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## Cost of Decoding a Genome Is Lowered

By [NICHOLAS WADE](#)

A Stanford engineer has invented a new technology for decoding DNA and used it to decode his own genome for less than \$50,000.

The engineer, Stephen R. Quake, says the low cost “will democratize access to the fruits of the genome revolution” by enabling many labs and [hospitals](#) to decode whole human genomes.

Until now only companies or genome sequencing centers, equipped with large staffs and hundreds of machines, have been able to decipher the three billion units in a human genome.

Dr. Quake’s machine, the Heliscope Single Molecule Sequencer, can decode or sequence a human genome in four weeks with a staff of three people. The machine is made by a company he founded, Helicos Biosciences, and costs “about \$1 million, depending on how hard you bargain,” he said.

Only seven human genomes have been fully sequenced. They are those of [J. Craig Venter](#), a pioneer of DNA decoding; [James D. Watson](#), the co-discoverer of the DNA double helix; two Koreans; a Chinese; a Yoruban; and a leukemia victim. Dr. Quake’s seems to be the eighth full genome, not counting the mosaic of individuals whose genomes were deciphered in the Human Genome Project.

An article describing the decoding of Dr. Quake’s genome, reported Monday in Nature Biotechnology, shows the degree of overlap between the DNA variations in his own genome and those in Dr. Venter’s and Dr. Watson’s.

For many years DNA was sequenced by a method that was developed by Frederick Sanger in 1975 and used to sequence the first human genome in 2003, at a probable cost of at least \$500 million. A handful of next-generation sequencing technologies are now being developed and constantly improved each year. Dr. Quake's technology is a new entry in that horse race.

Dr. Quake calculates that the most recently sequenced human genome cost \$250,000 to decode, and that his machine brings the cost to less than a fifth of that.

“There are four commercial technologies, nothing is static and all the platforms are improving by a factor of two each year,” he said. “We are about to see the floodgates opened and many human genomes sequenced.”

He said the much-discussed goal of the \$1,000 genome could be attained in two or three years. That is the cost, experts have long predicted, at which genome sequencing could start to become a routine part of medical practice.

The impediment to the medical use of genomes, however, is fast becoming not the technology but the ability to understand and interpret what the technology reveals.

The quest to uncover the genetic roots of complex diseases like [cancer](#), [diabetes](#) or [Alzheimer's](#), a primary goal of the Human Genome Project, recently stalled. Most of those diseases turn out to be caused not by a few common variants, as many biologists expected, but by an unmanageable number of rare variants, offering for the most part no clear target for drugs or diagnosis.

That genetic complexity has thrown into disarray many plans for personalized medicine, because for complex diseases and traits there is no obvious way to predict the status of a whole person from his DNA sequence.

There is much better knowledge about the genetic basis of many simple diseases — those caused by a single genetic variant — but most of those diseases are rare and account for a small fraction of the overall burden of disease.

Still, people trying to analyze their own DNA sequence are likely to find one or more of the single gene disease variants because those are the only ones understood so far.

Dr. Quake said that analysts were annotating his genome and had found a variant associated with heart disease. Fortunately, Dr. Quake inherited the variant from only one parent; his other copy of the gene is good.

“You have to have a strong stomach when you look at your own genome,” he said.

Dr. Quake said he was making his genome sequence public, as Dr. Venter and Dr. Watson have done, to speed the advance of knowledge.

“Scientists have a strong ethic for sharing data,” he said. “Venter’s and Watson’s genomes were incredibly helpful in analyzing mine, and I hope mine will have the same utility for others.”

Some experts believe the way around the current impasse in understanding the roots of complex disease will lie in sequencing the whole genomes of many people, including patients suffering from specific diseases. Cheaper methods of sequencing should help toward achieving that goal.

George Church, a leading biotechnologist at the Harvard Medical School, said that for clinical [genetics](#), DNA sequences needed to be decoded with an accuracy of only one error in every 10,000 to 100,000 DNA units. Dr. Quake said his machine had an accuracy of one error in every 20,000 units.

A real breakthrough in technology, Dr. Church said, would be the ability to sequence a human genome for \$5,000 with an accuracy of one error per 100,000 units.

Dr. Quake’s DNA sequencing machine, about the size of a refrigerator, works by splitting the double helix of DNA into single strands and breaking the strands into small fragments that on average are 32 DNA units in length.

The pieces of DNA are then captured on a glass slide. On each of those tethered strands a new helix is built up unit by unit in a way that generates light. The addition of each unit is recorded by a microscope in the machine, which can follow a billion DNA fragments at a time. Because the two strands of a DNA double helix are complementary, the sequence of new units that

attach to each growing strand reveals the identity of the units on the tethered strand.

A computer program then matches the billions of 32-unit fragments to the completed human genomes already on file and records the sites at which there are additions or deletions to the standard sequence, or a different DNA unit from the one most common in the population. The full set of those differences is what makes each individual unique