On the Spread of Epidemics in a Closed Heterogeneous Population

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Susceptible–Infected–Removed Model:

The population is divided into three groups:

$$S \longrightarrow I \longrightarrow R$$

The SIR ODE model (Kermack & McKendrick, 1927):

$$\begin{aligned}
&\dot{S}(t) = -\beta S(t) I(t), \\
&\dot{I}(t) = \beta S(t) I(t) - \gamma I(t), \\
&\dot{R}(t) = \gamma I(t), \qquad \text{(SIR model)} \\
&S(t) + I(t) + R(t) = N, \\
&S(0) = S_0,\ I(0) = I_0,\ R(0) = 0,\ S_0 + I_0 = N.
\end{aligned}$$

Ref: Kermack & McKendrick, 1927

Analysis of the SIR Model:

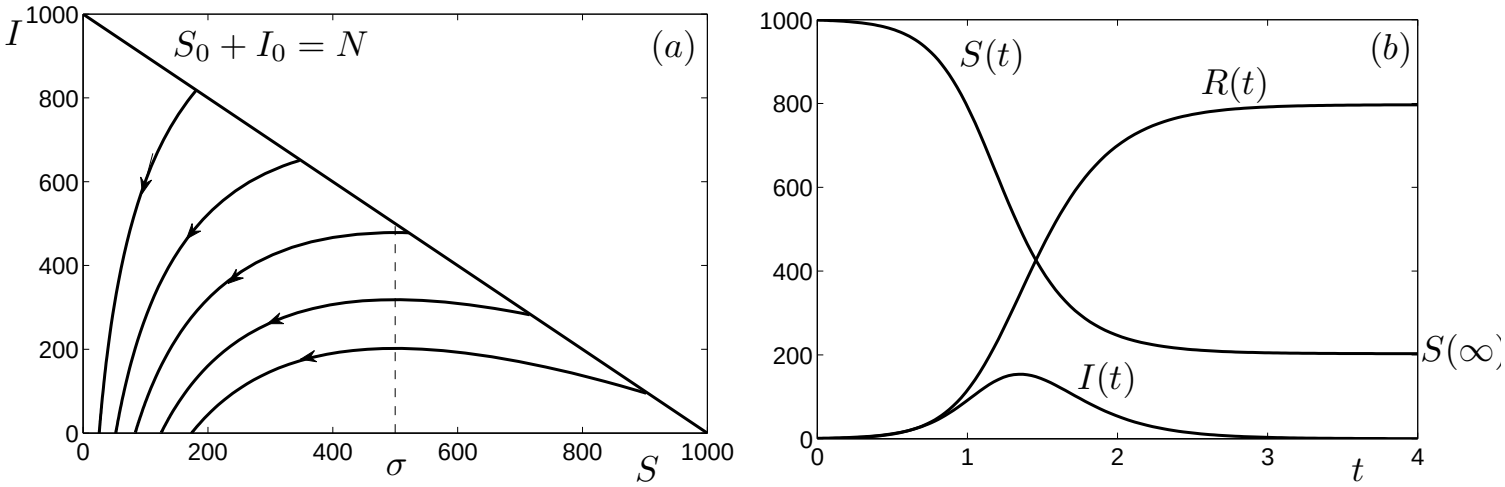


Figure: (a) The phase plane of the SIR model; (b) The integral curves

Theorem

Let the spread of an infectious disease in a closed population be described by the SIR model. Then epidemic occurs if and only if the basic reproductive number $\mathcal{R}_0 = N\beta/\gamma > 1$. *If epidemic occurs then the proportion of the susceptibles who escaped the infection* $(z = S(\infty)/N)$ *can be found as the only root of the equation*

$$z = \exp\{-\mathcal{R}_0(1-z)\}, \quad 0 < z < 1.$$

Assumptions Behind the SIR Model:

- A single infection triggers an autonomous process;
- The disease results in either complete immunity or death;
- Contacts are made according to the law of mass action;
- Individuals are infected for an exponentially distributed period of time;
- **All individuals are equally susceptible;**
- The population is closed;
- The population size is large enough to apply deterministic description.

Heterogeneous SIR Model:

$$\dot{S} = -\beta SI, \quad \dot{I} = \beta SI - \gamma I.$$

Here

$$\beta = ([\text{contact rate}] \times \mathbb{P}[\text{successful contact}])/N.$$

Let us assume that $\mathbb{P}[\text{successful contact}]$ takes only two values:

$$\begin{aligned} \dot{S}_1 &= -\beta_1 S_1 I, \\ \dot{S}_2 &= -\beta_2 S_2 I, \\ \dot{I} &= \beta_1 S_1 I + \beta_2 S_2 I - \gamma I. \end{aligned}$$

Here $S(t) = S_1(t) + S_2(t)$.

Ref: Gart, J.J.: Biometrics, 24:557–566, 1968

Heterogeneous SIR Model:

Discrete version:

$$\dot{S}_i = -\beta_i S_i I, \quad i = 1, \ldots, n,$$
$$\dot{I} = I \sum_{i=1}^{n} \beta_i S_i - \gamma I, \quad S(t) = \sum_{i=1}^{n} S_i.$$

Ref: Ball, F.: Adv Appl Prob, 17:1–22, 1985

Continuous version:

$$\frac{\partial}{\partial t} s(t,\omega) = -\beta(\omega) s(t,\omega) I(t),$$
$$\frac{d}{dt} I(t) = I(t) \int_{\Omega} \beta(\omega) s(t,\omega)\, d\omega - \gamma I(t),$$
$$s(0,\omega) = s_0(\omega),\ I(0) = I_0,\ S(t) = \int_{\Omega} s(t,\omega)\, d\omega.$$

Ref: Novozhilov, A: Math Biosc, 215:177–185, 2008

SI Model with Distributed Susceptibility and Infectivity:

Continuous version:

$$\begin{aligned}
\frac{\partial}{\partial t}s(t,\omega_1) &= -\beta_1(\omega_1)s(t,\omega_1)\int_{\Omega_2}\beta_2(\omega_2)i(t,\omega_2)\,d\omega_2 \\
&= -\beta_1(\omega_1)s(t,\omega_1)\mathsf{E}_t[\beta_2]I(t), \\
\frac{\partial}{\partial t}i(t,\omega_2) &= \beta_2(\omega_2)i(t,\omega_2)\int_{\Omega_1}\beta_1(\omega_1)s(t,\omega_1)\,d\omega_1 \\
&= \beta_2(\omega_2)i(t,\omega_2)\mathsf{E}_t[\beta_1]S(t), \\
\mathsf{E}_t[\beta_1] &= \int_{\Omega_1}\beta(\omega)p_s(t,\omega_1)\,d\omega_1 = \int_{\Omega_1}\beta(\omega_1)\frac{s(t,\omega_1)}{S(t)}\,d\omega_1, \\
\mathsf{E}_t[\beta_2] &= \int_{\Omega_2}\beta(\omega)p_i(t,\omega_2)\,d\omega_2 = \int_{\Omega_2}\beta(\omega_2)\frac{i(t,\omega_2)}{I(t)}\,d\omega_2, \\
s(0,\omega_1) &= S_0p_s(0,\omega_1),\ i(0,\omega_2) = I_0p_i(0,\omega_2).
\end{aligned}$$

General Theory of Heterogeneous Populations:

$$\frac{\partial}{\partial t}\, l(t,\omega) = l(t,\omega)F(t,\omega), \quad l(t,\omega) \geq 0,$$

$$F(t,\omega) = \sum\nolimits_{i=1}^{m_1} u_i(t,G_i)\varphi_i(\omega) + \sum\nolimits_{j=1}^{m_2} v_j(t,H_j)\psi_j(\omega),$$

$$G_i(t) = \int_\Omega g_i(\omega) l(t,\omega)\, d\omega = N(t)\mathsf{E}_t[g_i], \quad i = 1,\ldots,m_1,$$

$$H_j(t) = \int_\Omega h_j(\omega) p(t,\omega)\, d\omega = \mathsf{E}_t[h_i], \quad j = 1,\ldots,m_2.$$

Ref: Karev G.P.: J Math Biol, 60:107–129, 2010

Equivalent ODE System:

For the SIR model with distributed susceptibility

$$\dot{S}(t) = -\mathsf{E}_t[\beta]S(t)I(t), \qquad \mathsf{E}_t[\beta] = \int_\Omega \beta(\omega)p(t,\omega)\,d\omega,$$

$$\dot{I}(t) = \mathsf{E}_t[\beta]S(t)I(t) - \gamma I(t), \qquad p(t,\omega) = \frac{s(t,\omega)}{S(t)},$$

$$s(0,\omega) = S_0 p(0,\omega),\ I(0) = I_0,\ S(t) = \int_\Omega s(t,\omega)\,d\omega,$$

$$\mathsf{E}_t[\beta] = \frac{d}{d\lambda}\log \mathsf{M}_0[\lambda]\Big|_{\lambda=q(t)},$$

$$\dot{q}(t) = -I(t), \quad q(0) = 0,$$

$$\mathsf{M}_0[\lambda] = \int_\Omega \exp\{\lambda\beta(\omega)\}p(0,\omega)\,d\omega.$$

Homogeneous Model with Nonlinear Transmission Function:

Theorem

The heterogeneous SIR model with distributed susceptibility can be reduced to the homogeneous SIR model with a nonlinear transmission function in the form

$$\dot{S} = -h(S)I,$$
$$\dot{I} = h(S)I - \gamma I,$$
$$S(0) = S_0,\ I(0) = I_0,$$

where

$$h(S) = S_0 \left[\left. \frac{d\mathsf{M}_0^{-1}[\xi]}{d\xi} \right|_{\xi = S/S_0} \right]^{-1}.$$

Power Transmission Function:

Power transmission function:

$$T(S, I) = \beta S^p I^q.$$

Ref: McCallum, H., Barlow, N. & Hone, J.: Tr Ecol Evol, 16(6):295300, 2001.

Corollary

The power transmission function $T(S, I) = \beta S^p I^q$ *with* $q = 1$, $p = 1 + 1/k$ *in the homogeneous SIR model can be deduced from the mechanistic formulation of the SIR model with distributed susceptibility when the initial distribution is a gamma-distribution with the shape parameters* k.

Ref: Novozhilov, A.: Dyn Con Dis Impul Sys, 2009, 16:136–140.

Nonlinear Transmission Functions:

Heterogeneous SI model:

$$\frac{\partial}{\partial t} s(t,\omega_1) = -\omega_1 s(t,\omega_1) \int_{\Omega_2} \omega_2 i(t,\omega_2)\, d\omega_2,$$
$$\frac{\partial}{\partial t} i(t,\omega_2) = \omega_2 i(t,\omega_2) \int_{\Omega_1} \omega_1 s(t,\omega_1)\, d\omega_1,$$
$$s(0,\omega_1) = S_0 p_s(0,\omega_1),\ i(0,\omega_2) = I_0 p_i(0,\omega_2).$$

Corollary

The power transmission function $T(S,I) = \beta S^p I^q$ *with* $q = 1 + 1/k_2$, $p = 1 + 1/k_1$ *in the homogeneous SIR model can be deduced from the mechanistic formulation of the SIR model with distributed susceptibility and infectivity when the initial distributions are gamma-distributions with parameters* k_1, ν_1 *and* k_2, ν_2 *respectively.*

Ref: Novozhilov, A.: Dyn Con Dis Impul Sys, 2009, 16:136–140.

The Final Size of an Epidemic:

Theorem

Let $\hat{z} = S(\infty)/N$ be the proportion of the population that escapes infection in the population provided $I_0/N \to 0$. Then for the SIR model with distributed susceptibility, $\hat{z}$ can be found as the only solution of the equation

$$z = \mathsf{M}_0[-N(1-z)/\gamma],$$

satisfying the condition $0 < \hat{z} < 1$. This solution exists if and only if $\mathcal{R}_0 = \mathsf{E}_0[\beta]N\gamma^{-1} > 1$.

Remark: If $p(0,\omega) = \delta(\omega - \bar{\omega})$, $\beta(\bar{\omega}) = \text{const}$ then we obtain the well-known formula

$$z = \exp\{-\mathcal{R}_0(1-z)\}.$$

Ref: Ball, F.: Adv Appl Prob, 17:1–22, 1985

Ref: Novozhilov, A: Math Biosc, 215:177–185, 2008

The Final Size of an Epidemic. Examples:

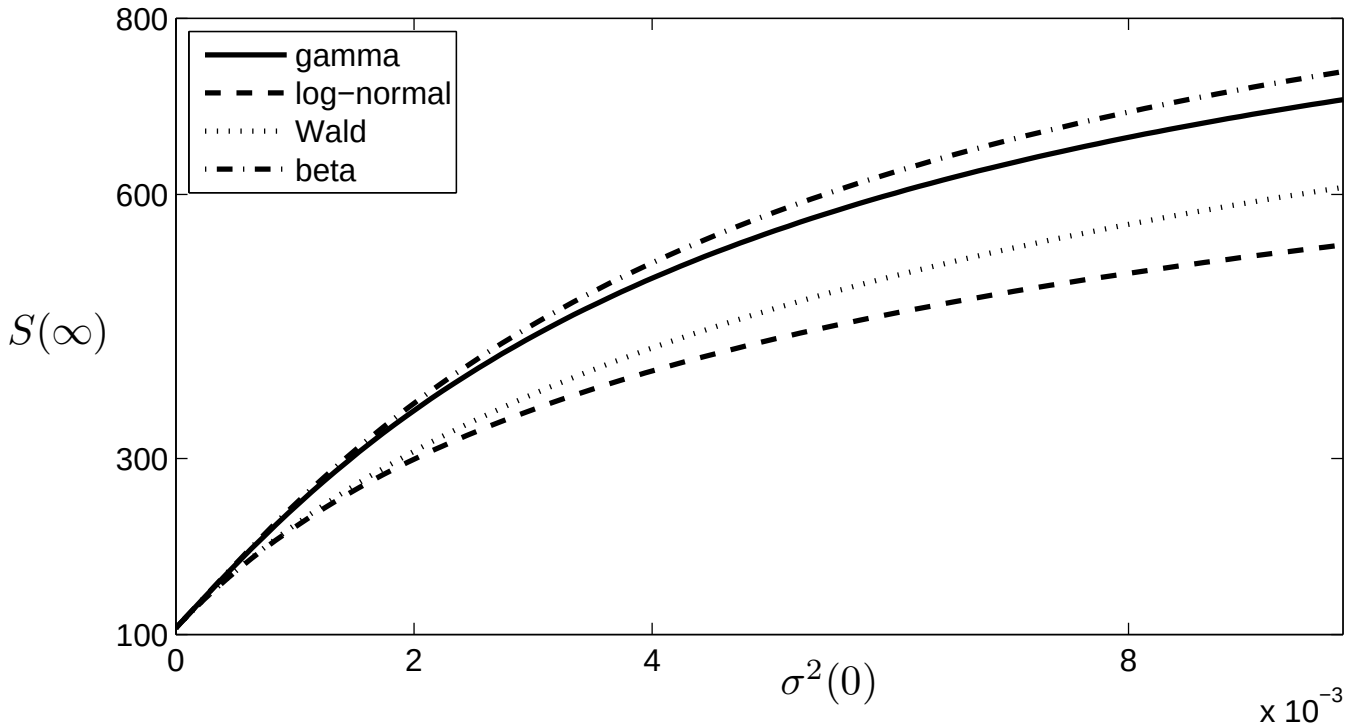


Figure: The size of the susceptible population that never gets infected versus the initial variance of the parameter distributions. The initial means are the same in all four cases. The parameters are
$S(0) = 999, I(0) = 1, \gamma = 20, \mathsf{E}_0[\beta] = 0.05, \mathcal{R}_0 = 2.5$

The Final Size of an Epidemic:

Theorem

Let

$$\tilde{\mathsf{M}}_0\left(\frac{\tilde{\mathcal{R}}_0}{\mathsf{E}_0[\beta]}(1-z)\right) \leq \mathsf{M}_0\left(\frac{\mathcal{R}_0}{\mathsf{E}_0[\beta]}(1-z)\right)$$

for any $z \in (0,1)$. *Then*

$$\hat{\tilde{z}} \leq \hat{z}.$$

Theorem

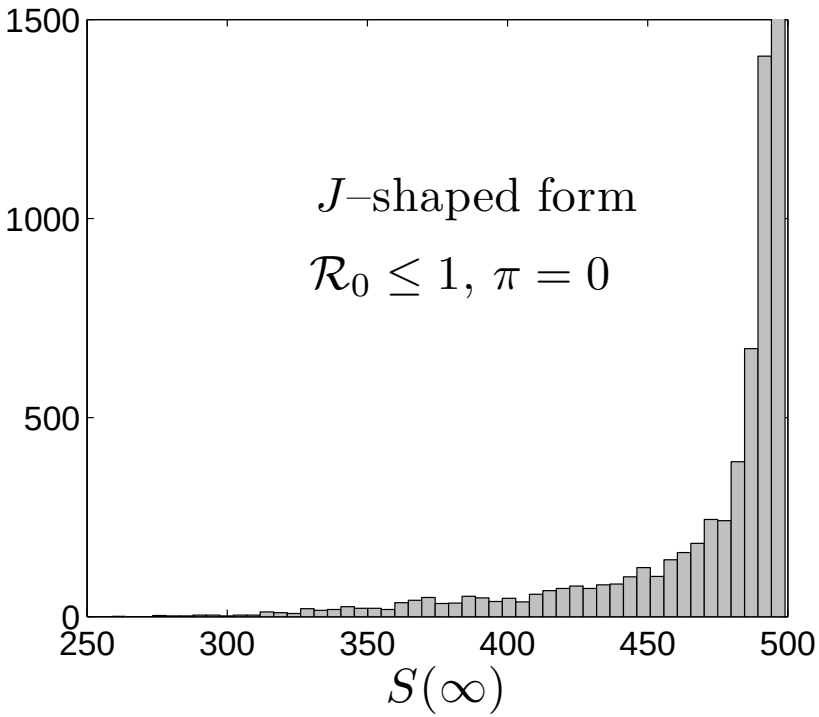
For any distribution of susceptibility, the final epidemic size satisfies

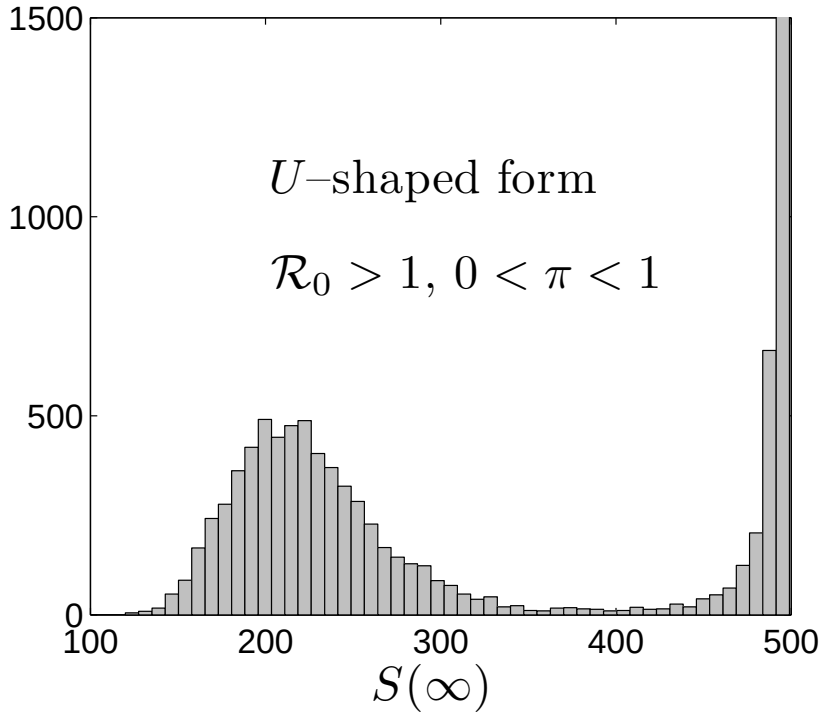
$$\frac{1}{1+cv^2}(1-z^*) \leq 1-\hat{z} \leq 1-z^*,$$

where z^* *is the solution to* $z = \exp\{-\mathcal{R}_0(1-z)\}$ *belonging to* $(0,1)$.

Ref: Catriel, G.: J. Math Biol, in press

Stochastic SIR Model:





Instead of two important quantities $\mathcal{R}_0$ (the basic reproductive number) and z (the final epidemic size) in the stochastic settings we have $\mathcal{R}_0$, π (the probability of disease invasion) and a random variable $z = S(\infty)/N$.

Stochastic vs Deterministic Epidemic Models:

Deterministic model:

1. The basic reproductive number $\mathcal{R}_0$ (the threshold parameter: if $\mathcal{R}_0 \leq 1$ then there is no epidemic)
2. The final size of an epidemic $S(\infty)$ (fixed number)

Stochastic model:

1. The basic reproductive number $\mathcal{R}_0$ (the threshold parameter: if $\mathcal{R}_0 > 1$ then there is a possibility of a major outbreak)
2. The final size of an epidemic $S(\infty)$ (random variable, which, if conditioned on the major outbreak, has an approximately normal distribution), $z = S(\infty)/N$
3. The probability of a major outbreak π ($\pi > 0$ iff $\mathcal{R}_0 > 1$)
4. The duration of an epidemic T (random variable)

Stochastic SIR model (Analytical Results):

Let $E_{n,m}$ be an epidemic process with n initial susceptible and m infective individuals. Let Z_n be the total number of infected individuals. Then

$$Z_n \xrightarrow{D} Z,$$

if $\mathcal{R}_0 \leq 1$, $\mathbb{P}[Z < \infty] = 1$, if $\mathcal{R}_0 > 1$, $\mathbb{P}[Z < \infty] = 1 - \pi$.
Moreover, conditional upon the epidemic becoming established

$$n^{-1} Z_n \xrightarrow{D} \tau, \quad n \to \infty,$$

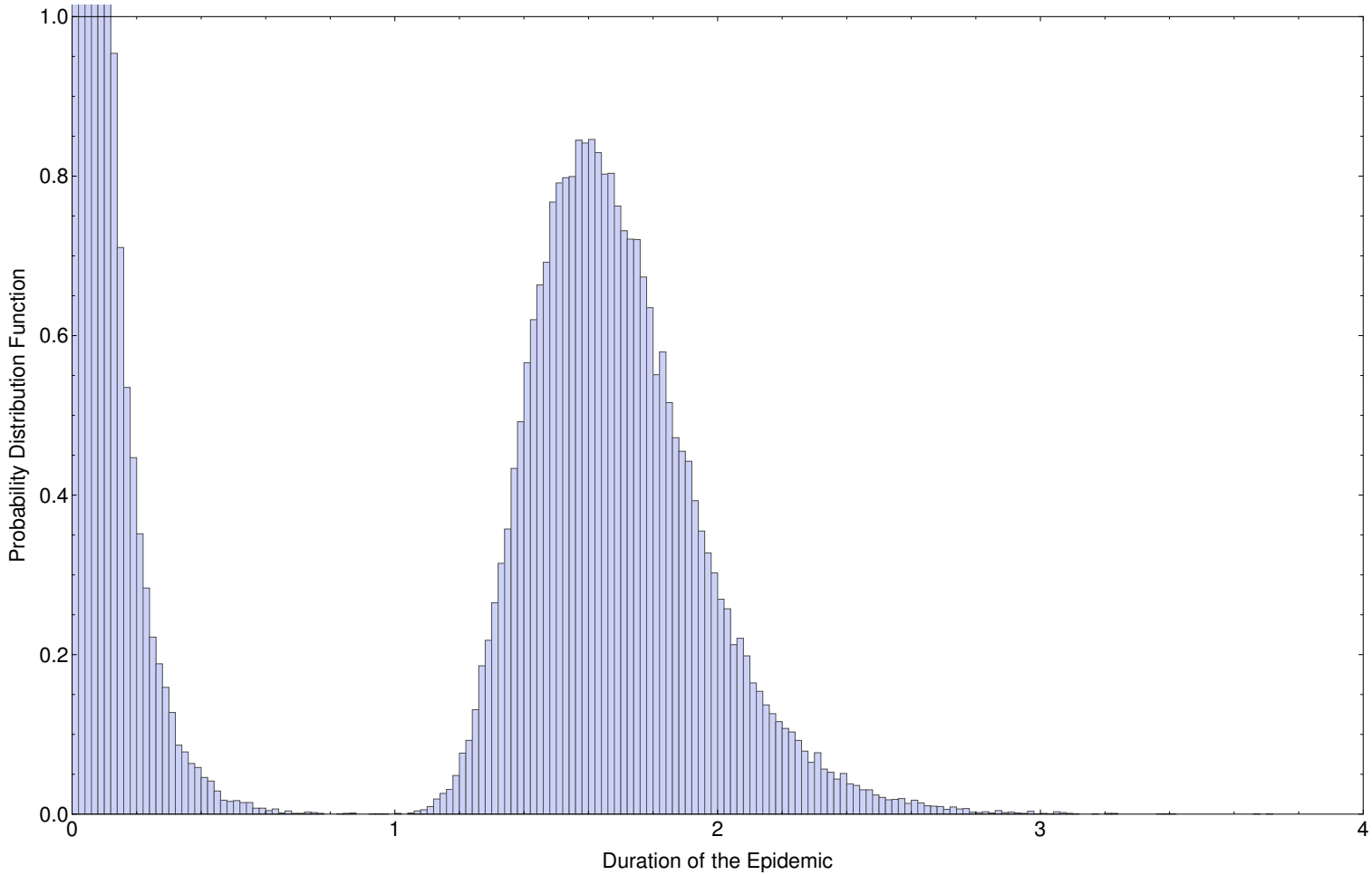
where τ is the root of $1 - \tau = e^{-\mathcal{R}_0 \tau}$, and

$$\frac{1}{\sqrt{n}}(Z_n - n\tau) \xrightarrow{D} \mathcal{N}(0, \sigma^2), \quad n \to \infty.$$

Ref: Ball, F.: Adv Appl Prob, 17:1–22, 1985

Ref: Scalia Tomba, G.: J Appl Prob 23:563–584, 1986

Duration of an Epidemic:



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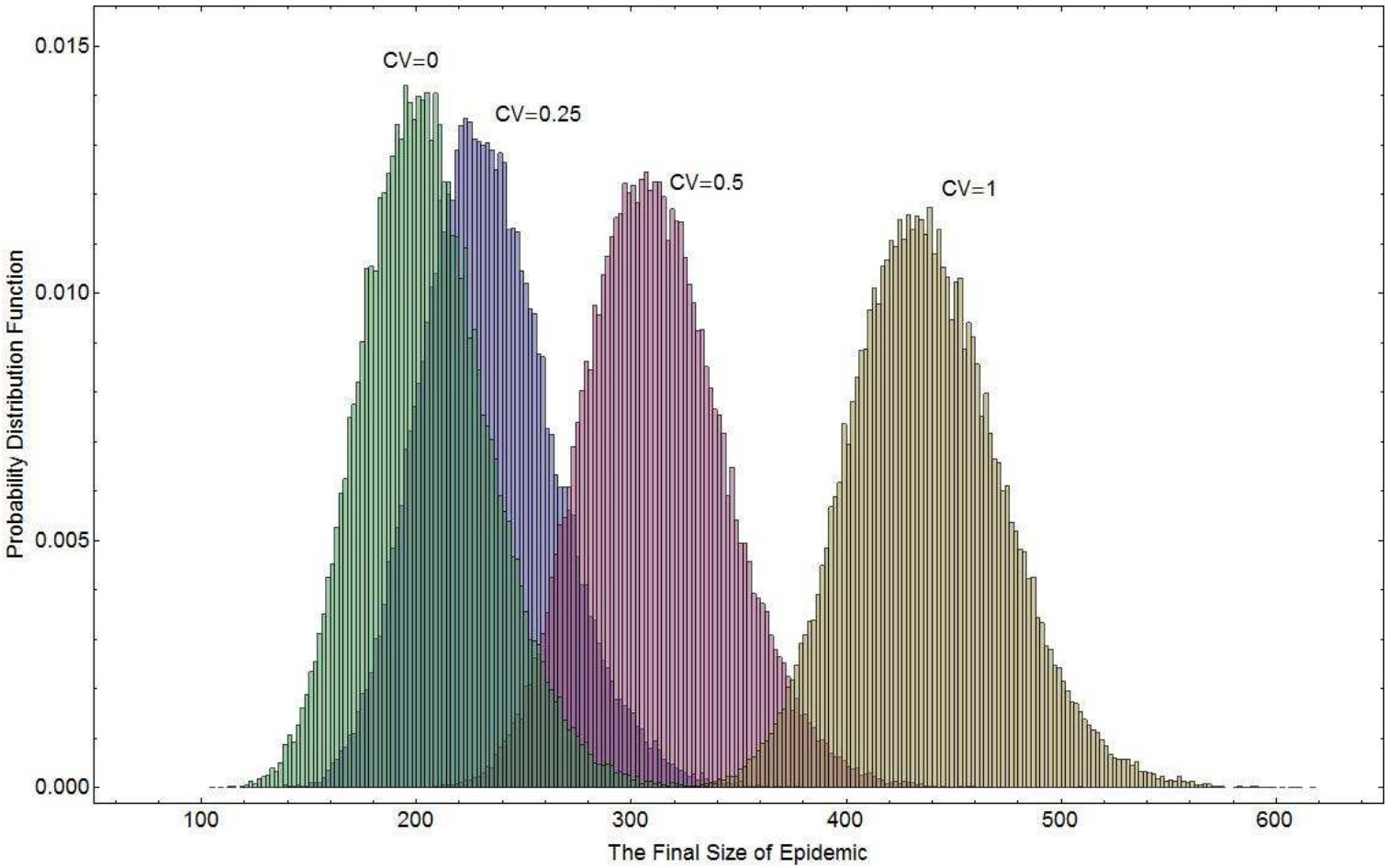
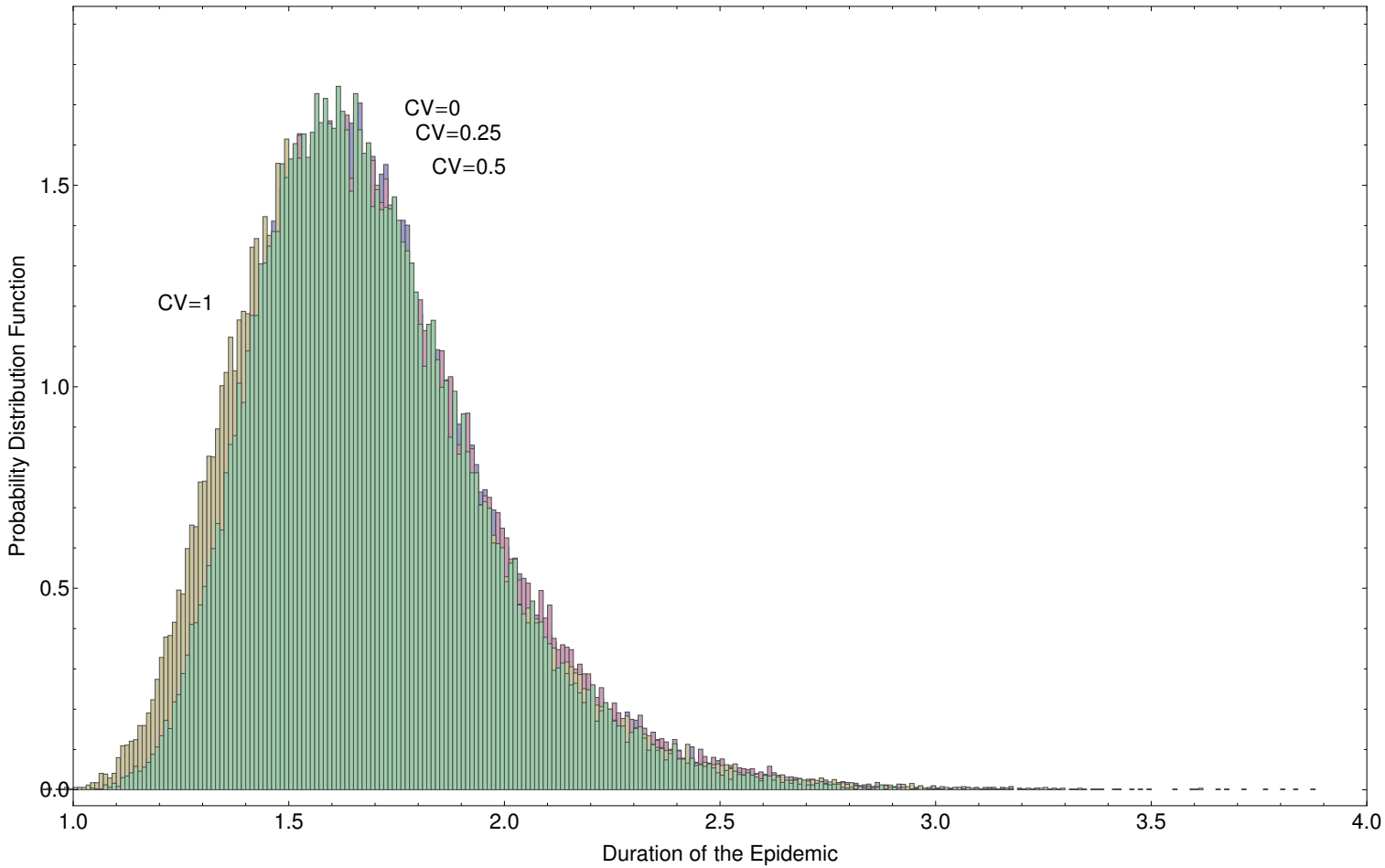


Duration of an Epidemic:



Simulation Results:

	$CV = 0$	$CV = 0.25$	$CV = 0.5$	$CV = 1$
$\mathsf{E}[z]$	0.203	0.232	0.310	0.436
$\widehat{\mathsf{E}[z]}$	0.204	0.233	0.311	0.437
$\widehat{\mathsf{Var}[z]}$	0.029	0.032	0.033	0.035
$\widehat{\mathsf{E}[T]}$	1.69	1.7	1.71	1.69
$\widehat{\mathsf{Var}[T]}$	0.262	0.269	0.278	0.288
$\widehat{\pi}$	0.5	0.498	0.497	0.514

Conclusions:

- There is a general technique applicable to the study of epidemics with distributed heterogeneity
- Using the theory of heterogeneous populations we obtain a simple equation for the final size of an SIR epidemic
- It can be shown that some heterogeneous models imply simple homogeneous models
- The results can be applied to stochastic epidemics conditioned on the occurrence of a major outbreak
- The final epidemic size is very sensitive to the population heterogeneity, whereas the probability of a major outbreak together with the distribution of the duration of the epidemic are not

Bratus, A. S., Novozhilov, A. S., & Platonov, A. P.: *Dynamical Systems and Models in Biology*, Moscow: FizMatLit, 2010, 400 pages.

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Thank you for your attention!

- Questions?

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