Analysis of RR Interval Entropies for Discrimination Between Wake and Sleep States

Santiago Flores-Chávez[†], Antonio Ravelo-García[‡§], Miguel Vizcardo Cornejo[†]

[†] Escuela Profesional de Física, Universidad Nacional de San Agustín de Arequipa, Arequipa, Perú
[‡] Institute for Technological Development and Innovation in Communications, Universidad de Las Palmas de Gran Canaria, Spain
[§] Interactive Technologies Institute (ITI/LARSyS and ARDITI), Funchal, Portugal

Abstract

This study use of Approximate Entropy (ApEn) for classification of sleep stages using R-R intervals derived from ECG signals. The results demonstrate that ApEn can effectively differentiate between sleep stages and wakefulness across varying embedding dimensions (m) and time windows. In lower dimensions, higher entropy values correspond to deeper sleep stages, while in higher dimensions, the relationship reverses, associating higher entropy with REM, light sleep, and wakefulness. The analysis also reveals that specific time windows (e.g., 5 minutes) and embedding dimensions (e.g., $m = 5$) improve the discrimination between sleep and wake states. These findings suggest that ApEn is a valuable tool for non-invasive sleep monitoring and classification. Further studies are recommended to explore its applicability in broader and more diverse populations.

1. Introduction

Sleep stage classification is typically performed through the manual evaluation of polysomnographic (PSG) records, a time-consuming process [1]. Although PSG is considered the gold standard for sleep monitoring, its high cost and complexity limit its scalability [2]. Electrocardiogram (ECG) data, specifically R-R intervals, offer a non-invasive alternative for classifying sleep and wakefulness states [3]. Approximate Entropy (ApEn) has been shown to differentiate between sleep stages, particularly between REM and non-REM sleep [4]. However, the impact of embedding dimensions and time windows on ApEn performance remains unclear. This study aims to evaluate ApEn's ability to classify sleep stages using R-R intervals derived from ECG, with an emphasis on optimizing embedding dimensions and time windows to improve accuracy in a heterogeneous population.

2. Method

2.1. Database

The data used in this study come from the *Haaglanden Medisch Centrum Sleep Staging Database*, publicly available on PhysioNet [5]. The database includes 151 full-night polysomnographic (PSG) recordings, collected in 2018 at Haaglanden Medisch Centrum (HMC) in the Netherlands [6]. The sample comprises 85 men and 66 women with a mean age of 53.9 ± 15.4 years. The records were randomly selected from patients referred for PSG evaluation for various sleep disorders, without applying additional exclusion criteria, aiming to assess the method's reliability in a heterogeneous population [7]. Each record includes EEG, EOG, chin EMG, and ECG signals, along with hypnograms annotated by sleep technicians at HMC. The data were anonymized, and their reuse was approved by the institutional review board of Zuid-West Holland (METC-19-065) [6]. The signals, sampled at 256 Hz and stored in EDF format [8], followed the guidelines of version 2.4 of the AASM manual [6]. The analysis focused on the ECG signal, specifically the RR intervals, to calculate Approximate Entropy (ApEn) during sleep and wakefulness stages.

2.2. Data preprocessing

Standard preprocessing techniques were applied to the R-R intervals, including normalization and filtering to remove artifacts and noise. Sleep segments were labeled according to the scoring system criteria [9], using high-pass (1 Hz) and low-pass (150 Hz) filters to eliminate baseline noise and interference, with a sampling frequency of 256 Hz [10]. ECG data and hypnograms were obtained from polysomnographic records in EDF format [6] and processed using the *mne* software, which allows direct reading of EDF/EDF+ files [10]. The processed ECG signal,

in voltage, has an average duration of 7 to 8 hours per patient [7]. The annotated hypnogram was used to identify the beginning and end of each sleep phase. Thirty-second intervals were labeled, structuring the ECG series and enabling the selection of time windows from 30 seconds to 10 minutes, facilitating the analysis of R-R intervals.

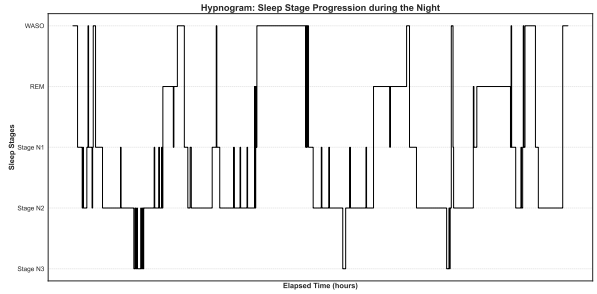

Figure 1. Hypnogram showing the distribution of sleep stages after preprocessing. It indicates the frequency and duration of each stage throughout the night.

To visualize the process of grouping ECG segments into different sleep stages, diagrams are presented in Figures 2 and 3. These diagrams illustrate the construction of time segments, from 300-second intervals to their combination representing sleep stages. This facilitates the understanding of how consecutive ECG segments are grouped based on sleep stages.

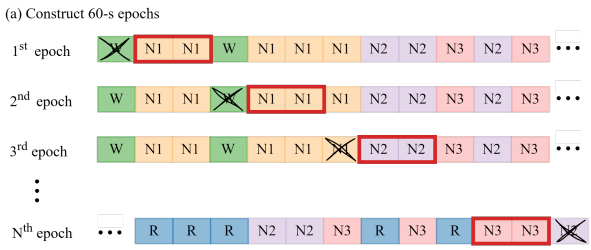

Figure 2. Construction of hypnograms in 300-second intervals through the grouping of consecutive ECG segments.

Finally, R-R intervals, representing the time differences between the R peaks of the ECG signals, were calculated using the Pan-Tompkins algorithm for QRS peak detection [11].

2.3. Calculation of Approximate Entropy (ApEn)

Approximate Entropy (ApEn) was calculated for each time window using embedding dimensions (m) from 1 to 5, with values stored alongside timestamps and sleep stages. The analysis, based on R-R intervals from ECG

Figure 3. Final distribution of sleep stages with the combination of ECG segments to form a long-term hypnogram.

signals, assessed the regularity and complexity of the time series. ApEn was computed following Pincus' definition [12]:

$$ApEn(m, r, N) = \frac{1}{N-m} \sum_{i=1}^{N-m} \log\left(\frac{A_i}{B_i}\right) \quad (1)$$

where m is the embedding dimension, r is the threshold, and A_i and B_i are proximity measures between vectors embedded in dimensions m and $m+1$. In this study, m ranged from 1 to 5, with $r = 0.5$ of the standard deviation (SD). Hypothesis tests were performed to evaluate ApEn's ability to discriminate between sleep stages and wakefulness, with a significance level set at p-value < 0.001. The Wilcoxon-Mann-Whitney test was used to compare the extracted features between different sleep stages and wakefulness [13].

3. Results

When calculating entropy values for R-R interval series grouped into 1-minute time windows and using embedding dimensions $m = 4$ and $m = 5$, clear differences are observed between the different sleep stages and micro-arousals, as shown in Figure 4. Similarly, the results for a 10-minute time window also exhibit variations, as depicted in Figure 5. Both graphs demonstrate significant differences in ApEn values across the various physiological stages, along with variations in the number of outliers and the quartiles generated for each data group.

A more general overview of the behavior of ApEn values, calculated for different embedding dimensions ($m = 1, 2, 3, 4, 5$), can be observed in Figure 6. In this case, ApEn values were calculated for an 8-minute time window, where this interval was found to better discriminate between the different physiological stages. However, for distinguishing between sleep and wakefulness stages, the 5-minute time window yielded better results, as shown in Figure 7.

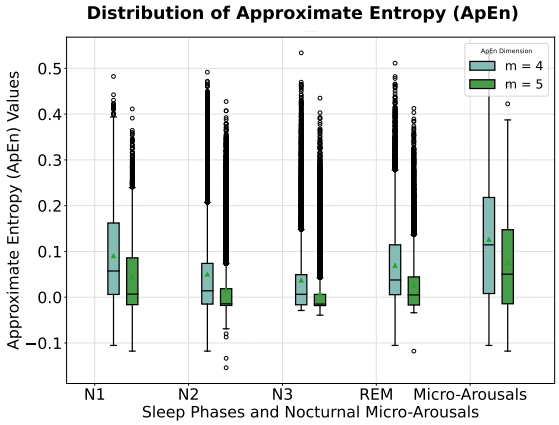

Figure 4. ApEn values calculated for 1-minute windows and embedding dimensions $m = 4$ and $m = 5$, showing differences between sleep stages and micro-arousals.

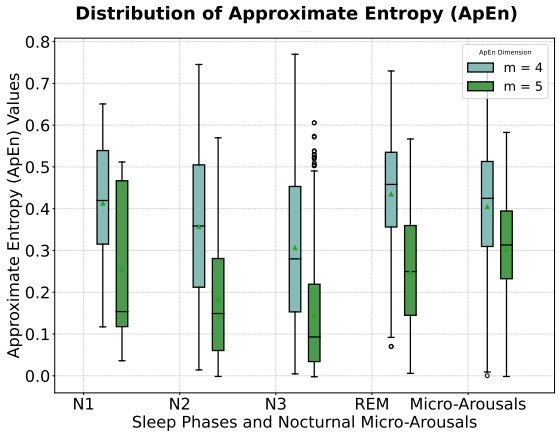

Figure 5. ApEn values calculated for 10-minute windows and embedding dimensions $m = 4$ and $m = 5$, showing differences between sleep stages and micro-arousals.

Figure 8 shows the clear difference between ApEn values calculated for sleep and wakefulness stages. The Mann-Whitney U statistical tests to evaluate whether the ApEn values belong to significantly different samples demonstrated significant discriminative ability between the two stages, particularly with $m = 5$ obtaining a p-value < 0.001.

4. Discussion

Approximate Entropy (ApEn) was validated as a useful metric for the classification of sleep stages based on R-R intervals. Previous studies confirm that at low embedding dimensions m, high entropy values are associated with deep sleep, while low values correspond to REM and wakefulness [3] [4]. However, at higher dimensions, this relationship is reversed, with high entropy values ob-

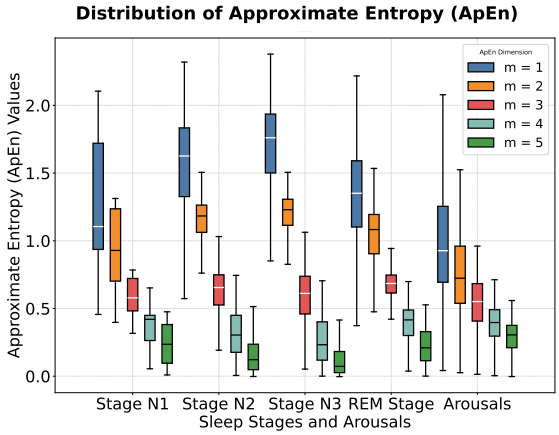

Figure 6. ApEn values calculated for an 8-minute time window and different embedding dimensions ($m = 1, 2, 3, 4, 5$), showing a clear differentiation between the physiological stages during the night.

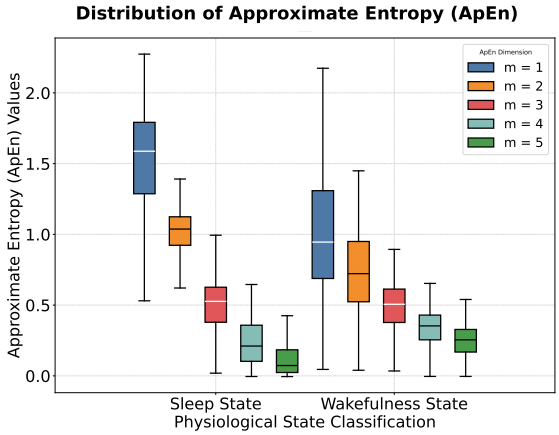

Figure 7. Comparison of ApEn values between sleep and wakefulness stages for a 5-minute time window, using embedding dimensions ($m = 1, 2, 3, 4, 5$).

served in REM, light sleep, and wakefulness, and low values in deep sleep. These results suggest a more complex dynamic in R-R intervals depending on the sleep stage. ApEn's ability to distinguish between physiological states varies with m and the time window used. To differentiate between wakefulness and sleep, a 5-minute window with $m = 5$ is more effective, while to distinguish between all stages, 8 or 10-minute windows with $m = 1$ or $m = 2$ are more suitable. One-minute windows with $m = 1$ or $m = 2$ may be useful if low deviation is sought and outliers are not relevant. This study improves differentiation between sleep and wakefulness stages, possibly due to the use of ECG signals specific to each stage. Unlike previous studies [4], which used signals from multiple stages, this work explores different time windows and embedding

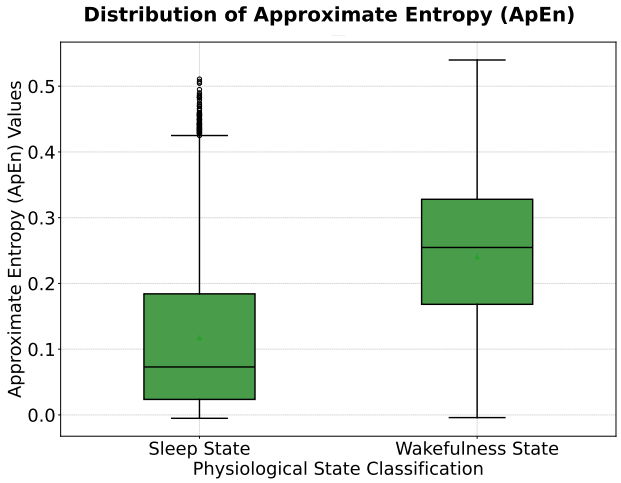

Figure 8. Differentiation between sleep and wakefulness stages using ApEn values, showing significant differences for $m = 5$ and 5-minute time windows.

dimensions m, optimizing differentiation. Further studies on larger and more diverse populations are recommended, and correlations with other patient characteristics should be explored. More research is also needed on the relationships between time windows and embedding dimensions m to optimize the use of ApEn.

5. Conclusions

This study validates Approximate Entropy (ApEn) as an effective tool for automatic sleep stage classification using R-R intervals from ECG signals, without the need for precise segmentation or data distribution assumptions. Results indicate that ApEn effectively discriminates between sleep and wakefulness across both low and high embedding dimensions, with better performance at higher values. At low m, higher entropy corresponds to deep sleep, whereas at higher m, higher entropy values are linked to REM, light sleep, and wakefulness. The analysis also shows that time window selection and m significantly impact ApEn's accuracy in differentiating sleep stages. Compared to previous studies, this work enhances the precision of sleep and wake discrimination, likely due to the use of ECG signals specific to each stage. The optimization of time windows and embedding dimensions suggests further potential for clinical applications and future research on sleep dynamics.

Acknowledgments

Universidad Nacional de San Agustin de Arequipa

References

[1] Berry RB, Brooks R, Gamaldo C, Harding SM, Lloyd RM, Quan SF, Troester MT, Vaughn BV. Aasm scoring manual updates for 2017 (version 2.4). Journal of Clinical Sleep Medicine May 2017;13(05):665–666.

[2] Pan Q, Brulin D, Campo E. Current status and future challenges of sleep monitoring systems: Systematic review. JMIR Biomedical Engineering August 2020;5(1):e20921.

[3] Han J, Han J, Park HJ, Park HJ, Park KS, Park KS, Jeong DU, Jeong DU. Estimation of rhythmic variations in r-r interval using nonlinear energy operator during sleep. Proceedings of the 20th Annual International Conference of the IEEE Engineering in Medicine and Biology Society Vol20 Biomedical Engineering Towards the Year 2000 and Beyond Cat No98CH36286 1998;.

[4] Yan C, Li P, Yang M, Li Y, Li J, Zhang H, Liu C. Entropy analysis of heart rate variability in different sleep stages. Entropy March 2022;24(3):379.

[5] Goldberger A Amaral L e. Physiobank, physiotoolkit, and physionet: Components of a new research resource for complex physiologic signals. PhysioNet 2000;101 (23), pp. e215–e220.

[6] Álvarez Estévez D. yRR. Base de datos de estadificación del sueño haaglanden medisch centrum. PhysioNet 2022; 1.1.

[7] Alvarez-Estevez D, Rijsman RM. Inter-database validation of a deep learning approach for automatic sleep scoring. PLOS ONE August 2021;16(8):e0256111.

[8] Alvarez-Estevez D. European data format. httpswwwedfplusinfospecsedftextshtml 2024;.

[9] Chriskos P, Frantzidis CA, Nday CM, Gkivogkli PT, Bamidis PD, Kourtidou-Papadeli C. A review on current trends in automatic sleep staging through bio-signal recordings and future challenges. Sleep Medicine Reviews 2021; 55:101377. ISSN 1087-0792.

[10] Gramfort A, Luessi M, Larson E, Engemann DA, Strohmeier D, Brodbeck C, Goj R, Jas M, Brooks T, Parkkonen L, Hämäläinen MS. MEG and EEG data analysis with MNE-Python. Frontiers in Neuroscience 2013; 7(267):1–13.

[11] Pan J, Tompkins WJ. A real-time qrs detection algorithm. IEEE Transactions on Biomedical Engineering 1985;BME-32(3):230–236.

[12] Pincus SM. Approximate entropy as a measure of system complexity. Proceedings of the National Academy of Sciences March 1991;88(6):2297–2301.

[13] Mann HB, Whitney DR. On a test of whether one of two random variables is stochastically larger than the other. The Annals of Mathematical Statistics 1947;18(1):50–60.

Address for correspondence:

Miguel Vizcardo Cornejo

Av. Independencia, Universidad Nacional de San Agustín, Escuela profesional de Física, Laboratorio Nro 305, Arequipa 04001, Perú.

mvizcardoc@unsa.edu.pe