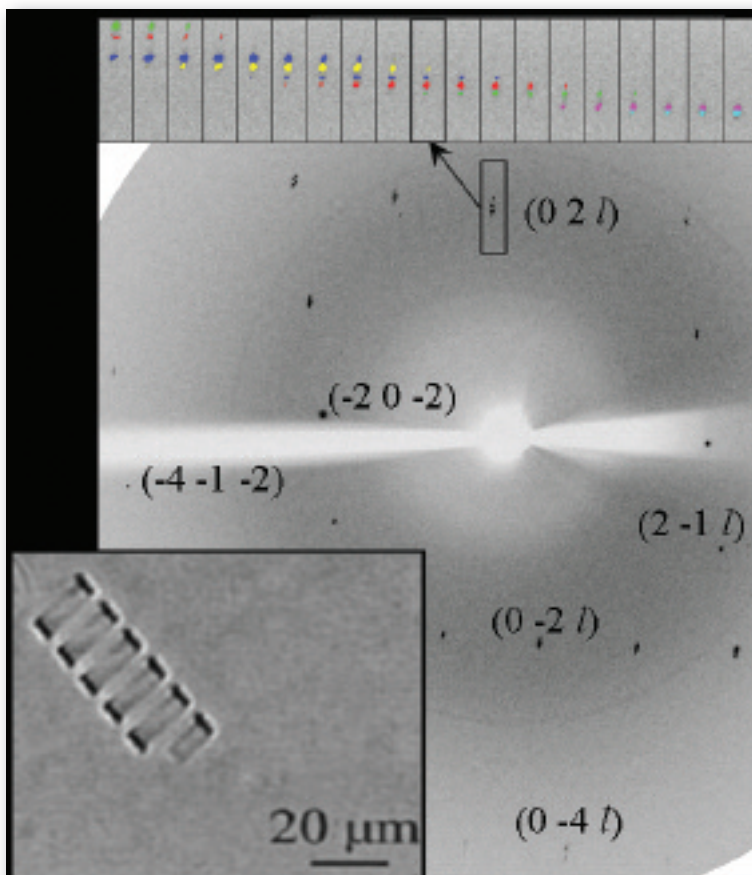


BIOLOGICAL SPRINGS FROM CHOLESTEROL RIBBONS?

Understanding the biological properties of cholesterol is a fundamental question that affects our health. One role of cholesterol is as a part of digestive bile in the gallbladder that aids in digestion of fats. However, in some cases, bile cholesterol becomes supersaturated and forms plate-like crystals of monohydrate cholesterol that seed the formation of cholesterol gallstones. The formation of these structures, while important to patients and their doctors, has also sparked the interest of lipid biophysicists for entirely different reasons. It turns out that bile cholesterol crystallization goes through a metastable helical ribbon intermediate. These helical ribbons of cholesterol are now being studied for their elastic properties. One such study, carried out at the SGX-CAT 31-ID-D beamline at the APS, casts light on the properties of cholesterol ribbons and could lead to new, bioengineered molecular devices.



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The x-ray-scattering studies of helical ribbons formed in multicomponent solutions of cholesterol solubilized by various surfactants carried out at the SGX beamline by colleagues from the Massachusetts Institute of Technology reveal important information about the structure of these cholesterol intermediates, showing that they are formed from single crystals. This provides a sound basis for understanding the elastic properties of these helices.

Initial observations came from studies that looked at cholesterol structures in natural bile. The cholesterol in those solutions appeared to form helical ribbons with two well-defined pitch angles of 11° and 54°. In an effort to understand how these ribbons are formed, the researchers studied cholesterol in solution with various surfactants. The surfactants are detergent-like molecules that help keep fatty molecules like cholesterol in solution. The group studied 11° helical ribbons that exhibited Bragg reflections by x-ray-scattering (Fig. 1). The Bragg reflections they observed were unusually arced through multiple adjacent images, possibly due to the curvature of the ribbons, and the team developed its own software to analyze the data and determine the dimensions of the unit cell. Their analysis confirmed that the ribbons are single crystals formed from the chiral cholesterol molecules. Further analysis revealed that the dimensions of the unit cell were similar to those of cholesterol monohydrate but three times longer in the direction of the *c* axis, which is perpendicular to the ribbon plane.

The researchers hypothesize that the helical ribbons are the result of two features of the crystals. The dimensions of the ribbon strip are determined by the rate of crystal growth along different crystallographic axes. Cholesterol monomers add more quickly in one direction than in the other two directions perpendicular to the first, and so one direction grows more quickly, forming the length of the ribbons. Second, the chirality of the molecules in the crystal creates different surface tensions on each side of the crystal, causing it to bend. This bending occurs at the 11° angle relative to the ribbon

edge, reflecting the underlying crystal structure. These helices have elastic properties just like a coiled spring. It is this property that authors hope to make use of in future work.

The elastic properties of the helical ribbons have offered a fortuitous surprise that may be useful in developing tools to make nanoscale measurements in biological systems. While this work had serendipitous roots in trying to understand a biomedical observation, the authors now speculate that the real value of these cholesterol ribbons may be in their biophysical properties as tiny springs. They plan to extend their work by developing ways to get homogeneously sized ribbons that could then be calibrated for their elastic constants. Once they know the strength of cholesterol springs of various radii and lengths, they can use light microscopy to measure forces. Another important problem is to develop means of functionalizing the ends of the springs so as to attach them to interesting biomolecules, with the objective of measuring the forces of various biological interactions. — *Sandy Field*

See: Boris Khaykovich¹, Chintan Hossain², Jennifer J. McManus³, Aleksey Lomakin³, David E. Moncton^{1,2}, and George B. Benedek^{2,3,4*}, “Structure of cholesterol helical ribbons and self-assembling biological springs,” *PNAS* **104**(23), 9656 (June 5, 2007).

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< Fig. 1. The lower left inset shows a typical helical ribbon of cholesterol. Above and behind this inset is a diffraction pattern of x-rays scattered by a flattened arc of another helical ribbon of larger radius. Such diffraction patterns demonstrate that each ribbon is a coiled crystalline strip. Detailed analysis of these patterns enables a determination of the unit cell of the cholesterol in the strip.

31-ID-D • SGX-CAT • Life science • Macromolecular crystallography, single-crystal diffraction, fiber diffraction, single-wavelength anomalous dispersion • 3.3-cm Undulator A • Accepting general users