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Who we are
The National Computational Science Alliance (Alliance) is a
partnership among more than 50 academic, government, and
industrial organizations from across the United States to proto-
type an advanced computational infrastructure for the 21st
century. This model infrastructure, called the Grid, will link
together advanced supercomputers, visualization environ-
ments, and mass storage devices into a powerful, flexible,
problem-solving environment. This computing environment
will be accessed via high-speed networks from anywhere in
the country—eventually, the world.

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cranks out thousands of copies. Molecular biophysicist David
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Slight structural variations within a stretch of DNA cause it to bend in ways that determine whether a gene sits dormant or cranks out thousands of copies. Scientists are uncovering how molecular dynamics govern this bending.
Blue eyes or brown, tall or short, susceptible to cancer or diabetes—our characteristics are written in the code of a twisting double helix. Unraveling that code has occupied molecular biologists since 1953, when James Watson and Francis Crick first proposed the double helical structure of DNA. This long molecule resembles a twisting rope ladder, the legs of which are identical groups of sugars and phosphates. The rungs, however, are composed of four kinds of bases. In genes, regions that code for proteins, the bases exist in any of 64 different groupings of three. These groupings, called codons, form the words of the genetic language—a language that carries the instructions for building and maintaining a living organism.

Over the years scientists have learned that a source of nuance in the meaning of this genetic language lies in structural variations that arise from differences in the sequence not of codons but of the bases themselves. Differences in base sequences encourage certain stretches of the double helix to fold back upon itself as if making a U-turn, while other stretches are straight as rods. Some stretches twist tightly, like an overwound rubber band, whereas others curve gently. These twists and bends often influence whether a gene sits dormant or turns on to crank out thousands of copies of a protein.

Today genetic engineers can design DNA with any base sequence, but they still cannot predict how it will twist or bend. To improve predictability, molecular biophysicist David Beveridge and his colleagues at Wesleyan University in Middletown, CT, are modeling DNA on the SGI Origin2000 computer at NCSA. Former graduate student Matthew Young, now at Rockefeller University in New York, generated the first glimpse of the bending action of a well-studied stretch of DNA called phased A-tract. The results, reported in the Journal of Molecular Biology, may lead to a fundamental understanding of the molecular forces that bend DNA.

Phased A-tract DNA, shown in red, is characterized by stretches of five to six adenine bases, or A-tracts, that recur after every twist of the helix. The bases are depicted as red stick diagrams projecting from the sugar-phosphate backbone toward the interior of the double helix. The other bases are depicted in purple. A-tracts somehow induce bending. At the end of this molecular dynamics simulation done at NCSA by David Beveridge, a molecular biophysicist at Wesleyan University, the phased A-tract DNA can be seen bending about 16 degrees. Also, the space between the ladder legs of the double helix is narrower at the lower end of the DNA fragment and within the A-tract segment.
Twists and turns

Scientists have long known that phased A-tract DNA bends and wraps around a multiprotein complex like a spool of thread. The wrapped spools, or nucleosomes, help pack DNA tightly inside the nucleus of the cell. Phased A-tract DNA is characterized by several evenly spaced stretches of five to six As, or A-tracts. (A is the abbreviation for adenine, one of DNA's four bases; guanine, G, thymine, T, and cytosine, C, are the others.) Earlier lab experiments proved that the presence of phased A-tracts results in bending, but these results did not tell scientists why the bending occurred.

Beveridge's group showed that unlike earlier DNA modeling programs, which yield odd and unrealistic DNA configurations, the new program yields realistic shapes and motions because it takes into account the structure's interactions with the cellular environment; that is, with the water and salt molecules that bathe the double helix.

Even a small piece of DNA is composed of thousands of atoms, each of which resembles electrically charged balls connected by springs. Each atom exerts a tiny force field that tugs and shoves all the other atoms, as do the water and salt molecules within the cell. Together these millions of tugs and shoves determine the detailed structure of a piece of DNA at a given moment. The only way to accurately predict how each atom moves from one moment to the next—a prerequisite to understanding DNA bending, says Beveridge—is to simulate all of these molecular dynamics on a supercomputer.

To predict how the phased A-tract DNA fragment would bend, Beveridge fed AMBER the standard Watson-Crick model of phased A-tract DNA, a ramrod-straight double helix. The program then computed the detailed molecular dynamics to simulate what the molecule would look like a split second later. “This is a powerful approach because we’ve made no assumptions about bending,” Beveridge explains. “We’re basically moving from one structure to another under Newton’s laws of motion. The results are a series of snapshots, one femtosecond, or quadrillionth of a second, at a time.” After weeks of runtime on the Origin2000, Young and Beveridge obtained 5 million consecutive snap-
shots, showing phased A-tract DNA in more detail than ever before. They then arranged these snapshots as frames in an animation. That animation shows, over 5 nanoseconds (billionths of a second) of simulated time, how phased A-tract DNA bends.

**Bending and protein binding**

A lot can happen to DNA in 5 nanoseconds. The phased A-tract DNA—straight as a rod at the start of the simulation—bent, straightened, and bent again. To test the accuracy of the computer model, Young and Beveridge also simulated a piece of DNA that was not expected to bend. The results revealed a crucial difference in how the two pieces of DNA behave: While the control DNA moved around in solution and bent temporarily, on average it was straight. The phased A-tract DNA, however, bent about 30 degrees in a single direction. Because the angle of bending was consistent with the results of lab experiments, they could scrutinize the details of the simulation to identify which of the three models most accurately represents phased A-tract bending. “The results essentially support the junction theory; that is, an essentially straight A-tract that is bent at junctions,” says Beveridge. But bending also occurs in the stretches of DNA that flank the A-tract.

Now that they have a basic understanding of how this piece of DNA bends, Beveridge and his colleagues will run DNA simulations to see how varying conditions inside the cell, such as salt concentration, affect bending. A preliminary run with the A-tract DNA has found that a saltier solution—one with a higher concentration of sodium—increases A-tract bending. Other DNA sequences also may bend and twist differently at different salt concentrations. Cells may, in fact, influence gene expression by altering the salt concentration inside their nuclei, Beveridge says.

Discerning the specific atomic forces that underlie DNA bending is not enough to understand the biological role of bent DNA, he adds. Genes are turned on when specific gene-activating proteins bind to specific stretches of DNA, and those segments of DNA are often bent. The next step, which Beveridge and his colleagues have already begun, is to run molecular dynamics simulations gauging the atomic forces that help proteins bind to bent DNA. The results may help scientists comprehend the molecular dynamics of how genes are turned on and off. Then the nuances of the genetic language will be that much clearer.

This research was funded by the National Institutes of Health.

http://access.ncsa.uiuc.edu/CoverStories/DNAbending

The concentration of salt and water molecules within a cell nucleus can dramatically affect DNA structure. The series of snapshots on these two pages, which are from the first molecular dynamics simulation to account for the influence of salt and water, depicts five nanoseconds of phased A-tract DNA moving in this solution. The full five-nanosecond simulation took five weeks on NCSA's SGI Origin2000 supercomputer. The multicolored spheres are counterions—ions of opposite charge—attracted to DNA because of its net negative charge.
Cosmologists need road maps, too. When the Sloan Digital Sky Survey begins surveying millions of distant galaxies, new computer models will help cosmologists interpret what they see.

In turn the survey data will help cosmologists determine the accuracy of their models.
The story of how galaxies were created can be told simply: After the big bang, quantum mechanical gurgling stirred a little unevenness into a swelling ball of matter and energy. Because some regions were denser than their surroundings, their gravitational attraction pulled yet more matter down onto them. Eventually these huge clouds of gas collapsed into galaxies and the stars within.

But this explanation of galaxy formation is no more a satisfying than a definition of weather that simply states that the sun heats the Earth’s atmosphere while temperature differences in the air swirl into winds. Although true, it doesn’t answer the interesting questions. What causes El Niño? Why does San Francisco average 62 degrees in July? Will it rain this weekend? Similarly, the quantum-fluctuations-collapse-into-galaxies tale doesn’t explain why a typical galaxy contains hundreds of billions of stars (as opposed to millions or quadrillions) or why many galaxies clump into clusters and clusters line up into bubble-like structures that span hundreds of millions of light-years with vast voids in between.

For insight into these questions, astrophysicists Thomas Quinn and George Lake, both at Alliance partner University of Washington in Seattle, create universes with computer models to understand how the real one came into being. “We hope to understand how clusters of galaxies form and to define the correct parameters for a cosmological model,” Lake says.

Mapping the universe

These computer models will help astronomers interpret what they’ll be seeing over the next few years. Within a few months, after instruments have been calibrated, a five- to seven-year project called the Sloan Digital Sky Survey will begin exhaustively mapping one-quarter of the night sky. During the project’s lifespan, a telescope in New Mexico will capture images of 100 million stars and 100 million distant galaxies. A second instrument called a spectrograph will break down the light from each star and galaxy into individual colors, which give information about distance and velocity.

Comparing numerical results with the images and spectrographic data from Sloan will enable astronomers to zoom in on several cosmological numbers: the density of mass in the universe, the fraction of matter that is unseen or dark, and a hypothetical force called the cosmological constant.

This is “quack equals duck” reasoning. If researchers can tweak their models so that their simulations produce something that looks like the real universe as mapped by Sloan, then the parameters in the simulations are probably close approximations of those in the real universe. Having reliable models will, in turn, help answer fundamental questions about the universe such as whether it will expand into nothingness or collapse upon itself.
Creating a universe, even a virtual one, is neither quick nor easy. Indeed, a simulation of the universe with enough detail to provide meaningful comparison with the Sloan data is far beyond the capabilities of even the fastest and biggest supercomputers. "There are some odd puzzles in how clusters look in the real universe that have not been replicated in any simulation," Lake says.

Fortunately, researchers do not need to simulate the whole universe in exquisite detail, just a small chunk of it.

Quinn and Lake—as well as graduate students Jeff Gardner and Joachim Stadel—take an approach similar to how hurricane forecasters produce their models. Since it's impossible to produce a detailed storm model for the entire globe, hurricane simulations focus on the areas where the hurricanes form and blow. However, hurricane researchers increase accuracy by also including coarser, less detailed models of global climate patterns, such as El Niño, that influence the number and strength of hurricanes.

Similarly, the University of Washington researchers first simulate the universe from primordial lumpiness to the present, about 15 billion years later. In this first simulation, the universe is represented by 47 million particles moving within a 3D grid according to the laws of gravity. Each side of the grid represents about 3 million light-years although, as with the real universe, the size of the universe increases—that is, the grid gets bigger—with the passage of time.

Although 47 million particles may seem like a lot, they provide only a coarse representation of the universe. "Each particle is about size of a galaxy," Quinn says. "We can't follow the details of galaxy formation. The simulation is detailed enough, however, to pick out large clusters and voids. Even at this low level of detail, one run of this coarse universe simulation consumes more than 15,000 CPU-hours on the SGI Origin2000 supercomputer at NCSA.

A second simulation focuses on one of the clusters seen in the first simulation, with the rest of the universe fuzzed out. "Where the cluster forms I throw down many more (smaller) particles," Quinn says. That allows researchers to see the finer structures of a cluster that were blurred out in the bigger view.

Although the second simulation uses fewer particles—5 million—and focuses on a smaller region of space, it is just as computationally challenging. The detailed structure in the clusters form much more quickly, which means the simulation has much smaller timesteps. Smaller steps mean that more steps cover the same period of time and the simulation takes longer to run.

"Now we're talking a few hundred particles making a galaxy," Quinn says. "A cluster in our simulation looks like a cluster in the sky. We'll have simulations in which we'll be able to see galaxy distribution."

How realistic are their simulations? A poster-size image of the sky hanging on the wall of Lake's office looks as if it had been shot through a telescope. "We have people come in and they say, 'Is it a picture of the sky?'" Lake says. "Nobody has ever done simulations of galaxy clusters that have caused people to ask that before."

In one sense, all cosmological models are quite simple: there's basically one force that drives the formation of everything from stars to galaxies to clusters of galaxies. That force is gravity, the same garden-variety gravity that pulls apples down from trees.
What astronomers don't precisely know is how much mass is in the universe, the amount and type of dark matter—the unseen 90 percent of the universe whose gravity keeps galaxies from flying apart—and the strength of the cosmological constant where empty space literally pushes against itself. In each simulation run, the researchers vary the mass, dark matter, and the cosmological constant so that each variation produces different results. For each run the researchers also calculate several statistical measures, such as the number of different-sized clusters and how close the clusters are to each other. They will be able to calculate these measures from the Sloan data as well. Presumably the simulation run that most closely matches the Sloan numbers is the one that contains the most nearly correct values for the universe's mass, dark matter, and cosmological constant.

**Clumping together into planets**

Having created a behemoth computer program to track the gravitational attraction between millions of chunks, Quinn, Stadel, and postdoc Derek Richardson wondered if the same code could applied to other astronomy puzzles. They found such a puzzle: the creation of the planets in our solar system.

The researchers started with the young solar system. The big planets—Jupiter, Saturn, Uranus, and Neptune—have already formed, but the inner solar system is still a disk of asteroids. Quinn wants to know if the computer simulations will produce Mercury, Venus, and Earth. “The goal is to follow them for a million years so that we can see the development of the Earth,” he says.

The equations are the same as in the cosmological simulations, but now each particle represents an asteroid a few tens of miles wide rather than a chunk of galaxy. An important difference in the simulations is the behavior of particles when their paths cross. When two particles cross in the galaxy simulation “you want them to pass through each other like a collection of real stars would,” Quinn says. That's a realistic assumption because each particle represents a clump of stars with empty space in between. Individual stars almost never collide with each other.

When each particle represents an asteroid, however, the story is different. “They're chunks of rock and they hit each other,” Quinn says. The two rocks can pulverize each other, bounce off each other, or stick together. Quinn's current computer runs assume that any collision between asteroids causes them to stick together. That's unrealistic, but it doesn't diminish the value of the simulations in providing an overview of the evolution of the early solar system. They show how, over the span of a few thousand years, asteroids orbiting in paths that later belong to Venus and Earth clump together into chunks hundreds of miles wide. These chunks will later coalesce into the planets.

The simulation also shows why the asteroid belt between Mars and Jupiter never coalesced into a planet. As Jupiter orbits the Sun, its enormous gravity nudges those asteroids into elliptical orbits, which cross paths much less frequently. Fewer collisions means fewer chances for them to form larger asteroids and fewer chances to form a planet.

The researchers are currently refining their algorithms to speed up their planetary calculations. When they're done, they'll have a virtual solar system to accompany their virtual universe. This research is funded by NASA and the National Science Foundation.

This research is funded by NASA and the National Science Foundation.

http://access.ncsa.uiuc.edu/CoverStories/GalaxyFormation

The University of Washington team.
Compounds ranging from rust to antifreeze are end products of molecular collisions that transfer oxygen atoms from one molecule to another. The efficiency of this all-important transfer process depends on the molecules’ orientations when they collide.

If theoretical chemist Robert Bach needs an example of his favorite research subject, he needn’t look any farther than the brown splotches on cars parked outside his office on the University of Delaware campus. These ubiquitous scars of rust are examples of oxygen-atom transfer, a process as fundamental to the chemical industry as beakers and test tubes. Using NCSA’s SGI Origin2000 supercomputer, Bach simulates the exchange of atoms between oxidizing agents and their targets, providing the chemical insights needed by his more test-tube-based colleagues to engineer new and more efficient industrial processes.

Robert Bach
University of Delaware
Through a complicated chain of events, moisture and the transfer of oxygen atoms from air to iron creates rust. The reactions that Bach and his team of postdoctoral fellows strive to understand are somewhat simpler. Much of their recent work focuses on peroxides, molecules whose lowest common denominator is a backbone of two oxygen atoms tied by a single chemical bond. When these oxidizing molecules encounter their target, called the substrate, they form a complex called a transition structure. In a chemical handshake lasting only one-trillionth of a second, the bond between the two oxygen atoms in the oxidizer is stretched to the breaking point and one of the oxygen atoms bonds to the substrate.

Understanding what Bach appreciatively refers to as the “sequence of miracles” that drives oxygen-atom transfer is much more than an academic pursuit. “There are myriad processes that transfer oxygen, and few of them are well understood mechanistically,” Bach says. For instance, the chemical industry uses the oxygen-atom transfer process to manufacture feedstocks for polymer plastics in the billions of pounds per year, not to mention antifreeze, airplane deicers, and the slippery surfactant molecules in soaps. “If you understand the mechanism of the process then, hopefully, you can use this knowledge to design new and more efficient oxidizing agents,” he says.

During 30 years of research, Bach has had his feet planted in both the academic and industrial worlds. From 1958 to 1962, he engineered solid rocket fuels for Thiokol Chemical Corporation. In 1962 he moved to the DuPont Experimental Station in Delaware, where he synthesized polymers and came up with a product that required 14 pounds of DuPont product per unit—a Lucite bowling ball—for which he received the first of 13 patents. But academia beckoned, and in 1967 he completed his PhD and embarked on a career in university research.

**Oxygen in transition**

In Bach’s calculations, the formation of the transition structure is the key event. Mathematical equations simulate the behavior and distribution of electrons and atoms when oxidizer and substrate collide. In the moment it takes the transition structure to form, the oxygen-oxygen bond is stretched and broken, and one of the atoms is jammed close enough to the substrate for a new bond to form. But as in all matters chemical, there’s no free lunch. A certain amount of energy—an activation barrier—must be surmounted for the transfer to occur. Bach explains it in mountaineering terms. “You go from A to B by climbing a hill,” he says. “The height of the hill is the activation barrier.”

The energy to climb the hill comes from the force of the collision between oxidizer and substrate. In any mixture, a certain percentage of the collisions will be forceful enough to transfer oxygen. But as any linebacker knows, the outcome of a tackle depends on more than just the strength of the hit.

The player’s posture is also critical—whether he lunges head-, shoulder-, or chest-first. That’s why Bach’s calculations account for the effects of geometry on the height of the activation barrier. Oxidizer and substrate can meet in various orientations, depending on the types, sizes, and numbers of chemical groups poking out from a molecule. The groups jostle, attract, and repel in ways that can be predicted mathematically, given sufficient computer horsepower.

In collaboration with organic chemist R. Stanley Brown, head of the Department of Chemistry at Queen’s University in Ontario, Bach’s team has probed the effect of geometry on oxygen transfer to ethylene and other substrates containing two carbon atoms joined by a double chemical bond. The transfer of oxygen to ethylene produces epoxides, three-membered rings consisting of two carbons and one oxygen. The process, called epoxidation, is of major interest to organic chemists because it is used to make many pharmaceuticals. Most of Bach’s current work focuses on epoxidation.
This transition structure exists for one-trillionth of a second. The distance separating $0_1$ from its neighbor has now been stretched to 1.82 angstroms.

**Efficient epoxidation**

The molecule that transfers oxygen to the ethylene can land face-on, like cymbals crashing, or it can come in perpendicular orientation, slicing into the middle of the ethylene molecule like a knife cutting into a slice of bread. The researchers wanted to determine which of the two encounters presents the lower energy barrier. Knowing that, chemists could tweak the geometry of the epoxidizer—snip off a group here, stitch in a group there—and perhaps design the fastest and most efficient epoxidation process.

In the industrial world, higher efficiency translates directly into cost savings. “The reaction that is most likely to happen is the one that has the lowest hill to climb,” Bach explains. “It’s like standing in a valley and you can go in several different directions; you’d prefer to climb over the lowest hill.” The results of the simulations were decisive. “There’s been some controversy over which of the two transition states is most favored,” Brown says. “Bach’s calculations are unambiguous that the perpendicular way is the best way, and it appears that our experimental results are showing the same thing.”

With the $0_1$ transfer complete, the peroxoformic acid has become formic acid and 1,3-butadiene has been transformed into an epoxide, with a triangular ring composed of $C_1 + C_2 + O_1$. 

Computational chemistry has come a long way since the late 1970s, when Bach did his first theoretical work on oxygen-atom transfer. At that time, computers were powerful enough to take on only stripped-down, simplified molecules. When sufficient computing power became available in the 1980s, Bach was among the first researchers to do high-level calculations on larger molecules and more complex reactions of the sort that chemists typically encounter in the real world. However, theory was still to a large degree caught in the shadows of experiment. “For the first 20 years, theorists tried to reproduce experiments to lend credibility to the theoretical methods,” Bach recalls. But now the gap between theory and experiment has begun to close, so much so that in some cases it’s “cheaper, faster, and easier” to run experiments on computers instead of test tubes, Bach says. “I think now that many theoreticians are going out and doing new chemistry.”

This research was funded by the National Science Foundation.

http://access.ncsa.uiuc.edu/CoverStories/Oxygen
Nearly half of newly hatched salmon die as they run to the ocean. Understanding how water flows around dams may improve their odds.

**Spring** is precarious for young salmon in the Pacific Northwest. From their nurseries in the mountain tributaries of the Columbia and Snake rivers, they are driven by instinct and warm spring temperatures to dash to the ocean. Many are no bigger than a baby’s thumb, yet they cover 500 to 1,000 miles over two months. Nearly half die along the way from exhaustion, disease, pollution, and predation, aggravated by the aftereffects of passing through dams and plunging over spillways.

These fatalities are disheartening to Larry Weber, a hydraulic engineer from, of all places, central Iowa. Since 1988 he and a team of researchers and model builders at the Iowa Institute of Hydraulic Research (IIHR) at the University of Iowa, an Alliance partner, have been working with a cadre of biologists and engineers in the Pacific Northwest to reengineer hydroelectric dams to be more salmon friendly.

Thomas Quinn, School of Fisheries, University of Washington
Survival rates for young salmon have climbed steadily—the rate is higher than it has been in three decades. Data from the U.S. Commerce Department’s National Marine Fisheries Service (NMFS), which is the lead organization for salmon management, show that in the early 1960s, 50 to 60 percent of salmon safely navigated the four dams crossed en route to the Pacific. The construction of more dams in the 1970s—bringing to eight the number of dams migrating salmon crossed—saw the overall salmon survival rate plummet to a dismal 25 to 30 percent. Today rates are back up to 50 to 60 percent because of dam reengineering efforts.

But juvenile survival rates that were adequate for maintaining a healthy adult salmon population in the 1960s are insufficient today. Consequently federal agencies are pushing for higher juvenile survival rates. NMFS would like per dam survival rates, which now average 85 to 95 percent, to reach 95 percent or better.

In what amounts to a race to save the salmon, the last few yards are the hardest. “We’ve already found the obvious fixes,” says John Ferguson, a biologist with NMFS. “Now we’re looking for the tough ones. And that’s going to require even more focus on the details.”

This is where Weber comes in. He and an IIHR team are helping engineers eke out incremental improvements by using their software called River3D, which models river dynamics—where the currents are fastest and how different columns of water mix as they plunge over the dam.

Last year Weber turned to NCSA for help in parallelizing his code to run simultaneously on several processors of the SGI Origin2000 supercomputer. With the code now ten-times faster, his team is producing some of the most detailed models available. Those details may be a way of making dams safer for salmon.

## Troubled waters

The trouble with dams is that they were designed to generate power not protect salmon. Near a dam, water velocity accelerates, yanking fish down 50 to 100 feet and into the housings of 20-foot-high turbines, which are similar to high-powered house fans. The fish are swept past stainless steel blades and out a draft tube. If the turbines are operating optimally, 99 percent of the fish pass through without a knick. The greater danger is the rapid change in pressure. Salmon emerge disoriented, suffering the equivalent of the bends, making them easy prey for gulls and northern pike patrolling the bases of the dams.

Most dams have intake screens in front of the turbine housings. The screens are intended to redirect fish to bypass pipes that dump them into the river downstream. But performance is fickle: if flow is too high, fish are pinned against the screens; if too low, fish swim under the screens and into the turbines.

Another solution is to send the salmon over the spillways—waterslide-like structures originally designed as safety valves when reservoirs approach flood stage. The drawback to spillways is their location. “What the designers forgot to consider is that salmon don’t instinctively know there are spillways 10 feet to their right and 30 feet down,” says Weber. “They have an underlying desire to get to the ocean… And the strongest currents are often those that lead straight to the turbines.”

A more pernicious hazard of spillways is gas bubble disease. That’s killing salmon at Wanapum Dam on the Columbia River in Washington state, where Weber’s IIHR team is now working. The vertical drop from spillways is only 50 feet. However, the fish plunge into a supersaturated pool that can be deadly, says Weber. The water at the base of the spillway is frothy from high levels of nitrogen and other dissolved gases entrained, or incorporated, as the water tumbles over the dam. “The fish absorb these entrained gases through their gills, and when they rise to the surface a few feet downstream, the dissolved gases want to come out of
solution and form a bubble again. With bubbles forming in their gills, fins, and bloodstream, they suffer severe cardiac problems," explains Weber.

New regulations by NMFS have unintentionally aggravated the problem. Dam operators are now required to pass 70 percent of salmon through the spillways during the spring fish run (April 15 to June 15). "Since 1 percent of the fish usually follow 1 percent of the flow, you have to pass 70 percent of your water through the spillway," says Weber. "That leads to greater incidences of supersaturated water and decreases the amount of water available for power generation."

**Water over the dam**

Weber's River3D modeling software is helping reduce dam-related hazards to fish by offering engineers and biologists a sense of the river's dynamics that is close to a salmon's perspective.

"No one else is doing quite the same thing as IIIHR," says Don Weitkamp, a fisheries biologist at the consulting firm Parametrix in Kirkland, WA, who has studied salmon for 30 years. "They deal with upstream and downstream flows. Theirs is 3D versus 2D, so you can follow the movement of fish. It covers thousands of meters instead of hundreds."

River3D models water flow through the dam—from its surface to the bed (that's sometimes 100 feet of water) and for four miles upstream of the dam from the blades of the turbines. (Flow dynamics within the turbine are still too complicated to model.) The model has been calibrated against a 1-to-50 scale model constructed in a pole barn 10 miles from the Iowa campus. IIIHR is one of only four hydraulic labs in the country with a physical scale model, which is one reason their models are so accurate.

Such detail and accuracy help engineers find the most effective locations for outlets so that a greater percentage of salmon find the spillways. The detail and accuracy also lead to better designs for intake screens. River3D models help reduce supersaturation by revealing how various water sources contribute to problems. For instance, Weber's team have discovered that discharges from the powerhouse, thought to dilute gas concentrations, are actually contributing to the problem at some dams.

River3D is also fast. Because all river construction in the Columbia Basin halts during the spring and summer runs, engineering teams have only six to nine months in which to evaluate data, design, and test new designs, then implement the most promising.

This summer the team is testing a fish behavioral component they've added to the software. They have integrated a particle tracer that replicates the behavior of fish in response to flow conditions and other stimuli. Programmers in NCSA's computational fluid dynamics group are further modifying the code to be massively parallel so it will work in realtime on the SGI Origin2000 system.

"We used to wait six to ten days per calculation," says Weber. "Now we get results back overnight. The hope is that we will get results back in an hour or less. Biologists will be able to go to a website and get hourly records of flow conditions against which they can compare the observed fish behavior."

Knowing which flow conditions signal salmon to dart left or right won't help more juveniles navigate the dams more safely this year. But maybe next year, at least for those that survive long enough to spawn. ▲

This research is funded by the U.S. Army Corps of Engineers and Public Utility District No. 2 of Grant County, Washington.

http://access.ncsa.uiuc.edu/CoverStories/SavingSalmon

Larry Weber, an environmental engineer at the Iowa Institute of Hydraulic Research at the University of Iowa, poses on a scale model of 5,000 feet of the Columbia River in the state of Washington. This physical model is used for calibrating the mathematical models used in reengineering dams to be more salmon friendly.
An Arterial View of Atherosclerosis

The fatty plaque that leads to strokes accumulates gradually in arteries. A new imaging method may enable physicians to gauge the extent of the buildup—without resorting to surgery—and to prescribe more targeted drug therapies.
Strokes debilitate more than 100,000 people in the United States each year and remain the third leading cause of death. Doctors know the usual cause is atherosclerosis—the gradual buildup of fatty plaque in the walls of arteries. The flow of oxygen-rich blood to the brain constricts until the vessels become clogged or burst. Unfortunately, knowing the usual symptoms doesn't help doctors offer their patients any better than stock advice: Exercise. Reduce your fat intake. Take medicines to reduce clotting and to lower cholesterol.

Robert Lodder, a pharmaceutical chemist at Alliance partner University of Kentucky, is trying to personalize advice for potential stroke victims. He is developing a new analysis tool that may make individualized drug treatment for atherosclerosis possible.

The only current way to study atherosclerotic plaque in detail is to examine samples removed during arterial surgery. However, oxidation during removal damages plaque samples both physically and chemically. Working with degraded samples outside of the artery forces researchers to draw unproven inferences about the growth and composition of plaque—making it all but impossible to screen new drug therapies.
Ladder is developing a noninvasive means of gauging the severity of atherosclerosis. Relying on the HP-Convex Exemplar SPP-2200 supercomputer at Kentucky, which is available to the Alliance through its Partners for Advanced Computational Services program, Ladder is combining a new imaging algorithm with near-infrared spectrometry so that he can analyze—in vivo—the composition and ultimate progression of arterial plaque.

**Strokes, plaque, and oxidation**

More often than not, the blockages associated with strokes are caused by atherosclerotic plaque that has accumulated in the carotid artery just below the skin of the neck. The rate of plaque accumulation varies widely from one person to the next depending upon, researchers now believe, the level of oxidized low-density lipoprotein (LDL—the so-called bad cholesterol) in a person’s blood.

As LDL travels through the bloodstream, it is exposed to oxygen in the blood, which changes LDL's chemical structure so that it can enter the cells of blood vessel walls directly instead of continuing on as part of bloodstream. Once inside the blood vessel wall, LDL works like a magnet, attracting cholesterol-carrying cells to form an increasingly large lesion of plaque just below the surface.

Although blood levels of oxidized LDL correlate to atherosclerosis, the contents of the lesion are more crucial than the contents of the blood in determining if a plaque lesion will lead to a stroke, explains Ladder. Whether or not a plaque lesion will cause a stroke is a complex function of the lesion's structure, size, chemical composition, and the stress exerted on it.

Ladder believes that near-infrared technology is a good candidate for detecting oxidized LDL because it uses light absorbency values to determine the specific chemical compositions of living organisms. With the carotid artery's close proximity to the skin, it should be possible to use a near-infrared camera to screen the artery for the plaque lesions that are likely to cause strokes.

**Mapping plaque**

Ladder began testing his theory in 1991 by gathering atherosclerotic plaque and brain data from rats, rabbits, and gerbils. He inserted two sets of microscopic nonimaging fiber optic cables into an animal's arteries, one set to transmit light from a tunable laser and the other to receive the resulting scattered light. He coupled the receiving fibers to two other devices, which calculated that the probability tissue samples were normal based on their near-infrared spectra. Using a computing algorithm he developed, Ladder converted the probabilities to images, then profiled the chemical composition of the animal's plaque lesions.

This pioneering work won an IBM supercomputing competition and the attention of a neurosurgeon who encouraged Ladder to refine his methods to study atherosclerotic development in humans.

Since 1993 Ladder has improved his algorithm to take advantage of more powerful parallel processors. He has also begun human research, analyzing plaque tissue taken from more than 200 volunteers undergoing plaque removal surgery. Standing just beyond the sterile field of the operating room, Ladder and his team use a near-infrared video camera and digitizer to collect 3,072 images and a multitude of visible light frames during a single surgery. These in vivo data are later compared against in vitro scans of the patient's excised plaque. Using a protein separation...
analysis method known as gel electrophoresis, Lodder's group study the pathology of excised plaques, correlating near-infrared plaque data to several specific proteins and to patient medical histories.

**Results can't come too soon**

Although Lodder's group have established the usefulness of near-infrared tools and techniques in plaque research, they have also exposed its shortcomings, among them an inability to observe atherosclerotic plaque development at the cellular level and the fact that the body's sodium ion concentrations interfere with near-infrared scanning results.

Such limitations have forced the group to develop their own equipment, which include a near-infrared scanning microscope and a hybrid spectrometer that relies on magnetohydrodynamic and acoustic resonance as well as near-infrared imaging. The first commercial version of this hybrid spectrometer will be on the tip of a coronary catheter probe and will be used to analyze plaque and blood clots. But before they can apply such a probe analysis method to humans, Lodder's group must do additional animal studies.

By medical standards, Lodder's research is progressing rapidly; however, their results can't come soon enough. At least five new drugs are now available for treating atherosclerosis, including Citicoline, which reduces free fatty acids, and Tirilizad, which scavenges for free radicals. But without more knowledge of how atherosclerosis occurs in living humans, prescribing specific drugs to treat specific stages of plaque development remains a matter of educated guesses and relying on the old standbys: Get more exercise....

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### The BEST algorithm

Lodder calls his near-infrared imaging algorithm BEST, for Bootstrap Error-adjusted Single-sample Technique. Lodder compares BEST to a rubber yardstick that is nailed at its center. Each end is able to stretch independently of the other, allowing it to form odd shapes. Because it automatically detects samples and situations unlike any encountered in the original calibration, BEST is more accurate than typical regression approaches for near-infrared imaging.

In addition to being more accurate, BEST is also faster. By using $O(n)$ instead of $O(n^2)$, BEST avoids matrix factorization, which typically breaks down in a calculation as the number of samples approaches the number of wavelengths.

Assimilation models developed using BEST can be compressed for lab PCs. For his large calculations, Lodder uses the HP-Convex Exemplar SPP-2200. The University of Kentucky recently established an Exemplar repository, which serves as the Alliance's primary point of contact for information about this computing system. The repository includes training materials, software libraries, applications, benchmarks, and information exchanges.
COMPUTATIONAL POWER BALANCING

Help for the Overloaded Processor

by

Holly Korab

One overloaded processor can bottleneck hundreds of processors. A new computing paradigm developed at NCSA enables the overworked processor to call for help.

Davood Tafti
NCSA

Weicheng Huang
NCSA
There are days when computing on parallel architecture machines is like managing an auto assembly line that is short on motors. Suddenly 127 processors grind to a halt as the computer waits for the 128th to finish its calculations. Instead of churning out answers, the processors are idle as they wait for an overloaded processor to catch up with the rest.

This inequity in the distribution of a problem's calculations is what programmers call a load imbalance. Until recently programmers had two ways of handling the problem. Either they could kick back and wait, consuming valuable—and scarce—computing time. Or, as most do, they could suspend their calculation and redistribute the load—a tedious undertaking even with help from load-balancing algorithms.

Two research scientists at NCSA—the leading-edge site for the Alliance—believe they now have a better alternative. Programmers can scrap load balancing altogether in favor of what the researchers are calling computational power balancing. Developed by Danesh Tafti and Weicheng Huang, this new paradigm for parallel computing dynamically adjusts the number of processors working on a particular calculation. If a processor is nearing overload, their system senses it and recruits an unused processor to share the calculations. Instead of one processor working on the calculations, suddenly there are two.

There's no need to redistribute the load, says Tafti: "We are suggesting that researchers leave the load as it is and instead balance the computational power. With our paradigm, processors can ask for help."

Tafti's idea for enabling processors to call for help originated in the fall of 1996 when NCSA received its first SGI Origin series supercomputer. Tafti and Huang had been writing parallel computing codes for distributed-memory parallel computers. These machines have dozens to hundreds of processors, with memory parceled out to each one. Distributed-memory computers can be extremely fast if programmed correctly. But writing code for these systems is difficult. Problems must be divided into chunks that can be computed simultaneously, then datasets must be assigned to the processor most likely to need them (or else the process slows as data are exchanged among processors).

Origin supercomputers are distributed shared-memory machines. Memory is still physically distributed among the processors; however, every processor can read and write data to every other processor, giving the illusion of memory being in one location. NCSA's largest Origin has 256 processors sharing memory.

This architecture is simpler for programmers because they have only a single memory to consider when designing their codes versus dozens to hundreds of distributed-memory machines. On shared-memory systems, codes will clunk through a calculation regardless of where data are assigned. To achieve high performance, though, programmers still need to choose carefully among memory blocks when assigning data because the data's locations affect the speed at which data are retrieved.

The impact of the Origin on Tafti and Huang's programming style wasn't immediate. Tafti continued designing his parallel programming codes using a collection of functions called Message Passing Interface (MPI). Designed for distributed-memory machines, MPI tells processors where data are located and shuttles them back and forth. Tafti stuck with MPI because it works on any parallel architecture. Codes that include MPI directives are also portable—that is, able to run on a variety of computing architectures. Also, MPI is efficient.

"The exercise you go through in writing an MPI program forces you to have memory locality," says Tafti. "A given processor will be working on what is in its own memory 99 percent of the time." Gradually, though, Tafti and Huang incorporated directives for the Origin's shared memory so that they could take advantage of both programming paradigms.

"I ran into instances within the same program where I started using shared memory and kind of shut off MPI," says Tafti.

It didn't take Tafti and Huang long to begin figuring out how these two capabilities could be used together. By embedding shared-memory directives, or instructions, under MPI processes, they could dynamically spin calculations onto new processors. They'd start their code running MPI. But when the load on a processor doubled, their code called upon the shared-memory directives to spawn a new thread—or process—on another processor. In this way an overloaded processor could get help as needed, eliminating potential bottlenecks.
In these four images, the grid on which the oscillations are being modeled is progressively refined in the areas where activity is greatest. This approach, called adaptive mesh refinement, benefits from computational power balancing, which dynamically adds processors to whatever portion of the model is experiencing the greatest number of calculations.

**Speed and flexibility**

The greatest beneficiaries of their new paradigm, say Tafti and Huang, are the many researchers experimenting with adaptive mesh refinement (AMR). AMR creates computational grids, or meshes, that vary resolution in response to the needs of a computation as a way of balancing the need for greater detail against the limits of computing power.

"This technique is used in almost every computational discipline," says Huang. "But historically, as the load increased on a given processor, the researchers had to remesh everything. They would take the mesh, divide it into smaller units, and rebalance the load. Our paradigm does this on the fly."

The early tests of their paradigm—which were performed with the help of Gang Wang, a former NCSA researcher who is now a research engineer at Pittsburgh-based Ansys—used static load imbalances. They took a mathematical program called a linear solver that was perfectly balanced for four processors and ran it on three, one of which was given twice the computational load of the other processors. This overloaded processor was coaxed into spawning an additional thread.

Recent tests accomplished the same under dynamic conditions; that is, the load changed over the course of the calculation. Huang and Tafti subjected a metal bar to an oscillating force and modeled its behavior. (The bar's oscillations either broke up or stabilized, depending on the size of the bar and the frequency of the oscillations.) Their code started with a simple grid, then subdivided it wherever greater detail provided by a more refined grid was needed. The code also called on extra processors when necessary. Most importantly, running their problem dynamically took no longer than running it on a set number of processors.

"We knew it'd work," says Tafti. "The real question was whether the flexibility our system offered was worth the overhead. There's a certain cost involved in monitoring the progress of the calculation and calling the additional processors. We had to find out if the costs were worthwhile. As it turned out, the 'effective CPU' was nearly the same as with the set processors."

To determine if computational power balancing is efficient and hence practical, the researchers compared the speed at which calculations were performed on various numbers of set processors versus processors that were called up on demand. The results show that the CPU time under both scenarios is nearly identical, indicating minimal computational costs involved in monitoring calculations and calling additional processors.

**Portability and policy**

Recently Tafti and Huang increased the system's portability. Originally their computational power-balancing system was limited to Origin machines. That changed with the OpenMP standard for shared memory, which became available last year.

Tafti and Huang have replaced the Origin-specific shared-memory directives with those for OpenMP.

A trickier issue to resolve will be operating policy. Most researchers compute on tightly scheduled supercomputers. Spare processors may not be available when applications require them. Institutions that allocate computing cycles will need to develop policies that accommodate fluctuating demands for processors within a single calculation. Tafti and Huang will defer that issue to others.

Policy issues aside, the potential benefits to researchers are enormous, says Tafti. "The bottom line is that computational power balancing provides more freedom and flexibility in computations. Many times application scientists have to juggle the physical reality of what they are trying to simulate and the computational reality of trying to get better performance with larger calculations. Our system helps scientists better map physical reality to computational requirements."

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http://access.ncsa.uiuc.edu/CoverStories/LoadBalancing
Buckyball

Carbon 60, buckminsterfullerene, buckyball—they're all names for the provocative geodesic structure that launched a whole new branch of chemistry. Since the buckyball's discovery in 1985, scientists have been investigating the potential of this remarkably stable, soccerball-like molecule for everything from nanoscale recording devices to chemical catalysts. This volume rendering and geometric isosurface is based on research by J. Bernholc, Q.M. Zhang, J.Y. Yi, and C. Brabec at North Carolina State University. The visualization, by NCSA's David Bock, uses a rainbow of colors to capture the buckyball's electron density. White represents the lowest density; dark blue the highest. Bernholc is a member of the Alliance's Executive Committee and Application Technologies Nanomaterials Team.