



Stephen J Smith

Professor of Molecular and Cellular Physiology, Emeritus

 NIH Biosketch available Online

 Curriculum Vitae available Online

Bio

BIO

Now enjoying emeritus status, Prof. Stephen Smith remains active with work in computational neuroscience microscopy and genomic data science. His recent explorations have unearthed transcriptomic evidence for a previous unrecognized ubiquity of local neuropeptide signaling and possible involvement of same in memory engram formation. Smith led an active Stanford laboratory (1990-2014) that explored brain development, structure, function, and disease progression. The lab's experimental approach typically began with invention of a new imaging method followed by applications of that method to attack previously intractable experimental challenges. Early on, Smith invented a novel fiber-optic spectrometer for calcium sensing that enabled the first detection and measurement of calcium transients in vertebrate neurons, the first quantitative measurements of presynaptic Ca transients, and the extraordinarily significant discovery of Ca influx through NMDA receptor channels. Later inventions led to numerous significant neuroscience discoveries, including retrograde actin flow within neuronal growth cones, intracellular Ca waves in astrocytes, the active role of dendritic filopodia in synaptogenesis, and the packeted delivery of synaptic protein components during synaptogenesis, and to the first optical measurements of single synaptic vesicle release, the first in vivo imaging of synaptotropic dendrite growth, and the first in vivo functional imaging measurements of visual receptive field development in a vertebrate animal. Smith's laboratory also invented a unique and now widely used high-resolution proteomic imaging method called "Array Tomography" and applied the method to explore the molecular architecture of cortical microcircuits in mouse and human. Smith went emeritus and closed his Stanford laboratory in 2014, taking an exciting new position as Senior Investigator at the Allen Institute for Brain Science in his hometown of Seattle, Washington. At the Allen Institute he freshened up his data science proficiencies, driven by that Institutes prodigious production of extremely high-quality neuroscience data. He is now an Allen Institute Investigator Emeritus and an Allen Neural Dynamics Fellow and plans a return to California and Stanford campus life in Spring 2024.

ACADEMIC APPOINTMENTS

- Emeritus Faculty, Acad Council, Molecular and Cellular Physiology
- Member, Bio-X
- Member, Wu Tsai Neurosciences Institute

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Stephen Smith remains active in the computational microscopy field and is also currently using data science tools to explore new transcriptomic perspectives on signaling by neuropeptides and other neuromodulators in brains of diverse animal species. These exploration have unearthed evidence for a previous unrecognized ubiquity of local neuropeptide signaling and possible critical involvement of such signaling in memory engram formation.

Teaching

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biophysics (Phd Program)
- Molecular and Cellular Physiology (Phd Program)
- Neurosciences (Phd Program)

Publications

PUBLICATIONS

- **A scalable and modular automated pipeline for stitching of large electron microscopy datasets** *ELIFE*
Mahalingam, G., Torres, R., Kapner, D., Trautman, E. T., Fliss, T., Seshamani, S., Perlman, E., Young, R., Kinn, S., Buchanan, J., Takeno, M. M., Yin, W., Bumbarger, et al
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- **Cell-type-specific neuromodulation guides synaptic credit assignment in a spiking neural network.** *Proceedings of the National Academy of Sciences of the United States of America*
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- **Transcriptomic evidence for dense peptidergic networks within forebrains of four widely divergent tetrapods** *CURRENT OPINION IN NEUROBIOLOGY*
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- **A community-developed open-source computational ecosystem for big neuro data.** *Nature methods*
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- **Mapping synapses by conjugate light-electron array tomography.** *journal of neuroscience*
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- **Fmr1 KO and Fenobam Treatment Differentially Impact Distinct Synapse Populations of Mouse Neocortex** *NEURON*
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- **Astrocytes mediate synapse elimination through MEGF10 and MERTK pathways** *NATURE*
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- **Astrocyte glypicans 4 and 6 promote formation of excitatory synapses via GluA1 AMPA receptors** *NATURE*
Allen, N. J., Bennett, M. L., Foo, L. C., Wang, G. X., Chakraborty, C., Smith, S. J., Barres, B. A.
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- **Deep molecular diversity of mammalian synapses: why it matters and how to measure it** *NATURE REVIEWS NEUROSCIENCE*
O'Rourke, N. A., Weiler, N. C., Micheva, K. D., Smith, S. J.
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- **Single-Synapse Analysis of a Diverse Synapse Population: Proteomic Imaging Methods and Markers** *NEURON*
Micheva, K. D., Busse, B., Weiler, N. C., O'Rourke, N., Smith, S. J.
2010; 68 (4): 639-653
- **Array tomography: A new tool for imaging the molecular architecture and ultrastructure of neural circuits** *NEURON*
Micheva, K. D., Smith, S. J.

2007; 55 (1): 25-36

- **Detection of glutamate release from neurons by genetically encoded surface-displayed FRET nanosensors** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Okumoto, S., Looger, L. L., Micheva, K. D., Reimer, R. J., Smith, S. J., Frommer, W. B.
2005; 102 (24): 8740-8745
- **Functional imaging reveals rapid development of visual response properties in the zebrafish tectum** *NEURON*
Niell, C. M., Smith, S. J.
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- **In vivo imaging evidence for strong effects of synaptogenesis on the growth of both dendritic and axonal arbors in zebrafish optic tectum**
Smith, S. J., Niell, C. M., Meyer, M. P.
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- **Stability and plasticity of developing synapses in hippocampal neuronal cultures** *JOURNAL OF NEUROSCIENCE*
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- **Optical detection of a quantal presynaptic membrane turnover** *NATURE*
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- **Quantitative analysis of cadherin-catenin-actin reorganization during development of cell-cell adhesion** *JOURNAL OF CELL BIOLOGY*
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- **The dynamics of dendritic structure in developing hippocampal slices** *JOURNAL OF NEUROSCIENCE*
Dailey, M. E., Smith, S. J.
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- **THE KINETICS OF SYNAPTIC VESICLE RECYCLING MEASURED AT SINGLE PRESYNAPTIC BOUTONS** *NEURON*
Ryan, T. A., Reuter, H., Wendland, B., Schweizer, F. E., Tsien, R. W., Smith, S. J.
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- **Data-driven synapse classification reveals a logic of glutamate receptor composition.** *bioRxiv : the preprint server for biology*
Micheva, K. D., Simhal, A. K., Schardt, J., Smith, S. J., Weinberg, R. J., Owen, S. F.
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- **Developing a Toolbox of Antibodies Validated for Array Tomography-Based Imaging of Brain Synapses.** *eNeuro*
Micheva, K. D., Gong, B., Collman, F., Weinberg, R. J., Smith, S. J., Trimmer, J. S., Murray, K. D.
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- **A synapse census for the ages.** *Science (New York, N.Y.)*
Micheva, K. D., Weinberg, R. J., Smith, S. J.
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- **Progress and Future Goals for Neuroscience** *NEURON*
Moser, M., Gallant, J. L., Hu, H., Buckner, R. L., Stevens, M. M., Smith, S. J.
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- **Distinctive Structural and Molecular Features of Myelinated Inhibitory Axons in Human Neocortex.** *eNeuro*
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- **A Computational Synaptic Antibody Characterization Tool for Array Tomography.** *Frontiers in neuroanatomy*
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- **Probabilistic fluorescence-based synapse detection.** *PLoS computational biology*
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- **Generation of a Functional Human Cortex from Pluripotent Stem Cells**
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2015: 671-78
- **Knowing a synapse when you see one.** *Frontiers in neuroanatomy*
Burette, A., Collman, F., Micheva, K. D., Smith, S. J., Weinberg, R. J.
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- **Synaptic molecular imaging in spared and deprived columns of mouse barrel cortex with array tomography.** *Scientific data*
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- **Astrocytes mediate synapse elimination through MEGF10 and MERTK pathways.** *Nature*
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- **Accelerated Experience-Dependent Pruning of Cortical Synapses in Ephrin-A2 Knockout Mice** *NEURON*
Yu, X., Wang, G., Gilmore, A., Yee, A. X., Li, X., Xu, T., Smith, S. J., Chen, L., Zuo, Y.
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- **The Use of Immunofluorescent Array Tomography to Study the Three-Dimensional Microstructure of Murine Blood Vessels** *CELLULAR AND MOLECULAR BIOENGINEERING*
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