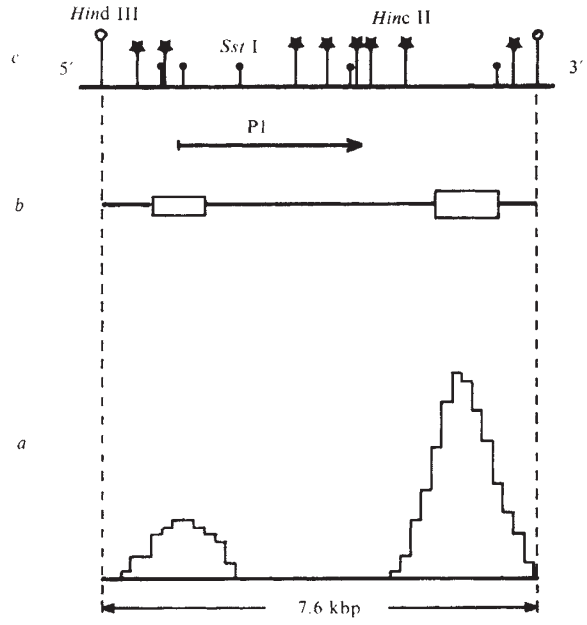

Fig. 3 Partial denaturation of cloned *Drosophila* DNA including the gene for the P1 protein. The DNA of the pBR322 recombinant pDm P1 (ref. 8) was linearized with the *Eco*RI restriction enzyme, denatured as explained in the text in 80% formamide at 24.5 °C, spread for electron microscopy and visualized as explained elsewhere[1]. *a*, Histogram of relative frequency of denaturation of any given segment of DNA, in relation to the ends of the molecule including pBR322 DNA. For higher precision the same measurements were realigned with respect to one of the denaturations in the *Drosophila* DNA and recorded as boxes with a length proportional to the average size of the denatured segment and a width porportional to the frequency of denaturation (*b*). *c*, A partial restriction map taken from refs 7, 8 of the cloned fragment used to position the P1 mRNA sequence.

Three main conclusions may be drawn from this analysis. (1) The fundamental features of A+T-rich linkers as observed in total DNA of chicken, duck, rat, mouse, man and *Drosophila* are found in specific cloned DNA fragments as well. In particular, the average size of the A+T-rich zones, and of the domains separating them, falls within the limits defined previously[1]. Furthermore, the characteristic homogeneous size of isolated linkers on the one hand and clusters of linkers, including A+T-rich linkers of more variable size on the other was also the case in the cloned DNA. (2) The most striking observation may be the clear-cut framing of both the α- and β-globin gene domains by the A+T-rich linkers. (3) The data on *Drosophila* show that A+T-rich linkers may frame individual genes and thus define putative units of gene function. Furthermore, considering recent sequence data of actin[9] and histone[10] genes, it may be the general case that genes or gene domains are placed between A+T-rich zones of the type described here.

Two correlations are of interest. First, the ~15 kbp of the chicken α-globin gene domain, as defined by the A+T-rich linkers, correspond to the maximal size of the transcriptional units found at pre-mRNA level for both the α- and β-globin genes in duck[11]. Recent data[5,12] have confirmed that in mouse and chick, pre-mRNA exists beyond the CAP–poly(A) boundaries. At the 3′ end of the chick $^{A}\alpha$-globin mRNA sequence a further 3 kbp of genomic DNA are co-transcribed[5]; this is about the distance separating, for example, the $^{A}\alpha$ gene from the next A+T-rich linker in the 3′ direction (compare with Fig. 1). Placing the largest (15 kbp) α-globin pre-mRNA reported[11] upstream from this termination point shows that the promoters for these maximal-size transcripts must be in or close to the 5′-framing A+T-rich linker. Second, the mapping of DNase hypersensitive sites, methylation sites and areas of transcriptional activity[5] also reveals correlations with the A+T-rich linker map given in Fig. 1 (see dotted lines and bold arrows). In the α-gene domain, the 3′-hypersensitive sites almost coincide with the corresponding A+T-rich linkers, and most of the methylated *Msp*I sites map within the same A+T-rich linker areas. A region of high DNase resistance correlates with the area immediately to the left of the A+T-rich linker which borders the 5′ end of the β-globin gene domain (dashed line in Fig. 1).

The present data confirm that the A+T-rich linkers are general elements of long-range DNA organization. Furthermore, the clearcut definition of the α- and β-globin gene domains and of the *Drosophila* P1 gene by these linkers suggests that they may have a role as organizational features defining domains of gene function. It is evident that DNA serves multiple functions, not all of which are directly involved in protein synthesis or transcription. The A+T-rich linkers, occurring outside the coding and transcribed areas, might also be involved in DNA functional organization at the chromosome/genome level.

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1. Moreau, J., Matyash-Smirniaguina, L. & Scherrer, K. *Proc. natn. Acad. Sci. U.S.A.* **78,** 1341–1345 (1981).
2. Dodgson, J. B., Strommer, J. & Engel, J. D. *Cell* **17,** 879–887 (1979).
3. Dolan, M., Sugamman, B. J., Dodgson, J. B. & Engel, J. D. *Cell* **24,** 667–677 (1981).
4. Engel, J. D. & Dodgson, J. B. *Proc. natn. Acad. Sci. U.S.A.* **77,** 2596–2600 (1980).
5. Weintraub, M., Larsen, A. & Groudine, M. *Cell* **24,** 333–344 (1981).
6. Lepesant, J.-A., Garen, A., Kejzlarova-Lepesant, J., Maschat, F. & Rat, L. *ICN-UCLA Symp.* Vol. 14 (eds Maniatis, T. & Axel, R.) (Academic, New York, 1979).
7. Lepesant, J.-A. *et al. Molec. appl. Genet.* (in the press).
8. Maschat, F. thesis, Univ. Paris VII (1981).
9. Firtel, R. A., Timm, R., Kimmel, A. R. & McKeow, M. *Proc. natn. Acad. Sci. U.S.A.* **76,** 6206–6210 (1979).
10. Grosschedl, R. & Birnstiel, M. L. *Proc. natn. Acad. Sci. U.S.A.* **77,** 7102–7106 (1981).
11. Reynaud, C.-A., Imaizumi-Scherrer, M.-T. & Scherrer, K. *J. molec. Biol.* **140,** 481–504 (1980).
12. Hofer, E. & Darnell, J. E. Jr *Cell* **23,** 585–593 (1981).

Errata

In the article 'Palaeontological documentation of speciation in Cenozoic molluscs from Turkana Basin' by P. G. Williamson, *Nature* **293,** 437–443 (1981), in Fig. 3 the top left principal components plot should be labelled '*A*', the top right '*B*', bottom left '*C*' and bottom right '*D*'. In the legend references to parts *a*–*d* of the figure should refer to the corresponding upper case.

In the letter 'Autoregulation of androgen production in a primary culture of rat testicular cells', *Nature* **293,** 737–738 (1981), the name of the second author was misspelt; the authors' names should read 'Eli Y. Adashi & Aaron J. W. Hsueh'.

In the article 'Glucocorticoids regulate expression of dihydrofolate reductase cDNA in mouse mammary tumour virus chimaeric plasmids' by F. Lee *et al.*, *Nature* **294,** 228–232 (1981), the first sub-heading on page 232 should read 'Mapping the 5′ end(s) of MMTV-*dhfr* RNA'.

Corrigenda

In the letter 'Immune (γ) interferon produced by a human T-lymphoblast cell line' by I. Nathan *et al.*, *Nature* **292,** 842–84 (1981), some of the reported interferon titres are inaccurate. A commercial interferon standard was used in many of the experiments. This preparation was checked against NIH human leukocyte standard; however, some of the commercial preparations used as laboratory standards were subsequently found to be defective, leading to an overestimation of interferon titres of approximately tenfold.

In the letter 'Expression of a human gene for interferon in yeast' by R. A. Hitzman *et al.*, *Nature* **293,** 717–722 (1981), refs 10 and 18 should read:

10. Faye, G., Leung, D. W., Tatchell, K., Hall, B. D. & Smith, M. *Proc. natn. Acad. Sci. U.S.A.* **78,** 2258–2262 (1981).
18. Staehelin, T., Hobbs, D. S., Kung, H., Lai, C. & Pestka, S. *J. biol. Chem.* **256,** 9750–9754 (1981).