

# Life & Brain GmbH Electrophysiology Services



NEUROPLASTICITY  
LIFE & BRAIN GmbH  
Sigmund-Freud-Str. 25  
53127 Bonn  
Tel.: 49-228-6885 215  
Fax.: 49-228-6885 296  
E-mail: [Heinz.Beck@ukb.uni-bonn.de](mailto:Heinz.Beck@ukb.uni-bonn.de)  
[www.lifeandbrain.com](http://www.lifeandbrain.com)

## WHO WE ARE

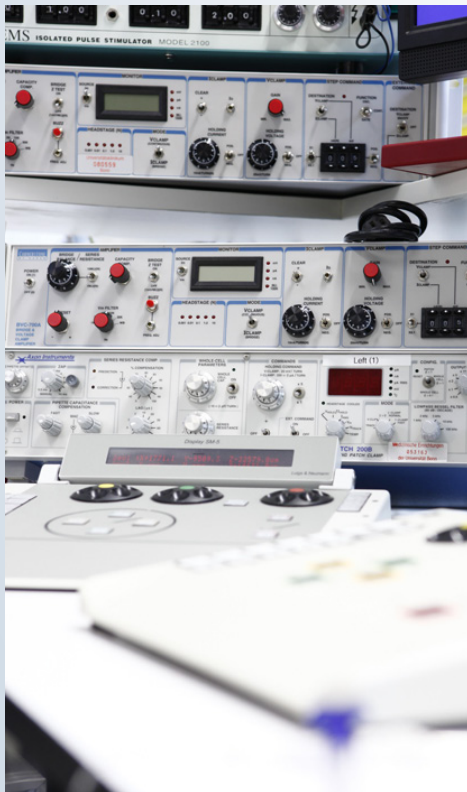


The NeuroPlasticity Platform provides contract research services to the Biotechnology and Pharmaceutical Industry and is an integral part of the Life and Brain GmbH. The development of new effective therapeutics for the majority of CNS diseases is challenged by the neuronal diversity and connectivity of the brain. This level of complexity requires

understanding of organizational principles and cell-type specificity. Electrophysiology and functional connectomics are key tools in elucidating mechanisms of action underlying the pathophysiology of CNS disorders and facilitating the development of new therapeutics.

## EVALUATE

We support preclinical R&D programs in the areas of Neurodegeneration, Neurocognition and Functional Connectomics by providing electrophysiological characterization of small molecules with focus on target engagement, efficacy and potency in acute rodent and human brain slices, cultured neurons and animal models.

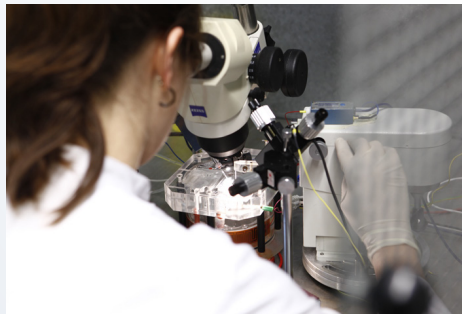


## DESIGN

We provide longstanding expertise in understanding CNS drug actions at the level of ion channels, receptors and cellular excitability, and their effects on complex neuronal networks.

In the field of **Epilepsy**, we focus on characterization of anticonvulsant therapies and pharmacoresistance, generally characterized by the failure of seizures to come under acceptable control in response to AED therapy. Overcoming resistance mechanisms is the most critical factor in the development of new anticonvulsant therapeutics with respect to clinical outcome as well as reduction of disease-related costs. As experts in pharmacoresistance we offer unique electrophysiological readouts for our clients to further drug development and competitive marketing activities.

In the field of **Functional Connectomics** we investigate the structure-function relationship of neuronal circuits using engineered RABV and AAV viruses as tracers of synaptically connected neuronal populations in combination with optogenetic/electrophysiological and histological methods.



## EXECUTE

Our team provides a flexible, highly skilled service with a proven track record of data quality and a keen sense for meeting corporate project timelines. Our collaborative culture ensures a well-designed study plan and execution.





# SERVICES

## **In vitro slice physiology**

Brain slices maintain functional local synaptic circuitry with preserved brain architecture, while allowing precise control of the extracellular environment and drug pharmacology. Replication of developmental aspects and regional specificity in brain slice preparations provides a suitable therapeutic screening system preceding in vivo efficacy studies.

## **Whole cell patch clamp**

Measurement of neuronal excitability on a single cell-level is used to evaluate effects of pharmacological agents on distinct neuronal cell types, receptors, ion channels or neurotransmitter systems. Whole cell recordings are tailored to the specific characteristics and mechanism of action of the investigational substance.

### **Synaptic transmission**

- paired-pulse facilitation, inhibition
- spontaneous postsynaptic currents
- basal synaptic transmission
- agonist/antagonist evoked postsynaptic current
- input/output properties
- pre/postsynaptic activity
- evaluation of feed-back and feed-forward inhibitory network motifs in CA1 neurons

## **Intrinsic firing properties and ion channels**

- voltage-dependent steady state activation and inactivation of ion channels (voltage-clamp recordings in isolated neurons)
- intrinsic firing properties (current clamp recording in slices)

## **Neuronal cell type characterization**

- pyramidal cell-interneurons-basket cells-olm cells-proximal dendritic cells

## **Safety and Toxicity**

Evaluation of unwanted drug effects on basal neurotransmission and convulsive activity.

- dose-response curves
- off-target activity
- excipient testing

## **Animal models of Epilepsy**

- pilocarpine model of epilepsy in male wistar rats
- pilocarpine model of epilepsy in male CD-1 mice
- kainate model of epilepsy in male wistar rats

## **Anticonvulsant drug pharmacology**

- pharmacosensitivity of voltage-dependent  $Na^+$  channels
- comparative  $Na^+$  channel-acting anticonvulsant activity
- anticonvulsant activity on neuronal inhibition/excitation

## **Neuronal in-vitro preparations**

- acutely dissociated dentate granule neurons
- acutely dissociated CA1 neurons

## **in vitro assays**

- voltage-clamp recordings from dissociated cells
- voltage-clamp recordings from transfected HEK293 and CHO cells

## **in-vivo assays**

- continuous telemetric EEG recordings in mice
- patch-clamp and extracellular recordings in mice

## **Connectomics**

- generation of RABV and rAAV virus constructs
- stereotactic virus delivery
- virus-mediated monosynaptic tracing from defined single neurons or neuronal populations
- whole brain tissue clearing
- image analysis and quantification of connected neurons
- microscopic visualization of connectomes

# HEAD OF THE NEUROPLASTICITY UNIT

## **Prof. Dr. Heinz Beck**

Dr. Beck studied Medicine in Cologne and was appointed a Professor of Experimental Epileptology and Cognition Research at the University of Bonn in 2004 and Head of the NeuroPlasticity unit within the Life & Brain GmbH in 2005. His interdisciplinary group has a strong track record investigating cellular and network mechanisms of excitability and synchronization in normal and diseased brain. A particular long-standing focus since more 20 years is the investigation of basic mechanisms of epilepsy in animal models and tissue obtained from epilepsy surgery. The group also has a particular track record in examining the mechanisms of CNS drug actions on the cellular and network level.



## REFERENCES

Function and developmental origin of a mesocortical inhibitory circuit. Kabanova A, Pabst M, Lorkowski M, Braganza O, Boehlen A, Nikbakht N, Pothmann L, Vaswani AR, Musgrove R, Di Monte DA, Sauvage M, Beck H, Blaess S. *Nat. Neurosci.* 2015 Jun;18(6):872-82.

Targeting pharmacoresistant epilepsy and epileptogenesis with a dual-purpose antiepileptic drug. Doerer A, Dickhof G, Reitze M, Uebachs M, Schaub C, Pires NM, Bonifácio MJ, Soares-da-Silva P, Beck H. *Brain.* 2015;138:371-87.

Function of inhibitory micronetworks is spared by Na<sup>+</sup> channel acting anticonvulsant drugs. Pothmann L, Müller C, Averkin R, Bellistri E, Miklitz C, Uebachs M, Remy S, Menendez de la Prida L, Beck H. *J. Neurosci.* 2014, 34(29):9720-35.

Fluorescent-protein stabilization and high-resolution imaging of cleared, intact mouse brains. Schwarz MK, Scherbarth A, Sprengel R, Engelhardt J, Theer P, Giese G. *PLoS One.* 2015; 10:e0124650.

Charting monosynaptic connectivity maps by two-color light-sheet fluorescence microscopy. Niedworok CJ, Schwarz I, Ledderose J, Giese G, Conzelmann KK, Schwarz MK. *Cell Rep.* 2012; 2(5):1375-86.

## CUSTOMERS



**LIFE & BRAIN GmbH**  
NeuroPlasticity

Sigmund-Freud-Str. 25  
53127 Bonn  
Tel.: +49 (0)228 6885 215  
Fax: +49 (0)228 6885 294  
[www.lifeandbrain.com](http://www.lifeandbrain.com)