by intrinsic genetic programs and phenotype determination regulated by extracellular signals. The authors are well positioned to dissect these two paradigms, for example, by using temporally inducible Cre lines to ablate Runx factors in DRG after establishment of the sensory circuitry.

One unresolved question is the role of the Runx binding partner CBFβ. CBFβ does not exhibit DNA binding affinity by itself but rather modulates Runx activities by changing its conformation (Ito, 2004). CBFβ is highly expressed in postnatal DRG and trigeminal ganglia (GNF, 2003). It will be most interesting through genetic analysis to determine the overlap in phenotypic consequences of CBFβ compared to Runx1 and Runx3 ablation in DRG neurons.

In sum, these three studies substantially expand our knowledge about transcriptional regulation of DRG neuronal identity and central axon patterning. They demonstrate that expression of Runx1 and Runx3 consolidate and specify traits of nociceptive and proprioceptive DRG neurons, respectively. The studies of Kramer et al. (2006) and Chen et al. (2006a) agree that Runx factors have critical functions in suppressing markers normally downregulated in specific populations during development. Chen et al. (2006a) further demonstrate a requirement for Runx1 in expression of a variety of proteins that are critical to the normal functioning of nociceptive neurons. Finally, both gain-of-function and loss-of-function studies show that Runx1 and Runx3 regulate sensory axon trajectories in the spinal cord toward appropriate terminal fields.

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Selected Reading

Arber, S., Ladle, D.R., Lin, J.H., Frank, E., and Jessell, T.M. (2000). Cell *101*, 485–498.

Caterina, M.J., Leffler, A., Malmberg, A.B., Martin, W.J., Trafton, J., Petersen-Zeitz, K.R., Koltzenburg, M., Basbaum, A.I., and Julius, D. (2000). Science *288*, 306–313.

Chen, C., Broom, D.C., Liu, Y., de Nooij, J.C., Li, Z., Cen, C., Samad, O.A., Jessell, T.M., Woolf, C.J., and Ma, Q. (2006a). Neuron *49*, this issue, 365–377.

Chen, A.I., de Nooij, J.C., and Jessell, T.M. (2006b). Neuron *49*, this issue, 395–408.

GNF. (2003). SymAtlas v1.1.1 (computer program). Genomics Institute of the Novartis Research Foundation.

Hall, A.K., Dinsio, K.J., and Cappuzzello, J. (2001). Dev. Biol. *229*, 263–270.

Inoue, K., Ozaki, S., Shiga, T., Ito, K., Masuda, T., Okado, N., Iseda, T., Kawaguchi, S., Ogawa, M., Bae, S.C., et al. (2002). Nat. Neurosci. *5*, 946–954.

Ito, Y. (2004). Oncogene *23*, 4198–4208.

Kramer, I., Sigrist, M., de Nooij, J.C., Taniuchi, I., Jessell, T.M., and Arber, S. (2006). Neuron *49*, this issue, 379–393.

Levanon, D., Brenner, O., Negreanu, V., Bettoun, D., Woolf, E., Eilam, R., Lotem, J., Gat, U., Otto, F., Speck, N., and Groner, Y. (2001). Mech. Dev. *109*, 413–417.

Levanon, D., Bettoun, D., Harris-Cerruti, C., Woolf, E., Negreanu, V., Eilam, R., Bernstein, Y., Goldenberg, D., Xiao, C., Fliegauf, M., et al. (2002). EMBO J. *21*, 3454–3463.

Molliver, D.C., Wright, D.E., Leitner, M.L., Parsadanian, A.S., Doster, K., Wen, D., Yan, Q., and Snider, W.D. (1997). Neuron *19*, 849–861.

Patel, T.D., Jackman, A., Rice, F.L., Kucera, J., and Snider, W.D. (2000). Neuron *25*, 345–357.

Patel, T.D., Kramer, I., Kucera, J., Niederkofler, V., Jessell, T.M., Arber, S., and Snider, W.D. (2003). Neuron *38*, 403–416.

Ritter, A.M., Lewin, G.R., Kremer, N.E., and Mendell, L.M. (1991). Nature *350*, 500–502.

Srinivas, S., Watanabe, T., Lin, C.S., William, C.M., Tanabe, Y., Jessell, T.M., and Costantini, F. (2001). BMC Dev. Biol. *1*, 4.

Taniuchi, I., Osato, M., Egawa, T., Sunshine, M.J., Bae, S.C., Komori, T., Ito, Y., and Littman, D.R. (2002). Cell *111*, 621–633.

Zylka, M.J., Rice, F.L., and Anderson, D.J. (2005). Neuron *45*, 17–25.

A Flashing Line
Can Warp Your Mind

Keeping pace with a constantly changing world requires the ability to make predictions about the future on a variety of timescales. A very basic example of this is the ability to predict the future location of a moving object in the brief time that it takes to perceive and respond to that object. In this issue of *Neuron*, experiments by Sundberg, Fallah, and Reynolds reveal a potential neural substrate for making short-range predictions about motion in visual area V4.

We are forever destined to live in the past. Due to neural transmission delays, the sensations we experience are always a fraction of a second behind the events that evoke them. The time differences involved may be slight, yet they represent a distinct disadvantage when dealing with a world full of moving objects, particularly if some of those objects are large, heavy, and rapidly approaching. How the primate visual cortex accurately estimates the position of moving stimuli in the face of neural tarrying is the subject of a current study by Sundberg, Fallah and Reynolds (Sundberg et al., 2006). By performing parallel studies in humans and monkeys, these authors provide perceptual and physiological evidence that a moving target shifts the position of neuronal receptive fields in extrastriate visual area V4, thereby creating a wrinkle in the fabric of visual space. The result is that we perceive not the true position of the target, but its presumed future whereabouts. This kind of short-range prediction allows us to keep a step ahead of our sluggish brains and regain a semblance of simultaneity with reality. In other words, we experience the present by predicting the future of things that happened in the past.

This all works out because inertia causes objects to move in a predictable manner—a tendency codified by Newton's First Law of Motion. But do our brains actually take advantage of this predictability? Some of the first evidence that they do came from the study of eye movements. The primate oculomotor system uses a variety of strategies to keep the image of a moving target on the fovea despite visual-motor processing delays. One such strategy is used when making rapid eye

movements called saccades. Careful studies have found that saccades are programmed based on an estimate of target position taken some 100 ms prior to the initiation of the movement (Gellman and Carl, 1991). For an object moving at a moderate speed, this delay could cause the eye to undershoot the target by an amount that is larger than the fovea itself. Yet saccades made to moving targets show no such error, because their programming includes a predictive component that compensates for the velocity of the target (Ron et al., 1989; Keller and Johnsen, 1990). These predictions require an intact striate cortex (Segraves et al., 1987).

In the perceptual domain, Donald M. MacKay discovered evidence of motion extrapolation while working in a darkened laboratory illuminated only by a strobe light and glowing instrument dials. During eye movements, the instrument dials sometimes seemed to move independently of their intermittently illuminated surroundings (MacKay, 1958). This effect can be reproduced in a dark room by using a light-emitting diode, a strobe light, and a ping-pong paddle. Attach the LED in the middle of the paddle's blade and adjust the strobe frequency to about five flashes per second. When the paddle is waved, the LED appears to float free of the surface to which it is attached. This phenomenon has come to be known as the "flash-lag" effect (Nijhawan, 1994), because the surface that is transiently illuminated by the flashing strobe appears to lag behind the continuously lit moving target.

Mislocalization of moving stimuli can be observed without the aid of a strobe light, as was demonstrated by Russell and Karen DeValois (DeValois and DeValois, 1991). They showed that a stationary window containing a set of moving bars (Figure 1) was perceived as being displaced in the direction of motion of the bars. The illusion is nicely demonstrated if one arranges three such stimuli in a column and alternates their direction. When the bars are set in motion, the stimuli appear dramatically misaligned (see Movie S1 in the Supplemental Data available online).

Sundberg et al.'s experiments take advantage of a similar motion illusion originally reported by Cai and Schlag (2001). In this case, the observer sees a moving blue line that briefly changes color to red. When queried about the position of the red line, observers consistently report that it appears ahead of its true location. That is, the red line appears displaced in the direction of motion. Sundberg et al. recorded from neurons in visual area V4 of awake monkeys viewing this stimulus. The investigators found that V4 neurons responded to the color change and that this response varied depending on the position of the flashed line within the receptive field. However, the critical observation is that the response evoked by the flash was modulated by the motion of the target as if the receptive field had shifted by a small amount. The direction of the receptive field shift was *opposite* to the direction of target motion, as if the cell had been recruited by a wave of activity preceding the target.

A number of explanations for the perceived mislocalization of moving stimuli have been proposed (see Nijhawan, 2002), but it isn't yet clear which is correct or even if there is a single phenomenon requiring a unitary expla-
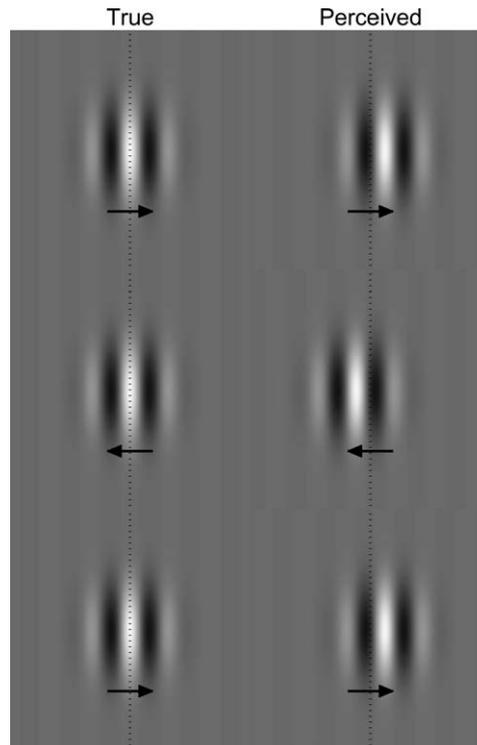

Figure 1. DeValois Motion Illusion

Motion illusion reported by DeValois and DeValois (1991). (Left column) Each stimulus is a set of light/dark bars within a stationary window. Three such stimuli are arranged in a column such that their centers are vertically aligned. (Right column) When the bars are set in motion, the perceived location of the stimulus is shifted.

nation. What is clear is that predictive responses are seen as early as the retina (Berry et al., 1999) and can be demonstrated in very simple neural network models. One such model is illustrated in Figure 2. It comprises a two-dimensional sheet of Hodgkin-Huxley neurons. The neurons have excitatory and inhibitory connections whose weights are determined by a two-dimensional "mexican hat" function. The network is spatially isotropic, yet a moving stimulus creates a traveling wave of activity the center of which tends to precede the stimulus (Figure 2A and Movie S2). The brief explanation for this behavior is that the moving target leaves a trail of refractory neurons in its wake so that spiking activity is shifted toward the leading edge. From the perspective of a single neuron in the network, activity anticipates both the arrival and departure of the stimulus. Hence, it is as if the receptive field of the neuron is shifted in a direction opposite to that of the stimulus motion. This is analogous to the effect observed by Sundberg et al. in area V4.

So far, then, there is evidence that moving targets can evoke predictive responses in at least two widely separated parts of the visual system. Given that a similar effect is seen in a generic network model, it is possible that the phenomenon is ubiquitous in visual cortex as well as other topographically mapped parts of the brain, including other sensory systems. But relating receptive field shifts to perception requires that the magnitude of the perceptual and physiological effects agree quantitatively. A strength of the Sundberg et al. study is that they
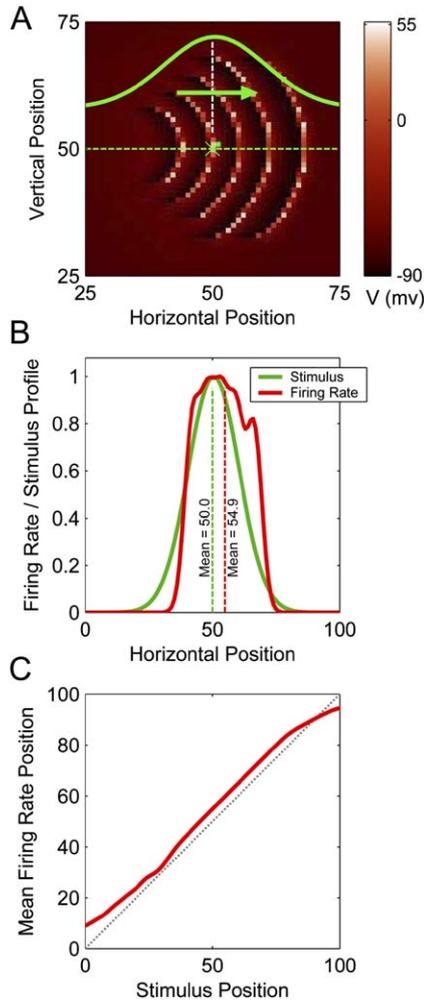
Figure 2. Neural Network Model Comprising a Two-Dimensional Array of Hodgkin-Huxley Neurons with Symmetric Excitatory and Inhibitory Connections

(A) Two-dimensional activity map where each location represents the membrane potential of a single neuron. The green curve represents a cross-section of the stimulus, which has a Gaussian luminance profile and is moving to the right (arrow). The green x represents the center of the stimulus.
(B) Stimulus profile (green) and average network activity collapsed across the vertical axis (red). The vertical lines indicate the centers-of-mass of the stimulus and network activity profiles.
(C) Stimulus position encoded by the network (y axis) against true stimulus position (x axis).

measured the perceived shift experienced by human observers and found that under some conditions it closely matched the neuronal shift in monkey V4. If one were to repeat the Sundberg et al. experiment in different visual areas and find receptive field shifts of different magnitudes, then one could argue that the area in which the neuronal shift most closely matched the perceptual shift plays a special role in the construction of visual awareness.

However, Sundberg et al. also found that V4 neurons had shifted receptive fields under conditions where human observers perceived no illusory displacement of the flashed stimulus. They therefore propose that V4 represents only one of several interpretations of the visual stimulus, with other interpretations being repre-

sented in other cortical areas. The brain then chooses the interpretation that best fits the sensory evidence and is consistent with prior experience and current behavioral goals. This idea recalls the "multiple drafts" model of consciousness proposed by Dennett and Kinsbourne (1992), in which perceptual representations are considered to be a product of the brain's interpretive processes, not a direct reflection of the sequence of events making up those processes. According to this view, subjective experience is similar to a movie spliced together from a Rashomon-like set of alternative scenarios. In the brain's editing room, even space and time can be manipulated so that we see what we expect to see.

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Selected Reading

Berry, M.J., Brivanlou, I.H., Jordan, T.A., and Meister, M. (1999). Nature *398*, 334–338.

Cai, R., and Schlag, J. (2001). J. Vis. *1*, 127a.

DeValois, R.L., and DeValois, K.K. (1991). Vision Res. *31*, 1619–1626.

Dennett, D., and Kinsbourne, M. (1992). Behav. Brain Sci. *15*, 183–247.

Gellman, R.S., and Carl, J.R. (1991). Exp. Brain Res. *84*, 660–667.

Keller, E., and Johnsen, S.D. (1990). Exp. Brain Res. *80*, 525–531.

MacKay, D.M. (1958). Nature *181*, 507–508.

Nijhawan, R. (1994). Nature *370*, 256–257.

Nijhawan, R. (2002). Trends Cogn. Sci. *6*, 387.

Ron, S., Vieville, T., and Droulez, J. (1989). Vision Res. *29*, 1103–1114.

Segraves, M.A., Goldberg, M.E., Deng, S.Y., Bruce, C.J., Ungerleider, L.G., and Mishkin, M.J. (1987). J. Neurosci. *7*, 3040–3058.

Sundberg, K.A., Fallah, M., and Reynolds, J.H. (2006). Neuron *49*, this issue, 447–457.