DISCRETE-TO-CONTINUUM MODELLING OF CELLS TO TISSUE

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Living tissues are composed of large numbers of cells packed together within an extracellular matrix. In order to understand the process of growth and remodelling in soft tissues that are subject to internal and external forces and strains, multiscale models that describe the interactions between individual cells and the tissue as a whole are needed. A significant challenge in multiscale modelling of tissues is to produce macroscale continuum models which rationally encode behaviour from the microscale (discrete cells). Over the years a number of highly successful approaches have been developed to rationally form macroscale models for multiscale processes such as solute transport and cell-cell signalling. However, such approaches have focused on homogenization techniques, which typically rely on underlying symmetries or periodicity on the smaller scales. We address the need for models that rationally incorporate the underlying mechanical properties of individual cells, without assuming homogeneity, symmetry or periodicity at the cell level. This challenge is particularly pertinent in modelling cardiac tissue, where the individual cells experience significant mechanical deformation in response to (periodic) electrical signalling. In particular, we are interested in cases where the mechanical properties of the cardiac cells may vary significantly between different regions of the heart (e.g. in disease or following a myocardial infarction).

We consider a single line of nonlinearly hyperelastic cells of finite size, with forces transmitted across the boundaries between neighbours. One or both ends of the line are fixed to represent free expansion or confinement. The dynamics of the array is given by a system of discrete 1D ODE's. Individual cells grow in volume and divide into two identical daughter cells. The parent cell divides its mass equally so that each daughter cell is half the total length of the parent cell, and an extra boundary at the midpoint of the parent cell is introduced. Two examples of resistance to motion are considered.

Firstly, we suppose that the cells are binding and unbinding to a fixed substrate, providing a resistive force is proportional to the speed of the cell relative to the substrate (Stokes dissipation). Secondly, we consider a local resistance to motion arising from the motion of a cell boundary relative to its neighbours so that the damping force is proportional to the rate of elongation of the cell (Kelvin dissipation).

Having constructed and solved the discrete model, we then use the methods of discrete-to-continuum upscaling to derive new PDE models using Taylor expansions local to each discrete cell, which requires that the properties of the individual cells (e.g. shear modulus) vary smoothly along the array. The discrete and PDE models are solved computationally for a range of imposed boundary and growth conditions.

We demonstrate excellent agreement between the solutions (including diagnostics such as pressure and stretch along the array) of the discrete and PDE models for a number of examples, including a ring of cells (e.g. myocytes) with a wave of active contraction, growth of incompressible neo-Hookean cells, and stress-dependent growth. Qualitative differences are found in long-time scaling laws for the growth of the array of cells for stress-dependent and independent cell division rules.

These methods provide a rational multiscale approach for deriving continuum models for soft tissues based on measured properties of individual cells. They can be extended to 2D and 3D.