

## THE 2014 NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE

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*Abstract*

The Nobel Assembly at Karolinska Institute has awarded The 2014 Nobel Prize in Physiology or Medicine with one half to Dr. John O'Keefe and the other half jointly to Dr. May-Britt Moser and Dr. Edvard I. Moser "for their discoveries of cells that constitute a positioning system in the brain".

In 1971, John O'Keefe and John Dostrovsky discovered place cells in the brain <sup>(1)</sup>. Based on previous reports that rats with hippocampal damage suffer from altered behavior in new environment and deficit in spatial learning, authors hypothesized that the neural system in hippocampus provides the animal with a spatial map of its environment. To demonstrate this, they implanted microelectrodes that could be moved inside the rat's brain, through the cortex and dorsal hippocampus, to search for active units. The activity of the units was monitored during spontaneous and elicited behaviors, auditory, visual, olfactory and tactile stimulation. As a result, certain units fired maximally when the rat was in a particular location facing a particular direction. This suggested that the hippocampus provides a cognitive mapping system, in which the activity of the cells- the place cells- specifies the orientation of the rat relative to its environment and the occurrence of particular stimuli whilst facing in that orientation. These active place cells would then activate other cells specifying adjacent spatial orientations, thus creating a map that can anticipate the sensory stimuli consequent to a particular movement. Through O'Keefe's discoveries, the cognitive map theory- that predicted that hippocampal damage in rats would result in the absence of exploration and place learning- found its demonstration.

May-Britt and Edvard Moser studied how information is processed in the entorhinal cortex, which is the interface between hippocampus and neocortex <sup>(2)</sup>. They provided evidence that the projections from entorhinal cortex to the hippocampus are topographically organized. Depending on the rat's position and the direction of movement, neurons are activated and these spatial signals are actively transformed into cohesive allosteric representations within the entorhinal cortex. Thus, the information about the rat's position is rep-

resented accurately in entorhinal cortex as well as in hippocampus. In 2005, May-Britt and Edvard Moser described the entorhinal cortex as a map-like structure that contributes to navigation <sup>(3)</sup>. They discovered grid cell-the basic unit of this map. The orientation and field size of grid cells were topographically organized, however their activation and spacing were not influenced by the transformation of the local environment or the visual deprivation. Thus, the grid-cell network forms an environment-independent spatial coordinate system. In this system, grid cells communicate with other types of neurons <sup>(4)</sup> - O'Keefe's place cells, head direction cells (which fire when animals face in a certain direction) and border cells (which fire when animals are near a border or an edge <sup>(5)</sup> - to integrate spatial information, memory formation, and decision-making.

This spatial-navigation system in hippocampus and entorhinal cortex frequently collapses in the early stages of Alzheimer's disease, and these patients cannot recognize the environment. The ground breaking discoveries of John O'Keefe, May-Britt Moser and Edvard Moser have contributed to our understanding of how specialized brain cells work together to create a map that enables us to navigate through environment, and opened new avenues for the treatment of Alzheimer's and other neurological disorders.

John O'Keefe, Ph.D, was born in 1939 in New York City, USA. He received his doctoral degree in physiological psychology from McGill University, Canada in 1967. He was a postdoctoral fellow at University College London, and was appointed Professor of Cognitive Neuroscience in 1987. He is currently Director of the Sainsbury Wellcome Centre in Neural Circuits and Behaviour at University College London.

May-Britt Moser, Ph.D, was born in Fosnavag, Norway in 1963 <sup>(6)</sup>. Together with her future husband Edvard Moser, she studied psychology at the University of Oslo and was awarded Ph.D. in neurophysiology in 1995. She was a postdoctoral fellow at the University of Edinburgh and subsequently a visiting scientist at University College London. She was appointed Professor of Neuroscience in 2000 at the Norwegian University of Science and Technology in Trondheim. She is a co-director and a founder of the Kavli Institute for Systems Neuroscience in Norway, as well as director of the Centre for Neural Computation at the Norwegian University of Science and Technology <sup>(7)</sup>. She is a member of the Royal Norwegian Society of Sciences and Letters, and the Norwegian Academy of Science and Letters.

Edvard Moser, Ph.D, was born in 1962 in Alesund, Norway <sup>(6)</sup>. He was awarded Ph.D. in neurophysiology from the University of Oslo in 1995. He was a postdoctoral fellow together with his wife May-Britt Moser at the University of Edinburgh and a visiting scientist in John O'Keefe's laboratory in London. In 1998, he became a Professor at the Norwegian University of Science and Technology in Trondheim. He is director and a founder of the Kavli Institute for Systems Neuroscience in Norway, as well as co-director of the Centre for Neural Computation at the Norwegian University of Science and Technology <sup>(7)</sup>. He is a member of the Royal Norwegian Society of Sciences and Letters, and the Norwegian Academy of Science and Letters.

### Sažetak

Nobelov komitet na Institutu Karolinska dodelio je Nobelovu nagradu za fiziologiju ili medicinu za 2014. godinu, tako što je polovinu dobio Dr John O'Keefe, a drugu polovinu su podělili Dr May-Britt Moser and Dr Edvard I. Moser „za njihovo otkriće ćelija u mozgu koje predstavljaju sistem za određivanje pozicije“.

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