Monte Carlo physics: A cautionary lesson

To simulate chance occurrences, a computer can't literally toss a coin or roll a die. Instead, it relies on special numerical recipes for generating strings of shuffled digits that pass for random numbers. Such sequences of pseudorandom numbers play crucial roles not only in computer games but also in simulations of physical processes.

Researchers have long known that the use of particular methods for generating random numbers can produce misleading results in simulations. Now Alan M. Ferrenberg, a computational physicist at the University of Georgia in Athens, and his co-workers have discovered that even "high-quality" random-number generators, which pass a battery of randomness tests, can yield incorrect results under certain circumstances.

The researchers report the findings in the Dec. 7 PHYSICAL REVIEW LETTERS.

Initially, the approach taken by Ferrenberg and his co-workers looked promising. They were interested in simulating the so-called Ising model, which features an abrupt, temperature-dependent transition from an ordered to a disordered state in a system in which neighboring particles have either the same or opposite spins.

To accomplish this goal, they selected a spin-flipping algorithm recently developed by Ulli Wolff of the University of Kiel in Germany and the new "subtract-with-borrow" random-number generator of George Marsaglia and Arif Zaman of Florida State University in Tallahassee (SN: 11/9/91, p.300). In preparation for simulating the three-dimensional Ising model, Ferrenberg tested this package on the two-dimensional version, which has a known answer. "I got the wrong result," Ferrenberg says.

Believing that the problem lay in how he had written his computer program, Ferrenberg spent three weeks looking for errors, but he found none. "As far as we could tell, we had exhausted every possibility – except the random-number generator," he remarks.

As a last resort, Ferrenberg substituted different random-number generators and, to his surprise, found that he came much closer to the correct answer by using a linear congruential generator, which has known defects.

"What we got out of this was that some random-number generators will work with one simulation algorithm and not with others," Ferrenberg says. "It's very discouraging."

"I am not at all surprised at the kind of results observed," comments J.A. Reeds of AT&T Bell Laboratories in Murray Hill, N.J. Reeds had encountered a similar problem with the Marsaglia-Zaman random-number generators in a different type of computation.

In an additional twist on the curious behavior of random-number generators, Shu Tezuka of the IBM Tokyo Research Laboratory in Japan and Pierre L'Ecuyer of the University of Montreal in Quebec have now proved that the Marsaglia-Zaman random-number generators are "essentially equivalent" to linear congruential methods. Therefore, these generators share many of the same characteristics and faults.

L'Ecuyer presented this analysis at this week's Winter Simulation Conference, held in Arlington, Va.

The uncertainty about how subtle, hidden patterns among digits spewed out by various random-number generators may influence simulation results presents researchers using so-called Monte Carlo methods with a serious dilemma, especially when the answer is not known.

"Since there is no reason to believe that the model which we have investigated has any special idiosyncrasies, these results offer another stern warning about the need to very carefully test the implementation of new algorithms," Ferrenberg and his co-workers conclude. "In particular, this means that a specific algorithm must be tested together with the random-number generator being used *regardless* of the tests which the generator has passed." *– I. Peterson*

Two strides toward a workable AIDS vaccine

In a development that they term "the most impressive . . . we have seen in any of our vaccine experiments," five AIDS researchers report they have used a vaccine made of crippled, but live virus to completely protect a group of monkeys from the simian form of AIDS. And in a second, separate finding with implications for the AIDS vaccine search, a research team has determined that AIDS viruses pick up bits of the cells they infect, perhaps as a means of improving their ability to latch onto and invade new cells.

The first discovery, by Ronald C. Desrosiers and four of his colleagues at the New England Regional Primate Research Center in Southborough, Mass., paves the way for the first human tests of an AIDS vaccine made of live human immunodeficiency virus (HIV), the virus that causes AIDS. For safety reasons, the only AIDS vaccines that have so far entered clinical trials consist of killed HIV, pieces of HIV, or other viruses with HIV genes.

Desrosiers and his co-workers hobbled a strain of simian immunodeficiency virus (SIV) by removing a gene called nef, which is thought to regulate the virus' ability to reproduce. They found that a single immunization with the live, hobbled virus allowed each of four rhesus monkeys to fend off infection following repeated injections of enough virulent SIV to infect 10 animals – even though the vaccine was administered more than two years previously. In contrast, Desrosier's group reports in the Dec. 18 SCIENCE, a control group of four monkeys that did not receive the immunization succumbed to the SIV infection and died.

The Massachusetts researchers say their results suggest that a similar strategy involving live HIV "may also be the most potent, effective vaccine for the prevention of AIDS" in humans. "If other vaccine approaches [now in clinical trials] indeed show little or no efficacy under field conditions, limited safety testing of live [disabled] HIV-1 in high-risk human volunteers seems warranted," they conclude.

Larry O. Arthur, director of the AIDS vaccine program at the National Cancer Institute's Frederick Cancer Research and Development Center in Frederick, Md., says Desrosier's team's results "move AIDS vaccine work a major step forward." However, he cautions, "it's going to be very difficult to show that a vaccine like that is safe enough for human volunteers."

A team led by Arthur reports the second AIDS vaccine development, which also appears in the Dec. 18 SCIENCE. Arthur and his colleagues found on the surfaces of HIV particles clusters of molecules that human immune system cells normally use to communicate with one another.

They suggest their finding might explain a puzzling result reported last year: Monkeys inoculated with human cells that had never been infected with SIV nonetheless resisted infection by the virus (SN: 11/23/91, p.328). At the time, some researchers thought the human cells had caused the monkeys' immune systems to make antibodies that could attack SIV as well as the foreign human cells. However, other researchers subsequently conducted experiments that ruled out such a cross-reaction scenario (SN: 2/1/92, p.71).

Arthur and his colleagues now suggest that the human cells might have protected the unvaccinated monkeys from later infection with SIV because both the human cells and the SIV particles bore proteins called the major histocompatibility complex (MHC) on their surfaces. The researchers found that both SIV and HIV contain more MHC proteins than they could have been expected to pick up at random as they budded off infected cells. Instead, Arthur says, "it appears the viruses may selectively concentrate these cellular proteins," perhaps to enable them to better stick to and infect other cells. To test the idea, he plans to administer human MHC proteins to monkeys to see if they protect the animals against SIV grown in human cells. *– C. Ezzell*