The Shape of Things to Come: Morphogenesis

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Introduction

One model for the way the shapes of assemblies of cells are controlled and by which bodies are patterned (*morphogenesis*) emphasises the effects of mechanical forces. Here we follow the discussion of Odell *et al*[1], but omit the biological evidence behind the model: consult the original papers for this. The sorts of phenomena this project treats are gastrulation and neurulation, that is, the folding of epithelia, or sheets of cells. A typical example is given in Figure 1, which shows a two-dimensional simplification, which might represent a slice through a fluid-filled tube.

[1] G. M. Odell, G Oster, P Alberch, and B Burnside. The mechanical basis of morphogenesis : I. epithelial folding and invagination. *Developmental Biology*, 85(2):446 – 462, 1981

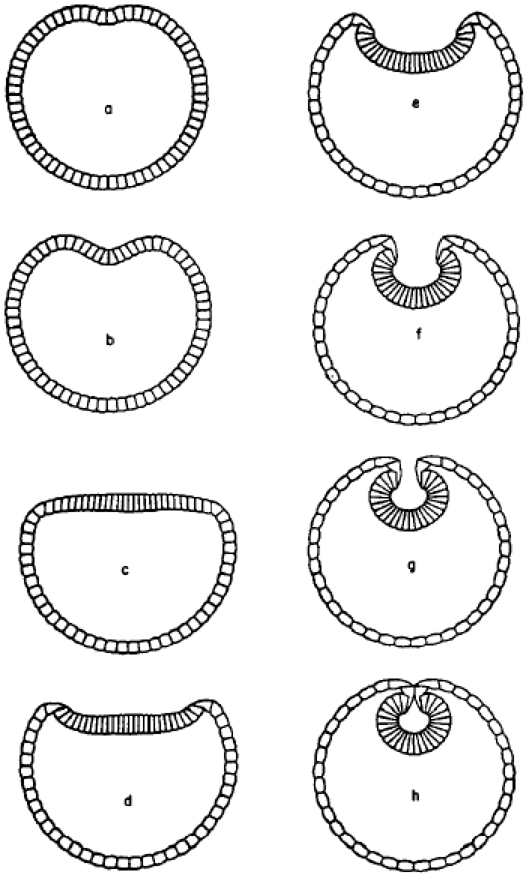

Figure 1: Simulation of amphibian neurulation (from Odell *et al* 1981.

The basis of the model is that each cell contains a special contractile domain. When stretched a small amount and released, these domains act as ordinary springs and return to their rest length. If stretched beyond a critical threshold, they contract to a new, shorter, rest length. As the volume of the cell remains roughly constant, this contraction causes the cell to become elongate in the other direction.

Mathematical Model

The whole process of shape changing is assumed to take place so slowly that inertial terms can be neglected, and the current length L of the contractile region can be described by the equation

$$\frac{dL}{dt} = \frac{k}{\mu}(L_0 - L),$$

where k is the elastic spring constant and μ represents viscous damping. What Odell *et al.* did was to consider the rest length of the spring, L_0, as a function of time in such a manner that the $L - L_0$ phase has two different stable regions. They took

$$\frac{dL_0}{dt} = \gamma(\epsilon_1^2 - LL_0)\left[\left(\frac{L-\eta}{\epsilon_3}\right)^2 + \left(\frac{L_0-\eta}{\epsilon_4}\right)^2 - 1\right],$$

where γ, ϵ_1, ϵ_3, ϵ_4 and η are constants and

$$\eta = 1 - \epsilon_3\epsilon_4\left(\epsilon_3^2 + \epsilon_4^2\right)^{-1/2}.$$

To ensure that the return to the contracted rest length is quite rapid, it is assumed that

$$k = k_0/L_0,$$

where k_0 is another constant.

Now a model is needed of the way in which cells try to maintain their shapes and interact.

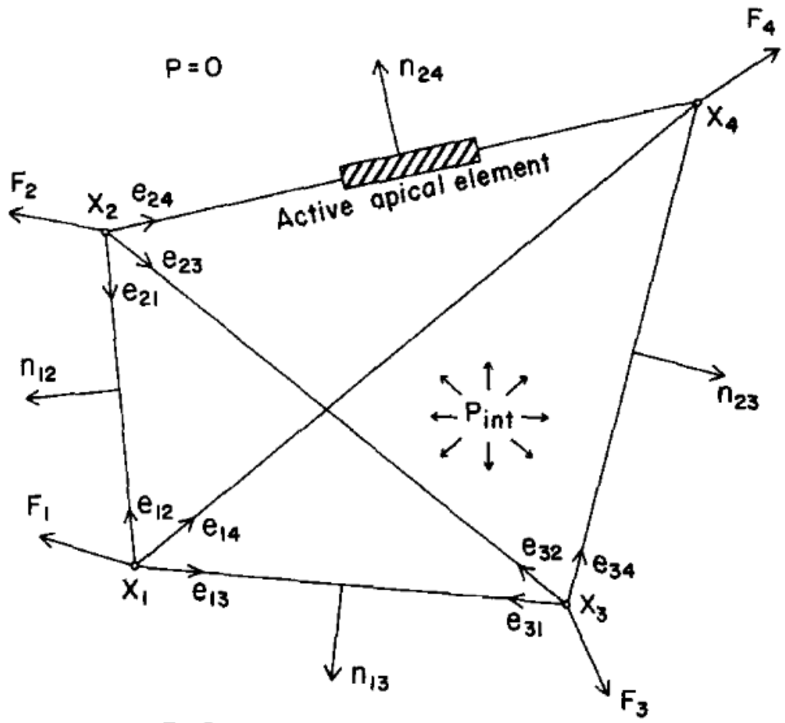

Figure 2: The forces on a cell. In setting up the equations, the normal pressure forces n_{ij} on each side are added to the corner forces. The shaded box is the nonlinear element, whilst the other sides and the diagonals are joined by linear damped springs.

Figure 2 shows how, in addition to the nonlinear side, a cell has an internal pressure, linearly elastic cell walls producing the forces

e_{ij}, and linearly elastic cross-braces (again giving forces e_{ij}). If we assume that the organism is composed of 2N cells, but remains symmetrical under reflection, we have to model the behaviour of only N cells. To rule out rigid motion and rotation of the whole organism, we fix one point and the orientation of one cell edge. If we work in two dimensions, and note that each corner is shared by 2 cells, we have a total of $4N + 4$ equations to set up and solve for the evolution of the organism.

Start with a circular ring of cells, with thickness h. Use N and h to determine the initial spring lengths by assuming that at the outset the cells are in equilibrium. You will find it helpful to set up Mathematica code to draw the configuration. Derive the coupled differential equations for the corner positions. Allow for the presence of a compressible fluid inside the organism. Then alter the length of the nonlinear spring in a few of the cells near the top of the organism and follow the development of the shape. The paper by Odell *et al* gives some suitable values for the parameters, and suggests that $N = 32$ gives reasonable results.

References

[1] G. M. Odell, G Oster, P Alberch, and B Burnside. The mechanical basis of morphogenesis : I. epithelial folding and invagination. *Developmental Biology*, 85(2):446 – 462, 1981.

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