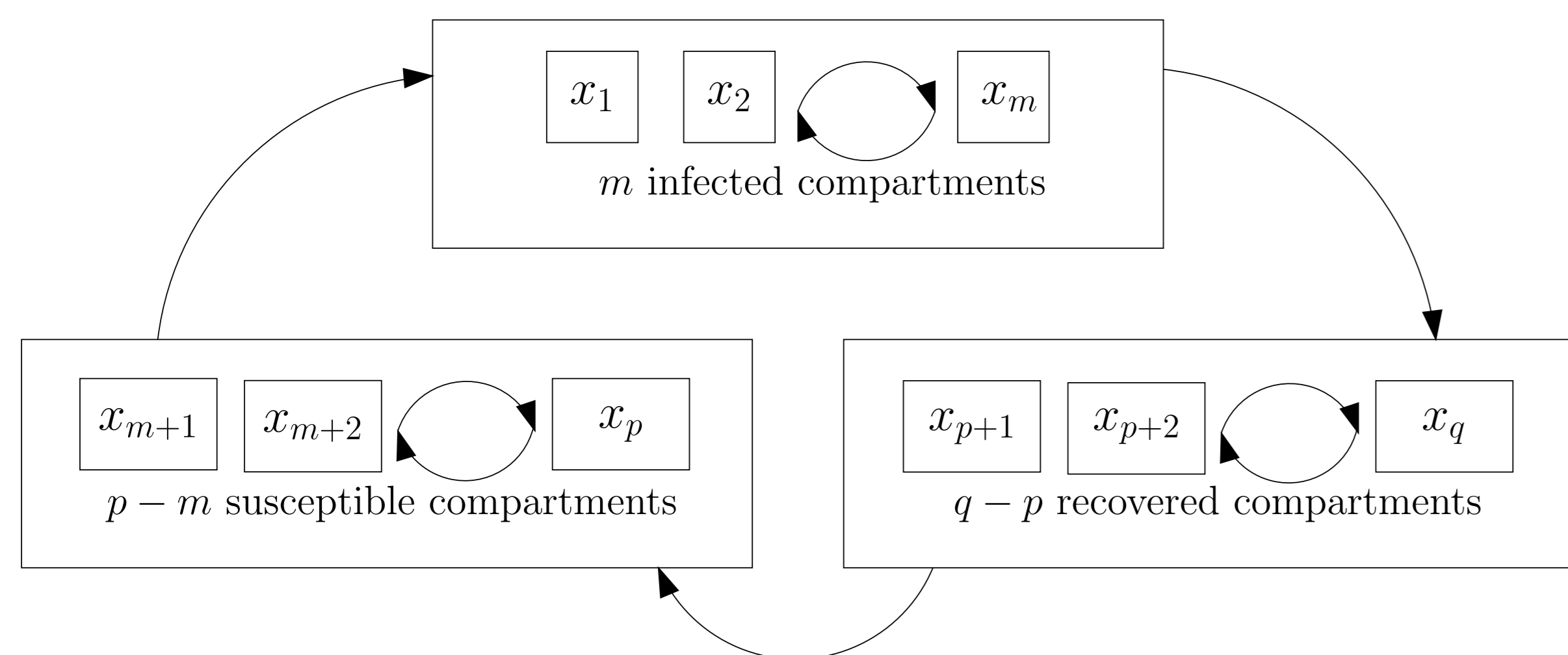




Deterministic Disease Models

The central modeling paradigm of mathematical epidemiology is the *compartmental model*, which tracks individuals as they transition between different disease compartments, classified by the compartment's ability to acquire and transmit infection. The state variable $x_i[t]$ counts the number of individuals in the i th compartment.



The spread of infection is most appropriately modeled stochastically as an individual-to-individual phenomenon. However, when populations are large and “well-mixed,” deterministic approximations often yield useful results.

Typically, the first goal of the analysis of any of these models is the identification of a function X of the parameters and a threshold value c such that a disease will become an “epidemic” if and only if $X > c$. This threshold test might detect:

- when a small initial infective population can grow in size
- if an outbreak will be larger than expected, based on the historical record
- whether the disease will establish an *endemic* presence

Mathematically, one might seek conditions on the parameters of the model such that:

- R_0 , the basic reproductive ratio, is > 1 , where R_0 is defined as “the expected number of secondary cases produced by a typical infected individual during its entire period of infectiousness in a completely susceptible population” [1].
- the *disease-free equilibrium* (DFE) of the model is locally asymptotically unstable
- an endemic equilibrium exists, i.e. the number of infected individuals is > 0 .

R_0 and the Stability of the DFE

When do these different conditions yield the same predictions for disease behavior? We'll focus on a discrete-time model, adopted from the framework presented in [2].

$$x_i[t+1] = h_i(x[t]) = x_i[t] + \underbrace{\mathcal{F}_i(x)}_{\text{new infections arising in compartment } i} - \underbrace{\mathcal{V}_i(x)}_{\text{transitions between compartments}}$$

Under biologically-reasonable assumptions on the forms of the functions $\mathcal{F}_i(x)$ and $\mathcal{V}_i(x)$, the following result holds.

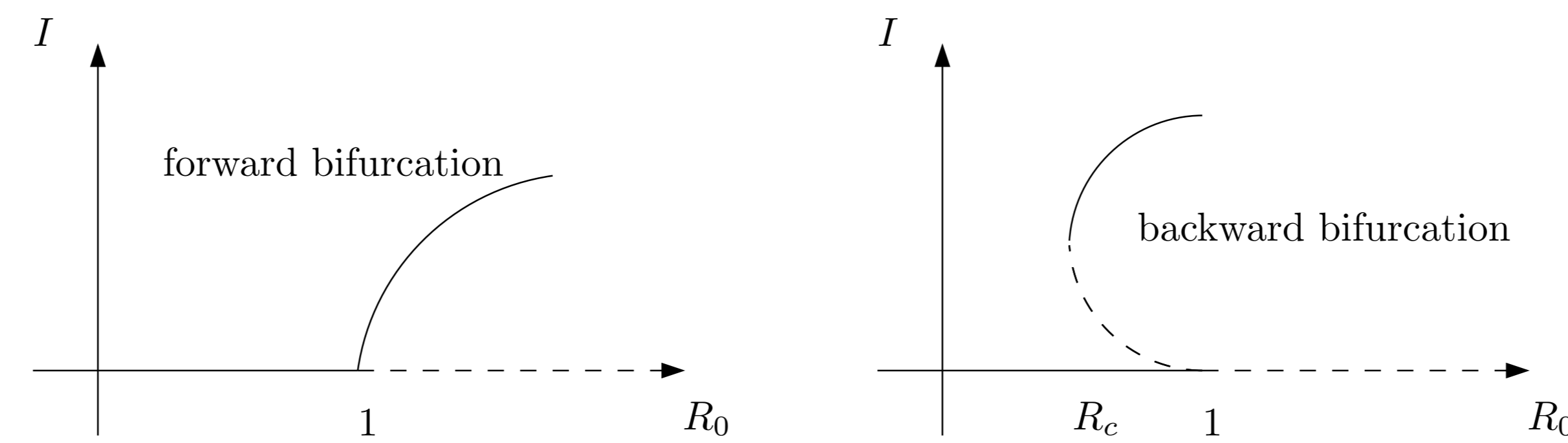
Theorem 1. If x_0 is a DFE, define the $m \times m$ matrices $F = \{f_{ij}\}$ and $V = \{v_{ij}\}$ as:

$$f_{ij} = \left. \frac{d\mathcal{F}_i}{dx_j} \right|_{x_0}, \quad v_{ij} = \left. \frac{d\mathcal{V}_i}{dx_j} \right|_{x_0} \quad \text{for infected compartments } i, j = 1, \dots, m$$

The DFE x_0 is locally asymptotically stable if and only if the spectral radius of $I + F - V$, $\rho(I + F - V)$, is less than 1, which occurs if and only if $R_0 = \rho(FV^{-1})$ is less than 1.

The Existence of Endemic Equilibria

Is the condition that $R_0 > 1$ also equivalent to the existence of an endemic equilibrium? Not in general! Define a variable $I = \sum_{i=1}^m x_i$, which counts the total number of occupants in all infected compartments, and consider a bifurcation diagram of I as a function of R_0 .



Locally, there are two types of possible behavior. In the forward bifurcation, a stable endemic equilibrium is “born” as R_0 increases past 1, while in the backward bifurcation, stable and unstable endemic equilibria exist for a parameter range that overlaps with the interval $R_0 < 1$. In this latter case, the number of initial infectives introduced into the population determines the long-term behavior. If the system is known to exhibit a unique forward bifurcation, then the conditions are equivalent.

In general, however, local information is not sufficient; for example, [3] describes an STD model that exhibits a forward bifurcation of the DFE and multiple endemic equilibria for $R_0 < 1$ and $R_0 > 1$.

A Network of Identical Individuals

Consider a population of identical groups of individuals interacting across the edges of a network according to a deterministic infection model. How does network topology influence disease dynamics? It is rare that complete information about the underlying contact network is known; one might only have estimates of some of the following statistics:

- total number of nodes and edges in the network
- maximum or minimum degree, network girth or diameter
- average degree and variance, degree distribution, or degree correlations
- the *growth* mechanism underlying the creation and evolution of the network

We'll interpret the unknown network structure as a random adjacency matrix \mathbf{A} , drawn from some distribution over the set of all adjacency matrices that satisfy the observed statistics. The following theorem describes a condition under which R_0 can be computed from $E[\mathbf{A}]$.

Theorem 2. For a network on n nodes, let x_i^j denote the number of individuals at node j and in compartment i . If the adjacency matrix of the contact network is $\mathbf{A} = \{\mathbf{a}_{ij}\}$, and the following conditions hold for the linearization of the system at a DFE x_0 :

$$\left. \frac{dh_i^j(x)}{dx_k^l} \right|_{x_0} = \delta_{ik}\delta_{jl} + f_{ik}\mathbf{a}_{jl} - v_{ik}\delta_{jl} \quad \text{for infected compartments } i, k = 1, \dots, m$$

then F and V can be represented as

$$\mathbf{F} = F_h \otimes \mathbf{A}, \quad \mathbf{V} = V_h \otimes I$$

for some matrices F_h and V_h and

$$R_0 = \rho(E[\mathbf{FV}^{-1}]) = \rho(E[F_h V_h^{-1} \otimes \mathbf{A}]) = R_{0,h} \rho(E[\mathbf{A}])$$

where $R_{0,h}$ is the basic reproductive ratio for a homogeneous population.

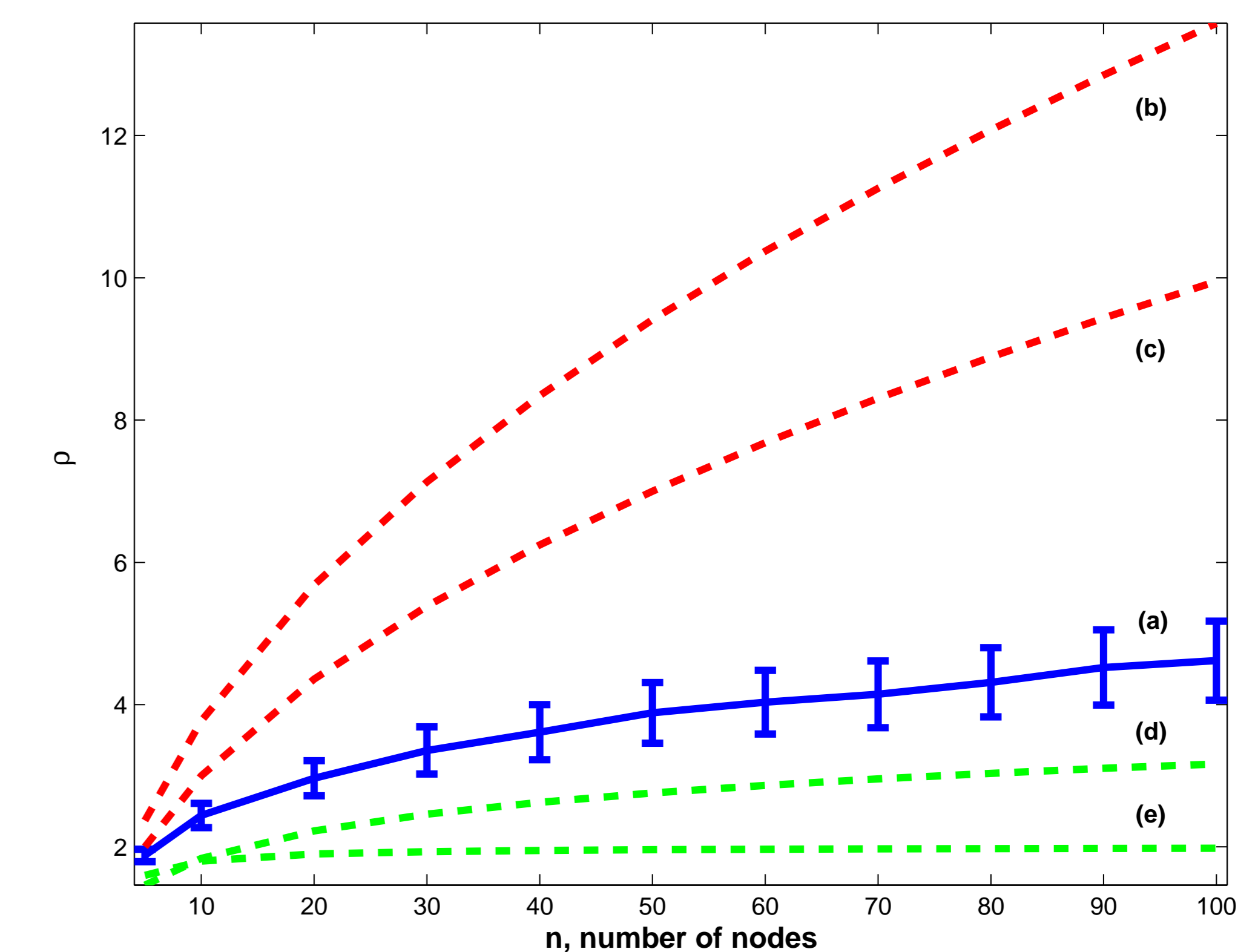
Bounding and Approximating R_0

Because adjacency matrices of undirected graphs are Hermitian,

$$\rho(E[\mathbf{A}]) \leq E[\rho(\mathbf{A})].$$

Thus, if it is possible to upper bound the spectral radii of all possible realizations of \mathbf{A} by a constant c , then $\rho(E[\mathbf{A}])$ is also upper bounded by c . Determining these bounds using the structural properties of the network is one of the tasks of *spectral graph theory*.

For example, consider a network generated by simple preferential attachment as described in [4]. The figure below compares some theoretical upper bounds and approximations with simulation results.



- (a) the mean (\pm std. dev.) of the spectral radius of the adjacency matrix of a simple preferential attachment model on n nodes ($n-1$ edges), taken over 100 trials.
- (b) an upper bound on $\rho(E[\mathbf{A}])$ obtained using the number of edges [5].
- (c) an upper bound obtained using the number of nodes, edges, minimum degree and maximum degree [6].
- (d) approximation assuming a degree distribution $\sim k^{-3}$, corresponding to preferential attachment, without degree correlations.
- (e) approximation assuming a homogeneous network on n nodes with $n-1$ edges distributed identically.

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