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movements. The activity of these neurons can be used to annul the retinal motion signal; consequently, saccade-induced motion is not perceived and external motion perception shortly after saccades is likely to be distorted (28). In addition, the sudden reversal of preferred motion direction demonstrates that tuning properties of cortical neurons are not necessarily static, but can be modified in the millisecond range.

References and Notes
18. Supplementary Web material is available on Science Online at www.sciencemag.org/cgi/content/full/295/5564/2460/DC1.
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Cortical Neurons Encoding Path and Place: Where You Go Is Where You Are

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We recorded neuronal activity in monkey medial superior temporal (MST) cortex during movement on a motorized sled. Most neurons showed a preferred heading direction, but some responded only when that heading was part of a particular path. Others responded only when the animal was at a certain place in the room, regardless of its path to that place. Video simulations of the self-motion scene evoked path, but not place, responses. Stationary positioning in the room revealed location preferences that matched place preferences recorded during movement. We conclude that MST encodes heading, path, and place information to support visuospatial orientation.

Most MST neurons (73%, 46/63) showed significant direction tuning (Fig. 1B), identified by the circular net vector (Z of circular distribution P < 0.05) (20, 21).

Clockwise (CW) and counterclockwise (CC) circular paths presented the same headings in reversed sequences with identical headings on opposite sides of the room. Nevertheless, many neurons had similar heading preferences on CW and CC paths (Fig. 1C), although 40% (25/63) showed at least a two-fold difference (22) between CW and CC response amplitudes (Fig. 1D).

Most neurons with comparable CW and CC response amplitudes preferred the same heading on both paths (Fig. 2A), but some preferred opposite headings. The neuron in Fig. 2B preferred rightward CW headings and leftward CC headings with both responses corresponding to the front of the room. This neuron was more affected by place-during-movement than by heading or path.

We used circular statistics (21) to describe heading, path, and place-during-movement selectivity. The sample’s distribution of direction-
ality showed no predominant heading preference. About half (46%, 21/46) of the neurons showed significant directionality on only one path. The remaining neurons (54%, 25/46) showed significant directionality on both preferred headings (CW-CC difference < 50°) but many (20%, 9/46) with opposite preferred headings (CW-CC difference > 100°). This creates the discontinuous distribution of directional differences separating heading and place preference neurons during movement (Fig. 2C).

We assessed the contributions of visual motion and translational movement by recording responses under three conditions (23): optic flow video simulations presented while the monkey was stationary, optic flow presented with matching CW or CC translational movement, and translational movement presented in darkness (no optic flow). Fig. 3, A to C, shows a neuron’s preference for leftward headings on the CC path with optic flow alone (3A) or with translational movement (3B), but not with movement alone (3C); a typical response pattern (24).

Optic flow with movement evoked a continuum of CW/CC response amplitude differences (Fig. 3D) like that seen during movement past the room-mounted lights (Fig. 1D). In contrast, CW/CC directional differences were always < 90° during simulated optic flow with movement (Fig. 3E), with no place-during-movement preferences (differences ≈ 180°) like those seen during movement past the room-mounted lights (Fig. 2C). We used optic flow simulating movement in front of a wall or through a cloud of dots (24), both evoked the heading-path response continuum without place-during-movement effects.

The source of selectivity for place-during-movement was explored by positioning the monkey at four stationary locations on the circular path while it viewed the room-mounted lights (19). Neuronal activity varied with the monkey’s stationary position in place preferences on a scatter plot of CW and CC response contrast (ordinate, C) versus the difference between CW and CC preferred directions (abscissa) for the 25 neurons with significant CW and CC responses.

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Fig. 1. Path-dependent heading selectivity. (A) The monkey viewed either a light-array or a video projection screen during translational sled movement on a circular path. (B) Spike-density histograms and raster displays of a neuronal response showing a left-forward heading preference that is stronger with CW motion (left). (C) A neuron’s responses to 16 heading intervals revealing greater CW heading selectivity. (D) Contrast ratios of CW and CC response amplitudes at the neuron’s preferred heading. 73% showed significant directionality (Z statistic) on at least one path.

Fig. 2. Heading and place preferences. (A and B) Spike-density polar plots (spikes/s) and net vectors (radial lines) with respect to heading (22). (A) Responses of a neuron with similar heading preferences on both paths (CW = 237°, CC = 276°). (B) A neuron with opposite heading preferences (CW = 67°, CC = 262°); a place preference for the right front of the room. (C) Heading and place preferences on a scatter plot of CW and CC response contrast (ordinate, C) versus the difference between CW and CC preferred directions (abscissa) for the 25 neurons with significant CW and CC responses.
the room (Fig. 4A) and was not attributable to ocular vergence (25) or disparity (26) effects: there was no relationship to distance from the wall (Fig. 4B), and all light stimuli were on the plane of fixation (27).

Stationary location effects were related to place-during-movement preferences in two ways. First, significant stationary location effects were more common (78%, 7/9) in neurons with place-during-movement preferences (CW/CC directional differences >100°) than in neurons (38%, 6/16) with heading preferences (CW/CC directional differences <50°). In addition, the preferred stationary location was close to the preferred place-during-movement (Fig. 4C).

These experiments reveal that MST encodes both instantaneous heading direction and the path to that heading. Path-dependent heading responses from simulated optic flow show the influence of the context (16, 28) created by heading sequences. The absence of context effects with other stimuli (29) suggests a critical role for heading sequences that represent a naturalistic path.

The heading-path response continuum must be separate from place preferences, because they are double-dissociated: Optic flow simulations yield path, but not place-during-movement, preferences; and stationary positioning yields location effects without a path. Nevertheless, path and place effects might interact. Stimulus sequence effects could support path integration and update position in the hippocampal place map (14, 15, 30). Hippocampal place information might feed back to create location effects when the monkey is stationary and path effects when the monkey is moving. Such reciprocal interactions may transform self-movement signals into a cognitive map; converting where you go, to where you are.
Molecular Determinants for the Tissue Specificity of SERMs

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Selective estrogen receptor modulators (SERMs) mimic estrogen action in certain tissues while opposing it in others. The therapeutic effectiveness of SERMs such as tamoxifen and raloxifene in breast cancer depends on their antiestrogenic activity. In the uterus, however, tamoxifen is estrogenic. Here, we show that both tamoxifen and raloxifene induce the recruitment of corepressors to target gene promoters in mammmary cells. In endometrial cells, tamoxifen, but not raloxifene, acts like estrogen by stimulating the recruitment of coactivators to a subset of genes. The estrogen-like activity of tamoxifen in the uterus requires a high level of steroid receptor coactivator 1 (SRC-1) expression. Thus cell type-- and promoter-specific differences in coregulator recruitment determine the cellular response to SERMs.

Tamoxifen and raloxifene are selective estrogen receptor modulators (SERMs) that bind the estrogen receptor (ER) and modulate ER-mediated gene transcription. Tamoxifen is an effective treatment for all stages of hormone-responsive breast cancer and can prevent breast cancer in high-risk women (J). However, tamoxifen has partial estrogenic activity in the uterus and is associated with an increased incidence of endometrial hyperplasia and cancer. Raloxifene, approved for the prevention and treatment of osteoporosis in postmenopausal women, also appears to prevent...