A Note on Gani's Models on Phage Attachment to Bacteria

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Mimeograph Series No. 121

September 1967

*This investigation was supported in part by U. S. Public Health Service Grant GM-10525-04.

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Abstract

In this note, the solution for the distribution of the relevant random variables has been obtained for Gani's "general stochastic model" [1] for the attachment of phages to bacteria, for the special case with $r = 1$, where r is the upper limit to the number of phage particles that can become attached to a bacterium. This distribution is then compared with the corresponding distribution already obtained by Gani [1] under his "simplified stochastic model". It is found that in general the simplified model appears to be a good approximation to the general model only when the total number ν_{00} of phages is much larger than the total number n_{00} of bacteria. The distribution of the time it takes before either all the bacteria (when $n_{00} < \nu_{00}$) or all the phages (when $n_{00} > \nu_{00}$) are exhausted, is also considered under the general model with $r = 1$.

*This investigation was supported in part by U. S. Public Health Service Grant GM-10525-04.

1. Introduction

In a recent paper, Gani [1] has considered a stochastic analogue of a deterministic model for the attachment of phages to bacteria in suspension considered earlier by Yassky [3]. Among others, the underlying assumptions of these models are (i) that the duration of observation is short enough not to cause any multiplications or deaths of both bacteria and phage particles and (ii) that there exists an upper limit r to the number of phage particles that can become attached to a bacterium. In [1] Gani first considers a general stochastic model, henceforth called 'model A', where it is assumed that the probability of attachment during $(t,t+\tau)$ of a phage to bacterium already carrying i phages is $\lambda_i n_i(t)\nu_0(t)\tau + o(\tau)$, where $n_0(t)$, $n_1(t)$, $\cdots$,$n_r(t)$ are the numbers of bacteria at time t with $0, 1, 2, \cdots, r$ phages respectively, with $n_{00} = \Sigma_{i=0}^{r} n_i(t) = n_0(0)$ and the random variable $\nu_0(t)$ is the number of unattached phages at time t with $\nu_0(0) = \nu_{00}$. Here λ_i's($\lambda_i = 0$ for $i \geq r$) are some nonnegative constants. In particular it is assumed that $\lambda_i = i\alpha + \beta$; $i = 0, 1, 2, \cdots, r-1$ where β is nonnegative and α is such that λ_i are nonnegative. Having found the differential equation associated with this model rather untractable to solution, Gani considers a simplified stochastic model, henceforth called as 'model B', where $\nu_0(t)$ instead is a assumed to be nonrandom having the form originally given

by Yassky as

$$v_0(t) = \frac{v_{00}(m\alpha+\beta)}{m\alpha+\beta\ \exp[n_{00}(m\alpha+\beta)t]}\ , \qquad (1)$$

where $m = v_{00}/n_{00}$. $v_0(t)$ as given in (1) may be regarded as the mean number of unattached phages at time t. It is assumed as before that the probability of attachment during $(t,t+\tau)$ of a phage to bacterium already carrying i phages is $\lambda_i n_i(t) v_0(t)\tau + o(\tau)$, where $v_0(t)$ is given by (1). The relevant distribution of the vector $(n_0(t), \cdots, n_r(t))$ under model B turns out to be of the multinomial form. Reader is referred for details to Gani ([1], [2]).

The purpose of this note is two-fold. First is to find the exact distribution of the random variables involved under model A for the special case with $r = 1$, where it was found possible to solve the equations directly using the laplace transform approach. The case of single infection $(r=1)$ may be of interest by itself in its applications to this as well as other fields. In the present case however when $v_{00} \prec\prec n_{00}$, the case with $r = 1$ may be regarded as a good first approximation. The second purpose is to compare the above distribution with the corresponding one obtained by Gani under his simplified model B.

2. Gani's Stochastic Model A.

We shall restrict ourselves to the case with $r = 1$, so that it is sufficient to consider the distribution of $n_1(t)$,

since $n_0(t) \equiv n_{00} - n_1(t)$ and $\nu_0(t) \equiv \nu_{00} - n_1(t)$. Let $P_k(t) = \Pr(n_1(t) = k)$; $k = 0, 1, \cdots, M$, where $M = \min(\nu_{00}, n_{00})$. Following Gani, we have

$$\begin{cases} \dfrac{dP_0}{dt} = -\lambda_0 n_{00}\nu_{00}P_0 \\ \dfrac{dP_k}{dt} = -\lambda_0(\nu_{00}-k)(n_{00}-k)P_k \\ \qquad\qquad + \lambda_0(\nu_{00}-k+1)(n_{00}-k+1)P_{k-1}; \quad k = 1, 2, \cdots, M . \end{cases} \tag{2}$$

Let

$$Q_k(\Theta) \equiv \int_0^\infty e^{-\Theta t}P_k(t)dt; \quad k = 0, 1, \cdots, M; \quad \mathrm{Re}(\Theta) > 0 . \tag{3}$$

Next, the transforms of equations (2) are taken, using the boundary conditions $P_k(0) = 1$ if $k = 0$ and zero if $k > 0$, leading to the recurrence relation between Q's as

$$\begin{cases} Q_0 = \dfrac{1}{\Theta+\lambda_0 n_{00}\nu_{00}} , \\ Q_k = \dfrac{\lambda_0(\nu_{00}-k+1)(n_{00}-k+1)}{\Theta+\lambda_0(\nu_{00}-k)(n_{00}-k)} Q_{k-1}; \quad k = 1, 2, \cdots, M , \end{cases} \tag{4}$$

and thence to their values

$$\begin{cases} Q_0 = \dfrac{1}{\Theta+\lambda_0 n_{00}\nu_{00}} \\ Q_k = \lambda_0^k\left[\dfrac{\nu_{00}!\ n_{00}!}{(\nu_{00}-k)!(n_{00}-k)!}\right]\cdot\prod_{i=0}^{k}[\Theta + \lambda_0(\nu_{00}-i)(n_{00}-i)]^{-1} \end{cases} \tag{5}$$

Rewriting the product in Q_k of (5) in terms of partial fractions we have for $k = 0, 1, \cdots, M$,

$$Q_k = \frac{\nu_{00}!\, n_{00}!}{(\nu_{00}-k)!\,(n_{00}-k)!} \sum_{i=0}^{k} \frac{C_{ik}}{\theta+\lambda_0(n_{00}-i)(\nu_{00}-i)} \tag{6}$$

where $C_{00} = 1$ and

$$C_{ik} = \prod_{\substack{j=0 \\ j\neq i}}^{k} [(i-j)(n_{00}+\nu_{00}-j-i)]^{-1} \tag{7}$$

Finally, taking the inverse of Q_k with respect to time t, we immediately obtain the desired distribution of $n_1(t)$ given for $k = 0, 1, 2, \cdots, M$ by

$$P_k(t) = \frac{\nu_{00}!\, n_{00}!}{(\nu_{00}-k)!\,(n_{00}-k)!} \sum_{i=0}^{k} C_{ik} \exp[-\lambda_0(n_{00}-i)(\nu_{00}-i)t] \,. \tag{8}$$

Unfortunately the expressions for $E(n_1)$ and higher moments of $n_1(t)$ are rather involved and hence we shall not touch them here. It is clear however that since $n_1(t)$ is a non-decreasing function of t, $n_1(t) \uparrow M$, a.s. as $t \to \infty$. Again if T denotes the time it takes before either all the bacteria or all the phage particles are exhausted, depending upon whether $n_{00} < \nu_{00}$ or $n_{00} > \nu_{00}$, we have

$$\begin{aligned} F(t) \equiv \Pr(T \leq t) &= P_M(t) \\ &= \frac{\nu_{00}!\, n_{00}!}{(|n_{00}-\nu_{00}|)!} \sum_{i=0}^{M} C_{iM} \exp[-\lambda_0(n_{00}-i)(\nu_{00}-i)t] \,, \end{aligned} \tag{9}$$

with

$$F(\infty) = \frac{\nu_{00}!\, n_{00}!}{(|n_{00}-\nu_{00}|)!}\, C_{MM} = 1;\ F(0) = \sum_{i=0}^{M} C_{iM} = 0 \ . \qquad (10)$$

From (9), one can easily find the moments of T, for instance

$$E(T) = \frac{\nu_{00}!\, n_{00}!}{(|n_{00}-\nu_{00}|)!} \sum_{i=0}^{M-1} \frac{-C_{iM}}{\lambda_0 (n_{00}-i)(\nu_{00}-i)} \ . \qquad (11)$$

3. Some limiting results and comparison between the two models

For the case with $r = 1$, we must take $\beta = -\alpha = \lambda_0$, so that under model B, $\nu_0(t)$ of (1) assumed to be nonrandom is given by

$$\nu_0(t) = \frac{\nu_{00}(n_{00}-\nu_{00}) \exp[-\lambda_0(n_{00}-\nu_{00})t]}{n_{00}-\nu_{00}\ \exp[-\lambda_0(n_{00}-\nu_{00})t]} \ . \qquad (12)$$

Under model B, $n_1(t)$ turns out to be a binomial random variable. More specifically, if $p_k(t)$ denotes $\Pr[n_1(t) = k]$ under model B, then from [1] we have for $k = 0, 1, \cdots, n_{00}$

$$p_k(t) = \binom{n_{00}}{k} a^k (1-a)^{n_{00}-k} \ , \qquad (13)$$

where

$$a = \frac{\nu_{00}(1-\exp[-\lambda_0(n_{00}-\nu_{00})t])}{n_{00}-\nu_{00}\ \exp[-\lambda_0(n_{00}-\nu_{00})t]} \ . \qquad (14)$$

It may be remarked here that because of the introduction of a deterministic element in model B (namely, treating $\nu_0(t)$ as nonrandom unlike in model A), one may be tempted to conclude that variance of $n_1(t)$ should be smaller under model B than under model A. This however is not necessarily true as will be

exhibited below specially for the case where $\nu_{00} < n_{00}$, the case which arises fairly commonly in practice. One simple explanation for this is as follows: when $\nu_{00} < n_{00}$, whereas one starts with ν_{00} phage particles at time zero and the number $\nu_0(t)$ decreases with t deterministically under model B, there is always a positive probability of $n_1(t)$ taking a value greater than the available total number ν_{00} of phage particles; in fact

$$\Pr(h_1(t) > \nu_{00}) = 1 - \sum_{k=0}^{\nu_{00}} p_k(t)$$

$$= n_{00}\binom{n_{00}-1}{\nu_{00}} \cdot \int_0^a x^{\nu_{00}}(1-x)^{n_{00}-\nu_{00}-1}\,dx \,. \qquad (15)$$

It is this scatter of the distribution of $n_1(t)$ beyond point ν_{00} that is partly responsible for a greater variability in $n_1(t)$ under model B than that under model A.

In the following we shall study the behavior of the distribution of $n_1(t)$ under models A and B for three different limiting cases: (i) when $t \to \infty$ (ii) when $n_{00} \to \infty$ and $\lambda_0 \to 0$ such that $n_{00}\lambda_0 \to \delta$ and (iii) when $\nu_{00} \to \infty$ and $\lambda_0 \to 0$ such that $\nu_{00}\lambda_0 \to \mu$.

Case (i). When $n_{00} \leq \nu_{00}$, it is easy to verify that in both models as $t \to \infty$, $\Pr(n_1(t) = k) \to 0$ for $k < n_{00}$ and $\Pr(n_1(t) = n_{00}) \to 1$. On the other hand when $n_{00} > \nu_{00}$, whereas in model A, $P_k(t) \to 0$ for $k \neq \nu_{00}$ and $P_{\nu_{00}}(t) \to 1$ as $t \to \infty$; in model B however, for $k = 0, 1, \cdots, n_{00}$,

$$\lim_{t\to\infty} p_k(t) = \binom{n_{00}}{k} \left(1 - \frac{\nu_{00}}{n_{00}}\right)^{n_{00}-k} \left(\frac{\nu_{00}}{n_{00}}\right)^{k} . \qquad (16)$$

Clearly in this case then, for large t, the variance of $n_1(t)$ under model A is neglible; whereas under model B it is quite significant, unless $\nu_{00} \approx n_{00}$.

Case (ii). If we let $n_{00} \to \infty$ and $\lambda_0 \to 0$ in such a manner that $n_{00}\lambda_0 \to \delta$, then we find under model A, for $k = 0, 1, \cdots, \nu_{00}$; that

$$\lim P_k(t) = \binom{\nu_{00}}{k} e^{-\delta(\nu_{00}-k)t} (1 - e^{-\delta t})^{k} . \qquad (17)$$

Thus the random variable $n_1(t)$ tends to be binomially distributed in the limit, with

$$E(n_1(t)) = \nu_{00}(1 - e^{-\delta t}); \; Var(n_1(t)) = \nu_{00}\, e^{-\delta t}(1 - e^{-\delta t}) \qquad (18)$$

The situation is somewhat different under the simplified model B when we let $n_{00} \to \infty$ and $\lambda_0 \to 0$ in a similar manner. Here the limiting distribution is Poisson with parameter $\nu_{00}(1 - e^{-\delta t})$ so that for $k = 0, 1, 2, \cdots$,

$$\lim p_k(t) = \frac{1}{k!} [\nu_{00}(1 - e^{-\delta t})]^{k} e^{-\nu_{00}(1 - e^{-\delta t})} , \qquad (19)$$

and in the limit

$$E(n_1(t)) = \nu_{00}(1 - e^{-\delta t}) = Var(n_1(t)) . \qquad (20)$$

On comparing (18) and (20), we find that whereas the $E(n_1(t))$ is same for both models, $Var(n_1(t))$ is again found to be smaller under model A than that under model B.

Case (iii). If instead we let $\nu_{00} \to \infty$ such that $\lambda_0 \nu_{00} \to \mu$, one finds as expected that the limiting distributions of $n_1(t)$ under the two models coincide; the common limiting distribution is binomial with the

$$\Pr(n_1(t) = k) = \binom{n_{00}}{k} e^{-\mu(n_{00}-k)t} (1 - e^{-\mu t})^k ; \qquad (21)$$

for $k = 0, 1, \cdots, \nu_{00}$.

In conclusion, we may remark that in general the simplified model B appears to be a good approximation to the stochastic model A, as far as the distribution of $n_1(t)$ is concerned, only when ν_{00} is much larger than n_{00}. However this is restricted only to the case with $r = 1$; for the case with $r > 1$, the present results are only suggestive.

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