Oscillatory neural networks are ensembles of neurons responsible for a wide variety of periodic behavior patterns. Much of what is known about the neuronal basis of rhythmic behaviors has come from the analysis of oscillatory neural networks in invertebrates. With invertebrates it is possible to identify component cells and synapses and work with them repeatedly; this review will be restricted to only these systems. The kind of networks we will be discussing are those capable of generating oscillatory activity without requiring some sensory input, although many do require some form of tonic excitation. Such networks are commonly referred to as central pattern generators (CPGs), and the goal of most efforts towards their analysis has been to try to explain their operation in terms of the cellular and synaptic properties of the neurons involved. To fully consider oscillatory networks, it will not only be necessary to examine their mechanisms when completely isolated but also when under the influence of neuromodulatory pathways.

There has been considerable progress since neuronal oscillators were last reviewed (20, 38, 39). Several are now known in enough detail that a reasonable explanation of their mechanisms can be in hand, and many others are far enough along that at least an idea of some components of their total mechanism can be suggested.

In this review we will first consider the possible ways in which neuronal oscillators may work, then, after stating the criteria used to identify network
TYPES OF OSCILLATORY NETWORKS

There are two ways that neuronal oscillators could work: one or more cells embedded in a network would have the property of endogenous bursting (cell-driven oscillators), or else the network itself would produce bursts as a result of synaptic interactions (network oscillators).

If a cell can be completely isolated from any synaptic input as well as from bloodborne substances (2), and the cell is still able to produce bursting pacemaker potentials, it can be considered a true endogenous burster. The most important feature of this cell is that it contains the intrinsic conductances necessary to produce slow waves of potential (28, 90). Superimposed upon these conductances may be the voltage-sensitive conductances necessary to generate spikes, and in these cases the cell will burst periodically. In some cases, neuromodulatory inputs or hormonal agents are necessary to unmask the conductances inducing the slow waves of potential (4, 48, 51). Such cells can be termed conditional bursters.

When neurons with intrinsic burstiness are connected with excitatory or inhibitory synapses to other neurons, complex phase relationships among a large number of cells can be established. In circuits without endogenous bursters, oscillatory activity can be generated as a function of the connections alone. Such circuits fall into two main categories, those with predominantly inhibitory connections only and those made up of both excitatory and inhibitory connections. One example of the latter type appears to be emerging from recent work on the locust-flight CPG.

Perhaps no system has had more importance as an impetus for the detailed cellular study of neuronal oscillators than the locust-flight motor-pattern generator. As a result of Wilson’s demonstration that the basic flight motor pattern could be produced without sensory feedback (91), the idea that invertebrate central-pattern generators might serve as good models for the unit analysis of oscillatory networks became firmly entrenched. The locust CPG, however, has been remarkably refractive to intracellular analysis, and until recently (65), virtually nothing has been known about this network. Despite the fact that the details of the oscillator have remained elusive, an enormous amount of information is available regarding the role of sensory feedback. Interestingly, many investigators now feel that sensory feedback serves a larger role than just increasing the frequency of the CPG output, as was originally postulated (91, 92). Recent work has shown that phasic sensory input can both entrain the CPG (87) as well as reset it (3, 34).

This is not to say that a flight-motor CPG does not exist and have powerful effects on the wing-muscle motor neurons, but that the real flight motor may be made up of both central and peripheral components, i.e. the sensory feedback may be part of the oscillator (1, 86). Whether this is the case or not, dual intracellular recordings from interneurons in the flight-pattern generator have now been made (65) and reveal a network that has interneurons able to both drive motor neurons and participate in pattern formation. No endogenously bursty cells have as yet been found, and the pattern appears to be the result of the many excitatory and inhibitory synaptic interactions.

Most of the networks that have been described are made up of predominantly inhibitory synapses. Several types of such networks are particularly noteworthy. Reciprocal inhibition has been suggested for some time to be the driving mechanism behind alternate bursting (6, 93). Such networks require a source of tonic excitatory drive, as well as some form of fatigue (such as accommodation) so that firing on the active side can be terminated.

A second form of inhibitory network known as recurrent cyclic inhibition has been described to account for leech swimming (21, 37, 75). This mechanism would permit more phases than the two seen with reciprocal inhibition and in addition does not require that fatigue properties be present. The principal evidence put forward to support this type of mechanism being the basis for leech swimming was that the Stent-Friesen circuit (20) could produce bursts in the correct phase relationships when modeled with electronic neuromimics (21).

The data that was modeled, however, was unfortunately very weak—in most cases monosynapticity was not proven and virtually nothing was known about the synaptic parameters or the intrinsic properties of the cells involved. Nevertheless, this oscillator now appears in some introductory textbooks, unfortunately, as an example of a neuronal network oscillator whose detailed mechanism has been explained (12, 71).

The predictions that derive from the Friesen-Stent model have recently been tested both by a series of ingenious lesion experiments and the findings of a swim-initiating neuron (85). These experiments have demonstrated that a single ganglion can, contrary to the model, produce the swimming rhythm. The cells that had originally been described do have properties that would suggest that they are part of the oscillator circuit, and they probably do play some role in pattern generation. But because these new results cannot be explained by the Stent-Friesen circuit, it should be considered at best incomplete and probably conceptually incorrect.

The third class of oscillator also appears to be of a hybrid form—those in which the oscillatory pattern is generated by both bursty cells and network interactions (mixed oscillators). These, in fact, may turn out to be the most predominant form, and because each mechanism would tend to reinforce the other, these networks would be both more robust and reliable.

An example of such a mixed oscillator is the feeding CPG of the snail...
Lymnaea. The rhythmic output of this system is due mainly to the endogenous capabilities of neurons in the N1 group to oscillate (66). The actual pattern, however, appears to be due to the properties of the inhibitory connections between the N1 group and the N2 and N3 groups, but the details of the connections and the mechanism involved have not yet been worked out.

EXAMPLES OF OSCILLATING NEURAL NETWORKS

In order to understand in mechanistic terms how a neural network can produce a rhythmic-patterned output, it is necessary to explain at least qualitatively: (a) What is the source of the rhythmicity? (That is, why do the neurons display cyclic activity?) and (b) How is the pattern produced? (That is, what determines the sequence of firing of the neurons in one cycle?) To answer these two questions, several criteria must be fulfilled:

1 Identification of the Neurons in the Network

First, all of the neurons active during the rhythm must be oscillatory. Second, it is necessary to distinguish those which are directly participating in the genesis of the rhythm from those which are only driven. There is not always a decisive test that makes this distinction. Nevertheless, if an evoked transient perturbation in the activity of one neuron resets the overall rhythm, this neuron is likely to be an element of the rhythm generator. It can also be a neuron that has access to, but is not part of, the rhythm generator (see 38). When possible, the identification can be confirmed by photoactivation of the cell (47), which must result in a measurable and irreversible alteration of the rhythm if the cell is an important part of the oscillator.

Because a systematic search of a ganglion is the only way of finding such cells, and because some ganglia contain thousands of cells, knowing whether or not one has identified all of the cells in an oscillatory network remains one of the most persistent problems.

2 Determination of the Synaptic Relationships Between the Neurons

This is critical, and many circuits are misunderstood only because the wiring diagram has not been completely worked out. Monosynapticity must be demonstrated, and this requires simultaneous intracellular recordings from the pre- and postsynaptic neurons. Moreover, several tests for monosynaptieity should be used concurrently to avoid errors (see 5, 12). Note that when the presynaptic neuron is nonspiking, monosynaptieity is almost impossible to demonstrate.

3 Characterization of the Intrinsic Properties of the Elements and of the Synapses

In cell-driven oscillators, the individual properties of the neurons play the major role. It is also clear, however, that even in network-driven oscillators the intrinsic properties of at least some neurons can play an important role either in the process of rhythm generation or in the organization of the pattern (22). Finally, in any circuit, knowledge of the individual synapses in more or less quantitative terms (e.g., strength, time course, facilitatory properties) is essential.

At the present time, there are only a few circuits for which most of these criteria have been successfully met; these will be considered next.

THE LOBSTER CARDIAC GANGLION: A CELL-DRIVEN OSCILLATOR

One of the smallest neuronal networks capable of generating coordinated oscillatory activity is the nine-celled cardiac ganglion of the lobster. This system produces bursts of motor impulses that drive the heart muscle at a frequency of 20-50 per minute. The ganglion consists of five motor neurons (cells 1-5), sometimes called large cells, and four interneurons (cells 6-9), which are referred to as small cells. All of the cells in the ganglion are connected to each other with nonrectifying electrotonic synapses so that during oscillatory activity they all tend to fire at about the same time. The four small cells are posteriorly located and have axons confined to the ganglion. These axons run anteriorly in the ganglionic trunk and make electrotonic connections as well as chemical excitatory synapses onto processes of the large cells within the ganglionic neuropil (for review see 31).

There is general agreement that both large and small cells are able to show endogenous bursting but that the primary control comes from the small cells (19, 43, 77, 81). Recent work has shed considerable light on the problem of how the small cells are able to provide this control, particularly with regard to cycle period and burst duration. Two types of conductance mechanisms appear to be involved: one that causes the production of pacemaker potentials, and the other that leads to the production of a regenerative depolarizing potential (78-80). This latter potential is termed a driver potential and has properties similar to those of the plateau potentials found in lobster stomatogastric neurons (67, 68). Cells with this property will not burst spontaneously but do have the capability of bursting as a result of some depolarizing input. This capability means that a population of such cells can form complex phase relationships, something that spontaneous bursters cannot. Because only the small cells have the conductances necessary to generate pacemaker potentials, these serve as the trigger for producing driver potentials and subsequent bursts.
The smaller cells fire first, and the EPSPs that they put onto the large cells trigger driver potentials and bursts in them. The slow driver potentials have a longer plateau (duration) in the small cells than in the large ones. There are also a greater number of spikes and a higher rate of firing in the small cells, due to lower thresholds and less accommodation. It appears that in normal circumstances the cardiac burst is initiated in the small cells, which produce coordinated but not absolutely synchronized action potentials leading to the production of EPSPs in the large cells. This triggers a burst in the large cells that is synchronized by their electronic connections. If spikes from the small cells are blocked by means of a ligature, the reduced synaptic input shortens the large cell burst, but they continue to produce coordinated bursting as a result of electrotonic conduction. If this is also removed, there is now some question as to whether or not the large cells can generate bursts (78).

The principal role of the EPSPs is to increase burst duration, this being the only deficit produced when spikes are blocked with TTX. One notes in this system the crucial role played by the extensive electrotonic interconnectivity in terms of coordinating the oscillations.

**TRITONIA SWIM OSCILLATOR: A NETWORK OSCILLATOR**

The sea slug, *Trionia diomedea*, escapes from predators by a series of dorsal and ventral flexion movements termed swimming (36, 89). During the swim, dorsal flexion neurons (DFN) and ventral flexion neurons (VFN) fire antagonist bursts of impulses to the dorsal and ventral musculature (88).

Complete isolation of the ganglion containing both the pattern-generating interneurons and motor neurons does not prevent the production of alternating bursts in the motor nerves when an appropriate input nerve is electrically stimulated (15, 16).

Four groups of premotor interneurons have been found that appear to be responsible for generating the pattern (23–26, 76). Recordings made from these interneurons in isolated brain preparations during " fictive" swimming have the following characteristics:

1. Alternating bursts occur between the dorsal swim interneurons (DSI) and two classes of ventral swim interneurons (VSI-A and VSI-B).
2. The third class of interneuron termed cerebral cell 2 (C2), fire after the DSI burst and continue through the initiation of the VSI bursts.
3. All of the bursts are superimposed onto a prolonged depolarizing ramp that declines as the swim progresses but is initially responsible for maintaining the swim activity (41).

The four classes of interneurons have been demonstrated to be part of the swim CPG by showing that current pulses that advance or delay their bursting can reset the entire motor pattern (25, 27). Monosynapticity has been demonstrated not only between the interneurons making up the CPG (26), but also between the interneurons and the dorsal and ventral flexion motor neurons (25, 35).

The principal synaptic mechanism underlying the swim oscillator appears to be reciprocal inhibition paralleled by delayed excitation (24). Note from Figure 1 that the oscillator consists of two sides, the DSI and the VSI. Synergists within these groups are coupled by reciprocal excitation. However, the two sides themselves are coupled via reciprocal inhibition. The monosynaptic inhibitory pathway from DSI to VSI is paralleled by a delayed excitatory pathway via the C2 interneuron. The mechanism underlying the oscillations emanating from this network can be described as follows:

1. The swim cycle begins when the DSI interneurons are depolarized and begin to fire.
2. When the DSI's fire, they inhibit the VSI's and excite C2.
3. C2 fires simultaneously with the DSI's for a short period, but although the VSI's are being inhibited by the DSI's, they are also receiving excitation from C2 that eventually causes them to start firing.
4. Once VSI starts firing, it inhibits both the DSI's and the C2, thus terminating their bursts.
5. Now VSI is no longer receiving any excitation from C2 and its spike frequency declines, releasing the DSI's from inhibition and starting the cycle over again.

The oscillation will continue as long as the ramp depolarization is sufficient to make the DSI's fire at a high enough frequency, following their release from inhibition, to bring C2 to threshold. Crucial for the operation of this network is a delay between the onset of inhibition and the onset of excitation to

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**Figure 1.** The neuronal network for generating the swim motor pattern in *Trionia diomedea* consists of three types of cells. The dorsal swim interneuron (DSI) and the ventral swim interneuron (VSI) are premotor to the dorsal and ventral flexor muscles. The C2 interneuron plays an important role in the generation of the pattern because it is excited by DSI and inhibited by VSI. Excitatory synapses are represented in this and subsequent figures by triangles, while inhibitory synapses are represented by circles.
the VSI. Two separate mechanisms, one for each class of VSI, appear to be involved. VSI-A receives a dual-action inhibitory-excitatory synapse from C2 (27), so that although its initial effect is inhibitory, it changes to excitation after a delay of 1–1.5 seconds. VSI-B, on the other hand, shows a delayed response to C2 excitation as a result of having a fast transient potassium current ("A current" of Connor & Stevens, 13), activated by depolarization. This current keeps the membrane from becoming depolarized by the EPSPs from C2. The A current inactivates after a few seconds, allowing the VSI-B neurons to fire.

This circuit is an excellent example of a network oscillator: the pattern emerges from the network as a whole, no single cell being capable of producing bursts. The network relies on both synaptic interactions and the intrinsic membrane properties of the individual neurons to generate the motor pattern.

**LEECH HEARTBEAT: A MIXED OSCILLATOR**

The circuit that controls the leech heartbeat is probably one of the best examples of a mixed oscillator. Lecitho circulaion is governed by two longitudinal vessels that constrict with a period of 10–30 seconds. The rhythmic contractions are driven by segmental pairs of motor neurons (HE cells of Thompson & Stent, 82) that innervate the parietal muscles of the left and right heart tubes in the corresponding segment. Each heart tube has two different contraction patterns: (a) a peristaltic pattern with a longitudinal wave of contraction going forward and corresponding to successive bursts of spikes in the HE cells from posterior to anterior on the corresponding side; and (b) a nonperistaltic pattern with an almost synchronous constriction of all the regions of the tube, corresponding to synchronous bursts of HE cells on the corresponding side.

When one heart tube behaves in a peristaltic mode, the other behaves in a nonperistaltic mode. Approximately, every 50 cycles, the two heart tubes trade roles (11, 83).

After isolation of the ventral nerve cord, recordings from the vascular motor nerves show a fictive heartbeat with the pattern described above (8). This demonstrates the presence of a heartbeat CPG within the CNS. The corresponding circuit is one of the best known, with almost all of the participating neurons and synapses identified. There is a set of segmental interneurons, the HE cells, and each ganglion from the first and the seventh contains a collateral pair. All of the HE cells project posteriorly and inhibit the ipsilateral HE cells. The HE cells produce bursts of impulses with the heartbeat rhythm, which are interrupted by barrages of EPSPs coming from other HE cells (Figure 2A) (11, 84). Recent work has elucidated the main mechanisms involved (8, 58–60).

We first consider the timing of the heartbeat, i.e. the rhythm generator. A perturbation imposed on any of the HN1 to HN4 neurons in the circuit resets the phase of the oscillation in the whole network (60). Conversely, the same test applied to any other neuron fails to reset the rhythm. This suggests that the eight HN interneurons form the circuit for the heartbeat rhythm. Because the HN cells of the first two ganglia (HN1 and HN2) have their spike-initiating zones in the fourth ganglion, a preparation containing only the third and fourth ganglion can still produce the pattern.

The circuit for G3 and G4 is a closed loop of six elements connected by reciprocal inhibition. In such a loop there are two functionally stable states: in the first, HN3L, HN1–2R, and HN4L are firing, and the other intercalated elements remain silent (Figure 2B). In the second, HN3R, HN4R, and HN1–2L are firing and the others are silent (Figure 2C). One burst of spikes in the three elements corresponding to the first stable state is always followed by one burst of spikes in the three elements corresponding to the second stable state. Considering only the HN3 and HN4 neurons (Figures 2B, 2C) that serve as the output of the rhythm generator to the rest of the circuit, then in one of the segments (either segment 3 or 4), when one neuron fires, the other is silent, and in successive segments (segments 3 and 4), the ipsilateral neurons are either firing or are silent at the same time. Switching from one state to the other occurs when an inactive HN3 (Figure 2B) or an inactive HN4 (Figure 2C) starts to recover from inhibition. The ability to recover is probably governed by the endogenous regenerative properties of these cells, which can oscillate when synaptic inhibition is blocked (9, 10).

The timing of the pattern appears to be governed by a separate mechanism.
The circuit just described is able to generate the heartbeat rhythm, but cannot be responsible directly for the two patterns displayed by the whole circuit or for the regular switch that occurs between these two patterns for a given heartbeat

With regard to the latter point, it is known that it is the behavior of the two HNS cells that determines the pattern (8). Depending upon the particular relationship, each HNS bursts in antiphase with the ipsilateral HNS-HN4 interneurons. Moreover, each HNS cell can be silenced by additional tonic inhibitory input, which remains from 20 to 50 cycles, the left and right HNS being alternatively inhibited. When one HNS cell is active, the other is silent and the heart tube ipsilateral to the active HNS displays nonperiodic behavior while the heart tube ipsilateral to the inactive HNS displays peristaltic behavior.

The existence of a switching oscillator, able to alternately remove the spiking activity of each HNS, must be postulated and remains to be identified.

Returning to the first point, the wiring diagram (Figure 2A) shows that on the side ipsilateral to an HNS active cell, all the interneurons that govern the HE motor neurons (e.g. HN3, 4, 6, and 7) are bursting in phase (and HNS in antiphase). On this side, all the HE motor neurons produce synchronous bursts of spikes and the heart tube displays a nonperiodic behavior. Conversely, on the side contralateral to an active HE, the HN6 and 7 fire roughly in antiphase with the HN3 and HN4 cells. On this side, and proceeding rearwards along the nerve cord, there is a blending of inhibitory inputs at different phases onto the motor neurons, and the heart tube displays a peristaltic behavior. The analysis of the heartbeat-pattern generator provides a remarkable example of how a circuit displaying complex metaplastic coordination can be worked out.

LOBSTER PYLORIC SYSTEM

Neuronal oscillators in the lobster stomatogastric ganglion produce two rhythmic motor patterns that control the striated musculature of the stomach (70). Although the patterns are quite variable in vivo (18, 62), an isolated preparation consisting of the stomatogastric, the esophageal, and the paired commissural ganglia will produce extremely regular and robust oscillatory activity for many hours. The stomatogastric ganglion contains only 30 neurons, 14 of which comprise the pyloric oscillator.

The oscillatory properties are derived mainly from the synaptic interactions and intrinsic cellular properties of motor neurons, although there is one interneuron. When the principal input nerve to the stomatogastric ganglion (the stomatogastric nerve) is cut or blocked, the pyloric rhythm ceases or is greatly slowed down, depending on the species. This suggests the requirement for factors extrinsic to the stomatogastric ganglion are necessary for maintenance of the oscillation, although it is clear that these factors need not contain phasic timing information.

The pyloric neurons produce a three-phase cycle (Figure 3A) with one dilator phase (PD, AB) and two successive constrictor phases (LP, PY). The highly simplified version of the circuit (Figure 3B) is derived from older results (32, 44, 45) in which the results obtained with the new cell photoactivation technique (47) have been added (17, 49, 69).

Utilization of this technique has resulted in a qualitative explanation of the pyloric oscillatory mechanisms (69). The main features are:
1. When the inputs to the stomatogastric ganglion are intact, all of the pyloric cells show an intrinsic bursting capacity even if synaptically isolated from other cells.
2. If the PD and AB cells are removed from the network, the remaining cells will continue to oscillate as long as the inputs from the commissurals are intact. If the inputs are blocked, all oscillation ceases.
3. Tonic stimulation of the reduced network on the ganglion side of the stomatogastric nerve block turns on the oscillator, which continues to operate for several minutes after the end of the stimulating volley. It is clear, therefore, that the PD-AB cells are not necessary for the production of oscillatory activity as long as the inputs to the ganglion are intact. It has also been demonstrated, using the photoactivation technique, that PD and AB cells have quite different physiological characteristics. Although the PD and AB cells are strongly coupled to each other, they do not make the same sets of connections of the LP and VD cells. Where they do make the same sets of connections, each may produce PSPs with different time courses, and in fact each uses different transmitters (17).

The presence of the inputs from the commissural ganglia confers at least two special properties: burstiness and the ability to generate plateau potentials (68).

**Figure 3** (A) The three-phase burst pattern of the pyloric system is shown schematically. The period in a combined preparation is approximately 0.5 seconds. (B) The neuronal network for generating the pyloric pattern; circles represent inhibitory synapses and the resistors represent electronic connections.
However, in ganglia that have been isolated and in which the AB cell has been photoactivated, minimal reciprocal inhibitory subsets of the pyloric network can still produce alternate bursting (49). This is the first demonstration of a real “half-center” oscillator in a biological system and shows that a patterned activity can be generated through the interconnection of neurons that would otherwise fire tonically.

The actual mechanism for the generation of the oscillatory pattern can be described when the ganglion is connected via the stomatogastric nerve to the commissural and esophageal ganglia as follows:

1. The VD-to-LP and the PD-to-LP cell pairs oscillate out of phase, due to their reciprocal inhibitory synaptic connections and their input-induced burstiness. If AB was not present, the VD and the LP would fire at about the same time.

2. The PDs put strong inhibition onto the PY and IC cells, causing them to be inhibited during the time of the PD bursts. However, both the LP cell and the IC cell recover before the PY cells, which have a built-in rebound delay (32). The delay explains why the rhythm occurs in three phases.

3. The AB cell not only puts strong synapses onto all of the other cells of the network, it is also strongly coupled to the PD cells so that in the intact network PD and AB always fire together. Under these conditions, VD will also be strongly inhibited by AB, overcoming the weak electrotonic connection to PD. Because VD is also inhibited by LP and IC, it will be constrained to fire during the PY period.

4. The AB cell also acts as the overall frequency controller for the network. As well as shutting off the other cells, rebound from AB’s strong inhibitory drive acts to accelerate the progression of bursts within the pattern. The existence of the pyloric pattern derives from both the oscillatory properties of the individual neurons in combination with the multiple reciprocally inhibitory interactions within the network. The phase relationships are a result of the synaptic connectivity, the relative synaptic strengths, postinhibitory rebound, rebound delay and the kinetics of the plateau, and bursting pacemaker potential mechanisms. The overall cycle frequency is determined by the AB cell both as a result of its oscillatory behavior and the strong synapses it makes with the other cells.

SPECIAL CELLULAR AND SYNAPTIC PROPERTIES OF OSCILLATORY NETWORK NEURONS

What are the most important cellular and synaptic properties involved in the production of oscillatory patterns? Although every known property may play some role (7), the examples just discussed have shown the following to be most crucial:

1 Bursting Pacemaker Potentials (BPPs)

In many oscillatory networks there are cells with regenerative bursting properties (see J. Connor, this volume) that are essential for the generation of the rhythm and/or the organization of the pattern (8, 48, 78). One important point, however, is illustrated by the oscillatory neurons in the stomatogastric circuit. Here it has been shown that the ability to generate BPPs can require synaptic inputs that are inducing or unmasking the cyclical conductance changes that govern the oscillations of the membranes (48, 51, 54). Although this may be a means for turning an oscillatory circuit on and off, it also shows that the isolation that is necessary to work out a circuit can result in the loss of fundamental properties necessary to understand how the circuit works.

2 Plateau Potentials (or Driver Potentials)

Neurons able to develop plateau potentials are not endogenous bursters because they normally do not develop any pacemaker potentials. Nevertheless, if some input drives their membrane potential to a given threshold, they develop a plateau potential (68) or driver potentials (78) that can be directly compared to the second phase of the membrane trajectory of an endogenous burster. The ability of a neuron to produce plateau potentials is unmasked by tonic inputs in some cases (53, 67, 68). This input is also able to continuously control the kinetics of the regenerative jumps of potential that start or terminate a burst of spikes (14). Using this mechanism, the input can continuously control the phase at which the neuron delivers a burst of spikes in the cycle (50, 53). These results are important from two points of view. First, they show that the pattern can be continuously controlled by the tonic discharge of an intrinsic input. Second, they demonstrate that the modulation of the output may occur via changes in the intrinsic properties of the elements, properties that must now be considered in a dynamic perspective.

3 Postinhibitory Rebound (PIR)

With the large number of inhibitory synapses present in oscillatory networks, PIR becomes an important parameter. The termination of inhibition can, as a result of PIR alone, cause a burst of spikes in the postsynaptic cell. Modeling studies have shown it to be important in maintaining the alternate firing pattern of reciprocally inhibitory networks (57). The kinetics of the PIR determines the time at which a postsynaptic cell starts firing, so that two cells receiving the same inhibition can fire afterwards at two different phases if they have different rebound kinetics (32).

4 Repetitive Firing Properties (Frequency Adaptation)

Spikes-frequency adaptation (55) is an intrinsic property of a neuron that can have important implications in shaping the pattern of oscillatory activity. For
example, in *Trionia*, some neurons respond to constant depolarization with a decelerating burst, whereas others respond with an accelerating burst (24, 25). This means that in one case a burst can stop before the end of the underlying synaptic drive and in another case can start long after the beginning of the drive (i.e., excitation can be delayed). Delayed excitation—caused by the development of a transient potassium conductance (A current) in some *Trionia* cells—is a property that, as noted, can greatly affect phase relationships (22).

5 Graded Transmitter Release

This may be common in oscillatory circuits. This form of transmission has been described for the lobster pyloric generator (29, 61) as well as the cardiac oscillator (78). It has also been implicated in other oscillatory networks that are less completely known, such as the cockroach walking system (56), the lobster scaphognathite (gill-bailer system) (46, 72), and the crayfish swimmeret system (33).

CONTROL OF OSCILLATORY NETWORKS

No oscillatory networks exist free of controlling inputs, but an exhaustive treatment of the elements that can be involved in this control, such as command fibers (40), coordinating fibers (74), and phasic sensory feedback (30), is beyond the scope of this review. However, some new data are especially germane to the general concept of neuronal network oscillators and must be considered.

Higher Order Oscillators

Included in the concept of CPGs was the premise that they were free of control by higher order oscillators located "upstream" (see 30). Recently, however, several examples of possible "master" oscillators have been documented.

The best example is found in the lobster pyloric system. In *Homarus* two pyloric oscillators have been identified, one in the stomatogastric ganglion (the pyloric CPG) and one in the higher order commisural ganglion (the commissural pyloric oscillator, CPO) (64). The oscillatory behavior of the CPO is determined by an endogenous burster neuron (CP). This neuron delivers cyclical monosynaptic excitation to the PD-AB group of the pyloric CPG and as a result entrains the entire pyloric rhythm. According to the instantaneous sensitivity of the PD-AB group, the CPG can be entrained with different ratios of coordination (1:1, 1:2, 1:3 and so on) (50). Although not directly demonstrated, the CPO could also entrain each neuron of the pyloric CPG with a coordination mode that was a function of its instantaneous sensitivity to the input. In other words, the CPO would be acting as a master oscillator controlling the frequency of the CPG as a whole as well as the frequency of each neuron in the CPG.

Recently described neuromodulatory inputs acting on the regenerative properties of all the neurons of the pyloric CPG can be responsible for the instantaneous sensitivity of the neurons to CPO inputs (14).

A comparable situation has now been described for the *Homarus* gastric CPG (63), where another higher order oscillator has been identified in the commissural ganglia. It is interesting to note that this oscillator (the CGO) receives phasic input from the CPO and strong phasic input from a proprioceptor associated with a gastric muscle (A. J. Simmers & M. Moulins, unpublished observations). This means that such a higher order oscillator can act as an interface between the CPG and several inputs capable of modifying it.

Finally, a similar independent high order oscillatory interneuron has also been described in the snail feeding system (66). This neuron (termed SO) monosynaptically excites a group of putative CPG interneurons and as a result is able to control the frequency of CPG activity.

Modulatory Inputs

Describing oscillatory circuits in terms of wiring diagrams and cell properties can allow us to understand how a circuit works, but they do not offer any explanation of the flexibility encountered in the intact animal. While sensory feedback can account for immediate, cycle-by-cycle flexibility, evidence is now accumulating that suggests that neuromodulatory mechanisms can be the origin of a more fundamental type of flexibility.

Recently it has been shown that the *Homarus* pyloric pattern can be completely modified by the tonic discharge of an identified interneuron (APM) (53). This cell appears to act monosynaptically on all the neurons of the oscillator and causes changes in phase relationships, the duration of bursts for several of the neurons, the firing frequency within the bursts, and the frequency of the rhythm itself. The efficacy of the synapses inside the network and the efficacy of the extrinsic inputs (such as the CPO) are modified in such a way that a new pattern appears (52). It has now been shown (14) that all of the modifications arise due to changes in the regenerative properties of the pyloric cells. In other words, the circuit is itself flexible in terms of its expression, and the control over this flexibility is insured by the control over the intrinsic properties of the cells (50).

Similar changes in synaptic efficacy have now been obtained by application of several neurotransmitters or neuromodulatory substances (42). It can be surmised that there are probably several neuromodulatory pathways acting in parallel and differentially on the pyloric neurons and able to "shape" the pyloric pattern in such a way that the pyloric CPG can produce a large repertoire of motor patterns. Although drastic, the effects of APM are only a small example of what can be produced using such mechanism in a small network.

Finally, the possibilities of "rewiring" neural circuits can be considered as a means by which a functional circuit can be specified from within the context of
a larger network. In the network that produces swimming in Tritonia, Getting has suggested that two different circuits can be specified, depending upon the strength of the swim-initiating stimulus. It may be difficult before long to consider a particular network as forming the basis for the generation of an oscillatory motor pattern. Future research may show that in these complex systems, extrinsic influences may be able to continuously rewire and rebuild circuits and that the idea of a specific fixed circuit should be abandoned.

SUMMARY

Despite the fact that a large number of neuronal oscillators have been described, there are only a few good examples that illustrate how they operate at the cellular level. For most, there is some isolated information about different aspects of the oscillator network, but too little to explain the whole mechanism. Two quite remarkable features do seem to be emerging from ongoing studies, however. One is that there are very few generalizable features common to neural oscillators. Many utilize reciprocal inhibitory circuits and endogenous burst-generating currents to some extent. All that have been well worked out utilize a combination of both cellular and network properties, but little else in the way of common mechanism is noteworthy.

Perhaps the most interesting aspect of recent work is the ability of a particular oscillator to produce a large repertoire of different outputs. This is separate and in addition to changes occurring via phasic sensory feedback. It is in fact a radical functional "rewiring" of the network in response to neuromodulators. The CPG circuits represent only the most basic form of a g-ven pattern.

Finally, concerning the role of sensory feedback in generating oscillatory patterns, the concept of the CPG as a group of neurons able to produce oscillatory patterns without any sensory feedback is, in our opinion, still valid. There is no doubt that some oscillators may be quite weak when isolated, but they can still produce bursts with firing sequences similar to those seen in vivo. The fact that sensory feedback can both control and enhance the oscillations has never been in doubt. Similarly, entrainment of the pattern by sensory feedback does not mean that the receptor is part of the generator, only that it has access to it (as do command and coordinating fibers). The real question remains: Can a group of cells produce an oscillatory pattern without phasic sensory input? We must answer this affirmatively even for the insect-flight motor CPG, while emphasizing the fact that for this system sensory feedback plays a larger role than in most other CPGs. Most neural oscillators will probably fall on some continuum between those like insect flight, which need and use a large amount of phasic feedback, and those that can oscillate in a near-normal manner without it.

Oscillatory Neural Networks

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CIRCADIAN NEURAL RHYTHMS IN MAMMALS

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INTRODUCTION

Only in the last few decades has the study of circadian rhythms attracted the interest of a large number of life scientists. This is somewhat surprising in view of the fact that the vast majority of biochemical, physiological, and behavioral phenomena show profound diurnal fluctuations. In nature these diurnal rhythms are normally synchronized with 24-hour environmental rhythms such as the light-dark cycle. However, even under constant environmental conditions in a laboratory setting, most diurnal variations persist (50a). This finding, along with other experimental evidence, has demonstrated that these diurnal fluctuations are endogenous rhythms and are driven by an internal biological clock (50a). These rhythms are referred to as “circadian” rhythms—from the Latin circa diem, meaning about a day, because their period under constant conditions is close to, but rarely exactly, 24 hours.

A primary objective of circadian rhythm researchers over the past two decades has been to identify and localize biological clocks in living tissue. Various experimental findings suggest that the circadian system in multicellular animals consists of more than a single circadian oscillator. Support for this hypothesis includes the observation that isolated glands and pieces of tissue can continue to show circadian oscillations in culture (72) and the fact that various rhythms within a single organism sometimes free-run with different circadian periods during exposure to constant environmental conditions (3, 37, 74). Despite the data indicating that the circadian system is multioscillatory in nature, there is a good deal of evidence to suggest that within a given species, a small number of specific neural structures serve as “driving” or “master” circadian pacemakers regulating many different circadian rhythms.

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