SI Text

Solution of the Age-Structured Model with Uniform Age Distribution. In the age-structured model, if the initial distribution of ages is uniform, given by $n_i(a) = \hat{n}_i/t_i$, then the stem cell population is given by

$$N_0(t,a) = \frac{\hat{n}_0}{t_0}(2a_3)^n \quad \text{for } (n-1)t_0 < t-a \le nt_0. \qquad \textbf{[34]}$$

If the cell cycle times satisfy $t_1/t_0 = p/q$, where p and q are integers, the general solution for the semidifferentiated cells, at the points where $t - a = qnt_1$, is given by

$$\begin{aligned} N_1(a+qnt_1, a) &= \frac{\hat{n}_1}{t_1}(2b_3)^{qn} \\ &+ \frac{2a_2\hat{n}_0/t_0}{(2a_3)^p - (2b_3)^q}\left((2a_3)^{p-1} + \sum_{k=1}^{q-1}(2b_3)^{q-k}(2a_3)^{\lfloor kp/q \rfloor}\right)\left[(2a_3)^{pn} - (2b_3)^{qn}\right], \end{aligned} \qquad \textbf{[35]}$$

where $\lfloor\cdot\rfloor$ denotes integer part.

Relating the Age-Structured and Continuous Models. We relate the age-structured and continuous models for the case in which all cells start with age zero, and the age-structured solution is given by **6**–**8**. To find the total stem, semidifferentiated and fully differentiated cell populations at a given time in the age-structured model we integrate the age distribution function over all possible ages. For the stem cell population, integrating **6** gives

$$\begin{aligned} \hat{N}_0(t) &= \hat{n}_0 \int_0^{t_0} \sum_{n=0}^{\infty} \delta(t - nt_0 - a)(2a_3)^n \, \mathrm{d}a \\ &= \hat{n}_0 \sum_{n=0}^{\infty} (2a_3)^n \left[\int_0^{t_0} \delta(t - nt_0 - a)\, \mathrm{d}a\right] \\ &= \hat{n}_0 (2a_3)^{\lfloor t/t_0 \rfloor}. \end{aligned} \qquad \textbf{[36]}$$

The last equality follows since the only δ-function which gives a non-zero integral is that satisfying $nt_0 < t < (n+1)t_0$, which picks out the single value $n = \lfloor t/t_0 \rfloor$ from the sum. If t is much greater than t_0, so that $\lfloor t/t_0 \rfloor \approx t/t_0$, we have

$$\hat{N}_0(t) \approx \hat{n}_0(2a_3)^{t/t_0}. \qquad \textbf{[37]}$$

For the semidifferentiated cell population, integrating **7** gives

$$\begin{aligned} \hat{N}_1(t) &= \hat{n}_1 \sum_{m=0}^{\infty}(2b_3)^m \left[\int_0^{t_1} \delta(t - a - mt_1)\, \mathrm{d}a\right] \\ &+ 2a_2\hat{n}_0 \sum_{n=1}^{\infty}\sum_{m=0}^{\infty}(2a_3)^{n-1}(2b_3)^m \left[\int_0^{t_1} \delta(t - a - nt_0 - mt_1)\, \mathrm{d}a\right]. \end{aligned} \qquad \textbf{[38]}$$

The integral of the first δ-function picks out the value $m = \lfloor t/t_1 \rfloor$, while that of the second picks out the value $m = \lfloor t/t_1 - nt_0/t_1 \rfloor$, giving

$$\hat{N}_1(t) = \hat{n}_1 (2b_3)^{\lfloor t/t_1 \rfloor} + 2a_2 \hat{n}_0 \sum_{n=1}^{\lfloor t/t_0 \rfloor} (2a_3)^{n-1} (2b_3)^{\lfloor t/t_1 - nt_0/t_1 \rfloor}. \quad \textbf{[39]}$$

The sum can be evaluated exactly at the times $t = rt_0 t_1$, where r, t_0, and t_1 are integers, giving the approximation

$$\hat{N}_1(t) \approx \hat{A}(2a_3)^{t/t_0} + \left(\hat{n}_1 - \hat{A}\right)(2b_3)^{t/t_1}, \quad \textbf{[40]}$$

where

$$\hat{A} = \frac{2a_2 \hat{n}_0 f_1}{(2a_3)^{t_1} - (2b_3)^{t_0}}, \quad \text{and} \quad f_1 = \sum_{n=1}^{t_1} (2a_3)^{t_1 - n} (2b_3)^{\lfloor (n-1)t_0/t_1 \rfloor}. \quad \textbf{[41]}$$

For the fully differentiated cell population, integrating **8** gives

$$\begin{aligned}\hat{N}_2(t) = \hat{n}_2 \sum_{p=0}^{\infty} (1-c)^p \left[\int_0^{t_2} \delta(t - a - pt_2)\, \mathrm{d}a\right] \\ + 2b_2 \hat{n}_1 \sum_{m=1}^{\infty} \sum_{p=0}^{\infty} (2b_3)^{m-1} (1-c)^p \left[\int_0^{t_2} \delta(t - a - mt_1 - pt_2)\, \mathrm{d}a\right] \\ + 2a_2 \hat{n}_0 (2b_2) \sum_{n=1}^{\infty} \sum_{m=1}^{\infty} \sum_{p=0}^{\infty} (2a_3)^{n-1} (2b_3)^{m-1} (1-c)^p \left[\int_0^{t_2} \delta(t - a - nt_0 - mt_1 - pt_2)\, \mathrm{d}a\right].\end{aligned} \quad \textbf{[42]}$$

The first δ-function picks out the value $p = \lfloor t/t_2 \rfloor$, the second picks out the value $p = \lfloor t/t_2 - mt_1/t_2 \rfloor$, and the third picks out the value $p = \lfloor t/t_2 - nt_0/t_2 - mt_1/t_2 \rfloor$, giving

$$\begin{aligned}\hat{N}_2(t) = \hat{n}_2 (1-c)^{\lfloor t/t_2 \rfloor} + 2b_2 \hat{n}_1 \sum_{m=1}^{\lfloor t/t_1 \rfloor} (2b_3)^{m-1} (1-c)^{\lfloor t/t_2 - mt_1/t_2 \rfloor} \\ + 2a_2 \hat{n}_0 (2b_2) \sum_{n=1}^{\lfloor t/t_0 - t_1/t_0 \rfloor} \sum_{m=1}^{\lfloor t/t_1 - nt_0/t_1 \rfloor} (2a_3)^{n-1} (2b_3)^{m-1} (1-c)^{\lfloor t/t_2 - nt_0/t_2 - mt_1/t_2 \rfloor}.\end{aligned} \quad \textbf{[43]}$$

Estimating $t/t_0 - t_1/t_0 \approx t/t_0$ for large times in **43**, and choosing $t_2 = t_1$, the resulting sums can again be evaluated exactly at times $t = rt_0 t_1$, where r, t_0, and t_1 are integers, giving the approximation

$$\hat{N}_2(t) \approx \hat{B}(2a_3)^{t/t_0} + \hat{C}(2b_3)^{t/t_1} + (\hat{n}_2 - \hat{B} - \hat{C})(1-c)^{t/t_2}, \quad \textbf{[44]}$$

where

$$\hat{B} = \frac{2a_2 \hat{n}_0 (2b_2)}{2b_3 - (1-c)} \left(\frac{f_1}{(2a_3)^{t_1} - (2b_3)^{t_0}} - \frac{f_2}{(2a_3)^{t_1} - (1-c)^{t_0}}\right), \quad \hat{C} = \frac{2b_2(\hat{n}_1 - \hat{A})}{2b_3 - (1-c)}, \quad \textbf{[45]}$$

and

$$f_2 = \sum_{n=1}^{t_1} (2a_3)^{t_1 - n} (1-c)^{\lfloor (n-1)t_0/t_1 \rfloor}. \quad \textbf{[46]}$$