Neural Information Processing

Fabrizio Gabbiani, *Baylor College of Medicine, Houston, Texas, USA*
Jens Midtgaard, *University of Copenhagen, Copenhagen, Denmark*

Introductory article

Article Contents

The central nervous system (CNS) is specialised in processing information originating from a variety of internal and external sources. Its basic information processing units are 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. The information processing capabilities of animal brains are quite distinct from those of existing man-made machines, being characterised by their resilience to noise, their capacity to learn and generalise, as well as their ability to participate in complex social behaviours.

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 organisation, 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. Since the early days of brain research, many analogies between neural and engineering approaches to information processing have been drawn and cross-fertilisation has enriched both fields. One such example is the discovery of artificial neural networks. Yet, at present there is no comprehensive theory of neural information processing in the same sense as there exists for instance in the field of applied mathematics a well defined theory of communication: information theory.

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The central aim of information theory is to quantify the rate at which information can be reliably transmitted through general communication channels. As such, information theory does not directly apply to neural information processing since the function of neural cells and networks is not only to transmit information, but also to process it. Early sensory systems, where external stimuli are converted to neural signals, may be one notable exception (de Ruyter van Steveninck and Laughlin, 1996). Yet, neuroscientists often compute the rate of information transmission of neuronal systems in bits per second, interpreting them as generalised measures of correlation (Thomson and Kristan, 2005). This interpretation goes beyond the more focused significance imparted to information rates in the context of information theory. One notable benefit of this approach is that it is model independent. One equally notable drawback is that such bit rates are usually difficult to interpret because of complex numerical issues and lack of natural normalisation. Newer correlation measures may in the future resolve these problems (Speed, 2011). Finally, we note that a refined theory of reliable computation in the presence of noise exists, but is not directly applicable to neural function as it is restricted to digital computations (Gács, 1986). Thus, unravelling the mechanisms employed by the nervous system to process information and abstracting general rules for neural information processing remains an outstanding scientific challenge of our time. Although no brain area is yet sufficiently well understood to unambiguously guide this process, we outline in the following the known experimental foundations and exemplify some approaches that might be useful to this end. In the following, we use the terms 'information', 'processing' and 'coding' in a colloquial sense, in agreement with common usage in the field. **See also**: Brain Evolution and Comparative Neuroanatomy; Neural Networks and Behaviour

Sensory Neurons: Conveyors of Information from Outside and Inside the Body into the CNS

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 specialised in the collection and processing of signals originating outside the body (exteroreception) such as the classic senses of vision, audition, touch, smell and taste. Further, many animals are thought to be able to detect the earth's magnetic field or the pattern of light polarisation in the sky for the purpose of long term travel, such as seasonal migrations (Homberg *et al*., 2011; Gould, 2010). All these sensory systems monitor signals that are generated largely independently 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 (Moss and Surlykke, 2010) 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 (Bullock and Heiligenberg, 1986). **See also**: Prey Detection by Bats and Owls; Sensory Processing in Invertebrate Motor Systems; Sensory System Organization; Sensory Systems in Vertebrates: General Overview

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 that is used to control the heart, are monitored inside the animal's body. **See also**: Proprioceptive Sensory Feedback; Sensors of External Conditions in Vertebrates

Receptor cells match the ecology and lifestyle of animals

Sensory information is gathered by various types of receptor cells specialised 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 commonly found throughout the animal kingdom. In primates, they come in two main types, rods and cones, used for low light level vision and colour vision, respectively. In addition, a subclass of ganglion cells of the mammalian retina is light sensitive, providing information to brain regions involved in regulating circardian rhythms (Schmidt *et al*., 2011). 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 for instance able to detect light changes with a much higher temporal resolution than human photoreceptors or than closely related hovering insects (O'Carroll *et al*., 1996). Similar adaptations are found in other sensory modalities. **See also**: Adaptive Gene Loss in Vertebrates: Photosensitivity as a Model Case; Colour Vision

Sensory neurons span a wide range of configurations inside and outside the CNS

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, whereas their axonal terminals arborise 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. **See also**: Hair Cells; Vertebrate Peripheral Nervous System

There are many exceptions to this general rule: the sensory neurons that enter the spinal cord, called dorsal root ganglion cells, possess specialised 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 (see **Figure 2a**). **See also**: Olfaction; Visual Cascade

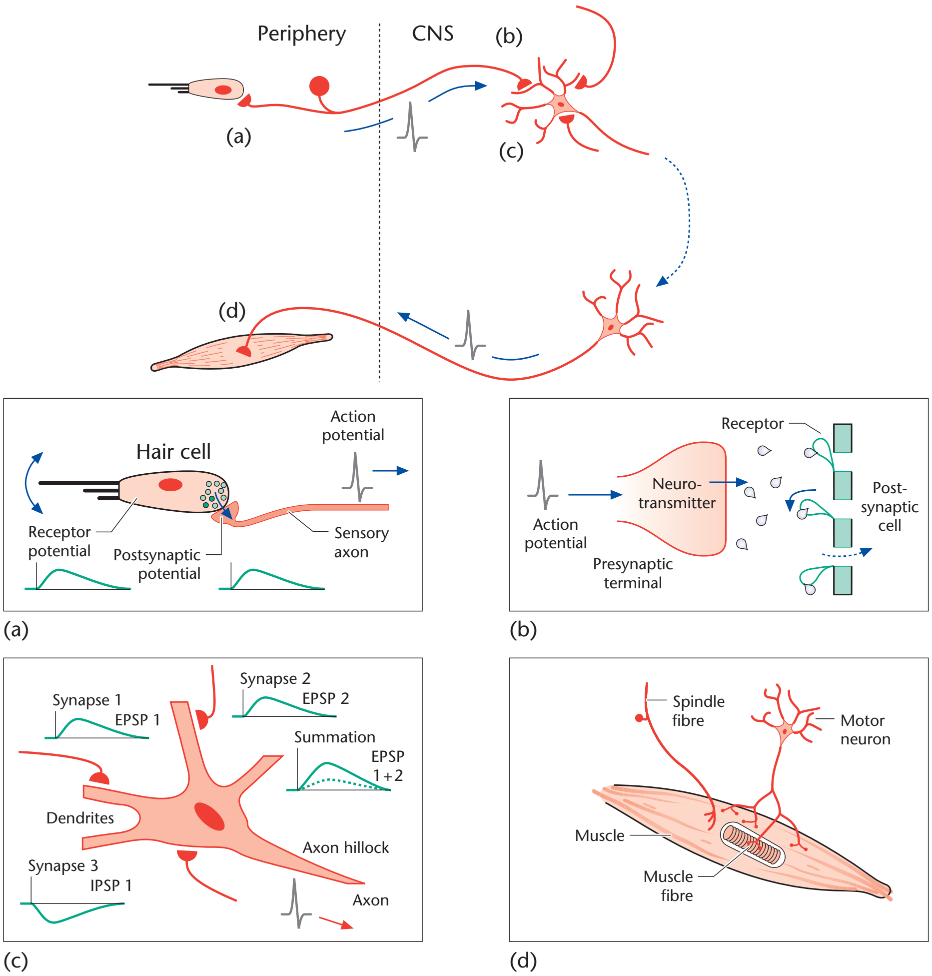


Figure 1 Information processing by nervous systems. Sensory stimuli are transduced at the periphery by receptor cells and action potentials travel along the axons of sensory neurons towards the central nervous system (CNS). In the CNS, sensory information is processed by interneurons, eventually causing motor neurons to fire action potentials issuing specific motor commands for peripheral muscles. (a–d) illustrate in more detail some steps of this process. (a) In hair cells of the inner ear, transduction is caused by mechanical movement of cilia located at the tip of the receptors (double arrow). (b) 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 synapses. (c) An action potential causes the release of neurotransmitter that binds to receptors located on the postsynaptic cell membrane. This opens channels across the membrane allowing ions to flow and modify the cell's membrane potential. Synapses are usually located in the dendrites or on the cell body of neurons. (d) 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) that 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. 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. 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. Motor neurons make contact with single muscle fibres at the neuromuscular junction. Sensory information also originates in muscles via several types of sensory afferent fibres such as muscle spindles.

Transduction by Sensory Neurons: The Conversion of Modality-Specific Stimuli to a Common Electrical Code

The first step towards the acquisition of sensory information consists in 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

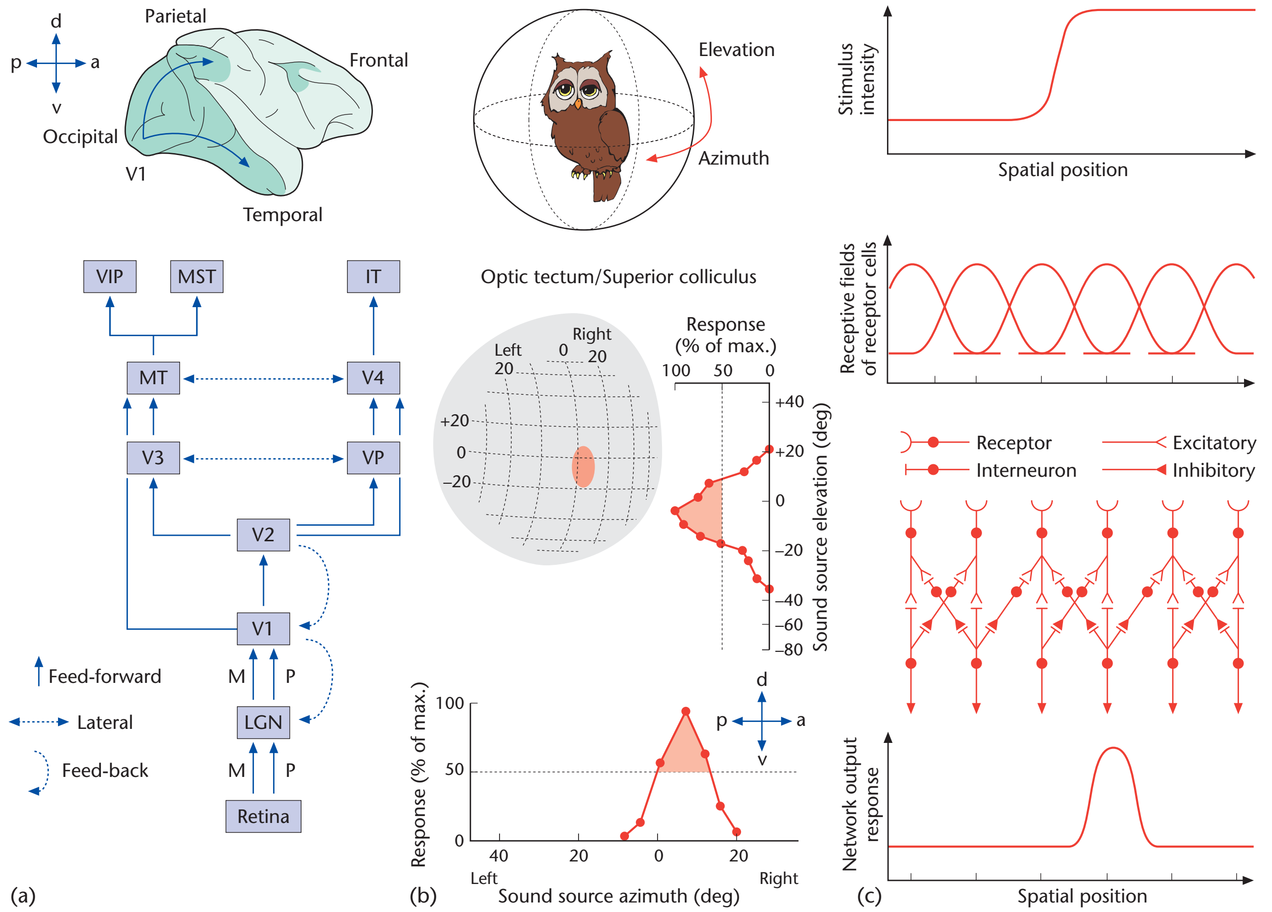


Figure 2 Common principles of CNS information processing. (a) In monkeys, visual information is processed by more than 30 densely interconnected subcortical nuclei and cortical areas (only a few areas and connections are illustrated here). The areas on the left (from V1 to VIP and MST), as well as the 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, with permission from Oxford University Press; Distler *et al.* (1993) *Journal of Comparative Neurology* **334**: 125–150. Copyright © 1993. Reprinted by permission of Wiley-Liss, Inc., a subsidiary of John Wiley & Sons Ltd. (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. Copyright © 1986, with permission from Elsevier Science; Cohen and Knudsen (1999) *Trends in Neurosciences* **22**: 128–135. Copyright © 1999, with permission from Elsevier Science. (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.

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 (McLaughlin and O'Leary, 2005). **See also**: Sensory Transduction Mechanisms; Synapses

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 synchronise their activity. **See also**: Chemical Synapses

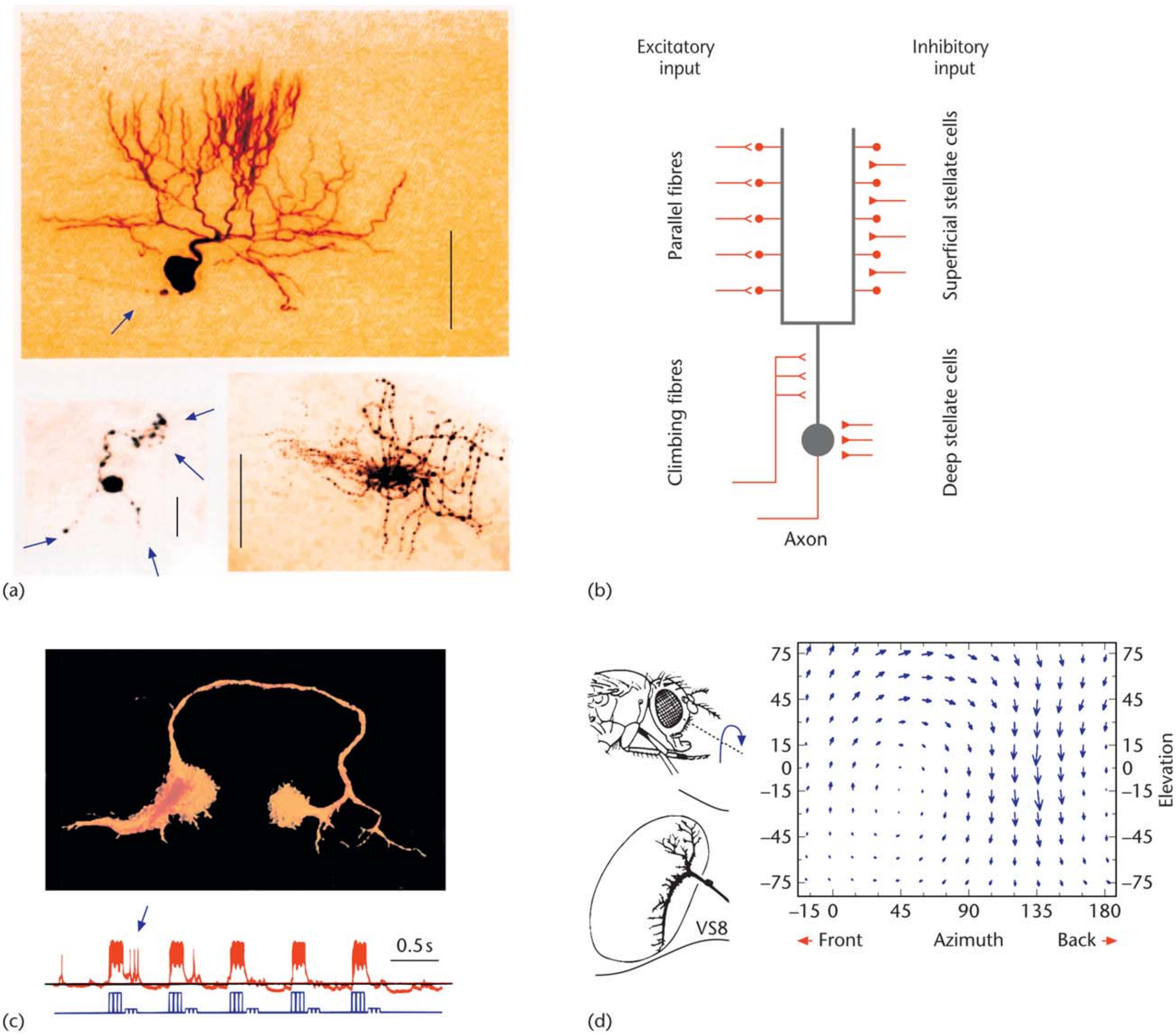


Figure 3 Diversity of neuronal shape and function. (a) Example of three types of neurons found in the cerebellum, a hindbrain structure involved in the execution of complex motor programmes. Purkinje cells (top; bar, 100 µm) are inhibitory output elements, which send their axons (arrow) to the deep cerebellar nuclei and other regions of the brainstem. They have an extensive dendritic tree that arborises 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. Copyright © 1994. American Association for the Advancement of Science; Yuste and Tank (1996) *Neuron* **16**: 701–716. Copyright © 1996 Cell Press. (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.

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. **See also**: Ion Channels; Membrane Potential; Olfactory Receptor Neurons

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 (Gu *et al*., 2005). 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.

In invertebrates, communication between CNS neurons often takes place by graded-potential chemical synapses that smoothly translate a variation in presynaptic membrane potential into a variation in postsynaptic membrane conductance (Juusola *et al*., 1996). The postsynaptic effect can be excitatory or inhibitory. The advantages of such signalling include speed and the fine-grained nature of the transmitted signal. The disadvantages include attenuation of electrical signals with distance along dendrites and axons and their susceptibility to noise. Similar trade-offs are encountered in man-made computational devices (Sharpeshkar, 1998). Further, due to the quantal and stochastic nature of chemical transmission, achieving a large dynamic range requires a large number of synaptic vesicles (Niven and Laughlin, 2008). In vertebrates, similar analogue signalling has been reported at several synapses of the CNS (Alle and Geiger, 2008). **See also**: Action Potentials: Generation and Propagation; Axons; Invertebrate Nervous Systems

Information coding by action potentials

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 specialised parts of the receptor cell. The encoding of sensory stimuli as sequences of spikes is accompanied by data reduction: most of the temporal and amplitude information present in the graded receptor potential is discarded during this process. Action potentials are also responsible for the long-distance propagation of information between neurons within the central and peripheral nervous systems. Although trains of action potentials mediate information transmission in all-or-none format, they differ substantially from the 0–1 bits used to encode digital information streams within a computer. Bits are delimited in time by a precise central clock, synchronising and confining their temporal validity across the entire machine. In contrast, action potentials are usually only loosely synchronised across neurons and time.

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 precise information content depends not only on the biophysical characteristics of the neuron, such as its peak firing rate and capability to track stimulus variations, but also on the type of stimulus encoded, for example naturalistic versus highly random, such as white noise. Further, the timescale 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. Rate codes are easy to study experimentally in single neurons, and can be readily decoded postsynaptically. However, rate coding carries a temporal penalty, is energetically costly, and suffers from diminishing information returns when discriminating fine differences in rate (Niven and Laughlin, 2008).

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 the presence of light stimuli by firing only two or three spikes in approximately 100 ms under low light conditions (Barlow *et al*., 1971). 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 in a single neuron, 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 (Krahe and Gabbiani, 2004).

The temporal patterning of spikes distributed across a population of neurons is often thought to convey information. For instance, during olfactory stimulation, a common synchronising 'clock' signal is revealed through oscillations in the local field potential, a measure of extracellular voltage fluctuations reflecting the averaged activity of large populations of primary olfactory sensory neurons. In these populations, the pattern of spikes is updated at each new cycle of the local field potential oscillation. In the vertebrate hippocampus and related cortical areas, coding of the animal's spatial location seems to rely in part on the relative timing of spikes between pyramidal neurons. Peaks in the rhythmic LFP reflect the timing of synaptic activation of the majority of neurons, whereas individual cellular spiking shifts to precede the LFP peaks during acquisition of new spatial locations (Burgess and O'Keefe, 2011; Buzsáki and Draguhn, 2004). Latency or phase population codes may also mediate information transfer from the eye to the brain in retinal ganglion cells (Gollisch and Meister, 2010), and may be at work in olfaction (Smear *et al.*, 2011).

In the olfactory system, information about the precise identity of an odour appears to be gradually refined through the time-evolving spiking of primary olfactory sensory neurons. This is consistent with the finer discrimination of odours requiring more time (Friedrich, 2006). **See also**: Action Potential: Ionic Mechanisms; Action Potentials: Generation and Propagation; Neuronal Firing Pattern Modulation; Repetitive Action Potential Firing

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. This phenomenon is termed hyperacuity, and is also a feature of the neural encoding of interaural sound timing differences in barn owls and mammals. In the visual domain, the ability to resolve features below the spacing of individual photoreceptors on the retina is called spatial hyperacuity. Although the mechanism is unknown, it is also thought to rely on improved coding of visual information through neuronal populations (Westheimer, 2009). Results from insect-inspired sensors indicate that micro-scanning eye movements may result in hyperacuity (Kerhuel *et al.*, 2012), as do pixel shifting strategies in electronic cameras.

Noise and CNS function

Noise is unavoidable in CNS function and has multiple sources, starting with the external sensory signals themselves (Faisal *et al.*, 2008). Vision has for instance evolved photoreceptors sensitive to single photons. This also means that the stochastic variance inherent in natural light sources has to be taken into account when the CNS detects weak light stimuli or determines differences in light intensity (Block, 1992). For hearing, the lowest limit of detection seems close to the floor set by random molecular processes in the ear (Block, 1992). Within the CNS, fluctuations in ion channel activation and synaptic transmission contribute to the imprecision of neural coding. Such features may set a lower limit for the diameter of axons that can reliably transmit spikes without being susceptible to random variations in ion channel activation, leading to spontaneous spikes. In the motor system, noise occurs during the neuromuscular activation process. At a cost, noise can be combatted by temporal or population averaging, for instance (Niven and Laughlin, 2008). On the other hand, noise has been suggested to increase the sensitivity to weak stimuli just below detection threshold (Ermentrout *et al.*, 2008). In addition, an invariable relationship between some sensory stimuli and behaviour may be detrimental, for instance in predator avoidance (Domenici *et al.*, 2008). Although the mechanisms underlying this particular motor variability remain largely unknown, these examples suggest that in some circumstances the CNS may exploit inescapable noise.

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 specialised in the processing of sensory information. A common organisational 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 organised hierarchically: areas farther away from the sensory periphery process more complex stimulus properties than areas closer to it. In addition, parallel pathways specialised 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. **See also**: Cells of the Nervous System; Cerebral Cortex; Sensory Processing in Invertebrate Motor Systems; Vertebrate Central Nervous System; Visual System

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 specialised 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 organised 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, or echo-timing in bats. 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 organisation 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**). However, maps are not always organised topographically. In rodents, visual cells selective for the orientation of bars follows a 'salt and pepper' distribution, in contrast to the orderly arrangement found in primates, for example. Place cells, head direction cells and grid cells of the hippocampal formation build spatial maps related to an animal's navigation in its environment (Derdikman and Moser, 2010) but appear to be distributed randomly within their associated areas irrespective of species, as is the case for olfactory cortical maps. **See also**: Brain Imaging: Observing Ongoing Neural Activity; Motor System Organization; Spinal Network Development; Topographic Maps in the Brain

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 (Wolfe *et al*., 2010), 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. One factor affecting the size of a neuronal pool is the potential correlations between the firing rate of its neurons caused by synaptic interconnections. Even weak correlations have an impact on the amount of information that can be carried within such a pool as well as on its optimal information encoding and decoding strategies (Nienborg and Cumming, 2010). **See also**: Touch

What a single neuron is coding for is conventionally determined by finding the stimulus to which it responds best. In vision, early investigations have centred on simple stimuli such as high-contrast dots or bars and their orientation (Masland and Martin, 2007). The best stimulus can be either stationary or moving, as long as it is within the receptive field of the cell recorded from. In this way cellular tuning curves can be obtained. Some cells are tuned to complex aspects of a sensory stimulus (**Figure 3b**). However, evidence at the single synapse level shows that cells also receive substantial input from stimuli away from their best one, providing a basis for the wide tuning curves observed (Varga *et al*., 2011).

Active sensing

Motor behaviour is sometimes used to actively find and select sources of sensory information. In the retina of primates, a central region called the fovea contains a high density of cone photoreceptors that is rapidly moved from one position to the next several times per second. The corresponding eye movements are called saccades. In this way, the metabolically costly concentration of foveal photoreceptors can be directed to acquire a detailed sampling of a particular part of the environment. Similar saccadic movements are executed by a variety of animals for active vision; in insects such as flies they are called 'body saccades'. In humans, finger movements are another well-known example of active sensing. In addition, depth cues for 3-D vision and the direction to sound sources in hearing may be obtained by head movements, for instance. Further, scent-tracking in moths involves a close connection to flight control and navigation, as the entire animal moves in relation to an odour source. Active sensing can also impose temporal periodicity to sensory neuron activation. Vibrissal whisking in rodents (Deschênes *et al*., 2011), and respiration and sniffing in the context of olfaction (Wachowiak, 2011) may lead to the synchronous activation of participating neuronal populations. This temporal patterning could be used in time-based population coding schemes. **See also**: Oculomotor System; Olfaction; Touch

Active sensing, and more generally motor activity, usually has an impact on the input experienced by sensory neurons. For example, a saccadic eye movement will completely change the image of the external world mapped on the retina. Yet, the visual system seamlessly interpolates between such eye movements and we perceive the world as stable. Functionally, this is achieved because information about the upcoming movement is sent from the motor centres initiating it to visual sensory centres. This allows them to factor out the expected visual changes caused by the voluntary motion of the eye. Such information is called 'corollary discharge' or 'negative image' since it cancels predictable changes in sensory input (Niven and Laughlin, 2008). A visual corollary discharge pathway involved in this cancellation mechanism has been identified in the visual system of primates. The network mechanisms of corollary discharge have been best characterised in weakly electric fish and neurons implementing corollary discharge have been identified in the auditory system of the cricket (Crapse and Sommer, 2008). Active sensing, such as saccades and other eye movements, raise the question of the strategies employed for information sampling. For instance, small fixational eye movements have been likened to random walks with avoidance of already visited areas. Such information gathering strategies may share similarities with the selection of efficient foraging strategies. **See also**: Foraging

Diversity of Neuronal Size, Shape and Physiology

In the CNS, neurons lying between the sensory and motor neurons are often called interneurons. This term encompasses an enormous range of nerve cells and bears a different significance from animal to animal. In the leech, several 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 sometimes known with great precision. In the case of the roundworm *C. elegans*, even the complete wiring diagram or connectome of the brain has been obtained at the electron microscopic level (White *et al.*, 1986). In contrast, in mammals the number of interneurons involved in most behaviours and their connections is nearly impossible to characterise with accuracy, although the pathways and areas involved are usually reasonably well known. **See also**: Advanced Techniques for Cell Lineage Labelling in Drosophila; Coordination, Integration and Behaviour in Invertebrates; Modulatory and Command Interneurons for Behaviour; Neural Networks and Behaviour

Neurons are composed of distinct anatomical and functional compartments

In spite of their diversity (**Figure 3**), neurons share many common features within and across such diverse species as leeches and monkeys. Neurons are subdivided in specialised 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**). The arrival of an action potential in a presynaptic neuron causes the release of a neurotransmitter substance that 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 specialised 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. **See also**: Axons; Dendrites; Neurons; Neurotransmitter Receptors in the Postsynaptic Neuron; Neurotransmitter Release from Presynaptic Terminals

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 depolarisation of the cell membrane), or inhibitory, bringing it farther away from this threshold (i.e. leading to a hyperpolarisation of the cell membrane; **Figure 1c**). Activity in only approximately 50–100 excitatory synapses is required to reach firing threshold in a pyramidal neuron with approximately 30 000 excitatory inputs, consistent with the notion of sparse coding. At the other extreme, in cerebellar granule cells for instance (**Figure 3a**), one or two out of four inputs are sufficient. Any permutation of a sufficient number of inputs could in principle give rise to similar axonal spiking. Thus, given the wide tuning curves of sensory cells, a cell's axonal output may not tell recipient neurons unequivocally about the presence of any particular feature in the input to the cell.

Besides channels responsible for synaptic transmission, which are gated by neurotransmitter molecules, the dendritic membrane 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. Other neurons have different capabilities for temporal patterning of spikes, determined by the specific expression of voltage and calcium-sensitive ion channels in their membrane. Often each anatomical compartment of a neuron expresses different types of such ion channels. Synaptic input to different parts of the cell will thus encounter different integrational properties in their postsynaptic targets. Since the activation of such intrinsic conductances is dependant on previous activity of the cell over a timescale of up to a minute, it is generally difficult to foresee the net effect of a given synaptic input. Within an anatomically defined type of neurons, small variations in intrinsic membrane properties may increase population information transfer (Padmanabhan and Urban, 2010).

Although action potentials usually propagate forward along the axon from the spike initiation zone towards their postsynaptic targets, they sometimes also invade the dendritic tree of the neuron. Such backpropagating action potentials (bAP) are thought to be involved in learning through regulation of the strength of synaptic inputs and of the active conductances present in the dendrites. In addition, bAPs are under the influence of local intrinsic conductances and synaptic input in individual dendritic branches, which may restrict their backpropagation. Traditionally, spikes are postulated to initiate in the low-threshold proximal part of the axon called the spike initiation zone. Ample evidence suggests that individual dendritic branches may initiate local spikes, which could subsequently result in axosomatic spikes. The behavioural roles of such dendritic events are not yet clear, even if they could carry relevant information, for example, about stimulus-orientation in retinal ganglion cells. Dendritic spike initiation suggests that there may exist several units for 'decision making' in a large neuron.

In the olfactory system and the thalamus, dendrodendritic synapses are prominent, and local input-output regions using dendritic spikes and graded potentials may play a role in sensory processing. Retrograde transmitter release from dendrites to presynaptic boutons may affect axodendritic synaptic transmission in many other brain regions. Yet another form of communication between neurons is volume transmission of neurotransmitter substances in the extracellular space and their subsequent action on synaptic or extrasynaptic receptors. Documented examples include the action of highly diffusable chemicals such as nitric oxide and GABA release by neurogliaform cortical interneurons (Philippides *et al.*, 2005; Oláh *et al.*, 2009). One practical consequence of these unconventional mechanisms of neurotransmission is that the recording of axosomatic spikes will not provide a full picture of the output of a neuron. At the conceptual level, theories based on such spike data will not provide the full picture of internal CNS information processing. **See also**: Dendrites; Neurotransmitters; Repetitive Action Potential Firing; Synaptic Integration; Voltage-gated Potassium Channels

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.

Female crickets for instance listen to male calling songs and use this auditory information to localise 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. **See also**: Auditory Processing; Calcium and Neurotransmitter Release; Calcium Channels in Presynaptic Terminals; Potassium Channels

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 specialised 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 (Borst *et al.*, 2010). In the locust, one neuron specialised in detecting object approaching on a collision course with the animal is closely related to tangential cells. The ionic conductances and dendritic mechanisms subserving its function are also well understood (Fotowat and Gabbiani, 2011).

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*, specialisations 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* hyperpolarise 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 depolarisation of the membrane. **See also**: Cell Locomotion; Cilia and Flagella; Paramecium

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**). In this way, the anatomical distribution of the sensory afferents' synaptic terminals onto the motor neuron pool embodies a basic sensory-motor transformation map. Yet, the knee-jerk reflex is conditional, and may be suppressed or enhanced by other input to the motor neurons. 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. **See also**: Motor Output from the Brain and Spinal Cord; Spinal Reflexes

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 localises external sources of heat, such as preys, through infra-red receptors.

Topographic sensory representations project on to movement maps

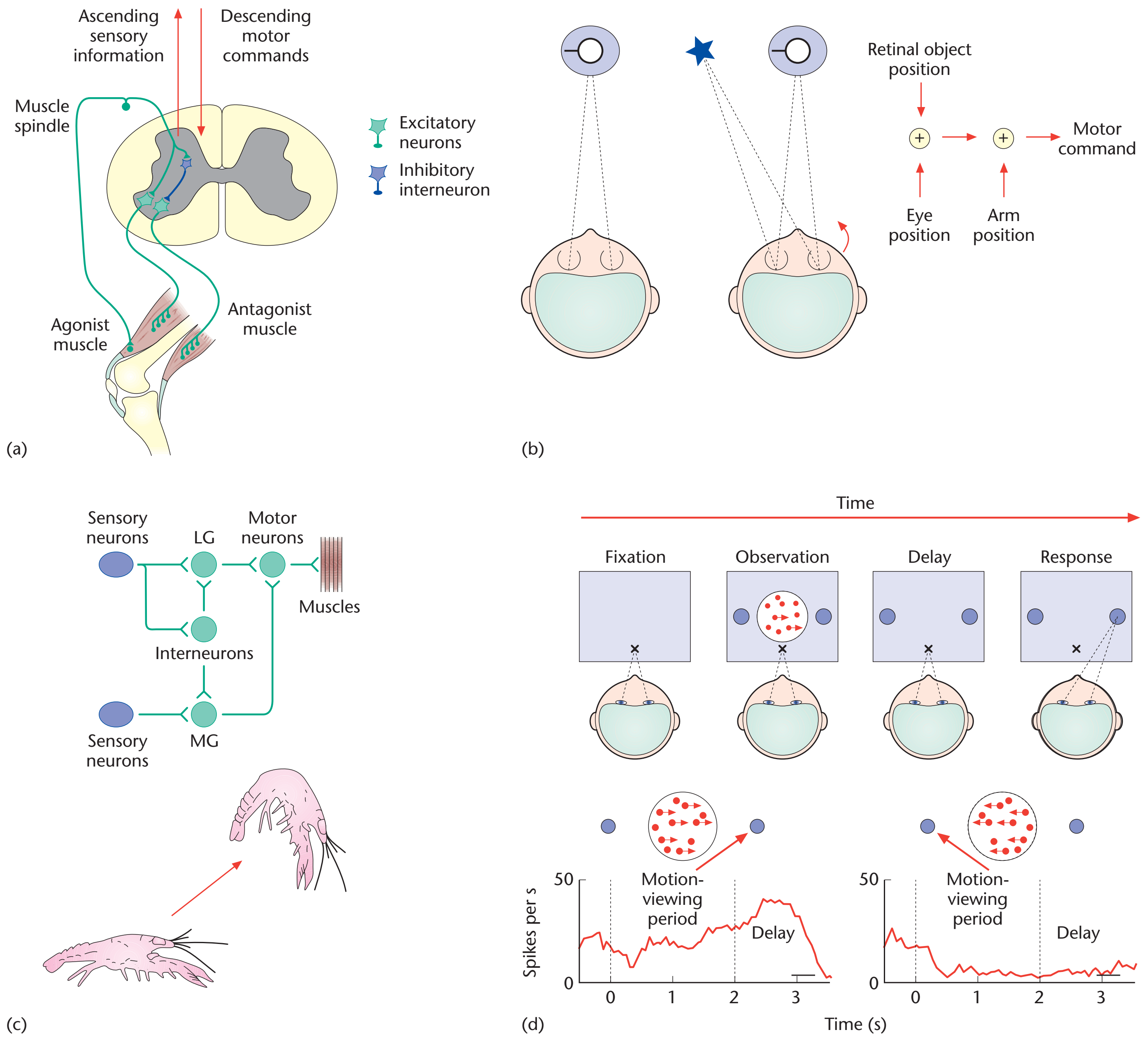
When reaching for a visually identified object such as a cup lying on a table, the object spatial position is initially encoded through the location of stimulated photoreceptors on the retina of both eyes. This information needs to be translated in reference to the body and integrated with the current 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. **See also**: Neurons and Neural Networks: Computational Models

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 (Bogacz *et al*., 2009). In single cells, any process resulting in a change in output could be called a decision. The factors affecting such changes in cells and dendrites have already been discussed.

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 (Palmer and Kristan, 2011). In invertebrates, they can sometimes be related to the activation of 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


Ascending sensory information
Descending motor commands
Muscle spindle
Excitatory neurons
Inhibitory interneuron
Agonist muscle
Antagonist muscle
(a)
Retinal object position
Motor command
Eye position
Arm position
(b)
Sensory neurons
LG
Motor neurons
Muscles
Interneurons
Sensory neurons
MG
(c)
Time
Fixation
Observation
Delay
Response
Spikes per s
50
0
Motion-viewing period
Delay
0
1
2
3
50
0
Motion-viewing period
Delay
0
1
2
3
Time (s)
(d)

water, away from visual or mechanical stimuli (**Figure 4c**). **See also**: Coordination, Integration and Behaviour in Invertebrates

Decision processes have been studied in monkeys trained in a wide range of tasks, such as interpreting and selecting 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. Models indicated that such decisions rely on the activation of a threshold number of neurons in these premotor areas.

The term ‘decision-making’ is also used for the description of the collective behaviour of social insects such as ants and bees, and more broadly in the analysis of behavioural choices, including social interactions in humans, for instance in the fields of neuroeconomics and game theory. Behavioural decision making often incorporates the concept of ‘utility’ or ‘value’, which may be embodied in brain circuits for reward and aversion. These aspects of decision-making are outside the scope of this article. **See also**: Addiction; Cognitive Neuroscience; Decision-making and Neuroeconomics; Neuroeconomics

Motor Neurons: Conveyors of CNS 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. **See also**: Autonomic Nervous System

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 a muscle fibre 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. **See also**: Motor Neurons and Spinal Control of Movement; Nervous Control of Movement; Nicotinic Acetylcholine Receptors in Muscle; Postsynaptic Membranes at the Neuromuscular Junction: Molecular Organisation

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 timescales: 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.

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 for 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, with permission from Elsevier Science. (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, with permission from Cell Press.

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. **See also**: Muscle Contraction: Regulation

The oculomotor system offers a particularly attractive model for the quantitative study of movement generation. The precise focusing and stabilisation 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** and **b**). These include the vestibuloocular reflex, which stabilises 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. **See also**: Oculomotor System

The spatial and temporal organisation of motor programmes ensures the precise timing of activation of agonistic and antagonistic muscles. Although this organisation 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, zebrafish and lampreys or walking in cats and mice are controlled by networks of neurons called central pattern generators (CPGs) (**Figure 5c** and **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 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 instructive 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. **See also**: Central Pattern Generators

Time, Neural Processing and Behaviour

Behaviourally relevant timescales range from nanoseconds to an organism's lifetime, whereas many time-dependent cellular properties of neurons cover a range from submilliseconds to minutes. Thus, behavioural decisions and reaction times will often leave little opportunity for longer-lasting cellular properties to take immediate effect. For instance, in insects, sensory-motor processing times can be as short as 30 ms, whereas in mammals sensory processing times alone lasts typically on the order of 100 ms. In mouse olfaction for example, only one sniff can bring odour discrimination and a motor response in less than 200 ms. These processing intervals leave little room for elaborate neural coding schemes, although spike latencies in single cells and population coding could be involved. During multimodal integration, the nervous system must overcome differences in processing speed and conduction delays across sensory modalities (King, 2005). In practice, a time window of a few milliseconds may allow for stimuli from different modalities to be perceived as occurring simultaneously. Time delays in sensory and motor processing mean that animals invariably react to past events. Hence, to interact with fast moving objects both these sensorimotor delays and the projected object trajectory must be taken into account (Gollisch and Meister, 2010). This means that motor systems may include ways to anticipate future events or even build a predictive model of the external world. The vertebrate cerebellum has been postulated to be one region that may carry out such predictive motor plans.

Since no central brain clock has ever been identified, in contrast to that of digital computers, it is not clear how neurons organise their activity into a coherent whole during ongoing behaviour. Synchronised rhythmic synaptic activity, manifesting itself as oscillations in the local extracellular electrical potential has attracted much attention as a window into the dynamic organisation of neuronal ensembles (Buzsáki and Draguhn, 2004). Such rhythms cover a range of frequencies from about one to a hundred cycles per second and sometimes more. It has also been suggested that oscillatory activity in the olivo-cerebellar circuit may determine a fundamental time interval for motor processing (Llinás, 1988). However, no universally accepted picture of correlated neuronal activity has yet emerged, nor is it generally understood how the classical concepts of static sensory, navigational and motor maps would merge with the rhythmic organisation of dynamically evolving neuronal subpopulations. **See also**: Oscillatory Neural Networks

Circadian clocks and rhythms on longer timescales, such as annual rhythms, are not discussed here. **See also**: Circadian Rhythms; Oscillatory Neural Networks

Which Computational Rules for the CNS?

Abstracting general rules for neural information processing is an underlying driving force for much of the research described in this article. Yet, the molecular and cellular construction of brains and the intricacies of behavioural testing represent formidable experimental obstacles. In no brain area do we know for instance the wiring diagram with any degree of certainty (i.e. its connectomics) and new cell types are regularly discovered even in well-known areas such as the retina and the cerebellum. The profound influence of anaesthetics on neuronal firing patterns has

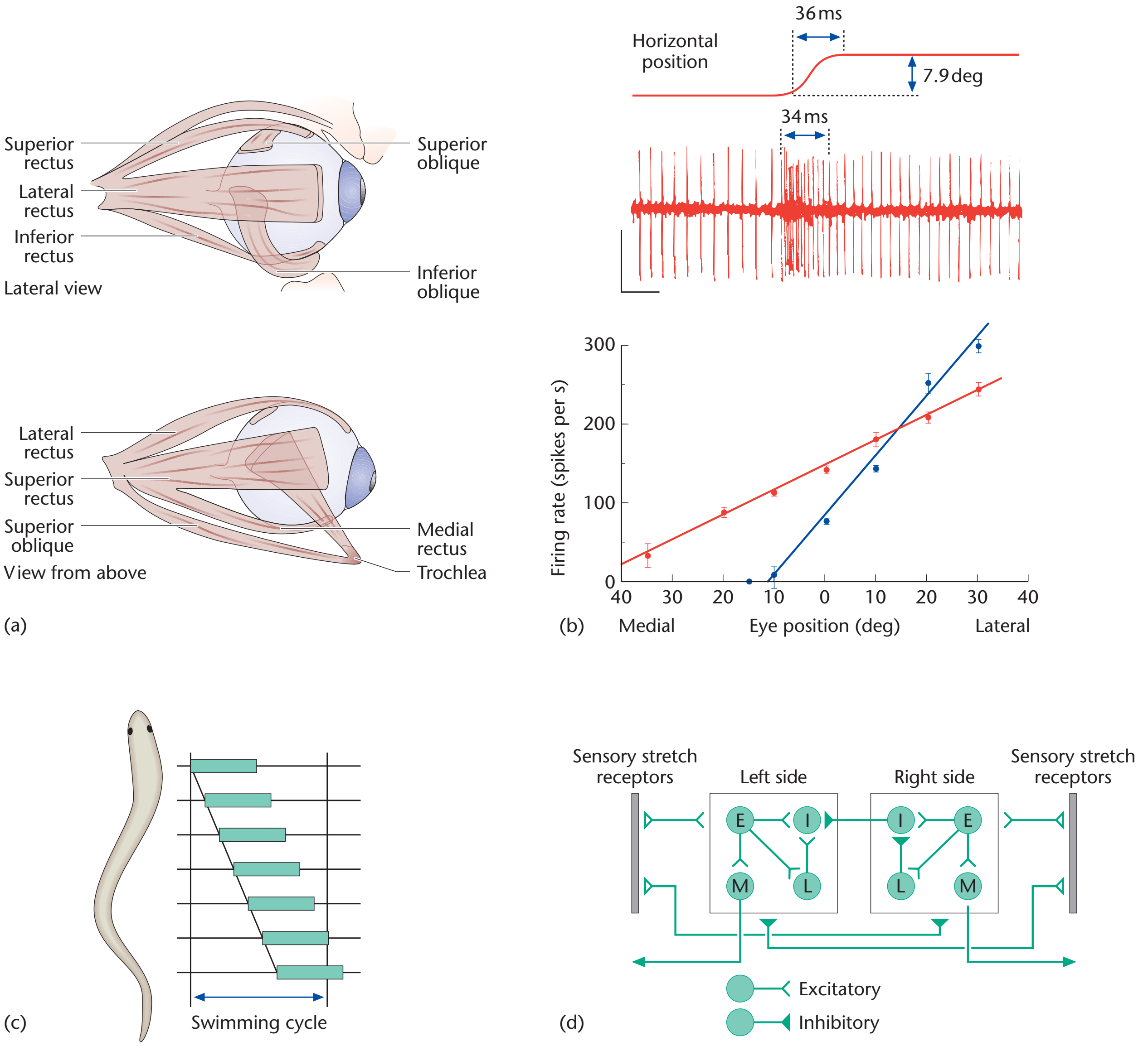


Figure 5 (a) Anatomy and relative positioning of extraocular muscles. The muscular apparatus for eye movements consists of four recti (superior, inferior, lateral and medial) and two oblique muscles (inferior and superior). The superior oblique muscle passes through a pulley of bone called the trochlea. (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. Copyright © 1989, with permission from Elsevier Science. (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. Copyright © 1995, with permission from Elsevier Science.

become clear (Smear *et al.*, 2011), casting doubt on the wisdom inferred from neuronal responses and on the models of brain function derived under such conditions. Early concepts of sensory processing and response selection gave much emphasis to the faithful transfer of stimuli to and within the brain. Yet, short behavioural response times and the limited bandwidth for axonal information transfer, combined with the stereotyped, but nonetheless species-specific allotment of neural estate to relevant functions may indicate that brains in effect come equipped with embedded information regarding the likely sensory inputs they will face and correspondingly appropriate responses. How these notions from bottom-up neurobiology can be quantified and related to rules of information processing remains unclear. Conversely, behavioural studies indicate, for instance, that mammalian sensory-motor processing may in some circumstances be described using Bayesian inference both at the sensory and motor levels (Angelaki *et al.*, 2011). These observations provide an attractive and comprehensive organisational principle, of relevance for the implementation of similar behaviours in robots, for instance. However, while neurons may be able to carry out Bayesian statistical calculations (Ma *et al.*, 2008), even simple neuronal look-up tables could in principle implement similar behaviours (Churchland and Sejnowski, 1992), leaving much experimental work to be done to sort out the underlying biological implementations in cells and networks.

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 human perception and cognition, 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 (Rivera-Alba *et al.*, 2011), or the relation between energy consumption and the efficiency of neural computations (Niven and Laughlin, 2008). These factors play an important role in driving the evolutionary process, and have been quantified, although they remain difficult to manipulate. Over the course of time, the information processing capacity of nervous systems has been compared with human-made technology, from mechanical calculators, telephone switchboards and digital computers up to quantum computers. Such metaphors and other borrowed concepts may be of help, but may also unwittingly restrain experimental design and the interpretation of physiological data. That such metaphors are often difficult to reconcile with current experimental facts only serve to underscore that the topic of neuronal information processing is still far from being understood and continues to offer rich opportunities for scholarly investigation. **See also**: Learning and Memory

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