A Virtual Reality Model of the Rat Hippocampus From Magnetic Resonance Microscopy Image Stacks

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The hippocampus is an important region of the mammalian brain that has been implicated in a variety of cognitive functions, including the consolidation of episodic and declarative memories in humans, and spatial navigation in rodents. A great deal of experimental data has been accumulated on hippocampal anatomy, electrophysiological, and behavioral involvement. Yet, the link between structure, activity, and function in the hippocampus at the cellular and system level is far from understood. The hippocampus proper consists of two interposed cortical folds, namely the dentate gyrus (DG), and the Cornu Ammonis, often divided in regions CA3 and CA1 on the basis of cellular connectivity. Each of these regions is itself constituted by three layers that correspond to the organization and orientation of the principal cells' dendritic fields. The DG principal neurons, granule cells, project their dendrites in the molecular (outer) layer, and axons in the hilus (inner layer). The CA principal neurons, pyramidal cells, project their basal dendrites and axonal hillocks in the oriens (outer) layer, and apical dendrites in the radiatum (inner) layer. Granule cells receive synaptic inputs from the Entorhinal cortex, and project to CA3. CA3 neurons project to CA1, and CA1 neurons project back to the Entorhinal cortex, both directly and through the Subiculum. All of these pathways, as well as the additional commissural and extrinsic connections, and the local interneuronal network, are highly layer-specific.

In order to build a quantitative representation of this complex anatomical organization, we are creating a virtual reality model based on high-resolution experimental data. Here we present the computational approach to the 3D surface and volume reconstruction of the hippocampus based on image stacks from ex-vivo micro MRI of a rat brain. From each image, the contours of the DG granular and molecular layers, and of the CA pyramidal and oriens layers, are semi-manually traced using the SynapseWeb IGL_Trace tool (http://synapses.mcg.edu). With this step, all external and internal hippocampal boundaries are acquired based on contrast (water content), using standard rat atlases (Swanson's and Paxinos') as validation references. Surface rendering of the resulting stack of contours (pixel-based closed polygons) is achieved by means of an iso-surface extraction algorithm, namely the Regularised Marching Tetrahedra (http://mi.eng.cam.ac.uk/~gmt11/research/volume.html). Finally, the 3D surfaces are volume-rendered by sequentially applying an algorithm to find all the points inside the closed polygons in each section.

The resulting VRML model is suitable for the integration and visualization of cellular level details, by incorporating fully reconstructed and digitized neurons in the appropriate volumes, and by algorithmically orienting the dendritic principal axes with respect to the curvature of the tissue. The addition of projecting axons to this construct constitutes an original example of the potential of this approach for the elucidation of the relationship between system and cellular level neuroanatomy that underlies network connectivity.

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