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Evolutionary Dynamics

Assignment #04s

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Wednesday 14th November, 2012

1.1 Allometric scaling

We know (from lecture and an article 'Some Dynamic Aspects of HSC') that a number of active HSC follows negative allometry (power law) to mass of mammal with scaling exponent 0.75.

$$N_{sc} \approx M^{0.75}$$

That means that to get to know the number of Active HSC in any mammal we just need to calibrate that power law by experimentally getting to know N_{sc} and M of any mammal. It was done for cats and humans, so for humans $M = 70$ and $N_{SC} = 385$, so

$$N_{sc} = N_{sc_0} \times M^{0.75}$$
$$385 = N_{sc_0} \times 70^{0.75}$$
$$N_{sc_0} = 15.9088$$

Now, we can estimate the number of active HSC in hamster (average M=100gm = 0.1 kg), so

$$N_{sc} = 15.9088 \times 0.1^{0.75} \approx 2.3$$

Same for blue whale (M =100 000 kg, http://www.marinemammalcenter.org), so

$$N_{sc} = 15.9088 \times 100000^{0.75} \approx 89461$$

The range of total number of HSC is the same for all mammals and approximately equal to 11000...22000, so it is the same for hamster and blue whale.

2.1 Hematopoietic multicompartment model

K – number of compartments (successes, i.e. cell manages to move to k-th compartment)

E – probability of differentiation.

D – number of additional non-differentiating divisions which cell underwent before entering k-th compartment (failures, i.e cell failed to move to the next compartment).

So, $K + D$ is equal to the total number of cell divisions before k-compartment. D follows negative binomial distribution (in our case $P(D) = NBin$ is a probability of D failures (staying in the same compartment) before k successes (jumping into next compartment) occurred).

2.1.1 a

So, we know that expectation of $NBin$ distribution (i.e expected number of staying in the same compartment before reaching k-th compartment) can be calculated as follows:

$$E[D] = \sum_{d=0}^{\inf} dP(D=d) = \sum_{d=0}^{\inf} d \binom{k+d-1}{d} (1-\varepsilon)^d \varepsilon^k$$

$$\sum_{d=1}^{\inf} d \frac{(k+d-1)!}{d!(k-1)!}(1-\varepsilon)^d \varepsilon^k = \sum_{d=1}^{\inf} \frac{(k+d-1)}{(d-1)!(k-1)!}(1-\varepsilon)^d \varepsilon^k$$

$$k\frac{1-\varepsilon}{\varepsilon} \sum_{d=1}^{\inf} \frac{(k+d-1)!}{(d-1)!(k)!}(1-\varepsilon)^{d-1} \varepsilon^{k+1}$$

by change of variable $z = d-1$, we have:

$$E[D] = k\frac{1-\varepsilon}{\varepsilon} \sum_{z=0}^{\inf} \frac{k+z}{!} z!k!(1-\varepsilon)^z \varepsilon^{k+1} = k\frac{1-\varepsilon}{\varepsilon} \sum_{z=0}^{\inf} \binom{(k+1)+z-1}{z} (1-\varepsilon)^z \varepsilon^{k+1} = k\frac{1-\varepsilon}{\varepsilon}$$

So, for reaching $k = 30$ compartment (the last one, i.e to differentiate to a red blood cell) with e=0.85, we will expect the following number of identical divisions:

$$E[D] = k\frac{1-\varepsilon}{\varepsilon} = \frac{(30 \times (1-0.85))}{0.85} = 5.29$$

2.1.2 b

During the leukemia the self renewal probability $(1-e)$ increases by 15%, (so we can calculate a new $e = 0.827$) and in that case we will expect the following number of non-differentiated divisions till red blood cell formation:

$$E[D] = k\frac{1-\varepsilon}{\varepsilon} = \frac{(30 \times (1-0.827))}{0.827} = 6.25$$

To compute the number of leukemic cells, one should solve the following equation:

$$\frac{N_k}{N_{k-1}} = \frac{2\varepsilon}{2\varepsilon - 1} \times \frac{r_{k-1}}{r_k}$$

In the stationary condition, we assume $\frac{r_k}{r_{k-1}} = r$ and we can assume that r remains constant at $r = 1.27$ as claimed in (Dingli er al, *"Compartmental Architecture and Dynamics of Hematopoiesis"*, PlosOne, 2007, e345). Then:

$$\frac{N_k}{N_{k-1}} = \left(\frac{2\varepsilon}{2\varepsilon - 1} \times \frac{1}{r}\right)^k N_0 = N_k$$

$$\left(\frac{1.654}{0.654} * \frac{1}{1.27}\right)^{30} * 1 = N_{30} = 917,464,597$$

3.1 Treatment of chronic myeloid leukemia

4.1 One-dimensional Fokker-Planck equation

5.1 Diffusion approximation of the Moran process

6.1 Absorption time in the diffusion approximation