Population and disease models

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1 The SIR epidemic

1.1 The SIR model

We begin with a classical epidemic model based on ideas of En'ko (1889), Ross (1911) and Kermack and McKendrick (1927); see Bailey's (1975) book.

We begin with a closed population of $N+1$ individuals, of whom I_0 are originally infected, and the remainder S_0 are susceptble to the disease. Mixing is homogeneous. Let S_t and I_t denote the numbers of susceptibles and infectives at time t. There are two transitions possible at any time:

1. *Infection*: $I \to I+1$, $S \to S-1$, at rate $\alpha I(S/N)$.
2. *Removal*: $I \to I-1$, S unchanged, at rate βI.

The former rate comes from the 'law of mass action' analogy. The number of susceptibles can only decrease.

1.2 Differential equation formulation.

Interpret the rates as average drifts. This gives the equations

$$\frac{dS}{dt} = -\alpha I(S/N); \qquad \frac{dI}{dt} = \alpha I(S/N) - \beta I. \tag{1.1}$$

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Rewriting in terms of normalized variables $s = S/N$, $i = I/N$, this gives

$$\frac{ds}{dt} \;=\; -\alpha i s; \qquad \frac{di}{dt} \;=\; \alpha i s - \beta i. \tag{1.2}$$

Initial condition: $s_0 = S_0/N$, $i_0 = I_0/N$; $s_0 + i_0 = 1 + 1/N$.

Solution curve.

$$\frac{di}{ds} \;=\; -1 + \beta/(\alpha s),$$

integrated to give

$$i + s - (\beta/\alpha)\log s \;=\; \text{constant} \;=\; i_0 + s_0 - (\beta/\alpha)\log s_0,$$

or

$$i - i_0 \;=\; f(s_0) - f(s) \;\approx\; (s - s_0)f'(s_0),$$

for s close to s_0.

Basic reproduction number.

$$R_0 \;:=\; \alpha/\beta,$$

the average number of new infections caused by a single infective in an uninfected population. Note that thus $f(s) = s - (1/R_0)\log s$, so that, if $s_0 = 1$, then, as s gets a little smaller, i becomes smaller that i_0 if $f'(1) < 0$, whereas i becomes larger than i_0 if $f'(1) > 0$. This leads to the following:

Threshold theorem.

If $R_0 < 1$, only a small epidemic occurs. If $R_0 > 1$ there will be a large epidemic.

Final size. If $R_0 > 1$, then the final proportion of susceptibles s_∞ is the smaller positive solution s to the equation

$$i_0 \;=\; f(s) - f(s_0). \tag{1.3}$$

1.3 Stochastic formulation.

Interpret the rates as jump rates of a pure jump Markov process $(S(t), I(t))$ in continuous time. The state space is $\{(S, I) \in \mathbb{Z}_+^2 \colon S + I \le N + 1\}$, hence finite; the process begins with $S(0) = S_0$ and $I(0) = I_0$, and stops when $I(t)$ first reaches zero.

The Kolmogorov forward equations. Defining $\mathbb{P}_0$ to mean $\mathbb{P}_{S_0,I_0}$ and

$$p_{kl}(t) \;:=\; \mathbb{P}_0[(S(t),I(t))=(k,l)], \quad k\geq 0, l\geq 0,$$

we have

$$\frac{dp_{kl}}{dt} \;=\; \beta(l{+}1)p_{k,l+1}{+}\alpha\frac{(k+1)}{N}(l{-}1)p_{k+1,l-1}{-}\left(\alpha\frac{k}{N}l+\beta l\right)p_{kl}, \quad k\geq 0, l\geq 0,$$

if $p_{kl}(t)=0$ for all $l<0$. Multiply the k,l equation by $u^k v^l$ and add: if

$$F(t;u,v) \;:=\; \sum_{k\geq 0}\sum_{l\geq 0} p_{kl}(t)u^k v^l,$$

then we get

$$\frac{\partial F}{\partial t} \;=\; \beta(1-v)\frac{\partial F}{\partial v}+\frac{\alpha}{N}v(v-u)\frac{\partial^2 F}{\partial u\partial v}. \tag{1.4}$$

This yields moment equations, by taking partial derivatives of (1.4) with respect to u and v, and then setting $u=v=1$. For instance, writing

$$\begin{aligned} m_S(t) \;&:=\; \mathbb{E}_0 S(t) \;=\; \frac{\partial F}{\partial u}(t;1,1),\\ m_I(t) \;&:=\; \mathbb{E}_0 I(t) \;=\; \frac{\partial F}{\partial v}(t;1,1), \end{aligned}$$

then the first partial derivatives of (1.4) give

$$\begin{aligned} \frac{dm_S}{dt} \;&=\; -\frac{\alpha}{N}\mathbb{E}_0\{S(t)I(t)\};\\ \frac{dm_I}{dt} \;&=\; -\beta m_I(t)+\frac{\alpha}{N}\mathbb{E}_0\{S(t)I(t)\}. \end{aligned}$$

The deterministic differential equations result from these moment equations by setting

$$\mathbb{E}_0\{S(t)I(t)\} \;=\; \mathbb{E}_0 S(t)\mathbb{E}_0 I(t) \;=\; m_S(t)m_I(t),$$

so that possible correlation is effectively being ignored. This is a simple example of the 'moment closure' heuristic.

1.4 Sellke's model.

Sellke (1983) assumed the following:

1. Each susceptible needs a random cumulative amount of exposure to disease organisms before becoming infected.

2. Each infective exposes each susceptible equally to disease organisms, until removal.

In detail, he supposed:

1. Susceptibles have independent exp(1) distributed infection thresholds, $L_1, L_2, \ldots, L_{S_0}$.

2. Each infective exposes each susceptible to infection at rate α/N, until removal; the infectious periods are independent and exp(β) distributed (i.e. having mean $1/\beta$).

The 'forgetting property' of the exponential distribution leads to the following:
Curious fact: this model generates *exactly the same* stochastic process as the SIR-Markov model above.

Exploiting Sellke's construction.

1. Order the infection thresholds $L_{(1)} < L_{(2)} < \ldots < L_{(S_0)}$.

2. Let the total per capita exposure generated by the I_0 initial infected individuals be $U_0 := (\alpha/\beta N)T_0$ (with T_0 having Gamma distribution $\Gamma(I_0, 1)$).

3. Let the amount of per capita exposure generated by the kth infected individual be $(\alpha/\beta N)T_k$ (the T_k's being independent exp(1) distributed random variables). Write

$$U_k \;:=\; \frac{\alpha}{\beta N}\left\{T_0 + \sum_{j=1}^{k} T_j\right\}.$$

4. The kth smallest infection threshold can be expressed as

$$L_{(k)} \;=\; \sum_{j=1}^{k} \frac{V_j}{S_0 - j + 1},$$

where the V_j are independent exp(1) random variables.

The epidemic stops after exactly k infections have occurred, $0 \le k \le S_0 - 1$, if

$$U_k - L_{(k+1)} \;\le\; 0; \tag{1.5}$$

the total exposure generated by the initial infectives and the k next infected individuals is not enough to infect any of the remaining susceptibles.

This reduces discussion of the final size, and related questions, to a stopping problem for a partial sum process $W_k := \sum_{j=0}^{k} Z_j$, built from independent but not identically distributed random variables

$$Z_0 \;=\; \frac{\alpha T_0}{\beta N} - \frac{V_1}{S_0}; \qquad Z_k \;=\; \frac{\alpha T_k}{\beta N} - \frac{V_{k+1}}{S_0 - k}, \quad 1 \le k < S_0.$$

Note that

$$\mathbb{E}W_k \;=\; \left\{\frac{\alpha I_0}{\beta N} - \frac{1}{S_0}\right\} + \sum_{j=1}^{k} \left\{\frac{\alpha}{\beta N} - \frac{1}{S_0 - j}\right\} \;=:\; \mu(k) \tag{1.6}$$

$$\approx \left\{\frac{\alpha I_0}{\beta N} - \frac{1}{S_0}\right\} + \frac{\alpha k}{\beta N} + \log\left\{\frac{S_0 - k}{S_0}\right\}. \tag{1.7}$$

So $\mathbb{E}W_k = 0$ when, from (1.7) and writing S_∞ for the corresponding value of k, we have

$$\left\{\frac{\alpha I_0}{\beta N} - \frac{1}{N}\right\} + \frac{\alpha}{\beta}\frac{S_0 - S_\infty}{N} + \log\left\{1 - \frac{S_0 - S_\infty}{S_0}\right\} \;\approx\; 0,$$

which, with $s_\infty = S_\infty/N$, gives

$$f(s_\infty) \approx i_0 + f(s_0),$$

in agreement with (1.3).

Sellke's construction: the CLT.

One can use Sellke's method to prove a central limit theorem for the final size $S(\infty)$, when $N \to \infty$, if $S_0 \sim N s_0$ for s_0 *fixed*. Note that the process

$$\{\sqrt{N}(W_{Nu} - \mu(Nu)),\ u \geq 0\}$$

has a Gaussian limit Y as $N \to \infty$, and that Y can be written as

$$Y(u) \ := \ \int_0^u \left\{(\alpha/\beta)^2 + (s_0 - v)^{-2}\right\}^{1/2} \, dB(v),$$

where B is a standard Brownian motion. In particular,

$$\operatorname{Var} Y(u) \ = \ u(\alpha/\beta)^2 + \frac{u}{s_0(s_0 - u)}.$$

Let $N\tau_N$ denote the random time at which W hits zero, so that $S_0 - S(\infty) = N\tau_N$. Then, by Anscombe's theorem,

$$-\sqrt{N}\mu(N\tau_N) \ \to_d \ \mathcal{N}(0, (s_0 - s_\infty)\{R_0^2 + 1/(s_0 s_\infty)\}).$$

Since $N\tau_N = S_0 - S(\infty) = S_0 - S_\infty + (S_\infty - S(\infty))$, where we recall that S_∞ is the fixed value obtained by solving $\mu(S_0 - S_\infty) = 0$, we obtain from (1.7) and by Taylor's expansion that

$$\mu(N\tau_N) \ \sim \ \frac{\alpha}{\beta N}(S_\infty - S(\infty)) - \frac{S_\infty - S(\infty)}{S_\infty};$$

hence it follows that

$$N^{-1/2}(S(\infty) - S_\infty) \ \to_d \ \mathcal{N}(0, \sigma^2),$$

with

$$\sigma^2 \ = \ (s_0 - s_\infty)\{R_0^2 + 1/(s_0 s_\infty)\})/\{R_0 - 1/s_\infty\}^2.$$

The discussion above did not allow for the possibility that, by chance fluctuation, the stochastic process W may have fallen below zero very early in the trajectory, even though the deterministic average curve does not. The probability that this occurs can be addressed as an absorption problem for a random walk with drift. See also the later chapters.

Sellke's construction: severe epidemics.

Suppose that, as $N \to \infty$, $\alpha = \alpha_N$ becomes large, and hence $R_{0N} = \alpha_N/\beta$ becomes large also. Then, from (1.3), we have $s_\infty \sim e^{-R_{0N}}$ small, and the CLT suggests that $S(\infty) \approx \mathcal{N}(S_\infty, S_\infty)$, since $s_\infty \ll 1$ and $1/s_\infty \mathcal{G} R_{0N}^2$. This suggests a Poisson approximation (Daniels (19??)).

Let

$$E' \;:=\; \frac{R_{0N}}{N}\left\{T_0 + \sum_{j=1}^{S_0} T_j\right\}$$

be the total conceivable per capita infectious exposure generated if the whole population became infected. Define

$$S' \;:=\; \#\{i\colon L_i > E'\}.$$

Note that, if $L_i > E'$, individual i can never become infected.

Use the *Stein–Chen method*. Conditional on E',

$$S' \;\sim\; \mathrm{Bi}\,(S_0, e^{-E'}),$$

and is at total variation distance at most $e^{-E'}$ from $\mathrm{Po}\,(S_0 e^{-E'})$. Also, $E' = R_{0N}(1+N^{-1/2}Z)$ with Z a very well-behaved random variable with zero mean and variance close to 1. So S' is close to having a mixed Poisson distribution (error $O(e^{-R_{0N}})$), and, again by the Stein–Chen method, this is in turn close to Poisson $\mathrm{Po}\,(S_0 e^{-R_{0N}})$. (Error now at most $O(R_{0N}^2 e^{-R_{0N}})$).

The true total exposure at the end of the epidemic is not quite E', because the S' individuals that were never infected should not contribute to the exposure. This makes a mean difference of about $S' R_{0N}/N$ to the total. On average, there are about

$$S_0 e^{-R_{0N}} (R_{0N}/N) S'$$

individuals i with L_i between $E' - S' R_{0N}/N$ and E', and if this number is much smaller than 1, Poisson approximation will not be upset, though the error in the approximation may be increased. Carrying through the calculations shows that good Poisson approximation is obtained if $R_{0N} \geq (1-\gamma)\log N$ for any $\gamma < 1/2$. See also Ball and Barbour (1990) for a more general setting.

1.5 The En'ko–Reed–Frost epidemic.

This is an epidemic in discrete time. Infectives contact individuals independently of one another, each other with fixed probability p/N, and any susceptibles contacted become infected.

The time index is 'generations of infection'; start with (S_0, I_0). At time m, conditional on (S_{m-1}, I_{m-1}), we have

$$S_m \;\sim\; \mathrm{Bi}\,(S_{m-1}, (1-p/N)^{I_{m-1}}); \quad I_m \;=\; S_m - S_{m-1}.$$

This is a 'chain–binomial' model; p corresponds to R_0. It also has an interpretation in terms of the $G_{n,p}$ Bernoulli random graph.

The model is used mostly for constructing explicit likelihood functions for small households, in order to estimate (in particular) p or R_0 for within household spread of infection.