An SIS Epidemic in a Large Population with Individual Variation

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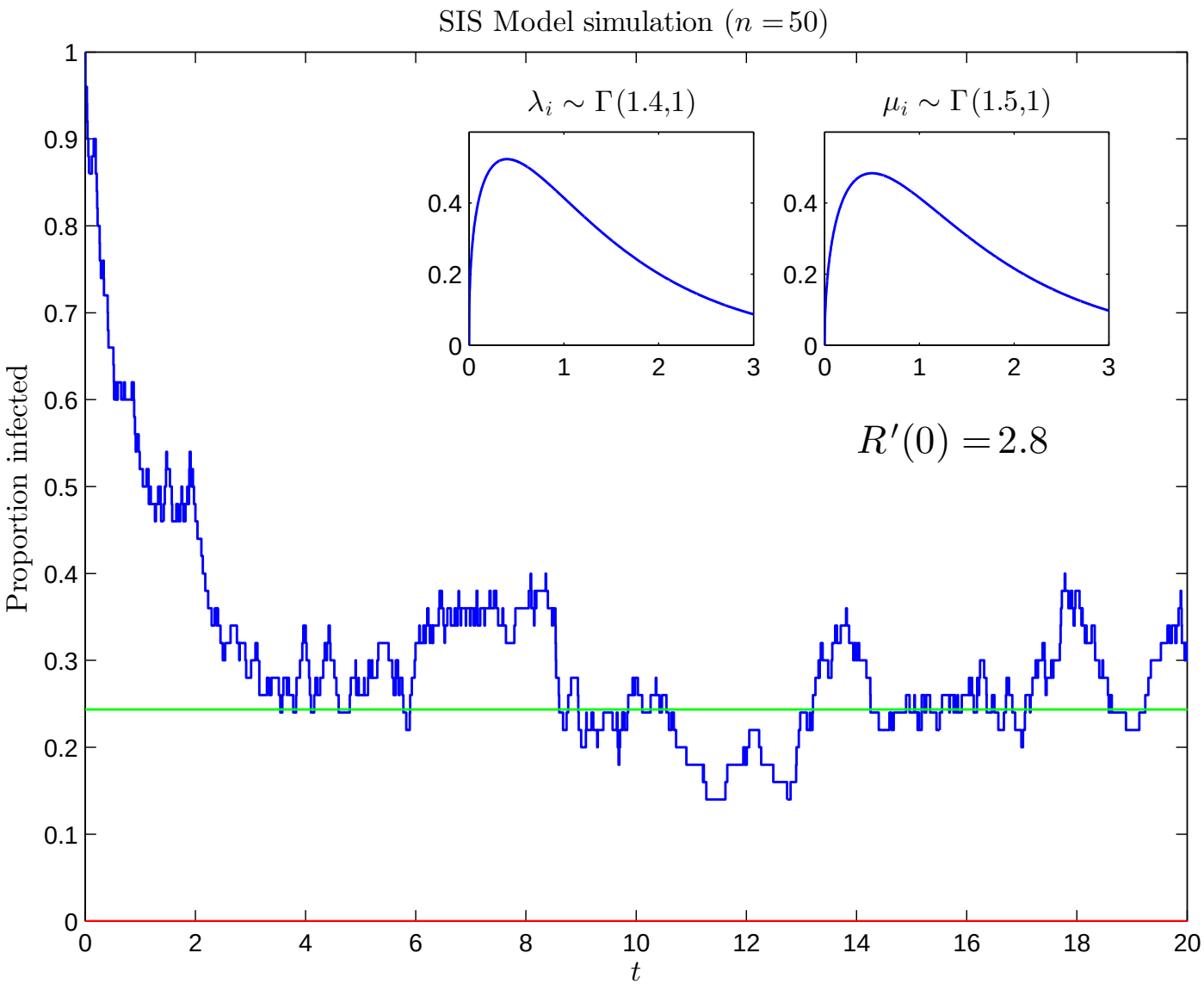
Main message



Collaborator

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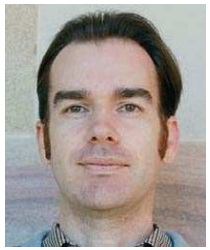
Department of Mathematics
University of Queensland



McVinish, R. and Pollett, P.K. (2012) A central limit theorem for a discrete-time SIS model with individual variation. *Journal of Applied Probability* 49, 521–530.

McVinish, R. and Pollett, P.K. (2013) The deterministic limit of a stochastic logistic model with individual variation. *Mathematical Biosciences* 241, 109–114.

The Stochastic SIS Model

The *SIS (Susceptible-Infectious-Susceptible) Model* was introduced by Weiss and Dishon to study infections, in a closed population of n individuals, that do not confer any long lasting immunity:

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$$Y \to Y + 1 \quad \text{at rate} \quad \frac{\lambda}{n} Y(n - Y) \qquad \text{(infection)}$$

$$Y \to Y - 1 \quad \text{at rate} \quad \mu Y \qquad \text{(recovery)}$$

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It is an example of the *stochastic logistic model* first proposed by Feller:

> Feller, W. (1939) Die grundlagen der volterraschen theorie des kampfes ums dasein in wahrscheinlichkeitsteoretischer behandlung. *Acta Biotheoretica* 5, 11–40.

Behaviour for large n

We can prove a *law of large numbers*, which shows that the proportion of infectives $Y(t)/n$ converges in probability uniformly over finite time intervals to the solution of the ODE

$$\dot{y} = \lambda y(1-y) - \mu y = \lambda y(1-\rho-y),$$

where $\rho = \mu/\lambda$, namely

$$y(t) = \frac{(1-\rho)y_0}{y_0 + (1-\rho-y_0)e^{-\lambda(1-\rho)t}}, \qquad y(0) = y_0,$$

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Theorem

If $Y(0)/n \to y_0$ as $n \to \infty$ then, for all $T > 0$ and for any $\epsilon > 0$,

$$\lim_{n\to\infty} \Pr\left(\sup_{0\le t\le T} \left| \frac{Y(t)}{n} - y(t) \right| > \epsilon \right) = 0.$$

Aside: "We will give the name *logistic* to the curve" - Verhulst 1845

Cette équation étant intégrée donne, en observant que $t=0$ répond à $p=b$,

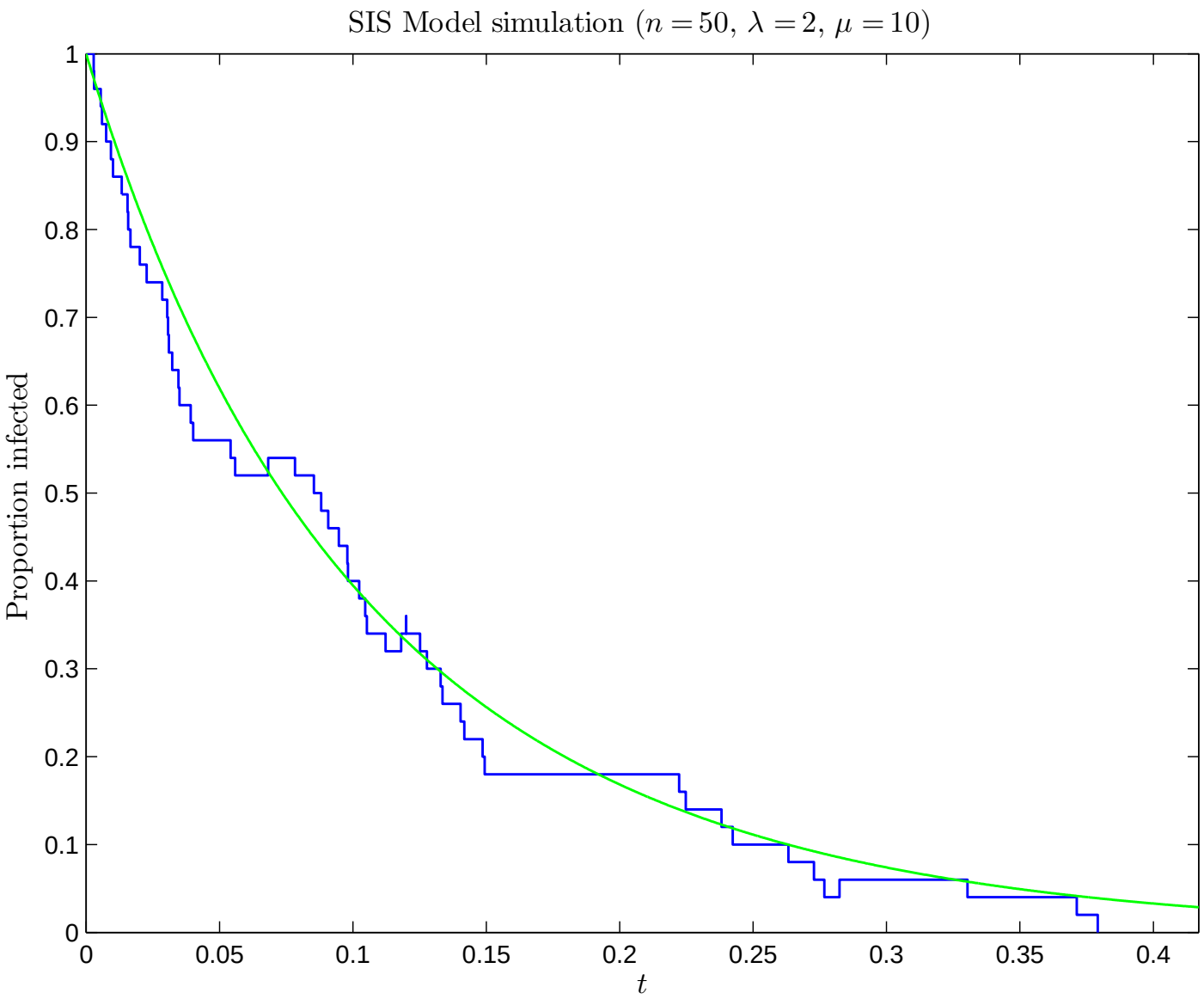
$$t = \frac{1}{m} \log. \left[\frac{p(m - nb)}{b(m - np)} \right] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Nous donnerons le nom de *logistique* à la courbe (*voyez la figure*)

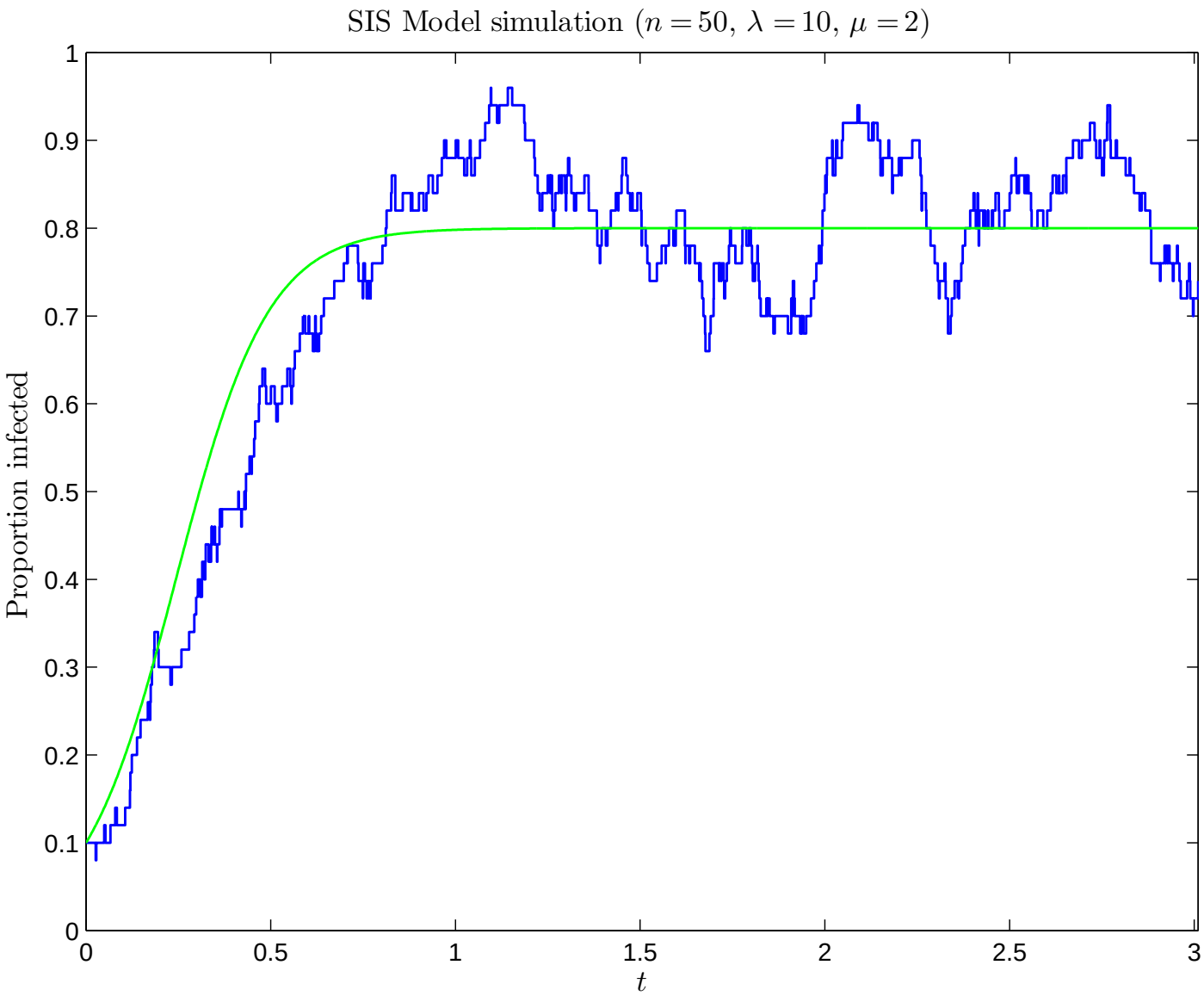
tenu compte de la propriété dont jouissent les denrées alimentaires, de se multiplier dans une progression plus rapide que l'espèce humaine, lorsque le sol est nouvellement cultivé. Mais cet âge d'or de la société n'existe plus depuis longtemps pour les nations européennes. Quant aux ressources qu'un grand peuple peut tirer du commerce étranger pour se procurer des subsistances, il nous suffira de rappeler que, d'après les calculs de M. Moreau de Jonnès, la récolte de la France, en blé seulement, est de 70 millions d'hectolitres, et que pour transporter une pareille masse, il faudrait 88,000 navires de cent tonneaux! Qu'on juge alors de la quantité des autres denrées alimentaires. Lors même qu'une partie considérable de la population française pourrait être nourrie de blés étrangers, jamais un gouvernement sage ne consentira à faire dépendre l'existence de millions de citoyens du bon vouloir des souverains étrangers.

Verhulst, P.F. (1845) Recherches mathématiques sur la loi d'accroissement de la population. *Nouveaux mémoires de l'Académie Royale des Sciences et Belles-Lettres de Bruxelles*.

Infection dies out quickly ($\lambda < \mu$)



Infection becomes endemic ($\lambda > \mu$)



Individual variation

Suppose now that the population is heterogeneous in that individuals have different characteristics: individual i ($i = 1, \ldots, n$) has

- an exponentially distributed recovery period with mean μ_i^{-1} ($\mu_i > 0$);
- a resistence level λ_i^{-1} ($\lambda_i > 0$); and,
- when infected, contributes κ_i to the infective potential of the population.

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- when infected, contributes κ_i to the infective potential of the population.

Let $X_i^{(n)}$ be 1 or 0 according to whether individual i is infected or not, and let $X^{(n)} = (X_1^{(n)}, \ldots, X_n^{(n)})$ be the state of the population.

The model

Suppose $(X^{(n)}(t),\, t \geq 0)$ is a continuous-time Markov chain on $\{0,1\}^n$ with transitions

$$(\ldots,0,\ldots) \to (\ldots,1,\ldots) \quad \text{at rate} \quad \lambda_i f\left(\frac{1}{n}\sum_{j=1}^{n} \kappa_j X_j^{(n)}\right)$$

$$(\ldots,1,\ldots) \to (\ldots,0,\ldots) \quad \text{at rate} \quad \mu_i.$$

$$\uparrow$$

Position i $(i = 1,\ldots,n)$

The function $f : \mathbb{R}_+ \to \mathbb{R}_+$ is assume to be Lipschitz continuous.

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Notice that the disease free state $\mathbf{0} = (0,0,\ldots,0)$ is the sole absorbing state and the remaining states form a communicating class from which $\mathbf{0}$ is accessible (and indeed reached with probability 1).

The model

For this talk take $\kappa_i = 1$ and $f(x) = x$, so that our Markov chain has transitions

$$\begin{aligned}(\ldots, 0, \ldots) &\to (\ldots, 1, \ldots) \quad \text{at rate} \quad \lambda_i \bar{X}^{(n)} \\ (\ldots, 1, \ldots) &\to (\ldots, 0, \ldots) \quad \text{at rate} \quad \mu_i,\end{aligned}$$

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Position i $(i = 1, \ldots, n)$

where $\bar{X}^{(n)} = \frac{1}{n} \sum_{j=1}^{n} X_j^{(n)}$ (the *proportion* of the population that is infected).

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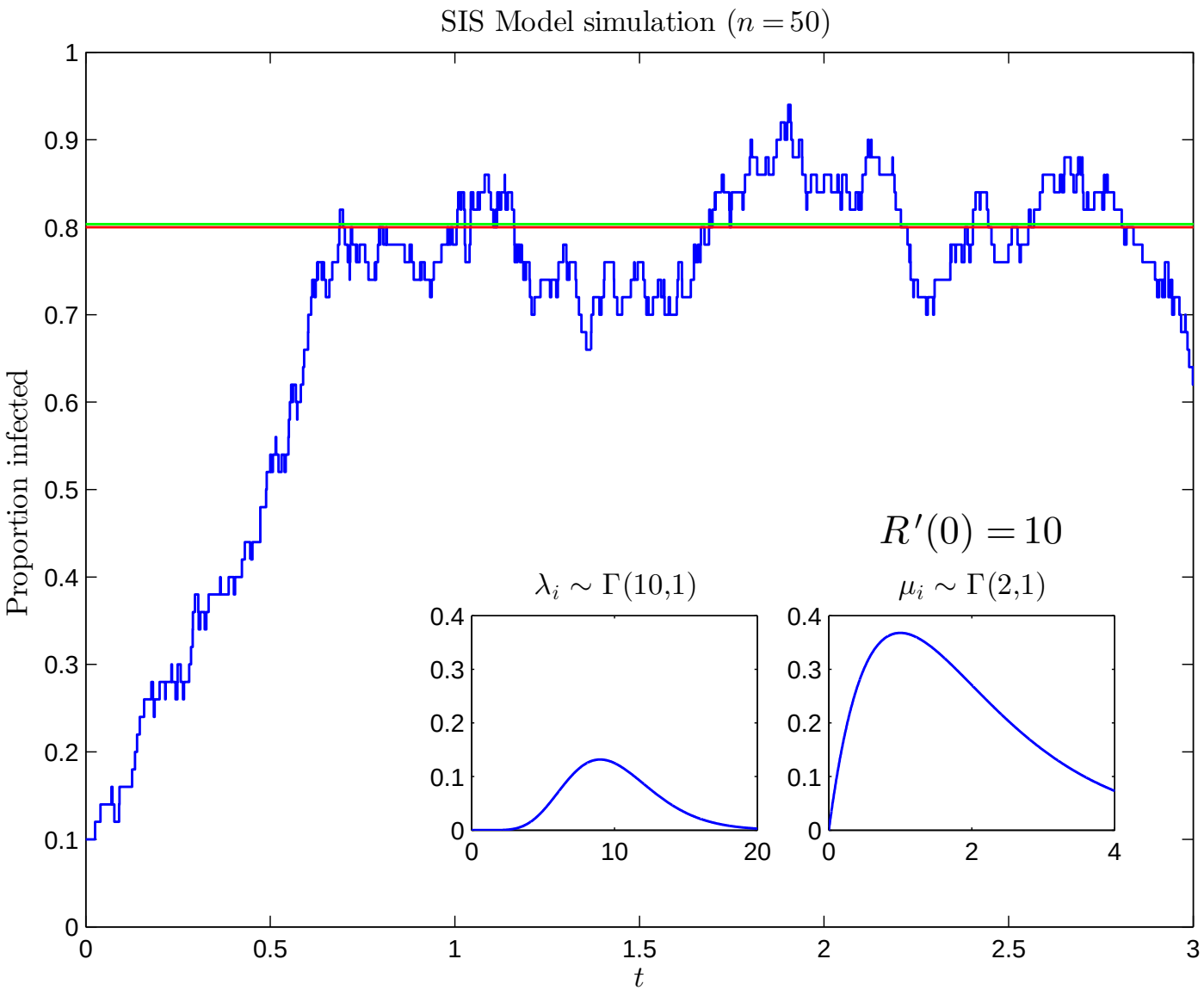
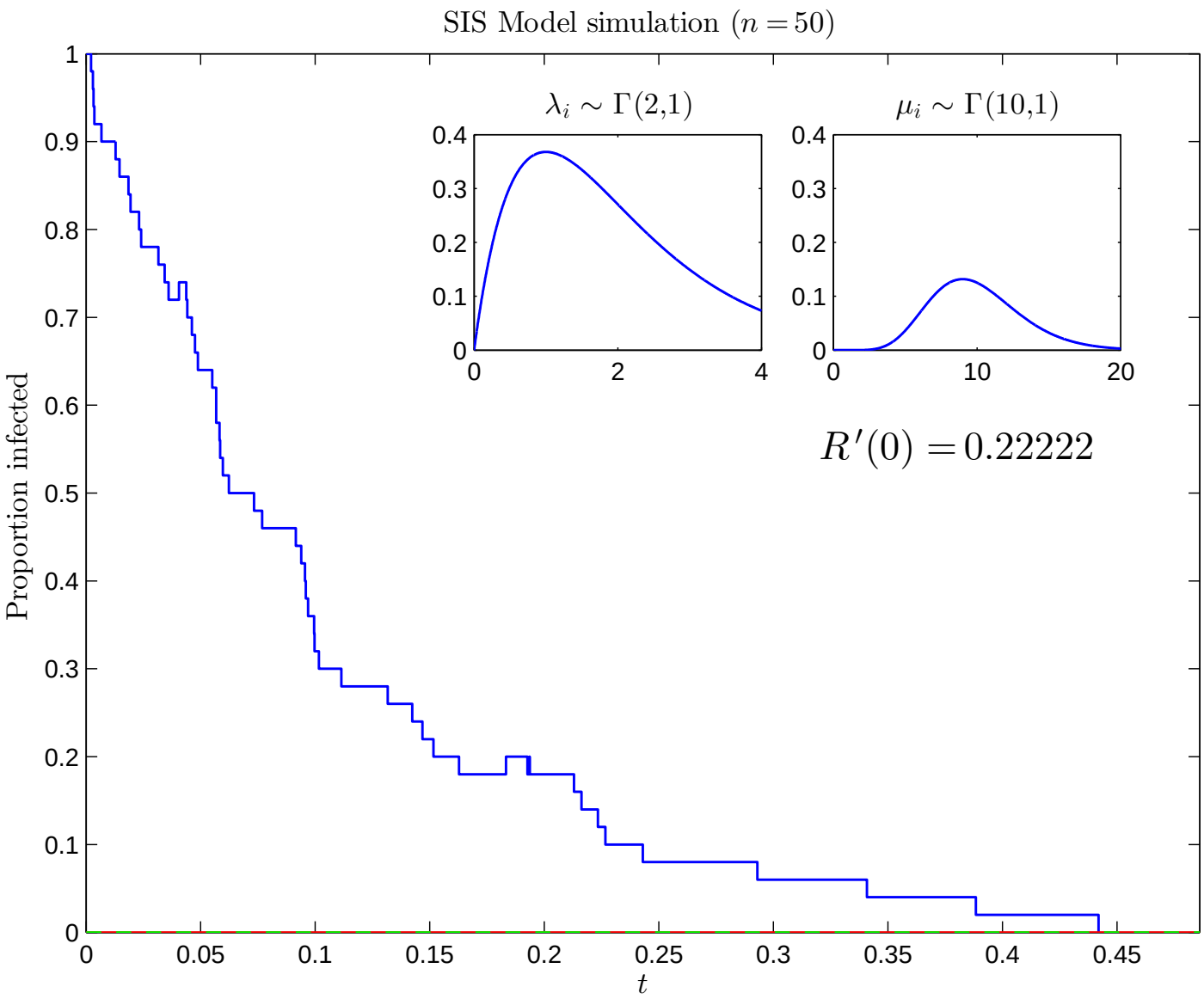
The plan: to get a handle on large n behaviour, and, then, to determine conditions for endemicity.

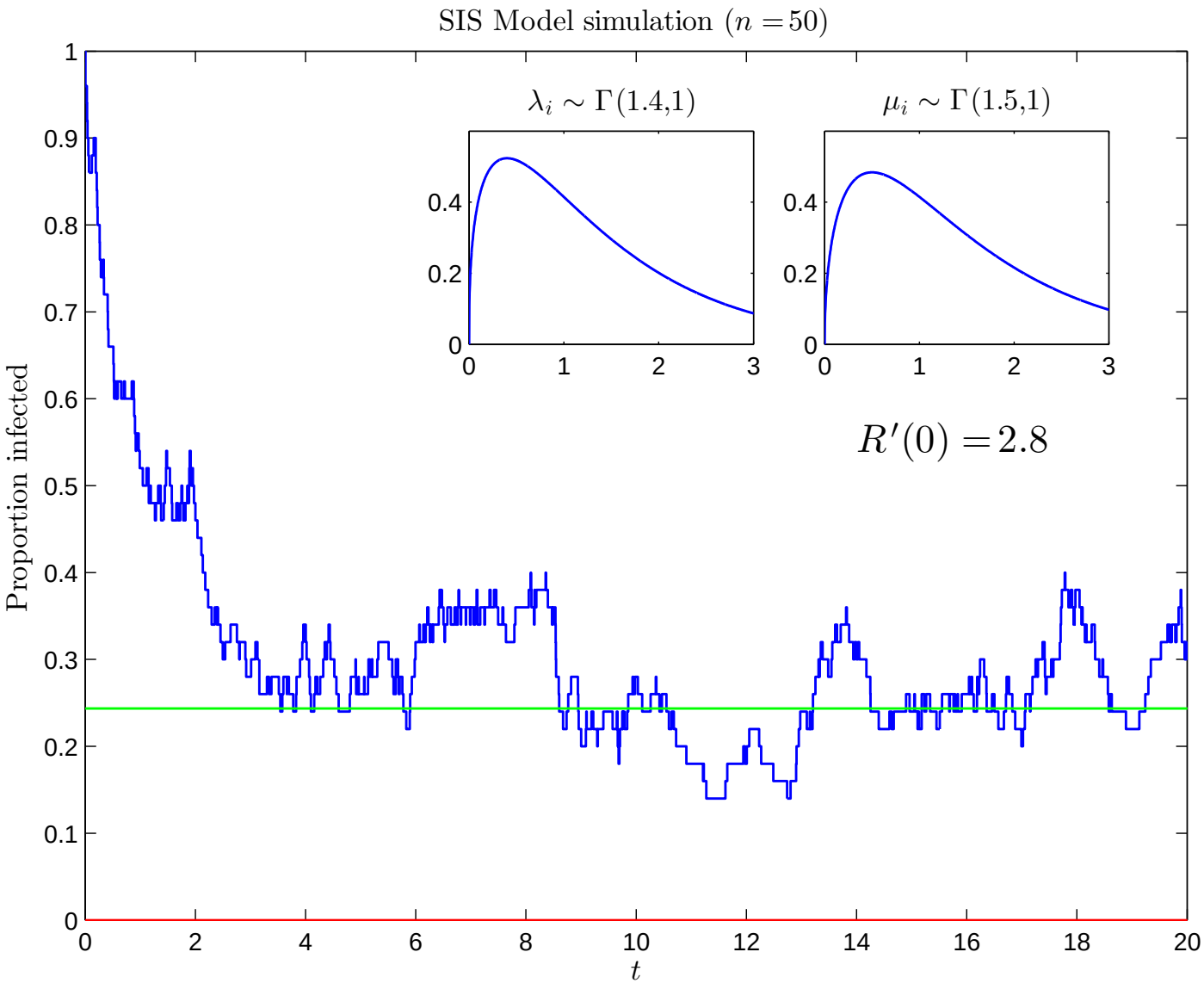
Endemicity (persistence of the epidemic)



Disease free state is globally stable



Endemicity!


SIS Model simulation $(n = 50)$
$\lambda_i \sim \Gamma(1.4,1)$
$\mu_i \sim \Gamma(1.5,1)$
$R'(0) = 2.8$
Proportion infected
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Our approach - Point processes

Think of the individual characteristics $\theta_i := (\lambda_i, \mu_i)$ as (random) points in some subset S of $\mathbb{R}^2_+$.

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Define sequences of random measures $(\sigma^{(n)})$ and random-measure-valued processes $(m_t^{(n)},\ t \geq 0)$ by

$$\sigma^{(n)}(B) = \#\{\theta_i \in B\}/n, \qquad B \in \mathcal{B}(S),$$

$$m_t^{(n)}(B) = \#\{\theta_i \in B : X_{i,t}^{(n)} = 1\}/n, \qquad B \in \mathcal{B}(S).$$

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We are going to suppose that $\sigma^{(n)} \xrightarrow{d} \sigma$ for some non-random (probability) measure σ.

Our approach - Point processes

Equivalently, we may define $(\sigma^{(n)})$ and $(m_t^{(n)})$ by

$$\int h(\theta)\sigma^{(n)}(d\theta) = \frac{1}{n}\sum_{i=1}^{n} h(\theta_i)$$

$$\int h(\theta)m_t^{(n)}(d\theta) = \frac{1}{n}\sum_{i=1}^{n} X_{i,t}^{(n)}\ h(\theta_i),$$

for h in $C_b(S)$, the class of bounded continuous functions that map S to $\mathbb{R}$. (Here $\theta = (\lambda, \mu)$.)

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For example ($h \equiv 1$),

$$m_t^{(n)}(S) = \int m_t^{(n)}(d\theta) = \frac{1}{n}\sum_{i=1}^{n} X_{i,t}^{(n)} \quad \text{(proportion infected)}.$$

A measure-valued limiting process

Theorem

Suppose that $\sigma^{(n)} \xrightarrow{d} \sigma$ *and* $m_0^{(n)} \xrightarrow{d} m_0$ *for some non-random measures* σ *and* m_0. *Then, the sequence of measure-valued processes* $(m_t^{(n)},\ t \geq 0)$ *converges weakly to the unique solution* $(m_t,\ t \geq 0)$ *of*

$$(h, m_t) = (h, m_0) + \int_0^t L(h, m_s)\, ds, \quad h \in C_b(S),$$

where (notation) $(h, m) = \int h(\theta) m(d\theta)$, *and*

$$L(h, m_t) := m_t(S) \left(\int \lambda h(\theta) \sigma(d\theta) - \int \lambda h(\theta) m_t(d\theta) \right) - \int \mu h(\theta) m_t(d\theta).$$

The limiting process

Lemma

For all $B \in \mathcal{B}(S)$ and $t \geq 0$, $m_t(B) \leq \sigma(B)$.

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In particular $m_t << \sigma$, and so m_t has a (uniquely determined σ-a.e.) Radon-Nikodym derivative ϕ_t (≥ 0) with respect to σ: $m_t(B) = \int_B \phi_t(\theta)\sigma(d\theta)$.

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Now, "differentiate" both sides of

$$(h, m_t) = (h, m_0) + \int_0^t L(h, m_s)\, ds,$$

with respect to σ. We get ....

The limiting process

Corollary

The Radon-Nikodym derivative $\phi_t(\lambda, \mu)$ satisfies

$$\phi_t = \phi_0 + \int_0^t \left(\lambda(1 - \phi_s) \int \phi_s(\theta')\sigma(d\theta') - \mu\phi_s \right) ds.$$

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Any equilibrium point ϕ_{eq} must satisfy

$$0 = \lambda(1 - \phi_{\text{eq}}) \int \phi_{\text{eq}}(\theta')\sigma(d\theta') - \mu\phi_{\text{eq}}.$$

Equilibria of the limiting process

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On setting $\psi = \int \phi_{\mathrm{eq}}(\theta)\sigma(d\theta)$, we see that

$$\phi_{\mathrm{eq}}(\lambda, \mu) \; (= \phi_{\mathrm{eq}}(\theta) \;) = \frac{\lambda\psi}{\lambda\psi + \mu},$$

and so, on integrating this over $(\lambda, \mu) \in S$, we find that ψ must solve the equation

$$\psi = R(\psi) := \iint \frac{\lambda\psi}{\lambda\psi + \mu} \sigma(d\lambda, d\mu).$$

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Our stability criteria are expressed in terms of

$$R'(0) = \iint \frac{\lambda}{\mu} \sigma(d\lambda, d\mu) = \mathbb{E}(\lambda_i/\mu_i).$$

Stability

Theorem

(a) If $R'(0) \leq 1$, *then* $\psi = 0$ *is the only fixed point of* R, *and* $\phi_{\mathrm{eq}} = 0$ *is globally stable, that is, for all* ϕ_0, $\phi_t \to 0$ *on* S. *The latter entails* $m_t(B) \to 0$, *for all* $B \in \mathcal{B}(S)$, *and hence the disease free state is globally stable.*

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(b) If $R'(0) > 1$, *then* R *has two fixed points,* 0 *and a positive fixed point* ψ_*, *and (subject to mild extra conditions), if* $(m_0(S) =)\ (\phi_0, \sigma) > 0$, *then*

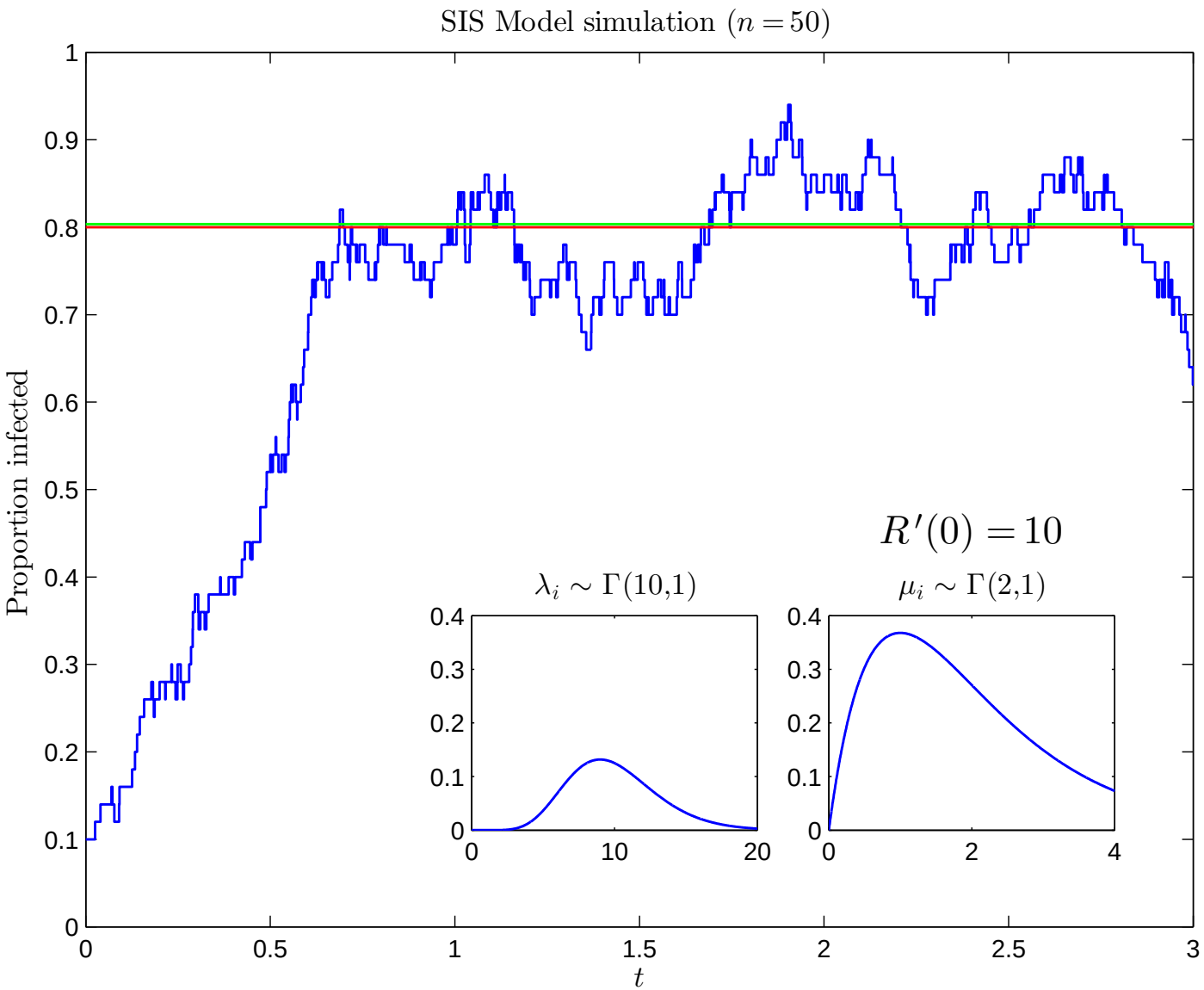
$$\phi_t \to \phi_* := \frac{\lambda\psi_*}{\lambda\psi_* + \mu}.$$

The latter entails $m_t(B) \to m_*(B)$, *for all* $B \in \mathcal{B}(S)$, *where*

$$m_*(B) = \int_B \phi_*(\theta)\sigma(d\theta) = \iint_B \frac{\lambda\psi_*}{\lambda\psi_* + \mu}\sigma(d\lambda, d\mu),$$

implying endemicity.

Endemicity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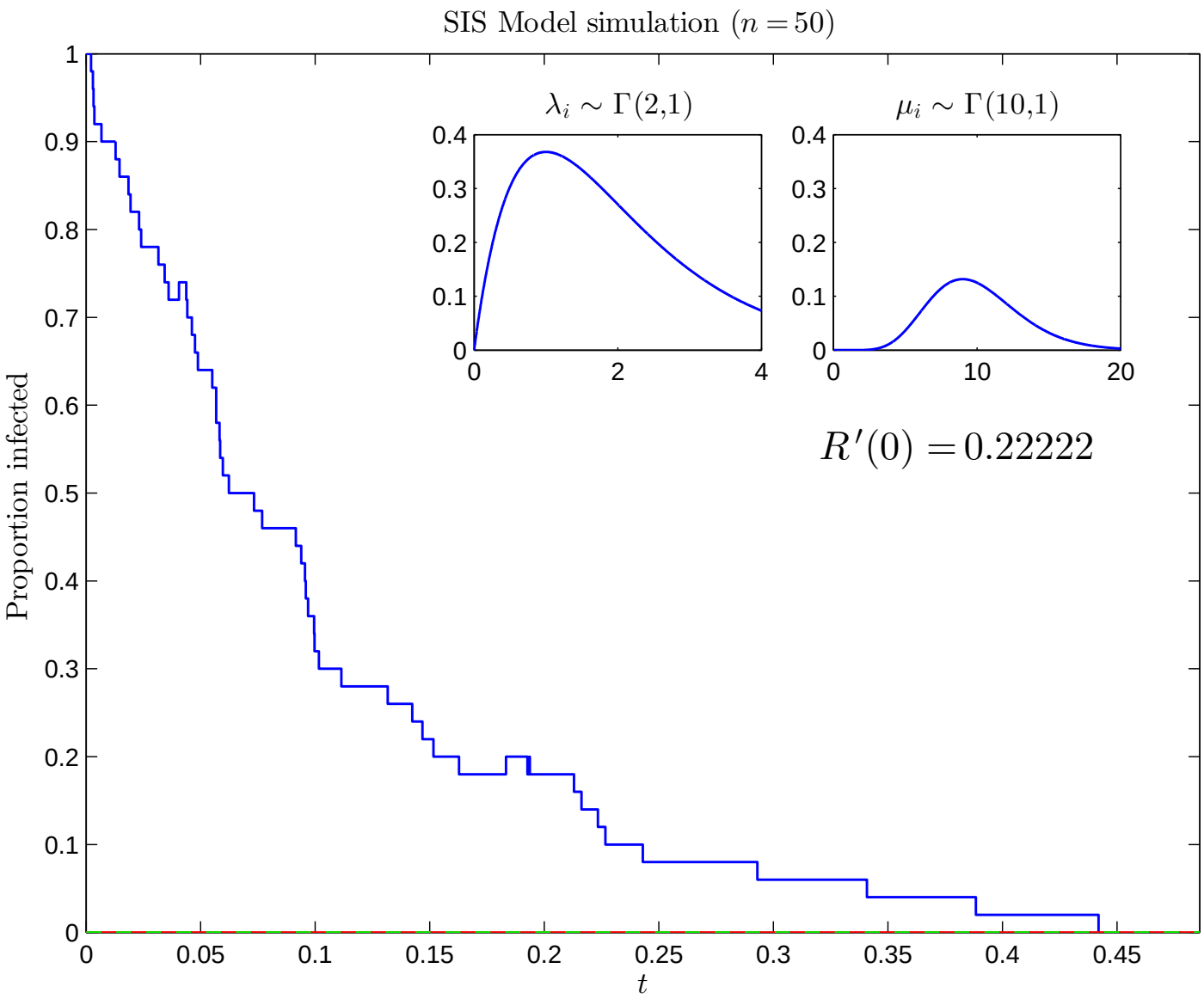

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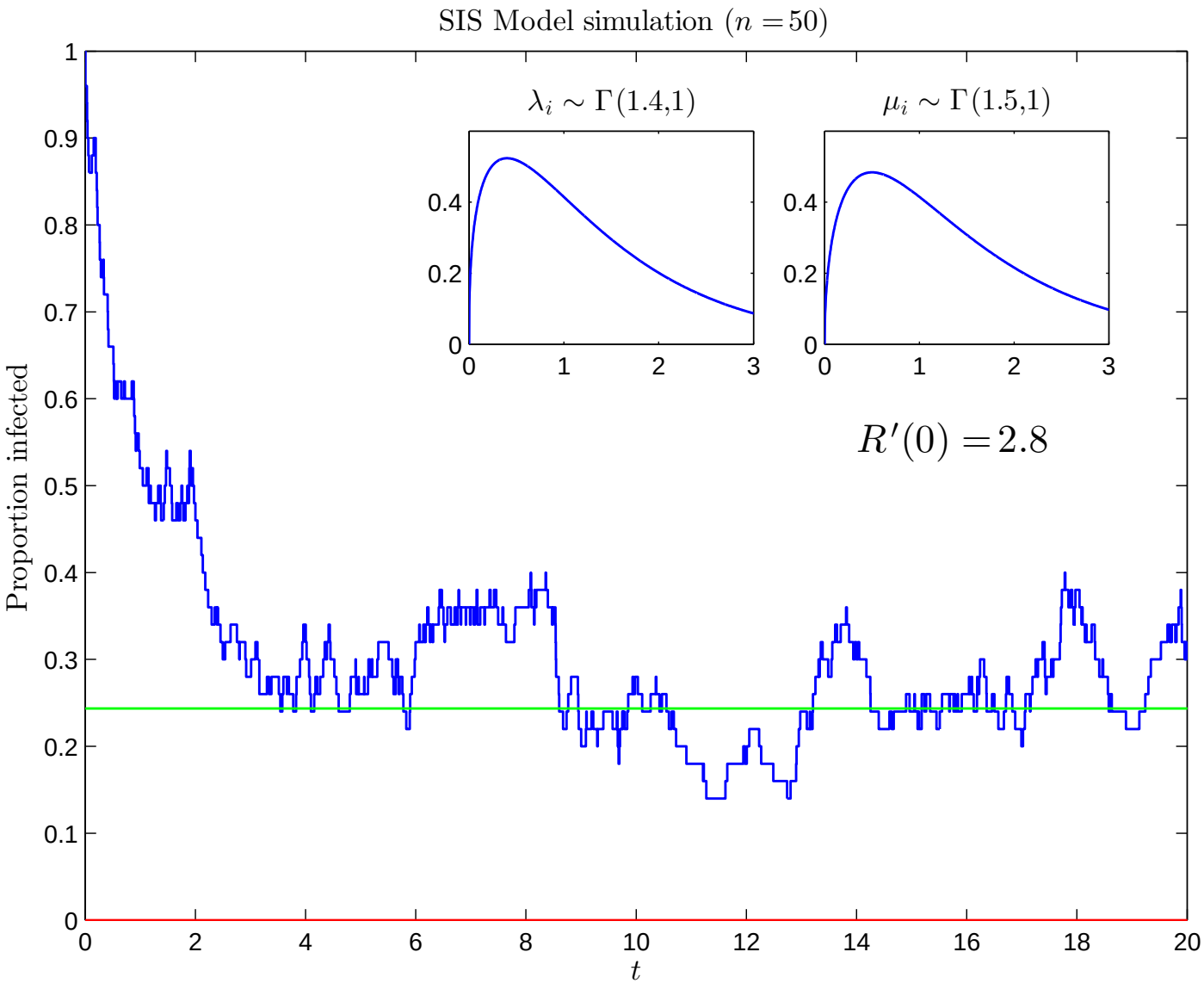
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