Collaborative computational frameworks and the growth problem

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Growth in biological tissue is a direct outcome of cascades of complex, intracellular, biochemical reactions involving numerous species, their diffusion across cell membranes, and transport through the extracellular matrix. Both reaction and transport are influenced by mechanics in a number of ways, and much of our modelling work thus far [1, 2] has been aimed at gaining a deeper understanding of the biophysical bases underlying these influences.

When treated as a continuum (usually in the context of mixture theory [3] to accommodate multiple interacting species, as in our previous work), a formal axiomatic treatment can be used to derive a general set of governing equations which specify how the mass, momenta and energy of each constituent species of the tissue evolve with time. These relations do provide a great deal of insight into the general behaviour of growing tissue treated as mixtures, the nature of the coupling between different physics and, with the incorporation of additional axiomatic principles (such as the Clausius-Duhem inequality), provide hints for constitutive specification.

Even so, when attempting to tailor a general continuum field formulation for a specific tissue growth problem, several basic modelling choices need to be made, which include:

- Determining which species need to be incorporated (collagen, proteoglycans, different kinds of cells, extra-cellular fluid, sugars, proteins ...)
- Appropriate constitutive relationships for the stress response of load-bearing species
- Specific models used for the various biochemical reactions,
- Determination of realistic boundary conditions
- Judicious introduction of additional constraints (such as tissue saturation)

When attempting to address some of these fundamental questions, it often proves useful to experiment *in silico*; constructing simple test cases to help shape ideas. This requires a computational framework that is not only efficient, but functions at a sufficiently high level so that it can evolve easily with our understanding of the problem.

In this context, the `FEniCS` project (a collaborative project for the automation of computational mathematical modelling based on the finite element method [4]) serves as an appropriate foundation to construct a computational tool kit specifically tailored to the needs of the tissue growth modelling community. Since it allows researchers to pose their problems directly in terms of the weak forms of the partial differential equations arising from the theory, it allows them to focus on higher-level modelling questions and not be hindered by specific implementation issues. As preparatory steps for implementing a common, robust computational tool kit for the growth problem, several relevant improvements to core `FEniCS` components are currently actively being worked upon, including automated symbolic

linearisation of classes of nonlinear forms, improved support for finite deformation and fluid-structure interaction, and adaptive mesh refinement/enrichment toward (goal-oriented) error control.

These enhancements will better help the creation of a common computational infrastructure customised for modelling growth. Since it is an open source project, anyone is free to obtain, use, study and extend the code. This will allow researchers and students to both contribute their own expertise, as well as learn from others, enhancing common understanding of the problem.

Such a computational framework would furnish a powerful tool that can easily be tailored to answer specific questions–ranging from those pertinent to viscoelastic aspects of the mechanical response of growing tendons under different loading conditions, to quantitative investigations of the efficacy of drugs based on how they are administered, to understanding the cellular processes associated with tumour growth.

References

[1] K. Garikipati, E. M. Arruda, K. Grosh, H. Narayanan, S. Calve, *A continuum treatment of growth in biological tissue: the coupling of mass transport and mechanics*, Journal of the Mechanics and Physics of Solids **52** (2004), 1595–1625

[2] H. Narayanan, E. M. Arruda, K. Grosh, K. Garikipati, *The micromechanics of fluid-solid interactions during growth in porous soft biological tissue*, Biomechanics and Modeling in Mechanobiology (2008), *Accepted*

[3] C. A. Truesdell, R. A. Toupin, *The Classical Field Theories*, Handbuch der Physik, band III/1 (1960), Springer-Verlag, Berlin

[4] A. Logg, *Automating the finite element method*, Archives of Computational Methods in Engineering **14** (2007), 1886–1784