Appendix: Stability of the homogeneous solution

The integration of the "stress-modulated growth" illustrated in the previous section predicts a spatially homogeneous solution, parametrically depending on the time-dependent growth rate. The growth $g(R;t)$ is independent of the radial position because the stress is the same everywhere. In such a purely mechanical setting we now study the stability of the homogeneous solution (20) and (25). In other words, the question is whether the spatial inhomogeneity observed in grown spheroids could be produced by the mechanobiological feedback, thus amplifying the spatial perturbations of the stress to yield inhomogeneous growth.

To investigate this hypothesis we consider the following perturbation of the homogeneous solution:

$$r(R,t) = \gamma g_0(t) R + \rho(R,t), \qquad \gamma g_0(t) R \gg \rho(R,t) \tag{32}$$

$$g(R,t) = g_0(t) + \delta(R,t), \qquad g_0(t) \gg \delta(R,t) \tag{33}$$

where γ and $g_0(t)$ are solutions of equations (21) and (24), respectively, and $g_0(0) = 1$. When the perturbed solutions are plugged in equations (21) and (24) and only first order terms are retained, the following linear equations are found

$$\left(\rho' + 2\frac{\rho}{R}\right)' = \gamma \, \frac{3-\gamma^2}{\gamma^2+1} \, \delta', \tag{34}$$

$$\dot{\delta} = \left(1 + 2\frac{g_0}{\kappa} - 2\frac{g_0}{\alpha} - 4\frac{g_0}{\kappa\gamma^2}\right)\frac{\delta}{\tau} + \frac{2}{3}\frac{g_0}{\kappa\tau\gamma^3}\left(\rho' + 2\frac{\rho}{R}\right). \tag{35}$$

Derivation of the former equation in space, derivation of the latter in time and cross substitution yields

$$\dot{\delta}' = \left(1 + 2\frac{g_0}{\kappa} - 2\frac{g_0}{\alpha} - 4\frac{g_0}{\kappa\gamma^2} + \frac{2}{3}\frac{g_0}{\kappa\gamma^2}\frac{3-\gamma^2}{\gamma^2+1}\right)\frac{\delta'}{\tau} \tag{36}$$

which determines the evolution in time of the spatial perturbation in the growth $g(t)$. Instability shows up if

$$\alpha\kappa\gamma^2(\gamma^2+1) > 2g_0\left(\alpha\left(1 + \frac{4}{3}\gamma^2 - \gamma^4\right) + \kappa\gamma^2\left(\gamma^2+1\right)\right), \tag{37}$$

for some $1 < g_0(t) < g_e$, where $0 < \gamma(p_D) < 1$.

The result (37) is negative versus our conjecture: it predicts a stabilization of the system for large enough growth g_0 which is not in agreement with experiments. If the purely mechanical system is stable, the reported inhomogeneity (large proliferation near the boundary, smaller internally) should instead be explained accounting for the role of nutrients.