Obtaining a Full Crypt Morphology

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Model with self-contact at a point

We model the crypt as a planar, elastic rod tethered to an underlying viscoelastic foundation, subject to heterogeneous growth. For simplicity and to enforce buckling at $t = 0$, we assume that the rod is inextensible. In this case, the current configuration, parametrised by s, is equivalent to the grown configuration, parametrised by S.

We consider the problem using a variational approach. Furthermore, if we assume symmetric self-contact, then we can reduce the problem to the half-interval, $[0, L_0/2]$. The contact point is assumed to occur at $s = s_1,\ x(s_1) = x_0 = L_0/2 - w$, where $w > 0$ accounts for the width of the lumen. We assume that contact traps interstitial fluid within the loop created by the contact region, which we will see enforces a pressure constraint on the force balance.

Initially, for convenience, we will minimise the energy functional assuming an elastic foundation, then replace the foundation by a viscoelastic law using force balance arguments.

The total energy functional to be minimised is given by:

$$\mathcal{E}\left[x, y, \theta, F, G, s_1\right] = \int_0^{s_1-} J ds + \int_{s_1+}^{\frac{L_0}{2}} J + pAds + \lambda C,$$

where the integrand $J[x, y, \theta, F, G]$ is given by

$J[x, y, \theta, F, G] = \frac{E_b}{2}(\theta')^2 + \frac{k}{2}y^2 + F(s)(x' - \cos\theta) + G(s)(y' - \sin\theta).$

The first term corresponds to the bending energy (assuming quadratic strain energy); the second term corresponds to the (elastic) foundation energy; the last two terms are point-wise constraints that impose the planarity assumption of the model due to the force densities, F and G.

The integrand $A = xy'$ imposes the area constraint in the contact region, where p is a Lagrange multiplier. That is, within the contact region, it is assumed

$$\int_{s_1+}^{\frac{L_0}{2}} Ads = \int_{s_1+}^{\frac{L_0}{2}} xy'ds = A_0.$$

This formula is derived by a straightforward application of Green's Theorem.

Finally, the last term,

$$C[x, s_1] = x(s_1) - x_0,$$

enforces the geometry of the contact condition.

To obtain the equations to be solved, consider the total variation of $\mathcal{E}$,

$$\delta\mathcal{E} = \mathcal{E}\left[x + \varepsilon\eta_1, y + \varepsilon\eta_2, \theta + \varepsilon\eta_3, F + \varepsilon\eta_4, G + \varepsilon\eta_5, s_1 + \varepsilon\eta_6\right] - \mathcal{E}\left[x, y, \theta, F, G, s_1\right],$$

where $\varepsilon \ll 1$ is an arbitrarily small parameter and $\eta_i(s)$ are functions that we assume vanish at the boundaries $s = 0$ and $s = L_0/2$.

We first expand the integrands J and A, the contact condition C, then the integral terminals. Expanding J in powers of ε, we obtain:

$$J[x+\varepsilon\eta_1, y+\varepsilon\eta_2, \theta+\varepsilon\eta_3, F+\varepsilon\eta_4, G+\varepsilon\eta_5] \tag{1}$$
$$= \frac{E_b}{2}(\theta'+\varepsilon\eta_3')^2 + \frac{k}{2}(y+\varepsilon\eta_2)^2 + (F+\varepsilon\eta_4)(x'+\varepsilon\eta_1' - \cos(\theta+\varepsilon\eta_3)) \tag{2}$$
$$+ (G+\varepsilon\eta_5)(y'+\varepsilon\eta_2' - \sin(\theta+\varepsilon\eta_3)) \tag{3}$$
$$= \frac{E_b}{2}\left((\theta')^2 + 2\varepsilon\theta'\eta_3' + \varepsilon^2(\eta_3')^2\right) + \frac{k}{2}(y^2 + 2\varepsilon y\eta_2 + \varepsilon^2\eta_2^2) \tag{4}$$
$$+ (F+\varepsilon\eta_4)(x'+\varepsilon\eta_1' - \cos\theta + \varepsilon\eta_3\sin\theta) \tag{5}$$
$$+ (G+\varepsilon\eta_5)(y'+\varepsilon\eta_2' - \sin\theta - \varepsilon\eta_3\cos\theta) \tag{6}$$
$$= J[x,y,\theta,F,G] + \varepsilon\Big[E_b\theta'\eta_3' + ky\eta_2 + F\eta_1' + F\eta_3\sin\theta + x'\eta_4 - \eta_4\cos\theta \tag{7}$$
$$+ G\eta_2' - G\eta_3\cos\theta + y'\eta_5 - \eta_5\sin\theta\Big] + O(\varepsilon^2). \tag{8}$$

Expanding A yields

$$A[x+\varepsilon\eta_1, y+\varepsilon\eta_2] = (x+\varepsilon\eta_1)(y'+\varepsilon\eta_2') \tag{9}$$
$$= xy' + \varepsilon x\eta_2' + \varepsilon y'\eta_1 + \varepsilon^2\eta_1\eta_2' \tag{10}$$
$$= A[x,y] + \varepsilon(x\eta_2' + y'\eta_1) + O(\varepsilon^2). \tag{11}$$

The contact condition expands straightforwardly to:

$$C[x+\varepsilon\eta_1, s_1+\varepsilon\eta_6] = x(s_1+\varepsilon\eta_6) + \varepsilon\eta_1(s_1+\varepsilon\eta_6) - x_0 \tag{12}$$
$$= x(s_1) + \varepsilon\eta_6 x'(s_1) + \varepsilon\eta_1(s_1) + \varepsilon^2\eta_6\eta_1'(s_1) - x_0 \tag{13}$$
$$= C[x,s_1] + \varepsilon\left(\eta_6 x'(s_1) + \eta_1(s_1)\right) + O(\varepsilon^2). \tag{14}$$

Now, considering the integrals requires a bit more work. In the region before contact, we have

$$\int_0^{s_1+\varepsilon\eta_6} J[x+\varepsilon\eta_1, y+\varepsilon\eta_2, \theta+\varepsilon\eta_3, F+\varepsilon\eta_4, G+\varepsilon\eta_5]ds = \int_0^{s_1+\varepsilon\eta_6} J + \varepsilon J_1 ds + O(\varepsilon^2) \tag{15}$$
$$= \left(\int_0^{s_1-} + \int_{s_1-}^{s_1+\varepsilon\eta_6}\right)[J+\varepsilon J_1]\, ds + O(\varepsilon^2) \tag{16}$$
$$= \int_0^{s_1-} J ds + \varepsilon\left(\int_0^{s_1} J_1 ds + \eta_6 J(s_1-)\right) + O(\varepsilon^2). \tag{17}$$

In the contact region,

$$\int_{s_1+\varepsilon\eta_6}^{\frac{L_0}{2}} J[x+\varepsilon\eta_1, y+\varepsilon\eta_2, \theta+\varepsilon\eta_3, F+\varepsilon\eta_4, G+\varepsilon\eta_5] + pA[x+\varepsilon\eta_1, y+\varepsilon\eta_2] ds \tag{18}$$

$$= \int_{s_1+\varepsilon\eta_6}^{\frac{L_0}{2}} J + pA + \varepsilon(J_1 + pA_1) ds + O(\varepsilon^2) \tag{19}$$

$$= \left(\int_{s_1+}^{\frac{L_0}{2}} - \int_{s_1+}^{s_1+\varepsilon\eta_6} \right) [J + pA + \varepsilon(J_1 + pA_1)]\, ds + O(\varepsilon^2) \tag{20}$$

$$= \int_{s_1+}^{\frac{L_0}{2}} J + pA ds + \varepsilon \left(\int_{s_1+}^{\frac{L_0}{2}} J_1 + pA_1 ds - \eta_6 J(s_1+) \right) + O(\varepsilon^2). \tag{21}$$

Putting it all together yields, at $O(\varepsilon)$,

$$\delta\mathcal{E} = \varepsilon \left[\int_0^{s_1} J_1 ds + \int_{s_1}^{\frac{L_0}{2}} J_1 + pA_1 ds + \eta_6 (J(s_1-) - J(s_1+)) + \lambda C_1 \right], \tag{22}$$

where

$$J_1 = F(\eta_1)' + ky\eta_2 + G(\eta_2)' + E_b\theta'(\eta_3)' + (F\sin\theta - G\cos\theta)\eta_3 \tag{23}$$

$$+ \eta_4(x' - \cos\theta) + \eta_5(y' - \sin\theta), \tag{24}$$

$$A_1 = x(\eta_2)' + y'\eta_1, \tag{25}$$

$$C_1 = \eta_6 x'(s_1) + \eta_1(s_1). \tag{26}$$

On $[0, s_1]$, integrating by parts and applying the boundary conditions that $\eta_i = 0$ at the boundaries yields:

$$\int_0^{s_1} J_1 ds = \int_0^{s_1} \Big[F'\eta_1 + (ky - G')\eta_2 + (F\sin\theta - G\cos\theta - (E_b\theta')')\eta_3 \tag{27}$$

$$+ \eta_4(x' - \cos\theta) + \eta_5(y' - \sin\theta) \Big] ds. \tag{28}$$

In order to minimise the energy functional $\mathcal{E}$, we require that the total variation vanishes. By the continuity lemma, this yields the following equations, in $[0, s_1]$:

$$x' = \cos\theta, \tag{29}$$

$$y' = \sin\theta, \tag{30}$$

$$F' = 0, \tag{31}$$

$$G' = ky, \tag{32}$$

$$(E_b\theta')' = F\sin\theta - G\cos\theta. \tag{33}$$

In the contact region, $[s_1, L_0/2]$, we have:

$$\int_{s_1}^{\frac{L_0}{2}} J_1 + pA_1 ds = \int_{s_1}^{\frac{L_0}{2}} \Big[(F' + py')\eta_1 + (ky - px' - G')\eta_2 + (F\sin\theta - G\cos\theta - (E_b\theta')')\eta_3 \tag{34}$$

$$+ \eta_4(x' - \cos\theta) + \eta_5(y' - \sin\theta) \Big] ds. \tag{35}$$

This gives us the following modified equations:

$$\begin{aligned} x' &= \cos\theta, && (36)\\ y' &= \sin\theta, && (37)\\ F' &= -py', && (38)\\ G' &= ky + px', && (39)\\ (E_b\theta')' &= F\sin\theta - G\cos\theta. && (40) \end{aligned}$$

Finally, considering what is left over gives the boundary conditions at self-contact. Expanding this in full:

$$\eta_6 \left[\frac{E_b}{2}(\theta')^2 + \frac{k}{2}y^2 + F(s)(x' - \cos\theta) + G(s)(y' - \sin\theta) \right]_{s_1-}^{s_1+} = \lambda\left(\eta_6 x'(s_1) + \eta_1(s_1)\right). \tag{41}$$

Imposing that these terms vanish yield continuity conditions (and also $\eta_1(s_1) = 0$, which I'm not sure how to eliminate) at $s = s_1$, which will be important for the numerics, while equating the x' terms gives an expression for λ:

$$\lambda = F(s_1+) - F(s_1-),$$

i.e. there is a jump in horizontal force at the contact point.

Self-contact over a region

Growth and material properties

At the moment, the growth stretch is assumed to depend solely on a Wnt-based chemical profile, which is highest in the base and minimal at the top.

$$\frac{\dot{\gamma}}{\gamma} = \exp\left(-\left(\frac{S_0 - 0.5L_0}{\sigma_W}\right)^2\right).$$

The differentiated cells are assumed to be twice as stiff as stem cells.

$$E_b(s) = 1 - 0.5\exp\left(-\left(\frac{s - 0.5l_0}{\sigma_E}\right)^2\right) = 1 - 0.5\exp\left(-\left(\frac{S_0 - 0.5L_0}{\gamma^{-1}\sigma_E}\right)^2\right).$$

For now, the foundation stiffness k is modelled to be spatially uniform, for heterogeneity was shown to have minimal effect on morphology in preliminary results.