Cognitive action control in rodents
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IMBIT Research program

**NeuroCore**

OptoRoboRat

**NeuroProbes**

Soft-FIB

**NeuroBots**

Machine-Brain-Interface
OptoRoboRat Project

OptoRat
- optical imaging of neuronal activity combined with optogenetic stimulation
- Freely moving rodent
- Neuronal data (2-photon imaging)
  - Head fixed rodent in virtual reality

Behavioral tracking
- Reconstructing complex movements in 3D
- Multi-camera tracking
- Closed loop control of virtual environment

Neuronal Decoding
- predict movements based on neuronal activity, extract knowledge about the role of individual neurons via backpropagation
- Extract behavioral patterns. Take out specific "neurons/layers" and observe behavioral outcomes.

Computer simulated rat
- simulate behavior based on neuronal data; compare learning rules in silico and in vivo
- Take out specific neurons and observe behavioral outcomes.

RoboRat
- apply biological control algorithms in a robotic scenario
- Take out specific "control parts" and observe outcome.

IMBIT
Intelligent Machine-Brain Interfacing Technology

Julian Ammer
Florian Steenbergen
Brice de la Crompe
Functional heterogeneity in the rat prefrontal cortex supports correctly timed responses

Dr. Stefanie Hardung

Zoe Jäckel
Our approach: A response preparation/inhibition task
Two error types: early and late responses

- Early release
- Late release

Hardung, …, Diester, *Current Biology* (2017)
Two error types: early and late responses

- Early release
- Late release

Hardung, ..., Diester, *Current Biology* (2017)
The no tone control

Hardung, ..., Diester, *Current Biology* (2017)
Post error slowing

Short trials

Long trials
Optogenetic manipulations

What is the causal impact of the PFC subsection in the task?

Hardung, …, Diester, *Current Biology* (2017)
Recording the effective spread of optical inhibition

**In vivo measurements**

<table>
<thead>
<tr>
<th>Distance to fiber tip (µm)</th>
<th>Cells responding to optical inhibition (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;400</td>
<td></td>
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<tr>
<td>400-800</td>
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<td>800-1200</td>
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<td>1200-1600</td>
<td></td>
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<tr>
<td>&gt;1600</td>
<td></td>
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</tbody>
</table>

Hardung, …, Diester, *Current Biology* (2017)
Effect of optical inhibition on behavior

Inhibition effect on reaction time

Change of RT [ms]

Short trial

Long trials

Delay

RT window

Late release

Early release

YFP control

Optical inhibition

n = 10

n = 9

Hardung, …, Diester, *Current Biology* (2017)
The traffic light in the PFC

- PL suppresses the urge to act
- IL enhances the urge to act
- VO influences the reaction to the tone
PL plays are very clear role in this task
PL inhibition versus excitation have opposing effects

inhibition

excitation

Change of error rate (%)

15
10
5
0
-5
-10
-15
-20

**

n.s.

***

1.0 s
0.5 s
Delay
RT window

1.0 s
0.5 s
Delay
RT window

20Hz,
2 ms pulse width

Zoe Jaeckel & Dominic Lau
Optogenetic excitation results in similar effects in all three structures

Inhibition

Excitation

Change of error rate (%)

1.0 s
0.5 s

Delay
RT window

PL
IL
VO

20Hz, 2ms pulse width
Direct comparison of PL, IL, and VO stimulation

Fiber position | fMRI response at 30Hz stimulation (5s block design)
---|---
PL | PL
IL | IL
VO | VO
Common response of PL, VO, IL stimulation

Stimulation: 5s block design, 10-40Hz

Labels based on the SIGMA rat brain atlas: https://doi.org/10.1038/s41467-019-13575-7
Take home message from opto-fMRI

- Optogenetic activation leads to far spread increase in neuronal activity with highly overlapping activation patterns
- We are currently running additional experiments including a PPI analysis

- Outlook: Establish correlation between behavior and network effect
Optogenetic dissection of cortico-subcortical interactions during movement control in rodents

Rat lever press training

Ephys recordings

Optogenetic modulation
Optogenetic dissection of cortico-subcortical interactions during movement control in rodents

Rat lever press training

\[\downarrow\]

Ephys recordings

\[\downarrow\]

Optogenetic modulation
LFP-burst based real-time neurofeedback in rats

Karvat, …, Diester, *Comm Biology* (2020)
Influence on beta bursts on vibrotactile perception - the task

Karvat, …, Diester, PNAS (2021)
Beta indicates a dynamic state that competes with detection of external stimuli
Optogenetic dissection of cortico-subcortical interactions during movement control in rodents

Rat lever press training

Ephys recordings

Local field potentials

Optogenetic modulation

Neurofeedback

On-line beta band filter

Burst detection

Changing task parameters
3D pose estimation enables virtual head fixation in freely moving rats
3D tracking of movements

FreiPose 3D tracking

Post hoc Triangulation

Cam 1

2D CNN feature extraction

Keypoint prediction via feature compression (e.g. argmax)

Cam 2

Feature channels

Triangulation of each keypoint independently

Cam 3

Keypoint output

Ambiguities/uncertainties have to be resolved at each individual view

FreiPose

Unproject and combine features

2D CNN feature extraction

Feature channels

Sparse voxel representation

3D Keypoint CNN predicts keypoint location

3D keypoint prediction

Schneider et al. (Neuron, in press)
Neuronal tuning to paw trajectories

17.68% (29/164) paw tuned neurons
(one-way ANOVA, Bonferroni-adjusted p< 0.05)

Schneider et al. (Neuron, in press)
Virtual head-fixation unmasked a large fraction of paw-tuned neurons

Number of tuned neurons

- 75 Tuned to body posture
- 6 Tuned to paw movements after virtual head-fixation
- 45 Tuned to paw movements without virtual head-fixation
- 5 Tuned to body posture without virtual head-fixation

Schneider et al. (Neuron, in press)
Outlook: Dynamic foraging task

- Reward
- Failure

<table>
<thead>
<tr>
<th>State switch</th>
<th>State switch</th>
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<tbody>
<tr>
<td>Left pokes</td>
<td></td>
</tr>
<tr>
<td>Left active</td>
<td></td>
</tr>
<tr>
<td>Right active</td>
<td></td>
</tr>
<tr>
<td>Right pokes</td>
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Reinforcement learning to extract individual strategies & link behavior to neuronal activity

Prof. Dr. Mansour Alyahyay

Prof. Dr. Joschka Bödecker
Reinforcement learning to extract individual strategies & link behavior to neuronal activity

\[ Q_k(s_t, a_t) \leftarrow \hat{f}(\Phi p(s_t), a_t) + \gamma \max_{a_{i+1}} \mathbb{E}_{s_{t+1} \sim \mathcal{M}} [Q_{k-1}(s_{t+1}, a)] \]

- **Testing**

- Prediction of behavior based on updated Q-values
- Release probability
- Execution period

Forward Q-learning
The role of OFC and motor cortex in reversal learning

Megan Schneck

Brice de la Crompe
In vitro slice work: Combination of patch-clamping and 2-Photon-Calcium-Imaging

Subgroup Cellular Neurophysiology

Philippe Coulon
Ashlyn Creamer

Cellular electrophysiological responses

isolated Ca\(^{2+}\) current

20 mV

100 ms

200 pA

Cellular Ca\(^{2+}\) responses

Ca\(^{2+}\) transient

F\(\text{C/FR}\)

60 s
Optogenetically stimulated Ca2+-transients in organotypical brain slice cultures
Acknowledgements