ON THE DERIVATION OF A MEAN GROWTH EQUATION FOR CELL CULTURES

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If $N(t)$ is the expected number of cells in a culture at time $t$, $\dot{N}(t)$ the corresponding time derivative, and $f(t - \tau)\, dt$ the probability that a cell of age $t - \tau$ at time $t$ will divide in the succeeding time interval $dt$, then according to Hirsch and Engelberg (this issue) there obtains the integral equation $\dot{N}(t) = 2 \int_{-\infty}^{t} f(t - \tau) \dot{N}(\tau) \, d\tau$ for describing the dynamics of the cell population. It is the purpose of this note to give two alternative derivations of this equation, one based on the age density equation of Von Foerster, and the other based on a generalized form of the Harris-Bellman equation describing the first moment of an age dependent, branching process. In addition, a probability model is posed from which the Von Foerster equation and, hence, the Hirsch–Engelberg equation readily follows.

Hirsch and Engelberg (this issue) have posed the equation

$$\dot{N}(t) = 2 \int_{-\infty}^{t} f(t - \tau) \dot{N}(\tau) \, d\tau \quad (1)$$

for describing the dynamics of a cell population. Here $N(t)$ is taken as the expected number of cells conditional on an initial distribution $\dot{N}(\tau) \, d\tau$ for $\tau \leq 0$, while $f(t - \tau) \, dt$ corresponds to the probability that a cell of age $t - \tau$ at time $t$ will divide in the succeeding time interval $dt$. Such an equation has an evident heuristic derivation, Hirsch and Engelberg [this issue], by noting that $\dot{N}(\tau) \, d\tau = dN(\tau)$ is the expected number of cells born in the time interval $\tau, \tau + d\tau$, and of these the fraction $f(t - \tau) \, dt \cdot \dot{N}(\tau) \, d\tau$ will divide in the time interval $t, t + dt$. Accordingly, summing these possible changes, one would obtain...
\[ dN(t) = 2 \int_{-\infty}^{t} f(t - \tau) \, d\tau \cdot dN(\tau) \]

in which the number 2 appears because upon division it is assumed that each cell gives rise to exactly two new cells. If we next assume that \( N(t) \) is differentiable, then

\[ \dot{N}(t) \, dt = 2 \int_{-\infty}^{t} f(t - \tau) \, d\tau \cdot \dot{N}(\tau) \, d\tau \]

and so

\[ \dot{N}(t) = 2 \int_{-\infty}^{t} f(t - \tau) \dot{N}(\tau) \, d\tau. \]

**Derivation From The Harris–Bellman Equation.** It is of interest that Harris and Bellman [1963] have derived the equation

\[ N(t) = 1 - G(t) + 2 \int_{0}^{t} N(t - u) \, dG(u) \quad (2) \]

representing the expected number of cells at time \( t \) that would result from a single cell born at time \( t = 0 \). Here \( G(t) \) represents the probability that a cell will have a life span equal to or less than \( t \). The derivation of (2) proceeds rigorously by first obtaining an equation for the generating function \( F(s, t) \) of the random variable \( Z(t) \) defined as the number of cells at time \( t \), given that \( P[Z(0) = 1] = 1 \), and then showing that \( \partial F(s, t)/\partial s \) exists for \( s = 1 \). The corresponding equation for \( \partial F(s, t)/\partial s \bigg|_{s=1} \) is then just (2). It would appear then that we might have a quick rigorous derivation of (1) if we made the assumption that \( N(t) \) and \( G(t) \) in (2) are differentiable, for then

\[ \dot{N}(t) = \dot{G}(t) + 2 \int_{0}^{t} \dot{G}(t - \tau) \dot{N}(\tau) \, d\tau \quad (3) \]

follows directly from (2) and it is easily shown that \( \dot{G}(t) = f(t) \). To see that (1) is almost (3) rewrite the former as

\[ \dot{N}(t) = 2 \int_{-\infty}^{0} f(t - \tau) \dot{N}(\tau) \, d\tau + 2 \int_{0}^{t} f(t - \tau) \dot{N}(\tau) \, d\tau \\
= 2 \int_{-\infty}^{0} f(t - \tau) \, dN(\tau) + 2 \int_{0}^{t} f(t - \tau) \dot{N}(\tau) \, d\tau \quad (4) \]

In the particular case in which \( N(\tau) \) for \( \tau \leq 0 \) has the form

\[ N(\tau) = \begin{cases} 0 & \text{for } \tau < 0 \\ 1 & \text{for } \tau = 0, \end{cases} \]