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As part of the joint colloquia organized by the Department of Chemistry and Chemical Biology at the Technical University of Dortmund

Prof. Dr. André Berndt

University of Washington, Seattle

will give a presentation with the title

"Chemistry in the Living Brain: New Tools to Measure Neurobiological Signaling"

The Berndt Lab at the Institute for Stem Cell and Regenerative Medicine, University of Washington (https://www.berndtlab.com) focuses primarily on developing fluorescent biosensors that can detect biochemical signals in neuronal networks in real time. The main aim is to monitor the activity of neurotransmitters, neuromodulators, hormones, ions, and intracellular signalling molecules in live tissue and behaving animals with high spatial and temporal resolution.

Abstract

Monitoring biochemical signals in the living brain with the sensitivity, speed, and specificity that neuroscience demands remains a fundamental challenge. Our lab addresses this by engineering genetically encoded fluorescent sensors that enable real-time, cell-type-specific imaging of molecular signals in vivo, and by developing the computational and screening platforms needed to do so systematically and at scale.

I will present two families of sensors built on the bacterial peroxide- sensing protein OxyR. By repositioning the circularly permuted fluorescent protein insertion site outside the reactive cysteine loop, we generated oROS-G, a reversible H2O2 indicator with kinetics that are approximately 7 times faster than those of the current gold standard, HyPer 7. Pairing oROS- G with oROS-HT, a far-red HaloTag-based variant targeted to the extracellular membrane, enables simultaneous, dual-compartment monitoring of hydrogen peroxide with subcellular resolution. We demonstrate applications in Alzheimer's disease models, opioid receptor signalling, and multiplexed redox imaging, and introduce fluorescence lifetime variants of both sensors for quantitative, expression-independent concentration measurements in tissues and freely moving animals.

We also engineered eNOVA, a genetically encoded estrogen sensor, which detects estradiol with sub-nanomolar sensitivity and high hormonal specificity. Validated in freely moving mice via fiber photometry, eNOVA enables direct visualization of neuroendocrine estrogen signalling in the brain, opening new avenues for studying sex differences in pain, neurodegeneration, and substance use disorders.

Finally, I will describe a machine learning pipeline trained on approximately 1,100 GCaMP calcium indicator variants that predicts gain-of-function mutations in silico. The resulting eGCaMP variants outperform GCaMP 6, 7, and 8 in signal amplitude and kinetics in cultured neurons and freely moving mice. We are extending this approach to red calcium indicators using Opto-MASS, a microwell-based platform that functionally screens more than 10,000 single mammalian cells per day and are using the resulting large-scale sequence-function datasets to train next-generation deep learning models.

References

1. Lee JD, Nguyen A, Gibbs CE, Jin ZR, Wang Y, Moghadasi A, Wait SJ, Choi H, Evitts KM, Asencio A, Bremner SB, Zuniga S, Chavan V, Pranoto IKA, Williams CA, Smith A, Moussavi-Harami F, Regnier M, Baker D, Young JE, Mack DL, Nance E, Boyle PM, Berndt A. Monitoring in real time and far-red imaging of H(2)O(2) dynamics with subcellular resolution. **Nature Chemical Biology** doi: 10.1038/s41589-025-01891-7.
2. Wait SJ, Expòsit M, Lin S, Rappleye M, Lee JD, Colby SA, Torp L, Asencio A, Smith A, Regnier M, Moussavi-Harami F, Baker D, Kim CK, Berndt A. Machine learning-guided engineering of genetically encoded fluorescent calcium indicators. **Nature Computational Science** doi: 10.1038/s43588-024-00611-w.
3. Lee JD, Won W, Kimball K, Wang Y, Yeboah F, Evitts KM, Neiswanger C, Schattauer S, Rappleye M, Bremner SB, Chun C, Smith N, Mack DL, Young JE, Lee CJ, Chavkin C, Berndt A. Structure-guided engineering of a fast genetically encoded sensor for real-time H_2O_2 monitoring. bioRxiv doi: 10.1101/2024.01.31.578117.

Time: **Friday, 28.08.2026 um 13:00 Uhr**
Location: **CP-02-182, Ersatzgebäude Chemie/Physik (OH4a), Campus Nord**

If you are interested in meeting André, please get in touch with
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