Under TheHood

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Continuum Mechanical Modeling of Biological Growth

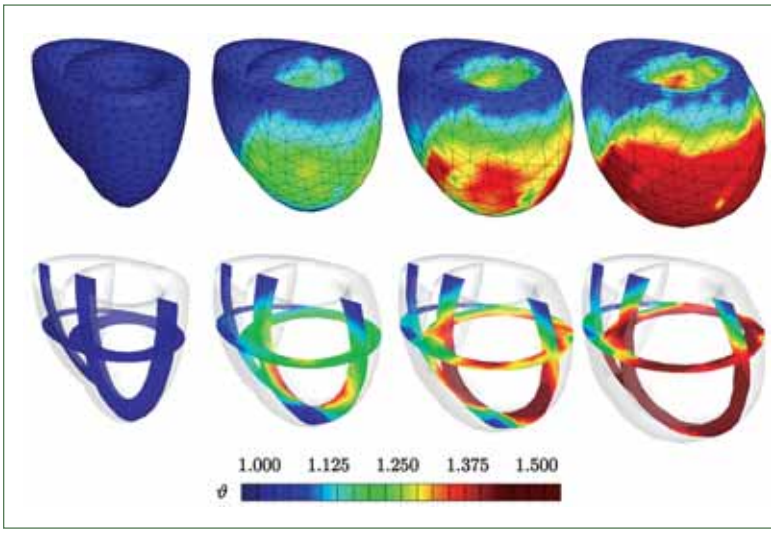
Unlike most classical engineering materials, biological tissues can adapt to external stimuli by growing in volume: Skin grows in response to wounding; muscles grow in response to exercise; cancer cells grow into tumors; and heart muscles become enlarged in response to high blood volume. To understand these adaptive processes and their role in various chronic diseases, it can be useful to study them in predictive computer models of cells, organs, organ systems and whole organisms.

As with most mechanical problems, volumetric growth can be described using continuum mechanics, a fundamental mathematical framework that describes the motion of and forces acting on a system while ignoring the discrete microscopic structure of the material under observation. Three sets of equations are used to model the system: kinematic equations, or equations of motion; constitutive equations, which model the behavior of the material; and balance laws of linear momentum, which are a generalized form of Newton's 2nd Law (force equals mass times acceleration).

But some aspects of continuum mechanics must be adjusted to address the unusual behavior of living materials. For example, unlike other materials that elastically snap back to their original shape after being stretched and released, growing tissues do not return to their original shape. The kinematic equations therefore need to account for reversible elastic and irreversible growth deformations. The precise definition of growth, and hence the exact form of this irreversible deformation, generally differs depending on tissue type and can ideally be tied to changes on the cellular or even molecular level.

For many tissues, growth may be expressed in the continuum mechanics framework as a matrix, which can be formulated in a particularly beautiful form with an intuitive interpretation of its entries. In the case of cardiac muscle growth, for example, these matrix entries can be interpreted on the molecular level as the addition of sarcomeres—the individual units that make up muscles—in series and in parallel to the existing sarcomere units. These changes result in changes on the organ level: adding sarcomeres in series results in the dilation of the cardiac muscle, while sarcomeres added in parallel results in the thickening of the cardiac muscle. Typically, the growth process is highly dynamic, and growth takes place until equilibrium between external mechanical stimuli and the growth process is reached. In its final configuration, the entries of the growth matrix will be proportional to the number of sarcomeres that were added to the tissue in series and in parallel. (Rausch MK, Dam A, Göktepe S, Abilez OJ, Kuhl E. Computational modeling of growth: Systemic and pulmonary hypertension in the heart. *Biomech Mod Mechanobio*, DOI:10.1007/s10237-010-0275-x.)

As one might imagine, the equations modeling this growth process are highly non-linear, reflecting the complex geometries and heterogeneous materials involved. As such, they typically must be solved numerically rather than analytically, which results in approximate solutions. Several numerical methods exist, such as the finite difference method (FDM) and the finite elements method (FEM). Both break down the partial differential equations describing a system into a set of algebraic equations that can then be efficiently solved using high performance computers. However, FEM has been shown to be advantageous for mechanical modeling of biological growth for a number of reasons. For instance, FEM allows us to discretize the given equations in space and time using a variety of different elements, to capture complex, ideally patient-specific, geometries. In summary, the combination of enhanced continuum theories and a powerful numerical method such as FEM now enables us to reliably predict biological growth across the different scales. This new information allows us to better understand, treat, and hopefully one day reverse the progression of pathological conditions, such as tumor growth, atherosclerosis, and heart failure. □



An idealized ventricle discretized in space and time. After spatial discretization, the model consists of 4000 elements. In this simulation, the heart undergoes growth in response to volume overload—too much blood and therefore, too much stretch in the left heart chamber. The color map denotes the amount of growth. A value of 1 (dark blue) corresponds to the normal number of sarcomeres within the heart cell. A value of 1.5 (red) indicates a 1.5-fold increase of sarcomere units.

DETAILS

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