



Presentation Abstract

Program#/Poster#: 853.1/G52

Title: The 3D structure of hippocampal extracellular space has sheets and tunnels

Location: Halls B-H

Presentation Time: Wednesday, Nov 17, 2010, 1:00 PM - 2:00 PM

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Abstract: The extracellular space (ECS) that surrounds synapses, axons, dendrites and glial cells in the neuropil is not as well studied or understood as intracellular compartments. First, the geometry is complex, consisting of tortuous passages that impedes diffusion. Second, EM images give an inaccurate picture because of tissue shrinkage during fixation and dehydration. We reconstructed the extracellular space inside a block of neuropil ($5 \times 6 \times 6 \text{ um}^3$) starting with a stack of 100 serial-section electron microscope images from adult rat hippocampus CA1 stratum radiatum. The reconstructed ECS from EM segmentation had a volume fraction of approximately 9%. Computational methods were used to expand the volume of the ECS to match the measured extracellular volume fraction (~20%). The geometry of the final reconstruction revealed an ECS structure composed of sheets with near uniform extracellular width (ECW) between pairs of cells punctuated by tunnels with ECW larger than the median at the junction of three or more cells. Half of the ECS volume is contained in sheets with a median extracellular width of 24 nm, and the other half is composed of tunnels with median extracellular width of 71 nm. The space between the sheets is likely to be filled with extracellular matrix and cell adhesion molecules that could impede the passage of molecules larger than 20 nm. In contrast, the tunnels form a network

surrounding the neurons and glial cells that could allow large molecules to travel long distances.

Disclosures: **J.P. Kinney:** None. **T.M. Bartol:** None. **B. Regner:** None. **C.L. Bajaj:** None. **K.M. Harris:** None. **T.J. Sejnowski:** None.

Keyword(s): EXTRACELLULAR
NEUROFIL
DIFFUSION

[Authors]. [Abstract Title]. Program No. XXX.XX. 2010 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience, 2010. Online.

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