Study of neuron-microelectrode junction formed via engineered synapse organizer

2120020 Kosuke Sekine

While the basic principles of information encoding and processing in neural circuits have not been uncovered, it is generally believed that the membrane potential dynamics of the constituent cells are closely involved. It is thus significant to develop techniques that enable detailed measurement of electrical activity in neurons in order to gain insight into the basic principles of circuit operation. Existing activity measurement methods can be classified into “optical” and “electrical” measurement methods. In the former, genetically encoded voltage indicators are expressed in the cells of a specific type to be measured. In order to achieve sufficiently precise measurements, it is essential to further improve the performance of optical probes, and many researchers are continuing their efforts for this direction. The latter uses microelectrodes, which generally enable stable recording with a good signal-to-noise ratio. The drawback has been the difficulty of spatial measurement, but recent developments such as flexible multi-electrode arrays are making it possible to measure neuronal activity at multiple points on a large scale. On the other hand, electrical measurement methods do not have the specificity for cell types that optical measurement methods have. The lack of cell type specificity is a critical disadvantage, since neural circuits are composed of diverse cell types, which are generally thought to play different roles in circuit function.

This study focuses on synapse organizers, a group of molecules involved in synapse formation and maintenance that have recently been identified, with the goal of forming specific junction structures between neurons and microelectrodes and developing them into basic principles for cell-specific electrical measurement methods that overcome the above drawbacks in the future. Chapter 1 describes the background of my research, and Chapter 2 discusses the molecular design of the synapse organizer using a molecular biological approach, resulting in the development of a compact engineered synapse organizer. In Chapter 3, it is demonstrated that the engineered synapse organizer can actually form specific junction structures between a metallic microelectrode and a neuron. The details of the function of the synapse-like neuron-microelectrode junction induced by this principle are not yet clear. Therefore, in Chapter 4, I developed microelectrodes simultaneously immobilized with glutamate fluorescent probes to analyze the function of this junction in terms of transmitter release. Thus, these research would serve as a basis for proof-of-principle experiment of the specific formation of neuron-microelectrode junctions via artificial synaptic organizers and physiological analysis of their properties, and this point is summarized in the last chapter.

Key word: neuron, electrical activity, synapse organizer, extracellular recording, cell type specificity