



DeepPsy

BIOMARKERS

In-house Analysis Software

Instructions for Use

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1 Label Information



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Medical Device

DeepPsy Biomarkers



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Certification Pending
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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

If you require a printed copy of these Instructions for Use, please contact DeepPsy AG using the contact details above. A printed copy will be provided free of charge by post within 7 calendar days of receiving your request.

For further information and support material, please visit the DeepPsy website at <https://manuals.deeppsy.io/>.

4 Product Description

The DeepPsy's Biomarkers medical device is a standalone software that DeepPsy specialists can use to analyze and compute physiological biomarkers from EEG and ECG data. Biomarkers are a broad subcategory of medical parameters – that is, objective indications of a physiological state – which can be measured accurately and reproducibly.



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

The medical device software is installed locally on a standard personal computer complying with the software specifications. The application allows specialists to:

- Select files of EEG and/or ECG data.
- Visualize and preview the selected EEG and/or ECG data.
- Data quality validation on the EEG and/or ECG files to ensure their suitability for biomarker analysis.
- Preprocessing the EEG and/or ECG data through a series of reproducible and quality-controlled steps to make it suitable for the computation of biomarkers. Preprocessing can be manual or automated.
- Compute EEG and/or ECG Biomarkers on preprocessed data.
- Generate a biomarker report: The information provided, along with the biomarkers, reflects the state-of-the-art scientific evidence in literature regarding the predictive properties of the included EEG and ECG biomarkers, presenting the current level of evidence from the literature.

The medical device can produce a set of files according to the configuration of the operator. These include the output biomarkers in numerical format, charts, and a report in an electronic document format such as Portable Document Format (PDF). Reports may be delivered to physicians.

Additionally, the software will communicate with a remote system hosted in a cloud service provider through the internet to perform basic functions such as authentication of the DeepPsy specialist, collection of logs, and telemetry.

4.1 Intended Purpose

DeepPsy Biomarkers is a 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. It is designed to analyze resting-state EEG and ECG recordings to compute physiological biomarkers.

A subset of the EEG and ECG biomarkers has been associated in the literature with psychiatric treatment outcomes and can assist in distinguishing subgroups of patients who may respond more favorably to specific treatments.

The information provided by the software is intended to be used only by physicians and is intended to influence treatment decisions only between treatments that are already indicated for the patient and that have a positive risk-benefit ratio. It is not intended to influence any diagnostic process or to establish or exclude any diagnosis. The treating psychiatrist remains fully responsible for diagnosis, indication, and final treatment choice.

4.2 Medical Indication

This can include conditions(s) or disease(s) to be screened, monitored, treated, diagnosed, or prevented.

The medical device is intended to provide additional information for medical professionals when treating with psychiatric disorders. It is designed to improve decision-making within the scope of treatments already indicated for the patient.

The DeepPsy Biomarkers software has been evaluated in clinical studies using EEG and ECG biomarkers in MDD population. Performance varies with biomarker and treatment type; detailed study data are available in the Clinical Evaluation Report.

This medical device is not intended to determine the indication or contraindication of a specific treatment. The responsibility for determining whether a treatment is appropriate or inappropriate for a patient rests solely with the medical professional.

Indication	Intervention	Biomarker	Sample Size	Effect Size	Estimated Power
MDD	Sertraline	APF	225	0.28	0.552
MDD	10Hz rTMS	APF	90	0.66	0.872
MDD	10Hz rTMS	APF	68	0.63	0.726
MDD	10Hz rTMS	APF	59	0.52	0.501
MDD	1Hz rTMS	APF	564	0.28	0.913
MDD	ECT	APF	564	1.07	1.000
MDD	Sertraline	APF	564	0.33	0.975
MDD	10Hz rTMS	APF	564	0.20	0.659
MDD	Escitalopram, Sertraline	Vigilance Slope	263	0.24	0.492
MDD	Escitalopram, Sertraline	Vigilance Slope	263	0.19	0.336
MDD	Citalopram, etc.	Vigilance Level	78	0.59	0.730
MDD	Escitalopram, Duloxetine	Vigilance Slope	79	0.47	0.541
MDD	Ketamine	Stage A	48	1.39	0.997
MDD	Ketamine	Stage A Prediction	48	0.79	0.764
MDD	CBT, SSRI	Stage 0	51	0.90	0.883
MDD	Escitalopram, Sertraline	FAA	203	0.30	0.566
MDD	Escitalopram, Sertraline	FAA	258	0.55	0.993
MDD	Escitalopram	FAA	56	0.68	0.705
MDD	SSRI, SNRI, Tricyclic	BPM	34	0.22	0.095
MDD	SSRI, SNRI, NDRI, TCA	BPM	28	0.63	0.362
MDD	Ketamine	BPM	47	0.60	0.521
MDD	Ketamine	HRV Power	47	0.42	0.291
MDD	Tricyclic	Log LF@week4	33	0.65	0.440
MDD	Tricyclic	Log HF@week4	33	0.48	0.267
MDD	Tricyclic	Log LF/HF@week4	33	0.08	0.056
MDD	Venlafaxine	BPM slope	184	0.26	0.419

Table 1: Clinical Study Data: Biomarker Performance Across Different Interventions and Indications

MDD: Major Depressive Disorder; GAD: Generalized Anxiety Disorder; OCD: Obsessive Compulsive Disorder.

4.3 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.

4.4 Patient Group

This can include age group, weight range, health, or condition.

The patient group includes any patient for whom a physician requests the respective additional information to support clinical decision-making within the scope of treatments



already indicated for that patient, provided that:

Patient condition:

- Patients with a diagnosis of depression or suspected depression.

Age group:

- The information provided by the DeepPsy Biomarkers Software is intended to be used only in Patients aged 18 and older.

Prerequisites:

- The treating physician has determined that a psychiatric treatment is needed for the patient.
- The treating physician has determined that the applicable treatment is indicated for the patient.

4.5 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.

4.5.1 General Manufacturer Claims

Type	Claim
Clinical Performance (Claim 1)	Our medical stratifies clinical responders and non-responders for the supported treatment modalities within different lines of treatment (first, second and third line therapies) and thereby achieves its intended purpose of providing information that supports treatment selection.
Clinical Benefit (Claim 2)	The device supports clinicians in selecting a treatment that is associated with a higher probability of symptom improvement within the respective line of treatment.
Safety and Risk Profile (Claim 3)	The device does not introduce additional clinical risks beyond those associated with standard clinical care.



5 Contraindications

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

- Is not intended to replace the expertise and guidance of a physician or psychotherapist.
- Is not intended to be used as a final, mandatory guideline or recommendation.
- The information provided by DeepPsy Biomarkers is not intended to drive diagnosis.
- Is not intended to decide whether a treatment is indicated.
- Is not intended to be used to make decisions about whether to undergo a psychiatric treatment or not.
- The DeepPSY Biomarkers report may only be used if the requesting physician has confirmed the absence of neurological or cardiac pathologies and the absence of clinically relevant medication effects on the EEG and ECG data.
- Not for self-diagnosis, self-treatment, or for making independent treatment decisions.
- Not for use in life-support or acute emergency settings.
- 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.



6 Cautions on DeepPsy Biomarkers Software

- Must be used only when requested and interpreted by a physician or psychiatric/medical institutions.
- Clinical decisions must always be made by a qualified medical professional 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.
- Use in elderly patients (>75) requires careful clinical interpretation.



7 Cautions on DeepPsy Biomarkers Report

- Must be used only when requested and interpreted by a physician or psychiatric/medical institutions.
- Clinical decisions must always be made by a qualified medical professional 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.
- Use in elderly patients (>75) requires careful clinical interpretation.

8 Limitations

8.1 Clinical Limitations

- The performance is unclear under the presence of neurological pathologies (in the EEG) or cardiac pathologies (in the ECG).
- Certain medication might influence the EEG and ECG patterns.
- The performance is unclear in patients with scalp abnormalities or head injuries.
- Performance may differ in elderly patients (>75) as EEG/ECG patterns can vary from those of typical adults.
- Use is restricted to approved geographic areas as per local regulatory authorization.
- Frontal alpha asymmetry (FAA) is used only for female patients, as the supporting predictive evidence is limited to that subgroup; it is not applied as claim-supporting treatment-selection information outside the female population.
- Using EEG/ECG data that does not meet the specified quality requirements may lead to unreliable results.

8.2 EEG and ECG data limitations:

- **Data length:** 3 minutes
- **Recording condition:** Resting state with eyes closed
- **Channel positioning:** Recommended: 10-20, Possible: 10-10, 10-05. We need at least: One electrode per lobe, one electrode on each side.
- **Channel number:** 19

- **Sampling frequency:** 250 Hz
- **ECG channel:** at least bipolar recording at one of the following: wrist, or neck, or breast
- Maximum length of recording is 3600 seconds. Longer recordings will be truncated.
- Maximum sampling frequency is 1000 Hz. Higher sampling frequencies will be down-sampled to 1000 Hz.

9 Safety Instructions & Technical Description

9.1 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



The software is not guaranteed to work in a virtualized environment. The only system where the software has been tested and shown to work is in [Parallels Virtual Machine](#).



Ensure that the software does not compete with resources against other compute-intensive software in the system. Running multiple resource-intensive applications simultaneously may significantly degrade performance and affect the reliability of the medical device.

Recommendation: Close unnecessary applications, especially those using significant CPU, RAM, or disk I/O before running DeepPSY Biomarkers. Consider dedicating a workstation specifically for medical device operations to ensure optimal performance and reliability.



Using a connection slower than the minimum required 20Mbps may result in data transmission delays, incomplete analysis, or connection failures. This could compromise the timely delivery of medical results and patient care.

Recommendation: Test your internet connection speed before using the software. If your connection is below 20Mbps, contact your IT department to upgrade the connection or consider using a wired connection instead of wireless. Ensure no other devices are consuming bandwidth during medical device operations.



Impact on the UI may occur on a slow computer or one starved of resources. Reduced system performance can lead to unresponsive interfaces, delayed data processing, and potential errors in medical data analysis.

Recommendation: If you experience slow performance, restart the computer before using the software, close all unnecessary applications, and ensure adequate free disk space. Consider upgrading system RAM or using a more powerful computer if performance issues persist. Monitor system resource usage during operation.



Minimum recommended monitor resolution of 1280x1024 or higher is required for proper display. Lower resolutions may cause interface elements to be cut off, making the software difficult or impossible to use effectively.

Recommendation: Check your monitor's native resolution in Windows Display Settings. If it's below 1280x1024, consider using a larger monitor or connecting to an external display with higher resolution. Ensure the display scaling is set to 100% to avoid interface scaling issues.

9.2 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.

9.3 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.

9.4 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.

10 Technical Specification

10.1 Biomarkers

10.1.1 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.

10.1.1.1 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].

10.1.1.2 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].

10.1.1.3 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].

10.1.1.4 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 dose escitalopram-intake [16]. Patients with bipolar depression have been found to exhibit a flatter aperiodic exponent when compared to healthy controls [17].

10.1.1.5 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 (EOG) 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].

10.1.2 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.

10.1.2.1 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].

10.1.2.2 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].

10.1.2.3 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].

10.1.2.4 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].

10.1.2.5 LF/(HF+LF) Ratio

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

10.2 Preprocessing Steps

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

10.2.1 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.

10.2.2 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).

10.2.3 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.

10.2.4 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.

10.2.5 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.

10.2.6 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.

10.2.7 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.

10.2.8 Independent Component Analysis (ICA) Filtering

This is a 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.

11 Performance Characteristics

11.1 Preprocessing Steps

The following table provides the performance specifications for all preprocessing steps.

Preprocessing Step	Performance Specification
ECG Preprocessing	
ECG Auto-Flip	Detects and corrects inverted ECG signals based on statistical polarity checks (Automatic, inspected by specialist)
Automatic Peak Detection	Detects R peaks in ECG traces (Automatic)
Automatic Peak Filtering	Filters out physiologically implausible peaks by applying minimum inter-peak interval threshold (Automatic)
Automatic Peak Correction	Identifies and corrects ectopic beats, interpolates missing peaks, removes physiologically implausible intervals (Automatic, optional)
Manual Peak Selection	Enables visual inspection and manual selection of missing ECG peaks (Manual)
EEG Preprocessing	
Bandpass Filter	EEG: Signal power preserved within 0.1–70 Hz band, attenuated (>20 dB reduction) for frequencies <0.05 Hz and >75 Hz; EOG: Signal power preserved within 0.05–70 Hz band, attenuated (>20 dB reduction) for frequencies <0.01 Hz and >75 Hz; ECG: Signal power preserved within 0.01–30 Hz band, attenuated (>20 dB reduction) for frequencies <0.005 Hz and >35 Hz (Automatic)
Notch Filter	Power at 50 Hz reduced by ≥ 20 dB compared to unfiltered signal; neighboring frequency content (± 5 Hz) preserved (Automatic spectrum analysis)
Interpolation for Broken Channels	Interpolated signal computed as weighted spatial average using spherical spline interpolation (per Perrin et al., 1989) (Automatic)
Re-referencing	EEG signals re-referenced to average of all channels (Automatic)
Epoching	Output data shape transforms from 2D matrix (nChannel \times pnts) to 3D matrix (nChannel \times pntsPerSegment \times nSegment) (Automatic)
Bad Segment Selection	Bad epochs visually identified by trained analyst and marked in metadata (Manual)
Independent Component Analysis	ICA applied to decompose EEG into independent components; artifact-related components identified and removed by trained analyst (Manual)

11.2 Biomarkers

The following table provides the performance specifications for all biomarker calculations.

Biomarker	Performance Specification
ECG Biomarkers	
Beat Per Minute (BPM)	Produces output range of 35–200 BPM; Achieves tolerance of ± 1 BPM vs. Kubios; Ensures $\geq 90\%$ of samples meet criterion
ECG Frequency Measures	Produces output LF, HF, LF/HF ≥ 0 ; Achieves adaptive tolerance of $\text{Max}(10 \mu\text{V}^2, 5\%)$ vs. Kubios; Ensures $\geq 90\%$ of samples meet criterion
BPM Slope	Ensures slope reflects correct direction (pos/neg/zero); Computes via linear regression on valid BPM values
EEG Biomarkers	
Alpha Peak Frequency (APF)	Produces output range of 8–13 Hz; Uses channel from predefined list; Achieves tolerance of < 0.25 Hz vs. MATLAB; Ensures $\geq 90\%$ of samples meet criterion
Frontal Alpha Asymmetry (FAA)	Produces output range of -1 to 1; Achieves tolerance of < 0.1 a.u. vs. MATLAB; Ensures $\geq 90\%$ of samples meet criterion
EEG Vigilance	Produces median vigilance of 0–6; Ensures percentages of stages per block sum to 1; Achieves declining slope in $\geq 85\%$ of cases; Ensures Stage A > B BPM is statistically significant
QEEG Powers	Produces power ≥ 0 in all frequency bands; Achieves tolerance of $\text{Max}(10 \mu\text{V}^2, 10\%)$ vs. MATLAB; Ensures $\geq 90\%$ of samples meet criterion

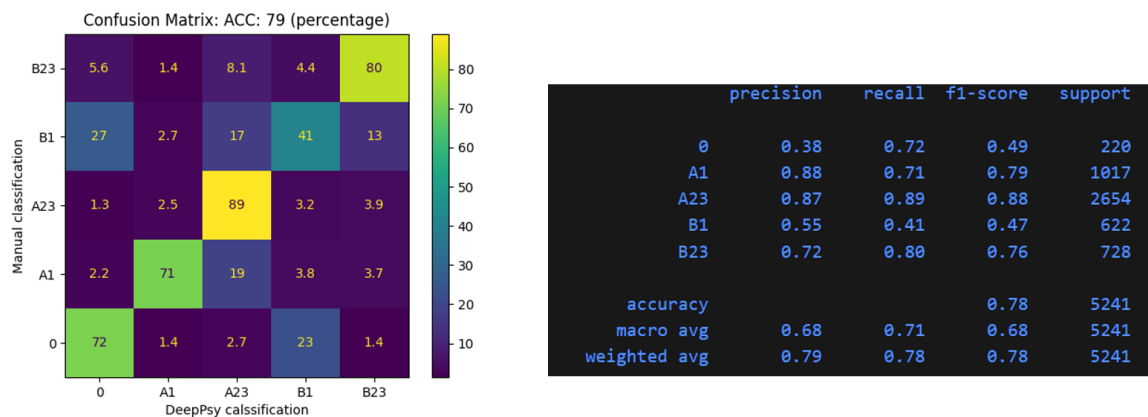


Figure 1: Performance of the VIGAZ algorithm for the calculation of EEG-Vigilance Regulation.

12 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.

13 Security Characteristics

The DeepPsy Biomarkers software implements a number of features to enhance the cyber-security aspects of the medical device, keeping the data safe and secure. As an operator, it's important to be aware of these features as some may impose limits on what can be done with the software. These features include:

- **Session Timeout:** When the user authenticates a session is created to keep track of their activity. This session expires after 5 continuous hours of use. Upon expiration, the user is logged out of the application and whichever activity they were performing is cancelled. Thus it's important to keep this in mind when using the software. If you suspect you might be close to reaching this 5-hour limit, it's recommended to save your work and restart the application.
- **Data Encryption:** All data that is transmitted between the application and the cloud servers is encrypted using the latest encryption standards. This ensures that the data is safe from evesdropping and tampering.
- **Events Logging:** Most actions performed by the user are logged and stored in a secure location. This is done to ensure that in case of a security incident, the logs can be used to trace back which actions may have triggered the incident.
- **New Release Enforcement:** Users of the medical device must always use the latest version of the software. Whenever a new version is released, older versions are disabled and users will not be able to login using them. This is done to ensure that the latest security patches are applied to the software. Please download the latest version of the medical device from the DeepPsy AG website.

14 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".

15 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.

15.1 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,

15.1.1 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.

15.1.2 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 <i>standard 1005</i> montage.

15.1.3 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

15.1.4 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

16 Operating Instructions

16.1 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.

16.2 Initialization Checks

Before the user can start using the application, the software will perform a number of checks to ensure that the system is ready to be used. If any of the checks fail, the user will present a dialog box with detailed information about the failed check and instructions on how to fix the issue. These checks are performed in the following order:

1. **Disk space:** the software will verify that at least 600 MB of free disk space is available for temporary files, downloads, and generated outputs.



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

2. **File permissions:** the software will verify that read and write permissions have been granted, so it can open input data and save analysis results to the selected output folder.
3. **Backend reachability:** the software will verify that the backend server is reachable through the internet, which is required for authentication and cloud-based operations.
4. **System time synchronization:** the software will verify that the local system time is in sync with the backend server time to avoid issues with authentication, logging, and time-based requests.
5. **Network bandwidth:** the software will verify that the available bandwidth is at least

20 Mbps to ensure reliable data transfer and acceptable performance.

Even if some of the checks fail, the user may still use the application. This measure was designed to assist the user in their work.

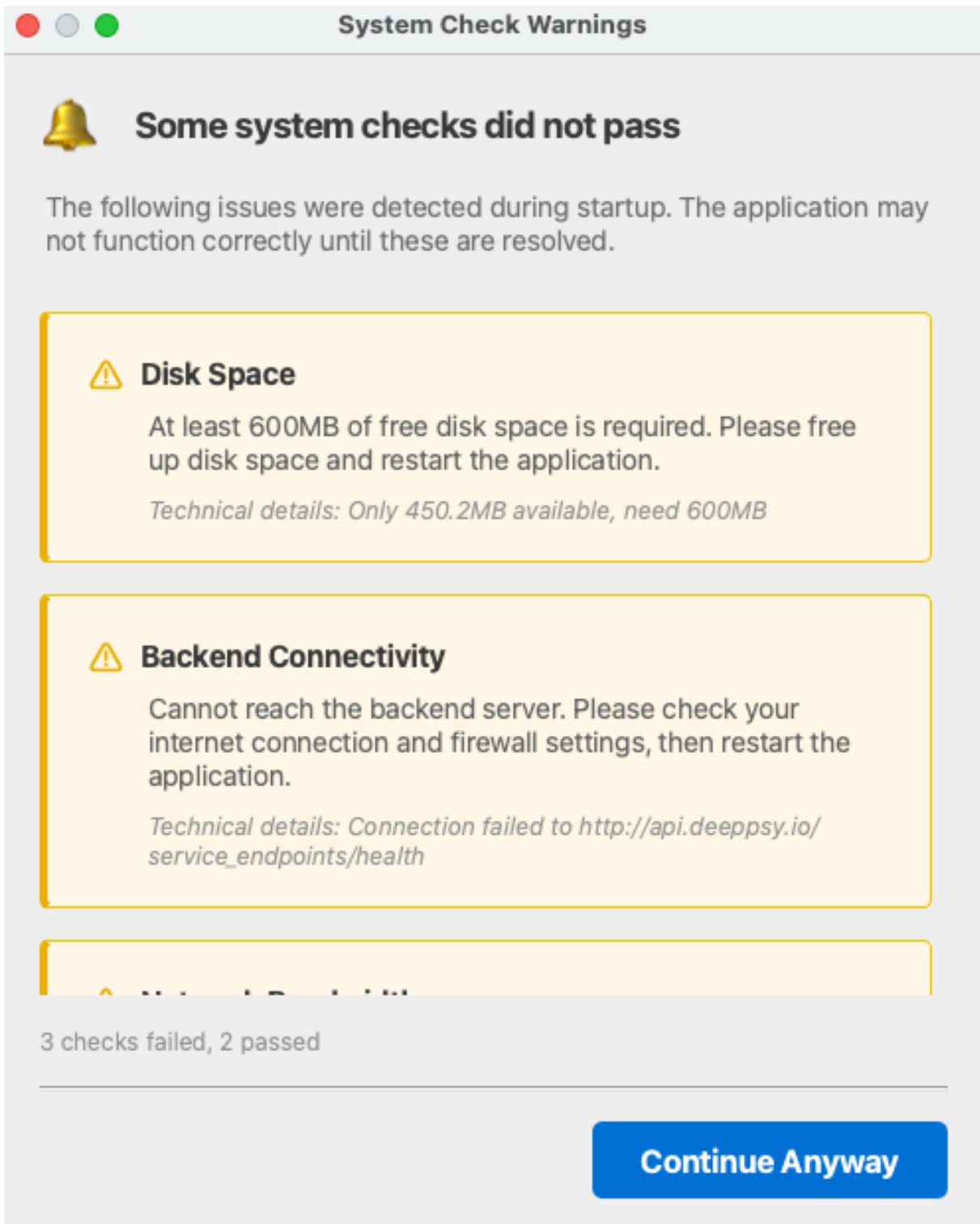


Figure 3: Initialization checks window.

16.2.1 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.

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 4: User authentication failed.

16.2.2 Analysis Modes

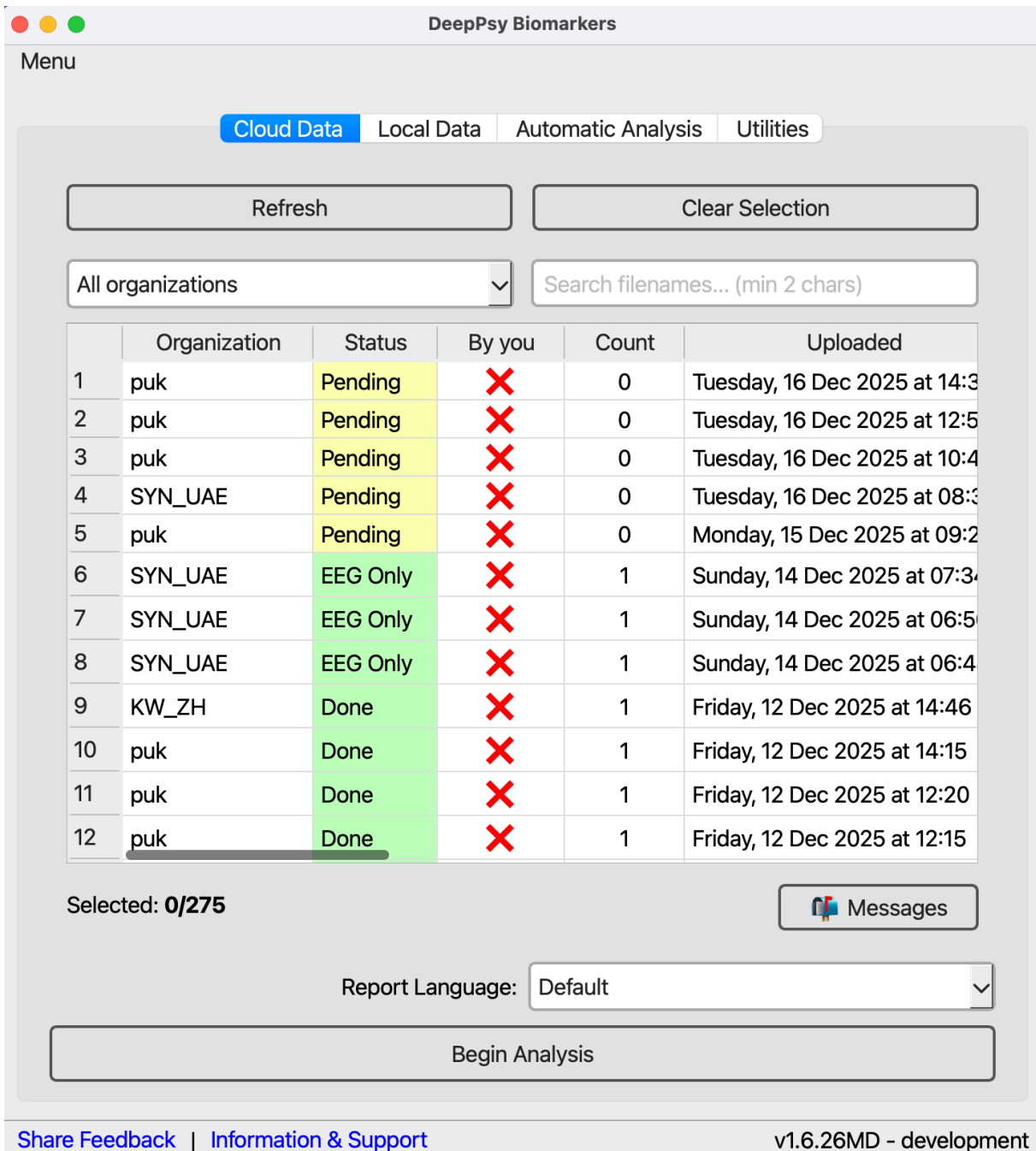
Following a successful user authentication, the application presents a dialog box with a tab bar offering three choices: Cloud Analysis, Local Analysis, and Automatic Analysis. One of these options may be selected by clicking on the corresponding tab in the tab bar. A description of each analysis type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

16.2.2.1 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.



DeepPsy Biomarkers

Menu

Cloud Data Local Data Automatic Analysis Utilities

Refresh Clear Selection

All organizations Search filenames... (min 2 chars)

	Organization	Status	By you	Count	Uploaded
1	puk	Pending	✗	0	Tuesday, 16 Dec 2025 at 14:3
2	puk	Pending	✗	0	Tuesday, 16 Dec 2025 at 12:5
3	puk	Pending	✗	0	Tuesday, 16 Dec 2025 at 10:4
4	SYN_UAE	Pending	✗	0	Tuesday, 16 Dec 2025 at 08:3
5	puk	Pending	✗	0	Monday, 15 Dec 2025 at 09:2
6	SYN_UAE	EEG Only	✗	1	Sunday, 14 Dec 2025 at 07:34
7	SYN_UAE	EEG Only	✗	1	Sunday, 14 Dec 2025 at 06:5
8	SYN_UAE	EEG Only	✗	1	Sunday, 14 Dec 2025 at 06:4
9	KW_ZH	Done	✗	1	Friday, 12 Dec 2025 at 14:46
10	puk	Done	✗	1	Friday, 12 Dec 2025 at 14:15
11	puk	Done	✗	1	Friday, 12 Dec 2025 at 12:20
12	puk	Done	✗	1	Friday, 12 Dec 2025 at 12:15

Selected: 0/275 Messages

Report Language: Default

Begin Analysis

Share Feedback | Information & Support v1.6.26MD - development

Figure 5: 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 meta-data 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.

Above the table, the dropdown allows the user to filter a specific organization's data items. If no organization is selected, all data items will be shown. The search filename is a basic search functionality that maps patterns to the filenames of the data items.

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.

16.2.2.2 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 several states:
 - **DONE** If it has already been successfully analyzed by an analyst
 - **EEG ONLY/ECG ONLY** The analysis was only partially completed, either the EEG or ECG analysis didn't complete.
 - **REJECTED** After completing the preprocessing, the analyst decided to reject it. This rejection is reflected in the report.
 - **BAD REPORT** After the report was printed, the analyst inspected it and did not accept it.
 - **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.
 - **NO REPORT** There was an error during the creation of the report and none was produced after the analysis.
3. **By you:** contains a cross or a checkmark depending on whether the analyst themselves analyzed this data item already.
4. **Count:** contains the number of times the data item has been analyzed by any analyst.
5. **Uploaded:** date in which the item was uploaded to DeepPsy's systems.
6. **Filename:** filename of the EEG/ECG data item. This field is important because often metadata information is encoded in the data item's name.
7. **Size:** size in MB of the file.
8. **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.
9. **Info:** a button opening a dialog with the history of analysis performed on the specific data item.

16.2.2.3 Analysis History Window

In the "Info" column, there's a button with a magnifying glass icon. Clicking on it opens a window with the history of analysis performed on the specific data item. This window is very useful in cases where it's necessary for a supervisor to inspect the work done by an analyst, or when it's necessary to obtain the metadata of a specific analysis.

The table shown in this window has the "Downloads" column, which contains three icons, by clicking on them the user can download the biomarkers file, PDF report, and actions metadata file, respectively, for the specific analysis.

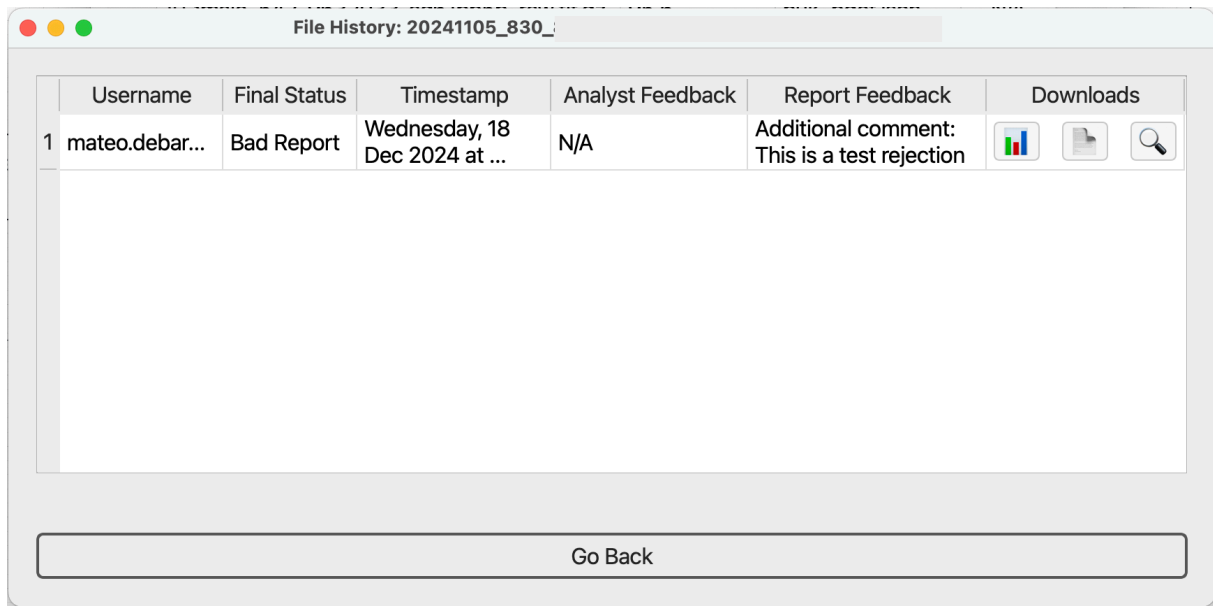


Figure 6: Analysis history window. It shows the history of analysis performed on the specific data item, as well as options to download the metadata produced by the analysis.

The rest of the columns have metadata about the analysis, such as the status, the analyst who performed it, and any feedback they provided, if any.

16.2.2.4 Messages Box

The messages button opens a dialog box with a list of messages that are attached to either an organization or a specific data item. These messages can come from several sources, and they're typically important to analyze a given data item.

The user has the option to read messages as many times as they want, and mark them as read, so that they can filter future important messages from unimportant ones.

The messages box is also available in the Analysis Window. There the messages will be filtered to only those relevant to the specific data item being analyzed at the moment..

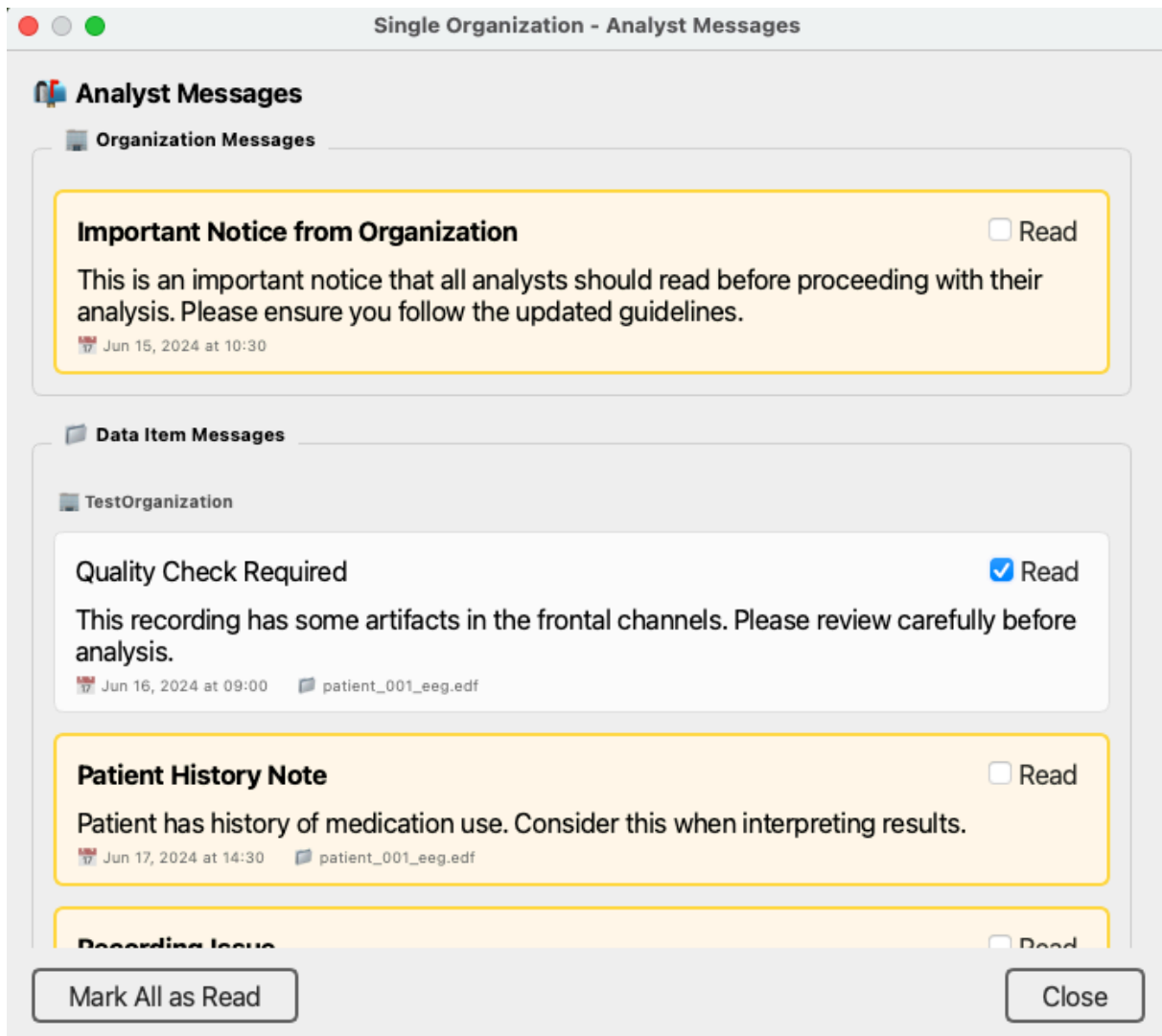


Figure 7: Messages box. It shows a list of messages that are attached to either an organization or a specific data item.

16.2.3 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.

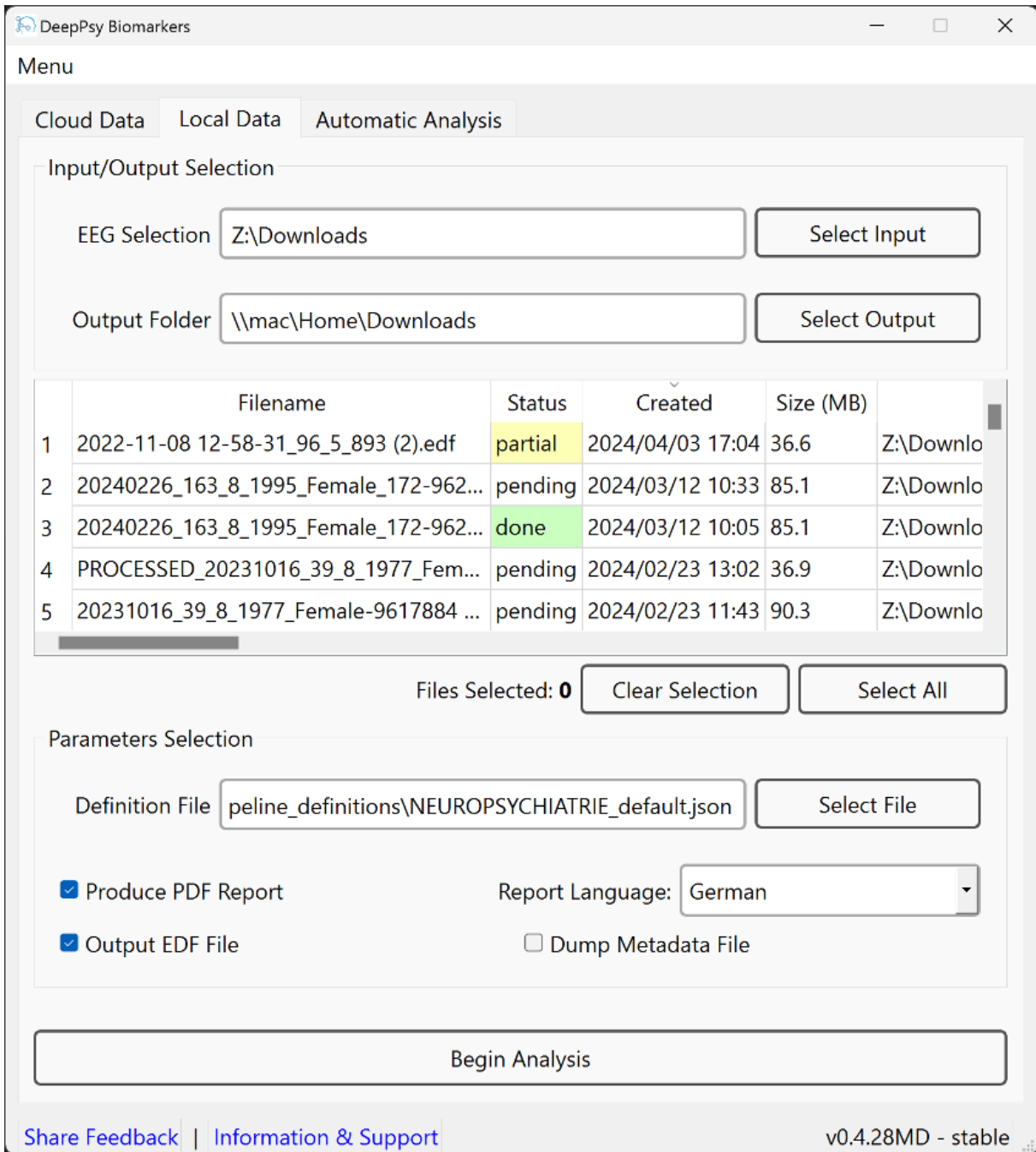


Figure 8: Local data analysis mode. Allows users to analyze data items located in their file system.

16.2.3.1 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 selected 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:/home/user/data_items".

16.2.3.2 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.

16.2.3.3 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.

16.2.4 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.

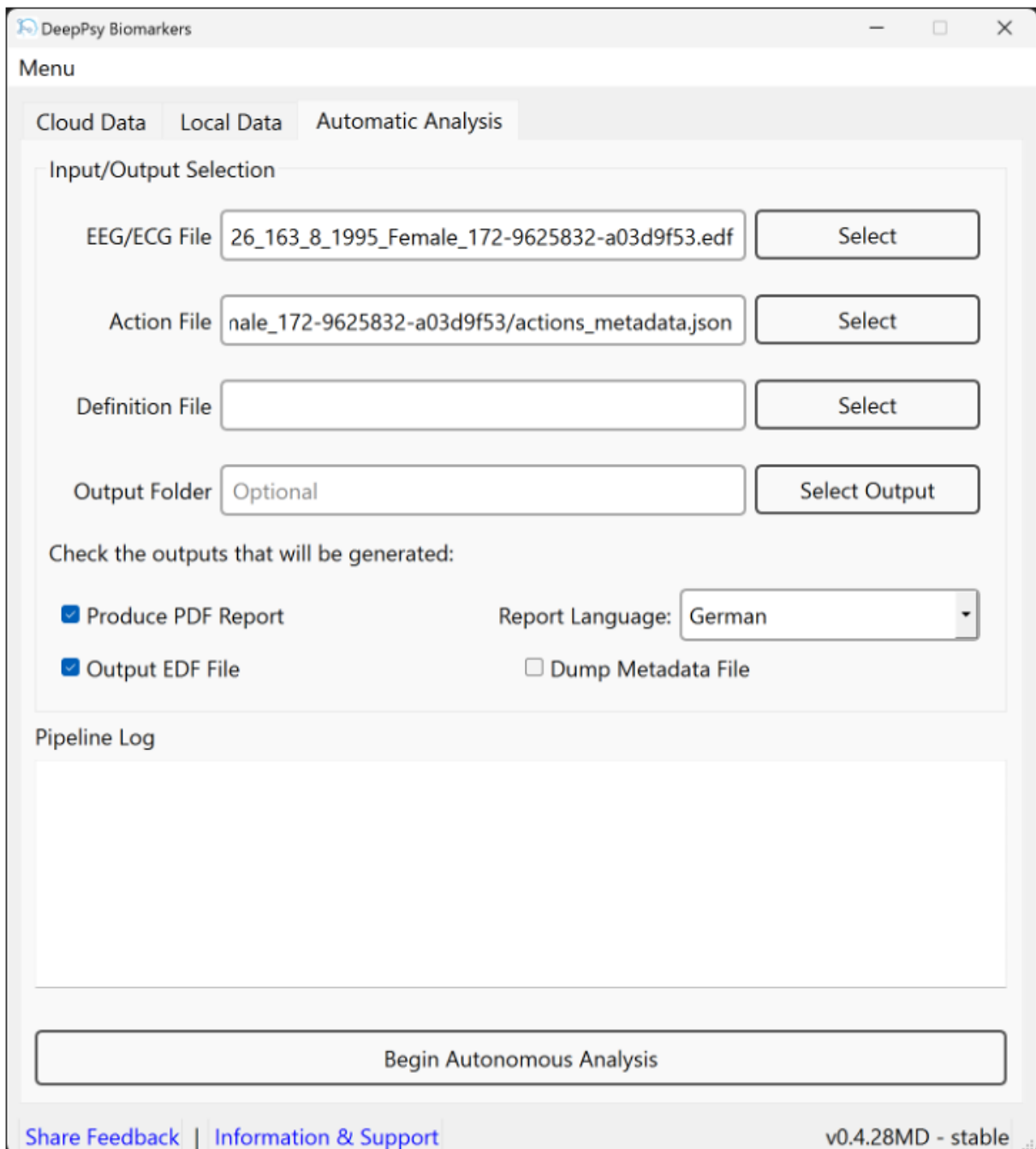
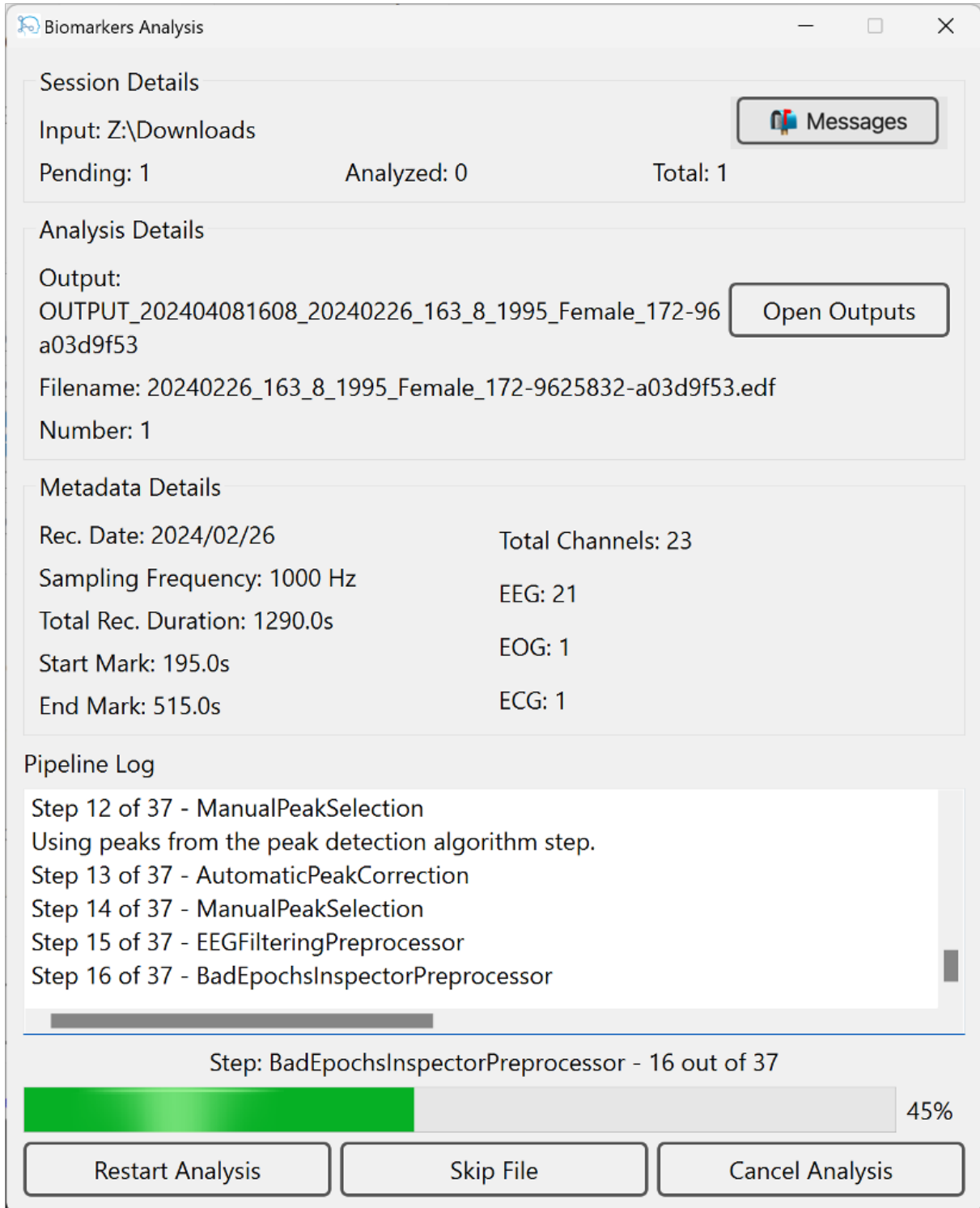


Figure 9: The automatic analysis mode. It's used to reproduce previous analyses without involvement from the user.

16.3 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:



The screenshot shows the 'Biomarkers Analysis' window with the following sections:

- Session Details:**
 - Input: Z:\Downloads
 - Pending: 1, Analyzed: 0, Total: 1
 - Messages button
- Analysis Details:**
 - Output: OUTPUT_202404081608_20240226_163_8_1995_Female_172-96a03d9f53
 - Filename: 20240226_163_8_1995_Female_172-9625832-a03d9f53.edf
 - Number: 1
 - Open Outputs button
- Metadata Details:**

Rec. Date: 2024/02/26	Total Channels: 23
Sampling Frequency: 1000 Hz	EEG: 21
Total Rec. Duration: 1290.0s	EOG: 1
Start Mark: 195.0s	ECG: 1
End Mark: 515.0s	
- Pipeline Log:**
 - Step 12 of 37 - ManualPeakSelection
 - Using peaks from the peak detection algorithm step.
 - Step 13 of 37 - AutomaticPeakCorrection
 - Step 14 of 37 - ManualPeakSelection
 - Step 15 of 37 - EEGFilteringPreprocessor
 - Step 16 of 37 - BadEpochsInspectorPreprocessor
- Progress Bar:**
 - Step: BadEpochsInspectorPreprocessor - 16 out of 37
 - 45% completion
- Control Buttons:**
 - Restart Analysis
 - Skip File
 - Cancel Analysis

Figure 10: 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.

16.3.1 Messages Box

The messages button opens a dialog box with a list of messages that are attached to either an organization or current data item being analyzed. These messages can come from several sources, and they're typically important to analyze a given data item.

If any messages are marked as unread for the current data item, the message box window will automatically open signaling, that there are important messages to read. These messages will continue

Messages must be marked as read otherwise they will continue to open for each new analysis which has this message attached to it. This is particularly important for organization messages.

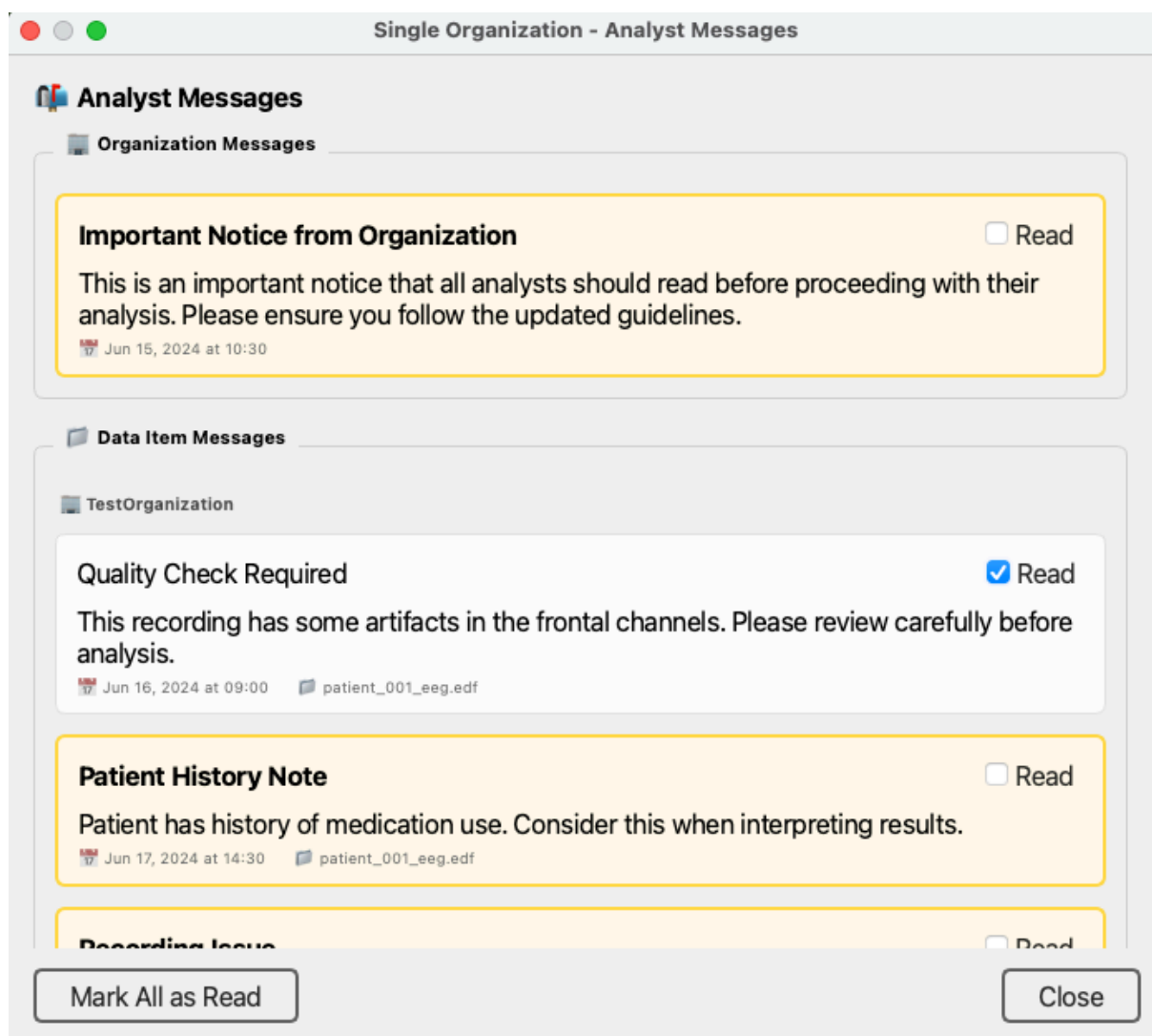


Figure 11: Messages box. It shows a list of messages that are attached to either an organization or a specific data item.

16.4 Analysis Results Dialog

the prepro The user will receive a confirmation dialog at the end of the analysis, where they will have to review the summary information of ccessing 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.

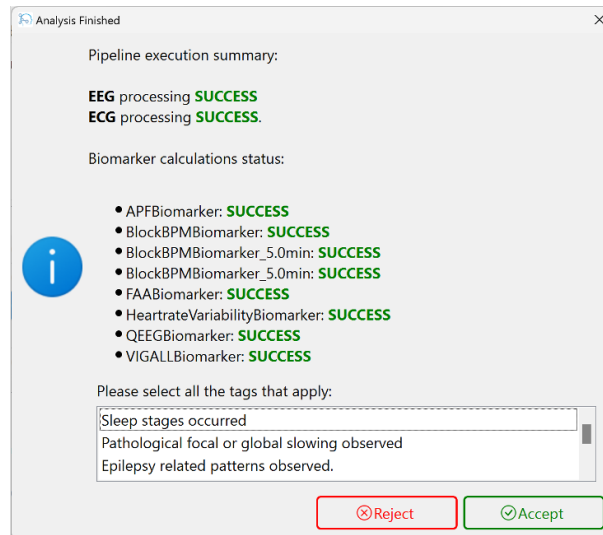


Figure 12: Status dialog showing that all calculation were successful.

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

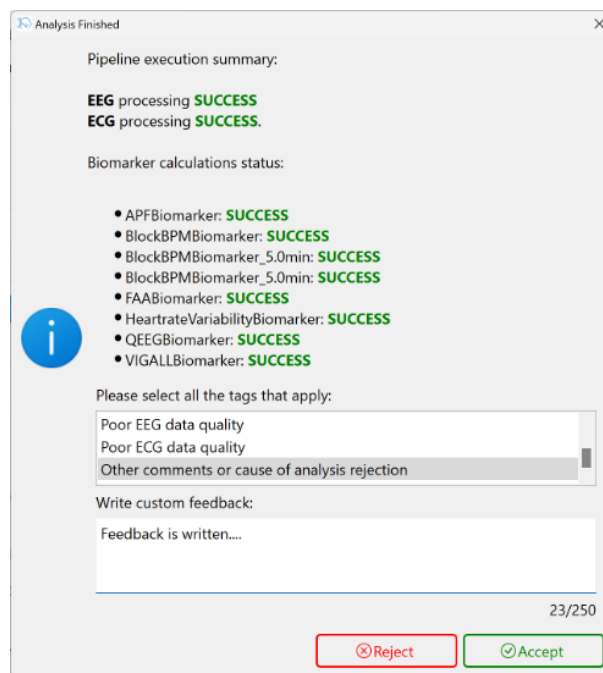


Figure 13: The user can leave feedback regarding the analysis by choosing the correct option in the status dialog.

16.5 Report Verification Dialog

After the end of an analysis, when the report has been produced, the user will be prompted to verify the integrity of the report. They will have the opportunity to open the report in a PDF viewer and verify its contents. If the report is not satisfactory, the user can reject it by clicking the "Reject" button. Additionally, the reject button will prompt for additional feedback to be provided by the user, briefly explaining why the report is being rejected. If the report is accepted, the user can continue to the next data item by clicking the "Accept" button.

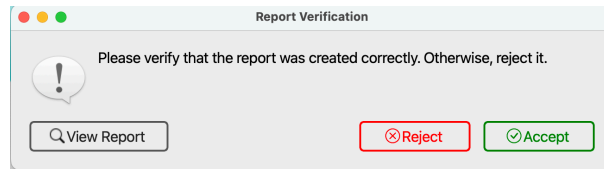


Figure 14: The report verification dialog appears at the end of the analysis, after the report has been produced.

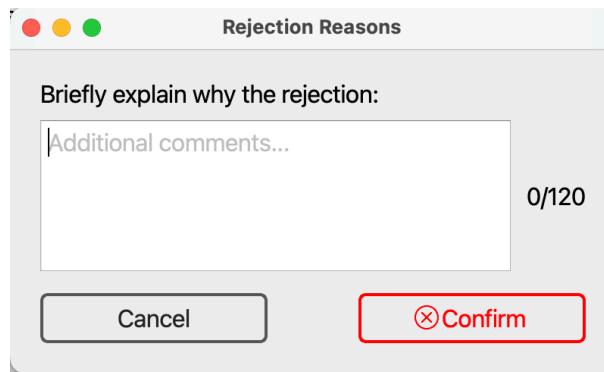


Figure 15: The user can leave feedback regarding the analysis by choosing the correct option in the status dialog.

16.6 Application Menu

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

16.6.1 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.

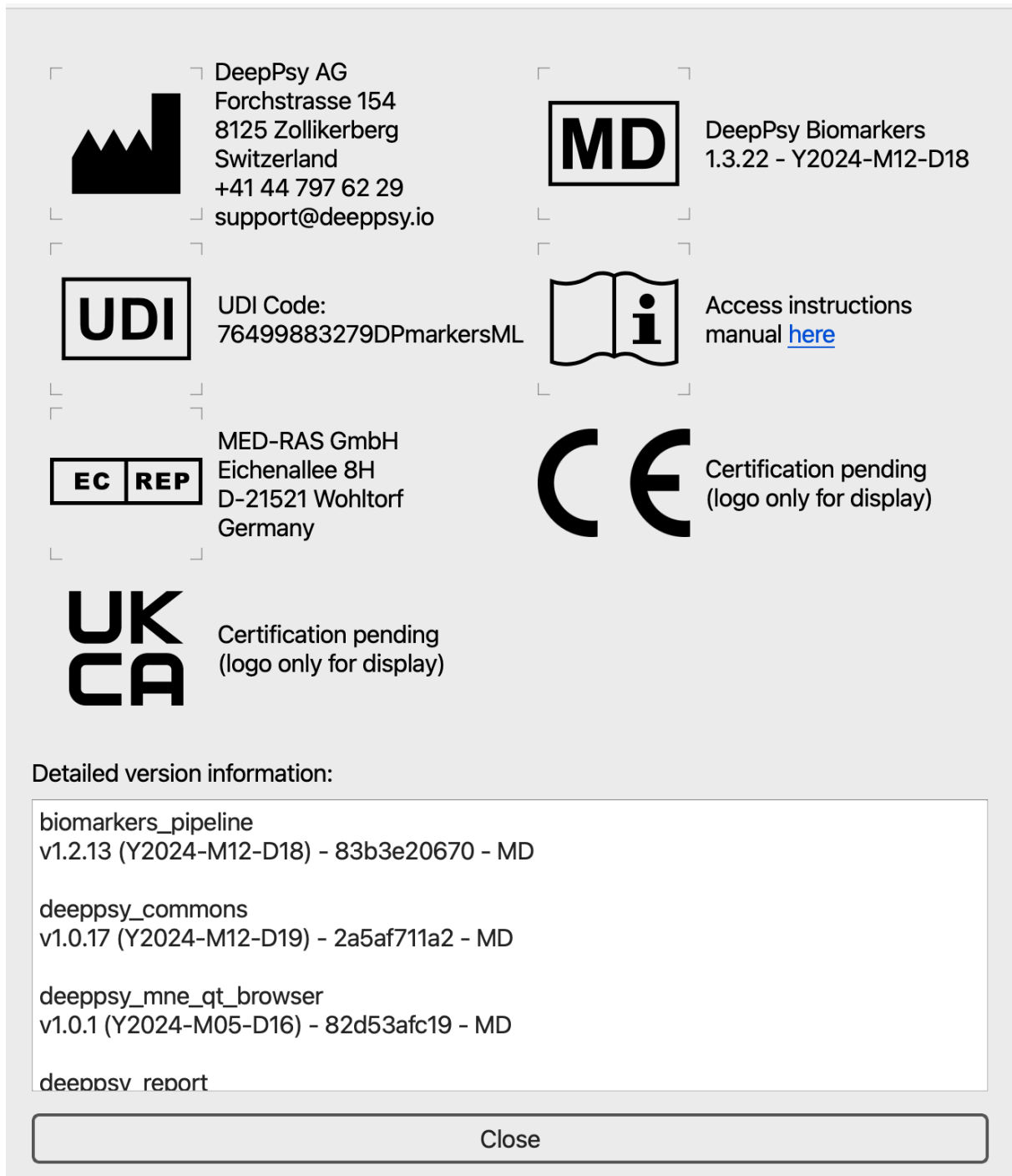


Figure 16: About dialog with important information about the application.

16.6.2 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".

16.6.2.1 General Options

This tab gather two specific configuration options "Parallelism Configuration" and "Timeout Options". The first one is used to configure how many cores to use in tasks that require parallelism, as well as the "backend" used to perform the parallel tasks. The second one is used to configure the timeout for different operations that require uploading data to the cloud server.

The parallelism option has three backends: "loky", "multiprocessing", and "threading". The first one is the default and recommended backend. The second one is a more traditional backend that uses the multiprocessing module. The third one is a backend that uses the threading module.

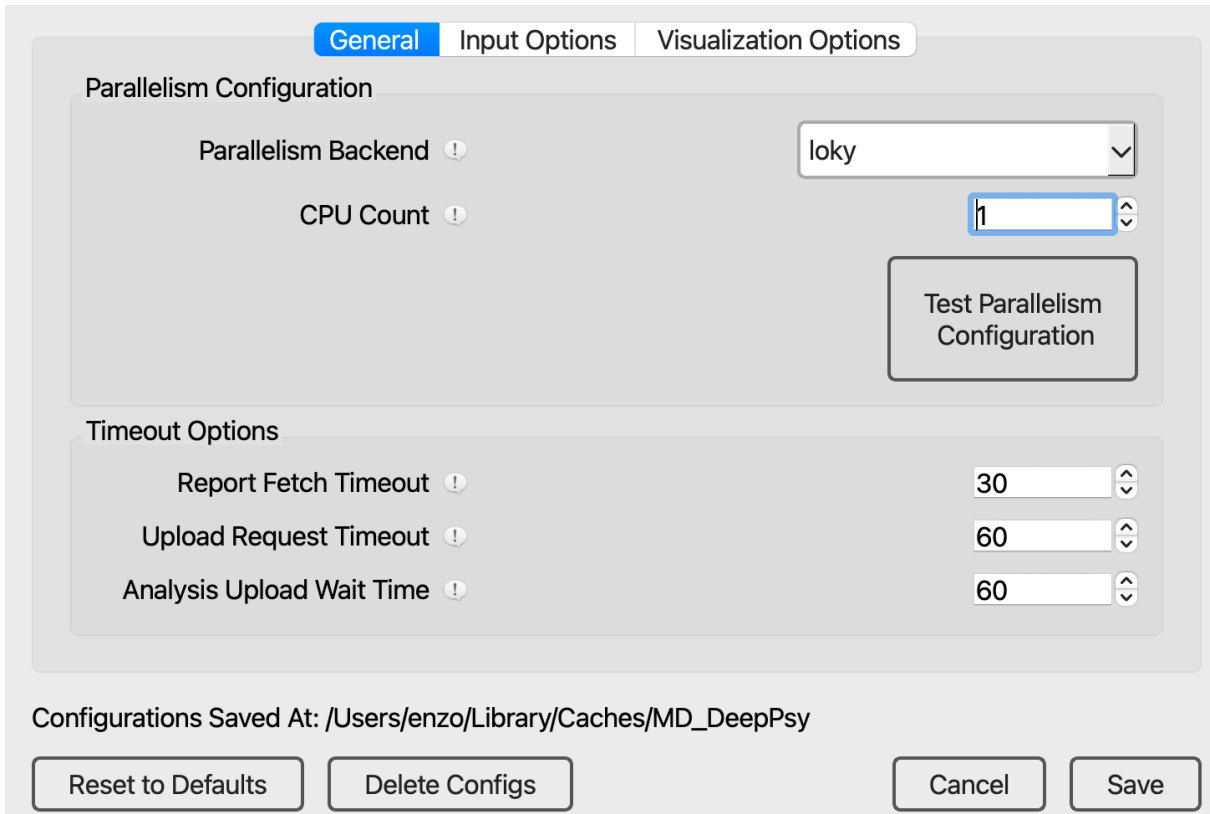
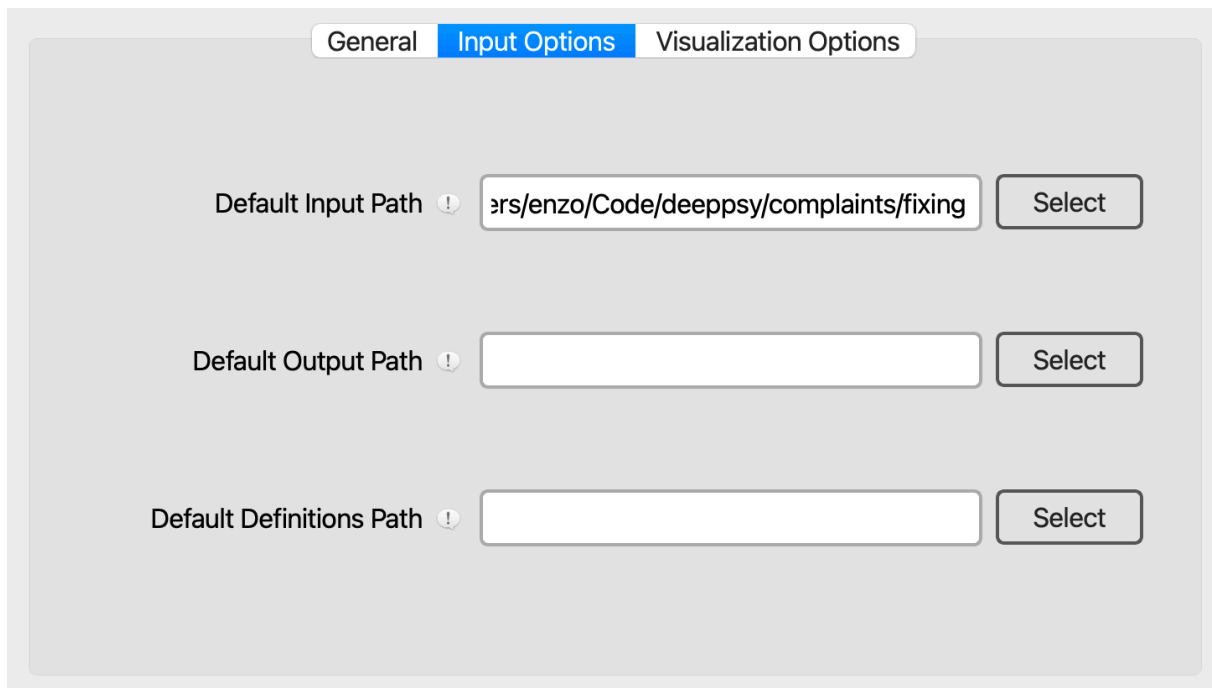


Figure 17: The configuration panel in the "general" tab. This screen contains the parallelism configuration, timeout options, and a group of buttons to administer the configuration options.

16.6.2.2 Input 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.



The screenshot shows a configuration window with three tabs: 'General', 'Input Options' (which is selected and highlighted in blue), and 'Visualization Options'. Below the tabs are three configuration items, each with a label, a text input field, and a 'Select' button. The first item is 'Default Input Path' with a warning icon and a value of 'ers/enzo/Code/deeppsy/complaints/fixing'. The second is 'Default Output Path' with a warning icon and an empty field. The third is 'Default Definitions Path' with a warning icon and an empty field.

Figure 18: Configuration parameters for the selection of the default analysis parameters.

16.6.2.3 Visualization Options

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.

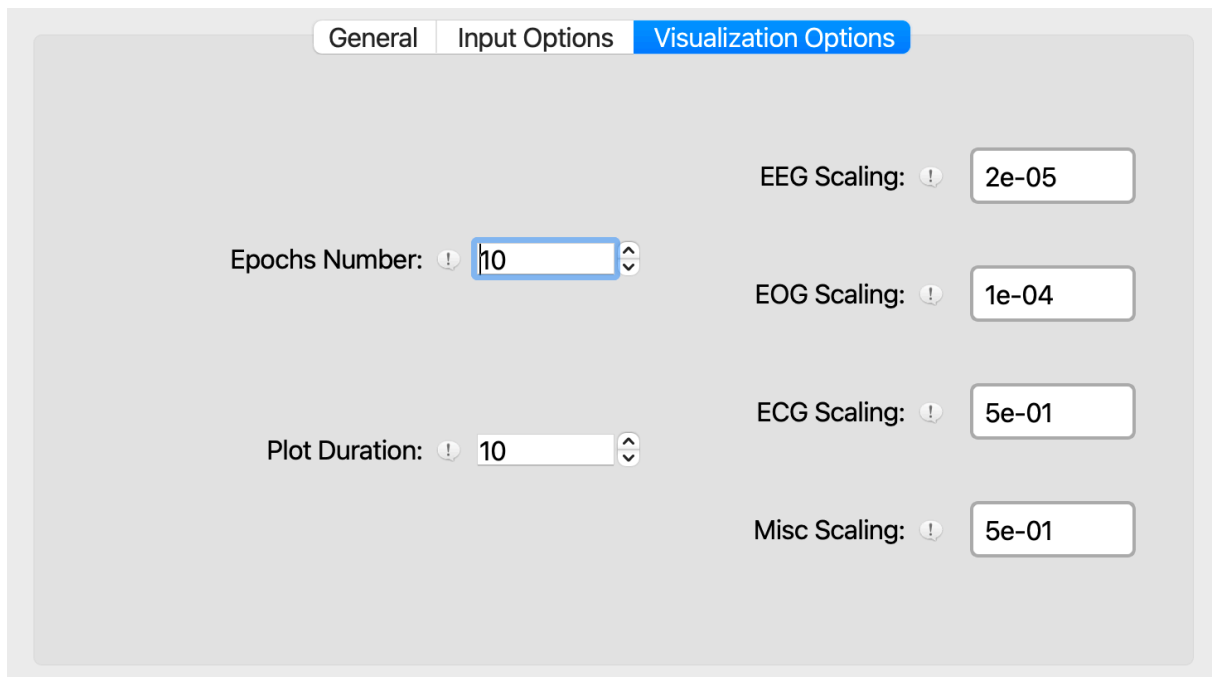


Figure 19: Configuration parameters for the signal browser. These options can be set directly in the signal browser as well.

16.6.3 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.

17 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.

17.1 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.

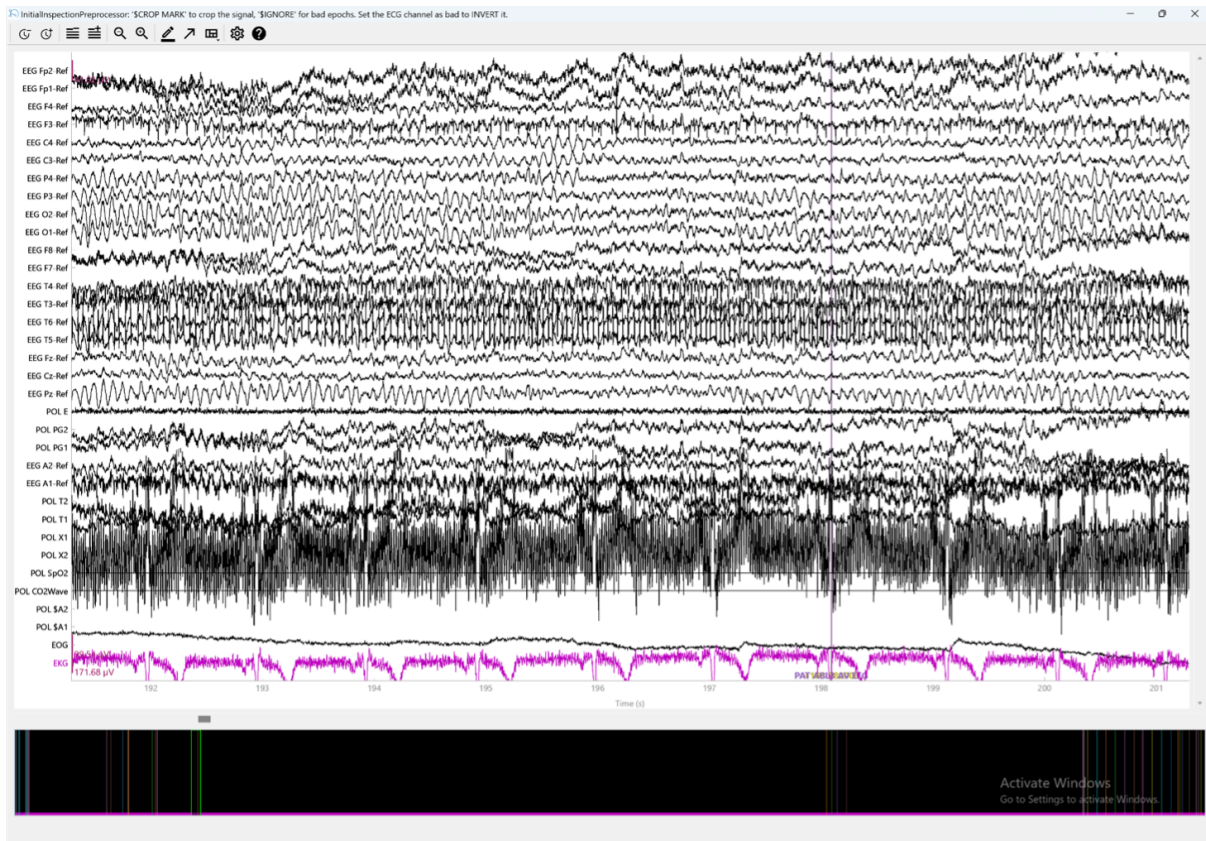


Figure 20: The signal display window used throughout the analysis pipeline.

17.1.1 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.

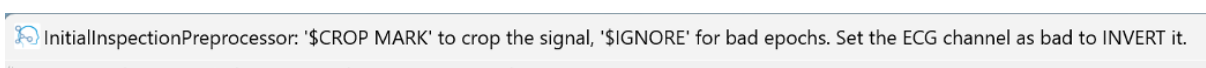


Figure 21: The signal window title bar contains important information about the current step in the analysis and the actions that the user must take.

17.2 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 22: 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.

17.2.1 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.

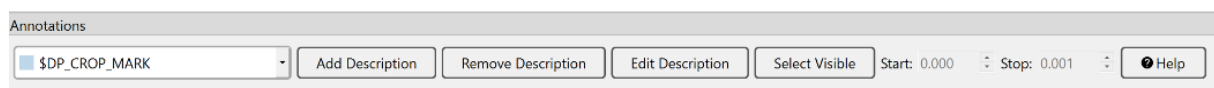


Figure 23: The command section of the signal display window contains a number of action items that the analyst can use to interact with the signals.

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.

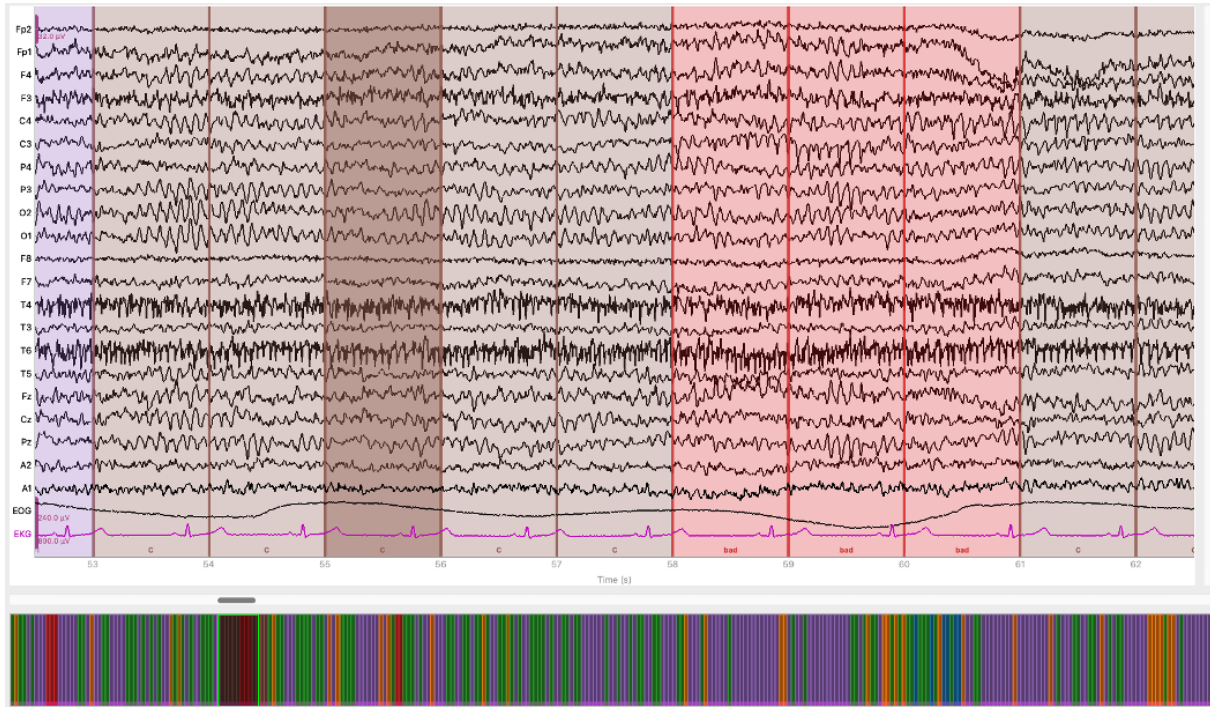


Figure 24: If too many different annotations are present in the signal screen, their colors will repeat across different annotation labels.

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.

17.2.2 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.

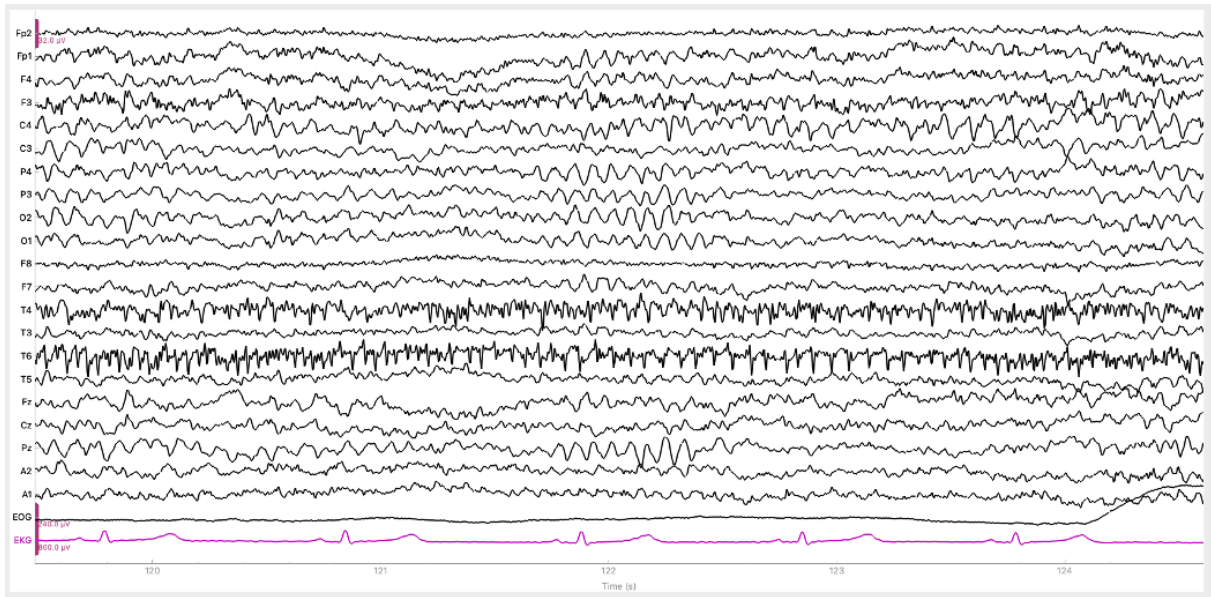


Figure 25: The signal screen displays the signals captured by each of the electrodes of the EEG or ECG recorder.

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.

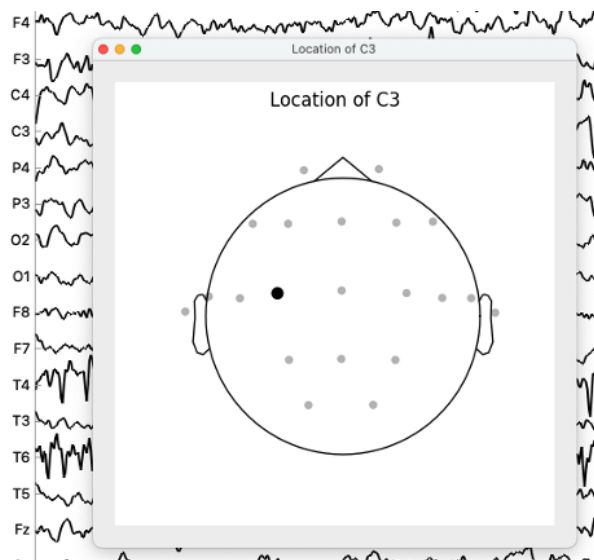


Figure 26: By left-clicking the label of an EEG channel, the user can visualize the electrode position. This is only possible after the "StandardMontageNamesPreprocessor" step has been executed.

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.

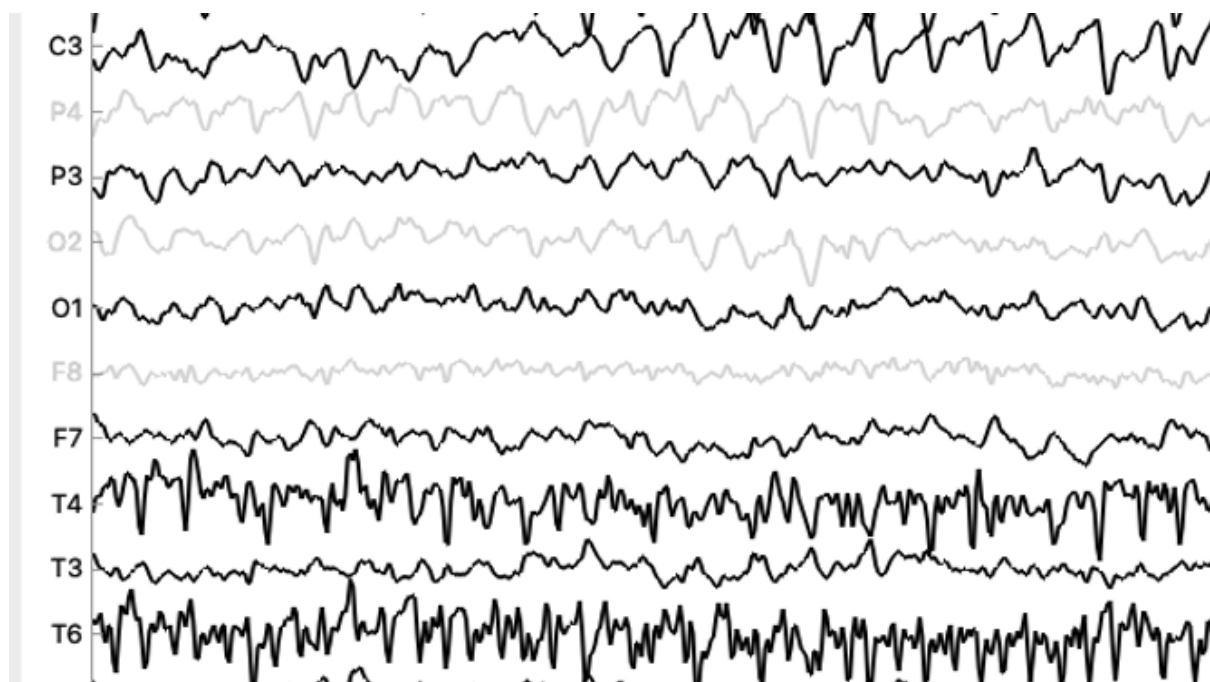


Figure 27: Channels can be selected by clicking either on the channel name or on top of the signal line. Selected channels will be grayed.

17.3 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.

17.3.1 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".

17.3.2 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.

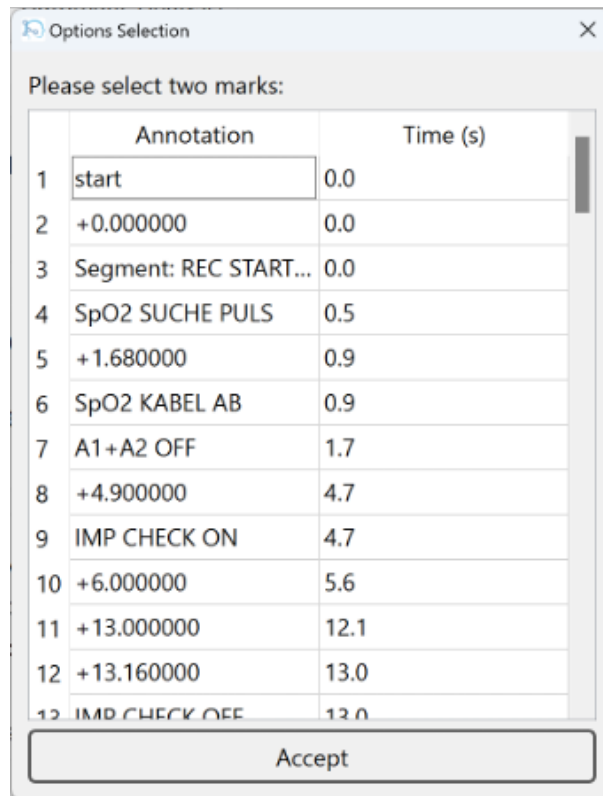


Figure 28: By left-clicking the label of an EEG channel, the user can visualize the electrode position. This is only possible after the "StandardMontageNamesPreprocessor" step has been executed.

17.3.3 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

17.3.3.1 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.

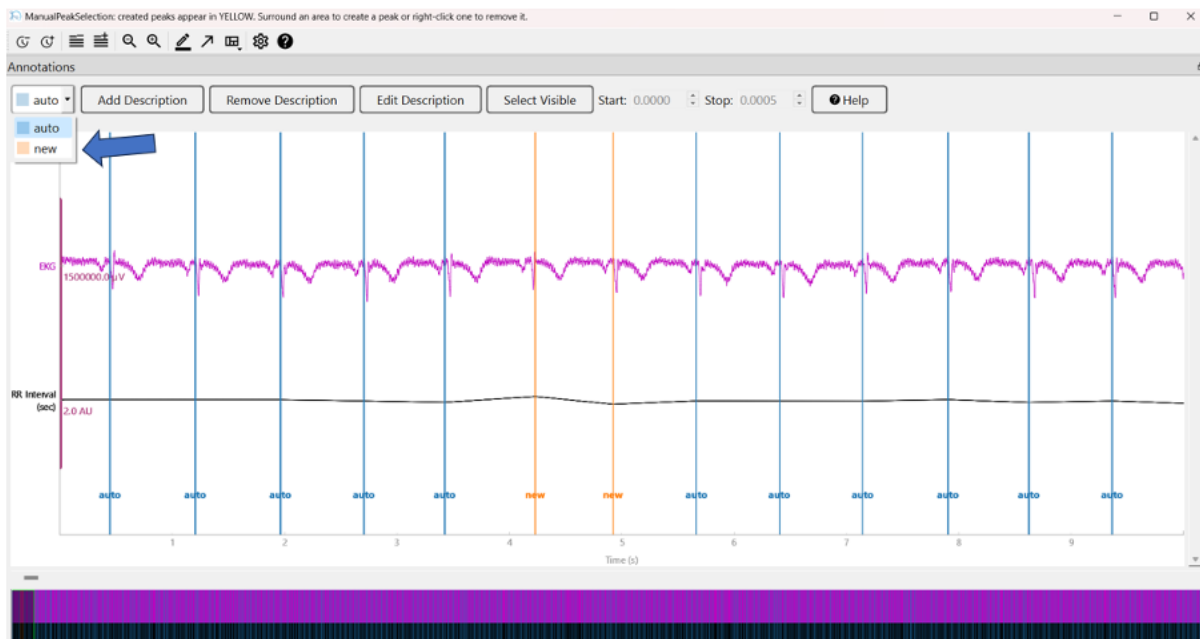


Figure 29: Select the correct annotation to interact with existing or newly created peaks. Notice that this ECG needed to be flipped at the beginning of the analysis, given the negative P and R waves.

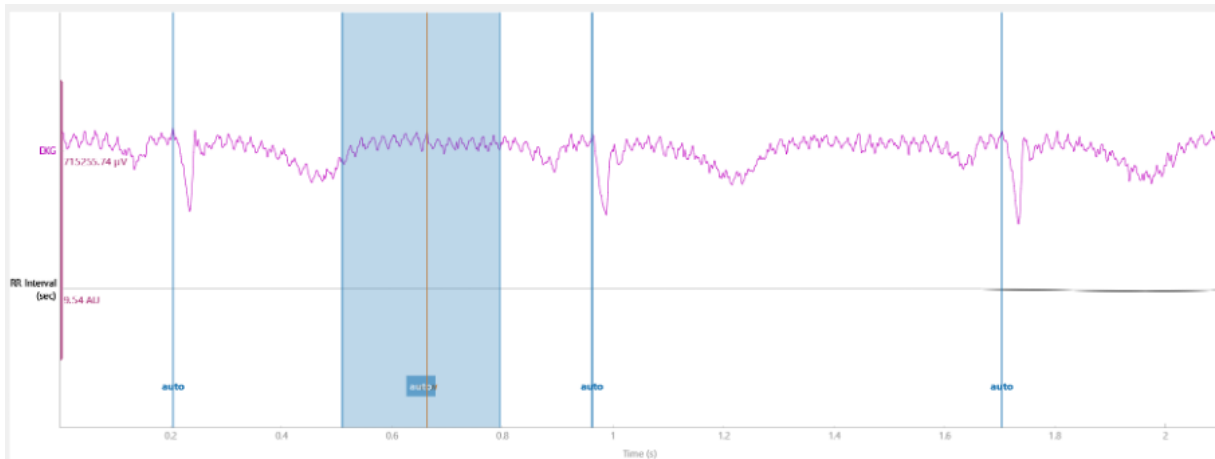
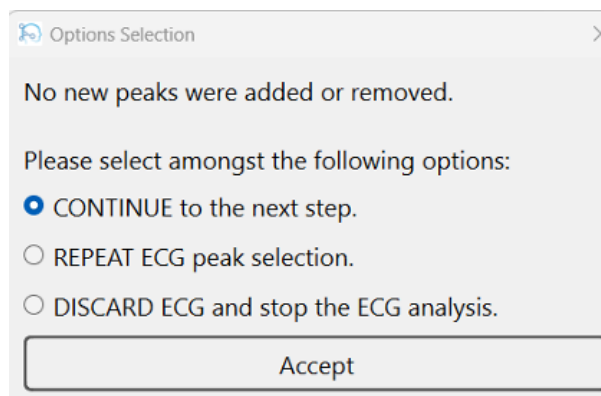


Figure 30: In this example, we can not delete the new peak we added (in orange), since we did not change the settings (the highlighted area is blue instead of orange).

17.3.3.2 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



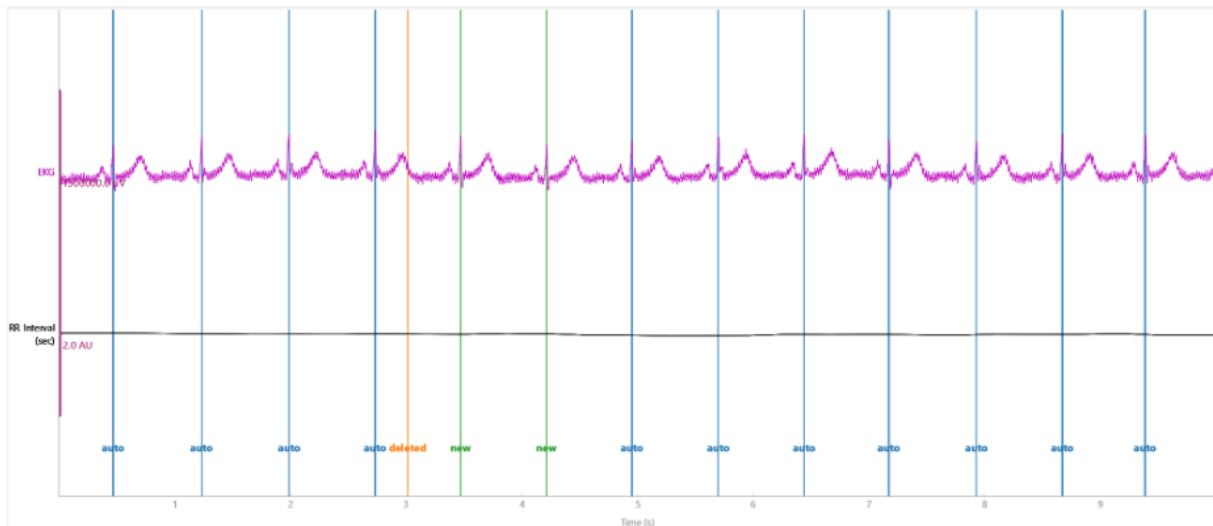


Figure 31: In this example, the algorithm removed the peak at 3s (in orange) to interpolate the peaks at around 3.5s and 4.1s (in green).

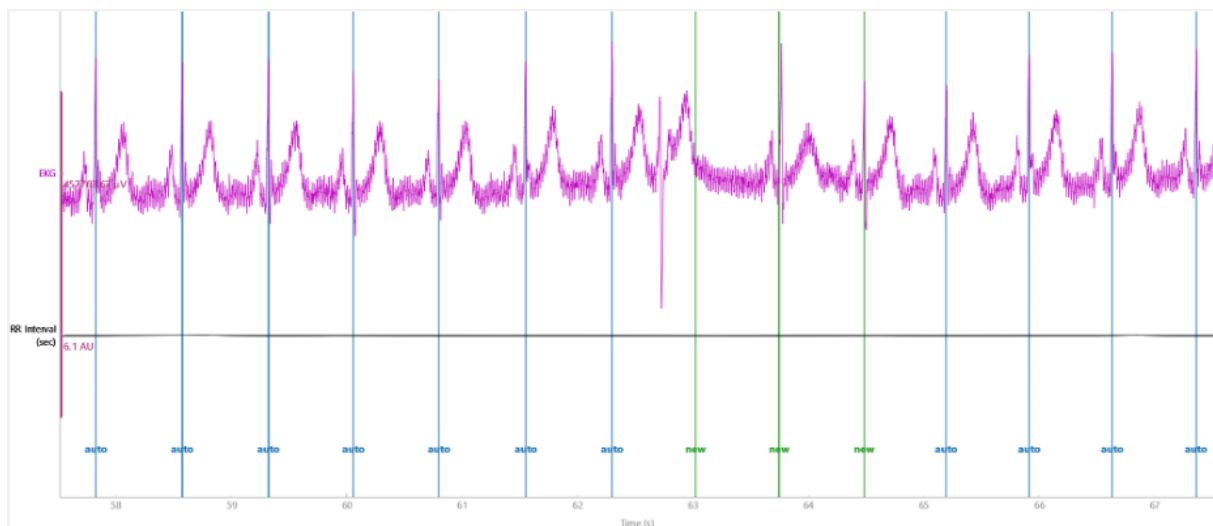


Figure 32: In this example, the algorithm interpolated three new peaks between 62s and 65s.

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.

17.3.4 EEG

17.3.4.1 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.

17.3.4.2 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.

17.3.4.3 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.

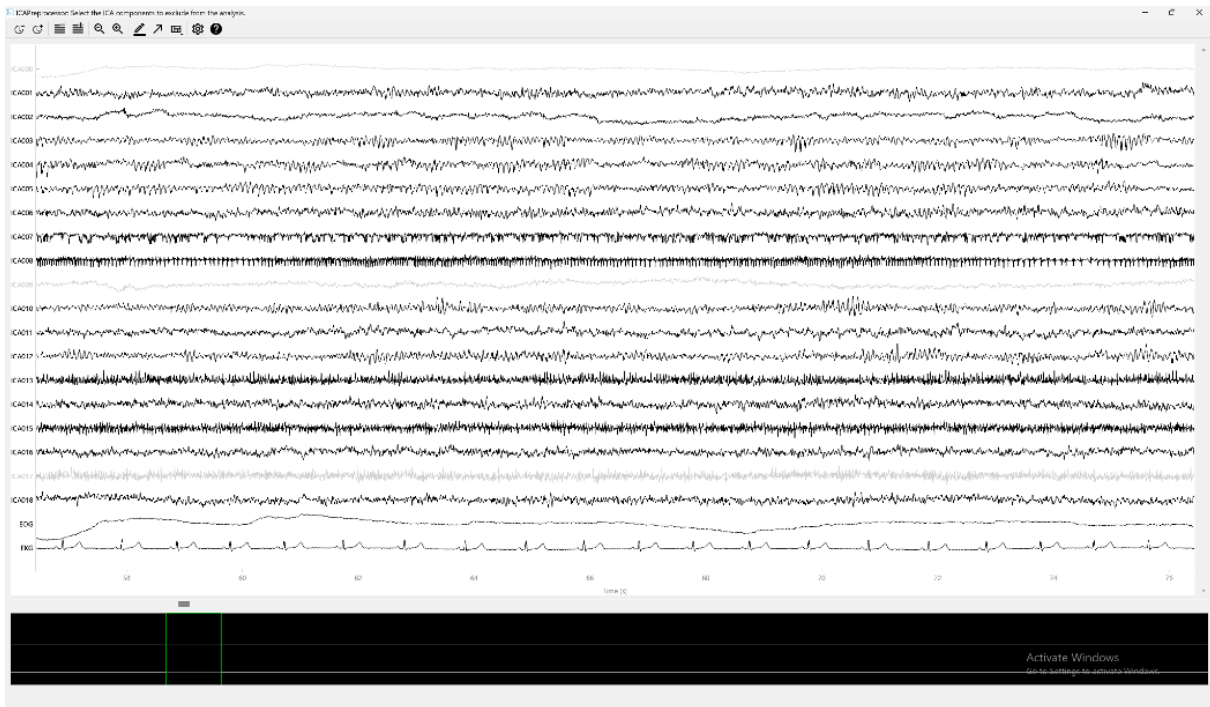


Figure 33: Each component is identified by a signal. Click on the signal or name label to select or deselect the component.

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

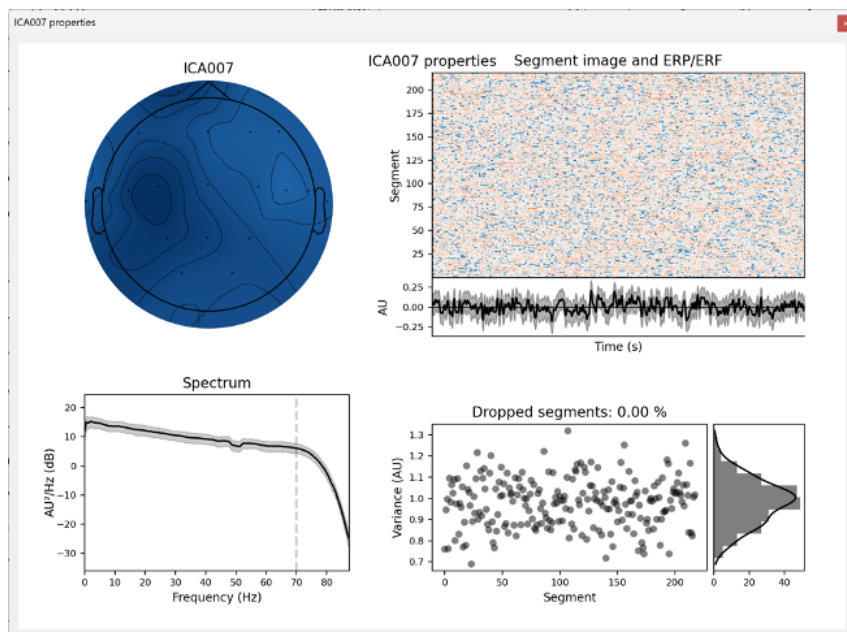


Figure 34: Right-clicking the component label will trigger the display of metadata for the component.

17.3.4.4 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.

17.3.4.5 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.

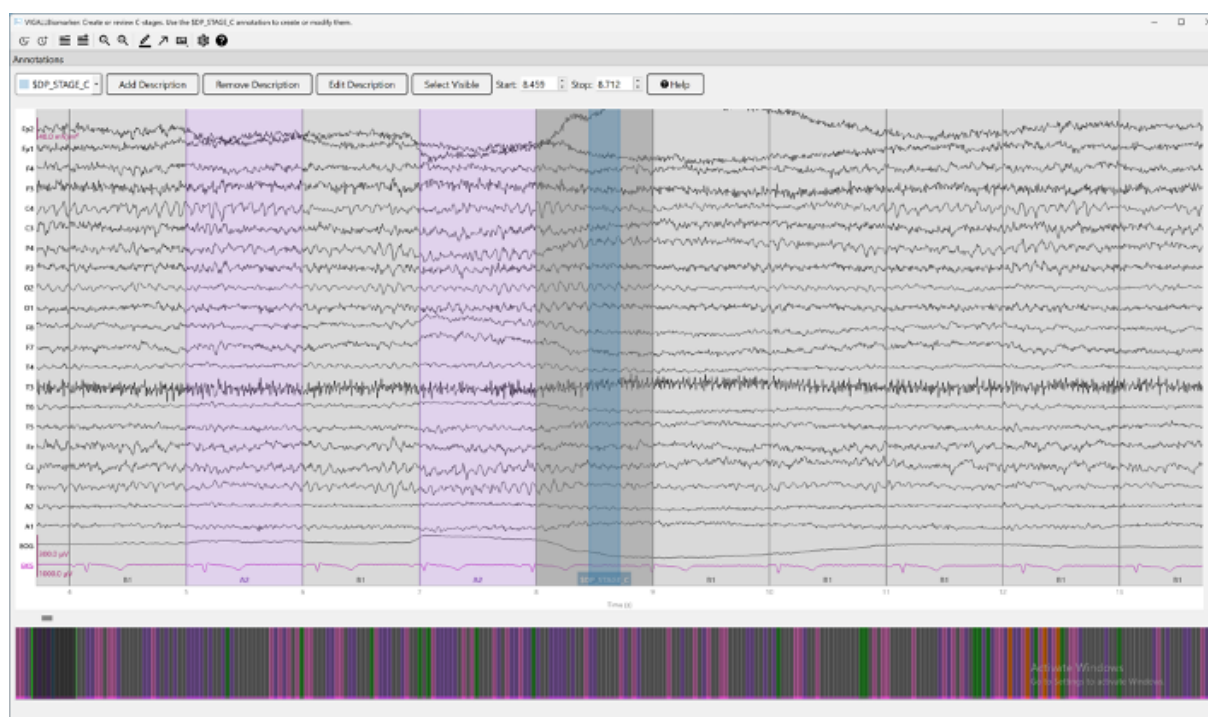


Figure 35: Place the "C stage" annotation in the signal browser to mark the beginning of the C stage.

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.

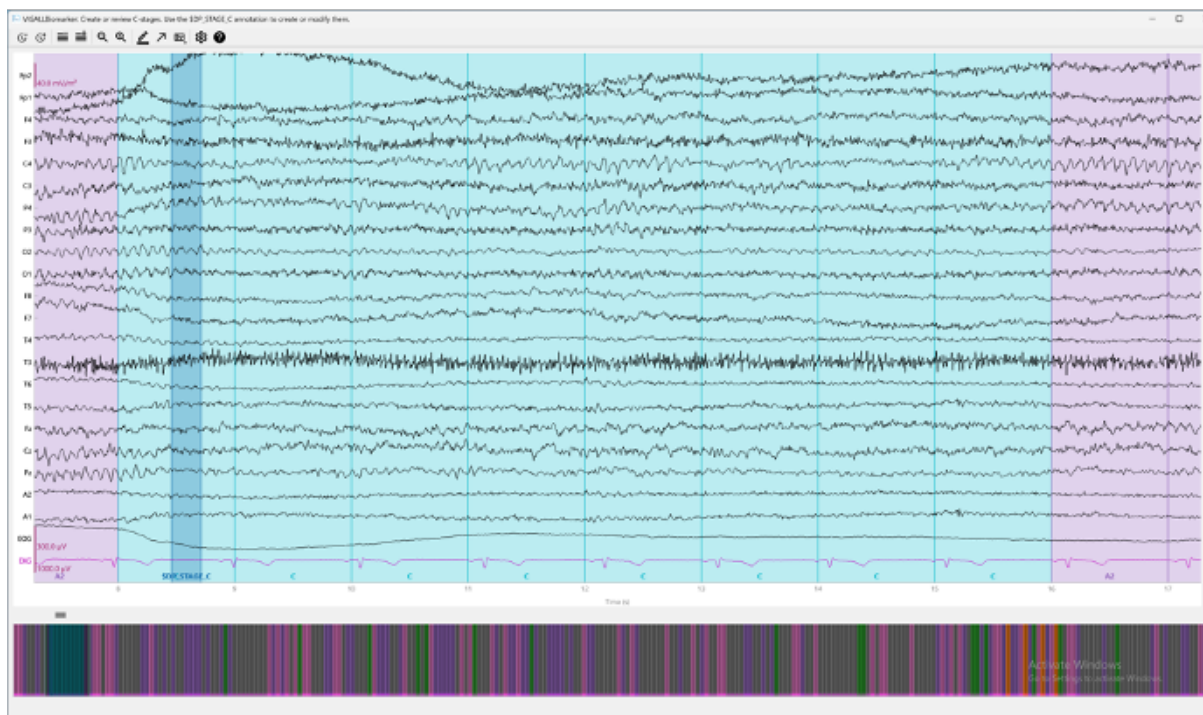


Figure 36: After placing the “C stage” annotation and closing the window, the user is displayed the resulting C stages.

If after viewing the produced C stages the user decides they 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.

18 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:

18.1 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 formats for human electrophysiological data.

18.2 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.

18.3 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 37.

18.3.1 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.

18.3.2 Indications & Contraindications

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

18.3.3 Biomarker Correlations

This sections lists the specific correlations between biomarkers, different conditions, and certified treatment options. This section contains in a more concise form, the same information as in the interpretations section. It's placed here for the convenience of physicians, who typically wish to have a quick overview of the correlations between the patient's physiological profile and the different conditions and treatments.

18.3.4 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.

18.3.4.1 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.

DeepPsy Name: [Redacted] Case ID: [Redacted]
 Patient ID: [Redacted] Report ID: [Redacted]
 Age: 56 Report Date: 19.12.2024
 Sex: Male Recording Date: 05.11.2024

EEG & ECG Biomarkers Report

- This report is intended to be used only by qualified medical practitioners.
- This report is intended to be used to improve decision-making within the scope of possible treatments already indicated for a patient.

- This report is not intended to be used to determine whether a patient should undergo treatment. It is also not intended to be used to determine if a treatment is indicated or contraindicated for a patient.
- This report is not intended for use in cases of neurological pathologies, scalp abnormalities, head injuries (in the EEG), or cardiac pathologies (in the ECG).
- This report is not intended to drive diagnosis, to be used as a vital signs monitor, or to be used in any situation where measured parameters could result in immediate danger to the patient.

Biomarker Correlations Summary

Condition	Treatment	Correlation
MDD	SSRI	Lower response rates than SSRI Vigilance Regulation 2min
	SNRI	Higher response rates than SSRI Vigilance Regulation 2min
	rTMS	10Hz left DLPFC has lower Response Rate than 1Hz right DLPFC Alpha Peak Frequency (APF)
	Ketamine (oral/i.v.)	Decreased response rates for Ketamine Heart Rate (BPM), Vigilance Regulation: A1 Stages
	ECT	Higher response rates for ECT and less side effects Alpha Peak Frequency (APF)

v1.3.22MD For any questions, please contact us at: +41 44 797 62 29 | support@deeppsy.io 1 of 5

DeepPsy Name: [Redacted] Case ID: [Redacted]
 Patient ID: [Redacted] Report ID: [Redacted]
 Age: 56 Report Date: 19.12.2024
 Sex: Male Recording Date: 05.11.2024

v1.3.22MD For any questions, please contact us at: +41 44 797 62 29 | support@deeppsy.io 2 of 5

DeepPsy Name: [Redacted] Case ID: [Redacted]
 Patient ID: [Redacted] Report ID: [Redacted]
 Age: 56 Report Date: 19.12.2024
 Sex: Male Recording Date: 05.11.2024

Biomarker Values

EEG	Value (first 2min)	Normal Interval (2 SD)
Alpha Peak Frequency (APF) [Hz]	9.0	(8.0 - 11.7)
Frontal Alpha Asymmetry (FAA)	0.3612*	(0.3 - 0.3)
qEEG Alpha [μV^2]	27.73	(0.0 - 144.0)
qEEG Beta [μV^2]	3.99	(0.0 - 16.0)
qEEG Delta [μV^2]	12.73	(0.0 - 16.0)
qEEG Gamma1 [μV^2]	1.32	(0.0 - 2.0)
qEEG Gamma2 [μV^2]	0.96*	(0.0 - 0.2)
qEEG Theta [μV^2]	10.33	(0.0 - 32.0)
Slow Basic Rhythm	No	(0.0 - 75.0)
Vigilance Regulation: 0 Stages (%)	0.0	(0.0 - 75.0)
Vigilance Regulation: A1 Stages (%)	12.9	-
Vigilance Level (Level)	4.0	(2.2 - 6.0)
Vigilance Mean (Level)	2.5	(2.24 - 6.0)
Vigilance Regulation 2min (Level/min)	0.0	(-0.5 - 0.4)
ECG		
Heart Rate (BPM) (beats/min)	61.0	(53.0 - 76.0)
Heart Rate Regulation (BPM Slope)	0.0	(-2.91 - 2.73)
Total HRV Power [m^2]	71.0	(0.0 - 8011.0)
Parasympathetic Activity (HF) [m^2]	49.17	(0.0 - 4320.0)
Sympathetic Activity (LF) [m^2]	21.8	(0.0 - 4262.0)
Relative Sympathetic Activity (LFn) (%)	30.7	(7.0 - 96.0)

Analysis Characteristics

- EEG analysis completed successfully. ECG analysis completed successfully.
- All biomarkers were computed successfully.

Recording Date: 05.11.2024
 Sampling Frequency: 1000 Hz
 Total Recording Duration: 1274s (21.2m) Analysis Interval: 60s - 241s (3.0m)
 Number of Channels: 23 Channel Types: EEG(21) EOG(1) ECG(1)
 Bad Channels Interpolated: F7 EOG Channel: EOG (POL PG1 - POL PG2)
 Number of Epochs: 132 Epochs with Artefacts: 49 (37.1%)
 ECG Peaks: 122 Peaks Corrected: None

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DeepPsy Name: [Redacted] Case ID: [Redacted]
 Patient ID: [Redacted] Report ID: [Redacted]
 Age: 56 Report Date: 19.12.2024
 Sex: Male Recording Date: 05.11.2024

Interpretations

EEG

- Alpha Peak Frequency (APF) [2, 3, 5, 19, 26]** In this EEG, a low Alpha Peak Frequency was found. In this case, for depressive symptoms, a 1Hz TMS protocols over the DLPFC may be more effective than 10Hz protocols over the left DLPFC. There is also a positive correlation with the response to Sertraline. ECT therapy shows particularly good response with low APF. In the case of ADHD, there is evidence suggesting that biofeedback methods might be more effective than Methylphenidate. (Evidence Level 2)
- Basic Rhythm Slow [1]** In this, a EEG normal Basic Rhythm Peak Frequency was found. No signs of generalized slowing of the basic EEG rhythm in this case. (Evidence Level 2)
- Percentage of vigilance stage A1 [11]** In this EEG, a low occurrence of vigilance stage A1 was found. In this case, low percentages of EEG-vigilance stage A1 are associated with a lower probability to respond to i.v. ketamine and oral ketamine. (Evidence Level 2)
- Vigilance Regulation 2min [12, 18, 20]** In this EEG increase or no initial decrease was found of vigilance during the first 2 minutes. For this case, literature shows lower response rates in depression to SSRIs and SNRIs can be more effective. (Evidence Level 2)

ECG

- Heart Rate (BPM) [14]** In this ECG, a low heart rate was observed. In this case correlation with less likely response to ketamine (i.v.) in depression. (Evidence Level 2)
- Heart Rate Regulation (BPM Slope) [18]** In this ECG, a decrease or no substantial increase in BPM was observed. In this case in depression, there is a correlation with lower response rates for venlafaxine (SNRI). SSRIs can be more effective. (Evidence Level 2)
- Sum of Parasympathetic and Sympathetic Activity [14]** In this ECG, low overall activity of the autonomic nervous system is observed. In this case, correlation with increased likelihood of response to intravenous ketamine in depression. (Evidence Level 2)
- Absolute parasympathetic Activation [15]** In this ECG, low absolute parasympathetic activation was observed. In this case correlation with an higher likely response to SSRI, CBT or combination in obsessive compulsive disorder. (Evidence Level 2)
- Absolute Sympathetic Activation [21]** In this ECG, normal absolute sympathetic activation is observed. In this case compared to the average population, total sympathetic activity is normal.
- Relative Sympathetic/Parasympathetic Activation [7]** In this ECG, a shift toward parasympathetic activity was observed. In this case no correlation with good response to Fluoxetine in generalized anxiety disorder. (Evidence Level 2)

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Figure 37: 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.

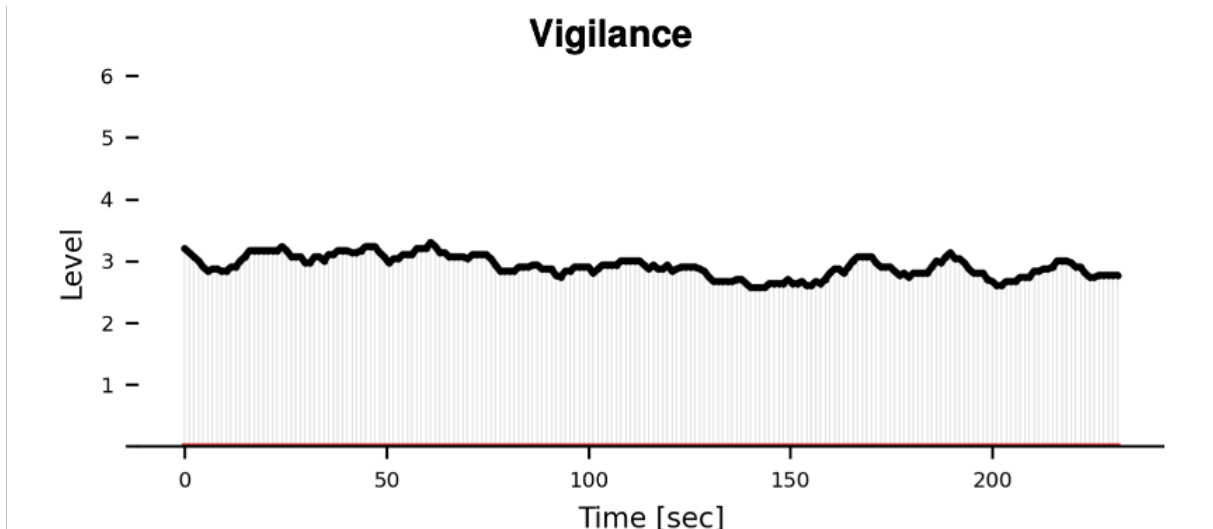


Figure 38: Vigilance of the subject throughout the EEG data item recording.

18.3.4.2 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 39: Slope of the patient's vigilance progression over the first two minutes of the signal.

18.3.4.3 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).

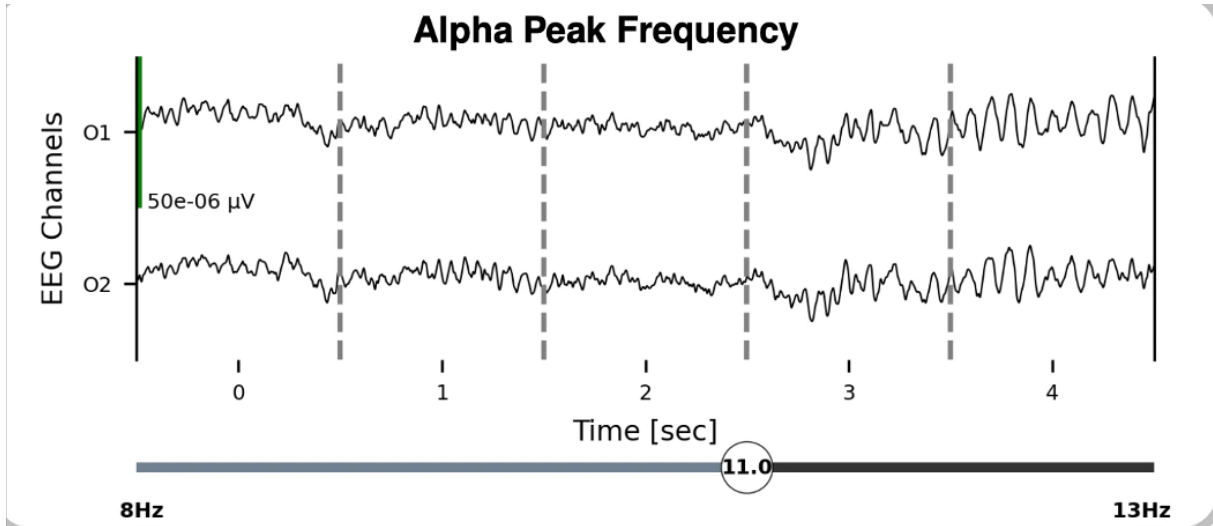


Figure 40: Alpha peak frequency plot.

18.3.4.4 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.

Frontal Alpha Asymmetry

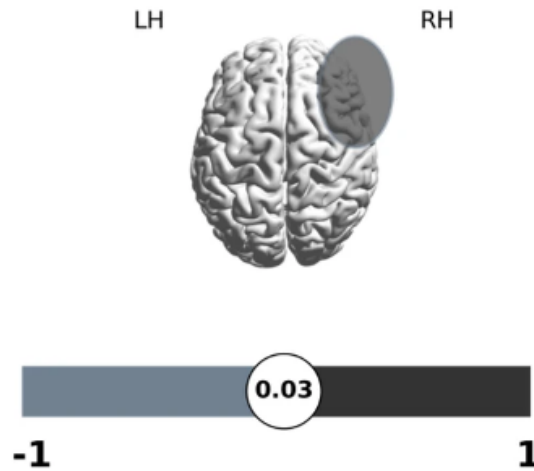


Figure 41: Frontal alpha asymmetry of the subject. It can be either left, right, or balanced.

18.3.4.5 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.

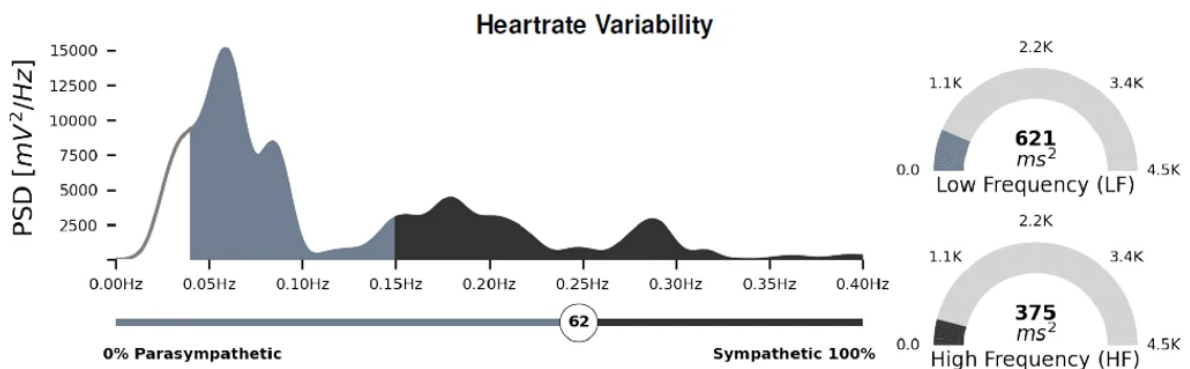


Figure 42: This plot contains several measures of the patient's heartrate variability.

18.3.4.6 Mean Beats Per Minute

Mean Beat Per Minute for the first 2 min recording.

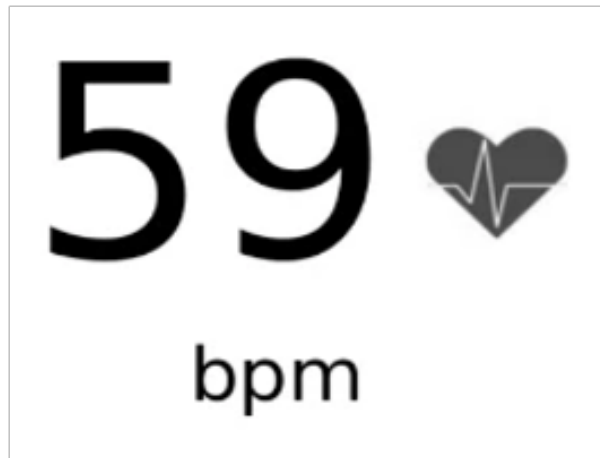


Figure 43: The mean beats per minute for the first two minutes of the ECG signal.

18.3.4.7 Heartrate Histogram

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

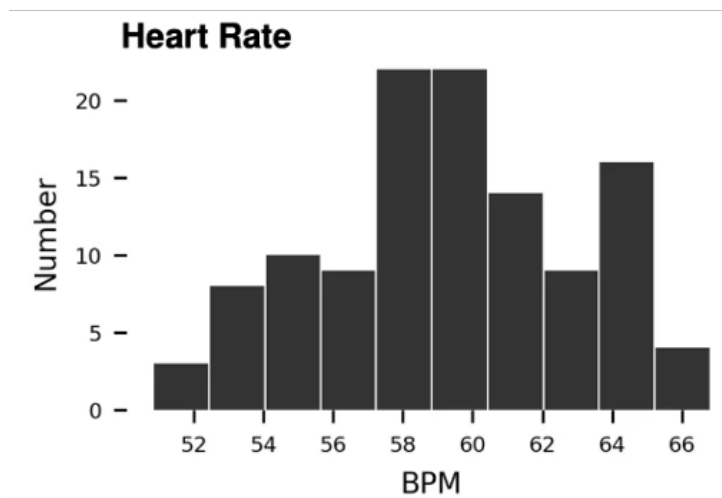


Figure 44: The histogram of the beats per minute for the analyzed ECG signal.

18.3.4.8 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 negative slope indicates a decrease in ANS-arousal.

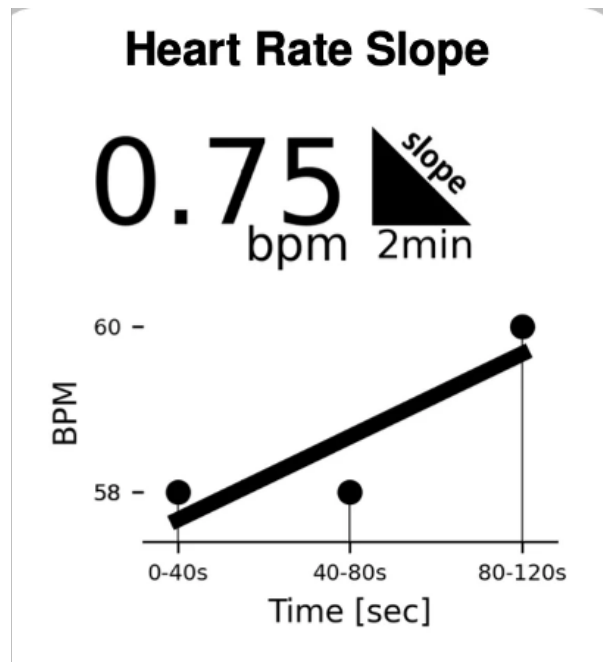


Figure 45: Slope of the heart rate over the first two minutes.

18.3.5 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.

18.3.6 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.
- **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.

18.3.7 Biomarker Interpretations

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.

18.3.8 References

The literature references used to produce the observations in the report. These are provided in the report in case the physician wishes to delve deeper into the literature supporting the findings we included.

18.4 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.

19 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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