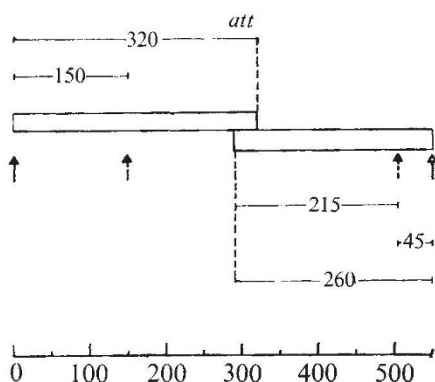


so there must be a hitherto undetected Hind III cut very close to one of the others. A new band appears when λ and λ pbio₁ DNAs are hybridised and digested sequentially with S1 and Hind III (Fig. 2b). In three separate experiments, the length of this DNA piece was determined as 320 base pairs. This band is not seen when the DNA in the hybridisation mix is digested with either enzyme separately, and represents DNA between Hind III cut 3 and the left end of the bio₁ substitution, since the right end of the bio₁ substitution is 9.7% λ (4,500 base pairs) away from the next Hind III cut^{1,6,7}.

The sum of the lengths of the Bam HI₃-att and Hind III₃-att DNA pieces is 580 base pairs. To obtain an independent estimate of this distance, we isolated the Hind III₃-Bam HI₃ piece (Fig. 2), which we call α . α can be cut by the restriction endonuclease Hinf I to yield three pieces, β , γ and δ (Fig. 2d). If the 5' ends of α are labelled using polynucleotide kinase and then digested with Hinf, only γ and δ are labelled (Fig. 2e). A fragment identical in mobility to δ is obtained by Hinf digestion of the Bam HI-att fragment (Fig. 2c). Thus δ is to the right, γ to the left, and β in the middle. The lengths of β , γ and δ as determined by ten separate measurements of their mobilities in gels are 360, 150 and 45 base pairs respectively, giving 555 base pairs for α . No other fragments have been detected, and the radioactivity present in the three bands after nick translation with α -³²P-dGTP is in the ratio 7.4:3.5:1, which is similar to the ratio of the fragment lengths, 8:3.3:1. Endonuclease Hha I also cuts α twice, yielding three fragments that are 470, 65 and 15 base pairs long, their sum being 550 base pairs. Mbo_{II} also cuts α twice yielding three fragments 380, 90 and 75 base pairs long, their sum being 545 base pairs. These values agree very well with the value obtained from the sizes of the Hinf fragments. We therefore have four independent measurements of the distance between Hind III cut 3 and Bam HI cut 3; 550, 555 and 545 from the Hha I, Hinf and Mbo_{II} pieces, 580 from the Hind III-S1 plus Bam HI-S1 pieces. The difference is too large to be accounted for by errors of measurement. No significant change in the observed size of the Bam HI₃-att piece was seen on increasing the amount of S1 nuclease twofold or decreasing it fivefold, so digestion of the single-stranded region with S1 was complete. One possibility is that a fragment or fragments have a mobility that does not correspond well to its

Fig. 3 Map of the attachment site region of λ . The sizes of the Hinf fragments form the basis of the map. Digestion of the Hinf fragments individually with Hha I and Mbo_{II} places the Hha I cuts 15 and 80 base pairs from the Hind III cut, the Mbo_{II} cuts 90 base pairs from the Hind III cut and 75 base pairs from the Bam HI cut. Marini and Landy²⁴ have also found a 380 base-pairs long Mbo_{II} piece containing att. The restriction endonucleases Hpa I, Hpa II, Hae II, Hae III, Hind II, Hind III, Bam HI, Sac III and Pst I do not cut within this DNA segment. Filled arrow, solid tail: Hind III; unfilled arrow, Bam HI; filled arrow, dotted tail: Hinf. Lengths of the fragments are given in base pairs.



real length²¹. A more interesting possibility arises from the fact that if a common region of homology^{22,23} is present in the attachment sequences of phage and host, the ends left by S1 in the attachment region will be at the junction between the common homology region and a recognition sequence (Fig. 1). In this case the ends should overlap by the length of the common homology region, so the discrepancy in the values obtained would indicate a common homology region of 20–25 base pairs (Fig. 3).

The position of the site of recombination is shown in Fig. 3. It is thus possible in this way to determine the physical map position of genetically-defined elements in large DNA molecules to within 20 nucleotides.

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- Davidson, N. & Szybalski, W. in *The Bacteriophage Lambda* (ed. Hershey, A. D.), 45–82 (Cold Spring Harbor Laboratory, New York, 1971).
- Ando, T. *Biochim. biophys. Acta* 114, 158–168 (1966).
- Vogt, V. M. *Eur. J. Biochem.* 33, 192–200 (1973).
- Hirsch, H. J. dissertation, Univ. Cologne (1973).
- Haggerty, D. M. & Schleif, R. F. *J. Virol.* 18, 659–663 (1976).
- Allet, B. & Bukhari, A. I. *J. molec. Biol.* 92, 529–540 (1975).
- Murray, K. & Murray, N. E. *J. molec. Biol.* 98, 551–564 (1975).
- Fiandt, M., Hradecna, Z. & Lozeron, H. A. in *The Bacteriophage Lambda* (ed. Hershey, A. D.) 329–354 (Cold Spring Harbor Laboratory, New York, 1971).
- Gottesman, M. E. & Weisberg, R. A. in *The Bacteriophage Lambda* (ed. Hershey, A. D.) 113–138 (Cold Spring Harbor Laboratory, New York, 1971).
- Yarmolinsky, M. B. in *Advances in the Biosciences* 8, 32–67 (Pergamon, Oxford, 1972).
- Echols, H. J. *J. molec. Biol.* 47, 575–583 (1970).
- Guerrini, F. J. *J. molec. Biol.* 46, 523–542 (1969).
- Davis, R. W. & Parkinson, J. J. *J. molec. Biol.* 56, 403–423 (1971).
- So, M., Gill, R. & Falkow, S. *Molec. gen. Genet.* 142, 239–249 (1975).
- Fanning, T. G., Schreier, P. H. & Davies, R. W. *Eur. J. Biochem.* 62, 173–179 (1976).
- Sanger, F., et al. *Nature* 265, 687–695 (1977).
- Wilson, G. A. & Young, F. E. *J. molec. Biol.* 97, 123–125 (1975).
- So, M., Gill, R. & Falkow, S. *Molec. gen. Genet.* 142, 239–249 (1975).
- Thomas, M. & Davis, R. W. *J. molec. Biol.* 91, 315–328 (1975).
- Clewell, D. B. & Helinski, D. R. *Proc. natn. Acad. Sci. U.S.A.* 62, 1159–1166 (1959).
- Maniatis, T., Jeffrey, A. & Kleid, D. G. *Proc. natn. Acad. Sci. U.S.A.* 72, 1184–1188 (1975).
- Zeiger, R. S., Salmon, R., Dingman, C. W. & Peacock, A. C. *Nature new Biol.* 238, 65–68 (1972).
- Signer, E. A. *Rev. Microbiol.* 22, 451–488 (1968).
- Schulman, M. & Gottesman, M. E. *J. molec. Biol.* 81, 461–482 (1973).
- Marini, J. C. & Landy, A. *Virology* 76, 196–209 (1977).
- Blin, N., Gabain, A. V. & Bujard, L. *FEBS Lett.* 53, 84–86 (1975).
- Cohen, S. N., Chang, A. C. Y. & Hsu, L. *Proc. natn. Acad. Sci. U.S.A.* 69, 2110–2114 (1974).

Erratum

In the article 'Direct demonstration of β -globin mRNA in homozygous Ferrara β_0 -thalassaemia patients, *Nature*, 266, 231–234, the author sequence should have read S. Ottolenghi, P. Comi, B. Giglioli, R. Williamson, C. Vullo, L. del Senno and F. Conconi. Figure 3 description line 2 should read Nuclear (a) and cytoplasmic (b) . . .