Neural circuits for cognition

Cerebellum microcircuit and neural forward models

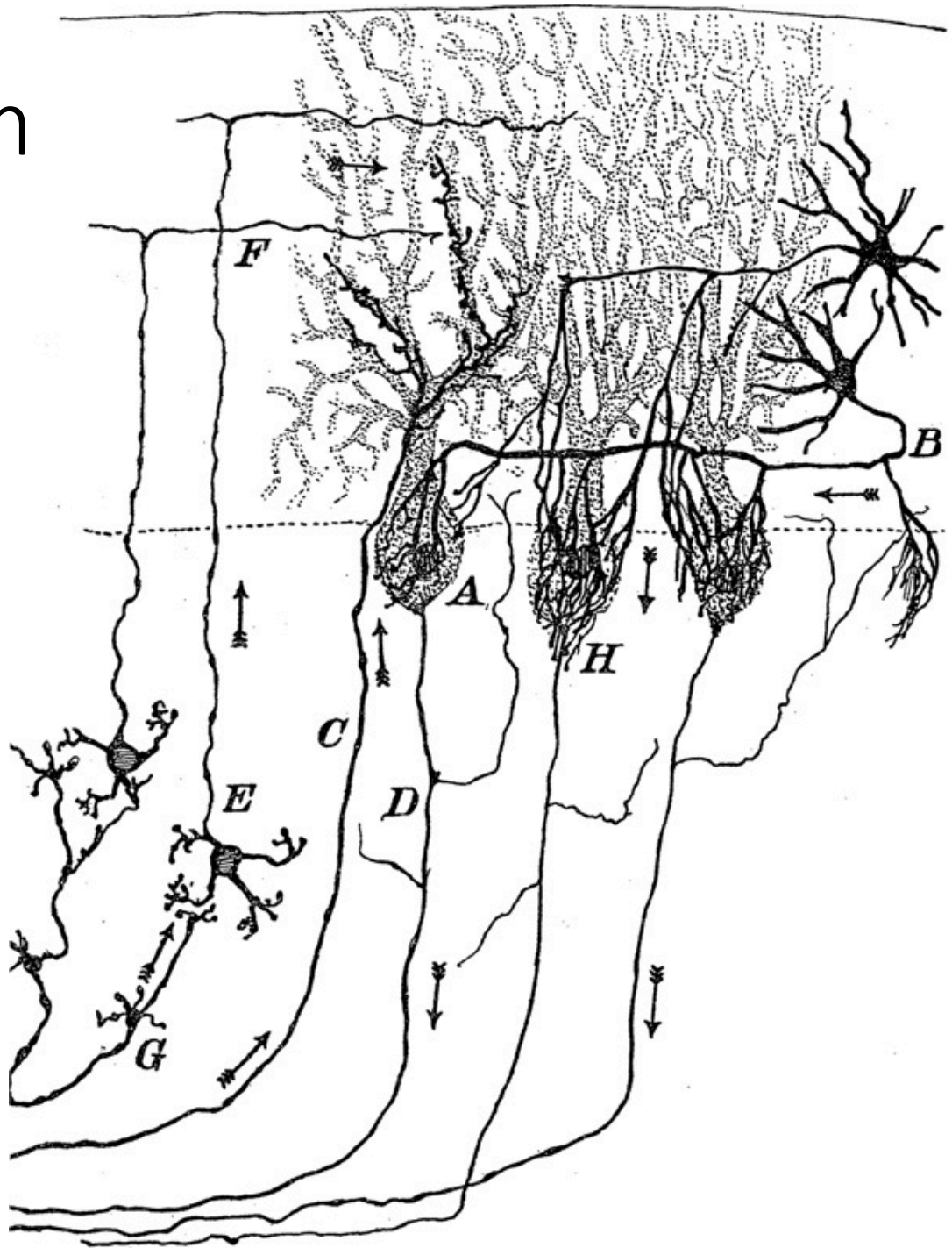
MIT Course 9.49/9.490

Instructor: Professor Ila Fiete

Cerebellum as internal model

Cerebellum

Cerebellar cells
Traced & drawn by Cajal



- 50% of neurons in brain are cerebellar (granule cells)
- 10% of volume
- Balance and posture
- Execution of smooth voluntary motor actions, motor learning
- Cognitive functions: ordering thoughts and actions to make a sandwich, verbal fluency, social interaction predictability, verbal working memory

Roles of cerebellum by region

- Most of the human cerebellum maps to association areas rather than the motor cortex. Those association areas also include executive control networks and the default network.
- Anterior damage → motor deficits
- Posterior damage → cognitive rather than motor deficits

In-class journal club II

Neuron
Perspective

The Cerebellum and Cognitive Function: 25 Years of Insight from Anatomy and Neuroimaging

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Twenty-five years ago the first human functional neuroimaging studies of cognition discovered a surprising response in the cerebellum that could not be attributed to motor demands. This controversial observation challenged the well-entrenched view that the cerebellum solely contributes to the planning and execution of movement. Recurring neuroimaging findings combined with key insights from anatomy and case studies of neurological patients motivated a reconsideration of the traditional model of cerebellar organization and function. The majority of the human cerebellum maps to cerebral association networks in an orderly manner that includes a mirroring of the prominent cerebral asymmetries for language and attention. These findings inspire exploration of the cerebellum's contributions to a diverse array of functional domains and neuropsychiatric disorders.

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Seeking a unified framework for cerebellar function and dysfunction: from circuit operations to cognition

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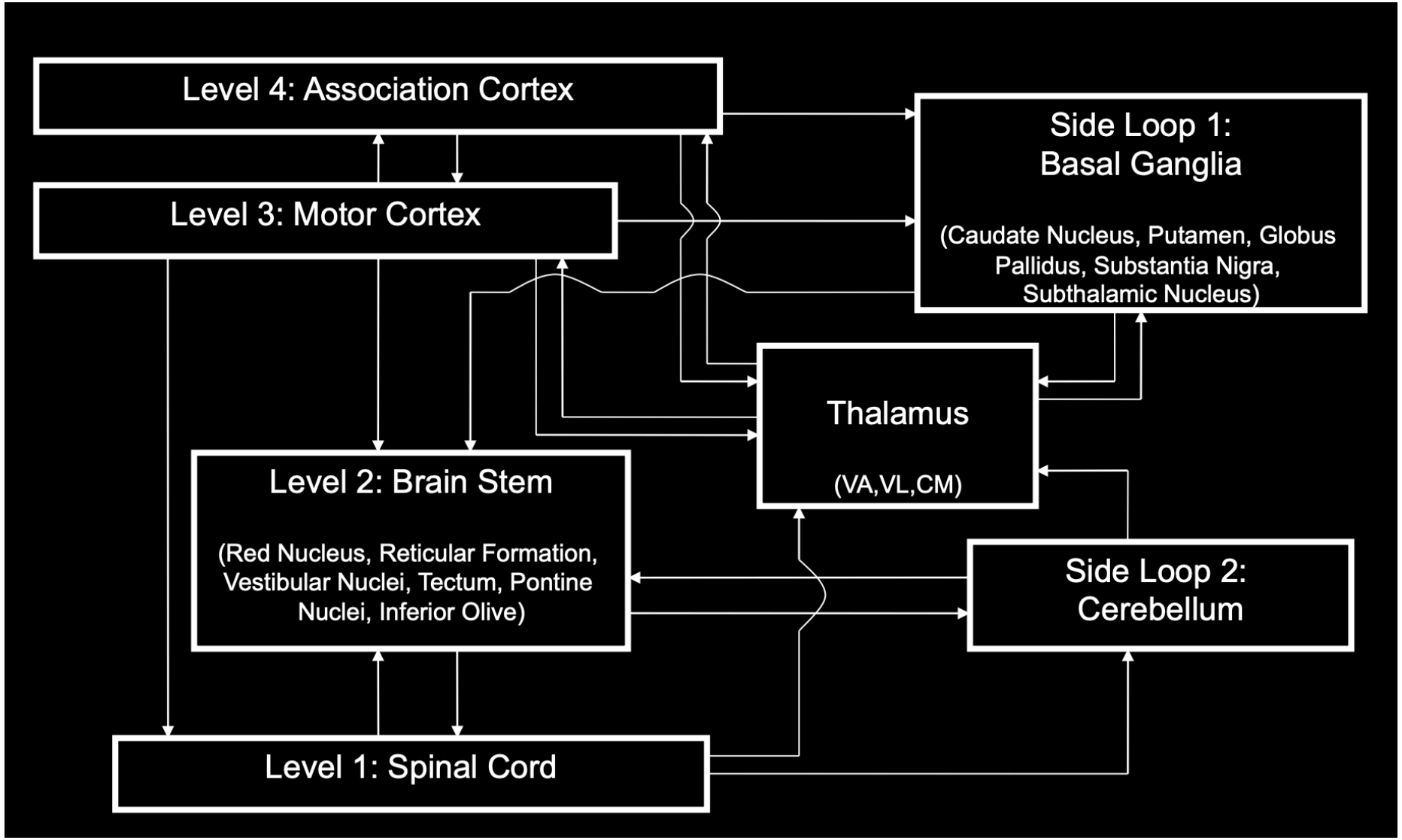
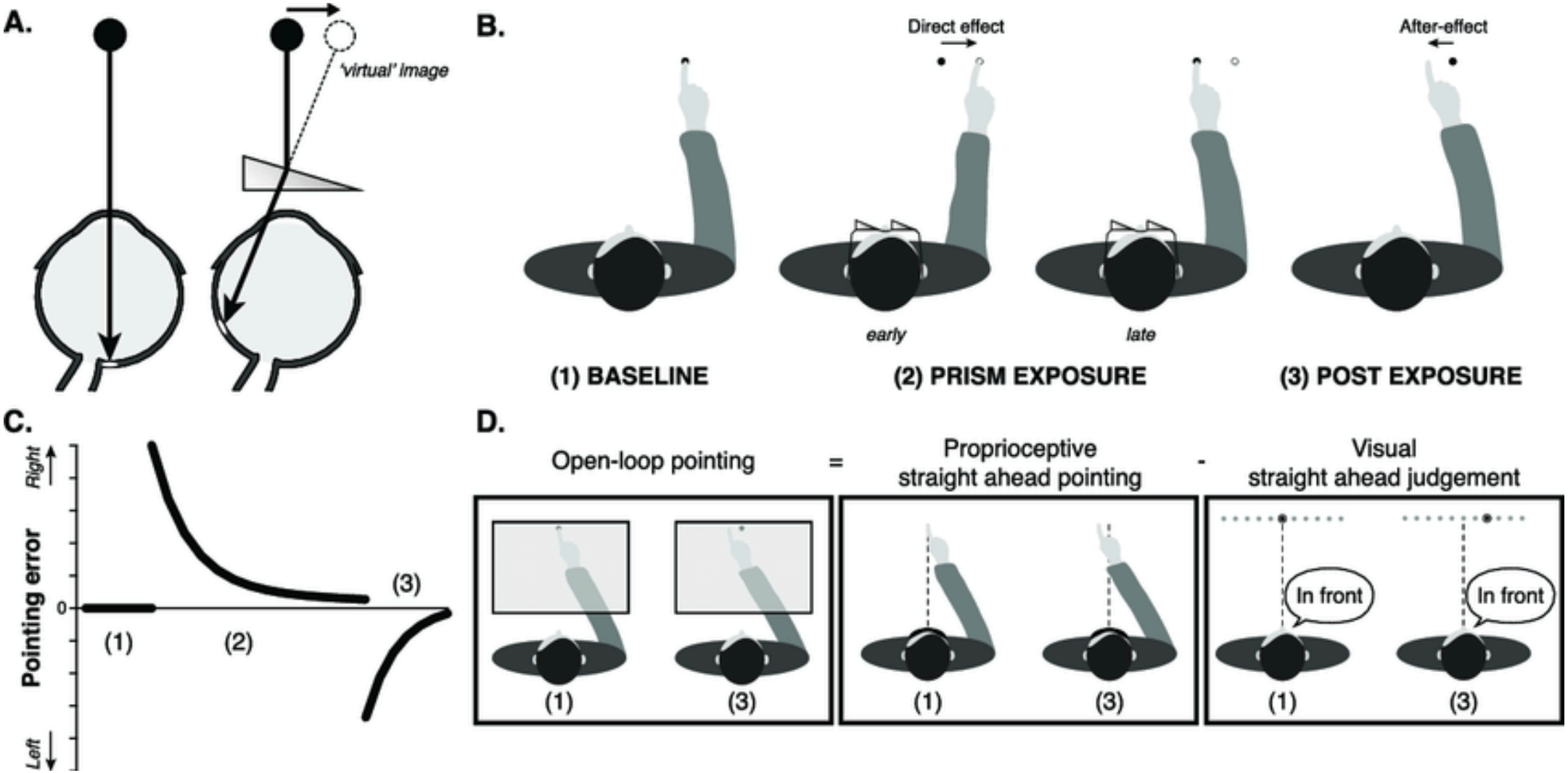
Following the fundamental recognition of its involvement in sensory-motor coordination and learning, the cerebellum is now also believed to take part in the processing of cognition and emotion. This hypothesis is recurrent in numerous papers reporting anatomical and functional observations, and it requires an explanation. We argue that a similar circuit structure in all cerebellar areas may carry out various operations using a common computational scheme. On the basis of a broad review of anatomical data, it is conceivable that the different roles of the cerebellum lie in the specific connectivity of the cerebellar modules, with motor, cognitive, and emotional functions (at least partially) segregated into different cerebro-cerebellar loops. We here develop a conceptual and operational framework based on multiple interconnected levels (a *meta-levels hypothesis*): from cellular/molecular to network mechanisms leading to generation of computational primitives, thence to high-level cognitive/emotional processing, and finally to the sphere of mental function and dysfunction. The main concept explored is that of intimate interplay between timing and learning (reminiscent of the "timing and learning machine" capabilities long attributed to the cerebellum), which reverberates from cellular to circuit mechanisms. Subsequently, integration within large-scale brain loops could generate the disparate cognitive/emotional and mental functions in which the cerebellum has been implicated. We propose, therefore, that the cerebellum operates as a general-purpose co-processor, whose effects depend on the specific brain centers to which individual modules are connected. Abnormal functioning in these loops could eventually contribute to the pathogenesis of major brain pathologies including not just ataxia but also dyslexia, autism, schizophrenia, and depression.

Keywords: cerebellum, cognition, motor control, timing, prediction, autism, schizophrenia, dyslexia

Motor organization and the cerebellum



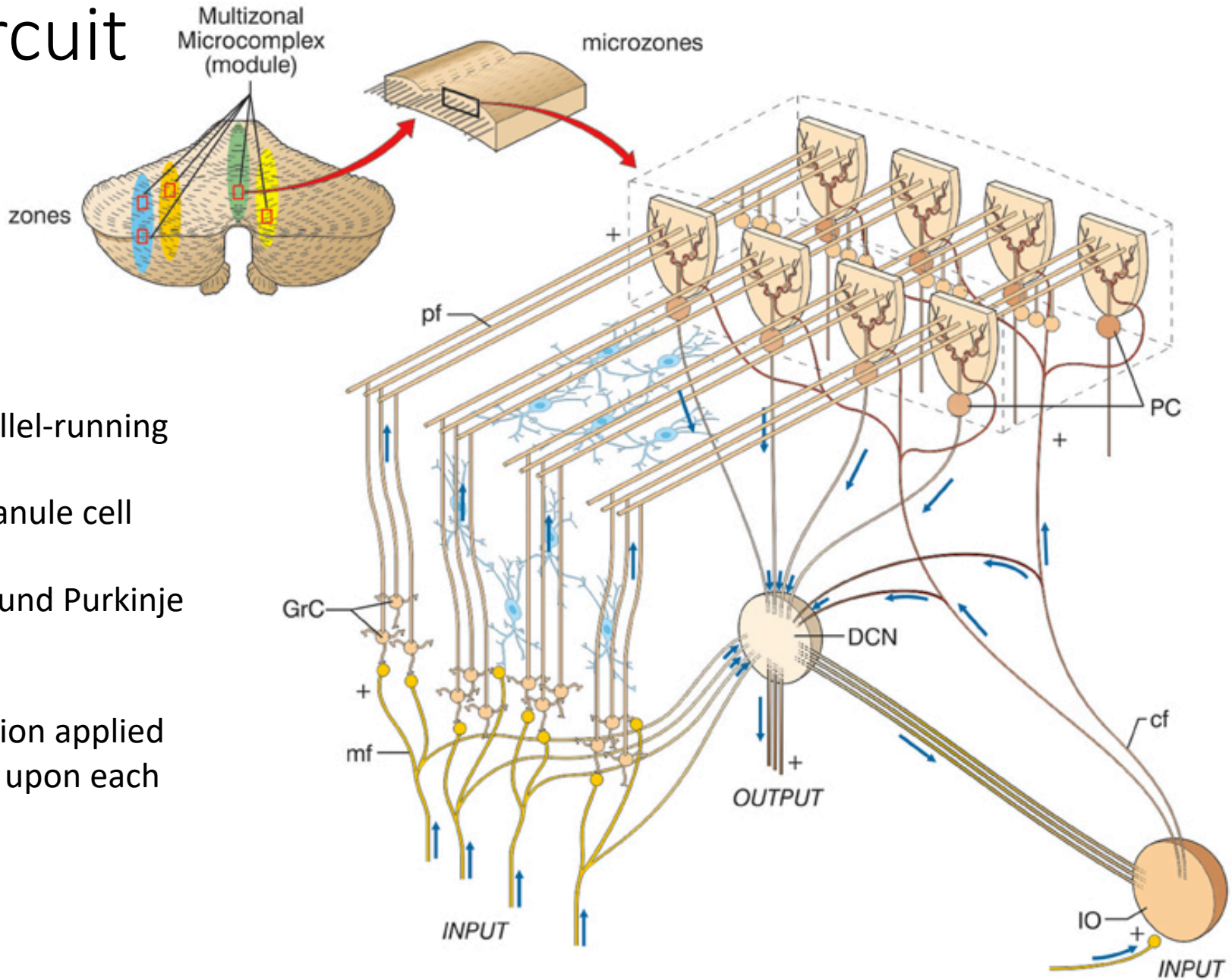
Prism adaptation: visuo-motor task



Prism glass experiment: multiple modules and cerebellum

- Gradual improvement to target after putting on glasses.
- Cerebellum-dependent: deficit in task learning with cerebellar disorder.
- Increased cerebellar activation related to discrepancy between movement goal and actual consequence.
- Removal of glasses (de-adaptation): gradual improvement back, slightly faster.
- Re-wear glasses (re-adaptation): rapid improvement to target – suggests that there was learning of new “module” for control, which can now be switched on.

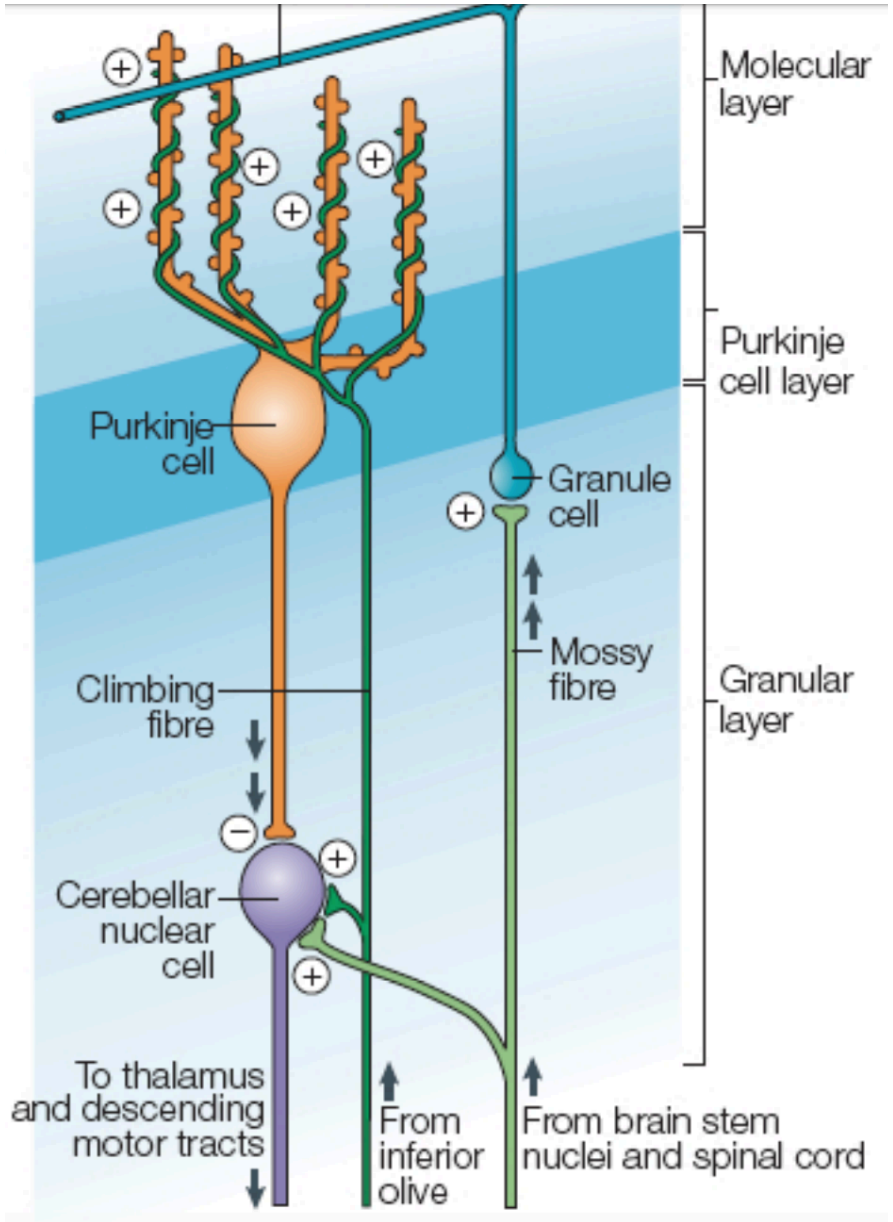
The canonically structured/repeating nature of the cerebellar circuit



Parallel fiber = long parallel-running granule cell axons.
Mossy fibers: contact granule cell axons.
Climbing fiber: wrap around Purkinje cells.

Suggests the same function applied to/operation performed upon each local set of inputs.

A closer look at the local circuit motif



Single AP in climbing fiber elicits burst (~4 spikes-wide complex spike) in Purkinje cells

Complex spikes have low rate: ~1/second.

Many simultaneously active granule cells (parallel fibers) drive simple spikes in Purkinje cells. High baseline rate of simple spikes.

Classic idea (Marr-Albus-Ito)

- Low-frequency complex spikes (CS) in Purkinje cells (thus climbing fiber) encode motor error/teaching signal.
- Mossy fibers provide motor command (efference copy), which arrive at Purkinje cells through the parallel fiber input.
- CF input instructs changes in the parallel-fiber to Purkinje cell synapse.
- The resulting simple-spike changes of Purkinje cells, the outputs of the cerebellum, cause changes in the behavior that reduce error.

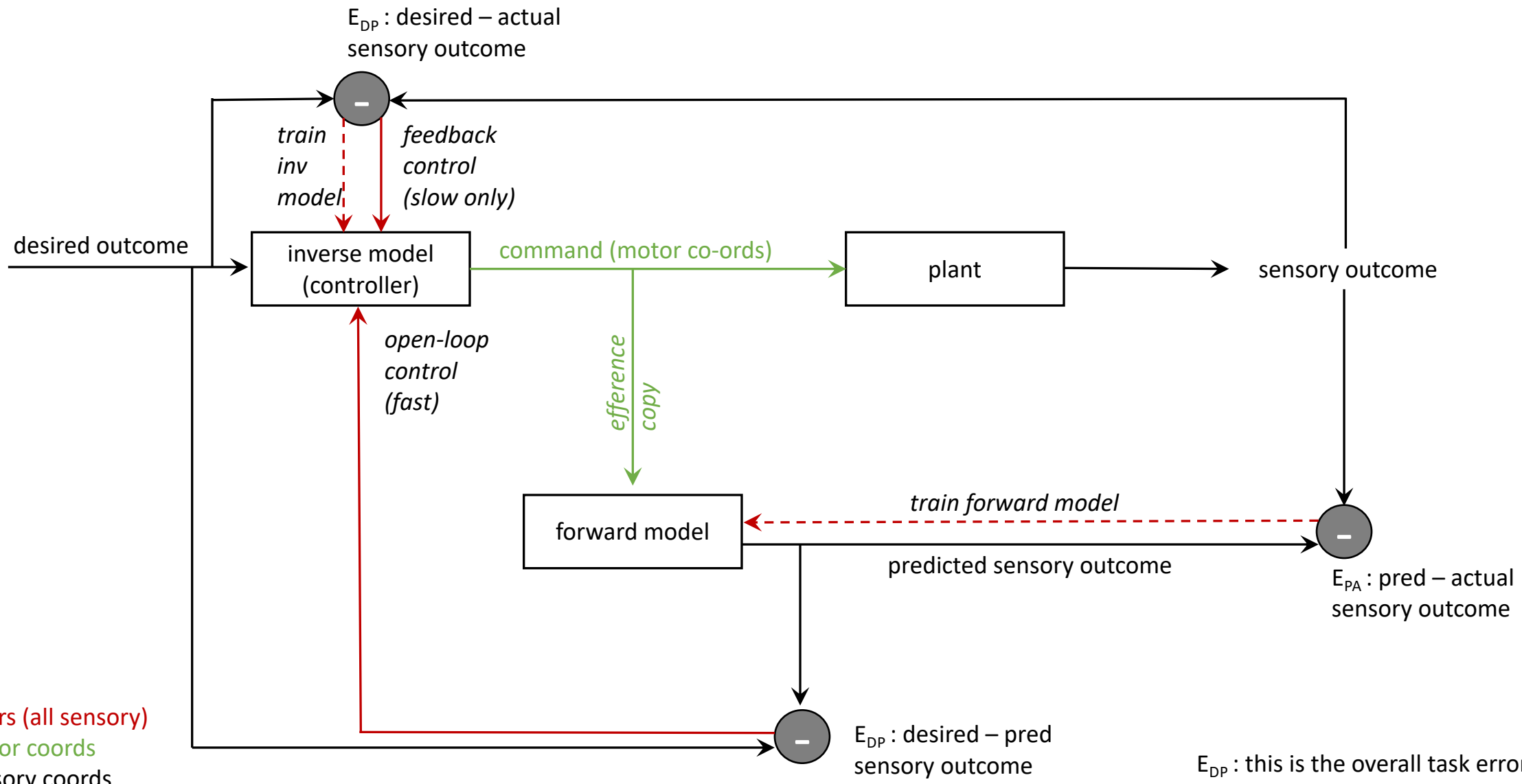
Classic idea (Marr-Albus-Ito)

- Low-frequency complex spikes (CS) in Purkinje cells (thus climbing fibers) encode motor error/teaching signal.
  - Support: CF complex spikes modulated by degree or retinal slip in smooth pursuit, VOR adaptation, ocular following
  - But: limited information; not graded; in saccadic adaptation task complex spike discharge increases with learning (as performance error decreases), persists after learning; in center-out reaching, CS not related to direction and speed errors
- Mossy fibers provide motor command (efference copy) to Purkinje cells via parallel fibers.
  - Parallel fibers carry not just motor command but also various sensory signals.
- CF input instructs changes in the parallel-fiber to Purkinje cell synapse.
- The resulting simple-spike changes of Purkinje cells, the outputs of the cerebellum, cause changes in the behavior that reduce error.

Short summary of status of Marr-Ito-Albus idea

- Climbing fibers (driving complex spikes in Purkinje cells) may not contain full error information, or even signal error at all during certain tasks.
- Parallel fibers (driving simple spikes in Purkinje cells) may not carry only motor efference, they also convey sensory error.

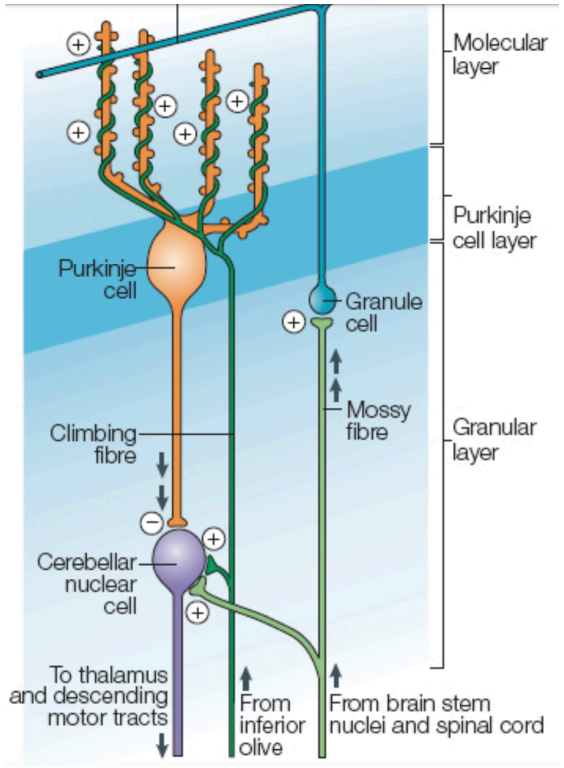
Alternate idea: Cerebellum as forward model. Review of fwd model

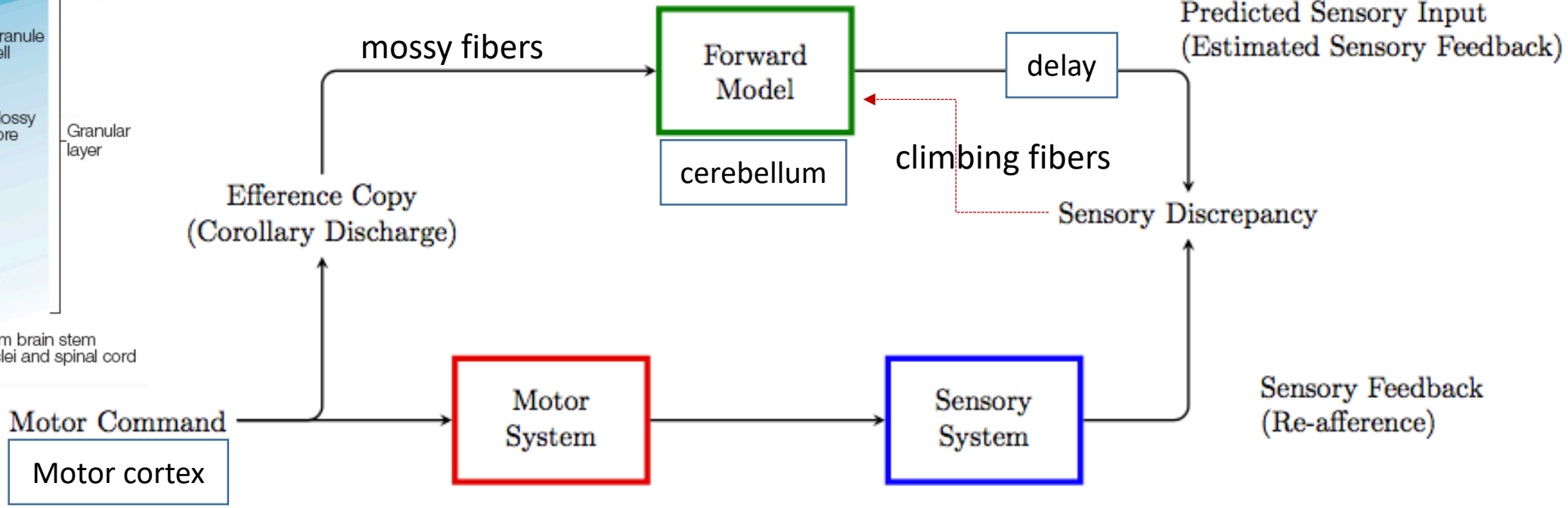


Errors (all sensory)
Motor coords
Sensory coords
Learning signal - -

E_{DP} : this is the overall task error to minimize!
The other three are proxy errors.

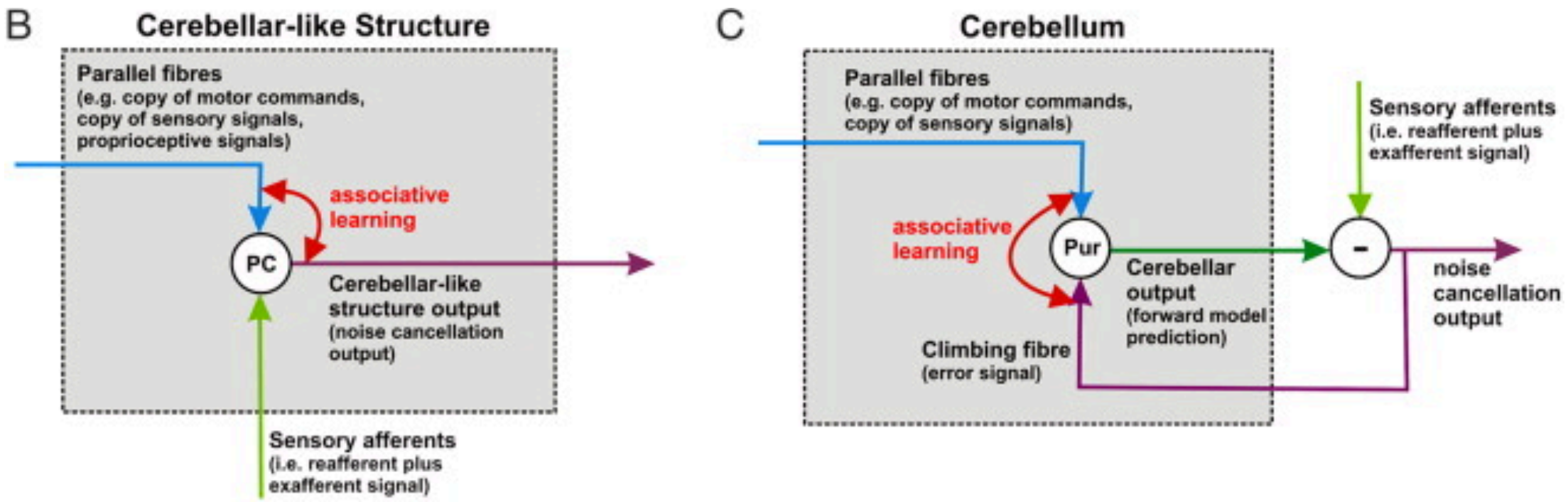
Alternate idea: Cerebellum as forward model?





Purkinje cell outputs

- The output of the cerebellum
- Firing of simple spikes related to sensory errors (position and velocity).
- Firing of simple spikes related to behavioral adaptation and performance.
- Firing does not encode load or muscle activity → not an inverse model
- Purkinje output consistent with cerebellum playing the role of a forward model (prediction)


B
Cerebellar-like Structure
Parallel fibres
(e.g. copy of motor commands,
copy of sensory signals,
proprioceptive signals)
associative
learning
PC
Cerebellar-like
structure output
(noise cancellation
output)
Sensory afferents
(i.e. reafferent plus
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C
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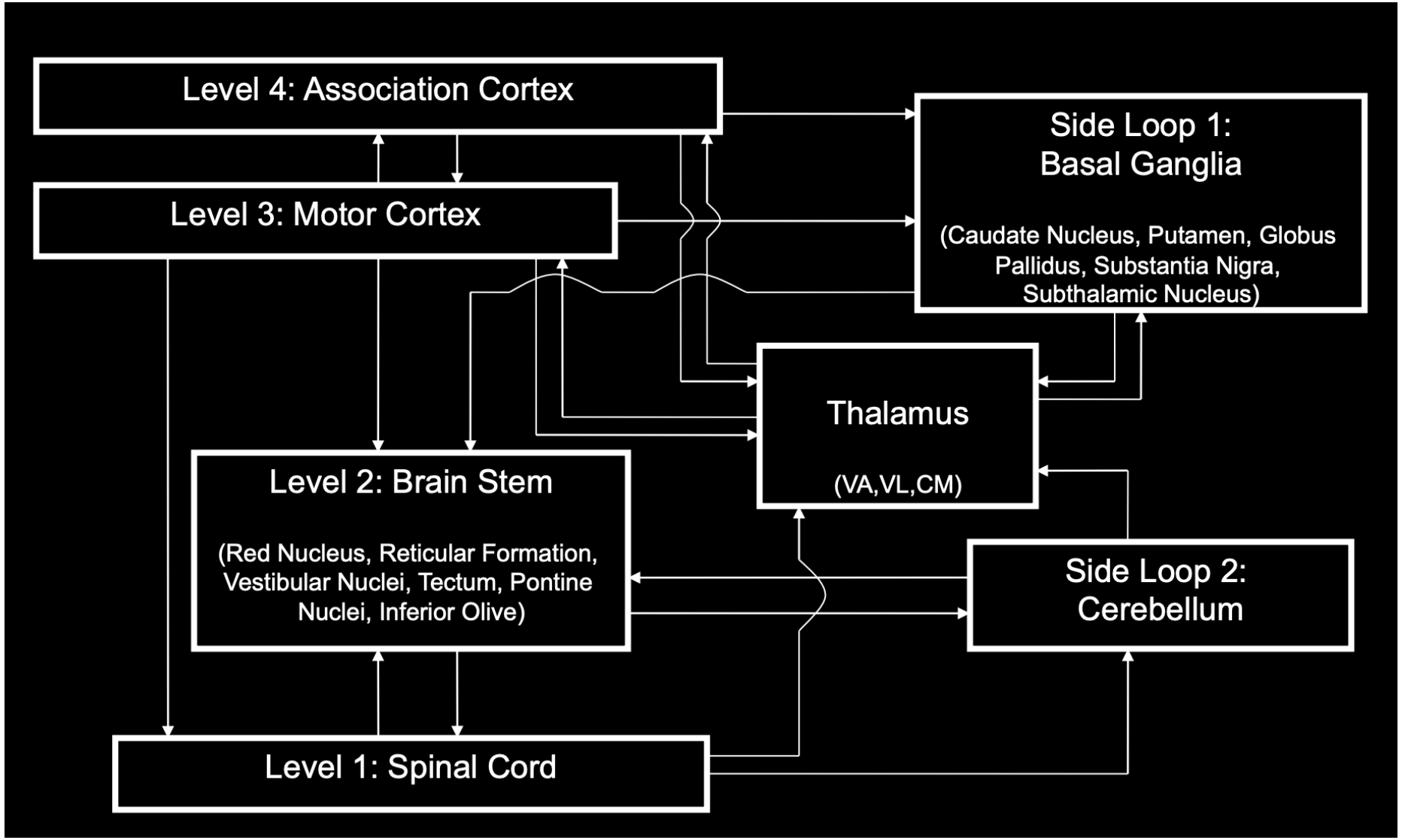
Pur
Cerebellar
output
(forward model
prediction)
-
noise
cancellation
output
Climbing fibre
(error signal)

Motor organization and the cerebellum



Cerebellum summary

- The Marr-Ito-Albus classic idea about cerebellum is motivated by cerebellar anatomy but is not fully consistent with existing data (and is also not a full computational model).
- The cerebellum appears to play a central role in forward modeling, and its tiling/repeating motif structure is suggestive of multiple modules.
- Despite its clear anatomical micro-organization, a precise computational model of cerebellum that also accords with the data is still lacking.