# SFI Bulletin

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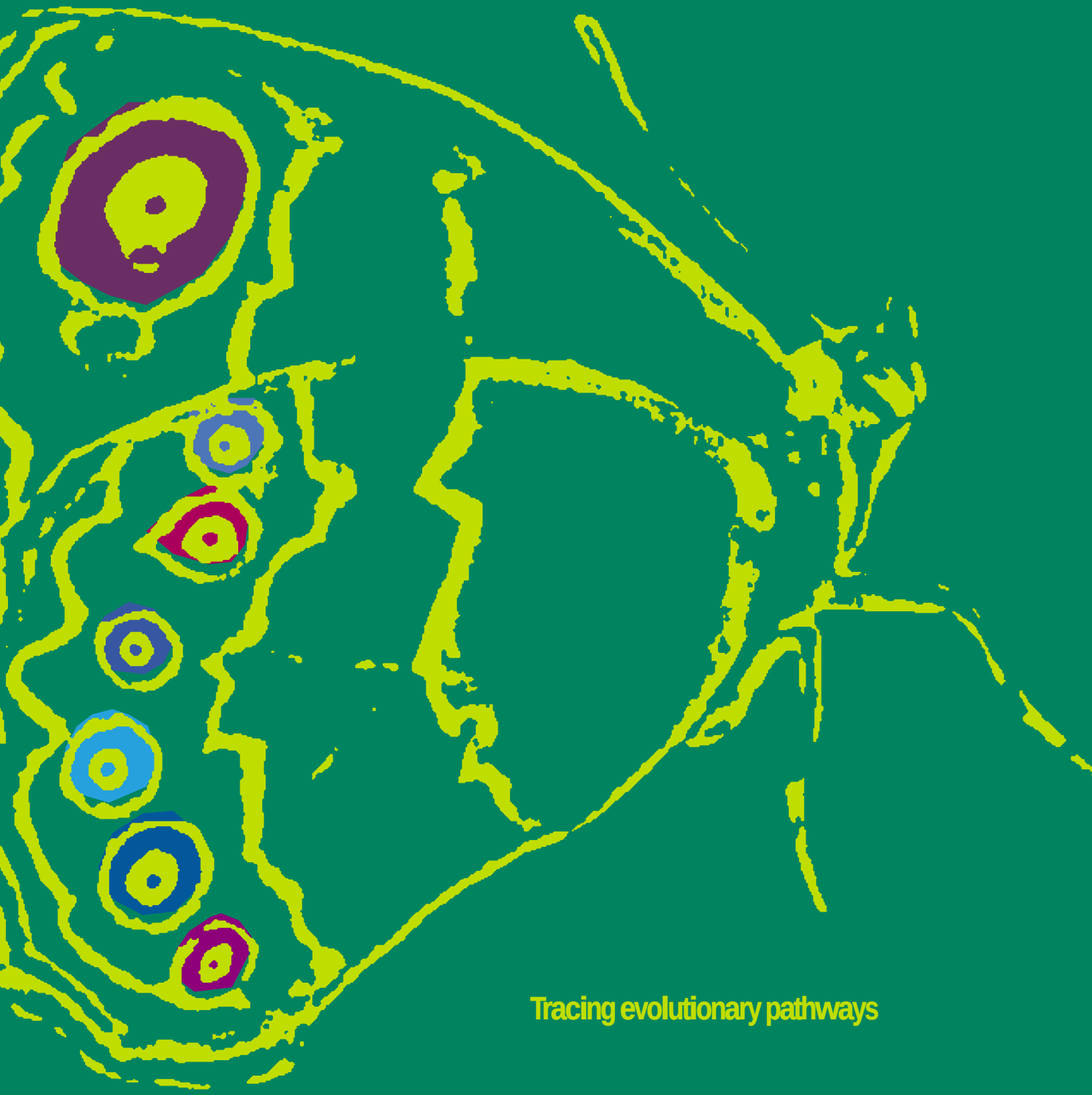

## Tracing evolutionary pathways

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The *Bulletin* of the Santa Fe Institute is published by SFI to keep its friends and supporters informed about its work. The *Bulletin* is free of charge and may be obtained by writing to Ginger Richardson at the address below.

The Santa Fe Institute is a private, independent, multidisciplinary research and education center founded in 1984. Since its founding, SFI has devoted itself to creating a new kind of scientific research community, pursuing emerging synthesis in science. Operating as a visiting institution, SFI seeks to catalyze new collaborative, multidisciplinary research; to break down the barriers between the traditional disciplines; to spread its ideas and methodologies to other institutions; and to encourage the practical application of its results.


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## EDITOR'S NOTE

Anyone who dislikes change should not work at SFI. The constant variation in the Institute's scientist roster, permutations in our research agenda, and the almost constant alterations in the campus environment can sometimes make your head spin. (I once came back to my office from getting a cup of coffee to discover that someone had taken over my desk. Really.) In SFI's early years folks like George Cowan and David Pines were fond of describing the endeavor as a "floating crap game," a clever metaphor that aptly depicted the fledgling organization's seemingly boundless flux.

As we approach the age of 20, many of our initial enthusiasms have matured into full-fledged, sustained research efforts. Entropy, however, appears to be a long way off; new approaches, research themes, and collaborators emerge here all the time. A glance at the table of contents for this issue illustrates the point.

We start with Ellen Goldberg's reflections on her seven years as SFI's president. Beginning in January 2003, Ellen will be concentrating full-time on one of her passions—education. She'll continue to be closely associated with SFI's program in cognitive neurobiology, and she will also be mentoring at-risk high school students. At the back of the magazine, George Gumerman, the Institute's interim vice president for Academic Affairs, shares his impressions since his arrival here this fall. (George actually has been deeply connected with SFI for many years, as both a Science Board and External Faculty member.) Janet Stite's profile of SFI's newest research professor, David Krakauer, focuses on this biologist's interest in how and why cells communicate, organize, transmit information, and make decisions. In another article we discuss entrepreneur Jim Rutt's work with Doyne Farmer's group on risk analysis.

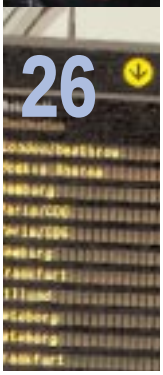
Finally, we highlight two new research initiatives. The first project, Innovation in Natural, Experimental, and Applied Evolution, will gather experts working in the range of evolutionary studies—from natural and experimental evolution to evolutionary computation and evolutionary engineering—for collaborative experimental and theoretical work. This work, an outgrowth of the Institute's founding programs in evolutionary dynamics and robustness, is supported by the David and Lucile Packard Foundation.

The second initiative, another follow-on project, is on robustness in social processes. Funded by the James S. McDonnell Foundation, this program's core questions center on the tension between staying the same and responding to change; opportunities for innovation, and vulnerabilities to collapse, on multiple scales; effects of interactions among slow variables such as cultural tradition and fast variables such as economic change; and, interwoven throughout, the role of learning. Come to think of it, maybe SFI should be on

Best wishes for the new year.









## FEATURES



## WORK IN PROGRESS



## NEWS



## TRANSITIONS



## IN EVERY ISSUE

# A Bold Past Points to a Promising Future

**BY ELLEN GOLDBERG**

OVER THE PAST SEVEN YEARS, as president of the Santa Fe Institute, I have witnessed the growth of an already extraordinary research institute into a highly innovative academic organization involving a network of physical, social, and natural scientists working together on problems addressing complex issues. I have seen the involvement of our business community in SFI research programs through the Business Network and meaningful interactions among the members of our Board with each other and the community of researchers associated with SFI. Further, SFI has grown to include theoretical and observational researchers from around the world including developing nations.

I have also grown with the Institute. Although I certainly knew that as president of the Institute, my intellectual life would expand to include a very different approach to science, I didn't realize how dramatic and exciting this change would be—every day I've been exposed to a new way of thinking and looking at the world. As I step down from the position of president, I'd like to share with you some of my experiences as a scientist involved with the Institute.

PHOTO: GUY AMBROSINO

But first, let me thank the founders of the Institute. George Cowan, Murray Gell-Mann, Phil Anderson, Ken Arrow, and David Pines, among many others, who had the vision to convene a group of outstanding researchers (in the early 1980s) to talk about creating an Institute that would be different from any existing academic organization—that would attract researchers from around the world to work on complex problems with a transdisciplinary approach. The Institute, incorporated in 1984, was meant to serve the research community by fostering and facilitating "risky" science by investigators who were courageous enough to collaborate with scientists from other fields in order to tackle difficult issues that could not be addressed in more traditional academic settings. In the nearly 20 years since its founding, SFI has lived up to this vision in full.

I started at SFI in January 1996, coming from an administrative position as associate provost for Research and dean of Graduate Studies at the University of New Mexico (UNM), as well as professor of microbiology at the UNM School of Medicine. In fact, it was in this latter role that I was first introduced to SFI and its research programs at that time. Unfortunately, not many New Mexicans, including those at the University, were familiar with SFI. But there were exceptions: In fact, it was Stephanie Forrest, a UNM computer scientist, and Linda Cordell, a UNM anthropologist, who introduced me to the Institute. They described SFI as a forward-thinking academic and research center that facilitated research across disciplines and encouraged "big"-scale thinking about complex problems.

Soon after, SFI entered into a partnership with several faculty members in the University's biology department—including Jim Brown, Terry Yates, and Jim Gosz—to compete for an NSF award as a National Center for Ecological Research and Synthesis (NCEAS). As associate provost for research at UNM, I worked with the dean of arts and sciences and the faculty—along with researchers and staff at SFI, including Mike Simmons and Ginger Richardson—to put together a proposal that would cement this partnership and would put SFI in a position to become a center for ecological research. Although ultimately we didn't get the grant (we came in second behind UC Santa Barbara), I personally became extremely excited about the potential collaborations that might grow between faculty members at UNM and SFI.

As an example, several years later, an introduction made at SFI brought Jim Brown (now External Faculty) and one of his students, Brian Enquist, together with Los Alamos Laboratory physicist Geoffrey West that resulted in an extraordinary SFI research program on scaling laws in biology. This program has gained momentum over the past six years and has been expanded to include other researchers from UNM, Los Alamos National Laboratory, and elsewhere. This work is generating worldwide interest in understanding scaling phenomenon in areas outside of biology and ecology. Could there be universal scaling laws? This is a provocative question that these researchers are attempting to address.

My own scientific background is immunogenetics. Even while associate provost and dean of Graduate Studies at UNM, I continued to run my NIH-funded laboratory at the School of Medicine. Beginning as a student at Cornell University Medical College and Sloan-Kettering Cancer Center and throughout my career, my research has always been experimental and reductionist in nature. I loved what I was doing, including my teaching responsibilities. Why, then, was I so intrigued about the theoretical research offered by SFI investigators? And furthermore, how could I have been lured away from a great job at UNM to become president of SFI?

The approach to research at SFI was very different from my own training, but I saw the incredible possibilities that could exist by bringing these two communities of theorists and experimentalists together. The research programs at SFI, then and now, look at the "big" picture and provide an environment in which risks may be taken. SFI research crosses intellectual boundaries, and enables researchers from disciplines as disparate as sociology and physics to work together on problems involving complex issues, such as what makes a system robust. As an immunologist who had worked on two single cell surface differentiation antigens for almost 30 years, I certainly understood the complexity of the immune system. I was, however, frustrated by the lack of interest by many of my colleagues to think about the "whole" immune system and all the interactions existing among and within the cells of this complicated, but fascinating biological network. Working with mathematicians who could help develop models of this kind of complexity was difficult to accomplish, especially at that time. There was little interest from traditional funding agencies to support this kind of interaction and research, and most of us, as experimental immunologists, had forgotten the mathematics that we learned as students. But there were a few researchers and private donors who saw the possibilities of this kind of collaboration—and one only had to look up the road from Albuquerque to Santa Fe to find them.

Ultimately the funding for this collaborative research in immunology did materialize. It did not come from a huge federal grant, but rather from a family foundation, the Joseph P. and Jeanne M. Sullivan Foundation. This funding supported the research of Alan Perelson (now External Faculty and Science Board) and his colleagues, including Avidan Neumann, a postdoctoral fellow at SFI, that eventually led to the exceptionally important breakthrough in understanding the dynamics of proliferation of the Human Immunodeficiency Virus. This in turn led to clinical trials and ultimately to the increased survival of patients harboring this deadly virus.

The Institute over the past seven years has expanded in physical size and number of researchers. In 1996-1997, we raised $4.5 million to expand the facility in order to decompress offices that housed anywhere from two to seven researchers and to increase the total number of researchers we could accommodate from 35 to 50. During these years, we also added to the diversity of our funding from federal agen-

cies, foundations, and businesses. In 1992 we had six members of our Business Network; by the end of 1996 we had 30 members. Now we have 50 active members. In 1996 we had funding from three federal agencies—the National Science Foundation, Department of Energy, and Defense Advanced Research Program Agency—and two foundations—the John D. and Catherine T. MacArthur Foundation and the Joseph P. and Jeanne M. Sullivan Foundation. Now we have successfully competed for funding from over ten federal agencies and private foundations to support our integrative core research as well as specific research programs. This year alone, we raised over $10 million in grants from such organizations.

This figure does not include private contributions. Over the past few years we have raised approximately $20 million to help expand the campus, renovate the main building, seed an endowment and reserve fund, supplement the core research budget, and provide funds to bring in researchers and convene workshops in developing nations worldwide.

What about changes in research directions? The vision and mission of the Institute remain constant: to conduct and foster scientific research that is transdisciplinary, excellent, fresh, and catalytic. At the same time SFI's research agenda changes over time. We have been able to spin off successful programs as they have become accepted by the mainstream scientific communities (leading to acceptance within university classrooms). At the same time we have initiated new programs that have received recognition as being risky, but extremely important. We have expanded our research agenda to include the social sciences. Although SFI has always had a strong economics program (thanks to the seminal workshop held at SFI back in 1987 with support from John Reed at Citibank), recently we have significantly increased our number of researchers interested in behavioral and social sciences. These researchers work together with the physicists and mathematicians who were always "at home" at SFI. Just looking at the transdisciplinary themes currently developed at SFI and the researchers who are involved, one can understand the uniqueness of this place. We have programs in human behavior, evolutionary dynamics, network dynamics, robustness and innovation, computation in nature, and social and economic interactions. And because of the unique approach at SFI—one only need look at the variety of researchers involved in any one project—it is obvious that a single researcher may be involved in work spanning from economic interactions to computation in nature to evolutionary dynamics. We find physicists working with linguists, biologists working with economists, computer scientists working with political scientists, and so on.

Why have we been so successful? We have a competent, dedicated staff of extremely intelligent people who are responsible for enabling researchers from around the world to do their work. We have resident faculty (who come to SFI, many of whom give up tenure positions at universities), external faculty, postdoctoral fellows, and graduate fellows who find themselves at home and comfortable in the environment provided by the Institute. We attract the best thinkers in the world. We attract researchers who are willing to learn the language of other disciplines, and who are courageous enough to "buck" the mainstream scientific community in order to pursue their own ideas. And we have a dedicated community of scientists who serve on our Science Board and Science Steering Committee, as well as a dedicated Board of Trustees, who find the science at SFI so fascinating they are willing to take time away from their own busy schedules to participate in scientific workshops and symposia. This also includes the 50 or so businesses who send representatives to SFI and who help organize workshops with our research community. Where else can you find such an incredible and sophisticated mix of individuals who work together to make an academic institute a success?

I will miss my role as president of the Santa Fe Institute. It is a wonderful place, and we are in an extraordinary position to make even more contributions to the scientific community and the world. I look forward to my future roles: involvement with SFI's Increasing Human Potential project—founded by George Cowan (the founding president of SFI), and working with high school students who just need a little encouragement to stay on track and in school. I feel as if I'm starting a new career and professional life.

One may ask why I chose to step down as president at this time? I've been in this position for seven years. As you can imagine from what I said above, they have been exciting, challenging, and extremely fulfilling years. At the same time, I have always felt that one should follow their passions. During the course of my tenure as president, I found that I was passionate about the Increasing Human Potential project and, if successful, the impact it could have on early childhood education in this country.

In conjunction with this program, I have felt, for as long as I could remember, that the world would be a better place if we paid more attention to the young student, especially those students not exposed to good education and learning environments. I also feel strongly that our educational system needs dramatic change. I'm at a point in my life where I could devote myself to this new challenge.

At the same time, I know SFI will be left in good hands and look forward to its growth and contributions to the research community. I want to thank everyone who has made this one of the highlights of my professional career.

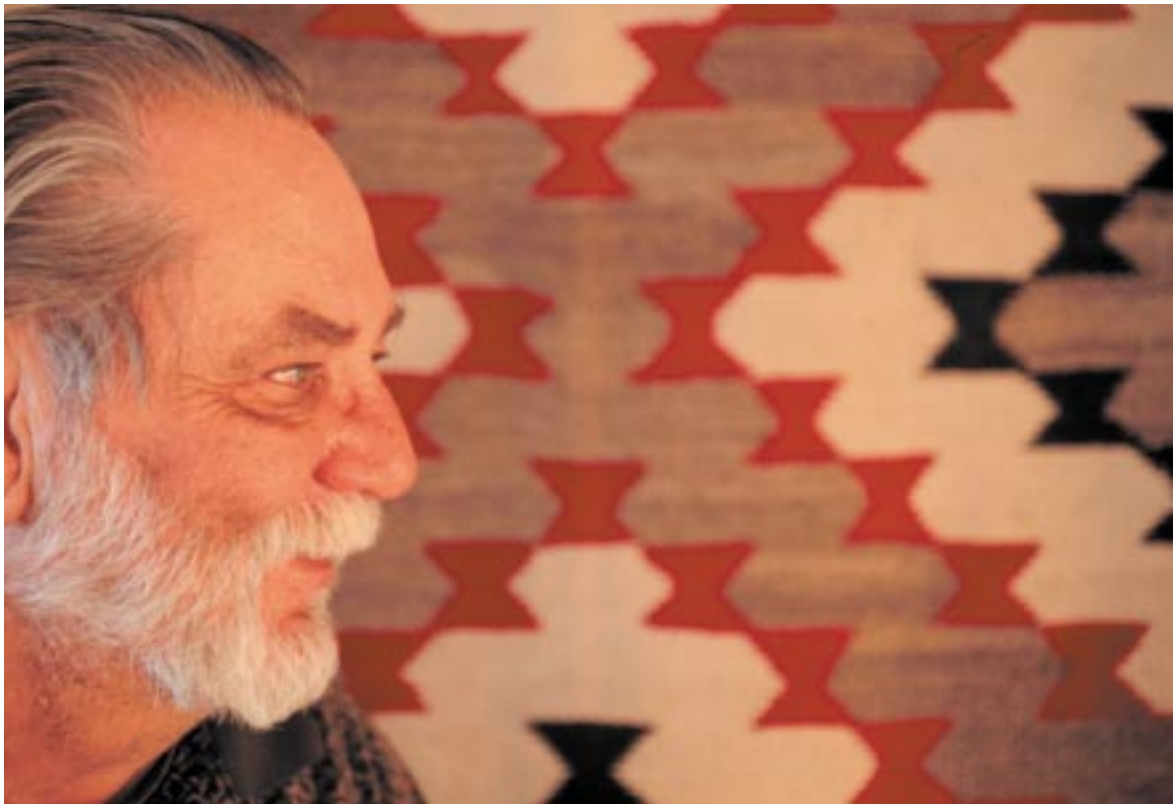


PHOTO: JULIE GRABER

## SFI: A COMPLEX, SELF-ORGANIZED ADAPTIVE SYSTEM

**BY GEORGE GUMERMAN**

When Ellen Goldberg called and offered me the position of interim vice president for Academic Affairs at SFI, I told her I felt I had been in training for the job for my entire professional career. As an archaeologist schooled in the 1960s and '70s, I was inculcated in a team-oriented, multidisciplinary research approach—the very essence of the SFI scientific endeavors. After a number of years in various SFI roles, I knew my own research predilections were well-suited to the Institute's style.

I have been advised that as acting vice president there isn't much I can change in one year, especially since SFI is between presidential appointments. Anybody in a temporary position is cautioned that the best strategy is to keep a low profile and simply make certain that programs function smoothly. While perhaps this is good advice, it is antithetical to my personality. SFI is still a relatively young institution, and its programs must continue to evolve; the Institute cannot afford to rest on its already considerable reputation.

What I had not realized is that the entire SFI organization, not just the researchers, is dedicated to the mission of team-oriented scholarship to more fully understand the past and present. SFI not only explores the nature of complex biological, physical, and cultural systems, but also, as is sometimes noted, the institution itself is an example of a complex, self-organized adaptive system. Theoretical biologists, computer scientists, evolutionary biologists, anthropologists, mathematicians, linguists, economists, physicists, political scientists, and assorted other academics come together from around the world to address various research domains. They are assisted in their vision by a dedicated and talented support staff and other contracted aides..

A few years ago one such staff memberaide, Venses Montano, and his family, gave to the Institute a telescope as a Christmas gift. Almost every evening, Venses, along with his wife, his children, and often some of his grandchildren, restores the Institute to a clean and tidy state, ready for another bout of scientific collaboration. With the telescope, the Montano family wanted to show their support of SFI science. They also wanted to help the researchers and visitors enjoy the mountain vistas available at the Institute.

With the assistance of the Montanos and the rest of the large and far-flung SFI family, I intend to help shape the Institute's agenda for as long as I remain the vice president for Academic Affairs. I trust I will do so with the same energy and dedication as the Institute's researchers and staff. Along the way, I also intend to enjoy the views.

# Robustness in Social Processes

IN A WORLD OF UNCERTAINTY, rapid change, and increasing complexity, one might think that failure of social processes should prove the rule rather than the exception. And yet both the past and the present provide many examples of social processes that we instinctively label as robust to failure, whether because of the agility with which they have responded to changing circumstances, or because of their record of surviving deliberate internal or external attack, or merely because they have proved so long-lived. Robustness is a term that captures our intuitive sense of one of the key determinants of long-term success or failure, but what do we mean by robustness, and what specific features of a social process contribute to its robustness or fragility?

SFI Research Professor Erica Jen is leading a new Institute-wide scientific initiative that will explore the emergence, pathways, and consequences of robustness in social processes. This work is supported by a generous three-year award from the James S. McDonnell Foundation. Founded in 1950 by aerospace pioneer James S. McDonnell, the foundation was established to "improve the quality of life," and does so by contributing to the generation of new knowledge through its support of research and scholarship.

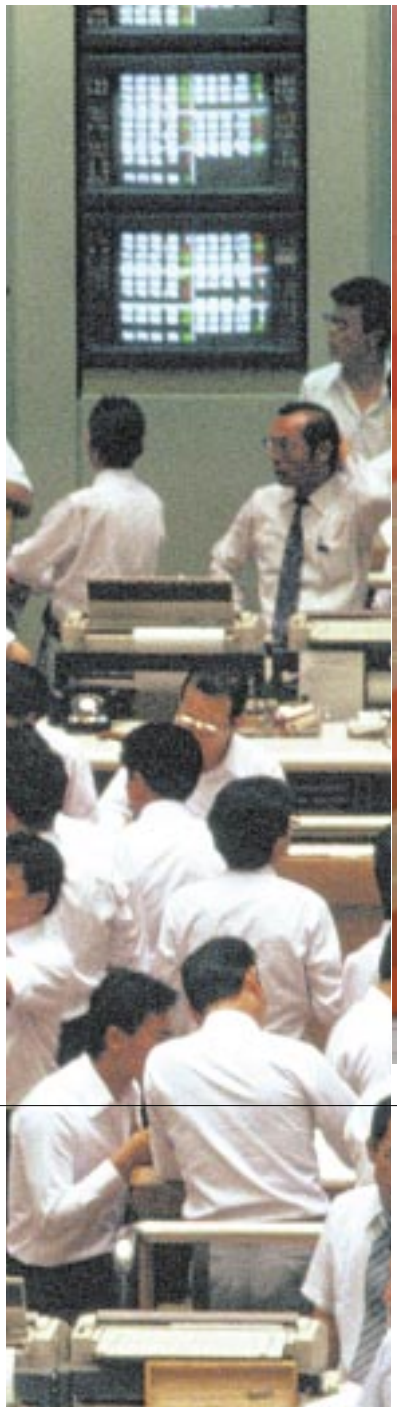
In the past few years, the concept of robustness has been the subject of growing interest in the natural and engineering sciences. Building on traditional fields such as stability, reliability, and control theory, the study of robustness has focused on the ability of a system to maintain specified features when subject to assemblages of perturbations either internal or external. The system of interest in robustness is typically not in equilibrium, and the perturbations are typically such that it is unrealistic to attempt estimations of their supports and distributions.

Preliminary progress has been made in the understanding of general principles of robustness especially in the context of evolutionary and developmental biology, ecology, and computer network design. The insights have stimulated a rich set of research programs, and, even more importantly, are contributing to new ways of thinking on issues ranging from the architecture of regulatory control, through the relation between performance and flexibility, to the evolution of general-purpose information-processing algorithms in these contexts.

In social contexts, however, the study of robustness has thus far not emerged as an explicit focus of research. However, potential interest is enormous. Examples of the questions that motivate the study of social robustness include:

- **Why do some social arrangements—monogamy, religious rituals, forms of property rights, markets, for example—persist over long periods and recur repeatedly despite significant adverse conditions, while others pass away quickly even in the absence of any serious challenge?**
- **How do social norms enhance or degrade the robustness of the socio-ecological-economic systems in which they operate?**
- **How can individuals and systems employ effective decision-making procedures in social situations where choices have unforeseeable consequences?**
- **What keeps a cultural tradition vital and open to innovation by the individuals participating in that tradition?**
- **What makes for a robust economy? Why for example did the Soviet system collapse with such speed? And why have the different former communist countries had such varied experiences in recovering?**

PHOTOS: GETTY IMAGES, EXCEPT LENIN MURAL COURTESY WESTSTOCK



These questions signal the core issues of interest: the tension between staying the same and responding to change; opportunities for innovation, and vulnerabilities to collapse, on multiple scales; effects of interactions among slow variables such as cultural tradition and fast variables such as economic change; and, interwoven throughout, the role of learning.

The project's approach will emphasize phenomenology and the use of case studies as the basis from which to abstract general principles of robustness. The goal is to explore the origins, mechanisms, and implications of robustness in social processes. The work is inherently transdisciplinary not only in considering case studies and theoretical analyses across the range of social sciences, but also in drawing upon recent advances in the study of robustness in non-social processes in biology, ecology, computer science, and engineering. It is important to note, however, that while this work will attempt to survey and to integrate diverse perspectives on robustness, it will in no way seek to unify all such perspectives, or to establish "universality principles" for robustness that would be inconsistent with the patent diversity and distinctiveness of the range of processes to which the concept applies.

The initial research themes focus on the usefulness of two complementary perspectives on robustness in social processes. The first (inspired in part by ecological studies) views robustness as characterizing a stage in the developmental history of a process. The social process will be analyzed as a set of dynamic interactions with feedback across multiple scales and in multiple dimensions on multiple networks. The question, then, is the role of these different dynamics in providing flexibility or rigidity in the response of the social process to uncertainty and change, and in leading to any of the future possibilities of innovation, persistence, degradation, or collapse.

The second perspective (inspired in part by engineering and computer science studies) views a social process—whether it be economic exchanges, the functioning of an organization, or an example such as decision-making either by individuals or by social systems—as distributed information-processing systems with feedback control. The goal is to understand the features such as error-correction or buffering that enable the process to perform successfully even with model uncertainty, unforeseeable consequences, conflicting data, and other complexities that could preclude the process from functioning as desired.

A major challenge is to construct new perspectives that incorporate useful aspects of the ecological and the engineering views described above, but that highlight the uniquely social features of social processes. Such features—including the critical role of cognition and learning, intentionality and identity, evolving cultural repertoires, and the extraordinary human capacities for effective behavior including deliberate collective action or the envisioning of alternative realities—impart to social processes their distinctive flavor of complexity, and are clearly key to any study of social robustness.

As an example of one result of these uniquely human capabilities, the deviant behaviors that challenge social system integrity are not accidental and uncorrelated (like mutations in biological models), but necessarily are sometimes intentional and coordinated. Moreover, humans adopt behaviors through cultural transmission processes that can be extraordinarily rapid and characterized by conformist learning (a tendency to adopt behaviors that are common, independently of other influences on learning such as relative payoffs). Study of factors such as the prevalence of conformist learning in social processes, and its implications for the likelihood of cataclysmic collapse or the persistence of multiple distinct outcomes, can be counted on to give rise to a radically new, and fascinatingly social, understanding of robustness.

The project will organize a range of activities—including workshops, visitor programs, postdoctoral fellowships, and student programs—around six major research themes.

Robust Decision-making will focus on the robustness of choice with unforeseeable consequences. Discussions will highlight the importance of issues including intentionality and the cognitive ability of social agents to observe outcomes, infer the reasons for those outcomes, and change their behavior accordingly.

**Robustness of Business Organizational Structures** will focus on the role of network structure in facilitating the dynamics leading to phenomena such as innovation or collapse in a social organization. Specifically, the research will explore the consequences for robustness of the ability of social agents functioning within a hierar-

chical structure to form social ties across all scales of the organization.

**Robustness of Political Agreements, States, and Regimes** will address the robustness of negotiated agreements that define a social structure such as a nation-state. In particular it will address the dynamics that enable some such agreements to survive internal or external shocks (such as events that challenge the beliefs of the involved parties, or shifts in interpretations of the agreements, or organized attempts to disrupt those agreements), while others collapse into conflict.

**Robust Institutions** will examine the social dynamics that contribute to robustness or fragility of institutions. One set of issues to be explored is the role of competition between groups in favoring those with more robust institutions, and the within-group processes of collective action that can serve to create the range of novel institutional forms on which between-group selection can act.

**Robust Economies** will consider issues of scale and levels in robust social processes. Included will be interactions between the slow variables of cultural patterns and the fast variables of economic change; the transference of robustness from one level to another; and mechanisms of robustness in organizations that are so large as to compromise the effectiveness of social norms.

The case studies in **Robustness of Cultural Traditions** will be instructive for the question of inference from the historical record. The discussions will attempt to disentangle the two aspects of "staying the same" versus "responding to change" that characterize robustness, with the goal of developing a methodology for examining the history of environmental or internal change, and the response of a social process to this change.

The program will bring together multigenerational teams—students and postdoctoral fellows together with senior researchers—from widely disparate scientific communities. The researchers will interact both with each other and with the broad-based community of researchers at SFI interested in complex adaptive systems. Research activities—that will begin in 2003—will include visitor programs, postdoctoral fellow and graduate student programs, working groups, and workshops on specific topics, as well as group meetings convened expressly to identify and to discuss cross-cutting conceptual issues.

**Robust Economies will consider issues of scale and levels in robust social processes**

# David Krakauer: Origins of an Evolutionary Biologist

PROFILE BY JANET STITES

PHOTO: JULIE GRABER

"Signs, signs, everywhere there's signs
Blockin' out the scenery, breakin' my mind.
Do this, don't do that. Can't you read the signs?"
—"Signs," Les Emmerson, Five Man Electrical Band

AS A YOUNG LECTURER AT OXFORD, theoretical biologist and Santa Fe Institute Resident Faculty member David Krakauer was honored to loan an elderly, distinguished professor copies of some rare science texts from his personal library. The professor died while still in possession of the books and Krakauer was left with a moral quagmire—to ask the widow for the books or to let it go. Mannered Brit that he is, he decided to let it go.

Some time later while browsing a famous Oxford used bookstore—known to be the recipient of many deceased professors' libraries—Krakauer came across the books. He took them to the clerk in hopes she would share in his enthusiasm for the fortuitous discovery and be happy to return them to their rightful owner. She was not. He tried to reason with her, telling her the story of the professor and showing her his own initials etched in each book. His efforts were rebuked and what could have been a sentimental—somewhat historic—book lovers' moment turned into an ugly exchange, with the otherwise affable Krakauer storming out of the shop.

Of course, Krakauer could have simply bought the books back, but that, according to him, was beside the point.

It's hard to picture the soft-spoken biologist, who will turn 35 at year end, the subject of a tiff in a university bookstore—used or otherwise—but it makes more sense as you start to study his work and realize that it's as much about communication as biology, and his reaction to the bookstore clerk as much frustration due to miscommunication as the loss of the books. What drives Krakauer as a biologist is the infinite problem of how and why cells communicate, how they organize, transmit information, and select and make decisions.

## EXPLORING THE GRAND ISSUES

It's no surprise then that Krakauer has a fascination with linguistics. Originally he wanted to be a writer. "But that would take some thought," he says in his self-effacing manner. "I'd have to invent something. I didn't have a good feel for it." But Krakauer was interested in the languages of math and computers, and had an affinity for biology. "I didn't want to do physics," he says. "Biology seems to be the natural science, other than anthropology, which seems to be most inclusive. It has the greatest breadth and allows you to deal with topics which would be of interest if you're working in the social sciences and the humanities."

Krakauer compares himself to the fox, curious about everything, and feels that theoretical biology versus being a lab biologist suits his personality. "I was never particularly gifted when it comes to lab work," he says. "I am fundamentally lazy."

At Oxford Krakauer worked on evolutionary theory, where he began to use mathematical models to study the evolutionary process. He did his doctorate in game theory and cognition and then started building models on the propagation of infectious diseases. When he met theoretical biologist Martin Nowak, his future took a turn. "He had an office next door," Nowak says, speaking now from his office at Princeton's Institute for Advanced Study. "But I never met him there. I met him at a party."

Nowak is all too happy to talk about Krakauer, his work and his potential. "He is one of the most creative minds in biology," he says. "He generates promising research ideas at a pace of about five a week."

Nowak attributes Krakauer as the inspiration

behind his own work on language. "He came to my house one night in Oxford and told me about an idea for modeling the evolution of language," Nowak says. "I dropped everything else I was doing and worked with him on that model for about a year. It was the beginning of something totally new."

When Nowak accepted a position to head the Theoretical Biology group at the Institute for Advanced Study, he brought Krakauer with him. Krakauer stayed three years until he joined SFI in April 2002.

Krakauer came to SFI as a full-time faculty member—a rare position. So how did he land a private office in a quiet corner of the Institute? The introduction was two-fold. SFI Research Professor Erica Jen reached out to Krakauer to join the Advisory Board of the robustness program at SFI, sponsored by the Packard Foundation. Subsequently, Walter Fontana met Krakauer while visiting the Institute for Advanced Study. Both recognized that his open-door, open-mind policy would prove valuable to the Institute.

"David is committed to no particular perspective or methodology," Jen says. "In fact, he relishes them all. And even more important, he refuses to do what almost all of us do to make a living. He refuses to focus on a particular level or scale or context in which a phenomenon is supposedly situated."

Fontana has as high praise. "David represents the mindset, the spirit of SFI more than any other researcher I have seen coming through this place in the past decade," he says. "He understands—and hence approaches—the grand issues of evolutionary biology in a special and rare way, because he has a deep knowledge of their history, their philosophical roots, and their epistemic structure. David also has a capacity for recognizing when these issues reappear in disguise elsewhere—in the social sciences, cognitive science, the visual arts, technology, politics, anthropology, and literature."

Indeed, the structure—or some might say, lack thereof—of the Santa Fe Institute was just the intellectual playground Krakauer longed for. "I had always worked on multiple topics from genetics, signal transduction, animal communication, human language, disease evolution," he says. "Walter felt that SFI was the kind of environment where you can get away with working on multiple topics which have a common theoretical underpinning. In most other establishments, that would almost seem frivolous. You have to work on a single topic."

But it wasn't strictly his work that captured Fontana's attention, but how he worked. "David believes in others and has leadership qualities," he says. "All this helps in the production of good scientific work, but, at the same time, reaches well beyond. David's mind is an interesting place, and such minds are vital for sustaining a small, lively, and irreverent interdisciplinary research community."

## HOW BIOLOGICAL INFORMATION IS PACKAGED AND PROPAGATED

It's clear Krakauer is relishing the environment of that community. His brain does not stop processing information for a moment. He is a sponge for knowledge and keen to make connections. His congeniality allows him to easily enjoy casual summer lunches in SFI's courtyard with physicists, political scientists, writers, and economists. When he leaves the table, he has new material to digest.

As you drill down into Krakauer's work, you see how all the connections begin to come together. He writes his own computer simulations, tending to work with smaller, mathematical models, which he believes allow him to capture the essence of a problem.

Jen explains his method this way: "David does not care about the kind of modeling that makes a phenomenon essentially into an epiphenomenon. He wants to understand something, and that means he models not the effects of the phenomenon, or statistical features of the phenomenon, but the actual mechanism by which the phenomenon is generated."

The backbone of Krakauer's work is evolutionary sign systems, with his fundamental interest being the way in which biological information is packaged and propagated. Most signs, he explains, come in the form

of a hormone or protein either attaching itself to the cell, or invading its nucleus.

One way Krakauer tracks and studies cell signaling methods is by studying disease, following the evolution of virus genomes. "How is it that a certain kind of information is represented and how is that information propagated reliably and robustly?" he asks.

Ultimately, studying micro-organisms allows Krakauer to utilize a plethora of data gathered from genome databases—which continue to grow—from all over the world.

But what confounds and discourages his colleagues in the lab—that is, the speed at which viruses can evolve—is valuable fodder for Krakauer's research. "If you're interested in evolutionary processes, it's nice if you can see some part of the evolutionary process unraveling in front of your eyes," he says. "Viruses and bacteria evolve on what for us is a developmental timescale. You can see the process of evolution and you see the constraints limiting the propagation of information."

Krakauer has two approaches to his research into the computational biology of a cell. "If you look at a system and take it to pieces to try to understand how it works, you want to understand the mechanics of a device," he says. "When we look at cells now, there is wonderful data. We can try to build parsimonious theories which explain as much of the data as we can." This type of mechanistic, atemporal theory is widely accepted and growing all the time, according to Krakauer.

More controversial, he explains, is historical theory. "How did something get put together over time? What are the stages through which the technologies passed?" Krakauer points to an essay written by Steven J. Gould in which Gould, as an argument for contingency in evolution, asserts (paraphrased by Krakauer), "If you were to re-run the tape of life, we would get a totally different set of outcomes." (Wonderful Life: The Burgess Shale and the Nature of History).

Krakauer has internalized this as a mission statement for theoretical biologists. "In some sense what a theorist tries to do is to determine the underlying laws of necessity in the evolutionary process," he says. "What outcomes do we observe today which are necessary or inevitable? Or what outcomes do we see today which were purely based on chance?"

Krakauer continues to work with scientists throughout the country and the world. Currently, he is collaborating with the Mt. Sinai School of Medicine in New York City, examining signal transduction. "This is an experimental group," he says. "They are lab-based. They collect data and do molecular experiments. I'm the theoretician of the project." He also continues to work with Martin Nowak at IAS, and Frans de Waal and Jessica Flak at Emory's Yerkes National Primate Research Center, among others.

### THE FATE OF A CELL

At SFI, Krakauer is working with Fontana, developing new theories for cellular signal transduction. One topic they are studying is determination of cell fate. How does a heart cell know it should become a heart cell? How does a brain cell know it should become a brain cell? "That decision is a kind of computational decision and it depends on things like positional information and signals sent from neighboring cells," Krakauer explains. "Traditionally, in developmental biology there has been a big concentration on how spatial position determines cell fate. What we're doing is looking at how that only goes so far. What you really want to ask is, `Okay, you're in this spatial position and you receive a signal, how do you process that information?'"

Krakauer likens the process to that of the nervous system making decisions based on rudimentary computation. Cells can receive multiple or even conflicting signals, he explains, and need to look at the balance of evidence and make a decision based on the strength of these signals. "On the basis of the incoming signal and its own internal signal," he says, "it's going to make a transition to a new state. That's almost the definition of a computation. This transition to a new state is what we're interested in."

Their interest has to do with picking up where Darwin left off.

"There is only one theory commonly accepted in the scientific community for the origins of biological complexity: Darwin's theory of natural selection," he says. "This is the one most people feel accounts for complexity; however, there is nothing intrinsic to the Darwinian theory that tells you why you should go from single cell to multi-cell, from multi-cell to division of labor.

"Darwin principally tells us that you have competition between types," he continues. "You have variation amongst those types. Those individuals that are best able to compete, to contribute to the gene pool, will leave the maximum amount of descendants and thereby be present in the future in greater frequency.

"But that doesn't tell you why we ever moved from the primordial sludge with proto-bacterial organisms that are very good competitors; how did they get more complicated? Why didn't they just stay like that?"

### TALKING CELLS

Krakauer believes the answer might be found by understanding how cells communicate. "Each of these changes in the level of biological organization requires a sophisticated, reconfiguration of a signalling system," he says. "So, in a sense, the focus on properties of signals—innovation, coordination, error, and redundancy—gives us some clues into how it is that these major transitions came about. How do you go from a single cell to a multi-cellular organism? Clearly those cells have to talk to each other."

**"A cell can simply lie about its own state."**

Innovation, coordination, error, and redundancy are concepts Krakauer wrestles with often.

Innovation and coordination, Krakauer explains, are categorized as "properties of origin." The terms beg questions. When he uses the term signal innovation, he asks, "Where does the signal come from?" When he uses the term coordination, he asks, "Once the signal has arisen, how does it get coordinated into the population?" For example, he explains, shifting back to the language of linguistics: "It's one thing for someone to discover a new term. It's another for everyone to know what that person is talking about. It must be embedded in a matrix of associations which is there to give it some function or semantic content."

Error, noise, and redundancy are outlined as "properties of robustness," which are needed to preserve and maintain the information in the cell. "What if the signal is subject to noise and it is misconstrued?" Krakauer asks. "How do you ensure that the receiver makes the correct interpretation?"

One way, he explains, is through redundancy. Redundancy allows for multiple copies of the same signal, or moreover, a set of signals where the removal of one of those signals leaves no obvious change in the meaning. It allows the organism to be more stable, but by virtue of the increased complexity, less efficient.

### USING CONTEXT TO TRANSLATE

Another problem with cell signaling, according to Krakauer, is "ambiguity." "This problem is ripe in signaling systems," he says. "In natural language, we would link the problem of ambiguity with a word like 'blind.' It can mean someone who can't see, or a certain kind of curtain."

To understand, the receiver turns to context, according to Krakauer. For example, in cell development there are signals where the same signal can tell the cell to become differentiated (heart cell? brain cell?) or divide. And what that particular signal does depends on the cellular context, the cell's state, and the cell's history. "Or the answer could be related to positioning," he says. "It's similar to the way we understand the meaning of a word because of its position in a sentence." Not being able to understand the context of the signal leads to "ectopic" growths, where you have one kind of cell emerging in a different tissue type.

### LYING CELLS

Continuing along the lines of miscommunication, Krakauer explains that sometimes the cells want to give the wrong information, that even cells can be full of deceit. "A cell can simply lie about its own state," he says, "The best example is that of a cancer cell, where a cell divides inappropriately." The cell divides as fast as it can, before its host can ascertain its danger.

When a virus enters into a cell, one response might be "cell suicide" (apoptosis) to keep the virus from entering neighboring cells. But some viruses block the cellular signal and consequently the cell can't commit suicide, so the virus spreads.

But the communication is not simple. "Say, as a cell, you were infected and you have a reduction in

your quality," Krakauer says. "How do you know when you've reached the lower threshold of acceptability? You might decide you're fine, but you can't really know what's fine because what's fine is defined relative to all the other cells. You might be making the wrong decision. The decision may need to be made collectively by the entire population."

### CONVEYING INFORMATION THROUGH SHAPE

"When you're looking at the way in which biology represents information, it does so in an incredibly complex variety of ways." Krakauer says. "The most obvious one is in sequences of bits, for instance, nucleic acids. Or you can look in proteins and see that the information is determined by the sequence of amino acids." Harder to grasp is the idea that information biology can also be carried in "shape." Shape-based information is analog, explains Krakauer. To replicate, the structure can somehow copy itself onto a template.

The fact that shape-based information is analog implies at least two things: (1) shapes can only carry a small number of messages – physics determines the number of stable protein conformations (not infinite as with combinations of nucleotides in DNA and RNA); and (2) there are no straight-forward mechanisms for correcting errors during inheritance (making them so called "limited heredity replicators"). This is in distinction to DNA and RNA, where carrying two strands solves the error correction problem.

By studying the dynamics of these limited-heredity replicators, and exploring diverse scenarios for shape-based propagation, Krakauer (working with Nowak, May, and Klug) found that polymer-based replication (one in which replication is more like crystal nucleation, growth, and fracture) is more plausible than copying one monomer's shape into another's. These microscopic signaling events at the protein level can then be used to understand the longer time scale of disease onset in Kuru, mad cow disease, and Creutzfeldt Jakob disease.

### COMMUNICATION REVOLUTION

In true SFI fashion Krakauer's interest in cell communication doesn't stop at biology or even linguistics. He sees patterns among cells that are eerily similar to patterns among humans—organizing as cultures and constantly sending signals and instructions for division of labor.

What will we have learned if we learn how cells communicate? Will we be able to send a signal to a cancer cell to prevent it from dividing? Will we be able to keep the HIV virus in check? Yes, asserts Krakauer, but not anytime soon.

"No one really understands how the inter-cellular circuitry works," he says. "We are far from intervention based on theoretical principles."

At this point in his career, Krakauer has more questions than answers, and that seems to suit him well. In his corner of the world, with a view of blue skies and snow-capped mountains, he is balancing writing computer programs for his projects, reading, researching papers, and attending SFI staff meetings. You get the sense he is right where he should be, physically and intellectually, and that he is in awe of his field.

"This is a pivotal moment in evolutionary biology," he says. "No one knows where it's going." He believes the ever-increasing efficiency of computers, combined with the ever-growing number and depth of biological databases, will allow biologists the ability to evolve their own theories faster, and that their work will become more and more entangled with information theory and culture.

"The twenty-first century will do for biology what the twentieth did for physics," he says. "Biology, computer science, and information theory: that's where the revolution is going to be."

Tell that to the bookstore clerk.

Janet Stites is a freelance science, technology, and financial writer based in New York City. She has written for *OMNI Magazine, Newsweek,* and *The New York Times* and was founder and publisher of *AlleyCat News*.


## A GLIMPSE AT KRAKAUER'S RESEARCH

To an outsider, the breadth of David Krakauer's interests seems paralyzing as he zigzags from prions to linguistics, from cellular signaling to mad cow disease, but to Krakauer it's the source of his inspiration. At his web site (www.santafe.edu/~krakauer/), he describes his ongoing research projects as encompassing "The Evolution of Sign Systems, Neurodegeneration, the Evolution of Apoptosis (cell death), Organelle Evolution & Development, Genome Organization, and Robustness." As well, he is most interested in genomic compression, i.e., the way in which to pack as much heritable information as possible, and has been collaborating with Jessica Flak (his wife) and Frans de Waal of the Yerkes National Primate Research Center at Emory University, studying communication among primates. Here's a glimpse of his projects.

### "The Evolution of Language"

Martin A. Nowak and David C. Krakauer
Institute of Advanced Study, Princeton, 1999

In this paper, Nowak and Krakauer approach language evolution based on evolutionary game theory via mathematical and computational modeling. They assume that in the early evolution of language, errors in signaling and perception would be common. And they argue that grammar—which provides context for words—originated as a simplified rule system that evolved by natural selection to reduce mistakes in communication.

### "Redundancy, Antiredundancy, and the Robustness of Genomes"

David Krakauer and Joshua Plotkin
Santa Fe Institute, 2002

In this paper Krakauer and Plotkin define "antiredundancy" as a hypersensitivity to mutation. Given that redundancy makes the system more cumbersome, the authors propose that large populations evolve antiredundant mechanisms for removing mutants, thereby bolstering the robustness of wild-type genomes, at the cost of losing some individual cells. Small populations, however, evolve redundancy to ensure that all individuals have a high chance of survival. They propose that antiredundancy is an essential mechanism for ensuring tissue-level stability in complex multicellular organisms and suggest it deserves great attention in relation to cancer, mitochodrial disease, and virus infection.

### "Red Queen Dynamics of Protein Translation"

David Krakauer and Vincent Jansen
Santa Fe Institute, 2002

In this paper Krakauer and Jansen suggest that the genetic code might serve as the first line of defense against infection as "host" translation strategies are constantly shifting through time to evade parasitism but where neither parasite nor host gains a systematic advantage. The term "Red Queen" is taken from Lewis Carroll's classic Alice's Adventures in Wonderland, in which the Red Queen is always moving, but not getting anywhere.

### "Selective Imitation for Private Sign System"

David Krakauer
Institute for Advanced Study, Princeton, 2001

In this paper, Krakauer uses game theoretic models to describe how signal imitation is investigated with a view to understanding how non-arbitrary (indexical) animal-style signals might evolve culturally into diverse, arbitrary signs. That is, how signals which everyone might understand become signals only distinguishable to a certain group (think baseball coaches, pitchers, and catchers). He suggests that private, arbitrary signs emerge as a result of selective imitation within a socially structured population and become the dominant force of communication.

### "Noisy Clues to the Origin of Life"

David Krakauer and Akira Sasaki
Santa Fe Institute, 2002

In this paper Krakauer and Sasaki show how "noise" and "drift" in the genome, generally considered inimical to the origin of life, can, in combination, give rise to conditions favorable to robust replication. The higher the level of developmental noise, the more mutations a population can tolerate, so replicators can evolve longer lengths than allowed by theories that only consider mutation and drift.

SFI BULLETIN WORK IN PROGRESS

# Four Complications in Understanding the Evolutionary Process

RICHARD C. LEWONTIN

# Four Complications in Understanding the Evolutionary Process

RICHARD C. LEWONTIN

## TAXONOMIC SPACE

IN ORDER TO DISCUSS complications that arise in the understanding of evolutionary processes, it is first necessary to make clear what the evolutionary explanation is to accomplish. For this purpose the concept of "taxonomic space" is a useful one. We owe this notion to G. Evelyn Hutchinson, but Walter Fontana and others have since used it in one form or another. This taxonomic space of organisms has a huge number of dimensions, each corresponding to some character that might be used in the characterization of an individual. If one looks at the occupancy of such a space one is struck by the fact that it has a structure to it. Individual organisms are clustered in the space and those clusters are themselves clustered. And there are clusters of clusters of clusters, rather like the stars in the cosmos. The most important thing for the evolutionist is that nearly the entire space is empty, not only when extant organisms are considered, but when all organisms known to have ever existed are considered. The measure of the emptiness of that space is nearly one, and the measure of the occupancy is nearly zero.

The real problem for the evolutionist is not to explain the kinds of organisms that have actually ever existed. The real problem for the evolutionist is how it is that most kinds of potential and seemingly reasonable organisms have never existed. The problem is to explain the location of the empty spaces in the clustered assemblage of occupied points. It is easy to describe organisms that have never existed. There are snakes that live in the grass, but there are no grass-eating snakes. Birds perch in trees, yet , aside from a few exceptions, they do not eat all that greenery around them, but rather spend a great deal of energy searching for food. So why are there virtually no leaf-eating birds? The fact that the measure of the unoccupied space is so big compared to the measure of the occupied space, means that explanations of that lack of occupancy are not so easy to come by. That most of the space is empty is expected since the dimensionality is enormous and only a relatively small number of organisms have come into existence since the beginning of life. Since there has only been one history of life the reason for the low occupancy in the total space is the finiteness of time.

## HIERARCHICAL CLUMPING

THE STRUCTURE OF THE OCCUPANCY is another matter. Organisms are underdispersed in taxonomic space and we need to understand the causes of the hierarchical clumping. One reason for hierarchical clumping in taxonomic space is simply that organisms arise one from another. If an organism is someplace in taxonomic space it is likely that its immediate descendants will be someplace close by in the space rather than someplace far away. It may not be that a particular region in the space is impossible to fill or that you can't get there from here, but that there has not been enough time for evolution to fill that space.

On the other hand, the structure of accessibility may make it impossible to get there from here without retracing the steps to a remote branch point that led from a distant ancestral state. One remarkable evolutionary example of not being able to get there from here is that no vertebrate has ever succeeded in evolving wings without giving up something. There are no hexapod vertebrates. Bats and birds have had to give up their forelimbs to produce wings. We will never evolve into a race of angels because we do not have the genotype that will allow for the possession of arms, legs, and wings. There is no general structural problem of evolving multiple limbs and multiple wings. Insects have succeeded in evolving six legs and four wings. So the problem for vertebrates is that of not being able to get there from here without retracing the evolution of vertebrates from invertebrates. In the absence of a very large numbers of trials such as we have in the case of the entire collection of vertebrates, we cannot know

whether a specific "hole" in the space is a consequence of the structure of accessibility or simply the chance result of a small sample size.

Taxonomic space may be clumped because there are ways of making a living that are so costly or have such a low survivorship and competitive ability in the face of already existing organisms that natural selection has prevented their occurrence except as rare mutational forms. Finally, there are some processes and structures that may simply not work given the general structure of the organisms in which they might occur. Despite the immense variation in methods of locomotion that animals have evolved, there are no organisms that move along the ground on wheels. Presumably this is a consequence of the problem of enervating and supplying nutrients to an axially rotating macroscopic structure.

## FOUR COMPLICATIONS

WHEN WE CONCERN OURSELVES with "innovation" and "novelty" in evolution we are concerned with the occupation of a region of the taxonomic space that has been previously empty. Unlike Walter Fontana's usage, novelty for the biologist is not the occupancy of a state that is somehow "difficult" to get to, but rather the more intuitive notion of the occupancy of a state that is a surprise, because it has never happened before despite a very large number of trials. Such novelties need not be very distant in the space from already existing forms and they need not be very large unoccupied regions, but may be in taxonomically quite small subspaces, as for example the evolution of a grass-eating snake. It is the pathways of evolution of novelties as I have defined them here that have shown a variety of possibilities that are themselves unexpected and whose occurrence should caution us against making easy model assumptions about what it takes to produce an evolutionary novelty.

## EMPTY SPACE DOESN'T TELL US MUCH

THE FIRST FACT that we must take into account is that we cannot judge how easy it is to create a novelty from the simple observation that parts of taxonomic space seem to have been avoided by organisms. There is a vast literature produced during the middle of the 20th century showing that there exists within species a large reservoir of standing genetic variation that can be used by selection to move a population to a position in the space that is not only currently unoccupied, but appears to be prohibited by some genetic or developmental constraint. The best known cases are those in which some aspect of the phenotype is invariant within a species, but variation between individuals can be produced by stressing the development either genetically or environmentally. By selecting among the variants the mean phenotype of the population can be changed and this change is heritable, demonstrating that there was genetic variation relevant to the character in the population but that under normal developmental circumstances this variation was hidden. That is, the development of the phenotype was buffered or "canalized" (Waddington, 1953; Rendel, 1959). Such changes can alter a character that is invariant not only within a species, but over a large taxonomic range, as for example placement of the three simple light receptors (ocelli) and their six associated sensory bristles on the head of all individuals in all species of the genus Drosophila. The ocelli are normally symmetrically placed, one anterior to the left, one to the right, and one posterior on the midline of the head (Figure 1a). Maynard Smith and Sondhi, (1960) succeeded in creating lines with only the posterior ocelli and, more surprisingly, lines in which the majority of individuals were asymmetrical (Figure 1b).

What is less well known is that allometric shape patterns that appear to be the consequence of unbreakable allometric relations that apply over many species of different size can also be changed by genetic variation already present within species. An example is the experiment of Anna Haynes (1989) on wing dimensions in *Drosophila*. Figure 2 shows two wing vein lengths that are negatively correlated among individuals within all species of *Drosophila* and between species means of all species in the genus. Haynes selected individuals in *Drosophila melanogaster* for which both measurements were larger (relative to a control length on the same wing) than the mean and, in another selected line, in which both were smaller than the mean. As a result in only 15 generations she succeeded in changing the correlation between the measurements from -.4 to +.2, breaking a genus-wide correlation. Such a genus-wide correlation seems an obvious candidate for a basic developmental

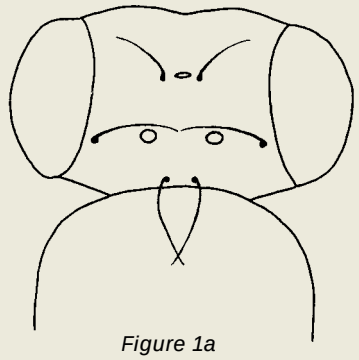


Figure 1a

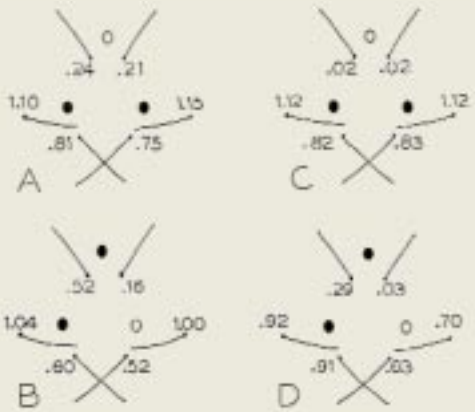



Figure 1b

*Figure 1* Ocelli and ocellar bristles in *Drosophila*. a) Normal pattern; b) result of selection for two ocelli in lines selected only for posterior ocelli (A,C) and for one anterior and one posterior ocellus (B,D). Numbers indicate the mean number of ocellar bristles at each position. (From Maynard Smith and Sondhi, 1960).

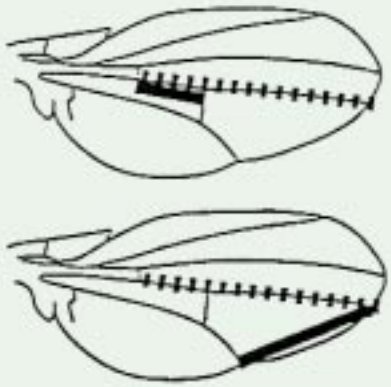


*Figure 2* Wing dimensions measured in the experiment of Haynes (1989). Dashed line is the control length. Solid lines are the lengths whose ratio to the control length is used as a basis for selection.

constraint, yet the experiment shows that it is trivially easy to break using the genetic variation that is already present in the species.

In this case we must conclude that the unoccupied region of the phenotypic space is easily accessible genetically and developmentally, but is empty because of natural selection. The same phenomenon was demonstrated for anterior and posterior eye spots on the wings of the butterfly *Bicyclus anynana* by Beldade et al. (2002). A strong positive correlation in the size of anterior and posterior eye spot size and other serially repeated features is the rule in butterflies and has been assumed to be a consequence of basic developmental mechanisms of anterio-posterior differentiation. The experiment reversed the correlation within 11 generations of selection. In both cases, despite the universality of the correlations in nature, there was enough genetic variation in growth relations within a population to allow a selective reversal within a few generations of the pattern.

A thorough aerodynamic modeling of the relation between fly size, lift, and wing dimensions in *Drosophila* might reveal a functional rule for the case of the fruit-flies. But, there are other selective reasons besides immediate function that keep regions of the space empty. There is a large literature showing that *Drosophila* females discriminate in their acceptance of courting males against individuals who deviate from the usual morphology for the species, as for example, deviant eye or body colors. It is this discrimination that prevents mating between species, but it also keeps the morphology of a given species within narrow bounds. It is part of the theoretical commitment of "evo-devo," the study of the evolution of development and the influence of developmental pathways on evolution, that shape is greatly constrained by basic developmental relations resulting from cell-to-cell signalling and gradients in gene transcription that are more or less fixed across a wide range of organisms. That may indeed be true for some features of development, but it is also clear that the observed constancy of some feature is not in itself a demonstration of such genetically determined invariance. At least for wings in flies and moths we must assume that natural selection is playing a stabilizing role in preventing evolutionary change in these organisms that is already possible with the genetic variability that they possess.

## SMALL CHANGES LEAD TO FUNCTIONAL NOVELTIES

THE SECOND COMPLICATION is that what we judge to be extremely small changes can produce what everyone would agree to be functional novelties. An example is a case in which a biochemical novelty may arise by a single very small molecular change. Newcomb, Campbell et al. (1997) found that the acquisition of organophosphate herbicide resistance in the blowfly, *Lucilia coprina*, is a consequence of a single amino acid substitution in the active site of a carboxylesterase that abolished that enzyme specificity and converted the enzyme to an organophosphatase. Figure 3 shows

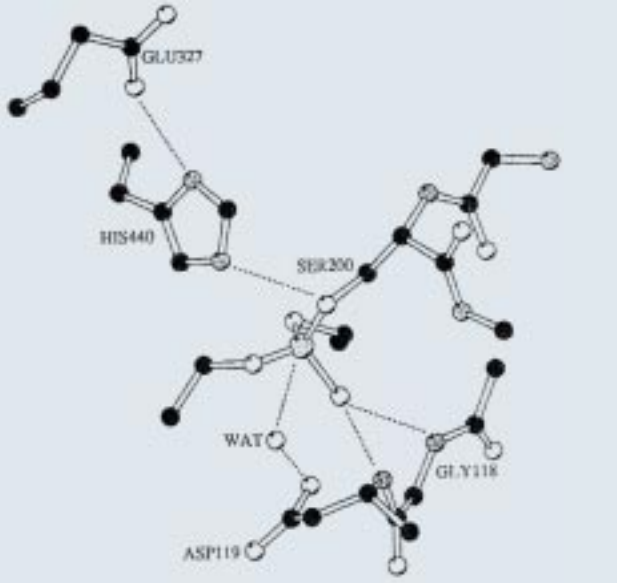



Figure 3 Molecular structure of active site of cholinesterase in *Lucilia coprina,* showing the water molecule bound at the aspartic acid residue (119) and the phosphate bound to the serine residue (200). (From Newcomb et al., 1997).

the three-dimensional structure of a closely related esterase with essentially the same structure as the carboxyesterase at the active site. The amino acid mutation that changed the function was the substitution of an asparagine residue for a glycine that allows a water molecule to be bound near the site of binding of the organophosphate. The structural change allows the molecule to participate in an attack on the phosphate bond, hydrolyzing it and destroying a molecule of the organophosphate. Thus, the qualitative change in specificity was a consequence of a small change in the angle at which the substituted amino acid was held in the folded molecule. That this change was not an extraordinary event was shown by the discovery of a second, different amino acid substitution that had the same effect. So, small genetic changes may lead to novel adaptive consequences.

## GETTING THERE FROM HERE

A THIRD COMPLICATION in the process of evolutionary change arises from the topology of accessibility of states, the problem of "getting there from here." One of the most illuminating and well-understood cases at the genetic level is Barry Hall's selection of a novel biochemical function in E. coli.

Hall (1978) set about to select *E. coli* that could use a novel carbon source, lactobionate, for its energy, instead of the usual lactose. For this purpose he used a gene, *ebg (*extra beta galactosidase) which had a low efficiency for cleaving the galactosidic bond of lactose and could be dispensed with in normal lactose metabolism. The first step in the experiment was to knock out the *lac* gene that codes for the normal beta-galactosidase, making a strain that required the ebg gene for normal lactose metabolism. Using a mutagen, he succeeded in accumulating mutations of ebg that would allow growth on lactobionate, but the evolutionary path to this state was not direct. He was not able to select directly for the new substrate. First he had to select for a control mutation such that the *ebg* gene would be transcribed even in the absence of lactose as an inducer of transcription. Next, he had to select for increased activity on lactose. Then these first selected stages had to be followed by a stage of selection for an intermediate substrate, lactulose, and then a strain that could ferment lactulose was successfully selected to grow on lactobionate. Moreover, at each stage there were several strains that possessed the same biochemical phenotype but only some of them could be further selected to the next stage. This result illustrates that the pathway through the space of genotypes from one phenotypic state to another is complex, rather like a maze with many dead ends. Only a restricted subset of all the pathways that lead to the first adaptation are open to the next so that evolution of a novelty may be very difficult to achieve. This suggests one reason for the apparent conservatism of intermediary metabolism.

## DIFFERENTIAL FITNESS

FINALLY, WE MUST CONSIDER the way in which differential fitness constrains the occupancy of the taxonomic space. Unfortunately the determination of fitness is a great deal more complicated than is usually supposed. It is easy to say that fitness of a type is its "relative probability of survival and reproduction" but turning that phrase into a coherent measure that can do work in evolutionary explanation is not so easy.

First, it is obvious that the fitness of a type depends on the environment in which the organism lives. But the environment is not independent of the organism. Organisms, by their biology, determine what aspects of the external world are relevant to them and constantly change their environment by their life activities. That means that as a collection of organisms evolves, their environment evolves with them. The

evolution of organism and environment may be described by a pair of coupled differential equations in which changes in both organism [d(org)] and environment [d(env)] are functions of both variables:

$$d(org)/dt = f(org, env)$$

$$d(env)/dt = g(org, env)$$

A consequence of the codependence of the properties of organisms and their environment is that the Darwinian fitness relations among competing types can be very complex. In particular, the relative fitnesses of genotypes may depend both on the population density of the organisms and on the relative frequency and identity of the competing types. An example of this can be seen in experiments on the effect of population density and composition in *Drosophila* (Lewontin, 1955; Lewontin and Matsuo, 1963). In these experiments newly hatched *Drosophila* larvae were placed on a measured amount of an agar medium on which yeast was seeded. An example of a typical result is shown in Figure 4 for an experiment on *Drosophila melanogaster* where the absolute probability of survival to adulthood of different genotypes was measured at different population densities. The highest probability of survival is not at the lowest density, but at an intermediate density (4-8 per vial). This intermediate optimum is a consequence of the larvae tunneling in the agar, which increases the surface area for yeast growth that is the food of the larvae. The effect can be abolished by making the food so soft that no tunnels are produced. The next step is to mix larvae of different genotypes at various densities to observe the relative probabilities of survival in competition. A typical result is shown in Figure 5 from an experiment on *Drosophila busckii*. The solid line is the predicted relative survival of two genotypes at different densities, the prediction coming from the absolute survival of the genotypes in pure culture. The dashed and dotted lines are the observed relative survivals in mixed culture at the various densities. What Figure 5 shows is that only at the optimal density (32 per vial for this species) is the actual relative survival predictable from the pure culture survivals. At the non-optimal densities one genotype is superior to the other, and the degree of this superiority depends both on total density and on the relative proportion of the two genotypes. That is, the force of selection is both density and frequency dependent.

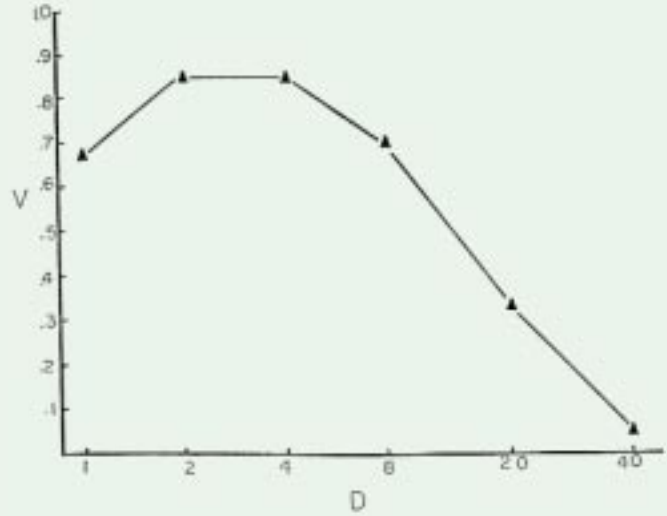



*Figure 4* Survival of *Drosophila* larvae as a function of density. (From Lewontin, 1955).

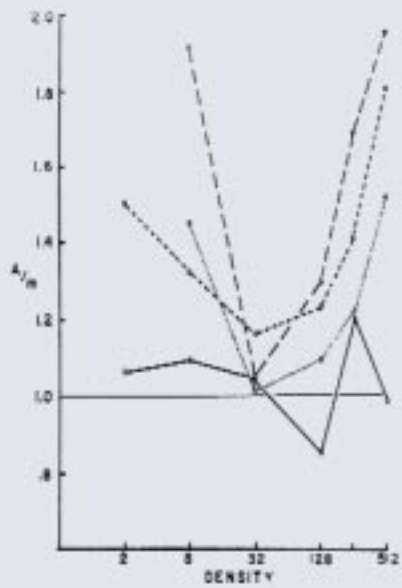



*Figure 5* Relative survival of two competing larval genotypes of *Drosophila busckii* as a function of density and composition. Solid line: predicted relative survival from pure culture experiments of Acme and mutant. Long dashes: observed relative survival in 75% Acme cultures; Short dashes: observed relative survival in 50% Acme cultures; Dots: observed relative survival in 25% Acme cultures. (From Lewontin and Matsuo, 1963).

The complications that arise from frequency dependence are even greater than those shown in the previous experiment. In experiments involving competition of several genotypes taken two at a time, Dobzhansky (1948) showed lack of transitivity of fitness. That is, genotype A is more fit than genotype B in an experiment involving only these two genotypes, and B is more fit than C in two-way competition, but

in three-way competition C beats A. If organisms play a game of scissors-paper-stone in which there is no simple transitivity of differential fitness, then no predictions of the actual outcome or application of game theory that depends on standard utility theory is possible without a detailed mapping of the fitness or utility space.

The difficulties of the concept of fitness are, unfortunately, much deeper than the problem of frequency and density dependence. The problem is that it is not entirely clear what fitness is. Darwin took the metaphorical sense of fitness literally. The natural properties of different types resulted in their differential "fit" into the environment in which they lived. The better the fit to the environment the more likely they were to survive and the greater their rate of reproduction. This differential rate of reproduction would then result in a change of abundance of the different types.

In modern evolutionary theory, however, "fitness" is no longer a characterization of the relation of the organism to the environment that leads to reproductive consequences, but is meant to be a quantitative expression of the differential reproductive schedules themselves. Darwin's sense of fit has been completely bypassed. The natural properties of organisms lead to differential reproductive schedules and these must somehow be mappable onto a quantitative function, fitness that can enter into formal prediction structures. There is also an implication that fitness is a scalar quantity since much of the informal argument of evolutionary theory characterizes one type as "more fit" than another. To make such a scalar work in prediction, a Standard Viability Model of reproduction has been created in which the organisms have discrete generations so that all can be regarded as being born simultaneously and all differences in fitness are the different probabilities of survivorship to sexual maturity.

Any relaxation from the Standard Viability Model produces serious problems in the definition of fitness. If there are differences in fertility and the organisms are sexually reproducing, then fertility, in the general case, is a function of the mating pair. Averaging over different mating combinations will provide a mean fertility of each genotype, but such means are necessarily frequency dependent so the quantitative values will change during the evolutionary process and even the ordering of type fitnesses may shift. The fitness of a genotype can then not be assigned apart from a statement of its frequency in the population and the rules of mating preferences. If we further relax the Standard Viability Model to include all those species with overlapping generations and reproduction that occur over an extended period of the individual's lifetime, then the totality of the reproductive information consists in the age schedule of relative mortality and fertility of different types, embodied in the probability of living from birth to age x, $l_x$, and the number of offspring, $b_x$, produced by an individual of age x in the interval x to x+dx. If the species is sexually reproducing, the vector of age-specific fertilities $b_x$ must be substituted by a matrix of the fertilities of couples $B_{xy}$ of females aged x and males aged y for each genotypic composition of the pair. These are then averaged to produce a matrix of frequency-dependent means for each genotype. These values change not only as frequencies change but as the population changes its age distribution. The attempt by Fisher to circumvent these complications by defining the fitness of a genotype as the root m of the Euler equation did not solve the problem because it confuses the rate of reproduction of a type with the rate of reproduction by a type, which are not at all the same thing in a sexually reproducing species, and also assumes that the population is at the stable age distribution which is not true for a population changing its type frequencies. But the problem is even worse.

It is the case that all the information about the relative reproductive behavior of types in the population is contained in the complete $l_x$ and $b_x$ schedules of all the genotypes (and, for sexually reproducing species, the age schedule of mating pairs and the frequencies of the different types). Yet this complete reproductive information is insufficient to predict whether a type will increase or decrease in frequency in the population! It is also necessary to know whether the population as a whole is growing larger, is stable in numbers, or is decreasing in numbers. The same type that may be favored in a growing population may be disfavored in a shrinking population. Suppose the only difference between two types is not in their total reproduction but in their age schedule of progeny production. A type that produces offspring at an early age will increase in relative frequency in a growing population because it has reproduced while the total population is still small. If the population is shrinking, however, it pays to postpone reproduction since the total popula-

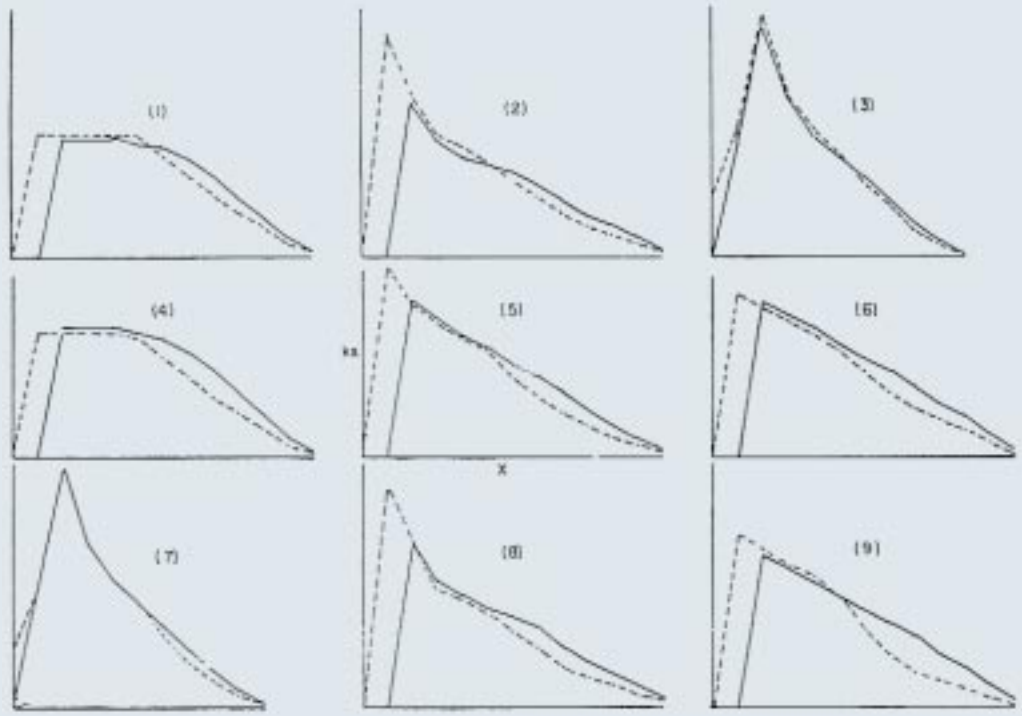



*Figure 6* Pairs of contrasting kx schedules for which frequency changes were calculated in populations of increasing and decreasing size. Abscissa: kx, ordinate: age, x. (From Charlesworth and Giesel, 1972).

tion will then be smaller at the time of reproduction of the tardy type.

Unfortunately, a simple examination of the reproductive schedules does not always reveal that one schedule is obviously "back-loaded" and one "front-loaded" as economists would put it. Figure 6 from the work of Charlesworth and Giesel (1972) shows a number of pairs of hypothetical relative reproductive schedules expressed as $k_x$, the product of $l_x$ and $b_x$. In cases 4, 5, 6, and 7, which of the two schedules was favored depended on whether the population was increasing or decreasing in total size. In cases 1, 2, 3, 8, and 9 there was no such contingency. There is no obvious common feature that would have allowed us to predict these classes. How, then, are we to assign relative fitnesses of types based solely on their properties of reproduction? But if we cannot do that, what does it mean to say that a type with one set of natural properties is more reproductively fit than another? This problem has led some theorists to equate fitness with outcome. If a type increases in a population then it is, by definition, more fit. But this suffers from two difficulties. First, it does not distinguish random changes in frequencies in finite populations from changes that are a consequence of different biological properties. Finally, it destroys any use of differential fitness as an explanation of change. It simply affirms that types change in frequency. But we already knew that.

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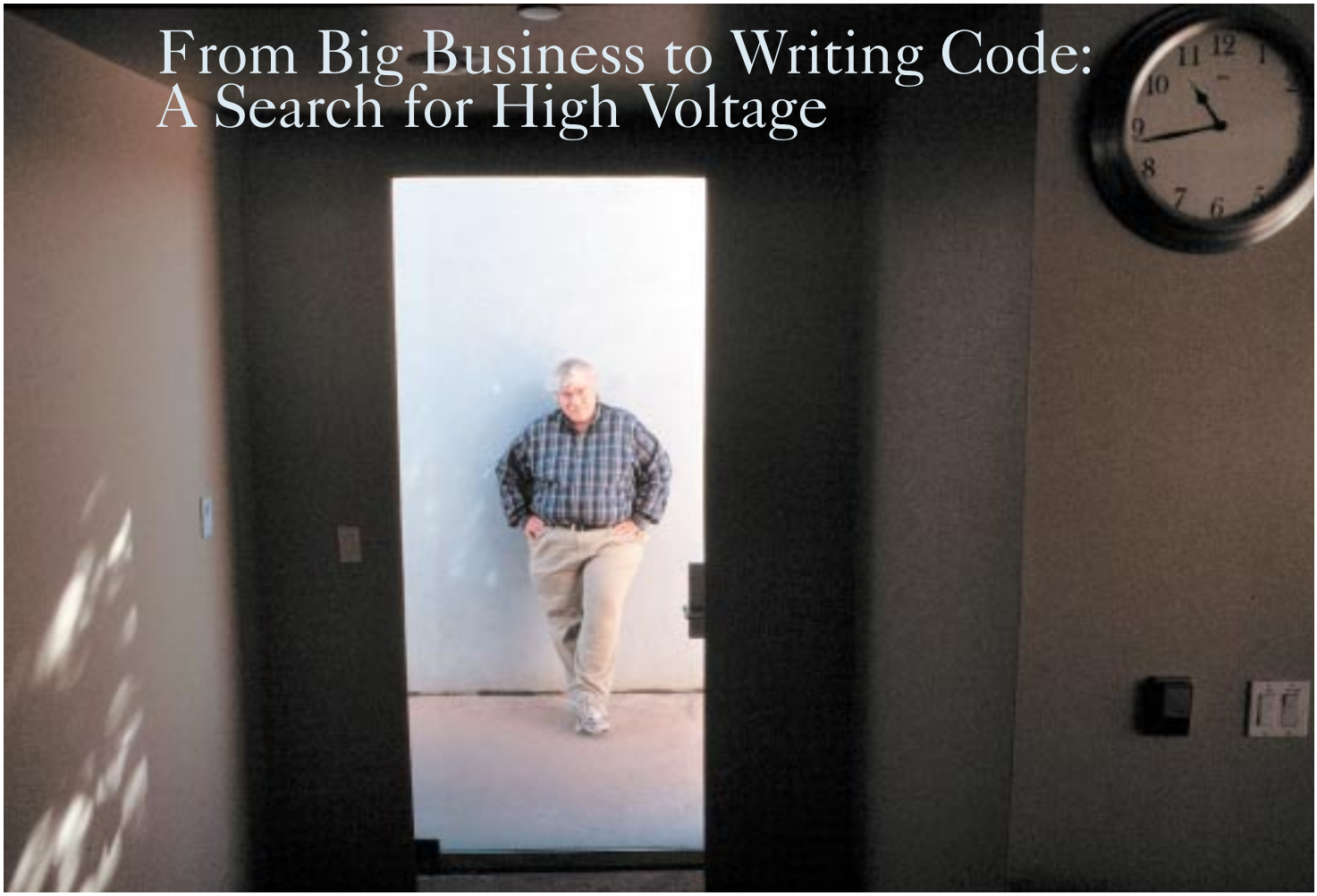
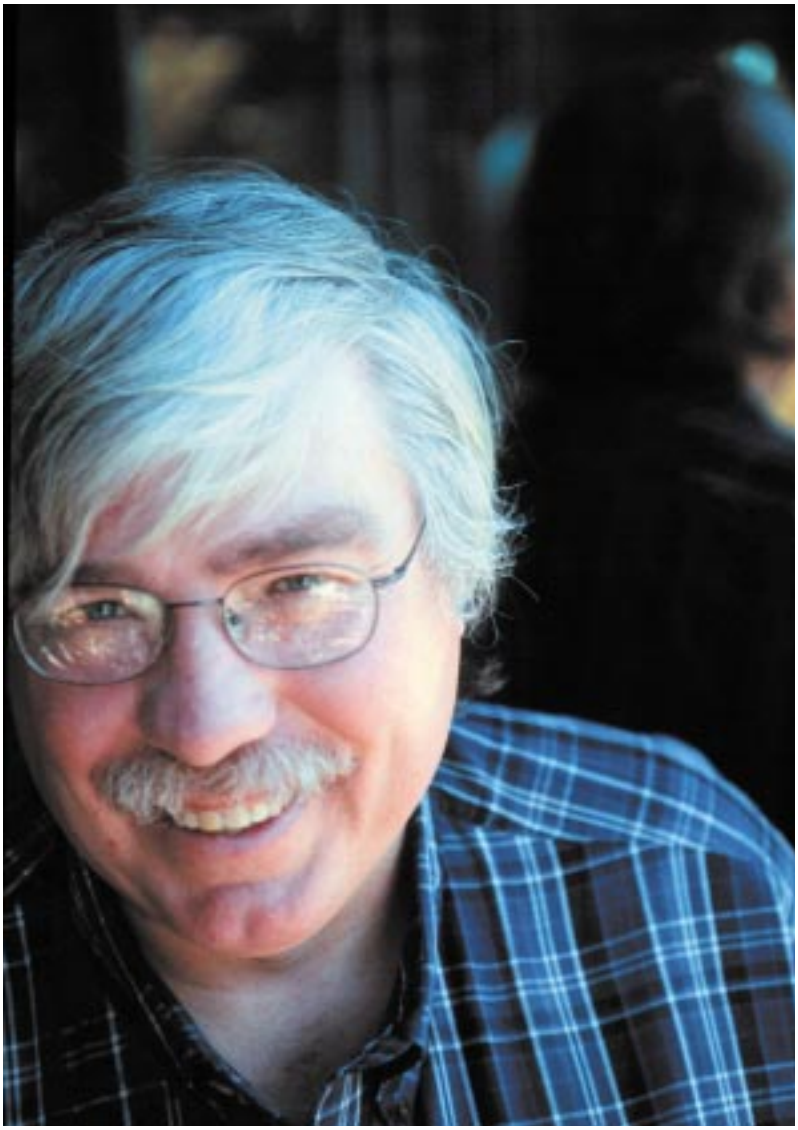
# From Big Business to Writing Code: A Search for High Voltage



BY LESLEY S. KING

JIM RUTT, RESEARCHER IN RESIDENCE AT SFI, HAS THE GIFT OF FORESIGHT. It manifests in an uncanny ability to take up hobbies that within five years time land him smack in the middle of national trends. It happened with personal computing, and again with the Internet. Now his focus has turned to complex adaptive systems (CAS), a subject that led him to SFI.

PHOTOS: JULIE GRABER



A man with an imposing presence, Rutt's very nature seems to make things happen. He took a business degree from MIT and parlayed it into the head position of Network Solutions, the company that manages Internet domains such as .com, .org, and .net. He negotiated Network Solutions' buyout by VeriSign, a $15.3 billion acquisition, through which he retained the titles of chief strategy officer for the company and president of its mass-market division.

He left that to do research in complex adaptive systems.

You've got to wonder what would make a CEO of a major corporation give up power lunches and six-figure paychecks to sit in an SFI office and write computer code. For Rutt, the decision was easy: "As a CEO you spend the day in meetings with zero voltage. It's a mile wide and an inch thick." In short, he's at SFI for the intellectual jolt and the depth of experience that comes from developing a body of knowledge.

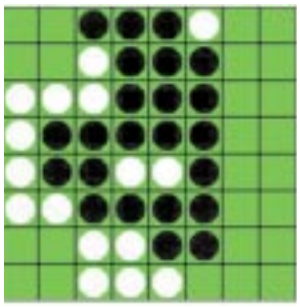
Most of his success in life has come through just such searches for knowledge. In 1979, when mainframe computers ruled the land, he spent what he termed "90 percent" of his net worth on a loaded Apple II personal computer, embarking early on a trend that didn't become significant until 1984. He used his Apple PC to explore the Internet beginning in 1989, well before people used it commercially; not until five years later, around 1993-1994, did the Internet become a significant business tool.

## PLAYING SMART GAMES

In 1997, as chief technology officer for Thompson Corporation, a big publishing company based in Toronto, Rutt came across a one-paragraph description of genetic algorithms, which are computational models of evolution. From there he searched Amazon.com and found one reference, John Holland's book, *Adaptation in Natural and Artificial Systems*.

This led him to complex adaptive systems, which Holland has defined as composed of many interacting and adapting agents. CAS theory has been used to better understand events on a small scale, such the human immune system, and on a much larger scale, such as the evolution of ecosystems.

"I read Holland's book and it started me thinking," says Rutt. From there he quickly swallowed up the works of John Koza, Melanie Mitchell, and David Goldberg. "I realized this field was wider than evolutionary computing. I saw it as a useful way of exploring many practical things," says Rutt.



By the fall of 2001, CAS was his main hobby. He wrote software game-playing agents that played Othello, a computerized board game in which players work to reverse (turn from black to

white or vice versa) their opponent's game pieces until one player occupies most of the board.

"I used evolutionary techniques to create neural nets and let the neural nets play Othello and let genetic algorithms generate the next generation of neural nets, and they got smarter and smarter. It was a little eerie. I felt the hair on my neck stand up," he says. "I hadn't told them anything other than the rules of the game."

Aware of his ability to make things happen, Rutt is careful where he directs his attention. "It's important that I don't go into these endeavors with hardcore business applications in mind. I like to learn the scope and richness of the field. When you do that an idea of real merit is likely to pop out."

## EXPLORING A BLACK ART

Even though this bold entrepreneur has sworn off starting any new companies during this phase of his life, opportunities seem to seek him out. After an article about his new interests appeared in The New York Times, he was flooded with requests. "It mostly triggered inbound inquiries from people looking for investment in their stupid ideas," says Rutt. However, one did catch his eye.

A software startup in Ottawa, Canada, Analog Design Automation (www.analogsynthesis.com), invited him to come and see their operation. "I liked them. There were six founders, none older than 27. They had bunk beds in their office, and we sat around chatting and drinking beer," says Rutt. The company's list of backers—Intel, Synopsis, and the Royal Bank of Canada—sweetened the deal, so Rutt agreed to be their chairman of the board.

It seems a bit odd that a forward thinker such as Rutt would be involved with analog. But, he explains, "They're using evolutionary computing and related CAS-style thinking to solve one of the big problems in the electronics industry."

It turns out that 18 percent of all integrated circuits still have analog components, and while companies such as Intel, Broadcom, Motorola, and Texas Instruments have used software to design digital integrated circuitry, analog presents a greater challenge. "The design of analog circuits until now has been pretty much a black art," says Rutt. "It's the slowest, most difficult part of the design process. It's often the bottleneck in getting new products out the door. Our optimization tools look to break that productivity bottleneck."

## CREATING "ECOSYSTEMS" OF EVOLVING TRADING AGENTS

Rutt takes care of business such as Analog Design Automation during his first cup of coffee in the morning. The rest of the day he works as part of Doyne Farmer's group simulating financial markets. Among other things the group uses a computer model of a financial market to study the attributes of markets, posing questions such as, "Where does the spread come from?"


London Stock Exchange limit order book

The group benefits from Rutt's participation. "He brings great enthusiasm, energy, and intelligence to everything he does," says Farmer. More specifically, Rutt has, as Farmer says, "dived into the problem of how agent ecologies emerge and how they affect the market."

After his first introduction to the group's concepts, even before Rutt had come to SFI, he started working on that very problem, setting out to, as he states it, "write a smart agent that could trade against the market and make money." But, he asked himself, "How can you make money when the price is a random walk?" So he created a smart trading agent that traded in the otherwise "random limit order market," which is based on the limit order book. The limit order book is a device that stores demand and effects trades. It is the primary mechanism for price formation in most modern financial markets. Through use of this, Rutt found that the trading agent could make an actual "profit" in the model market.

Where will he go with this? His goal is to eventually create complete "ecosystems" of evolvable trading agents that create a very realistic looking market solely by trading amongst themselves. Such a smart agent-based model market would be a useful testbed in understanding the real interplay between types of investors such as "technicians," "value investors," "market makers," etc., in real markets, especially how the side effects of their strategies change the market itself.

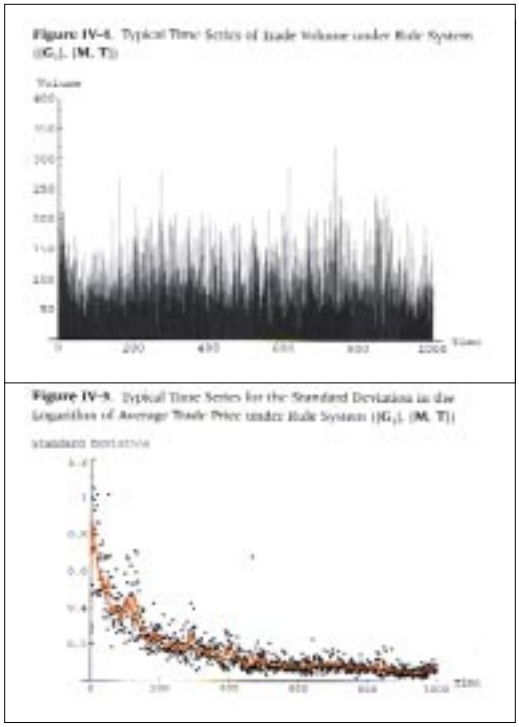
The group is fortunate to have real data from the London Stock Exchange (LSE). "We have every order, including all the limit orders in the LSE data, so it's very fine grained. We can even recreate the state of the order book through time," says Rutt.

"I hope to gain an understanding of how various classes of investors interact to produce the phenomenon that is the market. My particular interest is in trying to understand volatility. Why do stock prices fluctuate so much, even for mature and stable companies?

A fully functional model could possibly explain this."

## SURVIVING WITHIN A SUGARSCAPE

While at SFI, Rutt is also directing his gaze toward simulated societies, expanding on the work of Rob Axtell and Joshua Epstein on Sugarscape. He met Axtell at the Brookings Institute and later read Axtell and Epstein's book, *Growing Artificial Societies*. Sugarscape simulates the interaction of adaptive agents as they perform basic survival activities such as searching for food and trading. This takes place on an artificial landscape with sugar as the main commodity—thus it's called a Sugarscape. In this model, Epstein and Axtell hope to be able to decode collective phenomena, such as economies, ecosystems, epidemics, social revolutions, arms races, and wars, by uncovering simple local rules that generate them.



Figures from *Growing Artificial Societies*

"I want to add into Sugarscape production and technological evolution, and see what kind of societies you can grow," says Rutt. With his background in those areas, and the tenacity with which he approaches any subject, the model, and maybe even society, will likely benefit.

Lesley S. King is a freelance writer whose articles have appeared in *Audubon* and *The New York Times*.

# Innovation in Natural, Experimental, and Applied Evolution

**SUPPORTED BY THE DAVID AND LUCILE PACKARD FOUNDATION**

*Natural selection may explain the survival of the fittest, but it cannot explain the arrival of the fittest.*

— *HUGO DEVRIES (1904)*

## Evolutionary Breakthroughs

ALL OF THE EXTRAORDINARY organizational forms and behavioral strategies that we witness in nature have arisen through the process of inheritance with diversification and selection. The formal treatment of evolutionary dynamics is presently cast in terms of the changing frequencies of fixed entities: genes, linkage groups, individuals, and social groups. Yet it is the arising of these and other organizational structures—the emergence of novel entities—that is of profound interest, both theoretically and for the applications this understanding will facilitate.

Evolutionary innovation involves the acquisition of novel morphologies—behaviors or other attributes that open new niches, providing access to new ways of making a living. These include the major evolutionary transitions such as the origins of life and its major domains, the development of photosynthesis and other energy-capture methods, eukaryotes, and multicellularity. But it also includes the less sweeping innovations that solve more circumscribed problems. Artificially directed evolution has been applied with striking results to developing proteins, RNAs, viruses, and bacteria for specific functions. Evolutionary algorithms for the solution of mathematical problems have produced surprisingly non-intuitive solutions. In the evolution of digital organisms, we have witnessed both clever problem solving and major reorganizations such as the unanticipated emergence of parasites, parasite-resistant organisms, and hyperparasites.

A key to posing the questions appropriately, particularly with respect to potential applications, is the recognition that evolutionary innovation is recognizable only retrospectively. Organisms face an infinite number of problems and "work on" many of them simultaneously. An innovation represents a breakthrough solution to a problem not uniquely posed in advance.

The issue of evolutionary innovation is not new; many researchers have struggled toward its elucidation. Several recent developments, however, urge a renewal of effort. Technological advances have made the acquisition and manipulation of relevant data much easier: Many genomes have been completely sequenced. We can now measure the expression levels for all of an organism's genes simultaneously, providing unprecedented insight into cellular regulation. Quantitative developmental and paleontological data are much more abundant now than just 20 years ago. Experimental techniques for manipulating bacterial and viral evolution over thousands of generations have been developed, as have engineering techniques for harnessing evolution for the "design" of novel biological products. Recent advances in computing power permit systematic exploration of complex mathematical models, simulations of evolutionary systems, and statistical analyses of very large structured datasets. As a result, powerful theoretical perspectives have been gained on several key organizing principles.

In July 2002 the David and Lucile Packard Foundation made a generous two-year award to SFI to support new research on innovation in natural, experimental, and applied evolution. The David and Lucile Packard Foundation was created in 1964 by David Packard (1912-1996) and Lucile Salter Packard (1914-1987). The Foundation provides grants to nonprofit organizations in the broad program areas of conservation; population; science; children, families, and communities; arts; and organizational effectiveness and philanthropy. The Foundation provides national and international grants.

The innovation project, headed by Tom Kepler, former SFI vice president for Academic Affairs and now professor of biostatistics and bioinformatics at Duke University Medical Center and SFI External Faculty member will address questions such as:

**What are the most useful and elegant formal representations for open-ended evolutionary processes?**

**What drives evolutionary innovation, and what organizational circumstances control its rates of occurrence and success?**

**What are the relationships among innovations at distinct structural levels: genomic, developmental, morphological, and ecological?**

**How can technologists using directed evolution to design electronic circuits or to develop pharmaceuticals or, using evolutionary computation to solve formal problems, create conditions that encourage the discovery of innovative designs and solutions?**

The project will gather experts working in the range of evolutionary studies—from natural and experimental evolution to evolutionary computation and evolutionary engineering—for collaborative experimental and theoretical work.

The task is ambitious, but much groundwork has been laid, in many cases by researchers associated with the Institute. SFI Research Professor Walter Fontana and Leo Buss (Yale) have described the open-ended evolution of "autocatalytic sets" of abstract chemical reactions; External Faculty member Tom Ray's (University of Oklahoma) digital organisms, competing for CPU time, exhibit the unexpected emergence of parasitism and parasite resistance. SFI Research Professor Jim Crutchfield's and External Faculty member Melanie Mitchell's (Oregon Health and Science University) adaptive computation research elucidates the behavior of evolving algorithms. SFI Science Board member Richard Lewontin's (Harvard) and External Faculty member Douglas Erwin's (Smithsonian) combined empirical and theoretical work on life's major transitions examined the interplay of niche formation and speciation. Kepler's analysis of immunogenetic sequence data reveals complex relationships between somatic and germline evolution. Finally, Science Board member Frances Arnold (California Institute of Technology) uses directed evolution to explore the vast space enzyme functions never explored in nature and to engineer novel macromolecules.

## Mapping Many Possibilities

In most mathematical representations of systems evolving in time, the state space, or space of possibilities, is specified in advance. Mathematical population-dynamic models of evolution unfold on the space of gene frequencies with the genes and their relevant properties themselves specified at the outset. The state space for a mathematical theory of innovation is necessarily infinite (otherwise all possibilities can be enumerated in advance). Researchers will explore, therefore, mathematical representations in which the state space itself is constructed dynamically as populations evolve upon it, e.g., through the combinatorial assembly of fundamental building blocks of rules or forms, embodied in generative construction rules.

A theme running through much if not all of the mathematical thinking on these matters is that of the topological structure of maps from one space to another. For example, the replicative process maps genotype to genotype; genotype is mapped to phenotype via development; phenotype is mapped to fitness via interactions with the environment, broadly construed. The underlying spaces support a natural notion of distance, e.g., the number of point-mutations from one genotype to another, so these maps can exhibit discontinuities, mapping points nearby in one space to points quite distant in another. These features are known in mathematics as bifurcations and are well characterized in a large number of contexts.

Theoretical efforts will aim at studying the properties of these maps and developing methods for inferring their structure from data. Efforts will also aim at the development of compact representations of generative dynamical systems for use in applications.

## RNA Reveals an Intricate Interplay

Much theoretical work on RNA folding has been motivated by the relative simplicity of its genotype-phenotype map, illustrating the evolutionary interplay of environmental noise, plasticity, epistasis, and modulari-

ty on evolvability. Computational studies of RNA folding predict that sequences acquiring the same secondary structure form an extensive network connected by single-base changes such that large distances can be traveled in sequence space, jumping from neighbor to neighbor, without ever changing secondary structure. This work underscores the profound consequences of neutrality for evolutionary innovation. Neutrality enables phenotypic change by permitting the accumulation of phenotypically silent mutations that set the context for subsequent mutations to alter the phenotype.

Advances in laboratory techniques and the dramatic reduction in the costs for handling, synthesizing, screening, and amplifying arbitrary RNA sequences have rendered possible the systematic investigation of the structural and functional properties of RNA sequence space. Striking verification was obtained in Erik Schultes' experiments at the Whitehead Institute in which a wild-type hepatitis delta virus ribozyme (nuclease), was converted into a class III ribozyme (ligase) by walking a neutral path of roughly 40 mutations into the neutral network of the ligation function and from there another 40 neutral mutations to the naturally occurring ligation ribozyme.

This project will continue to clarify the structure of neutral networks by theoretical means by establishing an integrated theoretical/experimental effort with the Whitehead Institute to examine evolutionary innovation in the RNA system.

## Evolutionary Innovation in Deep Time

The rich array of comparative developmental data for animals, plants, and microbial groups has revealed far greater conservation of developmental control systems and gene regulatory interactions than had ever been anticipated. Together with the introduction of rigorous phylogenetic methods to establish evolutionary relationships between groups, this is increasingly allowing the reconstruction of the underlying basis for a variety of innovations, from limb formation to the evolution of flowers. Paleontologists have generated a detailed record for many of the most significant evolutionary innovations in the history of life, allowing us to place these events in an appropriate environmental context and evaluate the rates and timing of these events. Finally, ecological theory has kept pace with these other developments, allowing the construction of more realistic models than would have been true even five years ago. We are reaching a point where development, ecology, and paleontology are once again asking similar questions.

emergence of novel entities

acquisition of novel morphologies

surprisingly non-intuitive solutions

unanticipated emergence of parasites

"design" of novel biological products

Major turning points in the history of life, such as the spread of novel metabolic activities in the first billion years of earth history—including the spread of oxygenic photosynthesis, the development of multi-cellular life, the radiation of marine animals, and the development of terrestrial ecosystems—all share some basic similarities. In each case, innovation was constructed through an evolutionary triad of environmental challenge, genetic and developmental potentiality, and ecological opportunity. Changes in the physical environment often generated new possibilities, but successful conversion required the genetic (and for multi-cellular groups, developmental) inventions from which new ecological opportunities could be constructed. For example, the appearance of animals about 580 million years ago closely follows an increase in atmospheric oxygen and dramatic climatic perturbations. Although these may have increased evolutionary rates, they cannot have been responsible for the proliferation of new cell types and morphogenetic pathways required to form the diverse array of animal body plans, or for their assortment into a wide range of different ecological roles.

These similarities will form the foundation of an effort to develop a suite of models of evolutionary innovation designed to facilitate testing and further model development. One aim is to understand niche construction, through which lineages actively modify their environment to construct their own ecological role and consequently create niches for other species. Niche construction seems to be especially significant following mass extinctions; the course of this process may facilitate innovations that reorient evolutionary

useful and elegant formal representations

evolution of "auto-catalytic sets"

digital organisms

relationships between somatic and germline evolution

trajectories. Modeling efforts in this area have begun with relatively simple ecological and evolutionary models (logistic growth and multi-trophic models) but these will be expanded to include niche construction and other positive feedback elements to explore the full array of processes believed to be driving innovation. The hypothesis is that innovation during the major turning points in evolution involves a positive feedback process between genetics, development, and ecology. In essence, these processes construct an ecospace during the innovation and early diversification of the groups involved.

In contrast, many smaller scale events appear to be fundamentally different in the processes driving them, not simply in scale. These smaller scale events appear to involve refilling an existing ecospace rather than constructing a new one, as exemplified by the displacement of native North American ants by their Argentine cousins at the beginning of the 20th century. Contrast this with the evolutionary development of insect wings from primordial gills—an innovation that opened up a completely new way of making a living and engendered a consequent major reorganization of several ecosystems, including the development of flowering plants.

## Immunity and Pathogenesis

The coevolution of microorganisms and the vertebrate immune system has produced many extraordinary examples of innovation. For example, Variola major (the causative agent of smallpox) secretes proteins that act as cytokine receptor mimics, interfering with intercellular communication among the cells of the immune system. How did these molecules evolve? Were they "stolen" from the vertebrate genome? Further examples abound in which microorganisms have evolved extraordinarily surprising mechanisms of pathogenesis, as the case of HIV so clearly demonstrates.

The immune system itself operates on principles that seem to encourage innovation. Through a series of genetic mechanisms unique to the system, the receptors for foreign molecules are stochastically assembled from libraries of gene segments and further diversified by point mutation, gene conversion, and selection. It has been shown that, as mechanisms for searching, these processes are rendered more efficient by the incorporation of biases that avoid combinations known historically to be disadvantageous. For example, through evolutionary manipulation of the particular choice among several different DNA sequences that encode exactly the same protein, the mutation rate in immunoglobulin genes is higher in those parts that encode antigen-binding regions, and lower in those that encode structural elements. Further features of individual immune cells, such as their patterns of secreted cytokines, apparently are selected through combinatorial trial and error, and ultimately serve as the basis for the formation of transient functional modules.

The crucial event that sparked the rapid evolution of the adaptive immune system is believed to be the transfer of a transposable element from a bacterium to an early vertebrate. This element eventually inserted into a gene, encoding an adhesion molecule that was subsequently duplicated and diversified, thereby becoming the substrate for the recombinatorial diversification that is the hallmark of adaptive immunity. Once the transfer had been accomplished, how was the new molecular mechanism integrated into the regulatory apparatus of the cell? Though a rare chance event initiated the transformation, the question is how this initial singularity was able to precipitate the extraordinary reorganizations at the molecular, intracellular, and intercellular levels that led to the emergence of the entity that became the adaptive immune system.

The project will perform comparative statistical analyses of genomic, proteomic, and cell-biological data, both present in the literature and generated in the laboratory, to elucidate the co-organizational characteristics of pathogenesis and immunity contributing to the rapid generation of innovation in these systems.

## Self-perfecting Genetic Circuits

Cells routinely perform complex computational tasks that enable them to control the orchestration of thou-

sands of genes and communicate with other cells to manifest emergent properties such as growth and differentiation. Understanding and engineering the algorithms underlying the complex computational machinery of cells will have a significant impact in science and technology, particularly biotechnology, biocomputation, and medicine.

Project researchers will use laboratory evolution methods to explore innovation in genetic regulatory circuits in bacteria. Several notable recent reports demonstrate that it is possible to design and construct simple de novo genetic circuits such as a switch and an oscillator in E. coli. This work also revealed that implementation of even the simplest circuits in vivo requires tedious optimization of often poorly understood protein-DNA interactions and of mRNA and protein stabilities, among other parameters. Scientists in this project will use efficient, evolutionary design strategies for constructing functional de novo genetic circuits. They will use laboratory evolution methods to discover and optimize complex, functional genetic regulatory networks involving multiple repressors, operators, and promoters. The assumption is that evolution will prove to be generally applicable for optimizing individual "devices" as well as entire genetic circuits, and the goal will be to demonstrate how evolutionary searches are best performed in order to build libraries of devices and assemble them into functional circuits.

The research starts with the construction of genetic "logic gates" in bacteria. Each logic gate is a combination of one or more input proteins (mostly repressors) that controls expression of an output gene. Researchers will develop and evaluate various strategies for optimizing such logic gates using laboratory evolution methods. Starting at the device level, they will establish effective selection and screening methods to evolve better-performing circuits by improving individual components in the context of the whole circuit. The program will also explore means to interface in vivo genetic circuits with the outside environment by exploiting various natural transcriptional apparatuses that will be useful for applications such as sensors and gene therapy. Finally, the technologies developed at the device level will be applied to the construction of more complex circuits comprised of multiple logic gates. The technical goal is to develop strategies by which the circuits become self-perfecting under the pressure of artificial selection; only the cells that survive the selection (e.g., by producing the appropriate output protein) or perform as desired during high throughput screening, can grow and multiply. This allows a rapid search through large numbers of possible designs for those that function efficiently. The experimental research is complemented by detailed modeling studies that will allow "reverse engineering" of the evolution results and establishment of the mechanisms by which key circuit characteristics were obtained.

This research should establish a general strategy for de novo genetic circuit design and provide new insight into the natural algorithms of information processing in biological systems and biological complexity. It exploits, in powerful combination, the strengths of classical approaches in electrical circuit design (characterizing the "device physics" of gates, then composing circuits from well-understood components) with adaptation mechanisms (mutation and selection) that are the hallmark of biological systems.

**PROGRAM PARTICIPANTS**

**Frances Arnold**, Chemical Engineering, California Institute of Technology

**Mark Bedau**, Philosophy, Reed College

**Eric Bonabeau**, Engineering, Icosystem Corporation

**Jim Crutchfield**, Santa Fe Institute

**Doug Erwin**, Paleobiology, Smithsonian Institution

**Walter Fontana**, Santa Fe Institute

**Thomas B. Kepler**, Bioinformatics and Biostatistics, Duke

**David Krakauer**, Santa Fe Institute

**Laura Landweber**, Ecological Evolution, Princeton

**Richard Lewontin**, Zoology, Harvard

**Dan McShea**, Biology, Duke

**Rob Miller**, Immunology, University of New Mexico

**Melanie Mitchell**, Computer Science, Oregon Health and Science University

**Fred Nijhout**, Entomology, Duke

**Erik Schultes**, RNA, Whitehead Institute

**Ricard Solé**, Physics, Polytechnic University of Catalonia

**Andreas Wagner**, Biology, University of New Mexico

**Gunter Wagner**, Biology, Yale

# Bogotá, Budapest, Beijing, and Beyond

A number of exciting activities capture the growing pace and scope of the Institute's International Program. These include a workshop in Bogotá on settlements in civil wars, a complex systems summer school in Budapest, seven new international fellows, and a symposium in Beijing on intervention in complex systems.

Now in its third year, this global initiative continues to mature. During its first years, the Program has provided funding to support 19 fellowships, eight meetings, two summer schools, and a postdoctoral fellowship. It has also supported the visits of more than 25 international scholars to SFI, enabled the addition of international components to various Institute initiatives, and has made possible several trips by SFI researchers to the Program's targeted areas.

The project's aim is to spread SFI's scientific approach to countries throughout the world and conversely to introduce new scientific personnel and perspectives from the international community to the Institute. It targets especially areas where funding is not readily available for interdisciplinary activities, and where restrictions on the availability of funds may preclude extensive travel opportunities for educational purposes. Currently the project is focusing on participants and activities within China, India, Latin America, Africa, and Eastern Europe and the Former Soviet Union (FSU).

Funded by a generous grant from a private donor, this program is coordinated by SFI staff member Suzanne Dulle, who works closely with SFI resident and external researchers. The involvement of the research community has been identified as an increasingly important requirement to the success of the Program. As a result, each International Program workshop now involves at least one SFI scientist as a co-organizer. Additionally, each International Fellow visiting the Institute is assigned a residential mentor to encourage scientific interactions with the SFI community.

## SFI APPOINTS A NEW CLASS OF INTERNATIONAL FELLOWS

The third, 2002-2004, class of international fellows recently was selected from a pool of nearly one hundred applications. Juan Camilo Cárdenas is associate professor in the School of Environmental and Rural Studies at Pontificia Universidad Javeriana in Bogotá. His research focuses on the behavioral aspects of social life, and consequences to the environment. Cárdenas has worked with SFI researchers on projects related to land-use decisions, economic inequality, and political violence. Pablo Marquet is associate professor at the Center for Advanced Studies in Ecology and Biodiversity, Catholic University of Chile, Santiago. Marquet's research deals with the analysis of ecological systems, particularly the search for general and invariant principles that underlie the diversity and variability of these complex systems. Gabriel Mindlin is a professor in the Department of Physics at the University of Buenos Aires. Mindlin is researching the physics of birdsong, working toward a complete model that describes the physical operation of the avian vocal organ, as well as the brain architecture necessary to learn, recall, and produce vocalizations. Victor Sergeev is director of the Center for International Studies at the Moscow State Institute for International Relations. One of Russia's most eminent social scientists, Sergeev is interested in the application of cognitive and mathematical methods to the analysis of basic problems of economic and political theory. David Storch is affiliated with the Center for Theoretical Study at Charles University, Prague, Czech Republic. A zoologist and ecologist, Storch is interested in macroecological patterns, the role of environmental heterogeneity, and the interrelationships between them. Yuri Yegorov is assistant professor of economics at Central European University in Budapest. He works on mathematical formalization of models of economic interactions that are different from the "invisible hand" principle, and the development of a theory of economic fields. Martin Zimmerman is a full-time researcher at the National Science Council (CONICET) currently working in the physics department at the University of Buenos Aires. Zimmerman's research focuses on applications of network dynamics to social and economic problems.


PHOTOS: NANCY BUNDT

International Fellows are invited to make research visits to SFI during their two-year fellowship period, and they receive support in arranging meetings and workshops in their home countries. In September, for example, Fellow Nelly Kovalevskaya hosted a workshop in Novosibirsk, Russia, that explored how the complexity approach might be brought to bear on research within the Russian Academy of Science including work on biotic and abiotic adaptation, biospheric organization, and human/environmental co-evolution.

### ONLINE ACCESS TO INTERNATIONAL JOURNALS

A new benefit for Fellows this year is access to document delivery services in their home institutions. Individual accounts for each fellow are being set up with CISTI, the Canada Institute for Scientific and Technical Information, which will allow access to up-to-date information in science, technology, medicine, and other related fields. This service is being provided in response to requests from fellows whose home institutions are unable to provide affordable access to scientific journals.

### POSTDOCTORAL FELLOWSHIP GOES TO INTERNATIONAL FELLOW

A challenge in this program is finding ways to nurture enduring relationships in the target countries beyond the tenure of the fellowships. One strategy is to develop mechanisms that support sustained research collaborations. To this end, the International Program has created its first joint postdoctoral appointment: Fellow Han Jing has accepted a shared fellowship sponsored by SFI and the Institute of Systems Science (ISS) in Beijing. Han will work with Professor Guo Lei at the ISS but also spend a significant amount of time at the Institute.

### WORKSHOPS AND AN INTERNATIONAL SUMMER SCHOOL

In tandem with the Fellows' workshop initiatives in their home countries, SFI sponsors its own international workshops. In fact, nearly all SFI meetings feature rosters including international participants. What distinguishes international workshops from these is that they generally involve an international organizer or co-organizer, the venue is often in another country, and an explicit goal of the workshop, along with its scientific aims, is to extend the Institute's multidisciplinary research approach to new constituencies.

One such workshop was "Interdisciplinary Applications of Ideas from Nonextensive Statistical Mechanics and Thermodynamics" held last April at SFI, co-chaired by Murray Gell-Mann and Constantino Tsallis, a professor at the Brazilian Center for Physical Sciences in Rio de Janeiro. In June, former SFI Vice President for Academic Affairs Tom Kepler and Ivan Havel from Charles University in the Czech Republic co-hosted an "Evolutionary Innovation" workshop in Prague. In October 2002, Kepler and Guo Lei, director of the Institute of Systems Science at the Chinese Academy of Science, co-hosted a meeting in Beijing titled "Intervention and Adaptation in Complex Systems." A highlight of this meeting was a poster session that attracted papers from 21 of China's brightest young researchers, all of whom have become very interested in the study of complex systems.

Finally, last summer SFI joined with the Etvos Lorand University, Central European University, and the Collegium Budapest to co-sponsor a month-long Complex Systems Summer School in Budapest, Hungary.

### BOGOTA MEETING ON CIVIL WAR SETTLEMENT

In May 2003, SFI Visiting Researcher Elizabeth Wood (New York University) and International Fellow Juan Camilo Cárdenas are convening a meeting in Bogotá on "Obstacles to Robust Negotiated Settlements of Civil Conflicts." Empirical studies of civil war reveal a number of stylized facts and puzzles that call for explanation:

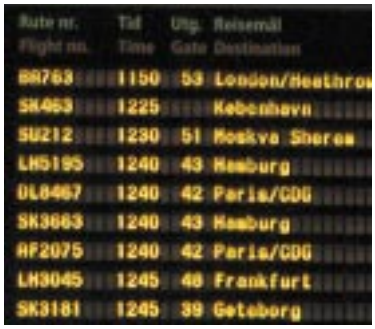
Contagion and path dependency. The spatial and temporal patterns of political violence exhibit strong proximity effects as well as path dependency, suggesting that both epidemiological models and models of punctuated equilibria may be illuminating.

Complex causation. State violence sometimes succeeds in repressing insurgency but sometimes foments it. A spiral of violence may ensue in some localities but be curtailed in otherwise identical communities.

Behavioral foundations of individual action. The reasons for participation in civil violence challenge conventional social science ideas: people are sometimes willing to participate despite very high risks to themselves and their families, often with little expectation of material gain.

Robust settlements. Some civil wars are durably resolved by negotiation (El Salvador, South Africa, Guatemala) while others, superficially similar (Angola, the Middle East, Colombia), appear resistant to negotiated resolution despite intense third-party involvement.

Participants will begin to apply the tools of complex dynamical systems, agent-based modeling, and evolutionary game theory to these issues, with a particular emphasis on the civil conflict in Colombia.




### TOWARD THE FUTURE

As the International Program continues to move through its cycle of growth and maturing, it is re-focusing on the goal of using the Program to improve SFI's own research programs by integrating a broader, more culturally diverse international group of participants. At the same time, and of equal importance, the Program, through its international meetings and schools, continues to seed interdisciplinary studies in the many targeted countries in which it is working.

# TRANSITIONS

## GEORGE COWAN AWARDED LOS ALAMOS MEDAL

SFI Distinguished Fellow George Cowan has received the highest honor Los Alamos National Laboratory (LANL) can bestow, the Los Alamos Medal, for his work on the early radiochemical evaluations of nuclear weapons. Cowan is Senior Fellow Emeritus at LANL. The award recognizes employees or groups that have made a contribution that changes the course of science, or has had a major impact on the lab.

## NEW SCIENCE BOARD MEMBERS

Science Board members advise on broad issues related to the SFI scientific agenda.

**Rodney Brooks** is director of the Massachusetts Institute of Technology (MIT) Artificial Intelligence Laboratory, and is the Fujitsu Professor of Computer Science at MIT. He is also chairman and chief technical officer of iRobot Corporation. Brooks' research is concerned with both the engineering of intelligent robots to operate in unstructured environments, and with understanding human intelligence through building humanoid robots. He has published papers and books in model-based computer vision, path planning, uncertainty analysis, robot assembly, active vision, autonomous robots, micro-robots, micro-actuators, planetary exploration, representation, artificial life, humanoid robots, and compiler design. Brooks' most recent publications include Cambrian Intelligence and Flesh and Machines. He is a founding fellow of the American Association for Artificial Intelligence (AAAI) and a fellow of the American Association for the Advancement of Science (AAAS). He starred as himself in the Errol Morris movie "Fast, Cheap and Out of Control."

**Lee Segel** is a professor in the Department of Computer Science and Mathematics at the Weizmann Institute of Science in Israel. Segel did his undergraduate work at Harvard, and received a Ph.D. in applied mathematics from MIT. After two years in the Aerodynamics Division of the National Physical Laboratory in England, he joined the Mathematics Department at Rensselaer Polytechnic Institute. Until 1968, Segel worked mainly on problems in nonlinear stability theory, but his major focus switched to theoretical biology starting with a sabbatical at the Sloan-Kettering Institute and Cornell Medical School in 1968-1969. He joined the Department of Applied Mathematics and Computer Science of the Weizmann Institute in 1973. Segel is a fellow of the American Association for the Advancement of Science (AAAS), editor-in-chief of the Bulletin of Mathematical Biology, and director of SFI's annual NIH-sponsored Summer Program in Mathematics and Biology.

## NEW MEMBERS OF THE SCIENCE STEERING COMMITTEE

The Science Steering Committee is a working group composed of Science Board and External Faculty members who provide ongoing guidance on SFI's scientific agenda. The terms of committee members are staggered, one quarter of the membership being appointed each year. The Committee welcomes three new members.

**Marcus Feldman** is Burnet C. and Mildred Finley Wohlford Professor in the School of Humanities and Sciences, Population Biology, at Stanford University. Feldman has made important contributions to evolutionary theory and population genetics, including the mathematical analysis of evolution in linked sets of genes, and of the means by which cultural evolution, considered alone and in combination with biological evolution, influences human behavior. At Stanford, Feldman's work uses applied mathematics and computer modeling to simulate and analyze the process of evolution focusing on topics such as evolution of complex genetic systems, the evolution of learning, the interaction of biological and cultural evolution, and mathematical and statistical analysis of molecular evolution.

SFI Research Professor **Erica Jen** is principal investigator for the Institute's McDonnell Foundation Founding Program on Social Robustness. Jen is currently program coordinator for the Packard Foundation project titled "A Founding Program on Robustness," and from 1999-2002 was principal investigator for SFI's Keck Foundation project on evolutionary dynamics. Jen served as the Institute's vice president for Academic Affairs from 1996 to 1999. Her current research focuses on robustness and the dynamics of switching.

**Geoffrey West** is a fellow at Los Alamos National Laboratory. His primary interest has been in fundamental questions in physics, especially those concerning the elementary particles and their interactions. West's long-term fascination in general scaling phenomena grew out of his work on scaling in quantum chromodynamics and the unification of all forces of nature. In 1996 this evolved into the highly productive SFI collaboration with James Brown and Brian Enquist on the origin of allometric scaling laws in biology and the development of realistic quantitative models for the structural and functional design of organisms.

## 2002 STEINMETZ FELLOW

The purpose of the Steinmetz Fellowship is to provide the opportunity for Complex Systems Summer School students to pursue research projects in complex systems and to participate in SFI scientific activities. The award is made to a participant of each year's School to support residency at the Institute the subsequent year. The Institute is grateful to Dr. Philip R. Steinmetz for his generous support of this award. Dr. Steinmetz is an alumnus of the 1990 Complex Systems Summer School.

**Jennifer Hallinan**, SFI's 2002 Steinmetz

PHOTO: JULIE GRABER

Fellow, is a research officer with the Institute for Molecular Biosciences at the University of Queensland in Australia. Her research interests are in systems biology, particularly the relationship between structure, function, and dynamics in intracellular interaction networks.

During her time at the Santa Fe Institute, she will work on modularity and mutational subnetworks in the yeast protein-protein interaction network. Large amounts of biomolecular data is currently being generated by molecular biologists; however, this data is incomplete and poorly characterized and thus difficult to use for systems-level modeling of biological systems. In order to make use of the data that currently exists, it is important to determine what proportion of an entire network must be available in order for useful inferences to be drawn. This project will address the extent to which structural and functional modularity in a network, together with an apparent bias in data collection towards genes and proteins of medical or financial significance, affect the data requirements for modeling of a system.

## 2002 REUS

Every summer the Institute welcomes a small number of motivated and talented undergraduates who benefit from exposure to the rich interdisciplinary mix of ideas at SFI. Students are matched with one or more mentors with meaningful research problems of interest to the student and to which the intern can make significant contributions. These mentorships have produced continuing collaborations and have resulted in several co-authored papers in the refereed literature. This summer SFI welcomed six participants to this NSF-supported program.

**Jeremy Barofsky** is currently a senior at Boston University, majoring in interdisciplinary economics. Barofsky worked with SFI McKinsey Professor Doyne Farmer to add a technical trading agent to Farmer's limit-order stock market simulation. The "trader" optimizes a negative auto-correlation in prices; using new price outputs, Barofsky analyzed the agent's effect on volatility and other variables.

**Lauren Childs** is majoring in mathematics and chemistry at Duke University, where she is a junior. She is a member of the Howard Hughes Research Fellows Program at Duke pursuing work in mathematical biology. Childs' project mentor was Tom Kepler, SFI vice president for Academic Affairs until his departure to Duke University in late summer 2002. As her SFI project, Childs modeled the interaction between affinity maturation and somatic mutation in the human immune system. Although considerable research has been done on this topic, it is gaining new attention with the discovery of the importance of activation-induced cytidine deaminase (AID) in somatic mutation.

**Sara Friedman** is a senior at U.C. Berkeley with a double major in applied mathematics and the interdisciplinary studies field of social science. Working with Research Professors Sam Bowles and Jim Crutchfield, Friedman formulated a two-player meta-agent game theory model to describe the co-evolution of a society and ecosystem with a circumscribed location.

**Janine Garnham** is a senior majoring in computer science at the Rochester Institute of Technology. She worked with SFI Researchers Walter Fontana, David Krakauer, and Homayoun Bagheri on a project focusing on long-term memory storage in the brain. A class of enzymes, the kinases, has been proposed to be involved in mechanisms underlying memory storage. Garnham's project modeled multiple-kinase networks and examined their dynamic behavior, particularly the number of potential steady states.

**Alex Herman** is a physics major at Wesleyan University. He continues to work with Science Board member Geoffrey West (Los Alamos National Laboratory and SFI) and colleagues to develop a general model for tumor growth, extending the group's work on allometic scaling principles.

**Jacob Usinowicz** is a senior majoring in human ecology (with a focus in the physical and biological sciences) at the College of the Atlantic. Jacob's research project with the SFI computational mechanics research group—including Jim Crutchfield and former Postdoctoral Fellow Cosma Shalizi—adapted the algorithms used in causal-state identification and machine reconstruction for use with data from two-dimensional systems. It is likely that this work will result in a publication co-authored with David Feldman, a faculty member at the College of the Atlantic and collaborator with the Crutchfield group.

## SARAH HAYES JOINS STAFF AS SFI MEETING MANAGER

**Sarah Hayes** recently joined the staff to manage meetings and events at the Institute. Sarah has been designing and orchestrating meetings and events for over 20 years. Her professional accomplishments include managing the executive seminar program at Control Data Corporation, video art direction for a Carnegie Hall tribute to Harry Chapin, and recently producing a new software product launch that was introduced at the Society for Biomolecular Screening in Edinbourgh, Scotland. Sarah has a B.A. in communication arts from the University of Wisconsin-Madison and an M.S. degree from Lehigh University.

**Per Bak**, 1948-2002

# TRANSITIONS

Physicist Per Bak, a professor at Imperial College in London and SFI External Faculty member, died October 2002 in Copenhagen. Bak received his doctorate from the Technical University of Denmark and went on to hold faculty positions at NORDITA (Copenhagen), Brookhaven National Laboratory, and the Niels Bohr Institute.

In 1987 Bak and two postdoctoral researchers, Chao Tang and Kurt Wiesenfold, presented their ideas on self-organized criticality in a much-cited paper in Physical Review Letters. Bak pursued the implication of this theory throughout his research career and brought his ideas to the general public in the book How Nature Works: The Science of Self-organized Criticality.

Bak was a fellow of the American Physical Society and the American Association for the Advancement of Science (AAAS) and a Member of the Danish Academy of Science. He received the Friedman Award in 1990 and was named a titular member of the European Academy of Sciences in 1997.

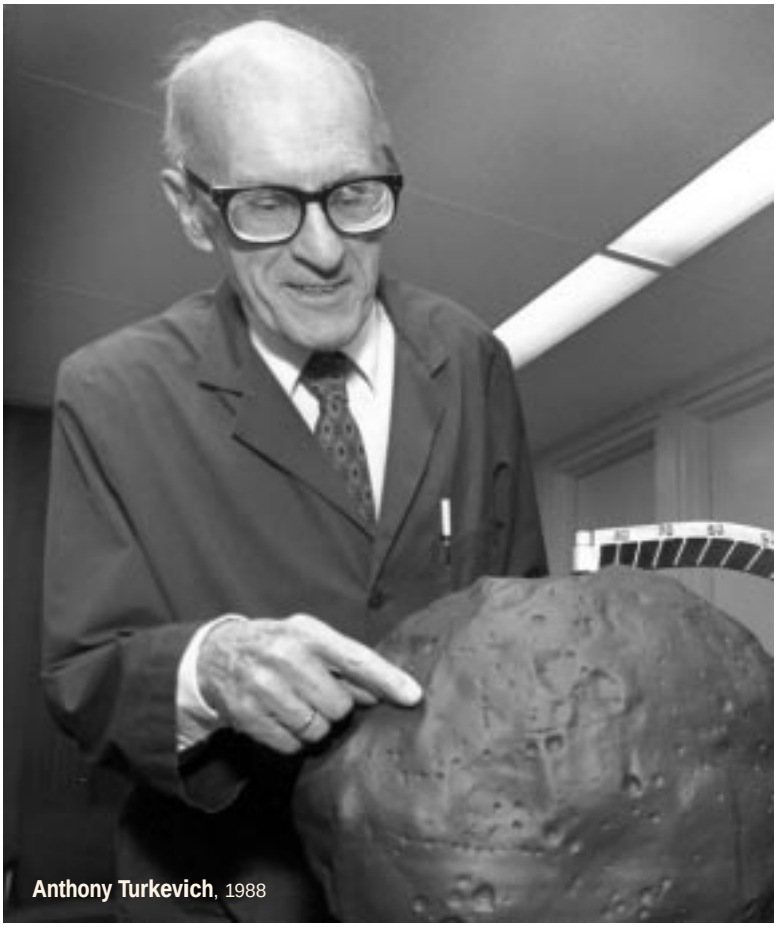
**Anthony Turkevich**, 1916-2002

Anthony "Tony" Turkevich, a founding member of the Santa Fe Institute and a former member of SFI's Board of Trustees, died in September 2002.

Turkevich was Professor Emeritus at the University of Chicago. He made a career of studying the physical and chemical composition of the universe. His research ranged from observing the fundamental properties of matter with particle accelerators to identifying the chemical composition of meteorites, the lunar surface, and the planets. In 1950, for example, he teamed up with Nobel laureate and University of Chicago physicist Enrico Fermi to calculate the elements produced in the big bang. During World War II, Turkevich was a member of the Manhattan Project, first at Columbia University, then at Chicago, and finally at Los Alamos National Laboratory (LANL).

Founding SFI President George Cowan recalls the early days working with Turkevich. "Tony was a visiting senior laboratory fellow at Los Alamos and attended the earliest meetings of the Laboratory Senior Fellows, which I chaired, dealing with possibilities for a new research institute. He contributed importantly to SFI's founding and policies." Indeed, at SFI's founding symposium Turkevich presented a paper entitled "Reconstructing the Past through Chemistry." He continued to participate in SFI business until he decided it had moved away from his expertise. He was one of several University of Chicago affiliates who helped found the Institute, including Murray Gell-Mann, Nick Metropolis, Herb Anderson, and Harold Agnew.

Turkevich's awards include the E.O. Lawrence Memorial Award from the Atomic Energy Commission in 1962, an honorary doctor of science degree from Dartmouth College in 1971, the Award for Nuclear Applications from the American Chemical Society in 1972, and the Boris Pregel Award from the New York Academy of Sciences in 1988. He was also elected to the National Academy of Sciences—one of the highest honors that can be accorded to a U.S. scientist—to the American Academy of Arts and Sciences, and as a fellow of the American Physical Society.



**Anthony Turkevich**, 1988

PHOTO CREDIT

# Summer 2003 Openings for Undergraduate Interns

This program is highly individualized. Undergraduate students work with SFI faculty mentors on an individual project focusing on some aspect of the computational properties of complex systems. Participants are expected to be in residence approximately ten weeks, within an approximate mid-May to mid-August window. Internships may be part- or full-time, although it is likely that most summer students will hold full-time positions.

Interns receive living stipends (from which housing costs are deducted) during their stay, along with support of round-trip travel expenses from their home institution. The Institute arranges for appropriate, affordable, shared housing arrangements in Santa Fe. Since this program is an educational rather than employment experience, stipends are expected to support a "no-gain/no-loss" situation for students (although previous, frugal interns have managed to save modest amounts out of their summer support).

Because Santa Fe lacks a full public transportation system, autos are provided to participants on a shared basis. Those interns who can bring their private transportation are urged to do so.

## ELIGIBILITY

Support is provided by a grant from the National Science Foundation (NSF) through the Research Experiences for Undergraduates program. Per NSF guidelines, it is open to U.S. citizens and permanent residents only. For the purposes of this program an undergraduate student is a student who is enrolled in a degree program (part-time or full-time) leading to a bachelor's degree. Students who are transferring from one institution to another and are enrolled at neither institution during the intervening summer may participate. College seniors graduating in 2003 are not eligible for this program, nor are graduating high school students who have not yet enrolled as undergraduates.

Mathematical or computational skills or experience (particularly knowledge of the rudiments of the Unix operating system and/or a programming language such as C) are favorably considered.

## TO APPLY

Provide a current resume, official transcript, and a statement of your current research interests and what you intend to accomplish during your internship. Please have three scientists who know your abilities write letters recommending you for this program.

Online: You may submit most of your application materials using an online application form at http://www.santafe.edu/reuannounce.html. We strongly encourage you to apply online in order to expedite your application.

Postal Mail/Courier: Alternatively, applications may be sent via postal mail. They must include your e-mail address and fax number. Do not bind your application materials in any manner. Send application packages to:

Summer Research Opportunities for Undergraduates
Santa Fe Institute
1399 Hyde Park Road
Santa Fe, New Mexico 87501

Transcripts and letters of recommendation: Transcripts must be official. If you apply by postal mail, transcripts and letters of recommendation may be included in the application package in sealed envelopes, or they may be sent directly to the address above. Letters of recommendation can also be e-mailed directly from the author to paul@santafe.edu.

Deadline: All application materials must be postmarked or electronically submitted no later than February 28, 2003.

Women and minorities are especially encouraged to apply.

For further information please contact Paul Brault, 505-984-8800, extension 235, or paul@santafe.edu.

# SFI COMMUNITY LECTURES 2003

**7January 29**

## Discounting, Karma, and Finessing the Future

### STEWART BRAND

*Co-Founder, Global Business Network , the All Species Inventory and the Long Bets Foundation; President, The Long Now Foundation (which is building a 10,000-year Clock and Library).*

Taking the future seriously usually means taking it fearfully. The fear is customarily structured in two broad ways. One is discounting, which dilutes the effect of expected (but unspecifiable) losses. Another, karma (the law of cause and effect) dreads expected (but unspecifiable) chains of consequences from present actions. Two common ways of coping include insurance, a way of monetizing both fears, and religious revelation, a way to escape both fears via an anticipated end-time (such as the promise of heaven or apocalypse).

However, there are other ways to take the future seriously. One, the use of multiple scenarios, can yield robust, adaptive strategies. Another, lengthening the time frame engaged, converges otherwise divergent interests toward inevitable altruism. Finally, acknowledging that surprise upon surprise is structurally built in, helps bias systems toward perpetual learning.

**February 16**

## Six Degrees: The Science of a Connected Age

### DUNCAN WATTS

*Associate Professor, Department of Sociology, Columbia University; author of Small Worlds: The Dynamics of Networks Between Order and Randomness (1999) and Six Degrees: The Science of the Connected Age. stet*

Whether they bind computers, economies, or terrorist organizations, networks are everywhere in the real world; yet until recently the fundamental nature of the networks themselves has remained shrouded in mystery. But in the past few years, a new generation of research has commenced that is rapidly revealing the rules by which networks grow, the patterns they form, and the way in which they drive collective behavior.

Starting from the "small world problem" from which the idea of six degrees was derived, Watts explains the science of networks and its relevance to a range of problems, from epidemics of disease to outbreaks of market madness, from individuals searching for information to business firms surviving crisis and change, and from the structure of personal relationships to the technological and social choices of entire societies.

**March 19**

## Avoiding Disasters in Deterministic Universes

### DANIEL DENNETT

*Distinguished Arts and Sciences Professor, Professor of Philosophy, and Director of the Center for Cognitive Studies, Tufts University; author of Darwin's Dangerous Idea (1995), Kinds of Minds (1996), and Brainchildren: A Collection of Essays 1984-1996 (1997)*

A ubiquitous bad habit of thought is supposing that whatever is determined is inevitable. This simple mistake lies at the heart of much of the anxiety about determinism (and the misbegotten fondness for quantum theoretical "solutions" to the problems of free will). These errors can be exposed with the help of several thought experiments involving Conway's Life (a computer game involving cellular automata theory) and chess-playing computers.

**April 16**

## Predicting Language Performance in Preschoolers: The Role of Infant Information Processing Abilities

### APRIL A. BENASICH

*The Center for Molecular & Behavioral Neuroscience, Rutgers University (Newark); Member, Santa Fe Institute Consortium for Increasing Human Potential*

A newborn is very different from a 12-, 24- or 36-month-old child as regards both brain and behavior. Given that so many changes occur over a short period of time, infancy is a particularly informative time to study behaviors that may reflect the underlying development of the brain. It is possible to follow the development of many abilities from their earliest appearance and to consider what impact experience, both social and perceptual, might have on their emergence. Language is a particularly fascinating "emergent ability" that has been of enduring research interest. Even after many years of study, however, the neural underpinnings and fundamental processes that support optimal language acquisition are not fully known.

Benasich will examine a fundamental skill that appears to be critical to the development of language—the ability to efficiently and accurately process rapid sequential sounds. Such rapid auditory processing (RAP) abilities can be measured to non-speech stimuli, such as tone doublets, or to early speech sounds, such as the consonant-vowel pairs "ba" and "da." Benasich's work strongly suggests that RAP in early infancy plays an important role in the facilitation of speech processing and the growth of language across early development in both normally developing children and children at risk for language disorders.

**May 5**

## The Future of Biological Diversity in a Crowded World

### LORD (ROBERT) MAY

*Professor of Zoology, Oxford University; President, The Royal Society*

Scientific advances of the past century have led to improvements in most peoples' lives, in both developed and developing worlds. But increasingly we recognize that many of these benefits have not been produced in a sustainable way, particularly as human populations continue to grow and the diversity and abundance of many other species diminishes. What happens in the future to our world, to us, and the creatures we share the world with, depends on the actions we take now.

**June 18**

## Spacesuit: 21 Stories and Statements on Technology and Design

### NICHOLAS DE MONCHAUX

*Architect and Assistant Professor of Design, University of Virginia; Recipient of the 2002 Dinkeloo Prize from the Van Alen Institute and the American Academy in Rome*

Why was the lunar spacesuit soft? In 1969, the costume worn by the Apollo astronauts on the surface of the moon consisted of 21 layers of different fabrics and materials, each with a distinct function. Many, if not all of these functions, could have been reduced to one or two hard surfaces; indeed there were contemporary proposals for such designs, which were proved more efficient—yet were not used. This lecture consists of 21 brief stories and statements that together shape an understanding the aesthetic, cultural, scientific, and institutional parameters that shaped the Apollo spacesuit. De Monchaux will discuss the lessons learned from the spacesuit's journey to the moon in terms of the past, the continuing changes in the body's relationship to technology, and the creation of this new century's culture, society, and designs.

**August 27**

## Where Mathematics Comes From

### GEORGE LAKOFF

*Professor of Linguistics, University of California at Berkeley*

How can a finite mind comprehend infinity in all of its forms in mathematics? How can numbers and formulas express ideas? Why does mathematics work in science?

The only mathematical ideas we can have are ideas the brain allows. Like other abstract ideas, mathematical ideas arise via conceptual metaphor, a mechanism for adapting the brain's sensory-motor system to constitute abstract thought. Lakoff discusses conceptual metaphors built into mathematical ideas, from arithmetic to higher mathematics, and explores the cognitive theory of mathematical ideas.

**October 29**

## Women, Men, and the Evolution of Spatial Navigation

### LUCIA JACOBS

*Associate Professor of Psychology, University of California at Berkeley*

An enduring mystery of animal behavior is the nature of true navigation—how an animal is able to home long distances over uncharted territory. Another puzzle of spatial orientation is the difference between the nature of navigation and spatial memory in women and men. What is the relationship between these curious sex differences and the nature of true navigation? A new model of the neural basis of navigation, mediated by an important memory structure, the hippocampus, suggests that not only do females and males use different frames of reference to navigate but that this difference has an ancient evolutionary history. Moreover, the difference is evoked not only in spatial navigation but also in thought processes that are spatially encoded. For mice and men, therefore, understanding a primitive cognitive universal such as spatial navigation may lead to a new understanding of abstract thought.

**November 18, 19, and 20**

**Tenth Annual Stanislaw Ulam Memorial Lecture Series:**

## The Coevolution of Organism and Environment

### RICHARD C. LEWONTIN

*Alexander Agassiz Research Professor, Museum of Comparative Zoology, Harvard University*

The usual view of evolution is that organisms are "adapted" to their environments by natural selection. This view assumes that the environment of an organism preexists and organisms are molded to fit into this already existent ecological "niche." In fact, organisms select, reorganize, alter, and destroy their environments as they evolve so that the environment and the organism are a coevolving pair in which both are equally the causes and the effects of the evolutionary process.

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Most talks take place on Wednesday evenings, beginning at 7:30. No reservations are necessary, but seating is limited.

Talks are generally held at the **James A. Little Theater** on the campus of the New Mexico School of the Deaf, 1060 Cerrillos Road, Santa Fe, or the **St. Francis Auditorium** at the Museum of Fine Arts on the plaza. Venues occasionally change. For information about the location of a particular talk, call (505) 984-8800 ext. 221. There is no admission charge.

Please contact the Santa Fe Institute to arrange for sign language interpretation if necessary.

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