I. Significance

Although EEG was the first neuroimaging modality {Berger, 1929 #161}, its uses gradually crystallizing into clinical neurophysiology and experimental psychology communities with relatively little methodological innovation or participation from biophysical engineering. EEGLAB began in 1997 as a laboratory software framework to support and exploit the consequences of innovative approaches to EEG analysis pioneered by Co-PIs Makeig and Delorme, including time/frequency analysis {Makeig, 1993 #49}, independent component analysis (ICA) {Makeig, 1996 #48}, soon extending to include brain connectivity analysis {Delorme, 2002 #139}, high-resolution EEG source imaging {Akalin Acar, 2008 #155}, and automated artifact rejection {Delorme, 2007 #4}. First fully introduced to the research community in 2001, EEGLAB has received NIH support since 2005, currently under R01-NS047293-[10-13]. By 2011, a survey of 687 researcher respondents {Hanke, 2011 #2} reported EEGLAB to be, by a wide margin, the software environment most widely used for electrophysiological data analysis worldwide. (*neuro.debian.net/survey/2011/results.html*). The EEGLAB reference paper {Delorme, 2004 #1} now has more than ***18,500 citations*** on Google Scholar, accumulating at a rate of 6.8 per day; the opt-in EEGLAB daily discussion email list links 6,281 researchers, and the EEGLAB news list reaches over 15,476 researchers worldwide. In addition, at least 146 EEGLAB plug-in toolsets have been released from our own and many other laboratories. During the 2018-2022 period, 5,926 individual messages from the international community of EEG researchers were posted to *eeglablist*, the EEGLAB mailing list. Since 2013, visits to the new EEGLAB website (*sccn.ucsd.edu/eeglab*) have increased by at least 8% per year (now at 1.1 million visits per year). The number of citations for the most widely used open-source EEG analysis environments (Fig. 1) shows that EEGLAB continues to grow faster than any other EEG analysis software environment. According to PubMed, since 2018, the EEGLAB reference article has been cited in papers funded by at least 397 NIH grants (with a total of $148M of funding). The EEGLAB environment is thus now a *de facto* world standard supporting a wide range of EEG and related research studies and teaching labs, as attested by the attached 98 letters of support (Appendix).

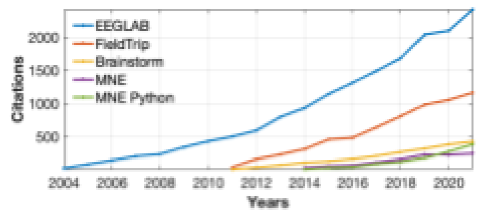


Figure 1. *Numbers of citations per year for the most popular EEG and MEG processing software packages.*

Our ongoing additions to the EEGLAB core and its many extensions make available a wide range of interoperable methods for performing multivariate statistics and causal analysis, accurate forward BEM and FEM head modeling from either individual subject MR head images or recorded 3-D electrode positions, equivalent dipole and distributed source location estimates, and general linear model (GLM) statistical analysis of source-resolved data measures.

We believe the current success of EEGLAB, judged by its broad, worldwide acceptance and use, rests on three factors: *First*, in now a period in which methods for the analysis of EEG and other electrophysiological signals are rapidly evolving after a long period of relative stasis, EEGLAB fills a widely felt need for an open source, readily customizable, and easily extensible analysis environment for electrophysiological signal processing – unlike the more nearly closed designs of nearly all other EEG software (commercial and noncommercial). *Second*, its multi-layer software architecture, extensive documentation, and live and online workshops have allowed EEGLAB to be adopted by a wide range of users, from beginning users first exploring their data using the EEGLAB GUI to advanced method developers making new algorithms and visualizations available to the wider research community through about ***150 EEGLAB plug-in tools*** and toolboxes that then appear in the EEGLAB GUI for immediate exploration and use by any interested EEGLAB user. *Third*, EEGLAB enables users to apply methods to their data not otherwise available to them, in particular those many research users who have no time or expertise to code new analysis methods themselves from their published descriptions.

The major significance and root innovation of the EEGLAB project are to assist the basic and clinical human electrophysiology research community in advancing their electrophysiological research methods beyond visual inspection of the EEG data and/or sole use of relatively simple scalp-channel averaged evoked-response and power spectral measures, and toward ever wider use and acceptance of EEG and other electrophysiological recording methods as a *spatiotemporally accurate*, *informative*, and in the case of scalp EEG, also *noninvasive*, relatively *low-cost*, and thereby *readily scalable* and *widely available 3-D functional brain imaging modality*, whereas intracranial recording *(iEEG)* provides a critical window into seizure dynamics necessary for planning successful surgeries for intractable epilepsies and other brain pathologies in difficult cases.

Progress during the current grant period. As detailed in our progress reports, in the preceding grant period, we have made significant progress under each of the three previous Specific Aims (SA). Some further details are reported under descriptions of the proposed work in the Approach section (following).

■ **PREVIOUS AIM 1: DEVELOP STATE-OF-THE-ART SIGNAL PROCESSING METHODS.** ***The Neuroelectromagnetic Forward problem Toolbox (NFT) EEGLAB plug-in.*** We improved the NFT plug-in for making electromagnetic Boundary Element Model (BEM) and Finite Element Model (FEM) head models. We refined our innovative ***skull conductivity and source location estimation algorithm (SCALE)*** for simultaneously estimating skull conductivity and the cortical distributions of 10-20 effective sources derived from the EEG data by independent component analysis (ICA) decomposition {Acar, 2022 #136}. SCALE combines a realistic Finite Element Method (FEM) head model built from magnetic resonance (MR) head image with the *effective source* scalp maps learned from the EEG data by ICA decomposition to estimate individual ***brain-to-skull conductivity ratio (BSCR)*** while inverse mapping the individual effective source densities to the cortical surface. To estimate the robustness of SCALE BSCR estimates, we applied SCALE to MR-image and high-density EEG data from ten subjects, five having data from 2-3 different tasks and sessions. As expected, across these (and all) subjects, the SCALE BSCR estimates differed widely (mean 40.6, range 18-78), but within-participant SCALE BSCR estimates across days and tasks were far more consistent (Std. Err of Mean, 1.6) {Acar, 2022 #136}. SCALE-optimized electrical forward head modeling can make high-resolution EEG brain imaging increasingly a reality.

Volumetric calculations using NFT: The most important variables for accurate EEG source localization are the different brain tissue geometries and conductances. To model brain tissue geometries, NFT tools were applied to structural neuroanatomical data from T1-weighted magnetic resonance images (MRI) collected using a Siemens Symphony Quantum 1.5T MR scanner {Walhovd, 2005 #127} at the University of Oslo. We performed the NFT-based head modeling for 47 older adult subjects with recorded 3D electrode locations and both EEG and MRI data, and calculated brain and CSF volumes and skull thickness for these subjects {Daniel, 2022 #154}.

Distributed source localization: We migrated the NFT plug-in code to GitHub with all its documentation. We also released a new version, including new tools to compute patch-based source space. We added Distributed EEG Source Localization and a new image segmentation module. Electrode co-registration has been modified to support sensors used in simultaneous EEG/MEG recordings. We evaluated different MEG forward problem solvers. Finally, we added MATLAB functions for solving the EEG distributed source localization/spatial distribution problem, making it easier to offload computation to High-Performance computing (HPC) resources via the Neuroscience Gateway (NSG, *nsgportal.org*).

Phase-amplitude coupling (PAC). We developed a new EEGLAB toolbox supporting computation of Phase-Amplitude Coupling (Fig. 2). A new tool to analyze PAC at the group level has been implemented to ensure its full integration into the EEGLAB STUDY statistics structure and platform. Our *Neuroimage* article described the toolbox, including a new method for time-resolved connectivity analysis using local mutual information phase-amplitude coupling (MIPAC) {Martínez-Cancino, 2019 #140} and its application to actual data.

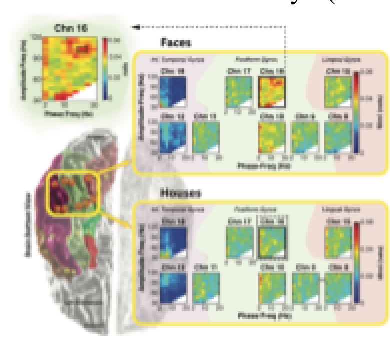


Figure 2. *A new phase amplitude coupling (PAC) measure applied to ECoG data.*

Independent Modulator Analysis Toolbox (IMAT). We developed a new toolbox, the Independent Modulator Analysis Toolbox, for decomposing spectral fluctuations of temporally independent EEG sources into 'spatial-spectrally' distinct spectral modulator processes. IMAT tools can separate alpha harmonics in the beta band from other beta band processes, high-frequency broadband (HFB) from narrow band high-frequency activities, etc.

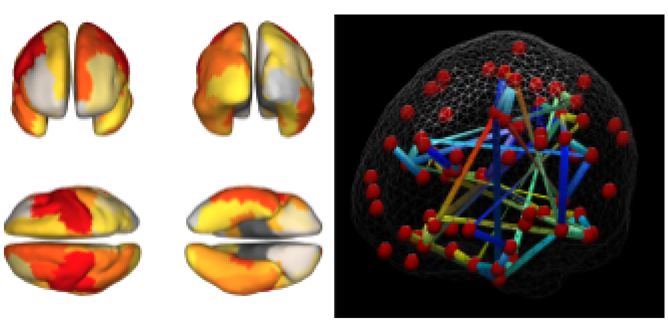


Figure 3. *Graphical output developed for the ROIconnect tool. The smooth cortical images show which brain areas interact the most with each other. The plot with the balls and rods indicates the strongest interactions between brain areas (each ball representing a region of interest).*

The ROIConnect tool. We have developed an EEGLAB plug-in, ROIconnect (see Fig. 3 below), for calculating network dynamics in collaboration with Stefan Haufe at Berlin University. First, we align the participant electrode montage to an MNI head model. Then we use LCMV beamforming to estimate the generating activity in cortical regions of interest (using the Desikan-Killiany surface atlas), then compute pairwise connectivity between these regions using cross-coherence, granger causality, directed transfer entropy, partial directed coherence, multivariate interaction measure, maximized imaginary coherency, or their time-reversed equivalents, allowing removal of some spurious connections {Pellegrini, 2022 #148}.

■ **PREVIOUS AIM 2: GROUP ANALYSIS AND META-ANALYSIS.** The ***Brain Imaging Data Structure (BIDS)*** research community-based specification initiative is establishing a common set of standards for MRI and fMRI {Gorgolewski, 2016 #95}, MEG {Niso, 2018 #128}, iEEG {Holdgraf, 2019 #129}, EEG {Pernet, 2019 #130} and other modality neuroimaging data. The BIDS standards facilitate organizing, archiving, sharing, and easily analyzing brain imaging data collected within and/or across studies and laboratories. Because of its wide use and acceptance, the EEGLAB *.set* format is one of only three that BIDS-EEG accepts. We developed an EEGLAB extension to import and export BIDS formatted data {Pernet, 2020 #131;Delorme, 2020 #142}. This ***EEGLAB BIDS plug-in*** has been used to export more than one-third (38 of 99) of the MEEG datasets on the NIMH-sponsored *OpenNeuro.org* and parallel *NEMAR.org* platform. EEGLAB imports BIDS studies, including EEG, MEG, and/or iEEG data, and supports processing either from the EEGLAB GUI or the MATLAB command line. The EEGLAB BIDS plug-in can currently import data for multiple tasks and sessions as well as behavioral data. EEGLAB and Brainstorm are the only two software environments that can import and process BIDS datasets, while EEGLAB and Fieldtrip are the only environments supporting the export of BIDS datasets. We also implemented full support in BIDS for HED-based EEGLAB event handling using our system of Hierarchical Event Descriptors (HED; *hedtags.org*, see below).

HED event annotation. Because of the central role that event-related data analysis plays in EEG and/or MEG (MEEG) experiments, choices about which events to report and how to annotate their full natures can significantly influence the value, reliability, and reproducibility of MEEG datasets for further analysis. Beginning in 2010, we proposed a set of syntax and vocabulary for event description in MEEG and other time series neuroimaging experiments {Bigdely-Shamlo, 2013 #39}. Further work examined the impact of various design decisions and provided a working template for organizing events in MEEG and other neuroimaging data {Bigdely-Shamlo, 2016 #50}. As the only system proposed to date for specifying the nature of events occurring during neuroimaging experiments, this Hierarchical Event Descriptor (HED) system was ***accepted into the BIDS framework*** in 2019**.** Work in the last few years has demonstrated how annotations using the new third-generation HED framework and tools can document events occurring during neuroimaging experiments, providing both human-readable and machine-actionable annotation, enabling automated both within- and across-studies analysis {Robbins, 2021 #143}. We have upgraded the graphic user interface tool, CTagger, that assists EEGLAB and other users in creating HED annotations, and have also updated EEGLAB event search and epoch extraction tools supporting HED-based epoching. As leaders in the HED Working Group, we have now received an award from the BRAIN Initiative to continue HED development (RF1MH126700; Co-PIs Makeig, Robbins, and Delorme).

The LIMO EEGLAB plug-in for statistical trial-by-trial analysis of M/EEG data using hierarchical linear models was developed in collaboration with Cyril Pernet {Pernet, 2020 #131} (Fig. 4). Almost any standard statistical design can be analyzed in EEGLAB using LIMO. Across subjects, analyses are performed using robust statistics coupled with bootstrap correction for multiple comparisons (including threshold-free cluster enhancement (TFCE), the only software to provide this superior correction method). We have created a new tutorial for LIMO and published a case use example {Pernet, 2020 #131}. In 2022, we remade the LIMO graphic interface and implemented BIDS support, including support for analysis spanning multiple BIDS sessions. We have also implemented IRLS (iterative reweighted least squares) optimization for GLMs.

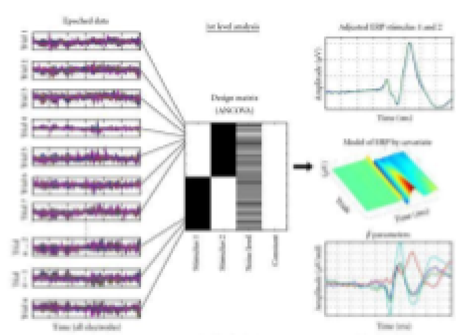


Figure 4. LIMO EEGLAB plug-in takes EEG data (left), and a design matrix (center) as input, and produces robust statistics (right).

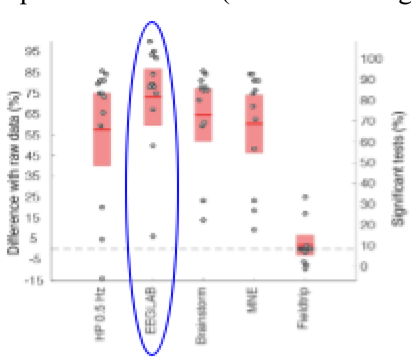


Figure 5. Comparison of EEG Analysis Pipelines applied to Event-related Data. *Here, cleaning scalp data using the EEGLAB standard pipeline unmasked significant evoked responses in more channels than other approaches {Delorme, 2022 #172}.*

Group-level modeling of effective source information flow. Unlike ROIconnect, which is based on regions of interest, the ***groupSIFT*** EEGLAB plug-in finds and models functional connectivity between ICA-resolved effective sources. As some of the characteristic sources might not be found in some subjects, standard LIMO methods cannot be used for group statistics. We, therefore, had to develop new statistical methods for group analysis. Following our first successful development and application of group-level source information flow to the study on children with a chronic tic disorder {Loo, 2019 #132}, we extended these tools for use in a clinical research collaboration in schizophrenia {Koshiyama, 2021 #144;Koshiyama, 2020 #145;Koshiyama, 2020 #146}.

Optimized automated processing pipelines. We developed several automated processing pipelines for EEG data, one of which we made available on the BrainLife platform (*brainlife.io*). We also processed 40 experiment datasets using EEGLAB tools as part of our NEMAR database award (R24MH120037; Co-PIs Makeig, Delorme, and Majumdar), for which we compared EEGLAB automated pipelines and other EEG signal-processing frameworks. We have extensively compared EEGLAB with other software packages, particularly the Fieldtrip, Brainstorm, and MNE open-source environments {Delorme, 2022 #172}. Commercial EEG analysis packages also exist, although an independent survey (2011) showed they are not as often used as open-source software {Hanke, 2011 #2}, mostly because of their lack of features, dependence on a specific operating system and weak scripting capabilities. Among the fully automated pipelines tested, EEGLAB performed best (Fig. 5). Of note, EEGLAB has ten core methods plus 28 plug-ins for automated artifact rejection, while Brainstorm has two, Fieldtrip one, and MNE one in a plug-in. EEGLAB automated artifact rejection methods are based on two now popular tools also developed in our laboratory: (1) ***Artifact Subspace Reconstruction (ASR)*** based on the projection of artifactual data onto a clean data subspace {Mullen, 2013 #12}, and (2) ***ICLabel***, a powerful ICA-based machine learning method we developed for identifying artifactual components, trained on 15,000 manually (crowd) labeled components {Pion-Tonachini, 2019 #157}. We conclude that, compared to other EEG software packages, ***the main advantage of EEGLAB is the variety of tools*** it has continued to make available to users and the more varied and (in many cases) innovative nature of these tools.

■ **PREVIOUS AIM 3: EEGLAB MAINTENANCE AND PORTABILITY.** The new and improved ***LabStreamingLayer (LSL) MATLAB Viewer/Recorder*** is a cross-platform EEGLAB plug-in (also available as a compiled stand-alone tool) for recording EEG and any concurrent data streams data using the LabStreamingLayer (LSL) protocol developed in our laboratory {Mullen, 2015 #116}, saving the data in the LSL native *.xdf* format and the EEG data as an EEGLAB *.set* dataset. LSL drivers are now available for 115 physiological and behavioral data acquisition systems (*labstreaminglayer.org*).

EEGLAB plug-ins. During this grant period (2018-22), 146 different EEGLAB plug-ins were downloaded a total of ***421,608 times*** (an 832% increase compared to the 2013-17 grant period). We have reprogrammed the plug-in handling mechanism and online submission website to include a new plug-in search feature, and have migrated the 43 EEGLAB plug-ins we maintain to their own GitHub repository. These 421,608 downloads do not include plug-ins distributed with the EEGLAB core code (data filtering *Firfilt,* equivalent dipole localization *Dipfit*, the recent *clean_rawdata*, and *ICLabel*). Popular plug-ins are data import plug-ins: ***BIOSIG***, an Austrian EEGLAB plug-in and toolbox (58,271 downloads), and ***File-IO***, developed by the Donders Center for Neuroimaging (26,505 downloads). The most popular data processing extension is ***Fieldtrip***, with 15,489 downloads. *Fieldtrip* is integrated into EEGLAB functions for source localization, likely explaining its popularity. The ***Cleanline*** plug-in for removing line noise was downloaded 8,929 times. **Third-party plug-in support.** EEGLAB actively supports contributed third-party plug-ins. For example, we developed a new way to tag discontinuities in data in EEGLAB to support continued compatibility with the ***ERPLAB*** plug-in (a separately NIH-supported project of Luck and colleagues, 5R01MH087450-12; 9,721 downloads). EEGLAB now has 28 plug-ins for artifact rejection, 45 plug-ins using ICA, 2 plug-ins for microstate analysis, etc.

EEGLAB releases. We have issued 8 EEGLAB releases during the supported period at a rate of two per year. Every release, a compiled version of EEGLAB *not* requiring a user MATLAB license, is also distributed – including compiled versions for Windows, Mac, and Linux (these now comprise 15-20% of all EEGLAB downloads). EEGLAB was downloaded more than 100k times in 2018-22 from the *eeglab.org* website and updated more than 12k times through the new (2022) EEGLAB auto-updating mechanism. These statistics do not include untrackable direct GitHub downloads.

Octave and Python support. We have enhanced support for EEGLAB scripts and functions to run on the free MATLAB-equivalent Octave software (*octave.org*). In 2020, we made the EEGLAB graphic user interface compatible with Octave. We have also worked on Python compatibility and are developing an interface enabling Python users to use any EEGLAB functions via MATLAB-compiled Python libraries.

EEGLAB repository. We have continued the development and maintenance of the ***EEGLAB GitHub repository***. From 2018 to 2022, 2628 commits were made to the EEGLAB repository to address bug fixes and introduce new features. We have also switched to using ***GitHub issues*** instead of Bugzilla reporting as our user communication manager. We closed all existing bug reports (more than 200) on Bugzilla in 2019 and are now monitoring bugs only on GitHub, where we have addressed 541 bug reports since 2019. There are currently 204 forks to our EEGLAB GitHub repository – made by developers or users who have created a copy of the EEGLAB repository on their GitHub account. Many other bug queries and other user feedback are addressed through our support email and EEGLAB list. ***Continuous Integration (CI)*** code maintenance is an integral part of robust software development. CI requires new proposed changes to the main codebase to be unit tested before merging. As we moved the EEGLAB software codebase to open-source GitHub, we configured the repository so that every new commit and/or pull request is automatically evaluated against all existing unit tests, ensuring changes to the codebase do not introduce bugs or unforeseen side effects.

EEGLAB documentation. We have migrated the full EEGLAB tutorial to the GitLab platform and have completely rewritten it and reorganized it with new examples and new tutorial datasets. Our YouTube channel now has 63 tutorial videos and 4.8k subscribers. The ***EEGLAB YouTube channel receives about 120,000 views per year***.

II. Innovation

The total innovation embodied in this proposal is *both* in (1) devising, testing, and making available tools representing research advances addressing challenges that restrict use and interpretation of human electrophysiology as a ***high-resolution functional cortical imaging modality*** suitable for use alone or in ***multimodal imaging paradigms***, and as well as in (2) continuing our ever-evolving process of design, maintenance, and distribution of *a* unique, *unified, and very widely accepted open-source framework of ready-to-use tools implementing advancing computational approache*s for the worldwide human electrophysiological research community, tools now supporting many hundreds of research projects (see 98 support letters in Appendix). Through ongoing collaborations with the established ***Neuroscience Gateway*** project (*nsgportal.org*), we will also continue to make computationally intense EEGLAB tools freely available to run on the Expanse supercomputer at UCSD (R01-EB023297) including immediate access to the NIMH/BRAIN initiative-sponsored OpenNeuro data archive (without need for data download) through our linked data, tools, and compute resource ***NEMAR.org*** (R24-MH120037).

High-resolution effective source separation and localization. An ongoing challenge is to develop robust tools for estimating the precise cortical areas over which local field potentials have become synchronous (or near synchronous), therein becoming effective source processes that contribute appreciably to scalp channel recordings, making them capable of being identified by ICA or other approaches {Delorme, 2012 #85}. We will further refine, optimize, and make available inverse problem approaches through our NFT toolbox, made yet more effective by our unique SCALE algorithm that estimates ***individual skull conductivity*** noninvasively, while optimizing the electrical forward problem head model and 10-20 given effective source distributions on the cortical surface ({Akalin Acar, 2016 #34}, 74 cites). For distributed localization of effective sources on the cortex, NFT uses SCS (Sparse, Compact, and Smooth) algorithm of Cao developed in our laboratory for MR head image-based location estimation of ***effective source distributions on the cortical surface*** {Akalin Acar, 2016 #34;Cao, 2012 #38}. SCS assumes that each effective source spatial distribution is indeed spatially sparse, compact, and smooth, and that its projection to the scalp surface can be modeled by a sum of activity in voxel-equivalent dipoles located within and oriented normal to the cortex. SCS requires that the relative position and orientation of every element of the cortical surface are known from the individual's MR head image and uses a multi-resolution patch basis built on a high-resolution cortical surface mesh to fit source distributions. Further, we will introduce tools to perform and validate our novel (though not yet unavailable) EMSICA spatiotemporal decomposition of (cortically projected) scalp EEG data and resultant cortical surface-based effective source clustering {Tsai, 2006 #92;Tsai, 2014 #120}. Effective source localization is also an important unsolved (and widely unrecognized) problem in ***iEEG and sEEG*** research (Fig. 12), one we will also address in this work with specialist collaborator Dora Hermes.

Functional effective source connectivity. Here we will compare (for the first time) two current approaches. One challenge associated with connectivity analysis between ***ICA-resolved EEG effective sources*** is that some sources might not be identified in some subjects. To address this issue, we propose to implement in our *GroupSIFT* plug-in a hierarchical Bayesian approach {Thompson, 2011 #163} as well as an innovative graph-based method. We are also co-developing an *ROIconnect* plug-in that identifies functional ***connectivity between brain regions of interest*** defined in MRI atlases using various methods, allowing reconstruction of simulated or actual EEG sources {Pellegrini, 2022 #148}. Here too, we propose a new approach evaluating whole-brain connectivity by computing pairwise connectivity between all LCMV beamforming-computed source densities, then identifying clusters of functional connections. We will compare this model to the already available simplified ROI-based modeling approach.

Mobile brain/body imaging (MoBI). Instead of representing body movements in terms of joint torques and angles, as is typical in robot design, we will implement and extend the approach of Tanaka based on inter-joint distances {Tanaka, 2018 #175}, quantities that arguably are more readily monitored by the nervous system. We will build and test tools to assess connectivity between details of motivated actions in this framework and source-resolved EEG dynamics

Continuity. Of course, none of the above innovations will be widely used or usable unless we continue to maintain the EEGLAB environment as a whole. A necessary element of this proposal is therefore to continue to support, validate, and document both new and existing EEGLAB-based tools and services. Providing valuable tools to the community necessarily involves a significant investment in testing, maintenance, and documentation. Supporting users and new user-contributed plug-ins is an essential service as well. Our existing track record over the past two decades demonstrates our ability to release and support software for thousands of users, and our capacity to adapt to new technologies, documentation formats, and software testing frameworks. NIH support of the EEGLAB software framework itself has been and remains critical to its mission – to support discovery and innovation in human electrophysiology.

III. Approach

■ AIM 1. HIGH-RESOLUTION EEG SOURCE IMAGING

Aim 1.1. High-resolution EEG source imaging. We will work on new methods to process EEG data involving high-resolution source imaging based on advances made by our team. Our ***Neuroelectromagnetic Forward modeling Toolbox (NFT)*** {Akalin Acar, 2010 #37} and ***Neuroelectromagnetic Inverse Source Toolbox (NIST)*** {Acar, 2022 #136} are perhaps the most precise broadly available toolboxes for inverse source localization, processing tissue surface meshes with up to 80,000 surface vertices (compared to 2,000 to 6,000 in other software). The reason for such precision is that cortical thickness inaccuracy in boundary element (BEM) or finite element method (FEM) models can lead to EEG source mislocalization {van den Broek, 1998 #133}. The head models in other software packages (Brainstorm, Fieldtrip, and MNE) are primarily tailored for MEG source localization, for which head model accuracy is less critical. Here, we will compare EEG effective source distributions to determine the trade-off between computation time and mesh resolution on the goodness-of-fit of the resulting source map estimates. ***Scanned electrode positions.*** Scanning of electrode positions using 3D photogrammetry is becoming increasingly popular - and now may be as simple as using a recent-model iPhone to acquire 3D head images. Thus, quickly scanning electrode positions *in situ* will likely become routine. We have released the ***get_chanlocs EEGLAB plug-in*** to streamline the manual procedure of clicking on each electrode position in the rotatable 3D head image (see Fig. 6) – performed once, during analysis rather than during subject preparation. We propose to develop a machine-learning-based tool to align montage-template electrode labels with the 3D head model automatically. To train the tool, we will use 3D image data from the Healthy Brain Network project {O'Connor, 2017 #166} (128-chan montage & 3D head images for >1,000 participants). We will also distribute and document the tools to easily construct label templates for other montages.

Figure 6. *Rotatable 3D head surface scan containing electrode position information.*

Aim 1.2. ICA-resolved sources. An ongoing challenge is to develop robust tools for estimating the precise cortical areas generating EEG (or iEEG) effective source processes identified by ICA decomposition (or any other method, e.g., beamforming). Once a participant's forward-problem head model is specified, and the scalp projection patterns (scalp maps) of one or more brain-based effective sources are identified from the data, one may estimate the spatial source equivalent dipole model or cortical surface distribution using various approaches. If the scalp map giving the signs and relative strengths of the source to the scalp channels has a nearly dipolar (or dual-dipolar) form, the source centroid(s) may be modeled using a single (or dual) dipole model {Delorme, 2012 #85}. With consultant Arthur Tsai of Academica Sinica (Taiwan), we will develop functionality to add EMSICA, a ***sparsifying decomposition of scalp EEG*** data following projection to the cortical surface (using an orthogonality constraint), and clustering of ICA-resolved EEG effective sources based on the nonlinear cortical co-registration available in Freesurfer {Tsai, 2014 #120}.

Aim 1.3. Use of template MNI brain. EEG is a relatively low-cost brain imaging method and has been used in the past as in effect a scalp imaging (rather than a 3D brain imaging) modality, most EEG laboratories do not acquire MR head images for their subjects. Of the 104 EEG experiment datasets currently released on *OpenNeuro.org*, only 11 contain the subject head images, and only 6 MR images *and* scanned electrode positions. Both are required for high-resolution source localization. How accurate can EEG effective source localization be when subject MR head images are not available? In a detailed simulation, we showed that using a template MR image decreases the accuracy of equivalent dipole source localization accuracy compared to using an individual subject image ({Akalin Acar, 2013 #35}, 242 cites). Some of our preliminary results suggest to us that template *model averages or medians* across individuals with similar electrode positions can enable more stable and accurate effective source localization. By estimating the localization errors, we may be able to compensate for them. No other software performs this type of correction to our knowledge. We will develop such a head modeling method and benchmark its efficacy on the very clean (MEG chamber-recorded) Henson & Wakeman EEG dataset {Wakeman, 2015 #134} for which individual head images are also available.

Critiques to high-resolution EEG source imaging. Some have argued, naively, that as nearby scalp EEG channel recordings are highly correlated, increasing the number of scalp channels provides little advantage in terms of usable signal. This is inaccurate, as others have shown improvement in source localization up to at least 128-256 channels {Chu, 2015 #135}. Deep learning models applied to EEG and MEG also show that increasing head coverage leads above 128 channels to improved classification performance {Défossez, 2022 #147}. Although this was not clear a decade ago, high-density EEG at 128 channels and above has undeniable advantages and is poised to become the norm. Some have argued that "low-resolution" source imaging methods such as the widely used *eLoreta* {Pascual-Marqui, 2002 #152} do not benefit from a high-density EEG montage. However, this is definitely not the case for localization methods including ***Linear Constraint Minimum Variance (LCMV) beamforming***. When compared by Pellegrini et al. {Pellegrini, 2022 #148} on connectivity calculated between simulated 97-channel EEG sources, connectivity accuracy using *eLoreta* did not exceed 70%, while for the same simulated data *LCMV* beamforming accuracy reached 99% . Unlike *eLoreta*, *LCMV* beamforming requires a precise head model and electrode coordinates. Both *eLoreta* and *LCMV* beamforming are now available in EEGLAB.

Aim 1.4. Connectivity analysis between regions of interest (ROIs). Effective source-resolved connectivity models estimate how brain effective sources affect each other as well as when and how these effects manifest. Connectivity models define a network of local brain sources plus connectivity measure values between them (in time, frequency, or time-frequency domains). They operate by finding relationships that prevail across single trials or time windows despite all other differences between them. EEG/MEG data typically derive from studies probing specific aspects of cognition through contrasts between conditions, subjects, event types, source activities, and effects. *ROIconnect* (planned for release next year) computes connectivity between regions of interest defined in MRI atlases using a variety of methods, with the recommended methods being the ***Multivariate Interaction Measure*** (MIM) and a ***time-reversed Granger Causal*** measure (TRGC) (Fig. 7). We have shown that it was possible to accurately reconstruct simulated EEG effective sources {Pellegrini, 2022 #148}. The *ROIconnect* plug-in will support four cortical fMRI atlases (two volumetric and two surface). However, reliance on fMRI atlases remains an issue. There is no reason for EEG effective source activities to arise precisely within single anatomy- or fMRI-defined regions. In addition, source location inaccuracy of even a few mm could cause it to be assigned to a different brain region.

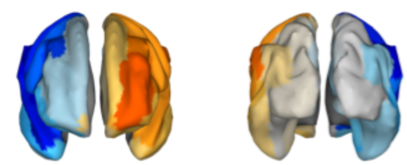
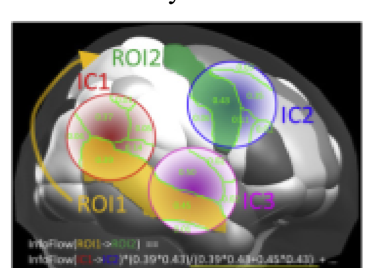


Figure 7. *Right vs left hemisphere TRGC connectivity during movement imagination in 68 cortical ROIs computed using ROIconnect {Pellegrini, 2022 #148}.*

Whole-brain connectivity. We therefore propose a new approach to compute pairwise connectivity between all LCMV-computed ROI estimates in a distributed source model. Significant connections will be assessed (uncorrected) through comparison to some other (or baseline) condition. We will then use an across-subjects cluster correction method to find which estimated ROIs are functionally connected to other ROI clusters. For example, in tasks requiring occipital-to-frontal cortex connectivity, we may expect an ROI cluster in the occipital cortex to granger-influence a cluster in frontal cortex. Our ***new multiple-comparison correction methods*** will be based on existing cluster methods we implemented in LIMO, generalizing them to multiple non-uniform dimensions. This correction method will ignore single-subject voxel connections that are not biologically plausible or not in common across some or many subjects.

What is the ideal number of brain ROIs for performing connectivity analysis? The whole brain analysis described above is impractical for routine analysis. We estimate that, using a 2,000-ROI volume mesh, computing whole brain connectivity on one minute of data would require about 700 core hours for the *MIM* measure and about 21,000 core hours for *TRGC* (about two years on a single-core workstation). This does not involve applying the clustering technique, which will also require dozens of hours. We can perform some analysis on this scale using the SDSC supercomputer (see Dr. Majumdar and Dr. Wuerthwein letters of support), but we also need to find a practical solution for routine applications. For each simulated source ROI model, we will gradually reduce the anatomic resolution of the ROI model (e.g., to use 2000, 1500, 1000, 750, 500, 375, 250, 198, 125, and 100 ROIs) and will assess the accuracy of the reconstructed *simulated EEG source connectivity*. We will then release *ROIconnect* with optimized suggested parameter selections. ***Group results.*** Group connectivity analysis across subjects will be performed using general linear model (GLM) analysis in *LIMO*. With consultant Dr. Pernet, *LIMO* will be extended to process connectivity analysis results while supporting most statistical designs, (ANOVA, regression, repeated measure ANOVA, ANCOVAs with arbitrary numbers of continuous and categorical variables, etc.).

Aim 1.5. Connectivity among ICA-identified effective source processes. *SIFT* {Delorme, 2011 #19} and ***groupSIFT*** {Loo, 2019 #132} are EEGLAB plug-ins supporting modeling of functional connectivity between ICA-identified effective sources. This ICA-based approach differs from that of many papers on EEG functional connectivity that use ROI beamforming approaches as described above {Gross, 2001 #158;Mahjoory, 2017 #149}. *SIFT* and *groupSIFT* first seek to characterize effective connectivity between subspaces of maximally independent effective sources compatible with an origin in one (or else two,



presumably anatomically coupled) cortical patch(es) {Delorme, 2012 #85}. Although computing connectivity between "independent" components may seem to be a contradiction, in practice ICA decompositions find cortical effective sources that are *maximally* – not completely – independent *at zero lag*. The high density of local vs. long-range neural connections in the brain may explain why ICA can separate effective sources localizing to compact cortical patches of cortex within which local field activities are then fully or partially synchronized, among which pairwise connectivities (*at non-zero lag*) may be assessed. Dozens of articles on functional connectivity between ICA components at the single subject and group levels have been published {Loo, 2019 #132;Koshiyama, 2020 #146;Koshiyama, 2020 #145;Koshiyama, 2021 #144}. ***Group analysis of connectivity matrices.*** One challenge associated with analysis of functional between ICA-derived effective source processes is that, while it is possible to find matching components in multiple subjects using cluster methods {Onton, 2006 #15;Campos Viola, 2009 #10;Bigdely-Shamlo, 2013 #13}, some efficient source clusters across the group may not include sources from every subject. Such missing network nodes renders group analysis difficult. In *GroupSIFT* {Loo, 2019 #132}, we have developed a method to assign effective sources to regions of interest (ROIs) and then compute pairwise connectivity (Fig. 8). However, this method depends on the cortical parcellation, and cannot reliably compute connectivities between neighboring brain ROIs. To address these issues, we propose implementing an innovative graph-based method based on an ***mHBL effective source connectivity model*** {Thompson, 2011 #163}. Fig. 9 shows a schematic of the generative model upon which the *mHBL* model is based. For each subject's multivariate EEG time series, we estimate three-dimensional spatial coordinates *f*or the ICA-derived brain effective sources (using *NFT* to fit optimal equivalent dipole source models) and obtain time-varying directed connectivities between each effective source pair using one of several measures, including multivariate autoregressive (MVAR) model fitting and Granger-causal analysis applied to the effective sources' time series. We assume that the collection of connectivity matrices is parameterized by a low-dimensional set of coefficients capturing the connectivity between all pairs of sources. We plan to instantiate one such parameterization involving smoothing using functional principal component analysis (FPCA) {Di, 2009 #164}. For a given subject population, we posit the existence of ***an unobserved population-level "meta-graph"*** where nodes represent EEG source densities and edges correspond to time-varying connectivities between all pairs of effective sources (nodes). We then assume that each subject's observed connectivity graph is a randomly-drawn sub-graph of the population-level graph**,** with subject-level random effects on spatial location and connectivity strength. Under an assumption of multivariate Gaussian distributions for the spatial locations of the population-level nodes, *mHBL* is a hierarchical generalization of a standard multivariate Gaussian mixture model for probabilistic clustering, combining data obtained from multiple partial "views" of the latent graph, i.e., subject-level source locations (nodes) and inter- and intra-node dynamics (graph edges), that incorporates subject-level differences in subgraph dimension. The goals of the *mHBL* model are: (1) To characterize the graph population graph, including the complete posterior distributions over locations and connectivities; (2) To correctly assign each subject effective source collection to nodes of the population-level graph; (3) To optimally address subject-level *missing data*, i.e., frequent cases in which the number of effective sources found for a given subject is lower than the number of population-level clusters (nodes). ***Validation.*** We will develop a series of simulations to evaluate the performance of *mHBL* under varying degrees of missing data. We will first define a ground-truth population graph consisting of a set of spatial nodes (cluster locations in the MNI "Colin27" standardized brain) with corresponding time-varying pairwise connectivity edges. The *mHBL* functionality will be released as a new group-analysis method within *groupSIFT*. To increase the numbers of effective source processes in each subject's data, we will also test computing multiple time-limited ICA models using multi-model *AMICA*.

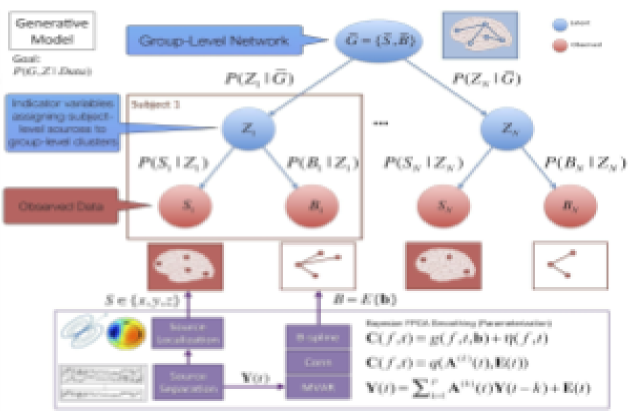


Figure 9. *Schematic of the mHBL generative model {Thompson, 2011 #163}.*

Aim 1.6. Comparison of groupSIFT and ROIconnect. We will compare the performance of the two connectivity plug-ins for source-resolved connectivity analysis on ***simulated and actual EEG data***. We will construct simulated data with connected sources with different numbers of sources, noise levels, and connectivity strength, then project these sources through a realistic forward model using *NFT*. We will then use each method to reconstruct source connectivity and will compute area under the curve (AUC) performance in detecting non-zero connectivities. We will also calculate the average pairwise difference between all ground truth sources and posterior mean connectivity estimates and will assess the Euclidean distance between spatial locations of centroids estimated by *GroupSIFT* and *ROIconnect*. We will also compare the results of the two methods on actual EEG data {Schalk, 2004 #67}. ***Group analysis.*** Although the data of individual subjects might differ, group analysis can identify underlying commonalities between subjects. We will assess the difference between the two approaches on simulated and actual data (*LIMO*-based cluster-based statistics for *ROIconnect*, and the *mHBL* group source connectivity model for *GroupSIFT*). We will simulate subject data by varying simulated source locations and connectivity strengths, and will assess the performance of each model by calculating differences from ground truth (errors in connectivity estimates and source cluster localization). To compare the two models as applied to actual data, we will use available ***data from a movement imagination task*** recorded on 109 subjects {Schalk, 2004 #67}, and will qualitatively compare the brain networks computed by the two models for relative strength and physiological plausibility.

■ **AIM 2: INTRODUCE AND DEMONSTRATE THE UTILITY OF NEW TOOLS FOR PROCESSING iEEG DATA.** Intracranial EEG (iEEG) recording is most commonly performed to plan surgery for epilepsy that is not treatable using pharmacological approaches and whose surgery target is unclear from other imaging and scalp recordings. Intracranial EEG recording (iEEG) uses two main methods, subdural electrode grids and/or strips (ECoG) or stereotactic (stereo) EEG (sEEG). ECoG was developed earlier and typically involves removing a large portion of the skull, while sEEG, currently the dominant clinical approach, uses long needle-like electrodes with up to 17 independent contacts in a several cm linear array that are inserted into small burr holes drilled in the skull, thereby reducing the level of brain swelling, patient discomfort, and risk of infection (Fig. 10). iEEG data offer a unique window into human brain activity at time scales supporting individual thoughts and actions. iEEG signals are about ten times larger than scalp EEG, as they are mostly attenuated while passing through the skull, and largely avoid contamination by scalp muscle activity, eye movements, and other non-brain source activities. Clinical iEEG data provide up-close (though still spatially sparse) information about activity in cortical (and, for sEEG, other) brain tissues at the sub-cm scale *and above*. In practice, sEEG recording is increasingly employed as it yields both cortical and subcortical data and has both clinical safety and patient comfort advantages. When active cortical or subcortical effective source or source network nodes are monitored simultaneously, iEEG signals can also reveal functional interactions between them. With its unique spatiotemporal resolution, iEEG/sEEG data complements the results of other human neuroimaging recording methods.

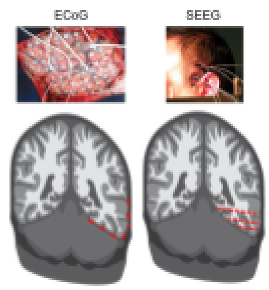


Figure 10. *(left) ECoG versus (right) SEEG recordings.*

Existing tools for iEEG. Tools currently available to flexibly process intracranial EEG are sparse and no open-source packages for sEEG data analysis currently exist. RAVE, an R and web-based tool to process iEEG data built with NIH support (5R24MH117529), offers a quite narrow range of signal processing capabilities and is currently not widely applicable (5 citations per Google Scholar). Fieldtrip, MNE, and Brainstorm do have dedicated tools and tutorials on processing intracranial data and coregistration of ECoG electrode locations with anatomical (MRI, CT) brain images, with again fewer applicable signal processing tools (iEEG+Fieldtrip citations, 198; Brainstorm, 91; and MNE, 55). Although EEGLAB currently has no spatial visualization or data co-registration functions dedicated to processing iEEG data, it is still often used and cited in iEEG research (109 cites). Under Aim 2.1 and 2.2, we propose to build, test, and release basic iEEG and sEEG data handling and visualization tools in EEGLAB, including ***innovative tools for visualizing locations of sEEG*** electrodes in an inflating cortical brain and co-visualization of co-registered electrode locations and white matter tractography {Huang, 2022 #167}. EEGLAB high-resolution source localization and imaging tools (cf. Aim 1) will also allow the joint analysis of iEEG and scalp EEG data when these have been recorded simultaneously.

Key personnel Dora Hermes is a leader in defining BIDS formats for iEEG data {Holdgraf, 2019 #129}. However, tools available to convert and process BIDS iEEG data remain limited, with EEGLAB at present the only open software environment with tools to import BIDS iEEG datasets. A critical need of the iEEG research community, going forward, is BIDS tools to properly annotate iEEG data, to export it into a standard format, and to read data stored in that format. BIDS and our *Hierarchical Event Descriptor (HED)* framework {Bigdely-Shamlo, 2013 #39;Robbins, 2021 #143} are ideal tools for this. Extended support for *BIDS / HED* formatting and annotation will allow the broad EEGLAB signal processing toolset to be applied efficiently to iEEG and sEEG data. Dr. Hermes is now building the first *HED* library schema (lexicon) to describe features of clinical EEG and iEEG data using the internationally accepted SCORE annotation lexicon {Beniczky,

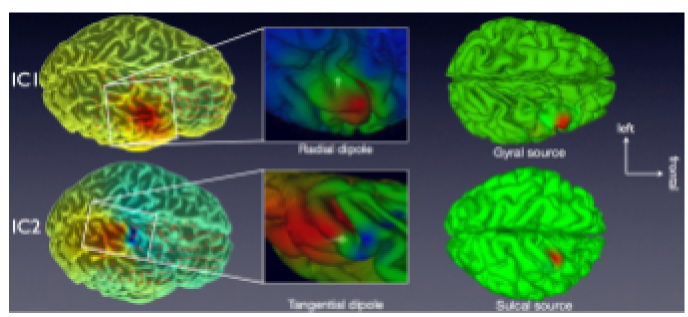


Figure 11. *High-resolution (right) versus equivalent dipole localization (middle) of two ICA-resolved ECoG data effective sources (left) using our NFT toolset. Results show that IC2 is a epileptic source located in s sulcus, while IC1 has a gyral origin.*

2017 #159}. With her guidance, we will collaborate with the *BIDS/HED* community to create a *HED* library schema for documenting iEEG connectivity measure data (now under development in BIDS initiative BEP017).

Aim 2.1. ICA decomposition of iEEG data. We will provide dedicated support functions in EEGLAB for computing and visualizing ICA decomposition results applied to iEEG and sEEG data. As we showed earlier ({Mullen, 2011 #168}, 12 cites; {Whitmer, 2010 #160}, 34 cites), ICA decomposition applied to data recorded by cortical ECoG electrode grids can reveal cortical effective source areas in sulci beneath the electrode grid surface (Fig. 11, lower row) as well as on gyri (top row). ICA decomposition of sEEG data has been little explored (cf. {Hofmanis, 2011 #165}, 4 citations only). Effective source activities may project to one or many sEEG electrodes, where their activities will be summed and recorded. This appears to be an ideal application for ICA decomposition, as its chief assumptions (linear signal summation at the electrodes, relative spatial effective source stationarity) are fulfilled. Fig. 12 shows a sample decomposition of 15 sEEG data channels (contacts on a single sEEG electrode) versus average reference). Independent component (IC) electrode weights (upper left) and IC time courses (lower right) account for near-always features in *multiple channels* within different cortical layers and areas (upper right). ***Modeling sEEG signal nonstationarity.*** As the sEEG effective source distributions may shift over longer recording times, we will test the application of multi-model adaptive mixture ICA (*AMICA*) decomposition {Palmer, 2008 #169}, also developed in our laboratory, to identify and characterize these shifts. *AMICA* can separate its training data into subsets, each most probable under one of the *AMICA* data models. Recent results support the observation that *AMICA* models often expose functional as well as numeric nonstationarities in the ICA effective source structure, for example, changes in sleep stage, in behavioral alertness during a continuous driving simulation {Hsu, 2017 #173}, and between periods of actively imagination of experiences inducing 15 different emotions {Hsu, 2022 #170}. As electromagnetic propagation through cortical neuropil can include both immediate (largely CSF-mediated) volume conduction as well as much slower intraneural propagation, we will also test the application of EEGLAB plug-in *CICAAR* (convolutive independent component analysis with an auto-regressive inverse model) {Dyrholm, 2007 #174}, also developed in our laboratory, to separate these factors. ***Validation.*** Validation will be performed with one of Dora Hermes' dataset (the same one used in figure 12). After the article describing this dataset is published in 2022, the data will be released publicly in BIDS format.

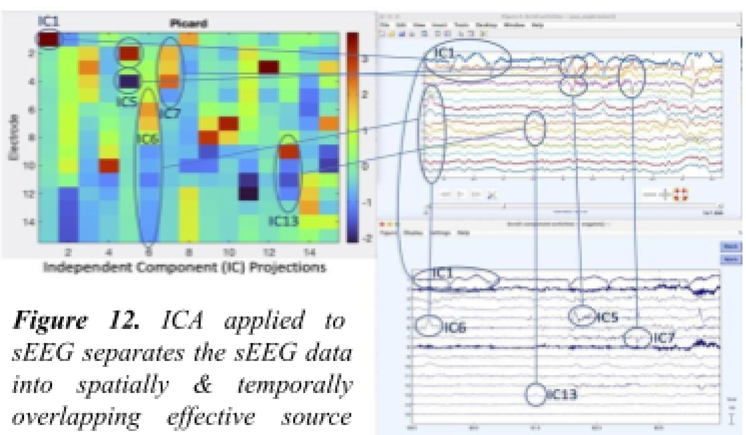


Figure 12. *ICA applied to sEEG separates the sEEG data into spatially & temporally overlapping effective source activities. (left) Columns show channel weights of the 15 ICs. (upper right) Phenomena in the raw sEEG data representing projections of single IC processes are circled. (lower right) IC effective source waveforms for the data. Data decomposition by Picard ICA (~5 minutes from 15 contacts along one sEEG electrode; average reference across the multi-electrode data).*

Aim 2.2. Connectivity analysis of iEEG sources. EEGLAB has a strong set of functional connectivity analysis tools based on multivariate quasi-granger causality, not available in any other toolbox (see Aim 1). These tools may assist in characterizing functional relationships (and characteristic as well as event-related delays) between sEEG effective sources. We will use another available dataset (*zenodo.org/record/1201560*) comprising both 96 ECoG and 56 sEEG data channels recorded in a single patient. The dataset contains pre-implant T1-weighted MRI, post-implant CT, and post-implant T1-weighted MR head images. The subject simply presses a button whenever (s)he hears a presented tone. We will first define MRI coordinate systems to allow FreeSurfer tools to extract scalp, skull, and cortical surfaces. We will then align these Freesurfer brain tissue meshes with the CT scan data. Electrode locations will be imported and aligned with the MRI, first coarsely, then more finely, using warping localization methods that minimize the distance of ECoG electrodes to the cortical surface. Once the alignment is performed, event-related spectral decomposition of the electrode activity will be performed to assess brain dynamics time-locked to auditory presentations and ensuing motor responses. We will perform ICA decomposition of the ECoG and/or sEEG data using *AMICA*, and will compute effective connectivity between effective sources, and will publish the results in one or more research articles detailing the methodological details, in an online tutorial and in an associated educational video detailing how to apply the tools on other iEEG data.

■ **AIM 3. MOBILE BRAIN/BODY IMAGING.** *We propose to add new, flexible multimodal data processing capabilities to the EEGLAB environment* by reformulating it to add support for processing multi-modal data including EEG, collected within the *mobile brain/body imaging (MoBI)* research framework {Makeig, 2009 #156}. First, we will add general support for performing ***multi-stream data visualization*** (Fig. 13), updating and optimizing the approach in our earlier multimodal browser, *MoBILAB* {Ojeda, 2014 #96}. We have extensive experience using the *LabStreamingLayer (LSL)* software and the associated multimodal *Extensible Data Format (.xdf)*, both developed in our lab. Synchronization of streams collected on different systems requires interpolation based on timestamps inserted into each data stream - in *LSL* these are introduced at a rate of 5 per second. In practice, LSL can achieve millisecond precision or better synchronization across nearly any number of concurrent data streams (e.g., in our experience, 40 streams of high-density EEG, video, audio, motion capture, etc.). We will then resample the different streams at the same sampling rate as the EEG (excepting still higher-bandwidth video and audio streams). Next, we will support the development of ***multimodal data processing measures including connectivity measures and statistics*** in the time and time/frequency domains. EEGLAB will thereby evolve to become multimodal software capable of processing different peripheral data types (EMG, ECG, GSR, and body temperature) as well as body motion capture and eye tracking data, taking advantage of their (now in place or under development) BIDS-defined standard formats. We will also provide documentation on using functions from the *WaveFormDataBase (WFDB)* toolbox and the *ECG-Kit* (*marianux.github.io/ecg-kit/*) to preprocess ECG data, extract peak latencies, and computing time-varying heart rate and heart rate variability (*macalester.edu/~kaplan/hrv/doc*). To integrate multimodal data collected using *LSL* into *BIDS*, we will propose and work to develop a new *BIDS* standard for storing multimodal *LSL* timestamp data streams, allowing full storage of multimodal *.xdf* data under *BIDS*.

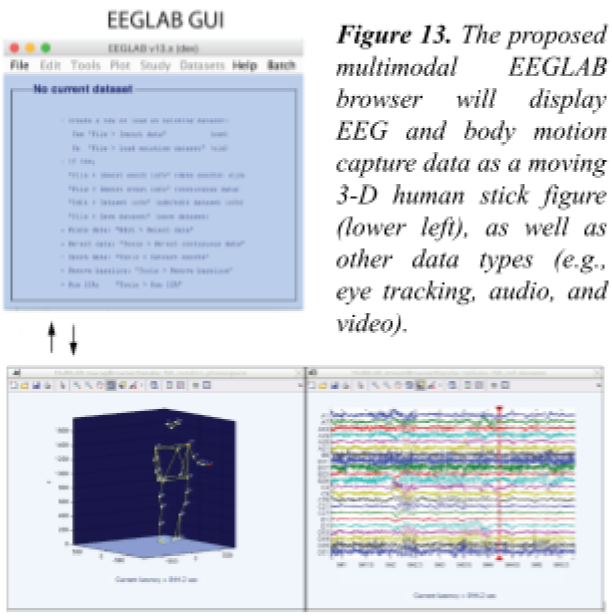


Figure 13. *The proposed multimodal EEGLAB browser will display EEG and body motion capture data as a moving 3-D human stick figure (lower left), as well as other data types (e.g., eye tracking, audio, and video).*

Aim 3.1. Visualizing and preprocessing MoBI data. In analyzing multimodal data, an ability to interactively review the multiple data streams is critical for selecting and evaluating data from a multimodal experiment. We will extend the *MoBILAB* multi-stream browser (*MSB*) {Ojeda, 2014 #96} that allows visual inspection, annotation, and sanity checking of recorded multimodal EEG and 3-D motion capture data (Fig. 13). Conversions of 3-D body motion capture data to generalized coordinates (its multiple time derivatives) will be extended. We will also introduce a method for transforming marker position data to a data-equivalent human body-centered reference frame recently introduced for upper limb movements by colleagues Tanaka and Sejnowski {Tanaka, 2018 #175}. Instead of representing body motion in terms of joint torques and angles as used in robotic design, Tanaka's approach uses a data-equivalent basis of ***inter-joint distances***, quantities that are more readily computed and monitored by the brain and body and that have more ecological relevance since our movements occur within peripersonal space (e.g., *space within reach)*. Transformed into this framework, body movement data should be suitable for analysis in conjunction with the effective source-resolved EEG (or iEEG) data. Multiple ***audio and video streams*** may be included in a multimodal *.xdf* recording. In the multistream browser, audio data will be visualized either as a time series or as a spectrogram, and a 'Play' button in the browser interface will play back audio and/or concurrent video (when available) for the currently selected browser time window. We will use the Java Media Framework, or Active X on Windows OS, to play video from disk for better stability. To mark events of interest, users will be able to add events manually or use automated scripts (for which we will make templates available). Combining lower-sampling rate ***eye gaze tracking data*** with higher-sampling rate EEG data allows fixation intervals to be identified precisely in the EEG and other high-rate data streams. We will develop a plug-in to perform efficient artifact correction for eye tracking data and to find fixations, to plot gaze trajectories in both 2-D and/or 3-D space in the multi-stream browser, and to compute time and time/frequency domain EEG dynamics time locked to eye movement events.

Aim 3.2. Inter-stream connectivity analysis. We will provide functions to compute connectivity between the different data streams. For this, functions available for EEG (using correlation, coherence, partial directed coherence, directed transfer entropy, and granger causality) will be adapted for multimodal connectivity analysis in the time and time/frequency domains. We will adapt the current EEGLAB group-data *STUDY* structure framework to implement statistical analysis of multimodal data measures within the general linear model (GLM) framework {Pernet, 2011 #33}. The multimodal EEGLAB methods will compute significance and confidence intervals using bootstrap approaches that provide unbiased estimates and may also be robust when applied to relatively few samples.

Aim 3.3. Test dataset. We will perform analysis on an existing laboratory dataset, our full body 3D maze exploration experiment dataset using a virtual 'audiomaze' paradigm {Miyakoshi, 2021 #176} to compute ***inter-joint distances and***

model dynamics of information transfer between reaching movements and EEG effective source dynamics. We will make available an EEGLAB tutorial on the analysis process for these (and/or any similar) MoBI data.

EEGLAB code maintenance and evolution. Supporting the most popular EEG software package is a large responsibility. Maintenance of large, complex open-source code involves housing and backing it up properly, making it readily available to users and developers, using proper identification for new versions that should retain backward compatibility, maintaining an automated testing process for side effects of any code changes, soliciting, handling, and responding to bug reports from users, and studying use patterns to distribute the programming effort properly. Although most of the EEGLAB release process is automated, we plan to ***make the entire release process fully automated***, reducing risk of operator error. We are currently not strictly ***enforcing backward compatibility*** but plan to put a framework in place to do so. We will ***simplify bug reporting*** by using built-in MATLAB functions and provide clear instructions on posting software reports and queries on GitHub. We will implement a mechanism to prompt users who have cloned EEGLAB from Git to update their local Git repository when needed. We will investigate expanding our online tools for anonymous opt-in acquisition of ***more detailed usage statistics*** from participating users to gain insights into common usage patterns. We will continue distributing a ***compiled EEGLAB release*** with each EEGLAB release, adding new plug-ins as they become available. For the first time, we will release EEGLAB as a ***compiled Python library***, making EEGLAB data structures and functions available to Python users, while *not* requiring them to have MATLAB installed. Here we will need to differentiate graphic and non-graphic functions, as when running on Python, graphic EEGLAB functions must use MATLAB/Java-based graphics, while some users may prefer to use native Python graphics only**.** Plug-ins are perhaps the most important feature of EEGLAB; we will continue to support ***versioning of plug-ins*** allowing users to update their plug-ins at any time and notifying all EEGLAB users of new plug-in releases. New user-developed plug-ins often incorporate naming conventions that conflict with existing EEGLAB or MATLAB functions, creating hard-to-find bugs; we will set up automated **pl*ug-in testing and certification methods*** to avoid this.

User Education. Our recent review comparing the available EEG software packages {Delorme, 2022 #172} revealed two surprising reasons for the success of EEGLAB: first, its plug-in system allows the organic diffusion and updating of new user-contributed tools; second, its ***documentation quantity and quality*** is sufficient for most users to take advantage of on their own. For this, maintenance of ***the EEGLAB website*** (*eeglab.org*, now migrated from MediaWiki to the Jekyll framework) is critical. We will continue to add new documentation including worked examples, and will improve ease of navigation by linking relevant pages to each other. Our educational ***EEGLAB YouTube channel*** now comprises 63 videos that have received about half a million views since the channel was created in 2018. We will continue to post new videos and will associate each with one or more tutorial pages on the EEGLAB website. Since 2019, we have released 13 ***quarterly EEGLAB newsletter*** issues to the >15k subscribers to our news list, featuring new developments in EEG research and EEGLAB plus profiles of longtime EEGLAB users and developers. Since 2018, despite the COVID pandemic we have organized four in-person ***EEGLAB workshops*** (in La Jolla, CA; Pittsburg, KS; France; Poland), plus two virtual workshops for US/European and Asia-Pacific time zones, respectively with over 1300 total participants.

Schedule of tasks. The Gantt diagram below indicates the planned tasks schedule. On a given row, we must complete a given task before the next one starts. Deliverables for each task are indicated in the proposal above (see the budget for the researchers' task assignment). Each sub-aim will lead to the publication of a journal article (a total of 11 planned).

	Year 1				Year 2				Year 3				Year 4				Year 5			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
SA1. HIGH-RES EEG (source imaging)	Aim 1.1						Aim 1.2						Aim 1.3							
SA1. HIGH-RES EEG (connectivity)	Aim 1.4						Aim 1.5								Aim 1.6					
SA2. NEW TOOLS FOR iEEG DATA	Aim 2.1												Aim 2.2							
SA3. MOBILE BRAIN/BODY IMAGING	Aim 3.1						Aim 3.2								Aim 3.3					

REFERENCES