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Supplemental information

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Supporting Materials

A reduced 1D stochastic model of bleb-driven cell migration

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S.1 Effect of parameters on total bleb displacement

Here, we include further studies on the parametric dependence of bleb events, with a focus on the total displacement per bleb event. The table below shows how the travel distance depends on D_g and K_m. When K_m is large, we expect that the protrusion formed in the membrane by that pressure when the adhesions are removed will be large, while if the hydrostatic pressure in the cell is low, the membrane expansion will be small. We find that while larger values of K_m lead to greater distances traveled, the bleb size actually decreases. If K_m is too small, the system becomes non-blebbing, while if K_m is too large, a secondary bleb is generated at the back. K_m can be interpreted as hydrostatic pressure inside the cell pushing the membrane outward.

Figure 1 plots is the color map of the distance traveled per bleb event. In general, as γ_m is increased the travel distance per bleb event is increased. It should be noted, however, that these changes are not that large, amounting to about a 10% difference over the parametric range.

Table 1: Predicted Effect of Biophysical Parameters on the Distance Traveled

Perturbation	Parameter	Effect on Distance Traveled
Increase drag	$D_g \uparrow$	Decrease
Increase hydrostatic pressure	$K_m \uparrow$	Increase

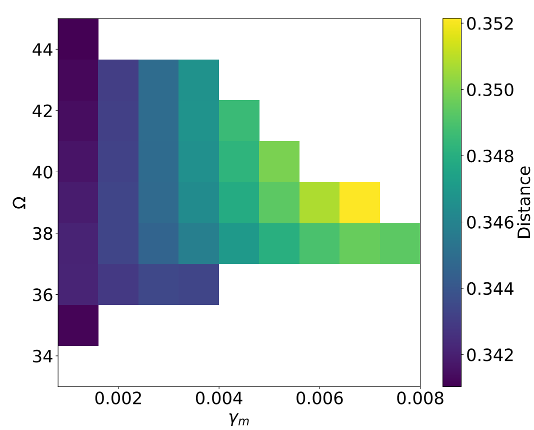

Figure 1: Traveling distance as Ω and γ_m change. Other parameters are the same as Fig. 2 of the main text. Note that only the excitable regime as plotted in Figure 4 of the main text is relevant for travel distance per bleb event.

S.2 Derivation of the asymptotic approximation process

A single bleb event consists of two random variables: the inter-blebbing time Δ and the traveling distance Q. Let us label the bleb events by $n = 1, 2, \cdots$. We determine the distribution information of the renewal process in terms of the gamma distributions. Introducing the blebbing time

$$T_n = T_{n-1} + \Delta_n, \quad T_0 = 0,$$

then one can write the renewal process by

$$X(t) = \sum_{T_n \leq t} Q_n H(t - T_n), \tag{1}$$

where $H(t)$ is the Heaviside function giving one if $t > 0$ otherwise zero. For given $T_1 = \Delta_1 = \tau_1$ and $Q_1 = \eta_1$, we have

$$X(t) = \begin{cases} 0, & t < \tau_1 \\ \eta_1 + X^*(t - \tau_1), & t \geq \tau_1 \end{cases}, \tag{2}$$

where $X^*(t)$ is identical with $X(t)$. Thus, applying the conditional expectation theorem gives

$$\begin{aligned} M_X(\xi, t) &:= \mathbb{E}[e^{\xi X(t)}] = \mathbb{E}\left[\mathbb{E}[e^{\xi X(t)} | T_1 = \tau_1, Q_1 = \eta_1]\right] \\ &= \int_t^\infty f_\Delta(\tau) d\tau + \mathbb{E}\left[1_{\tau_1 \leq t} \mathbb{E}[e^{\xi Q_1} e^{\xi X^*(t - T_1)} | T_1 = \tau_1, Q_1 = \eta_1]\right]. \end{aligned} \tag{3}$$

Since Q_1 and T_1 are independent, we have

$$M_X(\xi, t) = \int_t^\infty f_\Delta(\tau) d\tau + M_Q(\xi) \int_0^t M_X(\xi, t - \tau) f_\Delta(\tau) d\tau. \tag{4}$$

Since the moments of the approximation process satisfies

$$\mathcal{M}_k(t) := \mathbb{E}[X^k(t)] = \left.\frac{\partial^k M_X(\xi, t)}{\partial \xi^k}\right|_{\xi = 0},$$

for $k = 1, 2, \cdots$, taking derivatives with respect to ξ gives

$$\mathcal{M}_k(t) = \sum_{j=0}^{k} \mathbb{E}[Q^{k-j}] \int_0^t \mathcal{M}_j(t - \tau) f_\Delta(\tau) d\tau. \tag{5}$$

The time-averaged moments of the approximation process can be calculated by performing a Laplace transformation. Taking the Laplace transform of Eq. 5

$$\widetilde{\mathcal{M}}_k(s) = \widetilde{f}_\Delta(s) \sum_{j=0}^{k} \binom{k}{j} \mathbb{E}[Q^{k-j}] \widetilde{\mathcal{M}}_j(s), \tag{6}$$

and solving for $\widetilde{\mathcal{M}}_k(s)$ yields

$$\widetilde{\mathcal{M}}_k(s) = \frac{\widetilde{f}_\Delta(s)}{1 - \widetilde{f}_\Delta(s)} \left(\sum_{j=1}^{k-1} \binom{k}{j} \mathbb{E}[Q^{k-j}] \widetilde{\mathcal{M}}_j(s) + \frac{\mathbb{E}[Q^k]}{s} \right), \tag{7}$$

in accordance with $\widetilde{\mathcal{M}}_0(s) = s^{-1}$. In particular, the first moment takes the form

$$\widetilde{\mathcal{M}}_1(s) = \frac{\mathbb{E}[Q] \widetilde{f}_\Delta(s)}{s\left(1 - \widetilde{f}_\Delta(s)\right)}. \tag{8}$$

Performing integration by parts and l'Hospital rule yields

$$\begin{aligned} \lim_{t \to \infty} \frac{\mathcal{M}_1(t)}{t} &= \lim_{s \to 0} s \int_s^\infty \widetilde{\mathcal{M}}_1(s') ds' \\ &= \lim_{s \to 0} s^2 \widetilde{\mathcal{M}}_1(s). \end{aligned} \tag{9}$$

Substituting Eq. 8 into the above equation and another application of the l'Hospital rule gives

$$\lim_{t\to\infty}\frac{\mathcal{M}_1(t)}{t} = \mathbb{E}[Q]\lim_{s\to 0}\frac{s\widetilde{f}_\Delta(s)}{\left(1-\widetilde{f}_\Delta(s)\right)} = \mathbb{E}[Q]\lim_{s\to 0}\frac{\widetilde{f}_\Delta(s)+s\widetilde{f}'_\Delta(s)}{-\widetilde{f}'_\Delta(s)} = \frac{\mathbb{E}[Q]}{\mathbb{E}[\Delta]} := v_\infty, \tag{10}$$

according to the fact that

$$\widetilde{f}'_\Delta(s) = -\int_0^\infty t f_\Delta(t)e^{-st}dt \to -\mathbb{E}[\Delta],$$

as $s\to 0$. One can also calculate the asymptotic limit of the variance of the approximation process. Similar to Eq. 9, we have

$$\lim_{t\to\infty}\frac{\mathbb{E}[(X(t)-v_\infty t)^2]}{t} = \lim_{t\to\infty}\frac{\mathcal{M}_2(t)-(v_\infty t)^2}{t} - 2v_\infty\left(\mathcal{M}_1(t)-v_\infty t\right) = \lim_{s\to 0}s^2\left(\widetilde{\mathcal{M}}_2(s)-\frac{2v_\infty^2}{s^3}\right) - 2v_\infty s\left(\widetilde{\mathcal{M}}_1(s)-\frac{v_\infty}{s^2}\right). \tag{11}$$

Substituting the Laplace transform of the second moment

$$\widetilde{\mathcal{M}}_2(s) = \frac{1}{s}\left[\frac{\mathbb{E}[Q^2]\;\widetilde{f}_\Delta(s)}{1-\widetilde{f}_\Delta(s)} + 2\left(\frac{\mathbb{E}[Q]\widetilde{f}_\Delta(s)}{1-\widetilde{f}_\Delta(s)}\right)^2\right], \tag{12}$$

into Eq. 11 and performing l'Hospital rules yields

$$\lim_{t\to\infty}\frac{\mathcal{M}_2(t)-(v_\infty t)^2}{t} = \lim_{s\to 0}s\left[\frac{\mathbb{E}[Q^2]\;\widetilde{f}_\Delta(s)}{1-\widetilde{f}_\Delta(s)} + 2\left(\frac{\mathbb{E}[Q]\widetilde{f}_\Delta(s)}{1-\widetilde{f}_\Delta(s)}\right)^2\right] - \frac{2v_\infty^2}{s} = \frac{\mathbb{E}[Q^2]+2v_\infty^2\left(\mathbb{E}[\Delta^2]-2\mathbb{E}[\Delta]^2\right)}{\mathbb{E}[\Delta]}. \tag{13}$$

Similarly, one can determine the limit of the second term of Eq. 11

$$\lim_{t\to\infty}\mathcal{M}_1(t)-v_\infty t = \lim_{s\to 0}\frac{\mathbb{E}[Q]\widetilde{f}_\Delta(s)}{1-\widetilde{f}_\Delta(s)} - \frac{\mathbb{E}[Q]}{s\mathbb{E}[\Delta]} = \frac{v_\infty(\mathbb{E}[\Delta^2]-2\mathbb{E}[\Delta]^2)}{2\mathbb{E}[\Delta]}. \tag{14}$$

Substituting Eqs. 13 and 14 into Eq. 11, we finally have the asymptotic variance

$$\lim_{t\to\infty}\frac{\mathbb{E}[(X(t)-v_\infty t)^2]}{t} = \frac{\mathbb{E}[Q^2]+2v_\infty^2\left(\mathbb{E}[\Delta^2]-2\mathbb{E}[\Delta]^2\right)}{\mathbb{E}[\Delta]} - 2v_\infty\cdot\frac{v_\infty(\mathbb{E}[\Delta^2]-2\mathbb{E}[\Delta]^2)}{2\mathbb{E}[\Delta]} = \frac{\mathrm{Var}[Q]+v_\infty^2\mathrm{Var}[\Delta]}{\mathbb{E}[\Delta]} := \sigma_\infty^2. \tag{15}$$