Development of Complex Curricula for Molecular Bionics and Infobionics Programs within a consortial* framework**

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Consortium members

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**Molekuláris bionika és Infobionika Szakok tananyagának komplex fejlesztése konzorciumi keretben

***A projekt az Európai Unió támogatásával, az Európai Szociális Alap társfinanszírozásával valósul meg.

BEVEZETÉS A FUNKCIONÁLIS NEUROBIOLÓGIÁBA

INTRODUCTION TO FUNCTIONAL NEUROBIOLOGY

By Imre Kalló

Contributed by: Tamás Freund, Zsolt Liposits, Zoltán Nusser, László Acsády, Szabolcs Káli, József Haller, Zsófia Maglóczky, Nórbert Hájos, Emilia Madarász, György Karmos, Miklós Palkovits, Anita Kamondi, Lóránd Erőss, Róbert Gábriel, Kisvárdai Zoltán

Hippocampus

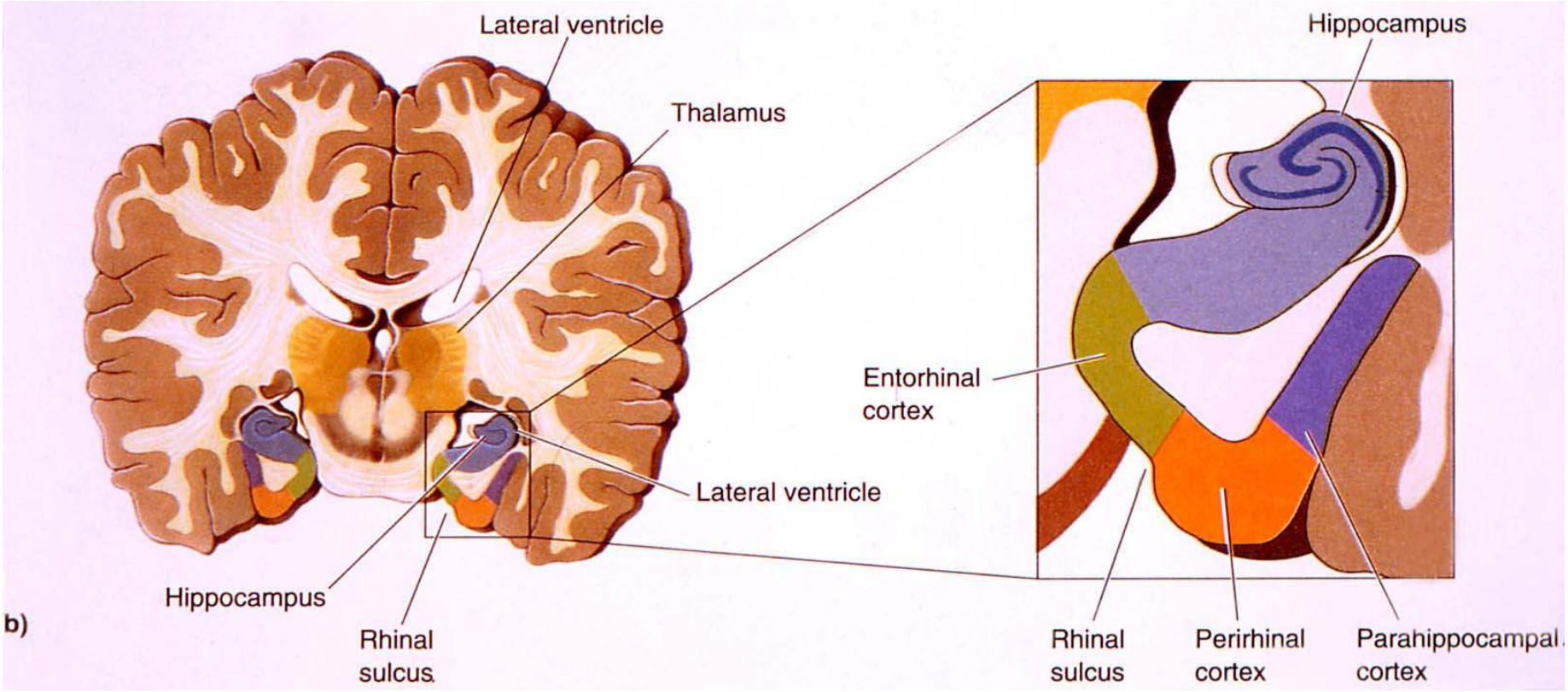
Imre Kalló & Tamás Freund

Pázmány Péter Catholic University, Faculty of Information Technology

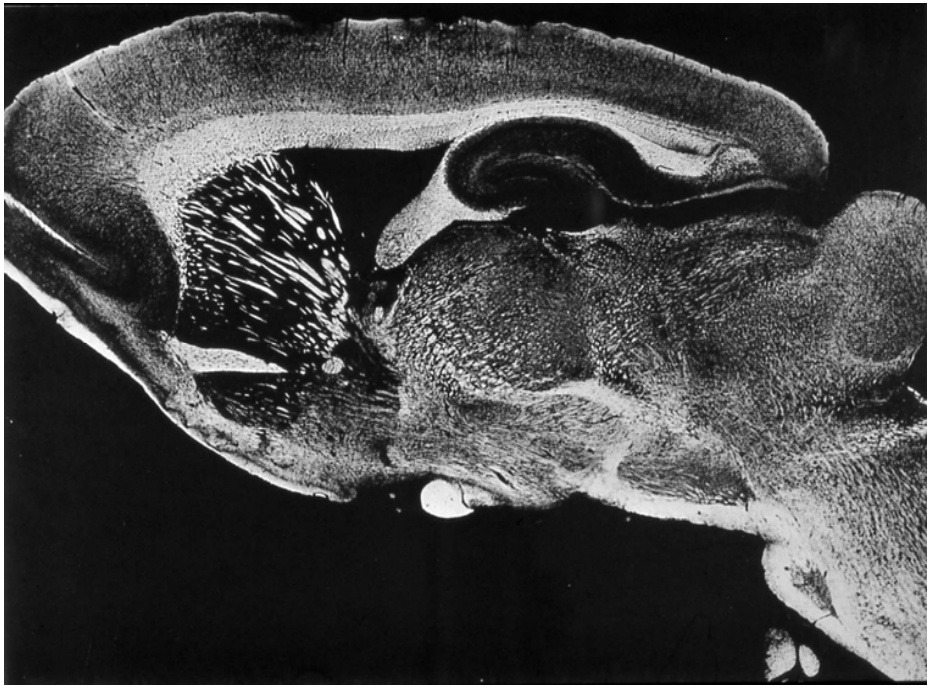
I. Subdivisions and microcircuitry of the hippocampus.
II. Interaction of excitatory and inhibitory cells.
III. Septo-hippocampal pathway.
IV. Theta oscillation, phase precession.
V. Subcortical input of the hippocampus.
VI. Gamma oscillation.

HIPPOCAMPUS

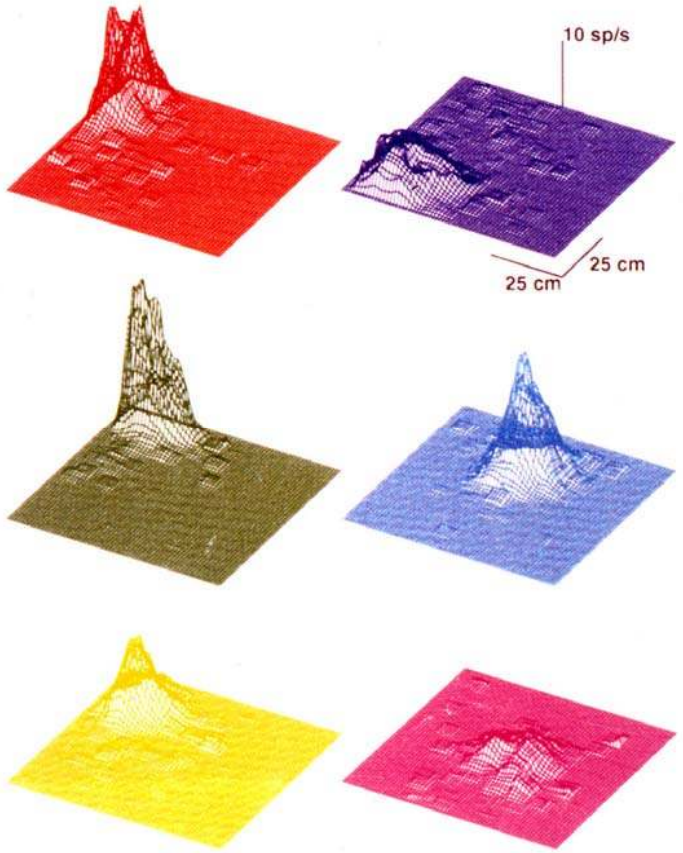
an archicortical area, which is in reciprocal connection to nearly all sensory and associative cortical areas via the entorhinal and perirhinal cortices



Compared to the entire cerebral cortex, the size of the hippocampus is much larger in rodents, than in humans. This size difference suggests that the memory traces are rather stored in the cerebral cortex.



The hippocampus is essential to acquire and associate different sensory informations. During philogenezis, it was however unneccessary for the hippocampus to grow parallel with the cerebral cortex to support the higher memory capacity in humans!



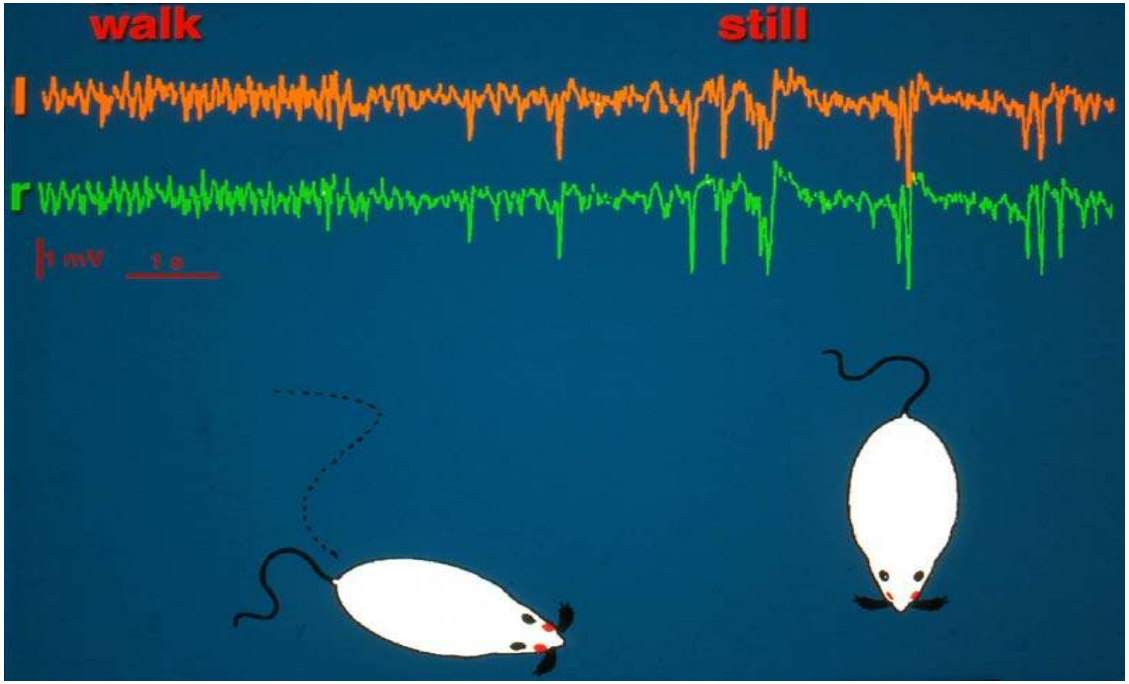
Most of the hippocampal neurons exhibit a so-called placefield-selectivity, which manifests in their increased discharge rate, when the experimental animal enters their specific ″encoded area″ in the field.

With the individual contribution of the place cells, the hippocampus generates a cognitive map of the animal's environment.

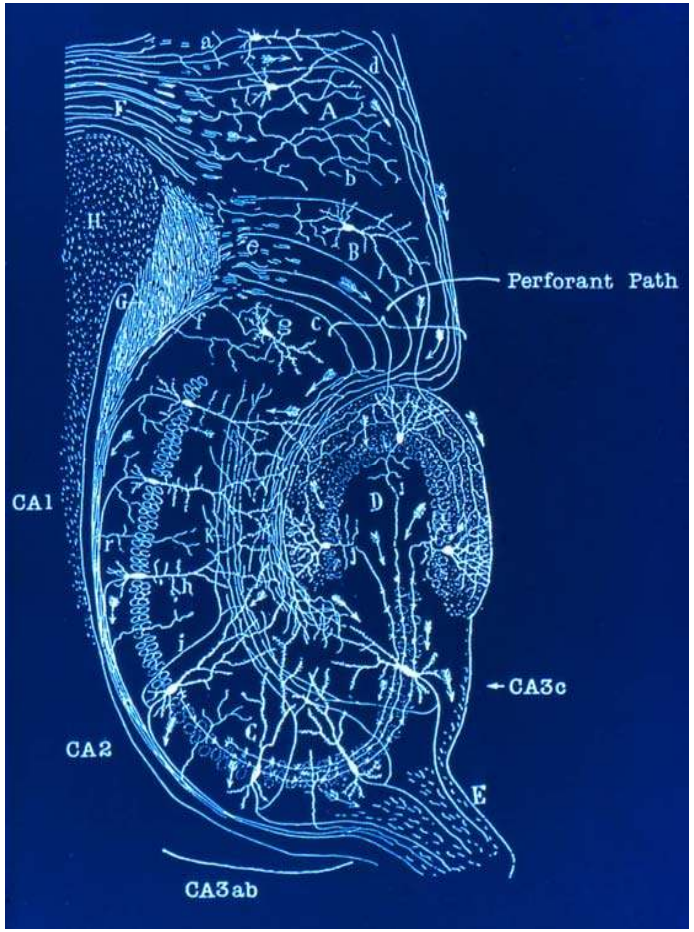
Two behavior-dependent activity patterns characterize the field potential (EEG) recorded from the rodent hippocampus

Theta activity (4-8 Hz oscillation) during exploration and paradox sleep

Sharp waves, fast, irregular EEG in conscious, resting state, during feeding and slow-wave sleep

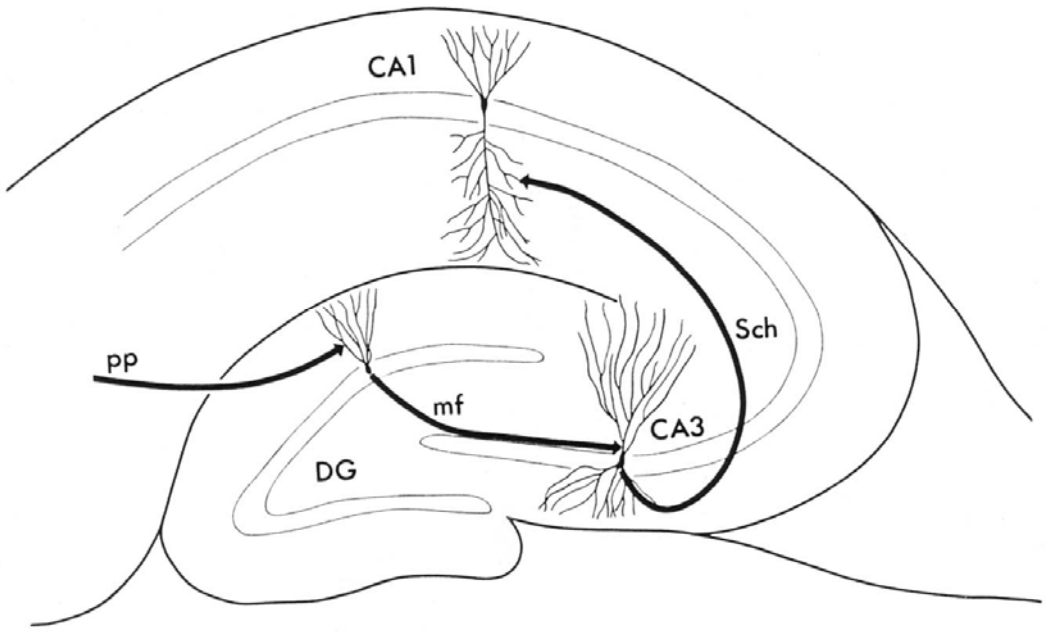


Major regions and pathways of the hippocampus



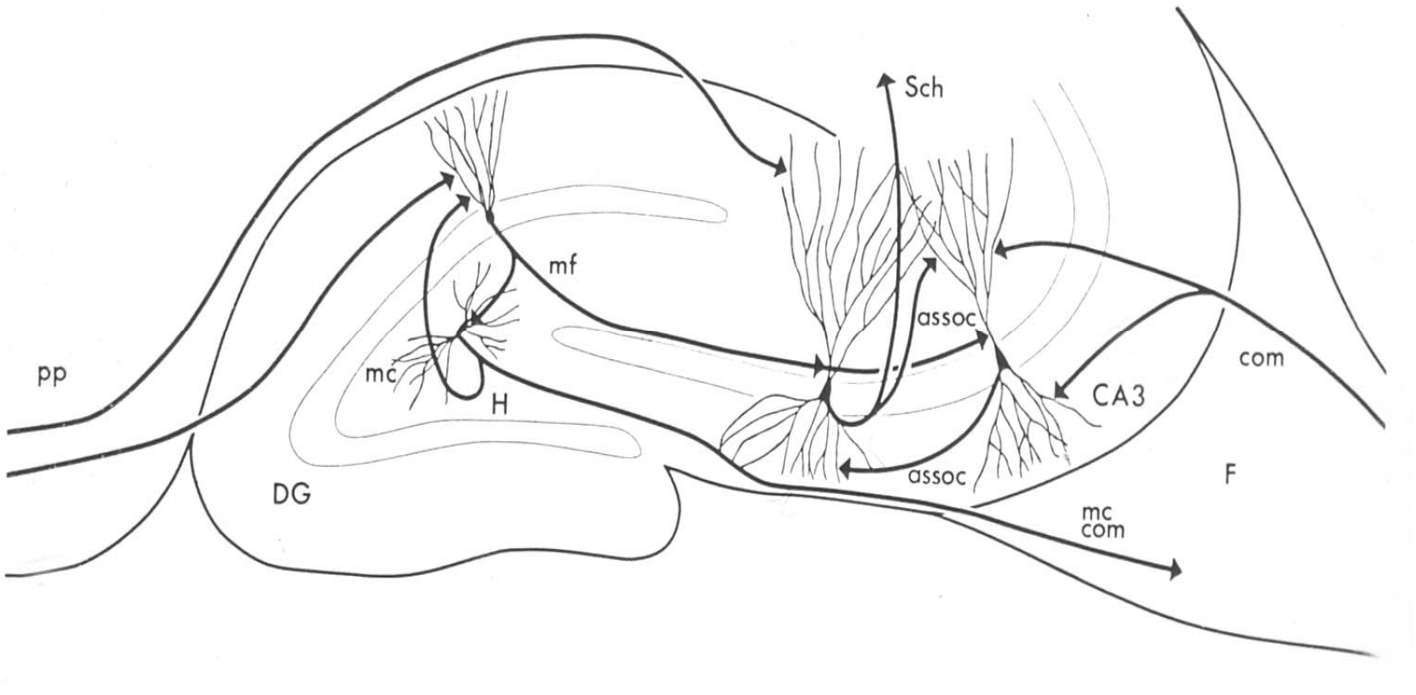
The primary excitatory input derives from the entorhinal cortex through the perforant pathway. It innervates the dendrites of granule cells in the molecular layer of the dentate gyrus, and the most distal part of the dendrites of CA1-3 pyramidal cells in the lacunosum-moleculare layer.

The trisynaptic loop of the hippocampus



The axons of the granule cells (mossy fibers) innervate the CA3 pyramidal cells, which in turn project (via the Schaffer collaterals in the radiatum and oriens layers) to the CA1 pyramidal cells. The latter cell population projects back to the entorhinal cortex.

Local recurrent connections in the hippocampus



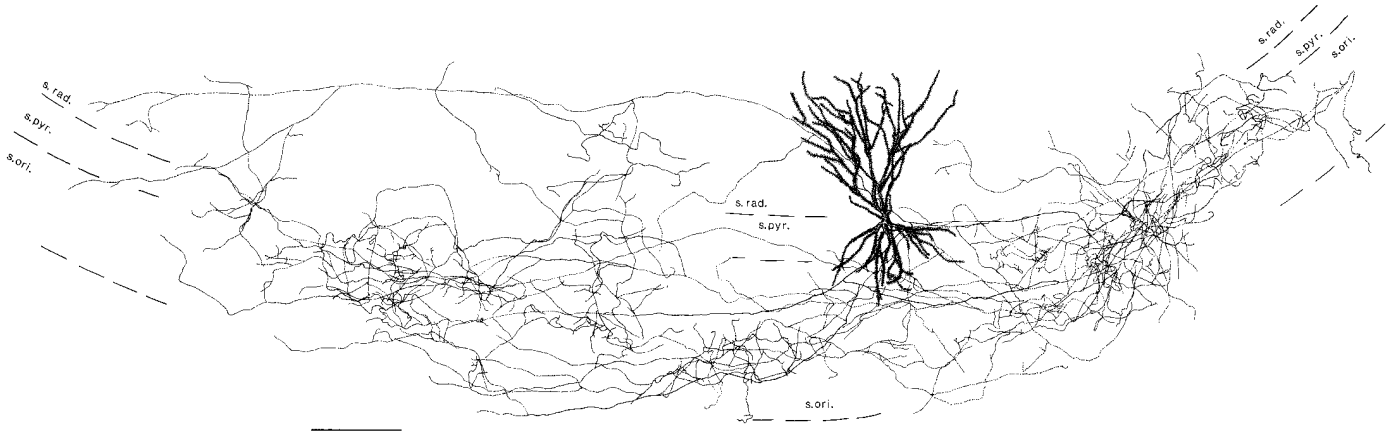
Local recurrent connections in the hippocampus

- Within the hilus, axons of the granule cells of the dentate gyrus, the mossy fibers, give off local collaterals, which then innervate interneurons and hilar mossy cells. Granule cells do not innervate themselves!!!
- Hilar mossy cells are the association cells of the DG. Their axons innervate the dendrites of granule cells extending quite far longitudinally within the inner third of the molecular layer.
- CA3 pyramidal cells establish extensive interconnections through their rich recurrent collateral-network.
- CA1 pyramidal cells do not innervate each other (!), their axons remain locally in the oriens layer, where they terminate on feed-back interneurons.

Neuronal phenotypes of the hippocampus

- Principal cells (excitatory ones – 90% of the neurons):
  - Pyramidal cells of the Ammon's horn
  - Granule cells of dentate gyrus (DG)
  - Hilar mossy cells (association cells of the DG)

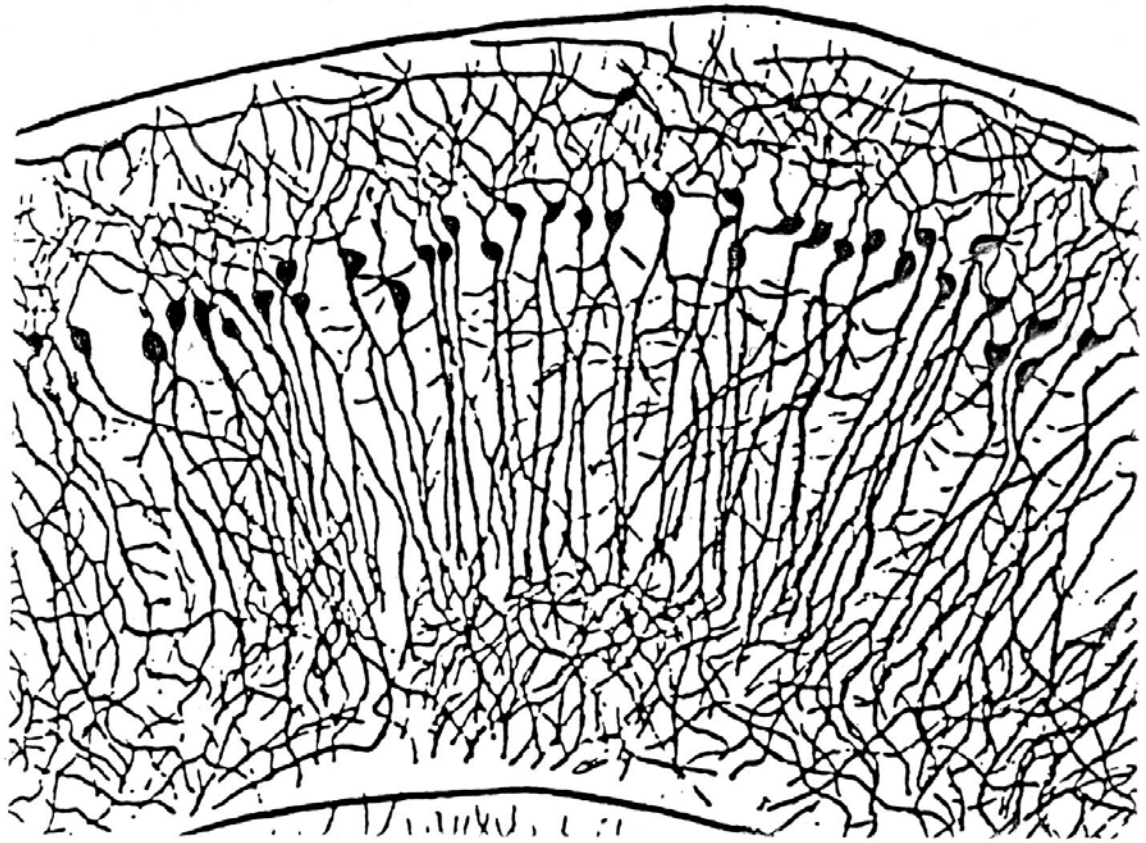
- Inhibitory interneurons (10% of the neurons): their neurotransmitter is γ-aminobutyric acide (GABA)



Principal (pyramidal and granule) cells, as major processing units of the hippocampus

They are excitatory cells, and use glutamate as neurotransmitter. Their dendritic tree receives about 15 to 20 thousands excitatory synapse, mainly from other pyramidal cells. Axons of CA3 pyramidal cells stimulate about 40 to 60 thousands other pyramidal cells in the CA1 and CA3 regions of the hippocampus forming a quasi randomly wired network, which is characterized with huge divergence and convergence. In contrast, the CA1 pyramidal cells establish local collaterals sparsely, which are restricted to the oriens layer and terminate mainly on inhibitory interneurons.

Principal cells are knit in a single (pyramidal) layer (stratum)



alveus

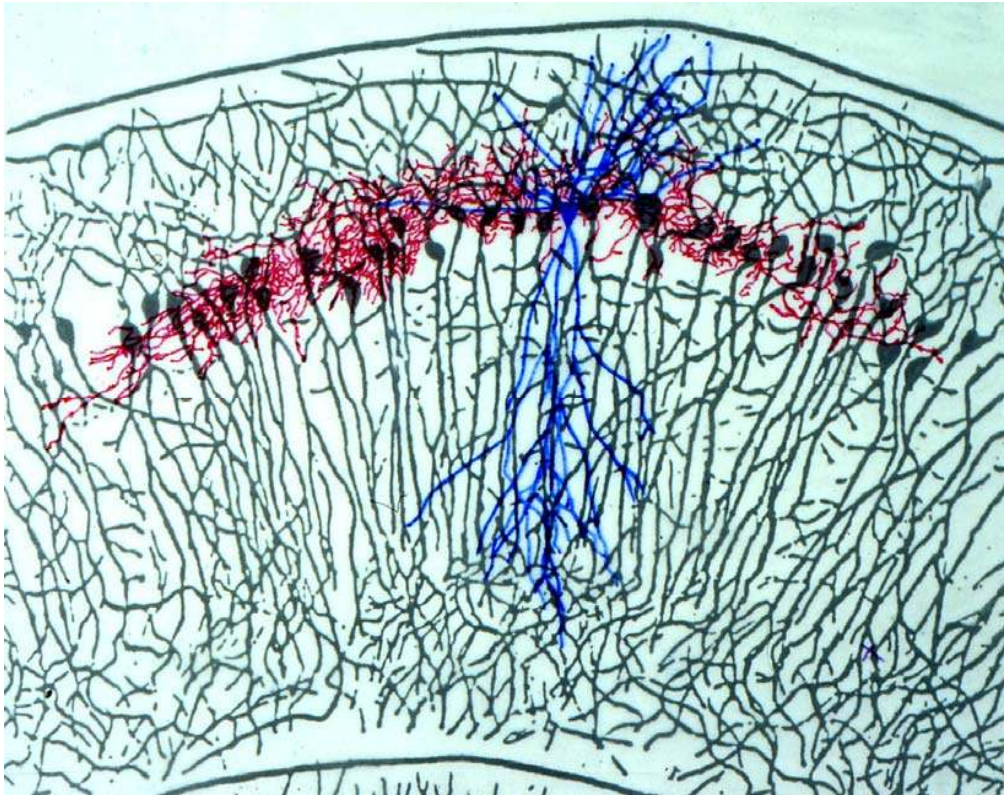
str. oriens

str. pyramidale

str. radiatum

str. lacunosum-moleculare

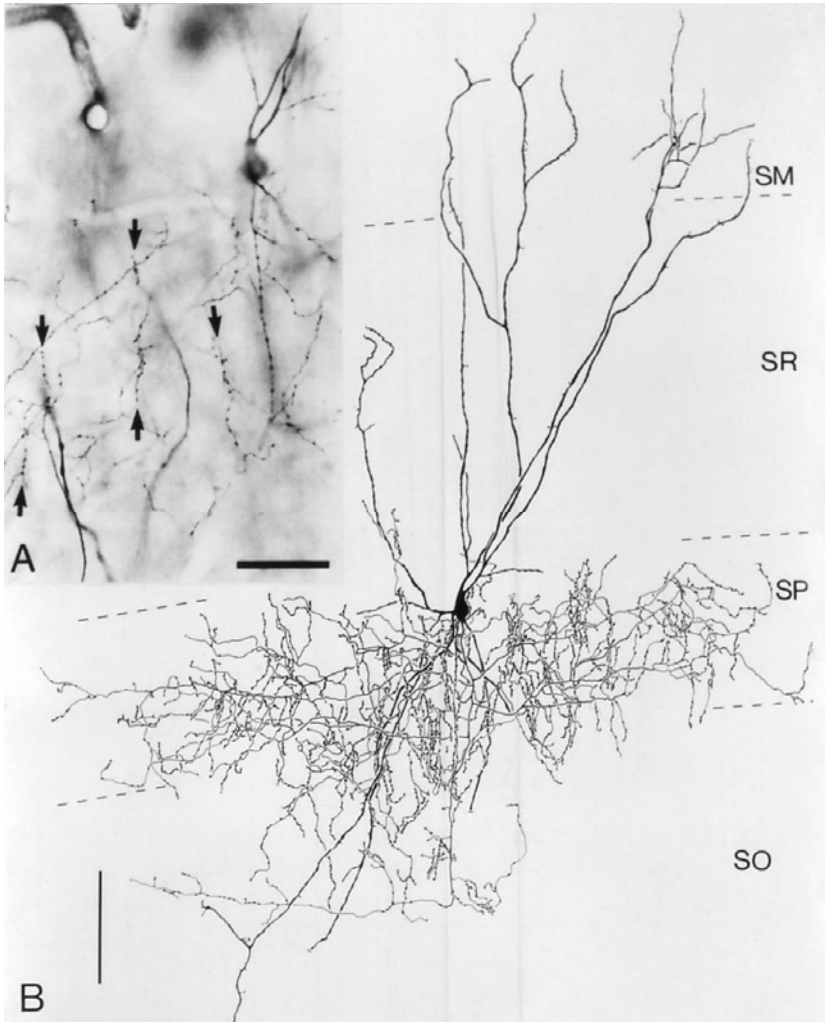
The axon of the perisomatic inhibitory cells (red) ramifies in the pyramidal layer by establishing multiple contacts on the soma, proximal dendrites and axon initial segment of the pyramidal cells.



Types: basket cells and axo-axonic (or chandalier) cells

One **basket cell** innervate the perikaryon and proximal dendrites of more than 1000 pyramidal cells.

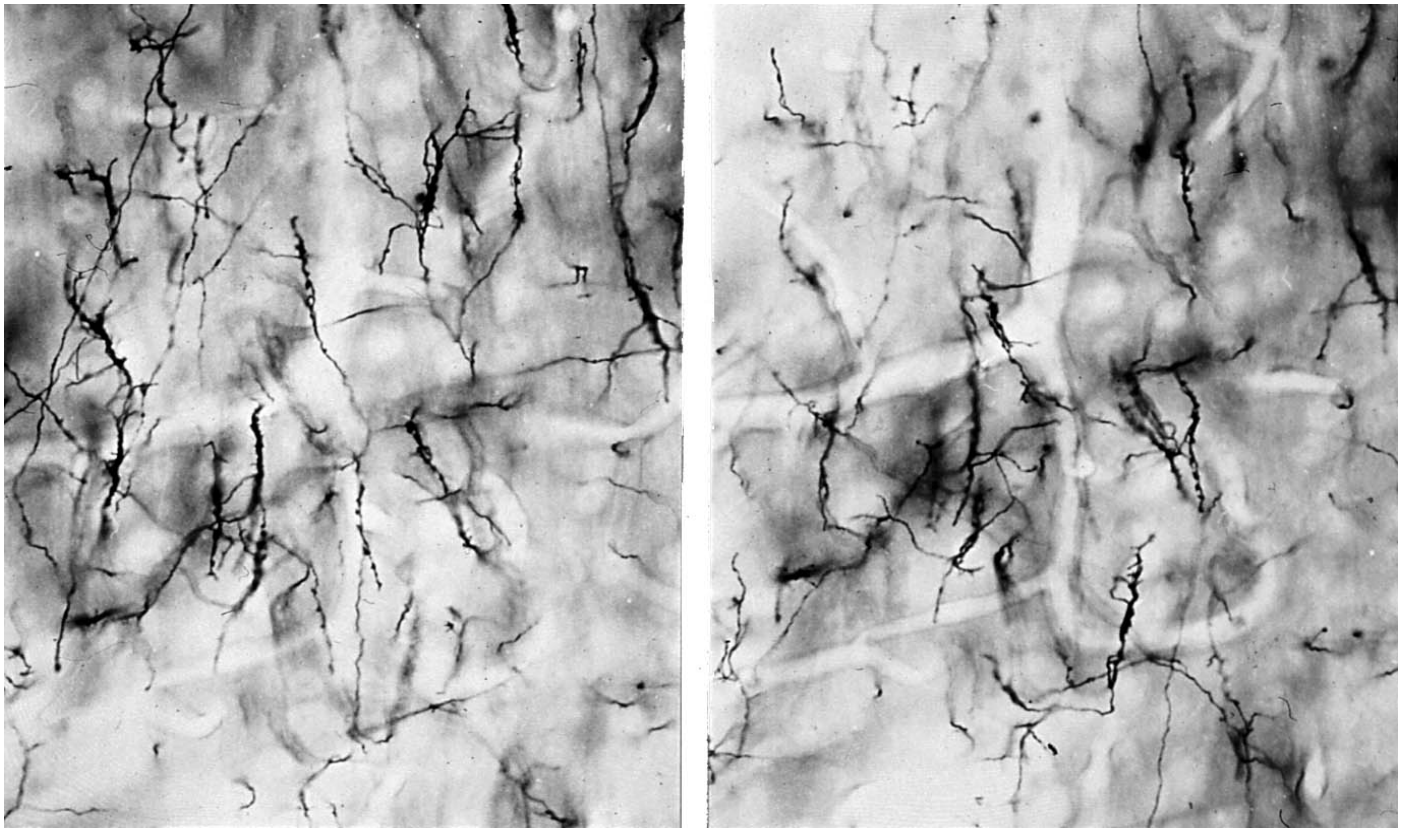
Laminar distribution of their dendritic tree (blue) is in overlap with that of the pyramidal cells.



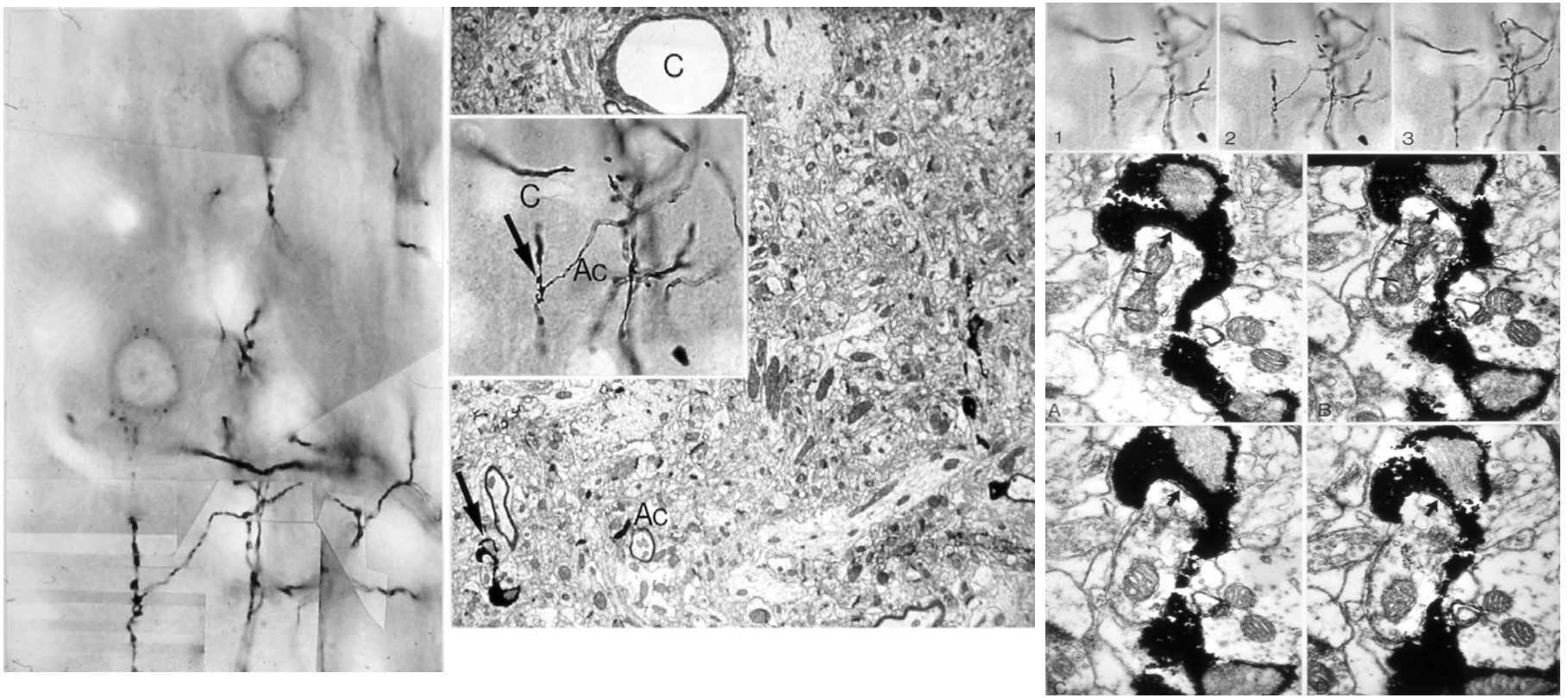
The axo-axonic (chandalier) cells

A type of perisomatic inhibitory cells, which innervates selectively the axon initial segment (AIS) of the pyramidal cells, where action potentials are generated.

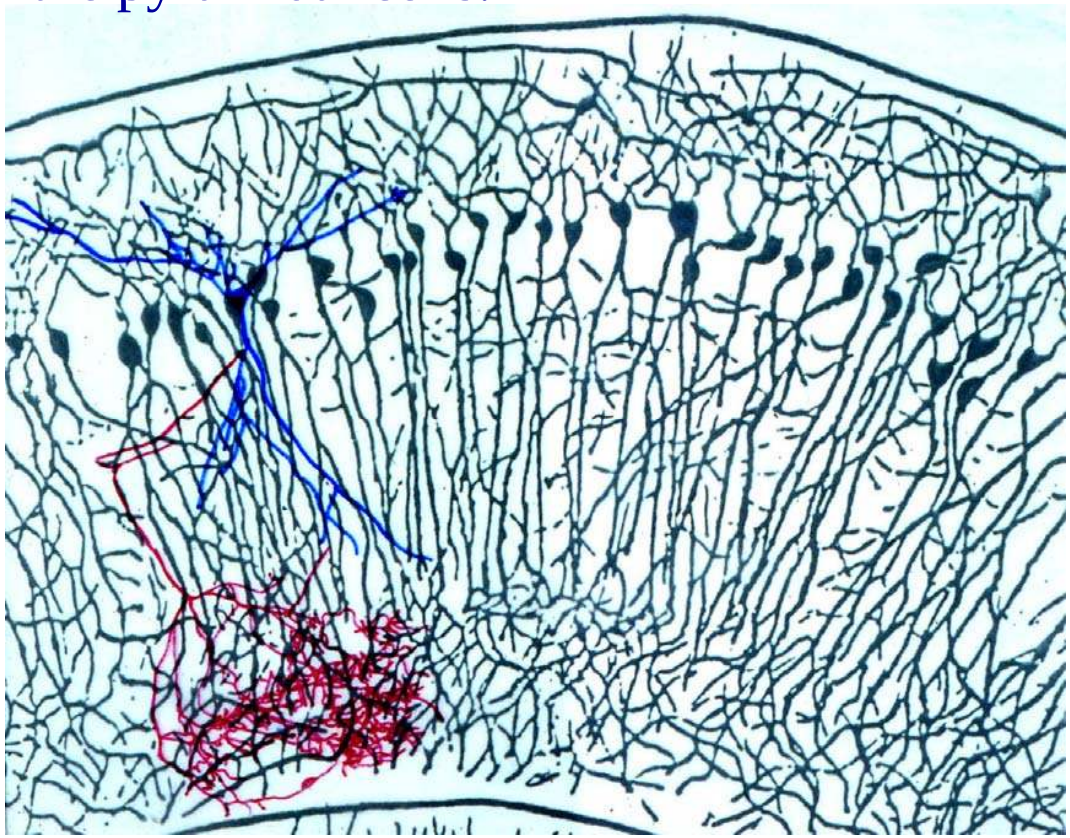
The axon of the axo-axonic cells forms vertical ribbons of boutons, each of which establish multiple, climbing-fibre-like contacts with the AIS of the pyramidal cells.



The axon of the axo-axonic cells forms vertical ribbons of boutons, each of which establish multiple, climbing-fibre-like contacts with the AIS of the pyramidal cells.

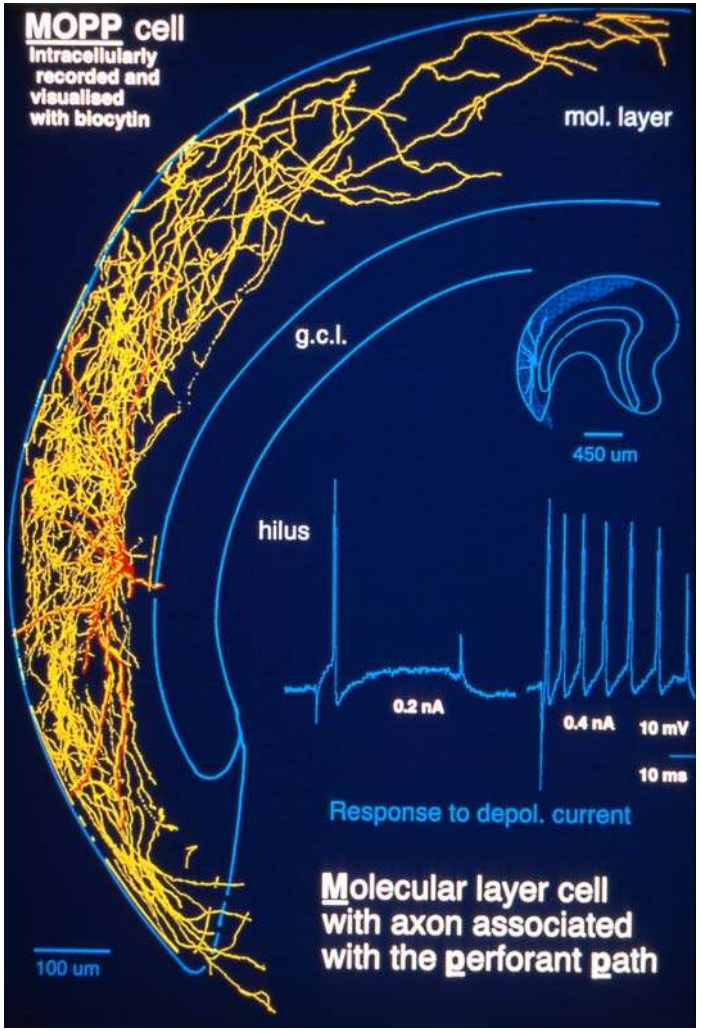


A type of dendritic inhibitory interneurons ramifies in the lacunosum-moleculare layer and establishes multiple contacts at the distal dendrites of the pyramidal cells.



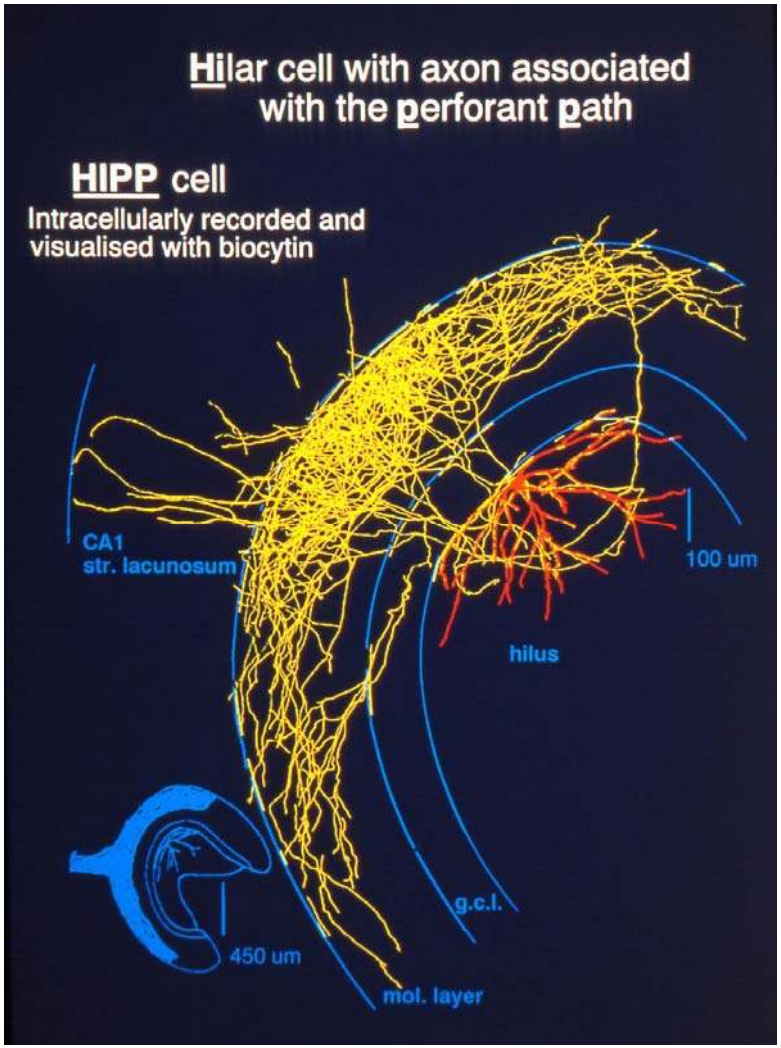
This type of interneuron is specialized for the control of entorhinal input.

The axon of other dendritic inhibitory interneurons terminate in the radiatum and oriens layers, where they regulate the input provided by the Schaffer collaterals.



The feed-forward way of dendritic inhibition

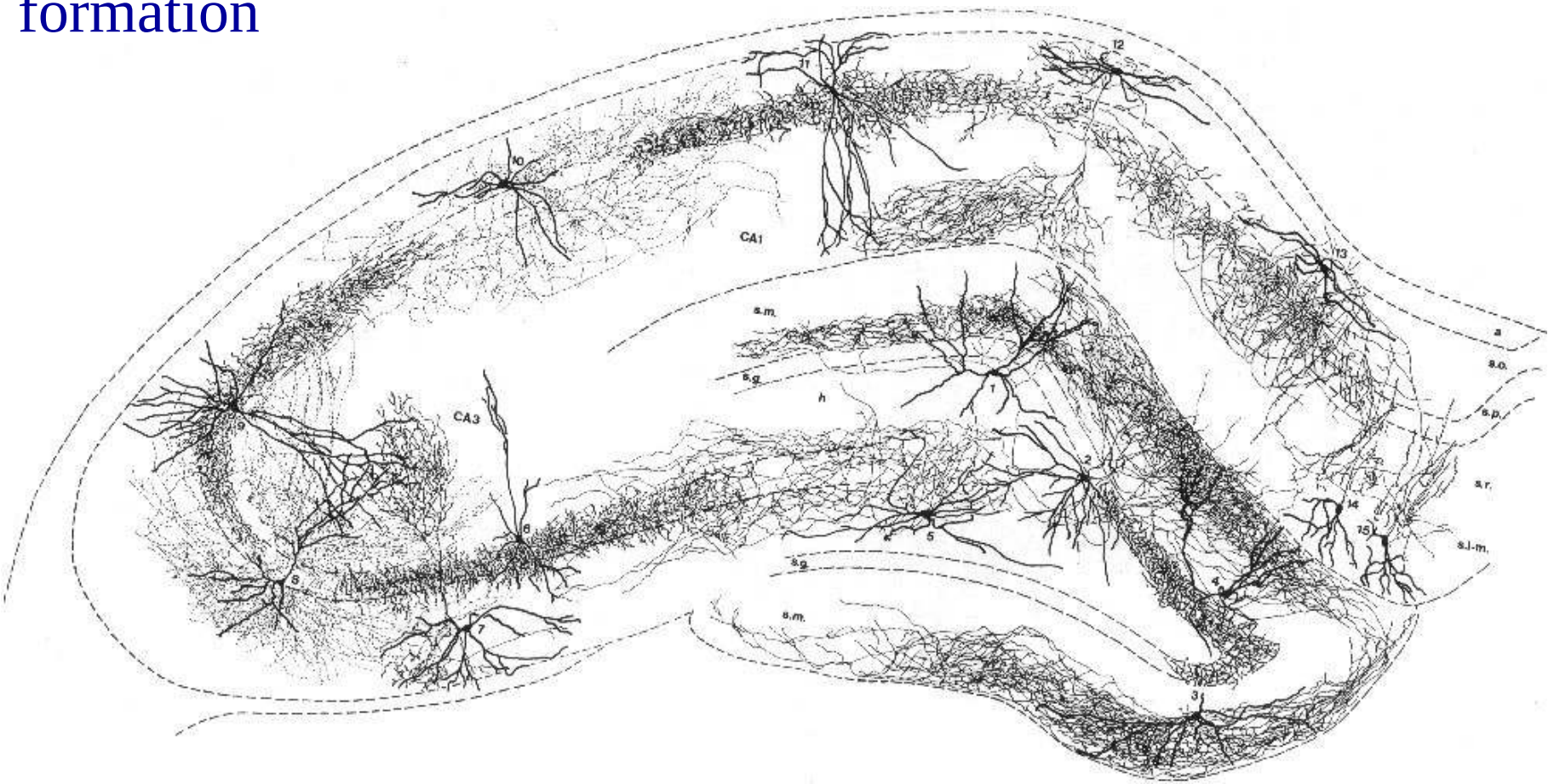
The dendritic tree (red) as well as the axon (yellow) of the dendritic inhibitory cell ramify in the outer two-third of the molecular layer, which receives the entorhinal input. This type of interneuron, therefore, can regulate the effectiveness of the pathway, which provides afferents to it, as well as to principal neurons. Through this type of interneurons, the entorhinal afferents regulate their own effectiveness at their activity-dependent manner.



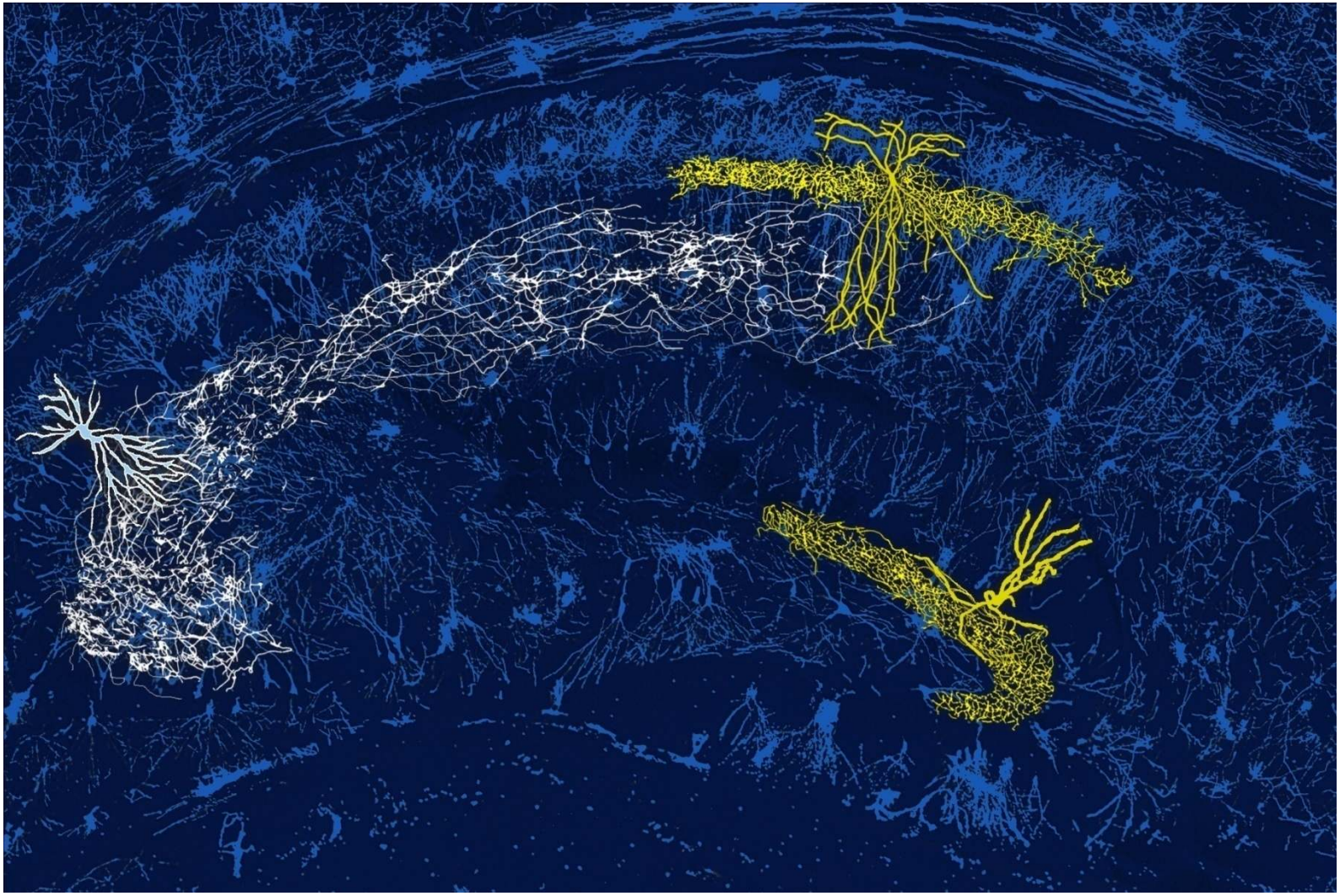
The feed-back way of dendritic inhibition

The axon (yellow) of this type of dendritic inhibitory cell ramifies in the outer two-third of the molecular layer, which receives the entorhinal input. The dendritic tree (red) is restricted to the hilus, where it receives input from the axon collaterals of granule cells. This type of interneurons regulates the effectiveness of the entorhinal pathway also at activity-dependent manner, but not primarily through the activity of the pathway itself, instead through the pathway-activated granule cell population.

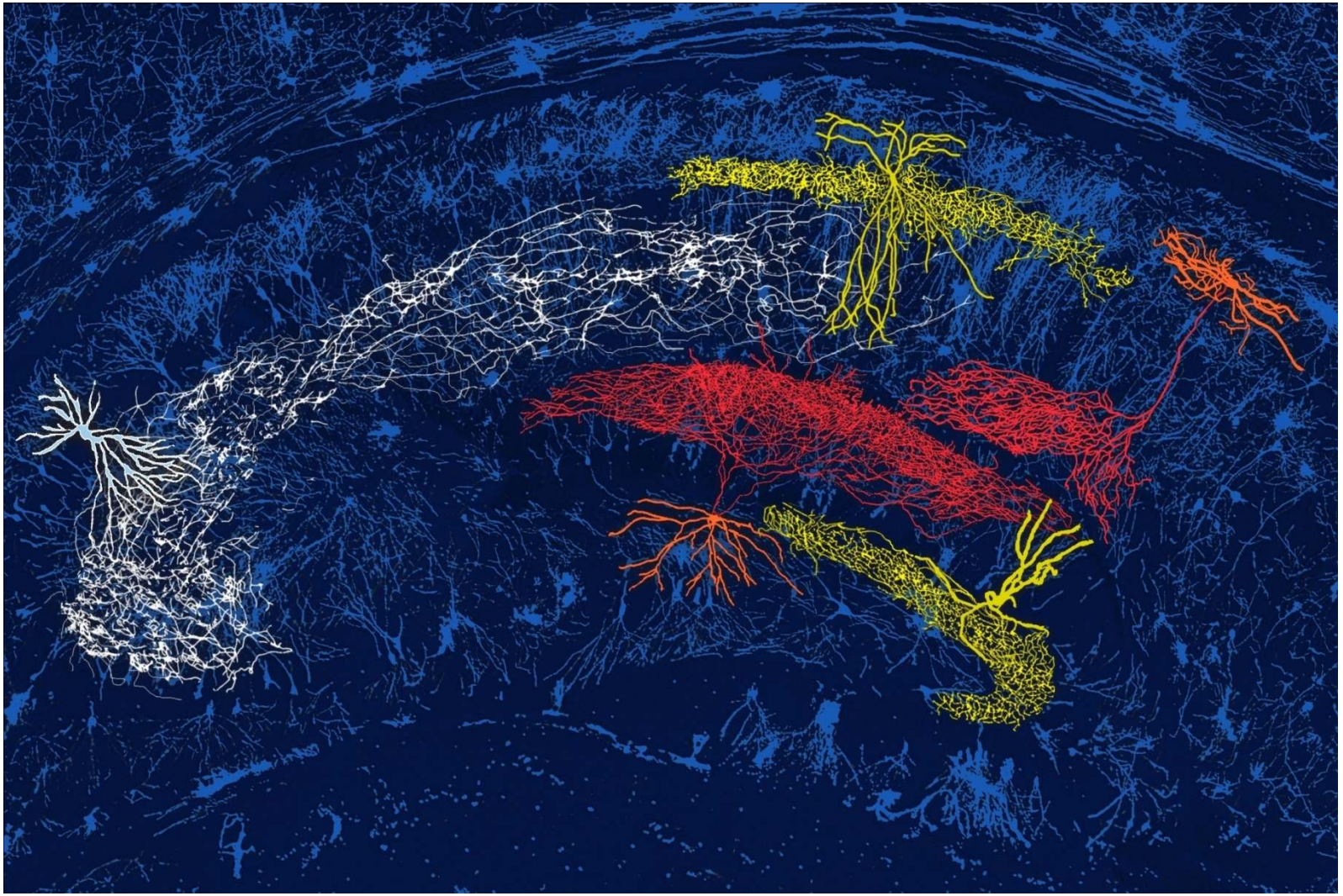
The major inhibitory interneuron-types of the hippocampal formation



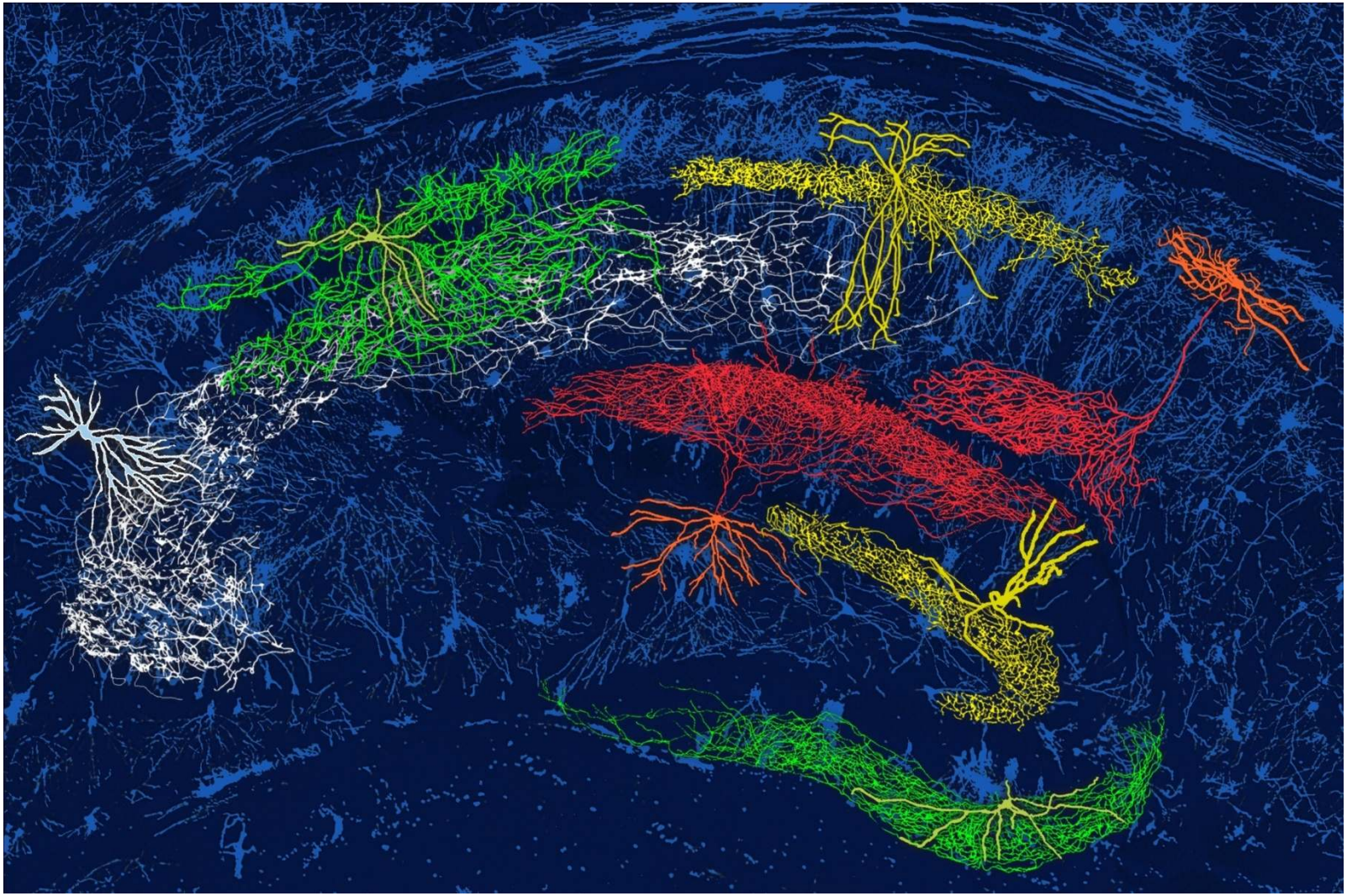
Introduction to functional neurobiology: Hippocampus



Introduction to functional neurobiology: Hippocampus

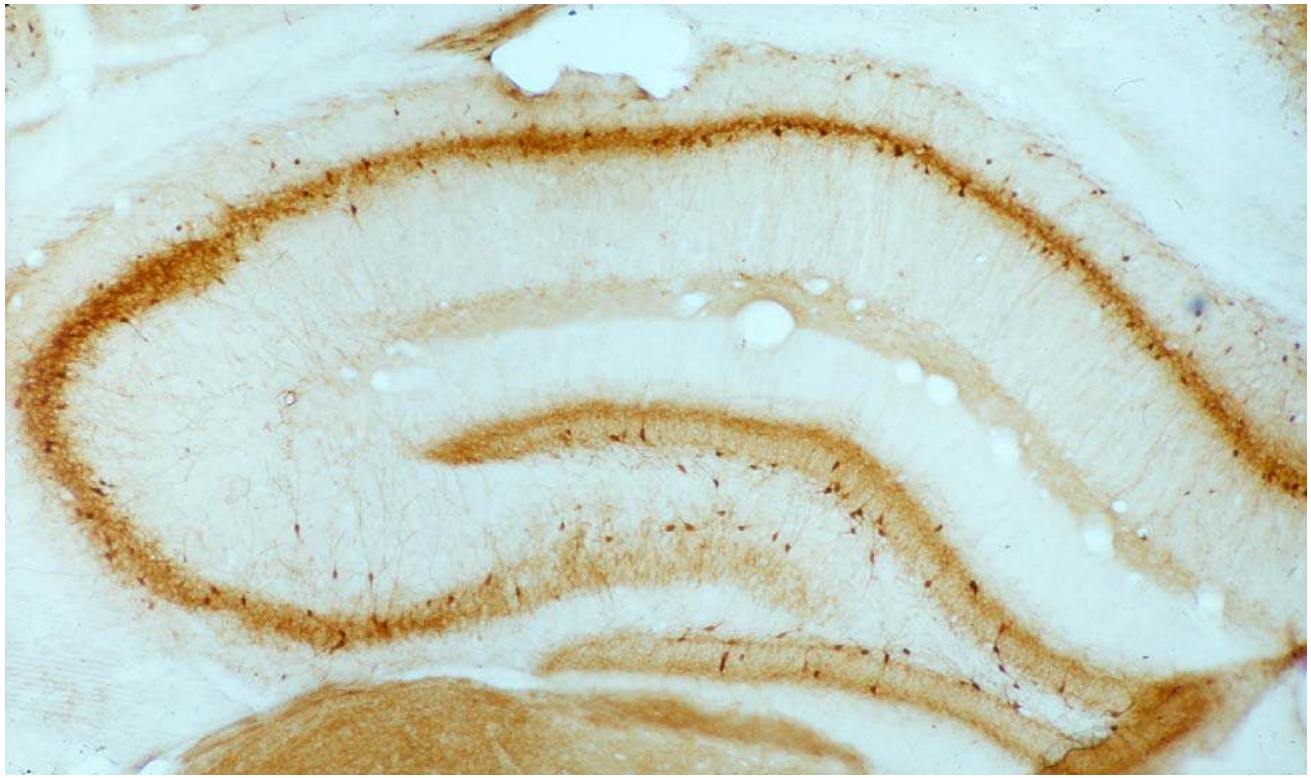


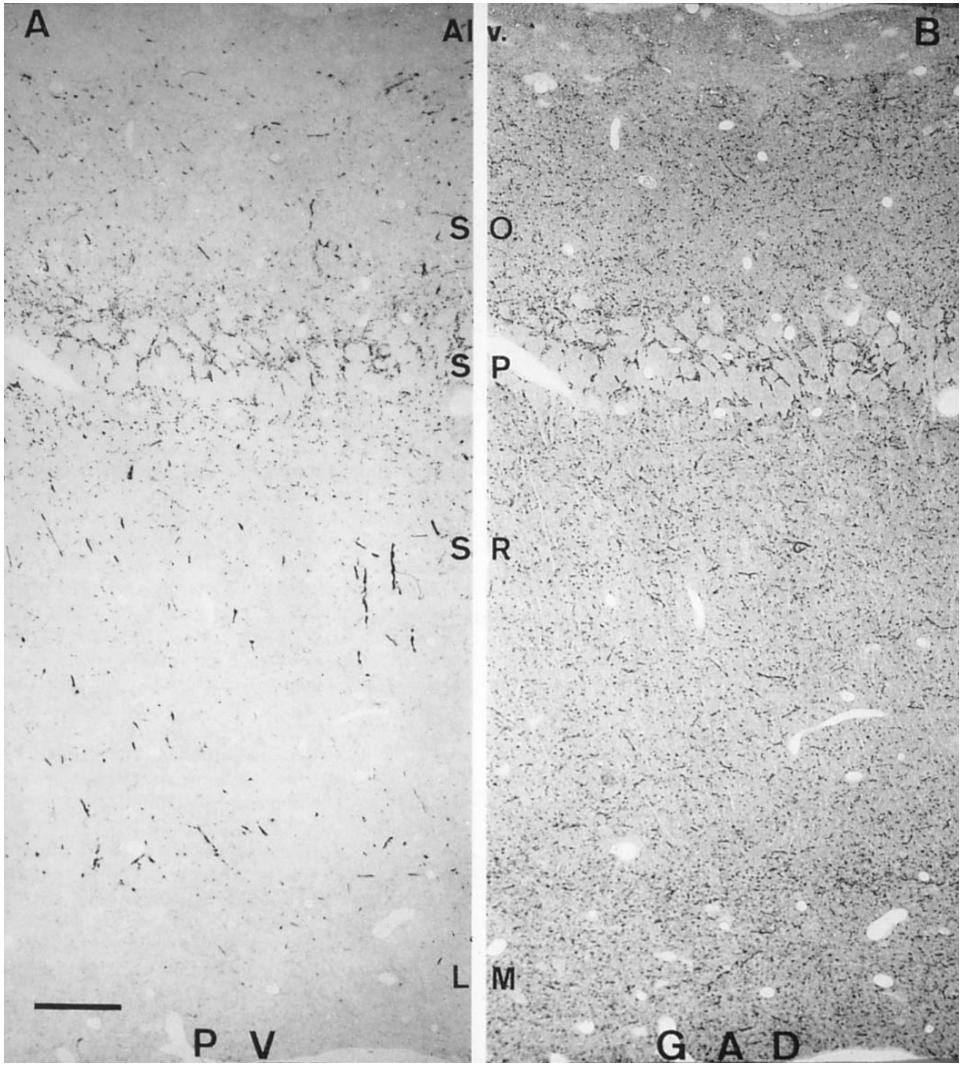
Introduction to functional neurobiology: Hippocampus



Neuropeptides and calcium-binding proteins are selectively present in certain inhibitory neurons

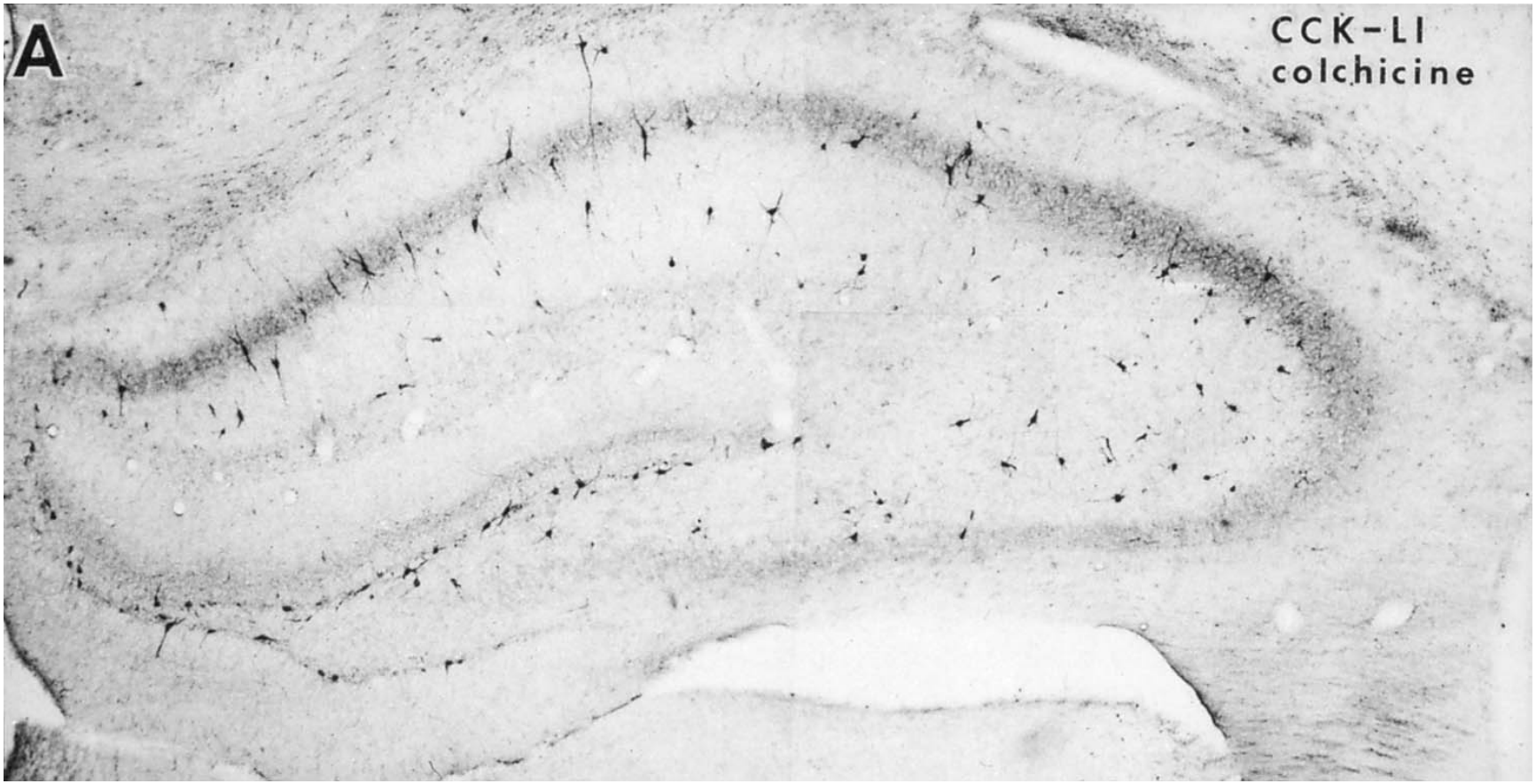
Parvalbumin: perisomatic inhibitory cells





GABAergic terminals are present in high density in all layers. In contrast, parvalbumin-containing terminals are almost exclusively in the pyramidal layer.

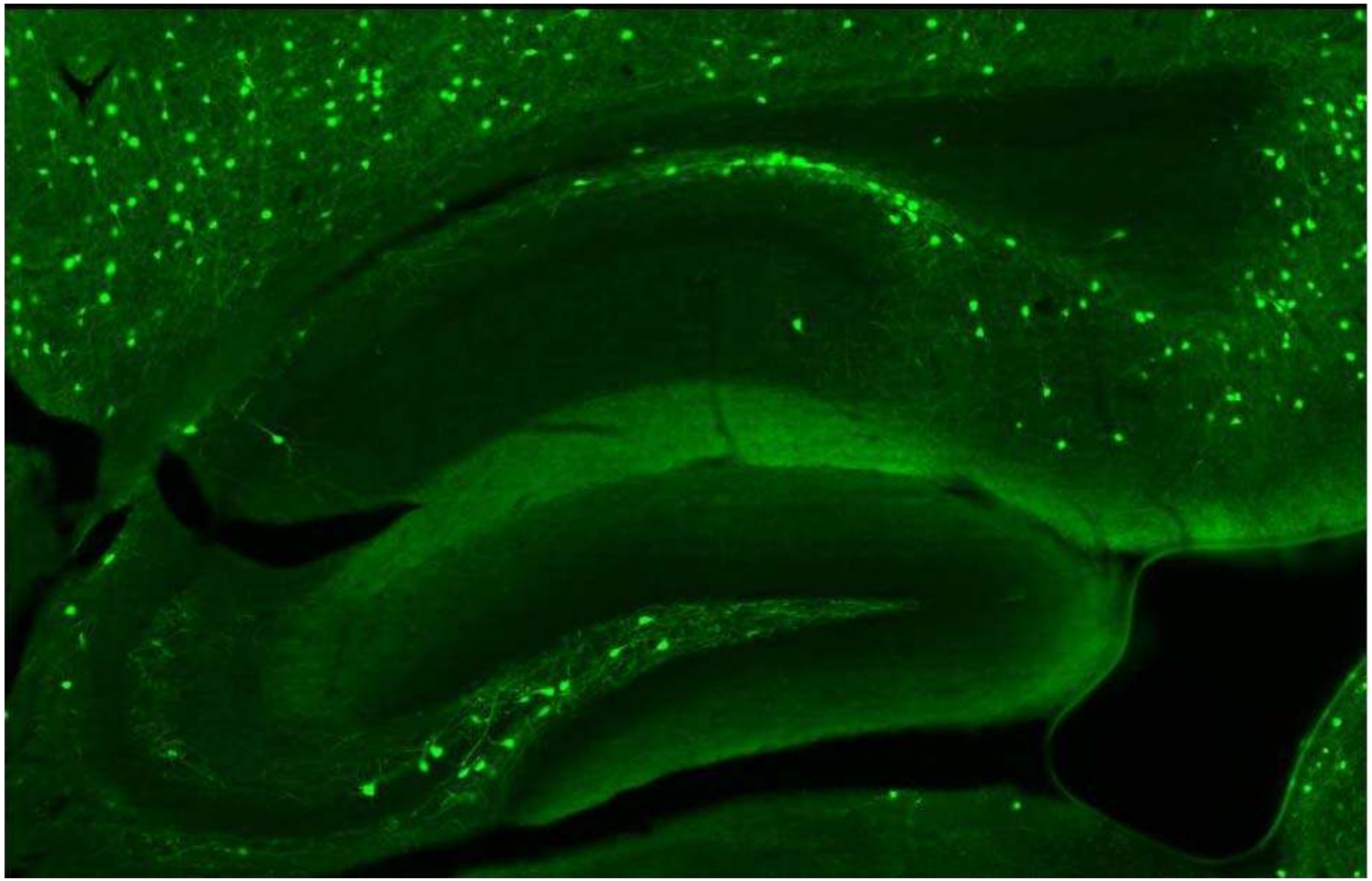
Cholecystokinin (CCK) are present also primarily in perisomatic inhibitory cells



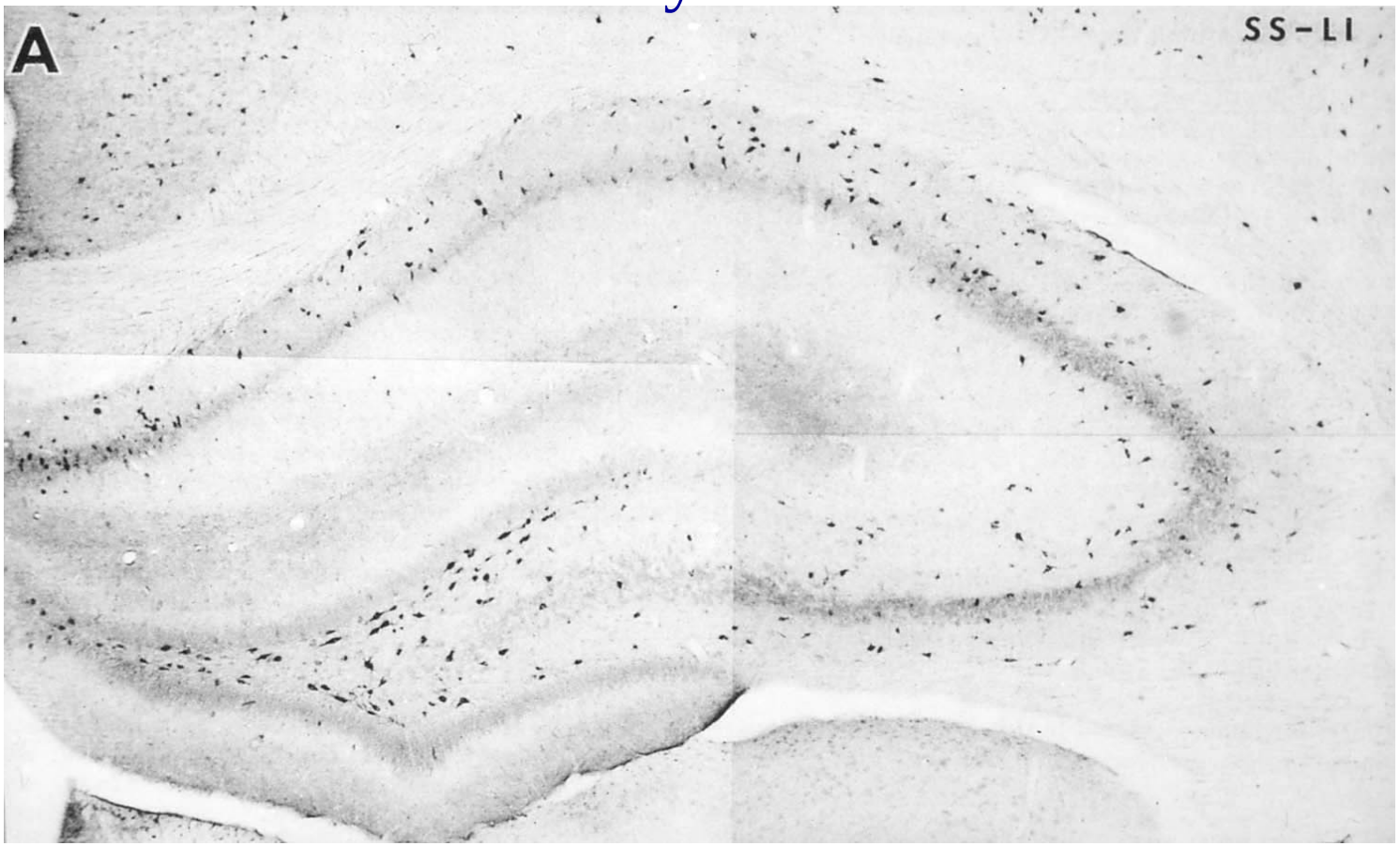
Som-ires-Cre



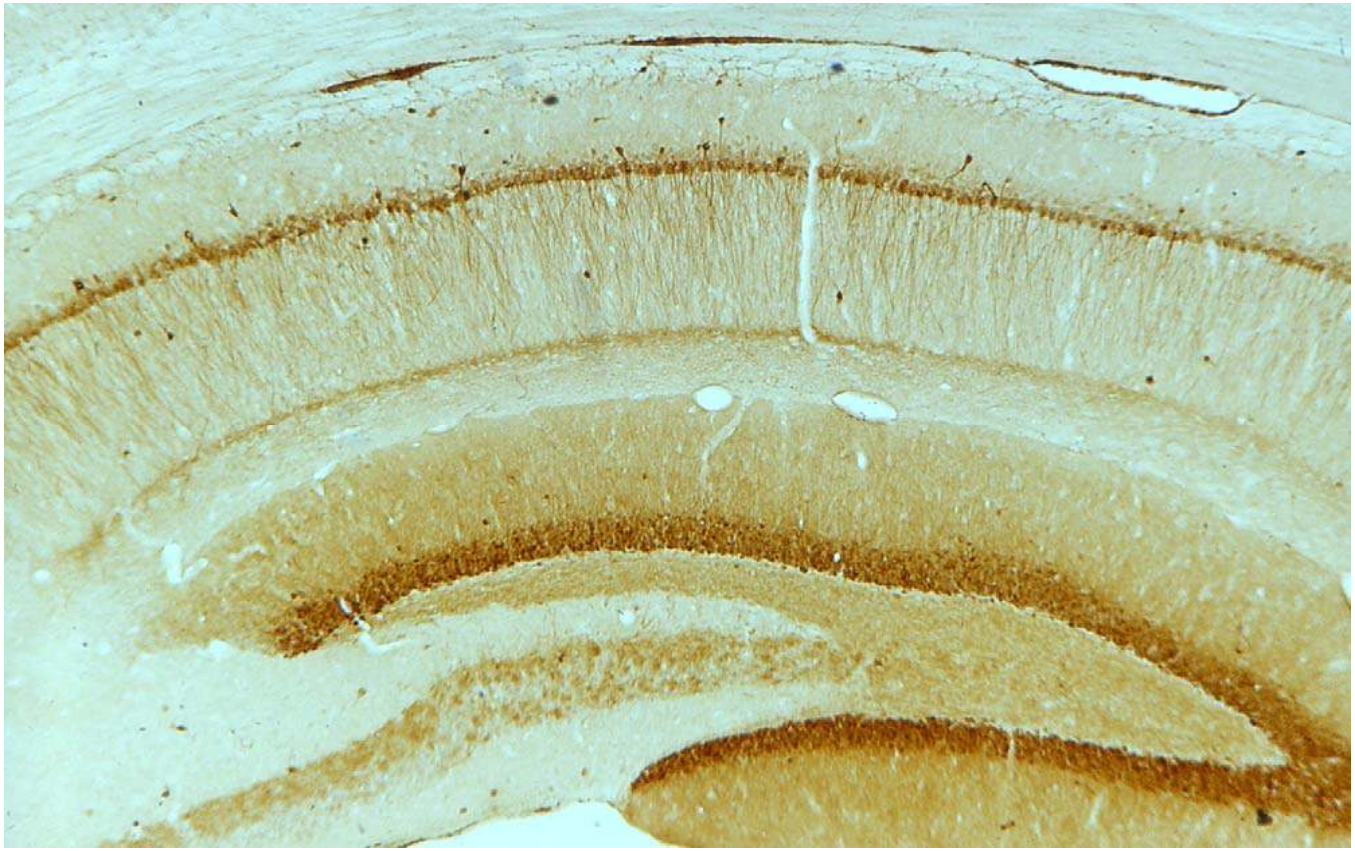
The O-LM cell axons in the hippocampus

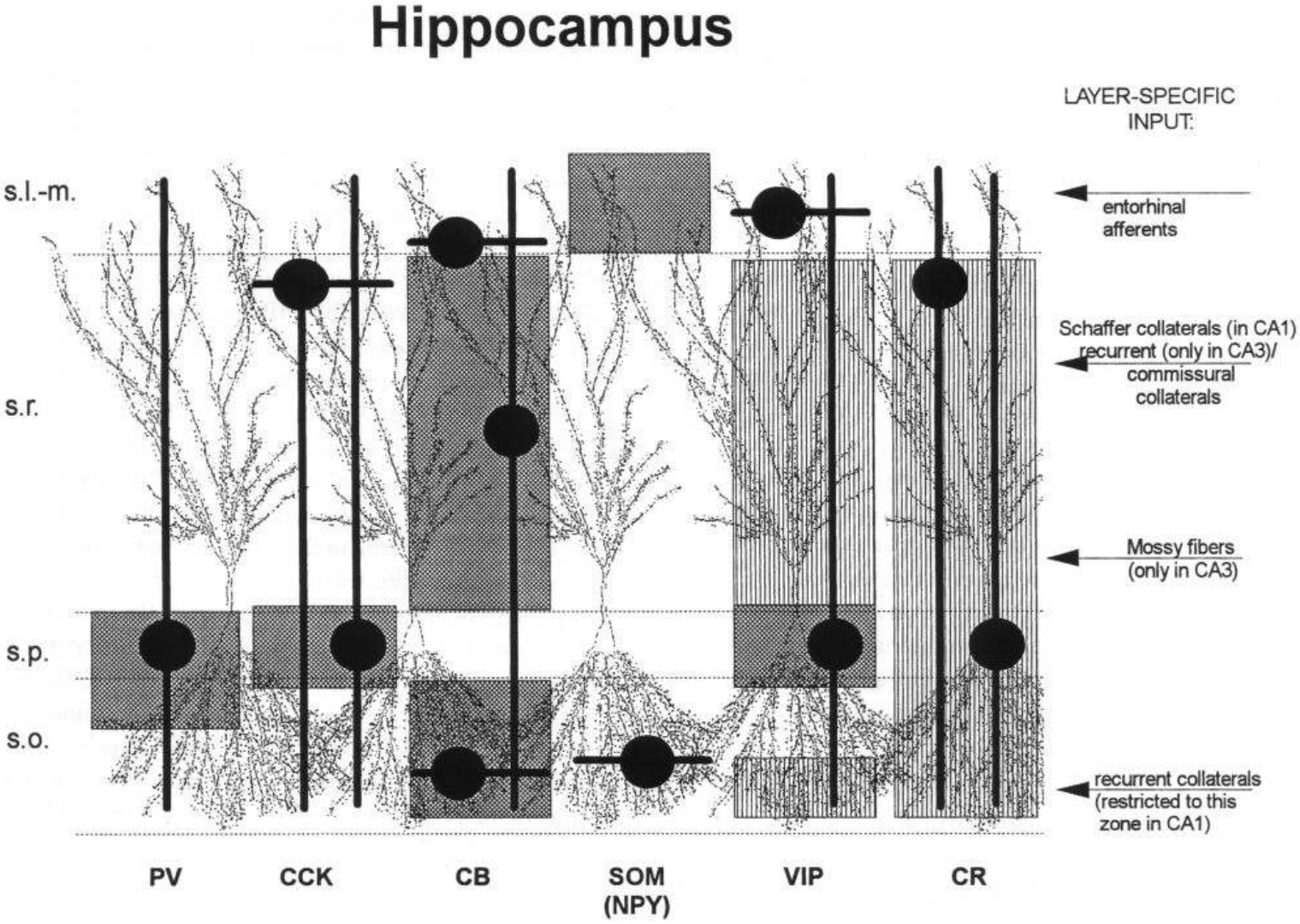


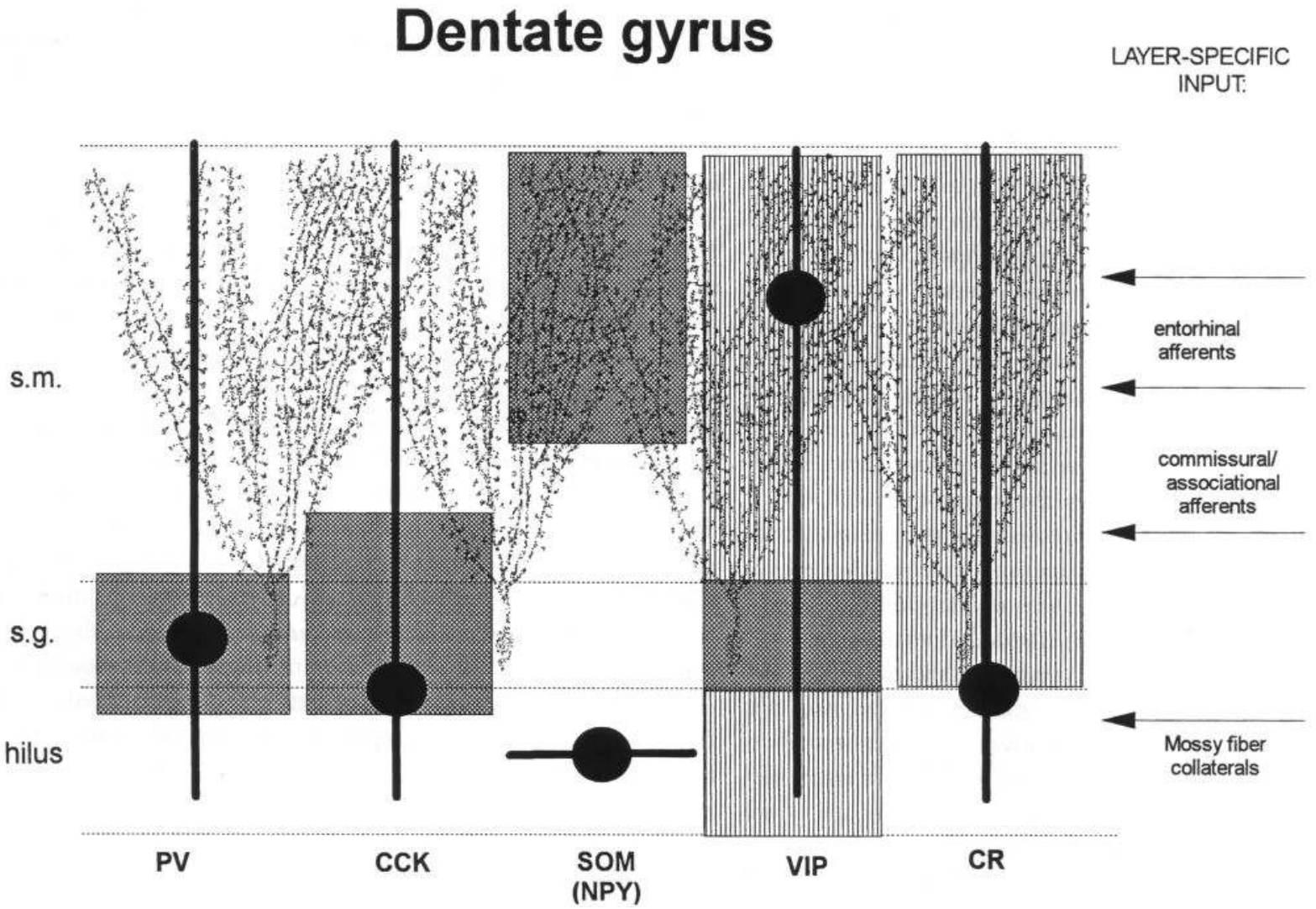
Somatostatin marks dendritic inhibitory cells, which exert inhibition in the layer of entorhinal afferents



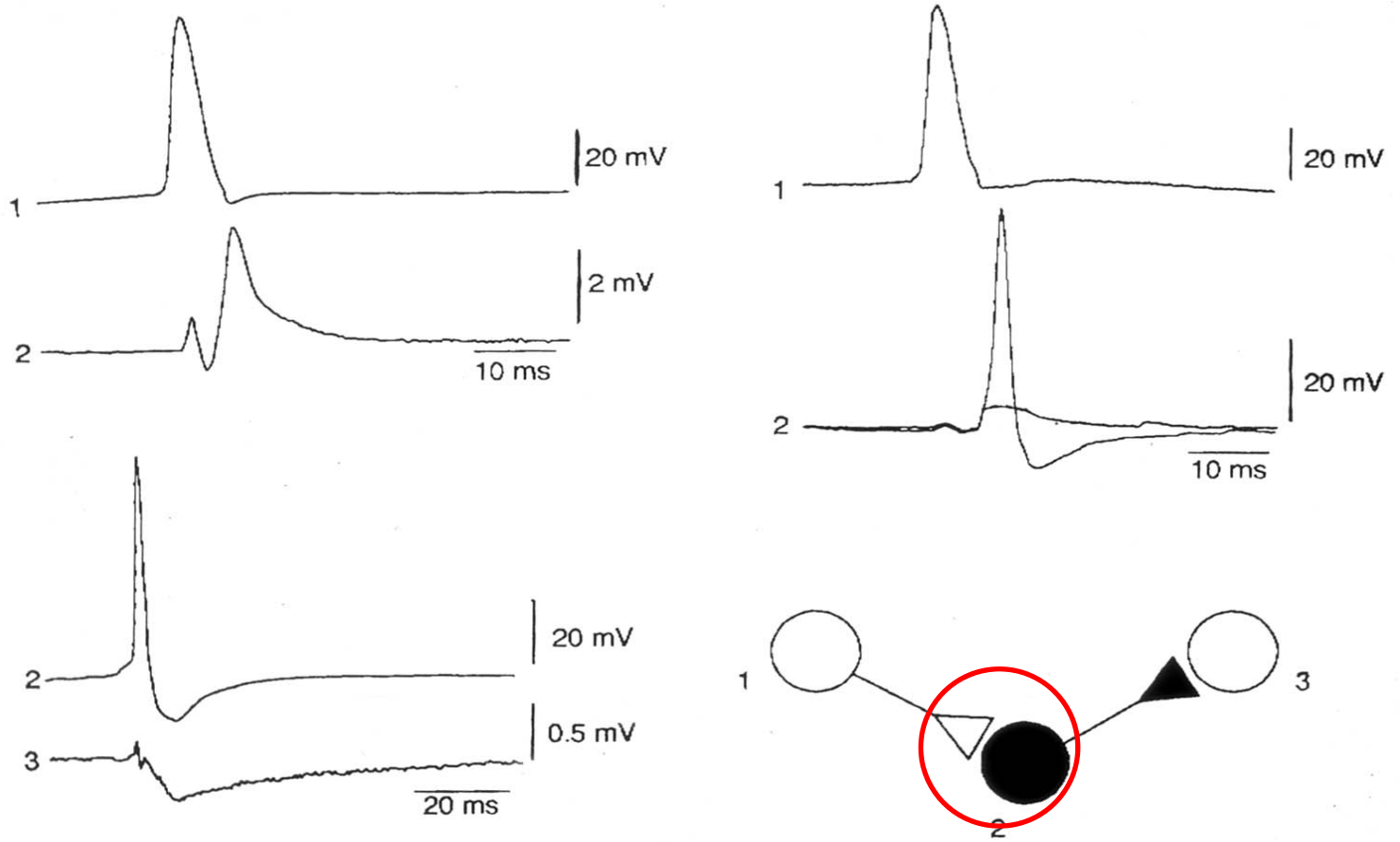
Calbindin is present in those dendritic inhibitory cells, which project to the layers also innervated by the Schaffer collaterals (radiatum and oriens) . Calbindin marks also the granule cells and the CA1 pyramidal cells.



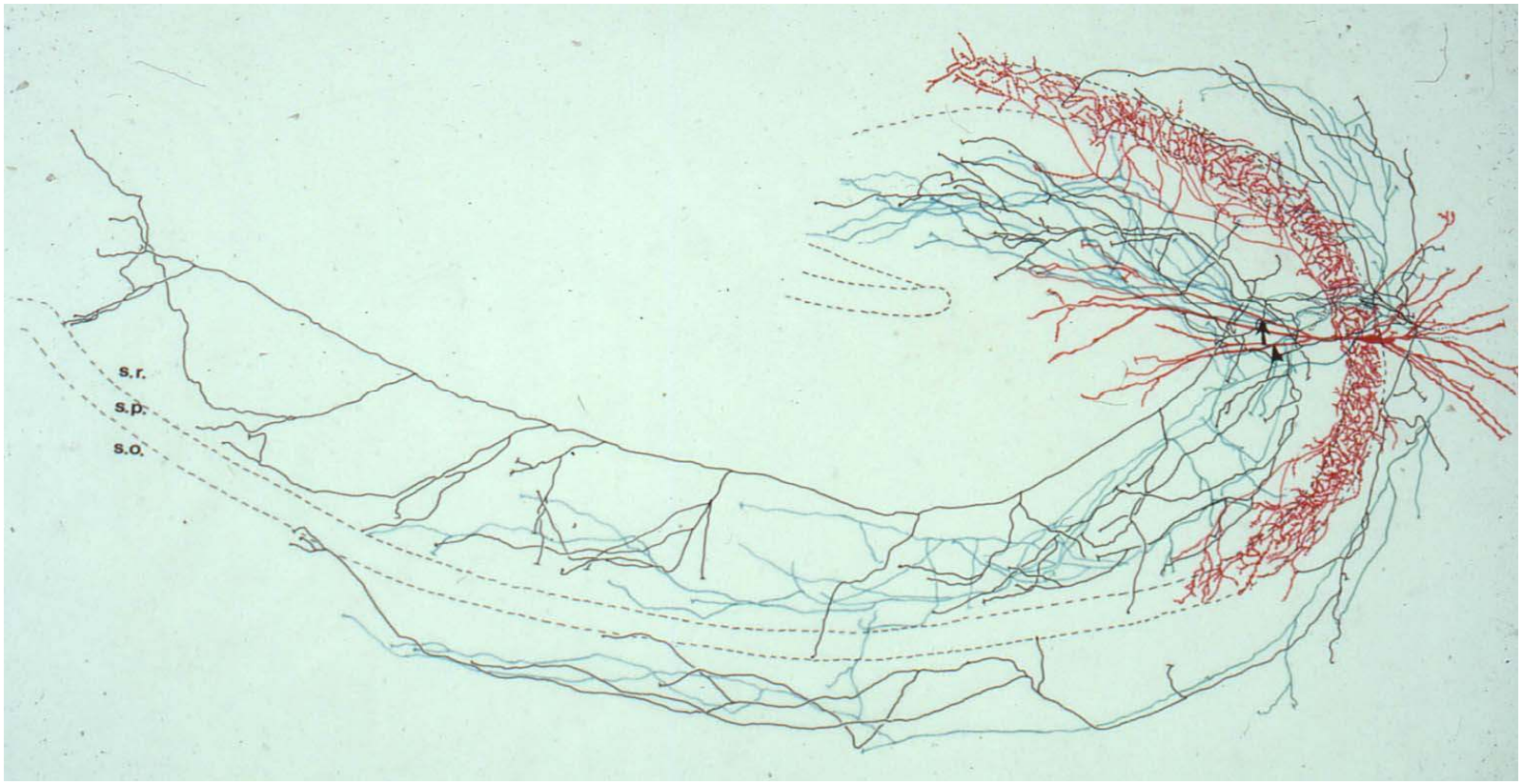

Hippocampus
LAYER-SPECIFIC INPUT:
s.l.-m.
s.r.
s.p.
s.o.
entorhinal afferents
Schaffer collaterals (in CA1)
recurrent (only in CA3)/
commissural collaterals
Mossy fibers (only in CA3)
recurrent collaterals (restricted to this zone in CA1)
PV
CCK
CB
SOM (NPY)
VIP
CR


Dentate gyrus
LAYER-SPECIFIC INPUT:
s.m.
s.g.
hilus
entorhinal afferents
commissural/ associational afferents
Mossy fiber collaterals
PV
CCK
SOM (NPY)
VIP
CR

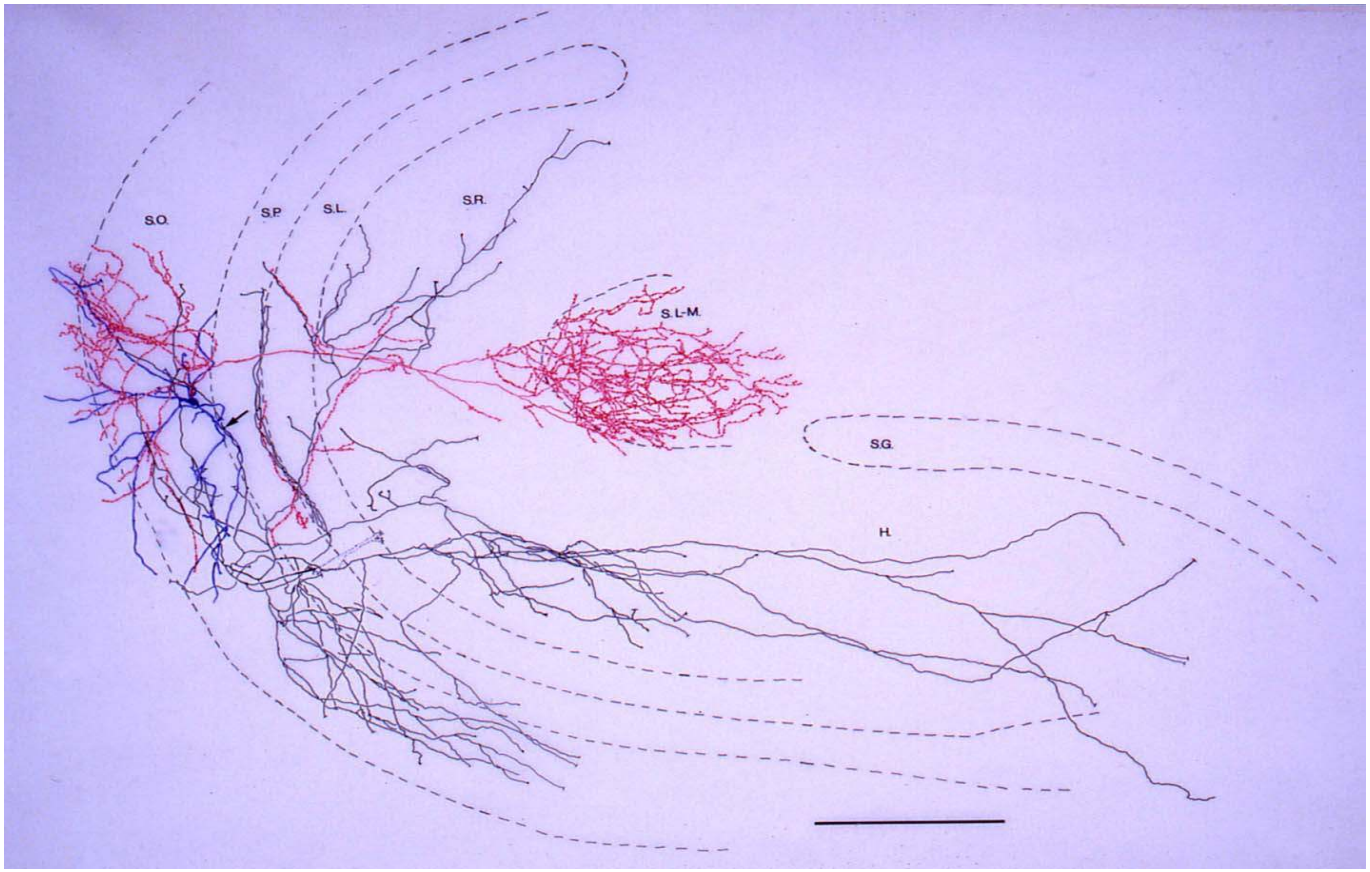
Interactions of excitatory and inhibitory cells can be studied with paired intracellular recordings



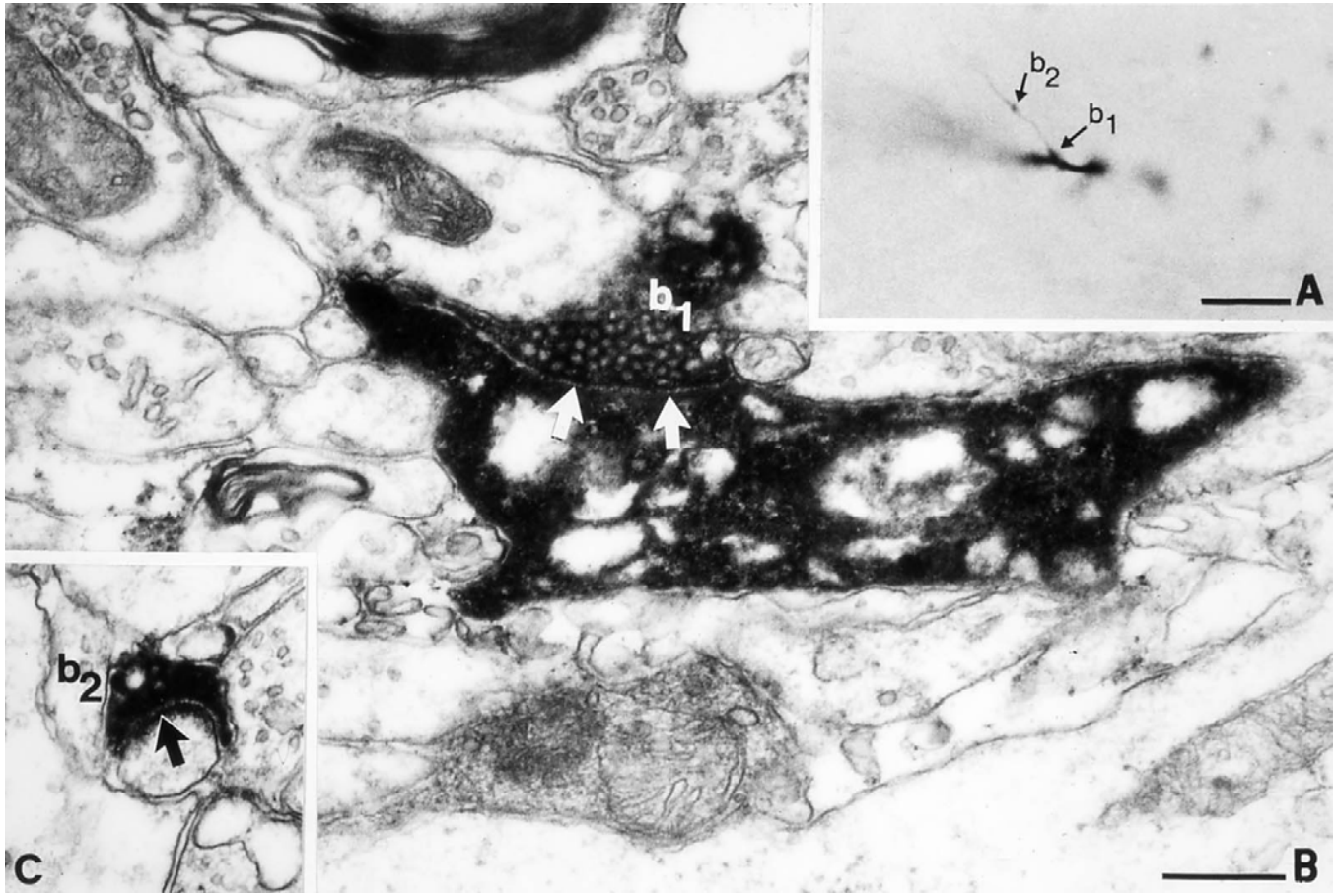
Pyramidal cells evoke large amplitude (2-3 mV) excitatory postsynaptic potentials (EPSP) in perisomatic inhibitory cells, usually through a single synapse. This is often sufficient to induce action potential in the target cell.



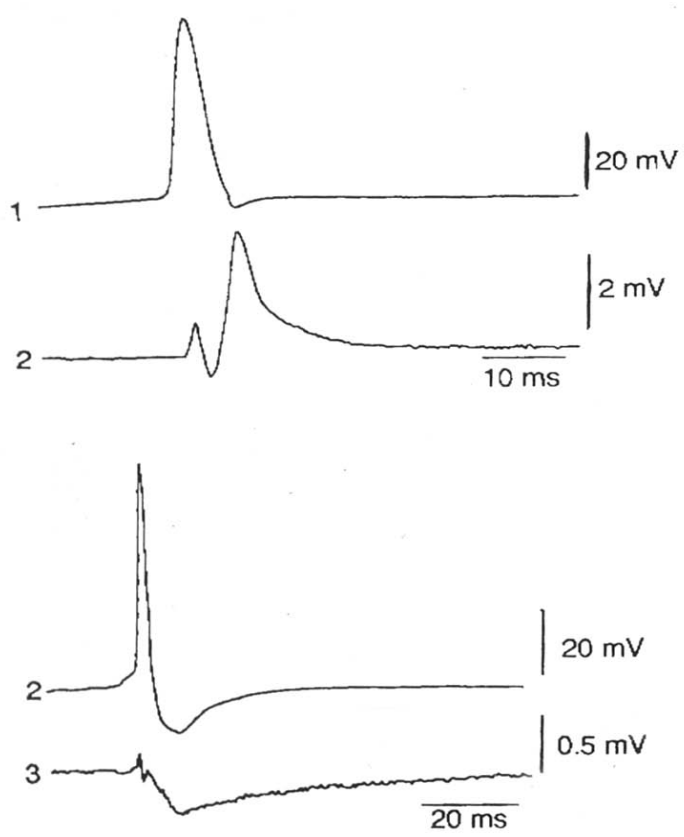
Similarly, dendritic inhibitory cells receive a very potent input from the pyramidal cells, mainly through a single synapse.

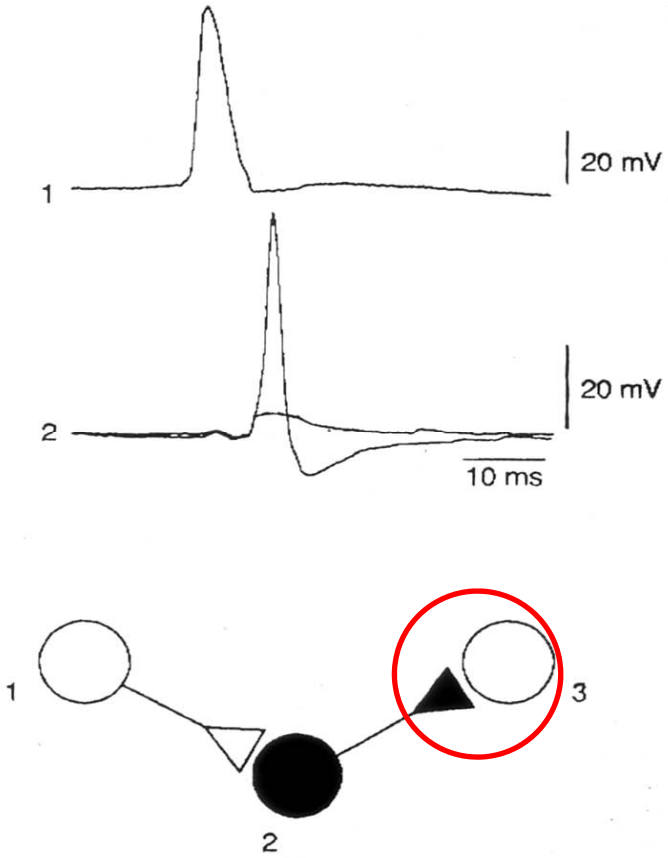


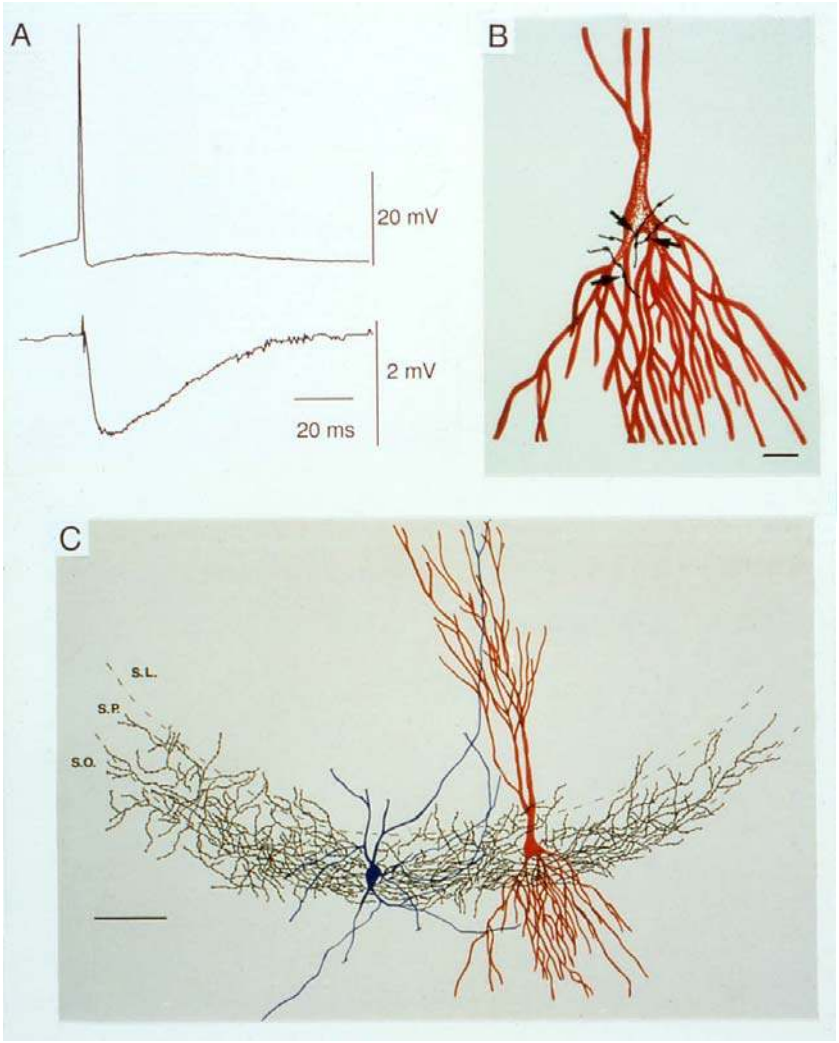
The pyramidal cell establish asymmetric synapses characteristic of the excitatory neurotransmission.



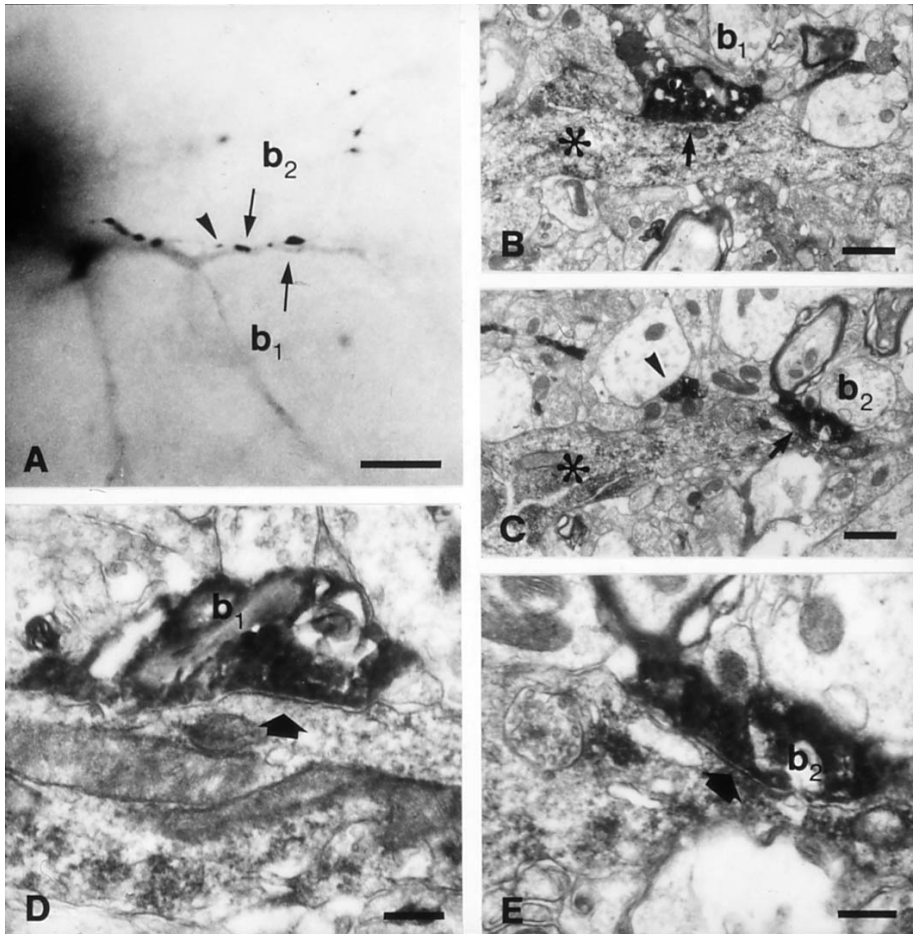
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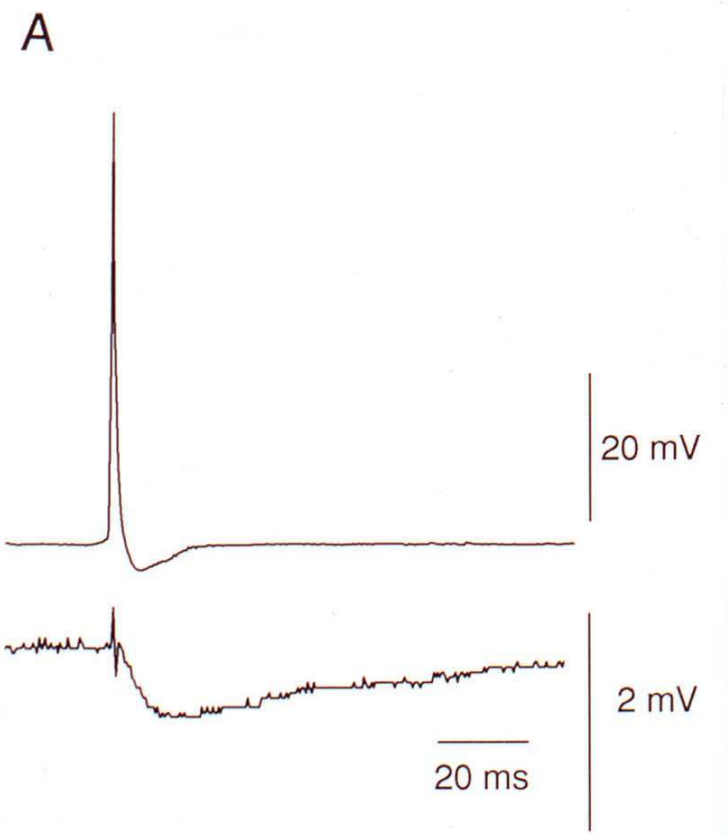


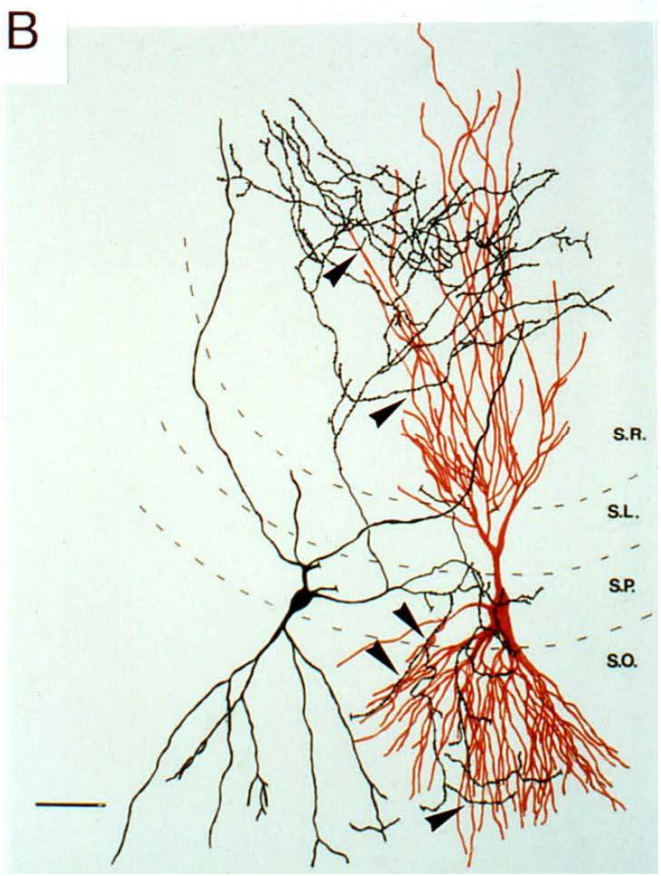
Basket cells (in blue) evoke large amplitude (2-3 mV) inhibitory postsynaptic potentials (IPSP) in the target pyramidal cells (in red), through an average of 2-8 axon terminals , which synapse on the soma and the proximal dendrites.



The basket cell establish symmetric synapses characteristic of the inhibitory neurotransmission.

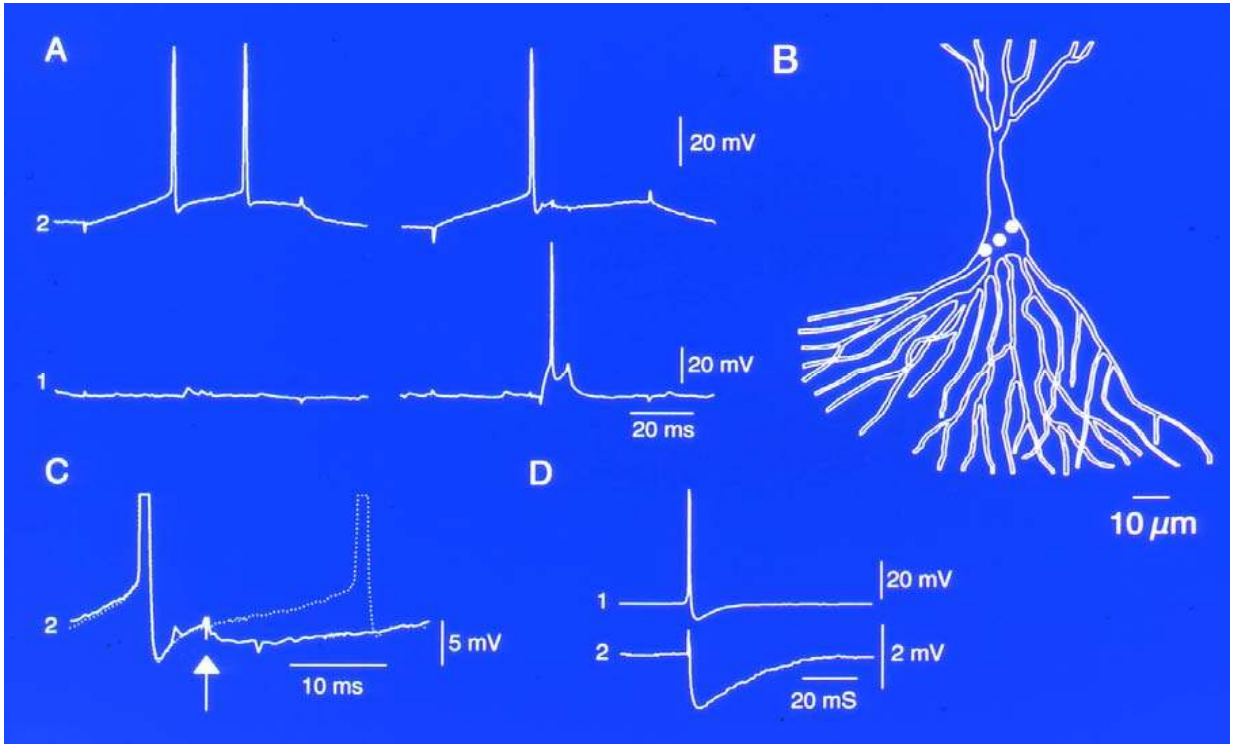
The dendritic inhibitory cells induce IPSPs (0,5-2 mV) in the pyramidal cells, through 3-18 synapses, which are located on the distal dendritic tree





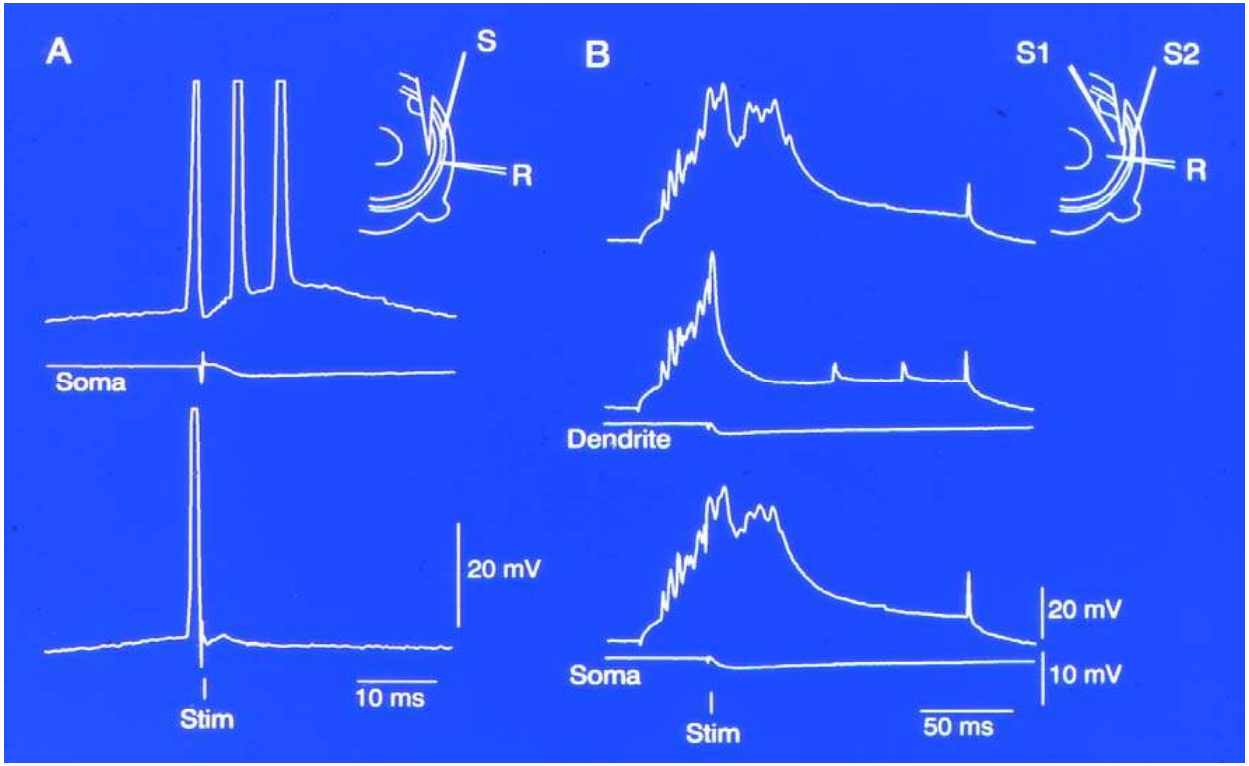
The perisomatic inhibition inhibit the firing activity of pyramidal cells very effectively

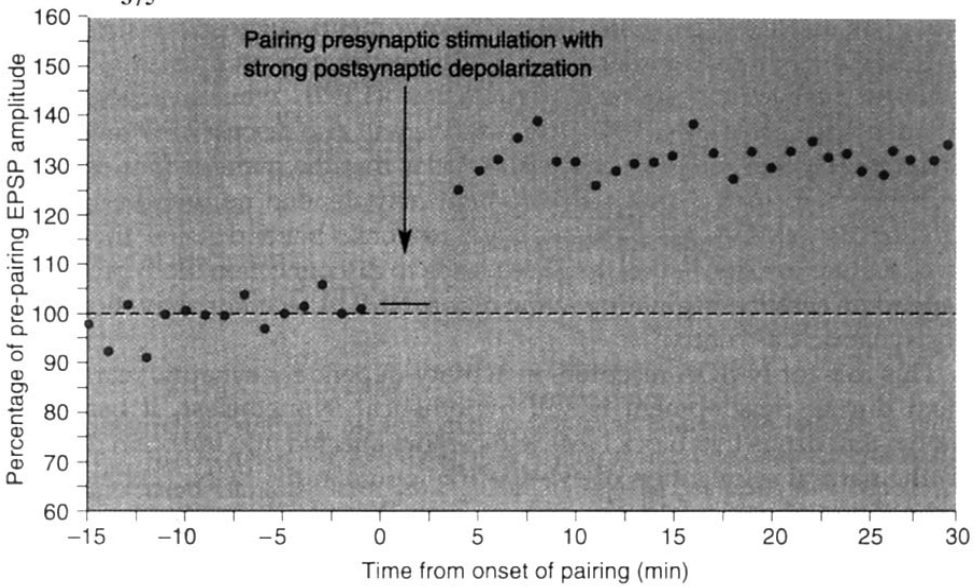
A single action potential of a single basket cell is capable to prevent the repetitive discharge of the pyramidal cells through 3 synaptic connection

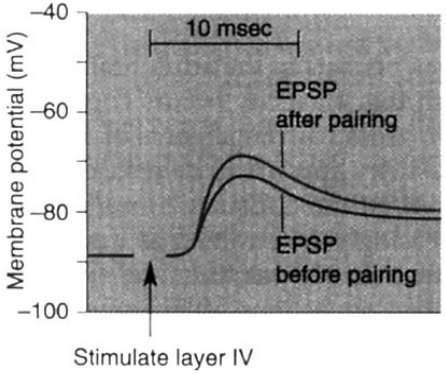


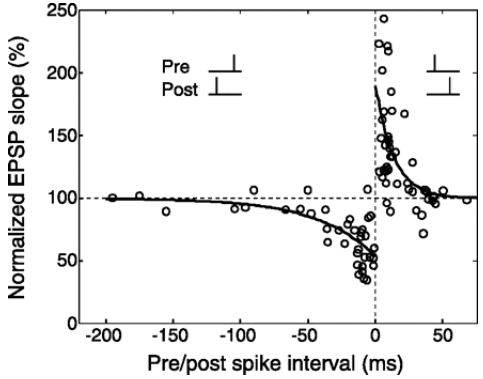
The dendritic inhibition regulates the effectiveness and plasticity of excitatory inputs of pyramidal cells

The dendritic inhibition prevents the opening of voltage-dependent calcium channels and the activation of NMDA receptors







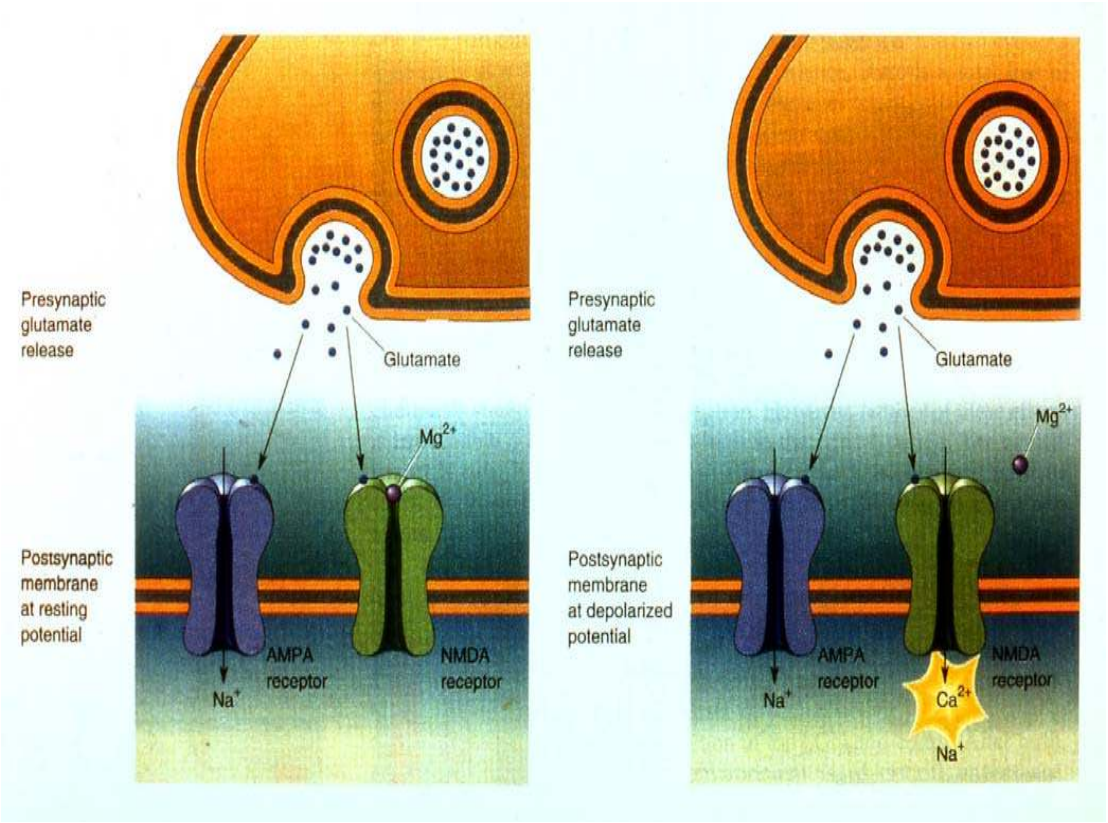


Why the precise synchronization is important?

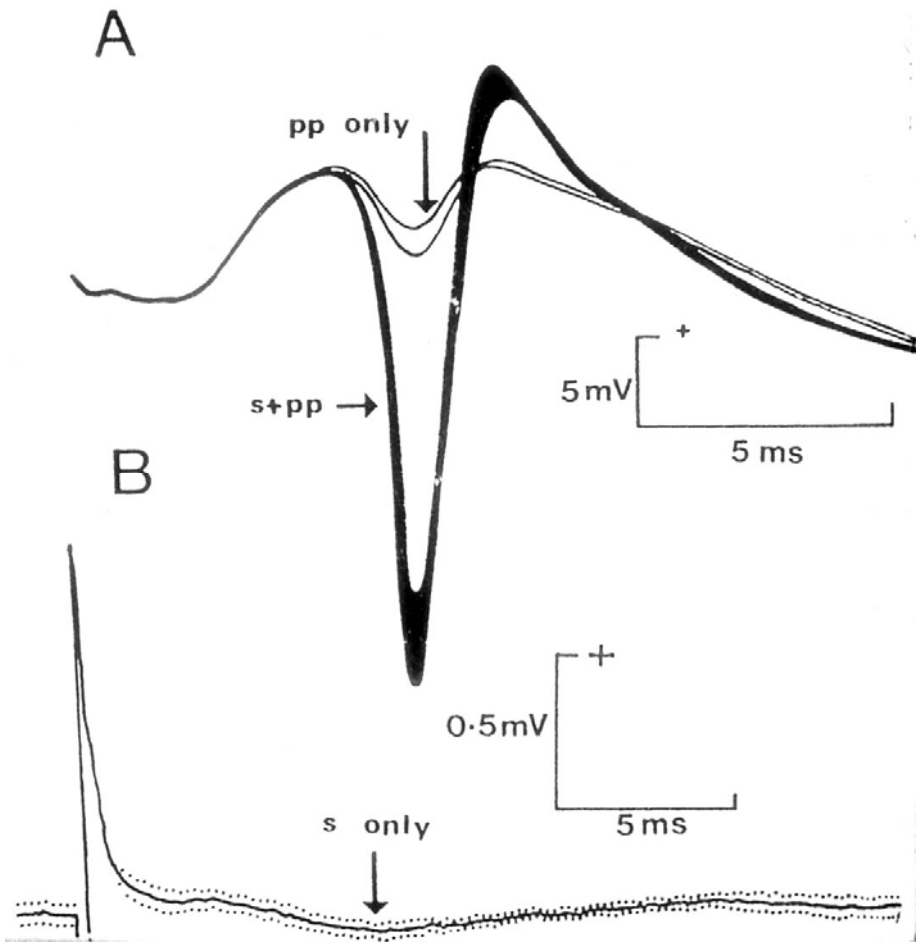
The concurrent discharge of the impulse provider and the receiver results in a lasting increase of the amplitude of the evoked excitatory synaptic potential.

The Long Term Potentiation (LTP) is the basic cellular mechanism of memory.

The NMDA receptors are ligand as well as voltage-dependent receptors. In their open state they transmit also calcium ions.

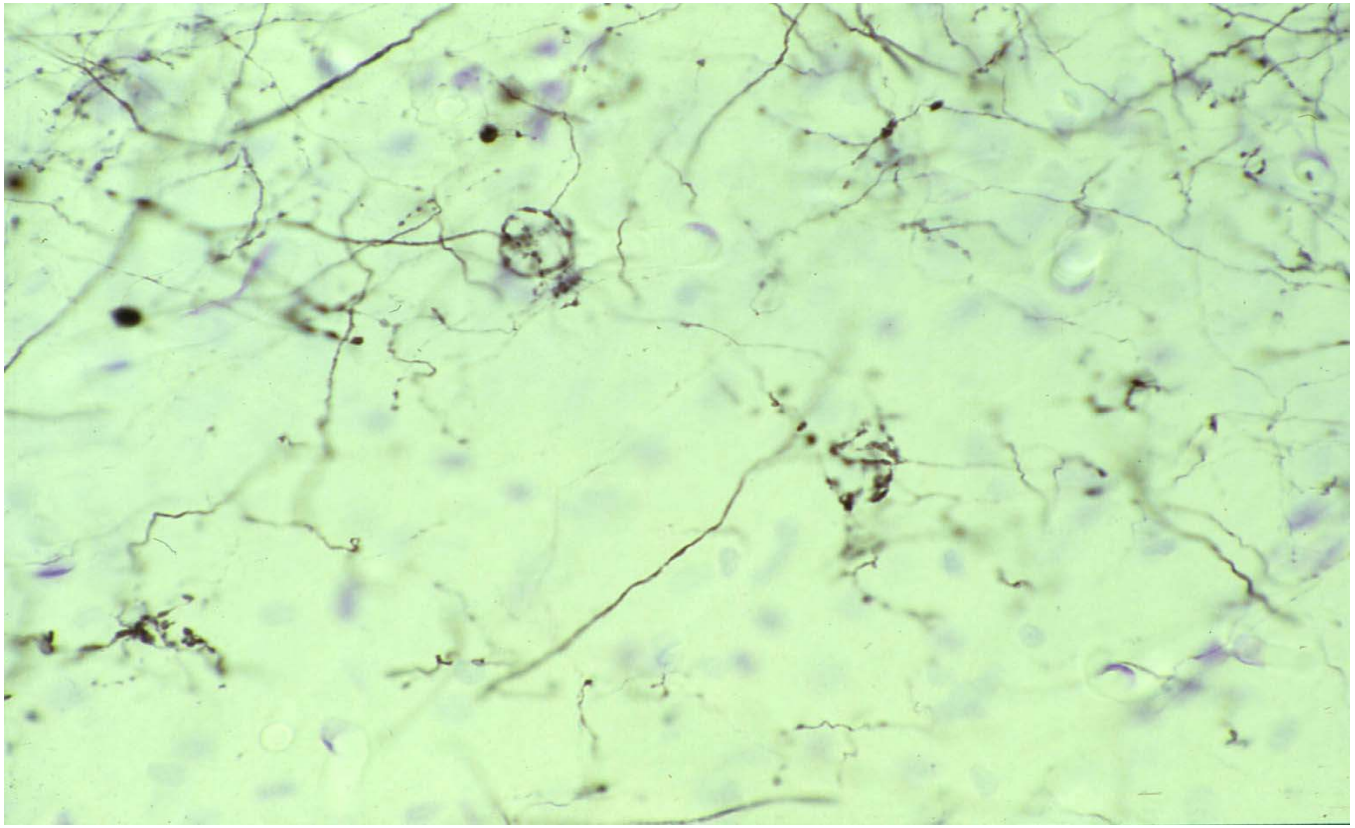


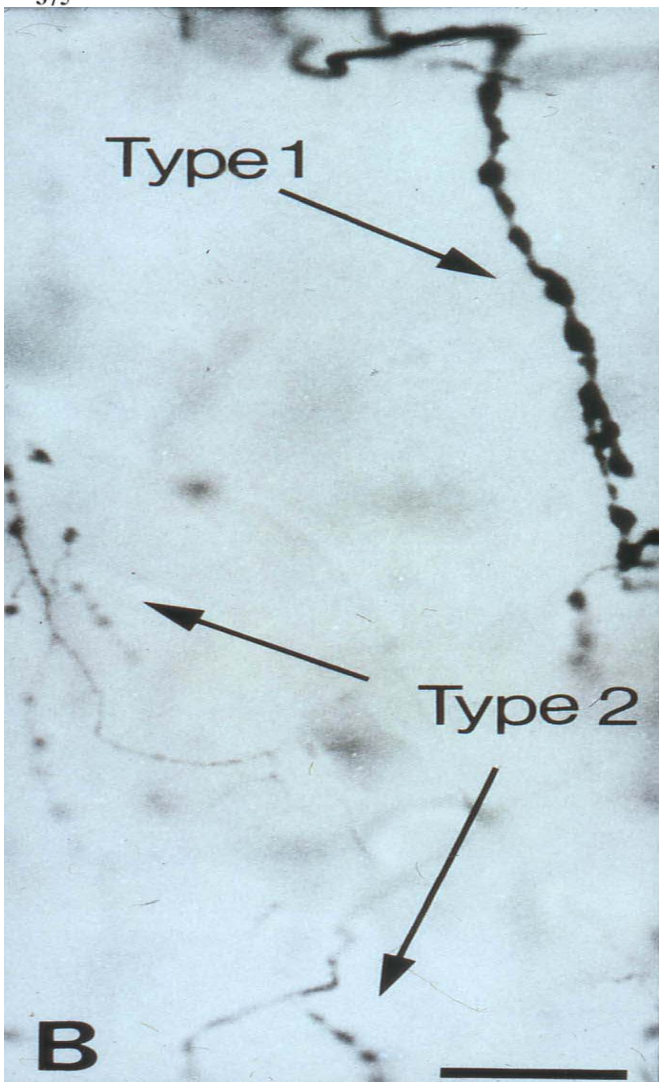
Precise synchronization of the discharge of pyramidal cells is the prerequisite for the induction of NMDA-mediated synaptic potentiation (LTP) since the synchronized retrograde propagation of action potentials tunes the release of Mg2+ blockage from the dendritic NMDA receptors (and the consequent Ca2+ influx) with the presynaptic transmitter release.



Stimulation of the septum alone does not evoke changes in the field potential recorded in the hippocampus, but increase the excitability of the hippocampal pyramidal cells. The increased excitability is not a response to a cholinergic stimulation, instead it is the result of a reduced inhibition in the hippocampus.

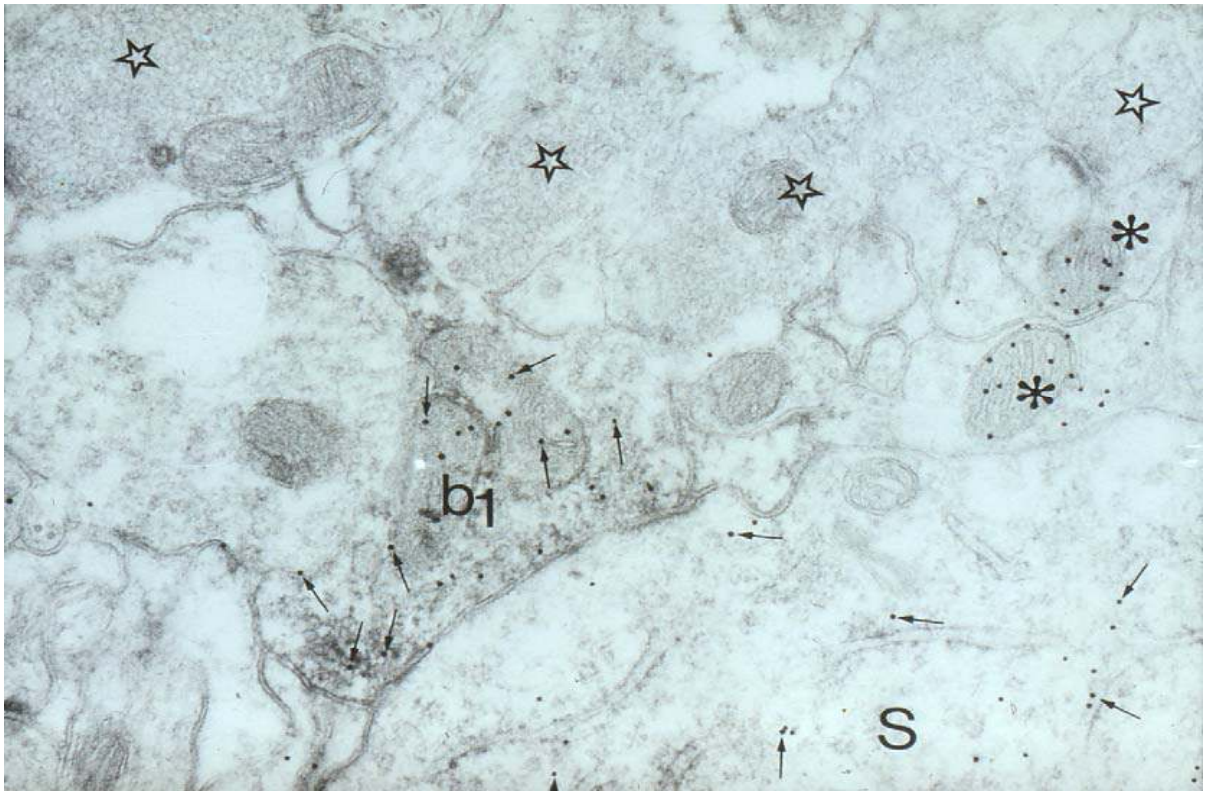
Axons from the septum provide a rich innervation of the hippocampus. Thicker fibers seem to surround perikaryons.

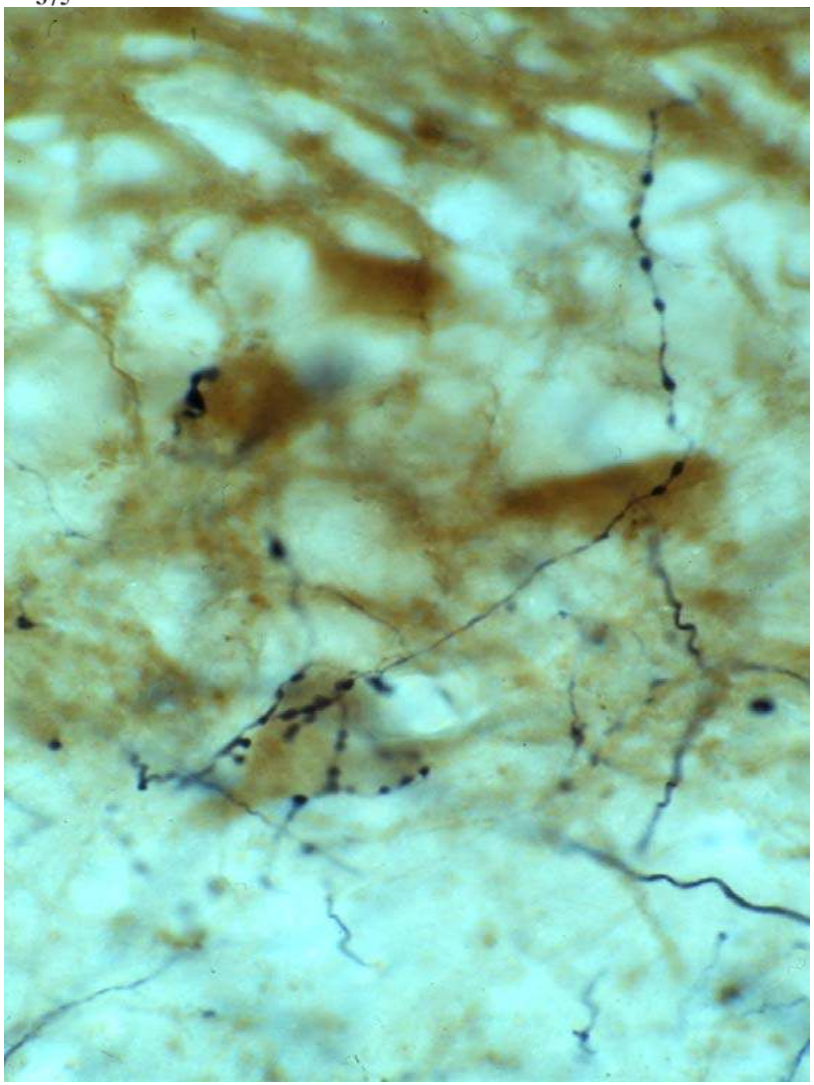




Two types of septohippocampal axons terminate in the hippocampus. They can be easily distinguished according to their thickness.

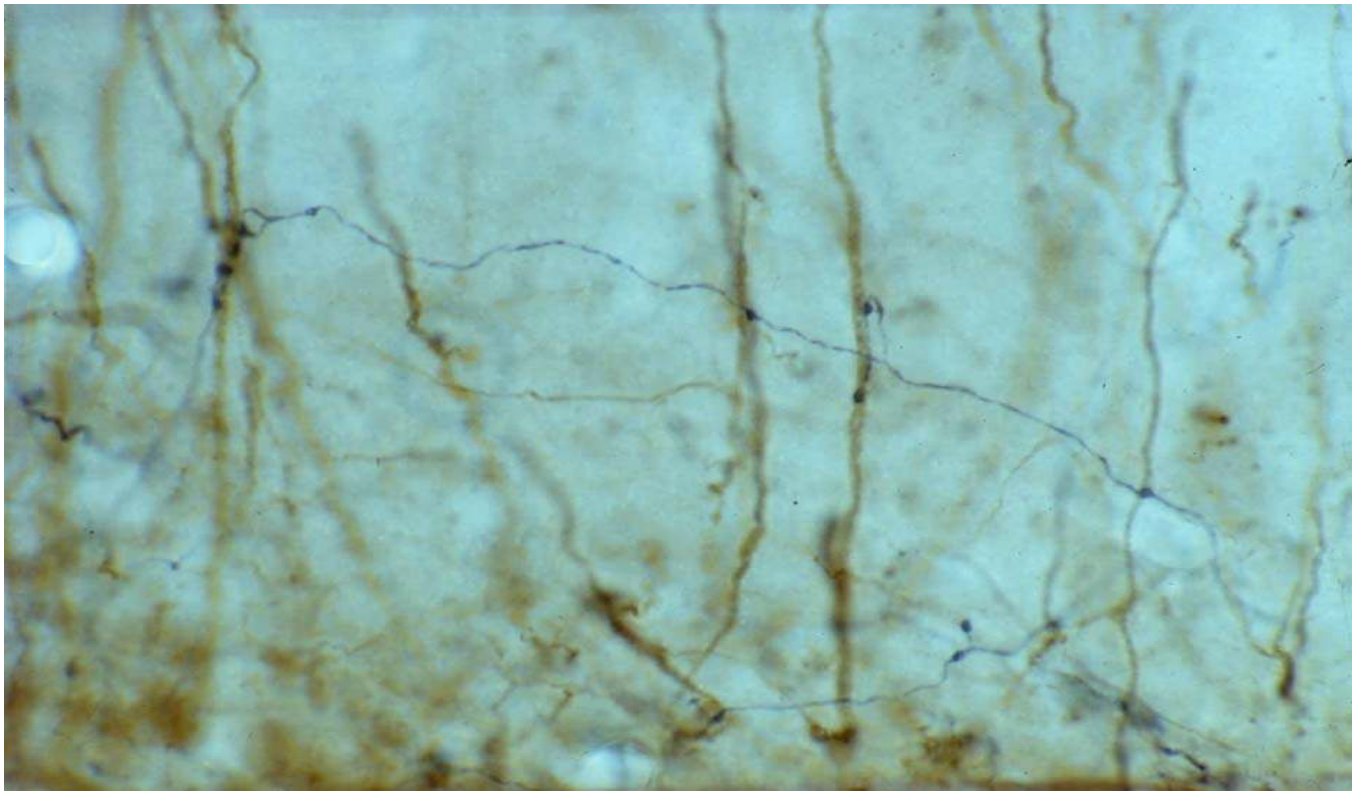
The thick septohippocampal fibers are GABAergic, which innervate the GABAergic interneurons of the hippocampus selectively.



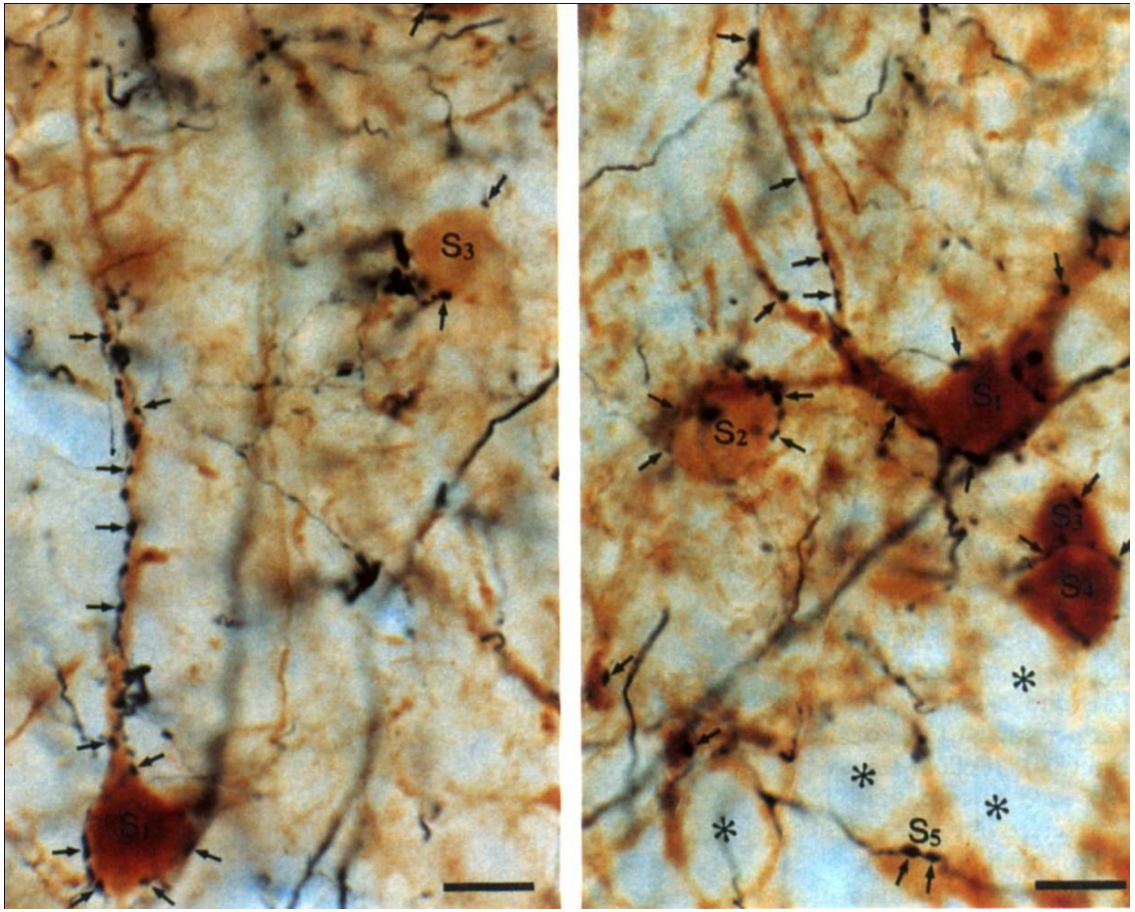


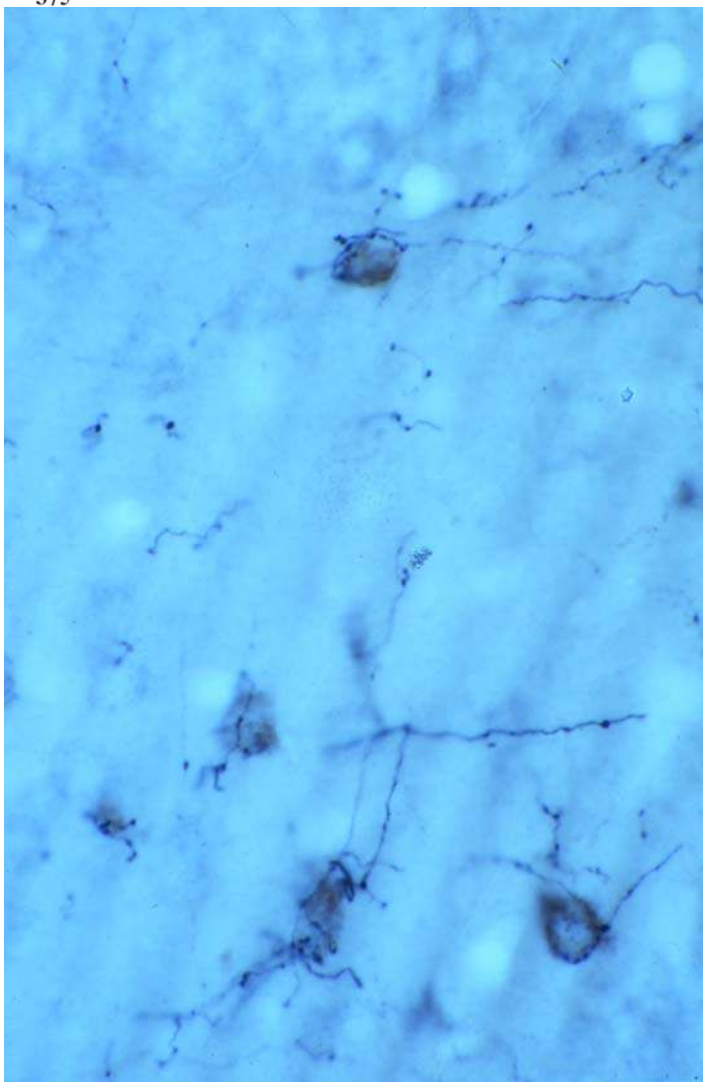
The calbindin-containing dendritic inhibitory cells (marked by brown reaction product) are selectively innervated by GABAergic septal fibers (black) .

Dendrites of the parvalbumin-containing basket cells (brown) are also selectively innervated by the septal GABAergic fibers (black).



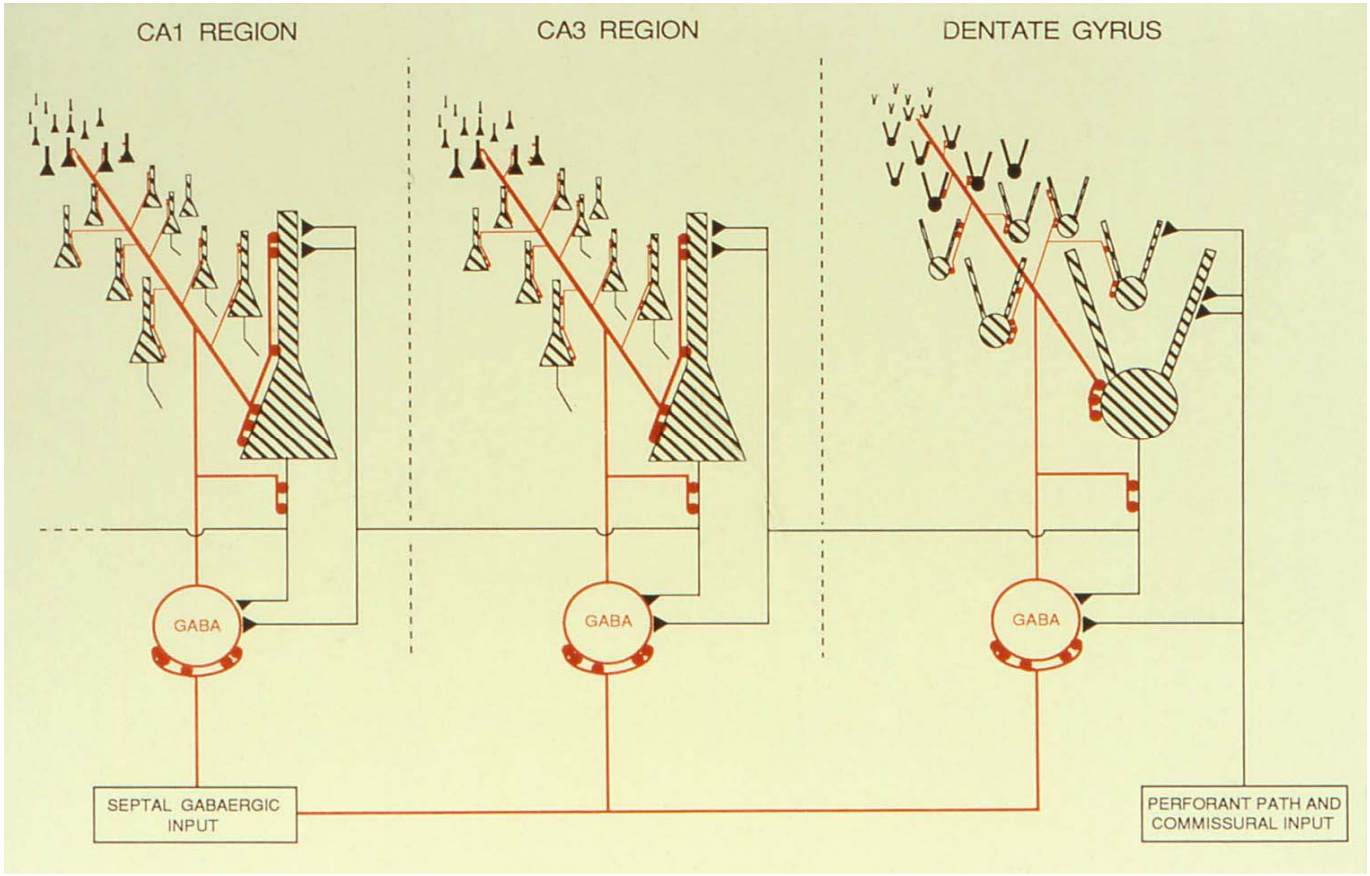
Multiple contacts are formed by septal afferents on PV-positive interneurons in a climbing fiber-like manner in the stratum oriens of the CA3 region.



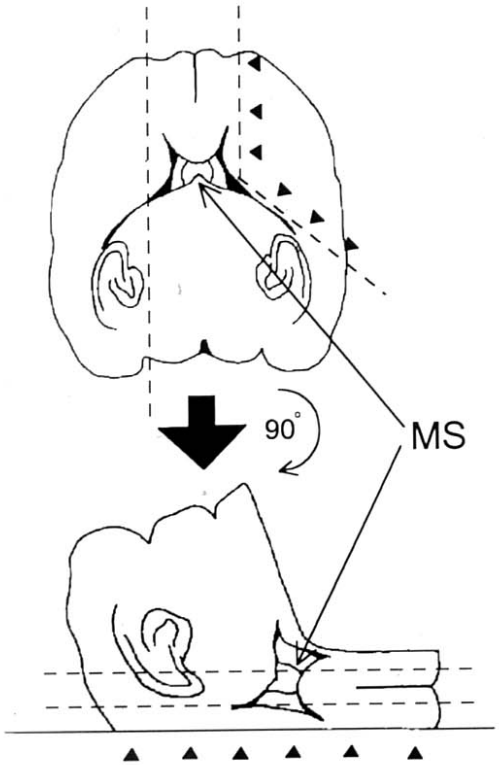


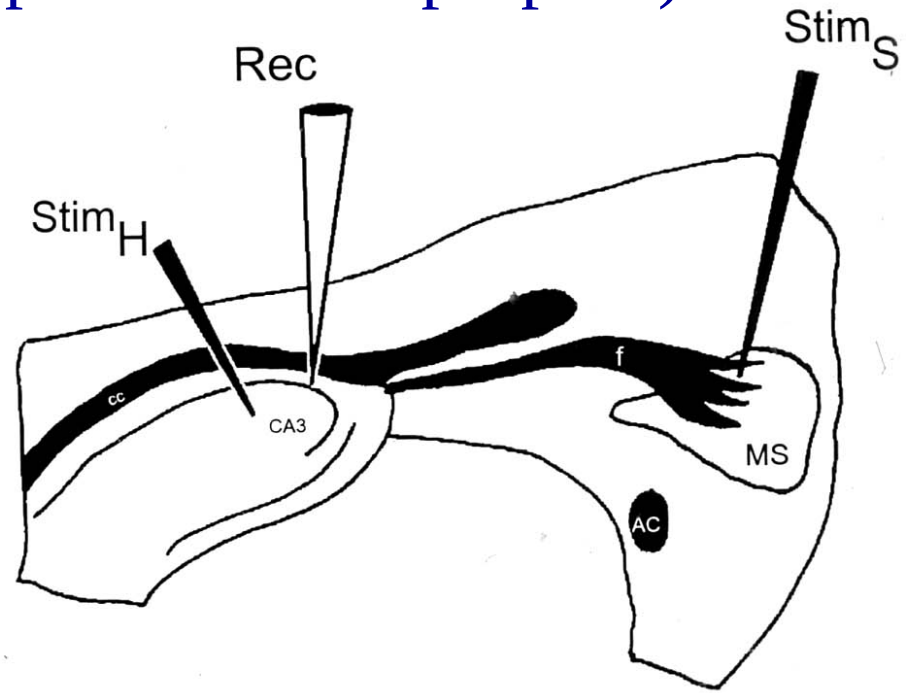
Another class of inhibitory interneurons, the somatostatin-containing dendritic inhibitory cells receive also a rich septal GABAergic innervation.

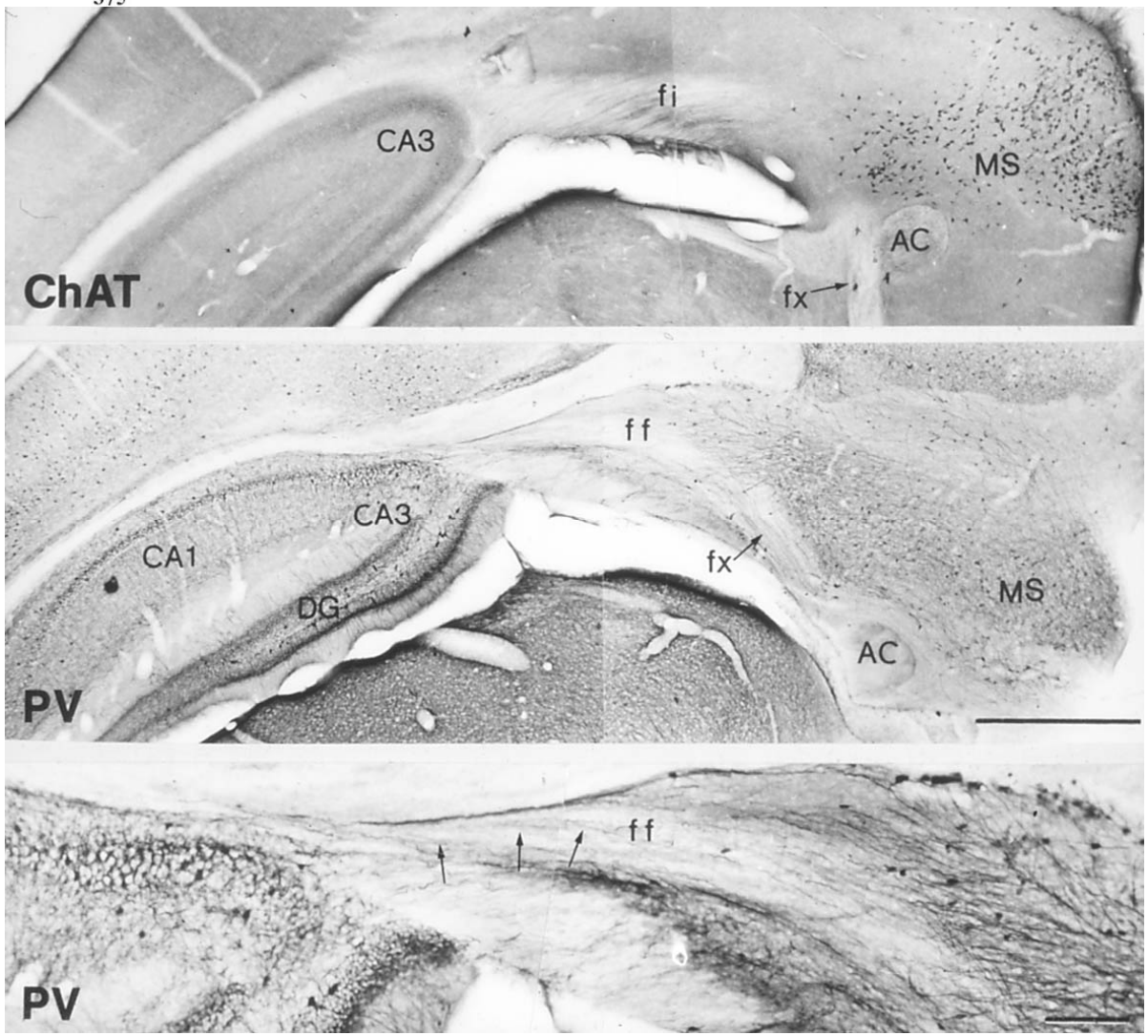
Principal neurons of the hippocampus are synchronised through GABA-GABA disinhibition



The septohippocampal GABA-GABA disinhibition has been demonstrated *in vitro* (a special septo-hippocampal slice was prepared for this purpose)

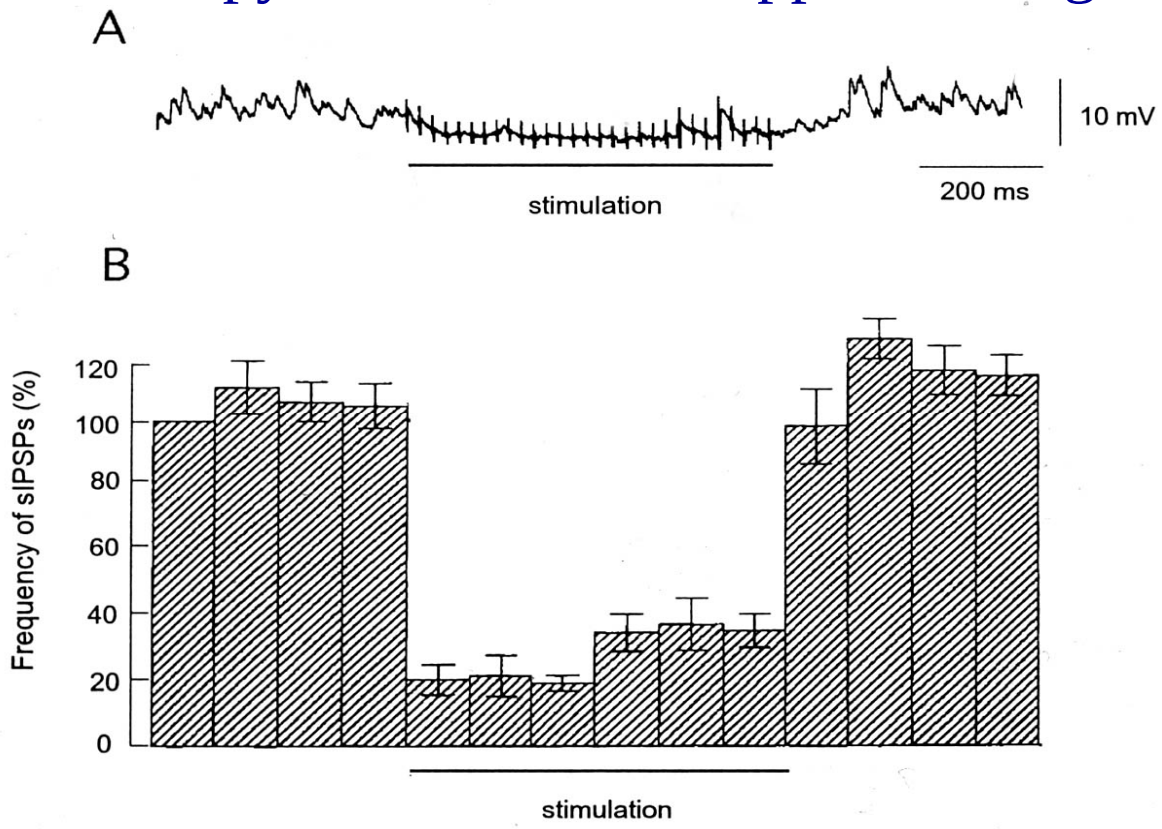




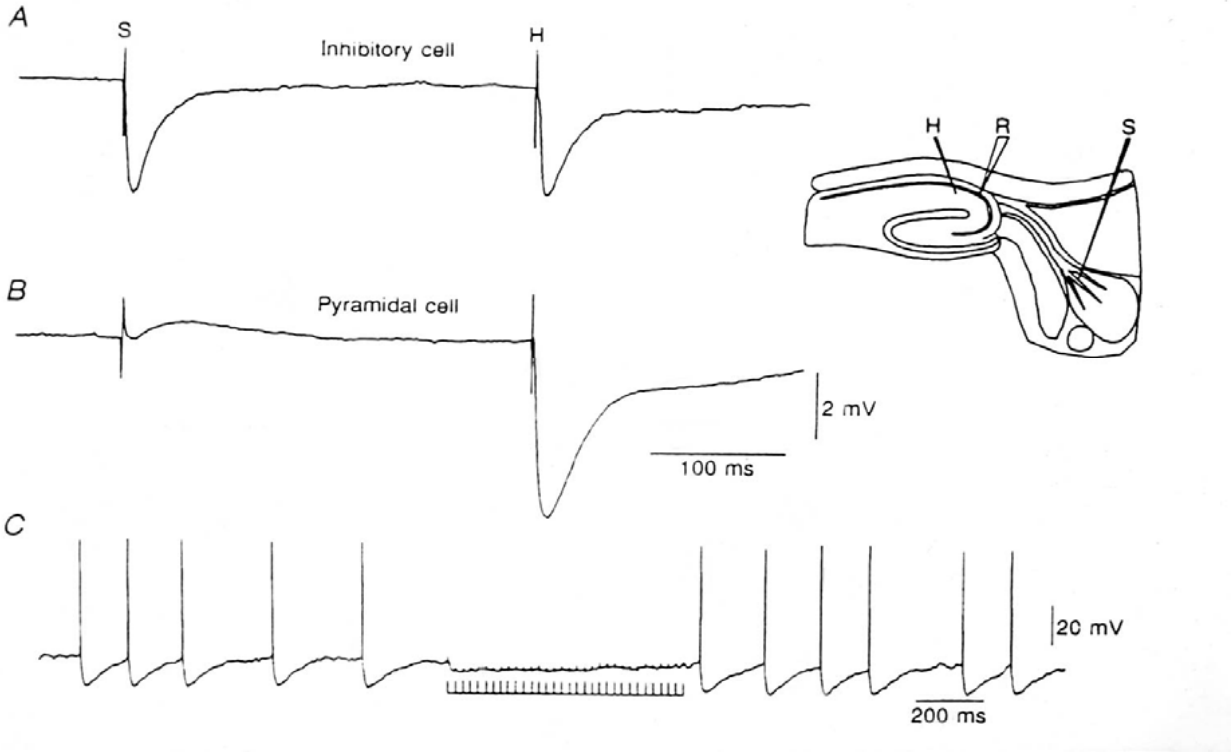


Distribution of cholinergic and GABAergic perikarya and fibers in the septo-hippocampal slices prepared for electrophysiology.

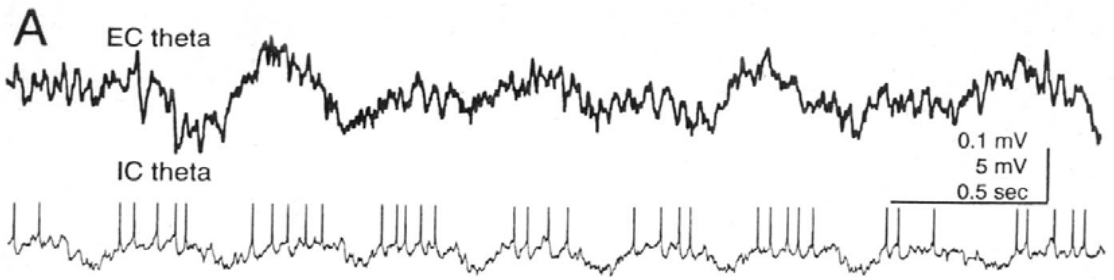
Stimulation of the septum silences the spontaneous activity of the inhibitory cells in the hippocampus. The spontaneous IPSPs recorded from the pyramidal cells disappear during the stimulation.

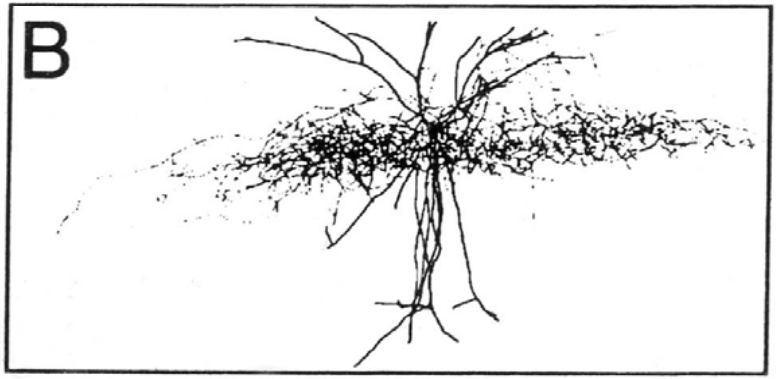


Stimulation of the septum induces (A) monosynaptic IPSPs in the hippocampal interneurons, and (B) slight depolarization of the pyramidal cells, which is a result of the disappearance of the spontaneous IPSPs. The firing interneuron is silenced by the stimulation of the septum (C).

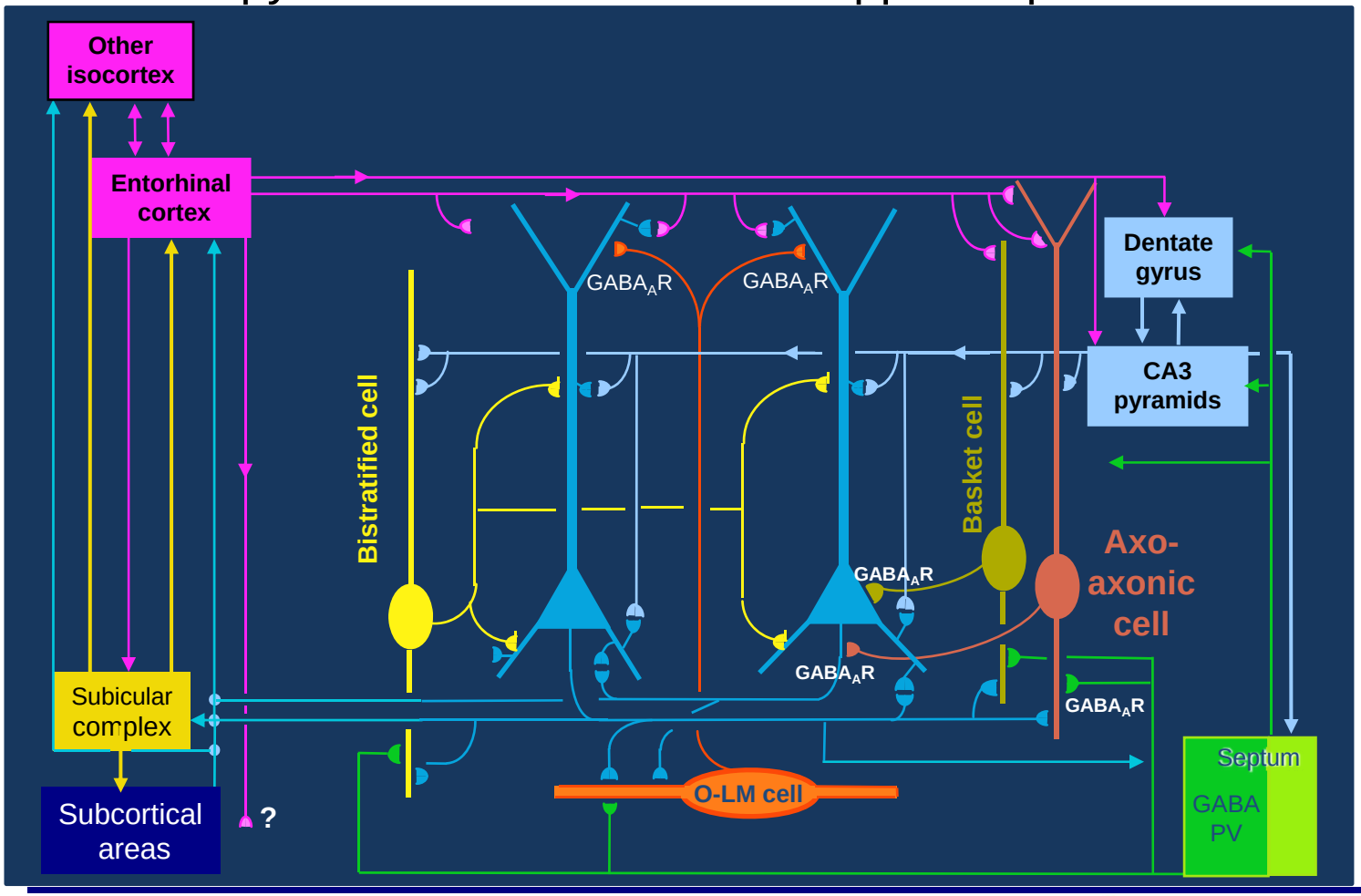


During theta activity basket cells produce trains composed of 4 to 5 action potentials. Each of the action potential „packets” are in overlap with the „hyperpolarization” phase of the EEG theta.



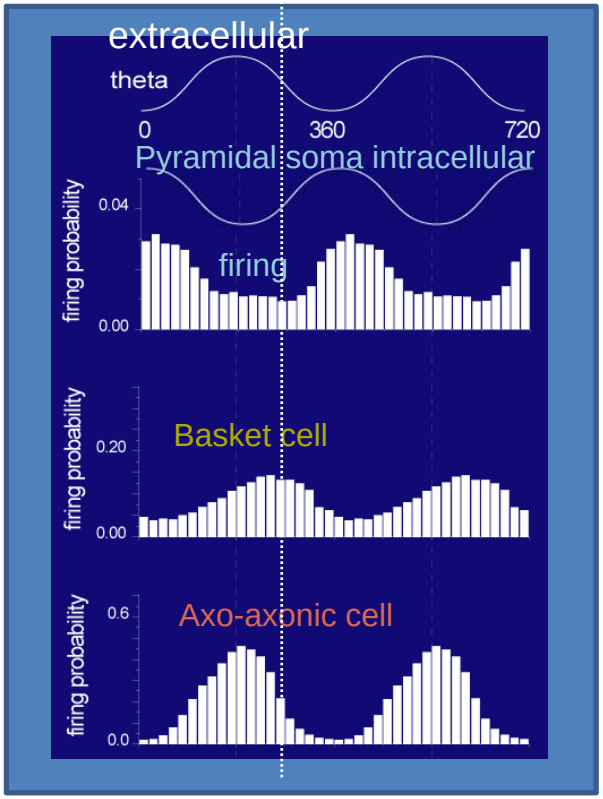


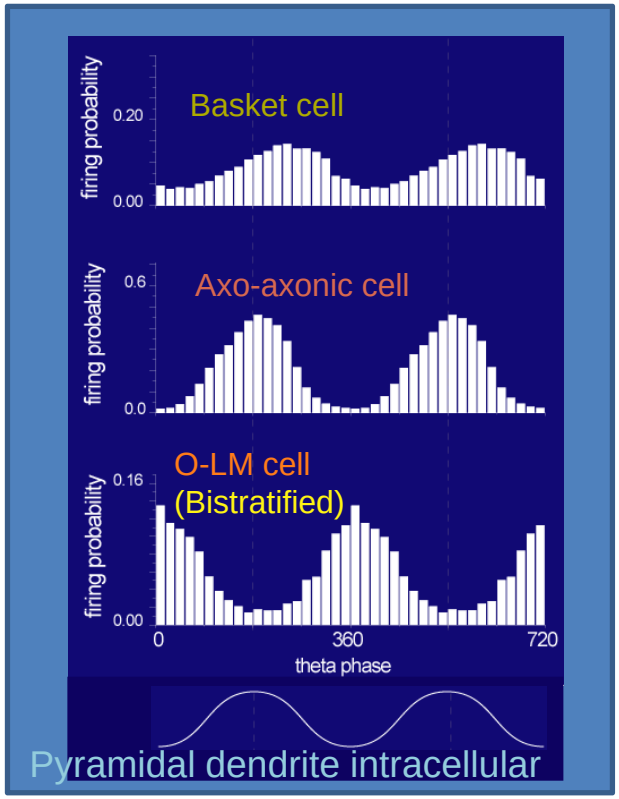
Synaptic and temporal organisation of GABAergic interneurons and pyramidal cells in the CA1 hippocampal area of the rat



Somogyi and Klausberger, J. Physiol. 2005. 562. 9-26.

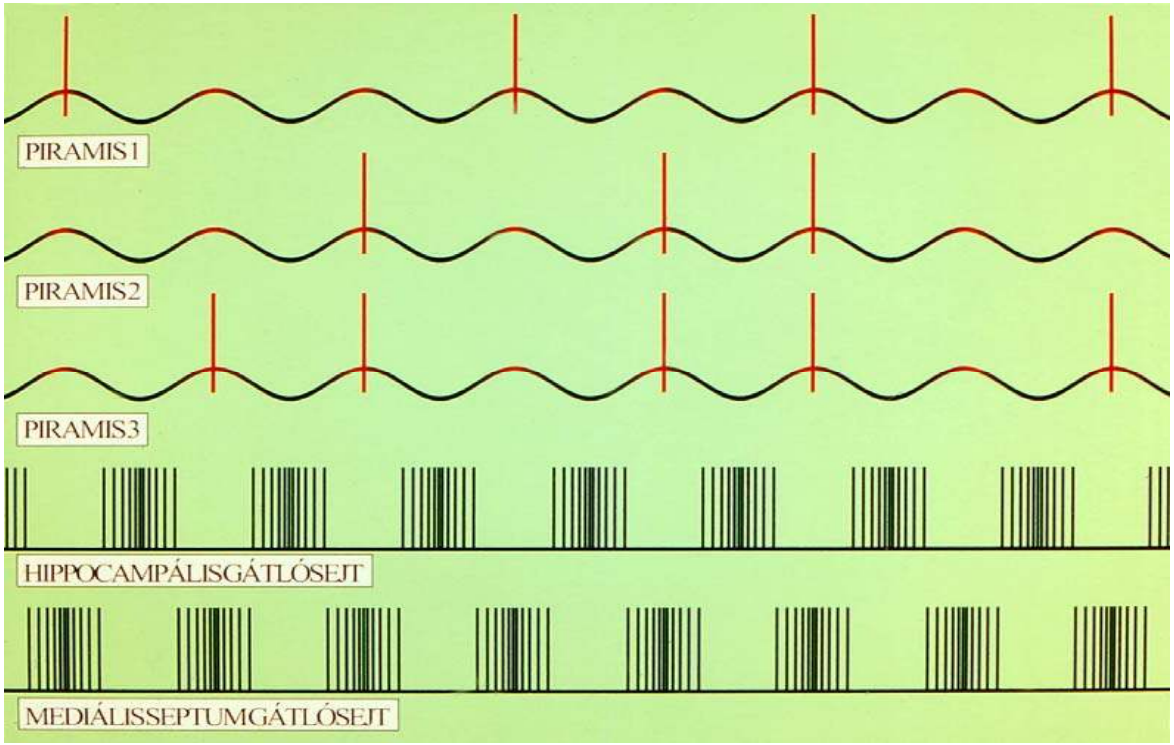
Theta oscillations in somata and dendrites of hippocampal pyramidal cells in vivo: activity-dependent phase-precession of action potentials





Kamondi A. and Buzsáki G. Hippocampus 1998;8(3):244-61

Membrane potential (excitability) of the hippocampal pyramidal cells oscillates at a synchronous manner, as they receive a rhythmic inhibition from the local interneurons. Activity of the local interneurons, in turn is rendered periodic by the septal GABAergic neurons.

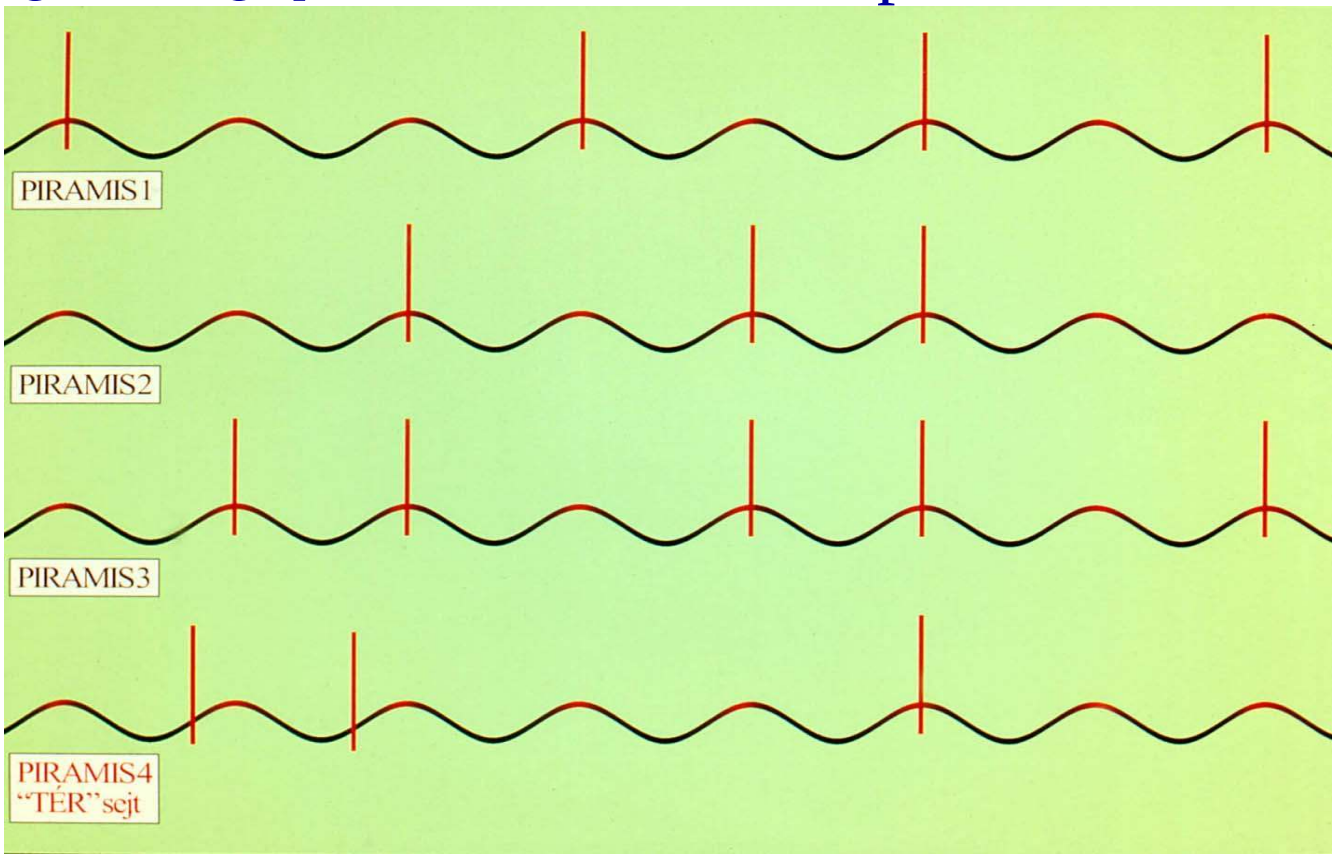


So, what is the theta oscillation for?

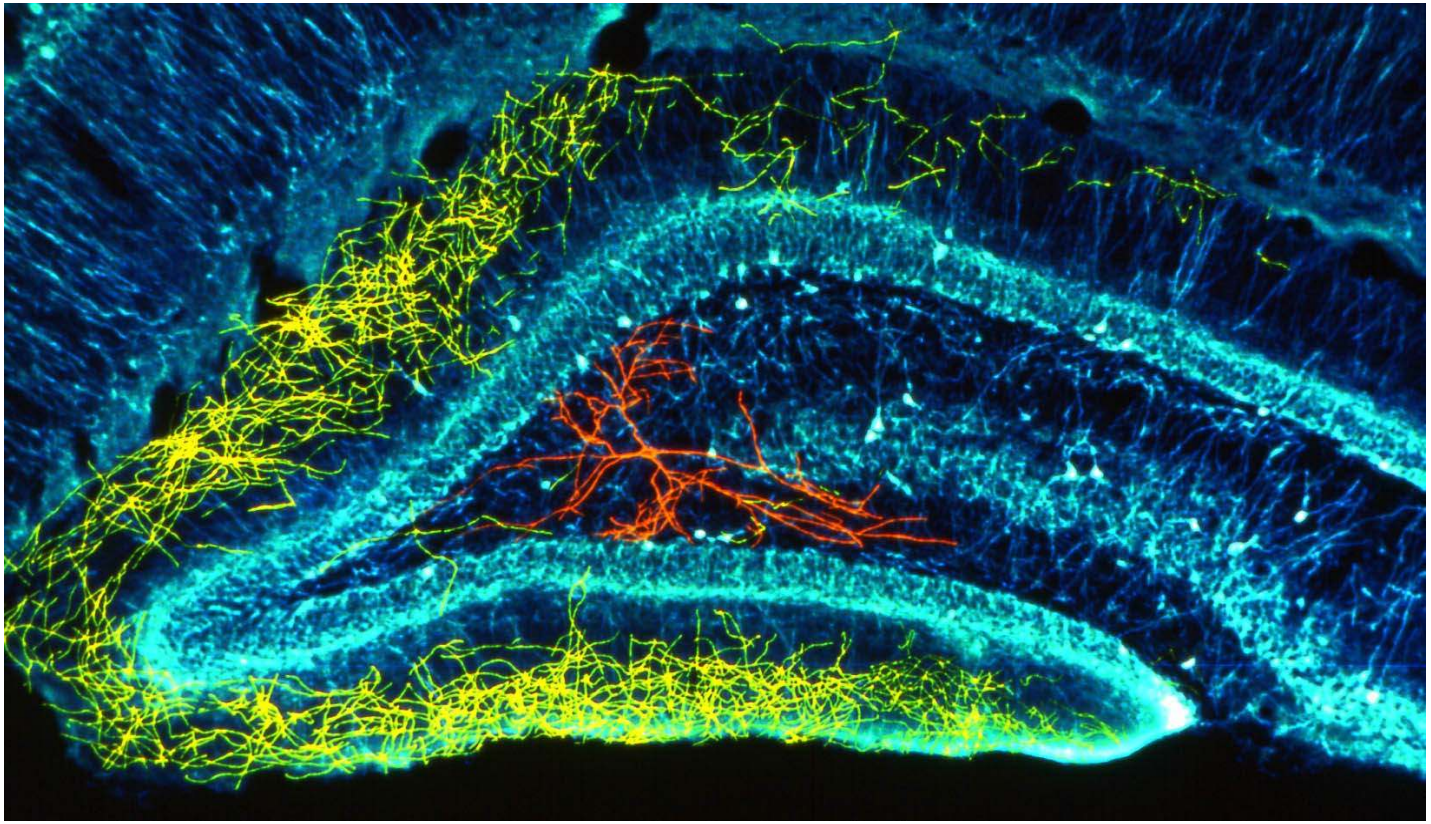
The function of the theta activity is most likely the temporal separation of the signal from the noise. The latter appear primarily at the crest phase, while the former at the trough phase of the theta. The perisomatic inhibition is increased at the trough phase, and can be overcome only by those cells, which receive an extra strong input at that moment.

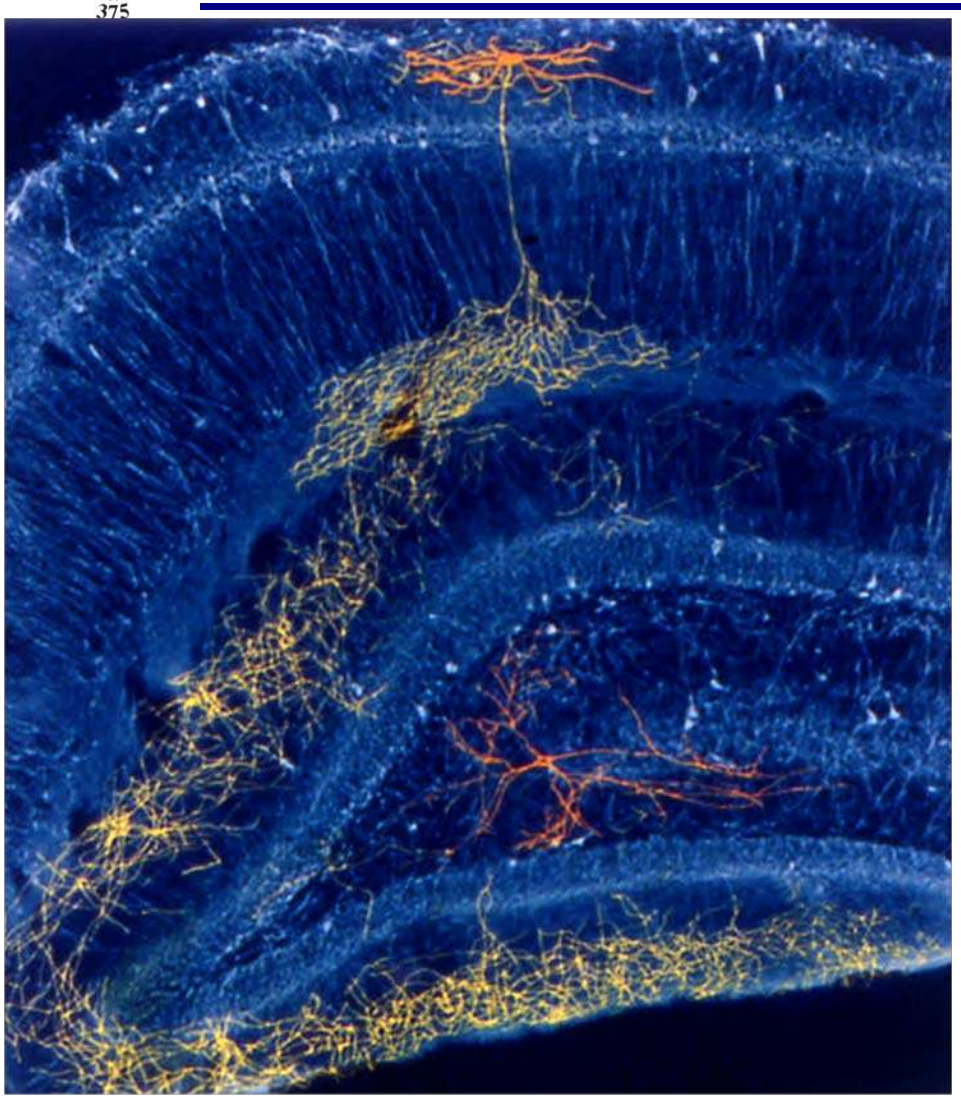
The noise-like background discharge of the pyramidal cells is localised to the crest phase of the theta activity. Those action potentials, which transmit specific signals, are fired during the trough phase!

Phase-precession



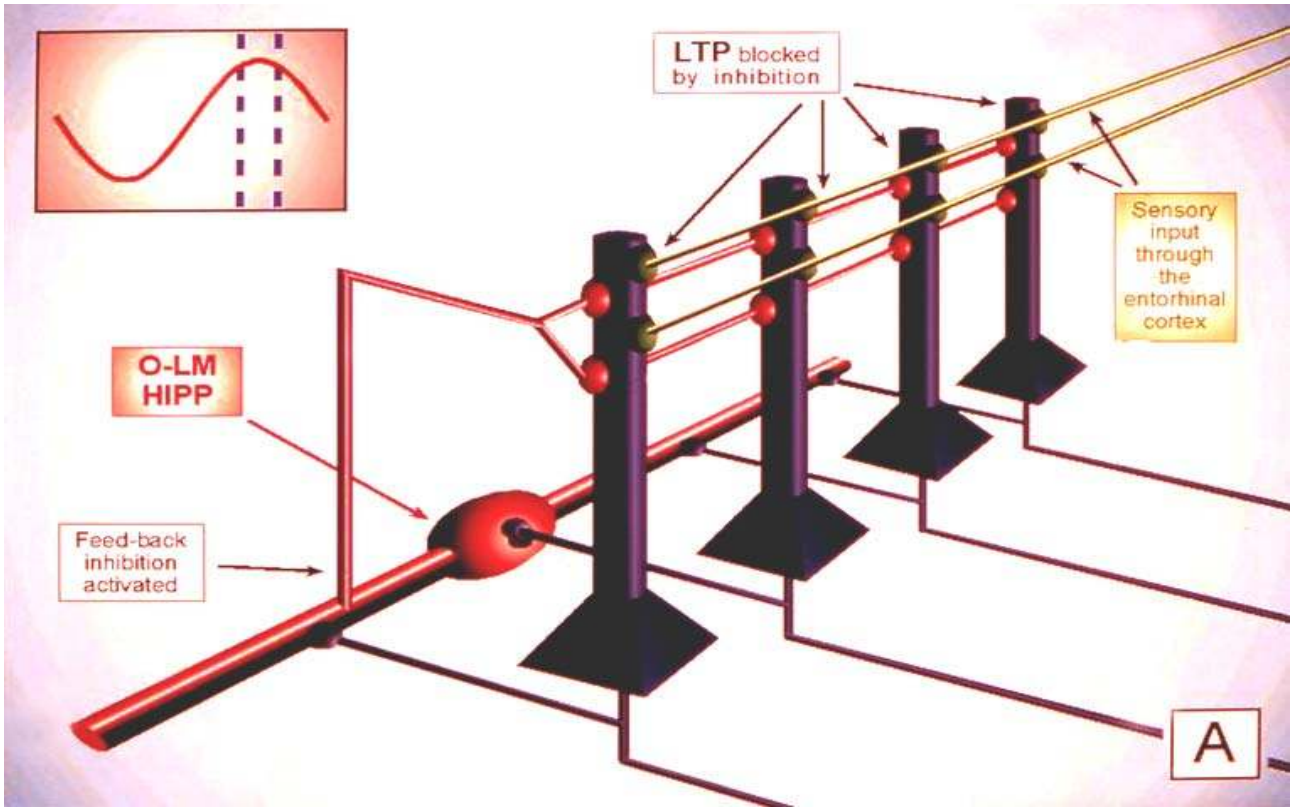
The role of the dendritic feed-back inhibitory cells is to prevent the synaptic potentiation during the noise-phase and to allow the synaptic potentiation during the signal-transmission phase.

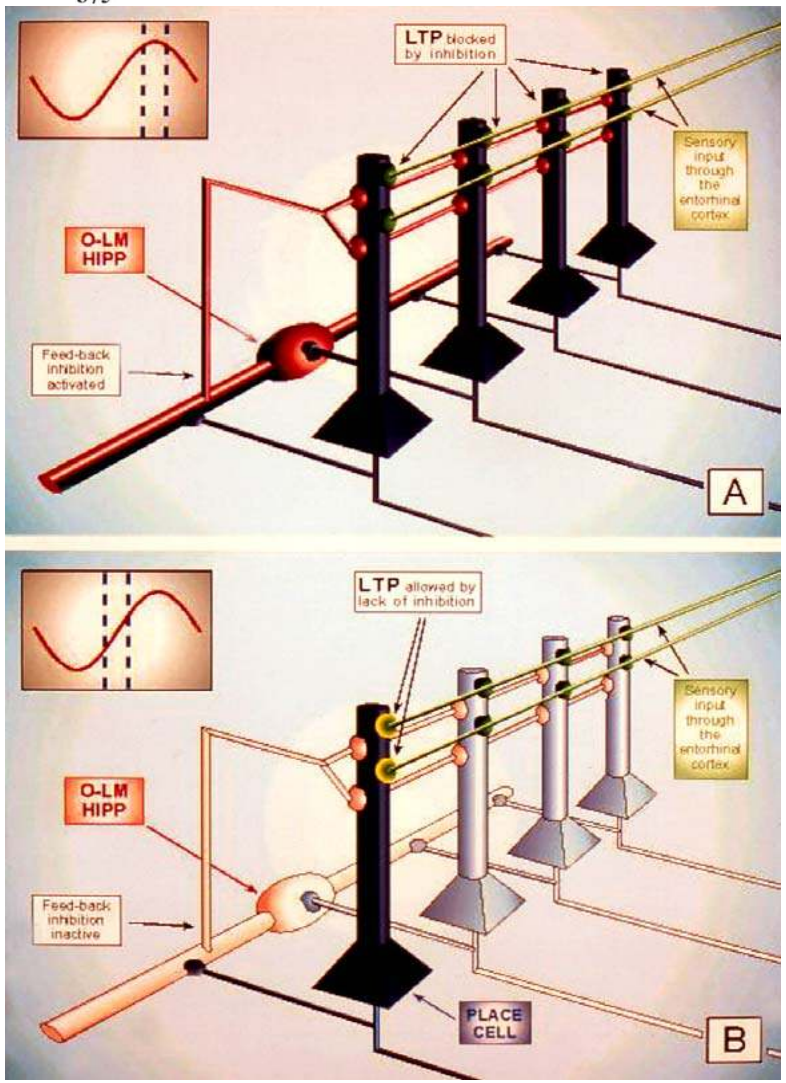




The CA1-3 regions also contain dendritic feed-back inhibitory cells, the axons of which terminate in overlap with the entorhinal pathway. The marker of these neurons is somatostatin.

Feed-back inhibition is activated most likely during the pick of the crest-phase of the theta oscillation, when most pyramidal cells fire. The feed-back inhibition reaches the distal dendritic tree concurrently with the retrograde propagating action potential and is capable to prevent potentiation by the even then arriving excitatory input!





Only cells (e.g. place cells) just mediating specific signals are able to fire during the trough-phase of the theta oscillation.

PHASE-PRECESSION

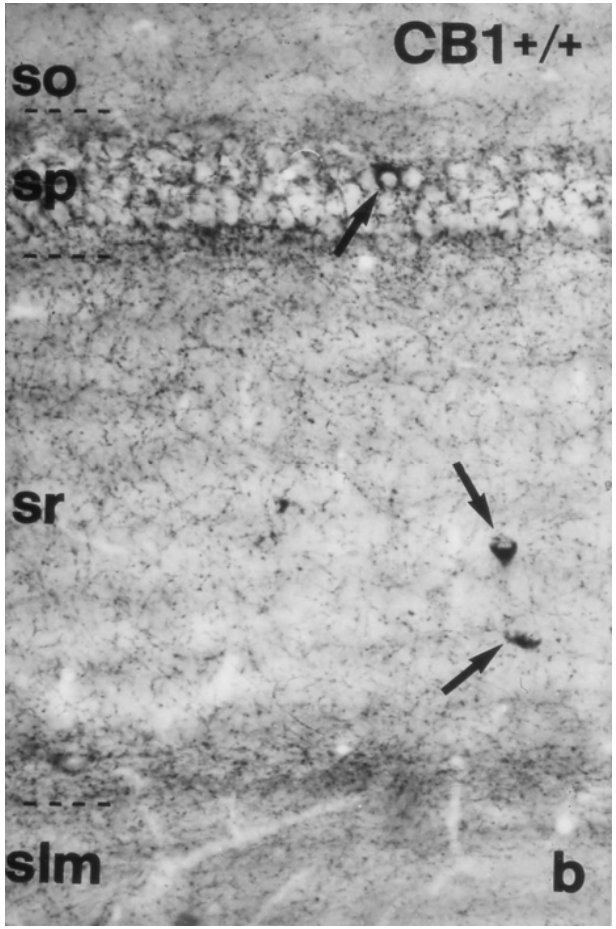
These are, however not sufficient in number to activate the feed-back inhibition. If action potentials of these neurons coincide with the firing of their afferent fibers, the connection will be potentiated. There is no dendritic inhibition, which could prevent it!

A possible mechanism of phase-precession

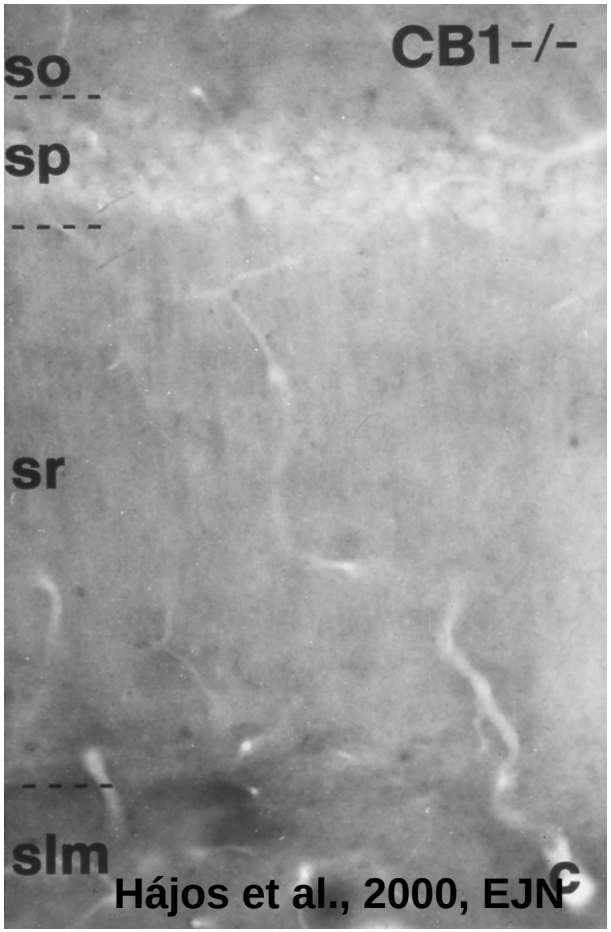
Function of the endocannabinoid signaling in the cerebral cortex

Hippocampal distribution of CB1 receptors

Immuno-reactivity in wild-type animals

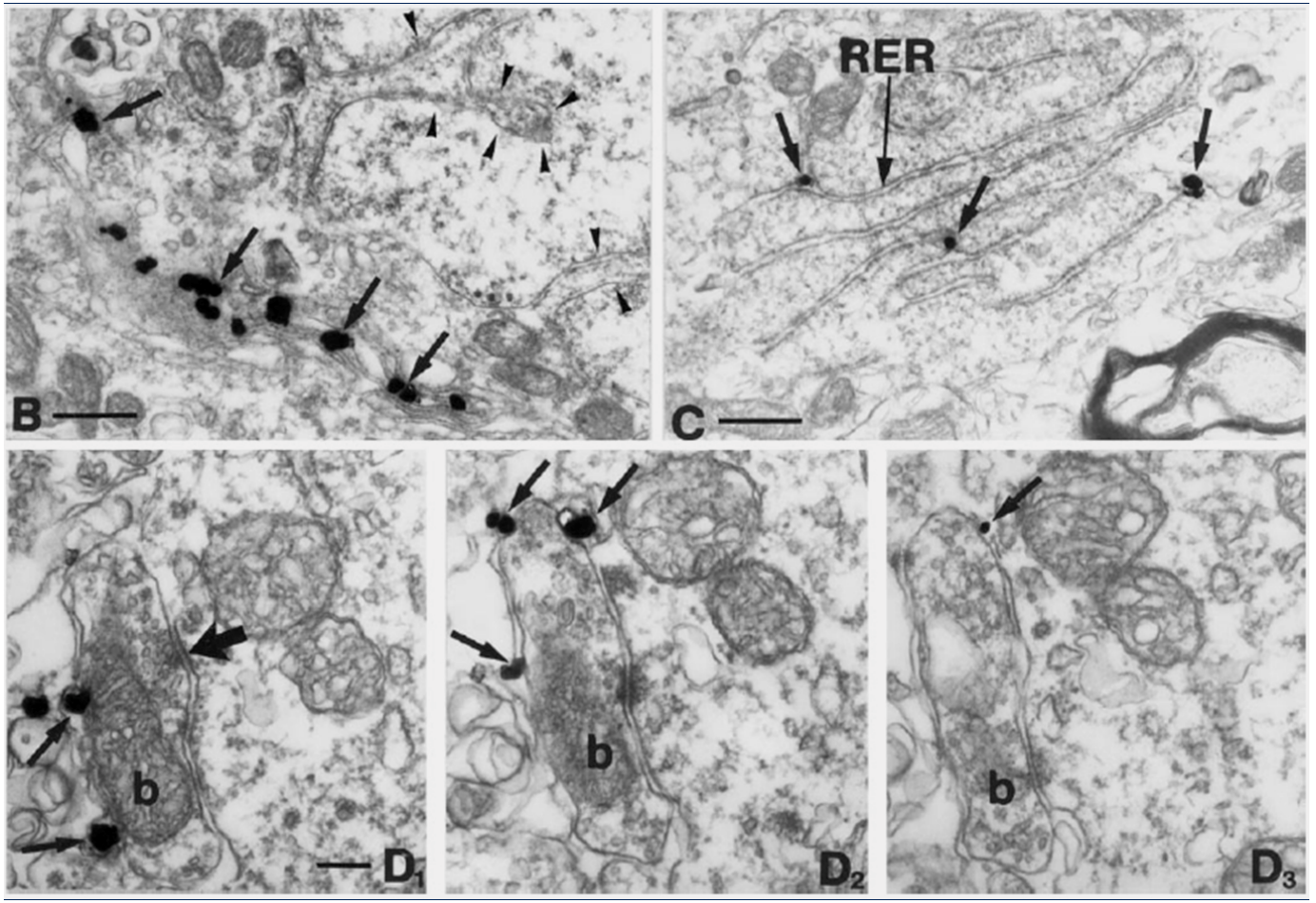


Control immuno-staining in KO animals

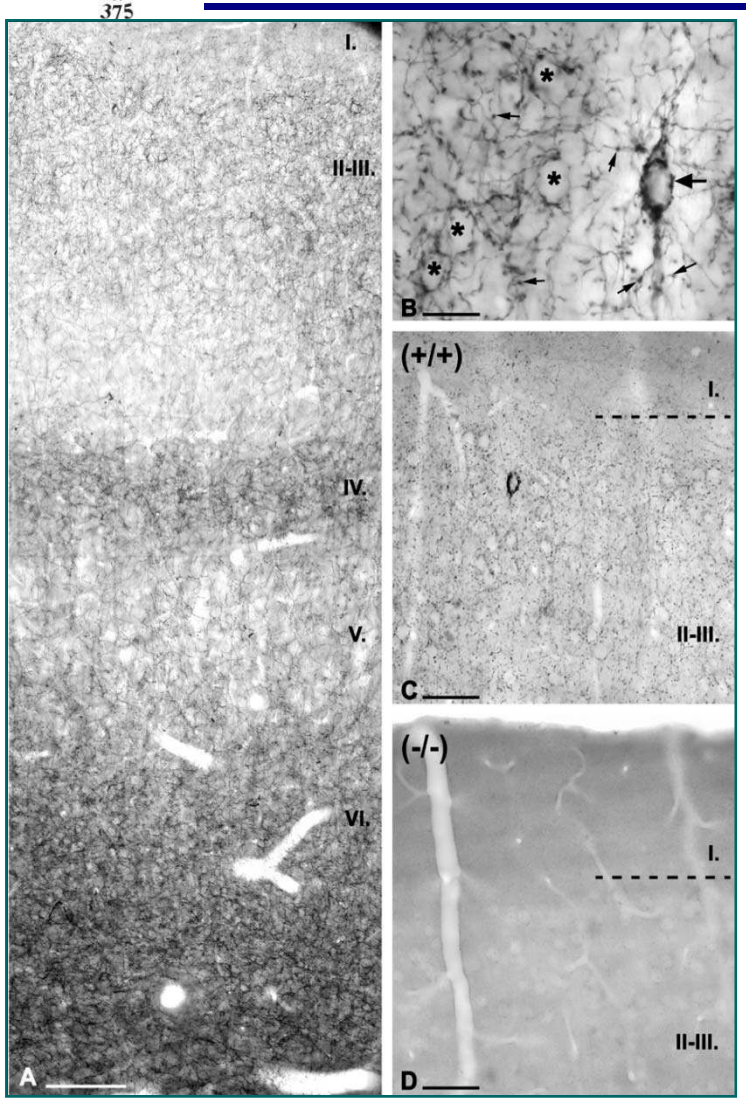


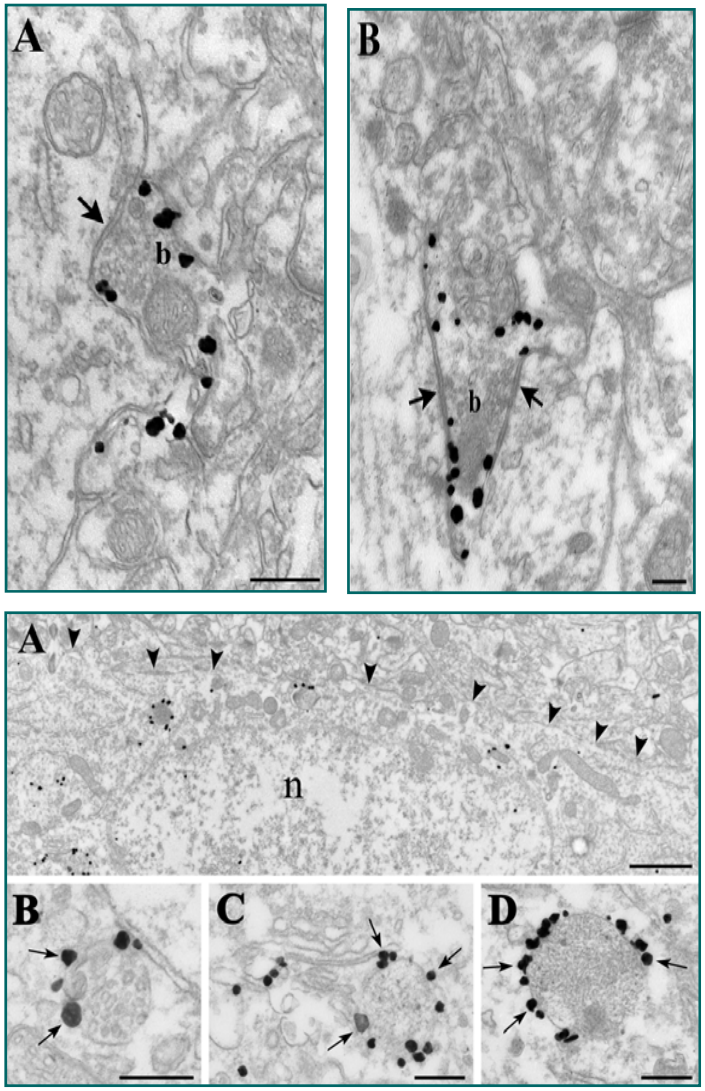
Hájos et al., 2000, EJN

CB1 receptors are located presynaptically on axon terminals

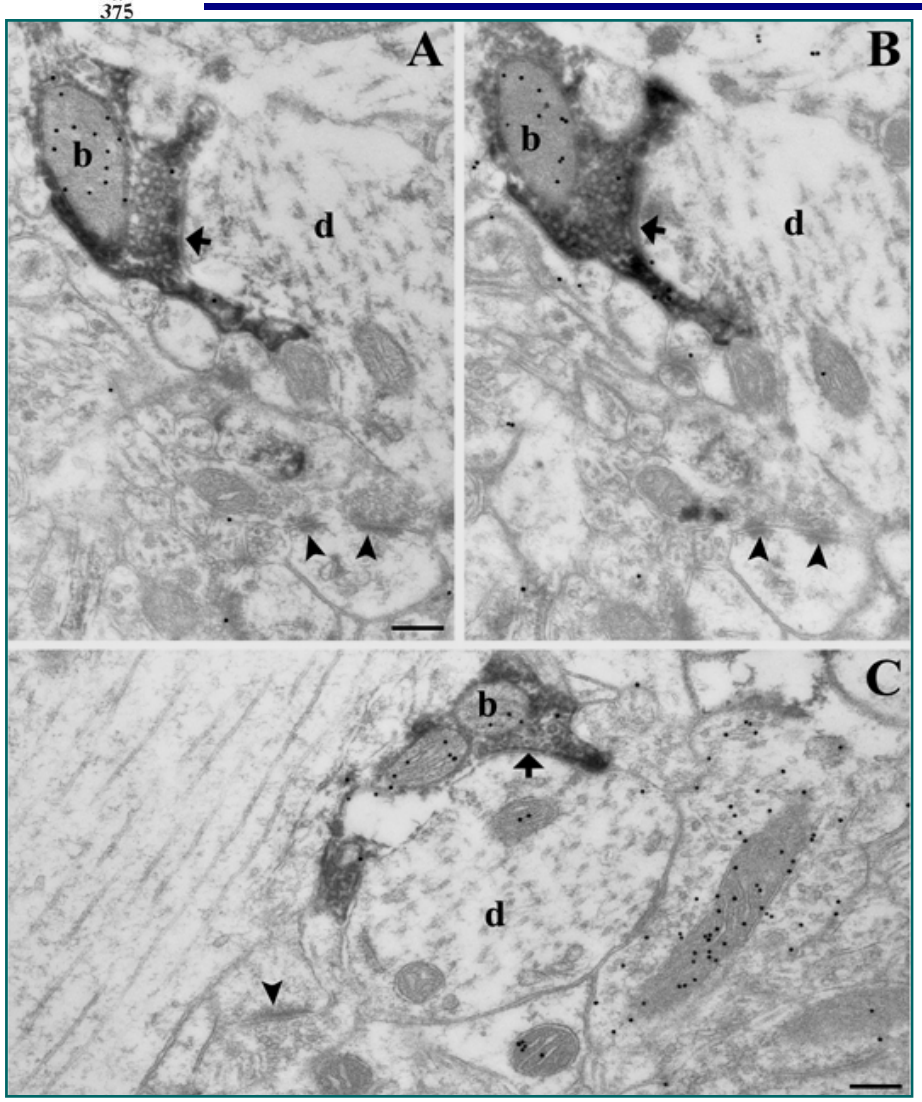


Introduction to functional neurobiology: Hippocampus





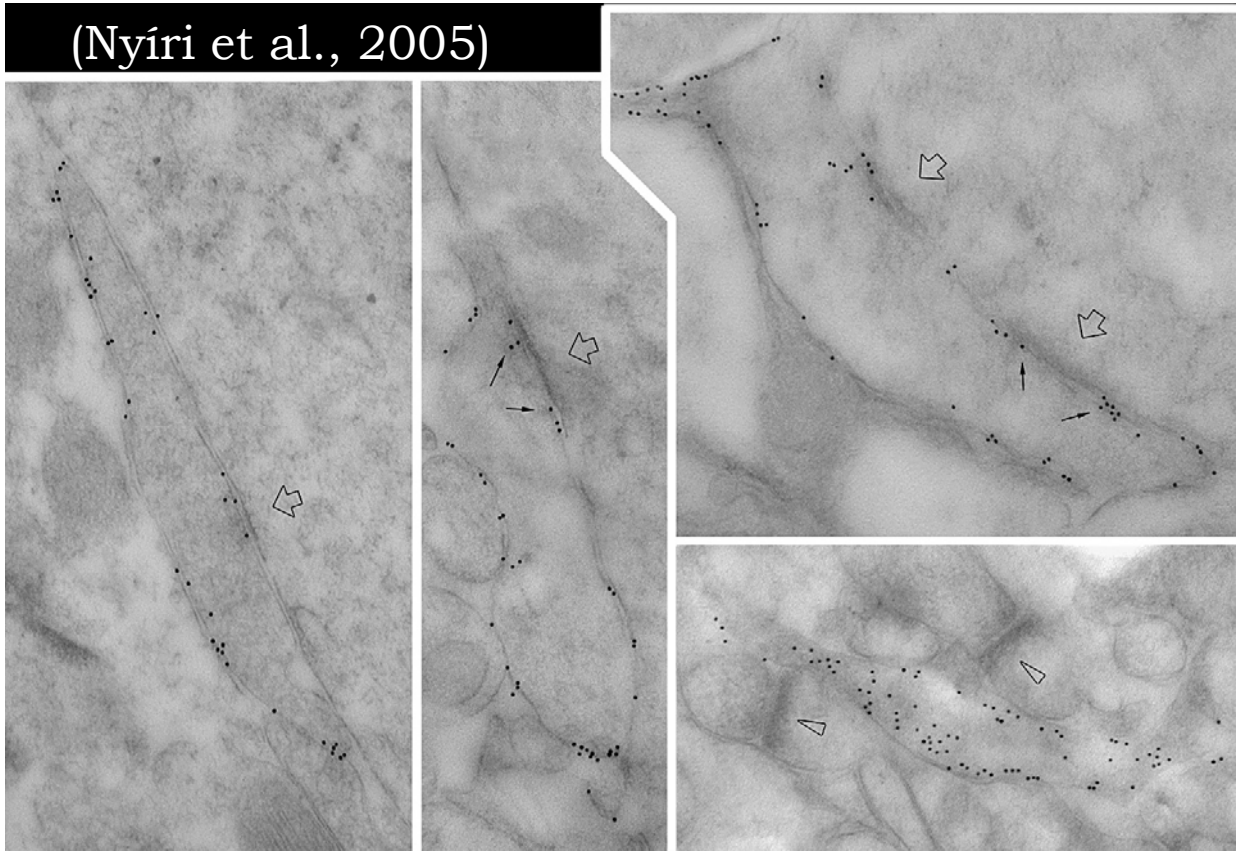
Bodor et al. (2005) J.Neurosci



CB1-positive axon terminals are immuno-reactive for GABA, and form symmet-rical synaptic contacts in the somatosensory cortex.

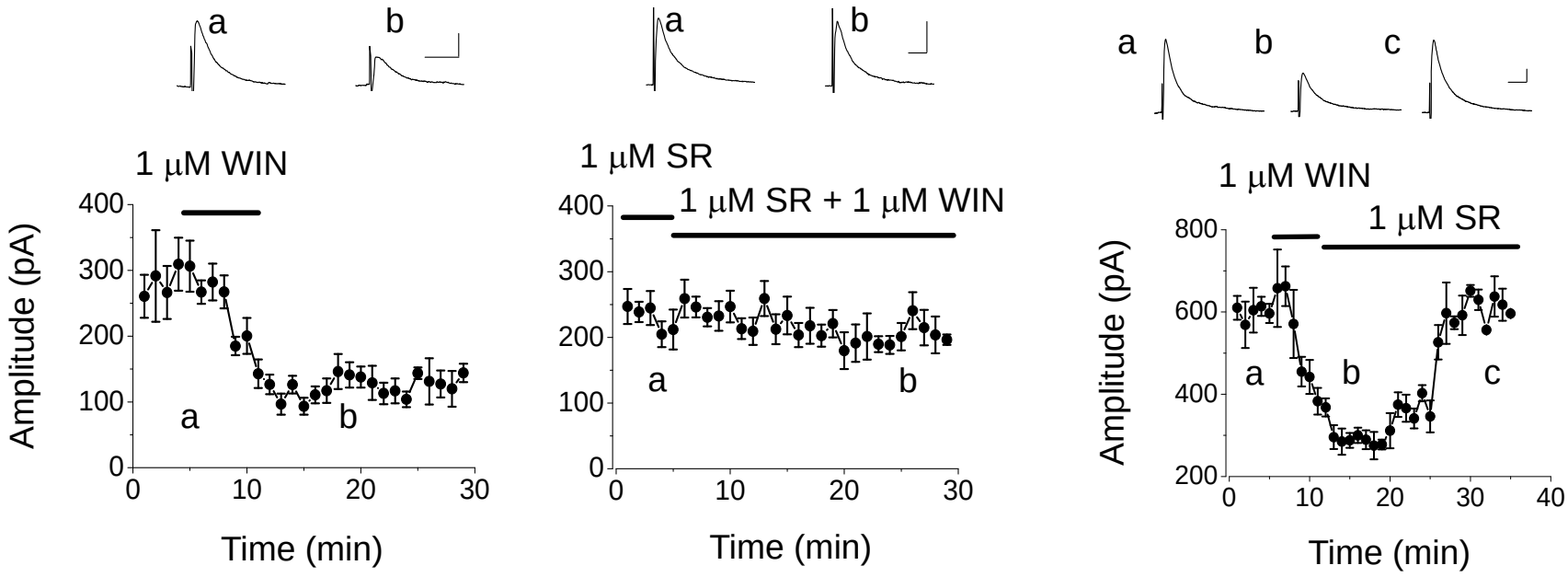
Bodor et al. (2005) J.Neurosci.

Quantitative subcellular localization of CB1 cannabiniod receptors on GABAergic axons in the hippocampus



Postembedding immunogold staining of serial ultrathin sections: av. **481** gold/term.

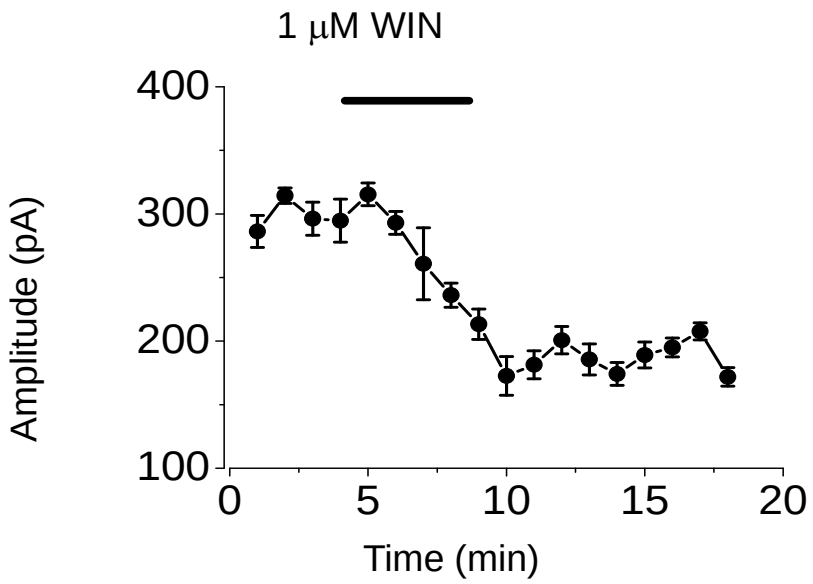
Activation of CB1 cannabinoid receptors inhibits evoked IPSCs in the hippocampus



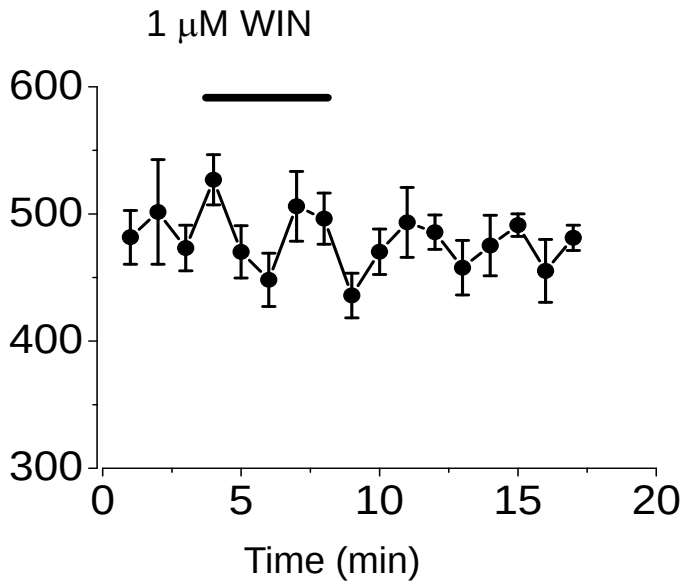
Hájos et al., EJN, 2000

Control:
The specific CB1-agonist is ineffective in CB1-KO animals

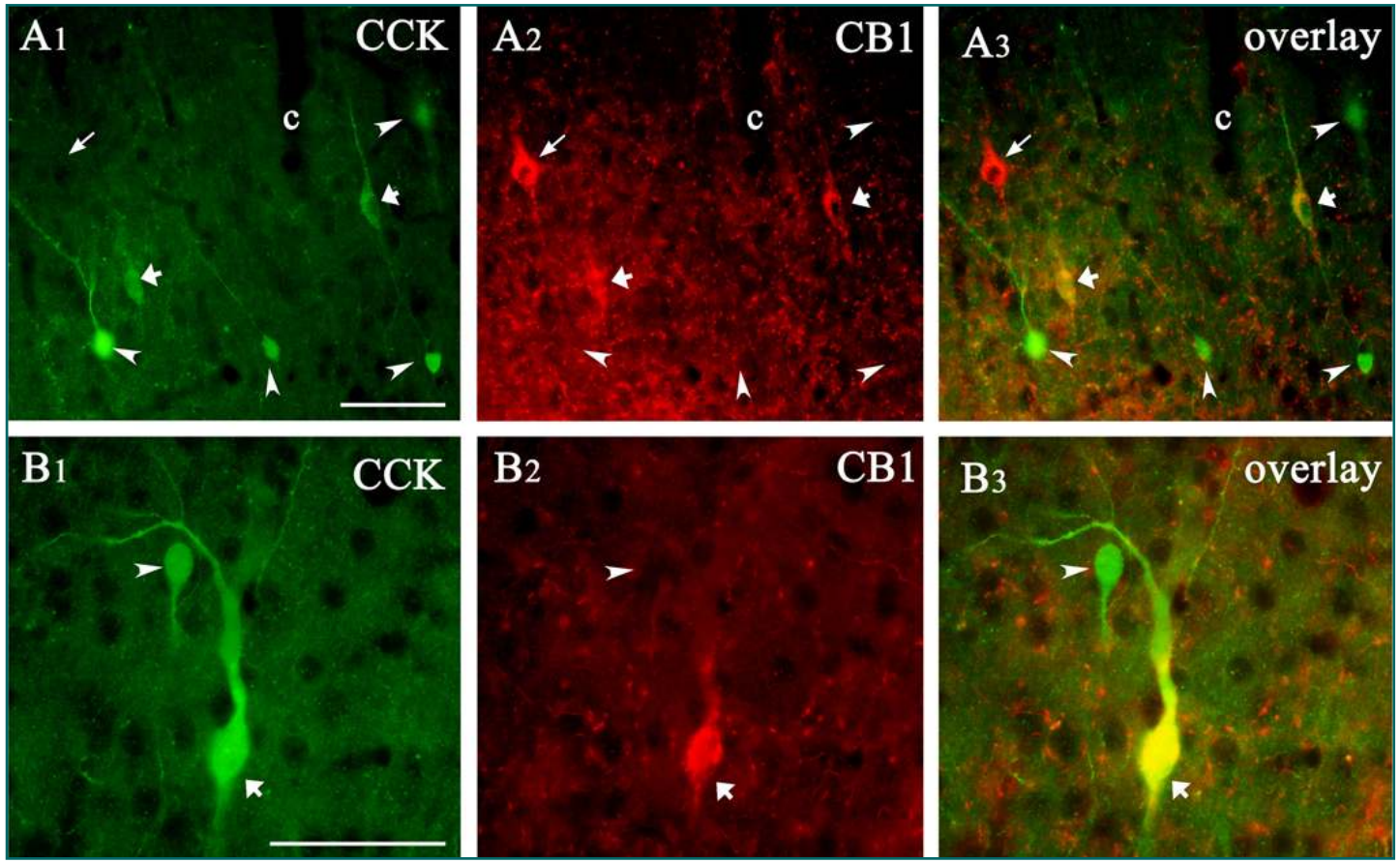
Mouse CB1 +/+



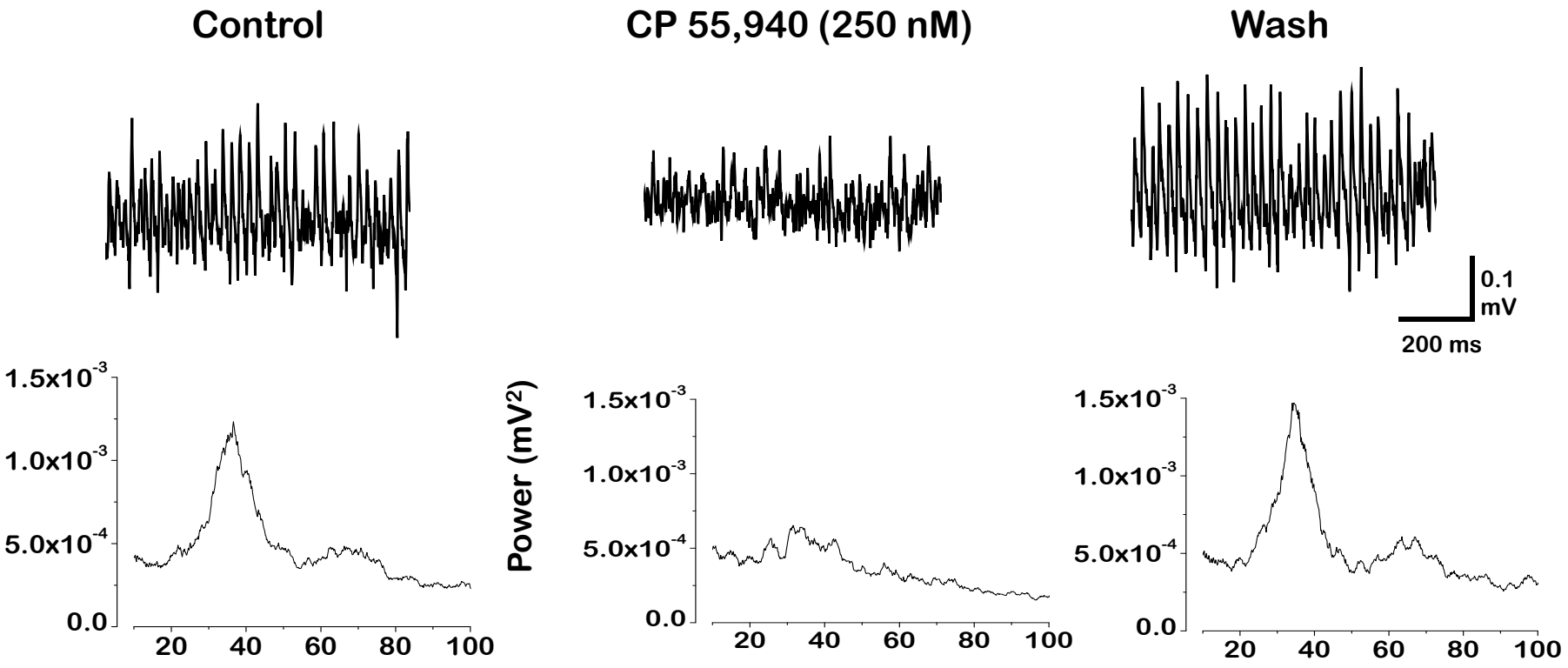
Mouse CB1 -/-



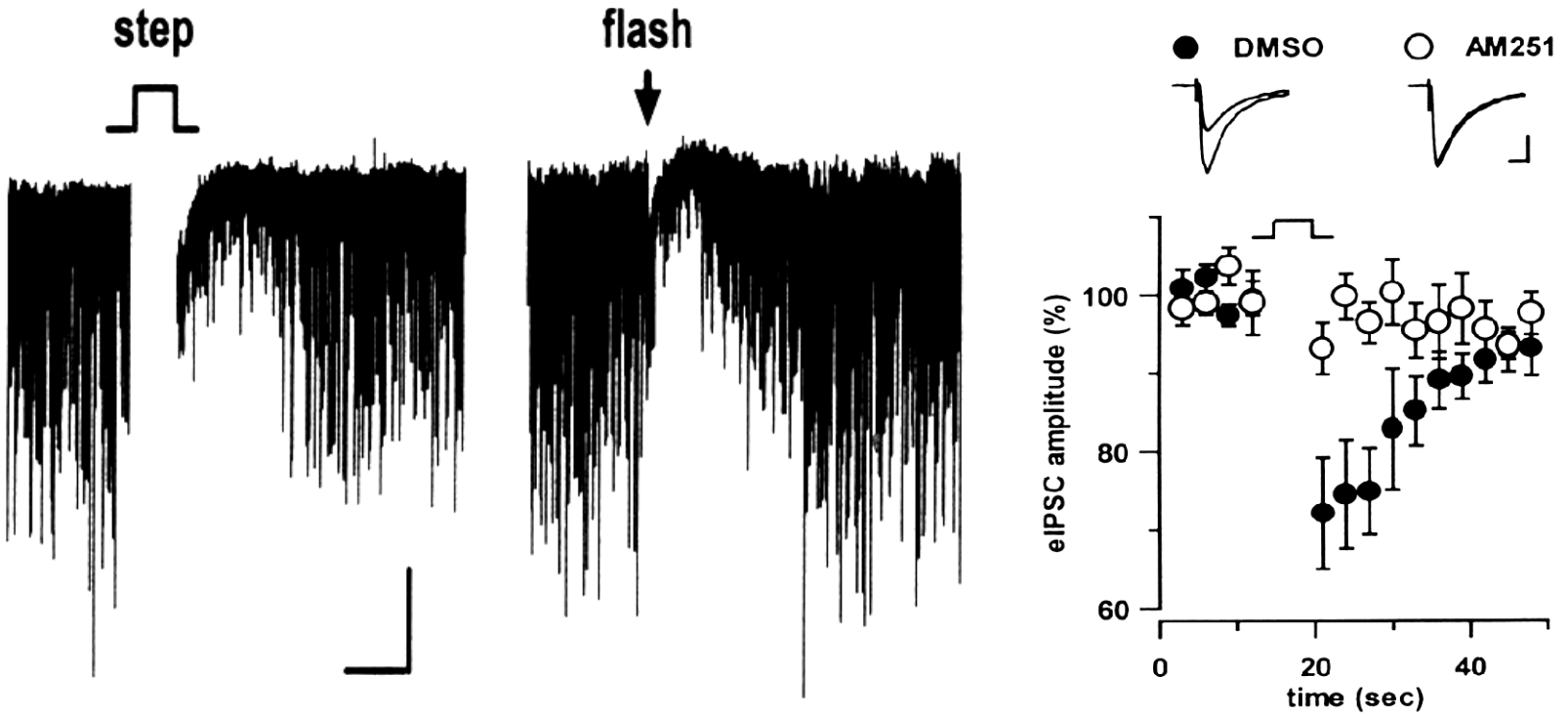
Large CCK-positive interneurons express CB1 receptors in the cortex and the hippocampus



CB1 receptor activation diminishes the power of gamma (40 Hz) oscillations in the hippocampus



Role of endocannabinoids and CB1 receptors in depolarization-induced suppression of inhibition (DSI)



Wilson and Nicoll (2001) Nature

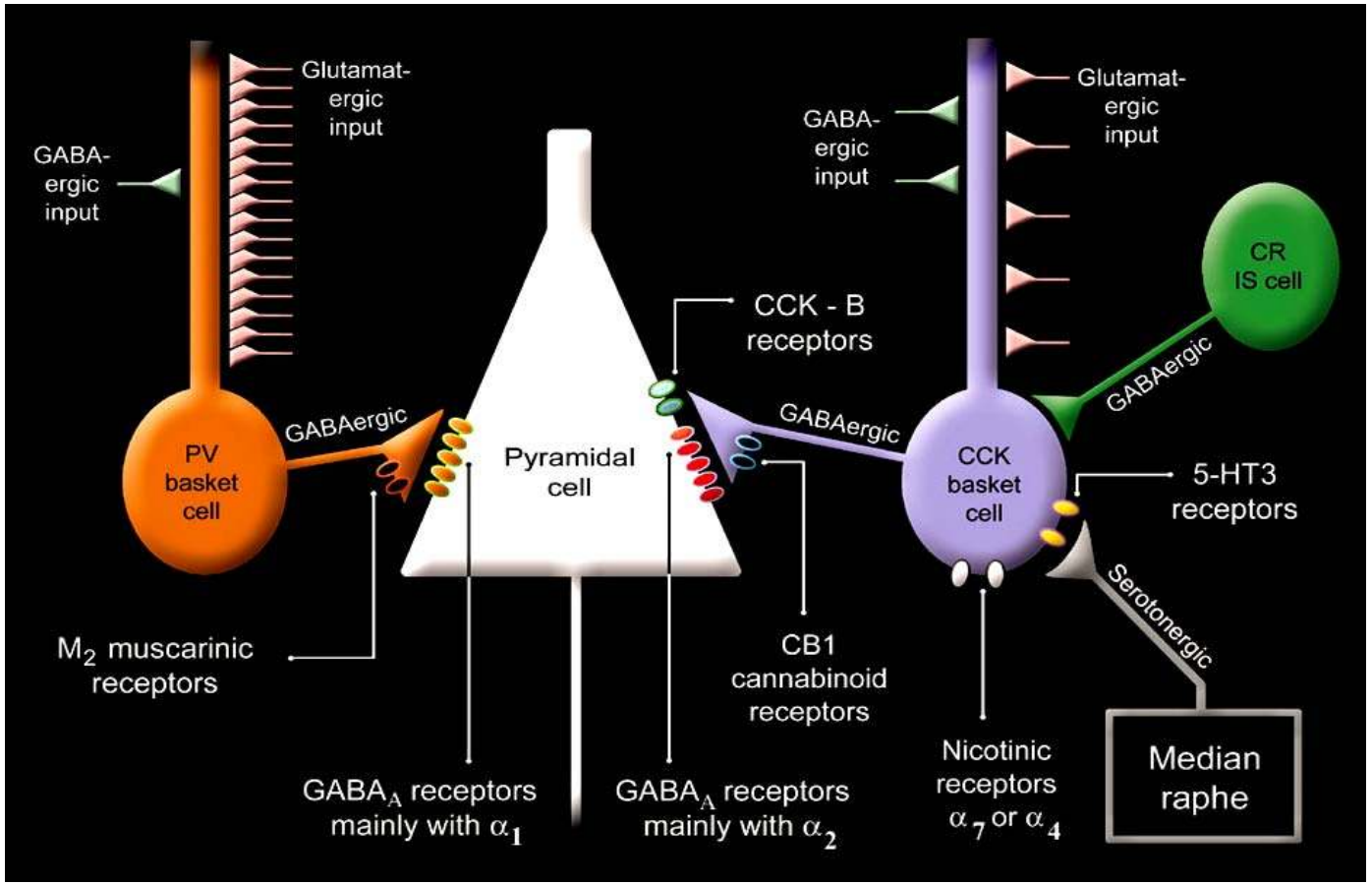
Wilson and Nicoll (2001) Nature

Why are there two different basket cell types (PV- and CCK-containing) to generate oscillations ?

One provides a rigid, non-plastic clock-work (these are the PV cells).

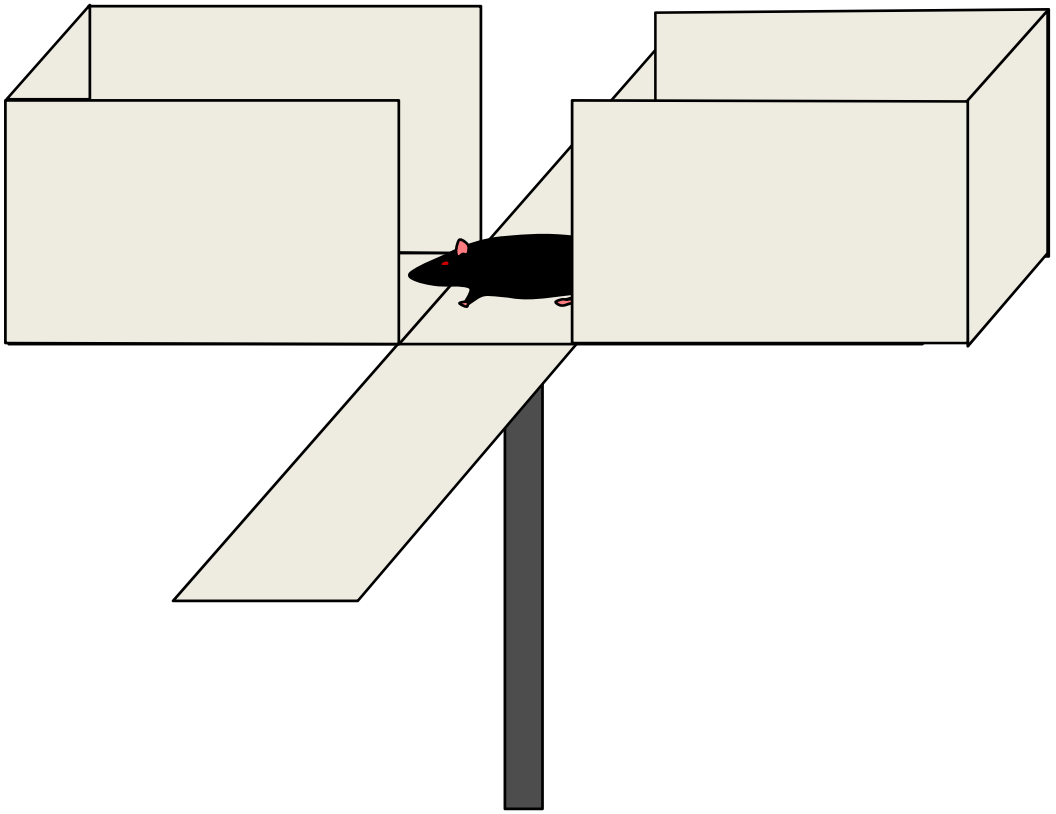
The other's role is fine tuning (CCK), and transmission of subcortical information related to affection and motivation

Introduction to functional neurobiology: Hippocampus

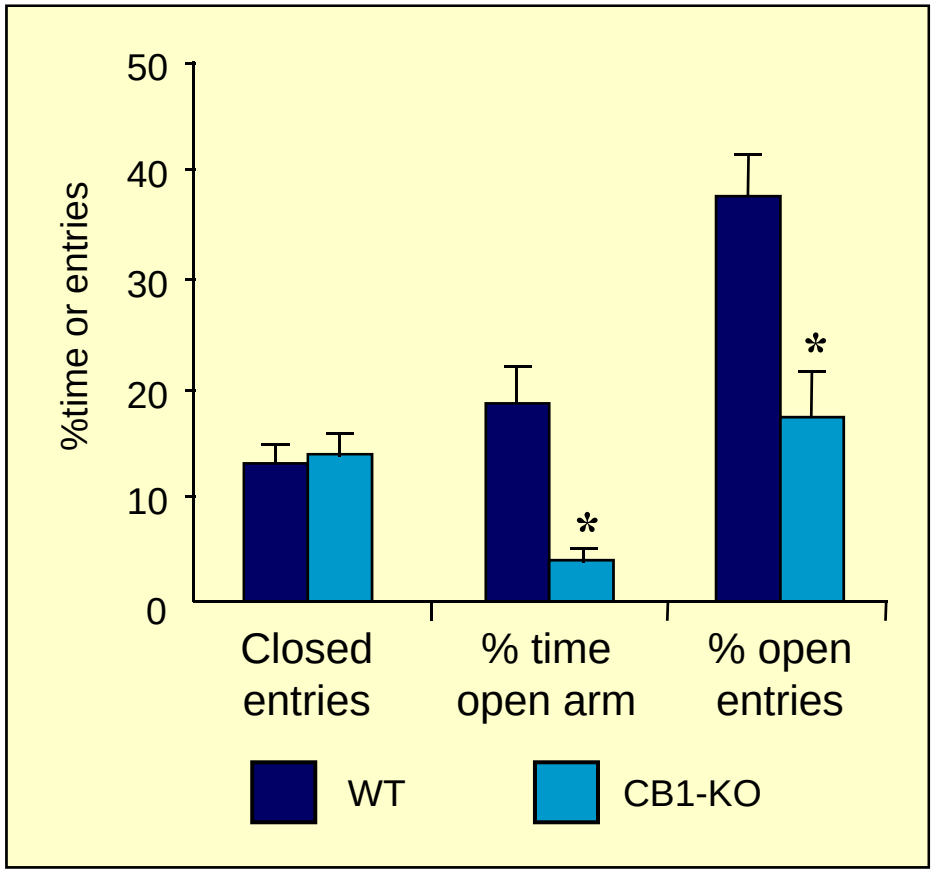


Freund T.F. and Katona I. (Neuron, 2007); Freund T.F. (TINS, 2003)

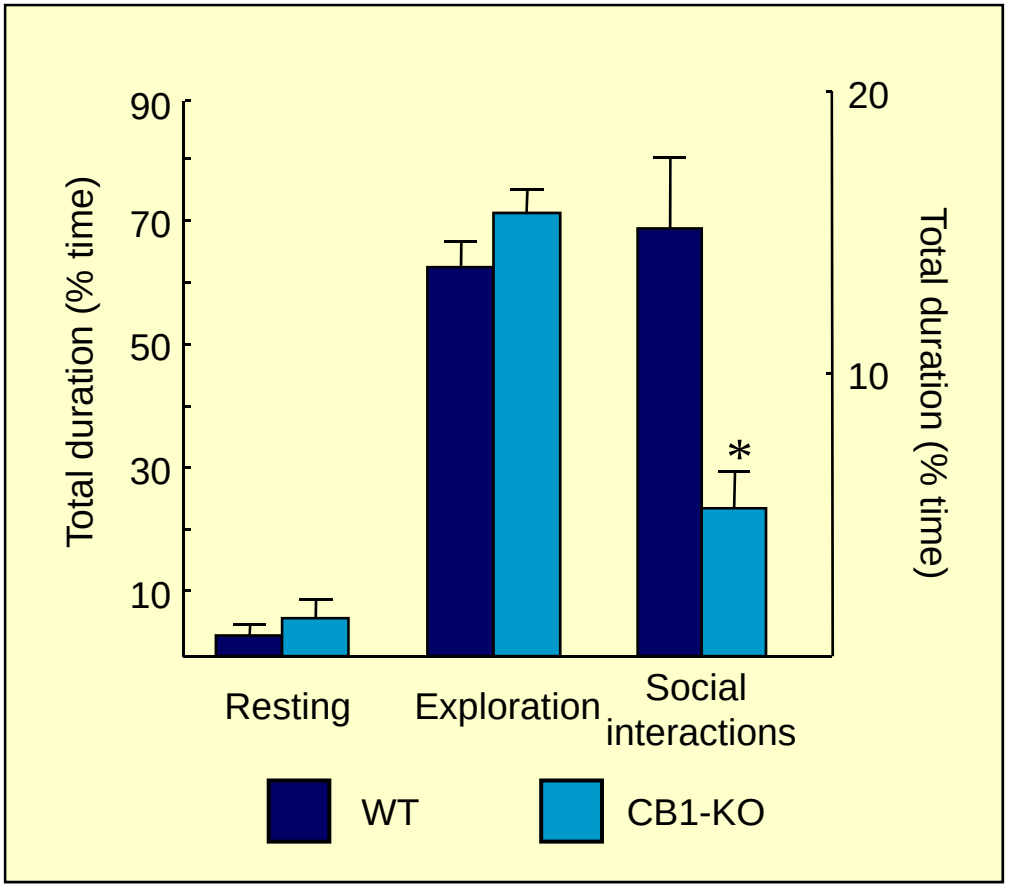
Anxiety of animals is tested on elevated plus maze



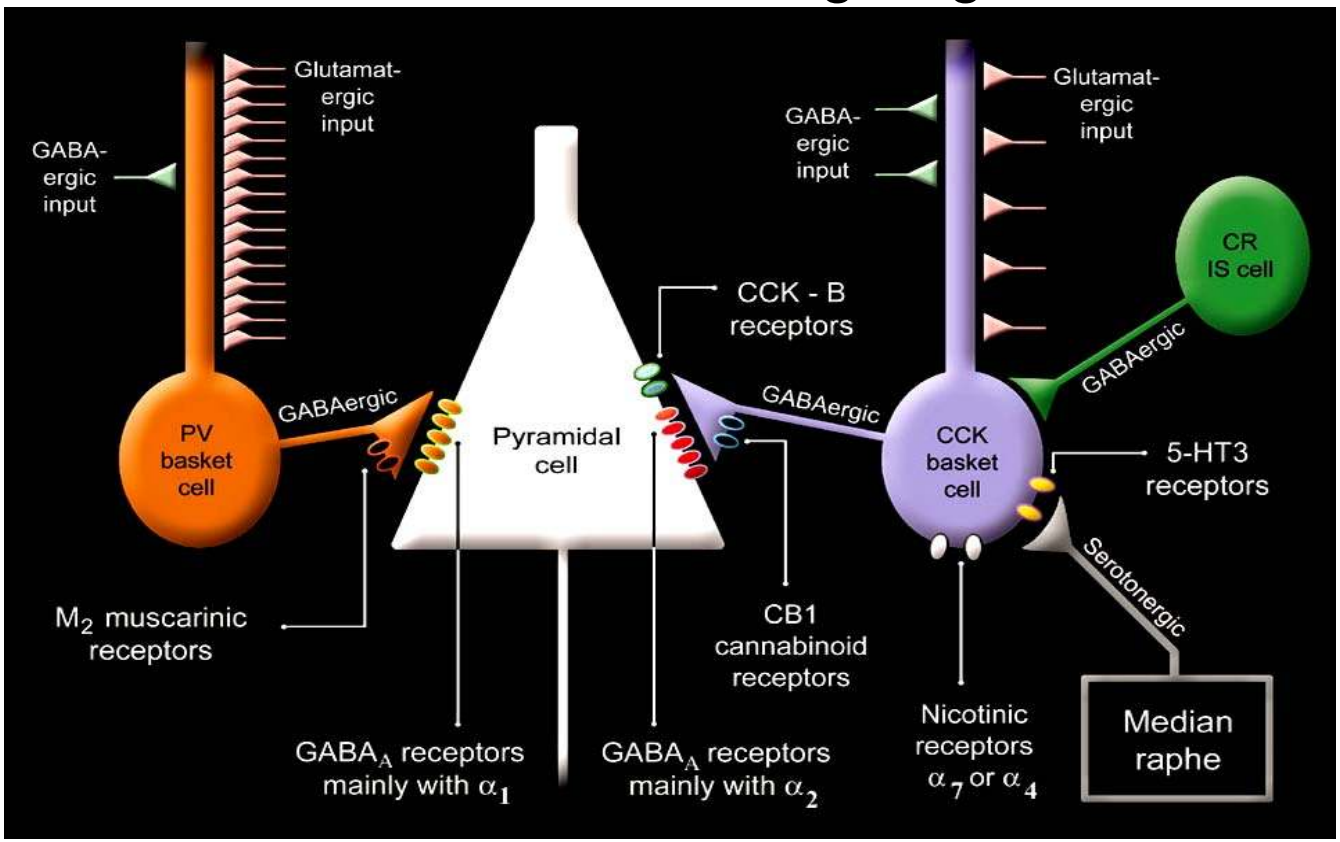
The behavior of wild type and CB1-KO mice on the elevated plus-maze



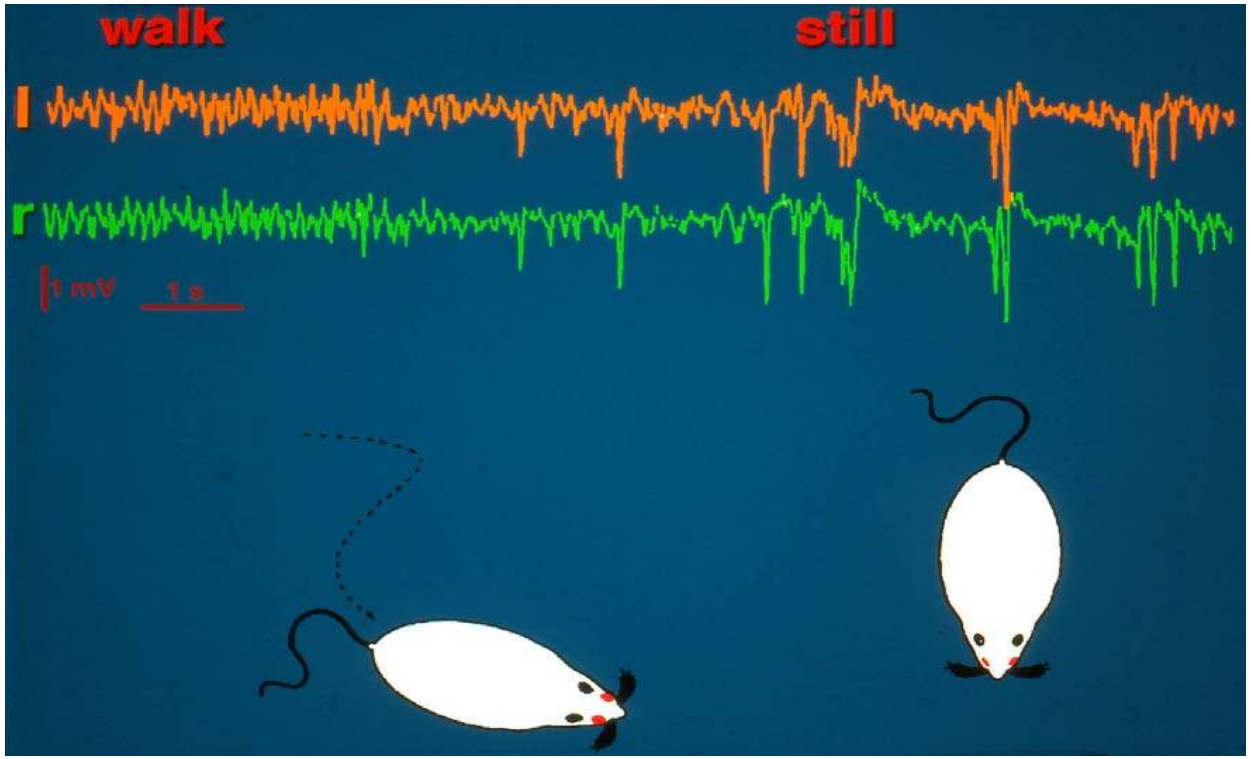
The behavior of wild type and CB1-KO mice in the social interaction test



Could individual cell types with all their complexity – rather than individual receptors or enzymes – be considered as drug targets?

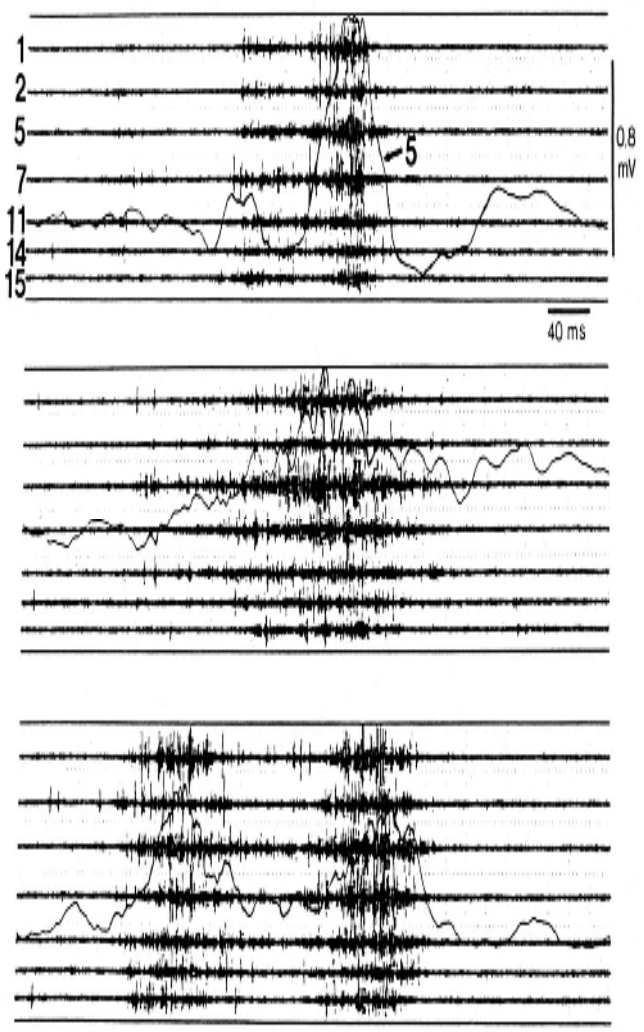


Two different, behavior-dependent electric (EEG) activity patterns recorded from the hippocampus.



Theta activity (4-8 Hz- and oscillation): during exploration and paradox sleeping

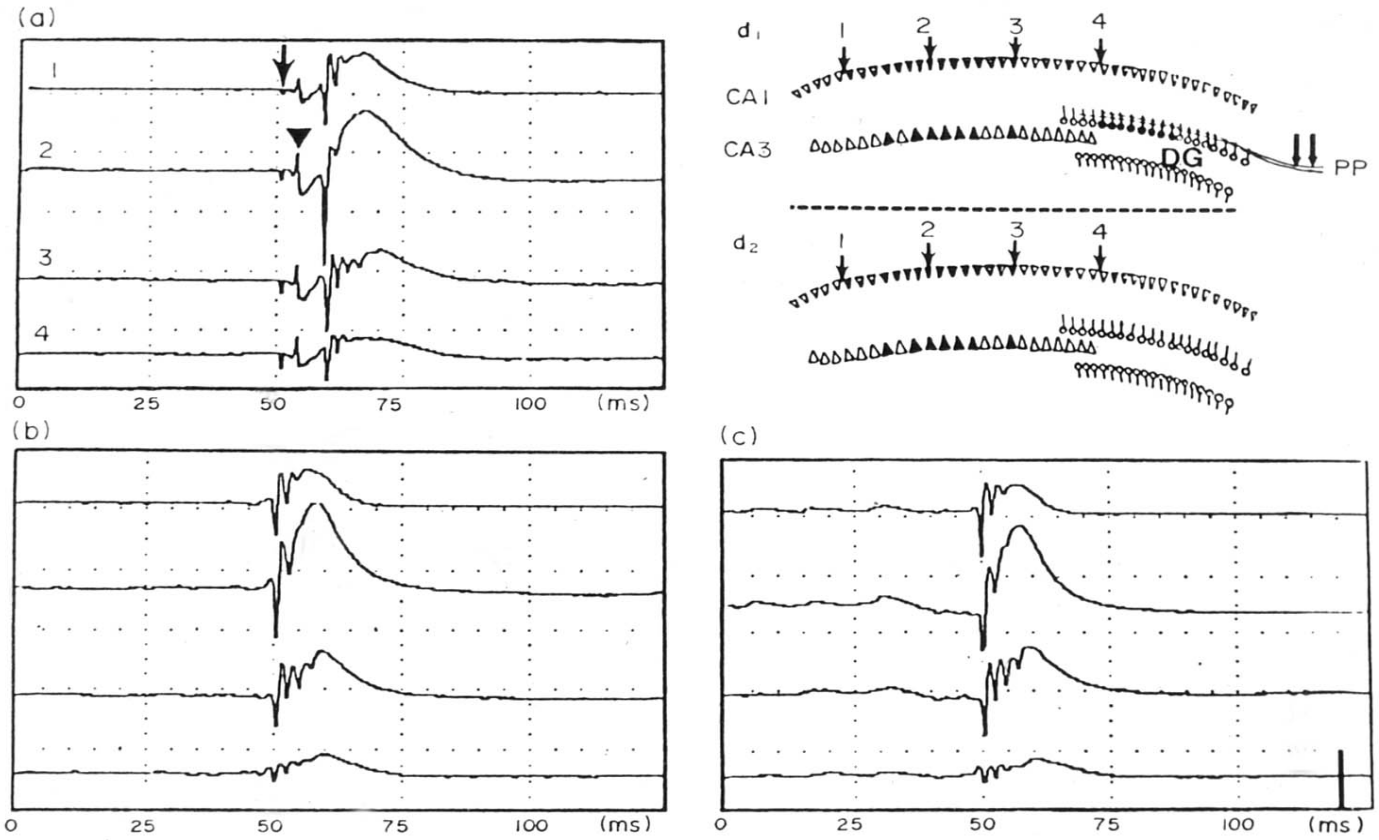
Sharp-waves, fast, irregular EEG in conscious, resting state, during feeding and slow-wave sleep



During sharp waves large percentage of hippocampal CA3 pyramidal cells produce synchronous bursts. During population burst activity, the participating neurons start and finish their burst activity in different time points; consequently spend different time with high firing activity. The longer is the participation, the stronger will be the synaptic connection to the other members of the mini networks.

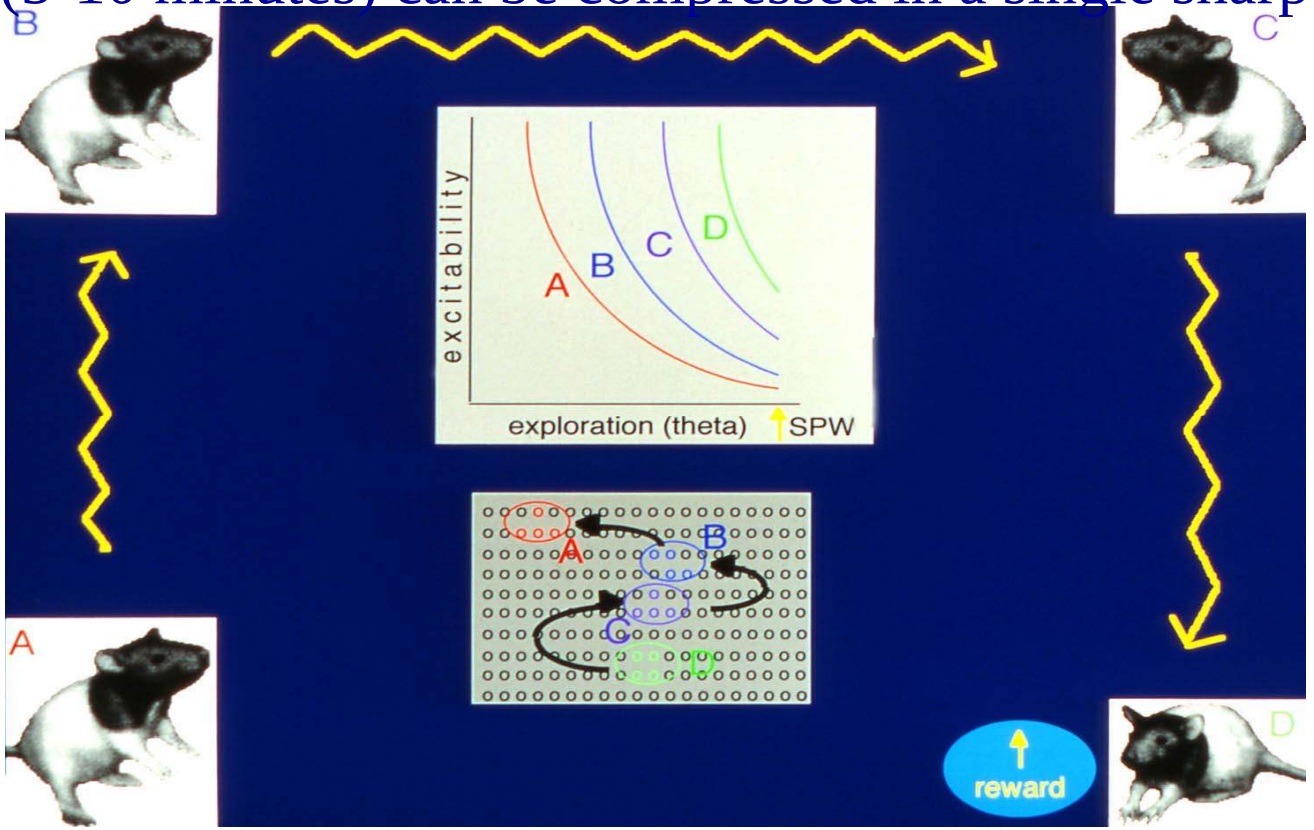
Buzsáki et al., 1986

An electric stimulus corresponding to a sharp wave potentiate a mini network in the CA3 region. Later, spontaneous sharp waves induced field potentials turn up in similar shape suggesting that neurons involved in the generation were the same.

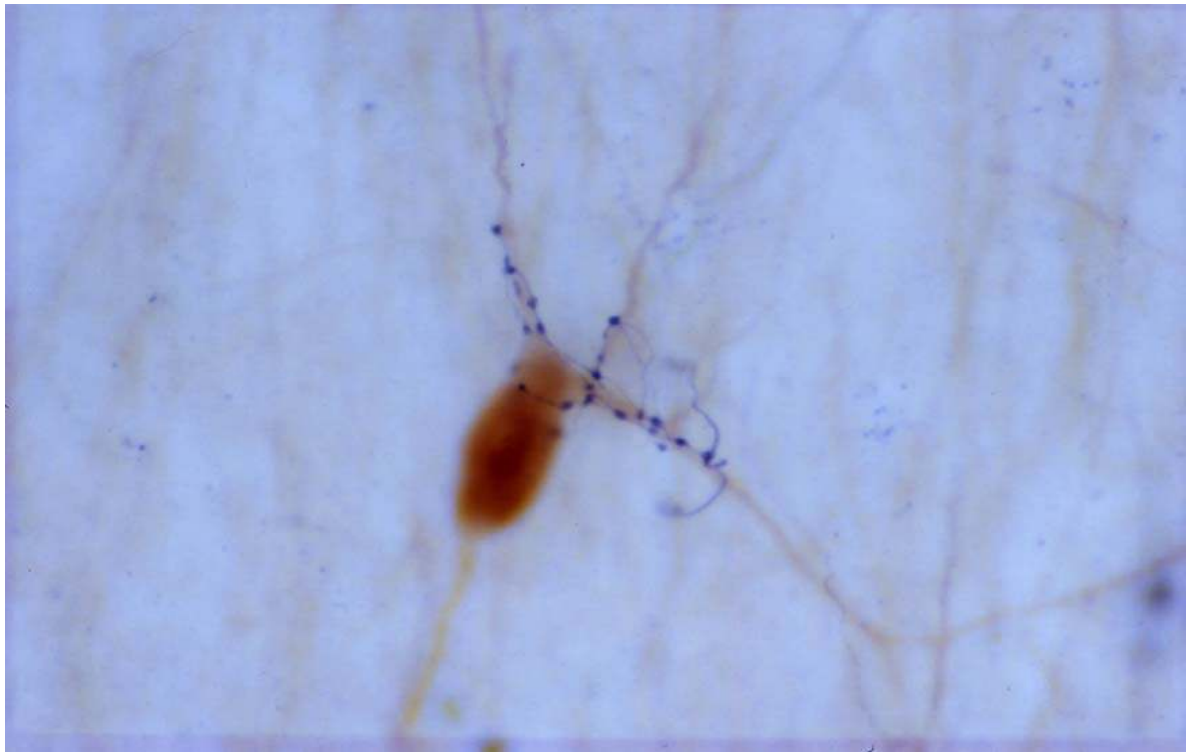


The two-phase memory model of Buzsáki

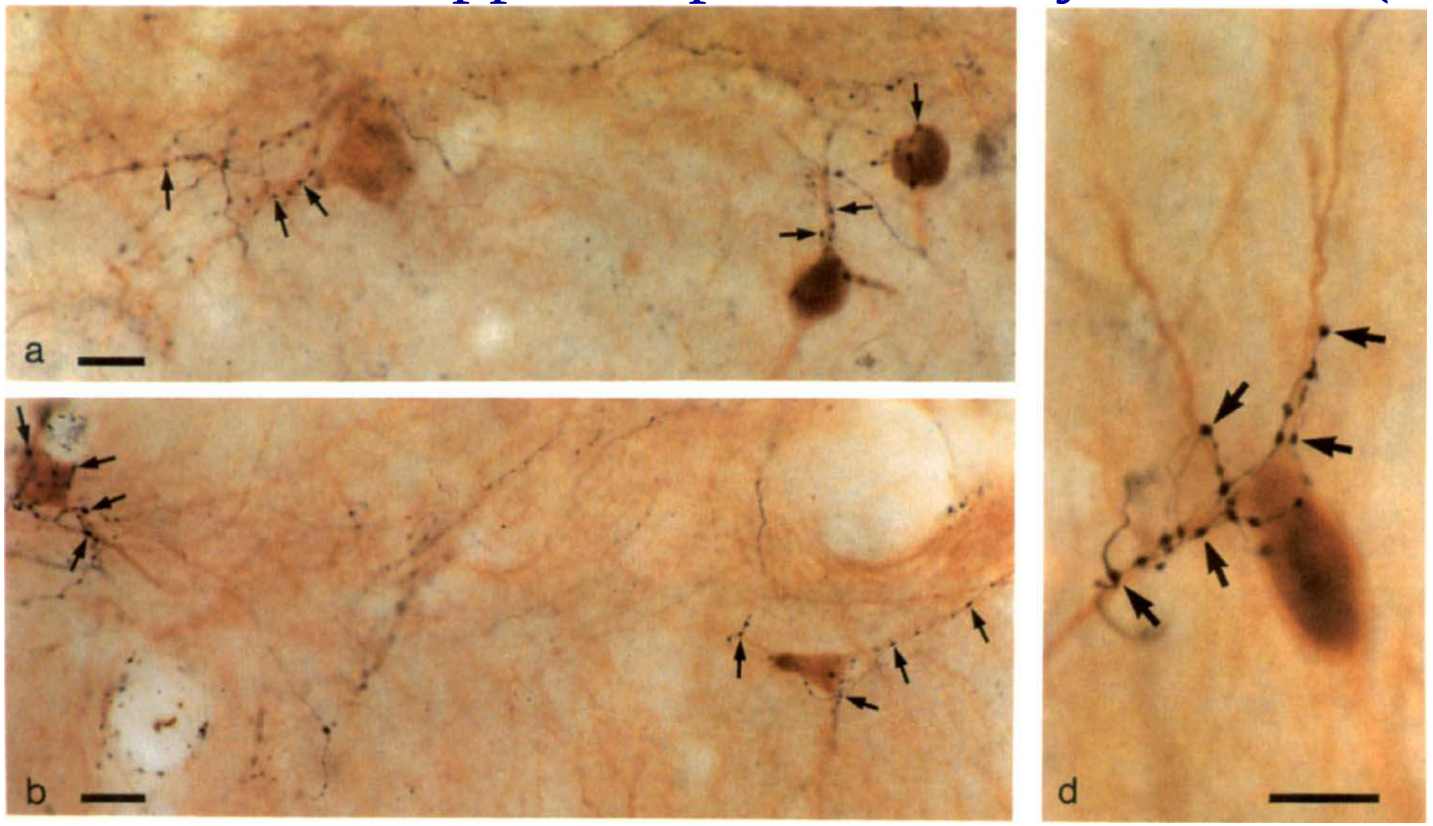
The full space-information of a relatively long exploration phase (5-10 minutes) can be compressed in a single sharp wave.

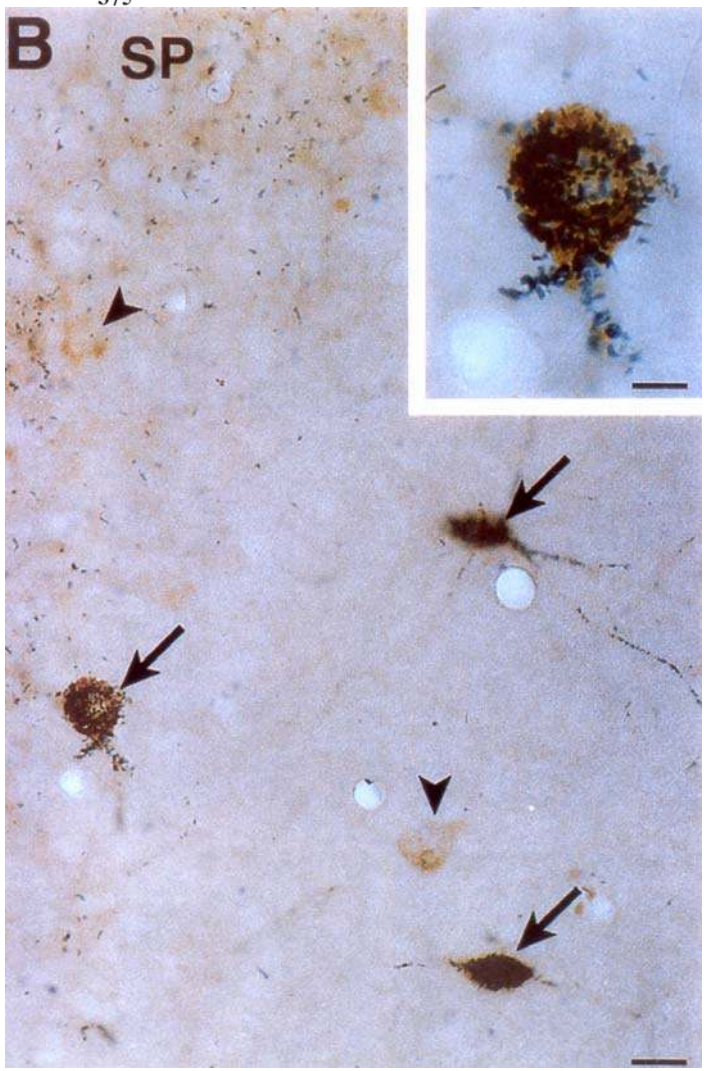


The serotonergic pathway originating from the raphe nuclei (dark blue reaction product) innervates selectively the hippocampal inhibitory neurons (brown).



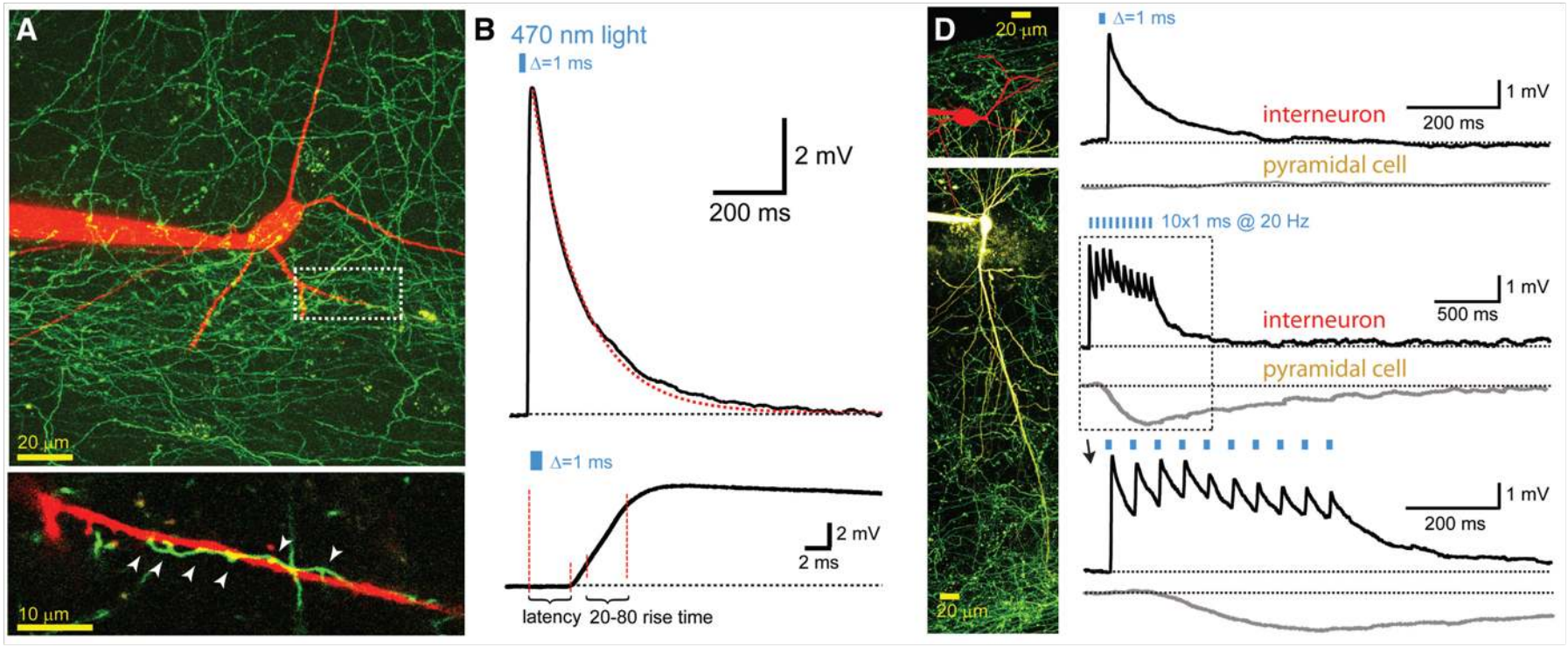
The serotonergic pathway originating from the raphe nuclei (black reaction product, arrows) establish multiple synaptic contacts with the hippocampal inhibitory neurons (brown).



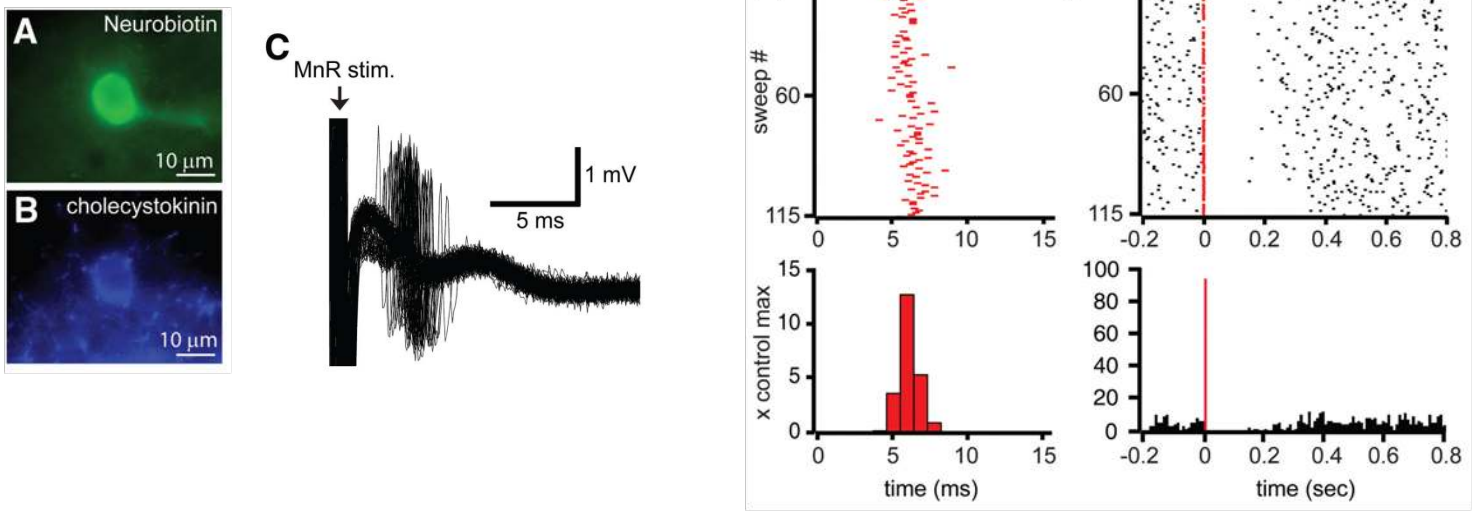


The only ionotropic receptor for serotonin is 5-HT3, the activation of which induces a fast excitation. These receptors are expressed exclusively by GABAergic interneurons, those which also contain CCK, VIP or calbindin. Serotonin, therefore excites interneurons responsible for perisomatic inhibition through 5-HT3 receptors. In addition, it inhibits the dendritic inhibition via presynaptic 5-HT1receptors at a non-synaptic manner.

Optical stimulation of raphe fibers excites hippocampal interneurons *in vitro*

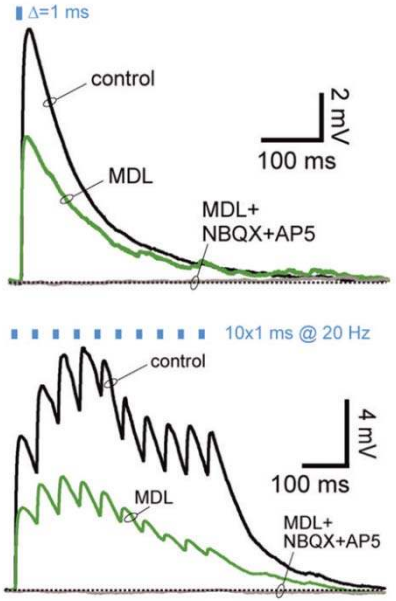


Electrical stimulation of raphe neurons excites hippocampal interneurons *in vivo*

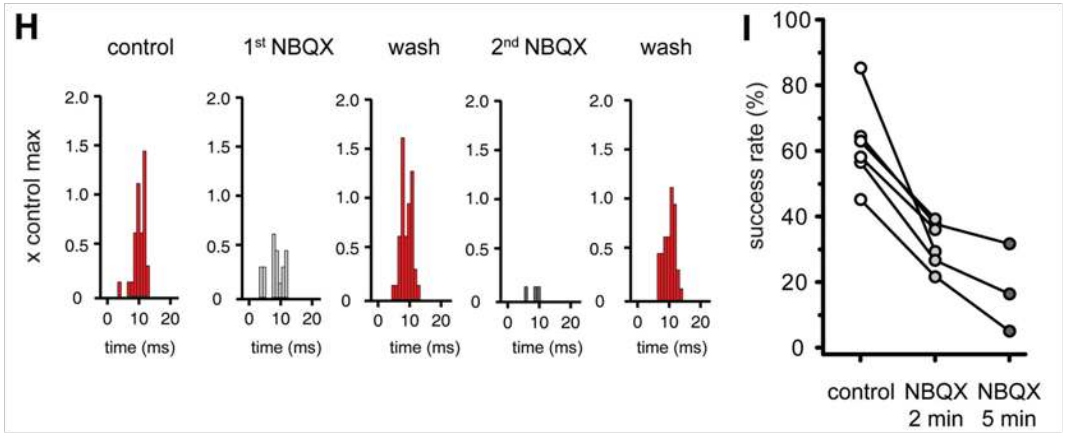


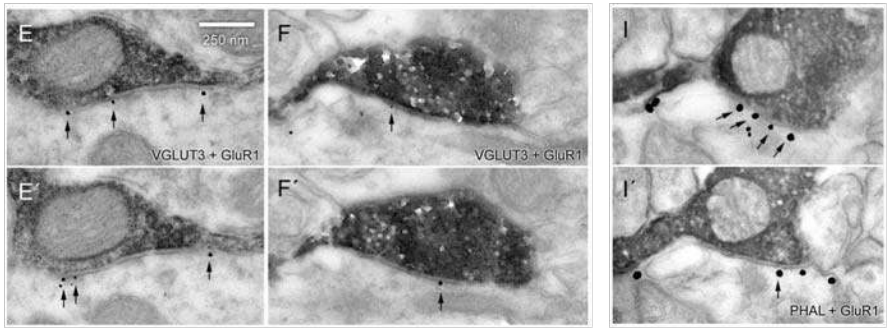
Fast activation is serotonin/glutamate-dependent...

In vitro

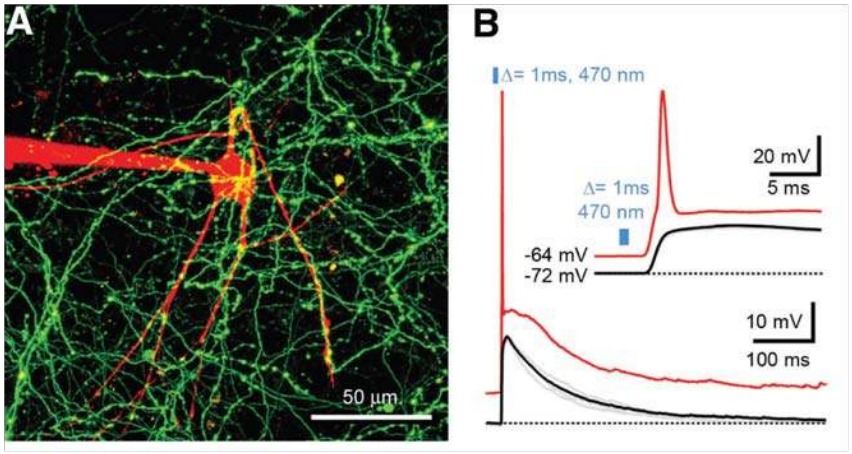


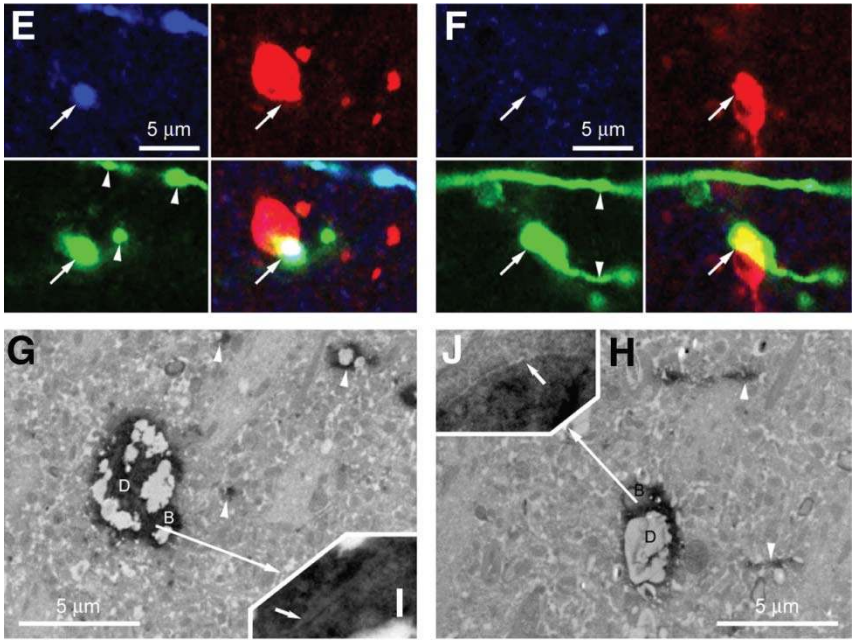
In vivo

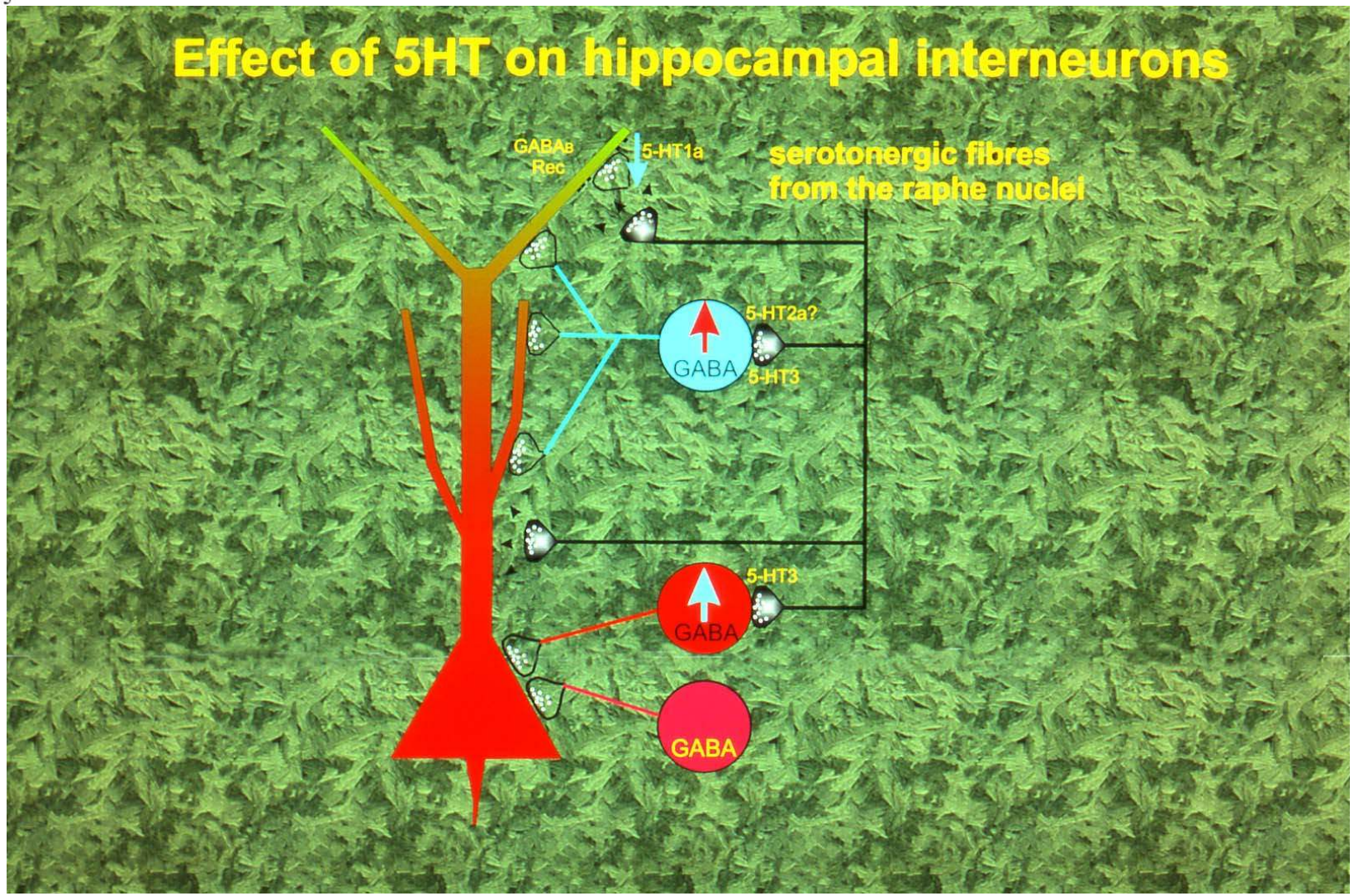


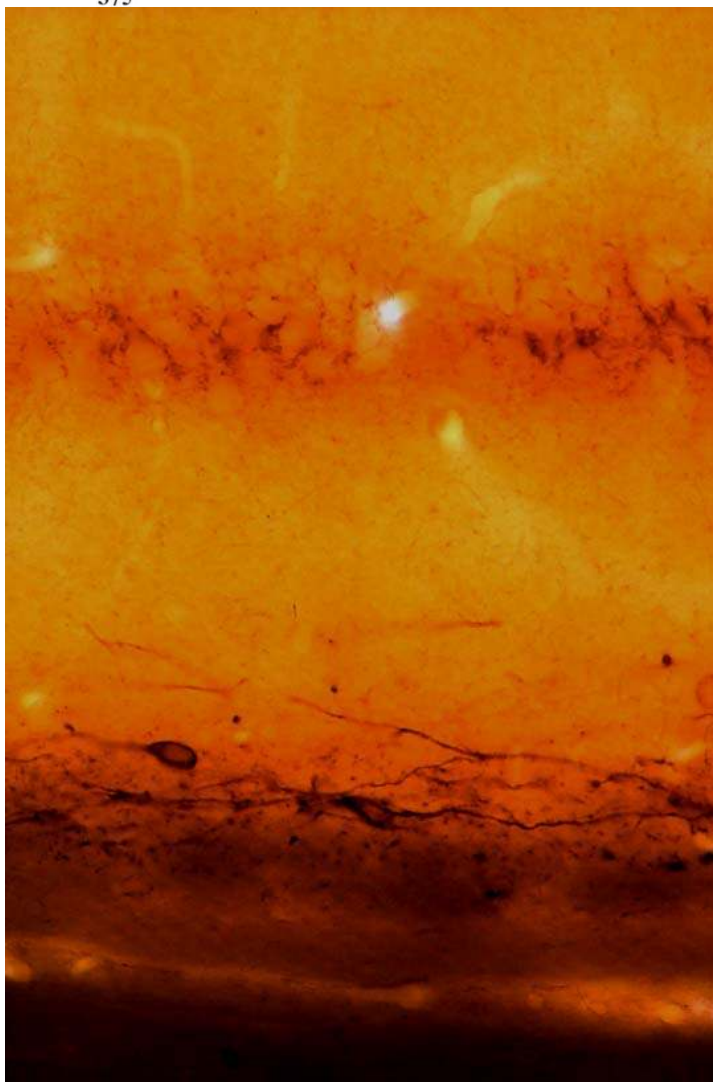


...and synaptic

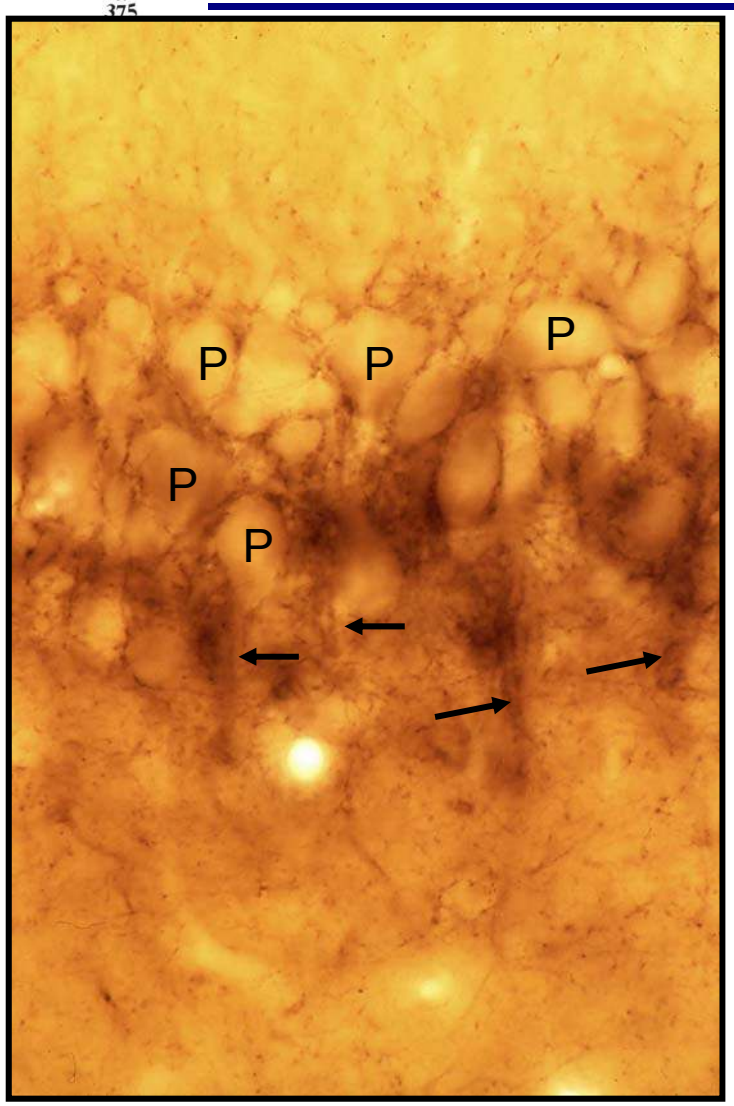





Effect of 5HT on hippocampal interneurons
GABAB Rec
5-HT1a
serotonergic fibres from the raphe nuclei
5-HT2a?
GABA
5-HT3
5-HT3
GABA
GABA

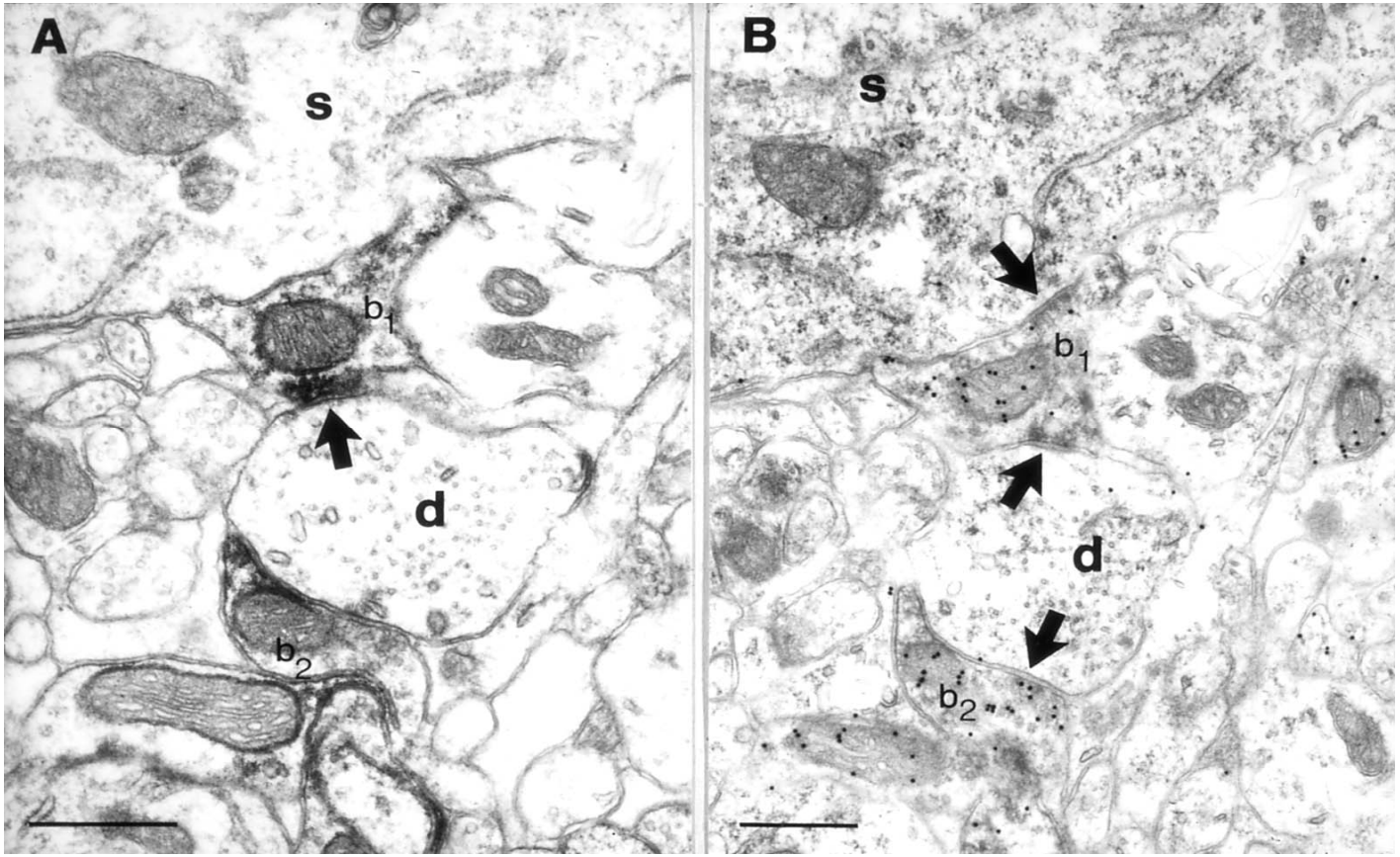


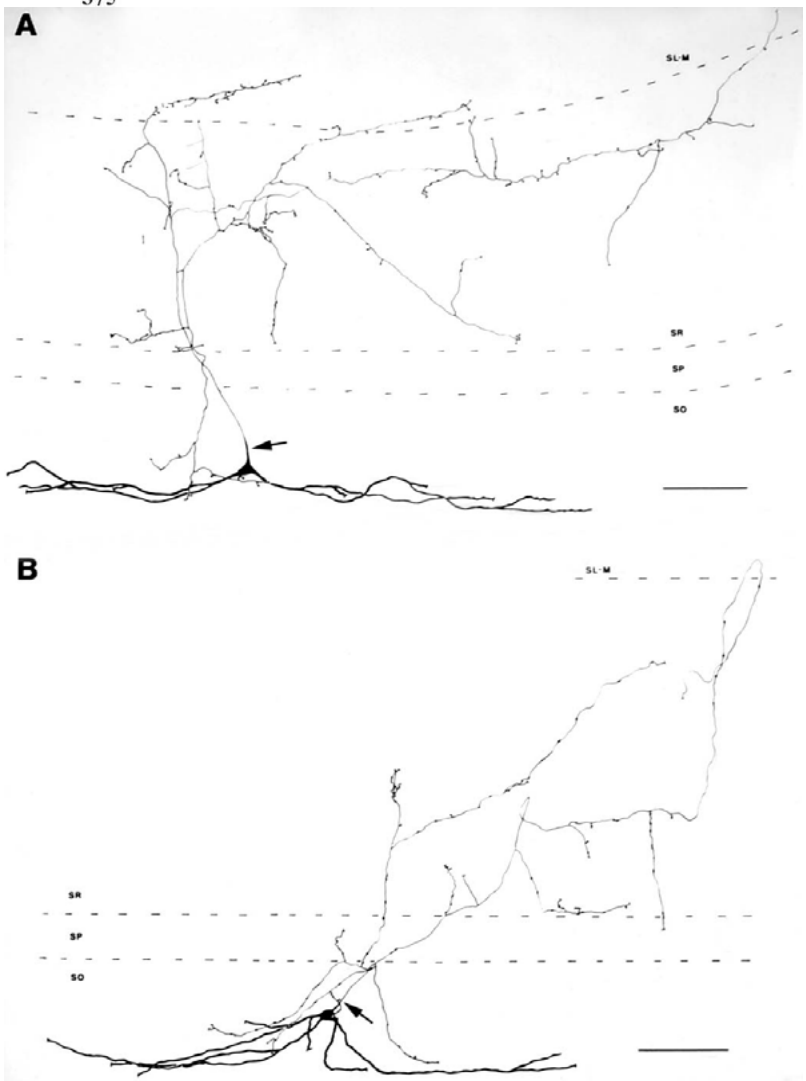
The m2 receptor of acetylcholine is also expressed selectively by interneurons. The receptor protein is present in the axon terminals of the perisomatic inhibitory neurons and in the dendritic tree of the dendritic inhibitory cells.



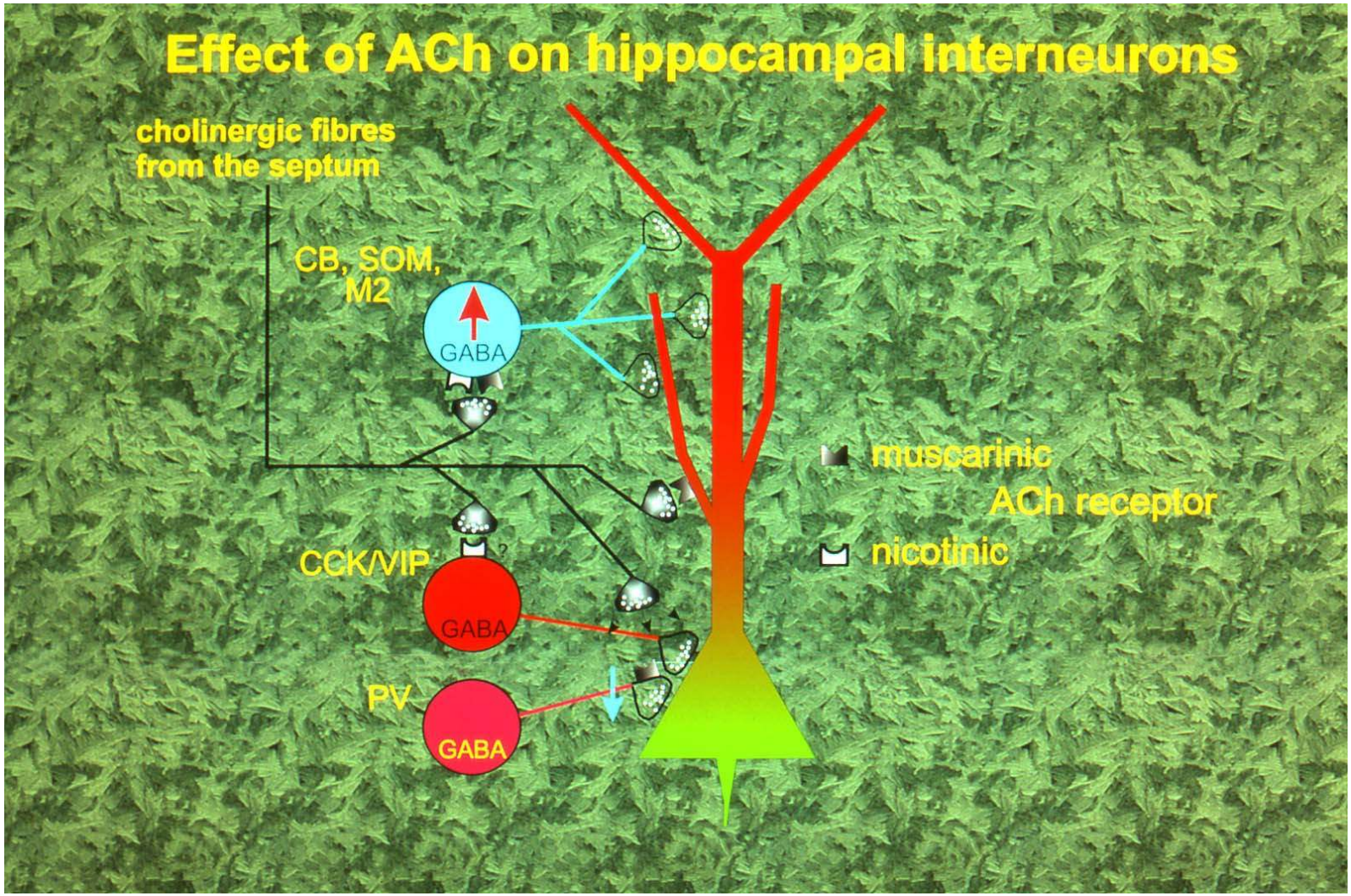
The m2-immunoreactive axon terminals (brown) are well visible around the soma (P) and axon initial segment (arrows) of the pyramidal cells. Activation of m2 receptors in the axon terminals of basket and axo-axonic cells inhibits GABA release, consequently it reduces the perisomatic inhibition through this type of the receptor.

The m2-immunoreactive terminals (b1 és b2) synapsing (arrows) onto the soma (s) and the dendrites (d) of the pyramidal cell, proved to be GABA-containing in the neighboring ultrathin sections (see the deposited gold granules).

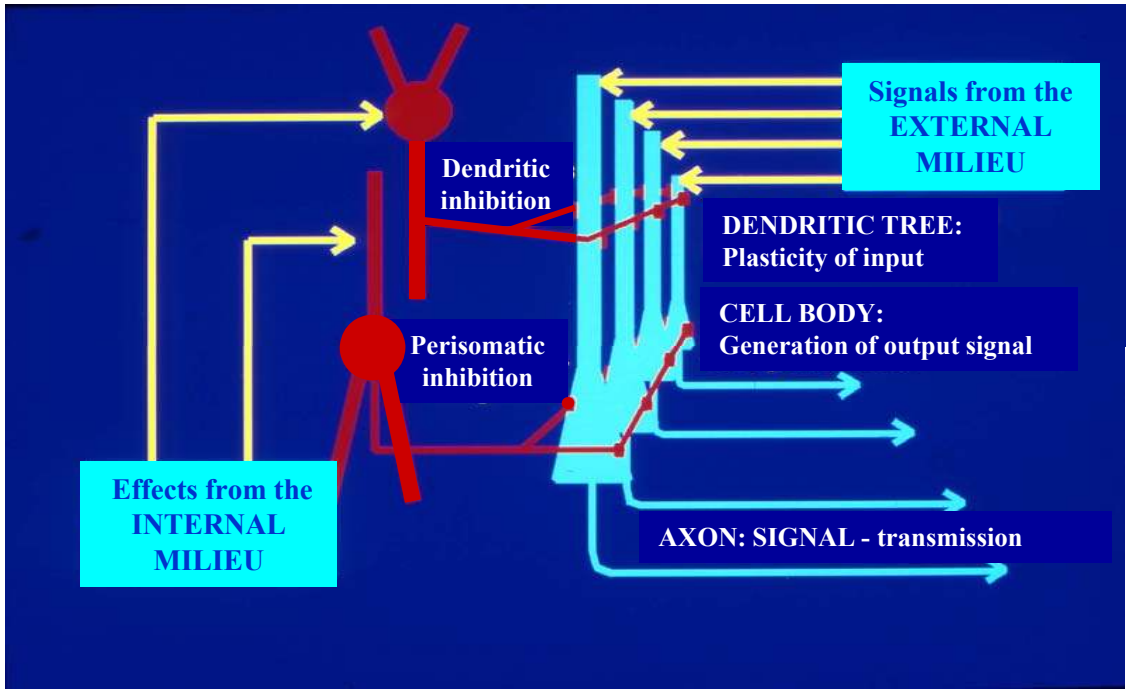




Those neurons , which express m2 receptors in the soma and dendritic tree, project to the layer of the apical dendrites of the pyramidal cells and are responsible for dendritic inhibition. The activation of m2 receptors located in the soma/dendritic tree of the interneurons enhances the cell's excitability. Acetylcholine therefore increase the dendritic inhibition through m2 receptors.


Effect of ACh on hippocampal interneurons
cholinergic fibres
from the septum
CB, SOM,
M2
GABA
CCK/VIP
?
GABA
PV
GABA
muscarinic
ACh receptor
nicotinic

The cerebral cortex exists in at least two functional states: in cholinergic activated state, as a simple relay nucleus, and in serotonergic activated state, as a structure of memory. The switch between the two states is established by subcortical pathways mediating information about the internal milieu (i.e. motivation, emotion and the physiological state) through the differentiated modulation of dendritic and perisomatic inhibitions.



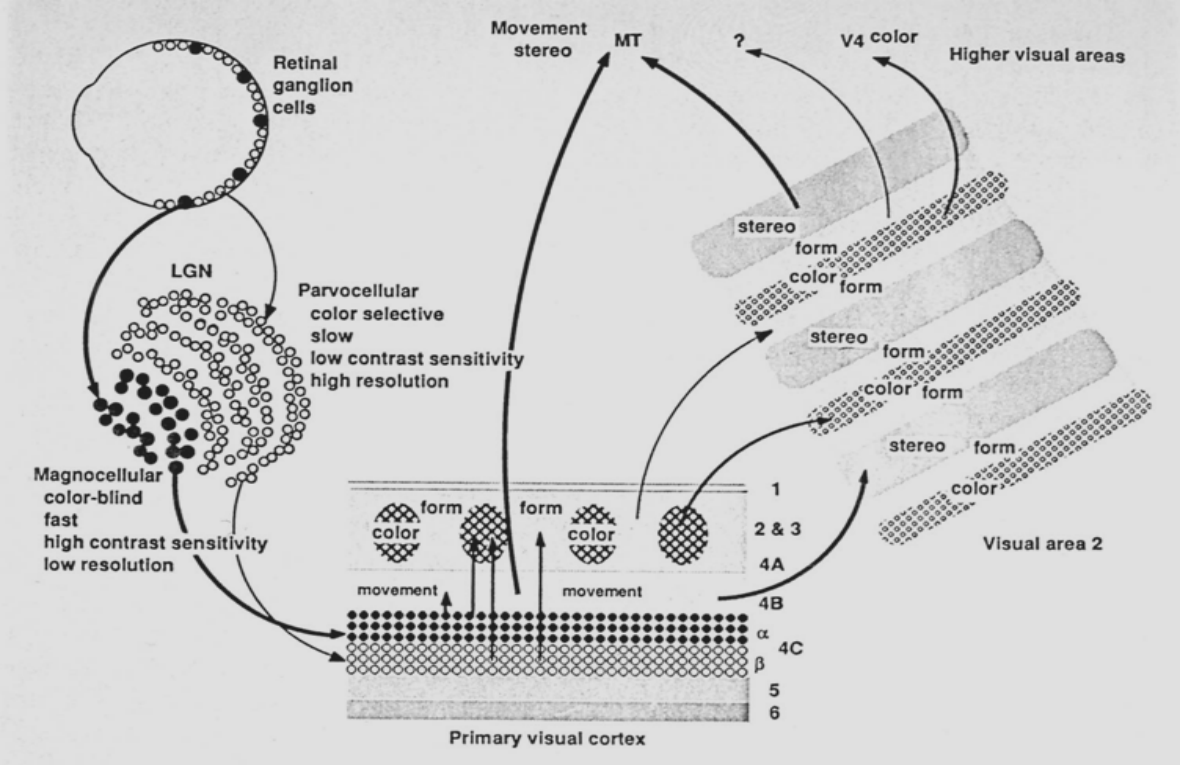
Gamma oscillation (40-100 Hz)

It ensures synchronization with 2 to 3 msec accuracy necessary for the synaptic potentiation

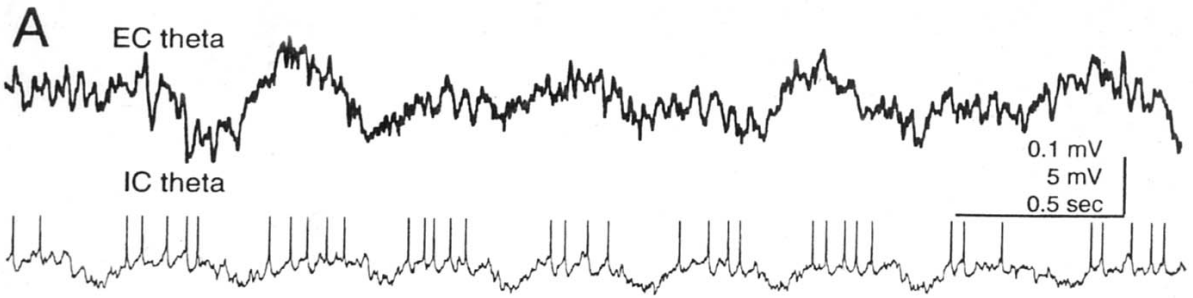
It is resolution for the „binding” problem

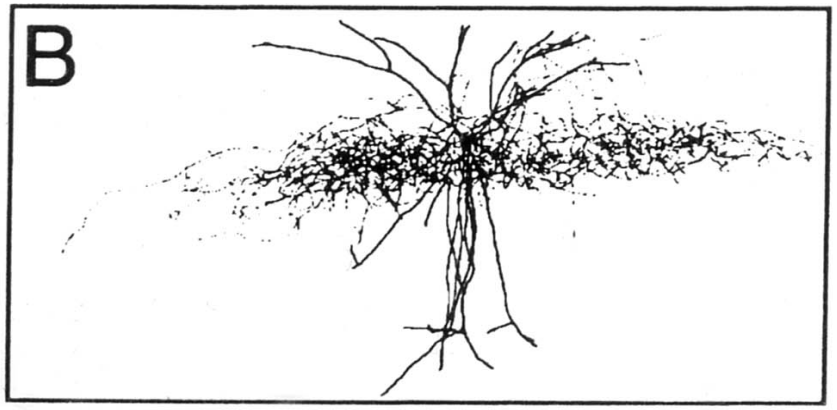
The binding problem

The pathways mediating various sensory modalities and submodalities do not converge in the brain, instead they diverge in the higher processing levels.



The EEG theta is characterised by „riding” waves with a frequency of 40-100 Hz.



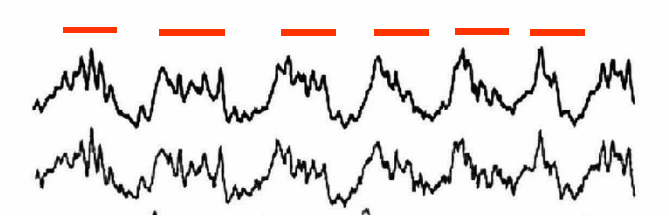


When can we record gamma oscillations in the hippocampus?

Theta oscillation during exploration **Irregular activity during consummatory behavior**

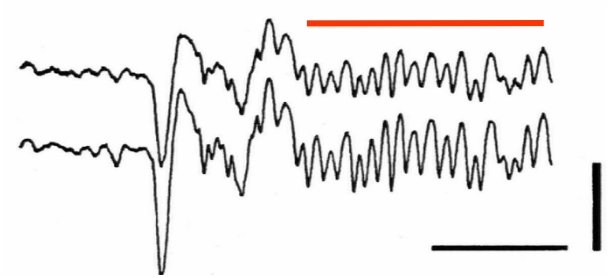


1. Theta nested gamma



Buzsáki et al., 2003

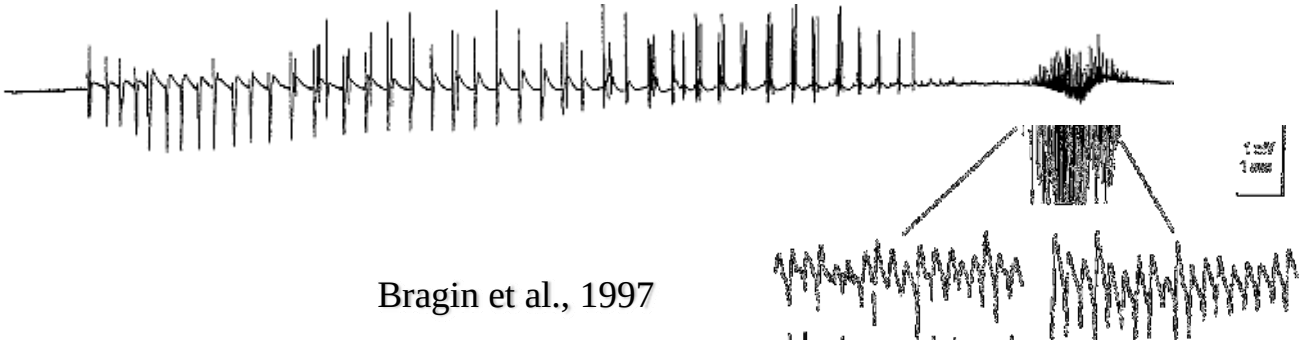
2. Tail gamma followes the sharp waves



Traub et al., 1996

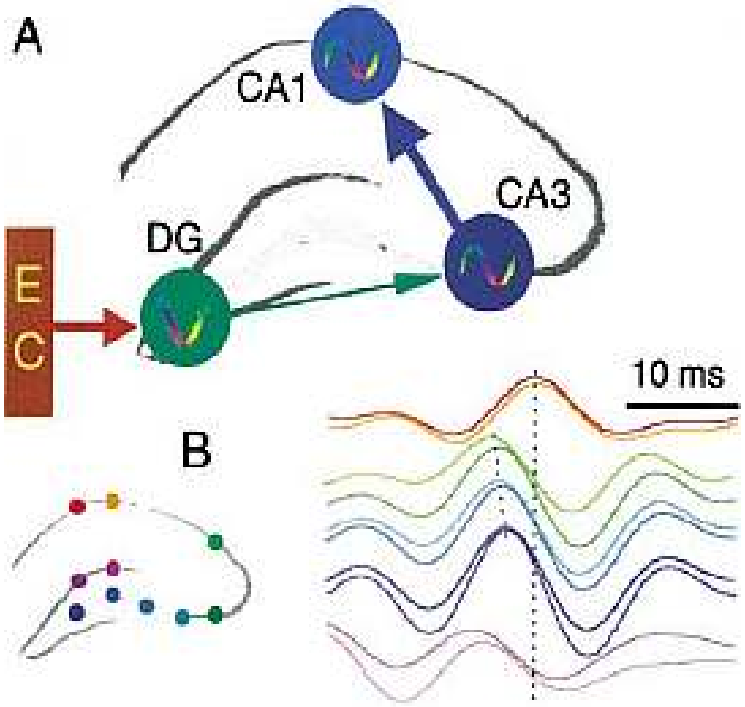
When can we record gamma oscillations in the hippocampus?

3. Epileptic discharges are followed by gamma oscillations



Bragin et al., 1997

Two independent gamma generators in the hippocampus

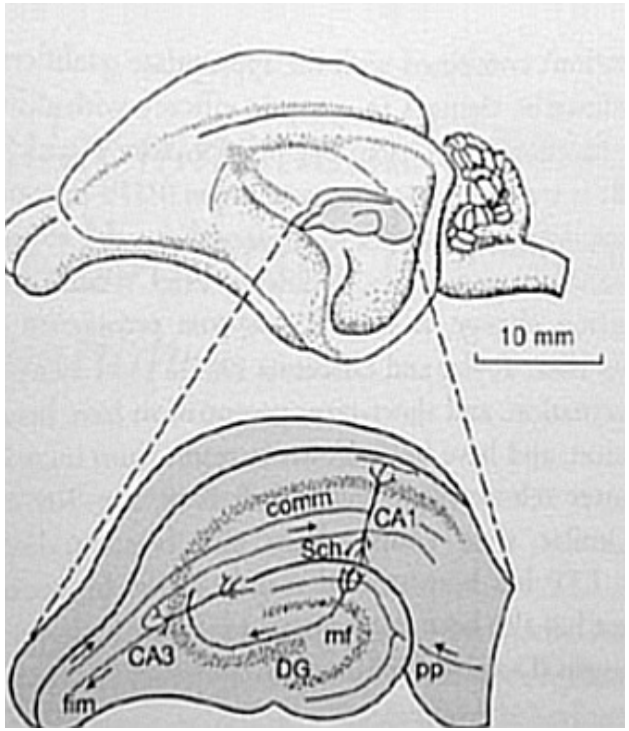


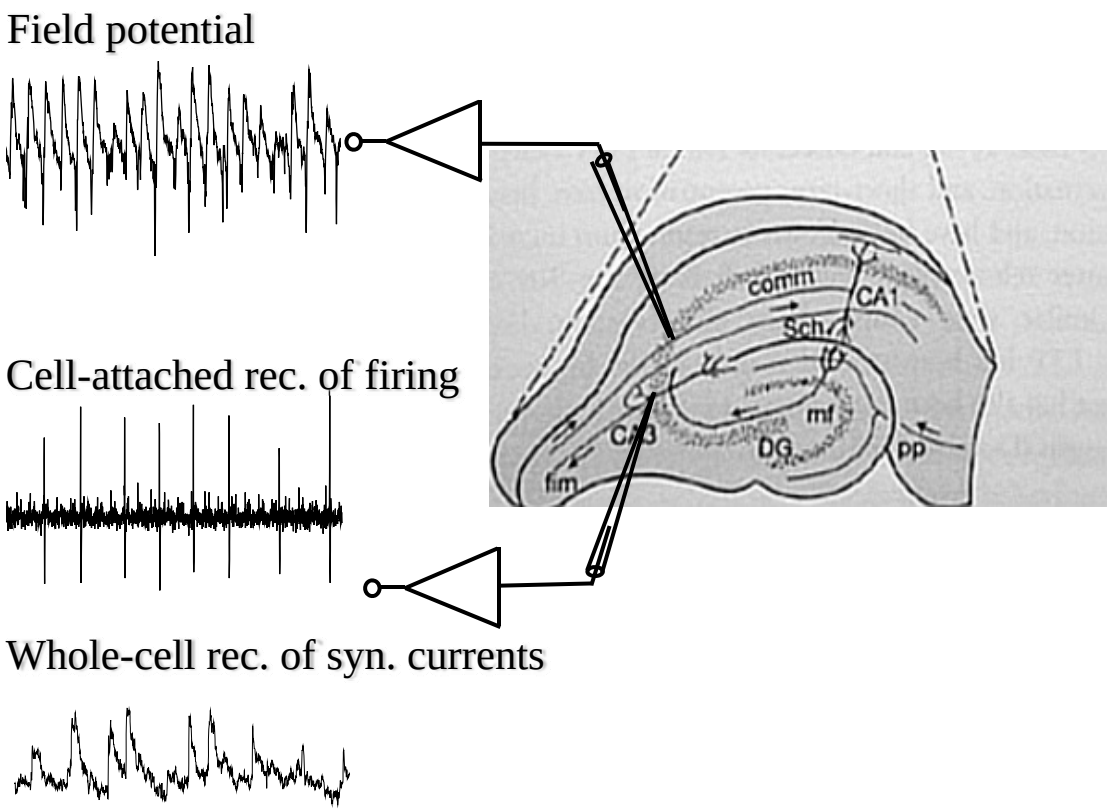
1. Gamma oscillations in the **dentate gyrus** are dependent on extra-hippocampal input

2. Gamma oscillations in the **CA3 region** are intrinsically generated and transmitted into the CA1 region

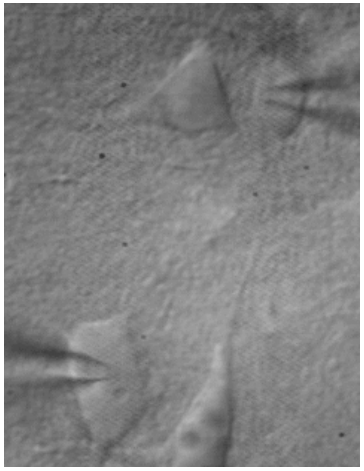
Bragin et al., 1995; Csicsvári et al., 2003

Carbachol-induced gamma oscillations in hippocampal slices

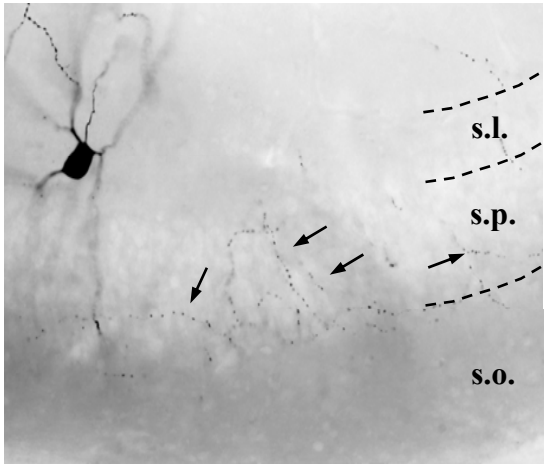




Recording carbachol-induced gamma oscillations in hippocampal slices



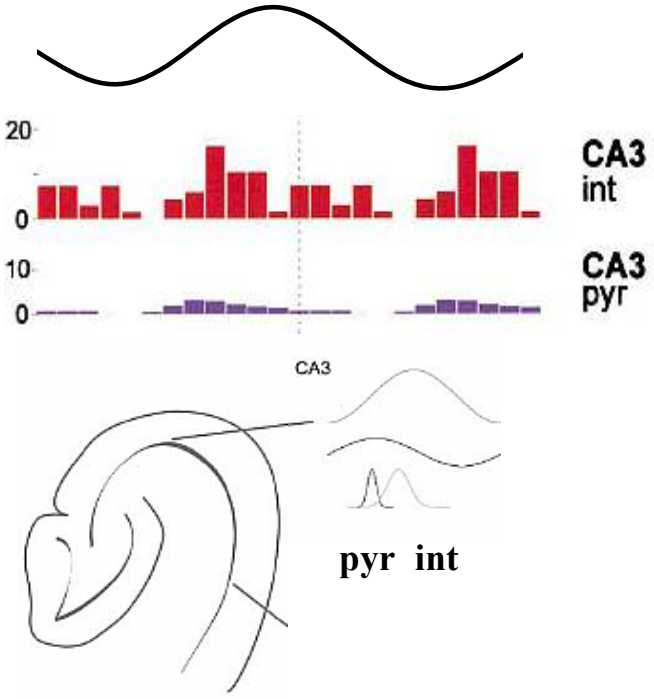
1. Firing characteristics of neurons
(frequency, phase, phase-coupling)
2. Properties of synaptic inputs
(both excitatory and inhibitory)
3. Anatomical identification
4. Imaging techniques



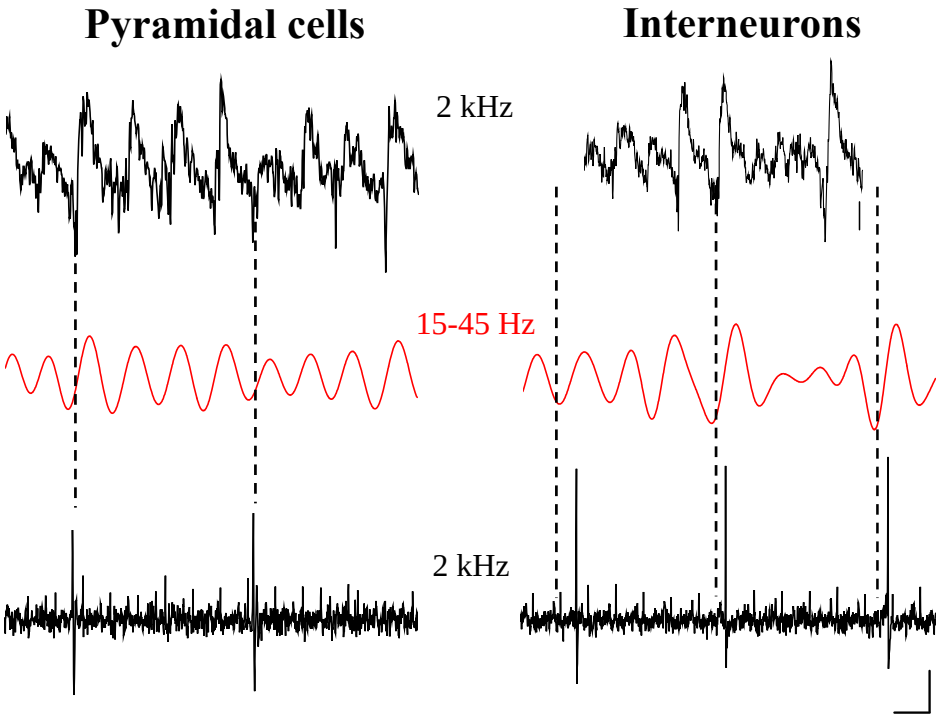
Comparison of *in vivo* and *in vitro* gamma oscillations

Firing of CA3 pyramidal cells is followed by the discharge of CA3 interneurons

In vivo



In vitro



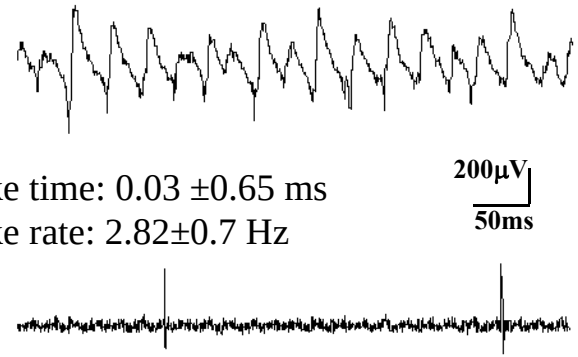
Csicsvári et al., Neuron, 2003

Hájos et al., J. Neurosci. 2004

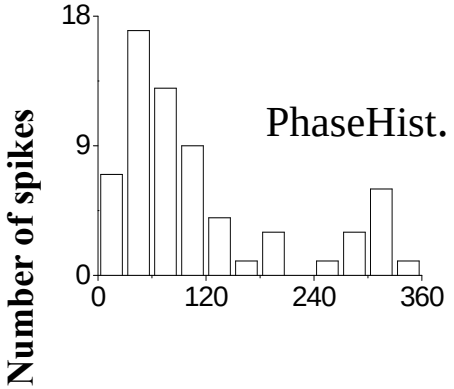
Firing properties of CA3 pyramidal cells and perisomatic inhibitory neurons during cholinergically induced gamma oscillations

Pyramidal cell

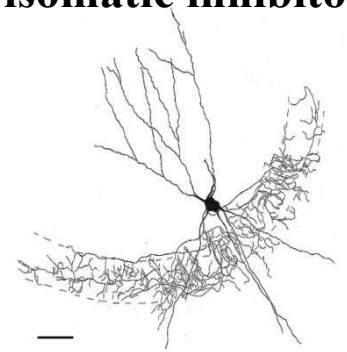


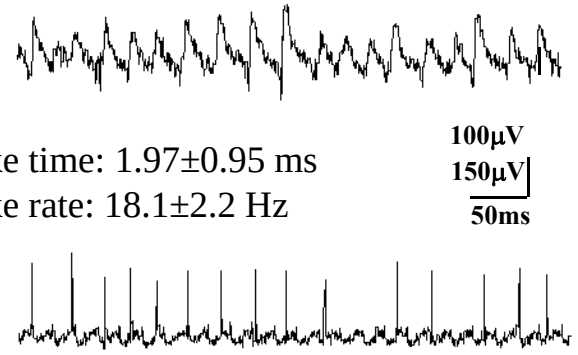


spike time: 0.03 ±0.65 ms
spike rate: 2.82±0.7 Hz

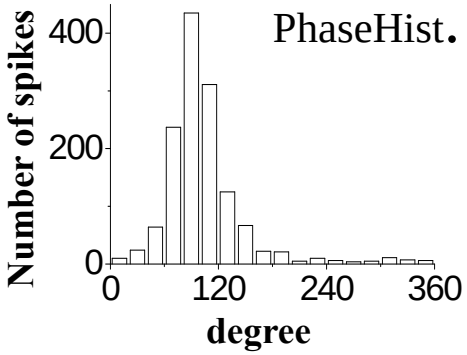


Perisomatic inhibitory cell

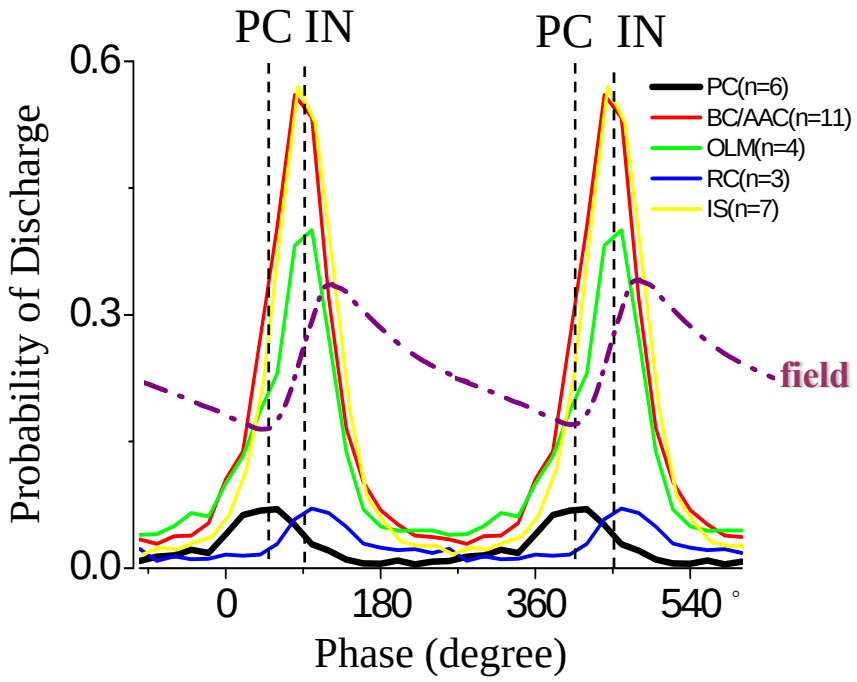


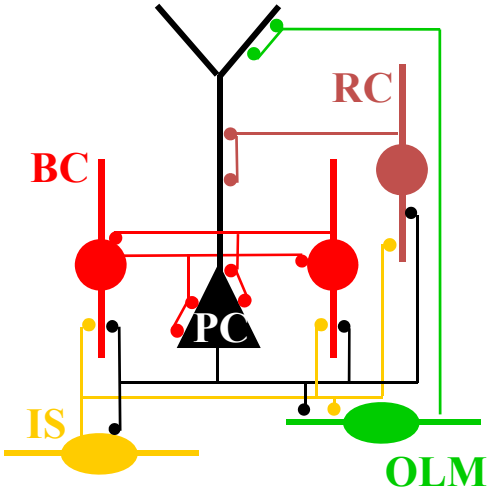


spike time: 1.97±0.95 ms
spike rate: 18.1±2.2 Hz

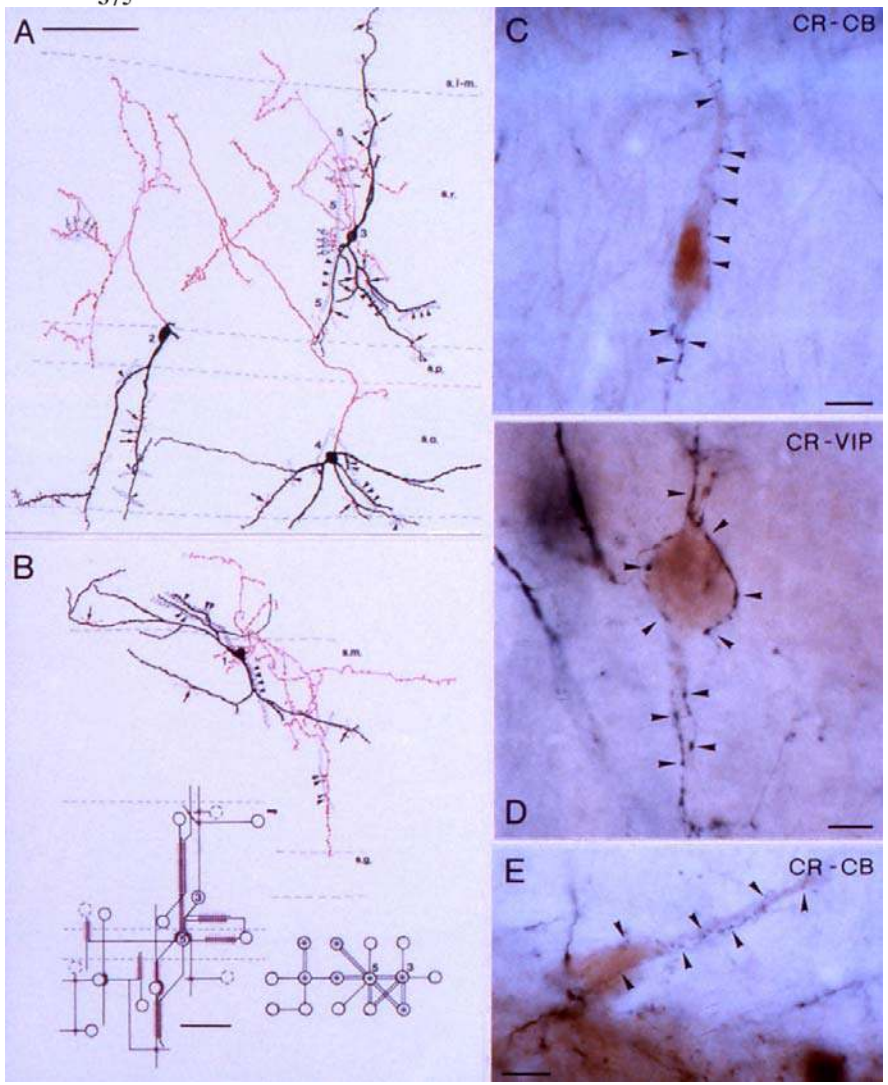


Behavior of distinct types of neurons during gamma oscillacions



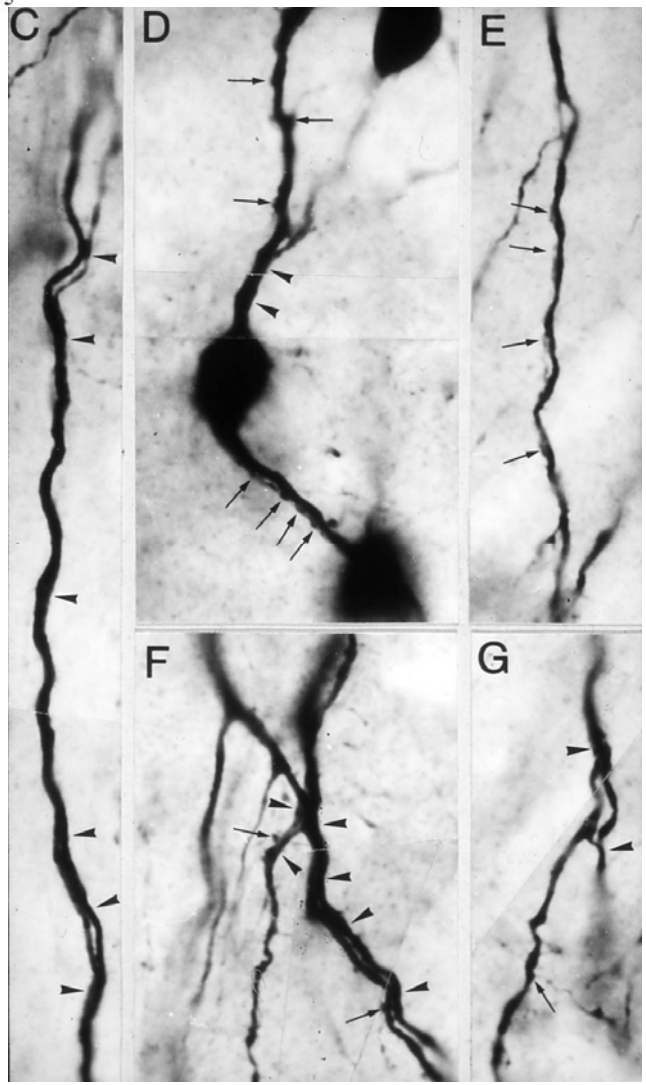


1. Pyramidal cells fire at the negative peak of the oscillations followed by the discharge of interneurons.
2. Perisomatic inhibitory cells and IS interneurons were the most active neuron types with strong phase coupling.
3. Dendritic-targeting interneurons fired with lower frequency and showed less significant phase-coupling.



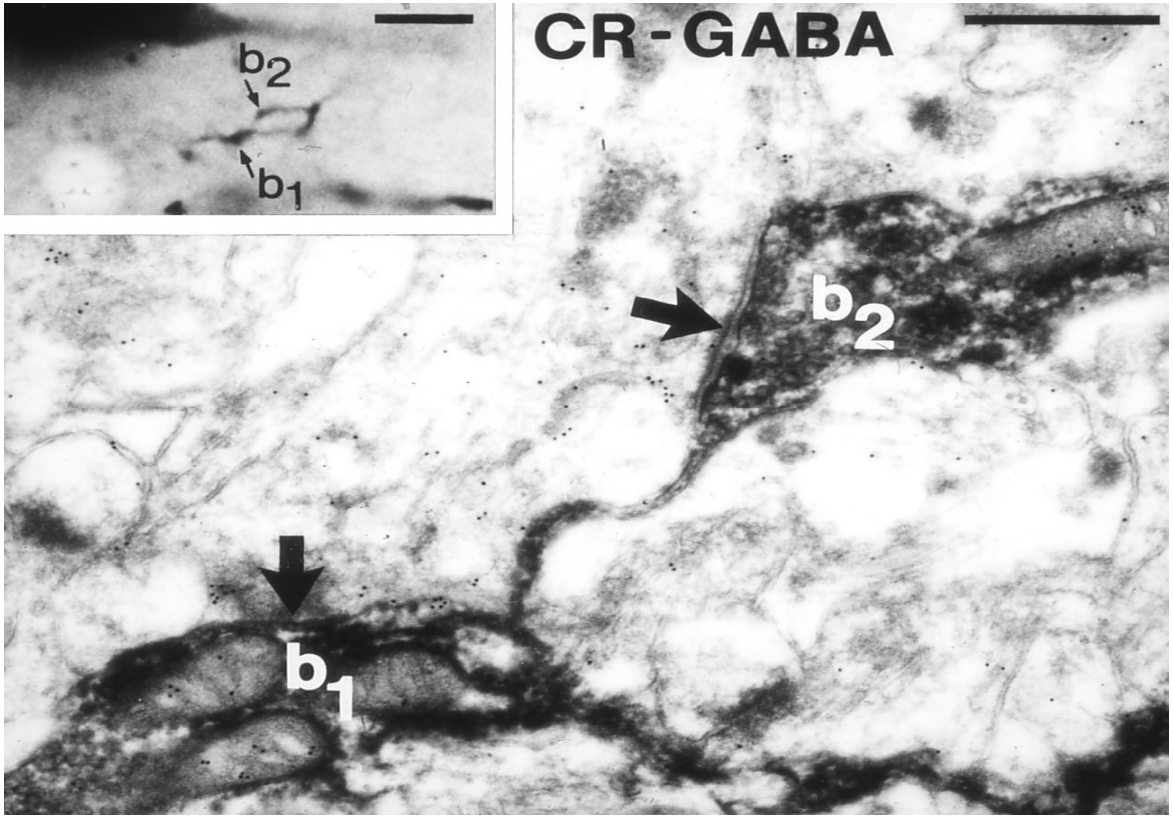
The calretinin-containing GABAergic cells are specilised for the selective innervation of other interneurons.

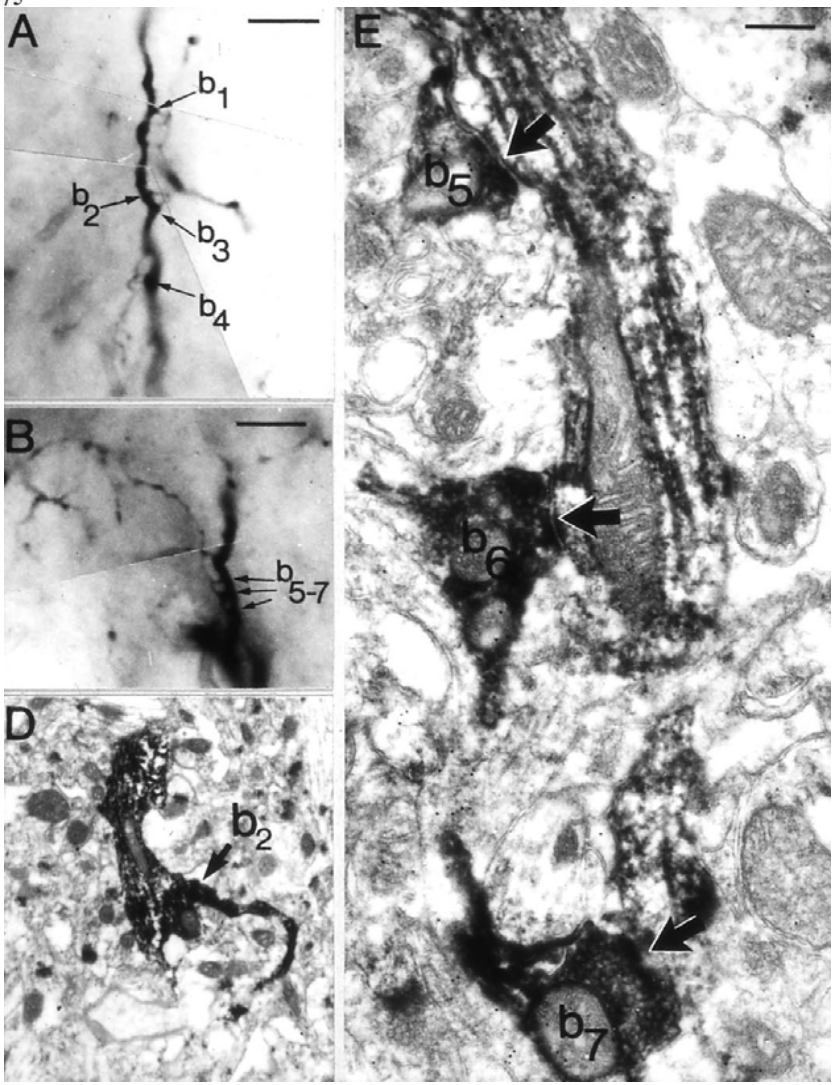
They are interconnected abundantly via dendro-dendritic and axo-dendritic connections.



The calretinin-containing interneuron-selective inhibitory cells exhibit rich dendro-dendritic connections

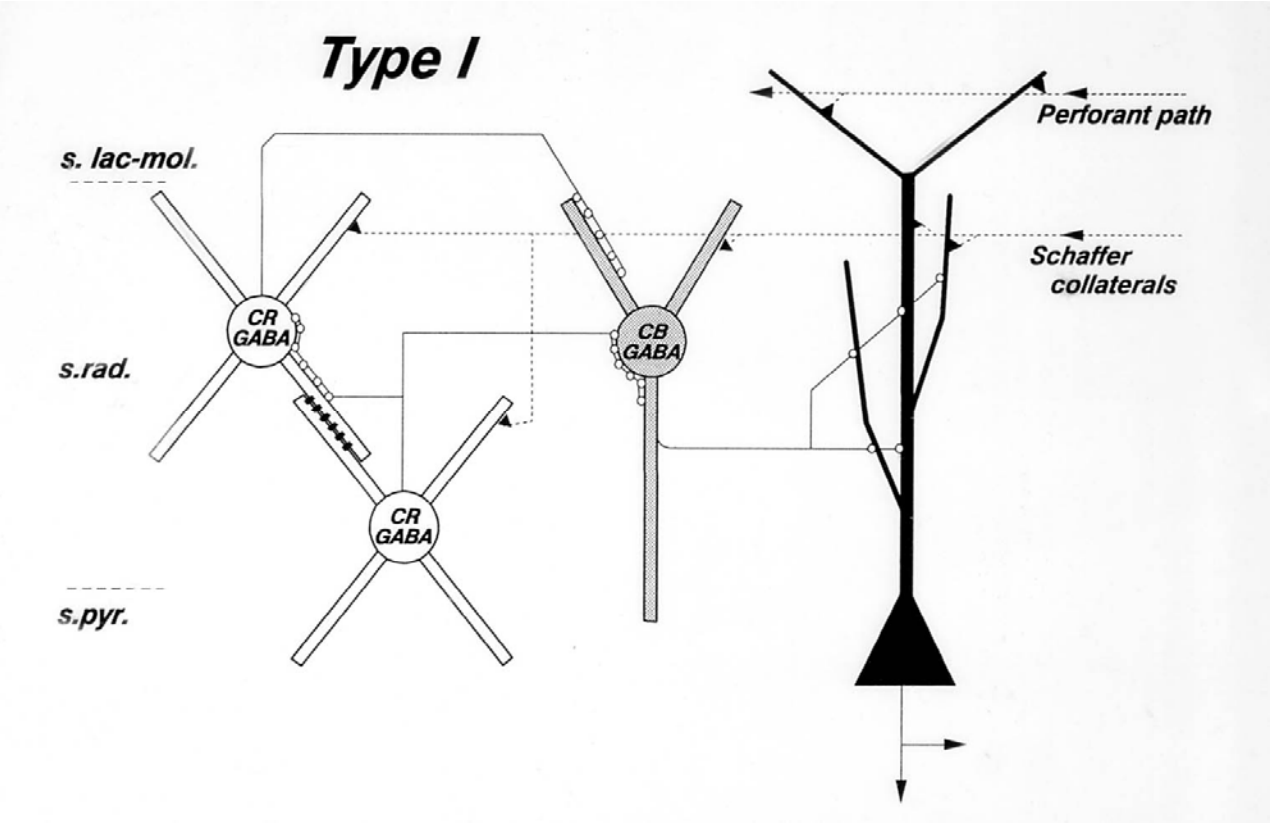
The calretinin-containing cells are GABAergic, and selectively innervate other GABAergic interneurons in the hippocampus



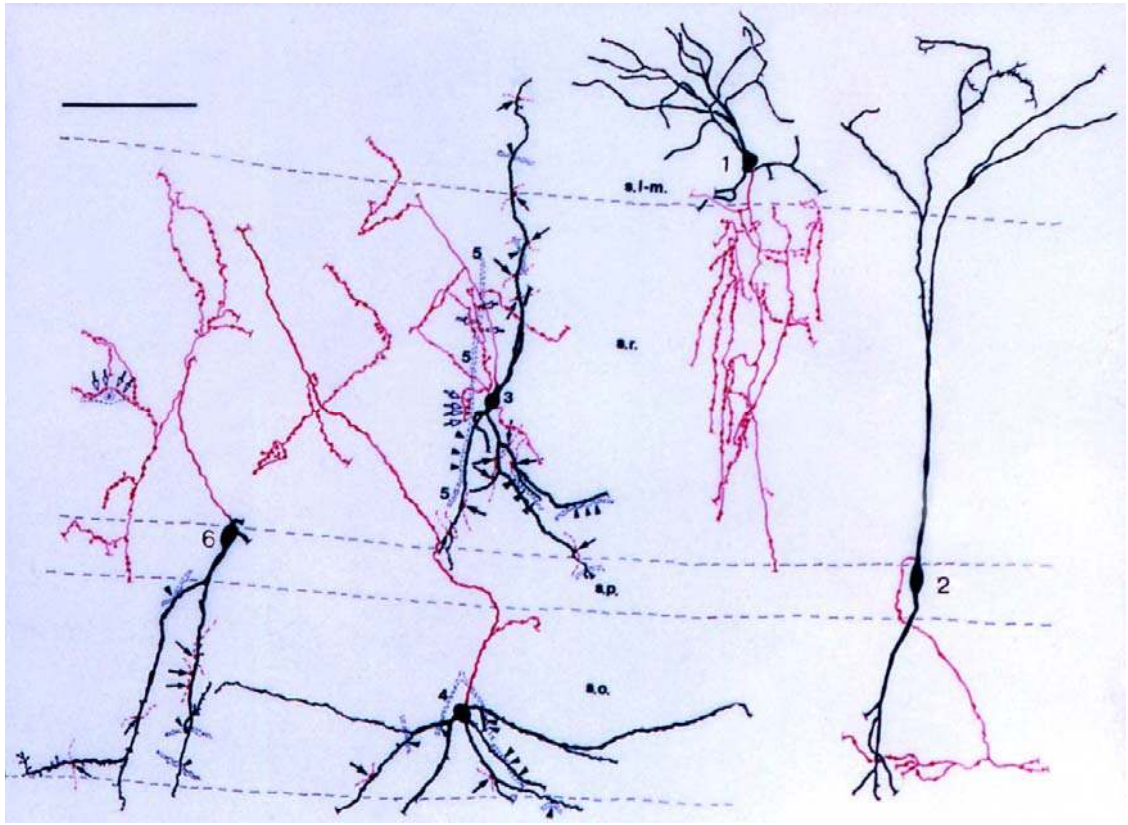


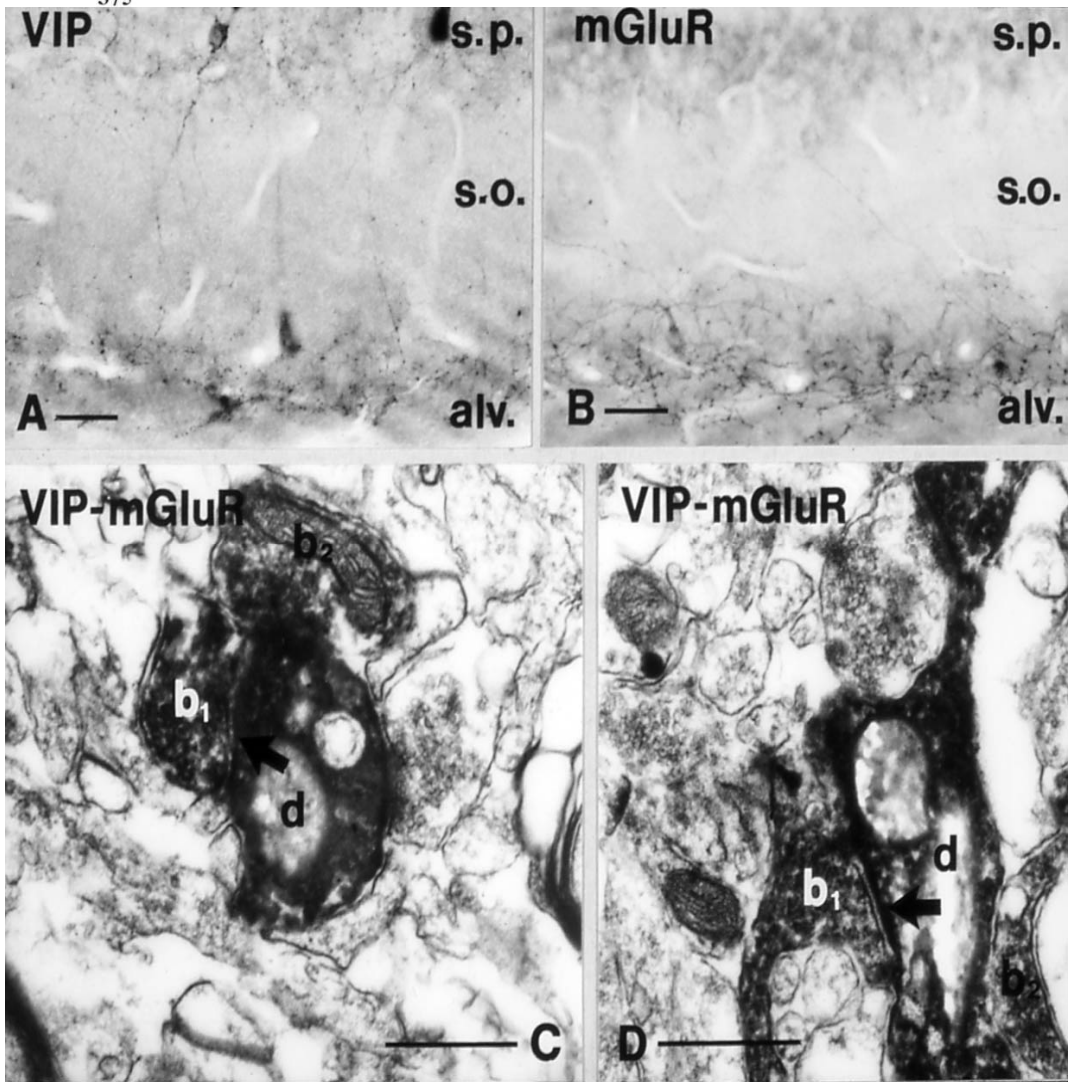
The calretinin-containing cells innervate each other abundantly, which facilitates their synchronization

Synchronization of inhibition is facilitated by the syncytial connections of calretinin-containing cells



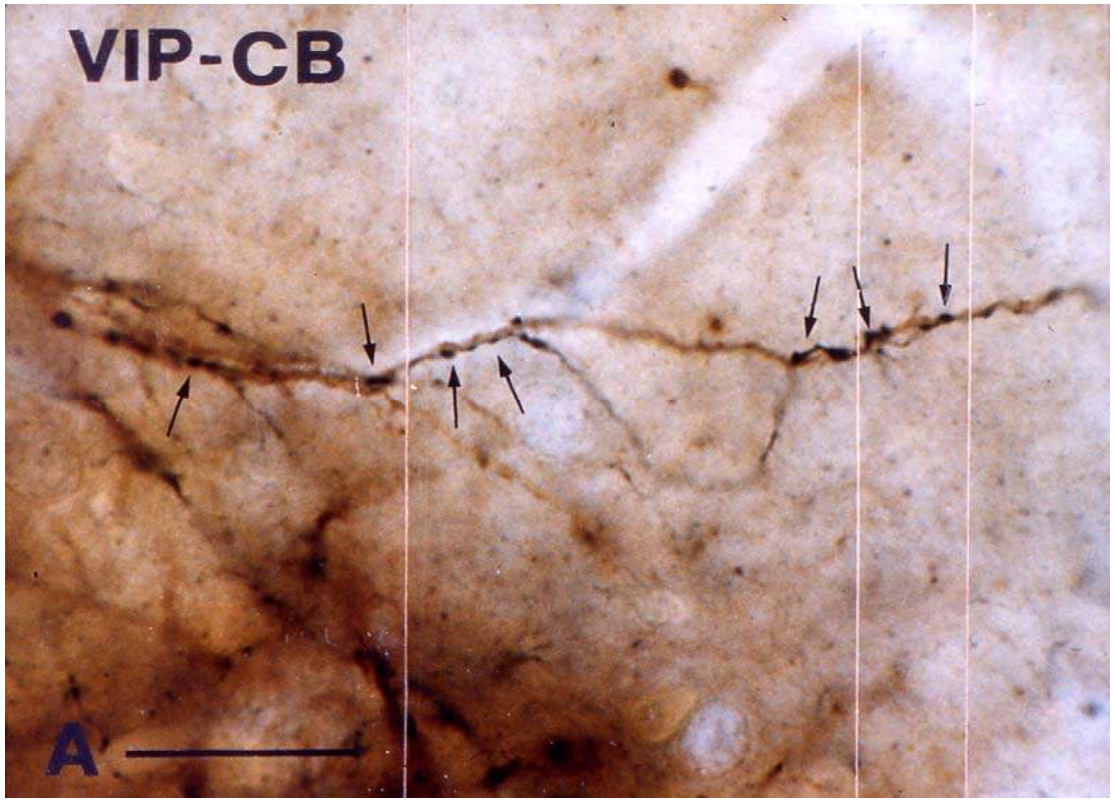
There are two subpopulations of VIP-containing GABAergic cells, which are specialised for the innervation of different inhibitory cells





VIP-containimg interneurons innervate abundantly the somatostatin-containing O-LM cells.

Axons of VIP-containing neurons (black, arrows) innervate selectively the interneurons in the str. oriens (brown, calbindin)



Hippocampal feed-back to the septum

The glutamatergic component derives from the pyramidal cells, and project to the lateral septum

The GABAergic component originates from the interneurons of the str. oriens, and projects to the medial septum