RNA Offers Clue to Life's Start

In answering the question of how life began, biologists can offer only plausible stories. One oft-described scenario highlights ribonucleic acids, or RNA, as the evolutionary link between life's chemical precursors and the first self-replicating cells. In contemporary cells, RNA carries genetic information and plays crucial roles in transforming genetic code into proteins.

To spawn the earliest living cells, RNA would have had to duplicate itself without the complex replicating enzymes and other chemicals used by cells. Researchers have found no such self-replicating molecules in nature.

Now, two molecular biologists claim their laboratory-modified RNA molecules can copy parts of themselves nearly unassisted. The researchers have yet to build an RNA molecule that can copy all of itself, but they say their work renders that goal realistic.

"If we can do this, it would show that self-replicating RNA could have been a major step in the evolution of life," says Jack W. Szostak of Massachusetts General Hospital in Boston. As a first experimental step, he and Jennifer A. Doudna have modified a type of RNA molecule — called a ribozyme — found in protozoans and some other organisms. Ribozymes' normal role is to extract themselves from larger RNA molecules that contain them.

Other researchers have shown that the protozoan ribozyme can use a short segment on its own molecular body as a template for linking a limited group of short nucleotide sequences, or oligonucleotides. In a commentary accompanying the researchers' report in the June 15 NATURE, Thomas R. Cech of the University of Colorado in Boulder notes that the modified ribozyme overcomes the limitations in the length and variety of sequences it can link.

Using genetic engineering, Szostak and Doudna removed the ribozyme's internal template and showed that the new ribozyme could connect separate oligonucleotides aligned on specially designed, external templates. They also found that certain chemical additives, which may cause subtle changes in the ribozyme or templates, enable the ribozyme to connect oligonucleotides of nearly any sequence. In its best performance, the ribozyme stitched five oligonucleotides into a string of 45 nucleotides, Doudna says.

Says Szostak, "I think this is a big step toward building a real replicase" — a self-copying molecule that might have evolved into living cells. He and Doudna hope to develop their system so it copies the several-hundred-ribonucleotide string that would coil into a new ribozyme. "If we could make a replicase and then enclose it in an appropriate membrane, we would have primitive cells," Szostak says.

Molecular biologist Norman R. Pace of Indiana University in Bloomington says the modified ribozyme system could lead to new tools for researchers who paste nucleotides together into new molecules. As for the origin-of-life question, he says, Doudna and Szostak's work adds another chapter to a plausible story that no one can prove true. — *I. Amato*

Biting off a record-breaking piece of pi

"Compute but verify" is the strategy at the core of a remarkable new method for calculating pi (π) — the ratio of a circle's circumference to its diameter. In a recent demonstration of the method's power, two mathematicians at Columbia University in New York City used it to compute pi to 480 million decimal places, shattering the previous record of 201 million digits (SN: 4/2/88, p.215).

Chudnovsky/Columbia

This computer-generated landscape represents statistical information about the first million digits of pi.

"Our goal is to develop a better understanding of the arithmetic properties of [constants such as pi]," says David V. Chudnovsky, who with his brother Gregory discovered the key formulas for the computation. With so many digits of pi now available for analysis, the Chudnovskys are seeing the first hints of subtle patterns in the distribution of pi's digits, suggesting the digits may not be truly random.

Computing pi also gives the largest and fastest computers a thorough workout, pinpointing subtle flaws in their hardware and software. "It is really the ultimate stress test — a cardiogram for a computer," Chudnovsky says. In the course of their calculations, the Chudnovskys identified unexpected quirks peculiar to the computers they used.

The new formula, or identity, discovered and used by the Chudnovskys expresses pi as a complicated sum. By evaluating more and more terms in such a sum, mathematicians get closer and closer to the true value of pi. This particular identity gets closer to pi faster than any other known formula.

But computing pi quickly isn't enough. Computers don't work correctly all the time, and an accidental change in even one bit of data could completely corrupt a computation. "The problem [of hardware faults] is totally beyond your control," Chudnovsky says. "If you don't have a way immediately to verify and recover the data, you would lose everything, and you wouldn't know it." To avoid such difficulties, the Chudnovsky method includes automatic verification and, where necessary, correction.

Using computer programs written in FORTRAN, the Chudnovskys tested their method on a Cray-2 and an IBM 3090. They computed at odd times over a period of 6 months, sometimes in segments only 15 minutes long.

The Chudnovsky method lends itself to group efforts. Much of the work of computing pi to a given number of decimal places can readily be divided among a large number of people, each working independently on a small computer. The Chudnovskys envision a "pi chain letter," with interested researchers, students and hackers combining their efforts to do multibillion-digit calculations.

Computing pi to billions of digits is important in the search for patterns among pi's digits. "Even a billion digits aren't really enough for doing a proper statistical analysis," Chudnovsky says. Although early results show some evidence for subtle relationships among the numbers, "we don't have enough numerical evidence yet." — *I. Peterson*