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Hydraulic control of mammalian embryo size and cell fate

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I. THEORY

We describe mathematically the growth and dynamics of the blastocyst following our previous work [1]. We model the blastocyst as a multicellular hollow spherical tissue shell, filled with fluid at a different pressure relative to the environment. Any osmotic imbalance or active pumping creates an inward flux of solvent that increases the radius of the shell while stressing its wall. When the wall stress is greater than a critical threshold, the wall ruptures leading to an outward flux that reduces the wall tension and deflates the shell. This deflation allows the rupture to heal, and the whole process repeats itself. While the total stress in the tissue shell has two components, a passive mechanical stress due to the lumenal pressure, and an active stress due to cellular actomyosin contractility, in our model we combine both contributions into a total stress.

As a first approximation, we assume that osmotic influx rate ($J_o = KP_{\rm osm}$) is constant and independent of the tension, and that the material follows a simple linear elastic-plastic law. For small strains below a yield stress (σ_y), the tissue is purely elastic, but it undergoes plastic deformation over the yield stress, with $\sigma_1 < \sigma_y < \sigma_2$. We write a set of equations for the evolution of the radius of the shell $R(t)$, the thickness $h(t)$, the hydrostatic pressure $P(t)$ and the wall stress $\sigma(t)$ that couples fluid permeation to the generation of tension in the tissue wall, and its intermittent release:

$$4\pi \frac{\mathrm{d}}{\mathrm{d}t}(R^2 h) = J_c \qquad \text{Cell vol. conservation} \tag{1}$$

$$\frac{\mathrm{d}R}{\mathrm{d}t} = K(P_{\rm osm} - P) - J_{\rm leak} - Q \qquad \text{Lumen vol. conservation} \tag{2}$$

$$\sigma = \frac{PR}{2h} \qquad \text{Tangent. force balance on shell} \tag{3}$$

$$\frac{\mathrm{d}\sigma}{\mathrm{d}t} = \frac{E}{R}\frac{dR}{dt} \qquad \text{Elastic constitutive eq.} \tag{4}$$

Here K is the areal permeability of the tissue wall, $P_{\rm osm}$ is the osmotic pressure, Q the water efflux rate after rupture per unit area of the shell, and E the elastic-plastic coefficient, where $E = E_0 + k\sigma$ for $\sigma < \sigma_y$, and $E = E_{\rm p}$ for $\sigma > \sigma_y$, being $E_{\rm p} < E(\sigma_y)$. We also assume that when the wall ruptures, outward flow through the hole can be modeled via a simple linear

Poiseuille-like relation coupling pressure to flux that reads

$$Q = \frac{1}{4\pi R^2}\frac{r^4 P}{\eta h} \tag{5}$$

where η is the viscosity of the solvent and r is the radius of the hole. We further assume that the time scale for hole closing, $\tau_{\text{hole}} \ll \tau_{\text{growth}}$, the time scale for blastocyst growth, so that we can approximate the opening of the hole as a sigmoid that depends on the wall stress. Then the hole has only two possible states, open and closed, and the transition between them occurs when the tension reaches the rupture tension $\sigma = \sigma_{\text{rupture}}$, leading to a hole of radius r_b, that closes when the fluid flow through the hole causes the tension to decrease to the healing tension, $\sigma = \sigma_{\text{heal}}$.

Finally, we introduce noise by allowing the rupture and healing tensions to fluctuate randomly around their average values following a Gaussian distribution with $\sigma_i \in \mathcal{N}(\bar{\sigma}_i, 0.2\sigma_i)$

As shown in [1], the change in radius from the initial value R_0 to the average value R_a follows $R_a \sim R_0(1 + \Delta\sigma/E)$, where $\Delta\sigma$ is the total change in stress. In our case where the elastic coefficient is a linear function of the stress, we expect R_a to be a linear function of R_0 because of dimensional arguments, but the slope of the relation will change as we depart from the linear regime.

For the simulations in Fig.4 of the Main Text we use the following parameters based on the experiments: the osmotic pressure $P_{\text{osm}} = 3\text{kPa}$, tissue permeability $K = 2.5\mu\text{m/kPa}\cdot\text{h}$, the initial radius of the cyst $R(0) = 25\mu\text{m}$, its thickness $h(0) = 5\mu\text{m}$, the initial hydrostatic pressure $P(0) = 0.4\text{kPa}$, the radius of the hole $r = 2.5\mu\text{m}$. We assumed that cells did not grow or divide during the experiments $J_{\text{c}} = 0$. For the calculations where the effect of leaking was explored, the elastic coefficient was set to $E = 5\text{kPa} + 2.5\sigma$ and $E_{\text{p}} = 49\text{kPa}$. The threshold stress for rupture and the yield stress were set in all the cases to $\sigma_c = 20\text{kPa}$ and $\sigma_y = 18.5\text{kPa}$. For the simulations where tissue stiffness was investigated, we assumed no leak $J_{\text{leak}} = 0$

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[1] Ruiz-Herrero, Teresa and Alessandri, Kévin and Gurchenkov, Basile V. and Nassoy, Pierre and Mahadevan, L. (2017).

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