1

Introduction to Electroencephalography

1.1 Introduction

The brain is the most amazing and complicated part of the human body and is responsible for controlling all other organs. The neural activity of the human brain starts between the seventeenth and twenty-third week of prenatal development. It is believed that from this early stage and throughout life electrical signals generated by the brain represent not only the brain function but also the status of the whole body. This assumption provides the motivation to study and understand the range of brain activities including normal brain rhythms, brain responses to stimuli, brain motor generators, and finally brain connectivity. One or more of these activities change in cases of brain disorder, disease, or abnormality. The brain status and often the entire body condition can then be recognized by applying advanced digital signal processing and machine learning methods to the electroencephalography (EEG) signals measured from the brain, and thereby underpin the later chapters of this book.

Although nowhere in this book do the authors attempt to comment on the physiological aspects of brain activities, there are several issues related to the nature of the original sources, their actual patterns, and the characteristics of the medium, that have to be addressed. The medium defines the path from the neurons, so-called signal sources, to the electrodes, which are the sensors where some form of mixtures of the sources (for the case of scalp electrodes) or individual sources (e.g. for subdural electrodes) are measured.

Understanding of neuronal functions and neurophysiological properties of the brain together with the mechanisms underlying the generation of signals and their recordings is however, vital for those who deal with these signals for detection, diagnosis, and treatment of brain disorders and the related diseases.

Examining brain activity or abnormality, however, is not limited to the use of EEG. For the abnormalities which affect the brain structure, different radiographical methods can be used. Also, for detecting the brain functional abnormalities, which is the main agenda for activity detection and functional monitoring, magnetoencephalography (MEG) and functional magnetic resonance imaging (fMRI) may be used. However, MEG is expensive and not readily accessible, and fMRI has very low temporal resolution and is not widely

EEG Signal Processing and Machine Learning, Second Edition. Saeid Sanei and Jonathon A. Chambers.

available. Therefore, EEG remains the main functional brain scanning modality as it is cheap, portable, and widely available.

We begin by providing a brief history of EEG measurements and looking at the journey from the time the brain function was initially recognized to the current time when new techniques in data processing, machine learning, and artificial intelligence have become popular research focuses.

1.2 History

The first understanding of the brain was in 1700 BCE when Imhotep lived in Egypt (in Edwin Smith Surgical Papyrus). At that time the hieroglyphic for 'brain' was presented as that in Figure 1.1. Then, during 460–379 BCE, Hippocrates discussed and introduced epilepsy as a disturbance of the brain. Since then many physicians, clinicians, and philosophers from around the world, particularly from Greece (Roman) and Iran (Persian), have encountered various brain diseases. In his Canon of Medicine (Al-Qanun fi al-Tibb), Avicenna (980–1037, also known as Abu Ali Sina), a Persian physician and philosopher, categorizes the causes of epilepsy into two main groups: those caused by brain diseases and those associated with the abnormalities and diseases of other organs.

However, the history of EEG, as an instrument to record the brain activity, goes back to when for the first time some activity of the brain was recorded or displayed. Carlo Matteucci (1811–1868, Pisa, Italy) and Emil Du Bois-Reymond (1818–1896, Berlin, Germany) were the first people who registered the electrical signals emitted from muscle nerves using a galvanometer and established the concept of neurophysiology [1, 2]. However, the concept of *action current* introduced by Hermann Von Helmholtz (1821–1894, Potsdam Germany) [3] clarified and confirmed the negative variations occurring during muscle contraction via measuring the speed of frog nerve impulses in 1849.

Richard Caton (British, 1842–1926) measured the brain activities of rabbits and monkeys from over the cortex in 1875. He discovered the electrical nature of the brain and laid the groundwork for Hans Berger to discover alpha wave activity in the human brain. He also placed two electrodes over the human scalp to record for the first time the brain activity in the form of electrical signals in 1875. Since then, the concepts of electro- (referring to registration of brain electrical activities) encephal- (referring to emitting the signals from head) and gram (or graphy), which means drawing or writing, were combined so that the term EEG was henceforth used to denote electrical neural activity of the brain.

Figure 1.1 Hieroglyphic symbol for the ancient Egyptian word for 'brain'.

Figure 1.2 Physiologists Adolf Beck (Polish, 1863–1942) on the left and Vladimir Pravdich-Neminsky (Ukrainian, 1879–1952) on the right who performed the first recording of brain activities from over the skull.

Fritsch (1838–1927) and Hitzig (1838–1907) discovered that the human cerebral can be electrically stimulated. Vasily Yakovlevich Danilevsky (1852–1939) followed Caton's work and finished his PhD thesis in the investigation of brain physiology in 1877 [4]. In this work he investigated the brain activity following electrical stimulation as well as spontaneous electrical activity in the brain of animals.

The cerebral electrical activity observed over the visual cortex of different species of animals was reported by Ernst Fleischl von Marxow (1845–1891). Napoleon Cybulski (1854–1919) provided EEG evidence of an epileptic seizure in a dog caused by electrical stimulation.

The idea of the association of epileptic attacks with abnormal electrical discharges was expressed by Kaufman [5].

Adolf Beck (Polish, 1863–1942) and Vladimir Pravdich-Neminsky (Ukrainian, 1879–1952) measured the EEG from over the skull of dogs. Therefore, these two scientists are indeed the pioneers in scalp EEG recording (Figure 1.2).

Pravdich-Neminsky recorded EEG from the brain, termed the dura, and the intact skull of a dog in 1912. He observed a 12–14 cycles s^{-1} rhythm under normal conditions which slowed under asphyxia and later called it the *electrocerebrogram*.

Although much research work on EEG principles and measurements has been performed by the above scientists, Hans Berger (1873–1941, Germany) was credited and named the first one for discovering and measuring human EEG signals. He began his study of human EEGs in 1920 [6]. Berger is well known by almost all electroencephalographers. He started working with a string galvanometer in 1910, then migrated to a smaller Edelmann model, and after 1924, to a larger Edelmann model. In 1926, Berger started to use the more powerful Siemens double coil galvanometer (attaining a sensitivity of 130 $\mu V\ cm^{-1}$) [7]. His first report of human EEG recordings of one to three minutes duration on photographic paper was in 1929. In this recording he only used a one channel bipolar method with fronto-occipital leads. Recording of the EEG became popular in 1924. The first report of 1929 by Berger included the alpha rhythm, as the major component of the EEG signals as described later in this chapter, and the alpha blocking response.

During the 1930s, the first EEG recording of sleep spindles was undertaken by Berger. He then reported the effect of hypoxia on the human brain, the nature of several diffuse and localized brain disorders, and gave an inkling of epileptic discharges [8]. During this time another group established in Berlin-Buch and led by Kornmüller, provided more precise

recording of the EEG [9]. Berger was also interested in cerebral localization and particularly in the localization of brain tumours. He also found some correlation between mental activities and the changes in the EEG signals.

Toennies (1902–1970) from the group in Berlin built the first biological amplifier for the recording of brain potentials. A differential amplifier for recording of EEGs was later produced by the Rockefeller foundation in 1932.

The importance of multichannel recordings and using a large number of electrodes to cover a wider brain region was recognized by Kornmüller [10]. The first EEG work focusing on epileptic manifestation, and the first demonstration of epileptic spikes was presented by Fischer and Lowenbach [11, 12].

In England, W. Gray Walter became the pioneer of clinical EEG. He discovered the foci of slow brain activity (delta waves), which initiated enormous clinical interest in the diagnosis of brain abnormalities. In Brussels, Fredric Bremer (1892–1982) discovered the influence of afferent signals on the state of vigilance [13].

Research activities related to EEGs started in North America in around 1934. In this year, Hallowell Davis illustrated a good alpha rhythm for himself. A cathode ray oscilloscope was used around this date by the group in St. Louis University in Washington, in the study of peripheral nerve potentials. The work on human EEGs started at Harvard in Boston and the University of Iowa in the 1930s. The study of epileptic seizure developed by Fredric Gibbs was the major work on EEGs during these years, as the realm of epileptic seizure disorders was the domain of their greatest effectiveness. Epileptology may be divided historically into two periods [14]: before and after the advent of EEG. Gibbs and Lennox applied the idea of Fischer based on his studies about picrotoxin and its effect on the cortical EEG in animals to human epileptology. Berger [15] showed a few examples of paroxysmal EEG discharges in a case of presumed petit mal attacks and during a focal motor seizure in a patient with general paresis.

As the other great pioneers of EEG in North America, Hallowell Davis, Herbert H. Jasper, Frederic A. Gibbs, William Lennox, and Alfred L. Loomis were the earliest investigators of the nature of EEG during human sleep. Alfred L. Loomis, E. Newton Harvey, and Garret A. Hobart were the first who mathematically studied the human sleep EEG patterns and the stages of sleep. At McGill University, Herbert Jasper studied the related behavioural disorder before he found his niche in basic and clinical epileptology [16].

The American EEG Society was founded in 1947 and the first international EEG Congress was held in London, United Kingdom around this time. While the EEG studies in Germany were still limited to Berlin, Japan gained attention by the work of Motokawa, a researcher of EEG rhythms [17]. During these years the neurophysiologists demonstrated the thalamocortical relationship through anatomical methods. This leads to the development of the concept of centrencephalic epilepsy [18, 30].

Throughout the 1950s the work on EEGs expanded in many different places. During this time surgical operation for removing the epileptic foci became popular and the book entitled *Epilepsy and the Functional Anatomy of the Human Brain* (Jasper and Penfield) was published. During this time microelectrodes were invented. They were made of metals such as tungsten or glass, filled with electrolytes such as potassium chloride, with diameters of less than 3 μm.

Depth EEG of a human was first obtained with implanted intracerebral electrodes by Mayer and Hayne (1948). Invention of intracellular microelectrode technology

revolutionized this method and was used in the spinal cord by Brock et al. in 1952, and in the cortex by Phillips in 1961.

Analysis of EEG signals started during the early days of EEG measurement. Berger assisted by Dietch (1932) applied Fourier analysis to EEG sequences which was rapidly developed during the 1950s. Analysis of sleep disorders with EEGs started its development in the 1950s through the work of Kleitman at the University of Chicago.

In the 1960s the analysis of EEGs of full-term and premature newborns began its development [19]. Investigation of evoked potentials (EPs), especially visual EPs, as commonly used for monitoring mental illnesses, progressed during the 1970s.

The history of EEG however has been a continuous process which started from the early 1300s and has brought daily development of clinical, experimental, and computational studies for discovery, recognition, diagnosis, and treatment of a vast number of neurological and physiological brain abnormalities as well as the rest of human central nervous system (CNS). At this time, EEGs are recorded invasively and noninvasively using fully computerized systems. The EEG machines are equipped with many signal processing tools, delicate and accurate measurement electrodes, and enough memory for very-long-term recordings of several hours. EEG or MEG machines may be integrated with other neuroimaging system such as fMRI. Very delicate needle-type electrodes can also be used for recording the EEGs from over the cortex (electrocorticogram), and thereby avoid the attenuation and nonlinearity effects induced by the skull. We next proceed to describe the nature of neural activities within the human brain.

1.3 Neural Activities

The CNS generally consists of nerve cells and glia cells, which are located between neurons. Each nerve cell consists of axons, dendrites, and cell bodies. Nerve cells respond to stimuli and transmit information over long distances. A nerve cell body has a single nucleus and contains most of the nerve cell metabolism especially that related to protein synthesis. The proteins created in the cell body are delivered to other parts of the nerve. An axon is a long cylinder, which transmits an electrical impulse and can be several metres long in vertebrates (giraffe axons go from the head to the tip of spine). In humans the length can be a percentage of a millimetre to more than a metre. An axonal transport system for delivering proteins to the ends of the cell exists and the transport system has 'molecular motors' which ride upon tubulin rails.

Dendrites are connected to either the axons or dendrites of other cells and receive impulses from other nerves or relay the signals to other nerves. In the human brain each nerve is connected to approximately 10 000 other nerves, mostly through dendritic connections.

The activities in the CNS are mainly related to the synaptic currents transferred between the junctions (called synapses) of axons and dendrites, or dendrites and dendrites of cells. A potential of 60–70 mV with negative polarity may be recorded under the membrane of the cell body. This potential changes with variations in synaptic activities. If an action potential (AP) travels along the fibre, which ends in an *excitatory* synapse, an excitatory post-synaptic potential (EPSP) occurs in the following neuron. If two APs travel along the same fibre over a short distance, there will be a summation of EPSPs producing an AP on the post-synaptic

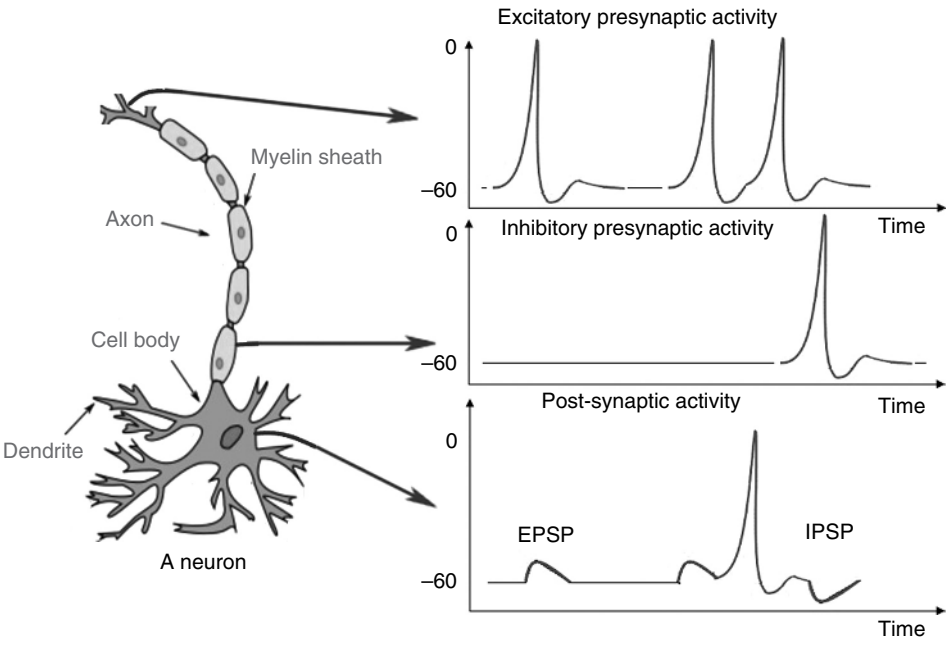

Figure 1.3 The neuron membrane potential changes and current flow during synaptic activation recorded by means of intracellular microelectrodes. APs in the excitatory and inhibitory presynaptic fibre respectively lead to EPSP and IPSP in the post-synaptic neuron.

neuron providing a certain threshold of membrane potential is reached. If the fibre ends in an *inhibitory* synapse, then hyperpolarization will occur, indicating an inhibitory post-synaptic potential (IPSP) [20, 21]. Figure 1.3 shows the above activities schematically.

Following the generation of an IPSP, there is an overflow of cations from the nerve cell or an inflow of anions into the nerve cell. This flow ultimately causes a change in potential along the nerve cell membrane. Primary transmembranous currents generate secondary ional currents along the cell membranes in the intracellular and extracellular space. The portion of these currents that flow through the extracellular space is directly responsible for the generation of field potentials. These field potentials, usually with less than 100 Hz frequency, are called EEGs when there are no changes in the signal average and called DC potential if there are slow drifts in the average signals, which may mask the actual EEG signals. A combination of EEG and DC potentials is often observed for some abnormalities in the brain such as seizure (induced by pentylenetetrazol), hypercapnia, and asphyxia [22]. We next focus on the nature of APs.

1.4 Action Potentials

AP is actually the information transmitted by a nerve. These potentials are caused by an exchange of ions across the neuron membrane and an AP is a temporary change in the membrane potential that is transmitted along the axon. It is usually initiated in the cell body and normally travels in one direction. The membrane potential depolarizes (becomes more

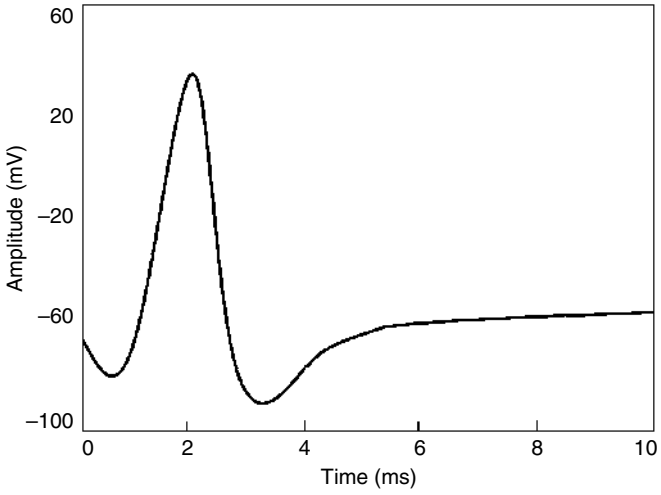

Figure 1.4 An example of an AP.

positive) producing a spike. After the peak of the spike the membrane repolarizes (becomes more negative). The potential becomes more negative than the resting potential and then returns to normal. The APs of most nerves last between 5 and 10 ms. Figure 1.4 shows an example of an AP.

The conduction velocity of APs lies between 1 and 100 m s^{-1}. APs are initiated by many different types of stimuli; sensory nerves respond to many types of stimuli, such as: chemical, light, electricity, pressure, touch, and stretching. Conversely, the nerves within the CNS (brain and spinal cord) are mostly stimulated by chemical activity at synapses.

A stimulus must be above a threshold level to set off an AP. Very weak stimuli cause a small local electrical disturbance, but do not produce a transmitted AP. As soon as the stimulus strength goes above the threshold, an AP appears and travels down the nerve.

The spike of the AP is mainly caused by opening of Na (sodium) channels. The Na pump produces gradients of both Na and K (potassium) ions, both are used to produce the AP; Na is high outside the cell and low inside. Excitable cells have special Na and K channels with gates that open and close in response to the membrane voltage (voltage-gated channels). Opening the gates of Na channels allows Na to rush into the cell, carrying a +ve charge. This makes the membrane potential positive (depolarization), producing the spike. Figure 1.5 shows the stages of the process during evolution of an AP for a giant squid.

For a human being the amplitude of the AP ranges between approximately −60 to 10 mV. During this process [23]:

I) When the dendrites of a nerve cell receive the stimulus the Na^+ channels will open.
II) If the opening is sufficient to drive the interior potential from −70 mV up to −55 mV, the process continues.
III) As soon as the action threshold is reached, additional Na^+ channels (sometimes called voltage-gated channels) open. The Na^+ influx drives the interior of the cell membrane up to about +30 mV. The process to this point is called depolarization.
IV) Then Na^+ channels close and the K^+ channels open. Since the K^+ channels are much slower to open, the depolarization has time to be completed. Having both Na^+ and K^+

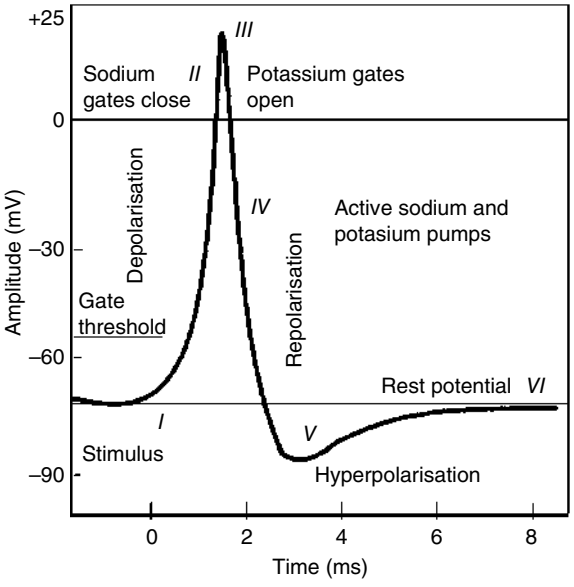

Figure 1.5 Changing the membrane potential for a giant squid by closing the Na channels and opening K channels. (Source: adapted from Ka Xiong Charand [23].)

channels open at the same time would drive the system towards neutrality and prevent the creation of the AP.

V) Having the K^+ channels open, the membrane begins to repolarize back towards its rest potential.

VI) The repolarization typically overshoots the rest potential to a level of approximately −90 mV. This is called hyperpolarization, and would seem to be counterproductive, but it is actually important in the transmission of information. Hyperpolarization prevents the neuron from receiving another stimulus during this time, or at least raises the threshold for any new stimulus. Part of the importance of hyperpolarization is in preventing any stimulus already sent up an axon from triggering another AP in the opposite direction. In other words, hyperpolarization assures that the signal is proceeding in one direction.

After hyperpolarization, the Na^+/K^+ pumps eventually bring the membrane back to its resting state of −70 mV.

The nerve requires approximately two milliseconds before another stimulus is presented. During this time no AP can be generated. This is called the refractory period. The generation of EEG signals is next described.

1.5 EEG Generation

An EEG signal is an indirect measurement of currents that flow during synaptic excitations of the dendrites of many pyramidal neurons in the cerebral cortex. When the brain cells (neurons) are activated, the synaptic currents are produced and propagate through the dendrites. This current generates a magnetic field measurable by EMG machines and a secondary electrical field over the scalp measurable by EEG systems.

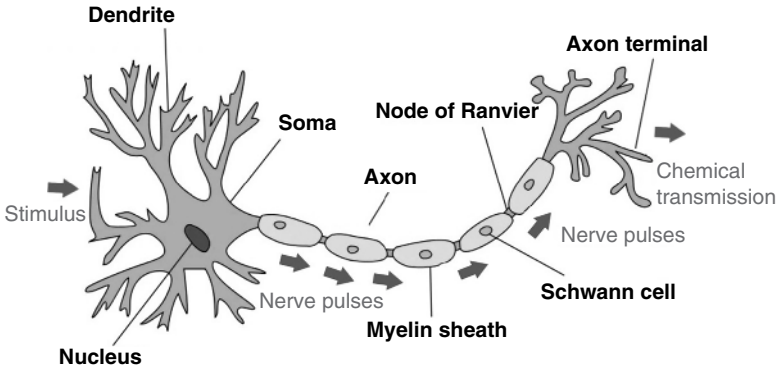

Figure 1.6 Structure of a neuron.

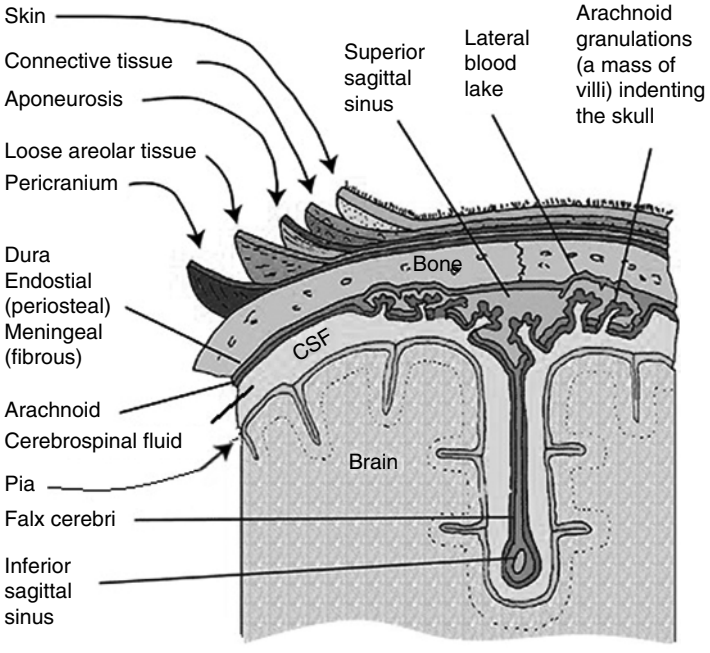

Figure 1.7 The head layers from brain to scalp.

Differences of electrical potentials are caused by summed post-synaptic graded potentials from pyramidal cells that create electrical dipoles between the soma (body of a neuron) and apical dendrites which branch from neurons (Figure 1.6). The current in the brain is generated mostly due to pumping the positive ions of sodium, Na^+, potassium, K^+, calcium, or Ca^{++}, and the negative ion of Cl^-, through the neuron membranes in the direction governed by the membrane potential [24].

The human head consists of three main layers of scalp, skull, brain (Figure 1.7) including many other thin layers in-between. In addition, the scalp consists of different layers such as

skin, connective tissue, which is a thin layer of fat and fibrous tissue lying beneath the skin, the loose areolar connective tissue, and the pericranium, which is the periosteum of the skull bones and provides nutrition to bone and capacity for repair. Conversely, the brain is covered by a thin layer of cortex, which encompasses various brain tissues. The cortex includes arachnoid, meninges, dura, epidural, and subarachnoid space. The skull attenuates the signals approximately one hundred times more than the soft tissue. Conversely, most of the noise is generated either within the brain (internal noise) or over the scalp (system noise or external noise). Therefore, only large populations of active neurons can generate enough potential to be recordable using the scalp electrodes. These signals are later amplified greatly for display purposes. Approximately 10^{11} neurons are developed at birth when the CNS becomes complete and functional [25]. This makes an average of 10^4 neurons per cubic millimetre. Neurons are interconnected into neural nets through synapses. Adults have approximately 5.10^{14} synapses. The number of synapses per neuron increases with age, whereas the number of neurons decreases with age.

Given the diversity in electric and dielectric properties of the head layers, the distribution of attenuation of brain discharges including cortical, subcortical, and hippocampal activities is not uniform over the scalp and is subject to nonlinearity. Therefore, to model the neuronal pathways or localization of brain activity sources an accurate head electrical model should be available.

From an anatomical point of view the brain may be divided into three parts: the cerebrum, cerebellum, and brain stem (Figure 1.8). The cerebrum consists of both left and right lobes of the brain with highly convoluted surface layers called the cerebral cortex.

The cerebrum includes the regions for movement initiation, conscious awareness of sensation, complex analysis, and expression of emotions and behaviour. The cerebellum coordinates voluntary movements of muscles and balance maintaining.

The brain stem controls involuntary functions such as respiration, heart regulation, biorhythms, neurohormones, and hormone secretion [26].

The study of EEG paves the way for diagnosis of many neurological disorders and other abnormalities in the human body. The acquired EEG signals from a human (and also from animals) may for example be used for investigation of the following clinical problems [26, 27]:

- Monitoring alertness, coma, and brain death.
- Locating areas of damage following head injury, stroke, and tumour.
- Testing afferent pathways (by EPs).
- Monitoring cognitive engagement (alpha rhythm).
- Producing biofeedback situations.
- Controlling anaesthesia depth (servo anaesthesia).
- Investigating epilepsy and locating seizure origin.
- Testing epilepsy drug effects.
- Assisting in experimental cortical excision of epileptic focus.
- Monitoring the brain development.
- Testing drugs for convulsive effects.
- Investigating sleep disorders and physiology.
- Investigating mental disorders.

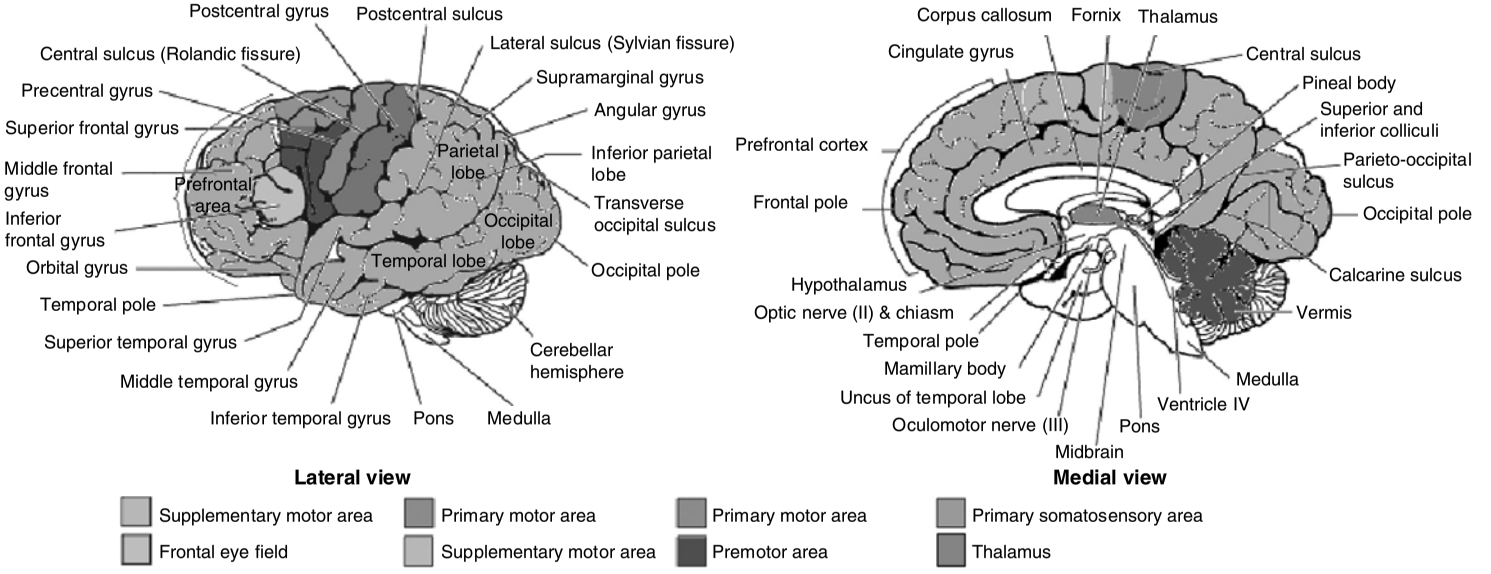

Figure 1.8 Diagrammatic representation of the major parts of the brain.

- Recognition of emotions for autistics.
- Monitoring mental fatigue for pilots and drivers.
- Providing a hybrid data recording system together with other imaging modalities.
- This list confirms the rich potential for EEG analysis and motivates the need for advanced signal processing techniques to aid the clinician in their interpretation. We next proceed to describe the brain rhythms, which are expected to be measured within EEG signals.
- Some of the mechanisms that generate the EEG signals are known at the cellular level and rest on a balance of excitatory and inhibitory interactions within and between populations of neurons. Although it is well established that the EEG (or MEG) signals result mainly from extracellular current flow, associated with summed post-synaptic potentials in synchronously activated and vertically oriented neurons, the exact neurophysiological mechanisms resulting in such synchronization to a given frequency band, remain obscure.

1.6 The Brain as a Network

Networks are already an integral part of human daily social, business, and intellectual life. Networking science is appealing to the field of neuroscience as the brain function stems from the communication and signalling between the neurons. The measured EEG amplitudes probed at each electrode have been the main parameter in evaluating brain function. Synchrony between left and right brain lobes gives further insight into detection of abnormalities such as mental fatigue and dementia and is associated with many other brain states such as emotions, as stated in the next chapter. The synchrony is often measured in the frequency domain where the variations in frequency and phase, corresponding to the time delay between the lobes, can be easily measured. More generally, recent developments in network science, however, have created a new direction in the study of brain normal and abnormal functions.

Although the fundamental concepts in network science originated from mathematics [28] and are used mostly in communications, a number of well established approaches, such as autoregressive modelling, have been used in characterizing the brain functional connectivity from the multichannel EEG. In addition, graph theory has become popular in designing effective classifiers which can segment the EEGs in time–space into the regions each encompassing a separate functionally connected brain region. In [29], a review of recent advances in neuroscience research in the specific area of brain connectivity as a potential biomarker of Alzheimer's disease with a focus on the application of graph theory can be studied.

Later in this book, we derive equations for the graphs applied to EEG in a similar way to those of brain connectivity estimators. We also observe that machine learning techniques such as deep neural networks can be directly applied to graphs for recognition of the brain state.

1.7 Summary

Following some details on EEG history, this chapter overviews the neuronal level analysis of the brain function. It also provides some information about the head anatomy. Generation of EEG signals as the result of signalling at the dendrite-dendrite or axon-dendrite

synapses and production of APs, is an important and fundamental concept covered in this chapter. It is also highlighted that normal brain rhythms, brain evoked responses, and brain connectivity are the outcomes of neuronal activities and should be treated differently to recognize the brain normal and abnormal states.

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