Non-linear sensory-motor transformations

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Function of the Vestibular System

Provide information about head motion relative to space and gravity to:

1) Stabilize the visual axis (VOR)
2) Maintain head and body posture (VCR and vestibulospinal reflexes)
3) Compute spatial orientation or ‘sense of balance’
4) Navigation

Semicircular canals
- sense angular rotation

Otoliths
- sense linear acceleration
Function of the Vestibular System

i. The VOR,

ii. Posture and balance, and

iii. Higher order vestibular processing
Function of the Vestibular System

i. The VOR,

ii. Posture and balance, and

iii. Higher order vestibular processing
Overview

Understanding how sensory pathways transmit information under natural conditions remains a major goal in neuroscience.

The vestibular system plays a vital role in everyday life, contributing to a wide range of functions from reflexes to the highest levels of perception and voluntary behavior.

Recent experiments have revealed that the sensorimotor transformations underlying postural control (i.e., via vestibulo-spinal reflexes) are characterized by significant and functionally significant non-linearities.
Sensorimotor transformations: Vestibulo-spinal Reflexes

1. Static Non-linearities
   - Boosting non-linearity in central vestibular neurons
   - Gain fields in the vestibulo-cerebellum

2. Dynamic Non-linearities
   - Suppression of Reafference and common strategies across systems
   - Learning in vestibulo-spinal reflex pathways
Recall from the last lecture:

Estimation of Gain versus Mutual Information

$$\text{MI} = \frac{-\log_2(\text{SNR}(f))}{\text{fr}}$$

Central cells are tuned for higher frequencies, but encode less information than afferents.

Massot, Chacron, and Cullen; 2011
Detection thresholds

Sadeghi, Chacron, Taylor, and Cullen; J Neurosci 2007
Comparison of Detection Thresholds

Behavioral Thresholds:

Grabherr et al, 2008: ~ 0.5 -1deg/s
Benson 1989: ~1deg/s

Cullen, Trends in Neuroscience 2012
Thus:

So far these results suggest that the detailed time course of vestibular stimuli encoded by canal afferents during rotations is not transmitted by central neurons.

Furthermore

- At first pass, our results suggest that higher vestibular pathways must integrate information from large (>20) central vestibular neuron populations in order to give rise to behaviorally observed detection thresholds.

- Notably, we assessed the quality of linear stimulus reconstruction by computing the coding fraction (Gabbiani, 1996; Rieke et al., 1996).

This raises the question: Is the assumption of linearity valid?
Sensorimotor transformations: Vestibulo-spinal Reflexes

1. Static Non-linearities
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Experiment: High pass, Low Pass, and Summed Noise
Central vestibular neurons respond nonlinearly to sums of noise stimuli.

Massot, Schneider, Chacron, and Cullen,
PLoS Biology 2012
In contrast, their afferent inputs respond linearly to sums of noise stimuli.

Massot, Schneider, Chacron, and Cullen,
PLoS Biology 2012
The central response nonlinearity is characterized by a strong (~50%) attenuation in neuronal sensitivity to low frequency stimuli when presented concurrently with high frequency stimuli.

The presence of a high frequency stimulus effectively ‘masks’ the coding of low frequency stimulus.
A comparable attenuation in neuronal sensitivity to low frequency stimuli is observed for sums of sinewaves (3 Hz + 17 Hz).
How do central vestibular neurons non-linearly Integrate their afferent input?
How do central vestibular neurons non-linearly integrate their afferent input?

Hypothesis: A static non-linearity in the input-output relationship of central neurons accounts for attenuation of low frequency responses.
Afferents display a nonlinear relationship between input head velocity and output firing rate.
Central neurons display a nonlinear relationship between input head velocity and output firing rate.

**Low Frequency Stimulus**

- **0-5Hz**
- **0-5Hz with 15-20 Hz**
- Linear fit

**High Frequency Stimulus**

- **15-20Hz**
- **15-20Hz with 0-5 Hz**
- Linear fit
How do central vestibular neurons non-linearly integrate their afferent input?

**Hypothesis:** A static non-linearity in the input-output relationship of central neurons accounts for attenuation of low frequency responses.
How do central vestibular neurons non-linearly integrate their afferent input?

We know the relationships between
i) afferent firing rate and head velocity, and
ii) central neuron firing rate and head velocity
How do central vestibular neurons non-linearly integrate their afferent input?

We know the relationships between
i) afferent firing rate and head velocity, and
ii) central neuron firing rate and head velocity

So, these relationships can be rescaled to plot the input-output relationship between:
afferent firing rate and central neuron firing rate
Central neurons display a static nonlinear relationship between their output firing rate and their afferent input.

Massot, Schneider, Chacron, and Cullen,
PLoS Biology 2012
Central neurons display a static nonlinear relationship between their output firing rate and their afferent input.

Note, curve obtained when low frequency is applied with high frequency has a lower slope. This occurs because the average central neuron firing rate is higher in this condition, than when the same stimulus is applied alone.
A simple model accurately predicts nonlinear central neuron responses to sums of low and high frequency stimuli.
With this model, we can now predict the % gain for different stimuli.

Higher frequency Maskers Produce greater Signal attenuation

Higher amplitude Maskers Also produce greater Signal attenuation

Massot, Schneider, Chacron, and Cullen,
PLoS Biology 2012
Thus the detailed time course of vestibular stimuli encoded by afferents during rotations is not transmitted by central neurons. This raises the question: Is the assumption of linearity valid?
Thus the detailed time course of vestibular stimuli encoded by afferents during rotations is not transmitted by central neurons. This raises the question: Is the assumption of linearity valid?

- Indeed it is not: We discovered a static boosting nonlinearity in the input-output relationship of central vestibular neurons accounts for this unexpected result.

- Notably, this nonlinear integration of afferent effectively extends the coding range of central neurons, and enables them to better extract the high frequency features of self-motion when embedded with low frequency motion during natural movements.
Functional Role of Central Vestibular Neurons

These neurons initiate vestibulo-spinal postural reflexes.

Stabilize posture during unexpected transient disturbances, or when falling, or locomotion on uneven surfaces.

These same neurons also likely transmit self-motion information to higher level areas that contributes to perception during everyday activities.

Note, however that self motion can be self-produced as well as externally applied....
Sensorimotor transformations: Vestibulo-spinal Reflexes

1. Static Non-linearities

   - Boosting non-linearity in central vestibular neurons
   - Gain fields in the vestibulo-cerebellum

2. Dynamic Non-linearities

   - Suppression of Reafference and common strategies across systems
   - Learning in vestibulo-spinal reflex pathways
Vestibular Cerebellum:
Nonlinear processing of vestibular and proprioceptive signals underlies the accurate computation of body motion

Question:
What information does the brain need to keep track of for you to keep your balance?
During passive self-motion,

Head and body motion are encoded in two distinct channels by the output neurons of the vestibular cerebellum

Unimodal neurons - respond to vestibular stimulation
   - encode head motion

Bimodal neurons - respond to vestibular and proprioceptive stimulation
   - encode passive body motion
Example Vestibulo-Cerebellar Neuron
Vestibular-only cell (Unimodal)

Brooks and Cullen, J. Neurosci., 2009
Example Vestibulo-Cerebellar Neuron
Vestibular+neck cell (Bimodal)

Brooks and Cullen, J. Neurosci., 2009
Brooks and Cullen, SFN 2007
Vestibular and neck inputs sum linearly

Unimodal cell

Bimodal cell

Head-on-body rotation

40 °/s

H_{on body} velocity

H_{space} velocity

B_{space} velocity

40 °/s

50 sp/s

Firing rate

50 sp/s

vestibular prediction

500 ms
Vestibular and neck inputs sum linearly

Unimodal cell

Bimodal cell

Head-on-body rotation

H_{on body} velocity

H_{space} velocity

B_{space} velocity

Firing rate
The **vestibular** responses of bimodal neurons depend on head-on-body position.
The **vestibular** responses of bimodal neurons depend on head-on-body position.
The **neck proprioceptive** responses of bimodal neurons also depend on head-on-body position.
Bimodal neurons encode **body motion**, and unimodal neurons encode head motion.

Brooks and Cullen, J. Neurosci., 2009
Neuronal representations of head versus body motion in the primate cerebellum

- Head motion is detected by the vestibular sensors
- No sensor directly encodes motion of the body in space
- However, humans can detect movement of the body and the head separately even in darkness (Mergner et al 1981).
- Body motion perception is thought to be a result the convergence of vestibular and neck proprioception signals
  1) Head motion encoded by VN neurons and uniimodal cerebellar neurons
  2) Body motion encoded by bimodal cerebellar neurons
Comparison of the proprioceptive and vestibular responses of bimodal neurons further reveals similar tuning in response to changes in head-on-body position.

Brooks and Cullen, J. Neurosci., 2009
This comparable tuning is required for bimodal neurons to encode body motion

In the case of the hypothetical neuron with overlapping tuning curves (panel A), the effect of head position is effectively cancelled.

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Brooks and Cullen, J. Neurosci., 2009
Vestibular Cerebellar Processing:
A nonlinear operation in which head-on-body position modulates the gain of vestibular and dynamic neck proprioceptive responses

Cullen, Current Opinion in Neurobiology, 2011
Consider the visual receptive fields of two neurons gain modulated (e.g., by eye position) in opposite ways without shifting.

- Eye position modulates the strength of response of the two input neurons, but does not cause them to shift.
- The summation of these two gain-modulated neural responses however can shift receptive fields in the output.
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- Eye position modulates the strength of response of the two input neurons, but does not cause them to shift.
- The summation of these two gain-modulated neural responses however can shift receptive fields in the output.
Thus comparison of the proprioceptive and vestibular responses of bimodal neurons further revealed that neurons show tuning in response to static changes in head-on-body position.

This raises the question: What is the functional significance of the observed tuning?

- To produce accurate motor control requires combining sensory signals with other postural information to transform the original sensory input from its native reference frame into another that is relevant to ongoing behavior.

- Vestibular sensory information is first encoded in a head reference frame because the sensors are located in the head. So, to generate appropriate postural responses, it is vital to integrate vestibular inputs with proprioceptive inputs.
Functional Role of Vestibulo-cerebellar Neurons

These neurons are a vital component of vestibulo-spinal postural reflexes, they project to multiple levels of the spinal cord.

Function: Integrate vestibular and proprioceptive inputs to ensure the generation of appropriate postural responses.

This is absolutely vital, since for the same vestibular input, the appropriate postural response will depend how the head is oriented relative to the body!

Again note, however that self motion can be self-produced as well as externally applied….
Sensorimotor transformations: Vestibulo-spinal Reflexes

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How does the vestibular system encode active self motion?
Differential processing of self-generated versus passive stimulation

1. Perceptual Stability: Helmholtz (1867) made the salient observation that tapping on the canthus of the eye, results in an illusionary shift of the visual world. However, we never see the world ‘shift’ when we make saccades.
Differential processing of actively-generated versus passive stimulation

1. Perceptual Stability: Helmholtz (1867) made the salient observation that tapping on the canthus of the eye, results in an illusionary shift of the visual world. However, we never see the world ‘shift’ when we make saccades.

2. Accurate Motor Control: In the vestibular system, the central neurons that receive direct afferent input, also project to motor centers to control vestibulo-ocular and -spinal reflexes.
Differential processing of self-generated versus passive stimulation

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For example, while vestibular-reflexes are essential for providing robust postural response to unexpected vestibular stimuli, they can be counter-productive when the goal is to make active head movements.
Differential processing of actively-generated vs. passive stimulation

1. *Perceptual Stability*: Helmholtz (1867) made the salient observation that tapping on the canthus of the eye, results in an illusionary shift of the visual world. However, we never see the world ‘shift’ when we make saccades.

2. *Accurate Motor Control*: In the vestibular system, the central neurons that receive direct afferent input, also project to motor centers to control vestibulo-ocular and -spinal reflexes.

3. Von Holst and Mittelstaedt (1950) proposed that an efference copy of the motor command was used distinguish between reafference and exafference.
Computing sensory reafference

This proposal is based on the idea that:

First, during active movements, the central nervous system sends a parallel “efference copy” of the motor command to sensory areas.
Computing sensory reafference

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As a result, this anticipatory signal is then subtracted from the incoming sensory signal to selectively remove that portion due to the animal’s own actions (i.e. reafference).
Computing vestibular reafference

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As a result, this anticipatory signal is then subtracted from the incoming sensory signal to selectively remove that portion due to the animal’s own actions (i.e. reafference).
Differential processing of actively-generated
Versus passive stimulation:
The vestibular system
Where and how does the brain make a distinction between active and passive head motion?

Balance and perception
Spinal cord (balance)
Higher Centers (perception)

Vestibulo-ocular Reflex

Vestibular afferents

Vestibular nuclei

PVP/FTN

VO
Experimental Setup

A. Spinal cord (balance) and Higher Centers (perception)

B. Diagram of a monkey sitting on a rotating platform

C. Rotation:
   - Active Head on Body
   - Passive Head on Body
   - Passive Whole Body

D. Translation:
   - Active Head on Body
   - Passive Head on Body
   - Passive Whole Body

Graphs showing rotation and translation velocity and acceleration over time.
First: Vestibular reafference is suppressed for head-in-space motion produced by active head-on-body rotations.
and for that produced by active body rotations.

I. Head-in-space motion produced by active head rotation

II. Head-in-space motion produced by active body rotation

Head-in-space velocity
Body velocity
Head-on-body velocity
Firing Rate
Moreover, neurons selectively encode **passive** motion during concurrent active/passive movements.

Roy and Cullen, J. Neurosci., 2001

Brooks and Cullen, under review
Where and how does the brain make this distinction between active and passive head motion?
Where and how does the brain make this distinction between active and passive head motion?
This distinction is not observed at the previous stage: Vestibular afferents similarly encode active and passive motion.

Regular Afferent

Irregular Afferent

Eq: \[ FR(t) = \text{bias} + g_v \dot{H}(t) + g_a \ddot{H}(t) \]
Where and how does the brain make this distinction between active and passive head motion?
During Passive Movements:
The Vestibular Sensors are Activated

Passive Whole-Body Rotation

Vestibular
During active movements:
Additional information is available for distinguishing between passive vs. active motion

1. Proprioception
2. Motor Command
3. Knowledge

Vestibular

Active Self-motion
Multimodal information is available from many sources that could potentially cancel vestibular information.
Cancellation of self-produced stimulation is not directly mediated by proprioceptive or by motor efference copy inputs.

Passive stimulation of neck proprioceptors

Generation of motor efference copy without head motion

Roy and Cullen, J. Neurosci., 2001
Roy and Cullen, J. Neurosci., 2004
Computing vestibular reafference

Active head movement

Motor command signal
Efference copy

Exafference

Sensor

Effector Muscle

Reafferece due to self generated motion

Vestibular reafference
Vestibular exafference
The current working model:
A central cancellation signal is produced if neck proprioceptor activation matches that expected as a result of the voluntary head movement.
The current working model:
A central cancellation signal is produced if neck proprioceptor activation matches that expected as a result of the voluntary head movement.
Test of the model:
There should be no cancellation if neck proprioceptive activation does not match that expected during the generation of an active head motion.

Brooks and Cullen, under review
Is this a Common Strategy among Sensory Systems?

Consider the question: *Why can’t you tickle yourself?*

Wolpert and colleagues developed a tickle robot to rigorously address this critical question.

**Condition 1:** the experimenter produces the stimulus to touch the participant’s left hand.

**Condition 2:** The participant self-produces the touch stimulus of his left hand using his right hand.
Is this a Common Strategy among Sensory Systems?

Condition 3: Introduction of a temporal or spatial mismatch (i.e. a delay or rotation, respectively) between the causal action and the resultant stimulation resulted in lower ratings of tickliness.

Blakemore et al., *J Cogn Neurosci.*, 1999
Neural Correlates of Sensory Cancellation

Human
For the same touch stimulus, activity in the right lateral cerebellar cortex showed a positive correlation with delay (i.e. more tickle).

Blakemore et al., *Neuroreport*, 2001

Electric Fish
Block EOD with curare, but the motor command that would normally elicit an EOD is still produced. When artificial experimental stimuli is paired with motor command, ELL neurons are modulated.

Bell., *Curr Opin Neurobiol*. 2001
Neural Correlates of Sensory Cancellation:

Together these studies suggest that the cerebellum is involved in signaling the sensory discrepancy between the predicted and actual sensory consequences of movements.

Consistent with the proposal that:

The cerebellum is involved in predicting the specific sensory consequences of movements, thereby providing the signal that is used to cancel the sensory response to self-generated stimulation.
The Big Open Question:

What mechanism support the comparison between sensory inputs and motor commands that are required for the distinction between active and passive motion at the level of the vestibular nuclei?
Support for the proposal that the cerebellum plays a role in the cancellation of vestibular reafference

1. Evidence from work in electric fish. The cerebellum-like electrosensory lobes provide the signal that is used to cancel the sensory response to self-generated stimulation (Bell and colleagues).

2. fMRI studies in humans Suggest that the cerebellum serves a similar role in the suppression of tactile stimulation during self-produced tickle (Blakemore, Wolpert and colleagues).

3. We have now begun to study whether the vestibular cerebellum might play a role in the cancellation of vestibular reafference.
The Vestibular Nuclei:
Processing is convergent and multimodal

Cortical Inputs
- parietoinsular vestibular cortex
- premotor area 6, 6PA,
- cingulate cortex areas 23cd, 23cv,
- somatosensory area 3a,
- intraparietal sulcus area 2v
- superior temporal cortex

Ocularmotor Inputs
- reticular formation
- nucleus prepositus hypoglossi

Cerebellar Inputs
- Fastigial
- Anterior Vermis

Vestibular Inputs
- semicircular canal afferents

Neck Proprioception
- via central cervical nucleus
During active motion, Unimodal Neurons no longer encode head-in-space motion.
and Bimodal Neurons no longer encode Body motion

Brooks and Cullen, Current Biology 2013
Moreover, during concurrent active/passive movements unimodal neurons selectively encode passive head motion.
And, bimodal neurons selectively encode **passive body motion**
What is the functional significance of the differential processing of active vs. passively motion by the cerebellum?
Effect of cerebellar inactivation on VO neuron responses

Neuron now shows comparable responses to active and passive motion consistent with a role for the cerebellum in reafferent suppression.
Summary:

Our results suggest that while vestibular afferents robustly encode both active and passive head motion, central neurons respond preferentially to passive motion.

This raises the question: What mechanism governs the differential encoding of active vs. passive motion?
Summary:

Our results suggest that while vestibular afferents robustly encode both active and passive head motion, central neurons respond preferentially to passive motion.

This raises the question:
How is reafferent vestibular stimulation suppressed?

- A cancellation signal is generated when the activation of proprioceptors matches the motor-generated expectation.

- Moreover, this central cancellation mechanism is highly adaptable.

- Cerebellar output neurons provide an explicit representation of unexpected motion, that contributes to the cancellation of vestibular reafference.
Functional Role of Central Vestibular Neurons

Neurons at the first central stage of vestibular processing:

- Detect specific features via non-linear transformations of their afferent input
- Respond preferentially to passive (versus active) motion
Sensorimotor transformations: Vestibulo-spinal Reflexes

1. Static Non-linearities

   - Boosting non-linearity in central vestibular neurons
   - Gain-fields in the cerebellum

2. Dynamic Non-linearities

   - Suppression of Reafference and common strategies across systems
   - Learning in vestibulo-spinal reflex pathways
Current hypothesis:

Suppression of vestibular reafference occurs when proprioceptive feedback matches that expected as a result of the motor command (as during normal active movements)

If this is true,

then reafferent suppression should not occur when the relationship between motor commands and sensory reafference is altered.
Experiment: Change the relationship between motor commands and sensory reafference via application of resistive torque: Behavior

Brooks and Cullen, in preparation
The time course of Behavioral Adaptation

1) The animal learns to adapt by trial 10.
2) Head overshoots the initial trajectory once resistance is removed.

Experiment: Change the relationship between motor commands and sensory reafference via application of resistive torque: Behavior

Brooks and Cullen, in preparation
Experiment:  Change the relationship between motor commands and sensory reafference via application of resistive torque: Neurons

Brooks and Cullen, in preparation
The Time Course:
Of Behavioural and Neuronal Adaptation are Comparable

Peak head velocity

Neuronal sensitivity

T=26 head movements

T=33 head movements

% change from control active movements

Trial number
Current hypothesis:

Suppression of vestibular reafference occurs when proprioceptive feedback matches that expected as a result of the motor command (as during normal active movements):
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Neurons at the first central stage of vestibular processing:

- Detect specific features via non-linear transformations of their afferent input
- Respond preferentially to passive (versus active) motion
Functional Role of Central Vestibular Neurons

Neurons at the first central stage of vestibular processing:

- Detect specific features via non-linear transformations of their afferent input
- Respond preferentially to passive (versus active) motion
- Internal model updated with a few movements

Stabilize posture during unexpected transient disturbances, or when falling, or locomotion on uneven surfaces.

These same neurons also likely transmit self-motion information to higher level areas that contributes to perception during everyday activities.
Sensorimotor transformations: Vestibulo-spinal Reflexes

1. Static Non-linearities
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Non-linear sensory-motor transformations
Vestibulo-spinal pathways
Vestibular compensation:
Neurophysiology of Vestibular Compensation
Neural Correlates of Prosthetic Stimulation
Is the differential processing of active and passively generated vestibular stimulation a general feature of all early vestibular pathways processing?

No, Consider the neurons that produce the VOR
This differential processing by different cell classes in the vestibular nuclei is consistent with their functional roles:

- **Vestibulo-ocular reflexes**
  - Suppression of vestibular information when goal is to move in space
  - Suppression of vestibular information when goal is to redirect gaze (gaze shifts)

- **Vestibulo-spinal reflexes**

- **Vestibulo-ocular reflexes**
Gain field theory

Constant receptive fields with gain modulation

Shifting receptive fields (deg)