Exploring new mechanobiological strategies for defining growth law in morphoelasticity

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Summary

Morphoelasticity represents one of the most consolidated theories for growth, remodelling and morphogenesis. However, many fascinating challenges remain partly unanswered. Among these, the identification of a general growth law adaptable to all living systems by avoiding *a priori* phenomenological kinematics and the way of connecting local growth and morphogenesis, mechanics and diffusion, represent two relevant open issues. To then explore these topics, we propose a strategy to trace back accretion, shaping and remodeling through mass balance. This should represent the sole dynamic equation to constrain the growth problem and to drive the biological, geometrical and constitutive transformations experienced by the living material, by providing complete information about species' proliferation, decay and mutual (interspecific) interactions, plasticity (mutation) as well as of diffusion mechanisms. Within a full-coupled framework, inhomogeneous rates depending on mechanical stresses and chemicals can be generalized to obtain consistent evolution laws, then applied to different growth problems.

Introduction

Mechanical stress, stress gradients and tissue mechanical properties are widely acknowledged as primary environmental factors influencing the tissue constituents at various scale levels, thereby orienting the growth of numerous biological systems, including muscles, arteries, bones, and cell structures [1, 2, 3]. Nevertheless, deriving thermodynamically and biologically consistent evolution dynamics for growth remains an unresolved issue. Indeed, in the absence of unique physical principles that would help to identify suitable forms of the growth, many growth kinematics are often assumed *a priori* based on phenomenological evidence or experimental results, by so pre-determining the structure of the growth tensor and limiting the mass-kinematics constitutive law to volumetric growth. However, in prescribing the kinematics of growth, some important aspects related to the interspecific interactions of biological constituents, as well as the inherent coupling of growth, remodeling and morphogenesis processes with actual mass evolution, seem not yet fully disclosed. In light of these observations, we aim to contribute to the field by exploring the impact of integrating leading cell-cell and cell-extracellular matrix (ECM) interactions on tissue development. To this end, as largely well known, evolutionary interspecific systems can be employed to analyze the dynamics of growth-related molecular processes in the context of body mass evolution. However, in absence of a consistent strategy, such systems are not sufficient to characterize the growth law. By starting from the generalization of the mass balance in finite regime, it has been possible to derive consistent evolution for the entire growth tensor without the need of uncoupling geometry from mass development, by providing a mechanobiology-based strategy to fully describe coupled growth, remodelling and morphogenesis processes in different contexts.

Results and Discussion

The proposed coupled strategy is analyzed with reference to some first paradigms and then can be extended to some multi-constituent systems involving more complex interspecific interplays. Results show how the inherent connection of microstructural properties, species flows and stress fields actually orient the internal re-organization of the material, by determining the overall change of both size and shape onto spontaneous growth directions. Some cases of interest are analyzed, with reference to problems of heterotypic tumor growth and arterial development, in which cell dynamics play a crucial role in determining residual stresses that drive the possibly anisotropic adaptation of such type of systems.

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