Development and Implementation of a Portable Real-Time fMRI Neurofeedback Protocol

Boston Children's Hospital — Until every child is well

Harvard Medical School Teaching Hospital

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Introduction

- One driving principle of neuroscience is plasticity, the brain's ability to modulate neural activity and connections in temporary and permanent ways.
- This process can be co-opted through neurofeedback, which presents an individual's own neural signals back to them to create neural and behavioral changes
- MRI neurofeedback (fMRI-NF) offers direct evidence of neuromodulation efficacy but is hindered by complex technical barriers
- We developed a user-friendly containerized real-time fMRI-NF protocol which facilitates the acquisition, processing, localization, and task and feedback display with low CPU/memory requirements.

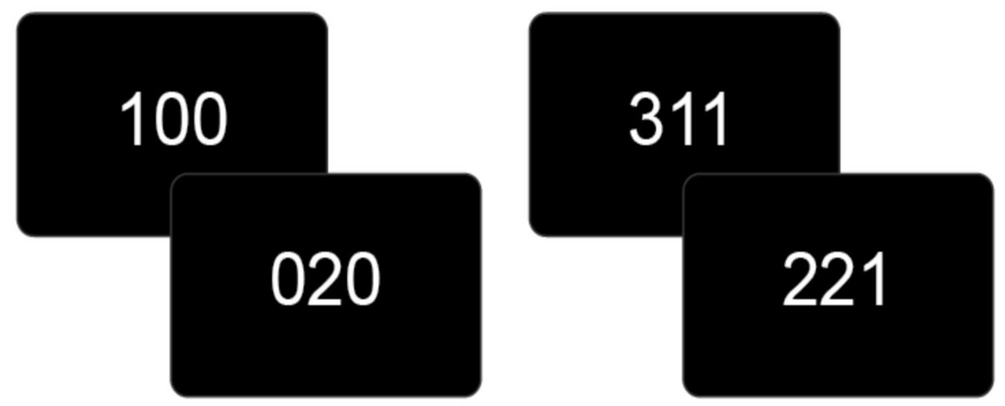
Our Ongoing Study on Stimulants, fMRI Neurofeedback and Motion

- In our study, we aim to use this real-time fMRI-NF protocol to replicate the effects of stimulant medications in individuals with ADHD, without the side effects that come with the usage of stimulant drugs.
- At the same time, by incorporating new analysis and registration software to better capture and correct for motion in a slice-by-slice method, we aim to refine our understanding of how motion affects ADHD neuroimaging results.

Participant Facing

Run Tasks to Localize Attentionally-Implicated Brain Regions and Measure Attention

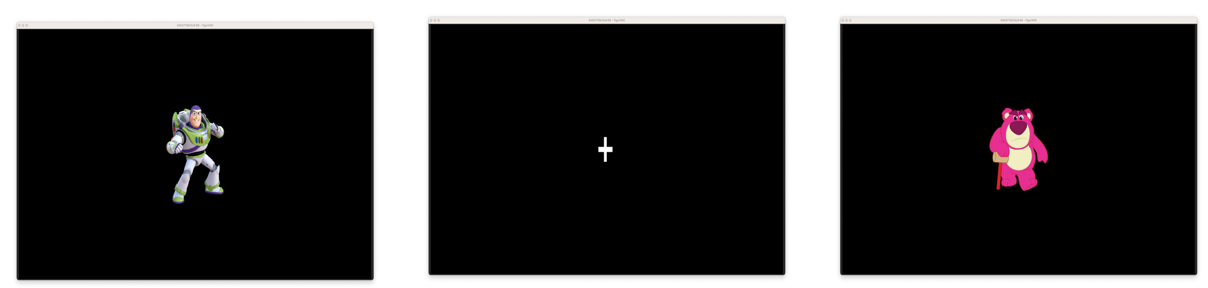
Multi-Source Interference Task (Bush & Shin 2006)**:** Activates attentional regions, namely the Anterior Cingulate Cortex, or ACC. For control trials, the paired digits are zero and the position of the target digit corresponds to its location. For interference trials, the distractor digits are non-zero and the target digits location is not the same as its value.



Control — Interference

Stop Signal Task: A go/no-go task where participants must press a button when they see a cartoon astronaut and refrain from pressing a button when they occasionally see a cartoon bear. Tasks of this nature, which requires participants to inhibit a response, has been shown to heavily involve the Right Inferior Frontal Gyrus, or RIFG (Rubia et al. 2003).

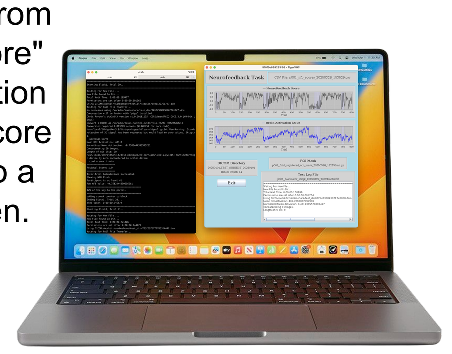
Press button (75% of trials) — Do not press button



Jittered interstimulus interval

Calculate Neurofeedback Metrics and Project Results to the MRI's Screen

The experimenter's laptop calculates brain activity from DICOMs, assigns a "score" to the brain ROI's activation level, and displays the score as a rocket's distance to a portal on the MRI screen.



The MRI streams DICOMs in real-time to a containerized Samba/SMB sharing server on the experimenter's laptop.

In an Ubuntu-based Docker image, we:

1. Calculate an ROI's brain activation for each DICOM using GLM residuals or mean intensity.
2. Normalize activation to a score (-1 to 1).
3. Visualize the score as a rocket moving toward a portal.

Display Tasks via a Containerized Virtual Display

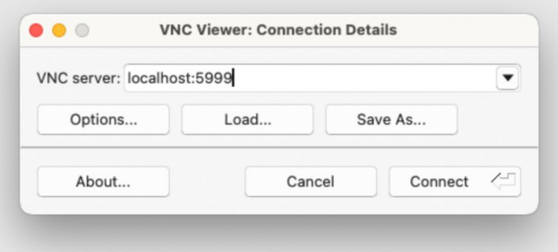
Inside the running Docker container

Xvfb
Creates virtual display (:99) with the MRI's screen parameters

X11vnc
Allows remote access to the virtual display

Connect to display

Users connect to the virtual display using the VNC Viewer of their choice



Our system utilizes a series of Docker containers controlled by a simple Command Line Interface, allowing experimenter control with no manual configuration, which can:

Researcher Facing

Register Atlas Region of Interest (ROI) masks to subject-space in real-time using either EasyReg or FSL, then Localize

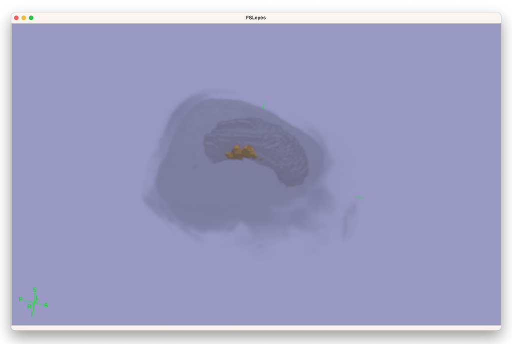
EasyReg Registration Pipeline: Through a series of scripts involving the transfer of files to/from Boston Children's High Performance Computing cluster and a local Docker container, an MNI-space mask is registered to a participant's brain using FreeSurfer's EasyReg, a machine learning tool for registration of brain MRI.

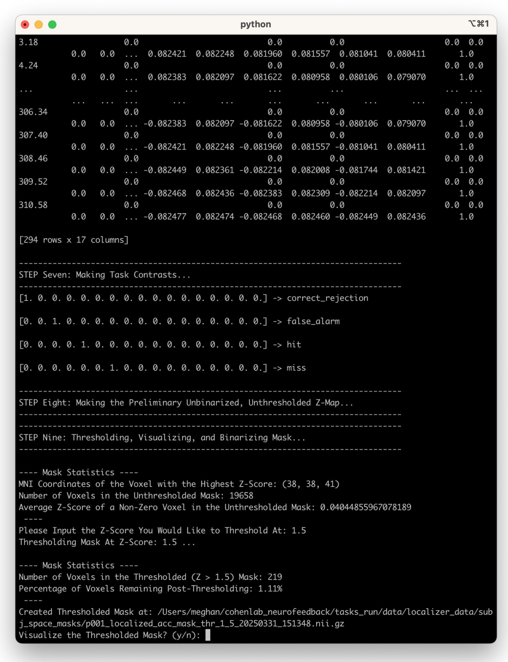
FSL Registration Pipeline: Using FSL's FLIRT and FNIRT tools, this script registers ROI masks to a participant's brain. It's process includes DICOM to NifTi conversion, skull-stripping and mask creation, affine and nonlinear registration, as well as mask binarization.

FSL Localization Pipeline: This pipeline localizes and creates a mask of a brain region (within a given registered brain region) based on activation from either the MSIT task or RIFG task. It allows the experimenter to choose the threshold activation level for voxels included in the outputted mask via visualization in FSLeyes.

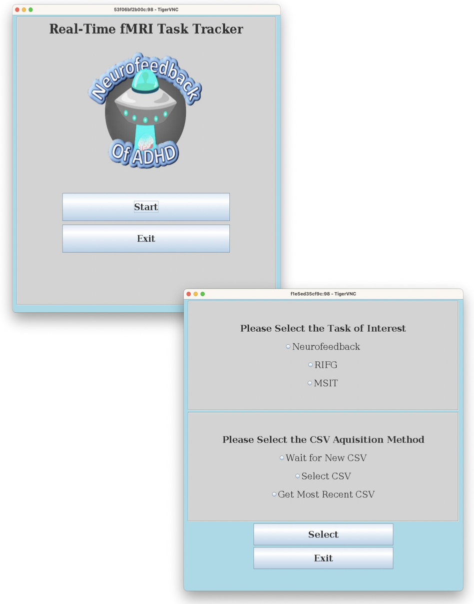
FreeSurfer

FSL

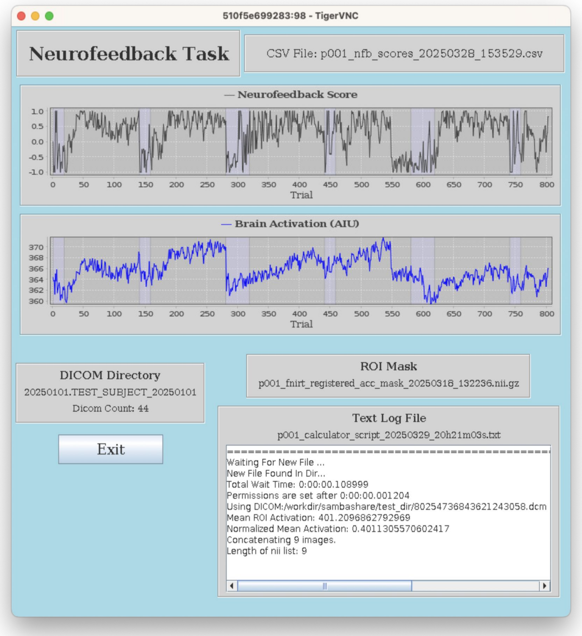




Provide immediate feedback on participant performance to experimenters via Graphical readout



A java-based graphical interface, containerized in a Docker image, can graph brain activation and task performance in real-time while showing task parameters and logs as they are updated.



Transfer DICOMs via a containerized OS-agnostic Samba/SMB sharing server to receive DICOM data transmitted from Siemens (XA30) MRI scanners with no manual configuration

MRI computer requests access to the SMB server on experimenter's machine

a Docker-containerized Linux-based SMB server on experimenter's machine accepts access

Client

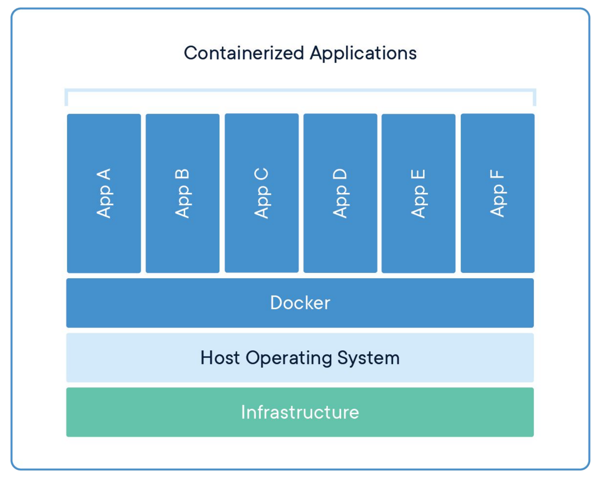
Requests

Responds

Server

Docker Ensures a Consistent Runtime Environment Across Host Machines

- From running fMRI task protocols to data visualization and analysis, Docker can streamline neuroscientific workflows
- Researchers can share Docker images, enabling collaborators to run identical setups without manual configuration
- Our images allow us to simplify complex fMRI neurofeedback software and protocols, limit manual installation and configuration, and provide a consistent runtime environment to run real-time experiments.



Summary

- We developed a portable, containerized real-time fMRI neurofeedback (fMRI-NF) protocol for Siemens (XA30) MRI scanners, designed to support neurofeedback research.
- Featuring low resource requirements and a CLI for experimenter control, it offers:
  - Real-time calculation of neurofeedback metrics and participant screen projection
  - Atlas ROI mask registration to subject-space using EasyReg or FNIRT
  - Localization of attention-related brain regions and tasks to measure attention
  - Immediate performance feedback via graphical readouts
  - Virtual display via a Docker-containerized VNC
  - File transfer via a containerized, OS-agnostic Samba/SMB server for DICOM data

Citations

Bush, G., Shin, L. The Multi-Source Interference Task: an fMRI task that reliably activates the cingulo-frontal-parietal cognitive/attention network. Nat Protoc 1, 308–313 (2006). https://doi.org/10.1038/nprot.2006.48

Rubia K, Smith AB, Brammer MJ, Taylor E. Right inferior prefrontal cortex mediates response inhibition while mesial prefrontal cortex is responsible for error detection. Neuroimage. 2003 Sep;20(1):351-8. doi: 10.1016/s1053-8119(03)00275-1. PMID: 14527595.