

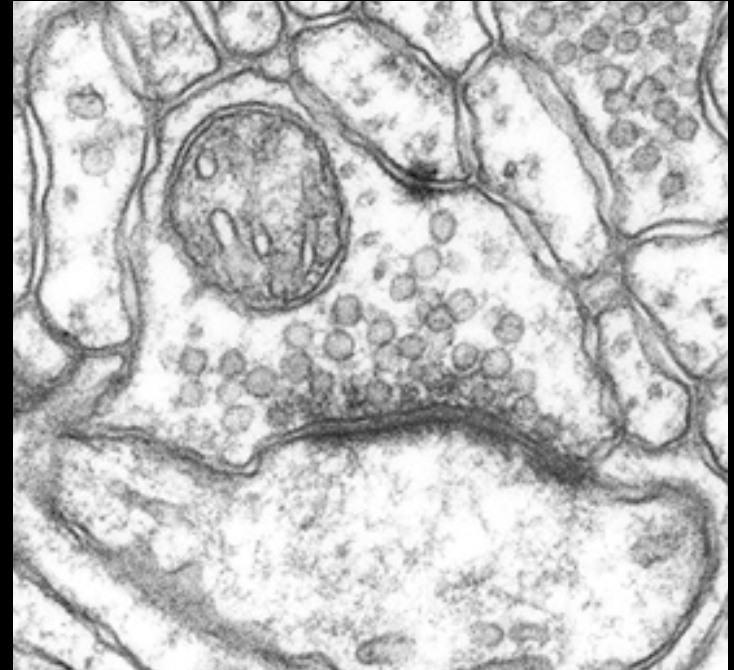
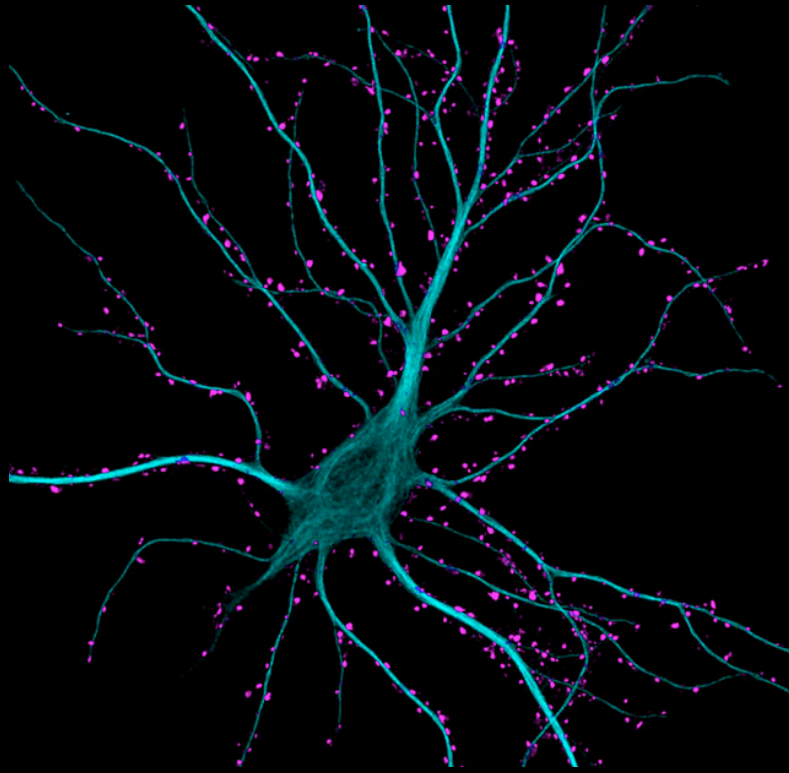
Building Synaptic Connections to Support Neuron to Muscle Signaling



Troy Littleton

The Picower Institute for Learning & Memory, MIT

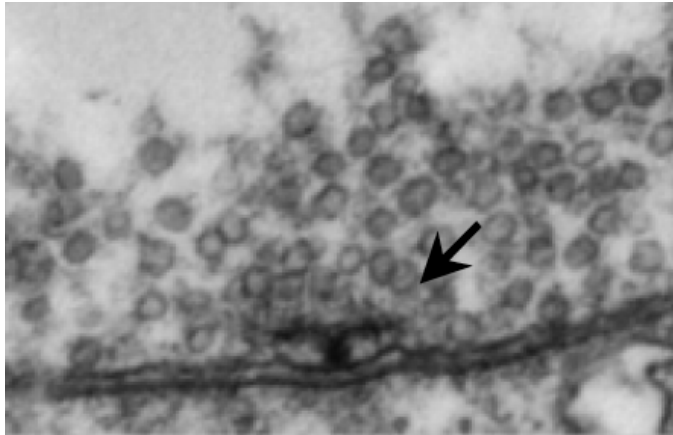
Synaptic Vesicle Fusion Drives Neuronal Communication



Synaptic Vesicle Fusion Occurs at Active Zones

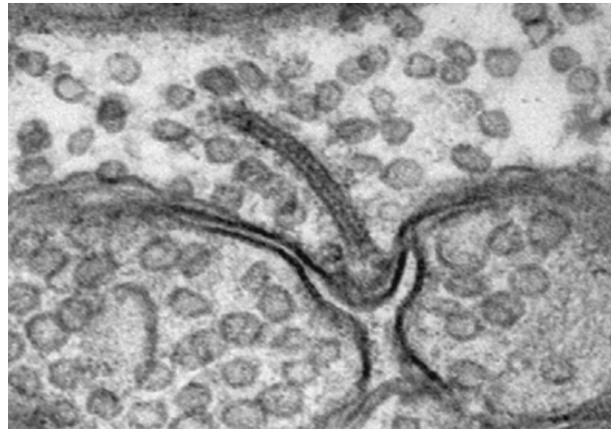
T-BAR STRUCTURE

Neuromuscular junction (NMJ)
D.melanogaster



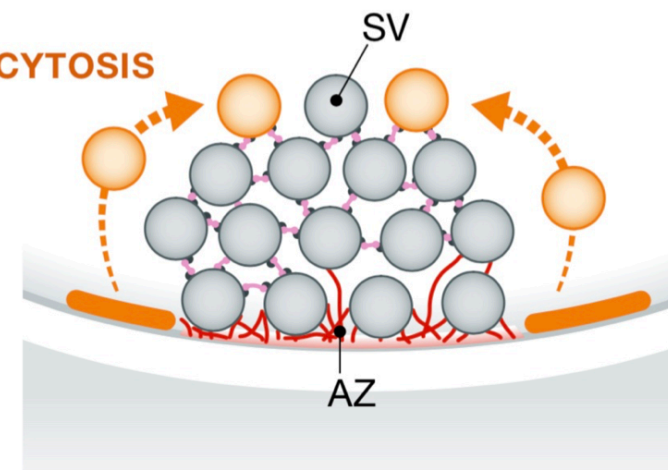
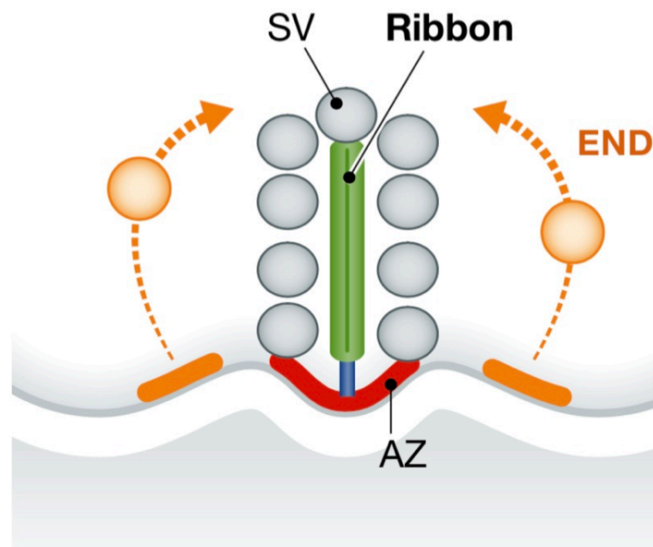
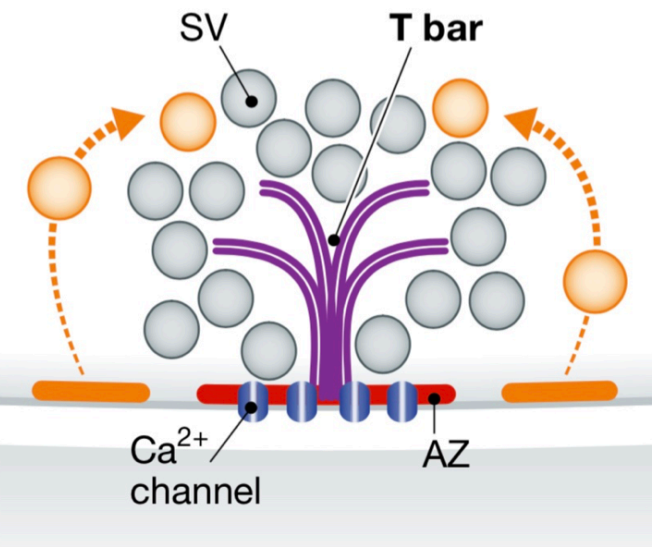
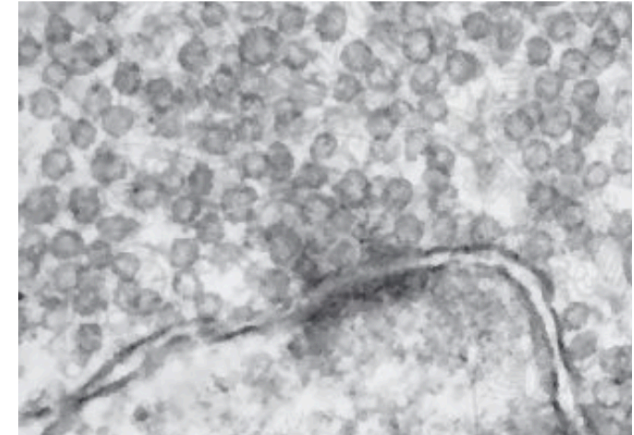
RIBBON SYNAPSE

Vertebrate photoreceptor cell
ribbon synapse

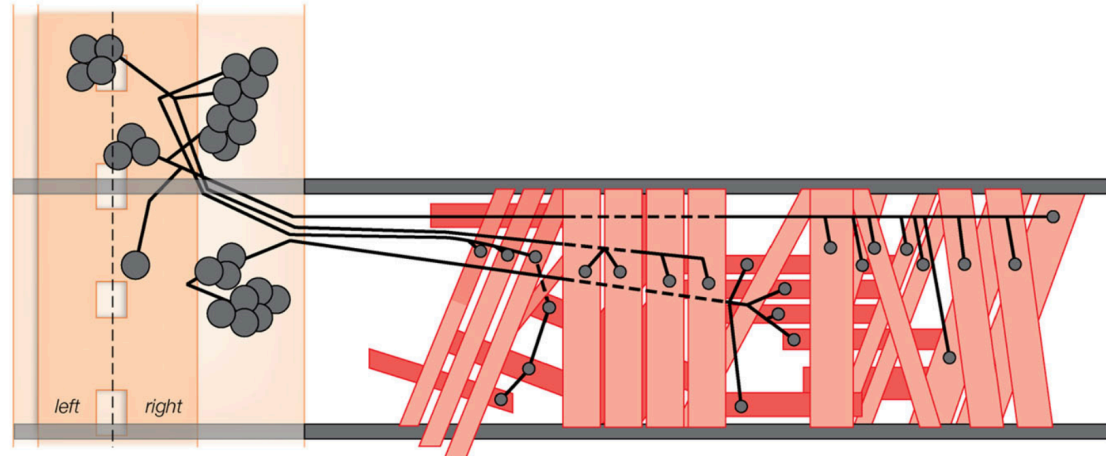
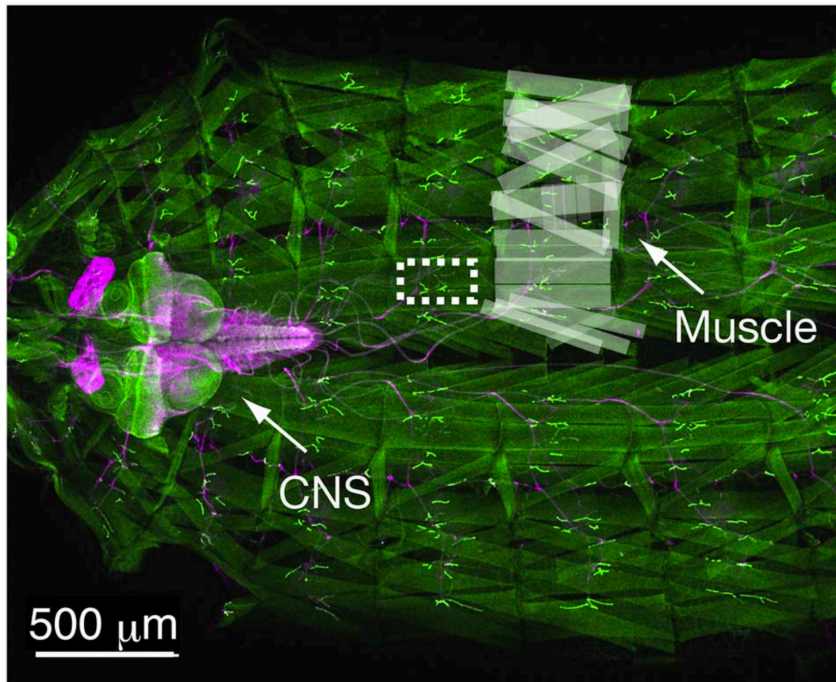
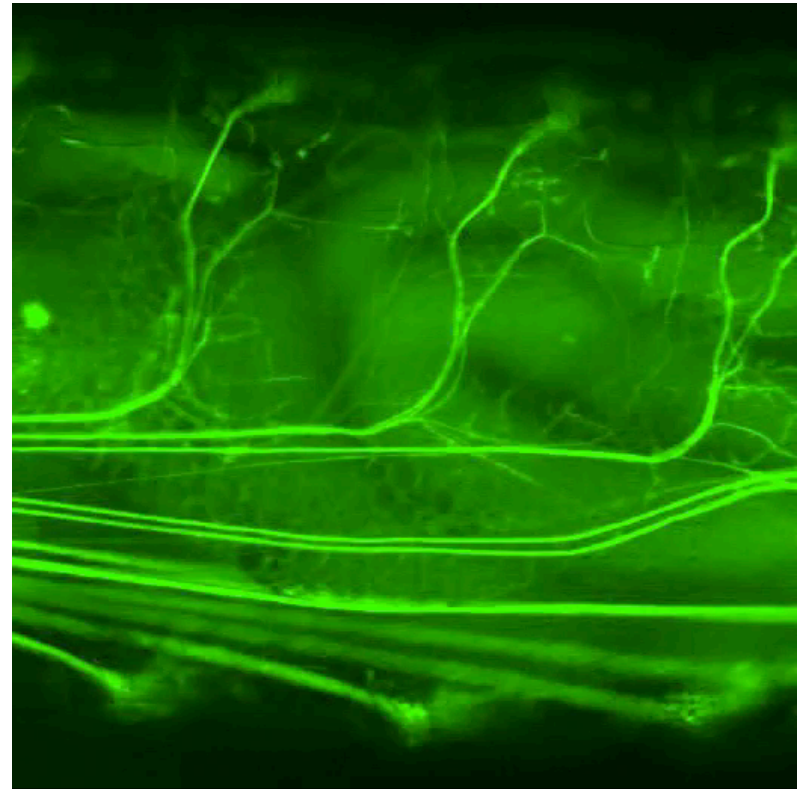
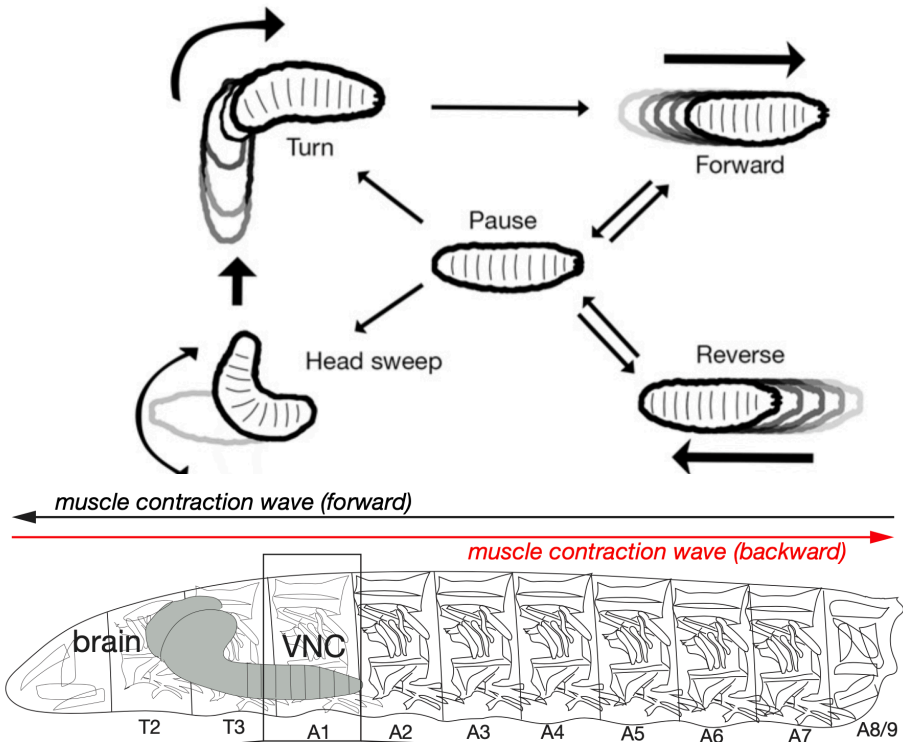


CENTRAL SYNAPSE

Vertebrate

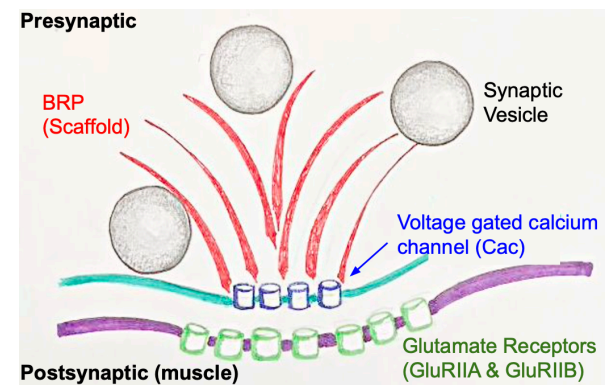
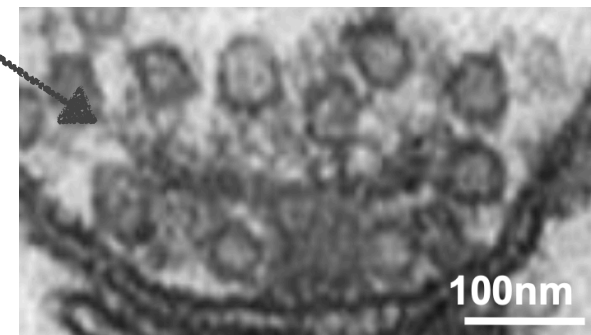
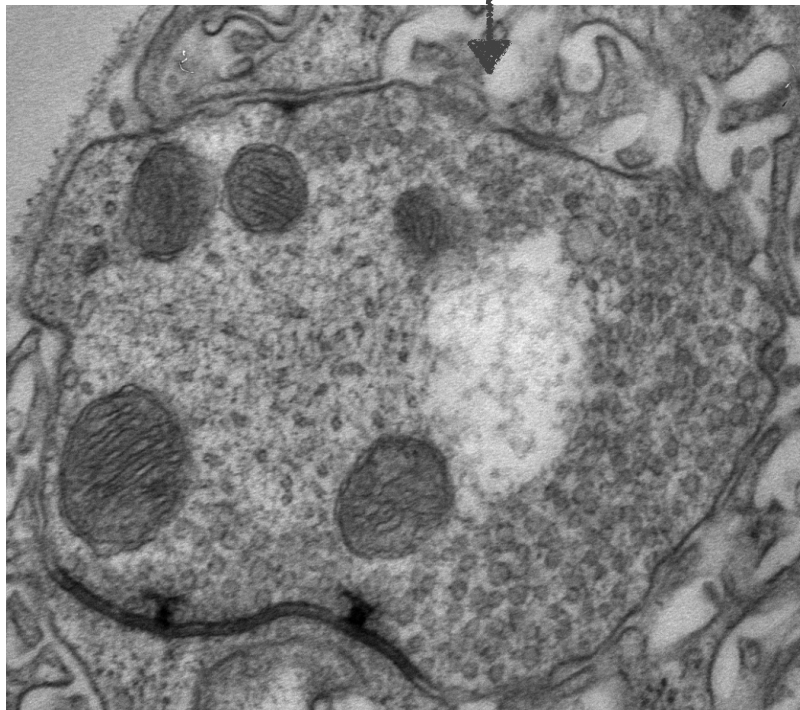
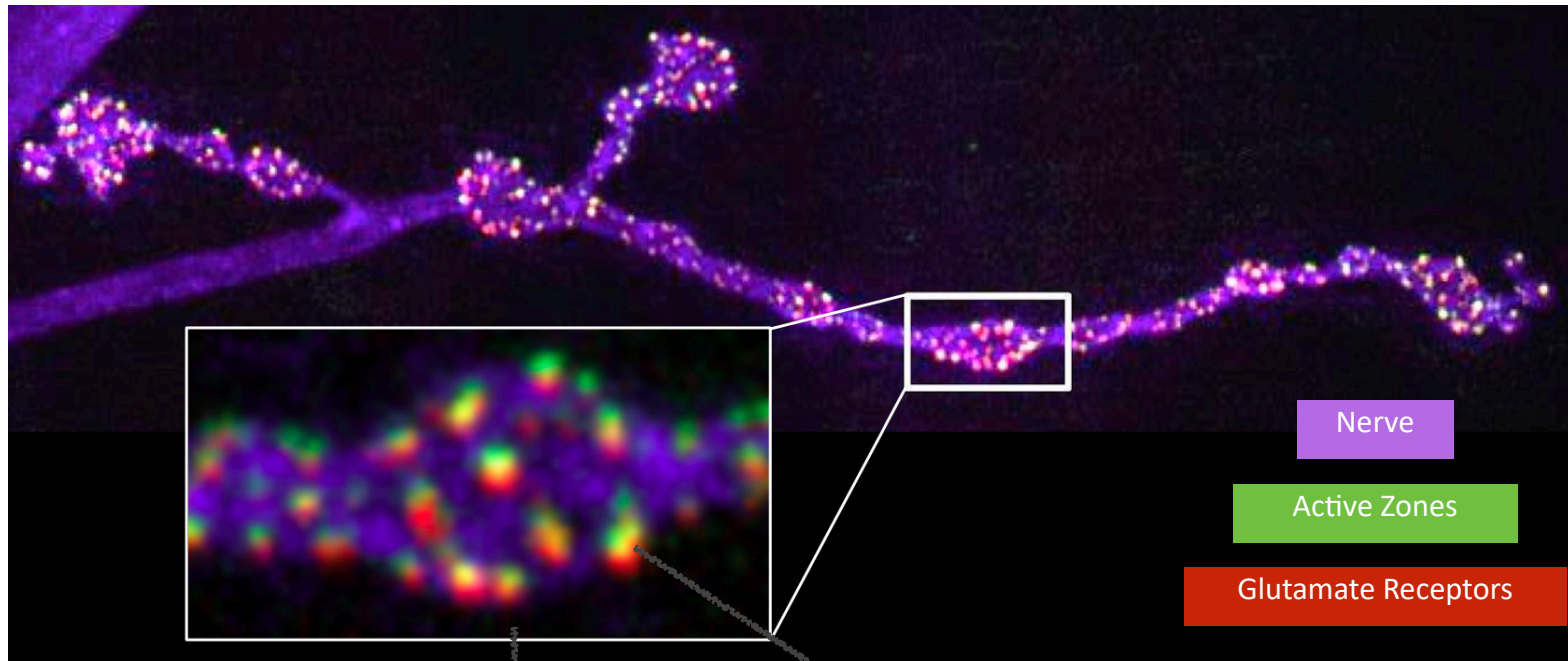


The *Drosophila* Larval Motor Circuit

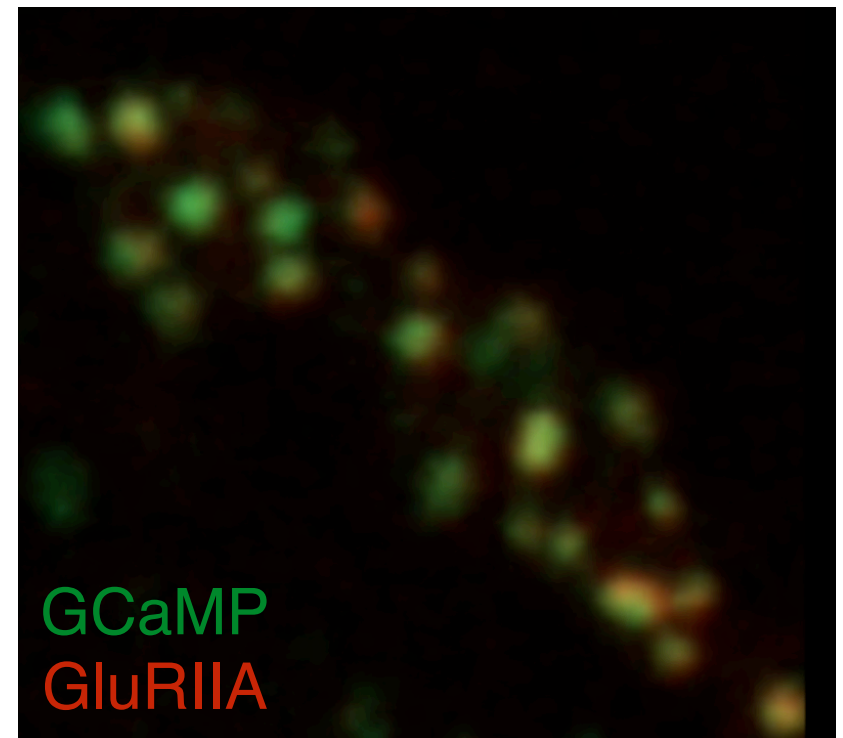
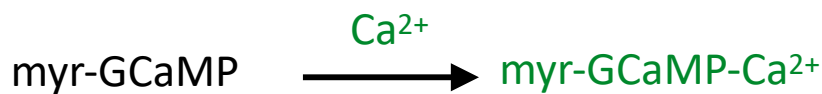
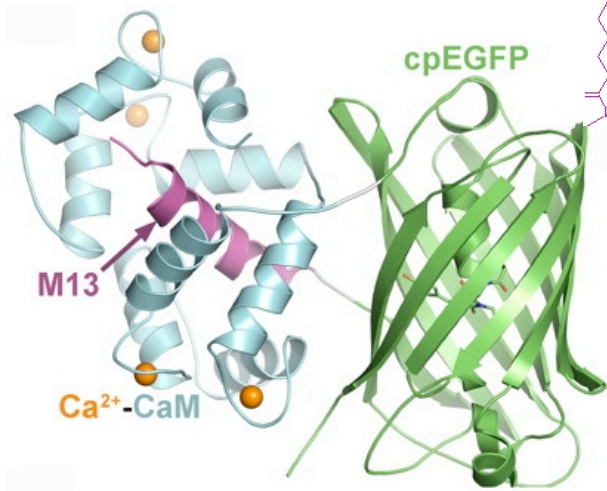
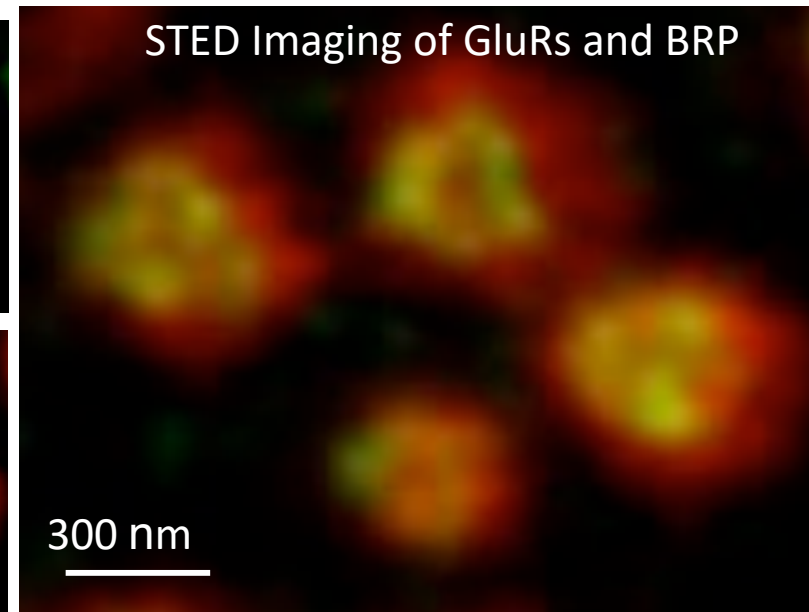
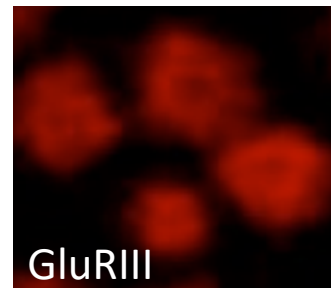
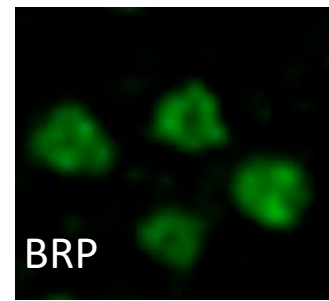
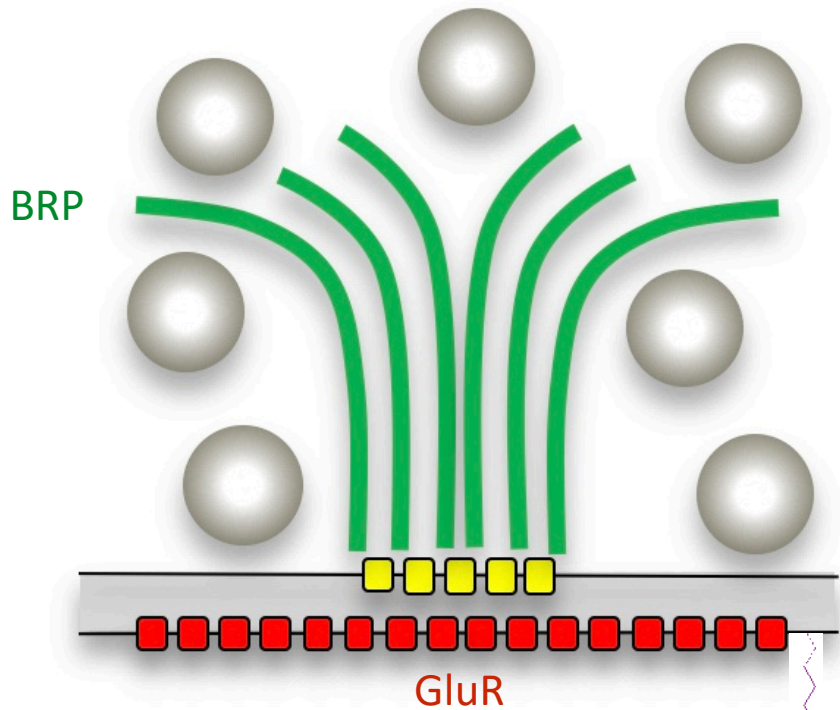


Clark et al, 2018; Zarin et al, 2019

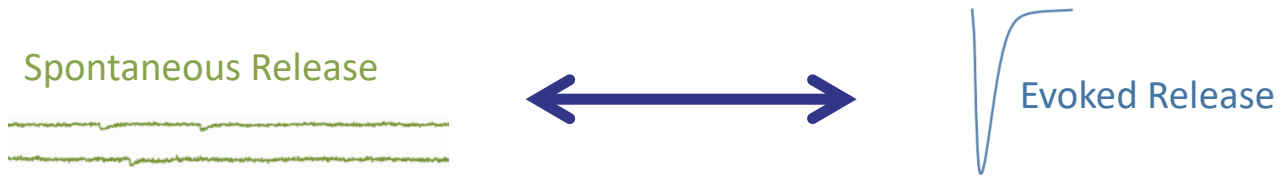
Organization of Synaptic Contacts at the *Drosophila* NMJ



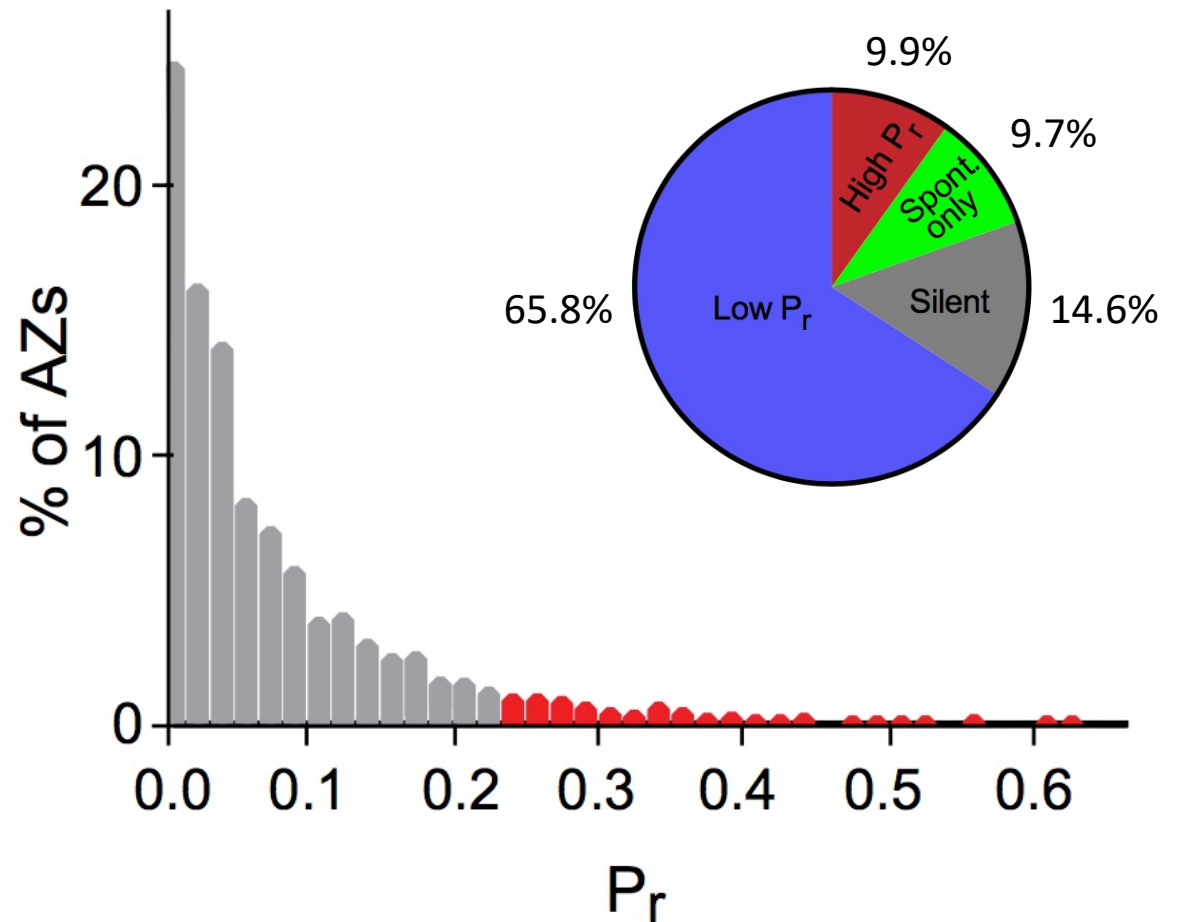
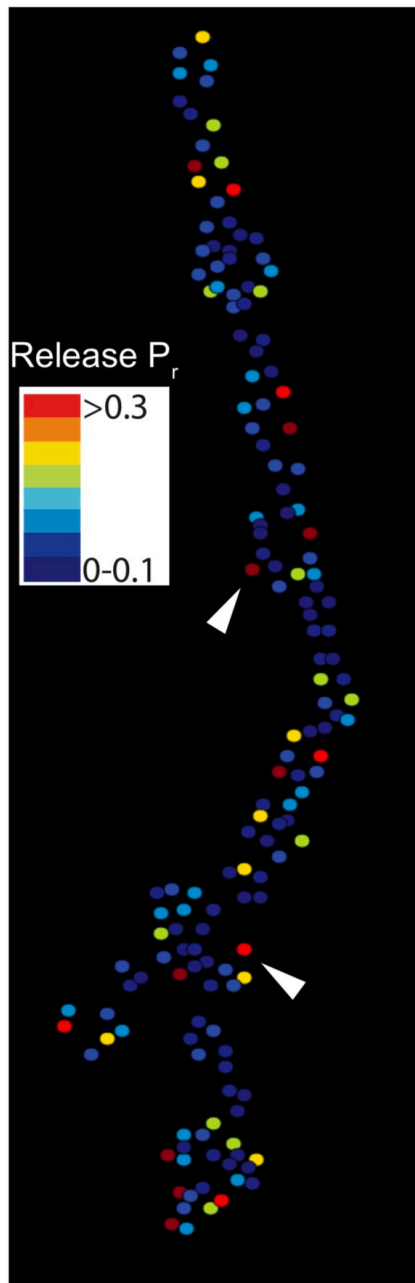
Matching of Presynaptic AZs to Postsynaptic GluR Fields



Visualizing Synaptic Transmission *In Vivo*

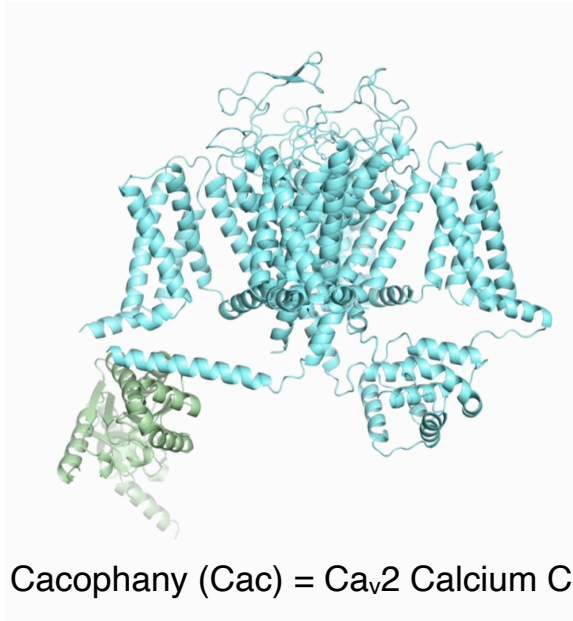


Evoked Release Probability is Heterogenous Across AZs

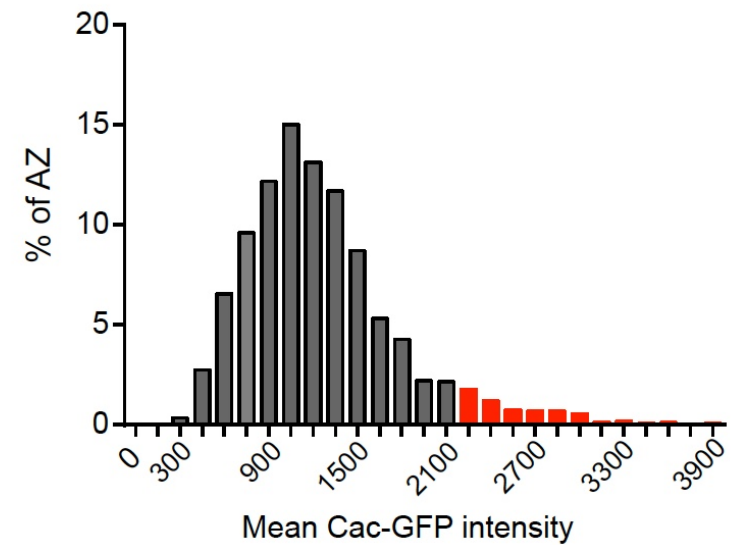
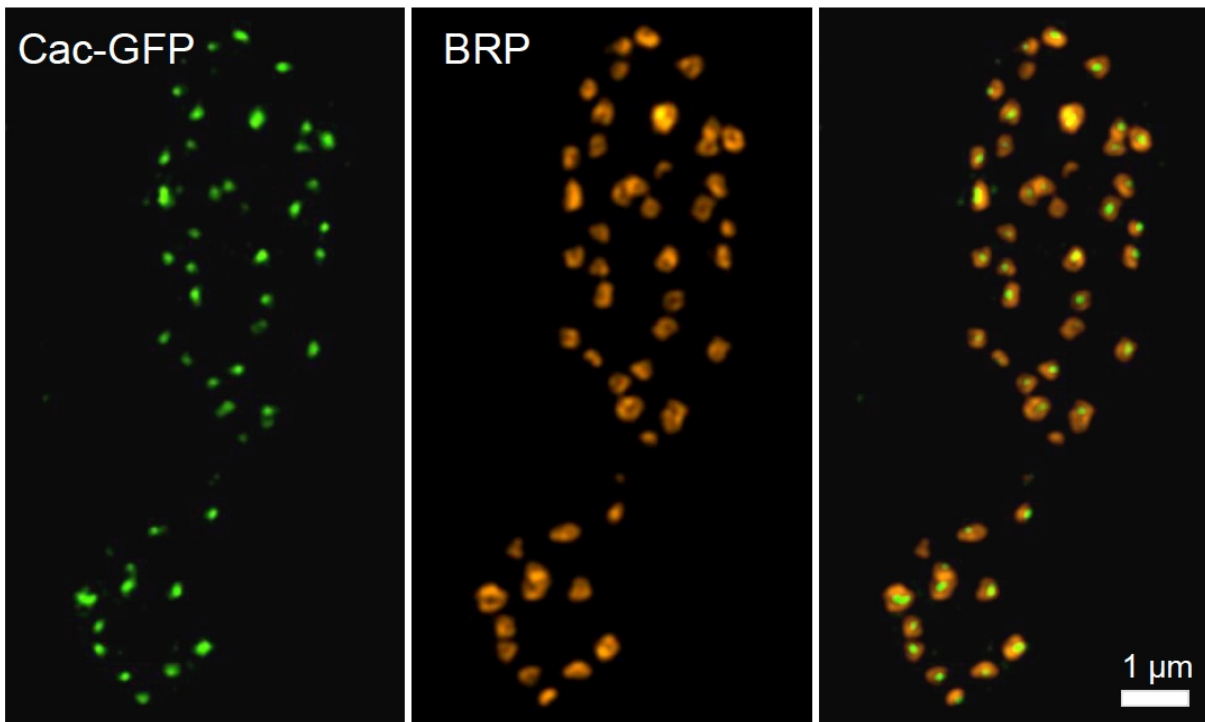
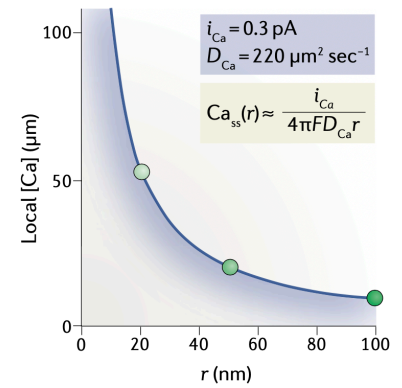
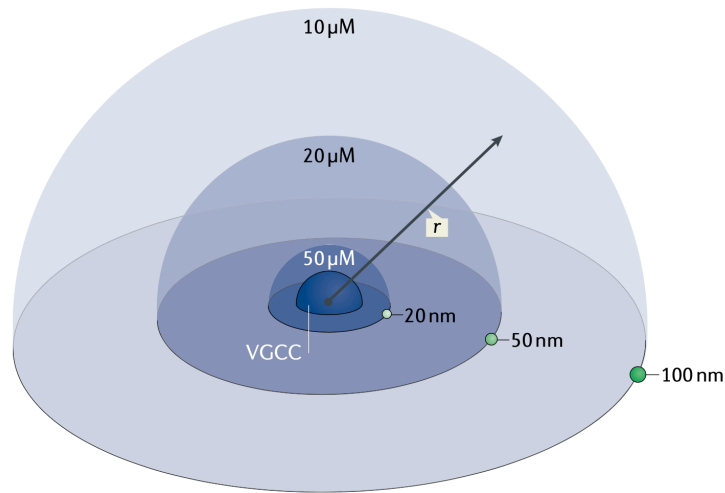


Average Active Zone Release Probability = 0.07

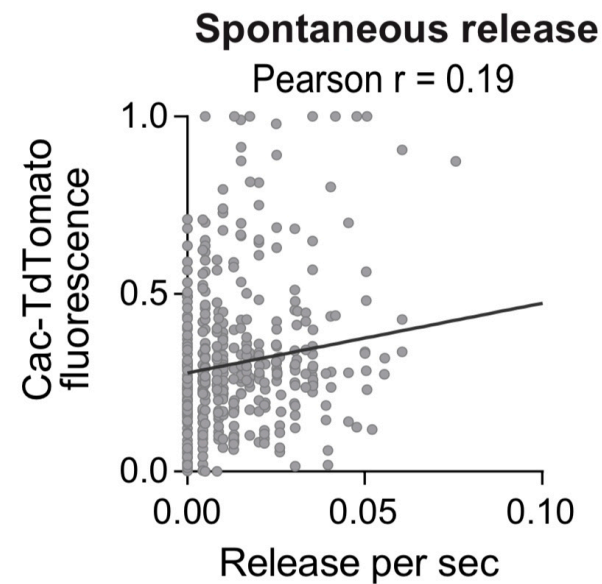
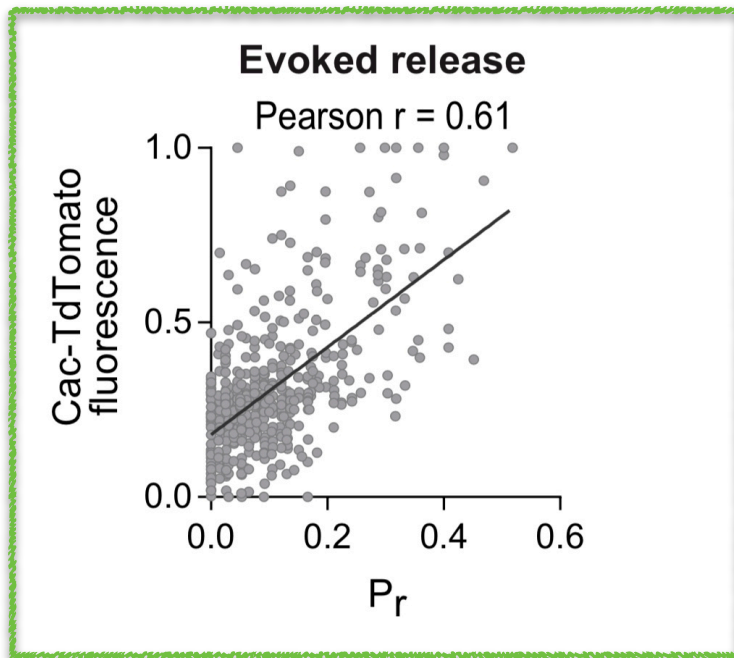
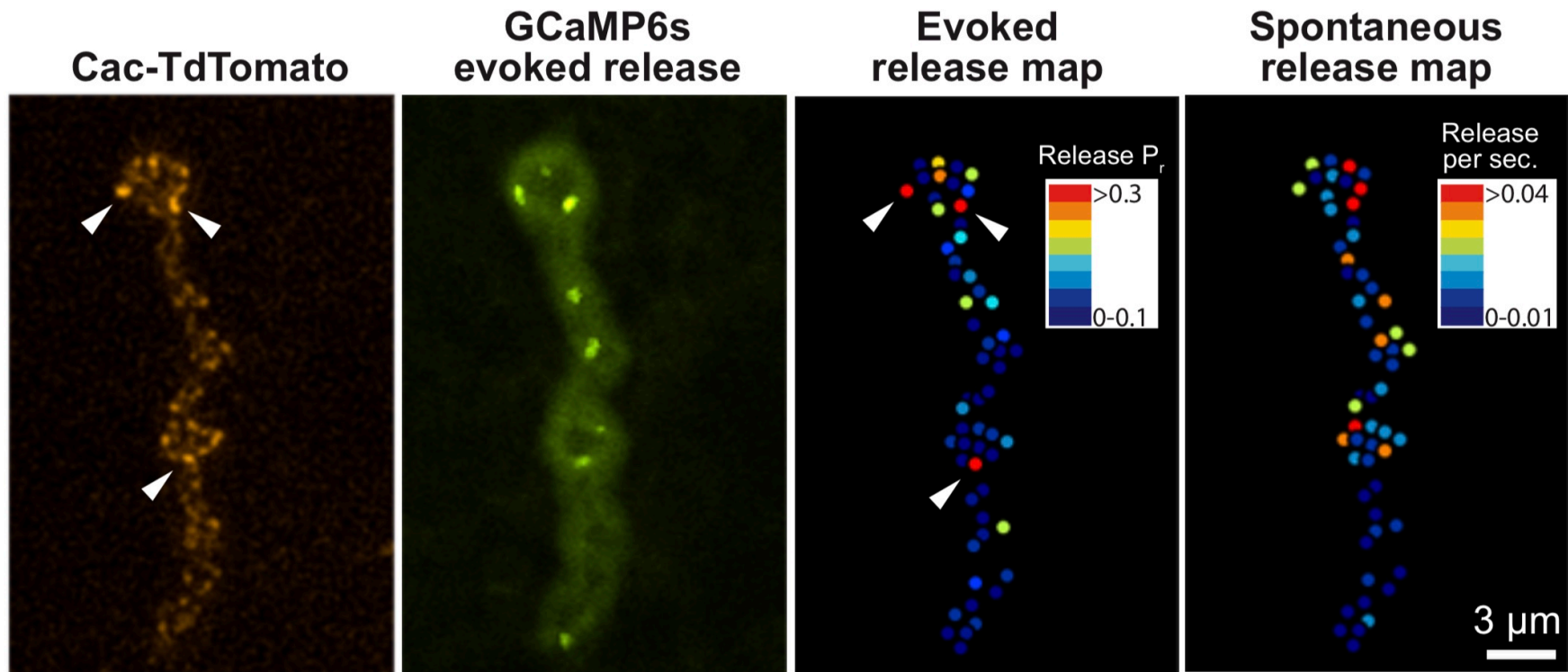
Active Zone Regulation of Synaptic Strength



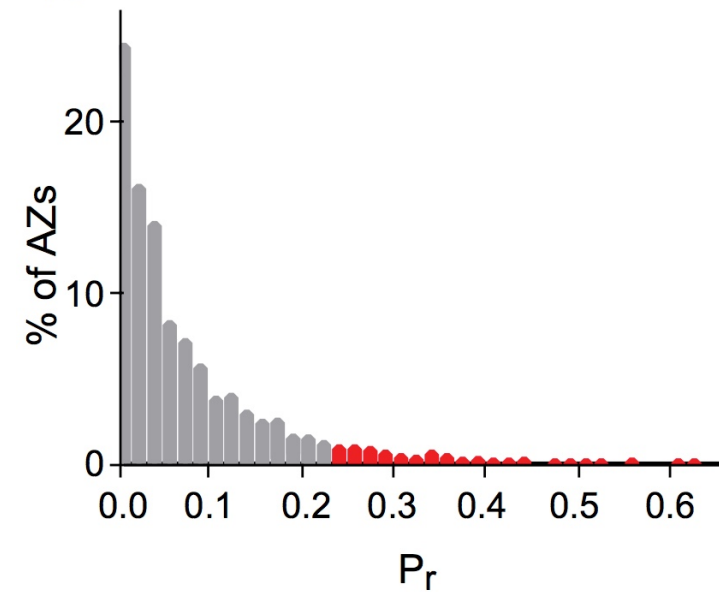
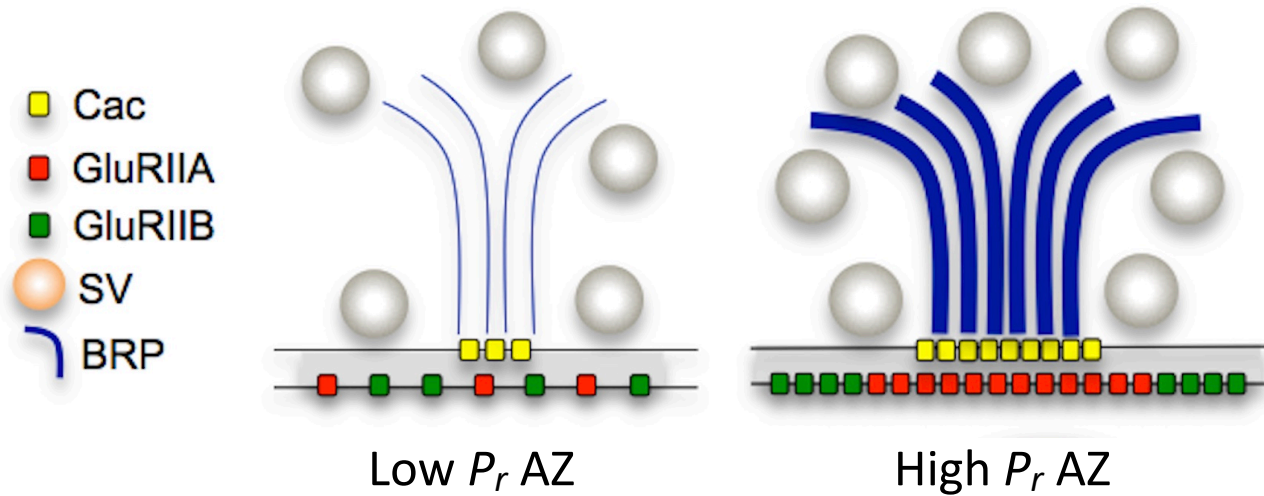
Cacophany (Cac) = Ca_v2 Calcium Channel



Correlation Between Calcium Channel Density and P_r

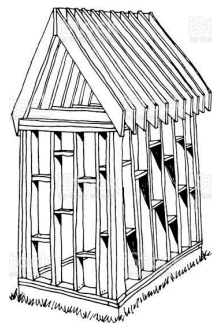
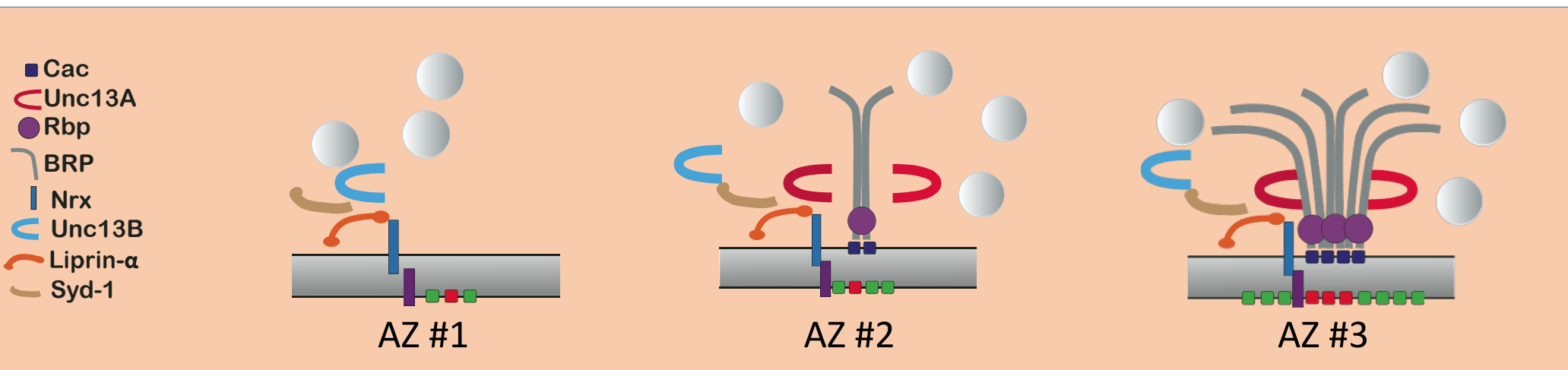


What is the Origin of AZ P_r Heterogeneity?



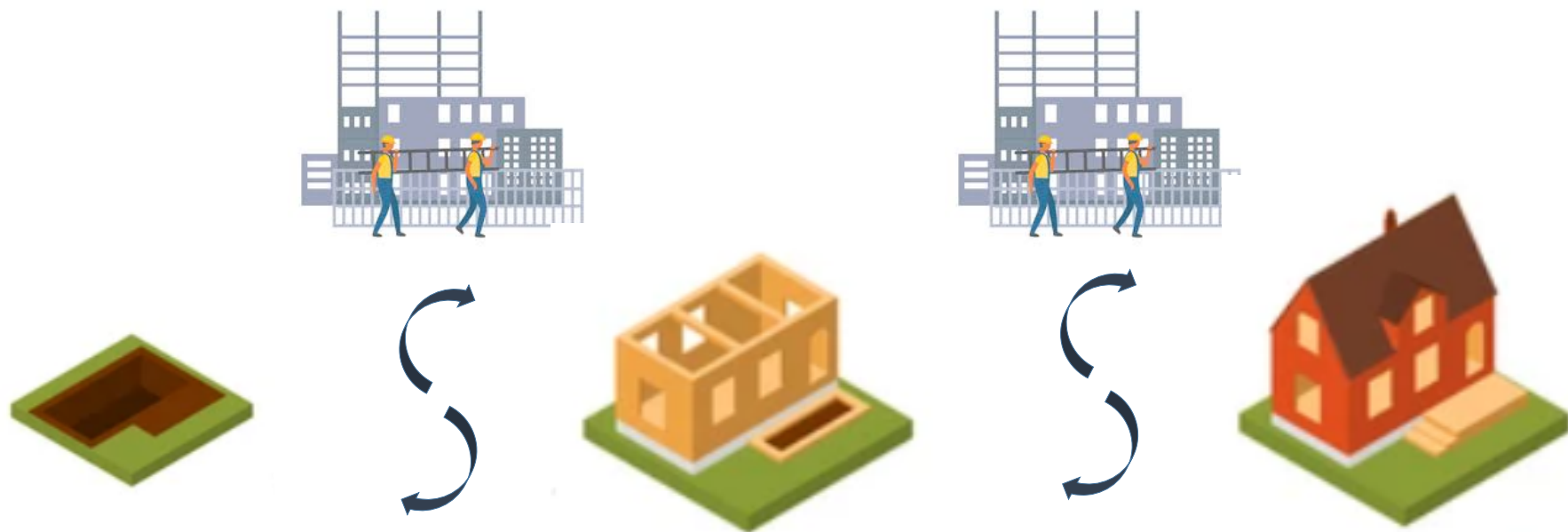
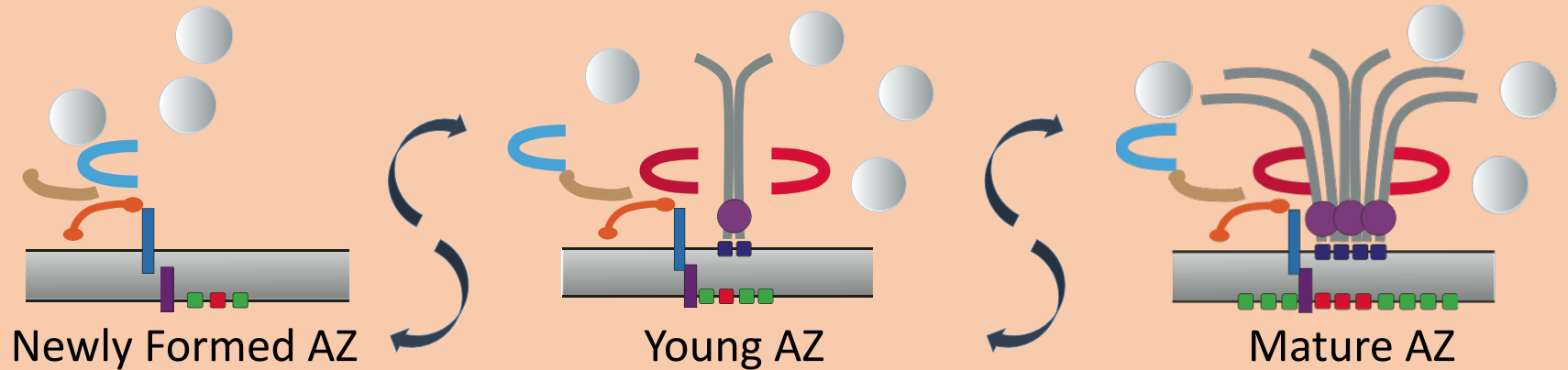
What is the Origin of AZ P_r Heterogeneity?

Model 1: AZs arrive preassembled and at a specific set strength

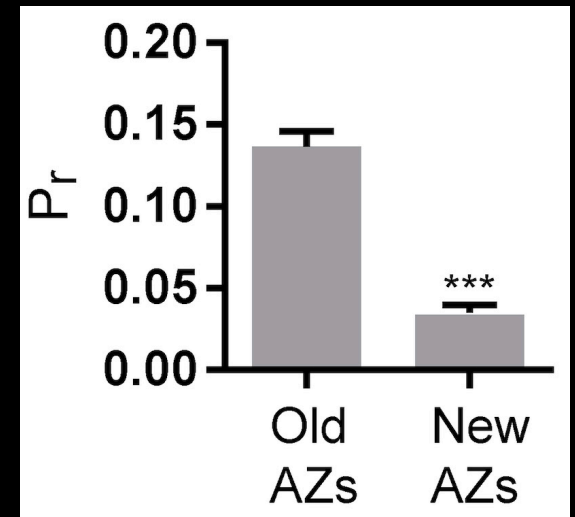
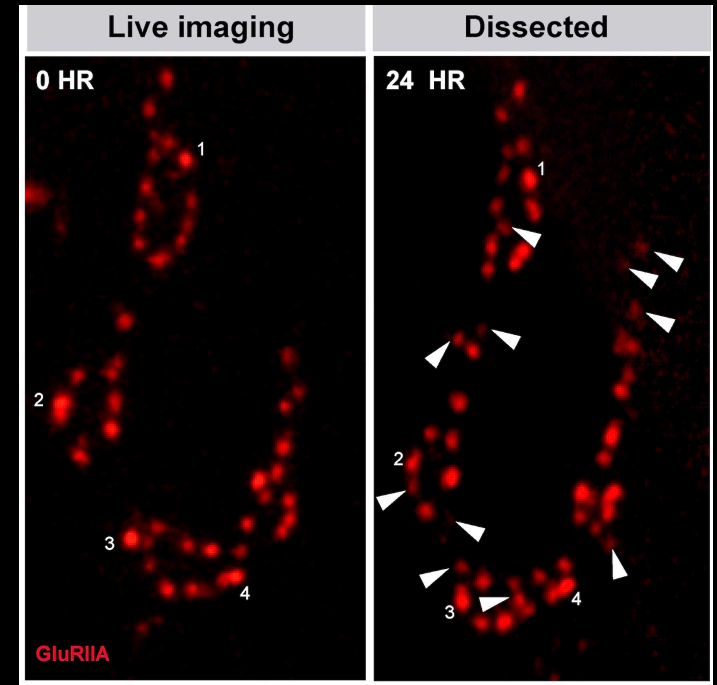
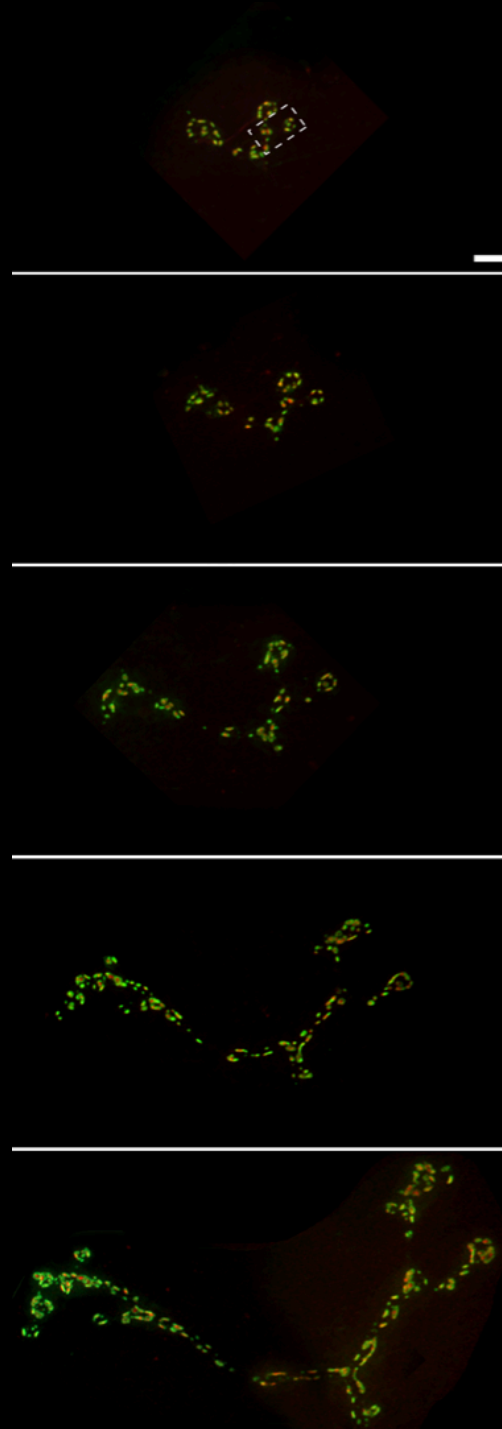
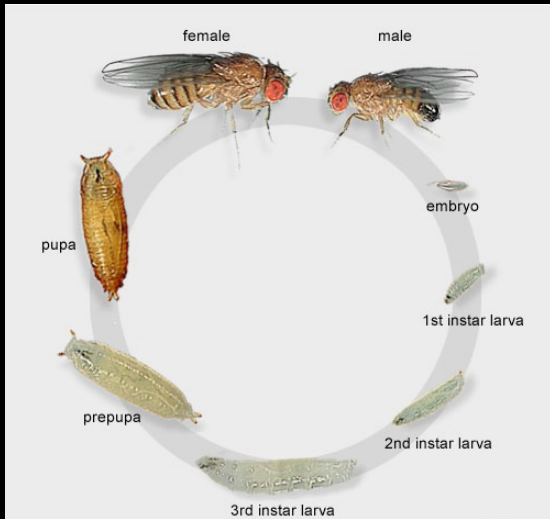


What is the Origin of AZ P_r Heterogeneity?

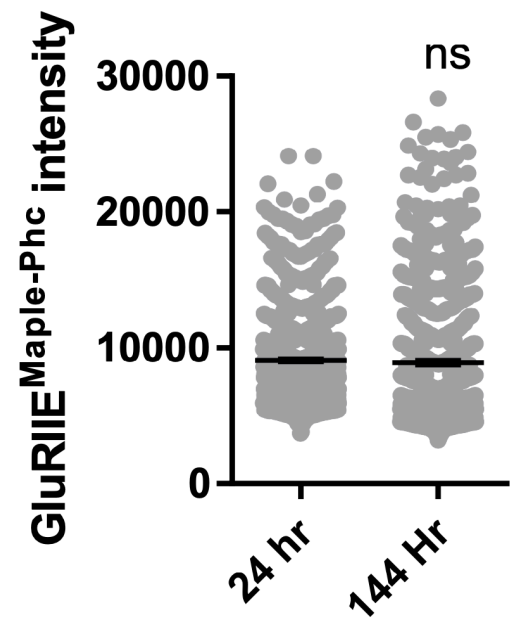
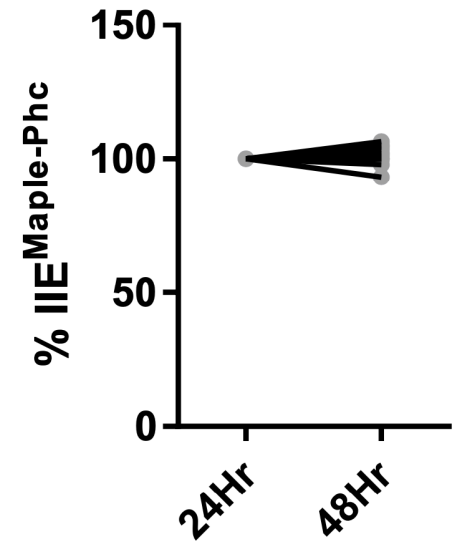
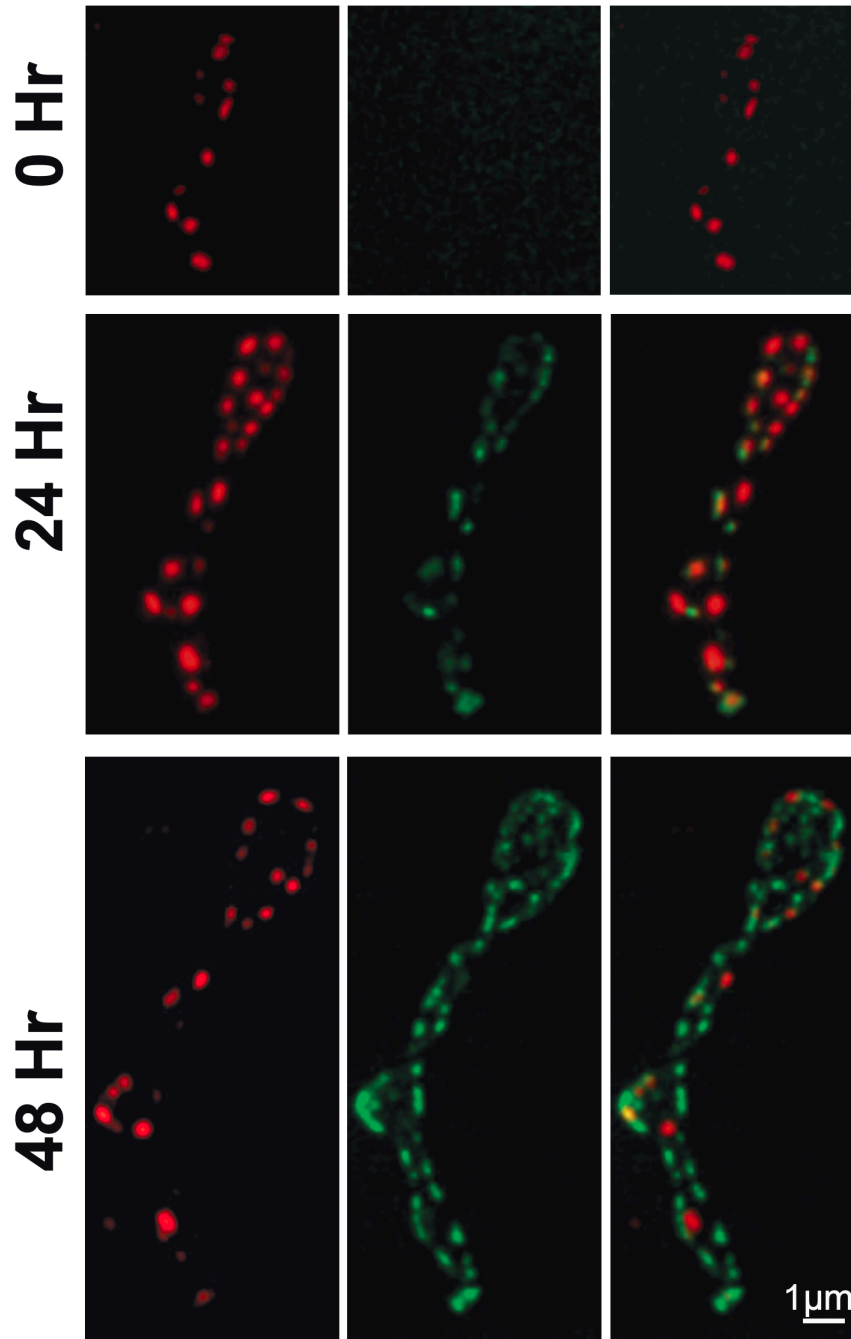
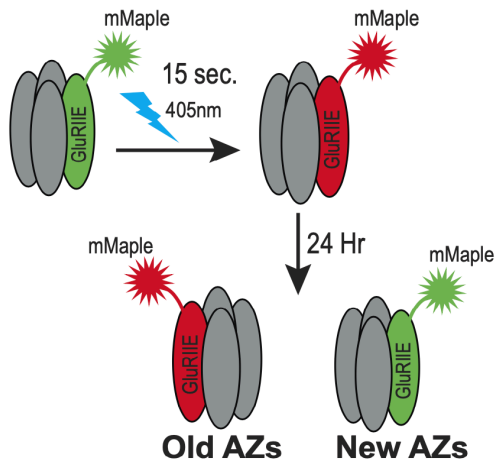
Model 2: AZ material assembles in a specific sequence over time at the synapse



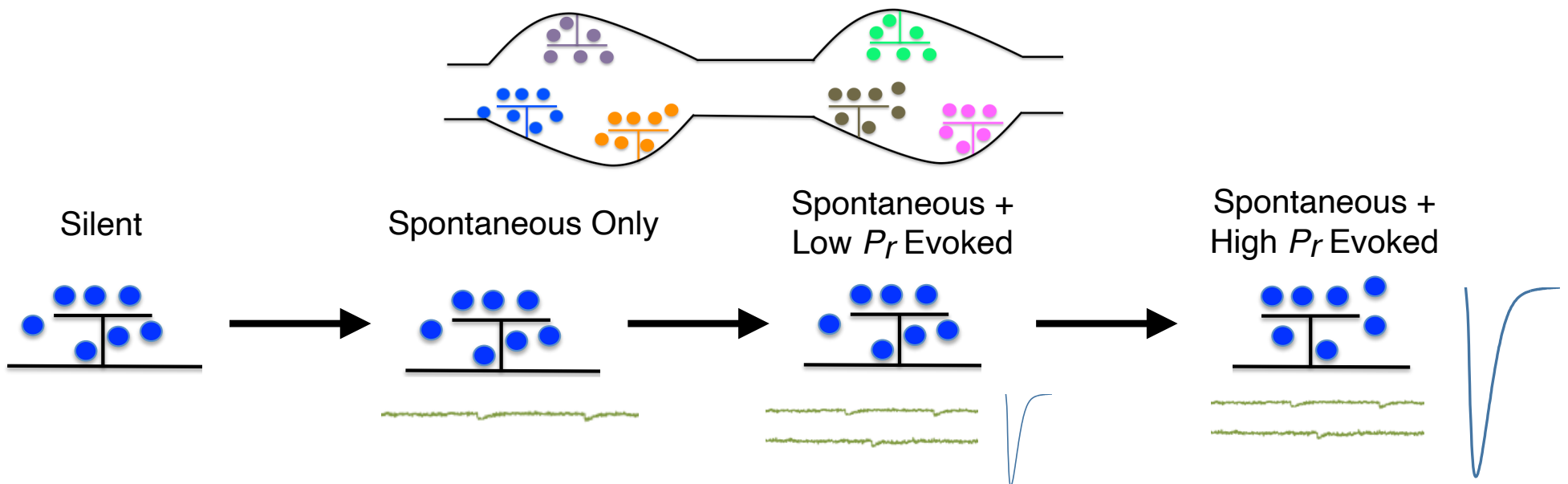
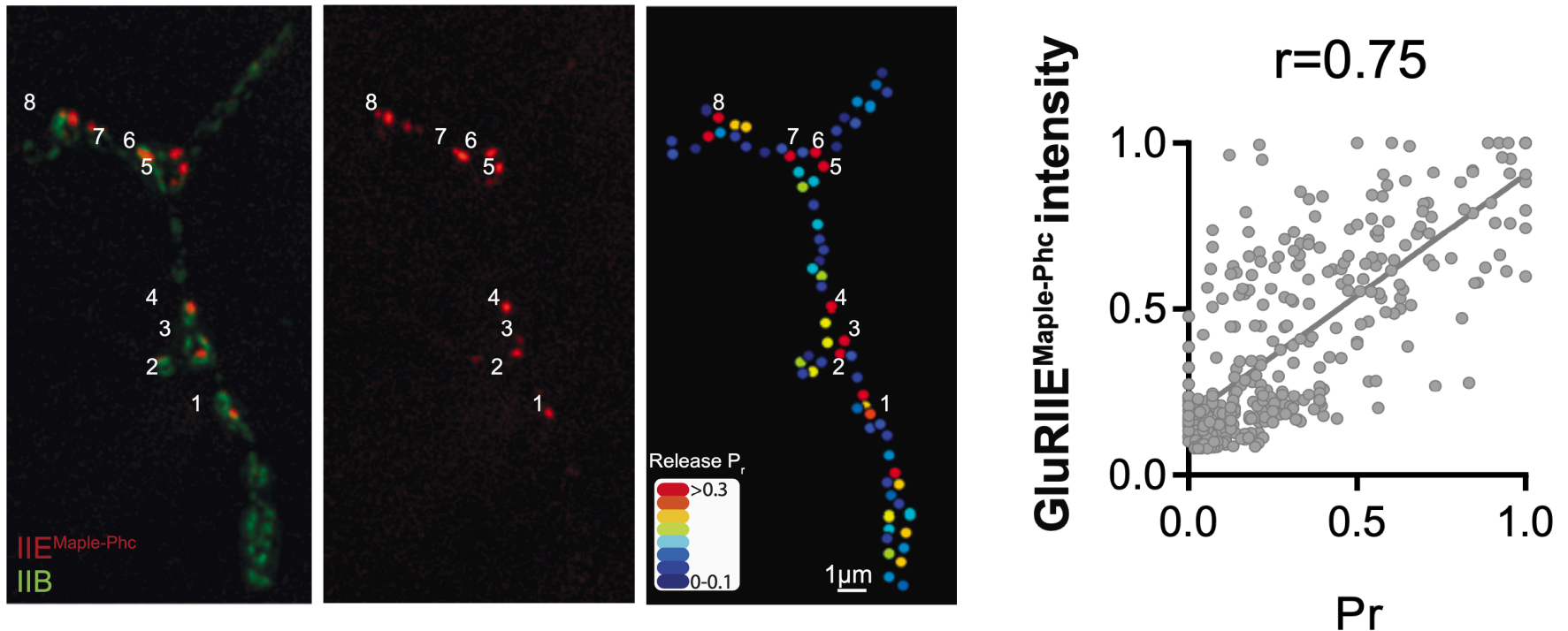
Synaptic Strength Develops Over Time



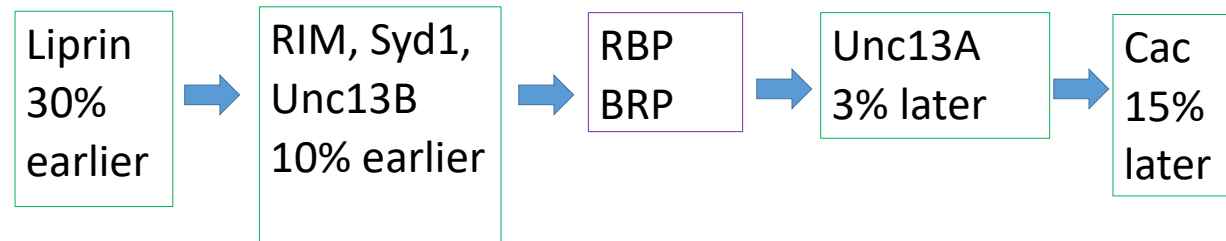
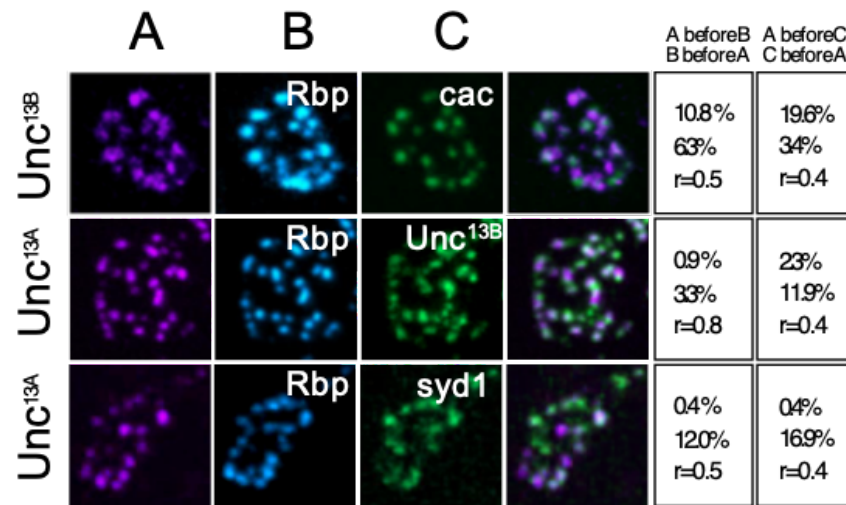
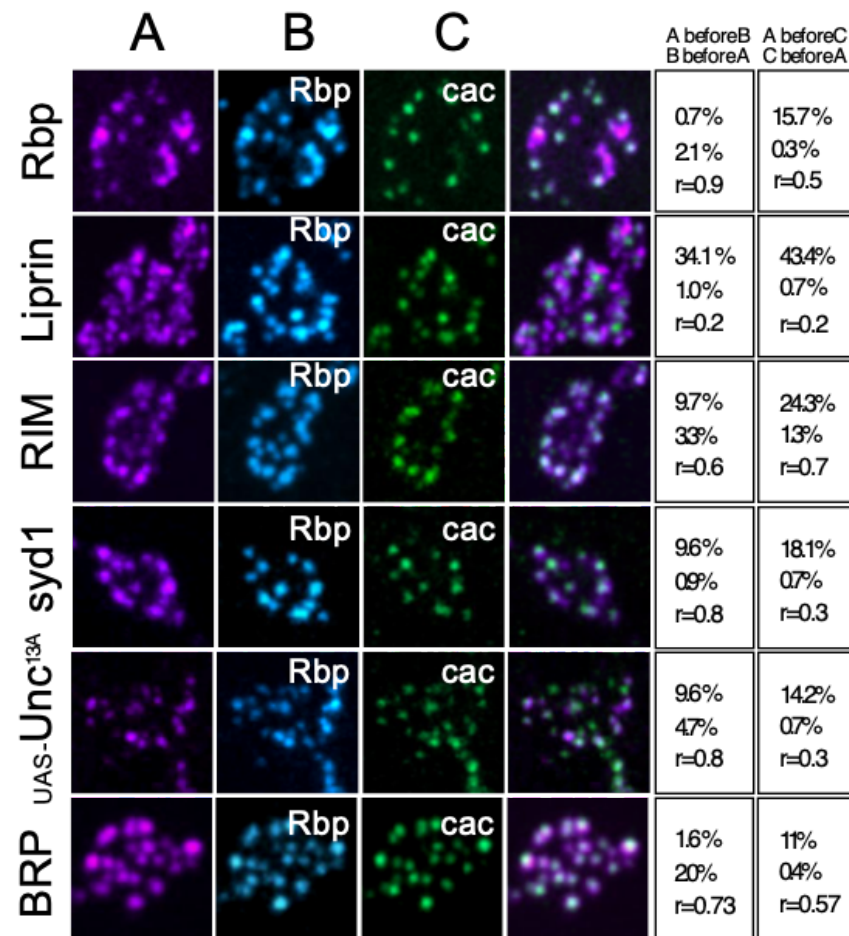
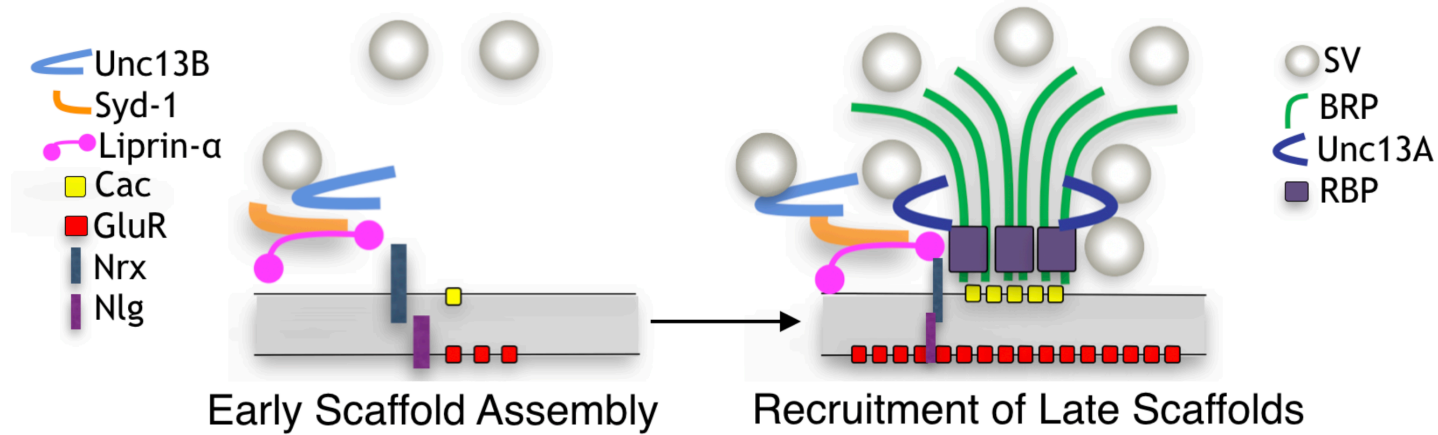
Time-stamping GluRs with mMaple



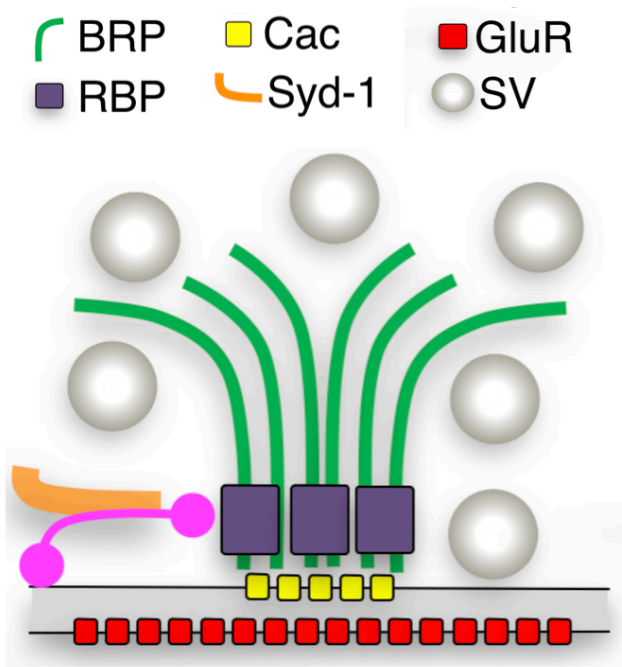
Active Zones With Variable Release Properties Reflect Developmental Maturation



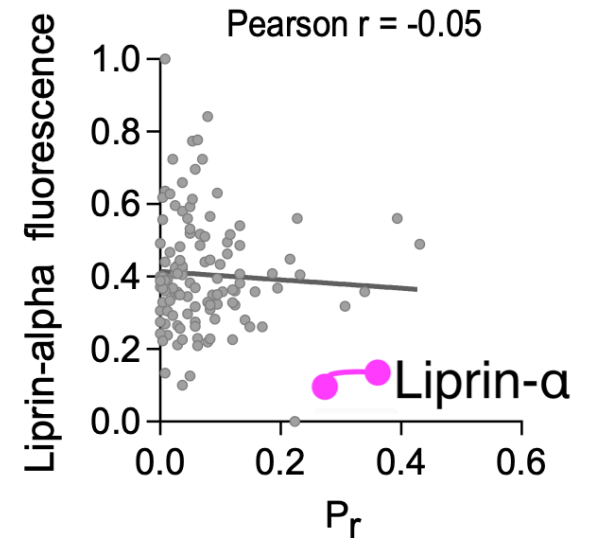
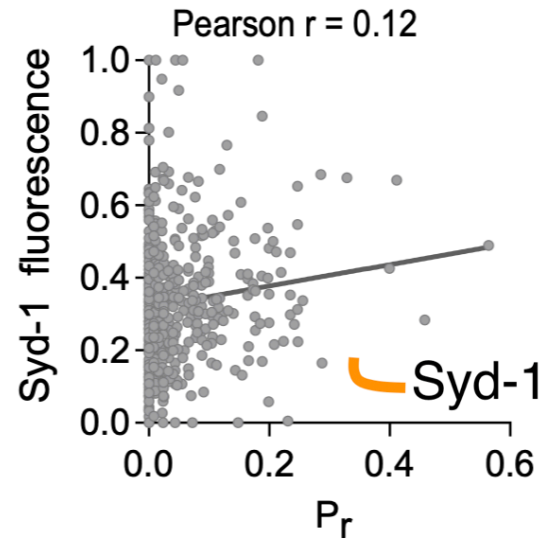
Active Zone Maturation Components and Timecourse



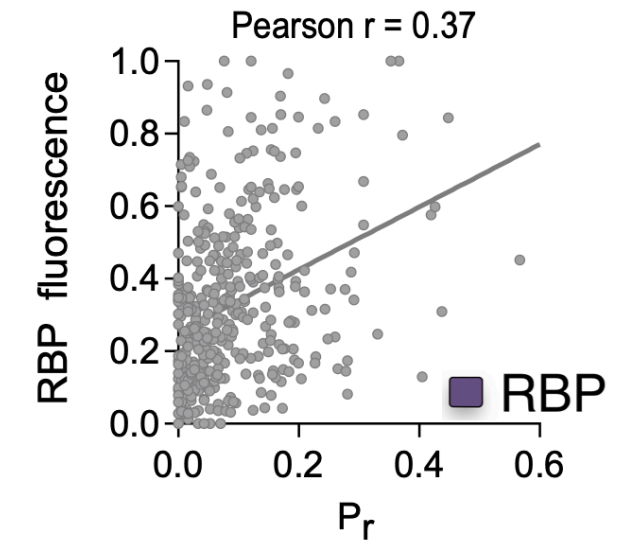
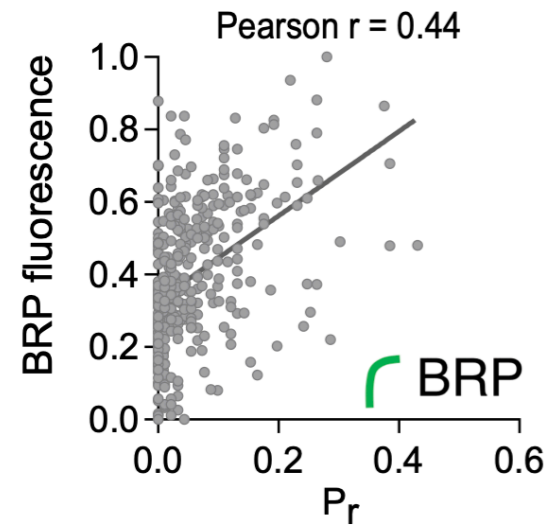
Presynaptic Correlations with Release Probability



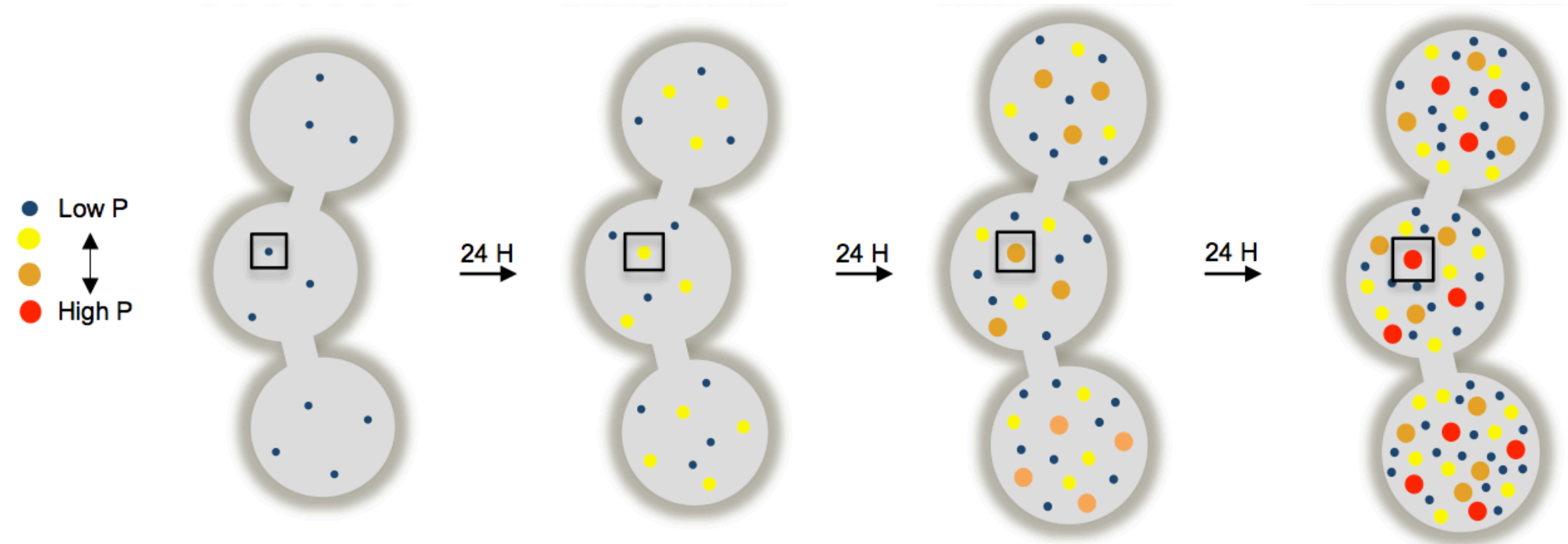
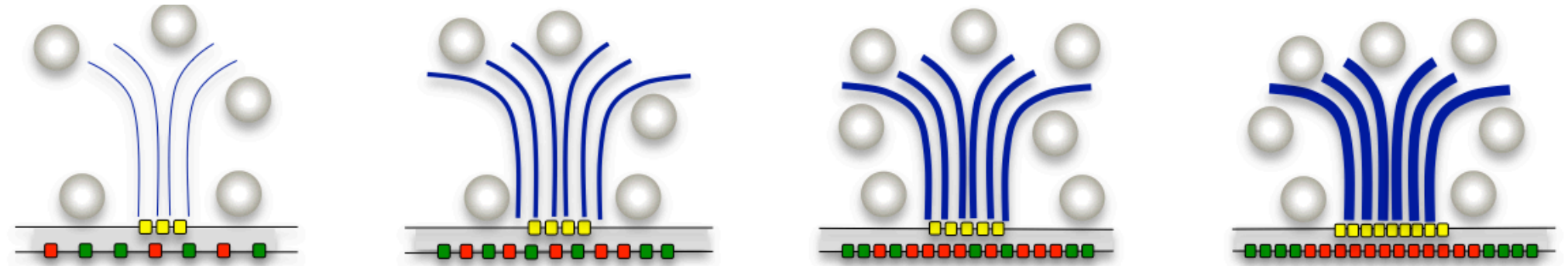
Early AZ Scaffolds



Late AZ Scaffolds

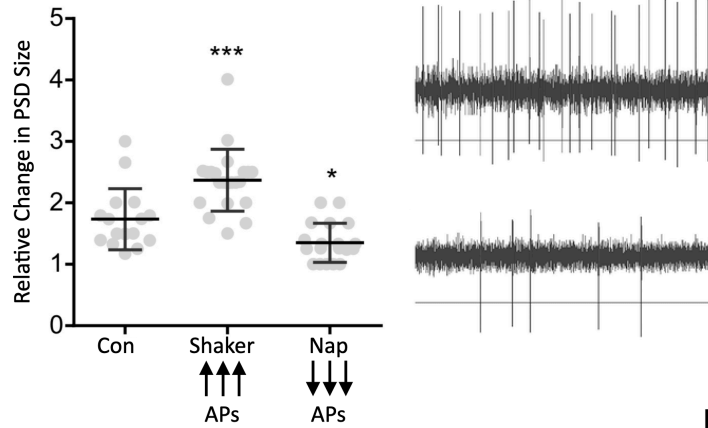


Model for Active Zone Release Heterogeneity

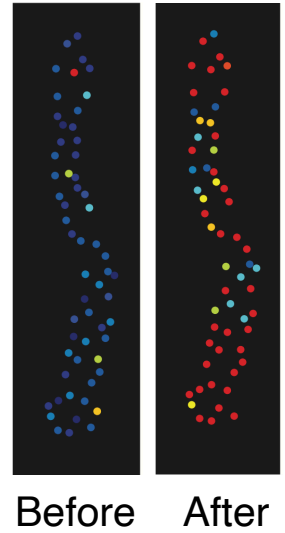
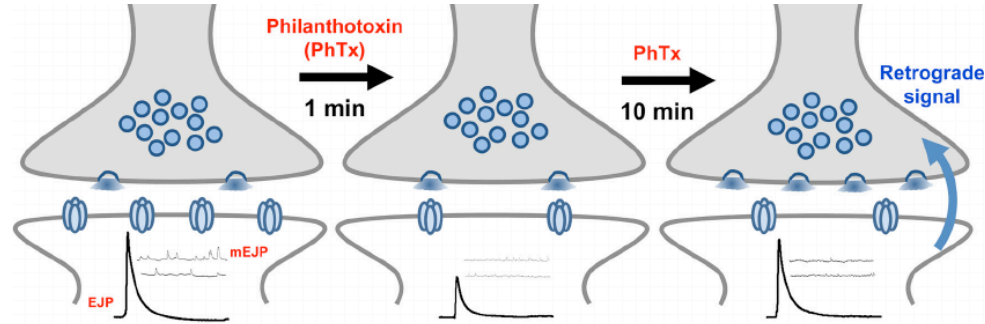


Ongoing Questions on Control of Presynaptic Output at AZs

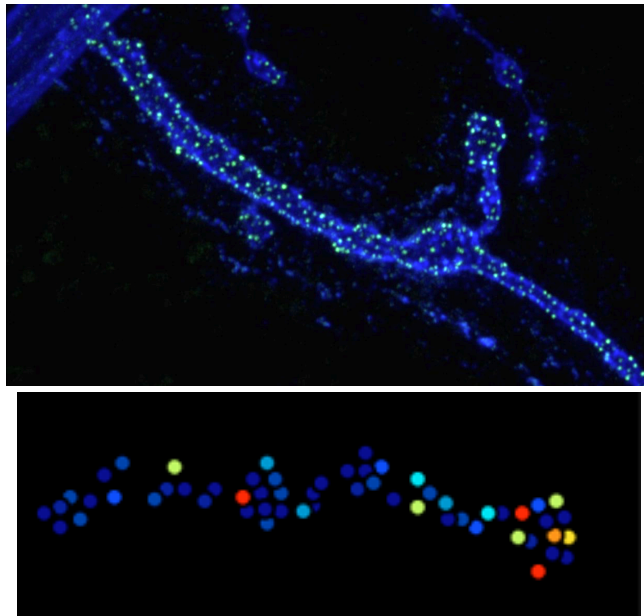
How Does Neuronal Activity Influence Synapse Formation?



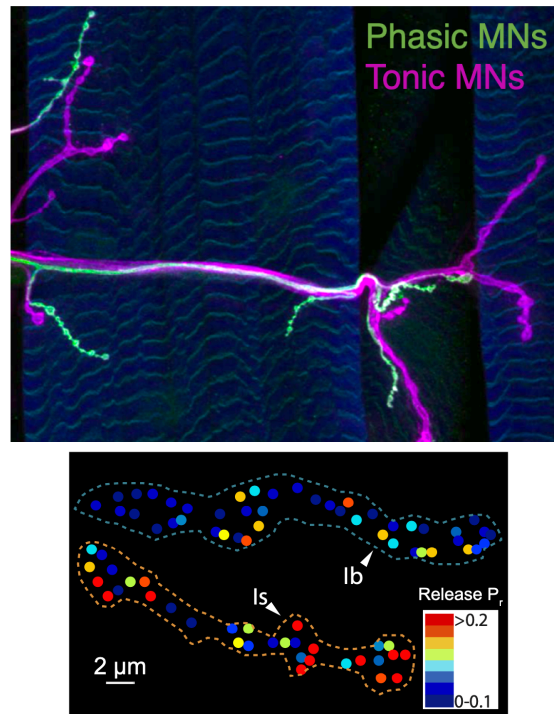
What Underlies Rapid Changes in P_r During Plasticity?



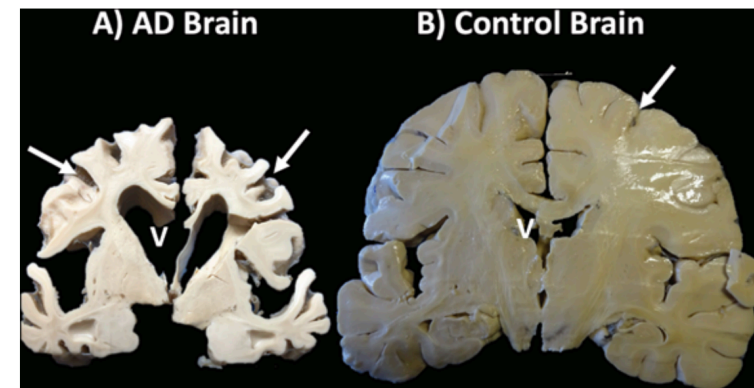
Mechanisms of AZ Material Capture and Maintenance



How are P_r Differences Across Neuronal Subtypes Set?



How does Disease Alter Synapse Assembly/Disassembly?



Reyes-Pablo et al, 2020



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