WHAT MECHANICAL QUANTITY DO CELLS REGULATE IN SOFT TISSUES?

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Background

In soft biological tissues, cells seek to establish and maintain a preferred mechanical state, the so-called homeostatic state. This state is marked by a specific (non-zero) tensile stress. However, so far, it remains controversial whether cells directly regulate stress or whether they primarily control some other target quantity from which tensile stress results as a consequence [1]. Understanding what target quantity cells are primarily regulating in soft tissues and how they are doing this is one of the key questions of currrent soft tissue biomechanics and mechanobiology. Answering it will be an important step towards predictive computer simulations of growth and remodeling in soft tissues, which play key roles in various areas ranging from tissue engineering to clinical healthcare (e.g., aneurysms).

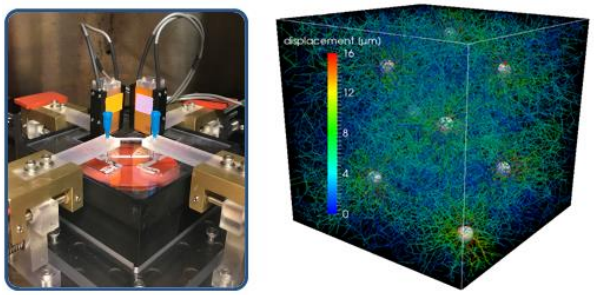

Figure 1: Combined experimental (left) and computational (right) framework to study interactions between cells and extra-cellular matrix (ECM)

Recent Advances

To identify the target qunatity cells regulate in soft tissues we developed a combined experimental [2] and computational [3] framework (Fig. 1). Our experimental setup allows well-controlled biaxial stress and strain states in tissue equivalents. Our computational framework models soft tissues as networks of discrete fibers and cells. The interactions between both are represented by a detailed model of focal adhesions.

We carefully validated our model and demonstrated that it can reproduce even complex phenomena such as the scaling relation between fiber density and homeostatic stress level.

Subseqently, combining extensive experimental and computational studies, we were able to identify the key factors and processes in the homeostasis of soft tissues, in particular the target quantity that cells regulate on short time scales [4].

Christian J. Cyron is currently full professor at the Department of Mechanical Engineering of Hamburg University of Technology and director of the Institute of Material Systems Modeling at Helmholtz-Zentrum Hereon, a major federal research laboratory in north Germany. He obtained his PhD in computational mechanics at the Technical University of Munich in 2011. From 2012 – 2014 he worked as postdoctoral associate at École Polytechnique, France, and Yale University. He has been working on computational modelling of mechanobiology for around 15 years and is an author of around 60 publications in peer-reviewed journals and 80 contributions to international and national conferences.

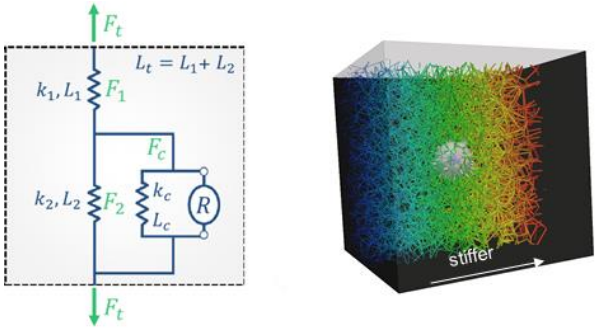

Figure 2: Microscopically informed continuum-scale model of growth and remodeling (left) and computer simulation of durotaxis (right)

Future directions

The insights provided by our combined experimental and computational framework open up several promising avenues of research. One relates to a new generation of microscopically informed continuum-scale simuluation models of growth and remodeling (Fig. 2, left), another one to a detailed analysis of complex cell-ECM interaction patterns such as durotaxis (Fig. 2, right), which opens up ways to enhanced tissue engineering

References

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