Developing high-throughput methods for structural analyses of macromolecular assemblies in cells, as imaged by electron tomography

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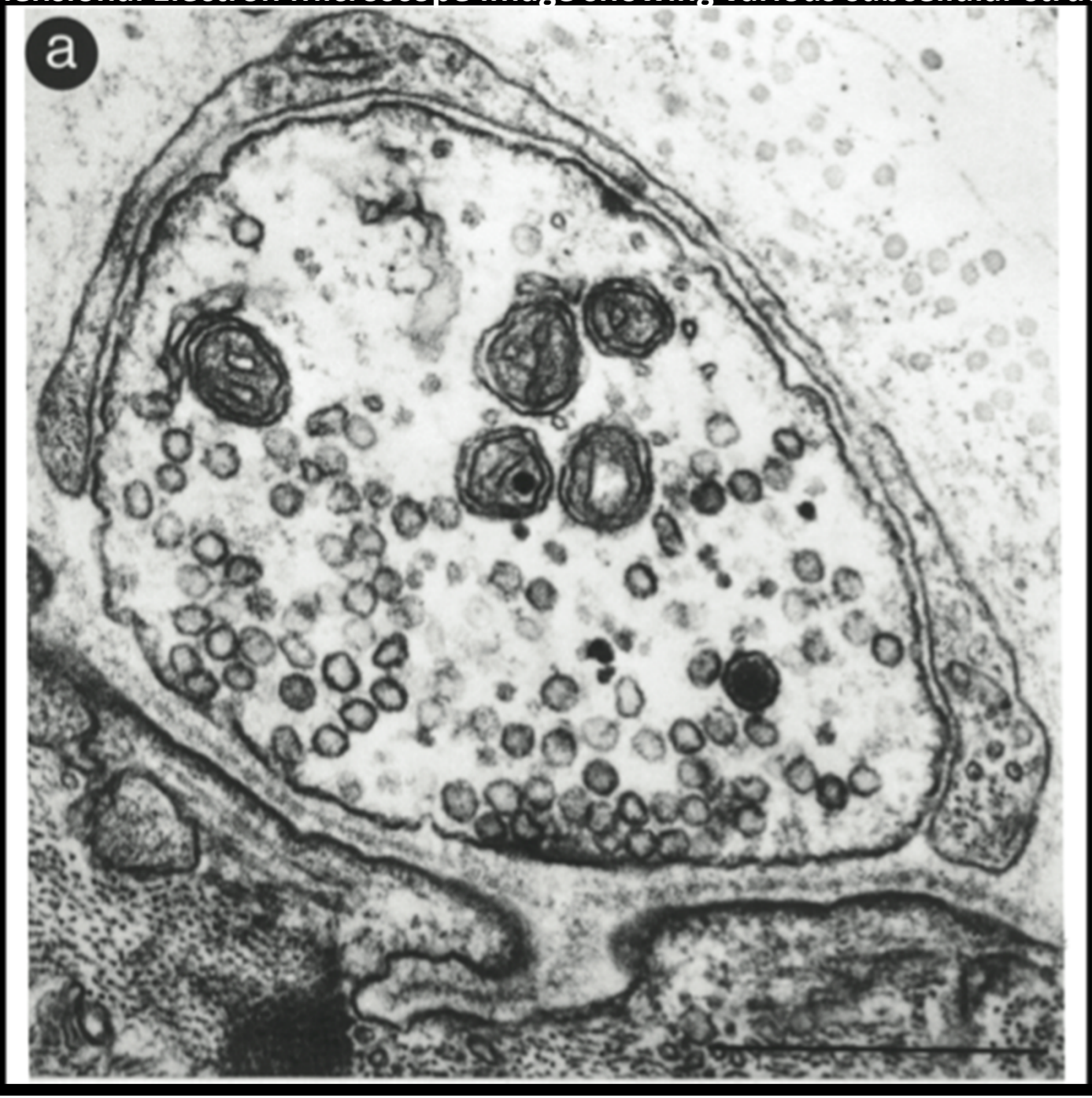
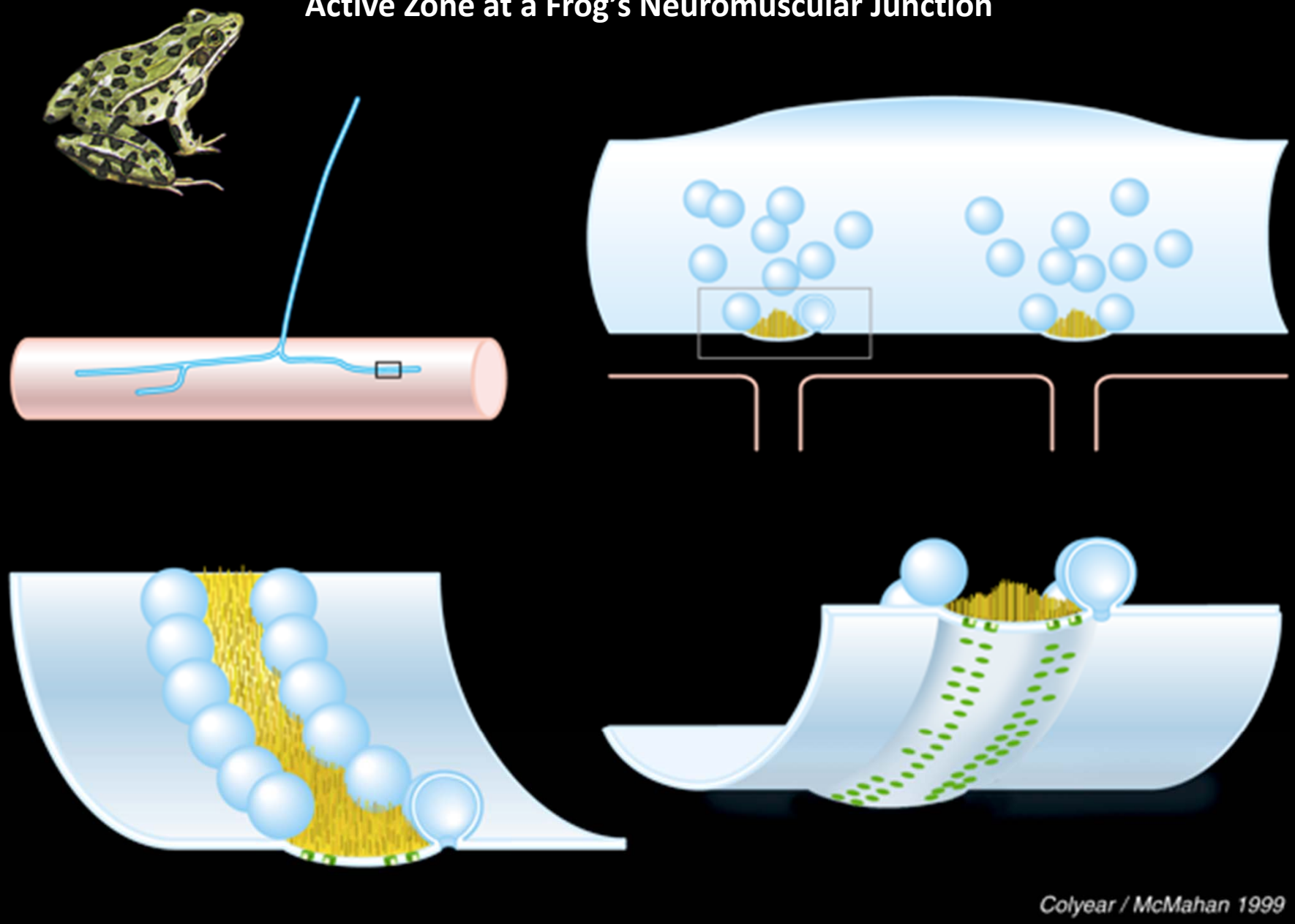
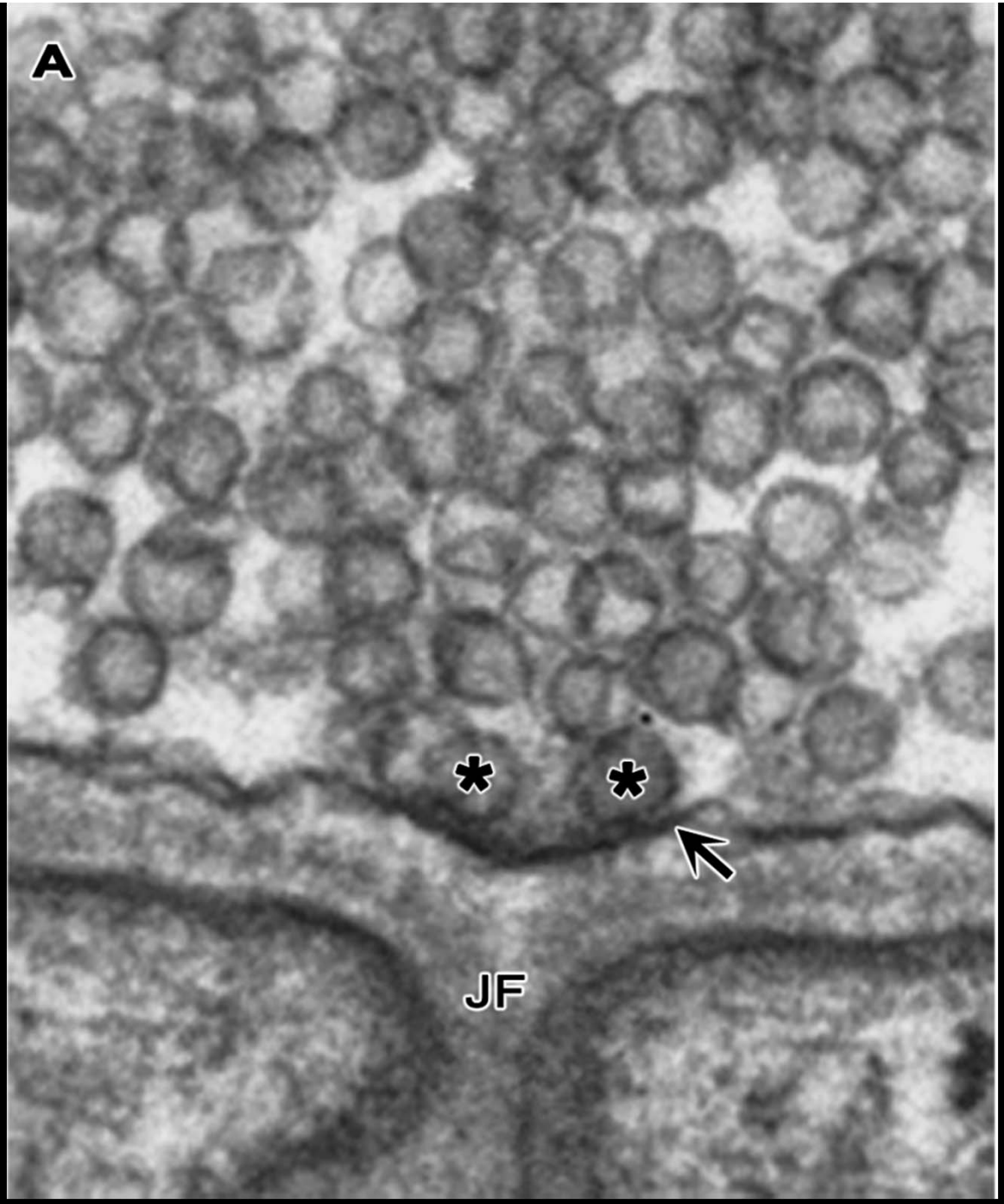
A 2-dimensional Electron Microscope Image showing various subcellular structures



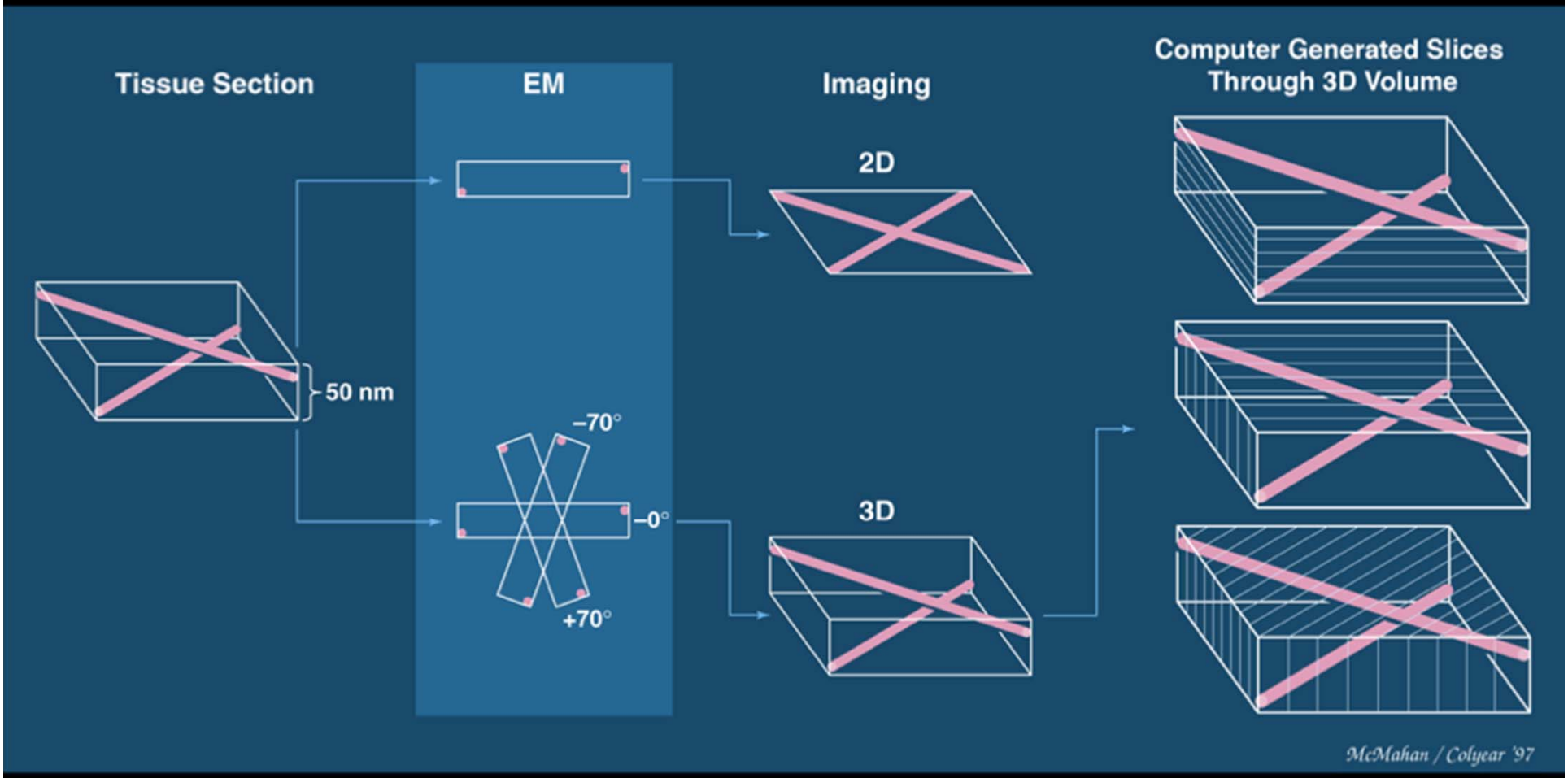
Active Zone at a Frog's Neuromuscular Junction





Lack of 3-dimensional structural information in 2D electron microscope images

Electron Tomography



Detailed 3-dimensional structural information can be provided by electron tomography.

Department of Neurobiology
Department of Structural Biology

Stanford University
Laboratory of Uel Jackson McMahan

Using EM3D©

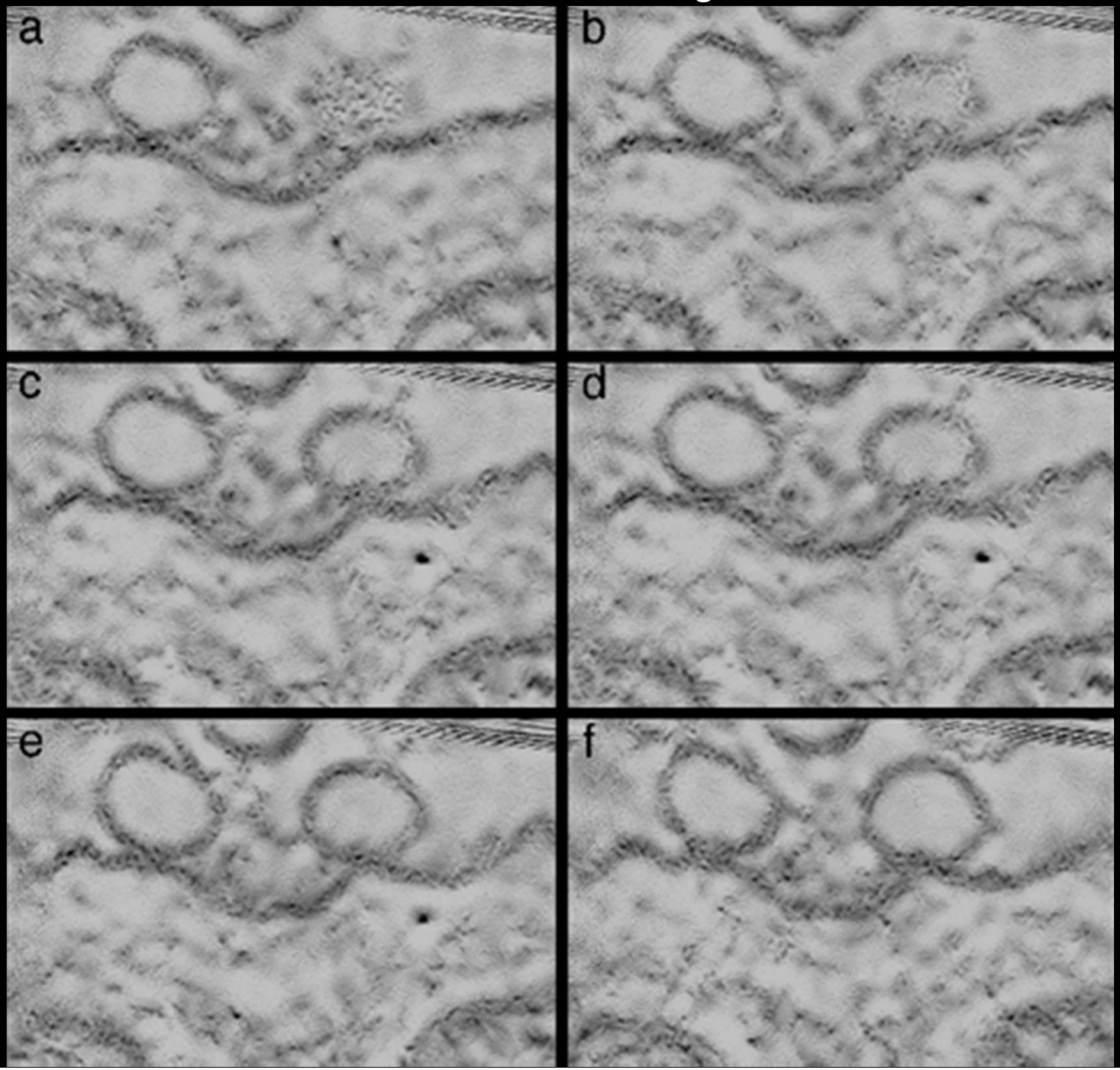
Software for Electron Microscope Tomography

David Ress, Mark Harlow, Robert Marshall, Cornelia Koch-Stoschek, David Yip,
Mira Roman and U.J.McMahan

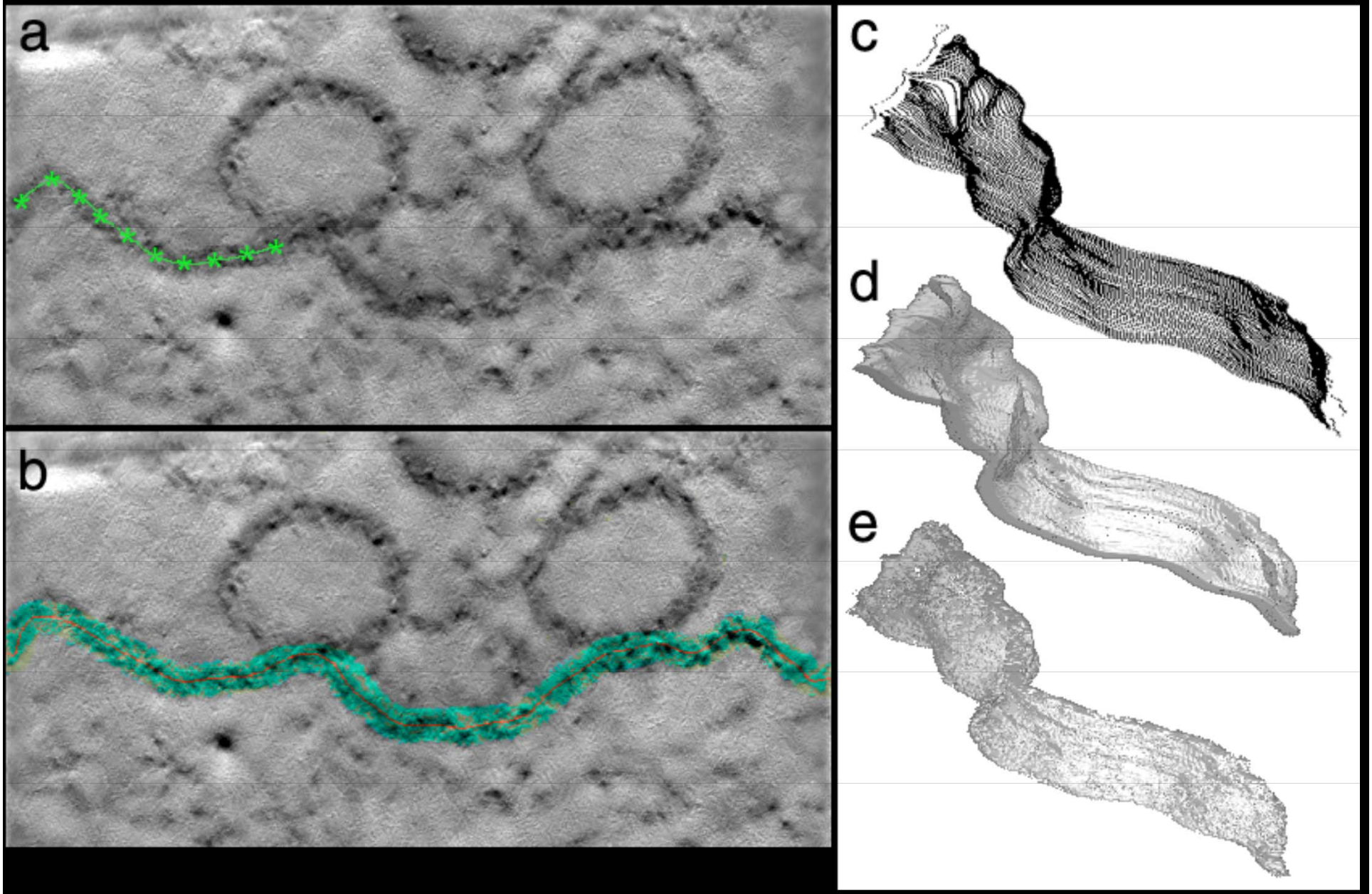
This Human Brain Project/Neuroinformatics
research is funded by the
National Institute of Mental Health

EM3D, a free electron tomography software package

Serial Virtual Slices at an Active Zone at a Frog's Neuromuscular Junction

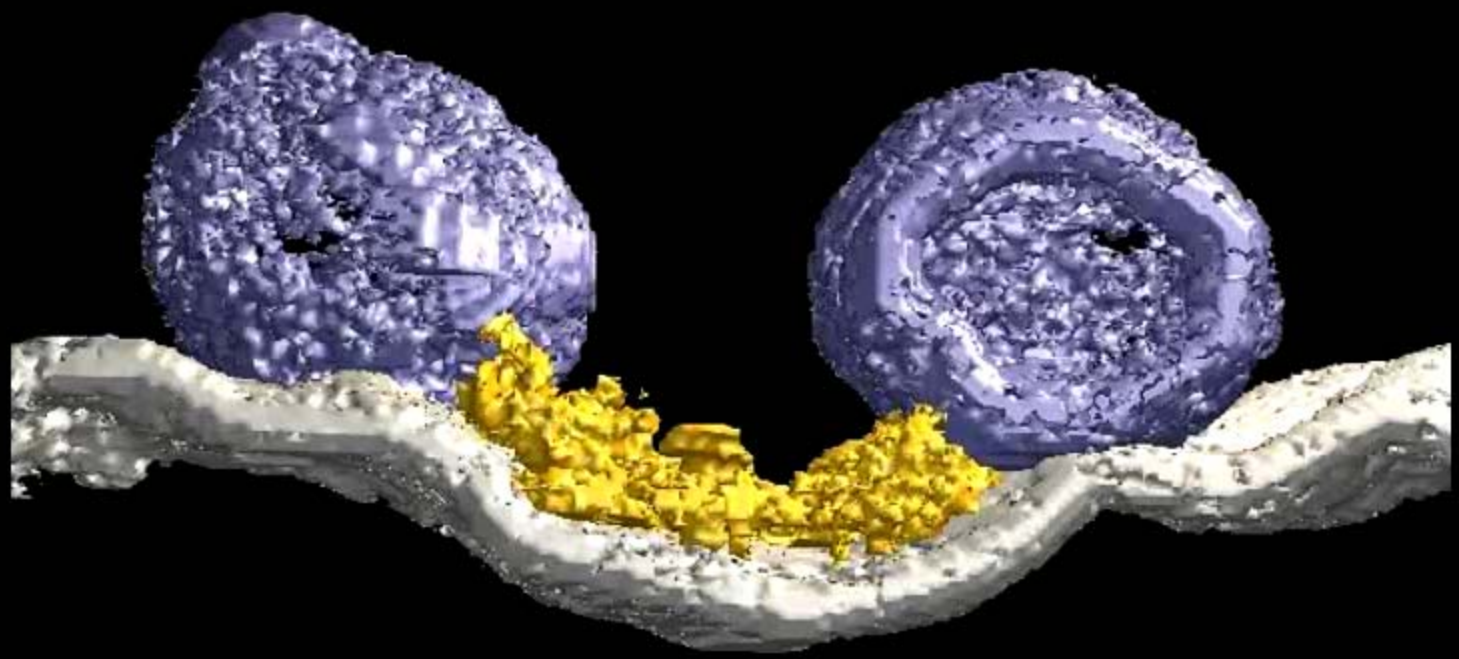


Segmentation and Surface Model generation of a structure of interest

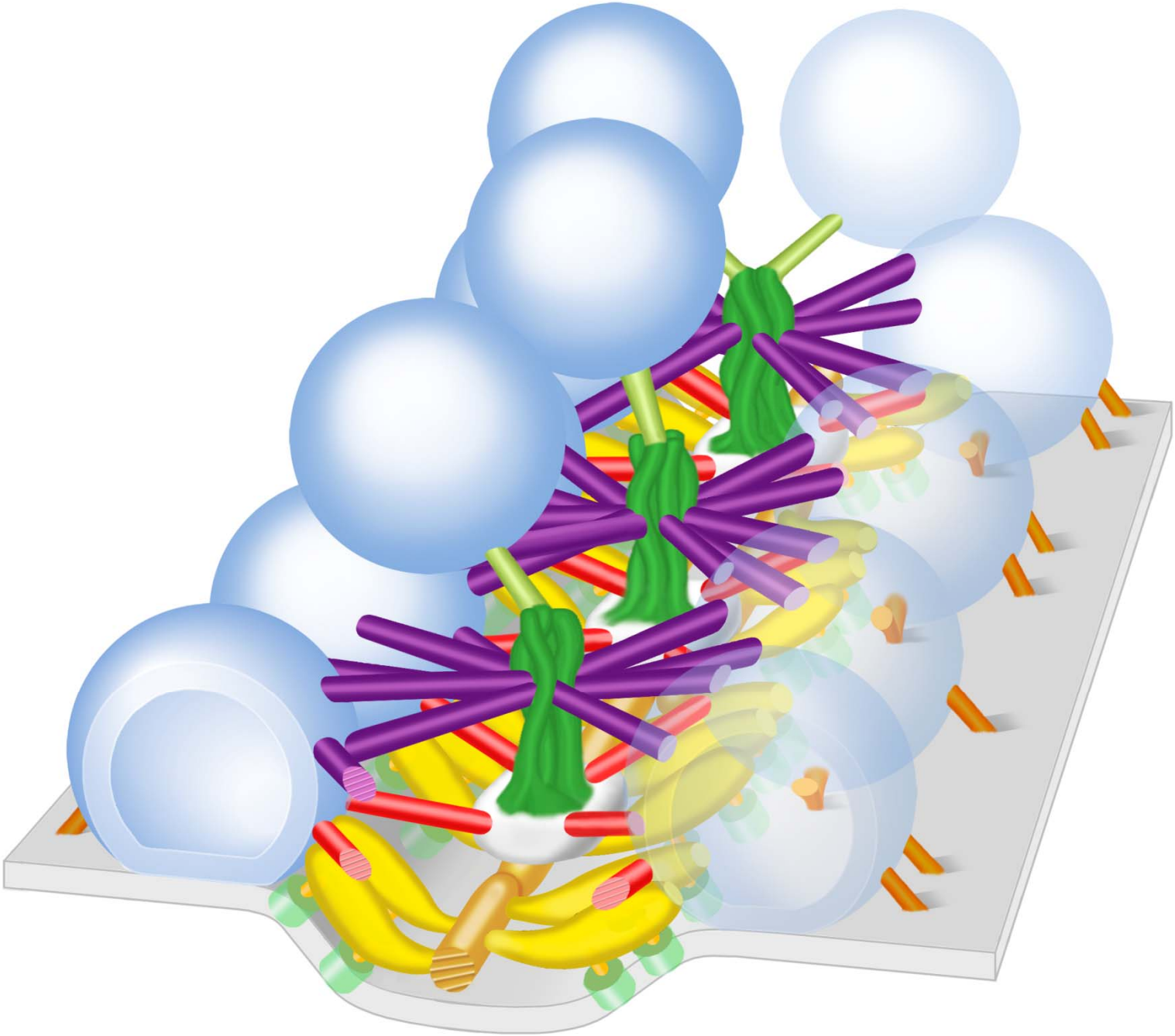


A Movie of Segmentation and Surface Model generation of a structure of interest

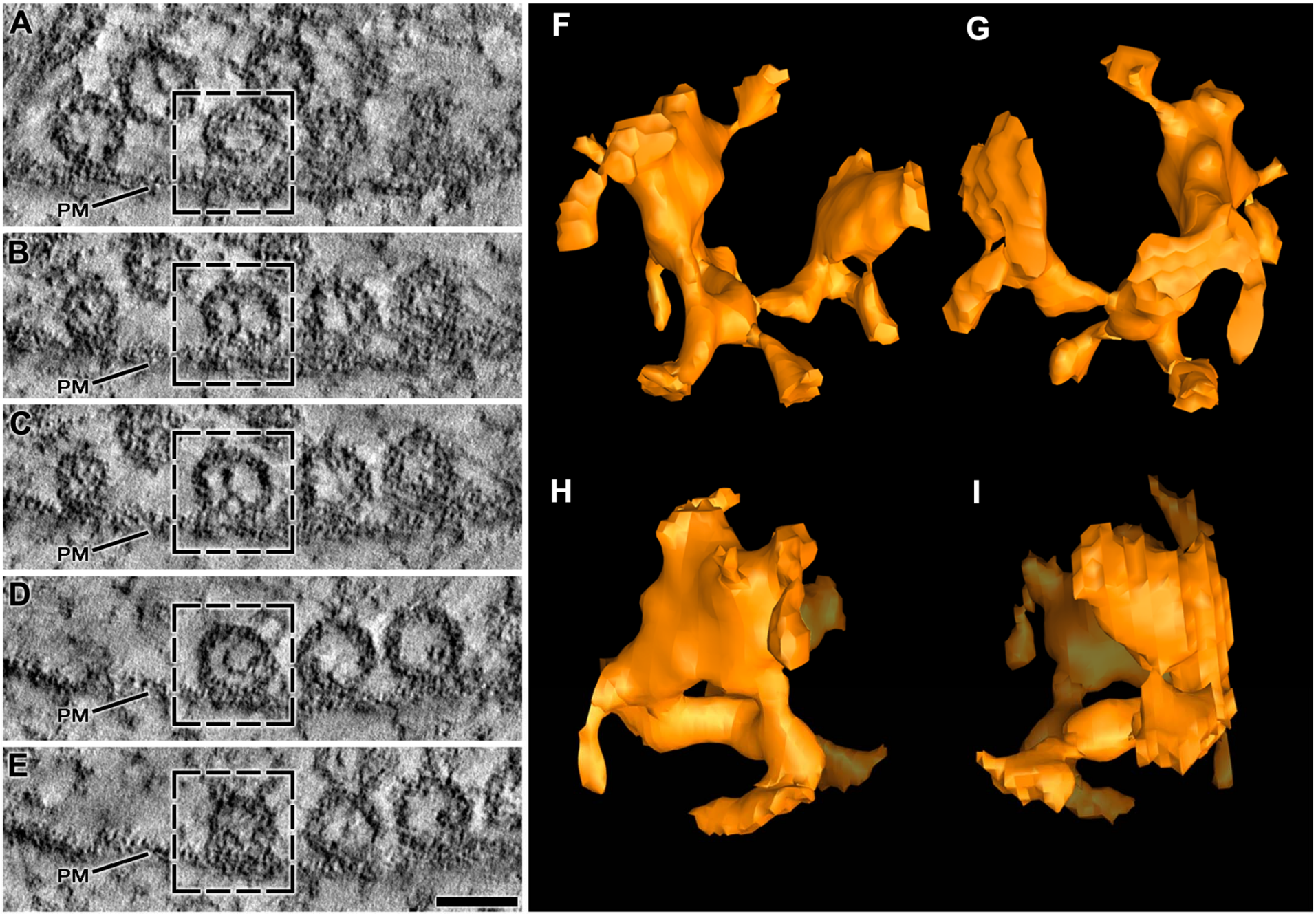
A Movie of High-resolution Surface Models of Structures at the Active Zone



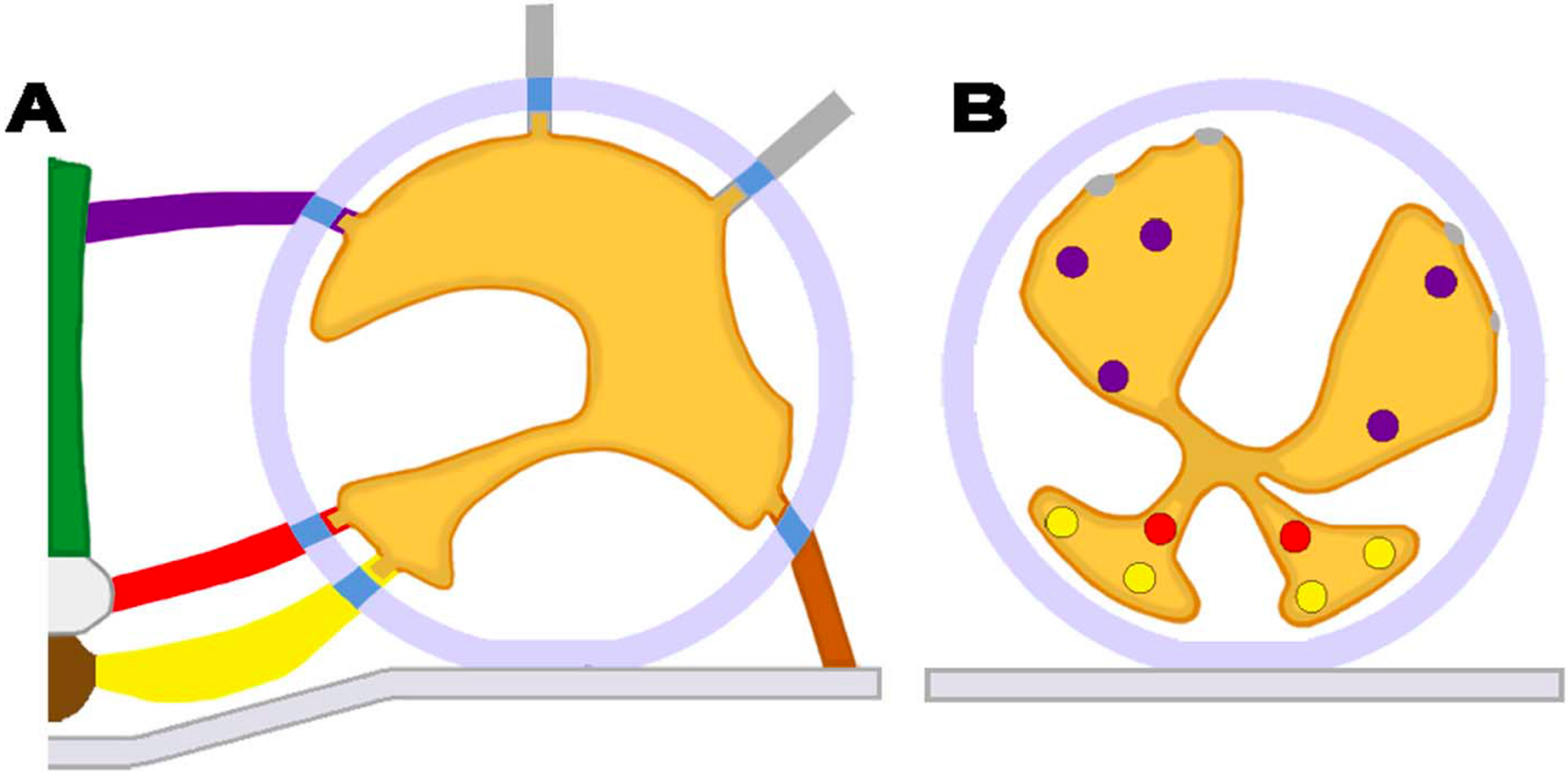
An Organization of the entire Active Zone Material at the Active Zone



An Organization of the Internal Structure inside a Synaptic Vesicle

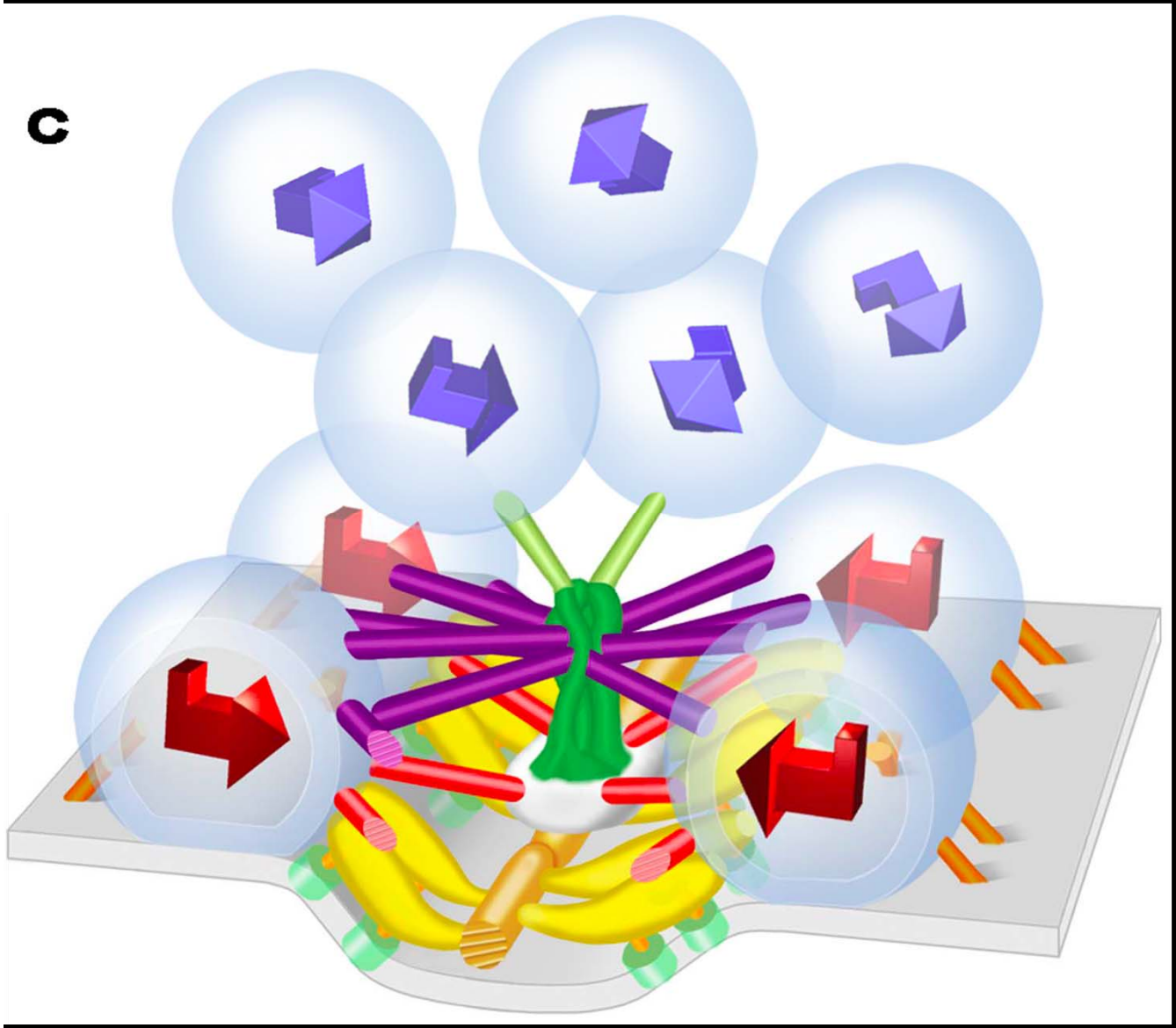


Linkage of the Internal Structure inside a Synaptic Vesicle with the Active Zone Material



Harlow ML, Szule JA, Xu J, Jung JH, Marshall RM, McMahan UJ. (2013) PLoS ONE 8(7): e69410. doi:10.1371/journal.pone.0069410

Organization of the Active Zone Material and Orientation of the Docked Synaptic Vesicles at the Active Zone



The findings based on our structural studies had required huge amount of time and effort from many colleagues (>10 years).

Jack McMahan
Jae Hoon Jung
Mark Harlow
David Ress
Joseph Szule
Jing Xu
Francisco F. de Miguel
Cornelia Stoschek
Mira Raman
David Yip

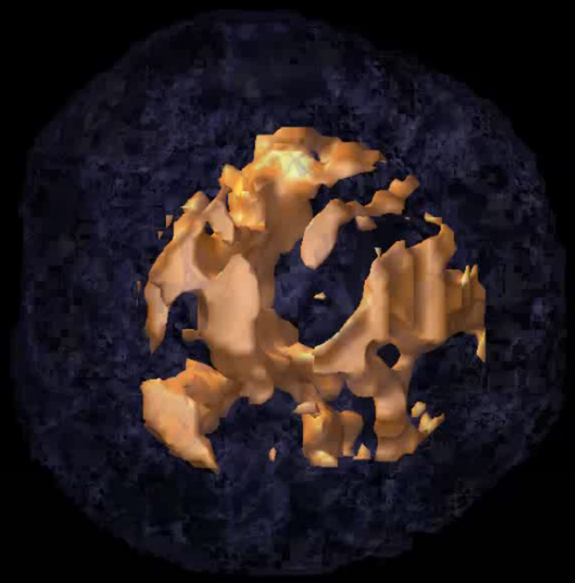
The procedure of structural analysis needs to be streamlined to handle increasingly growing large amount of volume data.

A Surface Model of Manually and Finely Segmented Internal Structure of a Synaptic Vesicle (>Weeks)

IDL TIFF file

Segmentation and surface model rendering require marked improvement to handle large volume data.

A Surface Model of Manually and Grossly Segmented Internal Structure of a Synaptic Vesicle (<hours)



IDL TIFF file

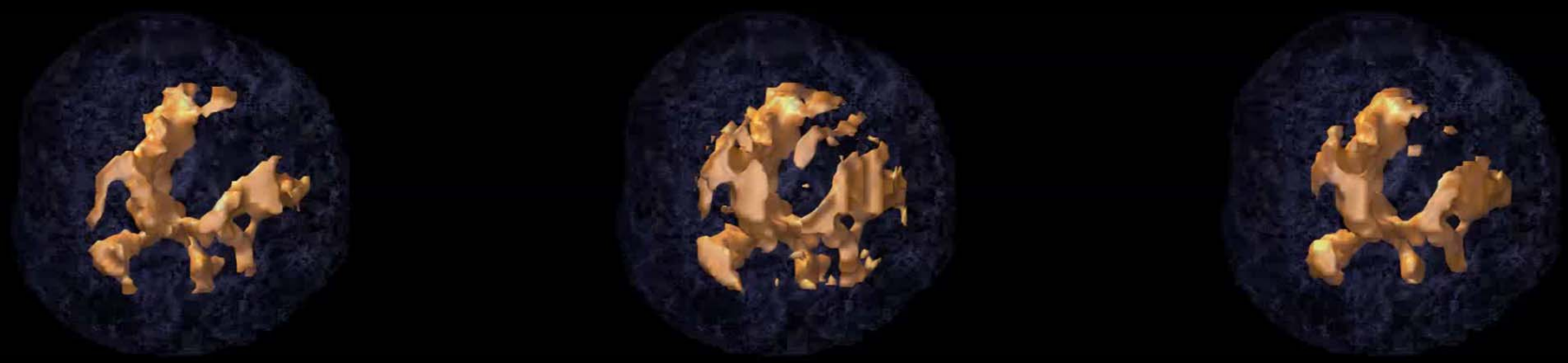
Gross segmentation and surface model generation are fast but noisy.

Automatically Refined Internal Structure of a Synaptic Vesicle after Gross Segmentation (~minutes)

IDL TIFF file

Automatic refinement of a gross segmented surface model is fast and decreases the noise level.

Automatic refinement of a grossly segmented structure enhances the efficiency of the processes of segmentation and surface model generation (>~100 fold)



Generally applicable to any structure in cells and materials for efficient structural analysis