The Nobel prize in Physiology or Medicine 2014
and related research at KTH Royal Institute of Technology
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The Nobel prize in Physiology or Medicine in 2014 was awarded to John O'Keefe and to May-Britt Moser together with Edward Moser for their discoveries of how neurons in the temporal lobe (on the side of your head, located inside the brain sort of where your ears are) code information about our surroundings.

The work of John O'Keefe shows how neurons in a brain region called hippocampus provide the brain with a code of where we are located. One such neuron fires its nerve impulses according to our position in a room (or outside). Each neuron has its own "favourite" location where it gets active and these neurons were therefore coined "place cells". Since all neurons have different favorite locations, most locations will trigger the activity of a number of neurons. The idea is that the brain, by "listening" to which group of neurons are active, can figure out where we are.

May-Britt and Edward Moser were studying the neighboring brain region called entorhinal cortex. Here, neurons do not have one single favorite spot, but many. In fact, these spots appear as corners in a triangular grid, and were therefore coined "grid cells". Intriguingly, the size of the triangles is different in different parts of entorhinal cortex so that in one end the triangles are small and in the other end they are large. It is assumed that the brain uses information from these neurons to decide where we are located and how we move.

Based on our earlier work (more about that further down), we proposed a model of how these grid cells obtain their firing properties, how they are able to fire their nerve impulses at the triangular points (Giocomo et al, Science, 2007). In this article, we suggest a computational model to explain the mechanism. We also provide experimental support for the model in that we show that the key component of the model, the ion channel named HCN, displays a gradient of change across the entorhinal cortex parallelling the gradient of change seen by Moser&Moser for the size of the triangles.

The idea to our model using the HCN-channel came from our previous work where we studied this ion channel both experimentally (Dickson et al., 2000, Giocomo et al., 2007) and using computational modeling (Fransén et al., 1998, 1999, 2004, Dickson et al., 2000). In particular, in 2004 we explained, based on our modeling work, how the membrane potential oscillations in the stellate neuron appear as a result of the activity of the HCN channel, how the HCN channel contributes to the after hyperpolarization of the stellate neuron and to the clustering of action potential firing. In our work by Giocomo (2007), our modeling of HCN channels were providing the key link between the magnitude of HCN channels observed experimentally and the neuronal oscillation frequency which formed the central component of the mechanism leading to grid firing. Furthermore, based on these models of the HCN channel and the stellate neuron where these channels are located, we also conducted modeling studies on entorhinal cortex network function (Fransén et al., 1999, Hasselmo et al., 2000, 2009, Giocomo et al., 2007).

Our work on stellate neurons built on the work by Angel Alonso, who pioneered the studies of entorhinal cortex (Alonso et al., Exp Brain Res 1987a,b; Alonso et al., Nature, 1989; Alonso and Klink, J Neurophysiol. 1993; Klink and Alonso, J. Neurophysiol. 1993).

References

A phase code for memory could arise from circuit mechanisms in entorhinal cortex
ME Hasselmo, MP Brandon, M Yoshida, LM Giocomo, JG Heys, ...
Neural Networks 22 (8), 1129-1138, 2009

Temporal frequency of subthreshold oscillations scales with entorhinal grid cell field spacing
LM Giocomo, EA Zilli, E Fransén, ME Hasselmo
Science 315 (5819), 1719-1722, 2007

Ionic mechanisms in the generation of subthreshold oscillations and action potential clustering in entorhinal layer II stellate neurons
E Fransén, AA Alonso, CT Dickson, J Magistretti, ME Hasselmo
Hippocampus 14 (3), 368-384, 2004

Computational modeling of entorhinal cortex
ME Hasselmo, E Fransen, C Dickson, AA Alonso
Annals of the New York Academy of Sciences 911 (1), 418-446, 2000

Properties and Role of I_h in the Pacing of Subthreshold Oscillations in Entorhinal Cortex Layer II Neurons
CT Dickson, J Magistretti, MH Shalinsky, E Fransén, ME Hasselmo, ...
Journal of neurophysiology 83 (5), 2562-2579, 2000

A biophysical simulation of intrinsic and network properties of entorhinal cortex
E Fransén, GV Wallenstein, AA Alonso, CT Dickson, ME Hasselmo
Neurocomputing 26, 375-380, 1999

Modeling the generation of subthreshold membrane potential oscillations of entorhinal cortex layer II stellate cells
E Fransén, CT Dickson, J Magistretti, AA Alonso, ME Hasselmo
Soc. Neurosci. Abstr 24 (814.5), 1998