Title of the Project:
Is Cortical High Frequency Brain Activity All Artifacts?

Supervisor:
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Background:
High-frequency oscillations were first discovered in the healthy rodent hippocampus through local field potential recordings and later observed in human **intracranial** recordings (1). Subsequent studies demonstrated that those are elevated in the seizure onset zone of patients with epilepsy (2), leading to their recognition as a biomarker for identifying the surgical onset zone and predicting surgical outcomes (3). Although the exact origins, mechanisms, and physiological roles of these oscillation remain unclear, in healthy brain, they have been linked to memory consolidation and cognitive processing (1). Looking at **cortical recordings** (EEG), high-frequency neural activity overlaps significantly with the spectral bandwidth of muscle activity (~20–300 Hz), raising concerns about contamination of EEG in frequency above 100 Hz. This has led to the routine application of a low-pass filter (120 Hz) to remove muscle artifacts in most EEG studies. However, recent studies have demonstrated that high-frequency oscillations in pediatric epileptic patients can be reliably recorded from scalp EEG (reviewed here [4]), prompting questions about whether EEG high-frequency components (oscillatory or non-oscillatory, between 200–499 Hz) might reflect real brain activity. To investigate this, we conducted 23 hours of recordings from nine animals, finding a strong correlation between high-frequency activity and wakefulness (5). Machine learning analysis suggested that this activity could serve as a clear marker to distinguish wakefulness from sleep (Figure 1). The next phase aims to validate these findings across species, including rats, monkeys, and humans using polysomnography.

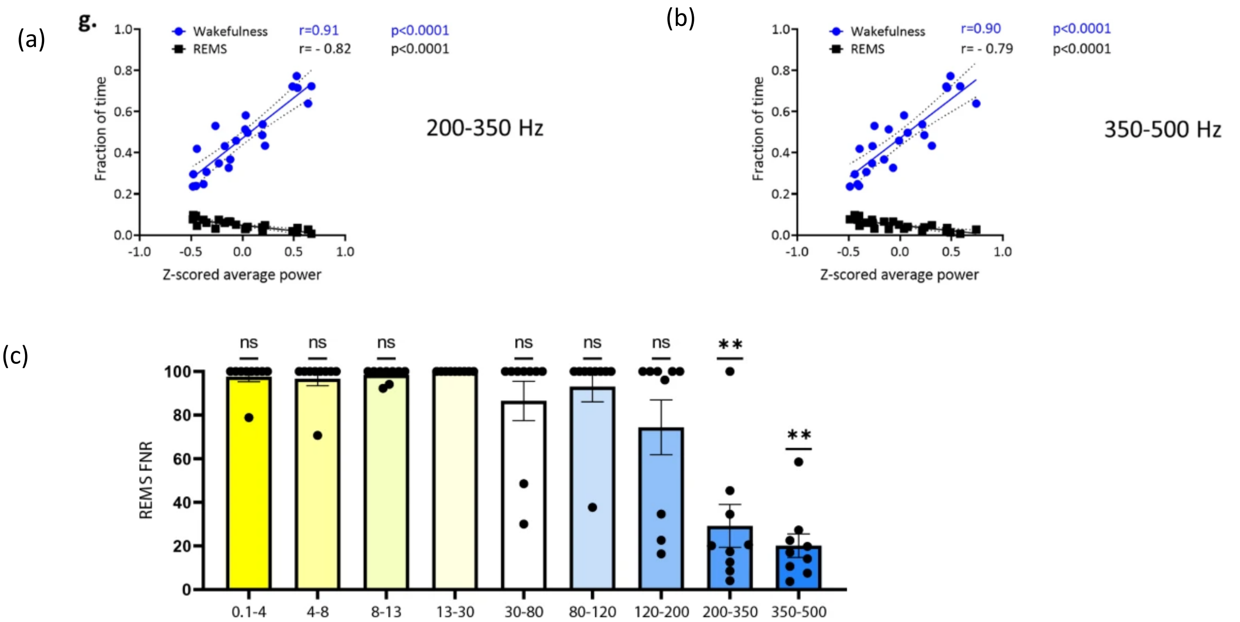

Figure 1. (a) and (**b)** show the significant positive correlation of wakefulness with the z-scored-average power of 200–350 Hz and 350–500 Hz, while REMS has a significant negative correlation with the value for each band ($p < 0.0001$, according to Pearson correlation coefficient test). **(c)** By limiting the algorithm to use only one frequency band, FNR (false negative ratio) in REMS prediction increased to almost 100 percent for 0.1–4 Hz, while it decreased significantly by choosing 200–350 Hz and 350–500 Hz ($p < 0.01$, according to one-sample Wilcoxon signed-rank test, compared with the hypothetical median of 100).

Completed Tasks:

- Developed a code to assess power, 1/f slope, permutation, and spectral entropy of high-frequency brain activity.
- Analyzed 23 hours of recordings from nine mice, with a sampling rate of 1000 Hz (Figure 1).
- Recorded six hours of data from five rats with a sampling rate of 2000 Hz.
- Recorded neural activity from four monkeys during wake, sleep, and anesthesia (database: http://www.neurotycho.org/).
- Primary analysis of eight hours of polysomnography, including HD-EEG from 29 healthy individuals with a sampling rate of 1000 Hz (database: https://doi.org/10.1038/s41597-024-03722-1). Our observations suggested very low high-frequency brain activity during N1, N2, N3, and REM sleep stages, with sporadic activity occurring primarily during wakefulness (Figure 2).

Upcoming Tasks:

- Comparative analysis of high-frequency brain activity measures in rats, monkeys, and humans, based on vigilance states.
- Application of machine learning techniques to distinguish vigilance states using high-frequency brain activity data.
- Artifact removal in human datasets, using ECG, ECOG, and EMG signals.
- Source localization for human data following the application of a 100 Hz low-pass filter.

Expectations from a Master's Student:

- A strong interest in biosignal analysis (EEG, EMG).
- Patience and creativity.
- Knowledge of programming.

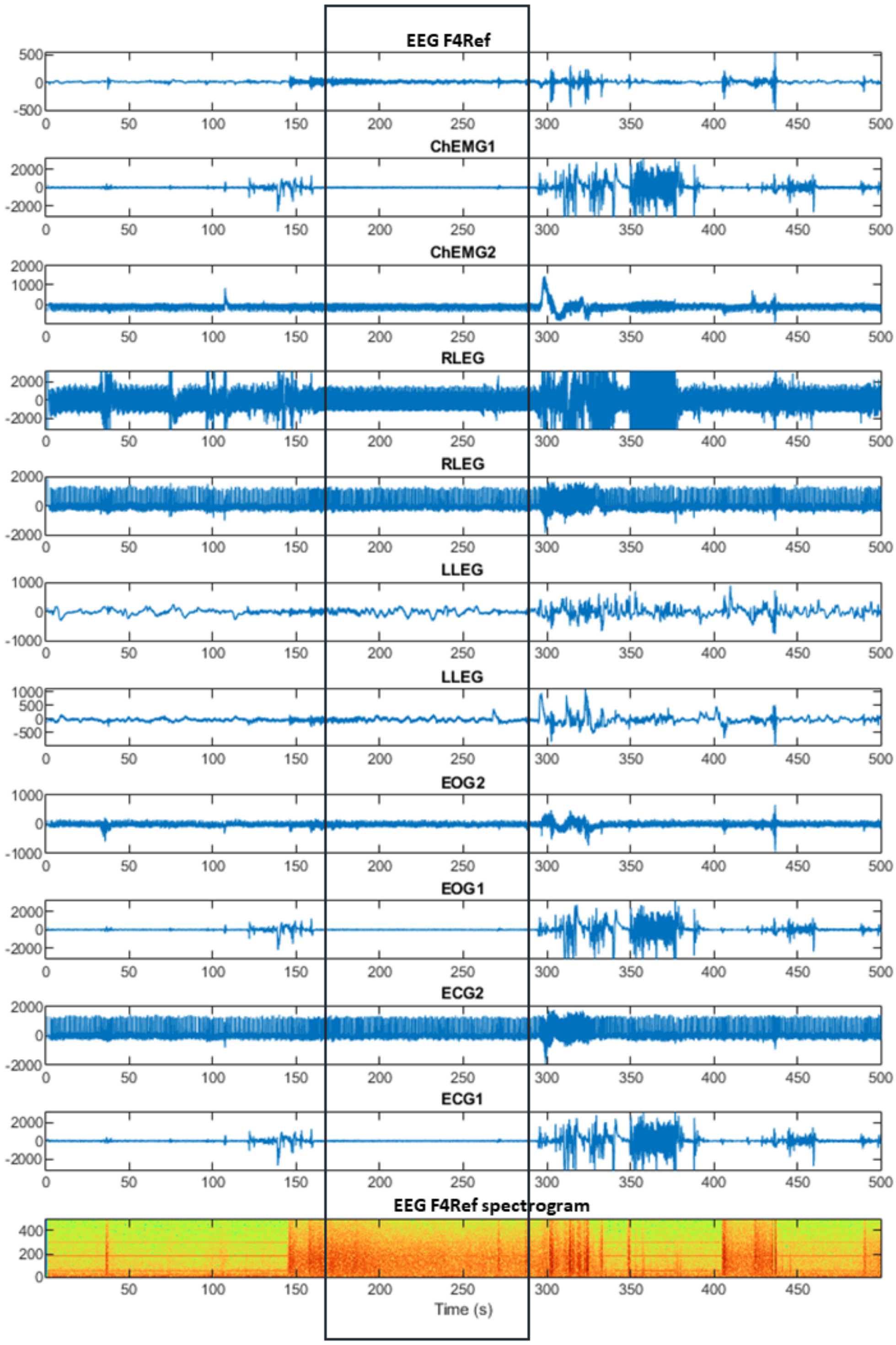

Figure 2. Representative example of 500 seconds of augmented wake epochs from a healthy individual, accompanied by the corresponding EEG spectrogram for the same period. During wakefulness, non-oscillatory brain activity is often associated with muscle artifacts. However, in certain intervals—such as the highlighted section (between 180 to 280 seconds in this example)—the activity in the EEG spectrogram appears to be independent of other channels, suggesting it may not be linked to muscle artifacts.

References:

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2) Park CJ, Hong SB. High frequency oscillations in epilepsy: detection methods and considerations in clinical application. Journal of Epilepsy Research. 2019 Jun;9(1):1.
3) Lin J, Smith GC, Gliske SV, Zochowski M, Shedden K, Stacey WC. High frequency oscillation network dynamics predict outcome in non-palliative epilepsy surgery. Brain Communications. 2024;6(1):fcae032.
4) Noorlag L, van Klink NE, Kobayashi K, Gotman J, Braun KP, Zijlmans M. High-frequency oscillations in scalp EEG: a systematic review of methodological choices and clinical findings. Clinical Neurophysiology. 2022 May 1;137:46-58.
5) Rahimi S, Soleymankhani A, Joyce L, Matulewicz P, Kreuzer M, Fenzl T, Drexel M. Discriminating rapid eye movement sleep from wakefulness by analyzing high frequencies from single-channel EEG recordings in mice. Scientific Reports. 2023 Jun 13;13(1):9608.