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The neural encoding of self-motion

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As we move through the world, information can be combined from multiple sources in order to allow us to perceive our self-motion. The vestibular system detects and encodes the motion of the head in space. In addition, extra-vestibular cues such as retinal-image motion (optic flow), proprioception, and motor efference signals, provide valuable motion cues. Here I focus on the coding strategies that are used by the brain to create neural representations of self-motion. I review recent studies comparing the thresholds of single versus populations of vestibular afferent and central neurons. I then consider recent advances in understanding the brain's strategy for combining information from the vestibular sensors with extra-vestibular cues to estimate self-motion. These studies emphasize the need to consider not only the rules by which multiple inputs are combined, but also how differences in the behavioral context govern the nature of what defines the optimal computation.

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Introduction

In everyday life as we move through the world, vestibular information is combined with cues from other sources in order to allow us to detect and perceive our self-motion. When self-motion is the result of an externally applied movement, such as riding as a passenger on the bus, the semicircular canals and otolith organs of the vestibular system encode rotation and linear acceleration information, while the visual system provides retinal-image motion (optic flow) cues. Furthermore, when self-motion is the result of voluntary movement, such as locomotion, sensory cues are not only provided by vestibular and visual systems, but also by the proprioceptive sensors of the muscles, tendons, and joints, which sense the relative position of neighboring parts of the body. Additionally, during voluntary movement, a motor command is generated to produce the movement, and thus

motor-derived information (i.e. a motor efference copy signal) is also available for integration with the existing multisensory cues to contribute to the brain's internal estimate of self-motion.

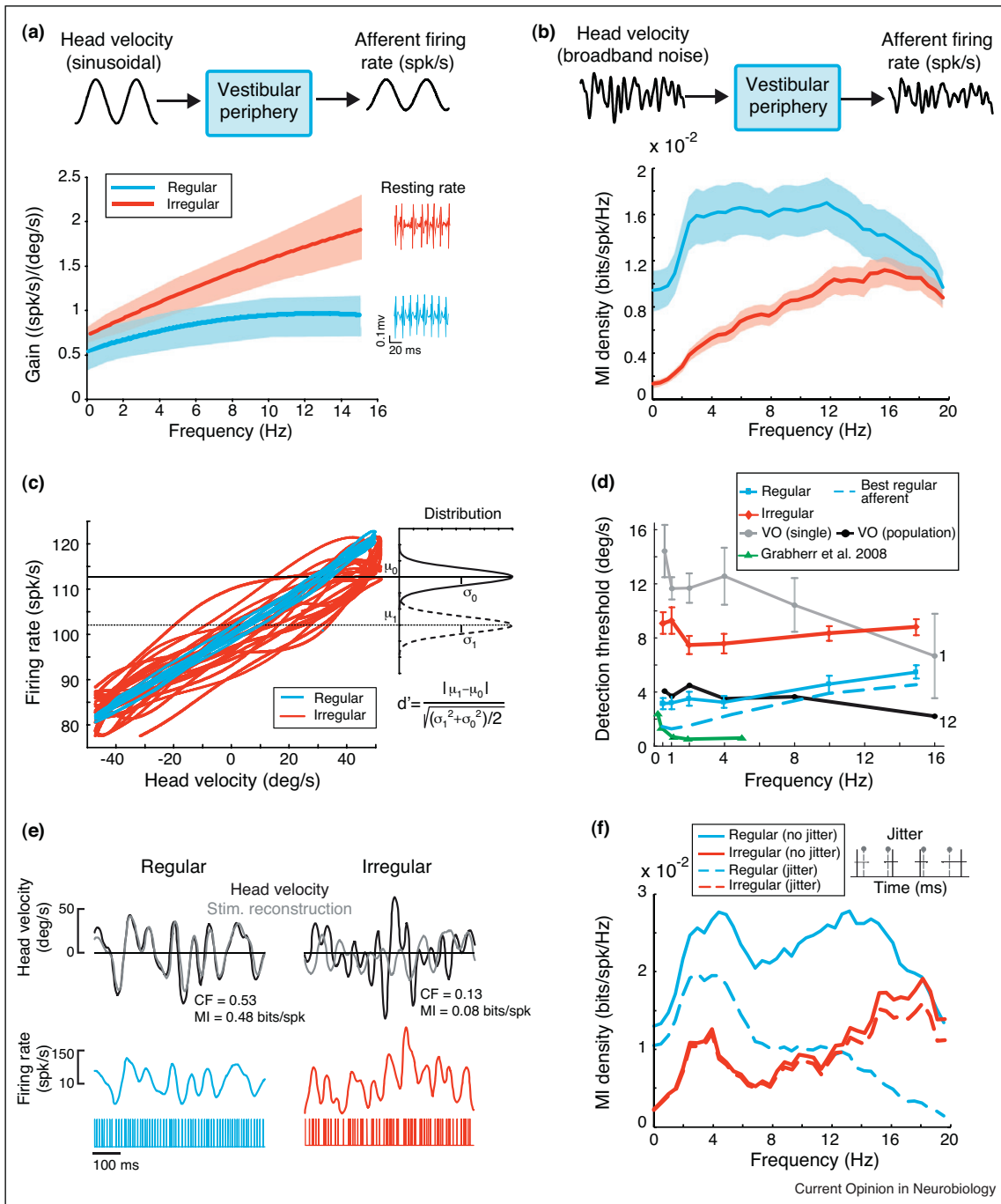
Recent work has made significant progress towards furthering our understanding of how the brain combines multimodal information to create a neuronal representation of self-motion. Here I review recent studies that have examined how the vestibular system encodes head motion information and integrates it with multimodal information cues (i.e. visual, proprioceptive, and efference copy information) to produce neural representations of self-motion during active versus passive self-motion. First, I will describe the early stages of vestibular processing. I next discuss the neural encoding of self-motion information provided by extra-vestibular cues including optic flow, proprioception, and efference copy signals. Finally, I consider strategies used for the integration of vestibular and extra-vestibular cues during active versus passive self-motion, and the implications regarding the neural encoding of motion in everyday life.

The vestibular system and the encoding of self-motion

The vestibular system detects motion of the head in space and makes a vital contribution to our subjective sense of self-motion and orientation relative to space. The end organs comprise two types of sensors: the three semicircular canals, which sense angular acceleration about three axes, and the two otolith organs (the saccule and utricle), which sense linear acceleration (i.e. gravity and translational movements). Information from the receptor cells of the semicircular canals and otoliths reaches the neural structures in the brain that contribute to our ability to estimate self-motion by means of the peripheral vestibular afferents of the VIII nerve [see [1] for review].

Vestibular afferents are categorized as either regular or irregular based on differences in their resting discharge variabilities (Figure 1a inset), which correspond to distinct morphological features at their peripheral terminations [2–4]. Traditionally, afferent responses to vestibular input have been characterized by estimating the gain and phase of the evoked modulation over several cycles of a stimulus at a specific frequency [5–9,10^{**}]. Figure 1a shows the average response gain and phase of semicircular canal afferents to rotations applied over a frequency range of 0–15 Hz [5]: a range which corresponds to that encountered during typical activities [11]. Notably, although irregular and regular afferents have comparable gains at frequencies of 0.5 Hz, irregular

Figure 1



The neural encoding of self-motion information at the earliest stages of vestibular processing. (a,b) Gain and mutual information density for populations of vestibular afferents. *a*, Population-averaged gains as a function of frequency for regular (blue line) and irregular (red line) afferents obtained during sinusoidal head rotations. The gray bands show 1 SEM. The inset shows resting discharge variability of an example regular (blue) and irregular (red) afferent. Irregular afferents have higher gains for higher frequencies. *b*, Population-averaged mutual information density curves for regular (blue line) and irregular (red line) afferents. These were relatively constant for regular afferents and increased with frequency for irregular afferents. *(c,d)* Detection thresholds for regular and irregular afferents. *c*, Plot of firing rate as a function of head velocity for an example regular (blue) and irregular (red) afferent during sinusoidal rotation of 0.5 Hz. The side inset shows a schematic representation of the firing-rate distribution during resting discharge (dashed line) and during stimulation (solid line). *d*, Population-averaged detection threshold values for regular (blue) and irregular (red) units at different frequencies of sinusoidal head rotation. Error bars indicate SEM. Data from Grabherr *et al.* (2008) are superimposed (green) for comparison. Population-averaged detection thresholds for single VO neurons (gray) as well as population of 12 VO neurons (black) are also reported. *(e,f)* *e*, Original head velocity (black) and reconstructed head velocities (gray) of an example regular and irregular afferent. *f*, Mutual information density curve obtained with (dashed) and without (solid) addition of 2 ms jitter for regular (blue) versus irregular (red) afferents. Addition of jitter decreased the mutual

afferents consistently display higher gains with increasing frequency.

The fact that irregular afferents have gains that are greater or equal to those of regular afferents over the physiological frequency range of natural head movements leads to the question: Why is it advantageous to have regular as well as irregular afferents in the vestibular system? The application of information theoretic measures to the vestibular system has helped to provide novel insights into the functional role of this afferent heterogeneity. To estimate information coding abilities across the same physiologically relevant frequency range, afferents can be stimulated using random (i.e. broad band noise) motion. Notably, in response to broad band noise stimulation regular afferents, in striking contrast to their response gains, consistently transmit more information than irregular afferents about head rotations for all but the highest frequency components of head motion (Figure 1b).

The observed differences in the information coding abilities versus sensitivities of regular and irregular afferents suggest different functional roles of each afferent class. For example, the more phasic irregular afferents could serve as highly sensitive event detectors, consistent with their greater sensitivities for high-frequency head rotations. In contrast, the more tonic regular afferents are likely to play a more important role in estimating the detailed time course of head rotations [10**,12]. Indeed, the higher information rates of regular afferents correspond to better (i.e. lower) detection thresholds than irregular afferents. Specifically, detection thresholds for frequencies less than 12 Hz are, on average, half as large for regular as irregular afferents (Figure 1c and d, compare blue and red traces). Importantly, however, even the most sensitive regular afferents (Figure 1d, dashed blue line) are still less sensitive than the behavioral detection thresholds of around 1°/s that have been measured in humans in response to rotational motion [13,14,15*].

Taken together these results suggest that neurons at subsequent stages of processing integrate inputs from vestibular afferent populations as well as from other sensory modalities to encode a precise representation of self-motion. For example, perceptual thresholds could be enhanced by pooling the activities of a large population of vestibular afferents, or alternatively, by selectively pooling the activities from a specific subset of afferents similar to the strategy describe in area MT [16]. Surprisingly, however, recent studies have shown that neurons in the first central stages of vestibular processing have thresholds that remain substantially larger than those measured perceptually [rotation: [17**],

translation: [18]]. Thus, a better understanding of population coding strategy used by central pathways will probably be required to reconcile the apparent discrepancy. In support of this view, is the recent report [17**] that combining the responses of multiple central vestibular neurons leads to detection values that nearly approach behavioral thresholds ($\sim 2.5^\circ/\text{s}$ vs. $0.5\text{--}1^\circ/\text{s}$). In addition to a population coding strategy, extra-vestibular cues – for example visual and/or proprioceptive information – could potentially further contribute to the construction of a neural estimate of self-motion. As will be considered below, the vestibular system is unique among sensory systems in that processing is inherently multimodal even at the first stage.

As a final point, it is important to note that to date all but one study has studied vestibular processing in relation to the information encoded by neuronal firing rates (i.e. rate coding). By artificially adding jitter to recorded spike trains, it has been recently shown that temporal coding coexists with rate coding at the vestibular periphery [Figure 1e and f; [10**]]. Specifically, regular but not irregular afferents (Figure 1f) encode information using a temporal code (i.e. information is carried by the precise timing of spikes). The implications of this finding are not yet fully understood, but could potentially provide an additional key to solving the mystery of the apparent disparity between neuronal and perceptual detection thresholds and the neuronal encoding of self-motion.

Extra-vestibular cues provide vital inputs for the estimation of heading: vestibular–visual convergence

Vestibular inputs are not our only source of information about self-motion. As we move through the world, vestibular information is combined with input from other sources, such as the retinal image motion. For example, when riding in a car, the visual system provides optic flow cues while the semicircular canals and otolith organs of the vestibular system encode rotational and linear head motion, respectively.

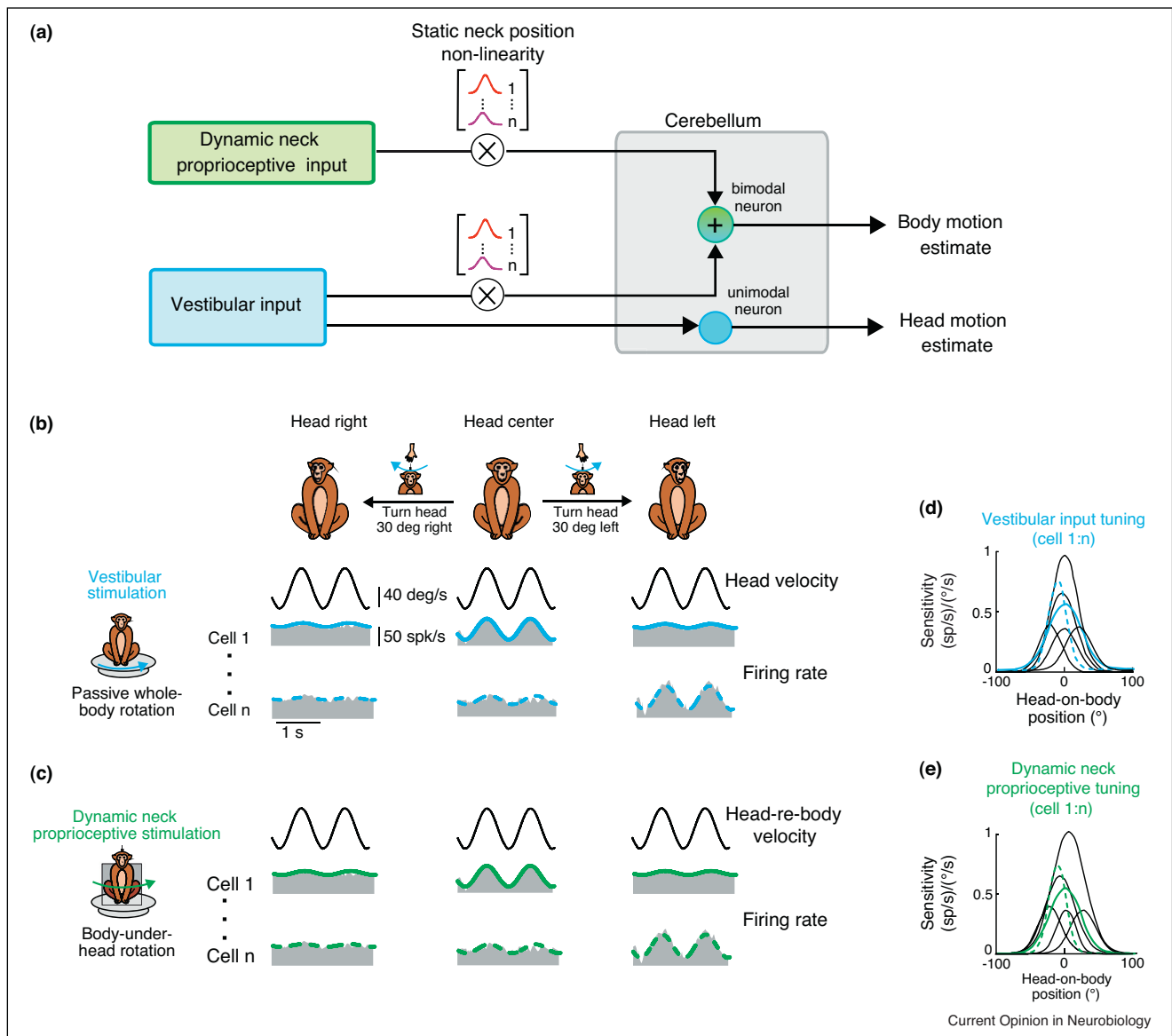
The ability of optic flow information to provide powerful sensations of self-motion when a subject is actually stationary have been long appreciated [19]. Distinct patterns of image motion simulating translation and rotation provide corresponding illusions of movement. The results of numerous studies [see [20] for review] provide support for the proposal that extrastriate visual cortex, most notably dorsal medial superior temporal extrastriate cortex (area MSTd) and area VIP are involved in the perception of the direction of self-motion during simulated translation (i.e. heading). Notably, electrical stimulation

(Figure 1 Legend Continued) information of regular but not irregular afferents significantly. By contrast, the addition of jitter had no significant effect on gain for either class of afferent (not shown). Inset shows example jittered (gray dots and lines) andunjittered (black lines) spike times. Data replotted with permission from Sadeghi *et al.* [17**] and Massot *et al.* [10**].

of either area can bias heading judgments suggesting a direct linkage between neuronal activity in both areas and heading perception. Quantitative analysis of neuronal responses to optic flow simulating self-motion shows that most neurons are sensitive to small heading changes, with some matching behavioral sensitivity [21]. Additionally,

the responses of MST [22] and VIP [23] neurons remain relatively stable in the presence of eye movements that distort the physical influx of optic flow information to the retina. This latter observation further supports the proposal that visual input to both areas is processed to provide an explicit representation of self-motion.

Figure 2



The neural encoding of body motion: the integration of vestibular and neck proprioceptive signals. (a) Schematic of the proposed mechanisms for vestibular-neck convergence in the rostral fastigial nucleus. The processing of both neck proprioceptive and vestibular inputs is characterized by a nonlinear operation in which head-on-body position modulates the gain of vestibular and dynamic neck proprioceptive responses. These two inputs sum linearly on bimodal neurons during combined stimulation, and because a given neuron has similar tuning to both sensory inputs it encodes body motion relative to space. (b) Vestibular sensitivity of two bimodal neurons (cell 1 and n) measured during whole-body rotation with the head oriented at different positions relative to the body (shown in cartoons). Note that cell 1 was most responsive when the head was centered on the body, while cell n was most responsive when the head was turned to the left. (c) Neck sensitivity of the same two bimodal neurons (cell 1 and n) measured during body-under-head rotation with the head oriented at different positions relative to the body (shown in cartoons). Again cell 1 was most responsive when the head was centered on the body, while cell n was most responsive when the head was turned to the left. (d,e) Turning curves (respectively) for vestibular (d, blue) and neck (e, green) sensitivities. The curves of cell 1 (solid) and cell n (dashed) are aligned, and have been superimposed on those of other bimodal neurons. Data replotted with permission from Brooks and Cullen [38**].

During actual motion in the light, the brain can combine visual (i.e. optic flow) information with vestibular cues to compute an optimal estimate of self-motion. Indeed neurons in areas MSTd/VIP that respond to optic flow stimuli also show tuning to translational motion in darkness [see [24] for review]. Moreover, the fact that tuning is eliminated following bilateral labyrinthectomy [25,26] has been taken as further support the view that extrastriate cortical neurons integrate visual and vestibular inputs to compute self-motion. In a series of recent studies, Angelaki, DeAngelis and colleagues have studied the rules that govern the interactions between visual and vestibular self-motion cues in macaque area MSTd. Notably, quantitative analysis of MSTd population activity [27**] has shown that the responses of neurons with congruent visual/vestibular heading preferences are well fit by weighted linear sums of their responses to each sensory input, where the relative weighting of each modality changes with the relative reliabilities of the two cues.

Extra-vestibular cues provide vital inputs for the estimation of body versus head motion: vestibular–neck convergence

During active self-motion, cues available from the proprioceptive sensors of the muscles, tendons, and joints can also be integrated with vestibular information to contribute to the brain's estimate of self-motion. In particular, the convergence of vestibular and neck proprioceptive inputs is known to underlie the ability of human subjects to perceive their body motion independently of their head motion [28]. Additionally, the integration of vestibular and proprioceptive information plays an important role in the control of balance and spatial orientation by ensuring that compensatory body movements account for the current position of the head relative to the neck [29,30]. Thus, a parallel effort has been made to understand the neural encoding of self-motion by studying vestibular-proprioreceptive integration.

The vestibular receptors of the inner ear sense only the motion of the head in space. Thus integration of vestibular and neck proprioceptive information is necessary to compute the estimate of body movement required to produce accurate postural reflexes. The first stages of vestibular processing in rhesus monkey are not characterized by vestibular–neck convergence; neurons in the vestibular nerve and nuclei of the rhesus monkey are insensitive to the passive stimulation of proprioceptors [[afferents: [5,31,32]]; [vestibular nuclei neurons: [33–36]]], and encode head-in space velocity. However, vestibular–neck convergence is evident at the next level of vestibular balance processing in the rostral fastigial nucleus (rFN) of the cerebellum. This nucleus, the most medial of the three deep cerebellar nuclei, receives direct input from the vestibular nuclei and contributes to the control of posture via the generation of vestibulospinal reflexes [reviewed in [37]]. Notably, approximately half of the neurons in the

rFN respond selectively to vestibular stimulation (termed unimodal neurons), while the other half respond to neck proprioceptive as well as vestibular stimulation (termed bimodal neurons) [38**]. By summing their sensitivities to these two sensory inputs, unimodal and bimodal cerebellar neurons encode explicit and separate representations of head and body motion, respectively [Figure 2a, [38**]].

Interestingly, the vestibular and neck inputs of bimodal rFN neurons sum linearly such that these neurons encode body motion, yet the processing of each individual modality is itself characterized by nonlinear operations. Specifically, neuronal sensitivities to proprioceptive and vestibular stimulation show tuning in response to static changes in head-on-body position. This is illustrated in Figure 2b and c, which shows the responses of two typical bimodal neurons to sinusoidal vestibular (Figure 2b) and neck proprioceptive (Figure 2c) stimulation when the head was positioned at different angles relative to the body. The responses of 'cell 1' to dynamic vestibular and proprioceptive stimulation are most robust with the head centered on the body, while those of 'cell *n*' are most robust when the head is turned to the left. For a given neuron, the widths, means, and amplitudes of the two tuning curves are well correlated (compare Figure 2d and e). The observed similarity in tuning of vestibular and neck proprioceptive responses is significant since it probably underlies the ability of each neuron to robustly encode the motion of the body in space; the responses of bimodal neurons sum linearly during combined stimulation as a result of the coherence in tuning between the two sensory cues. The relationship between this nonlinear processing of each modality and the reference frame transformation of vestibular inputs from head-centered to body-centered also known to occur in the rFN [39,40] requires further investigation. This will be an important area of research, since the transformation of the original vestibular input from its native reference frame (i.e. head) into a body reference frame is ultimately required for accurate motor control and sensory perception.

The vestibular system and the encoding of self-motion: reafference versus exafference

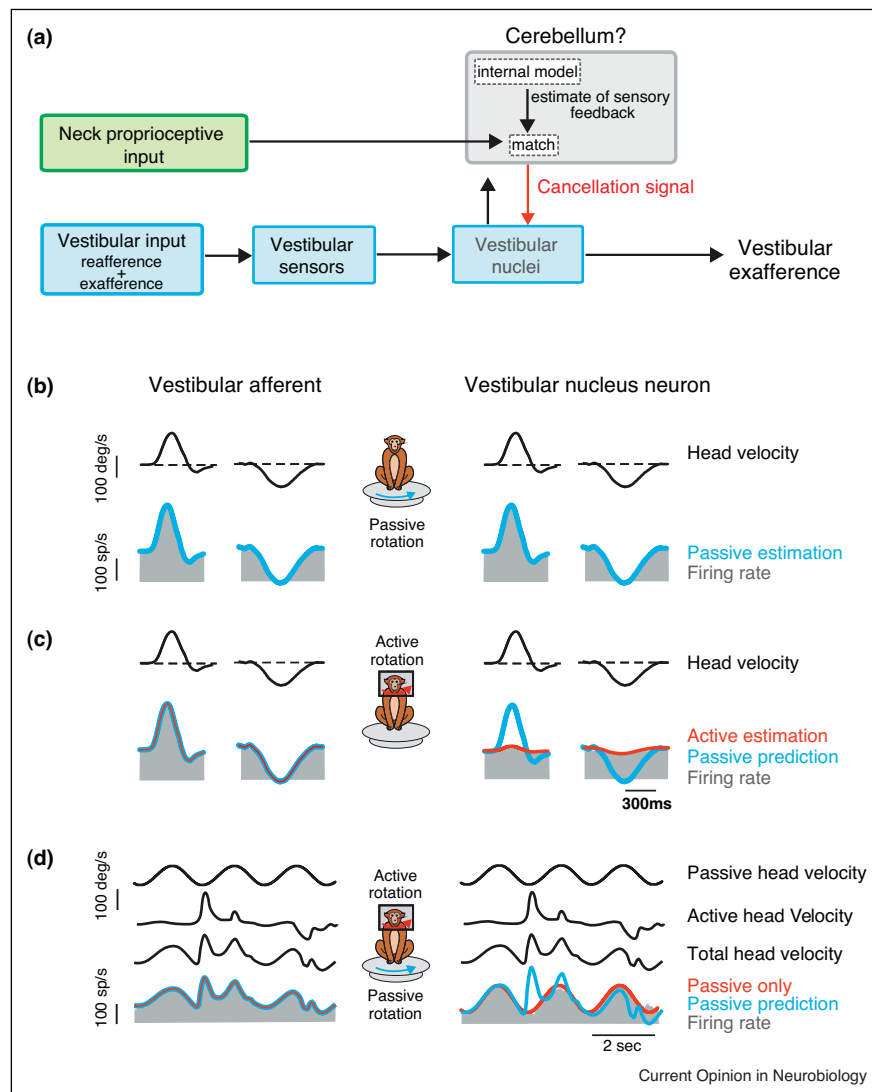
Thus far I have only considered neural representations of self-motion in response to passive movements. However, during daily activities such as walking and running, self-motion is also the result of voluntary movement. Notably, in this case the brain has access to its own estimate of self-motion by means of the motor command that is produced to make the movement. As a result, during voluntary self-motion, an additional cue (i.e. a motor efference copy signal) is available for integration with existing multisensory cues to compute an internal estimate of self-motion.

Recent studies in rhesus monkey have furthered our understanding of how the brain combines multimodal information to create a neuronal representation of

self-motion during voluntary movements [Figure 3a]. While vestibular afferents similarly encode active and passive self-motion [left column, Figure 3b and c; canal afferents: [5,31], otolith afferents: [32]], neurons at the first central stage of vestibular processing (i.e. in the vestibular nuclei) discriminate between active and passive motion. Notably, vestibular nuclei neurons that control posture and contribute to self-motion perception (i.e. Vestibular-Only (VO) neurons) – respond far more

robustly to passive movements than to self-generated head motion [right column, Figure 3b and c]. On average, VO neurons are ~70% less responsive to active than passive head motion [33,36]. Additionally when self-motion is the result of both active and passive motion, vestibular afferents reliably encode head in space motion, while their target VO neurons in the vestibular nuclei can respond selectively to only the passive component of head motion [compare left and right columns, Figure 3d].

Figure 3



Selective encoding of exafference during self-motion: computations to suppress the encoding of active motion. (a) Current model of the proposed mechanisms for the computation of vestibular exafference. Neck proprioceptive inputs are compared with the expected sensory consequence of neck motor command (internal model) in a putative matching center in the cerebellum. If these signals match, a cancellation signal is sent to VO neurons in the vestibular nuclei to remove exafference. (b, c, d) The responses of vestibular nuclei neurons but not vestibular afferents are attenuated during active self-motion. Comparison of the activity of an example vestibular afferent (left) versus an example vestibular nucleus neuron (right) during passive (b), active (c) and simultaneous active and passive self-motion (d) during which head in-space movement was the sum of the passive rotation generated by the turntable and voluntary head-on-body movements. The modulation of afferents was well described by a given afferent's sensitivity to passive motion (blue trace) while the modulation of vestibular nucleus neurons only encoded the passive component of the motion (red trace; prediction based on passive head motion only).

Data replotted with permission from Roy and Cullen [33,36].

It is noteworthy that, in contrast to the neuronal strategy used for combining vestibular–visual and vestibular–neck cues during passive self-motion, the mechanism underlying multimodal integration during active motion does not reflect a simple summation or reweighting of proprioceptive, vestibular and efference copy inputs. First, as noted above, vestibular nuclei neurons are not sensitive to activation of neck proprioceptors. Second, vestibular nuclei neurons are not directly influenced by the generation of a neck motor command (measured by quantifying neck torque) when the head is not allowed to move [36].

What mechanism underlies the suppression of the vestibular afferent input that represents active self-motion? Experiments in which the correspondence between intended and actual head movement were systematically controlled [36] have shown that a cancellation signal is generated only when the activation of neck proprioceptors matches the motor-generated expectation (i.e. the brain's internal model of the sensory consequences, Figure 3a). Accordingly, the interaction between vestibular, proprioceptive, and motor efference copy signals that occurs at the first central stage of vestibular processing cannot be described as a weighted linear sum of a neuron's responses to each cue, but instead is a more sophisticated computation that relies on an internal model of the expected relationship between the motor command and resultant sensory input (gray box, Figure 3a). The resultant suppression of expected self-motion information in the vestibular nuclei (termed refference) ensures that neurons selectively encode the unexpected component of the motion (termed exafference).

The 19th-century German philosopher and physicist, von Helmholtz [41], recognized that the ability to distinguish self-generated sensory events from those that arise as a result of changes in the external world is essential for perceptual stability and accurate motor control. Von Holst and Mittelstaedt [42] furthered this view by proposing the 'Principle of Refference', a conceptual framework in which a copy of the expected sensory outcome of a motor command (i.e. refference) is subtracted from the actual sensory signal to create a perception of the outside world (i.e. exafference). For example, in the specific case of vestibular stimulation experienced during self-motion, the brain would need to eliminate vestibular input resulting from voluntary movement of the head in space. Thus the results of recent neural recording studies comparing responses to active and passive self-motion are striking in that they provide evidence that the brain indeed implements the Principle of Refference in order to distinguish unexpected from expected self-motion, and does so at the first central stage of vestibular processing.

Evidence suggesting that the nervous system uses an internal model to estimate the outcome of motor commands has been provided by behavioral and theoretical

studies that have characterized motor control. In everyday life, the nervous system must consider the body and the world as a coupled dynamical system with properties that constantly vary. For example, over time the strength of each of our muscles will change as a result of fatigue, exercise, injury, aging, and so on. Recent studies using velocity-dependent force fields [43], rotating (Coriolis) rooms [44] and inertial perturbations [45,46] continue to provide new insight into how the nervous system adapts and generalizes to ensure accurate performance. The cerebellum has long been associated with motor adaptation, and recent neurophysiological findings support hypotheses that the cerebellum controls limb and eye movements in a framework, consistent with an internal model [see [47] for reviews, [48]]. Notably, the cerebellum is thought to compute the mismatch between the predicted and actual sensory outcome of motor commands in order to make fine adjustments to the control of actions. Future work will be required to demonstrate whether these same principles apply to the internal models that underlie the multimodal integration of vestibular, proprioceptive, and motor signals to eliminate self-generated vestibular information (refference).

As emphasized above, the ability to distinguish between self-generated and passive self-motion is necessary to ensure perceptual stability and accurate motor control. Studies of vestibular processing have revealed that the discrimination of active and passive motion requires the integration of motor with sensory (i.e. proprioceptive) signals (Figure 3a). Moreover, the results of recent studies of visual processing suggest that the brain also combines motor signals with visual sensory inputs in areas that contribute to the perception of self-motion. For example, the responses of MSTd neurons to virtual self-movement (i.e. optic flow fields) are enhanced during steering tasks in which monkeys are trained to steer a straight-ahead course using global patterns of optic flow [49]. Similarly, in the visual pathway of the fly – an excellent model system for studying visual-motor transformations – the application of a neuromodulator typically released during flight induces velocity-dependent alterations in the gain of optic flow-processing neurons [50•]. Regarding this latter finding it has been proposed that it may be more efficient to invest more energy in sensory processing during self-motion (i.e. flight) than to waste energy on underperforming motor control, and a comparable constraint may apply to the visual pathways of the driving monkey. Thus, as is the case in early vestibular processing, the neural representation of self-motion in visual pathways during active motion is unlikely to be a simple reweighting of inputs. Future work aimed at understanding the brain's strategy for constructing estimates of self-motion needs to consider not only the rules by which multiple inputs are combined to produce neural estimates of self-motion, but also how the behavioral context defines the optimal computation.

Conclusions

This review outlines recent advances in our understanding of the neural encoding of self-motion. The vestibular system detects motion of the head, making an essential contribution to our subjective sense of self-motion and orientation relative to space. Recent experiments provide novel insights into how single vestibular neurons, as well as populations of neurons, encode head motion information at the earliest stages of vestibular processing. During everyday life, extra-vestibular cues – for example visual and/or proprioceptive information – also contribute to the construction of neural estimates of self-motion. In particular, important progress has been made towards understanding the neural mechanisms underlying two specific computations: i) The computation of a robust estimate of self-motion during passive movements when visual as well as vestibular cues are available and, ii) The computation of the motion of neighboring parts of the body (e.g. body versus head motion) during unexpected (passive) motion that is required to ensure stable posture and perception. Importantly, however, the computational principles used for combining multiple sensory cues to encode passive motion do not directly translate to understanding the neural encoding of active motion. While neurons appear to perform a linear/weighted summation of their multimodal inputs during passive self-motion, recent work emphasizes that the brain uses an alternative strategy characterized by an inherently non-linear matching operation to discriminate expected (active) from unexpected (passive) self-motion. The mechanism underlying this complex computation, which is essential for perceptual stability and accurate motor control, is still not well understood, but presents an exciting challenge for future work.

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