## **SFI Bulletin**

2012, vol. 26



TIME AND CHANCE

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### Time, Chance and the Laws of History

BY DOUGLAS H. ERWIN Chair of the Faculty

Perhaps the greatest challenge for the study of complex adaptive systems lies in the historical fields of natural science, whether astronomy, geology, evolutionary biology, paleontology, or archaeology. In each of these fields, experimental approaches are limited, studying modern systems may not provide much insight into processes in the distant past, and chance (contingency) often plays an important role. This tension between the role of chance and the search for regular patterns that underlie historical processes is also found in a number of social and behavioral sciences, where the SFI community has been increasingly active. Economics and historical linguistics have long had a home at SFI, but efforts in behavioral economics, anthropology, sociology, and even history and law are more recent.

History has been described as "one damn thing after another." Good historians have always tried to identify more general patterns and processes from the mass of detail, and the same is true in the historical natural and social sciences. Some have a much easier task than others. Astronomy, for example, draws on the foundation of physics, the assumption (well-verified, but still an assumption) that the life span of elemental particles and the nature of physical laws have remained constant through time and space. Because the nature of the components of astronomical objects is fixed and subject to unvarying physical laws, physicists are confident they understand the underlying mechanisms of the system. This is true no matter how complex the historical evolution of a galaxy, how complex the system, and how difficult the prospect of modeling: for example, the interactions between galaxies. (There is also, of course, the small matter of dark energy.) Difficulties in forecasting the dynamics of a single planetary system within a galaxy do not undermine our fundamental understanding of a galaxy, any more than



How do we approach systems in which the laws themselves may be changing through time?

the inability to predict when a large earthquake will hit San Francisco undermines seismology.

In the case of most historical disciplines, the situation is more challenging, for five reasons. First, when generalizations exist, they rarely have the force or sweep of the laws of physics. Darwin's law of natural selection predicts the future change in gene frequencies of information-carrying material with variation. However, the complex mapping between genotype and the resulting phenotype means that predicting the course of selection may provide little insight into evolutionary dynamics. Evolutionary theory is largely an ahistorical theory about a historical discipline. Generalizations of greater scope may yet be identified, of course, but perhaps only by addressing more forthrightly this historical nature of these systems.

Second, the variety of actors and the variety of their interactions vastly swamps that of simpler physical systems. Identifying causal "laws" may thus require simpli-

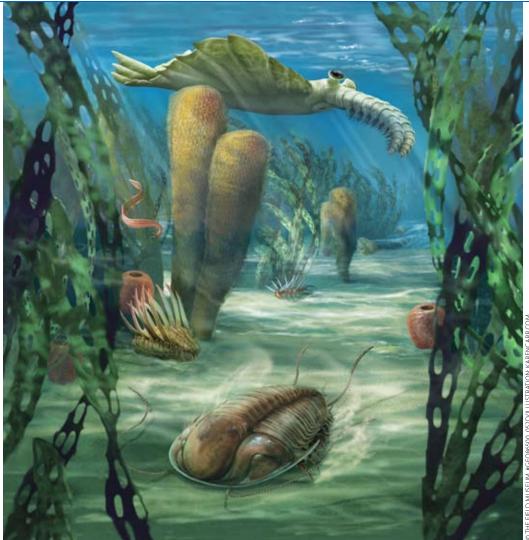
fications that render irrelevant the whole enterprise. The tensions between the assumptions of rational expectations in economics and the findings of behavioral economics are a case in point.

Contingency, or chance, is a third challenge. In his book about the exquisite 505 million-year-old fossils of the Burgess Shale and the explosion of animal diversity, the late Stephen Jay Gould famously argued that if we were able to redo the early history of animals, different groups might succeed. Perhaps the now virtually unknown priapulids (marine, mud-inhabiting, unsegmented worms) would be more common than annelids (earthworms and their allies) and arthropods would be a forgotten diversion. Many examples of the contingent success or failure of different clades (biological groups) have since been identified, and they challenge the belief that a study of patterns of change can yield a general understanding of process.

The fourth challenge is really an extension of contingency; the conscious behavior of components of many evolving systems can change the rules of the game, or at least some of them, some of the time. Each time financial analysts identify some property of a market, their drive to exploit it generally eliminates the arbitrage (or trading) potential (at a speed determined by the efficiency of the market). As conscious actions alter the interactions between the agents, any model requires learning.

Finally, unlike many physical laws, the generalities of biology, economics, and the human sciences may themselves evolve over time. Indeed one of the most exciting areas in modern evolutionary biology is identifying how the kinds of genetic and developmental variations have changed over time spans of hundreds of millions of years. These discoveries, made by comparative studies of living animals, raise questions about the utility of experimental manipulations of living species. If the nature of available evolutionary mutations has changed over time, then the range of evolutionary possibilities has changed as well. In the arena of technology we know this is true: Personal computers were an impossible technology in the Renaissance, or even in 1950.

These challenges do not mean that we cannot study complex adaptive systems in deep time. Rather, they provide us an exciting opportunity to extend the approaches pioneered at SFI over the past few decades, and to



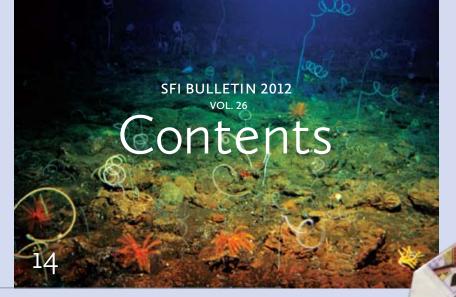
By exploring underlying complex interactions and forces of evolution, researchers formulate new understandings of the diversification of life during the Cambrian explosion 540 million years ago.

climates, deep oceans rich in sulfur and iron, or meteorites falling out of the sky, to cite a few recent discoveries, could never be imagined by Lyell. Empirical studies, and an open mind, can address this problem (good students, always sure their advisors are out of date, if not verging on senility, also help).

develop new tools and approaches. This is the case with that fifth, and perhaps greatest, challenge from my list: How do we approach systems in which the laws themselves may be changing through time, particularly if the conditions today provide only limited information about the rules applicable in the past (or, of course in the future)? In my field of geology, this problem was initially articulated by Charles Lyell in the 1830s and has been incorporated in the adage drilled into geology students ever since: "The present is the key to the past." But even Lyell's colleagues (with the surprising exception of Charles Darwin) did not believe him.

There are several problems with Lyell's perspective. Chief among these are that the present is really only a hypothesis about how the past works, and the range of mechanisms may be far greater than the limited sample size captured by modern scientific studies. Warm polar

The SFI scientific community has been confronting these challenges with increasing vigor over the past few years. Some of these efforts are chronicled in this issue. For example, SFI's Harold Morowitz and Eric Smith and their colleagues have generated a new approach to studies in the origin of life with their research on the evolution of metabolic networks. This is particularly relevant to the preceding discussion, because one vital implication of their work is that there may have been little scope for contingency in the evolution of these networks. If they are right, this, of course, suggests that carbon-based life forms elsewhere in the universe may have been constrained to similar metabolic pathways. This work exemplifies one of the strengths of SFI in addressing issues over time: Whether in evolution or economics, in many cases we will approach these problems from the perspective of how systems evolve. ◀



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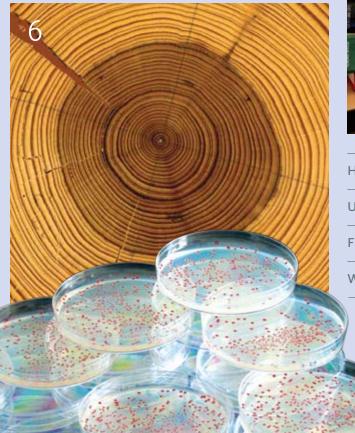
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## The Nature of Complexity

## Templeton Foundation Grant Supports SFI Research

JOHN TEMPLETON FOUNDATION

FI has been awarded a major new grant from the John Templeton Foundation to pursue fundamental understandings of the hidden regularities in complex biological and social systems.

As a philanthropic organization, the Templeton Foundation supports research on subjects ranging from complexity, evolution, and infinity to creativity, forgiveness, love, and free will. More about the Foundation is available at www.templeton.org.

The three-year, \$5 million SFI grant will generate new concepts and quantitative methods of general scientific and social value. It recognizes the opportunity presented by recent advances in data collection and computational power. According to the award, the grant "initiates a groundbreaking research program on the nature... of complexity with the potential for illuminating many hidden regularities in the biological and social worlds."

The project holds the promise of developing fundamentally new quantitative theories and focuses on "areas where new research and analysis are likely to make a real difference." Specifically, it supports exploration of the following questions:

- The evolution of complexity and intelligence on Earth, led by SFI External Professor David Krakauer (University of Wisconsin–Madison).
- The hidden laws that pervade complex phenomena, especially biological and social phenomena, led by SFI Distinguished Professor Geoffrey West.
- Universal patterns in the emergence of complex societies, led by SFI President Jerry Sabloff.

All projects seek to understand the interconnectedness among competition and cooperation. They also examine the increasingly efficient and robust means of acquiring and communicating information. The grant award states that the projects "consider the crucial role of multiple temporal and spatial scales in complex systems, why hierarchical and modular structure is ubiquitous, how mechanisms have evolved to exploit rapid changes in their surroundings, and how adaptive systems have found a way of overcoming and exploiting the rapid turnaround and loss of their most elementary components."

"These projects fit the progression of SFI science well," says President Jerry Sabloff. "Although they are quite different in terms of the complex systems they examine—from genes and neurons to large human social systems—they are all concerned with the fundamental processes underlying complexity and the evolution of complexity. These are questions SFI has been asking since its founding in 1984."

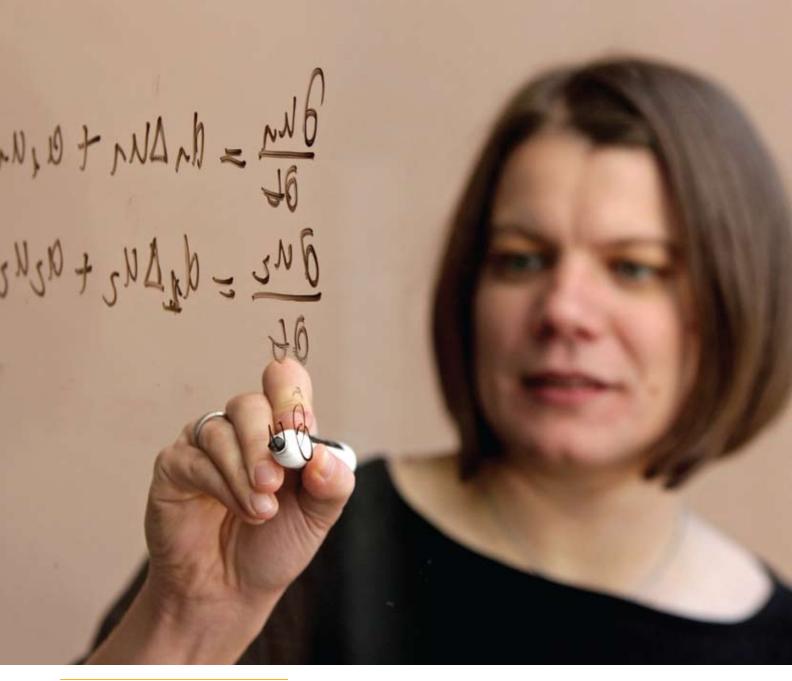
"With the Templeton Foundation's generous support," he adds, "we hope to make significant progress in understanding the principles that span and unify many complex systems."

### Coming Soon: Complexity Explorer

The Templeton grant also supports a significant education outreach project. As part of the grant, SFI will create an online resource called the Complexity Explorer. "At the Explorer's core will be a wealth of learning materials associated with the sciences of complexity," says SFI Vice President for Education and Outreach Ginger Richardson.

SFI has a long history of both developing the sciences of complexity and offering educational programs in complexity, says External Professor Melanie Mitchell, faculty coordinator for the Explorer project.

"The online resource is intended for all levels of teachers and learners interested in complexity, including



The online resource is intended for all levels of teachers and learners interested in complexity, including academics, graduate and undergraduate students, professionals, members of the public, and high school and middle school students.

academics, graduate and undergraduate students, professionals, members of the public, and high school and middle school students," she says.

A professor at a university might use the Explorer, for example, to interactively generate a recommended syllabus for a graduate-level course in complexity, along with supporting online exercises and simulations found in the Explorer's Virtual Lab. A professional interested in applying complexity to business problems could search for and find relevant

papers and paper summaries.

A student, who perhaps doesn't know where to start, will find definitions pertinent to the field and use multimedia demonstrations of complexity-related principles and concepts.

"Wherever I go, people ask me where they can learn more about complex adaptive systems," Mitchell says. "This project, supported by the Templeton Foundation, will transform a longtime need into a reality." ◀



### A Q&A WITH SFI PRESIDENT JERRY SABLOFF

he Santa Fe Institute has always challenged orthodoxy, probed freely across disciplines, and asked difficult questions. Here SFI President Jerry Sabloff gives his thoughts on how and why SFI asks big questions.

BULLETIN: The theme of this issue, "Time and Chance," is about long time scales. Why is the question of time scales such an important one for the sciences of complexity, and for SFI?

JERRY SABLOFF: Clearly, if you look at today's world, we operate on incredibly short time scales. In business, government, and our daily lives, we are measuring things in hours, days, weeks, months, sometimes years. But if you want to really understand the complex adaptive systems in our world and in our society, you need to examine longer time scales, because when you look only at the short term, you might perceive a variability as the norm, and you might easily miss the overall trajectory of a system. In business, that is very dangerous, because you can look at returns and assume you are viewing the trend, and your expectations adapt to what at a longer time scale appears like an oscillation.

From my perspective as an anthropologist, a focus on the short term can be a fatal miscalculation. You might have 50 years of warm, wet weather. Things are going well. You have plenty of crops. Trade is terrific. But you don't build up surplus. Then conditions return to what you would have seen as the true norm if you had taken a much longer-term view. And suddenly you are fighting for survival.

Left: Study of cities such as Dubai, which dates to 1095 and today boasts the world's tallest structure, helps SFI researchers determine whether the current trajectory of global urbanization is sustainable over the long term.

Thinking of SFI, one of our significant projects is the study of cities. If you look at what is happening with cities today, you will see one thing. But if you look at the emergence, growth, and evolution of cities over five millennia, you get a much richer view of the nature of cities and their potential future



trajectories. You get an incredible view of what pre-industrial cities were like, what industrial cities were like in the last two centuries, and then what the modern urbanization is like.

So for all those reasons, when you are looking at any problem, at least being aware of phenomena at a variety of time scales is really important.

BULLETIN: Why don't we, as a society, tend to think on bigger scales?

SABLOFF: It's hard to say. In business, it's probably related to the question of shareholder value and quarterly profits. In our area of science, one of the worrisome trends is that companies, particularly bigger ones, aren't willing to invest proportionally in research the way they used to. The results of basic research, or of a theoretical breakthrough, might be two decades or more out. Shareholders don't seem to want to hear about long-term investments. So very few CEOs and boards are willing to say, 'We expect three percent growth for the next five years, but if you hold onto your stock, in ten years we have a chance of enjoying astronomical growth.' Many companies, when they look five and ten years out, that's considered visionary thinking. We're fortunate to be working with the terrific SFI Business Network partners, many of whom are breaking out of this shortsighted mold.







The behavior of a complex system in more than one time scale often tells differing stories. Here, a view of AT&T stock on the Dow Jones over one-day, six-month, and two-year periods suggests vastly different performance interpretations.

**BULLETIN:** Why is it important, then, for SFI to ask big questions?

SABLOFF: Our society is facing a huge array of problems, and a number of them are either being ignored, or when they are faced, the solutions offered are variances of business as usual. Very few people are looking at the big questions with imagination. The importance of asking big questions is to say, 'Hey, the status quo is not working, and the

solutions are going to challenge business as usual.'

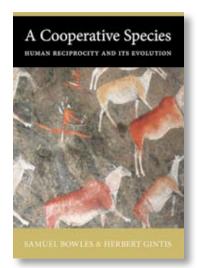
SFI is a good place to pose difficult questions that matter. Throughout our relatively short history of 27 years, we have been asking such questions and looking for answers from many perspectives and in ways that challenge assumptions. That's true, in part, because our reward systems are different from those of a university. Our faculty and external faculty are risk takers, intellectually, and we view failure as acceptable. Those factors, which are still very much alive today, and our terrific group of scholars, are the reasons SFI still is one of the best places in the world to ask the big questions and seek their answers in creative new ways.

**BULLETIN:** What are some examples of big questions that matter to you?

SABLOFF: A foremost question for me—because it relates to my own scholarly interests—is the long-term trajectory and future viability of urban systems. A number of faculty members at SFI are asking questions such as, Why did cities arise in the first place? Why was that a successful adaptation? Why have cities persisted for 5,000 years? Lewis Mumford said cities emerged and grew because they were places of safety, economic opportunity, and sacredness. But we should ask whether these are the key features of modern cities. That's not clear at all, in my mind. There are cities today where none of those attributes are true. So then the questions become: What purposes do cities serve today? Will the nature of cities change? Or is the current urban climate a harbinger of potential failure? Talk about big questions! The viability of cities is one in all of its ramifications, and one where a longer historical perspective is critical, and also challenging.

So a big question is one that gets at some major societal or human problem. It requires a new perspective. It hasn't been solved yet because it is challenging. And the answer is not going to be a normal, expected answer. If the answer was either easy, or there was a clear path to get at it, it wouldn't be a big question, because the solution would already be at hand. SFI's special role is to keep asking difficult questions and through them seek revolutionary insights.

## FRACTALS PARTS THAT REFLECT THE WHOLE Read more at www.santafe.edu/news.



### **DECADES OF INVESTIGATION**

by several SFI researchers, including Professor Sam Bowles and External Professor Herbert Gintis, culminated in their conclusion that cooperation within groups and a willingness to collaborate in conflict against outsiders co-evolved in the human species. Much of their research is compiled in a new book, A Cooperative Species: Human Reciprocity and Its Evolution (Princeton University Press, May 2011).

SFI HAS WELCOMED three eminent scholars as the first George A. and Helen Dunham Cowan Chairs in Human Social Dynamics, to be referred to as the Cowan Professors: anthropologist and SFI External Professor Robert Boyd of UCLA, economist Ricardo Hausmann of Harvard, and experimental psychologist Mahzarin R. Banaji of Harvard. **USING TECHNIQUES** borrowed from astrophysics, SFI Omidyar Fellow Simon DeDeo and External Professors David Krakauer and Jessica Flack sifted through 150 hours of observations Flack had collected on patterns of conflict in a monkey society. The researchers discovered evidence for a "conflict clock"—a social version of biological clocks like circadian rhythms—that predicts when animals will fight.

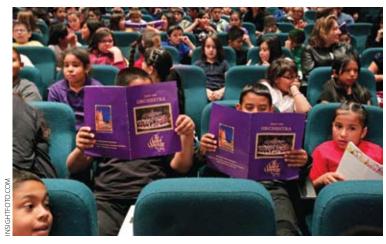
AS PART OF A GRANT from the Institute for New Economic Thinking, SFI Professor J. Doyne Farmer and External Professors Rob Axtell and John Geanakoplos are working to create an agent-based model of the economy that will help scientists, economists, and policy makers better understand past financial crises and possibly predict future crises.

### SCIENCE BOARD CO-CHAIR Stephanie

Forrest and her collaborators are working under a DARPA grant to develop a biologically inspired approach to software debugging a kind of natural selection for software. In effect, during each generation of a program's development, a group of slight variations are created and the best mutations are preserved. This process is repeated until the program functions.

TWO INSTITUTE **SCIENTISTS** gave talks at the 2011 TED Global event in Edinburgh, Scotland. SFI Distinguished Professor Geoffrey West explained how the world's cities are scaled versions of one another. SFI External Professor Mark Pagel described how language evolved in humans as a response to the evolutionary dilemma presented by social learning. Their talks are available at www.ted.com.

FOR THE THIRD TIME in as many years, SFI and the Santa Fe Symphony collaborated to produce a unique concert exploring the interface between music and science. "Voyages of Discovery III: Bach On the Brain," featured selected works of Johann Sebastian Bach interspersed with commentary by SFI Vice President and neuroscientist Chris Wood about the brain's response to sound and music. The event included two special concerts for New Mexico fourth graders.





# Watching Evolution Unfold

"In looking for the gradations by which an organ in any species has been perfected, we ought to look exclusively to its lineal

ancestors; but this is scarcely ever possible, and we are forced in each case to look to species of the same group, that is to the collateral descendants from the same original parent-form."

—Charles Darwin, On the Origin of Species, 1859

ichard Lenski has a front-row seat in the arena of evolution.

Back in 1988, he put 12 genetically identical strains of the bacteria *E. coli* in 12 flasks. He and his students then kept the bacteria on a glucose diet while the separate populations reproduced at a rate of more

than six generations per day. Every 500 generations, they

captured samples from each population and froze them for later comparison and experimentation.

Now, more than 54,000 gen-

erations later, Lenski's experiment encompasses the most generations ever examined in experimental detail. Armed with modern sequencing technologies and the vast stores of data contained in 23 years of frozen samples, he and his collaborators are learning a great deal about long-term evolutionary processes that in other species would take millennia to unfold.

Lenski, a member of SFI's Science Board, is the Hannah Distinguished Professor of Microbial Ecology at Michigan State University.

"My work uses *E. coli*, but it's not primarily about

*E. coli*," he says. "It's using *E. coli* in a very simple, artificial world to ask general, abstract questions about evolution, and explore the roles of chance and contingency."

It's the sort of experiment Charles Darwin might never have imagined as he sketched plants and animals in his notebooks, inferring their evolutionary histories from their modern characteristics. But, by expanding the boundaries of human perception, much as the telescope or radiography have, this experiment could serve as empirical high beams for modern evolutionary theory.

punctuated by periods of rapid mutation. By generation 20,000 in one population, for example, the team had found 45 mutations. At generation 26,000, a mutation affecting the bacterium's DNA metabolism arose, upsetting a relatively constant rate of genetic change and sparking a flurry of new mutations. By generation 40,000, some 653 mutations had occurred.

The team also found that a population of a given generation is in many respects more similar to the other independent lineages than to its own ancestors. For example, the levels of gene expression

# for 54,000 Generations—and Counting BY JOHN GERMAN

Lenski's *E. coli* strains are now distinct, each possessing unique traits that have resulted from many iterations that introduced both mutations—one of the random processes in evolution—and adaptation to their environment—a result of natural selection. By sequencing the genomes of generations of the bacteria, the researchers have been able to quantify rates of change and genetic differences among the populations.

They have gained important insights. Early changes in the bacteria, for example, appeared to be largely adaptive as the strains improved their fitness, and those early adaptations tended to progress in step-like sweeps of beneficial mutations. But adaptation-driven changes tended to slow down as the populations approached peak fitness, and later evolutionary changes tended toward the random.

These adaptive slow-downs were sometimes

**Left:** Because they reproduce so rapidly, *Escherichia coli* bacteria, often found in animal intestines, offer a unique opportunity to study evolutionary processes.

are strikingly similar for two strains that evolved separately—but in the same environment—for 20,000 generations. This suggests that overall, most of the genetic change in *E. coli* occurs as a result of selection and not by random drift.

In other words, if random drift were the dominant process, given enough time, the genomes and phenotypes from different lineages could be expected to diverge significantly. Instead, because different lineages evolve similarly, if not identically, there may be a common solution to the problems imposed by the glucose-limited environments in which all the populations have been living and evolving.

Still, adaptive and random genomic changes don't necessarily follow the same patterns. Even in a consistent environment, the interplay between adaptive and random is complex and can be counterintuitive, Lenski says. The researchers discovered, for example, that although most of the *E. coli* lineages continually adapted to the glucose diet, one population eventually figured out that the flasks contained citrate too, and evolved to

take advantage of the citrate as well as glucose.

Fortunately, with frozen samples, the researchers can replay the tape of the *E. coli's* evolutionary history. "We can go back and see how evolution might play out differently if given another chance," Lenski says. When the researchers took a second look at the evolution of the citrate-using bacteria, they found nearly two dozen more cases in which the bacteria evolved to use citrate. They also found that this change did not come about in any one mutational step, but instead required a series of mutations. Earlier mutations having nothing to do with citrate were required to set the stage for the eventual evolution of the new function, he says.

In another set of experiments spun off from the main experiment, Lenski's team pitted strain against strain in a battle for flask dominance, with



populations, as determined by accumulated mutations; the team dubbed this strain the "eventual winner." But they wanted to understand how it had achieved its victory, so they collected samples from the 500-generation freezer sample, and had the presumed winners and presumed losers compete against each other.

To their surprise, at the new 500-generation mark, the presumed losers had grown faster than the presumed winners, at a rate that would have driven the winners to extinction in 350 more generations. The presumed losers appeared, in other words, to be headed for victory. So what happened to change the outcome?

In a paper published in *Science* in March 2011, the team showed that the presumed losers (which a press release called the "hare" bacteria) had pulled ahead early with mutations that had given them a short-term advantage. But because of these early adaptations, the hares were not able to take advantage of later, more beneficial mutations. The ultimate winners (which the press release called the "tortoises"), on the other hand, enjoyed a large benefit from later mutations, allowing them to prevail.

Overall, says Lenski, the research shows that "mutations and their effects can't always be understood in isolation. With both the citrate users and the eventual winners, we showed that what had happened in earlier generations had unexpected and nonlinear effects in later generations."

More generally, Lenski emphasizes that "evolution in action"—that is, the fact that evolution is ongoing in the world around us—has many important implications and potential applications. "Evolutionary methods and concepts are used all the time to track the source of emerging pathogens and to understand the rise of resistance to antibiotics," he says, "and as human activities are changing the natural world in so many ways, we also need to ask how microbes and other organisms that perform key ecosystem services will respond."  $\blacktriangleleft$ 

The study has utilized thousands of petri dishes. Here, Zachary Blount, a researcher on the project, contemplates the vastness of *E. Coli* reproduction.

## FRACTALS PARTS THAT REFLECT THE WHOLE Read more at www.santafe.edu/news.

IN A Journal of Theoretical Biology paper, a group of scientists explores the prospects for general, predictive theories in biology akin to those in the physical sciences. The paper suggests that such theories take inspiration not only from physics, but also from the information sciences. SFI coauthors included External Professor David Krakauer, Faculty Chair Doug Erwin, External Professor Jessica Flack, Science Board member and External Professor Walter Fontana, Distinguished Professor Geoffrey West, and External Professor Peter Stadler.

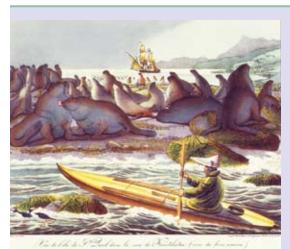
SFI WAS SELECTED to lead a three-year, NSF-sponsored model program called GUTS y Girls, designed to attract New Mexico girls to careers in science, technology, engineering, math, and information and communications technology-fields in which women are historically underrepresented.

### SFI DISTINGUISHED **PROFESSOR Geoffrey**

West and collaborators at MIT proposed a fractal geometry-inspired model that takes in basic meteorological data—such as annual temperature, precipitation, humidity, and solar radiation—and computes how tall a tree is likely to grow under those conditions. The team's research results, published in PLOS One, are consistent with local meteorological data and tree measurements obtained from the US Forest Service.



A STUDY BY former SFI Omidyar Fellow Jessika Trancik, former Graduate Fellow James McNerney, Professor J. Doyne Farmer, and External Professor Sidney Redner demonstrated a way to measure the interconnectedness of a technology's components and predict which technologies are likeliest to advance rapidly and which, due to their complexity, are likely to improve more slowly. The technique could serve as an aid for policy makers weighing technology investment decisions.



**Dunne** and colleagues from Idaho State University are using interviews, ecological observations, and archaeological studies to quantify how humans fit in their food webs on Sanak Island, Alaska, for the last 5,000 years. Such a "whole system" study of

the human roles in a food web has never been done.

SFI PROFESSOR Jennifer

MODERN HUMANS likely originated in southern Africa rather than eastern Africa as was generally assumed, according to the results of a Stanford University study that involved statistical analysis of the largest dataset to date of genetic diversity among African huntergatherer groups. SFI Science Board Co-Chair Marcus Feldman was the corresponding author.

IN THREE Stanislaw Ulam Memorial Lectures in three nights, SFI External Professor David Krakauer explored the extraordinarily convergent theories from math, physics, computation, and biology as they relate to the emergence of intelligence on Earth, and speculated about the future for biological intelligence in a world of distributed thinking machines.



### NOT YOUR GRANDFATHER'S

# Origin of Life THEORY

### BY KRISTA ZALA

ith just a glimpse, early Earth could almost be mistaken for a contemporary—but lifeless—landscape. A vast ocean swept shores in cycles, wind and rain chipped at cliffs, while vents and volcanoes leaked fresh compounds. Yet Earth's features and rhythms both above and below its surface did differ, often operating much more chaotically than those they've settled into over the eons.

The planet spun faster; days went by in half the time. The young moon was closer, drawing a much greater tidal swell—possibly rising as high as a kilometer instead of the few meters of today—and its proximity meant it simply looked bigger, too, though no creature was around to notice. The Earth's crust was more cracked, and the tidal bustle drove seawater through it like a hose blast-

ing a sponge rather than at today's trickle. Somehow, these conditions created life.

"From the solar system, through the formation of Earth, to the chemistry of rocks and water, the phylogenetic tree is clearly tied to the chemistry of Earth," says SFI External Professor Eric Smith. The question is, how did we get from thermodynamics to thoroughbred horses?

### **Sketching Life**

Origin of life theory has itself faced a rocky path. Amid the rise of chemistry as a science, the "vital force theory" drew a thick line between organic and inorganic chemicals, splitting Earth into biotic and abiotic worlds where living begat living all the way back to God's kitchen. The line remained impenetrable until the 19th century, when

the German chemist Friedrich Wöhler accidentally synthesized urea out of decidedly inorganic ammonium cyanate and opened scientific thinking to the wondrous possibility of chemical crossovers between life and the rest of Earth.

In the 1920s, Alexander Oparin and J.B.S. Haldane proposed the now-famous "primordial soup" theory: an early ocean rife with nutrients that provided the balanced breakfast for life to get its eventual start. Three decades later, Stanley Miller and Harold Urey demonstrated how organic molecules could arise from simple inorganic compounds under the right, vaguely prehistoric conditions.

Like all good science, those early revolutionary findings gave rise to many more directions for research: how the chemistry of rocks and water relates to Earth's position in the solar system, how the chemistry of Earth is tied to the tree of life, and which parts of biochemistry are absolutely fundamental to life.

Studies since then concerning the origin of life have branched across many disciplines including statistical physics, interstellar chemistry, geochemistry, microbiology, and computational biology. Quiet incremental advances in the shadows of research have been balanced by astounding discoveries and insights. At SFI, research indicates that any plausible origin of life theory is going to be broad and sophisticated, as well as a messy confluence of dynamic systems. In short, it's not going to be your grandfather's origin of life theory.

### Finding Life's Essence

SFI Science Board Chair Emeritus Harold Morowitz, a biochemist at George Mason University, has made the thermodynamics of living systems his life's work. When the discipline was just starting in the 1960s, the first approach was to study Mycoplasma; the bacterium with the smallest known genome and no cell wall seemed a natural starting point in cracking the great mystery of life. (Geneticist and co-founder of Synthetic Genomics Craig Venter is currently using it in his project to synthesize cells from a genome.) But as a clue to life's beginning it turned out to be a false lead. Rather than it being an ancient organism, Mycoplasma is a modern minimalist, having trimmed its superfluous functions and genes over time as it specialized its niche.

Later, while working with an origin of life group at NASA-Ames, Morowitz discovered how to make the amino acid glutamic acid—a main player in the citric acid cycle—from its precursor compounds without using enzymes. Reasoning that the process predated more sophisticated biomolecules that boost reaction speed, Morowitz decided to look at a potentially sturdy bridge between

Below: This Origin of Life timeline, part of the "Emergence" exhibit at the New Mexico Museum of Natural History, depicts 4.6 billion years of change, from early Earth's chaotic, lifeless era to the Blue Green Earth as we know it, with a relatively warm and stable climate that allows plants and animals to flourish.



"The core metabolism hasn't changed in the last four billion years," Morowitz points out, "but it's been kept alive in bacteria that turn over every 20 minutes."

geochemistry and life: the citric acid cycle.

The citric acid cycle stands as the metabolic heart of cellular respiration in all organisms that use oxygen. A true biofuel engine, it breaks down fats, sugars, and proteins, tapping the energy in the compounds' chemical bonds as it turns complex molecules into carbon dioxide.

"The core metabolism hasn't changed in the last four billion years," Morowitz points out, "but it's been kept alive in bacteria that turn over every 20 minutes." Such a tightly conserved mechanism indicates the pathway arose one of three ways. It could be simply an accident that happened and worked well (which Morowitz rejects as it doesn't lead to other useful questions about the emergence of life—i.e., it's a scientific dead end). It could be the best way to synthesize biologically useful compounds from inorganic surroundings, which the biosphere on Earth eventually or fortuitously happened upon. Or it could be the only way—which means it would be found everywhere in the universe where there is life.

"We could go to Mars and find the same intermediary metabolism," he says. "It could even mean that life will form on any planet with the right chemistry, temperature, and gravitational pull."

### A Fracture that Opens Everything to Sense

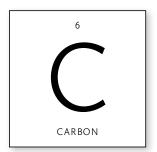
A major conundrum in origin of life theory was that the citric acid cycle relies on a steady source of complex organic molecules, which makes a fairly profound assumption that they run in rampant supply. (Plants,

in contrast, rely on the even more complex Calvin cycle to harness light energy and use it to build organic compounds from inorganic matter.) Where could these complex biomolecules have arisen?

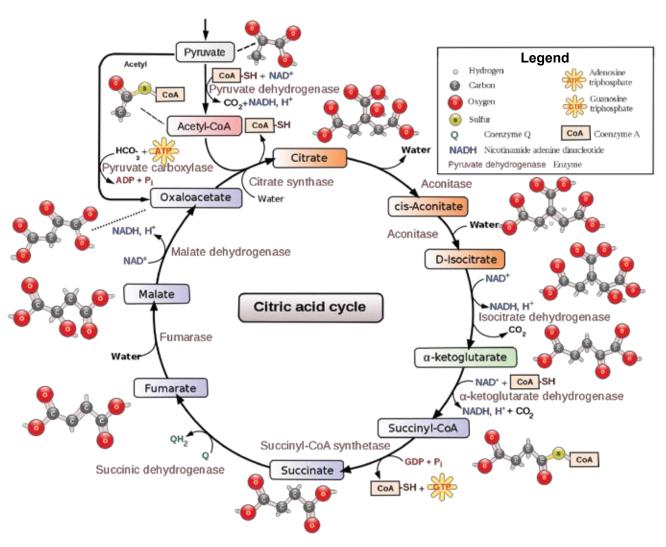
It took a voyage to the deep to boost origin of life theory. In 1977, Jack Corliss, Richard von Herzen, and Robert Ballard led the deep-water submersible Alvin to the oceanic trenches off the Galapagos, where they discovered life at the seemingly hostile hydrothermal vents. On examining the organisms thriving amid the scalding temperatures, immense pressures, and sulfur-spewing chimneys, they found some of the deepest-branching organisms on the tree of life. These included bacteria that ran the citric acid cycle—but in reverse.

The revelation that the cycle could run the other way "was like watching a fracture form that opens everything to sense," says Smith. After decades of struggling with the chickenor-egg paradox of complex and simple molecules that each required the other for its existence, the solution came from the lightless biosphere: The mechanism originally arose to build small molecules into bigger ones. What we call the reverse cycle was the original direction, and the only way it ran for the first billion years, he says.

Morowitz's recent work has shown that some small molecules can, in fact, speed metabolic reactions. He has also discovered how metals ranging through the transition elements of the Periodic Table from titanium to zinc, especially iron, cobalt, and nickel, can grab on to small organic molecules and nudge the cluster into an arrangement that catalyzes other biochemical reactions. Armed with such intriguing insights into the citric acid cycle development, Morowitz is now focusing on the stage where the compound citrate splits, adding a side path to form fatty acids, to determine why the cycle is







structured that way. "If it is the only solution, or the best one, to metabolism, we have to learn why it is so," he says.

### Miraculous or Inevitable?

Whereas Morowitz looks at the biochemical reactions from the top down, Smith is approaching the problem from the bottom up. A statistical physicist, Smith came to SFI in 2001 to pursue his interest in the processes by which order stems from dynamic systems. As he grew to know the SFI community, members recommended he meet Harold. "They remarked that when the two of you talk, you sound a lot alike, even though you talk about different things," he recalls.

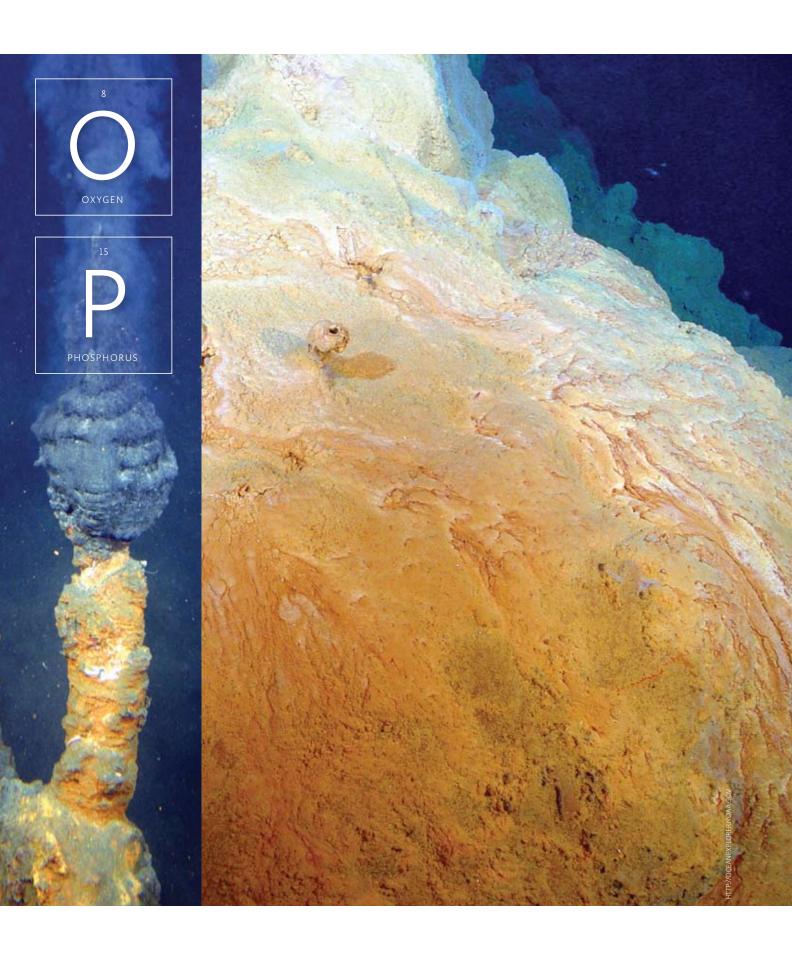
Smith turns conventional origin of life theory upside down. From a dynamic sys-

tems perspective, life may have been forced into existence as an outlet for the mounting free energy from the sun and geosphere. Rather than being miraculous, life could be inevitable. It could even be construed as a natural consequence of Earth's thermodynamic order, where the myriad and diverse high-energy systems on early, lifeless Earth "may have forced life into existence as a means to alleviate the buildup of free energy stresses," as he and Morowitz explained in a 2006 paper.

Recently, Morowitz and GMU colleague Vijay Srinivasan's search for a minimal metabolic pathway has whittled the field to about 125 molecular contenders, which Smith is drawing from in charting the drivers in the rise of metabolism.

Above: The citric acid cycle is a series of chemical reactions used by all aerobic living organisms to generate energy. In addition, the cycle provides precursors for the biosyntheses of compounds.





### **Exploring Metabolic Pathways**

SFI Omidyar Fellow Rogier Braakman brings a systems-level approach to reconstructing the deep evolutionary history of life. Braakman's interest in how chemical organization evolves prompted his graduate research in interstellar chemistry and led him to join SFI's 2006 Complex Systems Summer School in Beijing. Due to his interest in the bridging of the abiotic-biotic gap, he was drawn to Morowitz's and Smith's work. On a colleague's encouragement, Braakman contacted the two, who invited him to SFI in 2008. They've been working together on this puzzle ever since.

In contrast to traditional approaches to evolutionary history, which largely involve poring over the countless branches of the phylogenetic tree, Braakman took another approach. In his effort to map innovation of core metabolism through the biosphere, he focuses on the handful of core metabolic pathways that diversified around the split of the bacteria and archaea, traditionally the two main branches of the tree of life.

Braakman's recent work with Smith and Morowitz combines the constraints of physics and chemistry in developing an empirical framework that ties phylogenetics to metabolism. They hope to use it to determine what metabolic strategies organisms used at divergent points in the evolution of capturing carbon and turning it into biologically useful molecules. "If you can show how these pathways are related, and what guided their evolution, you can say a lot about the

Left: Hydrothermal vents and chimneys reside on the ocean floor. Upon examining the organisms thriving amid the scalding temperatures released from them, researchers found some of the deepest-branching organisms on the tree of life. These included bacteria that ran the citric acid cycle—but in reverse. Image courtesy of the New Zealand American Submarine Ring of Fire 2007 Exploration.

nature of life and evolution," says Braakman.

Like the bewildering, chaotic array of components and energy from which life emerged, the journey to an origin of life theory has leapt and stumbled through wild advancements and missteps amid overwhelmingly diverse efforts.

We couldn't be at our current stage of understanding without dozens of breakthroughs that have accumulated in all the areas that bear on the origin of life, Smith points out.

"Only in the last 30 years have fast computing and massive storage come together to bring deeper understanding," he adds.

From a dynamic systems perspective, life may have been forced into existence as an outlet for the mounting free energy from the sun and geosphere. Rather than being miraculous, life could be inevitable.

"Advances in statistical physics, genetic sequencing, and much richer understanding of interstellar chemistry, geochemistry, and biochemistry have brought us to the point where scientists can see from all sides how natural systems might have pushed, or pulled, life into existence."

Throughout the journey, "a lot of this work has been accomplished by researchers patiently trying to thoroughly understand particular systems, not expecting that a few 'big ideas' should command all the focus," he says. In other words, the next generation of SFI thinkers are well positioned to discover just how Earth's systems converged to squeeze life out of rock.  $\blacktriangleleft$ 

Krista Zala is a freelance science writer in Victoria, BC Canada, who balances computer-screen time with guiding kayak trips on the British Columbia coast.



### Cliodynamicists would like to see the historical fields

sharing methods among themselves and adopting approaches and theories from physics and other

## HISTORY AS SCIENCE

he past does not repeat itself, but it rhymes," Mark Twain once said, a reference to the patterns of history, perceived anecdotally.

Today, a new field is coalescing around the notion that historical patterns are, to some degree, measurable, and that the future can, also to some degree, be predicted. Researchers involved in the field call it "cliodynamics" after Clio, the Greek muse of history.

Scholars of human history traditionally have studied the past as a chain of idiosyncratic events, with each event a unique response to unique circumstances, says SFI External Professor David Krakauer. Historical fields such as paleontology have relied on collections of evidence—fossils, for example—to draw inferences about the past.

A few fields have made strides in approaching history as a science. In archaeology, for example, rigorous field survey methods have provided new, quantifiable information about the location, distribution, frequency, and organization of certain human activities. In population genetics, evolutionary outcomes are modeled as probabilities.

Cliodynamicists would like to see the historical fields sharing methods among themselves and adopting approaches and theories from physics and other long-quantified fields. The tools of complexity science are now beginning to make the task tractable, Krakauer says. Mathematical and computational techniques such as agent-based models, power-law relations, and more classical differential-equation models are in several fields helping scientists develop new theoretical frameworks, for example.

"A historical chronicle is like a random

sequence, with very high complexity," Krakauer says. "But if there's a pattern, you can dispense with details and give a more parsimonious description. This description can help reveal the general principles of historical dynamics as they apply across fields."

Scientists affiliated with SFI are playing key roles in the emerging field. In March 2011, a special issue of Cliodynamics, a peer-reviewed journal edited by longtime SFI collaborator Peter Turchin of the University of Connecticut, led with an editorial, "An Inquiry Into History, Big History, and Metahistory," by Krakauer, John Gaddis (Yale University), and Kenneth Pomeranz (UC Irvine). Its authors define "history" as the study of written records, "big history" as all reconstructions of the past that do not rely on written materials, and "metahistory" as the "patterns that emerge from both modes of inquiry that make generalization, and hence analysis, possible."

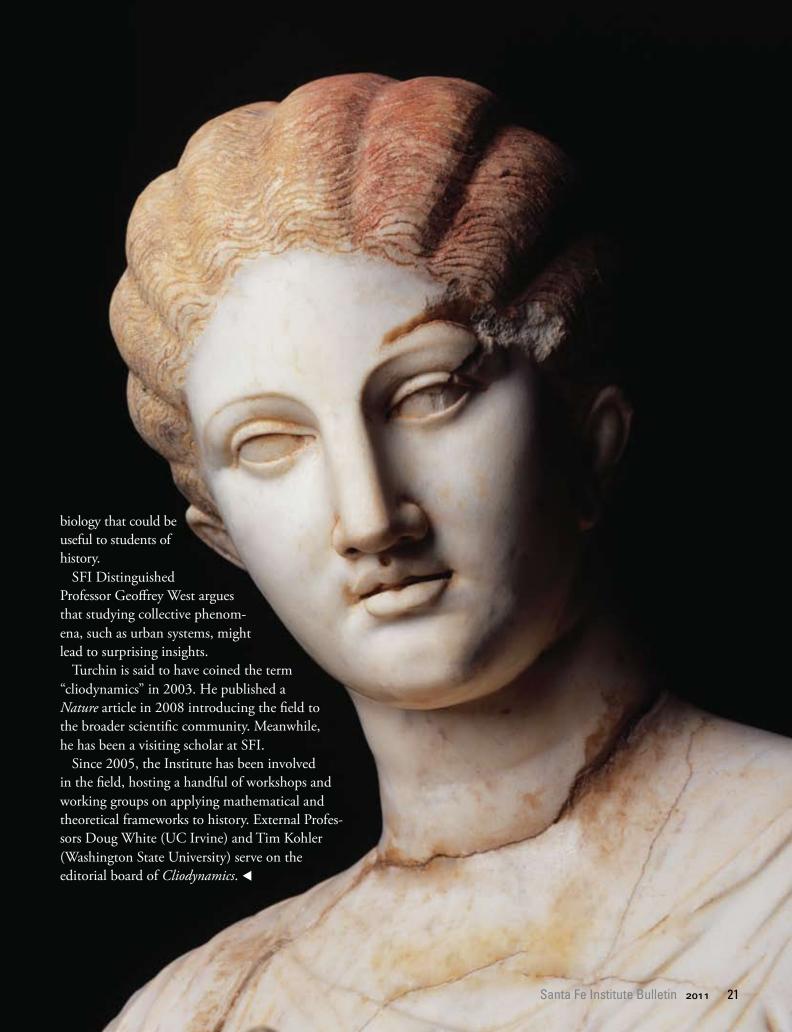
Also in the issue:

SFI Faculty Chair Doug Erwin explores how paleontologists deal with the vagaries of preservation, and how statistical techniques developed in biology have been applied to textual evidence.

SFI Distinguished Fellow Murray Gell-Mann illustrates how apparently complex histories and patterns can sometimes be organized using simple models of growth and scaling.

Krakauer shows how history often uses analogs of concepts and tools expressed quantitatively in the natural sciences, and introduces concepts from nonlinear dynamics, statistical physics, and evolutionary

Cliodynamics takes its name from Clio, the Greek muse of history, here rendered in marble: Roman 130-140 AD.



ight centuries ago, the Four Corners region of the US Southwest was bustling.
Regular rainfall coaxed crops from healthy soil, and the abundance of cottontails, jackrabbits, and mule deer made for choice meals. Tens of thousands of Ancestral Puebloans lived in adobe houses and cliff dwellings spread across an area the size of Napa County. Then, in the final decades of the 1200s, most everyone left. Drought, crop failure, and conflict all contributed to the society's collapse. But we don't exactly how the migration unfolded.

Clues from language, cultural artifacts, DNA, and human remains each provide pieces of the puzzle of human geographic history. Today, SFI researchers are re-examining these pieces, figuring out their collective significance, and applying novel insights to studies of civilizations past and present. Their research at the frontiers of genetics, linguistics, anthropology, and even economics is converging in a comprehensive approach to human migration. One early finding is that each migration story is unique.

BY KRISTA ZALA

"Most researchers assume that ancient migrations should leave consistent residues in human biology, language, and archaeology," says SFI Omidyar Fellow Scott Ortman, one of the archaeologists researching the history of the Four Corners. "But well-studied cases from the recent past show that they rarely do."

Ortman and others are confirming some old hunches and building cases for new accounts of migration. New techniques promise new evidence. Cheek swabs now produce enough DNA to help trace ancestral migrations. Computer models can help trace the evolution of human languages back to long before any word was ever written. By overlaying the improved evidence from many fields, some researchers hope to

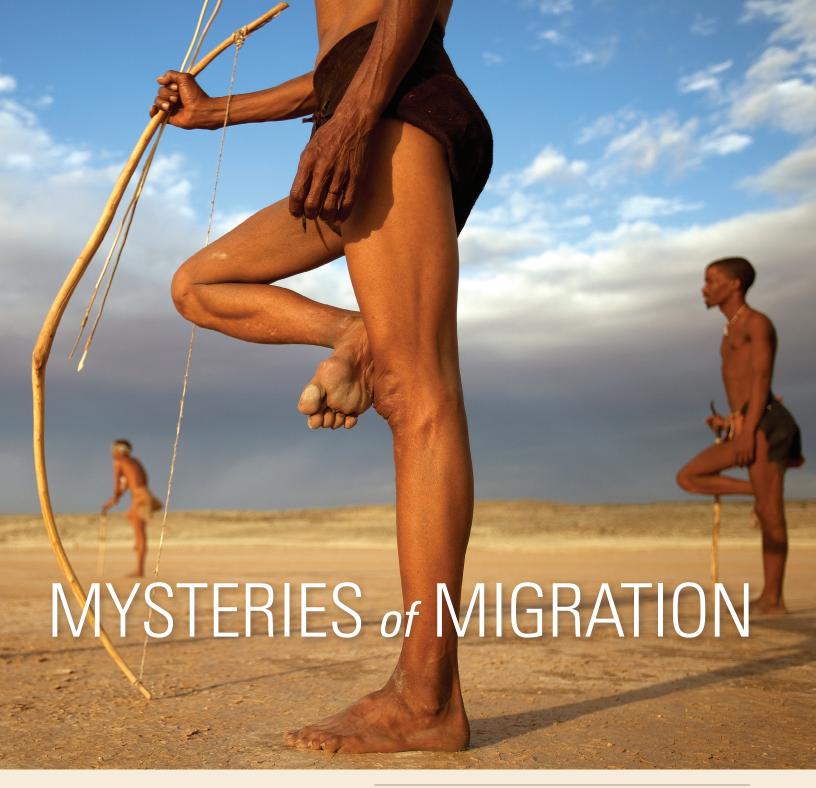
overhaul our understanding of migration and answer perhaps the most basic human question: Where did we come from?

### **Genes Reveal Clues**

Modern humans first left Africa 60,000 years ago, ultimately spanning the globe in a series of colonizations reflected in our genomic diversity variation today. Where that original migration started



ABOVE: DAN KITWOOD/GETTY IMAGES

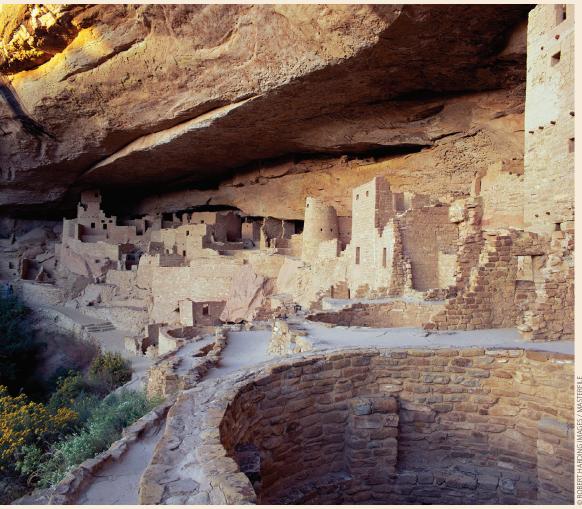


has been debated for decades. "Our belief used to be that the center of humans leaving Africa was in East Africa," SFI External Professor and Science Board Co-Chair Marcus Feldman says. "We've just never had enough people represented in our studies before."

Feldman is a geneticist at Stanford University and a pioneer in research on human origins and evolution. Using genetics and computational The  $\neq$ Khomani San strike traditional poses. Their African homeland could be the spot where modern humanity began.

biology, he and a team recently moved humanity's starting point considerably farther south.

He and colleagues analyzed the genetic sequences from 25 populations of modern-day huntergatherers, pygmies, and farming societies throughout southern, central, and eastern Africa.



Cliff dwellings nestle in the sandstone of Colorado's Mesa Verde National Park, what was, prior to the 13th century AD, a Four Corners settlement.

The team looked at sites on chromosomes where a lone nucleotide has altered from the standard sequence in what's known as an SNP (single nucleotide polymorphism, pronounced *snip*). All chromosomes (except the Y chromosome in males) get cut and mixed at each generation; the older a population, the more frequently its sequences have been shuffled; and the more mutations that have accumulated, the greater the genetic diversity.

In analyzing hundreds of thousands of SNPs, the team found that hunter-gatherers' sequences vary the most, both within their groups and compared to other African populations. Two in particular, the click-speaking South African

≠Khomani and the Bushmen in Namibia, stand out as most diverse. The earliest common ancestor among ≠Khomani and other KhoeSan speakers in southern Africa today dates to 40,000 years ago. Some Bushmen groups have remained there ever since, and some may have disappeared a long time ago. Thus those small groups that originally left Africa most likely derived from ancestors of today's KhoeSan speakers in southern Africa.

### Language Explains Roots

Language is nearly as easy to carry as genes. It's flexible too: When a group splits from its original population, the two lineages develop differently if they don't interact much. The French spoken in Quebec, for example,

is a 17th-century offshoot of the old country's lexicon, pronunciation, and even taboos: Today, people from France find Quebeckers' swear words charming. Similarly, not far from the Santa Fe Institute, mountain villagers speak a derivation of 16th-century Spanish brought from old Spain.

The French and Spanish cases of divergence prompted by geographic separation represent just a few examples of how languages behave like species. On a larger scale, a movement is afoot to study historical linguistics, using models and techniques borrowed from molecular evolution. In the latter, researchers analyze thousands of genetic sequences to uncover how related, and how old, species are. The nascent linguistics methodology

crunches thousands of similar words within and between languages to chart their lineages.

This isn't the first time well-meaning scientists tried to subject language to statistical analysis. Decades ago, attempts to quantify language evolution used unsophisticated statistical methods, with incorrect results deterring historical linguists. Since those early tries, both computing and statistics have grown enough to handle the phenomenal task of charting the evolution of language.

SFI External Professor Mark Pagel, an evolutionary biologist at the University of Reading, and colleagues took some steps a few years ago. The team used lexicons of three major language groups—Bantu in Africa, Indo-European, and Austronesian—to create evolutionary trees depicting the patterns and paces of language change and emergence. They found that, much the way species can speedily evolve in new settings, young languages burst with innovation in their infancy before slowing to relative stasis.

Subsequent work confirmed that a word's importance determines its resistance to change. Peripheral words like *bird* change faster than everyday words like *two*, where disagreement on meaning could lead to conflict.

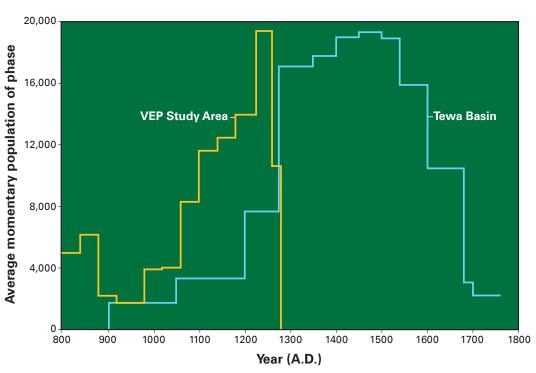
Back at the global scale, so many languages have deep-rooted similarities that they hint at a common ancestor, posits SFI Professor Tanmoy Bhattacharya, a statistical physicist at Los Alamos National Laboratory, who has turned his data-analysis skills to studying dynamics of change in language. "Today, we

don't care about answers that are *probably* so," says Bhattacharya. "We want to know *how* probably."

He, Pagel, and other SFI affiliates recently joined efforts to create two major systems that examine patterns of sound change and meaning change. Project members with SFI ties include SFI External Professor and physicist Eric Smith, External Professor and geneticist Jon Wilkins, Postdoctoral Fellow and network physicist Hyejin Youn, anthropologist Daniel Hrushcka of Arizona State University, and linguists William Croft and Ian Maddieson at the University of New Mexico.

In the first project, the team is quantifying sound changes in language by aligning corresponding sounds in similar words belonging to related languages. Drawing from the 29 closely related languages of the Turkic family, the team can construct an evolutionary tree of tongues, complete with probabilities of sound change for every branch.

In the second project, the team is looking



Population histories for the Four Corners (VEP) and northern Rio Grande (Tewa Basin) regions suggest a massive migration from the former to the latter during the 13th century AD.

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to trace how words have expanded, shrunk, or shifted their meanings. "If you learn that a word in, say, Basque means both 'water' and 'hazelnut,' would you be surprised?" asks Bhattacharya. "Across the world's languages, what patterns do you expect?" By measuring shifts in sound and meaning, the team hopes to build a system that scientifically analyzes language relationships. Ideally, the system will automate the routine work of processing countless data points, relieving the linguistics experts to interpret the results and advise on particular and peculiar instances.

### **Faces as Indicators**

Back in the Southwest, Ortman, the archaeologist, is putting genes, language, and culture together. He noticed the shrinking Four Corners towns coincided with swelling populations in the northern Rio Grande area, but confirming the link required evidence. With no DNA of the study subjects available, Ortman chose a proxy: craniofacial data. Skull measurements can indicate people's relatedness; across a population, the genetic structure and even the mating network emerge.

Ortman analyzed records from remains of 1,200 people found at a hundred sites across the Ancestral Pueblo world and found that, indeed, the northern Rio Grande population had originated in the Four Corners. He also found that residues of Four Corners society survived and persist in present-day Rio Grande pueblo languages. Oddly, however, the migrants chose the architectural and ceramic styles of their new home over those of their old one.

The Four Corners collapse represents just one of thousands of migrations. Societal features all jostle for prominence when cultures mingle, and

the melee rarely settles into consistent patterns. Trouble arises when researchers assume they will find the same patterns of change, in specific cases or in general. The lure of simplicity runs the risk of badly misrepresenting human history.

Traditionally, archaeologists have categorized elements of ancient cultures based on researchers' own backgrounds. The problem with this, Ortman continues, is that humans vary dramatically in how they classify and value experience, and such assumptions influence decision making. So to understand the cultural dimension of human history at the same level of precision as genetics or linguistics, the first step is to figure out how to identify, classify, and count the conceptions of the people who actually created the archaeological record. Ortman is working on a scientific approach for doing just that.

### **Metaphors Offer Answers**

People everywhere rely on metaphors to explain ideas. Analogies permeate languages. In English, for example, one collection of sayings for piquing interest uses fishing metaphors: Okay, I'll bite. He took the bait. They swallowed it hook, line, and sinker. He knows how to reel people in.

Concepts from everyday living are captured in language and can even be applied to other forms of expression, such as architecture or painting. Ortman's framework offers a means to describe cultures based on the distinctions the people themselves make.

To understand cultural elements at the Four Corners, Ortman is looking at the myriad ways Ancestral Puebloans utilized container metaphors to conceptualize their experience. He has quantified various elements that were important to the

Ultimately, human nature may be to join the migration once it starts: When enough people move away, the urge to **stay in the familiar place** is overcome by the urge to **stay amid the familiar culture.** 

people, including the bits of weaving imagery that appear on pots, the bits of pottery designs that appear in mural paintings, and the aspects of container technology that structured architecture and social organization. On a grander scale, the method also provides a basis for tracking how and why salient aspects of a culture change through time.

So why did the Four Corners people leave?

Ortman joins SFI External Professor Tim Kohler, an archaeologist at Washington State University, in making a model society that might point to some plausible reasons. They and researchers in hydrology, ecology, economics, and

computer science have built an agent-based model to simulate the Ancestral Puebloans' lives. In it, each household is an agent. Given initial conditions of climate and environment, the model simulates hundreds of years of people living their daily lives—collecting water and fuel, hunting and farming, exchanging meat and maize through good years and bad—to see how the inhabitants might have used their wild and domestic resources.

The team also drew from archaeological data from 9,000 sites to understand where farmers chose to live and use the local resources, how goods exchange influenced the forming and dissipating of villages, and why so many people left. By playing the model and data off each other, they learned that, beyond the basic water and land considerations, housing rules seemingly changed



In his paintings, Hopi/Tewa artist Dan Namingha utilizes ancient symbols often found on petroglyphs in the Four Corners region, including the spiral, which can depict migration. Courtesy of Niman Fine Art.

between waves of settlement, as households at later stages were built at less than optimal sites. The team also learned that maize levels dropped, but not necessarily enough to drive so many people away. Warfare, too, may have kept people huddled in villages for safety, even as some fled.

So, despite the tough times, more people left than needed to. Ultimately, human nature may be to join the migration once it starts: When enough people move away, the urge to stay in the familiar place is overcome by the urge to stay amid the familiar culture. The unknown is less intimidating if you face it with allies.  $\blacktriangleleft$ 

## FIGHTING HIV THE Evolution Solution

BY JULIE REHMEYER

IV seems to have learned a thing or two from Proteus. It constantly changes form, eluding the immune system much the way that mythological sea creature evaded Menelaus. Although a person typically gets infected with a single strain of the virus, after a decade of infection two HIV viruses in the body may differ by as much as 10 percent—a greater difference than that between the key regions of mouse and human DNA. So before the immune system has managed to grasp the first form of HIV, the virus has changed form enough to become unrecognizable.

For the past 20 years Bette Korber, an SFI external professor and a researcher at Los Alamos National Laboratory, has been hunting HIV, trying to develop a vaccine that could teach the immune system to grab onto the wily monster that causes AIDS. Now she and her team of researchers may have hit on something. The mosaic vaccine they have developed has entered Phase 1 clinical trials.

Every previous human vaccine attempt has either failed completely or has been only marginally use-

ful. Their trials have taken a fairly traditional approach, exposing the immune system to proteins from a few HIV strains and hoping the body would somehow be able to generalize and recognize other strains. Though disappointing, their failure hasn't been surprising: Two HIV viruses from different people in different parts of the world can vary by as much as 30 percent. Although a single vaccine might help the immune system with strains similar to the ones it's based on, it can't do much to stop the rest.

So vaccine researchers have continued to struggle with HIV's Protean tricks. In the early 1990s, Korber came up with a novel idea: She could design an artificial protein to resemble natural proteins from all the different strains. Then, if the body could learn to recognize that single protein, it might be able to spot a great variety of natural HIV proteins.

"People kept saying this would never work," Korber says. Proteins are complicated objects, other researchers argued, that won't fold up right if they're designed willy-nilly on a computer. But Korber noted that Two HIV viruses from different people in different parts of the world can vary by as much as 30 percent.

evolution itself, which produces HIV's tremendous variation, creates large, random changes in proteins, and those proteins seem to serve HIV's ends all too effectively. So she and her team stuck to her idea and produced a "consensus" protein, which is a kind of average of all of the global variants of each protein that makes up the HIV virus (one such protein, for example, forms part of the outer surface of the virus). Proteins are long strings of amino acids

chained together, and in each position along the chain, their artificial protein contained the amino acid that occurs most commonly in natural HIV viruses.

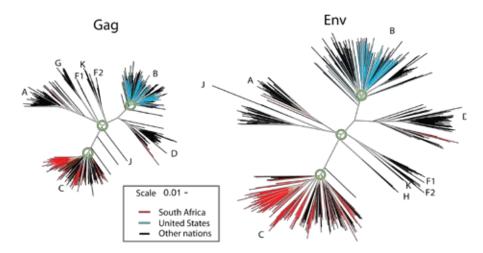
When Korber's colleagues for the experiment tested her vaccine, it caused vaccinated monkeys' immune systems to recognize many more variants of HIV than vaccines based on natural proteins had. Now that Korber's approach has shown success, she's received the ultimate compliment

from other researchers: Not only are other groups embracing her approach and pursuing similar ideas themselves, the success of the method is now seen by many as obvious.

The consensus vaccine is one of the approaches about to be tried in humans. Still, Korber and her team worried that it might not be good enough. Current HIV viruses could be so diverse that the body might not recognize their proteins as being related to the average, consensus protein.







A phylogenetic tree depicts the relatedness of different organisms and can be used to reconstruct lineages. In these trees, each branch tip represents an HIV sequence isolated from a different person. The different "clades" or branches are groups of genetically related sets of HIV sequences, designated by letters A, B, C...

So Korber and her team developed another way of designing an artificial protein, one that could be even more powerful. Because defending the body from outside attack is such a complex job, the human immune system takes a belt-and-suspenders approach, with independent, overlapping defenses. Traditional vaccines teach the body to quickly produce antibodies that can recognize proteins on the outer shell of a virus and mark the virus for destruction. Korber's team's new approach focuses on a different part of the immune system, the T cell. Rather than trying to detect freefloating viruses, T cells sniff out cells that have been taken over by viruses and then destroy them. A T-cell vaccine wouldn't stop infection entirely, but it would allow the immune system to fight back faster and keep the infection under control.

Healthy cells protect themselves

from these killer T cells much the way the Torah says the Israelites marked their homes' doorposts with lamb's blood to persuade God's angel of death not to harm them. Cells persuade the killer T cells to leave them unharmed by placing a little cup on the outside of their cell membrane and filling it with tiny, chopped-up bits of the proteins they're making. If the protein bits in the cup are from normal human proteins, the killer T cells will pass over the cell and leave it alone. But if the killer T cell recognizes a bit of viral protein in the cup, it mercilessly attacks.

Korber and her team hatched a plan to create a vaccine that could teach the T-cell assassins to recognize the wide variety of protein bits produced by variants of HIV. They did this by exposing the body to a set of proteins that were a kind of mosaic, pieced together from fragments of all the different HIV proteins.

Carrying this out was tricky, though. They couldn't simply smash together a bunch of protein bits at random, because the resulting protein might be unlike a natural HIV protein. If the cell chopped the protein up incorrectly, the killer T cells wouldn't learn to recognize infected

cells. Even worse, the cells could end up producing other harmless protein bits that would busy the immune system with useless reactions and distract it from its real work.

The problem was a stumper, one that had hung up previous groups that had tried a similar approach. So instead of relying on their own ingenuity to design the answer to the problem, Korber and her team set evolution—the very tool HIV uses in its shapeshifting stratagem—against the virus.

"We evolved the virus in the same way it evolves itself in people," Korber says. Rather than doing so inside the body, though, they did it inside a computer. The method is an application of the "genetic algorithm" concept developed in part by SFIers John Holland, Melanie Mitchell, and Stephanie Forrest. Korber and her team started with a database of every variant of a given protein produced by HIV and declared this their first "generation" of proteins. They then "mated" them to create a new generation.

Then the computer passed judgment on each of the proteins, deciding on its fitness. To do so, it chopped each protein into nine amino-acidlong bits, ranked those bits according to how commonly each occurs in natural HIV proteins, and added up those rankings. In creating the subsequent generation of proteins, the computer "bred" the high-scoring proteins more often than the low-scoring ones. After many generations, the highest-scoring set of proteins was chosen.

The result of this process was a set of proteins that contained a wide variety of the common protein bits from HIV viruses and very few uncommon ones.

Furthermore, within each small stretch of amino acids, their artificial proteins would look just like natural HIV proteins, making the body more likely to treat their protein as if it were real.

The team coded up the idea and ran it. The results, says Tanmoy Bhattacharya, an SFI professor and a member of Korber's team, were remarkable: "It beat all of our ideas hands down."

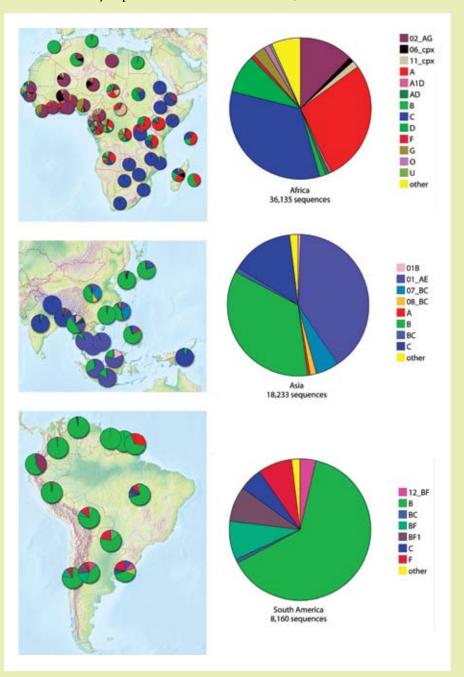
Then the long process of bringing their idea to reality began. Their colleagues in the experiment turned the virtual proteins into real ones and tested them in monkeys. The vaccine produced both an immune response to many more strains of HIV than a conventional vaccine and to many more strains than their own consensus vaccine.

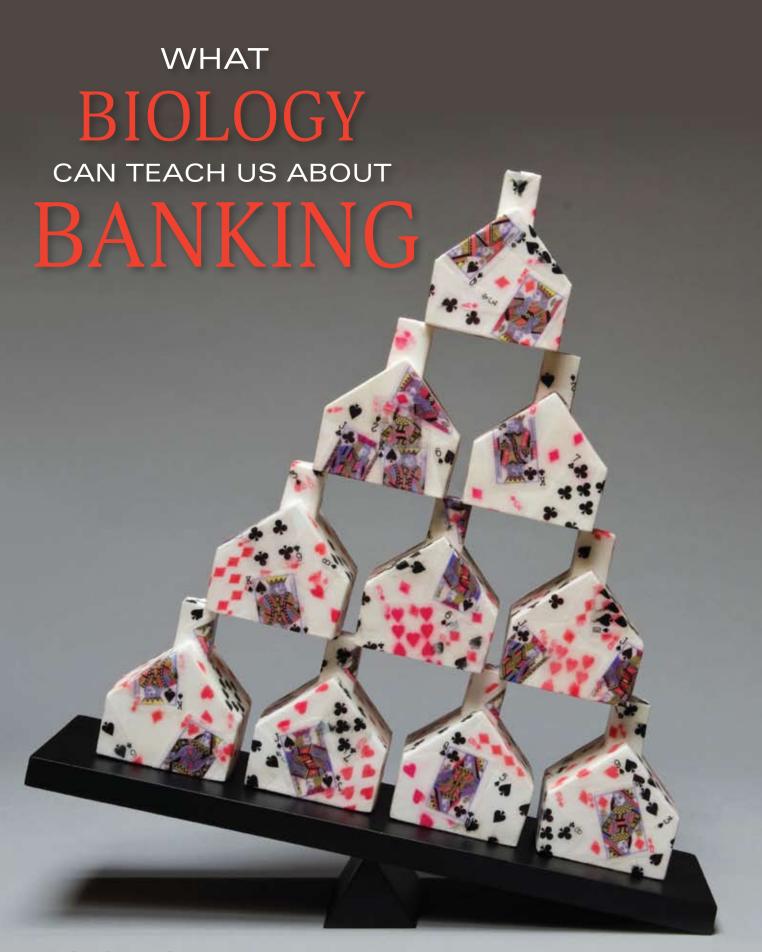
Both vaccines have entered Phase 1 clinical trials. These test how safe the vaccines are and also determine which vaccine—one based on a natural HIV strain, a consensus strain, or a mosaic combination—elicits the best immune response in humans. Though animal tests suggest that the mosaic vaccine is more powerful, results in humans might vary. Furthermore, the consensus vaccine is the least expensive to produce, making it advantageous if sufficiently effective. If successful, trials for efficacy will follow. While Korber is hopeful that this

Right: These maps reflect what researchers know about global distribution of HIV subtypes. The sequences are often single genes and fragments, so inter-subtype recombination is underestimated. They are not sampled randomly but are the product of all HIV studies with sequences submitted to GenBank.

new research will work, she's even more optimistic that the ideas behind the consensus and mosaic vaccines will at least contribute to an eventual vaccine. And a vaccine, she believes, is what we need. "People have made beautiful progress on treatments for HIV, but it is very expensive and difficult to deliver," she says. "You want to be able to protect people without having to give them drugs for life. A vaccine, if we could create one, would be the simplest and best solution."

Julie Rehmeyer is a math and science writer living in Santa Fe.





he behavior of nonlinear dynamical systems has been the unifying theme of my own nonlinear academic trajectory. Beginning as an undergraduate chemical engineer, I ended up with a PhD in theoretical physics, and roughly 10 years later transmogrified into a professor of biology at Princeton University. I believe the ways in which system risks can arise, and propagate, in different settings is best seen from many different perspectives. And it is increasingly clear that such a view of complex adaptive systems is critical to our future well-being, as we are indeed engulfed in complex, and often coupled, systems, from our environment to our social networks and our financial systems.

In my own subject of ecology, SFI has been a

SFI's "clean sheet of paper" approach to complicated problems has been important. It is my belief, however, that the recent—and continuing—worries about the performance of financial markets present SFI with its greatest-yet challenge and concomitant opportunity.

Figure 1 provides a striking illustration of the truly extraordinary growth in the amount of leveraged money swishing around within the UK banking system in recent years, arguably associated in part with the growth of computing power and contrasting greatly with the previous century's stability. Other countries show similar patterns. Much of this growth derives from increasingly complex financial instruments, which purport to reconcile greater returns with diminished risks.

In 2006 the US National Academy of Sciences

There are lessons to be learned about the disproportionate influence of big banks from relatively recent work on "superspreaders" of infectious diseases.

major player in understanding systemic risk, particularly in studies of the nonrandom network structures whereby real-world ecosystems reconcile complexity (many species interacting with each other) with persistence in naturally fluctuating environments. Given the additional shocks being imposed on ecological systems by human activities—overexploitation, habitat destruction, alien introductions, all compounded by climate change—such understanding is increasingly important. It is especially so as we strive to maintain a multitude of ecosystem services, not counted in conventional assessment of gross domestic product, but upon which we depend. In this general area, SFI professors such as Jennifer Dunne, Mercedes Pascual, and others are among the best in the business.

This is only one of several major areas where

(NAS) and the Federal Reserve Bank of New York (FRBNY) put together a prescient study, based on the observation that, while such complex "derivatives" and credit-default swaps seemed attractive at the level of individual financial institutions (henceforth brigaded as "banks"), essentially no one was considering the possible implications for the system as a whole. In addition to bankers and other economists, this NAS/FRBNY study drew in researchers from areas where some "read-across" seemed likely: ecology, infectious disease transmission, and the electricity grid.

Subsequent to the financial crisis that began in 2008, this issue of systemic risk has moved center stage. In the UK, studies of mathematical metaphors or "toy models" of banking systems have buttressed the intuition of central bankers, suggesting, for example, that all banks should revert

Such promotion of individual diversification, without corresponding attention to systemic risk, thus arguably contributed to our present problems.

to the somewhat higher capital reserves (or other liquidity) that they had previously held. These studies also suggest that big banks should hold relatively bigger such reserves than small banks (contrary to the trends of the nineties and noughties); there are lessons to be learned about the disproportionate influence of big banks from relatively recent work on "superspreaders" of infectious diseases.

Additionally, the stabilizing advantages of modular organization in complex systems, seen both empirically and theoretically in ecosystems, suggests a return to greater separation between retail and investment banking activities, along the lines of the US Glass-Steagall Act enacted in 1933. This legislation followed the recognition that a major factor in the Great Depression was banks leveraging casino activity with depositors' money. (Glass-Steagall was repealed at the high tide of free-market extremism that flourished toward the 20th century's end.) These measures, and broadly similar ones being aired in the US, not only

600 500 400 Percentage (%) 300 200 100 1880 1890 1900 1920 1940 1970 1980 1990 2000 1910 1950 1930 1960 Year

**Figure 1:** This graph illustrates UK bank assets expressed as a percentage of GDP, over the past century. The fast increase may be due to the amount of leveraged money circulating within the system.

march with the dynamical properties of sensible models of banking systems, but also are intuitively reasonable.

The recommendations of the UK's Independent Banking Commission, reported on September 12, 2011, are broadly along the above lines: in particular, higher capital reserves and retail banking activities to be structurally separated (by a strong but flexible "ring-fence") from wholesale and investment activity. Many bankers, however, argue against these recommendations and simply wish to get back on the roller coaster.

All these problems are compounded by the fact that there can be a conflict between what is best for any one bank viewed in isolation, and what is best for the system. This paradox is exemplified by the following toy model (Figure 2): Consider N banks and N distinct, uncorrelated asset classes, each of which has some very small probability, p, of having its value decline to the extent that a bank holding solely that asset would fail. At one

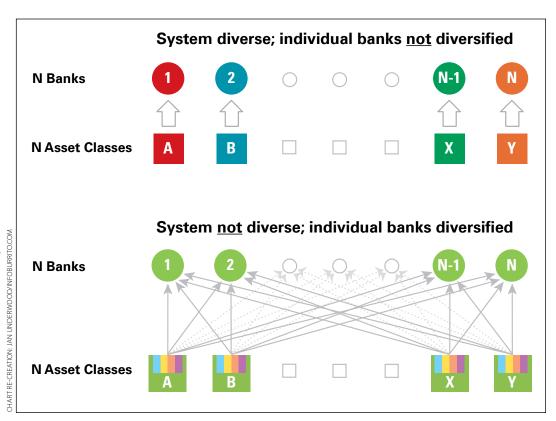
extreme, assume each bank holds the entirety of one of the N assets: the probability for any one bank to fail is now p, whereas that for the system is a vastly smaller p<sup>N</sup>. At the opposite extreme, assume all banks are identical, each holding 1/N of every one of the N assets: The probability for any one bank to fail is now much smaller than p, but all banks now being identically constituted, if one fails, all fail, and this probability is much bigger than pN (being of the general order e<sup>N</sup>p<sup>N</sup>). The former pattern minimizes diversification of individual banks but maximizes diversity of the system, whereas the latter does the opposite. Previous international banking

regulatory meetings, known as Basel I and II, had focused on individual banks and essentially disregarded the system as a whole. Such promotion of individual diversification, without corresponding attention to systemic risk, thus arguably contributed to our present problems.

My view is that considerations of systemic risk are very important, and that greater understanding of how to minimize the likely costs of problems cas-

cading through the system is needed. But I also believe it to be of even greater importance to have more sophisticated and reliable mechanisms for rating complex financial instruments. In retrospect, it is hard to believe anyone could have been so bewitched by illusionary mathematical elaboration of faulty assumptions as to rate collections of Triple B house mortgages as Triple A. There are both technical and social questions here: Not only was the mathematics underpinning the evaluation of complex derivatives (Arbitrage Pricing Theory) grossly unsound, but excessively diligent credit ratings agencies are unlikely to survive in a privatized system. How best to resolve this problem?

Underlying the problems of systemic risk and of proper evaluation of individual financial instruments is a deeper and even more difficult question, recently posed by Harvard's distinguished economist Benjamin Friedman. Beginning with the observation that the role of financial markets in a free-enterprise economy is the efficient allocation of investment capital, he went on to ask, "How much is it costing us to operate this financial system?" His answer: "A lot." Quan-



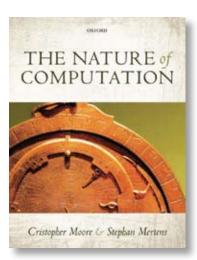
**Figure 2:** The top arrangement minimizes diversification of individual banks but maximizes diversity of the system, whereas the bottom arrangement does the opposite.

tifying this assessment he observed that, in the US 30 years ago the cost of running the financial system was 10 percent of all the profits earned in America. This rose to 20–25 percent 15 years ago, and just before the crisis hit, "running the financial system took one-third of all profits earned on investment capital."

I thus conclude by suggesting one important and appropriate task for the sciences of complexity, and for SFI. Take up Benjamin Friedman's challenge: "The time has come for a serious evaluation of the costs and benefits of running our financial system."

SFI Science Board member Lord Robert May, Baron May of Oxford, holds a professorship at Oxford University and is a fellow of Merton College. He was president of the Royal Society (2000–2005) and Chief Scientific Advisor to the UK Government, and head of its Office of Science and Technology (1995–2000).

## FRACTALS PARTS THAT REFLECT THE WHOLE Read more at www.santafe.edu/news.



A NEW BOOK by SFI Professor Cris Moore and External Professor Stephan Mertens, The Nature of Computation (Oxford University Press, July 2011), provides an overview of computational complexity and the state of the field of mathematics today.

BY ANALYZING A TENTATIVE FAMILY TREE for 2,135 past and present languages, SFI Distinguished Fellow Murray Gell-Mann and collaborator Merritt Ruhlen concluded in PNAS that the proto-language from which most modern languages descended likely featured a verb-last sentence structure.

IMPRINTING, the conditional expression of a gene in an individual, accounts for much of the evolutionary change not adequately described in classical genetic theory.



In a study published in 2011 in the American Naturalist, SFI Omidyar Fellow Jeremy Van Cleve, Science Board Co-Chair Marcus Feldman (Stanford), and Laurent Lehmann (University of Neuchatel) modeled notional populations over many generations and found that even minor population-wide demographic variables—such as small differences in maleto-female ratios and frequency of individuals' movement among groups—seem to play important roles in which alleles are imprinted in individual offspring.

A SPECIAL OCTOBER 2011 ISSUE of the journal *Chaos* includes several papers co-authored by researchers affiliated with SFI and chronicles the progress made since 1989 in developing quantifiable measures of complexity. The papers arose from a January 2011 SFI workshop organized by SFI External Professors Jim Crutchfield and John Machta.

### IS SUSTAINABLE DEVELOPMENT

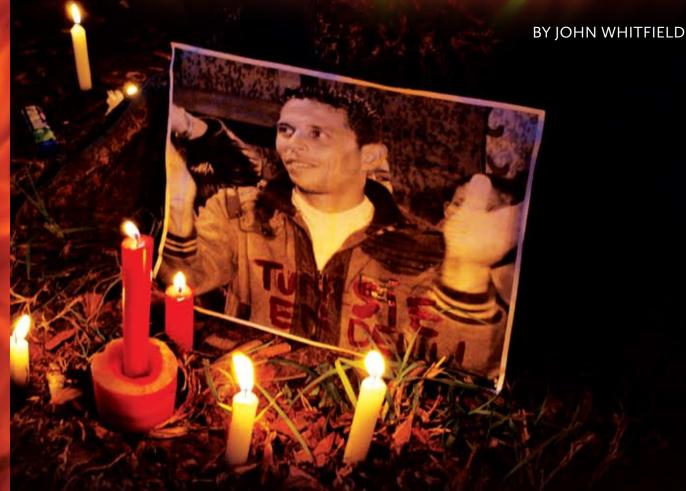
a science? In a study published in PNAS, SFI Professor Luis Bettencourt and Jasleen Kaur (Indiana University) assembled some 20,000 academic papers by 37,000 authors published between 1974 and 2010 and concluded that around the year 2000, worldwide research in sustainable development had coalesced to the point where most contributors were part of a single, global collaboration network, and the field was producing and drawing from unified sets of concepts and theories-evidence that "bodes well for the continued impact and longevity of sustainability science," wrote Bettencourt.

SFI OMIDYAR FELLOW Simon DeDeo, with External Professor David Krakauer (University of Wisconsin-Madison), has been awarded a \$339,000 Advancing Theory in Biology grant from the National Science Foundation to investigate biological processes using the tools of computer science. The study applies classical computational theory to understand



the unusual and counterintuitive ways living organisms (as opposed to engineered systems) collect information from their environments and use it to adapt, in processes DeDeo terms "natural computation."

## Individuals Matter?



n December 17, 2010, Mohamed Bouazizi, a Tunisian stallholder driven to despair by poverty, hopelessness, and police brutality, set himself on fire. He died less than one month later. Ten days after his death, demonstrations provoked by his act brought down the Tunisian government. Just under a month later, protestors overthrew the Egyptian government. The revolt spread to Bahrain, Syria, Yemen, and Libya, where in August 2011, Colonel Gaddafi's 42-year reign came to a violent end.

The Arab spring was built on the ability of powerless individuals to transform themselves into a collective force. The movements were effectively leaderless, and

no single man or woman played a decisive role—they self-organized, perhaps aided by the tools of social media. But what if Bouazizi had just gone home peacefully that day? Would something else have triggered the same events, or would those regimes still be in power?

Such questions cut to the heart of how we understand complex systems. Sometimes, the mass can be treated as one thing, such as when physicists study a cloud of molecules. They view the predictable

An informal shrine commemorates the life of Mohamed Bouazizi, the Tunisian stallholder who set himself on fire, sparking demonstrations that toppled the Tunisian government.

properties and behavior of the whole without worrying about what each component is up to. Researchers at the Santa Fe Institute have pioneered the application of similar techniques to biological and social aggregates. "Taking the tools of statistical mechanics and applying them to other fields is very much what SFI is doing," says paleontologist Doug Erwin, the Institute's chair of faculty. But the extent to which this approach is applicable is still unclear, which is why Erwin and SFI Vice President Chris Wood decided that the Institute's fall 2011 Business Network meeting should have the theme "Do Individuals Matter?"

Understanding emergence does not mean discarding the question of individuality and the role of individuals within a system. Rather, Erwin is one of a number of researchers seeking to understand what individuality is and how it comes

individuals. Professor J. Doyne Farmer, External Professor Duncan Foley and other SFI researchers have argued strongly, in fact, that agent-based models based on the rules of individual decision making should be at the heart of government economic policy making.

Bowles also thinks that balancing emergence against individuality could yield insights into history. The idea that individuals can effect historical change is sometimes disparaged as the "Great Man" view, in contrast to the structuralist view that historical change results from people being pushed by larger currents beyond their control. But Bowles cites many cases where individuals or small groups have brought about changes that deserve to be called historic. Examples include the dramatic increase in sharecroppers' claims on their harvest in West Bengal, the Russian revolution,

Bowles cites many cases where individuals or small groups have brought about changes that deserve to be called historic. All involved rapid shifts where one way of doing things, which had endured for millennia, crumbled and gave way to another.

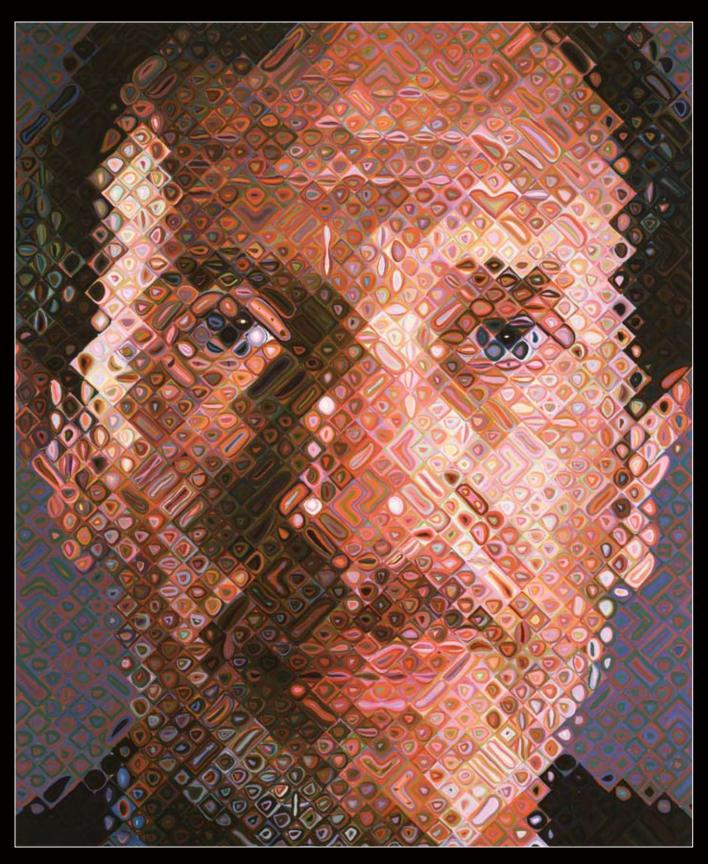
about, and how the differences and interactions between individuals at one level can lead to organization and behavior on a larger scale. "The issue of what an individual is matters a lot," he says.

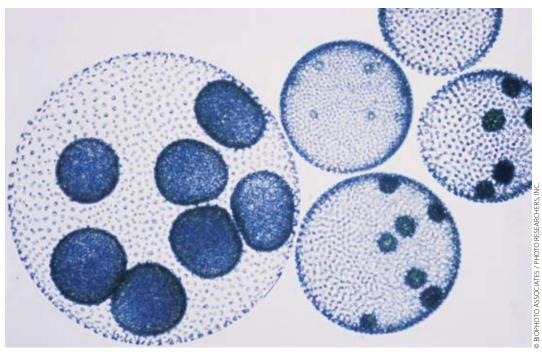
Human behavior is perhaps the most obvious area where SFI scientists consider both the individual and the collective. Behavioral economics, as practiced by SFI Professor Sam Bowles and External Professor Herbert Gintis, uses experiments to reveal the traits that underpin human decision making. People, it turns out, have a host of motives beyond simply maximizing expected material gains. They fear losing more than they desire winning, they copy their peers, they get overconfident when things are good, and they run scared when things change. They reciprocate, reward, and punish one another even at individual cost. You can only get a full picture of the economy if you understand what drives

the US civil rights movement, and the decline of foot-binding in China and of female genital mutilation in West Africa. All involved rapid shifts where one way of doing things, which had endured for millennia, crumbled and gave way to another.

So, when can a small number of people make a big difference? Bowles suspects that individual actions are important in societies poised on the cusp of two different states—when a society is, in other words, a dynamical system teetering between two stable equilibria, requiring only a small push to send it toward one state or the other. (With hind-sight, the Arab world seems to have been in just

Right: Relationships among individuals at one level can lead to organization and behavior on a larger scale. Here, artist Chuck Close combines hundreds of individual images to create a composite portrait.





*Volvox*, a colonial algae, defies definition because it is both an individual and a colony. Unlike multicellular organisms, a colonial organism, if separated, can survive on its own.

such a state, although detecting this beforehand is a difficult challenge, of course.)

Bowles compares this with the process of speciation, where long periods of stasis are followed by bursts of change, and where a small, isolated population of plants or animals can evolve independently into something new. "A lot of the machinery of speciation may explain the emergence of entirely new institutions in history," says Bowles. On the other hand, that doesn't mean the group doesn't matter. What humans do depends on both their individuality and their surroundings. "The beliefs and preferences people have are shaped by the kind of society they live in, and the way they make their living. It's implausible to take the individual as given, without recognizing that the individual is a product of what you're trying to explain," says Bowles.

A biologist would call this niche construction. It is the process by which individual animals and plants shape their environments, which in turn goes on to shape evolutionary history. Erwin believes that niche construction has been important in major evolutionary transitions, and

many have involved the creation of new types of individuals, as formerly independent entities have teamed up to make something novel. Examples include the merging of cells that gave birth to eukaryotes, or the merging of individual insects into a colony, or the merging of speakers of many dialects into a nation sharing a national language.

Over the past 25 years, most research has viewed major evolutionary transitions as arising from new ways

to transmit information, such as in the form of genes. Missing from this argument, says Erwin, is an appreciation of the wider context in which such changes take place. This includes the physical environment, such as the climate; the ecological environment, such as the networks of food webs and mutualisms; and the internal, biological environment, such as the networks of genes that control development and determine how information is used. "It's about trying to embed the issue of individuality in a larger context," says Erwin. "We need to understand the relationships between these things."

Erwin is particularly focused on understanding the ecological, environmental, and genetic conditions that may have facilitated the Cambrian explosion: the brief geological moment about 540 million years ago when the diversity of multicellular animals took off, and the range of body plans that we still see in today's animals made their debut in the fossil record. Just as in Bowles' view of humans and their societies, Erwin is interested in how individuals shape their environments and vice versa. One innovation in the Cambrian,

for example, was the emergence of organisms burrowing into the seabed as a way of life. This niche construction introduced oxygen into the sediment, encouraged microbial growth, and so increased the organic matter—food—available to life. Thus burrowing organisms changed the evolutionary pressures on their own and other species, and perhaps created new opportunities that led to increased diversity.

If you're talking about trilobites or snails, it's easy to understand what's meant by an individual. Biologists understand individuality by reference to properties such as an ability to replicate, or a clearly defined boundary with an environment. But many living things, such as viruses, or the clonal aspens growing in the hills around the Institute, don't fit neatly into such boxes. "Biology doesn't have a good definition of an individual,"

nant animals to recognize their place, because it reduces their costs of fighting. This frees up time and energy, and also allows new behaviors by increasing the differences—asymmetries—between individuals. The dominant members of a primate group, for example, can intervene in and subdue fights between their subordinates, because both parties recognize the dominants' superiority. This consensus is a statistic, a measure and memory of the environment that changes relatively slowly, despite change and turnover at the lower level. This is a common feature of hierarchically organized, multilevel systems, such as a body that remains recognizably itself even though it is always making and discarding cells.

A multicellular body and a primate power structure are very different in some ways, of course. But each gives its members, be they cells or mon-

"It's about trying to embed the **issue of individuality** in a larger context. We need to understand the relationships between these things."

says SFI External Professor Jessica Flack. To rectify this deficit, Flack and her collaborators are focusing on how different levels of organization—larger structures that emerge from the coming together of many individuals at a lower level—arise in biology.

Perhaps counterintuitively, she believes that a key process is conflict, arising through differences in individuals' interests or the information they have. This means that when individuals interact, they disagree with one another in some way. But repeated interactions allow each individual to gain a picture of its place within the whole, and so allow consensus to develop.

Primate groups, for example, have stable power structures that result from the outcome of many fights. Antagonism never stops, because individuals are always probing the hierarchy. But once there is broad agreement on who can dominate whom, it benefits both subordinate and dominate

keys, a predictable place in an uncertain and changing world. "There are fundamental features of both that are similar," says Flack. "A primary driver of evolutionary change is the reduction of uncertainty." She and her colleagues believe that the ability of conflict to create cohesion is an organizing principle that applies to both a body and a power structure, and they are working on extending these ideas into a definition of individuality based in information theory, says Flack.

Ultimately, they and other SFI researchers are showing that emergence and individuality are not opposites. Rather, they are different angles from which to see the world. But only when combined do they offer a whole picture.

John Whitfield is a London-based science writer and former writer-in-residence at SFI. He is the author of People Will Talk: The Surprising Science of Reputation.

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