preferentially observing more successful individuals, many of whom are more successful because they live in groups at stable cooperative equilibria (*9*). This can lead to a flow of decisions, strategies, and even preferences from more cooperative groups to less cooperative ones (*6*), or to a migration of individuals among groups (*10*) that favors the spread of the more cooperative equilibria.

Gürerk *et al*. address the issue of equilibrium selection with an elegant addition to the existing experimental work on public goods. In their experiment, individuals (the "players") choose between two different "institutions." In one institution, players can contribute money to a group project. The sum of all contributions to the project is augmented by a fixed percentage and then is divided equally among all players, regardless of their contributions. Previous experiments established that when this interaction is repeated, mean contributions to the public good drop to near zero (a noncooperative equilibrium). The other "sanctioning" institution is very similar, except that after players have contributed, they can pay to punish (reduce the payoff of) other players. When this interaction is played repeatedly (*11*) a substantial fraction of players punish low contributors, causing mean contributions to rise and stabilize near full cooperation (a cooperative equilibrium). Both institutions were run concurrently for 30 interactions and players could, initially and after each subsequent interaction (after seeing others' payoffs), choose their institution for the next interaction.

The principal findings of Gürerk *et al*. can be summarized simply. Initially, most players picked the institution without sanctioning possibilities. But, as usual, free-riders in the nonsanctioning institution started driving mean contributions downward, so cooperators, who hate being exploited by free-riders, started reducing their contributions. Meanwhile, in the sanctioning institution, punishers started driving contributions up by inflicting costs on noncontributors, despite the personal cost of punishing. After a few interactions, players from the nonsanctioning institution—presumably seeing the higher payoffs of those choosing the sanctioning institution—increasingly switched institutions. Notably, despite the incoming flow of migrants from the nonsanctioning institution, the mean contributions in the sanctioning institution consistently increased or held stable near full cooperation. In fact, most incoming migrants, consistent with local norms in their new setting, increased their contributions during their first interaction in the sanctioning institution, and a majority administered some punishment.

What does this tell us about equilibrium selection? First, the players' degree of rationality did not permit them to foresee the final outcome and select the higher payoff institution on the first interaction. Second, despite the stochasticity of human decisions, neither institution drifted to another equilibrium. What did happen is that once players from the lower payoff institution observed the higher payoffs of the other institution, they wanted to adopt either the practices of the higher payoff institution, or the decisions and strategies of those other players. Consistent with ethnographic and historical case studies (*12*, *13*), the present work provides an important experimental demonstration of cultural group selection in action, as the two alternative equilibria compete for shares of the total population.

The course charted by Gürerk *et al*. should spur more empirical work on how processes of equilibrium selection influence the evolution of institutional forms. Many questions remain to be tackled: for example, what happens if switching institutions is costly, or if information about the payoffs in the other institution is poor? Or, what happens if individuals cannot migrate between institutions, but instead can vote on adopting alternative institutional modifications? Such work can both help us understand how humans became such a cooperative species, and teach us how to build durable cooperative institutions that solve public goods problems and are readily spread.

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EVOLUTION

Reducible Complexity

Christoph Adami

How does biological complexity arise? The molecular evolution of two hormone receptors was traced from a common ancestral receptor. Through a series of mutations, receptors with distinct hormone binding properties evolved, one before the appearance of its cognate ligand.

If an elaborate lock fits an equally elaborate key, we immediately sense the purpose of design: The key was crafted with the idea of the lock in mind. We would not entertain the possibility that the match is accidental. When we come upon such lock-and-key pairs in nature, it is natural to ask how these pairs could have evolved via Darwinian evolution. At first glance, it seems that the key can only evolve to fit the lock if the lock is already present, and the lock cannot evolve except in the presence of the key (because without the key, it does not open). On page 97 of this issue, Bridgham *et al.* (*1*) take a closer look at this puzzle and discover a different answer in the molecular evolution of hormone-receptor interactions.

Charles Darwin was fully aware of the problems that such lock-and-key systems—should they exist in biology—would present to his theory because the theory relies upon step-by-step changes to a trait. Building a lock-and-key system appears to require at least two changes to happen simultaneously. He famously remarked that "if it could be demonstrated that any complex organ existed which could not possibly have been formed by numerous successive slight modifications, my theory would absolutely break down" (*2*). This concern has been seized upon by proponents of an "intelligent design" alternative to Darwinian evolution that proposes that complex systems—like those that display lock-and-key complexity—cannot evolve. The premise for the argument is that systems of a lock-and-key nature cannot evolve and are thus "irreducibly complex" (*3*), implying that only the lock-and-key combination, but not its parts, is complex. The argument continues that because such systems do exist in nature, and cannot have evolved, they must have been "designed."

Darwin already saw how such thorny issues could be resolved. He further explains in *The Origin of Species* that "if we look to an organ common to all the members of a large class…in order to discover the early transi-

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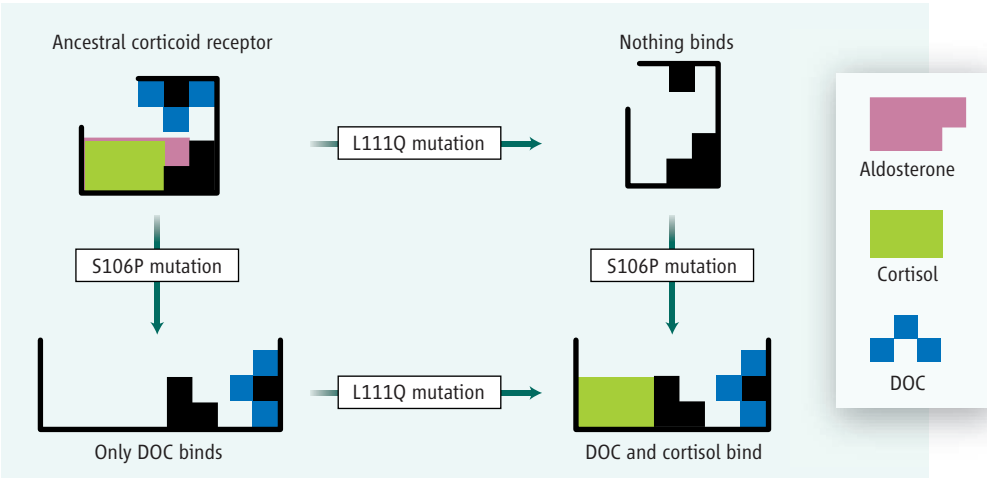
tional grades through which the organ has passed, we should have to look to very ancient ancestral forms, long since become extinct." In other words, Darwin suspected that viewing only the extant complex forms will obscure the path of evolution, and present an incomplete picture. But while the fossil record has yielded many intermediate forms that suggest a continuous evolution of traits, it is too often incomplete, and does not allow us to retrace the molecular history of a gene. Reconstructing the complete evolutionary history of a complex genetically encoded function (albeit a "computational" one) was achieved recently (*4*), and it experimentally vindicated Darwin's idea that the target of natural selection constantly changes, so that the complex feature of today may share very little with the original function. But while such computational investigations can be very satisfying, they might not convince everybody. It is therefore gratifying that it is now possible to reconstruct the ancestral genes of an existing species so that, as Darwin urged us to do, we can "look exclusively to its lineal ancestors" to understand a gene's evolution.

Bridgham *et al*. address one of the central concepts of the intelligent design argument. They did not study just any gene, but precisely a system that looks irreducibly complex: a hormone-receptor pair that we can think of as a biological lock and key. In vertebrates, the regulation of many cellular processes is controlled by steroid-receptor interactions that are highly specific. For example, cortisol activates the glucocorticoid receptor to regulate metabolism, inflammation, and immunity. In contrast, the mineralocorticoid receptor is activated by aldosterone, and controls electrolyte homeostasis, among other effects. This specificity is important, because the activation of the glucocorticoid receptor by aldosterone, for example, would be highly detrimental.

Phylogeny tells us that an ancestral corticoid receptor gave rise to the glucocorticoid receptor and the mineralocorticoid receptor in a gene-duplication event more than 450 million years ago. However, aldosterone evolved much later. Without aldosterone present, how could the mineralocorticoid receptor evolve to be activated by it? Doesn't the pair's specificity require the evolution of two traits at the same time, an event that appears highly unlikely?

Bridgham *et al*. took Darwin's advice and followed the line of descent to the ancestral corticoid receptor. Modern phylogenetic methods make it possible to reconstruct such inferred sequences and study the properties of these molecules in the laboratory. What the authors find is a surprise: Not only is the ancestral corticoid receptor sensitive to cortisol as expected, it is also activated by 11-deoxycorticosterone (DOC) and aldosterone. Because aldosterone was not present at the time, this sensitivity must be a by-product of sensitivity to another steroid, a promiscuity that can be exploited by evolution (*5*).

The next task was to determine how the mineralocorticoid receptor kept the aldosterone specificity, whereas the glucocorticoid receptor lost it. This is a tale of two mutations. More phylogenetic analysis revealed that precisely two amino acid substitutions resulted in the glucocorticoid receptor phenotype—aldosterone insensitivity and cortisol (and DOC) sensitivity. Could these two mutations have occurred one after the other? Bridgham *et al*. tested the effect of each of these mutations—replacement of leucine-111 with glutamine (L111Q) and replacement of serine-106 with proline (S106P)—alone on the reconstructed ancestral corticoid receptor and in the presence of the other mutation (see the figure). Of the two mutations, L111Q was the more damaging: Applying this mutation to the ancestral receptor destroyed its sensitivity to all three hormones. On the other hand, the S106P change reduced receptor activation by aldosterone and cortisol but did not change the sensitivity to DOC. In the presence of S106P, the effect of L111Q was quite different: It removed any sensitivity to aldosterone, and restored cortisol sensitivity. In other words, it produced the glucocorticoid receptor phenotype. The two mutations thus turned out to be strongly epistatic: Both reduce the fitness of the system (L111Q very strongly so), but together their effect is neutral or better.



Molecular evolution of a biological lock and key. A two-dimensional schematic picture of an ancestral hormone receptor that binds aldosterone, cortisol, and DOC. The L111Q mutation in the receptor is drastic because it eliminates receptor activation by any of the three molecules, modeled by an obstruction of the binding pocket. The mutation S106P, on the other hand, does not affect the binding of DOC, but both aldosterone and cortisol can bind only very loosely. However, the presence of both mutations allows cortisol to bind strongly again, whereas aldosterone no longer fits.

Can we determine the order in which these mutations appeared and can we understand how such epistatic effects arise? Structural changes very easily can lead to the type of epistatic interactions between mutations now documented in hormone receptor evolution, because such changes can condition the mutational effect. Thus, single mutations that confer different structural changes that depend on one another can conspire to give the impression of irreducible complexity. Although the mutation L111Q creates a possibly lethal phenotype when it occurs alone in the ancestral corticoid receptor, it confers the glucocorticoid receptor phenotype if it is preceded by the S106P mutation, which itself is nonlethal. Such interacting pairs of mutations are common and important in evolution.

Bridgham *et al*. conclude that the insensitivity of the glucocorticoid receptor to aldosterone most likely evolved by the S106P mutation followed by the L111Q mutation because the intermediate phenotype is still viable. Although this is the most parsimonious conclusion, the other sequence of mutation events cannot be ruled out. Indeed, the experiments following the line of descent of digital organisms in Lenski *et al*. (*3*) found, surprisingly, that occasional highly deleterious mutations were rescued by a partner mutation that conferred a beneficial trait. Thus, the highly deleterious partner of the pair can indeed come first, as long as the second mutation does not occur too late. In any case, the evidence is clear that such "multiresidue features" (*6*) can and do evolve. Understanding how they evolve requires taking into account

complex epistatic interactions that allow intermediate nonlethal states that might not appear obvious at first glance.

The Bridgham *et al.* and Lenski *et al.* (*4*) studies are of particular scientific interest, given the political attention given to intelligent design lately. Although these authors have not directly addressed this controversy in the discussion of their work—because the work itself is intrinsically interesting to biologists—such studies solidly refute all parts of the intelligent design argument. Those "alternate" ideas, unlike the hypotheses investigated in these papers, remain thoroughly untested. Consequently, whatever debate remains must be characterized as purely political.

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PHYSICS

New Additions to the Schrödinger Cat Family

Schrödinger cat states entail superpositions of seemingly opposite quantum states, metaphorically like a cat being both dead and alive. Femotsecond laser pulses can now induce photons into small and unbound Schrödinger kitten states.

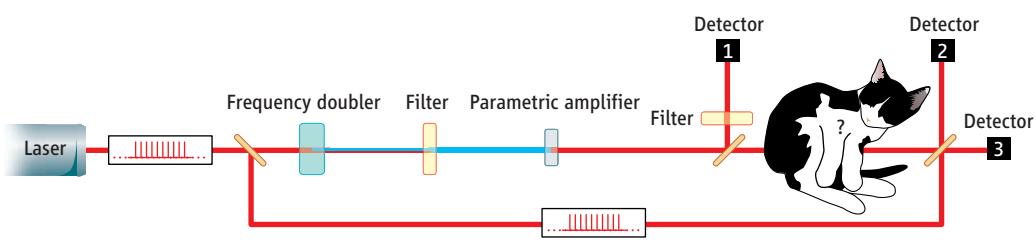
Nicolas Gisin

Can a cat be simultaneously dead and alive? Before the era of quantum physics, the answer would have been obvious to any reasonable person. But quantum physics is well known for being counterintuitive, as beautifully exemplified by Schrödinger's cat. In this famous example, a cat is hidden in a box and we do not know whether it is dead or alive until we make a measurement (by opening the box). According to quantum physics, the cat must exist in a quantum superposition of the "dead" and "alive" states—the cat is "dead-and-alive." Currently, experiments involving Schrödinger cats are still Gedanken experiments; however, technology is making huge progress. Recently, some states of the electromagnetic field mimicking small Schrödinger cats have been realized in optical cavities (*1*). As reported on page 83 of this issue, Ourjoumtsev *et al*. (*2*) have added to this strange family of quantum cats by creating flying Schrödinger kittens.

Historically, Schrödinger used his cat example to stress the oddness of quantum physics. In Schrödinger's opinion, superpositions of macroscopically distinguishable states could not exist. His example was thus presented as an argument against the completeness of quantum mechanics. Since Schrödinger's time in the 1930s, this remained a philosophical issue. But, in the past decade or so, physicists have made many of advances. On the theoretical side, it was understood that the main difficulty in producing Schrödinger cat–like states is decoherence, a phenomenon that quickly destroys the superposition of large objects if they are not perfectly isolated: The larger the object, the better it must be isolated to behave quantum mechanically. Decoherence doesn't answer all of the questions about cat states, and in particular, it doesn't help us understand the uniqueness of quantum measurement results. But it does answer qualitatively and quantitatively why Schrödinger cats are so fragile. An object twice as large must be exponentially better isolated. Understanding decoherence helps us to find ways around this problem. On the technology side, the new science of quantum information has given a huge impetus to new developments toward mastering individual quantum phenomena. Indeed, such mastery will open revolutionary new ways for information processing (*3*).

No physicist is really thinking of superposing actual cats, not even kittens. Any macroscopic system, or a mesoscopic system for that matter, would suffice to fill the entire physics community and beyond with wonder. In particular, it would suffice to demonstrate the superposition of a light pulse in a superposition of being "here" and "there." This should not be confused with a light pulse as it passes through a beam splitter. In this case, half of the pulse is transmitted and half is reflected, which is nothing strange (that is, as long as one doesn't think of the pulse as being made out of many photons, each photon in a superposition state of transmitted and reflected, an example of basic quantum strangeness). In contrast to a pulse passing through a beam splitter, a Schrödinger cat light pulse is a pulse that is entirely transmitted (with zero intensity reflected), superposed (that is, coexisting) with a pulse that is entirely reflected (with zero intensity transmitted).

In their effort to study cat states, Ourjoumtsev and colleagues from the Optics Institute in Orsay, near Paris, present a remarkable experiment (see the figure). They produced a (very small) Schrödinger kitten in the form of a tiny light pulse. To achieve this, they first pumped a nonlinear crystal to produce a light pulse of 180-fs duration, and this pulse has some special properties. Namely, the pulse contains photons that are quantum entangled in the way described by Einstein, Podolsky, and Rosen (EPR) more than 70 years ago. Next, they cleverly removed precisely one photon from the pulse.



Flying kittens. Simplified version of the experiment. A femtosecond laser creates a train of red pulses that are frequency doubled to create blue pulses. After the red is filtered out, the blue pulses are fed into a nonlinear crystal that "squeezes" the light into an EPR state. A single-photon detector (1) signals when one photon has been removed from the pulse by the beam splitter, and thus marks the creation of a quantum kitten. More detectors (2 and 3) are used to study the properties of the kitten pulse.

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