Supplementary Information for Energy barriers and cell migration in densely packed tissues†

Dapeng Bi*, J. H. Lopez*, J. M. Schwarz* and M. Lisa Manning*[a]

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1 Aboov-Weaire law

In a cellular packing where all vertices are three-edge coordinated, the coordination number of nearest adjacent neighbors are correlated and can be described by the empirical Aboav-Weaire law[1]:

$$\langle z_{n.n.}(z)\rangle \approx A + B/z, \tag{1}$$

where z is the coordination number of a given cell and $z_{n.n.}$ is the coordination number of its neighbor. The $\langle\ldots\rangle$ notation means averaging over all cells in the packing. As shown in Fig. 1, this also holds for the packings used in this work.

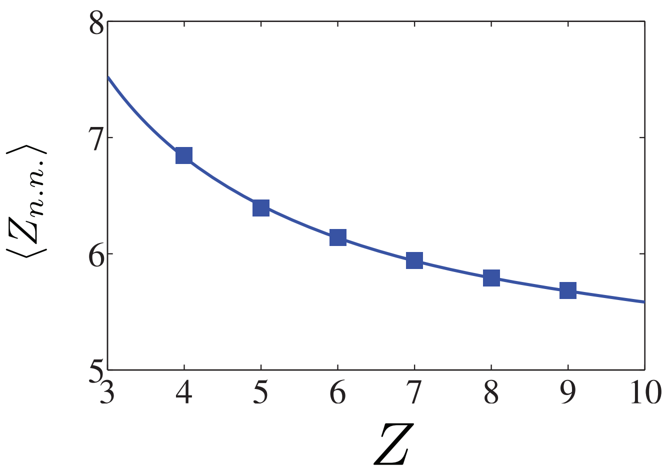

Fig. 1 The topological correlations from cell packings used in our simulations are represented by the blue squares. Z is the number of neighbors for a cell, and $\langle Z_{n,n}\rangle$ is the average number of neighbors of the nearest neighbors. The solid blue line is fitting using Aboav-weaire law, with A and B as fitting parameters

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* *Department of Physics, Syracuse University, Syracuse, NY 13244, USA Fax: +1 315 443 9103; Tel: +1 315 443 3920; E-mail: mmanning@syr.edu*
[b] *Syracuse Biomaterials Institute, Syracuse, NY 13244, USA*

Therefore, for the four cells involved in a T1 transition labeled S1,S2,E1 and E2, their topologies are not independent from each other. Statistically, given Z_{S1} and Z_{S2} it is possible to determine Z_{E1} and Z_{E2}.

2 Trap Model for glases

The trap model for glasses[2] models a system with a complex potential energy landscape, that is captured by a quenched distribution $\rho(\Delta u)$. The simple assumption is that the evolution between different metastable states occur via activated processes. The probability for a state to be in trap labeled by Δu at time t, $P(\Delta u,t)$, evolves according to the master equation[2]:

$$\frac{d}{dt}P(\Delta u,t) = -\omega_0 e^{-\Delta u/\varepsilon}P(\Delta u,t) + \omega(t)\rho(\Delta u). \tag{2}$$

In Eq. (2), the first term on the r.h.s. is the rate of escape from trap labeled by Δu. This is modeled as an activated process where the fluctuation is given by ε. In thermal systems $\varepsilon = k_B T$. ω_0 is an inherent attempt frequency which is assumed to be independent of ε. The second term on the r.h.s. of Eq. (2) is the rate of entering a trap with Δu, where a time dependent attempt frequency is given by

$$\omega(t) = \omega_0 \int_0^\infty d\Delta u P(\Delta u,t)\, e^{-\Delta u/\varepsilon}. \tag{3}$$

The rate of entering includes $\rho(\Delta u)$ which is the underlaying distribution of the trap depth Δu in the potential energy landscape.

Here we chose the form of $\rho(\Delta u)$ from the simulation result of the main text

$$\rho(\Delta u) = \frac{1}{\varepsilon_0}e^{-\Delta u/\varepsilon_0}. \tag{4}$$

2.1 Steady state solution

For this work we are interested in the steady state solution to Eq. (2) which is given by

$$f_{ss}(\Delta u) = \frac{\varepsilon - \varepsilon_0}{\varepsilon\,\varepsilon_0}e^{-\Delta u(1-1/x)} \tag{5}$$

where $x = \varepsilon/\varepsilon_0$. For $x < 1$ the system is glassy, since Eq. (5) is not normalizable. For $x > 1$ which is normalizable only when $x \geq 1$. The steady state distribution (Eq. 5 in main text) can also be written in terms of the trapping time $\tilde{\tau}$, which is the inverse of the escape rate $\tilde{\tau} = e^{\Delta u/x}$

$$g_{ss}(\tilde{\tau}) = f_{ss}(\Delta u)\frac{d\Delta u}{d\tilde{\tau}} \propto \tau^{-x}. \tag{6}$$

2.2 Two-time correlation function

We also study dynamics of the trap model in terms of two-time correlation for a particle starting in one trap at time $t = 0$ and remaining in the same at t. The probability that a state is in a trap labelled by Δu at $t = 0$ will stay in the same state Δu at time t is given by the homogeneous part of the solution of Eq. (2):

$$\mathscr{F}^{stay}_{\Delta u}(t) = f_{ss}(\Delta u)\exp\left[-\omega_0 e^{-\Delta u/x} t\right]. \tag{7}$$

A two-time correlation function can be defined by including the contribution from all initial traps Δu,

$$c_{trap}(0,t) = \int_0^\infty d\Delta u \mathscr{F}^{stay}_{\Delta u}(t) = \frac{x-1}{(\omega_0 t)^{x-1}}\int_0^{\omega_0 t} dw\, w^{x-2}e^{-w}. \tag{8}$$

A plot of $c_{trap}(0,t)$ for different values of $x = \varepsilon/\varepsilon_0$ is shown in Fig. 3(a) of the main text.

3 Soft Glassy Rheology model for tissues

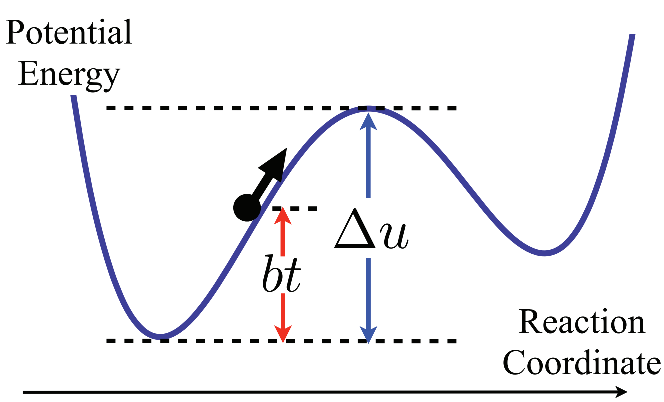

Fig. 2 A schematic of the model for glassy dynamics in tissues. Δu labels the trap (represented by the black dot with arrow). bt is the amount of energy generated as the cell moves in a directed manner.

Following the ideas of Soft Glassy Rheology[3], we model self-propelled, directed motion in a simple way, by assuming the cell generates energy at a constant rate b that allows it to traverse the Potential Energy Landscape. At time t, directed cell motion has consumed energy $\sim bt$, bringing it closer to a T1 rearrangement, and making the effective barrier height $\Delta u - bt$. There is also a finite probability for it to undergo a rearrangement due to non-directed fluctuations in its shape; we describe this as an activated process controlled by a temperature-like parameter ε. Then the rate for overcoming a barrier at time t can be written as

$$R = \omega_0 \exp\left[-(\Delta u - bt)/\varepsilon\right]. \tag{9}$$

After escaping a trap with the rate given in Eq. (9), the T1 four-cell region enters into a new trap chosen from the distribution $\rho(\Delta u)$. A master equation can be written[3] to describe the evolution of the four-cell T1 location:

$$\begin{aligned}\frac{\partial}{\partial t}P(\Delta u,t) =& -\omega_0 e^{-[\Delta u - bt]/\varepsilon}P(\Delta u,t)\\ &+\rho(\Delta u)\int d\Delta u'\,\omega_0 e^{-[\Delta u' - bt]/\varepsilon}P(\Delta u',t),\end{aligned} \tag{10}$$

where $P(\Delta u,t)$ is the probability that T1 location is in trap labeled by Δu at time t. On the r.h.s., the first term describes the rate of hopping out of a trap and second term is the total rate of entering trap with Δu, which is proportional to $\rho(\Delta u)$, the distribution of choosing a new trap.

Equation 10 can be rewritten in terms of non-dimensionalized time $s = \omega_0 t$ and energy $u = \Delta u/\varepsilon_0$

$$\begin{aligned}&\frac{\partial}{\partial s}f(u,s) =\\ &-e^{-(u-Bs)/x}f(u,s) + e^{-u}\int du' e^{-(u'-Bs)/x}f(u',s)\end{aligned} \tag{11}$$

where we have also introduced the dimensionless parameters $B = b/(\omega_0\varepsilon_0)$ and $x = \varepsilon/\varepsilon_0$.

The steady-state solution of Eq. 11 is the same as the result for the trap model Eq. (5):

$$f_{ss}(u) = (1-1/x)e^{-u(1-1/x)}, \tag{12}$$

which is not normalizable for $1 < 1/x$ or $\varepsilon > \varepsilon_0$. This indicates a glass transition at $\varepsilon = \varepsilon_0$.

The probability that a T1 location with u at $s = 0$ will stay in the same state u at time s is given by the homogeneous part of the solution of Eq. (11):

$$\mathscr{F}^{stay}_{u}(s) = f_{ss}(u)\exp\left[-\frac{x}{B}e^{-u/x}(e^{Bs/x}-1)\right]. \tag{13}$$

A two-time correlation function can be defined by including the contribution from all traps depths u,

$$c_{sgr}(0,s) = \int_0^\infty du\, \mathscr{F}^{stay}_{u}(t) = \frac{x-1}{y(s)^{x-1}}\int_0^{y(s)} dw\, w^{x-2}e^{-w}, \tag{14}$$

where $y(s) = \frac{x}{B}\left(e^{Bs/x}-1\right)$. We can define a caging time as the value of τ such that $C_{sgr}(0,\tau) = e^{-1}$. The dependence of τ on $x = \varepsilon/\varepsilon_0$ and $B = b/(\omega_0\varepsilon_0)$ is plotted in Fig. 3.

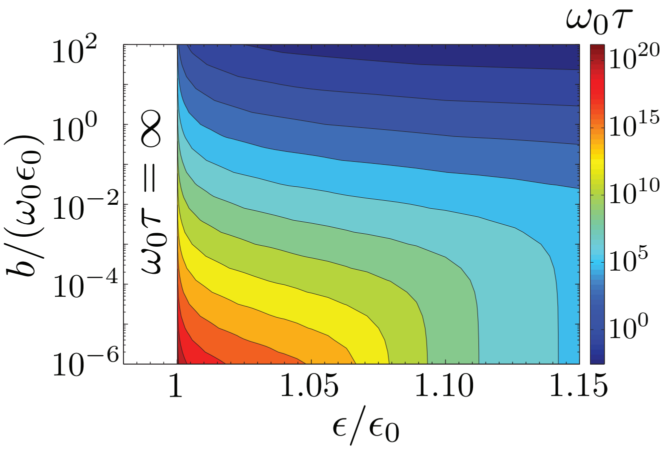

Fig. 3 Eq. (14) is used to define a caging time τ, such that $c(0,\tau) = e^{-1}$, as a function of the two dimensionless parameters of the model.

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