THE FIRST WORD/

THE EVOLUTIONARY METHOD

By Douglas McCormick

There are two buttons stuck to the bulletin board above the desk here. One (from a courier company) advises, "Don't Panic," which is the motto of that most estimable reference, *The Hitchhiker's Guide to the Galaxy*. The other button boasts, "Fast, Cheap and Out of Control," which is the motto, of sorts, of the Mobile Robots group at the Massachusetts Institute of Technology's Artificial Intelligence Laboratory. Rodney Brooks leads that group. We got the button from Brooks after meeting him at the Keystone Scientist-to-Scientist meeting last summer.

At the same meeting, we met Danny Hillis, the founder of Thinking Machines and inventor of the parallel-processing Connection Machine. (Brooks once built a pack-rat of a robot that would scoop up discarded cups and candy wrappers and dump them in a garbage can; he called it the Collection Machine.) Hillis ended the Keystone conference with a showing of *Liquid Selves*—a Peter Gabriel music video whose extraordinary, fluid graphical design was concocted by a computer. The computer is programmed to offer a flood of creative manipulations of images, accept the operator/designer's judgment that some images are interesting, and refine and combine the interesting manipulations to produce a final, stunning graphical statement.

The conference was organized by Ron Cape. As we noted here in October ("Light and Verity," *Bio/Technology* **10:**1063), Cape has just formed a company with Stuart Kauffmann, a biologist and computer researcher who found that most self-referencing systems (The state of C depends on the states of A and B. The state of D depends on the state of C. And A depends on C—a situation familiar to biochemist) slip into stable cycles after a very few sets.

The two books most recommended by participants were Stephen Jay Gould's *Wonderful Life* and Steven Levy's *Artificial Life*. We trotted right out and bought them both.

Artificial Life

Artificial Life, as it turns out, is about Hillis, Kauffmann, Brooks, and *Wonderful Life*...among many other things. Levy's book retells the experiences of a handful of researchers—biologists and computer scientists alike—as they try to abstract the essential processes of life and understand why living things live, die, beget, and change the way they do. As they discover, artificial life, developing *in silico* (as Levy puts it; we prefer *in electro*), shares several gross characteristics with real life:

It is bottom-up. Structure emerges from independent (or, rather, complexly interdependent) elements interacting with each other and some external environment. It grows from the simple, bottom layers up; rather than being imposed from the top down. Cellular automata, like John Conway's classic game of Life, clearly show emergent structure. Indeed, there is a theorem showing all von Neumann machines, as they are called, are equivalent, that any one can function as any other—that, time-scales aside, the pulsing patterns of Conway's Life display are the equivalent of a Cray supercomputer or...well, let's not say anything about the human brain.

It is self-organizing. The elements maintain cohesion and identity, and can even add to themselves despite disruptive forces in the environment.

It is genetic. The elements carry instructions that (1) prescribe ranges of reactions to the environment, (2) allow the element to reproduce copies of itself and its instructions through a mechanism that permits random variation.

It is Darwinian. Elements that satisfy some "fitness function" (one programmer used an operator called The Reaper) reproduce in large numbers; those that fail to measure up also fail to reproduce.

For the programmer, the lure of the evolutionary method is obvious. You set up your initial population (usually just strings of random numbers from 0 to 255, which the computer interprets as machine language instructions), establish a fitness function that will drive the system towards some desired result, and walk away. Come back an hour or a week later, and the program is written.

Hillis invented the Connection Machine, in part, to provide a petri dish where strings of ones and zeroes could struggle, reproduce, die, and evolve. Hillis's experiments found that sexual recombination, crossover, and pressure from parasites give genetic systems the variation and the goad needed to make them leap from merely local maxima of survival fitness to genetically distant peaks of even greater efficiency; using such methods, he "bred" random sequences of instructions into programs that can sort numbers more efficiently than any but a half score of the best human computer programmers could have dreamt of. Using a Toshiba lap-top (labeled "Containment Facility"), another investigator, Tom Ray, discovered that parasites and immune responses develop spontaneously in dynamic, self-replicating information-based systems. And a score of other people made a score of other discoveries that seem to relate directly to the much-discussed but seldom-dissected evolutionary forces that have made earthly life what it is today.

The Upshot

Evolution is not merely a theory any more. These researches clearly show that a bottom-up, iterative, evolutionary method is a powerful tool for developing variation and evaluating possibilities. And this is what makes them vital to biotechnology: There are on the order of 10^{80} nucleons in the universe; in theory, there are about 10^{130} possible 100-amino-acid peptides. Four billion years of evolution haven't even scratched the surface.

That datum is at the heart of what Dan Vapnek used to call "irrational drug design," the spaghetti method—you throw some at the wall see what sticks. Only, in this case, instead of a wall, one throws compounds at a receptor-affinity column—and sees what sticks. The column (or latterly a downstream reporter) is the fitness function. What is needed is an algorithm for developing variation—an approach being hotly pursued by the wave of "algorithm-based" start-ups that slipped in between the carbohydrate and neuroscience companies on one side and the anti-aging companies on the other—companies like Affymax, Darwin, Gilead, Houghten, Selectide, Tularik, and a few others.

References

Gould, Stephen Jay, 1989. *Wonderful Life: The Burgess Shale and the Nature of History*. W.W. Norton and Company (New York and London).

Levy, Steven, 1992. *Artificial Life: The Quest for a New Creation*. Pantheon Books (New York).