

Guest Editorial

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Highlight: Horizons in Neuroscience – Organoids, Optogenetics and Remote Control

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In September 2022 the Study Group “Molecular Neurobiology” of the German Society for Biochemistry and Molecular Biology (Gesellschaft für Biochemie und Molekularbiologie, GBM) organized an International Meeting entitled “Horizons in Neuroscience: Organoids, Optogenetics and Remote Control” at the Ruhr University Bochum, Germany (see Figure 1).

During this Meeting neuroscientists gathered from different areas of expertise to explore new perspectives on understanding and modulation of brain function. A special focus was on non-invasive methods. Selected contributions presented within this issue of *Biological Chemistry* comprise *in vitro* brain models, emerging aspects in optogenetics, advances in the remote control of regeneration in neuronal disease and analytical tools combining expansion microscopy and scanning ion conductance microscopy. A novel aspect for understanding human brain function arising from molecular archeological approaches is also included as a topical paper which was presented during the 30-year anniversary celebration of Biochemistry in Bochum on October 1st 2022 (see Heumann 2023).

In this paper Wulf Haubensak evolves the idea that humans share an anthropocentric fascination for the origins of mind, for what made us human, and what sets us apart from our closest relatives. With emerging evolutionary genetics and organoid technologies, it is now possible to deconstruct evolutionary processes on a molecular or cellular level from the bottom-up approach by functionally testing archaic alleles in experimental models. With this contribution, the authors want to bring together molecular/cellular and organism scientists with neuroscientists and archaeologist (Piszczek et al. 2023).

Using brain organoid culture models Christopher Esk summarizes recent approaches that apply genetic screening. As an example, CRISPR–human organoid–single-cell RNA

sequencing system was established: inducible CRISPR–Cas9-based genetic disruption was applied and single-cell transcriptomics established for a pooled loss-of-function screening in mosaic organoids. Mutation of the chromatin remodelling complex subunit ARID1B, which is involved in neural development and behaviour affected the fate transition of progenitors to oligodendrocyte and interneuron precursor cells. This phenotype was confirmed in patient-specific induced pluripotent stem cell-derived organoids highlighting the predictive power of such screens (Beirute-Herrera et al. 2023; Li et al. 2022).

Neuromuscular junctions are chemical synapses linking presynaptic motor nerve terminals and postsynaptic muscle cells. Using a 3D culture technique and hiPSC technology, insights from *in vivo* models can be complemented. Sarah Hörner provides a brief overview of different types of neuromuscular cocultures alongside examples of studies that have integrated Schwann cells (Hörner et al. 2023).

Annika Haak shows how to three dimensionally image membrane topographies a label- and contact-free technique named scanning ion conductance microscopy (SICM). Combined with expansion microscopy (Tillberg et al. 2016) the membrane surface and the underlying cytoskeleton of oligodendrocyte progenitor cell growth cones are visualized with a resolution surpassing Abbe’s diffraction limit (Haak et al. 2023).

Optogenetics emerges as a very powerful tool to manipulate microcircuit activity in many animal models and even in humans. Albrecht Stroh and collaborators argue that optogenetics will be used for an emulation of endogenous network activation, particularly taking advantage of the parallel development of optical imaging and systems integration concepts (Altahini et al. 2023).

Neurotransmitter and neuromodulators are crucial for the information flow between neurons and understanding their dynamics is the key to unravel their role in behaviour. Olivia Masseck reviews the increasing number of single-wavelength biosensors based on periplasmic binding proteins (PBPs) or on G-protein-coupled receptors (GPCR). Specifically, she develops a new family of genetically encoded serotonin (5-HT) sensors based on the native 5-HT_{1A} receptor and circularly permuted green fluorescent protein. This technology allows the detection of neurotransmitter release *in vitro* and *in vivo* with high spatial and temporal resolution (Kubitschke and Masseck 2023).

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Figure 1: Photo showing a group of participants coming together from Austria, Denmark, Great Britain, Italy, Japan, Sweden, and the USA to discuss the topic “Horizons in Neuroscience: Organoids, Optogenetics and Remote Control” at an International Meeting taking place on September 28th – 30th, 2022, at the Ruhr-Universität Bochum, Germany. (This picture is reproduced with permission by Biospektrum, Springer-Verlag GmbH, Germany.).

Mechanical force induces axon outgrowth and stimulates neuronal maturation, known as “stretch-growth” (Suter and Miller 2011). Here, Vittoria Raffa and collaborators discuss the main evidence supporting the role of microtubules as a signal hub for axon growth in response to a traction force generated by magnetic nanoparticles that are guided by an external magnet. Applying a tension to the axon appears to stabilize the microtubules, which, in turn, coordinate a modulation of axonal transport, local translation and their crosstalk (Falconieri et al. 2023).

Finally, Annika Guntermann presents an overview of autoantibodies in traumatic spinal cord injury. Infections remain the most common cause of death after traumatic spinal cord injury, likely due to the development of an immune deficiency syndrome. This, together with a somewhat contradictory development of autoimmunity in many patients, are two major components of the maladaptive systemic immune response (Guntermann et al. 2023).

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