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OpenNFT: An open-source Python/Matlab framework for real-time fMRI neurofeedback training based on activity, connectivity and multivariate pattern analysis

Yury Koush[a,b,c,*], John Ashburner[d], Evgeny Prilepin[e], Ronald Sladky[f,g,h], Peter Zeidman[d], Sergei Bibikov[i,j], Frank Scharnowski[f,g,h], Artem Nikonorov[e,i,j], Dimitri Van De Ville[b,c]

[a] Department of Radiology and Medical Imaging, Yale University, New Haven, USA
[b] Institute of Bioengineering, Ecole Polytechnique Fédérale de Lausanne (EPFL), Campus Biotech, Geneva, Switzerland
[c] Department of Radiology and Medical Informatics, University of Geneva, Geneva, Switzerland
[d] Wellcome Trust Centre for Neuroimaging, University College London, London, UK
[e] Aligned Research Group, 20 S Santa Cruz Ave 300, 95030 Los Gatos, CA, USA
[f] Department of Psychiatric, Psychotherapy and Psychosomatics, Psychiatric Hospital, University of Zürich, Lenggstrasse 31, 8032 Zürich, Switzerland
[g] Neuroscience Center Zürich, University of Zürich and Swiss Federal Institute of Technology, Winterthurerstr. 190, 8057 Zürich, Switzerland
[h] Zürich Center for Integrative Human Physiology (ZIHP), University of Zürich, Winterthurerstr. 190, 8057 Zürich, Switzerland
[i] Supercomputers and Computer Science Department, Samara University, Moskovskoe shosse str., 34, 443086 Samara, Russia
[j] Image Processing Systems Institute of Russian Academy of Science, Molodogvardeyskaya str., 151, 443001 Samara, Russia

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ABSTRACT

Neurofeedback based on real-time functional magnetic resonance imaging (rt-fMRI) is a novel and rapidly developing research field. It allows for training of voluntary control over localized brain activity and connectivity and has demonstrated promising clinical applications. Because of the rapid technical developments of MRI techniques and the availability of high-performance computing, new methodological advances in rt-fMRI neurofeedback become possible. Here we outline the core components of a novel open-source neurofeedback framework, termed *Open NeuroFeedback Training* (*OpenNFT*), which efficiently integrates these new developments. This framework is implemented using Python and Matlab source code to allow for diverse functionality, high modularity, and rapid extendibility of the software depending on the user's needs. In addition, it provides an easy interface to the functionality of Statistical Parametric Mapping (SPM) that is also open-source and one of the most widely used fMRI data analysis software. We demonstrate the functionality of our new framework by describing case studies that include neurofeedback protocols based on brain activity levels, effective connectivity models, and pattern classification approaches. This open-source initiative provides a suitable framework to actively engage in the development of novel neurofeedback approaches, so that local methodological developments can be easily made accessible to a wider range of users.

Introduction

About two decades ago, real-time functional magnetic resonance imaging (rt-fMRI) was introduced (Cox et al., 1995) and turned into a rapidly developing discipline. Neurofeedback based on rt-fMRI provides a training protocol that allows participants to voluntarily control their brain activity and connectivity (Caria et al., 2012; deCharms, 2008; Sitaram et al., 2017; Stoeckel et al., 2014; Sulzer et al., 2013; Weiskopf, 2012). Conventional measures of brain activity for fMRI-based neurofeedback continuously track the blood oxygen level dependent (BOLD) signal from a target region of interest (ROI). Most often, gradient-echo echo-planar imaging (GE-EPI) T2*-sensitive protocols and their extensions are used to acquire brain volume data in real-time (Weiskopf, 2012; Weiskopf et al., 2007b). Each GE-EPI voxel value is proportional to the BOLD signal, which is an indirect measure of underlying neural activity (Logothetis et al., 2001). The neurofeedback loop is closed when brain activity induced by the participant's efforts for regulation, is presented as the neurofeedback signal (LaConte, 2011; Sitaram et al., 2017). With the help of neurofeedback, participants can learn voluntary control over the own brain activity and connectivity. Such neurofeedback training has been shown to cause behavioral consequences, thus providing a scientific tool for investigat-

* Corresponding author at: Department of Radiology and Medical Imaging, Yale University, New Haven, USA.
E-mail addresses: yury.koush@yale.edu, yurykoush@gmail.com (Y. Koush).

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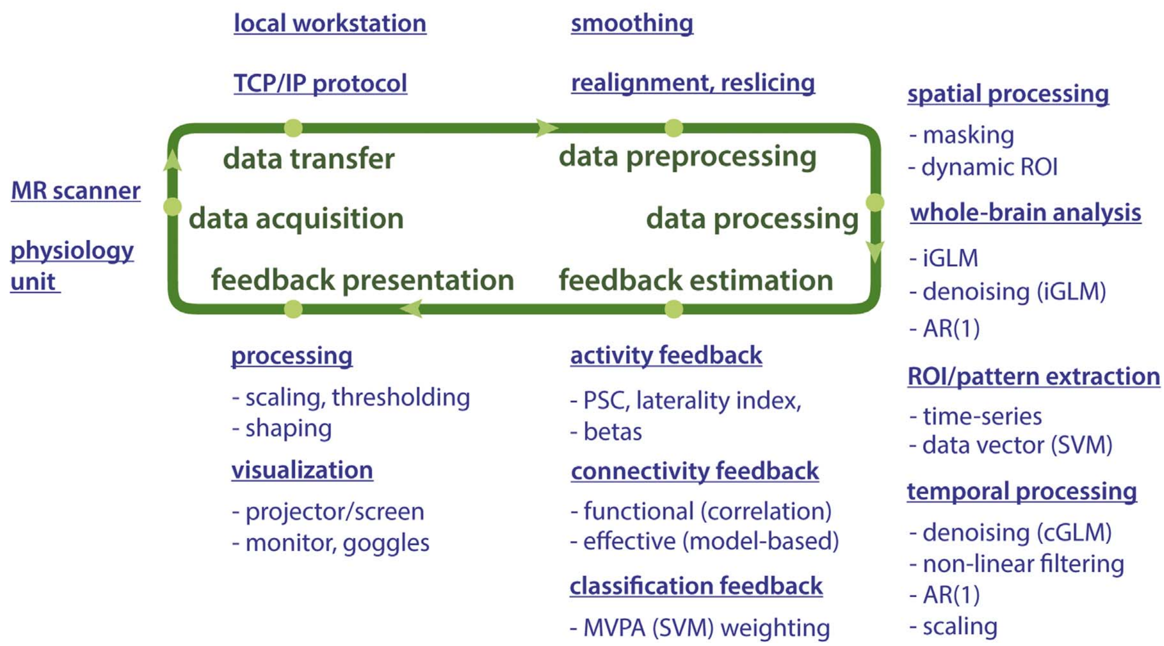

Fig. 1. An illustrative data flow for neurofeedback based on rt-fMRI that reflects the *OpenNFT* built-in functionality. MR – magnetic resonance, TCP/IP – transmission control protocol/ internet protocol, ROI – region of interest, PSC – percent signal change, GLM – general linear model, iGLM – incremental GLM, cGLM – cumulative GLM, AR(1) – autoregressive model of the first order, MVPA – multivariate pattern analysis, SVM – support vector machines.

ing the relationship between brain function and behavior (Sitaram et al., 2017; Sulzer et al., 2013). Likewise, neurofeedback allows neurological and psychiatric patients to normalize abnormal levels of brain activity that are associated with their disorder. It thus holds great promises as a drug-free and non-invasive experimental therapy that has been shown to be effective in depression, addiction, stroke, chronic pain, Parkinson's disease, and tinnitus (Haller et al., 2010; Hartwell et al., 2013; Li et al., 2013; Liew et al., 2016; Linden et al., 2012; Subramanian et al., 2011; Young et al., 2014) .

The conventional neurofeedback study involves defining the physiological target in terms of the brain ROI or network to be trained, assessing the participant's performance in terms of modulating brain activity, as well as the learning progression and the ability to transfer the trained regulation to an experimental situation without feedback. These experiments are challenging in terms of the evaluation of behavioral or therapeutic effects before and after learning (Sulzer et al., 2013). Therefore, neurofeedback studies can consist of multiple runs accompanying the neurofeedback ones, such as pre- and post-training tests and transfer runs. Neurofeedback studies range from short single-day neurofeedback session (deCharms et al., 2005) to relatively long experiments with up to 10 sessions spanned over several days (Shibata et al., 2011). Neurofeedback training sessions usually last approximately 1 h and consist of a few neurofeedback runs (Stoeckel et al., 2014; Sulzer et al., 2013). The runs are usually composed of alternating 10–30 s regulation and baseline blocks and last around 5–20 min each.

On the one hand, neurofeedback based on rt-fMRI is a rapidly developing and technically highly demanding approach. On the other hand, technical and methodological developments of the MRI hardware and software advance quickly, which, together with increasing availability of high-performance computing power, allows for more sophisticated real-time brain data processing approaches. The currently available software for rt-fMRI neurofeedback include the commercially available Turbo-BrainVoyager software (http://www.brainvoyager.com), and a few non-commercial software packages, such as FRIEND (https://www.nitrc.org/projects/friend/), which is written in C++ and based on the FSL libraries (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/), the AFNI real-time plug-in written in C (Cox et al., 1995) (https://afni.nimh.nih.gov/), scanSTAT written in C/C++ (Cohen, 2001) (http://www.brainmapping.org/scanSTAT/), BART written in C/C++ (Hellrung et al., 2015), and the FieldTrip extension for rt-fMRI written in Matlab (http://www.fieldtriptoolbox.org/). All of these software packages except for FieldTrip (which is non-GUI-based) are written in non-interpreted programming languages that require more sophisticated programming skills compared to interpreted languages. Thus, there is need for an open-source GUI-based multi-processing integrated framework written in more easy interpreted programming languages such as Python and Matlab, with a broad functionality asset for neurofeedback studies. However, despite the relative simplicity of programming in Matlab as compared to C/C++ or Java, it's GUI capabilities, parallel architecture implementation, and concurrent data processing performance is weaker. One solution to this problem is combining Matlab and Python, which allows for preserving the relative simplicity of programming in Matlab as well as an integration with other widely-used Matlab-based neuroimaging toolboxes, and for benefitting from the advanced GUI capabilities, parallel architecture and concurrent data processing of Python.

In this technical note, we provide a brief overview of the core neurofeedback data processing steps required to perform activity-, connectivity- and classification-based neurofeedback studies, and introduce an open-source framework, termed *OpenNFT*. This framework represents a parallel architecture and the set of core modules required to quickly design and test new neurofeedback experiments. The *OpenNFT* is written in an integrated Python/Matlab environment to facilitate concurrent functionality, high modularity, and the ability to extend the software in Python or Matlab into new directions depending on programming preferences, research questions, and clinical application. To demonstrate its capabilities, we describe three case studies covering neurofeedback based on coactivation patterns, advanced effective connectivity, and classification methods.