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# Increased Stiffness of Collagen Fibrils following Cyclic Tensile Loading

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## Abstract

Alterations in mechanical loading can induce growth and remodeling in soft connective tissues. Numerous studies have measured changes in the collagen structure and mechanical properties of cellularized native and engineered tissues in response to cyclic mechanical loading. However, a recent experimental study demonstrated that cyclic loading also caused significant stiffening and strengthening of acellular collagen constructs. In this work, we developed an anisotropic hyperelastic model of the collagen constructs to investigate whether the measured changes in the tissue-level properties can be attributed to changes in the anisotropic collagen structure and mechanical properties of the collagen fibrils. The model parameters describing the elastic properties, damage properties, and morphology of the fibril were fit to the stress-stretch response measured for the constructs subjected to different preconditioning strains and cycles. The results showed that the changes in the collagen anisotropy measured in experiments were insufficient to explain the increase in the stiffness and strength of the collagen constructs with cyclic loading and that the increase in the strength of the collagen constructs may be attributed mainly to the increase in the effective stiffness of the fibrils. These findings suggest that mechanical loading can induce changes in the stiffness and failure properties of the collagen fibril network through passive chemomechanical processes in addition to active cellular processes.

*Keywords:* collagen network, mechanical adaptation, network remodeling

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