localized inputs from hydrothermal (in the Pacific deep waters) or eolian (surface Indian Ocean waters) origin. The possibility cannot be discounted that the difference is caused by an experimental artefact, perhaps as a result of organic trace metal speciation. For instance, it is possible that the radioactive tracer[3] that was added to samples before Pt determination by GF-AAS, to verify the accumulation efficiency of the anion-exchange resin, did not reach equilibrium with organically complexed Pt. This is unlikely, as the samples were acidified to low pH; nevertheless, very stable metal-organic complexes such as of Cu and Ni occur in sea water[13,14], and a small amount of organically complexed copper is stable in acidified samples[15]. Furthermore, it is not impossible that complexation of Pt(II) by natural ligands is much stronger than with Cu(II) or Ni(II) if we consider the high value for α_{Pt} in sea water and the large shift in the reduction potential (>1 V, equivalent to a value for log $\alpha_{Pt\text{-formazine}} > 30$) on complexation of Pt(II) by formazone before voltammetric analysis[1]. Such organic complexing material, if present, should have been removed in the ultraviolet-photolysis step and would therefore not interfere with the voltammetric determination of Pt.

The interesting chemistry of platinum in the oceans should be investigated further if indeed the redox properties of Pt(IV)/Pt(II) and the strong complexation of Pt(II) can account for the observed differences in the Pt concentrations in the Pacfic and Indian oceans. □

Received 26 September 1988; accepted 2 February 1989.

1. van den Berg, C. M. G. & Jacinto, G. S. *Analytica chim. Acta* **211,** 129–139 (1988).
2. Hodge, V., Stallard, M., Koide, M. & Goldberg, E. D. *Earth planet. Sci. Lett.* **72,** 158–162 (1985).
3. Hodge, V., Stallard, M., Koide, M. & Goldberg, E. D. *Analyt. Chem.* **58,** 616–620 (1986).
4. Goldberg, E. D. *Pure appl. Chem.* **59,** 565–571 (1987).
5. Elderfield, H. & Bertram, C. J. Report on RRS *Charles Darwin* Cruise 15/86, Western Indian Ocean (1986).
6. Morley, N. H. & Statham, P. *Adv. underwat. tech. Ocean Sci. Offshore Eng.* **16,** 283–289 (1988).
7. Govett, G. J. S. *Handbook of Exploration Geochemistry* Vol. 3 (Elsevier, Amsterdam, 1983).
8. Elding, L. I. *Inorg. chim. Acta* **6,** 647–651 (1972).
9. Ringbom, A. & Still, E. *Analytica chim. Acta* **59,** 143–146 (1972).
10. Turner, D. R., Whitfield, M. & Dickson, A. G. *Geochim. cosmochim. Acta* **45,** 855–882 (1981).
11. Milazzo, G. & Caroli, S. *Tables of Standard Electrode Potentials* 376–383 (J. Wiley & Sons, Chichester, 1978).
12. Zika, R. G., Saltzman, E. S. & Cooper, W. J. *Mar. Chem.* **17,** 265–275 (1985).
13. van den Berg, C. M. G. & Nimmo, M. *Sci. tot. Envir.* **60,** 185–195 (1987).
14. Buckley, P. J. M & van den Berg, C. M. G. *Mar. Chem.* **19,** 281–296 (1986).
15. Kremling, K., Wenck, A. & Osterroht, C. *Mar. Chem.* **10,** 209–219 (1981).

ACKNOWLEDGEMENTS. We thank the captain and crew of RRS *Charles Darwin* for their help during the Western Indian Ocean cruise 15/86, J. D. Burton, N. H. Morley and P. Statham for permission to use their manganese data before publication and H. Elderfield and J. D. Burton for participation in the cruise. G.S.J. was supported by a fellowship from the United Nations Development Programme and the University of the Philippines.

Oscillatory responses in cat visual cortex exhibit inter-columnar synchronization which reflects global stimulus properties

Charles M. Gray, Peter König, Andreas K. Engel & Wolf Singer

Max-Planck-Institute for Brain Research, Deutschordenstrasse 46, D-6000 Frankfurt am Main 71, FRG

A FUNDAMENTAL step in visual pattern recognition is the establishment of relations between spatially separate features. Recently, we have shown that neurons in the cat visual cortex have oscillatory responses in the range 40–60 Hz (refs 1, 2) which occur in synchrony for cells in a functional column and are tightly correlated with a local oscillatory field potential. This led us to hypothesize that the synchronization of oscillatory responses of spatially distributed, feature selective cells might be a way to establish relations between features in different parts of the visual field[2,3]. In support of this hypothesis, we demonstrate here that neurons in spatially separate columns can synchronize their oscillatory responses. The synchronization has, on average, no phase difference, depends on the spatial separation and the orientation preference of the cells and is influenced by global stimulus properties.

We recorded multi-unit responses to appropriately oriented moving light bars simultaneously from 5 to 7 spatially separate sites in cortical area 17 of 13 adult cats. To determine the temporal relationship of the firing patterns recorded at two sites, we computed both the auto- and cross-correlation functions of the spike trains[4,5]. For 132 of 199 recording sites, the auto-correlation function of the responses was periodic, indicating that the neuronal responses were oscillatory. To establish an objective criterion for the occurrence of oscillatory responses, we fitted a damped sine wave (Gabor function) to the auto-correlograms. Responses were considered to be oscillatory when the fitted function had at least three peaks and when the amplitude of the sinusoidal modulation was significantly different from zero ($P < 0.05$) and exceeded 10% of the amplitude of the cross-correlogram recomputed after shuffling the trial sequence by one stimulus period. The frequency of these oscillatory responses ranged from 40 to 60 Hz (mean, 50 ± 6 Hz), was similar for different recording sites in the same animal and depended only slightly on stimulus configuration (orientation, direction)[2]. Of these 132 recordings, we selected 99 pairs in which oscillatory responses occurred simultaneously at two sites, and used these in cross-correlation analysis. Applying the same criteria used for auto-correlograms, 51 of the cross-correlograms had a significant correlation between the oscillatory responses.

Figure 1 illustrates a typical case in which neuronal responses were oscillatory and synchronized across spatially separate columns. Responses were recorded from five closely spaced sites near the representation of the area centralis of the retina. The receptive fields were overlapping but had different orientation preferences at adjacent sites. Stimulation with a light bar of 112° orientation evoked vigorous responses at sites 1, 3 and 5 but not at sites 2 and 4. As indicated by the periodic modulations of both auto- and cross-correlation functions, these responses were oscillatory and the oscillations were tightly correlated with zero phase difference. Changing the orientation of the stimulus to 22°, to maximize activation of the units at sites 2 and 4 produced synchronized oscillatory responses at these sites (data not shown). In all cases the correlations were abolished in the shuffled cross-correlogram[4–11].

When the recording sites had a larger spatial separation (>2 mm) the receptive fields were non-overlapping and could be stimulated independently. This enabled us to activate the

TABLE 1 Correlated oscillatory neuronal responses in area 17 as a function of spatial separation of recording sites and angular difference in preferred stimulus orientation

Angular difference of preferred orientation	Spatial separation 0.4–2.0 mm (overlapping fields)	Spatial separation 2.0–7.0 mm (non-overlapping fields)
0–22°	90% (28/31)	54% (7/13)
45°	73% (8/11)	0% (0/8)
67–90°	44% (7/16)	25% (1/4)

Data were taken from a total of 99 cross-correlograms in which simultaneous oscillatory responses were recorded from two electrodes in area 17. Correlograms computed for responses at sites separated by 8–12 mm ($n = 16$) were excluded. The correlograms were classified into six categories based on the difference in orientation preference of the neurons at the two recording sites and whether or not the receptive fields were overlapping. The results are presented as the percentage of recordings showing oscillatory correlations. The numbers in parentheses correspond to the number of oscillatory correlations and the total number of response pairs analysed for that category, respectively. The correlograms which showed no periodic modulation (48 out of 99) showed either a single peak centred around a 0 ms time delay ($n = 11$) or a flat distribution ($n = 37$).

units at each site even if their preferred orientations differed and to determine more precisely if the extent of correlations depended on the similarity of orientation preferences. Figure 2 illustrates the typical case where oscillatory responses in remote columns were synchronized if their orientation preferences were similar but showed no fixed phase relationship when the orientation preferences differed.

In two individuals we recorded at two sites separated by 7 mm in which the receptive fields were non-overlapping, had the same orientation preference and were aligned colinearly. This enabled us to co-activate the units at both recording sites with a single long light bar, as well as with two short, independently moving stimuli (Fig. 3). In both cases, the stimuli evoked oscillatory responses at each site. When the short light bars were moved in opposite directions over the two receptive fields, the respective responses showed no phase locking. When the two stimuli were moved in the same direction, however, the oscillations became weakly synchronized and this synchronization was markedly enhanced in each case when the responses were evoked with a single long light bar that co-stimulated the two receptive fields. This suggests that synchronization depends on global features of the stimuli such as coherent motion and continuity, which are not reflected by the local responses alone.

The probability for the occurrence of phase locking depended both on the distance between recording sites and on the angular difference between preferred stimulus orientations (Table 1). There was no phase locking of the oscillatory responses when the electrodes were separated by 7–12 mm ($n = 16$). At intermediate distances of 2–7 mm, when the receptive fields of the recorded neurons were non-overlapping, phase locking occurred mainly between neuronal groups with similar orientation preferences. The same trend was observed for more closely spaced neurons (0.4–2.0 mm), which had overlapping receptive fields but in these cases phase locking was also observed for cells with different orientation preferences. Phase locking of oscillatory responses typically occurred with a phase difference of 0 ms (32 out of 51) and the phase difference rarely exceeded ±3 ms.

Our auto-correlation data confirm that the responses of a large fraction of cortical neurons are oscillatory and that these oscillations are synchronous for cells that are close enough together to be recorded with a single electrode[1,2]. Thus, we could take advantage of multi-unit recordings for the cross-correlation analysis, considerably increasing the number of events per unit time and allowing us to confine the analysis to short epochs. Correlations between the firing probabilities of neurons in the visual cortex have been described previously[6–12] and shown to be dependent on orientation preference[6,9] but only one study has provided evidence for oscillatory correlograms[11]. This relative lack of evidence for oscillatory responses in the cortex has several possible explanations. First, only a fraction of cortical neurons have oscillatory responses[2]; second, averaging procedures mask the oscillations because they are not phase-locked to the stimulus[2]; and third, previous studies may have excluded oscillatory activity because cross-correlograms of rhythmic responses were interpreted as misleading[6,12].

The system of tangential intracortical connections[13–19], or the reciprocal projections from other cortical areas[20] may provide the anatomical substrate for the synchronization of oscillatory responses between remote columns. Common input from subcortical structures can be excluded because collaterals of geniculate afferents do not span sufficiently large distances and do not have oscillatory responses in this frequency range[1,2].

We propose that the synchronization of oscillatory responses in spatially separate regions of the cortex may be used to establish a transient relationship between common but spatially distributed features of a pattern[21]. Our data show that synchronization is sensitive to global features of stimuli such as continuity, similarity of orientation and coherency of motion. Synchronization may therefore serve as a mechanism for the extraction and representation of global and coherent features

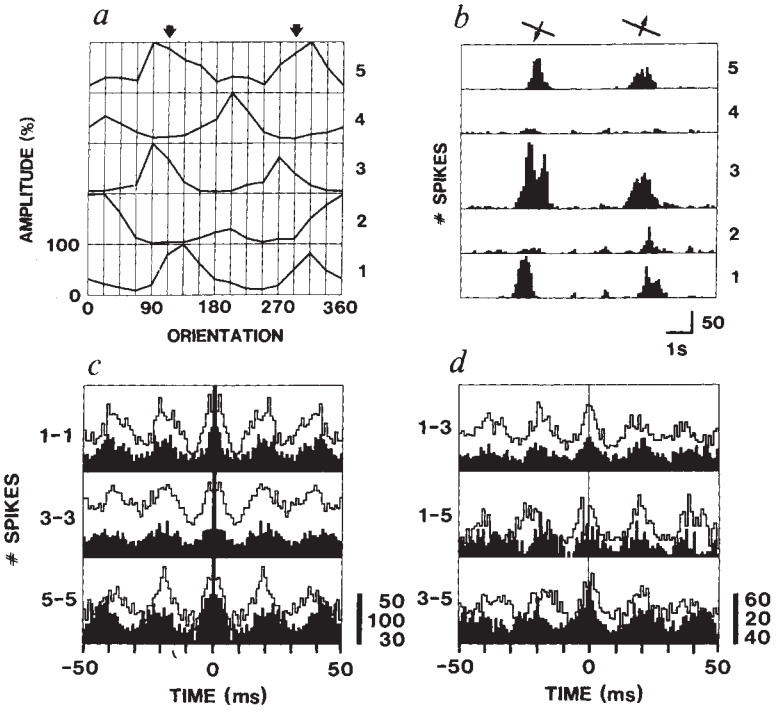

FIG. 1 Orientation-specific intercolumnar synchronization of oscillatory neuronal responses in area 17 of an adult cat. *a*, Normalized orientation tuning curves of the neuronal responses recorded from five electrodes spaced 400 μm apart and centred on the representation of the area centralis. Response amplitudes (ordinate) to stimuli of different orientations (abscissa) are expressed as a percentage of the maximum response for each electrode. The arrows indicate the stimulus orientation (112°) at which the responses were recorded in *b*, *c* and *d*. *b*, Post-stimulus time histograms recorded simultaneously from the same five electrodes at an orientation of 112°. Note the small difference in the latencies of the responses indicating overlapping but slightly offset receptive field locations. *c*, Auto-correlograms of the responses recorded at sites 1 (1–1), 3 (3–3) and 5 (5–5). *d*, Cross-correlograms computed for the three possible combinations (1–3, 1–5, 3–5) between responses recorded on electrodes 1, 3 and 5. Correlograms computed for the first direction of stimulus movement are displayed with unfilled bars with the exception of comparison 1–5 in *d*.

METHODS. Adult cats were prepared for acute physiological recordings from the visual cortex using standard procedures[2]. Anaesthesia was induced with a short acting anaesthetic (hexobarbital, 15 mg per kg or ketamine, 15 mg per kg) and then supplemented with a mixture of 30% O_2, 70% N_2O and 0.1–0.3% halothane. Multi-unit activity was recorded from an array of 4–6 closely spaced (300–500 μm) platinum–iridium electrodes (25 μm tip diameter) and an additional single electrode that was moved independently. The array was inserted in the vicinity of the representation of the area centralis. The single electrode was positioned anteriorly and advanced down the medial bank of area 17. All receptive field locations were within 15° of the area centralis. Spikes exceeding a threshold of twice the noise level were detected with a window discriminator and digitized with a resolution of 1 ms. All recordings used binocular stimulation after the receptive fields for the two eyes had been aligned using prisms. When neurons recorded from different electrodes had overlapping receptive fields but differing orientation preferences, we used a stimulus orientation that evoked a response at each site of at least half the maximal amplitude. Responses that did not meet this criterion and that did not overlap in time were excluded from the analysis. In the case of non-overlapping receptive fields we applied two independently controllable stimuli. For each trial the stimuli were moved across the receptive fields, at the preferred velocity, in both directions of movement perpendicular to the axis of orientation. Each trial lasted for 10 s and was repeated 10 times.

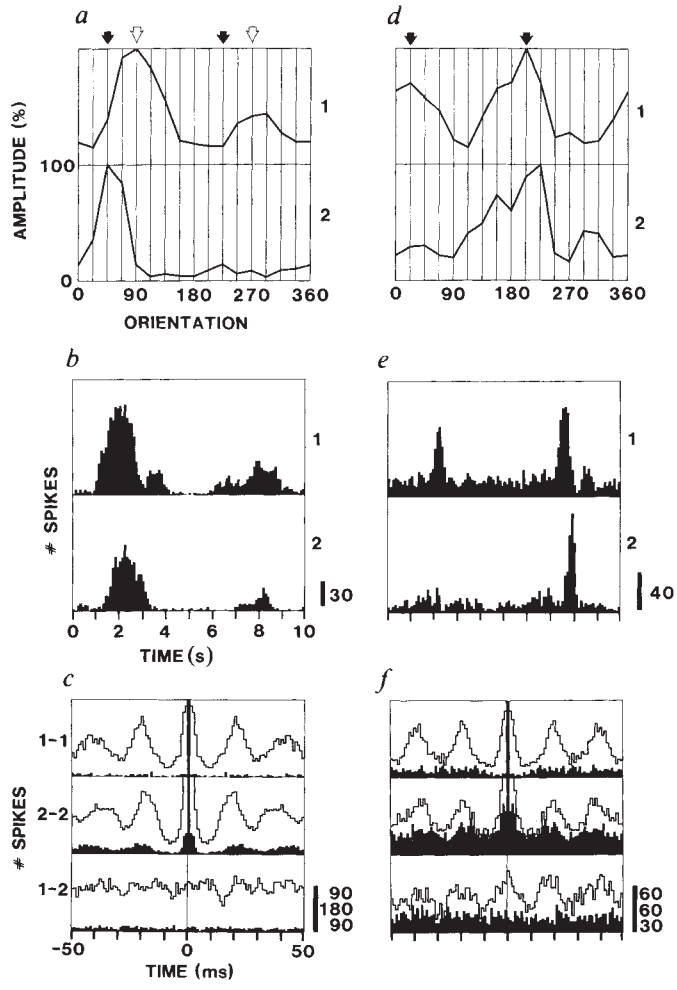

FIG. 2 Long-range inter-columnar synchronization of oscillatory responses depends on the similarity of orientation preference. *a*, Orientation tuning curves of multi-unit responses recorded at two sites (1 and 2) separated by 6 mm in area 17. The neurons had non-overlapping receptive fields and a clear difference in orientation preference of 45° (open and closed arrows). *b*, Post-stimulus time histograms of the responses recorded to stimulation of each receptive field at its own respective optimal orientation (open and closed arrows in *a*). *c*, Auto- (1–1, 2–2) and cross-correlograms (1–2) computed from the neuronal responses recorded from both electrodes revealed that oscillatory responses occurred at both sites but were not correlated. Unfilled bars are for the first direction of stimulus movement. *d*, Orientation tuning curves of multi-unit responses recorded from the same animal at two different cortical sites (1 and 2), separated by 7 mm. The neuronal responses at each site had similar orientation and directional preferences. *e*, Post-stimulus time-histograms of the activity recorded at each site in response to their optimal stimulus orientation of 22° (arrows in *d*). *f*, Auto- (1–1, 2–2) and cross-correlograms (1–2) computed from the neuronal responses recorded on the two electrodes demonstrate oscillatory responses at both sites which were correlated with zero phase difference. Unfilled bars are for the second direction of stimulus movement.

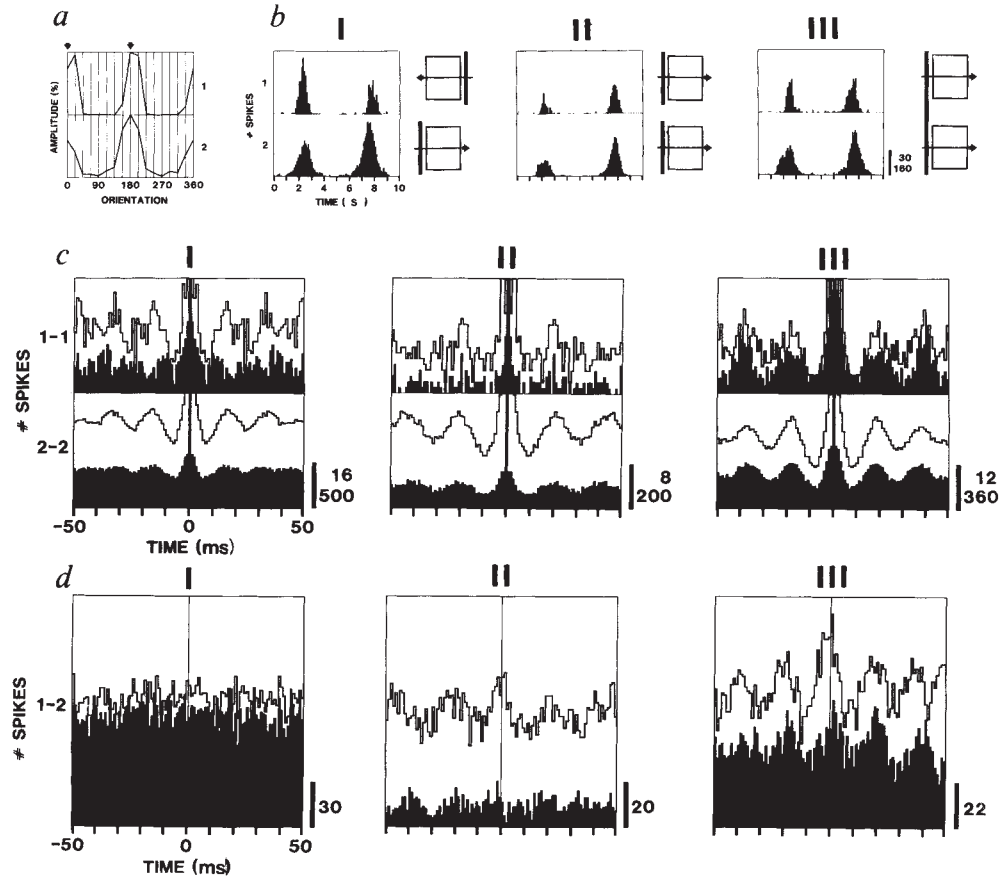

FIG. 3 Long-range oscillatory correlations reflect global stimulus properties. *a*, Orientation tuning curves of neuronal responses recorded from two electrodes (1, 2) separated by 7 mm show a preference for vertical light bars (0 and 180°) at both recording sites. *b*, Post-stimulus time-histograms of the neuronal responses recorded at each site for each of three different stimulus conditions: (I) two light bars moved in opposite directions; (II) two light bars moved in the same direction; and (III) one long light bar moved across both receptive fields. A schematic diagram of the receptive field locations and the stimulus configuration used is displayed to the right of each post-stimulus time histogram. *c*, *d*, Auto-correlograms (*c*, 1–1, 2–2) and cross-correlograms (*d*, 1–2) computed for the neuronal responses at both sites (1 and 2 in *a* and *b*) for each of the three stimulus conditions (I, II, III) displayed in *b*. For each pair of correlograms except the two displayed in *c* (I, 1–1) and *d* (I) the second direction of stimulus movement is shown with unfilled bars.

of a pattern. Such processes are crucial for the analysis of visual scenes and figure-ground segregation[3,22–26]. Synchronization of oscillatory responses may however also have a more general function in cortical processing because it is a powerful mechanism for establishing cell assemblies that are characterized by the phase and the frequency of their coherent oscillations. □

Received 17 October 1988; accepted 3 February 1989.

1. Gray, C. M. & Singer, W. *Soc. Neurosci. Abstr.* **404,** 3 (1987).
2. Gray, C. M. & Singer, W. *Proc. natn. Acad. Sci. U.S.A.* (in the press).
3. von der Malsburg, C. & Singer, W. in *Neurobiology of Neocortex (Proceedings of the Dahlem Conference)* 69–99 (eds Rakiç, P. & Singer, W.) (Wiley, Chichester, 1988).
4. Perkel, D. H., Gerstein, G. L. & Moore, G. P. *Biophys. J.* **7,** 391–418 (1967).
5. Perkel, D. H., Gerstein, G. L. & Moore, G. P. *Biophys. J.* **7,** 419–440 (1967).
6. Tso, D., Gilbert, C. D. & Wiesel, T. N. *J. Neurosci.* **6,** 1160–1170 (1986).
7. Toyama, K., Kimura, M. & Tanaka, K. *J. Neurophys.* **46,** 191–201 (1981).
8. Toyama, K., Kimura, M. & Tanaka, K. *J. Neurophys.* **46,** 202–213 (1981).
9. Michalski, A., Gerstein, G. L., Czarkowska, J. & Tarnecki, R. *Expl Brain Res.* **51,** 97–107 (1983).
10. Aiple, F. & Krüger, J. *Expl Brain Res.* **72,** 141–149 (1988).
11. Krüger, J. *Rev. Physiol. Biochem. Pharmac.* **98,** 177–233 (1983).
12. Hata, Y., Tsumoto, T., Sato, H., Hagihara, K. & Tamura, H. *Nature* **335,** 815–817 (1988).
13. Creutzfeldt, O. D., Garey, L. J., Kuroda, R. & Wolff, J.-R. *Expl Brain Res.* **27,** 419–440 (1977).
14. Gilbert, C. D. & Wiesel, T. N. *Nature* **280,** 120–125 (1979).
15. Rockland, K. S. & Lund, J. *Science* **215,** 1532–1534 (1982).
16. Mitchison, G. & Crick, F. *Proc. natn. Acad. Sci. U.S.A.* **79,** 3661–3665 (1982).
17. Gilbert, C. D. & Wiesel, T. N. *J. Neurosci.* **3,** 1116–1133 (1983).
18. Martin, K. A. C. & Whitteridge, D. *J. Physiol.* **353,** 463–504 (1984).
19. Kisvarday, Z. F. *et al. Expl Brain Res.* **64,** 541–552 (1986).
20. Montero, V. M. *Brain Behav. Evol.* **18,** 194–218 (1981).
21. Barlow, H. B. *Proc. R. Soc.* **B212,** 1–34 (1981).
22. Marr, D. & Poggio, T. *Science* **194,** 283–287 (1976).
23. Julesz, B. *Nature* **290,** 91–97 (1981).
24. Ballard, D. H., Hinton, G. E. & Sejnowski, T. J. *Nature* **306,** 21–26 (1983).
25. von der Malsburg, C. & Schneider, W. *Biol. Cybern* **54,** 29–40 (1986).
26. Nelson, J. I. in *Models of the Visual Cortex* (eds Rose, D. & Dobson, V. G.) 108–122 (Wiley, Chichester, 1985).
27. Gray, C. M. & Singer, W. *Eur. J. Neurosci.* Suppl. 1, 86.4 (1988).
28. Singer, W., Gray, C. M., Engel, A. & König, P. *Soc. Neurosci. Abstr.* **14,** 362.13 (1988).

ACKNOWLEDGEMENTS. The results presented in this study were presented previously in abstract form (refs 27, 28).

Transcripts of one of two *Drosophila* cyclin genes become localized in pole cells during embryogenesis

William G. F. Whitfield*, Cayetano González*, Ernesto Sánchez-Herrero†, & David M. Glover*‡

* Cancer Research Campaign, Eukaryotic Molecular Genetics Research Group, Department of Biochemistry, Imperial College, London SW7 2AZ, UK
† Department of Genetics, University of Cambridge, Downing Street, Cambridge, UK

CYCLINS, originally discovered in the eggs of marine invertebrates, are proteins which undergo dramatic cycles of synthesis followed by degradation at the metaphase–anaphase transition of cell division[1–3]. That they participate in the G_2–M transition is supported by the fact that when synthetic cyclin messenger RNAs from clam and sea urchin are microinjected into the G_2-arrested oocytes of *Xenopus*, they induce maturation[2,4]. The cyclin of fission yeast is the product of the *cdc13* gene, which is known to interact with *cdc2*, a gene required for the entry into mitosis[5–10]. We have cloned the genes that encode A-type and B-type cyclins from *Drosophila melanogaster* by virtue of their sequence similarity to oligonucleotides corresponding to conserved regions of the cyclin genes. We show that both genes encode abundant maternal mRNAs, but whereas the cyclin A mRNA is relatively uniformly distributed before cell formation, the cyclin B mRNA becomes localized to the developing pole cells. In larvae, cyclin A is expressed predominantly in brain and imaginal disks, whereas cyclin B transcripts are abundant in testes.

‡ To whom correspondence should be addressed.

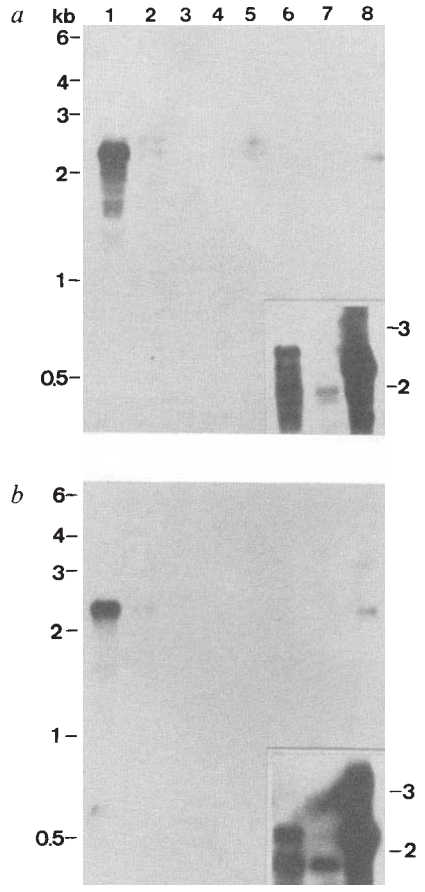

FIG. 1 Developmental northern blots showing the transcripts detected by cDNA clones of cyclins A (*a*) or B (*b*). Poly (A^+) RNA from the following developmental stages was analysed: lane 1, 0–2 h embryos; lane 2, 2–4 h embryos; lane 3, first instar larvae; lane 4, second instar larvae; lane 5, third instar larvae; lane 6, pupae; lane 7, adult males; lane 8, adult females. The autoradiograph shown was exposed for 15 h. The inset in the lower right-hand corner of each autoradiogram is an 80-h (cyclin A) or 60-h (cyclin B) exposure in which only the region containing RNA of ~2-kb from lanes *f–h* is displayed. Filters were reprobed with the *Drosophila ras* gene (*Dmras*64B) (ref. 16) as a control for uniform loading of RNA. The autoradiograph exposures indicated that the cyclin transcripts are 1–2 orders of magnitude more abundant than *ras* RNA in *Drosophila* embryos.

METHODS. An adult female *Drosophila* cDNA library in the bacteriophage vector λgt10 was screened with a ^{32}P-labelled oligonucleotide mixture of sequence: AA(A/G)TA(T/C)GA(A/G)GA(A/G)ATITA(T/C)CC (probe 1). Hybridizations and washings were carried out as recommended by Wood *et al.*[17]. Duplicate filters were screened in parallel with a second oligonucleotide mixture: AT(T/C/A)(C/T)TI(G/A)TIGA(T/C)-TGG(T/C)TIGT (probe 2). Positive plaques were purified by rescreening following the same protocol. The cDNAs fell into two classes: those that hybridized to both probes, and those that hybridized only to probe 1, cyclins A and B, respectively. We isolated three cyclin A cDNAs and four cyclin B cDNAs from $\sim 5 \times 10^4$ recombinant phage in this library. On rescreening, a 0–2 h embryo cDNA library, we isolated both cyclin A and B clones at a frequency of 0.002. The amino-acid sequence corresponding to probe 1 can be recognized within the amino-acid sequence derived from the sequence of the cDNA clones and is shown below in relation to amino acids 249–261 of clam cyclin A[2], and the corresponding regions of sea urchin cyclin[4] and *cdc13* (refs 7 and 8):

Clam A	L	A	A	**K**	**Y**	**E**	**E**	**I**	**Y**	**P**	P	D	V
Sea urchin	I	A	S	**K**	**Y**	**E**	**E**	**M**	**Y**	**P**	P	E	I
*cdc*13	I	A	S	**K**	**Y**	**E**	**E**	**V**	**M**	**C**	P	S	V
Drosophila A	I	A	A	**K**	**Y**	**E**	**E**	**I**	**Y**	**P**	P	E	V
Drosophila B	I	A	T	**K**	**Y**	**E**	**E**	**L**	**F**	**P**	P	A	I

The amino-acid sequence corresponding to probe 2 (in relation to amino-acids 196–208 of clam cyclin A) is as follows:

Clam A	M	R	C	**I**	**L**	**V**	**D**	**W**	**L**	V	E	V	S
Sea urchin	M	R	L	**I**	**L**	**V**	**D**	**W**	**L**	V	Q	V	H
cdc13	M	R	G	**I**	**L**	**T**	**D**	**W**	**L**	I	E	V	H
Drosophila A	M	R	S	**I**	**L**	**I**	**D**	**W**	**L**	V	E	V	S
Drosophila B	M	R	A	**V**	**L**	**I**	**D**	**W**	**I**	N	E	V	H

The cyclin A cDNAs hybridize *in situ* to salivary gland chromosomes at 68E, and thus correspond to a gene that has been independently cloned by Lehner and O'Farrell[18] and Y.-N. Jan (personal communication). The cyclin B gene hybridizes *in situ* to chromosome 2 at 59A. Northern blots using the cloned cDNAs as probes have been described previously[19].