Supplementary Materials

ScoreREM: A user friendly Matlab-GUI for rapid eye movement (REM) sleep microstructure (Phasic/Tonic) annotation and quantification

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This document summarises all functions of the ScoreREM application in detail using a sleep recording file from a public database in PhysioNet called the Haaglanden Medisch Centrum sleep staging database. This will facilitate the user to use the example to explore and understand ScoreREM's interface and capabilities.

Software configuration: MATLAB 2023b with Signal Processing Toolbox; Python 3.11.6 with the packages: 'numpy' 'pandas' 'pytz' 'mne' 'yasa' installed. Please refer to the installation support documentation in the repository for help with ScoreREM installation:
https://github.com/KiranKGR/ScoreREMGUI/tree/main/installation_support

Files used:

EDF:https://physionet.org/content/hmc-sleep-staging/1.1/recordings/SN001.edf

All files in this documentation referred to as EDF refers to this recording.

Hypnogram:https://physionet.org/content/hmc-sleep-staging/1.1/recordings/SN001_sleepscoring.edf

All files in this documentation referred to as hypnogram refers to this file.

Scenarios discussed:

Three of many scenarios are discussed below,

1. Scoring without a hypnogram.
2. Scoring given a hypnogram file.
3. Scoring given a marker file.

At each step where applicable detailed information on all available options is provided. ScoreREM is installed as a MATLAB app and is opened before proceeding further. Once opened the user will be provided a licence documentation followed by the python installation checks. The automated hypnogram generation and automated REM event scoring discussed below is applicable only if a compatible python installation is available and is identified by ScoreREM with error.

Scenario 1 : Scoring without a hypnogram.

Sleep recording EDF file is available with no hypnogram (i.e., sleep staging).

1. Step 1: Load the EDF file into ScoreREM. Click on ⬇ and choose the SN001.edf file and Click Open. (See Figure S1)
    a. The application gets the information on the sleep recording and checks for errors in the EDF file. If no error is found the application moves to the next step.
2. Step 2: The user can select the set of channels to be displayed based on the available channels (shown in Figure S2 A and B). In this example, SN001.edf contains only 4 EEG channels as seen in the figure.
    a. The application requires at least one EOG, one EEG and one EMG channel to proceed further. In case of only one EOG channel available the user has to assign the same EOG channel to both LOC and ROC.

3. Step 3: Once the channels are chosen, the user inputs the availability of hypnogram or marker file. In this example, the user chooses **'EDF Only'** option (see Figure S2 C).

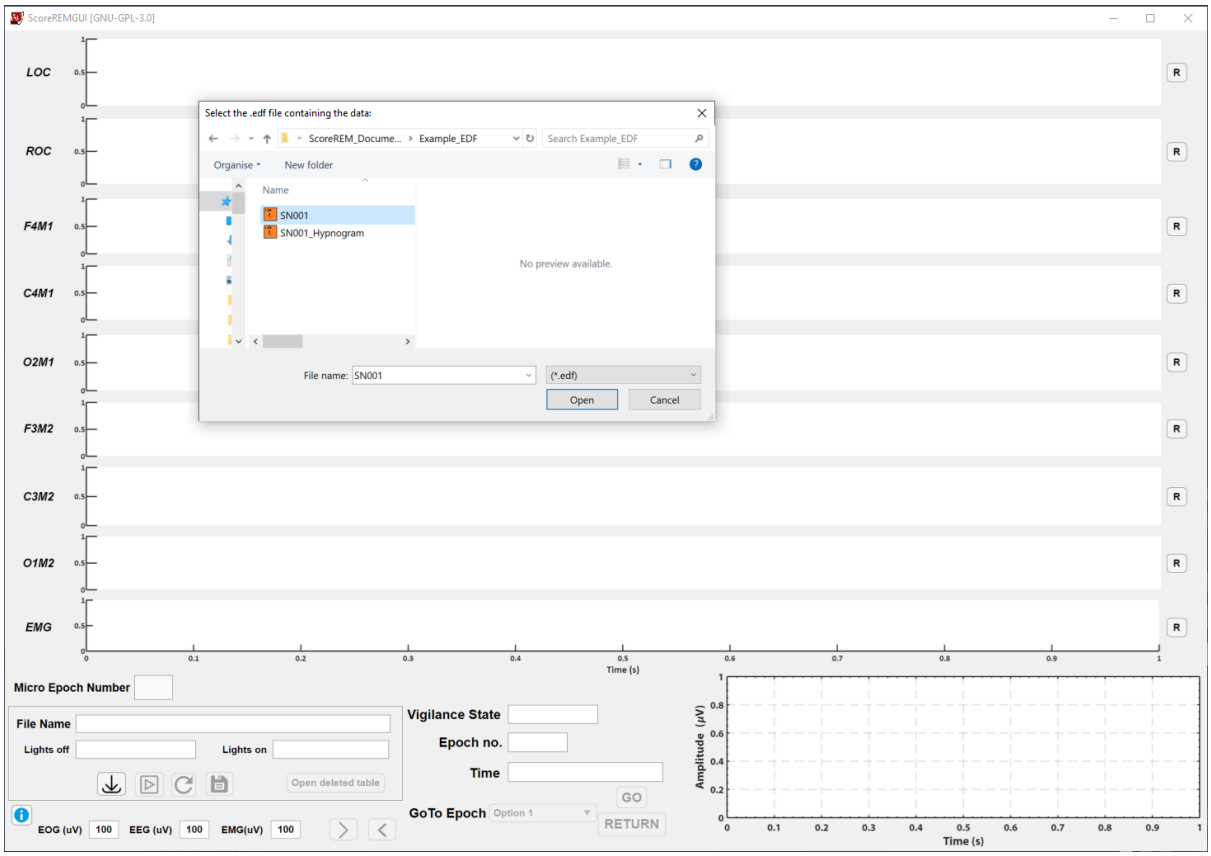


Figure S1. Load the EDF into ScoreREM. SN001.edf file is loaded as an example.

4. Step 4: With the 'EDF Only' option, if the python language interface and the required packages are found to be installed, the user is provided with the option to choose the channels to be input to the 'SleepStaging' function of the YASA package (see Figure S2 D and E).
    a. The application requires at least one EOG and one EEG channel to be selected for automatic sleep staging.
5. Step 5: At this stage, the automatic hypnogram is generated and used for segmenting and displaying the data down the application pipeline. The hypnogram is also saved in .xlsx format and .txt format (hypnogram format used by ScoreREM) in the EDF file path (See Figure S2 F). The format of the data exported allows for the hypnogram to be loaded into other programs (eg. EDFBrowser) (See Figure S2 G).
6. Step 6: At this stage, user initiates the data import, segmentation and preprocessing routines by clicking ▶ button,
    a. ScoreREM requests the choice of the micro epoch length in seconds as shown in Figure S3 A. The imported epoch-wise data is segmented based on this choice and sets the annotation resolution. The user can select either 1, 2 or 3 seconds micro epoch lengths.
    b. Next, the filter setting window is provided to the user, ScoreREM automatically detects the sampling rate of the EOG, EEG and EMG

channels and sets the range of the filter settings. ScoreREM uses a Butterworth second order filter via the filtfilt function to achieve zero lag filtering. The user is also provided with 50Hz or 60Hz power line interference removal option. The second order band stop filter is set between the frequency of interest (eg.: 50Hz) ±1Hz. (See Figure S3 B)

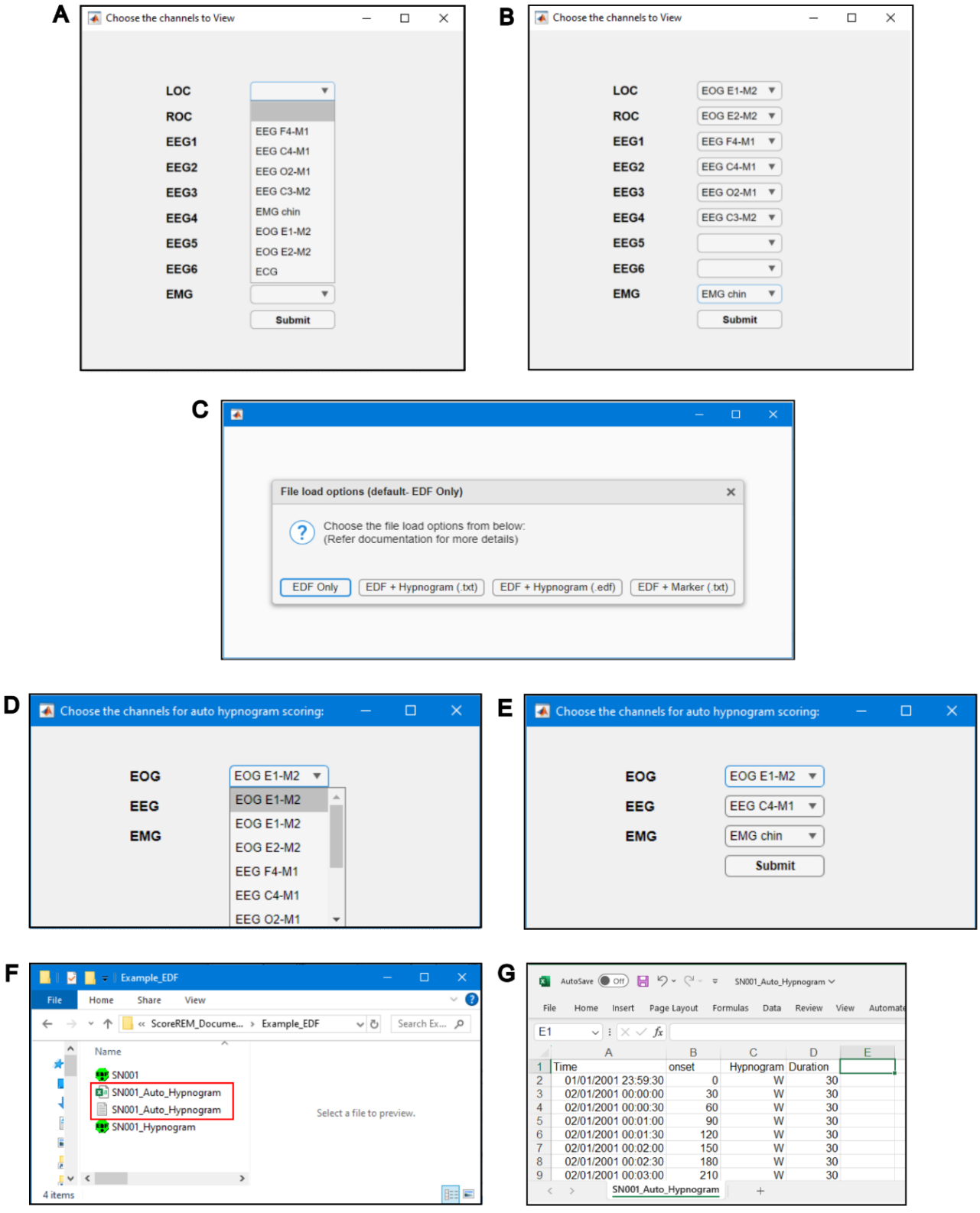


Figure S2. ScoreREM flow options based on loaded EDF file (SN001.edf).

c. Once the segmentation and filtering operations are performed, the user is presented with the option to choose Automatic scoring of Phasic/Tonic REM micro epochs (See Figure S3 C). If the user selects Yes, the ScoreREM uses the YASA 'rem_detect' function to get the REM events and add the labels into the annotation data of the app.

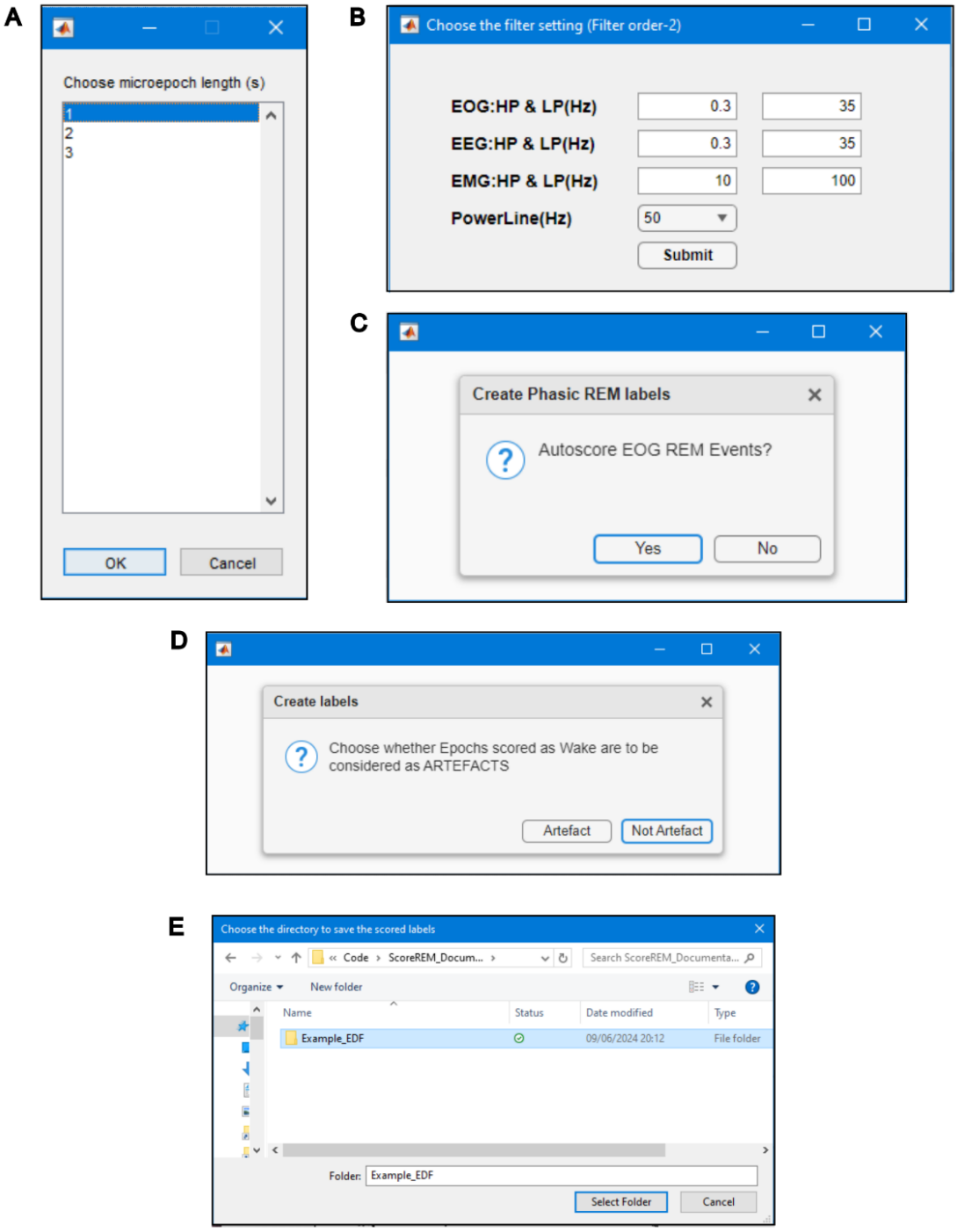


Figure S3. Data import and preprocessing options in ScoreREM.

d. The user can also choose to score all Wake epochs as Artefact or not Artefact. This affects the epoch-wise EEG spectrogram of the entire EDF exported in the final save (See Figure S3 D). If the user chooses yes, all wake epochs are marked as Artefact, and removed from the exported

spectrograms. It should be noted that any micro epoch marked as Artefact is removed when epoch-wise power spectrum is computed.

e. Finally, the user chooses the export folder (default name: *'ScoreREMdatafiles'*) location. The temporary autosave file of the annotations and the final export files are saved into this folder (See Figure S3 E).

7. Step 7: The user can now move between epochs in the recording or between REM epochs and annotate the labels. The user can also jump to a specific epoch to review or annotate and jump back to epoch of origin as shown in Figure S5 A. Keyboard shortcuts are used to perform these tasks.

Description of the keyboard navigation keys:
Keyboard controls:

- Press **Right** and **Left arrows** (or '**B**' and '**C**') to move between epochs.
- To move only between REM epochs, Press '**L**' and '**J**'
- To start micro epoch wise scoring Press '**I**' (enable) and '**K**' (disable)

[Unscored EOG looks Blue and if it is scored as Artefact looks Red]

[With micro epoch enabled by pressing '**I**' and micro epoch number not = 0]

- Press '**A**' and '**F**' to move between the micro epochs.

[Current micro epoch is highlighted between red dotted lines]
For Scoring the current micro epoch,

- Press '**Q**' and '**W**' to score LOC and ROC as ARTEFACT (Red))
- Press '**E**' to score Phasic REM (Orange) and
- Press '**R**' for Tonic REM (Purple))

[To change the prescored micro epoch label Press the key twice]
[Single key press of a prescored micro epoch clears the label (micro epoch looks Blue)]

8. Step 8: An example scoring is provided in Figure S4 A and B. Figure S4 A shows an REM epoch with a tonic micro epoch mis-scored as Phasic by the AutoREM scoring. The user first presses '**I**' to enable micro epoch-wise scoring. Then uses '**A**' and '**F**' to move between the micro epochs and move to the third micro epoch segment. The user then presses '**R**' twice to re-score the segment as Tonic (Purple) (Figure S4 B). Single press of '**R**' clears the auto scored Phasic label and then the second press relabels the micro epoch.
    a. The user can verify the scored label in the micro epoch label table shown in Figure S4 B.
9. Step 9: Once all the REM epochs are inspected and corrected, the user can export the labels by pressing  button. This action exports the scored labels and summary data to the *'ScoreREMdatafiles'* folder (See Figure S5 B and C). An example folder can be found in the ScoreREM repository (link: https://github.com/KiranKGR/ScoreREMGUI/tree/main/examplefiles/ScoreREMdatafiles).
10. Step 10: To resume the annotation process from a previous scored epoch location. The user can load the *'…scoredREMlabels….mat'* file to import the saved labels (See Figure S5 C).

Scenario 2: Scoring given a hypnogram file.

Sleep recording EDF file is available with a hypnogram (i.e., sleep staging) file (EDF or text file). Steps 1 and 2 are same as Scenario 1

1. Step 3: Once the channels are chosen, the user inputs the availability of hypnogram or marker file. In this scenario, the user chooses either '**EDF + Hypnogram (.txt)**' or '**EDF + Hypnogram (.edf)**' depending on the type of hypnogram available (see Figure S2 C).
    a. EDF + Hypnogram (.txt) - The hypnogram template for this case be found in the 'examplefiles' folder in the repository (https://github.com/KiranKGR/ScoreREMGUI/tree/main/examplefiles).
    b. EDF + Hypnogram (.edf) - The hypnogram is contained as an annotation in the EDF file uploaded.

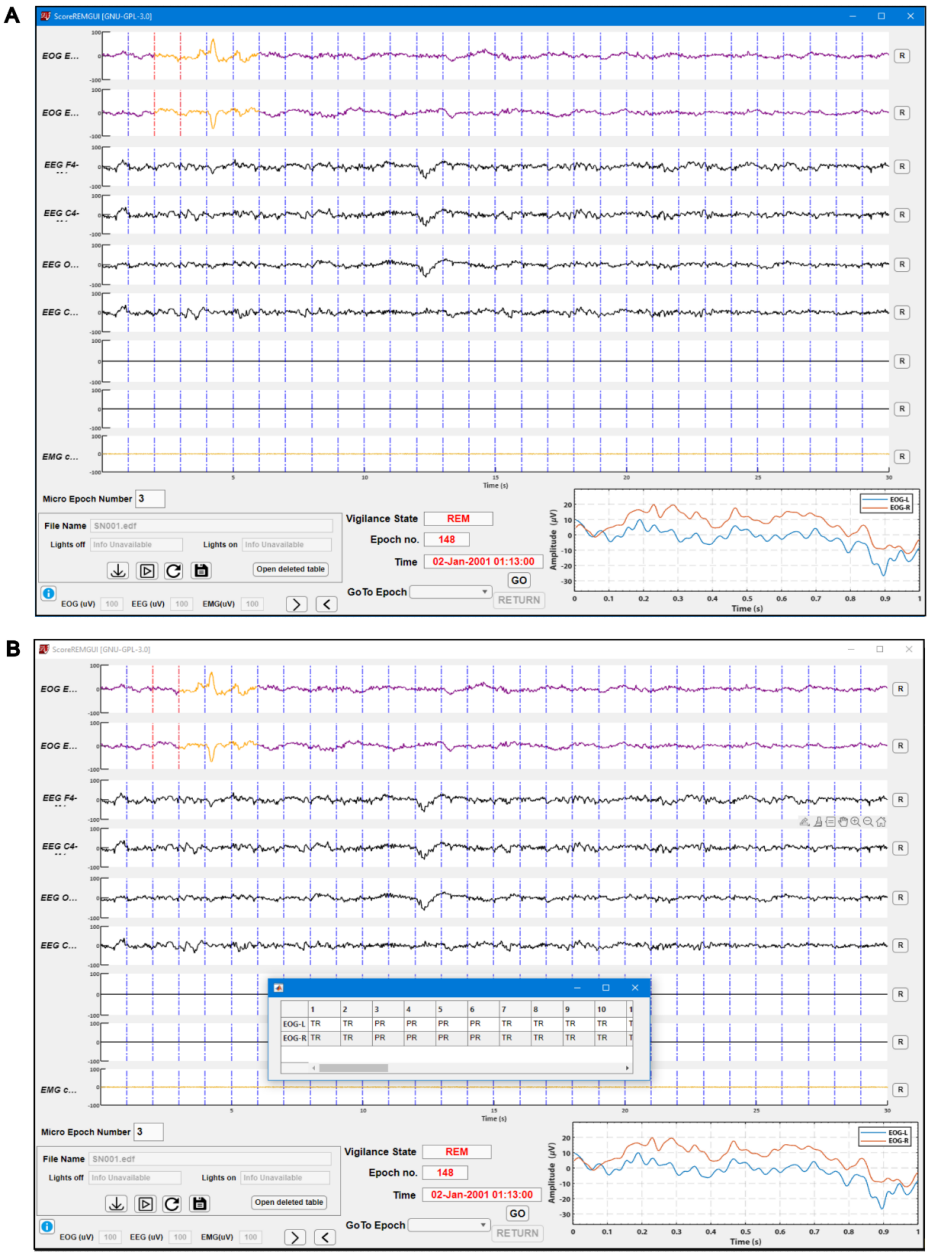


Figure S4. Micro epoch annotation (Artefact/Phasic/Tonic) in ScoreREM.

2. Step 4: For this example, in the SN001.edf file, the hypnogram is available as a .edf file and the option ‘EDF + Hypnogram (.edf)’ is chosen (Figure S3).
3. Step 5: Once the hypnogram is chosen. The user proceeds as given in Steps 6 to 10 of Scenario 1.

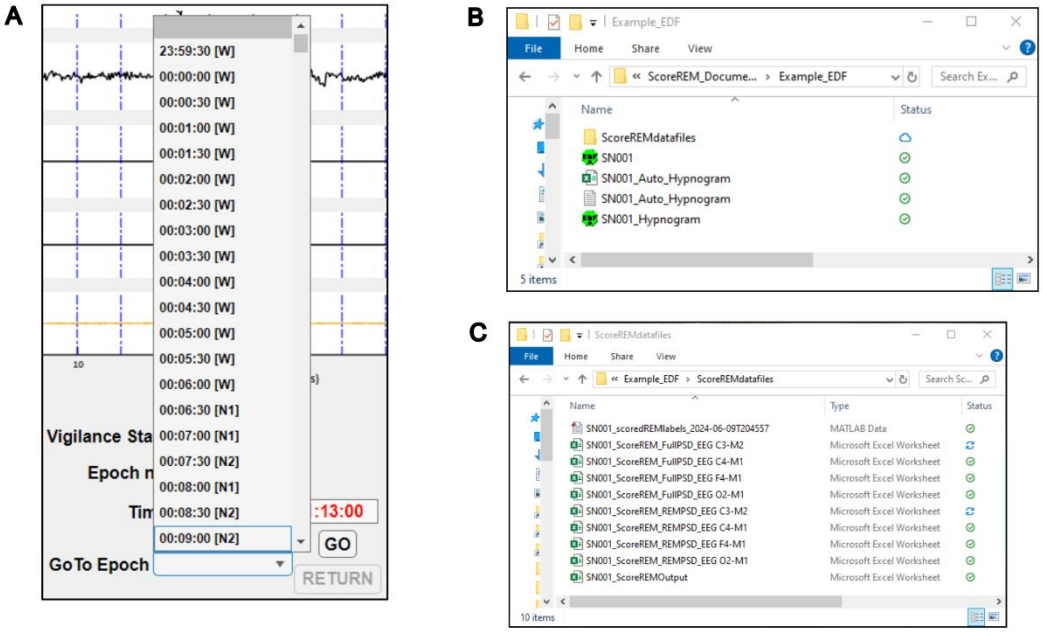


Figure S5 Epoch selection and export files in ScoreREM.

Scenario 3: Scoring given a marker file.

Sleep recording EDF file is available with a marker file containing Start time, Lights off and Lights on times. This option is used when the hypnogram is required to be scored or already scored starting from a timestamp that occurs after the recording start time in the EDF file. The Lights off and Lights on times are optional and is used by the summary generation process (summary measures are limited to lights off period) if available. Steps 1 and 2 are same as Scenario 1.

1. Step 3: Once the channels are chosen, the user inputs the availability of hypnogram or marker file. In this scenario, the user chooses ‘**EDF + Marker (.txt)**’ (see Figure S2 C). The Marker template for this case can be found in the ‘examplefiles’ folder in the repository (https://github.com/KiranKGR/ScoreREMGUI/tree/main/examplefiles).
2. Step 4: Following this, the user can choose to auto generate the hypnogram or upload a hypnogram (.txt) file. (see Figure S6 A).
4. Step 5: Once the hypnogram (.txt) is selected, ScoreREM allows the user to select the mapping of the loaded hypnogram to that of the standard five stage hypnogram as shown in Figure S6 B and C. Figure S6 shows an example where a R&K hypnogram is mapped on the standard five stage hypnogram. Notice the provision for multiple N3 and Artefact labels.

Following this step, the user proceeds as given in Steps 6 to 10 of Scenario 1.

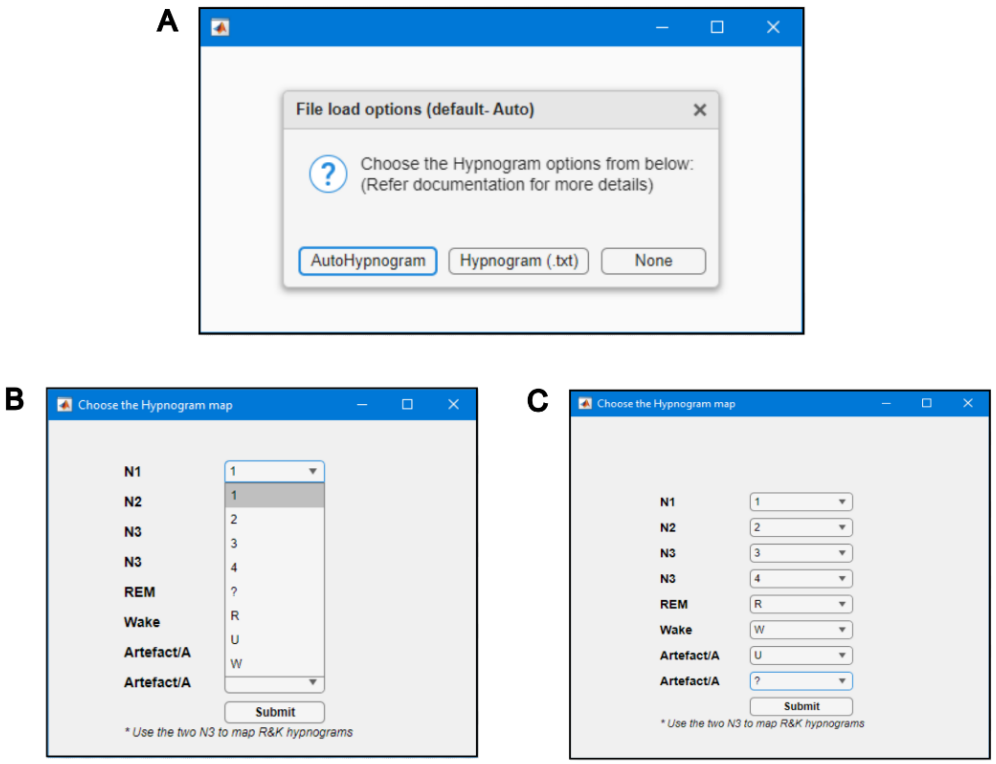


Figure S6. Hypnogram options with Marker file.

ScoreREM export file description

When the annotation perform is completed by the user and the save icon in ScoreREM is clicked, a total of 10 files are exported into the 'ScoreREMdatafiles' folder in the user selected save folder (See Figure S5 C). An example set of exported files can be found in the repository as described Step 9 and 10 of Scenario 1 above. The files and their description are provided below. The file specific changes to the filenames are highlighted in red. Filename is the name of the EDF file containing the sleep recording.

1. "*filename*_scoredREMlabels_*date*T*time*.mat": Scored annotations with the time and date of scoring. Contains the annotations/labels in the format used by ScoreREM. The user can use the file to reload (using reload button) the labels and start from the location they left off.
2. "*filename*_ScoreREMOutput.xlsx": Contains a total of 6 sheets.

- "Hypnogram" - Contains the hypnogram, information on the last epoch scored by the user and label definitions (See Figure S7 A).
- "Summary" - Contains the sleep summary measures. Definitions of all the 32 summary estimates is given in Table S1 and an example sheet in Figure S7 B. The estimation period is the total period of recording in the EDF file in the absence of the Light off and Lights on markers and over the lights off period when the markers are available. All definitions in the table are over the estimation period.
- "EOG-L-STR" "EOG-R-STR" - Annotated labels for the left and right EOG channels in string format. It contains epoch number alongside the first column and micro epoch segment number in the first row. The annotated labels are

provided as matrix of epoch number and micro epoch segment number (see Figure S7 C).

- "EOG-L-NUM" "EOG-R-NUM" - Annotated labels for the left and right EOG channels in numerical format in these sheets in a matrix format similar to the string labels.

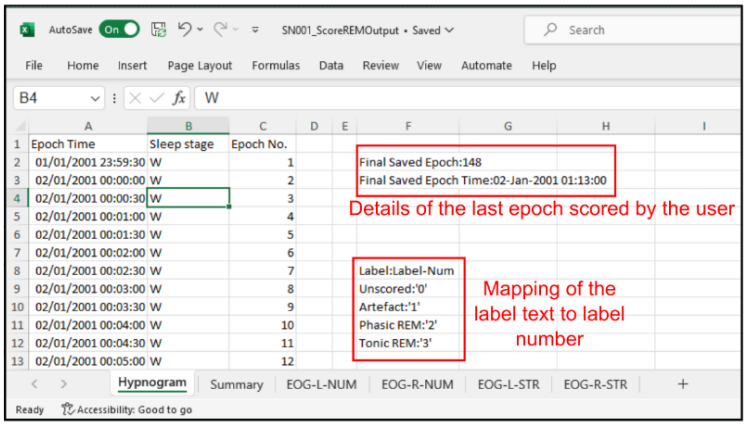
3. "*filename*_ScoreREM_REMPSD_*EEGchannelname*.xlsx: There are 4 sheets in this document. Contains the epoch wise Power spectral density (PSD) estimates (μV^2) of Tonic, Phasic and Artefact micro epochs in each of EEG channels in the sleep recording. The Tonic, Phasic and Artefact micro epochs are averaged over an epoch. Artefact free REM epoch power spectral estimates are provided in a separate sheet. A screen shot of an example file is given in Figure S7 D. The frequency resolution of the PSD estimates is determined by the micro epoch length (eg.: 1s provides 1Hz resolution)
4. "*filename*_ScoreREM_FullPSD_*EEGchannelname*.xlsx": Contains the epoch wise Power spectral density of artefact free micro epochs from the entire sleep recording for all chosen EEG channels. The micro epochs are averaged over an epoch excluding the ones scored as Artefacts. The frequency resolution of the PSD estimates is determined by the micro epoch length (eg.: 1s provides 1Hz resolution).

Table S1. Sleep summary metrics and their definitions.

Sleep metric	Units	Definition
REM_epoch_count	count	Total number of REM epochs in the estimation period
DUR_REM	min	Duration (in minutes) of rapid eye movement (REM) sleep
REM_LAT	min	Duration (in minutes) from the start of the estimation period and the first epoch of REM
PTST_REM	%	Percentage of REM sleep (duration in minutes) within the total sleep time
REMRATIO	ratio	Total duration of REM divided by the total duration of NREM
Phasic_event_count	count	Total number of Phasic REM micro epochs in REM
DUR_Phasic	min	Duration of Phasic REM micro epochs
PTST_Phasic	%	Percentage of Phasic REM sleep (duration in minutes) within the total sleep time
PREM_Phasic	%	Percentage of Phasic REM sleep (duration in minutes) within the REM sleep duration
Tonic_event_count	count	Total number of Tonic REM micro epochs in REM
DUR_Tonic	min	Duration of Tonic REM micro epochs
PTST_Tonic	%	Percentage of Tonic REM sleep (duration in minutes) within the total sleep time
PREM_Tonic	%	Percentage of Tonic REM sleep (duration in minutes) within the REM sleep duration
Artifacts_event_count_LOC	count	Total number of Artefact micro epochs in the LOC channel
Artifacts_event_count_ROC	count	Total number of Artefact micro epochs in the ROC channel
SOL	min	Duration (in minutes) between the start of the estimation period and the first epoch of NREM or REM

LPS	min	Duration (in minutes) between the start of the estimation period and the first consecutive 20 epochs (10 minutes) of NREM or REM
TRT	min	Duration (in minutes) between the start of the estimation period and the end of the estimation period
TST	min	Duration (in minutes) of epochs scored as NREM or REM excluding epochs of Wake within the estimation period
DUR_W	min	Duration (in minutes) of epochs scored as WAKE between the start and end of estimation period
DUR_N1	min	Duration (in minutes) of epochs scored as N1 between the start and end of estimation period
DUR_N2	min	Duration (in minutes) of epochs scored as N2 between the start and end of estimation period
DUR_N3	min	Duration (in minutes) of epochs scored as N3 between the start and end of estimation period
WASO	min	Duration (in minutes) of epochs scored as wake from SOL until end of estimation period
N2_LAT	min	Duration (in minutes) from the start of the estimation period to the first epoch of N2
N3_LAT	min	Duration (in minutes) from the start of the estimation period to the first epoch of N3
NumberOfAwakening	count	Number of blocks of consecutive epochs (2) of wake from LPS until end of estimation period
SEFF	%	Percentage of TST in TRT
PTST_N1	%	Percentage of N1 sleep (duration in minutes) within the total sleep time
PTST_N2	%	Percentage of N2 sleep (duration in minutes) within the total sleep time
PTST_N3	%	Percentage of N3 sleep (duration in minutes) within the total sleep time
PTST_NREM	%	Percentage of NREM sleep (duration in minutes) within the total sleep time

A



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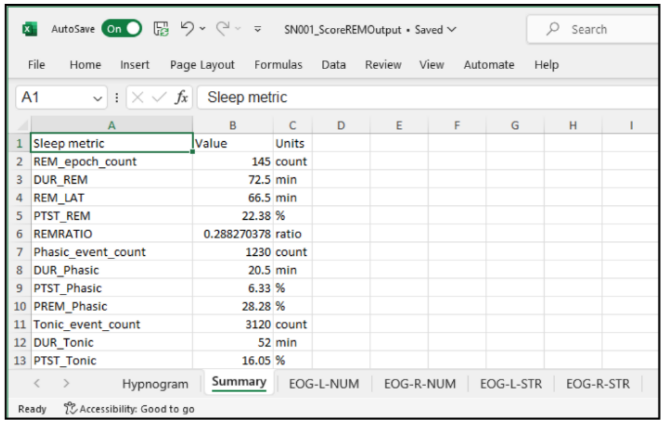

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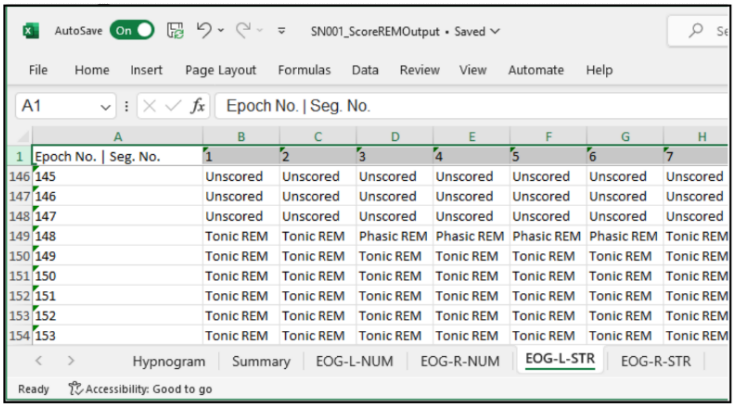

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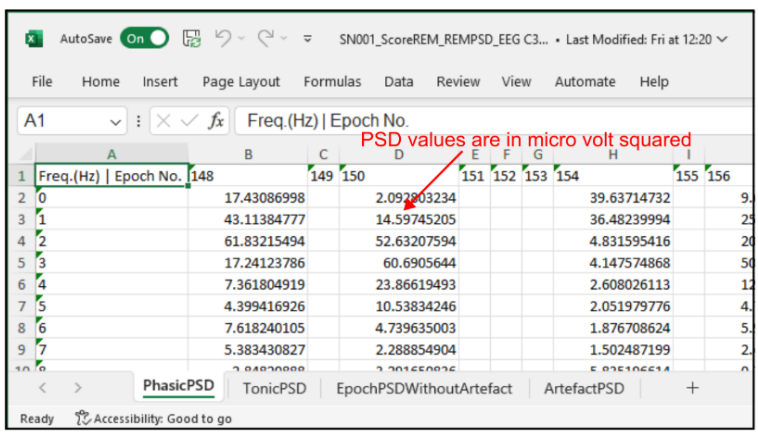

Figure S7. ScoreREM exported files.