

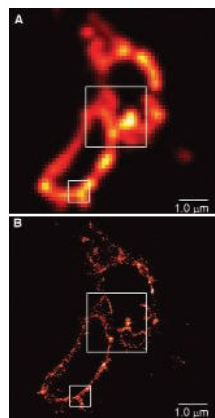
Areas to Watch in 2007

World-weary? Hardly. Four fledgling spacecraft will give planetary scientists plenty to ponder in 2007. Europe's COROT orbiting exoplanet hunter, scheduled for launch 27 December, should detect dozens of new "hot Jupiters" around other stars and may even bag its big quarry: signs of rocky planets just a few times the size of Earth. Closer to home, the Mars Reconnaissance Orbiter will take the sharpest-ever pictures of the martian surface and will use radar to look for rock layers—and ice—as much as 1 kilometer deep. The Venus Express orbiter will be going full tilt, and in February, New Horizons will send back snapshots of Jupiter en route to its 2015 rendezvous with Pluto.

Skulls and bones. In recent years, paleoanthropologists have uncovered new skulls, teeth, and lower limbs of the earliest members of our genus *Homo* at sites in the Republic of Georgia, China, and Kenya. In 2007, the first descriptions of these fossils should give clues to the identity of the first human ancestors to leave Africa about 1.8 million years ago—such as whether the bones all belong to one species (*Homo erectus*) or to two or more. Meanwhile, the long-awaited partial skeleton of *Ardipithecus ramidus*, an early human ancestor that lived in Ethiopia 4.4 million years ago, promises to shed light on how upright walking evolved in early hominids.

8 PEERING BEYOND THE LIGHT BARRIER.

Biologists got a clearer view of the fine structure of cells and proteins this year, as microscopy techniques that sidestep a fundamental limit of optics moved beyond



Clearly. New microscopy techniques resolve nanometer-sized features of proteins.

proof-of-principle demonstrations to biological applications. The advances could open a new realm of microscopy.

An ordinary microscope cannot resolve features smaller than half the wavelength of the light used to illuminate an object—about 200 nanometers for visible light. For years, physicists and engineers have devised schemes to get around the "diffraction limit," and this year, researchers used those techniques to do some real biology.

In April, researchers in Germany used a technique known as stimulated emission depletion (STED) to study the tiny capsules in nerve cells called synaptic vesicles. Each vesicle releases its load of neurotransmitter when it merges into the cell membrane. The

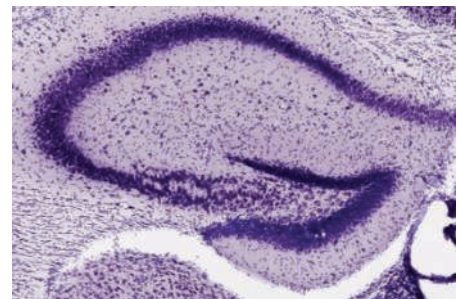
team showed that a protein in the vesicle remains clumped after the merger, suggesting that the clumps do not form from scratch when the process reverses to form new vesicles. The researchers tagged the proteins with a fluorescent dye and zapped the specimen with laser light to excite a spot as small as the diffraction limit allows. Then, by applying a pulse from a second beam with a dark "hole" in the middle, they squeezed the fluorescent spot down to a much smaller pinpoint of light. By scanning the beams across the sample and recording the level of fluorescence, the researchers assembled an image with a resolution of tens of nanometers. The team followed up with two other biological studies.

In August, another team imaged proteins within cells using a simpler technique known as photoactivated localization microscopy (PALM). The researchers used a fluorescent tag that had to be turned on with a pulse of light of one wavelength before it could be excited to fluoresce by light of another wavelength. By applying the first laser at a very low level, the researchers could turn on one tag molecule at a time. The molecule still produced a blurry spot when viewed through the microscope, but the researchers could nail down its position very precisely by finding the center of the blob. Repeating the process over and over, the team mapped proteins in cells with nanometer resolution. Two other groups introduced similar techniques this year.

Just how widely the techniques will be used remains to be seen. PALM is too slow to track dynamic processes, and STED requires fluorescent tags that can withstand intense excitation. Still, researchers are optimistic that more applications will follow, now that the diffraction limit is no longer a limit.

9 THE PERSISTENCE OF MEMORY.

How the brain records new memories is a central question in neuroscience. One attractive possibility involves a process called long-term potentiation (LTP) that strengthens connections between neurons. Many neuroscientists suspect that LTP is a memory mechanism, but proving it hasn't been easy. Several findings reported this year strongly bolstered the case.



Record keeper. Learning and LTP go hand in hand in the rodent hippocampus.

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Loads of new primate genes.

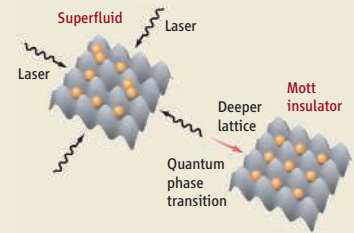
With the human and chimpanzee genomes sequenced, genetic research into our evolutionary past is scrambling up other branches of the primate family tree. Low-resolution maps of gorilla, rhesus macaque, orangutan, marmoset, and gibbon genomes are already available, and refined, error-free versions should be ready in 2007. In addition, look forward to rough drafts of the genomes of the galago, tree shrew, and mouse lemur. If things go as planned, a comparative analysis of all these genomes might finally begin to explain what sets humans apart.



A climate of change? The case for human-induced warming will grow even more ironclad as the Intergovernmental Panel on Climate Change releases its report in February. Meanwhile, the International Polar Year, opening in March, will feature climate research on Earth's coldest climes. And the world is watching the U.S. Congress, which, under Democratic control, is expected to pass some sort of mandatory emission regime, and President George W. Bush, whose response will be sure to shape the debate.

Whole-genome association studies. The trickle of studies comparing the genomes of healthy people to those of the sick is fast becoming a flood. Already, scientists have applied this strategy to macular degeneration, memory, and inflammatory bowel disease, and new projects on schizophrenia, psoriasis, diabetes, and more are heating up. But will the wave of data and new gene possibilities offer real insight into how diseases germinate? And will the genetic associations hold up better than those found the old-fashioned way?

Light crystals. Ultracold atoms continue to be one of the hottest areas in physics. Now researchers are loading the atoms into corrugated patterns of laser light known as optical lattices. The lattices work like artificial crystals, with the spots of light serving as the ions in the crystal lattice and the atoms playing the role of electrons moving through it. Optical lattices could help crack problems such as high-temperature superconductivity and seem sure to produce interesting new physics. Look for rapid progress in this burgeoning effort.



Scientists discovered LTP in the early 1970s, when experiments with rabbits showed that a brief barrage of electrical zaps could bolster synaptic connections between neurons in the hippocampus, a brain region tied to memory. Later studies revealed that drugs that block LTP, when given to an animal before it learns a new task, prevent new memories from being formed.

But some predictions of the LTP-memory hypothesis have been harder to test. One is that it should be possible to observe LTP in the hippocampus when an animal learns something. In January, Spanish scientists reported just such an observation in mice conditioned to blink upon hearing a tone. In August, another research team described LTP in the hippocampus of rats that had learned to avoid an area where they'd previously received a shock.

A study published in August addressed another prediction: that abolishing LTP after learning should erase what was learned. Researchers injected a compound that blocks an enzyme needed to sustain LTP into the hippocampus of rats after they'd been trained to avoid a "shock zone" in their enclosure. The treatment eradicated both LTP and the memory of the shock zone's location.

Although the new results add to evidence that LTP is a molecular mechanism of memory, much work remains. For example, researchers still haven't figured out how the

many forms of LTP identified in brain tissue relate to different kinds of memory. And they may have a while to wait for the ultimate test, which some call the "Marilyn Monroe criterion": inducing LTP at select synapses to create the vivid memory of an event, such as an evening with the voluptuous movie star, that never happened.

10 MINUTE MANIPULATIONS. Small RNA molecules that shut down gene expression have been hot, hot, hot in recent years, and 2006 was no exception. Researchers reported the discovery of what appears to be a new and still-mysterious addition to this exclusive club: *Piwi*-interacting RNAs (piRNAs). Abundant in the testes of several animals, including humans, piRNAs are distinctly different from their small RNA cousins, and scientists are racing to learn more about them and see where else in the body they might congregate.

PiRNAs made their grand entrance last summer, when four independent groups released a burst of papers describing them. In a sense, their sudden prominence is not surprising. The *Piwi* genes to which piRNAs bind belong to a gene family called Argonaute, other members of which

help control small RNAs known as microRNAs (miRNAs) and small interfering RNAs (siRNAs). Scientists already believed that the *Piwi* genes regulate the development and maintenance of sperm cells in many species. With the discovery of piRNAs, they may be close to figuring out how that happens.

Particularly intriguing to biologists is the appearance of piRNAs: Many measure about 30 RNA bases in length, compared with about 22 nucleotides for miRNAs and siRNAs. Although that may not sound like much of a difference, it has gripped biologists and convinced them that piRNAs are another class of small RNAs altogether. Also striking is the molecules' abundance and variety. One group of scientists found nearly 62,000 piRNAs in rat testes; nearly 50,000 of those appeared just once.

But beyond characterizing what piRNAs look like and finding hints that they can silence genes, scientists are mostly in the dark. Still to be determined: where they come from, which enzymes are key to their birth, and perhaps most important, what they do to an organism's genome. Stay tuned.

—THE NEWS STAFF

