بسم الله الرحمن الرحيم

Cerebellar Motor Function (Pt.2)

MID | Lecture 3

﴿ إِنِّي تَوَكَّلْتُ عَلَى اللَّهِ رَبِّي وَرَبِّكُمْ ۚ مَا مِنْ دَابَّةٍ إِلَّا هُوَ آخِذٌ بِنَاصِيَتِهَا ۚ إِنَّ رَبِّي عَلَىٰ صِرَاطٍ مُسْتَقِيمٍ ﴾

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Reviewed by: Omar Ibrahim

PHYSIOLOGY

رحلة اليقين مع سورة يس

بِسۡمِ ٱللَّهِ ٱلرَّحۡمَٰنِ ٱلرَّحِيمِ

وَنُفِخَ فِي ٱلصُّورِ فَإِذَا هُم مِّنَ ٱلۡأَجۡدَاثِ إِلَىٰ رَبِّهِمۡ يَنسِلُونَ ﴿٥١﴾ قَالُواْ يَٰوَيۡلَنَا مَنۢ بَعَثَنَا مِن مَّرۡقَدِنَاۜۗ هَٰذَا مَا وَعَدَ ٱلرَّحۡمَٰنُ وَصَدَقَ ٱلۡمُرۡسَلُونَ ﴿٥٢﴾

النفخة الأولى، هي نفخة الفزع والموت، وهذه نفخة البعث والنشور، فإذا نفخ في الصور، خرجوا من الأجداث والقبور، ينسلون إلى ربهم، أي: يسرعون للحضور بين يديه، لا يتمكنون من التأنِّي والتأخر، وفي تلك الحال، يحزن المكذبون، ويظهرون الحسرة والندم.

ويقولون: {يَا وَيْلَنَا مَنْ بَعَثَنَا مِنْ مَرْقَدِنَا} أي: من رقدتنا في القبور، لأنه ورد في بعض الأحاديث، أن لأهل القبور رقدة قبيل النفخ في الصور، فيجابون، فيقال لهم: {هَذَا مَا وَعَدَ الرَّحْمَنُ وَصَدَقَ الْمُرْسَلُونَ} أي: هذا الذي وعدكم الله به، ووعدتكم به الرسل، فظهر صدقهم رَأْيَ عين.ولا تحسب أن ذكر الرحمن في هذا الموضع، لمجرد الخبر عن وعده، وإنما ذلك للإخبار بأنه في ذلك اليوم العظيم، سيرون من رحمته ما لا يخطر على الظنون، ولا حسب به الحاسبون، كقوله: {الْمُلْكُ يَوْمَئِذٍ الْحَقُّ لِلرَّحْمَنِ} {وَخَشَعَتِ الْأَصْوَاتُ لِلرَّحْمَنِ} ونحو ذلك، مما يذكر اسمه الرحمن، في هذا.

Note that some Concepts and information were rearranged compared to the original lecture in order to enhance clarity and scientific flow.

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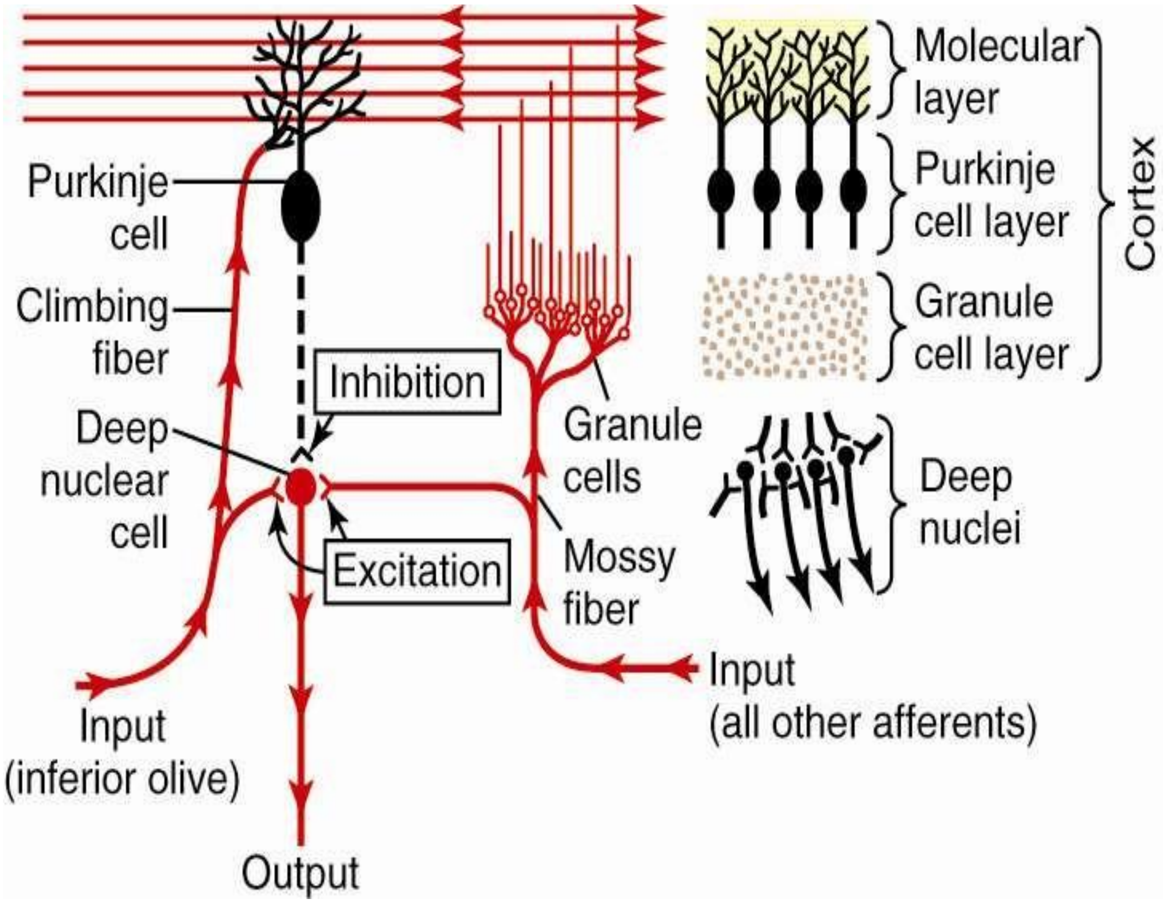
Organization of the Cerebellum

- ➢ During any voluntary action, muscles require:
- An initial **effective contraction**
- Followed by **controlled inhibition to dampen excessive movement**

- ➢ The cerebellum produces this **fine excitatory-inhibitory sequencing**, preventing tremor, overshoot, and incoordination.

- ➢ The **Functional Unit of the Cerebellum**: The cerebellum consists of **many repeating functional microcircuits**, each acting as a **movement-refining unit**. Each unit integrates incoming sensory-motor signals, processes them in the cerebellar cortex, and sends a precisely timed output through the deep cerebellar nuclei. (To be discussed thoroughly in the next slides)



Cerebellum Functional Unit

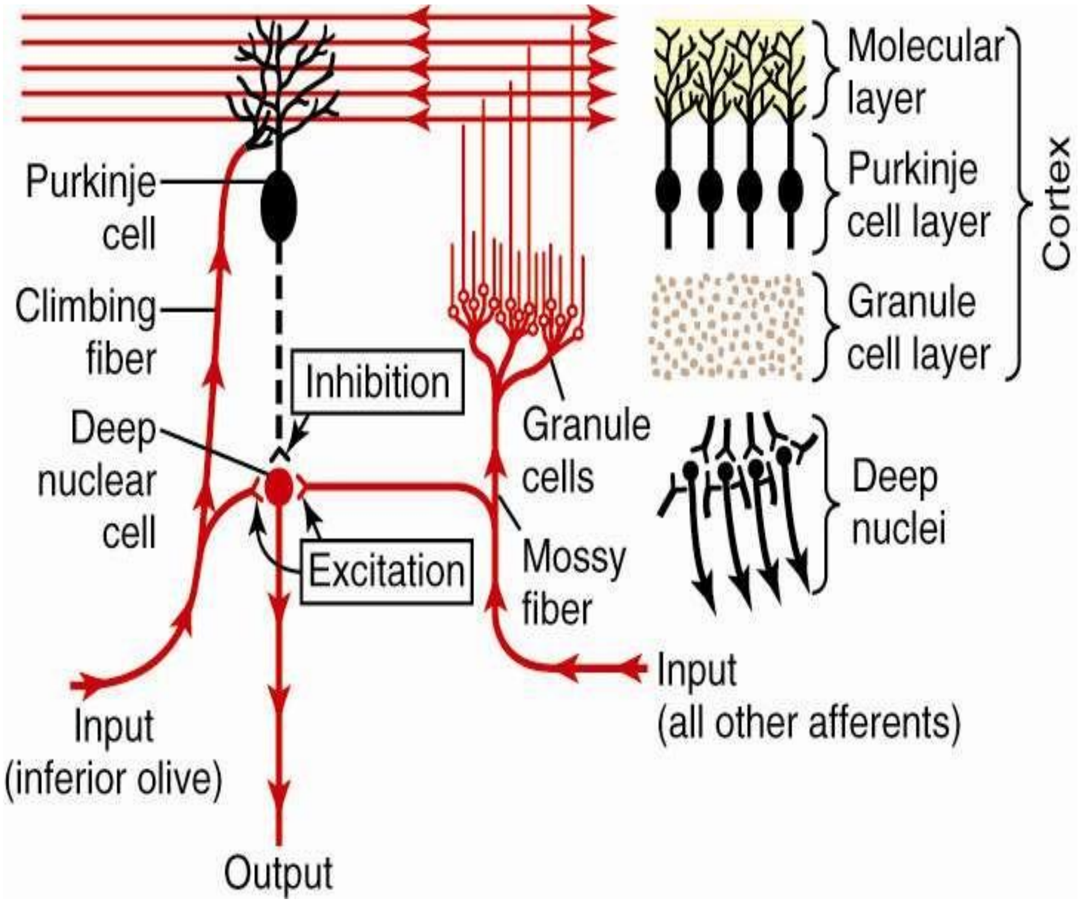
➢ Components of the Cerebellar Functional Unit:

1. **Afferent excitatory inputs (Excitatory Cells):**
- **Climbing fibers (From the Inferior Olivary Nucleus only)**
- **Mossy fibers (From the Cerebral Cortex, Reticular Formation and the Vestibular Nuclei)**

2. **Cortical neurons (found in the Cerebellar Cortex)**
- **Purkinje cells** (large **inhibitory neurons**)
- **Granule cells** (**Interneurons** that connect between the **Mossy cells** and the **Purkinjes**)

3. **Intracortical processes**
- **Parallel fibers** (axons of granule cells)

4. **Output structures**
- **Deep cerebellar nuclei neurons** (Ex: dentate, interposed, fastigial nuclei)



Cerebellum Functional Unit

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What actually happens inside one cerebellar functional unit?

➢ **Direct excitatory input to the deep cerebellar nuclei**

Before reaching the cortex, both:

- **mossy fibers**
- **climbing fibers**

Synapse **directly on neurons of the deep cerebellar nuclei,** producing an **initial excitatory discharge** from the deep nuclei, which facilitates **the beginning of muscle contraction.**

➢ **Indirect cortical pathway causing delayed inhibition**

At the same time, the same afferent fibers ascend to the cerebellar cortex **to stimulate the Purkinje cells:**

- Mossy Cells: activate **granule cells** → **parallel fibers** → **Purkinje cells**
- Climbing Cells: directly activate **Purkinje cells**

➢ **After cortical processing (Stimulation of the Purkinje Cells):**

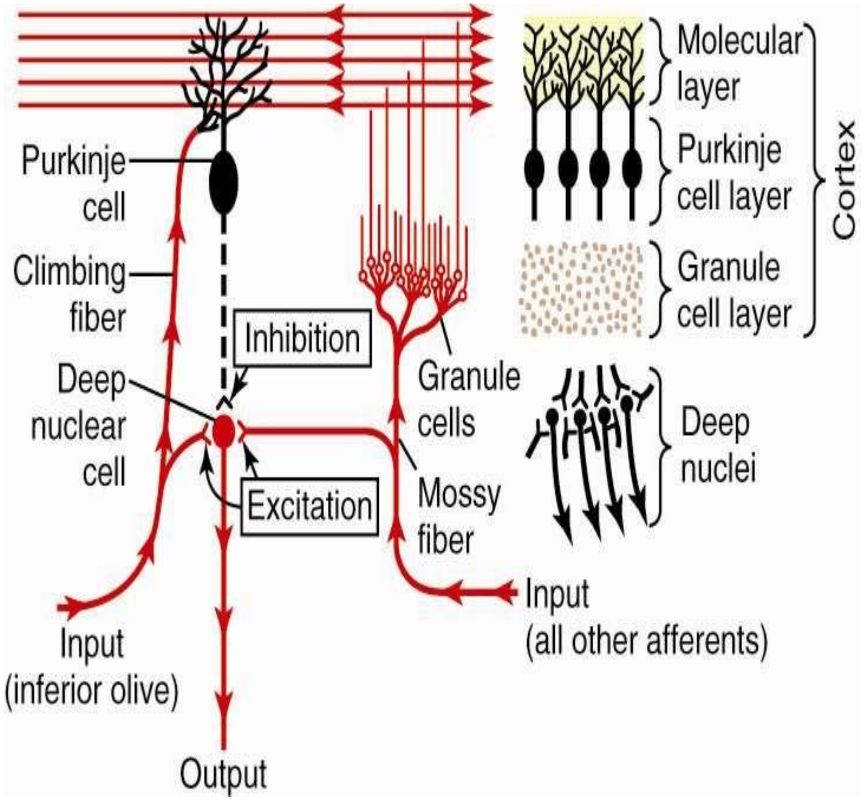
Purkinje cells send inhibitory signals to the deep nuclei.

This inhibition arrives **slightly later**, because cortical processing takes time.

➢ This produces:

- initial **facilitation of muscle contraction**
- then **damping and fine adjustment of movement**

preventing **overshoot, tremor,** and **uncoordinated motion.**



Cerebellum Functional Unit

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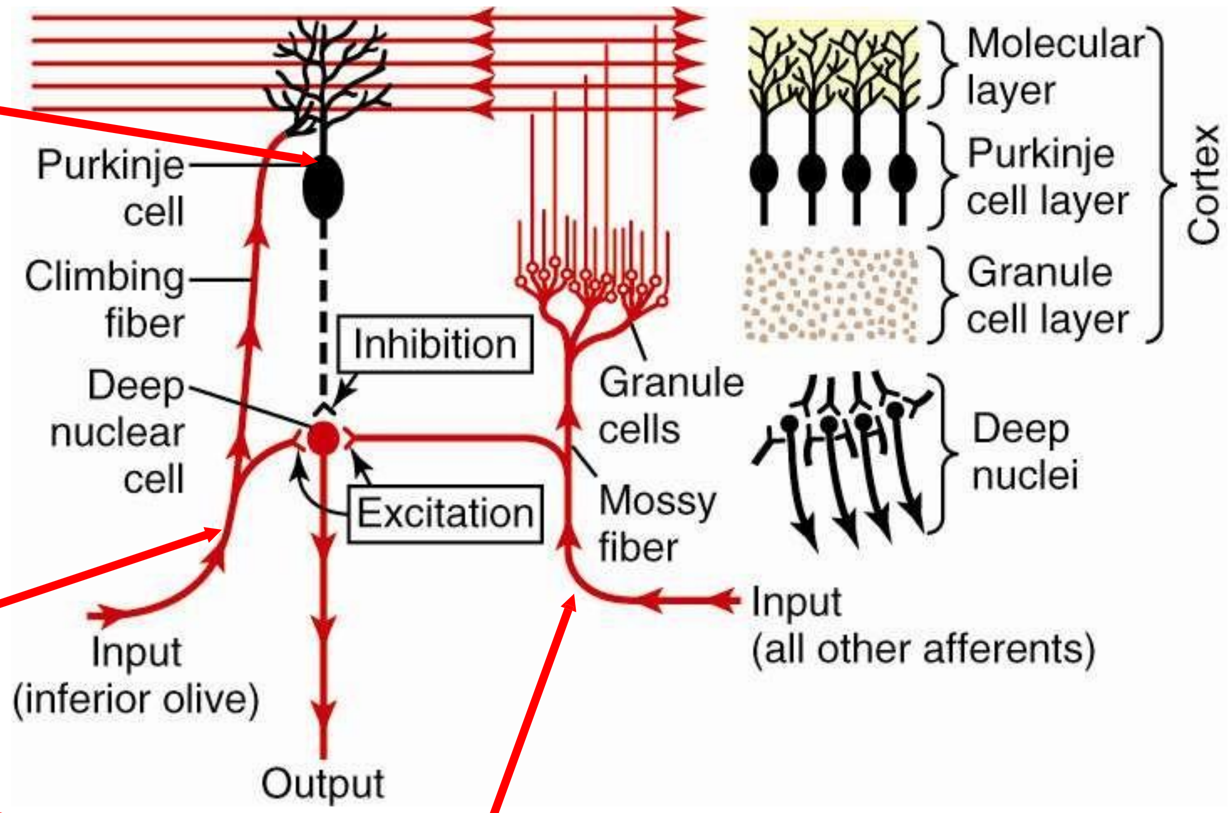
Neuronal Circuit of the Cerebellum

Deep nuclear cells receive excitatory and inhibitory inputs

Inhibitory from
Purkinje cells



Excitatory afferent
inputs from climbing
fibers and mossy fibers

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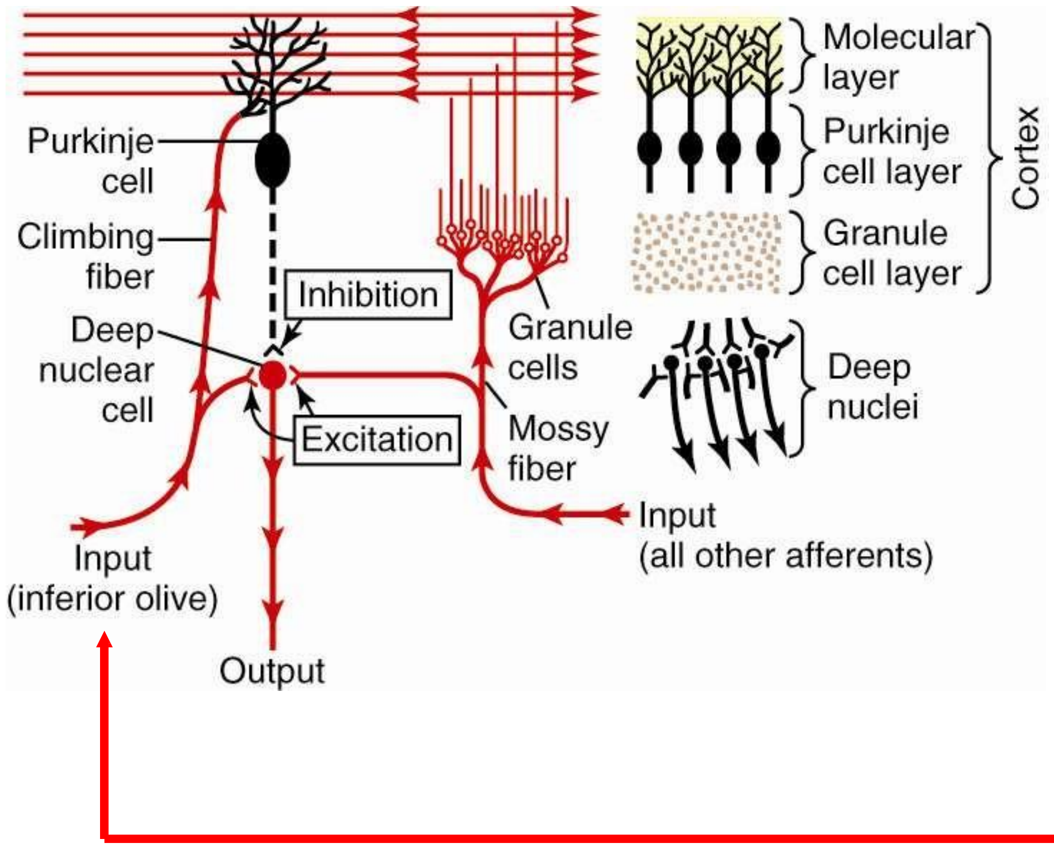
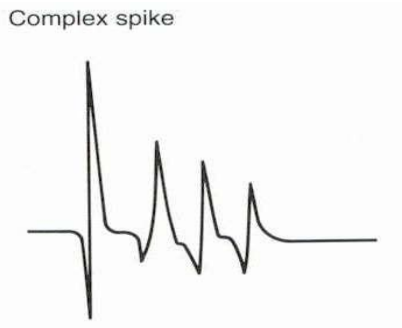
Neuronal Circuit of the Cerebellum



climbing fibers send branches to the deep nuclear cells before they make extensive connections with the dendrites of the Purkinje cell. Causes **complex spike** output from Purkinje cell. Multiple spikes in rapid succession ,these complex spikes are crucial for learning as they pair an initial excitation with the ability to adjust behavior based on previous input . *(To be discussed soon)*



all **climbing fibers** originate from the inferior olive

Mossy fibers vs Climbing fibers

- **After stimulating the deep cerebellar nuclei, mossy fibers** terminate in the **granular layer**, where they stimulate **granule cells** → **parallel fibers** → **Purkinje cells.**

- Because this stimulation is **indirect and brief**, it produces **single, short-duration spikes** in Purkinje cells **called simple spikes**.

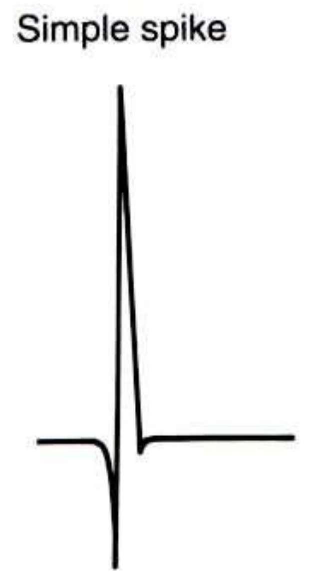
- These signals represent the **ongoing background motor information** in order to **help cerebellum continuously adjust movement.**

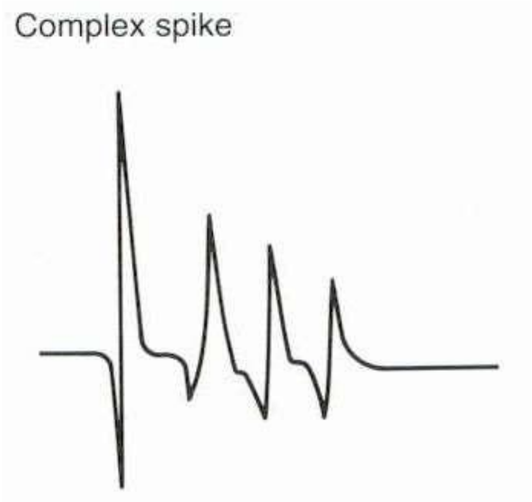
- These represent the **bulk of ongoing input signals** to the cerebellum.

- In contrast, **climbing fibers** form **prolonged, strong direct burst-like synaptic contact** with purkinje cell dendrites **called complex spikes.**

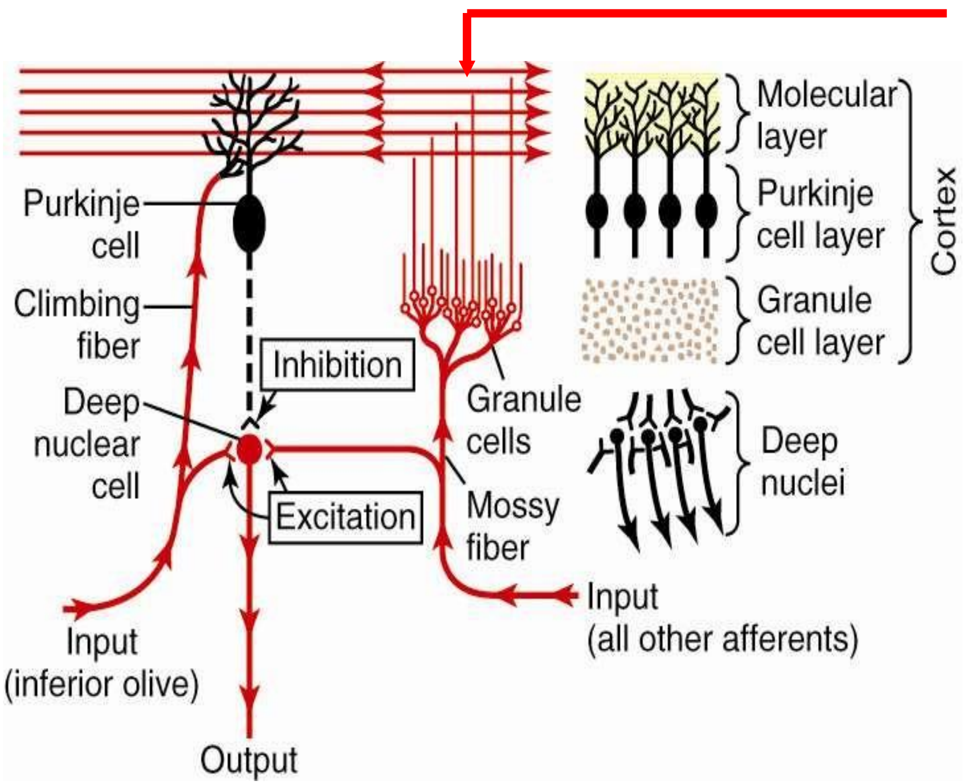
- These signals are essential for **Motor Learning**. *(Motor Learning to be discussed soon)*

- Additionally, in the **molecular layer**, inhibitory interneurons along the parallel fibers help **sharpen and refine cerebellar signals.**





Neuronal Circuit of the Cerebellum



granular cells send axons to the molecular cell layer where they divide and go a few mm in opposite directions to become parallel fibers in the molecular layer

About 500 - 1000 granule cells for every Purkinje cell, anywhere from 80,000 to 200,000 parallel fibers synapse with each Purkinje cell

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Deep Nuclear Cell Activity (Deep cerebellar nuclei)

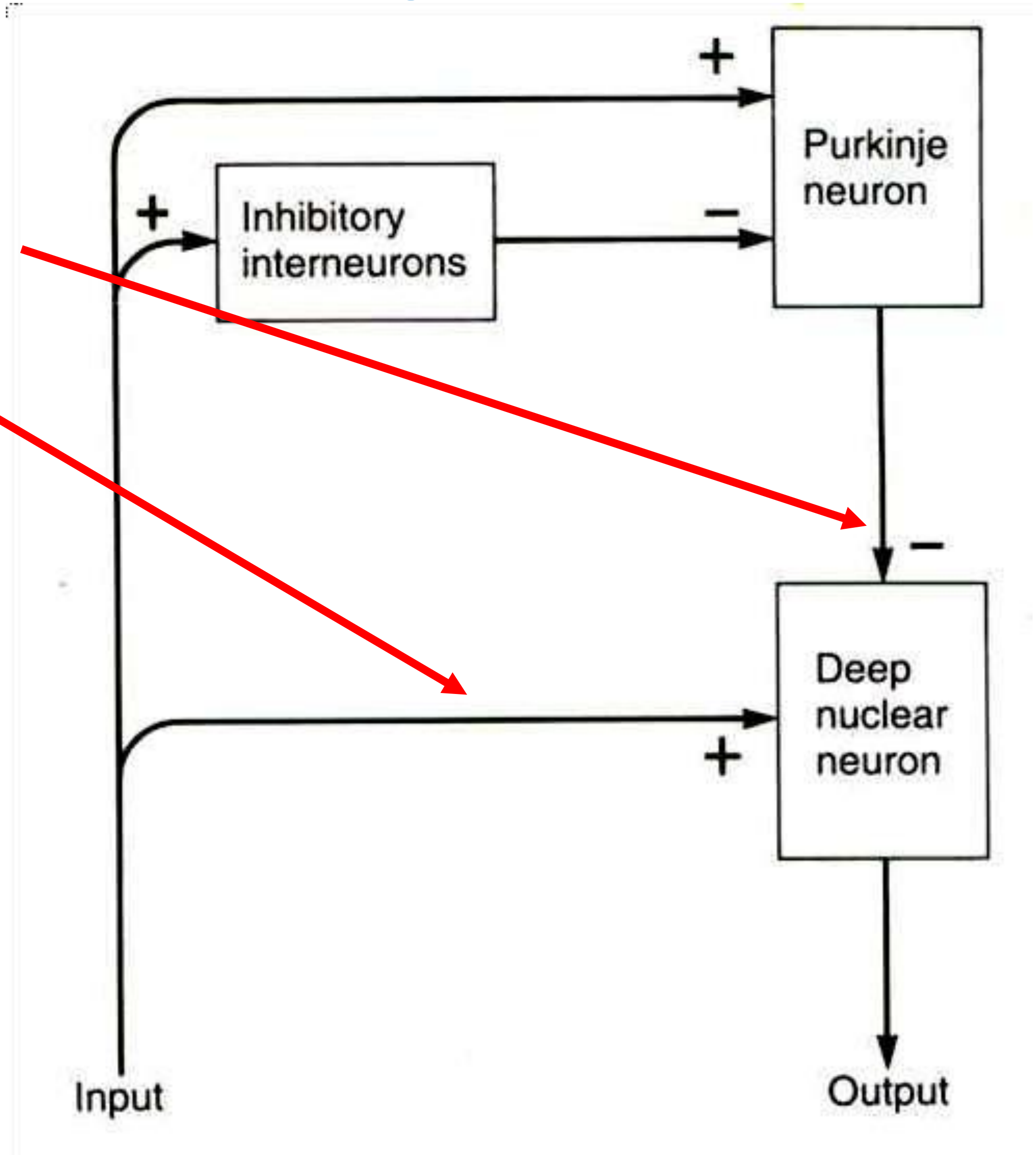
Inhibited by Purkinje cell input

Stimulated by both climbing and mossy fiber input

Normally the balance is in favor of excitation

Deep nuclear cell at first receives an excitatory input from both the climbing fibers and mossy fibers.

This is followed by an inhibitory signal from the Purkinje cells



Deep Nuclear Cell Activity

- At beginning of motion there are excitatory signals sent into motor pathways by deep nuclear cells to enhance movement, followed by inhibitory signals milliseconds later.
  - Provides a damping function to stop movement from overshooting its mark **ensuring it stops precisely at the intended point**
  - Resembles a delay-line type of electronic circuit for negative feedback

The Turn-On / Turn-Off Function

- The Cerebellum contributes to the rapid turn-on signals for agonist muscles and turn-off of antagonist muscles at beginning of a motion (This mechanism is especially important in **fast alternating movements**, such as typing or playing the piano.)
- Then it times the opposite sequence at the end of the intended motion
- Direct motor pathway via corticospinal tract is enhanced by cerebellum by additional signals to the tract or by signals back to the cortex

1. The initial motor command is first sent from the **cerebral cortex to the muscles via the corticospinal tract.**
2. After this, the **cerebellum analyzes the movement improves its precision**
3. It then sends **corrective feedback through the thalamus back to the motor cortex**, so the cortex can send a **more refined motor signal again to the muscles.**

The Turn-On / Turn-Off Function

- mossy fiber input also to Purkinje cells which activates them after a few millisec., this results in an inhibitory signal to the deep nuclear cell
- this inhibits the agonist muscle which stops its activity

Purkinje Cells Function to Correct Motor Errors

- Precise motor movement must be learned.
- Input from climbing fibers adjusts the sensitivity of Purkinje cells to stimulation by parallel fibers.
- This produces long-term changes in the responsiveness of Purkinje cells to mossy fiber input (e.g., signals from muscle spindles, Golgi tendon organs, and other proprioceptors).
- As a result, the feedback control of muscle movement is refined and improved.

➢ How do Climbing Cells and Purkinje Cells contribute to motor learning?
Input from **climbing fibers** produces **complex spikes** in Purkinje cells.
This input **modifies the sensitivity of Purkinje cells** to stimulation coming from **parallel fibers** (which carry mossy fiber information).

As a result, there is a **long-term change in the responsiveness of Purkinje cells** to sensory-motor input arising from structures such as:

- muscle spindles
- Golgi tendon organs
- other proprioceptors

This adaptive change helps the cerebellum **improve feedback control of muscle movement**,
allowing movements to become more accurate, smoother, and better coordinated with repeated performance.

Correction of Motor Errors

- **inferior olivary complex** receives input from:
  - corticospinal tract and motor centers of the brain stem
  - sensory information from muscles and surrounding tissue detailing the movement that actually occurs
- **inferior olivary complex** compares intent with actual function, if a mismatch occurs output to cerebellum through climbing fibers is altered to correct mismatch

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Role of the Inferior Olivary Nuclues

- Each cerebellar functional unit is organized around a single Purkinje cell.
- The inferior olivary nucleus may function in a manner somewhat **similar to the cerebellum.**
- It receives input from **corticospinal pathways, motor centers, and sensory information from large tactile receptors around the muscles**, and **compares** the intended movement with the actual movement performed.
- If a **mismatch is detected (which commonly occurs)**, cerebellar output through the climbing fibers is modified to help correct this error.
- The corrective signal is then transmitted to the cerebral cortex via the thalamus, allowing the cortex to issue a newly adjusted motor command.

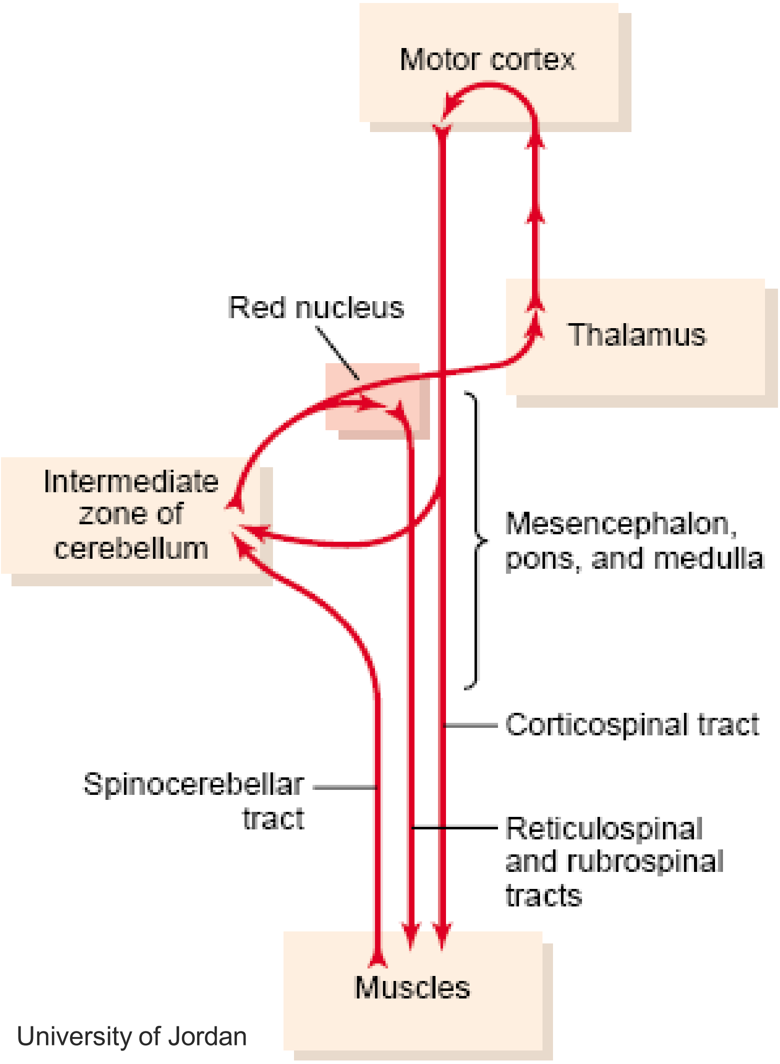
Motion Control by the Cerebellum

- **Most voluntary cortical movements are pendular (they swing back and forth).**
- Therefore, if uncoordinated, inertia and momentum are present, so the movement cannot stop exactly at the intended point, producing tremor.
- **For accurate limb movement, the limb must be accelerated and then decelerated in the correct sequence.**
- **The cerebellum calculates momentum and inertia** (using information about the rate of change from the muscle spindle and the Golgi tendon organ) **and initiates both acceleration and braking activity.**
- **If the cerebellum is damaged, an action tremor (pendular movement) occurs.**

Predictive and Timing Function of the Cerebellum

- motion is a series of discrete sequential movement
- the planning and timing of sequential movements is the function of the lateral cerebellar hemisphere **(lateral zone does not receive info about movement ,it gets cortical info about when to start or stop)**
- this area communicates with premotor and sensory cortex and corresponding area of the basal ganglia where the plan originates
- the lateral hemisphere receives the plan and times the sequential events to carry out the planned movement

Cerebellar Voluntary Control



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Cerebellar Voluntary Control (Summary)

- **Intermediate zone (also called Spinocerebellar Lobe):** receives proprioceptive feedback from **muscle spindles** and **Golgi tendon organs**, linking it functionally to the spinal cord.
- **Lateral zone (also called Corticocerebellar Lobe):** related to cortical motor planning.
- **Vermis (also called Vestibulocerebellar Lobe):** related to vestibular control of posture and balance.
- **Motor command pathway:**

Commands originate in the **motor cortex** → descend via the **corticospinal tract** (and **rubrospinal tract** from the red nucleus) → movement occurs → **sensory feedback returns to the cerebellum**.

- **Corrective loop:**

The cerebellum compares **intended vs actual movement** → sends corrective signals via **VA & VL thalamic nuclei** to the cortex → cortex issues a **refined command**.

- **Key concept:**

The cerebellum **does not send direct motor output to muscles**; it refines movement **indirectly through cortical pathways**, with rapid repeated corrections before and during motion.

Note: The doctor here mentioned that the vermis is also called "Vestibulocerebellar Lobe", however according to Guyton and Hall, it's the Foliculonodular Lobe which is called so because of its direct comuncication with the vestibular nuclei. Guyton and Hall mentions the Vermis as part of the "Spinocerebellar Lobe" along with the Paravermis

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Integration of Motor Control

- Spinal cord level
  - preprogramming of patterns of movement of all muscles (i.e., withdrawal reflex, walking movements, etc.).
- Brainstem level
  - maintains equilibrium by adjusting axial tone
- Cortical level
  - issues commands to set into motion the patterns available in the spinal cord
  - controls the intensity and modifies the timing

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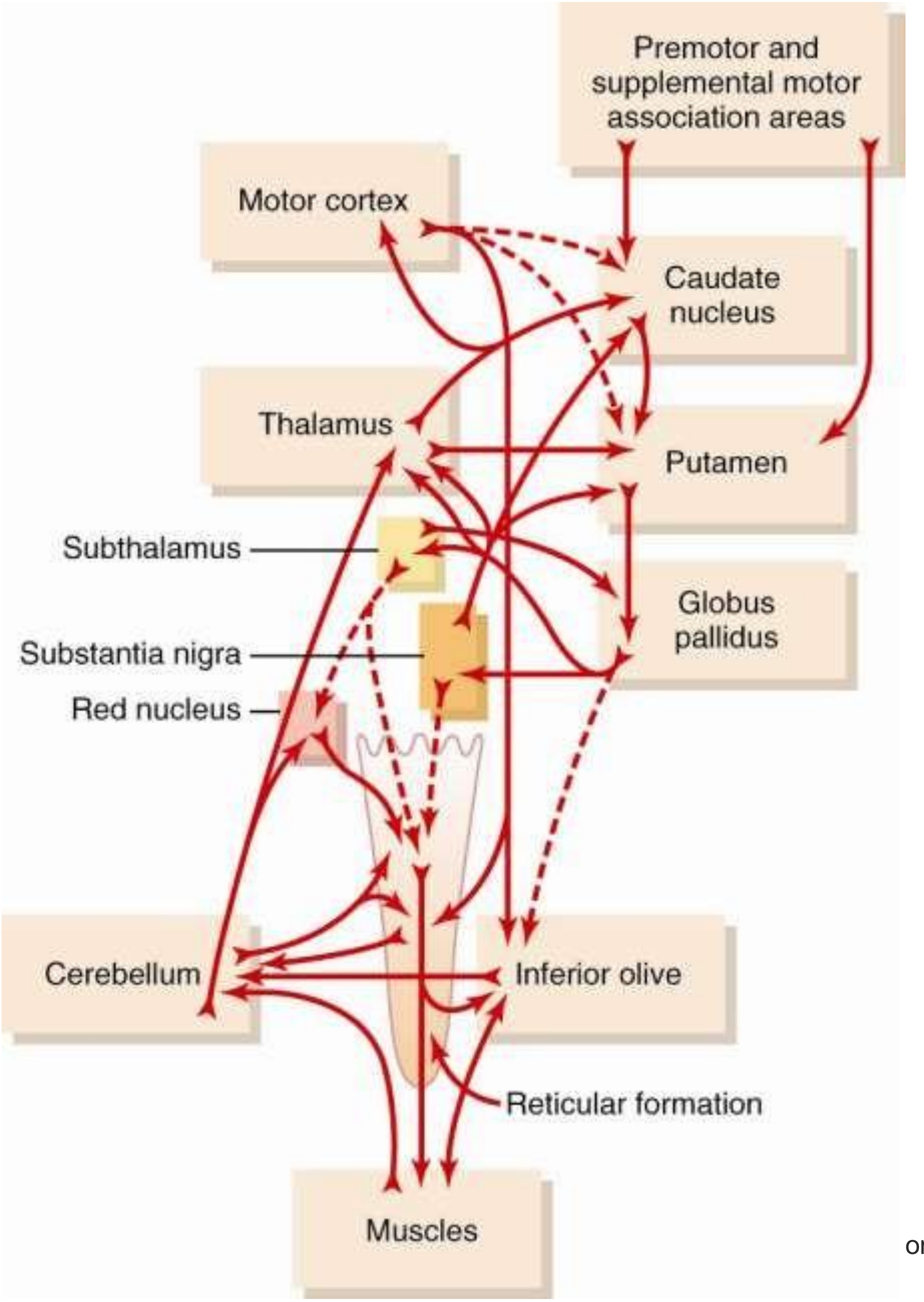
Integration of Motor Control (cont'd)

- Cerebellum
  - function with all levels of control to adjust cord motor activity, equilibrium, and planning of motor activity
- Basal ganglia
  - functions to assist cortex in executing subconscious but learned patterns of movement, and to plan sequential patterns to accomplish a purposeful task



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Overall scheme for integration of motor function

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Clinical Abnormalities of the Cerebellum

- All signs of cerebellar diseases are ipsilateral since there is double crossing- from cortex to pons and back to cortex
- Ataxia and intention tremor
  - failure to predict motor movement, patients will overshoot intended target, past pointing.
  - Dysequilbrium- ataxic (staggering) gait (drunken gait)
- Dysdiadochokinesia (Adiadochokinesia)
  - failure of orderly progression of movement
- Dysarthria
  - failure of orderly progression in vocalization
- Cerebellar nystagmus
  - intention tremor of the eyes when trying to fix on object.

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Clinical Abnormalities of the Cerebellum (Very important)

- **Cerebellar signs are ipsilateral**

→ because cerebellar pathways **cross twice** (cortex → pons → cerebellum → thalamus → cortex).

- **Most manifestations are motor in nature**

→ due to the cerebellum's primary role in **coordination and accuracy of movement.**

- **Movement initially becomes inaccurate**

→ cortical motor commands are **not precisely modulated**, so muscles receive **excessive or insufficient impulses.**

- **This causes overshooting of the intended target**

→ the limb moves **beyond the desired position (past-pointing).**

- **Visual and proprioceptive feedback then detects the error**

→ the cortex sends **repeated corrective impulses in opposite directions** (forward and backward).

- **These alternating corrections produce intention tremor**

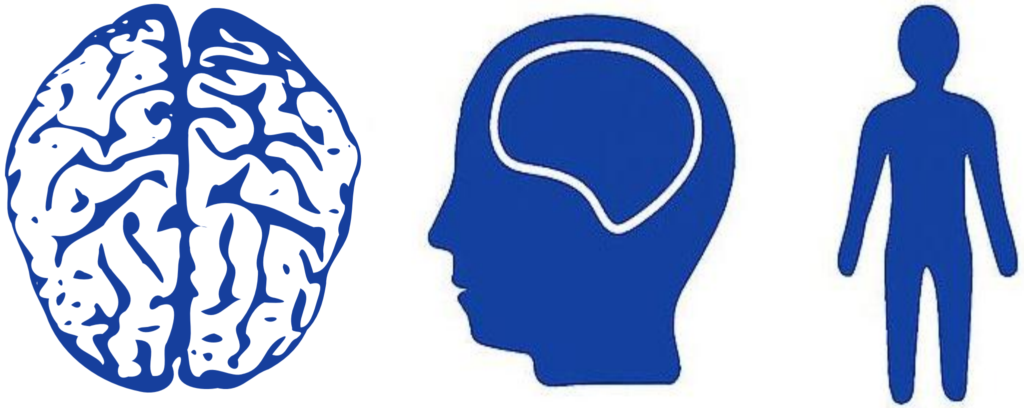
→ tremor becomes **more prominent as the limb approaches the target.**

Clinical Abnormalities of the Cerebellum (Cont'd)

- **Ataxia**
  - **General loss of coordination** of voluntary movements due to cerebellar dysfunction.
  - Can involve **limbs, gait, speech, or eye movements.**
- **Disequilibrium (especially in vermis lesions)**
  - Produces **ataxic, staggering gait**
  - Patient shows **swaying to either side with a wide-based stance** (feet kept far apart to maintain balance)
  - Gait resembles a "**drunken gait.**"

Clinical Abnormalities of the Cerebellum (Cont'd)

- **Dysdiadochokinesia:**
  - Rapid alternating movements (e.g., pronation-supination) become **slow, irregular, and poorly coordinated** due to impaired coordination between **agonist and antagonist muscles**.
- **Adiadochokinesia:**
  - **Complete inability** to perform rapid alternating movements.
- **Dysarthria:**
  - **Disordered speech articulation or vocalization**, with speech becoming **interrupted and irregular** due to incoordination of speech muscles.
- **Cerebellar nystagmus:**
  - **Abnormal, unsteady eye movements** with intention tremor when attempting to **fix gaze on an object**; the eyes cannot remain steady.
- **Note: Vestibular nystagmus** also exists (It is **rhythmic involuntary eye movement** caused by a **disturbance in the vestibular system)**



PHYSIOLOGY QUIZ LECTURE 3

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Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			