

## Using Serial EM to Map Organelle Contacts in Neurons

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Direct contacts between organelles, such as ER and mitochondria, are emerging as critical platforms for many biological responses in eukaryotic cells. Organelle contacts are emerging as critical signaling platforms in metazoan cells. In non-neuronal cells, many of the important physiological functions played by mitochondria such as  $\text{Ca}^{2+}$  uptake and lipid biogenesis require a specialized structural and functional interface with the smooth endoplasmic reticulum (ER). Recent data support a model whereby mitochondrial  $\text{Ca}^{2+}$  uptake can only occur upon Ryanodine and/or  $\text{IP}_3$  receptors-mediated  $\text{Ca}^{2+}$  release from the ER at sites of ER-mitochondria contacts, where  $\text{Ca}^{2+}$  transiently reaches high enough concentrations to open the mitochondrial calcium uniporter (MCU). The major limiting factors in studying the role of ER-mitochondrial contacts in shaping some of the functional properties of neurons are (1) to map their distribution throughout the dendrites of identified neuronal subtypes over large scales (hundreds to thousands of cubic microns) which requires serial electron microscopy and precise segmentation and reconstructions and (2) Developing a molecular toolkit allowing to manipulate their formation and/or dynamics at single cell resolution. I will report the progress we have made progress on both fronts including some published (Hirabayashi et al. Science 2017) as well as unpublished evidence.