Anatomy of the Cerebellum

The Brain's GPU

Computational Models of neural Systems

Lecture 2.1

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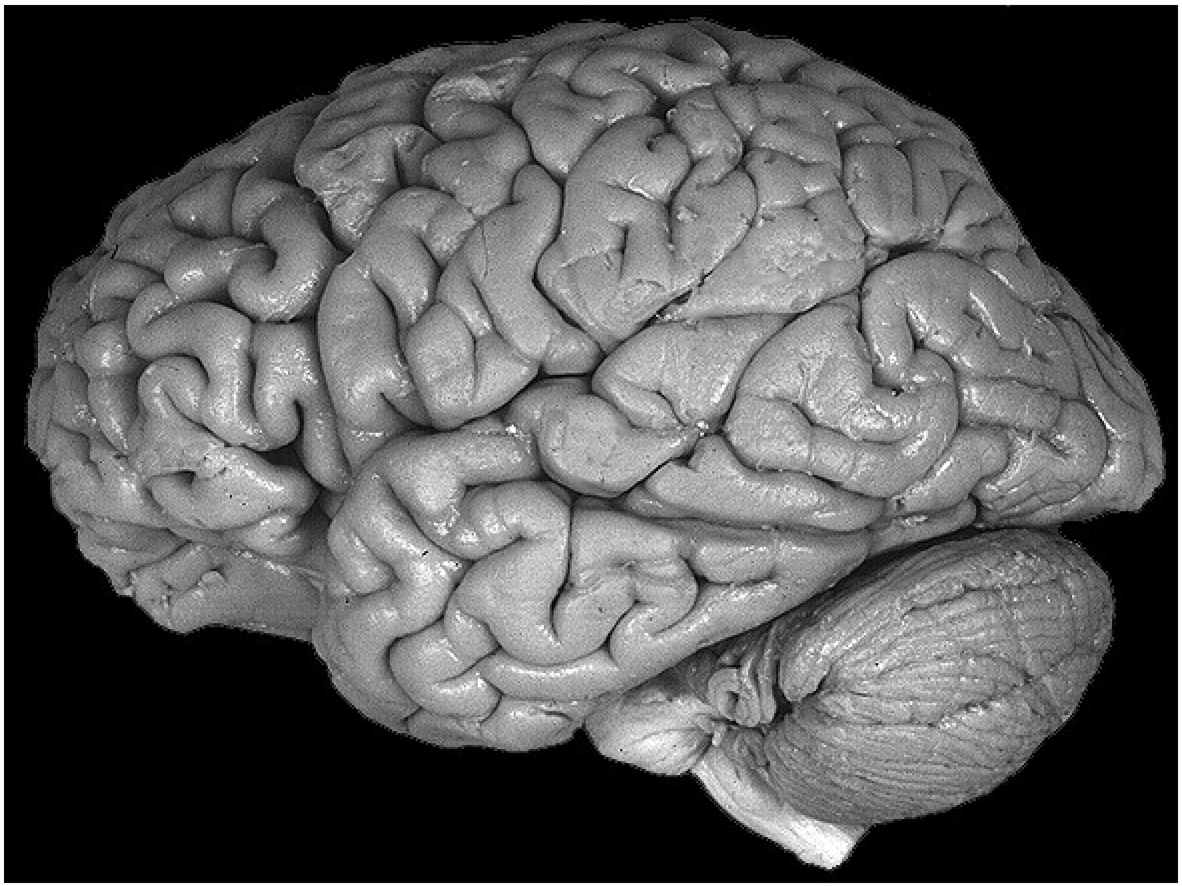
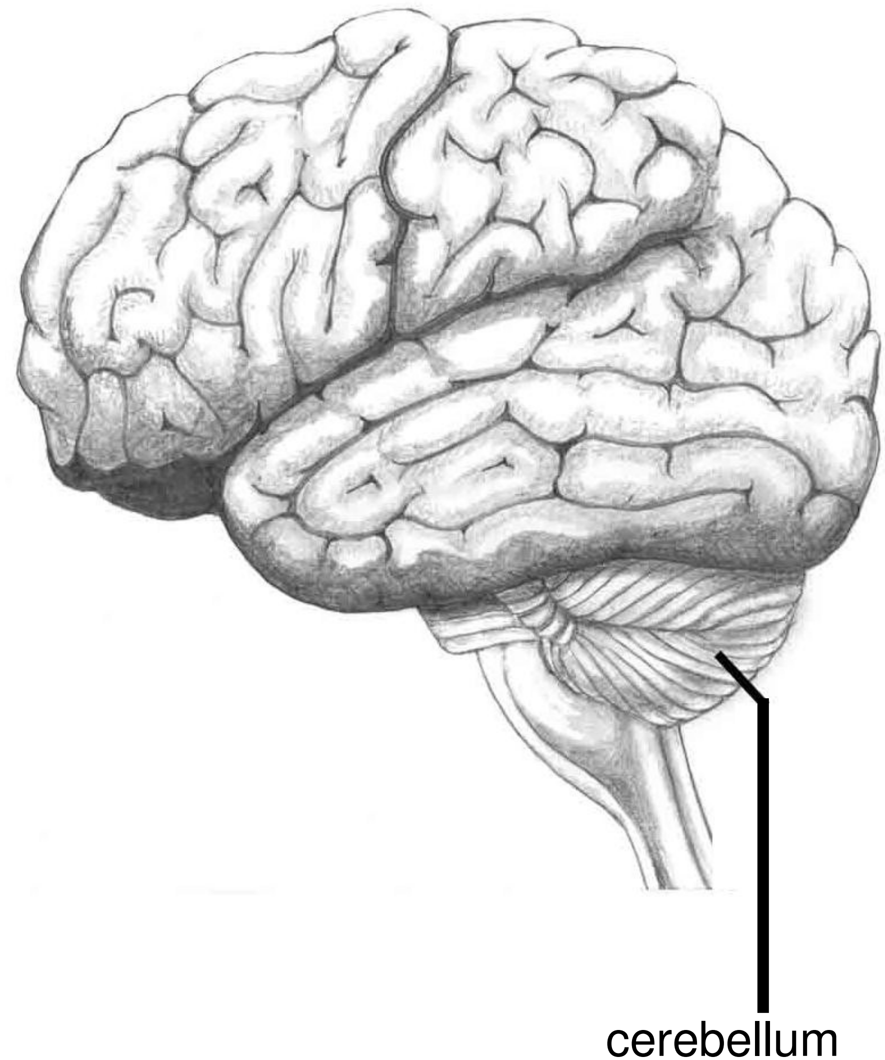
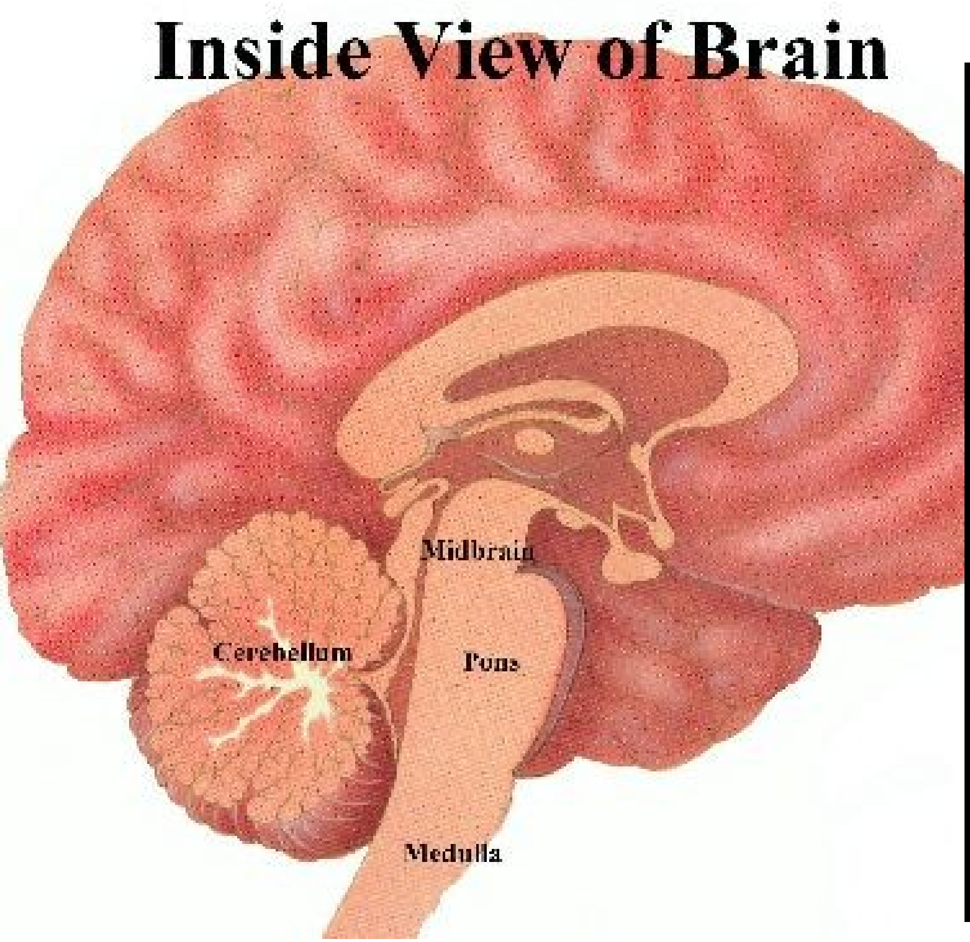
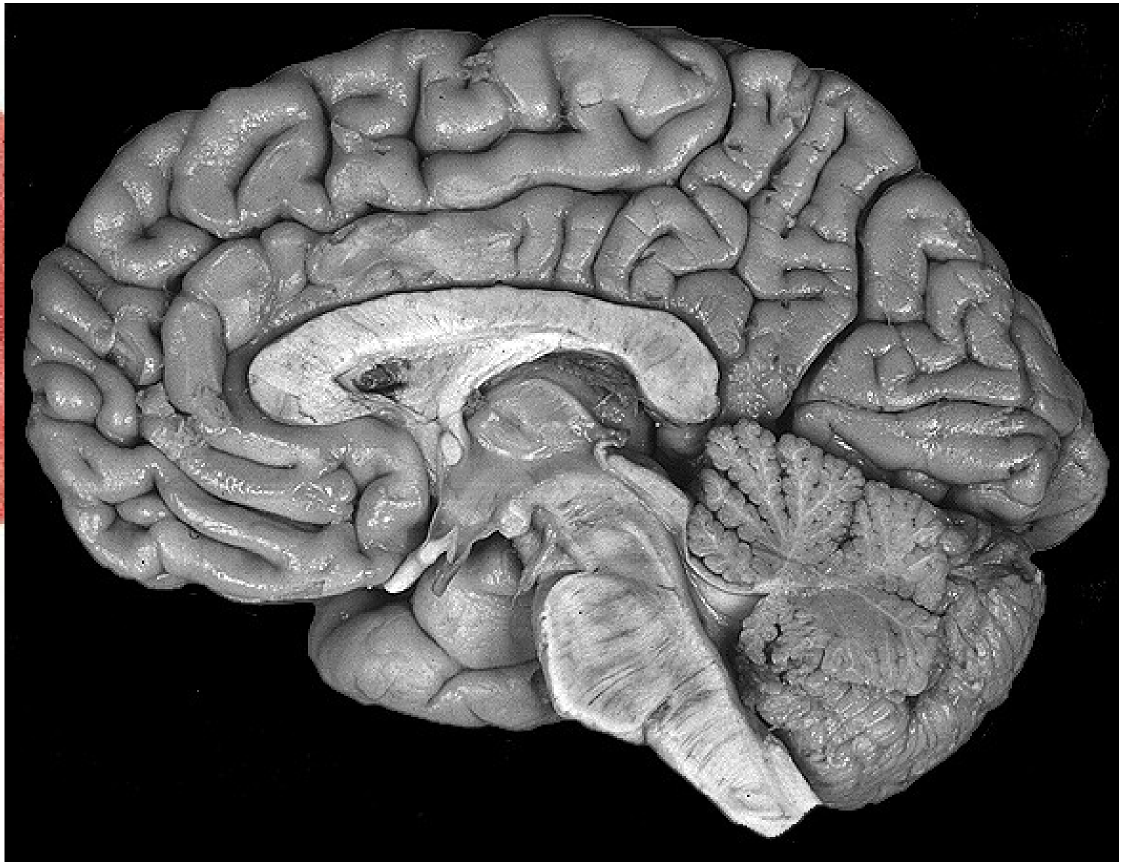
First Look



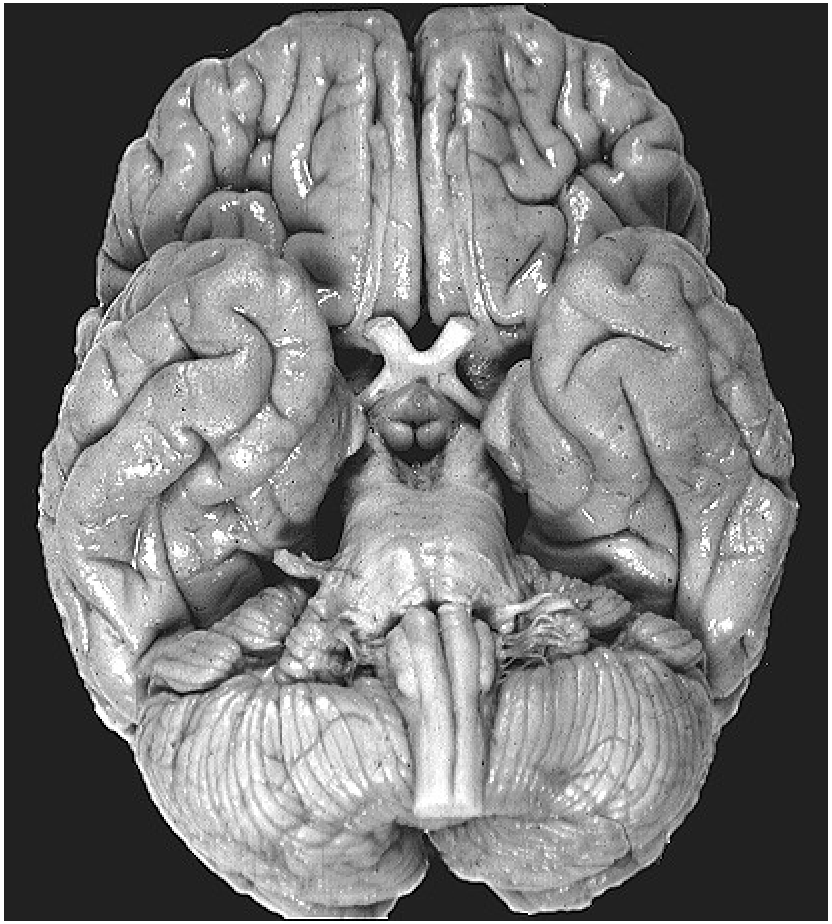


Lateral View





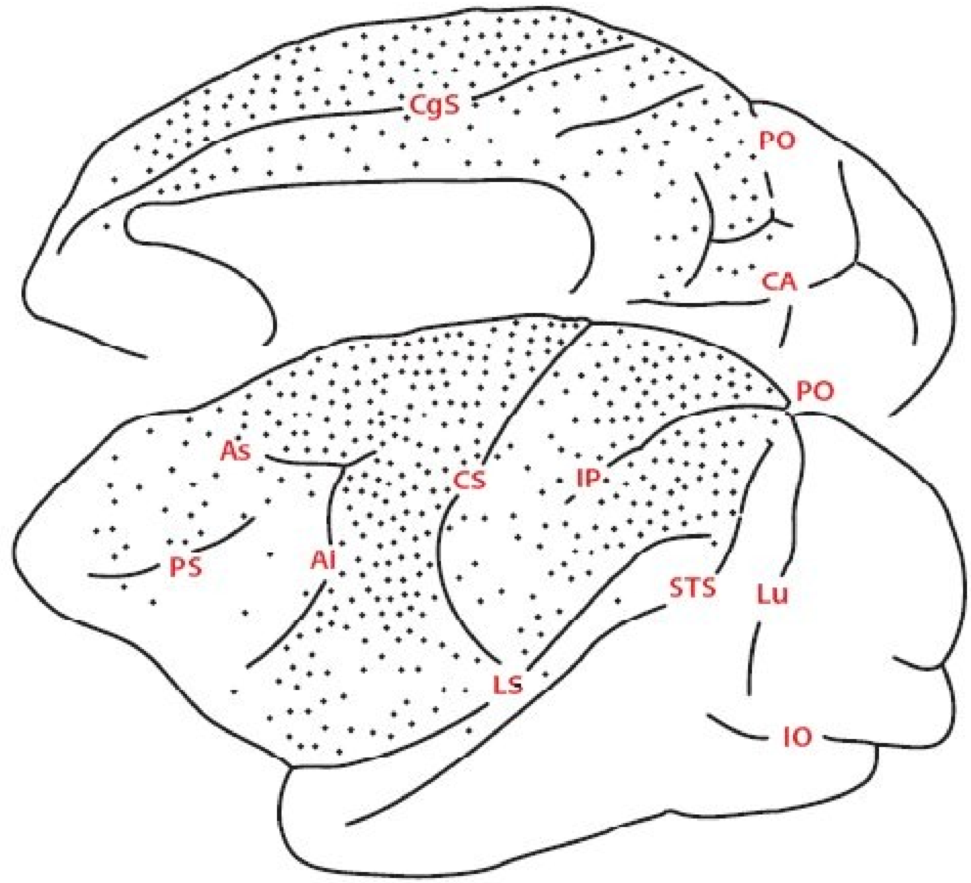
Ventral View

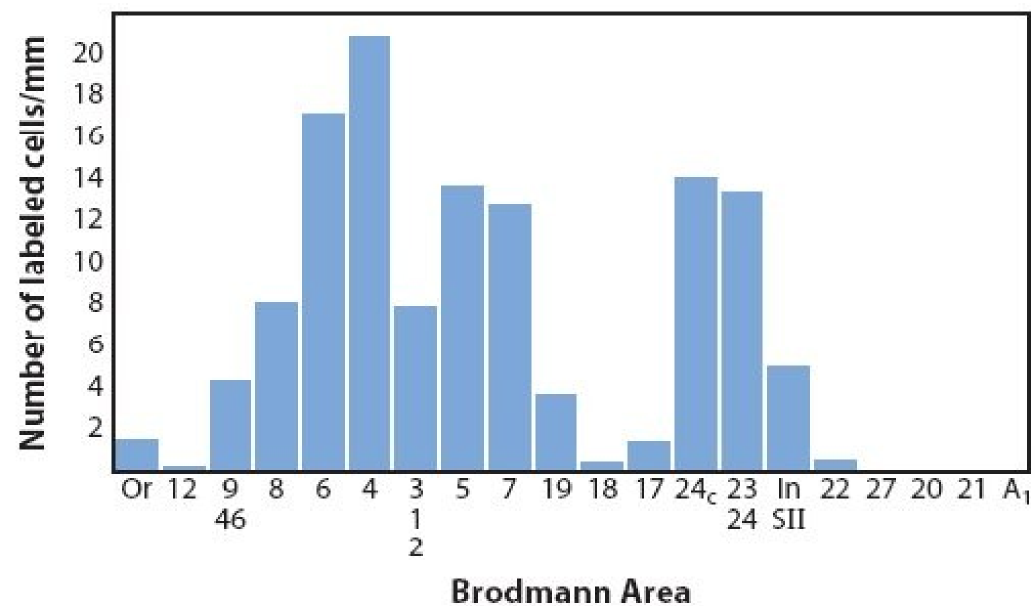


Basic Facts About the Cerebellum

- Latin for “little brain”.
- An older brain area, with a simple, regular architecture.
- Makes up 10% of brain volume, but contains over 50% of the brain's neurons and 4X the neurons of the cerebral cortex.
- Huge fan-in: 40X as many axons enter the cerebellum as exit from it.
- Necessary for smooth, accurate performance of motor actions.
- Example: moving your arm rapidly in a circle.
  - Involves many muscles in the arm, trunk, and legs.
- People can still move without a cerebellum, but their actions will not be coordinated. There can be overshoots and oscillations.

Cortical Projections to Cerebellum

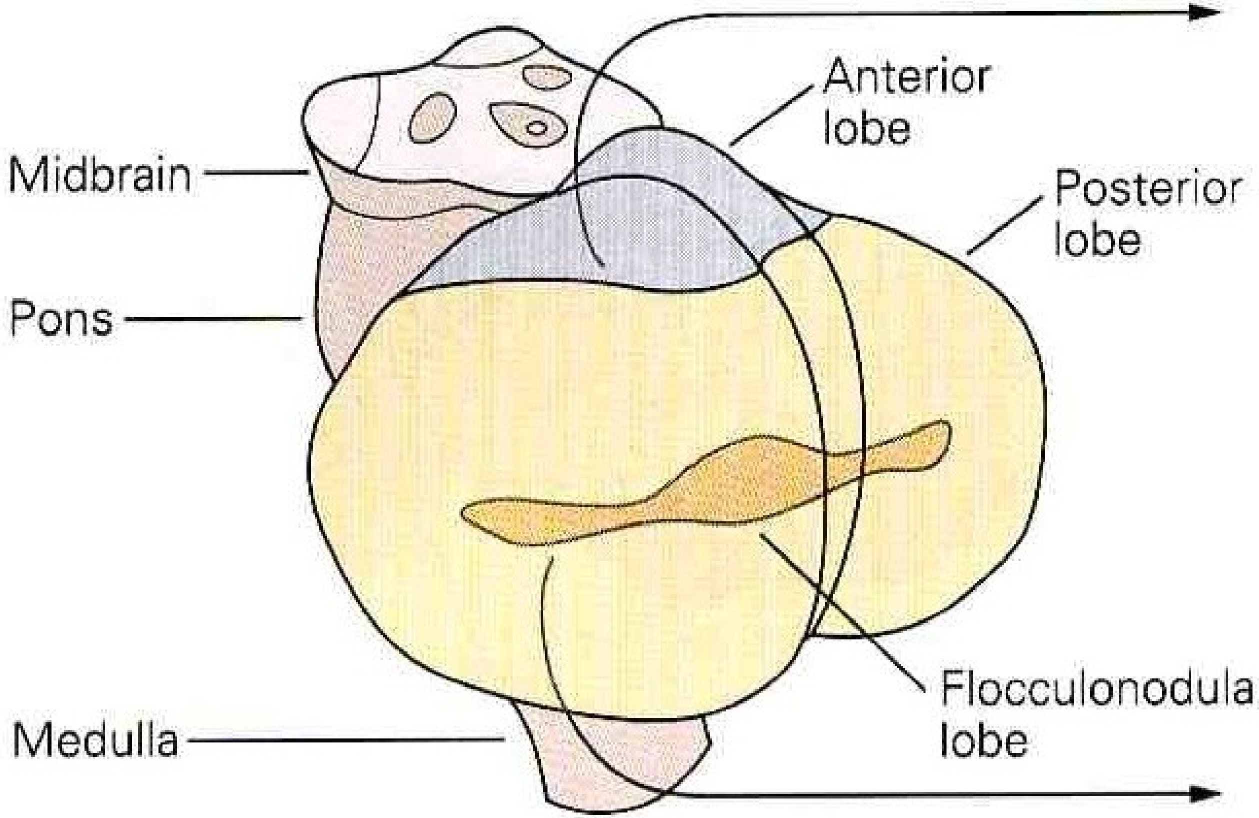




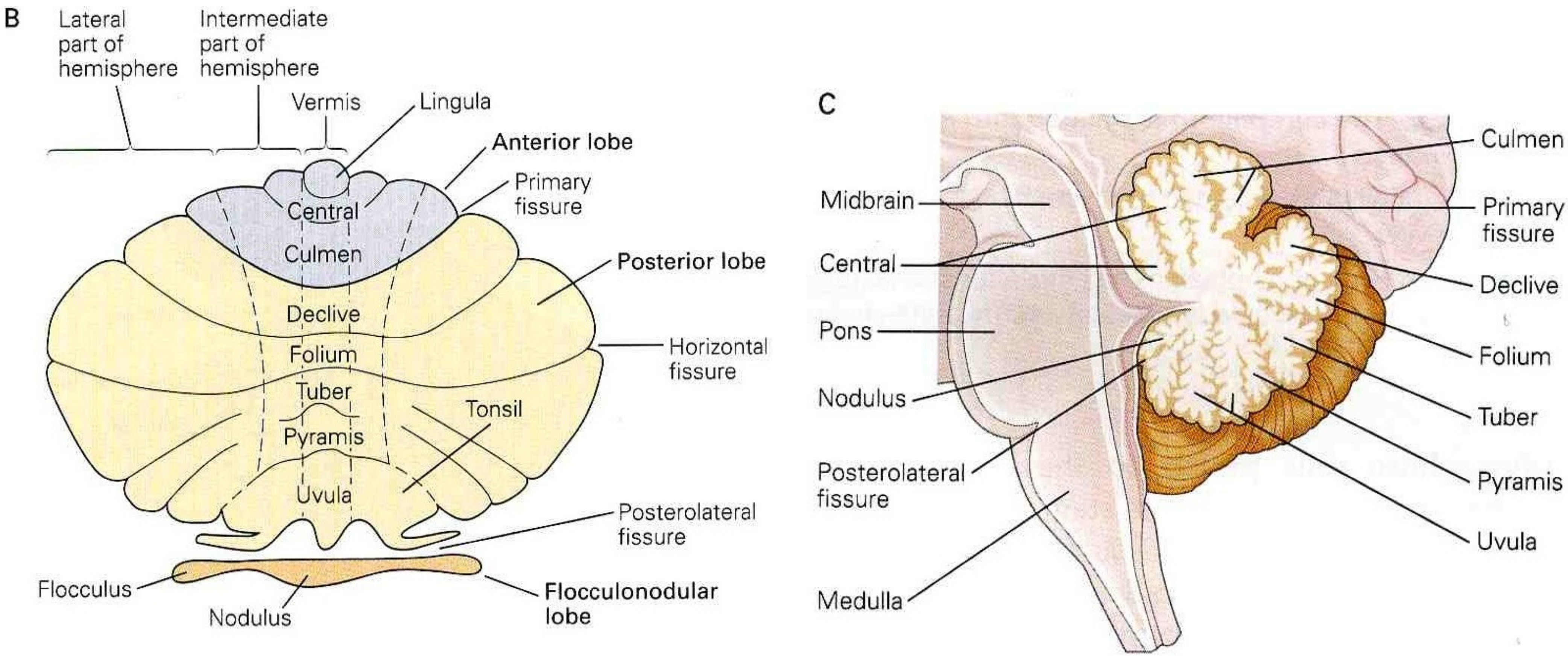
From Strick et al., Annual review of Neuroscience (2009), adapted from Glickstein et al. (1985) J. Comparative Neurology

Three Cerebellar Lobes

- Anterior (divided into 3 lobules)
- Posterior (divided into 6 lobules)
- Flocculonodular



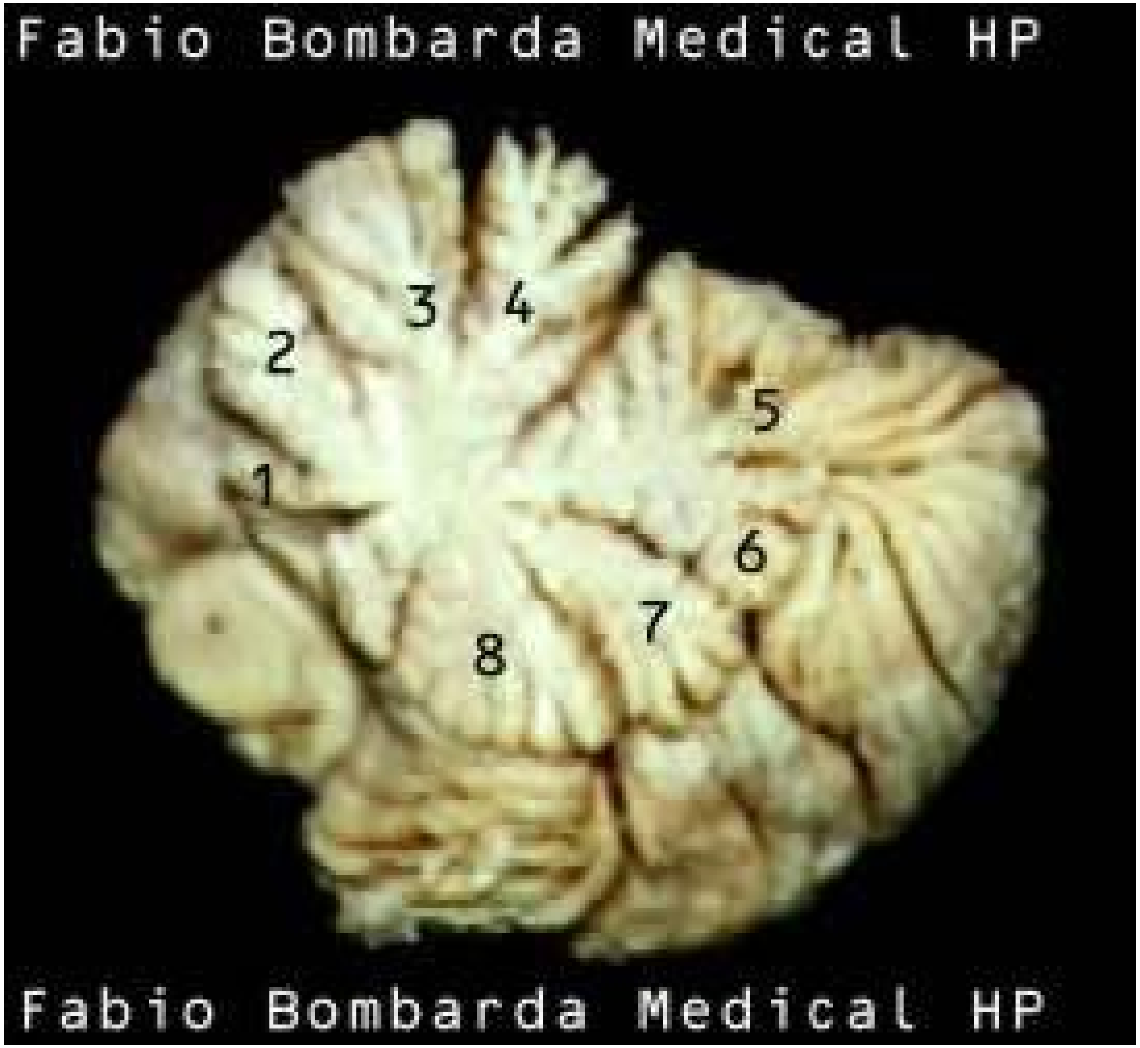
10 Lobules



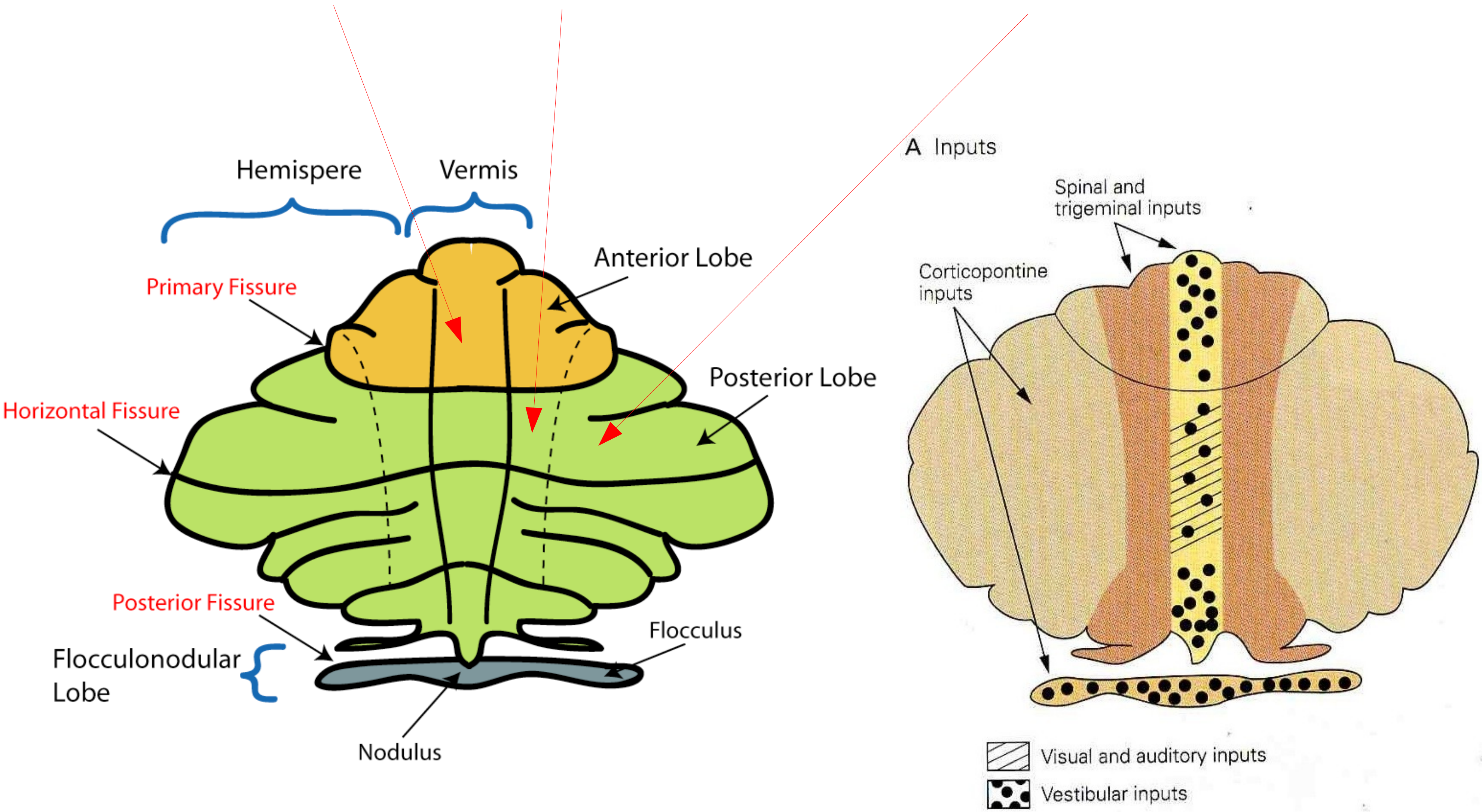
Lingula, Central, Culmen, Declive, Folium, Tuber, Pyramis, Uvula, Tonsil, Flocculonodular

8 of the 10 Lobules

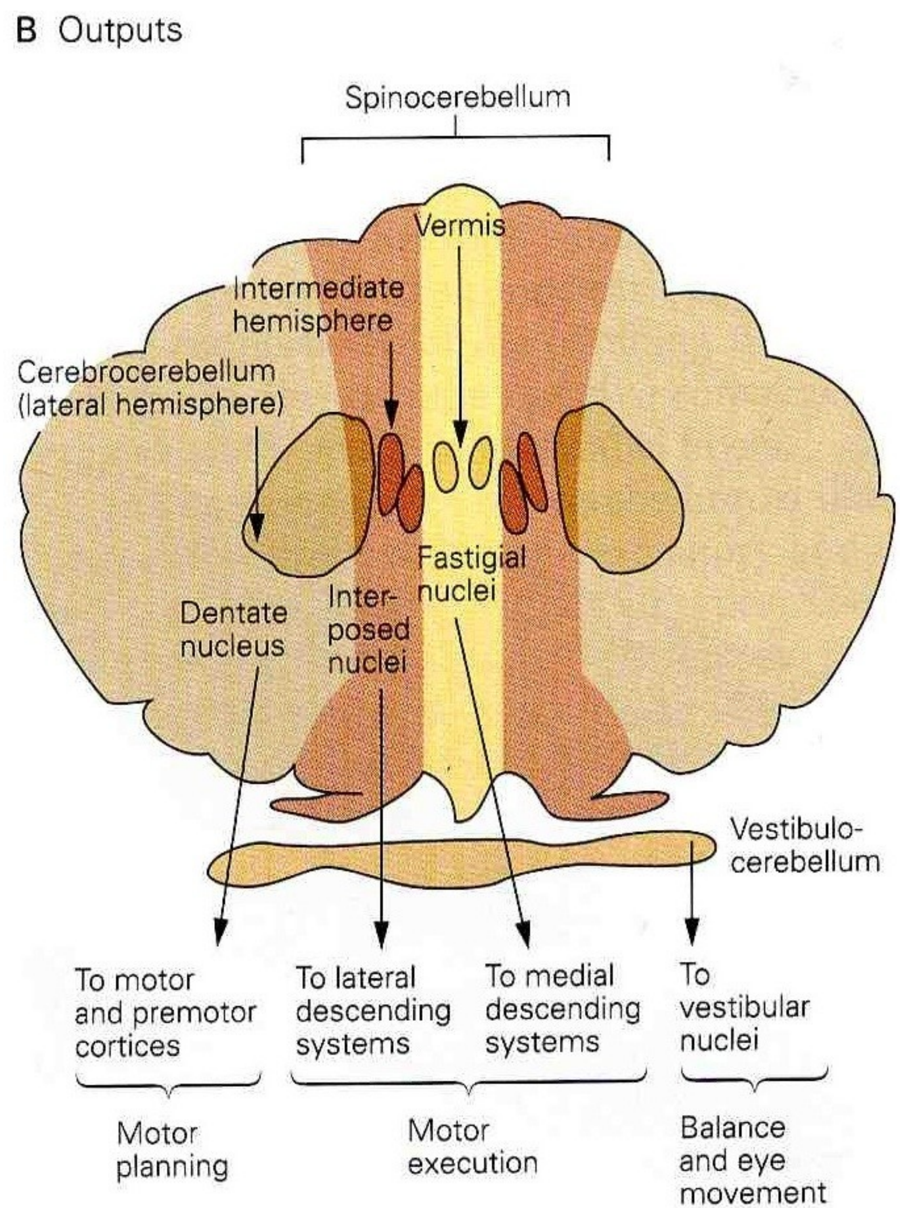
1. Lingula
2. Central Lobule
3. Culmen
4. Declive
5. Folium
6. Tuber
7. Pyramis
8. Uvulae



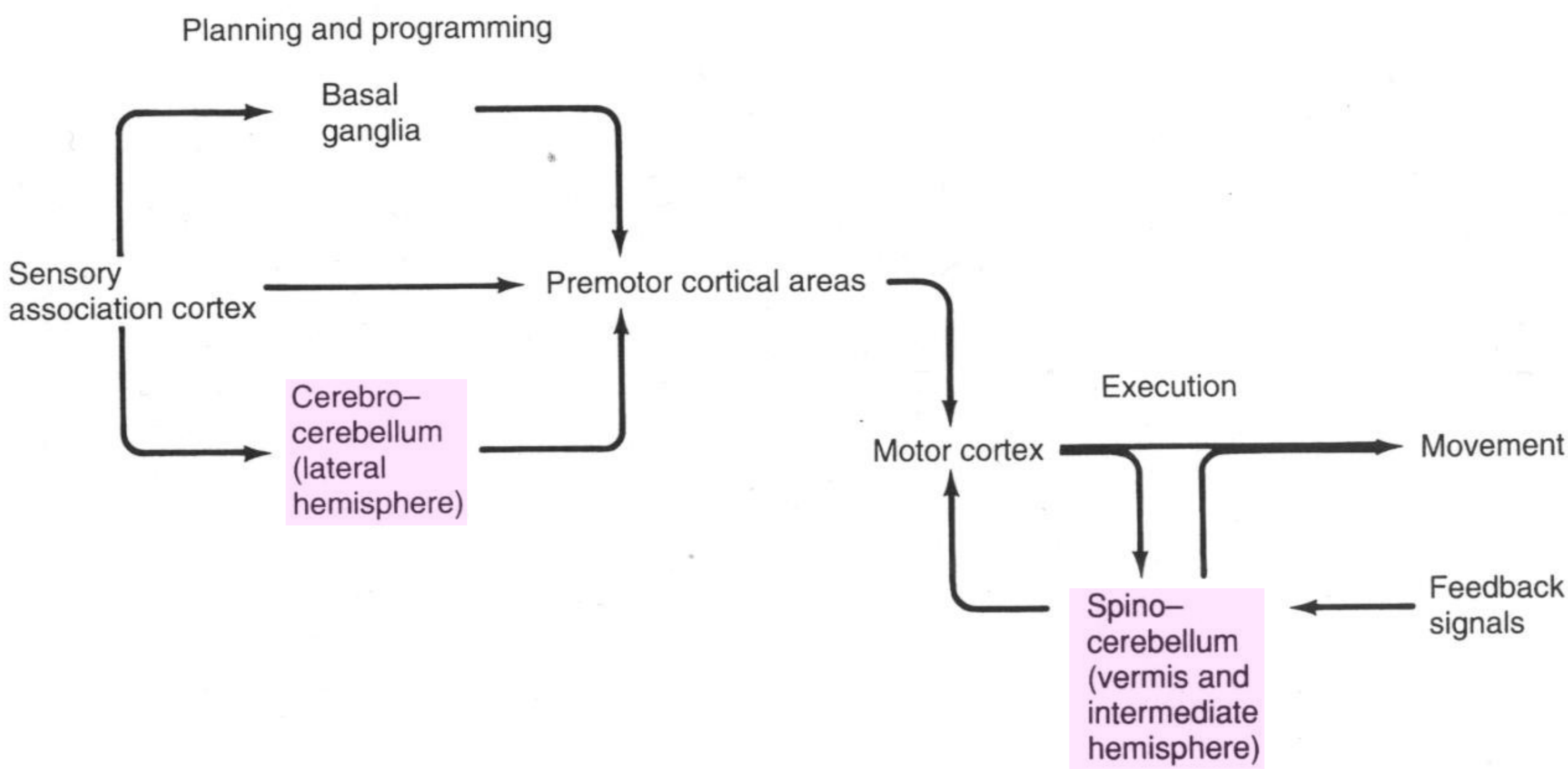
Vermis, and Intermediate and Lateral Zones



Spinocerebellum, Cerebrocerebellum, and Vestibulocerebellum

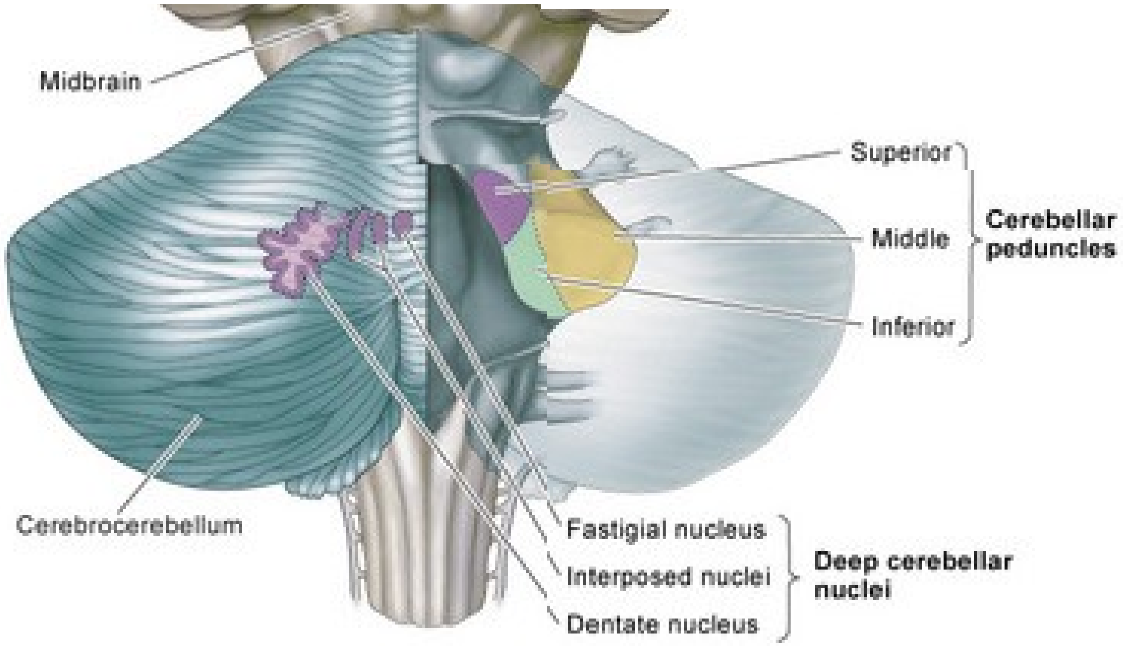


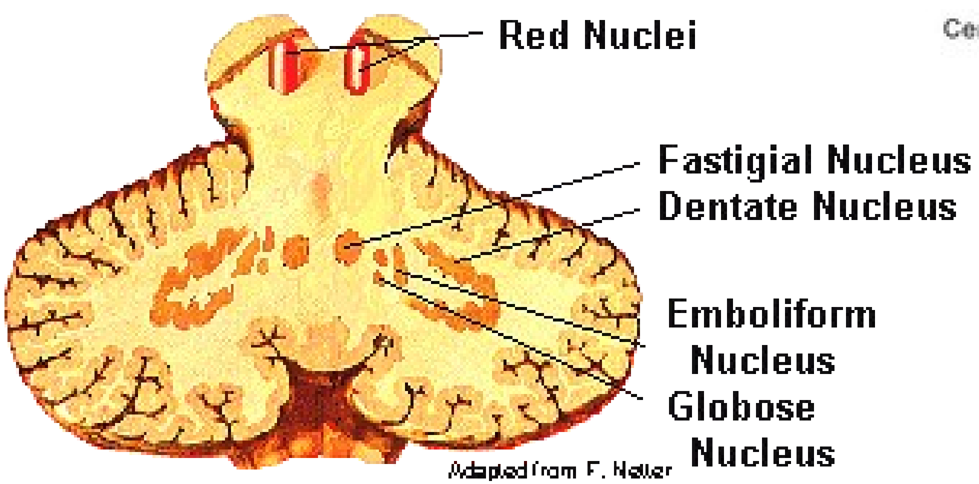
Control of Movement



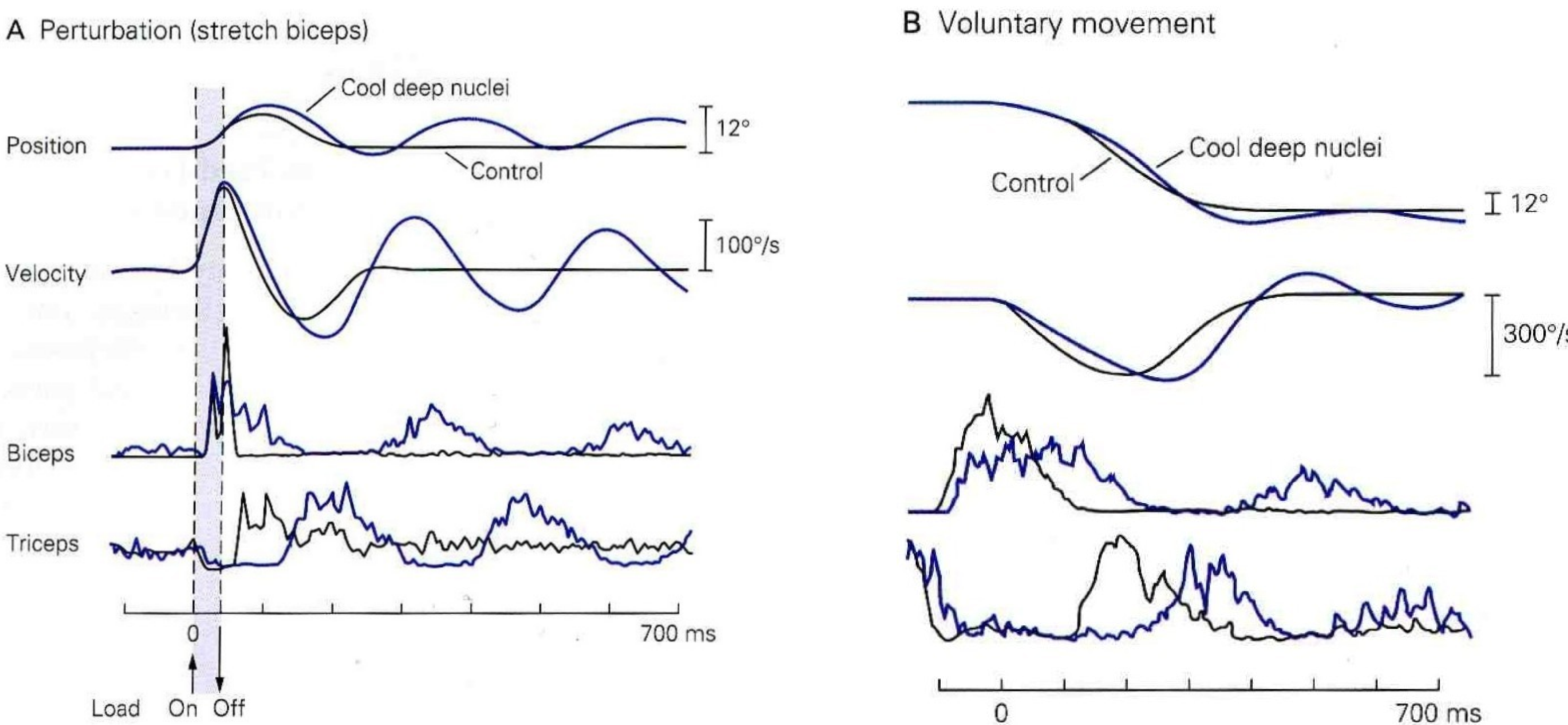
Deep Cerebellar Nuclei

- Fastigial nucleus ← vermis
- Interposed nuclei ← intermediate hemisphere
  - Globose
  - Emboliform
- Dentate nucleus ← lateral hemisphere

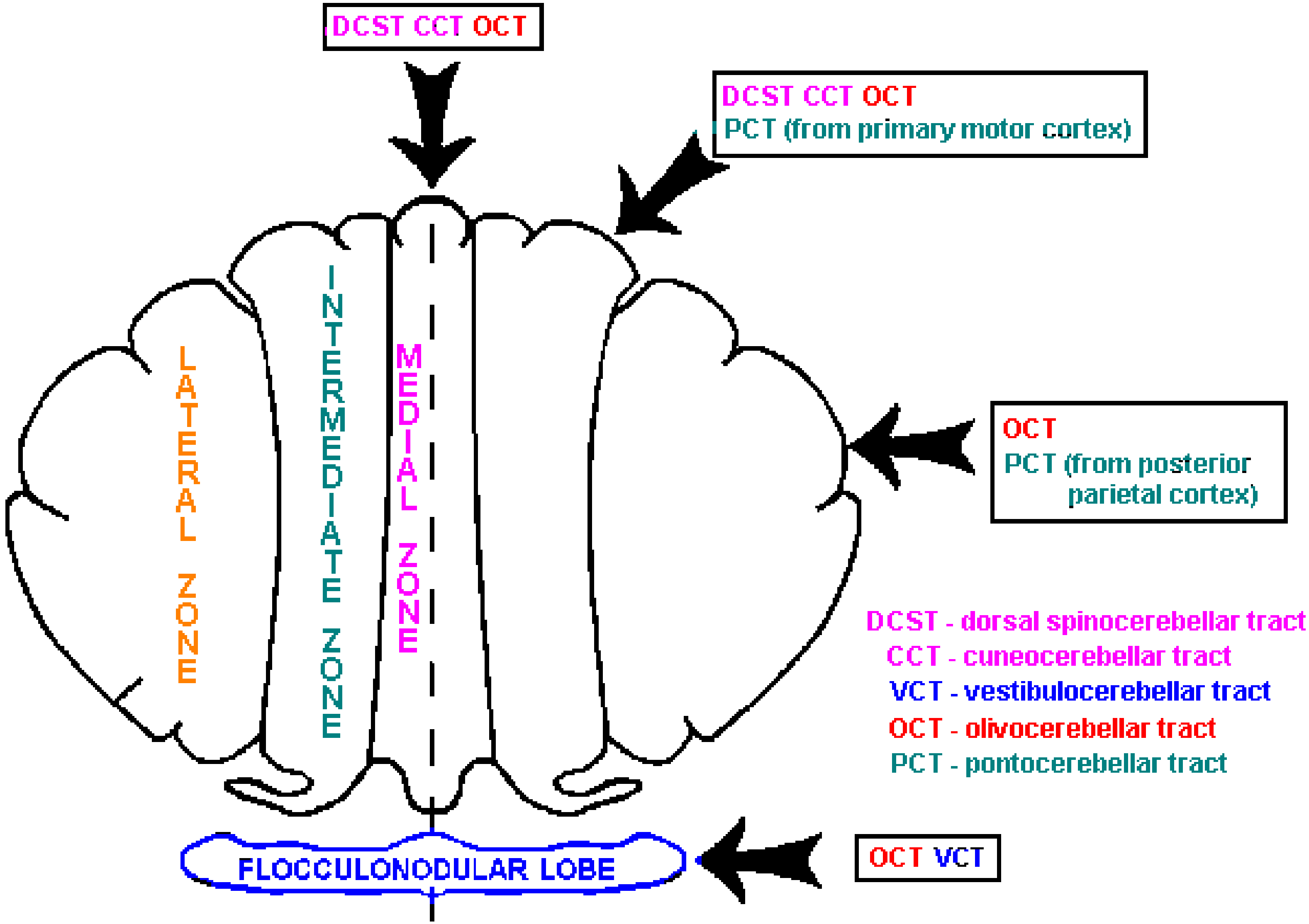




Cooling the Dentate and Interpositus



Input Pathways



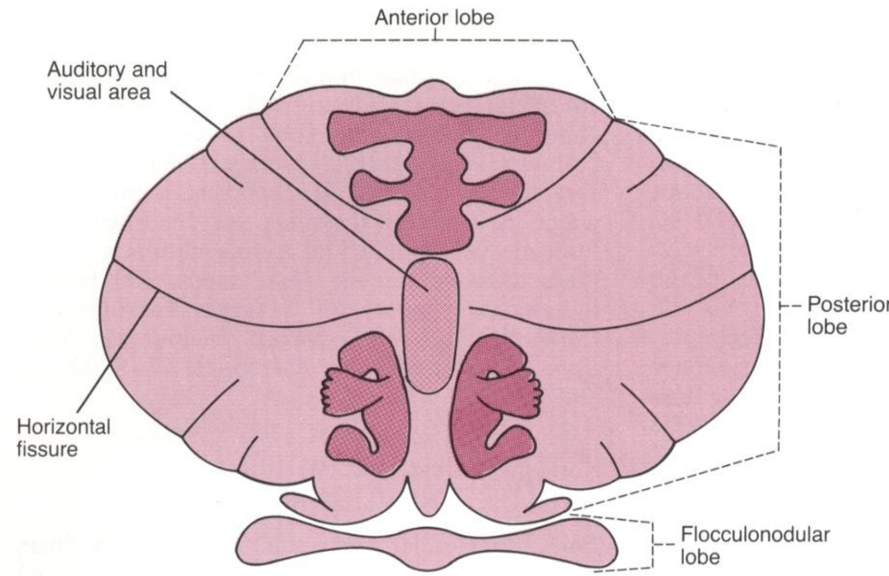
http://www.neuoanatomy.wisc.edu/cere/text/p3/zones.htm

Vestibulocerebellum

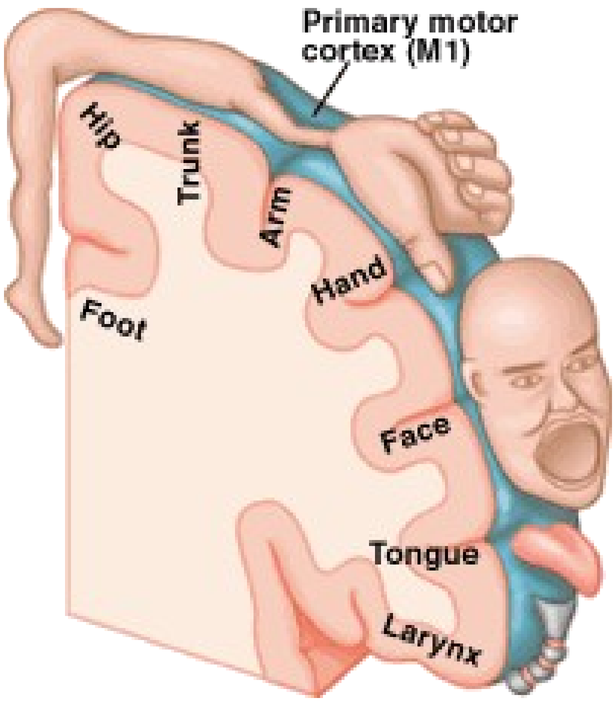
- Located in the flocculonodular node.
- Responsible for balance, eye movements, head movements.
- Modulates the VOR (Vestibulo-Ocular Reflex).
  - Experiment: push your eyeball with your finger.
- Receives input from the vestibular nuclei in the medulla and projects directly back to them, instead of deep cerebellar nuclei.
- Also receives direct input from the semicircular canals and otolith organs.
- Receive some visual information from lateral geniculate nucleus (thalamus), superior colliculi, and striate cortex, mostly relayed through the pons.

Spinocerebellum

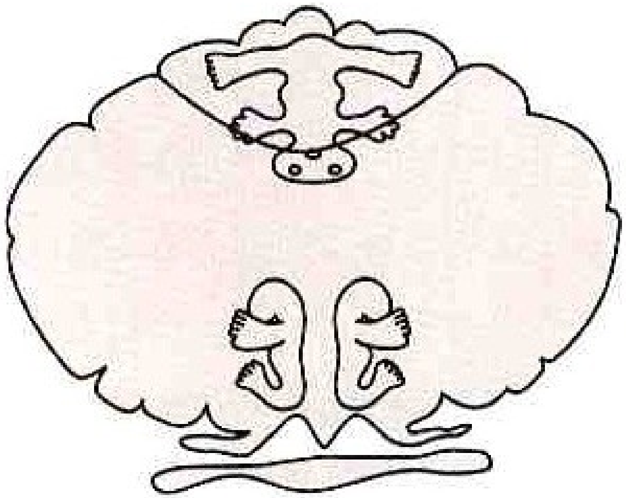
- Located in the central portion of the anterior and posterior lobes. Consists of the vermis and intermediate zone. Diverse inputs.
- Responsible for adjusting ongoing movements:
  - The vermis is concerned with balance and with proximal motor control. It projects to the fastigial nucleus.
  - The intermediate zone is concerned with distal motor control. It projects to the interposed nuclei (globose and emboliform).
- Contains two somatotopic maps of the body.
- Inputs from spinal cord: touch, pressure, limb position, motor efference copy.

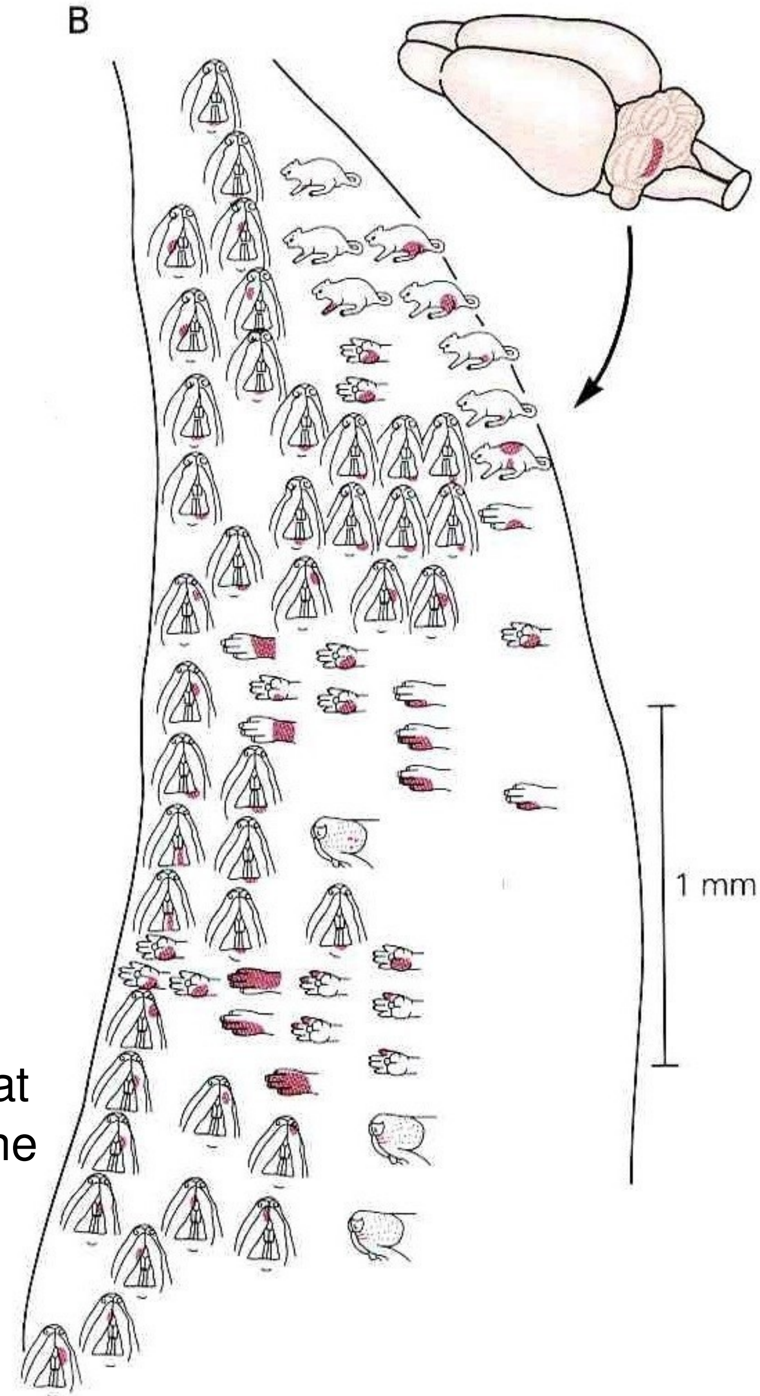


Homunculus in Motor Cortex



Fractured Somatotopy

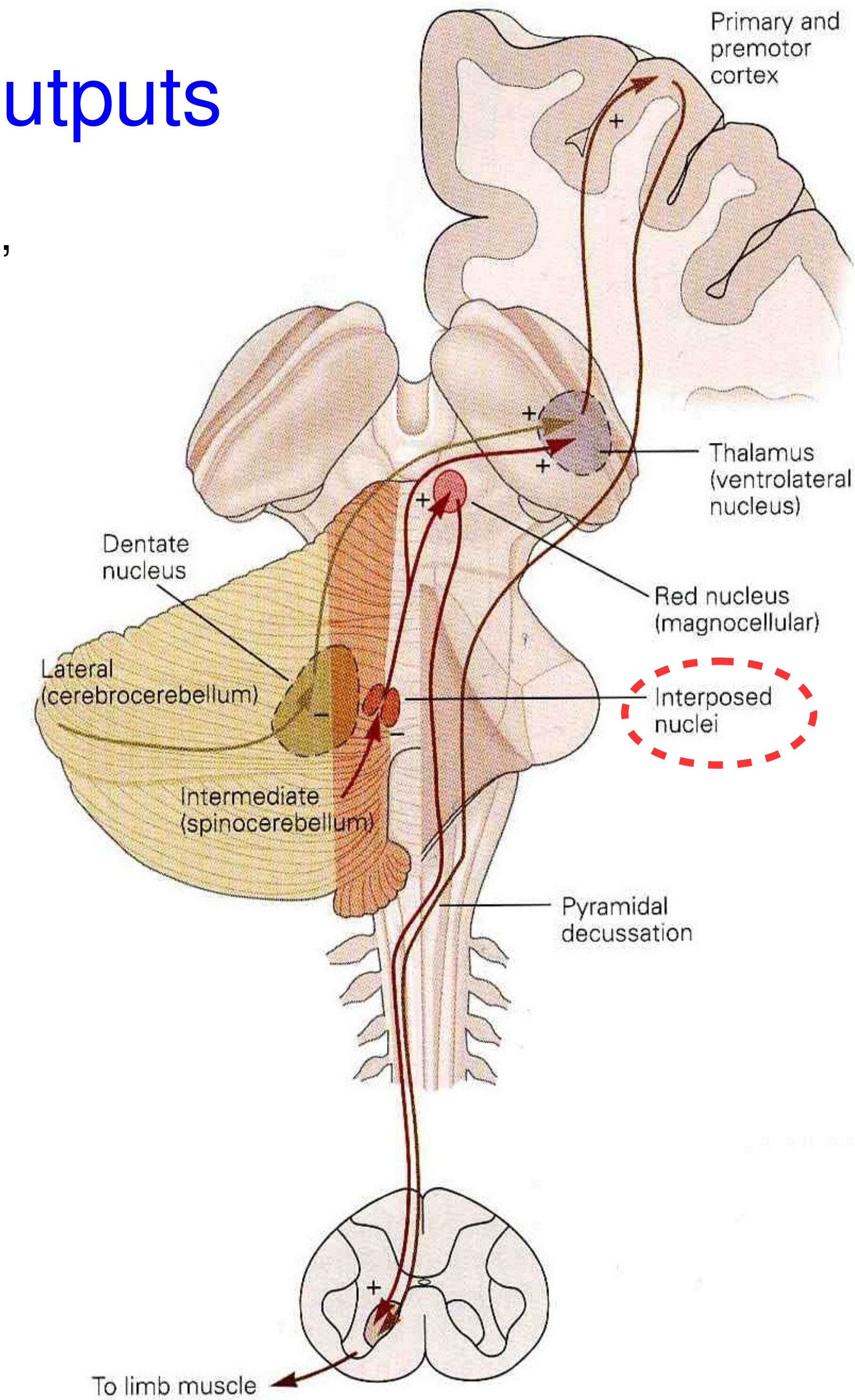




Representation of rat face and paws on the cerebellar surface.

Spinocerebellum outputs

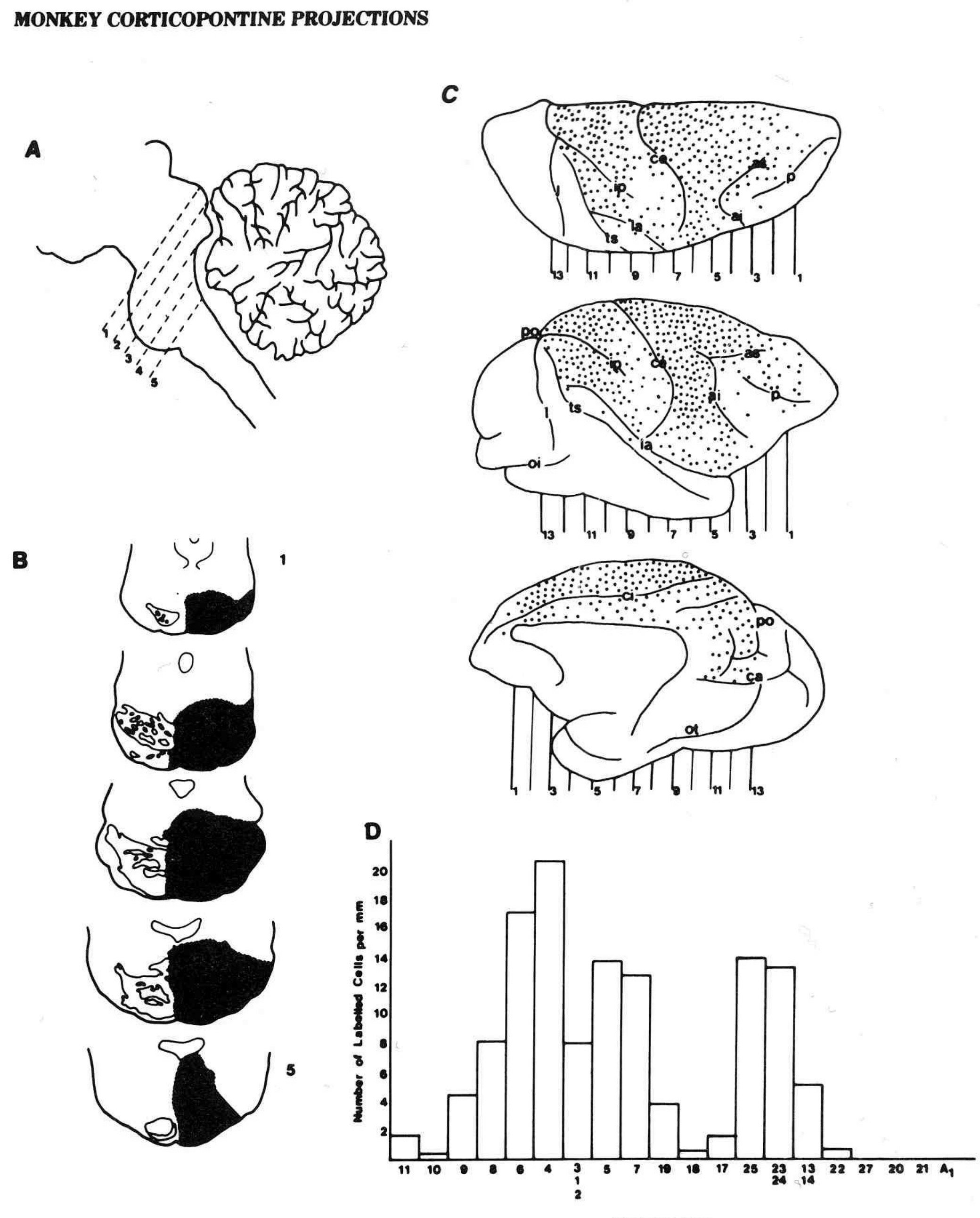
Projects to the interposed nuclei, thence to the red nucleus and thence to the spinal cord.



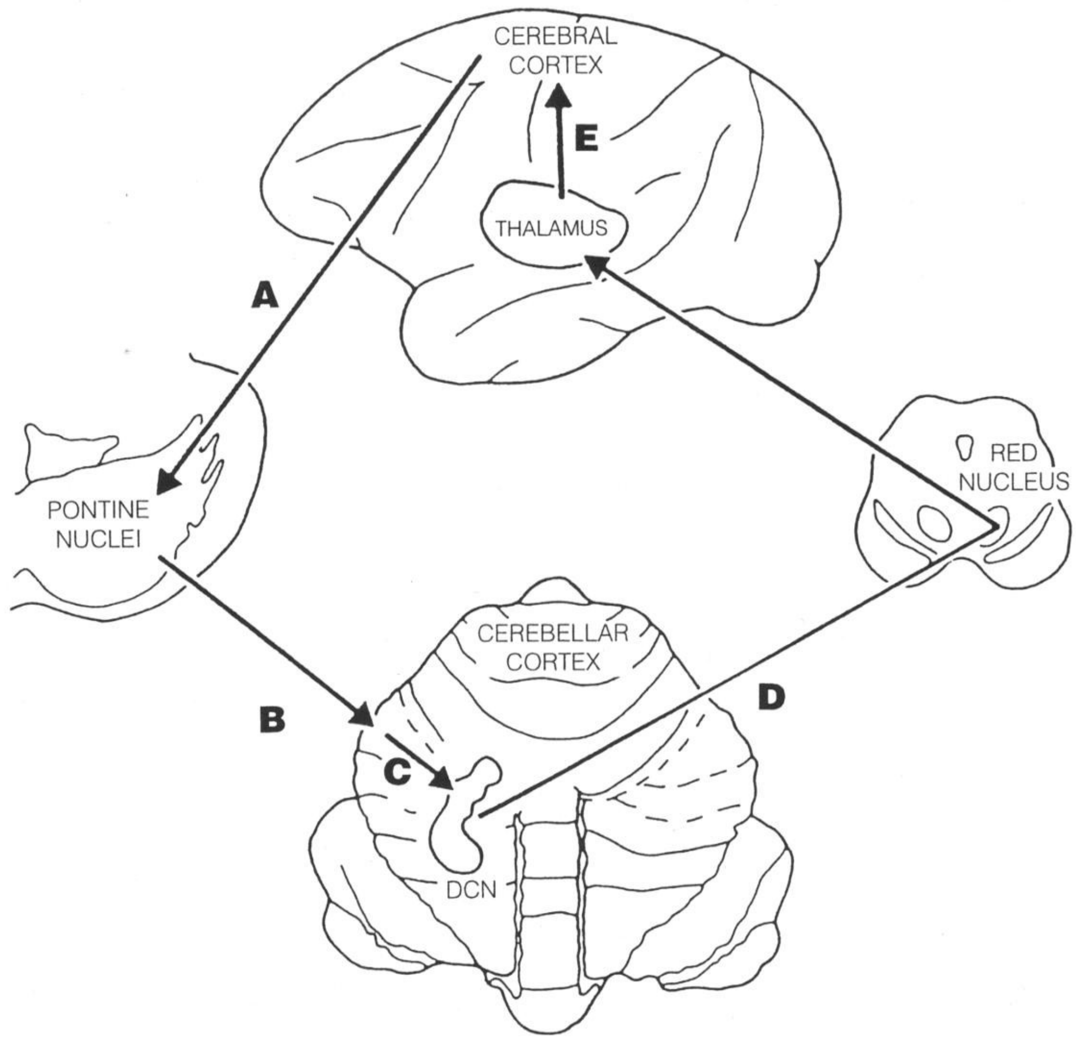
Cerebrocerebellum

- Located in lateral portions of anterior and posterior lobes.
- Responsible for planning of limb movements.
- Receives input from sensory and motor cortices, including secondary motor areas (premotor and posterior parietal cortices), via the <u>pontine nuclei</u>.
- Projects to the <u>dentate nucleus</u>, which in turn projects back to thalamic nuclei which project back to cortex.
- Lesions to the cerebrocerebellum produce delays in movement initiation, and in coordination of limb movement.
- May play a more general role in timing. Some patients with lesions in this area have difficulty producing precisely timed tapping movements

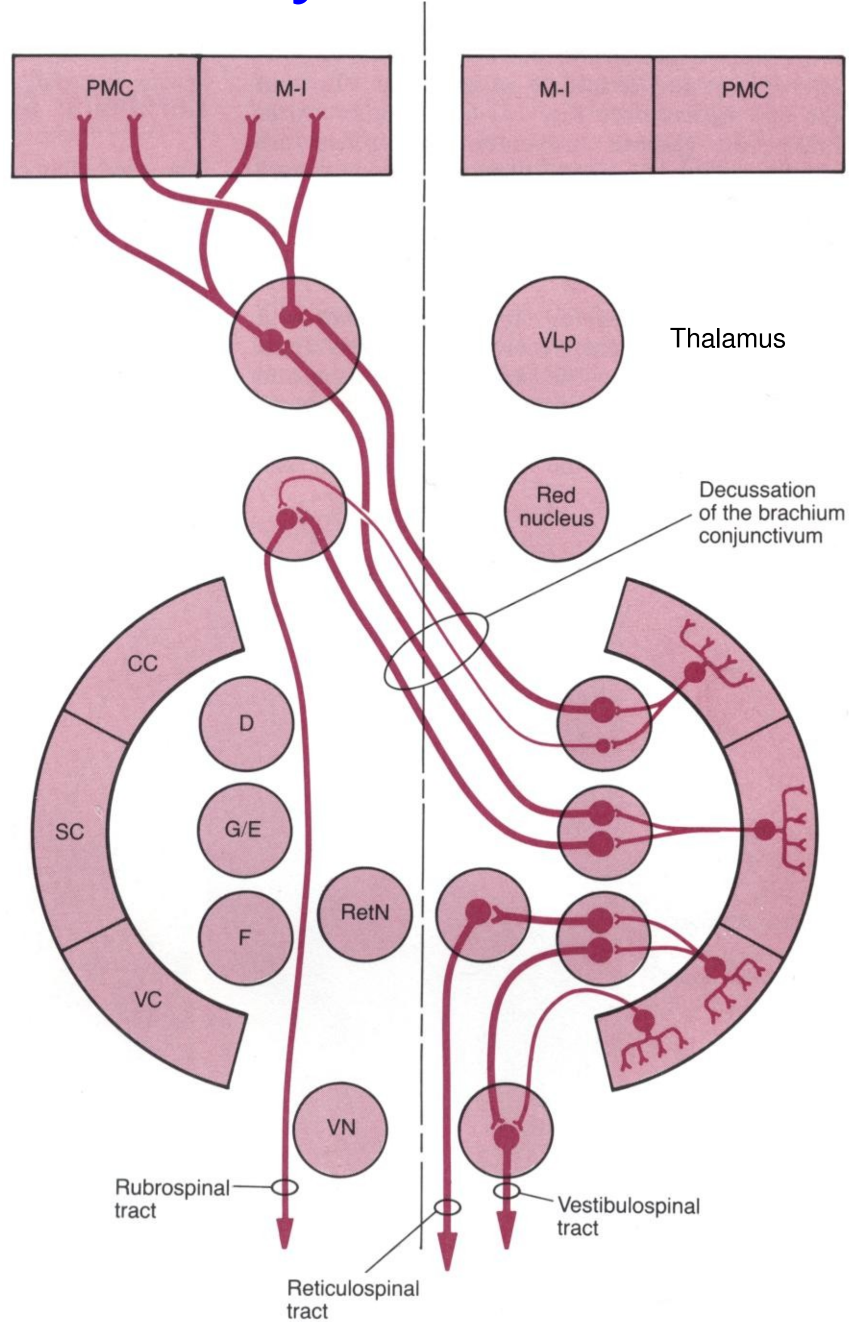
Corticopontine Projections in Monkey



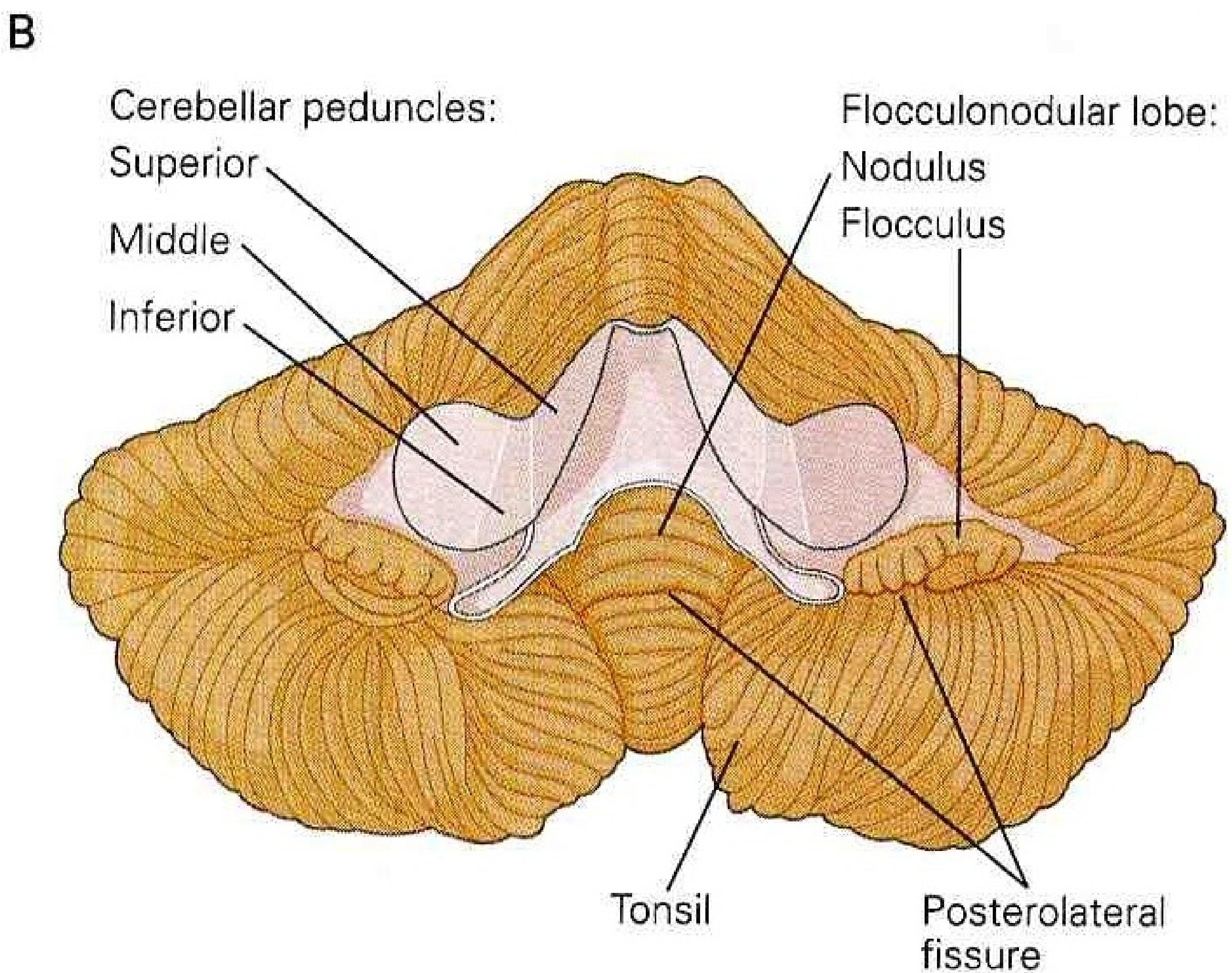
Cerebro-Cerebellar Circuit



Output Pathways of CC, SC, and VC



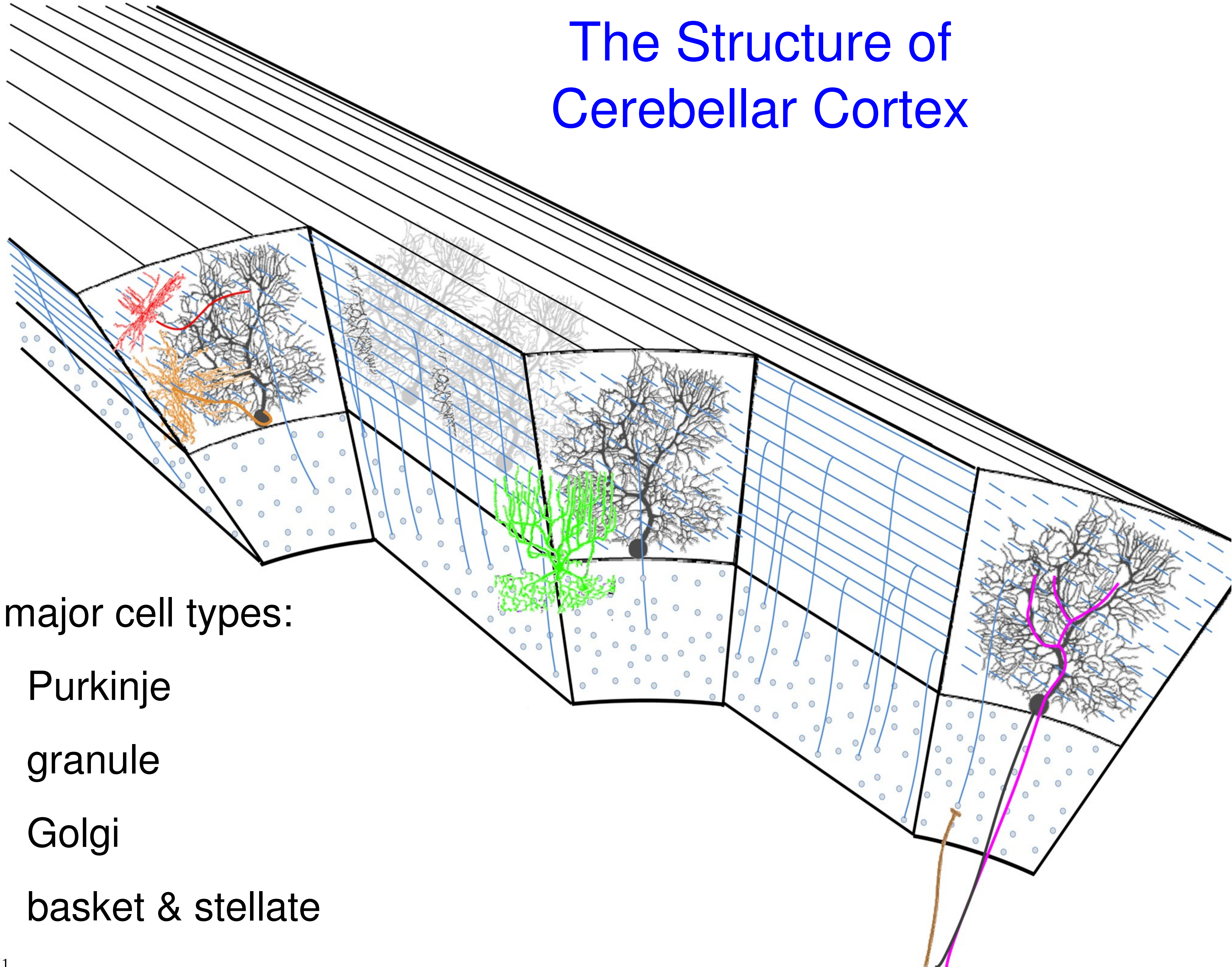
Cerebellar Peduncles: Large Fiber Tracts



Cerebellar Peduncles

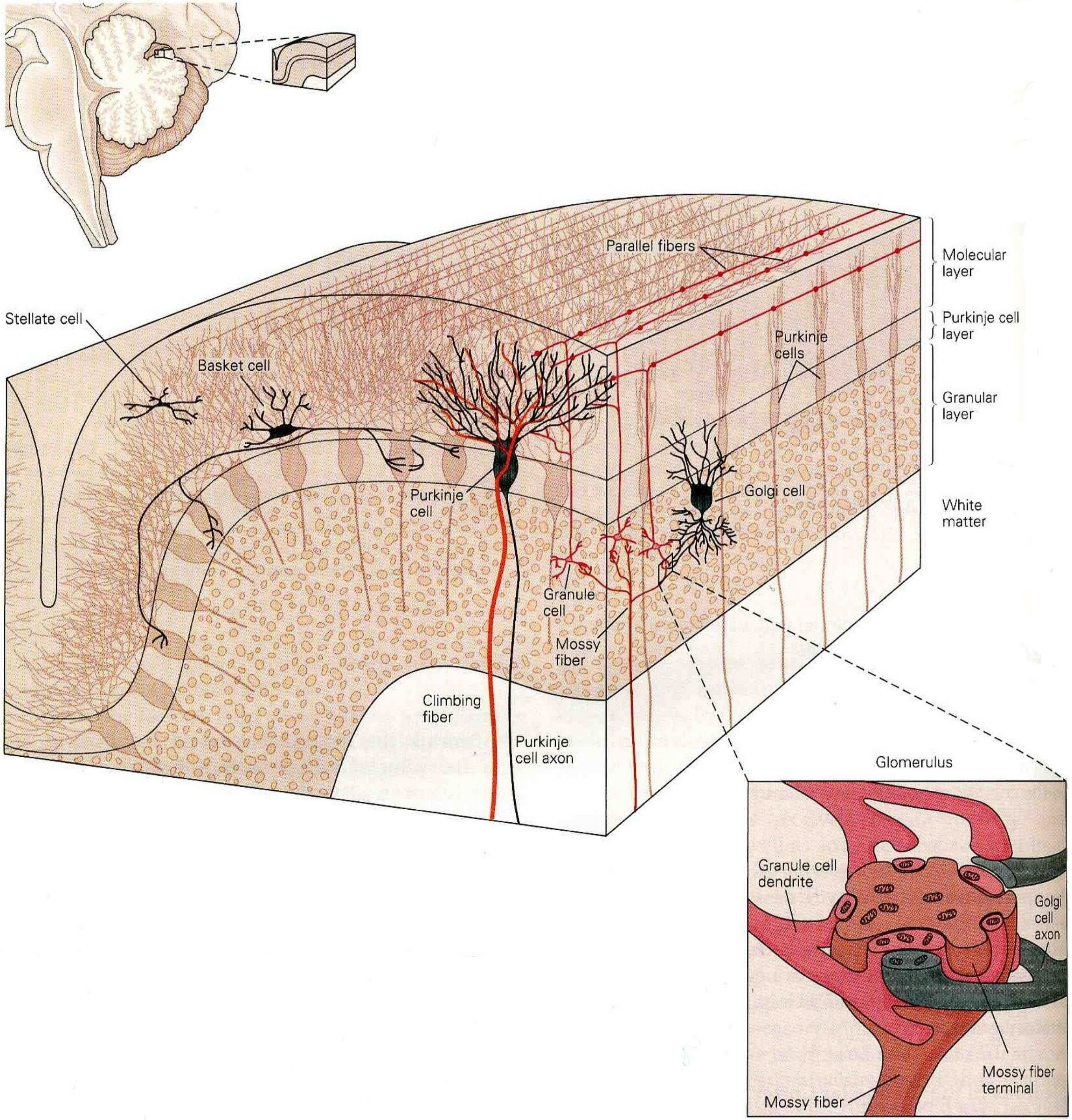
- Superior cerebellar peduncle
  - Contains most of the cerebellum's efferent (output) fibers, including all of those from the dentate and interposed nuclei.
  - Contains one afferent pathway: ventral spinocerebellar tract, carrying information from the lower extremity and trunk.
- Middle cerebellar peduncle
  - Carries input information from cerebral cortex via the pons.
- Inferior cerebellar peduncle
  - Carries afferent information from spinocerebellar pathways.
  - Carries olivocerebellar fibers (from inferior olive)

The Structure of Cerebellar Cortex



5 major cell types:

- Purkinje
- granule
- Golgi
- basket & stellate



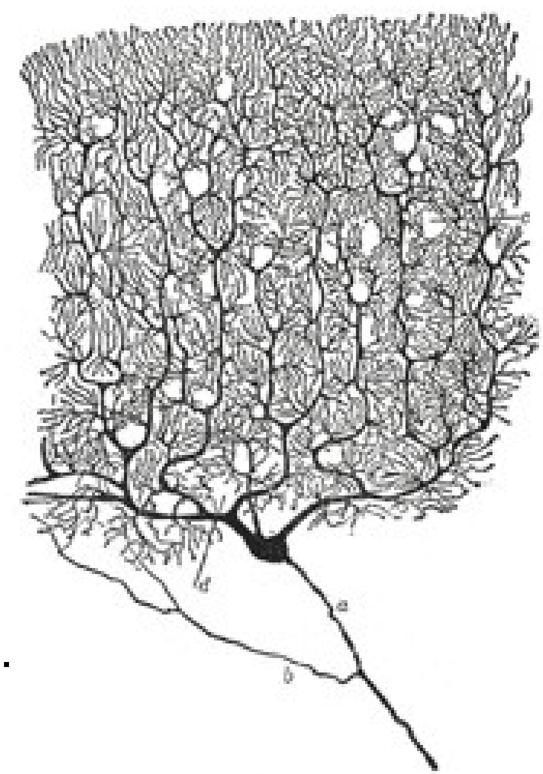
Parallel fibers
Molecular layer
Purkinje cell layer
Granular layer
White matter
Stellate cell
Basket cell
Purkinje cells
Purkinje cell
Golgi cell
Granule cell
Mossy fiber
Climbing fiber
Purkinje cell axon
Glomerulus
Granule cell dendrite
Golgi cell axon
Mossy fiber terminal
Mossy fiber

Purkinje Cells

- Cortex has three layers: granule, Purkinje, and molecular.
- Seven cell types:

  1. Purkinje cells: the largest cells in the brain. Principal cells of cerebellar cortex. 200,000 synapses each. Provide the only output pathway from cerebellar cortex.

Purkinje cell
drawn by Cajal

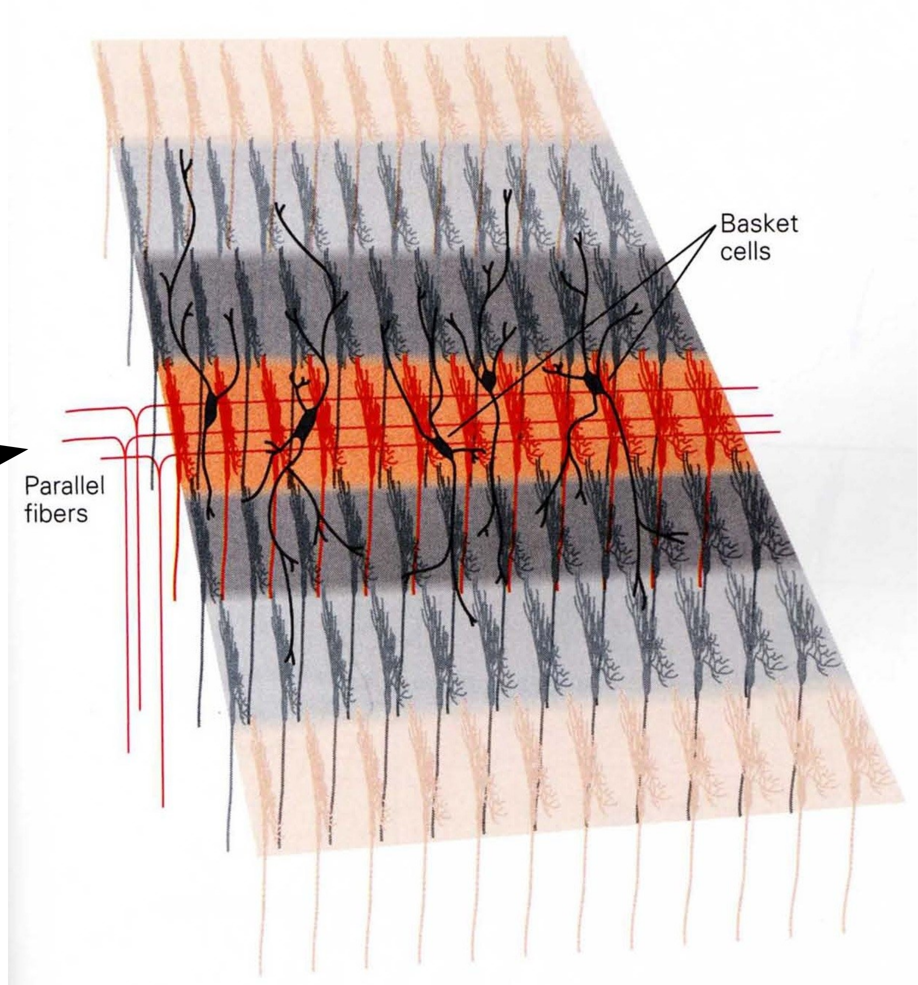


Purkinje cells are inhibitory and
use GABA as their neurotransmitter.

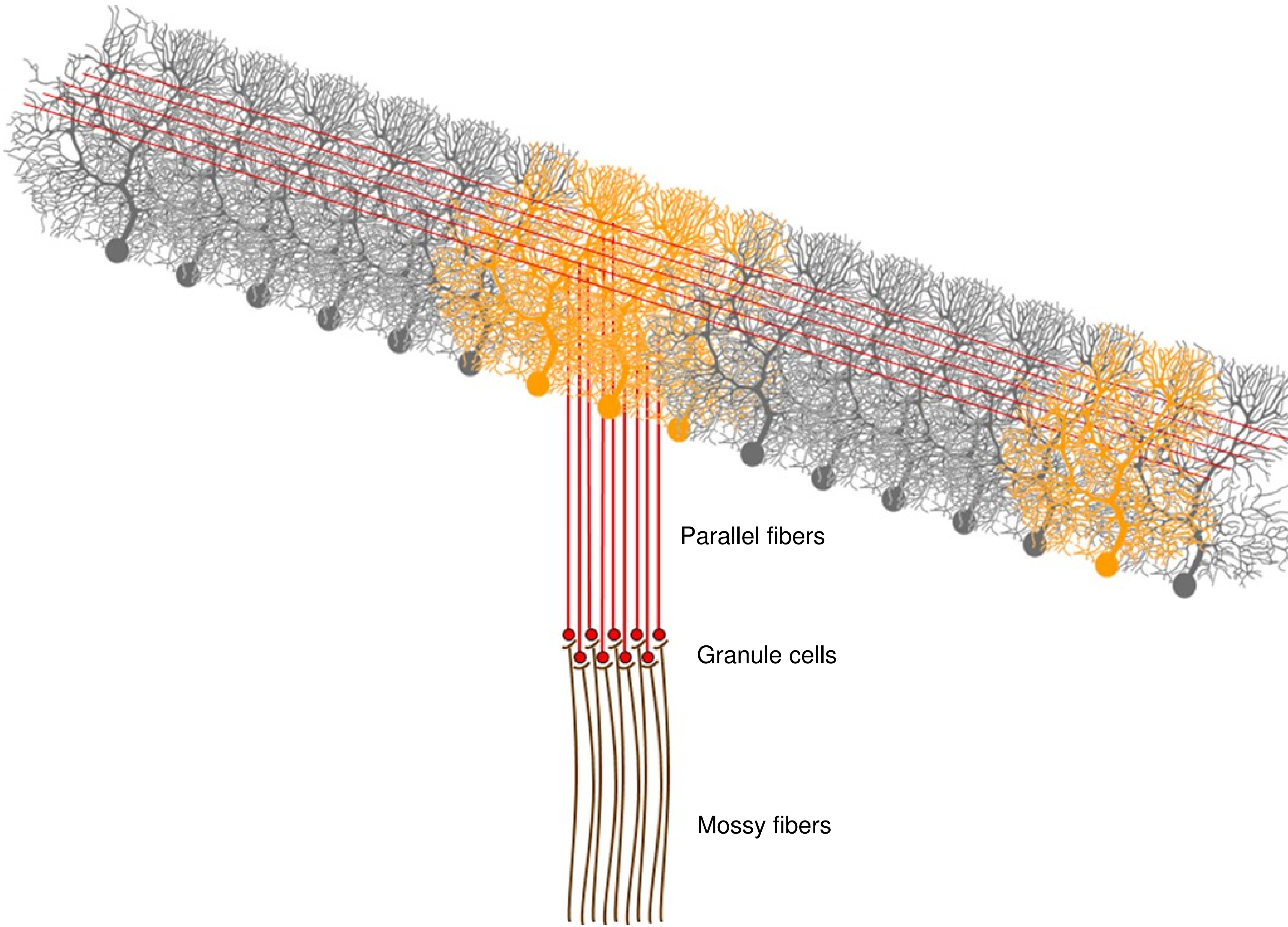
Granule Cells

2. Granule cells are the input cells of the cerebellar cortex. Their axons form the parallel fibers that innervate the Purkinje cells. About 10^{11} granule cells.

A cerebellar "beam"



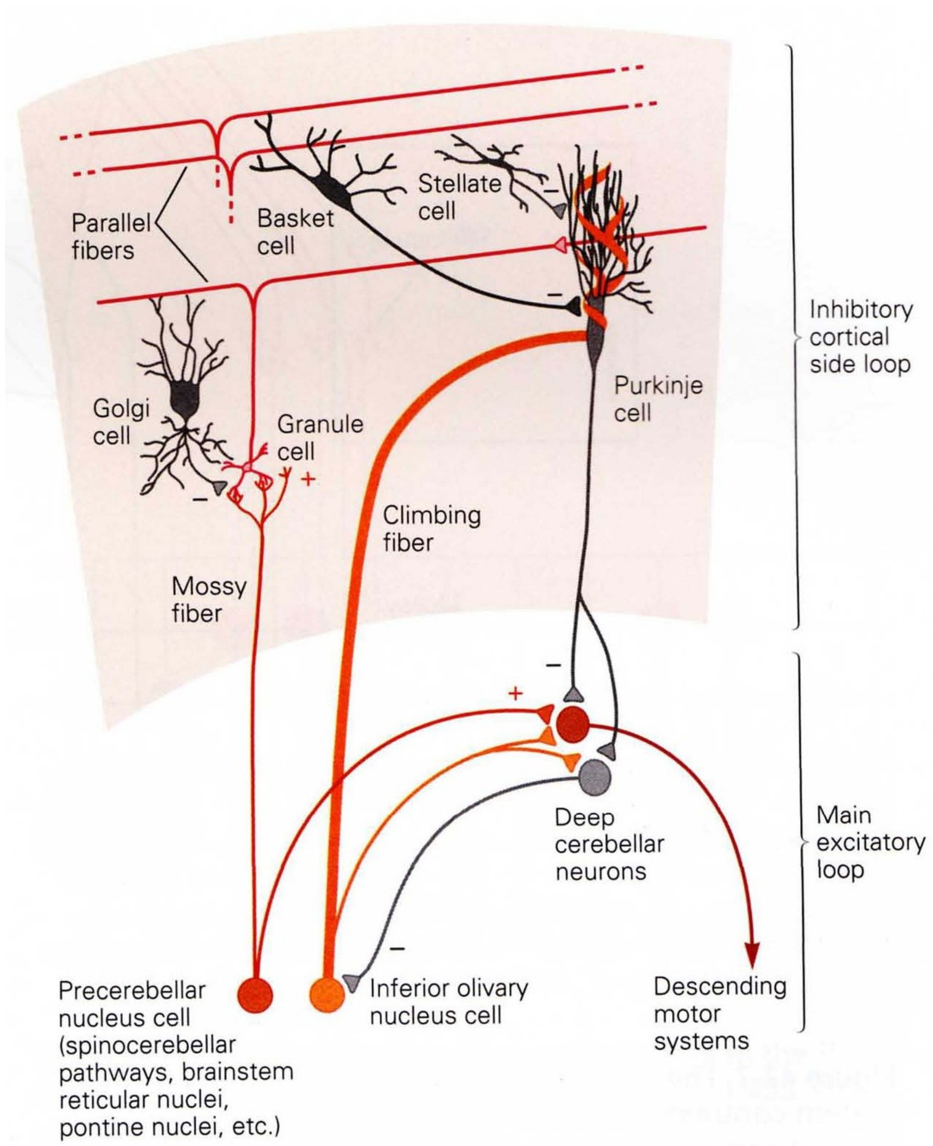
More Views of the Beam



Inhibitory Interneurons

3. Golgi cells: receive input from mossy and parallel fibers, and inhibit the mossy fiber to granule cell synapses, thus modulating the signal on the parallel fibers.
4. Basket cells: receive input from and inhibit the Purkinje cells, providing a kind of gain control. Short-range, possibly off-beam inhibition.
5. Stellate cells: apparently the same feed-forward inhibitory function as basket cells. Long-range inhibition.

Circuitry of Cerebellar Cortex



More Interneurons

6. Lugaro cells receive input from 5-15 Purkinje cells and project to basket, stellate, and Golgi cells.

7. Unipolar brush cells. Excitatory interneurons using glutamate as the neurotransmitter.

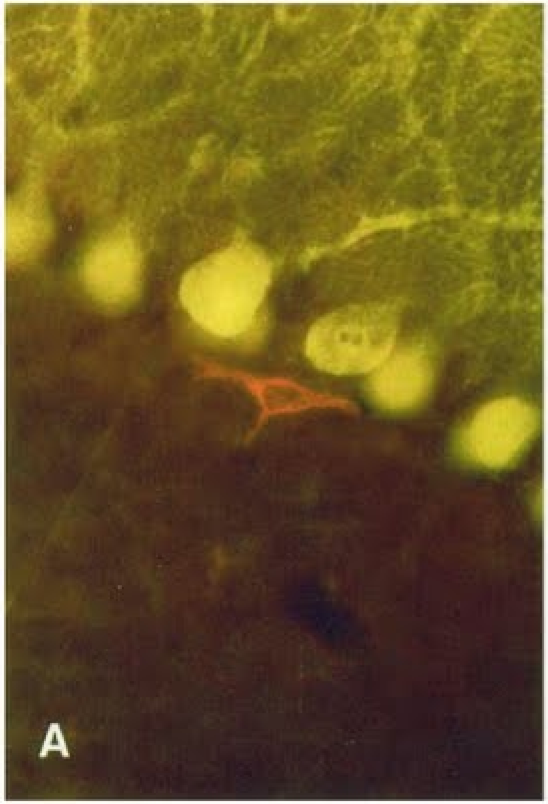
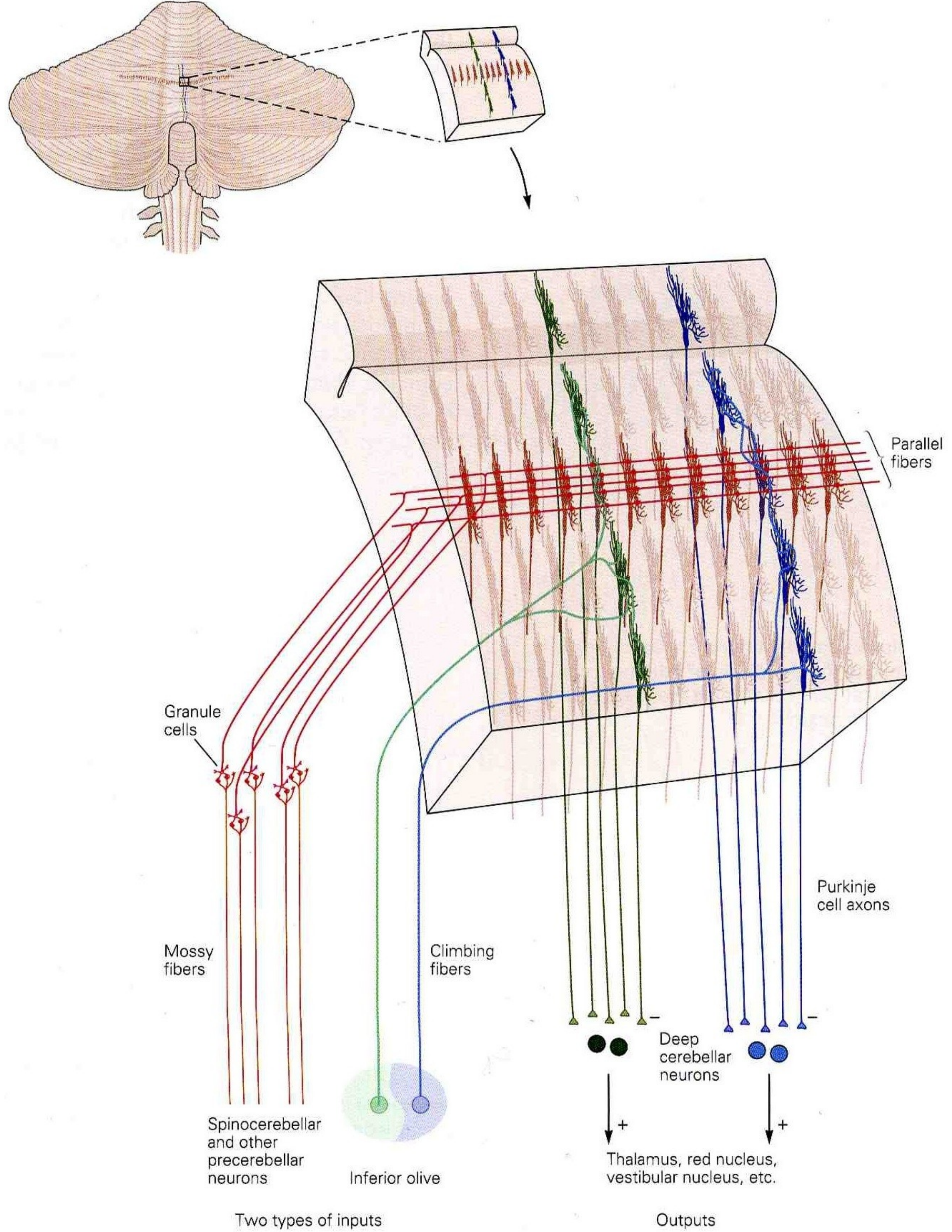


Fig. 7. **A:** Double-labeling studies show that anti-calbindin (yellow-green) and Cat-301 (red) recognize mutually exclusive sets of neurons. This is a photograph of a double-labeled section double-exposed under separate FITC and Texas red filters. The Cat-301 positive Lugaro cell is red and the calbindin-positive Purkinje cells are yellow-green.

Sahin M. and S. Hockfield. (1990). Molecular identification of the Lugaro cell in the cat cerebellar cortex. J.Comp.Neurol. 301, 575-584.

Inputs to Cerebellar Cortex

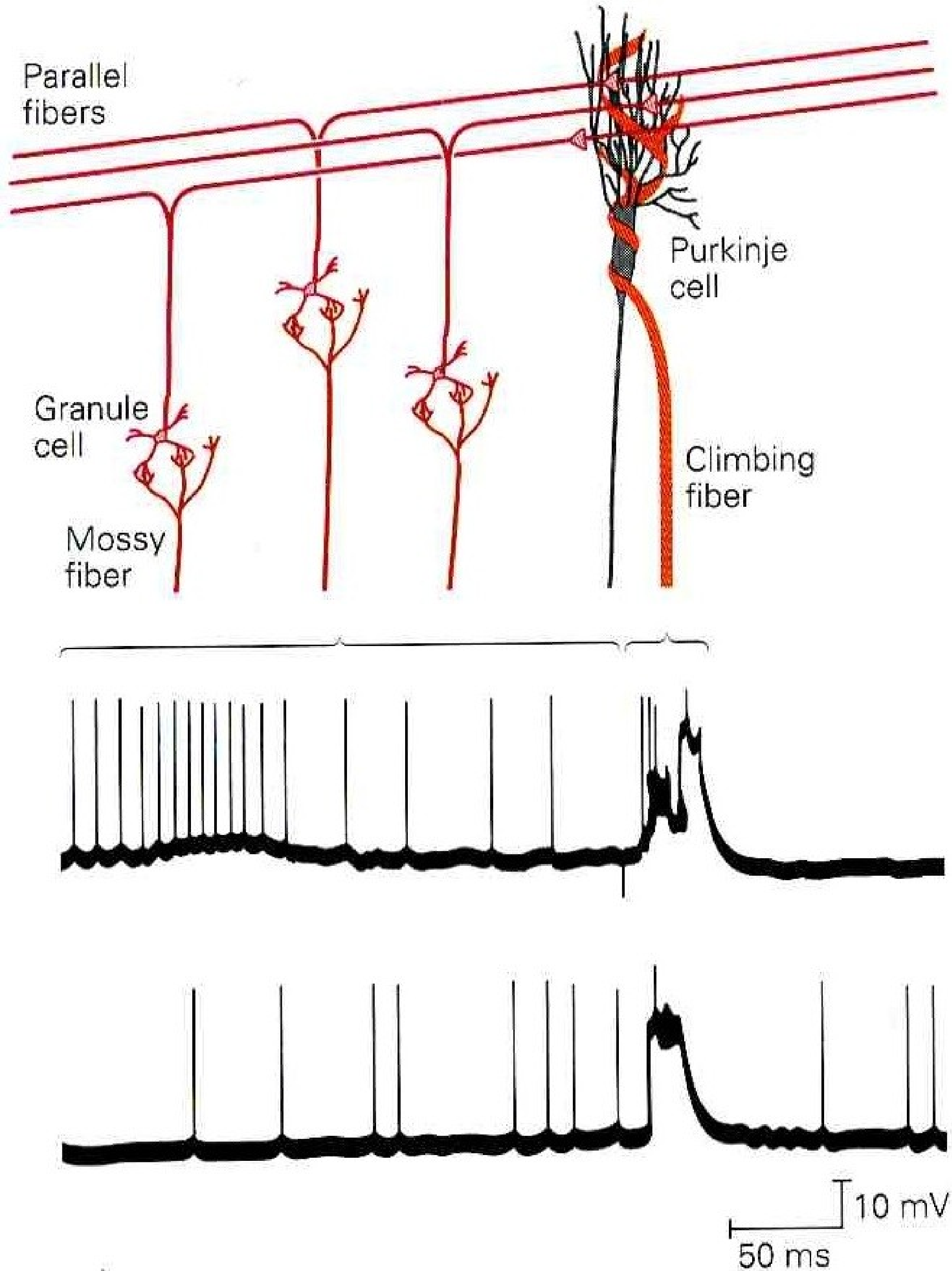
1. Mossy fibers from various sources (pons, medulla, reticular formation, vestibular nuclei) provide input to the granule cells, which in turn provide input to the Purkinje cells via the parallel fibers. (They also synapse onto Golgi cells.)
2. Climbing fibers from the inferior olivary nucleus contact Purkinje cells directly. Each Purkinje cells receives input from just one climbing fiber, but through 300-500 synapses. Complex spikes.
3. Modulatory projections from several brain areas (raphe nucleus, locus ceruleus, and hypothalamus). Neurotransmitters include serotonin, noradrenaline, and histamine.



Parallel fibers
Granule cells
Purkinje cell axons
Mossy fibers
Climbing fibers
Deep cerebellar neurons
Spinocerebellar and other precerebellar neurons
Inferior olive
Thalamus, red nucleus, vestibular nucleus, etc.
Two types of inputs
Outputs

Simple and Complex Spikes

- Simple spikes in a Purkinje cell are produced by parallel fiber input.
- Complex spikes are the result of climbing fiber input.

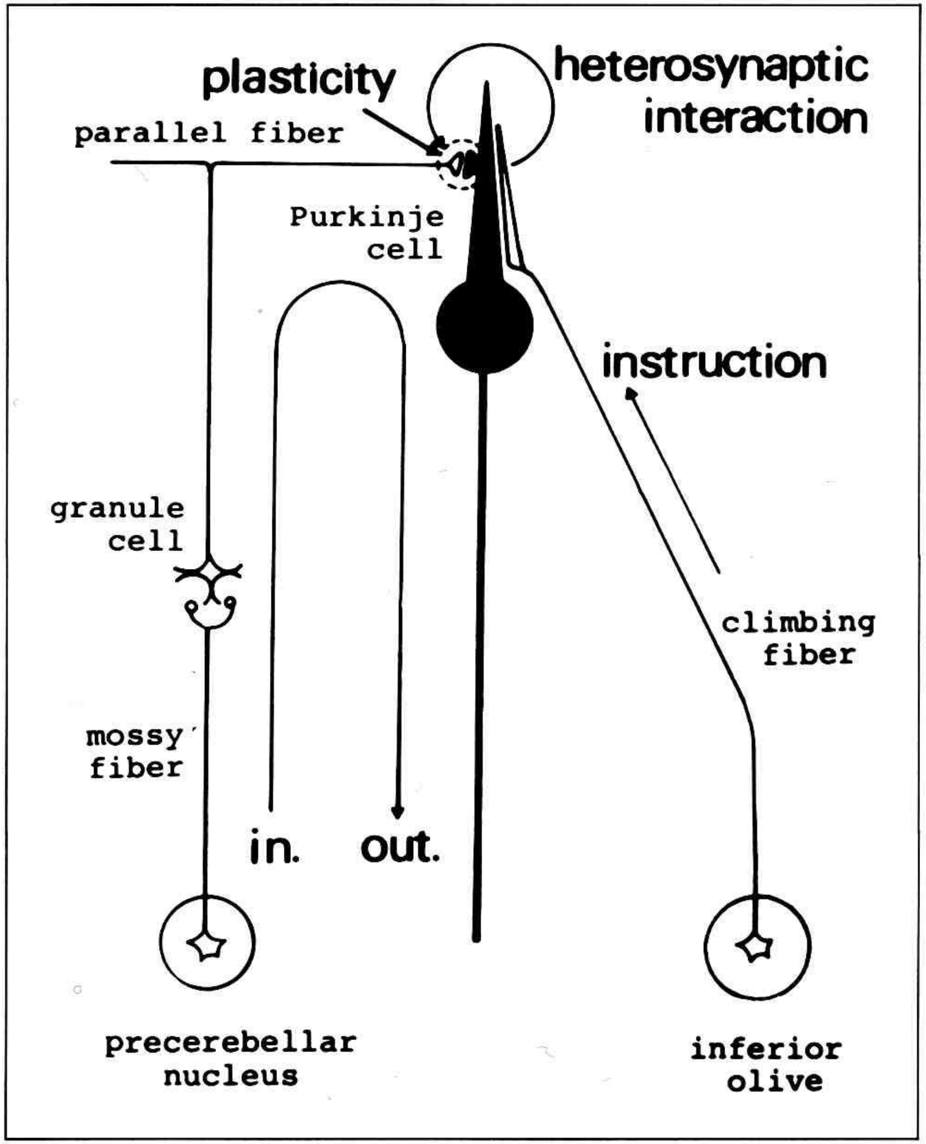


Output From Cerebellar Cortex

- Purkinje cells provide the only output of cerebellar cortex.
- Purkinje cells are inhibitory: they inhibit the cells in the deep cerebellar nuclei, and each other (via recurrent collaterals).
- The deep cerebellar nuclei project downward to pons, medulla, and spinal cord or upward to cortical motor areas via thalamus.
- The mossy fibers that project to granule cells also project to the corresponding cerebellar nuclei.
- The climbing fibers that project to Purkinje cells also project to the corresponding cerebellar nuclei.
- Hence, the nuclei integrate the inputs to cerebellar cortex (mossy and climbing fibers) with the outputs (Purkinje cell axons).

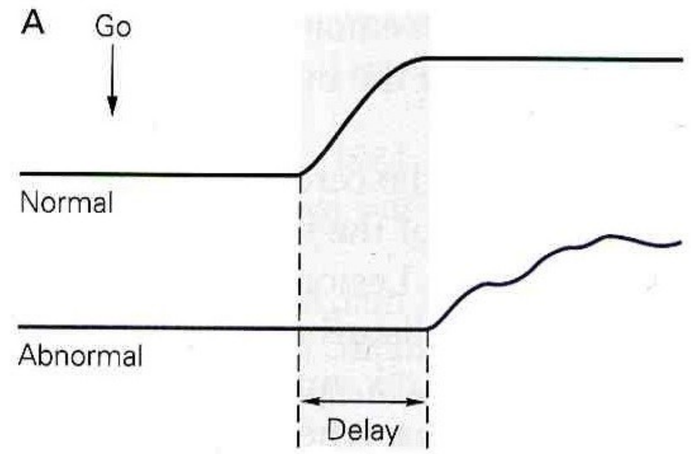
Learning in Purkinje Cells

- Parallel fiber input:
  - 200,000 synapses
  - generates simple slikes
- Climbing fiber input:
  - projection from inferior olive
  - each PC contacted by only 1 CF
  - “teaching signal”
  - generates complex spikes
  - causes LTD at parallel fiber synpases

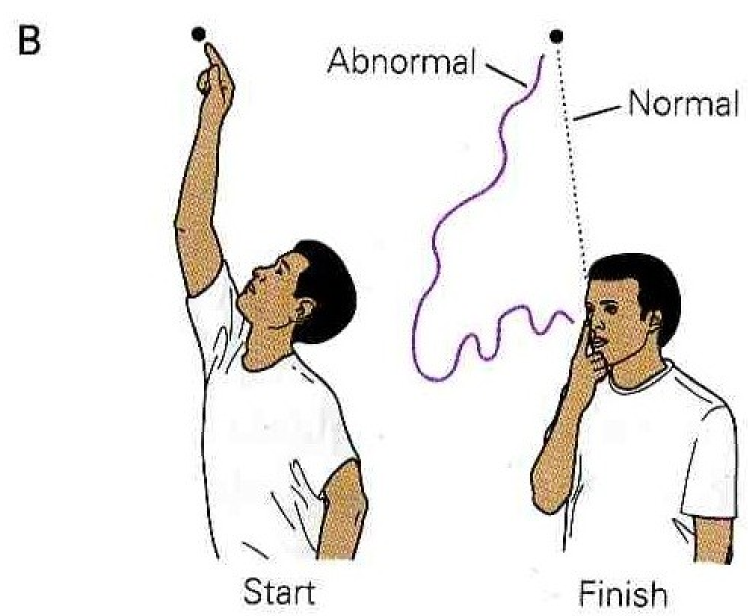


Effects of Cerebellar Disease

A) Delayed onset of movement relative to normal subjects.



B) Inaccurate estimates of range and direction, and unsmooth movement with increasing tremor as finger approaches the tip of the nose.



What Does the Cerebellum Do?

1) Real-time motor control

- Fine-tuning the vestibular-ocular reflex (VOR), an open-loop control system (just three synapses), and ocular following response (OFR).
- Recalibration of saccadic eye movements
- Cerebellar lesions impair motor coordination but don't cause paralysis.

2) Motor learning

- Marr-Albus pattern associator theory of cerebellar cortex
- Learning muscle combinations to effect desired movements

What Does the Cerebellum Do?

3) Classical conditioning

- Thompson: rabbit eyeblink conditioning
- Conditioning is abolished by cerebellar lesion but can eventually be recovered even with cerebellum absent.
- Korsakoff's patients acquire the eyeblink response but can't remember the training procedure, which they underwent just the day before.

4) Possible role in higher level cognition?

- *Much of the cortex* projects to the cerebellum, although the heaviest projections are from motor and somatosensory areas.
- Some patients with cerebellar lesions exhibit language difficulties.
  - Tasks for patient studies: articulatory rehearsal; verb generation
  - Imaging studies show differential cerebellar activation for nouns vs. verbs

Embodied cognition?

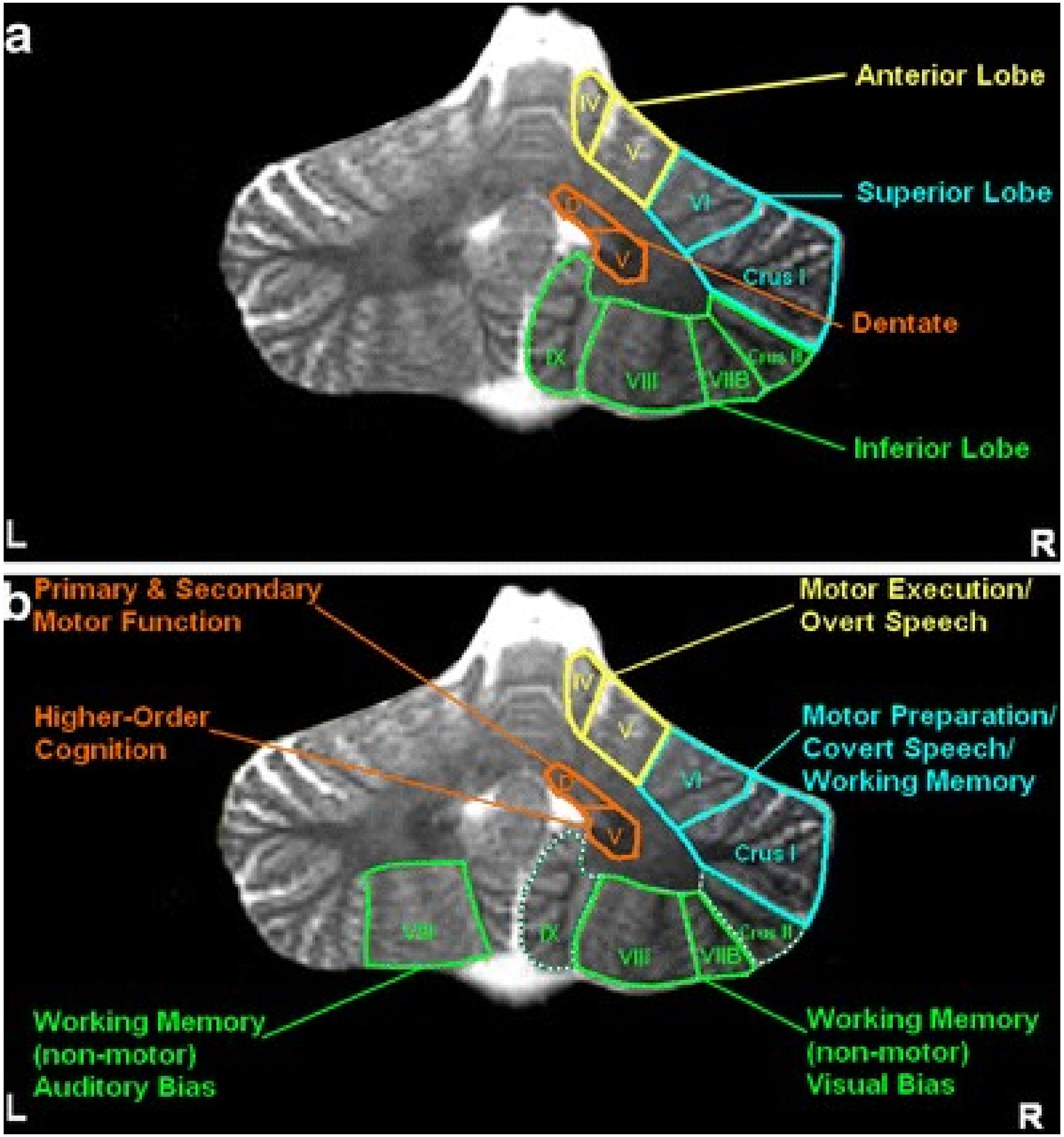
Cerebellar Activation in Language Tasks

- Articulatory rehearsal: working memory for:
  - words
  - letters
  - not figures, Korean characters (for non-Korean speakers)
- Verb generation
  - banana $\rightarrow$ “peel”
  - produces activation in right lateral cerebellum
  - not seen for noun generation

Functional MRI of Cerebellum in Verbal WM

Marvel & Desmond, 2010:

- Medial regions of anterior cerebellum support overt speech.
- Lateral portions of superior cerebellum support speech planning and preparation (e.g., covert speech)
- Inferior cerebellum is active when info is maintained across a delay; independent of speech.



Why Is the Cerebellum Attractive for Modeling?

- Simple circuit diagram, compared to cerebral cortex.
  - Only a few cell types, organized in just three layers.
  - Regular structure: parallel fiber beams, etc.
  - Computation is local: no long-range connections (?)
- Uniform throughout.
  - All portions have the same wiring pattern.
  - Suggests that all portions are performing the same computation.
- We <u>think</u> we know what it's doing (motor control, timing) but...

  "The range of tasks associated with cerebellar activation ... includes tasks designed to assess attention, executive control, language, working memory, learning, pain, emotion, and addiction."
  – Strick, Dum, and Fiez (2009)