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## The other cortex: surface-based analyses of the hippocampus

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The hippocampus (or archicortex) has a complex folded laminar structure that can be fully appreciated in the multiplanar views afforded by 3D BigBrain [1]. Here, we will look at how analysis of the hippocampus and hippocampal subfields can be performed using the same principles as surface-based analysis of the neocortex and neocortical parcels [2]. That is, at high resolution the various folds or ‘digitations’ within the hippocampus resemble neocortical gyrifications. By carefully fitting a surface to these folds, we extract depth-wise profiles of neuronal distributions across the 3D BigBrain hippocampi. Two complementary sets of results show that: i) within the hippocampus, unsupervised clustering of these profiles yields boundaries that almost perfectly overlap with the classical definitions of hippocampal subfields [3], and, ii) between the hippocampus and neocortex, there exists a continuum or gradient of changes in profile similarity, with greatest complexity in the neocortex [4].

In the domain of MRI, spatial resolution is considerably lower but with strong prior information a surface can accurately fit the folds of the hippocampus along its natural anterior-posterior and medial-lateral 2D axes [5]. Using MRI data from the Human Connectome Project dataset [6], we show that structural measures track the hippocampus’ medial-lateral axis, whereas resting state connectivity (rsfMRI) tracks its anterior-posterior axis. That is, examining structural measures like thickness, gyrification, and curvature, there are clear differences across the medial-lateral extent of the hippocampus in line with the hippocampal subfields. However, the primary differences in functional connectivity are aligned along the anterior-posterior axis of the hippocampus in a geodesic fashion. That is, the anterior hippocampus tends to show greater connectivity with anterior temporal and inferior frontal regions of the neocortex, whereas the posterior hippocampus tends to show greater connectivity to the anterior cingulate, medial visual, temporal-parietal junction, and lateral frontal neocortex.

Together these results present a simple model for understanding the hippocampus: it shows a stereotyped microstructure across its medial-lateral axis that repeats across its anterior-posterior axis with different input/output connectivity to the rest of the brain. This organizing principle is obviated by treating the hippocampus as a 2D folded structure with two natural geodesic axes rather than as a subcortical volume with subfields as subvolumes, as in many previous works.

### References

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