U-Sleep: resilient to AASM guidelines

Luigi Fiorillo\textsuperscript{1,2*}, Giuliana Monachino\textsuperscript{1,2†}, Julia van der Meer\textsuperscript{3}, Marco Pesce\textsuperscript{3}, Jan Warncke\textsuperscript{3}, Markus H. Schmidt\textsuperscript{3}, Claudio L.A. Bassetti\textsuperscript{3}, Athina Tzovara\textsuperscript{1,3}, Paolo Favaro\textsuperscript{1} and Francesca D. Faraci\textsuperscript{2}

\textsuperscript{1}*Institute of Informatics, University of Bern, Neubrückstrasse 10, Bern, 3012, Switzerland.
\textsuperscript{2}Institute of Digital Technologies for Personalized Healthcare | MedITech, Department of Innovative Technologies, University of Applied Sciences and Arts of Southern Switzerland, Via la Santa 1, Lugano, 6962, Switzerland.
\textsuperscript{3}Sleep Wake Epilepsy Center | NeuroTec, Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Freiburgstrasse 16, Bern, 3010, Switzerland.

*Corresponding author(s). E-mail(s): luigi.fiorillo@supsi.ch; giuliana.monachino@supsi.ch; julia.vandermeer@insel.ch; marco.pesce@insel.ch; jan.warncke@insel.ch; markus.schmidt@insel.ch; claudio.bassetti@insel.ch; athina.tzovara@inf.unibe.ch; paolo.favaro@inf.unibe.ch; francesca.faraci@supsi.ch;†These authors contributed equally to this work.

Abstract

AASM guidelines are the results of decades of efforts aiming at standardizing sleep scoring procedure, in order to have a commonly used methodology. The guidelines cover several aspects from the technical/digital specifications, e.g., recommended EEG derivations, to detailed sleep scoring rules accordingly to age. In the context of sleep scoring automation, deep learning has demonstrated better performance compared to many other techniques. Usually, clinical expertise and official guidelines are fundamental to support automated sleep scoring algorithms in solving the task. In this paper we show that a deep learning based sleep scoring algorithm may not need to fully exploit the clinical knowledge or
to strictly follow the AASM guidelines. Specifically, we demonstrate that U-Sleep, a state-of-the-art sleep scoring algorithm, can be strong enough to solve the scoring task even using clinically non-recommended or non-conventional derivations, and with no need to exploit information about the chronological age of the subjects. We finally strengthen a well-known finding that using data from multiple data centers always results in a better performing model compared with training on a single cohort. Indeed, we show that this latter statement is still valid even by increasing the size and the heterogeneity of the single data cohort. In all our experiments we used 28528 polysomnography studies from 13 different clinical studies.

**Keywords:** Automatic sleep scoring, deep learning, AASM guidelines

1 Introduction

Since its origin in the late 1950s, polysomnography (PSG) has been at the centre of sleep medicine testing with the main aim of standardizing and to simplifying the scoring procedure. A common methodology has fostered clinical research and improved sleep disorder classification and comprehension. A PSG typically involves a whole night recording of bio-signals. Brain activity, eye movements, muscle activity, body position, heart rhythm, breathing functions and other vital parameters are monitored overnight. PSG scoring involves the procedure of extracting information from the recorded signals. Sleep stages, arousals, respiratory events, movements and cardiac events must be correctly identified. Wakefulness and sleep stages, *i.e.* stages 1, 2, 3 and rapid eye movement (REM), can be mainly described by three bio-signals: electroencephalography (EEG), electrooculography (EOG) and electromyography (EMG). Clinical sleep scoring involves a visual analysis of overnight PSG by a human expert and may require up to two hours of tedious repetitive work. The scoring is done worldwide accordingly to official standards, *e.g.*, the American Academy of Sleep Medicine (AASM) scoring manual [1].

Artificial intelligence (AI) is a powerful technique that has the potential to simplify and accelerate the sleep scoring procedure. In literature over the last two decades, a wide variety of machine learning (ML) and deep learning (DL) based algorithms have been proposed to solve the sleep scoring task [2–7]. DL based scoring algorithms have shown higher performances compared to the traditional machine learning approaches. Autoencoders [8], deep neural networks (DNNs) [9], U-Net inspired architectures [10, 11], convolutional neural networks (CNNs) and fully-CNNs [12–21], RNNs [22, 23] and several combinations of them [24–33] have been recently proposed in sleep scoring. The possibility to extract complex information from a large amount of data is one of the main reasons to apply DL techniques in PSG classification. Another significant advantage is the ability to learn features directly from raw data,
by also taking into account the temporal dependency among the sleep stages.

In literature we find many examples about how clinical guidelines have been exploited when trying to support ML and DL based algorithms. The oldest Rechtschaffen and Kales (R&K) [34] or the updated AASM [1] scoring manuals have been designed to cover all the aspects of the PSG: from the technical/digital specifications (e.g., assessment protocols, data filtering, recommended EEG derivations) to the scoring rules (e.g., sleep scoring rules for adults, children and infants, movement rules, respiratory rules) and the final interpretation of the results. To date, all the sleep scoring algorithms, both ML or DL based, are trained on sleep recordings annotated by sleep physicians according to these manuals. For example, Stephansen et al. [27] they pre-filtered the sleep recordings as indicated in the AASM guidelines before feeding them to their scoring system; almost all of the algorithms mentioned above were trained using recommended channel derivations and fixed length (i.e., 30-second) sleep epochs. However, it still remains unknown whether a DL based sleep scoring algorithm actually needs to be trained by following these guidelines. A decade ago, it was already highlighted that sleep is not just a global phenomenon affecting the whole brain at the same time, but that sleep patterns such as slow waves and spindle oscillations often occur out-of-phase in different brain regions [35, 36]. Hence, the usage of multi-channel derivations, but not necessarily the ones indicated in the AASM guidelines, may be sufficient to reach high performance with our DL based scoring algorithms. Furthermore, in the AASM manual and in previous studies [37, 38], age has been addressed as one of the demographic factors that mainly change sleep characteristics (e.g., sleep latency, sleep cycle structure, EEG amplitude etc.). To the best of our knowledge, it has never been attempted before to incorporate this information within a sleep scoring system; it could reasonably improve its performance.

To date, all the efforts have focused on optimizing a sleep scoring algorithm in order to be ready to score any kind of subject. Data mismatch and data heterogeneity is one of the biggest challenges to address. The performance of a sleep scoring algorithm on a PSG from an unseen data distribution (e.g., different data domains/centers) usually drastically decreases. A common objective among researchers is to increase the model generalizability, i.e., the ability of the model to make accurate predictions over different or never seen data domains. In recent studies, Phan et al. and Guillot et al. [31, 39] propose to adapt a sleep scoring architecture on a new data domain via transfer learning techniques. They demonstrate the efficiency of their approaches in addressing the variability between the source and target data domains. Perslev at al., Olesen et al. and Vallat et al. [11, 40, 41] propose to train their sleep scoring architectures on tens of thousands of PSGs from different large-scale-heterogeneous cohorts. They demonstrate that using data from many different sleep centers improves the performance of their model, even on never seen
data domains. In particular, Olesen et al. [40] show that models trained on a single data domain fail to generalize on a new data domain or data center.

In our study we did several experiments to evaluate the resilience of an existing DL based algorithm against the AASM guidelines. In particular we focused on the following questions:

(i) can a sleep scoring algorithm successfully encode sleep patterns, from clinically non-recommended or non-conventional electrode derivations?

(ii) can a single sleep center large dataset contain enough heterogeneity (i.e., different demographic groups, different sleep disorders) to allow the algorithm to generalize on multiple data centers?

(iii) whenever we train an algorithm on a dataset with subjects with a large age range, should we exploit the information about their age, conditioning the training of the model on it?

We ran all of our experiments on U-Sleep, a state-of-the-art sleep scoring architecture recently proposed by Perslev et al. [11]. U-Sleep has been chosen mainly for the following reasons: it has been evaluated on recordings from 15660 participants of 16 different clinical studies (four of them never seen by the architecture); it processes inputs of arbitrary length, from any arbitrary EEG and EOG electrode positions, from any hardware and software filtering; it predicts the sleep stages for an entire PSG recording in a single forward pass; it outputs sleep stage labels at any temporal frequency, up to the signal sampling rate, i.e., it can label sleep stages at shorter intervals than the standard 30-seconds, up to one sleep stage per each sampled time point.

In the original implementation of U-Sleep we found an extremely interesting bug: the data sampling procedure was not extracting the channel derivations recommended in the AASM guidelines, as stated by the authors in [11]. Instead, atypical or non-conventional channel derivations were randomly extracted. This insight triggered the above mentioned question (i).

Our contributions can be summarized as follows: (1) we find that a DL based scoring algorithm is still able to solve the scoring task, with high performance, even when trained with clinically non-conventional channel derivations; (2) we show that a sleep scoring model, even if trained on a single large and heterogeneous data domain, fails to generalize on new recordings from different data centers; (3) we demonstrate that the conditional training based on the chronological age of the subjects is unnecessary.
2 Results

2.1 Datasets and model experiments

We trained and evaluated U-Sleep on 19578 recordings from 15322 subjects of 12 publicly available clinical studies, as done previously [11].

In this study we also exploit the Bern Sleep Data Base (BSDB) registry, the sleep disorder patient cohort of the Inselspital, University hospital Bern. The recordings have been collected from 2000 to 2021 at the Department of Neurology, at the University hospital Bern. Secondary usage was approved by the cantonal ethics committee (KEK-Nr. 2020-01094). The dataset consists of 8950 recordings from patients and healthy subjects aged 0-91 years. The strength of this dataset is that, unlike the ones available online, it contains patients covering the full spectrum of sleep disorders, many of whom were diagnosed with multiple sleep disorders and non-sleep related comorbidities [42]; thus providing an exceptionally heterogeneous PSG data set. EEG (F4-M1, F3-M2, C4-M1, C3-M2, O2-M1, O1-M2) and EOG (E2-M1, E1-M2) standard derivations have been considered in our experiments. The signals are recorded at 200Hz. The recordings are manually scored by sleep experts according to the AASM rules. An overview of all the open access (OA) datasets and the BSDB dataset along with demographic statistics is reported in Table 1. In Supplementary Notes: Datasets, we report a detailed description of all the OA datasets.

The data pre-processing and the data selection/sampling across all the datasets is implemented as described in [11] (see subsection 4.1). In contrast with the recommendation of the AASM manual, no filtering was applied to the EEG and the EOG signals during the pre-processing procedure. Most importantly, we found that in their model implementation atypical or non-conventional channel derivations were erroneously extracted. In fact, the data extraction and the resulting sampling procedure were creating totally random derivations, see Supplementary Table 6, obviously different to those recommended in the AASM guidelines. In this study, we examined the resilience of U-Sleep with respect to the strict AASM guidelines. To this aim, we extracted the channel derivations following the guidelines (as was originally meant to be done in [11]), to better understand the impact of channel selection on the overall performance. Below we summarize all the experiments performed in our work on U-Sleep:

(i) We pre-trained U-Sleep on all the OA datasets using both the original implementation selecting the atypical channel derivations (U-Sleep-v0), and our adaptation following AASM guidelines (U-Sleep-v1). We split each dataset in training (75%), validation (up to 10%, at most 50 subjects) and test set (up to 15%, at most 100 subjects). The split of the PSG recordings was done per-subject or per-family, i.e., recordings from
Table 1 Datasets overview with demographic statistics. Missing values are due to study design or anonymized data. On the BSDB dataset, we compute the age and the sex values on the 99.1% and on the 98.6% of the whole dataset, respectively, because of missing age/sex information. Datasets directly available online are identified by ✓, whilst datasets that require approval from a Data Access Committee marked by (✓). BSDB is a private dataset.

| Datasets | Recordings | Age in years ($\mu \pm \sigma$) | Sex % (F/M) |
|----------|------------|-------------------------------|-------------|
| [43, 44] ABC (✓) | 132 | 48.8 ± 9.8 | 43/57 |
| [43, 45] CCSHS (✓) | 515 | 17.7 ± 0.4 | 50/50 |
| [43, 46] CFS (✓) | 730 | 41.7 ± 20.0 | 55/45 |
| [43, 47, 48] CHAT (✓) | 1638 | 6.6 ± 1.4 | 52/48 |
| DCSM ✓ | 255 | - | - |
| [43, 49] HPAP (✓) | 238 | 46.5 ± 11.9 | 43/57 |
| [43, 50] MESA (✓) | 2056 | 69.4 ± 9.1 | 54/46 |
| [43, 51, 52] MROS (✓) | 3926 | 76.4 ± 5.5 | 0/100 |
| [53, 54] PHYS ✓ | 994 | 55.2 ± 14.3 | 33/67 |
| [53, 55] SEDF-SC ✓ | 153 | 58.8 ± 22.0 | 53/47 |
| [53, 55] SEDF-ST ✓ | 44 | 40.2 ± 17.7 | 68/32 |
| [43, 56] SHHS (✓) | 8444 | 63.1 ± 11.2 | 52/48 |
| [43, 57, 58] SOF (✓) | 453 | 82.8 ± 3.1 | 100/0 |
| BSDB | 8884 | 47.9 ± 18.4 | 66/34 |

the same subject or members of the same family appear in the same data split. In Supplementary Table 7 we summarize the data split on each OA dataset. We evaluated both U-Sleep-v0 and U-Sleep-v1 on the test set of the BSDB dataset. We also evaluated the models on the whole BSDB dataset, to test on a higher number of subjects, with a higher heterogeneity of sleep disorders and a wider age range. A model pre-trained on the OA datasets and evaluated directly on the BSDB dataset is what we will refer to as direct transfer (DT) on BSDB.

(ii) We exploited the BSDB dataset to evaluate whether a DL based scoring architecture, trained with a large and a highly heterogeneous database, is able to generalize on the OA datasets from different data centers. We split the BSDB recordings in training (75%), validation (10%) and test set (15%). We ran two different experiments on U-Sleep-v1: we trained the model from scratch (S) on the BSDB dataset; we fine-tuned (FT) the model pre-trained in (i) on the BSDB dataset, by using the transfer learning approach (see subsection 4.2). Then, we evaluated both (S) and (FT) on the test set of all the OA datasets and the test set of the BSDB dataset.

(iii) We exploited the BSDB dataset to investigate whether U-Sleep needs to be trained by also having access to chronological age-related information. We split the BSDB dataset in seven groups, according to the
Table 2 (i) Performance of U-Sleep-v0 and U-Sleep-v1, pre-trained on the OA datasets, and evaluated on the test set of the BSDB dataset, and on the whole BSDB$_{100\%}$ dataset, i.e. both direct transfer (DT) on BSDB. We report the F1-score (%F1), specifically the mean value and the standard deviation ($\mu \pm \sigma$) computed across the recordings.

| Datasets | U-Sleep-v0 | U-Sleep-v1 |
|----------|------------|------------|
| BSDB     | 72.5 ± 12.2| 72.5 ± 12.0|
| BSDB$_{100\%}$ | 72.9 ± 12.4| 72.9 ± 12.4|

age categories of the subjects [37], resulting in $G = 7$ subdatasets, see Supplementary Notes: Age Analysis. We further split the recordings of each subdataset in training (75%), validation (10% at most 50 subjects) and test set (15% at most 100 subjects). We ran three different experiments on U-Sleep-v1: we fine-tuned the model by using all the training sets of the seven groups (FT); we fine-tuned seven Independent models by using the training set of each group independently (FT-I); we fine-tune a single Sandwich Batch Normalization model (exploiting the batch normalization layers, see subsection 4.3), to add the condition on the age-group-index $G$ for each recording (FT-SaBN). These last two experiments have been replicated considering only two age groups, i.e., babies/children and adults, as recommended in [1], resulting in two additional fine-tuned model (FT-I and FT-SaBN for $G = 2$). We then evaluated all of the fine-tuned models on the independent test test of each age group.

In Supplementary Table 8 we summarize the two different data split sets, in experiment (ii) and experiment (iii), on the BSDB dataset.

2.2 Performance overview

(i) Clinically non-recommended channel derivations. In Table 2 we compare the performance of U-Sleep pre-trained on all the OA datasets, with (U-Sleep-v0) and without (U-Sleep-v1) using randomly ordered channel derivations. There is no statistically significant difference between the two differently trained architectures evaluated on the test set of the BSDB dataset (paired t-test $p-value > 0.05$). Most importantly, we found no difference in performance with the direct transfer also on the whole BSDB$_{100\%}$ dataset (paired t-test $p-value > 0.05$). These results clearly show how the architecture is able to generalize regardless of the channel derivations used during the training procedure, also on a never seen highly heterogeneous dataset.

(ii) Generalizability on different data centers with a heterogeneous dataset.

In Table 3 we report the results obtained on U-Sleep-v1 pre-trained (i) on the OA datasets, and evaluated on all the test sets of the OA datasets
Table 3 (ii) Performance of U-Sleep-v1, pre-trained on the OA datasets, and evaluated on all the test sets of the OA datasets and on the test set of the BSDB dataset. We also report the performance of U-Sleep-v1 trained from scratch (S) or fine-tuned (FT) on the BSDB dataset, and evaluated on all the test sets of all the available datasets. We report the F1-score (%F1), specifically the mean value and the standard deviation ($\mu \pm \sigma$) computed across the recordings.

| Datasets | Training on OA | Training on BSDB |
|----------|----------------|------------------|
|          | U-Sleep-v1     | U-Sleep-v1 (S)   | U-Sleep-v1 (FT) |
| ABC      | 73.6 ± 11.4    | 71.4 ± 13.9      | 69.0 ± 12.5     |
| CCSHS    | 84.9 ± 5.1     | 77.3 ± 7.2       | 77.3 ± 6.7      |
| CFS      | 76.6 ± 11.6    | 70.2 ± 10.8      | 70.9 ± 10.2     |
| CHAT     | 82.1 ± 6.5     | 72.9 ± 8.0       | 68.8 ± 8.7      |
| DCSM     | 79.3 ± 9.3     | 71.5 ± 11.2      | 69.3 ± 10.5     |
| HPAP     | 73.8 ± 10.8    | 68.9 ± 11.1      | 67.9 ± 12.5     |
| MESA     | 72.7 ± 10.8    | 68.5 ± 14.3      | 68.7 ± 11.9     |
| MROS     | 71.4 ± 12.1    | 61.7 ± 13.7      | 63.9 ± 13.2     |
| PHYS     | 74.2 ± 10.7    | 72.9 ± 11.2      | 73.2 ± 11.4     |
| SEDF-SC  | 77.8 ± 7.9     | 75.8 ± 8.0       | 77.9 ± 7.7      |
| SEDF-ST  | 77.2 ± 10.1    | 64.3 ± 15.4      | 67.5 ± 12.4     |
| SHHS     | 76.9 ± 9.7     | 70.9 ± 9.3       | 73.0 ± 8.9      |
| SOF      | 74.8 ± 9.8     | 64.6 ± 12.6      | 67.5 ± 11.2     |
| avg OA   | 76.5 ± 10.6    | 69.9 ± 11.9      | 70.2 ± 11.1     |
| BSDB     | 72.5 ± 12.0 (DT) | 77.6 ± 11.3    | 77.3 ± 11.4     |

and on the test set of the BSDB dataset. We also show the results obtained on U-Sleep-v1 trained from scratch (S) on the BSDB dataset, and the results obtained on the model pre-trained in (i) on OA and then fine-tuned (FT) on the BSDB dataset. Unlike what we expected, both the models (S) and (FT), trained with a large and a highly heterogeneous database, are not able to generalize on the OA datasets from the different data centers. The average performance achieved on the OA with (S) and (FT) models is significantly lower compared to the performance of the model pre-trained on OA (paired t-tests $p-value < 0.001$). Whilst, with both (S) and (FT) we show a significant increase in performance compared to the direct transfer (DT), on the test set of the BSDB dataset (paired t-tests $p-value < 0.001$). We also found that the training from scratch results in significantly higher performance (paired t-test $p-value < 0.001$) on the BSDB dataset, compared to the performance of the fine-tuned model. No significant difference (paired t-test $p-value > 0.05$) occurs between (S) and (FT) evaluated on the average performance on OA datasets. The pre-training on the OA dataset was not beneficial for the model fine-tuned on the BSDB dataset. With a large number of highly heterogeneous subjects, we can directly train the model from scratch on the dataset. However, we have to mention that the main advantage of using the fine-tuned model is that it reaches same
Table 4 (iii) Performance of U-Sleep-v1 on a single model fine-tuned on all the training set of the seven BSDB groups (FT); on seven/two models fine-tuned on the independent training set of each group (FT-I) with $G = 7$ and $G = 2$ respectively; and on a single model fine-tuned on all the training set of the seven/two BSDB groups conditioned (FT-SaBN) by $G = 7$ and by $G = 2$ groups respectively. All the fine-tuned models are evaluated on the associated test set of each group. We report the F1-score ($\%$F1), specifically the mean value and the standard deviation ($\mu \pm \sigma$) computed across the recordings. B: Babies (0-3 years); C: Children (4-12 years); A: Adolescents (13-18 years); YA: Young Adults (19-39 years); MA: Middle Aged Adults (40-59 years); E: Elderly (60-69 years); OE: Old Elderly ($> 70$ years). When $G = 2$ we have the following two groups $G_1 = \{B \cup C\}$, $G_2 = \{A \cup YA \cup MA \cup E \cup OE\}$, further details in Supplementary Notes: Age Analysis.

| Subsets | FT (G=1) | FT-I (G=7) | FT-I (G=2) | FT-SaBN (G=7) | FT-SaBN (G=2) |
|---------|----------|------------|------------|---------------|---------------|
| B       | 74.9 ± 6.8 | 74.1 ± 6.6 $^G_1$ | 74.8 ± 6.2 $^G_1$ | 72.2 ± 7.7 | 72.6 ± 7.7 |
| C       | 75.0 ± 9.8 | 74.9 ± 9.2 $^G_2$ | 75.9 ± 9.1 $^G_1$ | 74.8 ± 8.9 | 75.6 ± 10.1 |
| A       | 82.7 ± 13.7 | 80.0 ± 14.6 $^G_3$ | 82.8 ± 13.6 $^G_2$ | 82.3 ± 13.7 | 82.0 ± 14.0 |
| YA      | 80.8 ± 11.5 | 80.6 ± 11.6 $^G_4$ | 80.6 ± 11.6 $^G_2$ | 80.3 ± 11.9 | 79.9 ± 11.9 |
| MA      | 80.4 ± 7.8 | 79.90 ± 8.0 $^G_5$ | 79.8 ± 8.2 $^G_2$ | 79.6 ± 8.0 | 79.4 ± 8.3 |
| E       | 75.7 ± 10.1 | 74.2 ± 10.7 $^G_6$ | 74.9 ± 10.2 $^G_2$ | 74.5 ± 10.6 | 73.9 ± 10.9 |
| OE      | 75.2 ± 11.7 | 73.9 ± 11.0 $^G_7$ | 74.9 ± 11.3 $^G_2$ | 73.8 ± 11.7 | 74.0 ± 11.3 |
| avg     | 77.9 ± 10.7 | 77.0 ± 10.8 | 77.6 ± 10.7 | 76.9 ± 11.0 | 76.8 ± 11.1 |

(iii) Training conditioned by age. In Table 4 we show the performance of U-Sleep-v1 fine-tuned (FT) on all the training sets of the seven BSDB groups, i.e., single model. We also report the performance achieved using the training set of each group independently (FT-I) with $G = 7$ and $G = 2$ respectively (i.e., seven and two models), and the performance achieved using the training set of the seven/two BSDB groups conditioned (FT-SaBN) by $G = 7$ and by $G = 2$ groups respectively (i.e., single model). The mean and the standard deviation of the F1-score ($\%$F1), are computed across the recordings of the test set of each of the seven BSDB age groups. Comparing both the experiments (FT-I and FT-SaBN) and types of grouping ($G=2$ and $G=7$) with the baseline (FT), we did not find a statistically significant increase of the performance in any of the subgroups (paired t-test $p$-value $> 0.05$). Despite the lack of significant performance differences in our age-conditioned models, REM sleep seems to be less accurately predicted for small children, if the training data set only consists of data from adults (see Supplementary Figure 13, confusion matrix for test $\{CH\}$ against Model 1b). This is an interesting finding since small children exhibit more REM sleep (see Supplementary Figure 10). Visual scoring guidelines for small children differ from the guidelines for adults, with REM sleep scoring strongly relying on irregular respiration [59]. However, overall these results show that, despite
the age-related differences, the architecture is able to deal with different age subgroups at the same time, without needing to have access to chronological age-related information during the training procedure.

3 Discussions

In this paper we demonstrate the resilience of a DL network, when trained on a large and heterogeneous dataset. We focused on three of the most significant aspects: channel derivation selection, multi centre heterogeneity needs and age conditioned fine tuning. Channel derivations do have complementary information, and a DL based model resulted resilient enough to be able to extract sleep patterns also from mismatched, atypical and clinically non-recommended derivations. We showed that the variability among different sleep data centers (e.g., hardware, scoring rules etc.) needs to be taken into account more than the variability inside one single sleep center. A large database such as the BSDB (sleep disorder patient cohort of the Inselspital, with patients covering the full spectrum of sleep disorders) did not have enough heterogeneity to strengthen the performance of the DL based model on unseen data centers. Lastly, we show that a state-of-the-art DL network is able to deal with different age groups simultaneously, mitigating the need of adding chronological age-related information during training.

The resilience of the DL based model to the atypical or non-conventional channel derivations is fascinating. The model still learns relevant sleep patterns while solving the scoring tasks with high state-of-the-art performance on multiple large-scale-heterogeneous data cohorts. Although this is a remarkable finding, it would be useful to further investigate the reasons why the DL model is still able to encode clinically valid information. DL has been criticised for its non-interpretability and its black-box behavior, factors that may actually limit its implementation in sleep centers. Future works should focus on solving the following open question: which sleep patterns/features our DL algorithms are encoding/highlighting from the typical/atypical channel derivations?

AASM scoring rules have been widely criticized over the years, for many aspects. The scoring manual has been designed to consider the sleep stages almost as discrete entities. However, it is well-known that sleep should be viewed as a continuum/gradual transition from one stage to another. A growing consensus suggests that we should reconsider the scoring rules and the entire scoring procedure. Given the high variability among the individual scorers and different sleep centers, more efforts should be made to improve the standardization of the methodology. This variability inevitably affects the performance of any kind of algorithm, since all algorithms are learning from the noisy variability of labels given by physicians. A relevant finding of this paper is indeed that the heterogeneity given by data coming from different sleep data centers (e.g., different sleep scorers) is much more relevant than
the variability coming from patients affected by different sleep disorders. This latter insight raises a research question yet to be answered, i.e., how could we define and quantify the heterogeneity of a sleep database? To what extent could we consider a database heterogeneous enough, to allow the algorithm to generalize across different data domains/centers?

The age-related findings leave room to an important observation: the DL algorithm is intrinsically encoding age-related features, which may not be categorized into discrete age-subgroups. As sleep should be considered as a continuous physiological process, the hyperspace of features associated to the respective age-subgroups should be considered continuum as well. We are forcing the algorithm to learn sleep patterns based on the chronological age of the subjects, but actually there are many other factors that the DL model is taking into account.

To our knowledge, our study on the automatic sleep scoring task is the largest in terms of number of polysomnography recordings and diversity with respect to both patient clinical pathology and age spectrum.

Our final consideration relates to the general approach to solve the automated scoring dilemma. DL algorithms have reached better performance than feature based approach, DL is definitely able in learning features alone. DL better resemble the unconscious wide and comprehensive knowledge of the human beings, that cannot be discretized in a set of well defined features. Being the AASM so widely criticized, being the sleep labels so noisy (e.g., due to high inter- and intra- scorer variability), and being sleep so complex: could we delegate to a DL algorithm totally the scoring procedure? Could an unsupervised approach, that does not use labels, be the solution?

4 Methods

4.1 U-Sleep architecture

U-Sleep \cite{11}, optimized version of its predecessor U-Time \cite{10}, is inspired by the popular U-Net architecture for image-segmentation \cite{60–62}. Below we briefly describe U-Sleep architecture, for further details we refer the reader to \cite{11}.

U-Sleep is a fully convolutional deep neural network. It takes as input a sequence of length \( L \) of 30-second epochs and outputs the predicted sleep stage for each epoch. The peculiarity of this architecture is that it defines the general function \( f(X; \theta) : \mathbb{R}^{L \times i \times C} \rightarrow \mathbb{R}^{L \times K} \), where \( L > 0 \) is any positive integer, \( \theta \) are the learning parameters, \( L \) is a number of fixed-length windows with \( i \) sampled points each, \( C \) the number of PSG channels and \( K \) the number of sleep stages. Hence, U-Sleep takes in input any temporal section of a PSG (even the whole PSG) and output a sequence of labels for each fixed-length
$i > 0$ window. Ideally $L \cdot i > 4096$, because U-Sleep contains 12 pooling operations, downsampling the signal by a factor of 2. The architecture requires at least $C = 2$, one EEG and one EOG channel, sampled/resampled at 128Hz, with $K = 5$ \textit{i.e.} awake, $N1, N2, N3, R$.

U-Sleep architecture consists of three learning modules as shown in Figure 1.

- The \textit{encoder} module is designed to extract feature maps from the input signals, each resulting in a lower temporal resolution compared to its input. The module includes 12 encoder blocks. Each block consists of a 1D convolutional layer, one layer of activation function - \textit{i.e.} exponential linear unit (ELU), a batch normalization layer and one max-pooling layer.
- The \textit{decoder} module is designed to up-scale the feature maps to match the temporal resolution of the signals in input. We can interpret the output of the decoder as a high-frequency representation of the sleep stages at the same $f_s$ of the input signal (\textit{e.g.}, with $f_s = 128Hz$, output one sleep stage each $1/128Hz$). The module includes 12 decoder blocks. Each block consists of a nearest neighbour up-sampling layer (\textit{e.g.}, with a \textit{kernel size} = 2, the length of the feature map in input is doubled), a 1D convolutional layer, one layer of ELU activation function and a batch normalization layer. Then, a skip connection layer combines the up-scaled input with the output of the batch normalization layer of the corresponding encoder block. Finally, a 1D convolution, a ELU non-linearity and a batch normalization are applied to the stacked feature maps. The output has the same temporal resolution of the signal in input.
- The \textit{segment classifier} module is designed to segment the high-frequency representation output of the decoder into the desired sleep stage prediction frequency. The module consist of a dense segmentation layer (\textit{i.e.}
U-Sleep: resilient to AASM guidelines

1d convolution layer with a hyperbolic tangent activation function), an average-pooling layer (e.g., with kernel_size = stride_size = 30sec * f_s considering the same prediction frequency of a sleep scorer) and two 1D convolutional layers (the first using an ELU activation function, and the latter using a softmax activation function). The output of the segment classifier is a $L \times K$, where $L$ is the number of segments and $K = 5$ is the number of sleep stages.

The sequence length $L$, the number of filters, the kernel and the stride sizes are specified in Figure 1. The softmax function, together with the cross-entropy loss function, is used to train the model to output the probabilities for the five mutually exclusive classes $K$ that correspond to the five sleep stages. The architecture is trained end-to-end via backpropagation, using the sequence-to-sequence learning approach. The model is trained using mini-batch Adam gradient-based optimizer [63] with a learning rate $lr$. The training procedure runs up to a maximum number of iterations, as long as the break early stopping condition is satisfied.

Unlike [11], we consider early stopping and data augmentation as regularization techniques. As stated in [64] “regularization is any modification we make to a learning algorithm that is intended to reduce its generalization error but not its training error”. Early stopping and data augmentation do so in different ways, they both decrease the regularization error.

**Early stopping.** It provides guidance on how many iterations can be run before the model begins to overfit [65]. The training procedure is stopped as soon as the performance (i.e. F1-score) on the validation set is lower than it was in the previous iteration step. In our experiments, before hastily stopping the learning procedure, the algorithm runs for an additional number of iterations (by fixing the so called patience parameter). The model with the highest performance is the one we finally save.

**Data augmentation.** The signals in input are randomly modified during training procedure to improve model generalization. Variable length of the sequences in input are replaced with a Gaussian noise. For each sample in a batch, with 0.1 probability, a fraction of the sequence is replaced with $N(\mu = \hat{\mu}, \sigma^2 = 0.01)$, where $\hat{\mu}$ is the mean of the sample’s signals. The fraction is sampled with a log-uniform distribution $\{\text{min} = 0.001; \text{max} = 0.33\}$. With a 0.1 probability at most one channel is entirely replaced by noise.

The training parameters (e.g., adam-optimizer parameters beta1 and beta2, mini-batch size etc.) are all set as stated in [11]. The learning rate, the early stopping patience parameter and the maximum number of iterations have been changed to $10^{-5}$, 100 and 1000 respectively, to let U-Sleep converge faster. The architecture has several hyperparameters (e.g., number of layers, number/sizes of filters, regularization parameters, training parameters etc.) which could be optimized to tune its performance on any dataset. We decided
to not systematically tune all these parameters, as this is out of our scope, but to fix them for all the experiments, as done in the original network.

**Data pre-processing.** The signals are resampled to 128Hz and rescaled (per channel and per-subject), so that, for each channel, the EEG signal has median 0 and inter quartile range (IRQ) 1. The values with an absolute deviation from the median above 20*IQR are clipped. The signals outside the range of the scored hypnogram are trimmed. The recordings scored according to Rechtschaffen and Kales rules results in six scoring classes, *i.e.* awake, N1, N2, N3, N4, and REM. In order to use the AASM standard, we merge the N3 and N4 stages into a single stage N3. The loss function for stages as MOVEMENT and UNKNOWN is masked during the training procedure.

**Data sampling.** U-Sleep is trained using mini-batch Adam gradient-based optimizer. Each element in the batch is a sequence/segment of $L = 35$ EEG and EOG 30-second signals/epochs from a single subject. Each sequence/element is sampled from the training data as follows. (1) dataset sampling: one dataset is selected randomly. The probability that a dataset $D$ is selected is given by $P(D) = \alpha P_1(D) \cdot (1 - \alpha)P_2(D)$, where $P_1(D)$ is the probability that a dataset is sampled with a uniform distribution $1/N_D$, where $N_D$ is the number of available datasets, and $P_2(D)$ is the probability of sampling a dataset according to its size. The parameter $\alpha$ was set to 0.5 to equally weight $P_1(D)$ and $P_2(D)$; (2) subject sampling: a recording $S_D$ is uniformly sampled from $D$; (3) channel sampling: one EEG and one EOG are uniformly sampled from the available combinations of channels in $S_D$ (*e.g.*, if 2 EEG and 2 EOG channels are available, four combinations would be possible); (4) segment sampling: a segment of EEG/EOG signals of length $L = 35$ is selected as follows: first uniformly sample a class from $W, N1, N2, N3, R$, then select randomly a 30-second epoch scored with the sampled class and finally shift the chosen epoch in a random position of the segment of length $L$.

### 4.2 Transfer learning

We define transfer learning quoting the following clear and simple statements: "Transfer learning and domain adaptation refer to the situation where what has been learned in one setting (*e.g.*, distribution $P_1$) is exploited to improve generalization in another setting (say, distribution $P_2$)" by [64]; or in other words "Given a source domain $D_S$ and learning task $T_S$, a target domain $D_T$ and learning task $T_T$, transfer learning aims to help improve the learning of the target predictive function $f_T(\cdot)$ in $D_T$ using the knowledge in $D_S$ and $T_S$, where $D_S \neq D_T$ and $T_S \neq T_T$" by [66].

Formally, let $P_1 = D_S = \{X_S, Y_S\}$ denote the data domain $S$ with the biosignal/feature space $X_S$ and the corresponding label space $Y_S$. Let $T_S$ denote the task in the domain $S$ maximizing the conditional probability distributions $P(y_S|x_S)$, where $x_S \in X_S$ and $y_S \in Y_S$. Similarly, let $P_2 = D_T = \{X_T, Y_T\}$ denote the data domain $T$ with the biosignal/feature space $X_T$ and the
corresponding label space $Y_T$. $T_T$ denote the task in the domain $T$ maximizing the conditional probability distributions $P(y_T|x_T)$, where $x_T \in X_T$ and $y_T \in Y_T$. The transfer learning technique aim to improve the learning of the distributions $P(y_T|x_T)$ given what we previously learned from $D_S$ and $T_S$, where $D_S \neq D_T$ or $T_S \neq T_T$.

Overall the transfer learning approach have the following advantages: (1) the time-complexity of the training phase on the target domain (i.e., fine-tuning procedure) is drastically reduced in respect to that required if the learning process is made from scratch; (2) it does not require a big-sized training set, making the approach feasible when labelled data are missing; (3) the source model is already pre-trained, hence the hyperparameters are already tuned/optimized. This allow to reach quickly high performances on the target task without re-designing the model and without lose its generalization capabilities. As highlighted in [66], we can define two macro-classes of transfer learning approaches. Inductive transfer refers to those scenario in which both the task and the domain are different in the source and target model; transductive transfer defines a method in which the model adapts to a different target domain where, however, the source and the target task are the same. Transductive transfer is exactly what we do in our experiments, where $T_S \equiv T_T$, as the task is always to perform sleep staging with the same set of sleep classes/stages.

The main challenges when handling with transfer learning are "what" transfer, "when" transfer and "how" transfer. "What" refers to the data domain shifts (e.g., different hardware, different subject distributions with different disorders) and the disagreement between the predictions of the model and labels given by different physicians. "When" is not the major issue here as we will perform the transfer only once, and directly on the whole target dataset available. "How" is the most challenging decision. The process involves overwriting a knowledge from a small-sized database to a previous big-sized knowledge (result of a long training process). In this scenario, one concern is to avoid ending up in what the data scientists call catastrophic forgetting: "Also known as catastrophic interference, it is the tendency of an artificial neural network to completely and abruptly forget previously learned information upon learning new information" by [67].

Even if it is conceptually easy to understand, avoiding its occurrence is not trivial. To partially bypass this phenomena we fine-tune the architecture on the target domain using a smaller learning rate.

In our experiments we will first pre-train the architecture on the data-source domain $S$ (e.g., a set of different domains/databases \{ $S_{DB_1}, S_{DB_2}, ..., S_{DB_n}$ \}), then we fine-tune the model on the data-target domain $T$. Formally, we first minimize the loss function $L_S$, resulting in the learned parameters $\theta$: 
argmin_θ = \sum_{(x,y) \in D_S} L_S(x, P(y|x), P_\theta(y,x)) \tag{1}

The parameters θ of the pre-trained model will be used as the starting point on the data-target domain T. To transfer the learning on the new domain T, we fine-tune all the pre-trained parameters θ' = θ (i.e. the entire network is further trained on the new data domain T):

argmin_{θ'} = θ = \sum_{(x,y) \in D_T} L_T(x, P(y|x), P_\theta(y,x)) \tag{2}

4.3 Conditional learning

Basically all the sleep scoring architectures learn in a conditional way. The aim is to maximize the conditional probability distributions P(Y|X), where X are the sequences of the biosignals in input and Y are the corresponding ground-truth labels. For each epoch x_t in input the models aim to maximize the conditional probability distribution P(y_t|x_t), where y_t is the t-th one-hot encoded vector of the ground-truth label. Hence, the model is trained to minimize the prediction error conditioned only by the knowledge of X.

We know that the sleep data X often come from different sources or data domains. Even in the same cohort, subjects with different demographics and sleep disorders may occur, resulting in significant shifts in their sleep data X distributions. Imagine to have in the same data cohort G different groups of subjects \{g_1, g_2, ..., g_G\}, with \(g_1 = \{healthy\}, g_2 = \{sleep-\text{apnea}\}\) and so on. This additional information about the group (i.e. the sleep disorder group \(g_i\)) to which the subject belongs can be given in input to the model. So, we can either train G fully separated models, each maximizing G different P(Y|X) functions, or either train a single model maximizing the conditional probability distributions P(Y|X, \(g_i\)). The latter - i.e. train the joint model with the additional condition \(g_i\) - is the smartest approach; the tasks are similar enough to benefit from sharing the parameters and the extracted features.

We decided to exploit the batch normalization layers to insert the additional knowledge in the training of our model. In literature different normalization variants have been proposed by modulating the parameters of the vanilla batch normalization (BN) layer [68–72]. We decided to exploit the Sandwich Batch Normalization (SaBN) approach recently proposed in [73].

The vanilla BN [74] normalizes the samples in a mini-batch in input by using the mean μ and the standard deviation σ, and then re-scales them with the γ and β parameters. So, given the feature in input \(f \in \mathbb{R}^{B \times C \times H \times W}\), where \(B\) is the batch size, \(C\) is the number of channels and \(H\) and \(W\) are the height and width respectively, the vanilla BN computes:

\[ h = \gamma \left( \frac{f - \mu(f)}{\sigma(f)} \right) + \beta \tag{3} \]
where $\mu(f)$ and $\sigma(f)$ are the mean and variance running estimates (batch statistics, \textit{i.e.}, moving mean and moving variance) computed on $f$ along $(N, H, W)$ dimensions; $\gamma$ and $\beta$ are the re-scaling learnable parameters of the BN affine layer with shape $C$. Clearly, the vanilla BN has only a single re-scaling transform, indirectly assuming all features coming from a single data distribution. In [71], to tackle the data heterogeneity issue (\textit{i.e.}, images from different data domains/distributions), they propose the Categorical Conditional BN (CCBN), so boosting the quality of the generated images. The CCBN layer computes the following operation:

$$h = \gamma_g \left( \frac{f - \mu(f)}{\sigma(f)} \right) + \beta_g \quad g = 1, \ldots, G$$

where $\gamma_g$ and $\beta_g$ are the re-scaling learnable parameters of each $g$-th affine layer, where $g$ corresponds to the domain index associated to the input. The parameters of each affine layer are learned to capture the domain/distribution-specific information. In [73], instead, they propose the Sandwich Batch Normalization layer, an improved variant of the CCBN. They claim that different individual affine layers might cause an imbalanced learning for the different domains/distributions. They factorize the BN affine layer into one shared ”sandwich” BN layer cascaded by a set of independent BN affine layers, computed as follows:

$$h = \gamma_g (\gamma_{sa} \left( \frac{f - \mu(f)}{\sigma(f)} \right) + \beta_{sa}) + \beta_g \quad i = 1, \ldots, G$$

where $\gamma_{sa}$ and $\beta_{sa}$ are the re-scaling learnable parameters of the ”sandwich” shared affine BN layer, while, as above, $\gamma_g$ and $\beta_g$ are the re-scaling learnable parameters of each $g$-th affine layer, conditioned on the categorical input $g$. The SaBN enable the conditional fine-tuning of a pre-trained U-Sleep architecture, conditioned by the categorical index in input $g$.

### 4.4 Evaluation

In all our experiments we evaluate U-Sleep as stated in [11]. The model scores the full PSG, without considering the predicted class on a segment with a label different from the five sleep stages (\textit{e.g.}, segment labelled as 'UNKNOWN' or as 'MOVEMENT'). The final prediction is the results of all the possible combinations of the available EEG and EOG channels for each PSG. Hence, we use the majority vote, \textit{i.e.} the ensemble of predictions given by the multiple combination of channels in input.

The unweighted F1-score metric [75] has been computed on all the testing sets to evaluate the performance of the model on all the experiments. We compute the F1-score for all the five classes, we then combine them by calculating the unweighted mean. Note that the unweighted F1-scores reduce the absolute scores due to lower performance on less abundant classes such as sleep stage N1. For this reason, we also report in Supplementary Tables 9, 10, 11 and 12...
the results achieved in terms of weighted F1-score - i.e. the metric is weighted
by the number of true instances for each label, so as to consider the high imbal-
ance between the sleep stages. In that case, the absolute scores significantly
increases on all the experiments.

5 Ethical approval

Data usage was ethically approved in the framework of the E12034 - SPAS
(Sleep Physician Assistant System) Eurostar-Horizon 2020 program (Kan-
tonale Ethikkommission Bern, 2020-01094).

6 Data availability

The Bern Sleep Registry *BSDB*, the sleep disorder patient cohort of the Insel-
spital, University hospital Bern, is a not publicaly available. All other datasets
are in principle publicly available, most datasets require the user to complete
a data request form. The researchers and the use-case scenario need to be eli-
gible for a given dataset. In Table 1 we specify which datasets require approval
from a Data Access Committee and which are directly available online.

References

[1] Iber, C., Iber, C.: The AASM Manual for the Scoring of Sleep and Asso-
ciated Events: Rules, Terminology and Technical Specifications vol. 1.
American Academy of Sleep Medicine, Westchester, IL, ??? (2007)

[2] Ronzhina, M., Janoušek, O., Kolářová, J., Nováková, M., Honzík, P.,
Provazník, I.: Sleep scoring using artificial neural networks. Sleep medicine
reviews 16(3), 251–263 (2012)

[3] Şen, B., Peker, M., Çavuşoğlu, A., Çelebi, F.V.: A comparative study on
classification of sleep stage based on eeg signals using feature selection and
classification algorithms. Journal of medical systems 38(3), 18 (2014)

[4] Radha, M., Garcia-Molina, G., Poel, M., Tononi, G.: Comparison of fea-
ture and classifier algorithms for online automatic sleep staging based on
a single eeg signal. In: 2014 36th Annual International Conference of the
IEEE Engineering in Medicine and Biology Society, pp. 1876–1880 (2014).
IEEE

[5] Aboalayon, K., Faezipour, M., Almuhammadi, W., Moslehpour, S.: Sleep
stage classification using eeg signal analysis: a comprehensive survey and
new investigation. Entropy 18(9), 272 (2016)
[6] Boostani, R., Karimzadeh, F., Nami, M.: A comparative review on sleep stage classification methods in patients and healthy individuals. Computer methods and programs in biomedicine 140, 77–91 (2017)

[7] Fiorillo, L., Puiatti, A., Papandrea, M., Ratti, P.-L., Favaro, P., Roth, C., Bargiotas, P., Bassetti, C.L., Faraci, F.D.: Automated sleep scoring: a review of the latest approaches. Sleep medicine reviews 48, 101204 (2019)

[8] Tsinalis, O., Matthews, P.M., Guo, Y.: Automatic sleep stage scoring using time-frequency analysis and stacked sparse autoencoders. Annals of biomedical engineering 44(5), 1587–1597 (2016)

[9] Dong, H., Supratak, A., Pan, W., Wu, C., Matthews, P.M., Guo, Y.: Mixed neural network approach for temporal sleep stage classification. IEEE Transactions on Neural Systems and Rehabilitation Engineering 26(2), 324–333 (2018)

[10] Perslev, M., Jensen, M., Darkner, S., Jennum, P.J., Igel, C.: U-time: A fully convolutional network for time series segmentation applied to sleep staging. Advances in Neural Information Processing Systems 32 (2019)

[11] Perslev, M., Darkner, S., Kempfner, L., Nikolic, M., Jennum, P.J., Igel, C.: U-sleep: resilient high-frequency sleep staging. NPJ digital medicine 4(1), 1–12 (2021)

[12] Tsinalis, O., Matthews, P.M., Guo, Y., Zafeiriou, S.: Automatic sleep stage scoring with single-channel eeg using convolutional neural networks. arXiv preprint arXiv:1610.01683 (2016)

[13] Vilamala, A., Madsen, K.H., Hansen, L.K.: Deep convolutional neural networks for interpretable analysis of eeg sleep stage scoring. In: 2017 IEEE 27th International Workshop on Machine Learning for Signal Processing (MLSP), pp. 1–6 (2017). IEEE

[14] Zhang, J., Wu, Y.: Complex-valued unsupervised convolutional neural networks for sleep stage classification. Computer methods and programs in biomedicine 164, 181–191 (2018)

[15] Chambon, S., Galtier, M.N., Arnal, P.J., Wainrib, G., Gramfort, A.: A deep learning architecture for temporal sleep stage classification using multivariate and multimodal time series. IEEE Transactions on Neural Systems and Rehabilitation Engineering 26(4), 758–769 (2018)

[16] Cui, Z., Zheng, X., Shao, X., Cui, L.: Automatic sleep stage classification based on convolutional neural network and fine-grained segments. Complexity 2018 (2018)
U-Sleep: resilient to AASM guidelines

[17] Olesen, A.N., Jennum, P., Peppard, P., Mignot, E., Sorensen, H.B.: Deep residual networks for automatic sleep stage classification of raw polysomnographic waveforms. In: 2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), pp. 1–4 (2018). IEEE

[18] Patanaik, A., Ong, J.L., Gooley, J.J., Ancoli-Israel, S., Chee, M.W.: An end-to-end framework for real-time automatic sleep stage classification. Sleep 41(5), 041 (2018)

[19] Sors, A., Bonnet, S., Mirek, S., Vercueil, L., Payen, J.-F.: A convolutional neural network for sleep stage scoring from raw single-channel eeg. Biomedical Signal Processing and Control 42, 107–114 (2018)

[20] Yildirim, O., Baloglu, U.B., Acharya, U.R.: A deep learning model for automated sleep stages classification using psg signals. International journal of environmental research and public health 16(4), 599 (2019)

[21] Fiorillo, L., Wand, M., Marino, I., Favaro, P., Faraci, F.D.: Temporal dependency in automatic sleep scoring via deep learning based architectures: An empirical study. In: 2020 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), pp. 3509–3512 (2020). IEEE

[22] Michielli, N., Acharya, U.R., Molinari, F.: Cascaded lstm recurrent neural network for automated sleep stage classification using single-channel eeg signals. Computers in biology and medicine 106, 71–81 (2019)

[23] Phan, H., Andreotti, F., Cooray, N., Chén, O.Y., De Vos, M.: Seqsleepnet: End-to-end hierarchical recurrent neural network for sequence-to-sequence automatic sleep staging. IEEE Transactions on Neural Systems and Rehabilitation Engineering, 1 (2019). https://doi.org/10.1109/TNSRE.2019.2896659

[24] Supratak, A., Dong, H., Wu, C., Guo, Y.: Deepsleepnet: a model for automatic sleep stage scoring based on raw single-channel eeg. IEEE Transactions on Neural Systems and Rehabilitation Engineering 25(11), 1998–2008 (2017)

[25] Biswal, S., Sun, H., Goparaju, B., Westover, M.B., Sun, J., Bianchi, M.T.: Expert-level sleep scoring with deep neural networks. Journal of the American Medical Informatics Association 25(12), 1643–1650 (2018)

[26] Malafeev, A., Laptev, D., Bauer, S., Omlin, X., Wierzbicka, A., Wichniak, A., Jernajczyk, W., Riener, R., Buhmann, J.M., Achermann, P.: Automatic human sleep stage scoring using deep neural networks. Frontiers in Neuroscience 12, 781 (2018)
[27] Stephansen, J.B., Olesen, A.N., Olsen, M., Ambati, A., Leary, E.B., Moore, H.E., Carrillo, O., Lin, L., Han, F., Yan, H., et al.: Neural network analysis of sleep stages enables efficient diagnosis of narcolepsy. Nature communications 9(1), 5229 (2018)

[28] Back, S., Lee, S., Seo, H., Park, D., Kim, T., Lee, K.: Intra-and inter-epoch temporal context network (iitnet) for automatic sleep stage scoring. arXiv preprint arXiv:1902.06562 (2019)

[29] Mousavi, S., Afghah, F., Acharya, U.R.: Sleepeegnet: Automated sleep stage scoring with sequence to sequence deep learning approach. PloS one 14(5), 0216456 (2019)

[30] Seo, H., Back, S., Lee, S., Park, D., Kim, T., Lee, K.: Intra-and inter-epoch temporal context network (iitnet) using sub-epoch features for automatic sleep scoring on raw single-channel eeg. Biomedical Signal Processing and Control 61, 102037 (2020)

[31] Phan, H., Chén, O.Y., Koch, P., Lu, Z., McLoughlin, I., Mertins, A., De Vos, M.: Towards more accurate automatic sleep staging via deep transfer learning, IEEE Transactions on Biomedical Engineering 68(6), 1787–1798 (2020)

[32] Supratak, A., Guo, Y.: Tinysleepnet: An efficient deep learning model for sleep stage scoring based on raw single-channel eeg. In: 2020 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), pp. 641–644 (2020). IEEE

[33] Phan, H., Chén, O.Y., Tran, M.C., Koch, P., Mertins, A., De Vos, M.: Xsleepnet: Multi-view sequential model for automatic sleep staging, IEEE Transactions on Pattern Analysis and Machine Intelligence (2021)

[34] Rechtschaffen, A., Kales, A.: A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects. (1968)

[35] Nir, Y., Staba, R., Andrillon, T., Vyazovskiy, V., Cirelli, C., Fried, I., Tononi, G.: Regional slow waves and spindles in human sleep. Neuron 70(1), 153–169 (2011)

[36] Siclari, F., Bassetti, C., Tononi, G.: Conscious experience in sleep and wakefulness. Swiss Arch Neurol Psychiatry 163, 273–8 (2012)

[37] Ohayon, M., Carskadon, M., Guilleminault, C., Vitiello, M.: Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: Developing normative sleep values across the human lifespan. Sleep 27, 1255–73 (2004). https://doi.org/10.1093/sleep/27.7.1255
U-Sleep: resilient to AASM guidelines

[38] Kocevska, D., Lysen, T.S., Dotinga, A., Koopman-Verhoeff, M.E., Luijk, M.P., Antypa, N., Biermasz, N.R., Blokstra, A., Brug, J., Burk, W.J., et al.: Sleep characteristics across the lifespan in 1.1 million people from the netherlands, united kingdom and united states: a systematic review and meta-analysis. Nature human behaviour 5(1), 113–122 (2021)

[39] Guillot, A., Thorey, V.: Robustsleepnet: Transfer learning for automated sleep staging at scale. IEEE Transactions on Neural Systems and Rehabilitation Engineering 29, 1441–1451 (2021)

[40] Olesen, A.N., Jørgen Jennum, P., Mignot, E., Sorensen, H.B.D.: Automatic sleep stage classification with deep residual networks in a mixed-cohort setting. Sleep 44(1), 161 (2021)

[41] Vallat, R., Walker, M.P.: An open-source, high-performance tool for automated sleep staging. Elife 10, 70092 (2021)

[42] Mathis, J., Andres, D., Schmitt, W., Bassetti, C., Hess, C., Schreier, D.: The diagnostic value of sleep and vigilance tests in central disorders of hypersonmolence. Sleep 45(3) (2022)

[43] Zhang, G.-Q., Cui, L., Mueller, R., Tao, S., Kim, M., Rueschman, M., Mariani, S., Mobley, D., Redline, S.: The national sleep research resource: towards a sleep data commons. Journal of the American Medical Informatics Association 25(10), 1351–1358 (2018)

[44] Bakker, J.P., Tavakkoli, A., Rueschman, M., Wang, W., Andrews, R., Malhotra, A., Owens, R.L., Anand, A., Dudley, K.A., Patel, S.R.: Gastric banding surgery versus continuous positive airway pressure for obstructive sleep apnea: a randomized controlled trial. American journal of respiratory and critical care medicine 197(8), 1080–1083 (2018)

[45] Rosen, C.L., Larkin, E.K., Kirchner, H.L., Emancipator, J.L., Bivins, S.F., Surovec, S.A., Martin, R.J., Redline, S.: Prevalence and risk factors for sleep-disordered breathing in 8-to 11-year-old children: association with race and prematurity. The Journal of pediatrics 142(4), 383–389 (2003)

[46] Redline, S., Tishler, P.V., Tosteson, T.D., Williamson, J., Kump, K., Browner, L., Ferrette, V., Krejci, P.: The familial aggregation of obstructive sleep apnea. American journal of respiratory and critical care medicine 151(3), 682–687 (1995)

[47] Marcus, C.L., Moore, R.H., Rosen, C.L., Giordani, B., Garetz, S.L., Taylor, H.G., Mitchell, R.B., Amin, R., Katz, E.S., Arens, R., et al.: A randomized trial of adenotonsillectomy for childhood sleep apnea. N Engl J Med 368, 2366–2376 (2013)
[48] Redline, S., Amin, R., Beebe, D., Chervin, R.D., Garetz, S.L., Giordani, B., Marcus, C.L., Moore, R.H., Rosen, C.L., Arens, R., et al.: The childhood adenotonsillectomy trial (chat): rationale, design, and challenges of a randomized controlled trial evaluating a standard surgical procedure in a pediatric population. Sleep 34(11), 1509–1517 (2011)

[49] Rosen, C.L., Auckley, D., Benca, R., Foldvary-Schaefer, N., Iber, C., Kapur, V., Rueschman, M., Zee, P., Redline, S.: A multisite randomized trial of portable sleep studies and positive airway pressure autotitration versus laboratory-based polysomnography for the diagnosis and treatment of obstructive sleep apnea: the homepap study. Sleep 35(6), 757–767 (2012)

[50] Chen, X., Wang, R., Zee, P., Lutsey, P.L., Javaheri, S., Alcántara, C., Jackson, C.L., Williams, M.A., Redline, S.: Racial/ethnic differences in sleep disturbances: the multi-ethnic study of atherosclerosis (mesa). Sleep 38(6), 877–888 (2015)

[51] Blackwell, T., Yaffe, K., Ancoli-Israel, S., Redline, S., Ensrud, K.E., Stefanick, M.L., Laffan, A., Stone, K.L., in Men Study Group, O.F.: Associations between sleep architecture and sleep-disordered breathing and cognition in older community-dwelling men: the osteoporotic fractures in men sleep study. Journal of the American Geriatrics Society 59(12), 2217–2225 (2011)

[52] Relationships between sleep stages and changes in cognitive function in older men: the mros sleep study. Sleep 38(3), 411–421 (2015)

[53] Goldberger, A.L., Amaral, L.A., Glass, L., Hausdorff, J.M., Ivanov, P.C., Mark, R.G., Mietus, J.E., Moody, G.B., Peng, C.-K., Stanley, H.E.: Physiobank, physiotoolkit, and physionet: components of a new research resource for complex physiologic signals. circulation 101(23), 215–220 (2000)

[54] Ghassemi, M.M., Moody, B.E., Lehman, L.-W.H., Song, C., Li, Q., Sun, H., Mark, R.G., Westover, M.B., Clifford, G.D.: You snooze, you win: the physionet/computing in cardiology challenge 2018. In: 2018 Computing in Cardiology Conference (CinC), vol. 45, pp. 1–4 (2018). IEEE

[55] Kemp, B., Zwinderman, A.H., Tuk, B., Kamphuisen, H.A., Obery, J.J.: Analysis of a sleep-dependent neuronal feedback loop: the slow-wave microcontinuity of the eeg. IEEE Transactions on Biomedical Engineering 47(9), 1185–1194 (2000)

[56] Quan, S.F., Howard, B.V., Iber, C., Kiley, J.P., Nieto, F.J., O’Connor, G.T., Rapoport, D.M., Redline, S., Robbins, J., Samet, J.M., et al.: The sleep heart health study: design, rationale, and methods. Sleep 20(12),
1077–1085 (1997)

[57] Cummings, S.R., Black, D.M., Nevitt, M.C., Browner, W.S., Cauley, J.A., Genant, H.K., Masiolli, S.R., Scott, J.C., Seeley, D.G., Steiger, P., et al.: Appendicular bone density and age predict hip fracture in women. Jama 263(5), 665–668 (1990)

[58] Spira, A.P., Blackwell, T., Stone, K.L., Redline, S., Cauley, J.A., Ancoli-Israel, S., Yaffe, K.: Sleep-disordered breathing and cognition in older women. Journal of the American Geriatrics Society 56(1), 45–50 (2008)

[59] Grigg-Damberger, M.M.: The visual scoring of sleep in infants 0 to 2 months of age. Journal of clinical sleep medicine 12(3), 429–445 (2016)

[60] Ronneberger, O., Fischer, P., Brox, T.: U-net: Convolutional networks for biomedical image segmentation. In: International Conference on Medical Image Computing and Computer-assisted Intervention, pp. 234–241 (2015). Springer

[61] Falk, T., Mai, D., Bensch, R., Çiçek, Ö., Abdulkadir, A., Marrakchi, Y., Böhm, A., Deubner, J., Jäckel, Z., Seiwald, K., et al.: U-net: deep learning for cell counting, detection, and morphometry. Nature methods 16(1), 67–70 (2019)

[62] Brandt, M., Tucker, C.J., Kariryaa, A., Rasmussen, K., Abel, C., Small, J., Chave, J., Rasmussen, L.V., Hiernaux, P., Diouf, A.A., et al.: An unexpectedly large count of trees in the west african sahara and sahel. Nature 587(7832), 78–82 (2020)

[63] Kingma, D.P., Ba, J.: Adam: A method for stochastic optimization. arXiv preprint arXiv:1412.6980 (2014)

[64] Goodfellow, I., Bengio, Y., Courville, A.: Deep Learning. MIT press, ??? (2016)

[65] Prechelt, L.: Early stopping—but when? In: Neural Networks: Tricks of the Trade, pp. 55–69. Springer, ??? (1998)

[66] Pan, S.J., Yang, Q.: A survey on transfer learning. IEEE Transactions on knowledge and data engineering 22(10), 1345–1359 (2009)

[67] McCloskey, M., Cohen, N.J.: Catastrophic interference in connectionist networks: The sequential learning problem. In: Psychology of Learning and Motivation vol. 24, pp. 109–165. Elsevier, ??? (1989)

[68] Dumoulin, V., Shlens, J., Kudlur, M.: A learned representation for artistic style. arXiv preprint arXiv:1610.07629 (2016)
[69] De Vries, H., Strub, F., Mary, J., Larochelle, H., Pietquin, O., Courville, A.C.: Modulating early visual processing by language. Advances in Neural Information Processing Systems 30 (2017)

[70] Huang, X., Belongie, S.: Arbitrary style transfer in real-time with adaptive instance normalization. In: Proceedings of the IEEE International Conference on Computer Vision, pp. 1501–1510 (2017)

[71] Miyato, T., Kataoka, T., Koyama, M., Yoshida, Y.: Spectral normalization for generative adversarial networks. arXiv preprint arXiv:1802.05957 (2018)

[72] Xie, C., Tan, M., Gong, B., Wang, J., Yuille, A.L., Le, Q.V.: Adversarial examples improve image recognition. In: Proceedings of the IEEE/CVF Conference on Computer Vision and Pattern Recognition, pp. 819–828 (2020)

[73] Gong, X., Chen, W., Chen, T., Wang, Z.: Sandwich batch normalization: A drop-in replacement for feature distribution heterogeneity. In: Proceedings of the IEEE/CVF Winter Conference on Applications of Computer Vision, pp. 2494–2504 (2022)

[74] Ioffe, S., Szegedy, C.: Batch normalization: Accelerating deep network training by reducing internal covariate shift. In: International Conference on Machine Learning, pp. 448–456 (2015). PMLR

[75] Sokolova, M., Lapalme, G.: A systematic analysis of performance measures for classification tasks. Information processing & management 45(4), 427–437 (2009)

7 Acknowledgements

F.D.F. was supported by SPAS: Sleep Physician Assistant System project, from Eurostars funding program. P.F. was supported by the Interfaculty Research Cooperation (IRC) Decoding Sleep: From Neurons to Health & Mind, from the University of Bern, Switzerland. A.T. was supported by the IRC Decoding Sleep: From Neurons to Health & Mind, from the University of Bern, and the Swiss National Science Foundation (#320030_188737). The National Sleep Research Resource was supported by the National Heart, Lung, and Blood Institute (R24 HL114473, 75N92019R002). The Apnea, Bariatric surgery, and CPAP study (ABC Study) was supported by National Institutes of Health grants R01HL106410 and K24HL127307. Philips Respironics donated the CPAP machines and supplies used in the perioperative period for patients undergoing bariatric surgery. The Cleveland Children’s Sleep and Health Study (CCSHS) was supported by grants from the National Institutes of Health (RO1HL60957, K23 HL04426, RO1 NR02707, M01 Rrmpd0380-39).
The Cleveland Family Study (CFS) was supported by grants from the National Institutes of Health (HL46380, M01 RR0080-39, T32-HL07567, RO1-46380). The Childhood Adenotonsillectomy Trial (CHAT) was supported by the National Institutes of Health (HL083075, HL083129, UL1-RR-024134, UL1 RR024989). The Home Positive Airway Pressure study (HomePAP) was supported by the American Sleep Medicine Foundation 38-PM-07 Grant: Portable Monitoring for the Diagnosis and Management of OSA. The Multi-Ethnic Study of Atherosclerosis (MESA) Sleep Ancillary study was funded by NIH-NHLBI Association of Sleep Disorders with Cardiovascular Health Across Ethnic Groups (RO1 HL098433). MESA is supported by NHLBI funded contracts HHSN268201500003I, N01-HC-95159, N01-HC-95160, N01-HC-95161, N01-HC-95162, N01-HC-95163, N01-HC-95164, N01-HC-95165, N01-HC-95166, N01-HC-95167, N01-HC-95168 and N01-HC-95169 from the National Heart, Lung, and Blood Institute, and by cooperative agreements UL1-TR-000040, UL1-TR-001079, and UL1-TR-001420 funded by NCATS. The National Heart, Lung, and Blood Institute provided funding for the ancillary MrOS Sleep Study, "Outcomes of Sleep Disorders in Older Men," under the following grant numbers: R01 HL071194, R01 HL070848, R01 HL070847, R01 HL070842, R01 HL070841, R01 HL070837, R01 HL070838, and R01 HL070839. The Sleep Heart Health Study (SHHS) was supported by National Heart, Lung, and Blood Institute cooperative agreements U01HL53916 (University of California, Davis), U01HL53931 (New York University), U01HL53934 (University of Minnesota), U01HL53937 and U01HL64360 (Johns Hopkins University), U01HL53938 (University of Arizona), U01HL53940 (University of Washington), U01HL53941 (Boston University), and U01HL63463 (Case Western Reserve University).

8 Author contribution
All authors contributed to the design of the study; L.F. and G.M. implemented the system and conducted all the experiments; L.F., G.M. and F.D.F. wrote the paper with feedback from J.v.d.M, A.T., M.S. and P.F.; The BSDB dataset was extracted and prepared by J.v.d.M and M.P.; All authors approved the final paper.

9 Competing interests
The authors declare no competing interests.

10 Additional information
Publisher’s note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.
U-Sleep: resilient to AASM guidelines

Luigi Fiorillo¹,²*, Giuliana Monachino¹,²†, Julia van der Meer³, Marco Pesce³, Jan Warncke³, Markus H. Schmidt³, Claudio L.A. Bassetti³, Athina Tzovara¹,³, Paolo Favaro¹ and Francesca D. Faraci²

¹*Institute of Informatics, University of Bern, Neubrückstrasse 10, Bern, 3012, Switzerland.
²Institute of Digital Technologies for Personalized Healthcare | MeDiTech, Department of Innovative Technologies, University of Applied Sciences and Arts of Southern Switzerland, Via la Santa 1, Lugano, 6962, Switzerland.
³Sleep Wake Epilepsy Center | NeuroTec, Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Freiburgstrasse 16, Bern, 3010, Switzerland.

*Corresponding author(s). E-mail(s): luigi.fiorillo@supsi.ch; giuliana.monachino@supsi.ch; julia.vandermeer@insel.ch; marco.pesce@insel.ch; jan.warncke@insel.ch; markus.schmidt@insel.ch; claudio.bassetti@insel.ch; athina.tzovara@inf.unibe.ch; paolo.favaro@inf.unibe.ch; francesca.faraci@supsi.ch;
†These authors contributed equally to this work.
SUPPLEMENTARY MATERIAL

Supplementary notes

Dataset

We report a detailed description of all the datasets used in our experiments.

**ABC.** The Apnea, Bariatric surgery, and CPAP database consists of 132 recordings from 49 patients with severe obstructive sleep apnea and morbity obesity (BMI from 35 to 45) [1, 2]. EEG signals (F4-M1, F3-M2, C4-M1, C3-M2, O2-M1, O1-M2) and EOG signals (E2-M1, E1-M2) have been considered in our experiments. The signals are recorded at 256Hz, and hardware low-pass filtered and high-pass filtered at 105Hz and at 0.16Hz respectively. The recordings are manually scored by sleep experts according to the AASM rules. For more information we refer to https://doi.org/10.25822/nx52-bc11 and https://clinicaltrials.gov/ct2/show/NCT01187771.

**CCSHS.** The Cleveland Childrend’s Sleep and Health Study consists of children and adolescents recordings. In our experiments we consider 515 recordings from adolescents aged 16-19 years. The recordings are collected in three different hospitals around Cleveland, Ohio, US [1, 3]. EEG signals (C4-A1, C3-A2) and EOG signals (ROC-A1, LOC-A2) have been considered in our experiments. The signals are recorded at 128Hz, and hardware high-pass filtered at 0.15Hz. The recordings are manually scored by sleep experts according to the AASM rules. For more information we refer to https://doi.org/10.25822/cg2n-4y91.

**CFS.** The Cleveland Family Study is a family-based study on sleep apnea disordered subjects. The database consists of 2284 subjects from 361 families [1, 4]. We consider recordings of 730 subjects from 144 families (whence full whole-night PSG were available). For this specific database, the data split (train/val/test set) is done by considering subjects and family belonging (i.e., all the family members appear in the same data split). EEG signals (C4-A1, C3-A2) and EOG signals (ROC-A1, LOC-A2) have been considered in our experiments. The signals are recorded at 128Hz, and hardware low-pass filtered and high-pass filtered at 105Hz and 0.16 Hz respectively. The recordings are manually scored by sleep experts according to the AASM rules. For more information we refer to https://doi.org/10.25822/jmyx-mz90.

**CHAT.** The Childhood Adenotonsillectomy Trial database consists of 1638 recordings (452 baseline, 407 follow-up and 779 control) from 1232 children post-adenotonsillectomy-surgery aged 5-10 years. The recordings are collected in six different sleep centers in Massachusetts, Missouri, New York, Ohio and Pennsylvania [1, 5, 6]. EEG signals (F4-M1, F3-M2, C4-M1, C3-M2, O2-M1, O1-M2, T4-M1, T3-M2) and EOG signals (E2-M1, E1-M2) have been
considered in our experiments. The signals are recorded at 200Hz (or higher in other sleep centers), and different hardware filtering given the different acquisition systems. One recording has been excluded - EOG missing. The recordings are manually scored by sleep experts according to the AASM rules. For more information we refer to https://doi.org/10.25822/d68d-8g03 and https://clinicaltrials.gov/ct2/show/NCT00560859.

DCSM. The Danish Centre for Sleep Medicine database consists of 255 recordings from patients with potential and non-specific sleep related disorders. No demographic is available for the database. EEG signals (F4-M1, F3-M2, C4-M1, C3-M2, O2-M1, O1-M2, T4-M1, T3-M2) and EOG signals (E2-M1, E1-M2) have been considered in our experiments. The signals are recorded at 256Hz, and band-pass filtered between 0.3Hz and 70Hz. The recordings are manually scored by sleep experts according to the AASM rules. For more information we refer to https://sid.erda.dk/wsgi-bin/ls.py?share_id=fUH3xbOXv8.

HPAP. The Home Positive Airway Pressure database consists of 373 recordings (238 considered in our experiments) from obstructive sleep apnea patients aged over 18 years. The recordings are collected in seven different US sleep centers [1, 7]. EEG signals (F4-M1, F3-M2, C4-M1, C3-M2, O2-M1, O1-M2, T4-M1, T3-M2) and EOG signals (E2-M1, E1-M2) have been considered in our experiments. The signals are recorded at 200Hz, no filtering applied. Nine recordings have been excluded - EOG and/or reference channels missing. The recordings are manually scored by sleep experts according to the AASM rules. For more information we refer to https://doi.org/10.25822/xmwv-yz91 and https://clinicaltrials.gov/ct2/show/NCT00642486.

MESA. The Multi-Ethnic Study of Atherosclerosis consists of 2237 recordings (2056 considered in our experiments) from a cohort of black, white, Hispanic and Chinese-American subjects aged 45-84 years [1, 8]. EEG signals (Fz-Cz, C4-M1, Cz-Oz) and EOG signals (E2-Fpz, E1-Fpz) have been considered in our experiments. The signals are recorded at 256Hz, and hardware low-pass filtered at 100Hz. The recordings are manually scored by sleep experts according to the AASM rules. For more information we refer to https://doi.org/10.25822/n7hq-c406.

MROS. The database is a subset of the larger study Osteoporotic Fractures in Men (MrOS), involving 5,994 community-dwelling men aged over 65 years [1, 9, 10]. In our experiments we consider 3926 recordings (2900 from visit 1 and 1026 from visit 2) from 2903 subjects, which underwent in-home overnight PSG. EEG signals (C4-A1, C3-A2) and EOG signals (ROA-A1, LOC-A2) have been considered in our experiments. The signals are recorded at 256Hz, and hardware high-pass filtered at 0.15Hz. Seven recordings have been excluded - EOG channels and/or sleep stage annotation files missing. The recordings are manually scored by sleep experts according to the AASM
U-Sleep: resilient to AASM guidelines

rules. For more information we refer to https://doi.org/10.25822/kc27-0425.

**PHYS.** The database from the 1028 PhysioNet/CniC Challenge consists of 1985 recordings (994 labelled considered in our experiments) from patients with potential sleep disorders [11, 12]. EEG signals (F4-M1, F3-M2, C4-M1, C3-M2, O2-M1, O1-M2) and one EOG signal (E1-M2) have been considered in our experiments. The signals are recorded at 200Hz. The recordings are manually scored by sleep experts according to the AASM rules. For more information we refer to https://physionet.org/content/challenge-2018/1.0.0/.

**SEDF-SC & SEDF-ST.** The Sleep-EDF Expanded database consists of 197 recordings from two subset studies. The Sleep-EDF Sleep Cassette (SEDF-SC) consists of 153 recordings from 78 healthy subjects aged 25-101 years. The Sleep-EDF Sleep Telemetry (SEDF-ST) consists of 44 recordings from 22 healthy subjects with mild difficulty falling asleep (two recordings collected for each subject, i.e., one after temazepam intake and one after placebo intake) [11, 13]. EEG signals (Fpz-Cz, Pz-Oz) and one EOG signal (ROC-LOC) have been considered in our experiments. The signals are recorded at 100Hz. The recordings are manually scored by sleep experts according to the Rechtschaffen and Kales scoring rules, and re-aligned to the AASM rules as described at the end of this section. For more information we refer to https://doi.org/10.13026/C2C30J.

**SHHS.** The Sleep Heart Health Study consists of 8444 recordings (5793 from visit 1 and 2651 from visit 2) from 5797 patients with sleep-disordered breathing aged over 40 years [1, 14]. EEG signals (C4-A1, C3-A2) and EOG signals (ROC-A1, LOC-A2) have been considered in our experiments. The EEG and EOG signals are recorded at 125Hz and 50Hz respectively, and hardware high-pass filtered at 0.15Hz. The recordings are manually scored by sleep experts according to the Rechtschaffen and Kales scoring rules, and re-aligned to the AASM rules as described at the end of this section. For more information we refer to https://clinicaltrials.gov/ct2/show/NCT00005275 and https://doi.org/10.25822/ghy8-ks59.

**SOF.** The database is a subset of the larger study Osteoporotic Fractures (SOF). In our experiments we consider 453 recordings (from visit 8), which underwent in-home overnight PSG [1, 15, 16]. EEG signals (C4-A1, C3-A2) and EOG signals (ROC-A1, LOC-A2) have been considered in our experiments. The EEG and EOG signals are recorded at 128Hz, and hardware high-pass filtered at 0.15Hz. The recordings are manually scored by sleep experts according to the Rechtschaffen and Kales scoring rules, and re-aligned to the AASM rules as described at the end of this section. For more information we refer to https://doi.org/10.25822/e1cf-rx65.
Age analysis

(G=7) Age Groups by [17]

Inspired by the meta-analysis of quantitative sleep parameters from childhood to old age reported in [17], we decided to study, and then run all our experiments, on the following seven age groups: Babies (B; 0-3 years), Children (C; 4-12 years), Adolescents (A; 13-18 years), Young Adults (YA; 19-39 years), Middle Aged Adults (MA; 40-59 years), Elderly (E; 60-69 years), Old Elderly (OE; >70 years). Unlike in [17], we also considered the additional group of Babies, uncovered in their study. In Figure 1 and in Table 1, respectively, we show the age distribution of the BSDB dataset in the seven age groups, and we report the number of recordings, the age range, the age mean and standard deviation ($\mu \pm \sigma$) and the male/female percentage (M/F) for each group. For each PSG of the BSDB dataset we compute the following ten sleep parameters: Total Sleep Time (TST), Sleep Period Time (SPT), Wake After Sleep Onset (WASO), Sleep Latency (SL), Sleep Efficiency (SE), Percentage of N1 stage ($pN_1$), Percentage of N2 stage ($pN_2$), Percentage of N3 stage ($pN_3$), Percentage of REM stage ($pREM$) and Number of stage shifts per hour ($n_{\text{shift}}$). In Table 2 we report the mean and standard deviation ($\mu \pm \sigma$) of each sleep parameter for each age group. We also show the boxplots in Figures 2-11 computed on each sleep parameter and for each age group. In some of these plots emerge the continuous positive/negative trend on the specific sleep parameter from babies to old elderly subjects.

(G=2) Age Groups by AASM [18]

With sleep-specific age groups we refer to those suggested by the AASM scoring manual [18]. Indeed, it provides two sets of rules for visual sleep scoring, i.e., babies/children and adults.

The age boundary between the two groups is not well defined; in particular, it is not clear which group the subjects in the age range between 13 and 18 (adolescents) belong to. Therefore we started considering two groups plus the adolescents’ group: Babies/Children (CH; 0-12 years), Adolescents (A; 13-18 years), Adults (AD; < 19 years).

In Figure 12 and in Table 3, respectively, we show the age distribution of the BSDB dataset in the three age groups, and we report the number of recordings, the age range, the age mean and standard deviation ($\mu \pm \sigma$) and the male/female percentage (M/F) for each age group. We used U-sleep to evaluate if the PSGs of the Adolescents were closer to the Babies/Children’s recordings or to the Adults’ recordings. We run two different experiments on U-Sleep-v1: in experiment_1 we merge the recordings from the Adolescents with the Babies/Children; in experiment_2 we merge the recordings from Adolescents with the Adults. In both the experiments (1, 2), we fine-tuned two different models (a, b), resulting in four independently trained models: (1a) fine-tuning on $G_{1a} = \{CH \cup A\}$; (1b) fine-tuning on $G_{1b} = \{AD\}$; (2a)
fine-tuning on $G_{2a} = \{CH\}$; (2b) fine-tuning on $G_{2b} = \{A \cup AD\}$. For each experiment, we tested both the models (a) and (b) on the test set of the three groups $\{CH, A, AD\}$. In Table 4 we report the macro F1-score ($\%F1$), specifically the mean value and the standard deviation ($\mu \pm \sigma$), computed across the recordings. In bold we indicate the best performance achieved on each test set. We compared with a paired t-test the performance of the four models tested on the Adolescents. The model (2b), fine-tuned on $\{A \cup AD\}$, performs significantly better ($p-value < 0.05$) on the Adolescents than the model (1a), fine-tuned on $\{CH \cup A\}$, suggesting that Adolescents tend to be similar to Adults. This is confirmed by the fact that also the model (1b), fine-tuned on $\{AD\}$, performs better ($p-value < 0.05$) on the Adolescents than the model (1a), even without Adolescents’ recordings in the training set. The models (1b) and (2b), fine-tuned on Adults without or with Adolescents, reach the same performance (paired t-test $p-value > 0.05$), hence confirming again the statement above. We might conclude that the Adolescents belong to the Adults’ group, so as to run all the age conditioning analysis on the following two sleep-related age groups: $G_1 = \{B \cup C\}$ and $G_2 = \{A \cup YA \cup MA \cup E \cup OE\}$.

For both $\{CH\}$ and $\{AD\}$ we obtain the same performance (paired t-test $p-value > 0.05$) with the two models fine-tuned on the group itself, with or without Adolescents. However, we reached significantly lower performance (paired t-test $p-value < 0.01$) with the other two models fine-tuned on the complementary group. This latter statement strengthens the basic assumption that babies/children and adults are two clearly different groups for the deep learning scoring algorithm.

In Figure 13 we report the confusion matrix for each of the five models (0, 1a, 1b, 2a, 2b) and each of the three test sets $\{CH, A, AD\}$. With model (0) we refer to the model fine-tuned on the whole training set, regardless of the subjects’ age.
Noisy labels, uncertainty and query procedure

The visual scoring is a highly subjective procedure. In the last decades, [19–22] have been reporting high inter-scorer variability, i.e. the agreement between different scorers is of about 70%-80%. The labels we are using to train our sleep scoring algorithms are commonly annotated by a single scorer. It is well-known that the AASM scoring rules leave space for subjective interpretation. Hence, we are actually transferring the scorer’s subjectivity in our models. The labels should be considered noisy by nature. This noise may generate uncertainty during the training procedure. In our study we also exploit the label smoothing regularization technique to introduce additional noise on top of our labels, to better evaluate the uncertain predictions given from our model. In [23, 24] it has been shown that label smoothing helps improving robustness when learning with noisy labels.

The predicted sleep stage for each fixed-length $i > 0$ window comes with a probability value $\hat{p}$. As stated in [25], the probability value associated with the predicted sleep stage should mirror its ground truth correctness likelihood. When this happens the model is well calibrated. In [25] we also showed label smoothing [26] to be a suitable technique to improve the calibration of the model. In this study, we also train U-Sleep with the label smoothing techniques, to add some noise on the labels, to better calibrate the model and to evaluate its impact on our uncertainty estimate procedure. In a standard training of a neural network, the cross-entropy loss is minimized using the hard targets $y_k$ (i.e. hot encoded targets, ‘1’ for the correct class and ‘0’ for the other). When the model is trained with the label smoothing technique, the hard targets are weighted with the uniform distribution $1/K$ (eq. 1), and the cross-entropy loss is minimized using the weighted mixture of the targets (eq. 2).

$$y_k^{LSU} = y_k \cdot (1 - \alpha) + \alpha/K$$  \hspace{1cm} (1)

$$H(y, p) = \sum_{k=1}^{K} -y_k^{LSU} \cdot \log(\hat{p}_k)$$  \hspace{1cm} (2)

where $\alpha$ is the smoothing parameter, $K$ is the total number of classes, $y_k^{LSU}$ the targets smoothed with the uniform distribution, and $\hat{p}_k$ the softmax output probabilities. We fix the $\alpha$ smoothing parameter equal to 0.1.

We exploit the ensemble of the $M$ different predictions (i.e. one prediction for each combination of channel in input) and the query procedure introduced in [25] to estimate the model uncertainty, and consequently the uncertain predictions. We can compute the mean $\mu_{i,k}$ (eq. 3) and the variance $\sigma^2_{i,k}$ (eq. 4) of the $M$ predictions for each sleep stage $k$:

$$\mu_{i,k} = \frac{\sum_{m=1}^{M} \hat{p}_{m,i,k}}{M}$$  \hspace{1cm} (3)

$$\sigma^2_{i,k} = \frac{\sum_{m=1}^{M} (\hat{p}_{m,i,k} - \mu_{i,k})^2}{M}$$  \hspace{1cm} (4)
where $\hat{p}_{m,i,k}$ is the output probability for the sleep stage $k$ of the m-th prediction for the $i$-th 30-second epoch. The final prediction $\hat{y}_i$ of the model will be given by $max(\mu_i)$, which we will refer to as $\mu_{\max}$, along with the assigned variance value $\sigma^2\mu_{\max}$. As proposed in [25], the mean $\mu_{\max}$ and the variance $\sigma^2\mu_{\max}$ can be used as indicators of the model uncertainty. High $\mu_{\max}$ and low $\sigma^2\mu_{\max}$ indicate that the model is confident about its prediction, i.e. low degree of uncertainty. In this study, we use only the $\mu_{\max}$ query procedure introduced in [25], i.e., on each subject we select a fixed percentage of epochs with the lowest $\mu_{\max}$ value. It has been shown to be more efficient compared to the query procedure via $\sigma^2\mu_{\max}$. The query procedure requires the selection of a threshold $q\%$ on the distribution of the mean values. The selection criterion of the threshold value $q\%$ is based on a reasonable percentage of epochs to be re-sent to the physician for a secondary review. In our study we fix $q\%$ equal to 5%, as done in [25].

We found that training $U$-$Sleep$-$v1$ on the OA datasets with the label smoothing technique results in a significant decrease in performance compared to the baseline pre-trained in (ii) without label smoothing (paired t-test $p$-value < 0.001). Nonetheless, by adding some noise on the label during the training, we are able to select a significantly higher number of misclassified epochs among the selected ones (paired t-test $p$-value < 0.001). We thus succeed to better detect the uncertain predictions, see Table 5.
List of Figures

Fig. 1 Age distribution of the BSDB dataset in the seven age groups by [17].
Fig. 2  Boxplots on the Total Sleep Time for each age group (G=7).

Fig. 3  Boxplots on the Sleep Period Time for each age group (G=7).
**Fig. 4** Boxplots on the Wake After Sleep Onset for each age group (G=7).

**Fig. 5** Boxplots on the Sleep Latency for each age group (G=7).
Fig. 6  Boxplots on the Sleep Efficiency for each age group (G=7).

Fig. 7  Boxplots on the Percentage of N1 stage for each age group (G=7).
Fig. 8 Boxplots on the Percentage of N2 stage for each age group (G=7).

Fig. 9 Boxplots on the Percentage of N3 stage for each age group (G=7).
**Fig. 10** Boxplots on the Percentage of REM stage for each age group (G=7).

**Fig. 11** Boxplots on the Number of stage shifts per hour for each age group (G=7).
**Fig. 12** Age distribution of the BSDB dataset in the three age groups by AASM [18].
**Fig. 13** Fine-tuning performance (confusion matrix) on \(\{CH, A, AD\}\).
List of Tables

Table 1  Age groups by [17] overview with demographic statistics.

| Age groups | Recordings | Age in years (range) | Age in years (µ ± σ) | Sex % (F/M) * |
|------------|------------|----------------------|----------------------|---------------|
| B          | 151        | 0-3 1.6 ± 1.1        | 44/56                |
| C          | 246        | 4-12 7.8 ± 2.6       | 43/57                |
| A          | 177        | 13-17 15.3 ± 1.4     | 41/59                |
| YA         | 2106       | 18-39 29.7 ± 6.3     | 42/58                |
| MA         | 3655       | 40-59 50.4 ± 5.5     | 31/69                |
| E          | 1546       | 60-69 64.0 ± 2.8     | 30/70                |
| OE         | 988        | 70-91 75.1 ± 4.1     | 30/70                |

Table 2  Sleep parameters.

|        | TST (min) | SPT (min) | WASO (%) | SL (min) | SE | n shift (n/h) | pN1 (%) | pN2 (%) | pN3 (%) | pREM (%) |
|--------|-----------|-----------|----------|----------|----|---------------|---------|---------|---------|----------|
| all    | 340.2     | 402.0     | 15.7     | 18.1     | 84.3 | 20.8          | 20.2    | 44.6    | 17.9    | 14.5     |
| ± 83.7 | ± 71.4    | ± 13.6    | ± 25.1   | ± 13.6   | ± 7.8 | ± 15.1        | ± 14.2  | ± 12.3  | ± 7.6   |
| B      | 452.0     | 539.6     | 15.8     | 23.5     | 84.2 | 14.7          | 13.0    | 32.6    | 29.4    | 23.9     |
| ± 85.8 | ± 88.5    | ± 11.4    | ± 30.4   | ± 11.4   | ± 5.4 | ± 10.0        | ± 14.0  | ± 10.9  | ± 9.3   |
| C      | 430.2     | 465.9     | 7.5      | 20.3     | 92.5 | 12.9          | 8.0     | 36.5    | 36.5    | 17.0     |
| ± 73.3 | ± 75.9    | ± 7.4     | ± 28.3   | ± 7.4    | ± 4.1 | ± 6.6         | ± 11.6  | ± 13.4  | ± 6.9   |
| A      | 377.8     | 415.2     | 9.0      | 18.7     | 91.0 | 14.7          | 8.9     | 41.0    | 32.1    | 15.1     |
| ± 79.3 | ± 85.0    | ± 10.6    | ± 30.1   | ± 10.6   | ± 5.2 | ± 6.7         | ± 11.1  | ± 10.9  | ± 6.3   |
| YA     | 371.1     | 414.9     | 10.9     | 16.1     | 89.1 | 18.1          | 14.0    | 44.4    | 21.4    | 15.8     |
| ± 93.9 | ± 90.8    | ± 11.4    | ± 22.4   | ± 11.4   | ± 6.5 | ± 10.9        | ± 13.3  | ± 10.9  | ± 7.3   |
| MA     | 336.3     | 393.7     | 14.7     | 16.7     | 85.3 | 21.8          | 20.1    | 46.5    | 16.1    | 14.5     |
| ± 66.8 | ± 55.4    | ± 12.1    | ± 22.8   | ± 12.1   | ± 7.4 | ± 13.3        | ± 13.8  | ± 10.9  | ± 7.3   |
| E      | 311.4     | 389.6     | 20.3     | 20.0     | 79.7 | 22.8          | 25.3    | 45.1    | 14.5    | 13.0     |
| ± 72.6 | ± 56.8    | ± 14.7    | ± 26.5   | ± 14.7   | ± 8.1 | ± 15.9        | ± 14.6  | ± 11.9  | ± 7.5   |
| OE     | 287.8     | 385.6     | 25.7     | 22.6     | 74.3 | 23.4          | 31.9    | 41.5    | 13.8    | 11.6     |
| ± 73.4 | ± 53.2    | ± 15.7    | ± 32.0   | ± 15.7   | ± 8.3 | ± 19.3        | ± 15.8  | ± 12.2  | ± 7.4   |
**Table 3** Age groups by AASM [18] overview with demographic statistics.
* The percentage sex % (F/M) has been computed on different percentage (from 99.4% up to 99.5%) of the total recordings for each age group, given the lack of availability of the gender information.

| Age groups | Recordings | Age in years (range) | Age in years ($\mu \pm \sigma$) | Sex % (F/M) * |
|------------|------------|----------------------|-------------------------------|---------------|
| CH         | 397        | 0-12                 | 5.4 $\pm$ 3.7                | 43/57         |
| A          | 177        | 13-17                | 15.3 $\pm$ 1.4               | 41/59         |
| AD         | 8295       | 18-91                | 50.6 $\pm$ 15.6              | 34/66         |

**Table 4** Performance of *U-Sleep-v1* fine-tuned on $\{CH, A, AD\}$. We report the F1-score (%F1), specifically the mean value and the standard deviation ($\mu \pm \sigma$) computed across the recordings. Best shown in bold.

| Test Subsets | Experiment 1 | Experiment 2 |
|--------------|--------------|--------------|
|              | (1a) $\{CH, A\}$ | (1b) $\{AD\}$ | (2a) $\{CH\}$ | (2b) $\{A, AD\}$ |
| CH           | $75.3 \pm 8.0$ | $68.2 \pm 12.4$ | $75.4 \pm 7.9$ | $71.8 \pm 10.2$ |
| A            | $76.5 \pm 19.1$ | $82.9 \pm 13.7$ | $78.4 \pm 18.1$ | $82.8 \pm 13.6$ |
| AD           | $72.1 \pm 13.0$ | $77.7 \pm 10.9$ | $72.2 \pm 13.3$ | $77.5 \pm 10.8$ |
Table 5 Performance of U-Sleep-v1, pre-trained on the OA datasets, and evaluated on all the test set of the OA datasets (avg OA) with and without (i.e., U-Sleep-v1 pre-trained in (ii)) label smoothing. We report the F1-score (%F1), referred to the epochs kept after the $\mu_{\text{max}}$ query selection procedure ($q\%$ threshold value fixed to 5%), and we report percentage of misclassified epochs among the rejected with query (%miscl.). Specifically, we report the mean value and the standard deviation ($\mu \pm \sigma$) computed across the recordings.

| Dataset | w/o label smoothing | w/ label smoothing |
|---------|---------------------|--------------------|
| avg OA  | %F1                 | µ ± σ              |
|         | 78.1 ± 11.2         | 72.5 ± 12.4        |
|         | %miscl.             | 51.1 ± 9.5         | 53.7 ± 10.6 |

Table 6 Atypical and/or randomly ordered channel derivations. U-Sleep channel extraction for each open database: (U-Sleep-v0) atypical and/or randomly ordered channel derivations are extracted from the available channels; (U-Sleep-v1) correctly ordered channel derivations are extracted from the available channels, i.e., expected clinical derivations meant to be extracted in [27].

| Datasets | Channel type | U-Sleep-v0 | U-Sleep-v1 |
|----------|--------------|------------|------------|
| ABC      | EEG          | F3-F4      | F3-M2      |
|          |              | O1-C3      | F4-M1      |
|          |              | C4-F4      | C3-M2      |
|          |              | E2-C3      | C4-M1      |
|          |              | O2-F4      | O1-M2      |
|          |              | M1-C3      | O2-M1      |
|          | EOG          | M2-F4      | E1-M2      |
|          |              | E1-C3      | E2-M1      |
| CCSHS    | EEG          | LOC-C4     | C3-A2      |
|          |              | M2-ROC     | C4-A1      |
|          | EOG          | M1-C4      | LOC-A2     |
|          |              | C3-ROC     | ROC-A1     |
| CFS      | EEG          | A2-A1      | C3-A2      |
|          |              | C3-C4      | C4-A1      |
|          | EOG          | ROC-A1     | LOC-A2     |
|          |              | LOC-C4     | ROC-A1     |
| CHAT *   | EEG          | M2-E1      | F3-M2      |
|          |              | F4-T4      | F4-M1      |
|          |              | C3-E1      | C3-M2      |
|          |              | E2-T4      | C4-M1      |
|          |              | C4-E1      | T3-M2      |
|          |              | T3-T4      | T4-M1      |

Continued on next page
## U-Sleep: resilient to AASM guidelines

| Datasets | Channel type | U-Sleep-v0 | U-Sleep-v1 |
|----------|--------------|------------|------------|
|          |              | M1-E1      | O1-M2      |
|          |              | O2-T4      | O2-M1      |
| EOG      | O1-E1        | E1-M2      |
|          | F3-T4        | E2-M1      |

| DCSM     | EEG          | F3-M2      | F3-M2      |
|          | F4-M1        | F4-M1      |
|          | C3-M2        | C3-M2      |
|          | C4-M1        | C4-M1      |
|          | O1-M2        | O1-M2      |
|          | O2-M1        | O2-M1      |

| HPAP **  | EEG          | F3-M2      |
|          |              | F4-M1      |
|          |              | C3-M2      |
|          |              | C4-M1      |
|          |              | O1-M2      |
|          |              | O2-M1      |
| EOG      |              | E1-M2      |
|          |              | E2-M2      |

| MESA     | EEG          | E2-Fpz    |
|          |              | Fpz-Cz    |
|          | C4-M1        | Cz-Oz     |
|          | E1-Fpz       | C4-M1     |

| MROS     | EEG          | E1-C4     |
|          |              | C3-M2     |
|          | M1-C3        | C4-M1     |
| EOG      | M2-C4        | E1-M2     |
|          | E2-C3        | E2-M1     |

| PHYS     | EEG          | F3-M2      |
|          | F4-M1        | F4-M1      |
|          | C3-M2        | C3-M2      |
|          | C4-M1        | C4-M1      |
|          | O1-M2        | O1-M2      |
|          | O2-M1        | O2-M1      |

| SEDF-SC  | EEG          | Pz-Oz      |
|          | Fpz-Cz       | Fpz-Cz    |
| EOG      | EOG          | EOG       |
| SEDF-ST  | EEG          | Pz-Oz      |
|          | Fpz-Cz       | Pz-Oz      |

*Continued on next page*
| Datasets | Channel type | U-Sleep-v0 | U-Sleep-v1 |
|----------|--------------|------------|------------|
| EOG      | EOG          | EOG        |
| SHHS     | EEG          | C4-A1      | C4-A1      |
|          |              | C3-A2      | C3-A2      |
|          | EOG          | EOGL-PG1   | EOGL-PG1   |
|          |              | EOGR-PG1   | EOGR-PG1   |
| SOF      | EEG          | LOC-A2     | C3-A2      |
|          |              | A1-C4      | C4-A1      |
|          | EOG          | C3-A2      | LOC-A2     |
|          |              | ROC-C4     | ROC-A1     |

* The CHAT dataset has recordings where we may find a different order of EEG and EOG sensors for different edf files. Consequently, in the U-Sleep version where they were erroneously extracting atypical and/or randomly ordered channel derivations (U-Sleep-v0), we can generate multiple combinations of incorrect derivations. In Table we report the most frequent incorrect EEG and EOG derivations.

** The HPAP dataset has recordings where we can find a different order of EEG and EOG sensors for each edf file, resulting in different combinations of incorrect derivations for each recording. For that reason, we preferred not to report the incorrect and completely random combinations of derivations between the different recordings.


### Table 7
Data split on the OA datasets. We report the total number of recordings, and the number of recordings used to train, validate and test the U-Sleep architecture in the experiment (i).

| Datasets | Recordings | Train | Valid | Test |
|----------|------------|-------|-------|------|
| ABC      | 132        | 93    | 15    | 24   |
| CCSHS    | 515        | 387   | 50    | 78   |
| CFS      | 730        | 531   | 95    | 104  |
| CHAT     | 1638       | 1438  | 70    | 130  |
| DCSM     | 255        | 190   | 26    | 39   |
| HPAP     | 238        | 178   | 24    | 36   |
| MESA     | 2056       | 1906  | 50    | 100  |
| MROS     | 3926       | 3728  | 69    | 129  |
| PHYS     | 994        | 844   | 50    | 100  |
| SEDF-SC  | 153        | 115   | 15    | 23   |
| SEDF-ST  | 44         | 30    | 6     | 8    |
| SHHS     | 8444       | 8226  | 77    | 141  |
| SOF      | 453        | 339   | 46    | 68   |

### Table 8
Data split on the BSDB dataset. We report the total number of recordings, and the number of recordings used to train, validate and test the U-Sleep architecture in the experiments (ii) and (iii).

| Datasets | Recordings | Train | Valid | Test |
|----------|------------|-------|-------|------|
| (ii)     | -          | 8884  | 6658  | 882  | 1344 |
| B        | 151        | 111   | 14    | 26   |
| C        | 246        | 185   | 26    | 35   |
| A        | 177        | 132   | 17    | 28   |
| (iii)    | YA         | 2066  | 1902  | 58   | 106  |
| MA       | 3636       | 3482  | 51    | 103  |
| E        | 1539       | 1378  | 55    | 106  |
| OE       | 988        | 829   | 53    | 106  |
Table 9 (i) Performance of $U$-Sleep-$v0$ and $U$-Sleep-$v1$, pre-trained on the OA datasets, and evaluated on the test set of the BSDB dataset, and on the whole BSDB$^{(100\%)}$ dataset, i.e. both direct transfer (DT) on BSDB. We report the weighted F1-score ($\%wF1$), specifically the mean value and the standard deviation ($\mu \pm \sigma$) computed across the recordings.

| Datasets     | Training on OA |
|--------------|----------------|
|              | $U$-Sleep-$v0$ | $U$-Sleep-$v1$ |
| BSDB         | 77.8 ± 10.9    | 77.9 ± 10.8    |
| BSDB$^{(100\%)}$ | 78.2 ± 11.1    | 78.3 ± 11.2    |

Table 10 (ii) Performance of $U$-Sleep-$v1$, pre-trained on the OA datasets, and evaluated on all the test set of the OA datasets and on the test set of the BSDB dataset. We also report the performance of $U$-Sleep-$v1$ trained from scratch (S) or fine-tuned (FT) on the BSDB dataset, and evaluated on all the test set of all the available datasets. We report the weighted F1-score ($\%wF1$), specifically the mean value and the standard deviation ($\mu \pm \sigma$) computed across the recordings.

| Datasets     | Training on OA |
|--------------|----------------|
|              | $U$-Sleep-$v1$ | $U$-Sleep-$v1$ (S) | $U$-Sleep-$v1$ (FT) |
| ABC          | 81.3 ± 8.5     | 78.9 ± 10.1       | 76.5 ± 10.1       |
| CCSHS        | 90.3 ± 4.6     | 85.3 ± 6.3        | 85.4 ± 5.9        |
| CFS          | 87.8 ± 6.6     | 82.2 ± 7.9        | 82.8 ± 7.2        |
| CHAT         | 86.4 ± 4.8     | 79.3 ± 6.7        | 76.5 ± 7.5        |
| DCSM         | 90.5 ± 4.4     | 81 ± 8.9          | 79.1 ± 9.7        |
| HPAP         | 80.6 ± 7.5     | 75.8 ± 9.6        | 74.5 ± 11.7       |
| MESA         | 84.2 ± 7.2     | 79.1 ± 12.9       | 79.6 ± 9.3        |
| MROS         | 85.3 ± 7.0     | 75.5 ± 10.5       | 77.4 ± 9.8        |
| PHYS         | 80.5 ± 8.6     | 79.2 ± 8.9        | 79.2 ± 9.0        |
| SEDF-SC      | 86.7 ± 5.5     | 85.1 ± 5.6        | 86.6 ± 5.3        |
| SEDF-ST      | 83.5 ± 4.5     | 73.6 ± 8.3        | 74.9 ± 6.4        |
| SHHS         | 86.6 ± 6.3     | 81.6 ± 7.1        | 83.5 ± 6.5        |
| SOF          | 85.6 ± 6.5     | 75.6 ± 10.9       | 78.4 ± 9.9        |
| avg OA       | 85.7 ± 7.1     | 79.7 ± 9.4        | 80.0 ± 9.0        |
| BSDB         | 77.9 ± 10.8    | 82.2 ± 9.4        | 82.0 ± 9.4        |
**Table 11** (iii) Performance of *U-Sleep-v1* on a single model fine-tuned on all the training set of the seven *BSDB* groups (FT); on seven/two models fine-tuned on the independent training set of each group (FT-I) with $G = 7$ and $G = 2$ respectively; and on a single model fine-tuned on all the training set of the seven/two *BSDB* groups conditioned (FT-SaBN) by $G = 7$ and by $G = 2$ groups respectively. All the fine-tuned models are evaluated on the associated test set of each group. We report the weighted F1-score (%wF1), specifically the mean value and the standard deviation ($\mu \pm \sigma$) computed across the recordings. B: Babies (0-3 years); C: Children (4-12 years); A: Adolescents (13-18 years); YA: Young Adults (19-39 years); MA: Middle Aged Adults (40-59 years); E: Elderly (60-69 years); OE: Old Elderly ($> 70$ years). When $G = 2$ we have the following two groups $G_1 = \{B \cup C\}$, $G_2 = \{A \cup YA \cup MA \cup E \cup OE\}$.

| Subsets | FT (G=1) | FT (G=7) | FT-I (G=7) | FT-I (G=2) | FT-SaBN (G=7) | FT-SaBN (G=2) |
|---------|----------|----------|------------|------------|---------------|---------------|
| B       | 79.2 $\pm$ 7.4 | 78.7 $\pm$ 7.2 | 77.6 $\pm$ 8.5 | 79.5 $\pm$ 6.7 | 77.2 $\pm$ 7.9 |
| C       | 80.8 $\pm$ 9.5 | 80.7 $\pm$ 8.9 | 81.1 $\pm$ 7.7 | 81.5 $\pm$ 8.0 | 81.4 $\pm$ 7.9 |
| A       | 87.3 $\pm$ 10.8 | 86.0 $\pm$ 13.4 | 87.0 $\pm$ 10.7 | 87.0 $\pm$ 10.8 | 86.2 $\pm$ 11.3 |
| YA      | 85.9 $\pm$ 9.3 | 85.6 $\pm$ 9.4 | 85.4 $\pm$ 9.5 | 85.5 $\pm$ 9.4 | 84.6 $\pm$ 9.8 |
| MA      | 84.1 $\pm$ 6.2 | 83.5 $\pm$ 6.6 | 83.4 $\pm$ 6.4 | 83.5 $\pm$ 6.6 | 82.9 $\pm$ 6.9 |
| E       | 80.5 $\pm$ 8.3 | 79.4 $\pm$ 9.0 | 79.6 $\pm$ 8.9 | 80.0 $\pm$ 8.2 | 79.0 $\pm$ 9.4 |
| OE      | 79.8 $\pm$ 9.6 | 78.9 $\pm$ 9.4 | 79.1 $\pm$ 9.7 | 79.4 $\pm$ 9.5 | 78.8 $\pm$ 9.4 |
| **avg** | 82.5 $\pm$ 9.0 | 81.8 $\pm$ 9.4 | 81.9 $\pm$ 9.2 | 82.2 $\pm$ 8.9 | 81.4 $\pm$ 9.34 |

**Table 12** Performance of *U-Sleep-v1*, pre-trained on the OA datasets, and evaluated on all the test set of the OA datasets (avg OA) with and without (i.e., *U-Sleep-v1* pre-trained in (ii)) label smoothing. We report the weighted F1-score (%F1), referred to the epochs kept after the $\mu_{\text{max}}$ query selection procedure ($q\%$ threshold value fixed to 5%), and we report percentage of misclassified epochs among the rejected with query (%miscl.). Specifically, we report the mean value and the standard deviation ($\mu \pm \sigma$) computed across the recordings.

| Dataset | w/o label smoothing | w/ label smoothing |
|---------|---------------------|-------------------|
| **avg OA** | %F1 87.4 ± 7.3 | 82.5 ± 9.8 |
|          | %miscl. 51.1 ± 9.5 | 53.7 ± 10.6 |
References

[1] Zhang, G.-Q., Cui, L., Mueller, R., Tao, S., Kim, M., Rueschman, M., Mariani, S., Moblney, D., Redline, S.: The national sleep research resource: towards a sleep data commons. Journal of the American Medical Informatics Association 25(10), 1351–1358 (2018)

[2] Bakker, J.P., Tavakkoli, A., Rueschman, M., Wang, W., Andrews, R., Malhotra, A., Owens, R.L., Anand, A., Dudley, K.A., Patel, S.R.: Gastric banding surgery versus continuous positive airway pressure for obstructive sleep apnea: a randomized controlled trial. American journal of respiratory and critical care medicine 197(8), 1080–1083 (2018)

[3] Rosen, C.L., Larkin, E.K., Kirchner, H.L., Emancipator, J.L., Bivins, S.F., Surovec, S.A., Martin, R.J., Redline, S.: Prevalence and risk factors for sleep-disordered breathing in 8-to 11-year-old children: association with race and prematurity. The Journal of pediatrics 142(4), 383–389 (2003)

[4] Redline, S., Tishler, P.V., Tosteson, T.D., Williamson, J., Kump, K., Browner, I., Ferrette, V., Krejci, P.: The familial aggregation of obstructive sleep apnea. American journal of respiratory and critical care medicine 151(3), 682–687 (1995)

[5] Marcus, C.L., Moore, R.H., Rosen, C.L., Giordani, B., Garetz, S.L., Taylor, H.G., Mitchell, R.B., Amin, R., Katz, E.S., Arens, R., et al.: A randomized trial of adenotonsillectomy for childhood sleep apnea. N Engl J Med 368, 2366–2376 (2013)

[6] Redline, S., Amin, R., Beebe, D., Chervin, R.D., Garetz, S.L., Giordani, B., Marcus, C.L., Moore, R.H., Rosen, C.L., Arens, R., et al.: The childhood adenotonsillectomy trial (chat): rationale, design, and challenges of a randomized controlled trial evaluating a standard surgical procedure in a pediatric population. Sleep 34(11), 1509–1517 (2011)

[7] Rosen, C.L., Auckley, D., Benca, R., Foldvary-Schaefer, N., Iber, C., Kapur, V., Rueschman, M., Zee, P., Redline, S.: A multisite randomized trial of portable sleep studies and positive airway pressure autotitration versus laboratory-based polysomnography for the diagnosis and treatment of obstructive sleep apnea: the homepap study. Sleep 35(6), 757–767 (2012)

[8] Chen, X., Wang, R., Zee, P., Lutsey, P.L., Javaheri, S., Alcántara, C., Jackson, C.L., Williams, M.A., Redline, S.: Racial/ethnic differences in sleep disturbances: the multi-ethnic study of atherosclerosis (mesa). Sleep 38(6), 877–888 (2015)

[9] Blackwell, T., Yaffe, K., Ancoli-Israel, S., Redline, S., Ensrud, K.E.,
Stefanick, M.L., Laffan, A., Stone, K.L., in Men Study Group, O.F.: Associations between sleep architecture and sleep-disordered breathing and cognition in older community-dwelling men: the osteoporotic fractures in men sleep study. Journal of the American Geriatrics Society 59(12), 2217–2225 (2011)

[10] Relationships between sleep stages and changes in cognitive function in older men: the mros sleep study. Sleep 38(3), 411–421 (2015)

[11] Goldberger, A.L., Amaral, L.A., Glass, L., Hausdorff, J.M., Ivanov, P.C., Mark, R.G., Mietus, J.E., Moody, G.B., Peng, C.-K., Stanley, H.E.: Physiobank, physiotoolkit, and physionet: components of a new research resource for complex physiologic signals. circulation 101(23), 215–220 (2000)

[12] Ghassemi, M.M., Moody, B.E., Lehman, L.-W.H., Song, C., Li, Q., Sun, H., Mark, R.G., Westover, M.B., Clifford, G.D.: You snooze, you win: the physionet/computing in cardiology challenge 2018. In: 2018 Computing in Cardiology Conference (CinC), vol. 45, pp. 1–4 (2018). IEEE

[13] Kemp, B., Zwinderman, A.H., Tuk, B., Kamphuisen, H.A., Oberye, J.J.: Analysis of a sleep-dependent neuronal feedback loop: the slow-wave microcontinuity of the eeg. IEEE Transactions on Biomedical Engineering 47(9), 1185–1194 (2000)

[14] Quan, S.F., Howard, B.V., Iber, C., Kiley, J.P., Nieto, F.J., O’Connor, G.T., Rapoport, D.M., Redline, S., Robbins, J., Samet, J.M., et al.: The sleep heart health study: design, rationale, and methods. Sleep 20(12), 1077–1085 (1997)

[15] Cummings, S.R., Black, D.M., Nevitt, M.C., Browner, W.S., Cauley, J.A., Genant, H.K., Mascioli, S.R., Scott, J.C., Seeley, D.G., Steiger, P., et al.: Appendicular bone density and age predict hip fracture in women. Jama 263(5), 665–668 (1990)

[16] Spira, A.P., Blackwell, T., Stone, K.L., Redline, S., Cauley, J.A., Ancoli-Israel, S., Yaffe, K.: Sleep-disordered breathing and cognition in older women. Journal of the American Geriatrics Society 56(1), 45–50 (2008)

[17] Ohayon, M., Carskadon, M., Guilleminault, C., Vitiello, M.: Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: Developing normative sleep values across the human lifespan. Sleep 27, 1255–73 (2004). https://doi.org/10.1093/sleep/27.7.1255

[18] Iber, C., Iber, C.: The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications vol. 1. American Academy of Sleep Medicine, Westchester, IL, ??? (2007)
[19] Danker-hopfe, H., Anderer, P., Zeitlhofer, J., Boeck, M., Dorn, H., Gruber, G., Heller, E., Loretz, E., Moser, D., Parapatics, S., et al.: Interrater reliability for sleep scoring according to the rechtschaffen & kales and the new aasm standard. Journal of sleep research 18(1), 74–84 (2009)

[20] Rosenberg, R.S., Van Hout, S.: The american academy of sleep medicine inter-scorer reliability program: sleep stage scoring. Journal of clinical sleep medicine 9(01), 81–87 (2013)

[21] Younes, M., Raneri, J., Hanly, P.: Staging sleep in polysomnograms: analysis of inter-scorer variability. Journal of Clinical Sleep Medicine 12(06), 885–894 (2016)

[22] Muto, V., Berthomier, C., Schmidt, C., Vandewalle, G., Jaspar, M., Devillers, J., Chellappa, S., Meyer, C., Phillips, C., Berthomier, P., et al.: 0315 inter-and intra-expert variability in sleep scoring: comparison between visual and automatic analysis. Sleep 41(suppl_1), 121 (2018)

[23] Goodfellow, I., Bengio, Y., Courville, A.: Deep Learning. MIT press, ??? (2016)

[24] Lukasik, M., Bhojanapalli, S., Menon, A., Kumar, S.: Does label smoothing mitigate label noise? In: International Conference on Machine Learning, pp. 6448–6458 (2020). PMLR

[25] Fiorillo, L., Favaro, P., Faraci, F.D.: Deepsleepnet-lite: A simplified automatic sleep stage scoring model with uncertainty estimates. IEEE Transactions on Neural Systems and Rehabilitation Engineering 29, 2076–2085 (2021)

[26] Szegedy, C., Vanhoucke, V., Ioffe, S., Shlens, J., Wojna, Z.: Rethinking the inception architecture for computer vision. In: Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition, pp. 2818–2826 (2016)

[27] Perslev, M., Darkner, S., Kempfner, L., Nikolic, M., Jennum, P.J., Igel, C.: U-sleep: resilient high-frequency sleep staging. NPJ digital medicine 4(1), 1–12 (2021)