to use the nanotip as the "drain" in a particular kind of transistor (called a MOSFET transistor), as reported at the meeting by Junji Itoh of the Electro-Technical Laboratory in Tsukuba, Japan. By controlling the voltage in the transistor, researchers can control the rate at which electrons flow out of the nanotip. In Itoh's device, emission fluctuated by only a few percent, a solution that could make the field-emitter arrays more readily usable.

So far no flat-panel displays on the market actually use field-emitter arrays, but Robert Pressley from Candescent Technologies (formerly Silicon Video Corp.) in San Jose, California, says that his company expects to manufacture such displays in about a year. "We are now at the stage of putting the assembly line together," he says. They hope that their design, in which several thousand molybdenum nanotips illuminate each pixel on command, will be a competitor for the high-end LCD market.

Meanwhile, researchers haven't forgotten the traditional CRTs, reporting sizable increases in electron emission in thermionic cathodes, for example. And at the meeting, a Philips Research Laboratories team unveiled a fully working prototype of a flat-panel display that is basically an adaptation of a conventional CRT. Rather than emitting electrons from many single points adjacent to the screen, as the nanotip-based FEDs do, this device relies on a linear array of common thermionic cathodes mounted in the bottom of a flat tube less than 1 centimeter thick, with a phosphor screen on one side and supporting struts in the middle.

These internal pillars keep the flat sides of the vacuum vessel apart and also guide the electrons to the screen, says team leader Gerard van Gorkom. When an electron hits a strut, the strut responds by emitting exactly one secondary electron. The emitted electrons thus "follow" the path laid out by the struts, so researchers can precisely direct the electrons to the screen. "It is very nice technology," says Pressley. "To me it is amazing that no one stumbled on that before," agrees Brad Pate of Washington State University. "If the price is right, this is a real winner."

But apparently, not everyone thinks so: In April, Philips decided to discontinue development of the device because it had no partners in the project. "We do not exclude the possibility that others will take up this project," says van Gorkom, who hopes that Philips might one day restart the project. But even if Philips backs away from this device, the flurry of results seems likely to help computer screens of the future shed their portly profiles in favor of a trim silhouette.

–Alexander Hellemans

Alexander Hellemans is a science writer in Brussels.

MEETING BRIEFS

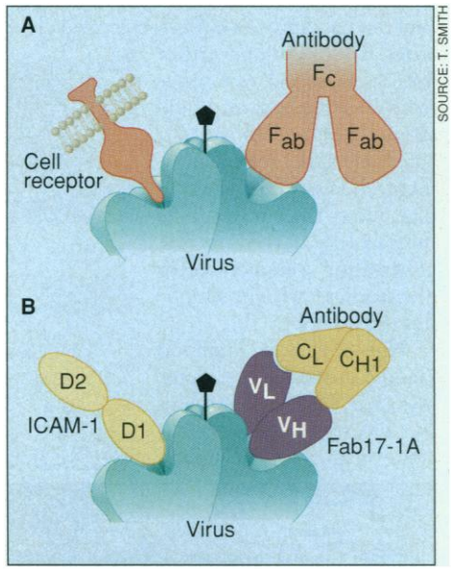
Crystallographers Pinpoint What Goes Where

SEATTLE—In structural biology, as in real estate, location is key. And by tracking x-rays or other high-energy sources as they scatter off crystallized biomolecules, crystallographers can pinpoint locations of structures that perform crucial biological functions. At the International Union of Crystallography XVII Congress and General Assembly, held 8 to 17 August, researchers using the technique reported insights into the evasiveness of viruses and the failure of AIDS drugs, among other topics.

Cold Virus Betrays Potential Achilles' Heel

Science still has no cure for the common cold. Fortunately, the immune system has its own remedies. New findings presented at the meeting reveal one immune strategy, showing that antibodies, immune proteins that attack invaders, can directly block features on rhinoviruses, the cold-causing culprits. The conclusion overturns previous assumptions about antibody behavior, and may serve as a model for anti-cold remedies that could supplement the natural defenses.

Researchers have long known that the surfaces of many viruses are pocked with tiny crevices, which help them infect cells by latching onto complementary-shaped protrusions on the cell surfaces. Researchers also believed, however, that the crevices play a secondary role as well, helping viruses evade immune detection. If antibodies plugged up these crevices, they could not only keep the virus from binding to the cell, they could mark the virus for later destruction by the immune system's heavy artillery. But crystal structures of the surfaces of viruses suggested that the crevices in rhinovirus are so small that antibodies' bulky heads wouldn't be able to wedge their way in. Instead, researchers believed, the antibodies simply try to smother the crevices by lying on top of them. But viruses, being slippery beasts, could presumably counter this by altering amino acids on their outer coat, causing the antibodies to lose their grip.



SOURCE: T. SMITH

A better fit. (A) Older theories held that antibodies lay atop the cold virus; (B) the new view shows that they plug into viral crevices.

Yet after crystallizing rhinovirus particles with antibodies bound to them and bombarding them with x-rays, Purdue University crystallographer Thomas Smith and his colleagues came up with a different picture. Their map of the complex showed that part of the head groups from rhinovirus antibodies do, in fact, fit snugly in the viral crevices. The implication, Smith says, is that crevices' shapes evolved solely to boost a virus's ability to invade its victim's cells, not to avoid antibody interference.

"It's a very important finding," says molecular biologist Ian Wilson of the Scripps Research Institute in La Jolla, California, for it points researchers toward designer drugs that might be able to affect the crevice interior, limiting the ability of the virus to bind to target cells.

A Better Handle on AZT?

AZT has never amounted to the AIDS wonder drug that many had hoped it would be. At the meeting, a group from the Max Planck Institute for Molecular Physiology in Dortmund, Germany, reported a clue to the compound's shortcomings: AZT's molecular structure may make a poor "fit" with the cellular enzyme needed to transform it into an active, antiviral form.

AZT, or azidothymidine, stops viruses like HIV from replicating by preventing them from using the nucleotide thymidine to translate the RNA in their genome into DNA inside the cells they invade. The drug's structure

is very similar to thymidine, so it can slip into thymidine's place in a growing DNA chain. But because the drug lacks the oxygen-containing hydroxyl group that chain-building enzymes use to attach the next link, its incorporation stops the DNA chain's growth.

AZT's problem, however, is getting into that DNA chain in the first place. Before it can be inserted, cellular enzymes must add a series of three phosphate groups to one end of the molecule; one of these phosphates eventually goes on to become part of DNA's backbone structure. The enzymes do this job quite nicely with thymidine. But despite AZT's resemblance to the nucleotide, about 96% of the drug molecules never acquire more than one of the three phosphate groups.

To better understand what's going awry, Arnon Lavie, Jochen Reinstein, and their colleagues at the Max Planck have been trying to compare how both AZT with one phosphate group (AZT-P) and thymidine bind to thymidylate kinase (TmpK), the enzyme that adds the second of the three phosphate groups. At the meeting, the researchers revealed the first part of this comparison: the structure of thymidine bound to TmpK.

It shows that thymidine has a hydroxyl group that fits snugly into the TmpK binding pocket, helping the two molecules to interact. AZT, however, lacks this key hydroxyl group. In its place AZT has a bulky nitrogen-containing cluster, known as the azido group, and the researchers argue that it probably doesn't fit into the TmpK pocket nearly as neatly; the poor fit may even shift the position of the drug molecule in the enzyme's pocket. The effect might be to prevent the enzyme from adding another phosphate group, says Lavie.

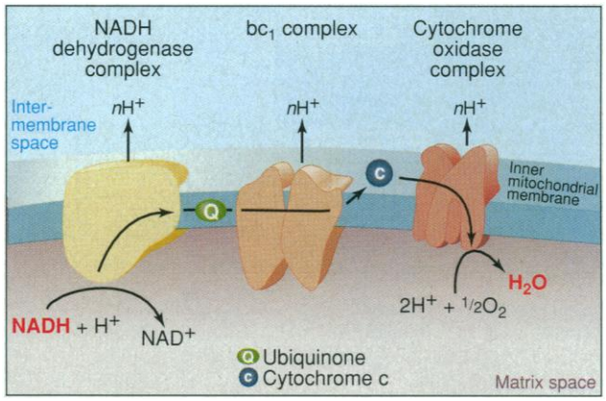
The Max Planck group is now trying to confirm this scenario by crystallizing AZT in conjunction with TmpK. Although the team doesn't have the final answer yet, "it's an interesting experiment to pursue," says Hiroaki Mitsuya, head of experimental retrovirology at the U.S. National Cancer Institute's medicine branch in Bethesda, Maryland. If the group's theory holds up, they hope to come up with alternate forms of the drug that make the connection more readily—and perhaps live up to a few more of the early hopes. Yet Carl Dieffenbach, a molecular biologist and virologist at the National Institute of Allergy and Infectious Diseases in Bethesda cautions that a better binding form of AZT may face problems. One, he says, is that if AZT is too readily transformed into its activated form, its incorporation in DNA could be overly toxic, harming healthy cells as well as halting a deadly virus.

SOURCE: ALLERTS *ET AL.*, *MOLECULAR BIOLOGY OF THE CELL*, 2ND ED.

Peering Into the Cell's Engine Room

Peeking under the hood of a cell's power plant, crystallographers have taken their first good look at a crucial part of the biochemical power train: one of the five essential protein complexes that convert energy into the cellular fuel known as ATP. The Seattle meeting showcased complex #3, a giant molecule known as cytochrome bc_1.

"It's a spectacular structure," says Ian Wilson, a molecular biologist at the Scripps Research Institute in La Jolla, California. Not only is it one of the largest membrane-bound proteins ever mapped—composed of 11 protein-based subunits—Wilson notes, but the molecule also performs an intricate task: orchestrating separate flows of negatively charged electrons and positively charged protons through different portions of the molecule. The new structure, worked out by Nobel laureate crystallographer Johann Deisenhofer and his team at the University of Texas Southwestern Medical Center in Dallas in conjunction with Chang-an Yu and his colleagues at Oklahoma State University in Stillwater, provides a reality check for models of this electronic shuffle.



Power train. Cytochrome bc_1 *(center)* shuffles electrons along cellular energy pathways; a new study shows how this happens.

Scientists have known since the 1960s that cytochrome bc_1 and its four enzymatic partners strip electrons from compounds such as NADH that originally hijack the charges from food metabolites such as glucose and fatty acids. Cytochrome bc_1, which like its partners straddles a membrane inside the mitochondria, uses some of the siphoned energy to pump protons outside this membrane, creating an electric potential that other enzymes use to drive ATP synthesis.

Models of the cytochrome had suggested that it sends the electrons down a pair of electronic "bucket brigades," each consisting of a pair of iron-containing groups. The positions of the groups in the new structure support those models, says Deisenhofer. And the new view of the complex provides some tentative hints about how it manages to pump protons through its core.

One hint is that the task may be carried out by a series of amino acids, such as glutamic acid, that can be ionized so they carry a negative charge. The charge attracts the positively charged protons, which then flit from amino acid to amino acid through the molecule, says Deisenhofer. But he adds that water molecules incorporated into the protein could be serving the same role.

Researchers will have to wait to settle that question, because the current resolution of the complex is not sharp enough to pin down the position of tiny water molecules. Scientists are currently trying to grow higher quality crystals that will give an even better look into the cellular engine room.

Germ Warfare

Warriors in the microbial world may be hard to see, but they sometimes have weaponry that would have made King Arthur's knights blanch with fear. *Escherichia coli* bacteria, for example, impale their bacterial foes with harpoonlike proteins that are so lethal that just one thrust is enough to dispatch a victim. In Seattle, researchers got their first atomic-scale look at the structure of one of these miniature lances—and new clues to why it is so deadly.

Relatively speaking, the *E. coli* harpoon isn't all that miniature: Known as colicin Ia, it contains a central shaft made up of coiled helices that is 160 angstroms long—roughly twice as long as the previous coiled record-holder. This new elongated structure caught crystallographers' imagination. "Most [protein] structures are very compact and globular," says Wim Hol, a biochemist at the University of Washington, Seattle. The new bacterial toxin, however, "is the most unglobular structure I've ever seen. It's really remarkable."

The harpoon's structure also makes it a natural killer, says Robert Stroud, who led the team from the University of California, San Francisco, that crystallized the molecule. He explains that the molecule, which is actually shaped like a hairpin, contains three distinct domains. At one end, the first domain appears designed to bind to receptors on the target cell. The second, located at the hairpin turn, wedges its way through the internal periplasm. The third, at the far end, situated just opposite the first, inserts itself into the plasma membrane, a protective sheath inside the cell wall. Having holed its opponent, the molecule then creates an ion channel that quickly kills the cell by selectively siphoning out key cell nutrients.

–Robert F. Service