TENDON GROWTH AND HEALING: THE ROLES OF REACTION, TRANSPORT AND MECHANICS

HARISH NARAYANAN, ELLEN M. ARRUDA, KRISHNA GARIKIPATI AND KARL GROSH

Department of Mechanical Engineering
University of Michigan
Ann Arbor, Michigan 48109, USA
hnarayan@umich.edu

As a substantial step toward understanding the mechanical and biochemical influences leading to the development of soft tissue, this current exposition enhances our recently-proposed general formulation of growth [1], by making it more applicable to the biophysics of growth in soft tissue; specifically tendon. Tendons are largely acellular and avascular in their mature state, resulting in an ideal setting to study the factors affecting collagen growth; collagen being the most important structural protein in soft tissue. The broad applications of the theory include studies of injury mechanisms, musculoskeletal wound healing, scarring, surgical repair, pathological hypertrophy/atrophy, an understanding of ageing, as well as drug efficacy and interaction.

Our formulation is within the context of open system thermodynamics. It involves the introduction of additional quantities (including mass sources/sinks, mass fluxes, terms for energy and momentum transfer between species), and deduces consequences for balance laws. We now utilise *enzyme kinetics* as a more physiologically relevant means of representing the biochemistry. This necessitates the introduction of additional interacting species, which result in more partial differential equations to solve, as well as adding to the modelling choices to be made. These choices and the constitutive framework will also be discussed. Moreover, we reformulate the governing differential equations for reaction-transport to represent the incompressibility constraint on the fluid phase of the tissue. This correction enables a straightforward implementation of numerical stabilization for the hyperbolic, or advection-dominated, limit (see, for e.g., [2]).

A finite element implementation employing a staggered scheme is utilised to solve the coupled nonlinear partial differential equations that arise from the theory. Nonlinear projection methods are used to handle incompressibility, mixed methods for stress-gradient driven fluxes and energy-momentum conserving algorithms are used for dynamics. Motivated by our experimental model, an *in vitro* scaffold-free engineered tendon formed by self-assembly of tendon fibroblasts [3], several numerical examples are solved in this context demonstrating biophysical aspects of growth. Particular cases of note include the simulation of damage healing by introducing mass source terms which mimic cell signalling to produce more collagen preferentially in wounded regions, and comparisons between bolus and gradual doses of nutrients, allowing for an introductory study of drug efficacy based on how it is administered.

References

[1] K. Garikipati, E.M. Arruda, K. Grosh, H. Narayanan and 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**, 1595–1625, 2004.

[2] T. Hughes, L. Franca and M. Malle, "A new finite element formulation for computational fluid dynamics: VII. Convergence analysis of the generalized SUPG formulation for linear time-dependent multidimensional advective-diffusive systems," *Comp. Methods in Applied Mech. Engrg.* **63(1)**, 97–112, 1987.

[3] S. Calve, R. Dennis, P. Kosnik, L. Baar, K. Grosh and E.M. Arruda, "Engineering of functional tendon," *Tissue Engineering* **10 (5)**, 755–761, 2004.

Keywords: tendon, growth, enzyme-kinetics