other sightings," explains Tavani, "you worry that it might have been an artifact."

Given the coverage history of the Crab by the two telescopes, the detection of three gamma flares thus far suggests that the Crab does it once or twice a year. If so, it will be interesting to see whether, as theorist Jonathan Arons (University of California, Berkeley) suggests, the recurrences are quasi-periodic. In any case, the Crab is now under close surveillance, not only by the gamma-ray telescopes but also by the *Hubble Space Telescope* and the *Chandra X-Ray Observatory*. With their much finer angular resolutions, the *HST* and *Chandra* could pinpoint anomalies to small structures within the nebula.

In fact, the *AGILE* team's paper[1] included follow-up observations by the *HST* and *Chandra* about a week after last September's flare, observations that show suggestive brightening of several structures near the terminal shock. "It's no smoking gun," says Tavani, "but they might be afterglows at longer wavelengths."

"Our way forward is clear," says Blandford. "The new monitoring regime should let us see if any local structures are brightening in x rays or the visible *in coincidence* with the next gamma flare. That would be an important clue for theorists."

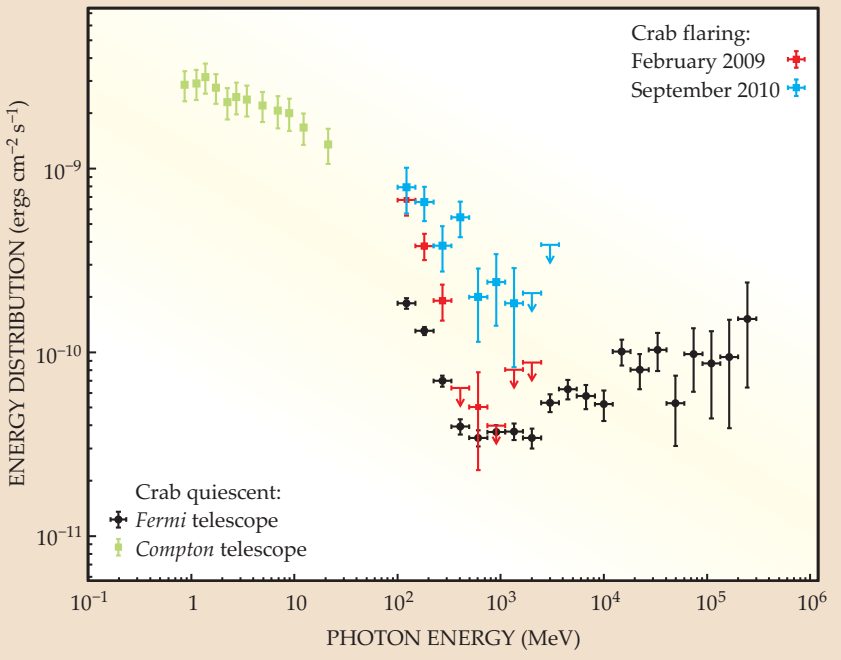

Figure 3. Spectral energy distribution of gammas from the Crab Nebula with energies above 100 MeV, as recorded by the *Fermi Gamma-Ray Space Telescope* in the nebula's normal quiescent state and during two gamma flares. (Arrows indicate upper limits.) The trough near 1 GeV in the quiescent spectrum is thought to indicate the divide between sub-GeV gammas produced by synchrotron radiation and the higher-energy gammas produced by inverse Compton scattering. The points below 20 MeV are older, quiescent-state data from the *Compton Gamma-Ray Observatory*. As in figure 2, the 33-ms pulsed component is excluded from all the plotted spectra. (Adapted from ref. 2.)

A unique laboratory

The Crab is the only place where relativistic astrophysical phenomena can be studied with the requisite spatial and temporal resolution. Aside from its proximity, the Crab also has the virtue of neatness—as supernova remnants go. Some supernovae leave behind a black hole rather than a neutron star, and the remnant nebula is powered by messy and often episodic accretion of nearby material. The Crab Nebula, by contrast, harbors very little baryonic material, and its luminosity is powered almost entirely by the steady but very gradual slowdown of the pulsar's spin.

Supernova remnants are thought to be the principal intragalactic source of cosmic rays. But the scarcity of protons in the Crab Nebula means that it is, at best, a feeble cosmic-ray source. That's probably true of most pulsar-wind nebulae. "But they're excellent laboratories for studying the physics of acceleration associated with relativistic outflows," says Arons. Relativistic outflows from active galactic nuclei, for example, are conjectured to be the principal extragalactic sources of cosmic-ray protons with energies above 10^{19} eV. But no observation has as yet been able to assign such ultrahigh-energy particles to any specific source.

In that regard, the data from the Crab's September flare set a new record: The flare's spectrum and its fast decay make it clear that the flaring GeV gammas come from synchrotron radiation by electrons that have somehow been accelerated to 10^{15} eV. "Those PeV electrons," Buehler points out, "are the highest-energy particles anyone has yet been able to associate with a specific astrophysical object."

Bertram Schwarzschild

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Time reversal produces optical focusing in scattering media

A technique hatched from concepts in acousto-optics and phase conjugation could be ideal for biomedical imaging and therapy.

A focused beam of light can trap a colloidal sphere, cause a specific neuron to fire, or deliver a lethal dose of energy to a cancerous cell. In biomedicine, focused light can perform nearly all the same sensing, diagnostic, and therapeutic functions as targeted x rays, without inducing harmful ionization.

Delivering light to internal tissue and organs, however, is not a straightforward task. In air or other transparent media, optical focusing is a simple matter of geometry—shape a beam with a curved lens and its rays will converge on ballistic trajectories toward a target. Scattering media such as biological tissues are not so cooperative. At penetration depths much larger than the scat-

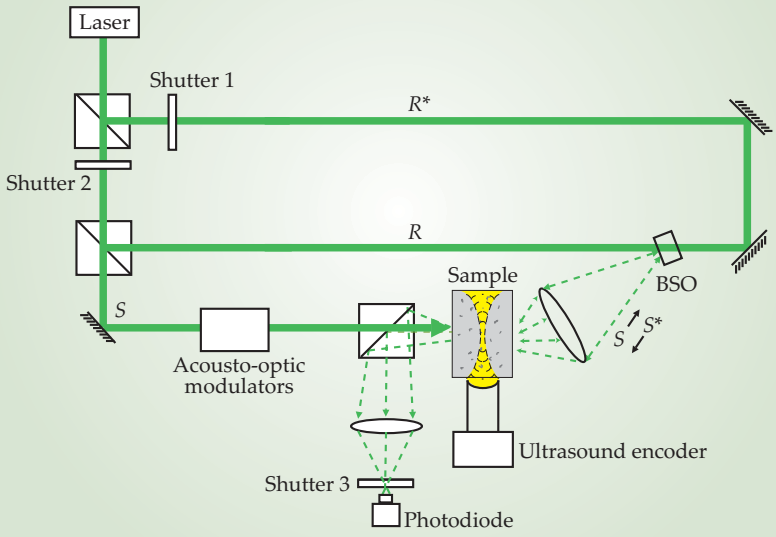

Figure 1. The TRUE setup. The time-reversed ultrasonically encoded (TRUE) focusing technique begins with shutter 1 open and shutters 2 and 3 closed, so that interference between the sample beam *S* and the reference beam *R* constructs a hologram in the photorefractive bismuth silicon oxide (BSO) crystal. Acousto-optic modulation ensures that the hologram encodes only the light that passes through the ultrasound focus. To read the hologram, shutter 1 is closed and shutter 2 is opened. The reconstruction beam *R** then generates a phase-conjugated copy *S** that retraces a path toward the virtual source. Shutter 3 can be opened to read the output signal with a photodiode. (Adapted from ref. 2.)

tering mean free path, a beam becomes distorted beyond recognition. In biological tissue, that mean free path is just 100 μm or so, roughly the width of a human hair.

Until recently it wasn't clear that focusing light in a scattering medium—a feat akin to guiding escaped molecules of perfume back into a bottle—was even possible. A few years ago, researchers from the University of Twente in the Netherlands demonstrated that it was.[1] But their method, and others that followed, called for embedding a fluorescent particle at the focal point—an impracticality for most biomedical applications. Now Lihong Wang (Washington University, Saint Louis), his graduate student Xiao Xu, and his postdoc Honglin Liu have devised a way to focus light several centimeters deep within a tissuelike medium without the help of an embedded particle.[2]

Guiding light

The diffusive effect of light scattering is a familiar nuisance in astronomy. Dynamic scattering in Earth's atmosphere distorts bright stars, causing them to twinkle, and renders fainter stars nearly invisible.

Astronomers figured out, however, that they could compensate for the distortions by using a bright guide star—either a real star or an artificial one produced with lasers—and a deformable mirror. The key was recognizing that the tortuous paths traced by light in scattering media, though seemingly random, are in fact deterministic and, at short-enough time scales, approximately fixed. Thus, by continually adjusting the mirror to correct the image of the guide star, it's possible to produce a high-resolution view of both the star and its surrounding sky. (See the article by Laird Thompson, PHYSICS TODAY, December 1994, page 24.)

That adaptive optics approach inspired the 2008 Twente experiment, led by Allard Mosk, in which a fluorescent particle—the guide star—was embedded inside a sample of zinc oxide pigment. A light beam aimed at the particle could then be shaped with a spatial light modulator, pixel by pixel, to find the pattern that produced the brightest fluorescence. Using that procedure, the researchers shaped a beam that delivered 20 times more light to the guide star than did an unmodulated beam.

But shaping light beams with spatial light modulators is a time-consuming endeavor. By the time the optimal beam can be calculated for a sample of living tissue, the tissue's scattering properties will already have changed. Further complicating matters is the need to embed a particle at the location of interest.

As Wang and company realized, however, the guide star need not be an actual particle, and the light-modulating technique need not involve computationally intensive algorithms. In fact, the essential ingredients for fast, noninvasive light focusing were already in common practice. The innovation was to put them together.

The main ingredients

Central to Wang and company's approach was a technique known as ultrasonic encoding. Oscillating density fluctuations associated with a focused ultrasound field alter a medium's refractive and scattering properties, so that the frequency of passing light is shifted either up or down by the acoustic frequency. (See the article by Mathias Fink and Mickael Tanter, PHYSICS TODAY, February 2010, page 28.) Although light that passes through the focus continues to scatter, the shift in frequency tags it as having emanated from a virtual source. And since ultrasound scatters much more weakly than light, that virtual source can be positioned several centimeters deep in a biological tissue.

But ultrasonic encoding doesn't focus light; rather, it does the opposite: It identifies the light that emerges from a focus. The second challenge, then, would be to get the encoded light to retrace its steps. Again, a suitable technique—phase conjugation—was already well established. (See the article by Mathias Fink, PHYSICS TODAY, March 1997, page 34.) In fact, in 2008 a team led by Changhuei Yang (Caltech) demonstrated that a phase-conjugate hologram could effectively "unscatter" light by redirecting it back through a scattering medium to its point of origin.[3]

Says Wang, "It dawned on me that if you could use ultrasound to make a virtual guide star, you could use a phase-conjugating mirror to redirect light back to a point inside the sample. Why didn't I think of this earlier?"

Soon thereafter, Wang and company began work on the prototype for time-reversed, ultrasonically encoded (TRUE) optical focusing. The design, illustrated in figure 1, uses acousto-optic modulators to downshift the frequency of a sample beam by an increment f before it enters the scattering medium. Then portions of the beam that pass through the ultrasound focus are modulated up by the same increment f. Of the light that emerges from the scattering medium, only the ultrasonically encoded part shares the frequency of the reference beam. Thus only the encoded light contributes to the stationary interference pattern that writes a hologram into a photorefractive crystal.

Once the hologram is recorded, the sample and reference beams are blocked and the hologram is read with a reconstruction beam. From there, the movie plays backwards: Diffraction in the photorefractive crystal produces a phase-conjugated copy of the ultrasonically encoded light, which reenters the sample, retraces the original scattering paths, and converges at the focus.

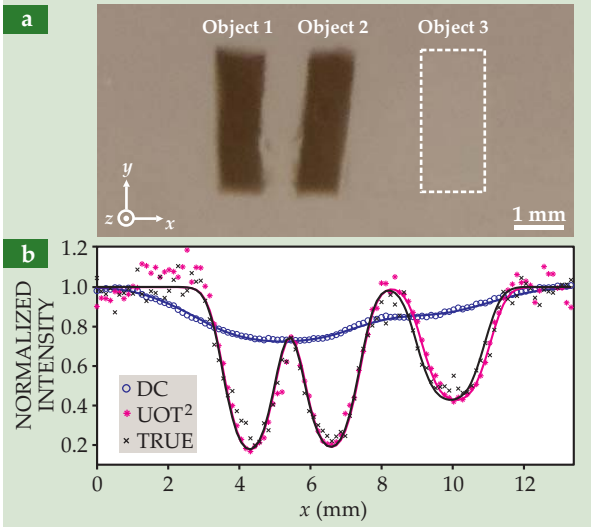

Figure 2. TRUE tomography. **(a)** A 10-mm-thick scattering slab embedded with three objects along its midplane—two absorbing, one transparent but strongly scattering—provided a test for time-reversed ultrasonically encoded (TRUE) focusing. **(b)** The slab was tomographically imaged by passing laser light through it in the z-direction and the output intensity is measured as a function of the laser's x-position. Due to scattering, direct transmission of light (DC) was insufficient to resolve the embedded objects. But by using TRUE to focus light at the midplane, each object could be distinguished with submillimeter resolution. That the TRUE signal was equal to the square of the signal produced with ultrasound-encoded optical tomography (UOT^2) confirms that the time-reversed light converged at the focus. (Adapted from ref. 2.)

TRUE in action

To test the technique, the team tomographically imaged a 10-mm-thick slab of intralipid, a fatty-acid emulsion that has a scattering mean free path of about 0.4 mm, shown in figure 2. Embedded along the slab's midplane were three blocks—two absorbing and one strongly scattering—each about a millimeter thick. Using TRUE to focus light at the slab's midplane, the team was able to distinguish the blocks with submillimeter resolution.

But the goal was to focus light, not simply to image objects. To confirm that TRUE was achieving that end, the team compared the TRUE image with one obtained by simply detecting the ultrasonically encoded output in the sample beam—a technique known as ultrasound-encoded optical tomography. In UOT, light passes through the virtual source just once. In TRUE focusing, it passes twice—once during the encoding step and again during the focusing step. Therefore, in theory, the TRUE signal should be roughly the square of the UOT signal, a result that was borne out by the data.

Wang and company envision a host of potential applications for TRUE focusing, including high-resolution imaging, phototherapy, and photogenetics. Some of those applications, however, require that the TRUE process get faster. Currently, the entire process—writing the hologram, opening and closing shutters, and reading the hologram—takes about 200 ms. The scattering properties of thick living tissues can have correlation times as short as 1 ms. Wang is optimistic, however, that the technique can be sped up with the aid of faster photorefractive materials.

The team is also looking to incorporate a higher-intensity reconstruction beam to increase what are currently modest focal intensities. There is work to do, says Wang, "but we're moving in the right direction." Mathias Fink (ESPCI in Paris), for one, seems to share that sentiment: "My guess is that many other groups will end up adopting this approach. In fact, we're trying to do it in our lab right now. It's a really good idea, a really nice step."

Ashley G. Smart

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