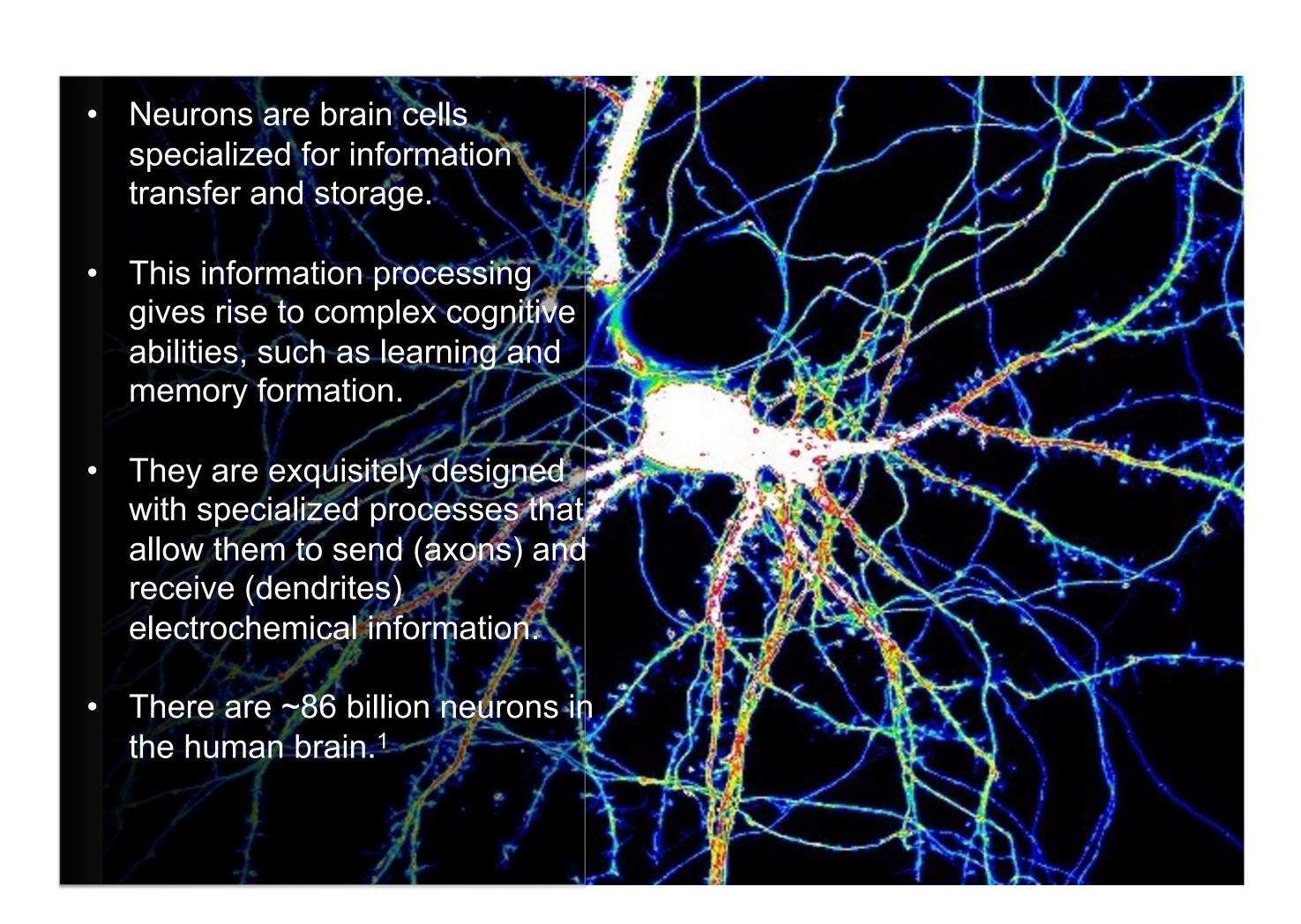
# Synapse Formation in Human Brain Development

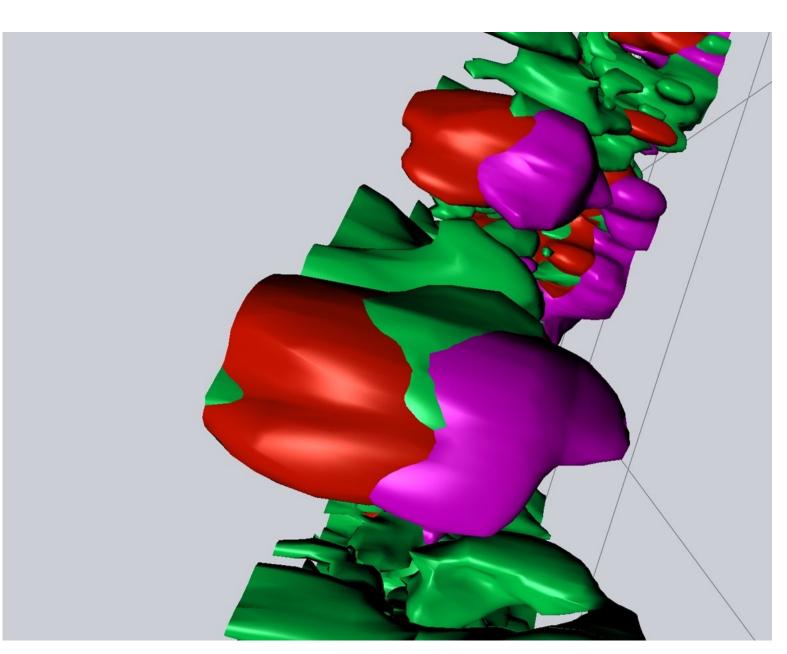
KAREN LITWA, PHD
ANATOMY AND CELL BIOLOGY, BRODY SCHOOL OF MEDICINE



#### WHAT IS A NEURON



#### WHY STUDY SYNAPSES



Synapses mediate information transfer.

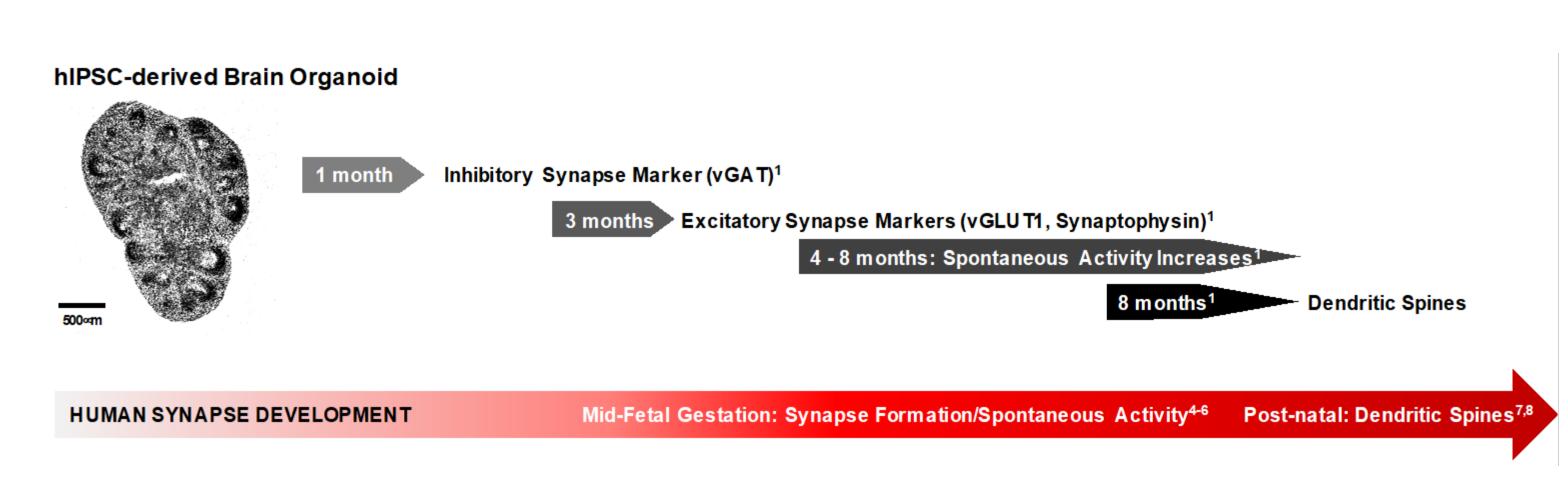
The pre-synaptic axon terminal sends information in the form of neurotransmitters across a synaptic cleft.

These neurotransmitters can then bind to receptors on the post-synaptic compartment, eliciting information transfer in the form of electrical activity, known as action potentials.

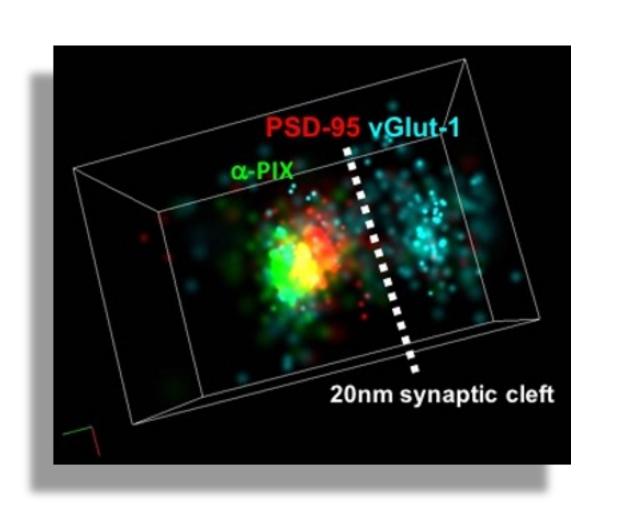
Understanding how synapses form will unravel mysteries of the brain, such as learning and memory formation.

This research will also help us to address how genetic mutations and environmental factors give rise to neurodevelopmental disorders, potentially leading to novel therapies.

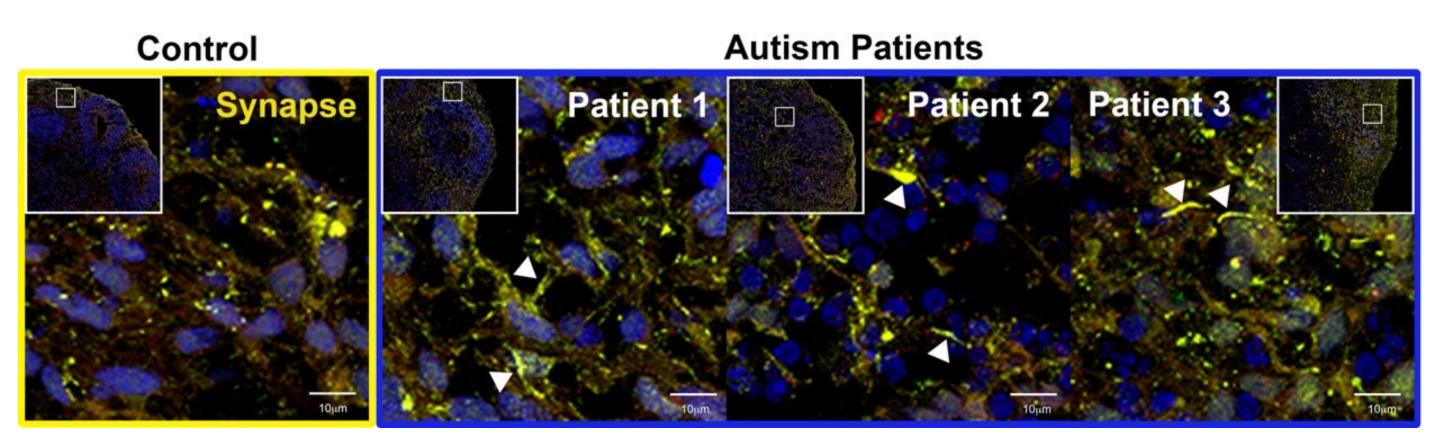
These discoveries may also allow us to rebuild synapses when they are lost in neurodegenerative diseases.



### HOW DO WE STUDY SYNAPSES

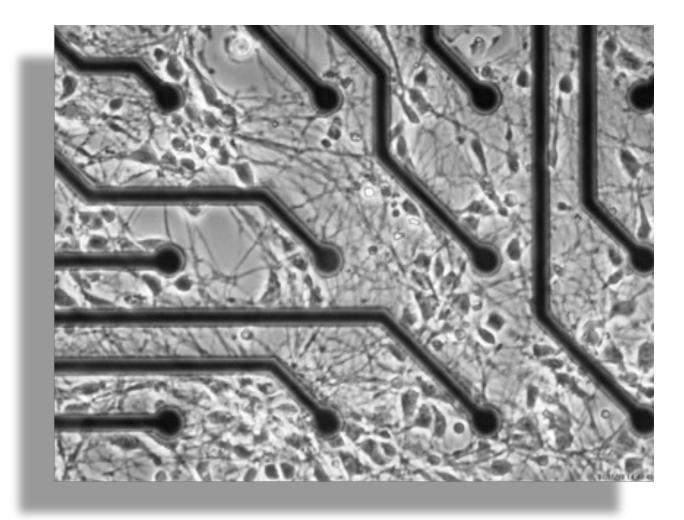


We visualize the formation of individual synapses with STORM super-resolution microscopy.<sup>3-6</sup>

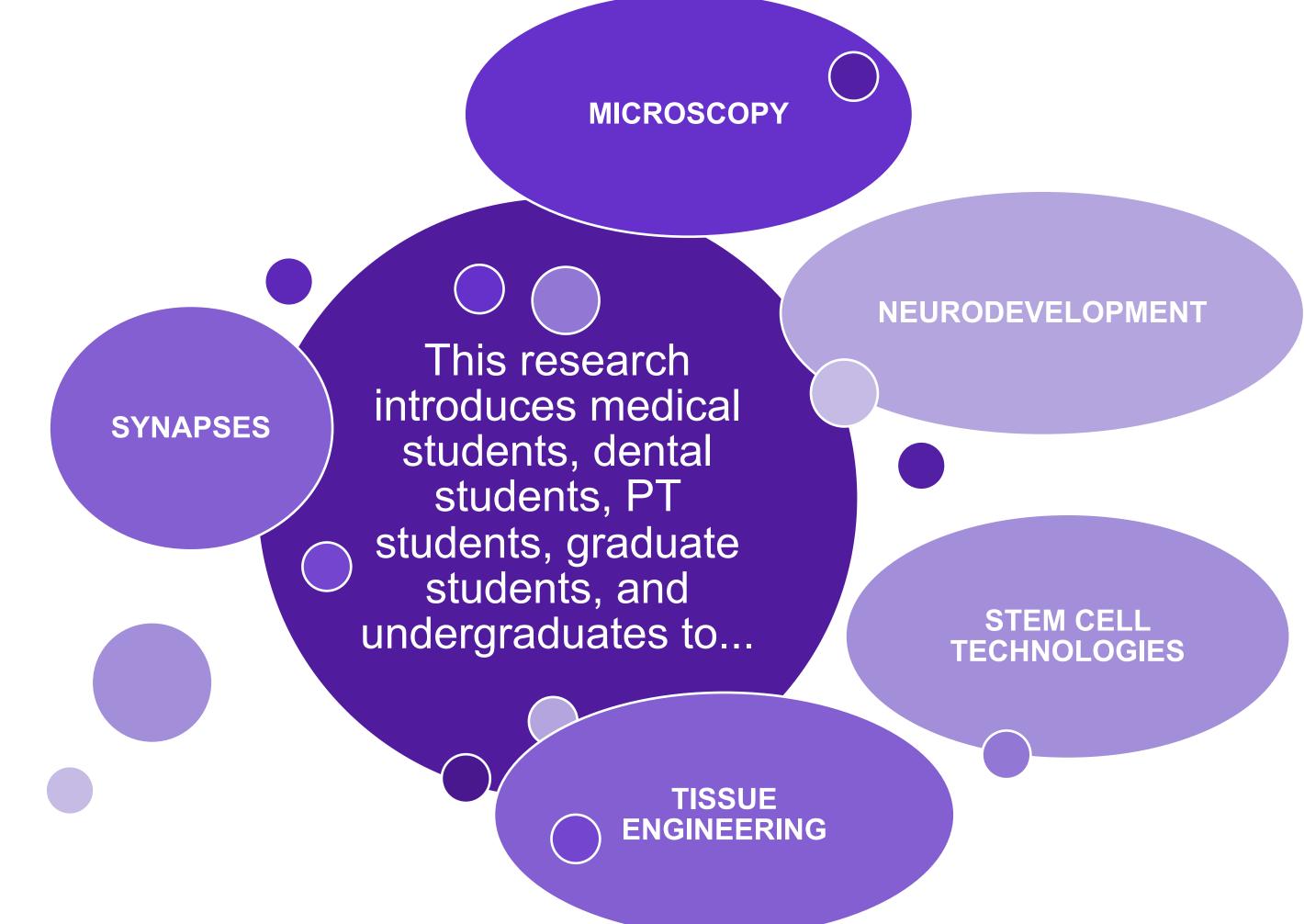


We develop human brain models from patient samples, allowing us to observe the emergence of synaptic alterations. We can also assess how different treatments impact synapse formation.<sup>3-7</sup>

We use microelectrode arrays to record electrical information transfer at synapses.<sup>4-7</sup>



Together, these technologies allow us to study how synapses form and function in brain development.



# WE BUILD BRAINS! WE ARE ALSO BUILDING THE NEXT GENERATION OF SCIENTISTS!

## How is teaching through biomedical research preparing students for STEM careers?

Innovate

optimize

experiments to test your hypothesis

Master

cutting-edge technologies

experiments to test your hypothesis

the ability to effectively share science



### **ACKNOWLEDGEMENTS**

I am extremely grateful to the amazing scientists with whom I get to share this journey of research discovery. I would especially like to thank my lab manager, Michelle Cobb, for always making sure we are equipped to do awesome science! I would also like to thank the Joani Zary in the histology core and Debajit Bhowmick in the flow cytometry core for providing amazing resources for our research. Finally, this research is currently funded by NSF CAREER AWARD 2144912

NIH R21 Award 1R21AT011371-01A1







- . Herculano-Houzel S. The remarkable, yet not extraordinary, human brain as a scaled-up primate brain and its associated cost. Proc Natl Acad Sci U S A. 2012 Jun 26;109 Suppl 1(Suppl 1):10661-8. doi: 10.1073/pnas.1201895109. Epub 2012 Jun 20. PMID: 22723358; PMCID: PMC3386878.
- 2. Wilson ES, Newell-Litwa K. Stem cell models of human synapse development and degeneration. Mol Biol Cell. 2018 Nov 26;29(24):2913-2921. doi: 10.1091/mbc.E18-04-0222. PMID: 30475098; PMCID: PMC6329912.
- 3. Wilson E, Rudisill T, Kirk B, Johnson C, Kemper P, Newell-Litwa K. Cytoskeletal regulation of synaptogenesis in a model of human fetal brain development. J Neurosci Res. 2020 Nov;98(11):2148-2165. doi: 10.1002/jnr.24692. Epub 2020 Jul 26. PMID: 32713041.
- 4. Papariello A, Taylor D, Soderstrom K, Litwa K. CB1 antagonism increases excitatory synaptogenesis in a cortical spheroid model of fetal brain development. Sci Rep. 2021 Apr 30;11(1):9356. doi: 10.1038/s41598-021-88750-2. PMID: 33931678; PMCID: PMC8087674.
- 5. Wilson E, Knudson W, Newell-Litwa K. Hyaluronan regulates synapse formation and function in developing neural networks. Sci Rep. 2020 Oct 5;10(1):16459. doi: 10.1038/s41598-020-73177-y. PMID: 33020512; PMCID: PMC7536407.
- 6. Wilson ES, Litwa K. Synaptic Hyaluronan Synthesis and CD44-Mediated Signaling Coordinate Neural Circuit Development. Cells. 2021 Sep 28;10(10):2574. doi: 10.3390/cells10102574. PMID: 34685554; PMCID: PMC8533746.
- 7. Tate K, Kirk B, Tseng A, Ulffers A, Litwa K. Effects of the Selective Serotonin Reuptake Inhibitor Fluoxetine on Developing Neural Circuits in a Model of the Human Fetal Cortex. Int J Mol Sci. 2021 Sep 28;22(19):10457. doi: 10.3390/ijms221910457. PMID: 34638815; PMCID: PMC8508811.