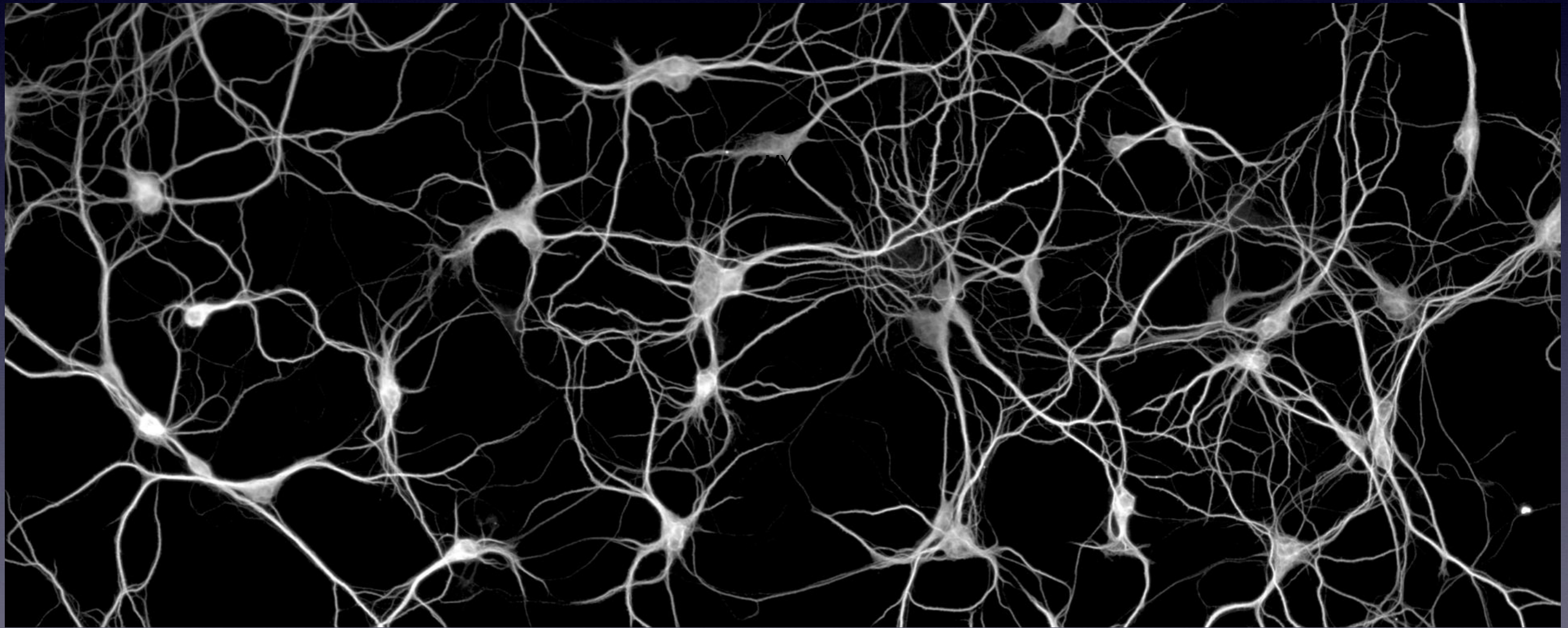


Long Lasting Proteins Long Lasting Memories

Richard L. Huganir
Department of Neuroscience
Kavli Neuroscience Discovery Institute
Johns Hopkins University School of Medicine



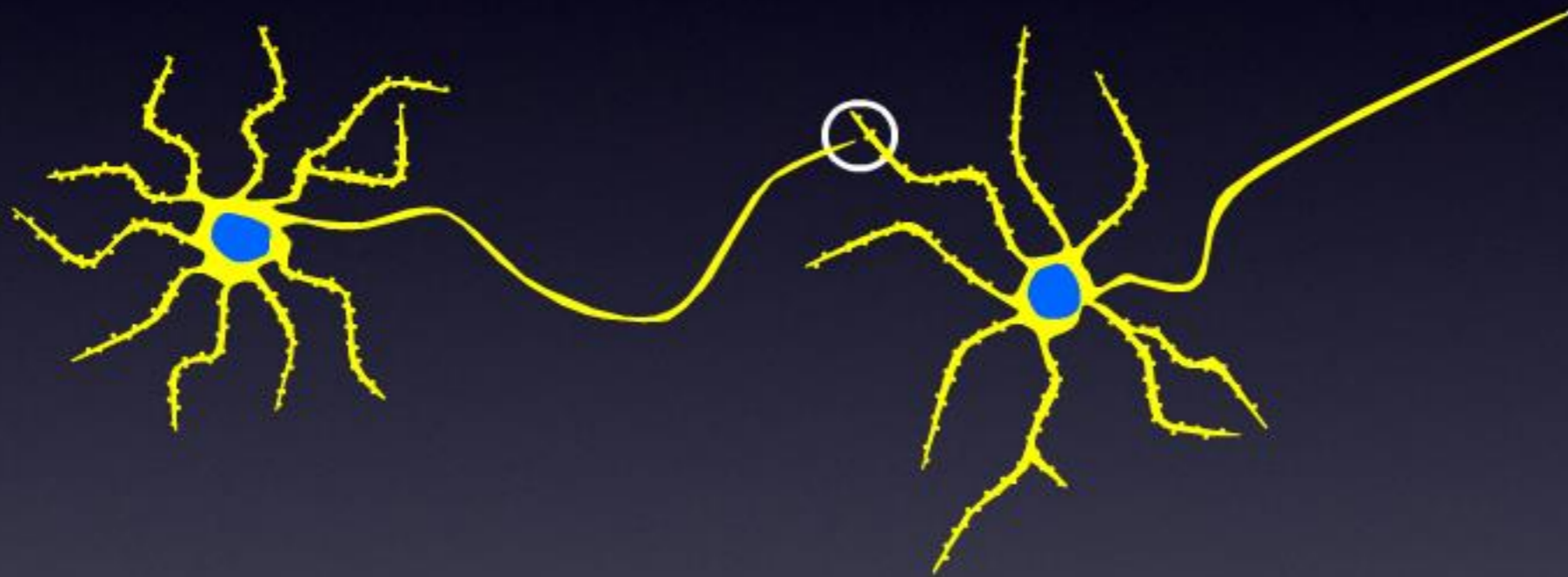
The Brain is a Network of 100 Billion Neurons



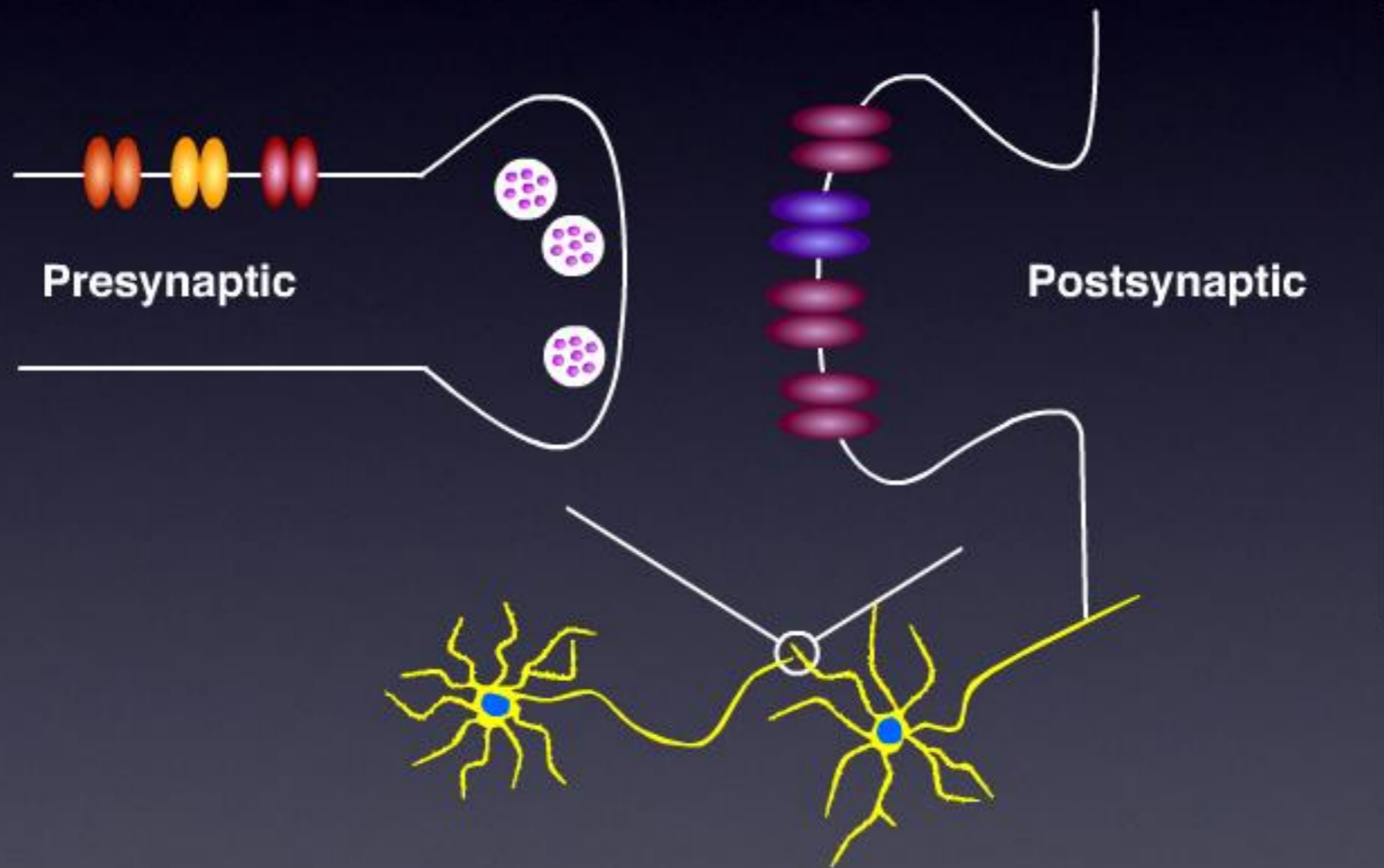
The Brain is a Network of 100 Billion Neurons that Form Millions of Neuronal Circuits



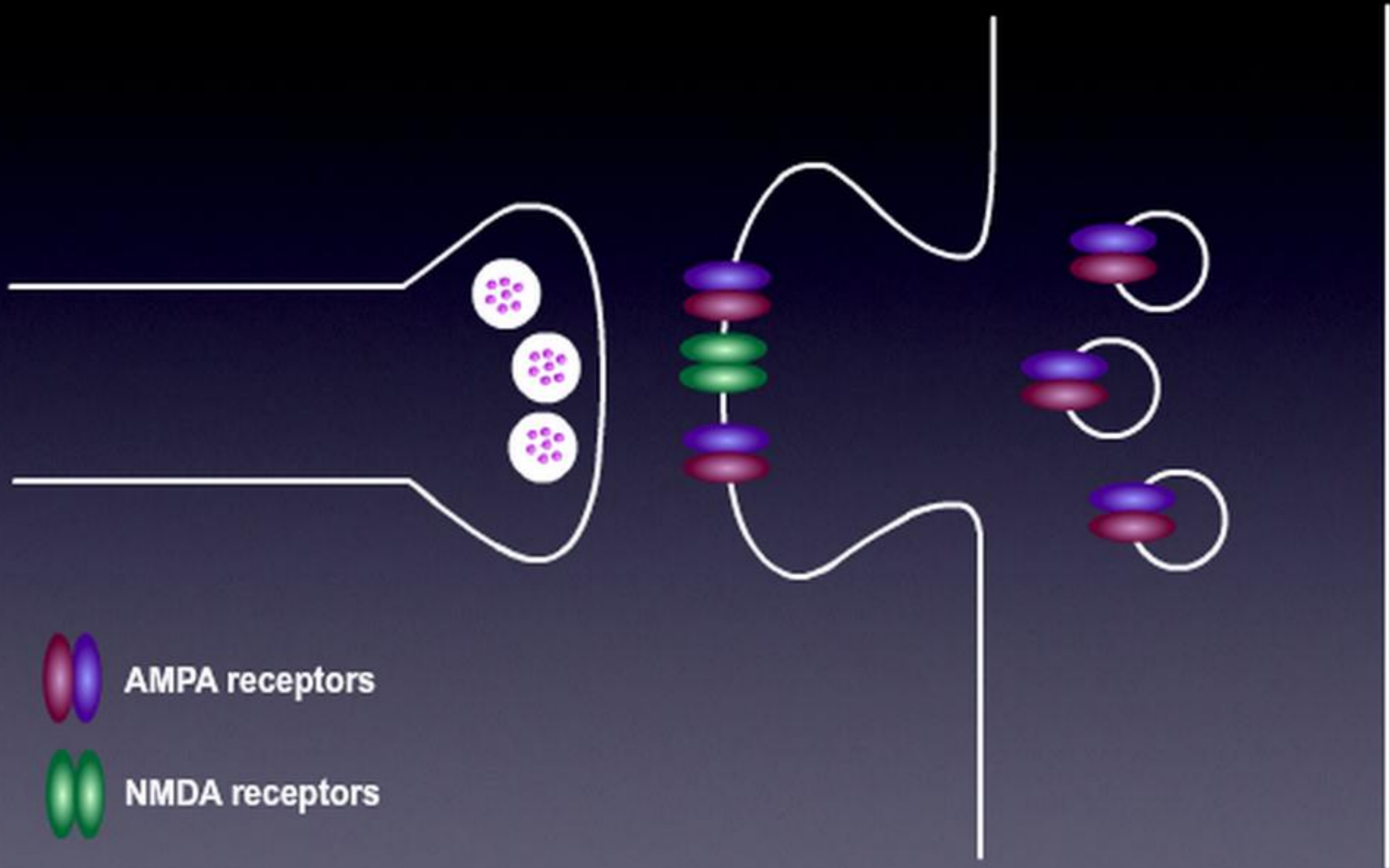
The Brain has Quadrillions of Synapses



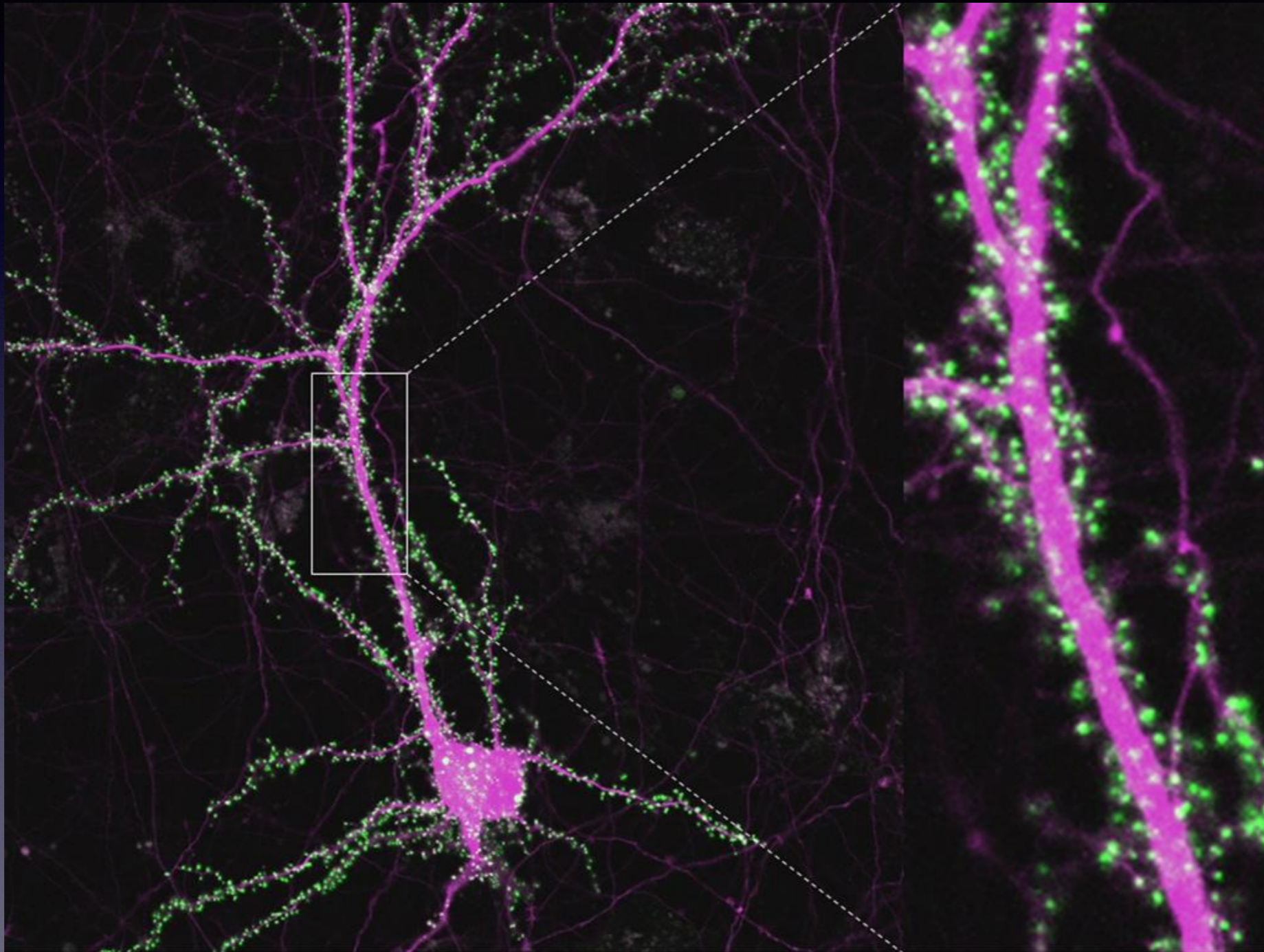
Synaptic Transmission



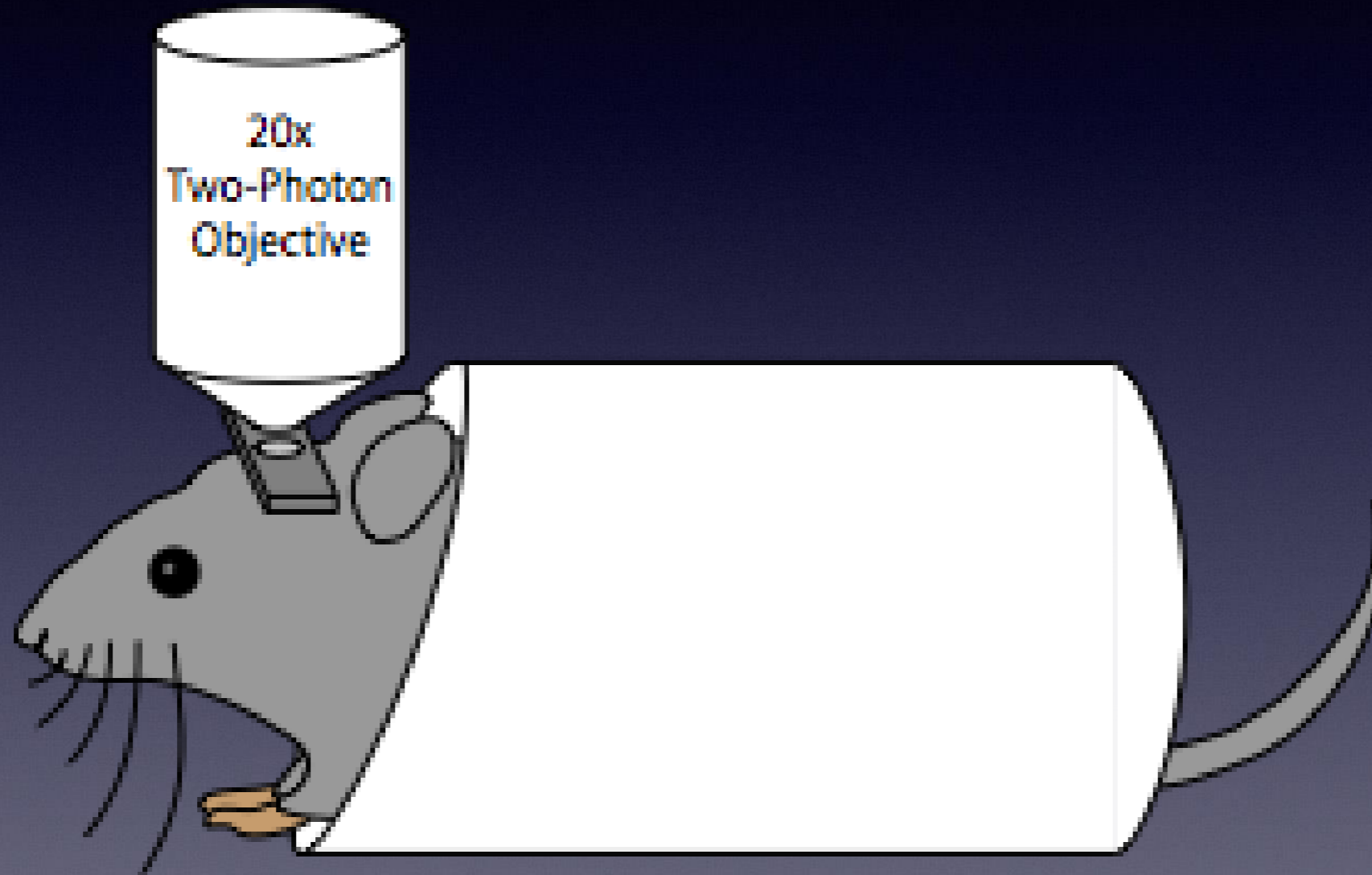
Long-Term Potentiation: Learning and Memory



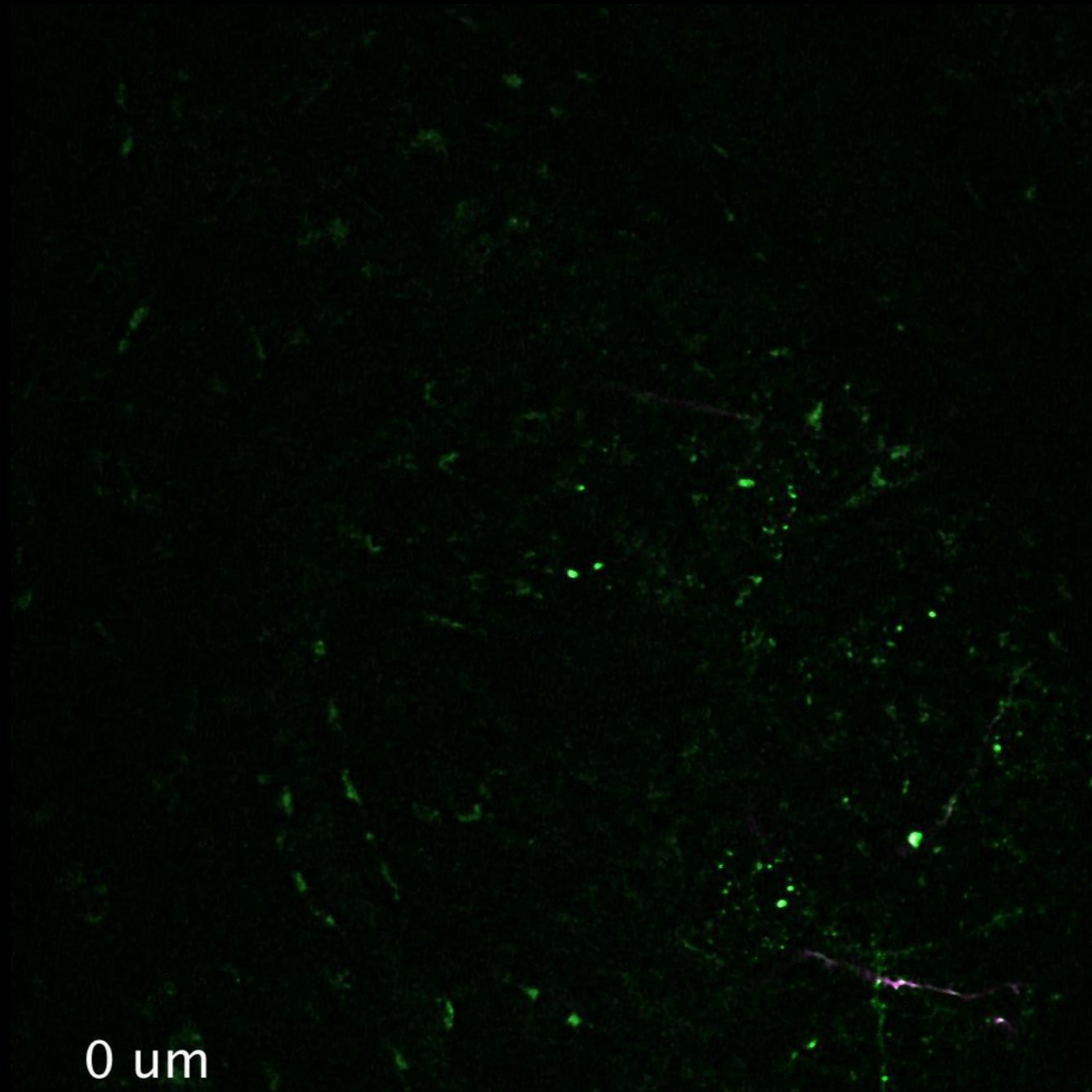
Visualizing Receptors in Neurons in a Dish



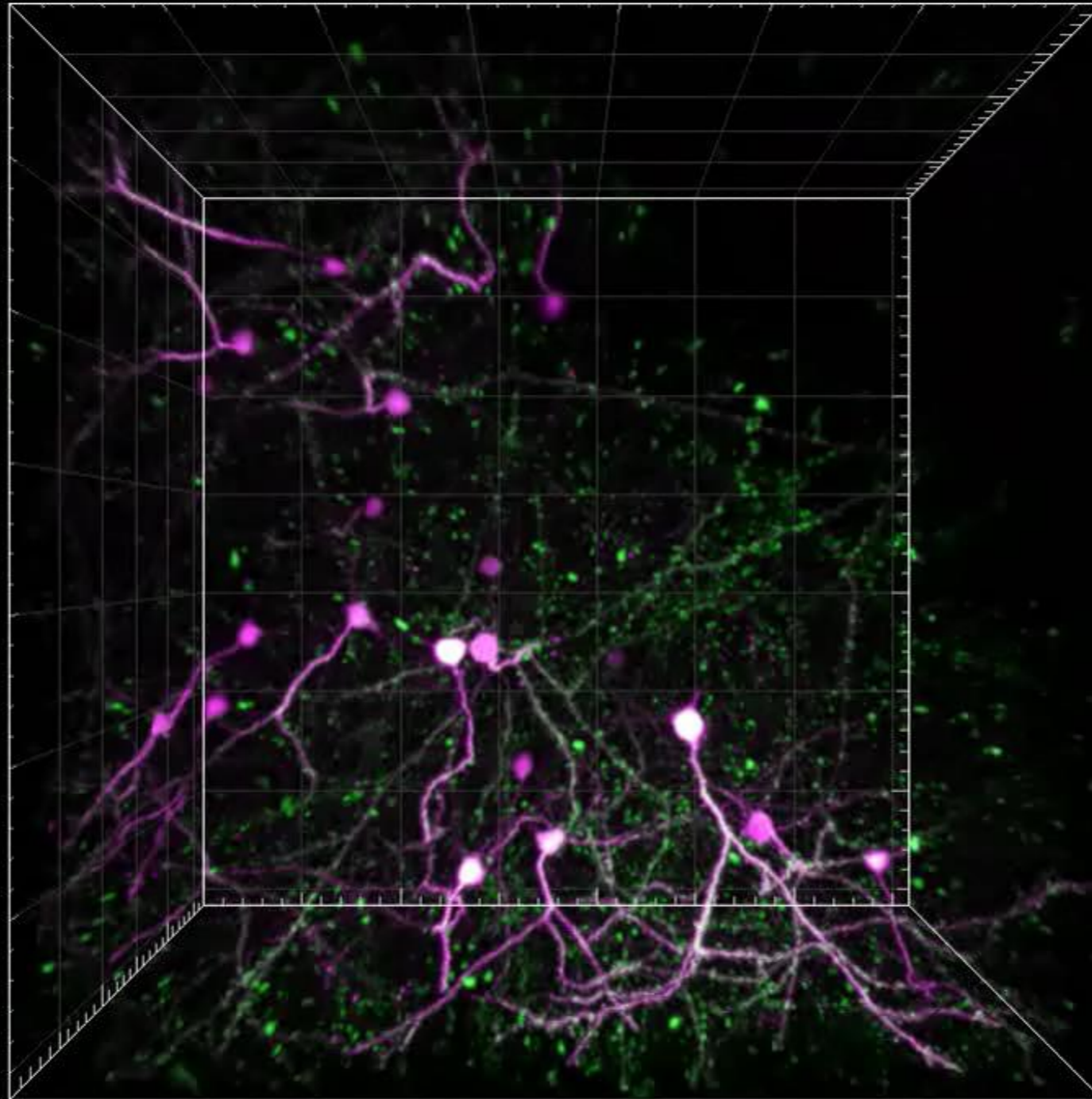
Visualizing Receptors in Neurons in a Live Mouse



Visualizing Receptors in Neurons in a Live Mouse



Visualizing Receptors in Neurons in a Live Mouse

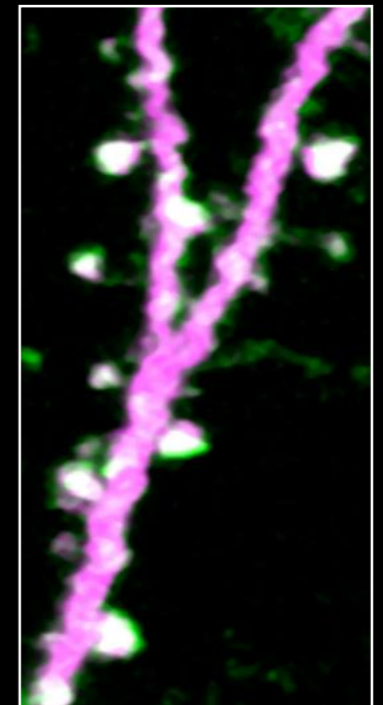
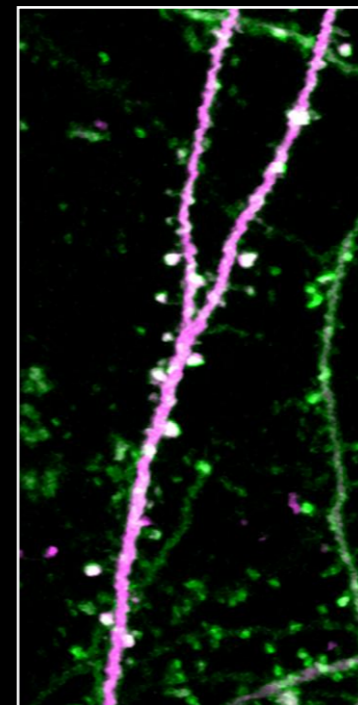
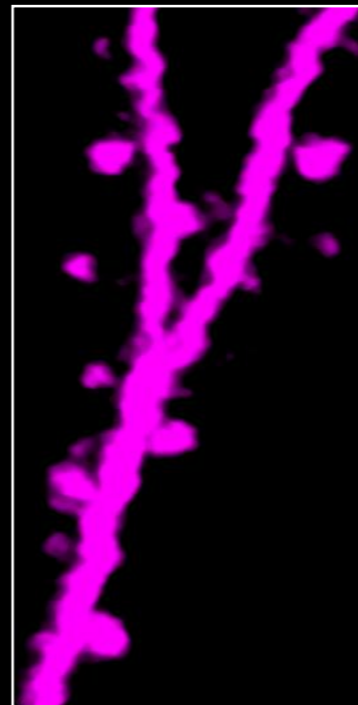
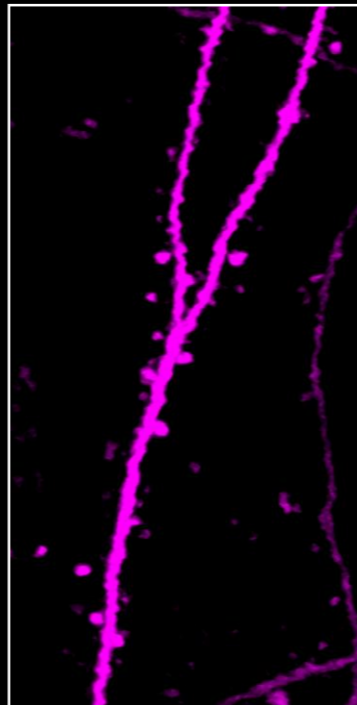
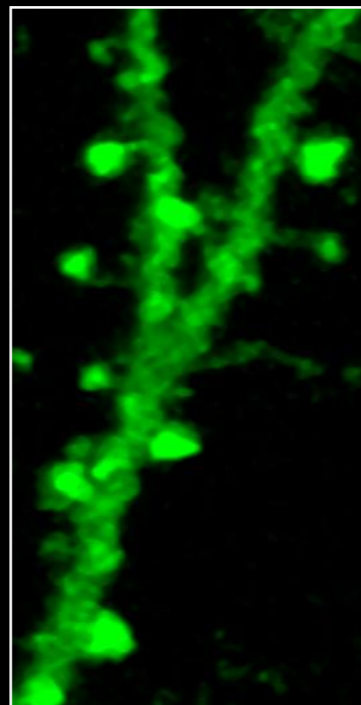
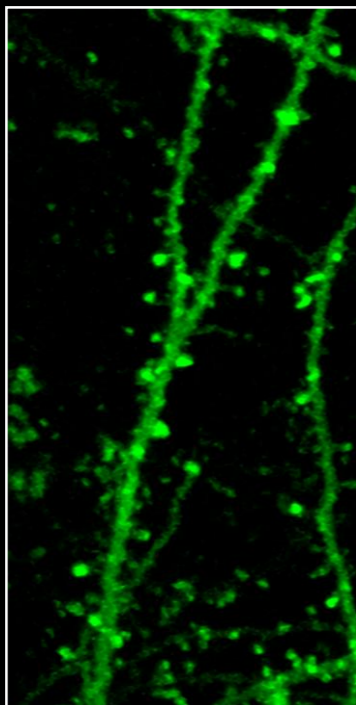
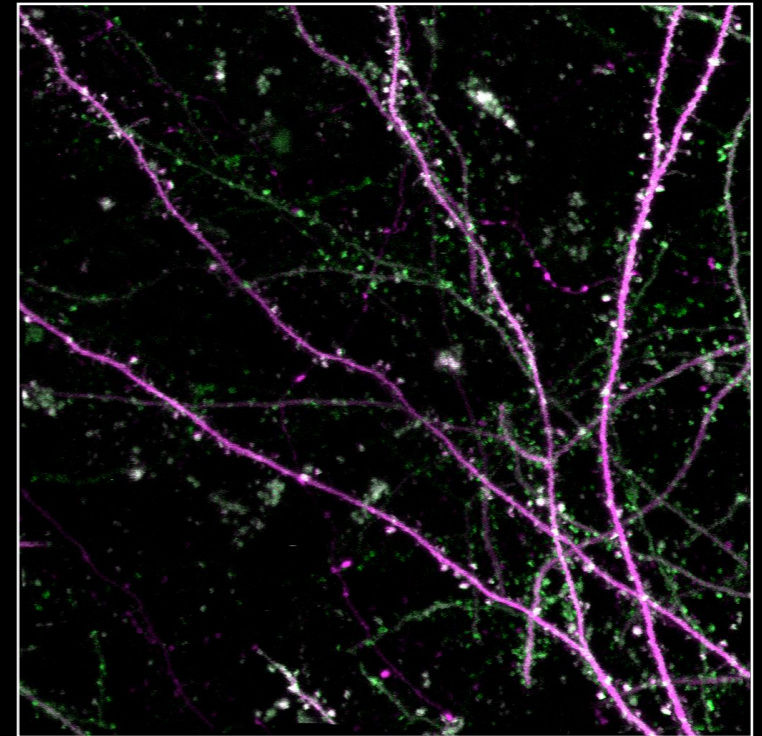
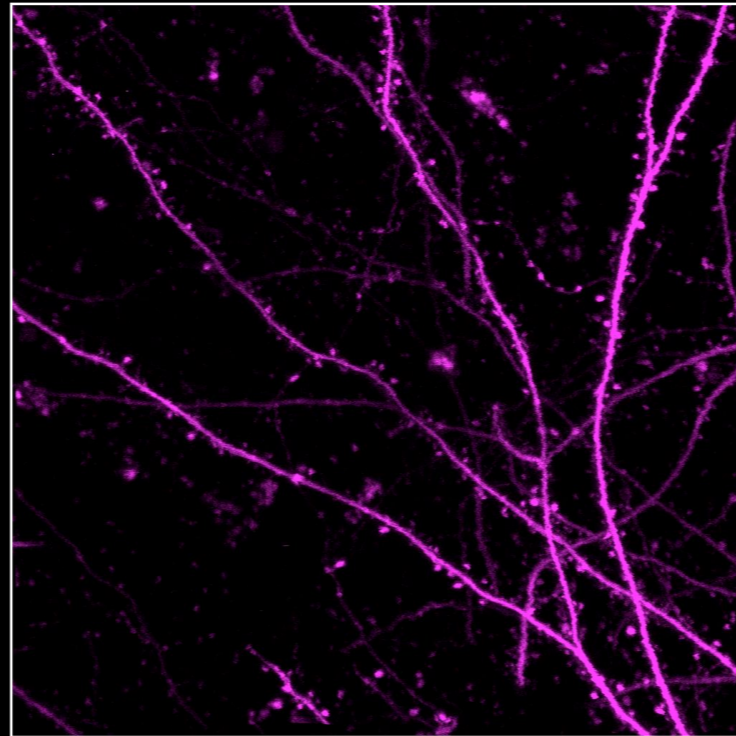
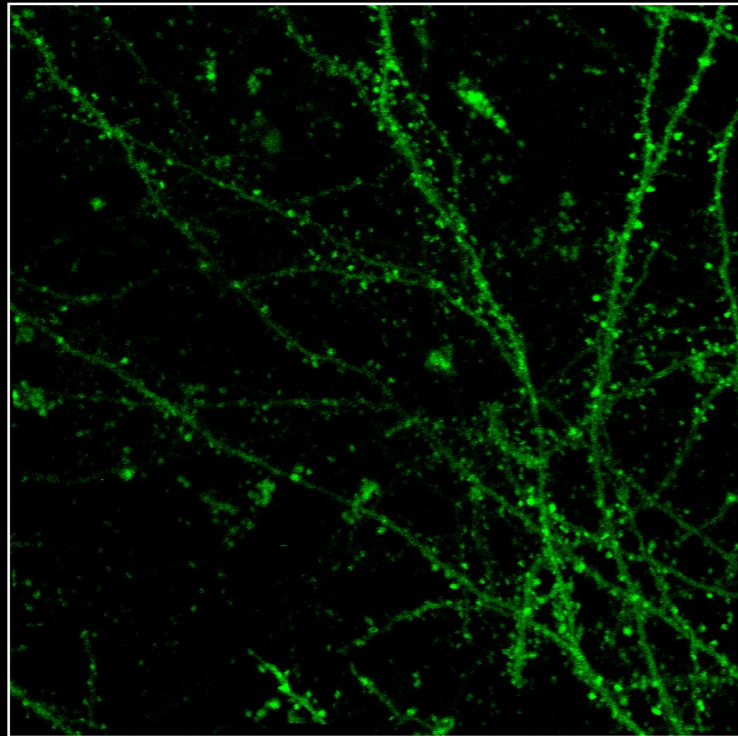


Visualizing Receptors in Neurons in a Live Mouse

Receptors

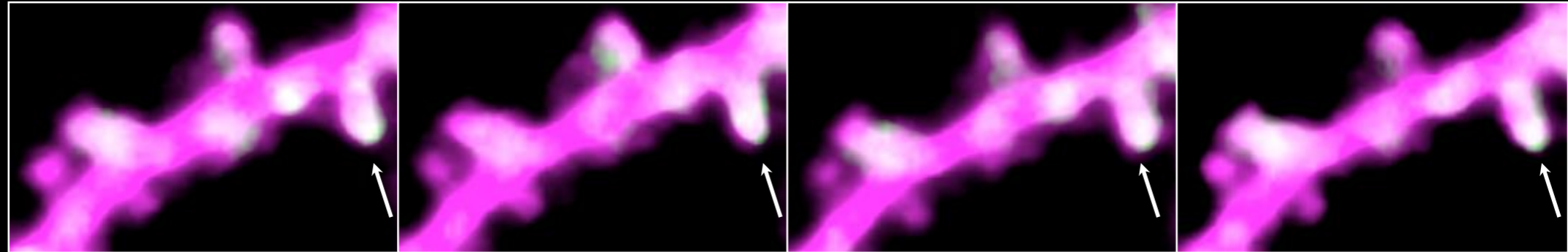
Structure

Merged

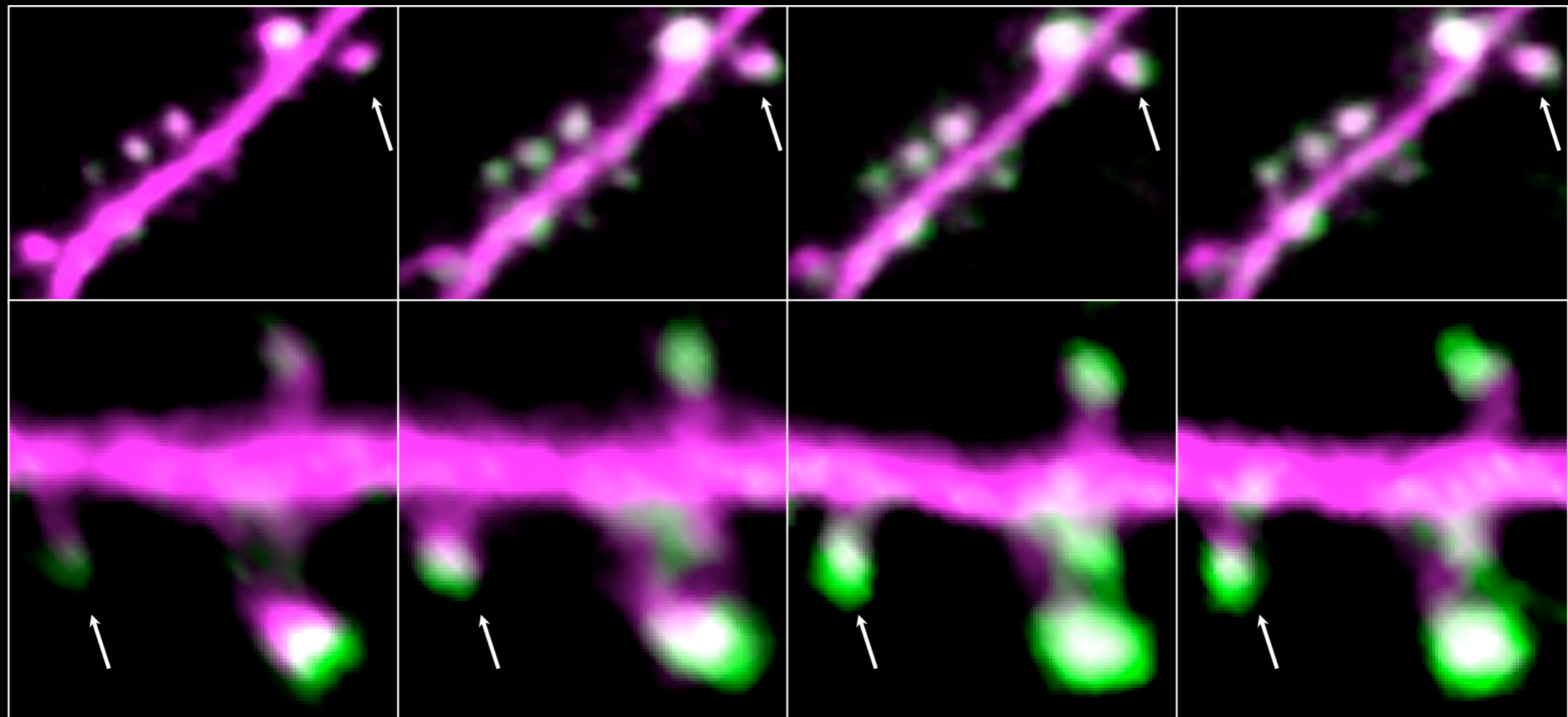


Visualizing Long Term Potentiation in a Live Mouse

Control



Learning



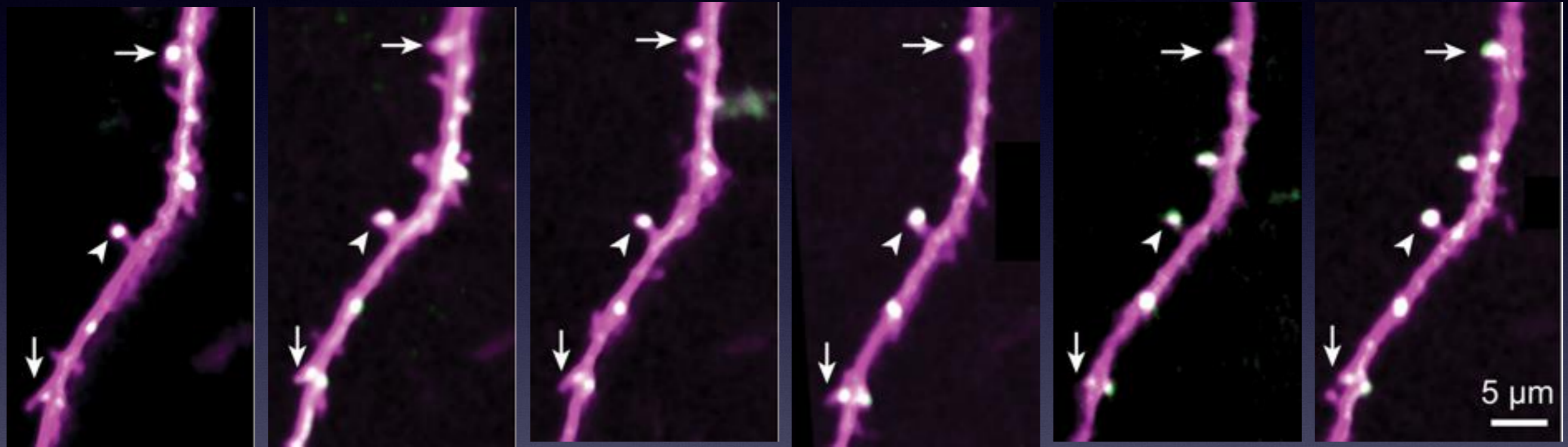
0 hour

1 hour

2 hour

3 hour

Visualizing Stable Strong Synapses in a Live Mouse



Day 1

Day 4

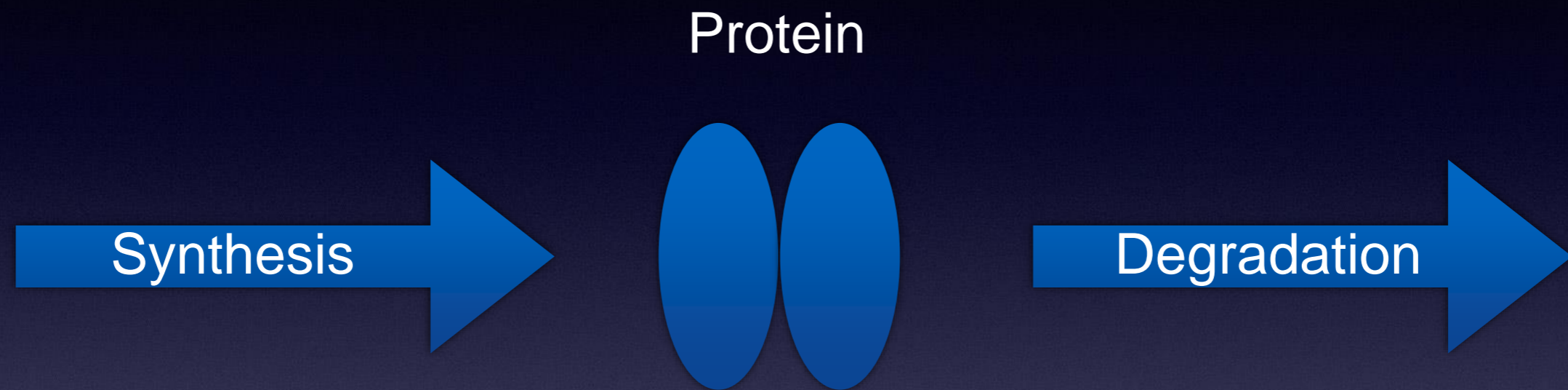
Day 7

Day 14

Day 14

Day 28

Protein Stability is Determined by Degradation Rate

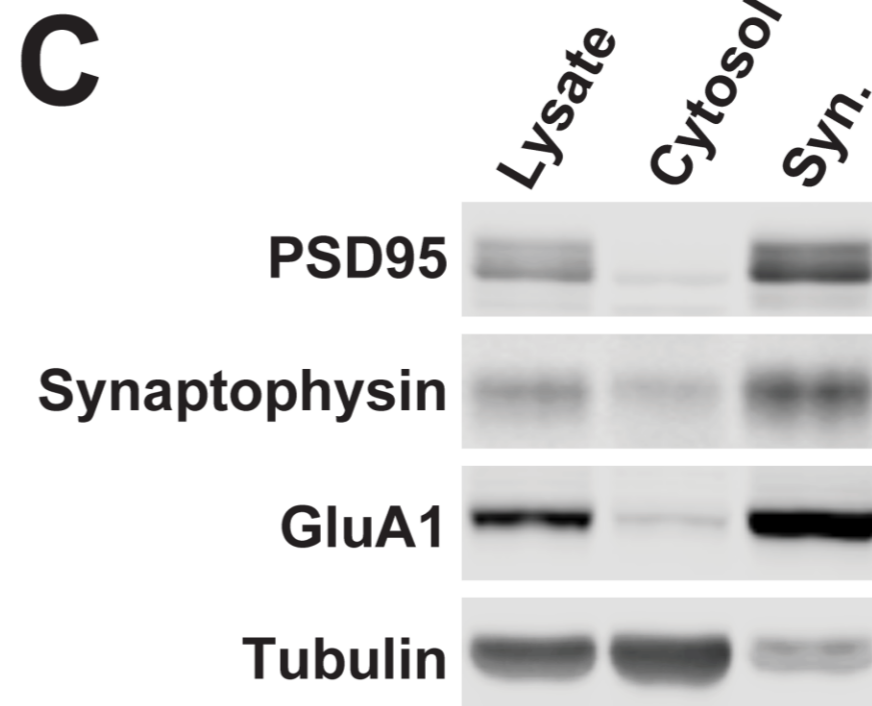
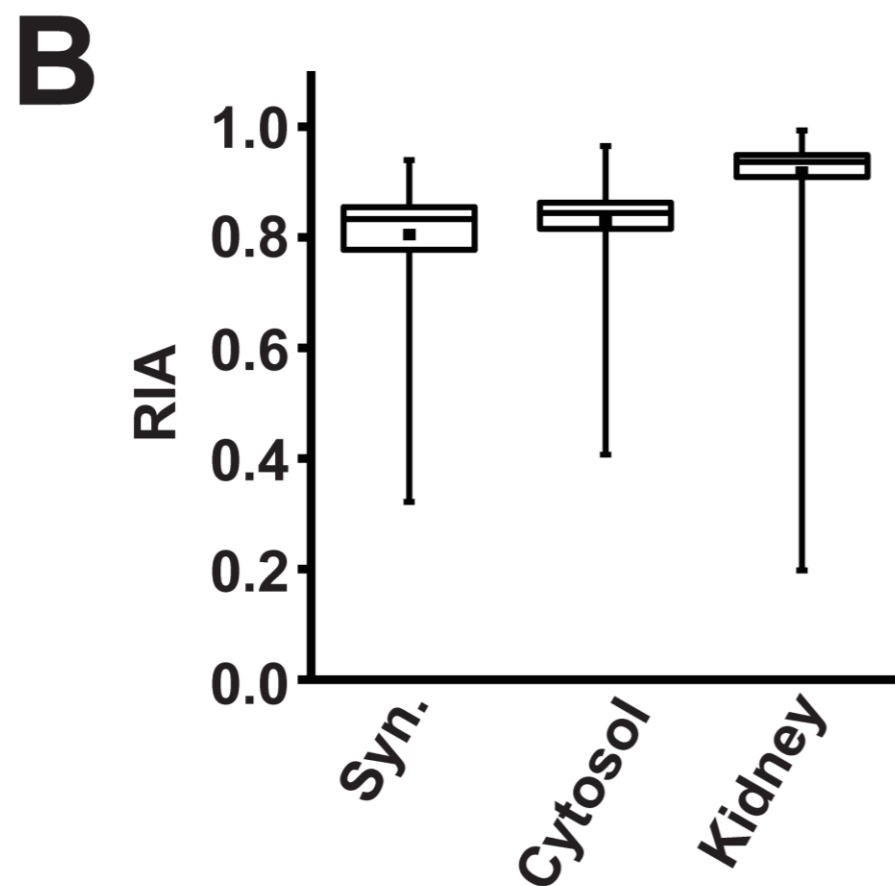
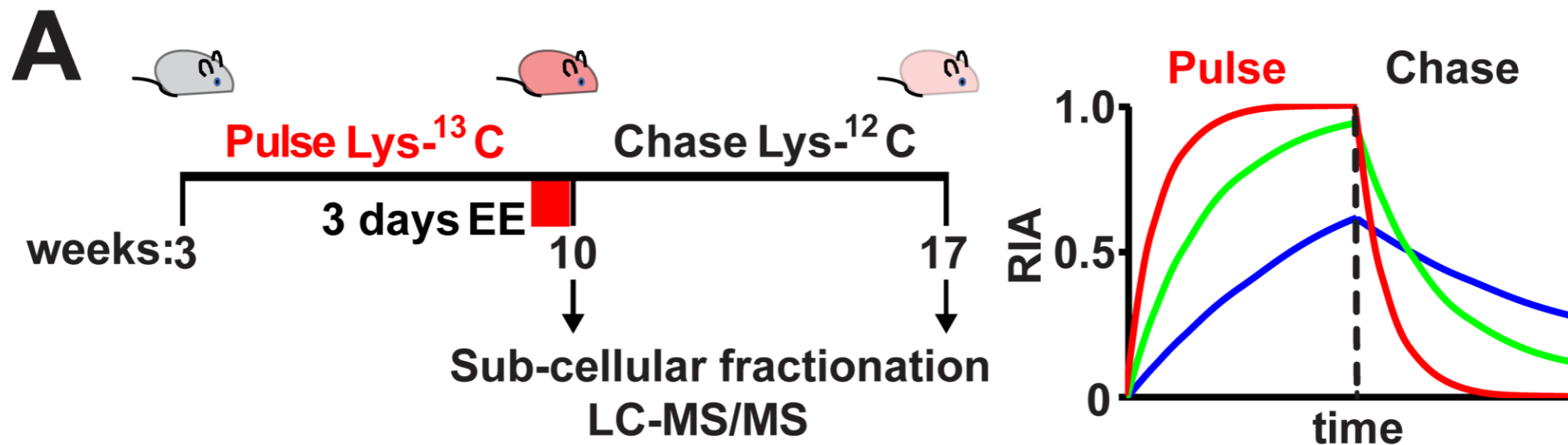


Most Proteins last 1-7 days

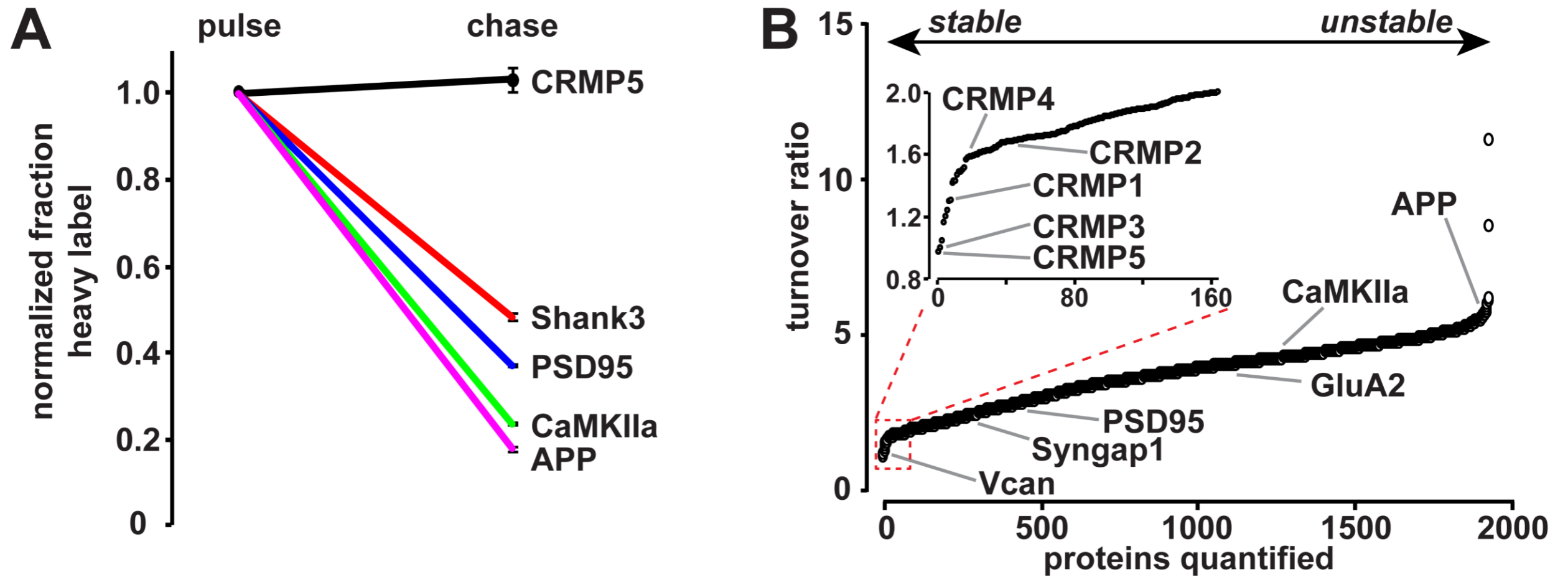
Collagen (cartilage) and Crystallin (eye lens) last decades ~ 100 years

Are there Long Lived Proteins in Synapses?

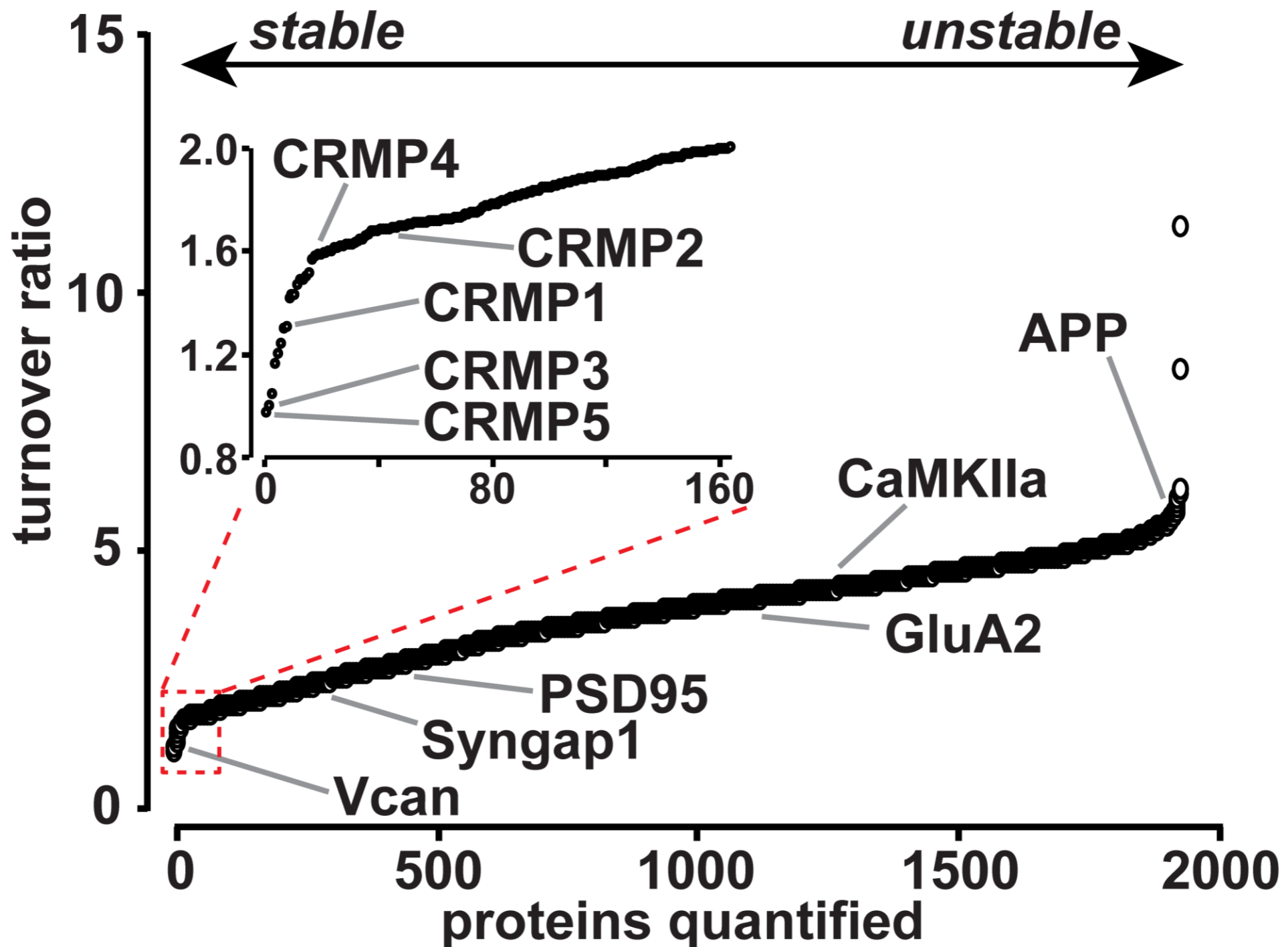
Stable Isotope Labeling in Mice: SILAM



Pulse/Chase Heavy and Light Isotope Abundance is Used to Measure Protein Turnover



Pulse/Chase Heavy and Light Isotope Abundance is Used to Measure Protein Turnover



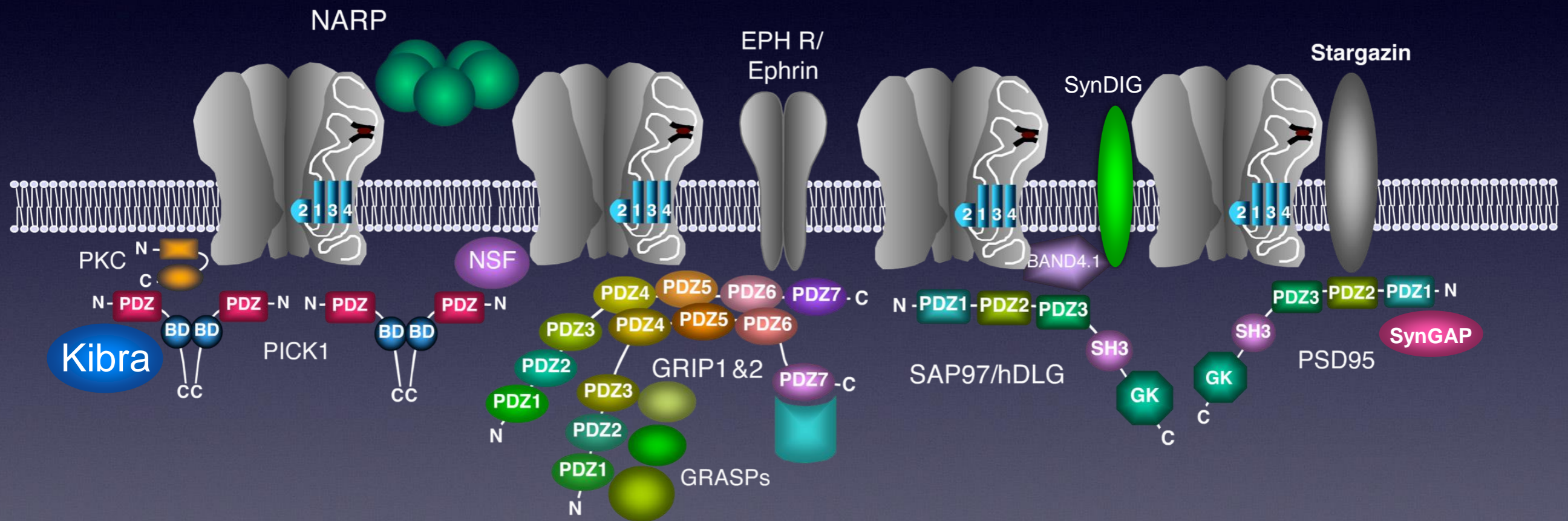
What Happens to Long Lived Proteins Over Time?



Osteoarthritis

Does Damage to Synaptic Long Lived Proteins
Contribute to Age Related Memory Disorders?

Regulation of Receptors and Cognitive Function



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