binds several hundred thousand times more tightly to a nicotinic receptor from the central nervous system, where neurons process pain information, than to one that tells muscles to contract. For epibatidine, that ratio was only 57 to 1. "They came upon a compound that gets rid of the toxic effects of epibatidine and still has analgesic capabilities," says Daly. "I would not have thought it possible."

And in at least one test, ABT-594 appeared to be nonaddictive. Rats that were taken off ABT-594 after being treated with a high dose for 10 days did not suffer the withdrawal symptom of appetite suppression seen after treatment with opioids. Other researchers point out, however, that ABT-594's mechanism of action raises the possibility that it will lead to other forms of dependency. "The company would hope that their drug isn't addicting because it doesn't act through the opioid receptor," says Fields. "But nicotine is addictive, too."

The big question now is whether this early promise will be borne out when the compound is tested in humans. An indication ought to come in a few months when the first results from the European safety trials become available. "We're crossing our fingers and anxiously looking forward to the summer," says Michael Williams, Abbott Labs vice president of neurological and urological drug discovery.

–Evelyn Strauss

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IMAGING

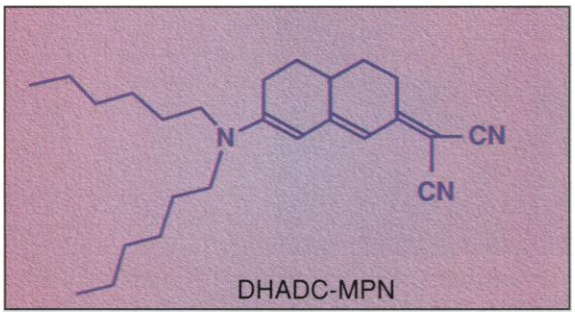
Putting the Infrared Heat on X-rays

Doctors would love to put an old workhorse—x-rays—out to pasture. Although x-rays are still an indispensable tool for diagnosing everything from broken pinkies to lung tumors, the energetic beams can damage DNA, posing a slight cancer risk. Infrared light, which can pass through tissue harmlessly, could bring a softer touch to medical imaging. But to turn it into a serious rival for x-rays, researchers need a simple way to compose an image from the few infrared photons that pass directly through tissue without getting scattered. In this issue of *Science*, a team from the University of Arizona in Tucson and the California Institute of Technology (Caltech) in Pasadena reports about a light-sensitive polymer that might do the job.

The polymer, described on page 54, can change its optical properties in response to a subtle play of light: the interference between the few infrared photons traveling straight through a scattering medium and a separate infrared beam. The result is a pattern called a hologram, from which a three-dimensional (3D) image of the tissue can be reconstructed. Until now, separating the few straight-shooting photons from the scattered stragglers to make an image has required unwieldy gas-, liquid-, or crystal-based detectors, but the new polymers are easy to handle and cheap to process into film. "They could be very useful," says Robert Alfano, an imaging researcher at the City College of New York. But experts acknowledge that infrared systems are a long way from the clinic, because these systems so far can only image thin tissue slices.

For years, researchers have been tinkering with polymers that store holograms made by visible light. Storing an image requires relatively simple physics: Two laser beams—one carrying information about the image to be stored and the other a "reference" beam—intersect in the polymer, setting up an interference pattern of bright and dark areas. "Sensitizing" compounds in the polymer's lit regions absorb photons, which excite electrons to a higher energy level. Electrons from a surrounding matrix of charge-conducting molecules rush to fill the gaps in the electron shells, resulting in transient positive charges that ripple through the matrix until getting trapped in the dark region. The light-dark interference pattern thus is reproduced in the polymer as a pattern of corresponding positive and negative charges.

These islands of charge attract a third class of compounds in the polymer: dye. The stringy dye molecules themselves are polarized, having opposite charges on either end. The positive end swivels toward a cluster of negative charge, and vice versa. This reorientation alters the polymer's index of refraction, or the speed at which light moves through the film. The 3D pattern of varying refractive index is a hologram. As long as the charges remain fixed in one of these photorefractive polymers, a hologram persists. When lit up by another laser beam, the polymer diffracts the photons in a pattern, reproducing the original image.



KIPPELEN ET AL.

Seeing the IR light. New dye molecule may help usher holographic imaging into the medical lab.

The research team, led by Arizona's Bernard Kippelen and Nassar Peyghambarian, and Caltech's Seth Marder, realized that such holograms might be useful for medical imaging. Most photorefractive polymers, however, are sensitive to visible light, which tissues readily absorb or reflect. To exploit the near-infrared light that is best for probing tissue, Kippelen and his colleagues added a new sensitizer to standard polymers that releases positive and negative charges after absorbing infrared photons.

This modification alone was not enough to make the polymer useful for medical imaging. The researchers also had to boost the polymers' signal-to-noise ratio to record the few photons that make it through tissue. To do so, they created new dye molecules that are adept at orienting their charged ends in the weaker electric fields created by fewer incoming photons. The souped-up polymer had the same sensitivity as the best visible-light photorefractive polymers, while receiving four times fewer photons.

Next, Kippelen's group set out to reproduce the image of the number "5" in a photorefractive film. First, they generated an infrared laser pulse and split it into two separate beams. One beam passed through a transparent "5" in an otherwise opaque sheet of photographic film. Photons emerging from the "5" passed through polystyrene beads floating in an organic solvent, a scattering medium used to simulate human tissue, before impinging on the polymer. Inside the polymer, the first wave of photons—which had emerged unscattered—crossed paths with others from the second beam that had been routed around the barriers and timed to arrive simultaneously. As photons from the two beams interfered, they reproduced the "5" as a hologram that could be read by another infrared beam. Scattered photons arrived too late to set up an interference pattern with the second beam; thus they were unable to muddy the hologram.

Similar feats have been accomplished using cesium vapor and other materials as the holographic storage medium, says Irving Bigio, a holographic storage expert at Los Alamos National Laboratory in New Mexico. But the new polymer films, he says, "look far easier to use." Major obstacles remain, however, before these new photoreactive polymers appear at the doctor's office. The key hurdle, Bigio says, is that no infrared technology designed so far can image tissue thicker than about 1 centimeter. The hunt is now on for new schemes to boost the number of usable photons, or make the most of the ones that get through. Until these efforts pay off, however, x-rays will remain a radiologist's best friend.

–Robert F. Service