Hand-feeding also became the preferred method of rearing foundlings—with sometimes disastrous results. During the last quarter of the 18th century, for example, 10,227 babies died at the Dublin Foundling Hospital—a mortality rate of 99.9%.

The wet-nursing and artificial-feeding trend gradually died out by the end of the 18th century, for a variety of reasons. A major one, according to Fildes, is that medical writers began to focus their attention on the health and well-being of mothers. In addition, Fildes writes, "there was an apparent decline of the husband's influence in decisions about how his children were to be fed."

What Fildes shows in her book, says Schofield, is that, "for most people, their preconceptions [about infant feeding] will be incorrect." It is, he says, "a very interesting piece of work." ■ **GINA KOLATA**

National Academy Looks at Human Genome Project, Sees Progress

A year after the Human Genome Initiative began, biologists are beginning to come to terms with the goals and organization of the project; specialized centers are proposed

In what will be one of its most rapidly produced committee reports, the National Academy of Sciences is preparing a commentary on the current initiative to map and sequence the human genome. The Academy's committee on the topic, convened under the Board on Basic Biology, had its first meeting at the end of January and plans to publish its conclusions by June.

The committee, chaired by Bruce Alberts of the University of California in San Francisco, joins a growing list of national bodies currently contemplating this major project, and this includes the Department of Energy (DOE), the National Institutes of Health (NIH), and the Office of Technology Assessment. Like members of a traveling circus, appointees to these various committees often overlap and find themselves moving from meeting to meeting to discuss the same issues with the same colleagues. "The ratio of talk to progress is still high," says Charles Cantor of Columbia University Medical School and a member of the Academy's committee, "but people are moving toward a consensus about how this project should be structured."

The fact that ideas of structure and organization are now being seriously considered is significant and reflects a real evolution of the biological community's response to the prospect of a megaproject of a scale and cost more familiar to physical scientists. "It is clearly no longer a question of whether the project ought to be done," commented University of California biologist Russell Doolittle after the Academy committee's recent gathering, "but of how fast it will be done."

Cantor agrees. "The idea of the project went through a period of doubt, when the biological community heard of the huge initial estimates of cost [$3 billion] and became concerned about the potential diversion of funds from other research," he says. "But now there is a much more upbeat tone."

The principal organizational idea that began to emerge from the Academy committee's discussions was the establishment of about half a dozen research centers that would concentrate on specific aspects of the problem, including mapping, sequencing, technology development, and data analysis. This arrangement would allow the exploration and development of new approaches to the problem to go along with what committee members kept referring to as "real science." The business of ultimately trudging through all 3 billion bases of the human genome would, most agreed, have to be tackled in some kind of factory approach. "That's not science," commented Walter Gilbert of Harvard University, "that's production."

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Although the Academy committee's discussion gave a sense that the human genome project was at last on its way, there was also a clearer recognition than has been apparent at previous gatherings that the practicalities are going to be even tougher than at first acknowledged. It was not that the committee heard any startling new evidence or covered new territory, but, as one member observed, "people got past the rhetoric" and faced up to the practical limitations of current techniques. The tenor of the discussion, not the substance, was different—it was more pragmatic, more self-critical. "There is a growing conviction that the technology is not yet good enough," says Lee Hood of the California Institute of Technology. "At worst, it might fail to complete the job, or at best it might be extremely expensive."

It is now little more than a year since the real push to characterize the human genome began, inspired principally by Charles DeLisi of the DOE's Office of Health and Environmental Research. Significantly, the name of the enterprise has proved to be mutable during that time, changing from the "Genome Sequencing Initiative" to simply the "Genome Initiative." What once was the rallying call—the entire nucleotide sequence of the human genome—has become muted, and in the Academy committee's formal statement of task it is characterized as "a subsidiary goal." The primary goal is "to map the human genome."

The ideal physical map of the human genome would actually be a line of bottles, each of which would contain DNA fragments about 40,000 bases long, the position of which on the genome would be accurately known. Producing individual fragments of this sort—which are known as cosmids—has been part of biologists' tool kit for some time. The challenge is to blanket the 30 billion bases of the human genome with overlapping cosmids so that there are no gaps in the map. That is a tough task, especially as some parts of the genome, particularly those with long stretches of repeated sequences, will prove very difficult to clone.

The Academy committee heard from Maynard Olson of his Washington University group's endeavors to produce much bigger clones, which potentially reduces the magnitude of the problem. Nevertheless, asked by Alberts "what scale of effort would be required to map the human genome using these approaches?" Olson replied, "huge." Sydney Brenner, of the Medical Research Council's Laboratory of Molecular Biology in Cambridge, England, reported on his group's progress with mapping the nematode genome using a technique that essentially "fingerprints" fragments of DNA. By now the Cambridge group has 860 such fragments, but, says Brenner, "these are islands, and we have to fill in the gaps."

The clearly stated limitations of mapping techniques so far available led to a recognition that a map, however good, might remain patchy for a long time. "The endgame is indeterminate," said Brenner, "and it shouldn't be counted in estimates of the cost of the project." The discussions also led to the notion of combining cosmid mapping with a restriction fragment length polymorphism (rflp) map, the latter forming a very much coarser scatter of markers that would serve to pinpoint the position of cosmids around the genome.

The development of new techniques both for mapping and sequencing is going to be crucial to bringing the genome project within manageable bounds, and Academy committee members were therefore delighted to hear from Harvard University's George Church about "multiplex sequencing." If it works, this low technology, parallel processing approach has the potential to improve sequencing by a factor of 10. Church and his colleagues are now putting the system to the test, and if it is successful they hope to have sequenced 90% of the *Escherichia coli* genome [which has 3 megabases] within a year.

The very real momentum that is now established behind the genome project nevertheless faces many uncertainties. For instance, proponents' interest in establishing a series of small, specialized centers reflects a recognition of the need for some sort of coordination and organization while maintaining flexibility, specifically in technology development. Although the prospect of trudging through the entire genome, whether mapping or sequencing, is widely described as being potentially immensely tedious, there is a fear that if a megacenter is established too soon to take on the job as a production task, then the technology might become frozen in its infancy. "A factory is not the place you solve problems," observed one committee member.

Together with questions of organization inevitably come questions of funding. The figure of $3 billion is rarely heard these days. Instead, estimates of something between $30 million and $50 million a year for 10 years are much more common, which brings the project well within a scale of annual expenditure that, for instance, the DOE could cope with if it so chose. The maneuvering is just beginning over which agency will eventually take charge of the principal responsibility for the human genome project. ■ **Roger Lewin**

Debate over Emergence of Human Tooth Pattern

For more than a decade, anthropologists have accepted that early human ancestors had a prolonged infancy period, like modern humans; this idea is now being challenged

"The question of standards might sound like a mild issue," says Holly Smith of the University of Michigan, "but it is really a massive disagreement." Smith is referring to the guts of a dispute that is fomenting between herself and Alan Mann of the University of Pennsylvania. The dispute centers on how you interpret the patterns of dental growth and development in our 2-million-year-old ancestors: are the patterns like those of modern humans or more like those of apes?

The disagreement, which so far has reached the scientific literature only in simple declarative form, extends beyond Smith and Mann and includes Timothy Bromage and Christopher Dean, two researchers at University College, London. Bromage and Dean believe, like Smith, that the teeth of the early hominids were distinctly primitive and apelike in their overall growth characteristics. Mann vigorously rejects the notion and insists that by at least 2 million years ago our ancestors had already evolved a pattern of dental development that is seen in modern man, *Homo sapiens*.

Smith and Bromage and Dean independently published their conclusions relatively recently, thereby challenging the conventional wisdom established by Mann more than a decade ago. Mann has been criticizing these conclusions during the past few months in several small seminars and now has two stinging critiques prepared for publication in the scientific literature. "Their analyses," he says, "are absolutely and completely wrong."

The distinction between the two patterns of dental growth is significant in this context because, as Washington University anthropologist Glenn Conroy says, "it affects the way you think about these creatures." The reason is that, by comparison with apes, modern humans have an extended period of infancy, which is important for the greater intellectual and social nurturing to which we must be exposed. If our earliest ancestors also had prolonged infancies, then it is perhaps legitimate to infer that they had already begun to assume a degree of humanness that is not shared by "mere" apes. Signs of prolonged infancy are directly reflected in the growth characteristics of the dentition: hence the interest in the teeth of the early hominids.

The suggestion by Smith, Bromage, and Dean that hominids of 2 million or so years ago were in general more apelike than humanlike falls very much in line with current thinking about human evolution. For instance, most anthropologists now agree that the evidence of molecular biology demonstrates a much closer genetic relationship and more recent common ancestry with the African great apes than had previously been contemplated. And there is a lot of talk nowadays about how some of the earliest hominids spent a good deal of time climbing trees, which has a distinct simian ring to it.

Overall, then, there has been a distinct shift during recent years from thinking about our earliest relatives as being quaint and hairy diminutive humans to characterizing them as bipedal apes. The question here, then, is how real is this trend? "I would term it a fashion," says Mann, who characterizes himself as one of the last old-time anthropologists.

The story began in the late 1960s with Mann's pioneering work applying x-ray analysis to the fossil remains of the cave site of Swartkrans in South Africa. Mann chose this site because it contained the largest collection of early hominid juvenile jaws available anywhere in the continent. The work has to be done on juvenile jaws, because you need to be able to see tooth patterns while development is still incomplete. Mann's conclusion, which he extended by further work in the early 1970s, was that the Swartkrans hominids had dental growth characteristics—and therefore duration of infancy—very like modern humans.

"I was concerned with looking for shifts," recalls Mann. "I felt that only minor genetic changes would be required to elongate the postnatal developmental stages. This would have an important effect on allowing animals to internalize a lot more information about their environment." Mann's conclusions were in harmony with ideas about hominid brain development that were then current, and the publication of his 1975