

# Comparison of randomized multifocal mapping and temporal phase mapping of visual cortex for clinical use



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## ABSTRACT

fMRI is becoming an important clinical tool for planning and guidance of surgery to treat brain tumors, arteriovenous malformations, and epileptic foci. For visual cortex mapping, the most popular paradigm by far is temporal phase mapping, although random multifocal stimulation paradigms have drawn increased attention due to their ability to identify complex response fields and their random properties. In this study we directly compared temporal phase and multifocal vision mapping paradigms with respect to clinically relevant factors including: time efficiency, mapping completeness, and the effects of noise. Randomized, multifocal mapping accurately decomposed the response of single voxels to multiple stimulus locations and made correct retinotopic assignments as noise levels increased despite decreasing sensitivity. Also, multifocal mapping became less efficient as the number of stimulus segments (locations) increased from 13 to 25 to 49 and when duty cycle was increased from 25% to 50%. Phase mapping, on the other hand, activated more extrastriate visual areas, was more time efficient in achieving statistically significant responses, and had better sensitivity as noise increased, though with an increase in systematic retinotopic mis-assignments. Overall, temporal phase mapping is likely to be a better choice for routine clinical applications though random multifocal mapping may offer some unique advantages for selected applications.

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## 1. Introduction

Functional magnetic resonance imaging (fMRI) is being used increasingly for mapping key brain structures prior to surgical treatment of tumors and other types of focal pathology. In such applications, the goal is to identify viable areas of the brain that might be at risk of damage due to resection, radiation or other invasive treatment. For tumors of the occipital lobe or adjacent portions of the parietal or temporal lobes, damage to visual cortex can cause partial or complete blindness or other disruptions of visual perception (Martin et al., 2012).

### 1.1. Temporal phase mapping

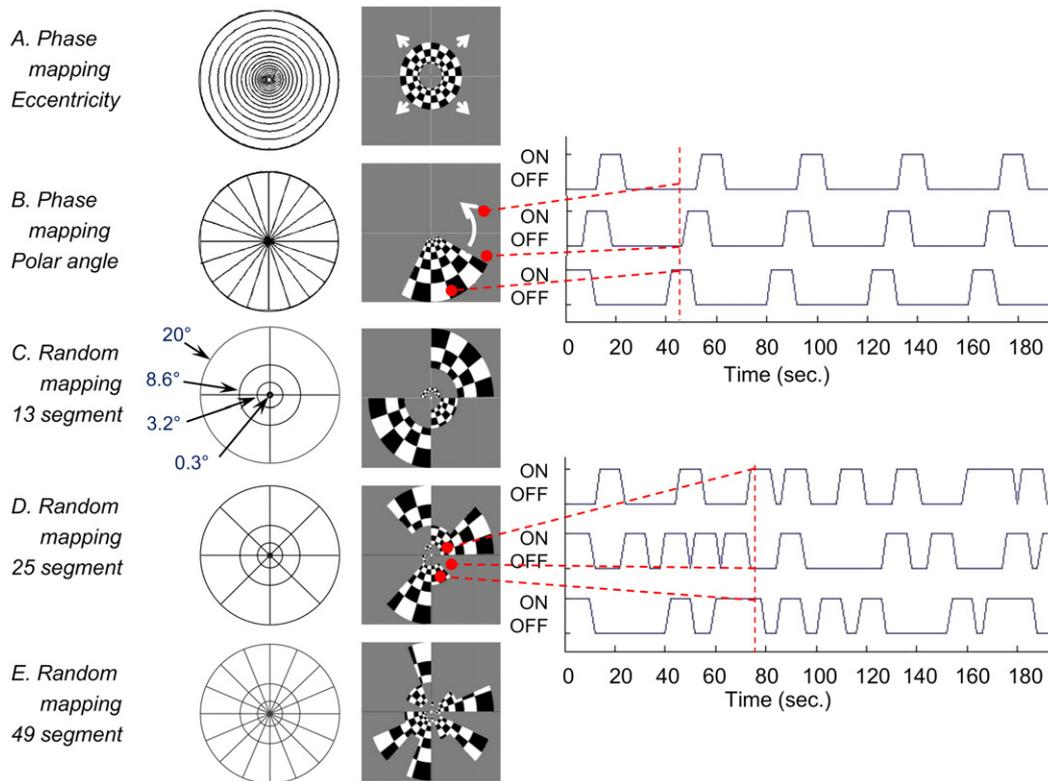
Conventionally, cortical maps of the visual field are charted using a temporal phase mapping technique that consists of a rotating checkered wedge, or an expanding checkered ring stimulus (Fig. 1A, B) (DeYoe et al., 1996; Engel et al., 1994, 1997; Sereno et al., 1995). Temporal

phase mapping can evoke robust responses in primary visual cortex (V1) and a number of extrastriate visual areas. Moreover, the checkered ring stimulus can identify cortical locations that support central vision, which if damaged can impair reading and other critical visual functions. The ability to identify the representation of central vision makes temporal phase mapping particularly useful for pre-surgical planning and generally superior to simple flashed checkerboards or pulsed lights (DeYoe et al., 2011). It is also time efficient in that all eccentricities or polar angles throughout the visual field can be mapped in less than 4 min. Temporal phase mapping has been used in a variety of clinical disorders, including inherited photoreceptor abnormalities (Baseler et al., 2002), amblyopia (Conner et al., 2007), glaucoma (Duncan et al., 2007a), albinism (Hoffmann et al., 2003), achiasma (Hoffmann et al., 2012; Sinha and Meng, 2012), scotoma (Sunness et al., 2004), long-period deprivation of visual input (Levin et al., 2010) and developmental reorganization of cortical visual field maps (Muckli et al., 2009). It has also played an important role in the ongoing debate over cortical plasticity (Baseler et al., 2011).

As illustrated in Fig. 1A and B, the fMRI signals produced by temporal phase mapping are periodic waveforms that are distinguished from each other by their temporal phases. As the wedge/ring sweeps through each visual field location, fMRI activation sweeps through retinotopically corresponding locations in visual cortex. The timing of the activation at a particular brain voxel is determined by the distance of a voxel's

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**Fig. 1.** Visual stimuli. A. Phase-based eccentricity mapping. Left to right: outlines of elementary ring steps; sample stimulus image composed of 4 elementary rings at one time point. B. Phase-based polar angle mapping. Left to right: outlines of 20 elementary wedge steps; sample stimulus image composed of 5 elementary wedges at one time point; stimulation sequences for three visual field locations indicated by red dots. C–E. Random multifocal stimuli for 13, 25 and 49 segments. D. (right) Three stimulation sequences associated with three visual field locations indicated by red dots.

“population receptive field” (pRF) (Dumoulin and Wandell, 2008) from the stimulus onset location plus a delay due to the sluggish hemodynamic mechanism responsible for the fMRI signal. Consequently, the ability to precisely locate the pRF of a given voxel is limited by the accuracy of the estimation of the temporal properties of the signal and the variability of the local hemodynamics. Computing the temporal phase of the fMRI signal is typically accomplished by cross-correlation with a reference waveform (e.g. sinusoid) (Bandettini et al., 1993; Saad et al., 2003) or through Fourier analysis (Boynton et al., 1996; Engel et al., 1997). Removing the additional phase delay caused by the BOLD hemodynamics can be achieved with fMRI scans using two stimuli moving in opposite directions, such as clockwise versus counterclockwise rotating wedges or expanding versus contracting rings (Serenó et al., 1995). For each voxel, the phases obtained with stimuli moving in opposite directions can be averaged to cancel out the phase shift caused by the hemodynamic delay. The resulting corrected time series can then be averaged across repetitions for improved signal-to-noise ratio (SNR).

The dependence of temporal phase mapping on precise timing of the fMRI signal makes it susceptible to signal distortions. Though correlation methods often used with temporal phase mapping can provide good immunity to some types of pulse or burst noise, other types of noise can blur the small phase difference of responses evoked by adjacent visual field locations, thus introducing errors in preferred stimulus location. In addition, if a voxel contains a mixture of neurons with spatially distinct receptive fields, as can occur for a voxel straddling a sulcus, then the voxel's response will be a sum of multiple (approximate) sinusoids having the same period but different phases. Such a sum, if non-zero, results in a single sinusoid with an erroneous phase that is intermediate between those of the true individual components. As a result, the estimated preferred stimulus location for that voxel will also be in error.

## 1.2. Randomized multifocal mapping

A potential solution to the problem of temporal distortion is to use a code-based mapping paradigm such as randomized multifocal stimulation. Fig. 1C–E illustrates multifocal visual stimuli consisting of multiple checkered segments that are each presented in a unique randomized temporal pattern. Multifocal stimulus paradigms have been used to explore visual cortex using a variety of neurophysiological techniques including visual evoked potentials (VEP) (Baseler et al., 1994; Slotnick et al., 1999), magnetoencephalography (MEG) (Tabuchi et al., 2002), and fMRI (Hansen et al., 2004; Vanni et al., 2005). In this approach, the stimulus segments to which a voxel responds can be identified by the unique ON/OFF pattern of the fMRI response. In other words, each stimulus sequence can be viewed as a unique temporal code for a specific region of the visual field. To identify which stimulus segments activate a particular voxel, a conventional multiple regression analysis can be employed with the unique time series of each stimulus segment used as a regressor (Ward, 2006).

Multifocal mapping has been tested in clinical applications including post-surgical mapping of primary visual cortex (Vuori et al., 2012), and the measurement of training-induced changes in the cortical representation of a hemianopic field (Henriksson et al., 2007). It has also been suggested that multifocal mapping might save time compared to the individual presentation of multiple static stimuli which could be beneficial for scanning elderly glaucoma patients (Duncan et al., 2007b).

One potentially important advantage of multifocal mapping is its ability to correctly identify voxels that respond to multiple separate locations in the visual field. Moreover, the unique ON/OFF ‘digital code’ associated with each stimulus segment potentially makes multifocal mapping more tolerant of temporal distortions. Indeed, computational simulations indicate that a random multifocal stimulus paradigm can

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