to one kind of pathogen, Anderson speculates that both humans and flies may have specific protein pathways for different invaders, although this isn't proven yet. Scientists hope that with a better understanding of how specific pathogens trigger the immune system, they might be able to selectively shut down certain proteins to treat inflammatory diseases.

Although researchers are still teasing out all the action of the various Toll proteins, they do know that Toll provides a link between the adaptive and innate immune systems. Naïve T cells—members of the adaptive immune system—that have not been exposed to antigens need two signals to become active. The first comes from the binding of an unfamiliar protein, or antigen, and the second comes from a protein called B7.1 and its relatives. And Janeway's work now links B7.1 to the innate immune system via the Toll pathway.

Janeway reported last summer that the active form of TLR4 increases production of B7.1. Immunologist Douglas Fearon of the Wellcome Trust in Cambridge, U.K., says that B7.1 may be a sort of red alert, released if the innate immune system, through its Toll-like receptors, has recognized an infectious invader.

While researchers pursue Toll proteins in hopes of medical applications, they are also thinking about what these new findings are telling us about evolution. Because the Toll immune proteins are similar across plants, flies, and mammals, most scientists think that the defense system arose before the divergence of plants and animals—perhaps at the dawn of multicellular life. Only later were the immune proteins co-opted by developmental systems. "You can't do anything as luxurious as making all sorts of fancy body parts without an immune response," says molecular biologist Michael Levine of the University of California, Berkeley.

It may be that only flies have used Toll in developmental roles, however—to date, there is very little evidence that Toll relatives are important for mammal or plant development. "In all of our experiments doing knockouts in mice, we've never seen a developmental phenotype," says David Baltimore of the California Institute of Technology in Pasadena, who helped characterize the NF-κB pathway.

Meanwhile, even as researchers continue to probe the functions of the Toll proteins, more of them continue to be uncovered. "We're not sure where this family ends," says molecular biologist Michael Karin of the University of California, San Francisco. "It's a very exciting field."

–GRETCHEN VOGEL

NATIONAL SCIENCE FOUNDATION

The Biocomplex World of Rita Colwell

In a discussion with *Science*, NSF's new director, microbiologist Rita Colwell, outlines her views on topics ranging from environmental research to computer science and educating students as well as the public

Biocomplexity. The word evokes images of the incredibly rich variety of the living planet, and it hints at the formidable scientific challenge of trying to understand such an intricate system. That twin message appeals to Rita Colwell, the new director of the National Science Foundation (NSF), who plans to make the study of biocomplexity a major new thrust for the $3.5 billion agency.

Last month Colwell, a microbiologist from the University of Maryland, was sworn in as the first woman to head the 48-year-old foundation, the government's flagship agency for the support of nonbiomedical academic research. She's no stranger to NSF, having served on its presidentially appointed oversight board under Reagan appointee Erich Bloch and as a longtime reviewer and grantee (*Science*, 13 March, p. 1622). "It's sort of like becoming president of your alma mater," she says. Her "campus" consists of a 5-year-old, 12-story building in Arlington, Virginia, that houses NSF's administrative staff of 1250, and the job comes with a 6-year term, sub-Cabinet rank, and an annual salary of $136,700. Earlier this month, Colwell, 63, met for 90 minutes with a group of reporters and editors at *Science* to discuss her plans for the agency.

Colwell takes the reins from physicist Neal Lane, now the president's science adviser and head of the Office of Science and Technology Policy (OSTP). Lane managed to win steady annual budget increases for both core programs and new facilities during nearly 5 years as director by emphasizing the agency's role as the government's major funder of basic academic research. With a deft wordsmith's touch, Lane successfully deflected congressional pressure to fund more applied research by redefining NSF's mission as "conducting basic research for strategic purposes" (*Science*, 20 December 1996, p. 2000). Similarly, by defining biocomplexity as "the interaction of biological, chemical, social, and economic systems," Colwell hopes to avoid the "baggage" attached to such related terms as biodiversity, which some conservative politicians see as a refuge for tree-hugging environmentalists, and sustainability, which some industrial leaders say smacks of bureaucratic meddling in the free market. She sees biocomplexity as a unifying theme for several NSF initiatives, some ongoing and others still in the planning stage (see the related News of the Week story, p. 1935).

Lane also championed the importance of undergraduate teaching and the need to explain to the public how long-term investment in research translates into a stronger economy, two issues that Colwell says are high on her agenda, too. "Seventy-five percent of the public is in favor of basic research," she says, citing a recent study. But "they don't understand it." And compared to what many companies spend on R&D to improve their products, she says the federal investment in science "is marginal."

Colwell's interest in science education also extends to the nation's elementary and secondary schools. And she believes that scientists must play a major role. "No group bears more responsibility for improving K-12 math and science education than the scientific community itself," she told a recent gathering of science writers. Using a variation on Clinton's 1992 campaign slogan to play on the current preoccupation with the millennium computer bug, Colwell punned, "It's not Y2K, stupid, it's K-12."

Information technology is another priority area, says Colwell, and her vision of the field extends far beyond computer science. "IT pervades the country's business," she says. "For instance, I think that the behavioral and social sciences are one

PHOTOS BY: SAM KITTNER

area that will benefit tremendously from this [increased speed and capacity]. … You don't just put machines together. You need to utilize them and make possible the sort of innovative thinking that takes you to the next stage."

In her meeting with *Science*, Colwell spoke passionately on topics ranging from an overemphasis on the Ph.D. as the gateway to a scientific career, through the need to help research-poor states, to greater collaboration with the National Institutes of Health (NIH), whose budget is four times larger than NSF's. Although she has said that the president's current predicament is not likely to affect support for R&D, she served notice on her political bosses that she won't sit by idly if a lame-duck Administration starts to ignore science. "I haven't any quarrel with the overall direction [of current R&D initiatives]," she noted. "There are ways that I want to shape it, however, and things I'd like to do to move more rapidly in certain directions."

What follows is an edited transcript of her remarks.

–JEFFREY MERVIS

On a boost for environmental research:

I think that the timing is right to build on the LEE [Life and Earth Environments] initiative with what I term biocomplexity. It's an attempt at understanding all the interrelationships between cells and organisms and between an organism and its environment. … We're taking all we know and utilizing it to build the type of models that we thought about 25 years ago that turned out to be so riddled with black boxes that we couldn't get the simulation we needed. But now, with the vastly increased power of computing and data mining, we can infuse a very strong science underpinning into environmental studies and make some dramatic gains in knowledge. …

What I like about a biocomplexity initiative is that it doesn't carry a lot of baggage. It's focused on science—bringing science into environmental studies. Right now, you get very narrow definitions of some terms. Biocomplexity is more than biodiversity. Biodiversity is part of it, especially with the genomic sequencing, which gives us a chance to learn a lot more about diversity without having to culture cells. But it's more than that, and more than just conservation or sustainability, although they are also important. …

On informal science education:

If you provide interesting exhibits, people will respond with their feet. That's been proven with aquaria, some of which are so popular that the museums have to replace the hand railings two or three times during the year. … [But measuring their impact] is an area that requires more behavioral research. It comes back to complexity, which is a hot subject these days. It's not so easy to assess the effectiveness of an educational program, and that's one reason why I would like to look more at research on learning. We've spent a lot of time focused on teaching, and yet we don't really know how people learn, how effectively people can have their learning enhanced, and the differences in how people learn.

On a recent report of a Ph.D. glut in the life sciences:

In the 1980s, NSF asked investigators to put graduate students on their research budgets, saying that it preferred to fund graduate students rather than technicians. But as often happens, the pendulum swung too far. There needs to be a balance. Well-trained technicians are needed to run equipment and labs, and what better way to provide opportunities for them than to build it into research grants. …

There's great respectability for those who want to be technicians, but we don't give them the opportunity. We've made it a sign of failure if you don't get a Ph.D. Other countries don't have this [negative] attitude. … With all the emphasis on graduate students, I'm not so sure that the question we're facing is one of overproduction. I think we have to look more closely at how we're using our resources. We've created a situation in the career pipeline where there is a bulge at the end of a postdoc and no place to go. …

On congressional earmarks to meet the research needs of "have-not" states:

The key is to link the local, state, and federal resources to build a collaboration. This kind of partnership is very important. We did a survey at [Maryland] and found there was a need for billions of dollars of research infrastructure. As a result, the governors of Maryland have made a serious commitment to solve this problem, and now the university is getting $90 million a year in state construction funds. But some states don't have a big enough tax base to draw upon, and they still need those facilities and research infrastructure.

There needs to be some way to provide a partnership—not a giveaway program, but a partnership—between city, state, and the federal government to make possible facilities that strengthen the science and engineering base that leads to economic growth. I didn't say an earmark. But I would like to see a program. Right now there isn't anywhere to go to get that done. It's very frustrating.

On the role of information technology:

I feel very strongly that computer science and research and the next-stage Internet and computation and the capacity to go 1000-fold greater in speed and volume of data handling are critical for the country's future. … We need to seize the opportunities open to NSF. There's strong interest at the Department of Energy for the weapons labs, and there's a clear need at NASA if they are going to go to Mars and continue to monitor climate change. All that takes research, and that's what NSF does best. I've met with [DOE Undersecretary] Ernie Moniz and [NASA Administrator] Dan Goldin and had long conversations with OSTP officials. The other agencies recognize that research is needed, and that's where NSF comes in. What they want to do will require the type of

advanced research that NSF funds. I see it as a really good working partnership. …

On why NIH receives larger funding increases than other science agencies:

What it tells me is that we're not making the case [for the value of research] as strongly as we need to. It's relatively easy to make the connection between the involvement of NIH and a cure for a disease, or for sequencing a gene that explains Alzheimer's. What's not so easy to make is the case that it's the fundamental research that allows that gene to be sequenced and that will provide a 30% return on investment for the economy, and that there's a relationship between our standard of living and our investment in science and technology. We don't make that case very well, and I'm open to ideas on how to do it better.

NETWORKS

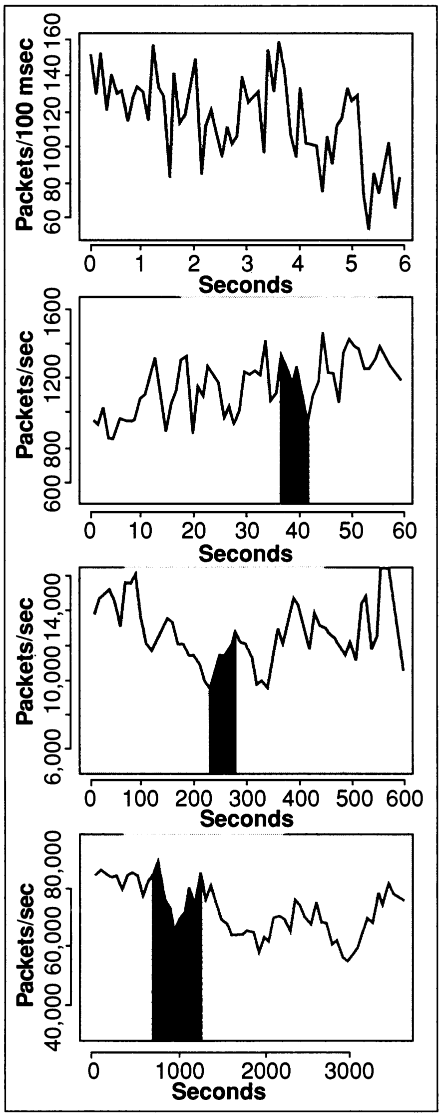
Fractals Reemerge in the New Math of the Internet

Traffic on the Internet has unpredictable bursts of activity over many time scales. This fractal behavior has implications for network engineering

Even a casual user of the Internet knows it is nothing like the phone system. Punch a number on your telephone, and the call will nearly always go through promptly, but click on a Web link or call up your e-mail for that urgent message, and you could be in for a long wait. This phenomenon reflects what may be the most fundamental difference between telephone service and the Internet: "It is no longer people doing the talking," says mathematician Rob Calderbank of AT&T Labs Research in Florham Park, New Jersey. Instead, it is computers talking to computers. As a result, he says, "the statistics of calling have completely changed."

Since the turn of the century, the telephone system has been built on the assumption that calls arrive at any link in the network in what's known as Poisson fashion: The likelihood of a call arriving at any given time is independent of earlier calls, for example, while call length varies only modestly. As a result, call volume fluctuates minute by minute, but over longer time scales the fluctuations smooth out. In contrast, AT&T mathematician Walter Willinger and his collaborators have shown that the machine chatter over the Internet is fractal. It has a wild, "bursty" quality that is similar at all time scales and can play havoc, Willinger says, with conventional traffic engineering.

When he first published that claim in 1993, other researchers regarded the idea as either wrong or meaningless. Willinger wasn't surprised by the reaction. Many mathematicians view the application of fractals to physical and social phenomena with some skepticism—after all, fractals have come and gone as fads in everything from hydrology and economics to biophysics. But as Willinger and network researcher Vern Paxson of the Lawrence Berkeley National Laboratory in California write in the September issue of the *Notices of the American Mathematical Society*, the fractal nature of local network traffic is now well established, and new studies have extended his analysis to the Internet as a whole. Indeed, the fractal mathematics of networks has become a fact of life for engineers designing everything from routers to switches. "Willinger's work has certainly changed the way we think about network traffic," says network researcher Scott Shenker at Xerox Palo Alto Research Center in California.



Self-similar. Internet traffic shows similar fluctuations over a range of time scales.

SOURCE: WILLINGER AND PAXSON, *NOTICES OF THE AMS*

The existing paradigm for what is known in the business as POTS, or Plain Old Telephone Service, dates back to the turn of the century and the work of a Danish mathematician named Agner Erlang, who derived a formula expressing the fraction of calls that have to wait because all lines are in use. "What he found empirically by going up to this little village telephone exchange and taking measurements with a stopwatch," says Calderbank, were the hallmarks of Poisson behavior. Call arrival times were random and independent of each other, and call durations clustered around an average value. Call frequency fell off rapidly at much longer durations.

The nature of communication—and its statistics—changed dramatically in the 1970s with the coming of what are called packet networks, beginning with Arpanet and ethernets and progressing to today's Internet. Not only did computers start doing most of the communicating, but the method of sending a message through the networks also changed. Whereas telephone networks hold open a continuous line for each call, packet networks break up a message into distinct information packets—maybe several hundred packets for a relatively small message—and send each one separately to its destination.

Despite these changes, says Paxson, researchers had such confidence in the Poisson paradigm that it continued to dominate their thinking. "People were writing papers," says Paxson, "and they would bend over backward to try to fit what they were seeing into the Poisson modeling framework, because it was so compelling."

In the late 1980s, however, Will Leland and Dan Wilson at Bell Communications Research (Bellcore) in Morristown, New Jersey, put together a hardware system that could, for the first time, accurately monitor and record the traffic flow on packet networks, much as Erlang had done for his local telephone exchange. Willinger, who was at Bellcore at the time and whose background was in probability theory, analyzed the resulting data in collaboration with Murad Taqqu, a Boston University mathematician. What they saw looked nothing like Poisson behavior.