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Neuroscience Award Honors Optical **Technique That sheds Light on the Living Brain**

TUM Professor Arthur Konnerth is one of four winners of this year's Grete Lundbeck European Brain Research Prize, a million-euro award for neuroscience. The 2015 Brain Prize is being awarded for "the invention, refinement and use of two-photon microscopy to provide detailed, dynamic images of activity in individual nerve cells, dendrites and synapses, thereby transforming the study of development, plasticity and functional circuitry of the brain."

Arthur Konnerth has led pioneering studies of how the brain works – in good health as well as under the effect of neurodegenerative diseases such as Alzheimer's – from intra- and intercellular functioning to behavior. Several ground-breaking discoveries have been enabled by his use of optical techniques, including two-photon microscopy, which allows highly specific observation of brain activity in living animals. Konnerth first worked at TUM in 1999–2000, when he conducted an essential part of the award-winning research (published in 2003). In 2006 he became the founding chair of TUM's Friedrich Schiedel Institute for Neuroscience. He is also a Carl von Linde Fellow of the TUM Institute for Advanced Study and a principal investigator in the Excellence Clusters SyNergy (Munich Cluster for Systems Neurology) and CIPSM (Center for Integrated Protein Science Munich).

From cells to circuits, in illness as well as health

In 2003 Konnerth and colleagues pioneered an imaging method that permitted for the first time the analysis of cortical circuits with single-cell resolution. This method is nowadays used in many laboratories worldwide to improve

TUM Prof. Arthur Konnerth, Friedrich Schiedel Institute for Neuroscience, shares in the million-euro Brain Prize for 2015.

Picture credit left: Heddergott / TUM
Graphics right: edlundsepp (source: Christine Grienberger / TUM)

our understanding of how the brain controls behavior in animals. More recently they further improved their method, allowing them in 2010 to observe a mouse in the act of seeing, with resolution that went beyond a single nerve cell to a single synapse. This achievement enabled them to map the functional links between brain cells in detail. The scientists combined two-photon flourescence microscopy – making it possible to look up to half a millimeter into brain tissue and view not only an individual cell, but even its fine dendrites – with the so-called patch-clamp technique, which let them conduct electrical signals to individual dendrites. This study showed for the first time that an individual neuron integrates input representing multiple sensory features into a well-defined, unique output signal: a decision, in essence, made automatically by a single nerve cell.

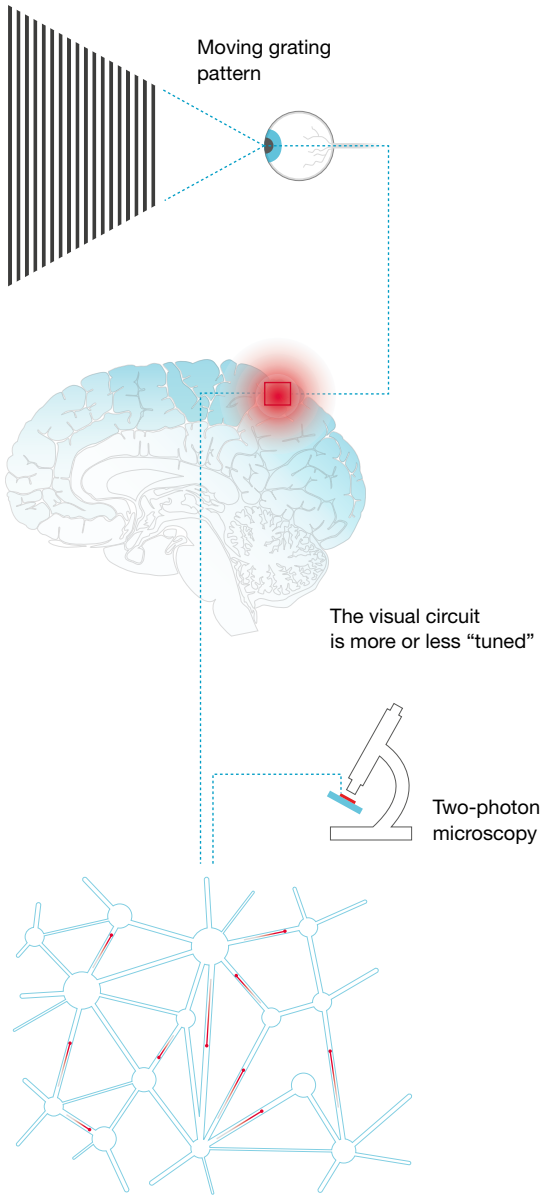
Observing distinct stages of Alzheimer's disease

Another key discovery came in 2012, from in vivo single-neuron experiments with a mouse model of Alzheimer's disease. Konnerth's group observed correlations between increases in both soluble and plaque-forming beta-amyloid – a protein implicated in the disease process – and dysfunctional developments on several levels: individual cortical neurons, neuronal circuits, sensory cognition, and behavior. Their results showed that these changes progress in parallel and that, together, they reveal distinct stages in Alzheimer's disease with a specific order in time.

In 2013, a combination of optical techniques shed light on the brain's "slow waves," rhythmic signal pulses that sweep through the brain during sleep and are assumed to play a role in processes such as the consolidation of memory. The slow waves can be observed in very early stages of development, and they may be disrupted in Alzheimer's and other diseases. In this study, two-photon microscopy was used in conjunction with optogenetics, an approach that enabled spatially defined stimulation of small numbers of neurons. Konnerth's group showed conclusively that slow waves start in the cerebral cortex, ruling out other longstanding hypotheses. The researchers also found that such a wave can be set in motion by a single tiny cluster of neurons. "Out of the billions of cells in the brain," Konnerth explained, "it takes no more than a local cluster of fifty to one hundred neurons in a deep layer of the cortex, called layer 5, to make a wave that extends over the entire brain."

Patrick Regan (TUM)

Studying the brain activity of a mouse while it is being visually stimulated with a moving grating pattern of light and dark bars. By observing in vivo with two-photon flourescence microscopy how neuronal signaling responded to the stimulation, Konnerth's team could characterize the visual circuit as being more or less "tuned" to specific orientations and directions of movement. The scientists were able to correlate these dysfunctional developments with distinct stages of Alzheimer's disease.



The Brain Prize

The Grete Lundbeck European Brain Research Prize – "The Brain Prize"– is awarded to one or more scientists who have distinguished themselves by an outstanding contribution to European neuroscience and who are still active in research. The sponsor of the prize is the Grete Lundbeck European Brain Research Foundation, a charitable, non-profit organization founded by the Danish Lundbeck Foundation. Arthur Konnerth shares the 2015 Brain Prize with Winfried Denk (Max Planck Institute of Neurobiology, Munich, Germany), David Tank (Princeton University, New Jersey, USA), and Karel Svoboda (Howard Hughes Medical Institute, Maryland, USA). The million-euro award is a personal prize, to be shared equally among the awardees. It was presented in Copenhagen on May 7 by Crown Prince Frederik of Denmark.