desynchronized and high frequency, whereas the latter is characterized by slow wave rhythms and is associated with a lack of activity in the acetylcholine-containing parabrachial terminals. In non-REM (slow-wave) sleep, inhibition is strongly active and a cycle of excitation and inhibition creates large rhythmic potentials in the thalamus and cortex. The effect of acetylcholine inhibits the inhibitory cells in the thalamus and excites the excitatory cells. This paradoxical action occurs because the two cells have different receptors for acetylcholine. As a result, the inhibitory cells are relatively inhibited and thus cannot contribute the inhibition that is necessary to maintain the rhythm.

In other neurons (e.g. in the olfactory bulb), noradrenaline (norepinephrine) reduces the release of inhibitory neurotransmitter. Noradrenaline and acetylcholine are also modulators of the intrinsic inhibition involved in firing frequency adaptation. Noradrenaline acts on channels that make the membrane slightly more negative, so potentiating the strength of adaptation. However, it also blocks firing frequency adaptation by blocking the activation of the membrane channels that normally open and act to slow the firing frequency. Acetylcholine has a similar effect. Both of these neurotransmitters are produced by neurons that form the diffusely projecting systems of the brain. Since these systems produce their relatively long-duration effects over a wide area of brain, they are probably involved in processes that alter the state of arousal or vigilance.

Further Reading

Evarts EV, Wise SP and Bousfield D (eds) (1985) *The Motor System in Neurobiology*. Amsterdam: Elsevier Medical Press.

Koch C (1999) *Biophysics of Computation*. New York: Oxford University Press.

Mize RR, Marc RE and Sillito AM (eds) (1992) *GABA in the Retina and Central Visual System. Progress in Brain Research*, vol. 90. Amsterdam: Elsevier Science Publishers.

Nicholls JG, Martin AR and Wallace BG (eds) (1992) *From Neuron to Brain*, 3rd edn. Sunderland, MA: Sinauer Assoc.

Shepherd GM (ed.) (1998) *The Synaptic Organization of the Brain*, 4th edn. New York: Oxford University Press.

Neural Oscillations

Intermediate article

Xiao-Jing Wang, Brandeis University, Waltham, Massachusetts, USA

CONTENTS

Oscillations represent a general feature of neural firing patterns, produced by dynamical interplay between cellular and synaptic mechanisms. Large-scale synchronous neural population rhythms reflect different behavioral states, play a role in neural synchronization that contributes to the neuronal encoding of sensory stimuli, or may be correlated with cognitive processes such as attention and working memory.

INTRODUCTION

Integrative operations in the brain involve coordinated neural firing patterns in large-scale neural networks. Ever since Hans Berger discovered distinct electroencephalogram (EEG) wave patterns in sleep and waking states in 1929, synchronous brain rhythms have been recognized as one of the most conspicuous types of neural population dynamics. Describing a 'mathematical outlook' of the cortex, Charles C. Sherrington wrote a half-century ago:

> A scheme of lines and nodal points, gathered together at one end into a great ravelled knot, the brain, and at the other trailing off to a sort of stalk, the spinal cord. Imagine activity in this shown by little points of light. Of these some stationary flash rhythmically, faster or slower. Others are travelling points, streaming in serial trains at various speeds. The rhythmic stationary lights lie at the nodes. The nodes are both goals whither converge, and junctions whence diverge, the lines of travelling lights. (Sherrington, 1951, p. 176)

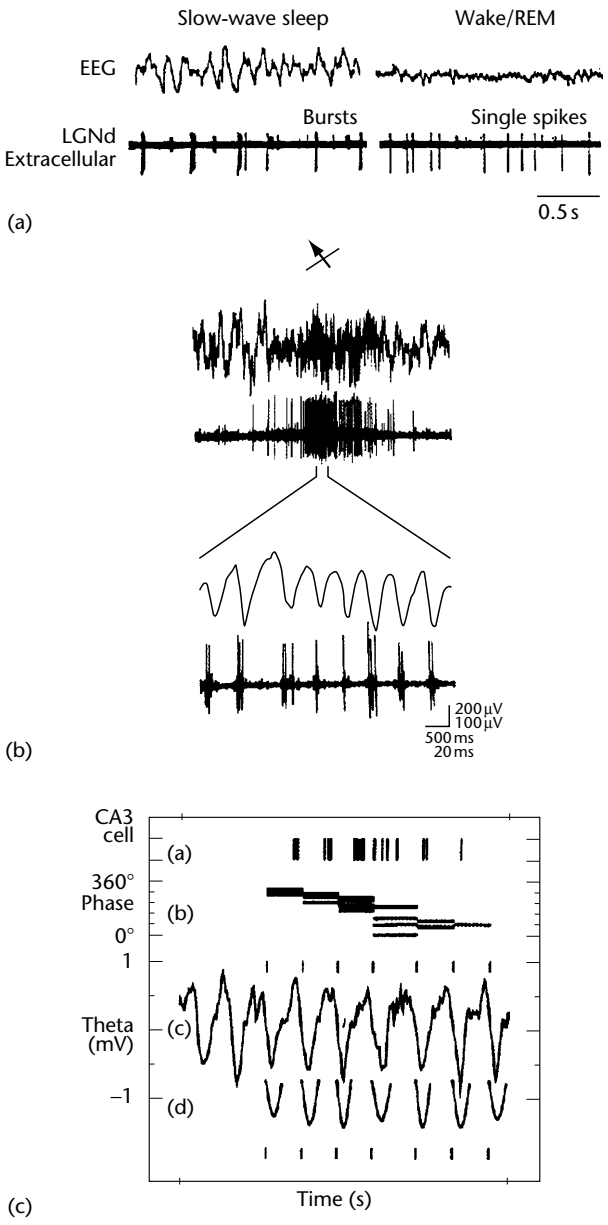

Figure 1. Neural rhythms correlated with behavior. (a) During slow-wave sleep, EEG shows slow synchronous oscillations and thalamic neurons in the dorsal lateral geniculate nucleus (LGNd) fire bursts of action potentials (left panels). In contrast, during waking or dreaming sleep (waking/REM), large-amplitude EEG oscillations are absent, and thalamic neurons fire single spikes tonically (right panels). Adapted from McCarley RW, Benoit O and Barrionuevo G (1983) *Journal of Neurophysiology* **50**: 798–818. (b) Multi-unit and local field potential from the cat primary visual cortex, in response to an optimally oriented light bar stimulus. In the upper two traces, the onset of the response is associated with an increase in *c.* 40 Hz oscillations, which are shown at an expanded timescale in the lower two panels. From Gray CM and Singer W (1989) *Proceedings of the National Academy of Sciences of the USA* **86**: 1698–1702. (c) Burst firing pattern of a hippocampal place cell and its relationship to the EEG theta rhythm as the rat runs through the place field on a narrow linear track. Upper panel: each spike is represented as a single vertical line. Middle panel: the phase of each spike relative to the theta cycle within which it falls is represented by a horizontal line. Lower panel: hippocampal theta rhythm is recorded at the same time as the neural spikes. Note that each successive burst moves to an earlier phase of the theta cycle than the previous burst, as shown by the descending staircase of the phase correlates in the middle panel. Adapted from O'Keefe J and Recces ML (1993) *Hippocampus* **3**: 317–330.

Today, there is a resurgence of interest in brain rhythms for two reasons. First, it is now known that neural rhythms occur in alert and behaving states (as well as in sleep), and that they may play important roles in cortical functions. Secondly, technical advances have led to significant progress in the elucidation of the cellular and synaptic mechanisms of these rhythms.

Broadly speaking, there are three categories of brain rhythms.

1. *Spontaneous rhythms* occur in brain states characterized by the absence of sensory inputs. These spontaneously occurring oscillations usually have low frequencies (< 15 Hz), and are remarkable for their large-scale synchronization across brain structures, detectable as large-amplitude brain waves by the EEG. Examples include the spindle rhythm (4–12 Hz) and delta rhythm (3–4 Hz) in the thalamocortical system, which are the hallmarks of non-dreaming sleep and disappear during dreaming sleep or wakefulness (Figure 1(a)). Spindle and delta rhythms are often temporally nested with another very slow rhythm (< 1 Hz).
2. *Induced rhythms* have been observed in waking states. They are typically evoked by external sensory stimulation and correlated with certain behaviors. In the olfactory bulb, fast synchronous oscillations (gamma at 30–60 Hz) can be induced by olfactory stimulation. For a given odor stimulus, the 'induced rhythm' (so named by E. D. Adrian, who discovered it) is synchronized transiently, in time (for a few hundreds of milliseconds), and only among a neural subpopulation which is selectively responsive to that particular odorant. Similarly, in the visual cortex of the cat and monkey, gamma oscillations were observed in evoked neural responses to optimal visual stimuli (Figure (1b)), and synchronization is realized within subgroups of neurons with similar stimulus specificity. Gamma oscillations are also present in the hippocampus and nearby limbic structures, where they are temporally nested with a slower, theta (4–10 Hz) rhythm. Theta rhythm occurs during exploratory movements and spatial navigation. Physiological studies of behaving rodents show that at any given time, only a subset

of hippocampal neurons that encode the animal's current (or immediate future) spatial location is synchronized at a particular phase of the theta cycle (Figure 1(c)).

Therefore, in contrast to the 'spontaneous rhythms', neural rhythms of the waking brain are usually characterized by the presence of a prominent fast oscillatory component (gamma at 30–60 Hz). Synchronization is subtle, typically confined to a restricted (possibly small) subpopulation within a brain area, and occurs intermittently by short episodes in time. The synchronous events propagate from one neural assembly to another (e.g., in response to varying stimuli).

3. *Pathological rhythms* are associated with certain neurological conditions, such as spike-and-wave patterns (3–4 Hz) of epileptic seizures, or tremors (3–8 Hz) characteristic of Parkinson disease. They may be viewed as pathological cases of low-frequency and extremely synchronous oscillatory brain states.

Are there general principles for the rhythmogenesis in the brain? Typically, a coherent neural network rhythm is generated within a relatively localized brain circuit, which is nevertheless composed of many hundreds or thousands of neurons. Therefore studies of the neural mechanisms underlying brain rhythms provide an excellent means of investigating how circuit dynamics emerge from the interplay between synaptic and intrinsic cellular properties. There are two general questions with regard to the mechanisms of a coherent oscillation.

1. What determines its oscillation frequency? Are there pacemaker neurons or is the rhythmicity largely a network phenomenon?
2. What are the synaptic mechanisms for network synchronization?

These two issues will be examined in turn.

CELLULAR PACEMAKER MECHANISMS

Single neurons in the CNS are endowed with a large repertoire of voltage- and calcium-gated ion channels, distributed across the dendritic and somatic membrane, which can give rise to complex neuronal dynamics. In general, oscillation occurs in a single cell, when a strong fast positive feedback (generating the rising phase of membrane voltage) interacts with a slower negative feedback (producing the decay phase of the cycle). Positive feedback within a cell can be provided by activation of voltage-gated inward Na^+ and/or Ca^{2+} currents, whereas negative feedback is mediated by either inactivation of inward currents or activation of outward K^+ currents. A group of neurons is described as pacemakers for a brain rhythm if (1) they are endowed with intrinsic membrane properties to display robust oscillations in a well-defined frequency range, and (2) that brain rhythm is critically dependent on the integrity of these cells.

Spindle sleep rhythm and rebound bursts in thalamic neurons

Spindle oscillations during quiet sleep originate in the thalamus, and have been reproduced *in vitro* in thalamic brain slices. It was discovered by Jahnsen and Llinás that thalamocortical projection cells and inhibitory neurons in the nucleus reticularis show two modes of firing patterns. On depolarization they discharge single spikes tonically, whereas on hyperpolarization they fire bursts of spikes, possibly in a rhythmic fashion (Figure 2(a), upper panel). During quiet sleep, thalamic cells are in the bursting mode and entrain the spindle oscillations in the entire thalamocortical system. Waking is associated with a switch of thalamic cells from the bursting to tonic firing mode, due to an increase in the neuromodulatory (cholinergic, noradrenergic and other) inputs.

The bursts of spikes are produced by a low-threshold voltage-gated Ca^{2+} ion channel I_T (of the T-type), which de-inactivates during hyperpolarization, and a hyperpolarization-activated cation channel I_h. Such a bursting mechanism is demonstrated by the single thalamic neuron model in Figure 2(a) (lower panel). Intuitively, rhythmic bursting can be generated as follows (Figure 2(a), upper panel). A hyperpolarizing input slowly activates I_h and de-inactivates I_T. The build-up of the I_T eventually leads to a depolarization wave that triggers a *rebound burst* of rapid (250–500 Hz) spikes. The burst is terminated by the inactivation of the same I_T at depolarized voltage, and the oscillatory cycle can start over again. The period of oscillation (*c*. 100 ms) is determined by the inactivation time constant of I_T and the activation time constant of I_h during hyperpolarization.

Gamma (c. 40 Hz) rhythm and chattering neurons in the neocortex

The mechanisms for the fast gamma (30–70 Hz) oscillations, commonly observed in waking and behaving states, have not yet been fully elucidated. In the neocortex, intrinsic gamma oscillations have been reported in a subclass of neurons termed 'chattering cells' (Figure 2(b), upper panel). These cells display repetitive burst firing in the gamma-frequency range, with intraburst spike rates of

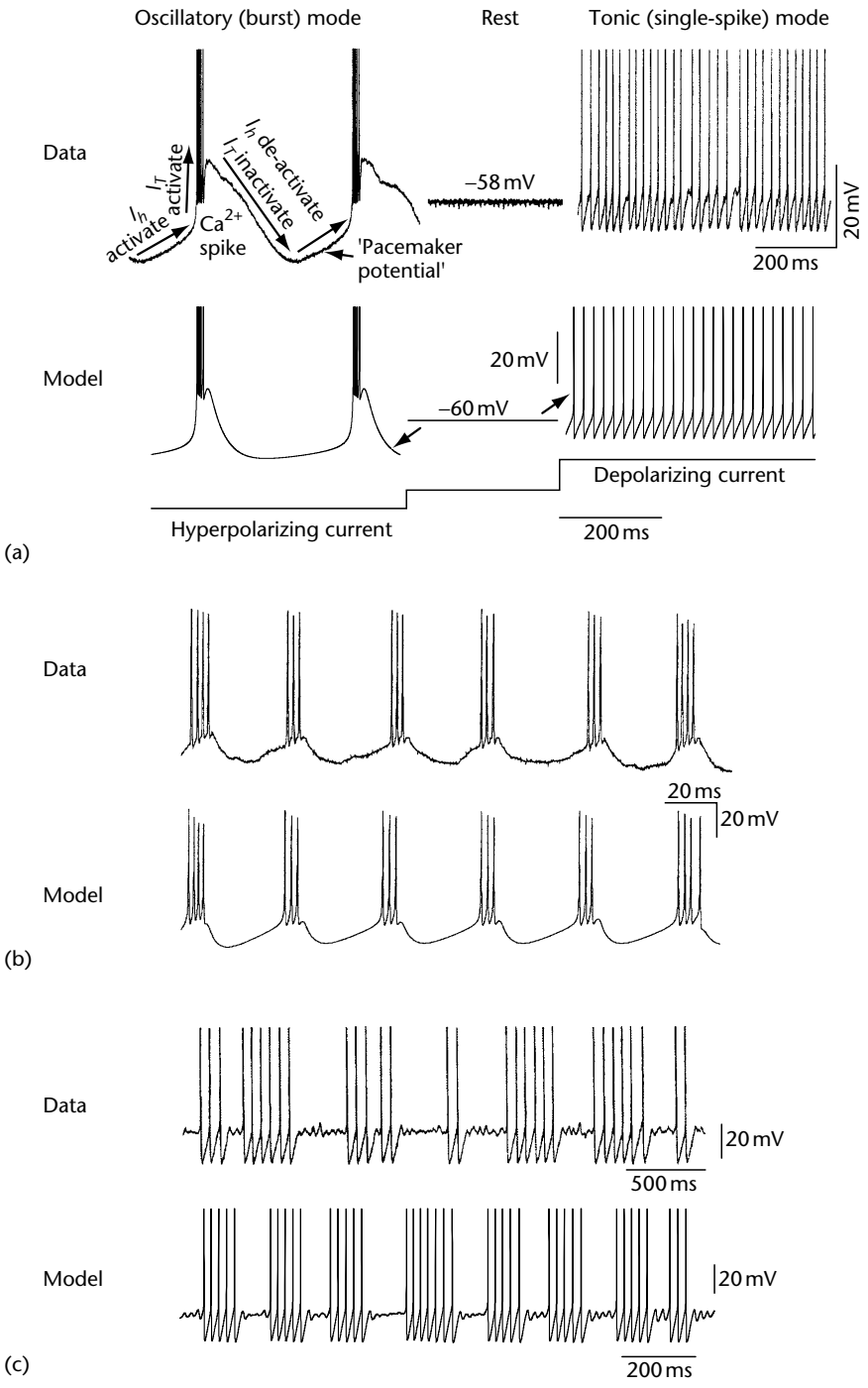

Figure 2. Intrinsic membrane oscillations of single neurons. Each panel shows experimental data and model simulations. (a) A thalamic relay cell displays two distinct spiking modes, namely tonic firing on depolarization, and burst discharges on hyperpolarization. Upper trace adapted from McCormick DA and Pape HC (1990) *Journal of Physiology* **431**: 319–342; lower trace adapted from Wang X-J (1994) *Neuroscience* **59**: 21–31. (b) A 'chattering' neuron from the cat visual cortex shows rhythmic bursting in the gamma-frequency range. Upper trace from Gray CM and McCormick DA (1996) *Science* **274**: 109–113; lower trace from Wang X-J (1999) *Neuroscience* **89**: 347–362. (c) A non-cholinergic (putative GABA-ergic) cell in the rat medial septum displays rhythmic alternations at theta frequency between 'clusters' of spikes and epochs of subthreshold membrane potential oscillations. Upper trace from Serafin M *et al*. (1996) *Neuroscience* **75**: 671–675; lower trace from Wang X-J (2002) *Journal of Neurophysiology* **87**: 889–900. The simulated oscillation is faster than the experimental data (see the different timescales), because the model simulation was performed at body temperature (37°C), whereas the *in-vitro* trace was recorded at 32°C.

300–500 Hz. A compartmental model suggests that the fast rhythmic bursting in chattering neurons is generated by a Ca^{2+}-independent ionic mechanism (Figure 2(b), lower panel). Instead, it relies on voltage-gated Na^+ currents in the dendrite. In this model, perisomatic action potentials propagate back to the dendritic sites, where an Na^+-dependent slow depolarization is produced, which in turn triggers more spikes in the soma. This somatodendritic 'ping-pong' interplay underlies a burst of spikes, which is terminated by the activation of a K^+ current. The de-activation of the K^+ current during hyperpolarization leads to recovery and eventually to the start of a new burst. Experimental evidence in support of such an Na^+-dependent, Ca^{2+}-independent mechanism has recently been reported from cortical slice studies. It has yet to be demonstrated that chattering neurons indeed play the role of pacemakers for gamma oscillations in the neocortex *in vivo*.

Hippocampal theta (7–10 Hz) rhythm and pacemaker neurons in the medial septum

The theta rhythm in the hippocampus and surrounding limbic structures is believed to be critically dependent on the input pathway from the medial septum, where pacemaker-like neural discharges have been observed. There are two major cell types in the septum, which are thought to play distinct roles in the generation of theta rhythm. Cholinergic cells slowly modulate the excitability of hippocampal neurons, whereas gamma-aminobutyrate (GABA)-ergic cells play the role of pacemakers. Recent physiological studies have revealed that non-cholinergic (putative GABA-ergic) neurons in the medial septum display robust intrinsic oscillations in the theta-frequency range, where clusters of spikes are inter-nested in time with episodes of *subthreshold membrane oscillations* (Figure 2(c), upper panel). Interestingly, similar membrane oscillations have been observed in single principal neurons of the rat olfactory bulb, which displays prominent gamma and theta rhythms. A conductance-based model (Figure 2(c), lower panel) suggests that such intrinsic rhythmicity can be generated by a low-threshold, slowly inactivating K^+ current I_{KS}. When the cell fires, the I_{KS} slowly de-inactivates during spike afterhyperpolarization, and a sufficiently large I_{KS} eventually terminates the spiking episode. When the cell does not fire spikes, I_{KS} slowly decreases due to inactivation, until the cell is sufficiently recovered and can start to fire again. The subthreshold oscillations are produced by the interplay between an Na^+ current and the low-threshold activation of I_{KS}. In this model, the periodicity of the theta rhythm is largely controlled by a single current (the I_{KS}) in septal GABA-ergic cells. This hypothetical mechanism has not yet been tested experimentally.

Summary

To summarize, some general remarks can be made. First, a single neuron can display different dynamic (e.g., single-spiking and bursting) modes, which depend on the membrane potential level and are under neuromodulatory control. Secondly, there are at least two general classes of ionic mechanisms for rhythmogenesis, one of which depends on an interplay between Na^+ and K^+ currents, while the other depends on Ca^{2+} currents. Putative pacemaker neurons for the gamma and theta rhythms of the waking brain seem to rely on Na^+ and K^+ currents, whereas pacemaker neurons for the spindle and delta sleep rhythms are critically dependent on Ca^{2+} currents.

Thirdly, a given set of ion channels can generate qualitatively different membrane dynamics, depending on their relative strengths or their distributions across the dendro-somatic membrane. For example, I_T gives rise to subthreshold oscillations (at about 10 Hz) rather than bursts in inferior olive cells that send climbing fibers to the cerebellum.

Finally, subthreshold oscillations and repetitive bursting may have different implications for synchronization of coupled neurons. Subthreshold oscillations could subserve a signal carrier for phase-locking and resonance, by virtue of the cell's sensitivity to small but precisely timed inputs (at the peak of the membrane oscillation cycle). On the other hand, bursts may provide a reliable signal for the rhythmicity to be transmitted across probabilistic and unreliable synapses between neurons.

SYNAPTIC NETWORK MECHANISMS

A neural circuit, whether it is thalamic, neocortical or hippocampal, consists of two major cell types, namely excitatory principal neurons and inhibitory interneurons. It follows that three types of synchronization mechanisms by chemical synapses can be envisaged: recurrent excitation between principal neurons, mutual inhibition between interneurons, and feedback inhibition through the excitatory–inhibitory loop.

Recurrent Excitation Model

Recurrent excitatory connections have historically been the first synchronization mechanism to undergo detailed experimental and computational analysis. This was motivated by the observation that blockade of synaptic inhibition in a cortical network led to extremely synchronous neural firing patterns which resembled epileptic discharges. Intuitively, mutual excitation is expected to synchronize coupled neurons, if cells that fire earlier in time excite the others and advance their firing times, so that the network is brought to fire in phase. However, model simulations of biophysically realistic coupled neurons have shown that synaptic excitation often delays rather than advances the firing time in the postsynaptic cell (e.g., if its predominant effect is to increase a voltage-gated K^+ current). Therefore the ability of mutual excitation to synchronize depends on the intrinsic membrane properties of the constituent neurons (Hansel *et al*., 1995; van Vreeswijk *et al*., 1995). In general, synchronization of normal brain rhythms is not realized by excitation alone, but depends critically on synaptic inhibition.

Interneuronal Network Model

Computational studies have revealed that reciprocal synaptic inhibition is capable of synchronizing certain rhythmic activities in an interneuronal network (Wang and Rinzel, 1992; van Vreeswijk *et al*., 1995). One general requirement for this mechanism is that the decay time of the inhibitory synaptic current should be long relative to the intrinsic membrane recovery time, and comparable with the oscillation period. For example, $GABA_B$-receptor-mediated inhibition with a time constant of 100–200 ms could in principle synchronize slow oscillations at a few hertz. $GABA_A$-receptor-mediated inhibition with a time constant of about 10 ms is too fast to syncronize an oscillation at a few hertz, but is sufficiently slow for a 40-Hz oscillation (with a period of about 25 ms) (Figure 3(a)). Indeed, a physiological study using *in-vitro* slices provided evidence that $GABA_A$-receptor-mediated inhibition in a hippocampal interneuronal network, without the involvement of pyramidal neurons, could give rise to coherent 40-Hz oscillations (Whittington *et al*., 1995).

Thus the interneuronal network model suggests a candidate scenario for the gamma rhythmogenesis in the hippocampus. Because this mechanism requires an optimal match between the synaptic time constant and the oscillation period, coherent network oscillations are possible only within a frequency range. In other words, synchronous oscillations with a well-defined frequency can be realized even without pacemaker neurons.

Feedback Inhibition Model

A competing network mechanism for coherent gamma oscillations is based on feedback between excitatory and inhibitory neural populations. W. J. Freeman first proposed this scenario to explain 40-Hz oscillations observed in the olfactory bulb. Similar models have been applied to the olfactory cortex and to the hippocampus.

A recent study (Fisahn *et al*., 1998) demonstrated such a scenario in hippocampal slices, where spontaneously occurring 40-Hz oscillations have been shown to depend on both excitatory and inhibitory synaptic transmissions. This experiment can be reproduced robustly in a network of pyramidal cells and interneurons, even in a randomly connected network model (Figure 3(b)). Thus the interneural network mechanism and the feedback inhibition mechanism do not have to be mutually exclusive. Rather, the two mechanisms are likely to operate cooperatively in a cortical network.

Note in Figure 3(b) that while the neural population as a whole oscillates in the 40-Hz frequency range, individual neurons fire more randomly and intermittently in time (at about 10 Hz for interneurons and only 2 Hz for principal cells), as is the case in the experiment of Fisahn *et al*. (1998). These intermittently firing dynamics are similar to neural firing activities during gamma rhythms of the intact brain. Such network dynamics cannot be adequately described in terms of coupled oscillators, with individual neurons firing regularly like a clock. A new conceptual framework is needed (Brunel, 2000) to describe coherent oscillations that emerge from complex and irregular firing patterns involving many thousands of neurons in a random network, in a very similar manner to the vivid picture envisioned by Sherrington 50 years ago.

Summary

A major conceptual advance resulting from experimental and computational work was the recognition that inhibitory neurons play a critical role in the synchronization of cortical networks. With the exception of pathological brain rhythms, synchronization of cortical oscillations appears to rely primarily on synaptic inhibition within interneuronal networks and/or through feedback between excitatory and inhibitory cells. Recent studies have

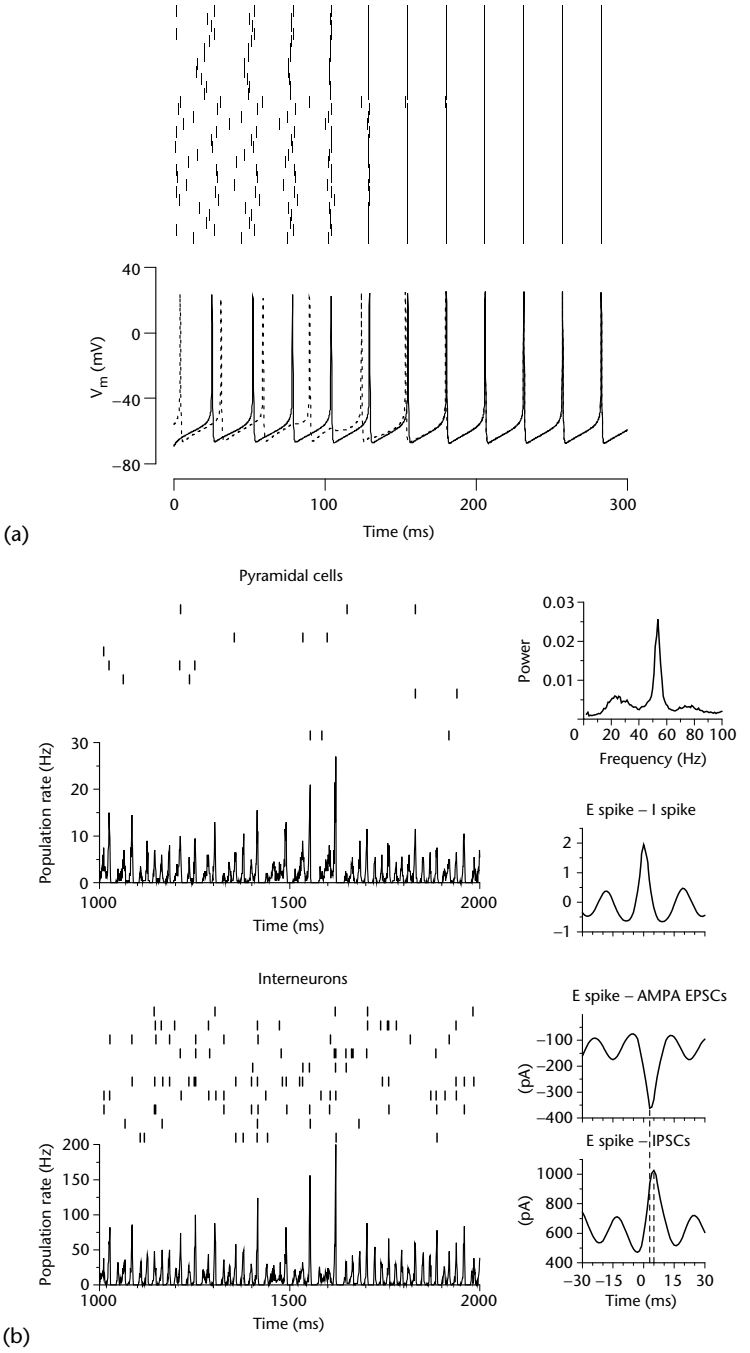

Figure 3. Synaptic mechanisms for network synchronization. (a) The interneuronal network model. A population of interneurons is synchronized at gamma frequencies, by mutually inhibitory connections mediated by $GABA_A$ receptors. Upper panel: the rastergram where each row of vertical bars represents spikes discharged by one of the neurons in the network. Neurons are intially out of phase, but quickly become perfectly synchronous after a few oscillation cycles. Lower panel: the membrane potentials of two neurons. From Wang X-J and Buzsáki G (1996) *Journal of Neuroscience* **16**: 6402–6413. (b) The feedback inhibition model. Computer simulation of a model with two neural populations (pyramidal cells and interneurons) in a sparsely connected random network. The network shows a collective oscillation at 55 Hz (see population rates, and the power spectrum), whereas single neurons fire spikes intermittently in time at low rates (2 Hz for pyramidal cells and 10 Hz for interneurons; see rastergrams). The spike discharges are synchronized to zero-phase between the two populations (second trace on the left), whereas the inhibitory synaptic current shows a phase lag of about 2 ms compared with the excitatory synaptic current (third and bottom traces on the left). From Brunel N and Wang X-J, unpublished data.

revealed that electrical coupling as well as chemical synapses between interneurons could contribute to network synchronicity, and that diverse subclasses of interneurons could be involved in different types of cortical rhythms.

POSSIBLE FUNCTIONS

Neural oscillations are obviously the modus operandi of central pattern generators – neural circuits that produce rhythmic motor movements such as respiration and walking. At the other end of the sensorimotor continuum, in the early stages of sensory information processing, the functional role of network rhythms is less obvious. Several proposals have been advanced, all centered on the idea that neural representation of sensory inputs is dynamic (as opposed to static), distributed in both space and time. This *dynamic stimulus-encoding hypothesis* is supported by data from the olfactory system, where an odor stimulus induces fast oscillations in a number of odor-specific neural assemblies, each of which is briefly synchronized at a different time epoch of the population response. Such activity patterns of oscillating neural assemblies in temporal sequence may be important for encoding, perhaps for temporally dissecting, and ultimately for identifying an odor stimulus. In the hippocampus, the spike times of a pyramidal cell progressively shift to earlier phases of the population theta cycle when the animal passes through the cell's spatial field (Figure 1(c)). Therefore spike firing time relative to a network oscillation cycle, in addition to the firing rate, may contribute to the hippocampal coding of spatial trajectory for animal navigation.

It has been proposed that neural synchronization provides a substrate for feature integration. For example, groups of neurons that detect different local features of a visual object can encode ('bind') the integrated whole image by synchronization of their spike discharges. Note that synchronization between neurons (which is a much more general phenomenon) does not necessarily imply oscillations. Indeed, unit-recording data from the visual cortex indicate that synchronization between nearby neurons can occur without oscillations, but long-range (> 2 mm) synchronization often occurs concomitantly with fast neural oscillations. Similarly, synchronization of a neural assembly in the motor cortex could reflect an integrated representation and association of movement features in a skilled action. This *temporal correlation hypothesis* for the 'binding problem' is still the subject of active debate. The contentious issues include the prevalence of the oscillatory activities in evoked neural responses, and the extent to which neural oscillations are correlated with sensory perception or motor behavior. Several physiological studies show that fast gamma-frequency-band oscillations in the primate motor cortex usually occur during the preparatory phase of a motor task, before the movement onset, rather than during the motor action itself. Therefore synchronous neural discharges may be associated with anticipation or planning.

Anticipation, planning, and other cognitive processes depend on association cortical areas. Neural circuits in these areas are believed to be highly recurrent, since reverberatory excitations are thought to generate the mnemonic persistent neural activities that are observed in association cortices. Since strongly recurrent network dynamics readily give rise to oscillations, it is possible that in the alert brain of behaving animals synchronous fast oscillations occur as a result of the activation of a highly recurrent cortical circuit (Wang, 1999). If this is so, one would expect an increased occurrence of cortical gamma oscillations with working memory or attention which requires top-down signals from the parietal and frontal cortices. Indeed, working memory (Pesaran *et al*., 2002) and selective attention (Fries *et al*., 2001) have been shown to enhance gamma oscillations in monkeys' cortices. These recent studies, if confirmed, suggest that fast (gamma) rhythm may be a characteristic sign of the engagement of strongly reverberatory cortical circuits in cognition and memory.

References

Brunel N (2000) Dynamics of sparsely connected networks of excitatory and inhibitory spiking neurons. *Journal of Computational Neuroscience* **8**: 183–208.

Fisahn A, Pike FG, Buhl EH and Paulsen O (1998) Cholinergic induction of network oscillations at 40 Hz in the hippocampus *in vitro*. *Nature* **394**: 186–189.

Fries P, Reynolds JH, Rorie AE and Desimone R (2001) Modulation of oscillatory neuronal synchronization by selective visual attention. *Science* **291**: 1506–1507.

Hansel D, Mato G and Meunier C (1995) Synchrony in excitatory neural networks. *Neural Computation* **7**: 307–337.

Pesaran B, Pezarls JS, Sahani M, Mitra PP and Andersen RA (2002) Temporal structure in neuronal activity during working memory in Macaque parietal cortex. *Nature Neuroscience* **5**: 805–811.

Sherrington CC (1951) *Man on His Nature*. Cambridge, UK: Cambridge University Press.

van Vreeswijk C, Abbott LF and Ermentrout GB (1995) When inhibition, not excitation, synchronizes neural firing. *Journal of Computational Neuroscience* **1**: 313–322.

Wang X-J (1999) Synaptic basis of cortical persistent activity: the importance of NMDA receptors to working memory. *Journal of Neuroscience* **19**: 9587–9603.
Wang X-J and Rinzel J (1992) Alternating and synchronous rhythms in reciprocally inhibitory model neurons. *Neural Computation* **4**: 84–97.
Whittington MA, Traub RD and Jefferys JG (1995) Synchronized oscillations in interneuron networks driven by metabotropic glutamate receptor activation. *Nature* **373**: 612–615.

Further Reading

Buzsáki G and Chrobak JJ (1995) Temporal structure in spatially organized neuronal assemblies: a role for interneuronal networks. *Current Opinion in Neurobiology* **5**: 504–510.
Gray CM (1994) Synchronous oscillations in neuronal systems: mechanisms and functions. *Journal of Computational Neuroscience* **1**: 11–38.
Laurent G (1996) Dynamical representation of odors by oscillating and evolving neural assemblies. *Trends in Neurosciences* **19**: 489–496.
Llinás RR (1988) The intrinsic electrophysiological properties of mammalian neurons: insights into central nervous system function. *Science* **242**: 1654–1664.
Marder E (1998) From biophysics to models of network function. *Annual Review of Neuroscience* **21**: 25–45.
Rinzel J and Ermentrout GB (1998) Analysis of neural excitability and oscillations. In: Koch C and Segev I (eds) *Methods in Neuronal Modeling*, 2nd edn, pp. 251–291. Cambridge, MA: MIT Press.
Steriade M, McCormick DA and Sejnowski T (1993) Thalamocortical oscillations in the sleeping and aroused brain. *Science* **29**: 679–685.
Traub R, Jefferys JGR and Whittington MA (1999) *Fast Oscillations in Cortical Circuits*. Cambridge, MA: MIT Press.

Neural Prostheses

Introductory article

John K Chapin, SUNY Health Science Center at Brooklyn, New York, USA

CONTENTS

A neural prosthesis is an electronic device that uses electrode stimulation to artificially activate muscle, nerve or brain tissue that has lost its normal functional capacity.

INTRODUCTION

A broad range of neural prostheses (or 'neuroprostheses') are now being developed to palliate neurological dysfunctions throughout the body. Nearly all of these devices transform electrical signals into neural signals by stimulating tissues through electrodes placed on the skin or implanted in peripheral or central nervous system (CNS) structures. The full potential of neural prostheses for restoring human nervous system function has not yet been achieved, though a few such devices are already widely used.

AUDITORY PROSTHESES

The cochlear implant is widely recognized as the most effective means for restoring auditory sensation in patients with sensorineural hearing loss. This disorder involves partial degeneration of the peripheral processes of spiral ganglion cells that normally carry auditory signals from the auditory receptor (hair) cells in the cochlea. The central processes of these ganglion cells, which normally transmit these auditory signals through the auditory nerve to the brain, are less affected. Cochlear implants bypass the degenerated peripheral processes by using microphones to record incoming sounds and then processing them into electrical signals that directly stimulate the neural fibers in the cochlea through implanted electrodes. Since the cochlea contains a 'tonotopic' map, multiple