COLLAGEN FIBRIL NANOMECHANICS

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Background

Collagens are the result of millions of years of biological evolution and compose a unique family of proteins. The majority of collagens provide mechanical support for biological tissues. The most abundant collagen molecules expressed by cells, e.g., types I, II, III, self-assemble into larger structures, known as collagen fibrils (CFs). CFs display a complex structural architecture, and their properties are tuned by the cells expressing them by imposing forces. In turn, CF mechanics influence cell behavior and because of this are important for tissue homeostasis. In this context, CFs are mechanically exposed to varying loading environments throughout the body, yet they perform and maintain mechanical functionality. CFs show nonlinear, elasto-visco-plastic behaviour, and therefore, determination of their mechanical properties is non-trivial. Advances in nanotechnology instrumentation opened the door to investigate the mechanics of individual CFs, but the number of samples tested to date is small and many open questions remain.

Recent Advances

The mechanics of isolated and individual CFs is a multiparameter problem (Figure 1). From research to date, several mechanisms influencing CF mechanics have been identified. These are hydration, composition, chemical modification, and structure. Hydration levels greatly affect both the tensile and transverse apparent modulus [1, 2]. The mechanical stiffness of CFs can be increased up to 6-fold in tension by reducing hydration [1]. CFs undergo enzymatic and nonenzymatic chemical modifications, i.e., attachment of adducts and cross-linking. These modifications, influence the longitudinal and transverse mechanical properties of CFs. However, while the extremes, i.e., very small vs. very high amounts of cross-linking have been studied, a full mechanistic understanding of properties related to such modifications is missing. In addition, cross-linking type and amount are also related to collagen turnover and pathologies. In idiopathic pulmonary fibrosis (IPF), for example, collagen cross-linking has been identified as a driver of pathology influencing CF mechanics and mechanobiology [3]. Further, also nonenzymatic glycation (*in vitro*) has been related to nanomechanical stiffening of CFs [4]. Lastly, CFs are heterotypic [5], and relative amounts of type I and III also affect CF mechanics [6]. In tension, CFs show a complex behaviour with up to three different phases [7]. So far, five deformation mechanisms have been proposed but a mechanistic understanding is lacking. Yet, viscous properties have been associated to hydrogen bond (H-bond) rupture/reformation and molecular sliding.

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Future directions

CFs are essential for human biomechanics and mechanobiology. Yet, our knowledge remains scarce, as the number of samples tested to date is on the order of a few hundred. To mechanistically understand CF mechanics and relate them to the complex multiparameter landscape (cf. Figure 1) significantly more studies of CF mechanics coupled with chemical analysis are required. Importantly, the full nonlinear elasto-visco-plastic behaviour needs to be assessed. This will not only deepen our understanding of CF mechanics in healthy tissues, but also the progression of connective-tissue pathologies.

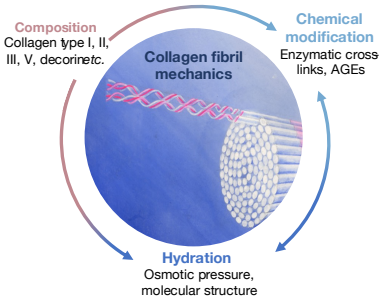

Figure 1: The multiparameter landscape of collagen fibril mechanics. Artists' impression of a collagen fibril. (courtesy of Lydia Andrioti).

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Acknowledgements

The works presented here would not have been possible without the contributions of P.J. Thurner, M. Jones, D.E. Davies, A. Carriero, M. Rufin, M. Nalbach, M. Handelshauser, A. Rohatschek, S. Desissaire, & K. Elsayad.