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# Q1 [MEG]PLS: A pipeline for MEG data analysis and partial least squares statistics

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## ABSTRACT

The emphasis of modern neurobiological theories has recently shifted from the independent function of brain areas to their interactions in the context of whole-brain networks. As a result, neuroimaging methods and analyses have also increasingly focused on network discovery. Magnetoencephalography (MEG) is a neuroimaging modality that captures neural activity with a high degree of temporal specificity, providing detailed, time varying maps of neural activity. Partial least squares (PLS) analysis is a multivariate framework that can be used to isolate distributed spatiotemporal patterns of neural activity that differentiate groups or cognitive tasks, to relate neural activity to behavior, and to capture large-scale network interactions. Here we introduce [MEG]PLS, a MATLAB-based platform that streamlines MEG data preprocessing, source reconstruction and PLS analysis in a single unified framework. [MEG]PLS facilitates MRI preprocessing, including segmentation and coregistration, MEG preprocessing, including filtering, epoching, and artifact correction, MEG sensor analysis, in both time and frequency domains, MEG source analysis, including multiple head models and beamforming algorithms, and combines these with a suite of PLS analyses. The pipeline is open-source and modular, utilizing functions from FieldTrip (Donders, NL), AFNI (NIMH, USA), SPM8 (UCL, UK) and PLScmd (Baycrest, CAN), which are extensively supported and continually developed by their respective communities. [MEG]PLS is flexible, providing both a graphical user interface and command-line options, depending on the needs of the user. A visualization suite allows multiple types of data and analyses to be displayed and includes 4-D montage functionality. [MEG]PLS is freely available under the GNU public license (<http://meg-pls.weebly.com>).

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## Introduction

In recent years, the theoretical and empirical focus of neuroscience has extended beyond the activity of individual brain regions to large-scale spatiotemporal patterns and neural interactions (McIntosh, 2000). There is a growing recognition that neural dynamics unfold over multiple scales of time and space (Honey et al., 2007), and that network interactions play an important role in cognition and behavior (McIntosh, 1998; Bressler and McIntosh, 2007).

Magnetoencephalography (MEG) is a neuroimaging technique that is well-suited for these experimental questions, as it measures electromagnetic neural activity across the whole brain with millisecond resolution (Hämäläinen et al., 1993). Surface measurements of magnetic fields can be used to facilitate 4-D source reconstruction (Van Veen and Buckley, 1988; Sekihara et al., 2005; Robinson and Vrba, 1999; Cheyne et al., 2007; Quraan and Cheyne, 2010), and to characterize the temporal

interactions between sources (Brookes et al., 2011; Srinivasan et al., 2007; Stam et al., 2007). Partial least squares (PLS) analysis is a multivariate statistical framework that can be used to identify distributed spatiotemporal patterns of neural activity that optimally relate to differences between cognitive tasks or to differences between groups of subjects (McIntosh et al., 1996; McIntosh and Lobaugh, 2004; Krishnan et al., 2010; McIntosh and Mišić, 2012). PLS can also be used to determine robust patterns of neural activity that correlate with behavior or demographic measures (McIntosh et al., 2008; Mišić et al., 2010b; Diaconescu et al., 2011). Finally, PLS can be used to assess the effect of experimental manipulations on functional interactions between specific seed regions (functional connectivity) (McIntosh et al., 1999, 2003), and on whole-brain patterns of functional connections (functional networks) (Vakorin et al., 2011; McIntosh et al., 2013).

Therefore, the MEG modality and the PLS framework are complementary and hold great potential for network discovery and analysis. A number of recent studies have demonstrated the benefits of a combined MEG-PLS approach for studying a wide range of cognitive tasks, including learning (Hopf et al., 2013), face processing (Mišić et al., 2010a, 2014b), as well as a wide range of populations, including healthy development (Mišić et al., 2010a), healthy aging (McIntosh et al., 2013), traumatic brain injury (Raja Beharelle et al., 2012), autism spectrum

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disorder (Mišić et al., 2014a) and mesial temporal lobe epilepsy (Protzner et al., 2010). At present, there exist a large number of well-established software packages and toolboxes that specialize for different aspects of MEG preprocessing (Oostenveld et al., 2011; Tadel et al., 2011; Friston et al., 2011), source reconstruction (Oostenveld et al., 2011; Tadel et al., 2011; Friston et al., 2011) and PLS analysis (McIntosh and Lobaugh, 2004; Kovacevic et al., 2013). However, there exists no unified platform that merges all of these functions, allowing the user to transition seamlessly from the raw sensor-level MEG data to a PLS network analysis in source space.

Here we present [MEG]PLS, a pipeline that consolidates MEG and PLS in a single framework. The pipeline is written in MATLAB (The Mathworks Inc., Natick, MA), a high-level programming language that is ideally suited for scientific computing as it is cross-platform and has a large number of scientific libraries. [MEG]PLS is modular and comprised of functions from several toolboxes specialized for different aspects of MEG processing and PLS analysis, including functions from FieldTrip (Donders, NL) (Oostenveld et al., 2011), AFNI (NIMH, USA) (Cox, 1996), SPM8 (UCL, UK) (Friston et al., 2011) and PLScmd (Baycrest, CAN) (McIntosh and Lobaugh, 2004; Kovacevic et al., 2013), all of which are extensively supported and actively developed by their respective communities. Specifically, [MEG]PLS facilitates MRI processing (coregistration and segmentation), MEG preprocessing (filtering, epoching, baseline correction, detrending and artifact correction), MEG sensor analysis (in both time and frequency domains), MEG source analysis (including multiple head models and beamforming algorithms), and combines these with a suite of PLS analyses. A visualization suite, designed for combined MEG–PLS analysis, allows the visualization of results in 4-D source space including whole-brain montages across time and various overlays of source time series. [MEG]PLS and all supporting libraries are open-source and under the GNU Public License.

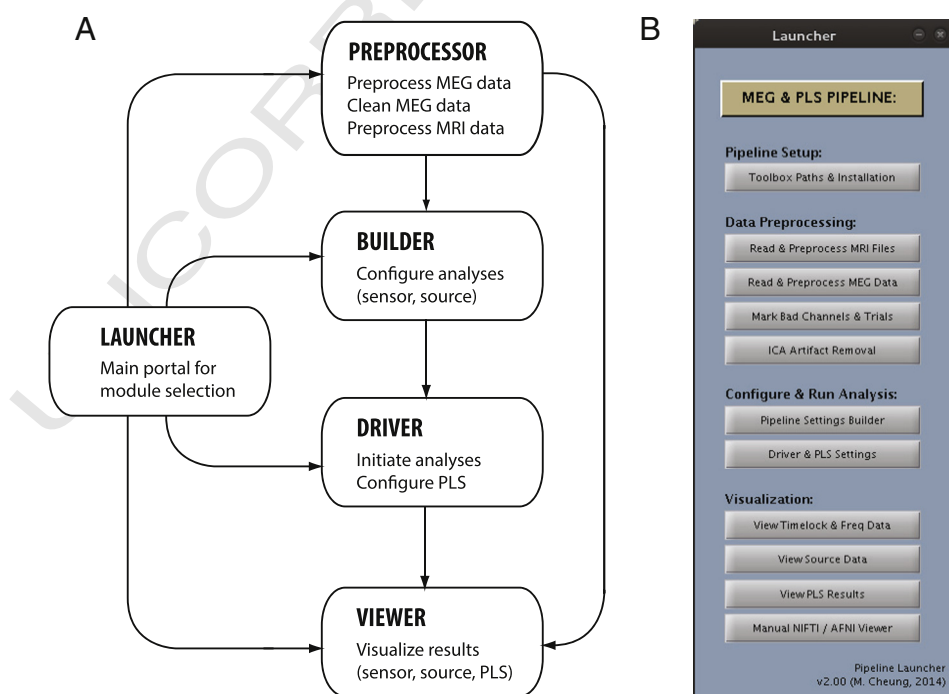
[MEG]PLS has both a graphical user interface (GUI) and a command-line interface, designed to accommodate users with varying programming experience. The comprehensive GUI is accessible and easy to use, allowing for core functions to be called interactively. The command-line interface offers flexibility for power-users, allowing users to write their own wrappers around base components, thereby encouraging

further development and community contributions. In both interfaces, [MEG]PLS permits full access to all core toolbox functions and their respective options. An extensive user guide has been included with [MEG]PLS along with detailed documentation and function help.

In the present report we give an overview of the functionality of [MEG]PLS, with an emphasis on the architecture and logic of the pipeline. We summarize the use and workflow of the primary [MEG]PLS modules and how they connect together into a unified framework. We then show how to navigate through [MEG]PLS by systematically working through a sample empirical dataset. We also note that earlier versions of the pipeline have been used to process and analyze data reported in Hopf et al. (2013), Fatima et al. (2013), and Doesburg et al. (2012).

## Methods

[MEG]PLS is organized around four main modules: the Preprocessor, Builder, Driver and Viewer (Fig. 1A). The Preprocessor reads and imports raw MEG and MRI files, and performs basic signal preprocessing, including filtering, epoching and artifact removal for MEG data, as well as coregistration, reslicing and segmentation for MRI data. Once the data are preprocessed, they are passed to the Builder module, which serves to configure settings and specify input files for sensor and source analyses. The Builder also includes settings for spatial normalization and file conversions following source reconstruction. The Driver module reads Builder-generated settings and initiates analyses. Importantly, the Driver also configures and runs PLS analyses on source-reconstructed data. As a result, the source reconstruction and PLS analysis are not configured simultaneously, but rather in two subsequent steps. In our experience, a user typically settles on a source solution, and then tries different types of PLS analyses. By keeping settings for the source reconstruction and PLS analysis separate, [MEG]PLS promotes experimentation, allowing users to try different types of post-localization PLS analyses without having to go back to reconfigure the Builder every time. The Viewer is a visualization suite, allowing the user to generate figures for sensor waveforms, time-frequency decompositions, individual or group-averaged source localizations, and PLS



**Fig. 1.** [MEG]PLS design and workflow. (A) [MEG]PLS is organized around a series of modules for data preprocessing, sensor analysis, source analysis, PLS analysis and visualization. (B) [MEG]PLS modules are accessed through a central launcher function. [Note: 2-column color image].

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