# How our tissues manage mechanical stress

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The collagen network (blue) and the hyaluronic acid chains (red) are entangled.

As a result forces in the hyaluronic acid can act on the collagen fibres. Credit: Justin Tauber

When running, breathing and moving, the body is continuously deforming. How do the tissues in the body deal with all these mechanical stresses? Publishing today in *Nature Physics*, researchers from Wageningen University & Research (WUR) and AMOLF institute show how the two principal components of soft tissues, collagen and hyaluronic acid, work together for finely tuning the mechanical response of our tissues.

This study advances the understanding of how biological matter precisely regulates its function by combining different components. Exploiting not only their individual properties, but also how these components interact, and thus opening the way for synthesizing novel polymeric materials.

An earlobe is soft when gently pulled. However, with more insistent pulling and more force, it will become very stiff. The skin and most of the soft tissues in the body, including earlobes, muscles and the cartilage in knees, have this extraordinary ability to drastically switch from soft to stiff when they are subjected to large deformation. This ability is crucial for biological functioning: when the tissue is soft, cells can move around. At the same time, the tissue has to protect the cells and should not break, and therefore becomes stiffer when the deformation becomes too large.

## Collagen networks in the skin

The physical origin of this special mechanical behaviour is the particular structure formed by the collagen proteins, called a sparse network. This was revealed in previous in-vitro studies, in which networks of collagen extracted from the skin of animals were formed directly inside a rheometer, an instrument that allows researchers to measure the response of a material while deforming it.

"However, real tissues are far more complex: they are composed of different molecules that have different sizes and interact with each other in still unknown ways," says Simone Dussi, postdoc in the WUR Physical Chemistry and Soft Matter group led by prof. Jasper van der Gucht. "Because of this complexity, real tissues are way more adaptive than the networks studied so far, made of only collagen. We were very excited to see the experimental results obtained at AMOLF by Federica Burla in the group of prof. Gijsje Koenderink. They systematically studied double networks where the second most abundant component of tissues, hyaluronic acid, was present. Its presence significantly changed the mechanical response of the composite networks and we were eager to understand why."

## Stiffer with hyaluronic acid

"In contrast to the rigid collagen fibres, hyaluronic acid is a much smaller and more flexible polymer that is electrostatically charged. Because of electrostatic interactions, a lot of stress is built up internally during the network formation. This stress becomes relevant when you deform the material, for instance, when pulling on it. Firstly, the networks with a larger amount of hyaluronic acid are already stiffer at small deformation and secondly, the switch to the even stiffer response occurs at a larger deformation," explains Justin Tauber, Ph.D. candidate in the same group. "We managed to construct a theoretical model and performed computer simulations that matched the experimental results. The key ingredients were identified: In addition to the network structure and the bending rigidity of the collagen fibres, the elasticity and the internal stress generated by the hyaluronic acid are crucial. The model allows us to make a step further in understanding how real tissues exploit the balance of all these effects. In addition, our findings can be translated into material science to create novel synthetic polymeric materials with more tunable properties."

Researchers are now investigating when and how these networks fracture, in another biology-inspired study from which they might gain inspiration for tougher man-made materials.

**More information:** Federica Burla et al. Stress management in composite biopolymer networks, *Nature Physics* (2019). DOI: 10.1038/s41567-019-0443-6

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