INTERFACES

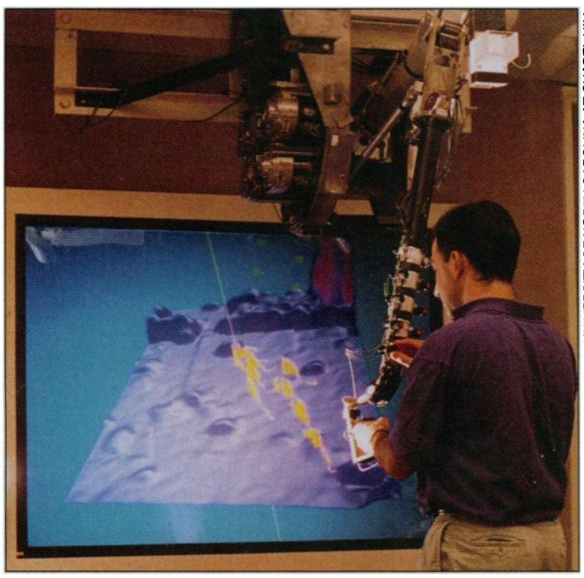
Taking the Data in Hand—Literally—With Virtual Reality

What does it feel like to push 100 atoms of gold around with the tip of an atomic force microscope? Not many have had the experience, but two of those who have say it feels like pushing bags of Jello across a rough surface with a screwdriver. The two in question, University of North Carolina (UNC) graduate students Michael Faldo and Mark Finch, were privy to a virtual reality (VR) display that immersed them in an atomic-scale world. With eyes on stereo video displays that turned the minute topography into a human-scale world and a hand on a "force-feedback" arm that moved and felt resistance just as the microscope tip did, Faldo and Finch were able to sense shapes and forces on the scale of atoms.

Faldo, Finch, and their colleagues in the Nanomanipulator collaboration—among them UNC physicists Sean Washburn and Richard Superfine and computer scientist Fred Brooks, and materials chemist R. Stanley Williams of the University of California, Los Angeles—make up one of the many research groups that are turning abstract data into visceral sensory experience through VR. At last month's SIGGRAPH '94, the 21st international conference on computer graphics and interactive techniques in Orlando, Florida, no fewer than 40 scientists presented VR displays of data or model results in fields ranging from theoretical physics and mathematics to earth sciences, chemistry, biology, and aerospace engineering.

How soon all these simulations of reality are going to pay off scientifically is another question. The hype that surrounds VR, researchers say, makes it difficult to assess the technology's true promise. And enthusiasts acknowledge that the real payoff may lie far in the future. "We're talking about stuff that looks very promising and very interesting and has many purposes but, boy, is it primitive," says Brown University computer scientist Andries van Damm. Robert Langridge, a pharmaceutical chemist at the University of California, San Francisco, argues simply that "to claim VR in its present incarnation is as far as it's going to go is truly foolish." Langridge, who has been doing computer graphics for almost three decades, goes on to say, "If I stayed in the field for 10 more years, just like everyone else, I would surely be using VR."

Already, researchers who have experienced VR say it can help them make sense of enormous databases or gain an intuitive grasp of unfamiliar processes. Virtual reality, says California Institute of Technology neuroscientist James Bower, can "provide data to our own pattern recognizer—our brain—in as rich a form as possible." Adds van Damm, "There are many ways of interacting with data that can't really be done well with a two-dimensional monitor, a mouse, and a keyboard. VR is about richer communication and therefore richer visualization and exploration."



UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL

At home in the nanoworld. The UNC/UCLA Nanomanipulator system allows a user to push a 100-atom gold particle across a surface, monitoring the process through 3D goggles *(not shown)* and a force-feedback arm.

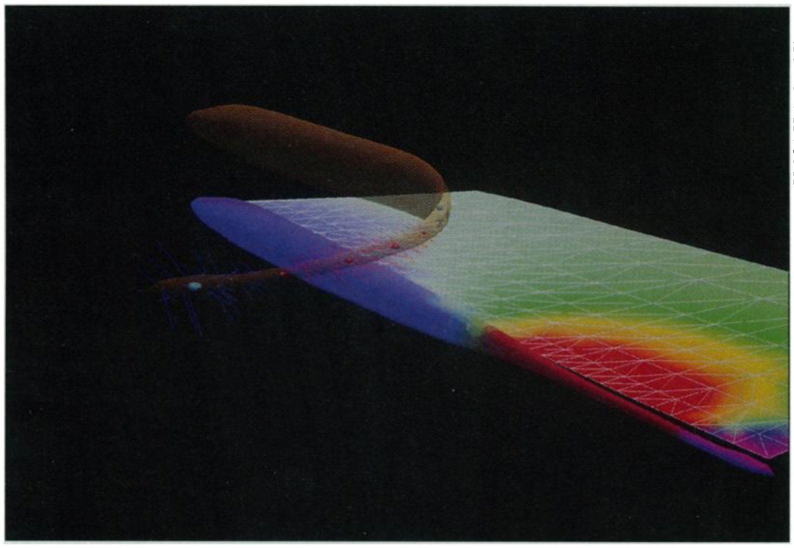
The centerpiece of VR is a three-dimensional visual display, usually an oversized set of goggles called a head-mounted display, which flashes images to the left and right eyes that differ enough to provide the impression of depth. A tracking system monitors head and eye movements so that as the user looks around the virtual world, the display changes accordingly, deepening the impression of three-dimensional reality. To allow the user to interact with this virtual world, some systems include a data glove that tracks hand movements and enables the user to point to and manipulate virtual objects. And the most sophisticated systems, such as the UNC/UCLA Nanomanipulator, have a force-feedback system—usually a mechanical tracking arm set up so that when the user acts on the virtual world, the virtual forces that result are calculated and reflected back to the mechanical arm and the user's hand.

One challenge still to be overcome before VR can become a widespread research tool is providing a high-resolution viewing device that weighs less than 10 or 20 pounds. "We give a lot of demonstrations to casual users," says William Wright, director of a UNC project to create computer graphics tools for biochemists and protein crystallographers, "and rarely does a person want to stay in the helmet more than a few minutes." The UNC program is generally considered the most advanced VR research program in the country, and yet only in the last few months, says Wright, "has our VR technology become good enough to be very useful."

Even when the technology has been made compatible with its human users, VR designers will still face the computational challenge of turning huge volumes of raw data, such as information from an atomic force microscope or the data points in a molecular model, into a virtual environment—then updating it fast enough so that it will change as the viewer's eyes shift. The rule of thumb among VR researchers is that the computers must update the virtual world at least 10 times per second; any slower, and a time lag will set in—quickly followed by nausea. "We're talking many millions of computations per second," says van Damm. And that's without adding to the computational burden by allowing the user to manipulate the virtual environment.

Easy-to-swallow gigabytes. Still, by combining computational brute force and ingenuity, researchers have been able to take data sets that would normally be far too large and unwieldy for easy understanding and turn them into almost magical displays of virtual reality. Take Steve Bryson's virtual wind tunnel project at the NASA Ames Research Center in Mountain View, California. In each run of the virtual wind tunnel, Bryson builds a computer model of the aircraft in question, then calculates the airflow around it for a three-dimensional grid of points extending outward from the vehicle surface. The result is what he calls "a god-awful array of numbers in three dimensions" describing air velocity, pressure, temperature, and a half-dozen other variables at each point. All of these numbers—easily a gigabyte of data—have to be graphically displayed and updated in real time, so the user can actually see how the airflow changes as, say, the plane's orientation changes.

Because solving the equations in real time would overwhelm any existing computer, Bryson uses a supercomputer to solve them beforehand, then stores the data. Later, a separate graphics computer taps into the data as needed to build a three-dimensional virtual image. Unlike a conventional wind tunnel, which must be off-limits to humans when it's operating, viewers can wander freely through the virtual one, inspecting the airflow from every angle as it rushes over the aircraft's contours.

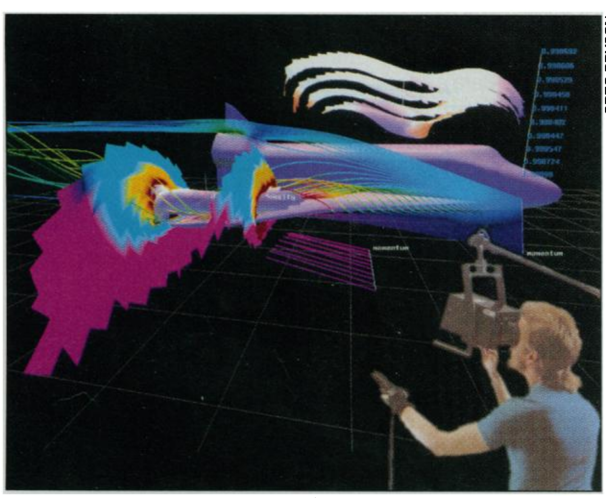


JAMES BOWER AND T. DEFANTI

The body electric. A VR display shows how the electric fields generated by a "weakly electric" fish respond to nearby objects and the fish's own motion.

"You're also wearing a data glove," adds Bryson, "so while you're walking around looking at this thing from different points of view, you can also add streamlines" or modify the model in other ways. By gesturing with the data glove, for example, the user can place a row of streamlines on a wing in order to trace how air cuts under and over the airfoil or spirals in a vortex. "Airflow around airplanes is a very complex three-dimensional phenomenon," says Bryson. "Virtual reality is vastly superior to your typical workstation monitor for visualizing these things."

Vivian Cody, a chemist at the Medical Foundation of Buffalo, is exploiting that superiority in a different realm. She has been using the UNC virtual reality technology to study enzyme structures, looking for clues to the design of drugs that would inhibit the enzymes. Cody begins by crystallizing an enzyme in the presence of a compound known to bind to it, "something that is a potential drug," she says. Then, following the standard procedure for determining the structure of biomolecules, she diffracts x-rays through the crystals to extract information about the positions of individual atoms and feeds the data into a computer, creating a three-dimensional model of the enzyme's structure.



GREG BRYSON

Tunnel vision. A virtual wind tunnel allows a user to explore the aerodynamics of a craft—in this case the space shuttle—and add visualization aids such as streamlines.

That model, says Cody, can reveal the geometry of the binding and which of the enzyme's amino acids take part in it. "Depending on what we find," says Cody, "we can suggest modifications that chemists can make to that drug to enhance its binding to that enzyme." But because the model might include the positions of as many as 500 atoms, it loses much of its richness when it is reduced to a flat display on a computer terminal. "If you want to see detail," says Cody, "you have to zoom in on the figure, but then the rest of the structure disappears off the screen, and you lose the perspective of the big picture. If you want the big picture, you get no details."

By displaying the molecular model in VR, says Cody, she can immerse herself in the structure, studying details without losing a sense of the entire molecule. And with the mechanical tracking arm, she can explore it by touch as well. "[The arm] allows you to feel the interactions of one molecule docking inside another," she says.

Exploiting the tracking arm as a three-dimensional mouse, Cody can "grab" a group of atoms in the drug molecule and try to move them into another docking orientation on the enzyme. The computer calculates the overall repulsion or attraction that would be generated by the electromagnetic forces among the atoms and sends the forces back through the arm to the user's hand. "As you try to drive through these passageways," she says, "you feel a repulsive force on the tracking arm....It gives you an idea of how difficult it is for these molecules to get together"—and perhaps a clue about how to make them bind more avidly.

Virtual worlds. Like Bryson, Cody relies on VR as a tool for making sense of otherwise overwhelming data sets. For some other researchers, however, VR plays another role: It's a means of projecting themselves into an unfamiliar world. Caltech's Bower and his colleagues, for example, have developed a VR system that opens a window on the capacity of some fish to sense electric fields, in particular the weakly electric species *A. leptorhynchus*. The fish, Bower explains, generates a weak electric field and, through receptors on its skin, picks up distortion in the field caused by nearby objects. "I don't know as a mammal what it means to be electrically active," he says. But by manipulating the three-dimensional VR display of the fish and its electric fields, he says, "we can look at the distribution of electric fields on the skin, interact with the field in real time, move objects closer or further away. We are really using virtual reality as a technique to understand the reality of a different animal."

Physicist Andy Hanson of Indiana University is working in a world that's every bit as alien to most human beings as that of the electric fish: the world of mathematical objects in four dimensions. And like Bower, he's trying to bring that experience closer to home. "Since we have a very good visual intuition for converting shaded two-dimensional objects into 3D structures in our heads," says Hanson, "I thought we might be able to develop the facility of converting what are in effect shaded three-dimensional images [seen in VR] into four-dimensional objects in our head." Instead of using a head-mounted display, Hanson presents the VR images in a "cave"—a room in which all four walls, ceiling, and floor are faced with high-definition, large-screen televisions. What the display actually looks like, however, is nearly impossible to describe, which is one of the problems of communicating the value of VR. It can't be conveyed in less than three dimensions. As one hematologist who uses VR puts it, "Once you take a picture of it, it's no longer virtual reality."

In the UNC/UCLA Nanomanipulator project, the world on display in the VR simulation is just as alien as that of electric fish and four-dimensional objects, but for a different reason: It's so small that it's invisible to our ordinary senses. The data driving the

Nanomanipulator display come from a tiny probe poised over a surface's bumpy atomic landscape. In its original form, conceived 5 years ago by Williams and Warren Robinett, a UNC computer scientist, the system was hooked to a scanning tunneling microscope (STM)—a device that maps surface contours from variations in an electric current running from surface to tip. Besides seeing the surface in a head-mounted display, the user could "feel" it through force feedback on a mechanical arm electronically linked to the STM tip and even sculpt it by pulling a trigger on the handgrip. A pulse of voltage fired from the STM tip, says Williams, would "dig out chunks of the surface or deposit pieces of the STM tip."

To sculpt with more finesse, the Nanomanipulator collaboration substituted an atomic force microscope (AFM) for the STM. Unlike the STM, the AFM physically traces the surface, like a phonograph needle. And although its resolution is coarser than an STM's, the AFM tip can actually push objects around on the surface. Explains Williams, "If you bump the AFM tip into something, you feel it on the mechanical tracking arm, and so you can start pushing things around as you might push a soccer ball around with your hand."

In the last week of June, the Nanomanipulator team exploited that ability to build what they call a nano-Stonehenge from 100-atom colloidal gold particles deposited onto an otherwise smooth gold surface. According to Russell Taylor, a UNC graduate student who helped build the original system, it took just 40 minutes "to assemble an aggregate of [these] balls on the surface and sweep the others away." Other researchers building atomic-scale structures without the benefit of VR, in contrast, often spend days on such feats.

Williams thinks the group's achievement may be a first step toward creating nanometer-scaled electronic circuitry. He's also dreaming of manipulating and modifying biological molecules such as DNA and proteins. "We could use an STM or AFM tip as a very fine scalpel to dissect a protein molecule or DNA molecule," he says. "Take it apart, put it back together, see if we can do it all using physical manipulation rather than chemical." The project could start right away if his group had "a good partner," says Williams: "someone who would have the knowledge of the biological molecules and the patience to actually play around with this thing."

And play, Williams says unapologetically, is still a pretty good word for the use of VR by the Nanomanipulator group—and that of many others. Interesting as it is, he says, "it's still at the stage of a pretty far-out research toy."

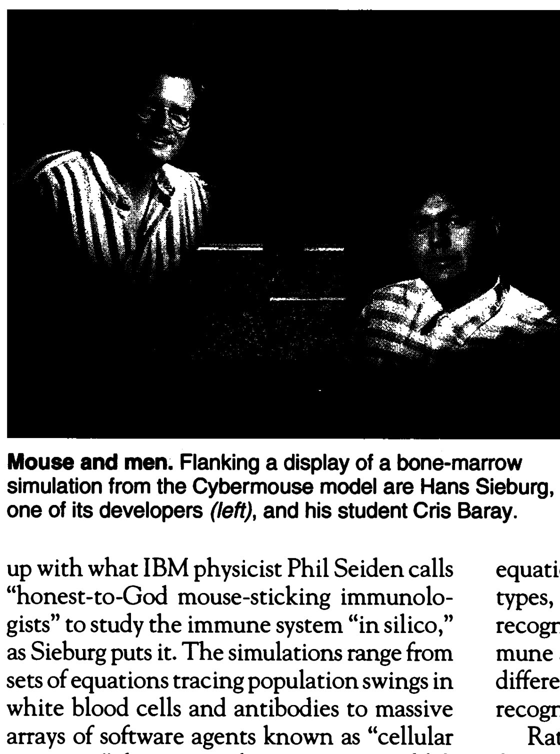
–Gary Taubes

BIOLOGICAL MODELING

Do Immunologists Dream of Electric Mice?

Call up Mosaic, a popular tool for exploring the Internet, and type http://bitmed.ucsd.edu. You'll see a logo that looks like a mouse and then a succession of menus. In a few moments, without leaving your desk, you'll be exploring the immune system of a mouse. With no more than a click of the (desktop kind of) mouse, you can manipulate a tiny syringe to inject cells or antigen, assay lymphocytes, and study how an immune response plays out in different tissues. Meet Cybermouse, an on-line virtual laboratory animal for exploring the immune system.

Cybermouse is the product of a collaboration between immunologist Don Mosier of the Scripps Research Institute in La Jolla, California, and mathematician Hans Sieburg of the University of California, San Diego and is just one example—albeit one of the most ambitious—of an expanding breed. In increasing numbers, computer scientists, physicists, and mathematicians are teaming up with what IBM physicist Phil Seiden calls "honest-to-God mouse-sticking immunologists" to study the immune system "in silico," as Sieburg puts it. The simulations range from sets of equations tracing population swings in white blood cells and antibodies to massive arrays of software agents known as "cellular automata" that mimic the interactions of different immune-system cells and tissues.


ALAN DECKER/SAN DIEGO SUPERCOMPUTER CENTER

Mouse and men. Flanking a display of a bone-marrow simulation from the Cybermouse model are Hans Sieburg, one of its developers *(left)*, and his student Cris Baray.

Regardless of which kind of model you're talking about, says Mosier, these computerized simulations can run experiments and test hypotheses that would be too time-consuming or difficult to do with live animals. "If we did them all in a mouse," he says, "it would take 10 years"—if they could be done at all. Adds Mel Cohen, a Salk Institute immunologist who learned his trade in the 1950s with Jacques Monod and François Jacob at the Pasteur Institute, "These computer models are the only way to take a large number of variables, take a system that is very complex, and study the effect of one variable on all the others."

Cohen and his colleagues aren't arguing that silicon-based immune systems can ever substitute fully for laboratory animals. But the simple, rigid logic of a computer is a good match to that of the immune system, argues Cohen's partner Rod Langman, a Salk Institute biologist. "[If I can] tell an incredibly stupid computer what to do... so that it can simulate immune response, then I must really have understood something about the immune system." Already, researchers have used computer simulations to make testable predictions about how the AIDS virus spreads through the immune system and how the system "remembers" a pathogen years after the original infection—and responds with a quick and vigorous counterattack.

One approach to putting the immune system on a computer was pioneered as early as the 1960s, when Los Alamos physicist George Bell developed a set of differential equations describing how antibody-producing white cells, called B cells, proliferate, differentiate, and secrete antibody in response to an antigen, in particular a foreign virus or bacteria. In 1986, theoretical immunologist Alan Perelson joined physicists Doyne Farmer and Norman Packard at Los Alamos to build on that strategy. As Perelson describes it, Bell's original equations followed the fate of some 40 B cell types, each one defined by a receptor able to recognize a different antigen. The actual immune system, however, has some 10 million different types of B cells, which is why it can recognize literally any antigen.

Rather than trying to write an equation for every possible B cell population and the antigen it responds to, Perelson, Packard, and Farmer developed a technique called metadynamics, in which the computer itself constructs the differential equations of the model. It does so in response to the interactions of bit strings representing the receptors of the various cell types. (Each cell and its progeny carry the same bit string—for in-