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High-throughput optogenetic functional magnetic resonance imaging with parallel computations

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HIGHLIGHTS

- A system enabling fast, high-throughput ofMRI studies is proposed.
- Highly optimized and massively parallel algorithms process 3D images in 12.80 ms.
- Enabled future real-time integration of advanced reconstruction and automatic registration.
- Higher effective temporal resolution is demonstrated by detection of initial dips.
- Proposed faster and more accurate parallel motion correction algorithm.

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ABSTRACT

Optogenetic functional magnetic resonance imaging (ofMRI) technology enables cell-type-specific, temporally precise neuronal control and the accurate, in vivo readout of the resulting activity across the entire brain. With the ability to precisely control excitation and inhibition parameters and accurately record the resulting activity, there is an increased need for a high-throughput method to bring the ofMRI studies to their full potential. In this paper, an advanced system facilitating real-time fMRI with interactive control and analysis in a fraction of the MRI acquisition repetition time (TR) is proposed. With high-processing speed, sufficient time will be available for the integration of future developments that further enhance ofMRI data or streamline the study. We designed and implemented a highly optimised, massively parallel system using graphics processing units (GPUs), which achieves the reconstruction, motion correction, and analysis of 3D volume data in approximately 12.80 ms. As a result, with a 750 ms TR and 4 interleaf fMRI acquisition, we can now conduct sliding window reconstruction, motion correction, analysis and display in approximately 1.7% of the TR. Therefore, a significant amount of time can now be allocated to integrating advanced but computationally intensive methods that improve image quality and enhance the analysis results within a TR. Utilising the proposed high-throughput imaging platform with sliding window reconstruction, we were also able to observe the much-debated initial dips in our ofMRI data. Combined with methods to further improve SNR, the proposed system will enable efficient real-time, interactive, high-throughput ofMRI studies.

1. Introduction

The ofMRI technology enables the systematic probing of brain circuitry with cell-type specific and temporally accurate control, while monitoring whole-brain network responses in vivo (Lee, 2012, 2011; Lee et al., 2010). The ability to control neurons with high specificity and an accurate readout, reflecting neural activity location and temporal firing patterns, provides an unprecedented opportunity to understand the whole brain neural network function. However, the increased degree of freedom in control (Fig. 1) and accurate readout requires a high-throughput method that can accelerate discoveries using ofMRI. To mediate high-fidelity ofMRI and provide potential for the future integration of more advanced methods to further improve the ofMRI image quality and efficiently streamline ofMRI studies, we propose a GPU-based

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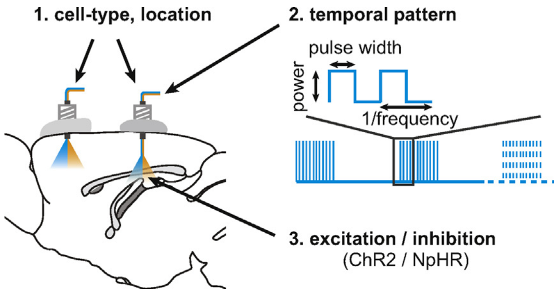

Fig. 1. ofMRI studies offer high degree of freedom in neural control. With ofMRI, the neural population is specifically controlled based on cell type, location, and temporal firing pattern. These cells can be specifically excited or inhibited, while whole brain responses can be observed with spatio-temporal accuracy. Thus, there is an important need to have the intelligent selection of control parameters through real-time feedback, which will accelerate scientific discovery in ofMRI studies.

parallel high-speed system enabling data reconstruction, motion correction, and analysis for a 3D volume in approximately 12.80 ms. With this high speed, the remaining time within a MRI acquisition repetition time (TR) can be used to integrate techniques such as iterative reconstruction (Fessler, 2007) for higher image quality, automatic segmentation (Lee et al., 2008b), anatomy/atlas registration, and brain connectivity analysis. Moreover, the high processing speed will increase the robustness of the studies, facilitating swift system recovery from potential operating system scheduling and network delays.

Since Cox et al. (1995) first published a real-time fMRI (rtfMRI) cumulative correlation analysis method in 1995, many different aspects of rtfMRI has been explored, e.g., real-time analysis (Bagarinao et al., 2003; Esposito et al., 2003; Gembris et al., 2000), real-time motion correction (Cox and Jesmanowicz, 1999), and real-time applications, such as brain machine interface and clinical diagnosis (Caria et al., 2011; Cohen, 2001; deCharms, 2008; Lee et al., 2009; Voyvodic, 1999; Weiskopf et al., 2004). Most of these widely used rtfMRI techniques are designed to reconstruct and analyse fMRI images after a complete 3D volume acquisition with a relatively long response time requirement. However, considering the future integration of advanced but typically computationally intensive techniques needed for the ofMRI studies to improve image quality and efficiency, we sought to further increase processing speed.

Real-time motion correction is also a critical part of the high-throughput interactive fMRI system. Because motion correction is typically an iterative process, most of the current algorithms are designed for offline processing (e.g. AIR, FSL and SPM (Friston et al., 1995; Jenkinson et al., 2002; Woods et al., 1992)). AFNI (Cox and Jesmanowicz, 1999) offers real-time motion correction at an approximately 51.31 ms/volume speed. We attempted to achieve even faster motion correction in order to optimise for future integration with computationally intensive processing.

In recent years, the GPU, which is rapidly evolving for massively parallel computations and devotes more transistors to computation than CPUs, has shown increasing potential for high-throughput rtfMRI systems. Many remarkable GPU speed increases have been reported (Ansorge et al., 2009; Eklund et al., 2010; Huang et al., 2011; Ruijters et al., 2008; Shams et al., 2010; Stone et al., 2008). Based on these successful results, we designed and optimised a series of new parallel algorithms for the GPU platform.

Using the proposed system, ofMRI studies can potentially be conducted with high efficiency, and optogenetic modulation parameters such as stimulation frequency, wavelength, power and pulse width can be controlled through live and accurate feedback from the impact of each stimulation across the entire brain. Tested on averaged high SNR phantom and ofMRI datasets, robust performance with high speed and accuracy was achieved in our system. Using sliding window reconstruction (Nayak et al., 2004; Riederer et al., 1988) in our proposed system, higher effective temporal resolution is achieved and the much-debated initial dips are also observed in our ofMRI data. Although initial dips can also be observed through offline sliding window reconstruction, the ability to perform this computationally intensive calculation in real-time clearly demonstrates the potential of our high-throughput system for future integration of advanced techniques to further improve ofMRI image quality and study throughput. In the following sections, detailed methods, analyses, results, and discussions are presented.

2. Methods

2.1. System architecture

We implemented the proposed high-throughput ofMRI algorithms on a custom-built parallel workstation connected to a 7 T Bruker Biospec MRI scanner (Fig. 2). Three levels of simultaneous processing were implemented on the high-throughput ofMRI workstation CPU threads. In level one, the raw data is received through a reliable Ethernet transmission protocol and pre-processed using a baseline correction method. In the second level, the pre-processed raw data is real-time reconstructed, motion corrected, and analysed through the proposed GPU-based massively parallel algorithms. At this level, we design the CPU thread as a master process that allocates parallel computing tasks to the slave GPU. In level three, the processed real-time images are displayed with analysis results.

2.2. Image acquisition pulse sequences

We utilised two types of MRI acquisition pulse sequences for our real-time scanning: a gradient recalled echo (GRE) multi-slice, interleaved-spiral readout sequence and a balanced steady-state free precession (b-SSFP) three-dimensional, interleaved stack-of-spiral readout sequence (Lee et al., 2008a, 2003; Miller et al., 2006; Scheffler and Lehnhardt, 2003). Spiral readouts were selected to achieve large volume coverage with high sampling speed. In addition, the interleaved acquisition provides the advantage of enabling high temporal resolution sliding window reconstruction (Meyer et al., 1992).

The GRE sequence was designed with a TR and echo time (TE) of TR/TE = 750/12 ms and a 30° flip angle. A total of 23 four-interleaf coronal slices (11.5 mm slice direction coverage) were obtained every 3 s. The b-SSFP sequence was designed to have TR/TE = 9.375/1.5 ms and a flip angle of 30°. A total of 32 ten-interleaf slices (16 mm slice direction coverage) were acquired every 3 s. The in-plane field of view (FOV) was 35 mm × 35 mm with a 0.5-mm slice thickness for both sequences. The GRE BOLD and b-SSFP data were reconstructed into 128 × 128 × 23 and 128 × 128 × 32 matrix-size images, respectively with a 0.273 mm reconstructed voxel size in both the x and y directions.

2.3. Reconstruction

2.3.1. Parallel gridding

In contrast to the data-driven conventional gridding method (Jackson et al., 1991) (Fig. 3a) that conducts convolutions sample by sample, our memory conflict-free gridding algorithm (Fig. 3b) calculates each Cartesian grid value in parallel using the following formula:

$$M_{grid}(m,n) = \sum_i (M_{spiral}(u_i, v_i) \cdot (w(u_i, v_i) \cdot C(m - u_i, n - v_i))) \quad (2.1)$$