BM3000
Foundations of Natural Intelligence

Emergence of gamma oscillations

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Gamma oscillations are network oscillations with a frequency between 30-90 Hz. An essential requirement for generating network oscillations is regular and synchronized neuronal activity. If a neuron traditionally fires action potentials, rhythmic activation of output synapses generates a periodic fluctuation in the intracellular membrane potential of all postsynaptic target cells. If several neurons fire action potentials regularly and synchronously, this fluctuating output signal is amplified, defining temporal windows of increased and reduced excitability in a larger population of target cells. The divergence of synaptic connections leads to a high spatial coherence of network oscillations. Although gamma oscillations occur in all cortical areas, they have been well-studied in the hippocampus,

Gamma oscillations can be evoked in-vitro by agonists of various metabotropic or ionotropic receptors. They can also be induced through the application of a potassium-rich solution. Potassium-induced oscillations in the CA1 and CA3 regions have intermediate properties, as GABAA receptor antagonists completely block them but are only partially inhibited by AMPA receptor blockers. Gamma oscillations can also be evoked in the dentate gyrus, entorhinal cortex, and somatosensory cortex27, although the underlying mechanisms have been less well investigated. GABA-mediated inhibition is necessary and sufficient for generating gamma oscillations induced by mGluR or kainate receptor activation. Application of a potassium-rich solution is likely to depolarize both interneurons and principal cells, and therefore potassium-induced oscillations have intermediate properties. mGluR- and kainate-receptor-dependent forms of gamma oscillation rely exclusively on fast inhibition mediated by GABAA receptors. mAChR-dependent types of oscillation require both fast inhibition and rapid excitation. Although the diversity of in vitro forms of gamma oscillation might be unsatisfying from a reductionist perspective, all of these forms are likely to be relevant in vivo, possibly reflecting region and state-dependence of mechanisms underlying hippocampal gamma oscillations.

In the presence of short delays, fast inhibition consistently supports synchronization, independently of whether delays are assumed to be constant or distance-dependent. Models based on shunting inhibition generate coherent gamma oscillations in a large region of the parameter space of mean tonic excitatory drive (Iμ) and synaptic peak conductance (g_{syn}), also covering experimental estimates of g_{syn}. Furthermore, they generate oscillations with greatly increased robustness against heterogeneity in the tonic excitatory drive. In comparison to the interneuron networks based on slow, weak and hyperpolarizing synapses, networks with fast, strong and shunting synapses tolerate a tenfold higher level of heterogeneity, up to ~70% .

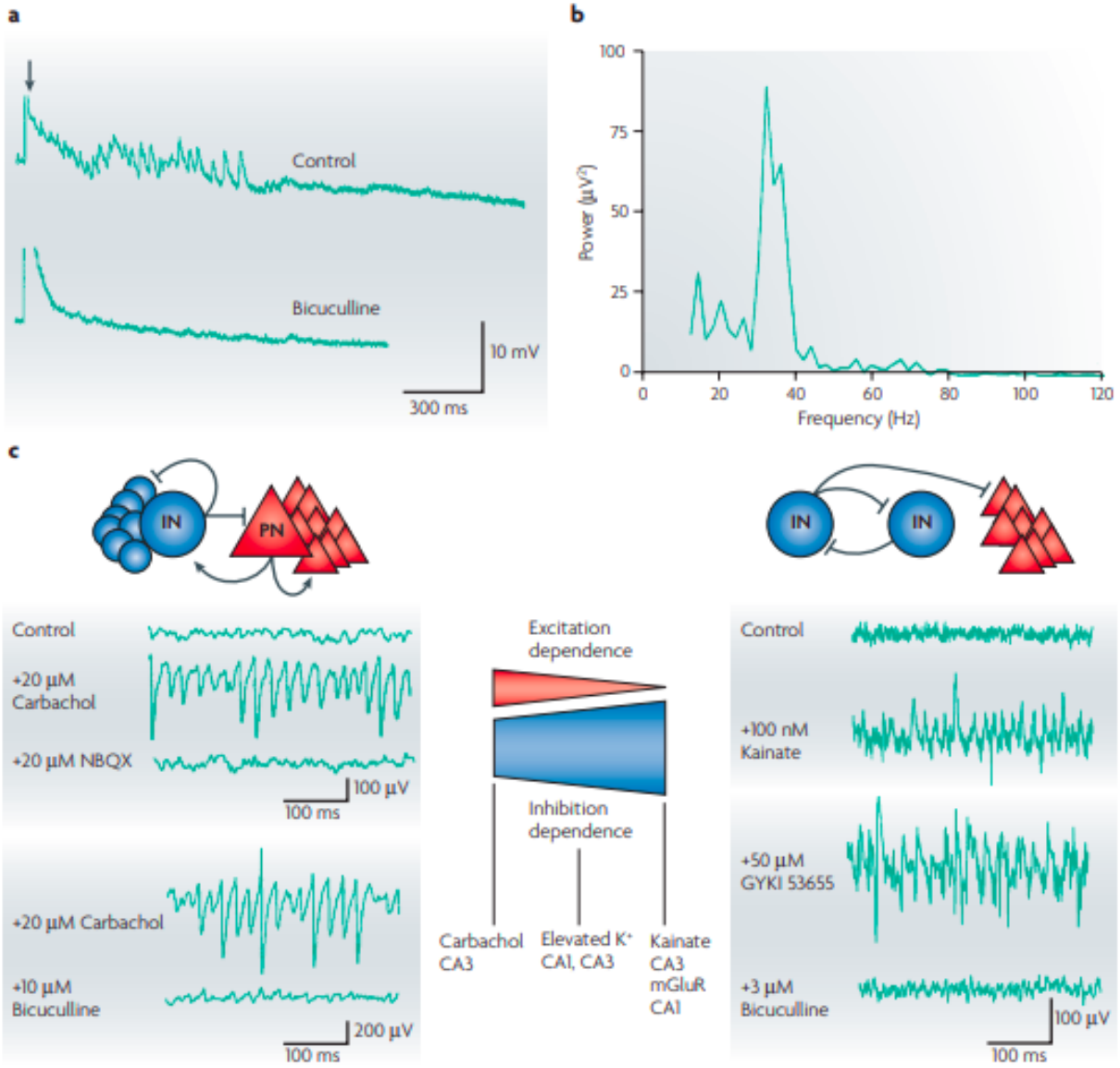

Figure 1 | **Networks of GABA-containing interneurons generate gamma oscillations *in vitro*. a** | Gamma oscillations in the hippocampal CA1 region evoked by tetanic stimulation (arrow) through activation of metabotropic glutamate receptors (mGluRs) *in vitro*. Gamma oscillatory activity was measured by whole-cell recording from a CA1 pyramidal neuron. Oscillations are blocked by the $GABA_A$ (GABA type A) receptor antagonist bicuculline. **b** | Power spectrum of the oscillations, showing the maximum at ~40 Hz. Similar oscillations can be recorded in the presence of blockers of fast excitatory synaptic transmission. **c** | Gamma activity in the hippocampus evoked by ionotropic or metabotropic receptor agonists *in vitro*. Left panel, carbachol-induced gamma oscillations in the CA3 subfield are blocked by both the AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid) receptor antagonist NBQX (2,3-dioxo-6-nitro-1,2,3,4-tetrahydrobenzo[f]quinoxaline-7-sulphonamide) and the $GABA_A$ receptor antagonist bicuculline. Right panel, kainate-induced gamma oscillations in the CA3 region are insensitive to the AMPA receptor antagonist GYKI 53655, but abolished by bicuculline. Gamma oscillatory activity was investigated with extracellular field potential recording. The schemes above the panels indicate putative mechanisms of gamma activity (IN, interneuron; PN, principal neuron). The red triangle and blue trapezoid (center) illustrate the relative dependence of oscillations on fast excitatory and inhibitory synaptic transmission in different paradigms. Panels **a** and **b** reproduced, with permission, from *Nature* REF. 17 © (1995) Macmillan Publishers Ltd. Panel **c** (left) reproduced, with permission, from *Nature* REF. 18 © (1998) Macmillan Publishers Ltd. Panel **c** (right) reproduced, with permission, from REF. 21 © (2004) Society for Neuroscience.

To generate gamma waves, The simplest possible model is a system of two synaptically connected neurons. If single neurons are described by integrate-and-fire models their synchronization properties can be determined analytically. All of these studies concluded that inhibitory interneuron networks can generate coherent oscillations in the gamma frequency range if the neurons are exposed to a tonic excitatory drive.

The two population model:

In the absence of chemical synapses, gap junctions can lead to synchronized activity in network models if the tonic excitatory drive is homogeneous. Modeling has shown that the propagation of both suprathreshold and subthreshold electrical events (including after hyperpolarizations) is important for the synchronizing effect of gap junctions. The two-population model of principal neurons (PNs) and interneurons (INs) contains four types of chemical synapse (IN–IN, PN–IN, IN–PN and PN–PN synapses). In addition, electrical synapses (for example, IN–IN and presumably PN–PN synapses via axo-axonic gap junctions) have to be considered. Although the full model is extremely complex, two limiting cases have been defined. In the first case, in which only chemical IN–IN and IN–PN synapses are present, the behavior of the PN–IN network approaches that of the pure interneuron network. In the second case, in which only PN–IN and IN–PN synapses are included, the behavior of the PN–IN network approaches that of a modified interneuron network, in which short-delay, monosynaptic inhibitory connections (IN–IN) are replaced by long-delay, disynaptic inhibitory connections (PN–IN–PN). Intriguingly, the full PN–IN network model can reproduce the activity pattern that is seen in interneurons (high frequency and high coherence) and principal cells (low frequency and low coherence; I.V., M.B. and P.J., unpublished observations) during gamma oscillations in-vitro and i- vivo.

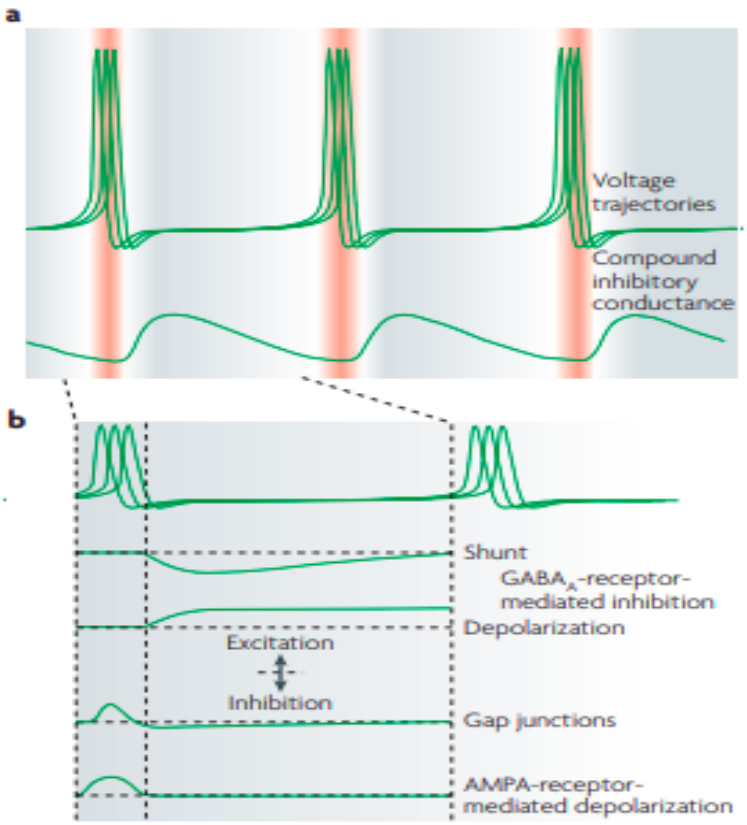

Figure 6 | **Several synaptic mechanisms underlie synchronization in interneuron networks during gamma oscillations.** Schematic summary of the contribution of different synaptic mechanisms to synchronization in oscillating interneuron networks. **a** | Voltage trajectories in three representative neurons and mean $GABA_A$ (GABA type A)-receptor-mediated compound inhibitory conductance in an oscillating interneuron network[68]. Temporal windows of high excitability (red) and low excitability (grey) follow in an alternating manner. **b** | Expanded view of one oscillation cycle, plotted together with the corresponding effects of $GABA_A$-receptor-mediated shunt, $GABA_A$-receptor-mediated depolarization, gap junction coupling, and AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid)-receptor-mediated depolarization (positive values, excitatory effect; negative values, inhibitory effect; arbitrary scaling in vertical direction). Note that the $GABA_A$-receptor-mediated shunt defines windows of low excitability, whereas the other three mechanisms define windows of high excitability.