

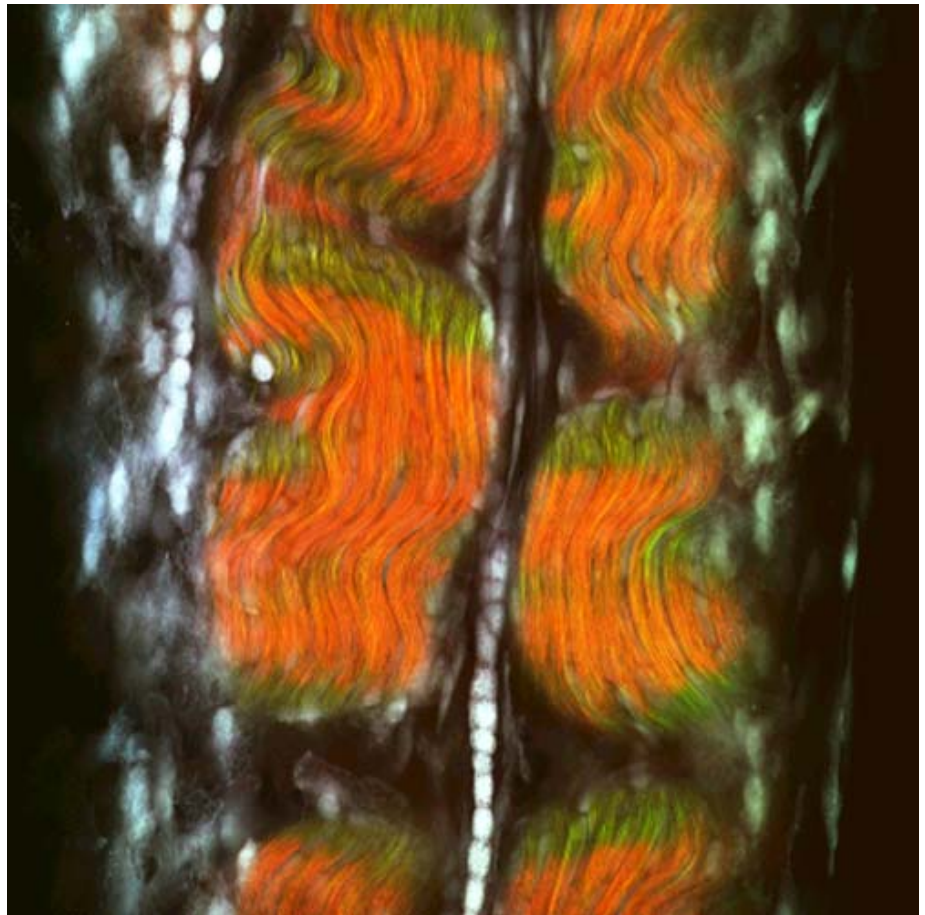
Structure of protein collagen seen at unprecedented level of detail

The structure and behavior of one of the most common proteins in our bodies has been resolved at a level of detail never before seen, thanks to new research performed at the Advanced Photon Source (APS) at the U.S. Department of Energy's Argonne National Laboratory.

Illinois Institute of Technology biologist Joseph Orgel used the high-energy X-rays produced by the APS to examine the structure of collagen, a protein that composes more than a quarter of all protein in the human body and forms the principal component of skin, teeth, ligaments, the heart, blood vessels, bones and cartilage. In these tissues, collagen molecules pack themselves into overlapping bundles called fibrils. These fibrils, which each contain billions of atoms, entwine themselves into collagen fibers that are visible to the naked eye.

Scientists have known the basic molecular structure of collagen since the 1950s, when several different international groups of scientists discovered that it had a triple-stranded helical structure. However, researchers had never before had the ability to study the structure of an entire fibril in the same way that they could study an individual collagen molecule, according to Orgel.

Orgel and his team performed diffraction studies on intact collagen fibrils inside the tendons of rat tails in order to understand just how the protein functioned within unbroken tissue. "We tried to draw a highly



A view of a rat tail tendon using second-harmonic generation microscopy. The collagen fibers show up in green and red.

accurate map of the molecular structure of tissues," Orgel said. "By doing so, we hope to transform a very basic understanding that we have of the molecular structure of tissue into a much more tangible form."

Since the scientists kept the tendon tissue intact, they could see how the collagen molecule binds to collagenases, a class of enzymes which when working properly help

to regulate the normal growth and development of animals but when malfunctioning can lead to the metastasis of cancerous tumors or rheumatoid arthritis. The visualization of this interaction could help drug developers to create an inhibitor to prevent the pathological action of the enzyme, Orgel said.

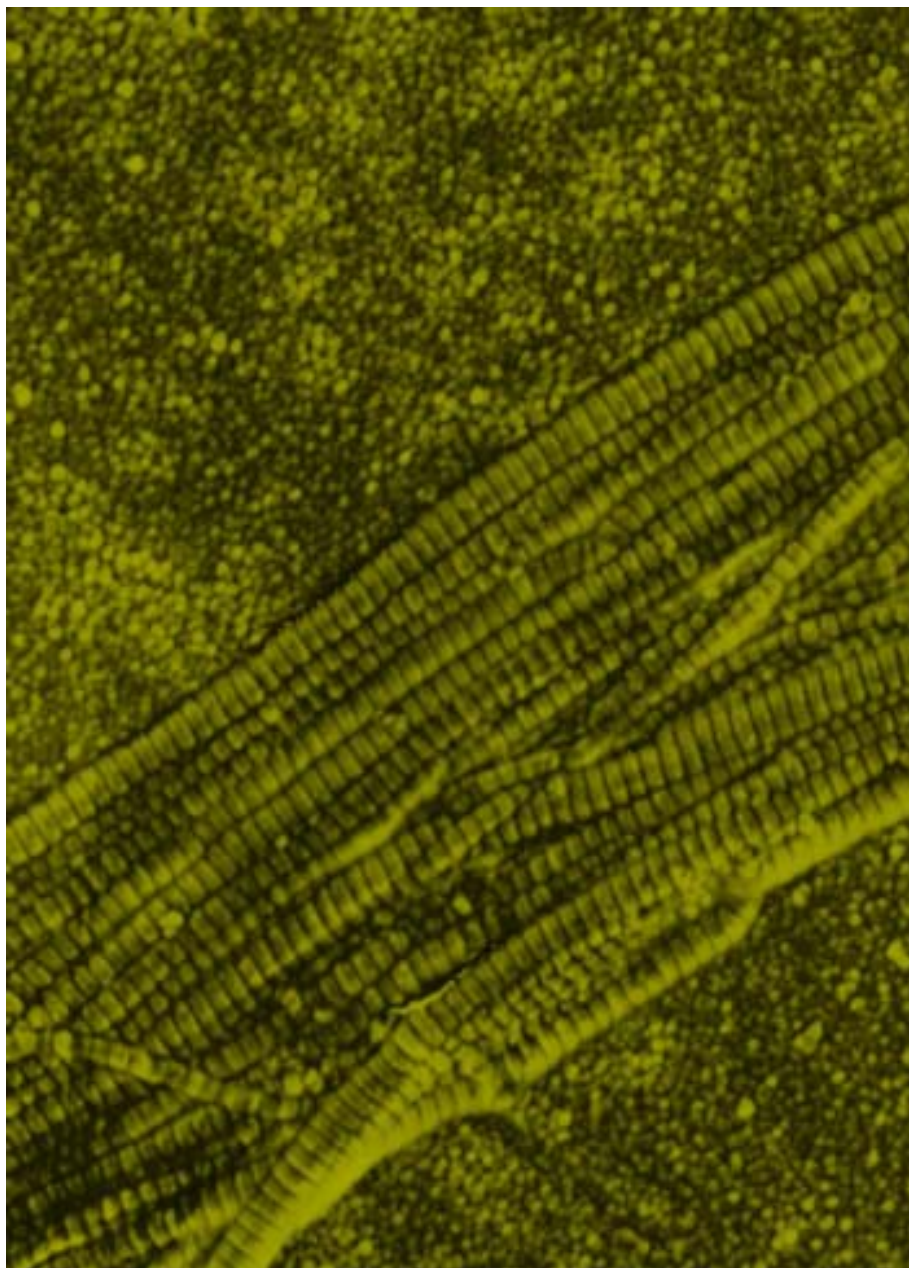
Previous studies of the structure of collagen had looked only at crystals

of small fragments of the protein, so scientists had little idea of how it looked within intact tissue. "It's impossible to get the information that we did by removing tiny chunks of the tissue," Orgel said. "We couldn't obtain this data by single-crystal crystallography. This research was made possible only because of the BioCAT beamline provided by the APS."

The research appears in the February 26 issue of the *Proceedings of the National Academy of Sciences*, and is available online at <http://www.pnas.org/cgi/reprint/0710588105v1>.

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By Jared Sagoff



An atomic-force-microscopy image of collagen fibrils in a collagen fiber.

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