Dissociated neuronal culture coupled to micro-electrode array: measurement of the network dynamics and application toward neural interface

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Primary neuronal cultures dissociated from different regions of the central nervous system have been a classical model for in vitro studies of neurobiological mechanisms. Developed at the beginning of the 80's, the Micro-Electrode Array (MEA) technique nowadays offers a useful experimental approach for in vitro electrophysiological investigations. Previous work demonstrated the possibility to use dissociated neuronal networks coupled to MEAs as a cell-based biosensor \cite{1}. The biocompatibility of the used materials and non-invasive nature of the extracellular measurement, make this system a perfect candidate to routinely record and evaluate the dynamics of the network behavior in spontaneous condition, either on short or long time-scales. This experimental system allows us to explore network properties, while preserving the morphological, molecular and functional properties of the individual neurons in the neocortex.

Here, we present our recent studies using neuronal culture coupled to MEAs: 1) principal properties of cultured neuronal networks revealed by long-term measurement of spatiotemporal dynamics. 2) development of neuronal network cultured on graphene-transferred MEAs. 3) neuronal cultures embodied in a closed-loop environment.

Primary neurons cultured on MEAs autonomously formed functional networks, after elongating axons and establishing synaptic connections (fig. 1A). The neuronal networks showed spontaneous uncorrelated firing within several days; the spontaneous spikes became synchronized bursts as the network grew (fig. 1B). The quantified activity as mean firing rate and bursting rate showed an initial increase and subsequent saturation during the 1-month culture period \cite{2}. As a result of quantification of synaptic density by immunostaining, it was clarified that the number of culture days to saturation from the initial increase in synaptic density corresponded to the electrical activity \cite{3}. In addition, we found the specific gene expression corresponded to the maturation of neuronal network.

Then, we present the study on the neuronal network cultured on graphene-transferred MEAs. As it has been widely known, graphene is a thin layer of pure carbon; it is a single, tightly packed layer of carbon atoms bonded together in a hexagonal lattice. We transferred single-wall graphene to MEA substrate and attempt to culture primary neuronal cells on the substrate. Interestingly, the culture on graphene-transferred MEAs showed higher number of spikes compared to conventional condition.

Finally, we present a new hybrid neuro-robotic architecture based on a neural controller bi-directionally connected to a virtual robot implementing a Braitenberg vehicle aimed at avoiding obstacles. The robot is characterized by proximity sensors and wheels, allowing it to navigate into a circular arena with obstacles of different sizes. As neural controller, we used neuronal cultures. These study offers a new framework for studying, in simplified model system, neuro-artificial bi-directional interfaces for the development of new strategies for brain-machine interaction.

References

\cite{1} Gross GW, et al., Neurosci Lett 1977;6;101-5. \cite{2} Ito D, et al., Neuroscience 2010;171;50-61. \cite{3} Ito D, et al., Brain Res 2013;1534;22-32.