Population and disease models

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5 Schistosomiasis, II

5.1 New model

The snails are no longer explicitly mentioned. We use M to denote the number of human hosts, whereas $H = H(t)$ will now denote the vector $(H_j(t),\ j \geq 0)$, with $H_j(t)$ the number of hosts having j parasites at time t: the structure of the distribution of parasites among hosts is now critical. Clearly, we have $\sum_{j\geq 0} H_j(t) = M$ for all t. Write $h_j = h_j(t) = H_j(t)/M$.

Infection: each host makes potentially infectious contacts at rate λ per unit time. The probability that the contact is with a j-host is then h_j (homogeneous mixing). Only uninfected (0-) hosts can become infected (concomitant immunity); if a 0-host contacts an i-host, the probability that he then becomes a j-host is p_{ij}. Typically, think of each of the i parasites in the i-host causing independent and identically distributed numbers of parasites in the newly infected host, each with mean θ. Then p_{ij} is the convolution of i copies of a distribution with mean θ, so that, in particular,

$$\sum_{j\geq 1} j p_{ij} \;=\; i\theta. \tag{5.1}$$

Parasite mortality: parasites die independently with rate μ.

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Transition rates:
Death of a parasite in an i-host:

$$H \;\to\; H - \varepsilon^i + \varepsilon^{i-1} \quad \text{at rate } i\mu H_i, \quad i \geq 1.$$

Infection changing a 0-host into a j-host:

$$H \;\to\; H + \varepsilon^j - \varepsilon^0 \quad \text{at rate } \lambda H_0 \sum_{i\geq 1} h_i p_{ij}, \quad j \geq 1.$$

Here, ε^i denotes a unit vector in the ith direction.

The model is easy to simulate, is 'reasonably' lifelike, but difficult to analyze.

5.2 Deterministic analysis.

The average rate differential equations yield

$$\begin{aligned} \frac{dh_i}{dt} &= (i+1)\mu h_{i+1} - i\mu h_i + \lambda h_0 \sum_{j\geq 1} h_j p_{ji}, \quad i \geq 1; \\ \frac{dh_0}{dt} &= \mu h_1 - \lambda h_0 \sum_{j\geq 1} h_j (1 - p_{j0}), \end{aligned} \tag{5.2}$$

now an *infinite* system of non-linear ODE's. Note that the approximation cannot now be justified by the theorems of Chapter 2, since they are essentially finite dimensional. General arguments for systems like this are very much harder.

Questions of interest: Threshold theorems? Equilibria?

5.3 Equilibria.

Take equations (5.2) with LHS set to zero; write $\bar{h}$ for $h(t)$, all t, and write $\Lambda := \lambda \bar{h}_0$. Multiply the i-equation by i, and add over $i \geq 1$:

$$0 \;=\; i\mu(i+1)\bar{h}_{i+1} - i\mu.i\bar{h}_i + \Lambda \sum_{j\geq 1} j\bar{h}_j.\frac{1}{j} p_{ji} i. \tag{5.3}$$

Now, since $\sum_{i\geq 1} p_{ji} i = j\theta$, we can write

$$\tilde{p}_{ji} \;:=\; \frac{1}{j\theta} p_{ji} i,$$

defining the elements of a *stochastic* matrix $\widetilde{P}$. Then (5.3) becomes

$$\begin{aligned} 0 &= i\mu y_{i+1} - (i-1)\mu y_i + \Lambda\theta \sum_{j\geq 1} y_j \tilde{p}_{ji} - \Lambda\theta y_i + (\Lambda\theta - \mu) y_i \\ &= (yS^{\Lambda})_i + (\Lambda\theta - \mu) y_i, \qquad (5.4) \end{aligned}$$

where we have written $y_i = i\bar{h}_i$, $i \geq 1$; and S^{Λ} is the infinitesimal matrix of a Markov jump process Y on $\mathbb{N}$.

If Y is *positive recurrent*, then there is certainly a solution to these equations for $\Lambda = \mu/\theta$, i.e. for $\bar{h}_0 = \mu/(\lambda\theta)$ — so this only works for $\lambda\theta > \mu$ — which we can call $\bar{y}$; and then any multiple of it is also a solution. The required solution $\bar{h}_i$ for $i \geq 1$ is then given by

$$\bar{h}_i = c\bar{y}_i/i, \qquad i \geq 1,$$

where c satisfies

$$c\sum_{i\geq 1} \bar{y}_i/i = 1 - \bar{h}_0 = 1 - \mu/(\lambda\theta).$$

Y is positive recurrent only if $\theta < e$.

5.4 Threshold theorems.

The parasites' viewpoint. In an (almost) uninfected population, a parasite enjoys

- average lifetime $1/\mu$;
- constant fecundity $\lambda\theta$.

So the average whole life expected number of offspring is their product:

$$R_0^p = \lambda\theta/\mu.$$

This suggests a threshold theorem with critical value $R_0^p = 1$, as usual.

The branching approximation. In an (almost) uninfected population, neglecting the (large) uninfected population, the transition rates become effectively:

Death of a parasite in an i-host:

$$\begin{aligned} H &\to H - \varepsilon^i + \varepsilon^{i-1} \quad \text{at rate } i\mu H_i, \quad i \geq 2; \\ H &\to H - \varepsilon^1 \qquad \text{at rate } \mu H_1. \end{aligned}$$

Infection changing a 0-host into a j-host:

$$H \to H + \varepsilon^j \quad \text{at rate } \lambda \sum_{i \geq 1} H_i p_{ij}, \quad j \geq 1.$$

Note that the total number of parasites,

$$P(t) := \sum_{i \geq 1} i H_i(t),$$

satisfies $\mathbb{E}P(t) = P(0)e^{(\lambda\theta - \mu)t}$, again suggesting that $R_0^p = 1$ should be critical. However, extinction means that $P(t) = 0$ eventually.

Criticality theorem for this branching process:

- If $\theta \leq e$, $\mathbb{P}$[extinction] $= 1$ if and only if $R_0 \leq 1$.
- If $\theta > e$, $\mathbb{P}$[extinction] $= 1$ if and only if $\frac{\lambda e \log \theta}{\mu} \leq 1$.

Heavily parasitized individuals. An individual with Y parasites at time 0 has about $Y(t) = Ye^{-\mu t}$ at time t later (as long as $e^{\mu t} \ll Y$). So $W(t) = \log Y(t)$ drifts at constant rate μ towards zero. At an infection event, say at time t, such an individual gives rise to a new individual with about $\theta Y(t)$ parasites, or, on the logarithmic scale, a new heavily infected individual with $W = W(t) + \log \theta$ parasites. This suggests a continuous state branching process for approximating the heavily parasitized individuals: the state of an individual (on the logarithmic scale) drifts at constant rate μ towards zero, and when zero is reached the individual dies. During its lifetime, it gives birth at constant rate λ, and the state of the child is $\log \theta$ larger than that of the parent. All individuals behave otherwise independently.

This model can be transformed by time and space scaling to an equivalent model, in which both drift and birth rate are 1, and the state of the child is larger than that of the parent by an amount $d = \lambda \log \theta / \mu$. Let P be the total number of particles ever in existence.

Criticality theorem.

- If $d \leq 1/e$, then $\mathbb{P}_w[N < \infty] = 1$ for all w, and indeed $1 \leq \mathbb{E}_d N \leq e$.

- If $d > 1/e$, then $\mathbb{P}_w[N < \infty] < 1$ for all w.

The interpretation is that, if $\lambda e \log \theta/\mu \leq 1$, the heavily parasitized individuals are not self-supporting, but rely on being created from time to time by the less heavily parasitized individuals. If $\lambda e \log \theta/\mu > 1$, the are self-supporting.

5.5 Initial growth rate

Assume the linear (branching process) approximation, in the deterministic setting. Classically, a linear process has exponential growth. So set $h_0 = 1$ in the differential equations (5.2), and ignore the $i = 0$ equation. Then the equations reduce to

$$\frac{dh^T}{dt} \;=\; h^T R,$$

a linear equation with constant coefficients, with the matrix R given by

$$R_{ij} \;:=\; i\mu\delta_{i-1,j} - i\mu\delta_{ij} + \lambda p_{ij}, \qquad i, j \geq 1,$$

where δ denotes the Kronecker symbol.

Note that the vector $v = (1, 2, 3, ...)^T$ satisfies $Rv = (\lambda\theta - \mu)v$, so that v is (formally) a positive eigenvector with eigenvalue $\lambda\theta - \mu$.

The parasites' view.

$$h^T v \;=\; \sum_{j\geq 1} j h_j \;=\; \text{mean number of parasites per host} \;=:\; m,$$

and

$$\frac{dm}{dt} \;=^*\; \left(\frac{dh}{dt}\right)^T v \;=\; h^T R v \;=\; (\lambda\theta - \mu) h^T v,$$

or

$$\frac{dm}{dt} \;=\; (\lambda\theta - \mu) m.$$

So $m \to \infty$ exponentially with rate $\lambda\theta - \mu$ if $R_0^p > 1$, whereas $m \to 0$ exponentially with rate $-(\mu - \lambda\theta)$ if $R_0^p < 1$. Again, suggests R_0^p as threshold quantity.

The hosts' view.

$$h^T \mathbf{1} \;=\; \text{prevalence of infection},$$

and $\frac{d}{dt}(h^T 1)$ gives nothing pretty. However, setting $y_j := jh_j e^{-(\lambda\theta-\mu)t}$ gives

$$\frac{dy^T}{dt} \;=\; y^T S,$$

with

$$S_{ij} \;:=\; (i-1)\mu\delta_{i-1,j} - [\lambda\theta + (i-1)\mu]\delta_{ij} + \lambda\theta\tilde{p}_{ij},$$

the infinitesimal matrix of a Markov jump process on $\mathbb{N}$ — in fact, $S = S^\Lambda$ when $\Lambda\theta = \lambda$. Hence

$$y_j(t) = |y(0)|\mathbb{P}_{y(0)}[Y(t) = j].$$

For example, if Y is positive recurrent, then $y(t) \to |y(0)|\pi$ in total variation, where $\pi_j > 0$ for all j and $\sum_{j\ge 1}\pi_j = 1$; then

$$h_j(t) \;\sim\; |y(0)|e^{(\lambda\theta-\mu)t}\pi_j/j,$$

and

$$h^T(t)\mathbf{1} \;\sim\; e^{(\lambda\theta-\mu)t}m(0)\sum_{j\ge 1}(\pi_j/j).$$

However, the process Y is positive recurrent if $\lambda\theta\log\theta < \mu$, and the 'parasite critical' value of λ is μ/θ: so Y is positive recurrent at the critical λ precisely when $\theta < e$, and things are different at the critical value otherwise. The asymptotic exponential growth rate is in all cases *not* the expected $\lambda\theta - \mu$ once Y is transient, which occurs for large enough ratio λ/μ, whatever the value of θ.