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The hippocampus (CA1, CA2 and CA3 areas and the dentate gyrus) together with the subiculum represents an associational area of the cerebral cortex intimately involved in mnemonic processes. Through its connections with other areas of the temporal lobe, the hippocampus contributes to the encoding, association, consolidation and recall of representations of the external and internal world in the combined firing rates and spike timing of glutamatergic pyramidal and granule cells. The hippocampus is thought to associate specific life events (items, episodes), on several time scales, in temporally determined firing sequences of neuronal assemblies (see chapter by Buzsaki). A single pyramidal cell can be part of several cell assemblies with different partners and contribute to different representations. Pyramidal cell assemblies are thought to be kept together and segregated from other assemblies by the dynamic strengthening and weakening of glutamatergic synaptic weights as well as by GABAergic interneurons. Interneurons generate cell domain and brain state dependent rhythmic changes in excitability, which are key for the formation, consolidation and recall of representations. Unsurprisingly, interneurons show intricate spatio-temporal diversity; e.g. the CA1 area is served by at least 21 types of resident GABAergic cell. I will attempt to allocate explicit roles for some of them, based on their previously published firing patterns *in vivo* as observed in identified neurons recorded in anaesthetised rats and on their putative equivalents in non-anaesthetised animals (Freund and Buzsaki, 1996; Somogyi and Klausberger, 2005; Klausberger and Somogyi, 2008).

Interneurons provide multiple modulatory operations, such as changing threshold, synchronisation, gain control, input scaling etc., and assist the network in the selection of pyramidal cells for cell assemblies. The spatio-temporal architecture of the network is beginning to be deciphered, but the computational roles of most of the specific synaptic links are not known beyond some general concepts. I concentrate on the spatio-temporal architecture of the *rat* hippocampus, which is by far the most extensively studied species anatomically and physiologically, although genetic engineering methods have provided key system level insights in the mouse. Events in the hippocampus need to be explained in the context of its interactions with input and output structures (Fig. 1). I often emphasise the limits of our knowledge in the hope of generating further interest in exploration and specific tests.

The hippocampus in the cortex (Fig. 1)

A parallel scheme of the hippocampus recognises a main reciprocal loop formed by projection from mainly layer III pyramidal cells of the entorhinal cortex to the subiculum/CA1 area, which project back to entorhinal cortex layer V. This primary loop is supplemented by the unidirectional loop of entorhinal mainly layer II projection to the dentate gyrus and the CA2/3 areas, the latter heavily innervating the CA1 area bilaterally (van Strien et al., 2009). The ventral hippocampus and the subiculum also innervate the prefrontal cortex, the perirhinal cortex and the amygdala in addition to widespread subcortical projections (Amaral and Lavenex, 2007; Cenquizca and Swanson, 2007). In order to analyse the factors that influence the integration of inputs by principal cells in multiple network states (for details see Buzsaki), it is necessary to have clarity about the cell types (Soltesz, 2005).

Neuron types

Two individual neurons belong to the same cell type if they deliver the same neuroactive substances to the same range of postsynaptic targets in the same temporal patterns in a brain state specific manner. Implicit in this definition is the similarity of synaptic input which allows the same input to output transformation. In an ideal case, the use of this definition requires a knowledge of the inputs, outputs, released neuroactive substances and temporal behavior of a cell in major brain states before it can be recognised. In most cases, all of this knowledge is not available for individual cells, only population data exist (Soltesz, 2005; Bota and Swanson, 2007). The population of cells however is often a mixture of distinct cell types, which means that no circuit level explanation can be obtained from the population data. Two examples illustrate this point. 1. The population of CA1 pyramidal cells project to at least 10 target areas outside CA1 (Cenquizca and Swanson, 2007), some of them are place cells, increase their firing rate during sharp wave/ripple events and some but not all of them express calbindin. It is not known if place cells include both calbindin negative and positive pyramidal cells, project to one, several or all of the 10 target areas and participate in ripple oscillations (see below). 2. The population of parvalbumin (PV) expressing GABAergic neurons innervate all postsynaptic domains of CA1 pyramidal cells from the axon initial segment to the distal tips of the apical dendritic tuft, but individual cells very specifically terminate on a restricted part of the pyramidal cell surface. Target domain selectivity is accompanied by a similar selectivity for distinct GABA release times during network oscillations. It is not possible to state if an observed result of perturbing parvalbumin cell activity is a consequence of altering a particular cell type and the resulting changed GABAergic action on a particular subcellular domain of pyramidal cells. These examples illustrate the need for caution in circuit level interpretation of network events with our rudimentary current knowledge.

Principal neurons and glutamatergic inputs (Figs. 1 & 2)

Glutamatergic inputs of different origin segregate to different parts of the dendritic tree of principal cells (van Strien et al., 2009). All glutamatergic extrinsic and intrinsic hippocampal axons innervate principal cells on dendritic spines and numerically fewer GABAergic interneurons in parallel. The CA1-3 areas have common organisational features and cellular properties with the supragranular neocortical layers, whereas the subiculum shares properties with the infragranular layers. The *CA3 pyramidal cells* ($2.5X10^5$ per hemisphere in rat) lie at the heart of hippocampal spatio-temporal organisation due to their very extensive axonal collateral system, each cell innervating a large and unknown number (estimated in the tens of thousands) of CA3, CA2, CA1 pyramidal cells and the dentate gyrus, in a topographically organised manner, bilaterally (Freund and Buzsaki, 1996). These synapses on the spines of principal cells show NMDA receptor dependent synaptic plasticity, and in the CA3 area have been proposed to play the role of pattern completion. This extensive axonal system is thought to form and store short term memories in synaptic weights. Pyramidal cells in CA3 and CA2 receive radially segregated lateral and medial perforant path inputs from *layer II glutamatergic cells of the entorhinal cortex* (appr. $1.2X10^5$ per hemisphere in rat), which also innervate dentate granule cells. In turn, *granule cells* (appr. $1.2X10^6$ in each hemisphere in rat) provide the mossy fiber input to the proximal apical dendrite of CA3, but not CA2 and CA1 pyramidal cells. Granule cells are exceptional amongst principal cells in that they do not form recurrent connections with each other and also store GABA in their terminals in addition to glutamate. The CA3 pyramidal cells closest to the hilus may not receive significant entorhinal input, and may represent a separate cell type under my definition. The dentate hilus contains the *mossy cells* which receive glutamatergic granule cell input, input from each other and hilar projecting CA3 pyramidal cells. Mossy cells innervate granule cells in the inner dentate molecular layer bilaterally.

Numerically the largest output of CA3 pyramidal cells is the bilateral Schaffer collateral/commissural pathway to *CA1 pyramidal cells* (appr. $3.8X10^5$ in each hemisphere in rat) terminating in str. oriens and radiatum in a topographical and sublaminar order (Amaral and Lavenex, 2007; van Strien et al., 2009). In str. lm., the distal apical dendritic tufts of pyramidal cells receive medial (in a septo-temporal band on the CA3 side) or lateral (in a band towards the subiculum) direct input from *layer III pyramidal cells of the entorhinal cortex* (appr. $2.5X10^5$ per hemisphere in rat) and the reuniens nucleus of the thalamus. Thus, CA1 pyramidal cells in different medio-lateral positions associate different entorhinal cortical information with parallel processed, and already combined medial and lateral

entorhinal cortical layer II, input from CA3 pyramidal cells. How these two major glutamatergic inputs cooperate in sculpting representations and discharging CA1 pyramidal cells is still not resolved, although the issue has been addressed by numerous stimulating hypotheses and models. The rhythmic firing of entorhinal and CA3 pyramidal cells in co-operative action with interneurons provides a rhythmic change in excitability of CA1 pyramidal cells during theta network oscillations. As a result, in each theta cycle (100-150 ms), the highest firing cell assembly at the trough of the pyramidal layer local field potential (LFP), represents the immediate future (next item) in a prospective manner, e.g. the next position of the animal (see chapter by Buzsaki).

The main outputs of the hippocampal formation are to the entorhinal, perirhinal and prefrontal cortices, the amygdala, the ventral striatum, the hypothalamus and the lateral septum (Amaral and Lavenex, 2007; van Strien et al., 2009). Although cognitive roles of the hippocampus are studied very extensively, a major output to the hypothalamus and the measurable functions henceforth may deserve more experimental scrutiny.

Subcortical inputs

The main thalamic input derives from the nucleus reuniens innervating the molecular layer of the subiculum and str. lm. of the CA1 area. Its role in hippocampal activity states has not been well defined. The medial septum sends a major cholinergic and GABAergic input to the hippocampus and is often considered as a pacemaker for one of the major network states, the theta rhythm. The cholinergic input synaptically innervates both interneurons and pyramidal cells and also exerts its action via non-synaptic muscarinic and nicotinic receptors. The rhythmically firing septal GABAergic neurons only innervate GABAergic interneurons of diverse types and receive GABAergic input from hippocampo-septal neurons (Freund and Buzsaki, 1996). Individual septal GABAergic neurons show various firing phases relative to the hippocampal theta rhythm and are thought to be responsible for the rhythmic inhibition of interneurons and the resulting rhythmic disinhibition of pyramidal cells (Borhegyi et al., 2004). A major outstanding question is, whether single septal GABAergic neurons innervate only those GABAergic neuron which share similar firing phases during theta. If this was the case, separate septal neuron populations with firing preference for one of at least four theta phases (trough, ascending, descending and peak) would be expected. Alternatively, or supplementing the above mechanism, a single septal GABAergic axon may innervate interneurons with diverse theta firing phases, and further intrahippocampal interactions may produce the shifts of the firing phases of different cell types. Another unresolved issue is the degree of divergence of single septal GABAergic axons to different areas of the hippocampus and the temporal lobe.

Like many other cortical areas, the hippocampal formation receives noradrenergic, dopaminergic, serotonergic, histaminergic and some orexyn containing subcortical inputs, which cannot be reviewed here. Within the serotonergic input, in addition to activating G protein coupled 5-HT receptors on principal cells and some interneurons, a subset of axons from the median raphe nucleus strongly innervate CCK/calbindin containing GABAergic neurons through excitatory 5-HT3 ionotropic receptors. It is not yet clear how 5-HT3 receptor activation contributes to interneuronal network roles.

Organising principles of GABAergic interneurons (Fig. 2, Table 1)

The co-operative action of interneurons and glutamatergic inputs provides rhythmic change in excitability during theta, gamma and ripple frequency network oscillations, which provides windows for co-ordinated pyramidal cell discharge enabling the formation of cell assemblies and representations. The term interneuron is used both for cells with exclusively local axon and for those that in addition project outside the area of their cell body location. Most interneurons receive inputs from the same extrinsic afferents that innervate their target principal cells, as well as, in a recurrent manner, from the principal cells. The weight of these two inputs may vary significantly from cell type to cell type. It is customary to describe extrinsic inputs as feed-forward and recurrent inputs as feed-back, but the presence of such connections does not mean that the action of one or the other alone leads to firing of the interneuron at any one time in the intact system. Interneurons having exclusively feed-forward (e.g. neurogliaform cell) or mainly feedback (e.g. O-LM cell) inputs are exceptional. During oscillations in a rhythmic, cyclical system with both excitatory and inhibitory inputs patterning discharge, it is not possible to delineate pure feed-back or feed-forward influences.

During a single theta cycle, a pyramidal cell assembly fires at highest rate at the trough of pyramidal layer LFP, when perisomatic inhibition is minimal but GABA release to dendrites is maximal. However, other pyramidal cell assemblies representing past and future items in a temporal sequences also fire at lower rate at earlier or later theta phases when the balance of perisomatic and dendritic GABA action is different from that at the trough of the LFP. The sequential firing of assemblies representing past, present and future items is then replayed in a time-compressed manner during high frequency ripple oscillations (see Buzsaki). Interneurons make multiple and essential contributions to temporal order and some predictions can be made about which cell types may be responsible for particular actions.

1. Interneurons are highly selective in their postsynaptic target domains, reflected in characteristic axonal shapes and laminar patterns. In addition to GABA they release cell type specific neuroactive substances, such as neuropeptides, nitric oxide and endocannabinoids. Each layer of the hippocampus contains the cell bodies of multiple groups of interneurons with different domain selectivity and molecular composition.
2. Interneurons having similar axons fire in a stereotyped, brain and network state dependent manner that differs from the firing of interneurons with different axons in at least one network state; this explains the need for independent cell types.
3. The axon initial segment of all pyramidal, granule and mossy cells receive GABAergic innervation from parvalbumin positive axo-axonic cells that generally do not innervate other domains of principal cells. Only axo-axonic cells provide significant innervation to the initial segment of principal cells. This design is unique to the cerebral cortex, and points to a specialized control of action potential generation and backpropagation. Axo-axonic cells are inhibited during sharp waves, but their inhibitory inputs are unknown.
4. The entire somato-dendritic domain is covered by two distinct sets of GABAergic synapses from neurons expressing either PV or cholecystokinin (CCK), but there are additional cell types that innervate only restricted domains and express neither of these molecules. The PV or CCK expressing cells release GABA at different preferred phases during theta oscillations.
5. Interneurons expressing CCK have high levels of CB1 cannabionid receptors on their axons and terminals, which suppresses GABA release upon the postsynaptic release of endocannabinoids evoked by depolarisation and calcium entry. Therefore, a firing postsynaptic neuron suppresses its GABAergic input from CCK expressing cells, which continue to release GABA to other innervated cells that do not fire. Such a selective reduction in inhibition of active cells increases contrast between active and inactive cell assemblies.
6. The soma and proximal dendrites of principal cells receive GABAergic innervation from three types of basket cells, which express either PV, CCK/VIP or CCK/VGLUT3. The consequences of VIP or VGLUT3 expression in the terminals of CCK positive GABAergic cells and possible differences in activity between these cells are not known.
7. Interneurons innervating the dendritic domain show the greatest diversity, pointing to a sophisticated GABAergic pre-and postsynaptic regulation of dendritic inputs and excitability. Different types of interneuron innervating the same dendrites may co-operate by synchronised action, or provide time-differentiated inputs in a given network state.
8. In the CA1 area, dendrite innervating interneurons associate their synapses mainly with one of the major glutamatergic input zones, the Schaffer collateral/commissural pathway in str. oriens and radiatum (bistratified cell, apical dendrite innervating cell, ivy cell, some projection cells), or the entorhinal/thalamic input zone in str. lm. (O-LM cell, perforant path associated cell, neurogliaform cell). This pairing of glutamatergic and GABAergic inputs provides a basis for pathway specific regulation of glutamate release by presynapic GABA and neuropeptide receptors.
9. The glutamatergic input zone segregation of GABAergic axons seem to hold for the dentate gyrus, as HIPP, MOPP and OML cells innervate the medial and lateral entorhinal input layers (Freund and Buzsaki, 1996; Ceranik et al., 1997). In turn, the HICAP cell and some CCK-expressing cells innervate the associational input zone innervated by mossy cells.

10. Less data are available on dendritic GABAergic innervation in the CA3 area. Interneurons have been shown having axonal output associated with str. oriens and radiatum (bistratified cell?), which are the CA3 pyramidal axonal input layers, or the mossy fiber input zone in str. lucidum (mossy fibre associated cell), or the entorhinal input zone (O-LM cell).
11. Some GABAergic neurons with cell bodies in CA1 also innervate the dentate gyrus, their axons freely crossing the hippocampal fissure, pointing to shared modulation of pyramidal and granule cells in as yet undefined ways.
12. Long-range projection GABAergic cells either cut across the boundaries of hippocampal areas (backprojection cells) or project outside the hippocampus proper, particularly to the subiculum (oriens-retrohippocampal cells, double projection cells, trilaminar cells, enkephalin expressing cells). Double projection cells innervating septal GABAergic cells, as well as retrohippocampal areas, also innervate pyramidal cells in str. oriens and radiatum showing similar spike timing to bistratified cells both during theta and ripple oscillations.
13. All GABAergic cells innervating pyramidal cells, except the axo-axonic cell, also make synapses with other interneurons, which may form a few percent (basket cells, bistratified cells) or up to half (trilaminar cell, enkephalin expressing cell) of their postsynaptic targets.
14. Three types of interneuron specific GABAergic cell were reported to innervate only other interneurons and express calretinin and/or VIP in the CA1 area (Freund and Buzsaki, 2006). Their network state dependent firing patterns are not known.
15. Interneurons are electrically coupled through somato-dendritic gap junctions. The selectivity of gap junctional coupling between different interneuron types remains to be tested, examples of coupling amongst PV expressing or neurogliaform cells have been documented.

Interneuron type specific contribution to rhythmic change in excitability

Assuming that information is stored in the synapses of principal cell spines, recalled and carried in their firing, it would be useful to explain how inputs are integrated to achieve the firing of hippocampal principal cells. Is the integration of several excitatory input pathways needed or can one pathway produce suprathreshold responses in a given network state or phase? Which interneurons contribute to the temporal structure of activity at a given time? A large amount of lesion, electrical stimulation, multisite recording and modelling work have addressed this question and is available in numerous reviews. Here, I consider possible mechanistic conditions necessary for pyramidal cell assembly activation in two well recognisable network states.

The theta oscillatory state (4-10 Hz) is associated with movement of the animal and REM sleep, and thought to enable encoding and recall of information and also modulates the amplitude of simultaneously occurring gamma oscillations (30-90 Hz) (O'Keefe and Nadel, 1978; Buzsaki chapter). Principal cells fire at very low average frequencies and they are silent for long periods indicating tonic inhibitory suppression. This has been demonstrated by in vivo intracellular recording and by the presence of theta-on interneurons (Freund and Buzsaki, 1996). When a pyramidal cell fires, e.g. because the animal entered the cell's place field, it can fire with high frequency bursts of action potentials modulated by the theta rhythm and phase precessing on subsequent theta cycles. The firing of entorhinal cortical layer II and III pyramidal cells is also theta modulated, phase precesses and their outputs to CA3/dentate and CA1, respectively, are phase shifted. Furthermore, theta modulated CA3 pyramidal cell firing is also phase shifted relative to average CA1 pyramidal cell firing. Therefore, there is no simple explanation of the relative contribution of the different excitatory pathways to the firing of a single principal neuron (see Buzsaki for hypothesis). It is clear however that principal cells are inhibited periodically with their lowest firing probability at the peak of the pyramidal layer theta LFP. Major contributors to this inhibition are the axo-axonic cell with maximum firing probability at the peak of theta, as observed in the anaesthetised rat. Theta modulation of basket cells has a broad tuning; the more numerous PV basket cells have maximum firing probability at the descending phase, whereas CCK basket cells fire at the ascending phase of theta. The combined output of basket cells weighted by their relative numbers also has a maximum at the peak of theta. Thus, a cooperative action of the four perisomatically terminating GABAergic cells reduces pyramidal cell firing at the peak of theta, the axo-axonic cells probably playing the major role (Klausberger and Somogyi, 2008).

In contrast to the perisomatic innervating cells, dendrite innervating bistratified, O-LM, ivy and projection GABAergic cells fire maximally at the trough of theta when pyramidal cells also have the highest firing probability. The dendritic GABAergic inputs increase the threshold, provide gamma frequency phasing of excitatory inputs, synchronise dendritic spikes and scale glutamatergic inputs via post- and presynaptic receptors. An example of the latter is NPY expression and likely release by bistratified and ivy cells acting on inhibitory presynaptic Y2 receptors on CA3 pyramidal cell terminals. The theta modulated GABAergic input to the most distal dendrites in str. lm. by O-LM cells contributes to the phase reversal of dendritic oscillations in the apical dendrites relative to the soma. The maximal discharge of double projection cells at the trough of theta innervating septal GABAergic neurons may help to set up the reciprocal oscillatory loop with the septum. Long-range theta modulated GABAergic output to the subiculum, the retrosplenial cortex and other related cortical areas by oriens- and radiatum-retorhippocampal cells contributes to the coherence of oscillations across different areas.

The second well defined network state is the synchronised discharge of pyramidal cells producing the *sharp wave* field potential (see chapter by Buzsaki) most easily seen in str. radiatum of the CA1 area and an associated ripple oscillation (140-200 Hz) in the pyramidal cell layer for about 50-100 ms (O'Keefe and Nadel 1978). The sharp wave/ripple event is driven by the synchronous discharge of CA3 pyramidal cells. The frequency of the event is modulated by the cortical up and down states, being more frequent in the first half of the up state. Sharp wave/ripple events also occur during awake consummatory behaviour and in short gaps in theta activity. What initiates sharp wave ripple events is not known, but Buzsaki (1989) suggested that a sudden drop in inhibition allows initiator pyramidal cells to trigger the replay of cell assembly sequences via glutamatergic synaptic links potentiated during encoding. Indeed, withdrawal of inhibition by the silencing of axo-axonic and O-LM has been demonstrated during ripple oscillations in CA1. Some CCK expressing and other GABAergic cells are also silent during some of the ripples (Fig. 2, and Klausberger and Somogyi, 2008). Particularly, the withdrawal of GABAergic inhibition from the axon initial segment may be crucial and causally linked to the development of synchronised pyramidal cell discharge in CA1. It remains to be tested if the same mechanism might also operate in other cortical areas involved in the sharp wave/ripple event. During the event, pyramidal cell spikes are phase locked to the trough of the ripple, which results in synchronised glutamate release to downstream targets. Such synchronisation is probably achieved by the ripple frequency phase locked firing of PV expressing basket and bistratified, as well as by trilaminar, double projection and some CCK expressing cells (Klausberger and Somogyi, 2008). The highest firing probability of PV basket and bistratified cells is just after the pyramidal cells on the rising phase of the ripple cycle. Thus pyramidal cell maximal firing at the trough is linked to a ripple periodic reduction in GABA release to the soma, the small oblique dendrites in str. radiatum and the basal dendrites. The rhythmic, phase locked firing of these two specific types of interneuron is consistent with their ability to temporally structure pyramidal cell discharge with ms accuracy.

The participation of the dendrite innervating bistratified cells is of particular significance in view of the ability of small oblique and basal dendrites to generate sodium spikes (Freund and Buzsaki, 1996; Losonczy et al., 2008). An oblique dendrite may receive about 600 glutamatergic and 25 GABAergic synapses; the latter number is about a quarter of GABAergic synapses on the entire soma (Megias et al., 2001) and comes from several cell types. The bistratified cells, which start to increase their firing during ripples earlier than the pyramidal cells that they innervate, are in prime position to synchronise dendritic electrogenesis within the same cell and between cells during ripples. Their main glutamatergic inputs are from CA3 and CA1 pyramidal cells (Ali et al., 1998). Bistratified cells probably release somatostatin and NPY with inhibitory effects; the latter, suppressing glutamate release from CA3 terminals via presynaptic Y2 receptors, which may contribute to the termination of ripples. Interestingly, amongst interneurons in the CA1 area, bistratified cells are most strongly coupled to gamma frequency LFP oscillations, the latter initiated by CA3 pyramidal cell discharge. Thus, bistratified cells mediate CA3 driven fast rhythmic GABAergic phasing of basal and small oblique dendrite excitability at both gamma and ripple frequencies. During ripples bistratified cells are joined by trilaminar and double projection cells which also discharge at ripple frequencies and innervate basal and oblique dendrites. This is a further example of cooperative action by several types of interneuron during a particular network state.

The above examples illustrate the need for the existence of numerous specific types of interneuron supporting the network to deliver temporally modulated pyramidal cell activity patterns. Complex though it may seem, our understanding of the system is still sketchy and most components have been described only qualitatively. E.g. the inputs of most interneurons are poorly known and some of them are completely unknown; consequently many of the proposals above are speculative and require imaginative experimental testing providing fertile ground for discovery.

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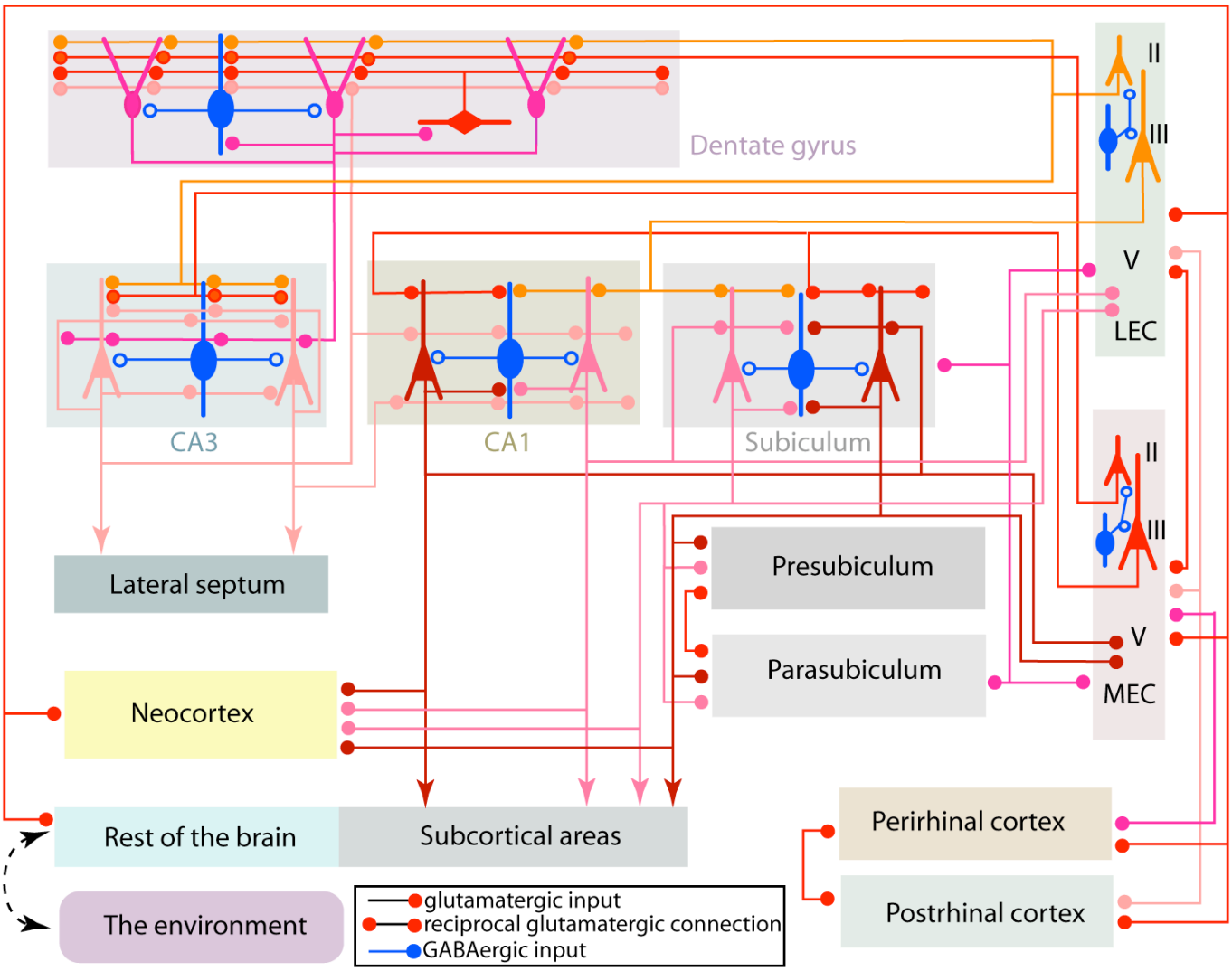
GABAergic interneuron							
Group	No	Suggested name (1)	Localized proteins useful for recognition (2,3)	CA1	CA3	dentate gyrus	To mossy cells
Soma, perisomatic innervating	1	axo-axonic	parvalbumin, sdm, a; GABA-A-R-a1 low, sdm	✔	✔	✔	✔
	2	basket	parvalbumin, sdm, a; GABA-A-R-a1 high, sdm	✔	✔	✔	not
	3	basket	CCK, s, a; VIP, s, a; CB1, a	✔	✔	✔	✔
	4	basket	CCK, s, a; VGLUT3, a; CB1, a	✔	✔	✔	✔
Stratum radiatum and oriens innervating	5	bistratified	parvalbumin, sdm SM, s, a; NPY s, a	✔	(✔)	?	?
	6	ivy	nNOS, s a; NPY, s GABA-ARa1, sdm	✔	✔	?	?
	7	Schaffer collateral associated	CCK, s, a; CB, s; CB1, a	✔	?	n.a.	n.a.
	8	apical dendrite innervating	CCK, s, a; VGLUT3, a; CB1, a	✔	?	n.a.	n.a.
	9	large calbindin	calbindin, sd, a	✔	?	?	?
	10	cholinergic	ChAT, sd, a; vAChT, a	✔	✔	?	?
Sratum lacunosum moleculare innervating	11	O-LM	SM, s, a; mGluR1a strong, sdm mGluR7a, it	✔	✔	✔, HIPP (4)	?
	12	perforant path associated	CCK, s, a; calbindin, s; CB1, a	✔	()	(✔) MOPP (5)	not
	13	neurogliaform	NPY, s; nNOS, s; alpha-actinin-2, s	✔	✔	?	?
Projection cells	14	radiatum retrohippocampal	M2 receptor, sdm; mGluR1a weak, sdm	✔	?	?	?
	15	trilaminar cell	M2 rec. strong, sdm; mGluR8a, it	✔	✔	?	?
	16	backprojection cell	?	✔	(✔)	?	?
	17	oriens retrohippocampal	calbindin, sd; M2 rec., sdm	✔	?	?	?
	18	double projection	calbindin, sd; SM, s; NPY, s; mGluR1a, sdm; mGluR7a, it	✔	✔	?	?
Interneuron specific cells	19	interneuron specific I.	calretinin, sd; mGluR1a weak		(✔)	?	?
	20	interneuron specific II.	VIP, s, a; mGluR1a weak	✔	(✔)	?	?
	21	interneuron specific III.	VIP, s, a; calretinin, sd, a; mGluR1a weak	✔	(✔)	?	?
	22	enkephalin expressing	ENK, s; VIP, s; mGluR1a weak, sdm	✔	(✔)	?	?
Regional projection	23	large nNOS positive	nNOS strong, sd, a; NPY, s, a	✔		?	?
	24	OML, outer molecular layer (6)	?	n.a.	n.a.	✔	n.a.
	25	CA3 hilar projection (7)	SM, s; NPY, s; mGluR1a, sdm	(✔)	(✔)	✔	?
CA3/dentate specialized cells	26	mossy fiber associated	CCK, s, a; CB1, a	n.a.	✔	?	(✔)
	27	densely spiny	calretinin, sd; NPY, s; SM, s	n.a.	✔	✔	?
	28	HICAP, hillar commissural assciational path assoc.	?	n.a.	n.a.	✔	?

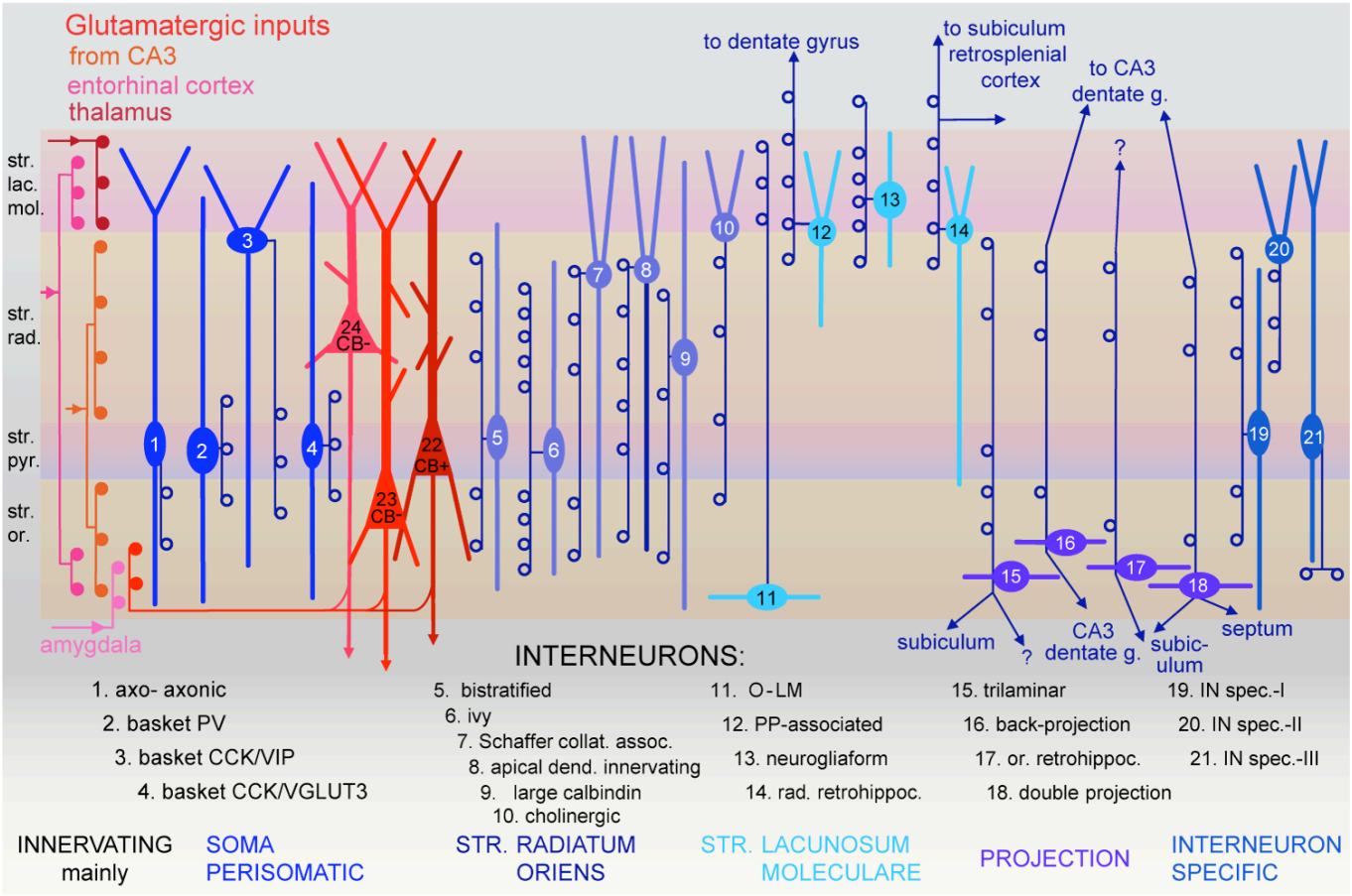
✔, strong evidence as a cell type; (✔), suggestive evidence, not proven; ?, not known; n.a., not applicable; sdm, somato-dendritic membrane; sd, soma and dendrite; a, axon; it, input terminals on soma and dendrite.

Table 1. Distribution of interneuron types across hippocampal areas and some molecules that in combination are useful for their grouping and/or recognition. Molecular combinations alone without information on synaptic input/output relationships are weak predictors of a cell type. The presence of some molecules in a single cell are mutually exclusive, but this is not indicated here. The same names and numbering are used as in figure 1; additional cell types are added here. The CA2 region is not listed separately, as the axons of many interneurons in the CA3 and to a lesser extent those in the CA1 area also innervate CA2. Interneurons mostly innervating only CA2 pyramidal cells also exist. Due to restrictions on references individual papers cannot be cited describing each result.
(1) Cell types with very partial characterisation may be absorbed into other cell types with further analysis.
(2) The subcellular locations of the highest concentration of molecular markers are indicated, but in some cases they may be present in other compartments as well.
(3) The listed molecules may not be detectable in every individual member of a cell type.
(4) I suggest that the HIPP cell (hilar perforant path associated) is homologous to the O-LM cells in the CA1 and CA3 regions in its hippocampal spatio-temporal position and role, although, unlike the O-LM cells, HIPP cells also project to the contralateral dentate gyrus.
(5) The MOPP cell (molecular layer perforant path associated) may correspond to perforant path associated cells of the CA1 area.
(6) Projects from the dentate outer molecular layer to the subiculum across the fissure.
(7) Projects from the CA3 area and the hilus to the septum with no other known long-range projection.



Somogyi fig. 1.

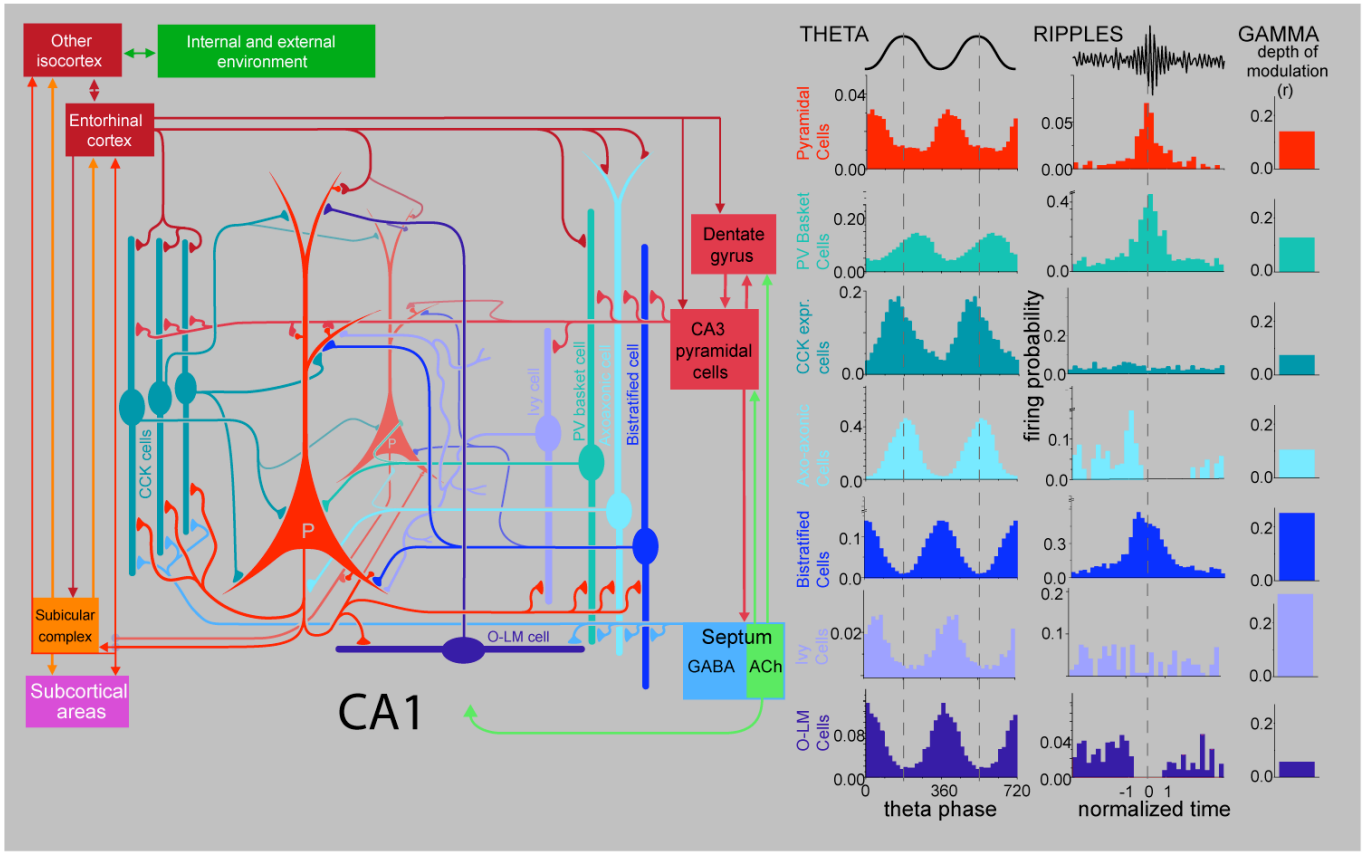
Fig. 1. Cortical relationships of the hippocampal formation.
Simplified schematic diagram based on data reviewed by van Strien et al. (2009). The main features are: 1. Glutamatergic inputs of different origins are segregated on the dendrites. 2. All external and internal glutamatergic pathways (shades of red) innervate both principal cells (pyramidal and granule) and GABAergic interneurons (blue). 3. The dentate gyrus and the CA3 area receive radially segregated layer II inputs from both the medial (MEC) and lateral (LEC) entorhinal cortex. 4. The combined and dentate/CA3 processed MEC and LEC information is transmitted to CA1 pyramidal cells. 5. The MEC and LEC are in reciprocal connections with different segments of the CA1 area and the subiculum, which however receive processed information from both MEC and LEC via the CA3 input. 6. Segments of the CA1 area innervate appropriate segments of the subiculum and either the lateral or medial entorhinal cortex. 7. Inter-areal GABAergic projections from the hippocampus to temporal lobe and the septum, from the perirhinal cortex to LEC and from the presubiculum to MEC are not shown.
Only one schematic interneuron is indicated and only some of the pyramidal cells and a limited number of connections are shown. Recurrent connections between pyramidal cells are only shown in the CA3 area. A mossy cell in the dentate gyrus is shown (red diamond). Numbers II, III and V in MEC and LEC denote layers.



Somogyi Fig. 2.

Fig. 2. Three types of pyramidal cell are served by at least 21 types of GABAergic interneuron in the CA1 area.

The laminar termination of five glutamatergic inputs are indicated on the left (boutons filled circles). Pyramidal cells are red, those located closer to str. radiatum express calbinin (CB+), the larger more loosely arranged cells towards str. oriens are calbindin negative as are those in str. radiatum that project to the accessory olfactory bulb. The somata and dendrites of interneurons are blue, cells 1-18 innervate pyramidal cells and interneurons to some degrees; cells 19-21 innervate mainly or exclusively other interneurons. Axons and the main synaptic terminations (boutons, open circles) are dark blue. Note the association of the output synapses of different sets of interneuron with the perisomatic region of pyramidal cells (left), and either the Schaffer collateral/commissural or the entorhinal pathway termination zones (right), respectively. Projection GABAergic neurons send long-range axons to related areas of the temporal lobe or the septum. Not all interneurons fit these categories (not shown). Abbreviations: str., stratum; lac. mol., lacunosum moleculare; pyr., pyramidale; or., oriens; g., gyrus; O-LM, oriens lacunosum-moleculare; PP, perforant path; retrohippoc., retrohippocampal projecting; IN spec., interneuron specific.



Somogyi Fig. 3.

Fig. 3. Spatio-temporal interaction between pyramidal cells and eight types of interneuron during network oscillations

Schematic summary of the main synaptic connections of pyramidal cells (P), three types of CCK-expressing cells, ivy cells and PV-expressing basket, axo-axonic, bistratified and O-LM interneurons. The firing probability histograms are averages from several cells of the same type; note different scales for the Y axis. Interneurons innervating different domains of pyramidal cells fire with distinct temporal patterns during theta and ripple oscillations. Their spike timing is coupled to field gamma oscillations to varying degrees (averages of several cells each type). The same somatic and dendritic domains receive differentially timed input from several types of GABAergic interneuron; e.g. CCK- and PV-expressing cells. Note that pyramidal cell firing probability is lowest at the peak of the pyramidal layer *theta* local field potential (LFP), when axo-axonic cells, which have the highest mean peak firing probability, fire maximally and the sum of CCK basket and PV basket cell firing probabilities are maximal. Therefore, the co-operative action of these three cell types cause a rhythmic lowering of pyramidal cell firing at the peak of theta and an increase in LFP *gamma oscillation*. Note also the similar theta phase coupling of dendrite innervating cells, roughly counter-phased with the perisomatic innervating cells, and the high gamma coupling of bistratified and ivy cells innervating basal and small oblique pyramidal cell dendrites. During *ripple oscillations,* axo-axonic cell GABA release to the axon initial segments is withdrawn, allowing maximal pyramidal cell discharge synchronized by PV basket and bistratified cells. Synaptic and electrical connections between interneurons are not shown for clarity, but most interneurons innervate other interneurons in addition to pyramidal cells (Freund and Buzsaki, 1996; Somogyi and Klausberger 1995; Klausberger and Somogyi, 2008).