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Mapping superficial white matter architecture on BigBrain

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INTRODUCTION.
The superficial white matter (SWM) is the layer of white matter (WM) located immediately underneath the cortex. This SWM contains subcortical U-fibers interconnecting adjacent brain gyri, which remain incompletely myelinated until later in life [1]. U-fibers play a key role in brain plasticity and aging, and alterations in these fibers have been observed in conditions such as autism, epilepsy, and Alzheimer's disease [2,3,4]. Despite its importance, the SWM has been understudied, primarily due to technical difficulties and limitations [5]. Recent advances in ultra-high field 7 Tesla magnetic resonance imaging (MRI) technology have enabled precise imaging and mapping of brain microstructure, leading to reliable research on the SWM. However, the structural and functional role of the SWM is still unclear and histological data could improve the understanding of these relationship. Specifically, BigBrain histological data could unravel complex microstructural properties by characterizing changes in intensity related to the SWM oligodendroglia organization5. In this regard, this study assesses histological features of the SWM, and evaluate its association to macroscale motifs of brain organization.

METHODS.
We preprocessed BigBrain histology data by correcting the outliers in temporal poles and intensity changes along the y-axes. To examine the SWM, we solved the Laplace equation over the WM domain. This was achieved by initially computing a Laplace field across the WM and subsequently shifting an existing WM surface along that gradient. Stopping conditions were set by the geodesic distance traveled. SWM surfaces were sampled at fifty depths, each separated by 0.06 mm, beneath the gray and white matter interface. The microstructure intensity profiles, depicting the intensity values of BigBrain features, are presented in Fig. A. Additionally, we sample the gray matter intensities to correlate the gray matter profile with its SWM at each vertex. Finally, we applied diffusion map embedding (DM), a non-linear dimensionality reduction on the data. Vertex-wise intensity profiles were cross-correlated, resulting in microstructural profile covariance (MPC) matrices that represent vertex-specific similarity in histological feature across the SWM. The MPC matrix was converted to a normalized angle affinity matrix, and diffusion map embedding was applied. This procedure identified eigenvalues (gradients) describing the main spatial axes of variance in inter-regional similarity of microstructural profiles. Gradient analyses were conducted using BrainSpace [6].

RESULTS
The spearman correlation between the gray matter and SWM intensity changes of BigBrain shows a positive pattern for most areas of the brain except the medial insula. (Figure A, bottom). After we applied DM, we observe that the two first eigenvalues or "gradients"explained ~75% of the variance. The principal gradient differentiated highly myelinated areas, like motor and pre-motor cortes from association areas (e.g. parieto-temporal and middle and superior frontal lobe).

CONCLUSIONS
We generated precise and reproducible SWM surfaces and proposed a novel method to study the cytoarchitectural similarity of the SWM on BigBrain. We observed a continuum between the gray matter lamination and the SWM structure that distinguishes it from the deep white matter. With this study, we open a new window to extend further cytoarchitectural studies to include the SWM.

Primary author: HWANG, Youngeun (McGill University)

Co-authors: Dr EVANS, Alan (McGill University); Dr BERNHARDT, Boris (McGill University); Dr TARDIF, Christine (McGill University); Dr RUDKO, David (McGill University); Ms CABALO, Donna (McGill University); Dr LEPPERT, Ilana (McGill University); Dr DEKRAKER, Jordan (McGill University); Dr RODRIGUEZ-CRUCES, Raul (McGill University); Ms THEVAKUMARAN, Risavarshni (McGill University)

Presenter: HWANG, Youngeun (McGill University)

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