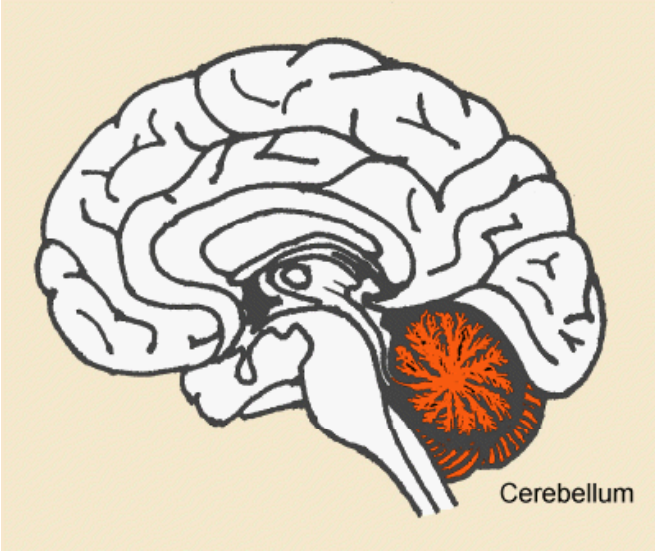
Cerebellum

- Overview and structure of cerebellum
- Microcircuitry of cerebellum
- Function of cerebellum
    -- vestibulo-ocular reflex
    -- adaptation and motor learning

Overview



- "small brain"

  10% of the weight but 50% of the number of neurons in the entire brain

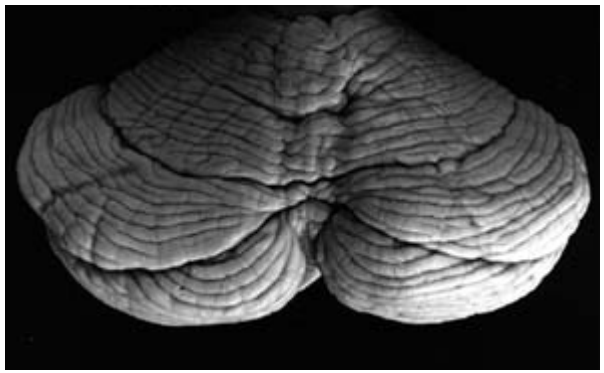
  (due to ~ 10^{11} granule cells)

- Cerebellar cortex:

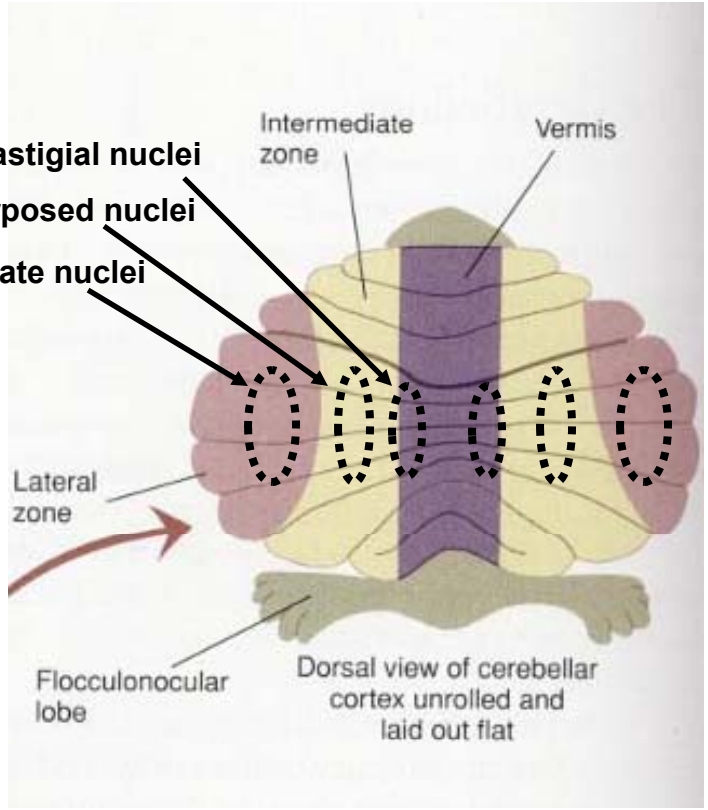
  highly regular structure – circuit modules

- Function:

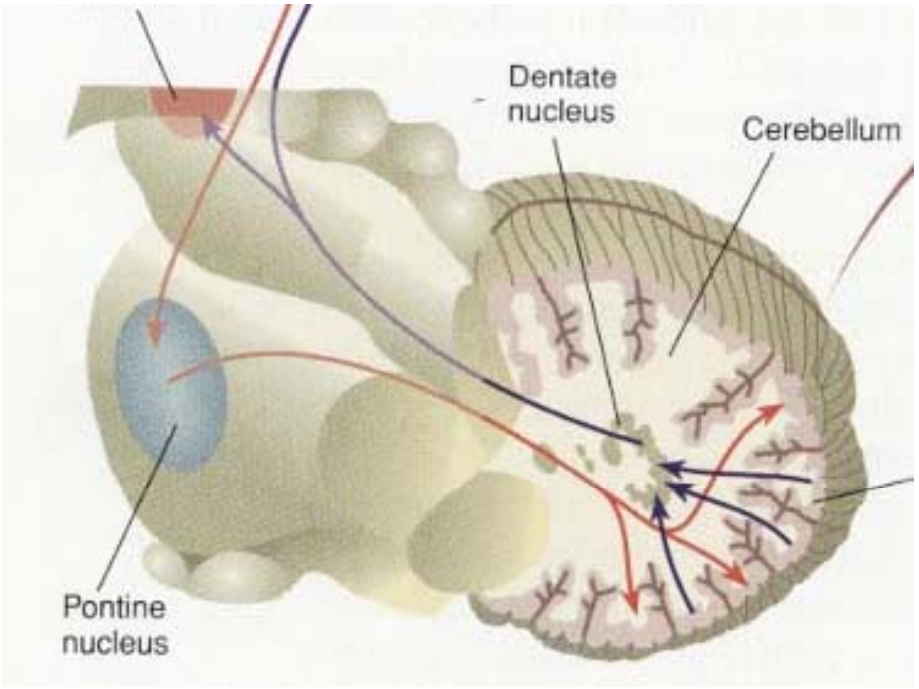
  coordination, balance, motor learning.



The cerebellum consists of the cerebellar cortex and a set of deep nuclei

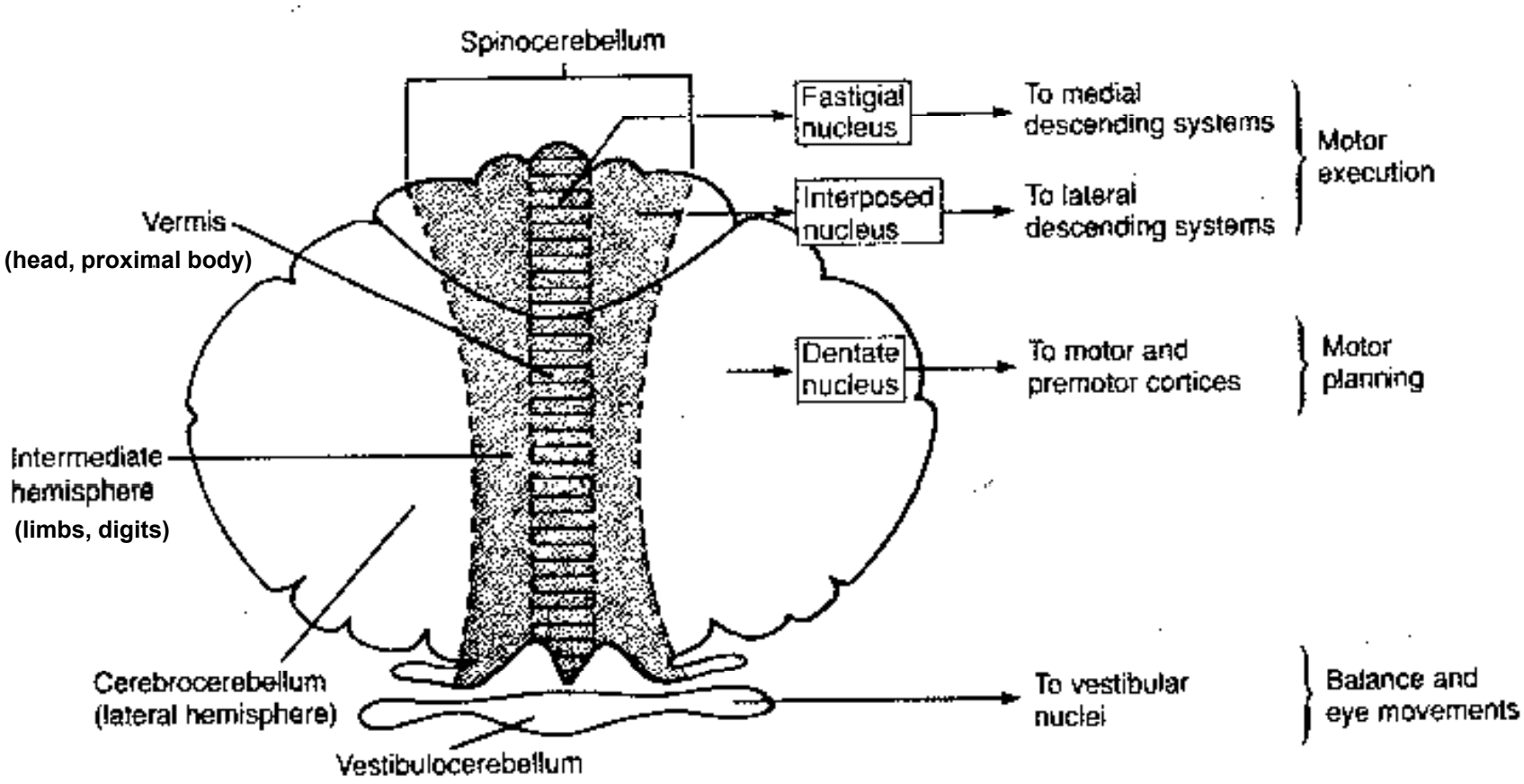


Dorsal view



Sagital view

Different regions of cerebellar cortex are connected to different deep nuclei, which carry out different motor functions



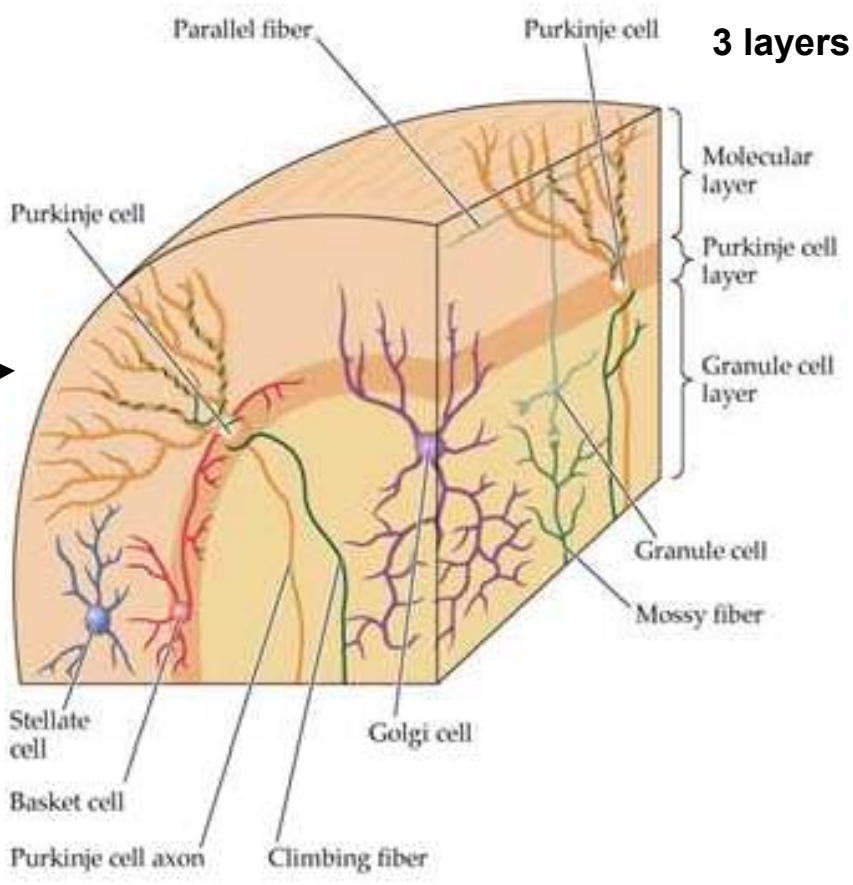
Microcircuitry of cerebellum

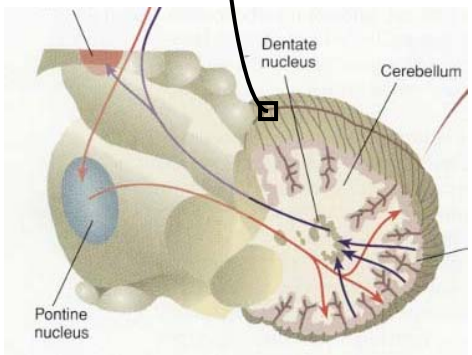
<u>5 cell types form 3 layers</u>

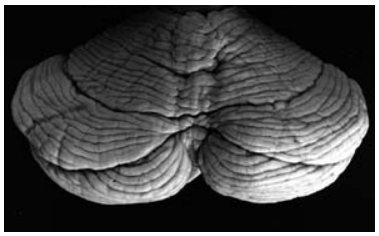
Stellate cell (inhibitory)
Basket cell (inhibitory)
(molecular layer)

Purkinje cell (inhibitory)
(Purkinje layer)

Golgi cell (inhibitory, large)
Granule cell (excitatory small)
(Granular layer)





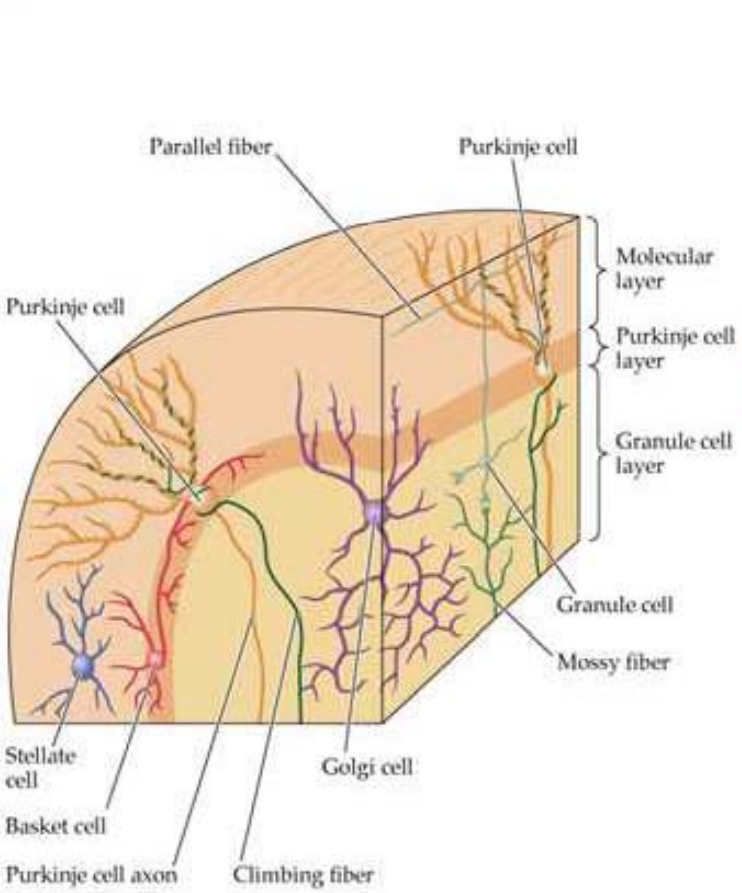


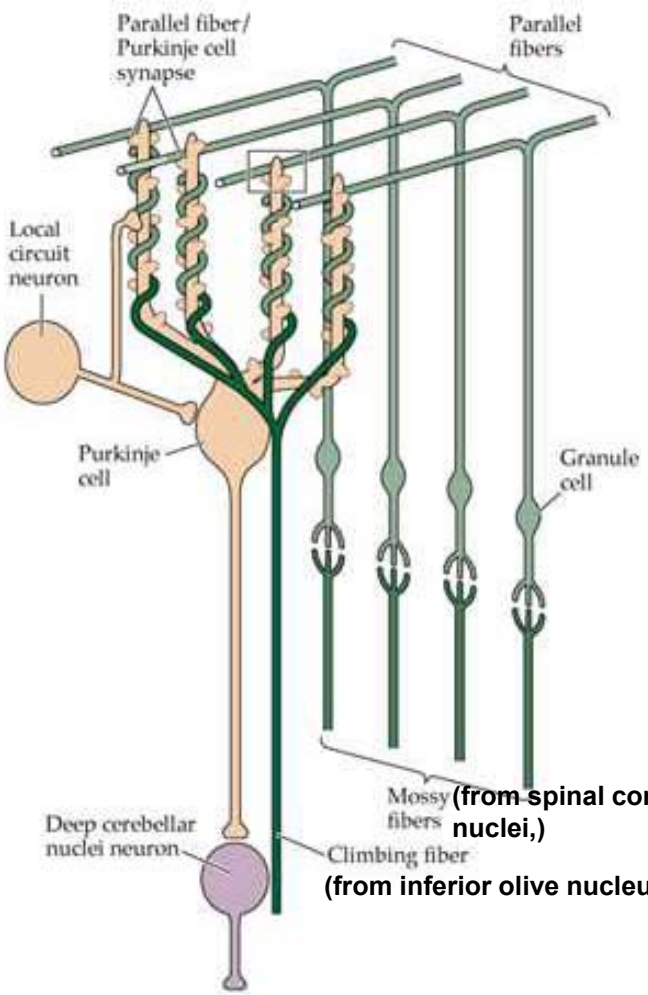
Inputs:

- Climbing fiber (“+”, excitatory, from inferior olive nucleus)
- Mossy fiber (+, from spinal cord & brain stem)

Output to deep nuclei:

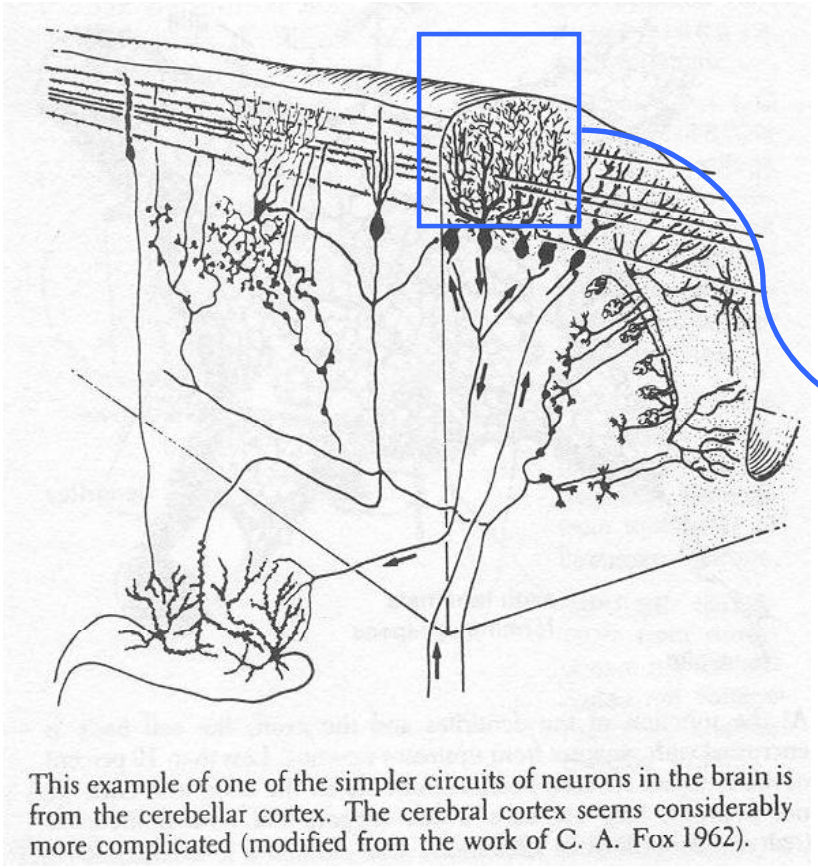
- Purkinje cell axon (“-”, inhibitory)





The main centers for synaptic integration: Purkinje cell

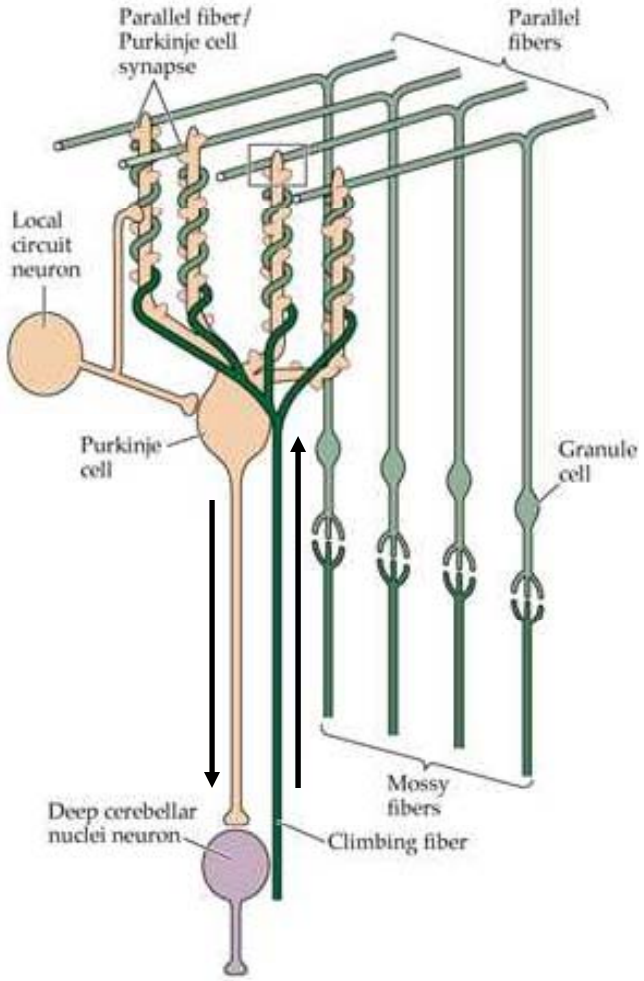
2-D dendritic tree with the plane perpendicular to the axis of long convolutions (folia) of the cortex

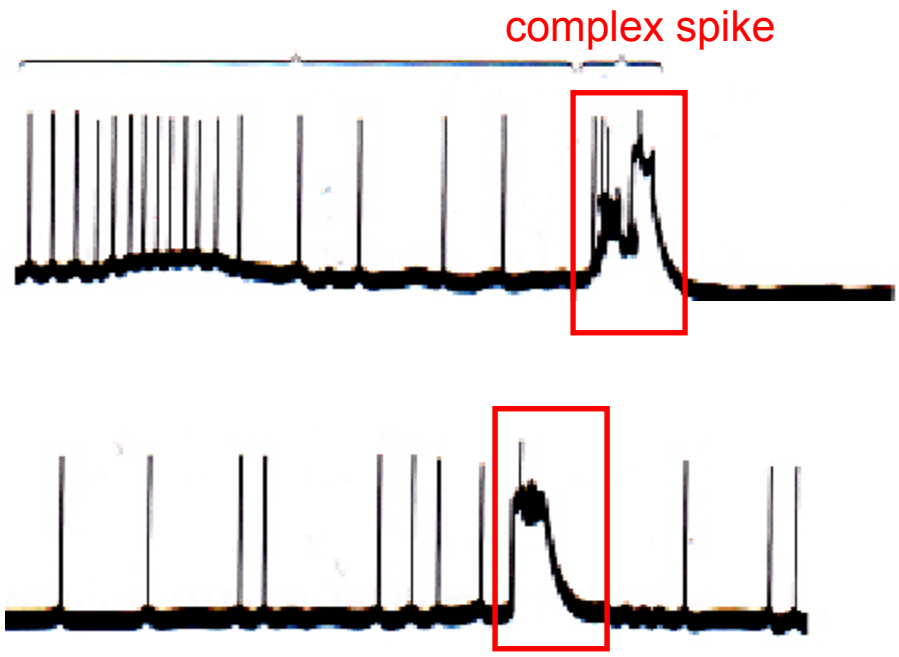


This example of one of the simpler circuits of neurons in the brain is from the cerebellar cortex. The cerebral cortex seems considerably more complicated (modified from the work of C. A. Fox 1962).

First direct pathway:

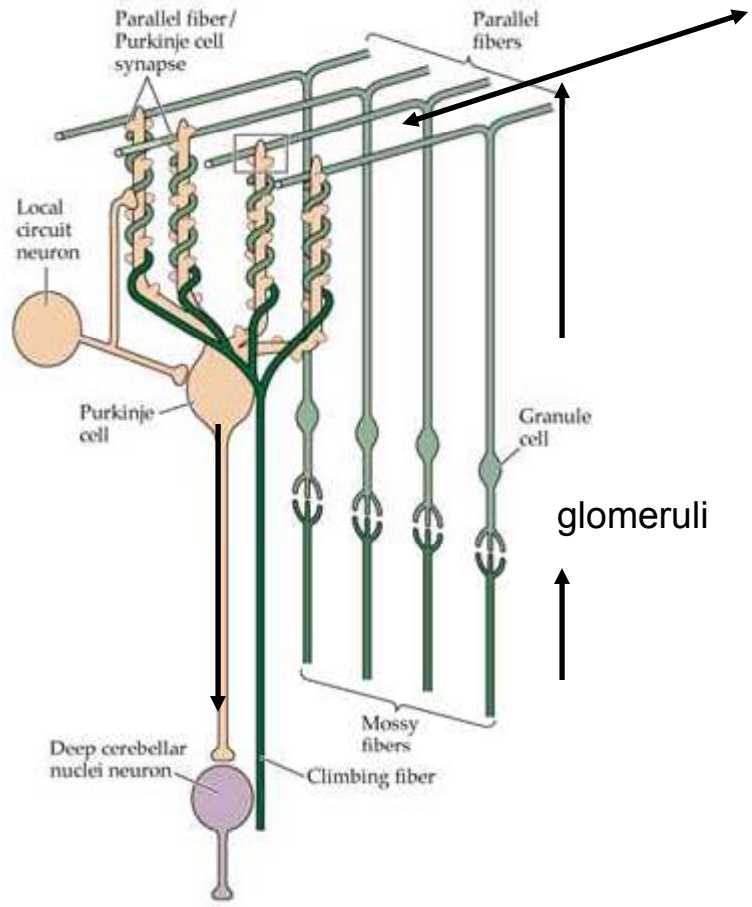
- Climbing fiber from inferior olivary nucleus (+) → Purkinje cells (-) → deep cerebellar nuclei
- Each climbing fiber projects to 1-10 Purkinje cells
- Each Purkinje cell receives input from a single climbing fiber (that forms many synapses)
- Powerful excitatory connection, each climbing fiber spike cause a burst of spikes in Purkinje cell (called a “complex spike”)



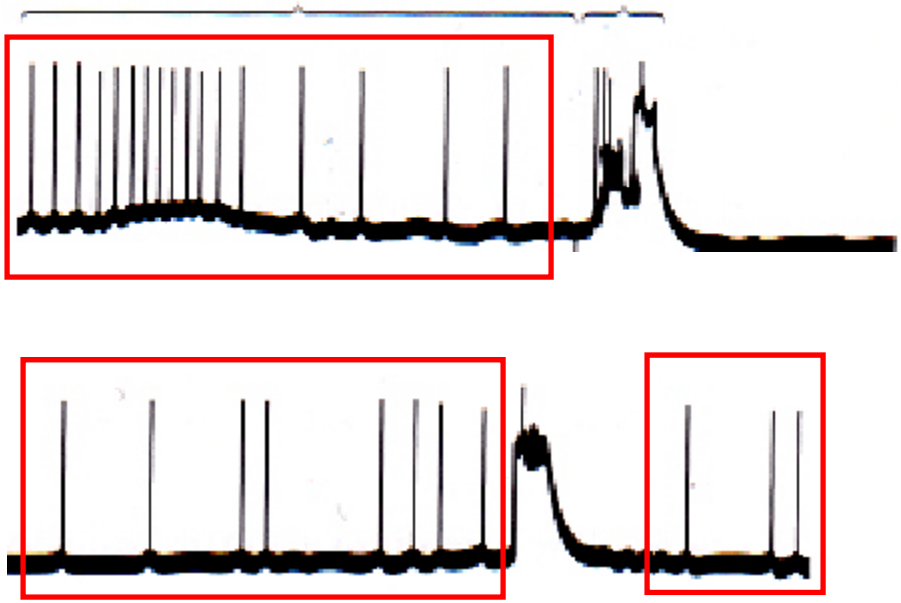


Second direct pathway:

- Mossy fibers from spinal cord and brain stem nuclei (+) → granule cells (axon: parallel fibers, +) → Purkinje cells (-) → deep nuclei
- each parallel fiber projects to thousands of Purkinje cells (high divergence)
- each Purkinje cell receives input from ~200,000 parallel fibers (high convergence)
- Weak excitatory connection, spatial and temporal summation of inputs from many parallel fibers causes a single spike in Purkinje cell (called a "simple spike")



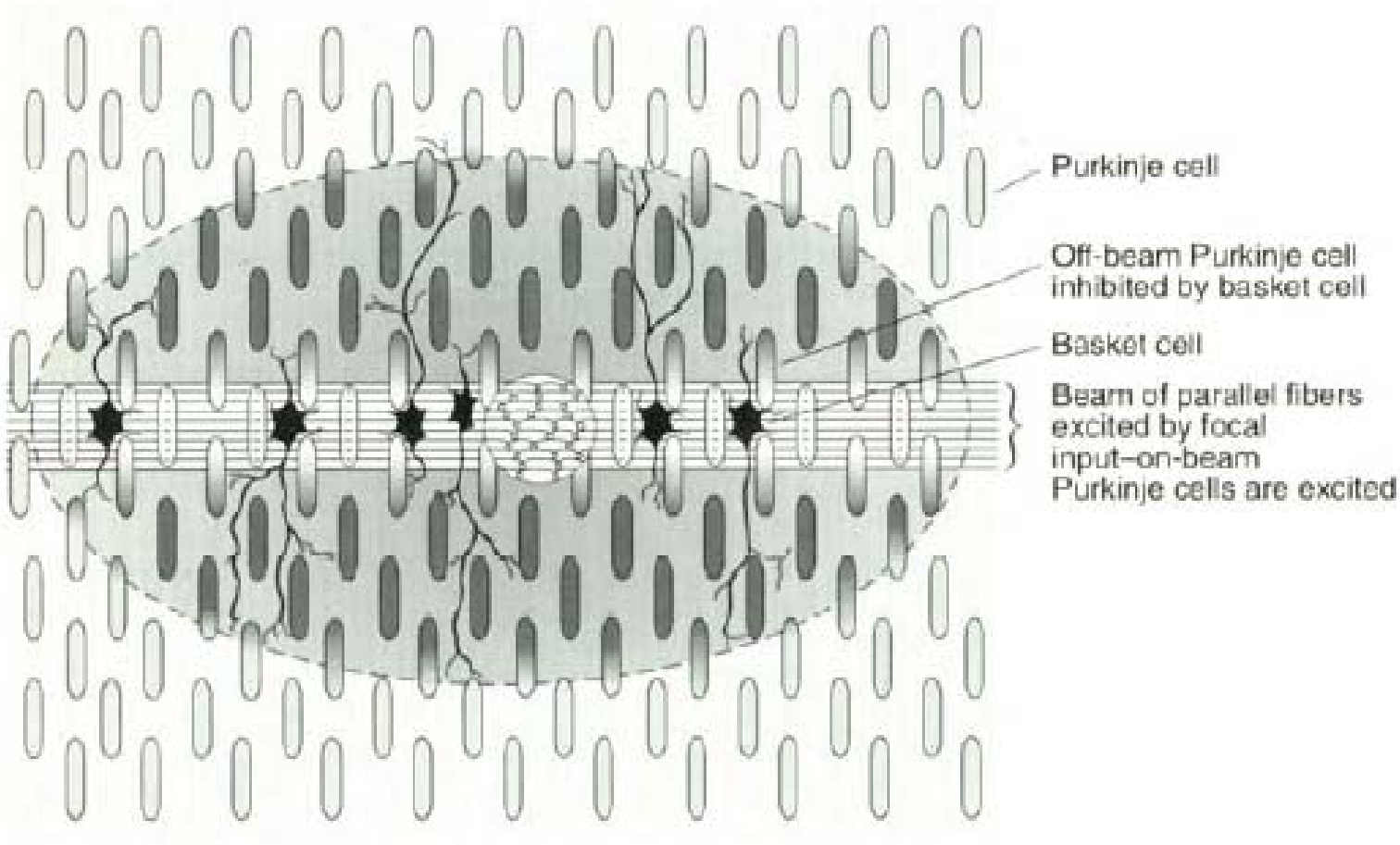
simple spikes



Indirect pathways mediated via inhibitory interneurons

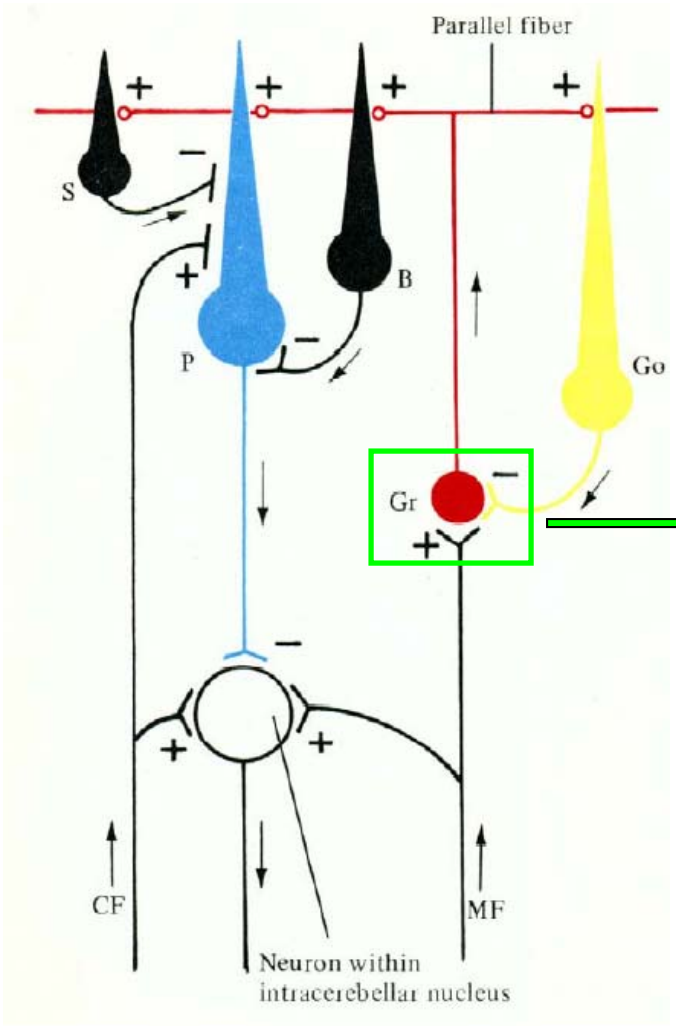
1. Lateral inhibition:

granule cells (axon: parallel fibers, +) → stellate and basket cells (-) → Purkinje cells in a different row (sharpening the excitation of Purkinje cells in the center along the "beam")

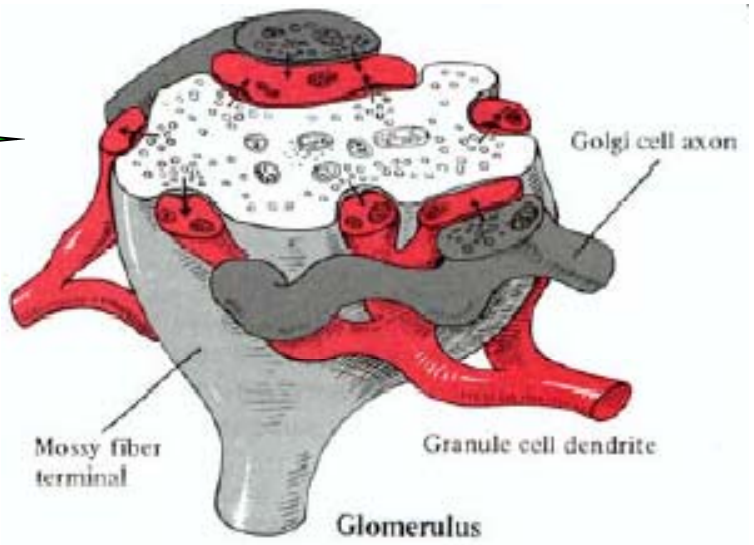


2. Negative feedback:

- granule cells (axon: parallel fibers, +) → Golgi cells (-) → granule cells



Feedback inhibition on granule cell dendrites in the synaptic complex, the cerebellar glomerulus (consisting of bulbous mossy fiber terminals and axon terminals of Golgi and granule cells axons)



Cerebellum Functions - 1. Vestibulo-ocular reflex

Vestibulo-Ocular Reflex

-- coordinated response that maintains the eyes on a fixed target when the head is rotated

Head rotation → vestibular labyrinth output + visual information
→ eye movement in opposite direction
→ image on the retina unchanged

Adaptation in Vestibulo-Ocular Reflex

-- Experiment on reversing L & R visual fields with prism glasses

Head rotation → eye movement in the same direction
→ image move further away
→ native V-O reflex is reduced (in a few days)
and eventually reverses direction

*** Lesion of vestibulo-cerebellum (flocculonodular lobe) → no adaptation**

Cerebellum Functions - 2. Eye-hand coordination

Dart-throwing Experiment:

Wearing eye prisms that bend the light path sideways

→ initial throws off to the side

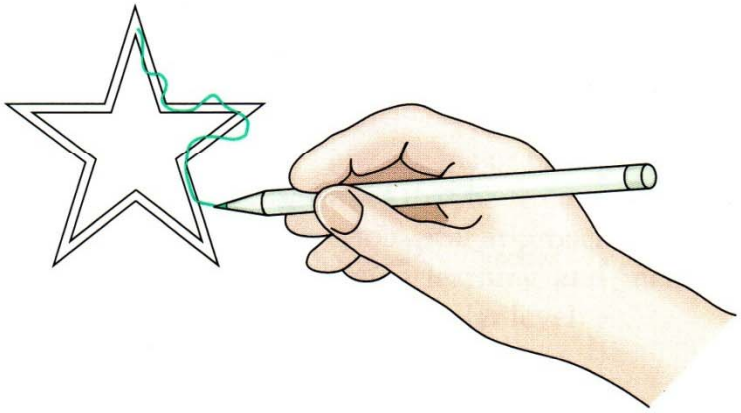
→ correct throws via adaptation of the motor system after 30 throws

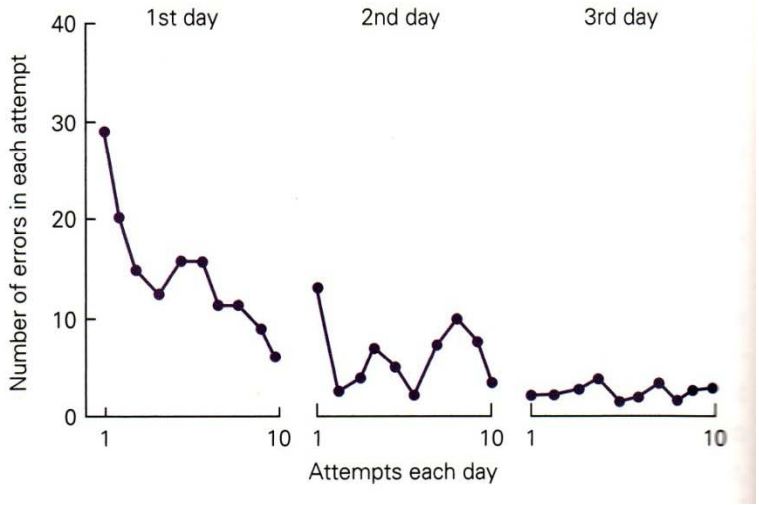
→ prism removal lead to off-target throws toward the opposite side

Patients with damaged inferior olive nucleus or inferior cerebellar peduncle show no adaptation

Cerebellum and motor learning

- During learning of a new motor task, subject makes mistakes, but the error reduces with practice
- The standard notion is that the “error signal” causes changes in brain circuits involved in motor control (e.g., cerebellum), thus improving motor performance





Patient H.M., who had bilateral removal of medial temporal lobe and lack of ability to form episodic memory, but motor learning is intact, indicating it is mediated by different brain structure

Cerebellum and Motor Learning

- Long-term Depression (LTD) - Simultaneous activation (within 100-200 ms) of climbing fibers and parallel fibers converging onto the same Purkinje cell (green circles) can cause LTD of parallel fiber → Purkinje cell synapse.

David Marr's hypothesis of motor learning:

1 Altering parallel fiber → Purkinje cell synapse select specific Purkinje cells to program or correct eye or limb movements.

2 During a movement, error signals (difference between expected and actual sensory inputs) represented by climbing fiber inputs induce LTD of parallel fiber synapses that activate the Purkinje cells concurrently.

3 Successive erroneous movements leads to successive LTD of parallel fiber inputs, leading to re-programming (correction) of the movement.