To the Editor:

We are writing to you concerning the paper "Optimal Estimation of Cell Movement Indices from the Statistical Analysis of Cell Tracking Data" by Dickinson and Tranquillo.[1] In that article, a function Φ is defined in Eq. AII3 and a closed form is given in Eq. AII11. Although the mathematical derivation is well-thought out and elegant, a critical portion of the derivation—namely, Eq. AII5—is given without justification. Here, we calculate Φ and show that the resulting equation differs from Eq. AII11.

The model for random walks which is used in the aforementioned article is an unbiased correlated random walk model of the type that has been used to model many different types of biological movement.[2,3] Specifically, the velocity of the walk at each point in time is $\mathbf{v}(t)$, the speed has constant root-mean-square, and the angle $\theta\ (t)$ of the tangent line to the walk can be given by a Wiener process with variance σ^2. For the purposes of this letter, we consider a special case of such walks where the speed is constant: $\mathbf{v}(t) = S$.

The velocity autocorrelation function is $\langle \mathbf{v}(t_1)\mathbf{v}(t_2)\rangle = \langle S^2 \cos\ [\theta\ (t_1) - \theta\ (t_2)]\rangle$. We see that $\theta\ (t_1) - \theta\ (t_2)$ is distributed normally with mean 0 and variance $(t_2 - t_1)\sigma^2$ (as it is a Weiner process) thus, the above expected value calculation can be written explicitly:

$$\langle\cos[\theta(t_1) - \theta(t_2)]\rangle = \frac{1}{\sigma\sqrt{2\pi(t_2 - t_1)}} \times \int_{-\infty}^{+\infty} e^{-x^2/[2\sigma^2(t_2-t_1)]} \cos x dx \qquad (1)$$

Computing this integral gives: $\langle \mathbf{v}(t_1)\mathbf{v}(t_2)\rangle = S^2 e^{-\sigma^2(t_2-t_1)/2}$. The quantity $P = 2/\sigma^2$ is known as the persistence time.[3] By extending this idea (computing the expected value integral), it is possible to derive a closed form solution for Φ. Consider the first term in Eq. A113. Again, as the speed is constant, we have:

$$\langle[\mathbf{v}(t_1)\mathbf{v}(t_2)][\mathbf{v}(t_3)\mathbf{v}(t_4)]\rangle = S^4\langle\cos[\theta(t_1)-\theta(t_2)]\cos[\theta(t_3)-\theta(t_4)]\rangle \qquad (2)$$

For notational simplicity, we will use the following shorthand: $\Psi = \langle\cos[\theta\ (t_1) - \theta\ (t_2)] \times \cos\ [\theta\ (t_3) - \theta\ (t_4)]\rangle$. For calculating Φ, we first notice that if $t_3 > t_2$, then the velocity autocorrelations are statistically independent and thus Φ vanishes. As a representative example for a nonvanishing case, consider the case where $t_1 < t_3 < t_2 < t_4$ (henceforth known as case A). This corresponds to Eq. AII6 in the Dickinson and Tranquillo article. Rotate into the coordinate frame where the curve angle at time t_1 is zero, that is, denote by $\phi_i + \theta_1$ the angle the curve takes at point t_i. Thus, in this case, we may rewrite Ψ as: $\langle\cos\ (\phi_2)\cos\ (\phi_4 - \phi_3)\rangle$. We, therefore, want to calculate the expected value of $\cos\ (\phi_2)\cos\ (\phi_4 - \phi_3)$, given that the first and second intervals overlap by $t_2 - t_3$. To calculate this expected value, we may integrate over all curves:

$$\Psi_A = \int_{-\infty}^{+\infty} d\phi_3 \int_{-\infty}^{+\infty} d\phi_2 \int_{-\infty}^{+\infty} \mathbf{P}_A(\phi_3, \phi_2, \phi_4)\cos(\phi_2)\cos(\phi_4 - \phi_3)d\phi_4 \qquad (3)$$

where $\mathbf{P}_A$ symbolically represents the probability that the curve will have rotated by angle ϕ_3 after time t_3, ϕ_2 after time t_2, and ϕ_4 after time t_4.

Performing this integration yields:

$$\Psi_A(t_1, t_2, t_3, t_4; P) = \frac{1}{2}\left(e^{2\,\sigma^2\,t_3+\frac{\sigma^2\,t_1}{2}} + e^{2\,\sigma^2\,t_2+\frac{\sigma^2\,t_1}{2}}\right) \times e^{-\frac{\sigma^2}{2}(t_4+t_3+3\,t_2)} \qquad (4)$$

Using a similar procedure as above for the other cases (B, C, and D), we obtain the general formula for when $\tau_1 < \tau_2 < \tau_3 < \tau_4$ (using the fact that $P = 2/\sigma^2$ to simplify Ψ):

$$\Psi(\tau_1, \tau_3, \tau_2, \tau_4; P) = e^{(\tau_1-3\,\tau_3+3\,\tau_2-\tau_4)/P} + e^{-(\tau_2-\tau_1+\tau_4-\tau_3)/P} \qquad (5)$$

Now multiply Ψ by S^4 and add in the second term in Eq. AII3 to obtain the full form of Φ. It can easily be seen that this is markedly different from the form given in Ref. 1 which is $\Phi = S^4 e^{-(\tau_4-\tau_1)/P}[e^{(\tau_3-\tau_2)/P} - e^{-(\tau_3-\tau_2)/P}]$.

Literature Cited

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