ENTROPY IN BIOLOGY

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Appendix to Lecture 12:

Analysis of the Laplace tranform of the probability density function for the binding time.

Appendix

Our asymptotic formula for $f(t)$ in the evaluation of k_{on}, equation (72), has the peculiar feature that the integral of $f(t)$ is infinite, even though $f(t)$ is supposed to be a probability density function.

Here, we would like to verify that the exact $f(t)$ actually does have integral 1, and we would also like to evaluate the mean time associated with it. The Laplace transform $\tilde{f}(s)$ is useful for both of these purposes, since

(A1) $$\int_0^\infty f(t)\,dt = \tilde{f}(0)$$

(A2) $$\int_0^\infty t\,f(t)\,dt = -\frac{d}{ds}\int_0^\infty e^{-st} f(t)\,dt\,\Big|_{s=0}$$

$$= -\frac{d\tilde{f}}{ds}(0)$$

Equations (A1) and (A2) show that we only need the constant and linear terms in the Taylor series for $\tilde{f}(s)$ about $s=0$ in order to evaluate the 0^{th} and 1^{st} moments of $f(t)$.

The formula (70) for $\tilde{f}(s)$ is exact. It involves the variable a, which is defined by the pair of equations (56-57). These equations are of the form

(A3) $$a \sinh \theta_0 - bL = \frac{r_0}{V} \frac{\lambda}{s(\lambda+s)}$$

(A4) $$a \theta_0 \cosh \theta_0 - bM = \frac{r_0}{V} \frac{\lambda}{s(\lambda+s)}$$

where

(A5) $$L = \psi \cosh(\psi - \psi_0) - \sinh(\psi - \psi_0)$$

(A6) $$M = \psi_0 \left(\cosh(\psi - \psi_0) - \psi \sinh(\psi - \psi_0) \right)$$

and where θ_0, ψ_0, ψ are given by (55).

Note that ψ_0 and ψ are both $O(\sqrt{s})$.

In the following we write Taylor series with as many terms as may be needed without explicitly noting the orders of the remainder terms.

Making use of the Taylor series for sinh and cosh, we get the following series for L and M:

(A7)
$$L = \psi\left(1 + \frac{1}{2}(\psi-\psi_0)^2 + \frac{1}{24}(\psi-\psi_0)^4\right) - \left(\psi-\psi_0 + \frac{1}{6}(\psi-\psi_0)^3 + \frac{1}{120}(\psi-\psi_0)^5\right)$$

$$= \psi_0 + \left(\frac{1}{2}\psi - \frac{1}{6}(\psi-\psi_0)\right)(\psi-\psi_0)^2 + \left(\frac{1}{24}\psi - \frac{1}{120}(\psi-\psi_0)\right)(\psi-\psi_0)^4$$

$$= \psi_0 + \frac{1}{3}\left(\psi+\frac{1}{2}\psi_0\right)(\psi-\psi_0)^2 + \frac{1}{30}\left(\psi+\frac{1}{4}\psi_0\right)(\psi-\psi_0)^4$$

(A8) $$M = \psi_0\left(\left(1 + \frac{1}{2}(\psi-\psi_0)^2 + \frac{1}{24}(\psi-\psi_0)^4\right)\right.$$
$$\left. - \psi\left((\psi-\psi_0) + \frac{1}{6}(\psi-\psi_0)^3\right)\right)$$
$$= \psi_0\left(1 + \left(\frac{1}{2}(\psi-\psi_0) - \psi\right)(\psi-\psi_0)\right.$$
$$\left. + \left(\frac{1}{24}(\psi-\psi_0) - \frac{1}{6}\psi\right)(\psi-\psi_0)^3\right)$$
$$= \psi_0\left(1 - \frac{1}{2}(\psi+\psi_0)(\psi-\psi_0)\right.$$
$$\left. - \frac{1}{8}\left(\psi + \frac{1}{3}\psi_0\right)(\psi-\psi_0)^3\right)$$
$$= \psi_0 - \frac{1}{2}\psi_0(\psi^2-\psi_0^2) - \frac{1}{8}\psi_0\left(\psi+\frac{1}{3}\psi_0\right)(\psi-\psi_0)^3$$

The three terms in the expressions for L, M that we have evaluated are

(A9) $$O(\sqrt{s}),\ O((\sqrt{s})^3),\ O((\sqrt{s})^5)$$

It will also be useful to evaluate L−M and we do this separately for each order.

The term that is $O(\sqrt{s})$ in L−M is

(A10) $$\psi_0 - \psi_0 = 0$$

The term that is $O((\sqrt{s})^3)$ is

(A11) $$\frac{1}{3}\left(\psi+\frac{1}{2}\psi_0\right)(\psi-\psi_0)^2 + \frac{1}{2}\psi_0(\psi+\psi_0)(\psi-\psi_0)$$

$$=\left(\frac{1}{3}\left(\psi+\frac{1}{2}\psi_0\right)(\psi-\psi_0)+\frac{1}{2}\psi_0\psi+\frac{1}{2}\psi_0^2\right)(\psi-\psi_0)$$

$$=\frac{1}{3}\left(\psi^2+\psi_0\psi+\psi_0^2\right)(\psi-\psi_0)$$

$$=\frac{1}{3}\left(\psi^3-\psi^2\psi_0+\psi^2\psi_0-\psi\psi_0^2+\psi\psi_0^2-\psi_0^3\right)$$

$$=\frac{1}{3}\left(\psi^3-\psi_0^3\right)$$

and the term that is $O\left((\sqrt{s})^5\right)$ is

(A12) $$\frac{1}{30}\left(\psi+\frac{1}{4}\psi_0\right)(\psi-\psi_0)^4+\frac{1}{8}\psi_0\left(\psi+\frac{1}{3}\psi_0\right)(\psi-\psi_0)^3$$

$$=\frac{1}{30}\left(\left(\psi+\frac{1}{4}\psi_0\right)(\psi-\psi_0)+\frac{15}{4}\psi_0\psi+\frac{5}{4}\psi_0^2\right)(\psi-\psi_0)^3$$

$$=\frac{1}{30}\left(\psi^2+3\psi_0\psi+\psi_0^2\right)(\psi-\psi_0)^3$$

Thus

(A13) $$L-M=\frac{1}{3}\left(\psi^3-\psi_0^3\right)+\frac{1}{30}\left(\psi^2+3\psi_0\psi+\psi_0^2\right)(\psi-\psi_0)^3$$

The solution of the pair of equations (A3-A4) for a is as follows:

$$(A14) \quad a = \frac{r_0}{V}\frac{\lambda}{s(\lambda+s)}\frac{L-M}{\Theta_0(\cosh\Theta_0)L - (\sinh\Theta_0)M}$$

To get first-order accuracy in s when evaluating this expression, we need both terms in the expression for $L-M$ that we have evaluated above, but in the denominator we only need the first two terms of L and the first two terms of M. This will become apparent as we proceed. Thus,

$$(A15) \quad a = \frac{r_0}{V}\frac{\lambda}{s(\lambda+s)}\frac{\frac{1}{3}(\psi^3-\psi_0^3) + \frac{1}{30}(\psi^2+3\psi\psi_0+\psi_0^2)(\psi-\psi_0)^3}{\psi_0\left(\Theta_0\cosh\Theta_0\left(1+\frac{1}{3}\left(\frac{\psi}{\psi_0}+\frac{1}{2}\right)(\psi-\psi_0)^2\right) - \sinh\Theta_0\left(1-\frac{1}{2}(\psi^2-\psi_0^2)\right)\right)}$$

Now recall from equation (55) that

(A16) $$\psi = \sqrt{\frac{S}{D}}\, R\,, \quad \psi_0 = \sqrt{\frac{S}{D}}\, r_0$$

Therefore, after canceling a factor of $(S/D)^{3/2}$ and also a factor of r_0, we get the following formula for a:

(A17) $$a =$$

$$\frac{1}{DV}\,\frac{\lambda}{\lambda+S}\;\frac{\frac{1}{3}\left(R^3-r_0^3\right)+\frac{S}{D}\,\frac{1}{30}\left(R^2+3Rr_0+r_0^2\right)\left(R-r_0\right)^3}{\left(\theta_0\left(\cosh\theta_0\right)\left(1+\frac{S}{D}\,\frac{1}{3}\left(\frac{R}{r_0}+\frac{1}{2}\right)\left(R-r_0\right)^2\right)-\left(\sinh\theta_0\right)\left(1-\frac{S}{D}\,\frac{1}{2}\left(R^2-r_0^2\right)\right)\right)}$$

and it follows that

(A18) $$4\pi a D (\theta_0 \cosh \theta_0 - \sinh \theta_0)$$

$$= \frac{\lambda}{\lambda + s} \left(1 - \frac{V_0}{V}\right) \frac{1 + s\tau_1}{1 + s\tau_2}$$

where

(A19) $$\tau_1 = \frac{1}{D} \frac{R^2 + 3Rr_0 + r_0^2}{10} \frac{4\pi}{3} \frac{(R - r_0)^3}{V - V_0}$$

(A20) $$\tau_2 = \frac{1}{D} \left(\frac{\theta_0 \cosh \theta_0}{\theta_0 \cosh \theta_0 - \sinh \theta_0} \frac{1}{3} \left(\frac{R}{r_0} + \frac{1}{2}\right) (R - r_0)^2 - \frac{\sinh \theta_0}{\theta_0 \cosh \theta_0 - \sinh \theta_0} \frac{1}{2} (R^2 - r_0^2) \right)$$

Also, let $\overline{\tau_2}$ be the same as τ_2 but with θ_0 replaced by $\overline{\theta_0}$. Recall that

(A21) $$\theta_0 = \sqrt{\frac{\lambda + s}{D}}\, r_0 \,, \quad \overline{\theta_0} = \sqrt{\frac{\lambda}{D}}\, r_0$$

So $\overline{\theta_0}$ is independent of s, and

(A22) $$\theta_0 = \overline{\theta_0} + O(s)$$

It follows that $\overline{\tau_2}$ is independent of s, and

(A23) $$\tau_2 = \overline{\tau_2} + O(s)$$

Substituting (A18) into equation (70) with τ_2 replaced by $\overline{\tau_2}$, we get the following result:

(A24) $$\tilde{f}(s) = \frac{\lambda}{\lambda + s}\left(\frac{V_0}{V} + \frac{\lambda}{\lambda + s}\left(1 - \frac{V_0}{V}\right)\frac{1 + s\tau_1}{1 + s\overline{\tau_2}}\right)$$

Equation (A24) is exact up to (but not including) terms of $O(s^2)$, and therefore it can be used to evaluate exactly the 0^{th} and 1^{st} moments of $f(t)$ by the recipes (A1) & (A2).

In this way, we get

(A25) $$\int_0^\infty f(t)\,dt = \tilde{f}(0) = 1$$

(A26) $$\int_0^\infty t\,f(t)\,dt = -\frac{d\tilde{f}}{ds}(0) =$$

$$\frac{1}{\lambda} + \left(1 - \frac{V_0}{V}\right)\left(\frac{1}{\lambda} + \overline{\tau}_2 - \tau_1\right)$$

Equation (A26) simplifies if we let $r_0 \to 0$ and $\lambda \to \infty$ but in such a way that $\overline{\theta}_0$ is constant. In this limit

(A27) $$\tau_1 \to \frac{1}{10}\,\frac{R^2}{D}$$

(A28) $$\overline{\tau}_2 \sim \frac{R^3}{3Dr_0\left(1 - \frac{\sinh\overline{\theta}_0}{\overline{\theta}_0\cosh\overline{\theta}_0}\right)}$$

$$= \frac{V}{4\pi D r_0\left(1 - \frac{\sinh\overline{\theta}_0}{\overline{\theta}_0\cosh\overline{\theta}_0}\right)}$$

Thus, in the limit that we are considering,

$$\int_0^\infty t\,f(t)\,dt \sim \frac{V}{4\pi D r_0\left(1 - \dfrac{\sinh \overline{\theta}_0}{\overline{\theta}_0 \cosh \overline{\theta}_0}\right)} \tag{A29}$$

and this is indeed the reciprocal of the expression (74) that we previously interpreted as the probability per unit time of binding.