Encoding and learning of movements by Purkinje cells of the cerebellum

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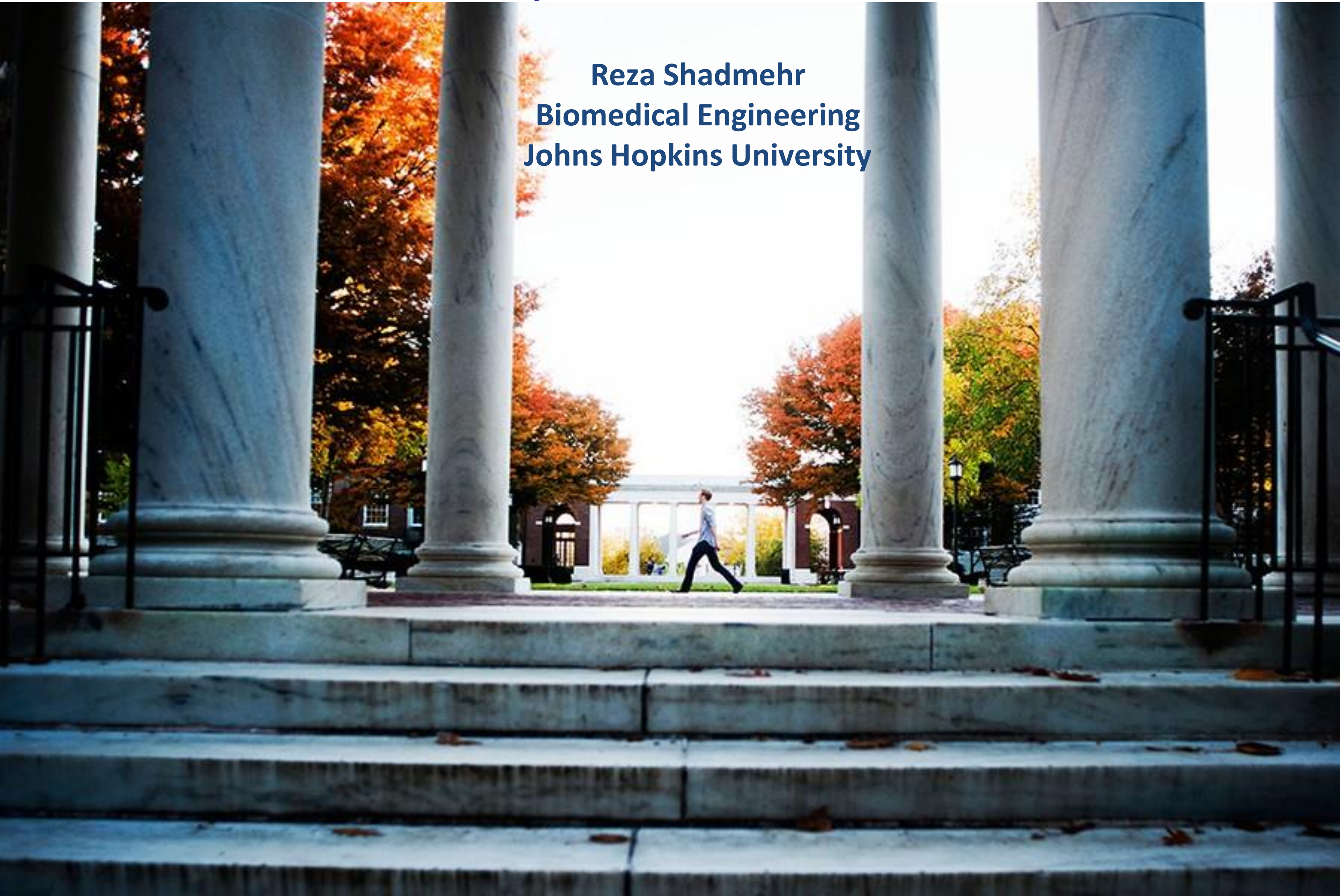
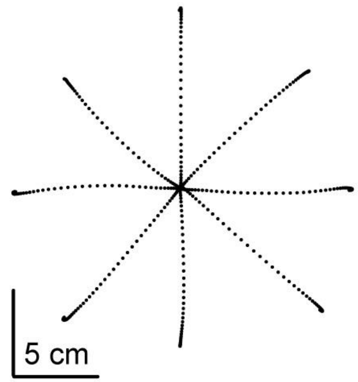
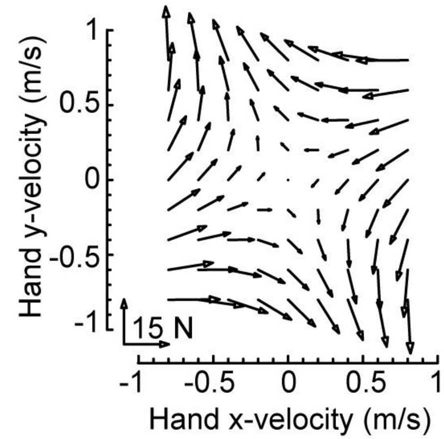


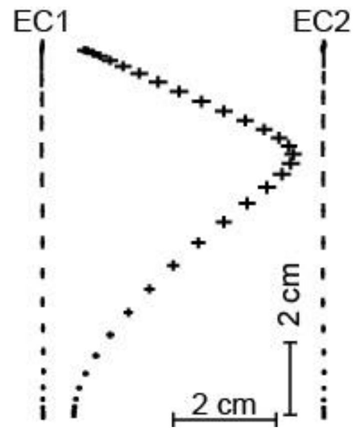
The force field paradigm

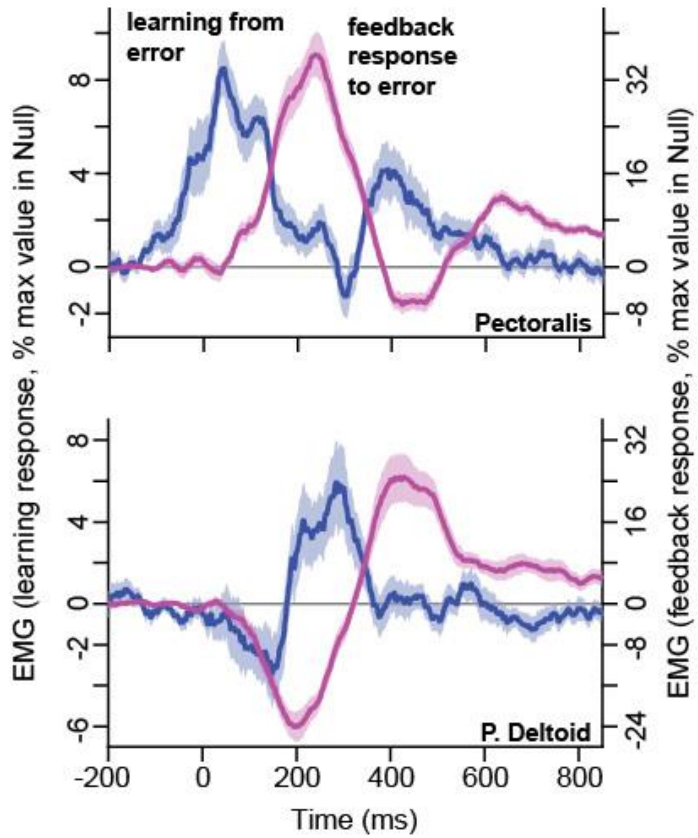




Shadmehr and Mussa-Ivaldi (1994)

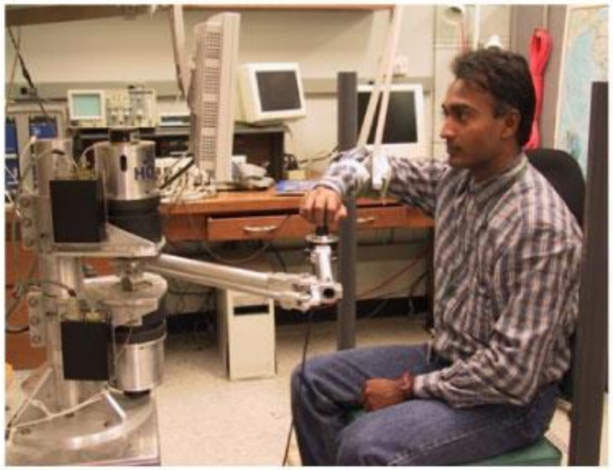
Reflex-generated error correction system as a teacher for the motor learning system

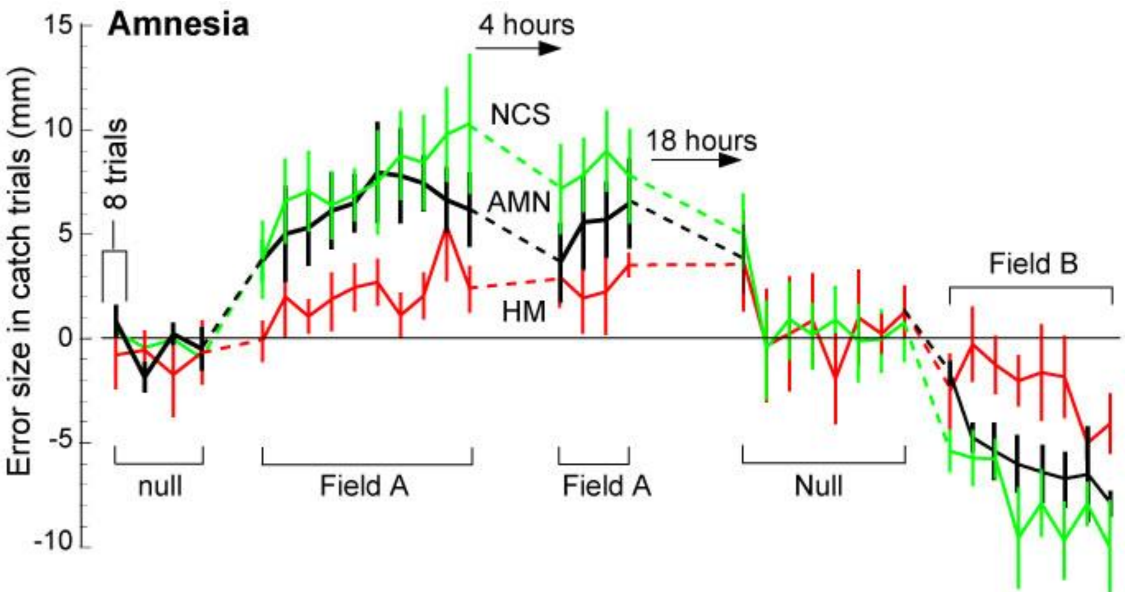




Albert and Shadmehr (2016)

The cerebellum as a crucial site for adaptation





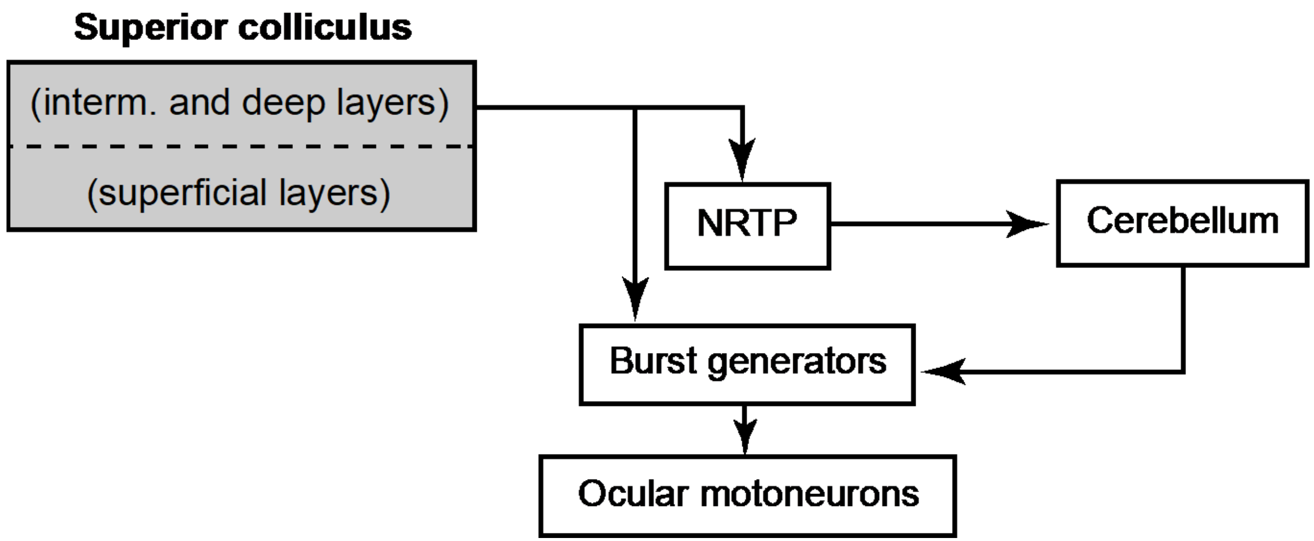
Shadmehr, Brandt, Corkin (1998); Smith and Shadmehr (2005)

Summary

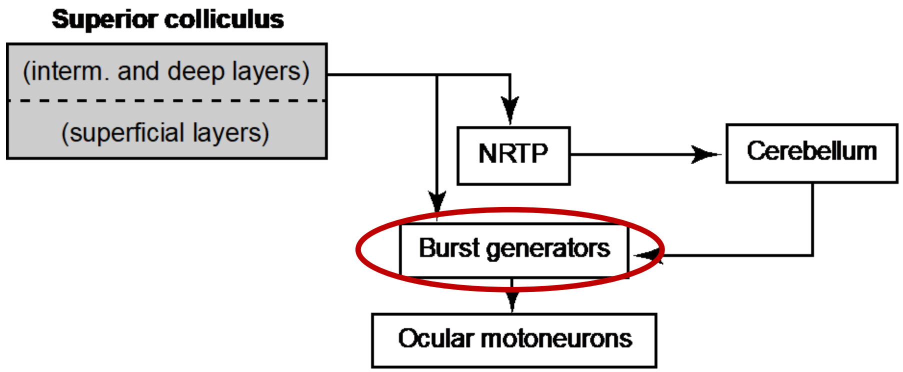
1. When we move an object, we need to predict and compensate for the physics of that object. Otherwise, our limbs will not move as we intended to.
2. With practice, our brain learns physics. This learning appears to depend on a teacher: the reflex generated feedback system.
3. The learning appears to depend on the cerebellum, as patients with basal ganglia disorders and temporal lobe disorders generally learn normally.

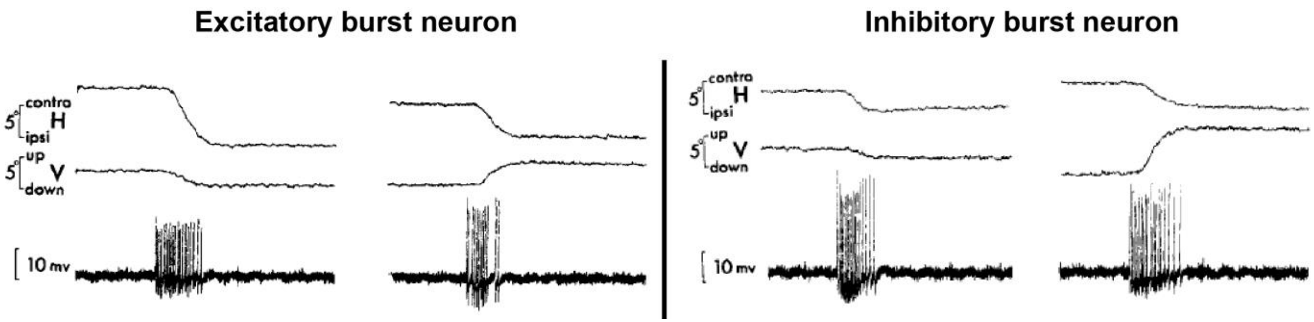
Plan

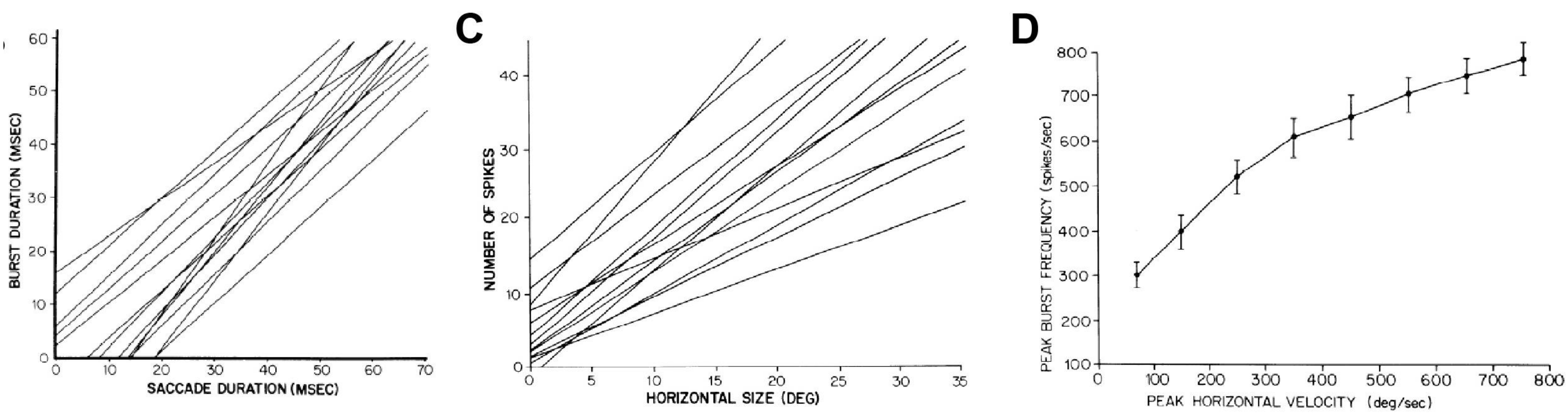
- Figure out how the cells in the cerebellum encode a movement.
- Figure out how this encoding changes with experience of error.


Superior colliculus
(interm. and deep layers)
(superficial layers)
NRTP
Cerebellum
Burst generators
Ocular motoneurons

Discharge of burst generator neurons exquisitely varies with movement kinematics

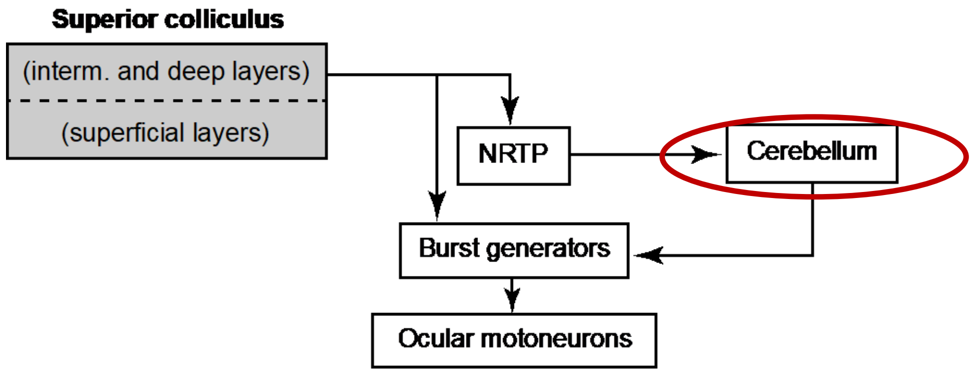


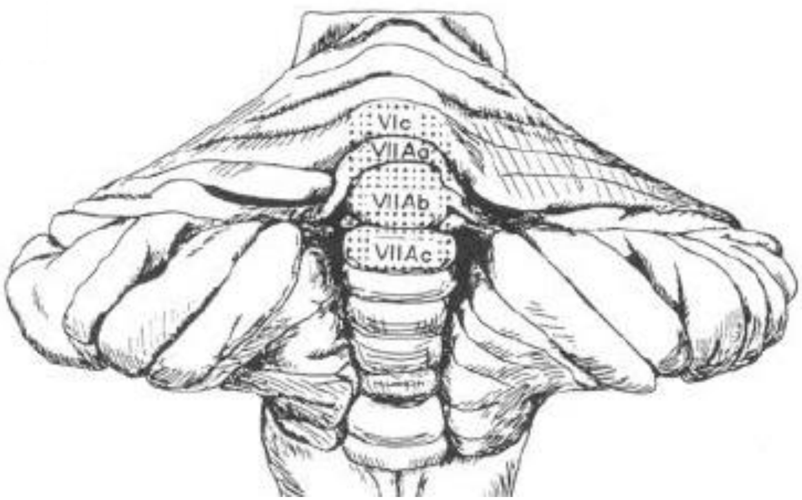




Strassman et al. (1986), Scudder et al. (1988)

Input to the cerebellum is via “mossy fibers”





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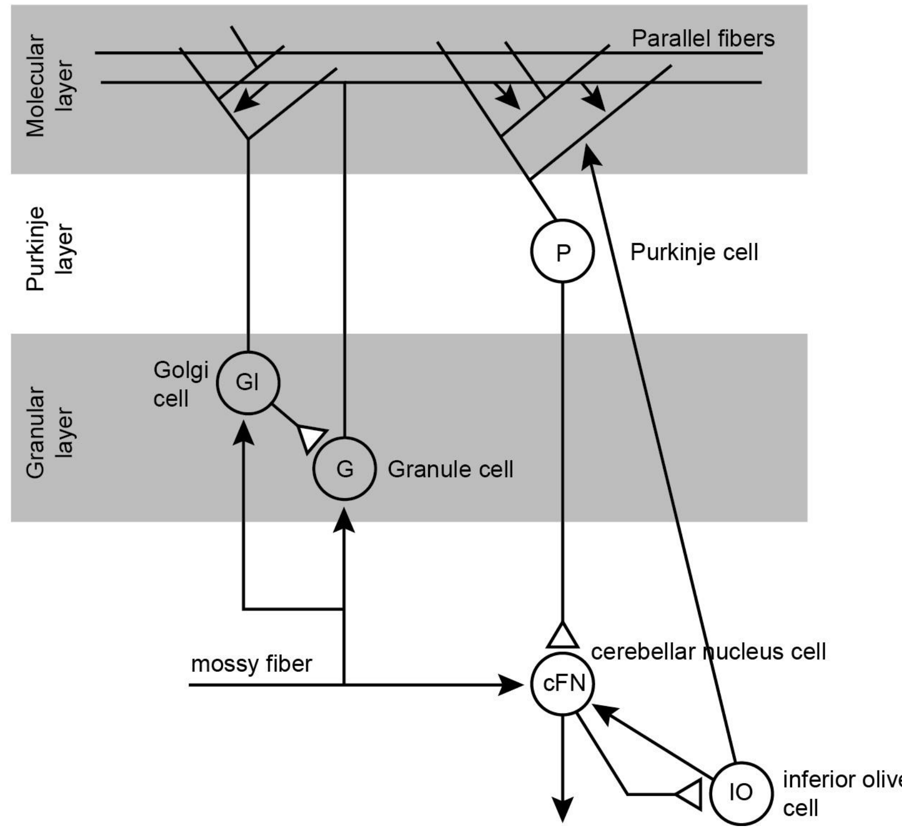
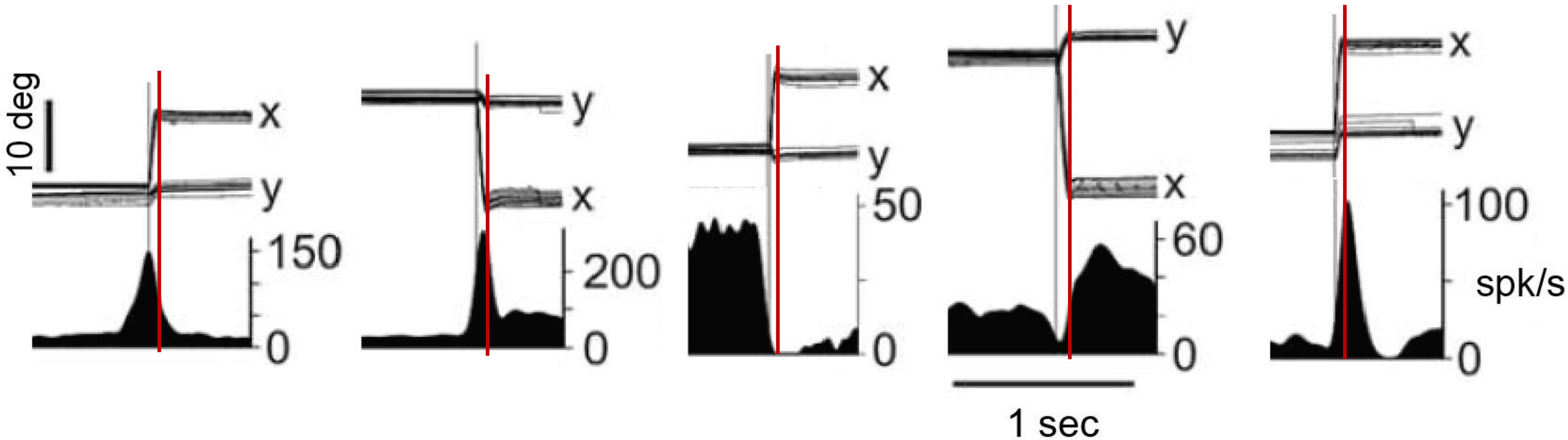


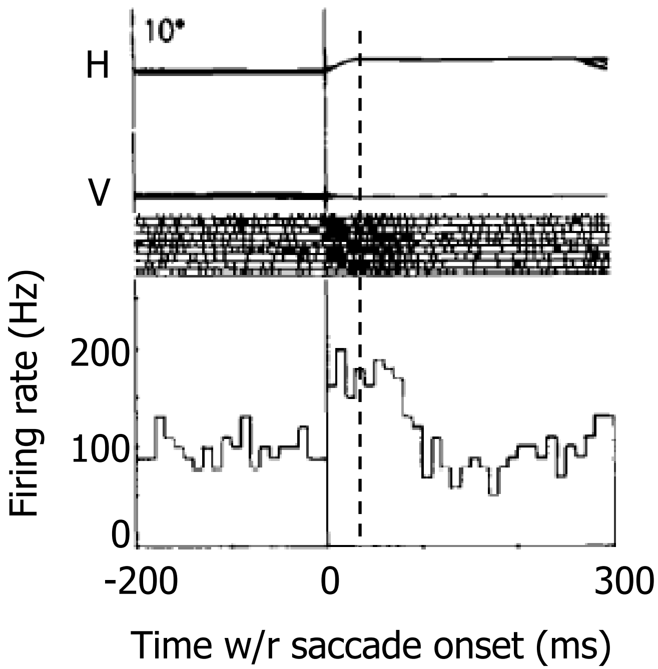
Activity of mossy fibers during saccades does not look like a copy of the motor commands



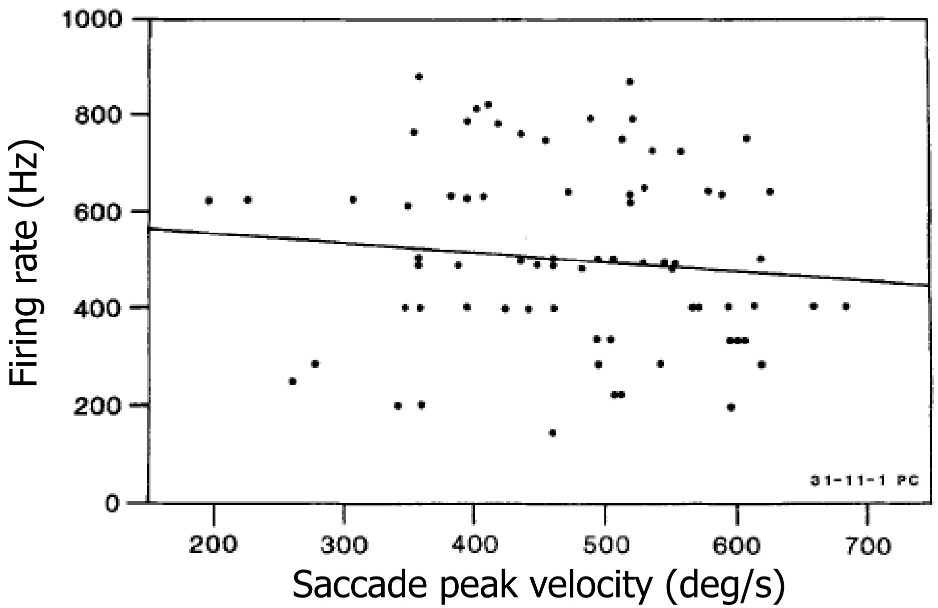
- Input to the oculomotor vermis of the cerebellum shows activity that bursts or pauses with saccades.
- The burst and pause durations appear to be generally longer than saccade durations.

Prsa et al. (2009)

Activity of Purkinje cells during saccades: no obvious coding of speed

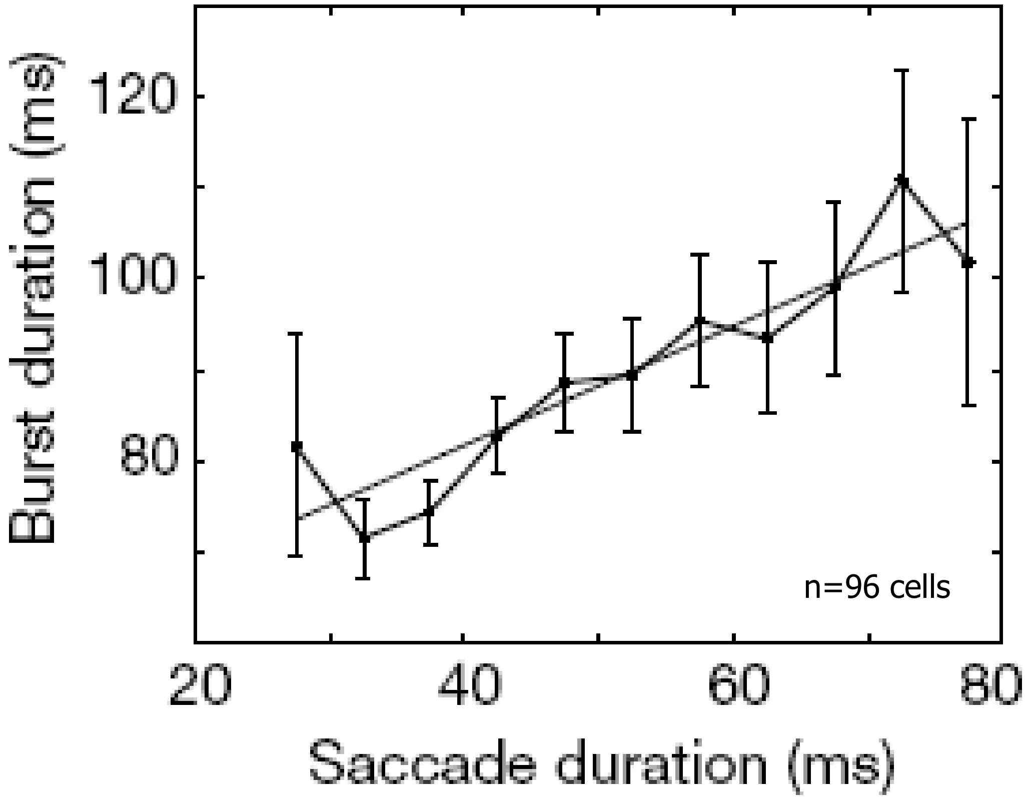


Ohtsuka and Noda 1995



Helmchen and Buttner 1995

A relationship between burst duration of P-cells and saccade duration at the population level



Thier et al. *Nature* (2000)

Summary

Execution of accurate saccades depends critically on the cerebellum, as evidenced by the deficits observed in patients and lesion studies.

These observations have suggested that discharge of Purkinje cells (P-cells) should be sensitive to the state of the eye during a saccade (e.g., its speed or direction).

This encoding has remained a long-standing puzzle: discharge typically lasts longer than a saccade, and shows little modulation with respect to saccade speed or direction.

Theoretical idea

Motor memories may be anatomically organized based on a tuning for errors. An error-addressable memory.

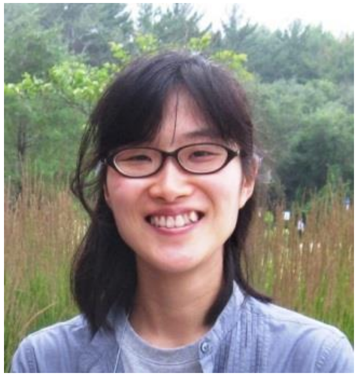
Herzfeld et al. (2014)

David Herzfeld
Johns Hopkins

Neurophysiological data

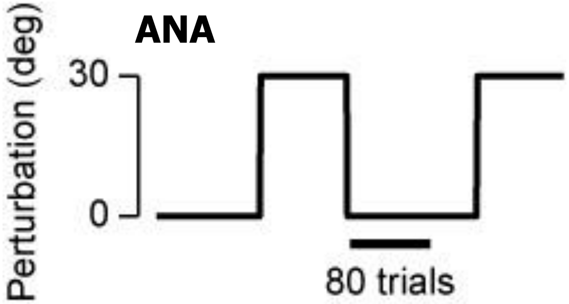
Herzfeld et al. (2015)

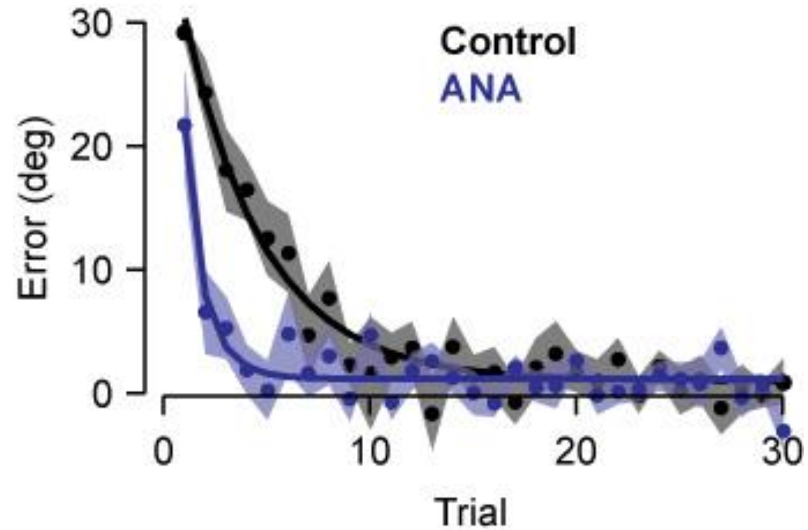
Herzfeld et al. (2018)

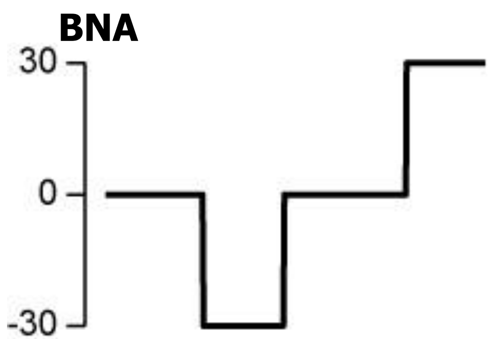


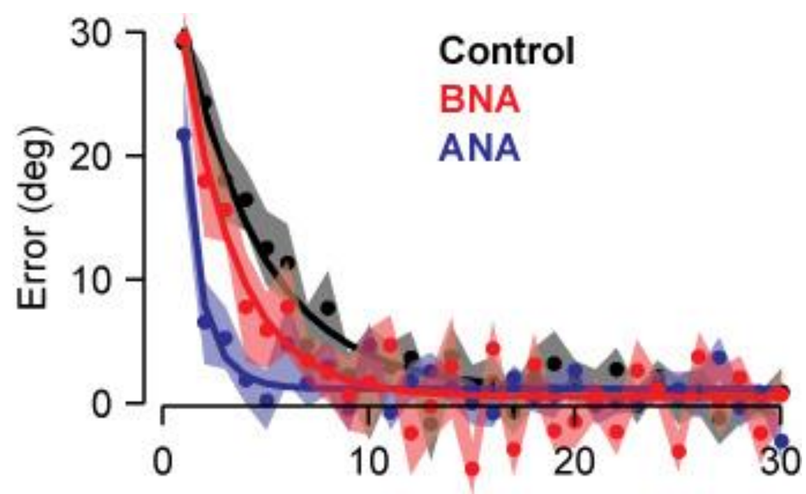
Yoshiko Kojima **Robi Soetedjo**
University of Washington

Two old problems in learning theory: savings and meta-learning

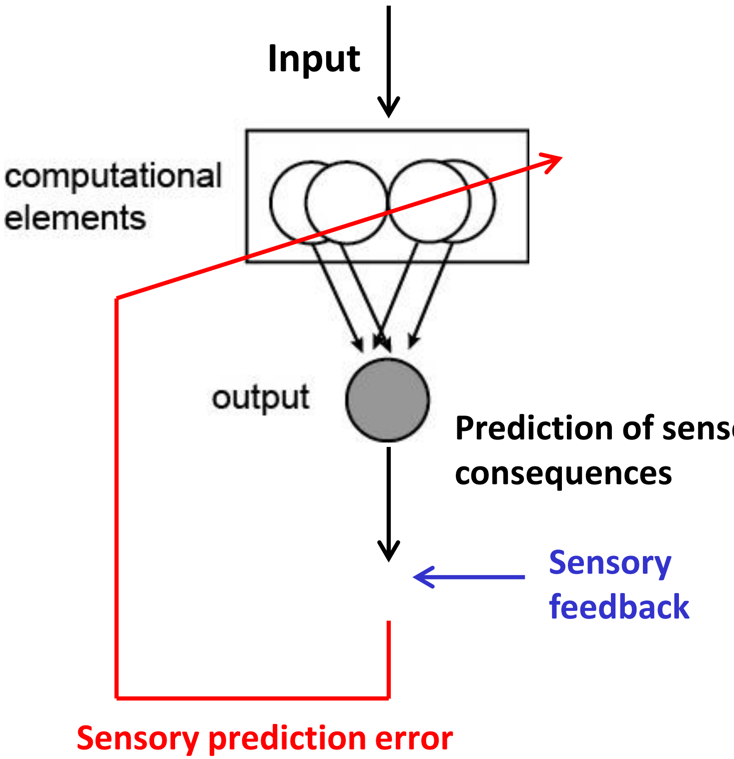








Idea: population coding based on a preference for error

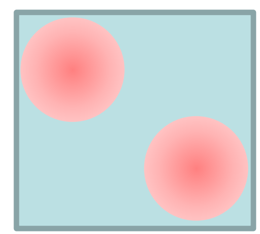


How are sensory prediction errors encoded in the nervous system?

The same way that sensory events are encoded: cells have a preference for direction of error, etc.

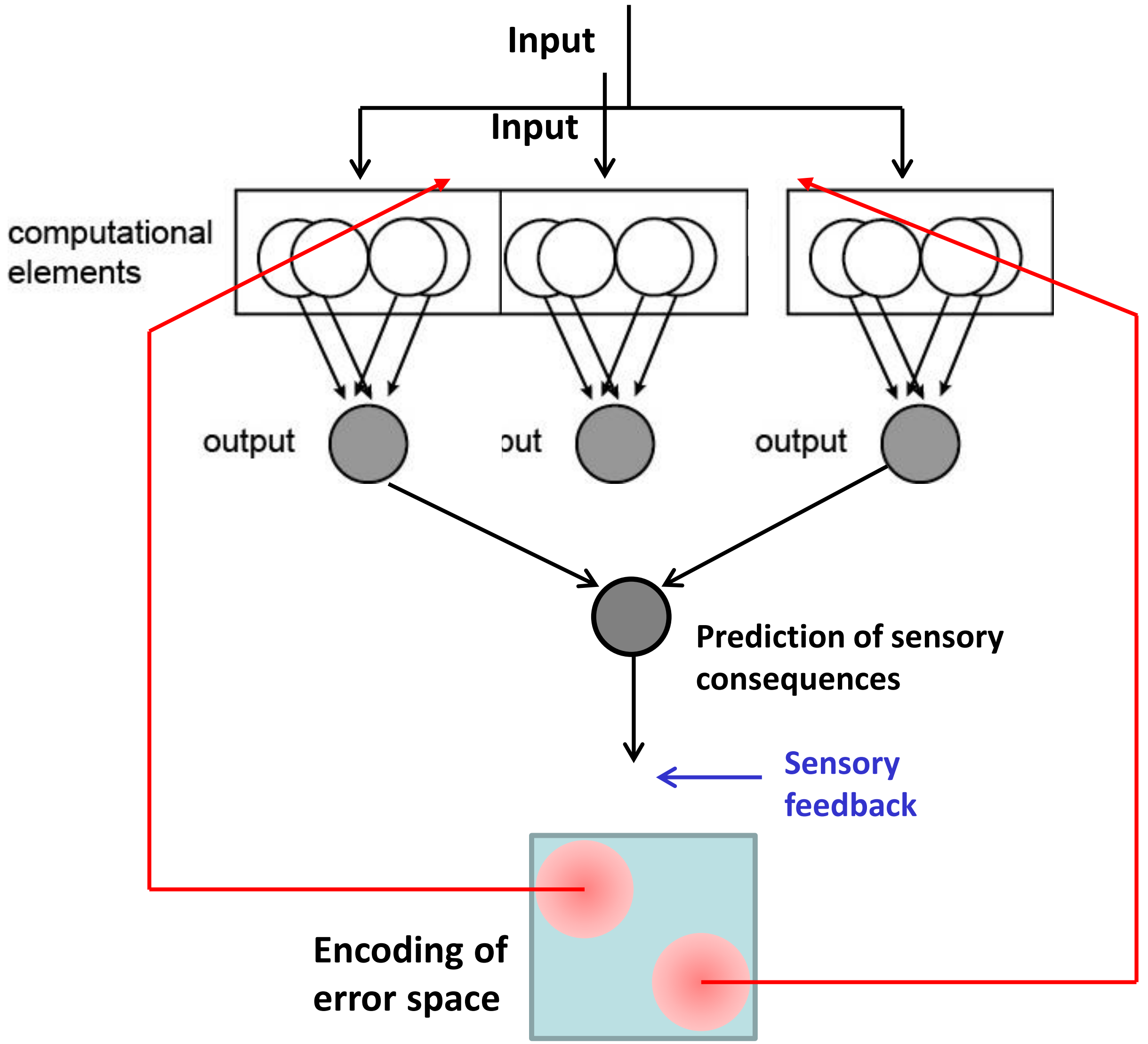
Example: if you throw a ball and it ends up to the right of the basket, that would be the preferred error for some cells, but the anti-preferred error for other cells.

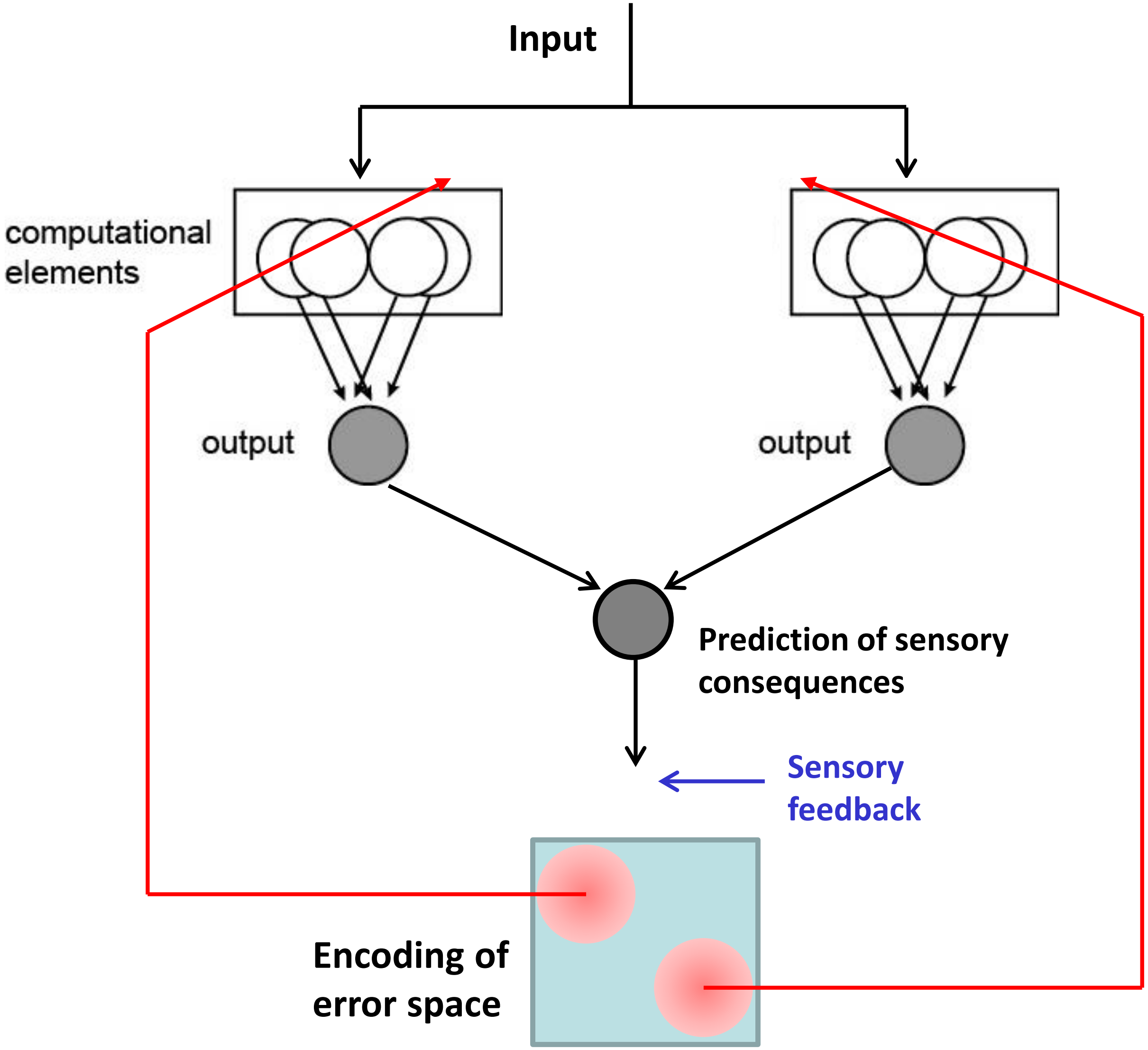
Encoding of error space

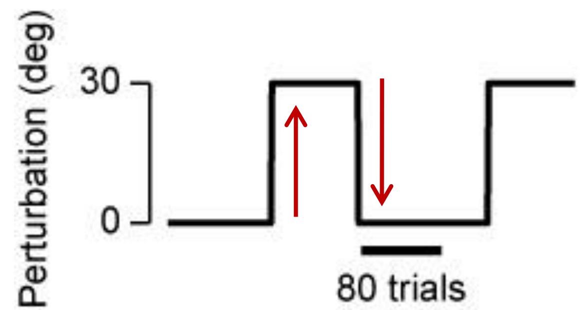


Herzfeld et al. (2014)

Idea: population coding based on a preference for error

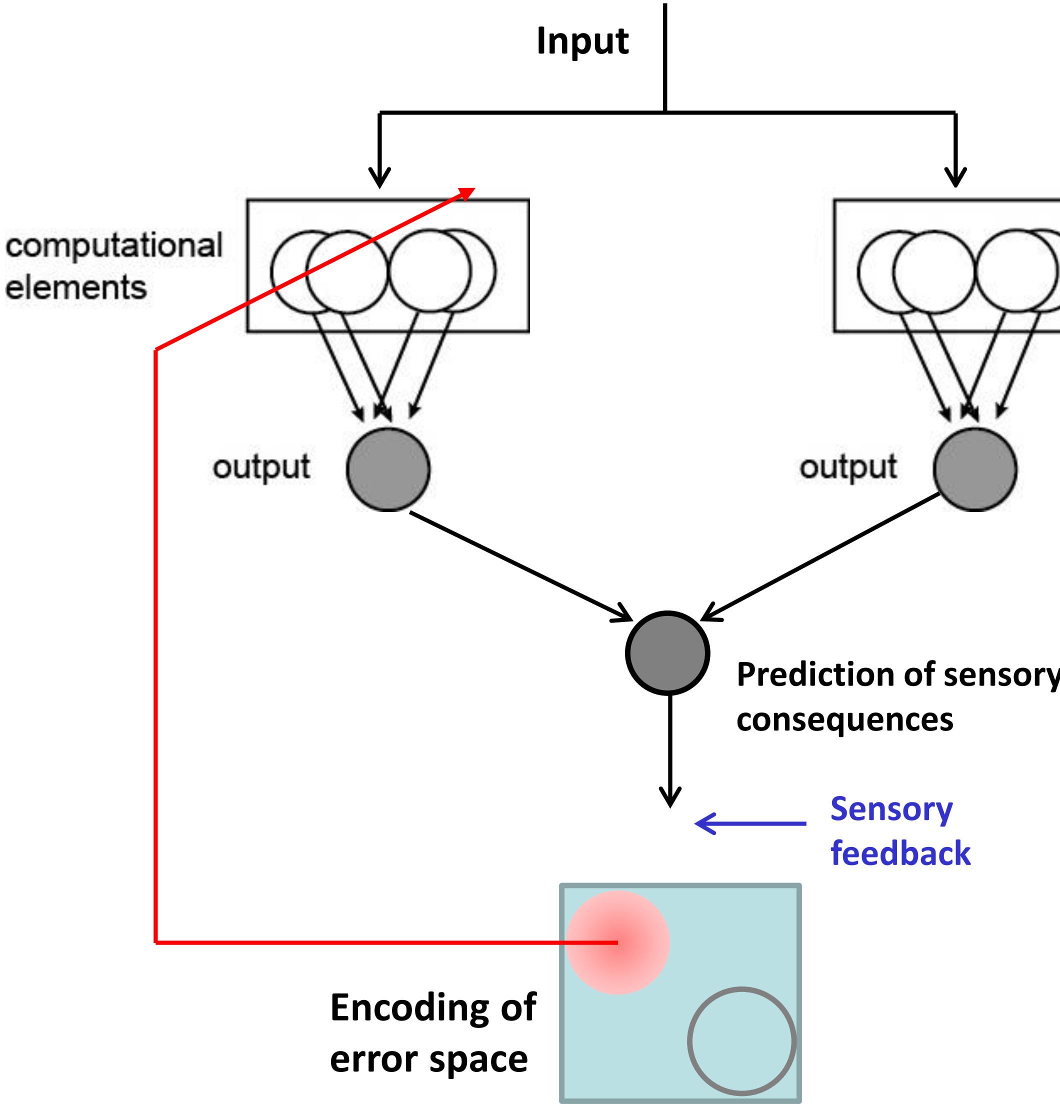


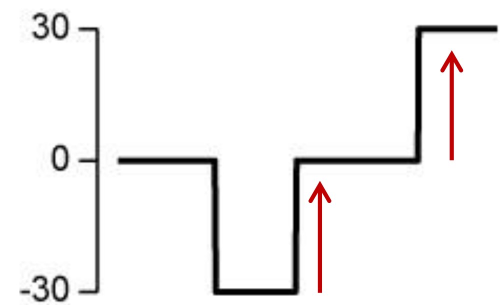




Reversal of error does not erase memory.

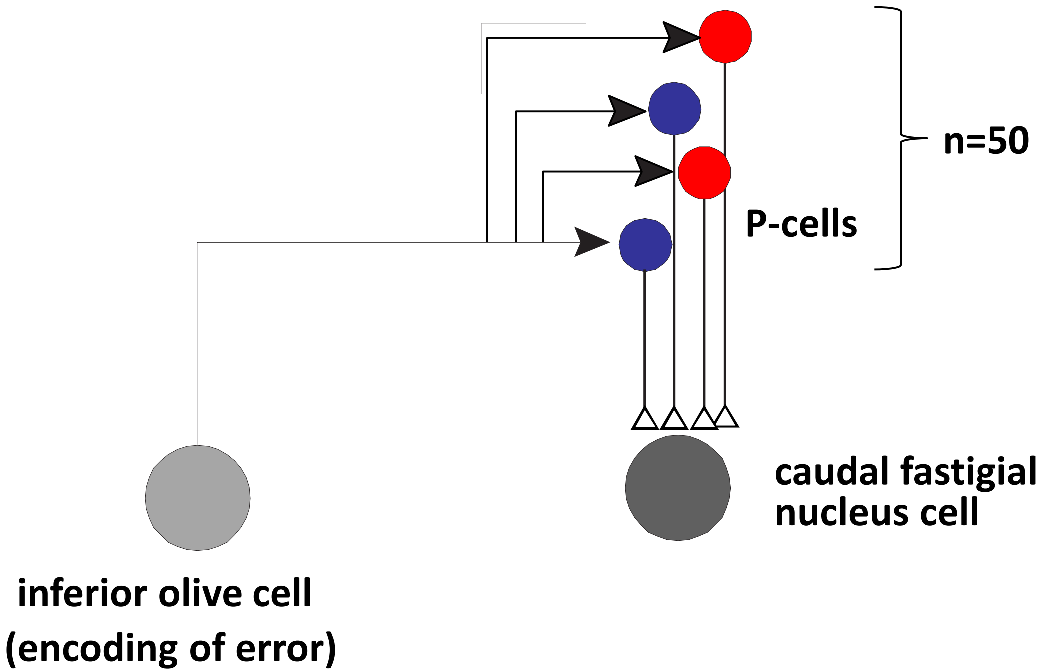
Adaptation and washout produce learning in two anatomically separate groups of cells.





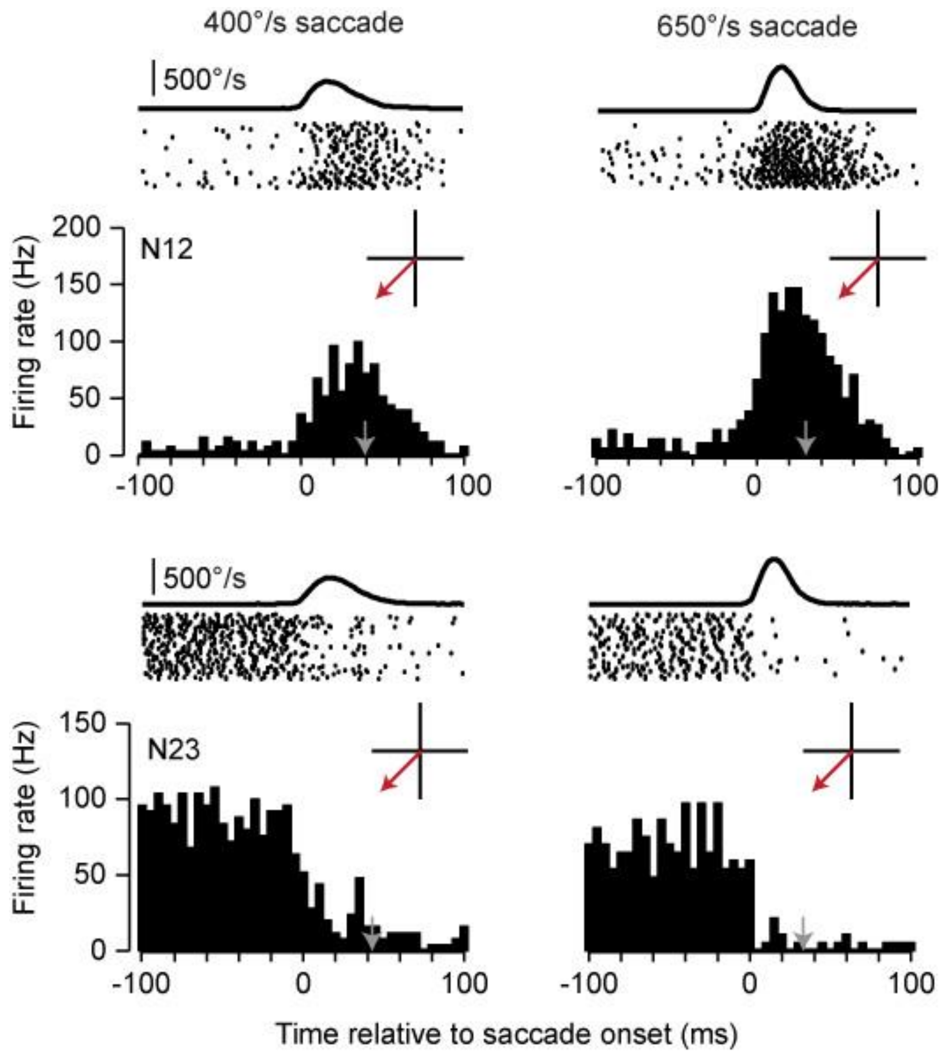
Meta-learning occurs because learning in two different circumstances shares a common pattern of errors. The common error engages the same micro-cluster of cells, and learning transfers from one context to another.

Idea: population coding in the cerebellum based on a preference for error

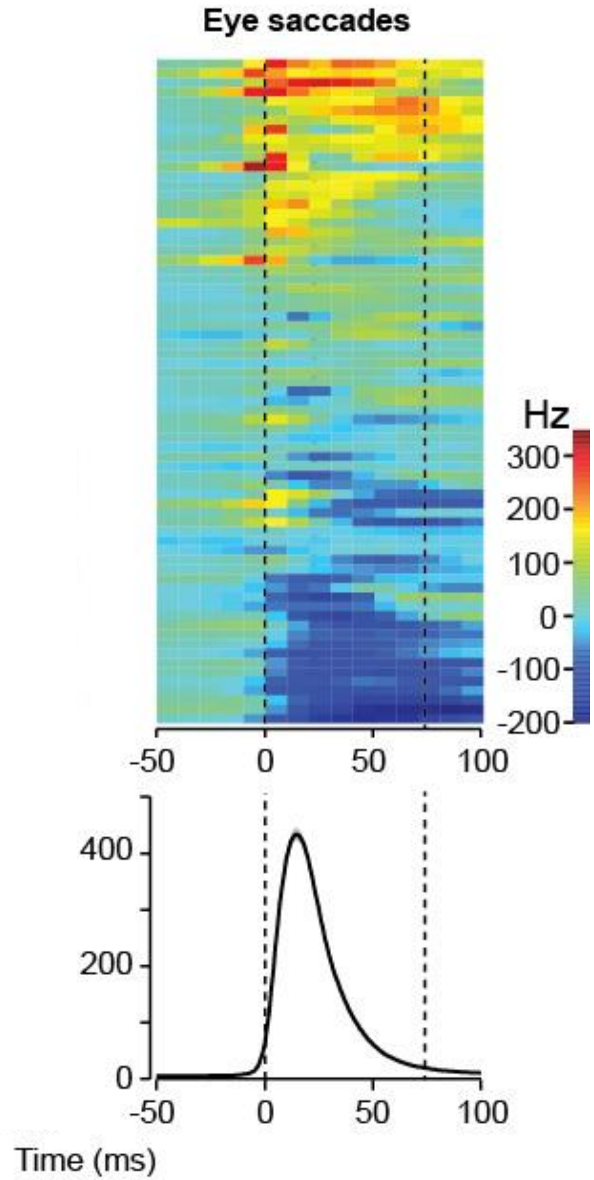


Bursters

Pausers

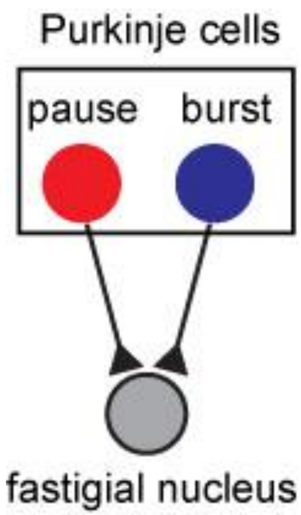


The diversity of activities in P-cells is not unique to saccades. A similar diversity is present for wrist movements.

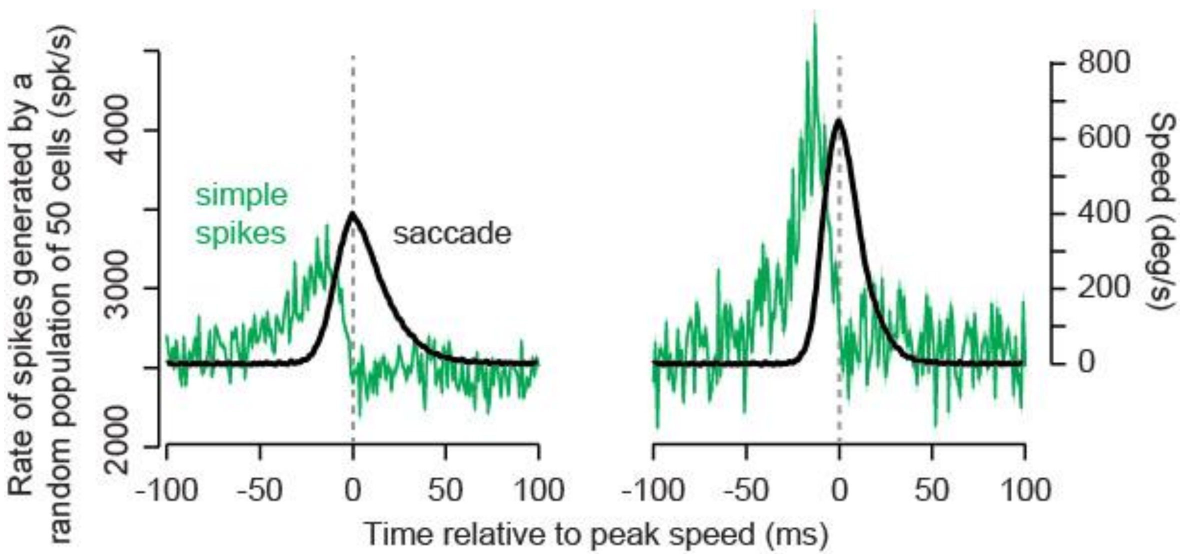


Ishikawa et al., 2014
Herzfeld et al., 2015

What does a cell in the deep cerebellar nucleus see?



Count the total number of spikes generated by the population in each millisecond of time.

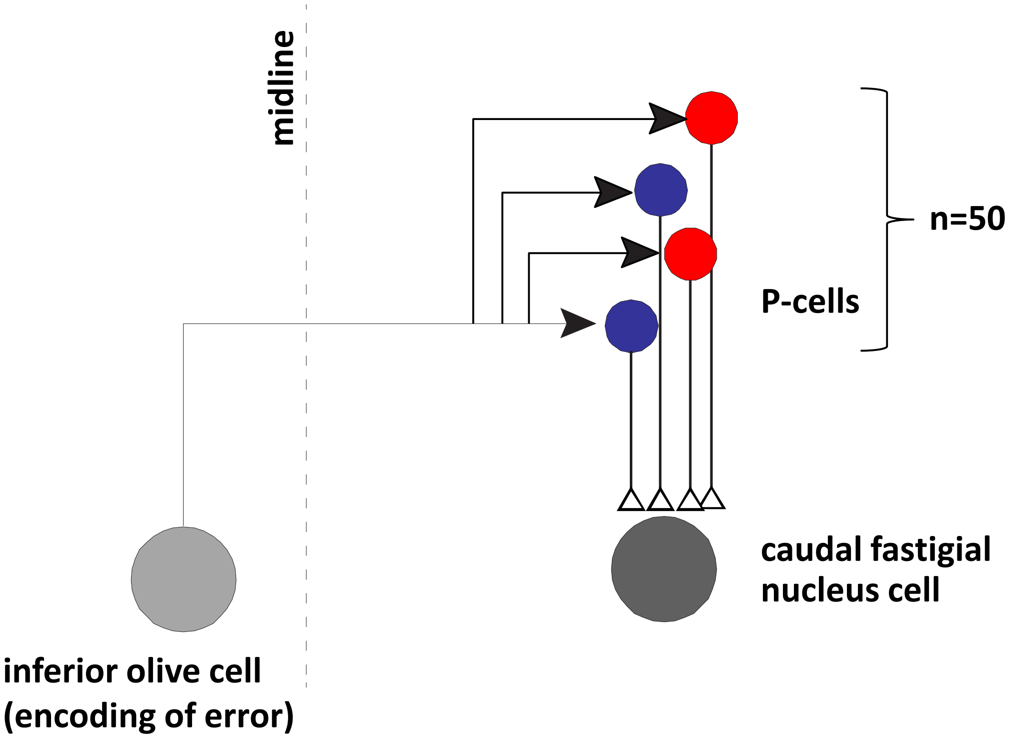


The converging inhibition at the fastigial nucleus resembles a prediction of future movement of the eye.

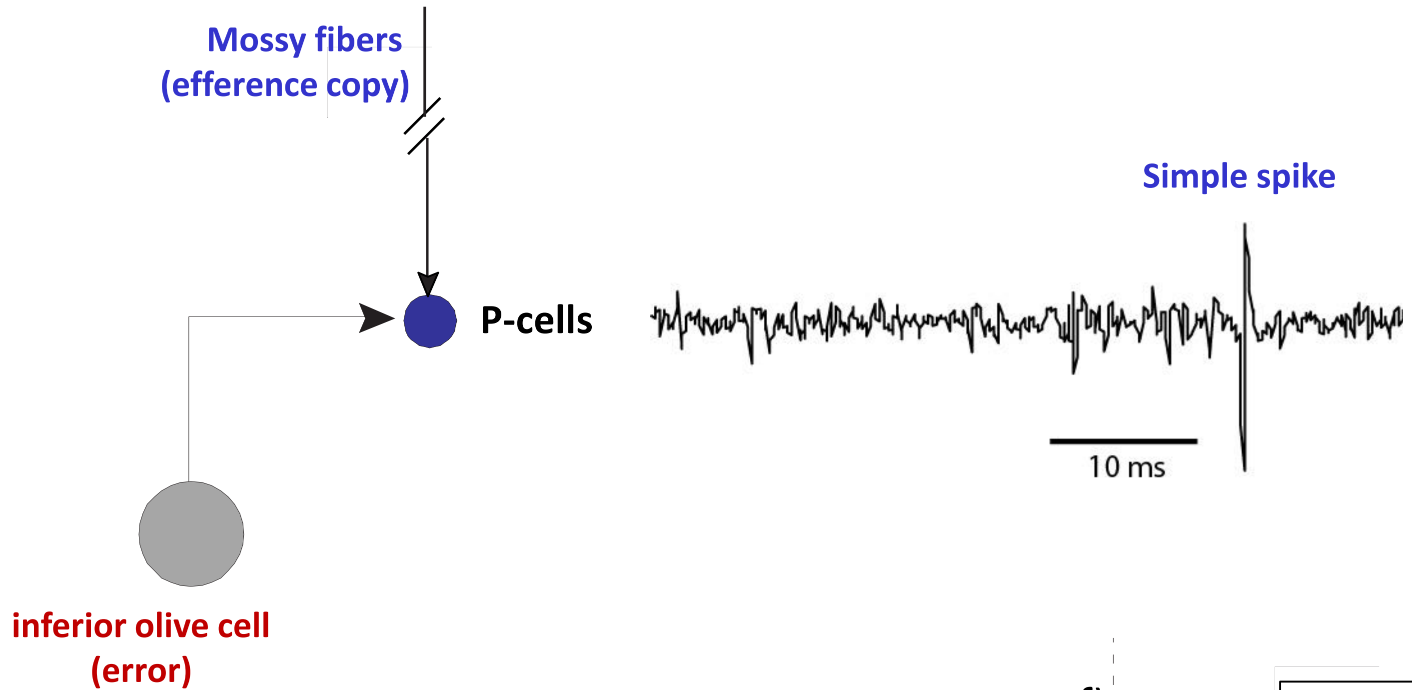
Main idea: the coding of saccade kinematics is not in the firing of individual P-cells, but in the population induced inhibition that is imposed on the target cell in the deep cerebellar nucleus.

What characterizes the population of P-cells that project onto the same nucleus cell?

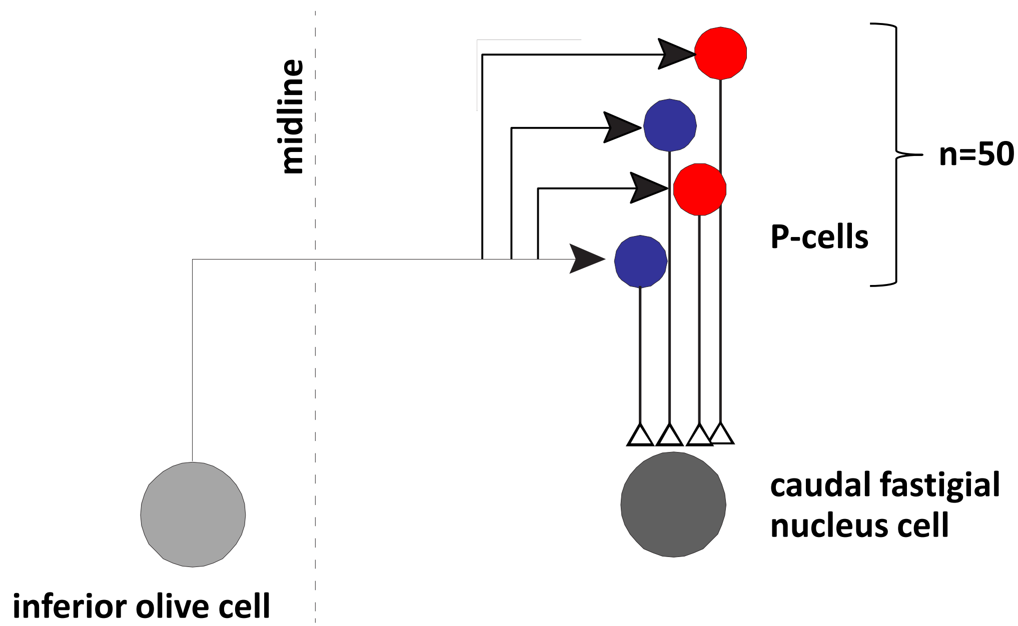
Hypothesis: the P-cells that project to a nucleus neuron are not selected randomly, but share a common input from the inferior olive (a common error signal).



Simple and complex-spikes of Purkinje-cells

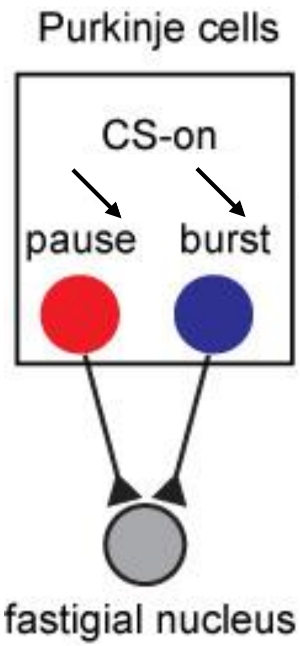


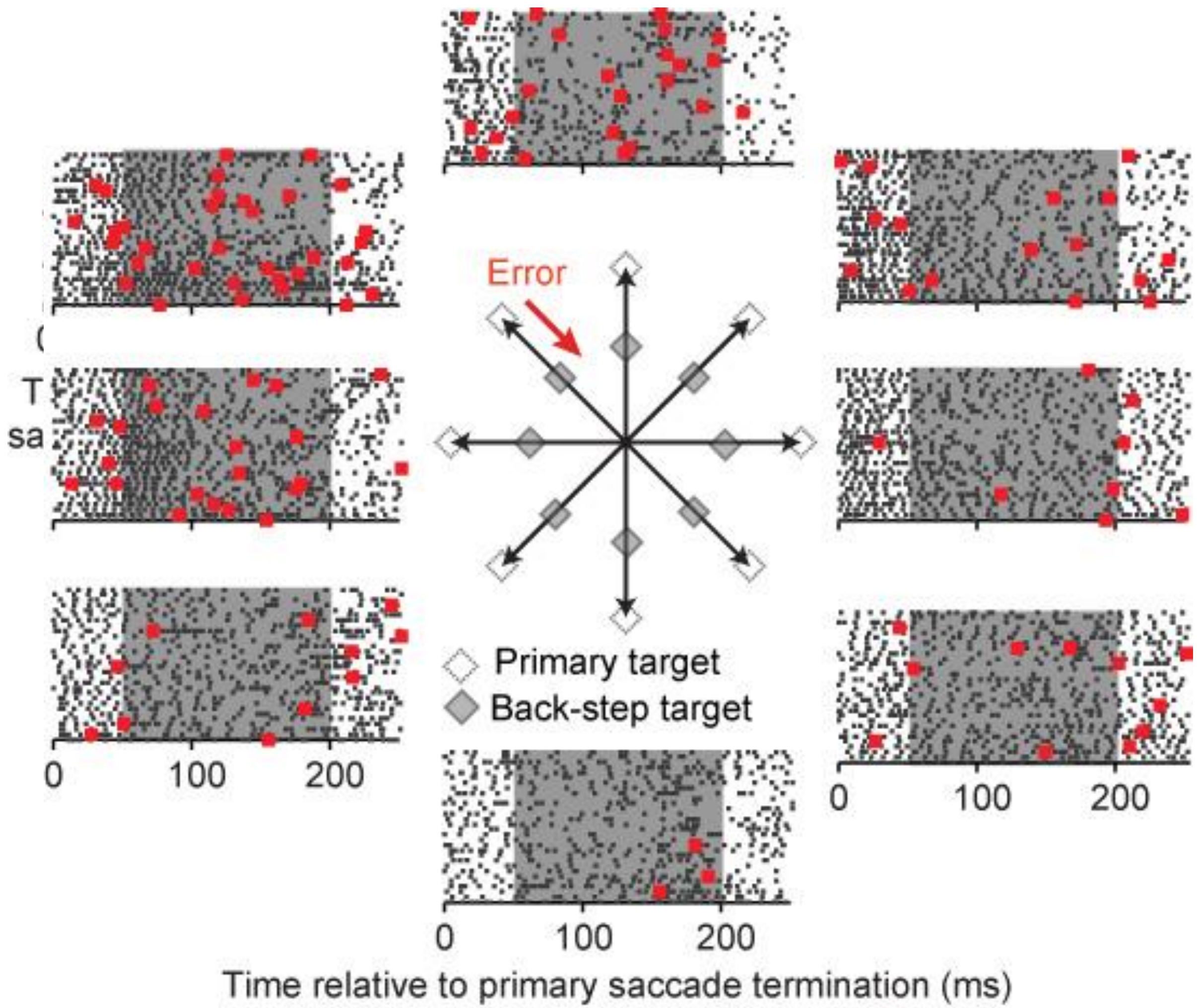
Hypothesis: the P-cells that project to a nucleus neuron are not selected randomly, but share a common input from the inferior olive (a common source of error).



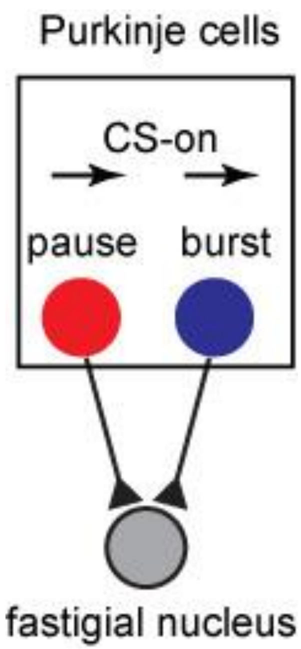
Idea: **the P-cell that connect to a nucleus neuron are not selected randomly, but by their complex spike properties**

Procedure to identify the complex spike properties of each P-cell

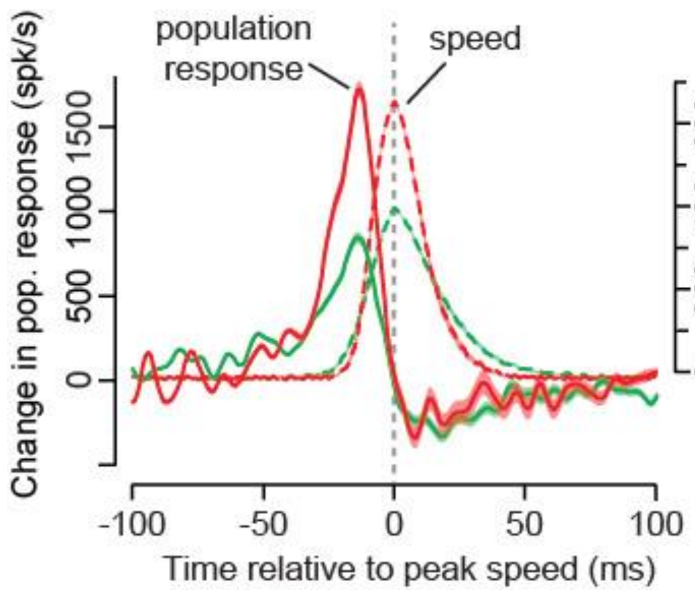


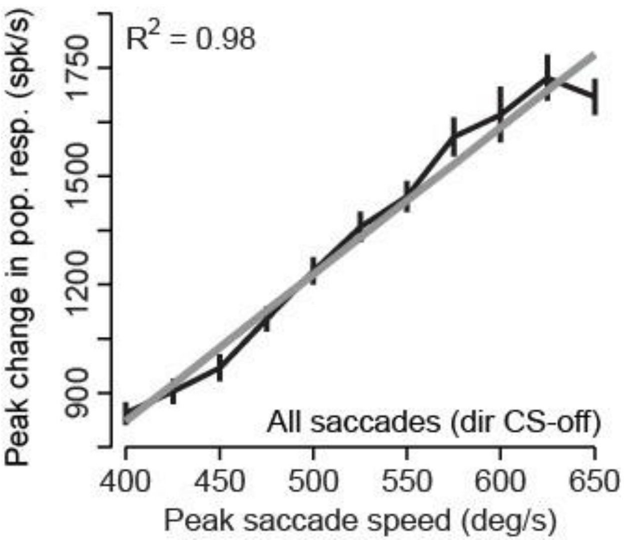


If P-cell projections to the nucleus are organized according to their CS field, then the inhibitory current predicts saccade velocity in real-time

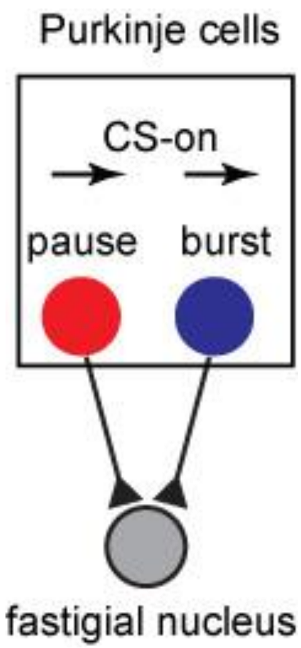


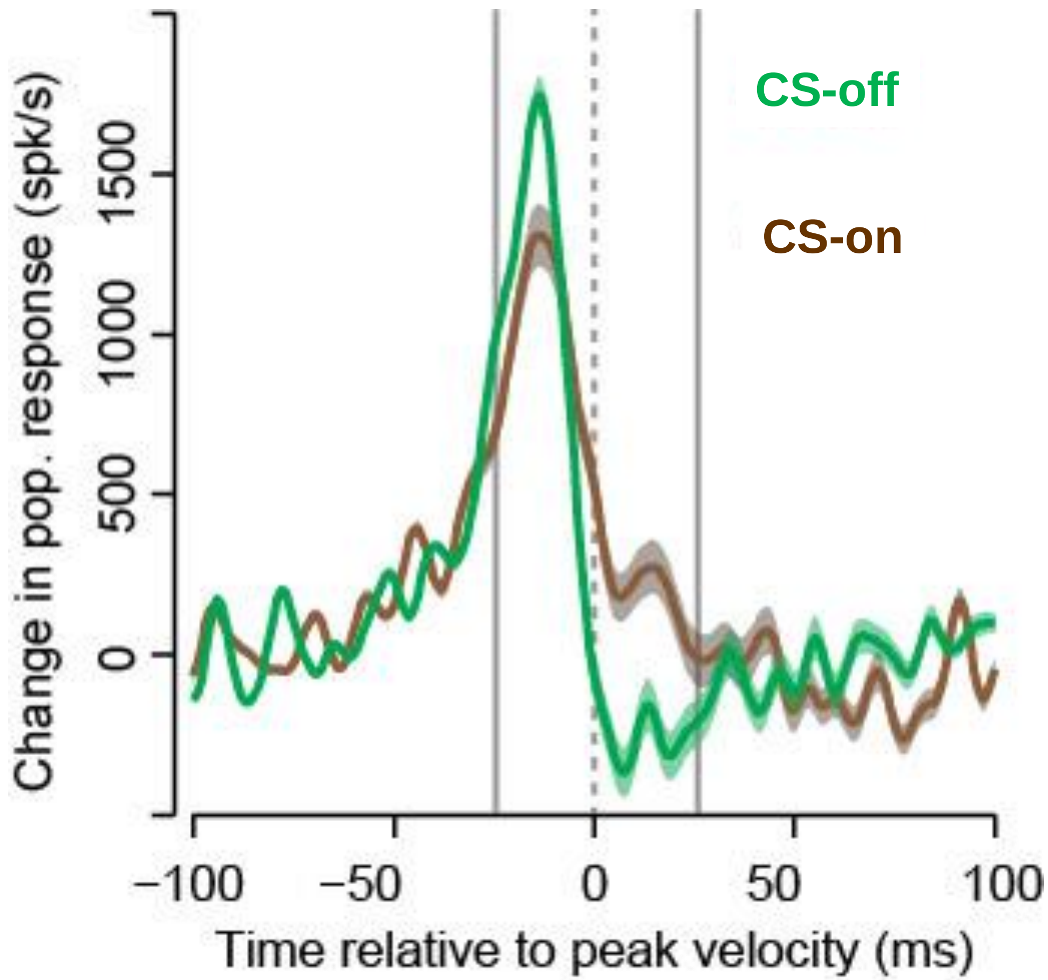
Saccade is in direction of CS-off



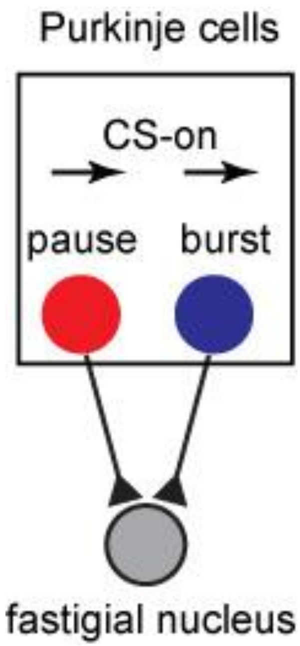


An encoding of saccade direction

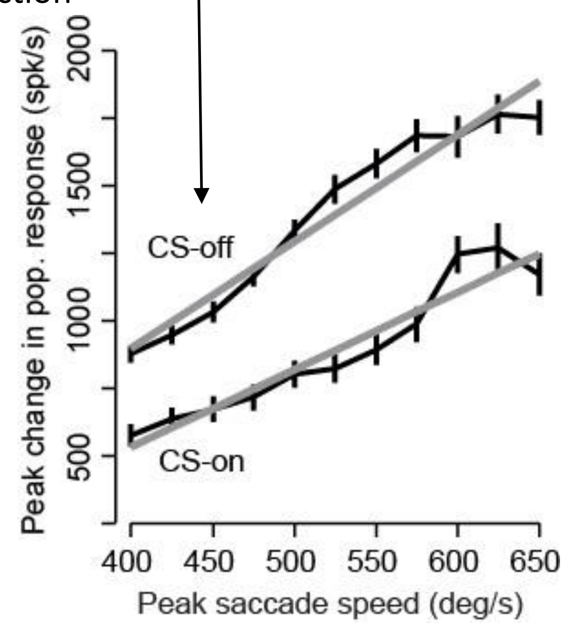




A gain-field encoding of saccade direction and velocity



Saccade direction



Population response (simple spikes)

Eye velocity in 2D space

Saccade direction

CS-off direction (complex spikes)

$$s(t) = \left|\dot{\mathbf{x}}(t+\Delta)\right| g(\theta, \theta_{cs})$$

$$g(\theta, \theta_{cs}) = a\cos(\theta - \theta_{cs}) + b$$

The problem

Firing rates of individual P-cells in the oculomotor vermis region of the cerebellum show little modulation with saccade amplitude or direction. How can these cells participate in control of eye movements if individually they show poor encoding of saccade kinematics?

The idea

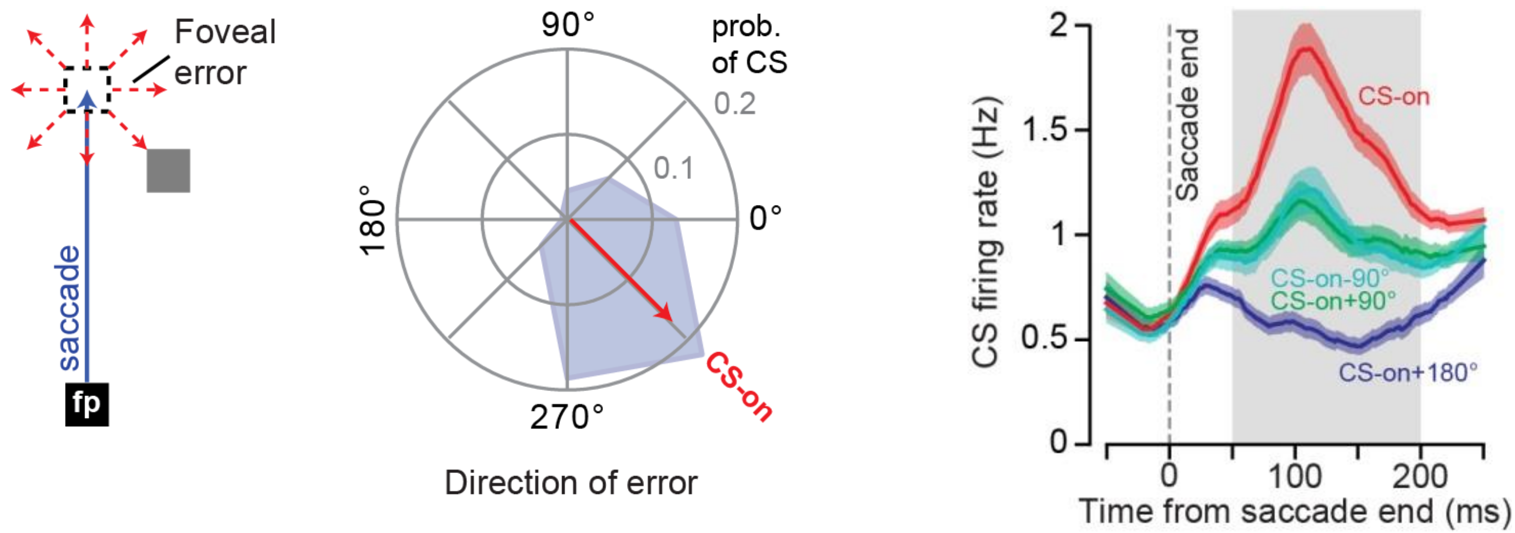
We imagined that the P-cells are organized into micro-clusters, wherein the cells in that micro-cluster project onto a single nucleus neuron, all receiving the same error signal from the inferior olive.

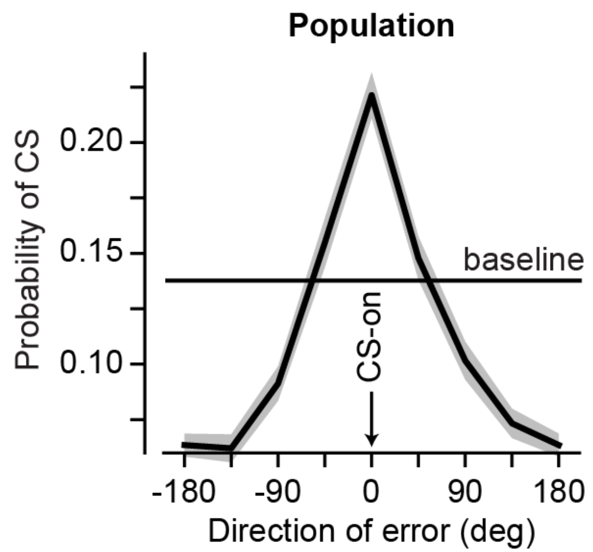
The result

1. We organized the simple spikes based on a coordinate system specified by the complex spikes. This revealed that within the micro-cluster, the P-cells together inhibited the nucleus cell with a pattern that predicted the real-time motion of the eye.

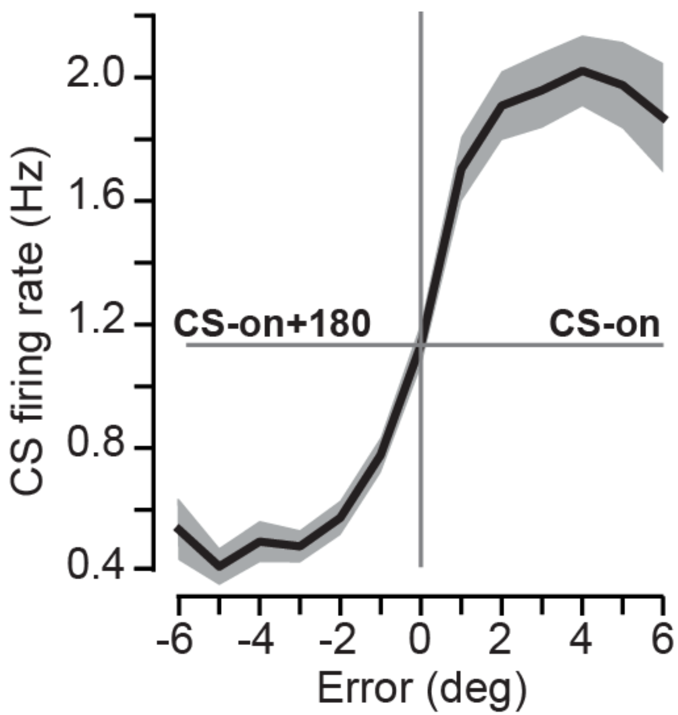
2. Within the micro-cluster, the P-cells together encoded saccade speed and direction via a gain-field.

Error direction is encoded in the probability of the complex spikes

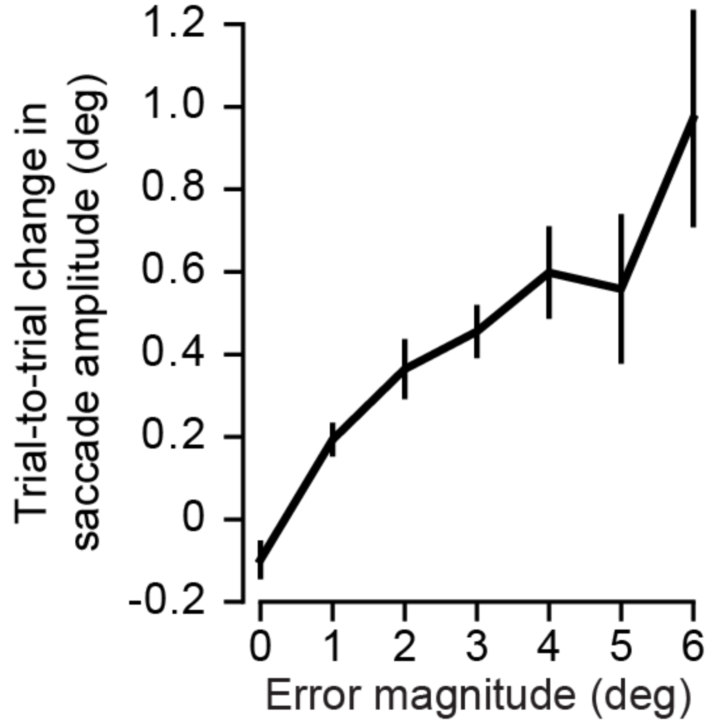




Encoding of error magnitude

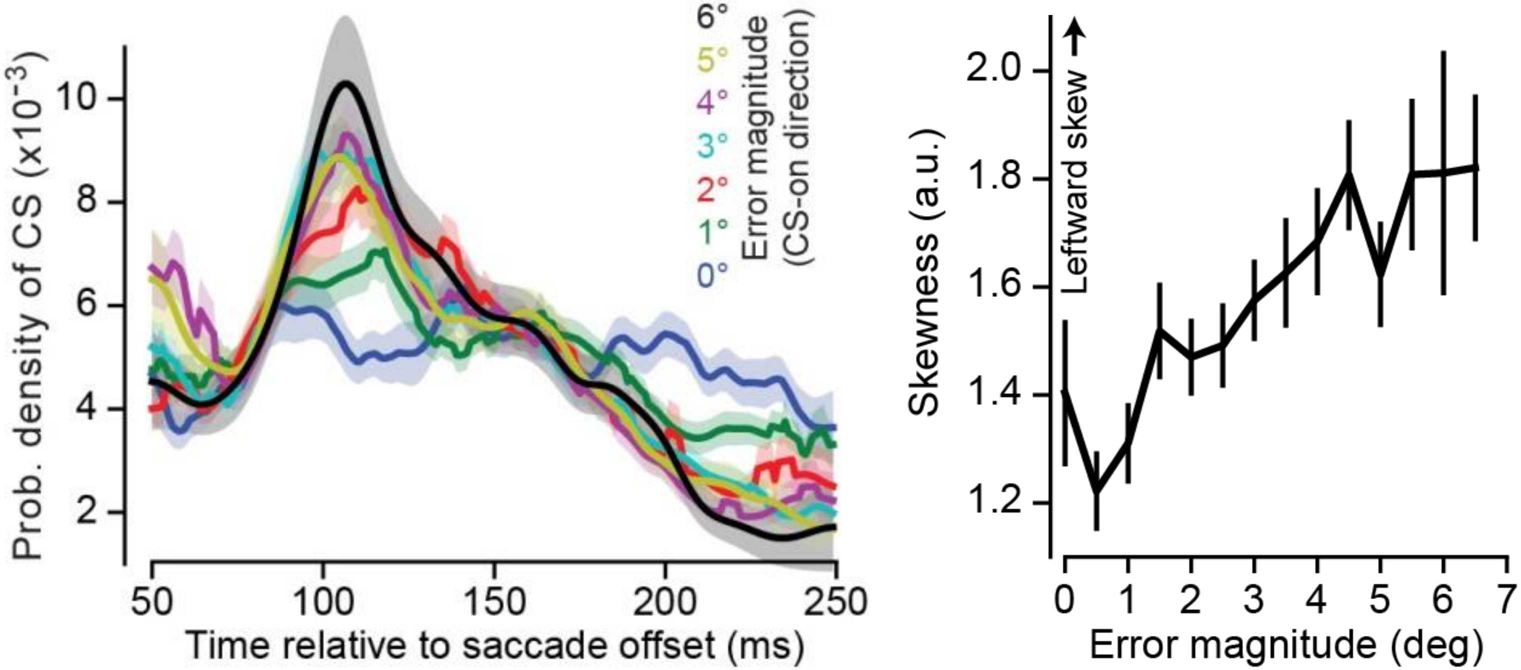


Probability of CS appears to encode direction of the error vector, but not its magnitude.



Learning from error depends on error magnitude.

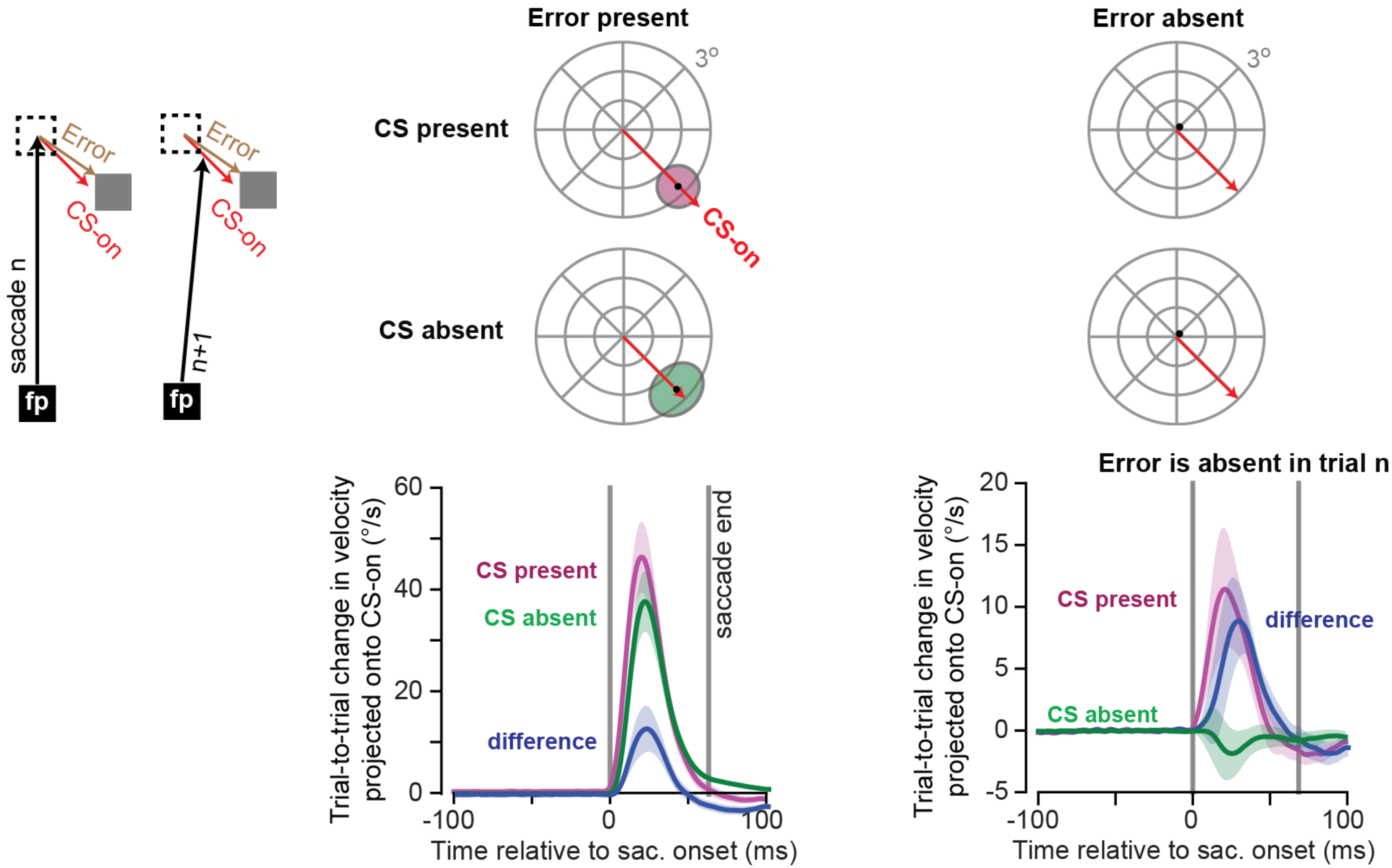
Encoding of error magnitude



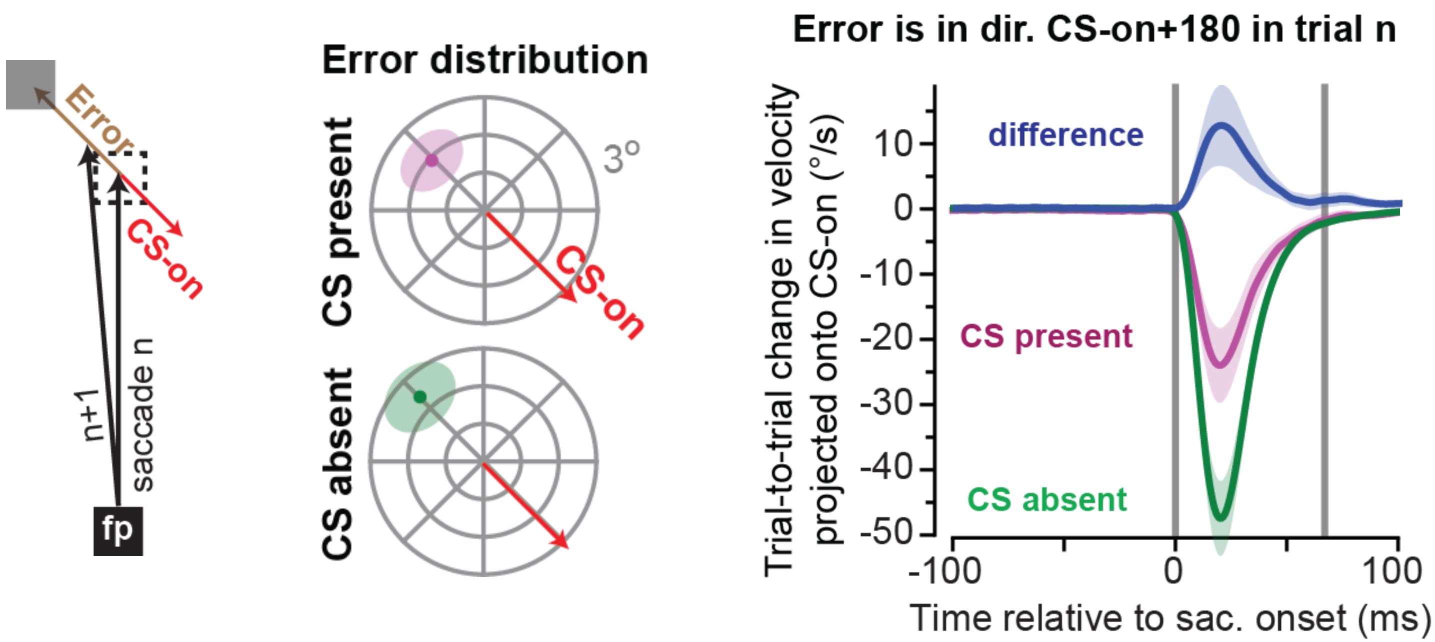
Error direction is encoded in the probability of the complex spike

Error magnitude is encoded in the timing of the complex spike: larger errors produce earlier complex spikes

What happens in the trial following experience of a complex spike?

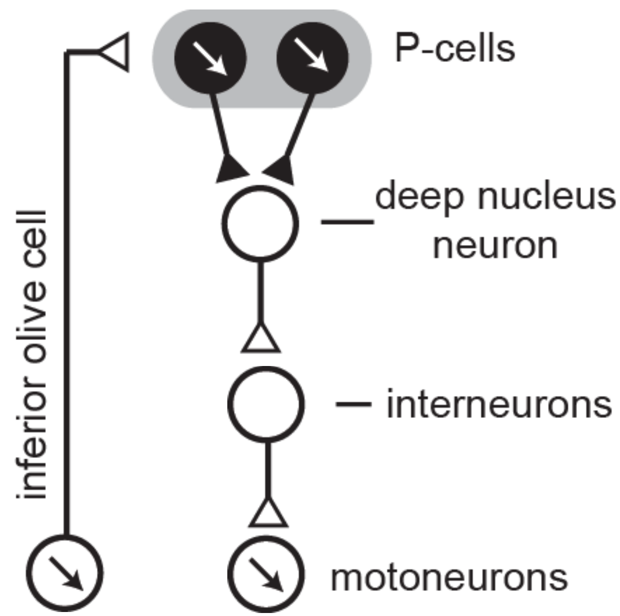


What happens in the trial following experience of a complex spike?

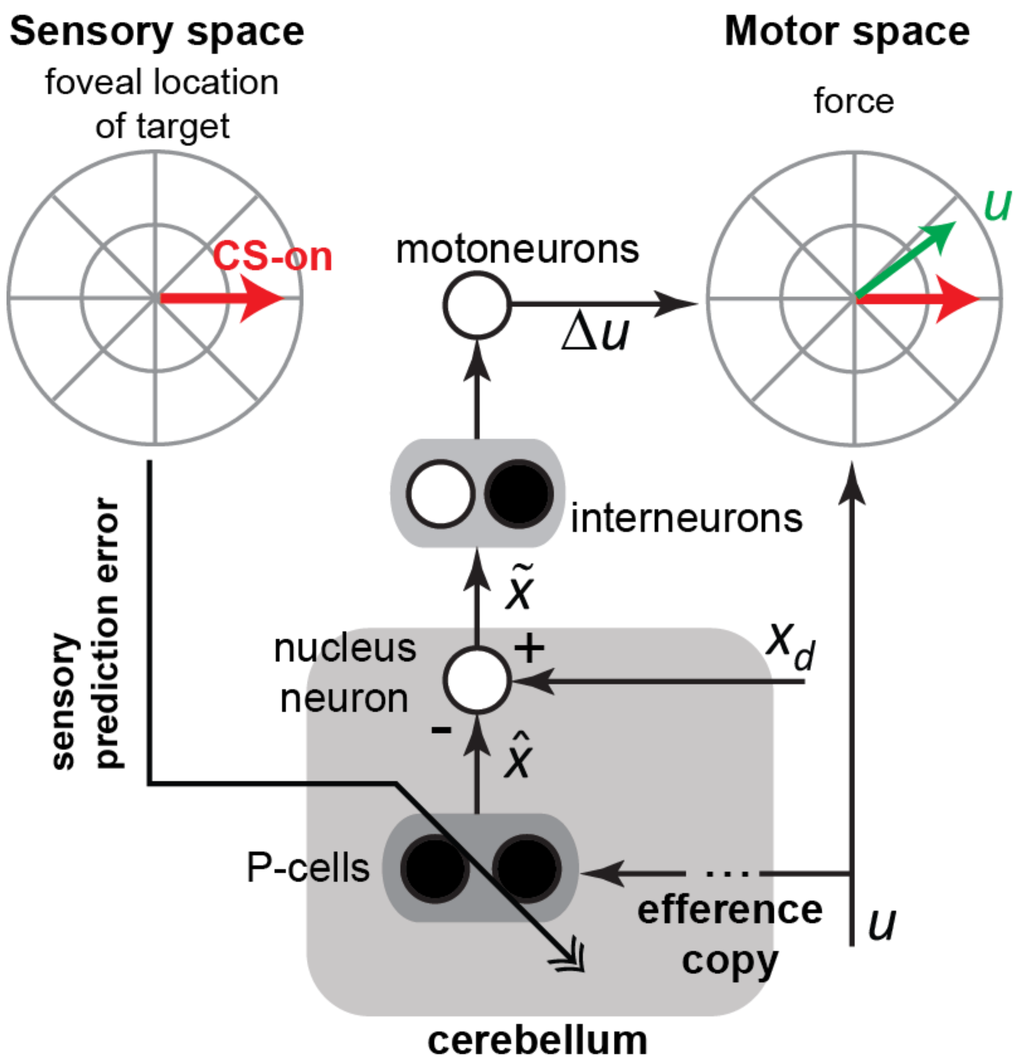


When a P-cell generates a complex spike, on the next trial the eye is pulled more in the CS-on direction of that P-cell

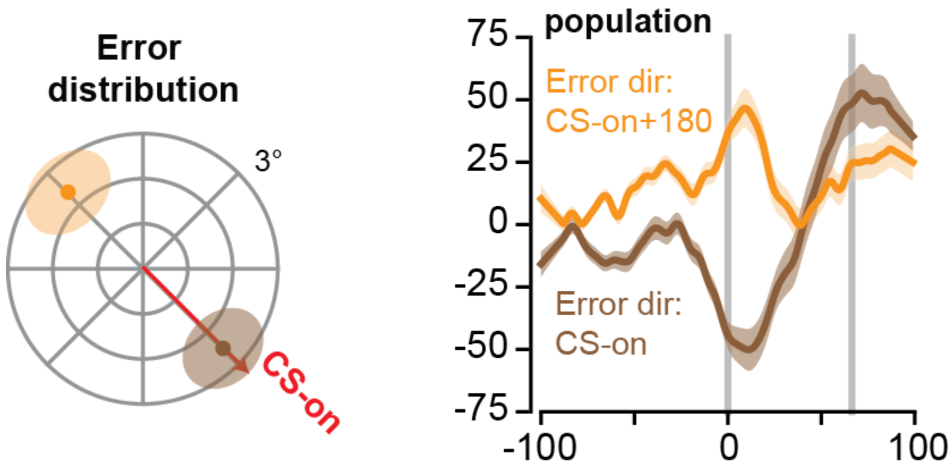
Hypothesized anatomy of the P-cell / deep nucleus projections to brainstem

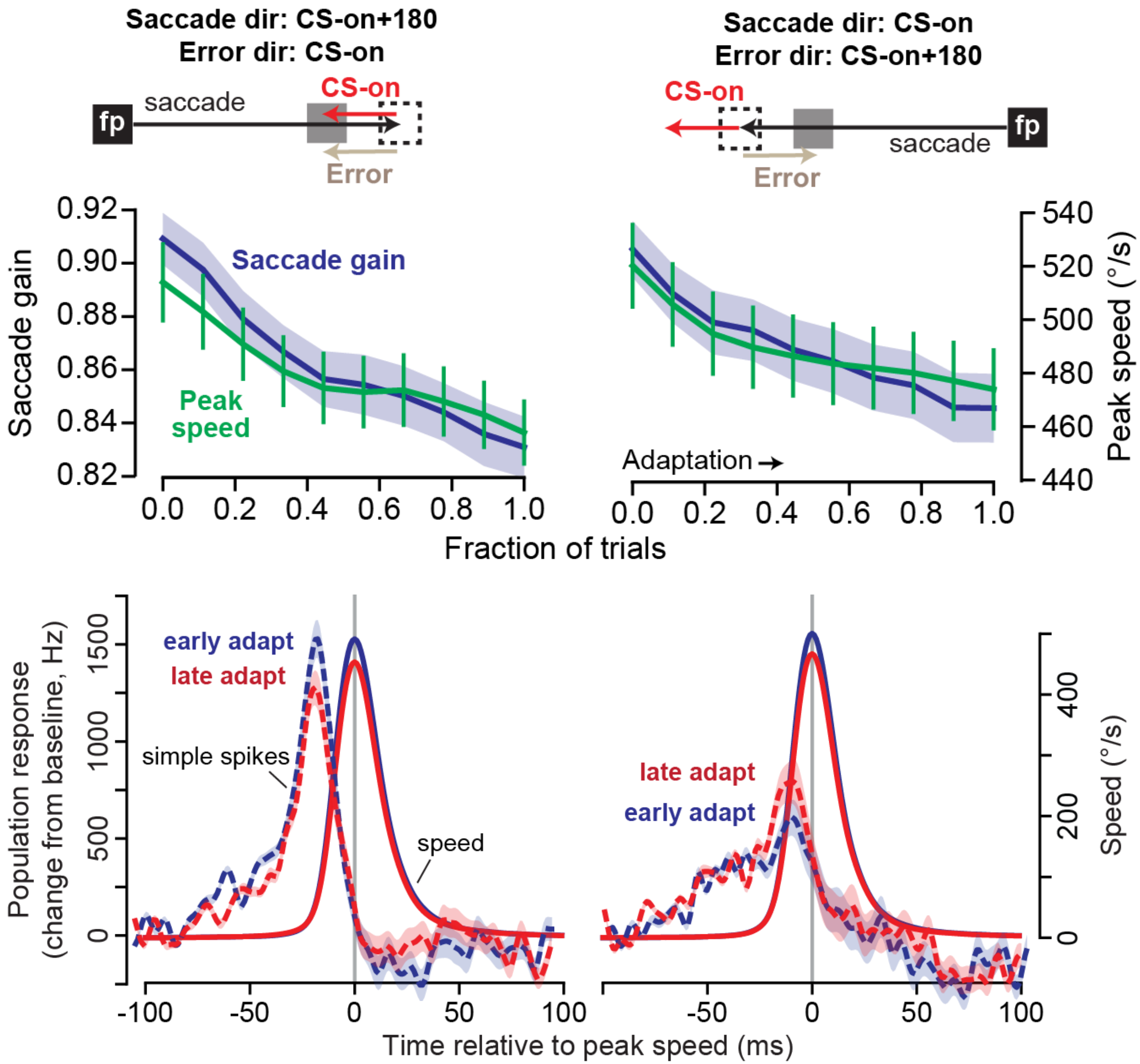


Function of the oculomotor region of the cerebellum



Effect of error on simple spikes





Saccade dir: CS-on+180
Error dir: CS-on
CS-on
saccade
fp
Error
Saccade dir: CS-on
Error dir: CS-on+180
CS-on
fp
saccade
Error
0.92
0.90
0.88
0.86
0.84
0.82
Saccade gain
Saccade gain
Peak speed
540
520
500
480
460
440
Peak speed (°/s)
Adaptation →
0.0 0.2 0.4 0.6 0.8 1.0
0.0 0.2 0.4 0.6 0.8 1.0
Fraction of trials
Population response (change from baseline, Hz)
1500
1000
500
0
early adapt
late adapt
simple spikes
speed
late adapt
early adapt
400
200
0
Speed (°/s)
-100 -50 0 50 100
-50 0 50 100
Time relative to peak speed (ms)

Limitations

- **The P-cells were recorded one at a time, but we analyzed them as if they were recorded in parallel.**
- **We do not really know the output of the cerebellum because we have no data from the mossy fibers that project to the nucleus neurons.**
- **Cerebellar output (from this region) is not just to brainstem motor nuclei, but also to superior colliculus and inferior olive. What are these projections computing?**

Summary

- **Population coding in the cerebellum may be based on anatomical organization of the P-cells based on their preference for error.**
- **If P-cells are organized in this way, then their simple spikes predict motion of the eyes in real-time as a gain-field.**
- **When a complex spike occurs, the simple spikes change on the next trial.**
- **This change coincides with a specific change in the motor commands: the eyes are pulled in the preferred error direction of those P-cells that produced a complex spike.**

Because of our wisdom,
We will travel far for love,
As all movement is a sign of thirst,
And speaking really says,
"I'm hungry to know you."

Hafez, 14th century Persian poet