School of Mathematical Sciences

G14TNS Theoretical Neuroscience

The nervous system of higher animals is very complex and highly nonlinear. The theory of nonlinear dynamical systems can be used to understand and explain neural phenomena at many different levels, including

- ion currents and action potentials
- short and long term memory
- visual hallucinations
- neural synchronisation
- motor control

This course explores the principles by which single neurons generate spikes, and synaptic networks generate waves and patterns fundamental for neurobiological function.

Biological Background

Central nervous system

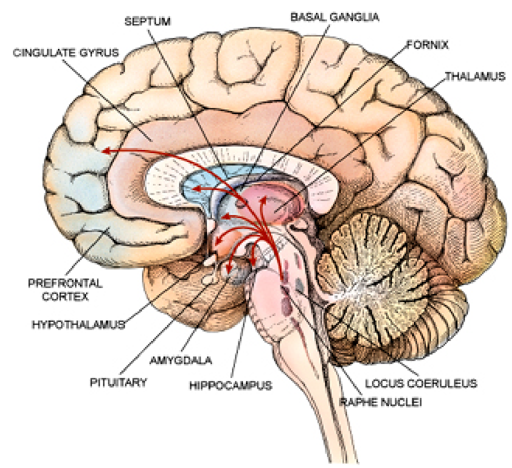
At the highest level of organisation, the central nervous system of mammals has the following broad structure:

- The main site of animal intelligence is the *cerebral cortex*. In humans it is the most highly developed part of the brain. Viewed superficially, the human cortex consists of a thin sheet about 0.2m^2 in area and 2-3mm thick. It is strongly convoluted and forms the exterior of both brain hemispheres. About 80 distinct cortical areas have been identified, each of which represents a highly parallel module specialised for a specific task. For example, in the visual cortex one can identify areas for the analysis of edge orientation, of colour shades, and of velocity, while other cortical areas contain modules for speech comprehension, face recognition, touch (somatosensory cortex) and planning and execution of movements (frontal and motor cortices). Additional areas (association areas) link information affecting combinations of sense, eg the smell of a red rose.
- The *thalamus* plays the role of a sensory gateway to the cortex. All information that flows to and from the cortex is processed by the thalamus. The thalamus is made of regions or nuclei, which make connections with specialised structures. For example, signals from the eye pass on their way to the cortex through a region of the thalamus called the lateral geniculate nucleus.

Various other structures in the brain play ancillary roles that are still not fully understood. Some of these are:

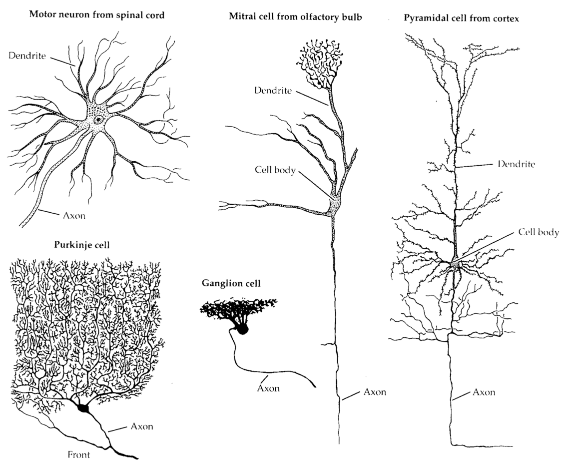
- The *hypothalamus* regulates the internal environment of the body (temperature, heart-rate, food intake etc.) through the control of involuntary movements and the secretion of hormones.

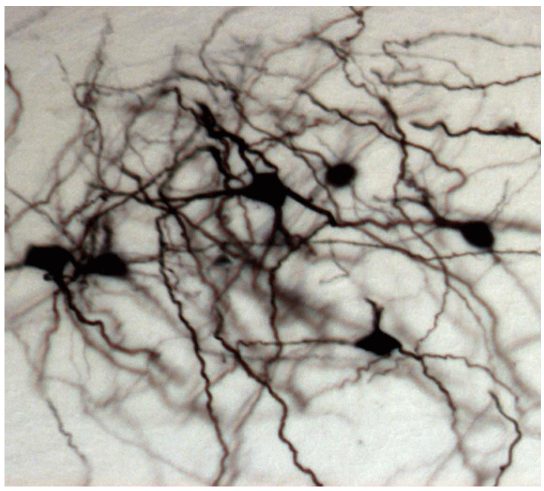
- The *reticular formation* coordinates and executes programs from the hypothalamus.
- The *cerebellum* is involved in the storage and retrieval of precise adjustments to sequences of coordinated movement.
- The *hippocampus* plays a key role in the storage of long term memories.



The neuron

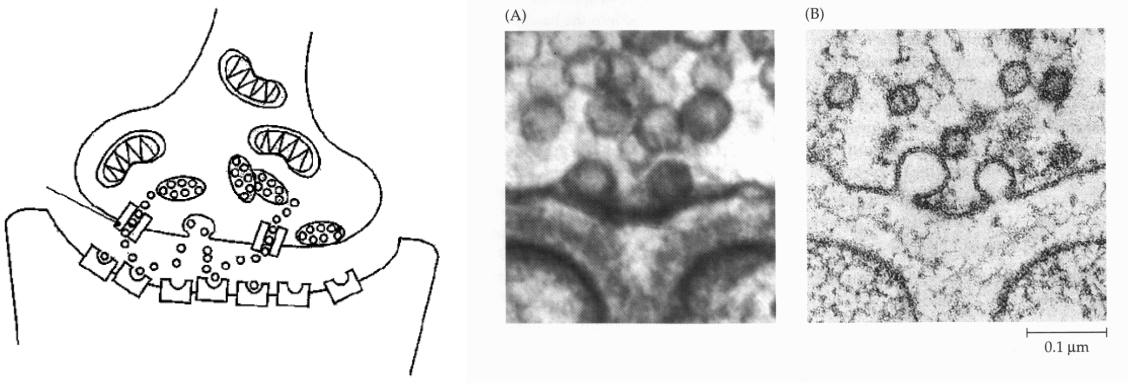
The fundamental processing unit of the central nervous system is the neuron. The total number of neurons in the human brain is around 10^{12}. In 1mm^3 of cortical tissue there are about 10^5 neurons.





- Three main structures can be identified in a typical neuron: dendritic tree, cell body or soma, and axon. These roughly correspond to the input, processing and output functions respectively. The *dendritic tree* is a branched structure that forms the main input pathway of a neuron. It sums the output signals received from surrounding neurons in the form of an electrical potential, which diffuses along the tree to the soma. If the total potential at the soma exceeds a certain threshold value, the neuron produces a short electrical spike or *action potential*, which is then conducted along the *axon*. The axon itself branches out so that the pulse is transmitted to several thousand target neurons.

- The contacts of the axon to target neurons are either located on the dendritic tree or directly on the soma, and are known as *synapses*. Most synapses are chemical contacts, that is, the arrival of an action potential at the synapse induces the secretion of a neurotransmitter that in turn leads to a change in the potential of the membrane of the target neuron. Depending on the type of synapse, an incoming pulse either causes an increase in electrical potential (excitatory synapse) or a decrease (inhibitory synapse).

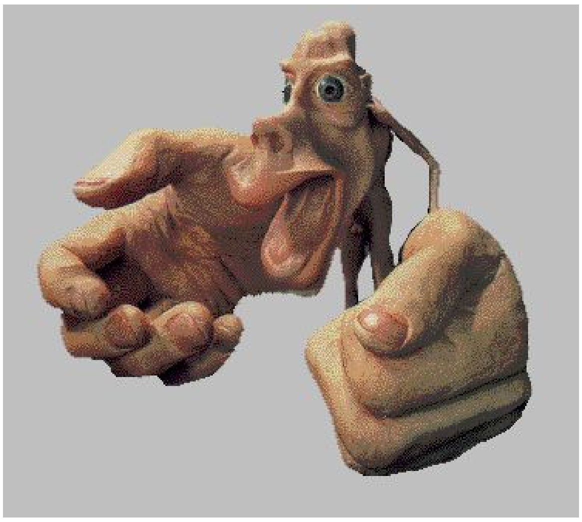


Left: Schematic diagram showing release of neurotransmitter as vesicle membrane fuses with end bulb membrane. Right: Electron micrograph showing how synaptic vesicles fuse with cell membrane as neurotransmiter is discharged.

- The total input to a neuron is continuous-valued (the resulting electrical potential at the soma), whereas the output is discrete (either it fires a pulse or it does not).
- A single neuron may have thousands, tens of thousands or hundreds of thousands of synapses. However, the brain as a whole is sparsely connected since a neuron will only be connected directly to a tiny fraction of other neurons.
- An action potential (spike) lasts about 1msec. Synaptic transmission can last from a few to a few hundred msec. Changes in synaptic potential induced by the arrival of an action potential can last from 1msec to many minutes.

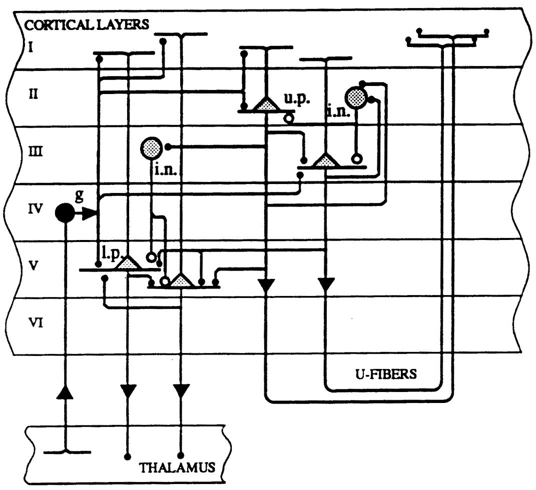
Organisational structures

- **Topographic maps**. A major principle of organisation within the sensory and motor systems is the topographic map. Most signals from the environment are received by the brain from *sensory surfaces* which are covered with receptors. Our largest sensory surface is the skin with its touch and thermal receptors. Probably our most important sensory surface is the retina. Both of these are two-dimensional. An example of a one-dimensional sensory surface occurs within the ear, where receptors are arranged along the spiral-shaped cochlea; each receptor is tuned to a particular frequency whose value depends on the spatial location of the receptor along the cochlea. Although the signals from a sensory surface to the corresponding primary sensory area in the cortex passes through several intermediate levels (eg thalamic nuclei), it is found that adjacent receptors in the sensory surface always connect to adjacent neurons in the cortex. Thus we have a so-called topographic mapping between the sensory surface and the cortical area. The fact that neighbouring processing elements are concerned with similar representations allows the brain to save considerably on its wiring. It is also significant that the topographic map is distorted, in the sense that some regions of the sensory surface occupy relatively larger regions of cortex. An example is the hand region of the somatosensory cortex.



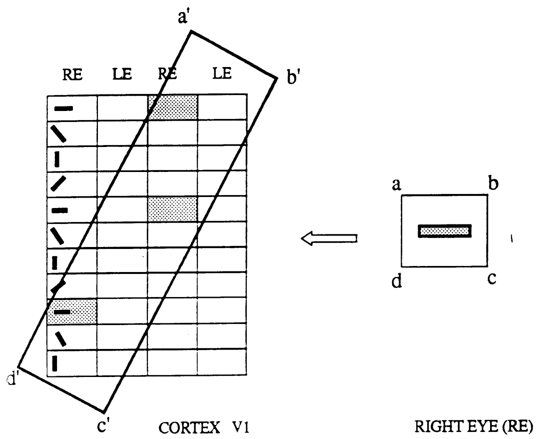
The human homunculus.

- **Layers**. Many brain areas display not only a topographic organisation, but also a laminar structure. All cortical areas consist of six layers (I-VI), one above the other, which differ in relative thickness. Broadly speaking, layer IV generally serves as input layer. The source of output connections to distant cortical regions is layer V, whereas layers I and II are the main output locations for short-range connections to surrounding neurons. These latter connections form the upper layer I. Layer VI sends output feedback to layer IV. Note that there are also two main classes of cortical neurons that are distinguished by shape and functional role. Pyramidal cells (about 80% of total neurons) have long-range axons and stimulate excitatory synapses of target cells, whilst star-shaped stellate cells have short-range axons and are usually inhibitory. It is believed that the important information is coded in the activity of the pyramidal cells, whereas the stellate cells act as a stabiliser of the system by inhibiting activity in excited regions.



The neuronal structure of the cortical sheet. i.n.: inhibitory neurons; g: granule cells; l.p.; lower pyramidal; u.p.;upper pyramidal neurons; solid circles: excitatory synapses; open circles: inhibitory synapses

- **Columns**. As well as the horizontal organisation seen in the laminae, cortical structures also display vertical organisation. It is found that cells with similar properties are arranged in vertical columns cutting across the various laminae. In visual cortex the dominant systems are the ocular dominance and orientation columns. Neurons lying within a single orientation column all respond selectively to bar stimuli of the same orientation. Similarly, cells lying at the centre of an ocular dominance column receive inputs from one eye. Binocular cells (inputs from both eyes) are found at the borders of left- and right-eye ocular dominance columns.



Cortical bands in V1. Horizontal stripes are bands sensitive to line orientation. Vertical stripes are bands of ocular dominance. A retinal region *abcd* in the right eye (RE) stimulated by a horizontal line projects on a receptive field*a'b'c'd'* and gives rise to cortical activities in the shaded areas.

- **Recurrent connections**. Forward connections from one area of the brain to another are generally matched by recurrent connections back to the area of origin.

Learning

- Adaptation in the central nervous system depends on local changes in the synapses of neurons. Such modifications alter the strengths of the connections between the neurons. There are several ways that such connectivity might be altered. (i) Postsynaptic changes in the dendrites might lead to the creation of new synapses or the removal of old ones. Existing synapses might be modified. (ii) Presynaptic changes in the axon might lead to changes in the amount of neurotransmitter released on arrival of an action potential. Alternatively, new axonal branches might be formed.

- A general principle of synaptic weight change is Hebb's rule:

  When an axon of cell A excites cell B and repeatedly or persistently takes part in firing it, some growth or metabolic change takes place in one or both cells such that the efficiency of A in firing B is increased.

  The simplest formal version of the Hebb rule for changing the strength $w_{\rm AB}$ of the weight from neuron A to neuron B is

$$\Delta w_{\rm AB} \propto {\rm F_A F_B}$$

  where $\rm F_A$ is the average firing rate (number of spikes per second) of neuron A and similarly for $\rm F_B$.