HUMAN & BIOTECHNOLOGY

Fields of Expertise TU Graz

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Gernot Müller-Putz,
Human & Biotechnology
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2021 is an anniversary year for Biomedical Engineering at TU Graz. The subject area is celebrating its 50th anniversary. As an elective subject bundle in the field of electrical engineering, one of the most successful teaching and research areas at TU Graz started in 1970/71 as an elective subject group: Biomedical Engineering. Only three years later, the specialized Institute of Electrical and Biomedical Engineering was founded under Stefan Schuy, later Rector of TU Graz. After a few years of development, the institute housed four departments: Biophysics, Medical Informatics, Medical Electronics and Health Care Engineering and two Ludwig Boltzmann Institutes (Assistive Technology, Medical Informatics and Neuroinformatics) as well as a testing facility for biomedical engineering. In 2001, the biomedical engineering branch of study was established as part of the electrical engineering diploma programme. In 2004, the organization was divided into four independent institutes: Genomics and Bioinformatics, Human-Computer Interfaces, Medical Technology, and Health Care Engineering with a European Test Centre for Medical Devices. Later, the Institute of Genomics and Bioinformatics was dissolved, and in 2007 the Institute of Biomechanics founded. The Bachelor's programme started in 2007, followed immediately by the Master's programme in Biomedical Engineering. Today, the institutes, including the Institute of Biomedical Informatics, are housed in the Biomedical Engineering Building at Stremayrgasse 16, which was renovated a few years ago.

At the Annual Conference of the Austrian Society for Biomedical Engineering, which took place at TU Graz, a festive evening was held to celebrate the anniversary. Rudolf Stollberger announced his retirement and received great applause, and his successor, Martin Uecker, was welcomed as head of the Institute of Biomedical Imaging.

After last year's call for FoE tenure-track positions, we were able to enlist Kerstin Lenk, who is setting up the Computational & Experimental Neuroscience working area at the Institute of Neural Engineering. She writes about her work in this issue of TU Graz research.

Kerstin Lenk

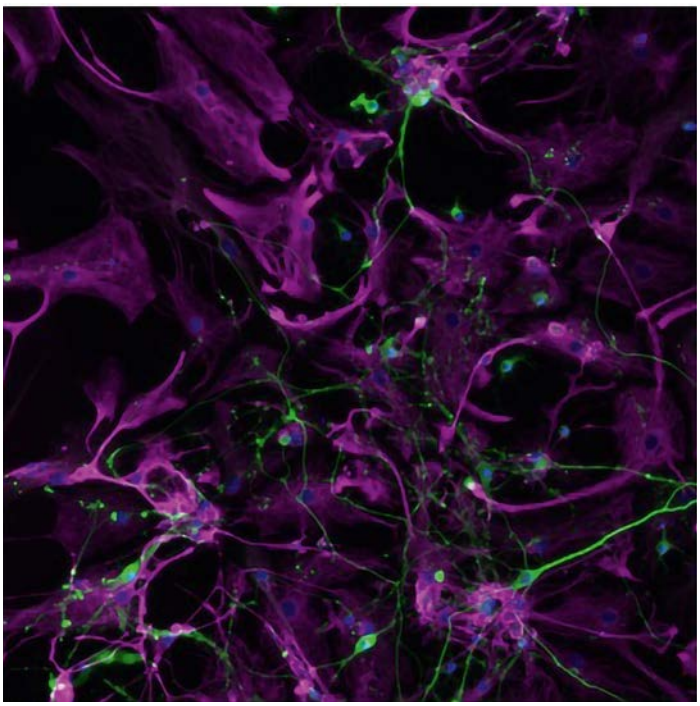
Computational Models of Neurons and Astrocytes in Studying Brain Dynamics in Health and Disease

Astrocytes are non-neuronal brain cells that contribute to the exchange of neurotransmitters and ions. They are involved in various cognitive functions like sleep and memory formation. Using computational models, we simulate the interaction between neurons and astrocytes. By perturbing parts of the signaling pathways, we investigate astrocyte behavior in diseases like Alzheimer's, epilepsy, and schizophrenia.

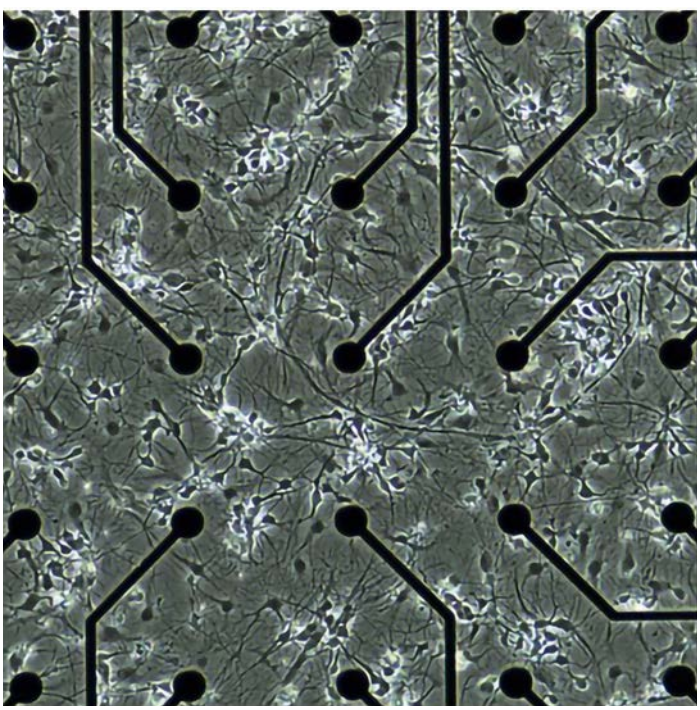
In the past, neurons in the brain were considered the sole contributors to cognitive function. This view has been changing over the last four centuries, and other non-neuronal cells are now being investigated as to whether or how they >

Kerstin Lenk
has been an assistant professor at the Institute of Neural Engineering since April 2021, focusing on computational neuroscience. The goal is to understand how neurons and other brain cells such as astrocytes interact with each other and how this interplay is disturbed in diseases.

Source: Hannah Pulferer



a)



b)

contribute to normal and pathological functions of the brain. One of these so-called glial cells are astrocytes, which even outnumber neurons in the human brain. They were initially described as star-shaped. A few main branches extend from the soma and subdivide in a very fine tree of subbranches. Hence, astrocytes look rather like a sponge. Astrocytes in the human brain are twenty times larger than their counterparts in rodents.

Astrocytes are involved in various homeostatic processes in the brain. They take up and release neurotransmitters and ions. Astrocytes are also connected to blood vessels in the brain and transport nutrients to neurons and other cells. They play a role in the sleep cycle and memory.

At a synapse, electrical and chemical signals can be passed from one neuron to another. An astrocyte can enwrap the synapse, and exchange neurotransmitters, ions, and nutrients with the contacted neurons. In the human brain, one astrocyte can contact up to two million neuronal synapses. Astrocytes also link to other astrocytes by gap junctions and, in this way, form non-overlapping domains. Hence, neurons and astrocytes build tightly interconnected networks (Figure 1a).

Figure 1:
a) Stained neurons in green, astrocytes in magenta, and the cell nuclei in blue.
b) Neurons and astrocytes distributed over the electrode field of a microelectrode array.
Source: Annika Ahtiainen, Tampere University

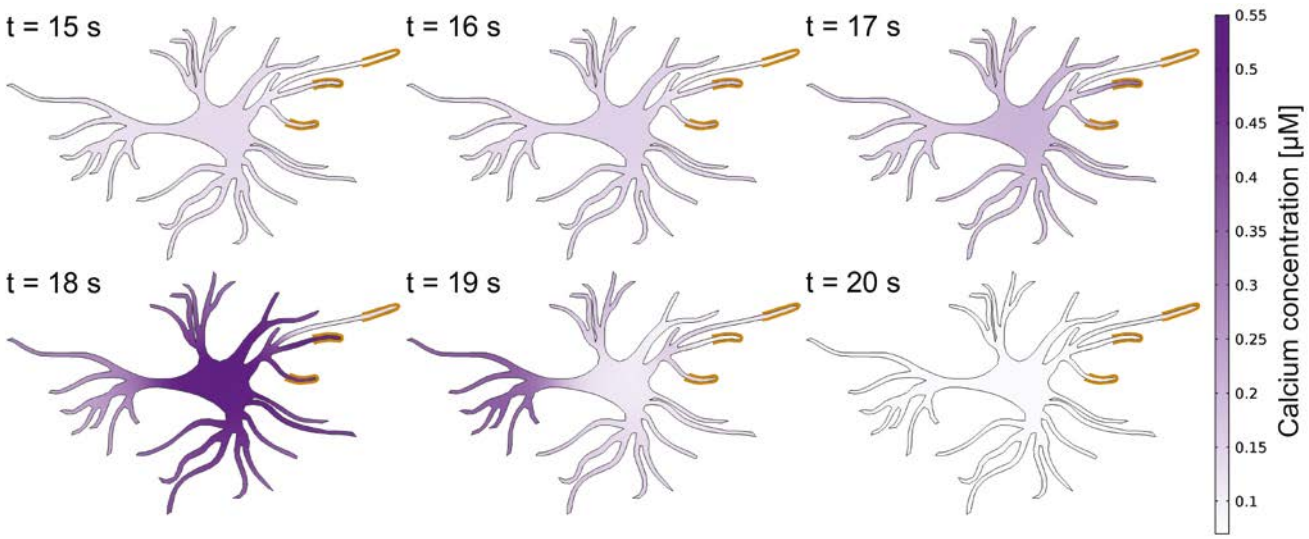


Figure 2: Simulation of the calcium dynamics over time (second 15 to 20) in an astrocyte. The astrocyte was stimulated by glutamate (indicated by the yellow lines at the tips of the astrocyte).
Source: Aapo Tervonen, Tampere University/ Kerstin Lenk

Unlike neurons, astrocytes are considered non-excitable, which means that they do not exhibit action potentials. Their primary signal is calcium and can be captured by means of calcium imaging. In this way, the binding of fluorescent molecules to calcium ions can be measured using microscopes. Astrocytes are involved in almost all brain pathology which influences the morphology and function of those glial cells.

At the Institute of Neural Engineering, one of our research areas is to develop computational models of single astrocytes (Figure 2) and in combination with neurons. As a first step, we analyze experimental data, for example, from calcium imaging and extract features such as the peaks in the signals. Then, we develop mathematical equations that describe underlying biophysical processes inside and outside of a cell. The parameters of the computational model are then adapted so that they resemble the experimental data at hand. One aspect that we investigate using the computational models is how different morphologies influence calcium and other ionic dynamics. Furthermore, we study the neuron and astrocyte interaction in larger networks. So far, we have been interested in specific aspects of the role of astrocytes in Alzheimer's disease, epilepsy, and schizophrenia. Using our computational models, we can study pathways in the astrocytes that are currently not accessible by experimental techniques or where the experiments are too expensive.

I learned about astrocytes during my time at the former Tampere University of Technology, now part of Tampere University, in Finland. There, we started to develop our first computational models of astrocytes. Side-by-side, we were also doing in vitro experiments with calcium imaging and microelectrode arrays (MEAs). Neuronal and astrocytic cells can be cultured on those MEAs (Figure 1b). These chips contain a field of electrodes over which the cells form a network over time (Figure 1b). After roughly a week, the first signal of electrical activity from the neurons can be measured. The networks can then be perturbated with chemicals or electrical stimulation, mimicking specific alterations in a disease. In collaboration with Christian Baumgartner and his PhD student Daniel Ziesel from the Institute of Health Care Engineering, we are currently establishing in vitro experiments with neuron-astrocyte co-cultures to be able to continue that research line.

One crucial part of our work is developing and implementing tools to analyze the experimental data, which we often do in close collaboration with our experimental partners. For example, we have written software to analyze electrical activity of neurons on MEAs and calcium imaging data of neurons and astrocytes. The analyzed results and insights from the in vitro experiments can also be used to build and refine our computational models.