Sharon Lubkin
North Carolina State University
e-mail: lubkin@eos.ncsu.edu
Oswaldo Lozoya
North Carolina State University/University of North Carolina-Chapel Hill

Mechanical control of spheroid growth: distinct morphogenetic regimes

We develop a model of transport and growth in epithelio-mesenchymal interactions. Analysis of the growth of an avascular solid spheroid inside a passive mesenchyme or gel shows that sustained volumetric growth requires four generic mechanisms: (1) growth factor, (2) protease, (3) control of cellularity, and (4) swelling. The model reveals a bifurcation delineating two distinct morphogenetic regimes: (A) steady growth, (B) growth arrested by capsule formation in the mesenchyme. In both morphogenetic regimes, growth velocity is constant unless and until a complete capsule forms. Comprehensive exploration of the large parameter space reveals that the bifurcation is determined by just two ratios representing the relative strengths of growth and proteolytic activity. Growth velocity is determined only by the ratio governing growth, independent of proteolytic activity. There is a continuum of interior versus surface growth, with fastest growth at the surface. The model provides a theoretical basis for explaining observations of growth arrest despite proteolysis of surrounding tissue, and gives a quantitative framework for the design and interpretation of experiments involving spheroids, and tissues which are locally equivalent to spheroids.