**METHODS**

The goal of the simulation study is to examine the validity of using principal component analysis for accurately predicting the V1 responses in real experimental settings. We incorporate experimental data and parameters from prior experiments whenever possible to achieve the highest level of realism. In particular appropriately simulating 1) the size and the geometry of the cortical activation and 2) the time courses should play important role when determining the success or failure of using PCA.

**SOURCE LOCALIZATION WITH MRI and fMRI**

The determination of the physiological geometry is performed with retinotopic f/MRI experiment (Ales et al. 2009). The f/MRI retinotopy is accurate to 2 mm of true activation, and should provide the simulation with ample realism. We have divided the 20 subjects into 2 groups. The first group (subjects 1 to 9) was presented with a stimulus with inner angle of 1.5 degrees and outer angle of 4 degrees. The latter group (subjects 10 to 20) was presented with the same stimulus in all aspects except for the overall size, which was 1.5 and 7 degrees inner and outer radius, respectively. Details regarding the f/MRI retinotopic experiment can be found in the methods section of Ales et al., 2009.

**THE PATCH FORWARD SOLUTION**

The bulk of detectable visual evoked potentials are generated by groups of pyramidal neurons located in layer 4 of the gray matter at the midpoint between the outer surfaces of the gray and the white matter. The pyramidal cells are organized in to columnar structures being aligned perpendicular to the cortical surfaces where they are located. Based on the physiology, the forward solutions **(F)** in our boundary element models are produced as follows. First, based on the individual T1-weighted MRI scans, 3-layer segmentation is generated defined by the surfaces of the scalp, gray, and white matter. The initial segmentation is performed using the Freesurfer software package (Dale et al., 1999; Fischl et al. 1999a) and resulted in approximately 150,000 mesh points per hemisphere at nearly uniform density. Typically, this number is sufficient for producing accurate and smooth cortical representation. Each mesh point is defined by the following properties:

1) a position vector from an arbitrary origin located at the center of the brain **(P)**

2) an orientation vector that denotes the normal to the cortical surface at the mesh position **(M)**

3) a scalar value denoting the area weights associated with the point **(a)**.

Note that if the discrete sampling of the cortical surfaces were done at exactly uniform density, then every area weighting value would be identical.

Generation of EEG lead fields **(L)** generally require the following: anatomical locations and orientations of sources, the conductivities of segmented layers, and the EEG sensors locations and co-registration information to align the sensors to the MRI coordinates. We have assumed the conductivities values of (XX, YY, ZZ) for the scalp, gray, and white matter segmentations as described in (XYZ, 1990) for all subjects. While individual variations in the conductivities exist, the selection of these representative conductivities is not expected to change the results of the simulation. The location of the EEG and co-registration information was collected during the original f/MRI experiment (Ales, 2009).

Ideally, we calculate the lead fields in the x-, y-, and z- directions for each anatomical mesh points available in the segmentation using the method described in (Nunez, 1990). The calculation of the lead field is computationally taxing, however, particularly for high throughput analyses involving multiple subjects. In an effort to balance the accuracies of forward solutions and the required computation time, we initially generate the lead fields only on a subset of the anatomical mesh points that we call the seed points. There are 10,242 seed points per hemisphere per subject. The calculation of the lead fields on the seeds was performed using MNE suite (Oostendorp and Van Oosterom, 1992).

To give a measure of mesh densities in physical dimensions, note that a 1 cm by 1 cm patch on the cortex is represented by approximately 170 mesh points. With the subsampling, approximately 12 of these are seeded, and contain their own calculated lead fields. The lead field values are then interpolated to all of the remaining mesh points. For operational simplicity, the interpolation is done with a routine that assumes the lead field value of the nearest neighboring seed. Due to the smoothness of the lead fields in the 3 cardinal directions, we believe this is a relatively accurate and fast interpolation scheme. The procedure produces sets of high density anatomical meshes with accurately interpolated forward solution and surface normal definitions.

To simulate the experimental data, we use the ‘patch forward solution.’ In many conventional simulation and source estimation studies, the M/EEG data is generated by simulating an equivalent dipole at a discrete location occupying zero physical area. In reality, a stimulus shown as a patch in visual field, such as multifocal dartboard, activates a measurable area on the visual cortex. The cortical patch representing the stimulus resides on a highly convoluted surface and the changes in orientation within its boundaries are complex and variable. The complexity and individual variability of these folding patterns must be taken into consideration when discussing the utility of source estimation methods. We suspect that simulating a dataset based on the activation of the entire cortical patch instead of the simplified equivalent dipole provides a more realistic method for simulating experimental data. (Hum brain mapping, George)

The increased realism of the forward model comes with a small computation cost since the calculation of patch forward solution is simple - the weighted sum of all individual forward solutions contained by the cortical patch. As an example, suppose a cortical patch representing a visual stimulus consists of *n* mesh points. Thus there are *n* associated individual lead fields L1, L2 … Ln, the orientation vectors M1, M2 … Mn, and the area weighting scalars a1, a2 … an. The forward solution per mesh point is the inner products between the normal vector and the lead field scaled by the area weighting values. The sum of all the contained forward solutions becomes the patch forward solution.

The use of patch forward solution brings up an important note about the necessity of opting for the high density lead fields. Because the patch forward solution sums up the signal contributions from discrete mesh points defined within the patch boundary, and because the orientations of these mesh points greatly affect the resulting forward solution, an insufficient spatial sampling could result in simulated topographies that are too unrealistically biased. By using all available orientation values that adequately reconstruct the cortical structures we can simulate the most realistic data available.

**SIMULATION OF EXPERIMENTAL DATA**

Stimulus

We simulate the EEG data in response to a check reversing 96-patch multifocal stimulus composed of 24 spokes and 4 rings (Figure. XYZ). The sizes of rings are increased from center to the outer most ring to account for cortical magnification. Due to the graduation of patch sizes based on eccentricities, the area of cortical activation is kept approximately constant for every patch. Each patch consists of 2 by 4 checks in tangential and radial directions with alternating white and black checks. The reversal of the checks produces visual evoked potential time locked to the reversal onset. Except for their respective spatial locations, every patch is assumed to be qualitatively identical and is expected to produce identical time course. We call this the “common response assumption” (CRA). For discussions about the validity of CRA, refer to the CRA section of the discussions.

The Activation Area

An important parameter in visual source simulation is the number and locations of active sources. The simulation should include the basic visual sources such as V1, V2, and V3, but depending on the experiment, should also account for external sources that involve other distant areas, such as the parietal or frontal sources. Peripheral sources would only be important if their activation is time-locked to the timing of the stimulus onset. In this study, we have examined the effectiveness of PCA for the simplified instances of having 1) only the three early visual sources V1, V2, and V3, or 2) the three visual sources with additional time-locked sources in the parietal areas.

The locations of visual sources are based on the retinotopy acquired from the fMRI studies. First, the outer boundaries of three visual areas are determined for the left and right hemispheres. Each visual area undergoes a series of sectioning to determine the appropriate active regions for each patch. The V1 area from the left hemisphere is first sectioned into two ventral and dorsal parts along the horizontal meridian, resulting in V1V and V1D. The V1V is sectioned into 4 equal parts in the direction of increasing eccentricities representing the four rings. It is further sectioned into 6 equal parts in the direction of increasing polar angles, representing the 6 wedges located upper-right visual field. These sectioning procedures are equivalently applied to all visual areas, namely V1V, V1D, V2V, V2D, V3V, and V3D for both hemispheres resulting in 96 cortical regions per visual source.

The Time Course

Accurate definition of neural responses to the stimulus is important. However, the time courses for the active sources are not easily obtainable for human visual experiments using non-invasive methods. The recent work by Ales et al. provides possibly the most accurate approximations of V1 and V2 visual sources using the multifocal dartboard stimulus to date. The V1 and V2 time courses estimated in their study is applied to the simulation for all subjects and patches. For V3, we have used a damped oscillator with natural frequency of 10 Hz, damping factor of 10, and peak latency at 100 milliseconds after the onset of the stimulus. For external parietal sources, another damped oscillator with the oscillation frequency 6 Hz, damping factor of 10, and the peak latency at 130 milliseconds. Since the true temporal dynamics of V3 and the external sources are unknown, we use these time courses as place holders. In accordance with the common response assumption, we apply the same set of time courses to all patches. The simulated time courses are normalized to 1.25, 1, 1 for V1, V2, and V3 respectively. The external sources are normalized to 0.1 or 0.5 for sensitivity analysis.

In this study, we show the results for simulations using signals with zero noise as it will allow for the most sensitive test of effectiveness of PCA. We have performed numerous multifocal dartboard stimulus experiments in the past, and due to the stability of VEP and repeatability of the experiments, very high levels of signal to noise ratio was shown to be readily attainable across all subjects in realistic settings.

Data Simulation

Given the patch forward solutions and the time courses, the data is simulated.

The symbols are p=patch index, e=sensor index, t=time index in samples, F= forward solution, T=evoked time response, V1-V3=visual source indices, and P=index for distant parietal source when active.

**DATA ANALYSIS**

Principal Component Analysis

The data analysis is performed with MATLAB. For PCA, we used the singular value decomposition (SVD) included in the standard version of MATLAB. SVD accepts a data matrix with e electrodes and t time samples, and outputs its decomposition as three 2 dimensional orthogonal matrices, and. The column vectors of U and C matrices, listed in the order of decreasing variances, have the physical interpretation of being the decomposed EEG sensor topographies and time response components, respectively. The data is collected for the 96 patches individually and thus the SVD analysis and data comparison can be performed on each individual patch independently. However, we have assumed common response assumptions during the data simulation and found it more appropriate to perform SVD after combining all existing patch data into a single ensemble dataset.