Tissue growth controlled by geometric boundary conditions: a simple model recapitulating aspects of callus formation and bone healing

The shape of tissues arises from a subtle interplay between biochemical driving forces, leading to cell growth, division and extracellular matrix formation, and the physical constraints of the surrounding environment, giving rise to mechanical signals for the cells. Despite the inherent complexity of such systems, much can still be learnt by treating tissues that constantly remodel as simple fluids. In this approach, remodelling relaxes all internal stresses except for the pressure which is counterbalanced by the surface stress. Our model is used to investigate how wettable substrates influence the stability of tissue nodules. It turns out for a growing tissue nodule in free space, the model predicts only two states: either the tissue shrinks and disappears, or it keeps growing indefinitely. However, as soon as the tissue wets a substrate, stable equilibrium configurations become possible. Furthermore, by investigating more complex substrate geometries, such as tissue growing at the end of a hollow cylinder, we see features reminiscent of healing processes in long bones, such as the existence of a critical gap size above which healing does not occur. Despite its simplicity, the model may be useful in describing various aspects related to tissue growth, including biofilm formation and cancer metastases.

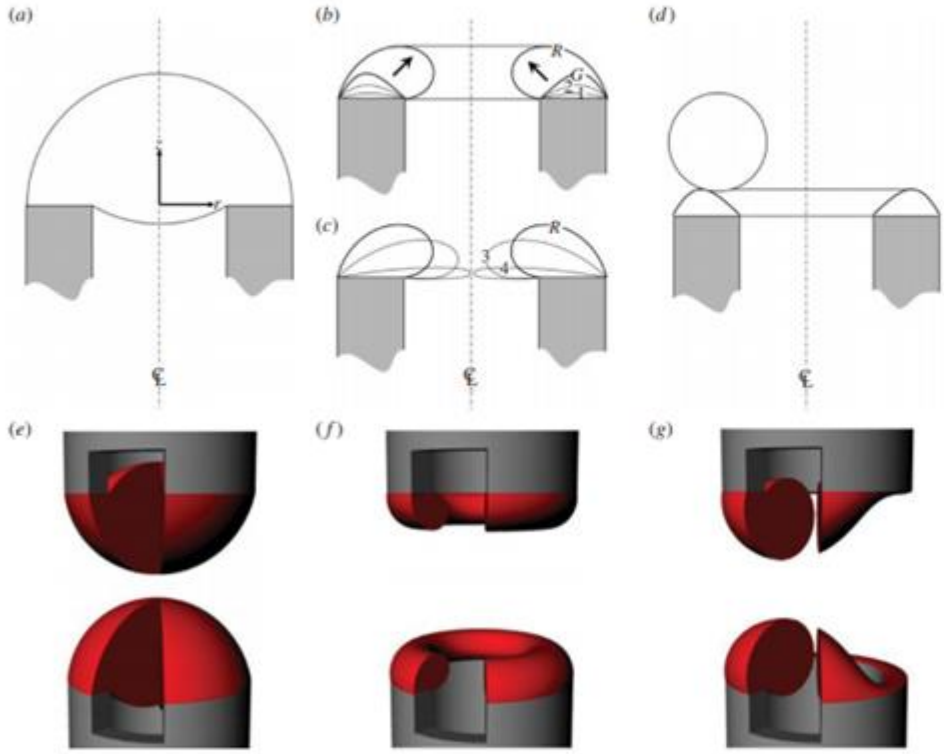

Figure 2. Topologically possible configurations with constant curvature sitting on the top of an open thick-walled cylinder. (*a*) A complete cap based on spherical calottes on the top and in the inner cylinder (both with same radius of curvature). These correspond to the stable branch S_3 in figure 3. (*b*) Nodoids partially covering the cylinder gap; nodoids labelled 1, 2 and *G* are on the stable branch S_1 in figure 3; nodoids between *G* and *R* (arrows) corresponds to the unstable branch U_1. (*c*) Further nodoids (labelled 3,4 and *R*) corresponding to the stable branch S_2 in figure 3. Such nodoids have the same curvature as those in (*b*) but a larger volume. (*d*) Nodoid with a spherical bulge (modelled by an adjacent droplet of identical mean curvature); nodoids with a spherical bulge correspond to the unstable branches U_2 and U_3 in figure 4. (*e–g*) Three-dimensional renderings of numerical simulations performed in Surface Evolver, for the topologies in (*a,b,d*). Note that the sketch in (*d*) is just an approximation of the real configuration shown in (*g*), neglecting the connecting zone between the spherical bulge and nodoid. *z* and *r* indicate the vertical and radial coordinates, respectively. (Online version in colour.)