step toward eventual use in patients, the discovery of the Tre recombinase proves that enzymatic removal of integrated HIV-1 from human chromosomes is a current-day reality.

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CHEMISTRY

Rhythm Engineering

A study of chemical oscillators shows how the synchronization of coupled elements can be engineered.

William L. Kath and Julio M. Ottino

Synchronized life cycles. This adult cicada from the 2007 Midwestern brood, and the larval nymph shell from which it apparently emerged, represent two stages of the insect's 17 year oscillatory life cycle. Kiss *et al.* (*4*) report how periodic events of this kind can be controlled.

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This May and June, a large brood of cicadas (see the figure) emerged in the Midwestern United States. The life cycles of these insects are synchronized, with periods of 13 or 17 years. These prime-number life cycles may make cicadas better able to survive, because predators with shorter life cycles cannot easily appear in large numbers at the same time (*1*, *2*).

Synchronized events of this kind may appear remarkable, but they are actually quite common. Nearly any system of coupled, similar oscillators tends to spontaneously self-organize (*3*). However, it is less straightforward to control synchronization such that it achieves a desired goal. On page 1886 of this issue, Kiss *et al.* (*4*) propose a method and carry out supporting experiments on a system of coupled chemical oscillators, demonstrating that synchronization can be controlled and engineered.

Humans use synchronized activity to their benefit. For example, if one synchronizes low-intensity microwave radiation in a resonant cavity with a specific atomic transition frequency, such as that of cesium, one obtains a highly accurate atomic clock (*5*). This technique, known as phase locking, is the modern-day equivalent of the observation made in 1665 by Christiaan Huygens that pendulum clocks can oscillate together as a result of vibrations transmitted along the wall between them. Today, synchronization is used to regulate power-system grids and to keep high-speed communication systems connected, such as for electronic funds transfers between banks. A spatially distributed network of synchronized atomic clocks is the basis for the Global Positioning System (*6*), which can pinpoint any location on Earth to a precision better than a meter.

But synchronization can also be detrimental, and in such cases it is best to disrupt it. For example, when London's Millennium Bridge opened in June 2000 to pedestrians, small oscillations of the bridge encouraged (or perhaps even forced) people to synchronize their walking; this in turn caused the amplitude of the oscillations to grow to a disconcerting level (*7*). Eventually, the bridge was retrofitted with additional vibration dampers at an additional cost of about 9 million U.S. dollars.

Can synchronization be controlled and engineered? And can this be done without knowing a priori all the details about the oscillators that are connected together, using only subtle control and preserving the system's fundamental nature? To address these questions, Kiss *et al.* consider a coupled set of limit-cycle oscillators—specifically, an array of 64 nickel electrodes in sulfuric acid. An individual electrode of this type will generate a periodic electrode potential (that is, a voltage) as a function of time as a result of the push and pull between opposing electrical and chemical forces. An array of such electrodes, uncoupled, will generate independent oscillations, and slight variances between them will eventually lead to oscillations that are out of phase with one another. What happens when these electrodes are coupled together, such that one electrode can sense what the others are doing?

Kiss *et al.* answer this question by turning to phase models (*8*). Such an approach works not with a traditional description of the electrode potential, but rather with the phase of an oscillation relative to some reference point [the phase is an angle that describes the position of an oscillator along the limit cycle's path in state space (*7*), that is, the periodic orbit after all of the transients have died out]. In the case of nearly identical oscillators that are all coupled to each other in an identical manner, the phase model reduces to a relatively simple system of equations involving an unknown interaction function.

A standard way to proceed would be to

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specify a feedback coupling and determine the resulting interaction function; this has been done, for example, for coupled neural oscillators (*9*). In what amounts to turning the problem on its head, Kiss *et al.* proceed in the reverse direction: They specify the interaction function that they would like to have (that is, the interaction function that generates some specified behavior), and then follow an optimization procedure to determine the feedback that generates it.

The result is a systematic procedure for generating a wide variety of dynamical behaviors. One of the simplest is synchronization, where all oscillations are at the same frequency and the phase difference between each pair of oscillators is constant. By carefully choosing the target interaction function, however, the optimized feedback allows dynamics that switch between different synchronized states, each with a distinct set of phase differences. Still another choice for the target interaction function produces complete desynchronization when the feedback control is turned on. This is the goal in anti-pacemaker applications when one needs to destroy some pathological global resonance.

There is a voluminous literature on the mathematics of coupled oscillators. The approach of Kiss *et al.* is unique in that it does not merely involve theoretical models of coupled nonlinear oscillators, or a comparison between such theoretical models and experimental results. Rather, it shows that such models can be made sufficiently accurate to provide precise control of experimental systems.

There are obvious limitations to the approach. The oscillators need to be sufficiently similar to one another, and the interactions must be independent of their spatial location—one cannot have specific arrangements in space, as for a school of fish or a flock of birds. In addition, there are cases of continuous spatiotemporal evolution, such as the Belusov-Zhabotinsky reaction, where one cannot identify specific agents and decompose the system into an array of discrete oscillators. But the method is worthy of further exploration. The ability to use a light touch is a strong plus, engineering change without altering the essential nature of the system. The possibility of doing so in the absence of detailed information about the elements of the system is another.

Ecological systems have a natural rhythm and, despite formidable obstacles, it may be tempting to look for applications in this area. The most promising applications, however, may arise in medical science and biological systems—not by creating order, but by destroying synchronization. Parkinson's disease and epilepsy are two compelling and challenging examples. The former is already being treated with some success using deep brain stimulation (*10*); it is hoped that further research into both the oscillations in the brain involved in such disorders and methods of the type introduced by Kiss *et al.* will, one day, lead to new, more effective ways of alleviating such conditions.

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BEHAVIOR

A Narrow Road to Cooperation

A new model of collective action shows how socially beneficial punishment can arise and evolve.

Robert Boyd and Sarah Mathew

In every human society, from small-scale foraging bands to gigantic modern nation states, people cooperate with each other to solve collective-action problems. They share food to ensure against shortfalls, risk their lives in warfare to protect their group, work together in building canals and fortifications, and punish murderers and thieves to maintain social order. Because collective action benefits everyone in the group, whether or not they contribute, natural selection favors noncontributors. So, why do people contribute? Everyday experience suggests that people contribute to avoid being punished by others.

But this answer raises a second question: Why do people punish? From an evolutionary perspective, this question has two parts: First, how can contributors who punish avoid being replaced by "second-order" free-riders who contribute but do not incur the cost of punishing? There has been much work on this topic lately, and plausible solutions have emerged (*1*–*5*). However, these solutions are not much good unless we can solve the second problem: How can punishment become established within populations in the first place? On page 1905 of this issue, Hauert *et al.* provide the first cogent answer to this question (*6*). Surprisingly, they find that punishment can become established if there are individuals who neither produce collective benefits nor consume collective benefits produced by others.

In previous models of the evolution of collective action, individuals in a group can either contribute and benefit from the public good (i.e., cooperate), or not contribute and benefit (i.e., defect). In the absence of punishment, defection wins. However, if punishment is possible and punishers are common, it does not pay to defect. But punishment is costly to impose. A rare punisher in a group of defectors suffers an enormous disadvantage from having to punish everyone in the group. This means that in very large populations, punishment can sustain cooperation when punishment is common, but punishing strategies cannot increase in numbers when they are rare (i.e., invade a population of defectors). In a finite population, random chance affects the number of each type that reproduce, and the resulting stochastic fluctuations allow punishers to eventually invade a population of defectors, even though selection favors defectors. However, it can take a very long time for this to occur, and thus, most of the time there is no punishment and no cooperation.

Hauert *et al.* provide a way out of this dilemma. They introduce a strategy that simply opts out of collective action. These "nonparticipants" neither contribute to the collective good nor consume the benefits, but instead pursue some solitary activity. Surprisingly, this innovation allows punishment to increase when rare. To see why, consider a population of defectors. Hauert *et al.* assume that nonparticipants get a

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