S1 Supplemental methods

Derivation of time-dependent mechanical parameters

Our primary concern is to obtain an expression for $r_1(t)$ and $r_2(t)$ used to formulate the time dependent mechanical parameter $\tau_y(t), \tau_c(t)$ and $k_b(t)$ of the 1D model. Let $a_{bleb}(t)$ and $a_{scar}(t)$ denote the actin concentration in the developing and old cortex at any time and a_0 the concentration of actin the mature cortex. Then we set $r_1(t) = \frac{a_{bleb}(t)}{a_0}$ and $r_2(t) = \left(1 - \frac{a_{scar}(t)}{a_0}\right)$. The expression for $r_1(t)$ is precisely the fraction of actin in the developing cortex at any time. The expression for $r_2(t)$ represents the fraction of actin lost in the degrading cortex, which correlates positively with the viscosity of the fluid within the bleb. It remains to obtain expressions for the actin concentration in the bleb cortex $a_{bleb}(t)$ and actin scar $a_{scar}(t)$.

Recently, we introduced the following linear model for actin a(t) and myosin m(t) dynamics during reformation of the bleb cortex and degradation of the actin scar [1],

$$\begin{aligned} \frac{da}{dt} &= k_a^{on} - k_a^{off} a(t), \\ \frac{dm}{dt} &= k_m^{on} a(t) - k_m^{off} m(t). \end{aligned} \tag{S1}$$

The model parameters were estimated using blebbing data from *Dictyostelium discoideum* cells migrating under the same experimental conditions used to obtain the data presented in this work. Here, k_a^{on}, k_a^{off} describe the polymerization and depolymerization rates of actin in the cortex. The estimated model parameters differ between reformation of the bleb cortex and degradation of the actin scar. Hence, we will denote the respective rates at the bleb cortex by $k_{ab}^{on}, k_{ab}^{off}$ and those at the actin scar by $k_{as}^{on}, k_{as}^{off}$. Whereas this model fits the experimental data on actin and myosin concentration in the reforming bleb cortex well, it was only able to capture the major trends of actin and myosin concentration in the degrading actin scar [1]. Nevertheless, the simplicity in the decoupling of actin dynamics from myosin make this an attractive model for estimating the relative concentration of actin in the bleb cortex and actin scar.

Solving for the actin concentration $a(t)$ from Eq. S1 we obtain

$$a(t) = \frac{k_{ab}^{on}}{k_{ab}^{off}} + \left(a(0) - \frac{k_{ab}^{on}}{k_{ab}^{off}} \right) e^{-k_{ab}^{off} t}$$

where $a(0)$ is the initial density of actin in the reforming cortex and $\frac{k_{ab}^{on}}{k_{ab}^{off}}$ is the equilibrium density of actin (referred to elsewhere as a_{rest}). At the reforming bleb cortex $a(0) = 0$, thus the relative actin density there is given by

$$a_{bleb}(t) = \frac{k_{ab}^{on}}{k_{ab}^{off}} (1 - e^{-k_{ab}^{off} t}). \tag{S2}$$

At the degrading actin scar $a(0) = a_0 \neq 0$. Our estimated value for k_{as}^{on} was near zero in [1]. Setting $k_{as}^{on} = 0$, we obtain the actin density

$$a_{scar}(t) = a_0 e^{-k_{as}^{off} t}$$

in the degrading actin scar.

S1.1 Steady-state analysis

The motivation for this section is two fold. First, we will determine the critical displacement u^0 and linker density ρ_a^0 necessary for initializing bleb expansion in the 1D model. Since bleb expansion is expected to stall over time, we will follow this analysis with an investigation of the parameters that control the steady-state bleb size.

Critical displacement and linker density

The initial conditions for our 1D bleb expansion model are the critical displacement u^0 and critical linker density ρ_a^0.To calculate these values, we set $\dot{u}(t) = 0$ and $\dot{\rho}_a(t) = 0$ in the 1D bleb expansion model

$$\frac{du}{dt} = \frac{F_{1D}}{(\tau_c + \tau_y)} - \frac{(k_b + k_a\rho_a)}{(\tau_c + \tau_y)}u \tag{S3}$$

$$\frac{d\rho_a}{dt} = k_{on}(\rho_0 - \rho_a) - k_{off}(u(t))\rho_a \tag{S4}$$

with all mechanical parameters fixed. This yields

$$\frac{F_{1D}}{\tau_c + \tau_y} - \frac{\left(k_b + k_a\rho_a^0\right)}{\tau_c + \tau_y}u^0 = 0 \tag{S5}$$

$$k_{on}\left[\rho_0 - \rho_a^0\right] - k_{off}(u^0)\rho_a^0 = 0. \tag{S6}$$

After substituting our driving force $F_{1D} = F_0 e^{-mu}$, our equilibrium solutions thus satisfy the following nonlinear system of equations

$$u^0 = \frac{e^{-mu^0}}{\left(k_b + k_a\rho_a^0\right)} \tag{S7}$$

$$\rho_a^0 = \frac{k_{on}\rho_0}{k_{on} + k_{off}^0 e^{\delta\beta k_a u^0}}. \tag{S8}$$

Steady-state bleb size

Recall that once the membrane detaches from the cortex, linker proteins are lost and no longer contribute to bleb dynamics. Hence, we set $\rho_a = 0$ and ignore its dynamics in the 1D model (Eq. S3). Our main equation for studying equilibrium bleb size is thus,

$$\dot{u} = \frac{F_{1D}(u)}{\tau_c(t) + \tau_y(t)} - \frac{k_b(t)}{\tau_c(t) + \tau_y(t)}u(t) \tag{S9}$$

which is non-autonomous. First we convert it to an autonomous system by using the exact forms of $k_b(t), \tau_c(t)$ and $\tau_y(t)$ given in the main paper and their rates of change

$$\begin{aligned}
\frac{dk_b}{dt} &= k_c\frac{\dot{a}_{bleb}(t)}{a_0} \\
\frac{d\tau_c}{dt} &= \tau_c^0\frac{\dot{a}_{bleb}(t)}{a_0} \\
\frac{d\tau_y}{dt} &= -(1-\theta)\tau_y^0\dot{a}_{scar}.
\end{aligned} \tag{S10}$$

Recall from Eq. S1 that

$$\dot{a}_{bleb} = k_{ab}^{on} - k_{ab}^{off} a_{bleb}$$
$$\dot{a}_{scar} = -k_{as}^{off} a_{scar}.$$

Therefore, the complete autonomous system becomes,

$$\begin{aligned}
\frac{du}{dt} &= \frac{F_{1D}(u)}{\tau_c + \tau_y} - \frac{k_b}{\tau_c + \tau_y} u \\
\frac{da_{bleb}}{dt} &= k_{ab}^{on} - k_{ab}^{off} a_{bleb} \\
\frac{da_{scar}}{dt} &= -k_{as}^{off} a_{scar} \\
\frac{dk_b}{dt} &= k_c \frac{(k_{ab}^{on} - k_{ab}^{off} a_{bleb})}{a_0} \\
\frac{d\tau_c}{dt} &= \tau_c^0 \frac{(k_{ab}^{on} - k_{ab}^{off} a_{bleb})}{a_0} \\
\frac{d\tau_y}{dt} &= (1-\theta)\tau_y^0 k_{as}^{off} a_{scar}.
\end{aligned} \tag{S11}$$

Steady state/equilibrium solution

At equilibrium, we have

$$\frac{du}{dt} = \frac{dk_b}{dt} = \frac{d\tau_c}{dt} = \frac{d\tau_y}{dt} = \frac{da_{bleb}}{dt} = \frac{da_{scar}}{dt} = 0,$$

resulting in the system of equations

$$\frac{F_{1D}(u)}{\tau_c + \tau_y} - \frac{k_b}{\tau_c + \tau_y} u = 0 \tag{S12}$$
$$k_{ab}^{on} - k_{ab}^{off} a_{bleb} = 0 \tag{S13}$$
$$-k_{as}^{off} a_{scar} = 0 \tag{S14}$$
$$k_c \frac{(k_{ab}^{on} - k_{ab}^{off} a_{bleb})}{a_0} = 0 \tag{S15}$$
$$\tau_c^0 \frac{(k_{ab}^{on} - k_{ab}^{off} a_{bleb})}{a_0} = 0 \tag{S16}$$
$$(1-\theta)\tau_y^0 k_{as}^{off} a_{scar} = 0.. \tag{S17}$$

We denote the equilibrium value of an arbitrary variable w as w^*. Note from Eq. S14 that $a_{scar}^* = 0$, which implies that Eq. S17 is trivially satisfied. From Eq. S13, $a_{bleb}^* = \frac{k_{ab}^{on}}{k_{ab}^{off}}$, which also implies that Eq. S16 and Eq. S15 are trivially satisfied. By allowing $t \to \infty$, we find that $\tau_y^* = \tau_y^0, \tau_c^* = \frac{\tau_c^0 k_{ab}^{on}}{a_0 k_{ab}^{off}}$ and $k_b^* = k_m + \frac{k_c k_{ab}^{on}}{a_0 k_{ab}^{off}}$. Therefore, from Eqn. S12,

$$F_{1D}(u^*) = k_b^* u^*.$$

Using the model for $F(u) = F_0 e^{-mu}$, the equilibrium bleb size, u^* can be obtained by solving the nonlinear equation

$$F_0 e^{-mu^*} - \frac{k_c k_{ab}^{on}}{a_0 k_{ab}^{off}} u^* = k_m. \tag{S18}$$

References

[1] E. Asante-Asamani, M. Dalton, D. Brazill, W. Strychalski, Modeling the dynamics of actin and myosin during bleb stabilization, Applied Mathematics for Modern Challenges (2024). doi:10.3934/ammc.2024002.
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