As for fractal viscous fingers, a major question in the mind of some researchers is the role of the non-Newtonian fluid used by Nittman, Daccord, and Stanley. While the use of such a fluid permitted the attainment of the negligible interface surface tension needed to get a fractal, it is also possible that the non-Newtonian character itself played an important role. Until this question is resolved, researchers cannot be sure that fractal behavior is a general characteristic of viscous fingers. Several experiments are planned in the hopes of resolving the issue.

—ARTHUR L. ROBINSON

Hopping Along the Chromosome

Chromosome "walking" has been a familiar exercise to molecular biologists for about 5 years. The technique allows the detailed mapping of relatively long stretches of DNA—nearly 250 kilobases (kb) is the best achieved so far. It has proved valuable for locating specific genes but suffers from the drawback of being tedious. An average walk requires four steps to traverse 100 kb, with each step taking up to 2 months.

A recently developed method, called chromosome "hopping" or "jumping," may have a decided advantage over walking for moving across long stretches of DNA. Hopping currently appears capable of spanning up to 100 kb at a time, about a fourfold improvement over walking. Ultimately, single hops of 500 or even 1000 kb may be possible. Moreover, walking proceeds by the progressive identification of overlapping cloned fragments of DNA and can be stopped in its tracks by a nonclonable region. In contrast, hopping does not require the cloning of all the DNA between the start and stop sites and may thus leap over DNA segments that are refractory to cloning.

The new technique originated independently in Sherman Weissman's laboratory at Yale University School of Medicine and that of Hans Lehrach at the European Molecular Biology Laboratory in Heidelberg. The approaches of the two groups are similar, says Francis Collins, who originally worked with Weissman and is now continuing his hopping research at the University of Michigan Medical School. Both aim at generating "junction fragments," in which the ends of DNA segments of a particular large size, say 100 kb, are brought together while most of the DNA in between the ends is removed (*1*). This is done, as shown in the diagram, by forming circles from the 100-kb pieces and then cutting them with a restriction enzyme. The resulting fragments are small enough to be cloned.

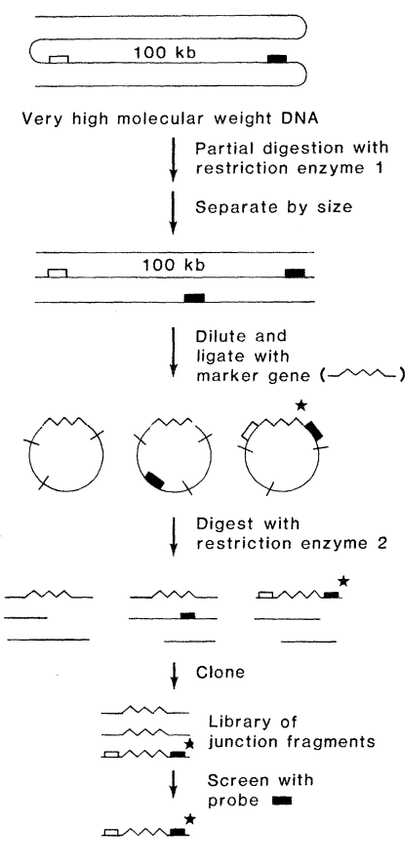
The final result is a library of junction fragments representing the 100-kb DNA fraction. Such a library can be produced in about 2 months, according to Collins, and once produced can be maintained and used indefinitely. Comparable libraries may also be constructed for additional DNA size classes. The library representing the desired length of the hop can then be screened with the probe that defines the start site, a procedure that also requires about 2 months. The junction fragment thus identified serves as a bridge between the start site and the destination and can provide a new probe for initiating a second hop, if that is desired.

The main disadvantage of hopping methods is that they entail a good deal of technical difficulty. Production of the junction fragment library initially requires a preparation of very high molecular weight DNA, and DNA is notoriously subject to mechanical breakage and digestion by cellular enzymes. In addition, DNA fragments longer than 70 kb cannot be separated by conventional gel electrophoresis. However, a new gel electrophoresis procedure, which was devised by David Schwartz and Charles Cantor of Columbia University College of Physicians and Surgeons for separating yeast chromosomes, is proving helpful in this regard (*2*).

Chromosome hopping should help in preparing detailed maps of large gene complexes. In addition, it may be useful for pinning down the defective genes that cause inheritable diseases, many of which are still unidentified. A probe that will identify a DNA sequence that is closely linked to the target gene is required to get the hop under way. Although such probes are currently rare, they are being avidly sought. One has already been found for the genetic locus of Huntington's disease (*Science*, 25 November 1983, p. 913).

The probe identifies a DNA sequence estimated to be some 3000 to 5000 kb distant from the Huntington's locus, a truly formidable distance to walk—but one that may be more amenable to hopping. In fact, Collins is collaborating with James Gusella of Massachusetts General Hospital in an attempt to identify the gene involved in Huntington's disease. As more markers for genetic disease loci are identified, there will be an even greater need for methods for moving rapidly along chromosomes.

—JEAN L. MARX



Scheme for chromosome hopping

The black box denotes the start site of the hop, for which there must be a probe, and the open box represents the destination some 100 kb away. Although it is not absolutely necessary, a marker gene (here denoted by the wavy line) may be inserted into the circles to make it easier to identify the junction fragments that contain the ends of large DNA segments.

References

1. F. S. Collins and S. M. Weissman, *Proc. Natl. Acad. Sci. U.S.A.* **81**, 6812 (1984).
2. D. C. Schwartz and C. R. Cantor, *Cell* **37**, 67 (1984).