Listening to the brain stars through nanotechnologies

Studies over the past 40 years are showing that neuro-centric vision of the brain is now outdated. It is emerging that astrocytes, a particular class of non-neuronal brain cells, characterized by a star-shaped morphology, play a central role in the structure and functions of the brain, such as memory and learning.

A work published in the Advanced Biosystems, a Wiley scientific journal, coordinated by Valentina Benfenati (CNR-ISOF), in collaboration with Annalisa Convertino and Luca Maiolo (CNR-IMM) reveals that, although they are so-called non-excitable cells, astrocytes have their own bioelectric activity. Their form of excitement and communication is not the "classic" nerve impulse, but rather it consists of small and slow variations of the local signal (of the order of millionths of Volt or billionths of Ampere) which last hundreds of milliseconds.

The difficulty of capturing these tiny signals derives from two main issues: the studies carried out on in vitro astrocytes, usually express different morphology and functions respect to astrocytes in vivo. Indeed, in vivo studies show that star-like morphology is necessary for astrocytes to function properly, and therefore much fundamental information is lost when we study astrocytes in vitro due to an experimental problem.

Furthermore, as the signals of the astrocytes are very small and very slow, it is necessary to engineer and develop electrodes with a particular shape and size (in the range of nanometers) together with an ad-hoc recording systems.

"In our work we have overcome this challenge thanks to the idea of using a forest of silicon nanowires covered with gold" says Annalisa Convertino. "The properties of these nanostructures allow on the one hand to both to differentiate the astrocytes and have a very efficient electrode-cell coupling ", continues Convertino. "The combination of these properties makes our microelectrode array an ideal recording system for listening to the language of astrocytes," says Luca Maiolo.

In fact, the work shows that the astrocytes grown on the silicon nanowire matrix, express a stellate and articulated morphology and the molecular and functional properties are more similar to those that these cells express in vivo. In addition tight junction between nanowire based electrodes and astrocytes processes enables extracellular recording of slow-frequency oscillations generated only by differentiated cells.

It is interesting to note that by applying protocols that mimic conditions that occur in diseases such as **epilepsy**, the intensity of astrocytes slow waves increased.

The authors envisage that astrocytes can actively contribute to the bioelectric activity of the brain.

"We are trying to validate the results in vivo, to verify whether this slow-wave bioelectrical communication in astrocyte plays a role in brain communication processes also related to memory formation or learning," says Benfenati. "The work paves the way for a smarter implementation and integration of nanotechnologies into the brain thus shedding new light on a global understanding of how brain works and how it is affected by diseases," says Convertino. "Technologies that target not only neurons but that allow us, aiming at the stimulation, recording and modulation of astrocytes, to have a more complete vision of how our brain works or how it gets sick" concludes Benfenati.

“We have used a multidisciplinary approach that is proving to be successful in dealing with such complex issues as the mechanisms of brain functioning." Said Dr Roberto Zamboni, Director of CNR-ISOF.

In fact, the 21 researchers involved in the project come from different scientific realities with skills in the fields of chemistry, material science, device physics, mathematics, bioengineering, neuroscience and neurophysiology. The multidisciplinary nature of the working group has therefore made it possible to look at the phenomenon from new and different perspectives, leading to a deeper understanding of how to monitor and modulate brain functions. "The vision is in itself attractive also for broader global strategies involving international and transoceanic partnerships." Adds Luigi Ambrosio, of the working group on "Advanced materials and nanotechnologies" Italian head of the joint working group of the Joint Commission of Italy-USA Cooperation in Materials Science & Technology, on behalf of the Ministry of Foreign Affairs and International Cooperation.

In fact, the work was mainly supported by the ASTROMAT research project funded by the Air Force Office of Scientific Research, Biophysics Programme, coordinated by Benfenati and Convertino.

The generation of glial interfaces could also have a significant impact on the industrial development of advanced health devices that aim to rekindle the brain where it appears to be off. But not only. Understanding the role of astrocytes in cognitive functions could also revolutionize fields such as bioengineering and robotics and artificial intelligence.

Who Consiglio Nazionale delle Ricerche: Istituto per la Sintesi Organica e la Fotoreattività (CNR-ISOF), Bologna; Istituto per la Microelettronica e Microsistemi (CNR-IMM), Rome; Istituto per i Polimeri, Composti e i Biomateriali (CNR-IPCB), Naples; Istituto per lo Studio dei Materiali Nanostrutturati (CNR-ISMN), Bologna; Fondazione Istituto Italiano di Tecnologia (IIT), Rehab Technologies IIT-INAIL Lab, Genoa; Università di Bologna, Dipartimento di Farmacia e Biotecnologie, FaBit, Bologna; US Air Force Research Laboratory, Wright-Patterson AFB, Dayton, OH, USA

What: E. Saracino, L. Maiolo, D. Polese, M. Semprini, A. I. Borrachero-Conejo, J. Gasparetto, S. Murtagh, M. Sola, L. Tomasi, F. Valle, L. Pazzini, F. Formaggio, M. Chiappalone, S. Hussain M. Caprini, M. Muccini, L. Ambrosio, G. Fortunato, R. Zamboni , A. Convertino, V. Benfenati. A Glial-Silicon Nanowire Electrode Junction Enabling Differentiation and Noninvasive Recording of Slow Oscillations from Primary Astrocytes, first published online on Advanced Biosystems.

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