Advanced imaging technologies reveal much that you can’t see.

Advanced imaging technologies have yielded a bounty of insights in disciplines ranging from physics to materials science to basic medical research.

At UC Santa Barbara, sonar imaging has enabled scientists to track methane bubbling up from the seafloor off the Goleta coast, magnetic resonance imaging is allowing neuroscientists at the university to investigate the workings of the mind, and atomic force microscopy—a technology pioneered here—is being used to watch proteins fold into the characteristic shapes that can be crucial to their function.

There’s tremendous activity across the campus in various modalities: using light, electrons, ultrasound, and MRI (magnetic resonance imaging), says UCSB’s Dean of Science Pierre Wiltzius.

While many researchers at the university are using such advanced imaging techniques as functional MRI and electron microscopy as tools in their work, others are focusing on developing imaging technologies and exploring new applications for them.

Some of the most cutting-edge imaging work going on at UCSB involves terahertz technologies, which utilize electromagnetic waves between infra-red and microwave, and atomic force microscopy, largely developed here and now used around the world in engineering and technology applications, and for basic biomedical research.

Right in the middle of the electromagnetic spectrum sits a poorly understood and underutilized resource: terahertz radiation.

This is the heart of the spectrum, researchers in the field like to say—the range from roughly 300 gigahertz to 3 terahertz between infrared radiation, which enables soldiers to see in the dark through night-vision goggles, and microwaves, which can transform a TV dinner from frozen solid to steaming in minutes.

This span of the electromagnetic spectrum is also referred to as the terahertz gap.
because it’s the last piece of the spectrum that really has not blossomed to what it could or should be,? says Wiltzius.

UCSB researchers, however, were some of the very early movers in terms of terahertz imaging and science,? Wiltzius adds. Now, the campus is probably one of the terahertz Meccas of the world,? says Mark Sherwin, director of UCSB?s Institute for Terahertz Science and Technology.

UCSB’s free electron lasers provide a source of terahertz radiation for researchers exploring its potential for imaging.

Here, scientists are working on ways of using terahertz imaging technology to examine wounds bandaged under layers of gauze, to detect skin cancers, and to watch proteins fold.

Terahertz waves are particularly useful because unlike visible light or infrared radiation, they can penetrate clothing, cardboard, wood, bricks, and to some extent, skin.

UCSB’s Elliott Brown, a professor of electrical and computer engineering, is working with Zach Taylor, Rahul Singh, Hua Lee, and Jon Suen of UCSB, and with colleagues in the School of Medicine at UC Los Angeles to explore potential applications of terahertz imaging technology in medicine and healthcare—in particular, to examine burns, which can be imaged through bandages, and to try to detect cancerous tissue.

Terahertz imaging reveals burn damage that’s not seen in the visible, infrared, or any other part of the electromagnetic spectrum,? Brown says. It shows up because terahertz radiation is incredibly sensitive to water concentration.?

Human tissue is water-based, so by using terahertz imaging, we can tell the difference between tissue types,? Brown says, and see the state-of-health of the tissue, which is usually correlated to water concentration.?

Because most cancer cells contain more water than healthy cells, Brown says terahertz imaging could be useful in picking up skin cancers. Our hope is to be able to detect cancerous conditions even before they would normally be flagged for biopsy,? says Brown, who, together with his collaborators at UCLA, is planning to investigate terahertz imaging of squamous-cell carcinoma and melanoma.

Terahertz imaging technology is unlikely, however, to supplant currently-used medical imaging technologies such as X-ray, magnetic resonance imaging (MRI), and positron emission tomography (PET), because terahertz waves can’t penetrate far into the body
because they are readily absorbed by water.

Gesturing at his stomach, Sherwin says, ?You?re not going to be able to see what?s going on in here.?

Terahertz imaging at a distance is a challenge, because absorption by water also limits how far terahertz radiation can travel through the atmosphere before it?s lost to water vapor, but there are plenty of ways of putting the technology to work in closer quarters.

NASA has used the technology to inspect the foam insulation on the outside of space shuttles, checking for voids in the foam layer like those that are thought to have lead to the loss of the shuttle Columbia in 2003. ?Terahertz radiation is perfect? for that application, Sherwin says.

It?s also been used to look through layers of oil paint in old artworks?showing the artists? first brush strokes, which they later painted over. ?There?s no reason we can?t do that here at UCSB,? Sherwin says.

The new full body scanning technology that?s now in place at major U.S. airports uses radiation that?s near the terahertz range to detect weapons and other prohibited items concealed beneath passengers? clothing.

At UCSB, Sherwin is using terahertz waves to peer into the workings of the human body. He?s developing ways of using terahertz technology to spy on proteins and see how they actually move?an improvement on common methods for studying proteins, which involve freezing or crystallizing them.

?Really understanding how proteins move is potentially revolutionary,? Sherwin says. ?Proteins are essentially molecular machines,? he explains. ?You?d like to know how the machines are put together?their structure?and you?d like to know their function, which often we do know. In addition, you?d like to know the mechanisms that they use to perform their functions?how they move.

?If we understand the functional dynamics of some proteins,? Sherwin adds, ?we may be able to intelligently design different proteins that do the same thing, or that do something we want them to do??a possibility with great potential for drug design, he says.

Links:

- Institute for Terahertz Science and Technology [2]
- Mark Sherwin [3]
- Elliott Brown [4]
The remarkable mechanical properties of abalone nacre (the inner mother-of-pearl layer of the shell, at left) are directly related to the material’s unique brick and mortar-like architecture (middle). Using AFM, researchers in the Hansma lab have been able to investigate atomic scale modifications to a growing crystal of calcium carbonate (right, upper) following the addition of abalone nacre proteins (right, lower).

Pinned to the wall of Physics Professor Paul Hansma’s office is an image of an atom, captured using atomic force microscopy (AFM) technology Hansma has pioneered over the last twenty years at UC Santa Barbara.

The picture is a clipping from the National Enquirer, a supermarket tabloid best known for salacious celebrity gossip and tales of politicians caught in compromising positions. Nonetheless, the tabloid ran the photo of an atom, accompanied by an accurate account of the achievement—to Hansma’s delight.

Atomic force microscopes are now ubiquitous in labs around the world, and AFM technology has enabled researchers to make groundbreaking discoveries and great progress in fields ranging from physics through biology to nanomaterials.

“Today’s science couldn’t be done without AFM,” says Dean of Science Pierre Wiltzius. “It’s put us on the map—it’s a true UCSB success story.”

AFM has allowed researchers to study the nanoscale structure of biological materials like bone, shell, and spider silk, and to examine atoms, cell membranes, and proteins in unprecedented detail.
Bone (upper), in this case a section though the trabecular, or “spongy” bone of a human vertebra, is composed of mineralized collagen fibrils. AFM has played a critical role in understand the nanoscale architecture of this material (middle), revealing both the individual banded collagen fibrils (boxed region), the inorganic mineral platelets, and the non-collagenous protein glue that binds the fibrils to one another. A schematic view of these components in shown in the bottom image.

“If you go to physics shows there are probably as many people selling AFMs as any other instrument,” Hansma says. “You see AFM images in all sorts of materials science presentations.”

AFM technology is widely used in the high-tech industry for both development and quality control.

“The killer apps for AFM have been imaging hard drive disc surfaces and integrated circuits,” Hansma says.

AFM—a type of scanning probe microscopy—uses a minute probe to investigate the surface of a sample, taking advantage of the interactions between the probe and the sample. Many kinds of forces can be measured using AFM, including mechanical
forces, chemical bonding, and capillary forces.

One of the advantages of AFM over other microscopy technologies is that samples can be non-destructively imaged under natural conditions—in air, or in liquids that mimic their natural surroundings—and without having to freeze, coat, or otherwise treat them.

Hansma and colleagues at UCSB have used AFM to study the glue that binds together layers of abalone shells, making them remarkably resistant to fracture, and to investigate the structure of spider silk—a material that’s incredibly strong, yet elastic.

In addition to research investigating the origins of toughness in these biological composites, the AFM also played a critical role in early studies aimed at understanding the mechanisms by which these materials were formed. In these studies the AFM was used to investigate in real time how abalone shell proteins interact at the atomic level with growing crystals of calcium carbonate, ultimately modifying their crystal structure and macroscopic morphology.

They have also used AFM to examine the molecular structure of human bone, gaining important insights into the origins of bone fracture resistance, and what goes wrong when bones become more easily fractured from age and disease, Hansma says.

Hansma and other UCSB researchers, including Daniel Morse and Galen Stucky, found a biopolymer in bone that acts like glue, holding together strands of mineralized collagen fibrils. This glue contains bonds that can uncoil or break and then reform, helping bone absorb stress without fracturing. This is the same kind of shock-absorbing substance the scientists earlier found in abalone shell.

“Our theory is that the glue we found in bone is very important,” Hansma says. “It prevents the separation of the mineralized collagen fibers—the beginning of a fracture.

The discovery has not only helped scientists understand the remarkable mechanical properties of bone, it’s helping researchers create new self-healing, shock-resistant materials. Hansma and his colleagues are also using the insights from their AFM studies of bone to develop diagnostic instruments to assess bone health in living patients.

Hansma’s hope when he first began working on AFM was that it would have biomedical applications. Although AFM isn’t yet used in clinical applications, there’s been progress in understanding human diseases, and the biomedical applications continue to grow, Hansma says.

Links:

- [Paul Hansma](#)
- [Bone glue discovery](#)

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