

Perturbative solution of the generating function for small f_0

We are interested in the linkage equilibrium statistic $\Lambda(f_0)$, defined as

$$\Lambda(f_0) \equiv \frac{\left\langle f_{ab}f_{Ab}f_{aB}f_{AB} \cdot e^{-\frac{f_A+f_B}{f_0}} \right\rangle}{\left\langle f_A^2(1-f_A)^2 f_B^2(1-f_B)^2 \cdot e^{-\frac{f_A+f_B}{f_0}} \right\rangle}, \quad (1)$$

where $f_A \equiv f_{Ab} + f_{aB}$, $f_B \equiv f_{aB} + f_{AB}$ and $f_A, f_B \lesssim f_0$. In the limit that $f_{Ab}, f_{aB}, f_{AB} \ll 1$,

$$\Lambda(f_0) \approx \frac{\left\langle f_{Ab}f_{aB}f_{AB} \cdot e^{-\frac{f_A+f_B}{f_0}} \right\rangle}{\left\langle f_A^2 f_B^2 \cdot e^{-\frac{f_A+f_B}{f_0}} \right\rangle}. \quad (2)$$

The moments follows from

$$\left\langle f_{Ab}^i f_{aB}^j f_{AB}^k \cdot e^{-\frac{f_A+f_B}{f_0}} \right\rangle = -f_0^{(i+j+k)} \partial_x^i \partial_y^j \partial_z^k H(x, y, z, t) \Big|_{\substack{x=1 \\ y=1 \\ z=2 \\ t=\infty}}, \quad (3)$$

where

$$H(x, y, z, t) \equiv \left\langle e^{-x \frac{f_{Ab}(t)}{f_0} - y \frac{f_{aB}(t)}{f_0} - z \frac{f_{AB}(t)}{f_0}} \right\rangle \quad (4)$$

is the joint moment generating function.

In the limit that $\theta = 2N\mu$ and f_0 are both small compared to one,

$$H(x, y, z, \tau) \approx 1 - \theta(H_A + H_B) + \frac{\theta^2}{2} (H_A + H_B)^2 \quad (5)$$

$$+ \theta^2 f_0 \Upsilon + \theta^2 f_0 \int_0^\tau d\tau' z(\tau') [\Phi_x(\tau') + \Phi_y(\tau') - \rho \Phi_x(\tau') \Phi_y(\tau')] \\ + \mathcal{O}(f_0^2) + \mathcal{O}(\theta^3),$$

where $\tau = t/2Nf_0$, $\gamma_A = 2Ns_A f_0$, $\gamma_B = 2Ns_B f_0$, $\rho = 2NRf_0$, and

$$H_A(x, \tau) \equiv \ln \left[1 + \frac{x(1 - e^{-\gamma_A \tau})}{\gamma_A} \right], \quad (6a)$$

$$H_B(y, \tau) \equiv \ln \left[1 + \frac{y(1 - e^{-\gamma_B \tau})}{\gamma_B} \right], \quad (6b)$$

$$\Phi_x(\tau') \equiv -\frac{[1 - e^{-\gamma_A(\tau - \tau')}] [\gamma_A + x(1 - e^{-\gamma_A \tau})]}{\gamma_A [\gamma_A + x(1 - e^{-\gamma_A \tau})]}, \quad (7a)$$

$$\Phi_y(\tau') \equiv -\frac{[1 - e^{-\gamma_B(\tau - \tau')}] [\gamma_B + y(1 - e^{-\gamma_B \tau'})]}{\gamma_A [\gamma_B + y(1 - e^{-\gamma_B \tau})]}, \quad (7b)$$

$$\Upsilon(x, y, \tau) = \int_0^\tau d\tau' \rho [x(\tau') + y(\tau')] \Phi_x(\tau') \Phi_y(\tau'). \quad (8)$$

The characteristic $z(\tau')$ is defined by

$$\partial_{\tau'} z(\tau') = -(\gamma_{AB} + \rho)z(\tau') - z^2(\tau') + \rho \frac{\gamma_A x e^{-\gamma_A \tau'}}{\gamma_A + x(1 - e^{-\gamma_A \tau'})} + \rho \frac{\gamma_B y e^{-\gamma_B \tau'}}{\gamma_B + y(1 - e^{-\gamma_B \tau'})} \quad (9)$$

with the initial condition $z(0) = z$, where γ_{AB} is the rescaled fitness of the double mutant.

Perturbative solution for $\Lambda(f_0)$ for neutral loci and weak recombination

In the absence of recombination, the equation above has an exact solution,

$$z_0(\tau') = \frac{\gamma_{AB} z e^{-\gamma_{AB} \tau'}}{\gamma_{AB} + z(1 - e^{-\gamma_{AB} \tau'})}. \quad (10)$$

In the limit that $\rho \ll 1$, corrections to the zeroth-order solution can be found by perturbatively expanding $z(\tau')$ as

$$z(\tau') \approx z_0(\tau') + \sum_{i=1}^{\infty} \rho^i z_i(\tau'). \quad (11)$$

Plugging the series expansion in the equation for $z(\tau')$ and matching the coefficients in front powers of ρ , we obtain for the first-order correction

$$\partial_{\tau'} z_1(\tau') \approx -\gamma_{AB} z_1(\tau') - 2z_0(\tau') z_1(\tau') - z_0(\tau') + \frac{\gamma_A x e^{-\gamma_A \tau'}}{\gamma_A + x(1 - e^{-\gamma_A \tau'})} + \frac{\gamma_B y e^{-\gamma_B \tau'}}{\gamma_B + y(1 - e^{-\gamma_B \tau'})}. \quad (12)$$

In the neutral limit, the equation above reduces to

$$\partial_{\tau'} z_1(\tau') \approx -\frac{2z}{1 + z\tau'} z_1(\tau') - \frac{z}{1 + z\tau'} + \frac{x}{1 + x\tau'} + \frac{y}{1 + y\tau'}. \quad (13)$$

This inhomogeneous linear ordinary differential equation can be solved by the method of variation of constants. The corresponding homogeneous equation

$$\partial_{\tau'} z_1(\tau') \approx -\frac{2z}{1 + z\tau'} z_1(\tau') \quad (14)$$

has solution in the form

$$z_1(\tau') \approx \frac{\phi(\tau')}{(1+z\tau')^2}, \quad (15)$$

where $\phi(\tau')$ is some function of τ' . Plugging Eq. (15) into Eq. (13), we obtain

$$\partial_{\tau'} \phi(\tau') \approx -z(1+z\tau') + \frac{x(1+z\tau')^2}{1+x\tau'} + \frac{y(1+z\tau')^2}{1+y\tau'}, \quad (16)$$

from where

$$\begin{aligned} \phi(\tau') &\approx - \int z(1+z\tau') d\tau' + \int \frac{x(1+z\tau')^2}{1+x\tau'} d\tau' + \int \frac{y(1+z\tau')^2}{1+y\tau'} d\tau' \\ &= \frac{1}{2}(1+z\tau')^2 + z\tau' \left(1 - \frac{z}{x}\right) + z\tau' \left(1 - \frac{z}{y}\right) \\ &\quad + \left(1 - \frac{z}{x}\right)^2 \ln(1+x\tau') + \left(1 - \frac{z}{y}\right)^2 \ln(1+y\tau') + C, \end{aligned} \quad (17)$$

where

$$C = \frac{1}{2} \quad (18)$$

is a constant determined by the initial condition $\phi(0) = 0$. Then,

$$\begin{aligned} z_1(\tau') &\approx \frac{1}{2} + \frac{1}{2} \frac{1}{(1+z\tau')^2} + \left(1 - \frac{z}{x}\right) \frac{z\tau'}{(1+z\tau')^2} + \left(1 - \frac{z}{y}\right) \frac{z\tau'}{(1+z\tau')^2} \\ &\quad + \left(1 - \frac{z}{x}\right)^2 \frac{\ln(1+x\tau')}{(1+z\tau')^2} + \left(1 - \frac{z}{y}\right)^2 \frac{\ln(1+y\tau')}{(1+z\tau')^2}. \end{aligned} \quad (19)$$

Substituting Eq. (19) into Eq. (11), we find

$$\begin{aligned} z(\tau') &\approx \frac{z}{1+z\tau'} + \frac{\rho}{2} + \frac{\rho}{2} \frac{1}{(1+z\tau')^2} \\ &\quad + \rho \left(1 - \frac{z}{x}\right) \frac{z\tau'}{(1+z\tau')^2} + \rho \left(1 - \frac{z}{y}\right) \frac{z\tau'}{(1+z\tau')^2} \\ &\quad + \rho \left(1 - \frac{z}{x}\right)^2 \frac{\ln(1+x\tau')}{(1+z\tau')^2} + \rho \left(1 - \frac{z}{y}\right)^2 \frac{\ln(1+y\tau')}{(1+z\tau')^2}. \end{aligned} \quad (20)$$

Thus, to the lowest order in ρ , the numerator of $\Lambda(f_0)$ follows as

$$\left\langle f_{Ab} f_{aB} f_{AB} \cdot e^{-\frac{f_A + f_B}{f_0}} \right\rangle \approx -\rho \theta^2 f_0^4 \left[- \int_0^\tau d\tau' \partial_x \Phi_x \partial_y \Phi_y \partial_z \frac{z}{1+z\tau'} \right] \quad (21)$$

$$\begin{aligned}
& - \int_0^\tau d\tau' \partial_x \Phi_x \partial_y \partial_z \frac{z}{y} \frac{z\tau'}{(1+z\tau')^2} \\
& - \int_0^\tau d\tau' \partial_y \Phi_y \partial_x \partial_z \frac{z}{x} \frac{z\tau'}{(1+z\tau')^2} \\
& + \int_0^\tau d\tau' \partial_x \Phi_x \partial_y \partial_z \left(1 - \frac{z}{y}\right)^2 \frac{\ln(1+y\tau')}{(1+z\tau')^2} \\
& + \int_0^\tau d\tau' \partial_y \Phi_y \partial_x \partial_z \left(1 - \frac{z}{x}\right)^2 \frac{\ln(1+x\tau')}{(1+z\tau')^2} \Bigg|_{\substack{x=1 \\ y=1 \\ z=2 \\ \tau=\infty}},
\end{aligned}$$

where

$$\partial_x \Phi_x \Bigg|_{\substack{x=1 \\ \tau=\infty}} = - \frac{(\tau - \tau')^2}{(1+x\tau')^2} \Bigg|_{\substack{x=1 \\ \tau=\infty}} = 1, \quad (22a)$$

$$\partial_y \Phi_y \Bigg|_{\substack{y=1 \\ \tau=\infty}} = - \frac{(\tau - \tau')^2}{(1+y\tau')^2} \Bigg|_{\substack{y=1 \\ \tau=\infty}} = 1. \quad (22b)$$

The first integral in Eq. (21) evaluates to

$$- \int_0^\tau d\tau' \partial_x \Phi_x \partial_y \Phi_y \partial_z \frac{z}{1+z\tau'} \Bigg|_{\substack{x=1 \\ y=1 \\ z=2 \\ \tau=\infty}} = - \int_0^\infty \frac{1}{(1+2\tau')^2} d\tau = -\frac{1}{2}. \quad (23)$$

The second (and third) integral in Eq. (21) can be evaluated as

$$- \int_0^\tau d\tau' \partial_x \Phi_x \partial_y \partial_z \frac{z}{y} \frac{z\tau'}{(1+z\tau')^2} \Bigg|_{\substack{x=1 \\ y=1 \\ z=2 \\ \tau=\infty}} = \int_0^\infty \frac{4\tau'}{(1+2\tau')^3} d\tau' = \frac{1}{2}. \quad (24)$$

Finally, we find the last (and the second to last) integral in Eq. (21) as

$$\int_0^\tau d\tau' \partial_y \Phi_y \partial_x \partial_z \left(1 - \frac{z}{x}\right)^2 \frac{\ln(1+x\tau')}{(1+z\tau')^2} \Bigg|_{\substack{x=1 \\ y=1 \\ z=2 \\ \tau=\infty}} = \int_0^\tau \frac{2\tau' - 2(3+2\tau') \ln(1+\tau')}{(1+2\tau')^3} d\tau' = -\frac{3}{4}. \quad (25)$$

Substituting Eq. (23), Eq. (24), and Eq. (25) into Eq. (21), we obtain

$$\left\langle f_{Ab}f_{aB}f_{AB} \cdot e^{-\frac{f_A+f_B}{f_0}} \right\rangle \approx -\rho\theta^2 f_0^4 \left[-\frac{1}{2} + \frac{1}{2} + \frac{1}{2} - \frac{3}{4} - \frac{3}{4} \right] = \rho\theta^2 f_0^4. \quad (26)$$

To the lowest order in θ , f_0 , and ρ , the denominator of $\Lambda(f_0)$ can be found as

$$\left\langle f_A^2 f_B^2 \cdot e^{-\frac{f_A+f_B}{f_0}} \right\rangle \approx \theta^2 f_0^4 \partial_x^2 \partial_y^2 H_A H_B \Big|_{\substack{x=1 \\ y=1 \\ \tau=\infty}} = \theta^2 f_0^4 \frac{1}{x^2 y^2} \Big|_{\substack{x=1 \\ y=1}} = \theta^2 f_0^4. \quad (27)$$

Thus, in the neutral limit for small ρ , $\Lambda(f_0) \approx \rho$.

Perturbative solution for $\Lambda(f_0)$ for strong selection or recombination

In the limit that γ_{AB} or ρ are large compared to one, we can rescale time in Eq. (9) so that

$$\partial_u z(u) = -z(u) - \epsilon z^2(u) + \alpha f(u) \quad (28)$$

with the initial condition $z(0) = z$, where $u = \tau'/\epsilon$ is the rescaled time, $\epsilon = 1/(\gamma_{AB} + \rho)$, $\alpha = \epsilon\rho$, $\beta_A = \epsilon\gamma_A$, $\beta_B = \epsilon\gamma_B$, and

$$f(u) = \frac{\beta_A x e^{-\beta_A u}}{\beta_A + \epsilon x (1 - e^{-\beta_A u})} + \frac{\beta_B y e^{-\beta_B u}}{\beta_B + \epsilon y (1 - e^{-\beta_B u})}. \quad (29)$$

We can solve Eq. (28) using a perturbation expansion in ϵ , defining

$$z(u) \approx \sum_{i=0}^{\infty} \epsilon^i z_i(u) \quad (30a)$$

and

$$f(u) \approx \sum_{i=0}^{\infty} \epsilon^i f_i(u). \quad (30b)$$

At zeroth order,

$$\partial_u z_0(u) = -z_0(u) + \alpha f_0(u) \quad (31)$$

with the initial condition $z_0(0) = z$ and hence

$$z_0(u) = ze^{-u} + \alpha e^{-u} \int_0^u e^{u'} f_0(u') du'. \quad (32)$$

At first order in ϵ ,

$$\partial_u z_1(u) = -z_1(u) - z_0^2(u) + \alpha f_1(u) \quad (33)$$

with the initial condition $z_1(0) = 0$ and hence

$$z_1(u) = \alpha e^{-u} \int_0^u e^{u'} f_1(u') du' - e^{-u} \int_0^u e^{u'} z_0^2(u') du'. \quad (34)$$

If $\gamma_A, \gamma_B \gg 1$, then the first two terms in Eq. (30b) can be found as

$$f_0(u) = xe^{-\beta_A u} + ye^{-\beta_B u} \quad (35)$$

and

$$f_1(u) = -x^2 \frac{1}{\beta_A} e^{-\beta_A u} (1 - e^{-\beta_A u}) - y^2 \frac{1}{\beta_B} e^{-\beta_B u} (1 - e^{-\beta_B u}). \quad (36)$$

Hence

$$z_0(u) = ze^{-u} - \frac{\alpha x}{1 - \beta_A} (e^{-u} - e^{-\beta_A u}) - \frac{\alpha y}{1 - \beta_B} (e^{-u} - e^{-\beta_B u}) \quad (37)$$

and

$$\begin{aligned} z_1(u) = & \frac{\alpha x^2}{\beta_A(1 - \beta_A)} (e^{-u} - e^{-\beta_A u}) - \frac{\alpha x^2}{\beta_A(1 - 2\beta_A)} (e^{-u} - e^{-2\beta_A u}) \\ & + \frac{\alpha y^2}{\beta_B(1 - \beta_B)} (e^{-u} - e^{-\beta_B u}) - \frac{\alpha y^2}{\beta_B(1 - 2\beta_B)} (e^{-u} - e^{-2\beta_B u}) \\ & + \left[z - \frac{\alpha x}{1 - \beta_A} - \frac{\alpha y}{1 - \beta_B} \right]^2 (e^{-2u} - e^{-u}) \\ & + \left[z - \frac{\alpha x}{1 - \beta_A} - \frac{\alpha y}{1 - \beta_B} \right] \left[\frac{2\alpha x}{\beta_A(1 - \beta_A)} (e^{-u(1+\beta_A)} - e^{-u}) + \frac{2\alpha y}{\beta_B(1 - \beta_B)} (e^{-u(1+\beta_B)} - e^{-u}) \right] \\ & - \frac{\alpha^2 x^2}{(1 - \beta_A)^2(1 - 2\beta_A)} (e^{-2\beta_A u} - e^{-u}) - \frac{\alpha^2 y^2}{(1 - \beta_B)^2(1 - 2\beta_B)} (e^{-2\beta_B u} - e^{-u}) \\ & - \frac{2\alpha^2 xy}{(1 - \beta_A)(1 - \beta_B)(1 - \beta_A - \beta_B)} (e^{-(\beta_A + \beta_B)u} - e^{-u}). \end{aligned} \quad (38)$$