ence between different 5HT treatments with the LTF test ($F_{4,25} = 7.86$; $P < 0.001$). There were no differences with the T1 ($F_{3,29} = 0.93$; $P = 0.44$) and STF ($F_{3,27} = 0.72$; $P = 0.55$) tests.
12. H. Kang and E. M. Schuman, *Science* **273**, 1402 (1996).
13. A factorial ANOVA indicated an overall difference in LTF among groups ($F_{2,12} = 4.99$; $P = 0.027$). Significant STF was expressed in all groups: controls, +154.8 ± 15.5%; synaptic-emetine, +92.9 ± 29.5%; somatic-emetine, +109.7 ± 33.6%; $P < 0.02$ in all cases.
14. The magnitude of coincident LTF in the controls as well as in the somatic-emetine (Fig. 3A) and somatic-emetine (4 to 6 hours) (Fig. 3B) groups is quite comparable [see also (*3*)]. However, the absolute magnitude of LTF in these groups is less than that observed in our initial experiments (Fig. 1). We do not know the source of this variability, but it underscores the importance of having each experimental group compared with its own set of controls (run simultaneously), which was the case in all our experiments.
15. STF: −16.0 ± 2.8%, NS (somatic-emetine); −15.5 ± 2.4%, NS (synaptic-emetine). LTF: −15.8 ± 10.4%, NS (somatic-emetine); −4.0 ± 12.2%, NS (synaptic emetine), paired *t* tests.
16. It is possible that our results reflect a capture-like mechanism [see (*8*)]. For example, if the 25-min 5HT pulse to the somatic compartment induced LTF at SN-INT synapses in the pleural ganglion, the synaptic pulse in the pedal ganglion could be viewed as inducing capture at the remote synapse. If true, this would extend the notion of capture in two ways: (i) in this case, protein synthesis is required immediately at the site of capture, and (ii) there is a tight temporal constraint (15 min) imposed on the induction-capture process occurring at two anatomically remote sites.
17. A. Barzilai, T. E. Kennedy, J. D. Sweatt, E. R. Kandel, *Neuron* **2**, 1577 (1989).
18. A factorial ANOVA showed a significant overall difference among groups ($F_{2,11} = 4.24$; $P = 0.043$).
19. The synaptic compartment (pedal ganglion) contains both the presynaptic SN terminals and postsynaptic MN neurites and somata. Thus the translation-dependent synaptic signal required for LTF induction (Fig. 3A) could be presynaptic, postsynaptic, or both. Distinguishing between pre- and postsynaptic contributions is experimentally feasible in this system [L.-E. Trudeau and V. F. Castellucci, *J. Neurosci.* **5**, 1275 (1995); D. L. Glanzman, *J. Neurobiol.* **25**, 666 (1994)]. Thus we are currently examining the effects of blocking translation in individual SNs and MNs.
20. The length of the connective is 2 to 3 mm, and the estimated rate of fast transport in *Aplysia* neurons is about 1.5 mm/hour [J. D. Gunstream, G. A. Castro, E. T. Walters, *J. Neurosci.* **15**, 439 (1995); R. T. Ambron, R. Schmied, C. C. Huang, M. Smedman, *ibid.* **12**, 2813 (1992)]. Thus communication between synapse and soma requires 40 min to >1 hour by this mechanism.
21. D. B. Jaffe and T. H. Brown, *J. Neurophysiol.* **72**, 471 (1994).
22. D. L. Senger and R. B. Campenot, *J. Cell Biol.* **138**, 411 (1997); R. Stoop and M. Poo, *Science* **267**, 695 (1995); A. Bhattacharyya *et al.*, *J. Neurosci.* **17**, 7007 (1997).
23. In CA1 cells of the hippocampus, the soma is not essential for induction of long-term synaptic plasticity (*12*) [U. Frey, M. Krug, R. Brodemann, K. Reymann, H. Matthies, *Neurosci. Lett.* **97**, 135 (1989)]; however, this does not indicate that the soma is unable to participate in the induction process, especially under conditions of subthreshold activation at remote synaptic sites.
24. Supported by National Institutes of Health grant F32-MH12004 to C.M.S. and National Institute of Mental Health grant RO1MH-14-1083 to T.J.C. We thank E. Kandel, S. McKay, and M. Sutton for helpful comments on a previous draft of this paper.

27 April 1999; accepted 13 August 1999

Shape Representations and Visual Guidance of Saccadic Eye Movements

Tirin Moore

One hallmark of primate vision is that the direction of gaze is constantly shifting to position objects of interest appropriately on the fovea, where visual acuity is greatest. This process must involve the close cooperation of oculomotor and visual recognition mechanisms because visual details must be translated into specific motor commands. This paper describes the correspondence between the presaccadic activity of V4 neurons and the degree of visual guidance of saccadic eye movements to objects of different form. The results suggest that neurons that participate in coding visual stimuli are also involved in guiding the eyes to prominent features of objects.

Because only a small fraction of the primate retina has heightened acuity, the point of fixation must constantly be moved about to allow detailed visual processing of objects of interest within the visual scene. Moreover, this must be done so that each change in gaze places the eye at convenient locations on the target stimulus once the movement is completed. For example, when scanning this text, the reader's eyes must accurately jump from word to word so that when each item is fixated it can be processed rapidly and the next eye movement can be planned. Studies of eye movements during reading have shown that the speed at which subjects scan text is determined partly by where each eye movement places the fovea within words and that for each word there appears to be an optimal landing position for the eye (*1*). To accomplish this requires that each individual eye movement be guided by detailed visual information obtained from locations peripheral to the current point of fixation. During all types of visual scanning, saccadic eye movements of both humans and monkeys follow the detail of visual images to a striking degree (*2*). This fact suggests that visual cortical mechanisms responsible for coding stimulus form are also actively involved in guiding eye movements to salient features of objects.

Most studies of oculomotor mechanisms have ignored the possible role of visually selective neurons in programming eye movement commands. Among the two apparent processing streams within the primate visual cortex (*3*), only the dorsal projecting visual areas, areas in the posterior parietal cortex, have been implicated in oculomotor control. In contrast, ventral visual cortical areas that contain neurons selective for stimulus features, such as color and orientation, have been primarily regarded as passive perceptual mechanisms (*4*). The major reason for this view is that dorsal stream visual areas contain neurons that respond in conjunction with saccadic eye movements and that electrical stimulation of some dorsal areas can evoke eye movements (*5*). There is, however, little evidence of the involvement of ventral stream visual areas in the programming of eye movements.

Extrastriate area V4 is the major source of visual input to the inferior temporal cortex (*6*), the terminus of the ventral stream; thus, neurons within V4 are very sensitive to stimulus form and color (*7*). Neurons within this area are modulated by focal attention in the absence of eye movements (*8*). However, they are also activated in advance of visually guided saccadic eye movements (*9*). The saccade-related activation within this area may merely reflect the fact that shifts in attention typically precede shifts in gaze, but it also may reflect a mechanism by which detailed visual information useful in guiding the eyes to salient features of objects is synchronized with the saccade command. We examined this possibility by studying the correspondence between neural activation preceding eye movements to targets of different form and the metrics of saccadic eye movements.

We recorded the activity of 91 single neurons in extrastriate area V4 of two monkeys (*Macaca mulatta*) performing a visually guided delayed saccade task. In this task, the monkeys were trained to make saccadic eye movements to stable visual stimuli presented within the visual receptive field (RF) of a V4 neuron (*10*). The response of a V4 neuron during the saccade task is shown in Fig. 1A. The responses of the neuron during the first half of each trial are aligned to the onset of

Department of Brain and Cognitive Sciences, Building E-25, Room 634, Massachusetts Institute of Technology, Cambridge, MA 02139, USA.

Present address: Department of Psychology, Princeton University, Princeton, NJ 08544–1010, USA. E-mail: tirin@princeton.edu

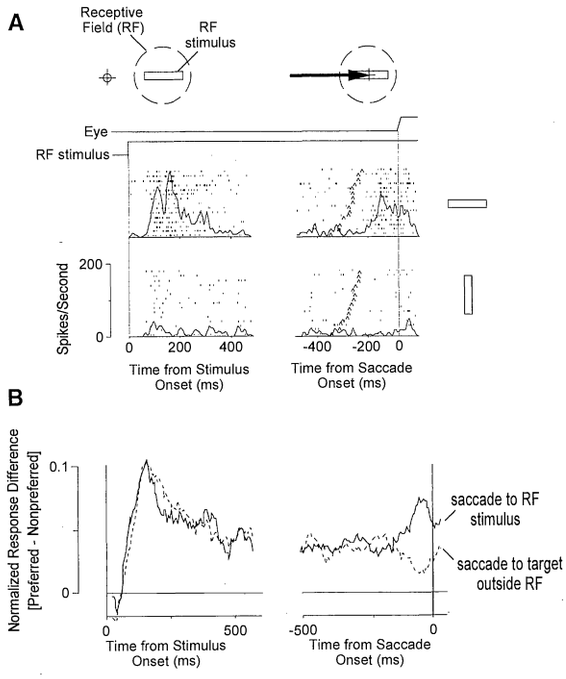

Fig. 1. Response of V4 neurons during the delayed saccade task. (**A**) Responses of a single V4 neuron during delayed saccadic eye movements to an oriented bar stimulus presented within the cell's RF. Each plot shows mean instantaneous firing rate superimposed over spike rasters obtained from individual trials. The cell's activity during the first half of each trial is aligned to the onset of the RF stimulus (left) and during the second half it is aligned to the saccade (right). Cartoon above illustrates the two phases of the trial. In the first half, the point of fixation (+) was on the fixation spot; in the second half, the monkey made a saccade to the RF stimulus (arrow). The saccade-aligned plots were sorted from top to bottom in order of increasing saccade latency and the cue to saccade (offset of the fixation spot) is indicated during each trial (^). (Top) Activity when the bar stimulus was presented at the preferred orientation. (Bottom) Activity when the nonpreferred orientation was presented. In both conditions, the monkey was required to make saccades to the bar stimulus at the end of the trial. When the preferred stimulus was presented, the neuron responded not only at the time of onset but also immediately before the monkey made a saccade to the stimulus. When the bar stimulus was presented at the nonpreferred orientation, the neuron responded at neither time. (**B**) Selectivity profiles of 83 V4 neurons during trials in which monkeys made delayed saccades to oriented stimuli within a cell's RF (solid) or to a target outside the RF (dashed) (*10*). Each response function is the mean difference in the normalized activity between trials in which the preferred and nonpreferred orientation was within the RF (*11*). Both selectivity functions are first aligned to the onset of the stimulus (left) and then to the initiation of the saccade (right). Note that when the saccade is made to the RF stimulus, the orientation selectivity reemerged immediately before the eye movement began. When the saccade was directed to a target outside the RF, the selectivity declined toward zero.

the visual stimulus and in the second half they are aligned to the onset of the saccadic eye movement. When the visual stimulus was presented to the cell's RF at the optimal orientation, the cell responded well at stimulus onset but then quickly adapted. The cell began to respond again just before a saccadic eye movement was made to the RF stimulus. When the least effective orientation was presented, the cell responded neither at the time of onset nor before the eye movement. This response is typical of neurons in area V4 during this task in that many of them respond in advance of saccadic eye movements to the RF and they do so in a way that depends heavily on which stimulus is the target. The temporal dynamics of orientation selectivity from 83 selective neurons recorded in two monkeys performing the delayed saccade task are plotted in Fig. 1B (*11*). The two functions show the response difference between preferred and nonpreferred stimulus trials when the monkey made saccadic eye movements to the RF stimulus or to a target outside the RF. As in Fig. 1A, trials are first aligned to the stimulus onset and then to the onset of the saccadic eye movement. The population response distinguished between preferred and nonpreferred orientations within the first 100 ms of stimulus presentation. This selectivity decayed by more than 50% within 500 ms even though the visual stimulus was still within the RF. Yet when a saccadic eye movement was directed to the RF stimulus, the selectivity increased again and peaked within 50 ms of the onset of the movement. The saccade-aligned selectivity recovered to about 75% of the initial stimulus-aligned selectivity. When an eye movement was directed instead to a target outside the RF, the response selectivity fell toward zero.

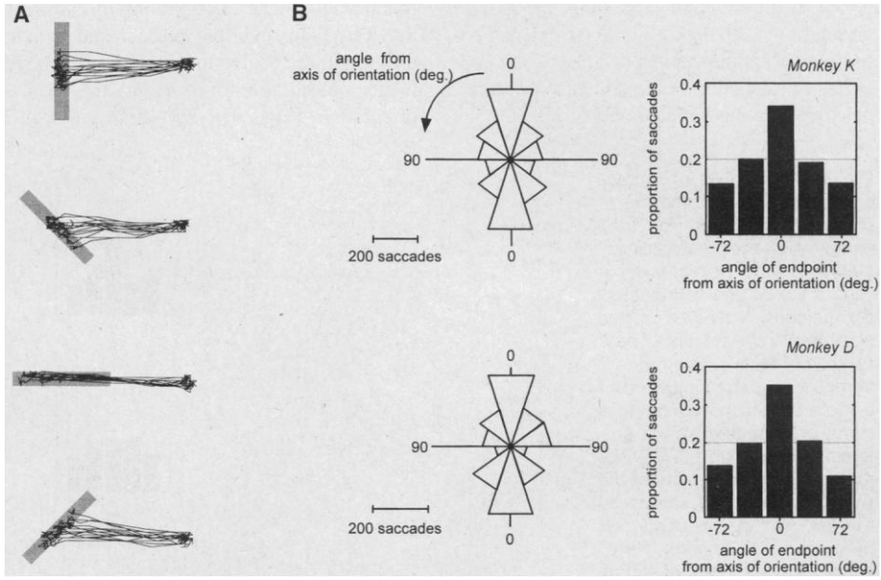

Fig. 2. Spatial distribution of endpoints of saccades made to visual targets varying in orientation. (**A**) Saccades made to oriented bar stimuli during the visually guided delayed saccade task. Individual saccade vectors obtained from a single block of trials (13 trials per orientation) are shown. (**B**) Distribution of saccade endpoints. Polar histograms (left) show angular distributions of saccade endpoints relative to the axis of bar orientation (normalized to vertical; 0); 10 angular bins, 36° per bin. Histograms on the right show the same distributions collapsed across the orthogonal axis of orientation, revealing the greater tendency of saccades to land near the axis of bar orientation (peak at 0). Dotted lines indicate proportions expected within each bin if the distributions are uniform. Observed distributions were significantly different from uniform (monkey K, $\chi^2 = 139$, $P < 0.0001$, $n = 2200$ saccades; monkey D, $\chi^2 = 131$, $P < 0.0001$, $n = 1624$ saccades). Oriented bars varied in size from about 0.1° to 0.3° × 1.0° to 3.0° and were positioned between 2.5° and 10° from the point of fixation.

The presaccadic activity in V4 therefore synchronizes a representation of the target stimulus with each saccadic eye movement. The fact that the presaccadic activation in V4

is visually selective at first prompted us to consider only its possible role in perception during eye movements (*12*), but upon examining the metrics of saccades, the need to also consider the relationship of this activity to the saccade command became apparent. Although our saccade task did not require the monkeys to accurately foveate the RF stimuli, both monkeys tended to do so by default. Moreover, they did so in a way that indicated they had taken into account the orientation of the stimulus before they initiated eye movements (Fig. 2A). For both monkeys, eye movements to oriented bar stimuli typically landed along the orientation axis of the bar stimulus. To quantify this behavior, we constructed angular histograms to examine the distribution of large samples of saccade endpoints with respect to the bar's orientation axis (Fig. 2B) (*13*). If one assumes that the monkeys' eye movements were not influenced by the orientation of the target stimulus, the endpoints should be equally distributed across all angles, forming a circular histogram. However, for both monkeys the proportion of endpoints was nonhomogeneous across angles, revealing a greater tendency of the fovea to land along the axis of orientation. Although all orientations had entirely overlapping centers of gravity, the endpoints of saccadic eye movements varied primarily along the bar's orientation axis.

This observation suggested that the presaccadic activity might be one mechanism by which saccades were guided by orientation information. We therefore examined the correspondence between presaccadic activation and the degree to which eye movements followed the orientation of the saccade target. If indeed the saccade-related activity contributes to the saccade command, one should expect a correlation between the level of presaccadic activation and the placement of the fovea with respect to the orientation axis. One might expect trials with the largest presaccadic activity to be accompanied by eye movements that land more accurately along the target's orientation axis. Likewise, trials with low presaccadic activity should be accompanied by eye movements that land randomly with respect to the target's orientation axis. In particular, this should be true when eye movements are made to each cell's preferred orientation.

For each neuron, we separated trials into two groups according the level of presaccadic activation when the cell's preferred orientation was the target of the saccade. We then compared distributions of saccade endpoints from trials with high or low presaccadic activation (*14*). The distributions of endpoints between high and low presaccadic activity differed in the degree to which the eye movements placed the fovea along the axis of orientation (Fig. 3). The trials in which presaccadic activity was high tended to precede eye movements that fell close the bar's orientation axis. In contrast, trials with poor presaccadic activity yielded more homogeneous distributions. This result indicates a correspondence between the degree of visual guidance and the level of presaccadic activation in V4.

Because the perception of fine visual details depends on those details actually falling on the fovea, placement of the fovea during normal visual scanning is crucial. Visually selective representations of visual targets peripheral to the point of fixation should therefore actively guide each successive saccade command. The presaccadic activation within areas such as V4 is perhaps the mechanism by which detailed visual information modifies oculomotor commands. The present observations suggest that neurons in V4 not only participate in the passive representation of visual stimuli but that they also contribute to the active guidance of saccadic eye movements. The fact that neurons in area V4 project directly to the parietal cortex, the frontal eye fields, and the superior colliculus (*15*) is consistent with this view, because each of the latter is more directly involved in oculomotor programming.

But is the presaccadic activation in V4 a motor response? The fact that the presaccadic activation in V4 depends primarily on the visual target (*12*), together with the fact that modulation of responses in V4 can be obtained in attentional tasks even when eye movements are withheld (*8*), appears to rule out a direct role for this area in triggering saccadic eye movements. Instead, the present observations suggest a distinction between mechanisms that initiate saccadic eye movements and mechanisms that actively guide them. Such a distinction is also supported by studies of the effects of microstimulation of extrastriate area MT. These studies show that microstimulation does not typically elicit saccadic eye movements but that it can nonetheless alter saccade vectors when eye movements are made to visual targets (*16*). Further experiments might examine the effects of microstimulation of other visually selective areas, such as V4, on the pattern of visually guided eye movements. Such experiments would potentially address the close link between visual coding and motor planning and, as the present results, expose the limitations of a strictly visual or motor interpretation.

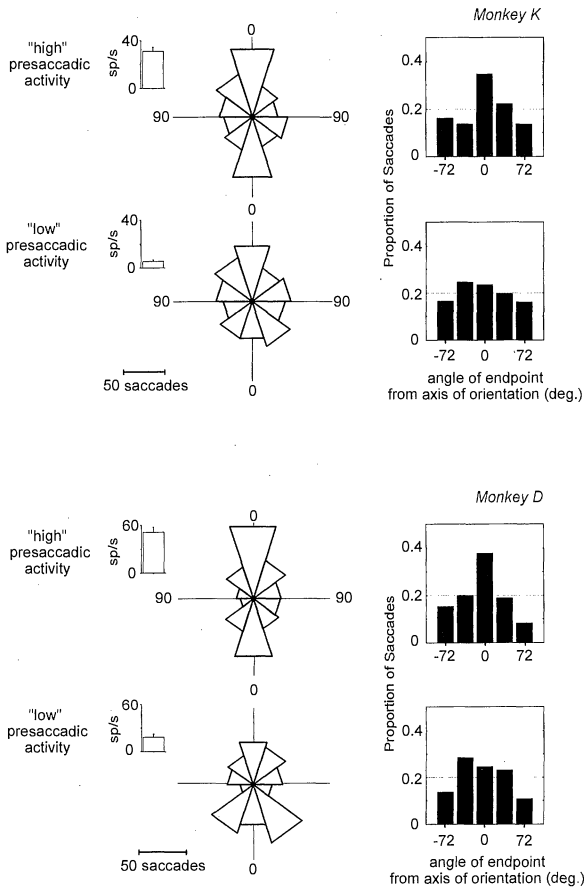

Fig. 3. Distributions of saccade endpoints relative to the axis of preferred orientation for trials during which the presaccadic activity was either high or low. For each of the 83 orientation selective neurons, trials were sorted according to the amount of neural activity (high or low) present immediately before initiation of a saccadic eye movement to a stimulus presented at the preferred orientation (*13*). The mean presaccadic activity of the two trial groups is shown by the bar plot in the upper left of each set of histograms. Histograms show the result of sorting the saccades according to the amount of presaccadic activity of individual neurns. Saccades landed closer to the orientation axis of the bar stimulus on trials when the presaccadic activity was high than on trials when the presaccadic activity was low. The two distributions of sorted trials were significantly different for both monkeys (monkey K, $\chi^2 = 15.5$, $P < 0.005$, $n = 556$ sorted trials; monkey D, $\chi^2 = 18.6$, $P < 0.001$, $n = 716$ sorted trials).

References and Notes

1. F. Vitu, J. K. O'Regan, M. Mittau, *Percept. Psychophys.* **47**, 583 (1990).
2. A. L. Yarbus, *Eye Movements and Vision* (Plenum Press, New York, 1967), pp. 171–211.
3. L. G. Ungerleider and M. Mishkin, in *Analysis of Visual Behavior*, D. J. Ingle, M. A. Goodale, R. J. W. Mansfield, Eds. (MIT Press, Cambridge, MA, 1982), pp. 549–586.
4. M. A. Goodale and A. D. Milner, *Trends Neurosci.* **15**, 20 (1992).

5. R. A. Andersen, *Annu. Rev. Neurosci.* **12**, 377 (1989); P. Their and R. A. Andersen, *J. Neurophysiol.* **80**, 1713 (1998).
6. R. Desimone, J. Fleming, C. G. Gross, *Brain Res.* **184**, 41 (1980).
7. R. Desimone, S. J. Schein, J. Moran, L. G. Ungerleider, *Vision Res.* **25**, 441, (1985).
8. J. H. R. Maunsell, *Science* **270**, 764 (1995).
9. B. Fischer and R. Boch, *Exp. Brain Res.* **44**, 129 (1981).
10. In the delayed-saccade task, the monkey was first required to fixate a central fixation spot within a <1° error window. Immediately after fixation, a visual stimulus was presented within the RF of the neuron under study and it remained there until the end of the trial. The monkey was required to maintain fixation on the fixation point for a delay of 1 s, while it waited for the appearance of a saccade target (0.25°) at one of two locations distant from the RF. In two-thirds of the trials, the saccade target appeared when the fixation spot was extinguished and the monkey was required to make a saccadic eye movement to the target. In the remaining trials, the saccade target did not appear; when the fixation spot was extinguished, the monkey was required to make a saccadic eye movement to the RF stimulus. Both conditions were identical until the cue to saccade (disappearance of the fixation spot) and were pseudorandomly interleaved. RF stimuli were light and dark bars presented at one of four orientations (0°, 45°, 90°, or 135°) on a 34 × 27 cm video monitor driven by a number nine graphics board (640 × 480 resolution). Eye position was monitored at 200 Hz with a scleral search coil (*17*). Neural activity and eye position data were both stored for off-line analysis. The activity of single neurons was recorded by standard electrophysiological techniques described in K. Zipser, V. A. F. Lamme, and P. H. Schiller [*J. Neurosci.* **16**, 7376 (1996)].
11. The mean normalized response of 83 orientation-selective neurons was first assembled into a matrix of response functions in which either the preferred or the nonpreferred stimulus was presented to the RF. A running difference function was then computed from a moving average of the activity from preferred and nonpreferred trials. The moving average was computed within a 50-ms window of activity, which moved in 5-ms steps. These difference functions were constructed from both stimulus-aligned and saccade-aligned activity. A neuron was considered orientation selective if its orientation tuning index (response to best orientation–response to worst orientation)/(response to best orientation + response to worst orientation) was >0.1.
12. T. Moore, A. S. Tolias, P. H. Schiller, *Proc. Natl. Acad. Sci. U.S.A.* **95**, 8981 (1998).
13. We determined the angular distribution of saccade endpoints by computing the angular position of each endpoint from an axis of orientation passing through the median saccade endpoint from a set of trials. Individual saccade endpoints were taken as the eye position coordinate obtained 60 ms from the start of the movement. Because the duration of saccades of ≤10° in amplitude is typically between 30 and 50 ms (*18*), this coordinate should represent the full displacement of the movement but still exclude corrective saccades. We detected the initiation of saccadic eye movements by computing the instantaneous eye speed from the 200-Hz eye position samples. Any eye speed of ≥50° per second that displaced the eye position >0.5° was considered the initiation of a saccadic eye movement.
14. We recorded the activity of each orientation selective neuron (n = 83) during 10 to 35 trials, from which there were an equal number of saccadic eye movements made to each RF stimulus. For trials in which the preferred orientation was the RF stimulus, we sorted the presaccadic activity during each set of trials in order of response magnitude. We sorted the trials according to a 50-ms window of activity preceding the onset of the saccadic eye movement. This time window centered on the peak in the presaccadic selectivity shown in Fig. 1B, namely, −75 to −25 ms with respect to the saccade onset. We then divided the sorted sets of trials into two groups: trials with the most activity and trials with the least. We divided odd-numbered sets of trials equally into two subsets, with the middle trial being omitted. No attention was paid to the degree to which the division of trials resulted in nonoverlapping distributions of response magnitudes. However, the difference between the two trial subsets was always >0.
15. G. J. Blatt, R. A. Andersen, G. R. Stoner, *J. Comp. Neurol.* **299**, 421 (1990); W. Fries, *ibid.* **230**, 55, (1984); J. D. Schall, A. Morel, D. J. King, J. Bullier, *J. Neurosci.* **15**, 4464 (1995).
16. J. M. Groh, R. T. Born, W. T. Newsome, *J. Neurosci.* **11**, 4312 (1997).
17. S. J. Judge, B. J. Richmond, F. C. Chu, *Vision Res.* **20**, 535 (1980).
18. D. A. Robinson, *J. Physiol. London* **174**, 245 (1964).
19. Supported by National Institutes of Health grant EY0067 and the McDonnell-Pew Foundation. This manuscript benefited from the valuable comments of P. H. Schiller, M. S. A. Graziano, C. G. Gross, and two anonymous reviewers.

10 May 1999; accepted 13 August 1999

Constitutive Activation of Toll-Mediated Antifungal Defense in Serpin-Deficient *Drosophila*

Elena A. Levashina,[1]*† Emma Langley,[1]*‡ Clare Green,[2] David Gubb,[2] Michael Ashburner,[2] Jules A. Hoffmann,[1] Jean-Marc Reichhart[1]§

The antifungal defense of *Drosophila* is controlled by the *spaetzle/Toll/cactus* gene cassette. Here, a loss-of-function mutation in the gene encoding a blood serine protease inhibitor, Spn43Ac, was shown to lead to constitutive expression of the antifungal peptide drosomycin, and this effect was mediated by the *spaetzle* and *Toll* gene products. Spaetzle was cleaved by proteolytic enzymes to its active ligand form shortly after immune challenge, and cleaved Spaetzle was constitutively present in *Spn43Ac*-deficient flies. Hence, *Spn43Ac* negatively regulates the Toll signaling pathway, and Toll does not function as a pattern recognition receptor in the *Drosophila* host defense.

Genetic analysis has established that the Toll signaling cascade controls the antifungal host defense of flies (*1*). In particular, Toll mediates the expression of the antifungal peptide drosomycin in the fat body cells by way of Rel-Cactus complexes, which are structurally and functionally equivalent to the vertebrate NF-κB–IκB complexes (*1, 2*). *Toll* (*Tl*) was initially identified as a gene that controls dorsoventral patterning in the *Drosophila* embryo (*3*). The *Tl* gene encodes a transmembrane receptor with extracellular leucine-rich repeats and an intracellular domain exhibiting marked similarities with the cytoplasmic domain of the interleukin-1 receptor (*4, 5*). A proteolytically cleaved form of the *spaetzle* (*spz*) gene product is thought to be the extracellular ligand of Toll both in embryonic development and in the immune response (*1, 5*). In the embryo, a proteolytic cascade, involving the Gastrulation defective, Snake, and Easter proteases, cleaves Spaetzle, a cysteine-knot growth factor, cytokine-like polypeptide (*5*). The genes encoding these three proteases are dispensable for induction of a Toll-mediated immune response (*1*). A human homolog of *Toll* was recently cloned and shown to activate signal transduction by way of NF-κB, leading to the production of pro-inflammatory cytokines (*6*). Studies performed with human cell lines suggest that a lipopolysaccharide (LPS)-binding and signaling receptor complex is assembled at the cell membrane where human Toll, in association with the MD-2 protein (*7*), interacts with LPS bound to the peripheral membrane protein CD14 (*8–10*). The LPS signal is probably transduced across the membrane by Toll, as mutations in this gene in mice lead to an LPS-unresponsive state (*11*).

Here, we have addressed the activation of the Toll receptor during the immune response of *Drosophila*. For this, we have used flies carrying ethylmethane sulfonate–induced mutations in the *necrotic* (*nec*) locus (*12*). The locus, which maps at position 43A, generates three transcripts encoding putative serine protease inhibitors of the serpin family (*13*). The *nec* mutants exhibit brown spots along the body and the leg joints, corresponding to necrotic areas in the epidermis. This mutant phenotype is rescued by a single

[1]UPR 9022 CNRS, Institut de Biologie Moléculaire et Cellulaire, 15 Rue René Descartes, Strasbourg 67084, France. [2]Department of Genetics, University of Cambridge, Cambridge CB2 3EH, UK.

*These authors contributed equally to this study.
†Present address: European Molecular Biology Laboratory, Meyerhofstrasse 1, Heidelberg 67117, Germany.
‡Present address: Wellcome/CRC Institute, Tennis Court Road, Cambridge CB2 1QR, UK.
§To whom correspondence should be addressed. E-mail: reichhart@ibmc.u-strasbg.fr