The Cerebellum

Anatomy

Electrophysiology

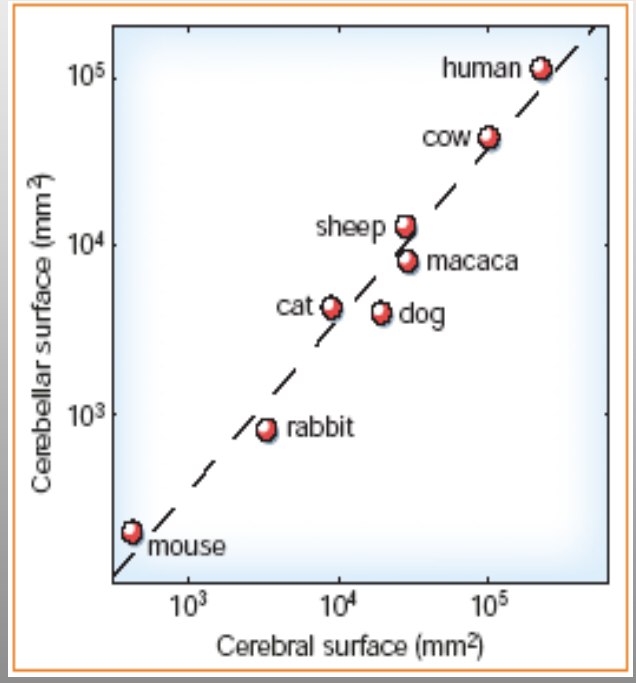
Learning

Function

Interesting fact about cerebellum #1

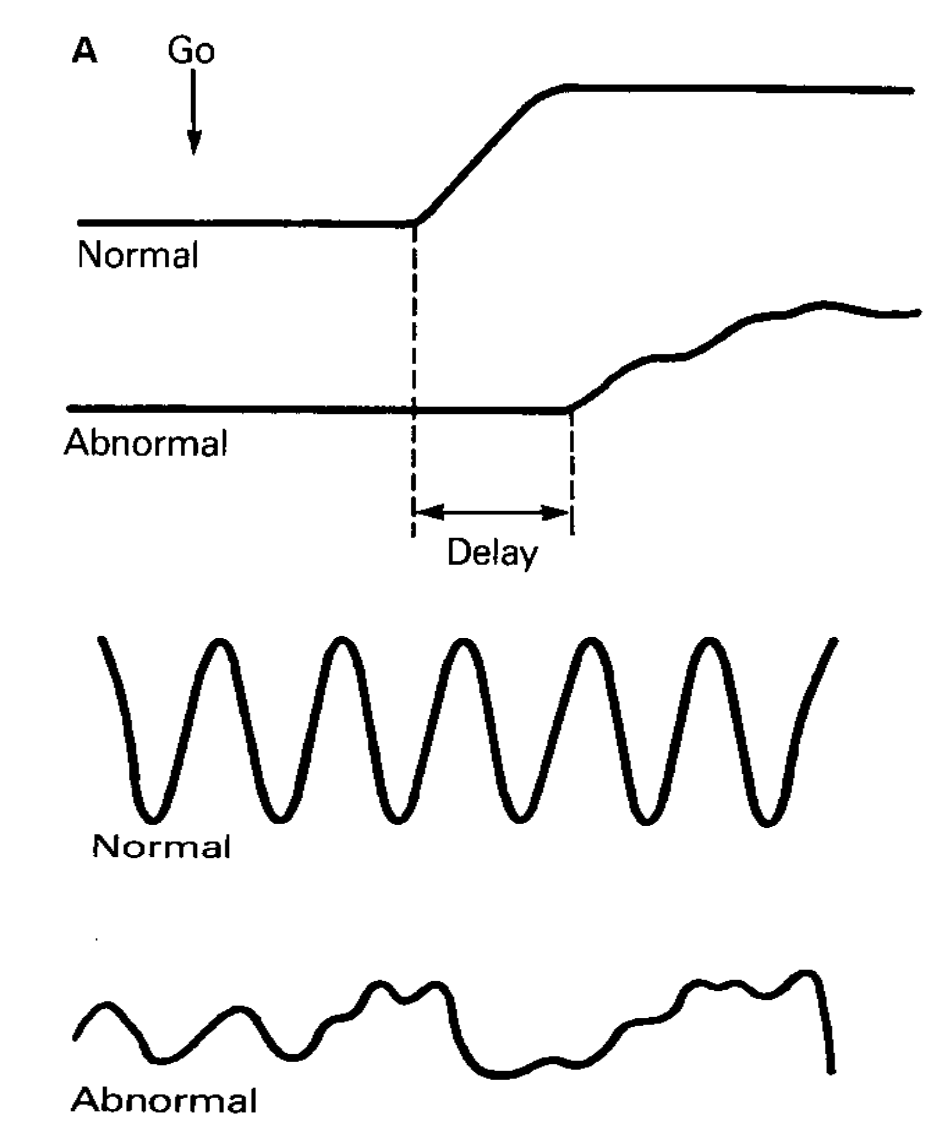
- Erasistratus (304-250BC): A Greek anatomist and a royal physician
  - The cerebral cortex and the cerebellar cortex are separate entities.
  - Cerebral cortex size and surface area related to intelligence of the species.
  - Cerebellar cortex related to motion, as larger animals possess larger cerebella.

Interesting fact about cerebellum #1

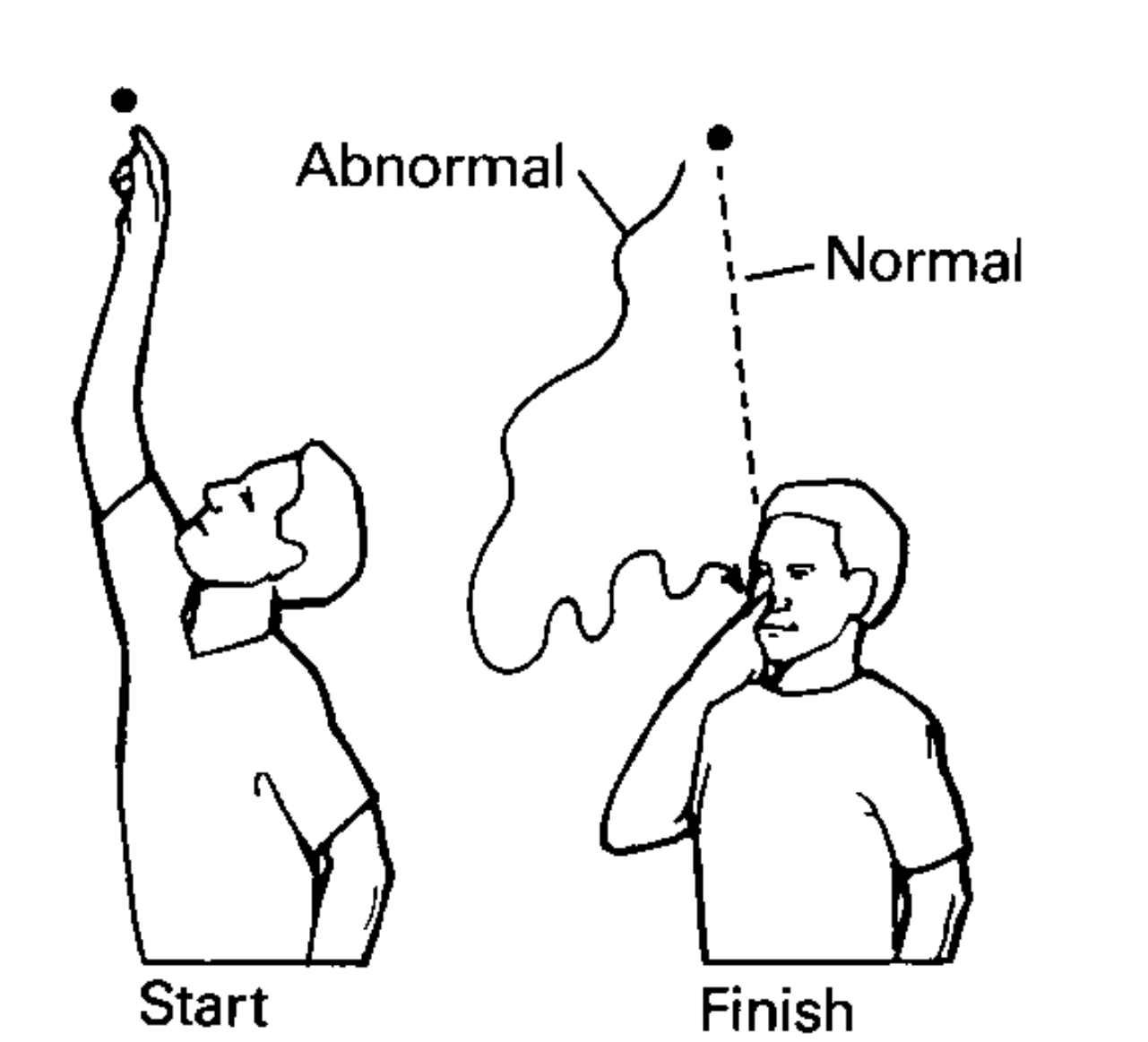


- Surface areas of cerebellum and cerebrum are linearly related.
- Half of the neurons in the CNS are in the cerebellum.

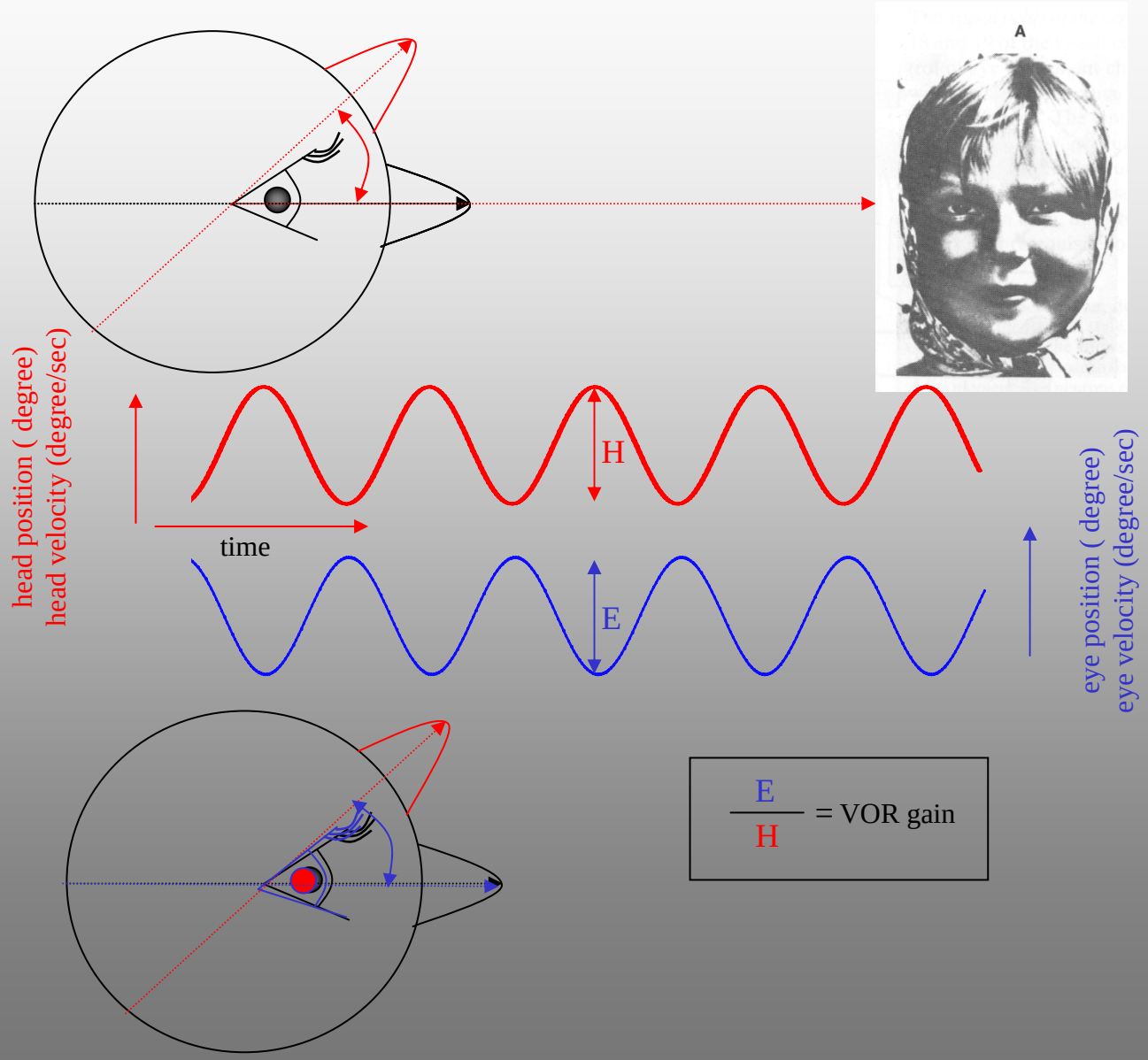
Motor control



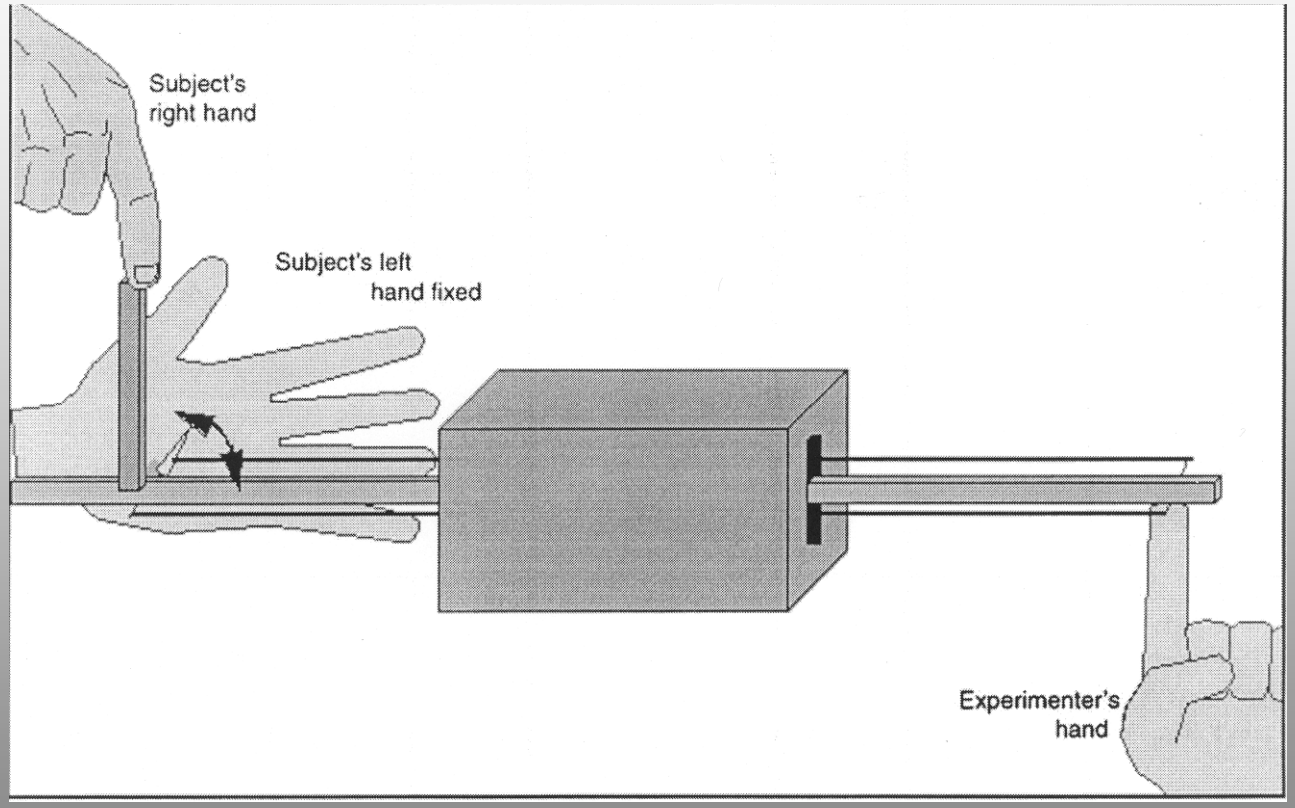
Motor control – dysmetria



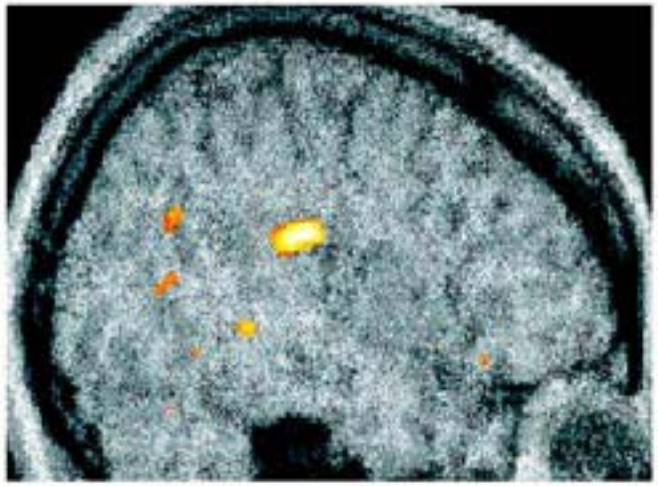
Vestibulo-Ocular Reflex

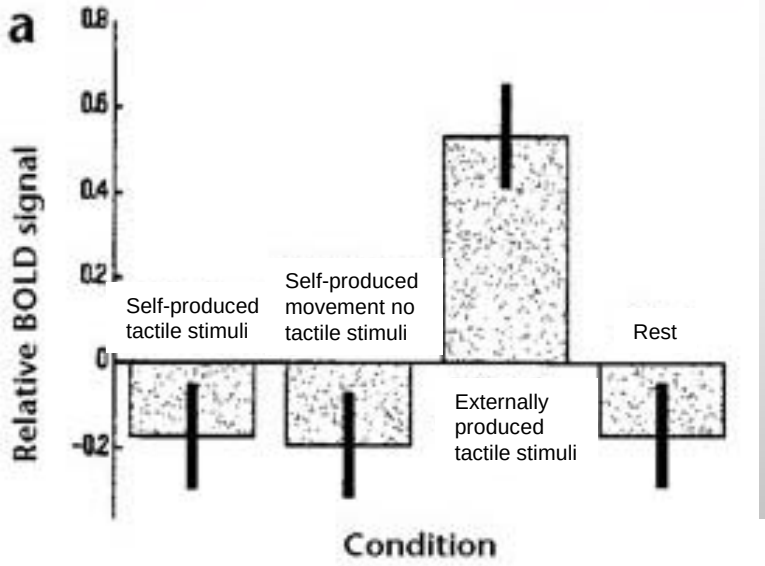


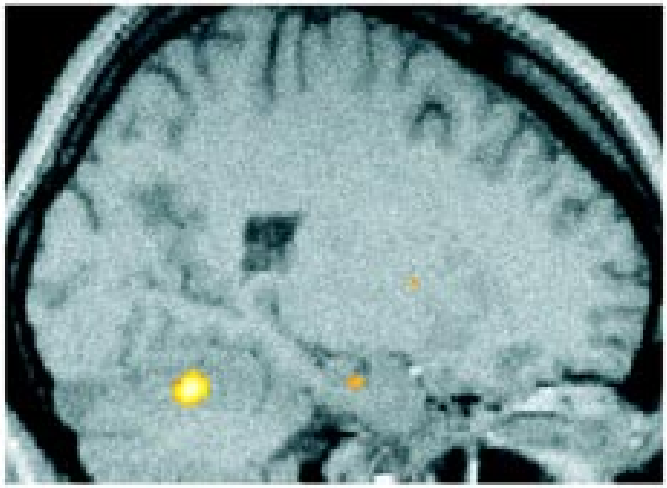
Stimulus expectation

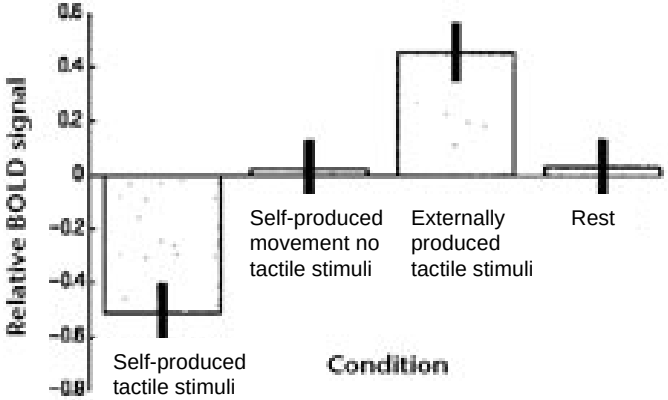


Somatosensory cortex



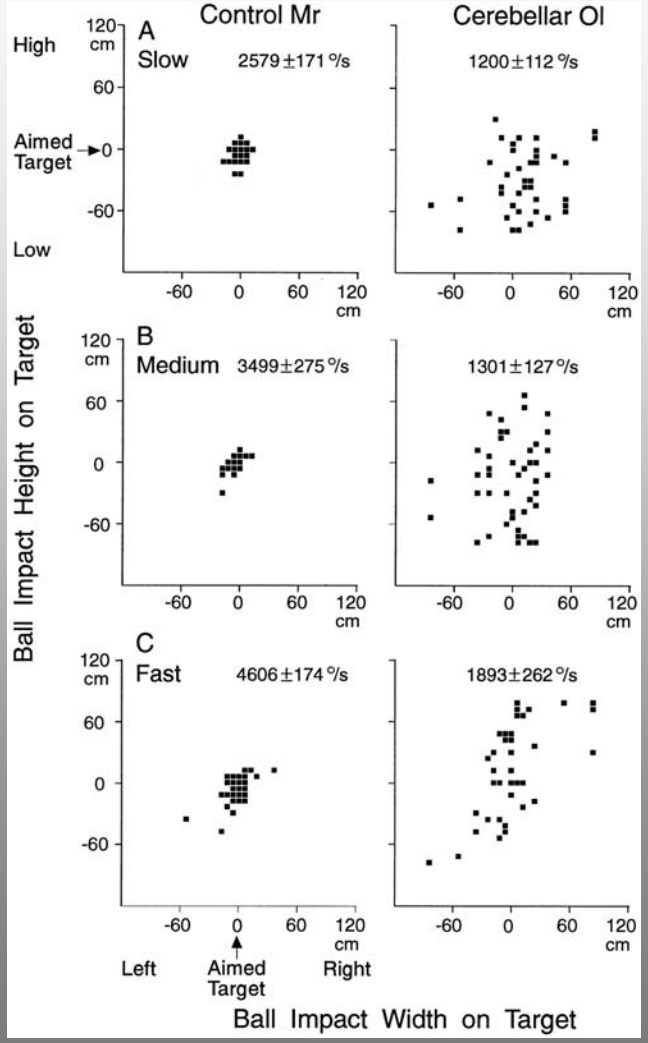


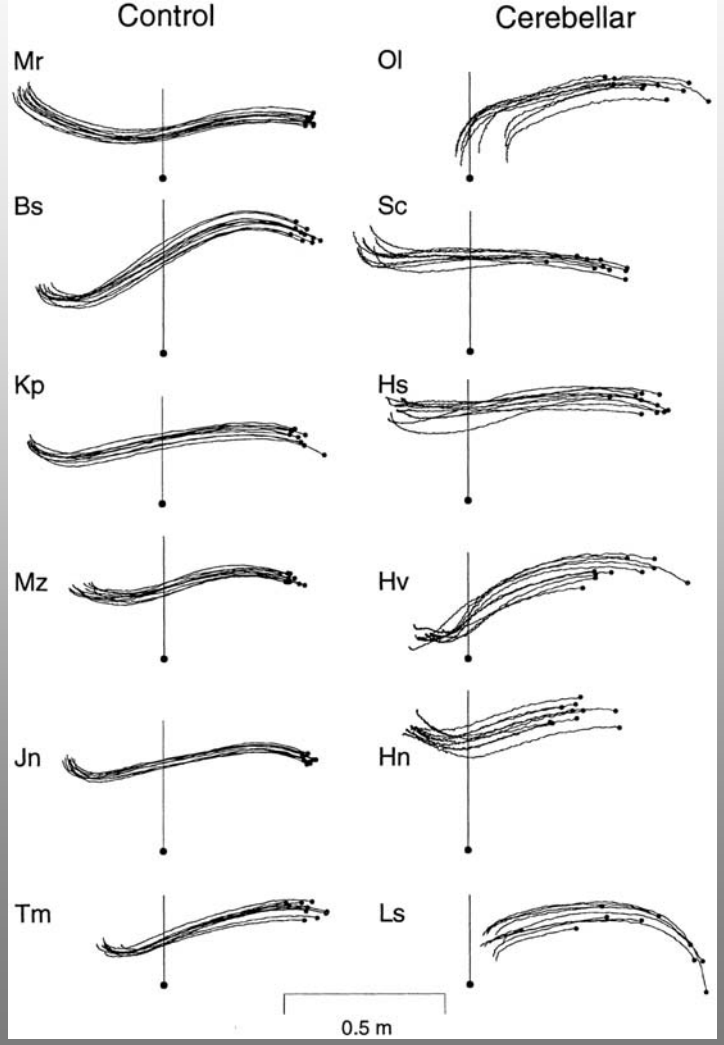




Cerebellar cortex

Multi-joint coordination and timing



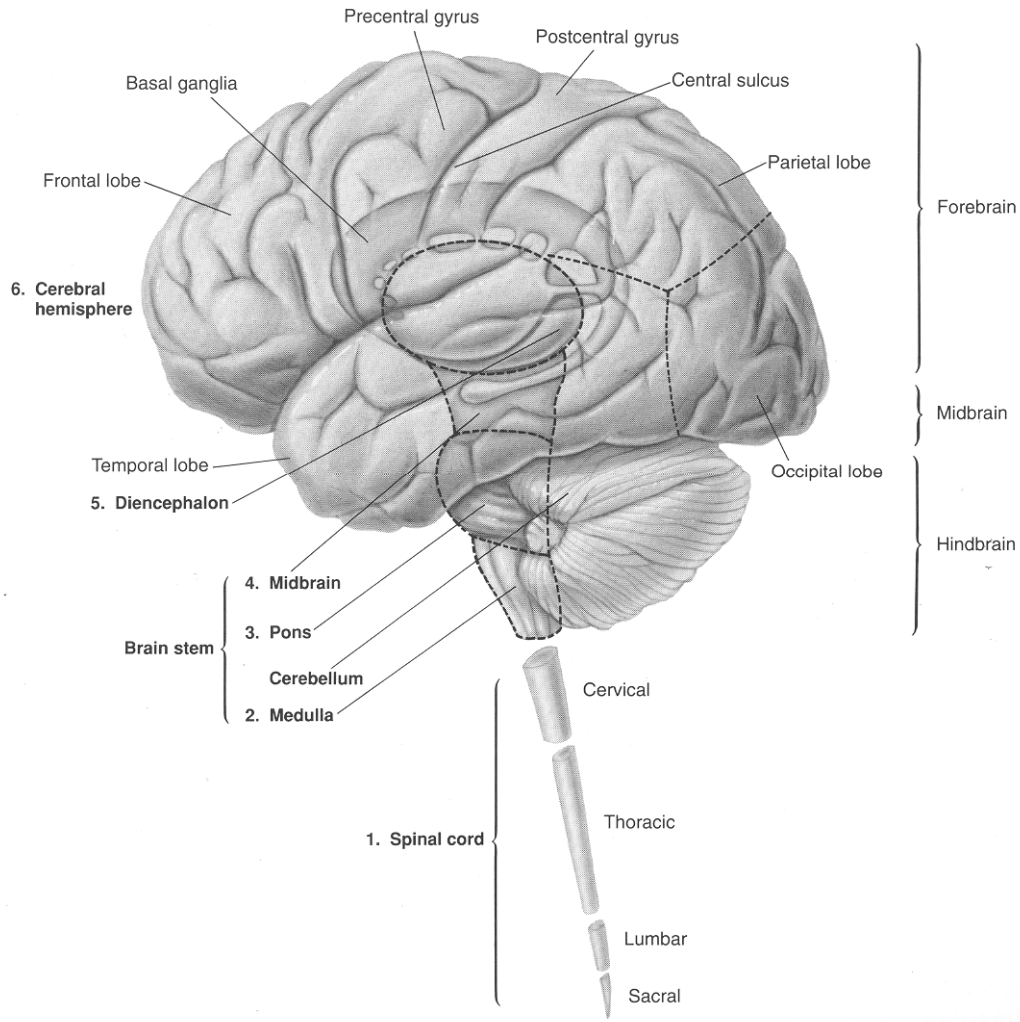


What is the function?

- Autism and cerebellum. An unusual finding with fMRI
- Human cerebellum plays an important role in memory-timed finger movement: An fMRI study
- The Cerebellum Contributes to Somatosensory Cortical Activity during Self-Produced Tactile Stimulation
- **Developmental dyslexia: the cerebellar deficit hypothesis**
- **The role of the cerebellum in cognition and behavior: a selective review.**
- Anticipatory Cerebellar Responses During Somatosensory Omission in Man
- **Neuroimaging evidence implicating cerebellum in support of sensory/cognitive processes**
- **Cerebellar Involvement in Response Reassignment Rather Than Attention**

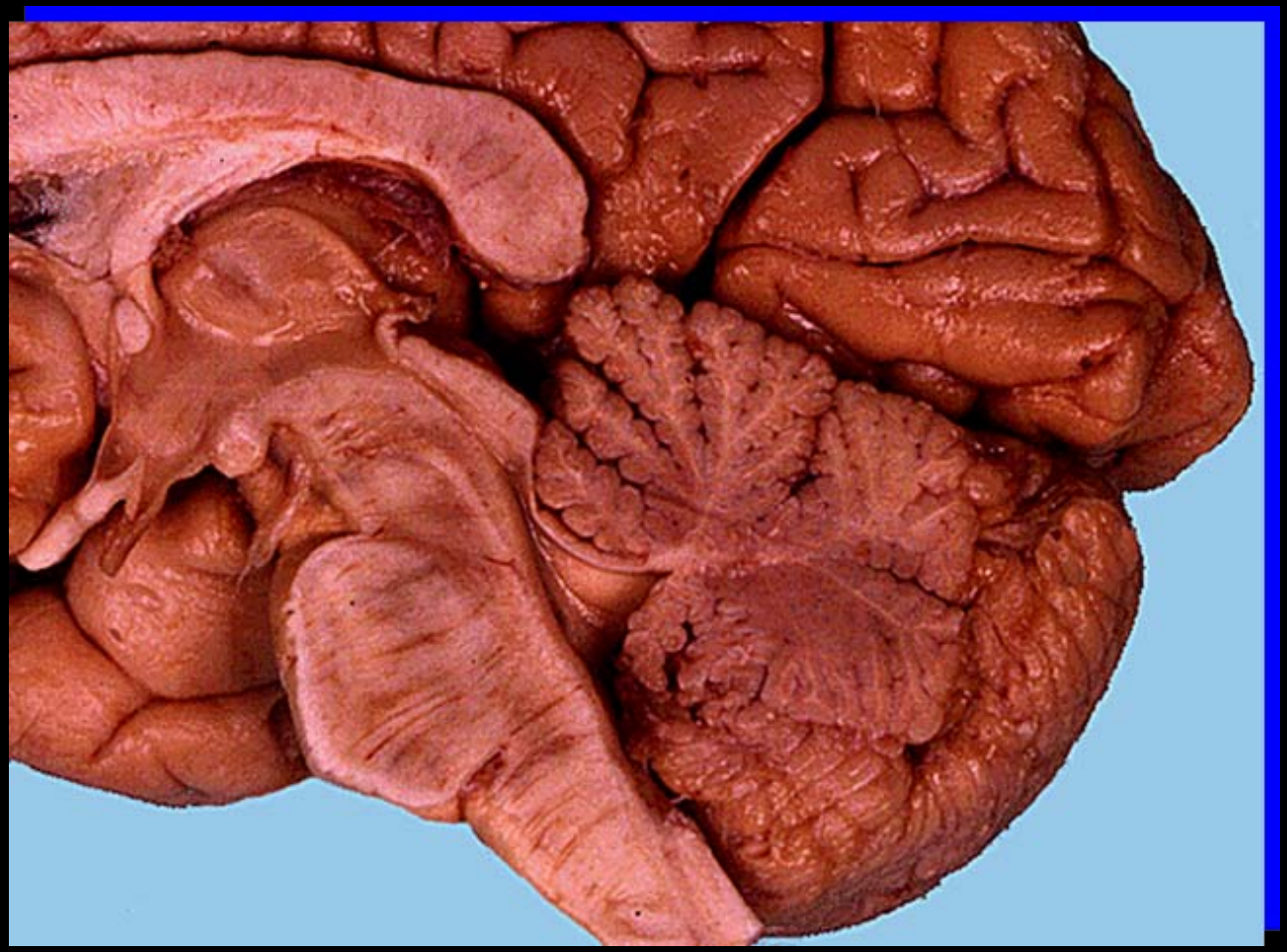
What does the cerebellum do?

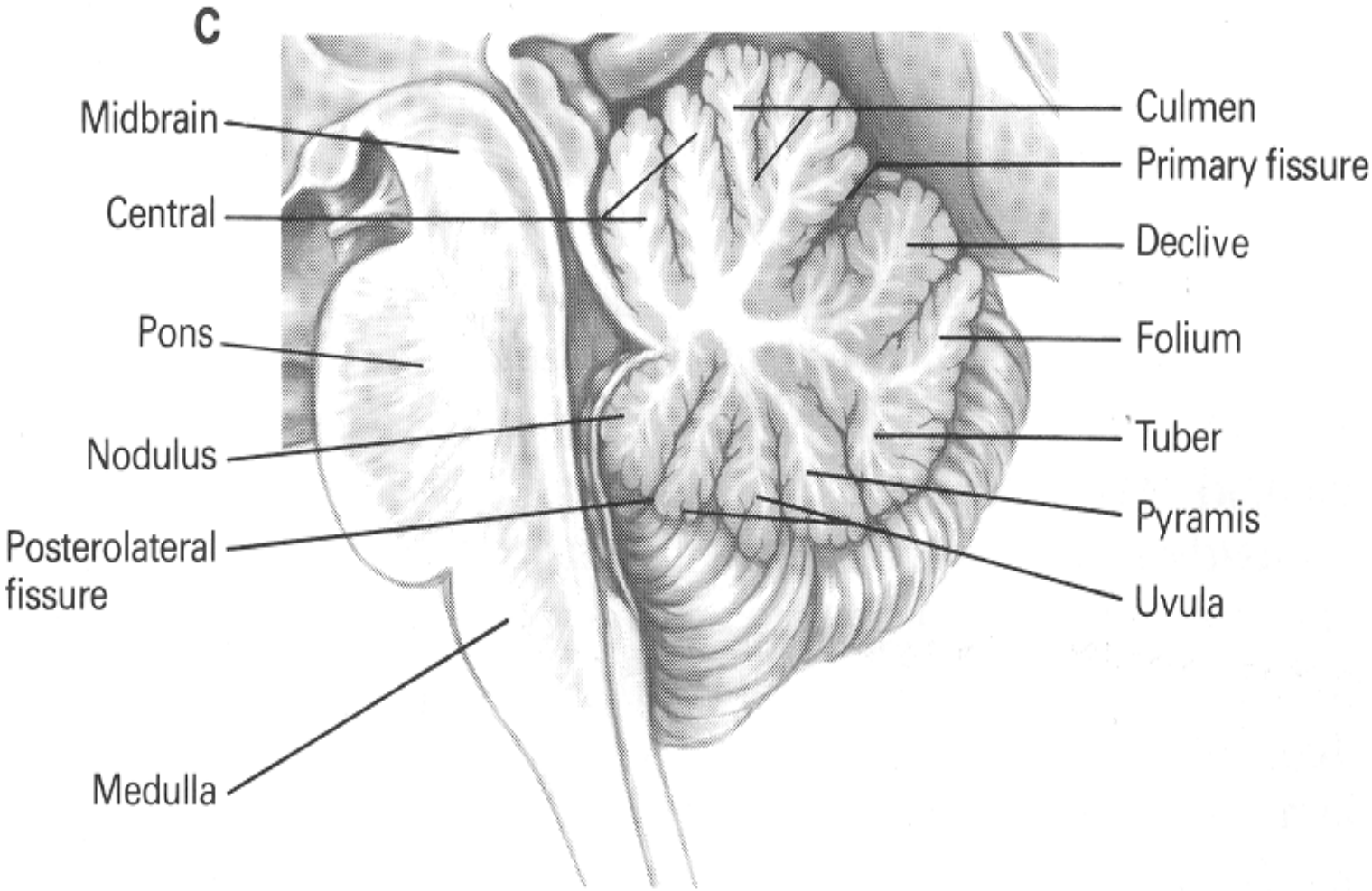
- Motor coordination
- Motor learning
  - Adaptation of the VOR
  - Eye blink conditioning
- Somatosensory processing
  - Discriminating surfaces
  - Self tickle
- Cognitive function
  - Autism
  - Dyslexia
  - Time perception



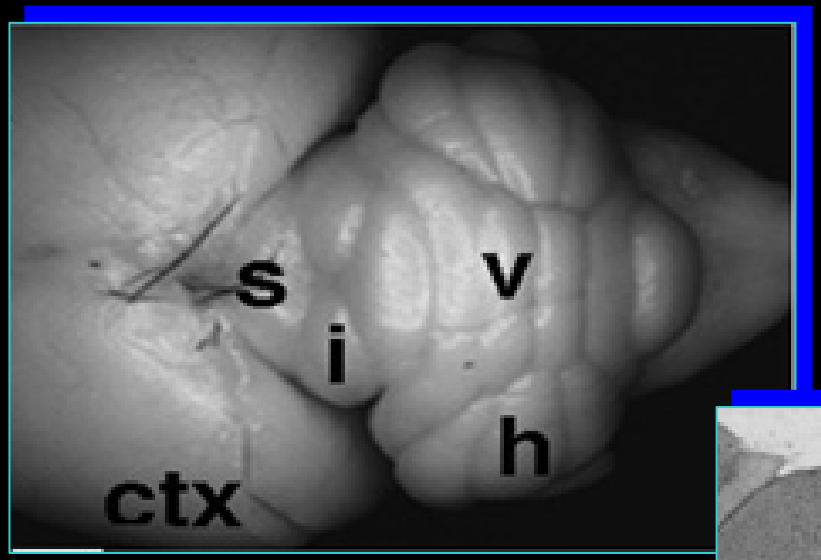
About 70% of the neurons in the central nervous system are located in the cerebellum

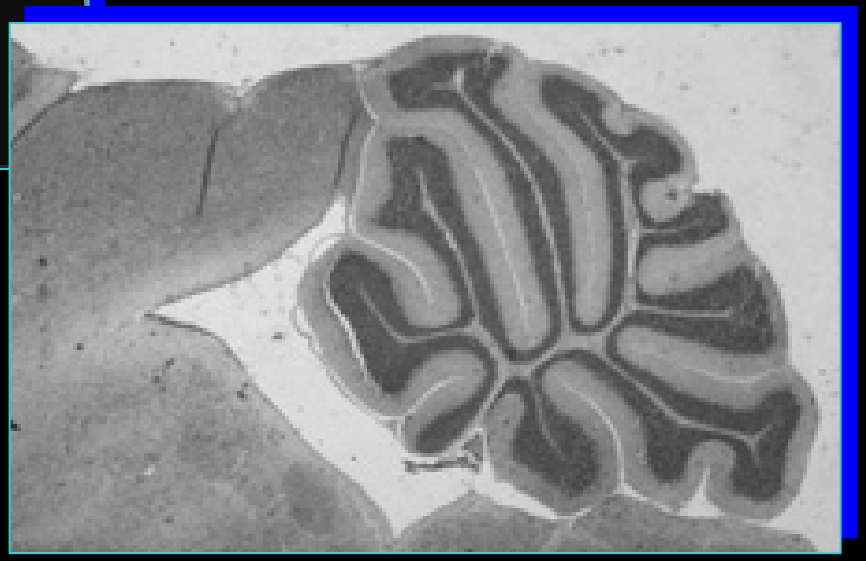
Mature Human Cerebellum

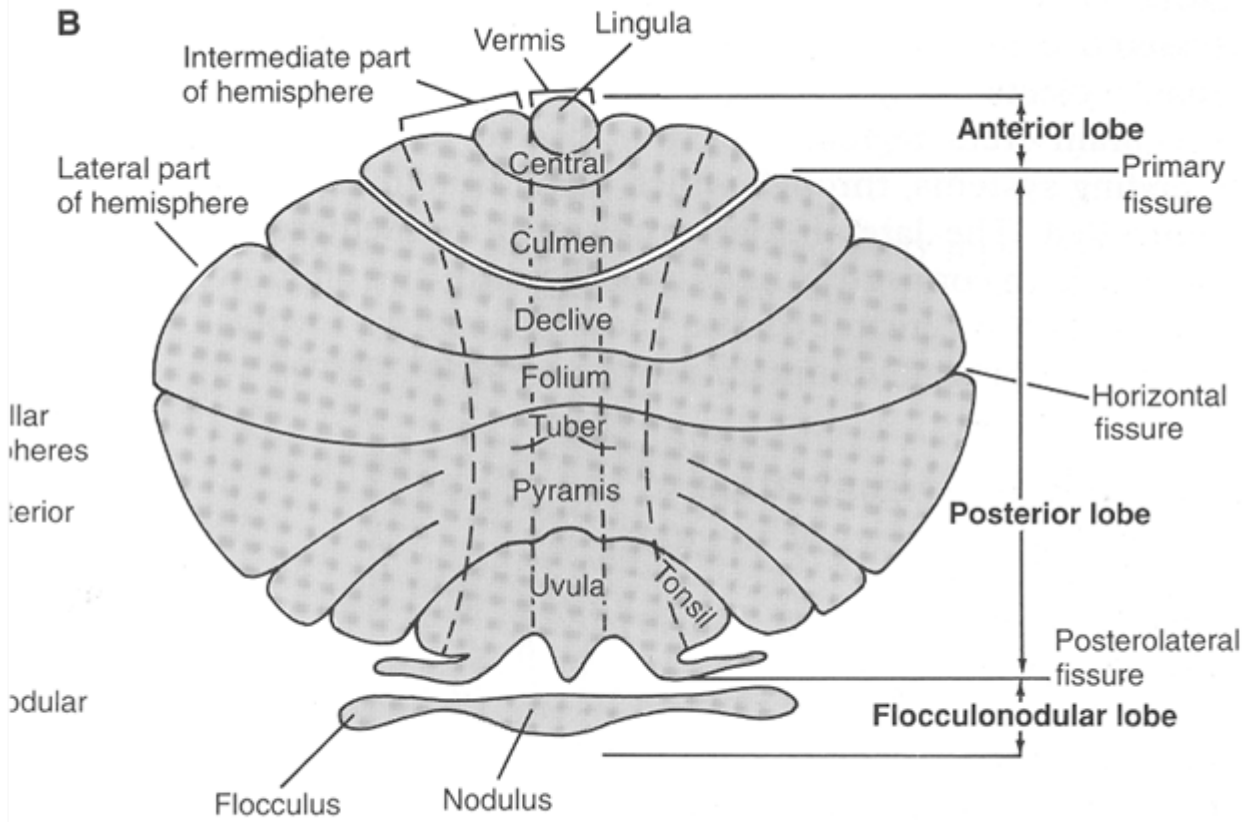



C
Midbrain
Central
Pons
Nodulus
Posterolateral fissure
Medulla
Culmen
Primary fissure
Declive
Folium
Tuber
Pyramis
Uvula

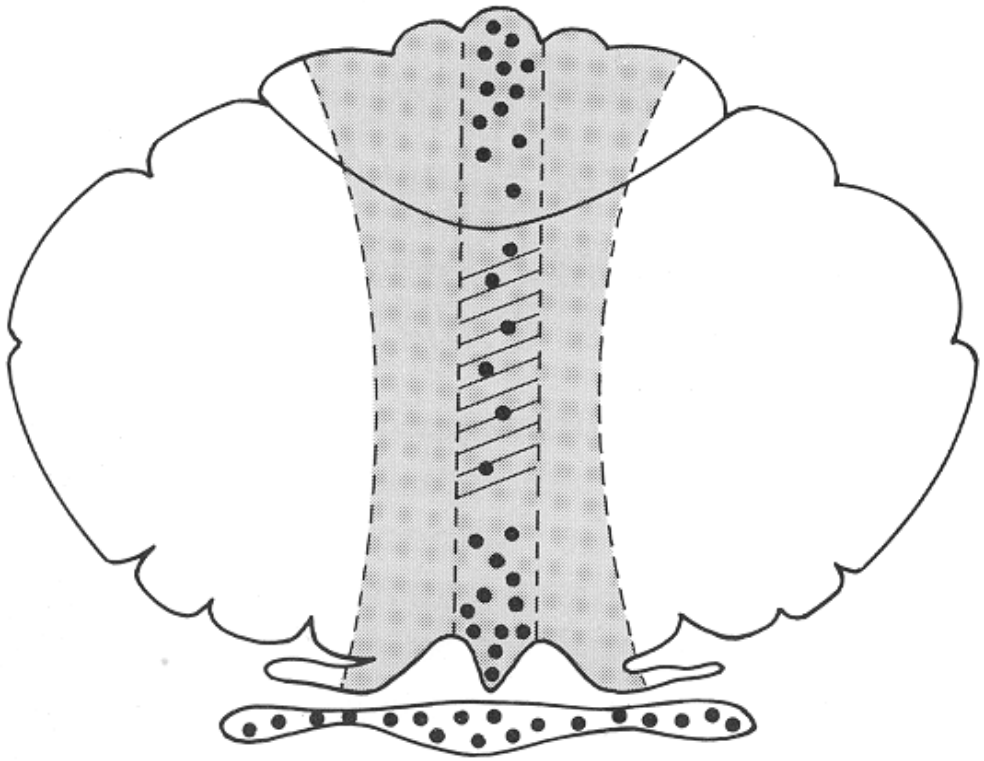
Mature Mouse Cerebellum






B
Intermediate part
of hemisphere
Vermis
Lingula
Lateral part
of hemisphere
Central
Culmen
Declive
Folium
Tuber
Pyramis
Uvula
Tonsil
Anterior lobe
Primary
fissure
Horizontal
fissure
Posterior lobe
Posterolateral
fissure
Flocculonodular lobe
Flocculus
Nodulus

B Inputs



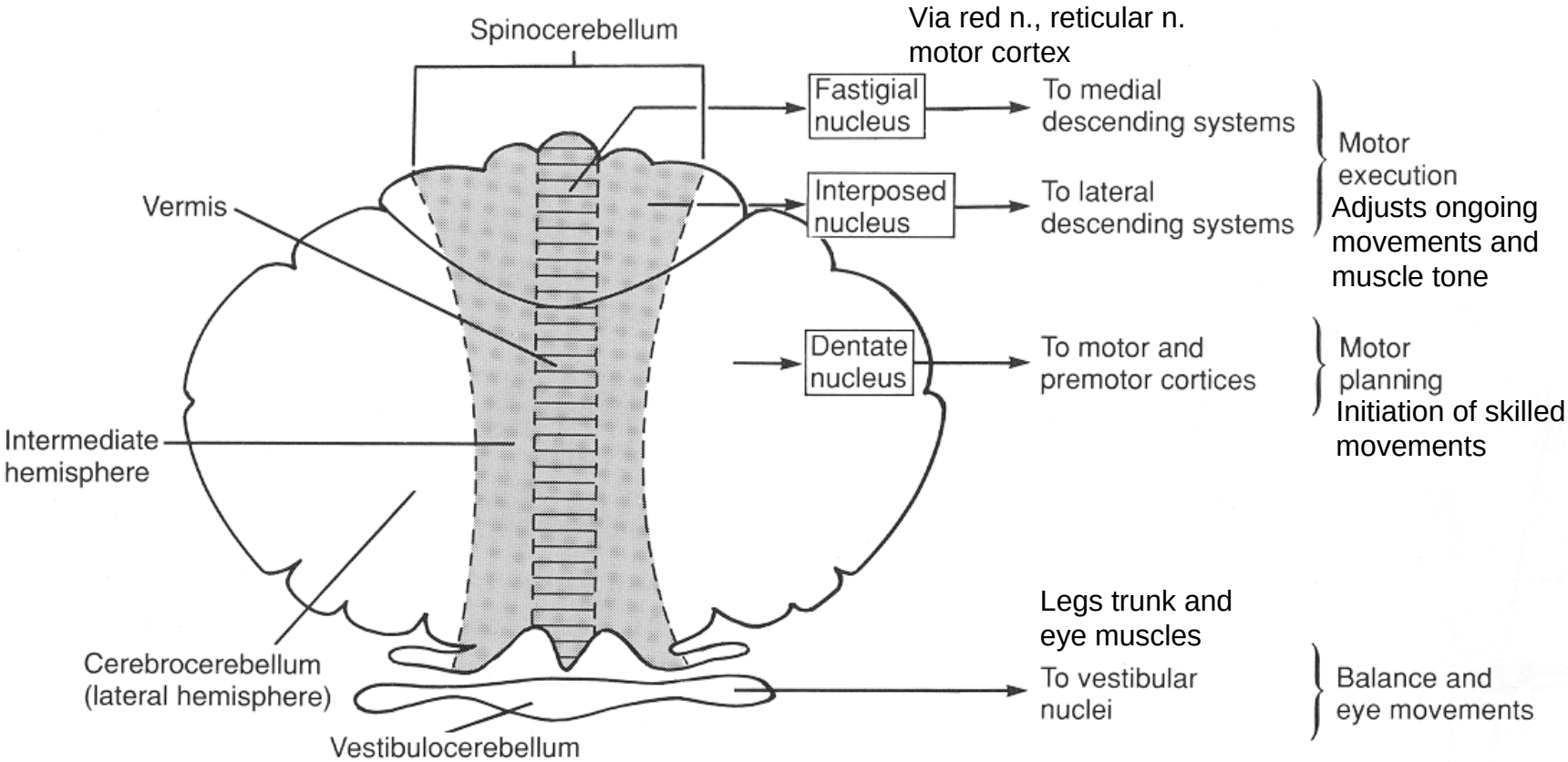
Corticopontine inputs (corollary discharge of motor command via pontine nuclei)

Spinal and trigeminal inputs (somatosensory and muscle afferents)

Visual and auditory inputs

Vestibular inputs

A Outputs


Spinocerebellum
Via red n., reticular n.
motor cortex
Fastigial nucleus
To medial descending systems
Motor execution
Adjusts ongoing movements and muscle tone
Vermis
Interposed nucleus
To lateral descending systems
Dentate nucleus
To motor and premotor cortices
Motor planning
Initiation of skilled movements
Intermediate hemisphere
Legs trunk and eye muscles
Cerebrocerebellum (lateral hemisphere)
To vestibular nuclei
Balance and eye movements
Vestibulocerebellum

Archicerebellum-Vestibulocerebellum

- The oldest part of the cerebellum.
- In fish: vestibular apparatus.
  - Coordinates eyes and trunk movements.
- In mammles: floccolonodular lobe & vermis.
  - Controls eye movements, and trunk equilibrium.

- Flocculonodular syndrome: Loss of whole body equilibrium. Swaying when standing, staggering when walking, tendency to fall (usually backwards), positional nystagmus.

Paleocerebellum - Spinocerebellum

- An old portion of the cerebellum.
- In reptiles:
  - coordinates trunk and limb movements.
- In mammles:
  - occupies the vermis & intermediate part of cerebellar body.
  - Controls posture & ongoing execution of limb movement.
  - Proprioception, spinocerebellar tracts.
- Failure of the spinocerebellum leads to ataxia.

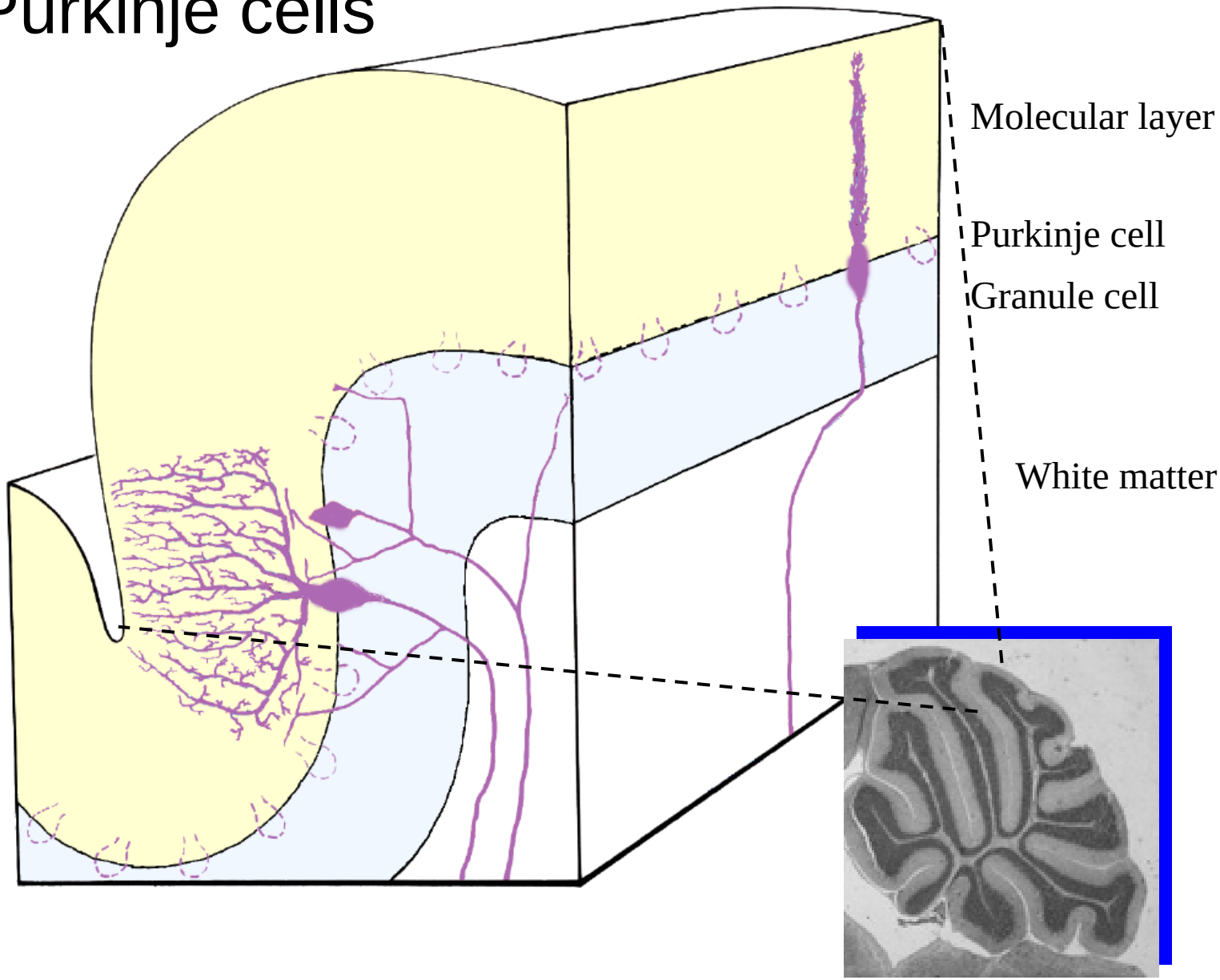
Neocerebellum-Pontocerebellum-Cerebrocerebellum

- The newest part of the cerebellum.
  - Developed phylogenetically in proportion to skilled movement.
- In man: 90% of cerebellar cortex.
  - synchronization of fine movements of the hands and fingers.
  - planning and initiation of movement (?)
- Failure of the cerebrocerebellum leads to intention tremor.

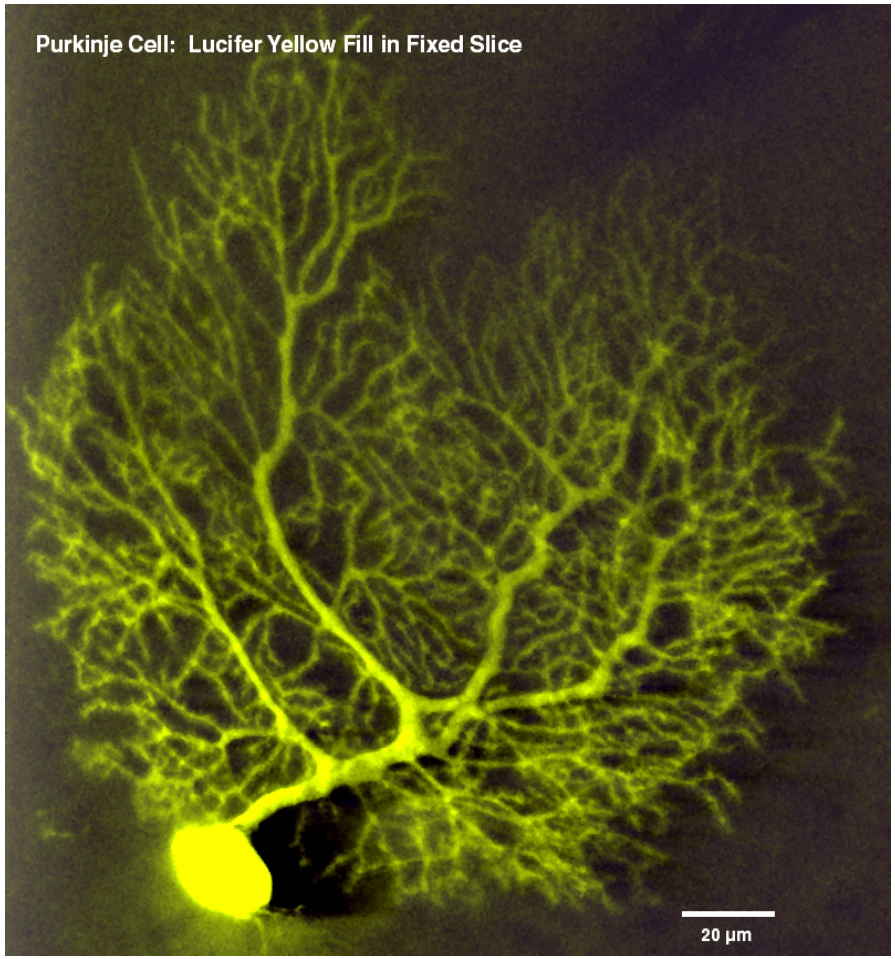
Cerebellar diseases

- Hypotonia – low muscle tone expressed in diminished resistance to passive limb displacement (knee jerk)
- Ataxia – lack of coordination
  - Delay in response initiation
  - Dysmetria – error in range of movement
  - Dysdiadochokinesia – error in rate and regularity of movements
  - Complex multi-joint movements deficit
- Intention tremor

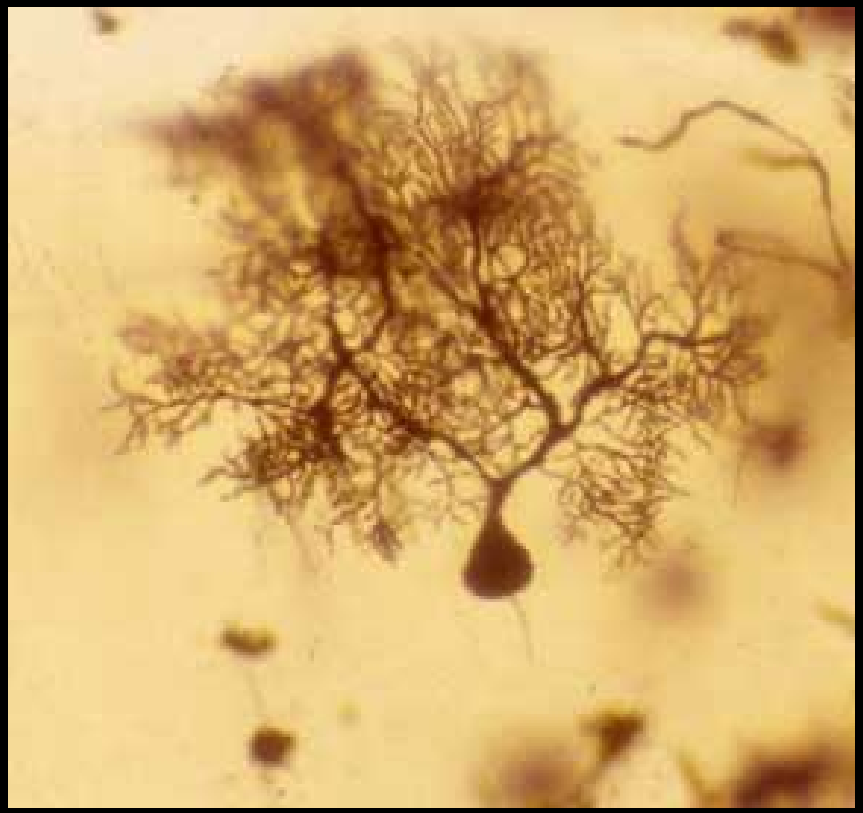
Purkinje cells



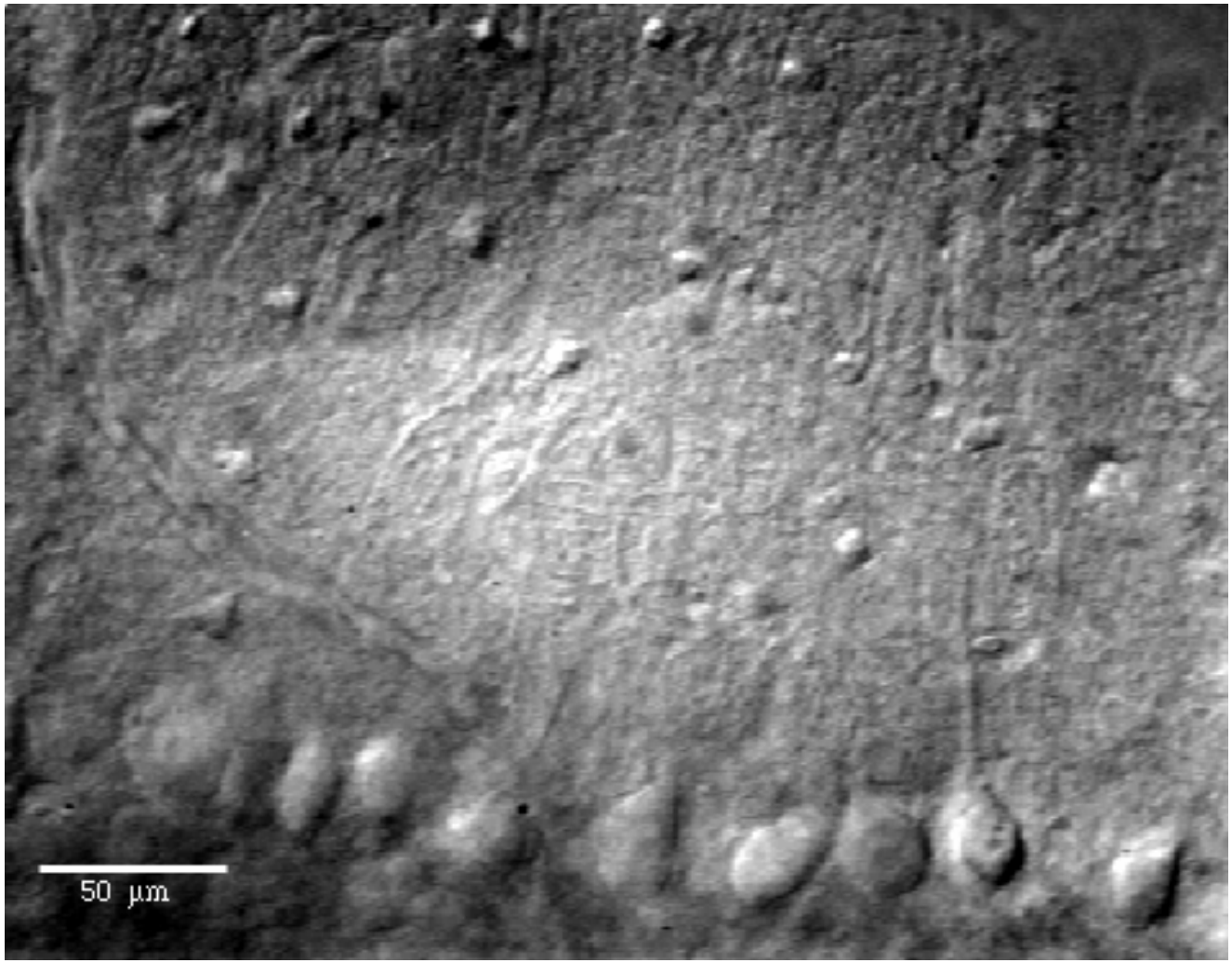
Purkinje cell (para-sagittal view using confocal microscopy, UCSD)



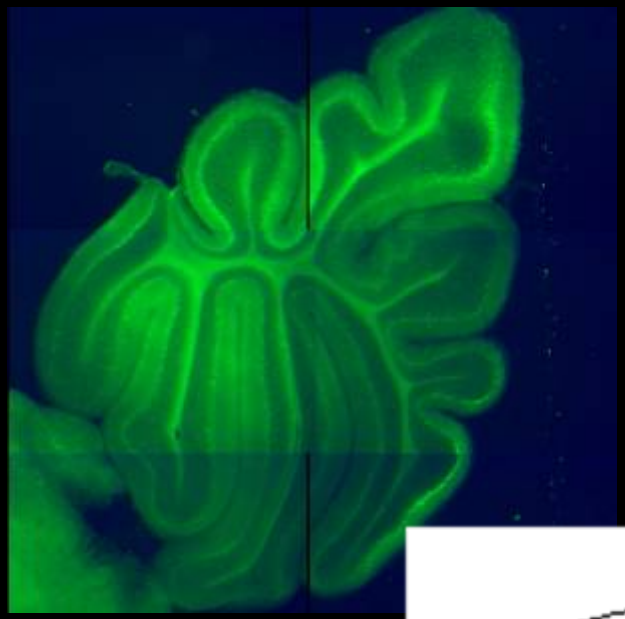
Purkinje Cells: Golgi Staining

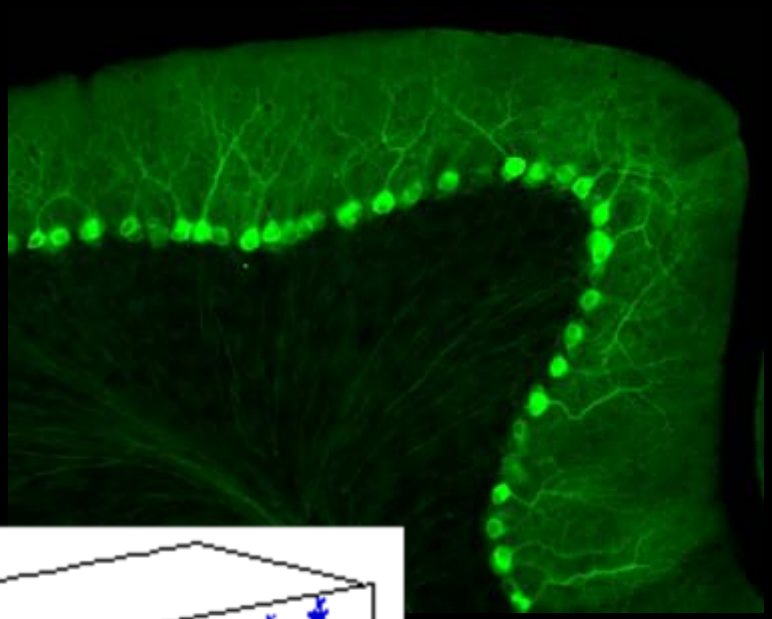


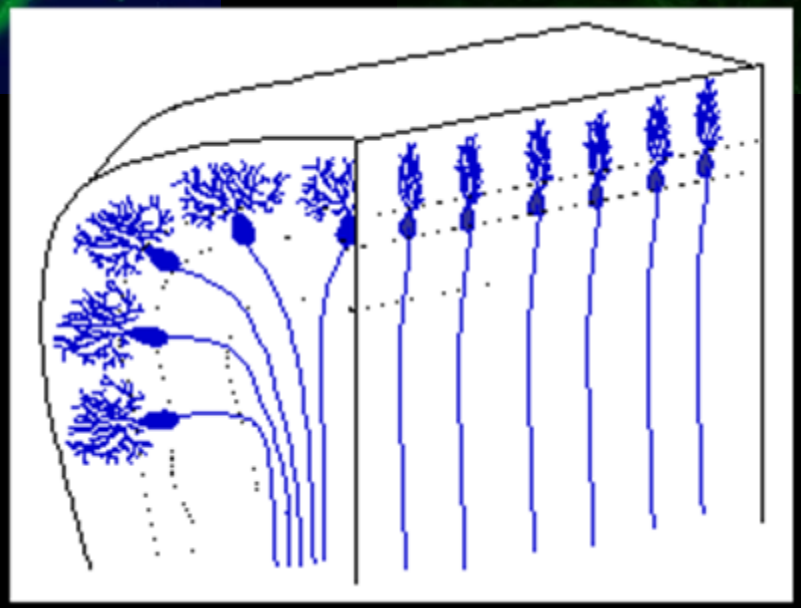
Purkinje cells form a monolayer



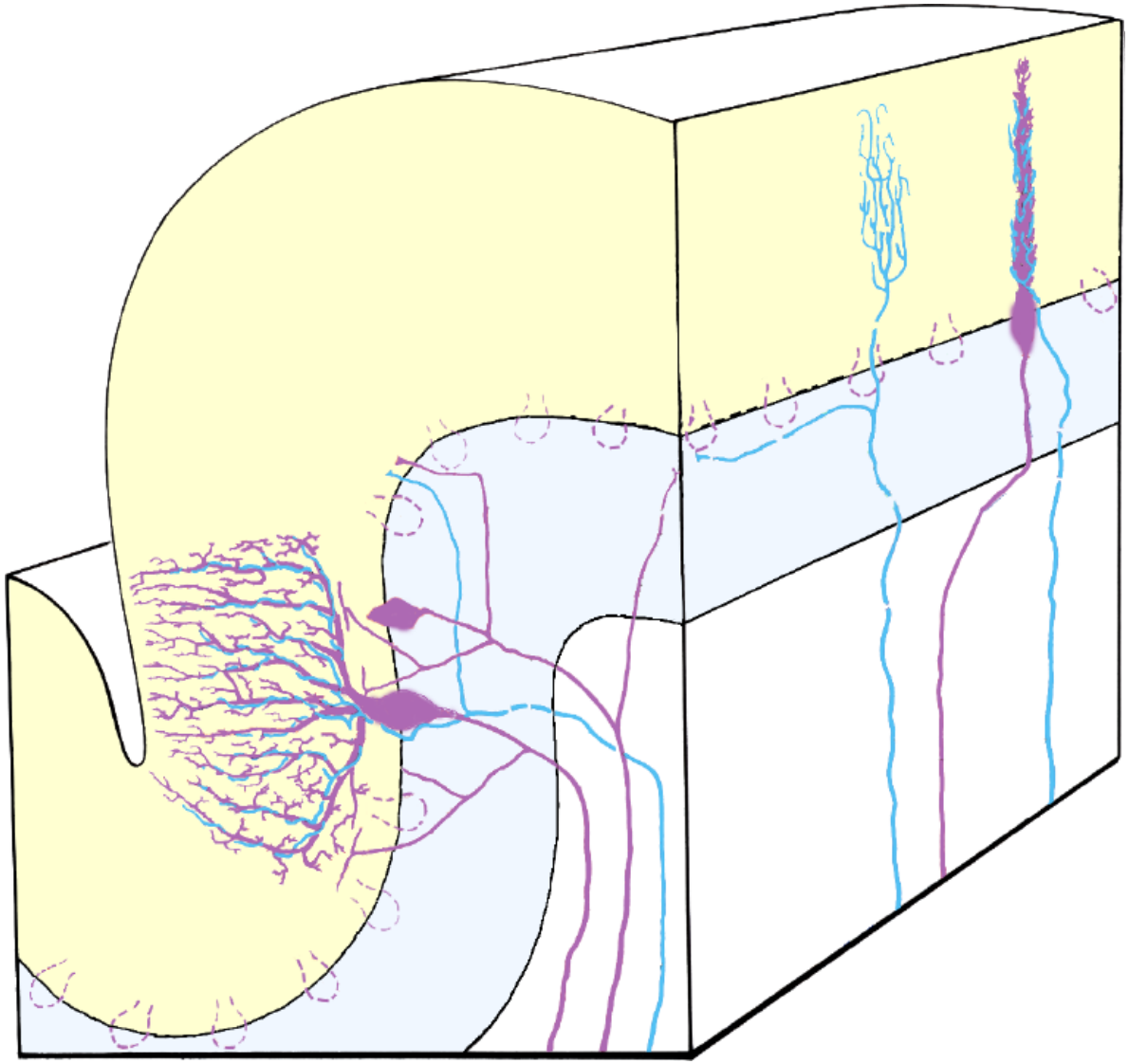
Purkinje Cell Layer



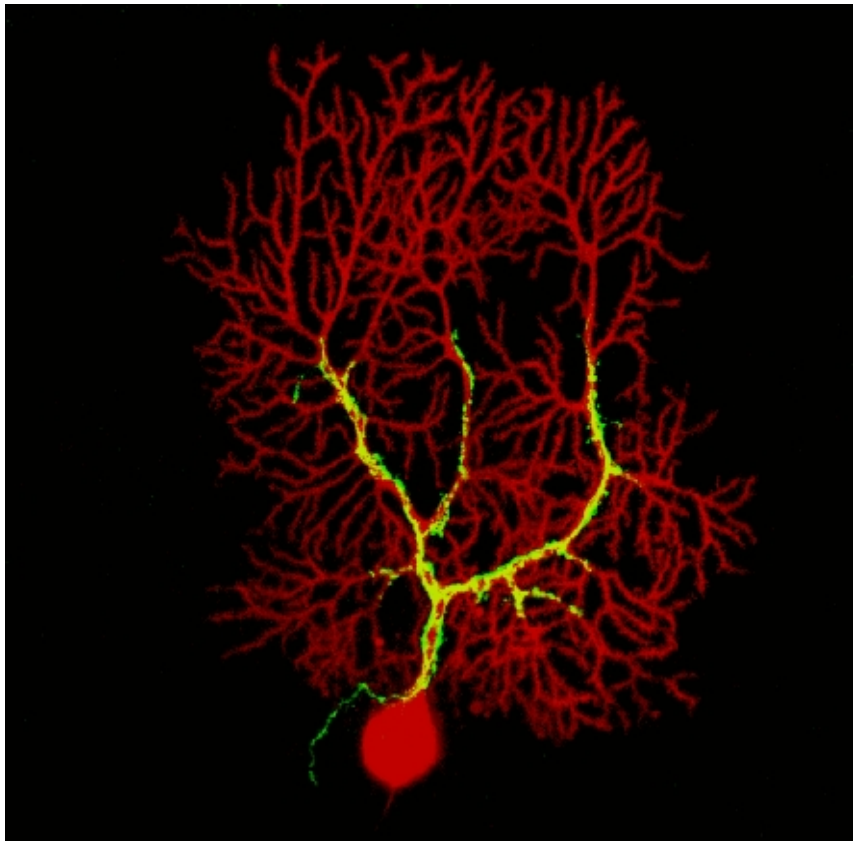


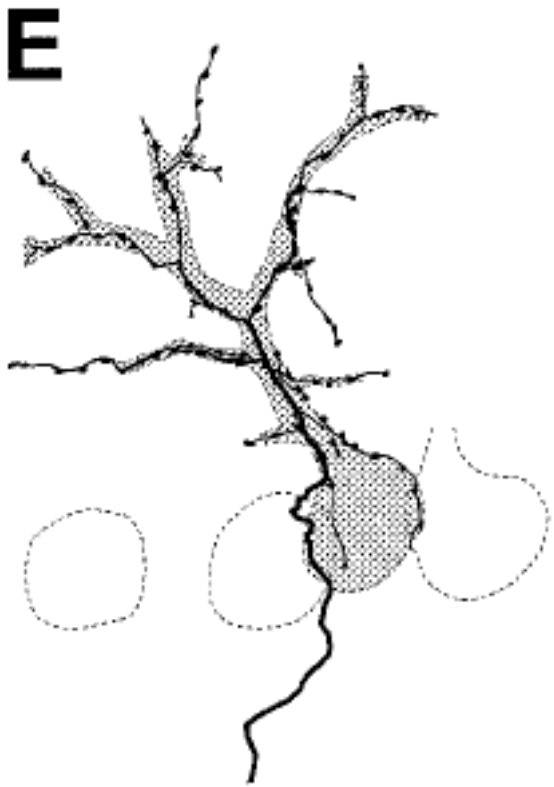


Climbing fiber input

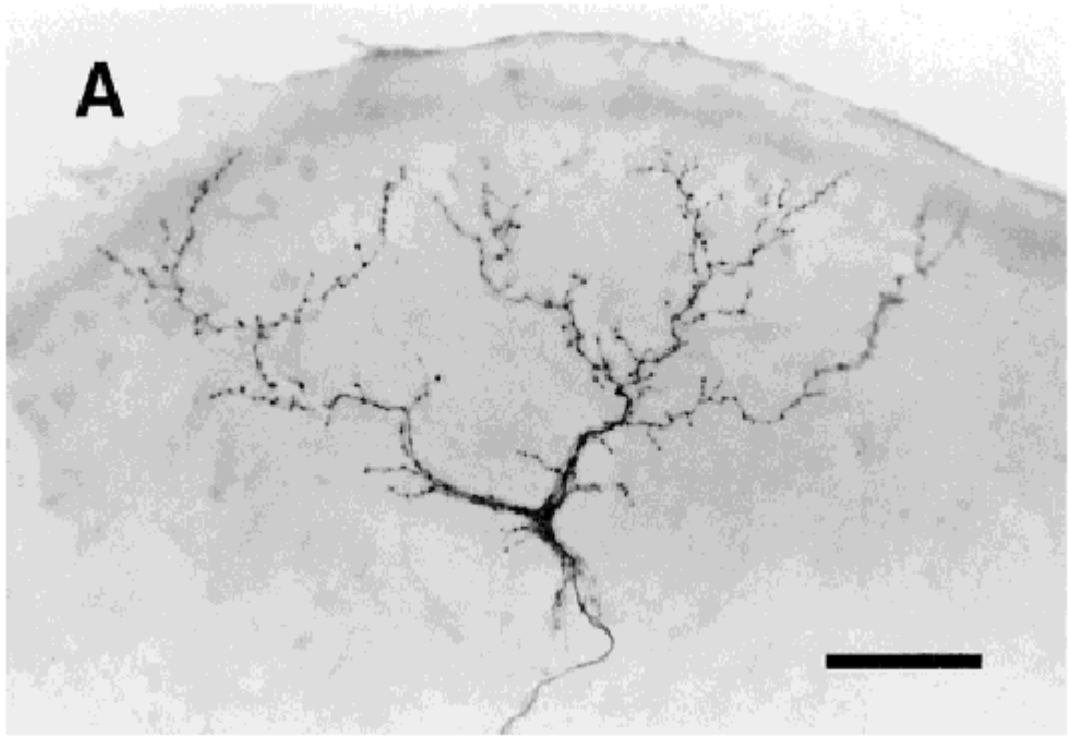


When CF meets PC

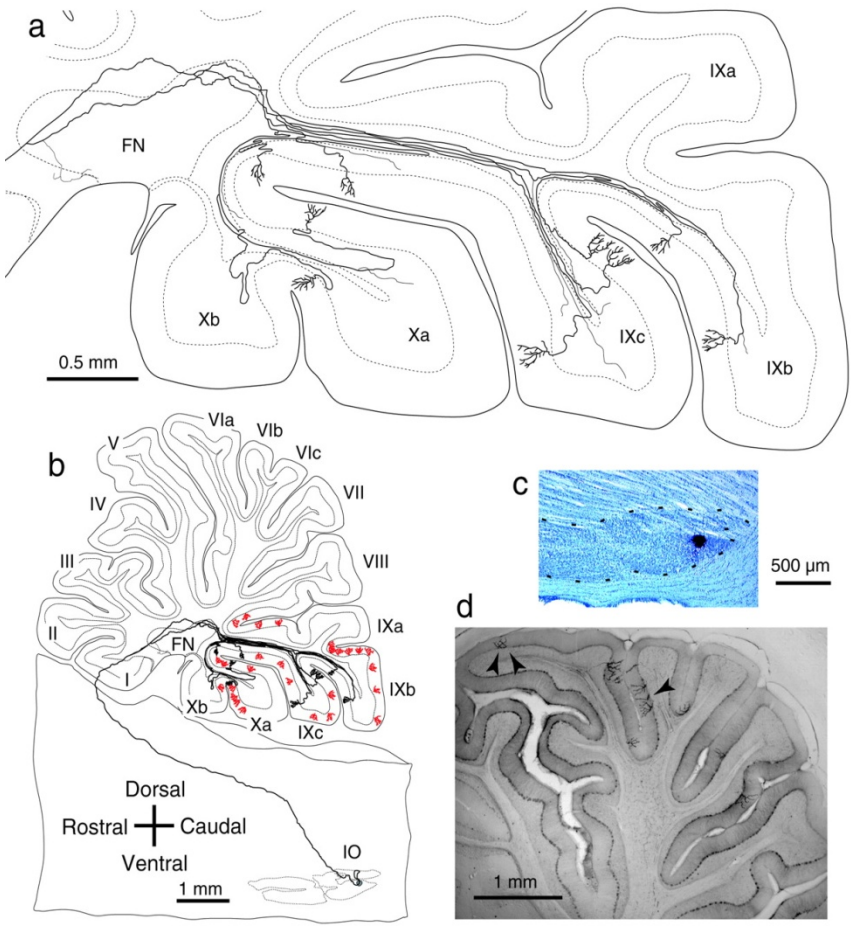




Terminal arborization of climbing fiber (CF) axon in the cerebellar cortex (biotin, Sugihara et al., 1999)



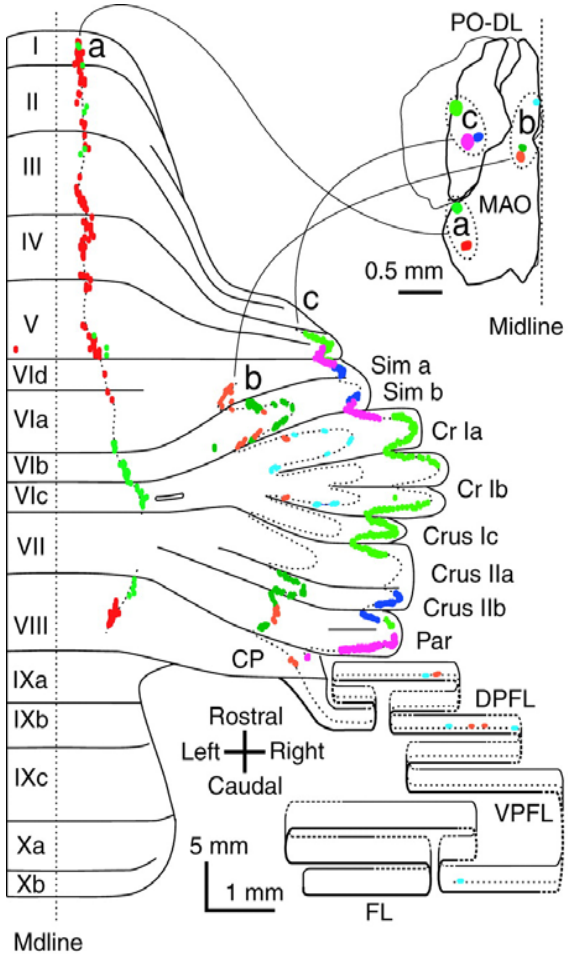
Inferior olive axons innervate Purkinje cells as climbing fibers



- Climbing fibers of one IO axon are restricted to a narrow longitudinal band.
- Each IO innervates 5-10 Purkinje cells.
- Each IO axon sends collaterals to the deep cerebellar nuclei.

Sugihara et al. J Neuroscience 2001

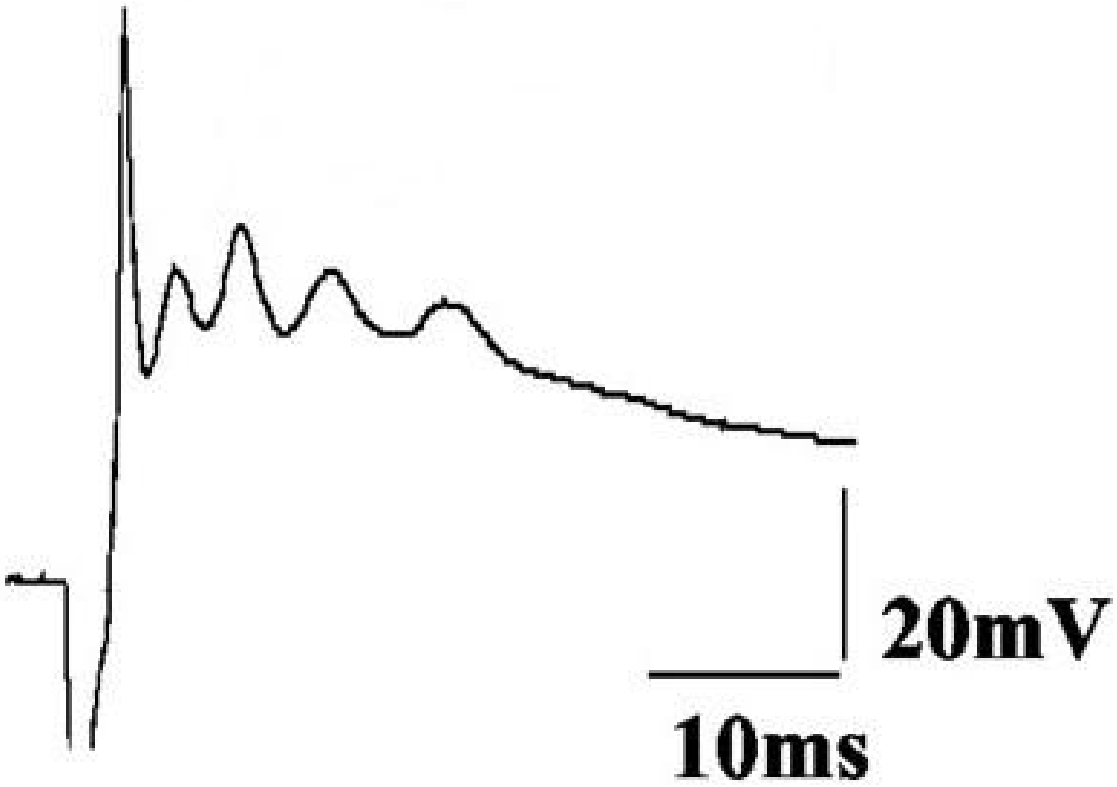
Proximal IO neurons innervate narrow longitudinal bands in CC



- Spatial organization of IO-CC inputs
- IO is contralateral to cerebellum
- IO receives inputs from many CNS sources

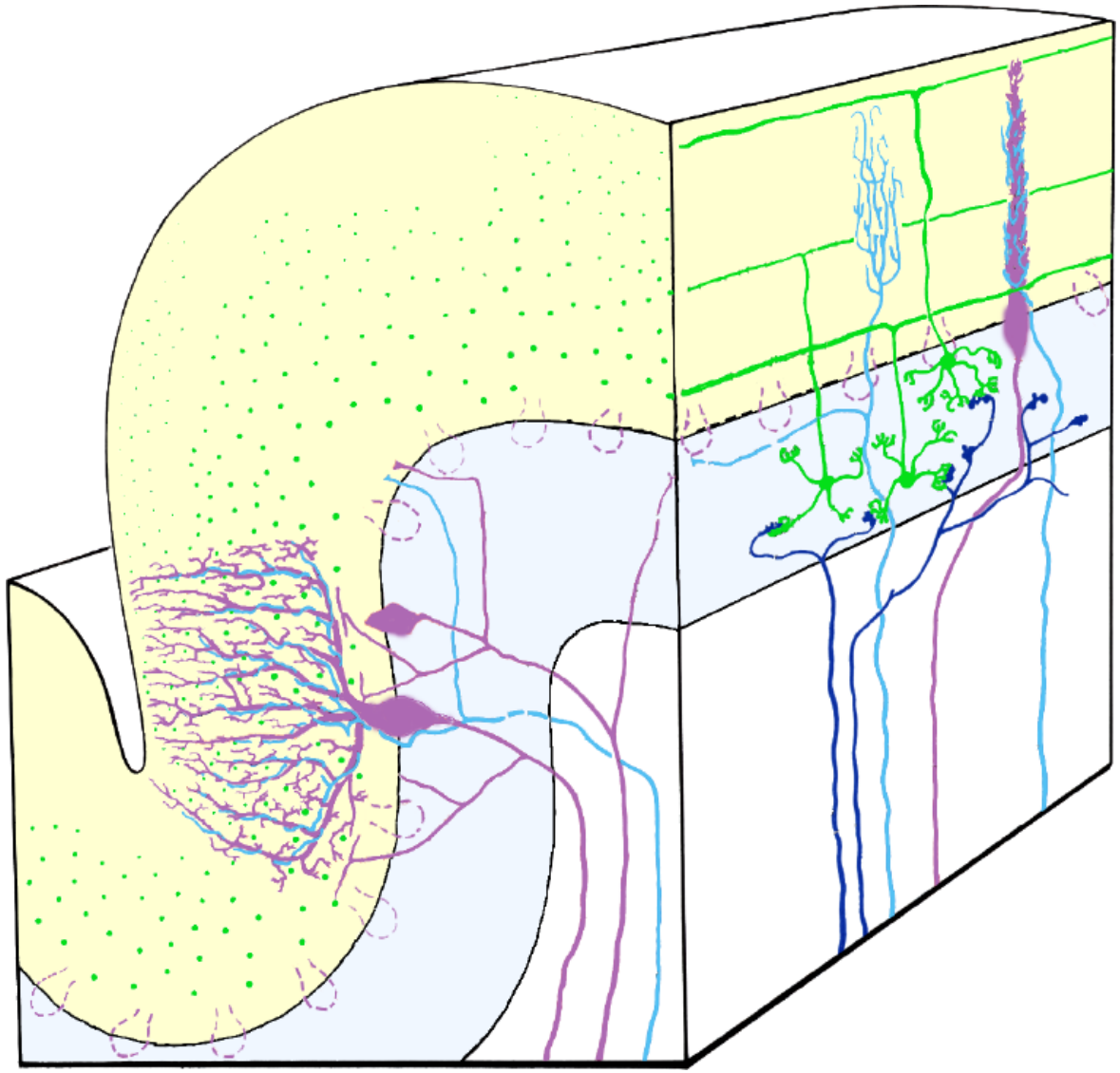
Sugihara et al., J Neuroscience 2001

The effect of CF input on Purkinje cells: the complex spike

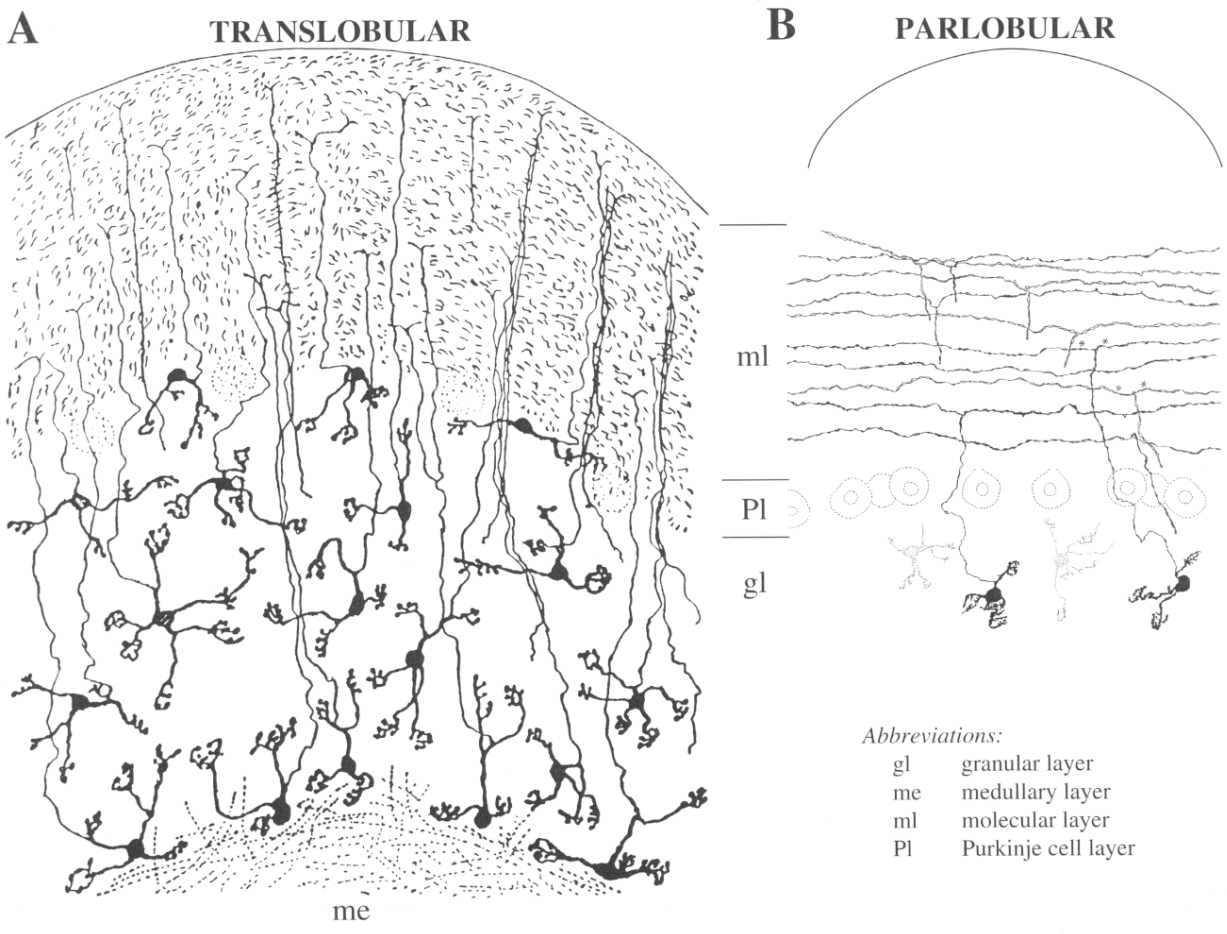


Weber et al., PNAS 2003

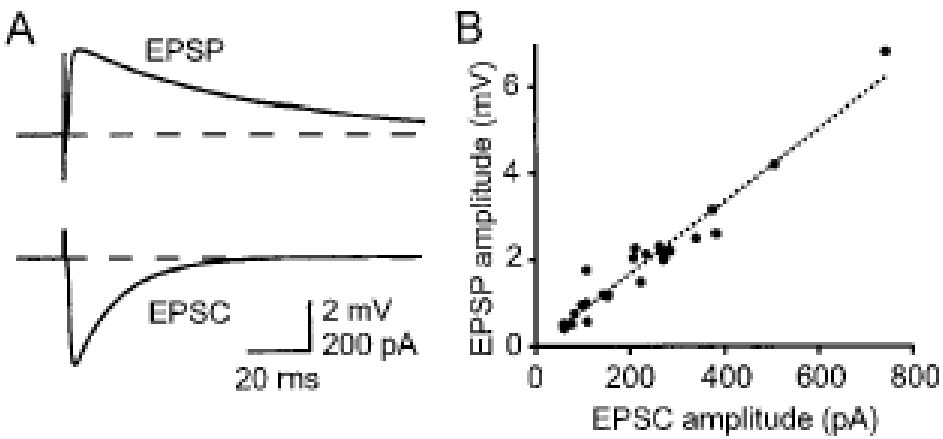
The mossy fiber input



Staining of granule cell parallel fibres (PFs)



The effect of PF input on Purkinje cells



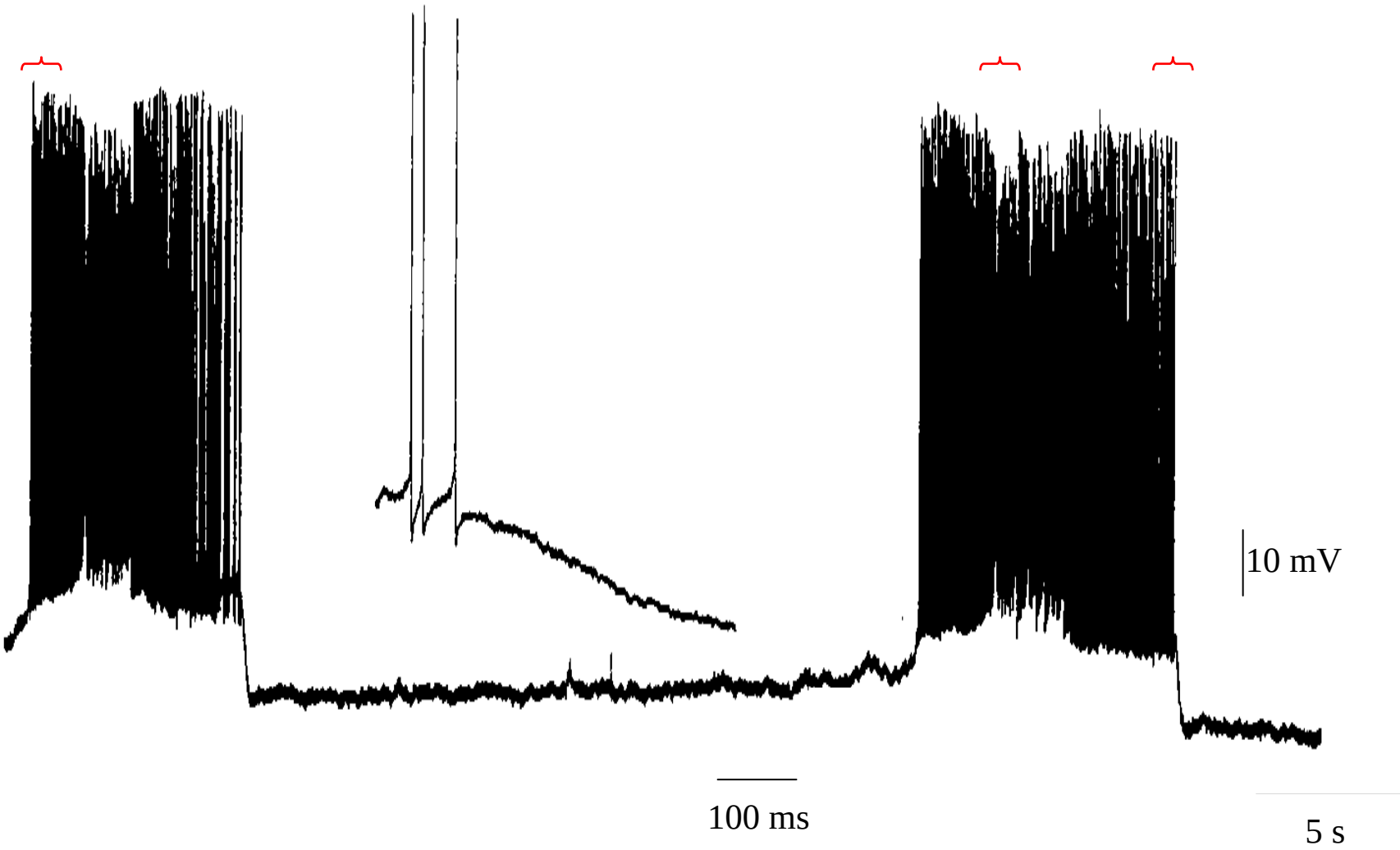
- A huge percentage (>85%) of PF-PC synapses are quiet
- The effective synapses are comparable and depolarize the cell on average by ~1mV

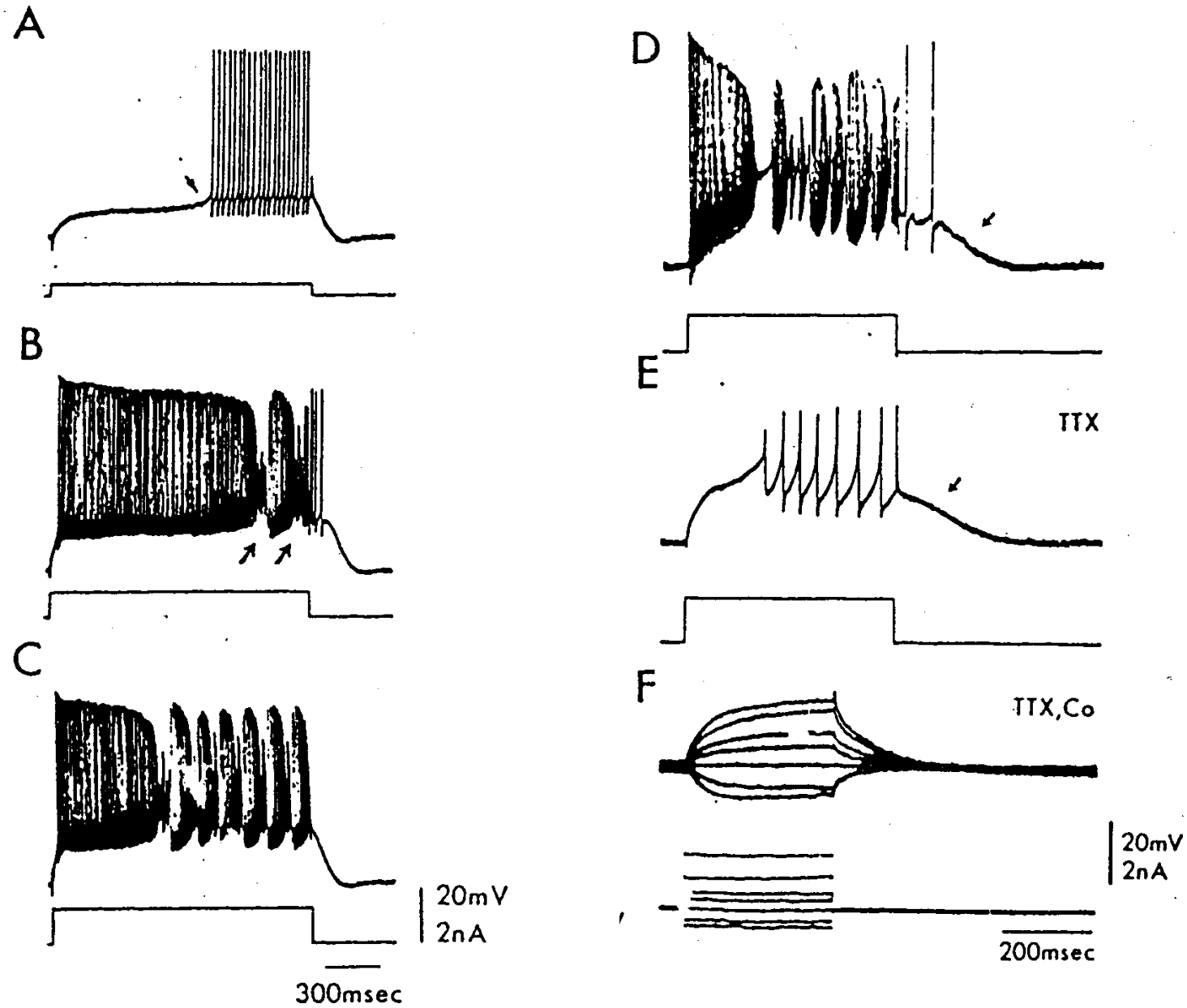
Let's talk some numbers

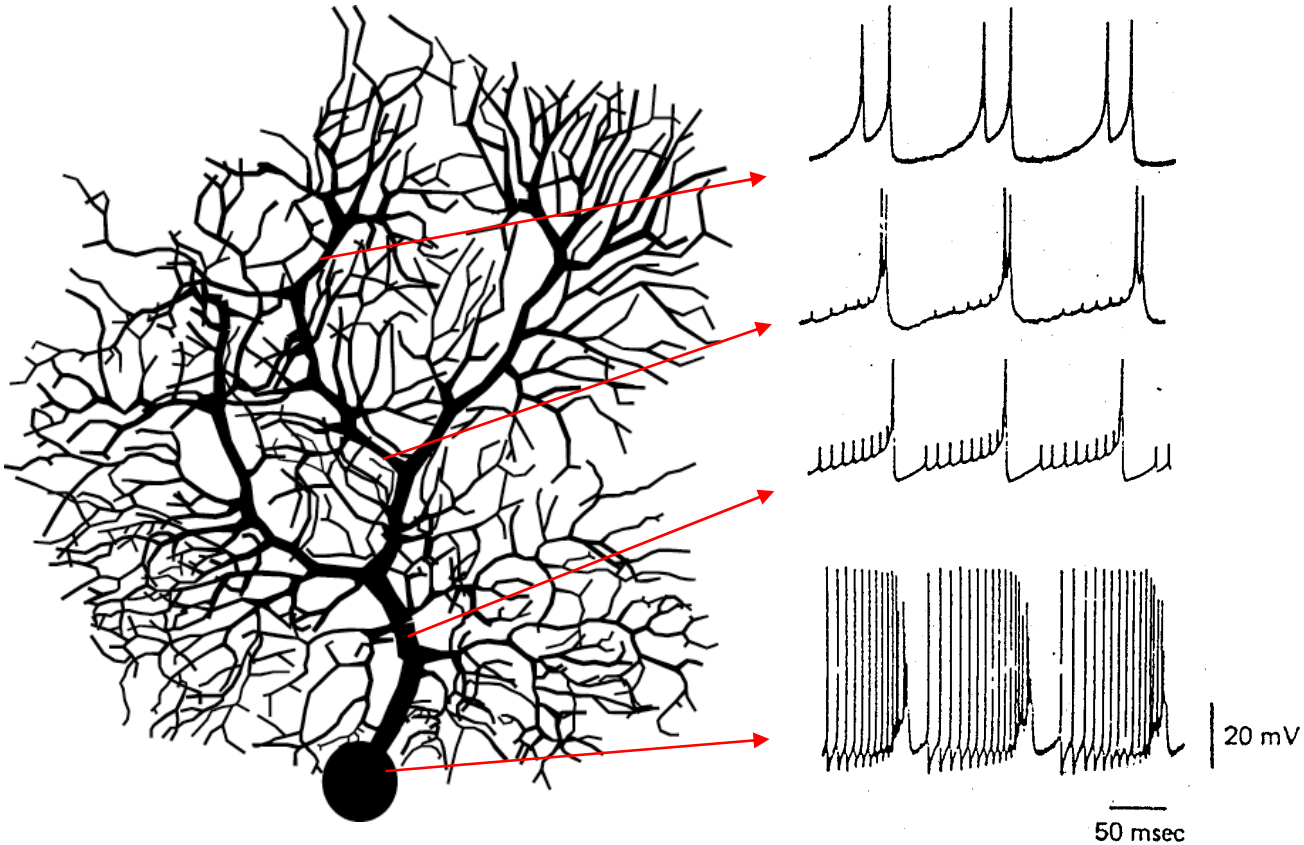
- There are about 10-20 million Purkinje cells in the human brain
- There are about 50-100 billion granule cells (and obviously a lot less mossy fibers)
- Each mossy fiber innervates about 400-600 granule cells in each folium
- Each Purkinje cell receives 100-200,000 PF inputs

What can be learned from it?

Electrophysiology of Purkinje cells




A
B
C
D
E
F
TTX
TTX,Co
20mV
2nA
300msec
20mV
2nA
200msec


20 mV
50 msec

Complex spikes occur at very low frequencies

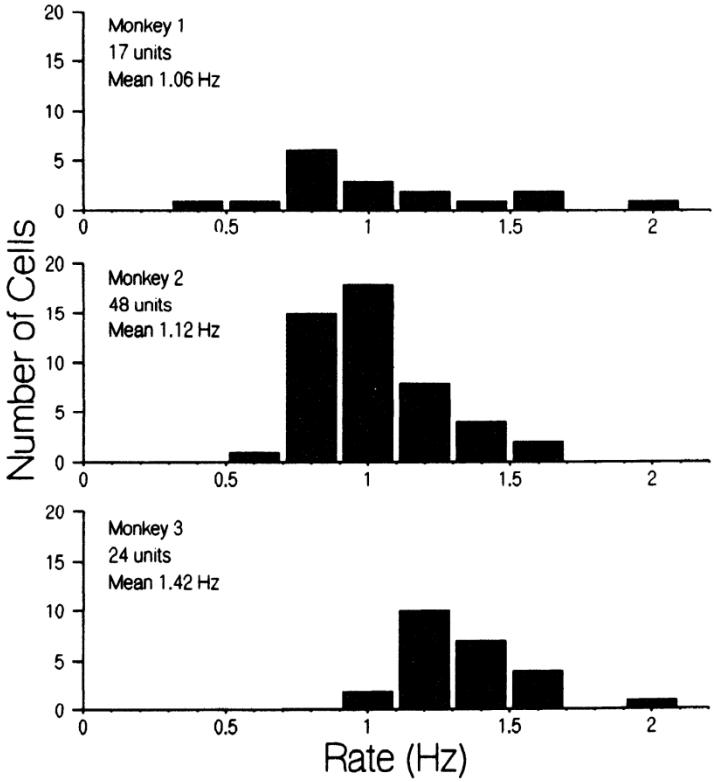
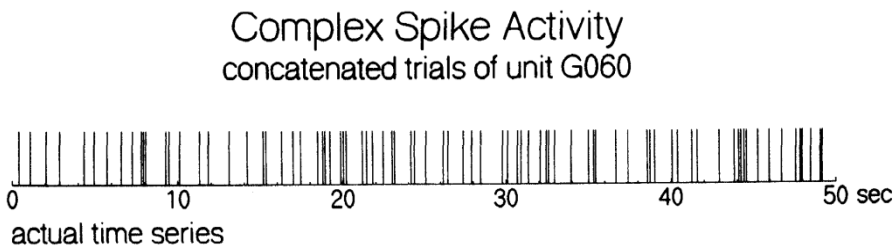
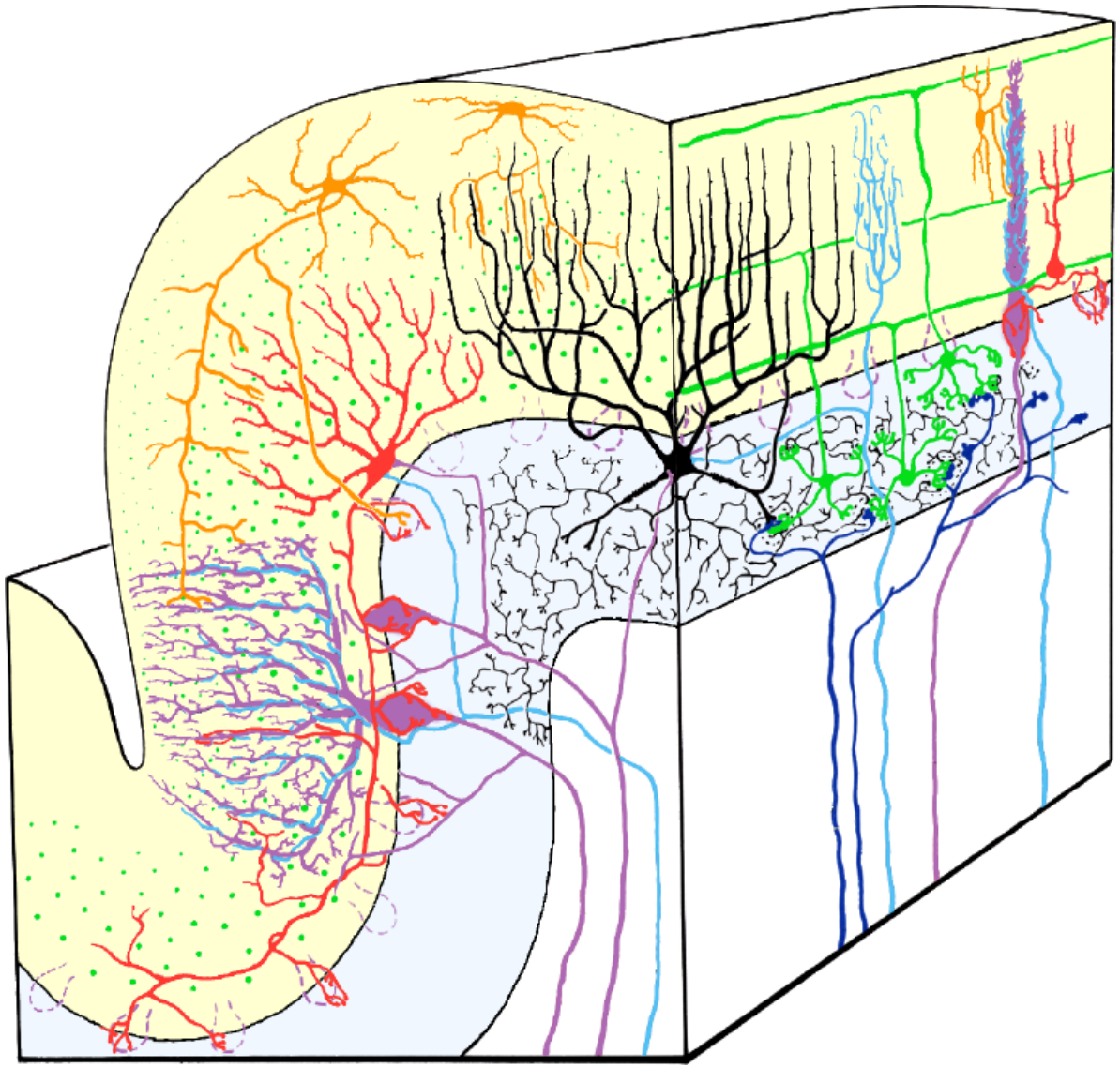


FIG. 2. Histogram of complex spike discharge rates of all the units used in this study, shown by monkey.



Keating and Thach, J Neurophys 1995

Inhibitory interneurons



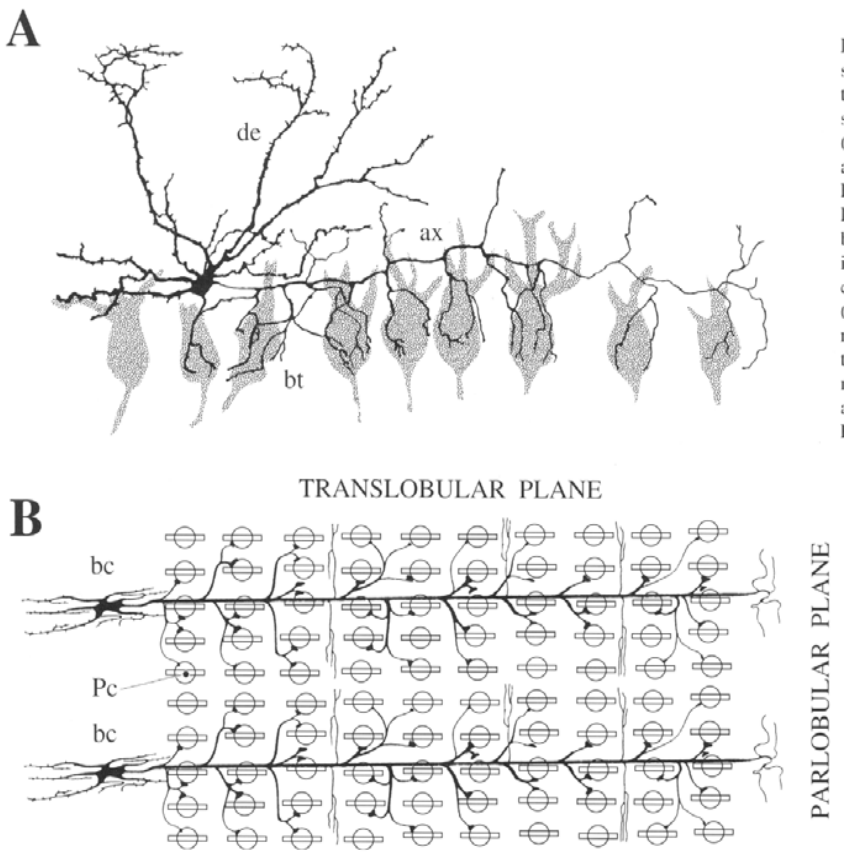
Molecular layer

Purkinje cell

Granule cell

White matter

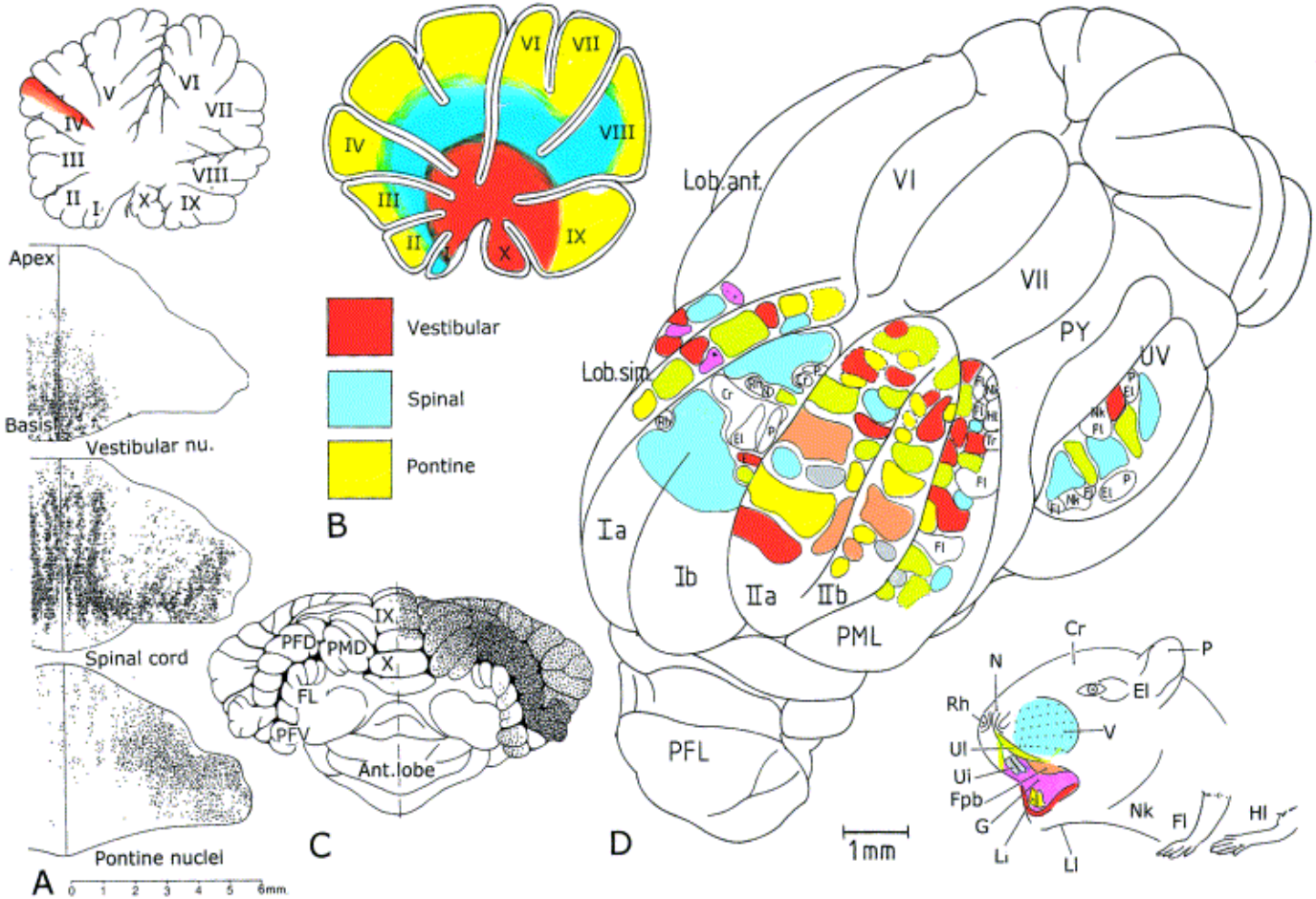
Molecular layer interneurons



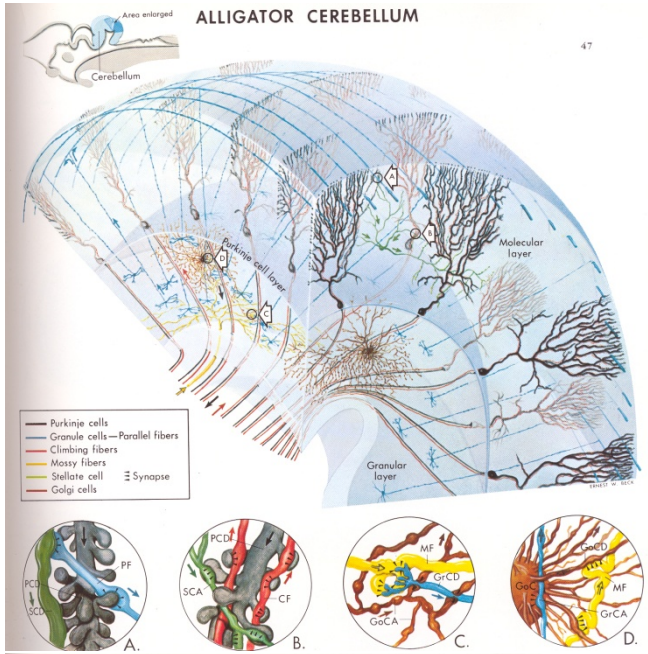
- Stellate and basket cells are interconnected chemically and electrically.
- They inhibit Purkinje cells.
- Their axonal axis is perpendicular to the PF axis – “lateral inhibition” to PF activity?

Cerebellar cortex: Cajal

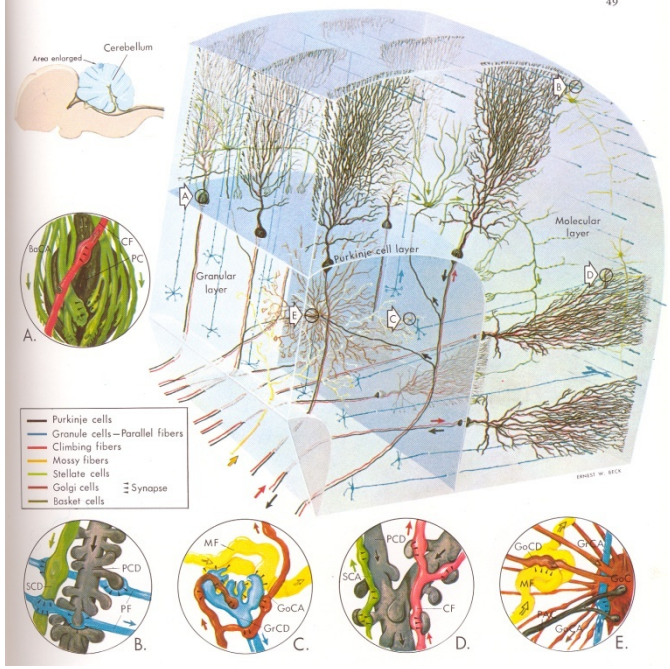
IV. Somatosensory maps in cerebellum



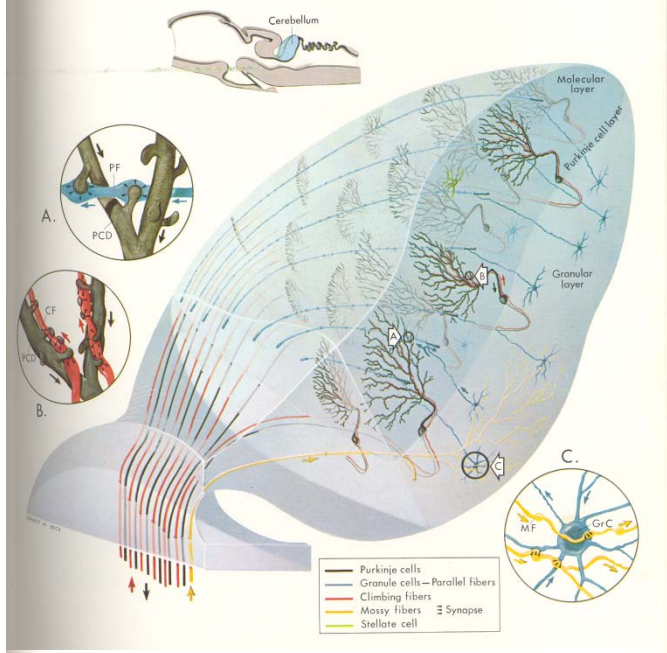
ALLIGATOR CEREBELLUM



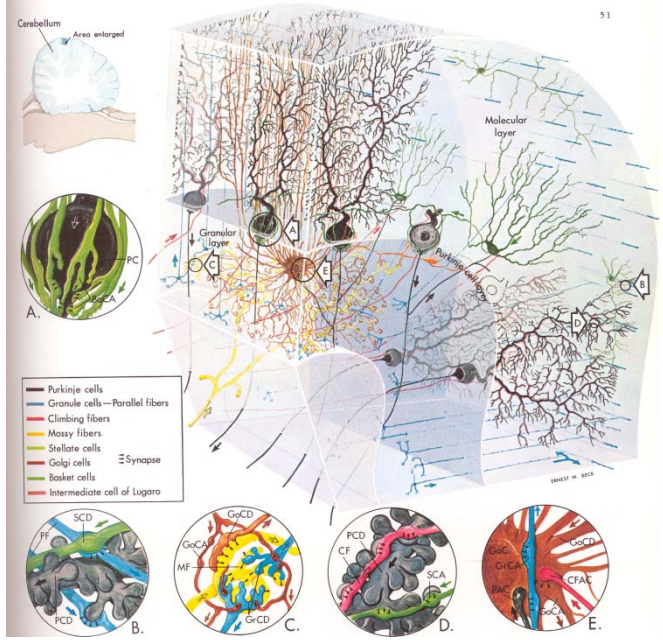
PIGEON CEREBELLUM



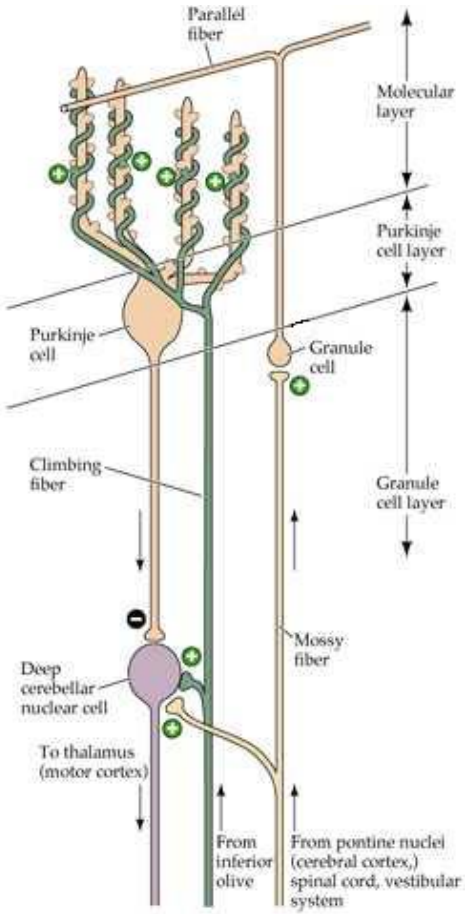
FROG CEREBELLUM



CAT CEREBELLUM



The cerebellum forms several feedback and feed forward networks



- Purkinje cells innervate deep cerebellar nuclei (DCN) : inhibitory output
- All cerebellar inputs send axon collaterals to the DCN (loops)

If so...

- Why do we need the MF-GC divergence only to then converge massively upon Purkinje cells?
- Why do Purkinje cells receive so many inputs?
- How do the two very different inputs to Purkinje cells interact?