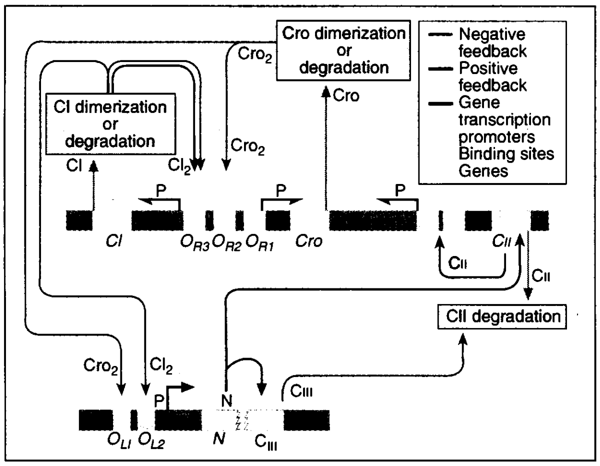
ing biological networks. At LBNL, for example, Arkin and his colleagues have begun using computer models together with experiments to track how viruses that infect bacteria "decide" whether to replicate inside their host or lie dormant, waiting for a better opportunity. Years of painstaking experimental measurements by numerous teams have shown that the five genes that push the virus either to replicate or lie dormant are controlled by six other genes: four promoters that turn on gene transcription, and two terminators that either partly or entirely shut it off. Embedded in this gene play are numerous positive and negative feedback loops: When one gene called *CI* that promotes the dormancy path is expressed, for example, it feeds back to amplify its own expression while diminishing the output of *Cro*, a gene that pushes immediate viral replication and release. Outside factors, such as the availability of nutrients and the presence of competing viruses, also act as inputs controlling which promoters are turned on and off.



Complex system. A web of interactions among a virus's genes and promoters determines whether it will lie dormant or replicate.

SOURCE: *TRENDS IN GENETICS* 5 (2), 67 (1999)

In most cases that feedback leads to predictable results: If food is present and competition is absent, the virus proliferates. But by modeling the entire network of interactions on the computer, the LBNL researchers found that the feedback control is inherently "noisy," so not all the viruses make the same decision under identical conditions—an adaptation that ensures some viruses will survive should the other path prove fatal. Understanding how to control such genetic switches could ultimately lead to new ways to control infections, says Arkin.

Still, even with these and other initial modeling efforts (see sidebars on pp. 80 and 82), many researchers argue that biological models have a long way to go before proving themselves. "[Models] haven't had a lot of respect among biologists," says Marc Kirschner, a cell biologist at Harvard Medical School in Boston. "They don't have enough of the biological character built in," and thus often don't reflect the true complexities of real biological systems. Arkin, Lauffenburger, and others say, however, that the new research in this area will improve the sophistication of the models by identifying common circuit motifs used in biological networks and incorporating more complex and realistic feedback mechanisms. Over time, the models will also benefit from better inputs, such as the amount of each protein present in real cells and their reaction and diffusion rates.

Other challenges loom. Among the biggest concerns, say researchers and administrators, are differences in research cultures. In physics, for example, postdocs are often treated like junior faculty, whereas in biology they typically have far less autonomy. Ironing out such differences is "one of the biggest problems we face," says Shapiro.

Promotions and tenure decisions could also prove to be sticking points. "People who work at the boundaries between disciplines are at a real disadvantage," says Chris Overton, who directs Princeton's bioinformatics center. "Who evaluates you for tenure and the quality of your work?" he asks rhetorically. Often, he says, people in one discipline or another fail to appreciate the work's full scope. What's more, discipline-bound funding departments within agencies such as the National Institutes of Health (NIH) or the National Science Foundation can be reluctant to fund interdisciplinary work seen as lying largely outside their area, and grant review panels made up of researchers in a single discipline may not fully understand an interdisciplinary project. Whether the money will be there to support new interdisciplinary programs "is a question we are all worried about," says Carlos Bustamante, a biophysicist at the University of California, Berkeley.

But NIGMS's Cassman says that his agency and others are creating niches for interdisciplinary science. Last year, for example, NIH announced a new bioengineering initiative to fund multidisciplinary research (*Science*, 5 June 1998, p. 1516). And interdisciplinary review panels, he says, are likely to follow. "When we've been able to promote an area of science, it is because it is ready," says Cassman. "From everything I hear about [the systems approach to biology], I think it is."

–ROBERT F. SERVICE

NEWS

Life After Chaos

After years of hunting for chaos in the wild, ecologists have come up mostly empty-handed. But the same equations that failed to find chaos are turning up stunning insights into how environmental forces and internal dynamics make populations rise and fall

The complexity of nature may be a beautiful thing, but it came pretty close to crushing Maria Milicich's spirit. On a typical morning 10 years ago she would take her motorboat out to the Great Barrier Reef, where she was studying the ecology of damselfishes. These brightly colored aquarium fish lay their eggs in nests at the reef's bottom. Each month the full moon triggers the larvae to hatch and emerge; they leave the reef and 19 days later return as mature larvae. Milicich wanted to figure out what determined how many larvae reached maturity, so she set up 2-meter-tall traps floating from buoys, each rigged with a light to attract the fish.

You might expect that Milicich would have found a regular pulse of new adults every month. Instead, she logged a wild gyration. When she checked her traps during some pulses, she found only a few fish, but during other months she would find thousands. On one visit to the reef she discovered that the trap had been dragged to the sea floor by a load of 28,000 fish.

Milicich searched for a cause for the fluctuations, seeking a link between the number of new adults and measurements she had made at the reef—everything from rainfall to the brightness of the moon. She tried hundreds of variables but came up empty-handed. Of course, many marine biologists had failed before her and simply labeled the supply of mature larvae as nothing more than random. That wasn't much consolation to Milicich. "To say that I felt depressed is an understatement," says Milicich, who now works as an ecological consultant to the Hong Kong government and private companies. "Something was clearly wrong."

Then Milicich had an epiphany. In 1990, she stumbled onto a paper in *Nature* that had invoked a strange kind of math to describe the abundance of phytoplankton off the coast of California. To decode her damselfish, Milicich had been trying to use linear equations—which produce results that are proportional to the values that go into them. But the paper's author, ecologist George Sugihara of Scripps Institution of Oceanography in La Jolla, California, had exploited nonlinear equations. What comes out of a nonlinear equation isn't proportional to what goes in; unlike linear equations, they may contain feedbacks and thresholds and other features that can yield complicated results. Sugihara's data looked as intractable as hers, yet they surrendered to his analysis. "When I read the paper, I thought, 'Bingo—this is what my data is, and this is what it needs,' " says Milicich.

Last month Milicich published a report in *Science* (5 March, p. 1528) with Sugihara and his graduate student Paul Dixon in which they cracked the damselfish cycle. Modeling it with nonlinear equations, they could account for the maddening dynamics with three factors: the moon's phase, turbulence around the reef, and winds blowing over the water. "From hundreds and hundreds of potential correlates, all of a sudden three dropped out, and they made perfect ecological sense," says Milicich. "An awesome feeling for an ecologist, I have to say."

Ecologists first began applying nonlinear dynamics to understanding the ups and downs of populations almost 30 years ago, and the field has gone through some drastic changes in recent years. When researchers began building nonlinear models of the ways that organisms might interact, they stumbled across what people in other fields were already calling chaos—a random-looking pattern produced by simple, nonrandom equations. Models were so rife with chaos that ecologists began searching for it in the real world, because it promised to overturn the old ideas ecologists had about the balance of nature. But it's a sign of the times that nowhere in the damselfish paper does the word "chaos" appear. Although chaos has become well established in other sciences such as physics, in ecology it remains elusive. "It's this great idea that really hasn't panned out all that well," says Dixon.

Yet chaos isn't the be-all and end-all of nonlinear dynamics, but only one type of pattern it produces. The same nonlinear equations that have failed to prove chaos in ecosystems are now helping researchers uncover how the fiendishly complex interactions of organisms with their own kind, with other species, and with weather send populations on erratic trajectories. "This is an area whose time has come," says ecologist Stuart Pimm of the University of Tennessee, Knoxville.

The rise and fall of chaos

The jagged oscillations in populations are nothing new to ecologists, but before the 1970s, they put most of the patterns down to the unaccountable effects of weather, disease outbreaks, and other sources of so-called environmental noise. If not for noise, they assumed, a population should naturally hover at an equilibrium. That assumption was shaken by the work of Sir Robert May in the 1970s. May was originally trained as a physicist, but while at the Institute for Advanced Study in Princeton, New Jersey, he was drawn to the thorny complexities that ecologists and biologists have to cope with. He started to explore simple ecological models, tracking how populations changed generation after generation. In a typical model, a population would swell toward an equilibrium level at a set rate; above that level, the population would decline.

May's model was simple, but the population of a preceding generation wasn't directly proportional to the current one. It might be more, it might be less, it might be the same. In other words, it was nonlinear. And May

Here and gone. Wind, waves, and the phase of the moon interact to produce drastic swings in damselfish populations.

CREDIT: BRUCE WATKINS/ANIMALS ANIMALS

discovered that a nonlinear model of ecology could produce complex patterns even if it was far simpler than anything in nature. When May ran his model at low growth rates, the population would hit equilibrium and stay there. But when May had the population reproducing like bunnies, it overshot its carrying capacity, triggering a population crash, followed by another rise. Rise and fall would then follow regularly, in a pattern known as a limit cycle. At even higher growth rates, the population tripped into a more complicated cycle. Instead of moving between one high and one low, it might hop between two of each, or four, or more. Finally, when the growth rate soared above a threshold, the population went berserk. From generation to generation, it hopped around in what looked like a purely random fashion.

Chaos was the name bestowed on this sort of random-looking pattern produced by a nonrandom equation. As other scientists were seduced by the erratic charms of chaos, they invented a more formal way to recognize it: By nudging the initial conditions of a chaotic system just a hair, you will drastically alter its future path. The rate of this divergence is called the Lyapunov exponent. A negative exponent means limit cycles and other at least somewhat regular behavior. A positive exponent means chaos.

May's work was "hugely influential," says Pimm, "because it showed if you take the simplest population model you can imagine that you'll get cycles and this special thing called chaos. What that told us immediately was that lurking in these descriptions that looked simple you've got very strange dynamics." Simple intrinsic factors such as growth rates might alone be enough to produce a lot of nature's complicated signal. It was so easy to find chaos in models, in fact, that it seemed likely that strong cases of chaos could be found in nature.

The excitement that many ecologists felt over the possibility had two sides. There was hope that the jagged oscillations found in nature could be explained by a few basic ecological rules. On the other hand, the sensitivity that chaotic systems had to their initial conditions meant that it would never be possible to predict what an ecosystem would do very far into the future. "You may even find all the simple rules, and yet prediction may be impossible," says May.

But from the start, May warned his colleagues that they would have a hard time finding chaos in the wild. By definition, it would look like a random pattern produced by the pushing and shoving of environmental noise. Ecologists struggled to find ways to filter out the noise in their data to get at the underlying dynamics, but they were not the ones to get the first strong signal of ecological chaos. Instead it came from the laboratory, where scientists can keep noise at a minimum. In 1997, biologist Robert Costantino of the University of Rhode Island, Kingston, and his colleagues reported bona fide chaos in captive flour beetles (*Science*, 17 January 1997, p. 389).

Costantino's lab has been raising the beetles in flasks of Blue Bonnet flour and brewer's yeast for over 20 years. After they hatch, the beetle larvae need about 2 weeks to grow into pupae, and another 2 weeks to reach reproductive age. Flour beetle dynamics are drastically nonlinear, because the beetles are cannibals, the adults eating eggs and pupae (and the larvae eating eggs as well). Cannibalism undermines the younger generation of beetles and can trigger a population crash. But it eventually leaves fewer adults around, which in turn means less cannibalism. A new batch of larvae can then reach adulthood in such high numbers that the population rebounds.

The researchers built a mathematical model of flour beetle population dynamics and tinkered with it, changing variables such as the adult mortality and the number of larvae each adult produced, and watched what kind of dynamics played out. They discovered that if adult mortality was high, the model became very sensitive to the rate of cannibalism, in some cases jumping to cycles and in others to chaos as they changed the rate. The researchers next turned to the actual beetles to see if they could create this behavior. They raised the adult mortality rate simply by regularly plucking out mature beetles. Then they mimicked different cannibalism rates by removing pupae from the flasks. At some rates the flasks reached an equilibrium; at others they fluctuated through cycles; at others they raged chaotically. Those were exactly the dynamics that Costantino's group had predicted from their model.

Outside the comfortable confines of the lab, though, things haven't gone so well. To find chaos in the wild, ecologists usually resort to historical records consisting of a few dozen data points. "Most of the data sets are really very bad; they're just awful," says Costantino, "and I don't mean to discredit any of the researchers who did the work." To try to make sense of them, researchers sometimes build a model out of the biology they consider important to the case they're studying—such as the rate at which a predator eats its prey. They can then turn these rates up and down like stereo knobs so that the equations produce a pattern like the real one. Other times they fit the data to an equation without bothering to figure out its biological meaning first. Then, by perturbing the model, they can find its Lyapunov exponent and determine whether the wild population is chaotic or not. For over 20 years ecologists have been using methods like these to hunt for chaos. And the result? "There is no unequivocal evidence for the existence of chaotic dynamics in any natural population," declares ecologist David Earn of Oxford University.

In 1995, for example, theoretical ecologists Stephen Ellner of North Carolina State University in Raleigh and Peter Turchin of the University of Connecticut, Storrs, surveyed all the long-term observations of wild populations they could find in the scientific literature and measured their Lyapunov exponents. They concluded that some were stable, many were verging on chaos, and only a few ambiguous, weak cases of chaos turned up.

To some ecologists, the way nature seems to sit on the edge of chaos, and not plunge deep into it as models might predict, is a fascinating puzzle. "I haven't seen any theory I believe that would predict this," says Turchin. It may be that a population's tendency toward chaos is buffered in some way that the models have missed. To study food webs, for example, ecologists often simplify them into linear chains. All the primary producers get thrown into one level; next up the chain are the herbivores, then the intermediate predators, and so on up to the top predators. These models can turn chaotic because oscillations in population density at one level generate oscillations at other levels. But some researchers argue that these chains ignore some important messiness in nature. A predator may depend strongly on a single species of prey, but it may sometimes switch to other species. Killer whales, for example, can switch from sea lions to sea otters (*Science*, 16 October 1998, pp. 390, 473). Or they may be omnivores like people or bears, picking their meals from many levels. Some predators may even snack on other species at the same rank in the food chain, or on their own species.

Last August a group of ecologists at the University of California (UC), Davis, showed how these additional connections could tame the tendency toward chaos. Ecologist Kevin McCann and his colleagues looked at the dynamics of a predator in a simple food chain. Next they compared this model to more complicated chains in which the predator switched between two prey species, or the prey had to compete with another species for its own food. They spent a lot of effort giving these more complicated models a realism that many earlier models lacked. For example, the efficiency with which their predators could catch prey was based on actual animal metabolism. A predator could only boost its success at hunting one prey species at the expense of its ability to hunt others.

At the mercy of weather. Harsh gales on islands off Scotland can synchronize fluctuating populations of feral sheep.

CREDIT: JUDITH SMITH

Predator populations that depended solely on one prey species slipped into chaos. But if the ecologists added in other connections between species—even if they were weak—the chaos disappeared. Changes in the population of one species no longer hit a linked species with full force. "It seems that for species to persist, nature is biased toward inhibitors and away from oscillators," says McCann. "That's just going to decrease the likelihood of chaos, no matter what."

Other ecologists don't take such a dim view of chaos. They still think it's out there in nature but playing hard to get. "There aren't a large number of examples that you can catalog, because there aren't a large number of systems out there for which we have long runs of data for all the variables," says May, who is now the Chief Scientific Advisor to the U.K. government. But if finding chaos means tracking a species for decades or centuries—as well as all its predators and pathogens and prey and the rainfall and so on—few ecologists may have the stamina (or the funding) to keep up the hunt.

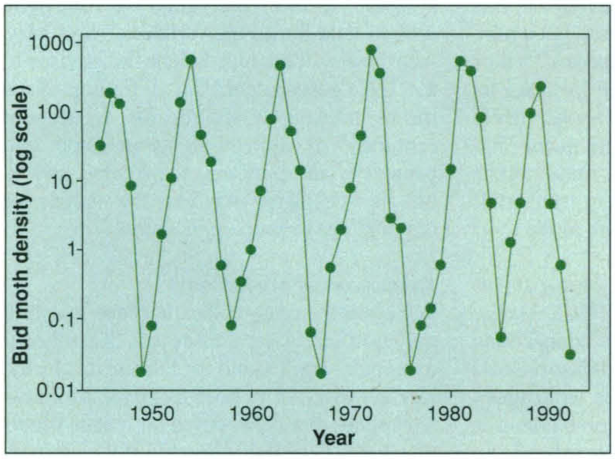
The powers of prediction

Whatever the final verdict on chaos in nature may turn out to be, the success of nonlinear dynamics won't stand or fall on it. "In the last few years we've been using the nonlinear techniques, but not focused on 'chaos versus nonchaos,' " explains Turchin. "We are now more interested in what are the forces that drive the spectacular population dynamics" seen in many species. Ecologists probing these forces were once limited to cumbersome experiments, such as closing off parts of a forest to predators. With the help of nonlinear mathematics, they can now get additional information from historical records.

Turchin, for example, is studying a pest known as the larch bud moth, which denudes larch trees in the Swiss Alps. The bud moth goes through cycles of 8 or 9 years in which its numbers can multiply 100,000-fold. Ecologists have been debating the cause of the cycles for as long as they've known about them. At one point a bud moth virus seemed to be the best candidate, but more recently the larches have taken the lead. An exploding moth population destroys larch needles faster than the trees can recover; the following year the trees muster only stubby needles that are a poor energy source for the moths.

Turchin and colleagues, working at the National Center for Ecological Analysis and Synthesis at UC Santa Barbara, have sifted through a 40-year bud moth census, as well as related ecological records. They then wrote out nonlinear equations representing the possible effects of each ecological factor—viruses, food quality, and so on—on the bud moth and tested them to see how closely they fit the bud moth's actual history. Their preliminary findings suggest that the plants have something do with the cycle, but they're not powerful enough on their own to produce it. The collapse of the needle supply does bring the explosion of bud moths to a stop. But a parasitoid wasp that lays its eggs in the caterpillar then seems to take over. The rise of the wasp lags behind the moths, and it continues after the moths have stopped their ascent. As a higher and higher proportion are parasitized and killed, the moth population crashes. When the moths bottom out, a window opens for the larches to recover. The bud moth crash spurs a wasp crash, then the cycle starts all over again.

The same kind of interaction from above and below in a food chain emerged when Nils Stenseth, an ecologist at the University of Oslo, looked at the snowshoe hare of Canada. Stenseth used a different method: Rather than make biologically plausible equations from the data, he let the actual data guide him through a statistical search for the best nonlinear equations. After he had a robust model, he looked at the variables. The animals, he discovered, were controlled by two factors; changes in food supply and populations of predators (mainly lynx) fit the job descriptions best. "People tend to belong to different schools—either it's the food supply or predation," says Stenseth. "But you really have to have both."



Bud moth boom and bust. The supply of the caterpillar's food, larch needles, and the depredations of a parasitic wasp interact to produce its population cycles.

You also have to have noise in the environment, ecologists are learning. Most ecological models (including nonlinear ones) have only looked at a particular species, or perhaps its food supply and predators. They haven't taken into consideration the effects of random variability coming into the model from the outside. In these models, every day is sunny. Now researchers are getting a better understanding of population dynamics by bringing noise into nonlinear models.

Bryan Grenfell of Cambridge University and his colleagues have been studying feral sheep on islands off Scotland using methods similar to Stenseth's. They found that at low populations, the sheep multiply in a straightforward, linear fashion. But above a certain threshold, as the sheep overgraze their island, they suddenly fluctuate in a nonlinear fashion. Randomly adding or subtracting a few sheep to a crowded island brings big changes to the dynamics of the population.

Their records also show that the population of sheep on neighboring islands has been rising and falling in tight synchrony since ecologists first started their census in the 1950s. Researchers have suspected that weather might synchronize separate populations, in the same way adjusting a slow clock every hour keeps it in synch with a faster one. But the sheep populations are so sensitive to random noise that weather ought to have the opposite effect, throwing them out of sync.

Grenfell and his colleagues resolved this paradox by incorporating weather into their nonlinear models, adding variables to their equations that described the harshness of the March gales that scour the islands, as well as the respite of calm Aprils. Their analysis showed that the weather is so intense that it can overcome the sensitivity of the sheep's dynamics. Not only does it bring down the sheep's numbers on neighboring islands at the same rate, but both populations subsequently cross the crucial threshold in the same year.

A powerful interaction between animals and their environment is responsible for the damselfish cycle as well, according to Dixon and his colleagues. Three days after hatching, the larvae have depleted their yolk sac and must start feeding in the outside world. Unable to swim far, they depend on turbulence to sweep them into contact with zooplankton. Too little turbulence won't give them enough food to survive; too much won't give them enough time to get it in their mouths. The full moon that triggers the larvae to hatch also brings with it high tides, which sweep the larvae away from the reef, letting them avoid predators while they mature. They return as mature larvae, but to get back, they need favorable winds to set up the right currents. Because their survival depends on several interacting factors, the fish can react dramatically to what looks like small amounts of noise.

If the turbulence and wind both jibe with the fish's needs at the right time relative to the full moon, they can reach adulthood in vast numbers. But if the factors go against the fish, their individual effects are multiplied. Say 90% of the fish get killed because of turbulence. If the returning winds also create a 90% mortality rate in the survivors, only 1% of the fish will reach adulthood. "If you play around with these losses, that alone can produce huge fluctuations," says Dixon.

Damselfish and feral sheep are only two examples of a growing list of organisms in which nonlinear dynamics seems to amplify noise. "The emergence of noise amplification as a very general factor is very exciting," says Ellner of North Carolina State. "Apparently there *is* some generality after all, even if it isn't the one that we looked for initially—that is, deterministic chaos."

Although nonlinear models are flexing their muscles at explaining the ebbs and flows of wild populations, experts say it is far too soon to apply them to conservation biology—designing reserves, for example, or understanding when a population drop is a natural fluctuation and when it's a sign of trouble. But the models are showing promise for helping scientists destroy unwanted organisms. Grenfell, for example, applies the same approach he brings to island sheep to diseases like measles. His work suggests that vaccination campaigns might work better if the constant low-level efforts now mainly practiced were punctuated by massive spurts. That would tend to synchronize disease levels in all regions of a country in the same way that March gales synchronize sheep, so that the crests and troughs of its cycle would be the same everywhere. If every town hits a low part of the cycle together, neighboring towns won't reinfect each other, and chances are better that the disease won't resurge.

For now, though, ecologists are just enjoying the fact that their models are working. "No one ever thought that the models were that good," admits Alan Hastings of UC Davis. "That to me is the biggest sign of progress." **–CARL ZIMMER**

Carl Zimmer is the author of *At the Water's Edge*.

SOURCE: (TOP) NILS STENSETH/UNIVERSITY OF OSLO; CREDIT: (BOTTOM) WERNER BALTENSWEILER