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Multiscale modelling in biomechanics

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This *Special Issue* emerged from two mini-symposia organised for the 7th World Congress of Biomechanics, held at Boston in July 2014. During these two symposia - and related sessions at the congress - it became evident that there is considerable potential and promise in the use of multiscale modelling and simulation in biomechanics, particularly in its potential to enable the discovery of new scientific knowledge and to enhance clinical decision-making and therapy.

Why do researchers in biomechanics feel the growing need to describe complex phenomena across different space-time scales? One reason is the "curse" of resolution. Resolution is defined as "the smallest interval of a measured signal that will still cause a change in the measurement result". We continue to face resolution limits not only in our sensors, but also in the storing, processing and ultimately understanding of observational quantifications. Thus, to explore from the infinitely small to the infinitely large with a finite resolution we need *scales*. In biomechanics, exploration of scales is motivated by our desire to understand biophysical phenomena of genes, molecules, cells, tissues, organs, organisms, and populations when affected by short-scale (e.g. injury) and long-scale (e.g. growth and aging) temporal changes. Another reason is that, in the spirit of reductionism, advances in genetics, molecular biology, and imaging provide increasingly more information at smaller and smaller scales. Yet, there is a pressing need to integrate this expanding knowledge base with that at other, higher, scales. Integrative modelling offers a promising descriptive and predictive potential.

The vast majority of traditional engineering theories rely on the assumption of "scale separation". A steel beam, used in construction, may have a length of say 5 m; its microstructural elements, called *grains*, have an average size of around 50 μm. Thus, between the (macro)structural and the microstructural element that forms it there is a scale separation of 10^5. This means that every small portion of the steel structure contains thousand of grains, whose properties can be described statistically within that small volume. Because of this we can accurately predict the mechanical behaviour of this steel beam using the information about its grains. As a biomechanical analogy, a human femur is roughly 0.5 m in length; it microstructural elements, the osteons, can be as long as 1 mm. So the scale separation for a human bone is only 10^2. This is not unique for bone; most tissues forming the human body have similar scale separations, if not less. In spite of this, most prior biomechanical research has focused on traditional engineering theories that assume scale separation, e.g., continuum theory. Notwithstanding its many benefits, limitations of the application of continuum theory to many aspects of tissue biomechanics have been discussed in the past [Harrigan, 1998]. It has only been more recent that investigators have started to explore systematically the possibility of accounting for more than one space-time scale in their models [Viceconti, 2011]. As our knowledge of biomechanics within individual scales increases, our capacity to adapt multiscale modelling and simulation strategies from traditional disciplines evolves; when, and if necessary, new computational approaches for multiscale biomechanical analysis will emerge naturally.

This Special Issue, far from exhaustive, provides a representative sample of multiscale modelling and simulation research as applied to various problems in biomechanics.

In “A survey on stochastic multi-scale modelling in biomechanics: computational challenges,” Marco Favino, Rolf Krause, and Igor V. Pivkin provide a literature review of contemporary computational methods used to model complex systems across scales.

In “Applications of computational models to better understand microvascular remodelling,” Walter Murfee and colleagues show how different scientific questions, in this case related to microvascular remodelling, can be more effectively answered by modelling processes at different scales when experimentation may be challenging.

In “A multiscale model for the study of cardiac biomechanics in the single-ventricle surgeries: a clinical case,” Alessio Meoli and colleagues use a multiscale approach to model the convoluted interactions between the heart and the rest of the circulatory system in pursuit of a clinical application.

In “Multi-scale modelling of the placental vasculature,” Alys Clark and colleagues use a multiscale simulation to predict the progressive vascularisation of the feto-placental circulation during pregnancy.

In “Multi-scale models of skeletal muscle reveal the complex effects of muscular dystrophy on tissue mechanics and damage susceptibility,” Kelley Virgilio and colleagues propose a multiscale model of skeletal muscles that integrates finite element analysis and agent-based modelling to explore the sensitivity of macroscopic properties to the variability of microscopic properties in healthy and pathological (i.e., Duchenne muscular dystrophy) conditions.

In “Multiscale cartilage biomechanics: technical challenges in realizing a high-throughput modeling and simulation workflow,” Ahmet Erdemir and co-workers explore the multiscale modelling of articular cartilage from a methodological point of view, considering the resolution of challenges that a large scale exploration of all regions and all possible loading conditions raises.

In “The inter-sample structural variability of regular tissue-engineered scaffolds affects significantly the micromechanical local cell environment,” Ana Campos Marin and Damien Lacroix use a multiscale modelling approach to an interesting tissue engineering problem, emphasizing the translational utility of *in silico* approaches.

In “Coupling intercellular molecular signaling with multicellular deformation for simulating 3D tissue morphogenesis,” Satoru Okuda and colleagues explore how multiscale modelling can be used to simulate the early stages of morphogenesis driven by signalling at molecular levels.

In “Stochastic modelling of muscle recruitment during activity,” Saulo Martelli and colleagues use an original approach to account for the stochasticity of neuromuscular control, an approach that finally enables the use of musculoskeletal dynamics to investigate pathological conditions as well.

In “Comparison of generic and subject-specific models for simulation of pulmonary perfusion and forced expiration” Kerry Hedges and colleagues explore another important methodological issue: the required degree of personalisation of multiscale models.

And last, but definitely not least, Mylena Mordhorst and colleagues show how multiscale modelling can be used to predict global manifestation of muscle activation, such as the EMG signal, from a multiphysics-based multi-scale description of the muscle contraction process, in “Predicting EMG signals under realistic conditions using a multiscale chemo-electro-mechanical finite element model”.

To see examples across many different physiological and pathological problems reinforce the evidence of how multiscale modelling is opening new doors to the exploration of the human body with mechanistic approaches. We hope the reader will find this collection of papers both informative and inspiring.

References

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