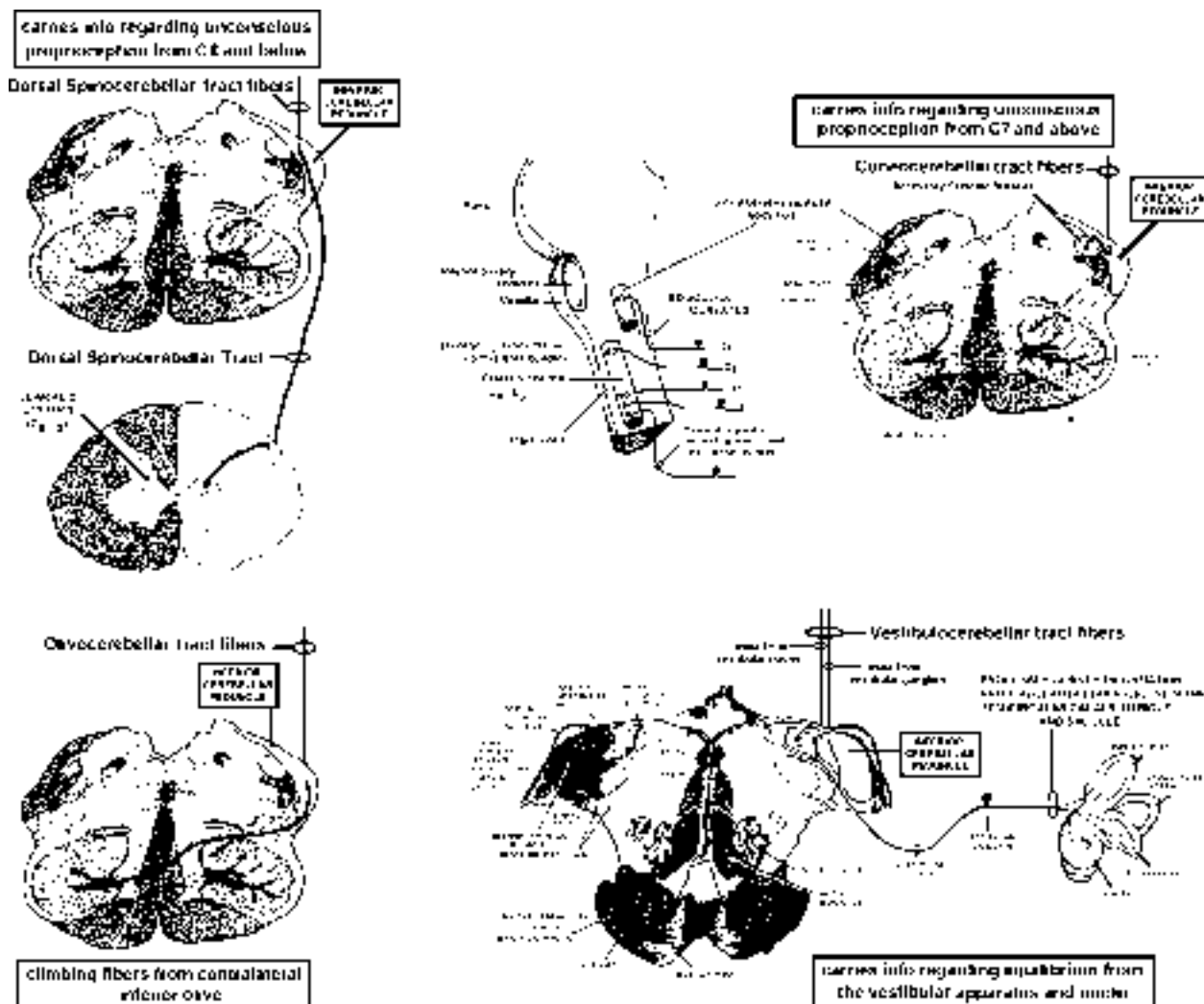# Cerebellum

We already know quite a bit about the cerebellum from our spinal cord and brain stem discussions. **Let's review our CURRENT STATE of knowledge.**

**CEREBELLAR PEDUNCLES** (bundles of fibers connecting the cerebellum with the underlying brain stem).

We know that the **inferior cerebellar peduncle** (restiform body) contains the **dorsal spinocerebellar tract** (DSCT) fibers. These fibers arise from cells in the **ipsilateral** Clarke's column in the spinal cord (C8-L3). We also know that this peduncle contains the **cuneocerebellar tract** (CCT) fibers. These fibers arise from the **ipsilateral** accessory cuneate nucleus. The largest component of the inferior cerebellar peduncle consists of the **olivocerebellar tract** (OCT) fibers. These fibers arise from the **contralateral** inferior olive. Finally, some of you might remember from Point 13 that **vestibulocerebellar tract** (VCT) fibers arise from cells in both the **vestibular ganglion** and the **vestibular nuclei** and pass in the inferior cerebellar peduncle to reach the cerebellum.

We also know that the **middle cerebellar peduncle** (brachium pontis) contains the **pontocerebellar tract (PCT)** fibers. These fibers arise from the **contralateral** pontine grey.

MI
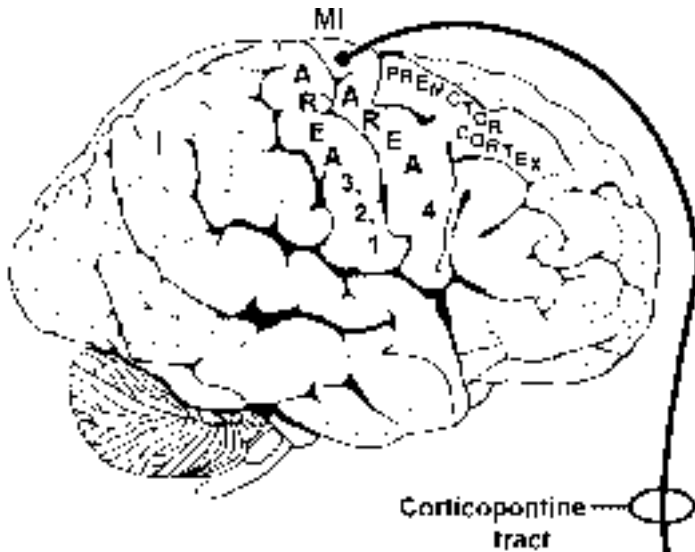
carries info that started in the contra
molor cortex and has been
relayed via the contra pontine grey

Pontocerebellar tract fibers —

MIDDLE
CEREBELLAR
PEDUNCLE

Corticopontine
tract

**Posterior
Parietal
cortex**

SMA
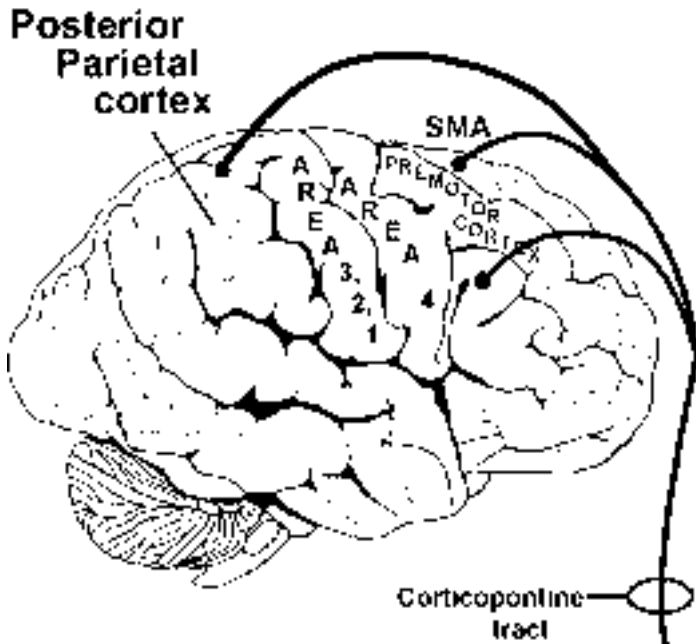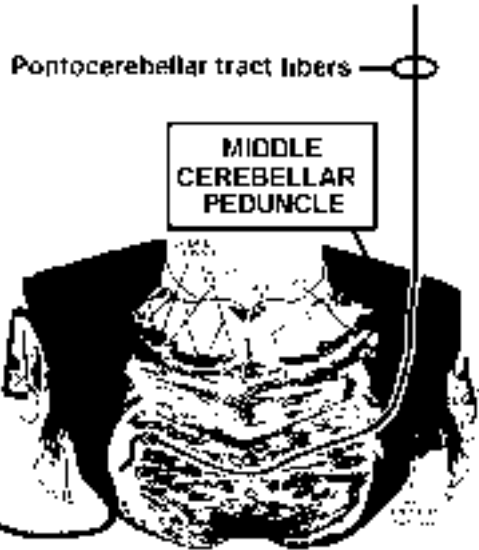
carries info that started in the contra
PPC, SMA and PMI and has been relayed
via the contra pontine grey

Pontocerebellar tract fibers —

MIDDLE
CEREBELLAR
PEDUNCLE

Corticopontine
tract
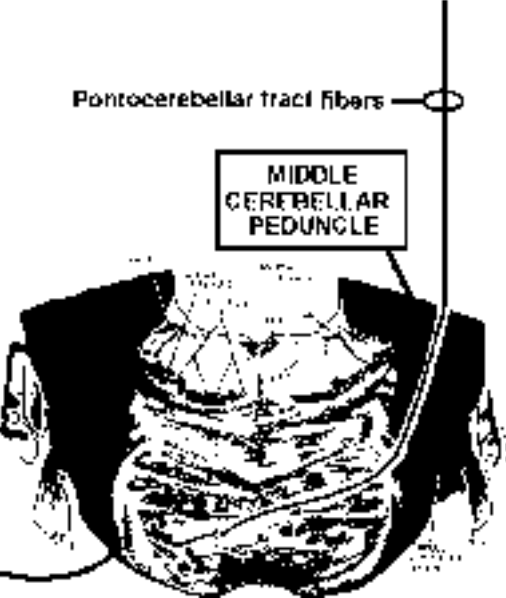
carries info rostral from interpositus and dentate
to the contralateral VA/VL and red nucleus

Superior
cerebellar
peduncle

Finally, we know that the **superior cerebellar peduncle** (brachium conjunctivum; Point 18) is the primary **efferent** peduncle of the cerebellum. It contains fibers that arise from several deep cerebellar nuclei. These fibers pass rostrally for a while (ipsilaterally) and then cross at the level of the inferior colliculus to form the decussation of the superior cerebellar peduncle. These fibers then continue rostrally to terminate in the red nucleus and the motor nuclei of the thalamus (VA, VL).

Fastigial

Globose

Emboliform

Dentate
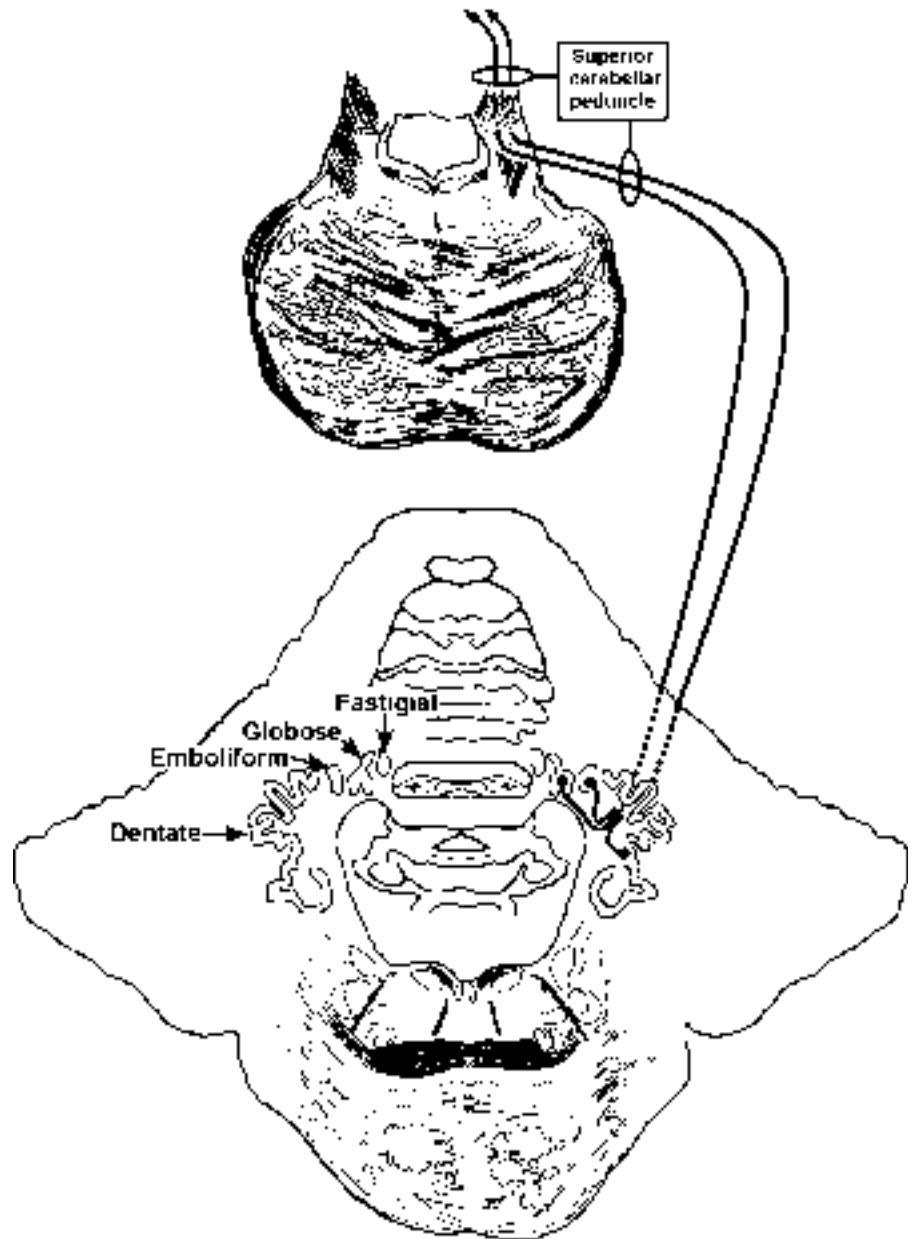
LET'S REVIEW

INFERIOR CEREBELLAR PEDUNCLE = **DSCT, CCT, OCT, VCT**

MIDDLE CEREBELLAR PEDUNCLE = **PONTOCEREBELLARS**

SUPERIOR CEREBELLAR PEDUNCLE = **EFFERENT FIBERS**

Try the questions below to see how you stand regarding the identity and components of the three cerebellar peduncles. Make sure you do this before moving on in the module.

1. **A**. Name the peduncle that lies adjacent to the fourth ventricle in the section below

   _____

   B. Where are the cells of origin of the axons in this peduncle?

   _____

LEVEL 7. ROSTRAL PONS

2. **A**. Name the peduncle present in the dorsal part of the section below

   _____

   B. Name four fiber tracts that contribute to this peduncle

   _____ _____ _____ _____

LEVEL 4. ROSTRAL MEDULLA

3. **A**. Name the peduncle present in the section below

—————————————————

B. Where are the cells of origin of the axons in this peduncle

—————————————————

LEVEL 5. MIDDLE PONS
- FACIAL COLLICULUS
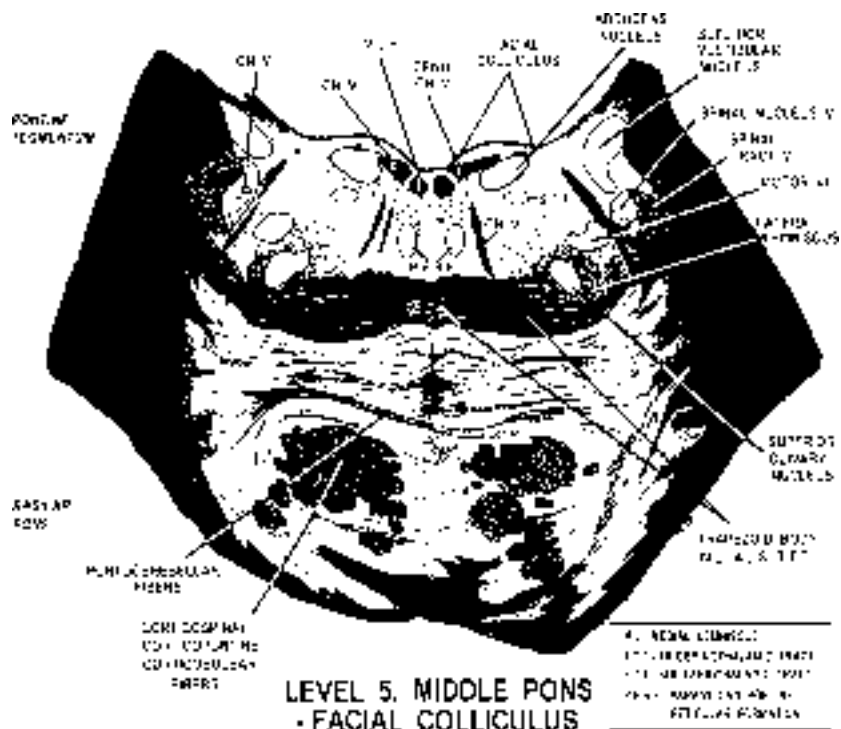
Now that you know the inputs to the cerebellum, we need to learn **WHERE** in the cerebellum each afferent terminates. If we look at the **dorsal view** of the cerebellum, you can approximate where most of these zones are. You can see the solid lines that run rostral (near the superior colliculus) to caudal (near the spinal cord). You can see such areas as the **vermis**, which is the medial worm-like part of the cerebellum. This vermis region was identified by the **OLD**- time anatomists and consists of the two (right and left) medial zones. You can also see the more laterally placed cerebellar **hemispheres**, which correspond mainly to the lateral zones. It is difficult to see the flocculonodular lobe as it is tucked underneath. In the lower of the two drawings, the flocculonodular lobe is shown at the caudal end of the dorsal view of the cerebellum. **The main point that you need to know is that different regions of the cerebellum receive different inputs and project to different parts of the brain stem and thalamus.**

Dorsal View
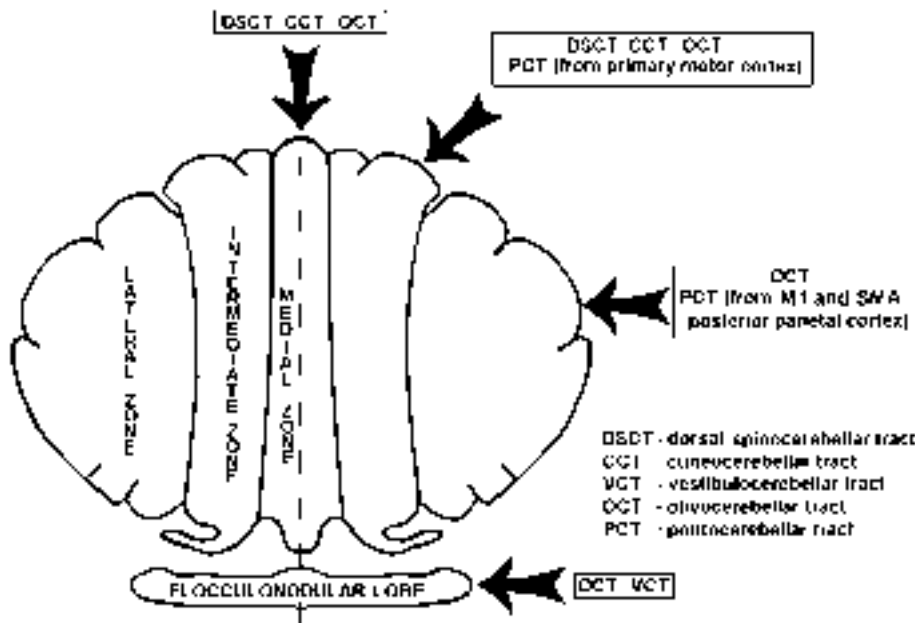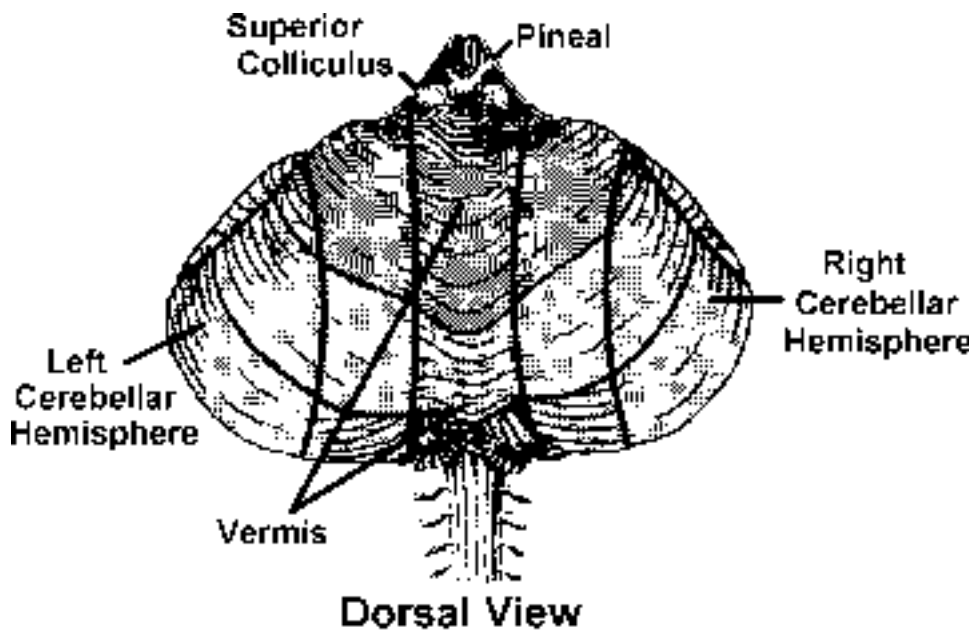
Zones of the cerebellum

The various cerebellar afferents that we have learned distribute to different zones of the cerebellum. Four different zones need to be considered. These are the 1) **medial zone**, 2) **intermediate zone**, 3) **lateral zone** and 4) **flocculonodular zone (or lobe)**. Let's consider the pathways that end in each zone or lobe.
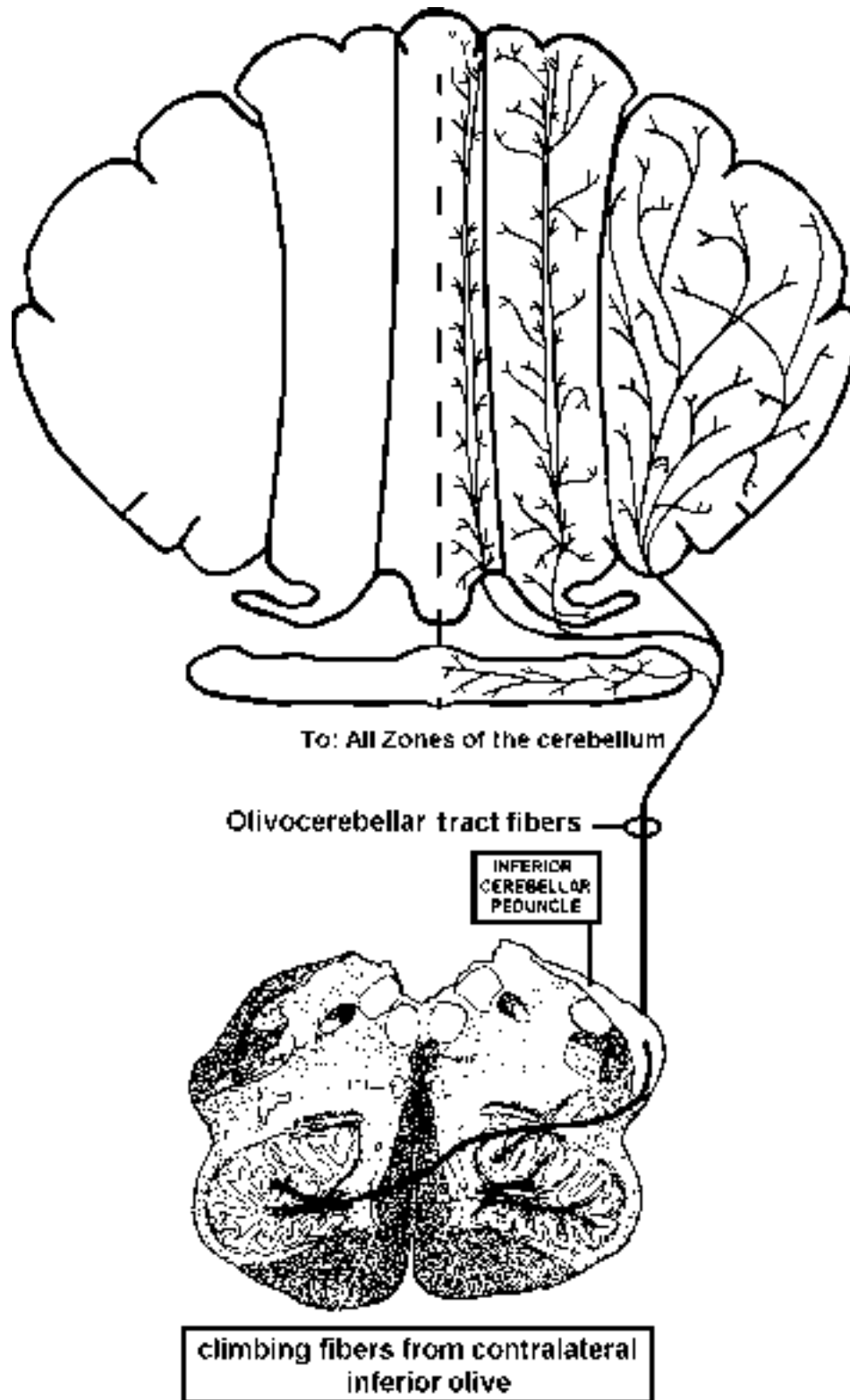
1. **olivocerebellar** fibers—distribute to the **ENTIRE** cerebellum
2. **dorsal spinocerebellar** and **cuneocerebellar** fibers—distribute to the **medial** and **intermediate** zones
3. **pontocerebellar** fibers—distribute to the **intermediate** and **lateral** zones

     A. Those pontine grey neurons that project to the **intermediate** zone of the cerebellum receive their corticopontine input from the **primary motor cortex** (area 4; *execution*).

     B. Those pontine grey neurons that project to the **lateral** zone of the cerebellum receive their corticopontine input from **posterior parietal** cortex (PMl and SMA). In comparison with the primary motor cortex,these areas are involved in **planning the motor act**.

4. **vestibulocerebellar** fibers—(arise from the vestibular ganglion and nuclei) distribute primarily to the **flocculonodular** lobe
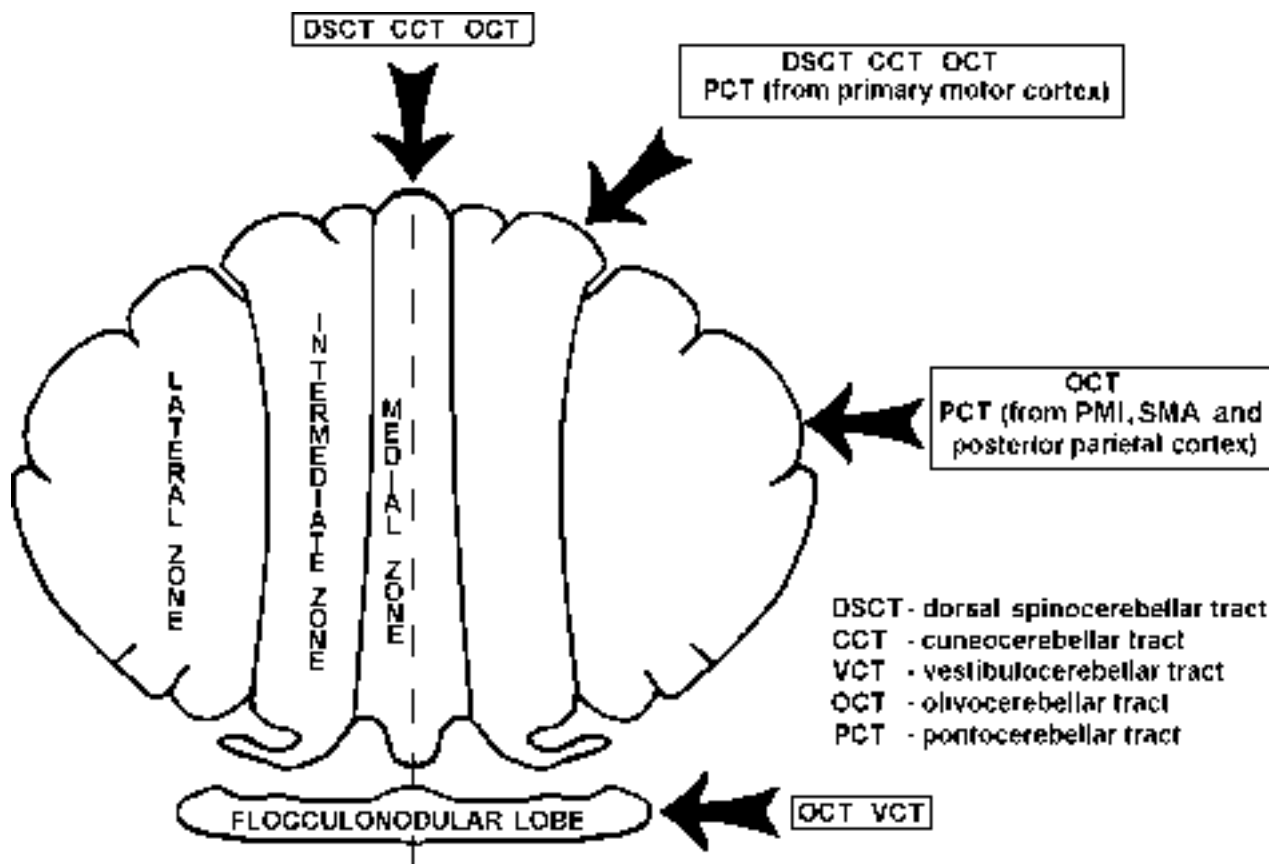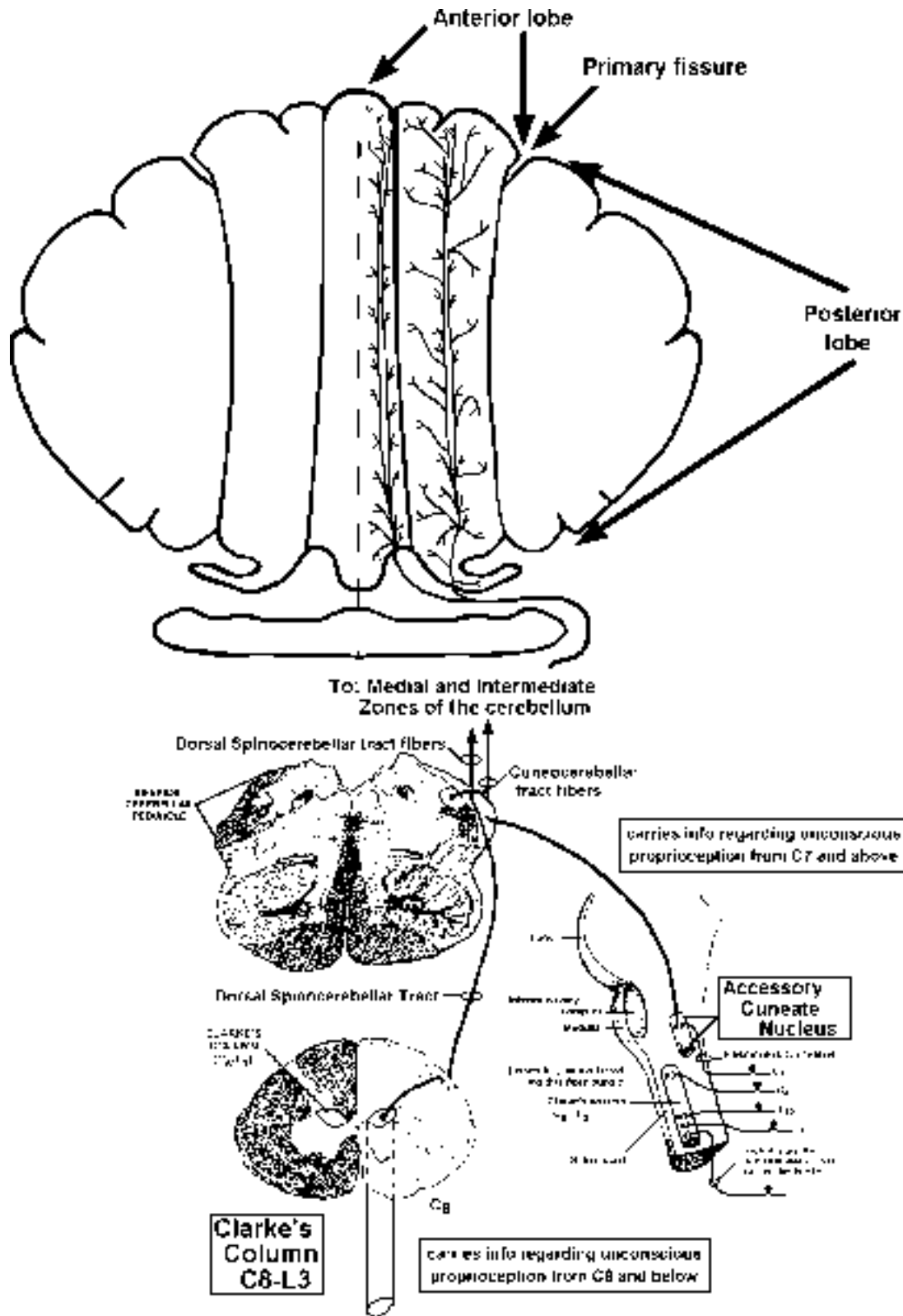
LET'S REVIEW

OLIVOCEREBELLAR FIBERS

The distribution of olivocerebellar fibers onto the flattened view of the cerebellum is shown. This is easy, since the fibers project to the entire cerebellum.

To: All Zones of the cerebellum

Olivocerebellar tract fibers —

INFERIOR
CEREBELLAR
PEDUNCLE

climbing fibers from contralateral
inferior olive

DORSAL SPINOCEREBELLAR AND CUNEOCEREBELLAR FIBERS

The DSCT and CCT pathways convey unconscious proprioception regarding the ipsilateral side of the body. They both project to the **medial** and **intermediate** zones.

Anterior lobe

Primary fissure

Posterior lobe

To: Medial and Intermediate
Zones of the cerebellum

Dorsal Spinocerebellar tract fibers

Cuneocerebellar tract fibers

carries info regarding unconscious
proprioception from C7 and above

Dorsal Spinocerebellar Tract

Accessory
Cuneate
Nucleus

Clarke's
Column
C8-L3

carries info regarding unconscious
proprioception from C8 and below

Pontocerebellar fibers that convey information from the primary motor cortex (MI or area 4) terminate within the intermediate zone. They overlap with DSCT and CCT fibers in this zone.

POSTERIOR PARIETAL AREA

LATERAL ZONE

INTERMEDIATE ZONE

MEDIAL ZONE

FLOCCULONODULAR LOBE

Corticopontine tract

POSTERIOR PARIETAL AREA = "planning"
AREA 4 = primary motor cortex
AREAS 3,2,1 = somatosensory cortex
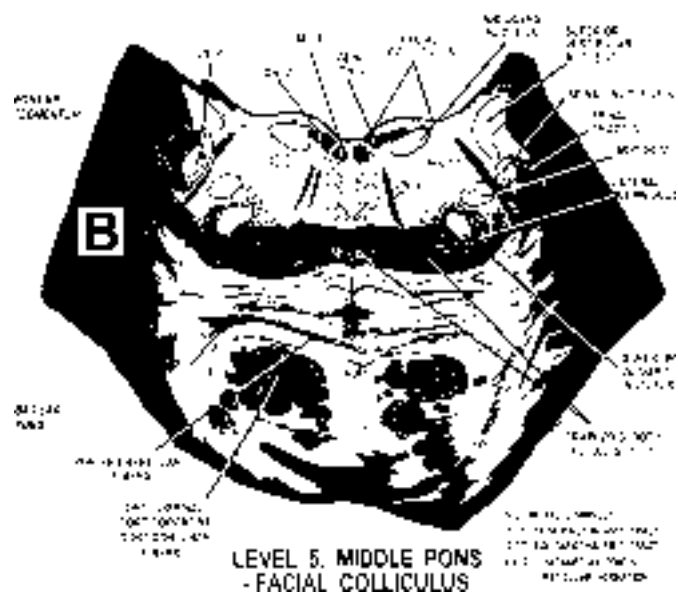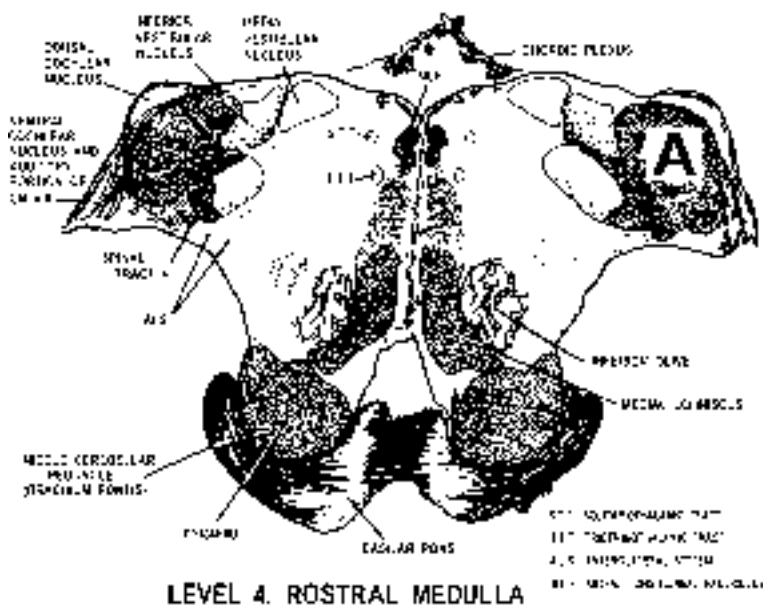
Middle Cerebellar Peduncle
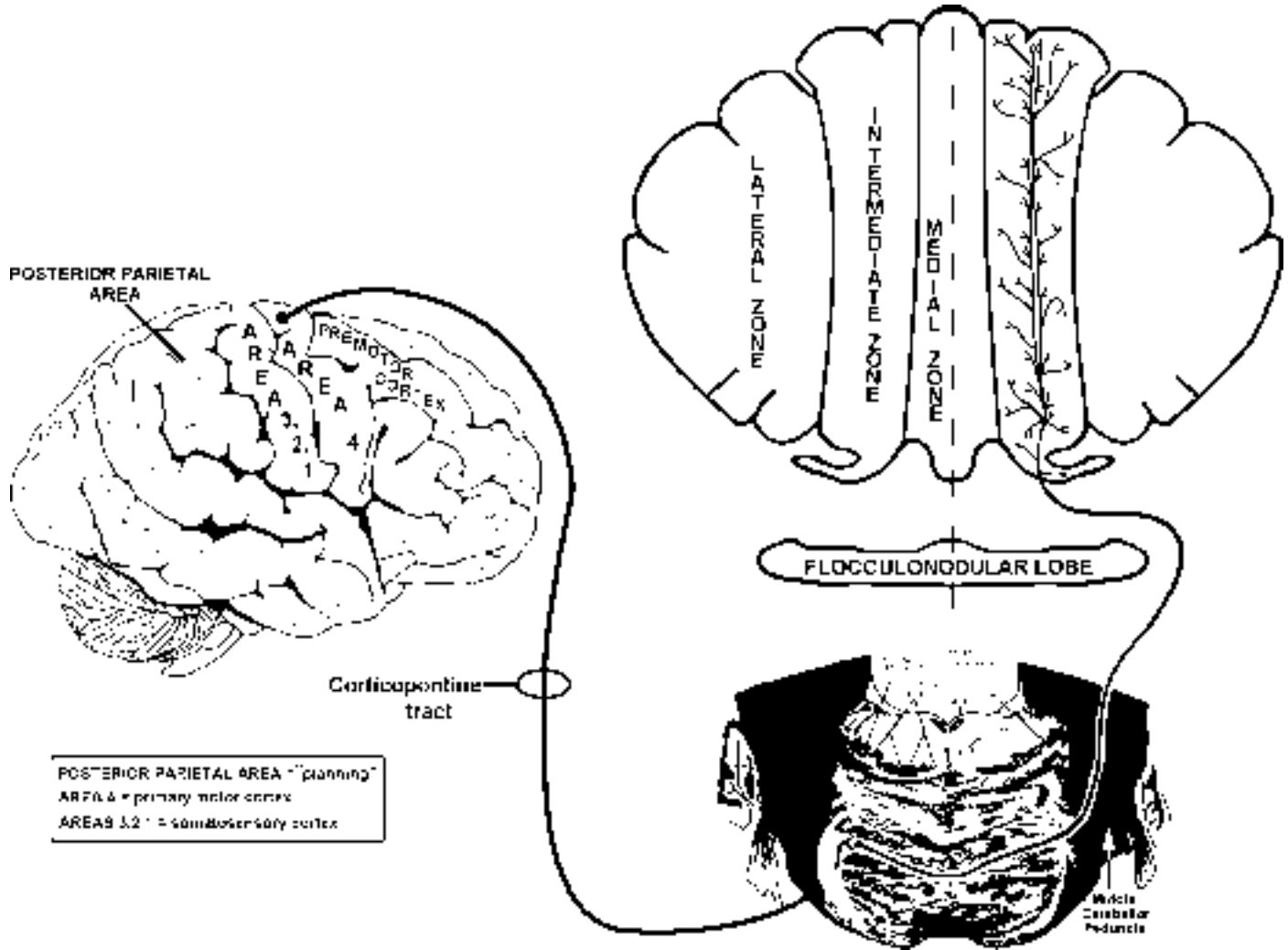
Pontocerebellar fibers that convey information from the **posterior parietal,** PMl and SMA (planning) areas of the cortex terminate within the lateral zone of the cerebellum.

Vestibulocerebellar fibers arise from the vestibular nerve and nuclei and terminate within the flocculonodular lobe.

LEVEL 4 ROSTRAL MEDULLA
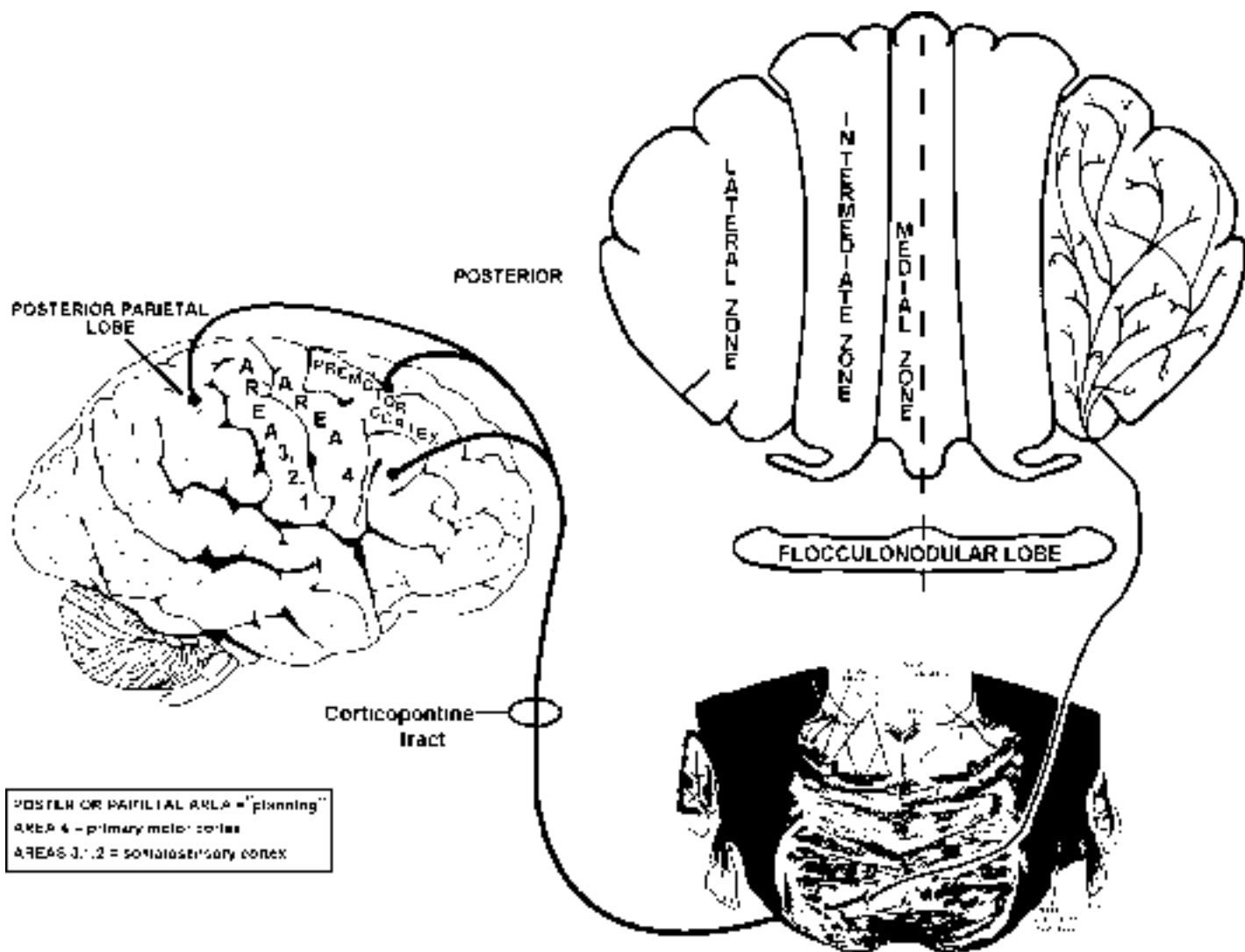
Now let's do some practice questions to make sure we understand the ***organization of inputs to the cerebellum***. Then we can move on to the deep cerebellar nuclei.

4. A. In the figure below, name the **zones** of the cerebellum that receive input from axons traveling within the structure labeled **A.** _____, _____, _____, _____

    B. In the figure below, name the **zones** of the cerebellum that receive input from the structured labeled **B.** _____, _____

LEVEL 4. ROSTRAL MEDULLA

LEVEL 5. MIDDLE PONS - FACIAL COLLICULUS

5. **The following questions relate to the labeled drawing below**.

A. Axons from **B** travel in which cerebellar peduncle?_____

B. Does **A** project to the same side of the <u>pons</u> and <u>spinal cord</u>?_____

C. Which cortical area(s) are is involved in "higher" planning of motor movements?_____

D. Which cortical area(s) send(s) information **(via the pons)** to the <u>lateral</u> zone of the cerebellum?_____

E. Which cortical area (**A** or **B**) send(s) information **(via the pons)** to the <u>intermediate</u> zone of the cerebellum?_____

F. Does either cortical area **A** or **B** send information **(via the pons)** to the <u>medial</u> zone of the cerebellum?   **YES   NO**

G. Does either cortical area **A** or **B** send information **(via the pons)** to the <u>flocculonodular</u> zone (or lobe) of the cerebellum?   **YES   NO**
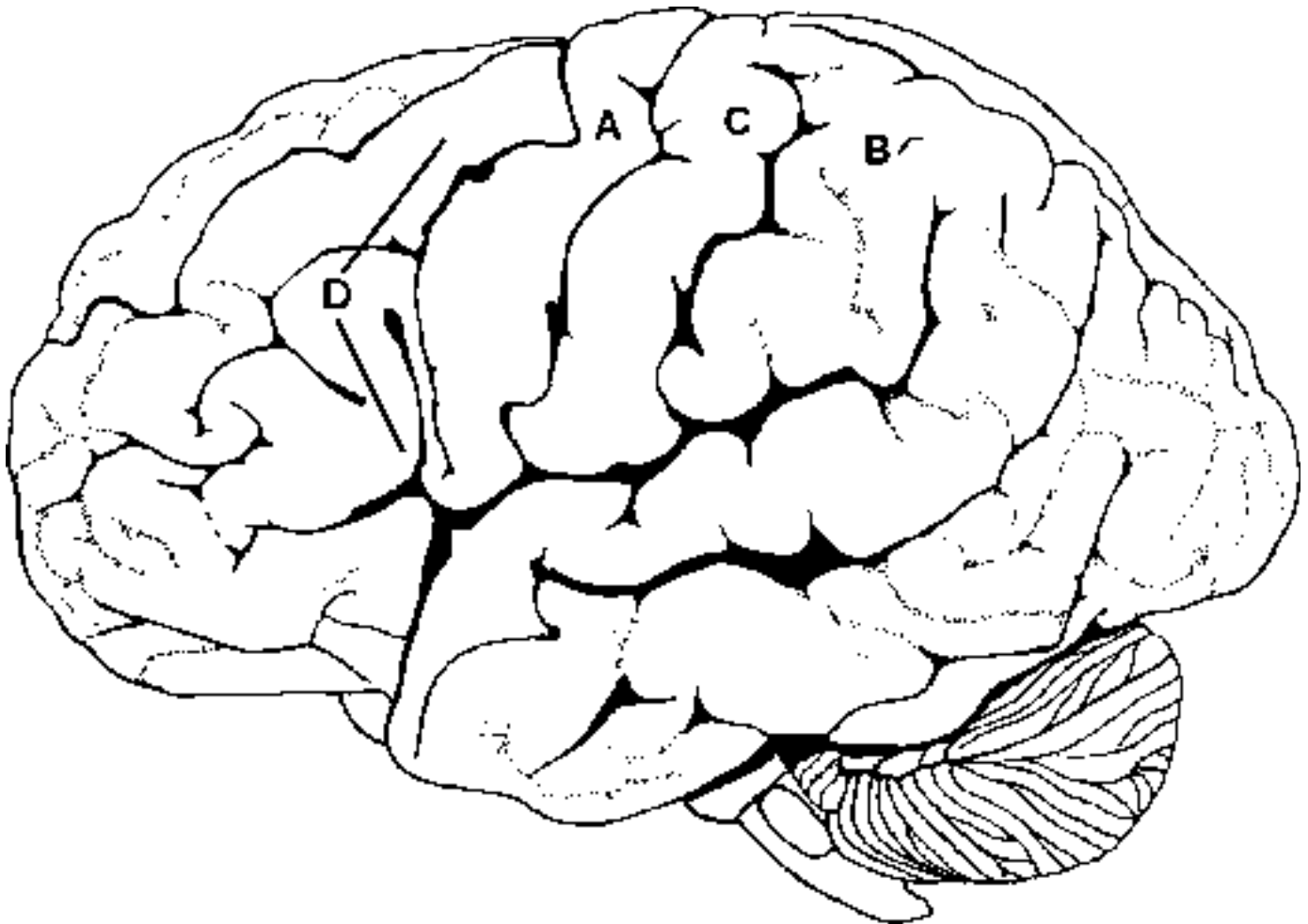
6. The following questions relate to the TWO labeled drawings below.

A. What cortical areas project to **D**?
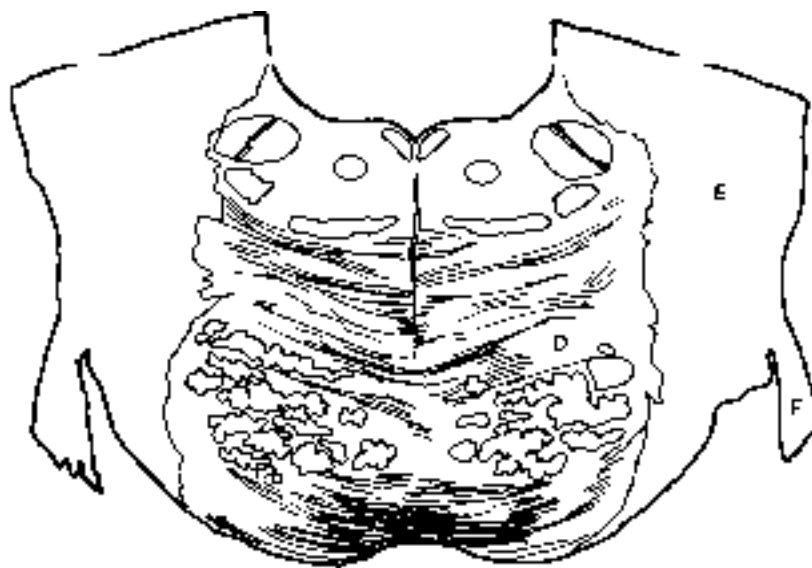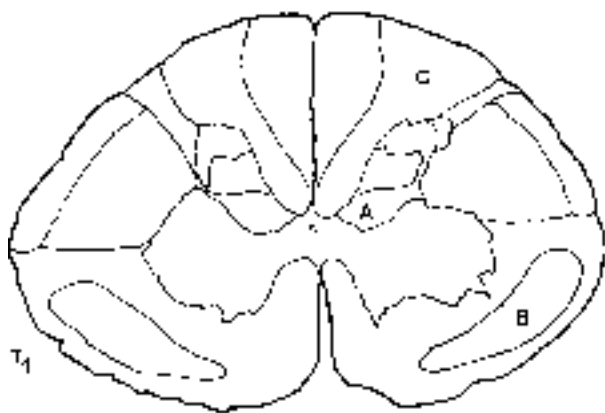
B. What zone(s) of the cerebellum are innervated by axons of the cells in **A**? (Clarke's column)

C. A complete lesion of **B** results in loss of pain and temperature (DON'T FORGET THE SPINAL
    CORD) from what level(s)?

D. Axons in **E** terminate in which zones of the cerebellum? _____and_____

E. Do axons with cell bodies in the motor cortex travel in **E**? _____

7. The following questions relate to the labeled drawing below.

A. Fibers from cells that lie in nucleus **A** project to which zone of the cerebellum?
_____

B. Cells in **A** project to the lateral zone of the right cerebellum via the middle cerebellar peduncle.
True or False?

C. **B** is the _____ cerebellar peduncle or _____body.

D. Vestibular input reaches the cerebellum via 2 pathways; peripherally from the
_____ and centrally from the _____.

E. True or False; axons of cells in **E** project directly to the cerebellum.

RIGHT   LEFT
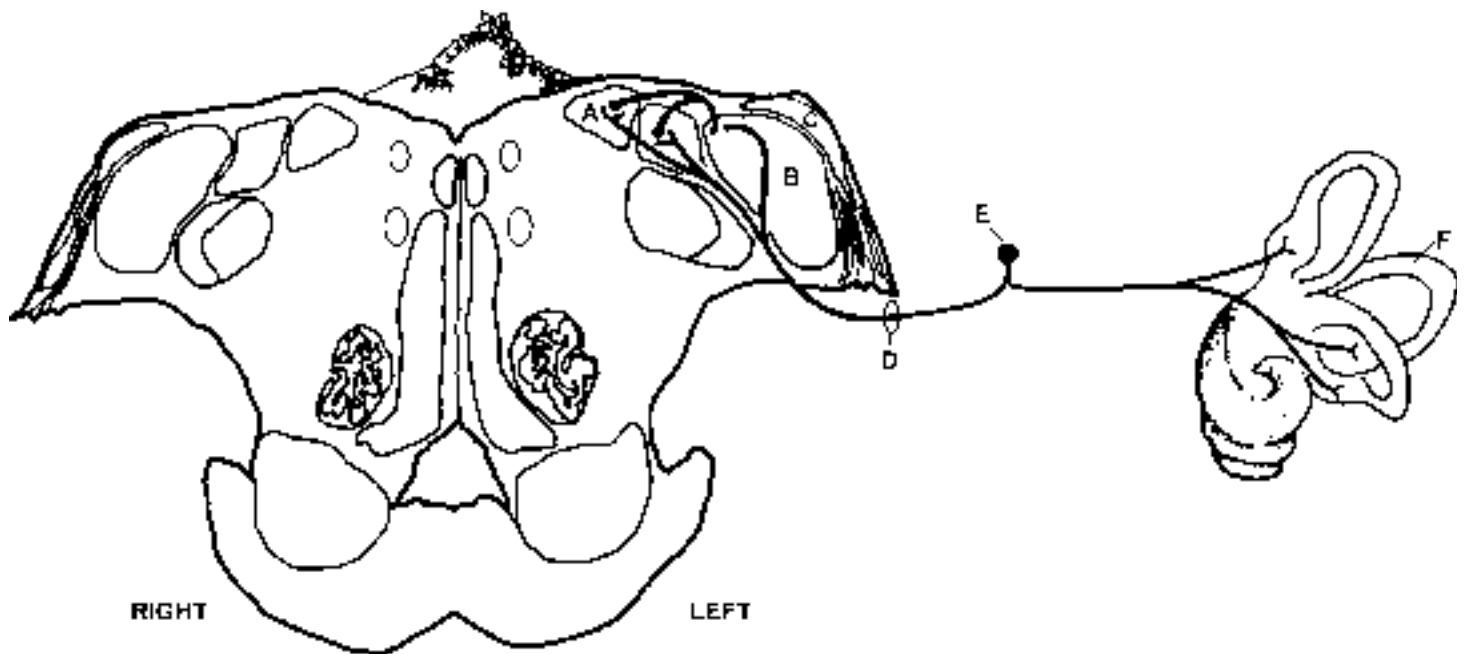
Deep Cerebellar Nuclei

The inputs to the cerebellum just discussed take part in some very complicated internal circuitry. An optional overview of this internal circuitry can be found at the end of this lecture, but it is not necessary for a good understanding of how the cerebellum influences movement. All you really need to know is that after all is said and done, the inputs to the cerebellum ultimately affect Purkinje cells of the cerebellar cortex a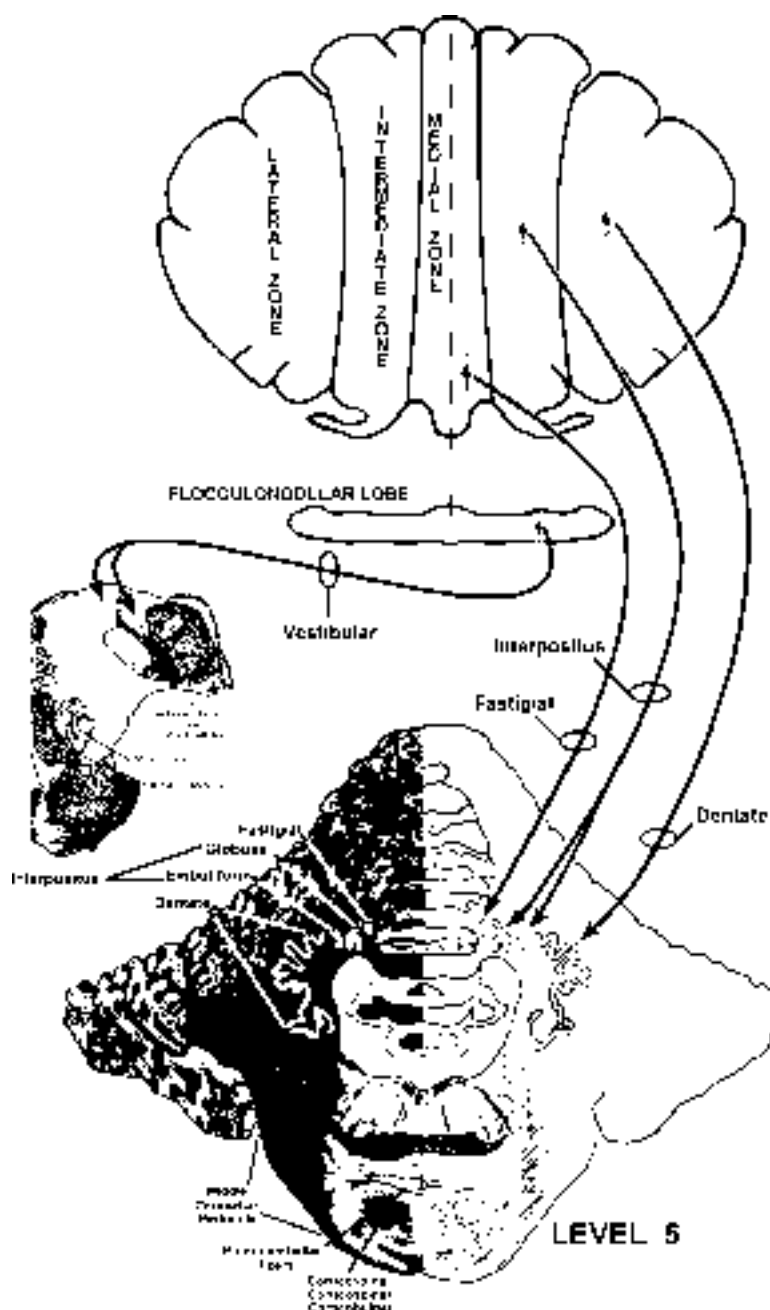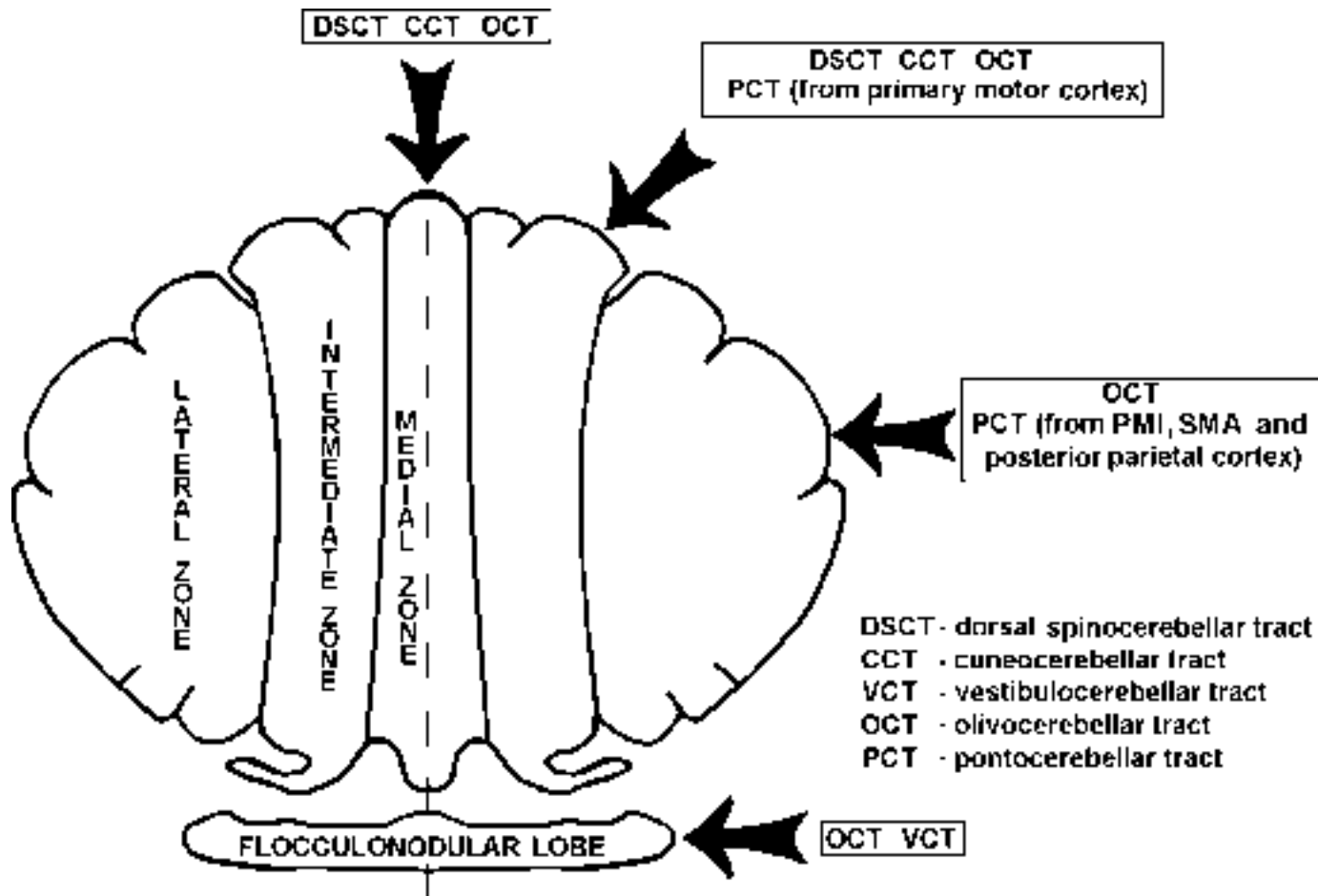nd the deep cerebellar nuclei. The Purkinje cells inhibit the deep cerebellar nuclei and ultimately affect the output of the cerebellum. Let's look at the distribution of Purkinje cell axons. Purkinje cells in the four different zones, MEDIAL, INTERMEDIATE, LATERAL AND FLOCCULONODULAR, project to different deep cerebellar nuclei. There are four deep cerebellar nuclei, fastigial, globose, emboliform and dentate (feel good every day) from medial to lateral.

Three of the four deep cerebellar nuclei can be seen below in an old friend from the brain stem, level 5. You have not seen the dorsal part of this section before, but it shows three of the four sets of **deep cerebellar nuclei**. The distribution of Purkinje cell axons to the cerebellar nuclei is actually quite easy to remember because it is topographically organized. The most **lateral** deep cerebellar nucleus, the **dentate**, receives its Purkinje cell input from the **lateral** zone of the cerebellum. Remember that this **lateral** zone of the cerebellum receives its input from olivocerebellar and pontocerebellar fibers carrying planning information. The **interpositus** nucleus (actually two nuclei, globose and emboliform) receives its Purkinje cell input from the **intermediate** zone of the cerebellum. The **intermediate** zone of the cerebellum receives its input from olivocerebellar and pontocerebellar fibers carrying information from primary motor cortex (area 4) **AND** from the DSCT and CCT. The Purkinje cells that innervate the medially located **fastigial** nucleus lie in the **medial** zone of the cerebellum which, as you remember, receives input from the DSCT, CCT and OCT.

Purkinje cells in the flocculonodular zone (or lobe) also need a deep nucleus. Unfortunately there isn't a deep nucleus left for the floccunodular zone, so the Purkinje cells of the flocculonodular lobe terminate in the **VESTIBULAR NUCLEI,** which we can consider as a "surrogate" deep cerebellar nucleus. Those Purkinje cell axons that are destined for the vestibular nuclei travel in the inferior cerebellar peduncle (along with the fibers from the vestibular nerve and nuclei that are entering the cerebellum.)


LEVEL 4 ROSTRAL MEDULLA

The signals from the Purkinje cells that terminate in the deep cerebellar nuclei are inhibitory. Think of the inhibitory signal as increasing or decreasing depending upon what is happening in the cerebellum (**see intrinsic circuitry at the end of section if interested**). Note that the deep cerebellar nuclei also receive **EXCITATORY** inputs from the collaterals of both mossy and climbing fibers as they pass through the deep white matter on their way to the overlying cerebellar cortex. The interplay of the inhibitory (Purkinje cell) and excitatory (mossy and climbing fiber) inputs to the deep nuclei determines their output signal to the other parts of the brain that we will discuss next.

DSCT CCT OCT

DSCT CCT OCT
PCT (from primary motor cortex)

OCT
PCT (from PMI, SMA and posterior parietal cortex)

LATERAL ZONE

INTERMEDIATE ZONE

MEDIAL ZONE

DSCT - dorsal spinocerebellar tract
CCT - cuneocerebellar tract
VCT - vestibulocerebellar tract
OCT - olivocerebellar tract
PCT - pontocerebellar tract

FLOCCULONODULAR LOBE

OCT VCT

LET'S REVIEW

## PURKINJE CELLS IN THE:

- *LATERAL ZONE* OF CEREBELLUM FEED INTO **DENTATE**

- *INTERMEDIATE ZONE* FEED INTO **INTERPOSITUS (globose and emboliform)**
- *MEDIAL ZONE* FEED INTO **FASTIGIAL**

- *FLOCCULONODULAR LOBE* FEED INTO **VESTIBULAR NUCLEI**
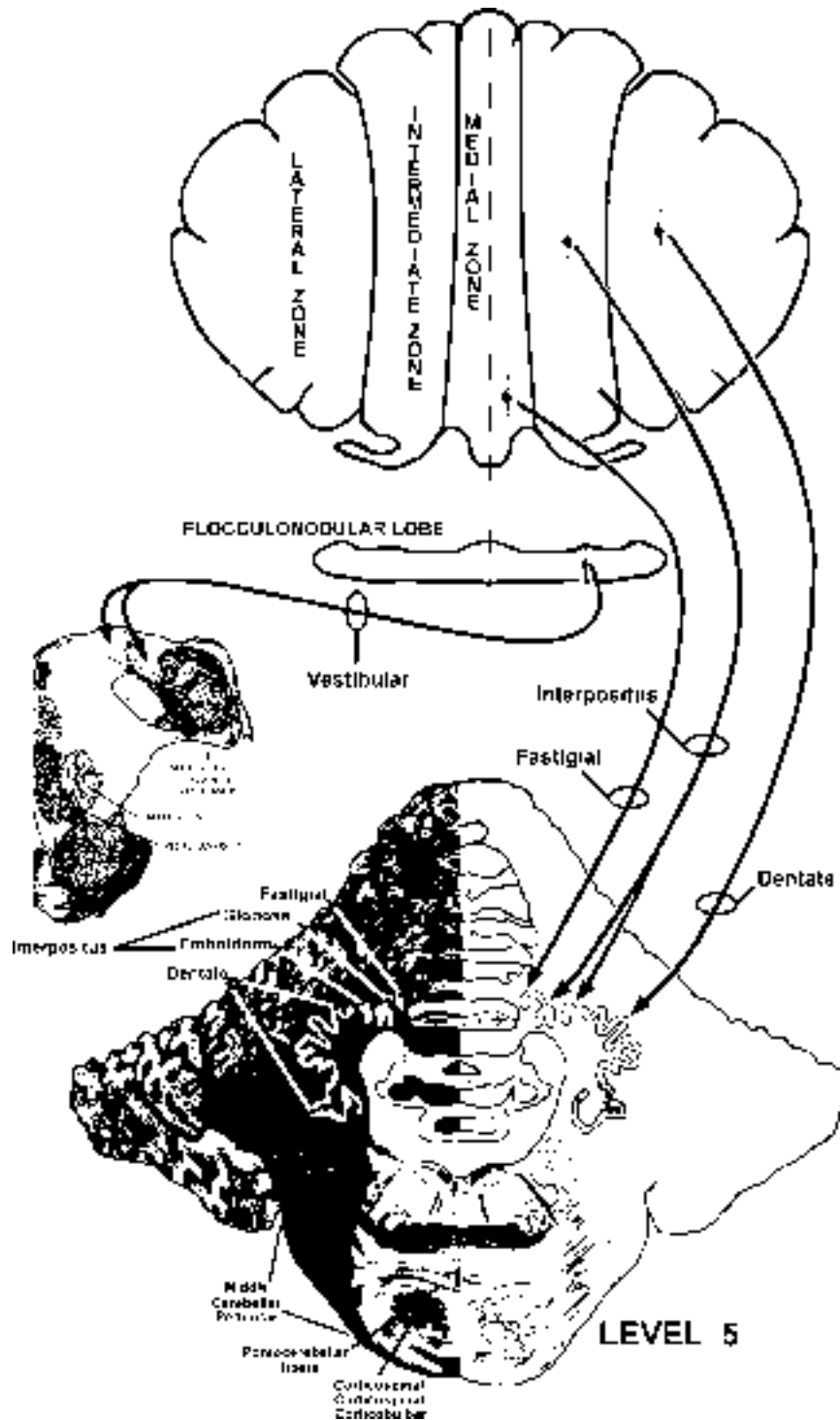
Now we can take the information out of the deep cerebellar nuclei and the vestibular nuclei to where it can do some good, i.e., to the spinal cord, brain stem and thalamus. We already know a lot of this from our discussions of the Superior Cerebellar Peduncle (Point 18) and the Vestibular Nuclei (Point 13).

The **dentate** nucleus projects primarily to the contralateral **VA/VL** nuclei of the thalamus via the **superior** cerebellar peduncle. Cells in VA/VL project to the premotor area (PM) and the supplementary motor area (SMA), both of which are motor "planning" areas. These cortical planning areas then project to primary motor cortex (MI or area 4) and from there the information is conveyed to the corticospinal system.
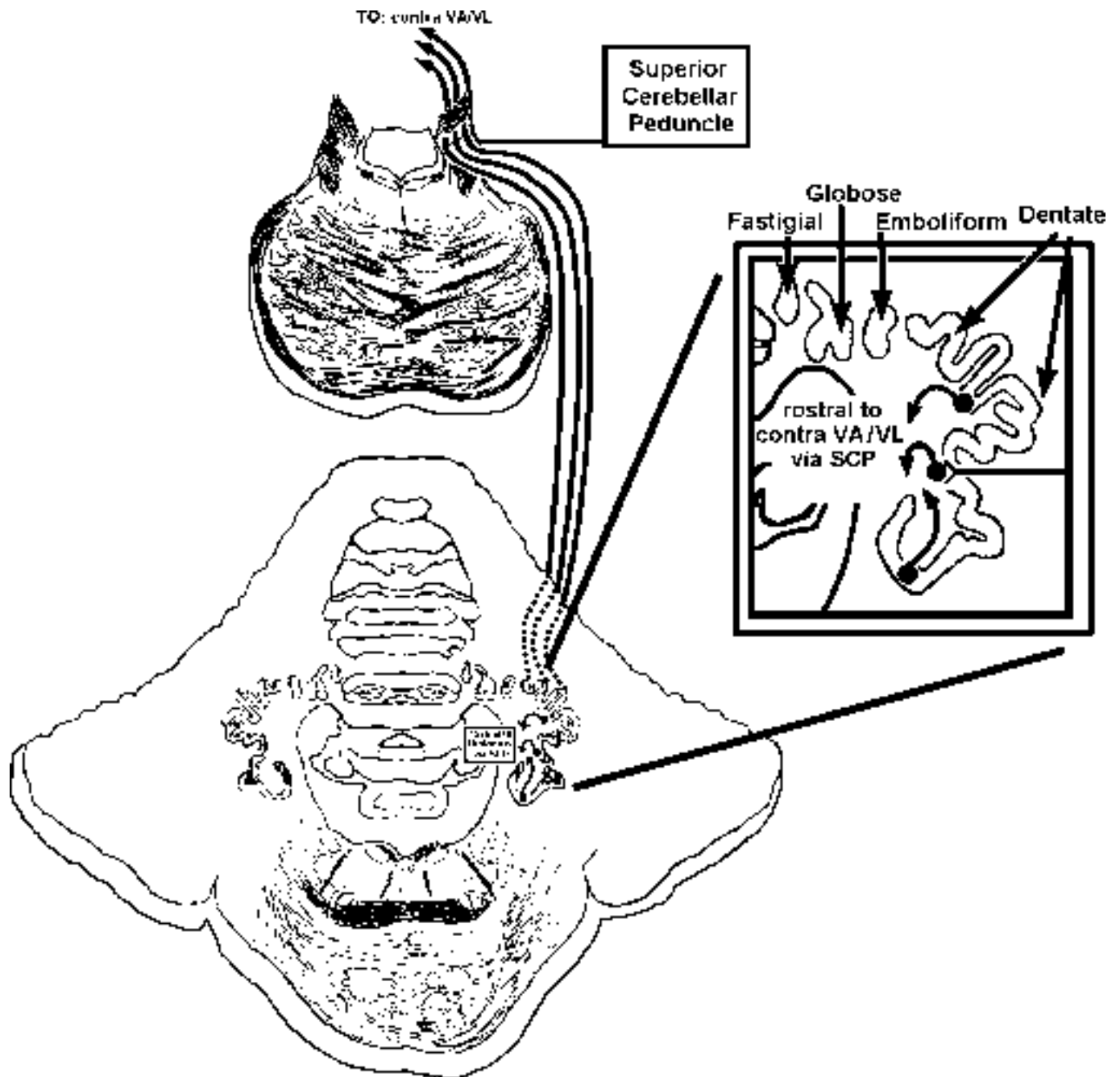
The **interpositus** nucleus projects to the contralateral **red nucleus** via the **superior** cerebellar peduncle. The ruber can then influence the **contralateral** spinal cord via the **rubrospina**l projection. Compared to the dentate, the interpositus influences the motor system more quickly. The interpositus also projects to cells in VA/VL, which in turn project directly to MI for any correction that is needed. The cells in VA/VL that project to PM and SMA receive input from the dentate, while those that project to MI receive their input from interpositus.
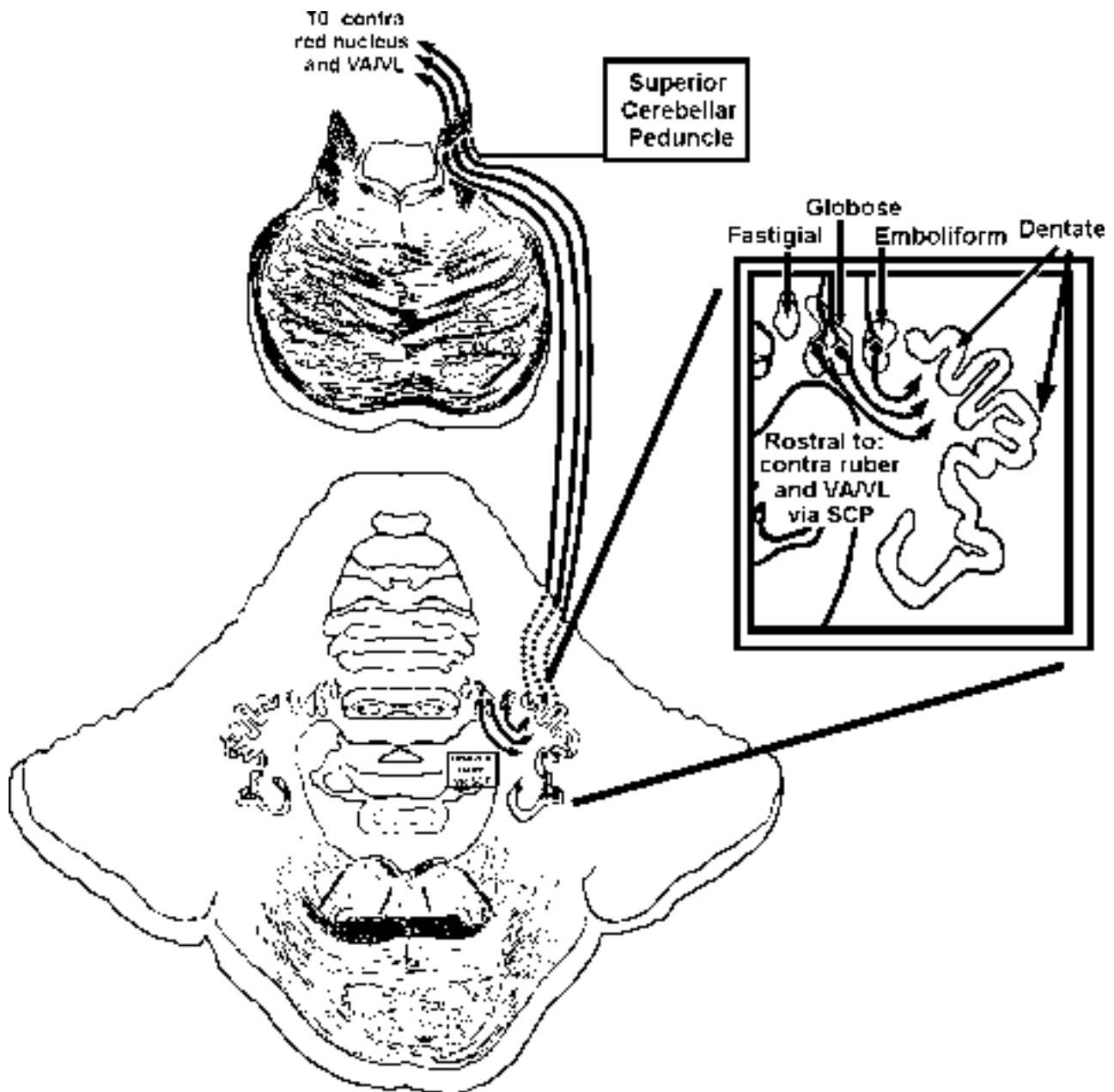
Now for the **FASTIGIAL** nucleus. To exit the cerebellum, the axons of cells in the fastigial nuclei take **two** routes that we did not discuss in the brain stem or spinal cord series of lectures. **Crossing** axons from the fastigial pass to the **vestibular** nuclei and **reticular formation of the pons and medulla** (not illustrated below). The greater number of fibers leaving the fastigial nucleus are uncrossed and pass via the inferior cerebellar peduncle to reach the **vestibular nuclei** and **reticular formation**. The **reticular formation** consists of cells that we did not identify in the brain stem series of discussions. They are kind of "left over", but nonetheless important, cells that project to the spinal cord as **reticulospinal** fibers. These fibers lie in the **ventral** funiculus. I have only illustrated the medullary reticular formation below. Don't worry about the pontine.
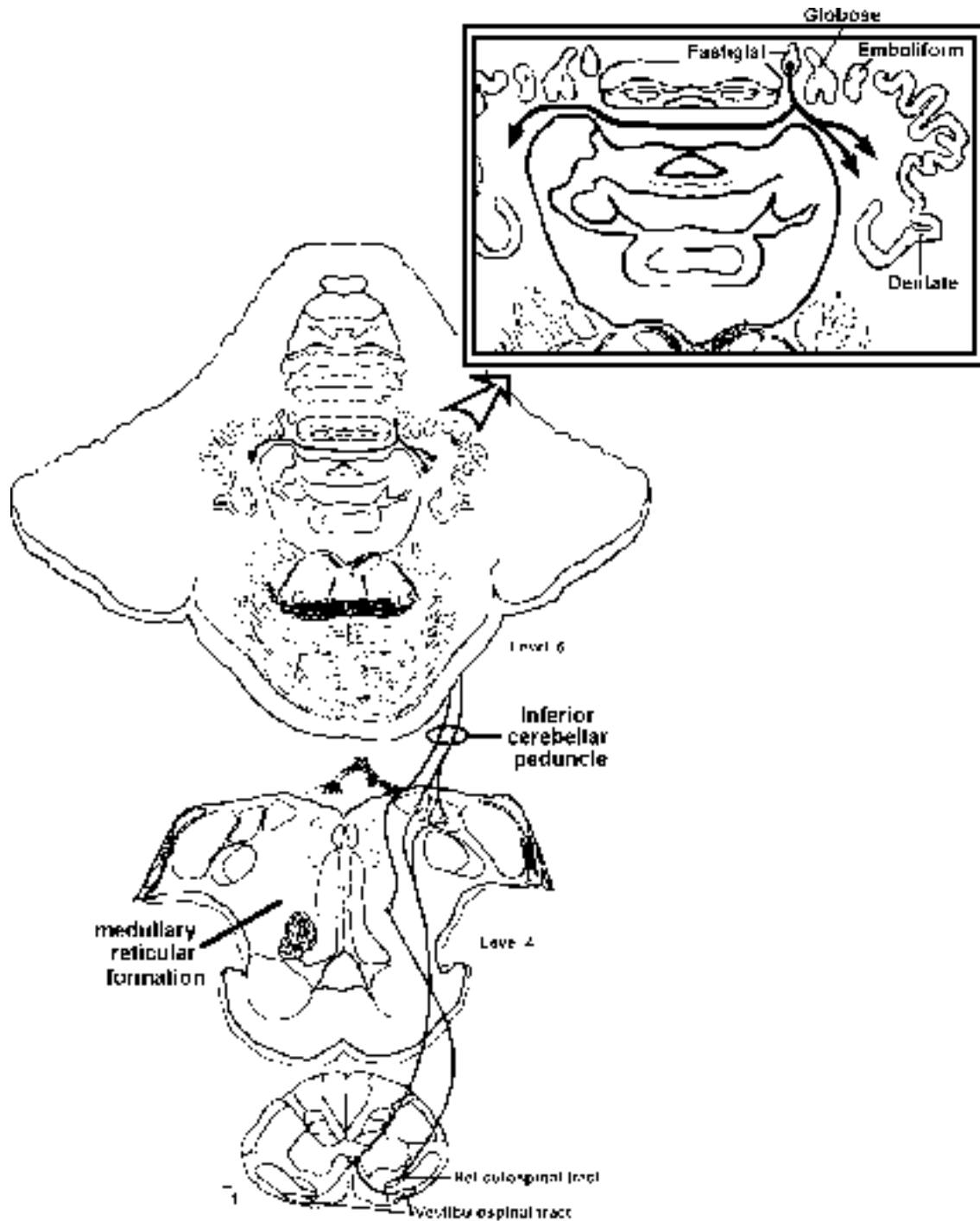
Finally, you already know that the **vestibular nuclei** (deep nuclei of the flocculonodular lobe) project to the **PPRF** and the **spinal cord** (via the MVST and LVST).

Medial Vestibulospinal Tract

Medial Vestibulospinal Tract

1. Cells of origin - medial vestibular nucleus.

2. Pathway is bilateral but ipsilateral projection is more dense.

3. Pathway innervates only cervical spinal cord. Influences mainly neck and axial muscles.

Lateral Vestibulospinal Tract

Lateral Vestibulospinal Tract

1. Cells of origin - lateral vestibular nucleus.

2. Pathway is uncrossed and courses the entire length of the spinal cord. Located in the ventral funiculus.

3. Pathway enables vestibular apparatus to influence the ipsilateral proximal limb muscles.

(LVST)

IN THE VENTRAL FUNICULUS

UNCROSSED

Putting it all together

Now, let's figure out what cerebellar circuitry might accomplish. I will use the example of the visually guided movement of reaching and grasping an apple from an apple tree. The visual information about the apple is carried from the retina to the cerebral cortex via pathways that we will discuss later in the course. This information eventually is sent to the **posterior parietal cortex**. Information from the **PPC** is conveyed to the PMl and in turn to the SMA. All of these planning areas project to the pons (corticopontine). The pontine grey neurons then relay the planning information to the contralateral **lateral zone** of the cerebellum via pontocerebellar fibers, which **everyone** knows by now are mossy fibers. The messages from these planning areas goes through the cerebellar circuitry. The Purkinje cell then sends a message to the dentate and the dentate projects to the VA/VL. This new message headed for VA/VL contains planning information for reaching out and grasping the apple. The message in VA/VL is then relayed back to the PMl and SMA which in turn feed into the primary motor cortex (area 4; the cells of origin of the corticospinal tract). Remember all of this happens before any movement has taken place.

You might ask, "what does the lateral cerebellum contribute to the planning that is not processed by PPC, PMl amd SMA? One hypothesis is that the lateral zone is involved in the storage and/or retrieval of long-term memory for motor skills. That is, circuitry in the lateral zone "learned" something about the movement that can now assist the PMl and SMA. Thus, when SMA, PPC and PMl information reaches the lateral zone (via corticopontine and then pontocerebellar fibers), specific cerebellar circuits that were laid down when the movement was initially learned are activated. So, information about the planned movement is contained not only in cortical areas but also in the lateral zone of the cerebellum.

Lesions of the lateral zone of the cerebellum and dentate result in errors in the **direction, force, speed, and amplitude of movements**. (Interestingly, these uncoordinated movements are being carried out by a healthy corticospinal tract. It is just that the corticospinal tract is receiving bad information). The "priming" of the corticospinal tract by the dentate is lost. It takes longer to get the movement going, the appropriate muscles contract for too long, and the movement stops too late. The result is incoordination or ataxia, which includes several symptoms or deficits. First there is **Decomposition of movements**, which means that instead of a nice smooth movement, the movement consists of jerky parts of the movement. **Dysmetria**, also called **past-pointing**, occurs when the patient tries to touch their nose with their finger. There is an inability to perform rapid alternating movements (pronation/supination) called **dysdiadochokinesis**. **Rebound phenomena** can be seen when you hold the patients tensed arm away from his/her sternum and chest and then let go. It will fly into their sternum. There also is tremor during the uncoordinated movement. This is called movement, or **intention tremor**. It is hard for me to explain why this might occur with lateral zone lesions but it might be due to the fact that there are problems in correctly stopping movements. This results in the movement going too far, after which there is a correction and then oscillations occur.

Now we have the planning signals from the lateral zone to MI. Information from MI is conveyed to cells in the spinal cord via the **corticospinal tract.** This information that is sent to the spinal cord from MI is also conveyed to the pontine grey (corticopontine fibers) and in turn to the **intermediate** zone of the cerebellum. As the movement to reach and grasp the apple evolves, the dorsal spinocerebellar and cuneocerebellar pathways convey what the muscles are really doing as

they reach out and grasp the apple. This incoming sensory information (what the muscles are actually doing) is then compared to the MI-corticospinal signal (conveyed to the intermediate zone via the corticopontine-pontocerebellar fibers) regarding what the muscles are **supposed** to be doing. If necessary, corrections are conveyed from the intermediate zone, via nucleus interpositus, to the red nucleus (rubrospinal tract, fast corrections) and MI (corticospinal tract).

The computations occurring in the intermediate zone involve mossy fiber barrages associated with the pontocerebellar fibers carrying information from MI about the **intended movement.** This information is somehow "compared" with information conveyed via the dorsal and cuneocerebellar fibers (what is really happening to the muscles). The Purkinje cell signals being sent to interpositus mix with the direct signals from mossy and climbing fibers, and an ongoing correction signal is sent to the red nucleus (quick adjustments via the rubrospinal tract) and back to MI (slower adjustments). This is carried from interpositus via the superior cerebellar peduncle.

Lesions of the intermediate zone and nucleus interpositus are thought to result in similar deficits as those in the lateral zone and the dentate. Such lesions interrupt the ability of the cerebellum to correct movements once they are started. In contrast to cells in the dentate nucleus, cell in the interpositus fire **after** the movement has begun. Such cells are involved in updating ongoing movements versus planning such movements (dentate).

The **medial zone** receives mainly dorsal spinocerebellar and cuneocerebellar information, and projects to the reticular nuclei and the vestibular nuclei. Lesions of this zone will result in a loss of fastigial **excitatory** drive to the ipsilateral vestibular nuclei, as well as the reticular nuclei. This means that the opposite vestibular nuclei are dominating. You know what that means as far as stumbling and nystagmus. CLUE-**ipsilateral** stumbling and **contralateral** nystagmus. In addition to the balance problems, the loss of inputs to the reticular nuclei has a powerful affect on the control of postural muscles which causes instability of the axial musculature.

Finally, The influence of the **vestibulocerebellum** (**flocculonodular** lobe) on the vestibular nuclei also plays a role in posture and balance. Remember that the Purkinje cells in the flocculonodular lobe are inhibiting the vestibular nuclei (while neurons in the fastigial nucleus are exciting them). Therefore a **lesion** of the **right** vestibular zone (or lobe) will "release" the **right** vestibular nuclei from inhibition. Thus the right vestibular nuclei are in dominance. You can take it from here regarding the directions of stumbling and nystagmus.

A classic sign of cerebellar damage is a decrease in tone (hypotonia). While this **hypotonia** is thought to result from malfunctioning of the descending control over the gamma efferent system, I will not discuss this any further.

Finally, there is incoordination of speech following cerebellar damage. This is called **dysarthria**.

WHAT ABOUT THE OLIVE?

Ever since the inferior olive first appeared back there in the brain stem, we have said "you will learn more about the olive later in the course." Well, here we are!! You already know that it projects to the contralateral cerebellum and the axons end as **climbing fibers**. Also, you know that olivocerebellar fibers terminate **throughout** the cerebellar cortex i.e., **they reach all four zones**. You even know a little bit about the circuitry of climbing fibers, in that they target deep nuclei and climb right up those Purk cells.

There is evidence that climbing fibers in the flocculonodular lobe might play a role in the plasticity of the **vestibulo-ocular reflex** (VOR; remember Point #13?). In this instance, plasticity refers to changes in the circuitry/functioning of the VOR. Hopefully you remember that the VOR helps stabilize the visual image on the retina as the head moves. So, a quick head movement to the **right** results in a compensatory horizontal conjugate eye movement to the **left**.

Now, consider what happens when you get a new pair of glasses. Say that they magnify things more than your old pair. This means that a **larger** compensatory eye movement is needed for the same degree head movement. Immediately after putting them on you notice things are a bit blurry and you might get dizzy. Remember, everything in the visual field is now **bigger** than before, so that during a head movement (over a certain number of degrees) to the **right**, the spot you are fixating on will move **more** to the **left** than before. Thus the eye movement to the **left** that is in reaction to the head movement to the **right** will **NOT** keep the image stable on the retina. The VOR is functioning as if you still have on your old glasses and the "gain" of the VOR is not large enough to move the eyes far enough to the **left** to stabilize the image. (Gain just refers to how much the eyes move in response to a certain head movement.

As you know, you do adjust after wearing the new lenses for a few hours/days. It is thought that this adjustment or adaptation of the gain is carried out by the olivocerebellar fibers that reach the flocculonodular lobe. For instance, a person who wore a new pair of glasses that were 2X the magnifying power of his/her old ones was found to have a VOR gain of **1.8** after a few days (1.0 is normal). How did this happen? You know that the vestibular nuclei receive information from the semicircular canals/CN VIII. They send the information to the flocculonodular lobe of the cerebellum via mossy fibers and also project to the contralateral PPRF, which in turn projects to the abducens nucleus. Thus, head **right**, increased firing of right CN VIII, left PPRF and left abducens; both eyes then go **left**.
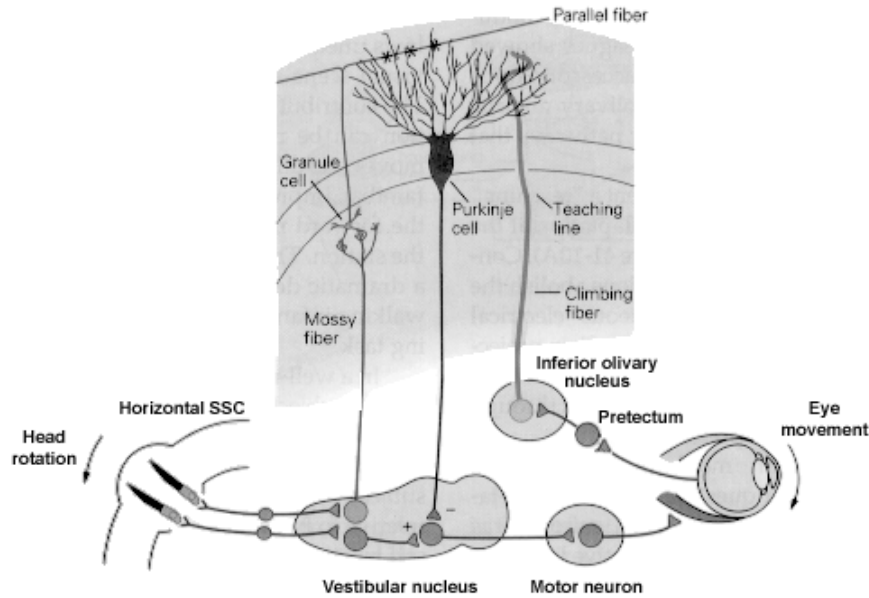
When the eyes move to the left, cells in the retina send information to an area of the rostral brain stem called the **pretectum**. These pretectal cells can tell if the eyes and head movements match. If they don't match, there is slippage/blurring of the image and the pretectal cells know it. They in turn tell the inferior olive about the slippage and the climbing fibers comprise a "teaching line" to instruct the Purkinje cells to fire **LESS**. They would do this by modulating the efficiency of the mossy fiber/granule cell input from the vestibular nuclei. If the gain of the VOR is too small for the head movement (new glasses), the climbing fiber input would somehow **decrease** the efficiency of the vestibular mossy fiber/granule cell/parallel fiber input to the cerebellum and the Purks would fire less. This would means **less** inhibition on the vestibular nuclei and a slightly **bigger** compensatory eye movement to the **left** (the degrees of head movement did not change). This would stabilize the image on the retina during the head movement. **It has been found that no such adaptation of the VOR can occur following lesions of the flocculonodular lobe.**

Granted, this is just the flocculonodular lobe and nothing has been said about olivocerebellars in the other three zones. Well, studies are in progress, but right now you have to be satisfied with the flocculonodular lobe.

REMEMBER—CLIMBING FIBERS=MOTOR LEARNING

8. Which of the following statements is correct?

    A. a Babinski sign is seen following cerebellar lesions
    B. cerebellar lesions result in atrophy
    C. a cardinal sign of cerebellar damage is hypotonia
    D. there are no speech problems following cerebellar lesions
    E. dysdiadochokinesia is another name for muscle weakness

9. Which of the following statements is correct?

    A. rebound phenomena refers to the inability to grab a rebound above the rim
    B. past pointing is a cardinal sign of corticospinal damage
    C. intention tremor is seen following lesions of the substantia nigra
    D. resting tremor is seen following lesions of the cerebellum
    E. atrophy is not a sign of cerebellar disease

10. Which of the following statements is correct?

    A. hypotonia could never result from defects in the gamma efferent system
    B. spasticity is associated with lesions of the lateral cerebellum
    C. both cerebral cortex and cerebellar deficits involve the ipsilateral side of the body
    D. weakness is not observed in cerebellar disease
    E. ataxia is a cardinal sign of cerebellar disease

11. Which of the following statements is correct?

    A. the fastigial nucleus projects to the red nucleus
    B. the presence of nystagmus suggests damage to the corticospinal tract
    C. the inferior olive is the sole source of climbing fibers
    D. the interpositus nucleus projects to the vestibular nuclei via the inferior cerebellar peduncle
    E. nystagmus is a sign of lower motor neuron disease

12. Which of the following statements is correct?

    A. a lesion of the **right** side of the flocculonodular lobe will result in **left** nystagmus
    B. a lesion of the **right** side of the flocculonodular lobe will result in staggering to the **right**
    C. a lesion of the **right** fastigial nucleus will result in staggering to the **left**
    D. a lesion of the **right** fastigial nucleus will result in **right** nystagmus
    E. a lesion of the **right** fastigial nucleus and the **right** vestibular nuclei will (in different cases) result in nystagmus of the **same** direction

Level 5
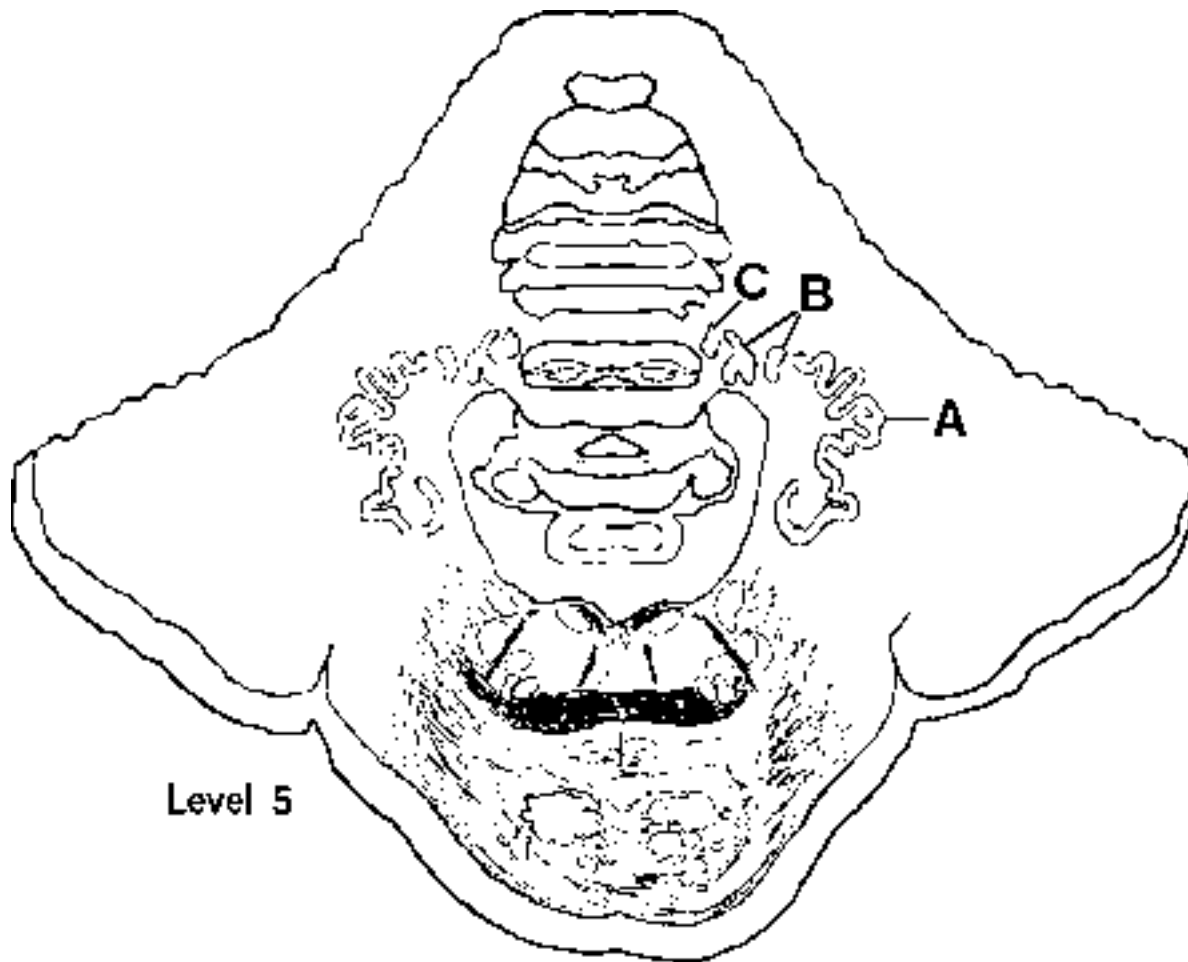
13. Which of the following associations are true?

A-planning
A-updating
A-posterior parietal cortex
A-VA/VL
A-PMl, PPC and supplementary motor cortex
A-reticular formation
A-vestibular nuclei
A-fires after movement
B-ruber
B-updating
B-reticular formation
B-primary motor cortex
B-vestibular nuclei
B-comparing and updating
B-fires before movement
C-nystagmus
C-reticular formation
C-ruber
C-VA/VL
C-bilateral efferent projection (but mostly ipsi.)

14. Which of the following is associated with cerebellar lesions?

    A. left nystagnmus following a lesion of the right flocculonodular lobe
    B. Babinski sign
    C. right nystagnmus following a lesion of the right fastigial nucleus
    D. hyperreflexia
    E. hemiplegia
    F. resting tremor
    G. apraxia
    H. rigidity
    I. bradykinesia
    J. hemiballism
    K. chorea
    L. atrophy
    M. anesthesia
    N. analgesia
    O. pronator drift
    P. intention (movement) tremor
    Q. rebound
    R. dysdiadochokinesia
    S. past-pointing

15. Which of the following statements regarding climbing fibers is **TRUE**?

    A. those ending in the flocculonodular zone arise from the inferior olive
    B. those ending in the medial zone arise from the inferior olive
    C. those ending in the intermediate zone arise from the inferior olive
    D. those ending in the lateral zone arise from the inferior olive
    E. all of the above are **TRUE**

16. Which of the following statements regarding mossy fibers is **TRUE**?

    A. those reaching lateral zone are solely pontocerebellar
    B. those reaching intermediate zone are pontocerebellar, DSCT and CCT
    C. those reaching medial zone solely DSCTand CCT
    D. those reaching the flocculonodular zone are from the vestibular ganglion and vestibular nuclei
    E. all of the above are **TRUE**

17. Which of the following statements is **TRUE**?

    A. Purkinje cells in the lateral zone excite the dentate
    B. Purkinje cells in the medial zone inhibit the vestibular nuclei
    C. Purkinje cells in the intermediate zone excite the fastigial
    D. Purkinje cells in the flocculonodular zone inhibit the fastigial
    E. Purkinje cells inhibit deep nuclei

18. Which of the following statements is **TRUE**?

    A. deep cerebellar nuclei excite their targets
    B. deep cerebellar nuclei inhibit their targets
    C Purkinje cells excite their targets
    D. deep cerebellar nuclei are inhibited by incoming climbing fibers
    E. deep cerebellar nuclei are inhibited by incoming mossy fibers

19. A 60 y.o. male presents with complaints of an unstable gait and some swaying of the trunk. His history is unremarkable except that for the past 15 years he has had increasing use of alcohol to his present level of approximately four hard liquor drinks per day. Most of his neurological exam is unremarkable. His walking gait is broad based, with short regular steps and his trunk is slightly inclined forward. A test of reflexes demonstrates some hypotonia in the proximal muscles, but nearly normal reflexes. He claims that he walks fine on flat ground, but has difficulty and stumbles a lot when he is on uneven ground. He says that people have commented about his gait for many years, but he is just beginning to think something may be wrong. Which of the following could be true of this patient?

    A. he probably has a tumor pressing on the superior cerebellar peduncle
    B. he probably has degeneration of the vermal regions of the cerebellum due to alcohol consumption
    C. an MRI of his cerebellum would show increased space between the folia of the vermal region and the anterior lobe
    D. all of his signs indicate damage to the lateral and intermediate zones of the cerebellum
    E. two of the above are true

20. A 45 y.o. woman presents with nausea, and tremor. Her history states she has been mildly hypertensive for many years, and has recently had TIAs (transient ischemic attacks). Her blood pressure is 180/120. A neurological exam shows a slight Horner's syndrome on the right, reduced pain and temperature sensation on the left, but all other sensations are normal. A motor exam demonstrates reduced tone in the right upper and lower limbs, dysmetria and past pointing, and an intention tremor on the right side. Movements of her right limbs seem to be most affected and when asked to perform a rapidly alternating movement with her right hand, she clumsily performs the task. She has a normal flexor plantar reflex bilaterally and nearly normal strength in all her limb muscles. Which of the following could be true of this patient?

    A. the Horner's syndrome and altered pain and temp sensations suggest damage to the ALS in the brainstem.
    B. this patient probably sustained a vascular accident affecting primarily the intermediate and lateral zones of the cerebellum.
    C. the inability to perform rapidly alternating movements is called dysdiadochokinesis.
    D. two of the above are true
    E. three of the above are true

CEREBELLAR PROBLEM SOLVING ANSWERS

1. A. superior cerebellar peduncle
   B. ipsilateral deep cerebellar nuclei

2. A. inferior cerebellar peduncle
   B. OCT, DSCT, CCT, VCT

3. A. middle cerebellar peduncle
   B. contralateral pontine grey

4. A. flocculonodular, medial, intermediate, lateral
   B. intermediate, lateral

5. **A.** none   **B.** no   **C.** B and D   **D.** B and D   **E.** A   **F.** no   **G.** no

6. A. motor, posterior parietal, premotor (SMA and PMl)
   B. medial, intermediate
   C. T3 and below (contra)
   D. intermediate, lateral
   E. no

7. A. flocculonodular
   B. false
   C. inferior, restiform
   D. vestibular ganglion, vestib. nuc.
   E. true

8. C	**13. A.** T; F; T; T; T; F; F; F;	**17. E**
	B. T; T; F; T; F; T; F;	
9. E	**C.** T; T; F; F; T	**18. A**
10. E	**14. P,Q,R,S**	**19. E (B and C)**
11. C	**15. E**	**20. E**
12. E	**16. E**	

Your colleague's who have taken this course before you have been so intrigued by the nervous system that many have written unforgettable songs. I have included one below and hopefully the authors or their friends will sing them sometime during this module.

YESTERDAY

Micheal Gelman and Alex Romashko
Class of 2000

Yesterday,
My cerebellum said "Come on let's play".
But now my lateral zone's gone away.
No input there from pontine grey.

Suddenly,
I've got no info from my PPC.
I can't wake up my CST.
My movements all come jerkily.

I don't plan too well, with VL or with VA.
Past-point, and I've found I rebound when held away.

There's no doubt,
In my premotor all lights are out.
It gets no news to think about.
My OCT just has no clout.

When I move, I go dysdiado-chokinetically.
Dentate cells, I've heard, get no word from Purkinje

Yesterday,
I moved smoothly, didn't go astray.
Now I can't get through the SMA.
Intention tremor's here to stay.

Mmm mmm mmm mmm mmm mmm mm…

The following pages are a detailed account of the current understanding regarding the intrinsic circuitry of the cerebellum. I have deliberately left it out of the discussion because it is not necessary for a good understanding of what the cerebellum does for motor control. I encourage you to read it for its academic merit, but you **will not** be tested on this information.
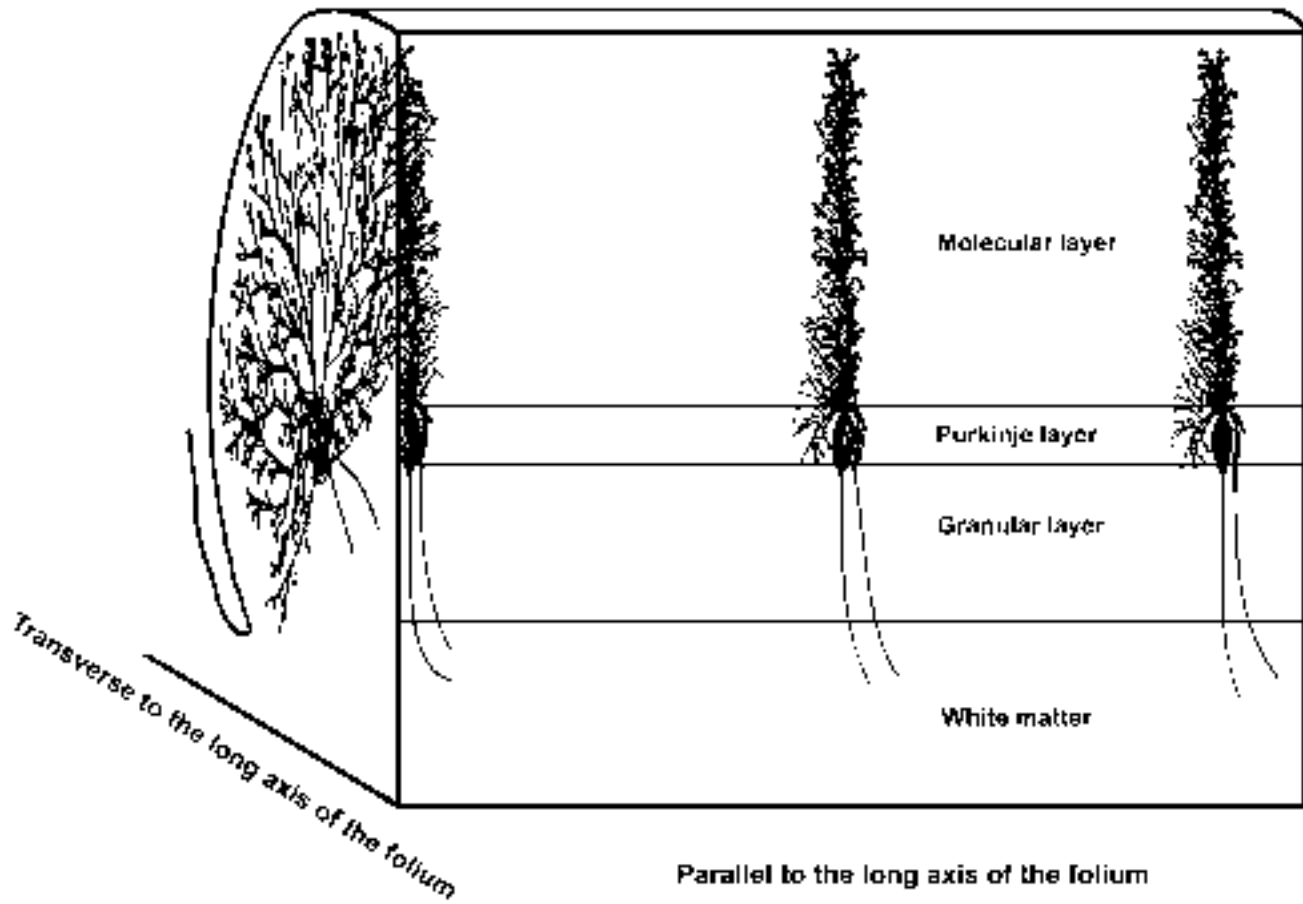
Circuitry (optional)

The internal circuitry of the cerebellum has been worked out in exquisite detail. Although it is not necessary for an understanding of cerebellar function, it may aid in your overall understanding of the complexity of the nervous system. The following is a complete description of this internal processing.
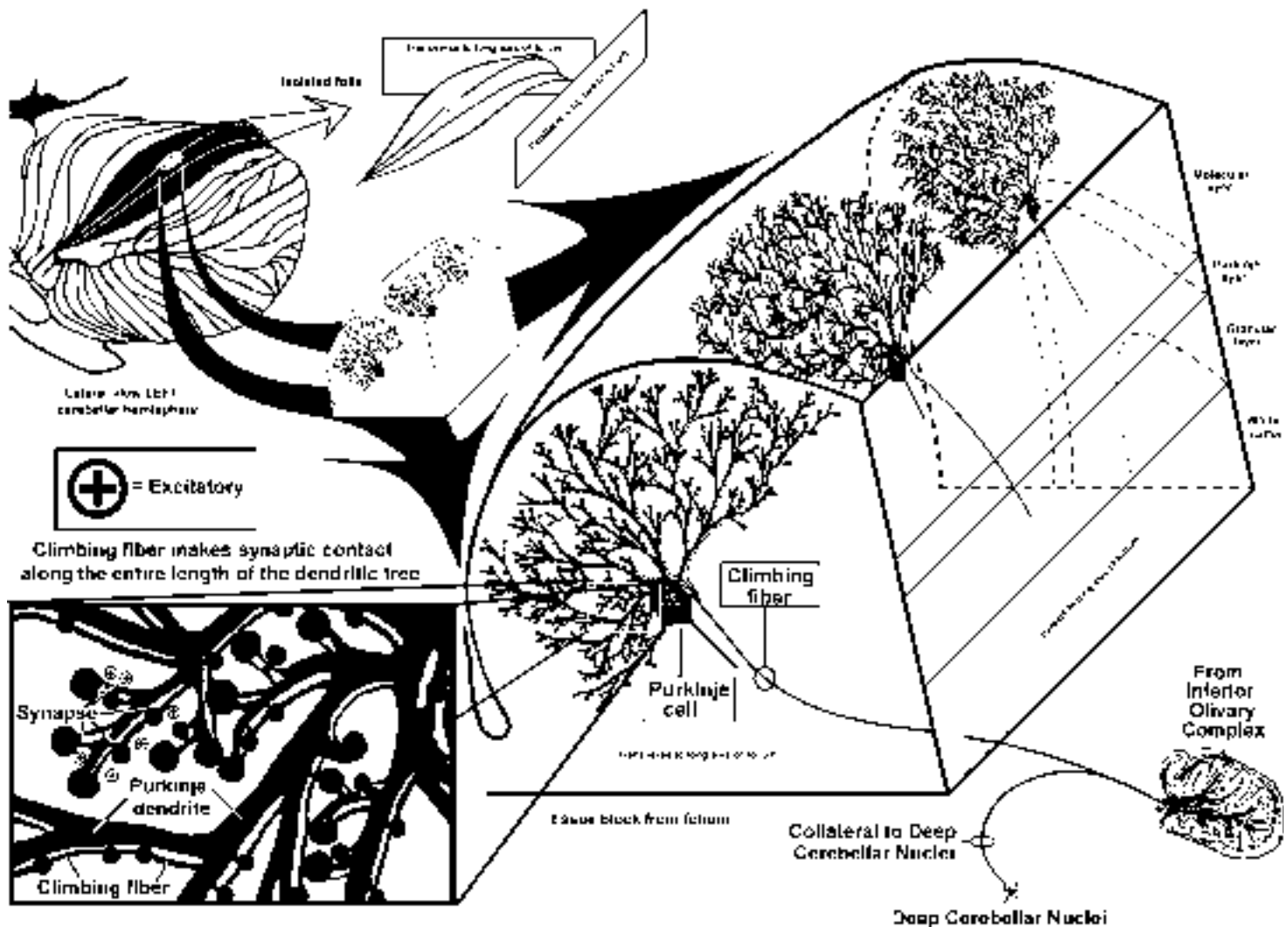
Before looking at the internal cerebellar circuitry, we need to **examine** how all of the little cerebellar folds or gyri, called folia (singular = folium) are organized. In the drawing below to the left are 3 isolated cerebellar folia. From the extracted tissue block at the right you can see that these folia can be sectioned either **PARALLEL** to their **LONG** axes or **TRANSVERSE** to their **LONG** axes. Each single folium is comprised of an outer cerebellar **CORTEX** (bark, peel, husk), which contains three cell layers, **molecular, Purkinje,** and **granule.** This cerebellar **cortex** overlies a deep zone of efferent and afferent fibers that we just call **white matter**. Within this dense aggregation of millions of fibers lie three sets of deep cerebellar nuclei (dentate, interpositus and fastigial). These deep nuclei **ARE NOT** shown in the drawing below, but we have already heard about the dentate and interpositus nuclei when discussing the superior cerebellar peduncle (Point 18). We will return to these nuclei later in the story.

You can see that the dendrites of the Purkinje cells (the most popular cells in the cerebellar cortex) are oriented **TRANSVERSE** or perpendicular to the **LONG** axis of the folium. Spread your fingers out and look at your palm. You are now looking at how a Purkinje cell dendritic tree looks when the folium is sectioned **TRANSVERSE** to its **LONG** axis.

tissue block from folium
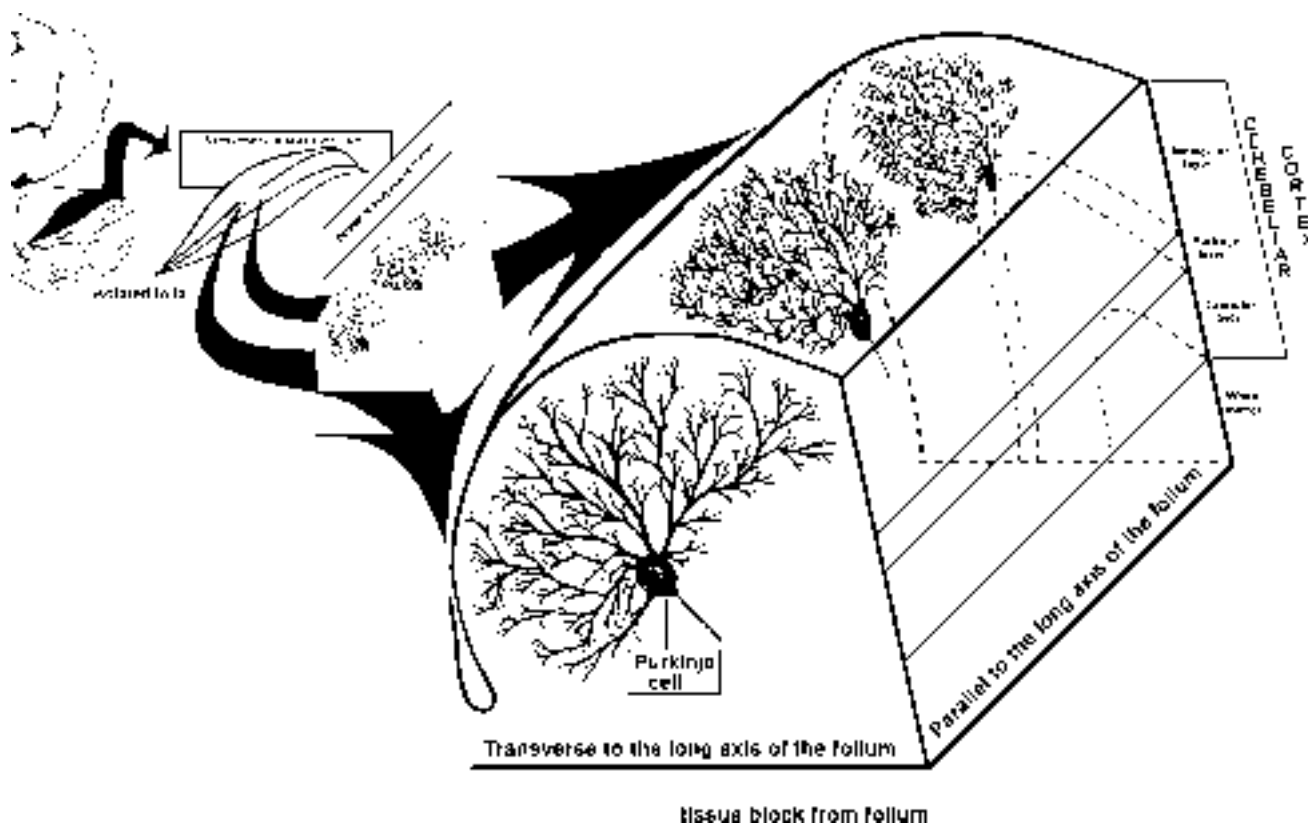
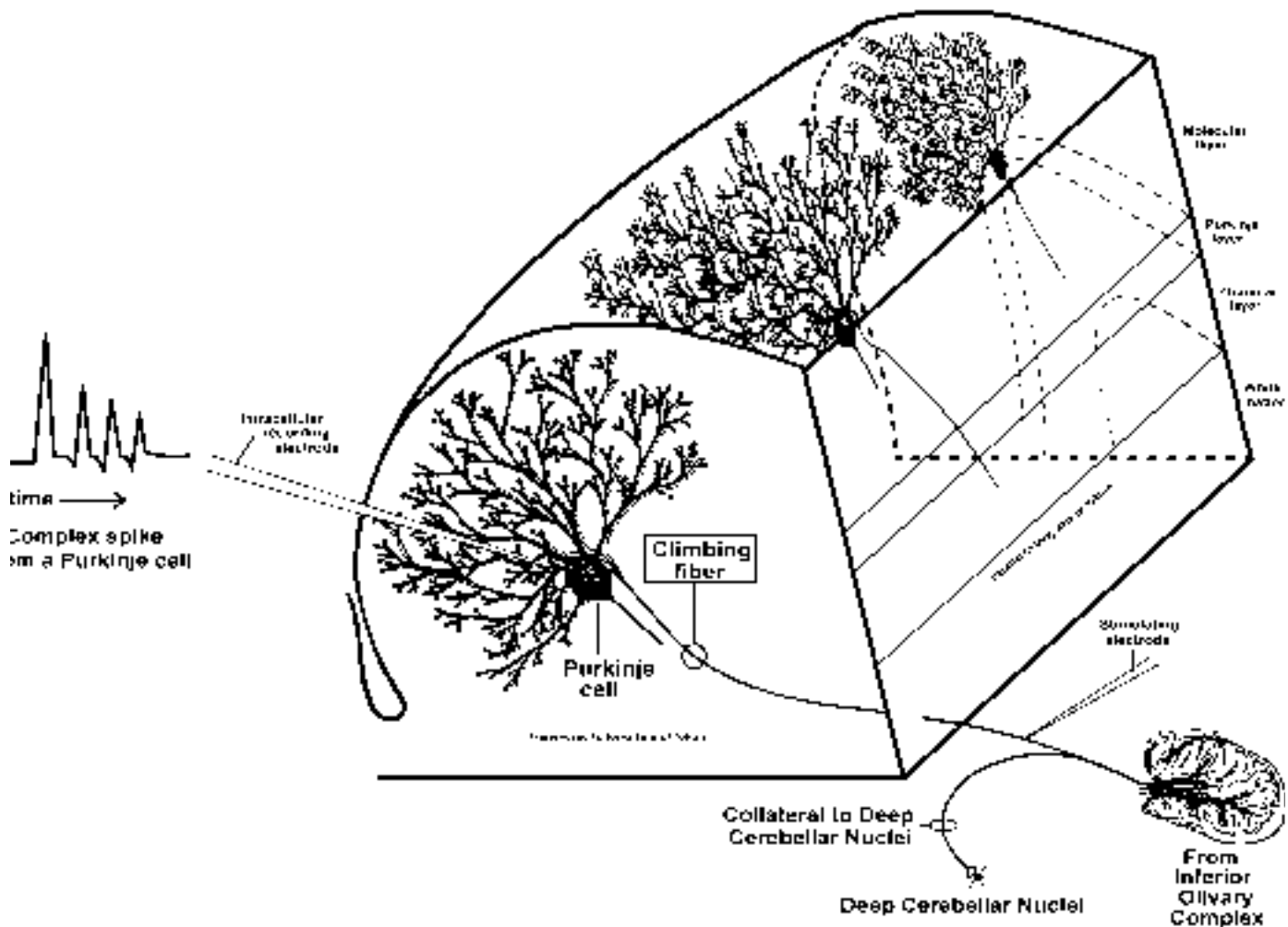Now, rotate your hand 90° and see how the dendritic tree of that same Purkinje cell looks when the folium is sectioned **PARALLEL** to its **LONG** axis. Sadly, you do not see the full extent of the Purkinje cell dendritic tree from this view. This is shown below.

Molecular layer

Purkinje layer

Granular layer

White matter

Transverse to the long axis of the folium

Parallel to the long axis of the folium

Climbing fiber makes synaptic contact along the entire length of the dendritic tree

= Excitatory

Synapse

Purkinje dendrite

Climbing fiber

Climbing fiber

Purkinje cell

From Inferior Olivary Complex

Collateral to Deep Cerebellar Nuclei

Deep Cerebellar Nuclei

Lets now schematize the basics of the internal cerebellar circuitry. First, we can look at an old friend who we first met at level 3 in the brain stem—**THE INFERIOR OLIVE**. Remember that, Dr. Harting told you that cells in the olive have axons that pass to the contralateral cerebellum as **climbing fibers**. These fibers go to all parts of the cerebellum, that is, they are not restricted to a particular zone. The drawing above shows that a climbing fiber sends a collateral to the deep cerebellar nuclei, which is excitatory, and then "climbs" up and like ivy, entwines and synapses all over the dendrites of the Purkinje cell. Each Purkinje cell receives input from only **1** climbing fiber axon, but each climbing fiber axon can split to innervate **several** Purkinje cells. **These climbing fiber-Purkinje cell synapses are excitatory.**

Complex spike from a Purkinje cell. Labels in the figure: Intracellular recording electrode; time; Complex spike from a Purkinje cell; Climbing fiber; Purkinje cell; Molecular layer; Purkinje layer; Granular layer; White matter; Stimulating electrode; Collateral to Deep Cerebellar Nuclei; Deep Cerebellar Nuclei; From Inferior Olivary Complex.

Since climbing fibers have synapses all over the dendritic tree of a Purkinje cell, their total excitatory action is extremely strong. In fact, the synaptic connection between the climbing fiber and the Purkinje cell is one of the most powerful in the nervous system. A single action potential in a climbing fiber elicits a **burst** of action potentials in the Purkinje cells that it contacts. This burst of action potentials exhibited by a Purkinje cell is called a **complex spike**. Climbing fibers are "lazy" (but strong), thus Purkinje cells exhibit complex spikes at a rate of about 1 per second. The illustration above depicts an intracellular recording from a Purkinje cell that has just been turned on by stimulating the climbing fiber a single time. This single climbing fiber stimulus has a powerful effect in that it results in **4 action potentials** (i.e., **complex spike**) of varying amplitudes in the Purkinje cell.
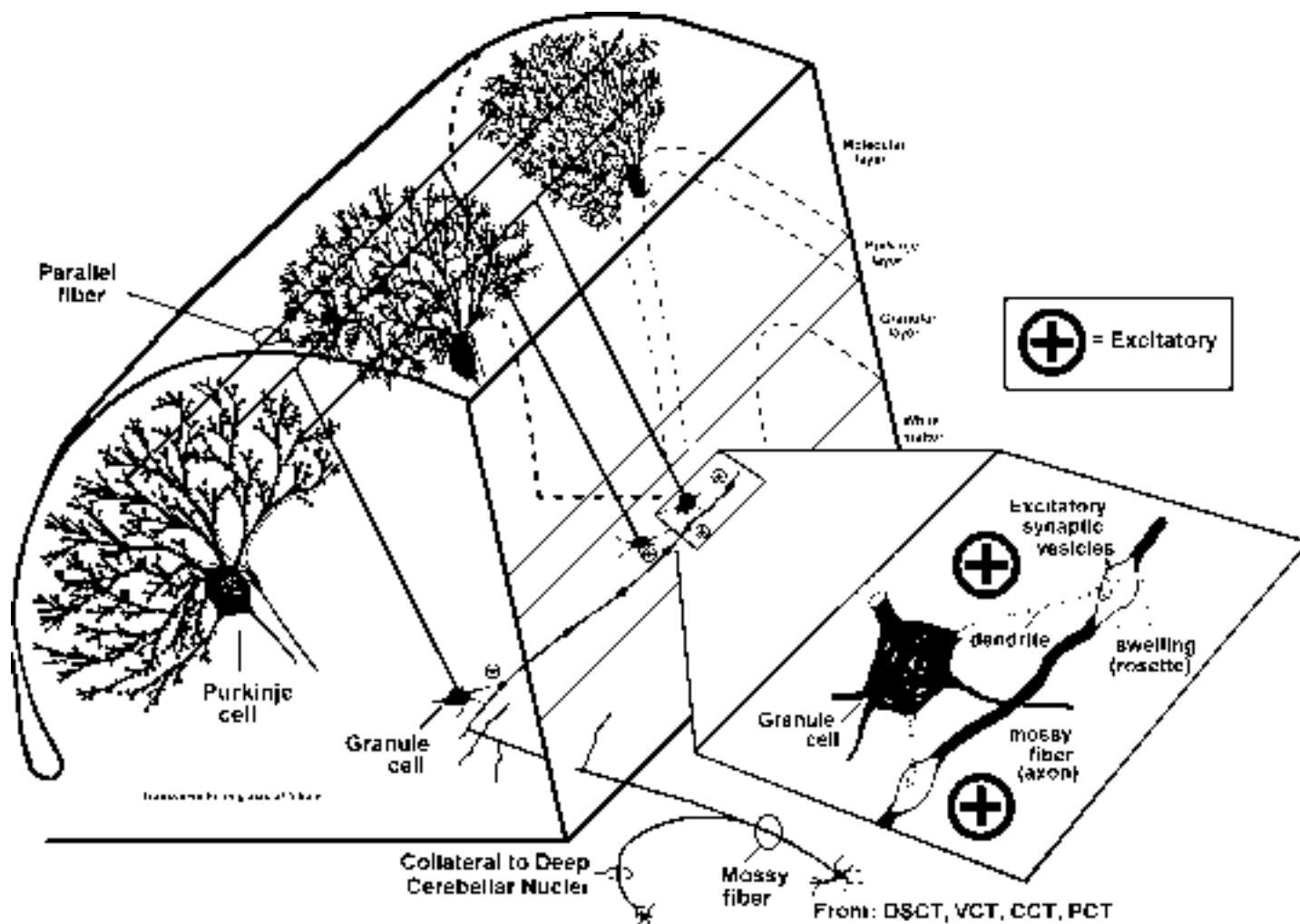
Now, what about branches of the **DSCT**, **CCT**, **VCT** and **PCT** that are destined for the cerebellar cortex. The axons of these inputs are called **MOSSY** fibers. Like climbing fibers, the information carried by mossy fibers is heading for the Purkinje cells. However, unlike climbing fibers, mossy fibers **DO NOT** go directly to the Purkinje cell. Each mossy fiber branches profusely in the white matter and has multiple (up to 50) swellings (resembling moss to the old time neuroanatomists) that contain round vesicles and synaptic thickenings. Each swelling, called a "rosette", is a synapse of the mossy fiber onto the dendrite of a granule cell. In the detail above you can see two rosettes contacting two different dendrites of the same granule cell. These are excitatory synapses. A rosette can also occur where the dendrites of several (up to 15) granule cells are contacted. Each mossy fiber can have up to 50 rosettes. You can see that there is considerable divergence of the mossy fiber signal.

Granule cells have long axons that pass dorsally through the granule and Purkinje, cell layers to reach the **molecular layer** of the cerebellar cortex, where they **bifurcate** and run **PARALLEL** to the long axis of the folium. These fibers, which are called **parallel** fibers, travel at **right** angles to the dendrites of the Purkinje cells (think of telephone lines running through a row of (flattened) trees in the fall after peak color). Each **parallel** fiber synapses upon and **excites** the dendritic spines of numerous Purkinje cells, but the synaptic effect of a **single** parallel fiber upon a Purkinje cell is extremely weak (contrast this with a climbing fiber). How then can the mossy fiber input fire the Purkinje cells? Well, what is needed is for many mossy fibers to fire rapidly and together, which causes many granule cells to fire together, which turns on **lots** of parallel fibers which then excite enough of the spines on a Purkinje cell to result in an action potential. When this occurs, the Purkinje cell exhibits what is called a **simple spike**. Such a spike in a Purkinje cell is shown below. In contrast to those lazy climbing fibers that fire about 1 per second (yet have a very powerful effect upon the Purkinje cell resulting in the **complex spike**), mossy fibers are really "gunners" (I use the term affectionately) in that they are always working. Thus they fire spontaneously and rapidly (50-100 per second) and cause (via the granule cells and parallel fibers of course) Purkinje cells to fire **simple spikes** at the same frequency.
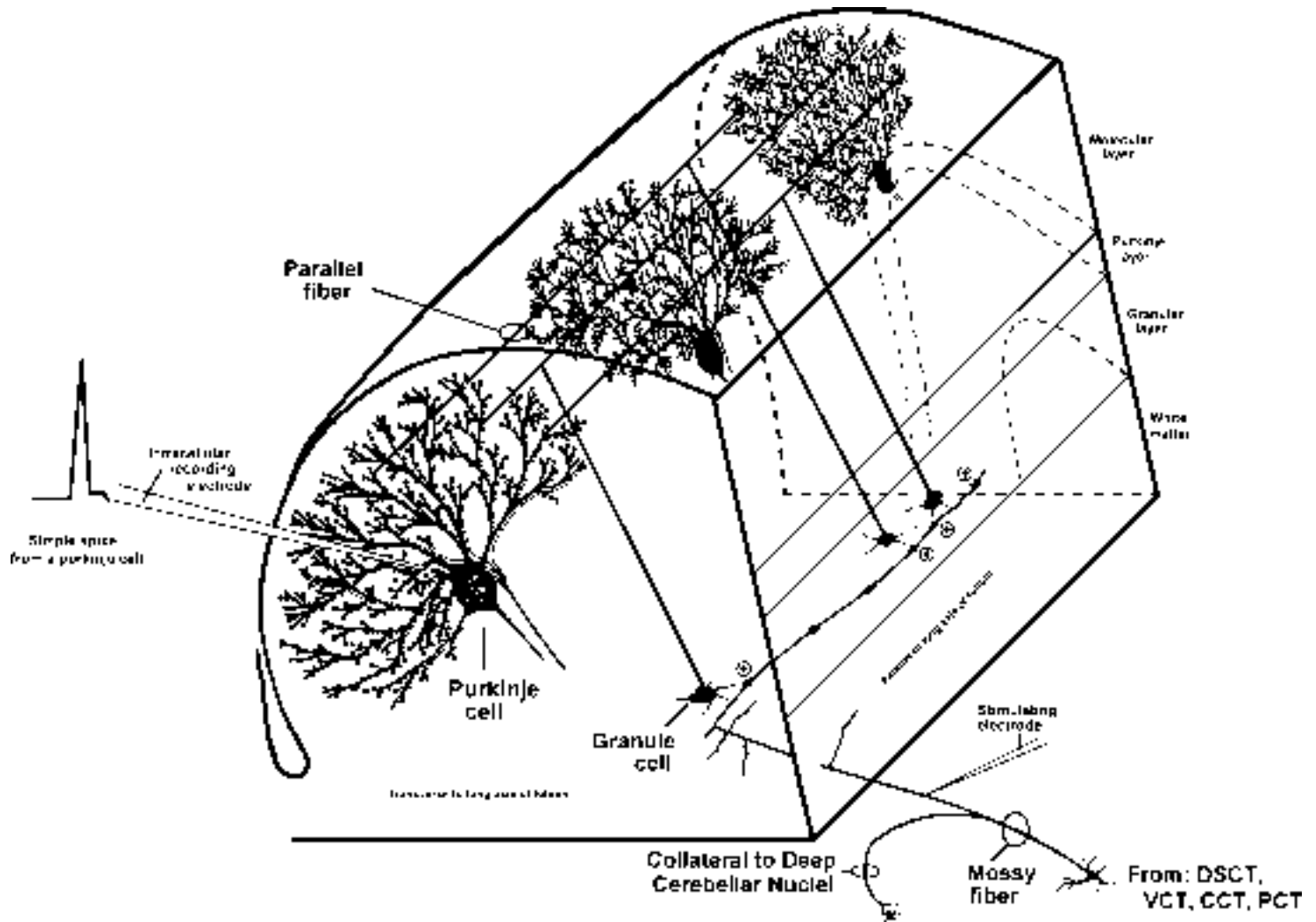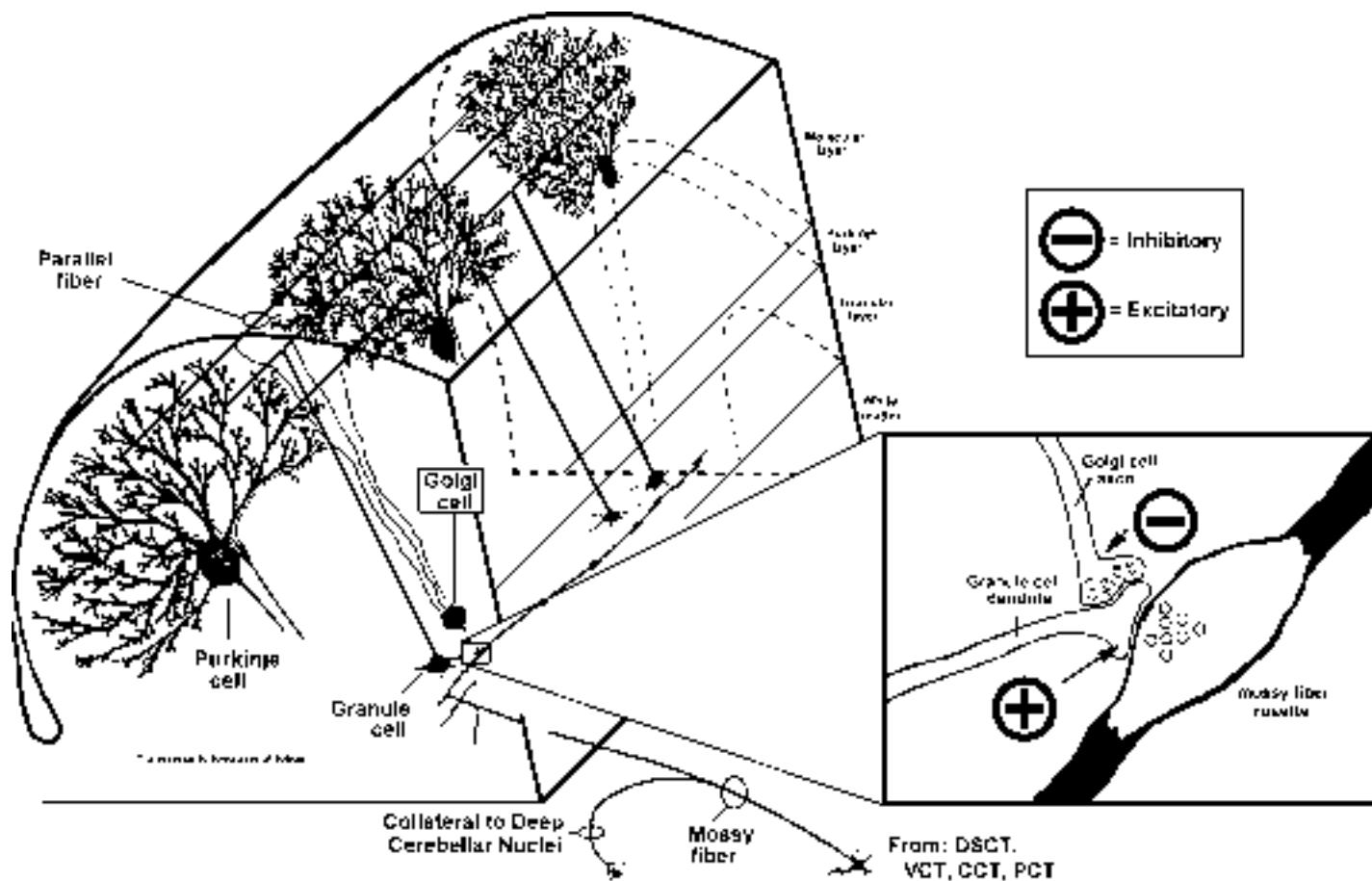
In addition to the climbing fiber and mossy fiber-granule cell-parallel fiber inputs that are **EXCITATORY**, there are cells in the cerebellum that are ***INHIBITORY***. The first cell that we will talk about lies in the granule cell layer and is called a Golgi cell (sorry there is no Golgi cell layer). Compared to the many millions of small granule cells (hence the name granule cell layer), there are relatively few Golgi cells and they are much larger than granule cells. The dendrites of the Golgi cells lie in the **molecular layer** (in no particular plane) and are **EXCITED** by the parallel fibers of granule cells. The axon of the Golgi cell enters into a complex arrangement with the **mossy fiber terminal-granule cell dendrite** (shown above) such that the Golgi cell axon **INHIBITS** (via GABA) the mossy fiber-granule cell relay. This is called **feedback** inhibition, because the Golgi cell inhibits information that is coming **into** the cerebellar circuitry.

The parallel fibers of granule cells (which travel in the molecular layer) also excite the dendrites of **basket** cells. Both the dendrites and somas of the basket cells lie in the molecular layer. These dendrites, like those of Purkinje cells, **lie in a plane that is transverse to the long axes of the folia**. The axons of basket cells also run in this plane (transverse to the long axis of the folia) and terminate on the somas of the Purkinje cells. The inhibition of Purkinje cells by the basket cell axons is called **feedforward inhibition**. Remember, **inhibition of the input=feedback** (Golgi cell axon-mossy fiber-granule cell relay) while **inhibition of the output=feedforward** (basket cell axon-Purkinje cell initial segment). Another way to look at these types of inhibition is whether the inhibiting cell is acting on an "earlier" or "later" cell in the cerebellar circuitry.
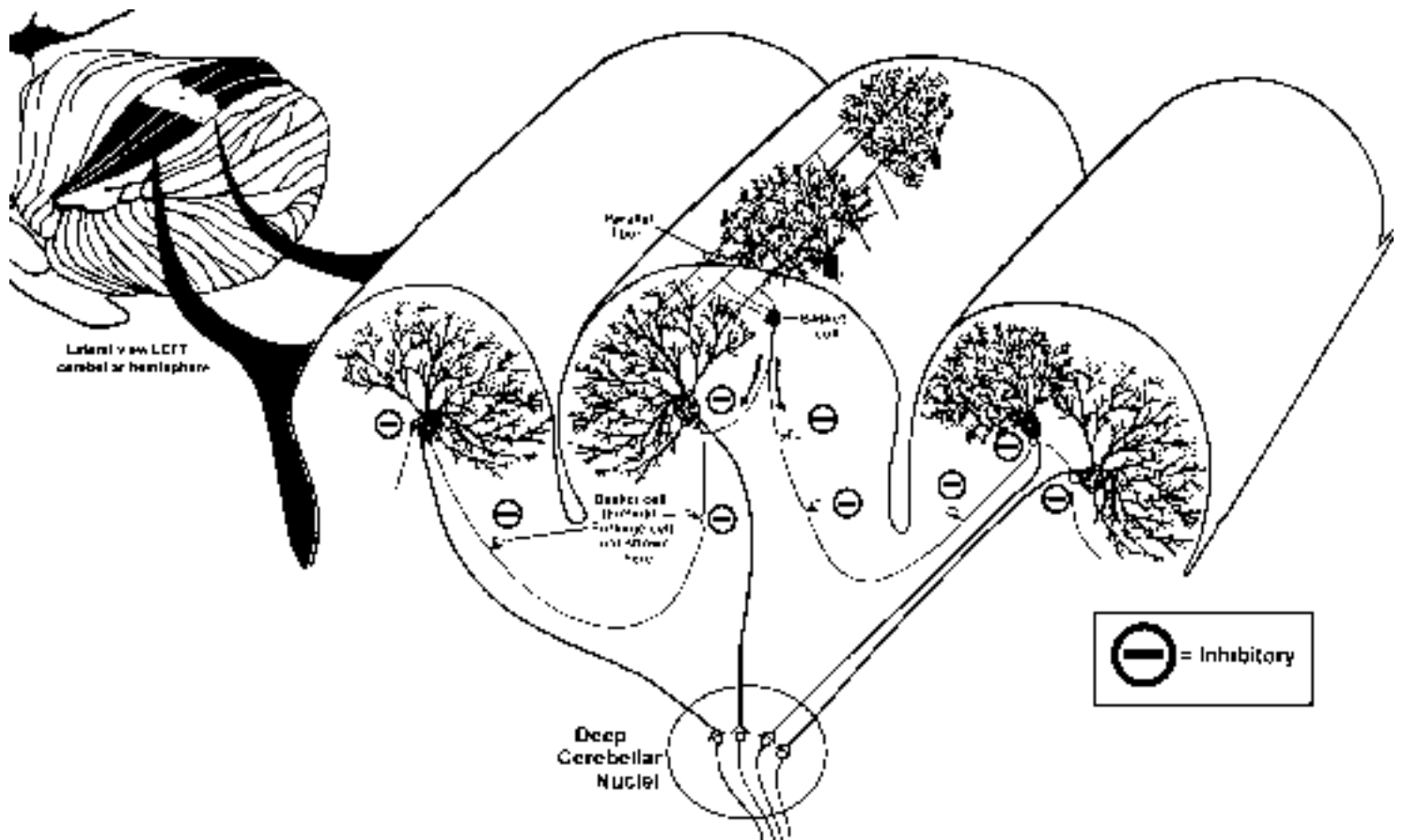
Those Crazy Inhibitory Cells

A

B
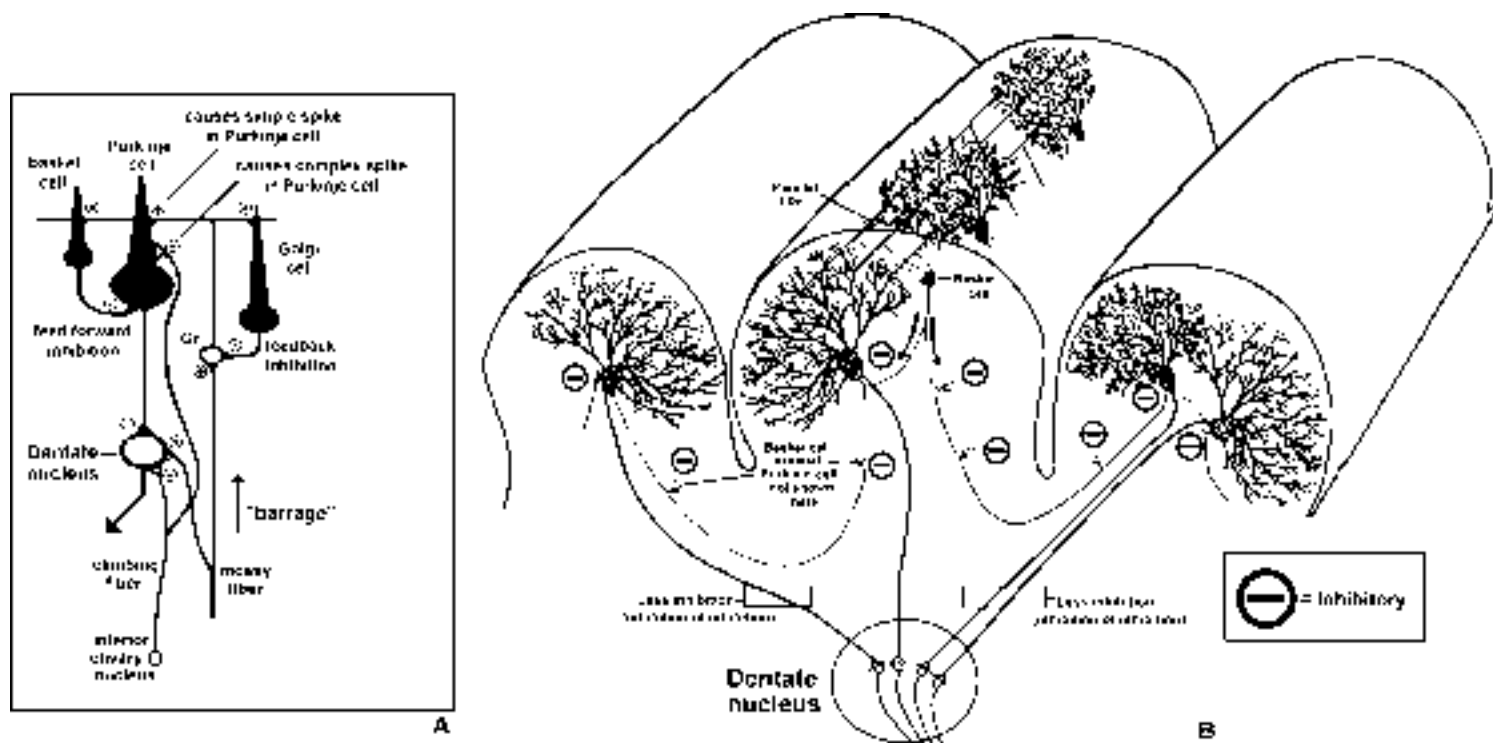
⊖ = Inhibitory

You might wonder what all of those inhibitory cells in the cerebellar cortex are doing. Let's look at the circuitry in the lateral zone (it will be somewhat similar in the other zones). Well, the **feedback** inhibition from the Golgi cell (see A above) could be a **temporal** (timing) control for sharpening the initial excitatory mossy barrage. That is, maybe for the cerebellum to do its "thing", only the very first part of the mossy fiber barrage of planning data is let through to the Purkinje cells. The **feedforward** inhibition via the basket cells (see B above) could be involved in **spatially** sharpening the planning of information signals. That is, as the parallel fibers associated with the mossy fiber barrage excite the Purkinje cells, the basket cells are inhibiting Purkinje cells on the flanks of the active zone. This would kind of emphasize a "hot" zone of Purkinje cell activity. The different firing rates and patterns of dentate neurons driven by the "hot" zone and the flanking zones are then conveyed to VA/VL, the PM and SMA, and in turn to MI (the cells of origin of the corticospinal tract). The cerebellum uses this spatial information in the planning of movements headed for the cells of origin of the corticospinal tract.

LET'S REVIEW

1. **all cerebellar inputs are excitatory**
2. **mossy** fibers=DSCT, CCT, PCT and VCT—terminate (excite) on granule cells
3. **climbing** fibers=OCT-terminate (excite) directly Purkinje cells (by-passes granule), cause complex spikes in Purkinje cell
4. **granule** cell is only excitatory cell in the cerebellar cortex-terminates (excites)   on
Golgi, basket and Purkinje cells—results in simple spikes in Purkinje cells (50-100/sec)
5. **Purkinje, Golgi and basket cells are all inhibitory**
6. basket=**feedforward** inhibition on Purkinje cells
7. Golgi=**feedback** inhibition on mossy fiber-granule cell relay
8. mossy and climbing fiber <u>collaterals</u> to the deep cerebellar nuclei are excitatory
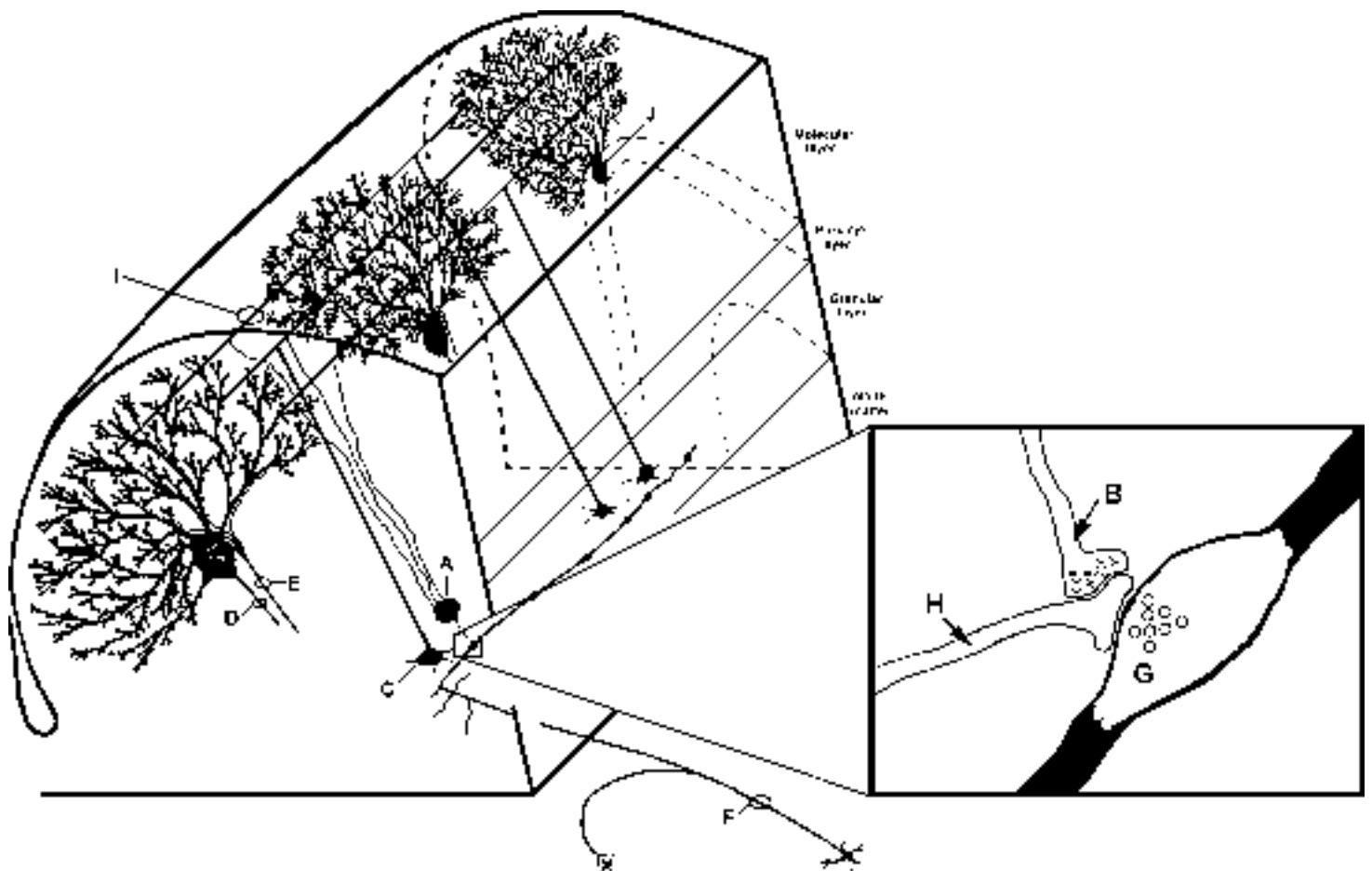
PRACTICE QUESTIONS ON CIRCUITRY

1. **Which of the associations below is/are correct**?

    A-stimulation results in a simple spike in a Purkinje cell
    B-axon terminates on Purkinje and Golgi cell dendrites
    C-axon excites deep cerebellar nuclei
    D-axon arises from inferior olive
    E-axon is excitatory
    F-swelling is called a rosette
    G-cell has strong effect on few Purkinje cells
    H-vesicles contain inhibitory transmitter
    I-cell body receives input from parallel fibers
    J-stimulation of this axon has a powerful effect upon the Purkinje cells
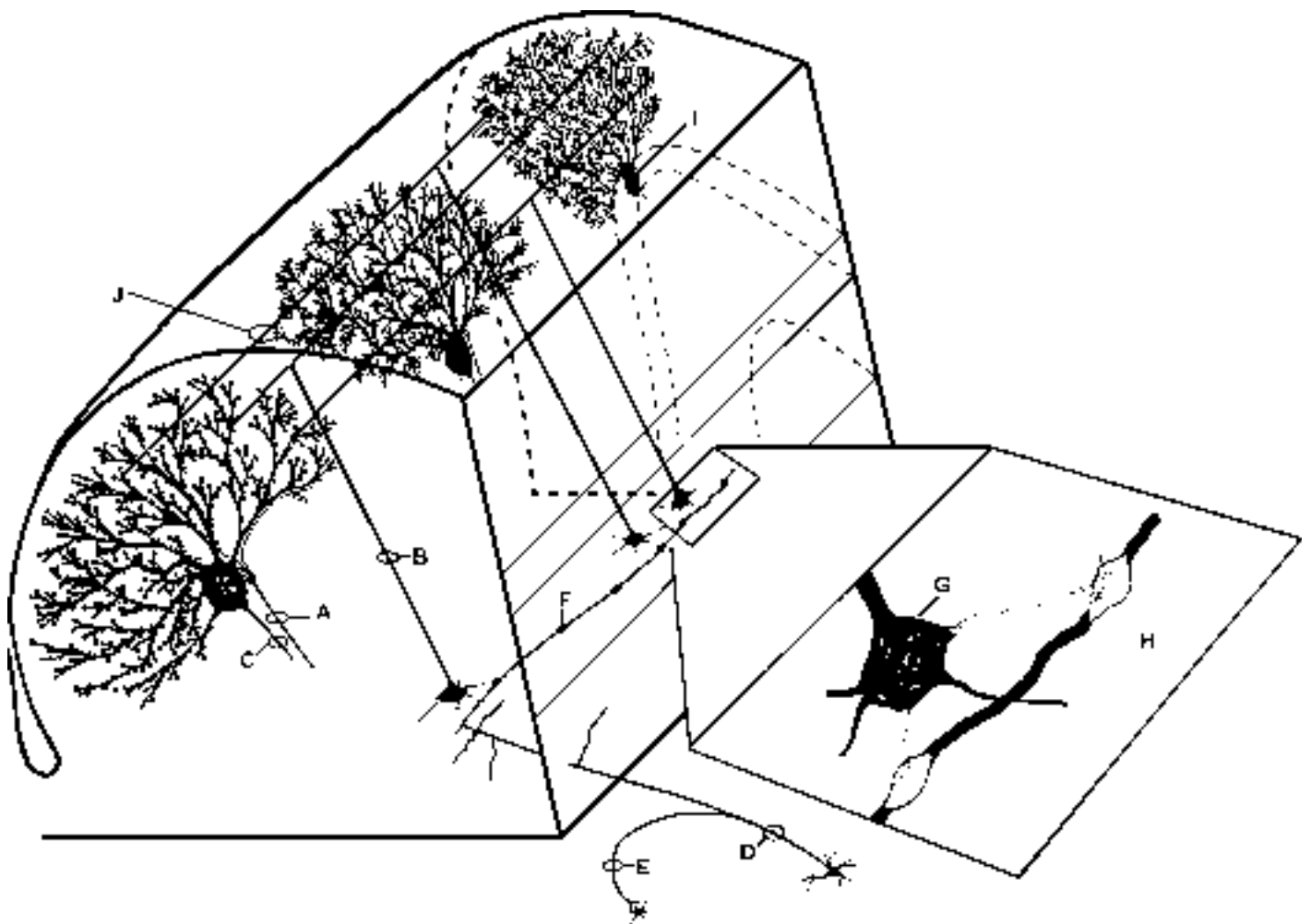
2. Which of the associations below is/are correct?

    A-cell is involved in **feedforward** inhibition
    B-axon is excitatory
    C-cell inhibits Golgi cells
    D-Purkinje cell axon
    E-axon innervates over 100 Purkinje cells
    F-axon could arise from vestibular ganglion
    G-swelling is part of climbing fiber
    H-dendrite lies in the granule cell layer
    I-axon synapses upon basket cell dendrites
    J-cell gives a complex spike upon climbing fiber stimulation

3. Which of the associations below is/are correct?

A-cells receive inhibitory input from mossy and climbing fibers and excitatory input from Purkinje cells
B-cell inhibits Gogli cells
C-"basket"
D-stimulation of axon excites basket cell
E-dendritic tree of cell lies in plane that is **parallel** to the long axis of the folium

4. Which of the associations below is/are correct?

    A-response of a Golgi cell
    A-response of a basket cell
    A-response of a Purkinje cell to mossy fiber stimulation
    A-response of a granule cell
    A-a simple spike
    A-a complex spike
    A-most common spike in Purkinje cells
    A-spike that occurs infrequently (versus another kind of spike)
    B-common spike in Purkinje cell
    B-response of a Purkinje cell to climbing fiber input
    B-response of a Purkinje cell to mossy fiber inputs
    B-response of a granule cell

A

B

5. Which of the following associations is/are correct regarding the drawing below?

   A-nucleus is the sole source of climbing fibers
   A-nucleus receives direct input from Purkinje cells in the medial zone of cerebellar cortex
   A-nucleus lies in the granule layer of the cerebellum
   B-nucleus receives direct excitatory input from Purkinje cells in the intermediate zone
   B-nucleus receives direct input from basket cells
   B-nucleus receives direct input from granule cells
   B-nucleus receives direct input from Golgi cells
   B-nucleus receives direct input from parallel fibers
   C-nucleus receives direct input from Purkinje cells in medial zone of cerebellar cortex
   C-nucleus receives direct excitatory input from Purkinje cells in the lateral zone
   C-nucleus receives direct input from basket cells
   C-nucleus receives direct input from granule cells
   C-nucleus receives direct input from Golgi cells
   C-nucleus receives direct input from mossy fiber rosette
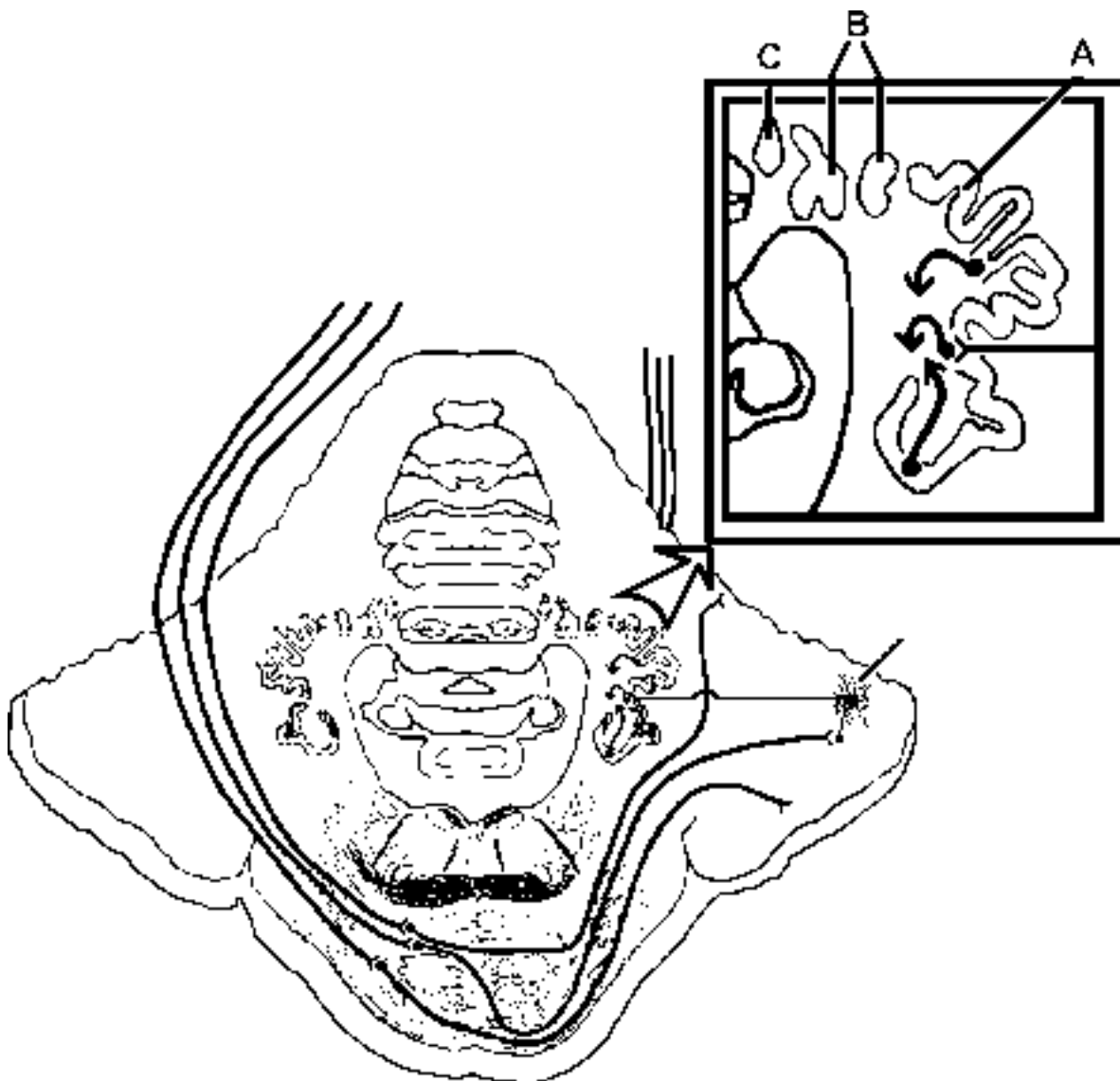
CEREBELLAR CIRCUITRY PROBLEM SOLVING ANSWERS

1. A. F; **B.** T; **C.** F; **D.** F; **E.** T;
 F. T; **G.** F; **H.** F; **I.** F; **J.** F

2. A. F; **B.** F; **C.** F; **D.** T; **E.** F;
 F. T; **G.** F; **H.** T; **I.** T; **J.** T

3. A. F; **B.** F; **C.** T; **D.** T; **E.** F

4. A. F; F; F; F; F; T; F; T
 B. T; F; T; F

5. A. F; F; F
 B. F; F; F; F; F
 C. T; F; F; F; F; F

SELF LEARNING Thursday, March 4, 11AM-12

Well, all of the lectures on Motor Systems have been given. Hopefully you will use this two-hour block of time to review. Finish those cerebellum questions and know those four cerebellar zones!!! Watch the review CD-ROM on Motor Systems again.

HOPEFULLY, YOU ARE BRINGING THINGS TOGETHER!!

Sorry to keep harping but you should have read and understood the www reading regarding **Parkinson's**, **Tourette Syndrome** and **Deep Brain Stimulation.** Moreover, the old stuff should be fixed in your brains. They are: 1) muscular dystrophy, 2) myasthenia gravis, 3) Guillain-Barre, 4) S1 radiculopathy, 5) amyotrophic lateral sclerosis (ALS), 6) Brown Sequard syndrome (spinal cord hemisection), 7) facial colliculus-vestibulo-cochlear, 8) lateral medullary (Wallenberg's) syndrome, 9) acoustic neuroma, 10) Weber Syndrome, 11) syringomyelia and 12) subacute combined systems disease. Finally, those power points on the "Integrated Motor Systems"power point for practice quiz #6 should be familiar!

YOU CAN ALSO GO UP TO THE LABS AND LOOK AT THE BRAIN IN ORDER TO VISUALIZE THE BASAL GANGLIA CEREBELLUM WE WILL BE UP THERE WAITING FOR YOU!!!!!!!

PREPARATION FOR QUIZ 6

Go to WEB-CT and do the Practice Questions for **Quiz #6**. This should be a pretty good test of your knowledge of the motor Systems. Work hard on those on-line quizzes so as to estimate your command of the information. Make sure you understand the **IMPORTANT** www reading on **Parkinson's**, **Tourette Syndrome** and **Deep Brain Stimulation.** You should remember the main points about 1) muscular dystrophy, 2) myasthenia gravis, 3) Guillain-Barre, 4) S1 radiculopathy, 5) amyotrophic lateral sclerosis (ALS), 6) Brown Sequard syndrome (spinal cord hemisection), 7) facial colliculus-vestibulo-cochlear, 8) lateral medullary (Wallenberg's) syndrome, 9) acoustic neuroma, 10) Weber Syndrome, 11) syringomyelia and 12) subacute combined systems disease. Finally, those power points on "Motor Systems power point for quiz #6" should be familiar!