

Press Release

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May 11, 2007

Neural cells in cross fire

Controversy evokes over fundamental question in neuroscience

In 1952, Alan Lloyd Hodgkin and Andrew Fielding Huxley proposed a quantitative description of the emergence of electrical impulses in neurons, for which they received the Nobel Prize. In April 2006, scientists working with Fred Wolf, BCCN Göttingen and Max Planck Institute for Dynamics and Self-Organization, showed for the first time evidence that not all cells conform to the Hodgkin-Huxley model. The publication of their results in the journal "Nature" has meanwhile evoked a controversy in the scientific community.

Neurons communicate by passing electrical impulses. When a neuron receives a signal, the voltage across its membrane changes. As soon as a certain threshold is reached, voltage-gated sodium channels in the membrane open up and sodium ions can pass into the cell. This in turn leads to a further increase of the membrane potential and a so-called "action potential" arises - the neuron now sends out a signal itself. According to the Hodgkin-Huxley model, the voltage across the membrane is the only trigger needed for voltage gated sodium channels to open. However, Wolf and his colleagues found that the Hodgkin-Huxley model cannot account for the emergence of action potentials in neurons of the cortex. The threshold value in these cells is very variable; at the same time, action potentials arise extremely rapidly. As they demonstrated, this can be easily modelled if one postulates that the sodium channels exert an influence on each other to open cooperatively.

It should not come as a surprise that questioning the universal validity of this fundamental equation was met with disbelief by some scientists. In the January issue of Nature, David McCormick, Yale University School of Medicine, and his colleagues published their doubts about Wolf's model. Action potentials in some neurons arise in a cellular process, the axon, at about 30 μm distance from the cell body. As the axon is however too thin to apply a pipette without destroying the structure, the membrane potential is generally measured at the cell body. McCormick points out that this could lead to artefacts. In a mathematical model he suggests how the rapid emergence of action potentials measured in the cell body may potentially be explained by the Hodgkin-Huxley model if such artefacts substantial. In addition, he attempts to measure the membrane potential at the site of its emergence by cutting off the axon and applying the



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pipette to a "bleb", which is formed by the nerve cell where its axon is cut. Data obtained in this way show a significantly slower emergence of action potentials than data published by Wolf et al.

In their reply published in the same issue of Nature, Wolf and colleagues can convincingly dispel both of McCormick's critiques. First, they point out that the removal of the axon results in a radical reorganization of the molecular structure, so that data obtained from measurements at the axon blob are not reliable. In addition to this, also McCormick's mathematical model cannot convince Wolf and his colleagues. While the model predicts the emergence of an action potential at a fixed threshold of $-55V$, measurements show that such a fixed threshold potential does not exist in real neurons. Thus, Wolf and his colleagues regard McCormick's model as yet another indication that the Hodgkin-Huxley model does not suffice to explain the emergence of action potentials in cells of the cortex. For the time being, Wolf's model appears to remain the most plausible hypothesis.

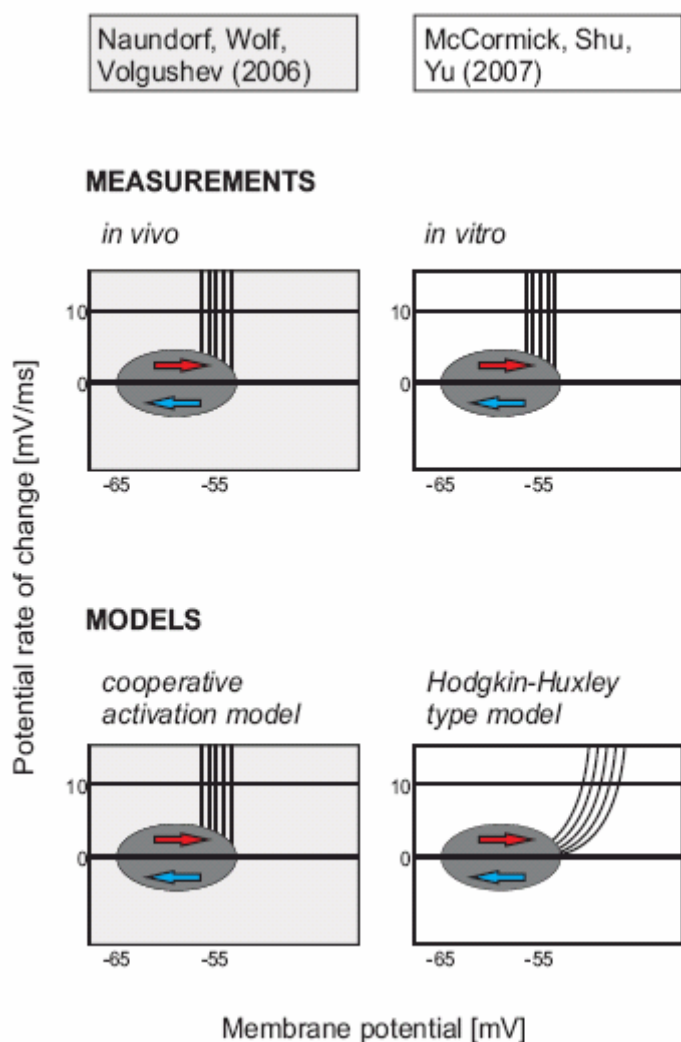


Figure: Schematic representation showing the emergence of action potentials based on measurements (top row) and mathematical models (bottom row). The potential over the neuronal membrane can rise (red arrow) or fall (blue arrow). While the Hodgkin-Huxley model predicts the emergence of an action potential at a fixed threshold, measurements show that a fixed threshold potential does not exist in real neurons. The threshold value in neurons of the cortex is very variable; at the same time, action potentials arise extremely rapidly. The model of Wolf and his colleagues (bottom left) reflects these measurements with far more accuracy. (source: Max Planck Institute for Dynamics and Self-Organization)



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Original publications:

Hodgkin and Huxley model - still standing?

McCormick, D.A., Shu, Y. and Yu, Y.

Reply by: Naundorf, B., Wolf, F. and Volgushev, M.

Nature, Volume 445, 4 January 2007

Naundorf, B., Wolf, F. and Volgushev, M.

Unique features of action potential initiation in cortical neurons

Nature, Volume 440, Number 7087, 2006

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The Federal Ministry of Education and Science (BMBF) has founded four Bernstein Centers for Computational Neuroscience (BCCN) in Berlin, Freiburg, Göttingen, and Munich. The interdisciplinary field of research combines experiments with data analysis and computer simulation on the basis of well-defined theoretical concepts. The central aim of Computational Neuroscience is to identify the neuronal basis of brain performance.

The BCCN Göttingen is a joint center of the Georg-August-University Göttingen, the Max Planck Institute for Dynamics and Self-Organization, the Max Planck Institute for biophysical Chemistry, the German Primate Center, and Otto Bock HealthCare GmbH.



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