Abstract / “Teaser Text”
When an Achilles tendon tears, impressively high forces have to be at work to rip it apart. But what makes a tendon strong? And what are its weakest links? Tendons, but also cartilage and ligaments, consist mainly of collagen. When we run or jump, it is collagen that withstands and transmits the forces. Surprisingly, collagen harbors particularly weak, sacrificial links that render the material stronger. These links can be considered the Achilles heel of the Achilles tendon. Collagen’s structure funnels external forces into these weakest links, the rupture of which still does not compromise the material’s integrity. It thereby translates mechanical stress into radicals, which can provide signals to the tissue to report on damage.

Introduction
It cracks when an Achilles tendon tears. This impressively shows the forces at work to separate this strong tendon into two parts. But what makes a tendon strong? And what makes it weak?
Tendons, as well as cartilage and ligaments, consist mainly of collagen, the most common protein in our body. It holds pretty much everything together in the body and is constantly subjected to large forces. And so the question arises as to where the vulnerability lies in the supposedly strong collagen of this tendon.

For the answer, we need to zoom in from the centimeter-long tendon to its components. The protein molecules of collagen are about one billionth of a meter thick and one millionth of a meter long. Always three of these long chains are coiled together to form a helix, a so-called triple helix. Much like a rope, this distributes the force. In collagen fibers, these helices are densely packed and arranged in parallel and also crosslinked with each other: there are struts to neighboring helices at the beginning and end of each helix, resulting in a dense network overall.

So what does it mean when the material tears, what does it mean on this smallest scale of protein molecules? Such a splitting of a molecule leads to so-called radicals: If the two electrons of a simple chemical bond separate, one electron follows one fragment, the other follows the other fragment. Radicals, i.e., individual electrons, are very reactive. They can cause damage to the material and accelerate its aging. But they can also be avoided or at least intercepted or even used elsewhere.
Results and Methods

Molecular Dynamics simulations can help to understand these processes on a much more detailed level than what is currently possible to see in experiments. Because of the many molecules that make up a collagen fibril, large simulations are needed to understand these phenomena on the molecular scale. This is where the resources from the SuperMUC-NG project came into play. We have been able to show that collagen forms radicals in a similar way to rubber bands. This is surprising because the fact that radicals can also form mechanically in biological materials was previously unknown. But where exactly do the chemical bonds in collagen break? One answer from our research is that collagen has very specific weak spots. These are located in the crosslinking between the helices. Interestingly, there are crosslinks that connect the helix twice on one side. One of these arms is exceptionally weak and tears particularly frequently. This arm in the crosslinking is therefore an “Achilles heel of the Achilles tendon”. What is remarkable about this weak point is that the crosslink is redundant here: if only one of the two arms tears, the crosslinking still remains. In materials science, this is called a "sacrificial bond," a bond that sacrifices itself. Nature seems to have come up with a special trick here, which has already been replicated with artificial materials. If a structure is designed so that there are particularly weak points that tear first but are unnecessary for the integrity of the material, then the structure is not only stable but can also absorb mechanical stress very well.

Ongoing Research / Outlook

Mechanobiology is a rapidly growing field that investigates how mechanical signals are translated into biological processes. Strong bonds for the structural integrity of molecules, cells, tissues, and even mechanisms are countered by weak spots that are built in so that the organism can sensitively respond to even the smallest mechanical signals and adjust biological processes accordingly. For example, skin can grow in the direction it is stretched by bone growth, and muscles can strengthen when they are heavily used. Athletes’ Achilles tendons are thicker than average. We currently only partially understand which molecules are responsible for these couplings of mechanics and biochemistry and how they perform this task. It is a surprising and new discovery that collagen is not just the tear-resistant material that makes up our Achilles tendon but also exhibits highly sophisticated chemical weak spots and reactions. Collagen is likely a kind of hub that can transmit mechanical stimuli to cells. We suspect that this knowledge can significantly contribute to understanding certain diseases and opening up new diagnostic and therapeutic pathways on the molecular scale. Examples include inflammation or pain due to mechanical overload, as well as arthritis or fibrosis.

References and Links

   https://doi.org/10.1016/j.bpj.2021.07.009
   https://doi.org/10.1038/s41467-023-37726-z