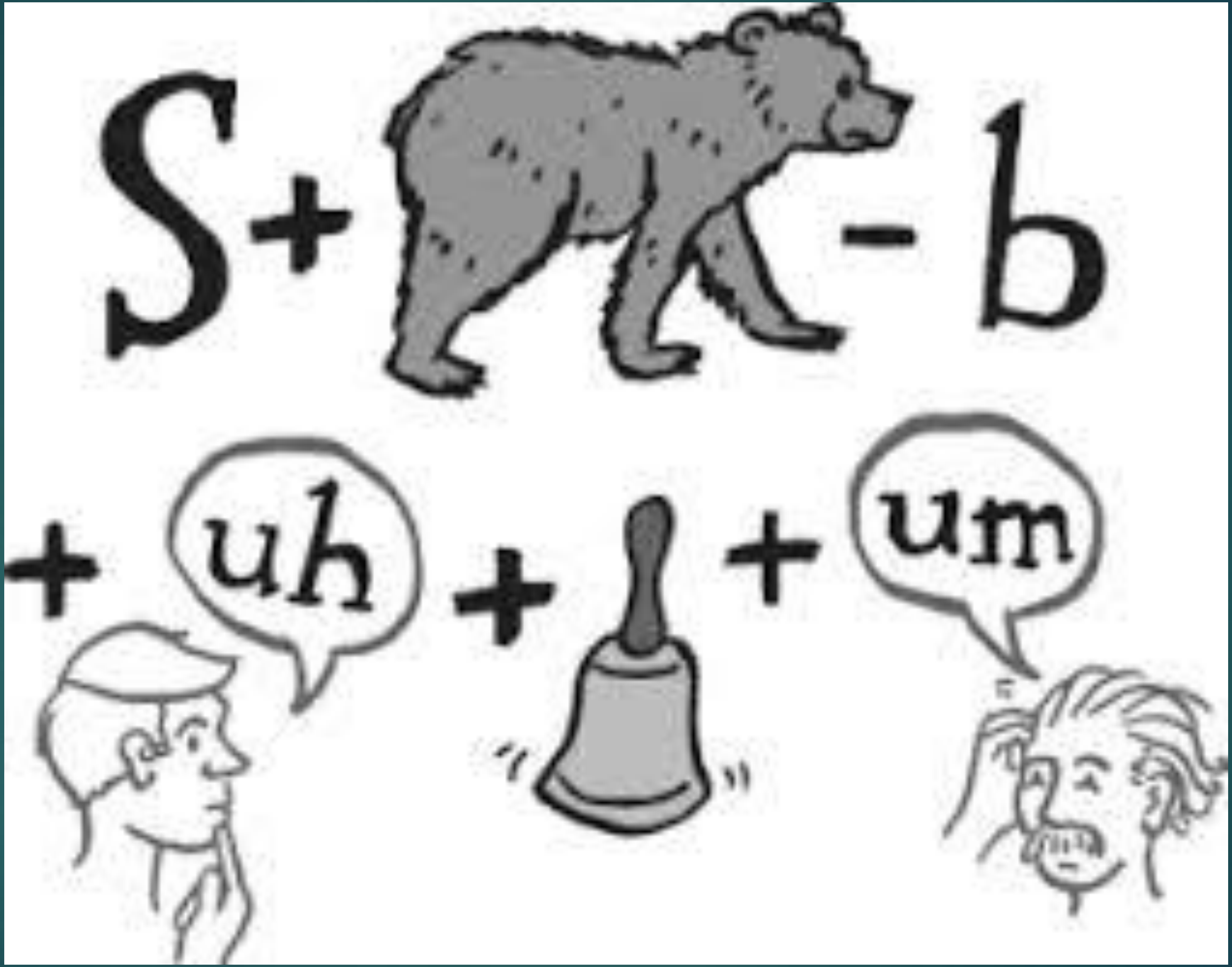
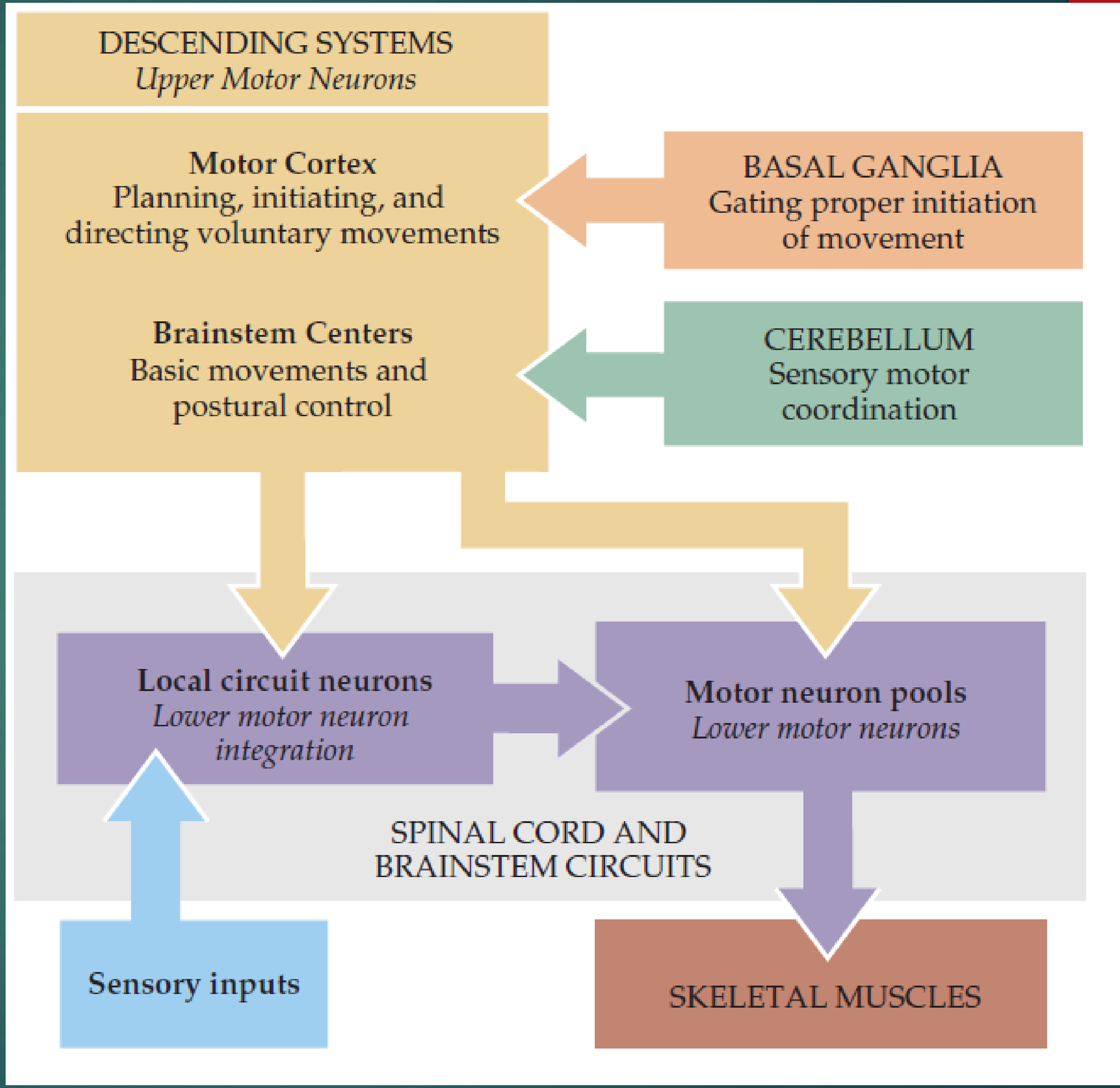


Sam Kean 2014

History of the Cerebellum

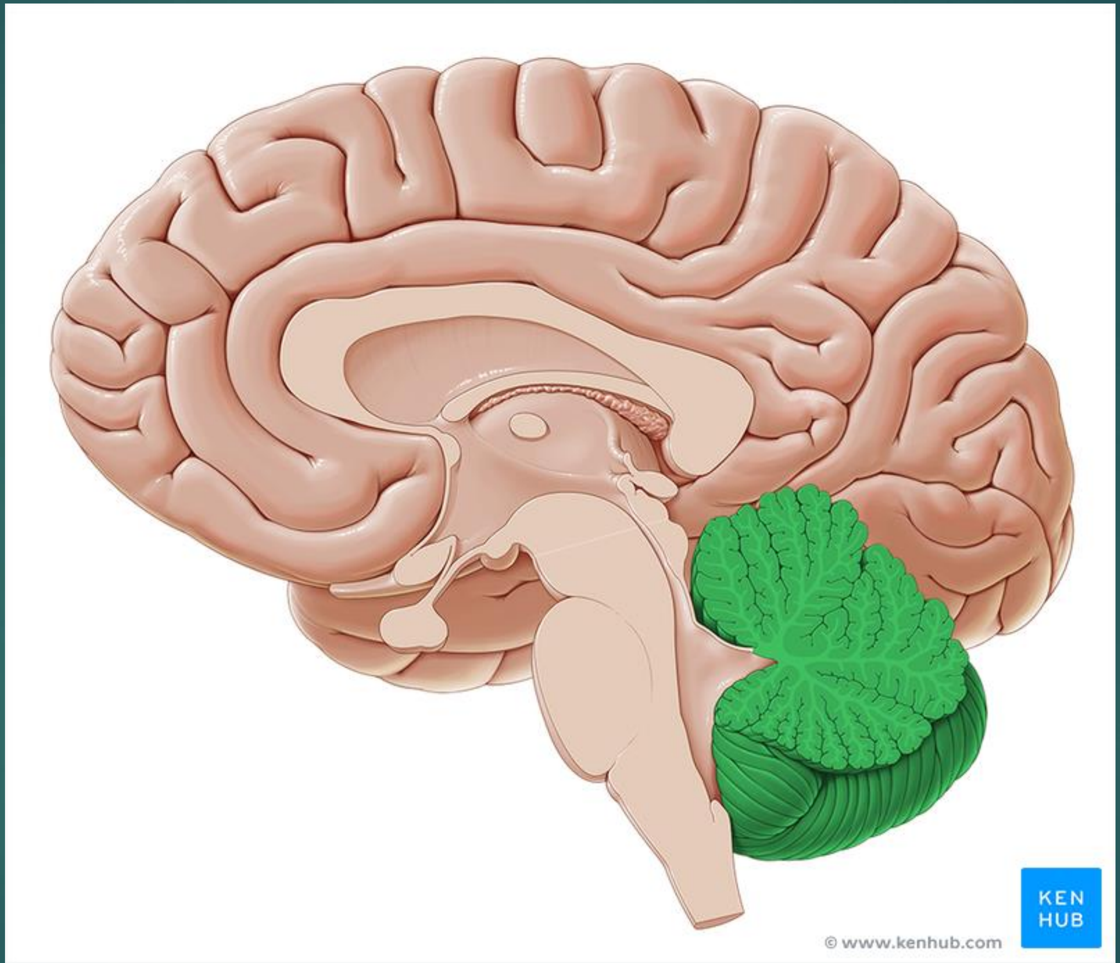
Dr. Angela Nietz

The cerebellum functions as a fast feedback loop allowing for fluid and coordinated movements



Purves 2004

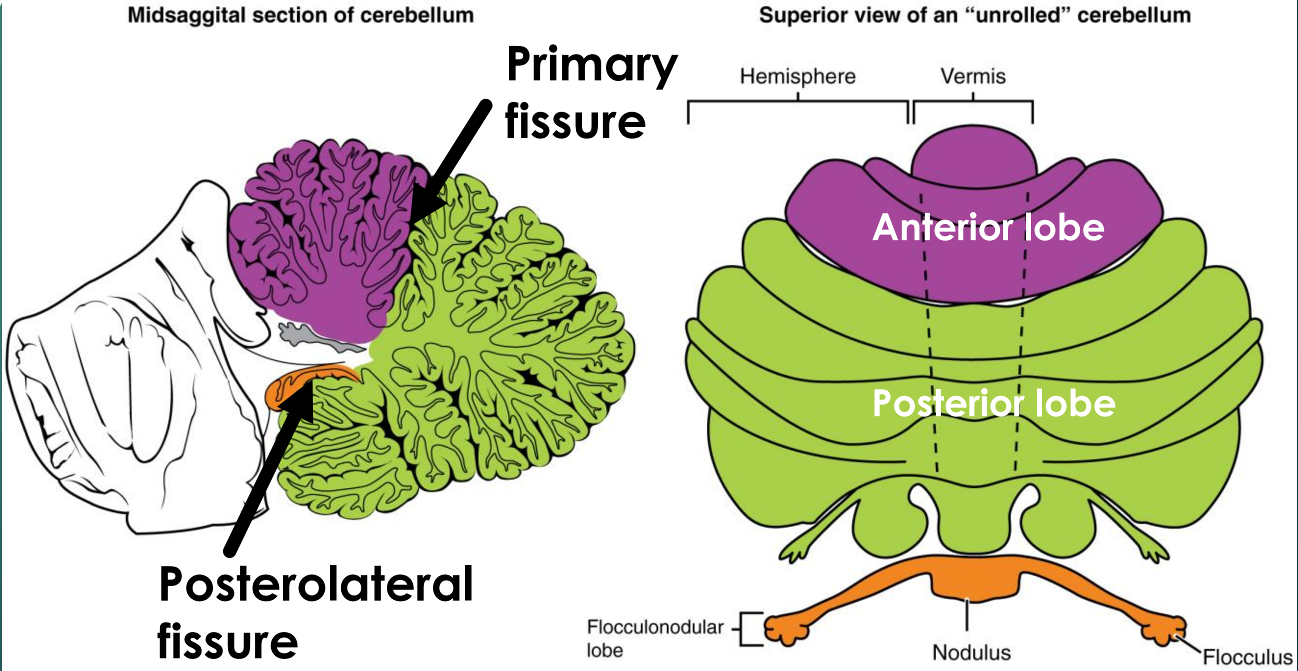
Gross Anatomy of the Cerebellum



Major lobes of the cerebellum (Bolk ,1906)

- Dutch anatomist - Recognized the cerebellar regions and named them in a way we still use today

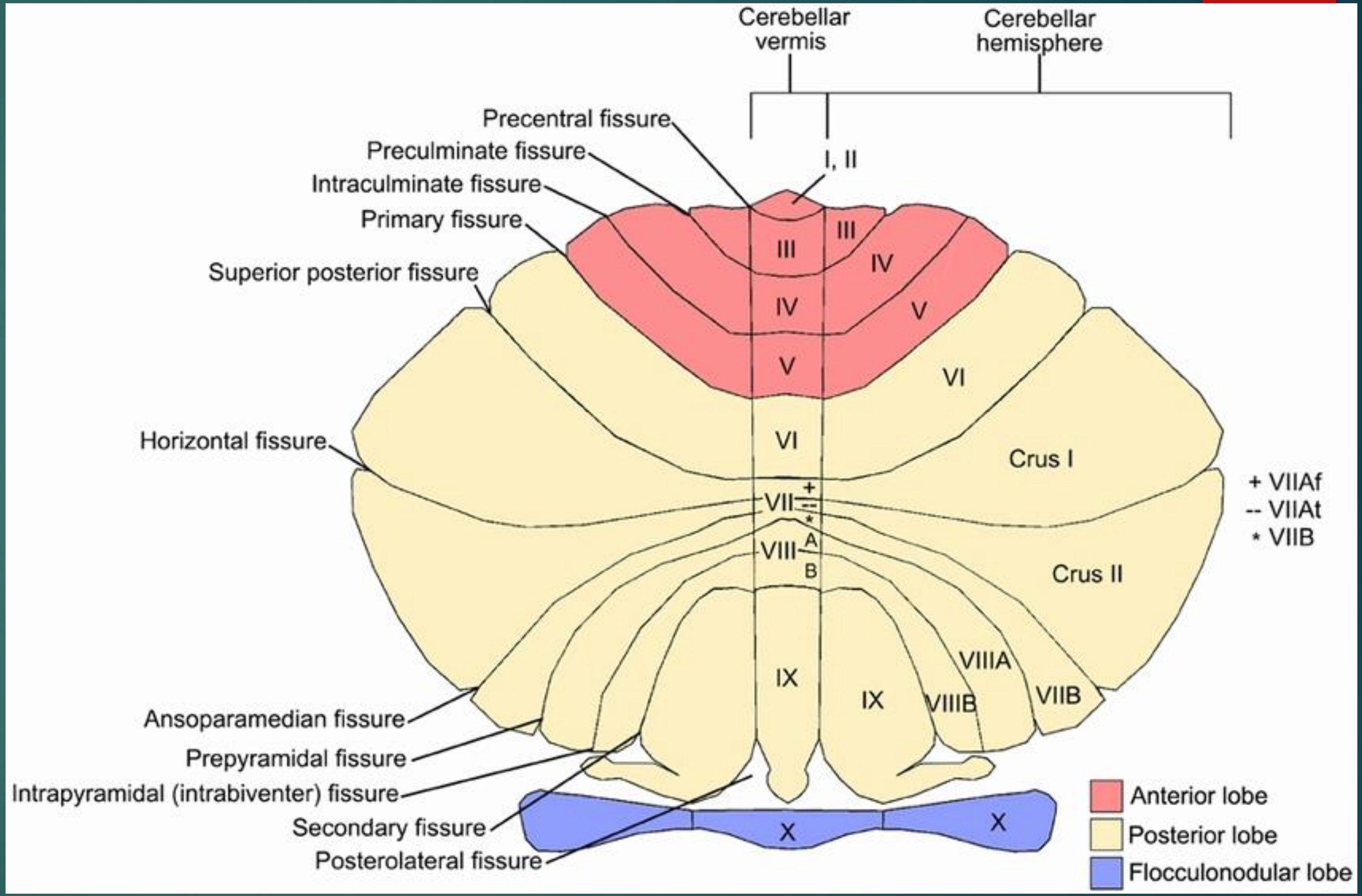
- There are 3 major lobes
  - Anterior lobe (above primary fissure)
  - Posterior lobe (below primary fissure)
  - Flocculonodular lobe
  (below posterolateral fissure)



https://www.memorangapp.com/flashcards/102836/N88%3A+Cerebellum+Structure+and+Function/

Subdivisions of the cerebellum

- Vincenzo Malacarne – first comprehensive description of the cerebellum (1776)
- Olof Larsell – Named cerebellar lobules using roman numerals (1934)
- Cerebellar lobules are also called folia
- We still use this naming system today
- There are 10 lobules total



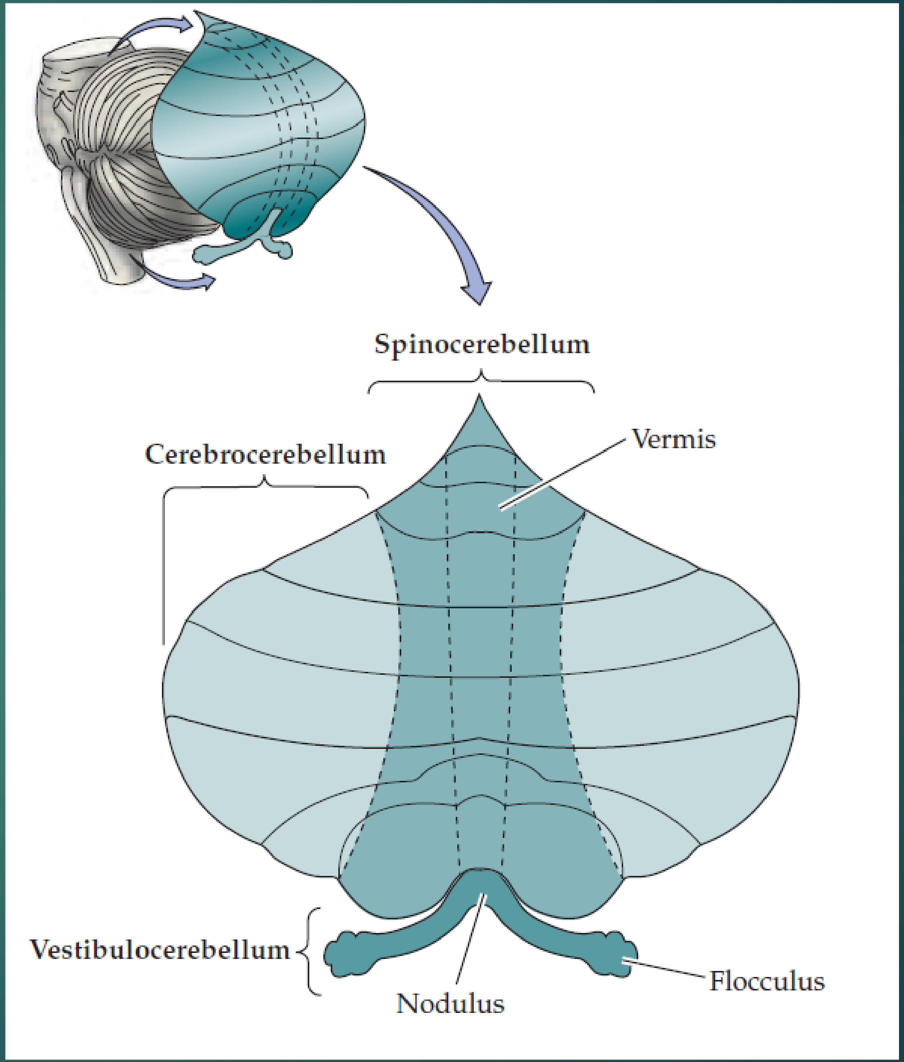
Manni and Petrosini 2004

Functional regions of the cerebellum

Cerebrocerebellum (lateral hemispheres) - coordination and planning of voluntary skilled movements

Spinocerebellum (vermis and intermediate parts of the hemispheres) – participates in motor control (walking), coordination and correction, posture

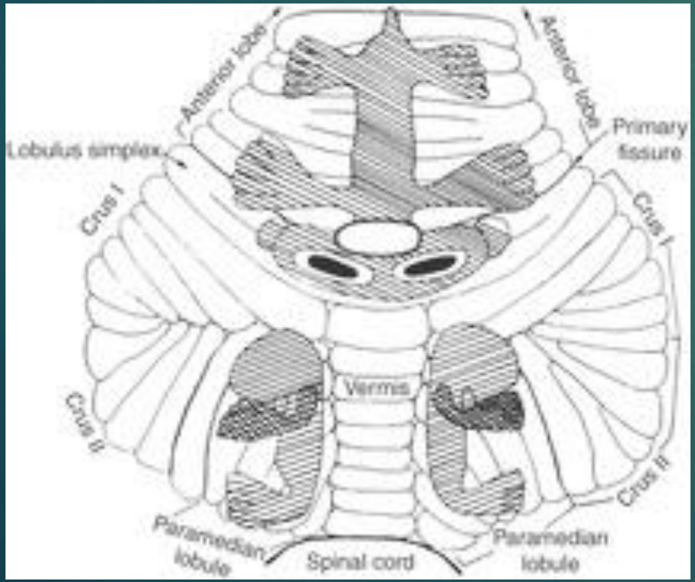
Vestibulocerebellum (flocculonodular lobe) – posture and balance maintenance and eye movements

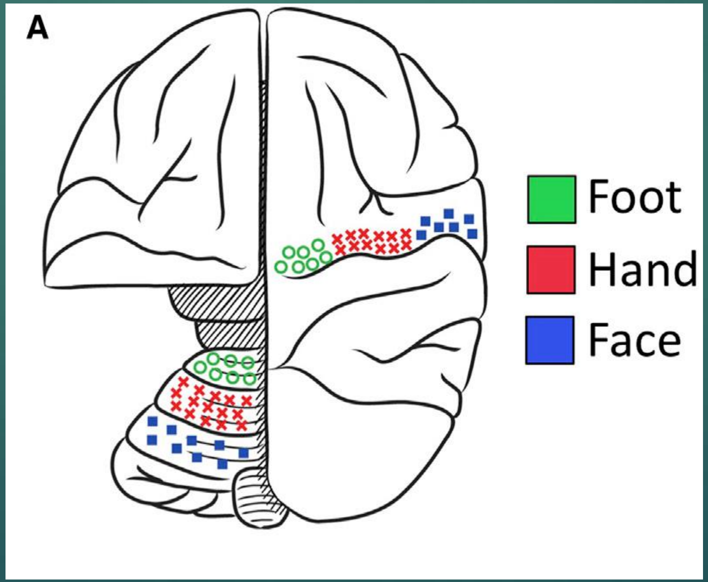


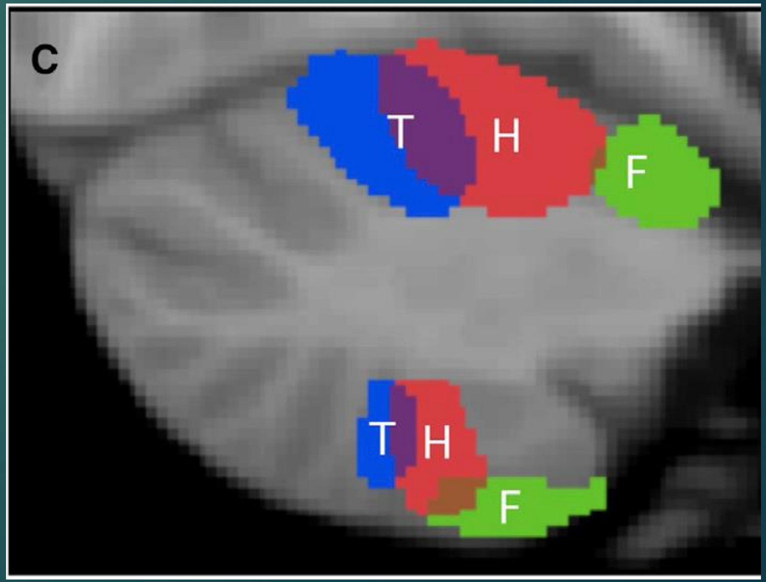
Purves 2004

Fractured somatotopy

- Two mirrored maps of the body
- First hypothesized by Bolk
- Revisited in the 1940’s when Edgare Adrian and Ray Snider recorded electrical activity in the brain of cats/monkeys while moving the limbs or providing sensation







Schmahmann 2012; Buckner 2013

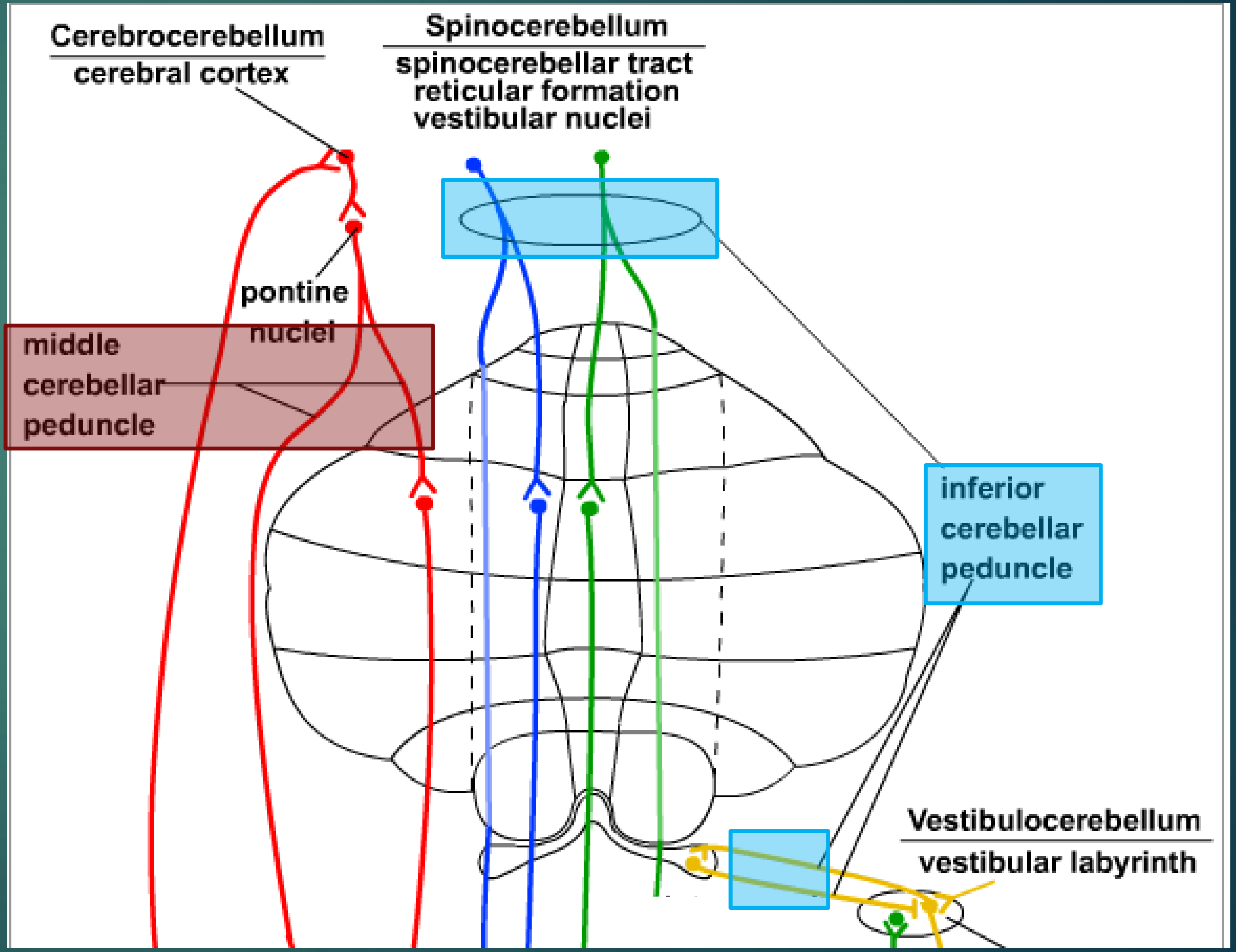
Cerebellar inputs (Jelgersma 1886-1932)

Inferior cerebellar peduncle

- Brings input from body via spinal cord, reticular formation, vestibular nuclei, and inferior olive
- Tells the cerebellum where the body is

Middle cerebellar peduncle

- Brings input from motor cortex to the pontine nuclei which is transmitted to cerebellum
- Tells the cerebellum where the body wants to be.

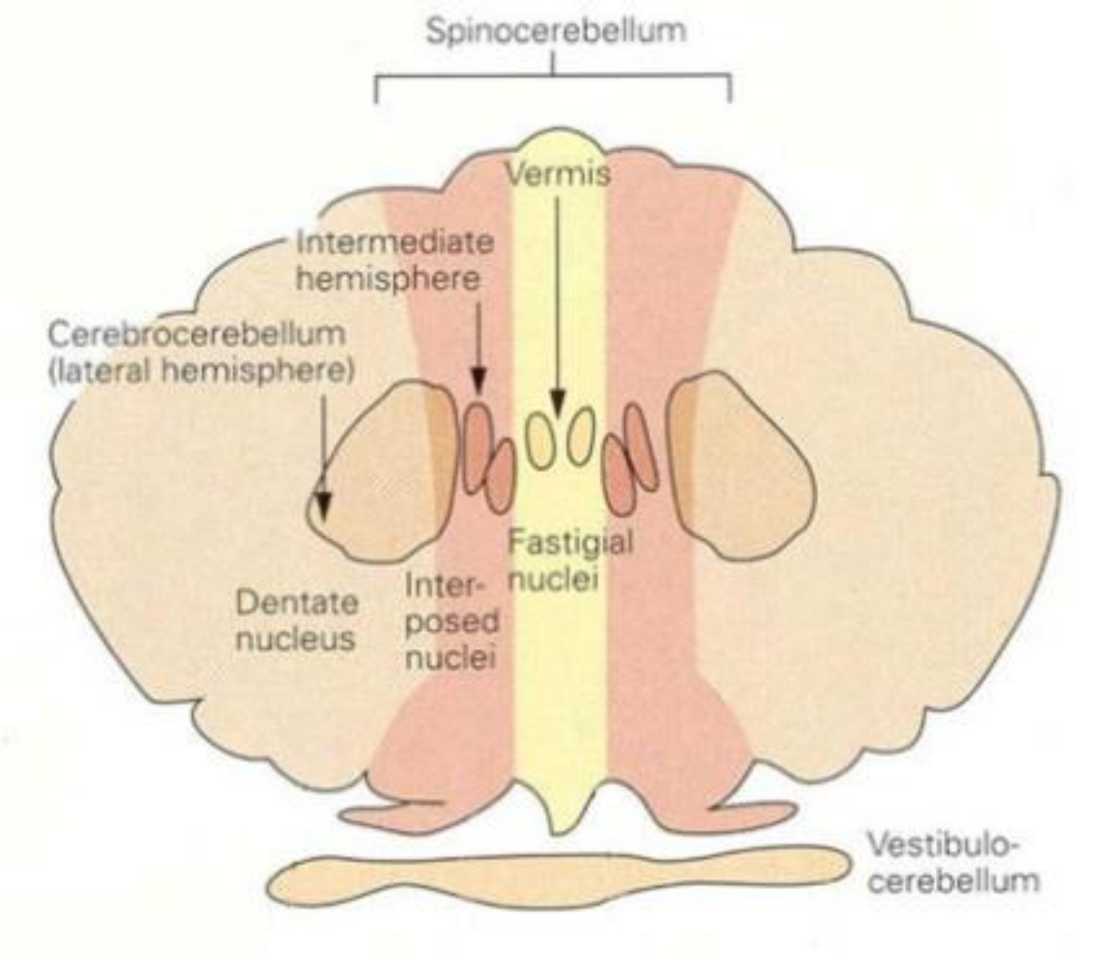


https://nba.uth.tmc.edu/neuroscience/s3/chapter05.html

Cerebellar output

- First described by Benedict Stilling (~1840)

- Four nuclei
  - Dentate (receives input from the cerebrocerebellum)
  - Globose & Eboliform (Interposed)nuclei (receive input from hemisphere near the vermis)
  - Fastigial (receives input from the vermis)



https://www.semanticscholar.org/paper/Back-42-The-Cerebellum-ClaudeGhezW.ThomasThach/5ed23b56eefbc821590ac81ba87c5102e57fa558/figure/5

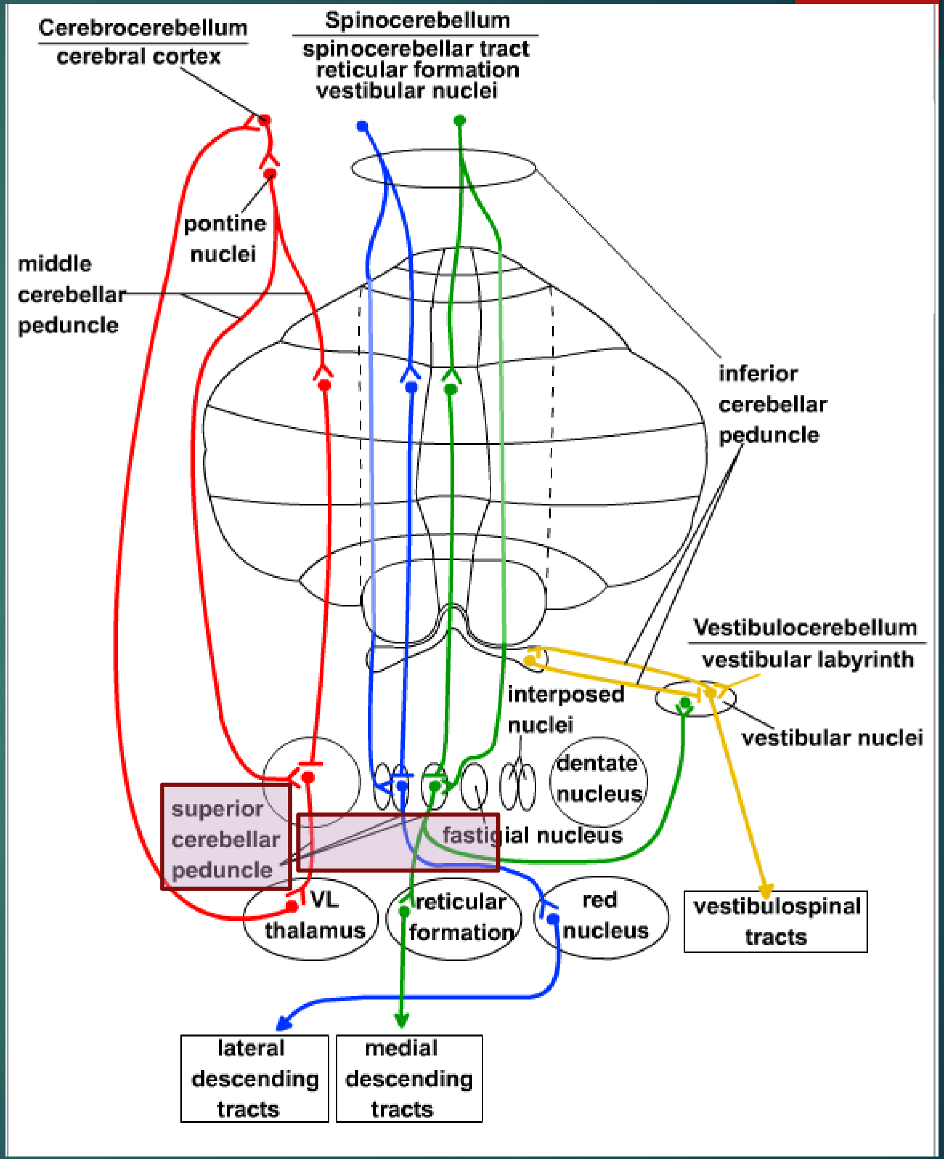
The cerebellar nuclei

- Sole output of the cerebellum
- Axons travel through the **superior cerebellar peduncle**

Dentate: outputs to **Ventral Lateral (VL)** nucleus of the thalamus and then to cortex

Globose/Eboliform: output to the **red nucleus** then to spinal cord and cranial nuclei

Fastigial: output to the vestibular nuclei and spinal cord

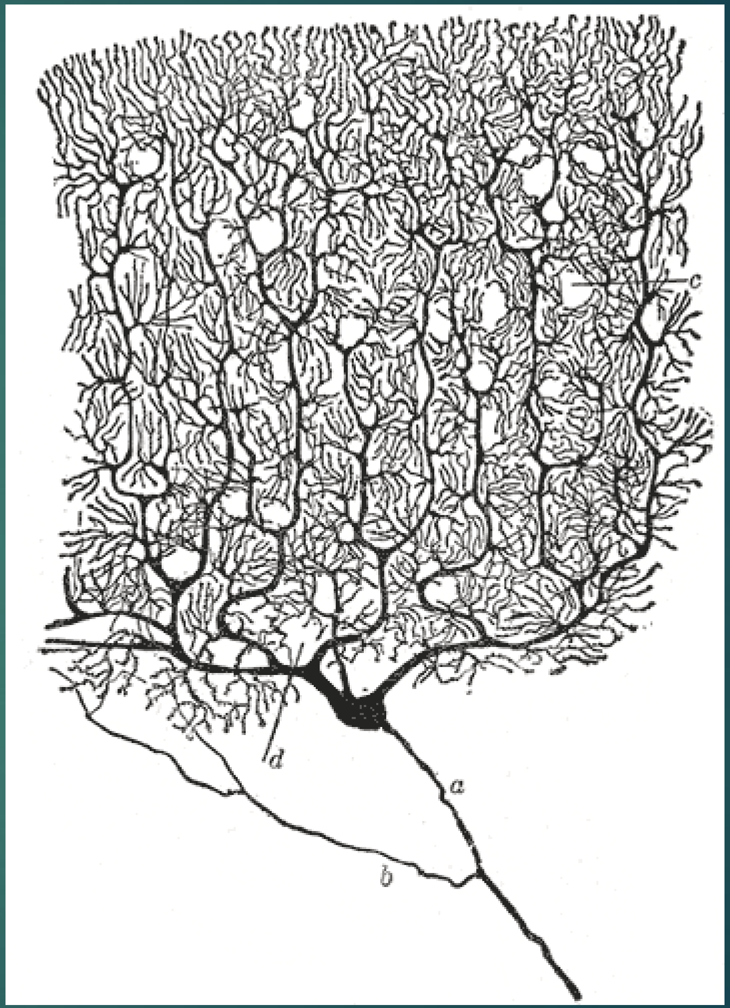


https://nba.uth.tmc.edu/neuroscience/s3/chapter05.html

Cerebellar microcircuitry

Purkinje cells are the principal neuron of the cerebellar cortex

- First described by Jan Evangelista Purkinje (1837)
- Cerebellar circuitry was further described by Santiago Ramon y Cajal (1894)



wikipedia

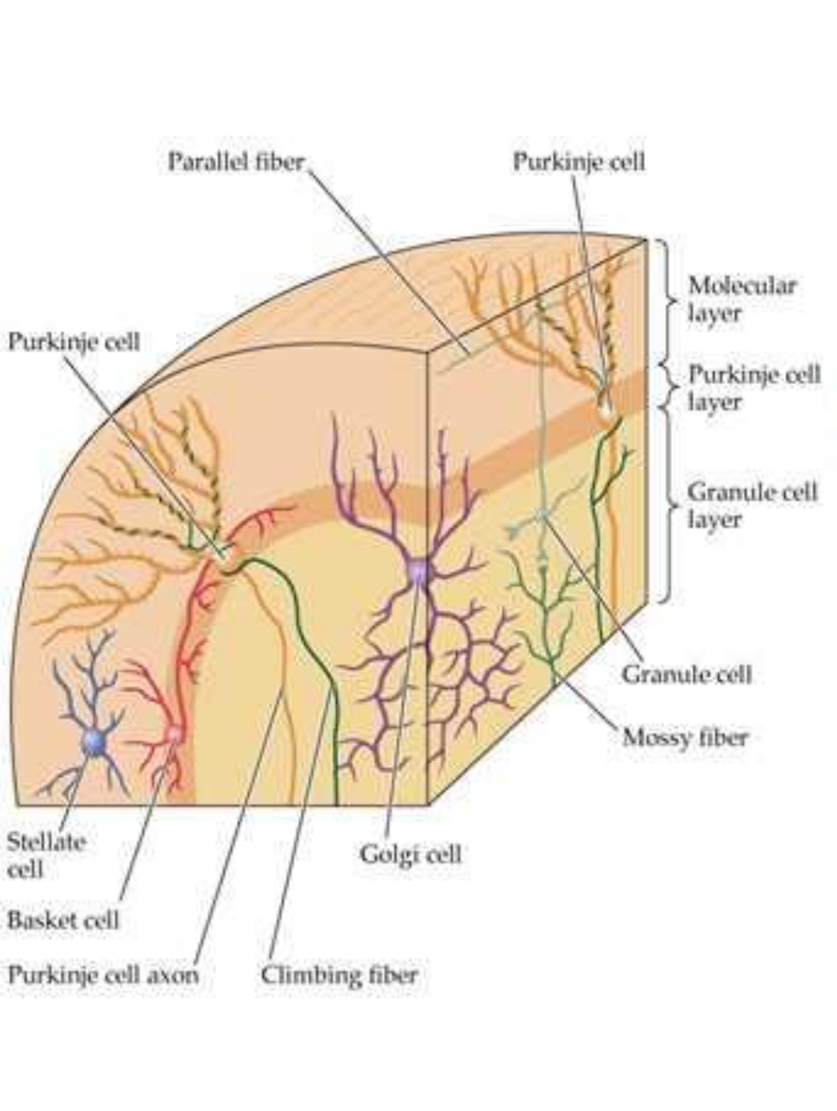
Cerebellar microcircuitry

Three major cell types:

- Purkinje cell
- Granule cell
- Molecular layer interneurons (basket & stellate cells)

Two major inputs:

- Mossy fibers
- Climbing fibers



Purves 2004

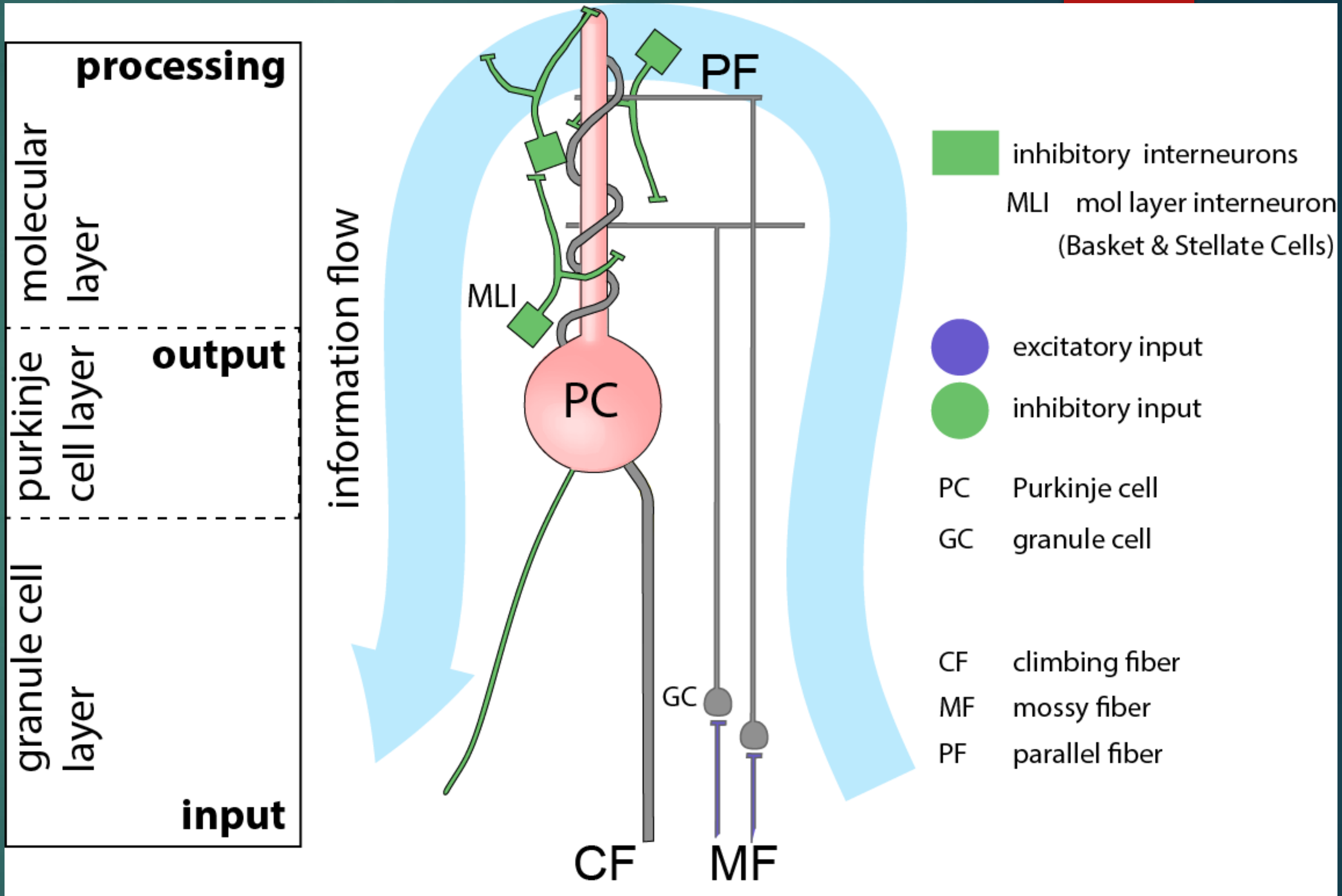
Cerebellar microcircuitry

Mossy fibers: axons of cells from cerebellar input pathways

Come through the pontine nuclei and various other regions through the middle and inferior cerebellar peduncles

Synapse with granule cells in the granule cell layer (input)

Give the cerebellum information about an outgoing motor command **(efference copy)** and the state of the body

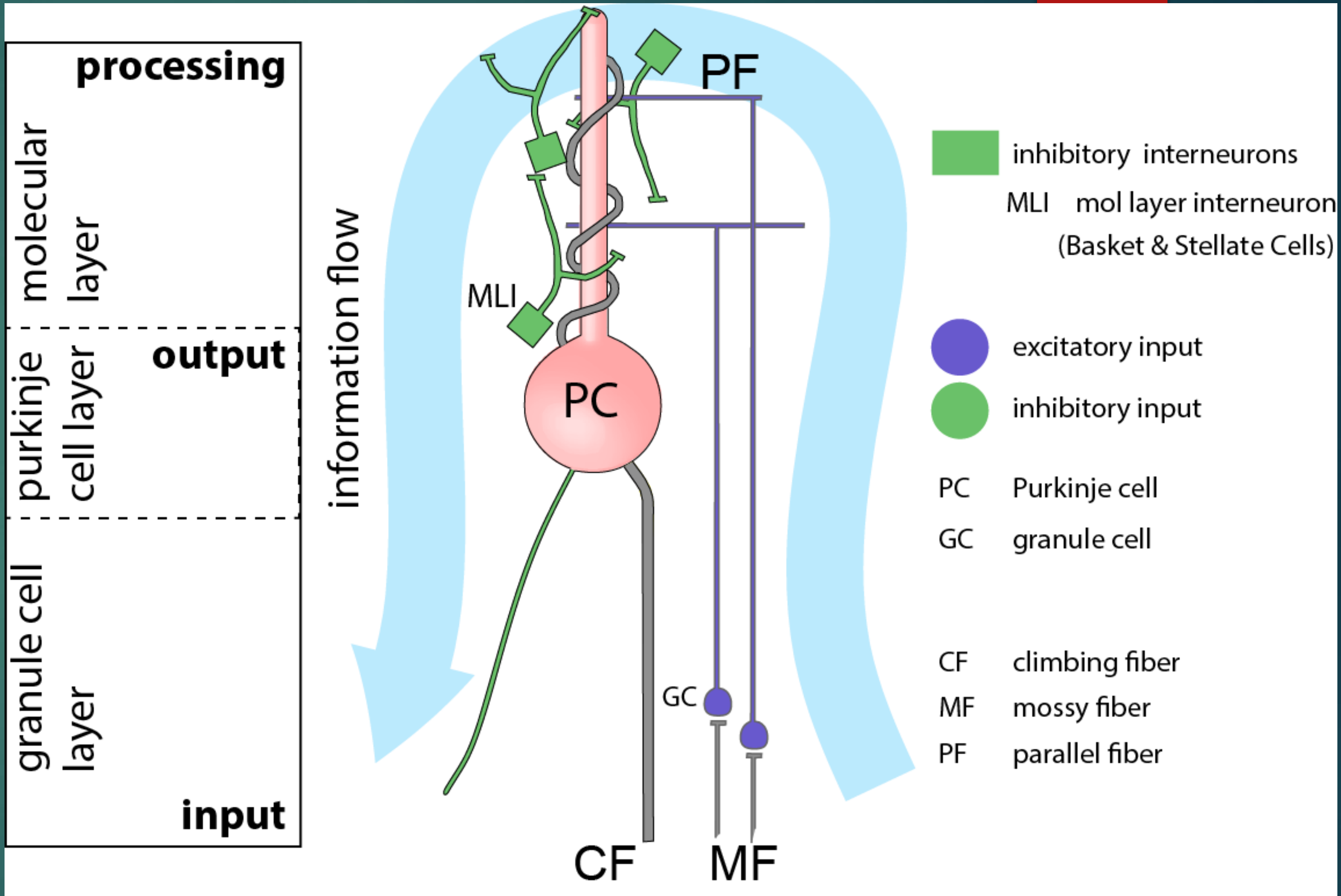


Cerebellar microcircuitry

Parallel fibers: the axons of granule cell ascend the cortex and branch like a telephone pole

Synapse with Purkinje cells

Transmit information from the mossy fibers to many Purkinje cells



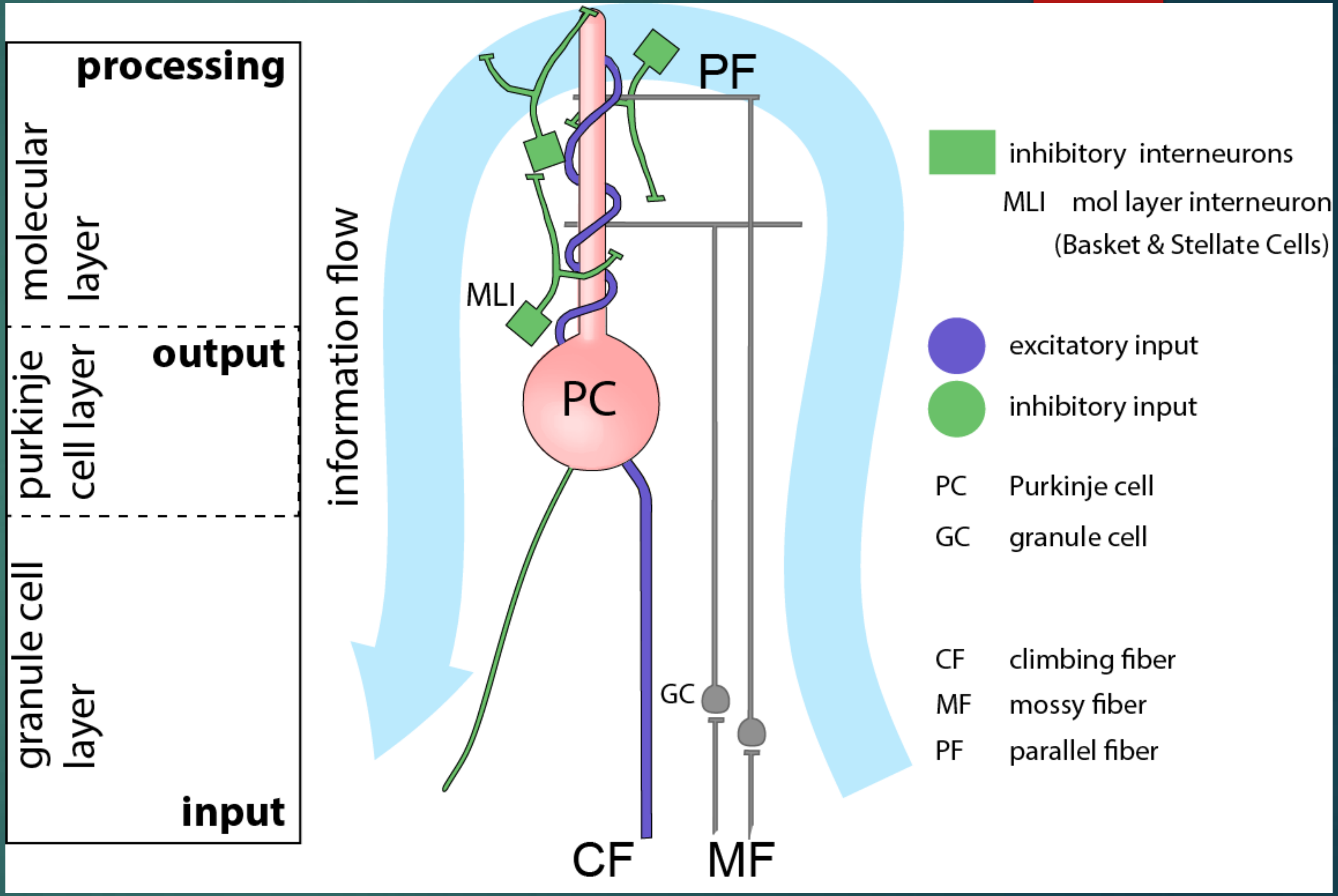
Cerebellar microcircuitry

Climbing fibers: the axons of cells in the **inferior olivary nucleus**

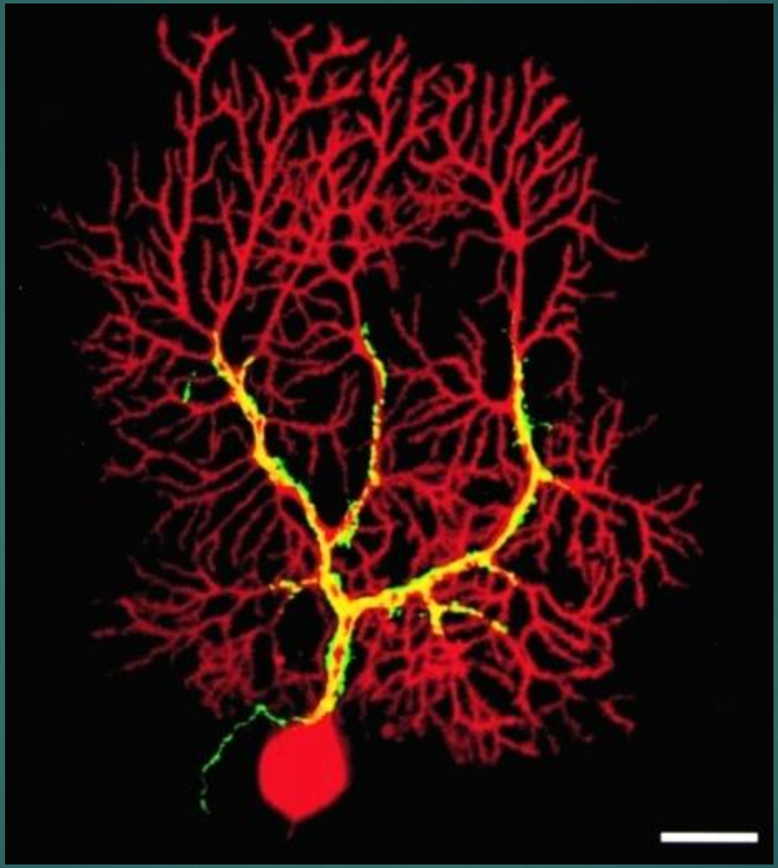
Ascend to the cortex through the inferior cerebellar peduncle

Make strong one to one synapses with Purkinje cells by climbing their dendrites

Convey errors in body movement



Cerebellar microcircuitry



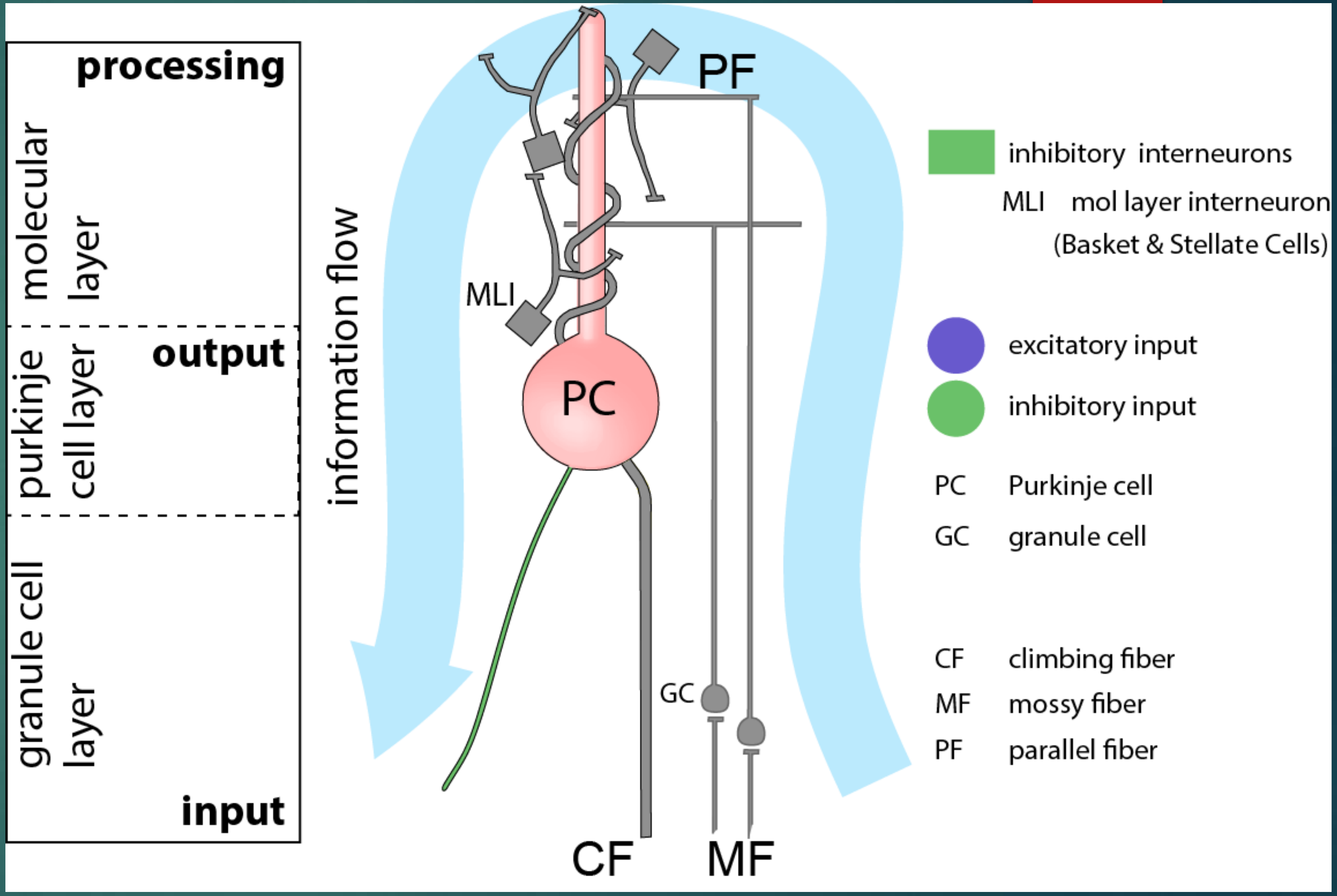
Kreitzer et al., 2000

Cerebellar microcircuitry

Purkinje cells: The sole output neuron of the cerebellar cortex

Process information about the body (compare the state of the body in reality to the desired state)

Send their axons to **inhibit** the deep cerebellar nuclei

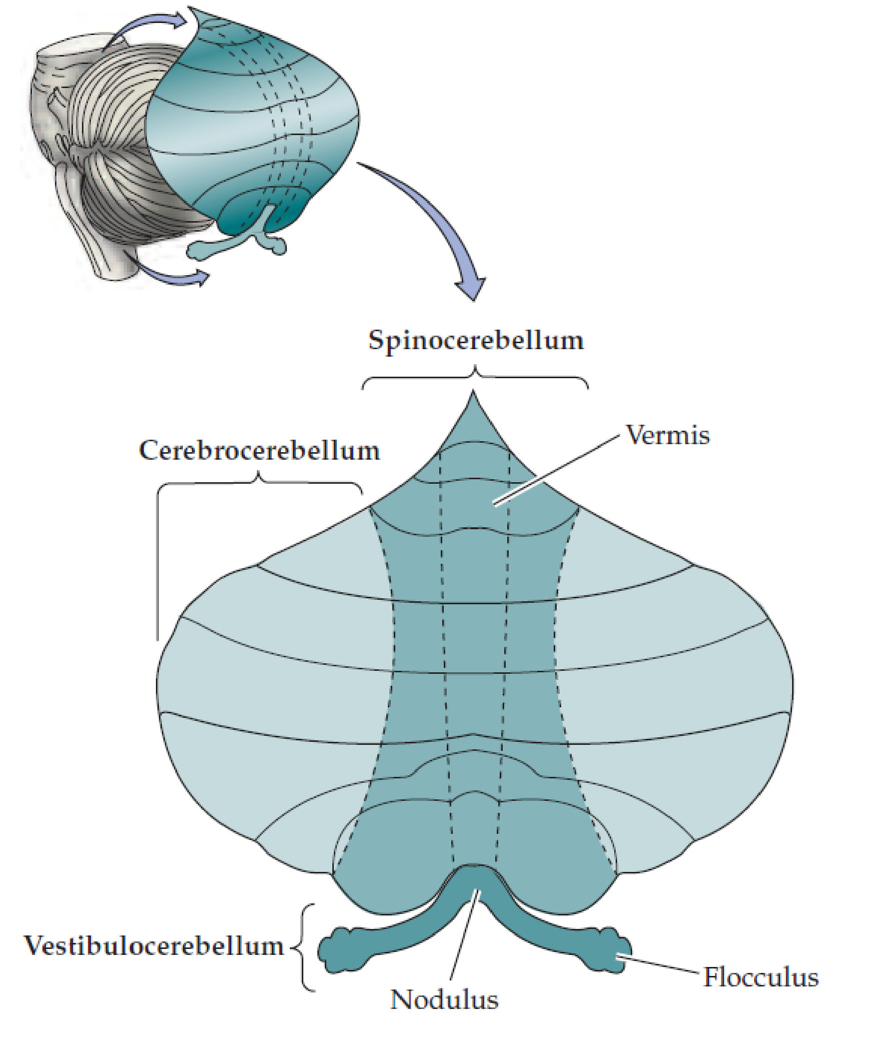


Functions of the cerebellum

Cerebrocerebellum – movement planning and motor learning

Spinocerebellum – movement coordination and correction, postural maintenance

Vestibulocerebellum – balance, eye movements (especially when the head moves)



Purves 2004

How did scientists figure this out?

Ans: They broke it and observed what happened

Luigi Rolando: first to suggest the cerebellum was critical for motor control by lesioning the cerebellum (1809)

Pierre Fluorens & Luigi Luciani: Figured out animals weren't paralyzed after destruction of the cerebellum; first to suggest the cerebellum was important for *coordinating* movement

Joseph Babinski & Gordon Holms (early 1900s): Observed uncoordinated and disjointed movements and unsteady gait/posture in patients with cerebellar damage; realized the deficits were on the same side of the body as the lesion

When things go wrong

Cerebellar Ataxia: uncoordinated movement , unsteady gait, difficulty with fine motor tasks

Caused by damage to the cerebellum (e.g stroke, head trauma, cerebral palsy)

Essential Tremor: shaking (tremor) of the hands, arms, head during voluntary movement

Appears to involve changes in cerebellar activity

https://pedclerk.uchicago.edu/page/ataxia

The laughing death

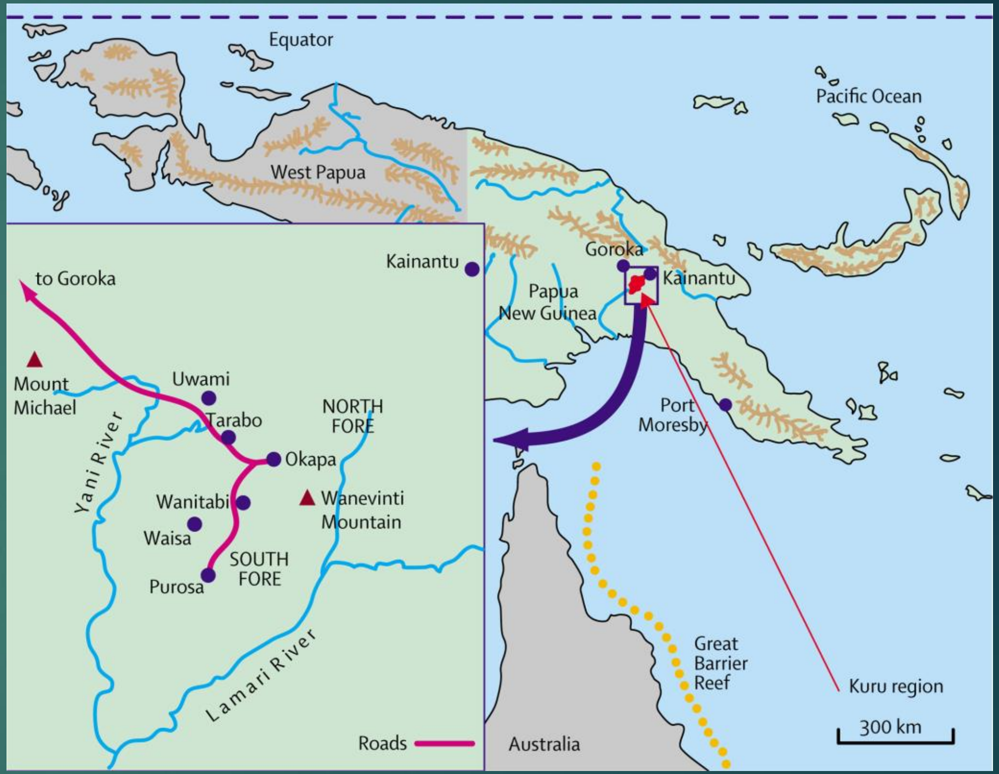
Kuru: the “shaking” disease (also called the laughing death due to suffers being prone to outbursts of laughter at the end of the disease)

Endemic to the Fore tribe of Papua New Guinea

First noted by Australians exploring Papua New Guinea in the 1950s

8-9 times higher prevalence in the kuru people than surrounding regions

Women and children disproportionately affected



The laughing death

Early Symptoms:

- Unsteady stance and gait
- Difficulty controlling muscles
- Uncoordinated movement
- Tremors
- Difficulty speaking

Late Symptoms:

- Severe tremor
- Near complete loss of motor control
- Difficulty swallowing
- Fits of laughter
- Eventual death due to secondary infections

Incubation period: 10 -13 years

Wikipedia

The cause of kuru

The Fore thought it was likely witchcraft

The Australian explorers thought it was psychosomatic

Michael Alpers thought to was due to funerary cannibalism practices

The Fore people often cooked and ate their dead to return their life force to the family

Women and children typically dined on the organs and brain, while men dined in muscles

Australian law banned cannibalism in its colonies which led to a decline in kuru in the region

The cause of kuru

1960’s: Daniel Carleton Gajdusek, a virologist, along with Michael Alpers begin the first experiments on kuru at NIH

Injected chimps with brain material from a deceased kuru victim

First to prove that kuru was transmissible by an infectious agent

Also showed it could cross the species barrier

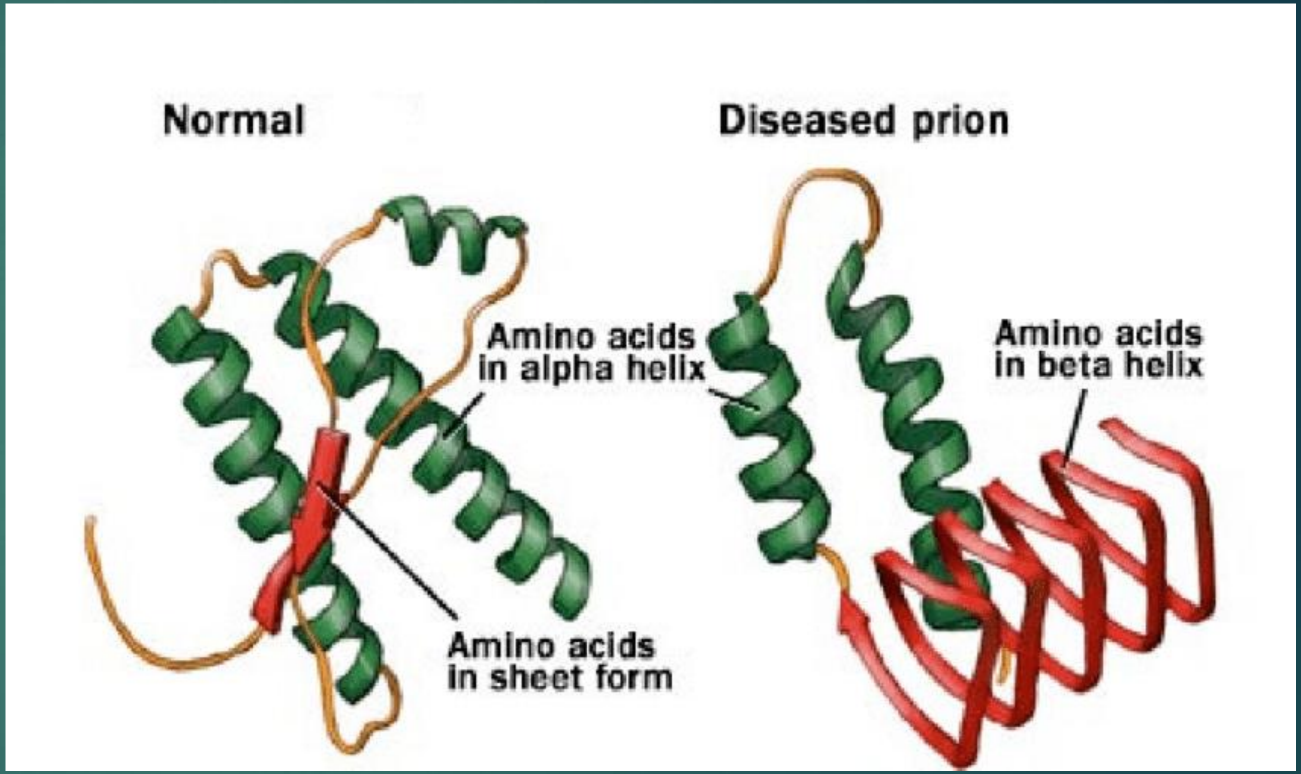
Won the Nobel prize for physiology or medicine in 1976

Today this disease is classified as one of the spongiform encephalopathies similar to scrapie, mad cow, and Creutzfeldt–Jakob disease

The cause of kuru

We now know this disease is caused by a prion, a misfolded protein that induces normal copies of the protein to misfold and leads to cell death

This was shown by Stanley Prusiner and his lab who won the Nobel Prize for physiology or medicine in 1997



Paudyal and Gillock 2017

What to know

The major anatomical regions of the cerebellum and fissures that separate them

The functional divisions of the cerebellum and what processes each are involved in

The major difference in the cerebellum’s somatotopic map and the map in the motor cortex

The major input pathways to the cerebellum (generally)

The function of the cerebellar nuclei and where they project to (thalamus, back to cortex, vestibular nuclei)

The major cellular inputs to the cerebellar cortex and Purkinje cells

Major functions of the cerebellum

Symptoms of cerebellar dysfunction

Major causes of kuru