Local mechanical characterization of soft fibrous materials

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Abstract

Soft collagenous tissues are highly heterogeneous at cell length scale. Local deformation mechanisms determine their mechanical properties and influence the behaviour of resident cells. Therefore, improved understanding of tissue biomechanics and mechanobiology requires mechanical characterization at the micrometer scale. Collagen is the most abundant protein found in the human body and represents the mechanically dominant components of soft tissues, such as skin. Better understanding the mechanical behaviour of collagen fibers and their interplay with the surrounding matrix would provide insights into various diseases related to collagen. In particular, it would allow us to better characterize the conditions of the extracellular matrix leading to the onset and progression of fibrotic diseases.
Current assessment of local mechanics of soft fibrous materials is based on micro- or nanoindentation. Atomic force microscopy (AFM) is a form of scanning probe microscopy that has found many applications in the mechanobiology field since its invention in the late 1980's. This tool, among its many functionalities, permits measurements of mechanical properties of biological tissues at the length scale of cells. However, depending on the tissue of interest, AFM indentation may not be sufficient for tissue characterization. In our previous study, two collagen hydrogels with different concentrations of collagen were measured with AFM-based nanoindentation (1). The results demonstrated that despite a 14-fold increase in collagen concentration, the apparent Young's modulus of the two collagen hydrogels were not significantly different (1). On the other hand, cells cultured within the two hydrogels behaved very differently in terms of their proliferative state (1). These results can be rationalized using a model which represents the collagen hydrogels in two parts: a discrete network model to exhibit the properties of the collagen fibers and a continuum solid to represent the matrix part of the hydrogel. The model confirms that the collagen fiber network is not activated by AFM-based nanoindentation (1).

In this contribution, we will present a novel approach for characterization of the local properties of soft fibrous materials. Our aim is to develop an experimental protocol which could activate fibers on this length scale. It is commonly understood that collagen fibers behave differently in compression and in tension and this led to the idea of comparing the mechanical response of collagen hydrogels when subjecting them to nanoindentation versus a nanoscale pulling force. Fluid force microscopy (FluidFM) has emerged as an advancement to AFM

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technology that incorporates nanofluidic channels into the AFM probes thereby allowing the suction or dispensation of fluids (2).

In our experiments, FluidFM-based suction is applied to collagen hydrogels of different compositions, and their response is compared against their nanoindentation behaviour. Using pulling forces instead of indentation was shown to distinguish between the two collagen hydrogels with different collagen concentrations. This approach provides insights into how collagen fibers respond to forces within their tissues and how these forces are transmitted and shared with other material components. Alongside this experimental work, we aim to rationalize these observations through computational modelling. A biphasic model represents the matrix part of the hydrogels, with a solid and liquid phase, and is combined with a discrete network model representation of the collagen fiber network. The improved protocols and models will be applied to skin samples, with the aim to contribute to the development of mechano-therapeutics for fibrotic diseases, such as systemic sclerosis, impaired wound healing, hypertrophic scarring or for the optimization of skin tissue-engineering.

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(2) A. Meister *et al.*, "FluidFM: Combining Atomic Force Microscopy and Nanofluidics in a Universal Liquid Delivery System for Single Cell Applications and Beyond," *Nano Lett.*, vol. 9, no. 6, pp. 2501–2507, Jun. 2009, doi: 10.1021/nl901384x.