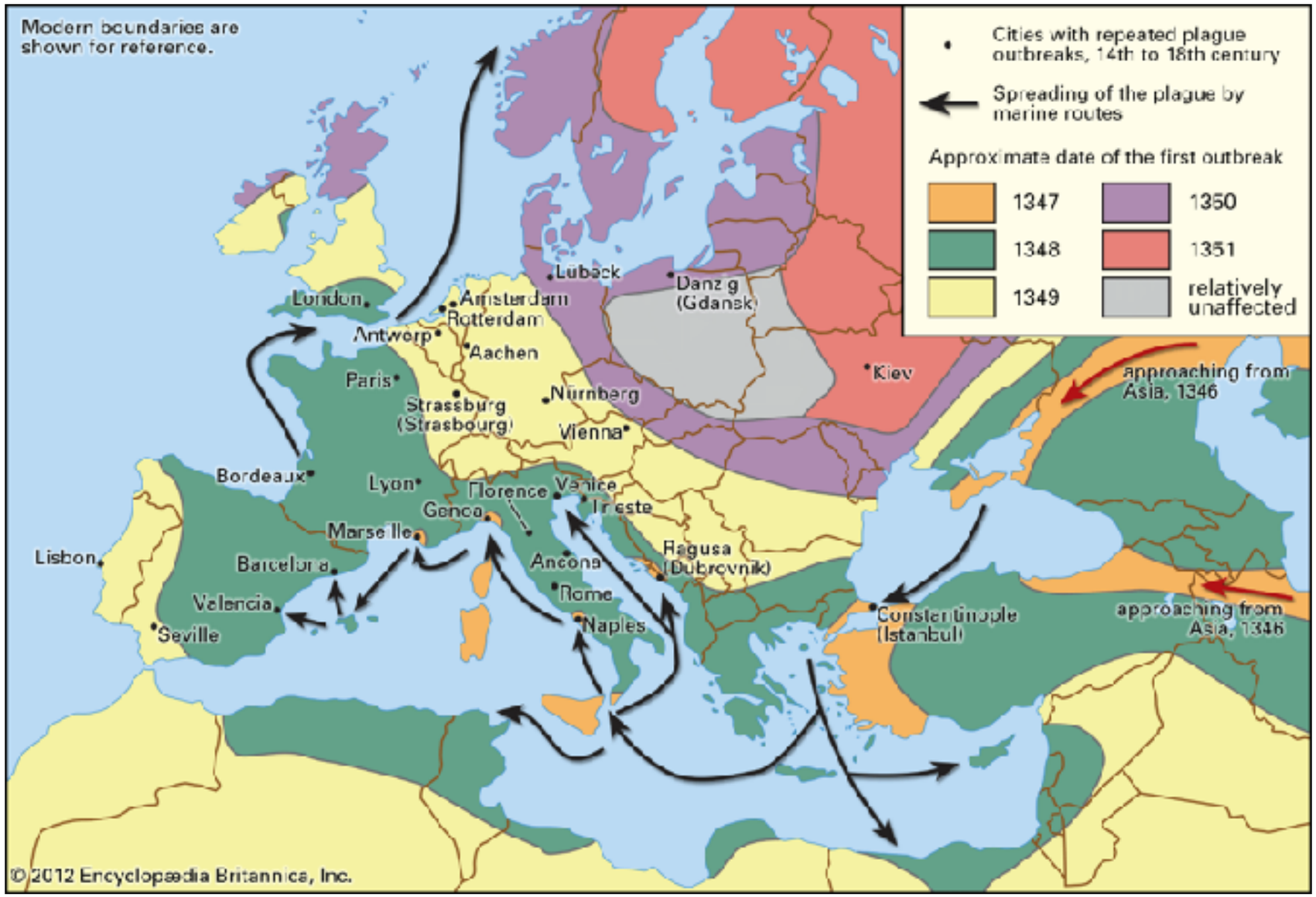
Ancient Civilization

[Pieter Bruegel (1563)]



- More population
- City: Dense population

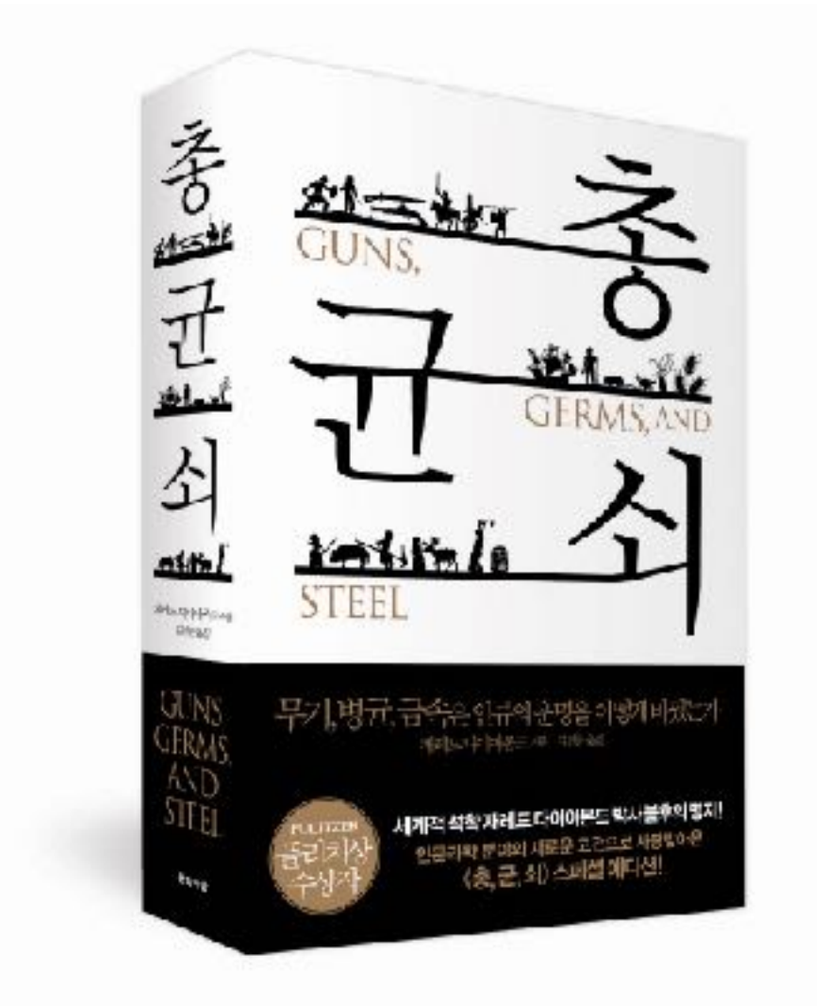
Black Death (Plague)



- One-third of the continent's population died.
- Decline of the church's power
- Wages high
- The end of feudalism

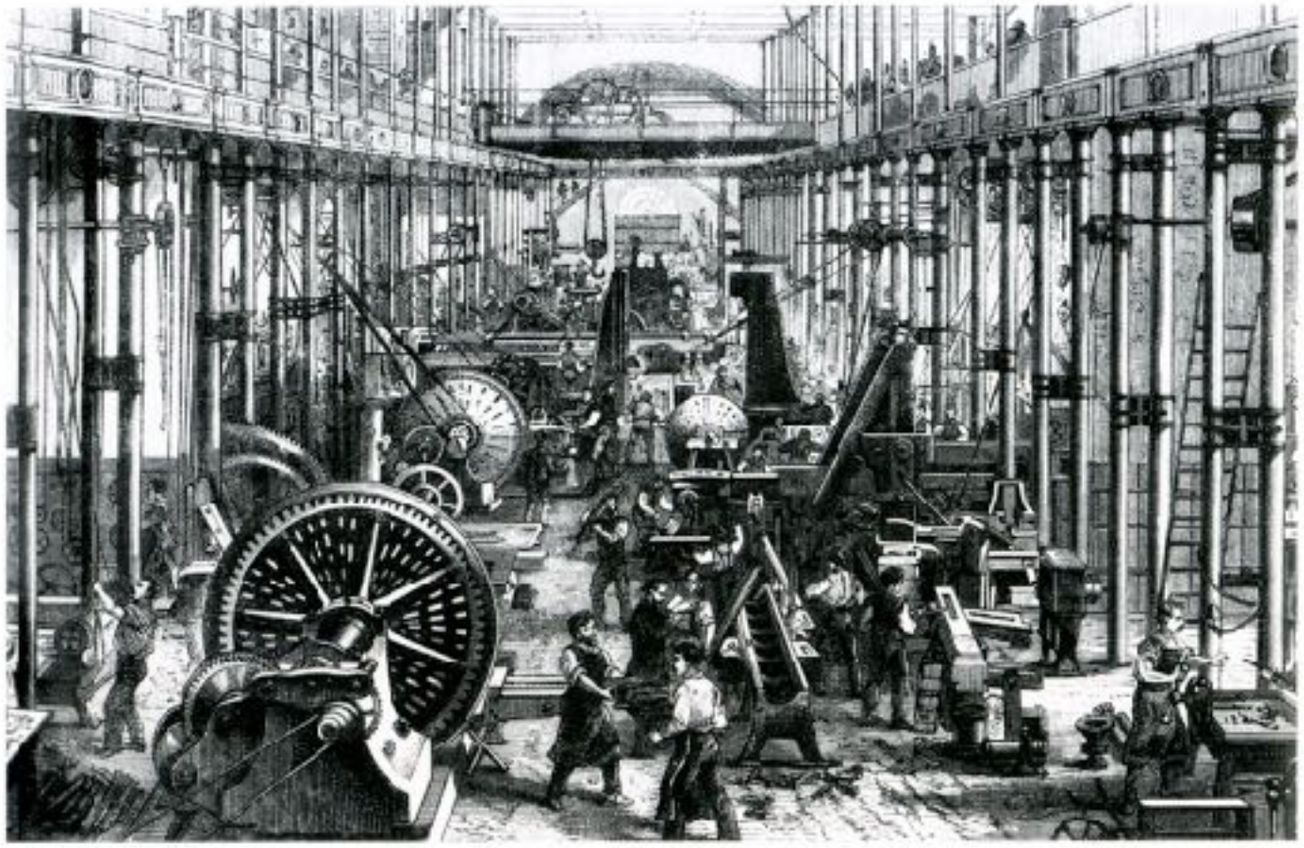
Native American Epidemics

[wikipedia]



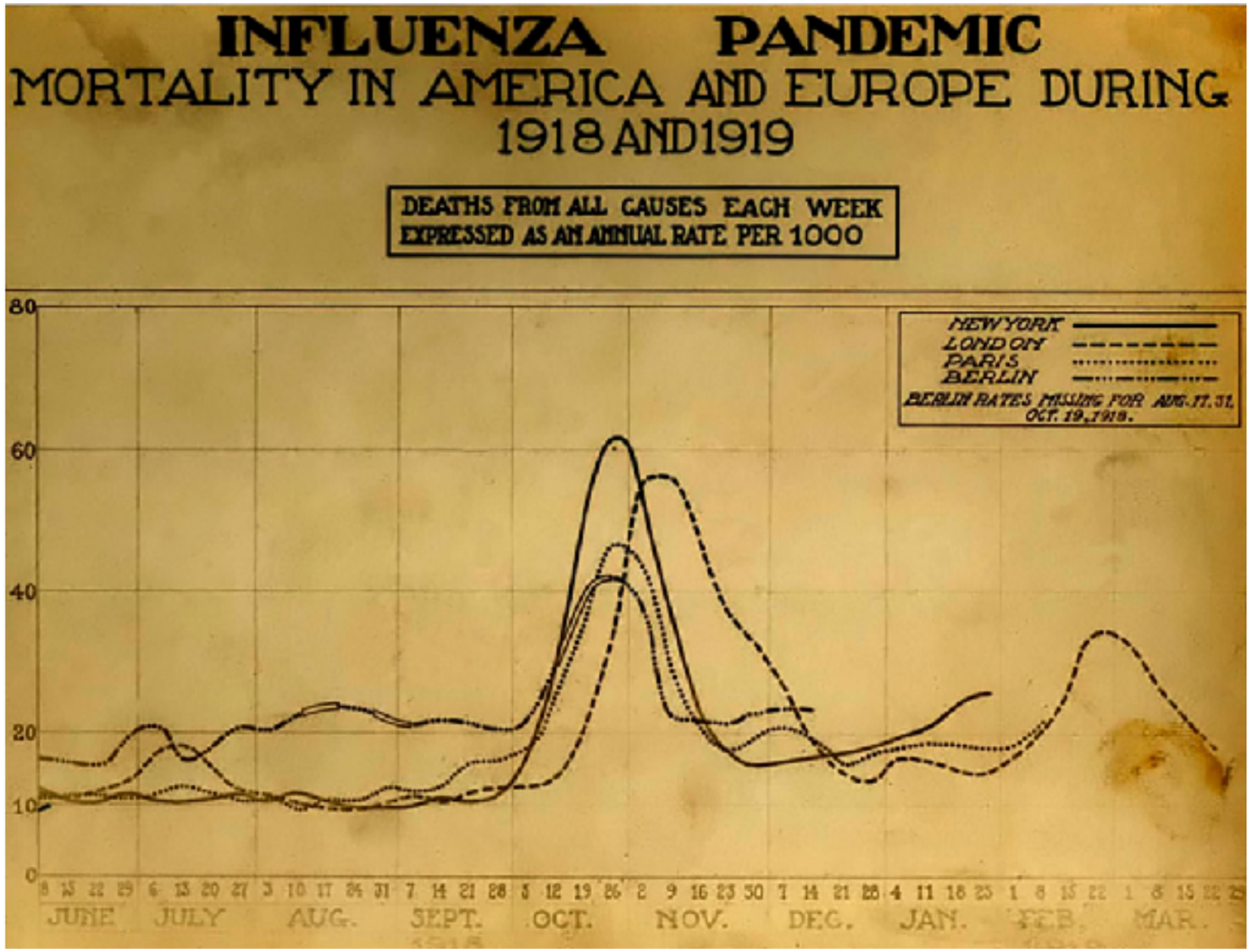
- Some believe that the death of more than 90 % of the native population of the New World was caused by Old world diseases.
- Cocoliztli (Salmonella) [Nat. Ecology & Evolution, 2, 520 (2018)]

The industrial revolution



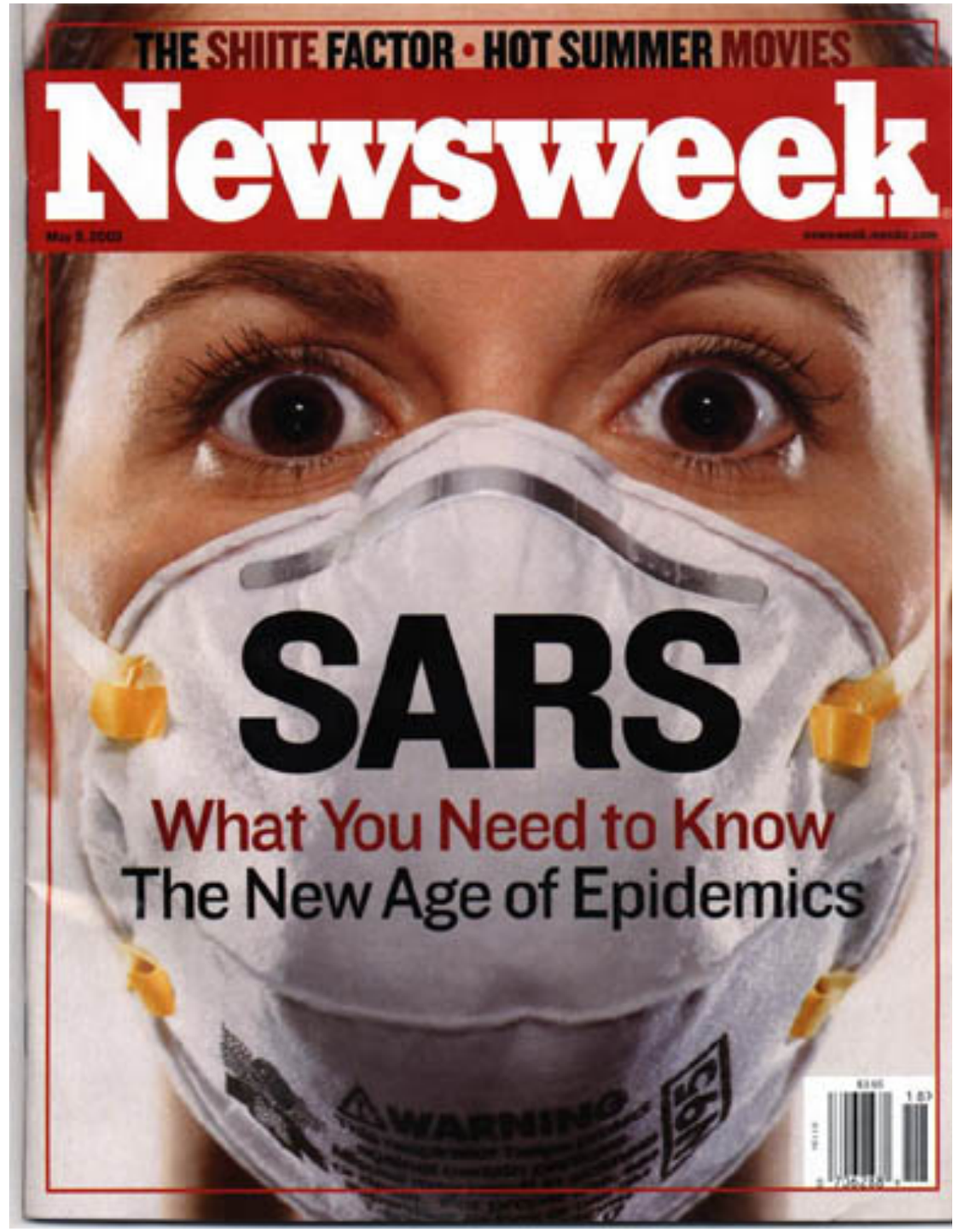
- City
- More and denser population
- High mobility

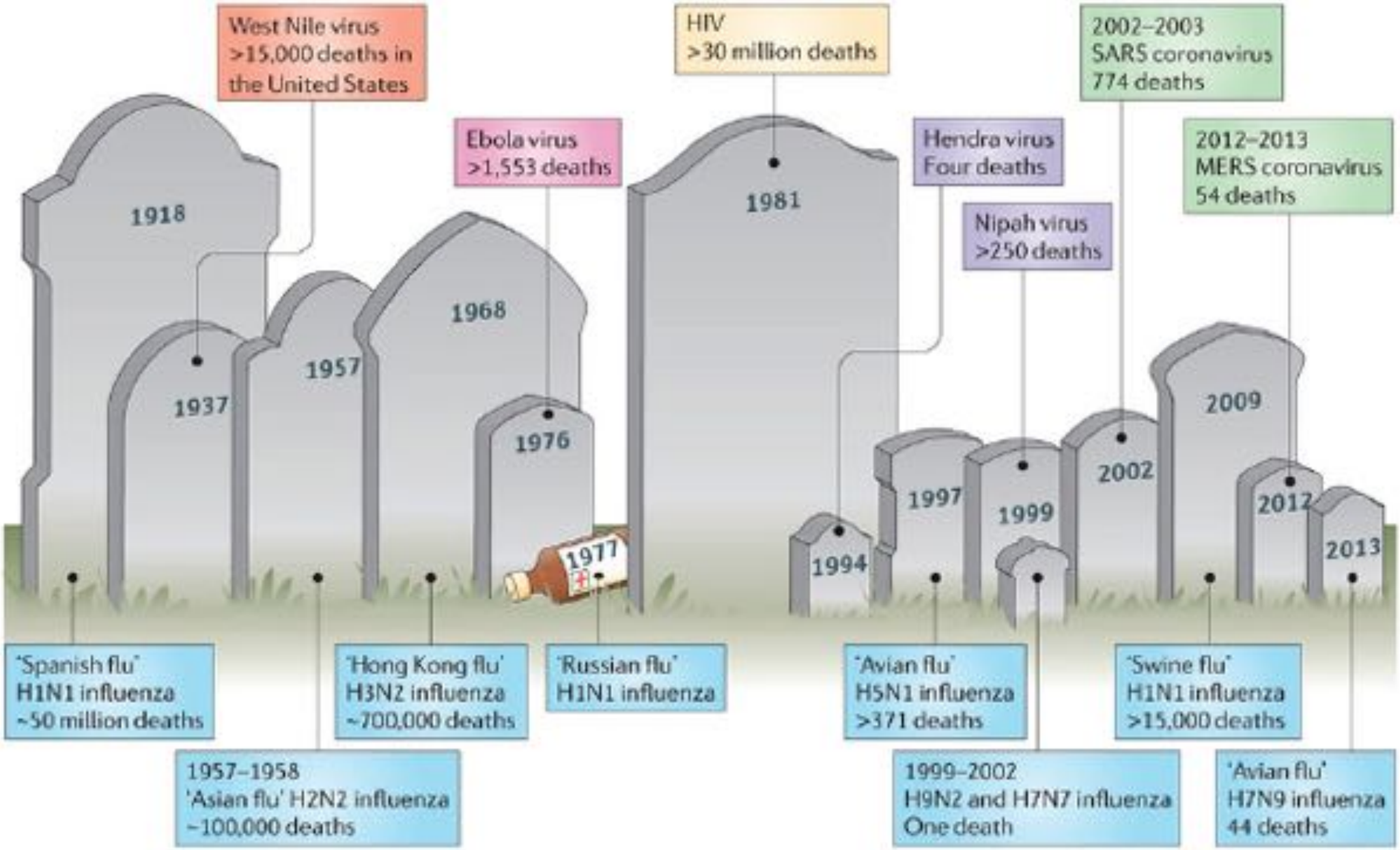
Spanish Flu (무오년 감기)



- From Feb. 1918 to Apr. 1920, Spanish flu infected 500 million (5억) people [wikipedia].
- The death toll is estimated to be between 17 and 50 million [wikipedia].

New Diseases

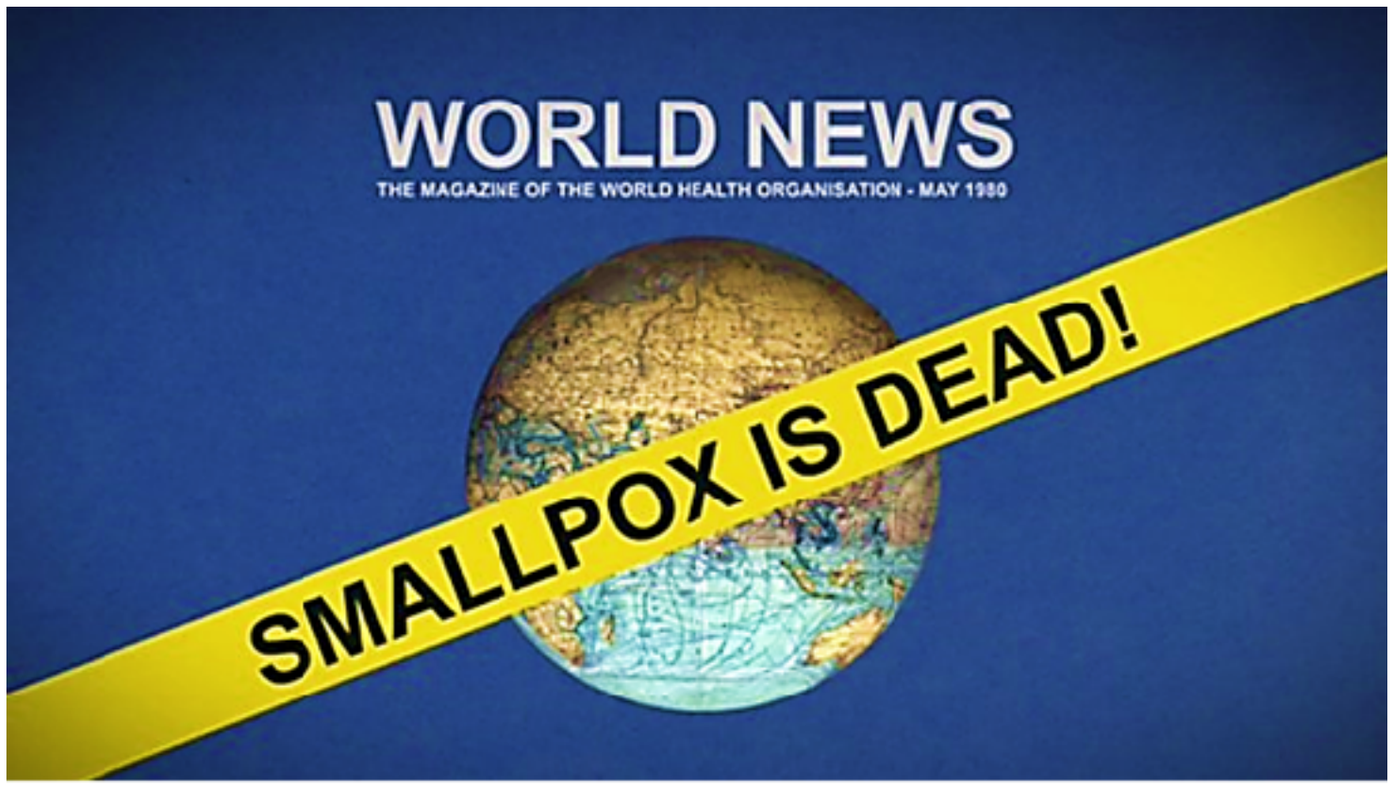




[Bean et al (2013)]

- Covid-19 (at least 1.7 million)

Vaccine and Herd Immunity



- Vaccinus (라틴어 젖소)
- “It is time to close the book on infectious diseases, and declare the war against pestilence won”, Dr. William H. Stewart (1969).

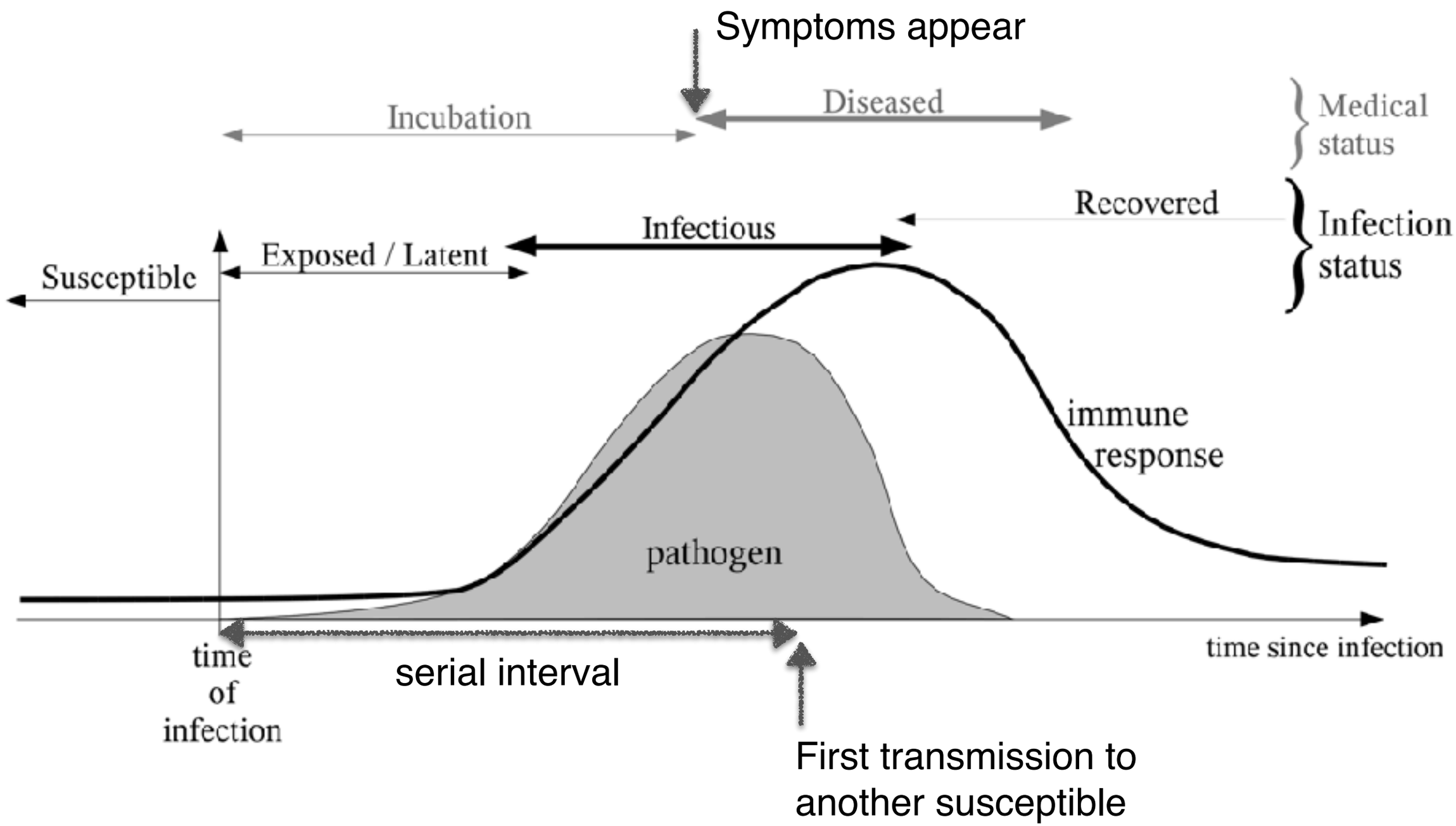
- Sanitary revolution

Mathematical Modeling of Epidemics

- In 1760 Daniel Bernoulli wrote the first epidemiological model, attempting prove the efficacy of inoculation against smallpox (천연두).
- W. Kermack and A. McKendrick published their theory of infectious diseases in a set of articles from 1927, 1932, and 1933 (Deterministic SIR model).
- One of the earliest of stochastic models is due to Reed and Frost in their class lectures at Johns Hopkins University in 1928, but they never published their work (Stochastic SIR model with discrete time).

  “I strongly urged Dr. Frost to publish his theory of the epidemic curve, but he thought it too slight a contribution”, E. B. Wilson’s note

Progress of a Disease



Purpose of Epidemic Models

- Aim of modeling: To describe, understand, and predict some real world epidemic phenomena
- Trade-off between *simple* and *realistic* models

simple	realistic
- Understanding mechanism	- Using real data
- Cause-effect relations	- Predict precisely

- Different geographic scale

Epidemic Models

- Compartments or classes:

  Susceptible, **I**nfected (Infectious, Infective), **R**ecovered (Removed), **E**xposed, etc

- Transmission:

  Contagious diseases (Influenza, Covid-19)

  Vector-borne diseases (Malaria, Dengue)

  Sexually transmitted diseases (HIV, Syphilis)

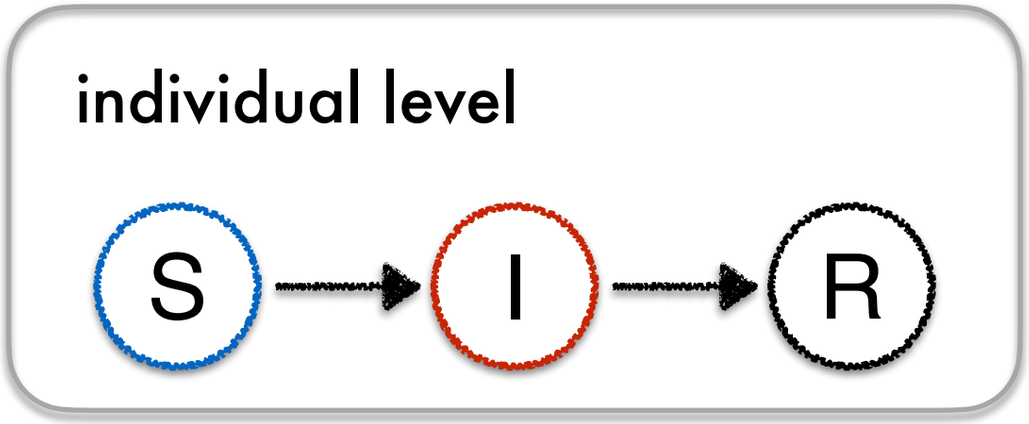
- Description:

  Deterministic or Stochastic

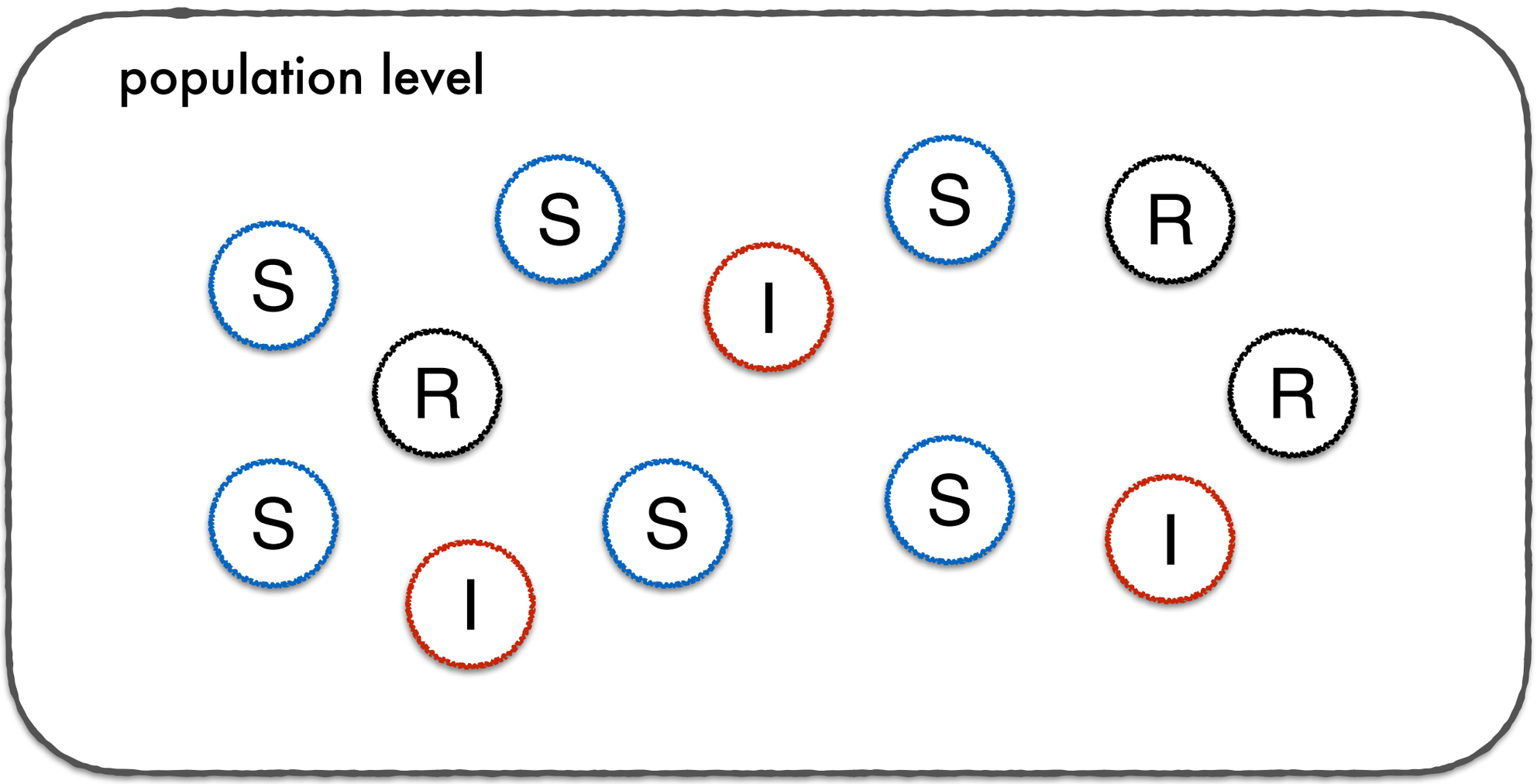
  Continuous or discrete time

  Fully-mixed, Networked, or Meta-population, etc.

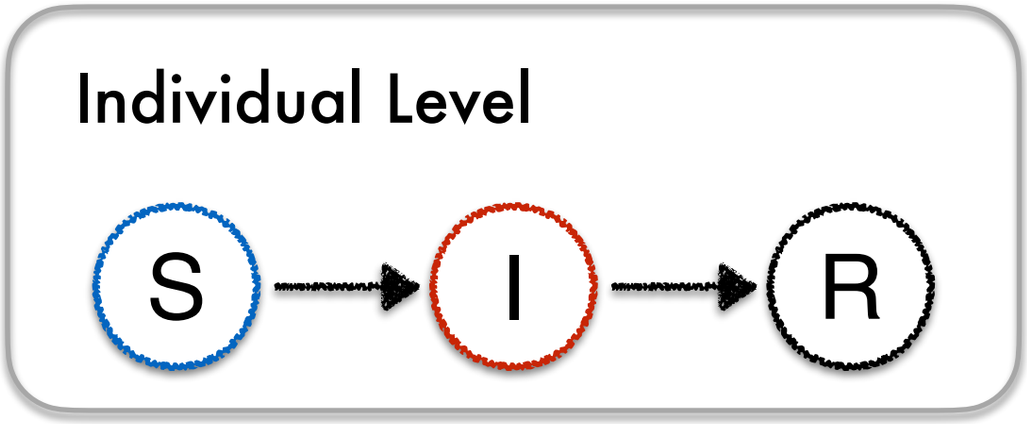
Compartmental Epidemic Model



- **S**usceptible: Healthy and susceptible to infections
- **I**nfected (infectious): Currently being infected and infective
- **R**ecovered (removed): Recovered and immune to infection



Susceptible-Infected-Recovered (SIR) Model

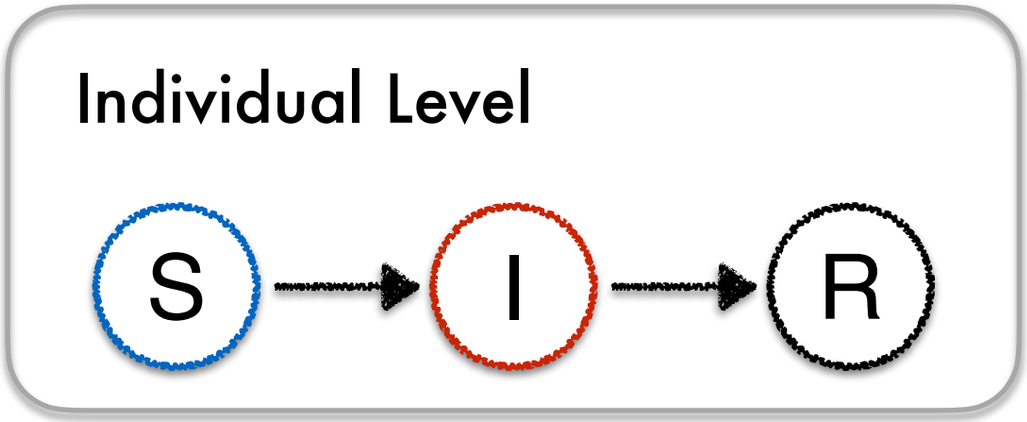


1. Infection: by ***interaction (contact)*** of the susceptible individual and an infectious one.

2. Recovery: the infected becomes susceptible, autonomously and spontaneously after a certain time.

- In a long time limit: there are S and R individuals.

SIR Model in a Well-Mixed Population



- Let S, X, and R be the number of S, I, and R individuals respectively.

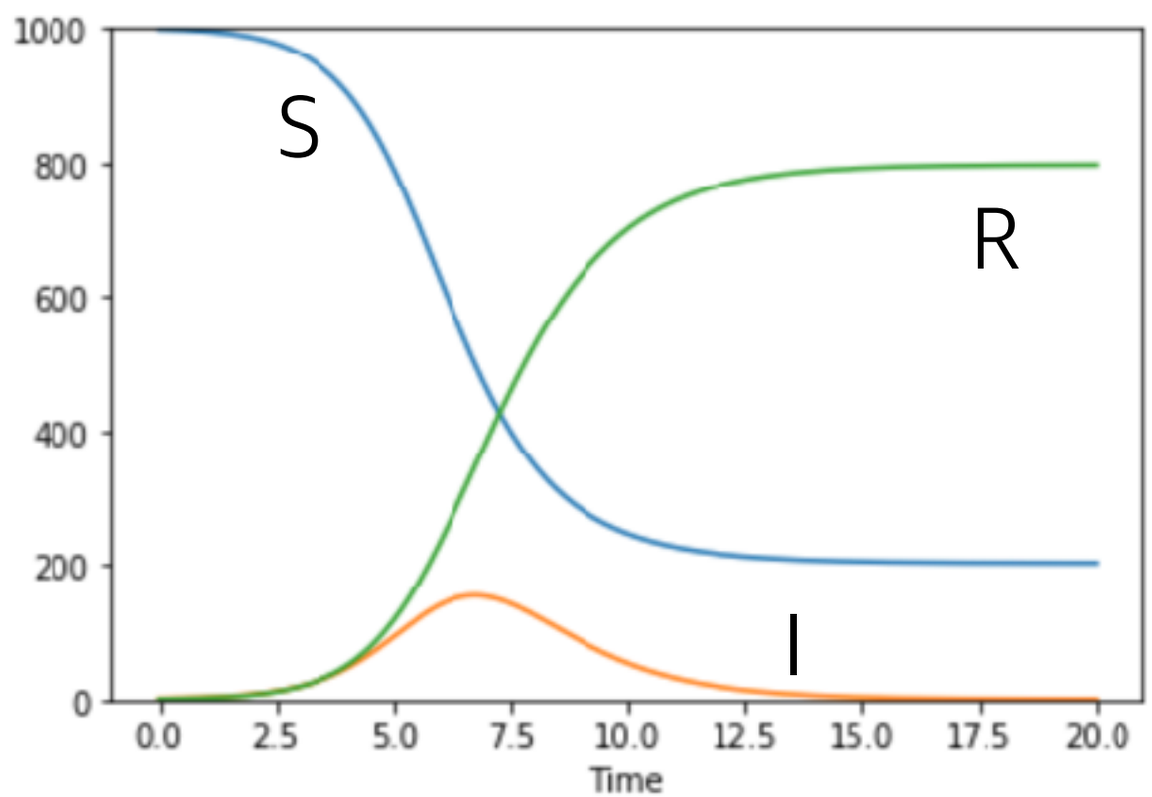
- Infection rate: β
  (the rate of contacts between an infected individual and all others)
- Recovery rate: γ

Eq. 1 $$\frac{dS}{dt} = -\frac{\beta}{N} SX,$$

Eq. 2 $$\frac{dX}{dt} = \frac{\beta}{N} SX - \gamma X,$$

Eq. 3 $$\frac{dR}{dt} = \gamma X,$$

$$S + X + R = N.$$



$$\beta = 2,$$
$$\gamma = 1,$$
$$N = 1000,$$
$$I_0 = 1.$$

SIR Model in a Well-Mixed Population

Let *s*, *x*, and *r* be the fraction of S, I, and R individuals in a large population limit.

Eq. 1 $\frac{ds}{dt} = -\beta s x,$

Eq. 2 $\frac{dx}{dt} = \beta s x - \gamma x,$

Eq. 3 $\frac{dr}{dt} = \gamma x,$

Eq. 4 $s + x + r = 1.$

$$-\frac{1}{\beta s}\frac{ds}{dt} = \frac{1}{\gamma}\frac{dr}{dt}.$$ (Eqs. 1 & 3)

$$\frac{ds}{dr} = -\frac{\beta}{\gamma}s. \longrightarrow s = s_0 e^{-\frac{\beta}{\gamma}(r - r_0)}.$$

Eq. 3
$$\begin{aligned}\frac{dr}{dt} &= \gamma x \\ &= \gamma(1 - s - r) \quad \text{(using Eq. 4)} \\ &= \gamma(1 - r - s_0 e^{-\frac{\beta}{\gamma}(r - r_0)}).\end{aligned}$$

At a steady state,

$$\begin{aligned} r &= 1 - s_0 e^{-\frac{\beta}{\gamma}(r - r_0)} \\ &\approx 1 - e^{-\frac{\beta}{\gamma}r}. \end{aligned}$$

Basic Reproduction Number

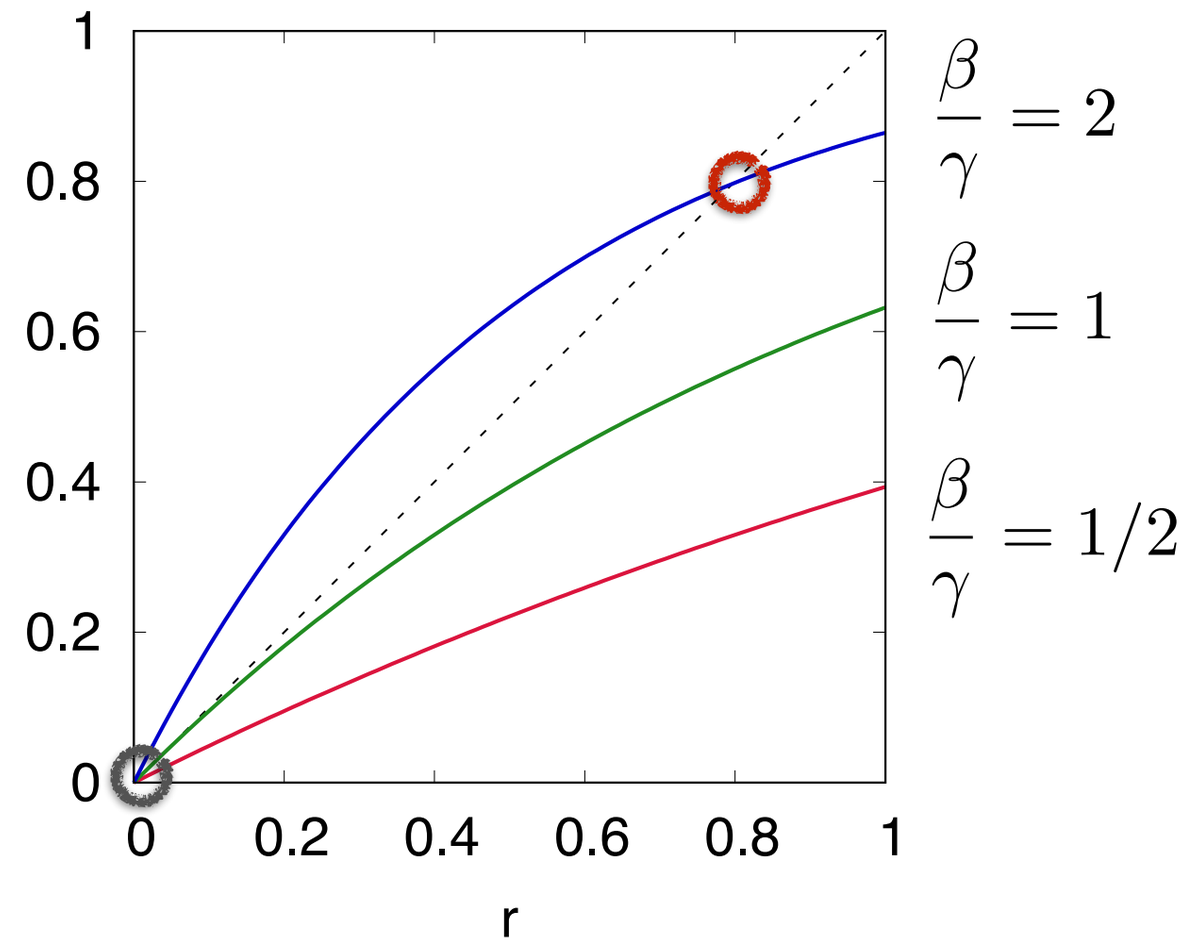
Self-consistent equation: $r^* = 1 - e^{-\frac{\beta}{\gamma} r^*}$.

$$f(r) = 1 - e^{-\frac{\beta}{\gamma} r}.$$

$$\frac{df}{dt} = \frac{\beta}{\gamma} e^{-\frac{\beta}{\gamma} r}.$$

$$\text{If } \frac{\beta}{\gamma} \leq 1 : r_\infty = 0,$$

$$\text{If } \frac{\beta}{\gamma} > 1 : r_\infty = 0 \text{ or } r^*.$$

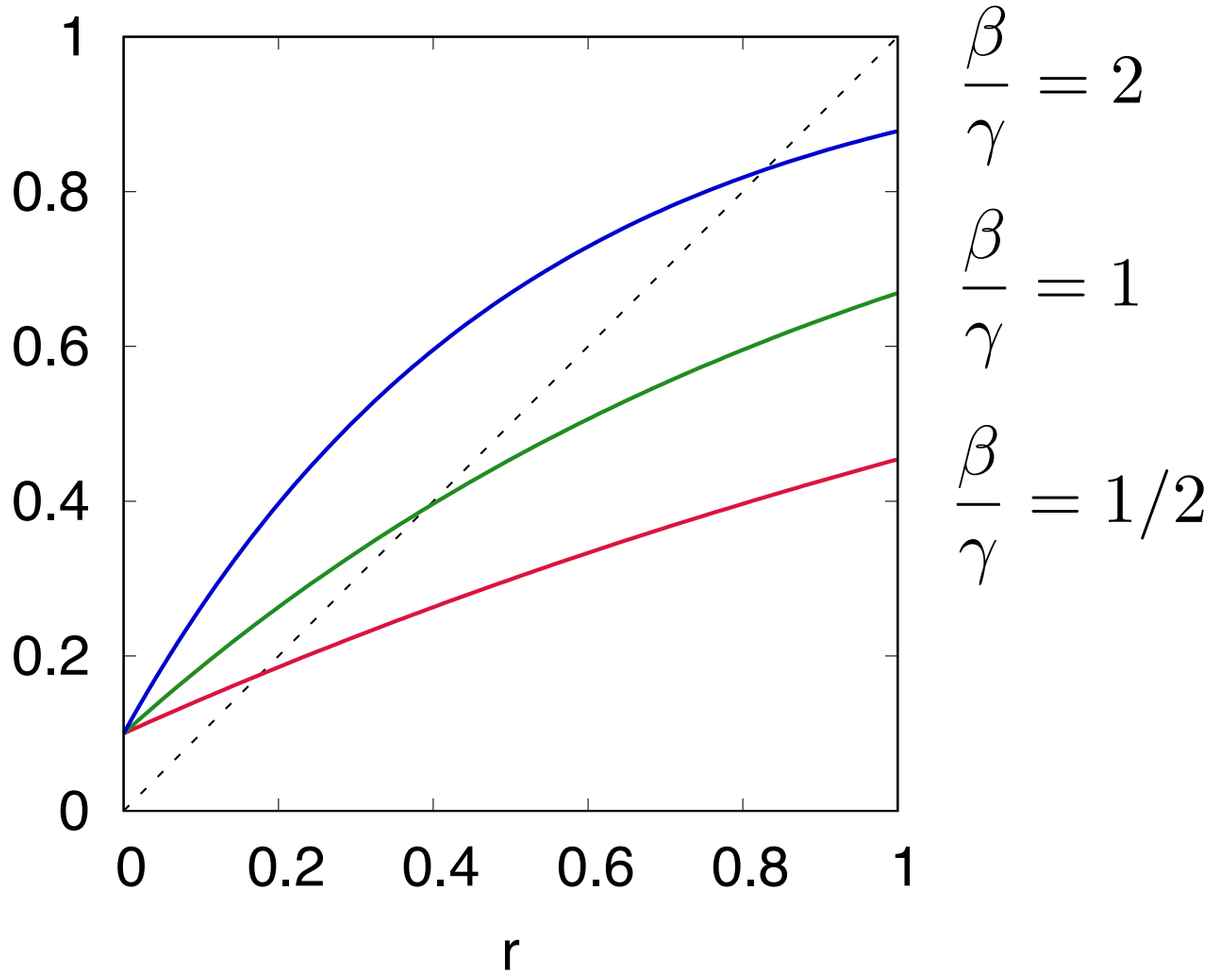


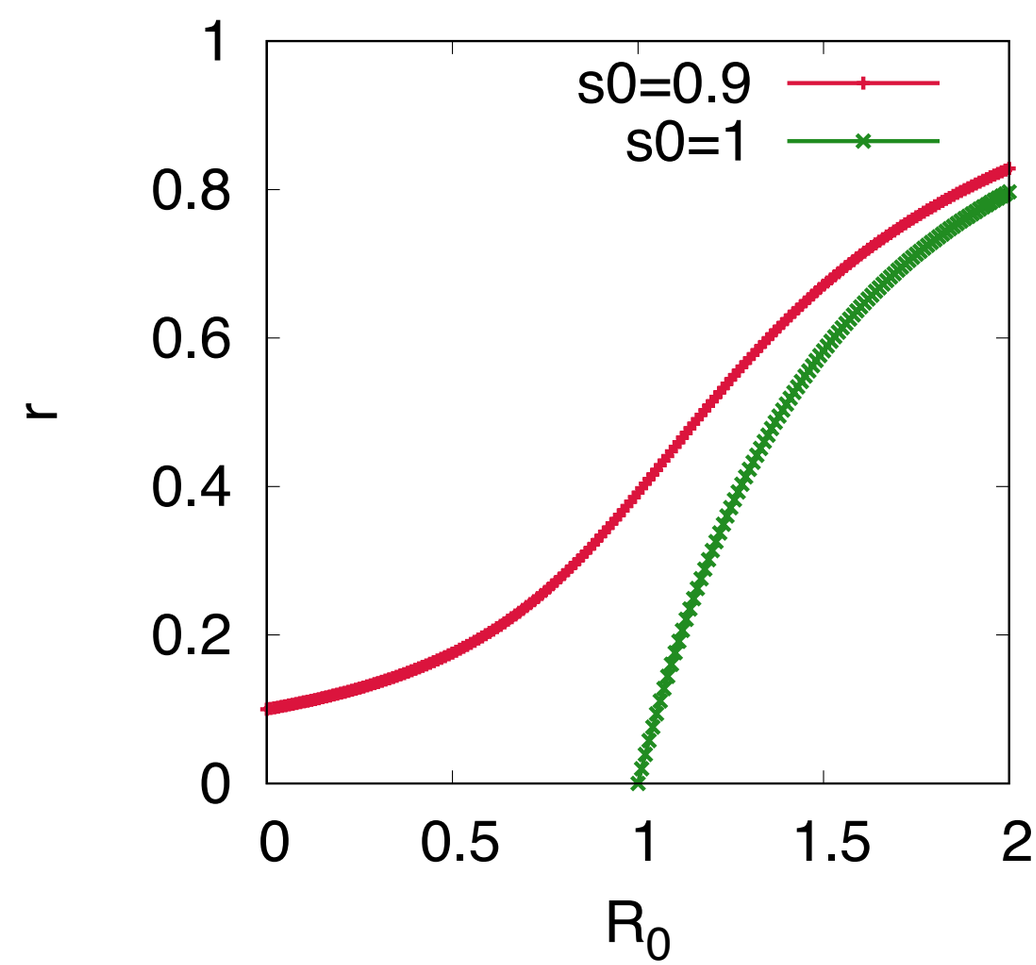
Basic Reproduction Number (Ratio): $R_0 = \frac{\beta}{\gamma}$.

→ The average number of secondary cases arising from a primary case in an entirely susceptible population.

SIR Model in a Well-Mixed Population

$$r = 1 - s_0 e^{-\frac{\beta}{\gamma}(r - r_0)}.$$





$$s_0 = 0.9, x_0 = 0.1, r_0 = 0.$$

Herd Immunity (1)

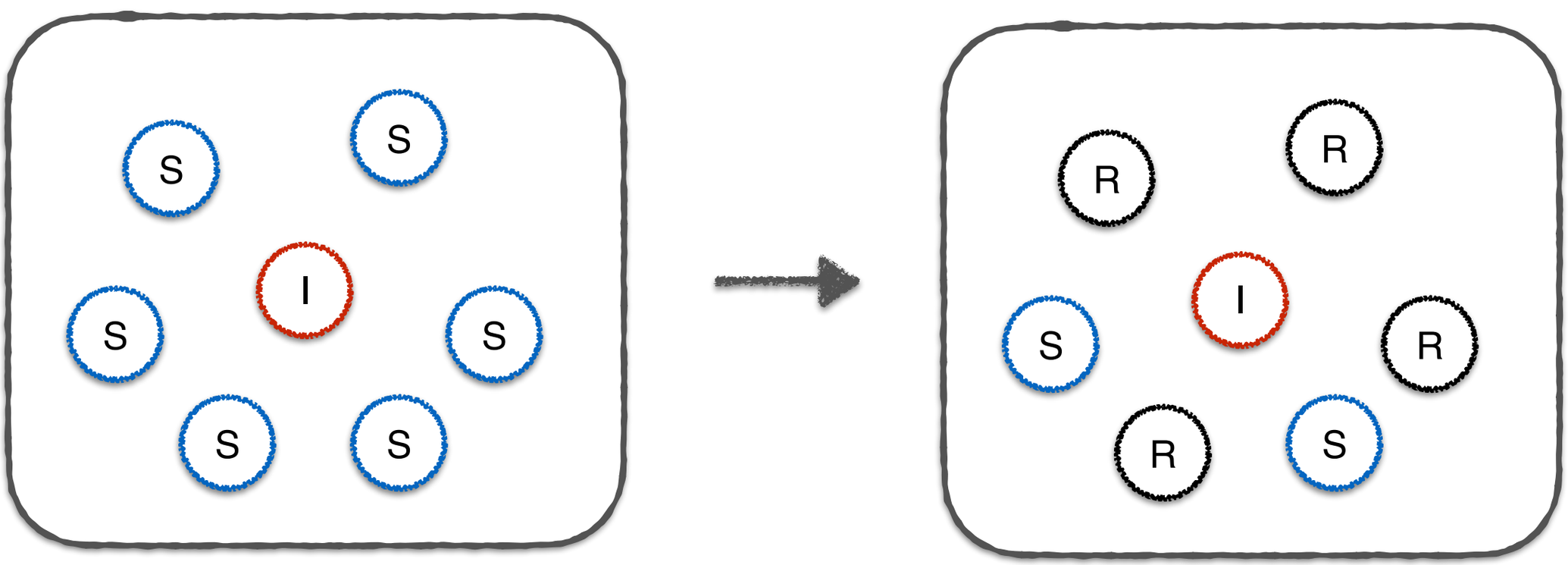
Eq. 2 $$\frac{dx}{dt} = (\beta s - \gamma)x$$
$$= \gamma(R_0 s - 1)x.$$

$\rightarrow$ $R_0 s \geq 1$

$\rightarrow$ $R_0(1 - r) \gtrsim 1$

Herd immunity threshold:

$$r_H = 1 - \frac{1}{R_0}.$$



$R_0 s < 1$

Herd Immunity (2)

Eq. 2 $$\frac{dx}{dt} = (\beta s - \gamma)x$$
$$= \gamma(R_0 s - 1)x.$$

$\rightarrow$ $R_0 s \geq 1$

$\rightarrow$ $R_0(1-r) \gtrsim 1$

Herd immunity threshold:

$$r_H = 1 - \frac{1}{R_0}.$$

For covid-19: 0.695 ~ 0.824

Values of R_0 of well-known infectious diseases (assayed before any social interventions)

	Disease	Transmission	R_0
홍역	Measles	Aerosol	12-18[1]
수두	Chickenpox (varicella)	Aerosol	10-12[2]
볼거리	Mumps	Respiratory droplets	10-12[3]
풍진	Rubella	Respiratory droplets	6-7[4]
소아마비	Polio	Fecal-oral route	5-7[5]
백일해	Pertussis	Respiratory droplets	5.5[6]
천연두	Smallpox	Respiratory droplets	3.5-6[7]
	COVID-19	Respiratory droplets and aerosol[8]	3.28-5.7[9][10]
	HIV/AIDS	Body fluids	2-5[11]
	Common cold	Respiratory droplets	2-3[12]
	SARS	Respiratory droplets	0.19-1.08[13]
	Diphtheria	Saliva	1.7-4.3[14]
	Influenza (1918 pandemic strain)	Respiratory droplets	1.4-2.8[15]
	Ebola (2014 Ebola outbreak)	Body fluids	1.5-1.9[16]
	Influenza (2009 pandemic strain)	Respiratory droplets	1.2-1.6[17]
	Influenza (seasonal strains)	Respiratory droplets	0.9-2.1[18]
	MERS	Respiratory droplets	0.3-0.8[19]
	Nipah virus	Body fluids	0.48[20]

[wikipedia]

Connections with Statistical Physics Models

SIR Model

- Exact mapping to bond percolation

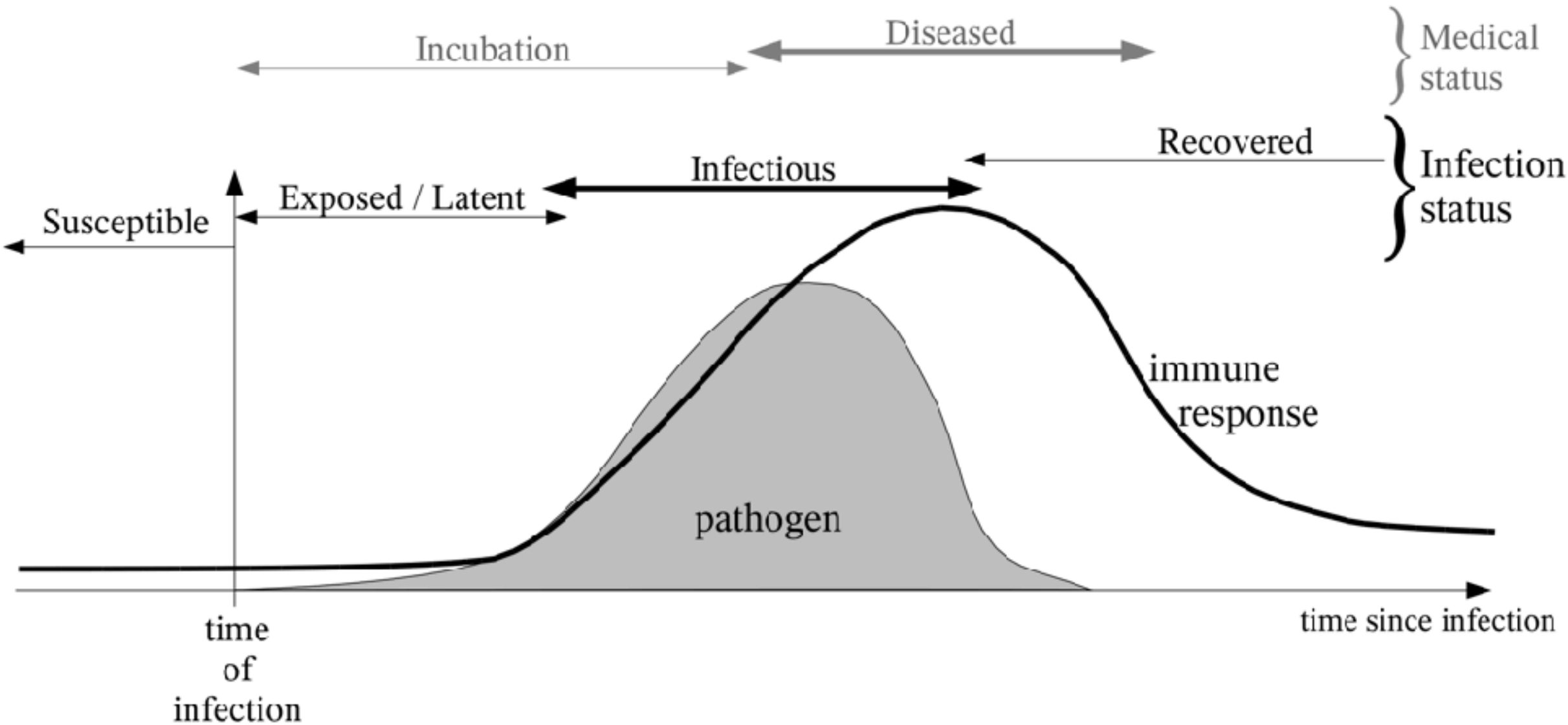
  [P. Grassberger, Math. Biosc. (1983); J. L. Cardy and P. Grassberger, J. Phys. A (1985);M. E. J. Newman, Phys. Rev. E (2002)]
- Forest Fire model (SIRS)

SIS Model

- Absorbing phase transitions
- Contact process [T. E. Harris (1974)]

  The “only” difference between the SIS and the CP is the number of offsprings that an active (infectious) individual can generate.

Compartmental Models in Epidemiology



- Population divided into compartments according to the disease status:

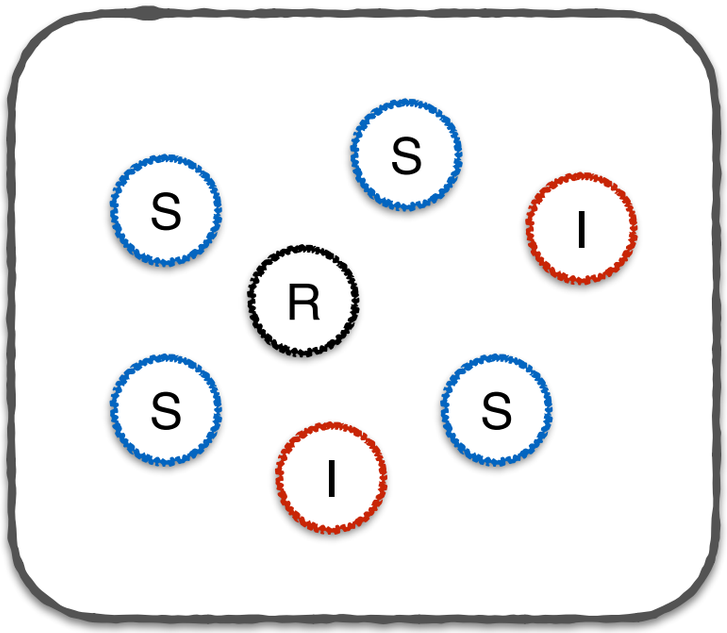
  Susceptible, **I**nfected (Infectious, Infective), **R**ecovered (Removed), **E**xposed, etc

Deterministic Epidemic Models

- Population sizes of each compartment are assumed to be functions of time.
- We assume a well-mixed population.
- Such approximation allows us to derive a set of differential (continuous time) or difference (discrete time) equations.
- An approximation to the mean of a random process.
- pros: easily tractable, accurate for large population
- cons: no randomness is allowed

- Basics: Infection Rate
- Susceptible-Infected (SI) Model
- Susceptible-Infected-Susceptible (SIS) Model
- Susceptible-Infected-Recovered (SIR) Model
- Basic Reproduction Number (Ratio)

Infection Rate



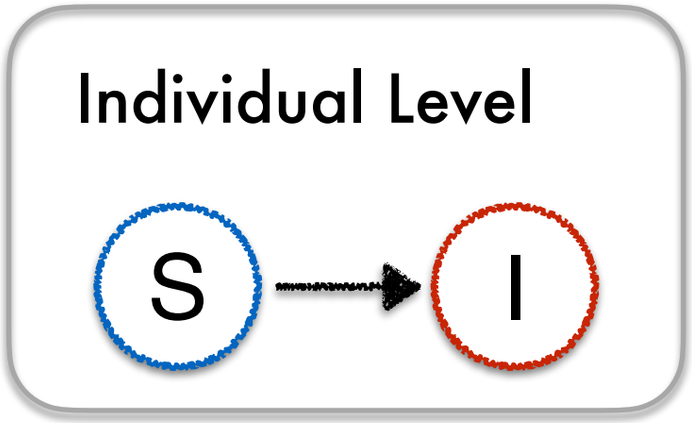
$$S_{t+1} = S_t - \left[1 - (1 - \frac{\beta}{N}\delta t)^{X_t}\right] S_t$$
$$\approx S_t - \frac{\beta}{N} S_t X_t \delta t.$$

$$\frac{dS}{dt} = -\frac{\beta}{N} SX.$$

$$\frac{ds}{dt} = -\beta s x.$$

(*s* and *x* are the fraction of S and I)

Susceptible-Infected (SI) model



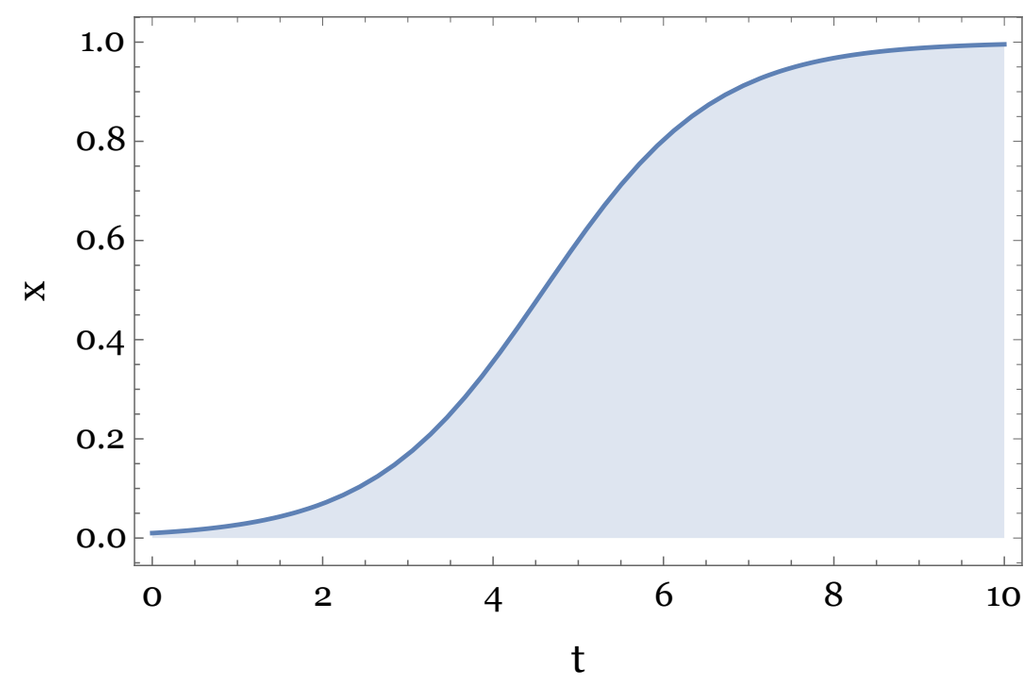
- Infection: by ***interaction (contact)*** of the susceptible individual and an infectious one.
- In a long time limit: all individuals are infected.

$$\frac{ds}{dt} = -\beta s x,$$
$$\frac{dx}{dt} = \beta s x.$$

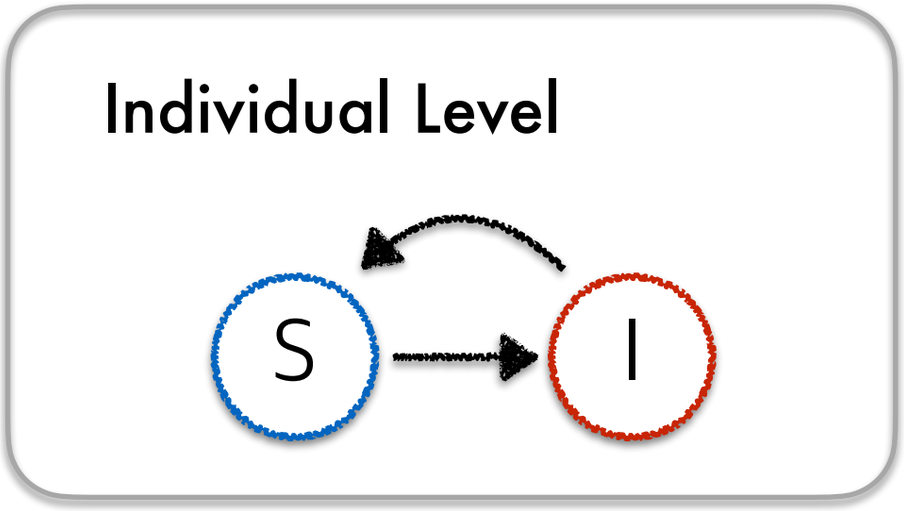
Logistic equation

$$\frac{dx}{dt} = \beta s x$$
$$= \beta(1-x)x.$$

$$x(t) = \frac{x_0 e^{\beta t}}{1 - x_0 + x_0 e^{\beta t}}.$$



Susceptible-Infected-Susceptible (SIS) Model

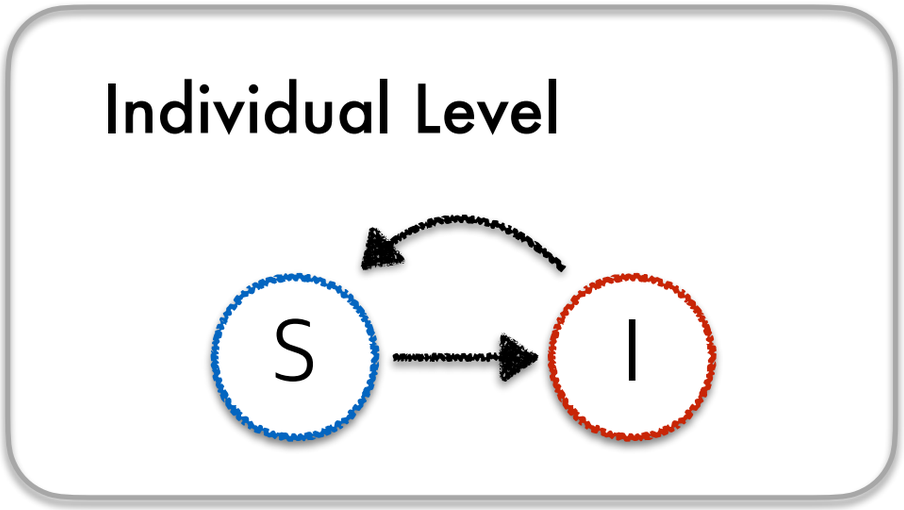


1. Infection: by ***interaction (contact)*** of the susceptible individual and an infectious one.

2. Recovery: the infected becomes susceptible, autonomously and spontaneously after a certain time.

- In a long time limit: active (S+I) or absorbing (S) phases.

Susceptible-Infected-Susceptible (SIS) Model



$$\frac{ds}{dt} = -\beta s x + \gamma x, \qquad \text{Eq. 1}$$

$$\frac{dx}{dt} = \beta s x - \gamma x, \qquad \text{Eq. 2}$$

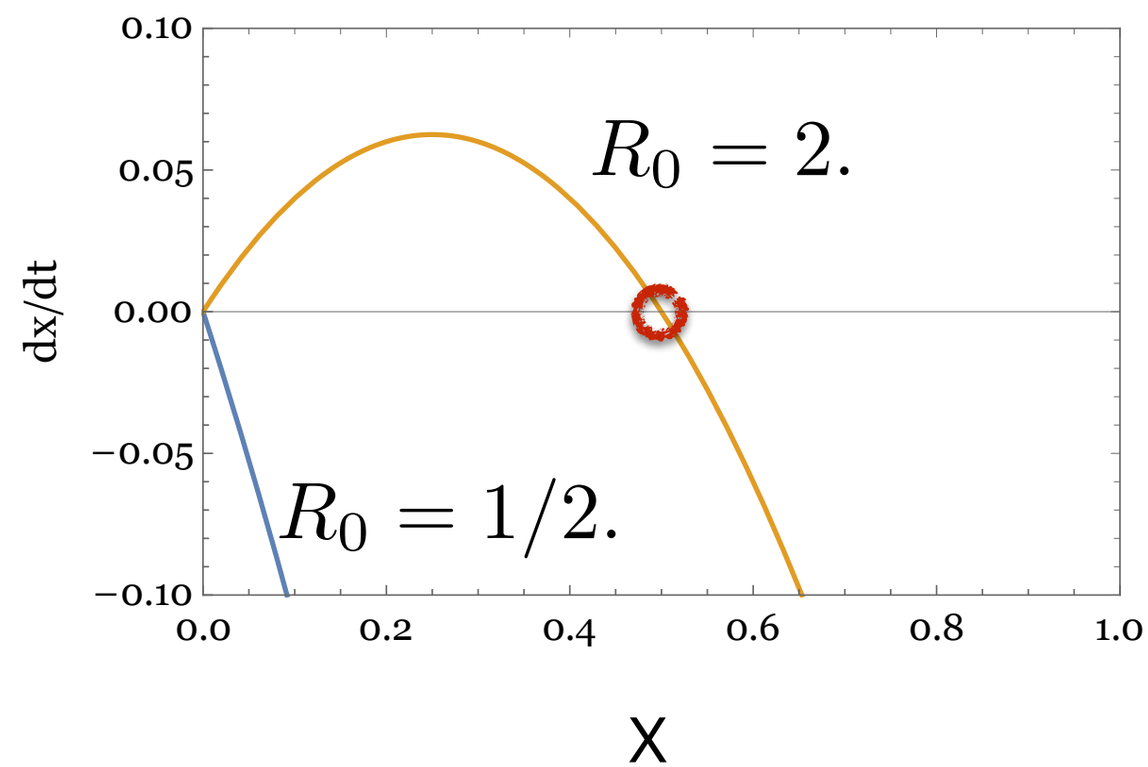
$$s + x = 1.$$

$$\begin{aligned}\frac{dx}{dt} &= \beta(1-x)x - \gamma x \\ &= \beta\left(1 - \frac{\gamma}{\beta} - x\right)x \\ &= \beta(x^* - x)x,\end{aligned}$$

$$\text{where } x^* = 1 - \frac{\gamma}{\beta} = 1 - \frac{1}{R_0}.$$

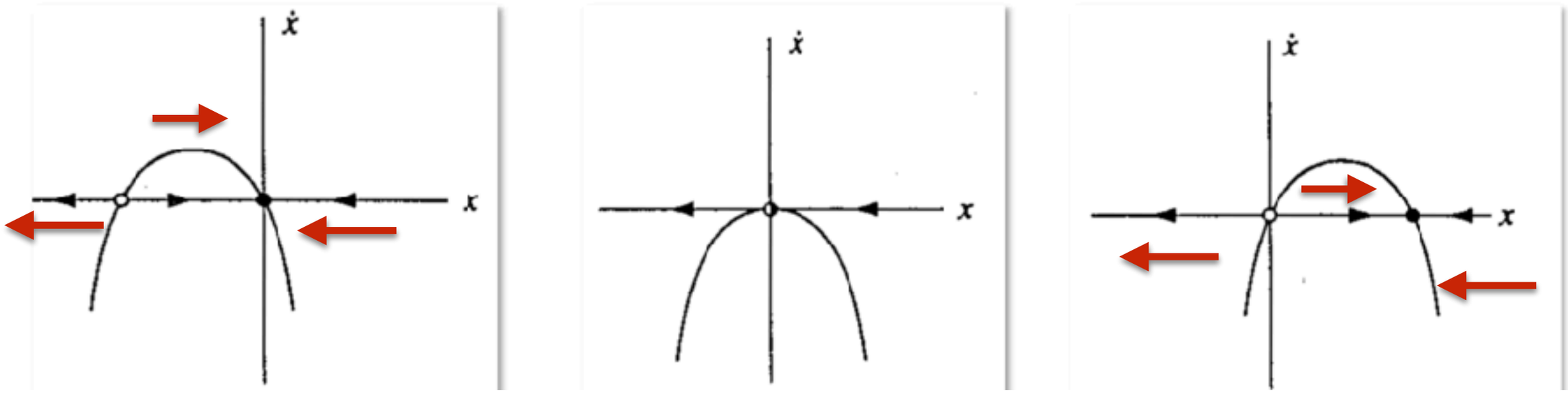
$$x(t) = \left(1 - \frac{1}{R_0}\right)\frac{Ce^{(\beta-\gamma)t}}{1 + Ce^{(\beta-\gamma)t}},$$

$$\text{where } C = \frac{\beta x_0}{\beta - \gamma - \beta x_0}.$$



Epidemic Spreading and Transcritical Bifurcations

$$\dot{x} = \beta(x^* - x)x \text{ where } x^* = 1 - \frac{1}{R_0}.$$



$x^* < 0.$ $\qquad$ $x^* = 0 \ (R_0 = 1)$ $\qquad$ $x^* > 0$

- Transcritical bifurcation: There is one unstable and one stable fixed point. Their stability is exchanged when they collide.

Susceptible-Infected-Susceptible (SIS) Model

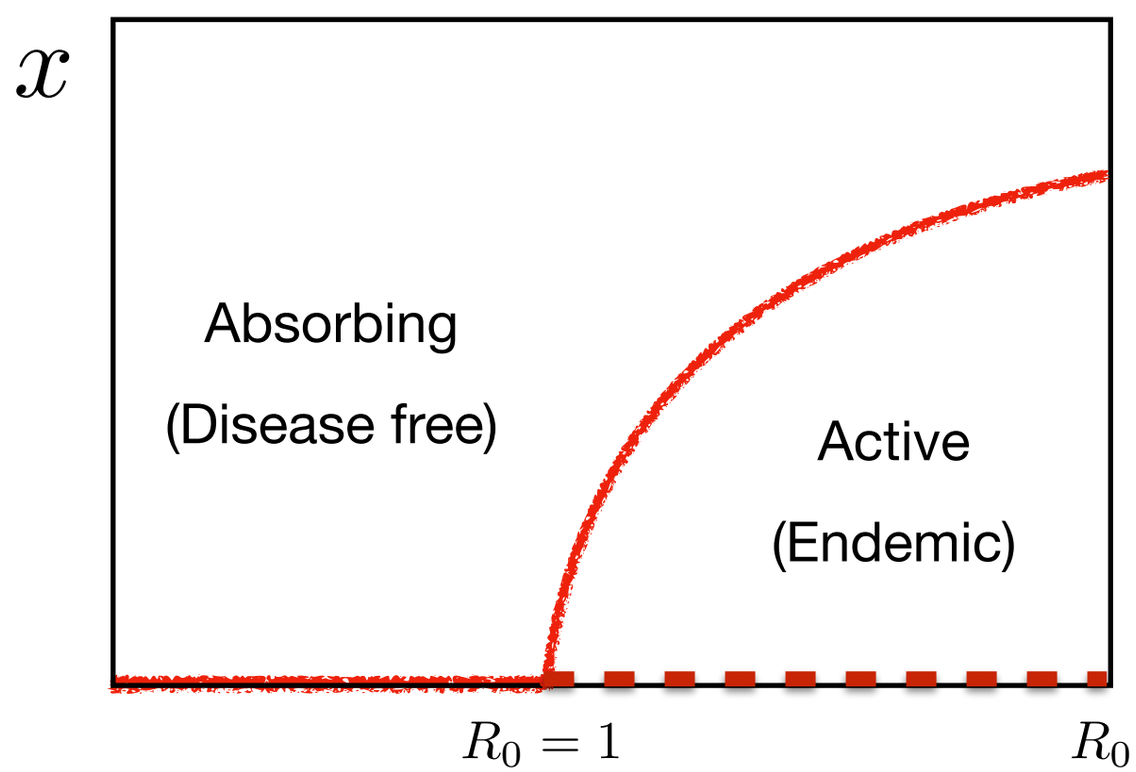
$$\dot{x} = \beta(x^* - x)x,$$

$$\frac{d\dot{x}}{dx} = \beta(x^* - 2x).$$

At $x = 0$,

$$\frac{d\dot{x}}{dx} = \beta x^*$$

$$= \beta - \gamma$$



$$x^* = 1 - \frac{1}{R_0}.$$

Susceptible-Infected-Recovered (SIR) Model

Let *s*, *x*, and *r* be the fraction of S, I, and R individuals in a large population limit.

Eq. 1 $$\frac{ds}{dt} = -\beta s x,$$

Eq. 2 $$\frac{dx}{dt} = \beta s x - \gamma x,$$

Eq. 3 $$\frac{dr}{dt} = \gamma x,$$

Eq. 4 $$s + x + r = 1.$$

$$-\frac{1}{\beta s}\frac{ds}{dt} = \frac{1}{\gamma}\frac{dr}{dt}.$$ (Eqs. 1 & 3)

$$\frac{ds}{dr} = -\frac{\beta}{\gamma}s.$$

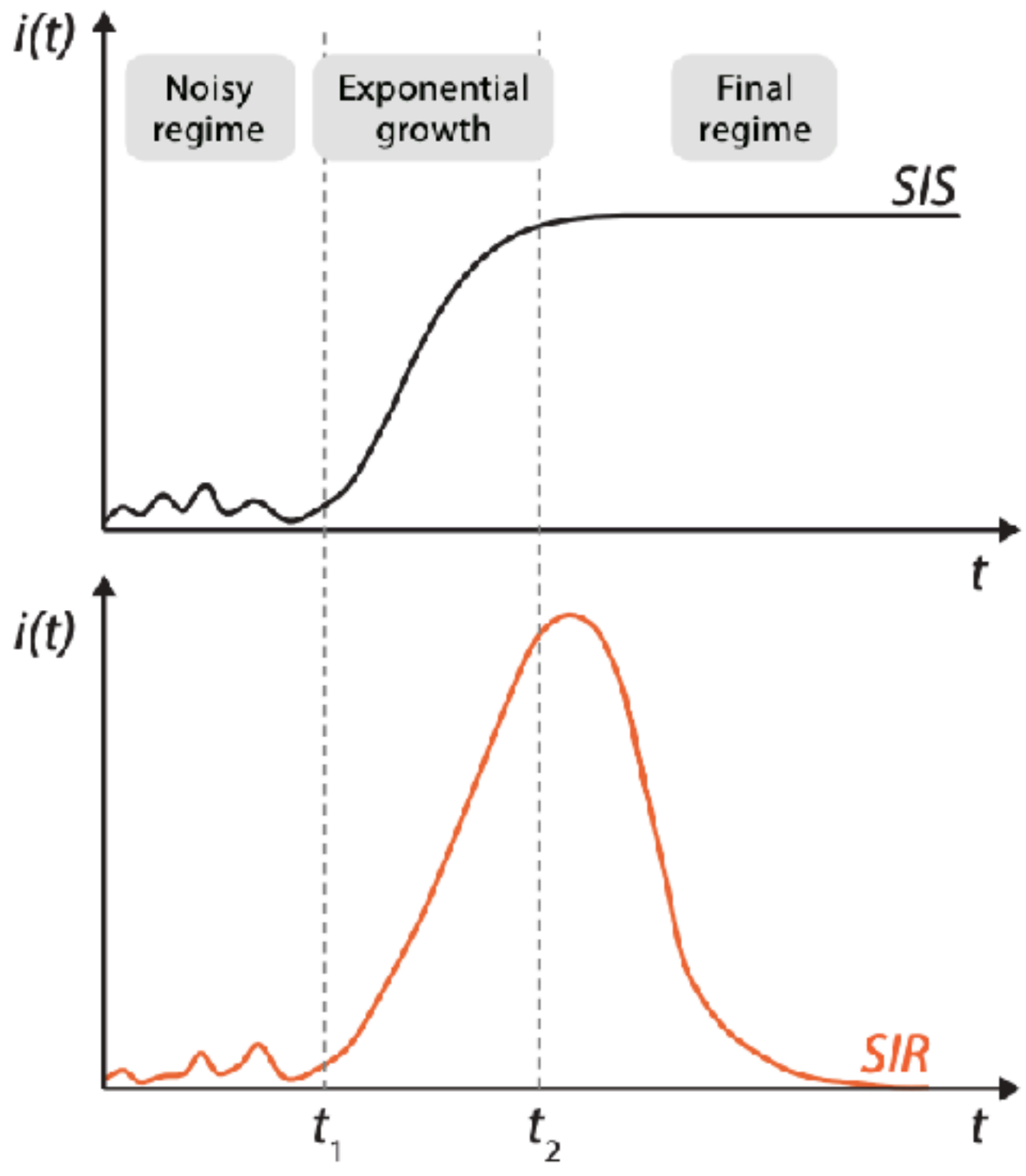
$$s = s_0 e^{-\frac{\beta}{\gamma}(r - r_0)}.$$

Eq. 3 $$\begin{aligned}\frac{dr}{dt} &= \gamma x \\ &= \gamma(1 - s - r) \quad \text{(using Eq. 4)} \\ &= \gamma(1 - r - s_0 e^{-\frac{\beta}{\gamma}(r - r_0)}).\end{aligned}$$

At a steady state,

$$\begin{aligned} r &= 1 - s_0 e^{-\frac{\beta}{\gamma}(r - r_0)} \\ &\approx 1 - e^{-\frac{\beta}{\gamma}r}. \end{aligned}$$

SIS and SIR Models



"Epidemic processes in complex networks", RMP (2015)

Basic Reproduction Number

When $s \approx 1$, $$\frac{dx}{dt} = \beta s x - \gamma x \quad \text{(Eq. 2)}$$
$$\approx (\beta - \gamma)x,$$

$$x(t) \approx x_0 e^{(\beta-\gamma)t}.$$

Basic Reproduction Number

$$R_0 = \frac{\beta}{\gamma}.$$

→ The average number of secondary cases arising from a primary case in an entirely susceptible population.

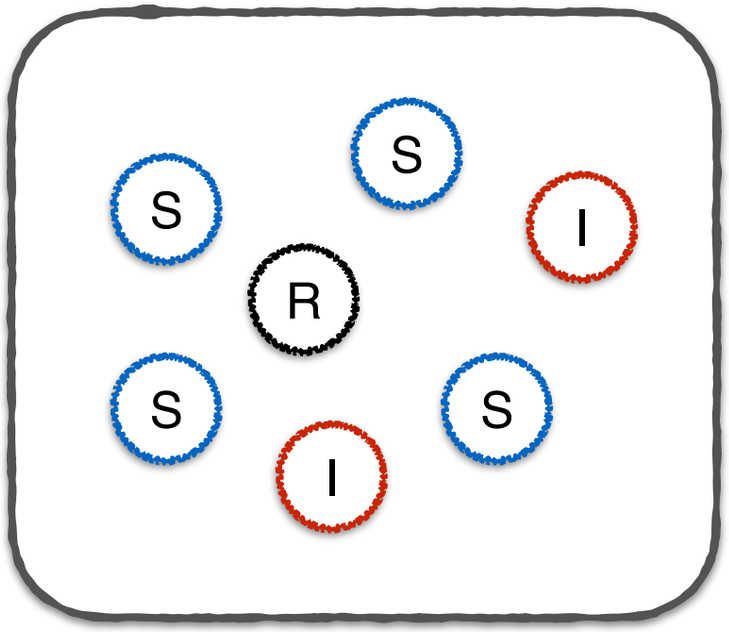
Infectious period: $\tau \approx \frac{1}{\gamma}.$

The average number of secondary cases: $\beta\tau = R_0.$

Stochastic Epidemic Models

- Epidemic processes are stochastic.

- Basics
- Branching Processes
  - Extinction Probability
  - Small outbreak size
  - Final epidemic size
- Generating Function



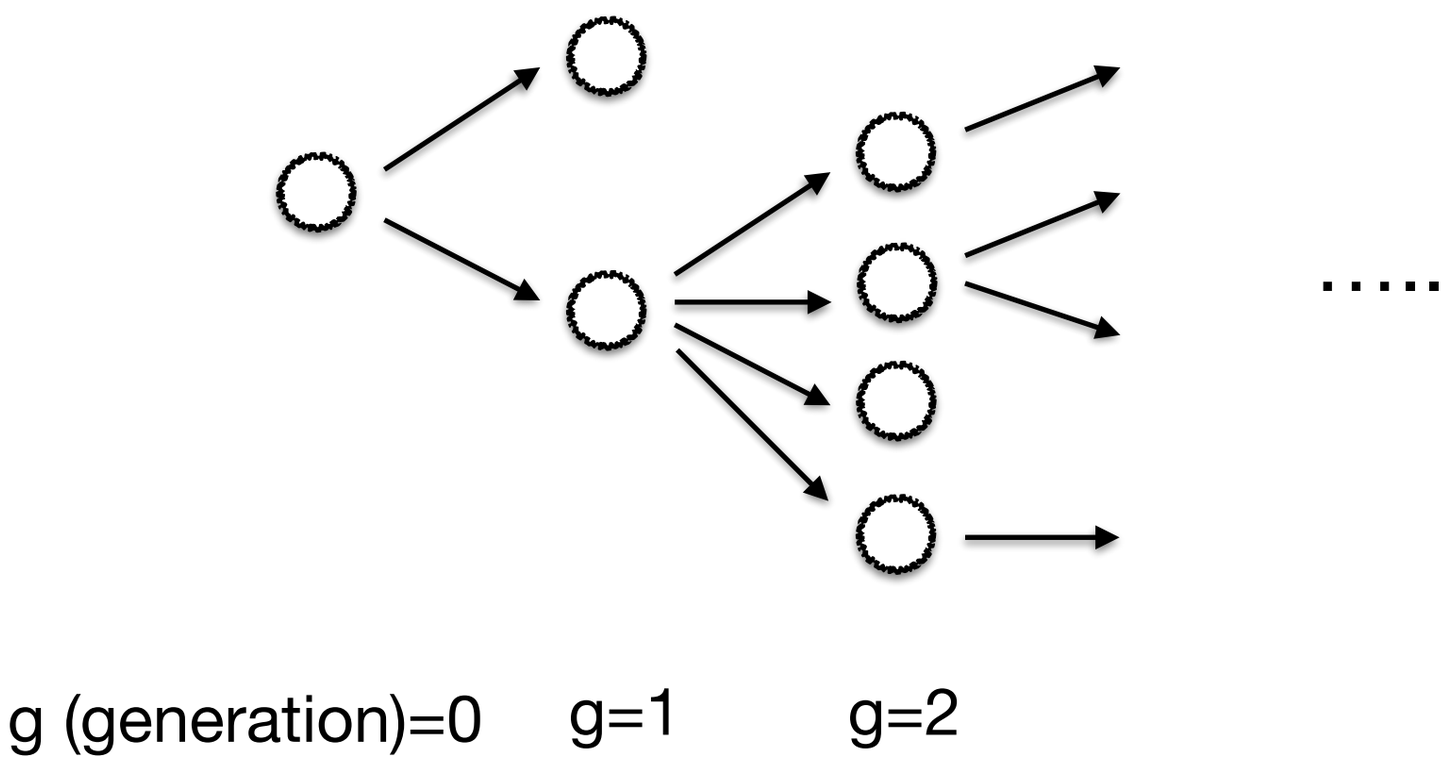
Basic Reproduction Number

Basic Reproduction Number R_0: the expected number of infections caused by an infected individual early in an outbreak.

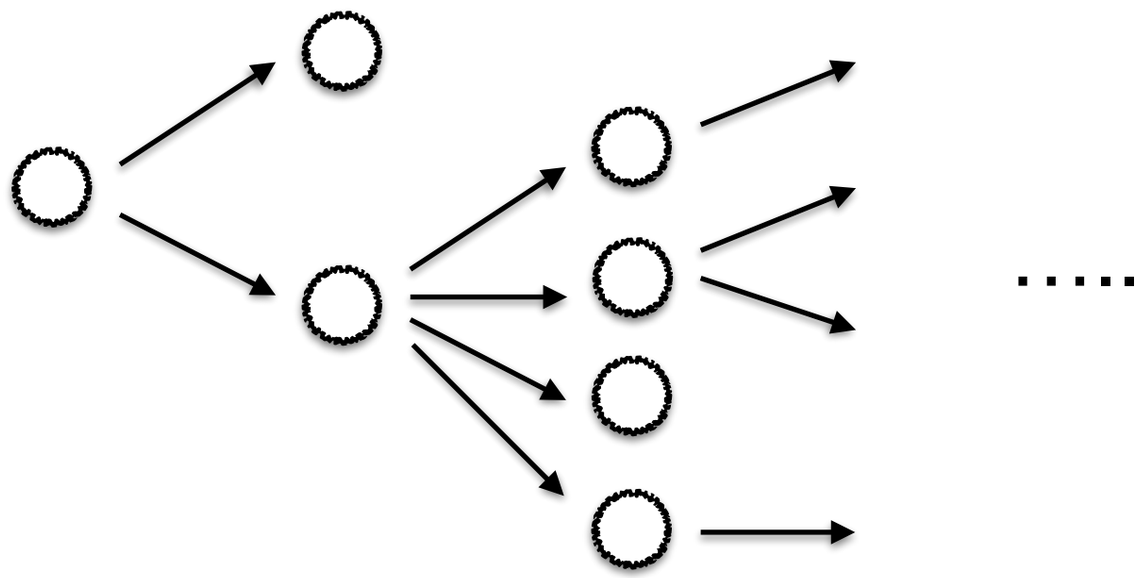
The average number of secondary cases: $\beta\tau = R_0$.

- Let us define *P(k)* as the probability of causing *k* infections (offspring).

$$R_0 = \sum_k kP(k)$$



Branching Process



g (generation)=0 g=1 g=2

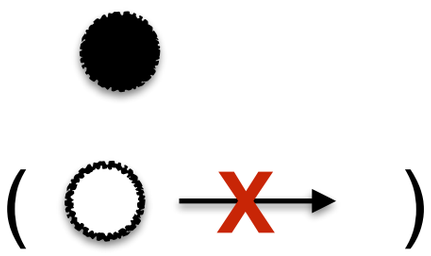
- Extinction probability
- Size distribution of small outbreaks
- Final size of epidemics

- Galton-Watson Process: The problem of extinction of families (1874)

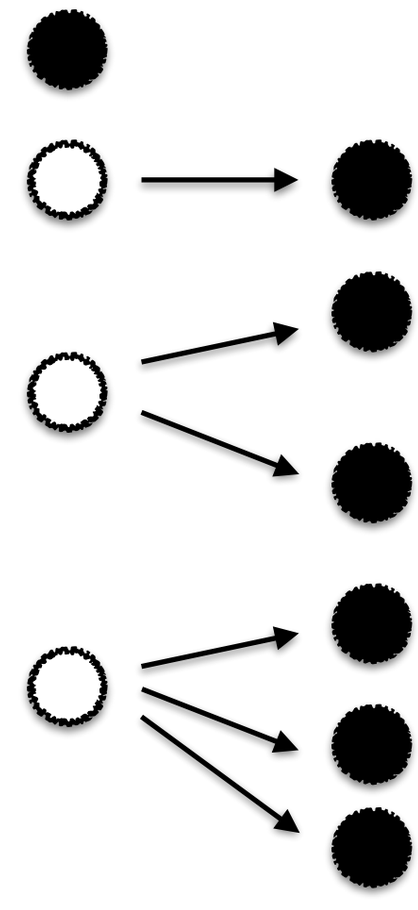
Extinction Probability (1)

- What is the probability that an outbreak goes extinct?
- The probability of causing *k* offsprings (infections): $P(k)$
- The probability that the longest generation is fewer than *g*: f_g

$f_1 = P(0).$

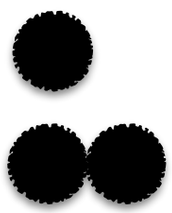


$$f_2 = P(0) + P(1)f_1 + P(2)f_1^2 + P(3)f_1^3 + \cdots$$



$+ \cdots$

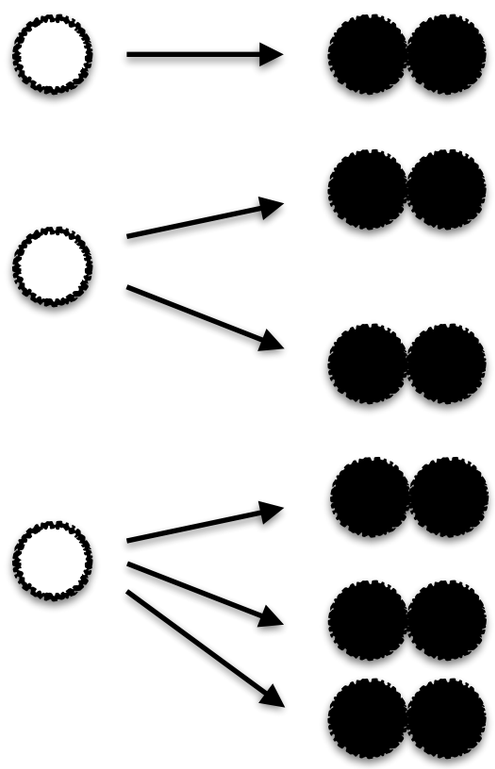
Extinction Probability (2)



$$f_1 = P(0),$$

$$f_2 = P(0) + P(1)f_1 + P(2)f_1^2 + P(3)f_1^3 + \cdots$$

$$f_3 = P(0) + P(1)f_2 + P(2)f_2^2 + P(3)f_2^3 + \cdots$$



$$+ \cdots$$

$$f_{n+1} = P(0)f_n^0 + P(1)f_n^1 + P(2)f_n^2 + \cdots$$

$$= \sum_k P(k) f_n^k$$

When $n \to \infty$: $f_\infty = \sum_k P(k) f_\infty^k$

Extinction Probability (3)

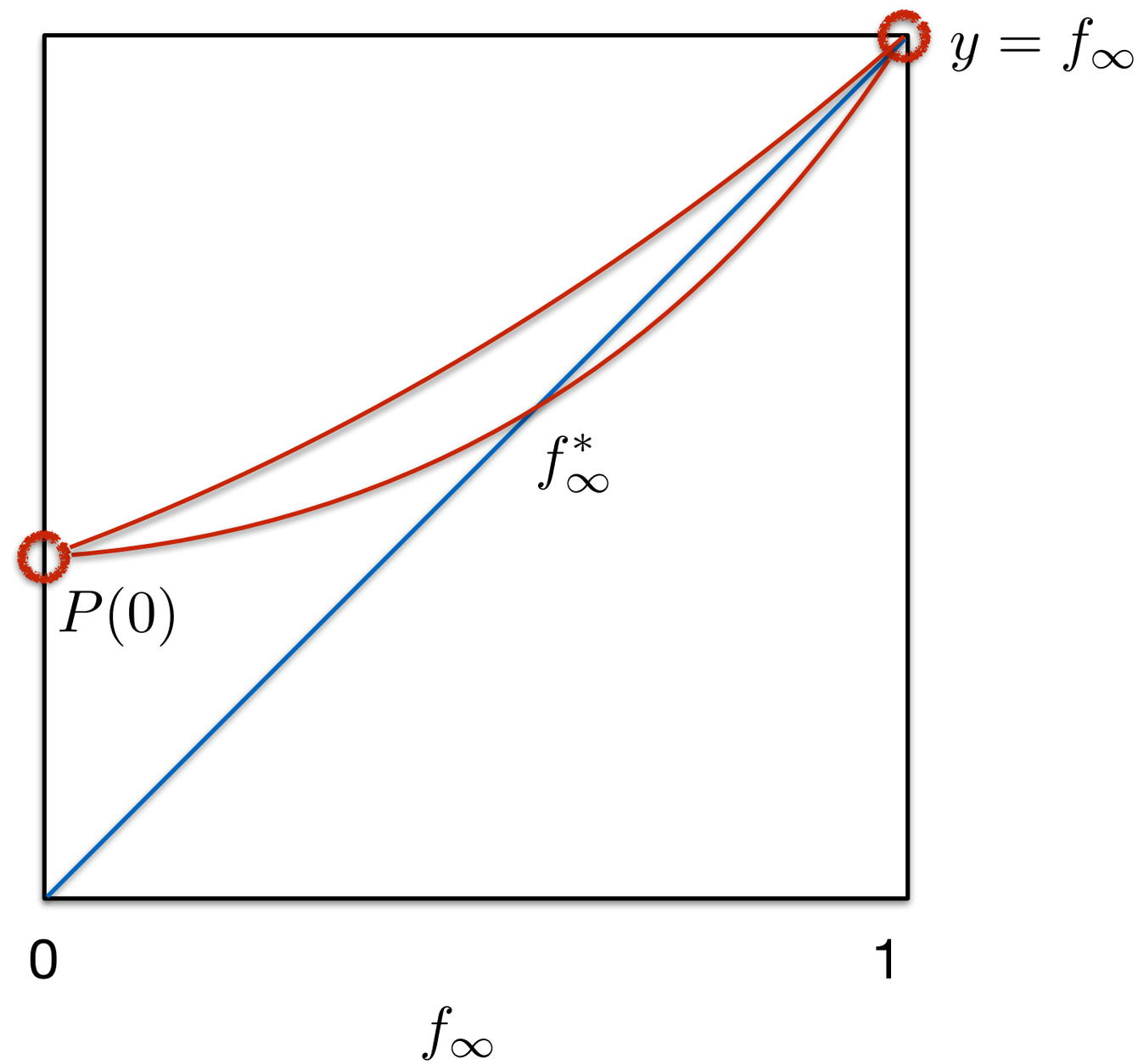
$$f_\infty = \sum_k P(k) f_\infty^k$$

$$f_\infty = 1: \quad \text{normalization}$$

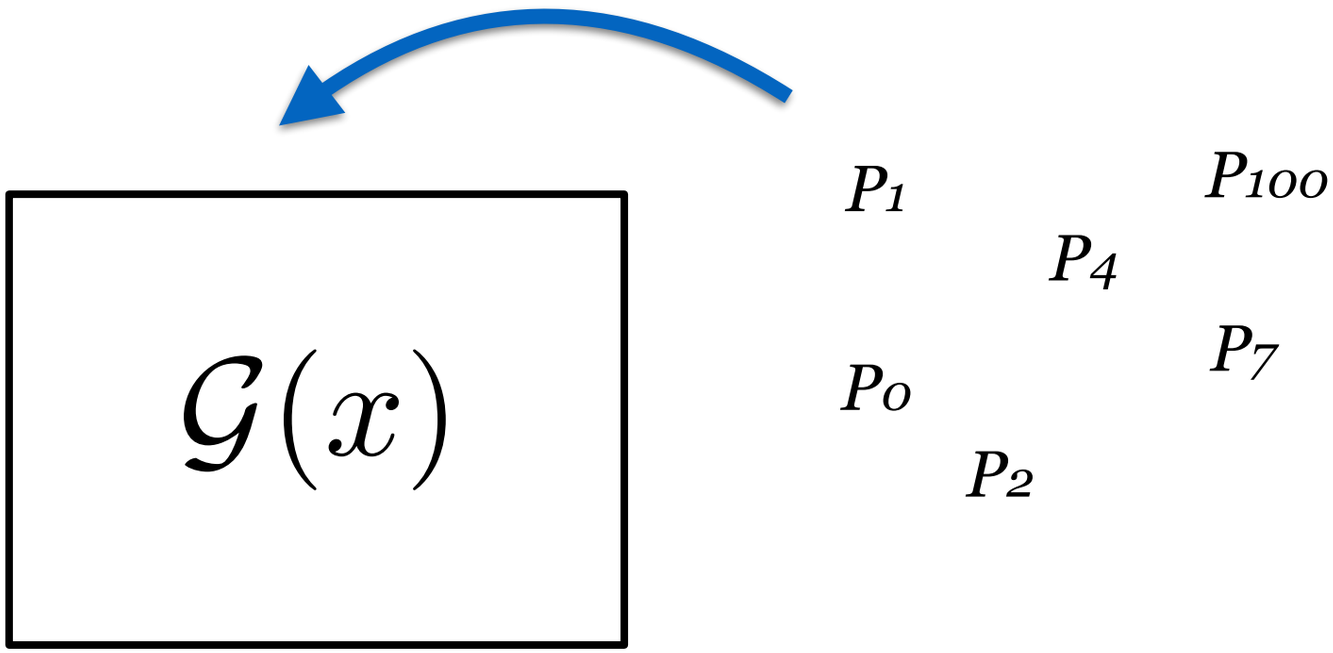
$$\sum_k kP(k) f_\infty^{k-1}|_{f_\infty=1} = \sum_k kP(k)$$
$$= R_0$$

If $R_0 < 1 : f = 1,$

If $R_0 > 1 : f = f_\infty^*$



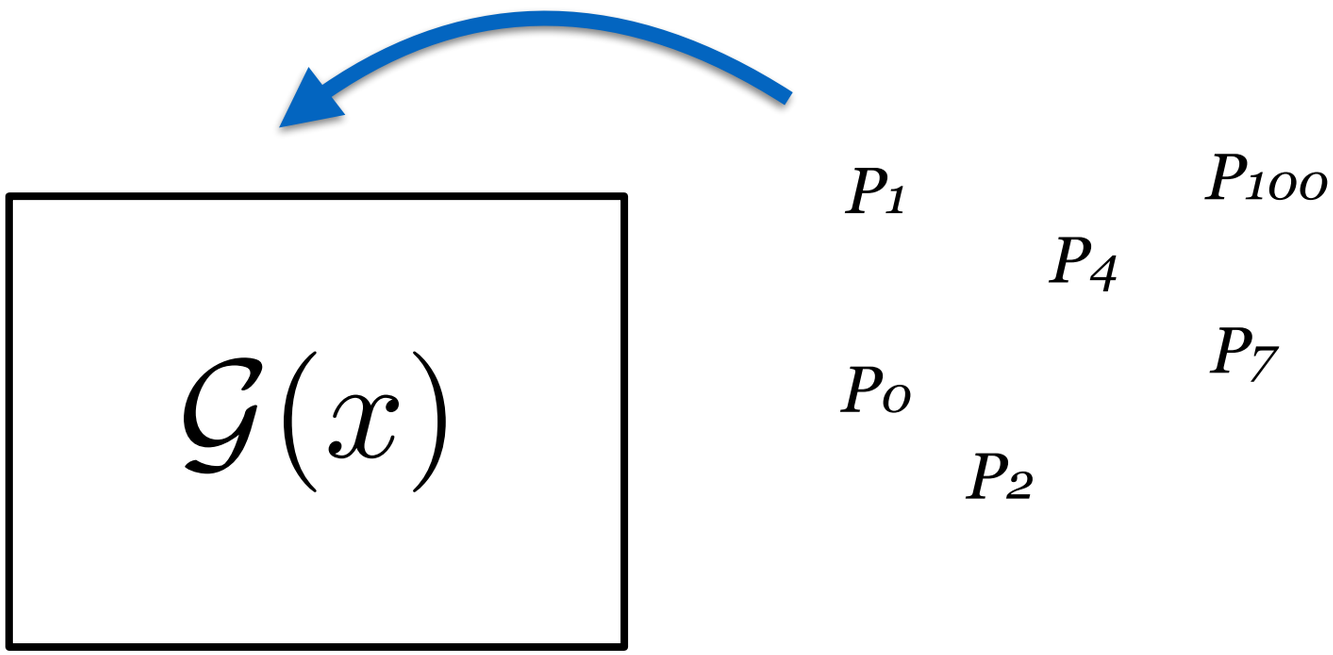
(Probability) Generating Function



$$\mathcal{G}(x) = P_0 + P_1 x^1 + P_2 x^2 + P_3 x^3 + \cdots$$

$$P_n = \frac{1}{n!} \frac{d^n \mathcal{G}(x)}{dx^n}\Big|_{x=0}$$

(Probability) Generating Function



$$\mathcal{G}(x) = P_0 + P_1 x^1 + P_2 x^2 + P_3 x^3 + \cdots$$

$$P_n = \frac{1}{n!} \frac{d^n \mathcal{G}(x)}{dx^n}\Big|_{x=0}$$

$$\mathcal{G}(x) = \sum_k P_k x^k.$$

$$1 = \mathcal{G}(1),$$

$$\langle k \rangle = \sum_k k P_k = \mathcal{G}'(1),$$

$$\langle k^n \rangle = \left(x \frac{\partial}{\partial x} \right)^n \mathcal{G}(1).$$

Extinction Probability using GF

- The probability of causing *k* offsprings (infections): *P(k)*
- PGF of *P(k)*: $G(x) = \sum_k P(k)x^k.$

$$f_{n+1} = P(0)f_n^0 + P(1)f_n^1 + P(2)f_n^2 + \cdots$$
$$= \sum_k P(k)f_n^k$$

When $n \to \infty$: $f_\infty = \sum_k P(k)f_\infty^k$

$$f_0 = 0,$$
$$f_1 = P(0) = G(0) = G(f_0),$$
$$f_2 = P(0) + P(1)f_1 + P(2)f_1^2 + \cdots$$
$$= \sum_k P(k)f_1^k = G(f_1),$$
$$f_3 = \sum_k P(k)f_2^k = G(f_2),$$
$$\cdots$$
$$f_\infty = G(f_\infty),$$

(Example 1) GF for Poisson Distribution

- The probability of causing *k* offsprings (infections): *P(k)*
- PGF of *P(k)*: $G(x) = \sum_k P(k) x^k.$

1. Assuming a Poisson distribution:

$$P(k) = \frac{e^{-\langle k \rangle} \langle k \rangle^k}{k!} = \frac{e^{-R_0} R_0^k}{k!}.$$

2. GF for the Poisson distribution:

$$\begin{aligned} G(x) &= \sum_k \frac{1}{k!} e^{-R_0} R_0^k x^k \\ &= e^{-R_0} \sum_k \frac{1}{k!} (R_0 x)^k = e^{R_0(x-1)}. \end{aligned}$$

3. Extinction probability:

$$f = e^{R_0(f-1)}.$$

(Example 2) GF for Bimodal Distribution

- The probability of causing *k* offsprings (infections): *P(k)*
- PGF of *P(k)*: $G(x) = \sum_k P(k) x^k.$

1. Assuming a bimodal distribution:

$$P(k) = \frac{1}{2}\delta_{k,0} + \frac{1}{2}\delta_{k,2R_0}.$$

2. GF for the bimodal distribution:

$$\begin{aligned} G(x) &= \sum_k \left(\frac{1}{2}\delta_{k,0} + \frac{1}{2}\delta_{k,2R_0} \right) x^k \\ &= \frac{1}{2}(1 + x^{2R_0}). \end{aligned}$$

3. Extinction probability:

$$f = \frac{1}{2}(1 + f^{2R_0}).$$

Product of Generating Functions

$$\mathcal{G}(x) = \sum_k P_k x^k = P_0 + P_1 x + P_2 x^2 + \cdots ,$$

$$\mathcal{F}(x) = \sum_\ell Q_\ell x^\ell = Q_0 + Q_1 x + Q_2 x^2 + \cdots .$$

$$\begin{aligned}
R_0 &= P_0 Q_0, \\
R_1 &= P_1 Q_0 + P_0 Q_1, \\
R_2 &= P_2 Q_0 + P_1 Q_1 + P_0 Q_2, \\
&\cdots \\
\mathcal{H}(x) &= R_0 + R_1 x + R_2 x^2 + \cdots \\
&= (P_0 Q_0) + (P_1 Q_0 + P_0 Q_1)x + (P_2 Q_0 + P_1 Q_1 + P_0 Q_2)x^2 + \cdots \\
&= \left(\sum_k P_k x^k \right) \left(\sum_\ell Q_k x^\ell \right) = \mathcal{G}(x)\mathcal{F}(x).
\end{aligned}$$

- Generating function: $G(x) = \sum_k P_k x^k.$
- Generating function for the sum of *n* numbers is: $[G(x)]^n$

Function Composition of Generating Functions

$$\mathcal{G}(x) = \sum_k P_k x^k = P_0 + P_1 x + P_2 x^2 + \cdots ,$$

$$\mathcal{F}(x) = \sum_\ell Q_\ell x^\ell = Q_0 + Q_1 x + Q_2 x^2 + \cdots .$$

1. Choose *k* from P_k
2. Choose *k* different values from Q_ℓ
3. *GF* of the sum of the *k* values: H(x)

$$\begin{aligned}\mathcal{H}(x) &= P_0 + P_1\mathcal{F} + P_2\mathcal{F}^2 + P_3\mathcal{F}^3 \cdots \\ &= G(F(x))\end{aligned}$$

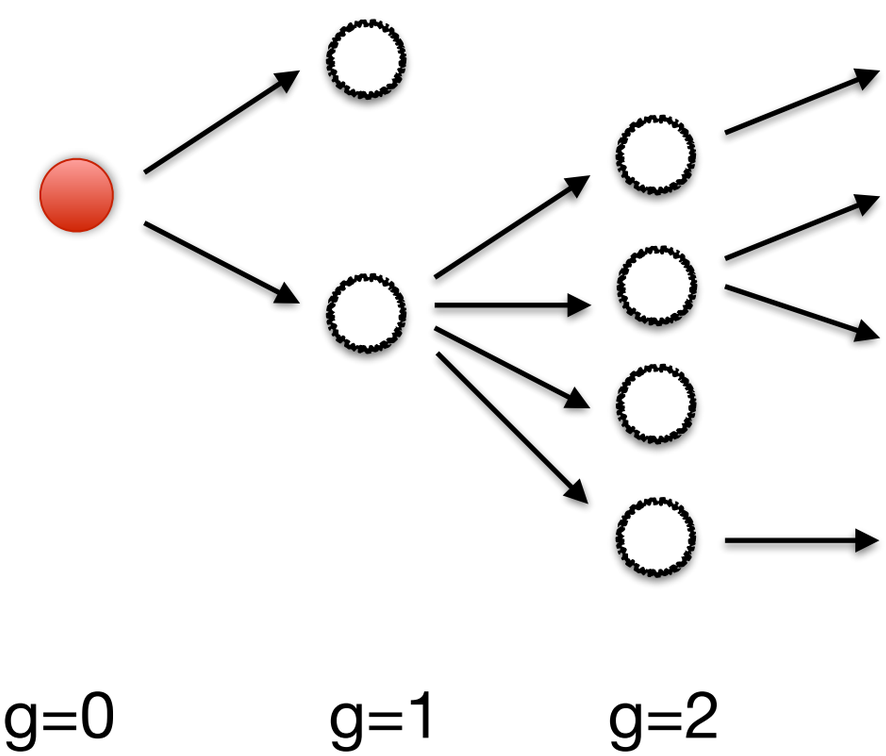
Size Distribution of Small Outbreak (1)

- The probability that the *completed* outbreak has size *s* in generation *g*: $Q_g(s)$
- PGF of $Q_g(s)$: $F_g(x) = \sum_s Q_g(s) x^s$

If the outbreak begins with a single seed,

$$F_0(x) = Q_0(0) + Q_0(1)x + Q_0(2)x^2 + \cdots$$
$$= Q_0(0) = 1.$$
$$F_1(x) = Q_1(0) + Q_1(1)x + Q_1(2)x^2 + \cdots$$
$$= Q_1(1)x = x.$$

Single seed

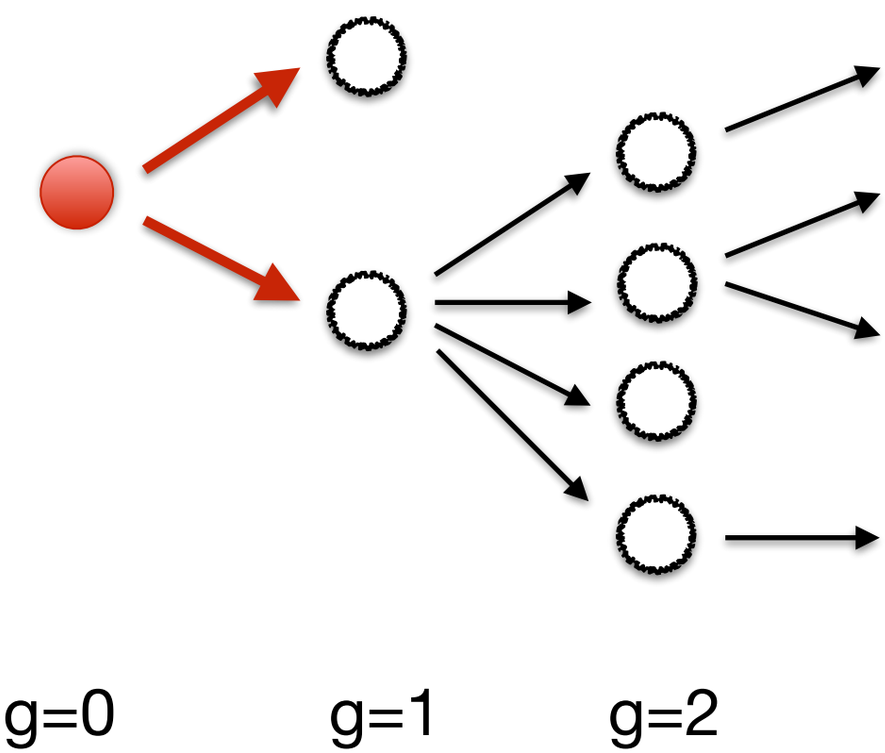


Size Distribution of Small Outbreak (2)

- The probability that the finite outbreak has size *s* in generation *g*: $Q_g(s)$
- PGF of $Q_g(s)$: $F_g(x) = \sum_s Q_g(s) x^s$

$$F_0(x) = 1,$$
$$F_1(x) = x,$$
$$F_2(x) = xG(x) = xG(F_1(x)),$$
$$F_3(x) = xG(F_2(x))$$

1. Initial infection in g=0: x
2. First offsprings in g=1: G(x)



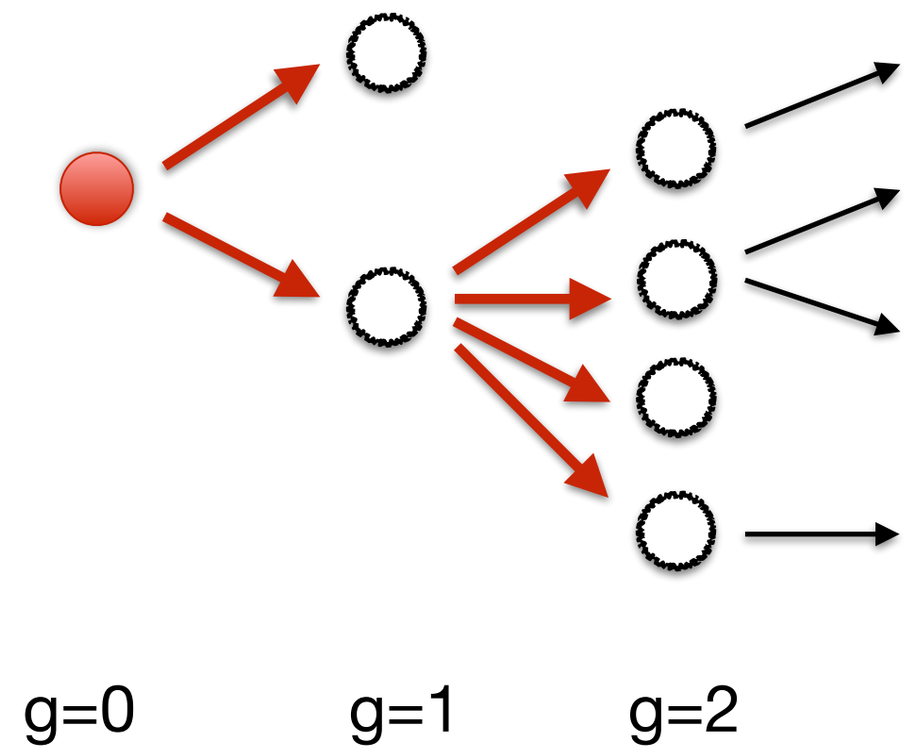
Note that the probability of causing *k* offsprings (infections): $P(k)$

PGF of $P(k)$: $G(x) = \sum_k P(k) x^k$

Size Distribution of Small Outbreak (3)

- The probability that the finite outbreak has size *s* in generation *g*: $Q_g(s)$
- PGF of $Q_g(s)$: $F_g(x) = \sum_s Q_g(s) x^s$

$$
\begin{aligned}
F_0(x) &= 1, \\
F_1(x) &= x, \\
F_2(x) &= xG(F_1(x)), \\
F_3(x) &= xG(F_2(x)), \\
&\dots \\
F_{n+1}(x) &= xG(F_n(x)).
\end{aligned}
$$



Size Distribution of Small Outbreak (4)

- The probability that the finite outbreak has size *s* in generation *g*: $Q_g(s)$
- PGF of $Q_g(s)$: $F_g(x) = \sum_s Q_g(s) x^s$

$$\boxed{\text{When } g \to \infty, \quad F(x) = xG(F(x)).}$$

$$\begin{aligned}\langle s \rangle &= \sum_s sQ(s) = F'(1) \\ &= [G(F(x)) + xG'(F(x))F'(x)]_{x=1} \\ &= 1 + G'(1)F'(1).\end{aligned} \longrightarrow \langle s \rangle = \frac{1}{1 - R_0}.$$

- Again, we find the epidemic threshold R_0=1.
- Note that here we assume that Q(s) is properly normalized.
- Above the epidemic threshold, we must have an infinite size of outbreak (that is "epidemic") with non-zero probability.

Size Distribution of Small Outbreak (5)

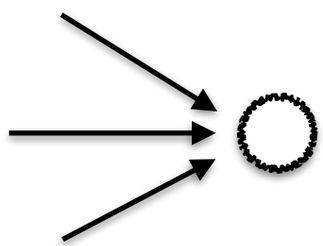
- Above the epidemic threshold, we need to redefine *F(x)* as the generating function only for outbreaks other than epidemic outbreaks (giant component in the language of percolation).

$$F(1) = \sum_s Q(s) = f_\infty, \text{ where } f_\infty \text{ is extinction probability}$$

$$\boxed{\begin{aligned} F(x) &= xG(F(x)), \\ f_\infty &= G(f_\infty). \end{aligned}}$$

Final Size of Epidemic

- Final fraction of recovered individuals



The distribution of the number of *incoming* arrows: *P(k)*

$$1 - r = P(0) + P(1)(1-r) + P(2)(1-r)^2 + \cdots$$
$$= \sum_k P(k)(1-r)^k = G(1-r).$$

$$P(k) = \binom{N}{k} q^k (1-q)^{N-k}, \text{ where } q = \frac{R_0}{N},$$

$$G(x) = \sum_k \binom{N}{k} q^k (1-q)^{N-k} x^k$$
$$= (1 - q + qx)^N = \left[1 + \frac{1}{N} R_0 (x-1)\right]^N$$
$$\approx e^{R_0(x-1)}.$$

$$r = 1 - G(1-r).$$

$$\rightarrow \quad r = 1 - e^{-R_0 r}$$

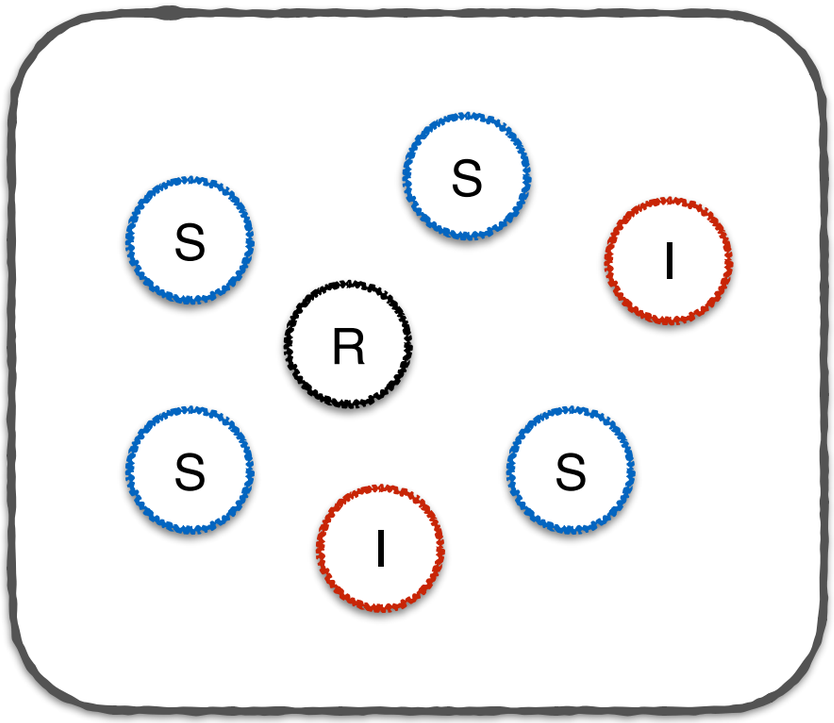
Epidemic Spreading on Complex Networks

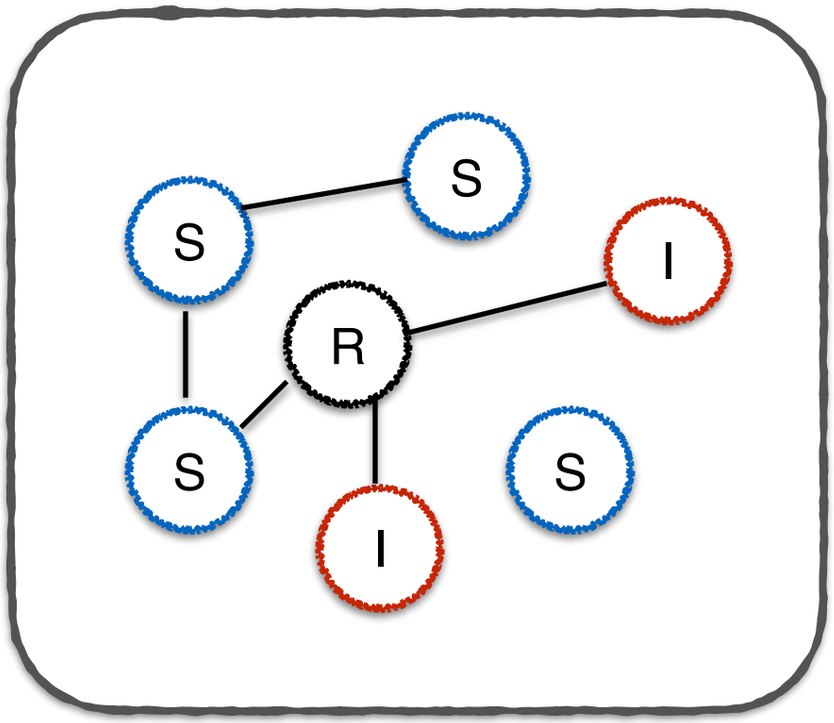
- Beyond a well-mixed population
- Contact networks can be important for contagious diseases (e.g., sexually transmitted diseases).

- Network measures and models
- SIS model on complex networks
- SIR model on complex networks
- Immunization protocols on networks
- Epidemic processes on a meta-population model
- Social contagion

Contact Networks

- Our society is not fully-mixed.





Network Measures

- A network is a collection of points (nodes, vertices) that are joined by a set of connections (links, edges).

- Adjacency matrix **A**: a_{ij}=1 if an edge is connecting nodes *i* and *j* and 0 otherwise.

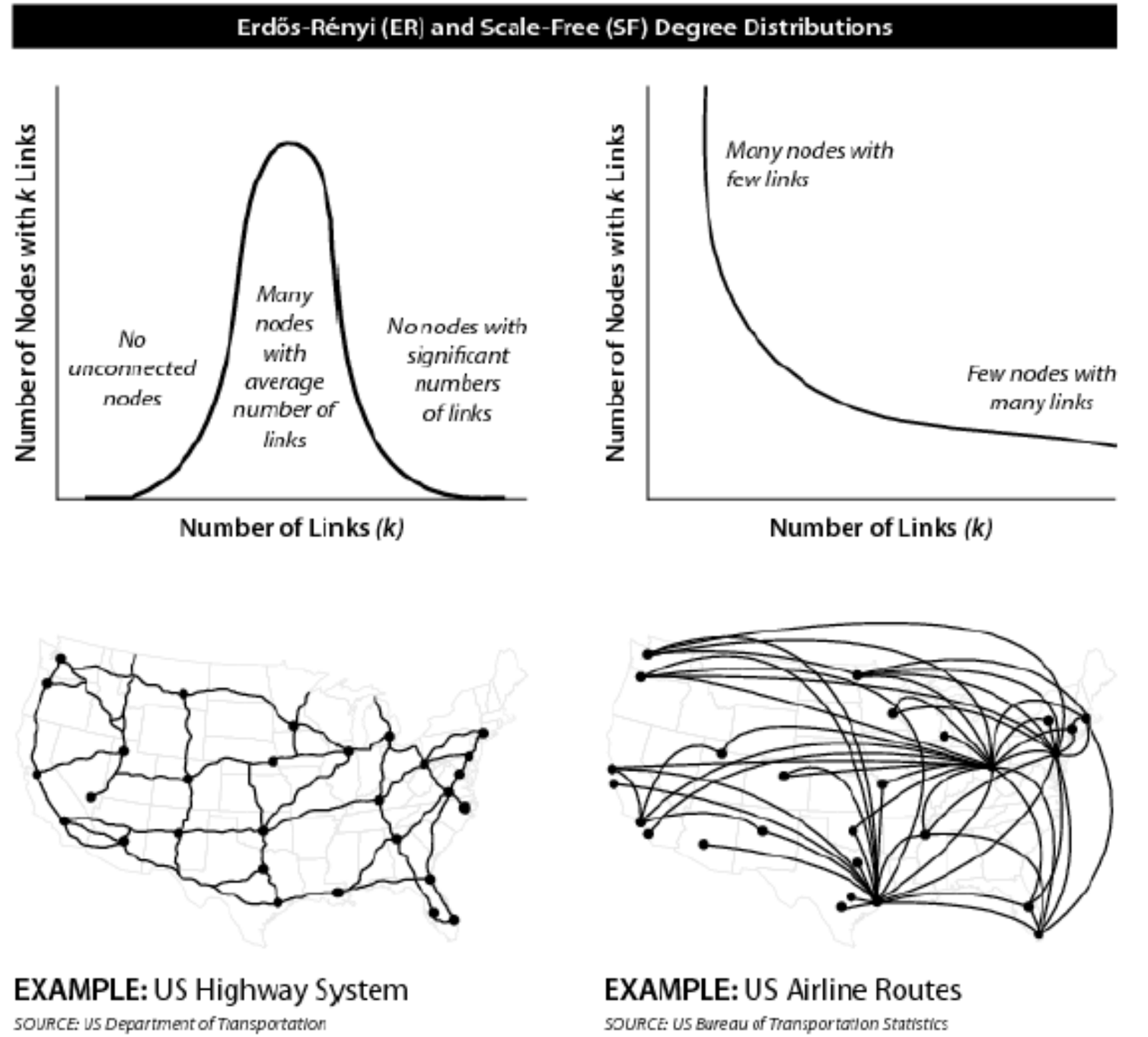
- Degree: The degree k_i of node *i* is the number of links connecting from *i.*

- Degree distribution *P(k)* is the probability that a randomly chosen node has degree *k*.

$$\sum_k P(k) = 1, \ \sum_k k^n P(k) = \langle k^n \rangle.$$

- Average degree: $z = \langle k \rangle$.

Homogeneous and Heterogeneous Networks



[Barabasi, Linked]

Network Models: ER

Erdos-Renyi (ER) networks

- Homogeneous
- ER network is constructed from a set of N nodes in which each one of the N(N-1)/2 possible links is present with probability p.
- In the limit large N and constant average degree (p=z/N), the degree distribution is approximately given by a Poisson distribution:

$$P(k) = \binom{N}{k} p^k (1-p)^{N-k},$$

$$G(x) = \sum_k \binom{N}{k} p^k (1-p)^{N-k} x^k$$

$$= (1-p+px)^N = \left[1 + \frac{1}{N} z(x-1)\right]^N$$

$$\approx e^{z(x-1)}.$$

$$P(k) = \frac{1}{k!} \frac{d^k G(0)}{dx^k}$$

$$= \frac{1}{k!} \frac{d^k}{dx^k} e^{z(x-1)}$$

$$= \frac{e^{-z} z^k}{k!}.$$

Network Models: SF

Scale-Free (SF) networks

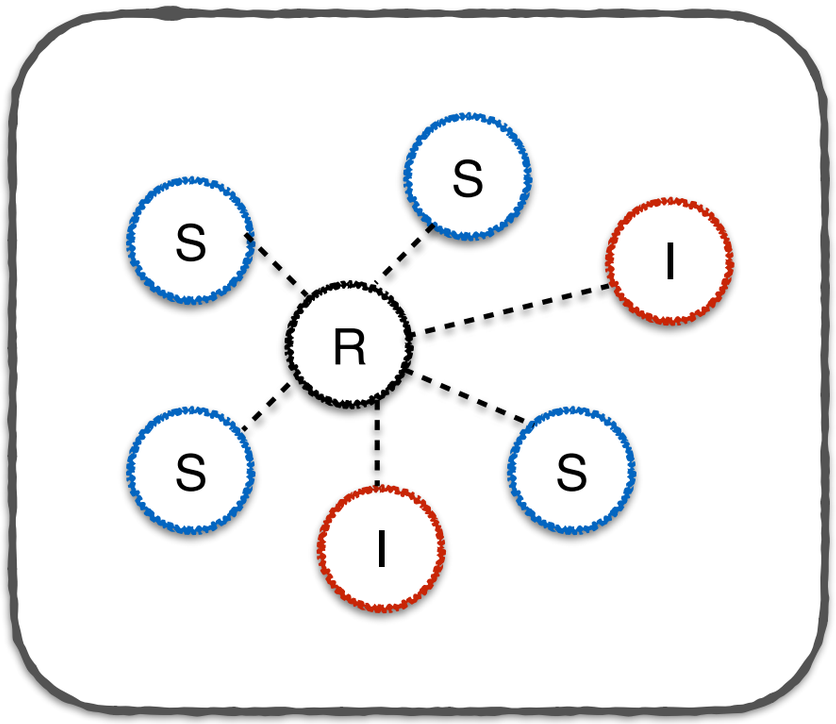
- Heterogeneous

$$P(k) \sim k^{-\gamma}$$

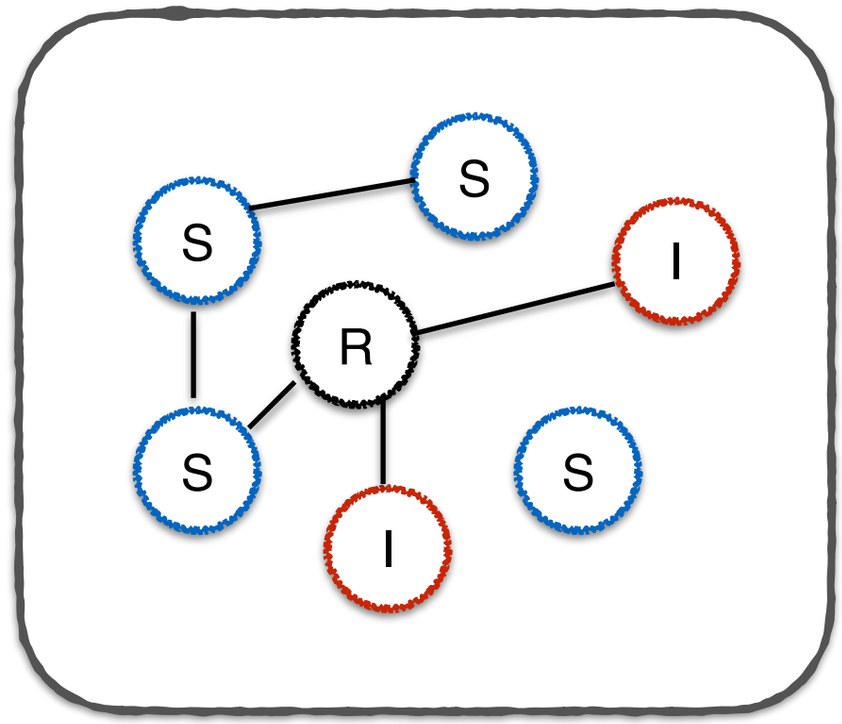
- Degree exponent takes a value between 2 and 3.
- The second moment of the degree distribution diverges in the thermodynamic limit.
- Non-negligible probability of finding nodes with very large k.
- Barabasi-Albert (BA) model, configuration model, static model, etc

Epidemic Spreading on Complex Networks

well-mixed



networked

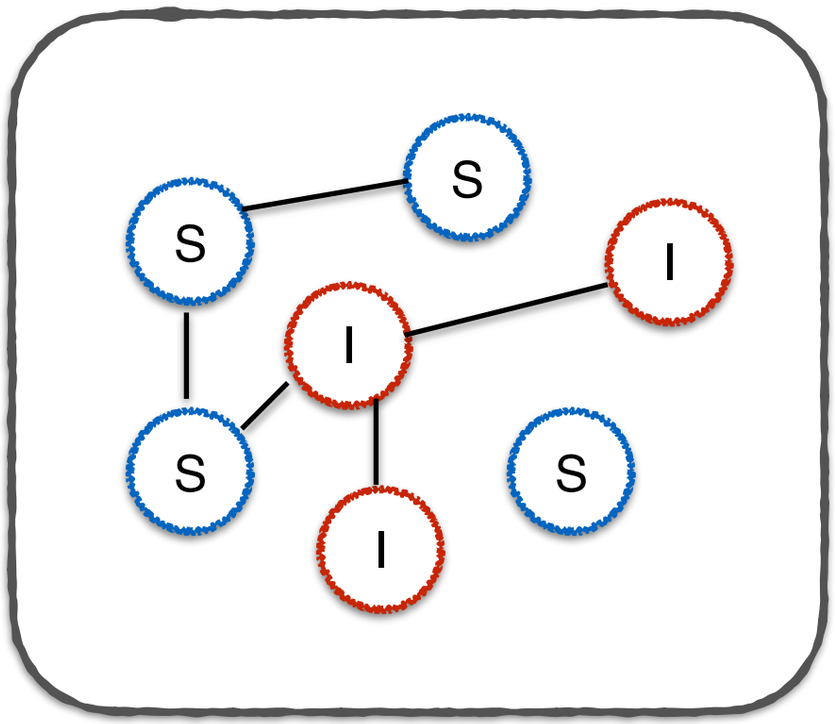


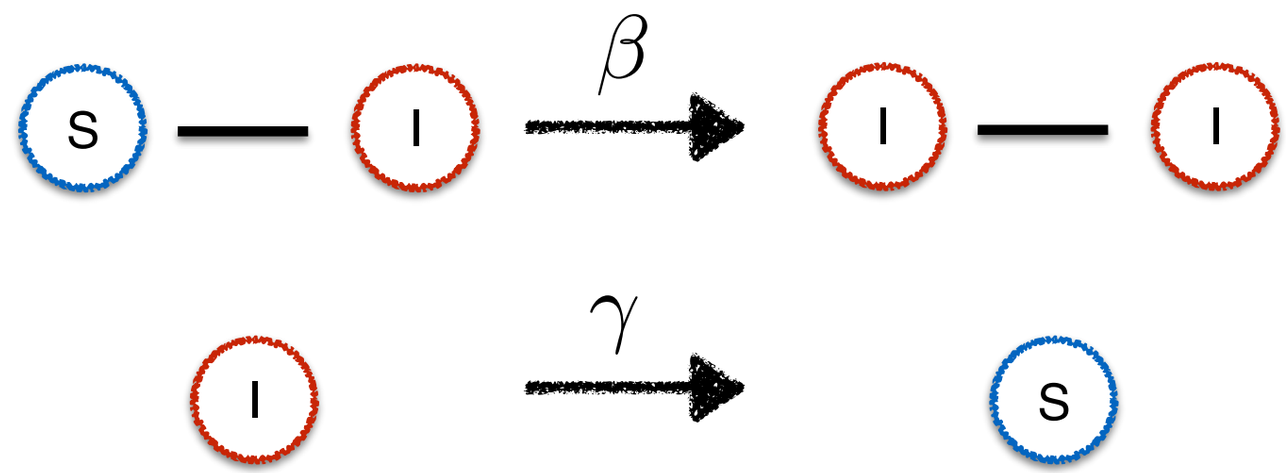
- the rate of contacts between an infected individual and all others
- the rate of contacts between two connected pair

$$N\beta \longleftrightarrow \beta$$

$$\beta \longleftrightarrow \beta/k$$

SIS Model on Complex Networks (1)





- (Naive) Mean-Field Approach

$$\frac{dx}{dt} = -\gamma x + \beta\langle k\rangle(1-x)x.$$

$$\text{Let } \gamma t \to t, \lambda = \beta/\gamma \longrightarrow \frac{dx}{dt} = -x + \lambda\langle k\rangle(1-x)x.$$

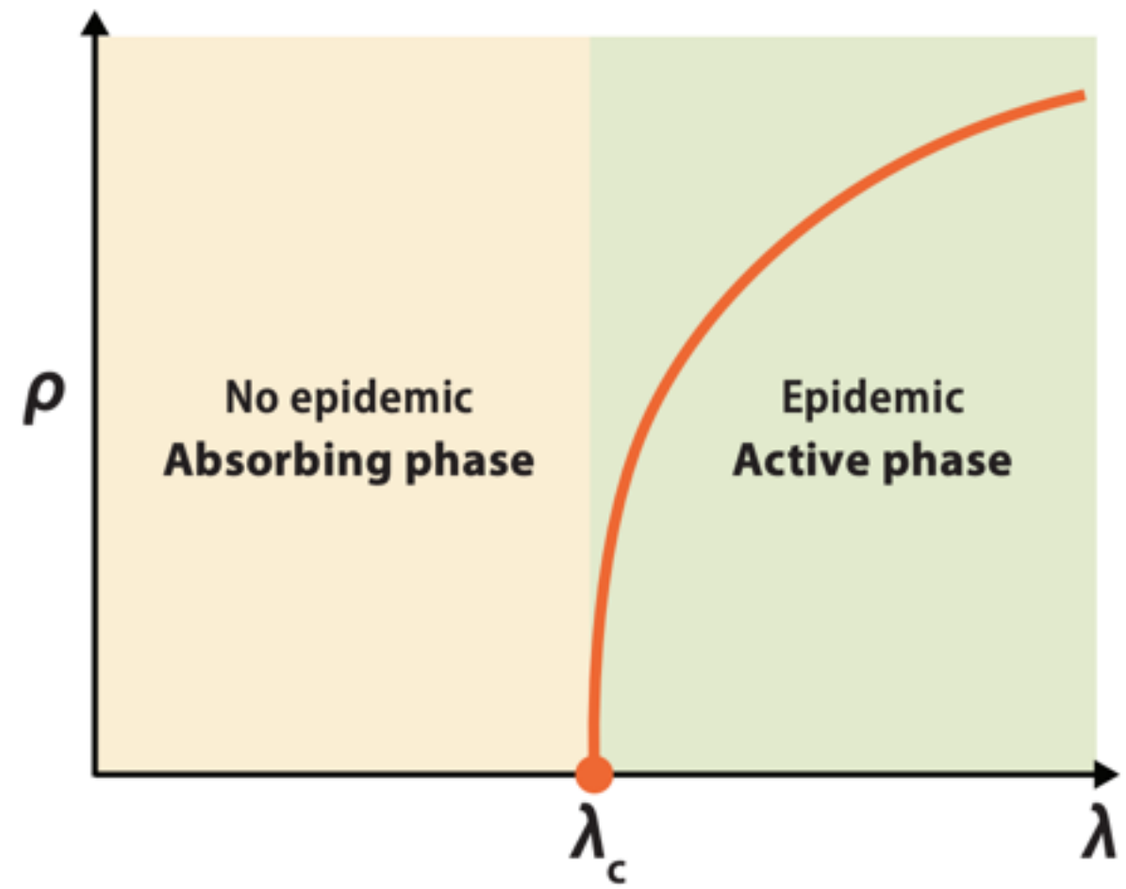
SIS Model on Complex Networks (2)

- (Naive) Mean-Field Approach

$$\frac{dx}{dt} = -x + \lambda\langle k\rangle(1-x)x.$$

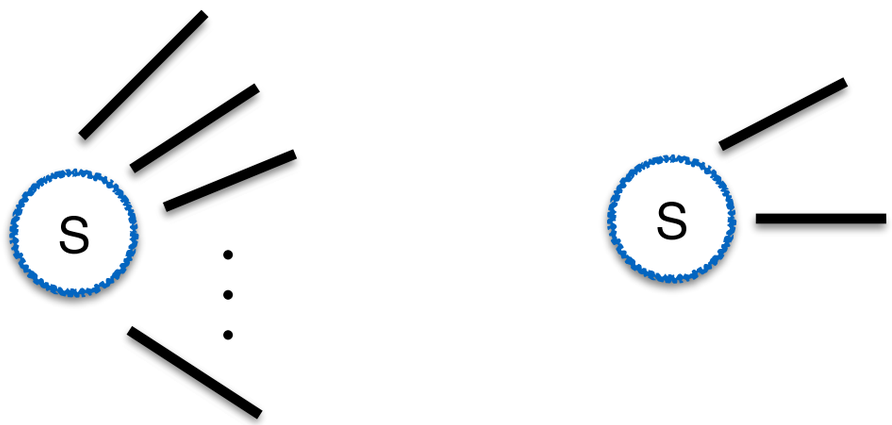
$$\longrightarrow \quad R_0 = \lambda\langle k\rangle = \langle k\rangle\frac{\beta}{\gamma}.$$

$$\longrightarrow \quad \lambda_c = \frac{1}{\langle k\rangle}.$$

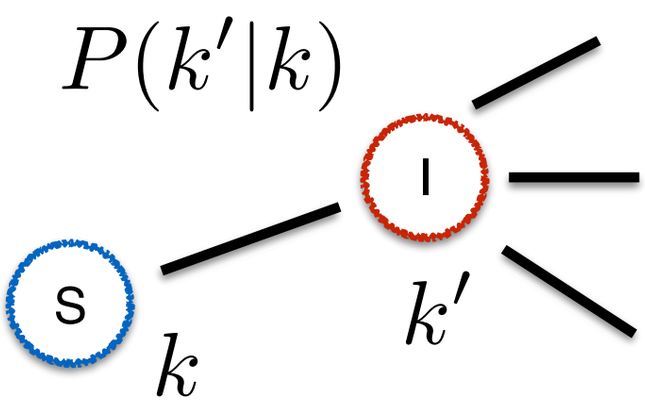


Adopted from “Epidemic processes in complex networks”, RMP (2015)

Heterogeneous Mean-Field Theory



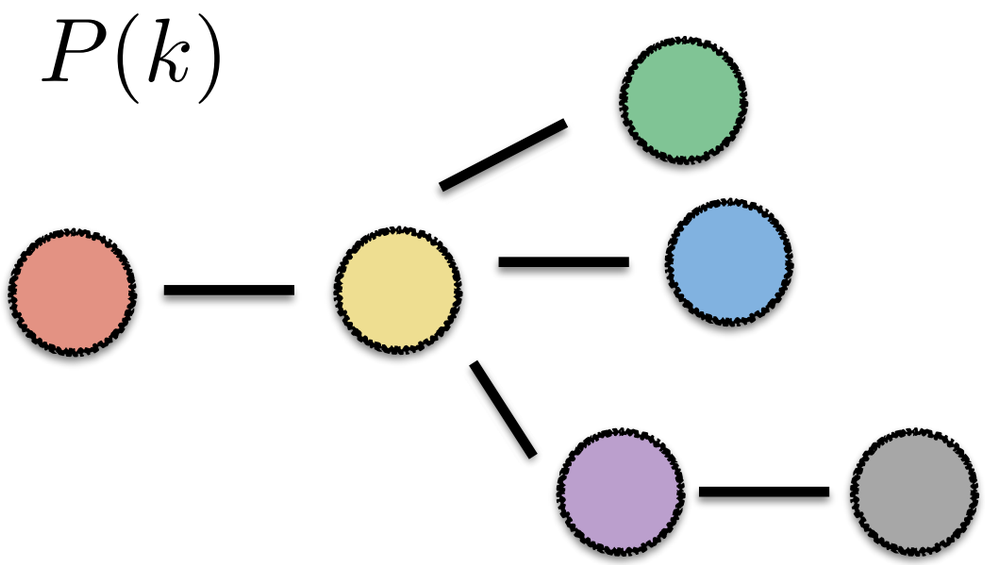
$$x_k \neq x_{k'}$$

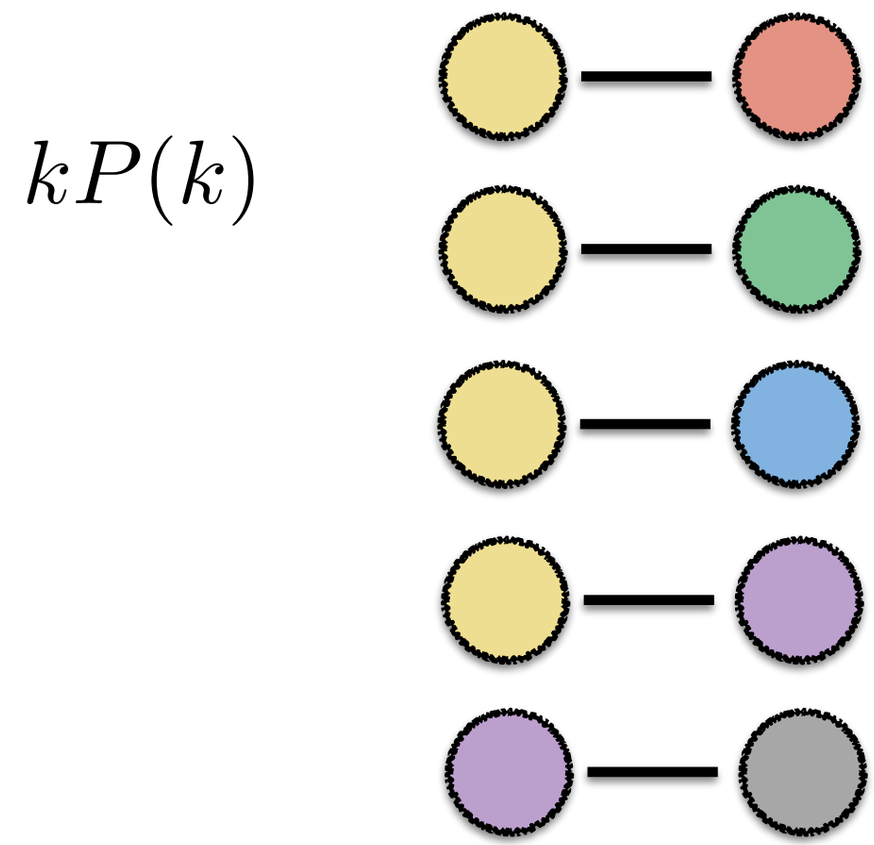


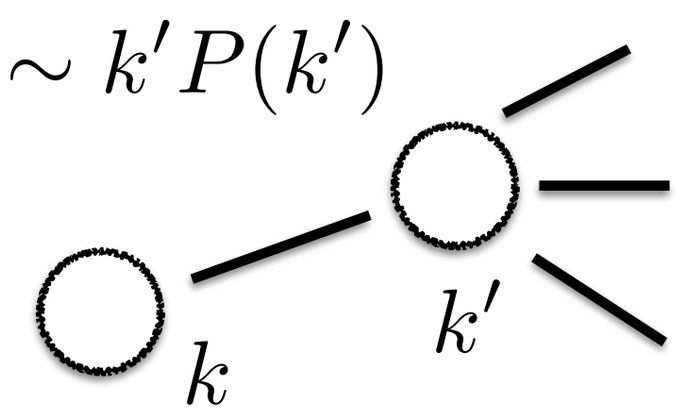
$$\frac{dx_k}{dt} = -x_k + \lambda k(1 - x_k) \sum_{k'} P(k'|k) x_{k'}.$$

- R. Pastor-Satorras and A. Vespignani, Epidemic spreading in scale-free networks, Phys. Rev. Lett., 86, 3200 (2001).

On a Uncorrelated Network







$$P(k'|k) = \frac{k'P(k')}{\langle k \rangle}.$$

Heterogeneous Mean-Field Theory

$$\frac{dx_k}{dt} = -x_k + \lambda k(1 - x_k) \sum_{k'} P(k'|k) x_{k'}$$

$$= -x_k + \lambda k(1 - x_k) \sum_{k'} \frac{k' P(k')}{\langle k \rangle} x_{k'}$$

Defining $\Theta = \sum_{k'} \frac{k' P(k')}{\langle k \rangle} x_{k'}$, in the steady state,

$$x_k = \frac{\lambda k \Theta}{1 + \lambda k \Theta}.$$

$$\longrightarrow \quad \Theta = \frac{1}{\langle k \rangle} \sum_k k P(k) \frac{\lambda k \Theta}{1 + \lambda k \Theta}.$$

Absence of Epidemic Threshold

$$\Theta = \frac{1}{\langle k \rangle} \sum_k kP(k) \frac{\lambda k \Theta}{1 + \lambda k \Theta}.$$

- Non-zero solution appears when the derivative of rhs at 0 is larger than unity.

$$\frac{1}{\langle k \rangle} \sum_k kP(k) \frac{\lambda k}{(1 + \lambda k \Theta)^2} \Big|_{\Theta=0} > 1 \longrightarrow \boxed{\lambda_c = \frac{\langle k \rangle}{\langle k^2 \rangle}.}$$

$$\langle k^2 \rangle = \int k^2 P(k) dk$$

$$\sim \int k^{2-\gamma} dk \to \infty \quad \text{if } 2 < \gamma \leq 3.$$

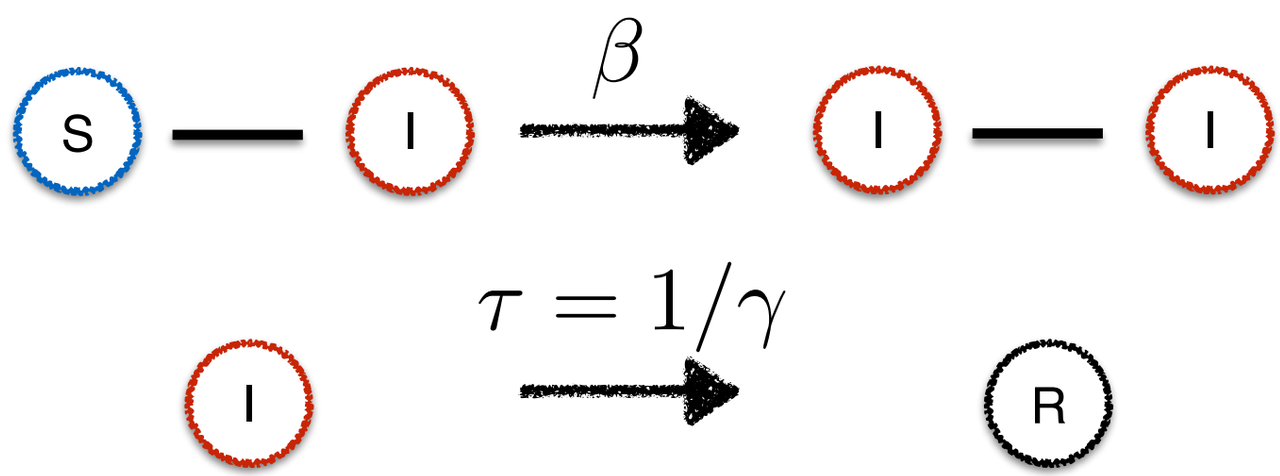
- Absence of epidemic threshold in SF networks

$$\lambda_c = \frac{1}{\Lambda}$$

QMF

- C. Castellano and R. Pastor-Satorras, PRL (2010); A. V. Goltsev, S. N. Dorogovtsev, J. G. Oliveira, and J. F. F. Mendes, PRL (2012); H. K. Lee, P.-S. Shim, and J. D. Noh, PRE (2013); M. Boguna, C. Castellano, and R. Pastor-Satorras, PRL (2013).

SIR Model on Complex Networks

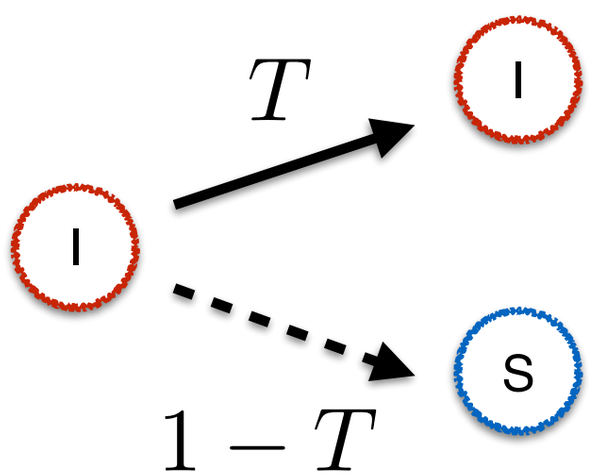


- Epidemic size (Final fraction of recovered nodes)
- Epidemic threshold
- M. E. J. Newman, The spread of epidemic disease on networks, Phys. Rev. E, 66, 016128 (2002).

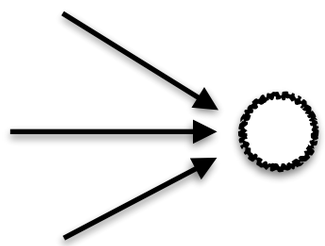
Transmissibility (Occupation Probability)

- Transmissibility *T* is defined as the probability that the infection will be transmitted from an infected node to a connected neighbor before recovery.

$$T = 1 - (1 - \beta\delta t)^{\tau/\delta t}$$
$$\approx 1 - e^{-\beta\tau}.$$



Final Size of Epidemic on a Network (1)



Degree distribution: *P(k)*

- Let us define *u* as the probability that a link is ***not*** active.

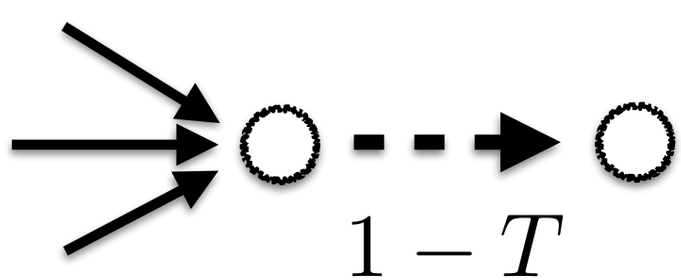
$$1 - r = P(0) + P(1)u + P(2)u^2 + \cdots$$
$$= \sum_k P(k)u^k.$$

Generating function: $G_0(x) = \sum_k P(k)x^k,$

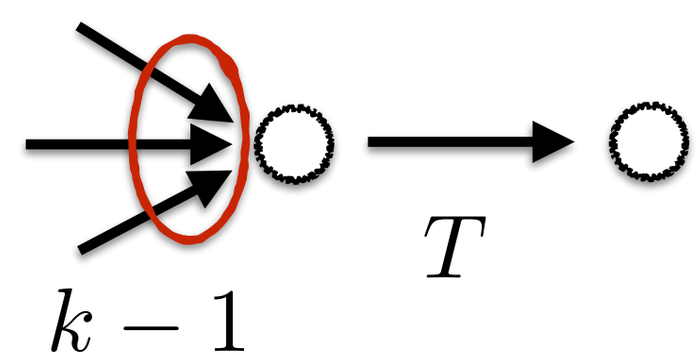
$$r = 1 - G_0(u).$$

Final Size of Epidemic on a Network (2)

$$u = (1 - T) + T \sum_{k=1}^{\infty} \frac{kP(k)}{\langle k \rangle} u^{k-1}.$$



or



Generating function: $$G_1(x) = \sum_{k=1}^{\infty} \frac{kP(k)}{\langle k \rangle} x^{k-1},$$

$$= \frac{G_0'(x)}{G_0'(1)} = \frac{1}{\langle k \rangle} G_0'(x).$$

$$\longrightarrow \quad u = 1 - T + TG_1(u).$$

Final Size of Epidemic on a Network (3)

1. Find transmissibility *T* for given β, τ

$$T = 1 - e^{-\beta\tau}.$$

2. Define the generating function for degree distribution *P(k)*

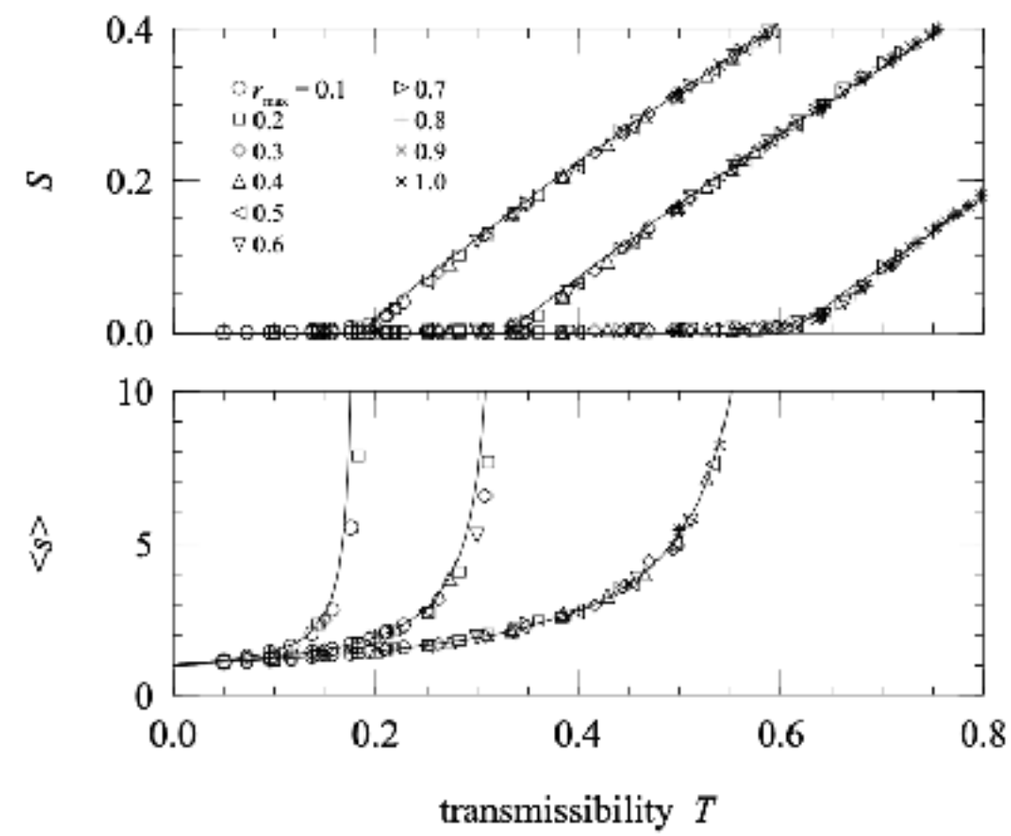
$$G_0(x) = \sum_{k=0}^{\infty} P(k)x^k, \quad G_1(x) = \sum_{k=1}^{\infty} \frac{kP(k)}{\langle k \rangle} x^{k-1}.$$

3. Obtain the probability *u:*

$$u = 1 - T + TG_1(u).$$

4. *Obtain the final size of epidemic:*

$$r = 1 - G_0(u).$$



Epidemic Threshold

- Self-consistency equation is given by

$$u = (1 - T) + T \sum_{k=1}^{\infty} \frac{kP(k)}{\langle k \rangle} u^{k-1}.$$

- *u=1* is a trivial solution, corresponding to *r=0* (no epidemic).
- Non trivial solution appears when the derivative of rhs at *u=1* is larger than 1.

$$T \frac{\langle k^2 \rangle - \langle k \rangle}{\langle k \rangle} > 1.$$

- The epidemic threshold is than:

$$T_c = \frac{\langle k \rangle}{\langle k^2 \rangle - \langle k \rangle}.$$

cf. threshold for SIS model

$$\lambda_c = \frac{\langle k \rangle}{\langle k^2 \rangle}.$$

(Example 1) Erdos-Renyi Networks

- The degree distribution is a Poisson distribution with average degree <k>.

$$G_0 = \sum_k \frac{e^{-z} z^k}{k!} x^k = e^{z(x-1)},$$

$$G_1 = \sum_{k=1}^{\infty} \frac{kP(k)}{z} x^k = \sum_{k=1}^{\infty} \frac{k e^{-z} z^k}{z k!} x^{k-1}$$

$$= \sum_{k=1}^{\infty} \frac{e^{-z} z^{k-1}}{(k-1)!} x^{k-1} = e^{z(x-1)}.$$

$$r = 1 - e^{z(u-1)},$$

$$u = 1 - T + T e^{z(u-1)},$$

$$= 1 - T(1 - e^{z(u-1)})$$

$$= 1 - Tr$$

$$\longrightarrow \quad r = 1 - e^{-zTr}.$$

$$T_c = \frac{1}{\langle k \rangle}.$$

(Example 2) Scale-Free Networks

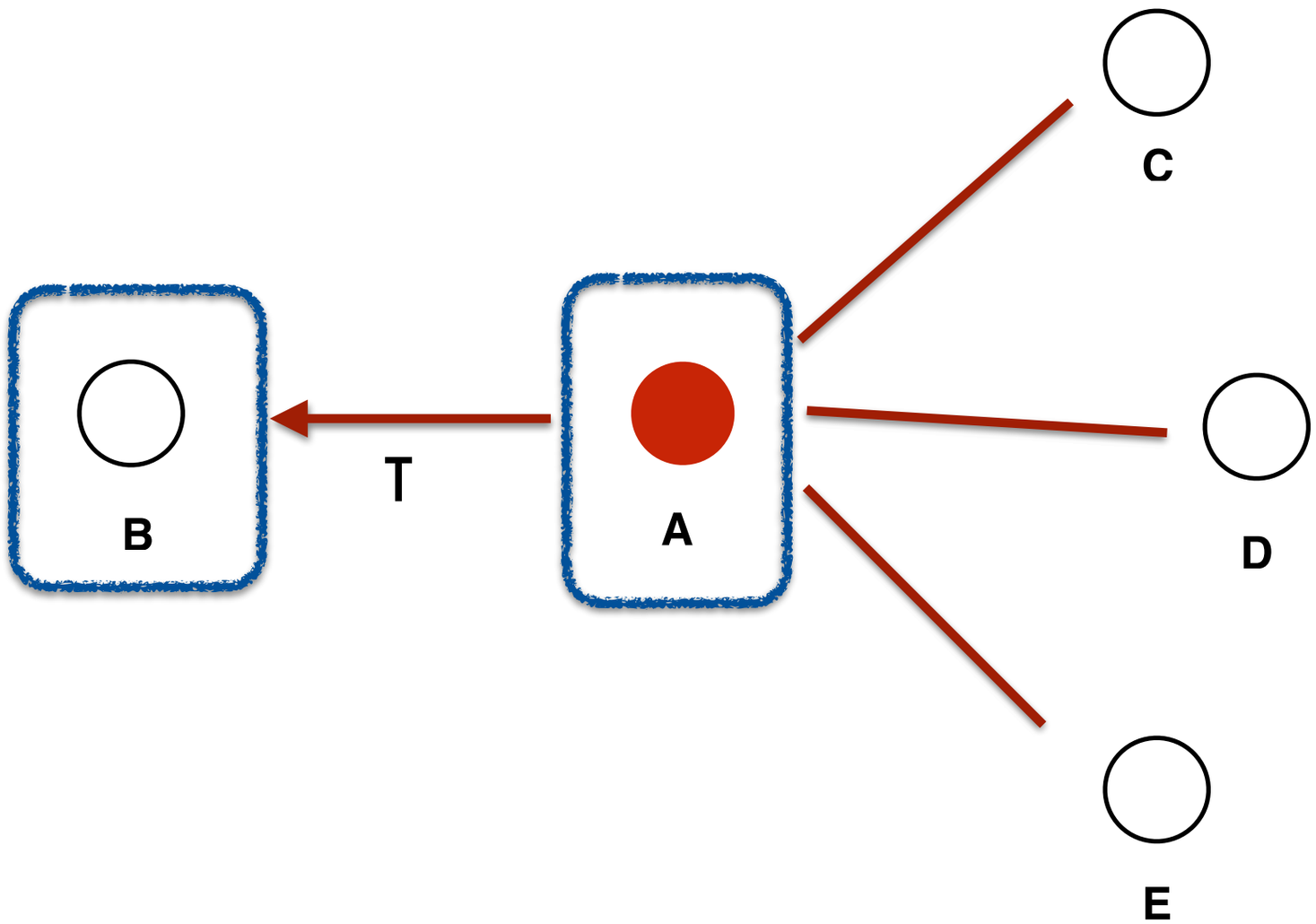
$$T_c = \frac{\langle k \rangle}{\langle k^2 \rangle - \langle k \rangle}.$$

$$\longrightarrow \quad \langle k^2 \rangle = \int k^2 P(k) dk$$

$$\sim \int k^{2-\gamma} dk \to \infty \quad \text{if } 2 < \gamma \leq 3.$$

- Absence of epidemic threshold in SF networks

Message-Passing Theory for Epidemic Spreading



Probability u_{BA} that ***B*** does not receive a message (disease) from ***A***:

$$u_{BA} = 1 - T(1 - u_{AC}\ u_{AD}\ u_{AE}).$$

Message-Passing Theory for Epidemic Spreading

On a locally tree-like network: $$1 - u_{ij} = T\left(1 - \prod_{k \in \partial j \setminus i} u_{jk}\right)$$

Final epidemic size: $$\rho = \frac{1}{N}\sum_i \left(1 - \prod_{j \in i} u_{ij}\right)$$

- pros: small networks, quenched disorder, node-level analysis
- cons: 2L equations, hard to apply to complex contagions

[B. Karrer, MEJ Newman, L. Zdeborova, Percolation on sparse networks, PRL (2014)]

Numerical Methods (discrete Time)

- Compare a network and the dynamical rules of epidemic processes.

1. Set $\delta t = \tau$.
2. Infection occurs btw a connected pair with prob = β
3. Infected nodes recover at next time step with prob = 1.
4. Repeat 2) and 3) until a steady state is reached.

1. Set δt as a small value.
2. Infection occurs btw a connected pair with prob = $\beta \delta t$
3. Infected nodes recover at next time step with prob = $\gamma \delta t$.
4. Repeat 2) and 3) until a steady state is reached.

Gillespie Algorithm (Exact and Efficient)

- Compare a network and the dynamical rules of epidemic processes.

1. Enumerate all possible events (including both infection and recovery) and define the rate *ai* of each event.
2. Calculate the sum of the rate of all possible events: $a = \sum_i a_i$.
3. Choose time of the next event from the exponential distribution (Poisson processes): $P(\delta t) = e^{-a\delta t}$.
4. Determine which event occurs.
5. Update the system state
6. Repeat 1) - 5) until a steady state is reached.

"A General Method for Numerically Simulating the Stochastic Time Evolution of Coupled Chemical Reactions", D. T. Gillespie, Journal of Computational Physics (1976).
"Exact Stochastic Simulation of Coupled Chemical Reactions", D. T. Gillespie, The Journal of Physical Chemistry (1977).

Controlling Epidemic Spreading

- Wearing a mask and Washing hands

  -> Reducing β

- Social distancing

  -> Reducing effective k and β

- Contact tracing and isolation

  -> Reducing τ

- Vaccination and Immunization

Immunization Strategy (1)

- Immunized nodes are effectively removed from the network, together with all links connecting to them.
- **Random Immunization**: Choose a fraction *p* of immunized nodes at random.

$$T \to T(1-p)$$

$$\longrightarrow \quad u = 1 - T(1-p) + T(1-p)\sum_{k=1}^{\infty}\frac{kP(k)}{\langle k\rangle}u^{k-1}.$$

$$\longrightarrow \quad T(1-p_c) = \frac{\langle k\rangle}{\langle k^2\rangle - \langle k\rangle}.$$

$$\longrightarrow \quad p_c = 1 - \frac{1}{T}\frac{\langle k\rangle}{\langle k^2\rangle - \langle k\rangle}.$$

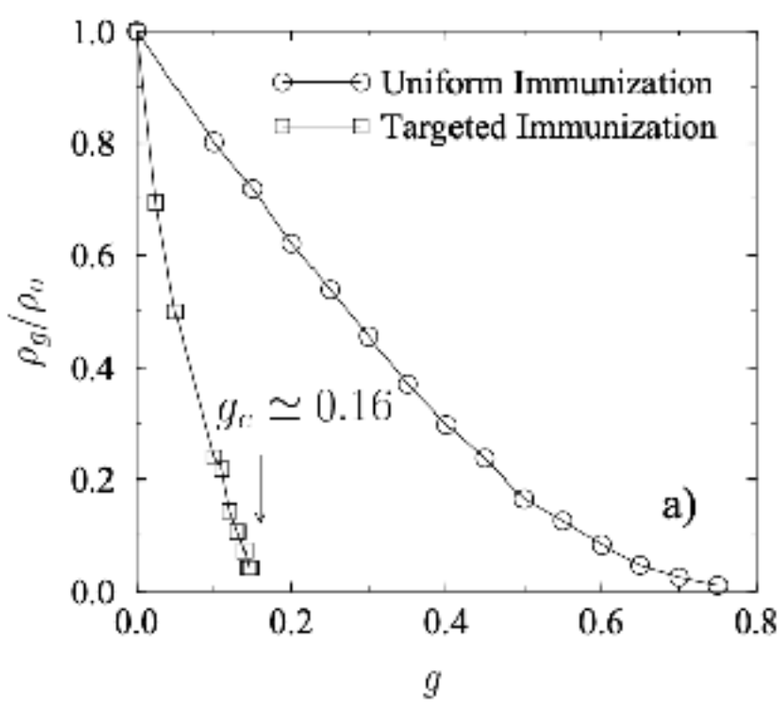
cf. well-mixed population

$$r_H = 1 - \frac{1}{R_0}.$$

Immunization Strategy (2)

- Not all the nodes play the same role in the spreading.
- **Hub Targeting Immunization**: Choose the immunization of a fraction *p* of nodes with largest degree.
- After deletion the nodes with highest degree, the degree distribution becomes then:

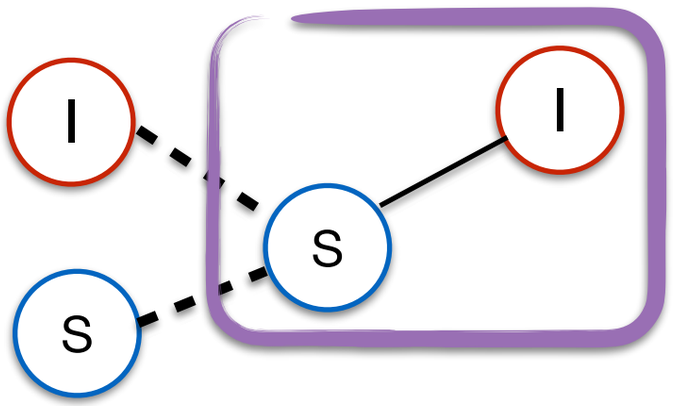
$$P(k) \to \sum_{k' \geq k}^{k_c} P(k') \binom{k'}{k} (1-p)^k p^{k'-k}.$$



"Immunization of complex networks",

R, Pastor-Satorras and A. Vespignani, PRE (2002).

Pair Approximation for Epidemic Spreading



$$\frac{dx}{dt} = -x + \lambda\langle k\rangle(1-x)x.$$

$$\ell_{SS}, \ell_{SI}, \ell_{II}.$$

$$\frac{d\ell_{II}}{dt} = \beta\ell_{SI} - 2\gamma\ell_{II} + \beta\ell_{SI}\ell_{SI}/s,$$

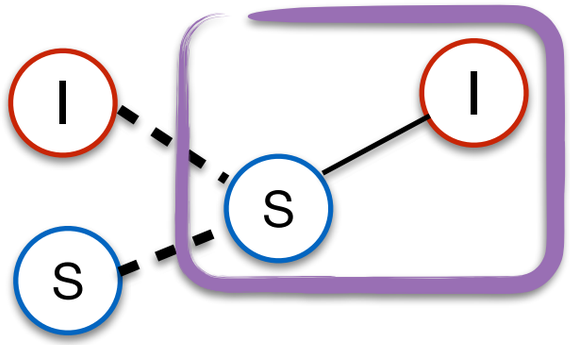
$$\frac{d\ell_{SS}}{dt} = -2\beta\ell_{SI}\ell_{SS}/s + \gamma\ell_{SI}.$$

- ℓ_{bc}/b is the probability that a given node with *b* has a *bc* link.

[J. P. Gleeson, PRX (2013)]

Epidemics on an Adaptive Network

- w = probability of rewiring for S-I pairs
- Pair approximation



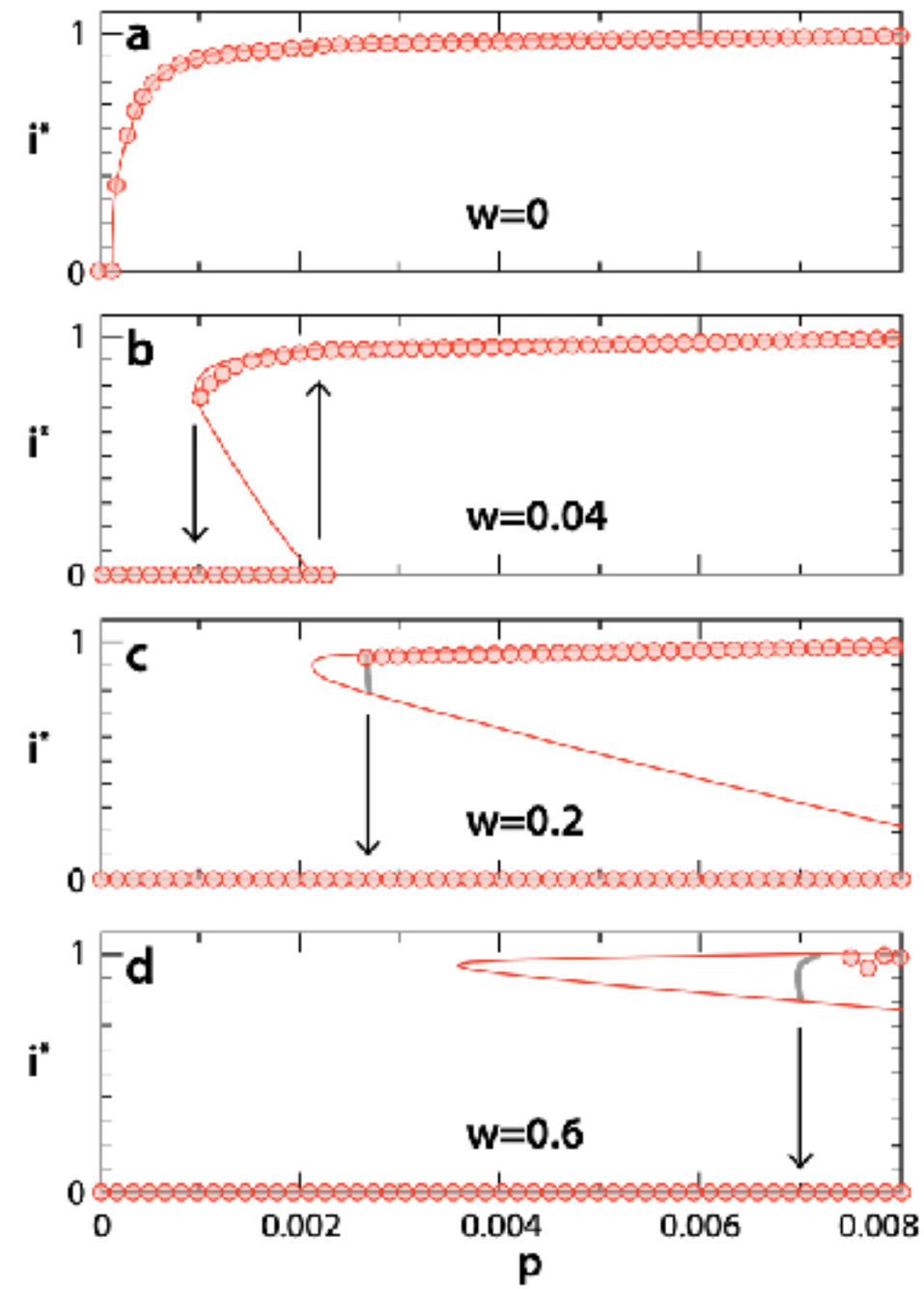
$$\frac{dx}{dt} = \beta \ell_{SI} - \gamma x,$$

$$\frac{d\ell_{II}}{dt} = \beta \ell_{SI} - 2\gamma \ell_{II} + \beta \ell_{SI} \ell_{SI}/s,$$

$$\frac{d\ell_{SS}}{dt} = (\gamma + \underline{w})\ell_{SI} - 2\beta \ell_{SI} \ell_{SS}/s.$$

- ℓ_{bc}/b is the probability that a given node with *b* has a *bc* link.

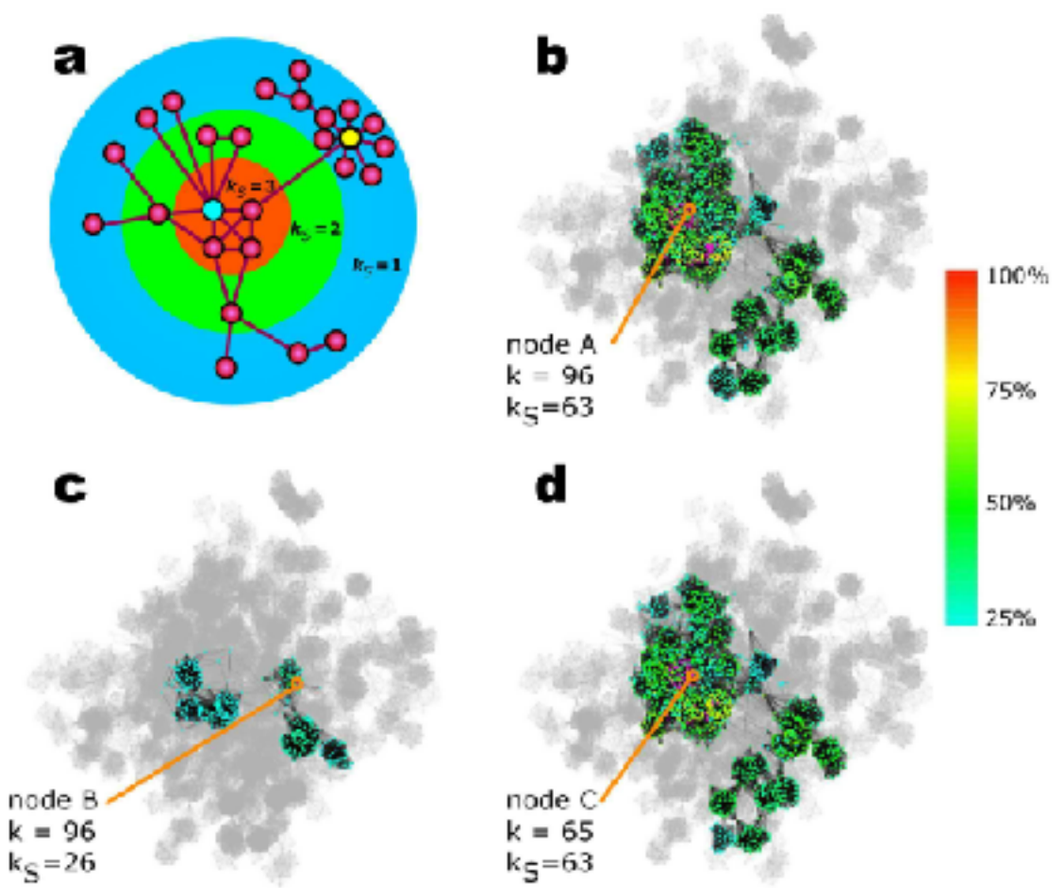
$$\beta_c = \frac{w}{\langle k \rangle [1 - e^{-w/\gamma}]}.$$

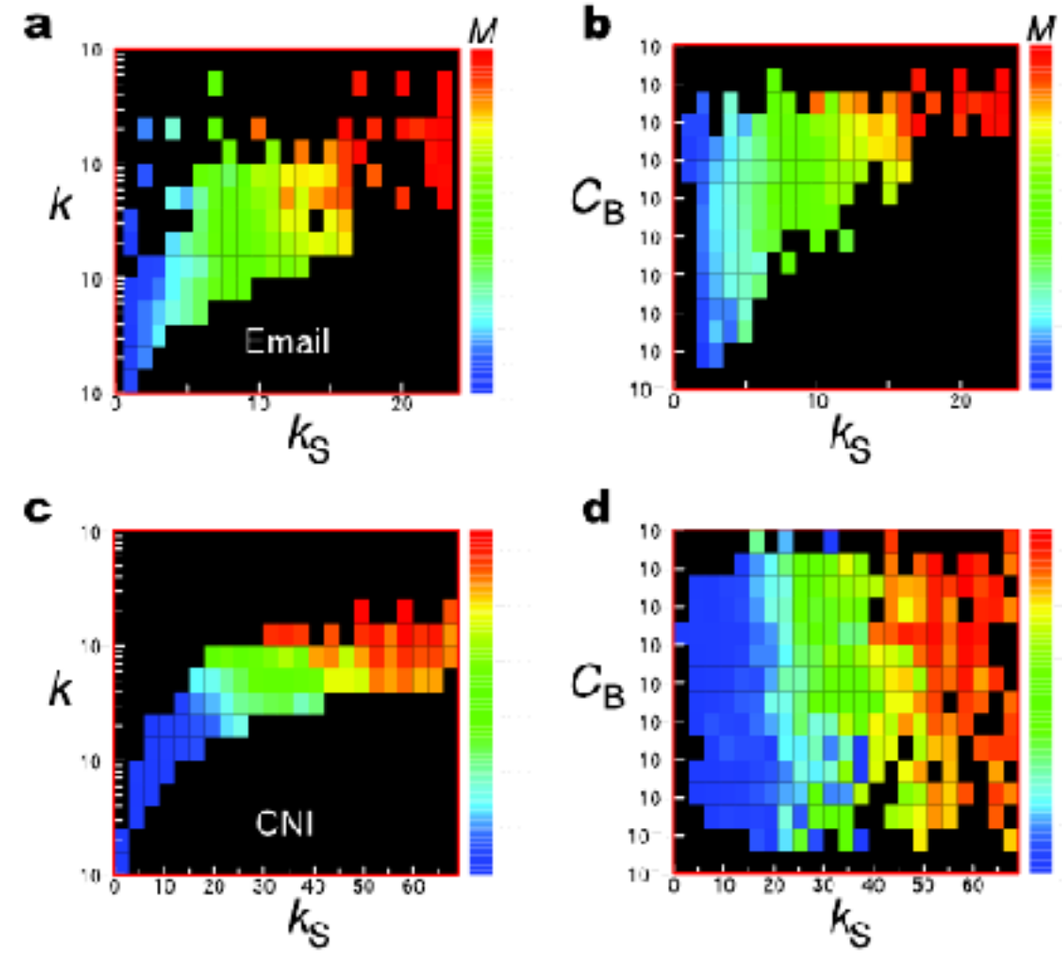


"Epidemic dynamics on an adaptive network", T. Gross, et al., PRL (2006).

Finding an Influential Spreader (1)

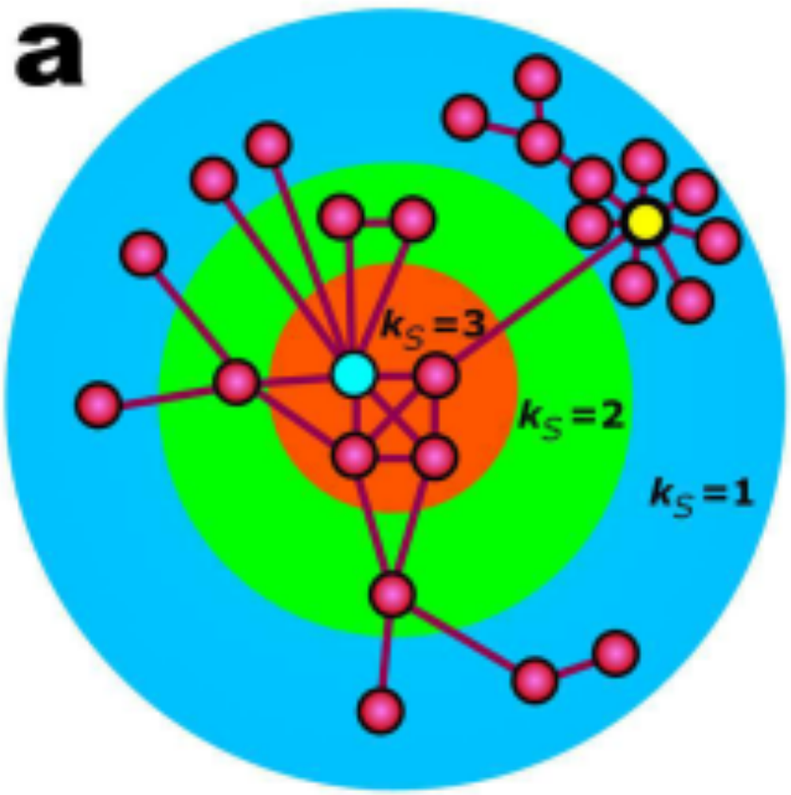
- Topological location of seed can affect the dynamics of epidemics.
- Influential spreader: What node should be chosen as initial seed in the SIR model in order to maximize the final epidemic?
- In order to quantify the influence of a given node *i* in spreading process, the average size of the infected nodes in an epidemic originating at node *i*.

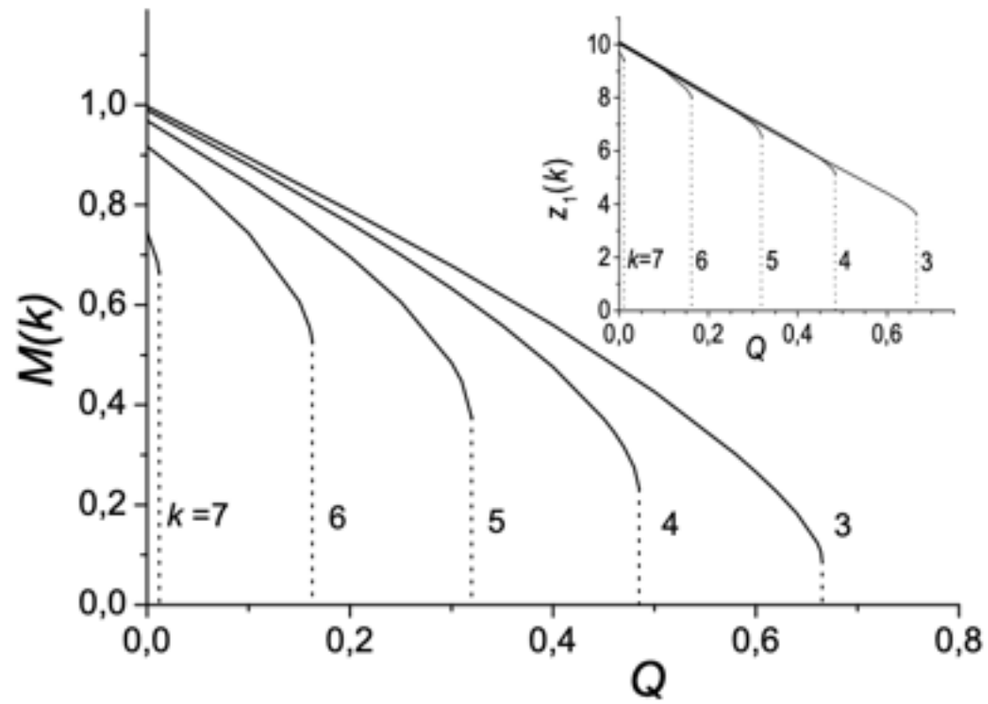




[M. Kitsak et al., Nat. Phys. (2010)]

Finding an Influential Spreader (2)





$$M_n = \sum_k P(k) \sum_{m=n}^{k} \binom{k}{m} (1-R)^m R^{n-m},$$

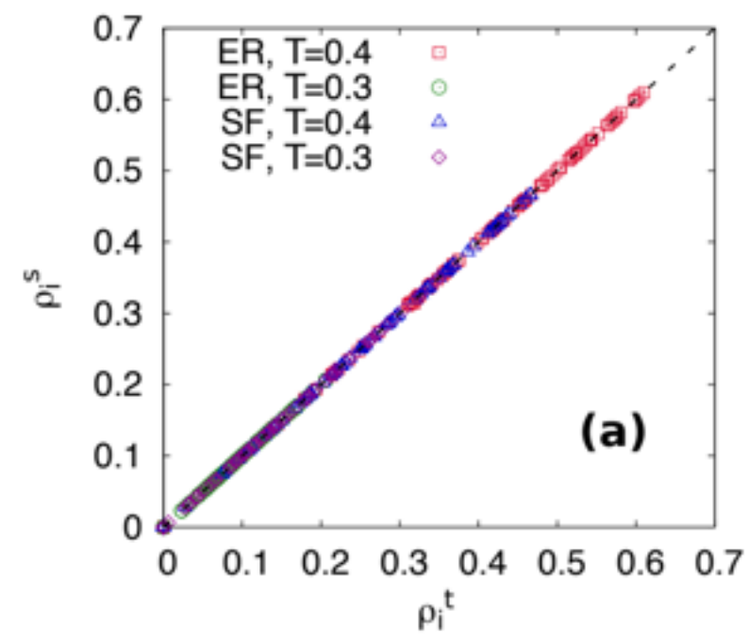
$$1 - R = \sum_k \frac{kP(k)}{\langle k \rangle} \sum_{m=n}^{k-1} \binom{k-1}{m} (1-R)^m R^{k-1-m}.$$

Finding an Influential Spreader (3)

- The probability of epidemic outbreaks:

$$P_i = 1 - \prod_{j \in i} u_{ij}.$$

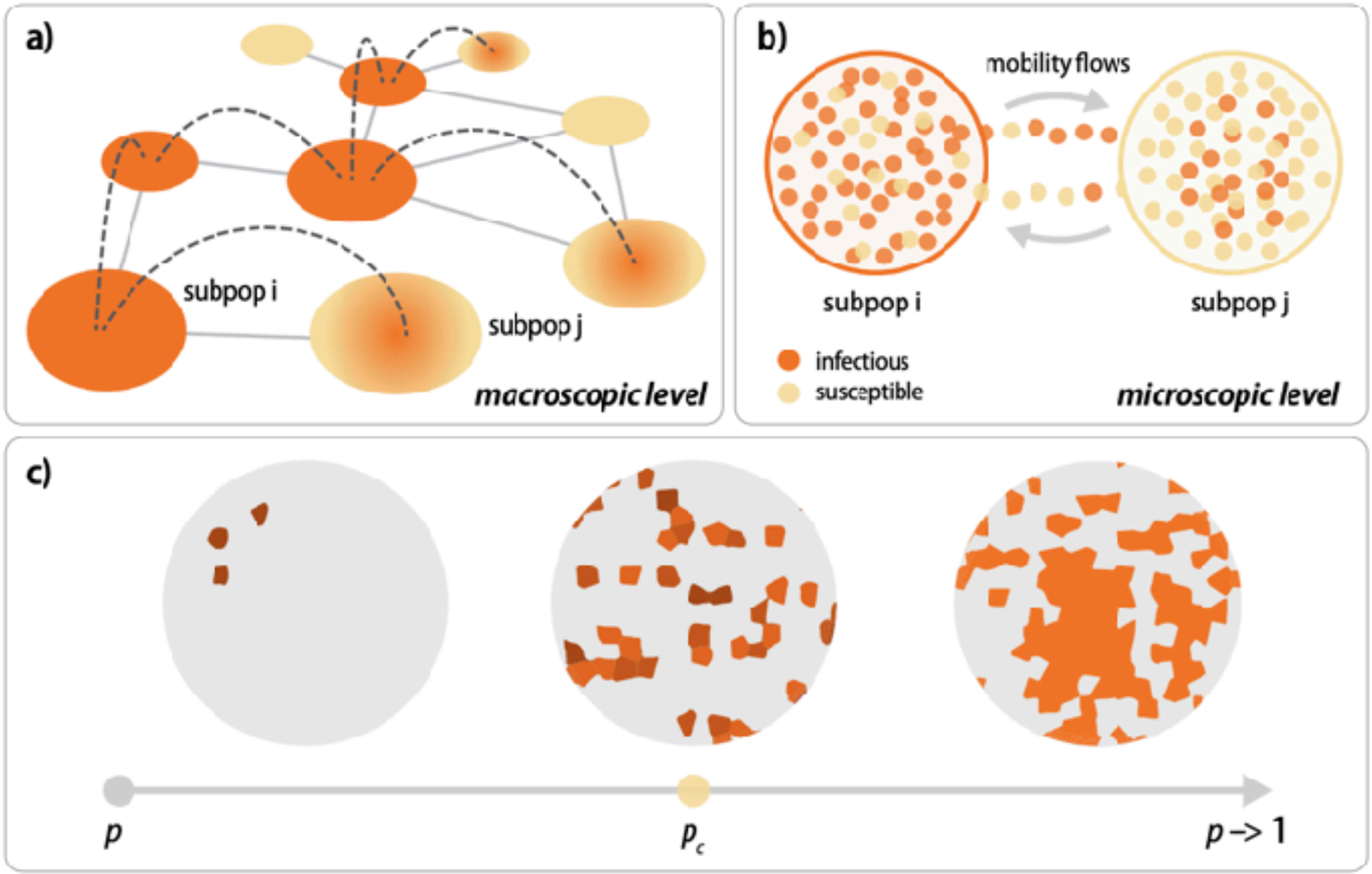
$$1 - u_{ij} = T \left(1 - \prod_{k \in \partial j \setminus i} u_{jk} \right)$$



[B. Min, EPJB (2018)]

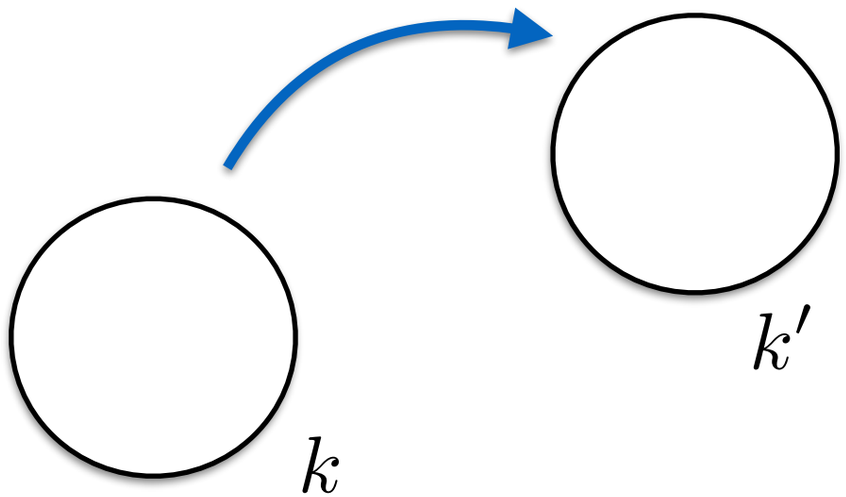
Epidemics on a Meta-Population Model (1)

- Macroscopic level: Diffusion in a network
- Microscopic level: Epidemic processes in a well-mixed population
- V. Colizza, R. Pastor-Sattoras, and A. Vespignani, Nat. Phys. (2007).



"Epidemic processes in complex networks", RMP (2015)

Epidemics on a Meta-Population Model (2)



- $1/\gamma$: average infectious period
- N_k: the number of individual in subpop with *k*
- $d_{kk'}$: movement rate from city with *k* to subpop with *k'*.
- $\lambda_{kk'}$: the number of infected seeds that may appear into subpop with *k' from subpop with k.*

$$\lambda_{kk'} = \frac{1}{\gamma} d_{kk'} \alpha N_k.$$

- prob that *n* seeds success to generate secondary infections

$$1 - \left(\frac{\gamma}{\beta}\right)^n = 1 - \left(\frac{1}{R_0}\right)^n$$

[V. Colizza and A. Vespignani, PRL (2007)]

Epidemics on a Meta-Population Model (3)

- D_k^n: the number of diseased subpopulation with *k* in *n*-th generation

$$D_k^{n+1} = \left(1 - \frac{D_k^n}{V_k}\right) \sum_{k'} D_{k'}^n (k'-1) P(k|k') \left[1 - \left(\frac{1}{R_0}\right)^{\lambda^{k'k}}\right].$$

Prob of finding not diseased subpop ≈ 1 (in the early stage)

$$\frac{kP(k)}{\langle k \rangle}$$

prob of outbreaks by traveled seeds kk'

$$\approx \lambda_{k'k}(R_0 - 1),$$

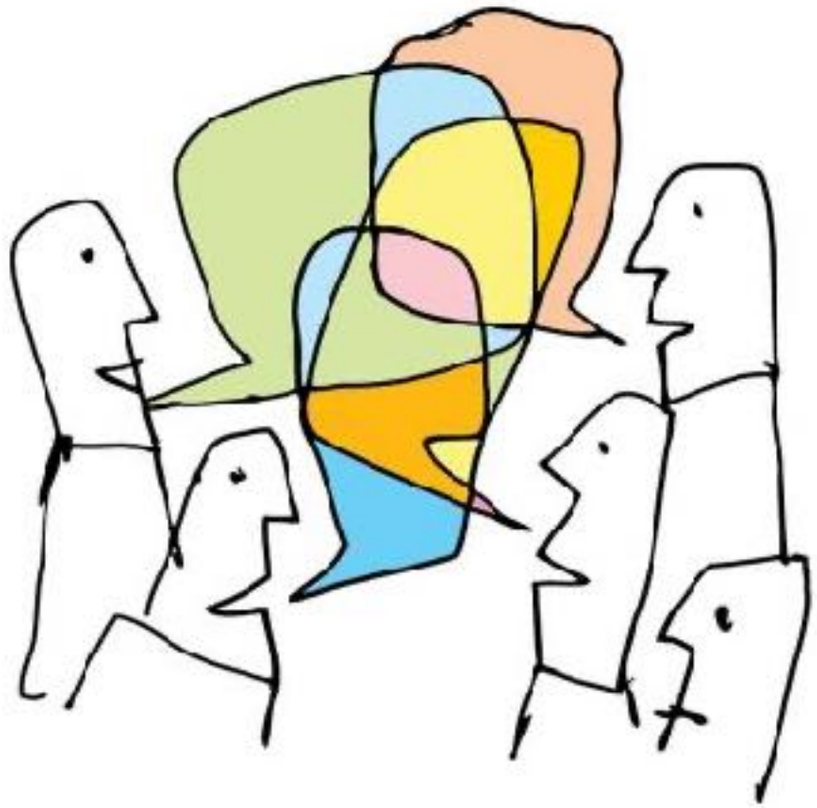
when $R_0 - 1 \ll 1$.

$$D_k^{n+1} \approx \frac{kP(k)}{\langle k \rangle}(R_0 - 1) \sum_{k'} D_{k'}^n (k'-1) \lambda_{k'k}.$$

$$(R_0 - 1) \frac{\langle k^2 \rangle - \langle k \rangle}{\langle k \rangle} \frac{1}{\gamma} \langle d \rangle \langle N \rangle \alpha > 1.$$

[V. Colizza and A. Vespignani, PRL (2007)]

Social Contagion

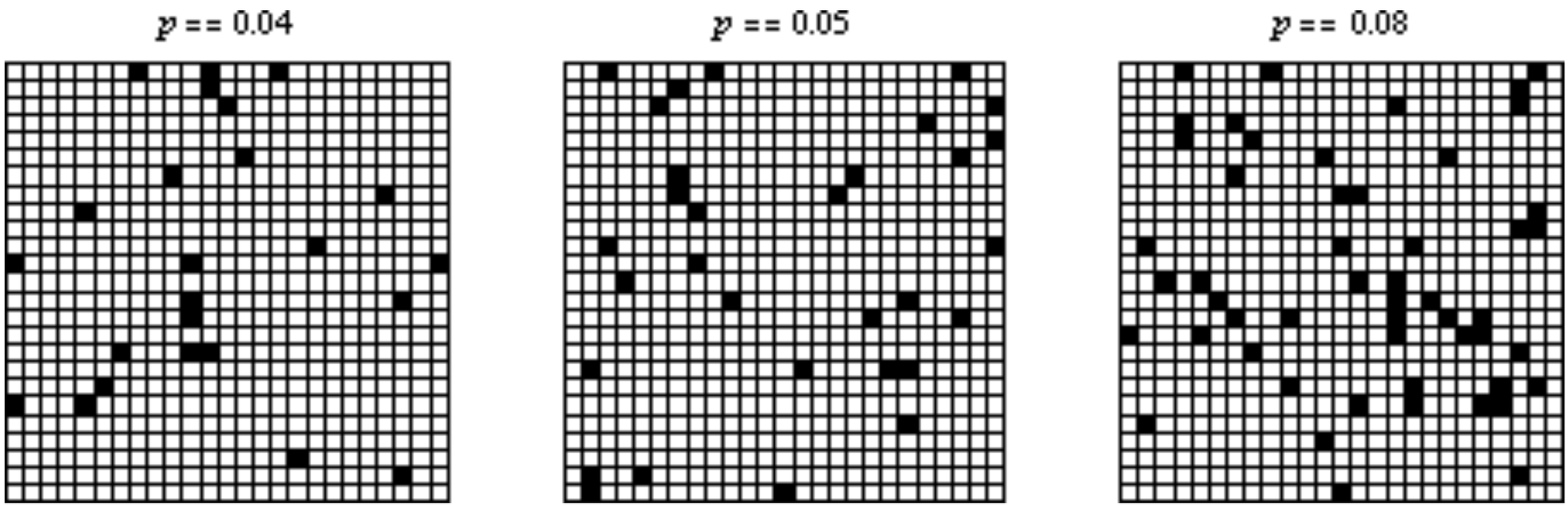


- Social contagion of behaviors and innovations.
- Threshold model
- Granovetter model (1978) and Watts' threshold model (2002).

Social Contagion

	Disease spreading	**Social Contagion**
Interaction	Pairwise (dyadic) interactions	Collective interactions
Rule	Single exposure	Multiple exposures
Phase transition	Continuous transitions	Discontinuous transitions
Models	SIR, SIS, etc	Threshold model, Bootstrap percolation, etc

Bootstrap Percolation



- More than one exposures are needed.
- Collective interactions among neighbors.
- Discontinuous phase transitions.

[J. Chalupa, P. Leath, G. R. Reich, JPC (1979), J. Adler, Physica A (1991)]

(Watts') Threshold Model

- Initially a certain fraction of nodes are active.
- A node becomes active if the fraction of active neighbors is larger than a threshold.

$$\rho = \rho_0 + (1-\rho_0)\sum_k P(k)\sum_{m=0}^{k}\binom{k}{m} q_\infty^m (1-q_\infty)^{k-m} F\left(\frac{m}{k}\right),$$

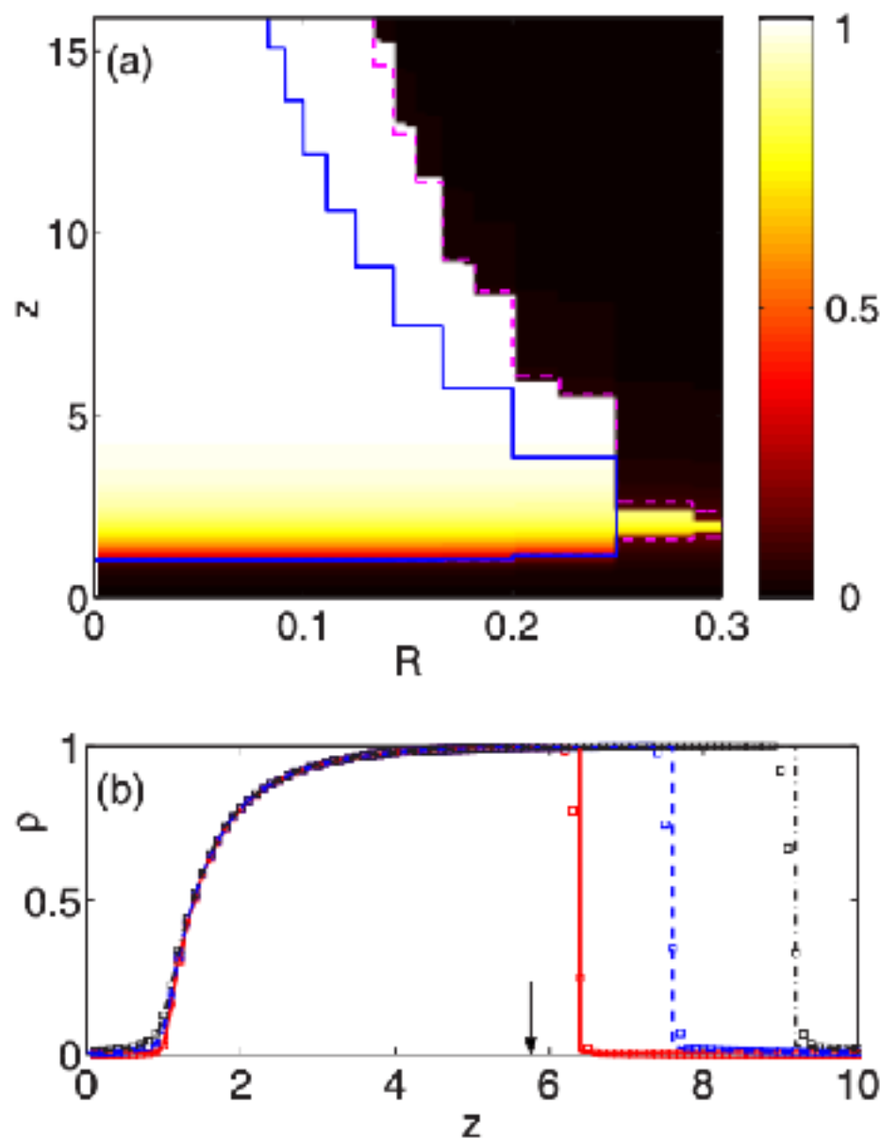
$$\text{where} \quad F\left(\frac{m}{k}\right) \ : \text{threshold function},$$

$$q_{n+1} = \rho_0 + (1-\rho_0)G(q_n),$$

$$G(q) = \sum_{k=1}^{\infty}\frac{kP(k)}{\langle k\rangle}\sum_{m=0}^{k-1}\binom{k-1}{m} q^m (1-q)^{k-1-m} F\left(\frac{m}{k}\right)$$

"A simple model of global cascade on random networks", D. J. Watts, PNAS (2002); "Seed size strongly affects cascades on random networks", J. P. Gleeson and D. J. Cahalane, PRE (2007)

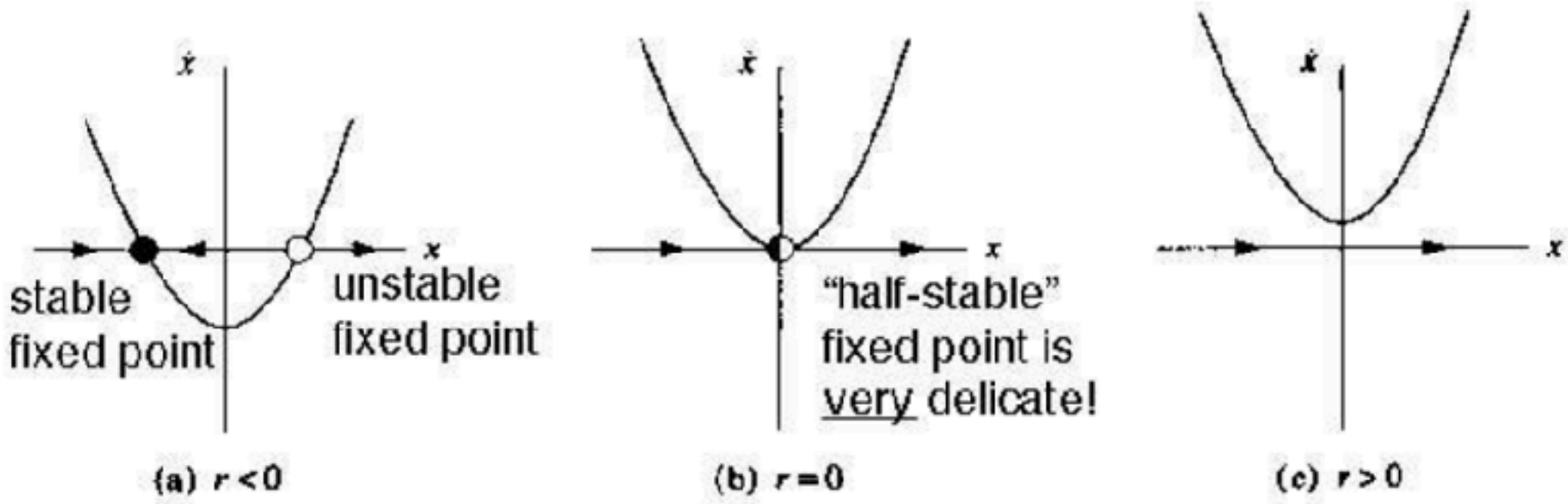
(Watts') Threshold Model



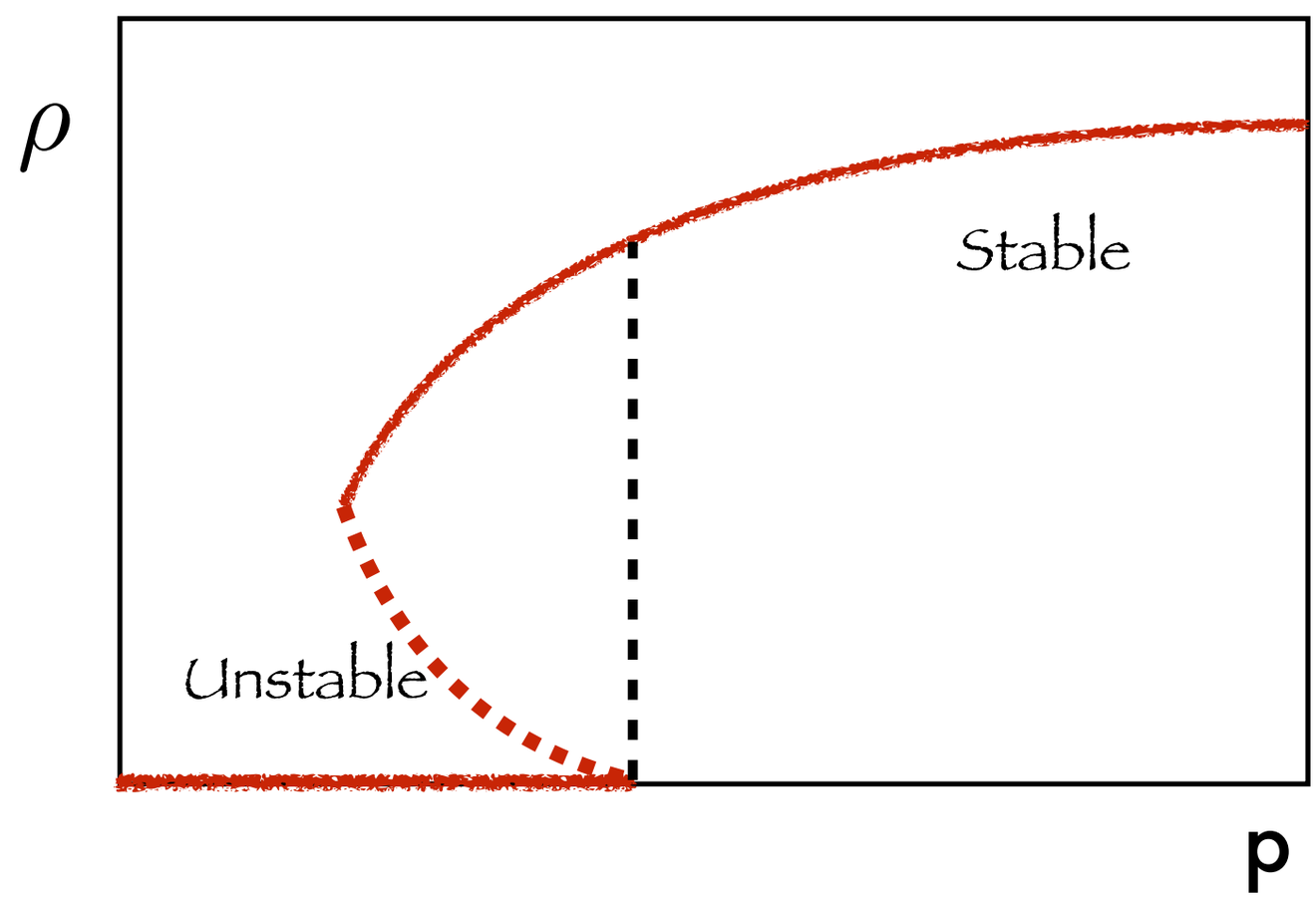
[J. P. Gleeson and D. J. Cahalane, PRE (2007)]

- Generalized epidemic model and cooperative epidemics

Saddle-Node Bifurcations

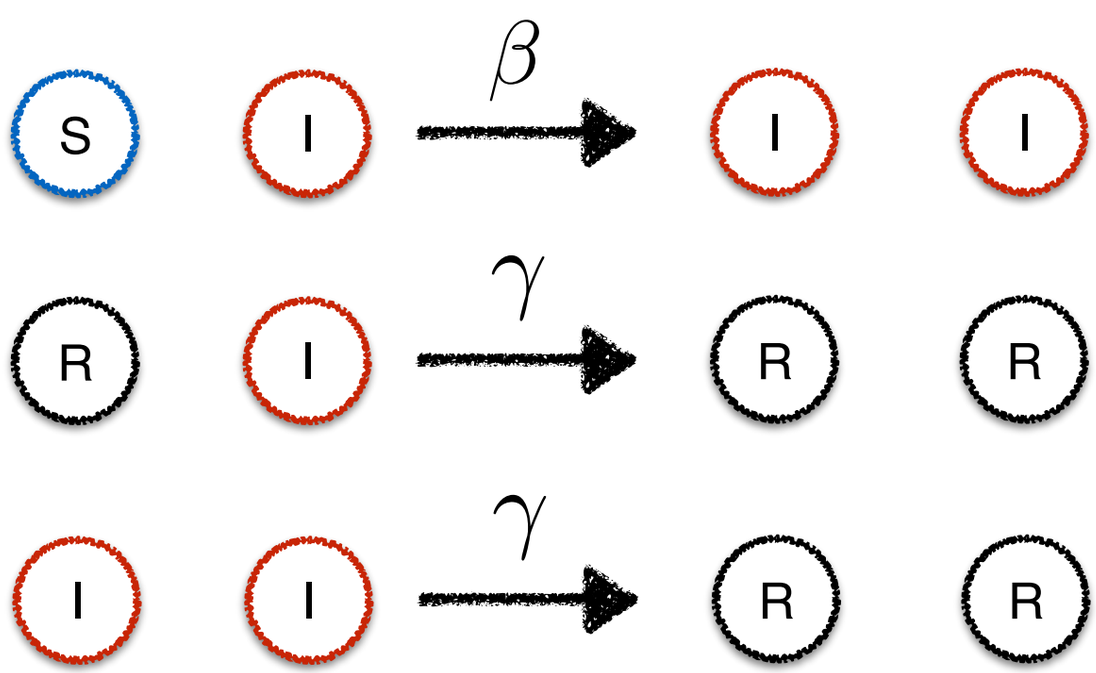


- Two fixed points (one stable and one unstable) disappear when they collide.



Rumor Spreading

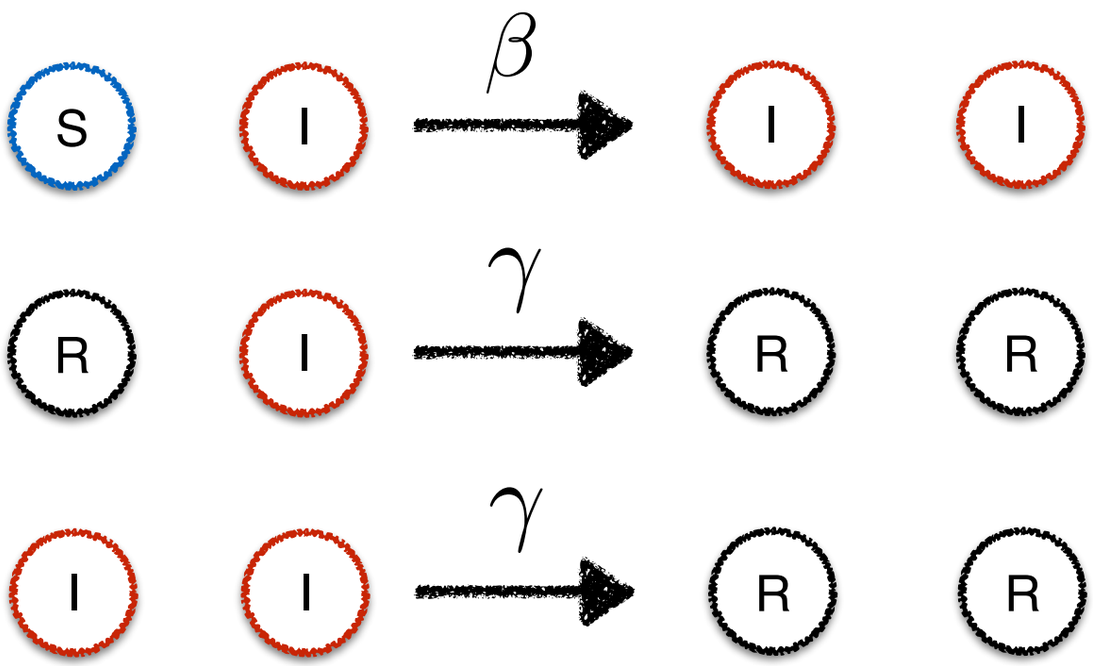
- A variant of the SIR model
- Recovery process does not occur spontaneously but is a consequence of interactions.
- Spreading a rumor is worth as long as it is new.
- If the recipient already knows the rumor, she might lose interest in spreading.



- S: ignorant
- I : spreader
- R : stifler

"Epidemics and rumours", Daley and Kendall, Nature (1964)

Rumor Spreading (1)



Eq. 1 $$\frac{ds}{dt} = -\beta s x,$$

Eq. 2 $$\frac{dx}{dt} = \beta s x - \gamma x^2 - \gamma x r,$$

Eq. 3 $$\frac{dr}{dt} = \gamma x^2 + \gamma x r.$$

Eq. 2 $$\frac{dx}{dt} = \beta s x - \gamma x^2 - \gamma x(1 - s - x)$$
$$= (\beta + \gamma) s x - \gamma x$$

$$r_\infty = 1 - e^{-(1+\beta/\gamma) r_\infty}.$$

Rumor Spreading (2)

$$r_\infty = 1 - e^{-(1+\beta/\gamma)r_\infty},$$

$$R_0 = 1 + \frac{\beta}{\gamma}.$$

- The final fraction of recovered nodes is positive for any values of parameters.
- Hubs are easily infected but then easily turn into recovered. And, they prevent the further spread of the rumor.

"Dynamics of rumor spreading in complex networks", Y. Moreno, M. Nekovee, and A. F. Pacheco, PRE (2004).

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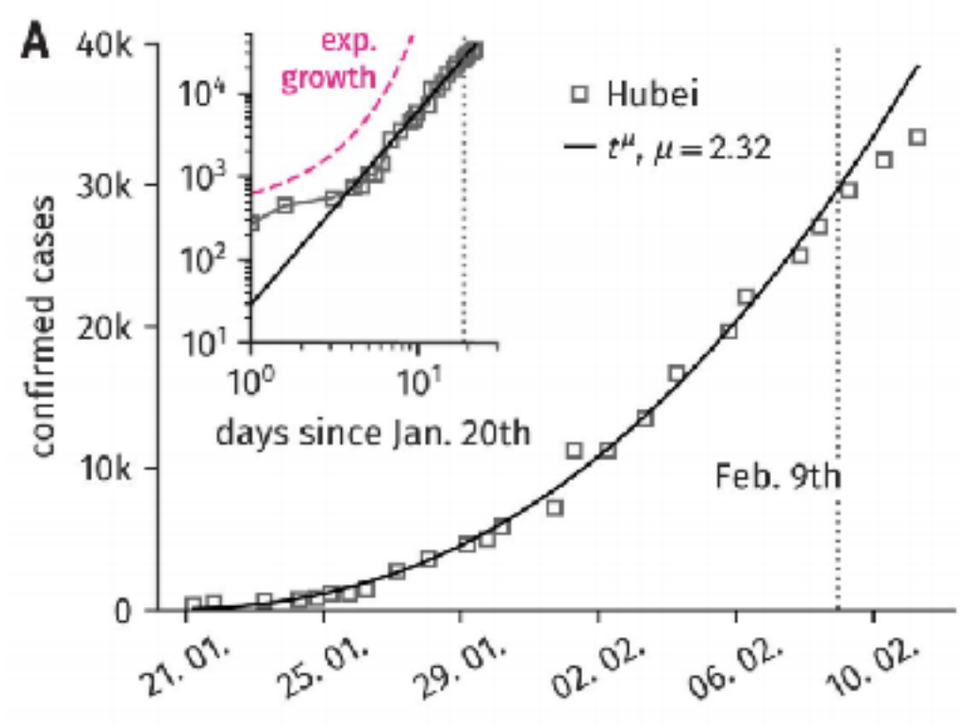
Summary and Outlook

- Prologue: some history
- Basics: Infections and Epidemic Models
- Deterministic Epidemic Models
- Stochastic Epidemic Models (Branching process)
- Epidemic processes on Complex Networks
- Spreading in other Domains

- Realistic static networks
- Temporal networks
- Non-Poissonian processes
- Multi-layer networks
- Generalized epidemic models
- Interacting pathogens

(Project 1) SIR-X Model on a Network

subexponential (power-law) growth



Containment rate (e.g. social distancing)

Quarantine rate

$$\partial_t S = -\alpha S I - \kappa_0 S$$

$$\partial_t I = \alpha S I - \beta I - \kappa_0 I - \kappa I$$

$$\partial_t R = \beta I + \kappa_0 S$$

$$\partial_t X = (\kappa + \kappa_0) I$$

1. Check the patterns of subexponential growth in other countries
2. Study the behavior of the SIR-X model on a network

Reference

1. “Effective containment explains subexponential growth in recent confirmed COVID-19 cases in China”, B. F. Maier and D. Brockmann, Science 368, 742 (2020).
2. https://github.com/datasets/covid-19

(Project 2) SIR model near Epidemic Threshold

- Study the behavior of SIR model near the epidemic threshold.
  - The distribution of cluster size
  - The distribution of lifetime

Reference

1. https://www.apctp.org/plan.php/statws2017/1794, Stochastic processes on complex networks (Lecture notes for 14th winter school), D.-S. Lee (2017) and references therein.
2. P. Grassberger, Math. Biosc. 63, 157 (1983) and J. Cardy and P. Grassberger, J. Phys. A 18, 267 (1985).