late the propagation of the action potential within the dendrite are important for activity-dependent synaptic development as well[15]. By manipulation of activity in individual neurons, Burrone *et al.*[9] suggest that activity-dependent refinement of synaptic connections is shaped by multiple mechanisms via positive and negative feedback (Hebbian and homeostatic, respectively) that are engaged in a developmentally regulated manner to provide a balance between rewarding active connections and ensuring network stability through maintenance of total synaptic strength.

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Hide, remember, seek

David Bradley and Pascal Wallisch

A new study shows persistent activity in frontal eye field neurons while monkeys track the imagined motion of a dot that has disappeared, and finds this activity is tuned for speed.

We often think of cortical sensory and motor systems as functioning separately, but in some situations, the distinction is blurred. A good example involves tracking a moving target that disappears momentarily behind an occluding object. Humans and monkeys accurately infer the motion of hidden targets, which presumably involves some form of persistent neural activity. This activity would not be easily classified as sensory, as no stimulus is visible; nor is it plainly motor activity, as no action has happened (and, indeed, none need happen at all).

Where, then, would one expect to find such activity? A good approach would be to look in cortical regions that have both sensory and motor characteristics. Such reasoning underlies a study in this issue by Barborica and Ferrera, who examined the activity of frontal eye field (FEF) neurons in monkeys performing a motion extrapolation task[1]. The FEF region is involved in planning and initiation of saccadic (rapid) eye movements, but the neurons there also have sensory characteristics[2]. The choice of the FEF was appropriate, as we will see, and the findings give a clear picture of how the brain amasses sensory cues and stores this information until a motor response requires it.

The authors first trained monkeys to look at a stationary spot on a computer screen (**Fig. 1**). Once the monkeys' gaze was thus fixed, a moving dot appeared, heading either toward or away from the fixation point. Moments later, the moving dot disappeared, as if behind an occluding object. The monkeys learned to extrapolate the dot's path, imagining where it would be at any particular time. Then the fixation spot disappeared. At this instant, the monkeys knew they had to look to the current location of the dot, effectively intercepting it as it moved along its hidden path. The actual target reappeared, as if from behind the occluder, after the saccade had begun, at approximately the time of interception.

To be sure the monkeys were extrapolating target motion and not simply scaling the size (distance) of their saccade to the initial speed of the target, the authors varied the duration of the occlusion period for a given target speed. Therefore, the monkeys could not know *a priori* how large to make their saccade,

as that would require them to know when the target would reappear.

The authors made three principal observations (**Fig. 2**). First, many FEF neurons remained active during the period of hidden motion. They therefore had the potential to store information about the invisible target. Second, these neurons' activity during the visible-motion stage was speed dependent; that is, most neurons responded differently to different target speeds. Because the time at which the hidden dot reappears depends on its speed (a faster dot will reappear sooner), it is logical that neurons would take this into account. Finally, each neuron's characteristic profile of responses to different speeds, called its 'speed tuning', was the same during the occluded period as it was during visible motion. This means that not only motion, but indeed the speed of motion, was represented during the memory period.

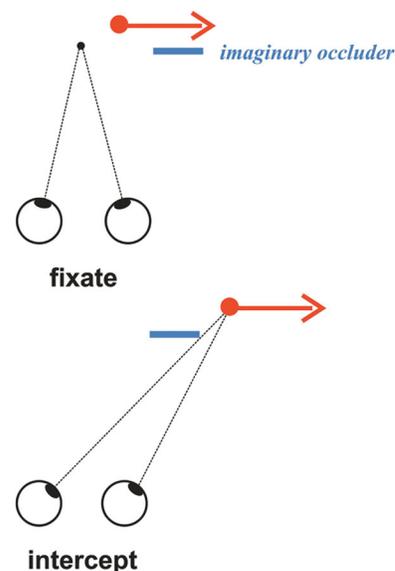In general, higher dot speeds require larger saccades, because for a given time

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Fig. 1. Experimental design. The monkey fixes his gaze on stationary spot while a target moves across the screen. The target disappears momentarily and then reappears at a random time. The monkey has to anticipate where the dot will reappear and make a saccade to that location.

Target visible Target occluded Saccade

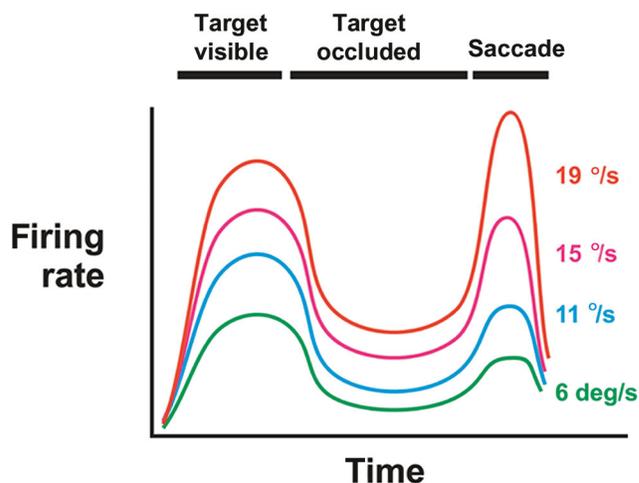**Firing rate**

19 °/s
15 °/s
11 °/s
6 deg/s

Time

Fig. 2. Hypothetical single-neuron data showing the basic result. While the target is visible, the neuron's response depends on target speed. When the target is invisible, the differential activity persists, thereby carrying information about target speed through the occlusion period.

of disappearance, the distance traveled is proportional to the speed. This fact is potentially problematic because FEF responses are linked to saccade amplitude[3], which could produce responses that would be mistaken for a speed effect. The authors used two controls to rule this out. First, by varying the duration of occlusion, saccade size was made to span a range of values for a given target speed. Also, by using different target speeds, they produced a range of saccade sizes for a given time of disappearance. This decoupling of speed, disappearance interval and saccade size made it possible to assess, by ANOVA, the effects of speed independently of any effects of saccade size and disappearance interval. As a second control, the initial period of dot motion was omitted on some trials. When the dot appeared from behind the imaginary occluder at its normal time of 'reappearance' (of course it had never initially appeared or disappeared in these control trials), monkeys looked at it as quickly as possible. The timing and size of the saccades were the same as in the ordinary trials, but in this case there was no informed way of representing target speed during the hidden period. In general, the correlations between dot speed and neuronal responses in experimental trials were apparent above and beyond any correlations observed during the control trials. This finding strongly supports the claim that speed is encoded during the occlusion period.

This is not the first study to show a persistent neural activity related to inferred motion. Eskandar and Assad

reported similar findings in LIP, a posterior parietal area, using monkeys trained to intercept an occluded, moving target[4]. What is distinct about the Barborica and Ferrera study design is its emphasis on the encoding and storage of information about speed. This has an important clarifying effect because persistent activities are otherwise hard to dissociate from such things as saccade preparation, attention effects, storage of position cues, and so on. The demonstration of a persistent representation of speed, in contrast, leaves little doubt that information about motion itself is being stored.

There are conceivably other ways of representing invisible target motion. For example, one could imagine a wave of activity traveling through a population of position-sensitive neurons. In this case, the extrapolated dot position could be deduced from the current location of the wave. The Barborica and Ferrera study, of course, does not exclude this possibility. But storing the speed, which could be done with just a handful of neurons, arguably makes more sense than recruiting an entire population to construct an activity wave.

When a moving target disappears, the location of its reappearance depends on the target speed and the time elapsed. Therefore, storing information about speed alone does not allow FEF neurons to anticipate the target's position. For this, the speed cue must be multiplied by time. But where is time encoded? It might happen in the FEF itself. Recent evidence suggests that FEF

neurons are sophisticated devices which amass, transform and store information needed to make saccades. For example, FEF neurons are involved in decisions about target relevance[5], attention shifts[6], the selection of targets for visual pursuit[7], and the integration of sensory information from various sensory regions[8] and over time[9] as required for planning a saccade. The Barborica and Ferrera study[1], which demonstrates the storage of information needed for future saccades, further supports the idea that the FEF embodies a kind of saccade-specific intelligence.

It would not be surprising, therefore, if the short-term passage of time were also represented in the FEF (or an associated area[10–12]). This representation could involve the changing activity of specific neurons, the shifting of activity between neurons, or a quantity that is broadly distributed over the neuronal population. It is easy to appreciate the importance of time in a region whose job it is to coordinate sensory input with motor behavior, especially if any form of anticipation is involved.

As with all important studies, the results of Barborica and Ferrera are intriguing as well as revealing, and they contribute to a crucial line of research that probes the boundaries between sensory and motor processing. Perhaps the most important outcome of these studies will be to suggest that no sharp boundaries exist.

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