4 Neuroglia, the Other Brain Cells*

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The name glia derives from the Greek work for glue and suggests what role these cells have been thought to play, namely holding together the rest of the brain tissue. While it is probably true that glial cells provide structural support for the neurons, which they outnumber in the brain by a factor of 9, research during recent years has revealed many more important functions these cells play in the central and peripheral nervous system. It is now understood that glia directs the neuronal growth in the developing brain. Oligodendrocytes produce coatings of myelin that electrically insulates axons and thus speed up propagation of electric pulses and microglia serve as immune cells to the brain.

An important species of glial cells are the start-shaped astrocytes. They appear as close partners to the neurons as they regulate the neuronal microenvironment, listen to the neuronal chatter, and feedback to the neuronal dynamics. Astrocytes pick up the neurotransmitter glutamate from synapses and convert it into glutamine. Glutamine is returned to the neurons where it can be converted back into glutamate when needed. It has been demonstrated recently that the synapses of neurons are disrupted minutes after the functions of glial cells in their surroundings had been disrupted with a chemical. Another important function of the astrocytes (and other glial cells) is to absorb K+ from the extracellular space. This is achieved by a large conductance for K+ and interconnectivity between astrocytes through gap junctions that permit rapid distribution of ionic products throughout the astrocytic network. This is particularly important for the neuronal system since K+ is released from the neurons after the action potential. The failure of the astrocytes of doing so, leads to neuronal depolarization and misfunction; cortical depression waves and migraine are being discussed as a consequence of astrocytic failure in tissues such as the visual cortex where astrocytes are rarer in favor of more neurons. The influence of glial cells on the EEG is discussed in Chap. 5.

Astrocytes sport a variety of receptors at their surface, receptors for the excitatory neurotransmitter glutamate, the inhibitory neurotransmitter GABA and the rarer kainate. These receptors allow the astrocyte to read neuronal messages. Although astrocytes do not develop long extensions such

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as the neurons, they send shorter extensions to envelope neuronal clefts where they sense and bind the neurotransmitter.

4.0.1 Voltage-gated Na$^+$ Channels in Astrocytes and Action Potentials

For a long time glial cells have been believed to be electrically passive since full cell recordings have indicated this. Patch clamp recordings from cultured rabbit Schwann cells [315] and rat astrocytes [316,317] have revealed that astrocytes do express voltage-gated Na$^+$, K$^+$ and Ca$^{2+}$ channels. For the formation of action potentials in neurons, the voltage-gated Na$^+$ channels are essential. There is evidence that the expression of Na$^+$ channels is influenced by the neuronal environment. Removal of neuronal tissue has led to almost complete loss of Na$^+$ channels in nearby astrocytes [318,319]. These findings suggest that the expression of ion channels in glial cells is dynamic and controlled by the micro-environment. In Schwann cells, the glial cell in which neurons of the peripheral nervous system are embedded in, the density of voltage-gated Na$^+$ channels is particularly large close to the nodes of Ranvier [320], the segments of axons that are not myelinated and active propagation re-shapes the dispersing electric signal. This suggests that Schwann cells serve as a local source of Na$^+$ channels for the nodal region of the neuronal axon. This theory is consistent with the observation that Schwann cells contain an intracellular pool of the Na$^+$ channel protein [320].

The astrocytes and the neurons in the central nervous system (CNS) are engaged in a similar symbiosis as are the Schwann cells and the neurons in the PNS [321,322]. Electrophysiological recordings from astrocytes from the optic nerve have revealed voltage activated transient Na$^+$ currents [323,324]. The presence of voltage-activated Na$^+$ currents suggest that astrocytes may elicit action potentials. This, however, is normally not the case for the following reasons [325]:

1. The density of Na$^+$ channels is normally much lower than in neurons.
2. The K$^+$ conductivity is higher than in neurons. The resting potential is therefore more negative and an even smaller portion of the smaller number of existing Na$^+$ channels is open.
3. The gap junction coupling between the astrocytes tends to clamp the voltage to a common fixed value and suppresses voltage variations and therefore, for example the formation of an action potential.

In pathological tissues, however, the situation can be different. In patients with temporal lobe epilepsy astrocytes from the seizure focus (where the seizure focus was in the hippocampus) have an approximately two orders of magnitude larger density of voltage-gated Na$^+$ channels. Careful studies of these astrocytes have revealed the following results [326]:

1. The resting membrane potential ($\approx -55$ mV) was significantly more depolarized than in normal cells ($\approx -80$ mV).