

# Comparing Mouse and Human Synapses with Automated Probabilistic Synapse Analysis

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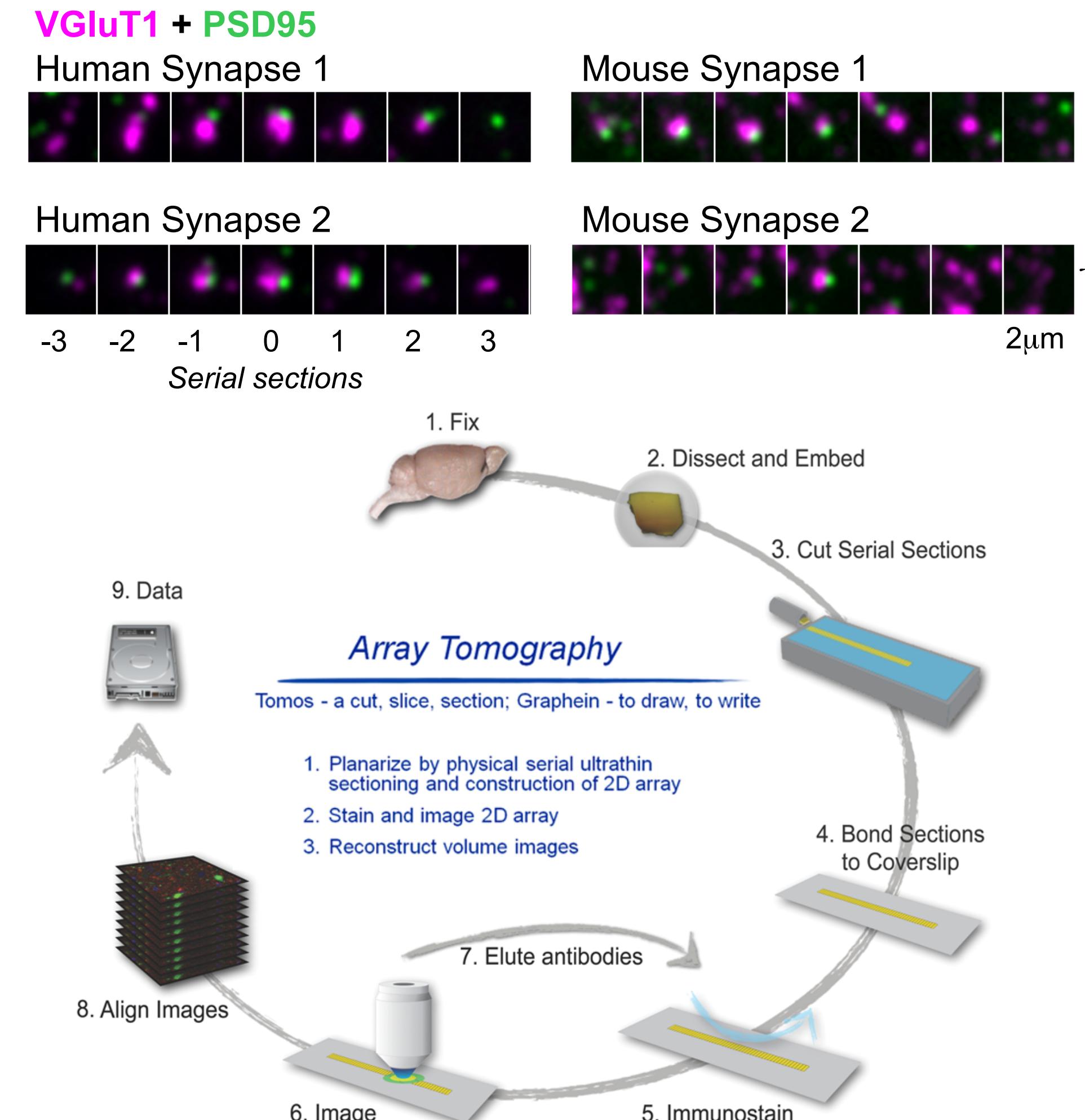
## Abstract

Mouse models are widely used in biomedical research, but do they provide a satisfactory model for *Homo sapiens*? Much of our current understanding of the molecular basis of neuropsychiatric diseases is based on studies in rodents, but surprisingly little is yet known about the similarities and differences between the synapses of mice and men, though this knowledge will be a crucial step toward developing new drugs directed at synaptopathies. The introduction of array tomography enables acquisition of hyperspectral proteomic data, allowing identification of multiple synapse subtypes in both mouse and human tissue, critical data that can allow this comparison. We had previously developed an automated query-defined probabilistic synapse detection algorithm and validated it in mouse brain tissue [1]. We now show that this algorithm performs equally well on human tissue obtained from brain surgeries, and use it to quantify similarities and differences between human and mouse synapses, with a focus first on excitatory glutamatergic synapses in neocortex. Our results show that excitatory synapse sizes and densities differ between mouse and human neocortex, with human synapses being larger and sparser. However, many of the correlations between the size of synapse postsynaptic densities and their AMPA and NMDA receptor content, previously documented in rodents, also hold true for human cortical synapses. We further refine this comparison by including variables such as the type of vesicular glutamate transporter present in the presynaptic bouton, the abundance of mitochondria, and the type of postsynaptic target.

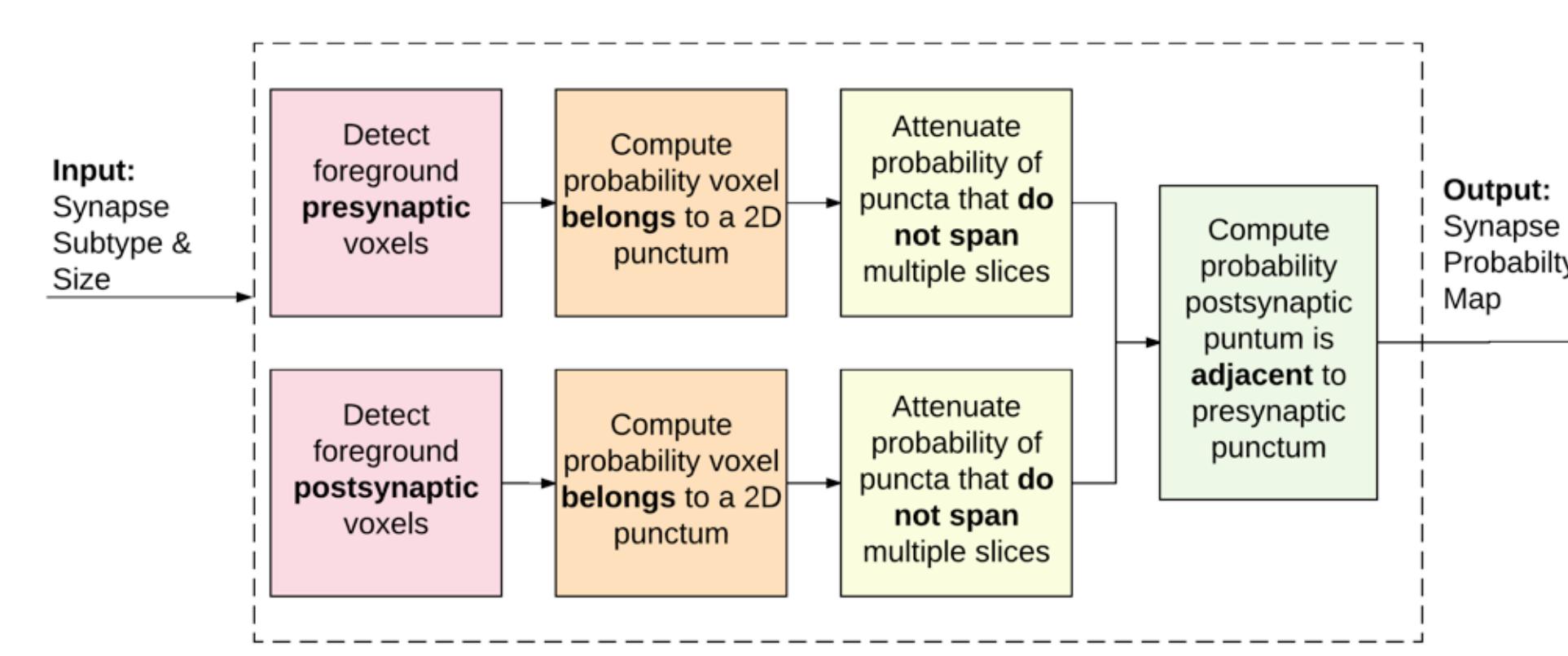
This computational approach opens a door to thorough comparison between human and animal model synapses, as well as to a data-driven discovery of novel synaptic arrangements in human brain. The methods developed for this application are readily applicable to other datasets. All data, code, and data derivatives will be made available after publication.

## Methods & Materials

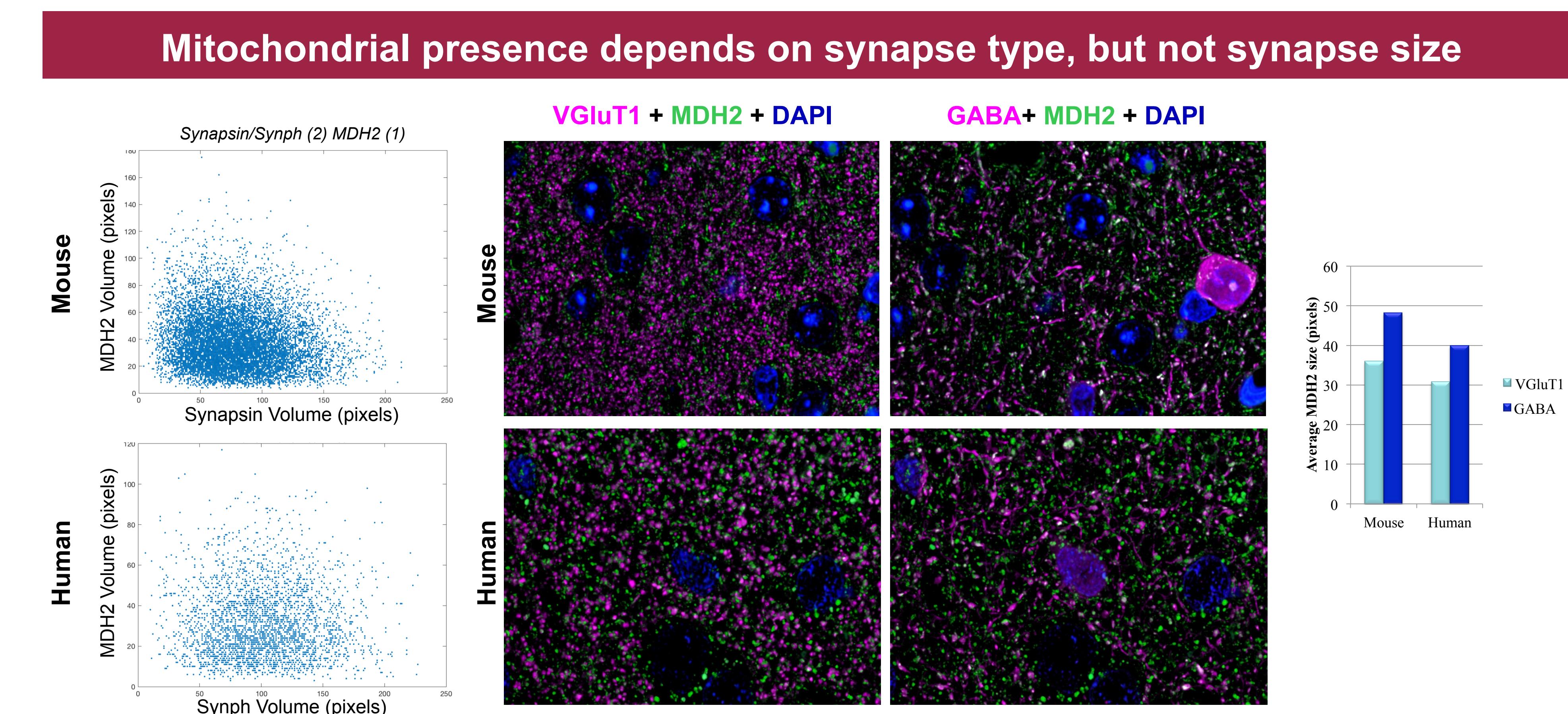
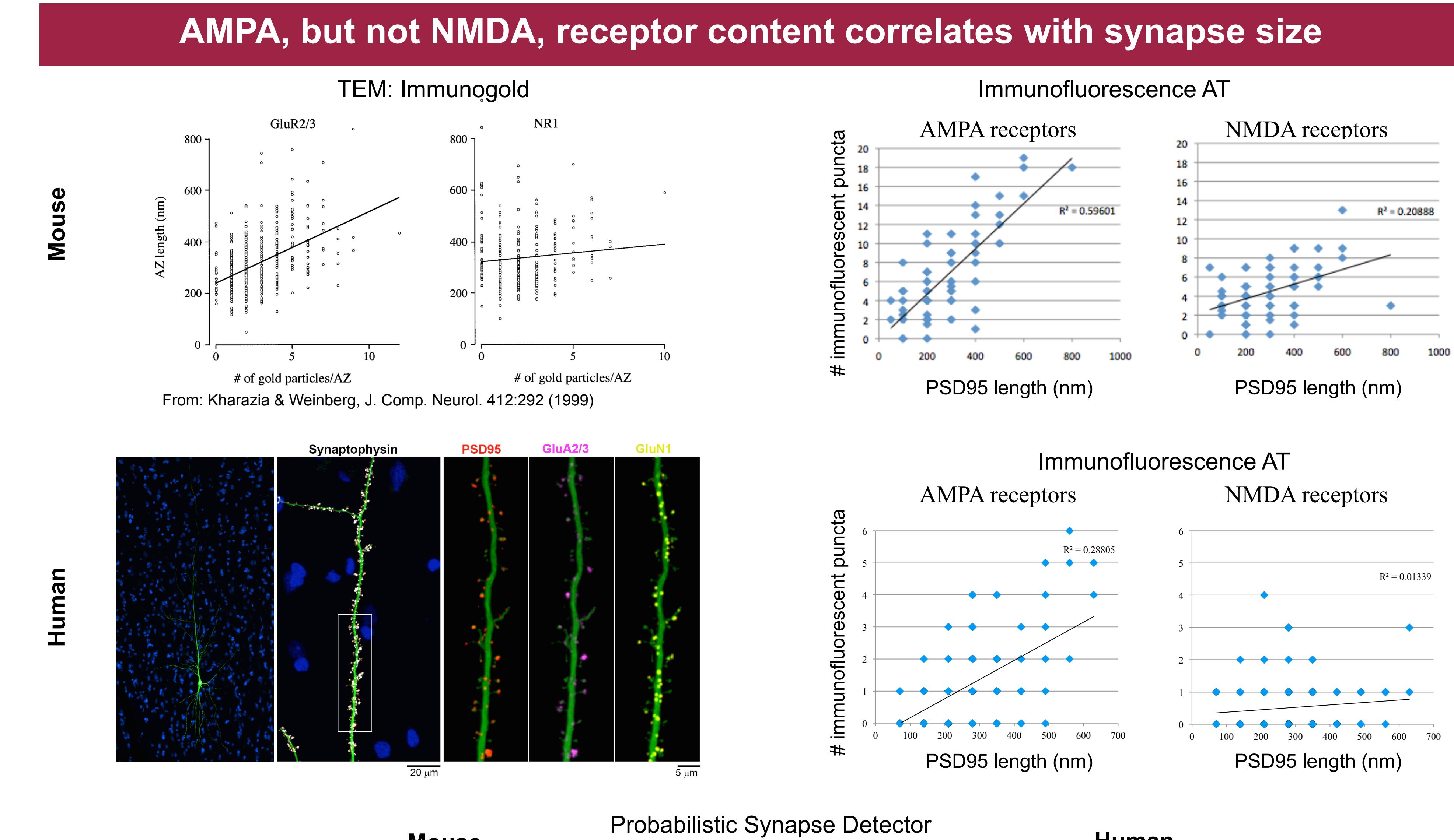
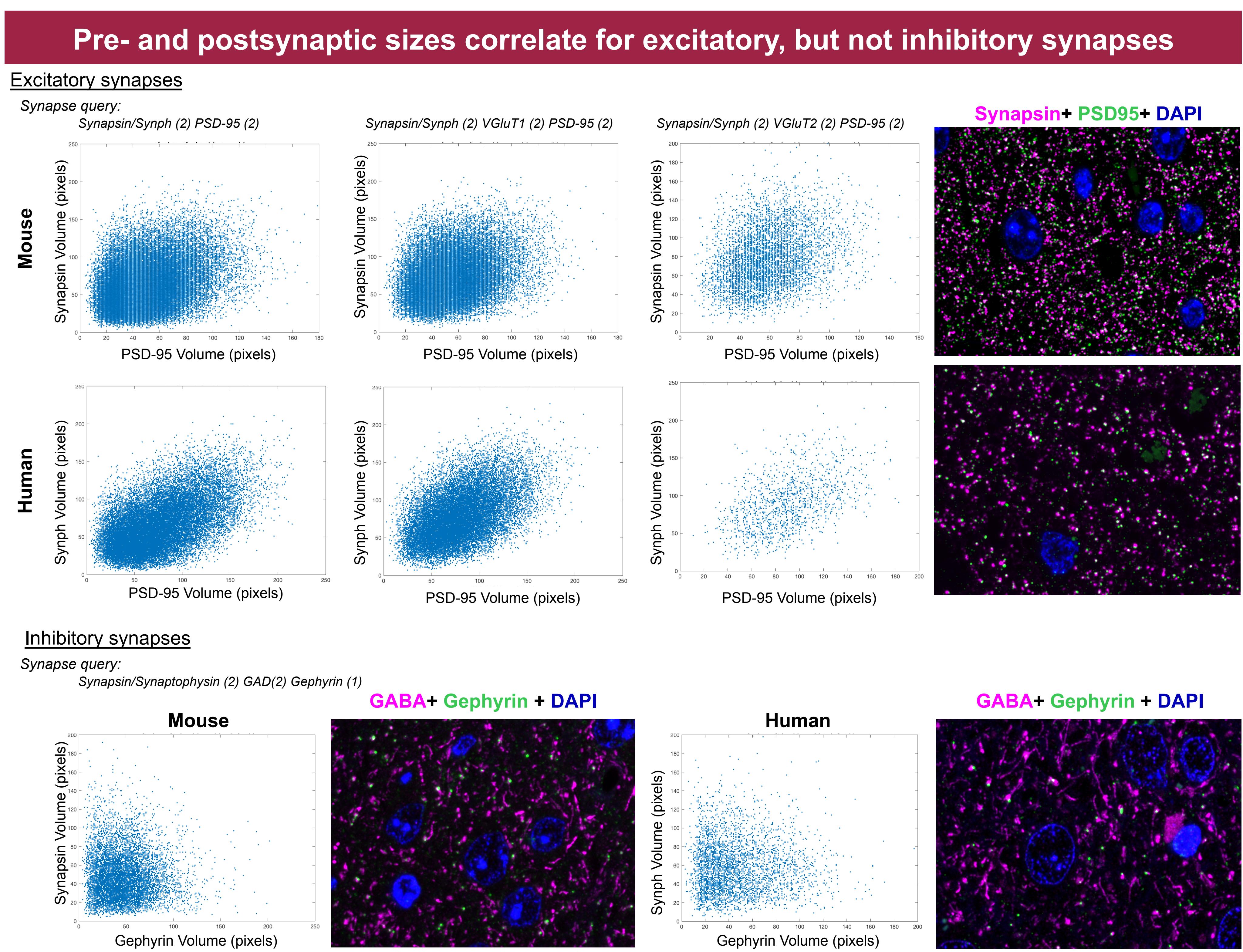
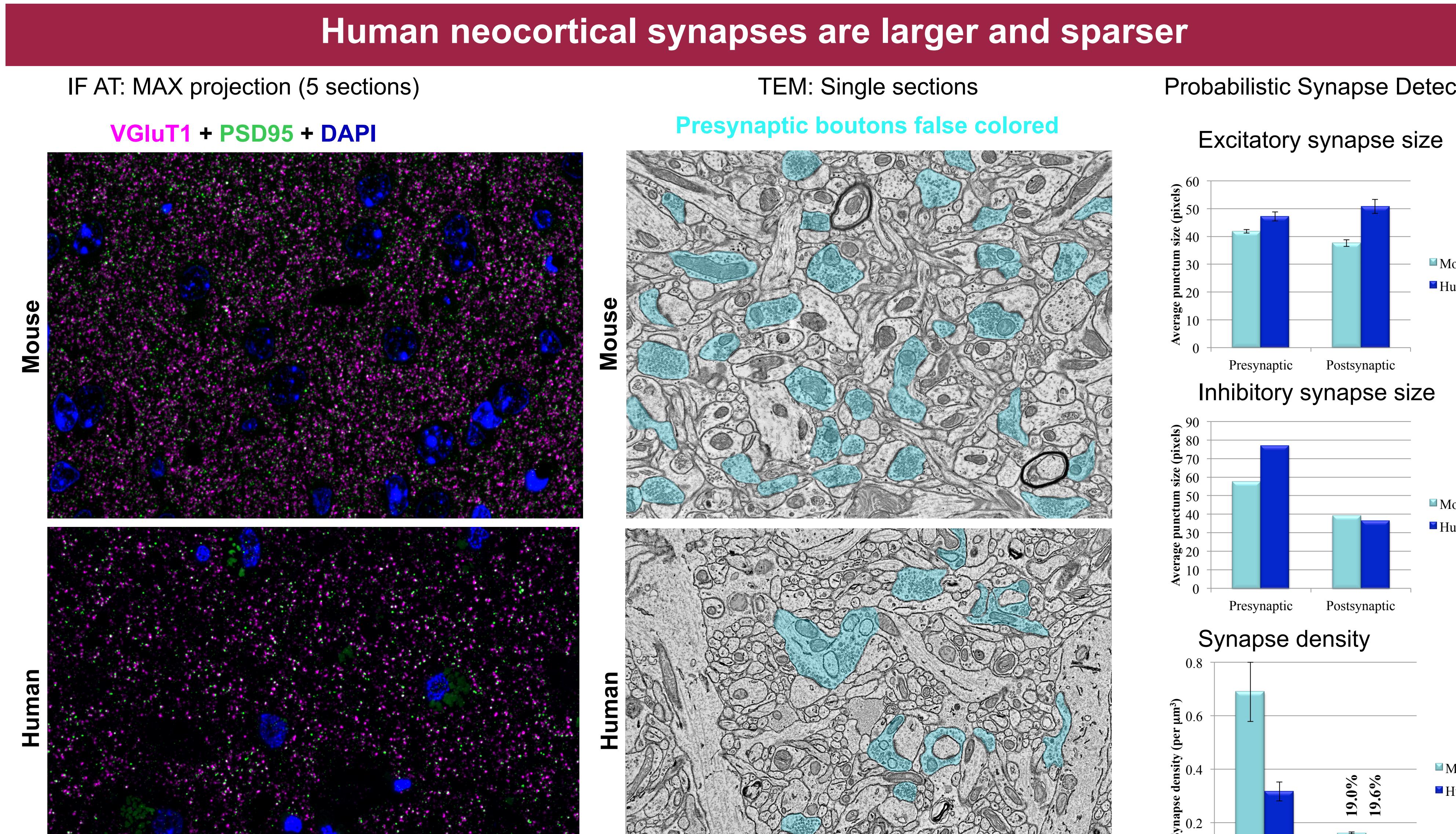
### Array Tomography



### Probabilistic Synapse Analysis



Simhal, Anish K., et al. "Probabilistic Fluorescence-Based Synapse Detection." PLoS Computational Biology, May 2017



## Acknowledgements

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