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Supplemental Information

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Supplementary material

Elastic deformation of the hole

Here, we show that in the elastic regime, the hole radius does not appreciably change from its initial radius. For times that are shorter than the typical viscoelastic timescale $\tau = E/\eta$, the change in the hole radius is governed by linear elasticity. For approximately flat shells, this is a problem of a two-dimensional annulus with boundary conditions of constant stress $\tilde{\sigma}_0$ that equals $\tilde{E}\varepsilon_0$ at infinity, where $\tilde{E}$ is the three-dimensional Young's modulus (E is the two-dimensional Young's modulus, which is related to $\tilde{E}$ by $E \sim \tilde{E} \cdot d$ where d is the shell thickness), and a size dependent line tension of the hole on the perimeter of the annulus. Force balance dictates

$$\frac{\partial \tilde{\sigma}_{rr}}{\partial r} + \frac{1}{r}\left(\tilde{\sigma}_{rr} - \tilde{\sigma}_{\theta\theta}\right) = 0 \tag{1}$$

where $\tilde{\sigma}_{ij}$ is the component of the stress tensor. In linear elasticity the stresses and strains are related by

$$\tilde{\sigma}_{ij} = \frac{\tilde{E}}{1+\nu}\left(\varepsilon_{ij} + \frac{\nu}{1-2\nu} tr\left(\varepsilon\right)\delta_{ij}\right) \tag{2}$$

where ε_{ij} are the components of the strain tensor and ν is the Poisson ratio. We work in a coordinate system in which the $\hat{z}$ axis is the symmetry axis of the annulus and $z = 0$ characterizes the midplane of the shell. From symmetry considerations, the θ component of the displacement vector $\vec{u}$ vanishes while other components are θ independent. This means that $\varepsilon_{rr} = \frac{\partial u_r}{\partial r}, \varepsilon_{\theta\theta} = \frac{u_r}{r}, \varepsilon_{zz} = \frac{\partial u_z}{\partial z}$ and $\varepsilon_{rz} = \frac{1}{2}\left(\frac{\partial u_r}{\partial z} + \frac{\partial u_z}{\partial r}\right)$ while all other components vanish.

The upper and lower surfaces of the shell are traction free. This means, for a thin shell, that all the components of $\tilde{\sigma}_{iz}$ can be approximated to be zero, in particular $\tilde{\sigma}_{zz} = 0$ which gives, using Eq. 2 and the relations between the strain and displacement components, $\varepsilon_{zz} = -\frac{\nu}{1-\nu}\left(\frac{\partial u_r}{\partial r} + \frac{u_r}{r}\right)$. Substituting this into Eq. 2 together with the relation between the strain and displacement components leads to:

$$\tilde{\sigma}_{rr} = \frac{\tilde{E}}{1+\nu}\left(\frac{\partial u_r}{\partial r} + \frac{\nu}{1-\nu}\left(\frac{\partial u_r}{\partial r} + \frac{u_r}{r}\right)\right) \tag{3}$$

$$\tilde{\sigma}_{\theta\theta} = \frac{\tilde{E}}{1+\nu}\left(\frac{u_r}{r} + \frac{\nu}{1-\nu}\left(\frac{\partial u_r}{\partial r} + \frac{u_r}{r}\right)\right) \tag{4}$$

Substituting these relations into Eq. 1 gives the differential equation

$$\frac{\partial^2 u_r}{\partial r^2} + \frac{1}{r}\frac{\partial u_r}{\partial r} - \frac{u_r}{r^2} = 0 \tag{5}$$

whose solution is

$$u_r = Ar + B\frac{1}{r} \tag{6}$$

where A and B are integration constants determined by the boundary conditions $\tilde{\sigma}_{rr}(r \to \infty) = \tilde{\sigma}_0$ and $d\cdot\tilde{\sigma}_{rr}(r = R_i) = \frac{T}{R_i}$. Using equations 6 and 3 allow us to express the radial component of the stress tensor as a function of r and the integration constants:

$$\tilde{\sigma}_{rr}(r) = \frac{\tilde{E}}{1+\nu}\left(\frac{1+\nu}{1-\nu}A - B\frac{1}{r^2}\right) \tag{7}$$

The expression above, together with the stress boundary conditions determines $A = \frac{(1-\nu)\tilde{\sigma}_0}{\tilde{E}}$ and $B = \frac{1+\nu}{\tilde{E}}R_i^2\tilde{\sigma}_0 - \frac{1+\nu}{\tilde{E}}\frac{R_i T}{d}$. Substituting the integration constants A and B into 6 with $R = R_i$ results in the displacement of the hole $u_r(r = R_i) = 2R_i\frac{\tilde{\sigma}_0}{\tilde{E}} - (1+\nu)\frac{T}{d\cdot\tilde{E}}$. In linear elasticity $T/d, \tilde{\sigma}_0 \ll \tilde{E}$, so that the change in the hole radius is negligible compared with the radius itself. We therefore conclude that in the short-time elastic regime, the hole radius is essentially unchanged for times smaller than the typical viscoelastic timescale τ, where the shell is approximated to respond elastically.

Derivation of the dynamical equations

To formulate the equations for the hole dynamics in case I, we have to account for the flow of the shell, the high-concentration, polymer solution and their coupling. We consider each of these in separate subsections.

Shell flow dynamics

For times larger than the typical viscoelastic timescale $\tau = \eta/E$, the shell flow is controlled by low Reynolds number hydrodynamics. We approximate the shell to be a three-dimensional incompressible, viscous thin film with a hole of radius R. The boundary conditions are: surface tension σ equals $E\varepsilon$ at infinity and an equivalent surface tension of $T/R(t)$ that arises from the line tension and the time dependent hole radius; the upper and lower surfaces of the film are traction free. We again work in a coordinate system in which the $\hat{z}$ axis is the symmetry axis of the annulus and $z = 0$ characterizes the midplane of the shell. Symmetry considerations dictate, that the θ component of the velocity field $\vec{v}$ of the shell vanishes and that v_r and v_z are θ independent. Using these symmetry arguments, the incompressibility condition is written as:

$$\nabla \cdot \vec{v}(r,t) = \frac{1}{r}\frac{\partial (r v_r)}{\partial r} + \frac{\partial v_z}{\partial z} = 0 \tag{8}$$

For a thin shell, the flow of the molecules is quasi two-dimensional in the plane of the shell while the change in its thickness is governed by its three-dimensional incompressibility. Thus, changes in the molecular rearrangements in the z direction occur almost instantaneously; v_z and its derivatives are therefore very small compared with their corresponding quantities in the radial direction.

Eq. 8 is therefore well approximated by $\frac{1}{r}\frac{\partial(r v_r)}{\partial r} = 0$, therefore $v_r = G(t,z)/r$. Since the upper and lower surfaces are traction free, the hydrodynamic stress tensor $\tilde{\sigma}_{zr}$ vanishes on both surfaces. For a thin shell, this means that $\tilde{\sigma}_{zr}$ is approximately zero throughout the thickness of the shell: $\tilde{\sigma}_{zr} = \tilde{\eta}\left(\frac{\partial v_z}{\partial r} + \frac{\partial v_r}{\partial z}\right) = 0$, where $\tilde{\eta}$ is the kinematic viscosity of the shell and is related to the surface viscosity η by $\eta = d \cdot \tilde{\eta}$. Neglecting $\partial v_z/\partial r$ means that v_r is approximately z independent, thus $v_r = G(t)/r$. The radial component of the hydrodynamic stress tensor is therefore:

$$\tilde{\sigma}_{rr} = -p + 2\tilde{\eta}\frac{\partial v_r}{\partial r} = -p - \frac{2\tilde{\eta}G(t)}{r^2} \tag{9}$$

where p is the pressure field in the shell that enters the Navier-Stokes equation. This hydrodynamic stress tensor, together with the boundary conditions at the circumference of the hole $\tilde{\sigma}_{rr}(r = R) = \frac{T}{R \cdot d}$ and at infinity $\tilde{\sigma}_{rr}(r \to \infty) \cdot d = \sigma$, determine $p \cdot d = \sigma$ and $\frac{R^2}{2\eta}\left(\sigma - \frac{T}{R}\right) = G(t)$, so that $v_r(r = R) = G(t)/R$.

However, the velocity at the circumference of the hole $v_r(r = R)$ is equal to the rate of change of the hole radius $v_r(r = R) = \dot{R}$, thus:

$$\dot{R} = \frac{R}{2\eta}\left(\sigma - \frac{T}{R}\right) \tag{10}$$

which describes the hole growth/healing due to a surface tension σ and a line tension T.

Outflow dynamics

On the scale of the entire shell, the curvature of the shell must be taken into account since it induces a pressure gradient between its two sides, as described by Young-Laplace law. In the presence of a hole, this pressure gradient drives outflow; the outflow decreases the volume and combined area A of the shell. Reduction of the shell area increases the packing density of molecules, which was (before nucleation of the hole) lower than its equilibrium value (due to the constriction), so that the lateral stresses and strains are relieved.

To account for the evolution equation of the combined area A due to outflow, which is determined by the hole radius R and pressure gradient Δp, we again use low Reynolds number hydrodynamics, where now $\vec{v}$ refers to the velocity of the solvent phase of the inner solution and the pressure p now refers to the pressure field inside the high-concentration, polymer solution. This time, the viscosity is not that of the shell but is the kinematic viscosity η_s of the solvent phase of the polymer solution. In the model of case I, a channel forms due to solvent phase flow in the dense, polymer phase. The channel is modeled by a tube of radius R and a contour length of d^*, which is greater than the actual shell thickness d and the hole radius R. In the limit of low Reynolds number, the flow is laminar, meaning that the fluid flow in parallel layers that do not mix. We again work in a cylindrical coordinate system, in which the axis of symmetry of the hole is the $\hat{z}$ axis and $z = 0$ characterizes the midplane of the effective cylinder. The equations governing the flow are the Navier-Stokes equation:

$$\nabla p = \eta_s \nabla^2 \vec{v} \tag{11}$$

and the incompressibility condition, which for laminar, cylindrically symmetric flow ($v_\theta =$

$v_r = 0$ and v_z, p are θ independent) becomes:

$$\nabla \cdot \vec{v} = \frac{\partial v_z}{\partial z} = 0 \tag{12}$$

$$\frac{\partial p}{\partial r} = 0 \tag{13}$$

$$\frac{\partial p}{\partial z} = \eta_s \left(\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial v_z}{\partial r}\right) + \frac{\partial^2 v_z}{\partial z^2}\right) \tag{14}$$

The boundary conditions we use for the velocity field are no-slip boundary conditions on the inner walls of the channel, which are $v_z\,(r = R, z) = v_r\,(r = R, z) = 0$. For the pressure, in the absence of end effects (applicable when $d^* \gg R$) the boundary conditions are set by the pressure gradient across the membrane (the pressure outside the shell is our reference and is set to zero): $p\,(r, z = 0) = -\Delta p$ and $p\,(r, z = d^*) = 0$. The solution of these equations with the specified boundary conditions is:

$$p\,(z) = \Delta p \left(\frac{z}{d^*} - 1 \right) \tag{15}$$

$$v_z = \frac{\Delta p}{4\eta_s d^*} \left(R^2 - r^2 \right) \tag{16}$$

The total outflow Q is calculated by integration of the velocity v_z over the area of the hole:

$$Q = \int_0^R 2\pi r dr \frac{\Delta p}{4\eta_s d^*} \left(R^2 - r^2 \right) = \frac{\pi \Delta p R^4}{8\eta_s d^*} \tag{17}$$

The pressure difference Δp is related to the surface tension by force balance across the shell (Young-Laplace law). Force balance dictates $\nabla \cdot \tilde{\sigma} = 0$ ($\tilde{\sigma}$ is again the three-dimensional stress tensor); in a spherical coordinate system, in which the origin is the center of the ruptured hemisphere the force balance equation becomes

$$\frac{\partial \tilde{\sigma}_{rr}}{\partial r} + 2\frac{\tilde{\sigma}_{rr}}{r} - \frac{1}{r}\left(\tilde{\sigma}_{\theta\theta} + \tilde{\sigma}_{\phi\phi} \right) = 0 \tag{18}$$

where $\tilde{\sigma}_{\theta\theta} = \tilde{\sigma}_{\phi\phi} = \sigma/d$ (the surface tension divided by the shell thickness) which is constant throughout the thin shell. The stress boundary conditions are $\tilde{\sigma}_{rr}\,(r = R_c) = -\Delta p$ and $\tilde{\sigma}_{rr}\,(r = R_c + d) = 0$, where R_c is the radius of the hemisphere (and the constriction cross section) and d is the actual thickness of the shell. Multiplying the force balance Eq. 18

by r^2 and integrating between R_c and $R_c + d$, gives the relation:

$$\Delta p \approx \frac{2\sigma}{R_c} \tag{19}$$

which becomes accurate for a thin shell where $d \ll R_c$. Substituting this relation in Eq. 17 results in:

$$Q = \frac{\pi \sigma R^4}{4\eta_s R_c d^*} \tag{20}$$

The outflow decreases the volume V_s of the deformed shell and causes the length L of the cylindrical part of the shell (see Fig. 1B) to decrease. This can be related to the change in the combined area A in the following way:

$$-Q = \frac{dV_s}{dt} = \frac{d}{dt}\left(\frac{4\pi R_c^3}{3} + \pi R_c^2 L\right) = \pi R_c^2 \frac{dL}{dt} \tag{21}$$

$$\frac{dA}{dt} = \frac{d}{dt}\left(4\pi R_c^2 + 2\pi R_c L\right) = 2\pi R_c \frac{dL}{dt} = -\frac{2Q}{R_c} \tag{22}$$

Substituting Eq. 20 in the relation above, results in an equation that describes the time evolution of the combined area A:

$$\frac{dA}{dt} = -\frac{\pi^2 \sigma R^4}{2\eta_s A_c d^*} \tag{23}$$

where $A_c = \pi R_c^2$ is the cross sectional area of the constriction. Together with Eq. 10 for the dynamics of the hole size, Eq. 23 forms a complete set of coupled equations that describe the dynamics of the rupture in the fluid-like regime. Using linear elasticity relation $\sigma = E\varepsilon$ the equation becomes:

$$\frac{dR}{dt} = \frac{E}{2\eta} R \left(\varepsilon - \frac{T}{ER}\right) \tag{24}$$

$$\frac{dA}{dt} = -\frac{\pi^2 R^4 E}{2\eta_s A_c d^*} \varepsilon \tag{25}$$

Dimensionless form of the equations

This set of equation is non-linear and cannot in general be solved analytically. However, solutions can be obtained in approximate manner using perturbation expansions of the variables, which first requires identification of the small parameters. This can be done by transformation of the equations to dimensionless form. We thus rescale the hole radius R by its initial radius R_i, the shell and constriction areas A and A_c by A_u and the time t by the typical viscoelastic timescale $\tau = \eta/E$. This results in the following set of equations:

$$\frac{d\tilde{R}}{d\tilde{t}} = \frac{1}{2}\tilde{R}\left(\varepsilon - \beta\frac{1}{\tilde{R}}\right) \tag{26}$$

$$\frac{d\tilde{A}}{d\tilde{t}} = -\frac{\rho^2\tilde{R}^4}{2\delta\tilde{A}_c}\varepsilon \tag{27}$$

where the parameters β, ρ and δ are $\frac{T}{ER_i}$, $\frac{\pi R_i^2}{A_u}$ and $\frac{\eta_s d^*}{\eta}$ respectively. henceforth, for brevity the tilde signs will be omitted from the rescaled variables. The theory is analyzed in the linear regime, so that the difference between the undeformed nuclear radius R_n and the constriction cross sectional radius R_c is small, i.e $R_n - R_c \ll R_n$. The radii R_n and R_c are related to the undeformed shell area and the constriction cross sectional area by $\pi R_c^2 = A_c$ and $4\pi R_n^2 = A_u$. Therefore $\tilde{A}_c = \frac{A_c}{A_u} = \frac{1}{4}\left(1 - \frac{R_n - R_c}{R_n}\right)^2 = \frac{1}{4} + O\left(\frac{R_n - R_c}{R_n}\right)$. However, in the linear elastic regime, the strain ε is also a small parameter; therefore the deviation of $\tilde{A}_c$ from $\frac{1}{4}$ is higher order in small terms, so that to leading order $\tilde{A}_c$ can be replaced by $\frac{1}{4}$. To linear order in ε the set of equations becomes:

$$\frac{dR}{dt} = \frac{1}{2}R\left(\varepsilon - \frac{\beta}{R}\right) \tag{28}$$

$$\frac{dA}{dt} \approx -\frac{2\rho^2 R^4}{\delta}\varepsilon \tag{29}$$

We further rewrite this using the strain ε, which is a variable which is more physical than the combined area and thus replace A by ε. The lateral strain ε is the ratio of the excess area to the undeformed area A_u and can therefore be written, in non-rescaled variables as $\varepsilon = \frac{A - \pi R^2 - A_u}{A_u}$ or in rescaled variables $\varepsilon = A - \rho R^2 - 1$. Therefore, the time derivative of the lateral strain is

$$\frac{d\varepsilon}{dt} = \frac{dA}{dt} - 2\rho R\frac{dR}{dt} = -\left(1 + \frac{2\rho R^2}{\delta}\right)\rho R^2\varepsilon + \rho R\beta \tag{30}$$

For the biologically relevant values of the initial hole radius of $R_i = 25$nm, which is of the order of the NPC channel size, and the undeformed shell radius of the order of the radius of the nucleus $R_n \approx 3\mu$m , $\rho \approx 1.73 \cdot 10^{-5}$. The value of the parameter $\delta = \frac{\eta_s d^*}{\eta}$ depends on the value of d^*. The equivalent three-dimensional, kinematic viscosity of the lamina (which equals η/d where d is the lamina thickness) is of the order of one kPa $\cdot$ s [1] (we assume that the contribution of the bilayers to the mechanical properties of the NE is small compare to the lamina); therefore the biologically relevant value of the ratio $\eta_s d/\eta$ is of the order 10^{-6} if η_s is taken to be similar to the kinematic viscosity of water (10^{-3} Pa $\cdot$ s). Choosing $d^*/d \approx 10 - 100$ to account for the tortuosity of the channel, we get $\delta \approx 10^{-5} - 10^{-4}$ and $\rho/\delta \approx 1 - 0.1$. Multiplying this by $\left(\frac{R}{R_i}\right)^2$, which can be much greater than unity when the rupture grows to its maximal size, we find $\frac{2\rho R^2}{\delta} > 1$. Thus, the evolution of the strain can be approximated by

$$\frac{d\varepsilon}{dt} = -\frac{2\rho^2 R^4}{\delta}\varepsilon + \rho R\beta \tag{31}$$

it should be stressed that this approximated form is more accurate when R is close to its maximal size, for $R \approx 1$ Eq. 30 should be used.

For completeness, we estimate in this subsection the value of the parameter β for the model of the lamina as a viscoelastic shell. To estimate β, we start by considering the origin of the line tension. In a coarse-grained view, the bulk of the shell is more hydrophobic than its surfaces (this is the driving force for the creation of the shell in aqueous solution). Thus, hole nucleation creates interface between the hydrophilic solvent and the hydrophobic bulk of the shell; this interface is thermodynamically unfavorable and drives bending of the shell around the circumference of the hole in order to eliminate this interface (see Fig 3. in [2]). This bending energy is results in a line tension, which is the energy of creating unit length of that interface. The bending energy per unit area of the shell is $f_B = \frac{1}{2}K\left(\kappa_1 + \kappa_2\right)^2$, but for bending around the hole one curvature is much larger than the other $\kappa_1 = \frac{2}{d} \gg \frac{1}{R} = \kappa_2$ (d is the shell thickness) so that $f_B = \frac{1}{2}K\left(\frac{2}{d}\right)^2$. The bending modulus K of a plate can be calculated using the equation $K = \frac{\tilde{E}h^3}{12(1-\nu^2)}$ where h is the plate thickness, $\tilde{E}$ and ν are the three-dimensional Young and Poisson moduli respectively [3]. Since the shell folds over itself, it can be viewed as a folded plate, thus $h = d/2$, and $\nu = 1/2$ due to three-dimensional membrane incompressibility. Therefore

$$T = d \cdot f_b = \frac{d\tilde{E}\left(\frac{d}{2}\right)^3}{24\left(1 - \left(\frac{1}{2}\right)^2\right)}\left(\frac{2}{d}\right)^2 = \frac{\tilde{E}d^2}{36} \tag{32}$$

It is important to note that the modulus $\tilde{E}$ that appears above is the three-dimensional Young's modulus, not the two-dimensional Young's modulus E. However, we expect the two to differ by a factor of the order of d, therefore we approximate $T = Ed/36$ in this subsection.

β equals (by definition) to $\frac{T}{ER_i} = \frac{d}{36R_i} \approx \frac{1}{72}$ ($d \approx 14nm$ [4]).

Perturbation analysis and estimate of maximal hole size R_m

The dynamics of the hole radius R and the combined shell area A are determined by the equations 28 and 29:

$$\frac{dR}{dt} = \frac{1}{2}R\left(A - \rho R^2 - 1 - \frac{\beta}{R}\right) \tag{33}$$

$$\frac{dA}{dt} = -2\alpha R^4\left(A - \rho R^2 - 1\right) \tag{34}$$

where $\alpha = \rho^2/\delta$. The dynamics of the hole growth at short times is determined by the value of α and there are two asymptotic limits of interest:

1. Outflow-driven dynamics: In this limit, the majority of the lateral strains due to the constriction are relieved by the outflow of the internal fluid. This limit is characterized by large initial holes (i.e., ρ is relatively large) and small effective dissipation length (i.e., δ is relatively small), which corresponds to values of α which are large $\alpha \equiv \frac{\rho^2}{\delta} \gg 1$. We now follow the perturbation analysis of this limit, beginning with an expansion of $R(t)$ and $A(t)$ as power series in the small parameter $1/\alpha$:

$$R = R^0 + \frac{1}{\alpha}R^1 + O\left(\frac{1}{\alpha^2}\right) \tag{35}$$

$$A = A^0 + \frac{1}{\alpha}A^1 + O\left(\frac{1}{\alpha^2}\right) \tag{36}$$

Rewriting the equations 33 and 34 so that the small parameter $1/\alpha$ appears instead of α gives:

$$\frac{dR}{d\tilde{t}} = \frac{1}{2\alpha}R\left(A - 1 - \rho R^2 - \frac{\beta}{R}\right) \tag{37}$$

$$\frac{dA}{d\tilde{t}} = -2R^4\left(A - 1 - \rho R^2\right) \tag{38}$$

where $\tilde{t} = \alpha t$. Substituting the expansions of R and A and matching the zeroth order terms give:

$$\frac{dR^0}{d\tilde{t}} = 0 \Rightarrow R^0 = 1 \tag{39}$$

$$\frac{dA^0}{d\tilde{t}} = -2\left(A^0 - 1 - \rho\right) \tag{40}$$

so that (the initial condition for A^0 is $A^0\left(\tilde{t}=0\right)=1+\varepsilon_0$)

$$A^0 = 1+\rho+(\varepsilon_0-\rho)\,e^{-2\tilde{t}} \tag{41}$$

For $\tilde{t} \ll 1/2$, the exponent in Eq. 41 can be linearized; this gives:

$$A^0 \;=\; 1+\varepsilon_0-2\,(\varepsilon_0-\rho)\,\tilde{t} \tag{42}$$

In the other limit, the exponent in Eq. 41 is very small, therefore $A^0 \approx 1+\rho$. This means that the lateral strain and stresses are now fully relieved, which corresponds to the regime of hole closing. The dynamics of hole closing is found by calculating the first order correction for R, again by matching orders:

$$\frac{dR^1}{d\tilde{t}} \;=\; \frac{1}{2\alpha}\left(A^0-1-\rho\right)-\frac{1}{2\alpha}\beta \tag{43}$$

for short times $\tilde{t} \ll 1/2$ (hole growth) :

$$\frac{dR^1}{d\tilde{t}} \;=\; \frac{1}{2\alpha}\left(A^0-1-\rho\right)-\frac{1}{2\alpha}\beta \tag{44}$$

$$R^1 \;=\; \frac{(\varepsilon_0-\rho-\beta)}{2\alpha}\tilde{t}-\frac{1}{2}\,(\varepsilon_0-\rho)\,\frac{\tilde{t}^2}{\alpha} \tag{45}$$

and for long times $\tilde{t} \gg 1/2$ (hole shrinking):

$$\frac{dR^1}{d\tilde{t}} \;\approx\; -\frac{1}{2\alpha}\beta \tag{46}$$

$$R^1 \;=\; C-\frac{1}{2}\beta t \tag{47}$$

where C is an integration constant that can be calculated from matching the two regimes.

2. Hole growth-driven dynamics: In this limit, the majority of the lateral strains are relieved by the growth of the hole. This limit is characterized by small initial holes (i.e., ρ is relatively small) and large effective dissipation length (i.e., δ is relatively large), corresponding to values of $\alpha \equiv \frac{\rho^2}{\delta} \ll 1$. Expanding R and A in in the small parameter α:

$$R \;=\; R^0+\alpha R^1+O\left(\alpha^2\right) \tag{48}$$

$$A = A^0 + \alpha A^1 + O\left(\alpha^2\right) \qquad (49)$$

Using this equation, equations 33 and 34 give, to zeroth order:

$$\frac{dA^0}{dt} = 0 \Rightarrow A^0 = 1 + \varepsilon_0 \qquad (50)$$

so that

$$\frac{dR^0}{dt} = \frac{1}{2}\left(-\left(R^0\right)^3 \rho + \varepsilon_0 R^0 - \beta\right) \qquad (51)$$

For short time when R^0 is of order unity, we find in the limit that $\rho \ll \varepsilon_0 - \beta$

$$R^0 = \frac{\beta}{\varepsilon_0} + \left(1 - \frac{\beta}{\varepsilon_0}\right) e^{\frac{1}{2}\varepsilon_0 t} \qquad (52)$$

The hole radius of course does not grow indefinitely but is bounded due to the contribution of the $(R^0)^3$ term in Eq. 51. The maximal hole radius can be calculated by searching for the steady state $\frac{dR^0}{dt} = 0$, which results in a polynomial equation of the third degree $(R^0)^3 \rho - \varepsilon_0 R^0 + \beta = 0$; the maximal value of R^0 is the largest real root of the three, which is equal to $\sqrt{\frac{\varepsilon_0}{\rho}} - \frac{\beta}{2\varepsilon_0}$ to first order in β. In the absence of outflow (zeroth order), the maximal hole radius is stable; this is the maximal hole radius in case II (for nucleoplasm as a homogenous viscous fluid) in which outflow is negligible during the exponential growth regime. Addition of slow outflow relieves some of the lateral strains and causes the hole to shrink. Since the lateral strain $\varepsilon = A - 1 - \rho R^2$ is close to zero when R is near its maximal value, Eq. 28 can be written approximately as $\frac{dR}{dt} = -\frac{\beta}{2}$ right after the hole reaches its maximal value. Therefore, the dependence of the hole size on time in this regime is approximately a linear function of time with a slope of $-\frac{\beta}{2}$. However, in the case that the effective dissipation length is too high, outflow will not mitigate the growth of the lateral strain ($\rho\beta R$ is not small compared to $-\left(1 + 2\rho R^2/\delta\right)\rho R^2 \varepsilon$ in 30). This in turn will slow the rate of hole radius decrease, which will return to the value of $-\frac{\beta}{2}$ for a small enough hole, since $\frac{1}{2}R\varepsilon$ will again be negligible compared with $-\frac{\beta}{2}$ in Eq. 28. In this limit, we predict a step-like bump in the dependence of the hole radius on time, which slightly slows the average shrinking rate of the hole. Numerical solutions of the equations over a wide range of effective dissipation lengths verify our prediction of the late-time behavior of the hole radius.

Estimate of the maximal hole radius

Up to this point, the early and late time dynamics of the hole radius have been calculated analytically for different asymptotic regimes. However, in order to fully characterize the dynamics, the transition between the early and late time regimes, or equivalently the maximal hole radius, must be determined. The time at which the transition (or maximal hole radius) occurs is derived from an identity as follows: Multiplying Eq. 29 by $-\frac{1}{4}\frac{\delta}{\rho^2}$ gives

$$-\frac{1}{4}\frac{\delta}{\rho^2}\frac{dA}{dt} = \frac{1}{2}R^4\left(A-\rho R^2-1\right) \tag{53}$$

Next, multiplying Eq. 28 by R^3

$$\frac{1}{4}\frac{d\left(R^4\right)}{dt} = \frac{1}{2}R^4\left(A-\rho R^2-1\right)-\frac{\beta}{2}R^3 \tag{54}$$

and substituting Eq. 53 into Eq. 54 gives

$$\frac{1}{4}\frac{d\left(R^4\right)}{dt} = -\frac{1}{4}\frac{\delta}{\rho^2}\frac{dA}{dt}-\frac{\beta}{2}R^3 \tag{55}$$

Integrating this identity above between the limits of $t=0$ and $t=t_f$ (the time in which the hole closes), using the initial and final conditions$R\left(t=0\right)=1, R\left(t=t_f\right)=0, A\left(t=0\right)=1+\varepsilon_0$ and $A\left(t=t_f\right)=1$ gives the identity:

$$\int_0^{t_f} R^3 dt = \frac{1}{2\beta}+\frac{1}{2\beta}\frac{\varepsilon_0\delta}{\rho^2} \tag{56}$$

It is important to remark that the final condition $A\left(t=t_f\right)=1$ is approximate since in principle, residual strains after healing are possible. However, in the range of parameters which are biological relevant the residual strain is negligible.

The identity in Eq. 56 serves as a constraint that can be used to approximate the transition time between the growth and hole closing regimes. We approximate the hole radius as a function of time to be a piecewise function, where in each regime it is characterized by the asymptotic early and late time dynamics as respectively calculated in equations 52 and 47 (the second applicable to both hole-growth and outflow-driven dynamics); the transition time, or the time at which the hole reaches its maximal radius, R_m can be found using Eq.

56. Denoting the transition time by t_m we split the integral into two regimes:

$$\int_0^{t_f} R^3 dt = \int_0^{t_m} R^3 dt + \int_{t_m}^{t_f} R^3 dt \tag{57}$$

The late-time ($t > t_m$) dependence of the hole radius in time is approximately $R(t) = R_m - \frac{\beta}{2}(t - t_m)$. Substituting this dependence into the second integral in the right hand side of 57, using $R(t_f) = R_m - \frac{\beta}{2}(t_f - t_m) = 0 \Rightarrow t_f - t_m = \frac{2R_m}{\beta}$ gives:

$$\int_{t_m}^{t_f} R^3 dt = \int_{t_m}^{t_f} \left(R_m - \frac{\beta}{2}(t - t_m)\right)^3 dt = \int_0^{\frac{2R_m}{\beta}} \left(R_m - \frac{\beta}{2}t'\right)^3 dt' = \frac{1}{2\beta} R_m^4 \tag{58}$$

Therefore, from equations 56, 57 and 58 it follows that

$$2\beta \int_0^{t_m} R^3 dt = 1 + \frac{\varepsilon_0 \delta}{\rho^2} - R_m^4 \tag{59}$$

For the case of hole-growth driven dynamics, which are characterized by $\frac{\delta}{\rho^2} \gg 1$, the identity above is approximately

$$R_m^4 + 2\beta \int_0^{t_m} R^3 dt \approx \frac{\varepsilon_0 \delta}{\rho^2} \tag{60}$$

Solving for t from Eq. 52 for the early-time ($t < t_m$) dynamics calculated in this limit,

$$dt = \frac{2dR}{\varepsilon_0 R - \beta} \tag{61}$$

the second term on the LHS of Eq. 60 becomes

$$\begin{aligned} 2\beta \int_0^{t_m} R^3 dt &= 2\beta \int_1^{R_m} \frac{2R^3 dR}{\varepsilon_0 R - \beta} \\ &= \frac{4\beta}{3\varepsilon_0} \left(\left(R_m^3 - 1\right) + \frac{3}{2}\frac{\beta}{\varepsilon_0}\left(R_m^2 - 1\right) + 3\frac{\beta^2}{\varepsilon_0^2}(R_m - 1) + 3\left(\frac{\beta^3}{\varepsilon_0^3}\right) \ln\left(\frac{R_m - \frac{\beta}{\varepsilon_0}}{1 - \frac{\beta}{\varepsilon_0}}\right)\right) \end{aligned} \tag{62}$$

As mentioned before, we take $\beta = \frac{1}{72}$, therefore $\frac{\beta}{\varepsilon_0} \approx \frac{1}{2}$. Substituting this ratio and the order of magnitude $R_m \approx 10$ shows that the value of the integral $2\beta \int\limits_0^{t_m} R^3 dt$ is smaller than R_m^4. We therefore neglect the integral so that Eq. 60 is approximately written as

$$R_m = \left(\frac{\varepsilon_0 \delta}{\rho^2}\right)^{\frac{1}{4}} \tag{63}$$

Eq. 63 can be written in dimensional units as $\frac{\pi R_m^2}{A_u} = \left(\varepsilon_0 \frac{\eta_s d^*}{\eta}\right)^{\frac{1}{2}}$, which predicts the ratio of the maximal hole area and the undeformed area (for fixed constriction cross-sectional area). This ratio increases as the square root of the initial strain ε_0, internal polymer solution kinematic viscosity η_s and the dissipation length d^*. ε_0 is the initial strain that drives hole growth, while the strain relief that limits hole growth decreases with increasing η_s or d^*, which limits the outflow and promotes hole growth. The maximal radius also decreases with the shell surface viscosity η, which slows the hole growth, thus allowing more strain relief by outflow.

This is an approximation that is accurate for small β and large ε_0. In conclusion, for hole growth-driven dynamics (relevant to case I in the main text) the hole radius as a function of time is approximated as:

$$R(t) \approx \begin{cases} \frac{\beta}{\varepsilon_0} + \left(1 - \frac{\beta}{\varepsilon_0}\right) e^{\frac{1}{2}\varepsilon_0 t} & t < t_m \\ \left(\frac{\varepsilon_0 \delta}{\rho^2}\right)^{\frac{1}{4}} - \frac{\beta}{2}(t - t_m) & t \geq t_m \end{cases} \tag{64}$$

where $\left(\frac{\varepsilon_0 \delta}{\rho^2}\right)^{\frac{1}{4}} = \frac{\beta}{\varepsilon_0} + \left(1 - \frac{\beta}{\varepsilon_0}\right) e^{\frac{1}{2}\varepsilon_0 t_m}$.

polymer extrusion as a model for chromatin herniation

To estimate the amount of herniated chromatin, we model the nucleoplasm as a fluid-filled network that comprises a high concentration polymer melt (chromatin) immersed in a viscous solution of water and small molecules. Herniation requires bending of the fibers to radii of curvature which are smaller than the size of the hole. For flow rates smaller than $\frac{k_B T}{\eta_s} \approx 5 \frac{\mu m^3}{s}$ (η_s being the kinematic viscosity of the solvent phase which is taken to be the kinematic viscosity of water) and in the absence of active process, the bending of the polymers is driven by thermal fluctuations [5, 6]. An upper bound for the flow rate can be calculated by taking Eq. 20 and replacing all the variables by their maximal values (R_m is taken to be the larger value predicted in case II). [All parameters in following equation have their true dimensions.]

$$Q < \frac{\pi E \varepsilon_0 R_m^4}{4\eta_s R_c d^*} \approx \frac{\left(A_d - A_u\right)^3}{4\pi\tau\delta R_c A_u} \sim 3\frac{\mu m^3}{s} \tag{65}$$

The actual maximal flow rate is expected to be much smaller than this upper bound since ε is close to zero when $R \sim R_m$, so that the condition $Q < \frac{k_B T}{\eta_s} \approx 5\frac{\mu m^3}{s}$ is surely satisfied for system of biological relevance. Thus, the herniation is not convective, but rather is driven by thermal fluctuations. In order to herniate, a polymer chain must bend to a radius of curvature that is smaller or equal to the radius of the hole R, for a length of at least πR such that a hemicircle is formed; otherwise it cannot slide outside of the hole. Due to the short screening length (Debye length) of the electrostatic interactions in the nucleus which we model, which is of the order of few nanometers [7], the inter- and intra-fiber electrostatic interactions can be neglected. Furthermore, for reasons that are not entirely clear, chromatin fibers in the nucleus may not be entangled [8]. Therefore, the prevalence of steric interaction when the polymer chains locally reorganizes in the vicinity of the hole and these interactions can be neglected as well. With these approximations, the minimal energy E_h of the configuration of the polymer chain that allows herniation arises only from bending, and can be written in terms of the persistence length l_p of the polymer (whose exact value for chromatin is unknown since the in-vivo microscopic structure of chromatin fiber is controversial [9]) as $E_h = \pi k_B T l_p/(2x)$ where x is the radius of curvature and T is the temperature.

The rate of polymer extrusion is therefore the sum over possible radii of curvature from 0 to the hole radius R of Boltzmann probabilities of the form $\nu_0 \exp\left(-\frac{\pi}{2} l_p/x\right)$, where ν_0 is a parameter with dimension of inverse time that represents the molecular kinetics and x is the summation variable. Since the exponent is negative and depends on $1/x$, the sum is dominated by the contribution of the term with the largest x. We thus approximate the extrusion rate by $\nu_0 \exp\left(-\frac{\pi}{2} l_p/R\left(t\right)\right)$, where $R\left(t\right)$ is the hole radius. The total amount of extruded polymer is obtained by integration of the above expression over the entire hole growth/healing cycle of the hole. Cases I and II of the dynamics differ in their prediction for the velocity of hole closing and the maximal hole radius R_m. We therefore calculate the amount of extruded polymer for a general case characterized by an exponential hole growth up to radius R_m followed by a decrease of the hole radius with a constant velocity α. [All variables here, including t have their true dimensions.]

$$L_c = \nu_0 \int\limits_0^{t_f} e^{-\frac{\pi l_p}{2R(t)}} dt = \nu_0 \tau \left(\int\limits_0^{t_m} e^{-\frac{\pi l_p}{2R(t)}} dt + \int\limits_{t_m}^{t_f} e^{-\frac{\pi l_p}{2R(t)}} dt \right) \quad (66)$$

Taking $\beta/\varepsilon_0 < 1$, $\exp\left(-\frac{\pi}{2} l_p / R(t)\right) \ll 1$ for small $R(t)$ and using Eq. 64, we find

$$L_c \approx \frac{\nu_0 \tau}{\alpha} \int\limits_1^{R_m} e^{-\frac{\pi l_p}{2R}} dR \approx \frac{\nu \tau}{\alpha} \left(R_m e^{-\frac{\pi l_p}{2R_m}} + \frac{\pi l_p}{2} \mathrm{Ei}\left(-\frac{\pi l_p}{2R_m} \right) \right) \quad (67)$$

where Ei is the exponential integral function that defined as $\mathrm{Ei}(x) = \mathcal{P} \int\limits_{-\infty}^{x} \frac{e^t}{t} dt$ (where $\mathcal{P}$ is the principal part).

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