



What then is the function of nuclear speckles? They could be sites for storage of splicing factors, or more simply sites where excess splicing factors accumulate, as indicated in a study of *Drosophila* polytene nuclei²⁸. It has been shown in yeast that splicing factors are present in large functional excess²⁹.

The approach described here can be extended to other genes in order to provide high spatial and temporal resolution of the transcription and processing of its pre-mRNA. The precise targeting of fluorochrome-labelled oligonucleotide probes to different regions of a large transcript, and the exact superimposition of these images by digital imaging microscopy, will allow a correlation of biochemical and structural events in the early life of an mRNA. □

Received 22 July; accepted 10 November 1994.

1. Spector, D. L. *Proc. natn. Acad. Sci. U.S.A.* **87**, 147–151 (1990).
2. Fu, X. D. & Maniatis, T. *Nature* **343**, 437–441 (1990).
3. Spector, D. L. *A. Rev. Cell Biol.* **9**, 265–315 (1993).
4. Xing, Y. & Lawrence, J. B. *Trends Cell Biol.* **3**, 346–353 (1993).
5. Rosbash, M. & Singer, R. H. *Cell* **75**, 399–401 (1993).
6. Carter, K. C., Taneja, K. L. & Lawrence, J. B. *J. Cell Biol.* **115**, 1191–1202 (1991).
7. Spector, D. L., Fu, X. D. & Maniatis, T. *EMBO J.* **10**, 3467–3481 (1991).
8. Huang, S. & Spector, D. L. *Genes Dev.* **5**, 2288–2302 (1991).
9. Xing, Y., Johnson, C. V., Dobner, P. R. & Lawrence, J. B. *Science* **259**, 1326–1330 (1993).
10. Sass, H. & Pederson, T. *J. molec. Biol.* **180**, 911–926 (1984).
11. Beyer, A. L. & Osheim, Y. N. *Genes Dev.* **2**, 754–765 (1988).
12. Vazquez-Nin, G. H., Echeverria, O. M., Fakan, S., Leser, G. & Martin, T. E. *Chromosoma* **99**, 44–51 (1990).

FIG. 4 Localizing sites of endogenous β -actin pre-mRNA splicing. **A**, Spatial correlation of unspliced and spliced β -actin RNAs. *In situ* hybridization signals detected using intron (a) and splice-junction (b) probes. (c), Overlay. **B**, Distribution of β -actin RNA relative to intranuclear speckles. Distributions of actively transcribed β -actin RNA (actin) relative to intranuclear speckles (SC35) in five representative cells. Nuclear β -actin RNA signals are indicated by arrows.

METHODS. Oligonucleotide probes contained 24 nucleotides complementary to actin sequence and 18 nucleotides of nonspecific sequence added to increase the fluorochromes. Intron-specific probes: IN1, 5'-GTCCCTGTGCAGAGAAAGCGCCCT-3'; IN2, 5'-CACGGCTAAGTGTGCTGGGGTCTT-3'; IN3, 5'-ATGAGGGCAGGACTTAGCTCCAC-3'; IN4, 5'-CTGACCTGCCAGGTCAGCTCAGG-3' complementary to the regions of 1,088–1,111, 1,744–1,768, 2,354–2,377 and 2,587–2,610. Splice-junction probes: SJ1, 5'-CACCATCACGCC/CTGGTGCCTGGG-3'; SJ2, 5'-CTCAAACATGAT/CTGGGTCATCTT-3'; SJ3, 5'-GGACTCCATGCC/CAGGAAGGAGG-3'; and SJ4, 5'-AGGAGCAATGAT/CTTGATCTTCAT-3' complementary to 1,028–1,039/1,074–1,085, 1,401–1,412/1,854–1,865, 2,281–2,292/2,388–2,399 and 2,559–2,570/2,683–2,694. Nonspecific sequences were: 5'-TTGCTTGCTTGCTTGCTT-3'. Morphometric analysis of nuclei was done on photographic images of optical sections from ten representative cells using a combined Image-Lab and Image-Measure program (Micro-Science, Inc.). The speckles occupied $31 \pm 7\%$ of the nucleoplasmic area (excluding nucleoli). Of ten β -actin RNA signals, three coincided with nuclear speckles and one was in contact.

13. Wu, Z., Murphy, C., Callan, H. G. & Gall, J. G. *J. Cell Biol.* **113**, 465–483 (1991).
14. Aebi, M. & Weissman, C. *Trends Genet.* **3**, 102–107 (1987).
15. LeMaire, M. F. & Thummel, C. S. *Molec. cell. Biol.* **10**, 6059–6063 (1990).
16. Baurén, G. & Wieslander, L. *Cell* **76**, 183–192 (1994).
17. O'Farrell, P. H., Edgar, B. A., Lakich, D. & Lehner, C. F. *Science* **246**, 635–640 (1989).
18. Shermoen, A. W. & O'Farrell, P. H. *Cell* **67**, 303–310 (1991).
19. Lawrence, J. B., Singer, R. H. & Marselle, L. M. *Cell* **57**, 493–502 (1989).
20. Valcarcel, J., Singh, R., Zamore, P. D. & Green, M. R. *Nature* **362**, 171–175 (1993).
21. Turner, B. M. & Franchi, L. *J. Cell Sci.* **87**, 269–282 (1987).
22. Voelkerding, K. & Klessig, D. F. *J. Virol.* **60**, 353–362 (1986).
23. Bridge, E., Carmo-Fonseca, M., Lamond, A. I. & Pettersson, U. J. *Virology* **67**, 5792–5802 (1993).
24. Wansink, D. G. et al. *J. Cell Biol.* **122**, 283–293 (1993).
25. Jackson, D. A., Hassan, A. B., Errington, R. J. & Cook, P. R. *EMBO J.* **12**, 1059–1065 (1993).
26. Fakan, S., Leser, G. & Martin, T. E. *J. Cell Biol.* **98**, 358–363 (1984).
27. Jiménez-García, L. F. & Spector, D. L. *Cell* **73**, 47–59 (1993).
28. Zachar, Z., Kramer, J., Mims, I. P. & Bingham, P. M. *J. Cell Biol.* **121**, 729–742 (1993).
29. Séraphin, B. & Rosbash, M. *Cell* **59**, 349–358 (1989).
30. Taneja, K. L., Lifshitz, L. M., Fay, F. S. & Singer, R. H. *J. Cell Biol.* **119**, 1245–1260 (1992).

ACKNOWLEDGEMENTS. We thank B. M. Turner for anti-3C5, J. A. Steitz for anti-Sm, X. D. Fu for anti-SC35, and A. J. Levine and T. Linne for anti-DBP antibodies; A. Femino for help with detection of the β -actin RNA; X.-c. Zhu for flanking regions of the human β -actin gene; and R. Singh, J. Valcarcel and M. Zapp for comments on the manuscript. This work was made possible by the UMMC Biomedical Imaging Facility and was supported by NIH grants to M.R.G. and to R.H.S.

ERRATUM

Signal transduction and regulation in smooth muscle

Andrew P. Somlyo & Avril V. Somlyo

Nature **372**, 231–236 (1994)

IN the UK edition of *Nature*, Figs 1 and 2 of this Review Article were accidentally transposed during the production process. □

PLEASE follow these guidelines so that your manuscript may be handled expeditiously.

Nature is an international journal covering all the sciences. Contributors should therefore bear in mind those readers who work in other fields and those for whom English is a second language, and write clearly and simply, avoiding unnecessary technical terminology. Space in the journal is limited, making competition for publication severe. Brevity is highly valued. One printed page of *Nature*, without display items, contains about 1,300 words.

Manuscripts are selected for publication according to editorial assessment of their suitability and reports from independent referees. They can be sent to London or Washington and should be addressed to the Editor. Manuscripts may be dealt with in either office, depending on the subject matter, and will where necessary be sent between offices by overnight courier. High priority cannot be given to pre-submission enquiries; in urgent cases they can be made in the form of a one-page fax. All manuscripts are acknowledged on receipt but fewer than half are sent for review. Those that are not reviewed are returned as rapidly as possible so that they may be submitted elsewhere without delay. Contributors may suggest reviewers; limited requests for the exclusion of specific reviewers are usually heeded. Manuscripts are usually sent to two or three reviewers, chosen for their expertise rather than their geographical location. Manuscripts accepted for publication are processed from the London office.

Nature requests authors to deposit sequence and crystallographic data in the databases that exist for this purpose.

Once a manuscript is accepted for publication, contributors will receive proofs in about 4 weeks. *Nature's* staff will edit manuscripts with a view to brevity and clarity, so contributors should check proofs carefully. Manuscripts are generally published 2–3 weeks after receipt of corrected proofs. *Nature* does not exact page charges. Contributors receive a reprint order form with their proofs; reprint orders are processed after the manuscript is published and payment received.

Categories of paper

Review Articles survey recent developments in a field. Most are commissioned but suggestions are welcome in the form of a one-page synopsis addressed to the Reviews Coordinator. Length is negotiable in advance.

Progress articles review particularly topical developments for a nonspecialist readership. They do not exceed 4 pages in length. Suggestions may be made to the Reviews Coordinator in the form of a brief synopsis.

Articles are research reports whose conclusions are of general interest and which are sufficiently rounded to be a substantial advance in understanding. They should not have more than 3,000 words of text (not including figure legends) or more than six display items and should not occupy more than five pages of *Nature*.

Articles start with a heading of 50–80 words written to advertise their content in general terms, to which editors will pay particular attention. The heading does not usually contain numbers, abbreviations or measurements. The introduction to the study is contained in the first two or three paragraphs of the article, which also briefly summarize its results and implications. Articles have fewer than 50 references and may contain a few short subheadings.

Letters to Nature are short reports of outstanding novel findings whose implications are general and important enough to be of interest to those outside the field. Letters should have 1,000 or fewer words of text and four or fewer display items. The first paragraph describes, in not more than 150 words and without the use of abbreviations, the background, rationale and chief conclusions of the study for the particular benefit of non-specialist readers. Letters do not have subheadings and contain fewer than 30 references.

Commentary articles deal with issues in, or arising from, research that are also of interest to readers outside research.

News and Views articles inform nonspecialist readers about new scientific advances, sometimes in the form of a conference report. Most are commissioned but proposals can be made in advance to the News and Views Editor.

Scientific Correspondence is for discussion of topical scientific matters, including those published in *Nature*, and for miscellaneous contributions. Priority is given to letters of fewer than 500 words.

Preparation of manuscripts

All manuscripts should be typed, double-spaced, on one side of the paper only. An original and four copies are required, each accompanied by artwork. If photographs are included, five sets of originals are required; for line drawings, one set of originals and four good-quality photocopies are acceptable. Reference lists, figure legends and tables should all be on separate sheets, all of which should be double-spaced and numbered. Three copies of relevant manuscripts in press or submitted for publication elsewhere should be included with submitted manuscripts, clearly marked as such. Five copies of revised and resubmitted manuscripts, labelled with their manuscript numbers, are required, together with five copies of a letter detailing the changes made.

Titles are brief and simple. Active verbs, numerical values, abbreviations and punctuation are to be avoided. Titles should contain one or two key words for indexing purposes.

Artwork should be marked individually and clearly with the author's name and, when known, the manuscript number. Ideally, no figure should be larger than 28 by 22 cm. Figures with several parts are to be avoided and are permitted only if the parts are closely related, either experimentally or logically. Unlettered originals of photographs should be provided. Suggestions for cover illustrations, with captions and labelled with the manuscript number, are welcome. Original artwork is returned when a manuscript cannot be published.

Protein/nucleotide sequences should ideally be in the three-letter and not the single-letter code for amino acids. One column width of *Nature* can accommodate 20 amino acids or 60 base pairs.

Colour artwork. A charge of £500 per page is made as a contribution towards the cost of reproducing colour figures. Inability to pay these costs will not prevent publication of essential colour figures if the circumstances are explained. Proofs of colour artwork may be sent to contributors under separate cover from their galley proofs.

Figure legends should not exceed 300 words and ideally should be shorter. The figure is described first, then, briefly, the method. Reference to a method published elsewhere is preferable to a full description. Methods are not described in the text.

References are numbered sequentially as they appear in the text, followed by those in tables and finally by those in figure legends. Only papers published or in the press are numbered and included in the reference list. All other forms of reference should be cited in the text as a personal communication, manuscript submitted or in preparation. Text is not included in reference lists. References are abbreviated according to the *World List of Scientific Periodicals* (Butterworths, London, 1963–65). The first and last page numbers are included; reference to books includes publisher, place and date.

Abbreviations, symbols, units and Greek letters should be identified the first time they are used. Acronyms should be avoided whenever possible and, if used, defined. Footnotes are not used in the text.

Acknowledgements are brief and appear after the reference list; grant and contribution numbers are not allowed.

Supplementary information is material relevant to Articles or Letters which cannot, for lack of space, be published in full, but which is available from *Nature* on request.

Submission. Manuscripts can be sent to the Editor at 4 Little Essex Street, London WC2R 3LF, UK or at 1234 National Press Building, Washington, DC 20045, USA. A telephone and fax number should be included. Manuscripts or proofs sent by air courier to London should be declared as 'manuscripts' and 'value \$5' to prevent the imposition of import duty and value-added tax.