International Conference 2017 - BrainLinks-BrainTools

Co-located with International Conference for Advances in Neurotechnology (ICAN)

June 28 to 30, 2017 - Merzhausen, Germany

BrainLinks
BrainTools
acting.thoughts
University of Freiburg

ICAN
International Conference for
Advanced Neurotechnology

Introduction

The International BrainLinks-BrainTools Conference 2017 held from June 28 to 30 in Freiburg, Germany, was a real success. For a period of three consecutive days it provided a great forum for 260 participants from all over the world to share their most recent insights into neurotechnology research and to discuss the future challenges of the field.

In eight detailed sessions, one of them jointly with the co-located International Conference for Advances in Neurotechnology (ICAN), this single track conference featured four insightful keynotes by renowned speakers and over thirty scientific presentations. Special attention was given to the topics of closed-loop interaction and longevity in particular, which turn out to be two emerging challenges in this field of research.

This conference brochure provides not only a summary of the conference but is also designed to recapture the atmosphere of an inspiring gathering of great research and innovative ideas in Freiburg.

Table of Contents

1	**Keynote Lectures**	**2**
1.1	Learning and Adaptation in Artificial Neural Networksfor the Control of Robots	3
1.2	Large-scale Recording of Local Field and Action Potentials	4
1.3	Achieving a Bionic Interface to Overcome Paralysis	5
1.4	The Challenge of Integrating High Density RecordingArrays into Brain Tissue	7
2	**Session Talks**	**10**
2.1	Functional and Structural Connectivity	11
2.2	Bidirectional Interaction with the Brain	14
2.3	Human-Device Interaction	16
2.4	Interfacing with Intracortical Probes	18
2.5	Clinical Applications	20
2.6	International Conference for Advanced Neurotechnology	23
2.7	Ethics and Outreach	28
2.8	Implant Development	29
3	**Conference Illustrated**	**32**
3.1	Comics	33

"The reason why time is so important is because even though the brain is not like a computer - it seems pretty slow - but even in that scale it is astonishingly fast."

(G. Buzsáki)

1 - Keynote Lectures

Four inspiring talks from the world's leading scientists

1.1 Learning and Adaptation in Artificial Neural Networks for the Control of Robots

Keynote Lecture, Florentin Wörgötter

Florentin Wörgötter, Third Institute of Physics, Biophysics, Georg-August University Göttingen, Germany

Conventional robot control, for example using PID controllers, often leads to unwanted properties, because these controllers are stiff, inflexible, and cannot easily adapt to new situations ("learn"). Here we will show how to implement modular neural control thereby creating increasingly complex behavior in several artificial agents.

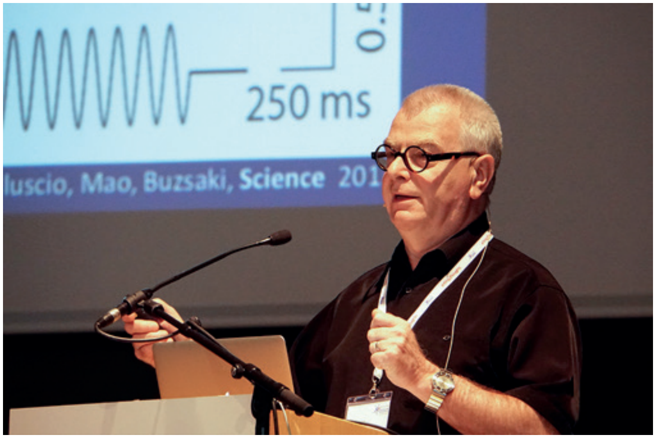
Different from conventional methods, neural control directly links signals from sensors via a set of network modules to the motors of the machine without explicit "rules". The machine thereby develops fast responses and flexible behavior and can adapt by ways of simulated neuronal plasticity to new situations. Here we will show several robots under neural control. Starting with an older study of a small biped robot RunBot, where signals from sensors are being processed by a network to create motor-control signals directly from neuronal elements. The little machine thereby develops a fast and flexible dynamic walking gait and can adapt by ways of simulated neuronal plasticity to new situations.

Next, we will demonstrate, how a small CPG, which operates initially in a chaotic domain, can – via neural chaos control – be driven into repetitive patterns, which are being used to determine the walking gait of an 18DOF hexapod robot.

Finally we will use a combination of Hebbian Learning and Reservoir Computing to teach a 7DOF robot arm to perform a very accurate Peg-In-Hole action. Taken together these approaches use modern theoretical results from the neurosciences and try to demonstrate that increasingly complex behavior can be obtained this way.

1.2 Large-scale Recording of Local Field and Action Potentials

Keynote Lecture, György Buzsáki



György Buszáki, NYU Neuroscience Institute and Department of Neurology, School of Medicine, New York University, New York, NY 10016, USA

To understand how function arises from the interactions between neurons, it is necessary to use methods that allow the monitoring of brain activity at the single-neuron, single-spike level and the targeted manipulation of the diverse neuron types selectively in a closed-loop manner.

Large-scale recordings of neuronal spiking combined with optogenetic perturbation of identified individual neurons has emerged as a suitable method for such tasks in behaving animals. Although these tools can be scaled to some extend, their invasive nature prevents recordings from tens of thousands of neurons. The invasive nature of electrodes is a major obstacle in human recordings. We addressed the latter challenge by developing an organic material-based, ultra-conformable, biocompatible and scalable neural interface array (the 'NeuroGrid') that can record both LFP and action potentials from superficial cortical neurons without penetrating the brain surface. Spikes with features of interneurons and pyramidal cells are simultaneously acquired by multiple neighboring electrodes of the NeuroGrid, allowing for isolation of putative single neurons.

Spiking activity demonstrated consistent phase modulation by ongoing brain oscillations and was stable in recordings exceeding one week. We demonstrate the effectiveness of NeuroGrids in intra-operative recordings in patients undergoing epilepsy surgery. The NeuroGrid constitutes an effective method for large-scale, stable recording of neuronal spikes in concert with local population synaptic activity, enhancing comprehension of neural processes across spatiotemporal scales and potentially facilitating diagnosis and therapy for brain disorders.

To fully exploit the potential power of these methods, multiple steps of technical innovation are needed. I will highlight the current state-of-the-art in electrophysiological recording methods, combined with optogenetics, and discuss directions for progress. In addition, I point to areas where rapid development is in progress and discuss topics where near-term improvements are possible and needed.

1.3 Achieving a Bionic Interface to Overcome Paralysis

Keynote Lecture, John P. Donoghue

John P. Donoghue, Wyss Center for Bio and Neuroengineering, Geneva, Switzerland

Combined engineering and neuroscience efforts since the beginning of the 21st century have led to major advances in achieving a brain computer interface that can reconnect the brain to the outside world for people with severe paralysis. In recent years humans with longstanding paralysis have been able to control computer cursors well enough to type at nearly half the speed of an able bodied typist, control multijoint robotic arms, and most recently to control their own limb to reach and grasp in order to eat and drink. These advances were accomplished with a neural interface system, we term 'BrainGate', that consists of a small 100 probe multielectrode array (MEA) implanted into the motor cortex. The array is connected via a plug and cable to external computers that decode patterns of neural activity into useful signals that can control computer systems, robots or functional electrical stimulation (FES) systems to move the paralyzed arm. Importantly, small neural ensembles sampled from a 4 x 4 mm patch of the 'arm' motor cortex are sufficient to provide whole arm reach and grasp signals and, while variable, useful signals are routinely recorded at least one year, and in one case more than 5 years before testing ended, suggesting both efficacy and long term viability of this technology.

Despite these successes, there are several challenges remaining to achieve a true bionic interface that can be routinely used by the hundreds of thousands each year who are unable to move after stroke, spinal cord injury, or neurodegenerative disorders. Barriers to an effective bionic replacement nervous system fall into interrelated neuroscience and engineering issues.

Decoding of neural signals into rich control signals is a complex challenge. Current control is both slower and less dexterous than can be achieved by an able-bodied person. We need to understand how best to sample and how to select and combine the most useful local field potentials and spiking signals to achieve desired device control. Decoding strategies are also based in our understanding of the nature of cortical information processing, which is essential in selecting signals and the methods to decode them. This knowledge influences the design of neural interfaces - e.g., what is the optimal sampling density, in which areas, in which layers? The above BrainGate investigational trial results were all achieved with a penetrating MEA, but the signals on this array are variable both day to day and over time, even though years of recording can be achieved.

Engineering with novel materials and designs might provide neural tissue interfaces that not only sample more stably, but are also able to sustain the sensor implant in the harsh, dynamic body environment, which appears to be the major cause of signal decline for the currently used MEA. It may be possible to obtain sufficiently useful signals from the cortical surface, although this is an unresolved question for human brain computer interfaces.

Engineering is also essential to replace the current percutaneous head pedestal, cabling and bulky signal processing components. It is now feasible, with current and emerging technology, to process high bandwidth, high channel count signals from fully implantable, wirelessly transmitting systems and to provide compact portable signal processing for continual home use. By addressing these key but very challenging issues, I am confident it will be possible in the coming years to provide a bionic nervous system that can be a practical solution not only for those with severe paralysis, but for those with more limited loss of movement, to restore independence and control through a physical nervous system that will restore communication and body movement.

1.4 The Challenge of Integrating High Density Recording Arrays into Brain Tissue

Keynote Lecture, Patrick A. Tresco

Patrick A. Tresco, Department of Bioengineering, University of Utah, USA

Long-term neural recording using implantable microelectrode arrays has provided important discoveries that have shaped our understanding of how the brain functions and have been used experimentally to treat such disorders as paralysis that provides hope for many suffering from this disability. At present this promising technology has been challenging to implement reliably, which limits its use as a basic science tool and threatens its broader clinical utility. Since its inception, the dominant design strategy for the technology has been an empirical build and test approach guided more by technical advances than a biologically informed rationale. Over the past two decades our group has studied how cortical brain tissue responds to different types of chronically implanted recording arrays and their implantation approaches.

This lecture will review what we have learned to date and attempt to point out similarities and differences in the FBR to single penetrating electrode arrays, which create minimal damage upon implantation, to those of much higher density that cause significantly more damage upon insertion.

In the spirit of advancing the technology, we also will review more recent efforts to modulate the FBR to high density recording arrays including discussing the impact of implantation choice and head stage components, the use of modeling approaches to inform design, novel immunomodulatory strategies and speculate on future design changes to enhance biocompatibility that are based on what we have learned from studying the FBR. The broader impact is to advance our collective understanding of how to improve the performance of next generation CNS implants.

"We have to realize that no matter what we put into the brain, it's gonna take the place of something important. There is very little space in the brain itself."

(Patrick A. Tresco)

"The problem that I see:
Our brains are smarter than we are."

(F. Wörgötter)

2 - Session Talks

Over thirty talks from international speakers

2.1 Functional and Structural Connectivity

J H Lee, J Hennig, C A Haas, S Rotter

Optogenetic fMRI and the Investigation of Global Brain Circuit Mechanisms

Jin Hyung Lee

Neurology and Neurological Sciences, Bioengineering, Neurosurgery and Electrical Engineering (Courtesy) Stanford University, USA

With the development of optogenetic functional magnetic resonance imaging (ofMRI), it is now possible to observe whole-brain level network activity that results from modulating with millisecond-timescale resolution the activity of genetically, spatially, and topologically defined cell populations. ofMRI is anticipated to play an important role in the dissection and control of network-level brain circuit function and dysfunction.

In this talk, the ofMRI technology will be introduced with advanced approaches to bring it to its full potential, ending with examples of dissecting whole brain circuits associated with neurological diseases utilizing ofMRI.

Modulation of Structural and Functional Connectivity in Mouse Brain Observed by MR

Jürgen Hennig

Department of Radiology, Medical Physics,
Medical Center - University of Freiburg

The brain is a closely interconnected network of networks. Insight and understanding how different areas are connected to and interact with each other can be achieved using mouse models, allowing the detailed investigation of changes of connectivity and networks after modulation. We have developed a standardized toolbox of measurement and evaluation procedures based on DTI (diffusion tensor imaging) and rsMRI (resting state fMRI) to investigate the network effects caused by different tapes of intervention including electric or sensory stimulation, pharmacological intervention, optogentics, as well as knock-out mice for highly specific modulations.

A consistent finding in several of our studies is that even very specific and/or local intervention typically affects the brain network as a whole. Any intervention creates a cascade of compensatory mechanisms leading to unexpected modulations in areas only indirectly related to the stimulus. Insight into such mechanisms is essential for planning of appropriate stimulation protocols in clinical applications.

Structural and Functional Reorganization of the Hippocampal Network in Epilepsy

Carola A. Haas

Research group Experimental Epilepsy Research,
Department of Neurosurgery, Medical Center - University of Freiburg

Temporal lobe epilepsy (TLE) is the most common focal epilepsy in adults. It is unknown whether pathological processes preceding epilepsy onset are indicators of later disease severity. Therefore, we performed longitudinal multi-modal MR to monitor hippocampal injury and tissue reorganization during epileptogenesis in a mouse mTLE model. We present evidence that the extent of early hippocampal neurodegeneration and progressive microstructural changes in the dentate gyrus translate to the severity of hippocampal sclerosis and seizure burden in chronic epilepsy.

Inferring functional networks from BOLD-related signals

Stefan Rotter

Reseach Lab Computational Neuroscience,
Bernstein Center Freiburg, Faculty of Biology, University of Freiburg

Dynamic brain activity is strongly influenced by the anatomical wiring that links different brain regions. We suggest a new method to infer this unknown connectivity from recorded activity by evaluating the dynamic interactions between subpopulations. We have applied our method to reconstruct the full connectivity matrix for 90 brain regions from whole-brain fMRI recordings, accounting for both the direction and the sign of each individual link. As the success of the procedure is difficult to assess, we used numerical simulations to establish reliability and robustness of the new method.

2.2 Bidirectional Interaction with the Brain

C Chestek, I Diester, U Egert

Neural Interfaces for Controlling Finger Movements

Cynthia Chestek

Biomedical Engineering, Michigan Institute for Computational Discovery and Engineering, University of Michigan, USA

Neural prosthetic devices may one day restore movement to people with paralysis or amputation. The natural next step is to control complex movements at the level of individual fingers. For amputation, our lab acquires signals from individual peripheral nerve branches, using small muscle grafts to amplify the signal in humans. For spinal cord injury, we implant Utah arrays into finger areas of motor cortex, and have successfully decoded finger flexion and extension using the ReFIT Kalman filter. Finally, we seek to increase the number of channels using 8 um carbon thread electrode arrays.

A Toolbox for Chronic Optophysiological Experiments in Freely Moving Rodents

Ilka Diester

Research Lab for Optophysiology, Faculty of Biology, University of Freiburg

Simultaneous recordings and manipulations of neural circuits that control the behavior of animals is one of the key techniques in modern neuroscience. Rapid advances in optogenetics have led to a variety of probes combining multichannel readout and optogenetic write in. The choice of the device is constrained by several factors such as the animal model, the structure and location of the brain area of interest, as well as the behavioral read out. Here we provide an overview of available devices for chronic simultaneous neural recordings and optogenetic manipulation in awake behaving rats.

Autonomous Optimization of Targeted Stimulation of Neuronal Networks

Ulrich Egert

Biomicrotechnology, Department of Microsystems Engineering,
Faculty of Engineering, Bernstein Center Freiburg, University of Freiburg

Electrical stimulation of the brain is increasingly used to treat neurological disorders. Machine learning (ML) has been proposed to find optimal stimulation settings autonomously but the interaction between stimulus and network activity makes it difficult to appraise the result. We used models of the interaction between stimulus and network to design a testable ML task. In this, the ML algorithm had to balance opposing effects of ongoing neuronal activity on stimulation efficacy. ML solutions were close to optimal stimulation efficacy. Such concepts could help to test ML performance in more complex networks.

2.3 Human-Device Interaction

T Brox, T Ball, W Burgard

Deep Learning for 3D Vision

Thomas Brox

Pattern Recognition and Image Processing, Computer Vision Group,
Department of Computer Science, University of Freiburg

Deep learning in image processing has focused mainly on visual recognition, where it has led to drastic improvements in quality. Other tasks in computer vision have been approached with deep learning much more slowly, and particularly 3D vision has been assumed to not benefit from deep learning at all. With a set of works we have shown that also the formulation of 3D vision tasks as learning problems outperforms the state of the art with classical methodology. Apart from improved accuracy and robustness, such formulations allow for interactive frame rates and are compatible with learning formulations of other tasks. This yields excellent conditions to combine 3D vision networks with interactive learning approaches, for instance in control settings.

Deep Learning with Convolutional Neural Networks for Brain Mapping and Interfacing

Tonio Ball

Research Group Translational Neurotechnology,
Department of Neurosurgery, Medical Center - University of Freiburg

Deep learning with convolutional neural networks (CNNs) recently led to substantial progress in many application areas including image classification and natural speech processing. Now, deep learning with CNNs can be used for EEG analysis in movement-related and cognitive including language-related settings, as well as in brain-computer interfacing for online robot control. Recent advances from deep learning research can help to improve performance for these tasks. Beyond BCI-control, deep learning may also offer new possibilities for mapping task-related information using EEG.

Perception and Learning for an Autonomous Brain-Controlled Mobile Manipulation Robot

Wolfram Burgard

Research Lab Autonomous Intelligent Systems,
Department of Computer Science, University of Freiburg

Autonomous robots acting in the real world are faced with a series of perception and learning problems to achieve and optimize their behavior. Within BrainLinks-BrainTools we developed novel approaches for an intelligent robot designed to support paralyzed people via an EEG-based brain computer interface. The task of the robot is to provide different services to the user including fetch and carry operations or serving a drink. For all approaches we developed to realize this robot we performed extensive experiments demonstrating their robustness and illustrating in which way they extend the state of the art.

2.4 Interfacing with Intracortical Probes

P Ruther, T Stieglitz, W Shain

Micro-Optical Tools with Integrated Light Sources to Interface the Brain

Patrick Ruther

Microsystem Materials Laboratory,
Department of Microsystems Engineering, University of Freiburg

The experimental method of optogenetics established in neuroscientific research, asks for advanced implantable micro devices to provide light for a temporally and laterally well-controlled optical stimulation of neural tissue. In BrainLinks-BrainTools and related national and international projects, we develop and apply optical probes which are based on silicon and polymer substrates comprising either light-emitting diodes (both commercial LED chips and thin-film LEDs realized at IMTEK) or laser diode chips combined with polymeric waveguides. The analysis of key device challenges in view of a save and long-term stable application is supplemented by experimental results on probe performance and respective in vivo applications in cortical brain tissue and in the cochlea.

Long-Term Performance of Flexible Thin-Film Electrode Arrays in Neural Implants

Thomas Stieglitz

Research Lab Biomedical Microtechnology,
Department of Microsystems Engineering, University of Freiburg

Flexible neural probes with integrated thin-film metallization have to stay stable and functional in chronic applications. We have investigated metal adhesion and electrode coating performance in intracortical, epicortical and peripheral nerve electrode arrays in chronic studies under electrical recording and stimulation conditions.

Electrode arrays remained stable up to years in animals in cortical implants as well as in humans in the peripheral nervous system for up to six months. Various probe designs and materials were assessed in MRI scans and showed less artefacts than conventional arrays.

Controlling Device Initiated Tissue Responses to Implanted Neural Prosthetics—the Major Impediment to High Fidelity, Long-term Performance

William Shain

Center for Sensorimotor Neural Engineering,
University of Washington, Seattle, WA, USA

Time-dependent performance decrement of implanted microfabricated devices has prevented their greater use. Device implant results in biological responses associated with insertion and sustained reactive responses. We have investigated both device design and brain cell function.

Studies investigating cell responses measured major brain cell types and tested our hypothesis that reactive cellular responses around implanted devices result from interference with cell-to-cell interactions resulting in microglia activation. Results suggest that incorporation of biological criteria into device design will provide necessary high-fidelity, life-time performance.

2.5 Clinical Applications

M Bartos, C Weiller, T Schläpfer, A Schulze-Bonhage

Distance-Dependent Inhibition Facilitates Focality of Gamma Oscillations in the Dentate Gyrus

Marlene Bartos

Systemic and Cellular Neurophysiology,
Institute for Physiology I, University of Freiburg

Gamma oscillations (30-150 Hz) in neuronal networks are associated with the processing and recall of information. We measured local field potentials in the dentate gyrus of freely moving mice and found that gamma activity occurs in bursts, which are highly heterogeneous in their spatial extensions, ranging from focal to global coherent events. Synaptic communication among perisomatic-inhibitory interneurons (PIIs) is thought to play an important role in the generation of hippocampal gamma patterns. However, how neuronal circuits can generate synchronous oscillations at different spatial scales is unknown.
We analyzed paired recordings in dentate gyrus slices and show that synaptic signaling at interneuron-interneuron synapses is distance-dependent. Synaptic strength declines whereas the duration of inhibitory signals increases with axonal distance among interconnected PIIs. By neuronal network modeling, we show that distance-dependent inhibition generates multiple highly synchronous focal gamma bursts allowing the network to process complex inputs in parallel in flexibly organized neuronal centers.

Anatomical Constraints for Compensation After Stroke

Cornelius Weiller

Department of Neurology and Neuroscience,
Neurocenter, Medical Center - University of Freiburg

External devices can be used to reclose disrupted internal closed-loops in brains (e.g. DBS in Parkinson's disease) or to provide temporary externalization to reinstall the internal closed-loops. After identifying the functional roles of anatomically defined loops in patient behaviour we present two studies, showing that one arm of the closed-loop is used for recovery of tool use and that intactness of this arm is a prerequisite for compensation.

The results are supported by a recent behavioural study and our own data on markers of recovery. Now the stage is set for an intervention study on strokes and how the concept may be generalized to other brain diseases.

The Clinical Promise of Neuromodulation of Reward Processing

Thomas Schläpfer

Division of Interventional Biological Psychiatry, Department of Psychiatry
and Psychotherapy, Medical Center - University of Freiburg

The recent introduction of Deep Brain Stimulation (DBS) for treatment resistant psychiatric disorders might very well lead to the most significant development in clinical psychiatry of the last forty years – possibly offering a rise of hope for patients to whom medicine had hitherto little to offer. Furthermore, translational research on neuromodulation will allow us to glean something about the underlying cause of patient's illnesses before figuring out a treatment that addresses the source of the problem. Major depression offers perhaps the best example of the rapid progress being made in understanding the biology of mental illness. Studies on the underlying neurobiology of major depression have typically focused on the description of biological differences between patients and healthy subjects such as alterations of monoaminergic or endocrine systems.

Psychotropic drugs work by altering neurochemistry to a large extent in widespread regions of the brain, many of which may be unrelated to depression. We believe that more focused, targeted treatment approaches that modulate specific networks in the brain – specifically structures mediating rewarding responses to emotional stimuli - will prove a more effective approach to help treatment-resistant patients. In other words, whereas existing depression treatments approach this disease as a general brain dysfunction, a more complete and appropriate treatment will arise from thinking of depression as a dysfunction of specific brain networks that mediate mood and reward signals. A better understanding of defined dysfunctions in these networks will invariably lead to a better understanding of patients afflicted with depression and perhaps contribute to a de-stigmatization of psychiatric patients and the medical specialty treating them.

Progress Towards Closed-Loop Interventions in Epilepsy

Andreas Schulze-Bonhage

Epilepsy Center at the University of Freiburg,
Department of Neurosurgery, Medical Center - University of Freiburg

Epilepsy is characterized by transient periods of abnormal neuronal synchronization, leading to functional brain disturbances called “seizures”. Established treatment consist in a continuous prevention of seizure occurrence. Closed-loop approaches in contrast aim at an early detection and rapid intervention during epileptic activity; presently used algorithms, however, lack in specificity and have an unclear potential to quench ongoing ictal activity. We report progress in monitoring excitability and in feature-based specific detection of seizures using machine-learning techniques at low energy consumption.

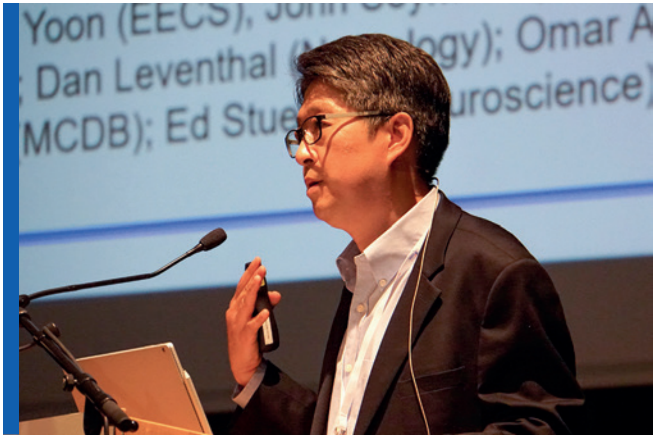
2.6 International Conference for Advanced Neurotechnology

E Yoon, U Oh, N Choi, K Harris, N Steinmetz, I Hanganu-Opatz, B Watson, J Seymour, S J Aton

International Partnership for Advancement of Neurotechnology: Challenges and Expectations

Euisik Yoon

Department of Biomedical Engineering,
Solid-State Electronics Lab, University of Michigan, USA



The International Partnership for the Advancement of Neurotechnology (IPAN) is an NSF funded project to develop hardware and software systems to advance one of the biggest scientific challenges: understanding the brain. The challenge is so grand that strong collaborations among leading international laboratories are essential to accelerate neurotechnology for advancement of science. Collaborative efforts among the partners (U. of Freiburg, U. of Hamburg, UCL, KIST, IME, NYU, UPR, Janelia, and U. of Michigan) focus on (i) identification of recorded neuron types, (ii) reconstruction of local neural circuits, and (iii) delivery of biomimetic or synthetic inputs in a cell-specific targeted manner. Collaborative efforts also focus on a cross-disciplined education program for next-generation scientists/engineers.

Introducing the Brain Science Institute of the Korea Institute of Science and Technology (KIST)

Uhtaek Oh

Brain Science Institute, KIST, Seoul 0272, Korea

The Brain Science Institute (BSI) of KIST is one of the leading neuroscience research institutes in Korea. Despite its short history, BSI performs remarkably well and competes with

global experts in neuroscience. BSI has four centers that specialize in neurobiology, functional connectomics, neurochemistry, and neural engineering.
Various techniques from gene mining to connectome or from synthesizing novel molecules to MEMS devices are our research power for applying to translational as well as basic research fields. With different disciplines and expertise of more than 250 workers, BSI continues to tackle the solutions to unanswered questions in neural diseases and basic neuroscience.

Anisotropically Organized Three-Dimensional Culture Platform for Reconstruction of Hippocampal Neural Network

Nakwon Choi

Center for BioMicrosystems, Brain Science Institute,
Korea Institute of Science and Technology (KIST), Korea

In native tissues, cellular and acellular components are anisotropically organized and often aligned in specific directions, providing structural properties for actuating biological functions. However, achieving desired alignment is challenging, especially in 3D constructs. By exploiting the elastomeric property of polydimethylsiloxane and fibrillogenesis kinetics of collagen, here we introduce a simple yet effective method to assemble and align fibrous structures in a multi-modular 3D conglomerate. Applying this method, we have reconstructed the CA3–CA1 hippocampal neural circuit three-dimensionally in a monolithic gel.

Neuropixels and Kilosort: Hardware and Software for Next-Generation Electrophysiology

Kenneth Harris

Quantative Neuroscience, University College London, London, GB

A new generation of silicon microelectrodes was funded by the Wellcome Trust, Gatsby Foundation, Allen Institute for Brain Sciences, and Howard Hughes Medical Institute.

These probes contain close to 1000 electrode sites, from which 384 can be recorded simultaneously via switching electronics close to the recording sites. An active circuit located at the probe base amplifies, filters, and digitizes the recorded physiological signals and streams them to a host computer for recording. Software for rapid processing of the resulting data has been developed that allows processing of the resulting data in close to real time.

Distributed Neuronal Populations Supporting Vision, Action, and Reward across the Mouse Brain

Nick Steinmetz

Institute of Neurology, University College London, London, GB

Behavior arises from neuronal activity patterns, but whether the relevant activity is private to a small number of brain regions, as typically studied, or instead distributed and coordinated widely across many regions, remains unknown. We used acutely-inserted Neuropixels electrode arrays with 384 recording sites to measure the activity of thousands of neurons in more than 40 regions of the mouse brain, while mice performed a visual discrimination task. We discovered representations of motor response execution and reward in essentially every recorded region, suggesting that relevant neuronal populations are highly distributed.

Cognitive Ontogeny in Health and Mental Illness: a Story of Right Communication

Ileana Hanganu-Opatz

Developmental Neurophysiology,
University Medical Center Hamburg-Eppendorf, Germany

Cognitive performance relies on the entrainment of neuronal networks in oscillatory patterns of electrical activity, as exemplified in the case of functional interplay between the prefrontal cortex and hippocampus. Coupling of neuronal networks in oscillatory rhythms emerges early during development. However, the contribution of coordinated activity for the maturation of neuronal networks remains largely unknown. The talk will introduce the mechanisms controlling the development of structural and functional coupling within prefrontal-hippocampal networks of rodents. Moreover, the dysfunction within hippocampal-prefrontal networks, switching from neonatal hypo- to juvenile hyper-coupling, will be characterized as a possible mechanism underlying the pathophysiology of cognitive deficits in neuropsychiatric disorders.

Regulation of Brain Activity by Brain State

Brendon Watson

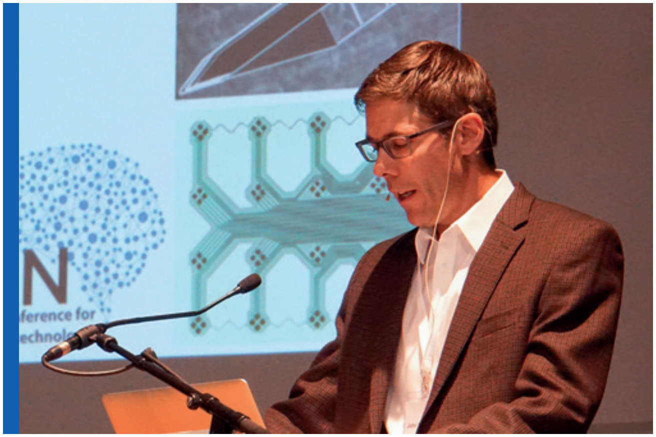
Weill Cornell Psychiatry Specialty Center, Weill Cornell Medical College, Cornell University, New York, NY 10065, USA

We take advantage of the capacity of silicon probes to record multiple neuronal units simultaneously to study network state. We recorded from frontal cortex of rats and we found that sleep and wake oppositely modulate the heterogeneity of spiking activity in the excitatory neuronal population. During wake, neurons fire with a wide variety of firing rates whereas firing rates homogenize progressively over sleep. We then preliminarily show that this heterogeneity of firing is also modulated when animals are given antidepressant drugs—implying that this metric indicates general network state.

Advances and Challenges in Optoelectrode Systems

John Seymour

Department of Electrical Engineering and Computer Science, College of Engineering, Michigan University, Ann Arbor, USA



The goal of our work is to ensure every neuroscience lab can easily use optoelectrodes to perform ever more sophisticated mapping tasks. So how do we get there?

The µLED and waveguide optoelectrode already have sufficient complexity and density for some experiments, but the software and connectivity should become seamless and simple. Critically the induced electrical artifacts from optical stimulation should be minimized so the filtered electrophysiology is uncorrupted. The system should also be capable of real-time control using any event trigger of the neuroscientist's choosing. I will discuss our efforts and collaboration with all of these challenges.

Slow Wave Sleep Oscillations Coordinate Neural Ensembles During Memory Consolidation

Sara J. Aton

Department of Molecular, Cellular, and Developmental Biology, University of Michigan, USA

Sleep has long been implicated in the process of memory formation, but the underlying mechanisms are unknown. Our lab has recently characterized changes in hippocampal network activity which are associated with long-term memory consolidation. These include increased coherent firing with slow wave sleep oscillations, and stabilization of network activity patterns over long (~24 h) timescales. We show recent data demonstrating that following learning, coherent firing associated with slow wave sleep is both necessary and sufficient for network stability and long-term memory formation.

2.7 Ethics and Outreach

E Chudler, O Müller

Research Neuroscientists as Science Communicators: Challenges and Opportunities

Eric H. Chudler

Department of Bioengineering, Department of Anesthesiology and Pain Medicine; Center for Sensorimotor Neural Engineering, University of Washington, Seattle, WA, USA

The public is fascinated by brain research but rarely interacts with scientists who are making the discoveries. Some researchers avoid such interactions because of perceived difficulties translating their work to novice audiences or fear their work will be misinterpreted. Opportunities for scientists to interact with the public include participation in science fairs, museum exhibits, community lectures and publications for lay audiences. These activities are rewarding not only for the audiences, but they also may benefit the scientist through grant funding and factor into promotion decisions.

Ethical Reflection on Neurotechnology and New Public Engagement Formats

Oliver Müller

Research Group Norms & Nature, Department of Philosophy, Norms & Nature, University of Freiburg

Different projects within BrainLinks-BrainTools deal with philosophical and ethical approaches to neurotechnology, including a broad variety of ethical engagement activities. On a theoretical level, central research topics encompass 'hybridity' as a normative base category, 'personhood' as an ethical core concept in clinical applications, and 'agency' in human-robot interactions. On a practical level, we aim at developing new types of participatory projects - especially with artistic partners. In order to promote a vivid debate on the societal and ethical implications of neurotechnology we create new forums for scientists in BrainLinks-BrainTools to discuss their findings and conceptual backgrounds. Thus, we aim to foster knowledge transfer and dialogue with the public.

2.8 Implant Development

O Paul, M Asplund, U Wallrabe

Silicon-Based Neural Probes for Minimally Invasive Neuroscience

Oliver Paul

Research Lab Microsystems Materials,
Department of Microsystems Engineering, University of Freiburg

Within BrainLinks-BrainTools we were able to make big steps in the progress of developing smart invasive neural probes. Relying on CMOS technology and designed for interacting with individual neurons, these probes are equipped with multiplexing and signal conditioning circuitry allowing neuronal signals to be simultaneously extracted from extended regions of the brain. Among the recent achievements of BrainLinks-BrainTools, a probe allowing 32 channels to be read out from among 1600 available recording sites will be described. With its small base, it is suitable for chronic experiments on freely behaving animals.

Tailor Made Electrode Surfaces for Long-Term Stable Intracortical Probes

Maria Asplund

Research Group Electroactive Coatings,
Department of Microsystems Engineering, University of Freiburg

For long term stable connections to be made possible, between neural probes and neurons, better surfaces are needed at the interface. Conducting polymers, especially PEDOT, are the perfect building blocks for tailoring biofunctionalized electrodes for this purpose. PEDOT based materials have low impedance and are stable during stimulation. By mixing in functional parts with the polymer we show how extra features can be added on the probe. Whether it is a non-biofouling membrane that is wished for, or local delivery of a biomolecule, PEDOT materials can contribute to the solution.

Non-Diffracting Light Beams for Optogenetics

Ulrike Wallrabe

Reseach Lab Microactuators,
Department of Microsystems Engineering, University of Freiburg

Quasi non-diffracting beams such as Bessel beams can be created, e.g., by an axicon, forming a self-interfering conical wavefront. These beams feature an extended focal zone and self-healing properties, which we aim to apply for optogenetic stimulation without penetrating brain tissue. With an array of blue laser diodes, micro-lenses and micro-axicons we can control multiple independent channels without the use of stiff fiber connections, as often used in nowadays stimulation devices. Our goal is to build an implantable depth-controlled tool for optogenetic stimulation of cortical areas.

"I had the opportunity to watch the BrainLinks-BrainTools program from the beginning and it is really wonderful to see all the success. It is really an impressive set of accomplishments."

(John P. Donoghue)

3 - Conference Illustrated

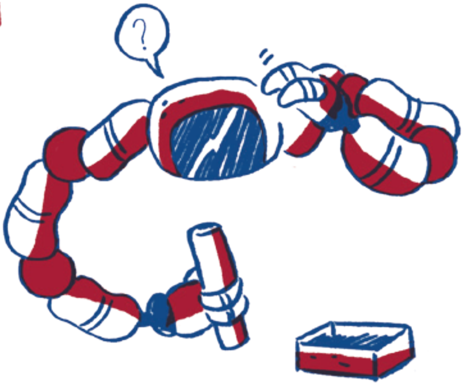
Illustrated Impressions of the 2017 Conference

FLORENTIN WÖRGÖTTER

NEURONS AND ROBOTS: USING NETWORKS TO CONTROL & LEARNING TO BEHAVE

SELF-ORGANIZATION OF LARGE NETWORKS
> 1000 NEURONS

THE ROBOT ARM



TWO INDEPENDENT TASKS:
1. ROTATE } THE OBJECT
2. TRANSLATE } THE OBJECT

REQUIRE
TWO INDEPENDENT NEURON POPULATIONS

LEARNING THROUGH RESERVOIR COMPUTING

LET'S TRAIN THESE GUYS!

problem:

CONVENTIONAL NETWORKS ARE TOO BIG

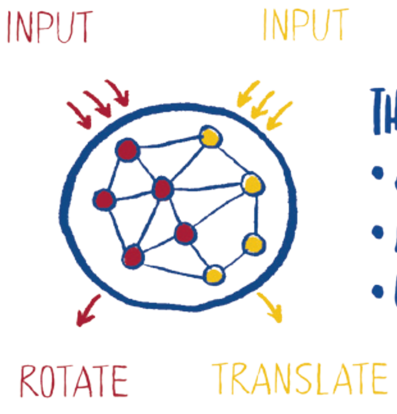
LEARNING AS A SOLUTION?

BUT HEBB LEARNING IS NOT STABLE ON ITS' OWN

combine with →

SYNAPTIC SCALING: NEURONS HAVE A DESIRED FIRING RATE CREATES STABILITY

AFTER A FEW LEARNING CYCLES LARGE NETWORKS RESTRUCTURE INTO SMALL BUT POWERFUL RESERVOIRS!

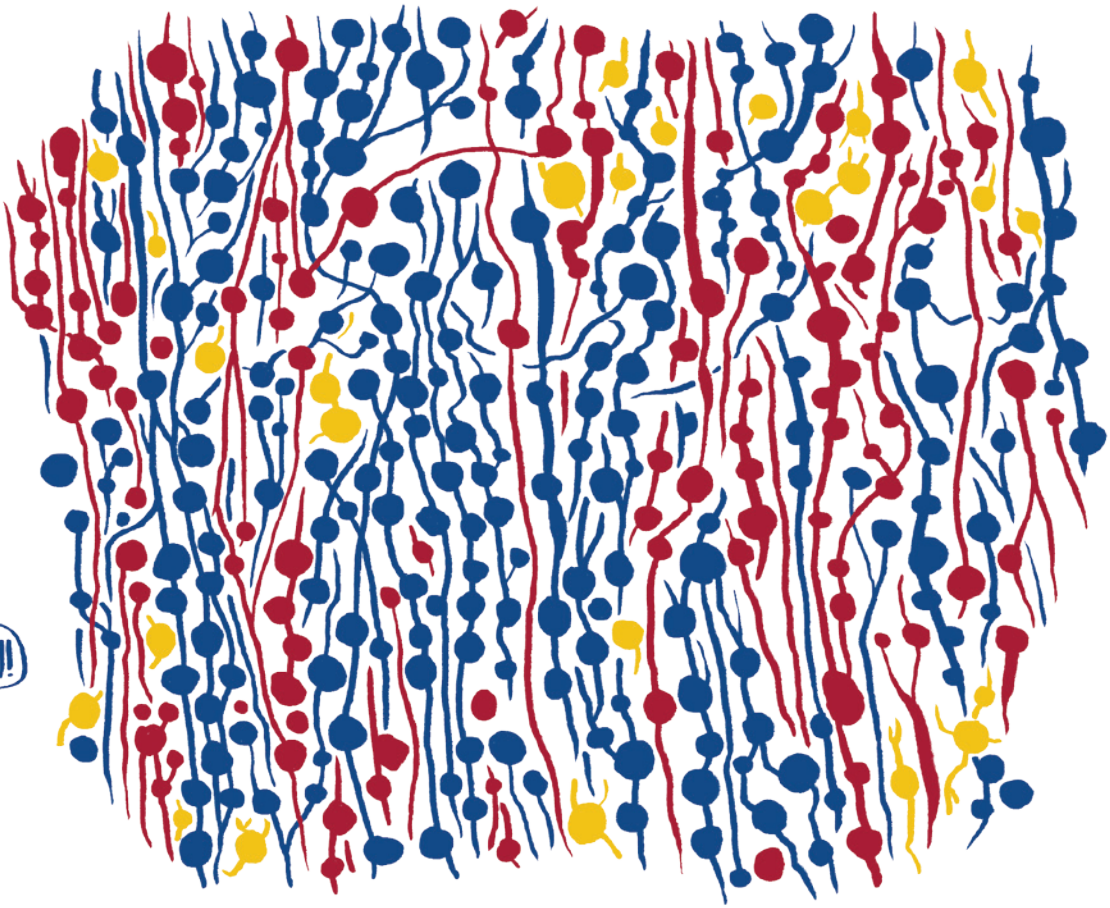


THESE RESERVOIRS:

- STORE DIFFERENT INFORMATION
- DO DIFFERENT COMPUTATION
- GROW ON DEMAND

GYÖRGY BUZSÁKI

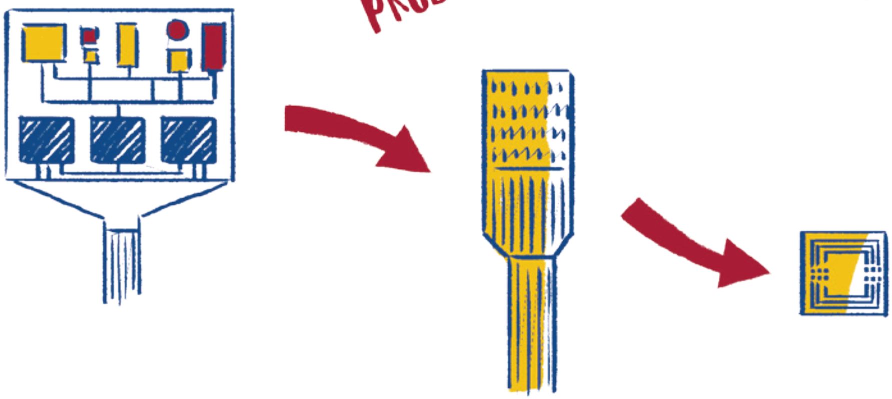
NEURONAL CIRCUIT EXPLORATIONS



HOW DO WE APPROACH THEM?

WITH **LARGE SCALE RECORDINGS** ON SINGLE NEURON LEVEL!

PROBES KEEP GETTING SMALLER AND LESS INVASIVE.



THE CHALLENGE BEING: NOT TO SACRIFICE RESOLUTION!

OUR TOOLS (STATE OF THE ART):

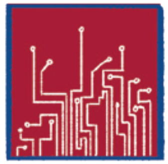
OPTOGENETIC ELECTRODES WITH NEURON–SIZED LEDS
→ TO RECORD FROM SINGLE NEURONS

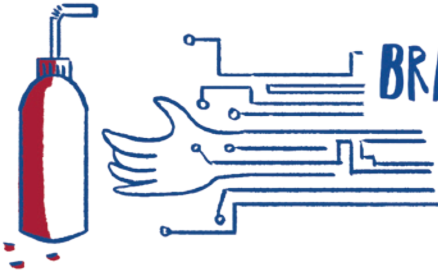
JOHN P. DONOGHUE

BRAIN COMPUTER INTERFACES:
MAKING THEM BETTER

OUR VISION @

BRAINGATE:





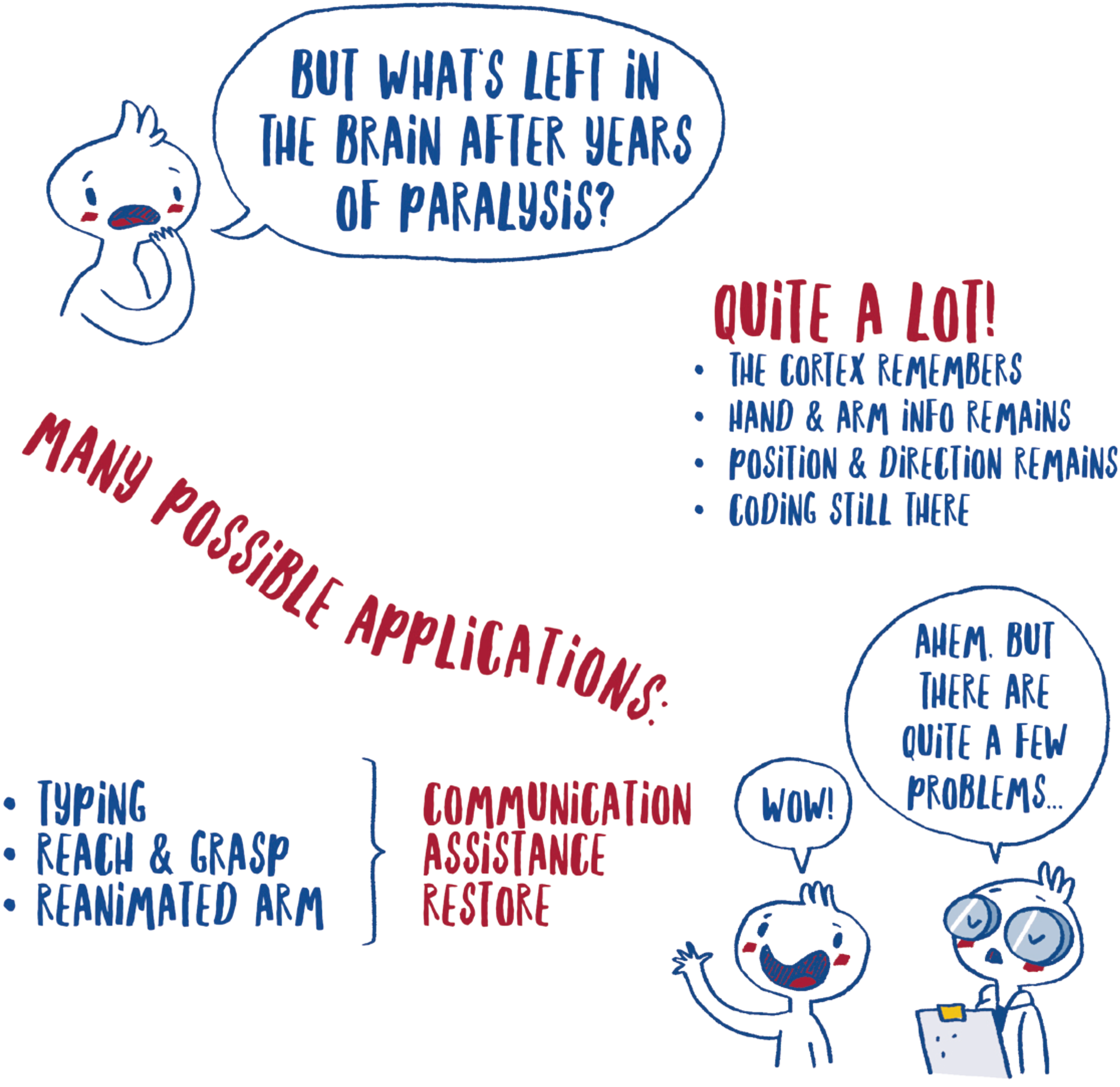
BRAIN COMPUTER INTERFACES TO RESTORE MOVEMENT TO A PARALYZED ARM

WHY?

>125.000 PEOPLE IN THE US SUFFER FROM STROKE OR SPINAL CORD IN-JURIES EACH YEAR!

WHO?

BRAINGATE: ~22 YEARS OF ACCUMULATED EXPERIENCE


BUT WHAT'S LEFT IN THE BRAIN AFTER YEARS OF PARALYSIS?
QUITE A LOT!
• THE CORTEX REMEMBERS
• HAND & ARM INFO REMAINS
• POSITION & DIRECTION REMAINS
• CODING STILL THERE
MANY POSSIBLE APPLICATIONS:
• TYPING
• REACH & GRASP
• REANIMATED ARM
COMMUNICATION
ASSISTANCE
RESTORE
WOW!
AHEM. BUT THERE ARE QUITE A FEW PROBLEMS...

PATRICK A. TRESCO

THE CHALLENGE OF INTEGRATING HIGH DENSITY RECORDING ARRAYS INTO BRAIN TISSUE

LONG-TERM NEURAL RECORDINGS

LEAD TO

IMPORTANT DISCOVERIES

HELP TO UNDERSTAND THE BRAIN

HELP TO TREAT DISORDERS

BUT

THEY ARE CHALLENGING TO IMPLEMENT

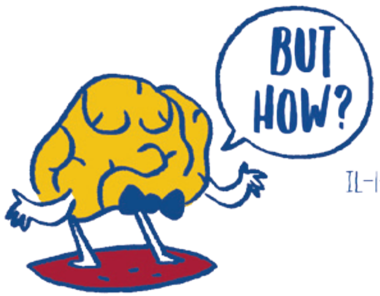
IN THE PAST, PEOPLE FOCUSSED ON ENGINEERING.

WE FOCUS ON BIOLOGY.

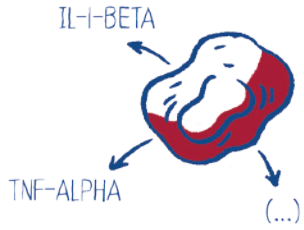
WE FOCUS ON THE BRAIN'S REACTION.

- to advance collective understanding
- to improve performance of implants

our goals: MOVE FROM EMPIRICAL BUILD-AND-TEST-APPROACH TOWARDS BIOLOGICALLY INFORMED APPROACHES

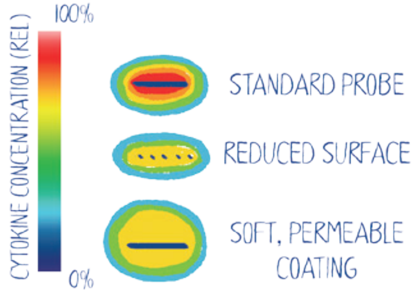


#1 BIOLOGY



ACTIVATED MACROPHAGES RELEASE PROINFLAMMATORY CYTOKINES > DRIVE INFLAMMATORY PROCESSES

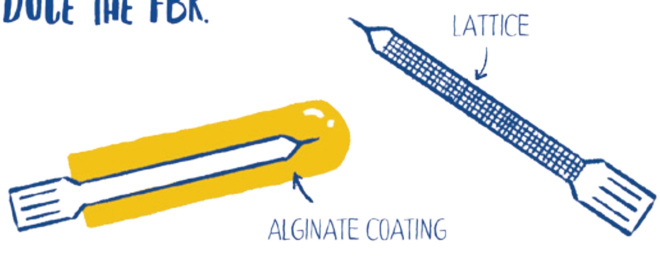
#2 PREDICTIVE MODELING



A MODEL OF CYTOKINE DISTRIBUTION SUBJECT TO THE SURFACE AREA OF PROBES

#3 DESIGN & ENGINEERING BASED ON #1 AND #2

REDUCING SURFACE AREA OR FACILIATING CYTOKINE-CLEARANCE SHOULD REDUCE THE FBR.



Imprint

Cluster of Excellence BrainLinks-BrainTools
University of Freiburg
Georges-Köhler-Allee 80
79110 Freiburg, Germany

Speaker of the Cluster: Prof. Dr. Wolfram Burgard
www.brainlinks-braintools.uni-freiburg.de

Concept & Layout
Daniel Hellweg
@ Graphic Design Agency, hKDM Freiburg, Germany
agentur.hkdm.de

Illustration
Veronika Mischitz
@ KIRSCHVOGELKANTINE Illustration, Esslingen, Germany
www.kirschvogelkantine.de

Photography (in part)
Hans-Peter Fischer
@ fischer fotodesign, Elzach, Germany
www.fischerfotodesign.de

NSF

DFG Deutsche Forschungsgemeinschaft

BrainLinks-BrainTools is a Cluster of Excellence funded by the German Research Foundation (DFG, grant number EXC 1086). The International Conference for Advanced Neurotechnology (ICAN) is funded and organized by the National Science Foundation's (NSF) International Program for the Advancement of Neurotechnology (IPAN).