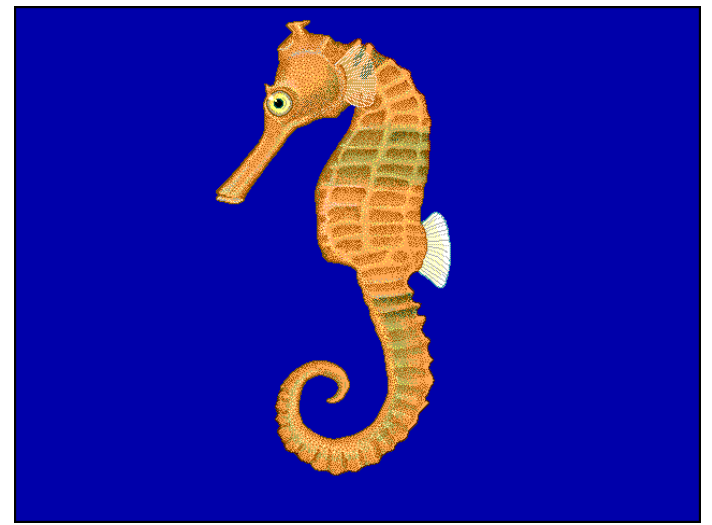# Anatomy of the Hippocampus
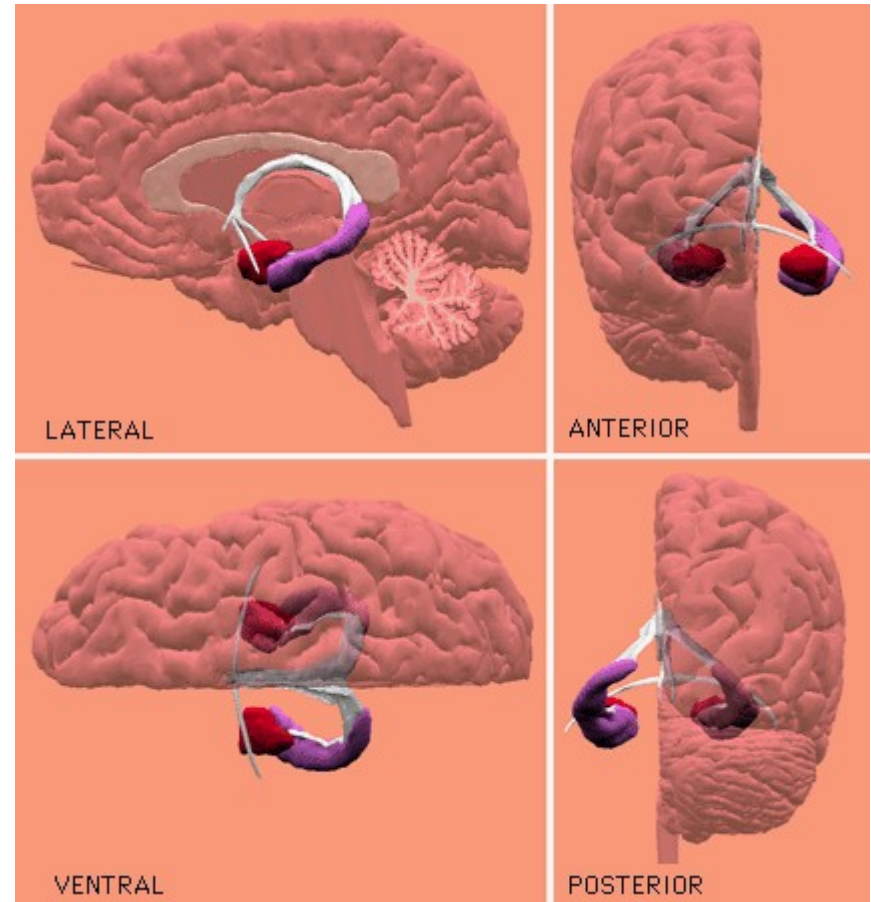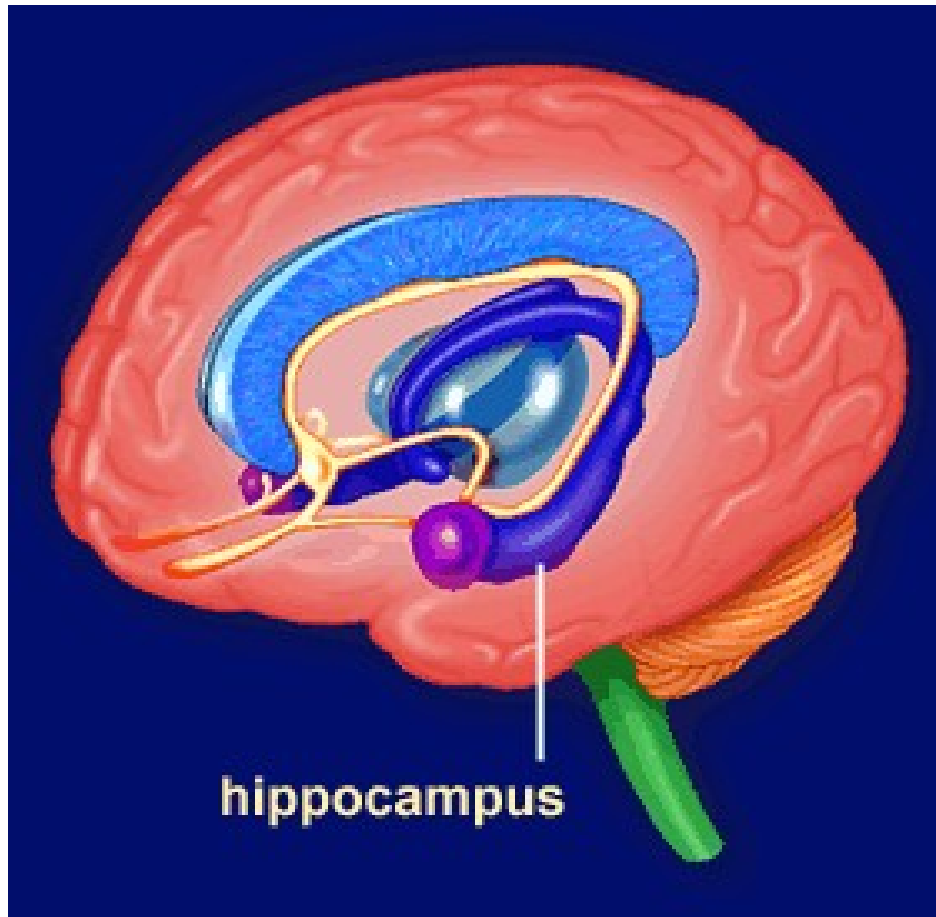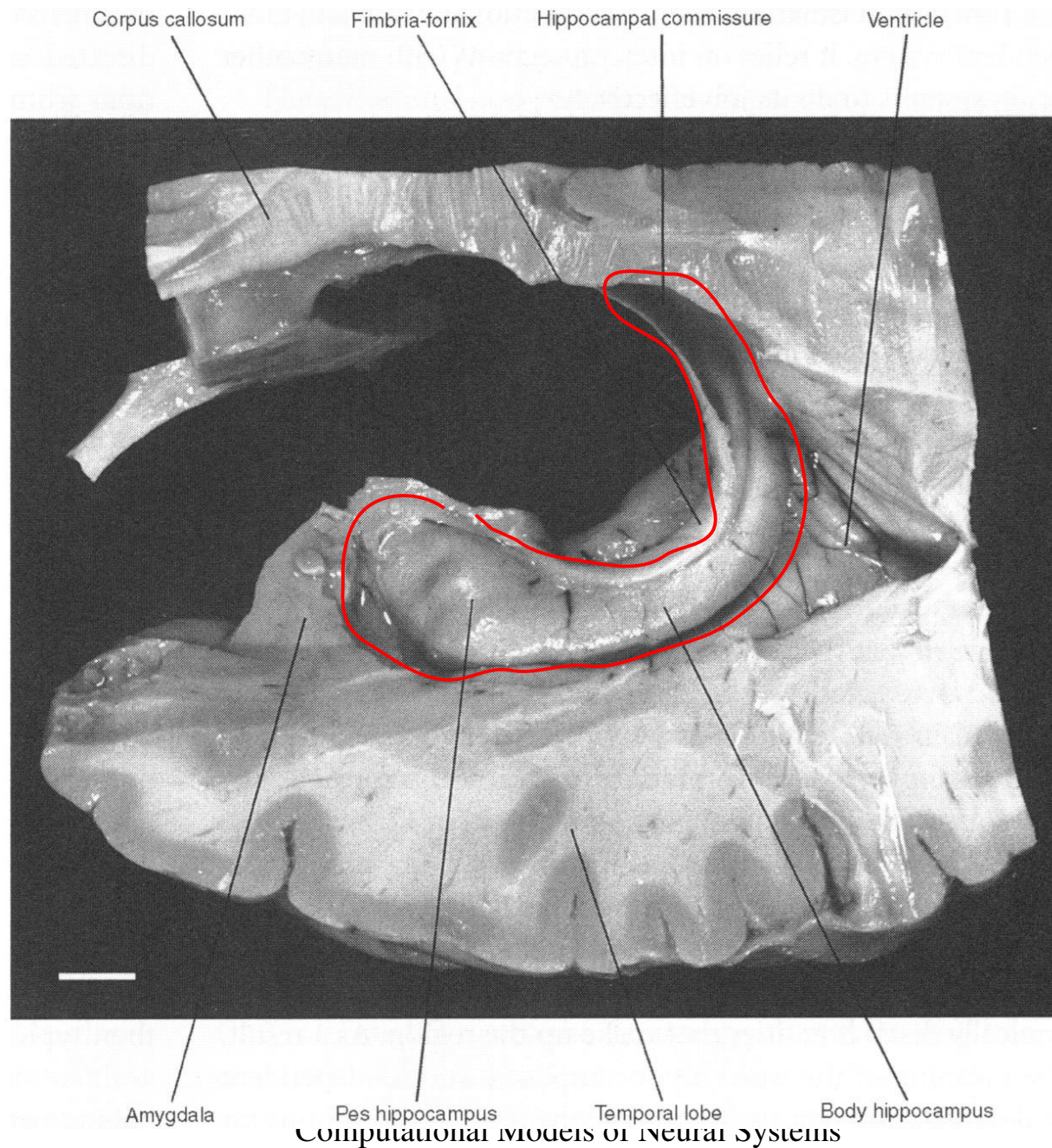
Computational Models of Neural Systems

Lecture 3.2

David S. Touretzky

September, 2021

Human Hippocampus

hippocampus

LATERAL

ANTERIOR

VENTRAL

POSTERIOR

Computational Models of Neural Systems

Human Hippocampus

Computational Models of Neural Systems

Hippocampus Means "Seahorse"
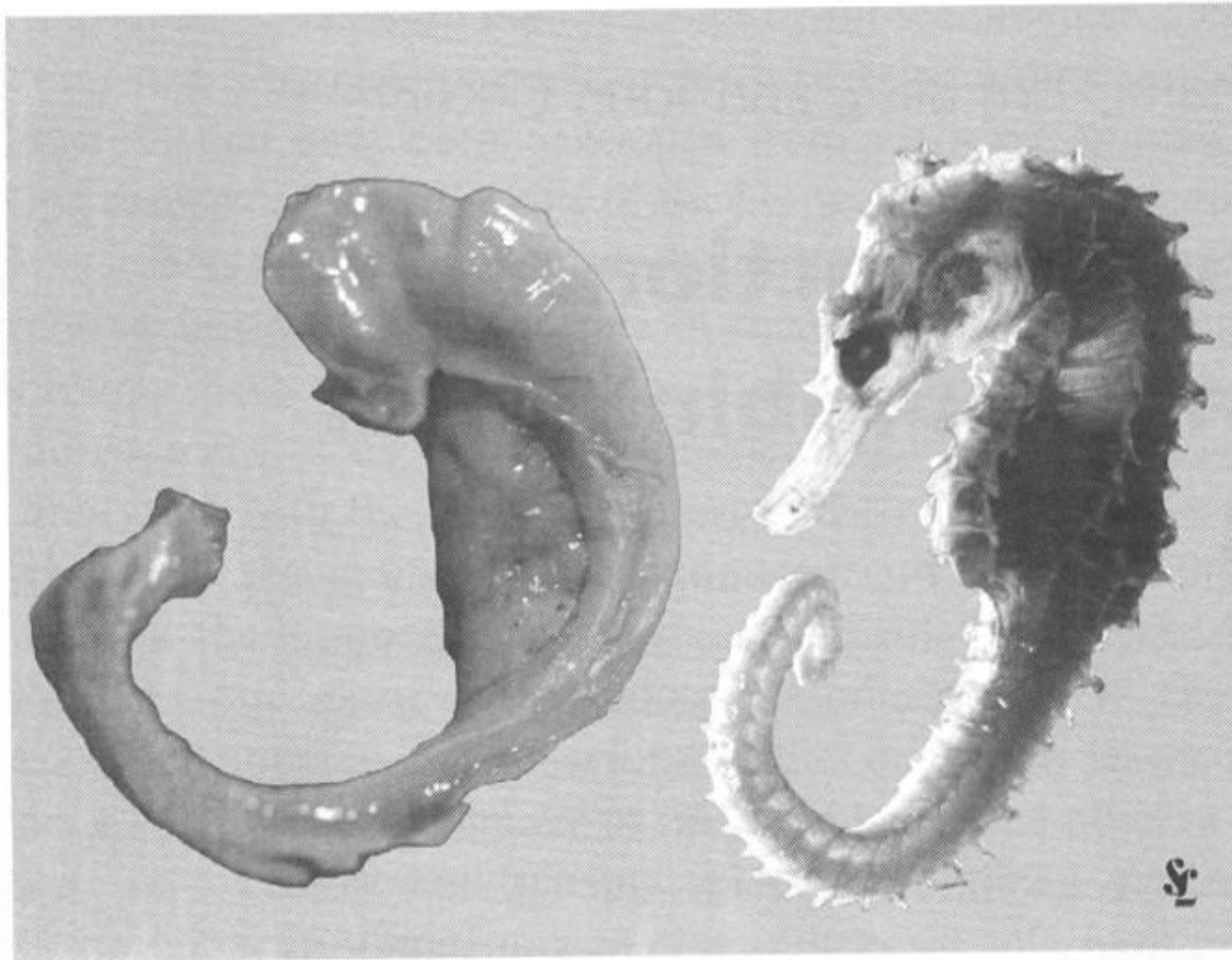
Dissected human hippocampus next to a specimen of *hippocampus leria*, one of several dozen species.

Computational Models of Neural Systems

Rat Hippocampal Formation

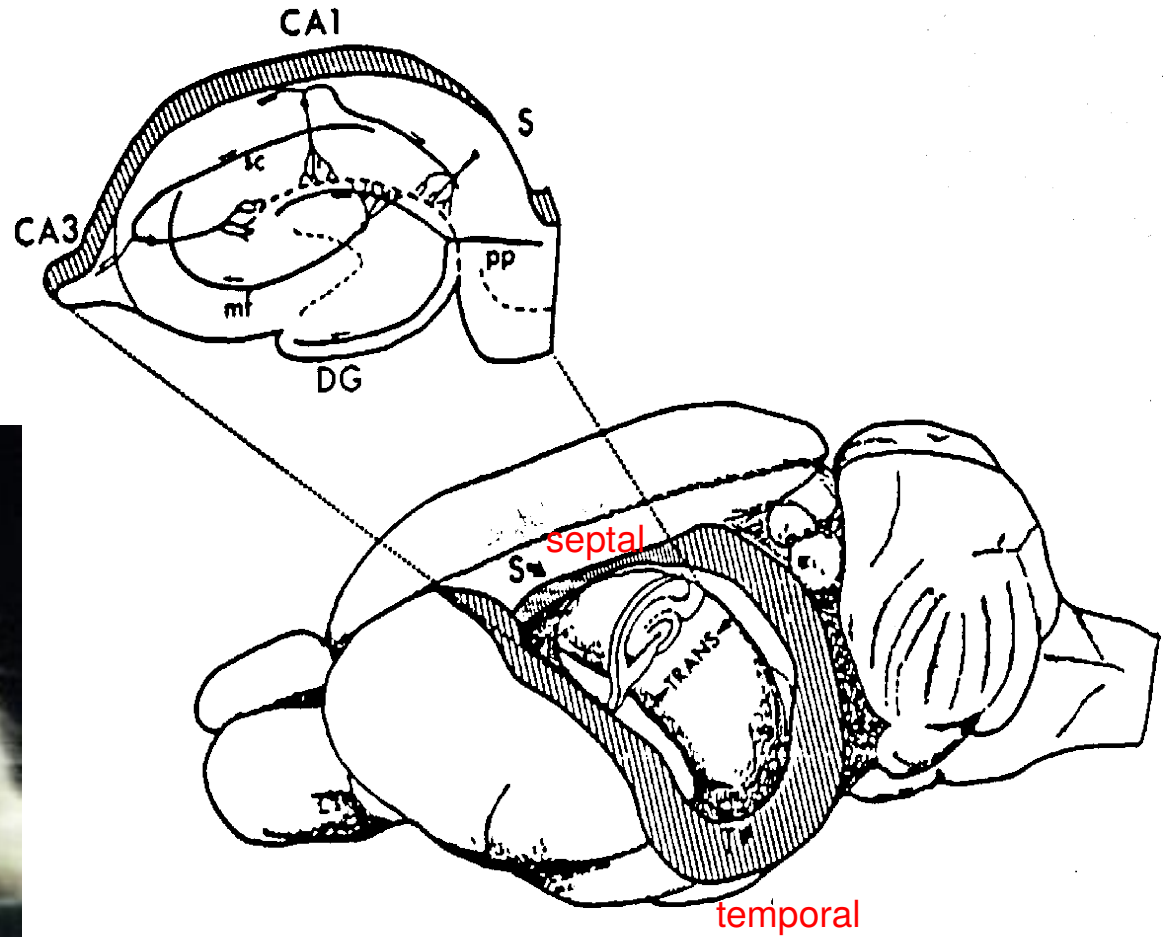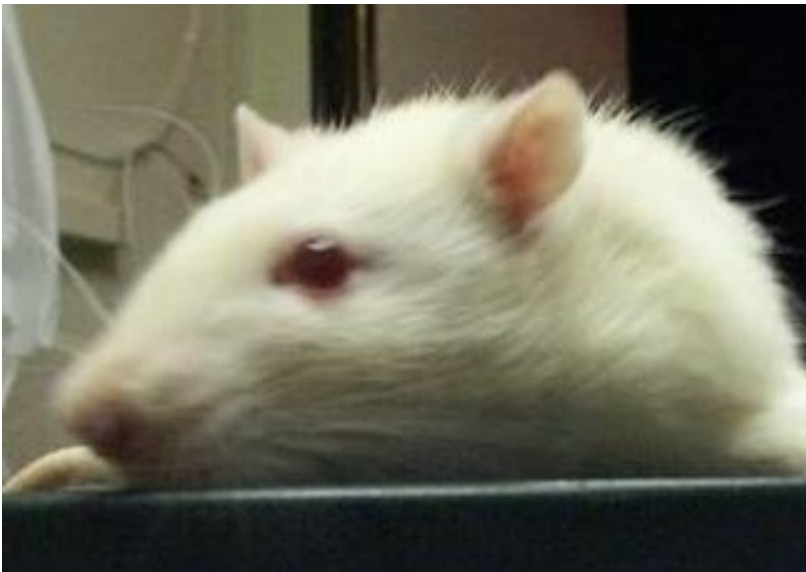
septal

temporal

From (Amaral & Witter, 1989)

Computational Models of Neural Systems

Ammon: Egyptian god with ram's horns

Computational Models of Neural Systems

Rat Hippocampal Formation

septal

temporal

CA1

CA3

dentate gyrus

entorhinal cortex

Computational Models of Neural Systems
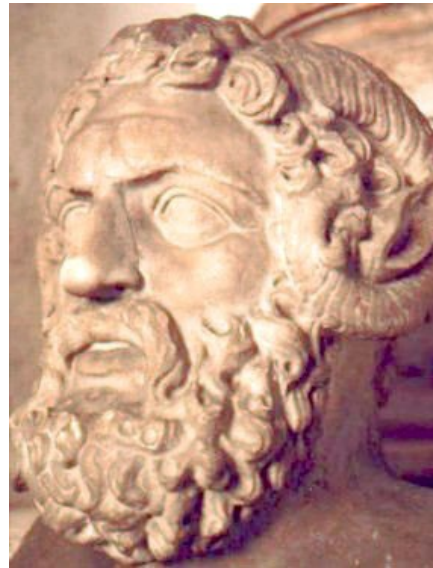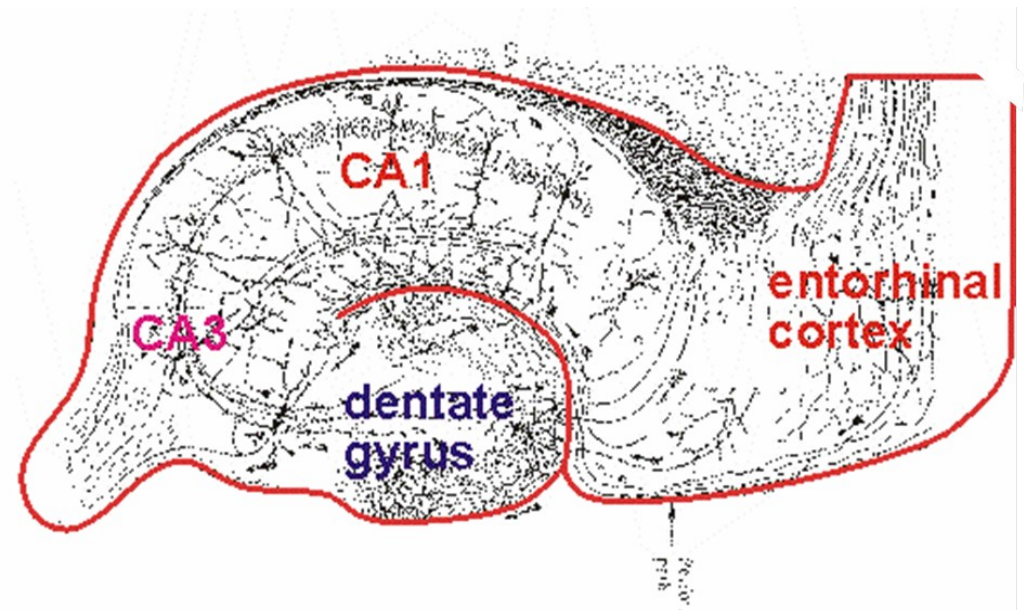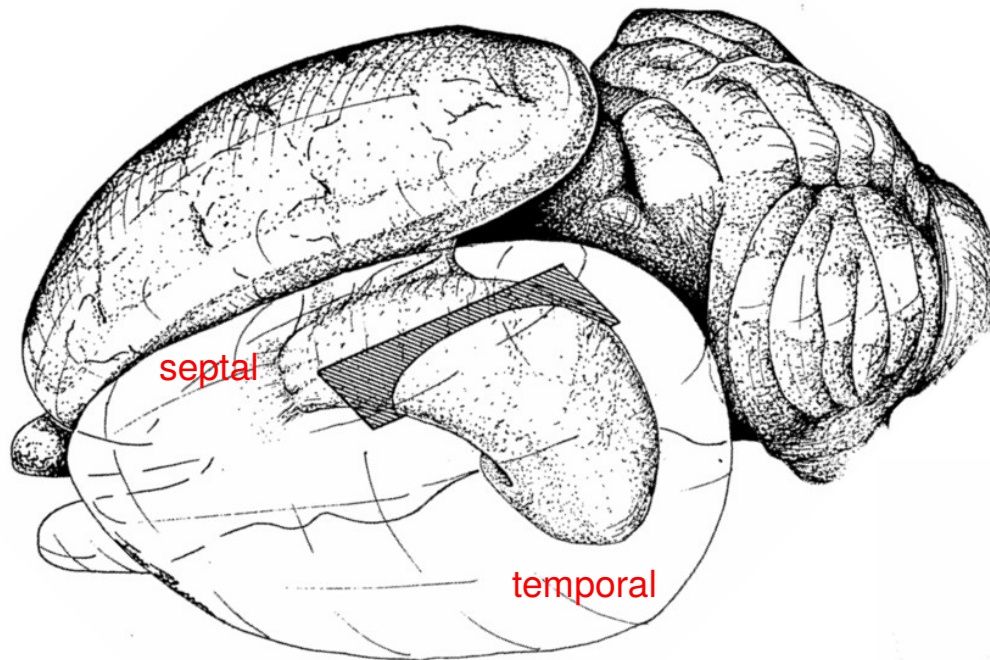
Components of Hippocampal Formation

- The "*hippocampus*" contains CA1 - CA3.

  CA = Cornu Amonis (Ammon's horn)

- The "*hippocampal formation*" includes CA, dentate gyrus ("tooth-like bump"), entorhinal cortex, subiculum, pre- and parasubiculum.

- Hilus (CA4): reciprocally connected to DG.

Ammon's Horn

Cornu ammonis (=CA)

Computational Models of Neural Systems
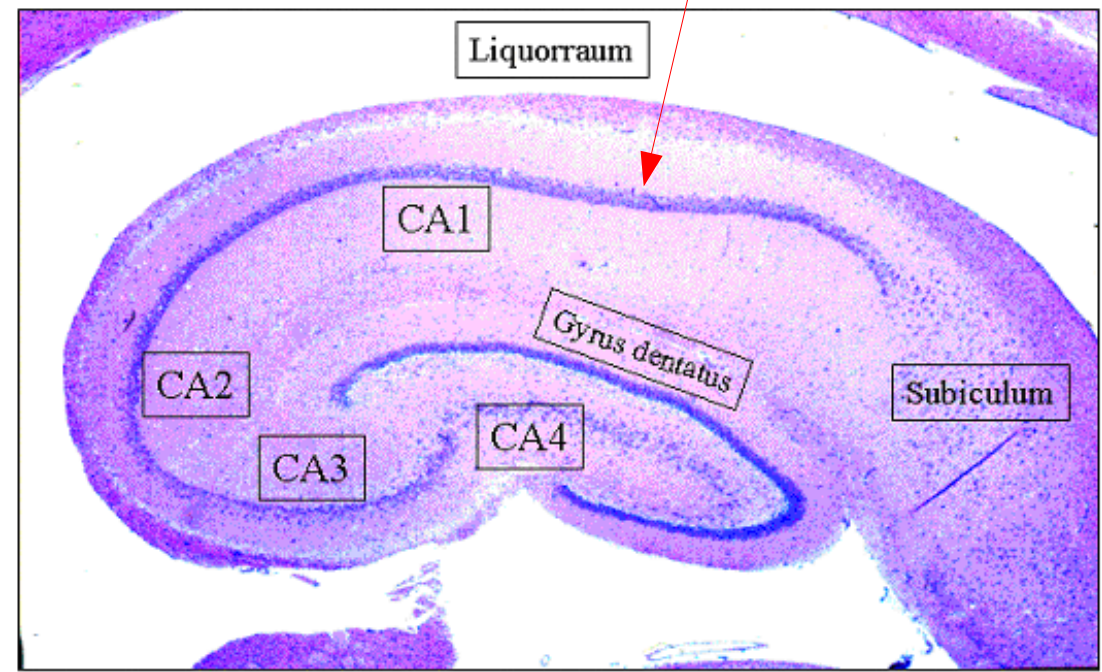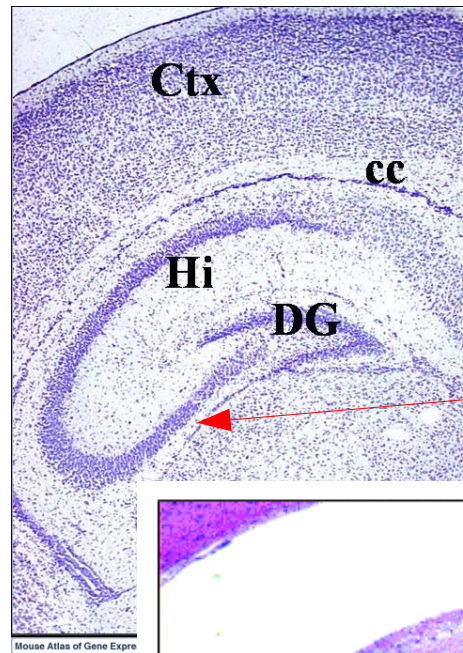
Early Anatomy: Cajal's Drawings

Rat Hippocampus

Computational Models of Neural Systems

Monkey Hippocampus

Computational Models of Neural Systems
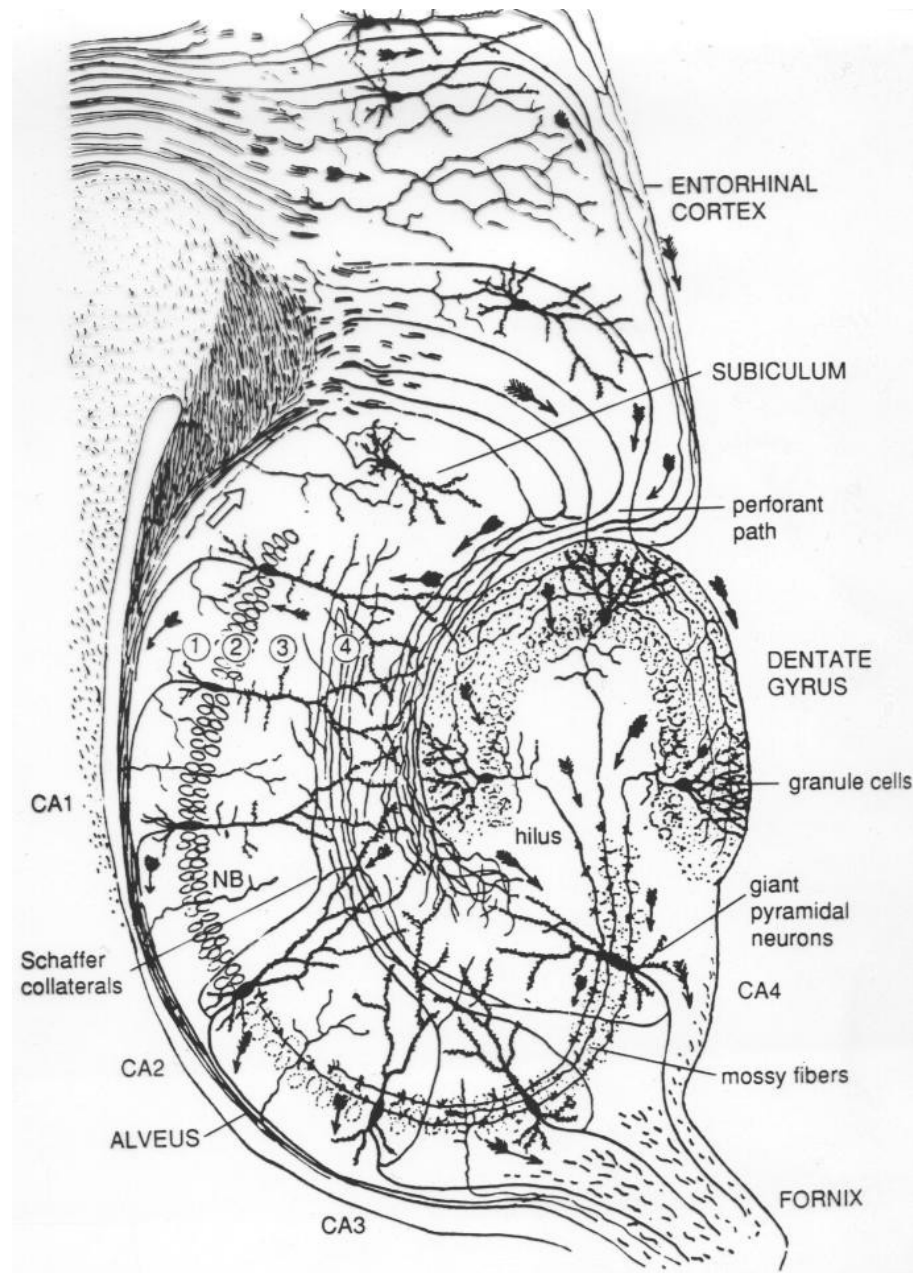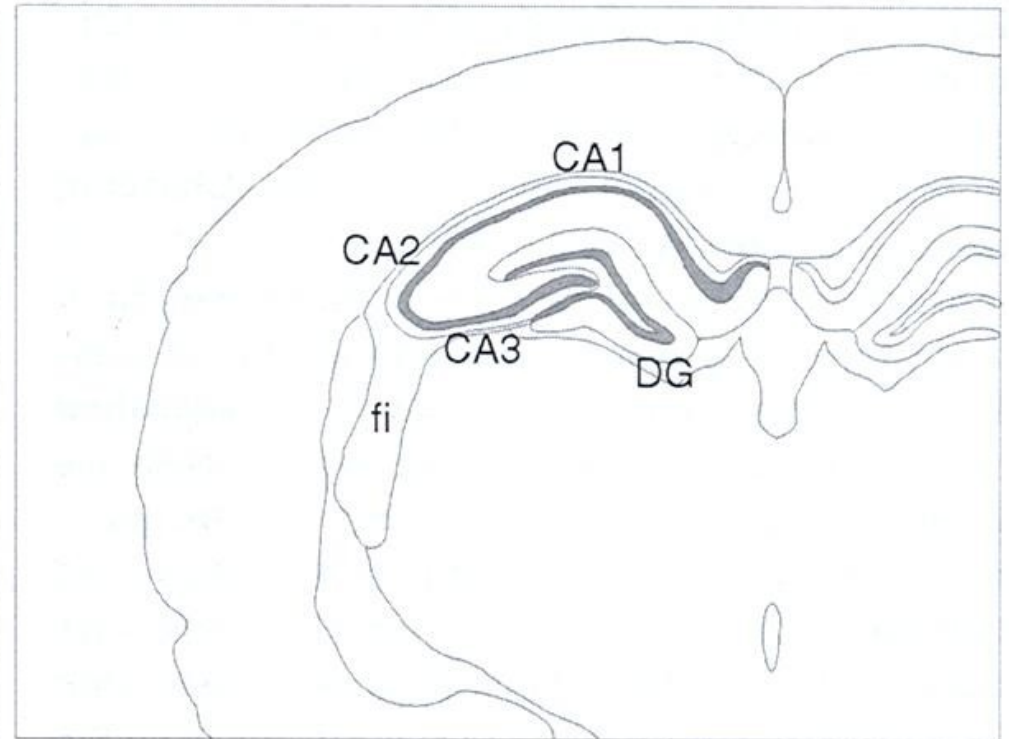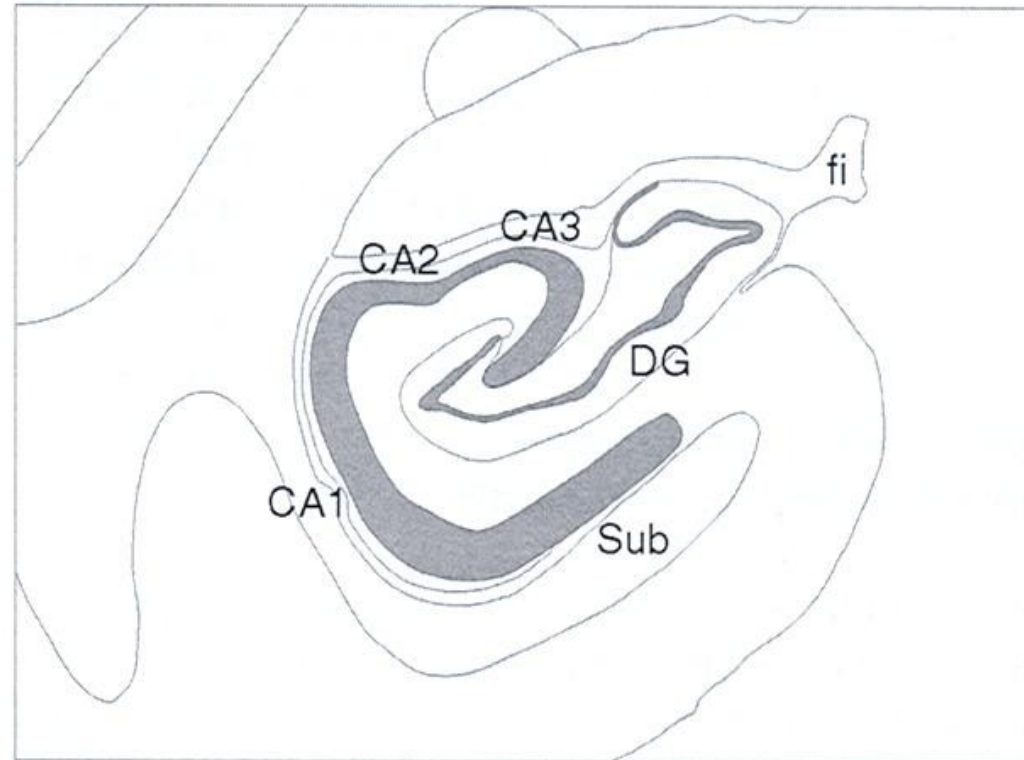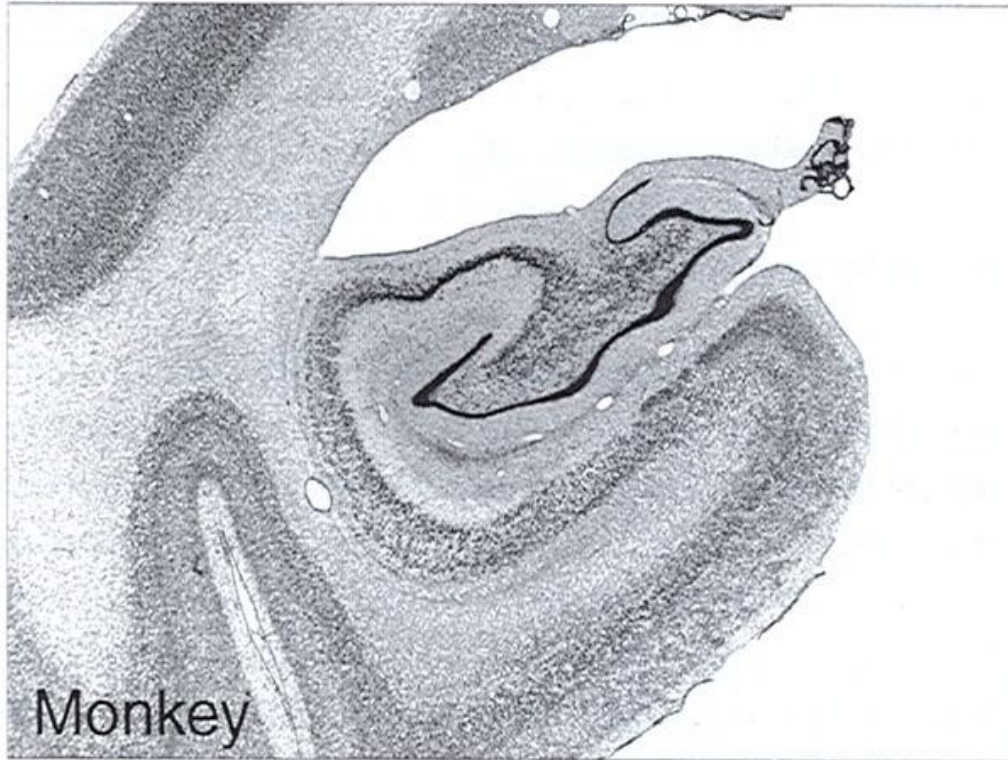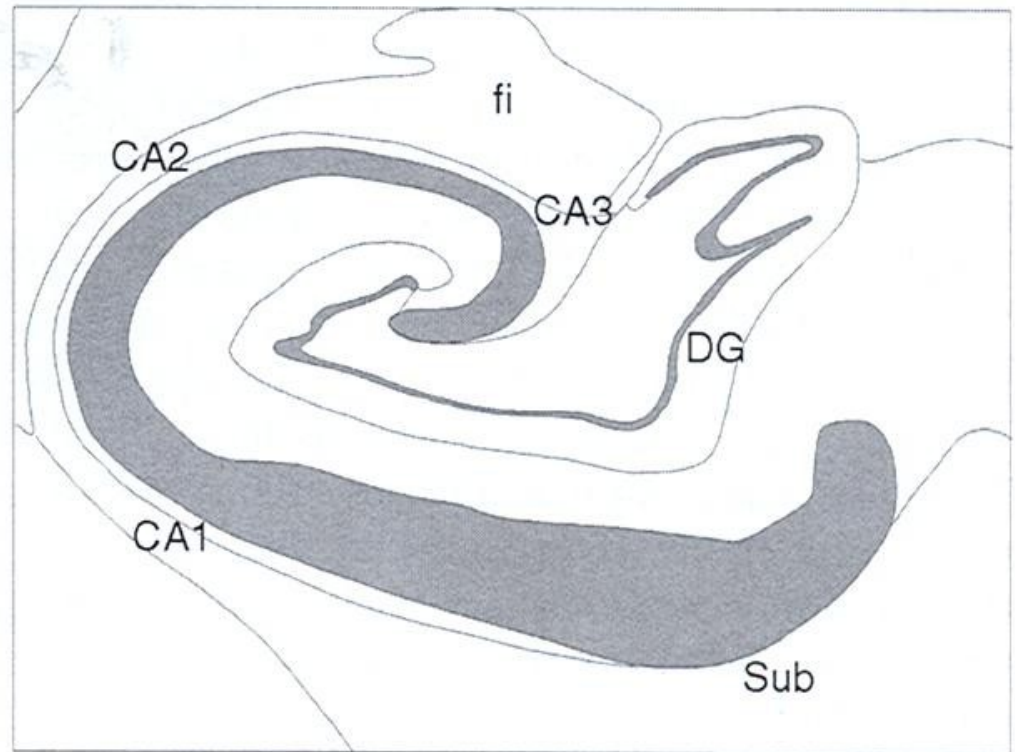
Human Hippocampus

The volume of the human hippocampus is about 100 times that of the rat, and 10 times that of the monkey.

Basic Circuit

Layer III perforant path

EC

Layer II perf. path

DG — Mossy fibers → **CA3** — Schaffer collaterals → **CA1**

Recurrent collaterals
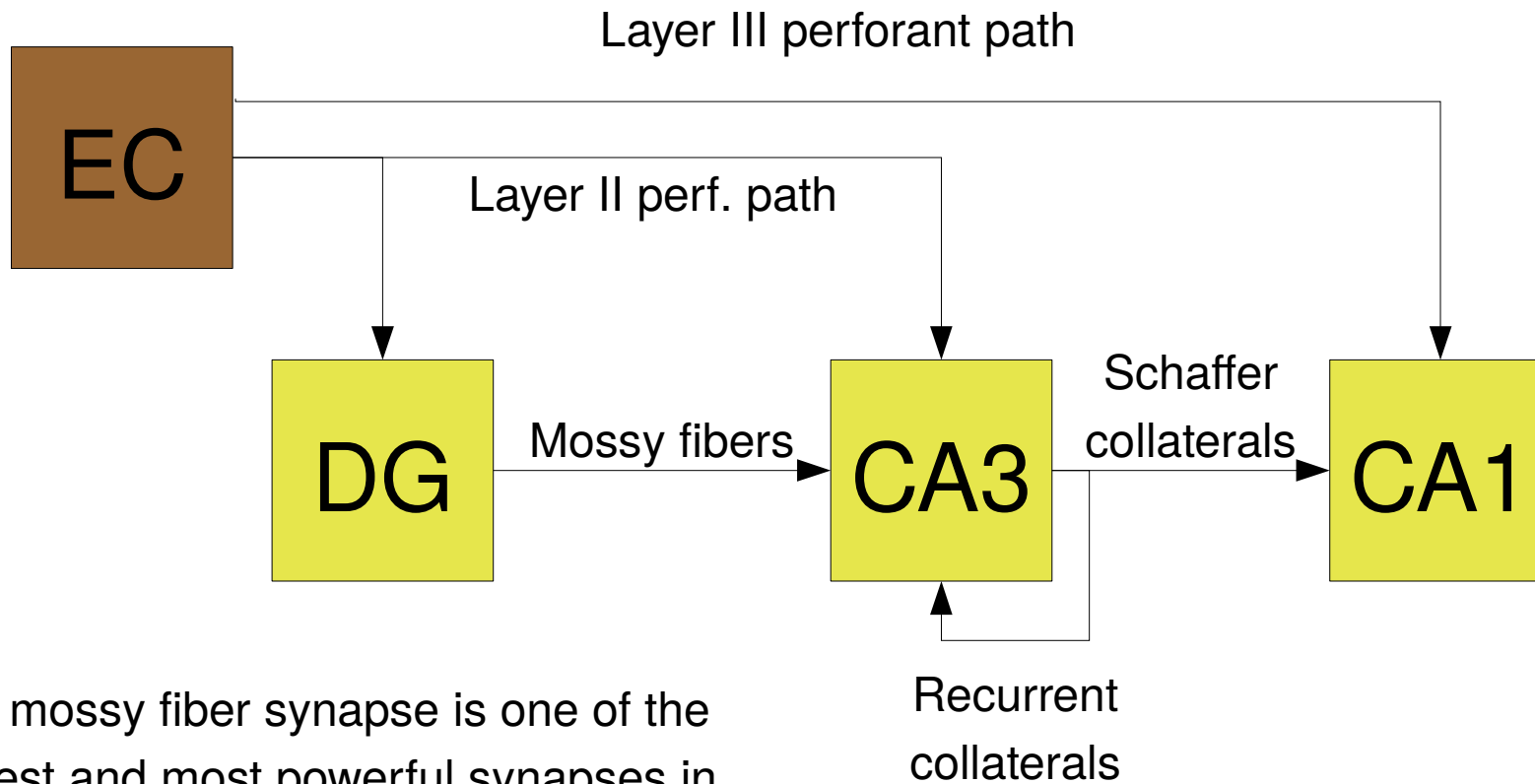
The mossy fiber synapse is one of the largest and most powerful synapses in the brain.

Connectivity Is Mostly Uni-Directional

Computational Models of Neural Systems
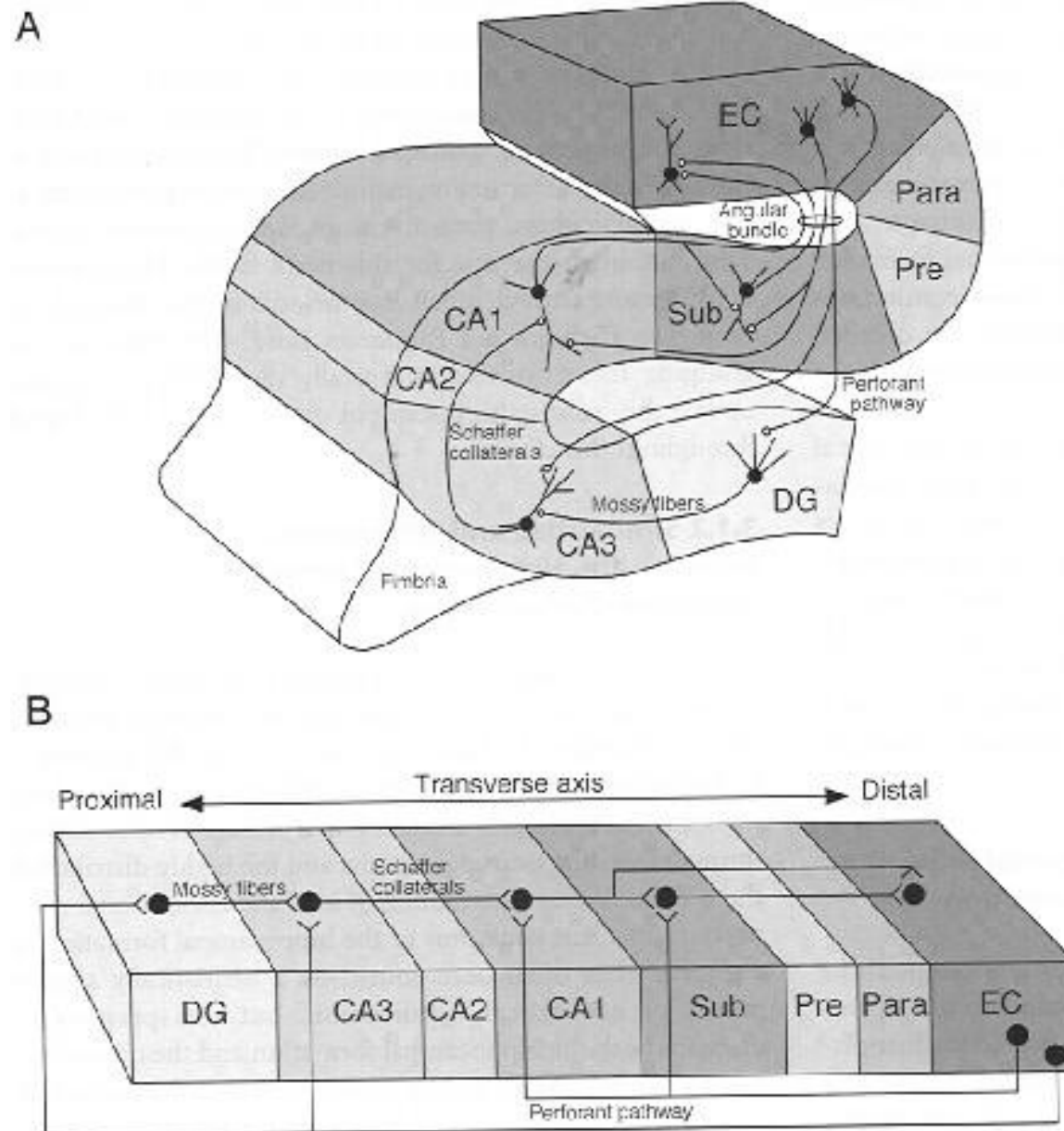
What About CA2?

- Small relative to CA3 and CA1

- Originally dismissed as a "transitional area"

- Driven by Schaffer collaterals from CA3

- Projects back to CA3 and to two layers of CA1

- Does not show activity-dependent LTP as found in CA3 and CA1

- In mice, contributes to social memory
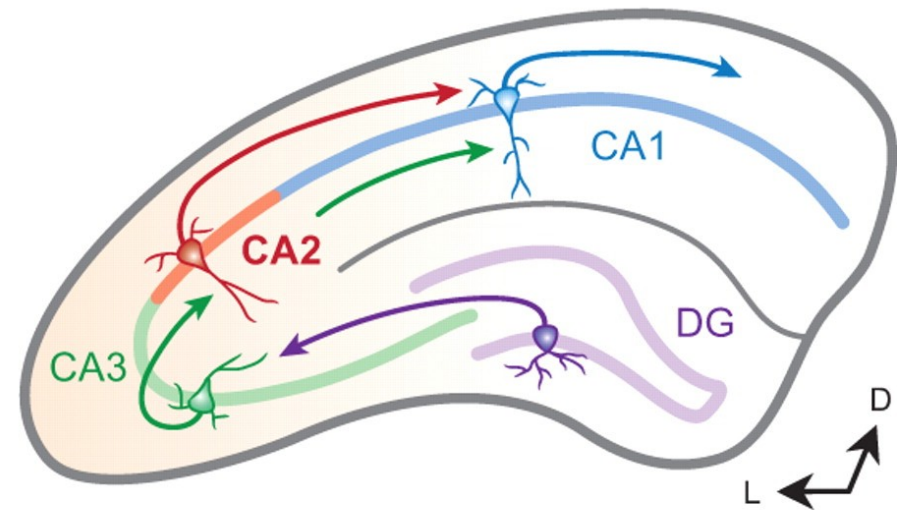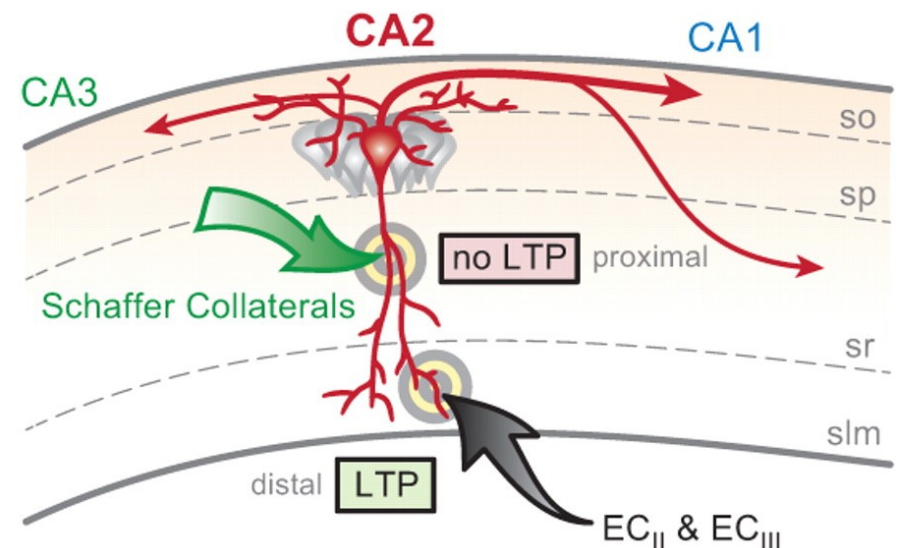
Caruana, Alexander, and Dudek (2012), Fig. 1

More of the Picture

- EC: entorhinal cortex
  - Layer II projects to DG/CA3
  - Layer III projects to CA1/Sub
  - CA1 & Sub project back to EC layer V

- DG: dentate gyrus
  - mossy fibers project to CA

- CA3
  - Schaffer collaterals to CA1

- Sub: subiculum

Computational Models of Neural Systems
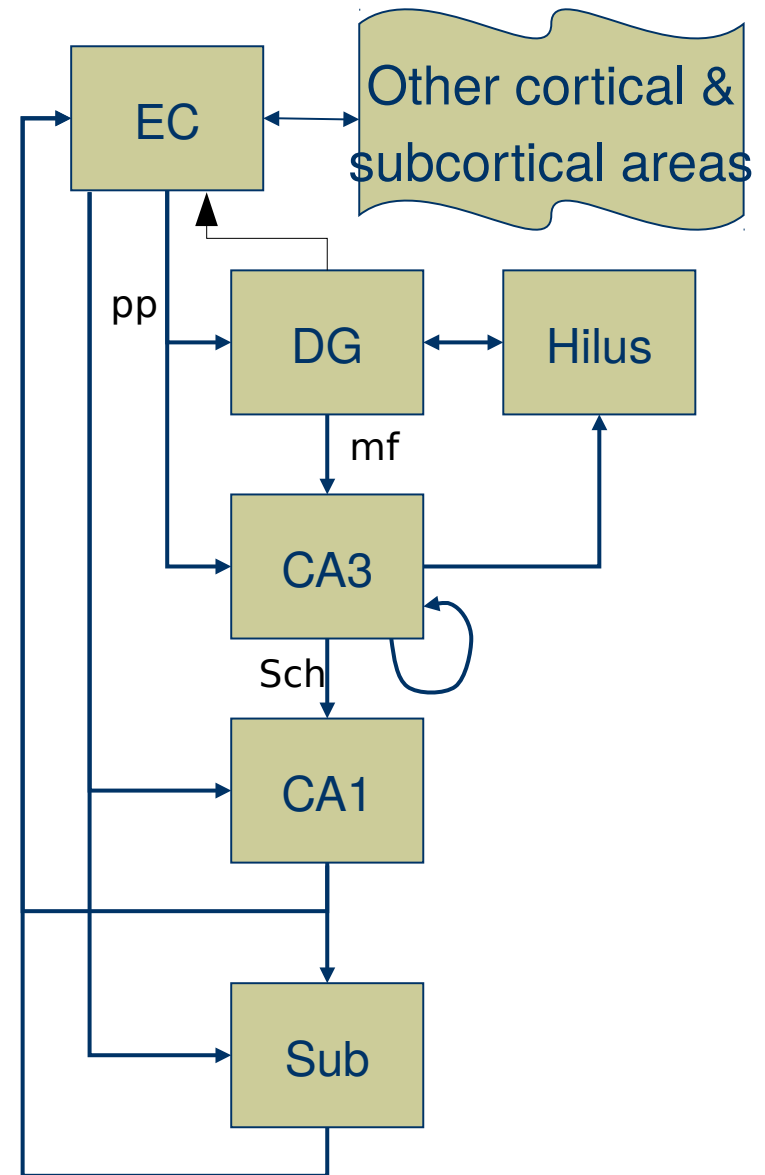
Even More
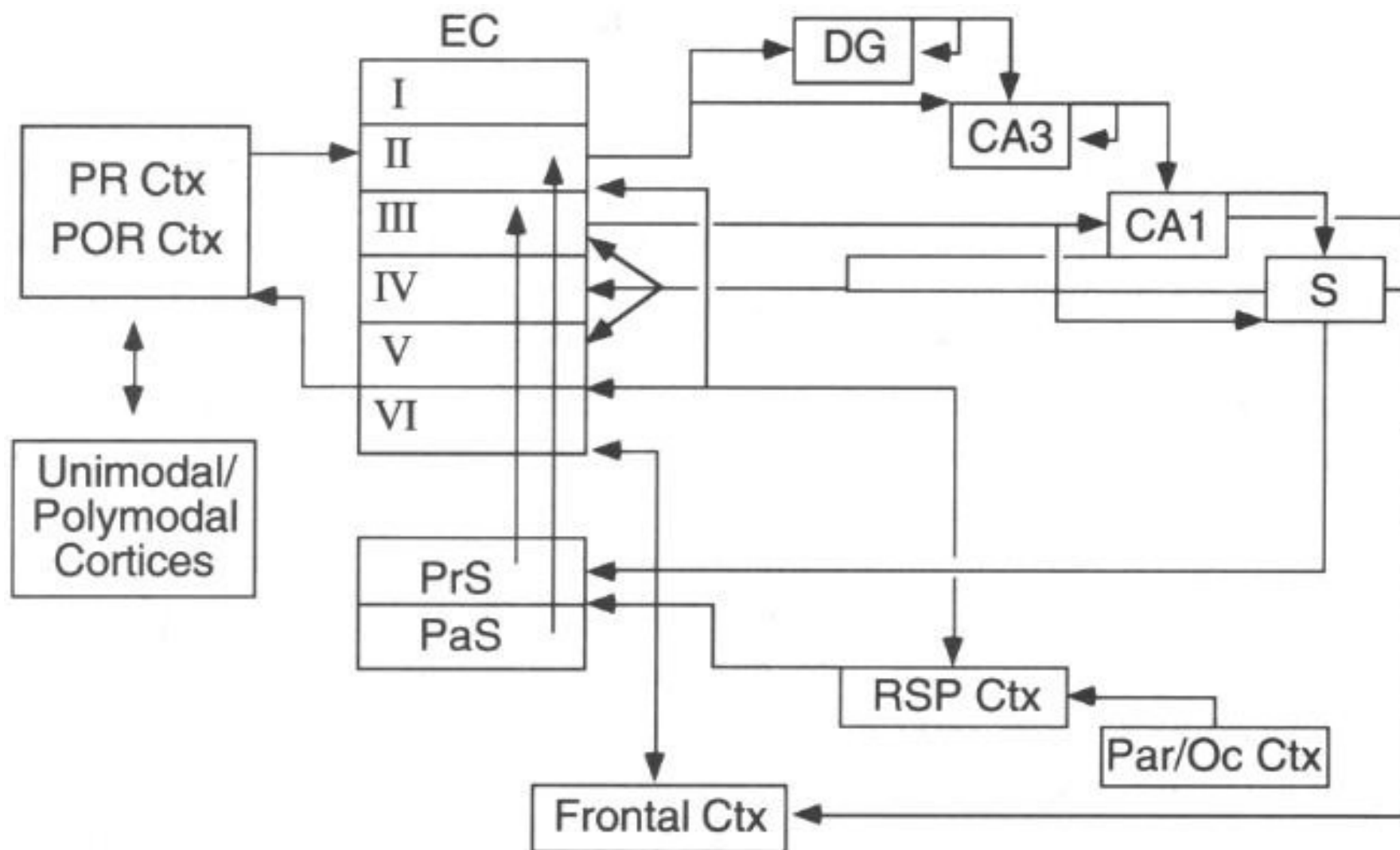
PR: perirhinal cortex; POR: postrhinal cortex; EC: entorhinal cortex; PrS: presubiculum; PaS: parasubiculum; DG: dentate gyrus; CA: Cornu amonis; S: subiculum; RSP: retrosplenial cortex; Par/Oc: parietal/occipital cortex

Three Major Fiber Systems

- Angular bundle from EC: perforant path (and more)

- Fimbria/fornix to subcortical areas
  - fimbria: red
  - fornix: yellow

- Dorsal and ventral commissures link hippocampi
  - dorsal: purple
  - ventral: green

Computational Models of Neural Systems
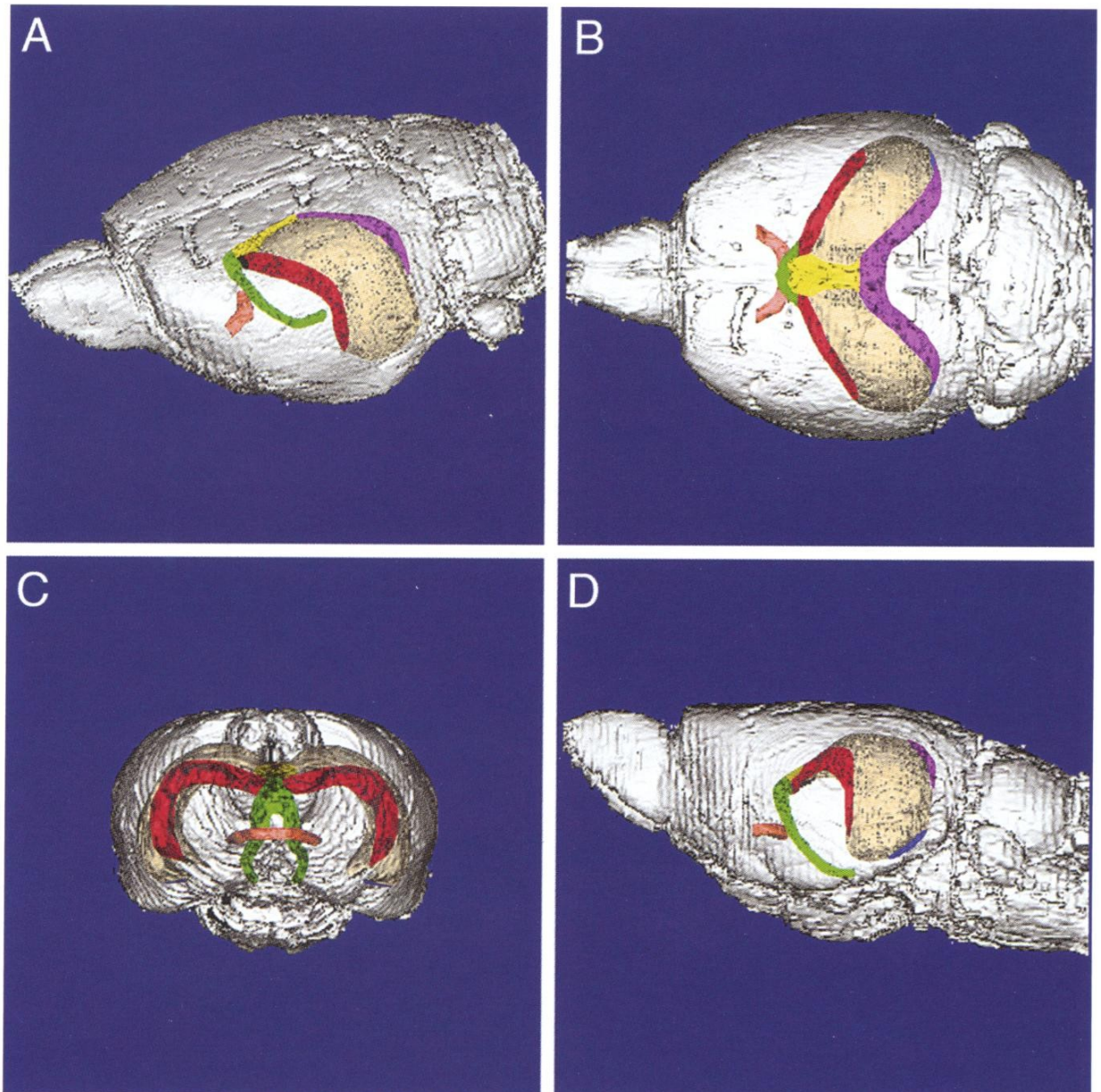
Alveus/Fimbria/Fornix

- Second input/output pathway for hippocampus (first is via angular bundle from EC)

- Communicates with subcortical structures: septal nuclei and mammillary bodies
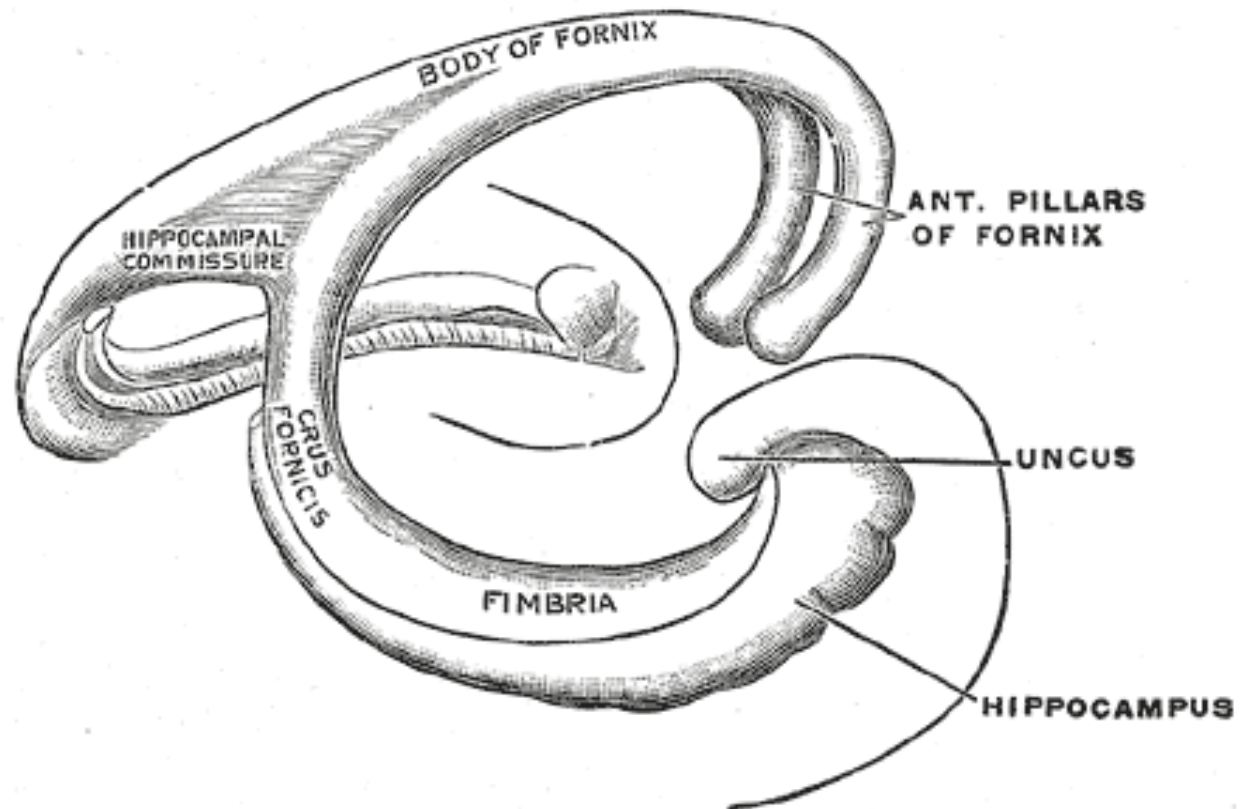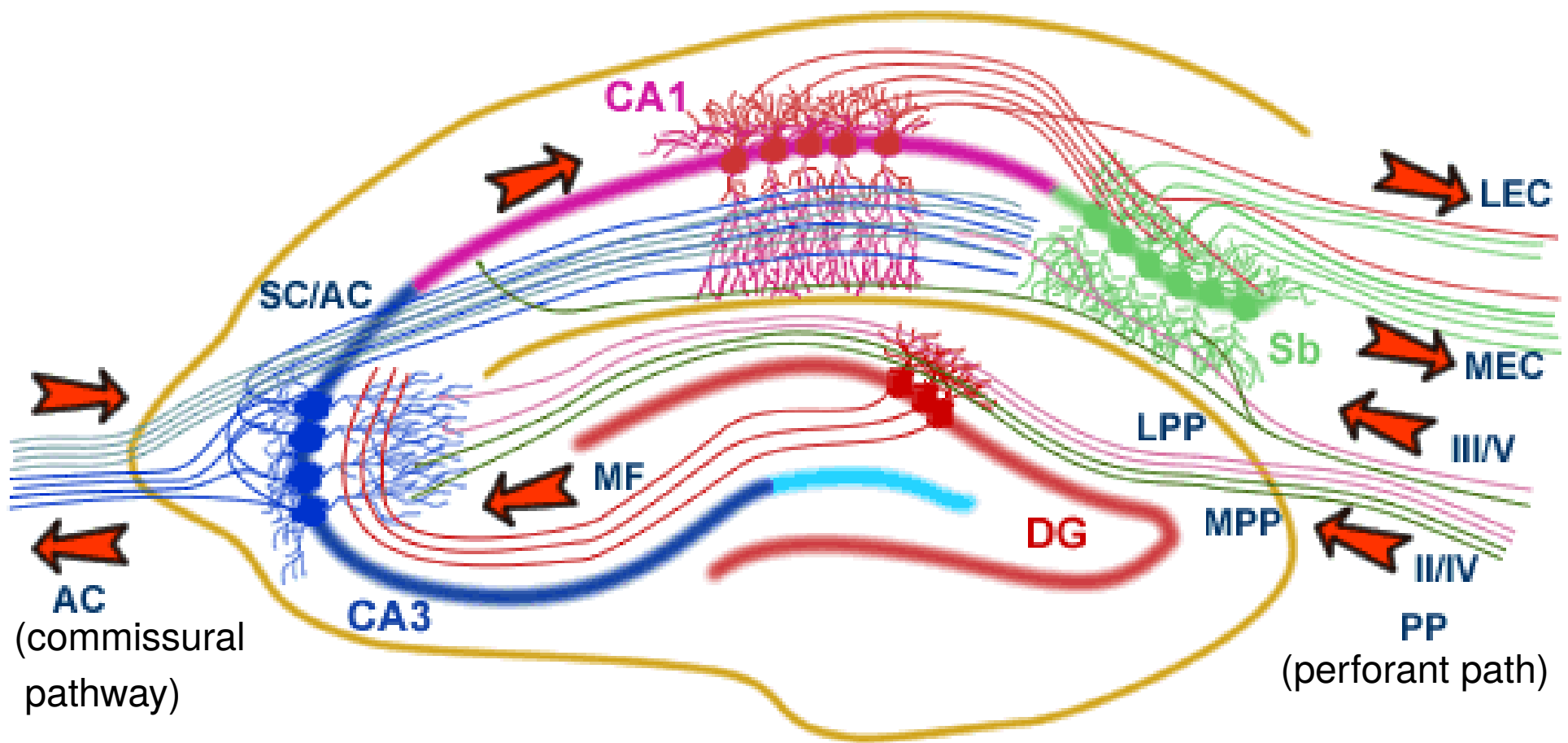
The Hippocampal Network: The hippocampus forms a principally uni-directional network, with input from the Entorhinal Cortex (EC) that forms connections with the Dentate Gyrus (DG) and CA3 pyramidal neurons via the Perforant Path (PP - split into lateral and medial). CA3 neurons also receive input from the DG via the mossy fibres (MF). They send axons to CA1 pyramidal cells via the Schaffer Collateral Pathway (SC), as well as to CA1 cells in the contralateral hippocampus via the Associational Commissural pathway (AC). CA1 neurons also receive input directly from the Perforant Path and send axons to the Subiculum (Sb). These neuron in turn send the main hippocampal output back to the EC, forming a loop.

Dendritic Arborization of Principal Cells

Figure 3–15. Dendritic arborization of the principal cells in the rat dentate gyrus (granule cells) and hippocampus proper (pyramidal cells). See the text for details.
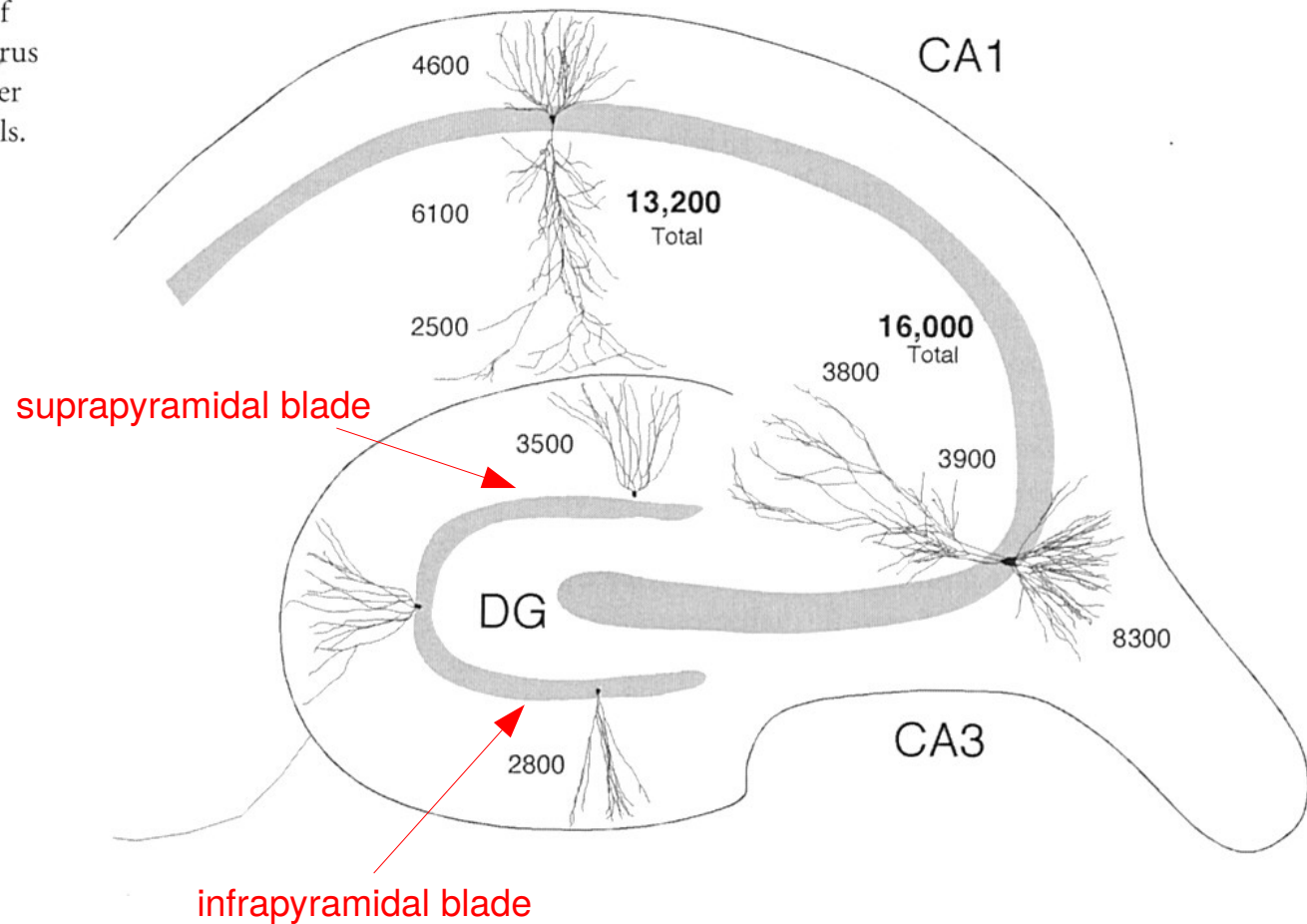
Structure of the Dentate Gyrus

- Granule cell layer holds principal cell bodies
  - their axons form the mossy fiber pathway
- Molecular layer: gc dendritic tree; afferent connections
- Polymorphic cell layer (hilus): interneurons, mf collaterals
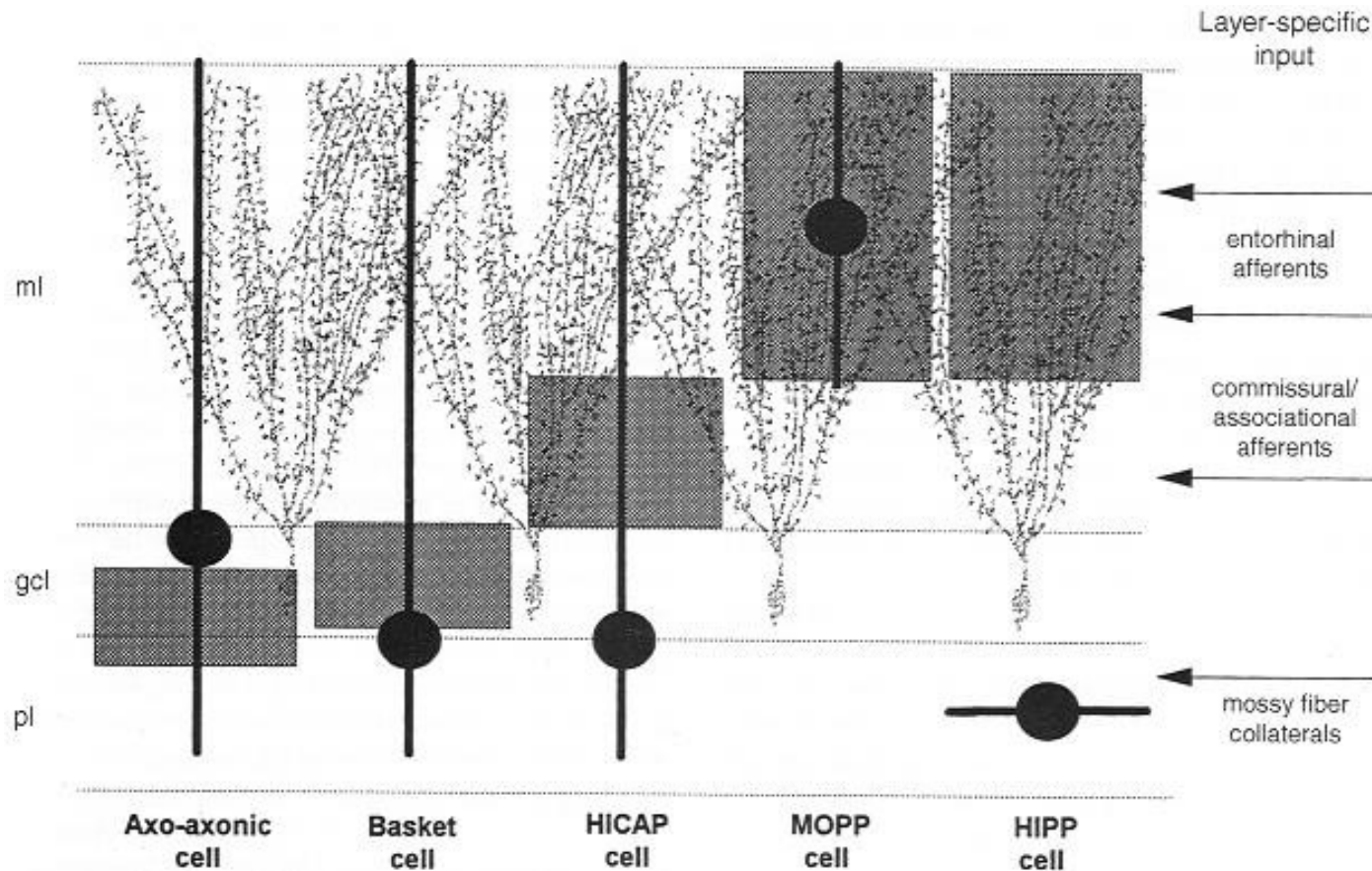
Mossy Fiber Synapse Onto CA3 Cells

- The dentate gyrus projection to CA3 terminates in large mossy fiber synapses.

- CA3 dendrites have "thorny excresences" with complex spine shapes. A mossy fiber can make 30-40 synapses within one excresence.

- Each granule cell contacts only about 15 CA3 pyramidal cells. Each pyramidal cell receives input from only about 72 granule cells.
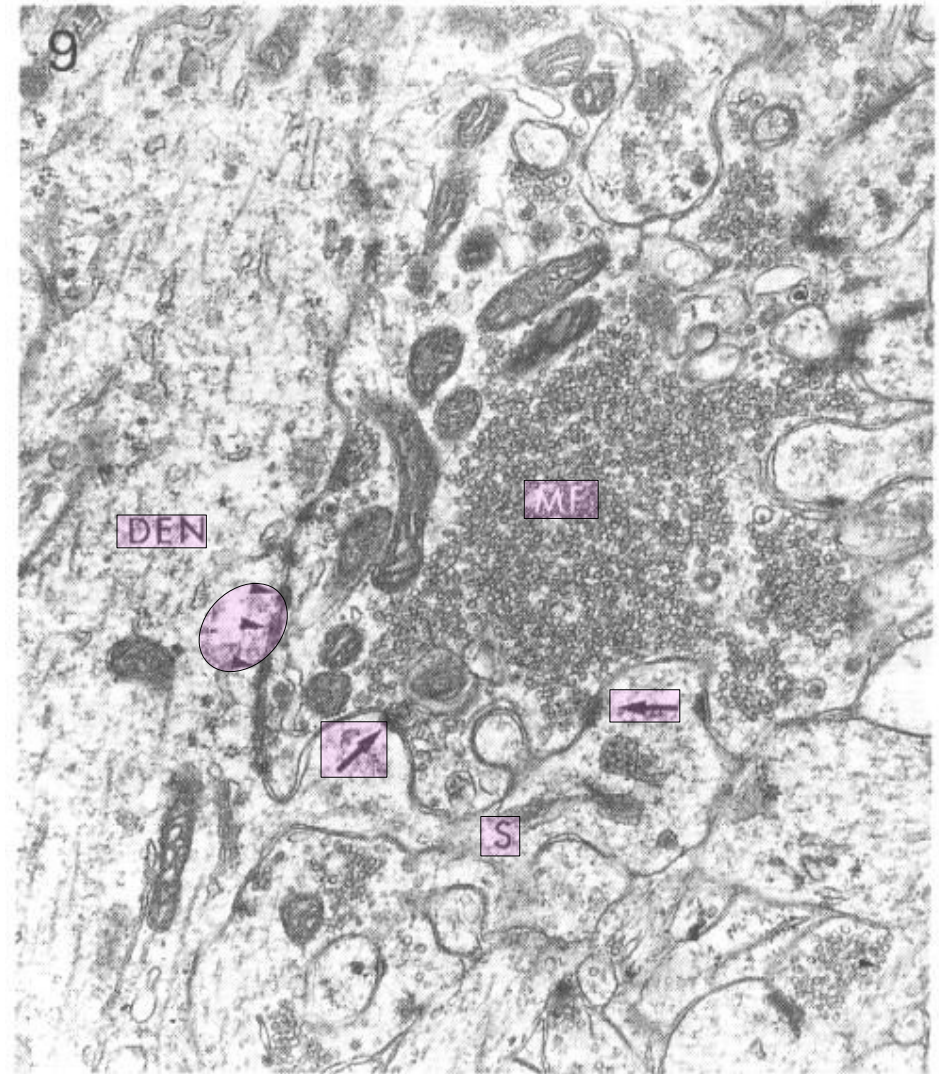
Structure of CA3

- stratum radiatum: entorhinal afferents; mossy fibers enter from DG, make synapses in s. lucidum

- stratum lucidum

- stratum pyramidale

- stratum oriens: recurrent collaterals

CA3 pyramidal cell

thorny excresences

sr

sl

pcl

so

Computa
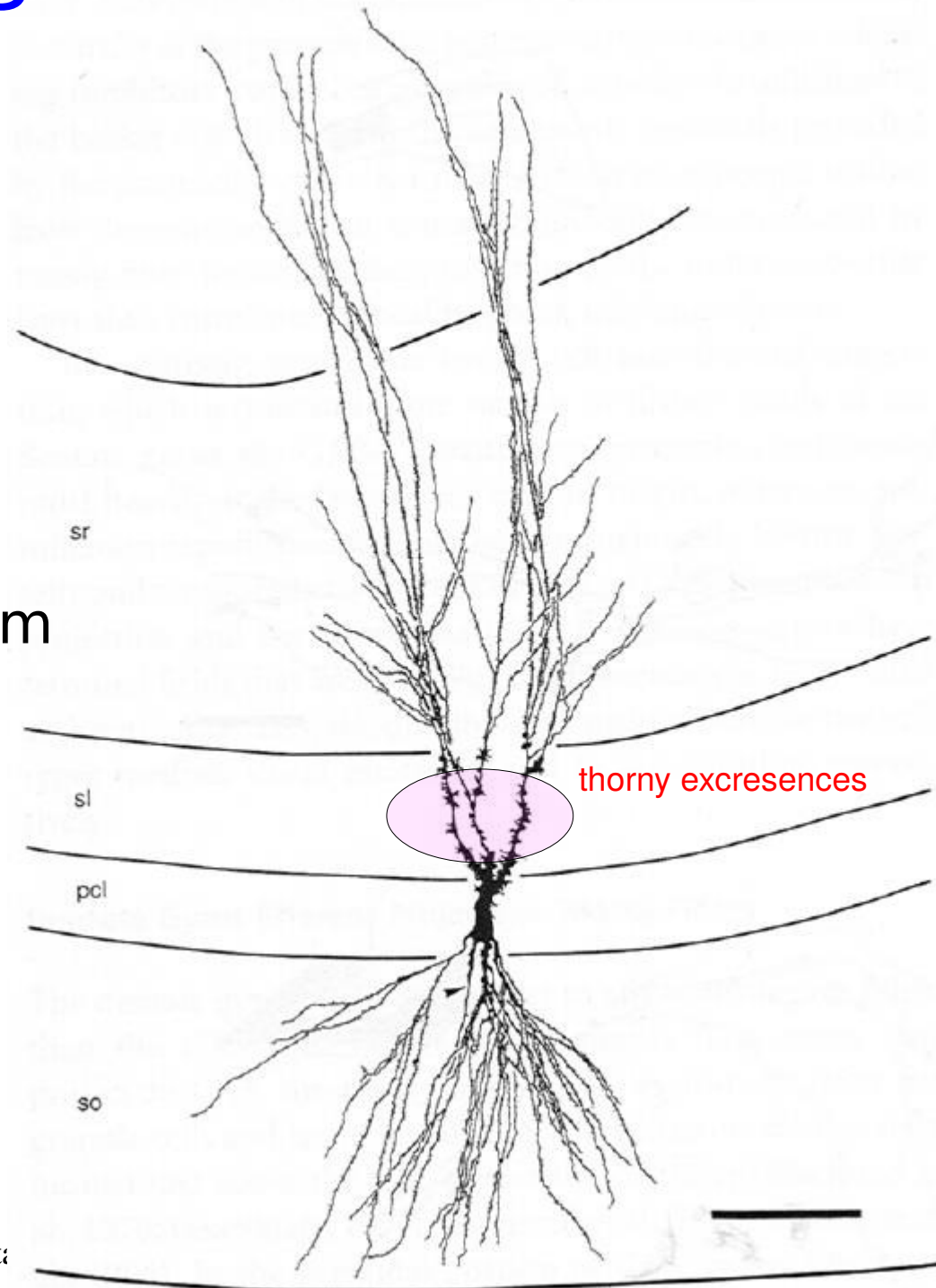
Structure of CA1

- stratum lacunosum-
  moleculare:
  entorhinal afferents

- stratum radiatum:
  Schaeffer collaterals,
  commissural fibers

- stratum pyramidale

- stratum oriens:
  Schaeffer collaterals

CA1 pyramidal cell

sl-m

sr

pcl

so

Computa

Interneurons in CA3/CA1

Entorhinal Cortex — Dentate Gyrus — CA3 — CA1 — Subiculum

EC layer II

EC layer III

LEA

MEA

II   III

Prox   Dist   Prox   Dist   Prox   Dist

1. Entorhinal Cortex
2. Perirhinal Cortex
3. Infralimbic Cortex
4. Mammillary Nucleus (rostral)
5. Nucleus Accumbens
6. Lateral Septal Region

1. Midline Thalamus
2. Entorhinal Cortex

1. Retrosplenial Cortex
2. Presubiculum
3. Anterior Thalamic Complex
4. Mammillary Nucleus (caudal)
5. Entorhinal Cortex

Layer II Projections

PERFORANT PATH
LAYER II

A

MEA   LEA

TEMPORAL   ±25%   SEPTAL

——— MPP
- - - LPP

MPP/LPP = medial/lateral perforant path

Layer III Projections

Computational Models of Neural Systems

Temporal-Lobe.com

Computational Models of Neural Systems

Some Numbers for the Rat

- Dentate Gyrus
  - 1.2 million granule cells
  - 4K basket cells
  - 32K hilar interneurons (20K mossy cells)

- CA3/CA1
  - 330K /420K pyramidal cells
  - various interneurons

- Entorhinal cortex layer II
  - Around 200K cells (20% interneurons?)

- Subiculum
  - Around 180K cells
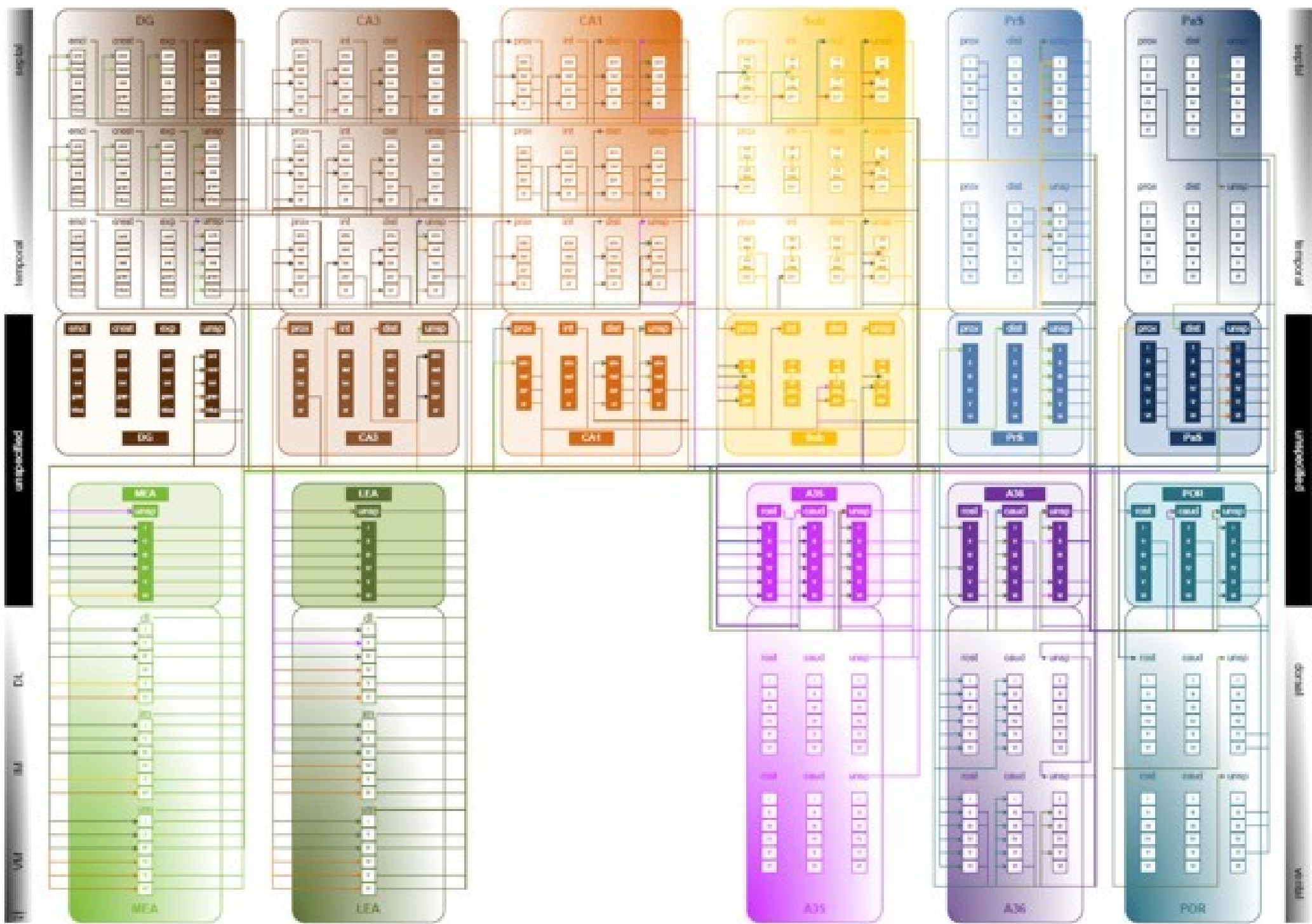
Computational Models of Neural Systems

Rat Connectivity

- Perforant path projection to DG

  - Around 4500 spines per granule cell (75% from EC)

  - One EC cells makes about 18,000 synapses with granule cells

- CA3: three distinct inputs

  - 50-80 mossy fibers from DG

  - 3,500 perforant path synapses from EC II

  - 12,000 recurrent collaterals from other CA3 cells

    - 8,000 to basilar dendrites (stratum oriens)
    - 4,000 to apical dendrites (stratum radiatum)

- CA1: inputs from CA3 and EC

  - From CA3 Schaffer collaterals: 4,500 basilar, 6500 apical synapses

  - From EC layer III: 2,500 synapses

Computational Models of Neural Systems
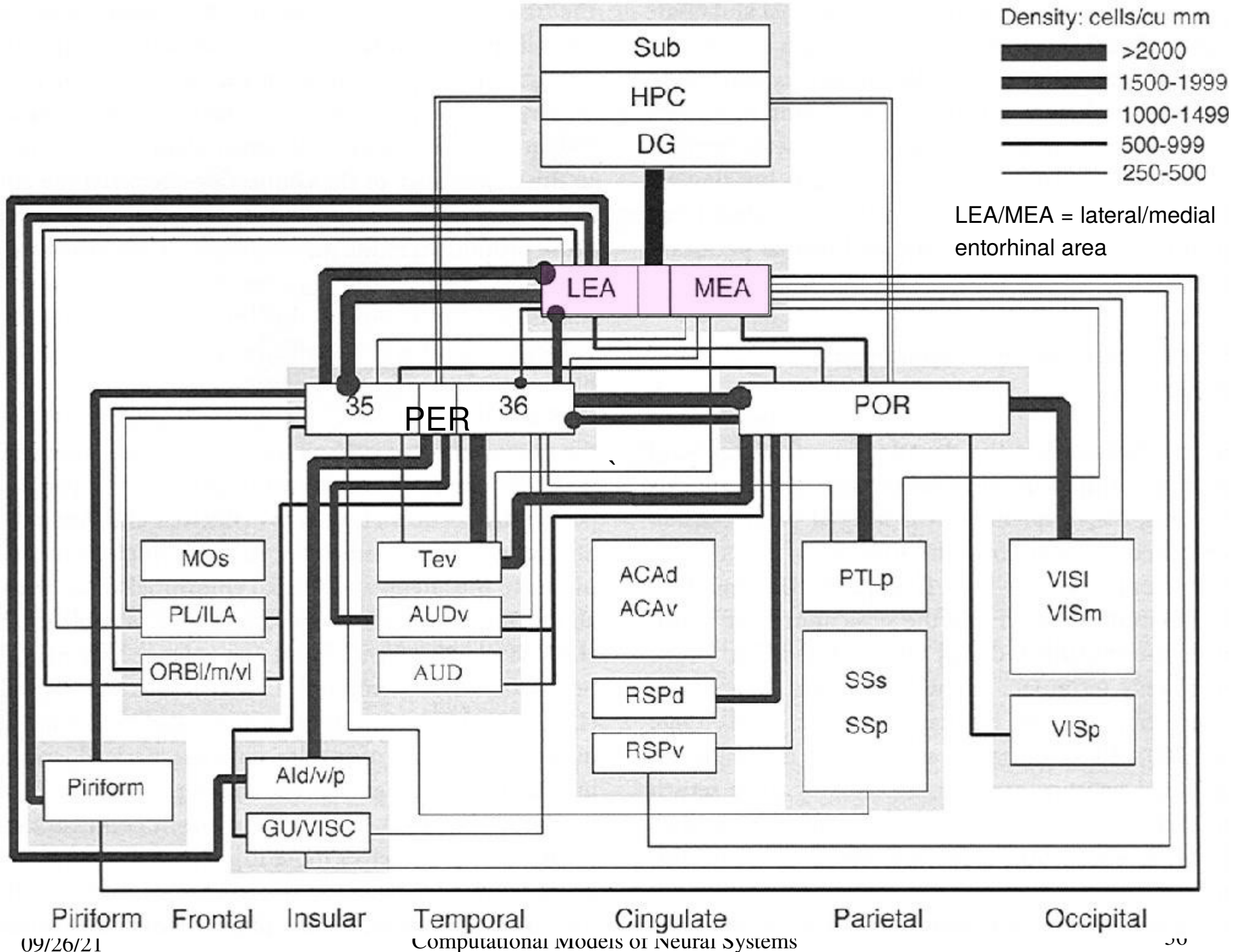
Why Does the Circuitry Look Like This?

- Why so many kinds of interneurons?

- Why have recurrent connections in some regions and not others?

- What do these regions compute?
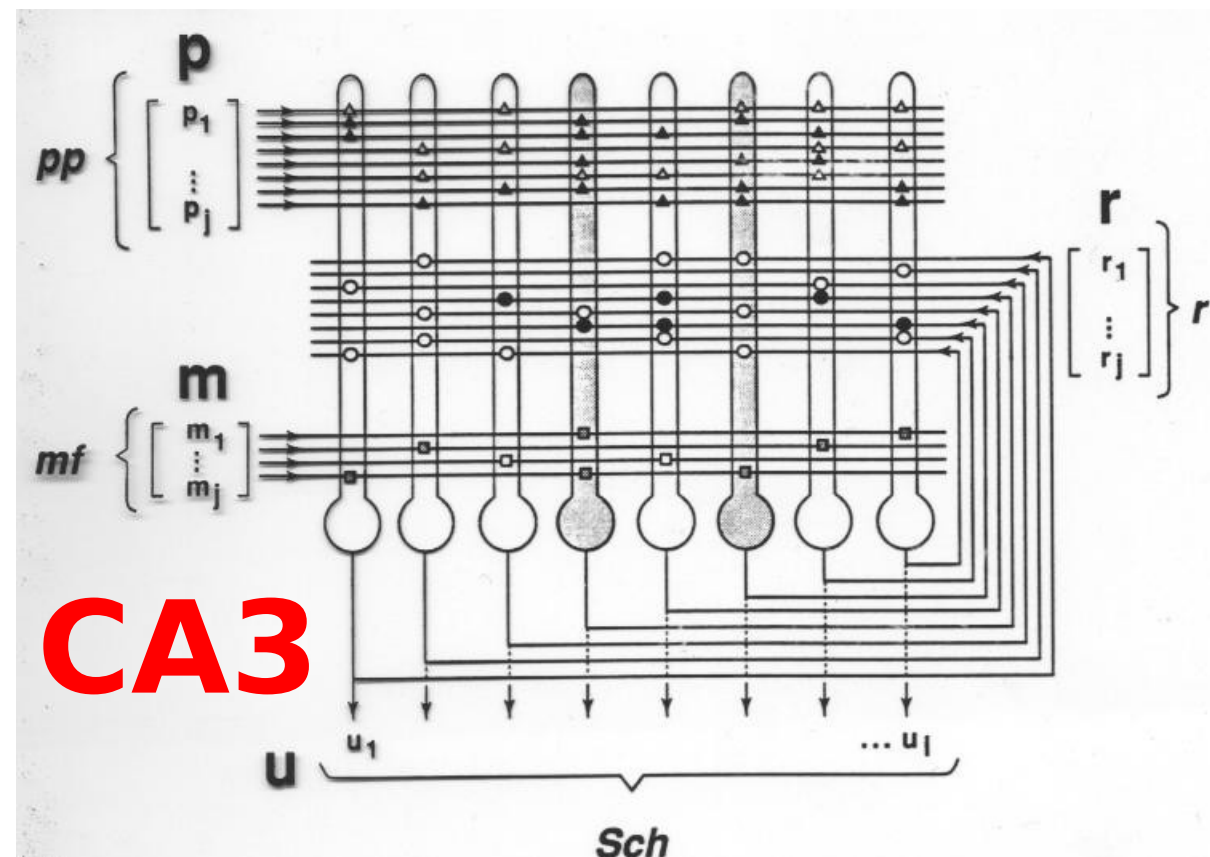
# The Hippocampus Is Very Well Connected to Other Brain Areas

Connected via EC and fimbria-fornix pathway to:

- Prefrontal / orbitorfrontal cortices

- Cingulate cortex

- Piriform cortex

- Perirhinal and Postrhinal cortices (sensory)

- Striatum

- Amygdala

- Septum

- Mammillary bodies

- Thalamus

- Hypothalamus

Computational Models of Neural Systems

Density: cells/cu mm
- >2000
- 1500-1999
- 1000-1499
- 500-999
- 250-500

LEA/MEA = lateral/medial entorhinal area

Sub
HPC
DG

LEA | MEA

35 | PER | 36 | POR

MOs
PL/ILA
ORBl/m/vl
Piriform
Ald/v/p
GU/VISC

Tev
AUDv
AUD

ACAd
ACAv
RSPd
RSPv

PTLp
SSs
SSp

VISl
VISm
VISp

Piriform   Frontal   Insular   Temporal   Cingulate   Parietal   Occipital

Neuromodulatory Projections to HC

Figure 3–21. Line drawing of horizontal sections through the rat hippocampal formation shows the distribution of *A.* noradrenergic, *B.* serotonergic, and *C.* dopaminergic fibers. (*Source:* Adapted from Swanson et al., 1987.

A

B

C
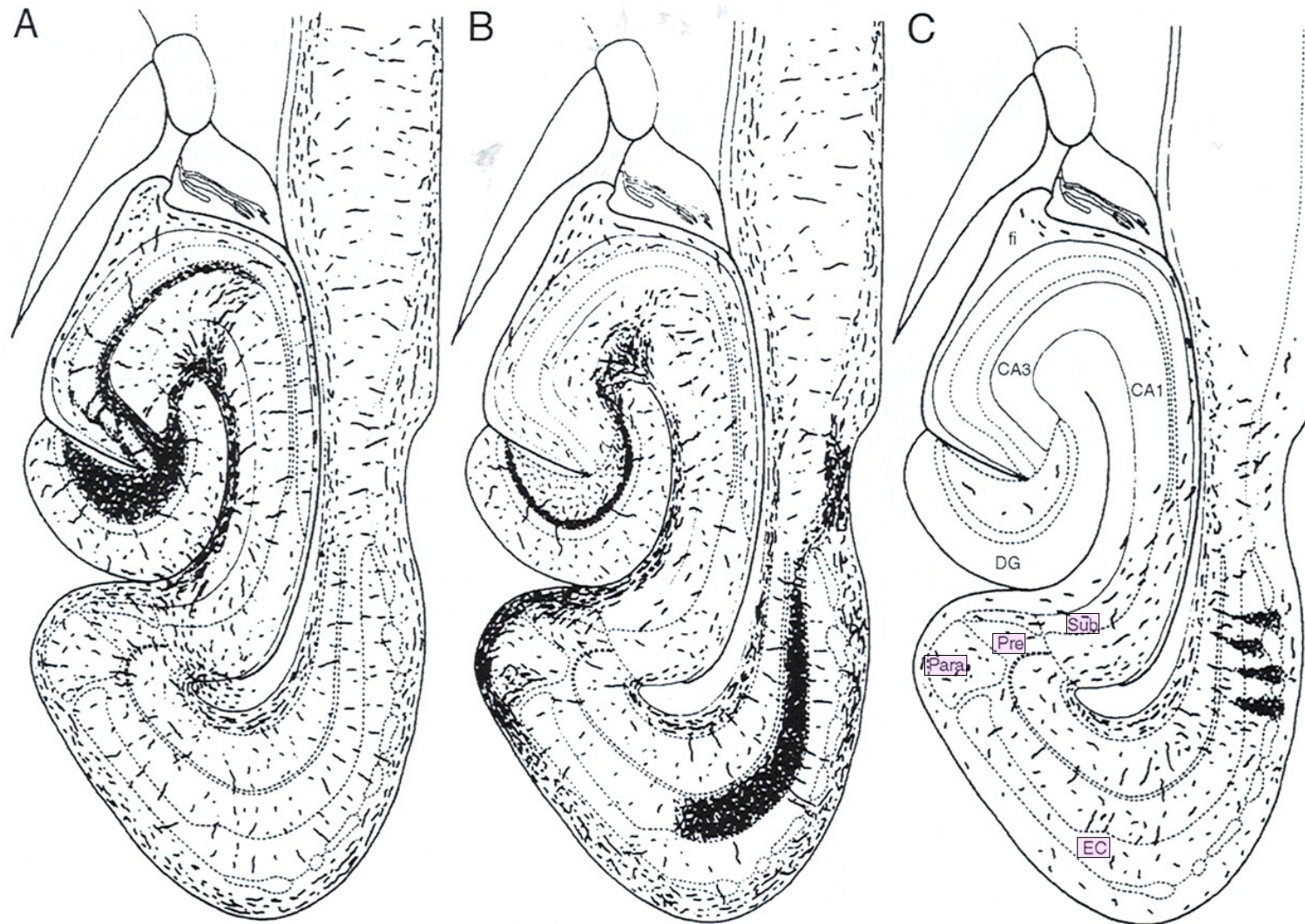
Noradrenaline
locus coeruleus

Serotonin
raphe nuclei

Dopamine
substantia nigra

NA: Attention
5HT: Mood
DA: Reward
ACh: Novelty

acetylcholine
medial septum

Hippocampal EEG

- ## Awake

  - Active exploration:

    - theta (8-12 Hz) plus gamma (40 Hz)

  - Resting:

    - LIA (Large-amplitude Irregular Activity) w/transient sharp waves

- ## Asleep

  - REM sleep: theta

  - Slow wave sleep: LIA

  - S-SIA: small-amplitude irregular activity (Jarosiewicz & Skaggs)

Hippocampal EEG

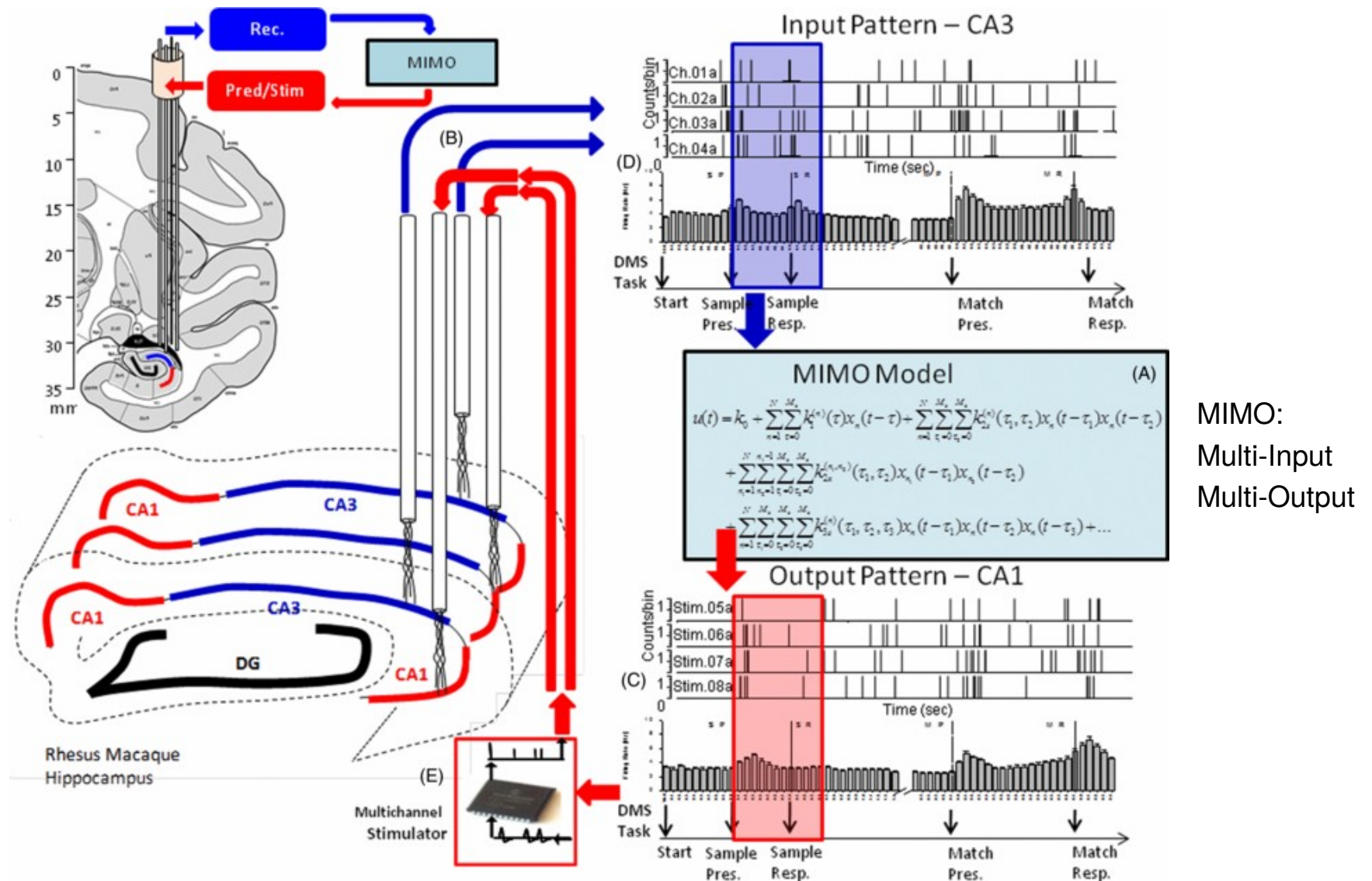Computational Models of Neural Systems
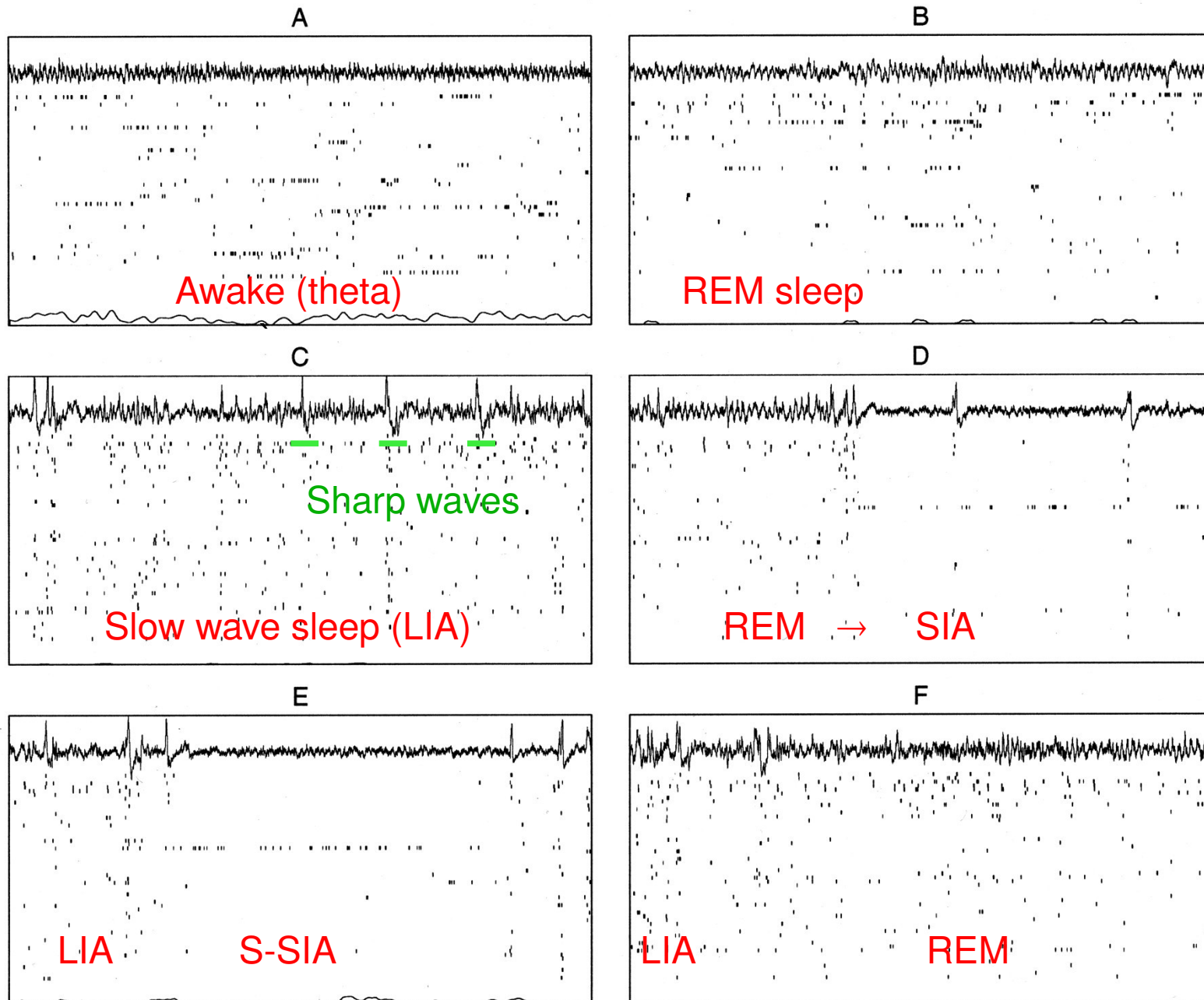
What Does the Hippocampus Do?

- Formation of new episodic memories?

  – Anterograde amnesia (H.M. and others)

- Cognitive map?

  – Place cells in rats; spatial attention cells in monkeys

- Configural association theory?

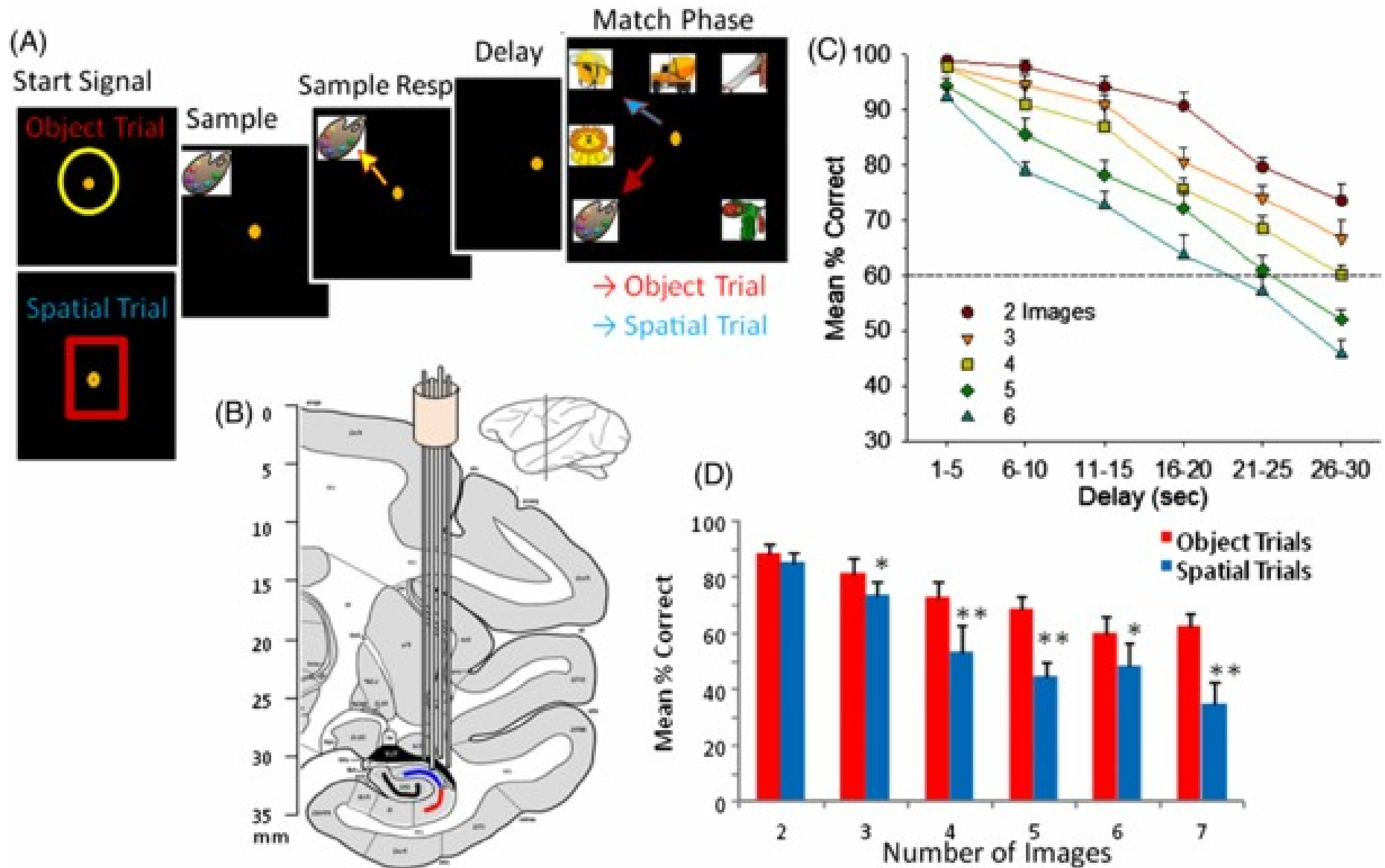 – Lesioned rats are impaired on tasks requiring them to recognize cue configurations

A Hippocampal Prosthesis?

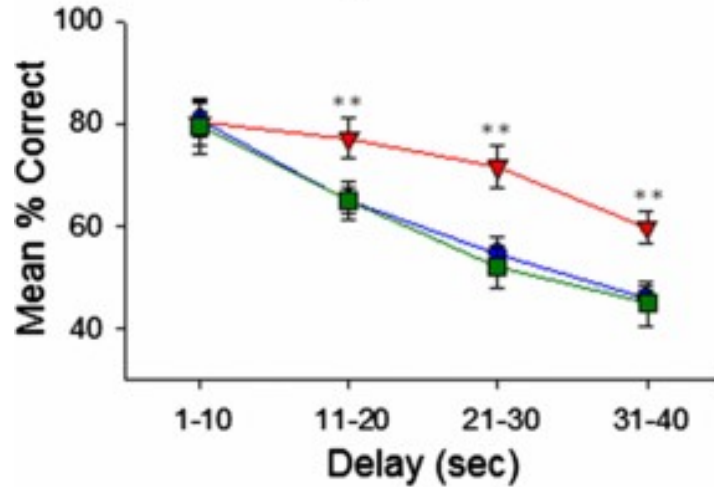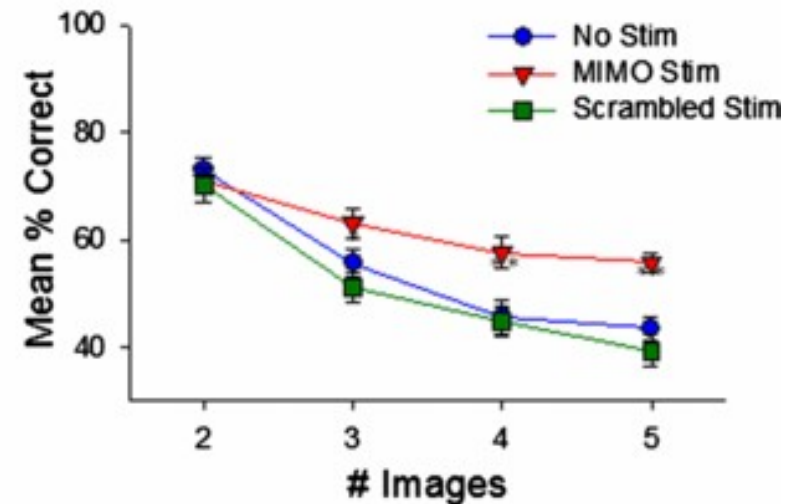- Hampson et al (2013) Journal of Neural Engineering, 10(6).

Computational Models of Neural Systems

Delayed Match to Sample Task

Computational Models of Neural Systems

Effects of Stimulation

MIMO Stimulation of Hippocampus

Computational Models of Neural Systems
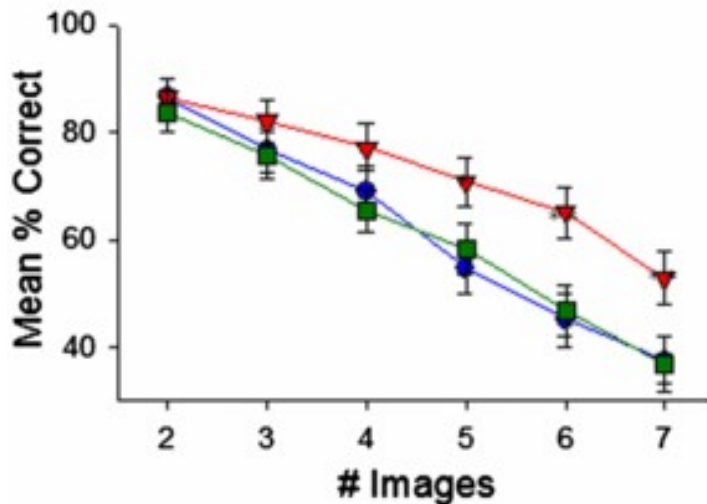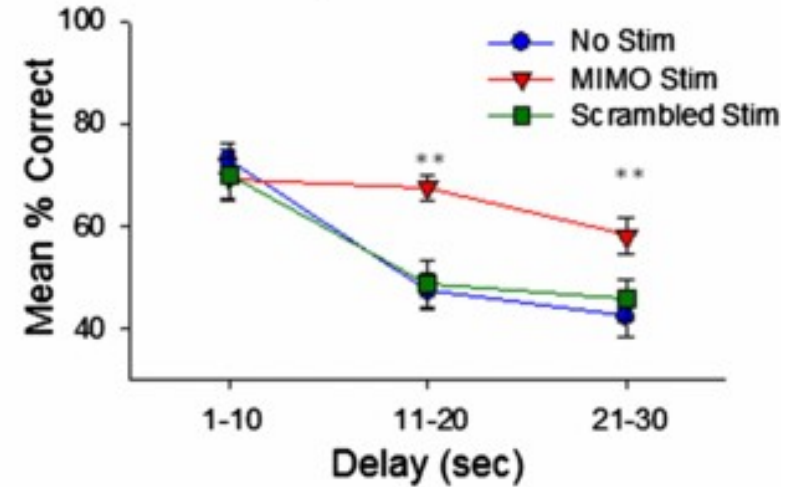
Results with Humans (2018)

Experiments done on epilepsy patients who had been implanted with electrodes to localize the source of their seizures.

Stimulation Effects within Memory Tasks

**p<0.001 vs. MIMO Stim