Human genetic map: Worth the effort?

When researchers last week in Chicago announced their success in constructing the rough map of a bacterium's entire genetic code, the new information added another line to the expanding book on deciphering the complete human genome. But because an organism's genome includes all of its genetic material, the current federal program to map the highly complex human genome is having some technical and political difficulties.

Charles R. Cantor of Columbia University said at the annual meeting of the American Association for the Advancement of Science that he and his coworkers had divided the genome of the common bacterium *Escherichia coli* into 23 pieces and had used a new method to prepare the DNA for study. He emphasized that the data are "sketches" of the *E. coli* genome, not a complete sequence of all its components.

Although the project took several researchers more than a year to complete, Cantor says current technology could shorten the time required to two or three weeks. The Columbia research was one of several pilot studies being conducted to see if such sketches can be used to map entire genomes, and its success was welcome news to those anxious to systematically map the genetic code.

But the *E. coli* genome is only about one-tenth the size of the smallest human chromosome. In turning to the human system, Cantor's group and another from Yale University currently are trying to map pieces of chromosome 6 (important in transplant compatibility) and chromosome 4 (involved in Huntington's disease) by using similar techniques.

Whether these latest efforts are successful or not, they have already yielded some unexpected results, according to Cantor. "The major surprise is . . . the human genome is mosaic," he says. "What this means is that genes for related functions appear to be clustered together in the chromosomes more than originally thought." As a result, segments of the chromosomes located near specific disease-causing genes may be used to a greater extent in diagnosis.

The promise of improved diagnosis and treatment for the more than 3,000 known genetic diseases is enticing, but at the same time frustrating. If it were uncoiled from the nucleus of a cell, human genetic material would stretch 2.7 meters. If the information stored there were printed out on paper, it would fill 200 Manhattan telephone books, or three years worth of daily newspapers, say scientists. And only 0.2 percent of the human genome has been decoded.

Just to process the data produced by mapping the entire human genome would require "an extraordinarily rich" computer base, possibly using artificial intelligence capability, says Mark W. Bitensky from Los Alamos National Laboratory in New Mexico. The Los Alamos lab and its so-called GenBank (a repository for genetic sequencing data) join Lawrence Livermore National Laboratory in California and Columbia University as the primary centers for the Department of Energy's (DOE) Human Genome Initiative (HGI).

All the nonscientific elements of modern science also can be found in the government's human genome project — international cooperation/competition, ethical questions about working with human genetic material, controversy over the high price for a fairly narrow area of research, basic science giving way to technology, and much more.

According to Charles P. DeLisi, from the DOE's Office of Health and Environmental Research and a principal supporter of HGI, if mapping of the human genome proceeds at its present-day pace, it will take 7,000 years to decipher the entire sequence. But with adequate financial and human resources, he claims that the HGI could supply the entire genome by the year 2000; DeLisi adds that the Japanese are building a robot capable of decoding DNA 1000-fold faster than methods currently used in the United States. DeLisi predicts that X-ray lasers or new types of scanning electron microscopes may be used in the U.S. effort.

Despite the technological dazzle, there are those biologists who ask about the economic and scientific costs of such a project, wondering whether it is, in Bitensky's words, "technological determinism rather than good science." The questions are similar to those being asked by physicists critical of the high-cost superconductor project. Reagan's proposed budget for fiscal year 1988 includes a $12 million request for the genome project (up from $2 million the previous year). A DOE advisory committee projected expenditures of $20 million to $40 million per year during the initial technology-development phase of the project; the second phase of actual sequencing may cost as much as $3 billion a year, says DeLisi, who is quick to point out that this estimate is based on current technology that would be replaced by less expensive methods.

Walter Gilbert, a Nobel laureate at Harvard University, calls decoding the human genome "the biology of the 21st century." And Bitensky says that "the insights that lurk in the genome are very exciting . . . comparable to the information that awaits us in outer space, or at the heart of particle physics." Whether that information is worth the cost is still being debated. — *D.D. Edwards*

Lake Nyos reported red and rumbling

The U.S. Agency for International Development (AID) officially released its final report Feb. 11 on the Lake Nyos disaster that killed at least 1,700 people last August when a gas cloud escaped from the Cameroon lake (SN: 1/17/87, p.36). The agency also made public "Lake Nyos Revisited," a preliminary report by two scientists sent to Cameroon by AID after a French and a Cameroonian geologist reported hearing rumbling and the sound of waves on the lake Dec. 30.

According to this preliminary report, written by Haraldur Sigurdsson at the University of Rhode Island in Kingston and William Evans from the U.S. Geological Survey in Menlo Park, Calif., the French and Cameroonian geologists also said they heard noises accompanied by flashes of light from the direction of nearby Lake Njupi. The report notes that at times in December both lakes were red.

During their visit to Lake Nyos Jan. 20-25, Sigurdsson and Evans conducted interviews, made temperature profiles, collected gas and water samples and did a bathymetric survey of the lake. They also visited Lake Njupi. Like the final AID report on the August event, "Lake Nyos Revisited" concludes that there is "no evidence of recent volcanic activity in the lake." Instead Sigurdsson, Evans and the other AID researchers who have visited the lake believe the August event was caused by a disruption of the layering of the lake, allowing carbon dioxide, which had been building up in the highly stratified lake, to escape.

Sigurdsson and Evans write that during their January visit they observed rockfalls from the cliffs surrounding the lake, and also noted scars on the cliffs from rockfalls or earlier landslides. They suggest that such a rockfall may have triggered the release of the August cloud. A rockfall might also have been the source of the noises heard by the geologists in December. If so, write Sigurdsson and Evans, it may have brought a little of the oxygen-deprived deep water to the surface. Iron in the rising deep water would then have been oxidized at the surface, giving the lake a reddish cast.

Both reports warn that Lake Nyos and other Cameroon lakes may still be hazardous. They recommend that anthropological studies be conducted to determine how unusual cloud emissions have been in the region. They also suggest that pipes be installed in Lake Nyos to siphon off the carbon dioxide that builds up at the bottom. According to an AID official, the international science teams sent to study Lake Nyos will meet in Cameroon March 16 to compare results. — *S. Weisburd*