varies in size from 10,000 bp to 1 Mb (Fig. 9b, p. 14). An advantage of this approach is the accessibility of these stable clones to other researchers. Contig construction can be verified by FISH, which localizes cosmids to specific regions within chromosomal bands.

Contig maps thus consist of a linked library of small overlapping clones representing a complete chromosomal segment. While useful for finding genes localized to a small area (under 2 Mb), contig maps are difficult to extend over large stretches of a chromosome because all regions are not clonable. DNA probe techniques can be used to fill in the gaps, but they are time consuming. Figure 10 is a diagram relating the different types of maps.

Technological improvements now make possible the cloning of large DNA pieces, using artificially constructed chromosome vectors that carry human DNA fragments as large as 1 Mb. These vectors are maintained in yeast cells as artificial chromosomes (YACs). (For more explanation, see DNA Amplification, pp. 18–20.) Before YACs were developed, the largest cloning vectors (cosmids) carried inserts of only 20 to 40 kb. YAC methodology drastically reduces the number of clones to be ordered; many YACs span entire human genes. A more detailed map of a large YAC insert can be produced by subcloning, a process in which fragments of the original insert are cloned into smaller-insert vectors. Because some YAC regions are unstable, large-capacity bacterial vectors (i.e., those that can accommodate large inserts) are also being developed.

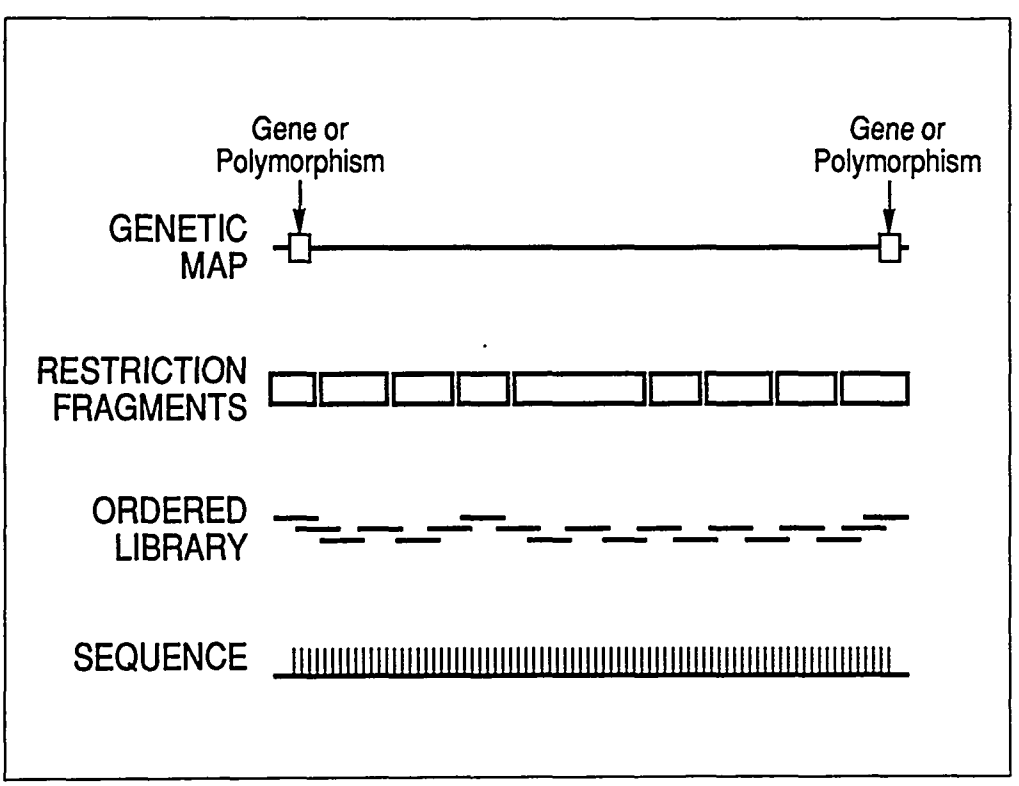

Fig. 10. Types of Genome Maps. *At the coarsest resolution, the genetic map measures recombination frequency between linked markers (genes or polymorphisms). At the next resolution level, restriction fragments of 1 to 2 Mb can be separated and mapped. Ordered libraries of cosmids and YACs have insert sizes from 40 to 400 kb. The base sequence is the ultimate physical map. Chromosomal mapping (not shown) locates genetic sites in relation to bands on chromosomes (estimated resolution of 5 Mb); new in situ hybridization techniques can place loci 100 kb apart. This direct strategy links the other four mapping approaches. [Source: see Fig. 9.]*