Sequencing Technologies

The ultimate physical map of the human genome is the complete DNA sequence—the determination of all base pairs on each chromosome. The completed map will provide biologists with a Rosetta stone for studying human biology and enable medical researchers to begin to unravel the mechanisms of inherited diseases. Much effort continues to be spent locating genes; if the full sequence were known, emphasis could shift to determining gene function. The Human Genome Project is creating research tools for 21st-century biology, when the goal will be to understand the sequence and functions of the genes residing therein.

Achieving the goals of the Human Genome Project will require substantial improvements in the rate, efficiency, and reliability of standard sequencing procedures. While technological advances are leading to the automation of standard DNA purification, separation, and detection steps, efforts are also focusing on the development of entirely new sequencing methods that may eliminate some of these steps. Sequencing procedures currently involve first subcloning DNA fragments from a cosmid or bacteriophage library into special sequencing vectors that carry shorter pieces of the original cosmid fragments (Fig. 11). The next step is to make the subcloned fragments into sets of nested fragments differing in length by one nucleotide, so that the specific base at the end of each successive fragment is detectable after the fragments have been separated by gel electrophoresis. Current sequencing technologies are discussed on p. 21.