anti-KS approaches.

One therapeutic strategy discussed at the meeting that some researchers believe is marginally effective is to attack the transformed cells with conventional cancer treatments. Another is to inhibit KS cell proliferation with inhibitors that block the action of the cytokines, immune system messengers that are believed to cause KS cells to proliferate; among the possibilities are inhibitory cytokines and the banned sleeping pill thalidomide. Gallo's lab has also promoted the use of human chorionic gonadotropin, a hormone that plays a key role in pregnancy and cures KS lesions in mouse experiments. Other potential KS drugs inhibit angiogenesis, the process by which new blood vessels are formed—blood vessels that cancer cells must have available to spread widely.

Susan Krown of the Memorial Sloan Kettering Cancer Center closed the conference by urging her colleagues "to look ahead to combining agents," even ones that don't appear promising by themselves. "I think we all need to be treatment artists to move the field forward," said Krown. And the hope is that if enough researchers make small steps forward, that might soon translate into a giant leap for people infected with HIV.

–Jon Cohen

PHYSICS

A Gentle Scheme for Unleashing Chaos

Chaotic systems behave unpredictably. So does the science of chaos, whose theories describe everything from planetary orbits to the irregular dripping of a faucet. Who could have predicted that just 5 years after learning how to summon the reliable Dr. Jekyll of periodicity from that unruly Mr. Hyde of chaos, researchers would want to reverse the process? "People have spent years trying to make chaos regular," says chaos researcher William Ditto of the Georgia Institute of Technology. "Now we are starting to see that irregularity is something good."

For certain biological behaviors, such as the electrical activity in the brain and heart, some researchers are beginning to think that chaos may be the norm. Pathological effects, they argue, including abnormal heart rhythms and epileptic seizures, could actually result from an excess of regularity. Now Ditto and his graduate student Visarath In, along with physicist Mark Spano of the Naval Surface Warfare Center in Silver Spring, Maryland, have come up with a way to restore complexity: a practical scheme for chaos "anti-control," in which precisely timed jolts make a system with a penchant for periodicity stay chaotic.

Although chaos control and anti-control have opposite goals, they are based on a common principle, spelled out in 1990 by Edward Ott, Celso Grebogi, and James Yorke of the University of Maryland. The key to mastering chaos, they determined, lies in the same quality that makes chaotic systems so hard to predict—their sensitivity to small perturbations. This sensitivity is called the "butterfly effect," after the classic example of a small perturbation that leads to big effects on the overall system: a hypothetical butterfly's wingbeat that ultimately changes a weather pattern. "If you can control the butterfly," says Ditto, "you can control the system."

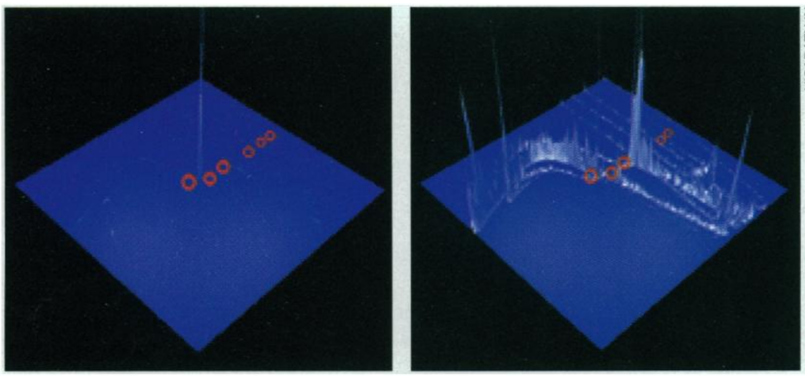
That same year, Ditto and his colleagues at the Naval Surface Warfare Center first demonstrated such control in the laboratory, coaxing the chaotic vibrations of a flexible metal ribbon in a changing magnetic field into periodic states with small magnetic nudges. Chaos control has since been applied to electronic circuits, lasers, chemical reactions, and more. Then last year, Ditto and Steven Schiff, a neurologist at George Washington University, announced that they had achieved the converse: maintaining chaos in brain tissue (*Science*, 26 August 1994, p. 1174). Using precisely timed electrical shocks, they manipulated the chaotic firing of neurons in slices of rat brains—a system where Ditto thinks the loss of complexity may cause "spiking" akin to epileptic seizures—to keep it aperiodic.

Some skeptics weren't convinced Ditto and Schiff had really demonstrated anti-control, arguing that the brain tissue's behavior may not have been truly chaotic in the first place. After all, says Tim Sauer, a physicist at George Mason University in Fairfax, Virginia, the electrical shocks weren't the tiny "butterfly" nudges that should be enough to influence a chaotic system. "You can control anything if you bang it around enough," says Sauer.

But now the blunt force of this first attempt has given way to calculation. Ditto and colleagues have returned with a general algorithm for anti-control, which they report in the 29 May issue of *Physical Review Letters*. It allows a computer to learn how to recognize signs that a system is approaching areas in its phase space called "loss regions," where it slips into periodic behavior. Researchers can then make small, precisely timed perturbations to the system, causing it to avoid the periodic traps.

Sauer, impressed by the technique, likens it to controlling a ball bouncing around a billiard table with irregular sides and a hole in the middle. The ball will follow a chaotic trajectory, but once in a while it will get stuck in the hole, which represents a loss region. By observing the table and learning to identify events that send the ball into the hole—say, a collision with a particular side at a particular angle—one can gain enough predictive power to "anti-control" the ball and keep it on its chaotic course. In this case that might entail tilting the table slightly when an encounter with the hole is imminent.

The group successfully tested their scheme on an oscillating metal ribbon that intermittently becomes trapped in periodicities. But Frank Moss, a physicist studying chaos in crayfish ganglia at the University of Missouri, says the method should also be well suited to detecting and maintaining chaos in biological systems, which are often plagued by noise and changing conditions. It doesn't demand complete knowledge of a chaotic system—its initial conditions or the differential equations describing it—just a relatively brief period of observation for finding the loss regions. And the scheme's reliance on subtle perturbations is well suited to sensitive living tissue.



VISARATH IN

Chaos resurrected. A chaotic attractor—a structure mapping chaotic behavior—shows how a system trapped in periodicity *(left)* is made chaotic again *(right)* when nudged at specific points *(circles)*. Peak height represents probability.

All of which has researchers thinking about the therapeutic potential of chaos anti-control. "There is a large prize at the end of the tunnel," says Moss. Ditto, for one, already has his eye on that prize; he has formed a company to develop an epilepsy "pacemaker" based on anti-control techniques. "Our goal," he says, "is to take it straight to the brain."

–Antonio Regalado