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A SIMPLE POPULATION MODEL FOR PHAGE REPRODUCTION

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In a recent paper on phage crosses, Hershey (1958) has raised a number of interesting problems in population and genetic processes. A very simplified model of phage reproduction may be imagined as follows: at time $t=0$ let n phage particles be released in a medium containing $N>n$ bacteria, and penetrate (infect) some bacteria, each with a probability $0<p<1$ of success. Only the bacteria free of phages reproduce in an ordinary birth-death process with constant parameters $\lambda>\mu>0$; meanwhile in any infected bacterium, the number of phages may be considered to grow in a birth process with parameter α. When exactly r phages are produced, the bacterium dies, and releases these particles; they immediately infect more bacteria, and the process continues until all bacteria are killed. We are interested in the time of extinction T of the bacteria.

We adopt as our basic time unit τ the mean time taken by an infected bacterium to break open. In the phage birth process, the probability that an r-th phage is produced in the interval t, $t+\delta t$ is

$$P_{r-1}\ (t)\ \ (r-1)\ \alpha\ \delta t,$$

where $P_{r-1}(t)=e^{-\alpha t}(1-e^{-\alpha t})^{r-2}$ is the probability that there are $r-1$ phages at time t. Thus the mean time τ for a bacterium to break open is

$$\tau=\int_0^\infty te^{-\alpha t}(1-e^{-\alpha t})^{r-2}(r-1)\ \alpha\ dt=\alpha^{-1}\textstyle\sum_{j=1}^{r-1}(-1)^{j+1}\binom{r-1}{j}j^{-1}. \qquad (1)$$

Starting with i phage-free bacteria, then after an interval of time τ, the average number of bacteria will be $ie^{\beta\tau}$ where $\beta=\lambda-\mu>0$. Clearly the average numbers of infected and phage-free bacteria just after times $0, \tau, 2\tau, \cdots$ will be:

Times	*Infected bacteria*	*Phage-free bacteria*
$0+$	np	$N-np$
$\tau+$	np^2r	$(N-np)e^{\beta\tau}-np^2r$
$2\tau+$	np^3r^2	$(N-np)e^{2\beta\tau}-np^2re^{\beta\tau}-np^3r^2$
$3\tau+$	np^4r^3	$(N-np)e^{3\beta\tau}-np^2re^{2\beta\tau}-np^3r^2e^{\beta\tau}-np^4r^3$
$\cdots$	$\cdots$	$\cdots$

In general, just after time $j\tau$, there will be $np^{j+1}r^j$ infected bacteria, and

$$e^{j\beta\tau}\{N-np\sum_{i=0}^{j}(pre^{-\beta\tau})^i\} = e^{j\beta\tau}\left\{N-np\frac{(pre^{-\beta\tau})^{j+1}-1}{pre^{-\beta\tau}-1,}\right\} \tag{2}$$

phage free bacteria.

For all the bacteria to die by time $T=(j+1)\tau_+$, $(j\geq 0)$, we require that

$$e^{j\beta\tau}\left\{N-np\frac{(pre^{-\beta\tau})^{j+1}-1}{pre^{-\beta\tau}-1}\right\}>0\geq e^{(j+1)\beta\tau}\left\{N-np\frac{(pre^{-\beta\tau})^{j+2}-1}{pre^{-\beta\tau}-1}\right\}$$

or, after taking logarithms and simplifying (if $pre^{-\beta\tau}>1$), we find that

$$\frac{log\left\{1+\frac{N}{np}(pre^{-\beta\tau}-1)\right\}}{log\ pre^{-\beta\tau}}-2\leq j<\frac{log\left\{1+\frac{N}{np}(pre^{-\beta\tau}-1)\right\}}{log\ pre^{-\beta\tau}}-1. \tag{3}$$

To gain some idea of the speed of the process, let us take $N=10^6$, $\tau=30$ (minutes), $\beta=.1$, $r=200$, $p=.7$; the following table gives values for T for different values of n.

n	$h=j+1$	$T=h\tau$
10^3	4	$T=120$
10^4	3	$T=90$
10^5	2	$T=60$
10^6	1	$T=30$
$10^k(k\geq 7)$	0	$T=0$

A far more interesting and complicated problem is the stochastic treatment of the present model. A second realistic problem arises if phage reproduction in an infected bacterium is treated as a birth-death process in which dead phages are in fact "mature", and can no longer reproduce; when the bacterium breaks open after the mature phages reach the number r, it is these only which are infective. Such a stochastic model would require the knowledge of the probabilities that r deaths have occurred in a birth-death process: this problem has not been fully solved. However, if the birth and death (maturation) parameters are η and γ respectively ($\eta>\gamma>0$), the deterministic approximation will give for the number $N(t)$ of survivors at time t

$$N(t)=e^{(\eta-\gamma)t},$$

and the time τ for r phages to have matured would then be given by

$$r=\int_0^\tau \gamma e^{(\eta-\gamma)t}\,dt,$$

whence

$$\tau=(\eta-\gamma)^{-1}\log\{1+(\eta-\gamma)r\gamma^{-1}\}\ . \tag{4}$$

With this value for τ, instead of the previous value (1), the remaining treatment remains unchanged for a deterministic model.

References

HERSHEY, A. D. *The production of recombinants in phage crosses.* Cold Spring Harbor Symposia on Quantitative Biology, **23** (1958), 19-46.

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