Marr-Albus Model of Cerebellum

Computational Models of Neural Systems

Lecture 2.2

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September, 2017

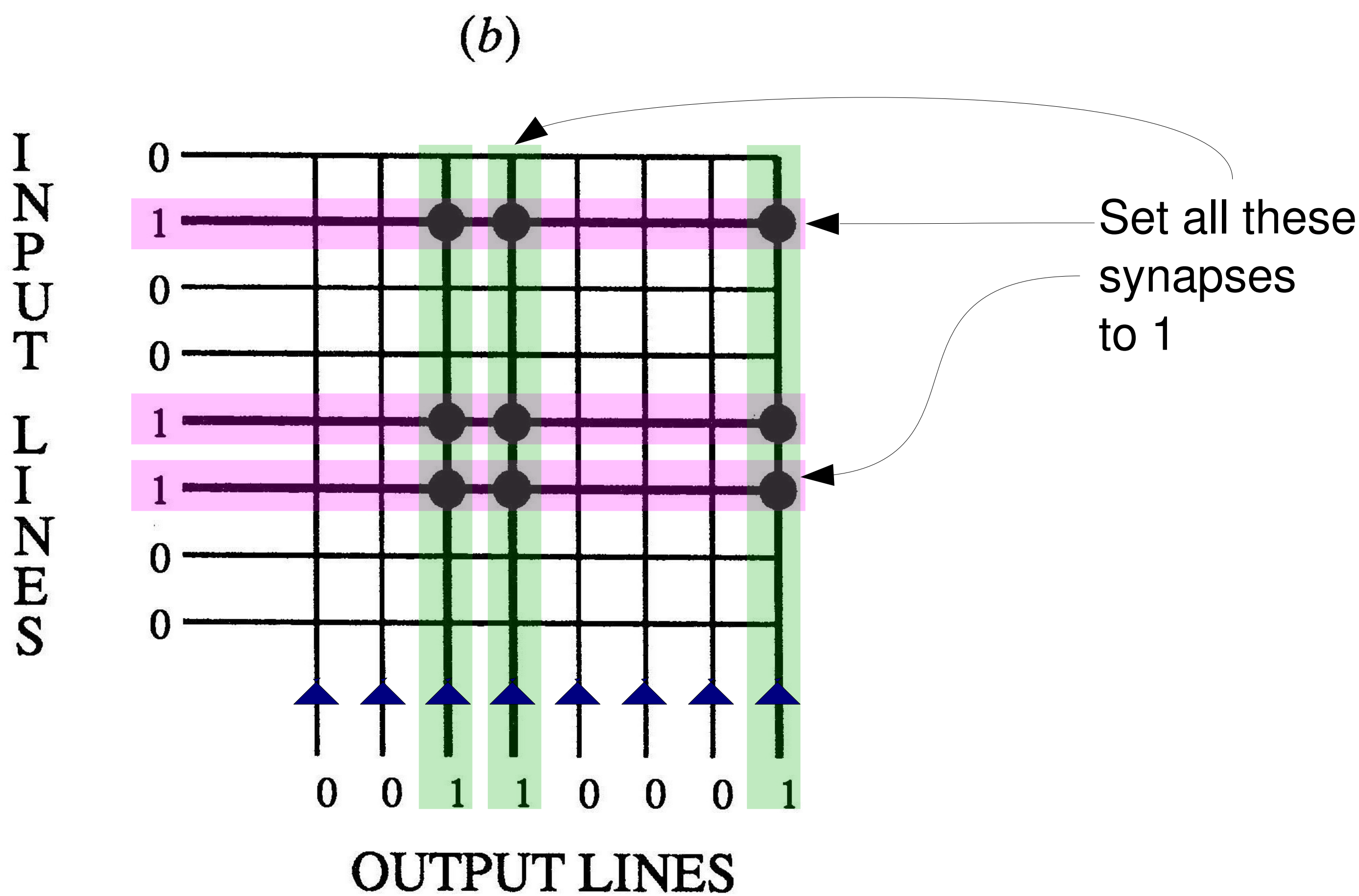
Marr's Theory

- Marr suggested that the cerebellum is an associative memory.
- Input: proprioceptive information (state of the body).
- Output: motor commands necessary to achieve the goal associated with that context.
- Learn from experience to map states into motor commands.
- Wants to avoid pattern overlap, to keep patterns distinct.

Albus' Theory

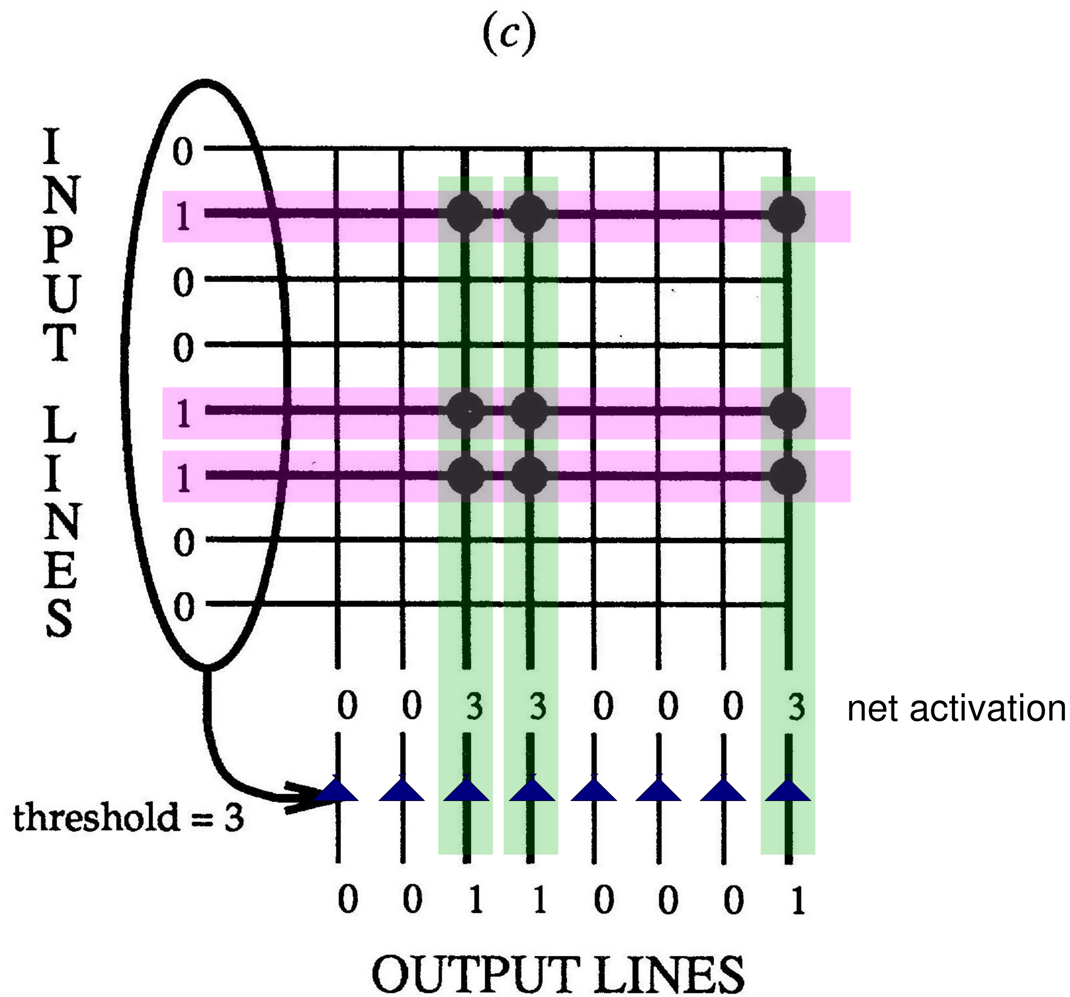
- Albus suggested that the cerebellum is a function approximator.
- Similar to an associative memory, but uses pattern overlap and interpolation to approximate nonlinear functions.
- Could explain how the cerebellum generalizes to novel input patterns that are similar to those for previously practiced motions.

Associative Memory: Store a Pattern

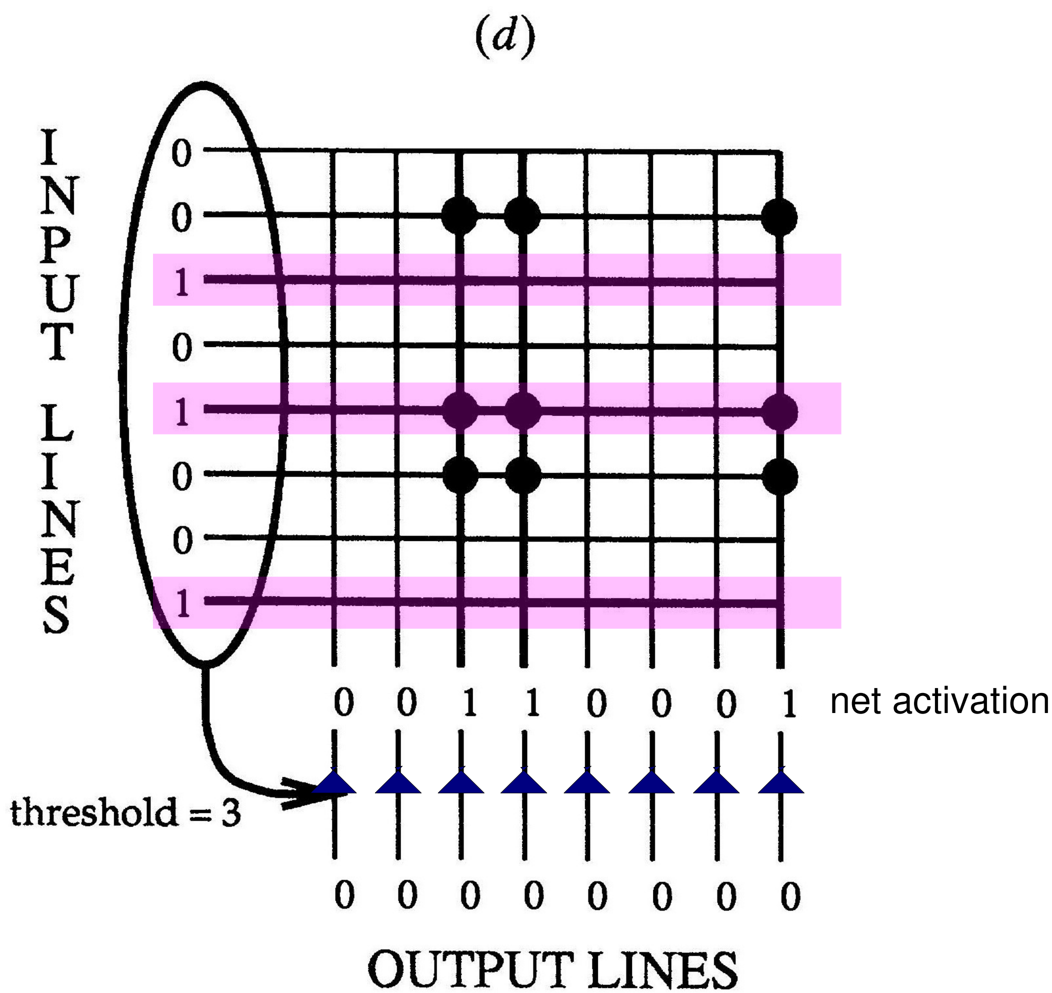


The input and output patterns don't have to be the same length, although in the above example they are.

Associative Memory: Retrieve the Pattern

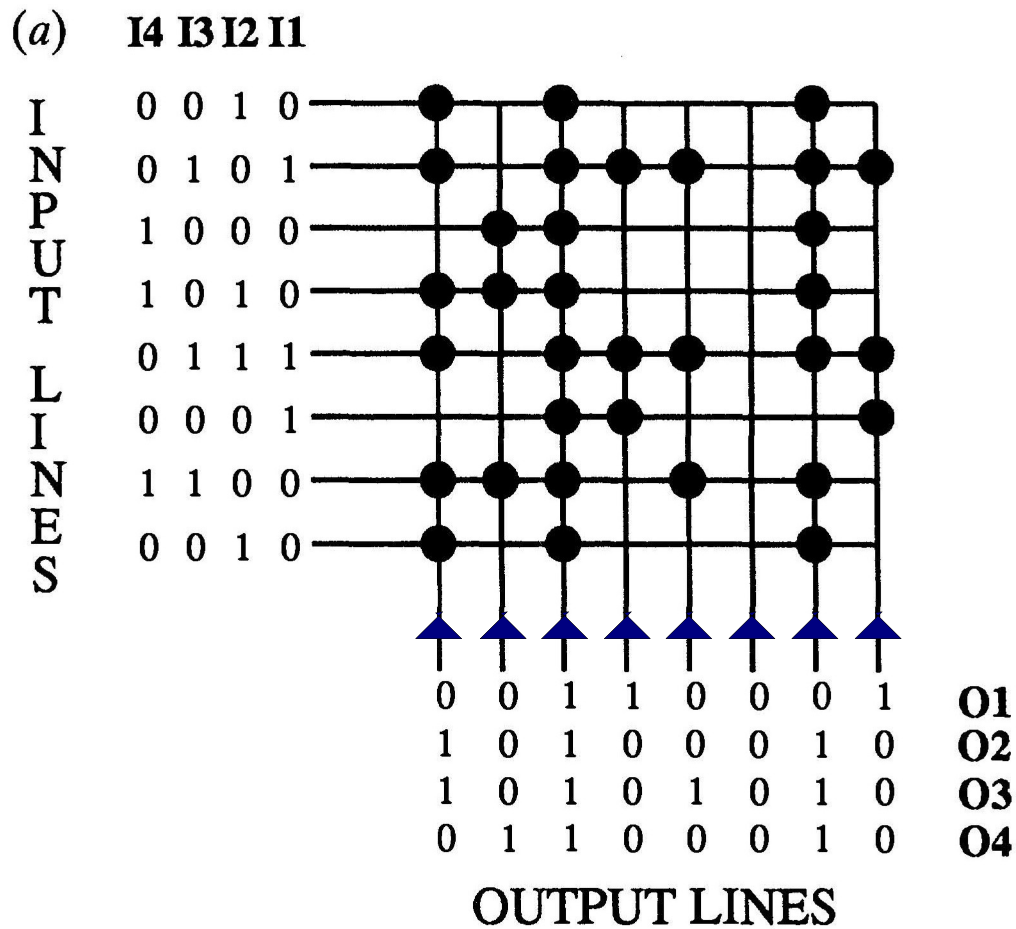


Associative Memory: Unfamiliar Pattern



Storing Multiple Patterns

Input patterns must be dissimilar: orthogonal or nearly so. (Is this a reasonable requirement?)



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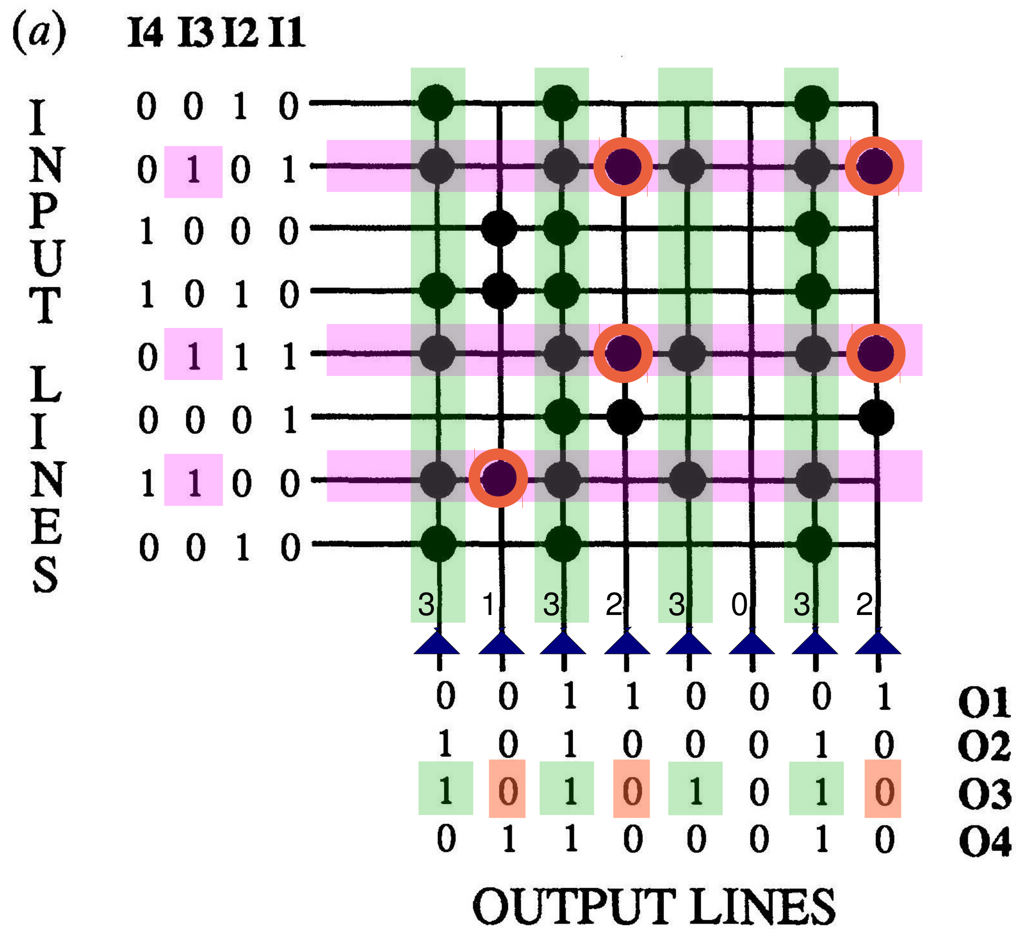
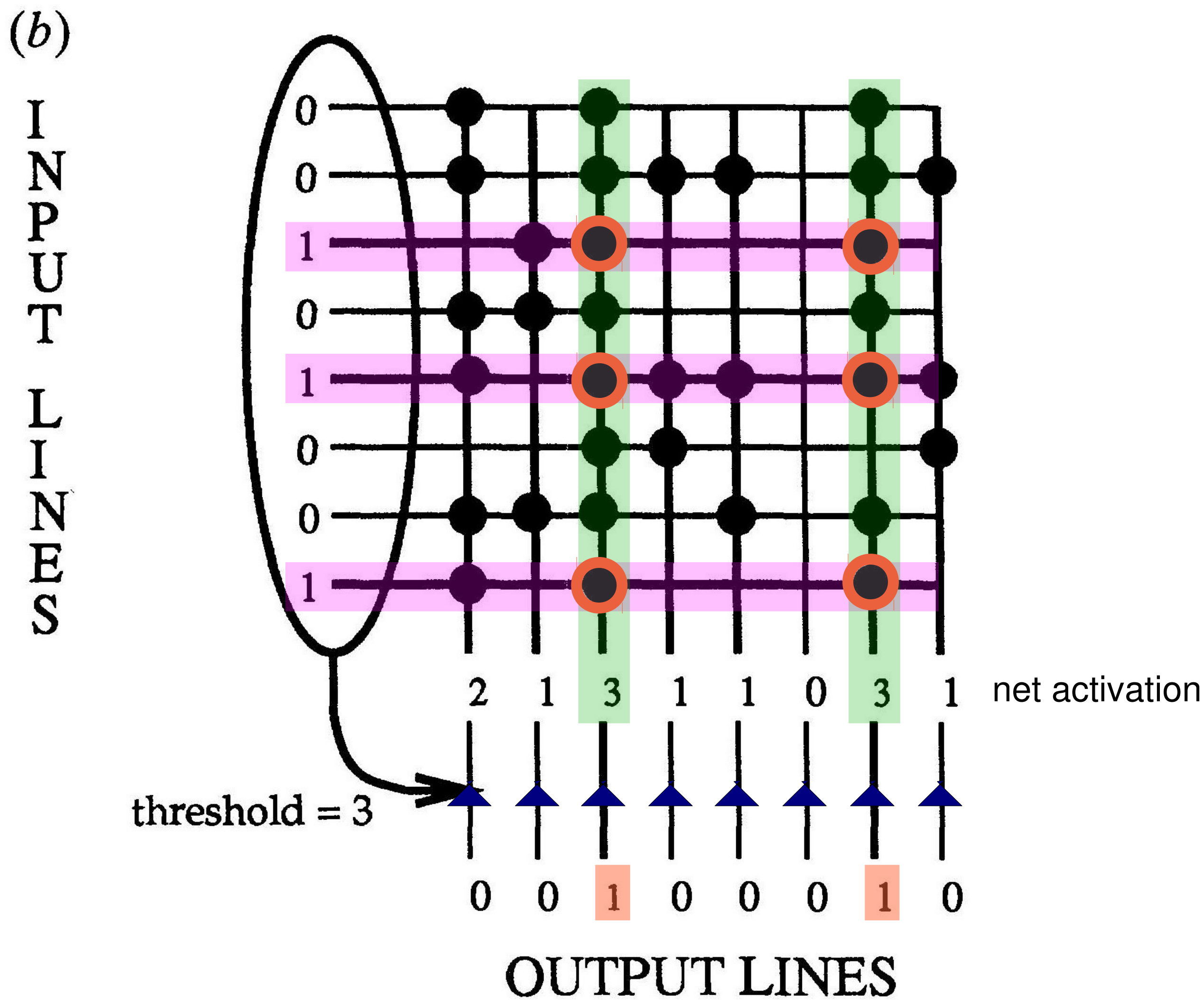
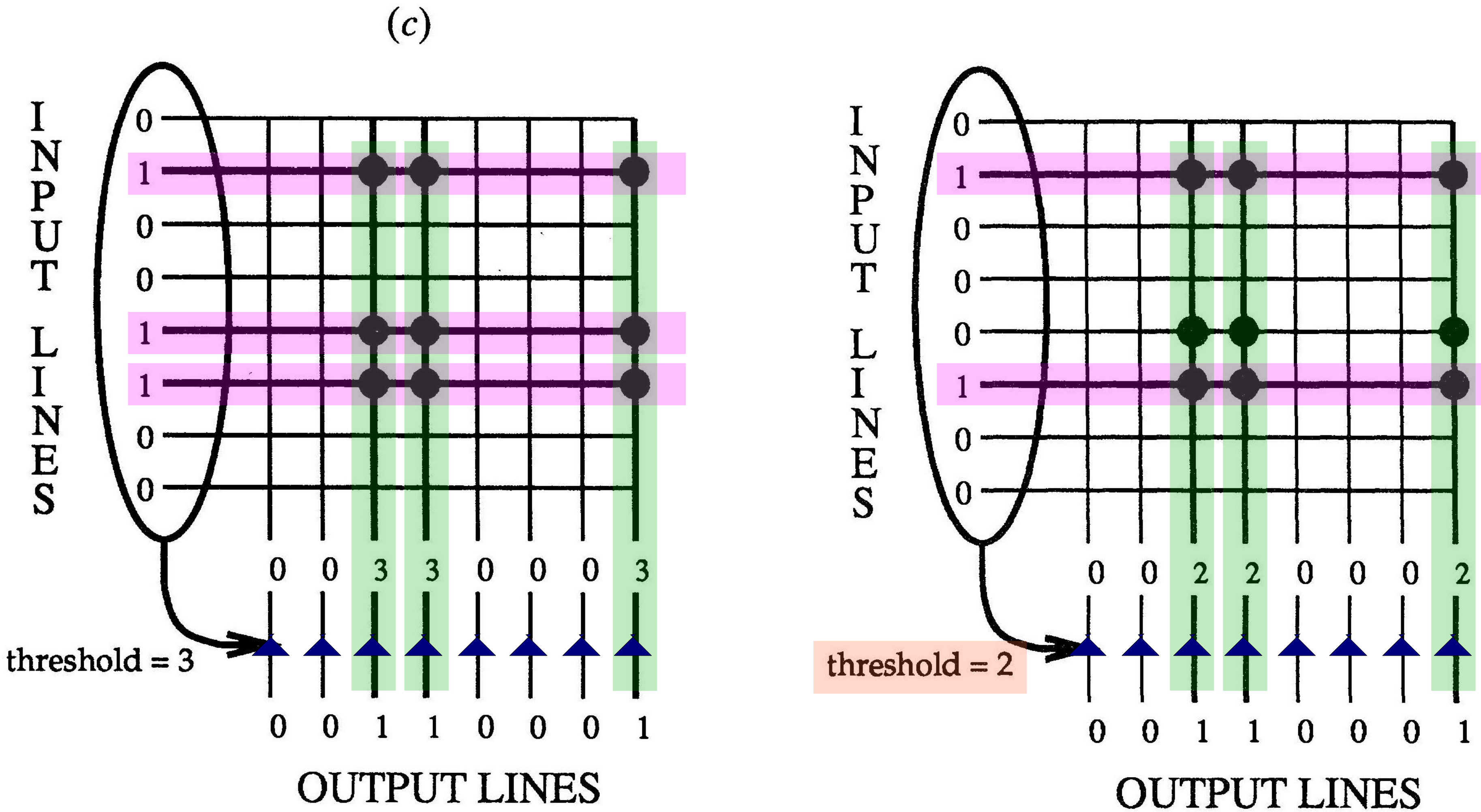


Noise due to overlap

False Positives Due to Memory Saturation

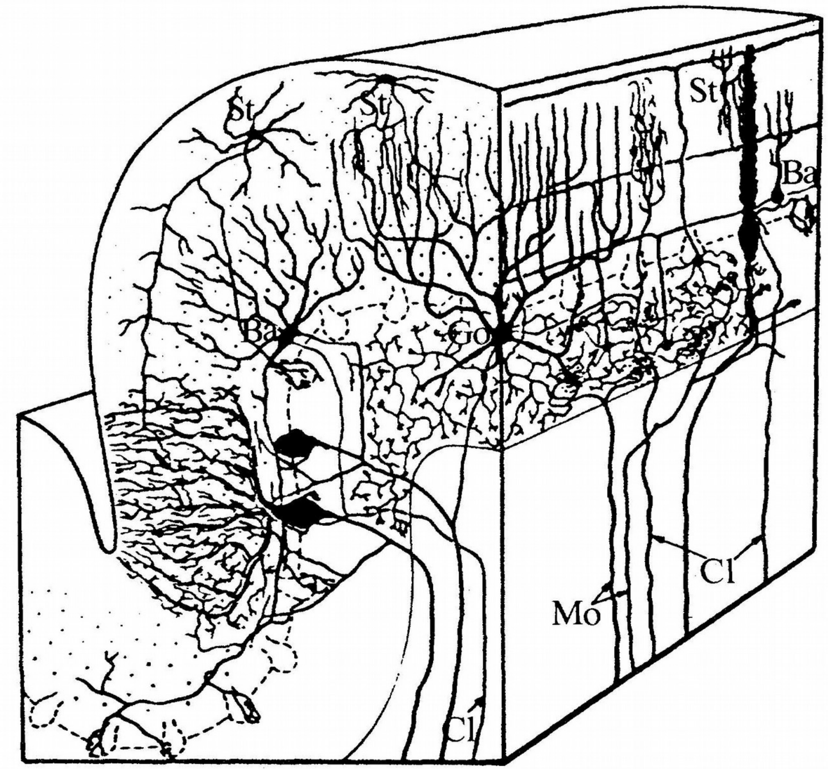


Responding To A Subset Pattern

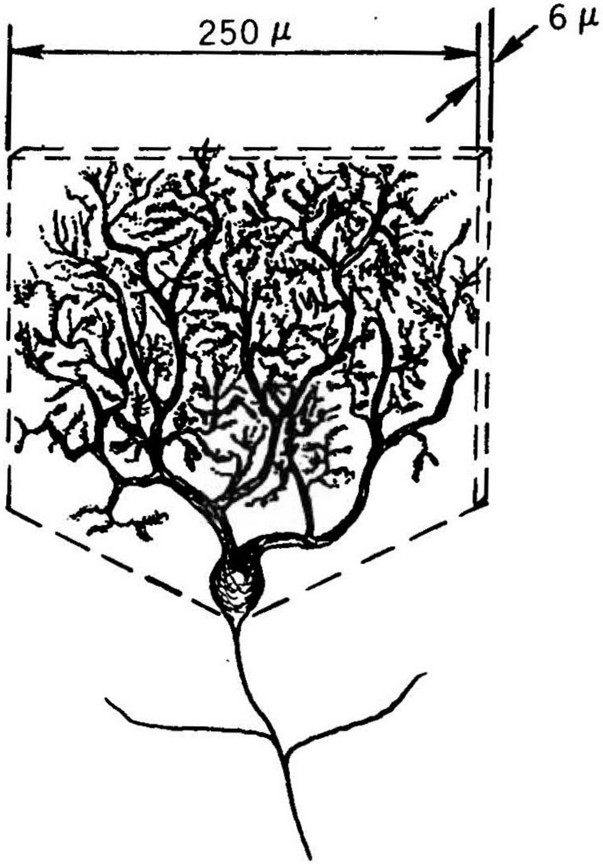


Training the Cerebellum

- Mossy fibers (input pattern)
  - Input from spinal cord, vestibular nuclei, and the pons.
  - Spinocerebellar tracts carry cutaneous and proprioceptive information.
  - Much more massive input comes from the cortex via the pontine nuclei (the pons) and then the middle cerebellar peduncle. More fibers in this peduncle than all other afferent/efferent fiber systems to cerebellum.
- Climbing fibers (teacher)
  - Originate in the inferior olivary nucleus.
  - The “training signal” for motor learning.
  - The UCS for classical conditioning.
- Neuromodulatory inputs from raphe nucleus, locus ceruleus, and hypothalamus.



Purkinje Cells



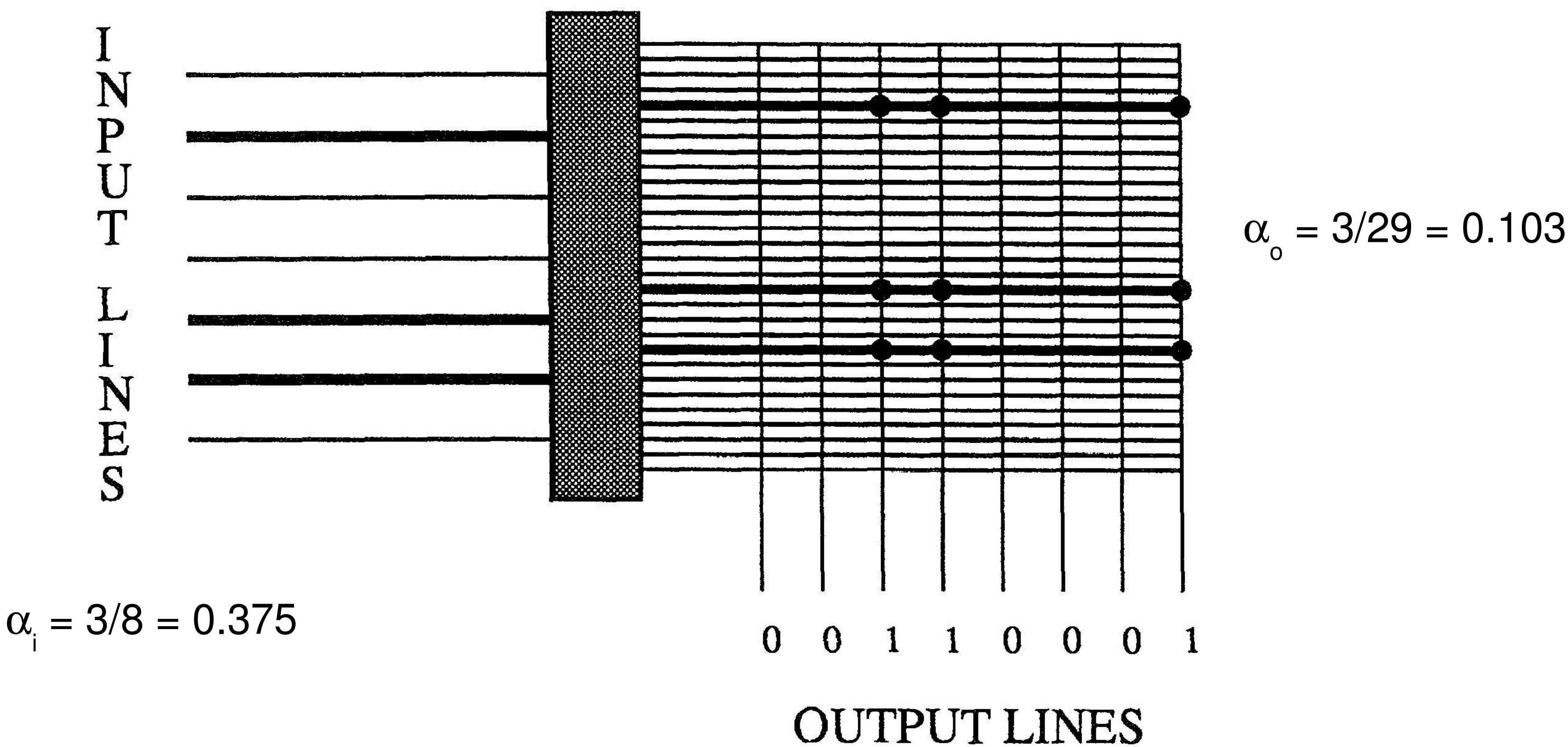
- The principal cells of the cerebellum.
- Largest dendritic trees in the brain: about 200,000 synapses.
- These synapses are where the associative weights are stored. (But Albus argues that basket and stellate cells should also have trainable synapses.)
- Purkinje cells have recurrent collaterals that contact Golgi cell dendrites and other Purkinje cell dendrites and cell bodies.
- Purkinje cells make only inhibitory connections.

Input Processing

- If mossy fiber inputs made direct contact with Purkinje cells, the cerebellum would have a much lower memory capacity due to pattern interference.
- Also, for motor learning, subsets of an input pattern should not produce the same results as a supserset input. Subsets must be recoded so that they look less similar to the whole.
    - “cup in hand”, “hand near mouth”, “mouth open”
    - “cup in hand”, “mouth open” (don't rotate wrist!)
- Solution: introduce a layer of processing before the Purkinje cells to make the input patterns more sparse and less similar to each other (more orthogonal).
- Similar to the role of the dentate gyrus in hippocampus.

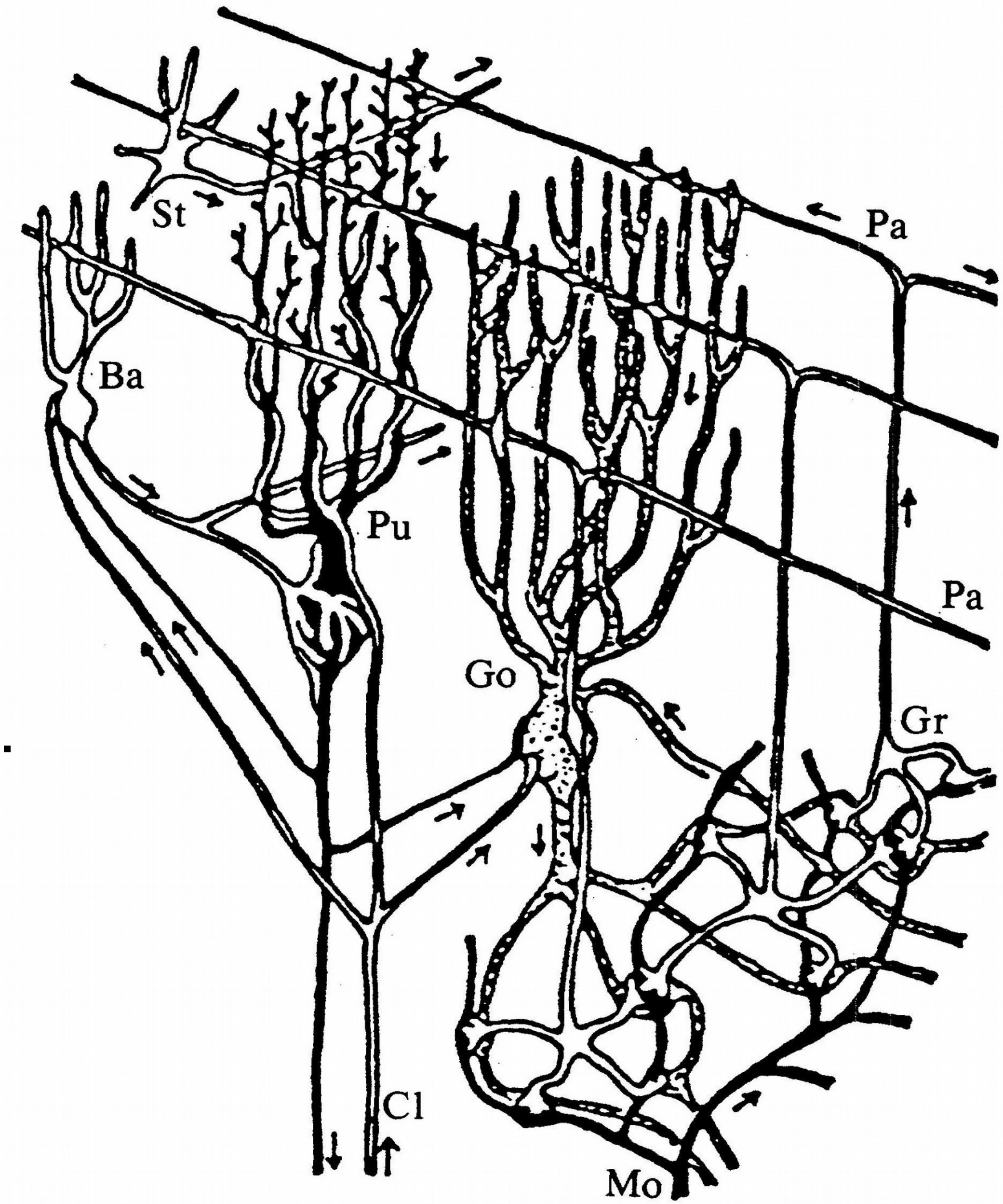
Mossy Fiber to Parallel Fiber Transformation: "Conjunctive Coding"

- Same number of active lines, but a larger population of units, produces greater sparsity (smaller α) and less overlap between patterns.



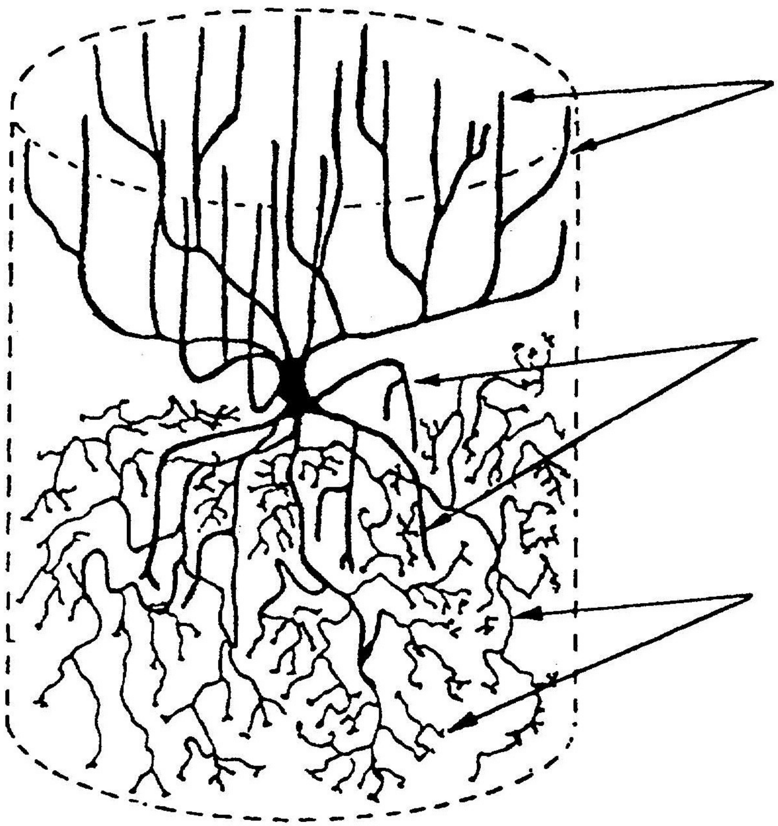
Recoding Via Granule Cells

- Mossy fibers synapse onto granule cells.
- Granule cell axons (called parallel fibers) provide input to Purkinje cells.
- Golgi cells are inhibitory interneurons that modulate the granule cell responses to produce 'better" activity patterns.

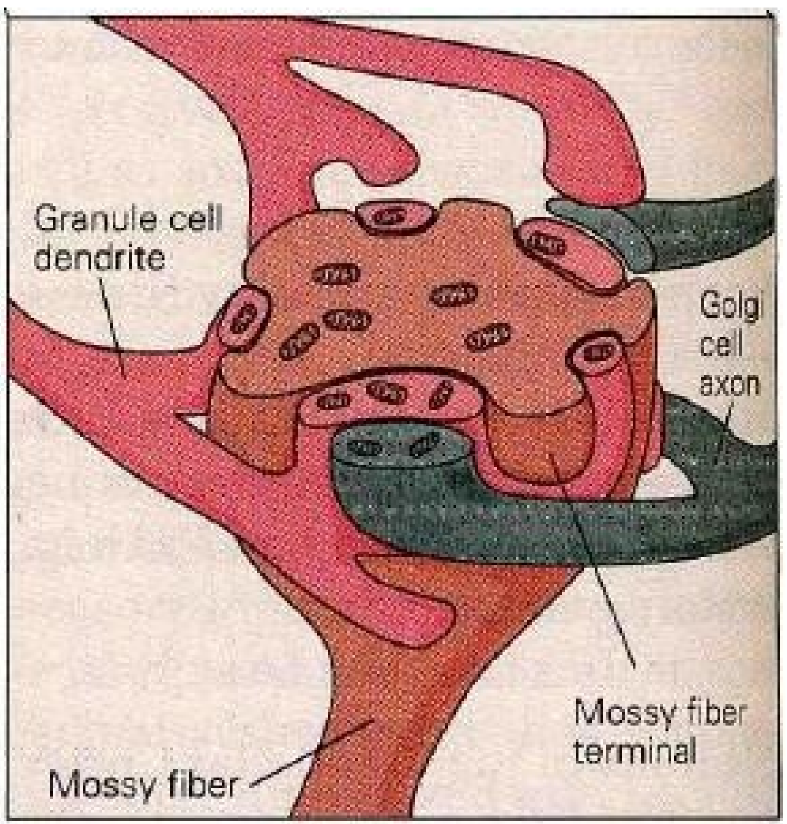


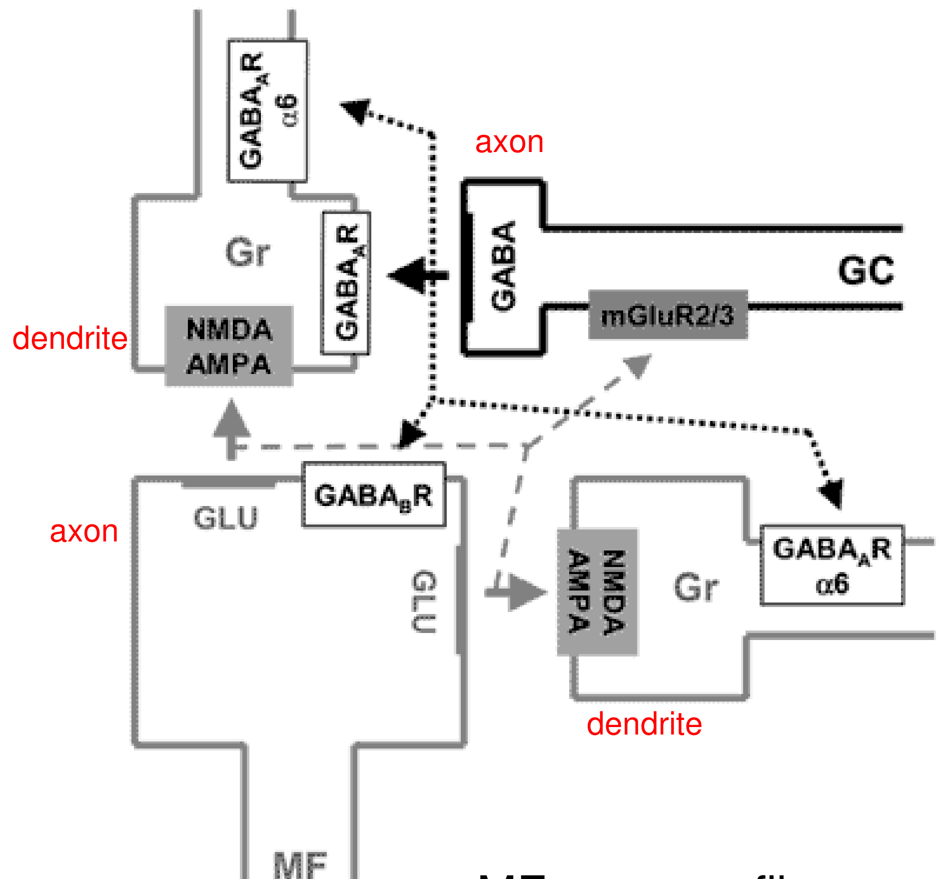
Golgi Cells

- Golgi cells monitor both the mossy fibers (granule cell inputs) and the parallel fibers (granule cell outputs).
- Mossy fiber input patterns with <u>widely varying</u> levels of activity result in granule cell patterns with roughly the <u>same</u> level of activity, thanks to the Golgi cells.



The Glomerulus

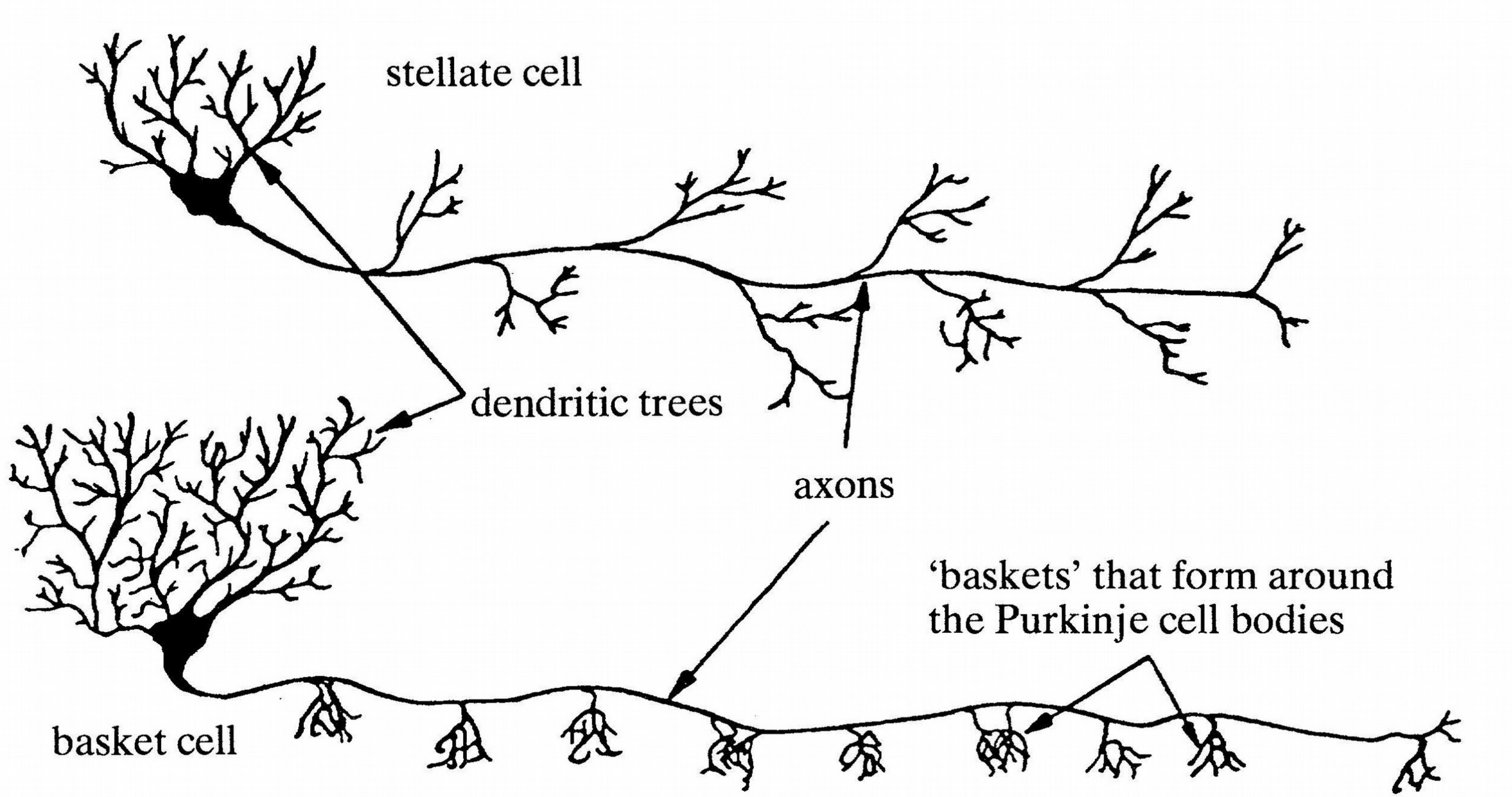




MF = mossy fiber
Gr = granule cell
GC = Golgi cell

Basket and Stellate Cells

- Inhibitory interneurons that supply short-range, within-beam inhibition (stellate) and long-range, across-beam inhibition (basket).



The Matrix Memory

- Weights: modifiable synapses from granule cell parallel fibers onto Purkinje cell dendrites.
- Thresholding: whether the Purkinje cell chooses to fire.
- Threshold setting: stellate and basket cells sample the input pattern on the parallel fibers and make inhibitory connections onto the Purkinje cells.
- Albus' contribution: synapses should initially have high weights, not zero weights. Learning *reduces* the weight values (LTD).
- Since Purkinje cells are inhibitory, reducing their input means they will fire less, thereby dis-inhibiting their target cells.

Marr's Notation for Analyzing His Model

α_m is the fraction of active mossy fibers
α_g is the fraction of active granule cells (parallel fibers)
N_m, N_g are numbers of mossy fibers/granule cells

$N_m \alpha_m$ = expected # of active mossy fibers
$N_g \alpha_g$ = expected # of active granule cells

A fiber that is active with probability α transmits
$-\log_2 \alpha$ bits of information when it fires

$N_m \alpha_m \times -\log_2 \alpha_m$ = information content of a mossy fiber pattern
$N_g \alpha_g \times -\log_2 \alpha_g$ = information content of a granule cell pattern
(but assumes fibers are uncorrelated, which is untrue)

Marr's Constraints on Granule Cell Activity

1. Reduce saturation: tendency of the memory to fill up.

$$\alpha_g < \alpha_m$$

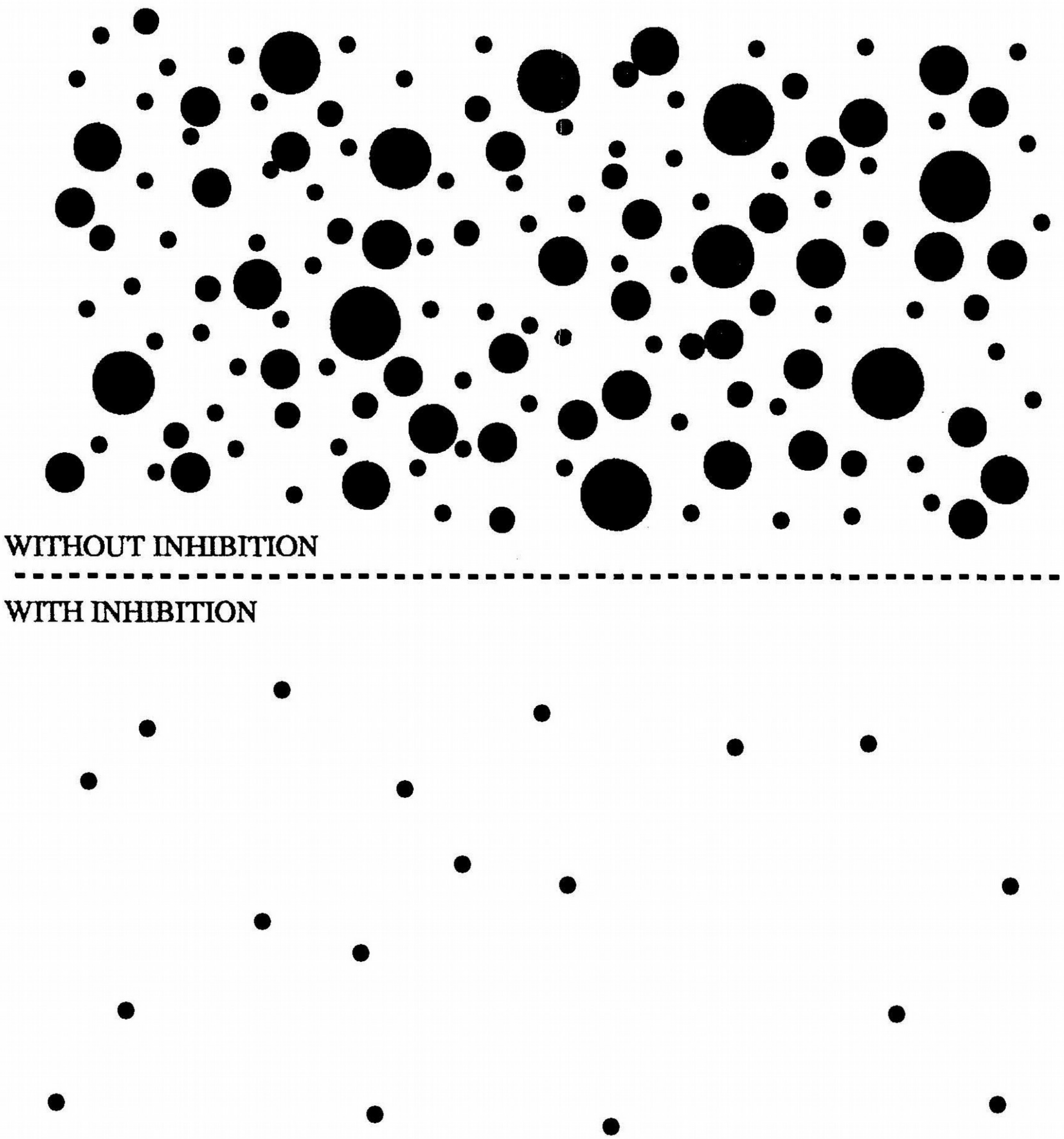
2. Preserve information. The number of bits transmitted should not be reduced by the granule cell processing step.

$$-N_g \alpha_g (\log \alpha_g) \geq -N_m \alpha_m (\log \alpha_m)$$

$$-\alpha_g (\log \alpha_g) \geq -\frac{N_m}{N_g} \alpha_m (\log \alpha_m)$$

3. Pattern separation: overlap is an increasing function of α, so we again want $\alpha_g < \alpha_m$

Golgi Inhibition Selects Most Active Granule Cells



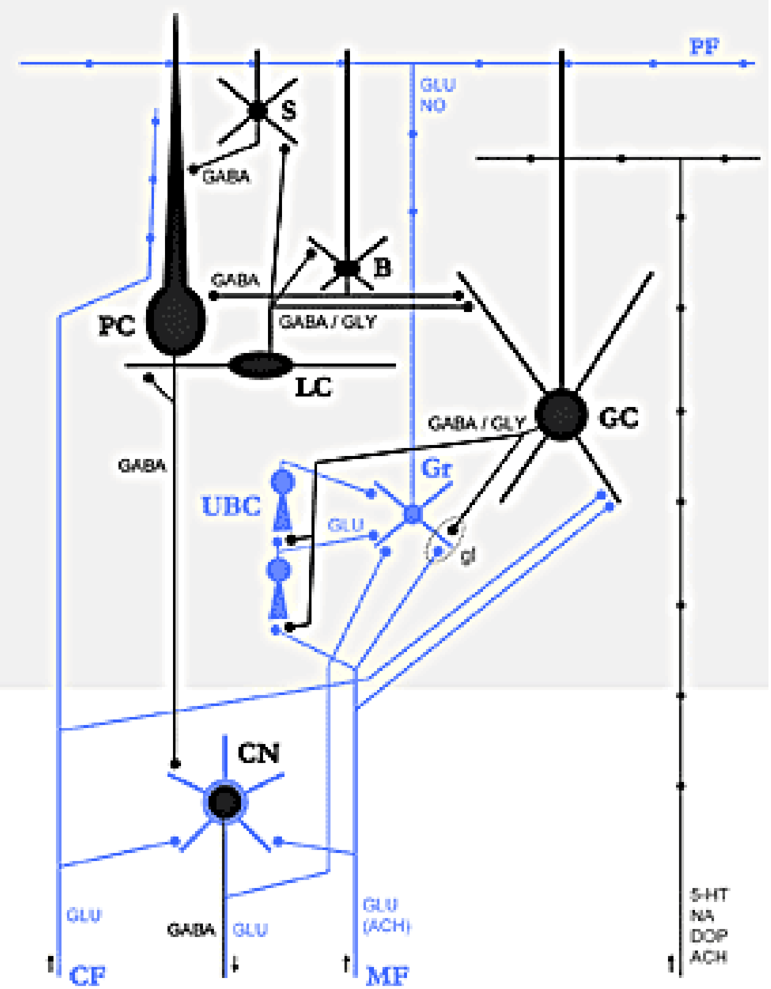
Summary of Cerebellar Circuitry

- Two input streams:
  - Mossy fibers synapse onto granule cells whose parallel fibers project to Purkinje cells
  - Climbing fibers synapse directly onto Purkinje cells
- Five cell types: (really 7 or more)
  1. Granule cells (input pre-processing)
  2. Golgi cells (regulate granule cell activity)
  3. Purkinje cells (the principal cells)
  4. Stellate cells
  5. Basket cells

  Feed-forward inhibition of Purkinje cells
- One output path: Purkinje cells to deep cerebellar nuclei.
- But also recurrent connections: Purkinje $\rightarrow$ Purkinje

New Cell Types Investigated Since Marr/Albus

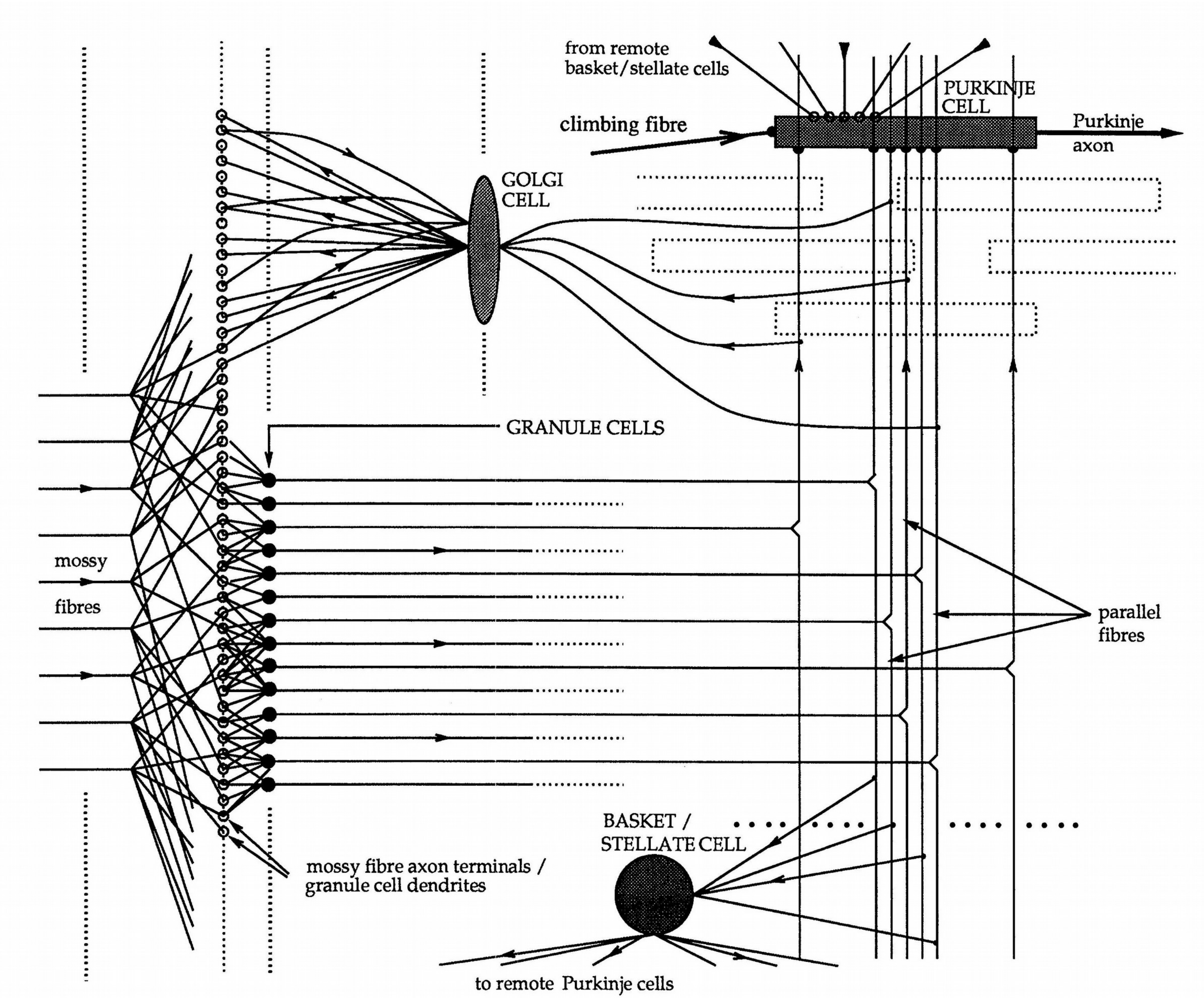
- Lugaro cells (LC): an inhibitory interneuron (GABA) that targets Golgi, basket and stellate cells as well as Purkinje cells. May be involved in synchronizing Purkinje cell firing.
- Unipolar brush cells (UBC): excitatory interneurons



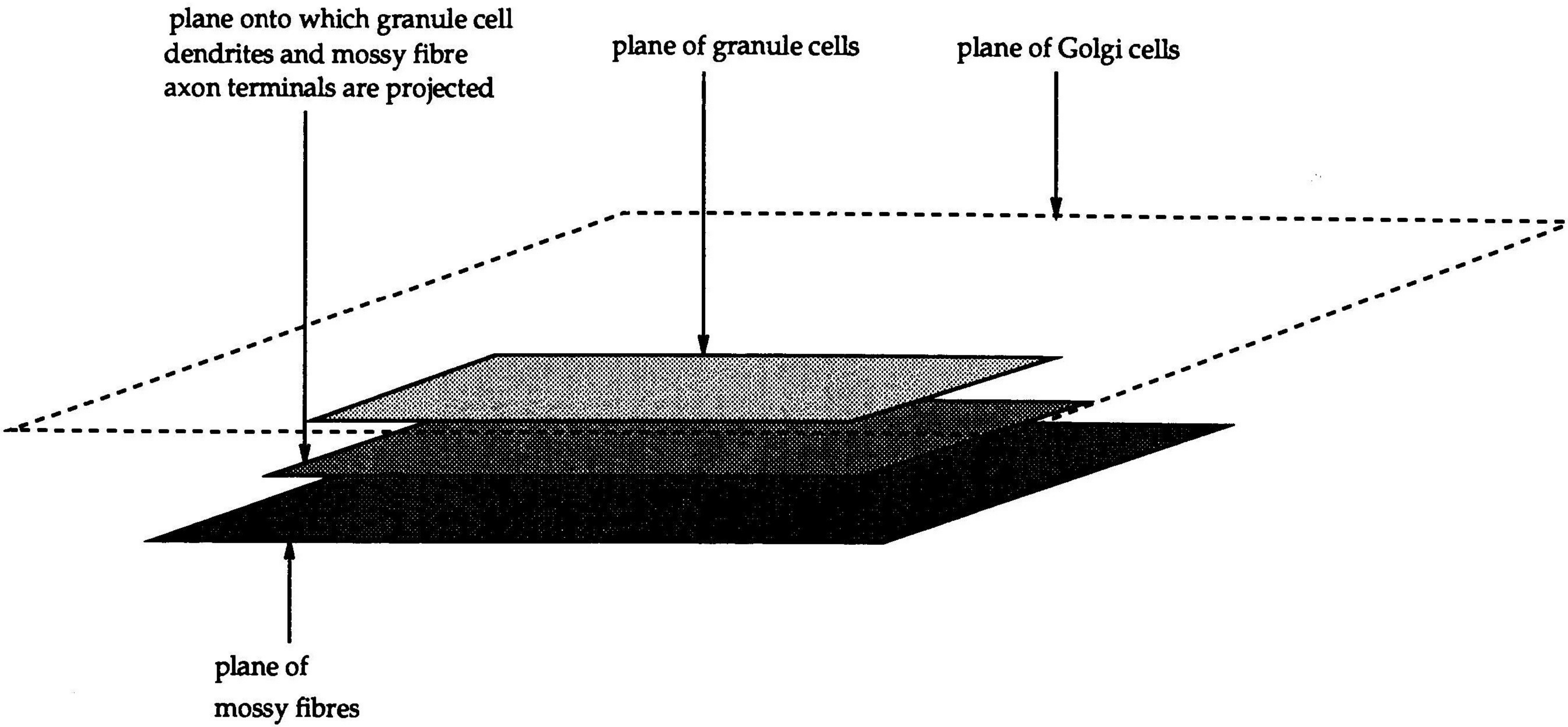
Tyrrell and Willshaw's Simulation (1992)

- C programming running on a Sun-4 workstation (12 MIPS processor, 24 MB of memory)
- Tried for a high degree of anatomical realism.
- Took **50 hours** of cpu time to wire up the network! Then, 2 minutes to process each pattern.
- Simulation parameters:
  - 13,000 mossy fiber inputs, 200,000 parallel fibers
  - 100 Golgi cells regulating the parallel fiber system
  - binary weights on the parallel fiber synapses
  - 40 basket/stellate cells
  - 1 Purkinje cell, 1 climbing fiber for training

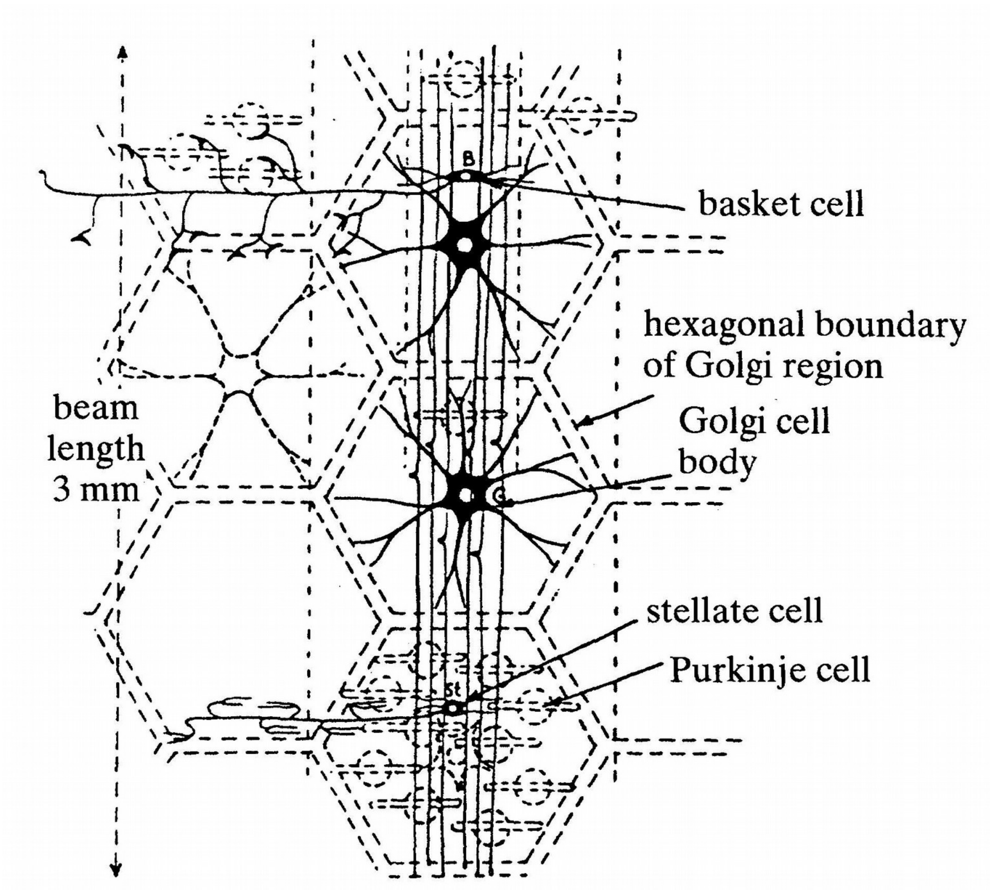
Tyrrell & Willshaw Architecture



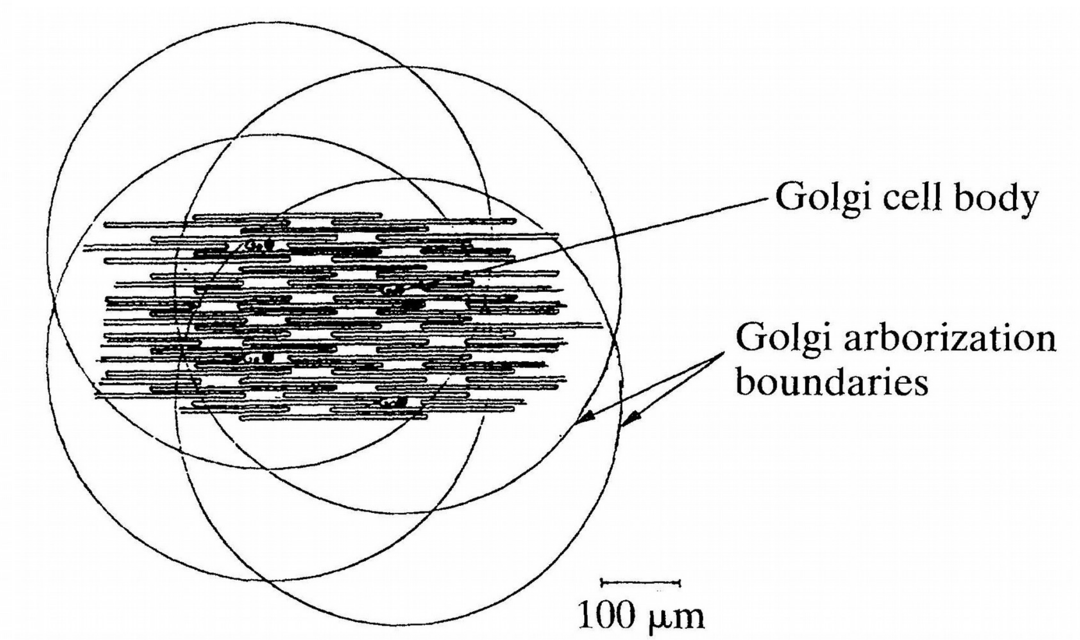
Geometrical Layout



Golgi Cell Arrangement

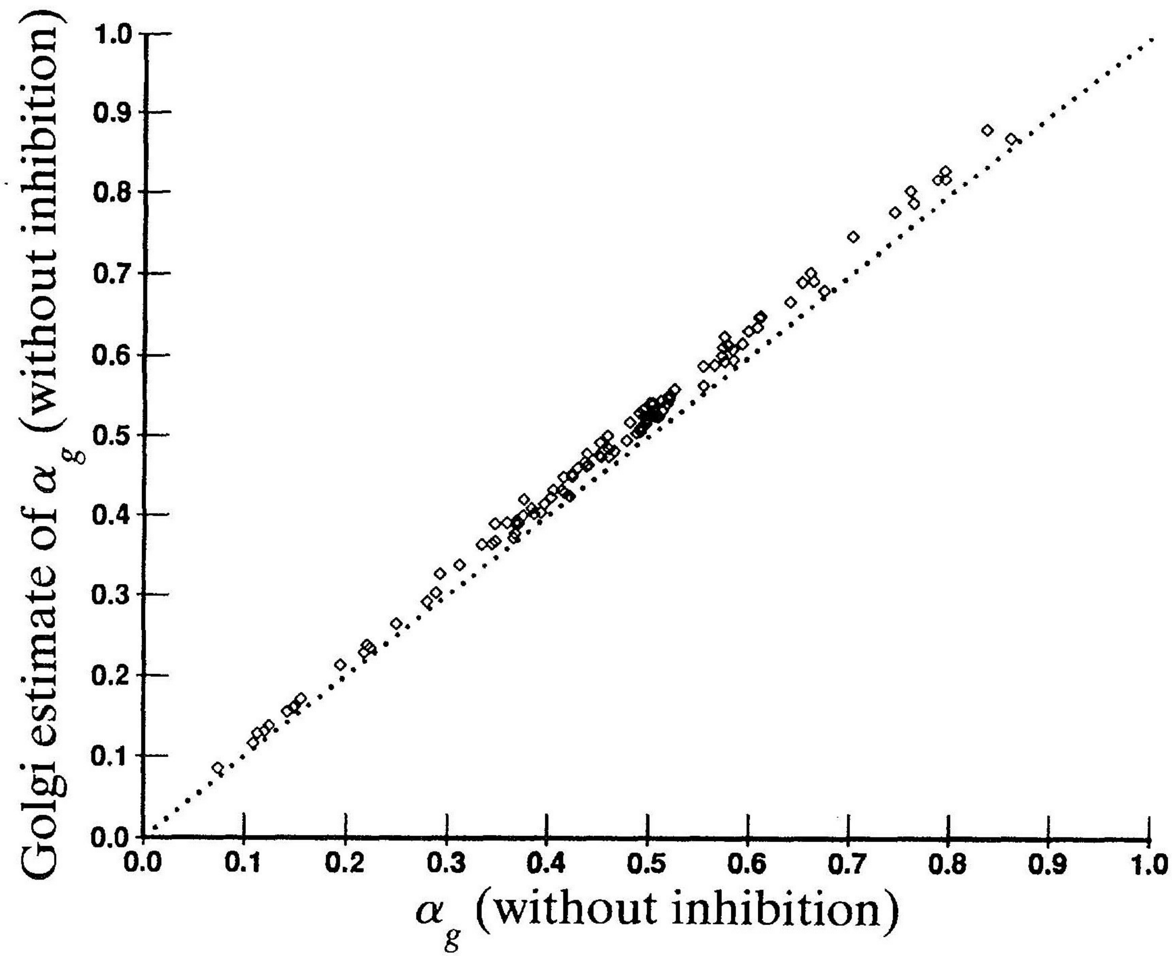


Marr

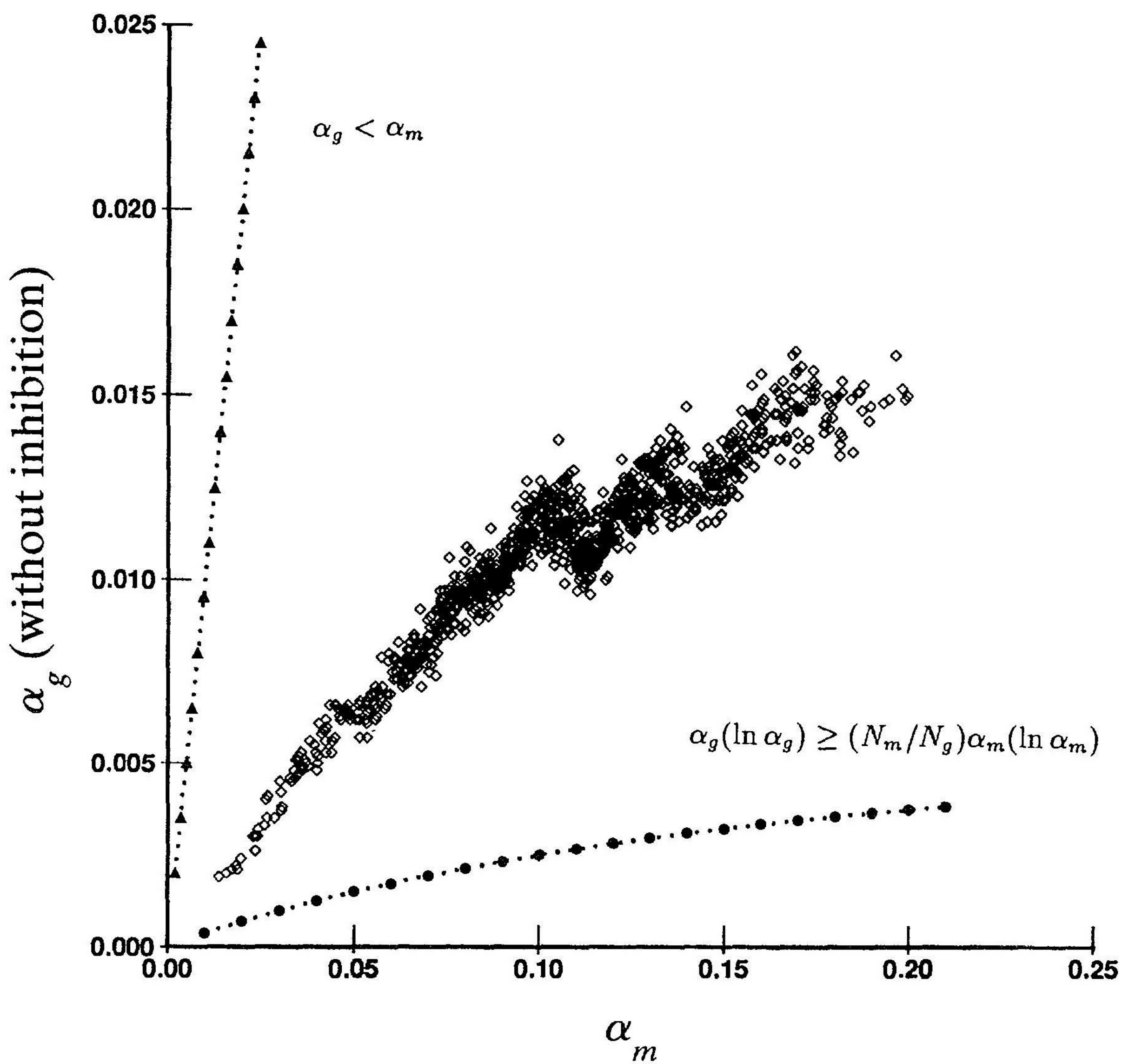


Albus

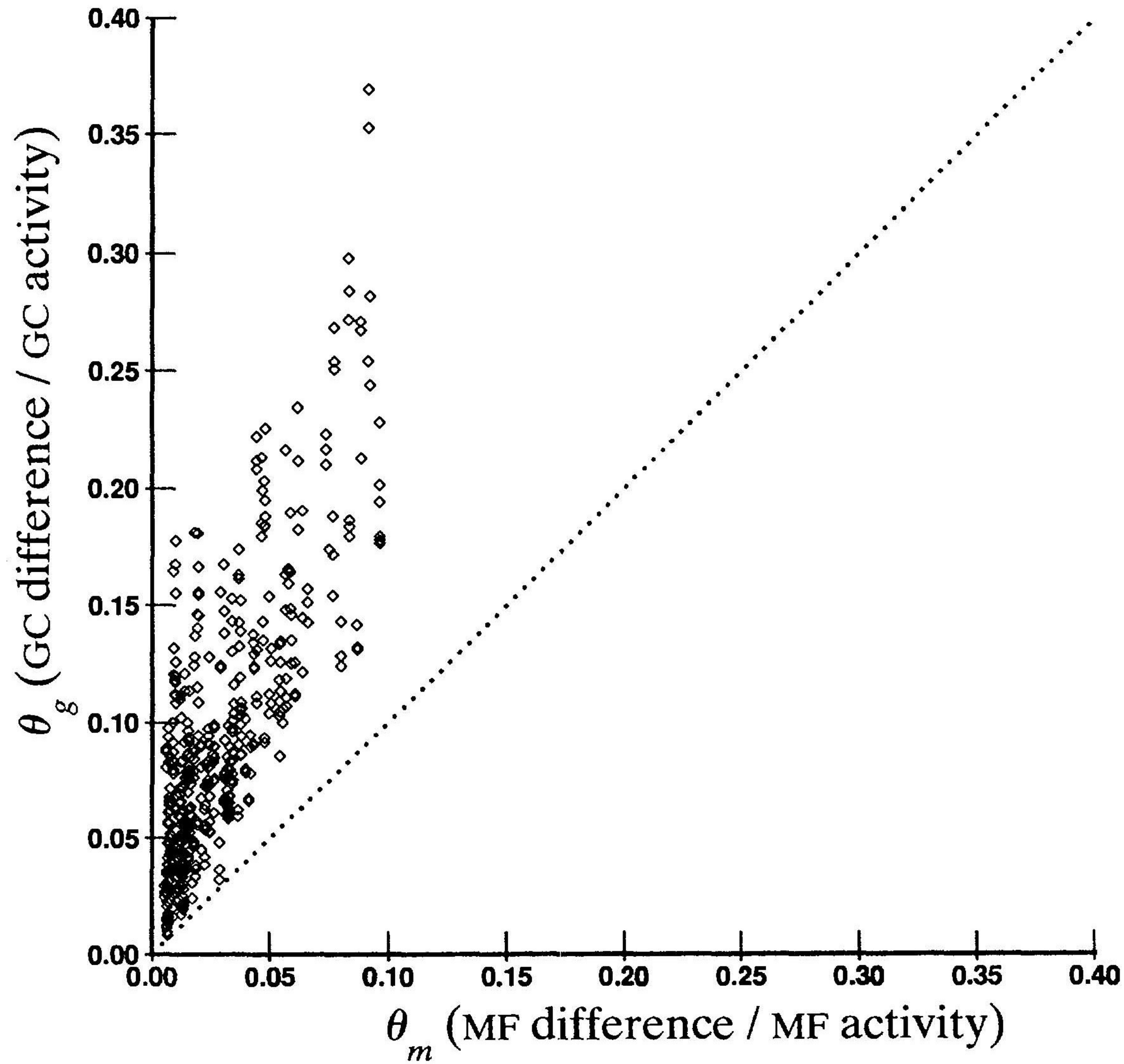
Golgi Cell Estimate of Granule Cell Activity



Golgi Cell Regulation of Granule Cell Activity



Granule Cells Separate Patterns



Pattern Separation by Granule Cells

Let's look at how two patterns are transformed by the granule cells.

Mossy fibers: input pattern.
Parallel fibers: output pattern.

Mossy Fibers		Parallel Fibers
$\alpha_M = 3/6 = 0.5$		$\alpha_G = 4/10 = 0.4$
1 1 1 0 0 0	$\rightarrow$	**1 0 1 1 0 0 0 1 0 0**
0 1 1 0 0 1	$\rightarrow$	**0 0 1 0 1 1 0 0 0 1**
$\theta_M = 2 / 6 = 0.33$		$\theta_G = 6 / 8 = 0.75$

Patterns have become <u>more</u> <u>sparse</u>: $\alpha_G < \alpha_M$

Patterns have also become <u>more</u> <u>distinct</u>: $\theta_G > \theta_M$.

Tyrell & Willshaw's Conclusions

- Marr's theory can be made to work in simulation.
- Memory capacity: 60-70 patterns can be learned by a Purkinje cell with a 1% probability of a false positive response to a random input.
- Several parameters had to be guessed because the anatomical data were not yet available.
- A few of his assumptions were wrong, e.g., binary synapses.
- But the overall idea is probably right.
- The theory is also compatible with the cerebellum having a role in classical conditioning.

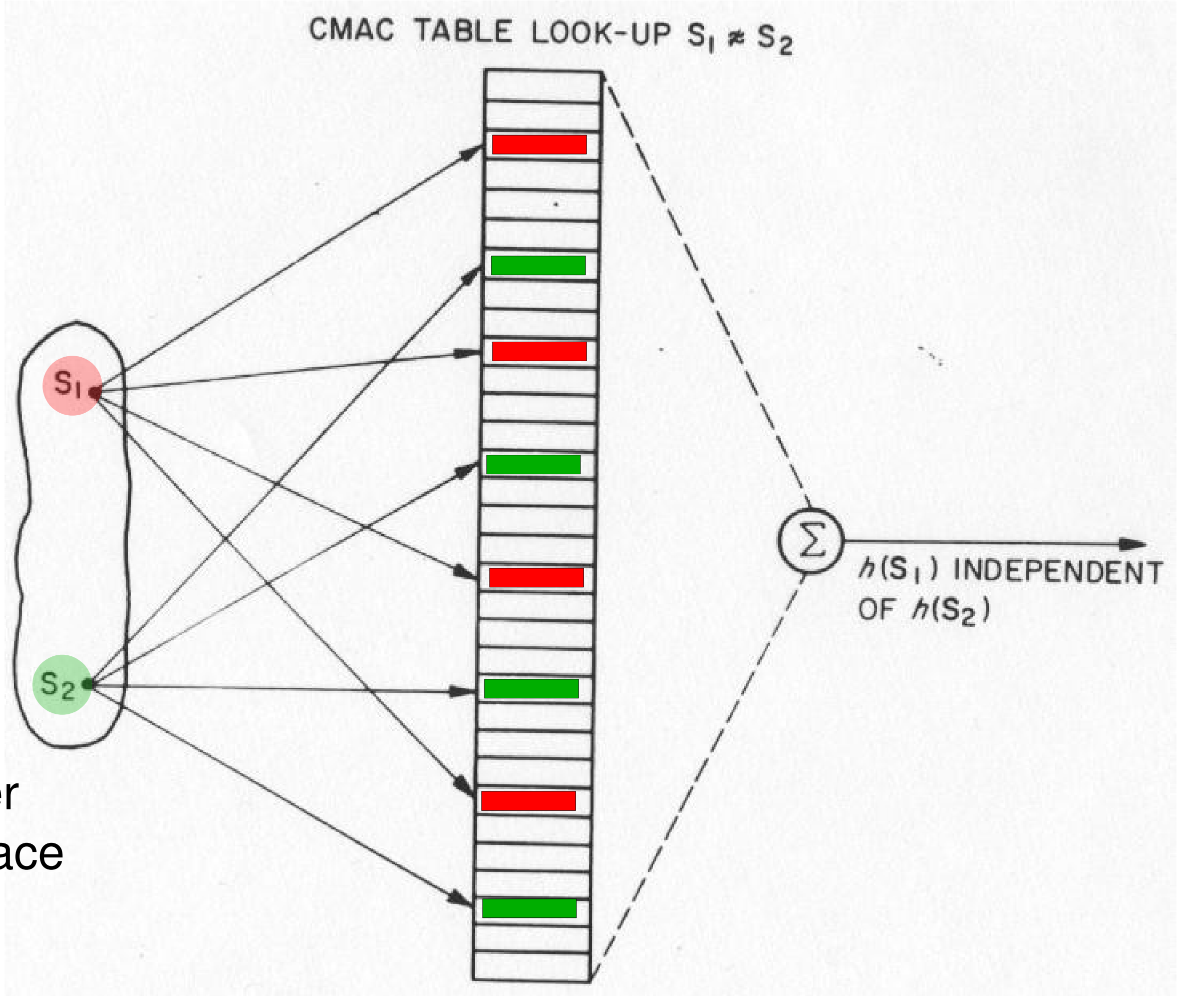
Marr's 3 System-Level Theories

- Cerebellum
  - Long-term memory but strictly “table lookup”.
  - Pattern completion from partial cues not desirable
- Hippocampus
  - Learning is only temporary (for about a day), not permanent.
  - Retrieval based on partial cues is important.
- Cortex
  - Extensive recoding of the input takes place: clustering by competitive learning.
  - Hippocampus used to train the cortex during sleep.

Albus' CMAC Model

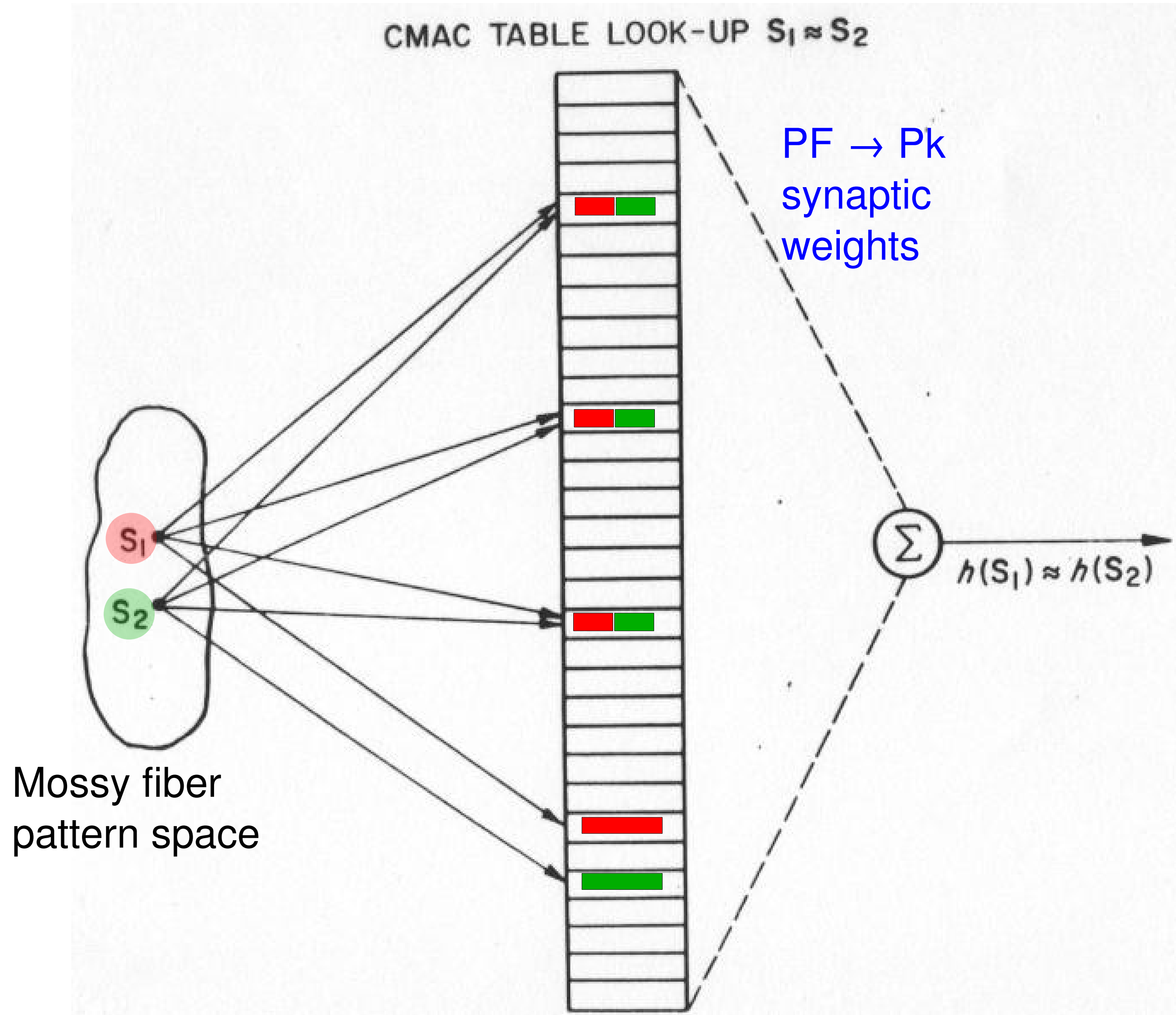
- Cerebellar Model Arithmetic Computer, or
  Cerebellar Model Articulation Controller
- Function approximator using distributed version of table lookup. In machine learning this is called “kernel density estimation”.

S_1 and S_2 far apart in pattern space: table entries don't overlap.



Mossy fiber pattern space

Similar Patterns Share Representations



Learning a Sine Wave

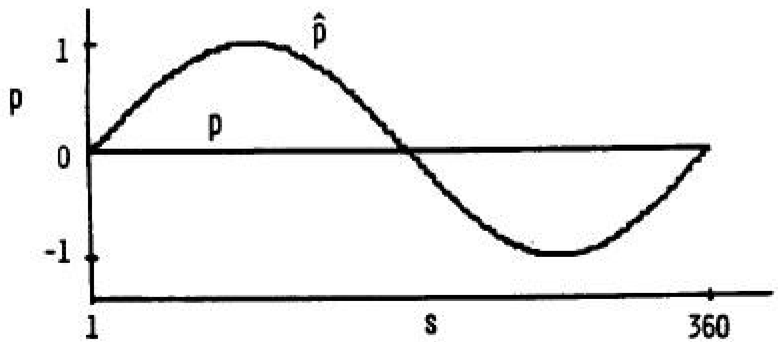


Fig. 1 ρ is the output from a one-input CMAC memory prior to any data being stored. $\hat{\rho}$ is the desired output. For this case the maximum error between ρ and $\hat{\rho}$ is 1.0 and the r.m.s. error is 0.707.

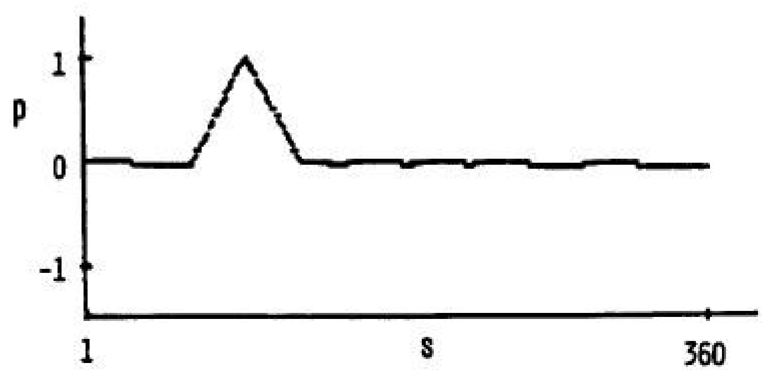


Fig. 2 The output of the CMAC memory after a single error correction data storage operation. ρ was set equal to 1.0 at $s = 90$. Maximum error is still 1.0 (at $s = 270$) and r.m.s error is now 0.625.

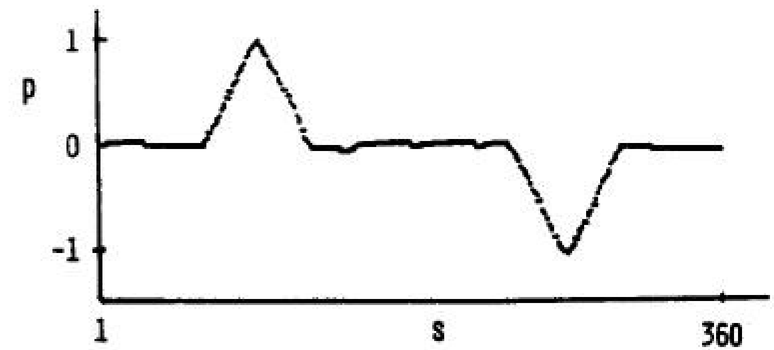


Fig. 3 After two data storage operations. Maximum error = 0.87 and r.m.s. error = 0.530.

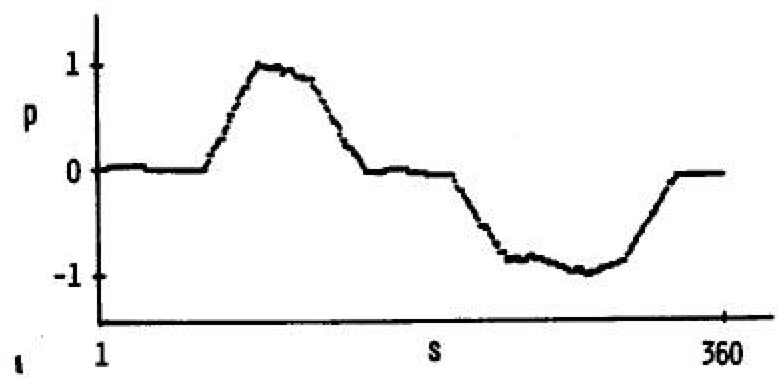


Fig. 4 After five data points are stored. Maximum error = 0.84 and r.m.s. error = 0.313.

Learning a Sine Wave

Fig. 5 After nine data points are stored. Maximum error = 0.33 and r.m.s. error = 0.081.

Fig. 6 After sixteen data points are stored. Maximum error = 0.09 and r.m.s. error = 0.033.

Learning 2D Data

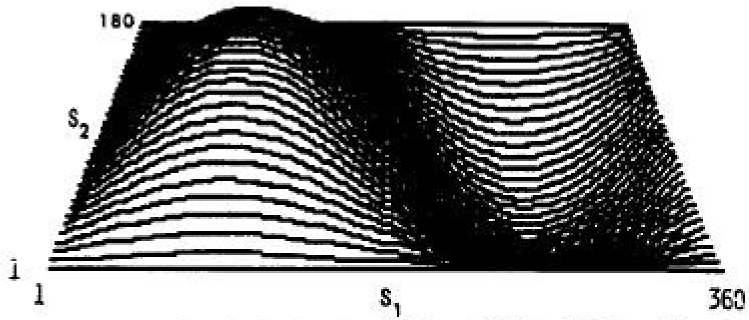


Fig. 7 A plot of a desired output $\hat{p}$ for a CMAC with two inputs. $\hat{p} = \sin\left(\frac{2\pi s_1}{360}\right)\sin\left(\frac{2\pi s_2}{360}\right)$

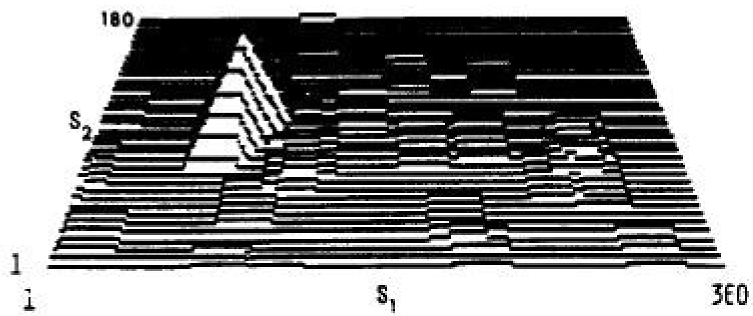


Fig. 8 The output of a two-input CMAC memory after a single error correction data storage operation. p was set equal to 1.0 at $s_1 = 90$, $s_2 = 90$.

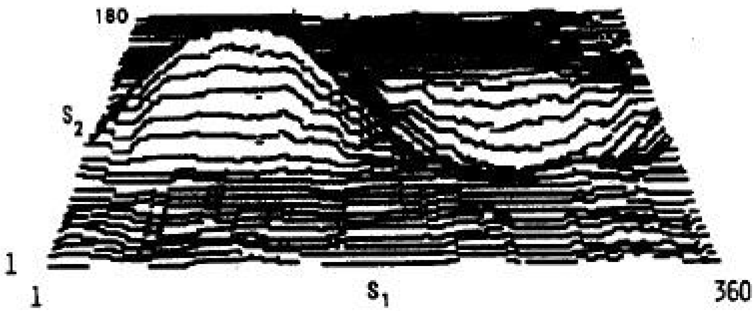


Fig. 9 The output of a two-input CMAC memory after sixteen data points were stored. A cross section of this figure in the $s_1 = 90$ plane is identical to Fig. 6.

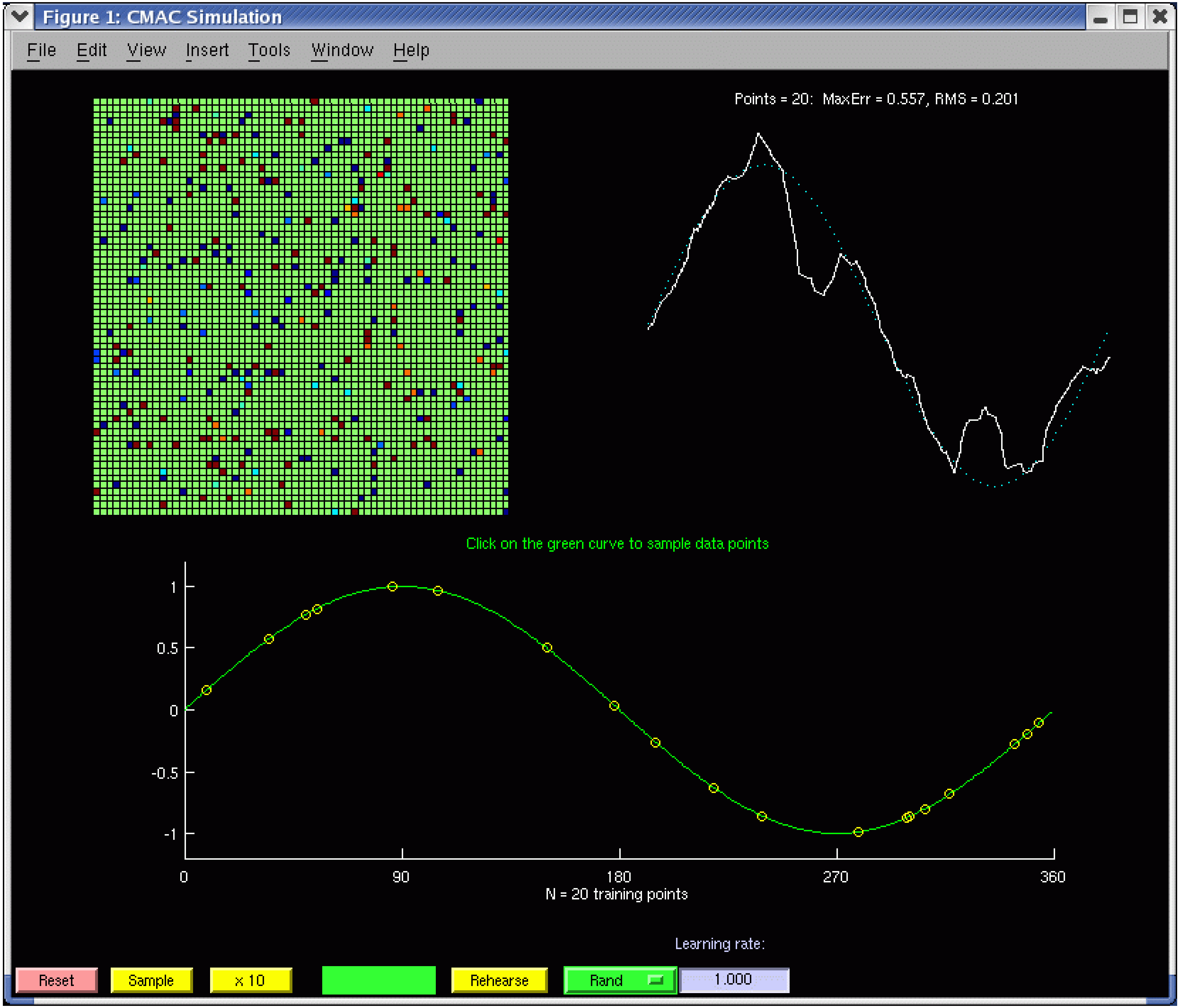
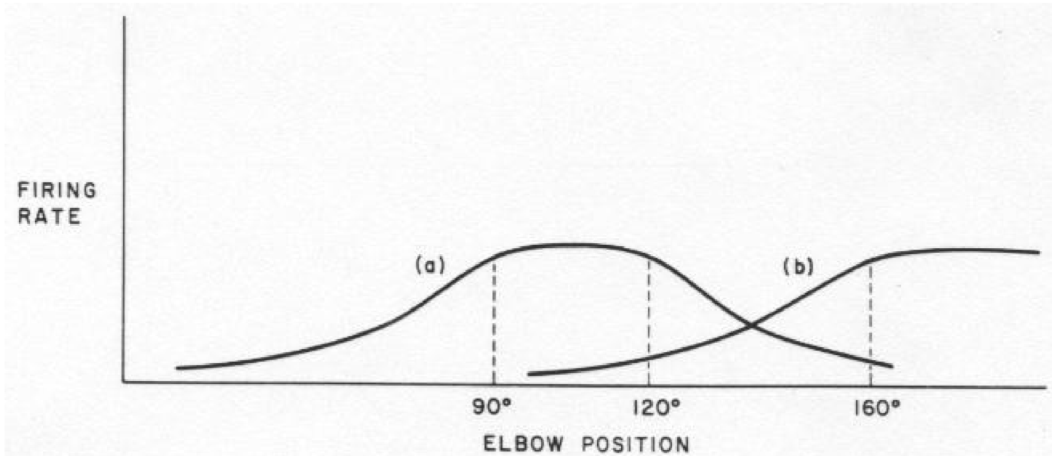
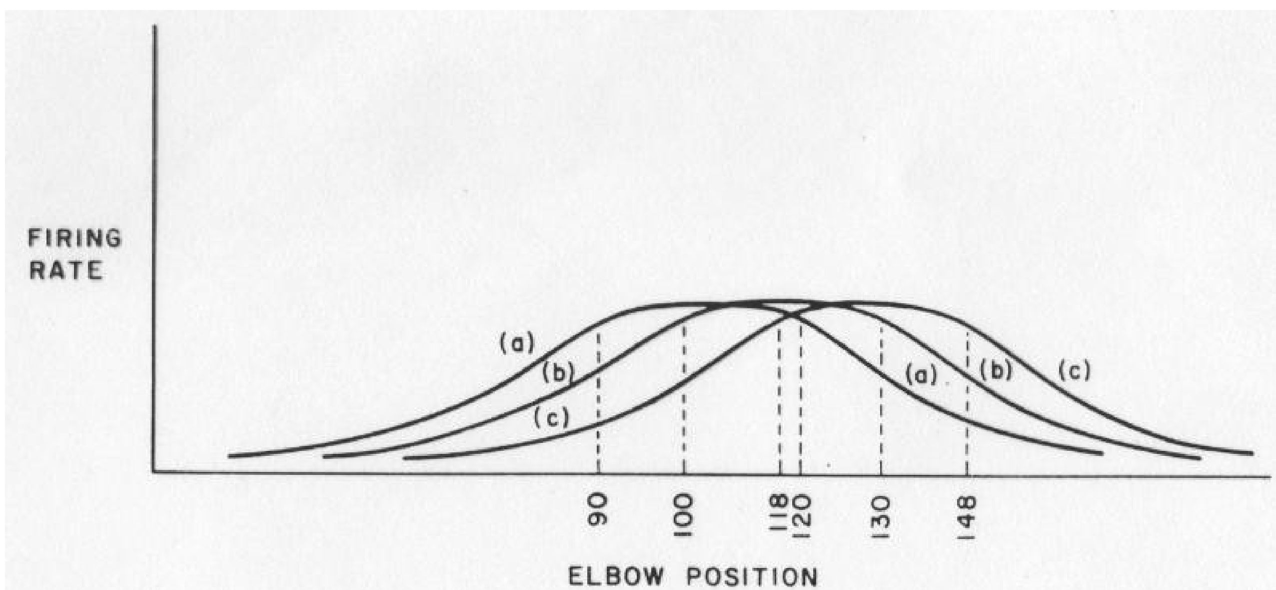


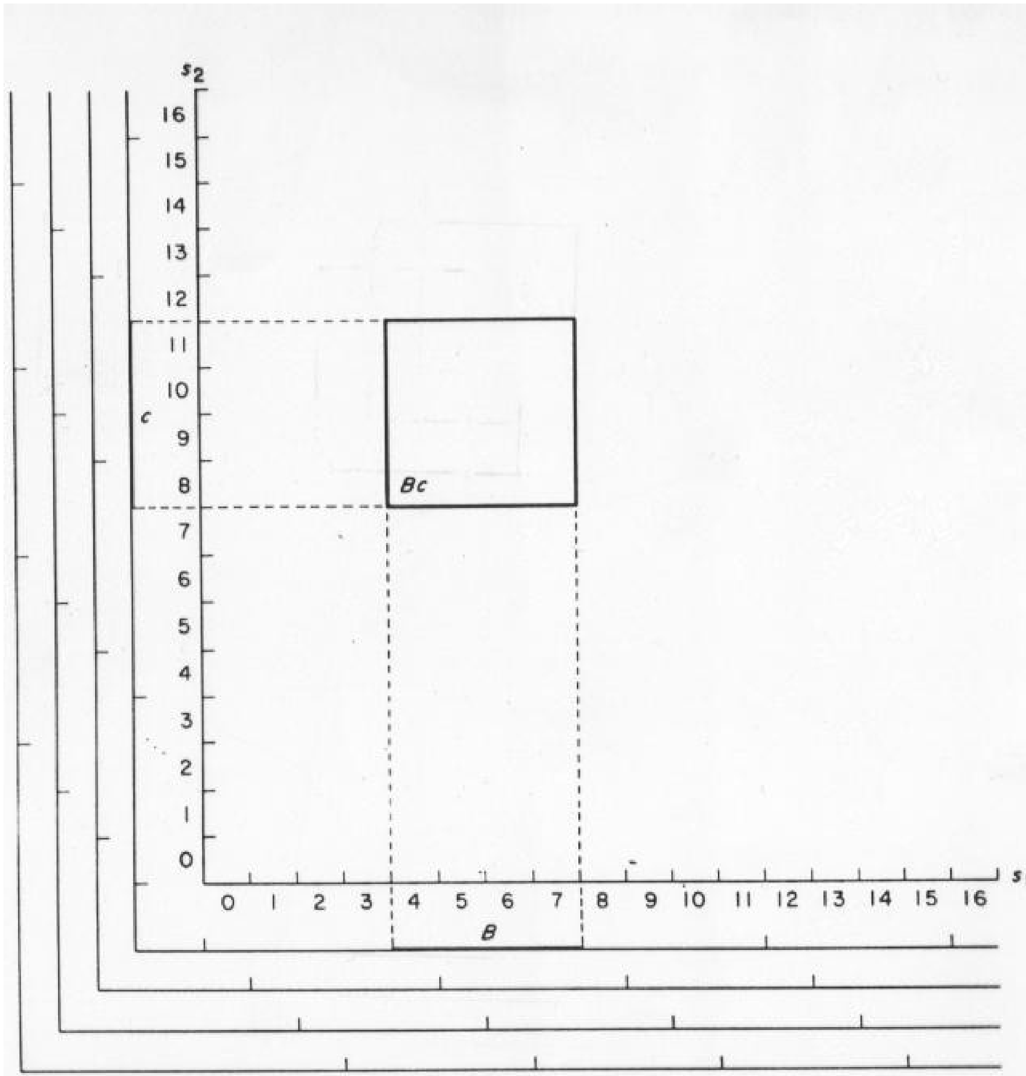
Figure 1: CMAC Simulation
File Edit View Insert Tools Window Help
Points = 20: MaxErr = 0.557, RMS = 0.201
Click on the green curve to sample data points
1
0.5
0
-0.5
-1
0
90
180
270
360
N = 20 training points
Learning rate:
Reset
Sample
x 10
Rehearse
Rand
1.000

Coarsely-Tuned Inputs Resemble Mossy Fibers

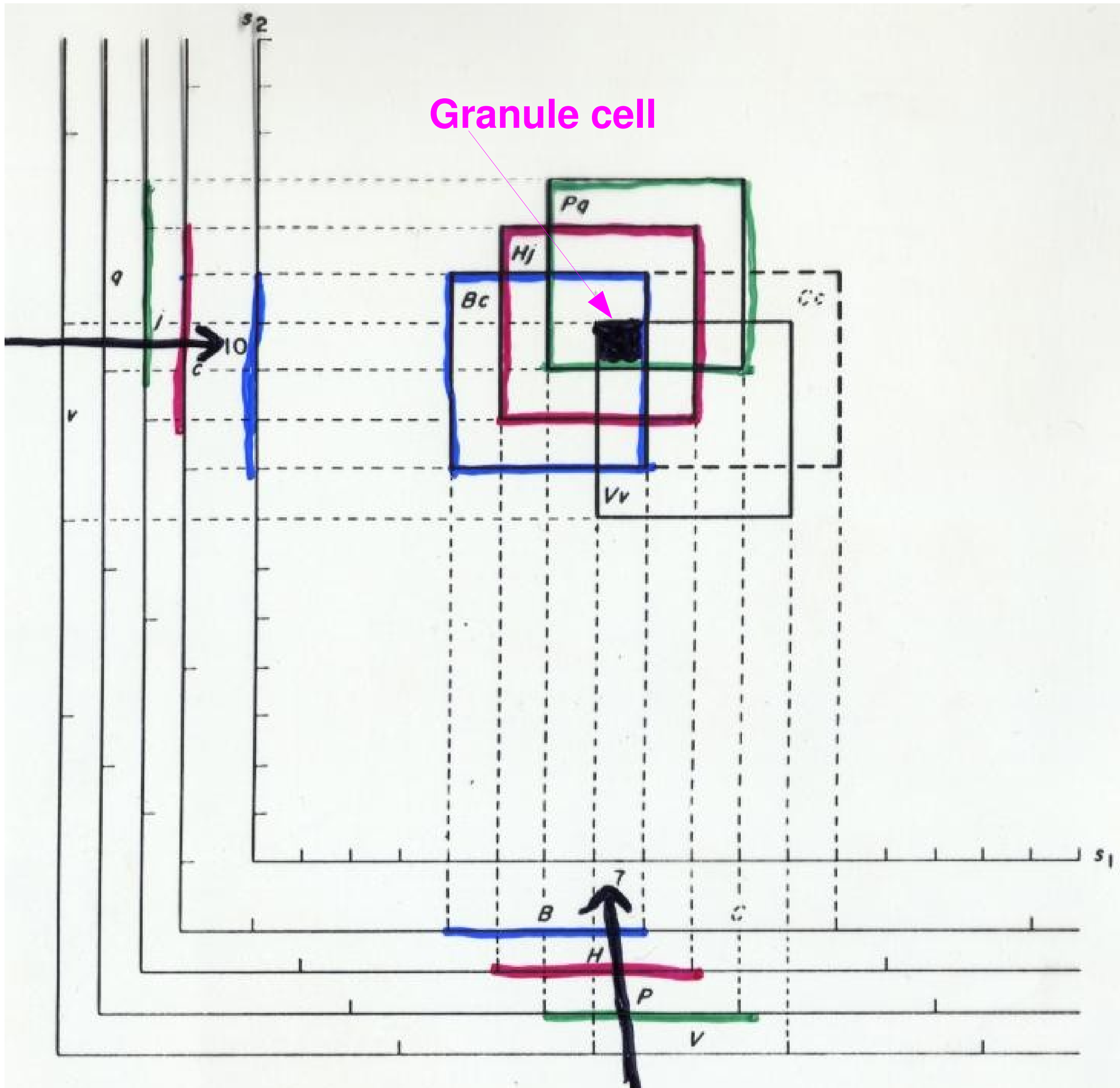




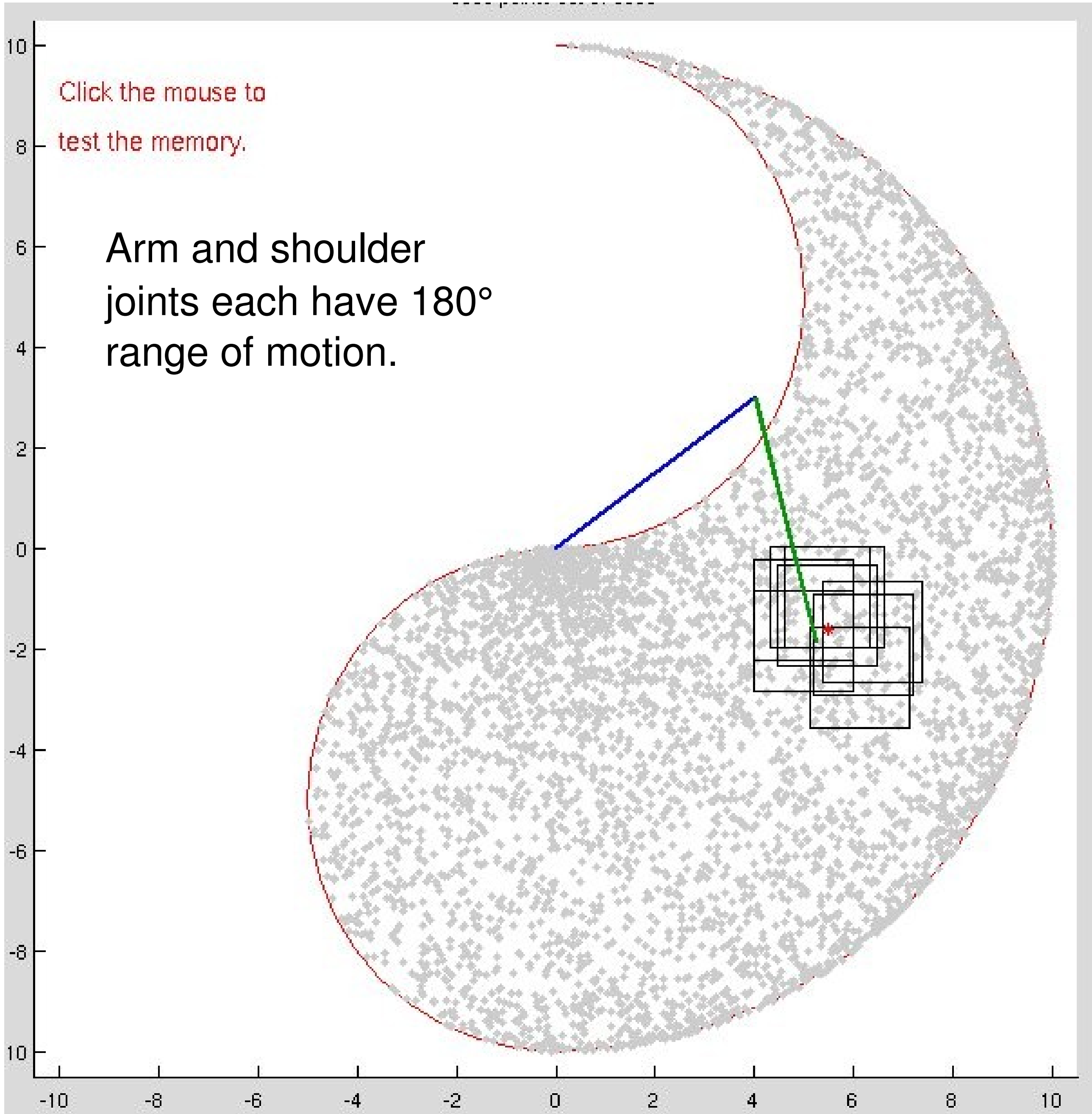
Coarse Tuning in 2D



Coarse Coding Using Overlapped Representations



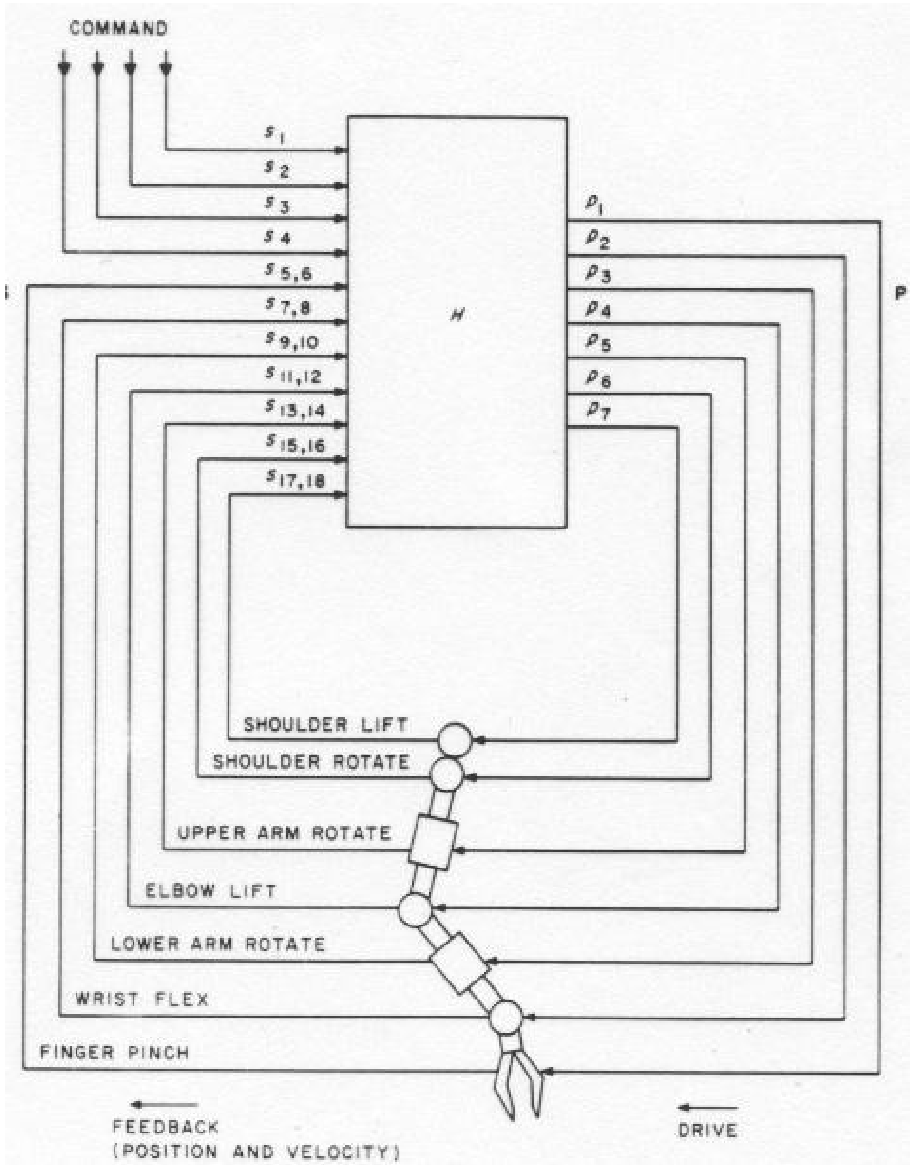
2D Robot Arm Kinematics



Arm and shoulder joints each have 180° range of motion.

Higher Dimensional Spaces

Motor control is a high dimensional problem.



CMAC Learning Rule

1. Compare output value *p* with desired value *p**.
2. If they are within acceptable error threshold, do nothing.
3. Else add a small correction Δ to every weight that was summed to produce *p*:

g is a gain factor ≤ 1
A is the set of active weights

$$\Delta = g \cdot \frac{p^* - p}{|A|}$$

If $g=1$ we get one-shot learning.
Safer to use $g<1$ to ensure stability.

CMAC = LMS (Least Mean Square) Learning

- CMAC learning rule:

$$\Delta = g \cdot \frac{p^* - p}{|A|}$$

Implicit: rule only applies to active units (units in set A)

- LMS learning rule:

$$\Delta w_i = \eta \cdot (d - y) \cdot x_i$$

Explicit: learning rate depends on unit's activity level

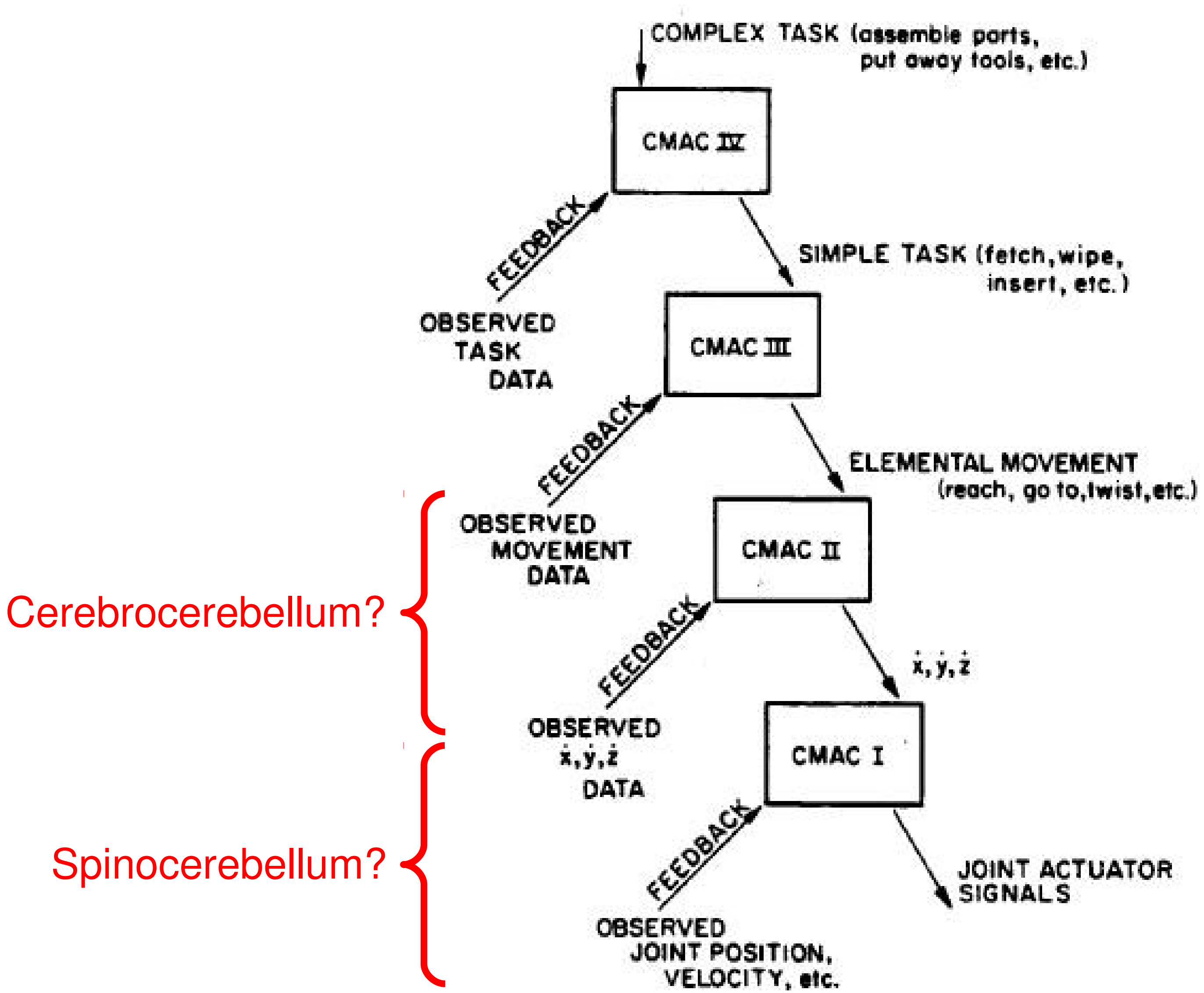
- Same rule!
- LMS could be used to store linearly independent patterns in a matrix memory.

Albus: Why Should Purkinje Cells Use LTD?

1. Learning must be Hebbian, i.e., depend on Purkinje cell activity, not inactivity.
2. Climbing fiber = error signal.
   Climbing fiber fires $\rightarrow$ Purkinje cell should <u>not</u> fire.
3. Parallel fibers make excitatory connections.

So: <u>reducing</u> the strength of the parallel fiber synapse when climbing fiber fires will reduce the Purkinje cell's firing.

Application to Higher Order Control?



Compare Marr and Albus Models

Marr:

- Focus on single Purkinje cell recognizing N patterns
- Binary weights (correct?)
- Binary output

Albus:

- Focus on PCs collectively approximating a function
- Continuous weights
- Continuous-valued output

Both use granule cells to recode input, decrease overlap.

Marr:

- Assumes learning by LTP

Albus:

- Requires learning by LTD

Both use static input and output patterns; no dynamics.

Newer Simulations using GPUs

- Mauk lab (2013): large scale simulation of cerebellum
  - 1024 mossy fibers; 1024 Golgi cells
  - 2^{20} (1,048,576) granule cells
  - 32 Purkinje cells
  - 128 basket cells; 512 stellate cells
  - Simulated on an Nvidia GTX580 GPU
  - Eyeblink conditioning, pole balancing tasks

- Yamazaki & Igarashi (2013): real-time spiking simulation
  - 102,000 granule cells
  - 1024 Golgi cells, 16 Purkinje cells, 16 basket cells
  - Runs in real-time on Nvidia GeForce GTX580
  - Robot arm control application

Complications

- PF $\rightarrow$ Pk synapses show LTP as well as LTD
- Connectivity is more complex than these models provide for:
  - Pk cells project to other Pk cells
  - Deep cerebellar nuclei (DCN) cells project to Golgi cells
  - Deep cerebellar nuclei cells inhibit cells in the inferior olive
  - Inferior olive cells are electrotonically coupled
- Plasticity is not limited to PF $\rightarrow$ Pk synapses
  - Plasticity of connections onto interneurons
  - Plasticity within DCN
- DCN is complex
  - At least 6 cell types
  - Multiple neurotransmitters (glutamate, GABA, glycine)

Experimental Issues to Consider

Why do some papers report results that conflict with others?

- It's easier to record in slice than in intact animals.
  - But slices are missing some input pathways because those axons get severed.
  - Slice experiments require artificial stimuli; experiments done with intact animals can use natural stimuli.
- Recording in intact animals may require anesthesia.
  - Anesthesia alters the behavior of neurons.
- Although the cerebellum is common to vertebrates, there may be differences between species.