Macrorestriction maps: Top-down mapping. In top-down mapping, a single chromosome is cut (with rare-cutter restriction enzymes) into large pieces, which are ordered and subdivided; the smaller pieces are then mapped further. The resulting macrorestriction maps depict the order of and distance between sites at which rare-cutter enzymes cleave (Fig. 9a). This approach yields maps with more continuity and fewer gaps between fragments than contig maps (see below), but map resolution is lower and may not be useful in finding particular genes; in addition, this strategy generally does not produce long stretches of mapped sites. Currently, this approach allows DNA pieces to be located in regions measuring about 100,000 bp to 1 Mb.

The development of pulsed-field gel (PFG) electrophoretic methods has improved the mapping and cloning of large DNA molecules. While conventional gel electrophoretic methods separate pieces less than 40 kb (1 kb = 1000 bases) in size, PFG separates molecules up to 10 Mb, allowing the application of both conventional and new mapping methods to larger genomic regions.

Contig maps: Bottom-up mapping. The bottom-up approach involves cutting the chromosome into small pieces, each of which is cloned and ordered. The ordered fragments form contiguous DNA blocks (contigs). Currently, the resulting "library" of clones

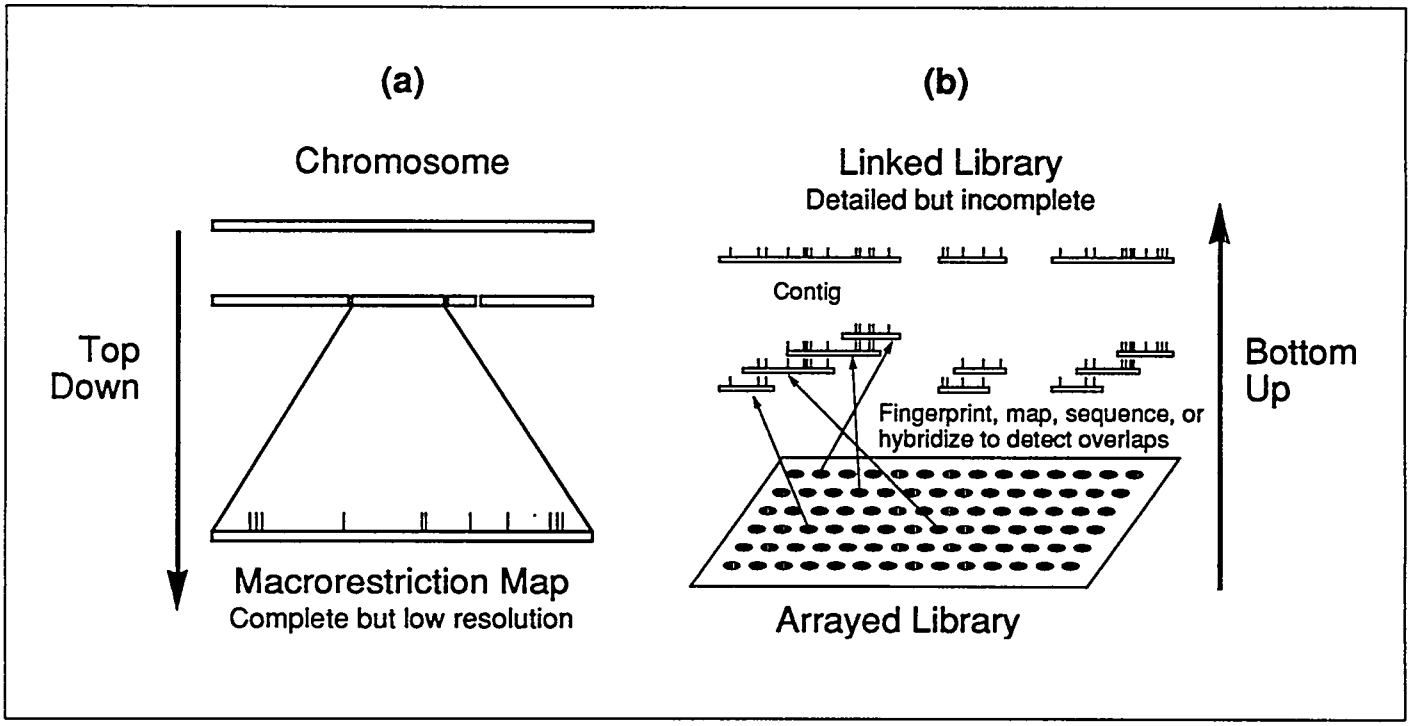

*Fig. 9. **Physical Mapping Strategies.** Top-down physical mapping **(a)** produces maps with few gaps, but map resolution may not allow location of specific genes. Bottom-up strategies **(b)** generate extremely detailed maps of small areas but leave many gaps. A combination of both approaches is being used. [Source: Adapted from P. R. Billings et al., "New Techniques for Physical Mapping of the Human Genome,"* The FASEB Journal *5(1), 29 (1991).]*