# Neural Information Processing

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The central nervous system (CNS) is specialized in processing information originating from a variety of internal and external sources. Its basic information processing units are called nerve cells, or neurons. Within the CNS, these elementary building blocks are densely interconnected in hierarchical and parallel pathways. Information originating from sensory neurons in contact with the body periphery is gradually transformed along these pathways to generate specific actions through signals relayed by motor neurons to peripheral organs.

## Introduction

Over the course of evolution animals have developed a rich set of capabilities to interact with their environment. The central nervous system (CNS) is the bodily system that, together with peripheral receptor and effector organs, is responsible for the acquisition of internal and external information, for its processing and for the generation of appropriate responses by the organism. This article provides an overview of the organization, circuitry and algorithms common to many neural systems across the animal kingdom with an emphasis on the processing of external stimuli and the generation of appropriate motor responses. A fascinating aspect of neural information processing is its power. Our visual system, for example, is able to solve – in real time – tasks that are far beyond the capabilities of any artificial vision system ever engineered. Indeed, unravelling the mechanisms employed by the nervous system to process information has often been identified as an outstanding scientific challenge of our time.

pendently of the animal. In addition, some organisms have evolved the ability to monitor the interaction of signals that they generate with the environment. Two important examples include bats and whales, which emit ultrasound calls and process their echoes, as well as certain fish, called weakly electric, which are able to produce and detect electric fields.

Apart from external stimuli, information about body orientation, the relative positioning of skeletal elements and the tension exerted by various muscles is critical to the control and coordination of body movements. These and other proprioceptive signals used by the autonomic nervous system to control the operation of inner organs, such as blood pressure which is used to control the heart, are monitored inside the animal's body.

## Sensory Neurons: Conveyors of Information from Outside and Inside the Body into the Central Nervous System

### Information from a variety of sources is needed for survival

Animals need to monitor a wide range of internal and external parameters to ensure proper interaction with their environment. A major source of information comes from senses specialized in the collection and processing of signals originating outside the body (exteroreception) such as vision, audition, touch, smell and taste. These sensory systems monitor signals that are generated largely inde-

### Receptor cells match the ecology and lifestyle of animals

Sensory information is gathered by various types of receptor cells specialized in the transduction of specific stimuli, such as light or sound, into electrical signals suitable for processing by the CNS. Photoreceptors are the receptor cells responsible for the transduction of light stimuli and are found throughout the animal kingdom. In primates, they come in two types, rods and cones, used for low light level vision and colour vision, respectively. Sound is detected in vertebrates by mechanoreceptors called hair cells (**Figure 1a**). Another type of proprioceptive mechanoreceptor cell, the muscle spindle, is responsible for signalling muscle stretch (**Figure 1d**). As organisms experience a wide range of life conditions, their receptor cells are often matched to the ecology of their environment and lifestyle. The photoreceptors of fast-flying flies are able to detect light changes with a much higher temporal resolution than human photoreceptors or than closely related
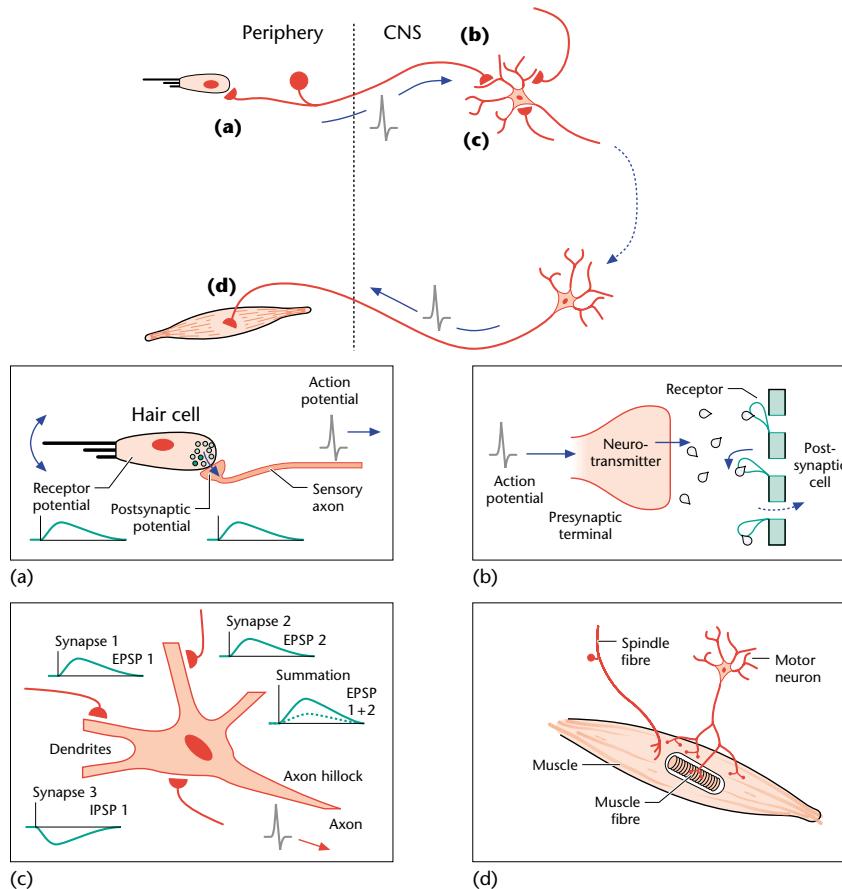
**Figure 1** Information processing by nervous systems. Sensory stimuli are transduced at the periphery by receptor cells and action potentials travel along the axons of sensory neurons towards the central nervous system (CNS). In the CNS, sensory information is processed by interneurons, eventually causing motor neurons to fire action potentials issuing specific motor commands for peripheral muscles. Panels (a–d) illustrate in more detail some steps of this process. In hair cells of the inner ear, transduction is caused by mechanical movement of cilia located at the tip of the receptors (double arrow, a). This generates a receptor potential and the release of neurotransmitter on to the sensory neuron terminal, which in turn generates a postsynaptic potential causing an action potential to travel along the sensory axon. In the CNS, information is conveyed between neurons by chemical synapes (b). An action potential causes the release of neurotransmitter that binds to receptors located on the postsynaptic cell membrane. This opens channels across the membrane, which allow ions to flow and modify the cell's membrane potential. Synapses are usually located in the dendrites or on the cell body of neurons (c). Synapses close to the spike initiation zone (the axon hillock) are often inhibitory; their activation causes the membrane potential to decrease with respect to its resting value, as illustrated by the inhibitory postsynaptic potential (IPSP) at synapse 3. When activated separately, synapses 1 and 2 generate excitatory postsynaptic potentials (EPSP 1 and 2). Often, simultaneous activation results in a change in membrane potential (dashed line of summation) which is smaller than the algebraic sum of the two individual EPSPs (EPSP 1 + 2, solid line of summation), indicative of nonlinear interactions between the two synaptic inputs. Motor neurons make contact with single muscle fibres at the neuromuscular junction (d). Sensory information also originates in muscles via several types of sensory afferent fibres such as muscle spindles.

hovering insects. Similar adaptations are found in other sensory modalities.

## Sensory neurons: cells bodies outside, synaptic terminals inside, the central nervous system

The information transduced by receptor cells is conveyed to the CNS by the axons of sensory neurons. The cell bodies of these second-order neurons are often located in ganglia outside the CNS, while their axonal terminals arborize in the CNS where they contact interneurons (**Figure 1**). In the auditory system, for example, auditory nerve fibres convey information transduced by hair cells to the cochlear nucleus in the CNS.

There are many exceptions to this general rule: the sensory neurons that enter the spinal cord, called dorsal root ganglion cells, possess specialized peripheral endings that act as receptors and do not originate from separate cells. Depending on the location of particular receptors, the axons of sensory neurons may travel for a few

millimetres (in the case of olfactory receptors located in the nose) or more than a metre (for touch receptors located at the tip of the toes) before reaching the CNS. This requires the encoding of information into actively propagated all-or-none action potentials or spikes. There are, again, many exceptions to this rule. Rod and cone photoreceptors use graded potentials to encode light intensity, and several layers of neurons precede the first long-distance transfer of visual information by retinal ganglion cells towards the thalamus and visual cortex.

# Transduction by Sensory Neurons: the Conversion of Modality-specific Stimuli to a Common Electrical Code

The first step in the acquisition of sensory information consists of the conversion of modality-specific stimuli to relatively stereotyped electrical events, called graded potentials and action potentials (spikes). In the CNS, this allows for interactions among neurons belonging either to the same or to different stimulus modalities. Following the conversion of sensory stimuli to universal electrical signals, their identity is preserved by the pattern of connections or synapses between neurons within the CNS. Here, specific classes of presynaptic neurons contact specific classes of target cells, called postsynaptic neurons. These contacts are specific at the subcellular level: particular classes of presynaptic cells contact specific regions of the postsynaptic neuron. The spatial distribution of synaptic innervation by various cell types (see **Figure 3b** for an example) is in part genetically determined.

Synapses fall in two broad categories: chemical synapses mediate the directional transfer of information from a presynaptic to a postsynaptic neuron, allowing signals from various presynaptic sources to be processed independently by different postsynaptic neurons. Electrical synapses, by contrast, often allow bidirectional exchange of information, enabling ensembles of cells to synchronize their activity.

## Receptor and synaptic potentials: analogue coding of information

In the nervous system, transduction is the process by which sensory stimuli (e.g. photons, pressure or chemicals) lead to a change in the membrane potential, the voltage gradient maintained between the inside and the outside of the receptor cell. Depending on the receptor cell type, a cascade of biochemical or mechanical events leads to a change in the opening probability of ion channels in the receptor cell membrane. The resulting flow of charged ions across the cell membrane results in the receptor potential, which is smoothly graded in amplitude with the intensity of

the stimulus (**Figure 1a**). This response represents an analogue coding of the sensory stimulus.

The duration of the receptor potential contributes to setting the time-window for the integration of successive sensory stimuli. It is specific to each receptor type, depending on factors such as the events involved in the transduction process and the electrical properties of the receptor cell. The integration time of a receptor cell may change dynamically depending on environmental conditions: photoreceptors often increase their integration time at low light levels when photons are sparse. In the CNS, information is propagated from one neuron to the next across synapses by means of synaptic potentials (**Figure 1c**), which are also graded and thus analogue.

## Action potentials: digital coding of information

The electrical properties of nerve cells cause graded synaptic or receptor potentials to be attenuated and low-pass filtered with distance from their generation site. Long-distance transmission of sensory information is ensured by conversion of these potentials to all-or-none, actively propagated, action potentials or spikes. In the case of receptor potentials, this conversion takes place either in second-order neurons synaptically stimulated by the receptor cells (**Figure 1a**), or in specialized parts of the receptor cell. The encoding of sensory stimuli as sequences of spikes is accompanied by data reduction: most of the time and amplitude information present in the graded receptor potential is discarded during this process. Action potentials are responsible for the long-distance propagation of information between neurons within the central and peripheral nervous systems.

## Information coding by action potentials

The information carried by spikes propagating along nerve cell axons is often determined by the instantaneous firing rate (in spikes per second) of the neuron. The time scale at which variations in instantaneous firing rate are relevant depends among other factors on the animal's need for real-time adjustments in its behaviour. In many cases, the time-window for integration of sensory inputs is short and the number of spikes carrying behaviourally significant information in each cell is low. In cats and toads, a few retinal ganglion cells seem to encode information about light stimuli by firing only two or three spikes in about 100 ms under low light conditions. The maximum firing rate of most neurons is on the order of a few hundred spikes per second, but the number of distinct stimulus intensities that can be encoded by neuronal spiking is limited by noise both in the transduction mechanism and intrinsically to the CNS. To encode the wide spectrum of natural stimulus intensities into this limited range, many neurons signal

stimulus changes with respect to the mean stimulus level. When changes in mean stimulus level occur, such as the change in mean lighting that we experience during a transition from an indoor to an outdoor setting, adaptation of the transduction process resets the reference level for the conversion of sensory stimuli to electrical events.

The pattern of spikes, such as the firing of bursts of closely spaced action potentials, sometimes carries significant information because it can favour the transmission of signals across synapses by a phenomenon called paired-pulse facilitation.

In bats and weakly electric fish the relative timing of spikes in multiple cells allows the reliable discrimination of time intervals as short as 10 ns by the animal, in spite of the fact that individual spikes have a duration on the order of 1 ms. A population of nerve cells can therefore encode information that would otherwise be outside the limited bandwidth and resolution set by the maximal firing rate and action potential duration in individual neurons.

# Central Processing of Sensory Information: Common Principles across Sensory Modalities

## Information is processed in parallel and hierarchical pathways

In the CNS, the afferent fibres of sensory neurons usually make divergent connections with interneurons specialized in the processing of sensory information. A common organizational principle is the segregation of nerve cells into anatomically restricted structures such as nuclei, which are found in invertebrates, in lower vertebrates and in subcortical brain structures of higher vertebrates. Similarly, the neocortex of higher vertebrates is subdivided into distinct modules called cortical areas (**Figure 2a**). These various nuclei or areas are interconnected by a rich arrangement of axonal fibre bundles or projections and organized hierarchically: areas farther away from the sensory periphery process more complex stimulus properties than areas closer to it. In addition, parallel pathways specialized in processing different aspects of a stimulus may arise at various levels of a sensory system. For instance, in the mammalian visual system, the parvocellular and magnocellular pathways arise in the retina and project to different layers of the lateral geniculate nucleus of the thalamus and visual cortex. These two pathways are thought to process colour and motion information relatively independently of each other. Separate pathways may converge at subsequent processing stages or exchange information through lateral connections.

A distinction can be made between feed-forward projections from areas closer to the periphery (and therefore at a lower level in the processing hierarchy) towards more specialized areas, and feedback projections which convey higher-level information towards the periphery (**Figure 2a**). These latter projections are thought to mediate top-down effects on sensory processing such as the focusing of attention on particular parts of the visual field, for example.

## Sensory information is organized in topographic maps

Many sensory areas process and encode information that depends on one or more continuous parameters such as the position of a receptor on the skin or the direction of motion at a particular location on the retina. Such variables are often represented topographically within a given area or nucleus (**Figure 2b**). This means that information corresponding to nearby positions in stimulus space is encoded by spatially nearby neurons, thus conserving the topography of the input variable. A similar topographic organization is also found in many motor areas for parameters specifying movements. One advantage of this representation is that it allows computations involving nearby inputs in stimulus space to be implemented in parallel by local connections at the neuronal level. In several modalities, lateral inhibitory networks implement the enhancement of 'edges' or discontinuities in the sensory input (**Figure 2c**).

## Sensory information is encoded by populations of neurons

The activity of single sensory neurons may well carry information that allows the conscious detection of weak stimuli, for instance touch stimuli or light. However, single neurons in a sensory pathway do not usually encode unequivocally a stimulus parameter such as the direction of motion of an object in the visual field. This results from two important characteristics of their responses to sensory stimuli. First, single neurons are typically broadly tuned and respond to a range of different stimulus parameters. Second, responses to the same stimulus vary because noise limits their accuracy. Precise information is therefore conveyed by neuronal population codes, which result from the simultaneous activity of many sensory neurons. The nature of these codes and the size of the neuronal pools involved are currently topics of active investigation.

# Diversity of Neuronal Size, Shape and Physiology

In the CNS, neurons lying between the sensory and motor neurons are often called interneurons. This term encom-
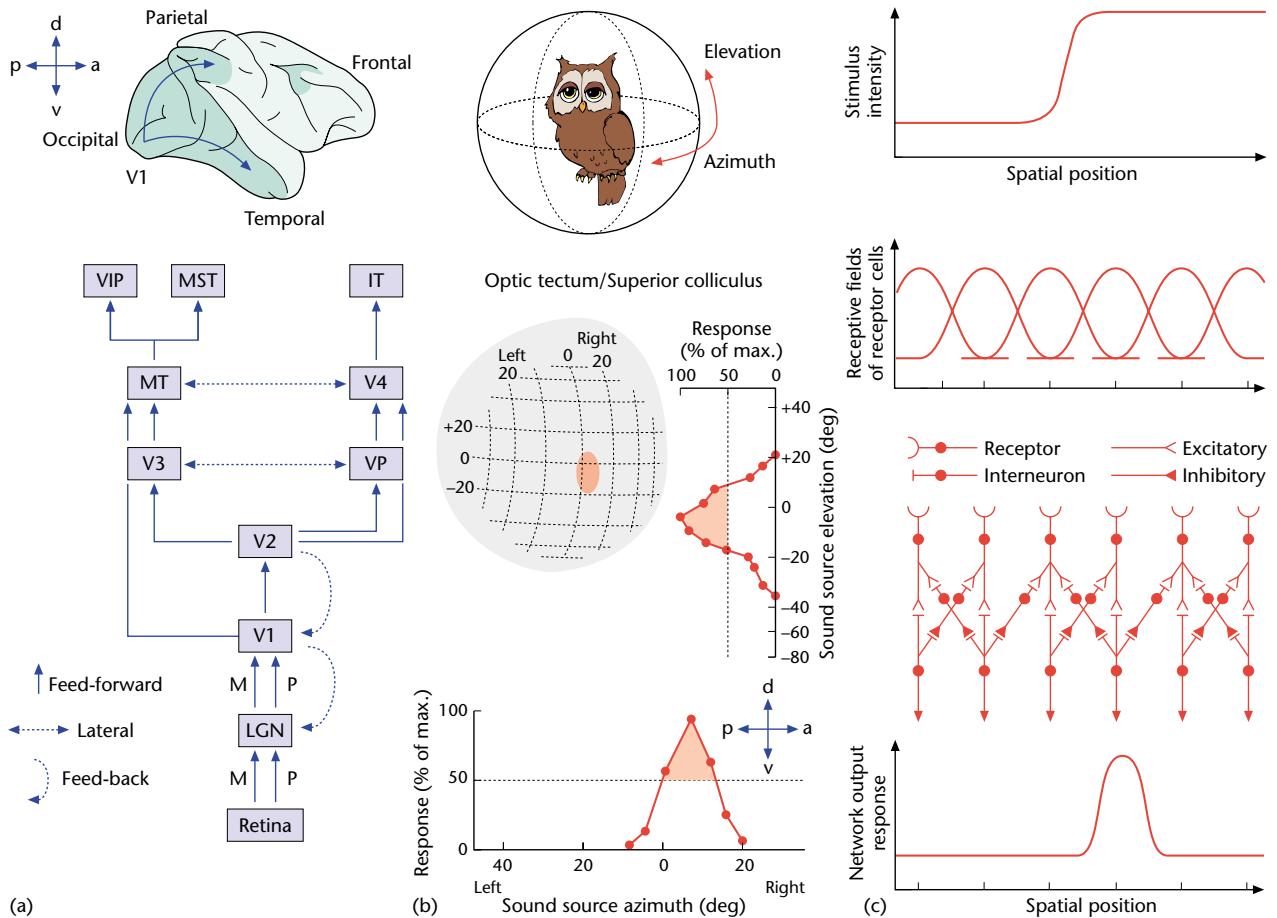
**Figure 2** Common principles of central nervous system information processing. (a) In monkeys, visual information is processed by more than 30 densely interconnected subcortical nuclei and cortical areas (only a few areas and connections are illustrated here). The areas on the left (from V1 to VIP and MST), as well as the subcortical magnocellular pathway, process mainly spatial and motion information. They are located in the occipital and parietal lobes (see the upper arrow in the lateral view of the monkey brain on top). The areas on the right (from V1 to IT), as well as the parvocellular pathway, are involved in object recognition and are located in the occipital and temporal lobes (lower arrow on top). Abbreviations: posterior (p), anterior (a), ventral (v), dorsal (d), magnocellular pathway (M), parvocellular pathway (P), lateral geniculate nucleus of the thalamus (LGN), visual area 1 (V1), visual area 2 (V2), middle temporal area (MT), ventral posterior area (VP), ventral intraparietal area (VIP), medial superior temporal area (MST), inferotemporal area (IT). Adapted from Felleman and Van Essen (1991) *Cerebral Cortex* **1**: 1–47; Distler *et al.* (1993) *Journal of Comparative Neurology* **334**: 125–150. (b) In the barn owl optic tectum (a brain structure equivalent to the mammalian superior colliculus) neurons are tuned to the location of sound sources in space. A reticular grid superimposed on the surface of the optic tectum indicates the location of sound sources eliciting optimal responses (maximal firing rates) for neurons at a particular location. The hatched area indicates the geometrical locus in space eliciting responses greater than 50% of maximum for a neuron centred close to 0 azimuth and elevation (this locus is often called the response field or receptive field of the cell). The top drawing illustrates how azimuth and elevation are defined (0 azimuth and elevation corresponds to a point in front of the animal in the median plane of the eyes). Adapted from Konishi (1986) *Trends in Neurosciences* **9**: 163–168; Cohen and Knudsen (1999) *Trends in Neurosciences* **22**: 128–135. (c) Lateral inhibition sharpens the response to stimulus edges. The top panel shows a stimulus with a sharp jump in mean value (such as a one-dimensional bar that is dark on the left and bright on the right). The middle panel illustrates the receptive fields of the six receptor cells shown in the network diagram below. The response of each cell is proportional to the stimulus intensity and depends on the spatial position of the stimulus. The bottom panel illustrates the response profile of interneurons after processing by a lateral inhibitory network. The peak output activity is centred on the edge of the stimulus.

passes an enormous range of nerve cells and bears a different significance from animal to animal. In the leech, some behaviours are implemented by simple neuronal networks consisting of three layers: sensory neurons, interneurons and motor neurons. In invertebrates, many neurons can be uniquely identified from one individual to the next, and their synaptic connections are known with great precision. In contrast, in mammals the number of interneurons involved in most behaviours and their connections is nearly impossible to characterize with accuracy, although the pathways and areas involved are usually reasonably well known.

## Neurons are composed of distinct anatomical compartments

In spite of their diversity (**Figure 3**), interneurons share many common features within and across such diverse species as leeches and monkeys. Neurons are subdivided in specialized anatomical compartments, which process neural information differently. The main region receiving and processing inputs from other neurons is the dendritic tree (**Figure 1c**; **Figure 3**). Incoming information is conveyed across specialized structures called synapses. The arrival of an action potential in a presynaptic neuron causes the release of a neurotransmitter substance which binds on to receptor molecules inserted in the membrane of the postsynaptic neuron and generates a synaptic potential in its dendritic tree (**Figure 1b**). The synaptic potentials of up to 100 000 presynaptic neurons can be processed within the dendritic tree of a single cell such as the Purkinje cell shown in **Figure 3a**. The final integration of this information occurs near the cell body, or soma, and results in a change in membrane potential that can, if it reaches a certain threshold value, result in the generation of an all-or-none action potential close to the axon hillock of the neuron (**Figure 1c**). The soma and axon hillock are often the site of powerful inhibitory synapses which can veto the generation of action potentials (**Figure 1c**). Action potentials are then actively propagated along the axon of the cell by means of specialized ion channels and eventually reach the synaptic boutons at the tip of the axon. There, they cause the release of neurotransmitter, which in turn results in synaptic potentials in their target neurons.

There are many exceptions to these general rules: in invertebrates the soma does not usually participate in the propagation of electrical signals. Some vertebrate and invertebrate neurons make synaptic contacts from dendrites to dendrites called dendrodendritic synapses, instead of the more common axodendritic synapses.

## Synaptic inputs, dendritic integration and spiking output

Many properties of single neurons contribute to the processing of information from the synaptic inputs to the spiking output. The geometry of the dendritic tree and the relative position of specific inputs with respect to one another is one factor influencing their processing. A wide range of different synaptic potentials may arise in a neuron, depending for example on the neurotransmitter released presynaptically and the type of receptor binding it postsynaptically. Broadly speaking, synaptic potentials can be either excitatory, bringing the membrane potential towards the threshold for action potential generation (i.e. leading to a depolarization of the cell membrane), or inhibitory, bringing it farther away from this threshold (i.e. leading to a hyperpolarization of the cell membrane;

**Figure 1c**). In general, the summation of synaptic potentials is not strictly additive because it results from the opening of ion channels and the flow of ions across the cell membrane (**Figure 1c**). This ion or current flow depends not only on the permeability or conductance of the open channels but also on the membrane potential itself, which changes dynamically as new synaptic events constantly impinge on the neuron. Besides channels responsible for synaptic transmission, which are gated by neurotransmitter molecules, the dendritic membrane often contains voltage-dependent ion channels that can boost or attenuate the effect of a synaptic potential along the dendrites. Similarly, ion channels located at or near the neuron soma influence significantly its subthreshold integration and spiking output. In the cat, thalamic neurons relaying information from the sensory periphery to the cortex possess ion channels that can switch the spiking output of cells from a tonic mode, in which spikes are generated relatively independently of one another, to a bursting mode, in which spikes tend to be clustered in small groups.

## Correlation of anatomy and physiology with function

Given the complex properties of single neurons, it has been a challenge to identify the computations that they perform and the role played by their anatomical and physiological properties in these computations. Some of the presently best understood cases involve identified interneurons found in invertebrates and lower vertebrates which can be studied repeatedly from one preparation to the next; two examples are presented, drawn from auditory and visual processing.

Female crickets listen to male calling songs and use this auditory information to localize and select their mating partners. An important aspect of auditory processing is the regulation of the threshold sound intensity at which neurons will respond to stimuli. Setting this response threshold appropriately allows females selectively to process the loudest calling song and ignore weaker ones. Similar gain-control mechanisms are found across species in most sensory modalities. In crickets, the gain-control mechanism that regulates dynamically the response threshold in one auditory interneuron is related to the intracellular calcium level (**Figure 3c**). In this, as in many other neurons, calcium enters the intracellular space through selective channels present in the membrane and regulates several key physiological parameters, including the activation of certain types of potassium channels which, by opening, can shift the membrane voltage level further away from the threshold for action potential generation.

In the fly, a class of identified interneurons called giant tangential cells plays an important role in the processing of motion information by the visual system. These cells are
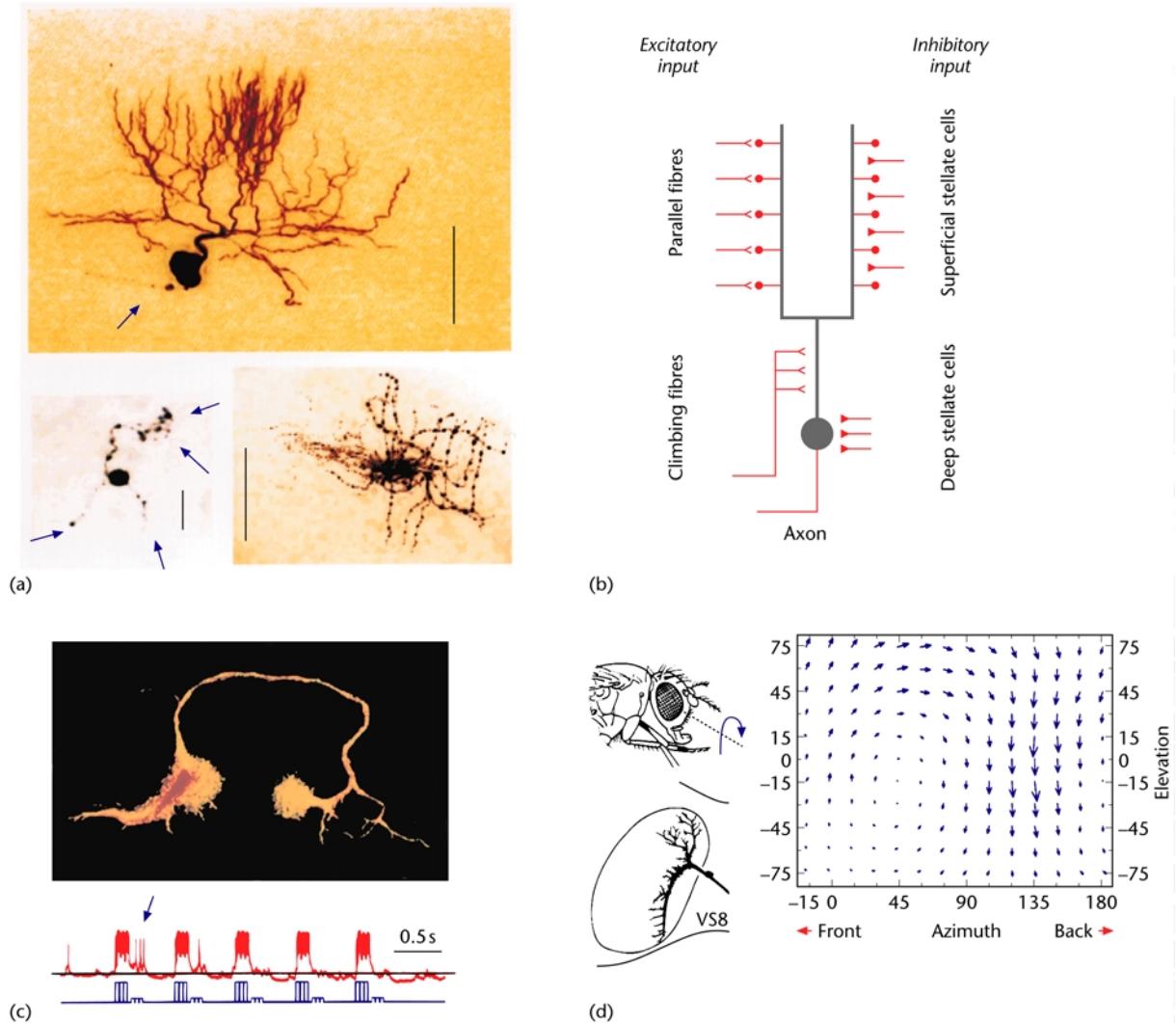
**Figure 3** Diversity of neuronal shape and function. (a) Example of three types of neurons found in the cerebellum, a hindbrain structure involved in the execution of complex motor programmes. Purkinje cells (top; bar, 100 μm) are inhibitory output elements which send their axons (arrow) to the deep cerebellar nuclei and other regions of the brainstem. They have an extensive dendritic tree that arborizes towards the surface of the cerebellum. A major source of excitatory input to Purkinje cell dendrites is relayed by granule cell axons, called parallel fibres. Granule cells (bottom left; bar, 10 μm) are tiny interneurons possessing only four dendrites, each receiving excitatory input (arrows) from extracerebellar brain regions. In addition, parallel fibres contact inhibitory interneurons called stellate cells (bottom right; bar, 100 μm) which also synapse on to different regions of the Purkinje cell dendritic tree (cells stained in the turtle). (b) Schematic summary of synaptic inputs to Purkinje cells (note that excitatory and inhibitory inputs shown on left and right are intermixed in the animal). In addition to the excitatory input mediated by parallel fibres and the inhibitory input from stellate cells, a second powerful source of excitatory input on proximal dendrites is provided by climbing fibres, which are the axons of neurons located in the inferior olive, a brainstem nucleus. (c) Gain control mechanism in the Omega neuron of the cricket. The bottom trace illustrates an experiment during which simulated male calling songs of strong (large pulses) and then weak intensity (small pulses) were presented while the membrane potential was recorded (top trace). Initially, the neuron responds with a vigorous burst of spikes to strong songs and by three spikes to a weak song (arrow). The response to weak songs rapidly decreases, reflecting an adjustment in the spiking threshold of the cell. This gain control mechanism is thought to be mediated by the influx of calcium into the cell, which can be monitored with fluorescent dyes and a camera system, as illustrated on top (adapted from Sobel and Tank (1994) *Science* **263**: 823–826; Yuste and Tank (1996) *Neuron* **16**: 701–716). (d) The dendritic tree of a giant tangential cell (VS8) in the brain of the fly is illustrated at the bottom left. This cell is sensitive to the motion of a small object over a large portion of the visual field. The direction of motion eliciting the strongest response varies systematically from location to location as illustrated on the right (larger arrows correspond to stronger responses; the arrow's direction indicates the motion direction eliciting the strongest response – see Figure 2b for a definition of azimuth and elevation). The cell is therefore expected to respond best to a rotation of the animal around the axis illustrated in the top left drawing, as will happen during flight (adapted from Krapp and Hengstenberg (1996) *Nature* **384**: 463–466).

specialized in detecting specific global patterns of motion of the surroundings that occur during flight when the animal turns with respect to its body axes (**Figure 3d**). This visual information is then relayed to motor centres for the control of flight muscles. The role played by the dendritic morphology as well as the ion channels present in the dendritic membrane of tangential neurons is understood in considerable detail.

# Transformations from Sensory Input to Motor Output

## Transformations and multimodal integration in single neurons

Changes in neuronal activity at successive levels of a nervous system reflect the gradual transformation from sensory information to motor signals. In its simplest expression, such transformations map sensory inputs on the surface of unicellular organisms to specific changes in their locomotor behaviour. In *Paramecium*, specializations located within the cell membrane and intracellular second-messenger systems combine to control the responses to touch stimuli. Such stimuli applied at the posterior pole of *Paramecium* hyperpolarize the cell membrane and increase cilia beating such that forward movement speeds up. Conversely, touch stimuli applied at the anterior pole reverse forward movement and lead to turning through a depolarization of the membrane.

In vertebrates, the spinal cord provides examples of direct coupling between primary sensory afferents (such as muscle spindles which convey muscle stretch information) and specific groups of motor neurons. The knee-jerk reflex is, for instance, implemented by direct connections between sensory and motor neurons (**Figure 4a**). More complex reflexes, such as the scratch reflex, arise from the projection of sensory inputs through spinal interneurons on to neuronal circuits that execute stereotyped motor sequences locally in the concerned body segments. In addition, spinal interneurons integrate descending inputs from the brain with primary afferent inputs and play a role in adapting reflexes and motor neuron activity to different functional requirements, such as maintenance of stance versus locomotion. Descending inputs from the brain are also directly responsible for the initiation and generation of voluntary movements.

Many motor acts are elicited in response to more than one sensory stimulus. The generation of orientation behaviours might, for example, result from the integration of visual and auditory information. Neurons responding to several sensory modalities, often called multimodal neurons, have been observed in vertebrates as well as in invertebrates. Identified multimodal interneurons in invertebrates, such as wind- and light-sensitive neurons

involved in locust flight control, provide good models to study the basis of multimodal sensory integration. In mammals, a notable example for the integration of visual, auditory and somatosensory inputs by single cells is found in the superior colliculus. This midbrain structure is thought to control orientation responses of the head or the eyes toward novel sensory stimuli. The optic tectum of pit vipers represents another example, where some cells receive both visual inputs and information from the pit organ, which localizes external sources of heat, such as preys, through infrared receptors.

## Topographic sensory representations project on to movement maps

When reaching for a visually identified object such as a cup lying on a table, the object spatial position is initially encoded through the location of stimulated photoreceptors on the retina of both eyes. This information needs to be translated in reference to the body and integrated with the current arm position to produce appropriate motor commands (**Figure 4b**). Such computations are called reference frame transformations or coordinate transformations. During such transformations, spatial information on the surroundings in relation to the organism is combined with sensory inputs and converted to a set of spatial and temporal motor commands appropriate for the particular task at hand. Their implementation from sensory maps to movement maps has been exemplified in the superior colliculus, where the superficial layers receive sensory inputs that are converted in deeper layers to spike activity patterns, thought to represent preferred action sequences for orientation behaviours.

Current research indicates that the posterior parietal cortex and the frontal lobes of monkeys (see **Figure 2a**) may also participate in reference frame transformations of multimodal sensory inputs leading to movement programmes.

## Decision-making in single cells and neuronal circuits

Besides multimodal integration and the reference frame transformations described above, the nervous system has to 'decide' on appropriate actions and plan the execution of motor acts. Such processes are likely to take place in parallel at many levels of the nervous system. Decisions may be based on a trade-off between speed and accuracy, depending on the consequences of not responding versus responding erroneously to a sensory stimulus.

Simple 'decision-making' systems are involved in the generation of escape, withdrawal and orientation reflexes. In many cases, even such 'simple' behaviours are conditional, depending on the state of the animal. In invertebrates, they can sometimes be related to the activation of
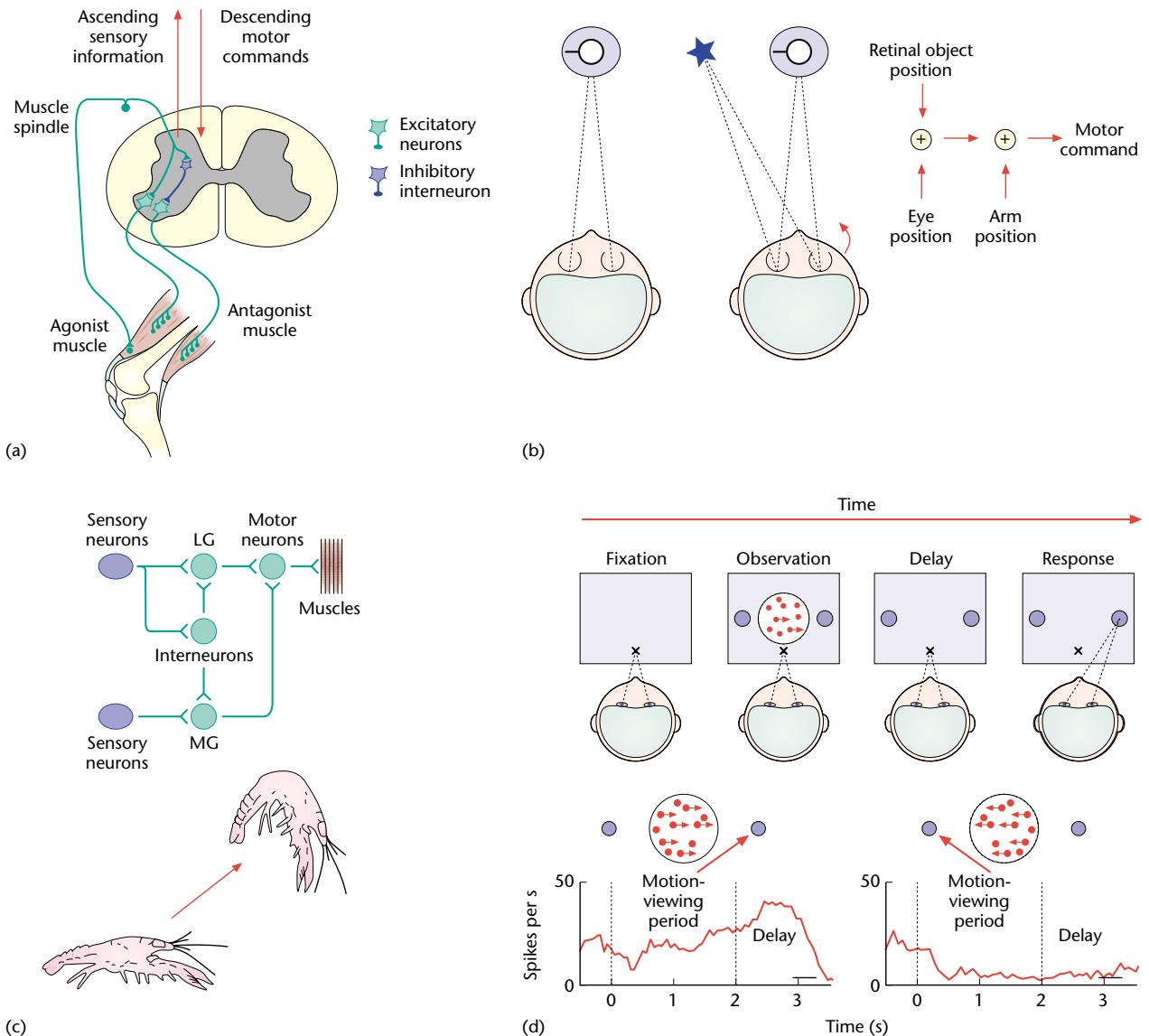
**Figure 4** (a) The knee-jerk reflex relies on direct synaptic connections between sensory and motor neurons. Muscle spindles that sense the stretch of the quadriceps muscle resulting from tapping the knee tendon excite a pool of motor neurons in the spinal cord causing contraction of the quadriceps (agonist) and inhibit a pool of motor neurons that contract the antagonist muscle via interneurons. This information is conveyed to the brain by ascending pathways. More complex voluntary behaviours such as reaching are controlled by descending pathways conveying motor commands from the brain. (b) Coordinate transformations are essential to proper execution of motor programmes. If a subject fixes a cup directly (left panel), its position on the retina will be different than if they are looking at something else (right panel). The retinal position of the cup must therefore be combined with eye position information relative to the head to provide the appropriate motor command moving the arm. (c) The crayfish tail-flip escape response illustrated at the bottom is mediated by a simple circuit comprising a pair of neurons on each side of the body called the lateral giant fibre (LG) and the medial giant fibre (MG). A single action potential in any of these neurons causes the activation of motor neurons in several body segments, resulting in the escape behaviour. Sensory neurons innervating LG and MG originate in part from different body segments. Interneurons play an important role in shaping the timing of the response (adapted from Edwards *et al.* (1999) *Trends in Neurosciences* **22**: 153–161). (d) Response of a neuron in a premotor cortical area during a direction discrimination task. The monkey observes a motion signal consisting of dots moving in either of two directions and is trained to report the direction of motion by an eye movement after a delay. The particular neuron illustrated at the bottom shows strong activity during the delay period for an eye movement to the right but not for an eye movement to the left, thus revealing the intention of the monkey. The small bar on each graph indicates the occurrence of the eye movement. Adapted from Leon and Shadlen (1998) *Neuron* **21**: 669–672.

single neurons, called command neurons. In the case of the crayfish escape behaviour, one spike in any of four neurons, the giant fibres, elicits a rapid bend of the abdomen that thrusts the animal through the water, away from visual or mechanical stimuli (**Figure 4c**).

Recently, decision processes have been studied in monkeys trained to interpret and select visual stimuli. In delayed action tasks, the animal is required to react after a delay period during which the visual stimulus has disappeared depending on its nature. The presented stimuli might, for instance, consist of a few dots moving left or right imbedded in a random background of flickering dots. The task consists of identifying the true direction of motion and reporting it by an eye movement towards either one of two target spots (left or right; **Figure 4d**). In such situations, nerve cells have been found in premotor cortical areas that are active during the delay period (i.e. after visual sensory stimulation has disappeared but before motor output) and that may participate in selecting the motor response. According to current models, such decisions rely on the activation of a threshold number of neurons in these premotor areas.

# Motor Neurons: Conveyors of Central Nervous System Output

Nervous system activity results in the activation of skeletal muscles, the stimulation of exocrine or endocrine secretions, the activation of the smooth musculature and effects on the immune system. All but the first aspect may be considered to be part of autonomic nervous system activity, which, while critical for survival and often part of the response to a sensory stimulus, will not be considered further. The control of skeletal muscles includes behaviours such as the maintenance of balance and posture, movement of the body and the limbs, and respiratory activity.

## Activation of single motor neurons causes muscle fibre contraction

Motor neurons are the nerve cells directly responsible for the activation of skeletal muscle fibres. In vertebrates, they send axons outside the CNS and contact single muscle fibres at the neuromuscular junction (**Figure 1d**). Just as for other chemical synapses, the arrival of presynaptic action potentials causes the release of neurotransmitter and the subsequent contraction of the activated postsynaptic muscle fibre. A given motor neuron in the vertebrate CNS innervates only one particular type of muscle cell. For a given spike activity, the force and the speed of the muscle response depend on its type, on training, and on the background level of neuromodulatory substances such as

adrenaline (epinephrine) and noradrenaline. The muscle response also depends on the number of muscle cells controlled by a single neuron and the firing rate of the motor neuron. The activity of motor neurons is matched to the electrical, biochemical and mechanical properties of the muscle cells they innervate.

## Temporal and spatial activity of motor neuron populations during movements

During movement, contraction of a given muscle depends on the number of active motor neurons contacting it. Different types of motor units may be recruited in different proportions depending on behavioural demands. The force and the resulting linear and angular accelerations may vary depending on loads, including the activation of antagonistic muscles, and on the angle of the joints controlled by a particular muscle. All these factors vary dynamically on different time scales: from instant to instant in relation to posture and load, and over longer time periods due to training, ageing or changes in bodyweight, for instance. In general, the number of possible motor neuron activation patterns leading to a given limb movement is very large and the question of how the CNS controls the instantaneous firing of each motor neuron is still unresolved.

The oculomotor system offers a particularly attractive model for the quantitative study of movement generation. The precise focusing and stabilization of visual images on the retina requires fine control of extrinsic eye muscles. These muscles comprise only three antagonistic pairs, which control a range of different eye movements (**Figure 5a, b**). These include the vestibuloocular reflex, which stabilizes images during head rotation, smooth tracking of moving visual targets, and vergence movements that are required to focus objects at different depths in the visual field. The neuronal basis of some of these movements has been analysed in considerable detail across vertebrate species ranging from goldfish to monkeys.

The spatial and temporal organization of motor programmes ensures the precise timing of activation of agonist and antagonistic muscles. While this organization is still imperfectly understood at higher levels of the CNS, our understanding of the generation of complex rhythmic movements by the spinal cord has progressed significantly. Many of these movements, like swimming in leeches and lampreys or walking in cats, are controlled by networks of neurons called central pattern generators (CPGs) (**Figure 5c, d**). During walking, for instance, the synaptic connections and electrical properties of CPG neurons permit the proper sequence of muscle contractions on one side of the animal and the alternating activity between the two sides. Sensory feedback from the skin and proprioceptive organs modulates this centrally generated activity. One future challenge will be to provide a
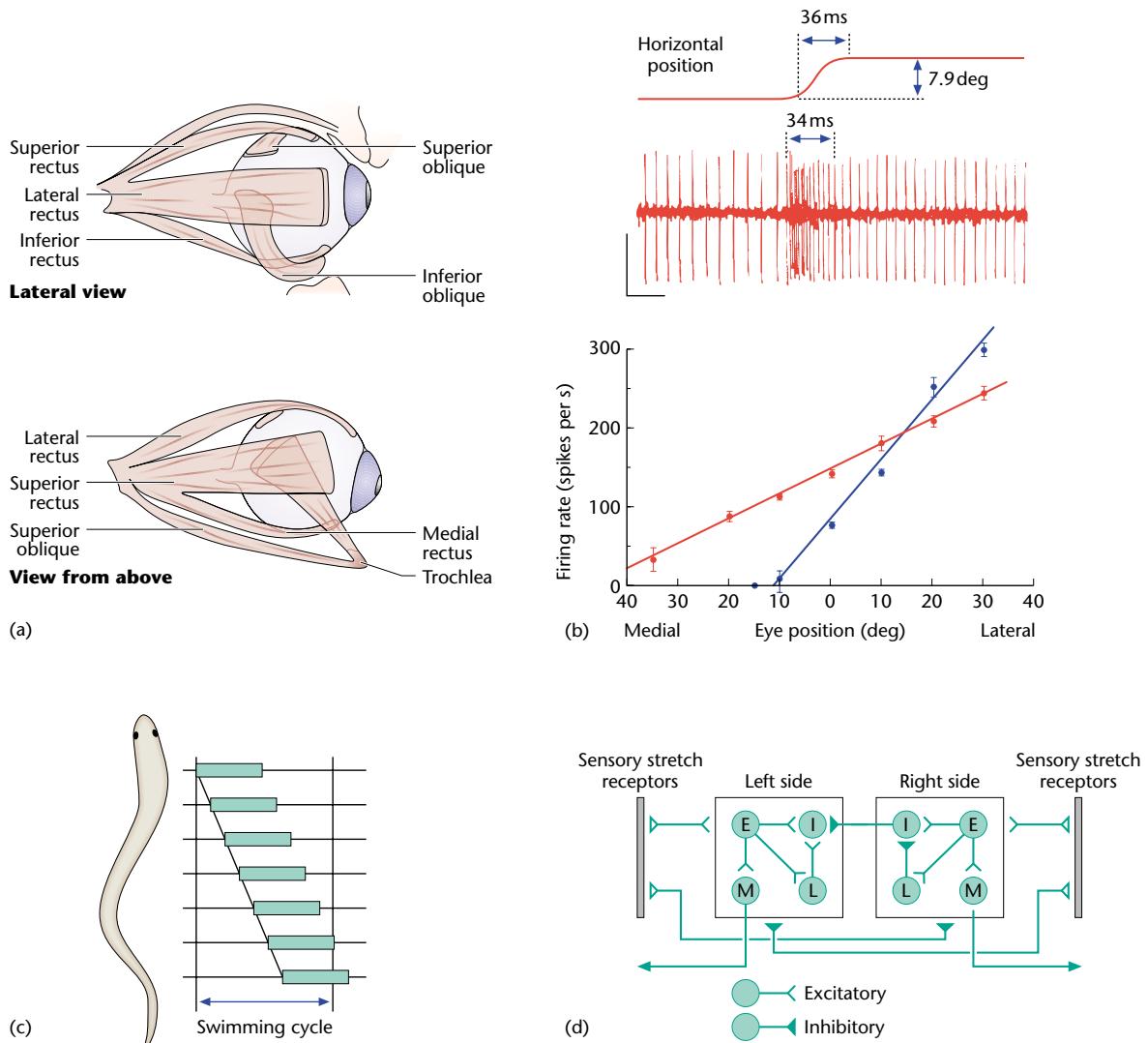
(a)

(b)

(c) Swimming cycle

(d)

Sensory stretch receptors — Left side — Right side — Sensory stretch receptors

E   I   I   E

M   L   L   M

< Excitatory

◀ Inhibitory

**Figure 5** (a) Anatomy and relative positioning of extraocular muscles. The muscular apparatus for eye movements consists of four recti (superior, inferior, lateral and medial) and two oblique muscles (inferior and superior). The superior oblique muscle passes through a pulley of bone called the trochlea. (b) Firing frequency of ocular motor neurons during fast eye movements and fixation. The top panel shows the action potentials recorded from a motor neuron during a fast horizontal eye movement, called a saccade, consisting of a 7.9° displacement of the eye following a 34-ms burst of spikes in the motor neuron. Note that the firing rate is constant before and after the movement and that it is higher after the movement than before it. The bottom panel illustrates the relationship between horizontal eye position and average firing rate in two different motor neurons. In both cases the relation between eye position and firing rate is linear, although the slopes and intercepts differ considerably. Adapted from Hepp *et al.* (1989) In: Wurtz and Goldberg (eds) *The Neurobiology of Saccadic Eye Movements*, pp. 105–212, Amsterdam: Elsevier. (c) Forward swimming in the lamprey is accomplished through an undulatory rhythmic movement of the body from head to tail which requires the coordination of muscle activity in successive body segments. As illustrated on the left, the phase of muscle activation is delayed from segment to segment during the swim cycle. Furthermore, in each segment, muscles contracting the body on the left and right side are activated in alternation. (d) Schematic diagram of the neuronal network (central pattern generator) located in the spinal cord which generates the motor pattern activating body muscles in each segment. On each body side a pool of excitatory interneurons (E) activates motor neurons (M) causing body contraction and simultaneously inhibits neurons on the opposite side via a pool of inhibitory interneurons (I). This mechanism ensures the alternate contractions of muscles on both sides during swimming. Sensory feedback from stretch receptors on each side of the body and the activation of lateral interneurons (L) also contribute to the motor pattern. Adapted from Grillner *et al.* (1995) *Trends in Neurosciences* **18**: 270–279.

comprehensive quantitative account of how the timing of muscle activation is determined centrally during natural movements, taking varying loads and other peripherally generated feedback into consideration. Particularly in-structive in this endeavour may be the cases of small robots, which simulate in real time the problems encountered by motor systems, complete with the mechanical properties of sensors, actuators and 'limbs'.

# Conclusions

This article is by necessity only a basic overview of the rapidly evolving field of study of neuronal information processing. Several aspects have not been considered, for instance the distinction of innate versus learned behaviour or the processes underlying learning and memory. Neither has consideration been given to the role played by physical constraints in the design of nervous systems, or the relation between energy consumption and the efficiency of neural computations. These factors undoubtedly play an important role in driving the evolutionary process, but are not easily quantified, let alone manipulated. Over the course of time, the information processing capacity of nervous systems has been compared with human-made technology, from mechanical calculators, telephone switchboards, digital computers up to quantum computers. Such metaphors are often difficult to reconcile with experimental facts and only serve to underscore that the topic is still far from being understood.

# Further Reading

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