Stiff yet supple hydrogel mimics cartilage

Magnetically aligned nanosheets give the material its rare combination of mechanical traits.

In the realm of bioengineering, hydrogels are something of an all-purpose material. Made up of networks of interlinked, hydrophilic polymers, they tend to be soft, biocompatible, and highly absorbent. They can be deployed as capsules for controlled-release drug delivery, thin films for contact lenses, and even sensing elements in breathalyzers.

In tissue engineering, hydrogels are often used as scaffolding to support cells as they grow into functional replacement tissue. Now researchers led by Takuzo Aida, Yasuhiro Ishida (both at Japan's RIKEN research institute), and Takayoshi Sasaki (Japan's National Institute for Materials Science) have designed a hydrogel that can serve as the tissue itself.[1]

The new material mimics the articular cartilage that lubricates our joints: It can support a heavy load along one direction while stretching and shearing with ease in the others. In real cartilage, that lubricating behavior is the result of a complex interplay among cells, collagen fibers, and a host of extracellular proteins. In the synthetic version, it's the product of a simpler recipe: The researchers mixed flakes of titanium oxide into a solution of hydrogel precursor molecules and let the strong field of a superconducting magnet do the rest.

Liquid crystals

Two decades ago, Sasaki was part of a team that discovered that by immersing titanium oxide, or titanate, in a solution of tetrabutyl ammonium, one could exfoliate layers of titanate that were a single unit cell thick.[2] Those nanosheets, thousands of nanometers wide and less than a nanometer thick, have shown promise as high-surface-area catalysts and as starting materials for the fabrication of thin films, nanotubes, and other nanostructures.

While experimenting with aqueous suspensions of the nanosheets, researchers in Aida's lab noticed an unexpected behavior: In an applied magnetic field of around 10 T, the sheets all aligned in the same direction, transverse to the magnetic flux. Not only that, they organized into layers that were spaced with the regularity of a crystal.

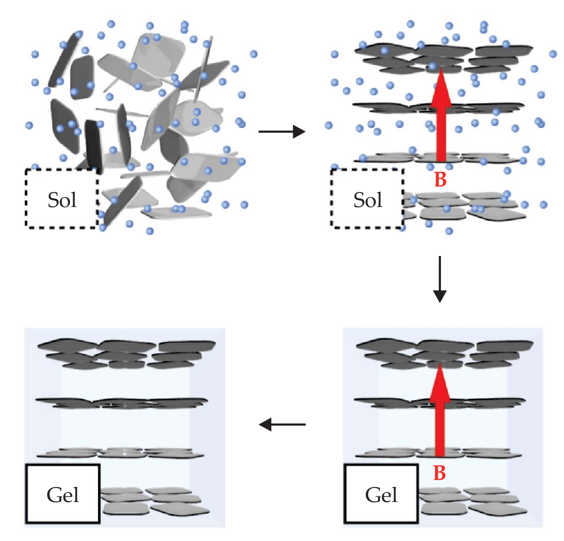

Figure 1. A cartilage-like hydrogel is prepared via a four-step process: Titanium oxide nanosheets are mixed into a solution of hydrogel precursor molecules; an applied magnetic field **B** orients the sheets into regularly spaced layers; the precursor molecules are polymerized to encase the nanosheets in a hydrogel matrix; and the magnetic field is removed. Coulomb repulsion between the negatively charged nanosheets stiffens the material in the direction normal to the layers but permits it to easily stretch and shear along the layer plane. (Adapted from ref. 1.)

That the nanosheets are influenced by a magnetic field is not, in itself, unusual. Titanate is known to be diamagnetic, so a magnetic field is expected to induce dipoles that give rise to an orienting torque. Indeed, similar ordering has been observed for liquid crystals comprising antimony phosphate nanosheets.[3] Most two-dimensional metal oxides, however, align with their surfaces parallel to a magnetic field. In that alignment, the nanosheets needn't face the same direction, much less adopt long-range, crystal-like order.

"It was a completely serendipitous discovery," says Aida. "I bought a superconducting magnet without any particular purpose in mind, and for a year it gathered dust. So I encouraged our lab members to use it for their own research, and we stumbled across something new."

Aida and his coworkers think the long-range ordering most likely emerges due to a combination of magnetic and electrostatic forces. The nanosheets carry negative charges, distributed along their surfaces, so they tend to repel each other when they're suspended in a dielectric medium such as water. Coaxed by a magnetic field to orient face-to-face, nanosheets will minimize their electrostatic repulsion by maximizing the distance between them. In a sufficiently concentrated suspension, the lowest-energy configuration is one in which the distances between facing nanosheets are uniform.

The resulting interlayer spacing can be quite large. At nanosheet concentrations of about 0.3%, the smallest for which the spontaneous ordering is seen, the spacing is about 50 nm, more than 70 times the thickness of the nanosheets themselves.

Cooking up cartilage

The magnetically induced structure that Aida and company observed was fleeting. When the magnetic field was removed, so, too, was the crystal-like order. The researchers figured they could lock in the order more permanently by encasing the nanosheets in a hydrogel. As illustrated in figure 1, they dispersed nanosheets in a solution of acrylamide monomers—common hydrogel precursor molecules—before applying the magnetic field. They then irradiated the mixture with UV light to initiate a photopolymerization reaction that converts the monomers into a polymer network. Then, after the magnetic field is removed, the nanostructure remains.

As figure 2 demonstrates, the anisotropic nature of the resulting material is evident even to the naked eye: Viewed along the axis normal to the nanosheet surfaces, the hydrogel is opaque; viewed edge-on to the nanosheets, it's virtually transparent. Diffraction spots observed in small-angle x-ray-scattering experiments confirmed the material's crystal-like order.

The team figured that the hydrogel's

structural anisotropy should, in theory, translate into a mechanical one. Specifically, electrostatic repulsion between the negatively charged titanate layers should stiffen the hydrogel in the direction normal to the nanosheets' surfaces. But because the layers are free to slide past one another, the material should remain easily deformable in the layer plane. That's precisely the behavior one would look for in a synthetic cartilage.

Tests of the hydrogel's material properties seem to bear out the group's intuition. The hydrogel's elastic modulus, a measure of its stiffness, was significantly larger in the direction normal to the layers than it was in the plane parallel to them. The disparity grew as the concentration of nanosheets increased; in samples with nanosheet concentrations of 1%, the highest concentration tested, the difference was more than a factor of two. The so-called storage modulus, a measure of a material's resistance to shear, showed similar directional dependence.

To be a viable cartilage replacement, the new hydrogel will need to show that it can endure much harsher loading cycles than those used in the researchers' preliminary measurements. And since the putative mechanism for the material's anisotropic behavior depends on electrostatic interactions, one would want reassurance that its properties would hold up in the highly ionic environment inside our bodies. To that end, Aida and his coworkers have taken a first step: They've shown that after a weeklong immersion in physiological saline—their longest experimental trial—the hydrogel retains its structural and mechanical properties.

Aida and his colleagues also see potential for the hydrogel as a vibration isolator; the material's mechanical

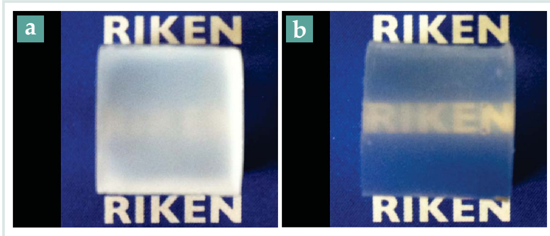

Figure 2. Now you see it, now you don't. This 1-cm^3 block of hydrogel has a magnetically induced nanostructure that makes it **(a)** opaque in one direction and **(b)** virtually transparent in another. (Adapted from ref. 1.)

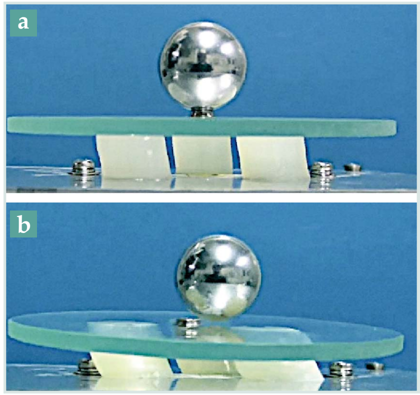

Figure 3. Keeping it on the level. A metal sphere balanced on a glass stage provides a test of a hydrogel's vibration-isolating capabilities. **(a)** When the stage is supported by 3-cm-diameter pillars of a nanostructured hydrogel, the sphere remains on its tee even as the underlying table shakes. The specially tailored hydrogel redirects the vibrational energy into horizontal modes. **(b)** Supported by pillars of a more conventional hydrogel, the stage wobbles and the sphere is sent tumbling. (Adapted from ref. 1.)

anisotropy causes it to concentrate vibrational energy into modes parallel to the embedded titanate layers. As a proof-of-principle experiment, the team balanced a glass plate atop hydrogel pillars supported by a mechanically oscillating table, as shown in figure 3. When the hydrogel's stiff axis is aligned vertically, the plate remains level, even as the table underneath it shakes. When the nanostructured hydrogel is swapped out for a more conventional hydrogel, the plate wobbles, and the sphere that rests above tumbles from its tee.

"The vibrational isolation capabilities are especially relevant and promising," says Aida. "After all, Japan is a country of earthquakes."

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References

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Giant impacts may explain the origin of chondrules

Long thought to be the building blocks of planets, the small orbs in meteorites may instead be a by-product of planetary accretion.

Chondrules, such as the one shown in figure 1, are millimeter-scale, previously molten droplets that make up more than half the volume of most meteorites that fall to Earth. Isotopic dating suggests they formed during the roughly 5 million years when the solar nebula was coalescing into solids (see the article by Robin Canup, PHYSICS TODAY, April 2004, page 56). Unfortunately, there's no consensus as to how they formed. The conventional and perhaps still leading view holds that chondrules originated as rapidly melted dust balls—flash heated by shock waves, lightning bolts, solar flares, or some other process—that crystallized in hours to days and sometime afterward became part of accreting

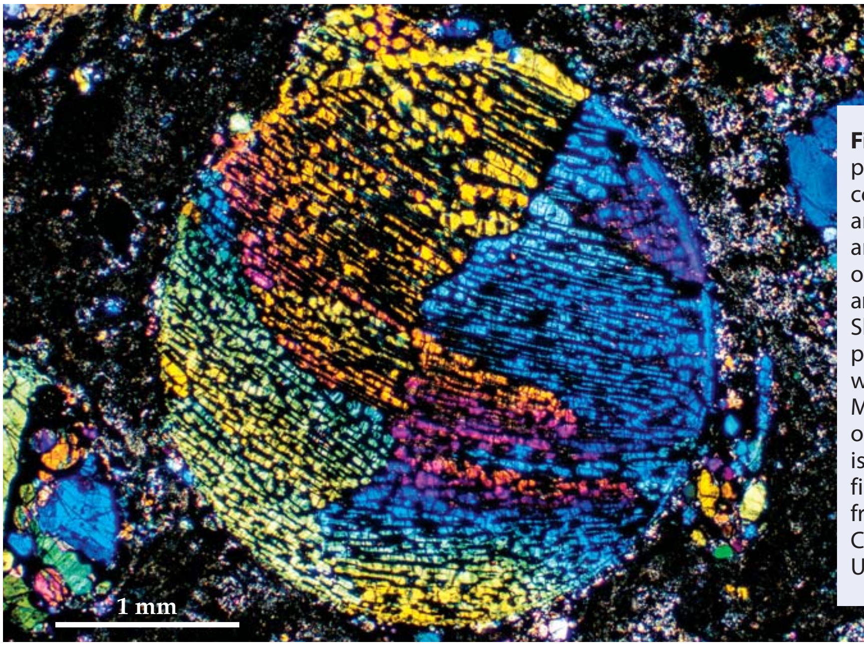

Figure 1. Crack open a meteorite and you'll probably find chondrules whose chemical compositions, millimeter-scale diameters, and igneous textures—the shapes, appearance, and crystal orientations of the mostly olivine and pyroxene minerals—constrain any compelling model of chondrule formation. Shown here sliced wafer thin and viewed in polarized light, this richly colored chondrule was embedded in a meteorite known as Maralinga. The barred texture shows the orientation of olivine crystals. The chondrule is surrounded by other inclusions and a fine-grained matrix (black) of mineral fragments. (Courtesy of Laurence Garvie, Center for Meteorite Studies, Arizona State University.)