Spatial scale estimation of columnar neuronal activity in cats' visual cortex based on the analysis of ultra-high-resolution CBV-weighted fMRI

X. Chen[1], F. Zhao[2], S-G. Kim[2], J. Tkach[1], and S. Strother[3,4]

[1]Radiology, Case Western Reserve University, Cleveland, Ohio, United States, [2]Neurobiology, University of Pittsburgh, Pittsburgh, PA, United States, [3]Rotman Research Institute, Baycrest, Toronto, Canada, [4]Medical Physics, University of Toronto, Canada

Introduction: With the development of high resolution functional MRI (fMRI), there has been increased interest in exploring the spatial scale of the structure of neural representations. Estimation of these spatial scales is often critical in neuro-imaging studies. On the one hand, the spatial scale plays an important role in determining the optimal size of spatial smoothing filters in post processing. On the other hand, the fMRI resolution that should be used to explore particular brain regions depends on the scale of the associated functional architecture. Using higher-resolution fMRI, more microscopic structures may be revealed in brain areas that are functionally homogeneous with standard lower resolution fMRIs [1]. In this study, we demonstrate a framework to estimate the spatial scale of columnar neuronal activity in a cat's primary visual cortex based on the analysis of ultra-high-resolution CBV-weighted fMRI data.

Materials and Methods: CBV-weighted fMRI signals were obtained in a 1-*mm* thick slice tangential to the surface of the cortex containing visual area 18, using gradient-echo data collection (in-plane resolution=0.15 x 0.15 mm^2, TE/TR=10*ms*/2*s*) at 9.4 *Tesla* after injection of MION contrast in an anesthetized cat [2]. Stimuli consisted of high-contrast moving gratings at two orthogonal orientations (0º vs. 90º or 45 º vs. 135º). Each epoch consisted of 10 baseline, 10 stimulus, and 9 baseline scans. Epochs for each of the orthogonal orientations were repeated about 40 times with a 30 second break between adjacent epochs. To avoid the non-stationary caused by injecting more contrast agent in the middle of the experiment, the data for 0º vs. 90º and 45 º vs. 135º were each split into 2 separate datasets, for a total of 4 datasets with a similar number of epochs at both orientations.

For each of the 4 datasets the NPAIRS software package[3] was used to perform a preliminary agnostic canonical variate analysis (aCVA) [4]. The aCVA identified HRF transient state scans that were removed before creating new datasets of smoothed images using Gaussian filters with 16 different FWHMs ranging from 0.0 to 1.0(mm). Within NPAIRS all epochs in each dataset were split, 25 times, into two independent split-half sets, each with same number of epochs at both orientations. For each split-half set, GLM analysis with the contrast and design matrix illustrated in **Fig.1A** was applied to the visual cortical area of the CBV data to investigate the differential iso-orientation pattern. By comparing the GLM results across independent split-half sets we extracted Z-scored SPMs and reproducibility metrics[3]. The reproducibility was compared across all FWHMs, and the highest reproducibility was defined as optimal.

For each of the 4 datasets, 100 new re-sampling datasets were also generated by bootstrapping the original dataset epochs100 times. The above mentioned procedure was applied to each of the new bootstrapped datasets to obtain the bootstrapped distribution of 100 optimal FWHMs.

A new data set of fMRI images with lower in-plane resolution of 0.225 x 0.225 mm^2 was also generated by down-sampling the K-space, and the procedure described above was also applied to this new dataset.

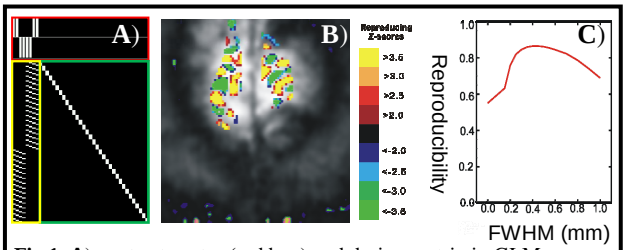

Fig.1, **A**) contrast vector (red box) and design matrix in GLM analysis; **B**) a GLM result based on a 0-90 º dataset smoothed by a Gaussian filter with FWHM of 0.45*mm*; **C**) Reproducibility as a function of the FWHM of the Gaussian smooth filter.

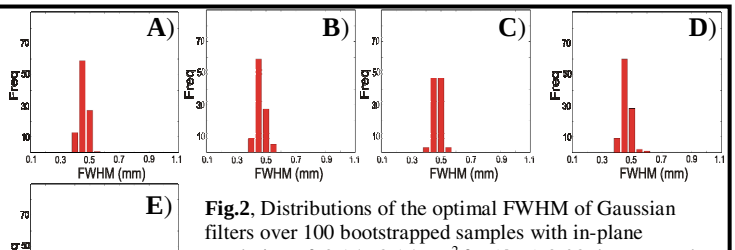

Fig.2, Distributions of the optimal FWHM of Gaussian filters over 100 bootstrapped samples with in-plane resolution of 0.15× 0.15 mm^2 for (**A**,**B**) 0-90 datasets and (**C**,**D**) 45-135 datasets; (**E**) Distribution of optimal FWHM for 0-90 dataset with resolution of 0.225× 0.225 mm^2.

Results and Discussion: Both **Fig.1B** and **Fig.1C** are based on dataset 1 of 0 º vs. 90 º. **Fig.1B** illustrates the differential columnar response to the stimulation at each orientation, with complementary iso-orientation spatial patches (Green=0 º, yellow=90 º) in the visual cortical area. **Fig. 1C** illustrates the reproducibility as a function of FWHM. The profile of reproducibility peaks at FWHM ≈ 0.45 mm. Similar differential patterns and reproducibility profiles were found for other datasets.

Figure 2 illustrates the distribution of optimal Gaussian filter FWHMs over 100 bootstrapping samples for 0-90 º datasets (**A**, **B**) and 45-135 º datasets (**C**,**D**). For a specific orthogonal orientation pair, the distributions based on different datasets are very similar. **Fig. 2E** illustrates the distribution of optimal FWHM for 0-90 º with lower in-plane resolution of 0.225 × 0.225 mm^2. We've found that independent of the stimulation orientations, the MR in-plane resolution, and the dataset, the distribution of optimal FWHM peaks at FWHM=0.45*mm*. Based on the matched filter theorem, there must be some underlying structure in the visual cortex that has a similar spatial scale of 0.45mm. Considering that the hemodynamic point spread function is narrower than intercolumn distance [5], we believe that the spatial scale of columnar CBV response in cats' visual cortex is approximately 0.45mm and our analysis framework provides a new way to estimate the scale of cat columnar neuronal activity. Compared to the traditional method using autocorrelation, our method is better in the sense that 1) it estimates the average scale of the iso-orientation region instead of the intercolumn distance; 2) it does not depend on the position and direction of the line along which the signal profile is obtained.

Conclusion: We demonstrated an fMRI analysis framework that is able to estimate the spatial scale of the columnar neuronal activity in cats' visual cortex. This framework has the potential to be extended to estimate the spatial scale of other important neuronal activities.

Ref.: [1] Grill-Spector, et al., Nature Neoroscience 9 (9):1177-1185, 2006; [2] Zhao, et al., NeuroImage 27 :416-424, 2005; [3] Strother et al., NeuroImage 15 :747-771, 2002 ; [4] Chen et al.; HBM abstract 2005; [5] Fukuda et al., J. Neurosci. 26: 11821-32, 2006.This work was in part supported by NIH grants EB002013 and EB003324.