DeepPsy

BIOMARKERS

In-house Analysis Software

Instructions for Use

02/05/2024

v1.0

Contents

1 Label Information

Manufacturer:
DeepPsy AG (https://deeppsy.io/)
Forchstrasse 154
8125 Zollikerberg
Switzerland

Medical Device
DeepPsy Biomarkers
Version: 1.0
Release Date: 26/04/2024

Unique Device Identifier
UDI-DI 76499883279DPmarkersML

2 Symbols Used in this Document

This symbol is used throughout this document to highlight sections that require special attention.

3 Contact & Incidents

In case of serious incident or near-incident caused by DeepPSY Biomarkers software, please immediately report to the Quality Assurance Officer. Alternatively, contact the DeepPsy AG using the information provided below.

Email	support@deeppsy.io
Phone Number	+41 44 797 62 29

In case you require this user manual in printed form, please contact DeepPsy AG using the information above.

4 Product Description

The DeepPSY Biomarkers is a in-house standalone software application that enables DeepPsy specialists to analyze data derived from electroencephalogram (EEG) and electrocardiogram

(ECG), and compute electrophysiological biomarkers. Biomarkers are a broad subcategory of medical parameters – objective indications of a physiological state that can be measured accurately and reproducibly.

The DeepPsy Biomarkers software is intended for in-house use by DeepPsy AG exclusively.

This medical device is a software that is installed locally on a standard personal computer, as detailed in the compatibility section. The application allows specialists to:

- Select EEG and/or ECG data files.
- Visualize and preview the chosen EEG and/or ECG data.
- Perform data quality validation on the EEG and/or ECG files
- Preprocess the EEG and/or ECG data through a series of steps, making it suitable for biomarker computation. This preprocessing consists of both manual and automated steps.
- Compute EEG and/or ECG biomarkers on the preprocessed data.
- Generate the the “DeepPSY Biomarkers’s Report” in PDF format.

The medical device is capable of producing a set of files according to the operator’s configuration. These include the raw biomarkers in numerical format (such as JSON files), and charts. Moreover, a report can be produced called ”DeepPSY Biomarkers’s Report” that can be provided to physicians.

Furthermore, the software communicates with a remote system hosted on a cloud service provider via the internet to perform basic functions such as authentication of the DeepPsy specialist, collection of logs, file uploads/downloads, and telemetry.

4.1 Intended Purpose

DeepPSY Biomarkers is a in-house standalone software that assists in displaying, analyzing, and providing information through the examination of electrophysiological signals derived from human electroencephalogram (EEG) and electrocardiogram (ECG) data. The software is exclusively intended for use within DeepPsy AG and by specialists accredited by DeepPSY AG. The information provided by the software is intended to be used by physicians, who have to exercise their professional judgment when using this information.

4.2 Intended User

The intended users of this software are qualified specialists trained in electrophysiology and accredited by DeepPsy AG. The software is intended to be used in-house only. The intended users of the information provided by the software are qualified medical practitioners, who need to exercise their professional judgment when using this information. The information are delivered in the form of a ”DeepPSY Biomarkers Report” outlined below.

4.3 Patient Group

The patient group includes any patient for whom a physician has requested the respective information. The information provided by DeepPsy Biomarkers are not intended to drive diagnosis, but to support clinical decision-making as an additional source of data.

The DeepPsy Report is not intended to be used under the presence of neurological pathologies (in the EEG) or cardiac pathologies (in the ECG).

DeepPsy Biomarkers is not intended to be used as vital signs monitor not in any situation where measured parameters could result in immediate danger to the patient. DeepPsy Biomarkers should not be used with patients in critical conditions nor as a substitute of a standard of care in serious or time-sensitive situations. The risk of software error or failure cannot be completely excluded.

4.4 Intended Clinical Benefit

This medical device is designed to offer insights into a patient's electrophysiological parameters. It also incorporates the latest findings from state-of-the-art literature in the field of precision psychiatry, which is intended to aid in the interpretation of these electrophysiological data.

The DeepPsy Biomarkers has the intended clinical benefit of improving patient quality of life by supporting the decision process for psychiatric disorders and their comorbidities by providing supporting information from patients electrophysiology.

4.4.1 General Manufacturer Claims

Type	Claim
Performance	Correctly read, process, and display the data according to the specification given by the operator. The medical device does not pose further risks beyond those that are already present in the state of the art.
Benefit	The information provided by the medical device allows for gaining insights into the patient's electrophysiology. The information provided by the medical device correlates with the likelihood of response to certain state-of-the-art treatments (Precision Psychiatry).
Non-Medical Related	The EEG/ECG analysis is fast and efficient.

⚠ 5 Contraindications

The DeepPSY Biomarkers software, DeepPSY Biomarkers's Report, and every other output:

- Is not intended to be used under the presence of neurological pathologies (in the EEG) or cardiac pathologies (in the ECG).
- Is not intended to replace the expertise and guidance of a physician or psychotherapist.
- Is not intended to be used to make decisions about whether to undergo a psychiatric treatment or not.
- Is not intended to be used as a final, mandatory guideline or recommendation.
- Is not intended to be used for self-diagnosis or self-treatment.
- Is restricted to the approved geographic areas.

⚠ 6 Cautions on DeepPsy Biomarkers Software

- DeepPSY Biomarkers is only intended to be used within the DeepPsy AG.
- DeepPSY Biomarkers must be used only for its intended purpose and not beyond that scope.
- DeepPSY Biomarkers must only be used by an authorized DeepPsy specialist who has the prerequisite training and accreditation by DeepPsy on electrophysiological signal data analysis.

⚠ 7 Cautions on DeepPsy Biomarkers Report

- DeepPSY Biomarkers Report must be used only when requested and interpreted by a physician or psychiatric/medical institutions.
- DeepPSY Biomarkers's Report must be used only as an additional source of information alongside other clinical and paraclinical sources of information, and the relevance of the report is weighed in the context of the entire clinical picture.
- DeepPSY Biomarkers's Report must be used only when the EEG and ECG data from which this report is generated come from certified medical device amplifiers.
- DeepPSY Biomarkers report can be used if the requesting doctor has reviewed the EEG and ECG data for neurological or cardiac pathologies or the influence of medications.

8 Safety Instructions & Technical Description

8.1 System Requirements

The DeepPSY Biomarkers medical device is a stand-alone software product compatible with personal computers with the following minimum characteristics:

Operating System	Microsoft Windows® 10 or higher
CPU	2 GHz or higher, 4 virtual cores or higher
RAM Memory	8 GBs or higher
Disk Space	At least 3 GBs of free disk space
Display Resolution	1280x1024 or higher
Graphics Card	OpenGL 2.0 with 16 MBs of RAM or more
Network	An internet connection of 20Mbps of bandwidth or higher

8.2 Network Requirements

The application should be able to access the internet, specifically, cloud servers located in the region where it will be used. Thus, it should not be constrained by a firewall or other security application from reaching these servers.

8.3 Safety Measures

In order to ensure the safe and controlled use of the medical device, the operator must authenticate prior to using the medical device. The authentication mechanism is based on a simple username and password combination, which are provided by DeepPsy AG to all individuals who are authorized to use DeepPSY Biomarkers.

8.4 Application Environment

The application must always be up-to-date. Whenever DeepPsy AG releases a new version, it shall be communicated to all operators with access to it. Medical device versions older than the latest version will become deprecated and won't function.

Additionally, for best performance, it's recommended that the least amount of resources from the machine are used for other applications while running the DeepPSY Biomarkers software, as these would deprive the latter of the resources needed for its timely operations.

While a slower performance does not pose a risk in the use of the software, it is the User's responsibility to ensure the safety of combined medical or medical-&-non-medical- devices particularly installed in the patient environment.

9 Technical Specification

9.1 Biomarkers

9.1.1 EEG-Based

The DeepPsy's Biomarkers derived from resting EEG data are associated with various psychiatric disorders, including attention-deficit/hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), dementia, schizophrenia, and depression. These biomarkers can also be used to identify patient subgroups within these disorders.

9.1.1.1 Power Spectrum (qEEG)

EEG data include information about neural activity from different brain sites at frequencies. However, due to its non-stationary nature, the data are analyzed using the complex Morlet wavelet transform instead of the common Fourier transform, as it provides better time-frequency resolution [1]. The mother wavelet is chosen to match frequencies ranging from 1 to 80 Hz using a logarithmic scale. The resulting wavelet coefficients are then divided into the following frequency bands: delta (1 - 4 Hz), theta (4 - 8 Hz), alpha (8 - 13 Hz), beta (13 - 30 Hz), gamma1 (30 - 45 Hz) and gamma2 (45 - 80 Hz). There is abundant evidence demonstrating that the EEG spectrum is related to different psychiatric disorders [2-4]. Additionally, an increase alpha appears to be a predictor to non-response to paroxetine in patients with OCD [5].

9.1.1.2 Alpha Peak Frequency (APF)

The individual APF is defined as the frequency at which the alpha power is at its maximum. Previous research has shown that APF is associated with aging [6], as well as treatment response in ADHD [7] and depression [8]. In ADHD, a slowing of APF has been identified as a

marker of treatment resistance [7], while in depression, it is indicative of poorer treatment outcomes for escitalopram and venlafaxine-XR [8].

9.1.1.3 Frontal Alpha Asymmetry (FAA)

FAA is determined by calculating the alpha power extracted from two frontal electrodes F3 and F4. It is computed using an average reference with the formula (F4-F3)/(F4+F3), and a positive FAA indicates greater right than left alpha activity. FAA has been found to be associated with several psychiatric disorders, including ADHD [9], OCD [10], psychosis [11], schizophrenia [12] and depression [13]. Moreover, in the studies with depression, a greater right FAA was reported in SSRI female responders but not in SNRI female responders [13,14].

9.1.1.4 Aperiodic Exponent (1/f-like slope)

Aperiodic exponent is characterized by a 1/f-like distribution, whereby the power decreases exponentially with increasing frequencies. It is estimated by fitting a power-law function to the power spectrum in the frequency range after removing the oscillatory peaks. Recent work suggests that cortical excitability can be represented by the 1/f-like slope of the power spectrum density, with a flatter slope indicating increased and a steeper slope indicating reduced cortical excitability [15]. Furthermore, the aperiodic exponent has been found to be positively related to plasma escitalopram levels and to be associated with single does escitalopram-intake [16]. Patients with bipolar depression have been found to exhibit a flatter aperiodic exponent when compared to healthy controls [17].

9.1.1.5 EEG-Vigilance Regulation

EEG-vigilance is used to identify and analyze different functional brain states from full wakefulness to sleep onset with closed eyes EEG and electrooculogram (ECG) data. Each 1s epochs was automatically classified into the following arousal states, resulting in a vigilance time-course: stage 0 (highest arousal), A1, A2, A3, B1, B2/3, C (lowest arousal, sleep onset, classified visually by sleep grapho-elements from an experienced rater). In a typical case, non-alpha activity with the absence of SEMs would first appear after closing eyes (stage 0). The alpha activity would then dominate gradually from occipital (A1) to central and frontal (A2), and to mainly centralized at frontal area (A3) along with the relaxation of the participant. Subsequently, alpha activity would disappear and be replaced by low amplitude activity with SEM (B1) then dominated by delta and theta activity (B2/3). According to the VIGALL framework of EEG wakefulness regulation, MDD patients tend to show a hyperstable wakefulness regulation with a less propensity toward relaxation and sleep stages in comparison to healthy subjects [18,19]. Independent replication has shown reliably that treatment responders to SSRI have a higher propensity toward low vigilance stages in comparison to patients with no response [20,21].

9.1.2 ECG-Based

For each ECG channel, several Heart Rate Variability features are computed in both the time and frequency domains. It has been shown that these biomarkers differ between responders and non- responders in the treatment of the depressive disorder.

9.1.2.1 Beats per minute (BPM)

The number of heartbeats per minute. For example, a high heart rate is predictive of response to SSRI, SNRI, and Ketamine [22,23].

9.1.2.2 Heart Rate Slope

The slope is computed from the linear regression curve for the mean heart rate of three consecutive blocks of 40s. This biomarker is an estimate of the arousal of the sympathetic autonomic nervous system activity (ANS). The ANS arousal profile reflects the responsiveness of the nervous system to specific drugs such as SSRI and SNRI [22].

9.1.2.3 High-Frequency Power (HF)

It measures the activity in the 0.15 – 0.40Hz range. It reflects the Parasympathetic nervous system activity. Some treatments, such as agomelatine, can increase the parasympathetic tone, whereas others, such as tricyclic drugs, can decrease it [24].

9.1.2.4 Low-Frequency Power (LF)

It measures the activity in the 0.04 – 0.15Hz range It reflects the Sympathetic nervous system activity. Depressive patients showed a significant reduction of LF compared to the control group [25].

9.1.2.5 LF/(HF+LF) Ratio

Normalized ratio of Low Frequency. It reflects the Sympathetic to Parasympathetic Autonomic Balance [26].

9.2 Preprocessing Steps

The main preprocessing steps that are available for being applied to the EEG/ECG data are:

9.2.1 Initial Inspection

The operator is shown the EEG/ECG without any preprocessing steps applied to it, that is in its raw form. They may choose to create annotations on the EEG to specify certain behaviors, such as where to crop it, or instruct the application to invert the ECG signal (multiply it by -1), to mitigate cases where the electrodes were inverted.

9.2.2 Data Cropping

It involves selecting the EEG/ECG data to be used in the computation of the biomarkers. Usually, the period of interest corresponds to the eyes closed condition during a given period of time (several minutes).

9.2.3 Channel Interpolation

Channels that have been identified as malfunctioning or displaying excessive noise are manually selected. These channels are then reconstructed based on the data from surrounding channels to retain the integrity of the spatial information in the data.

9.2.4 Filtering

In this automated step, high-pass, low-pass, and band-pass filters are applied to the EEG/ECG data to remove frequencies that are not of interest or are known to contain artifacts, such as electrical line noise or heartbeat signals.

9.2.5 Montage Changer

This automated step involves altering the reference points of the EEG/ECG channels to correspond with different electrode positions on the scalp or body. This re-referencing can help diminish background noise and enhance signal clarity. Typically, EEG/ECG recordings use custom labels for each electrode that are specific to the recording institution. These labels need to be converted to standardized electrode names that are universally acknowledged. By doing this, each channel is accurately associated with its respective electrode, guaranteeing that the biomarker calculations are based on precise scalp electrode placement information.

9.2.6 Channel Creation

Automatically combining or transforming existing channels to create new channels, which can provide different spatial perspectives of the electrical activity and can be critical for certain types of biomarker computation. Often, channels needed for the analysis appear in the data as two channels that need to be summed together in order to capture the prerequisite data. In this step, such channels are identified and a new one is created out of their composition.

9.2.7 Bad Segment Selection

A human rater manually reviews the EEG/ECG data to identify and tag segments of the recording that contain artifacts or noise that automated cleaning processes have missed, ensuring these segments are not used in further analysis.

9.2.8 Independent Component Analysis (ICA) Filtering

This is an semi-automated process where statistical properties of the data are used to separate out components of the signal that represent noise or artifacts (such as eye blinks or muscle movements) from those representing brain or heart activity, which can then be selectively removed from the data. The operator selects the components that need to be eliminated from the data and then the original signal is reconstructed leaving out the undesired sources.

10 Performance Characteristics

For each biomarker, the method of calculating its accuracy is specified in the *"Calculation Method"* column.

- Mean Absolute Precentage Error is shortened to MAPE.

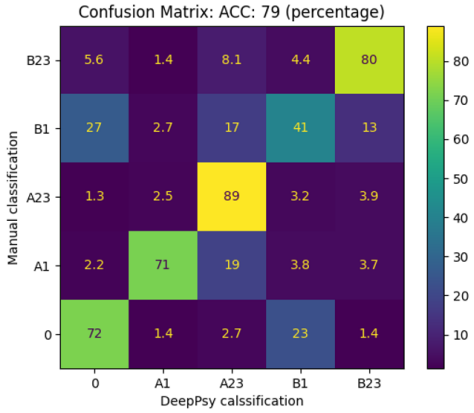
Biomarker	Accuracy	MAPE	Testing Accuracy
Alpha Peak Frequency (APF)	The discrepancy between the calculated values and the expected results is less than 0.25 95% should pass	0.001%	100%
Frontal Alpha Asymmetry (FAA)	The discrepancy between the calculated values and the expected results is less than 0.1 95% data should pass	0.52	100%
Power Spectrum (qEEG)	Discrepancy between the calculated values and the expected results is less than a passing criteria, which defined as the maximum between 10 and 10% of the expected values. 90% should pass	0.08%	100%
Beats per minute (BPM)	Discrepancy between the calculated values and the expected results is less than 1s.	0.006	94.5%
ECG Power	Discrepancy between the calculated values and the expected results is less than a passing criteria, which defined as the maxiumum between 10 and 5% of the expected values. 90% data should pass	0.009	91.74%
EEG-Vigilance Regulation	Refer to the confusion matrix in figure 1		

11 Installation & Uninstall

The application is bundled into a single, self-contained executable (.exe) file. In order to run the application you must:

1. Receive the executable (.exe) file from DeepPsy AG through an electronic means of communication such as email.
2. If the DeepPsy AG team provides a link for the download of the executable (.exe) file, proceed to download it.
3. Move the executable file to the desired final location where the application will reside.
4. Open the executable (.exe) file and wait for the application to load.
5. Authenticate using your credentials.

To uninstall the application, simply delete the executable (.exe) file.



	precision	recall	f1-score	support
0	0.38	0.72	0.49	220
A1	0.88	0.71	0.79	1017
A23	0.87	0.89	0.88	2654
B1	0.55	0.41	0.47	622
B23	0.72	0.80	0.76	728
accuracy			0.78	5241
macro avg	0.68	0.71	0.68	5241
weighted avg	0.79	0.78	0.78	5241

Figure 1: Performance of the VIGAZ algorithm for the calculation of EEG-Vigilance Regulation.

12 Configuration Requirements

To configure the DeepPSY Biomarkers system, you must use a pipeline definition file. This file, formatted in JavaScript Object Notation (JSON), specifies the operations to be performed by the application. The file organizes these operations into a sequence of steps, categorized into four groups based on their function. Additionally, each step can be configured using a set of parameters defined within the file. The various types of steps are:

- **Validator:** This step examines the incoming EEG/ECG data to confirm its appropriateness for the subsequent analysis. If the data fails this validation, the analysis is halted.
- **Preprocessor:** In this phase, the EEG/ECG data is either converted into a new format or specific metadata is extracted and conveyed to the subsequent steps.
- **Biomarker:** Utilizing the EEG/ECG data and any relevant metadata, this step calculates a particular biomarker.
- **Post-Processor:** This step further modifies the EEG/ECG data or derives additional metadata, sometimes employing insights gained from prior biomarker computations.

See the list of all available pipeline steps below in “List of Available Steps”.

13 Pipeline Definition

The pipeline definition is a document in JSON format which outlines the analysis template that the software will use to analyze data items. It’s a vital component of the analysis because it lays out exactly which steps shall be executed, in which order, and how to parametrize them, so as to tune them for the analysis of a specific data item. Typically, the DeepPSY IT department creates a custom pipeline definition for each set of EEG/ECG data items that will be analyzed, then it’s used by the analyst for their work.

⚠ Pipeline definitions are created in a controller manner so as to ensure there are no mistakes in them. As they’re a critical component of the analysis of data items.

13.1 List of Available Steps

What follows is a list of all the steps that may be applied to the EEG/ECG data item in order to obtain the desired outputs:

- **Technical Name:** precise name of the step used in the pipeline definition.
- **Manual Input:** whether the step requires the intervention of a human operator.
- **Step Type:** the kind of operation performed on the EEG/ECG input data. For a description of each step type refer to the "Configuration Requirements" section.
- **Signal Type:** whether this step operates on the EEG, ECG,

13.1.1 Validators

Technical Name	Manual Input?	Signal Type	Function
ECGChannelValidator	No	ECG	Check if an ECG channel is present. It checks against a predefined list of typical ECG channel names (ECG, EKG, etc)
CheckStandard-MontageValidator	No	EEG	Checks whether the data file has a standard montage. Less than 100 electrodes means it's standard.

13.1.2 Preprocessor

Technical Name	Manual Input?	Signal Type	Function
AnnotationsRemover-Preprocessor	No	EEG/ECG	Removes all the annotations in the EEG/ECG data item.
AutomaticPeakDetection	No	ECG	Detects peaks automatically.
AutomaticPeakFiltering	No	ECG	Implements a series of filters to remove bad peaks.
AutomaticPeak-Correction	Yes	ECG	Automatically corrects peaks, the operator can visualize the corrected peaks and decide from there.
BadEpochsInspector-Preprocessor	Yes	EEG	Allows the operator to select bad epochs and, optionally, select bad channels to interpolate, all in one step.
ChannelCreator-Preprocessor	No	EEG/ECG	Creates a new channel by adding other two channels (i.e. EOG = F7 - F8). Additionally, sets the correct channels type.

ContinuousData-MarkerPreprocessor	No	EEG	Used to preserve the selected bad epochs across other processing steps.
EEGFiltering-Preprocessor	No	EEG	Applies a series of common filters to the data.
ICAPreprocessor	Yes	EEG	Applies ICA preprocessing to the data. First it allows the operator to exclude channels from the ICA model training, then they may select individual components. Finally, they have a visualization of the post-processed data where they may decide to continue with the processing or stop there.
InitialInspection-Preprocessor	Yes	EEG/ECG	Displays the signal to the operator and allows them to create annotations with different purposes. It's useful to have an initial visualization of the data prior to any modification from the pipeline.
Interpolation-Preprocessor	Yes	EEG	Allows the operator to select channels to interpolate.
ManualPeakSelection	Yes	ECG	Operator selects/deselects peaks according to their criteria.
MarkCropperPre-processor	Yes	EEG	Allows the operator to select two annotations from which to crop the EEG signal.
ReReferencing-Preprocessor	No	EEG	Applies rereferencing, a common operation in EEG signal processing.
SetChannelType-Preprocessor	No	EEG/ECG	Sets the channel type to a list of predefined channel names. Used to set the ECG and EOG channel types.
StandardMontage-NamesPreprocessor	No	EEG/ECG	Applies a mapping to the electrode names to turn them into *standard 1005* montage.

13.1.3 Biomarkers

Technical Name	Manual Input?	Signal Type	Function
APFBiomarker	No	EEG	Alpha Peak Frequency
FAABiomarker	No	EEG	Frontal Alpha Asymmetry
QEEGBiomarker	No	EEG	qEEG Algorithm
VIGAZBiomarker	Yes	EEG	VIGAZ algorithm based on the vigilance of the patient
BlockBPMBiomarker	No	ECG	Beat per minute (BPM)
HeartrateVariability-Biomarker	No	ECG	Heart Rate frequency biomarkers

13.1.4 Postprocessors

Technical Name	Manual Input?	Signal Type	Function
VigallStageAnnonAdder	No	EEG	Adds the VIGAZ annotations to the processed EEG
ECGPeakAnnonAdder	No	ECG	Adds the ECG peaks to the final processed data

14 Operating Instructions

14.1 Main Screen

Upon launching the application, the user is presented with the primary interface as seen in figure 2, which displays the version (v0.4.28MD), the environment (stable), various hyperlinks for user feedback and access to supplementary information, particularly this IFU document, a menu bar with numerous options, and the login form.

By selecting the ”Share Feedback” link, a website is launched where users can provide their input. The user can open a dialogue that contains the application’s label information and more detailed information about the software’s version by clicking the ”Information & Support” link.

14.1.1 Log In

The primary interface of the software, commonly referred to as the ”Main Screen”, also incorporates forms designed to facilitate the process of user authentication and authorization. Access to the software is exclusively granted to individuals who have been specifically approved by DeepPsy AG and for whom a unique user account has been established. In the event that an individual does not possess a user account or encounters difficulties accessing the application despite a perceived entitlement, it is advised to contact DeepPsy AG for assistance and guidance.

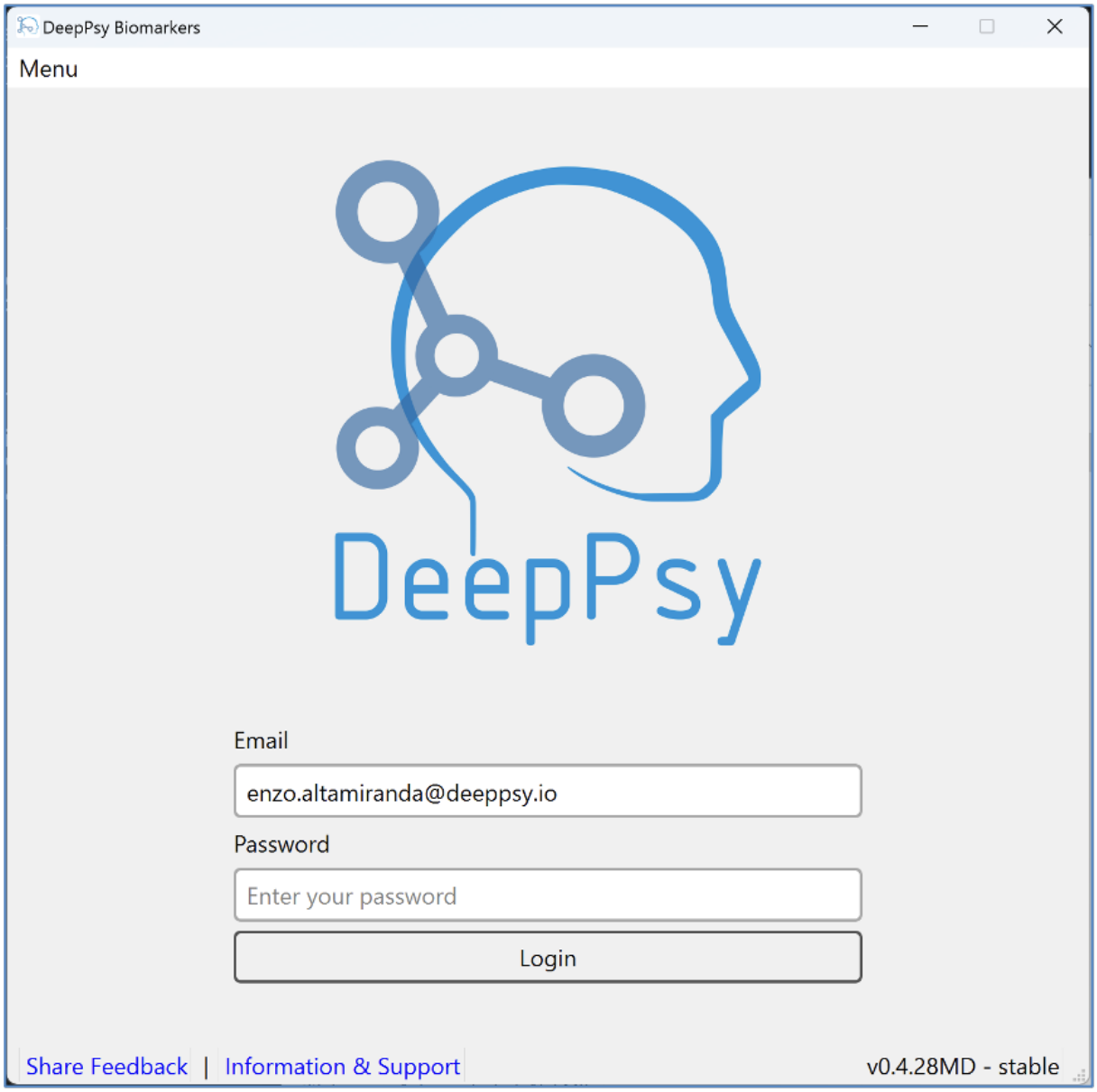


Figure 2: Screen presented to the user upon opening the application.

To authenticate, enter your email and password, then click the “Login” button. After a few moments, a successful authentication will direct you to the analysis screen. Otherwise, a relevant error message will be displayed. The most common error is an error in the credentials provided for authentication.

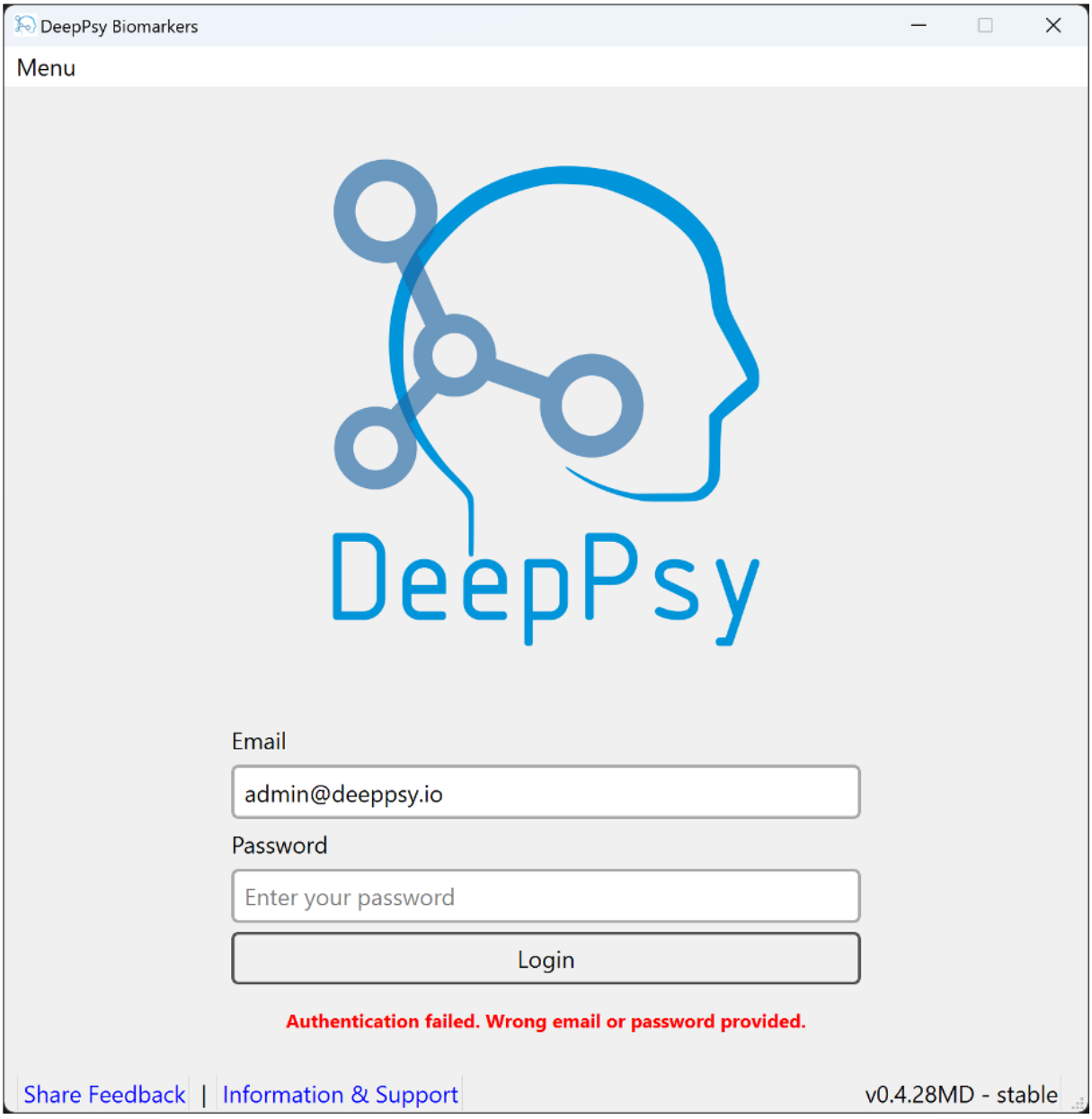


Figure 3: User authentication failed.

14.1.2 Analysis Modes

Following a successful user authentication, the application presents a dialog box with a tab bar offering three choices: Cloud Analysis, Local Analysis, and Automatic Analysis. One of these options may be selected by clicking on the corresponding tab in the tab bar. A description of each analysis type is provided below.

14.1.2.1 Cloud Data

This analysis mode is reserved for DeepPsy AG analysts who are responsible for the inspection and processing of EEG/ECG data items. Only authorized users will be able to access this mode of operations.

The Cloud Data mode allows analysts to directly access the EEG/ECG data items stored in the cloud. They may select a subset of items to analyze and the application will download them one by one for each analysis, respectively. Moreover, all required metadata needed for

the analysis, such as the Pipeline Definition, is downloaded alongside the data item, thus the analyst must not spend time deciding which configuration to apply and allows for the speedy analysis of subject data.

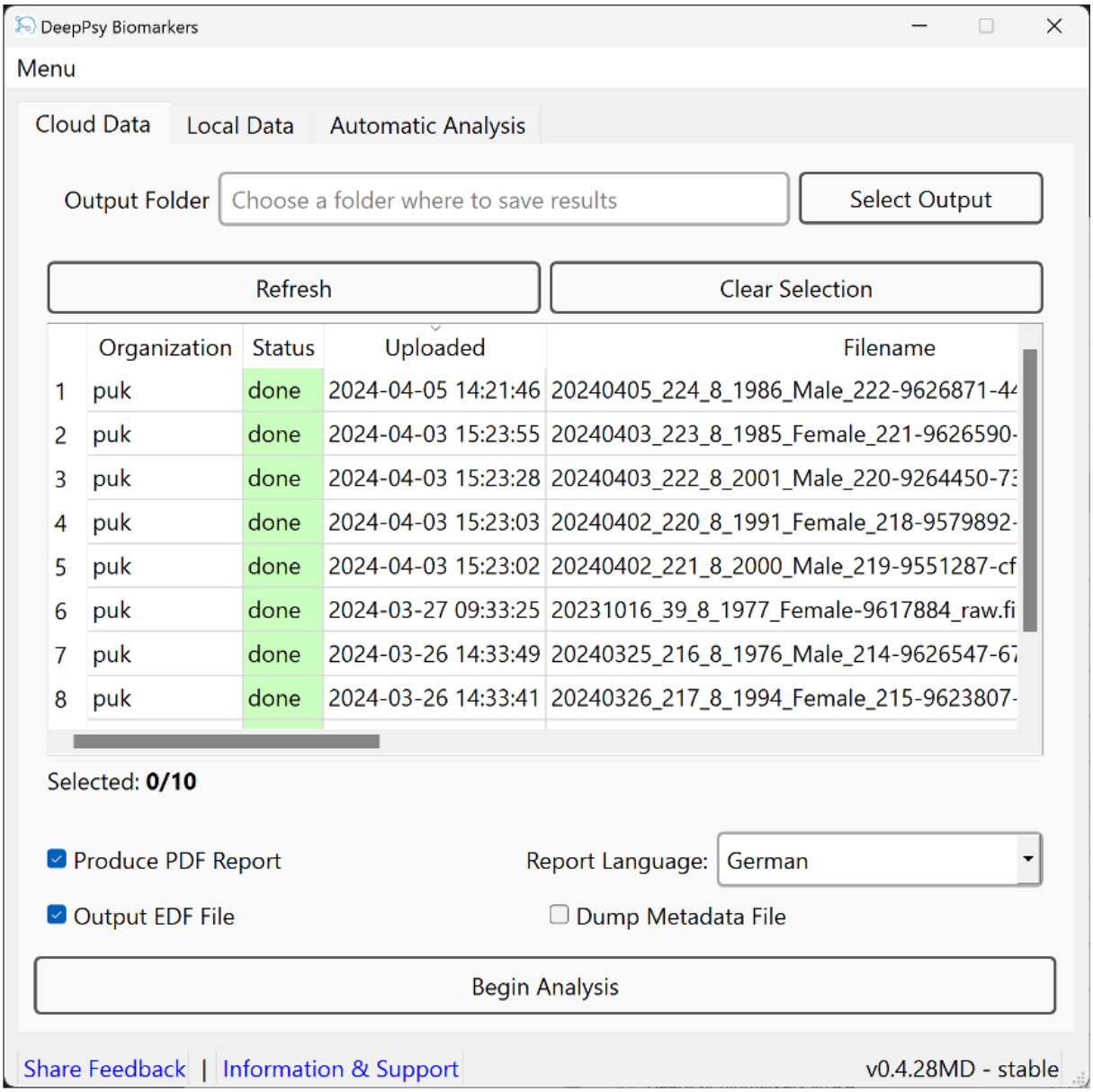


Figure 4: Cloud data analysis mode. Only available for DeepPsy specialists.

In this screen the user must select one or more items from the selection table, select an output folder where to place all the outputs from the analysis and specify some optional output parameters such as whether to produce a PDF report, the language, if it's required to output the processed data item in EDF format as well, and whether to dump the metadata file for each analysis which contains detailed information of the preprocessing data.

The data items table has two buttons "Refresh" and "Clear Selection". The first action refreshes the table, adding new items or updating existing ones. The second action clears the data items that have been selected, which are indicated by highlighted rows.

To start the analysis, the user must click the "Begin Analysis" button,once the data items and output folders have been selected. A confirmation window will appear prompting the user to confirm before proceeding. After confirmation, the analysis of the first data item begins.

14.1.2.2 Data Item Fields

The EEG/ECG data items table has a number of fields with metadata information, these are:

1. **Organization:** the specific entity, could be a hospital, a research institute, or some other organization, which provided the data to be analyzed by DeepPsy AG.
2. **Status:** The data can be in one of three states: 'done' if it has already been successfully analyzed by an analyst, 'pending' if it still needs to be analyzed, and 'error' if an error occurred during analysis, preventing its completion. In the case of an error, a member of the technical team must review and address the issue.
3. **Uploaded:** date in which the item was uploaded to DeepPsy's systems.
4. **Filename:** filename of the EEG/ECG data item. This field is important because often metadata information is encoded in the data item's name.
5. **Size:** size in MB of the file.
6. **Pipeline Definition:** the pipeline definition that will be used to process the data item. By default, there is an organization-wide pipeline definition which is used to process all items belonging to that organization. However, it is possible that within the organization some data items require a personalized pipeline definition. This field allows the analyst to know exactly which one would be used for the analysis.

14.1.3 Local Data

The Local Data analysis mode reads EEG/ECG data items from the user's computer. The screen has a number of fields and parameters that the user can change to configure their desired analysis.

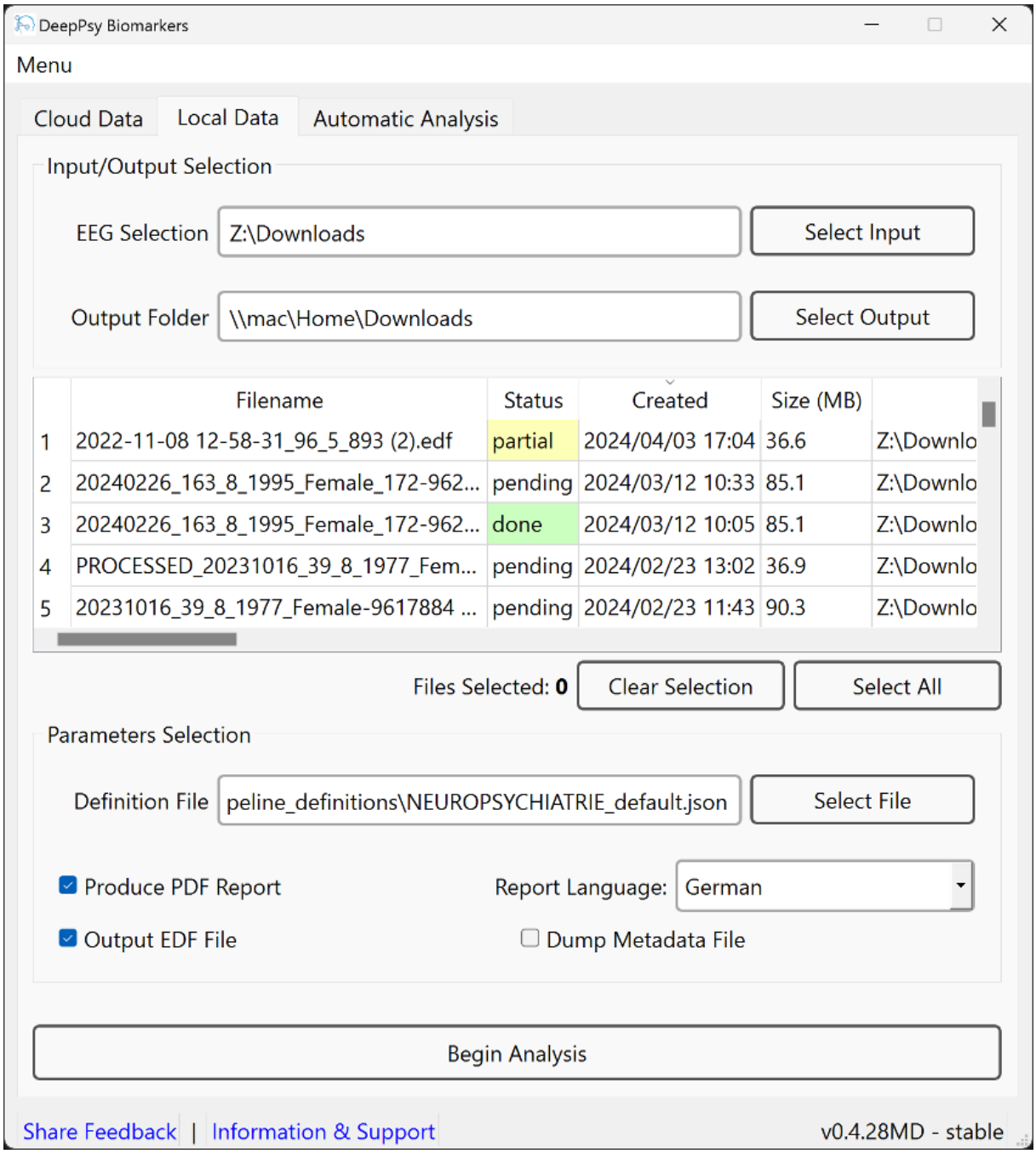


Figure 5: Local data analysis mode. Allows users to analyze data items located in their file system.

14.1.3.1 Input/Output Selection

The area has the “input field” and the “output field”. Prior to selecting data items, the user must select a folder containing the files. Upon selecting a folder, the software will recursively search through the subdirectories of the folder picking up all eligible EEG/ECG data items and using them to populate the selection table. If no EEG/ECG data items are found, then no items are shown in the table and the analysis cannot be performed.

The “output field” is an optional field that the user can use to select where all the outputs of the analysis will be stored in their filesystem. If the user does not select any output folder, then the outputs of the analysis will be stored in the same parent folder as each of the data items se-

lected for analysis. For example, if the data item is in “C:/home/user/data_itemsmy_data_item.edf”, then the outputs will be stored in a newly created folder inside “C:homeuserdata_items”.

14.1.3.2 Selection Table

The user can select the items to analyze by using the selection table. The table has a number of columns with metadata about each file and two buttons: “clear selection” and “select all”. These are convenience buttons that allow the user to select all items present in the table for analysis or clear the current selection.

The columns in the table are:

1. **Filename:** the name of the data item in the user’s filesystem.
2. **Status:** reflects the state of the specific data item, it’s “done” if the application can find a folder with the results of the analysis of the data item in the “output folder” location, “pending” if no analysis has been conducted yet, “partial” if there was an error in the EEG or ECG analysis, thus signaling that the analysis was only partially completed, and “error” in case there was a problem that prevented the completion of the analysis.
3. **Created:** time in which the file was placed in the filesystem.
4. **Size (MB):** size in MB of the data item.
5. **Path:** absolute path in which the file is located in the user’s filesystem.

14.1.3.3 Parameter Selection

This section allows the user to change the outputs produced by the analysis. They may request to generate a PDF report with details of the analysis, the language of the report. Whether to produce an EDF file with the processed data item, and, if required, produce a metadata file with detailed information on the outputs of the analysis along each step.

14.1.4 Automatic Analysis

The automatic analysis feature reproduces previous processing steps for a given EEG/ECG data item. While manual analysis involves activities like inspecting signals and selecting operation segments, automatic analysis utilizes a metadata file named ”actions_metadata.json” to record the specific actions that were performed. This feature efficiently repeats these actions as if executed by an analyst, automating the entire process.

This feature is not only essential for regulatory purposes, but it also helps the DeepPsy team reproduce an analysis that may have had issues.

The user must select the required parameters and begin the analysis by pressing the “Begin Automatic Analysis” button.

The user must provide the following information in the fields shown by the screen to reproduce the analysis:

1. **EEG/ECG File:** the original EEG/ECG data item prior to being processed by the analyst.
2. **Action File:** the file with the steps that were taken throughout the analysis. This file is created as an output of the analysis. Its contents are described here.
3. **Definition File:** this is the pipeline definition used to analyze the original EEG/ECG data item. This file is optional and it’s only included in this section for support of analyses performed with older versions. Recent versions include the pipeline definition used inside the actions metadata file, making it self-contained and avoiding having the user need to manage several different files.

4. **Output Folder:** the location where the output contents shall be created. This folder is optional. If no output folder is selected, all outputs will be stored adjacent to the file selected for analysis.

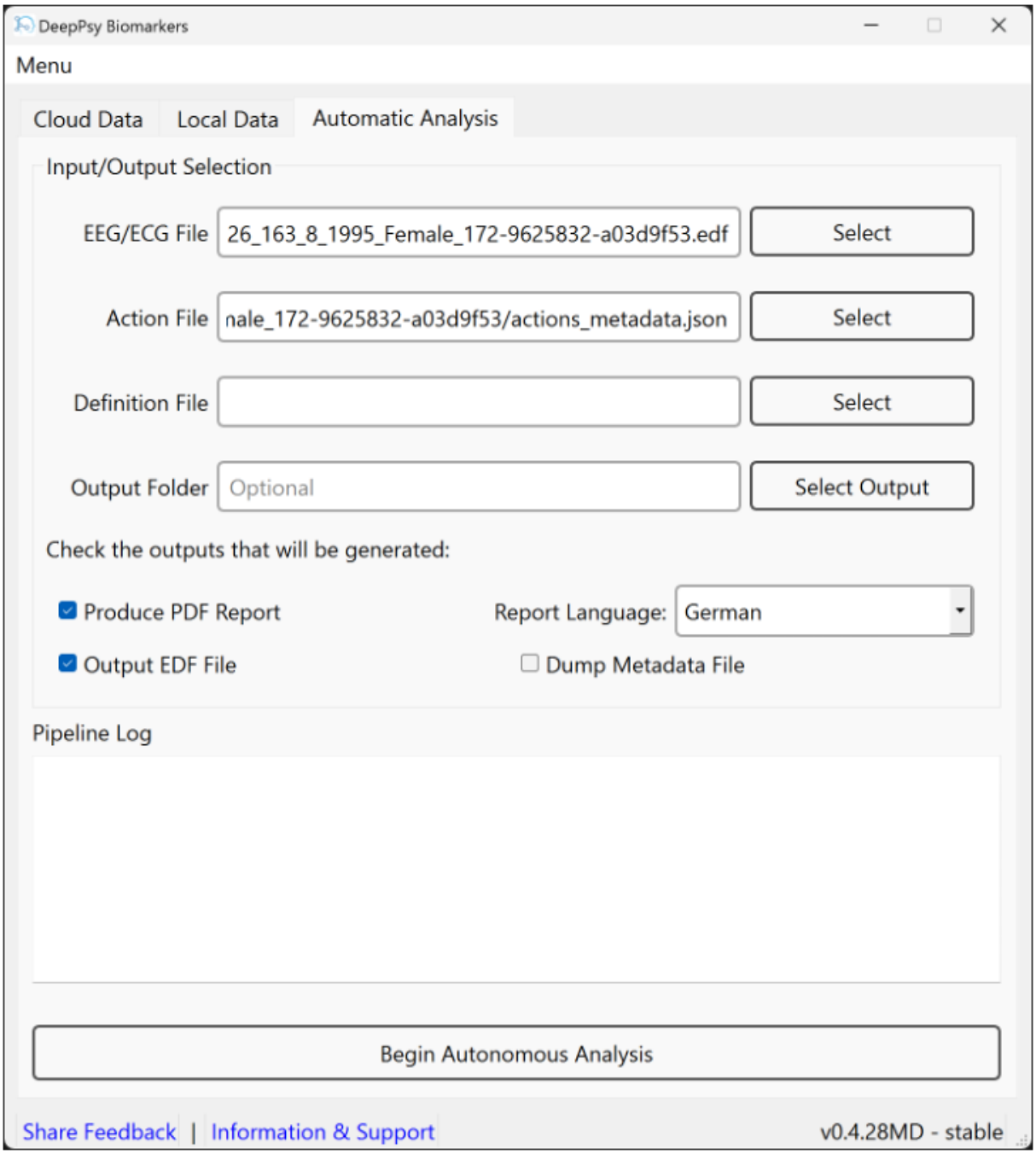


Figure 6: The automatic analysis mode. It's used to reproduce previous analyses without involvement from the user.

14.2 Analysis Window

This window opens immediately after the user begins the analysis of one or more data items. It contains basic information of the progress made in analyzing the group of data selected, as well as important metadata information of the current data item being processed. It has four sections: session details, analysis details, metadata details, and pipeline log. Session

details give information about the number of data items selected in this session, the number already analyzed and those pending. Analysis Details display the output folder name, filename and the number of the current EEG/ECG data item being analyzed. Additionally, it includes a button “Open Outputs” which opens a file system explorer window located in the folder where the outputs will be stored. Finally, the Metadata Details section contains the:

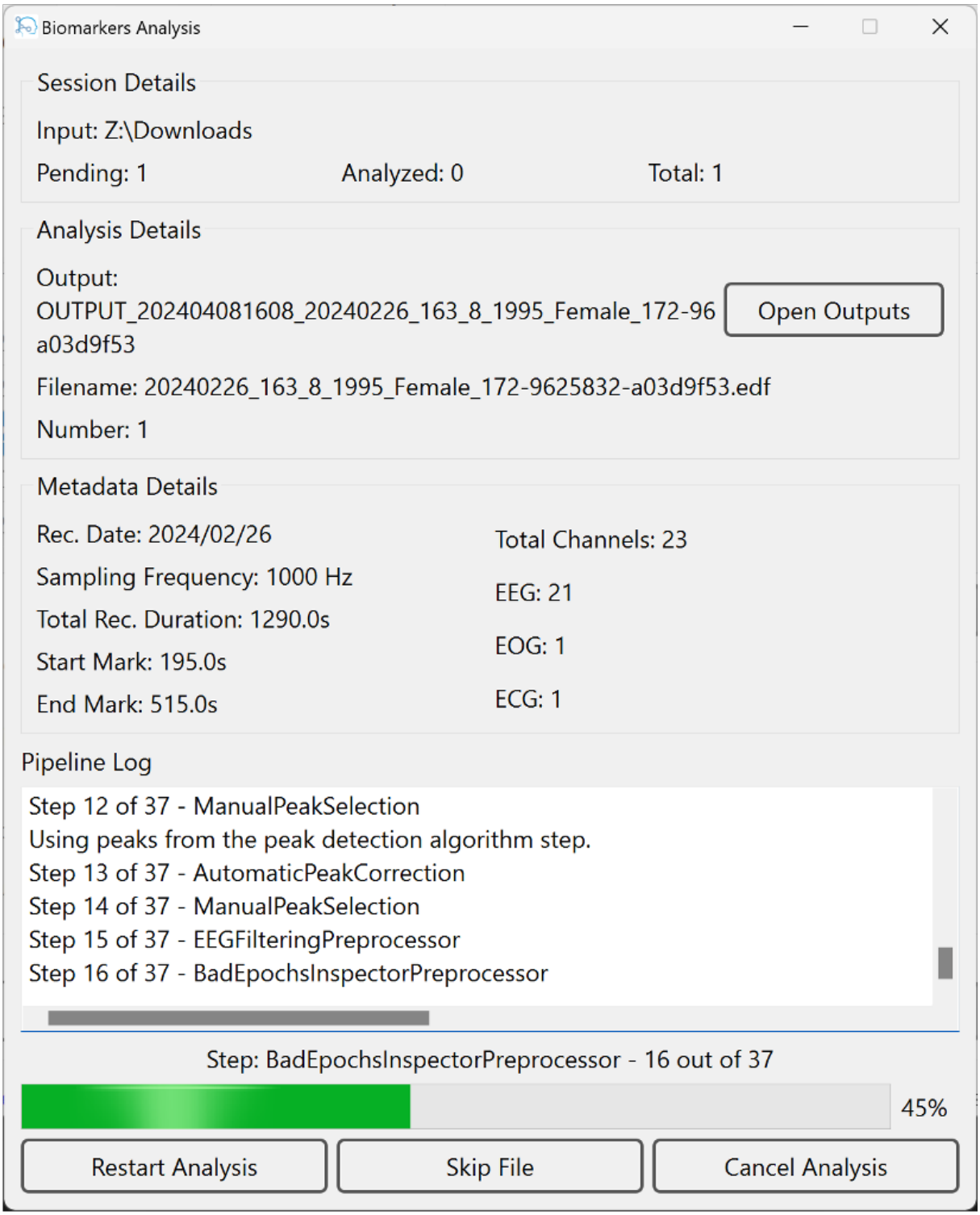


Figure 7: Cloud data analysis mode. Only available for DeepPsy specialists.

- **Recording Date:** date in which the EEG/ECG signal was recorded.

- **Total Channels:** total number of channels in the data item being processed. This number may change as the item moves through the processing steps.
- **Sampling Frequency:** sampling frequency of the signal.
- **EEG, EOG, and ECG:** total number of channels of each of these types, respectively.
- **Total Rec. Duration:** the total recording duration from the data item signal, at the moment it was first read by the DeepPsy Biomarkers and prior to any preprocessing applied to it, such as croppings.
- **Start Mark:** The point in time in which the signal shown by the signal browser starts. If no cropping has been applied to the signal in a preprocessing step, the start mark is 0.
- **End Mark:** The point in time in which the signal shown by the signal browser ends. If no cropping has been applied to the signal in a preprocessing step, the start mark is the same as the total recording duration.

The Pipeline Log area prints informative logs produced by the analysis pipeline as it progresses. Typically it informs the step in which the pipeline is currently in.

At the bottom of the screen there are three buttons, from left to right, these are the “Restart Analysis”, which makes the analysis start again from step 0, the “Skip File” button which stops the processing of the current data item and continues to the next one out of all that were selected when the analysis began, and finally, “Cancel Analysis” which stops the processing of the current data item and those of all subsequent data items, thus giving back control to the user and going back to the screen where they selected the data items to process.

14.3 Analysis Results Dialog

The user will receive a confirmation dialog at the end of the analysis, where they will have to review the summary information of the preprocessing performed and the biomarkers calculated. If at any point either the EEG or ECG preprocessing fails or the calculation for any of the biomarkers, they will be notified in this window. Additionally, they will have the option to select from a number of tags when patterns of interest are observed in the data items. This is useful to improve the quality of the datasets being built by DeepPsy.

The user may either accept or reject the analysis. The decisions made by the analyst will be recorded. Moreover, if they decide to reject the analysis, they must write the reason why it’s being rejected before they can continue.

To leave feedback, they must select the tag called “Other comments or cause of analysis rejection” and write the feedback in the form that appears. The feedback must be longer than 10 characters and shorter than 250.

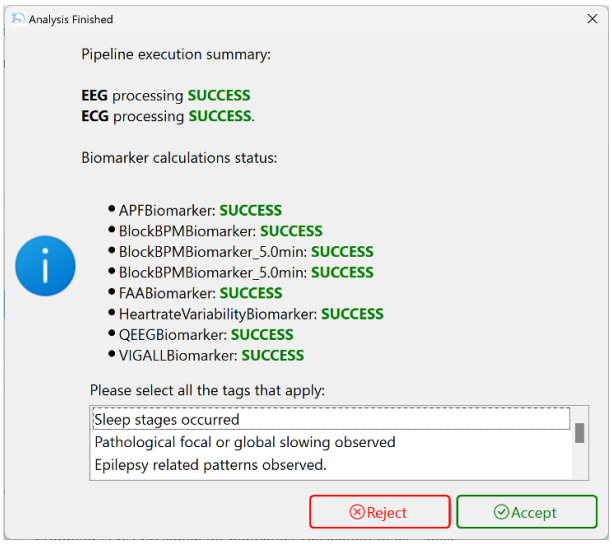


Figure 8: Status dialog showing that all calculation were successful.

The image below showcases how the user can leave custom feedback for the application.

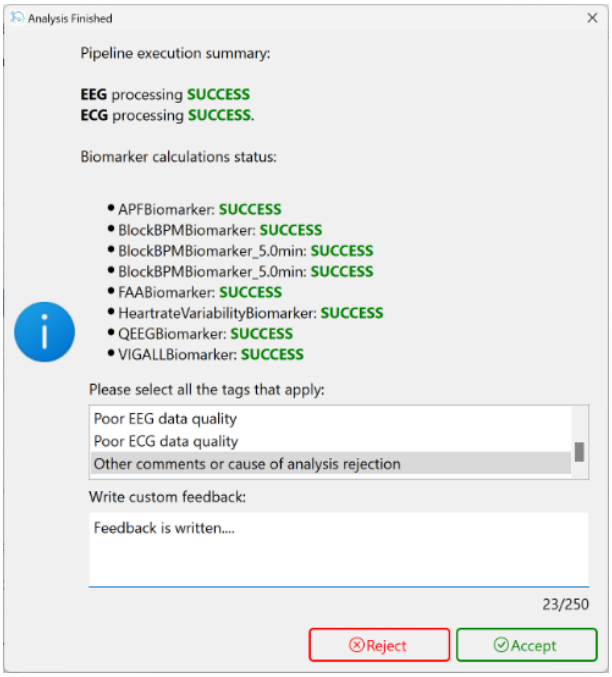


Figure 9: The user can leave feedback regarding the analysis by choosing the correc toption in the status dialog.

14.4 Application Menu

The application menu is accessible through the toolbar at the top of the main window. This section describes each of its options.

14.4.1 About

It's a dialog box that contains the "Label" information for the device, as well as other important identifying information, such as the version, release date, and release number for each of the major components of the DeepPsy Biomarkers package.

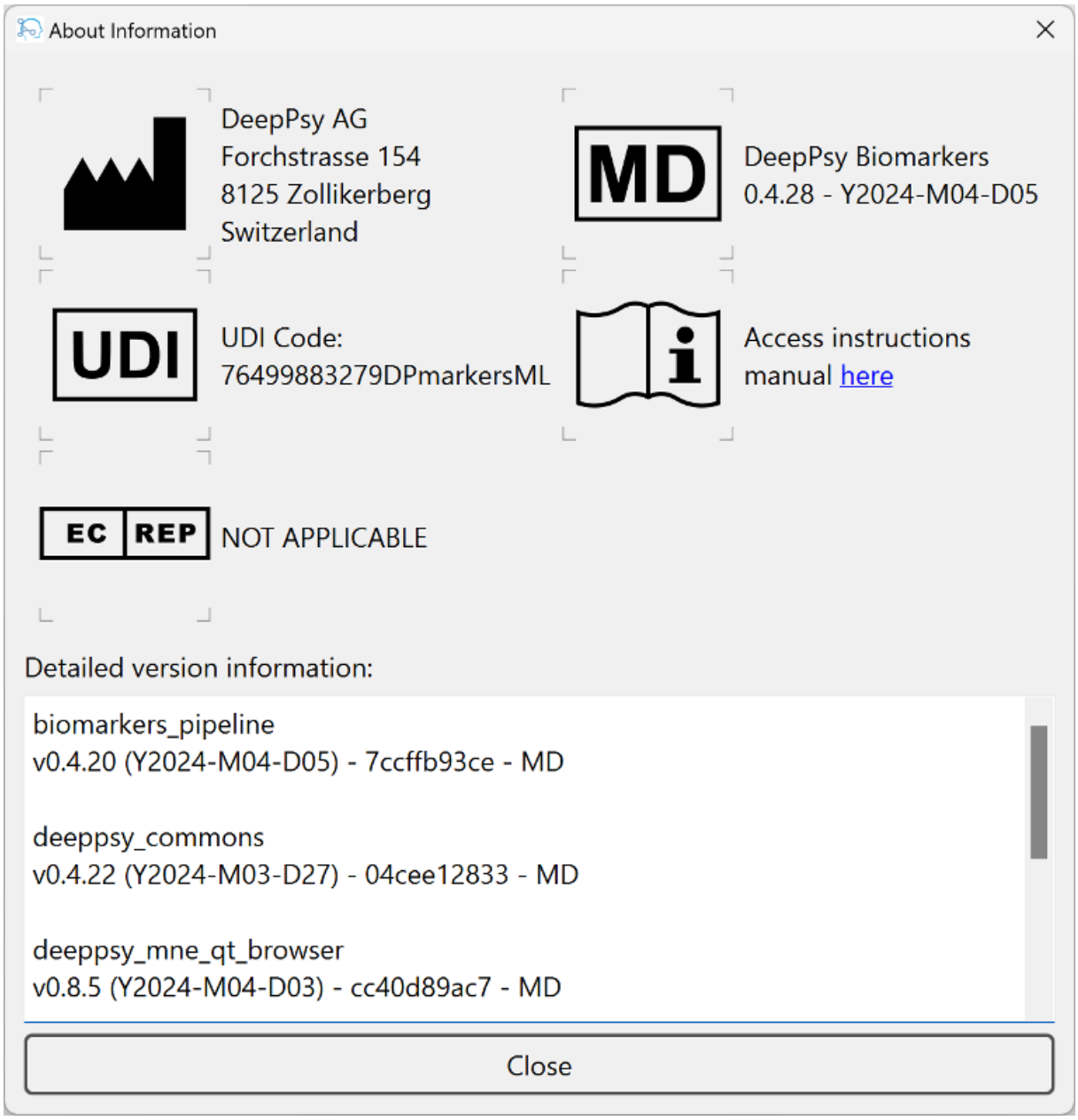


Figure 10: About dialog with important information about the application.

14.4.2 Configuration

A configuration panel with several options to establish default values for several features of the medical device. The intention of this configuration is to allow analysts to customize some of the characteristics of the application. There are two tabs: “Analysis Options” and “Plots”.

14.4.2.1 Analysis Options

Here you can set default paths for common parameter selection fields. Whenever you need to select a new input path, the default folder that will appear in the file explorer will be the path set here. Otherwise, it’s a system-specific path. Likewise for the default output and pipeline definition paths.

Figure 11: Configuration parameters for the selection of the analysis parameters.

14.4.2.2 Plots

This controls the appearance of the signal browser. The Plot Duration sets how many seconds to show in one whole pane of the signal browser. Increasing or decreasing this value will increase the "amount" of signal that will be displayed on the screen. The "Scaling" values refers to how the data item signals are displayed in the browser window. By decreasing the magnitude of the values the signals amplitudes will increase. These values can be set directly in the signal browser, however, some analysts might find it useful to select their preferred signal sizes by default.

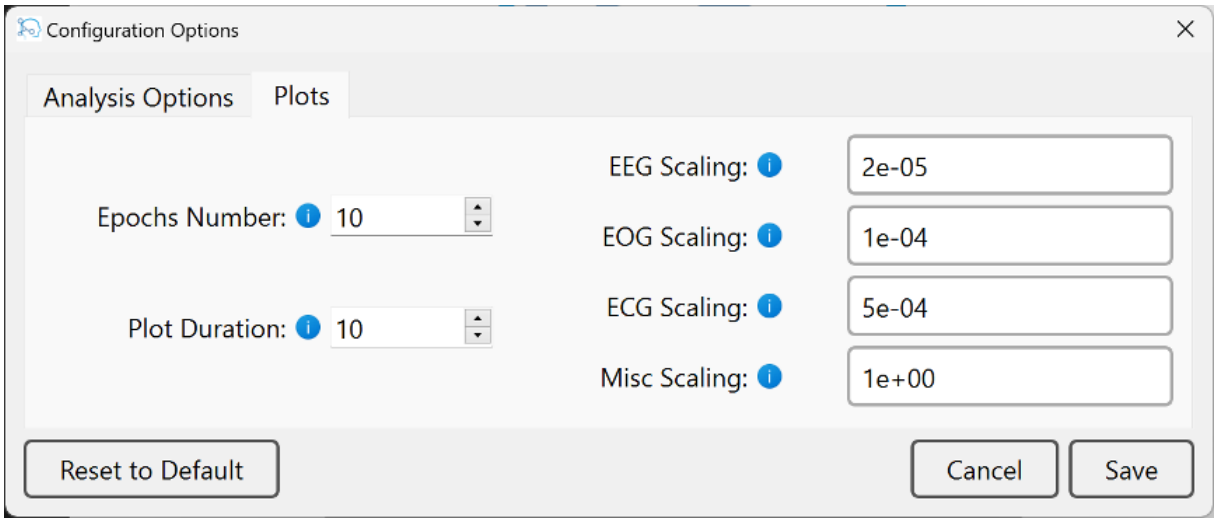


Figure 12: Configuration parameters for the signal browser. These options can be set directly in the signal browser.

14.4.3 Logout

By clicking in this menu option, the user is logged out from their session and they will have to authenticate again before they can use the system.

User sessions last for a maximum of 5 hours, which means they will have to login again every 5 hours if they keep their sessions open in the application.

15 Manual Analysis Instructions

The processing of data items is formed by a series of automatic and manual steps. Manual steps require the intervention of an analyst, while automatic steps perform their work unassisted.

In this section, we describe the elements of the signal browser which is used throughout the manual analysis pipeline, as well as each of the steps that require manual intervention from the analyst.

15.1 EEG/ECG Signal Browser

The signal browser is the basis of the manual preprocessing of data items. It is modeled after a standard signal browser used by many commercial software packages for the analysis of EEG data and it includes a substantial number of features and functionality to enable the accurate and speedy processing of data items.

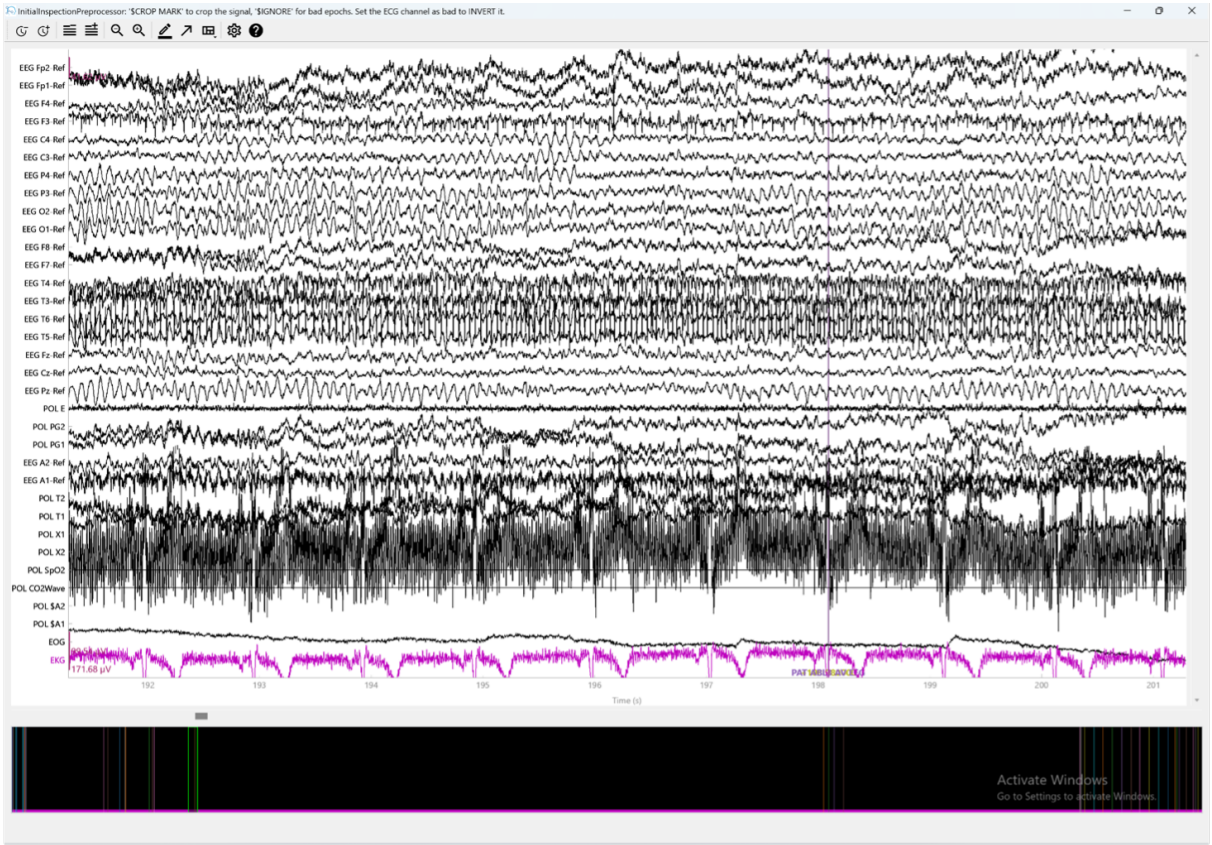


Figure 13: The signal display window used throughout the analysis pipeline.

15.1.1 Window Title

The signal browser window title bar holds important information about the current step in the analysis. The user can orient themselves about where in the analysis they are, and which actions they should take in the present screen by reading the window title.

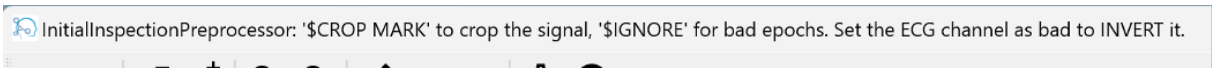


Figure 14: The signal window title bar contains important information about the current step in the analysis and the actions that the user must take.

15.2 Commands Bar

The commands bar can be found in the top-left corner of the signal screen. It includes a number of action items that the analyst can activate to help them interact with the signal.

Figure 15: The command section of the signal display window contains a number of action items that the analyst can use to interact with the signals.

The bar is divided in 5 sections, separated by a divider represented by a vertical line. These are explained below:

- **Time Points:** gives the analyst the option to increase or decrease the number of time points, that is the amount of signal time shown in the screen. By default, only 10s of signals are shown at a time.
- **Channel Quantity:** decreases or increases the number of channels shown at once in the signal screen. Having fewer channels allows each channel to appear in more detail on the screen.
- **Change Amplitude:** permits increasing or decreasing the amplitude of the signal, that is, changes its scale.
- **Options Toolbar:** the toolbar includes, in this order, an annotations mode toggler, a projectors toggler and an overview bar toggler. The annotations tool bar is very important and will be covered below, the remaining two items are not used in the pipeline.
- **Signal Configuration & Help:** the section includes two actions, one to toggle the signal presentation configuration and a help button which toggles a dialog with keyboard shortcuts for the different actions and commands available by the browser. The signal configuration item can be used to modify how the signal is presented. In some cases, it's possible to increase the display quality of the signal, reducing the number of artifacts at the expense of more computational requirements. This feature is useful in cases where the analyst must inspect subtle details in the signal in order to process it.

15.2.1 Annotations Mode

Annotations are markers used to highlight sections of interest in the data item signal. Annotations have three properties: an onset, a specific point in time in which the annotation begins, a duration, how much of the signal to mark, and a description, which is essentially a label identifying the annotation.

In selected steps, it's possible to toggle on the annotations mode, where the analyst may create, modify, and delete annotations from the data item. The annotations mode must be toggled on first before it's possible to manipulate annotations.

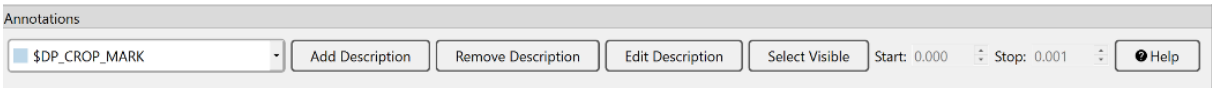


Figure 16: The command section of the signal display window contains a number of action items that the analyst can use to interact with the signals.

Most EEG/ECG data items contain a number of annotations that mark special segments of interest. All existing annotations are listed on the left side of the bar in a dropdown and ordered alphabetically. When a specific annotation label is selected, new annotations with that label can be created by simply left-clicking with the mouse and dragging it across a section of the signal. Right-clicking any existing annotation will delete it.

When there are no annotations defined in the data item, a new label must be added before it is possible to create new annotations. This can be done by clicking the “Add Description” button and selecting a new label for annotations. Similarly, it’s possible to delete annotations by clicking the “Remove Description” button, it will prompt the user to confirm that they wish to delete all annotations with the selected label.

The “Select Visible” button allows the user to toggle on or off certain annotations. This is specially relevant in cases where there are many annotations present in the data item and it is desired to reduce the noise in order to view the specific annotations of interest.

Annotations are identified by a specific color. The color is chosen automatically by the browser in order to maximize the contrast between them. However, when too many annotations exist in the data item, the colors may repeat themselves.

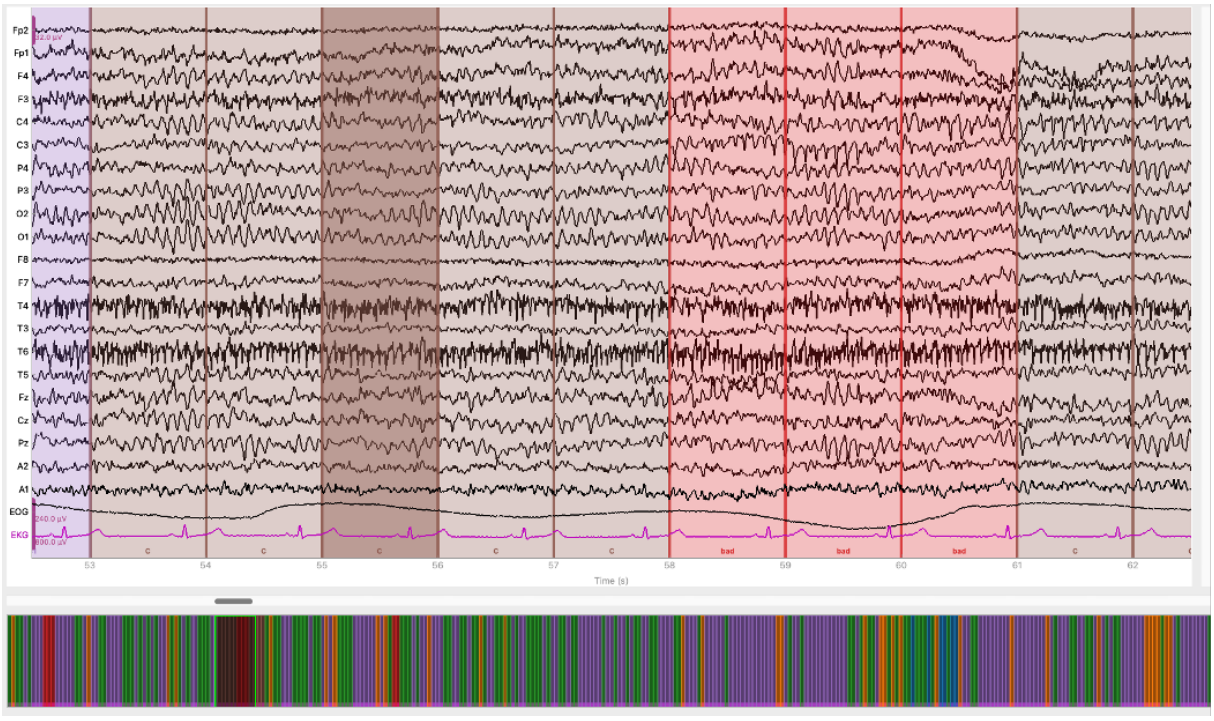


Figure 17: If too many different annotations are present in the signal screen, their colors will repeat across different annotation labels.

The browser supports editing the annotations by right-clicking. Right-clicking inside their interior and moving the mouse pointer will drag them around horizontally. Clicking in one of their edges and dragging will resize it accordingly, effectively changing the duration of the annotation.

15.2.2 Signals Screen

The signal screen is the section that displays the EEG/ECG signals. It is similar to many commercial signal browsers, giving the user options to visualize the data throughout the time axis.

The browser is also capable of displaying different types of signals: EEG, EOG, and ECG. Each type uses a different scale and sometimes a different color, in the case of ECGs. The scale of each signal type can be found on the edge of the signal screen to the left, next to the name of the first channel for each signal type. In the image below, the Fp2, EOG, and EKG channels have a pink bar next to their name identifying the scale.

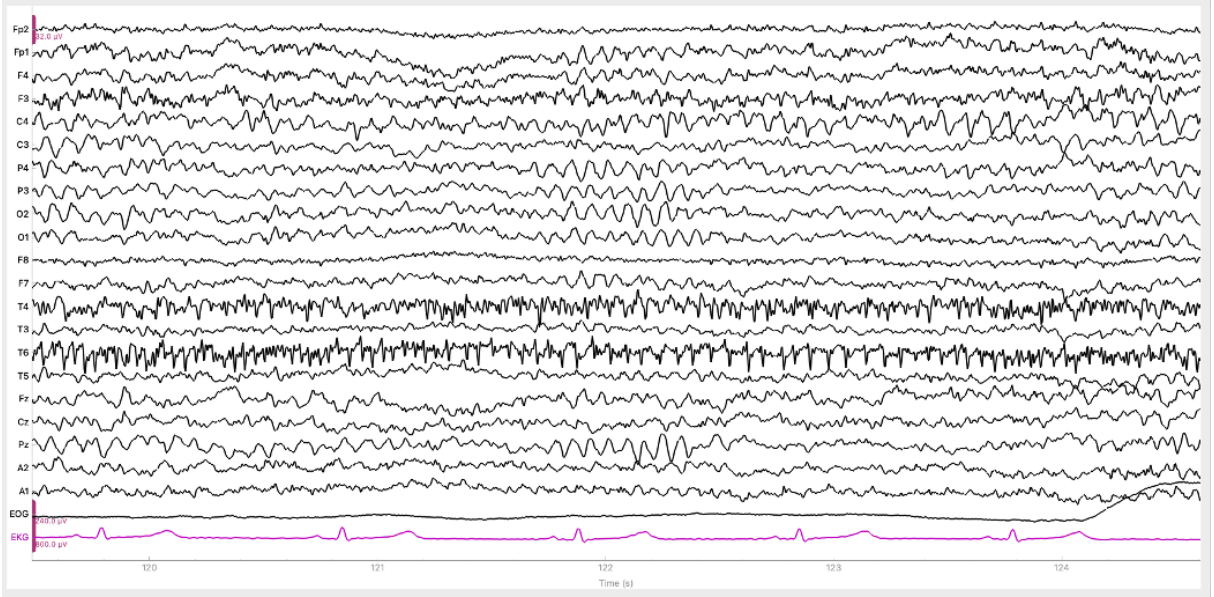


Figure 18: The signal screen displays the signals captured by each of the electrodes of the EEG or ECG recorder.

In some cases, it's possible to visualize the electrode position for an EEG channel. This will depend on whether the montage type is set, which is usually the case after the "StandardMontageNamesPreprocessor" has been executed. This visualization is activated by right-clicking on the channel name.

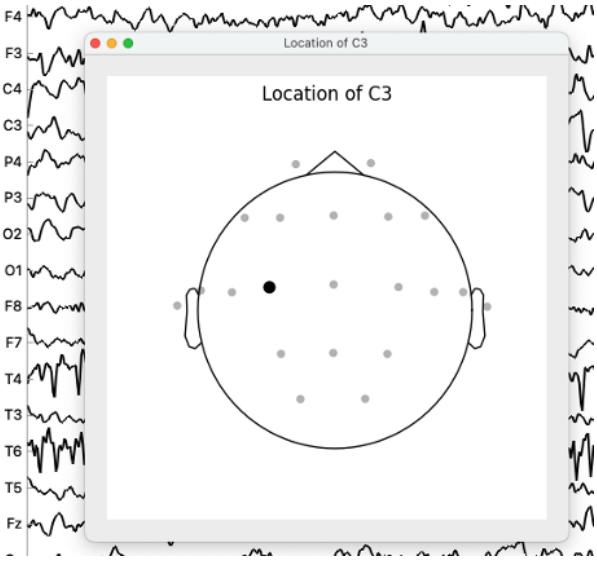


Figure 19: By left-clicking the label of an EEG channel, the user can visualize the electrode position. This is only possible after the "StandardMontageNamesPreprocessor" step has been executed.

An important feature of the Signal Screen is to select individual channels. This is done by left-clicking either on a channel name or on top of the channel signal line. Selected channels will become grayed. This operation is used to select bad channels that need to be ignored or interpolation, depending on the case.

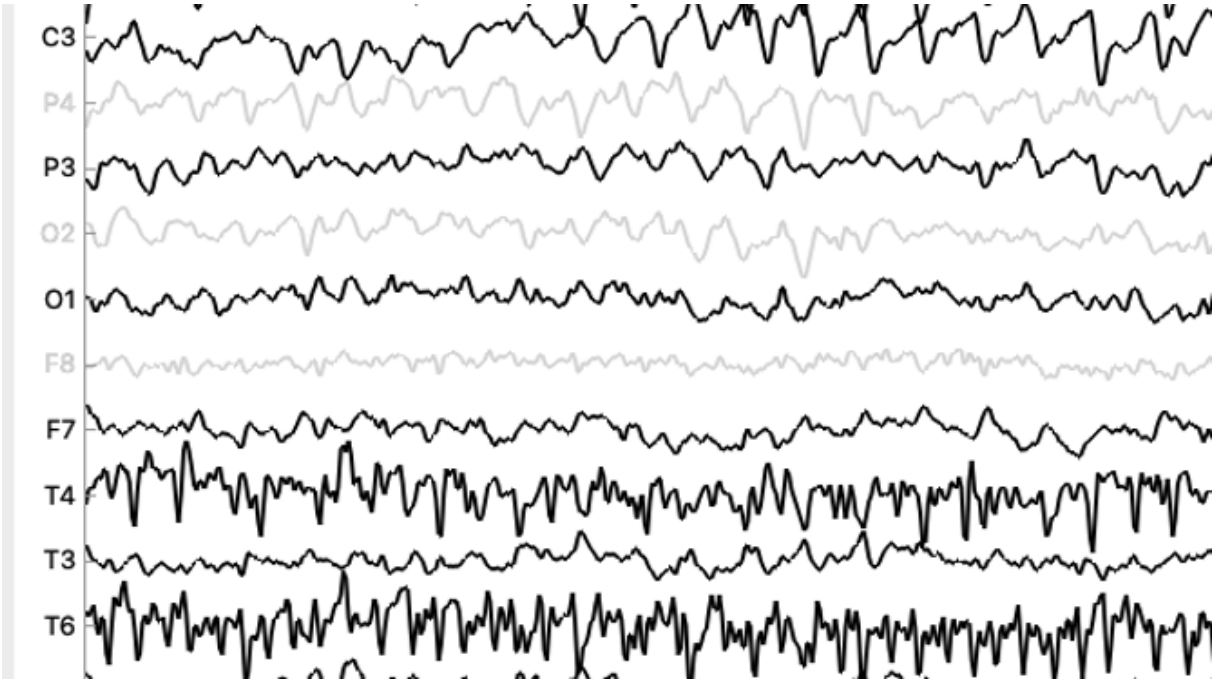


Figure 20: Channels can be selected by clicking either on the channel name or on top of the signal line. Selected channels will be grayed.

15.3 Manual Analysis Steps

What follows is a description of the pipeline steps that require manual input from the analyst to complete. These are divided into general, ECG, and EEG, depending on whether they apply

to the analysis of any, one or the other, respectively.

15.3.1 Initial Inspection Preprocessor

This is typically one of the first steps executed by the pipeline. It's used to allow the inspection of the data prior to any processing so that its suitability may be assessed. The analyst can check which annotations are present, the shape of the signal, and in some cases, whether the ECG signal needs to be inverted. This last action is necessary because often the electrodes used by the recording laboratory are inverted.

In this step the user can:

- **Mark Sections for Cropping:** the user may create annotations of type "$DP_CROP_MARK" wherever they wish to crop the signal. This type of signals will be made available in the MarkCropperPreprocessor step where the user may select them to define the region cropped.
- **Mark Bad Segments:** the user may create annotations of type "$DP_IGNORE". These will be picked up at a later step and automatically mark the annotated segments as bad.
- **Invert the ECG signal:** if a signal of type ECG is present in the data item, the user may select its channel to have it inverted. To select the channel they must left-click on the channel representing the ECG signal, in most cases "ECG" or "EKG".

15.3.2 Mark Cropper Preprocessor

This step allows the analyst to crop the signal with a region defined by annotations. The user is shown a dialog with the annotations in the data item alongside the onset at which they appear. The user must select two signals to continue. Additionally, the "start" and "end" labels are available to choose a crop region that start at 0.0 and/or ends at the last data point. If "$DP_CROP_MARK" annotations were created, they may be selected here.

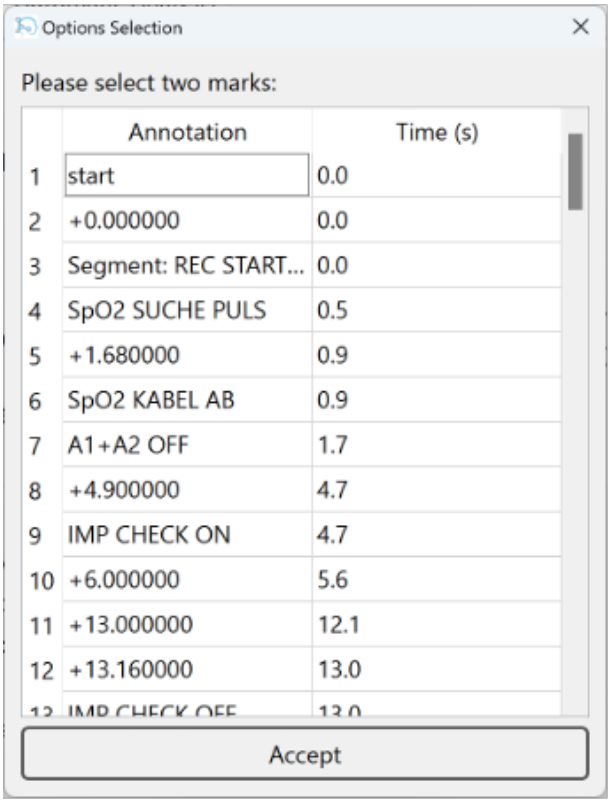


Figure 21: By left-clicking the label of an EEG channel, the user can visualize the electrode position. This is only possible after the "StandardMontageNamesPreprocessor" step has been executed.

15.3.3 ECG

In this section, we analyze the ECG in order to extract the R peaks to compute the different biomarkers. The user must check if the signal has a sinus rhythm and if the automatic detection of the R-peaks worked properly. In the different steps, the peaks can be added, deleted and interpolated. For example, peaks masked by artifacts can be removed and then be interpolated.

Exclusion criteria for an ECG:

- Irregular rhythm or absence of a sinus rhythm
- Need to interpolate more than 3 consequent peaks

15.3.3.1 Manual Peak Selection

The first screen of the ECG analysis allows you to check if the peak detection worked properly.

If a peak needs to be added, you must highlight the area around it. The algorithm will automatically select the maximum value in the area as the new peak. Each highlighted area will apply only one peak. You need to highlight as many areas as the number of peaks needed.

If a peak (or several) needs to be deleted, we have to click 'a' on the keyboard to be able to highlight it with the mouse (similarly as the previous step in which you highlight regions of the EEG). To remove a peak, you must right click on the highlighted region (if the area stays highlighted, a new peak will be added in the next step).

Once the screen is closed, the algorithm will remove the highlighted peaks and show the new peaks in orange. Please note that you can keep adding and removing peaks as many times as needed. You will be able to move to the next step only when no further modifications are applied. In case you want to remove a new peak, you need to make sure that the highlighted

area matches the color of the peak (orange in our case). You can select the correct setting by clicking new in the top left menu as shown below.

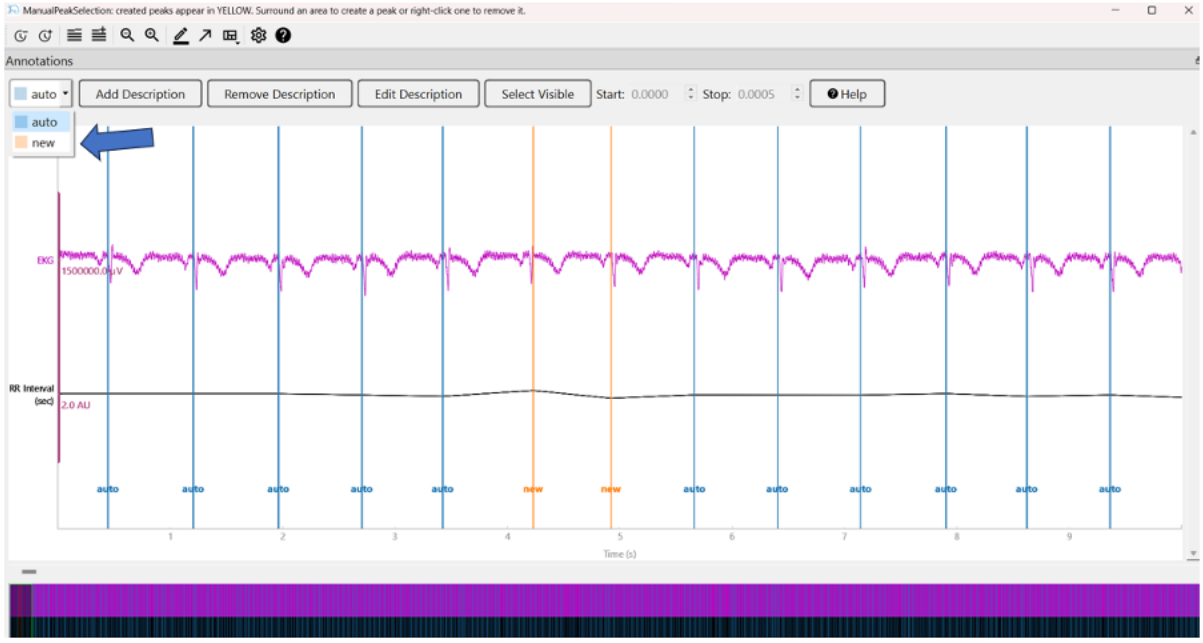


Figure 22: Select the correct annotation to interact with existing or newly created peaks. Notice that this ECG needed to be flipped at the beginning of the analysis, given the negative P and R waves.

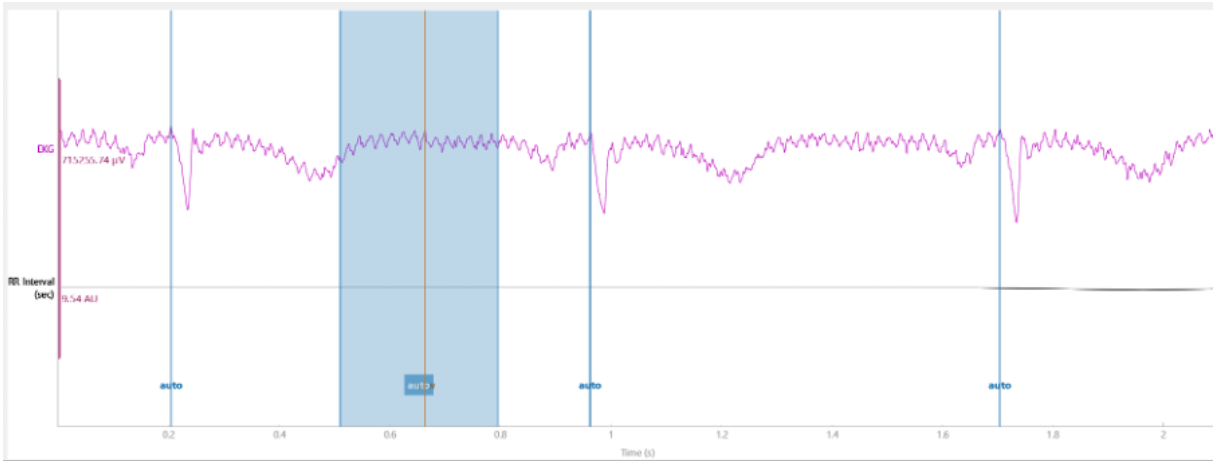
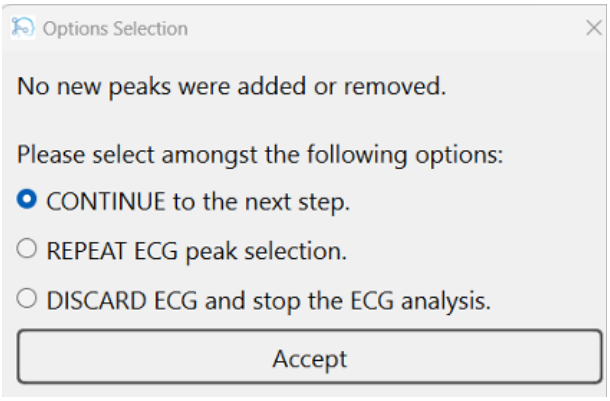


Figure 23: In this example, we can not delete the new peak we added (in orange), since we did not change the settings (the highlighted area is blue instead of orange).

15.3.3.2 Automatic Peak Correction

Once all the peaks have been selected or removed, a message will ask you if you want to continue the analysis, repeat the peak detection or discard the ECG



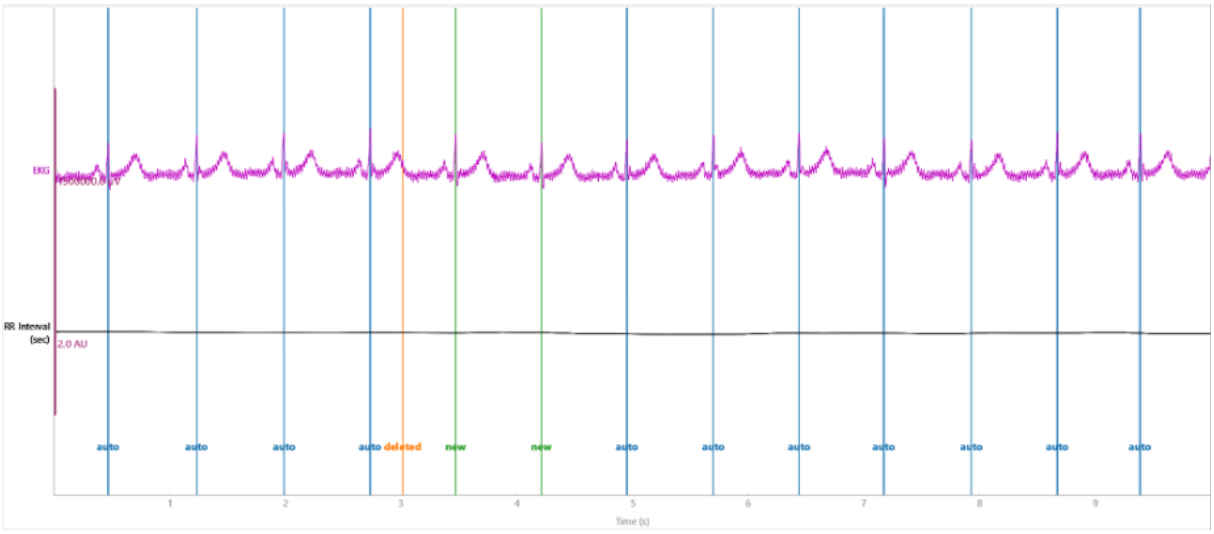


Figure 24: In this example, the algorithm removed the peak at 3s (in orange) to interpolate the peaks at around 3.5s and 4.1s (in green).

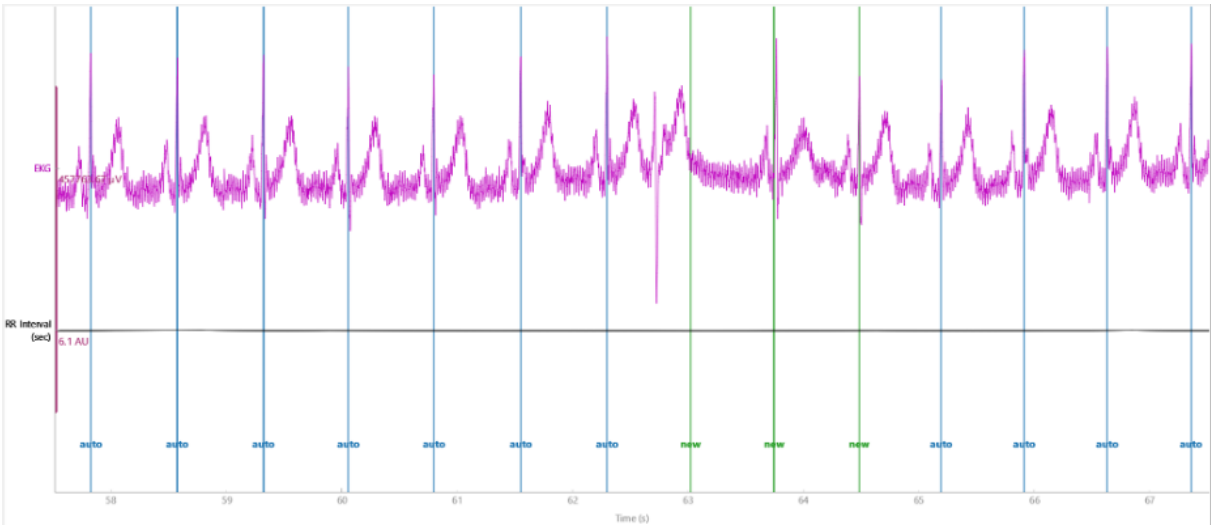


Figure 25: In this example, the algorithm interpolated three new peaks between 62s and 65s.

Once the screen is closed, you will be asked if you want to take into account the corrections. Please notice that you cannot select specific corrections to keep or discard.

15.3.4 EEG

15.3.4.1 Bad Epochs Inspector Preprocessor

This step gives the possibility of marking certain segments of the EEG signal as bad, so that further processing steps can exclude them from the analysis. Additionally, when the functionality is enabled, the user can select channels marking them as bad and triggering their interpolation. The interpolation is a process by which the channel is replaced by the weighted average of the surrounding channels coming out of the neighboring electrodes in the EEG recording machine.

This step is key to filter out parts of the signal which should not be regarded for the analysis and is an important part of the processing of EEG data.

The selection of bad time segments relies on annotations. The user must mark these segments using the "$DP_IGNORE" annotation, which is available in the annotations mode. The parts covered by this annotation will be transformed into adjacent 1s "bad" segments. This means that if the user covers the interval from 10.5s to 13.9s with the "$DP_IGNORE" annotation, the segments corresponding to 10s-11s, 11s-12s, 12s-13s, and 13s-14s, will be marked as bad.

Bad channels can be selected in this step if this feature is enabled in the parameters defined by the pipeline definition. The bad channels will be interpolated at the end of the step. The bad channel selection is done by left-clicking on the channel signal.

15.3.4.2 ICA Preprocessor

This step applies the Independent Component Analysis (ICA), that is a computational method used in the analysis of EEG (electroencephalography) data, which is fundamental in various neuroscience research and clinical applications. The step has three main phases: selection of channels to exclude, filter of ICA components, and validation of the EEG signal. Excluded Channels In this phase the user can select one or more channels to exclude from the ICA model fitting. The software presents the signal browser to the user and they may select which channels to exclude, if any.

The ICA step implicitly trains a model out of the EEG data and then uses it to fit the data, transform it into independent components and then present the results to the user. In this process, adverse noise in the signal is eliminated. In some cases, it's desirable to exclude some channels from the "fit" stage of this process, because they would adversely affect the process by making it focus on exceptionally noisy data, which the user plans to interpolate anyways.

15.3.4.3 Components Filtering

In this phase, the user is presented with the components coming out of fitting the data to the ICA model. They may select which components to exclude, if any, and can inspect metadata for each component by right-clicking the component name label on the left side of the browser.

The component selection is identical to the selection of channels in other steps. The ECG and EOG channels are also displayed, in cases where they're present in the original signal, since they can be helpful when deciding which components to filter out.

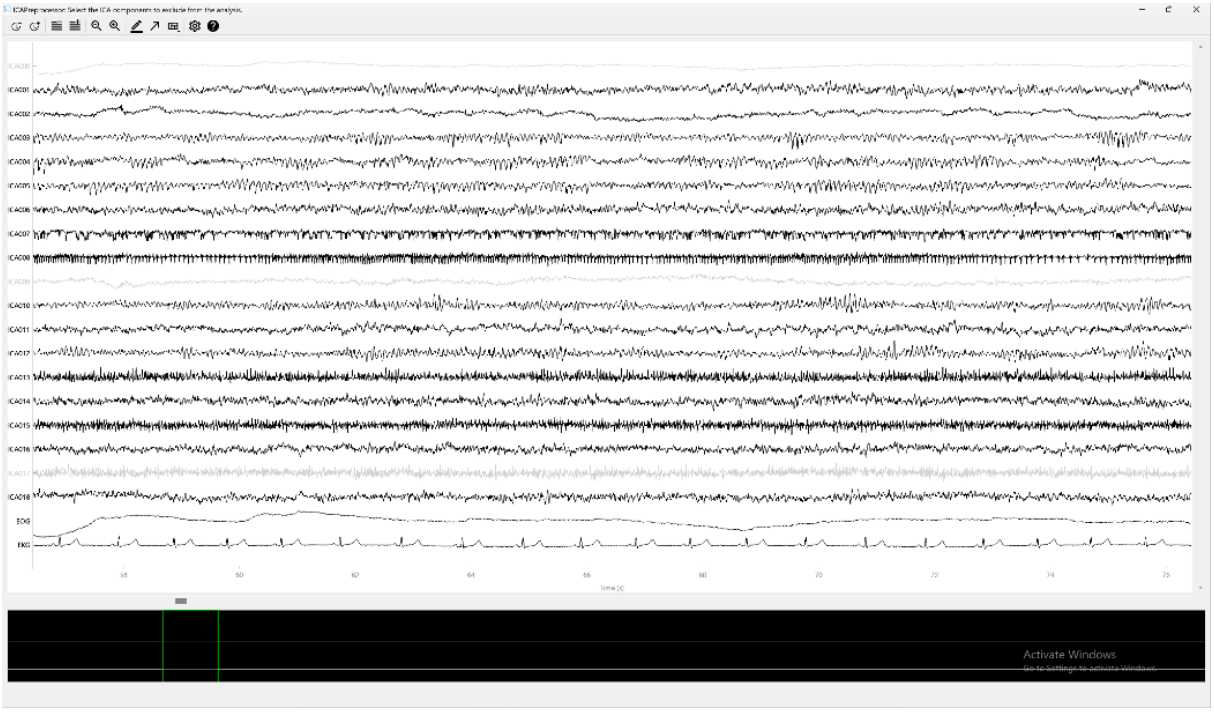


Figure 26: Each component is identified by a signal. Click on the signal or name label to select or deselect the component.

Right-clicking the component label creates a display with helpful metadata for each component.

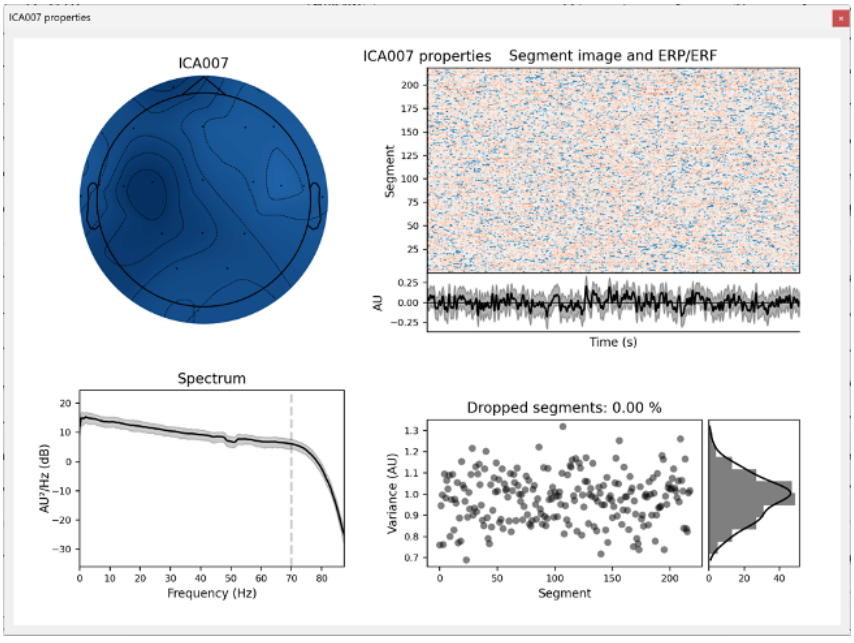


Figure 27: Right-clicking the component label will trigger the display of metadata for the component.

15.3.4.4 Validation of the EEG Signal

Once the component selection process is complete, users will be presented with the resulting EEG signal. They won't be able to interact with the signal at this stage, but they will have the

option to reselect the components for filtering, based on the information displayed in this signal screen. This additional feature allows users to assess whether any changes to the selected components are necessary.

15.3.4.5 VIGAZ Biomarker

This step gives users the option to manually select stages from the signal where the patient fell asleep. These are marked as annotations labeled “C stage”. The user is presented with VIGAZ annotated signal browser. They can create “$DP_STAGE_C” annotations anywhere in the signal. After closing the signal browser window, the subsequent 20 seconds will be marked as C stages, starting at the second where the annotation onset is located. The user creates a “$DP_STAGE_C” annotation and closes the signal browser window.

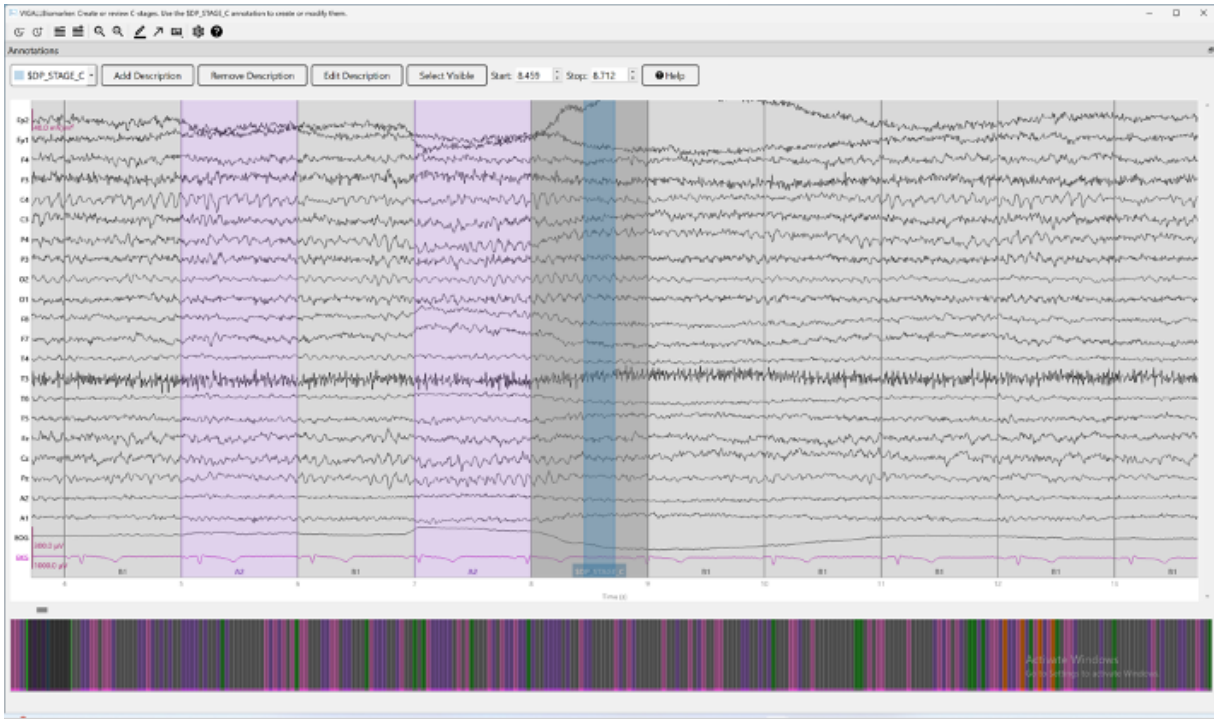


Figure 28: Place the ”C stage” annotation in the signal browser to mark the beginning of the C stage.

The user is then presented again with the signal browser window, but this time the segments starting at the annotation onset are marked with annotations labeled “C” after the C-stage.

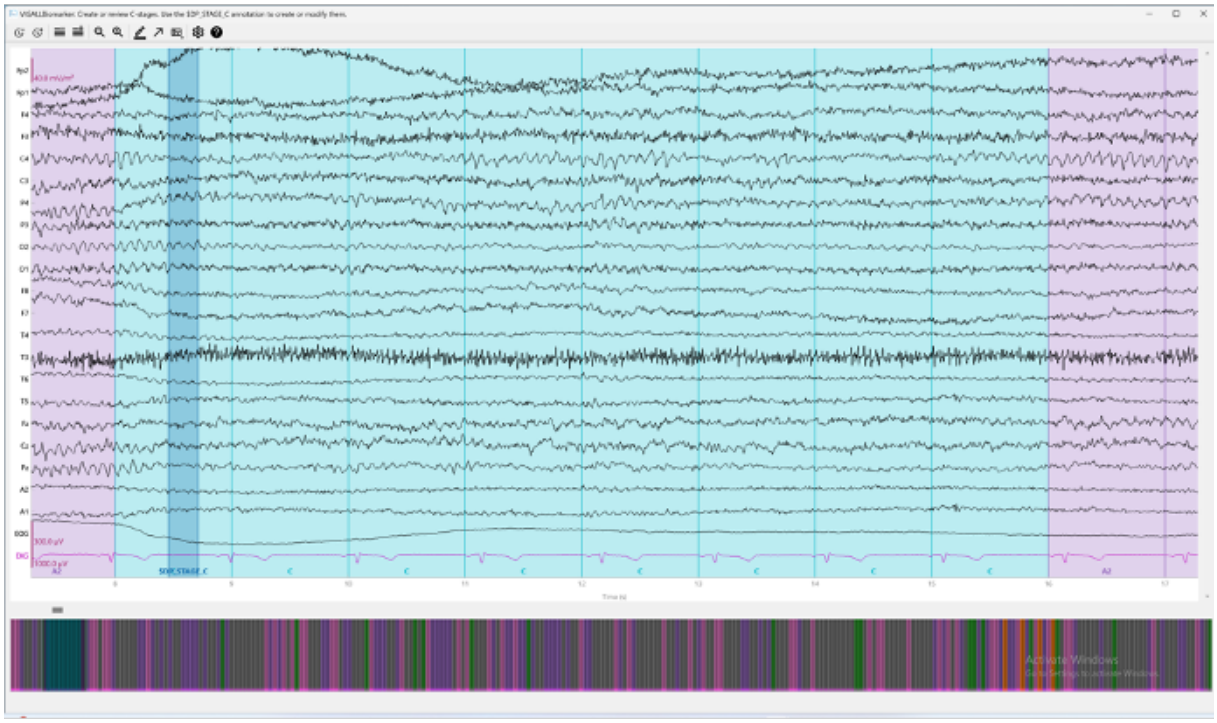


Figure 29: After placing the ”C stage” annotation and closing the window, the user is displayed the resulting C stages.

If after viewing the produced C stages the user decides the would like to revert the selection, they can delete the “$DP_STAGE_C” annotation they created, close the window, and the new screen will have removed the C stages that were previously created.

The user can repeat this process of adding or removing “$DP_STAGE_C” annotations indefinitely. As long as they keep changing any “$DP_STAGE_C” annotation in the signal, they will be presented with the screen again after closing it.

To finish the C stages and move onto the next step coming after VIGAZ, they must close the signal browser window without having made any changes to the annotations. Then they will be presented with the options to move on to the next step, keeping all the changes they made, discard them, and repeat the step again, having the option to rework on the C stages.

16 Analysis Outputs

The DeepPSY Biomarkers application creates several files as outputs of an analysis. Such outputs are located, by default, in the same path as the EEG/ECG data item, or in the selected output path in the parameter selection window. The outputs created by the pipeline are:

16.1 Processed EEG/ECG Data Item

This is the resulting EEG/ECG data item to which all the preprocessing steps have been applied. It reflects the work of the operator on cleaning the input data and adding special annotations such as ECG peaks and vigilance stages. The filename follows the format PROCESSED_«FILENAME».[FORMAT], where «FILENAME» is the name of the original data item and [FORMAT] can be either EDF (European Data Format) or FIF, two well known data format for human electrophysiological data.

16.2 Raw Biomarkers File

The raw biomarker file contains the biomarkers values that were specified in the pipeline definition and that were successfully computed. Additional metadata concerning the analysis and the input EEG/ECG data item are also included. The filename follows the format biomarker_«FILENAME».json where «FILENAME» is the name of the EEG/ECG data item.

16.3 Electronic Report

The DeepPSY Biomarkers medical device generates an electronic PDF report detailing the output from the DeepPsy pipeline, including biomarker values and interpretations for potential treatments based on the patient's electrophysiological profile. These interpretations assist physicians in making informed treatment decisions. The main sections of the report are shown in the figure 30.

16.3.1 Report Header

The report header contains metadata information that the report consumers can use to identify the patient. If available the age and sex of the patient are added to the report. Other fields are populated outside the context of this software.

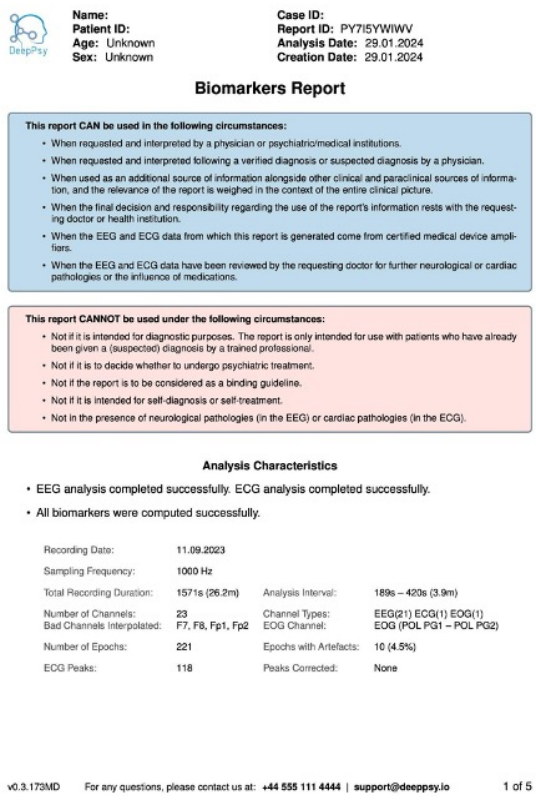
16.3.2 Indications & Contraindications

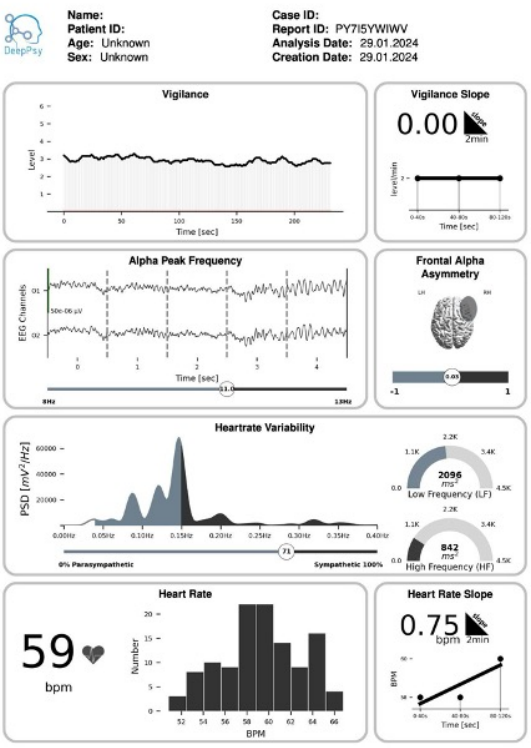
This section specifies the circumstances in which the report may or may not be used.

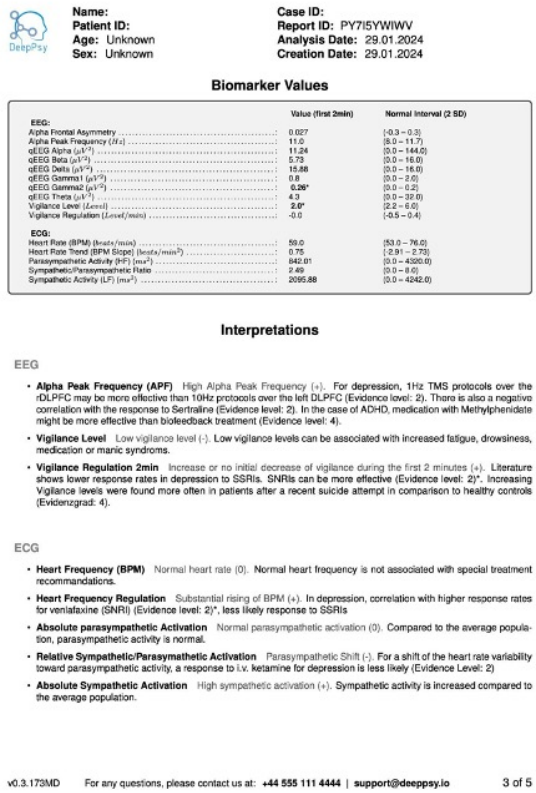
16.3.3 Analysis Characteristics

This section includes metadata related to the characteristics of the specific EEG/ECG data item and some of the actions taken during the analysis by the analyst. The list of items are:

- **Recording Date:** date in which the data item was recorded by the certified EEG/ECG machine.
- **Sampling Frequency:** how many data points can be found in a second of recording. Typically 1000 Hz.
- **Total Recording Duration:** the total amount of recording duration prior to any processing by the software.
- **Analysis Interval:** the specific time interval used for the production of the report.
- **Number of Channels:** how many channels are present in the data after processing.
- **Types of Channels:** the number of channels per type. Types can be EEG, ECG, or EOG.
- **Bad Channels Interpolated:** how many channels were deemed "bad" and interpolated.
- **EOG Channel:** what is the name of the channel identified as EOG, and how it was constructed. It could either have been present since the beginning of the analysis or constructed out of two existing channels.
- **Number of Epochs:** the number of 1s segments present in the data item after processing.
- **Epochs with Artifacts:** how many of the 1s segments were deemed unfit for analysis and thus not included.
- **Bad Epochs Percentage:** the percentage of 1s segments over the whole analyzed interval that were deemed unfit.







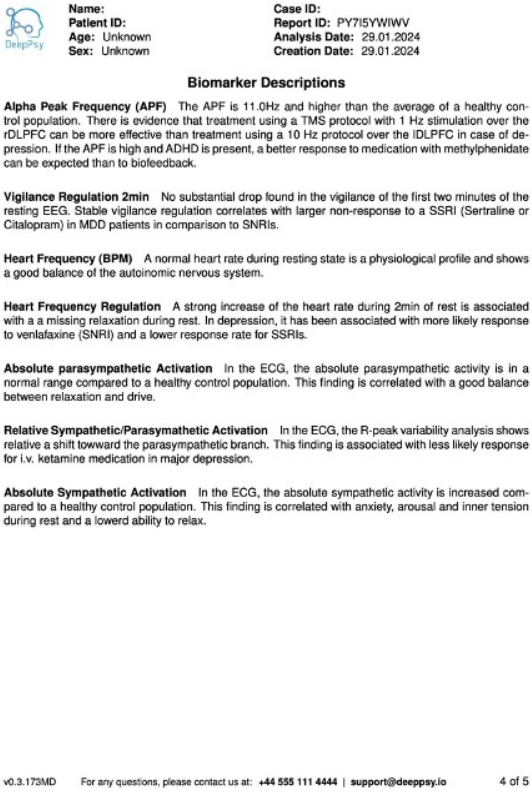


Figure 30: The four essential pages of the report. Please note that the real report might contain more pages, depending on the amount of text output based on the calculated biomarkers. However, the section order and general layout will remain the same.

- **ECG Peaks:** how many peaks were derived from the analyzed ECG signal.
- **Peaks Corrected:** how many peaks were added as part of the correction process for ECG signals with noisy segments.

16.3.4 Biomarker Plots

The report includes a number of plots that can be used to gain insights at a glance of the patient's physiological state. They're described in the following sections.

16.3.4.1 Vigilance

Time course of EEG vigilance (representing CNS-arousal). Each 1s epoch was automatically classified into the following arousal states using the algorithm-based Vigilance Algorithm Leipzig (VIGALL 2.0), resulting in a vigilance time-course: stage 0 (highest arousal), A1, A2, A3, B1, B2/3, C (lowest arousal, sleep onset, classified visually by sleep grapho-elements from an experienced rater). The VIGALL stages were assigned numerically with a range from 6 (stage 0) to 1 (stage C). Most individuals naturally undergo transitions between these different vigilance stages as part of their physiologic vigilance regulation. However, some individuals remain within the high vigilance stage, a condition referred to as "hyperrigid" or "hyperstable" vigilance regulation. Conversely, others exhibit rapid declines into the lower vigilance stage, signifying unstable vigilance regulation.

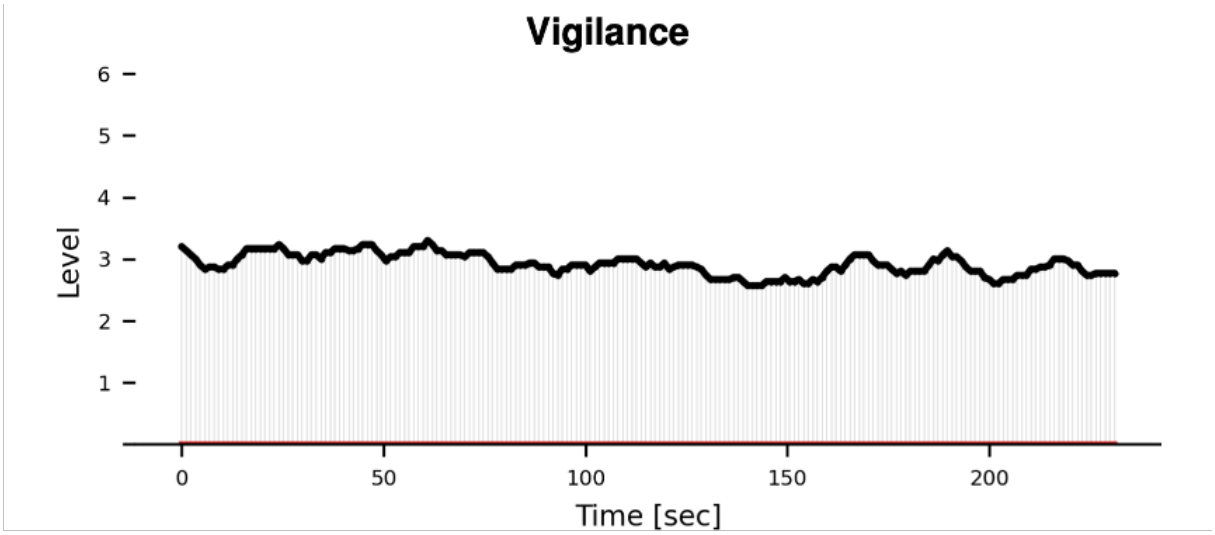


Figure 31: Vigilance of the subject throughout the EEG data item recording.

16.3.4.2 Vigilance Slope

Two-minute time series of CNS-arousal. The vigilance slope was calculated using linear regression the mean median EEG vigilance for each 40s block. A positive slope indicates an increase in alertness; a negative slope indicates a decrease in alertness.

Figure 32: Slope of the patient's vigilance progression over the first two minutes of the signal.

16.3.4.3 Alpha Peak Frequency

The alpha frequency frequency (APF) was determined as the frequency exhibiting maximal power within the alpha band (8-13 Hz) for the channel displaying the highest power. APF was plotted across consecutive 5s epochs. Research has linked APF with cognitive performance. Additionally, deviations in APF have been observed across various mental disorders, including Alzheimer's disease, mild cognitive impairment, psychosis, schizophrenia and attention-deficit hyperactivity disorder (ADHD).

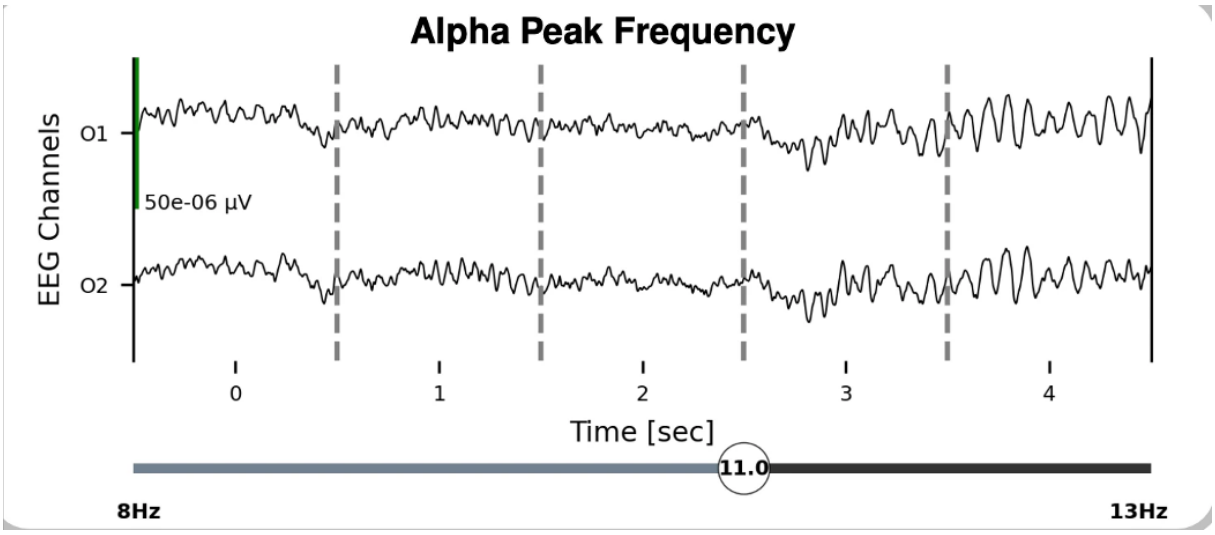


Figure 33: Alpha peak frequency plot.

16.3.4.4 Frontal Alpha Asymmetry

The hemisphere with greater frontal alpha power was highlighted for the frontal alpha asymmetry. A positive FAA (greater alpha power at the right hemisphere) indicates greater right than left alpha activity; a negative FAA (greater alpha power at the left hemisphere) indicates greater left than right alpha activity.

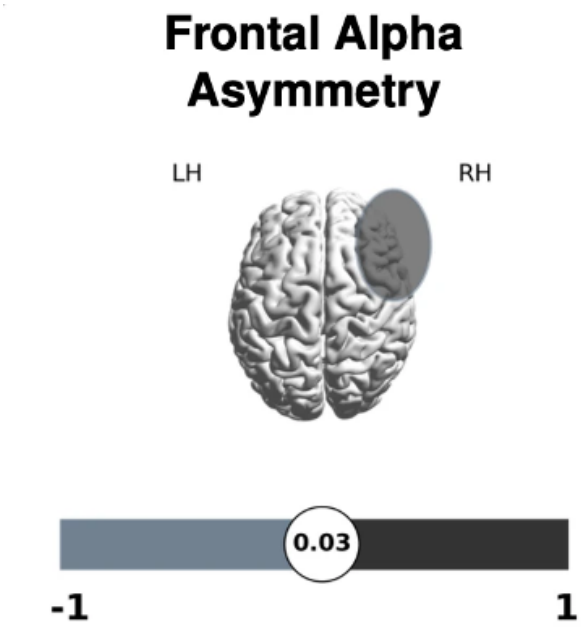


Figure 34: Frontal alpha asymmetry of the subject. It can be either left, right, or balanced.

16.3.4.5 Heartrate Variability

Low Frequency (LF - [0.04-0.15 Hz]) evaluates the influence on the heart rate from both the sympathetic and the parasympathetic via baroreflex mechanisms. However, LF is usually used to evaluate the sympathetic nervous system in the context of mental or physical stress. High LF reflects the adaptive capabilities in case of stress factors. Low LF is usually associated with a relaxation state.

High Frequency (HF - [0.14-0.4 Hz]) is commonly used to evaluate the parasympathetic nervous system through the modulation of the heart rate via the vagus nerve. High HF is associated with a relaxed state, where low HF might be associated with stress or anxiety.

The bottom bar shows LF/(HF + LF). This ratio [0-100%] shows the sympathetic to parasympathetic balance. A higher ratio represents a relative dominance of sympathetic activity or reduced parasympathetic activity, suggesting a stress response or heightened alertness state. A lower ratio suggests a dominance of parasympathetic activity, which is associated with relaxation and recovery states. This measure is different from LF/HF (not shown in the plots), and also reflects the balance between the sympathetic (LF) and parasympathetic (HF). High LF/HF is usually associated with stress whereas lower LF/HF with relaxation or recuperative states.

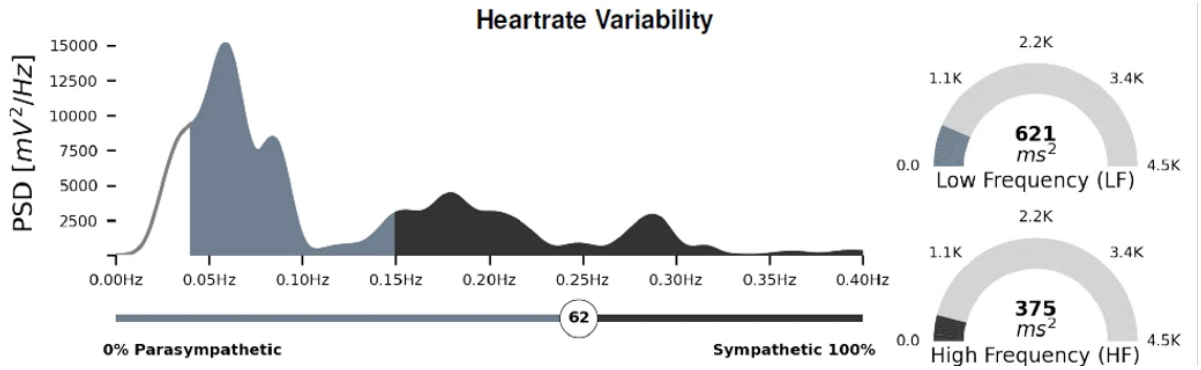


Figure 35: This plot contains several measures of the patient's heartrate variability.

16.3.4.6 Mean Beats Per Minute

Mean Beat Per Minute for the first 2 min recording.

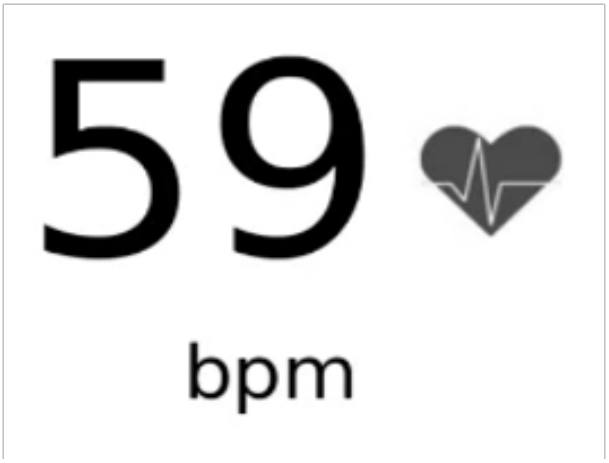


Figure 36: The mean beats per minute for the first two minutes of the ECG signal.

16.3.4.7 Heartrate Histogram

Histogram of beat per minute for the analyzed ECG signal interval.

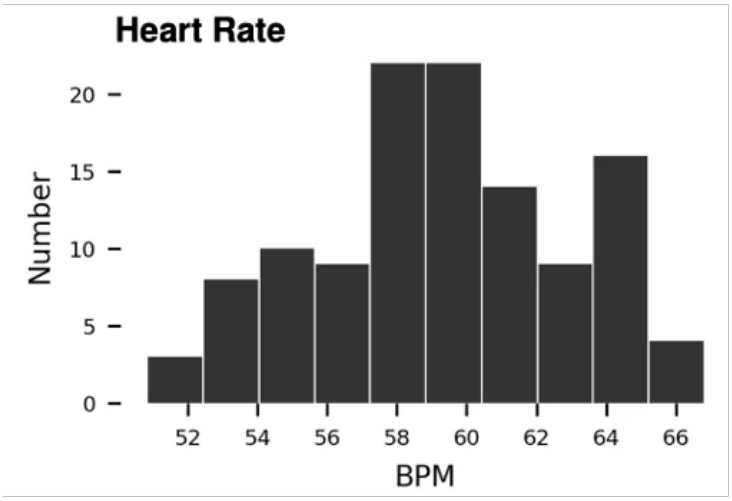


Figure 37: The histogram of the beats per minute for the analyzed ECG signal.

16.3.4.8 Heart Rate Slope

Two-minute time series of ANS-arousal. The heart rate slope was calculated using linear regression the mean BPM for each 40s block. A positive slope indicates an increase in ANS-arousal; a a negative slope indicates a decrease in ANS-arousal.

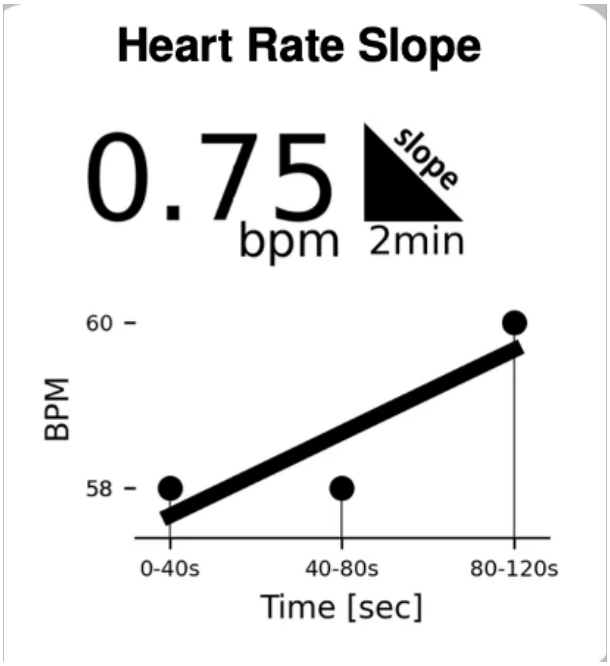


Figure 38: Slope of the heart rate over the first two minutes.

16.3.5 Biomarkers Values

These are the raw biomarker values obtained from the biomarker algorithms. They're ordered by whether they're EEG or ECG, and alphabetically. For each value, there are two columns. The first column presents the value itself. The second column expresses the range of values that the biomarker can take in a healthy subject. Lastly, values are shown in boldface and with an asterisk when they're outside the normal range.

The values are calculated using the first two minutes of the signal after it has been processed. The normal interval is within two standard deviations of the mean, obtained from a

database of healthy subjects.

16.3.6 Biomarker Interpretations & Descriptions

These represent observations and literature findings. The observations about which medications have correlated with other patients of a similar biomarker profile are included in this section.

16.4 Actions Metadata

The actions metadata file contains detailed information of the analysis performed by the operator of the software. It has a vital role in making the analysis reproducible as it includes information that permits the execution of the analysis without any human intervention.

17 References

Several paper references that can be useful for those that wish to delve deeper into the literature used to produce the observations in the report.

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