March 11-16 2022 WORLD SLEEP Rome • Italy

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Real-time Implementation of Sleep Staging using Interbeat Intervals

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CONFLICT OF INTEREST DISCLOSURE

With respect to this CME activity,

☐ **No**, I (nor my spouse/partner) do not have a relevant financial relationship.

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Nature of Relevant Financial Relationship (choose all that apply)	**Name(s) of Company or Companies**
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__X_ Full-time/Part-time Employee	Sleep Number Corporation
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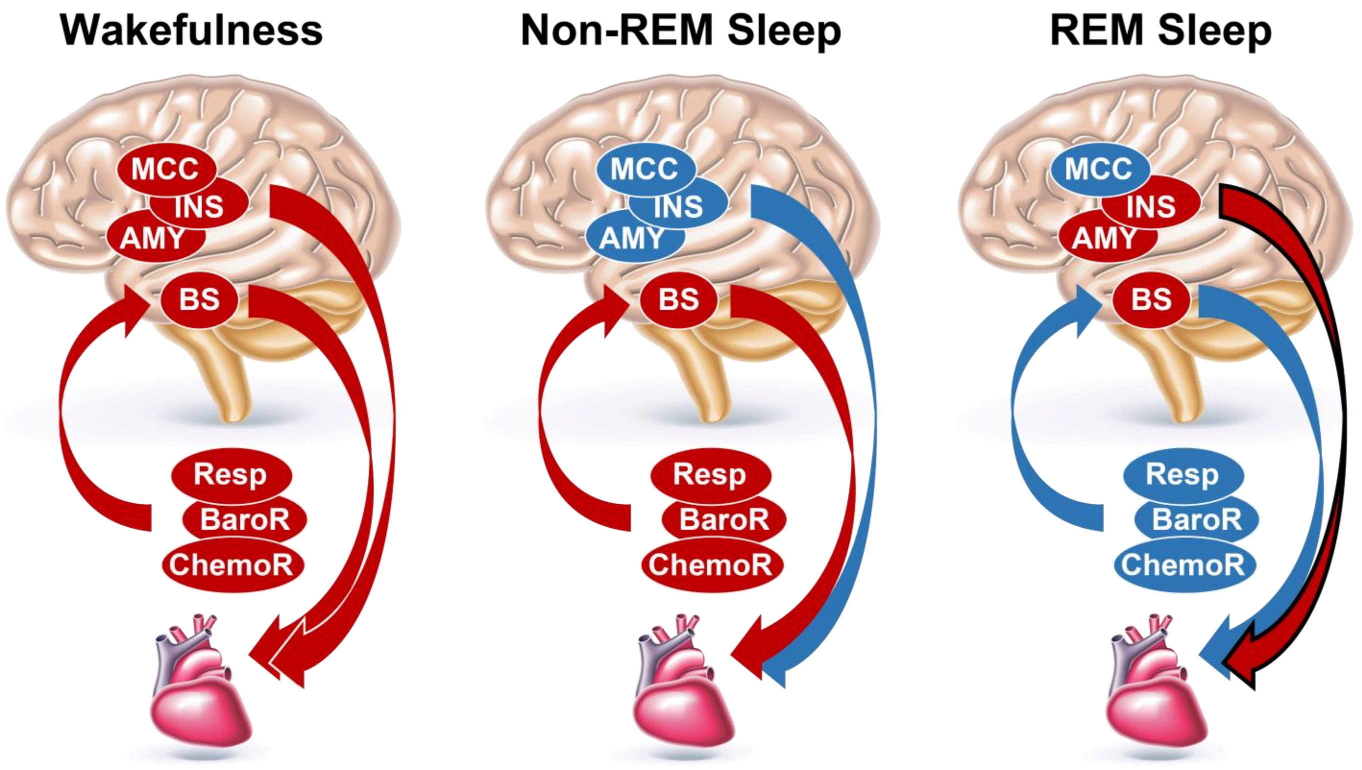
The activity of the autonomic nervous system changes according to behavioral state

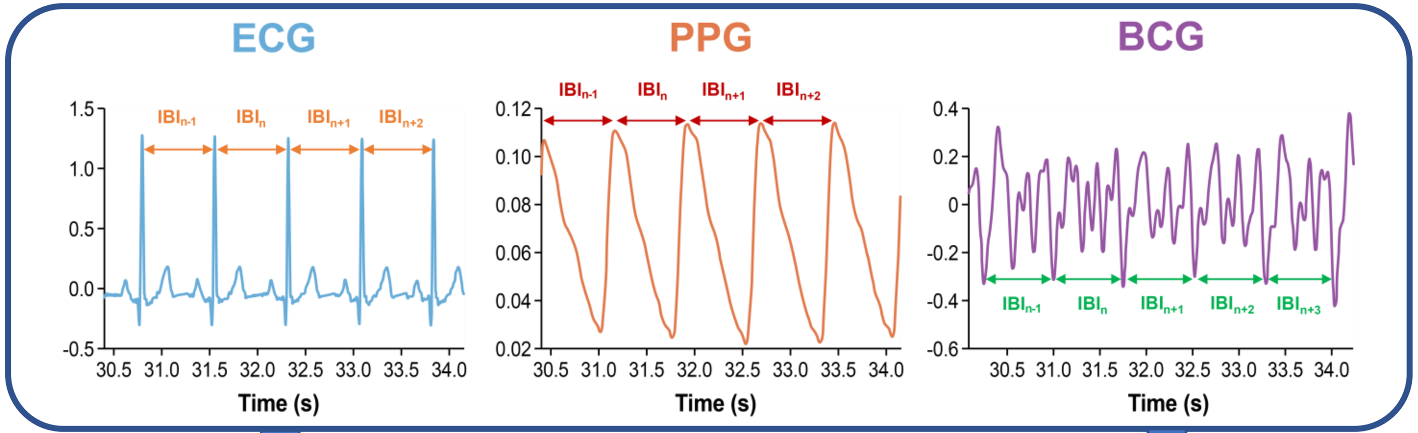


	Wakefulness	Non-REM Sleep	REM Sleep
Heart rate	↑	↓	↑
Sympathetic activity	↑	↓	↑
Parasympathetic activity	↓	↑	↓

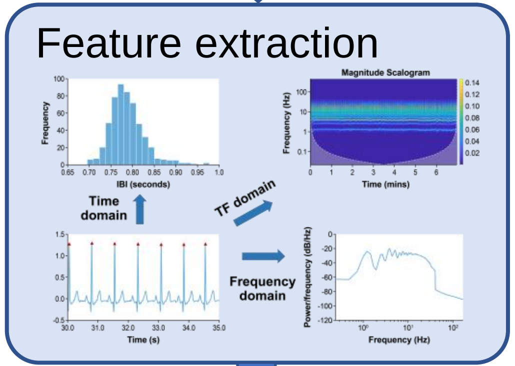
AMY, amygdala; BaroR, baroreflex; BS, brainstem centers; ChemoR, chemoreflex; INS, insula; MCC, midcingulate cortex; REM, rapid eye movement; Resp, respiration.
Modified image from: Chouchou F and Desseilles M. *Front. Neurosci.* 2014;8:402.

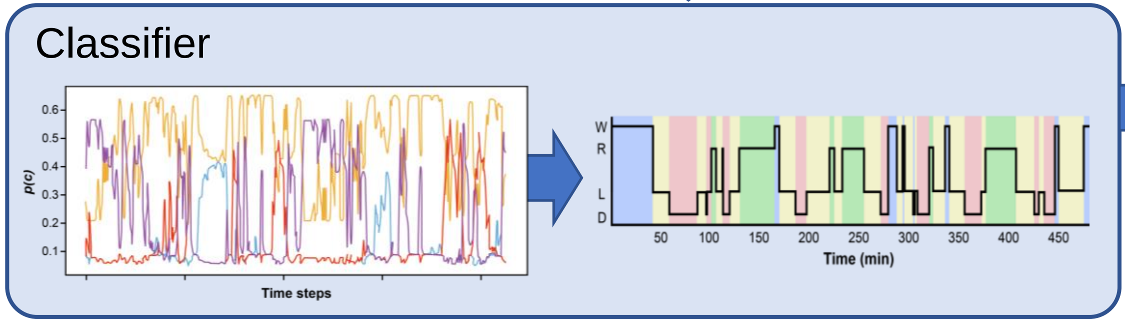
Sleep staging algorithms can be categorized into 2 groups

Examples of cardiac signals

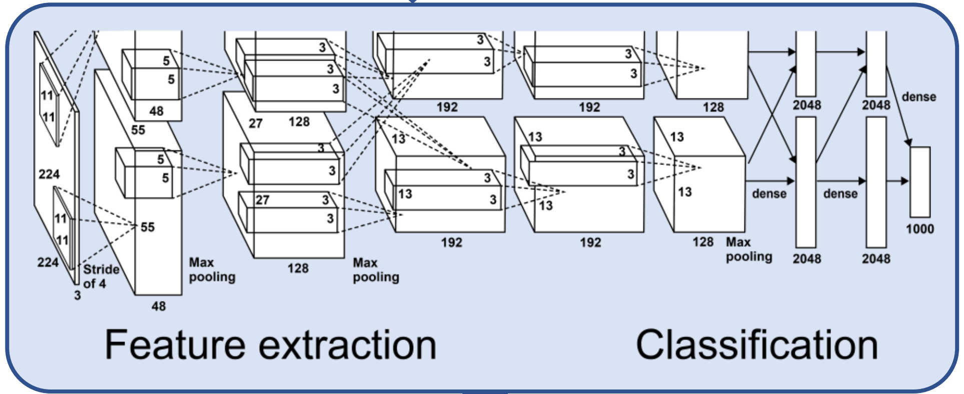


Classic sleep staging
feature extraction and classification





Representation learning
features are automatically discovered[a]

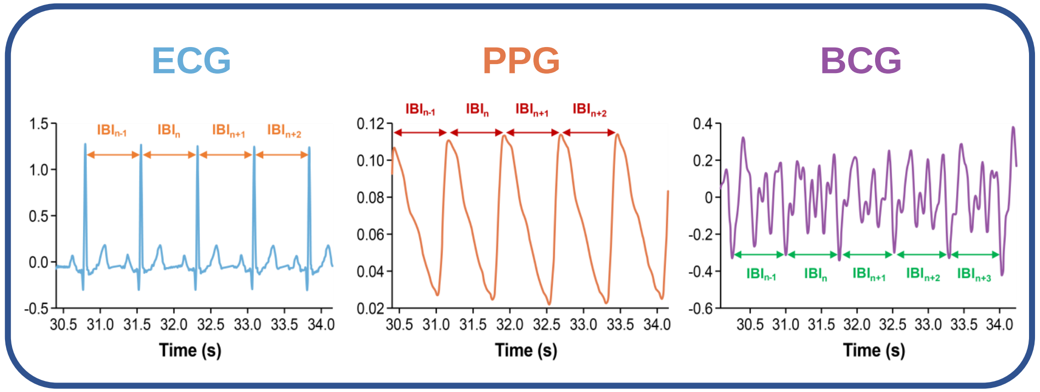


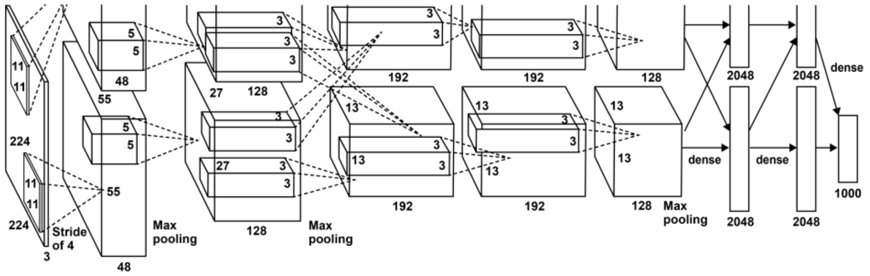
- Deep
- Light
- REM
- Wake

BCG, ballistocardiography; ECG, electrocardiogram; IBI, interbeat interval; PPG, photoplethysmography; REM, rapid eye movement; TF, time-frequency.

Study aim

- To develop a sleep staging representation-type of algorithm (deep neural network) that:
  - utilizes a variety of cardiac signals including ECG, PPG, BCG
  - can operate in real-time with sufficient accuracy
  - has a small memory footprint that enables micro-processor embedding
  - has low complexity





Feature extraction

Classification

- Deep
- Light
- REM
- Wake

BCG, ballistocardiography; ECG, electrocardiogram; IBI, interbeat interval; PPG, photoplethysmography; REM, rapid eye movement.

The ECG from 3 sleep data sets (D1, D2, D3) were used in this research

Dataset	Number of PSG recordings from unique subjects	Diagnosis
D1	994 ▪ ~50% for training ▪ ~20% for validation ▪ ~30% for testing 3× cross-validation	Healthy and apnea
D2-healthy	16	Healthy
D2-INS	9	Insomnia
D2-RBD	22	REM behavior disorder
D2-PLMD	10	Periodic limb movement disorder
D3	45	Healthy

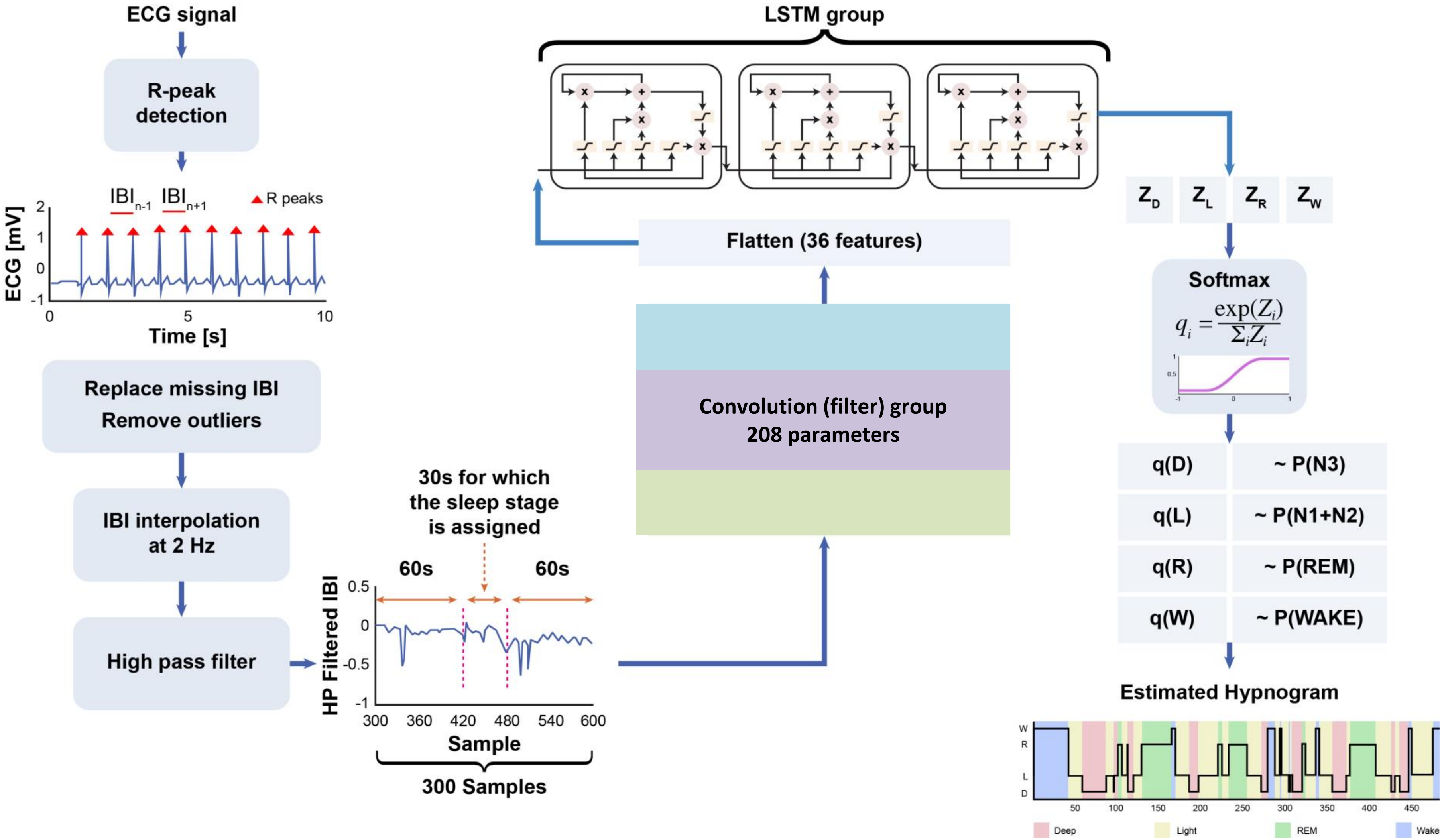
D2

Note: D1[1,2] and D2[2,3] are publicly available

ECG, electrocardiogram; INS, insomnia; PLMD, periodic limb movement disorder; PSG, polysomnography; RBD, REM behavior disorder; REM; rapid eye movement.

1. Ghassemi M et al. 2018 *In:* 2018 Computing in Cardiology Conference (CinC), 1–4; 2. Goldberger AL et al. *Circulation*. 2000;e215–e20; 3. Terzano M et al. *Sleep Med*. 2002;3:187–99.

Signal processing and deep neural architecture



D, deep; ECG, electrocardiogram; HP, high pass; IBI, interbeat interval; L, light; LSTM, long short-term memory; R/REM, rapid eye movement; W, wake.

Results show moderate agreement with manual scoring for the healthy datasets

Four-sleep-stage accuracy

Mean (SD)	D1-test	D2-healthy	D2-INS	D2-RBD	D2-PLMD	D3
Kappa	0.39 (0.16)	0.31 (0.08)	0.39 (0.13)	0.24 (0.09)	0.36 (0.12)	0.44 (0.09)
Accuracy	0.62 (0.13)	0.52 (0.06)	0.58 (0.12)	0.47 (0.06)	0.57 (0.11)	0.65 (0.07)

Three-sleep-stage accuracy

Mean (SD)	D1-test	D2-healthy	D2-INS	D2-RBD	D2-PLMD	D3
Kappa	0.46 (0.17)	0.35 (0.10)	0.41 (0.14)	0.30 (0.13)	0.42 (0.11)	0.52 (0.12)
Accuracy	0.73 (0.11)	0.65 (0.09)	0.64 (0.12)	0.59 (0.10)	0.68 (0.08)	0.76 (0.07)

INS, insomnia; PLMD, periodic limb movement disorder; RBD, REM behavior disorder; REM; rapid eye movement; SD, standard deviation.

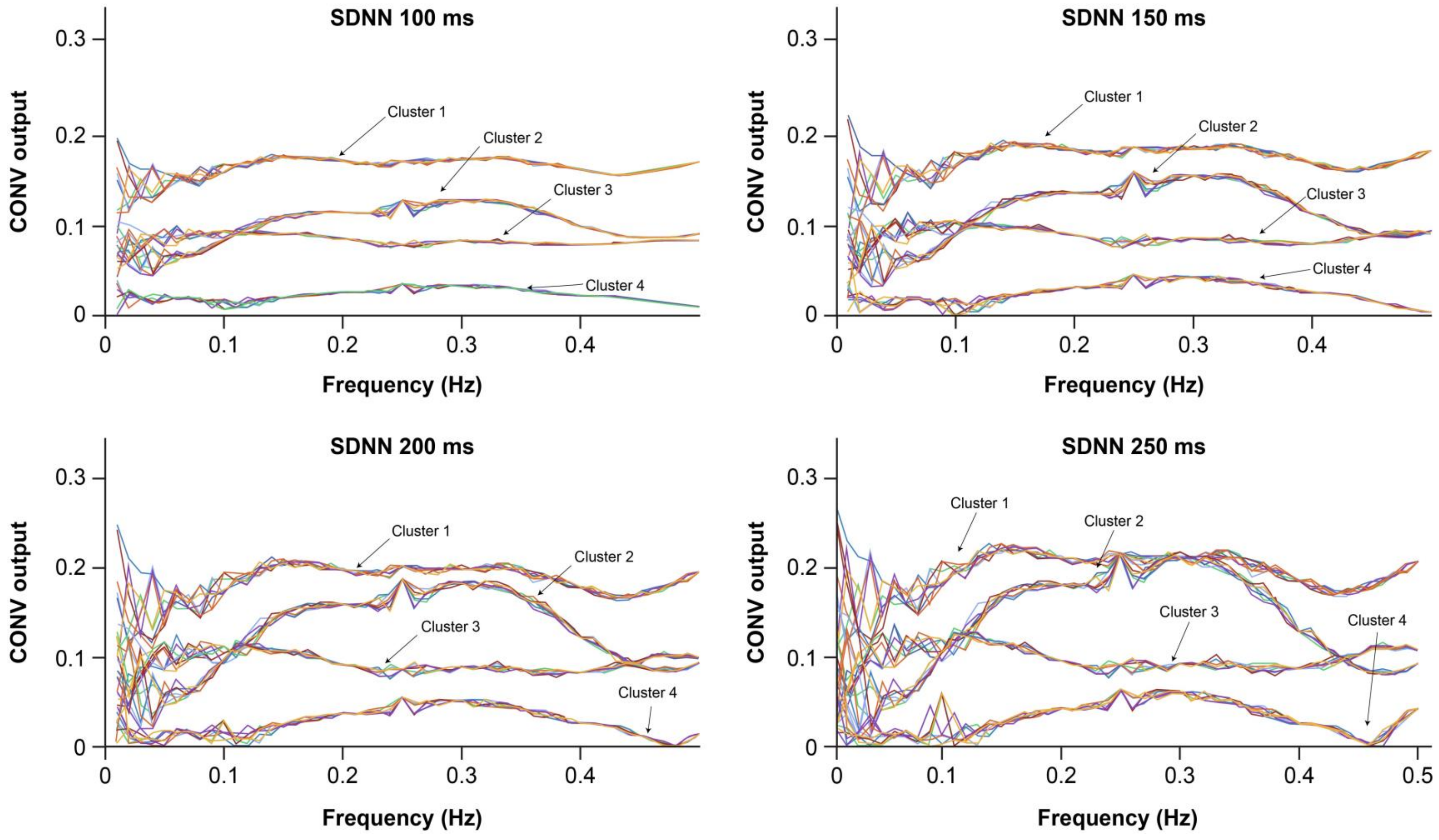
Model size, latency, and accuracy for comparable approaches

Approach	Kappa	Accuracy	Model size (# of parameters)	Type of model	Decision Latency (time)
Sridhar et al 2020[1]	0.66	0.77	1.5 M	DNN	> 6 hours
Radha et al 2019[2]	0.61	0.77	260 K	DNN	> 6 hours
Wei et al 2019[3]	0.55	0.78	10 K	Decision tree	5 minutes
Zhao and Sun 2021[4]	0.69	0.77	10 K	Decision tree	5 minutes
Our model	0.44	0.65	6408	DNN	150 seconds

DNN, deep neural network.

1. Sridhar N et al. *NPJ Digit Med*. 2020;3:106; 2. Radha M et al. *Sci Rep*. 2019;9:14149; 3. Wei Y et al. *IEEE Access.* 2019;7:85959–70.; 4. Zhao X and Sun G. *Entropy (Basel)*. 2021;23:116.

Qualitative analysis of the DNN's spectral response



- Four clusters could be distinguished, each with 9 components
- The cluster profiles show band-pass type of spectral responses
- The peak at 0.25 Hz that is most prominently visible for clusters 2 and 4 reflects typical respiration frequency (15 breaths/min)

CONV, convolution; DNN, deep neural network; SDNN, standard deviation of normal-to-normal intervals.

Conclusions

- Real-time interventions that compensate for sleep deficiencies[1] or boost beneficial aspects of sleep[2] require real-time sleep staging, preferably based on minimally obtrusive sensing
- We developed an algorithm that is minimally obtrusive, relying on IBI signals that can be extracted through contactless sensing to estimate the sleep stage of 30-second sleep epochs
- Our DNN model has several advantages:
  - **Small footprint:** 6408 parameters compared with > 100K parameters for other models relying on DNNs[3,4]
  - **Fast:** has the processing speed to provide real-time results
  - **Versatile:** can be potentially used across different platforms
  - **Accuracy:** moderate accuracy for 4 sleep stages and substantial accuracy for 3 sleep stages
  - **Interpretability:** the DNN's spectral response shows patterns consistent with cardiac activity during sleep
- Overall, our model shows promise for implementation across different platforms, and may enhance intervention strategies

DNN, deep neural network; IBI, interbeat interval

1. Raymann RJ et al. *Brain*. 2008;131:500–13; 2. Bellesi M et al. *Front Syst Neurosci*. 2014;8:208; 3. Radha M et al. *Sci Rep*. 2019;9:14149; 4. Sridhar N et al. *NPJ Digit Med*. 2020;3:106.

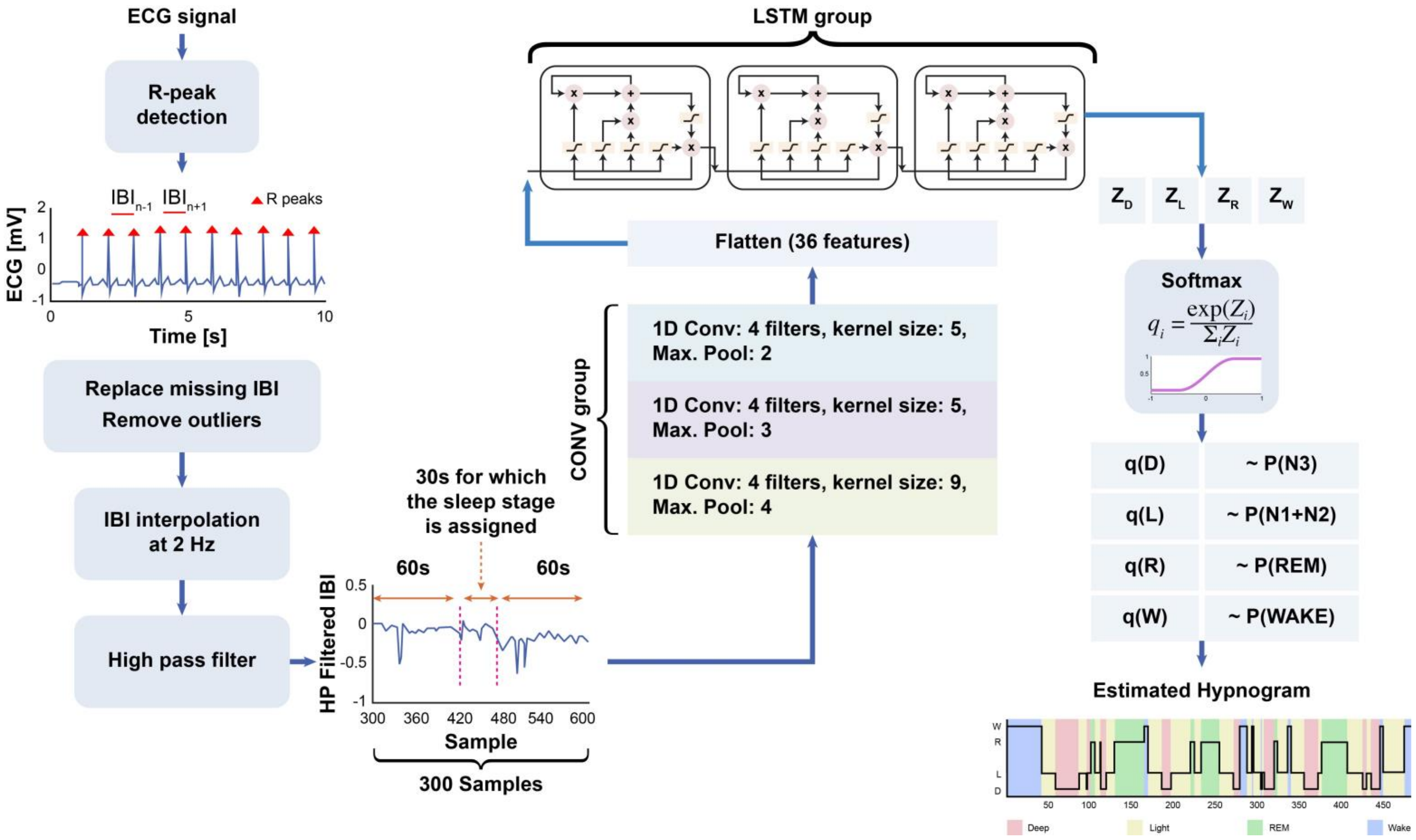
Disclosures and acknowledgments

- This research was supported by Sleep Number Corporation
- Gary Garcia-Molina, PhD and Jiewei Jiang are employees of Sleep Number Corporation, Minneapolis, MN, USA
- Shawn Barr, Cristina Jocson, Anna Pastushko, and Farzad Siyahjani provided insightful recommendations
- We thank the Computational Clinical Neurophysiology Laboratory and the Clinical Data Animation Laboratory, Massachusetts General Hospital, Boston, MA, USA , and the Sleep Disorders Center, Ospedale Maggiore, Parma, Italy, for making their datasets publicly available through PhysioNet.
- Medical writing support was provided by Rachel C. Brown, PhD, and Sandra J. Page, PhD, from Oxford PharmaGenesis Inc., Newtown, PA, USA, and was funded by Sleep Number Corporation

Full study results have recently been published in *Physiological Measurement*, and can be found at DOI: XXXX

Supplemental Slides

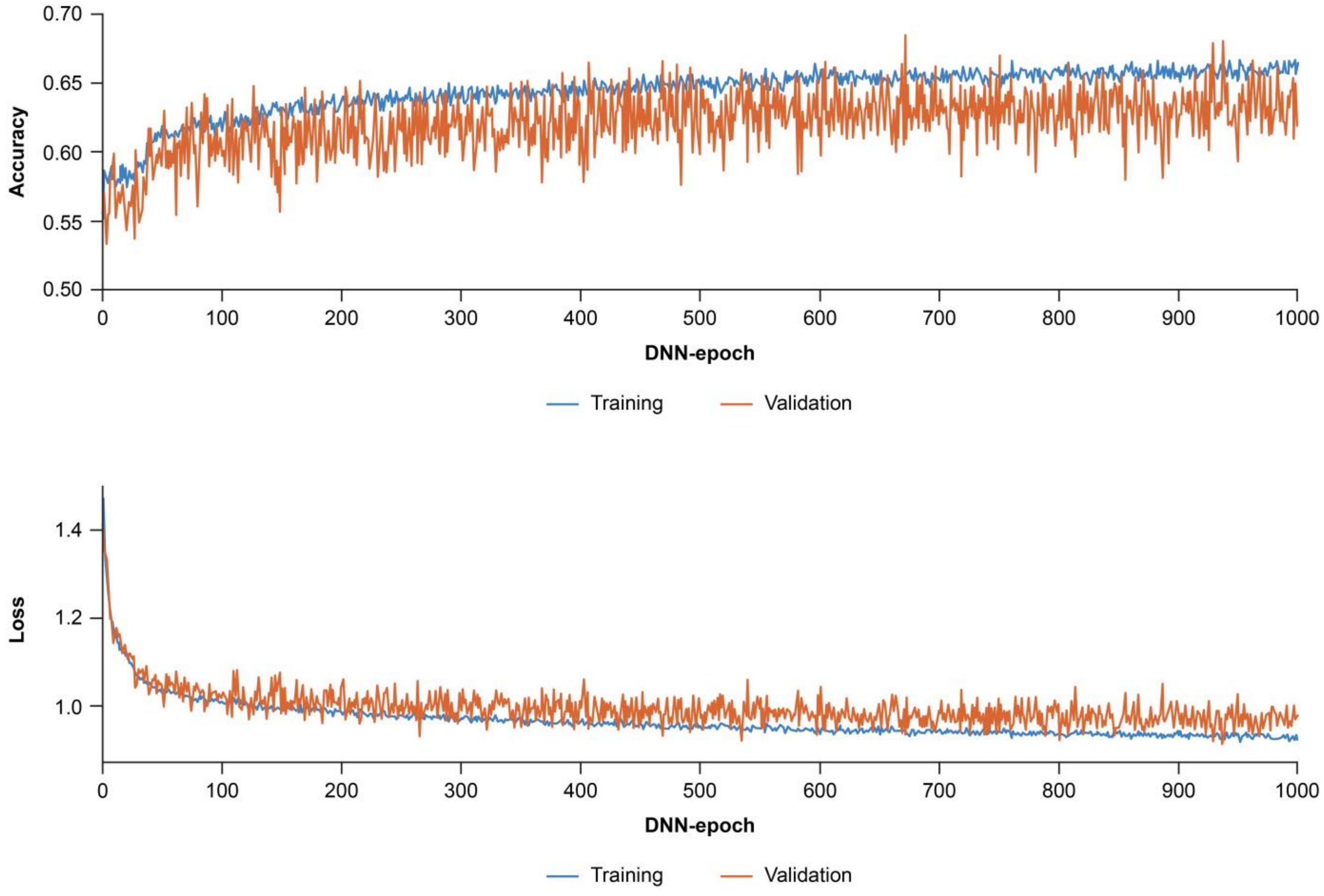
Overview of signal processing and DNN architecture



- The training and validation subsets of D1 were used to train the DNN
- Three-fold cross-validation was used
- DNN output approximated the probabilities of a window belonging to light, deep, REM, or wake stages
- Cohen’s Kappa, accuracy, and sensitivity/specificity per stage were determined
- Kappa was optimized using thresholds on probability ratios for each stage versus light sleep

1D, one dimension; CONV, convolution; D, deep; DNN, deep neural network; ECG, electrocardiogram; HP, high pass; IBI, interbeat interval; L, light; LSTM, long short-term memory; R/REM, rapid eye movement; W, wake.

DNN training and validation



- Our model included 6408 parameters
- Training accuracy increased with the DNN-epoch, while the validation accuracy fluctuated more than the training accuracy
- Both datasets showed an increasing trend in accuracy overall

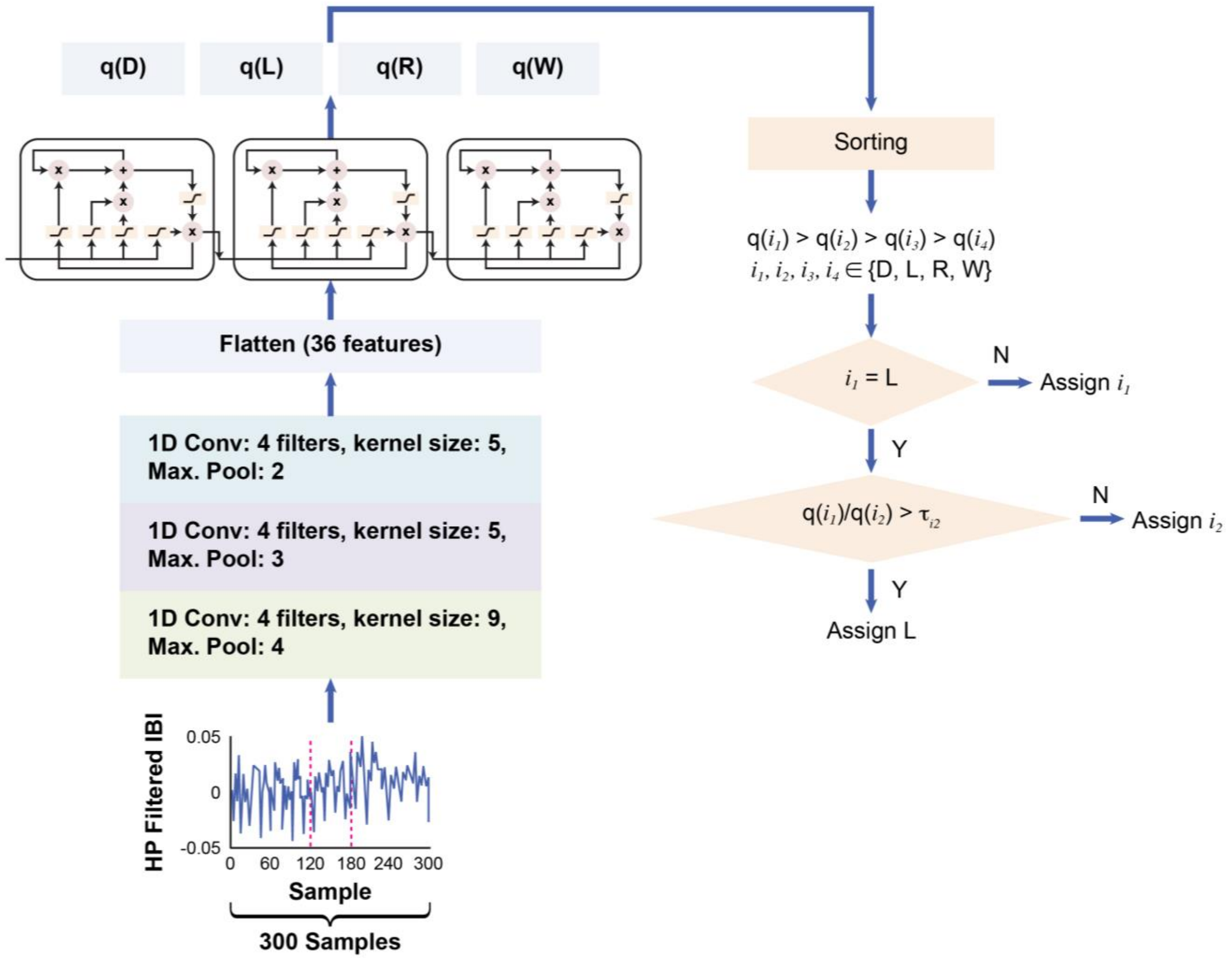
DNN, deep neural network.

Kappa optimization and correction of light sleep bias

- Given that light sleep is significantly more prevalent than other sleep stages, the DNN can be biased to detect light sleep
- To correct the bias, we analyzed the cumulative distribution functions of the probability ratio of light sleep versus other stages

$$\frac{q(L)}{q(D)}, \frac{q(L)}{q(R)}, and \frac{q(L)}{q(W)}$$

- This analysis allowed us to increase Kappa by performing a confirmation step when q(L) is the highest probability produced by the DNN



1D, one dimension; Conv, convolution layer; D, deep sleep; DNN, deep neural network; HP, high pass; IBI, interbeat interval; L, light sleep; N, no; R, rapid eye movement; W, wake; Y, yes.

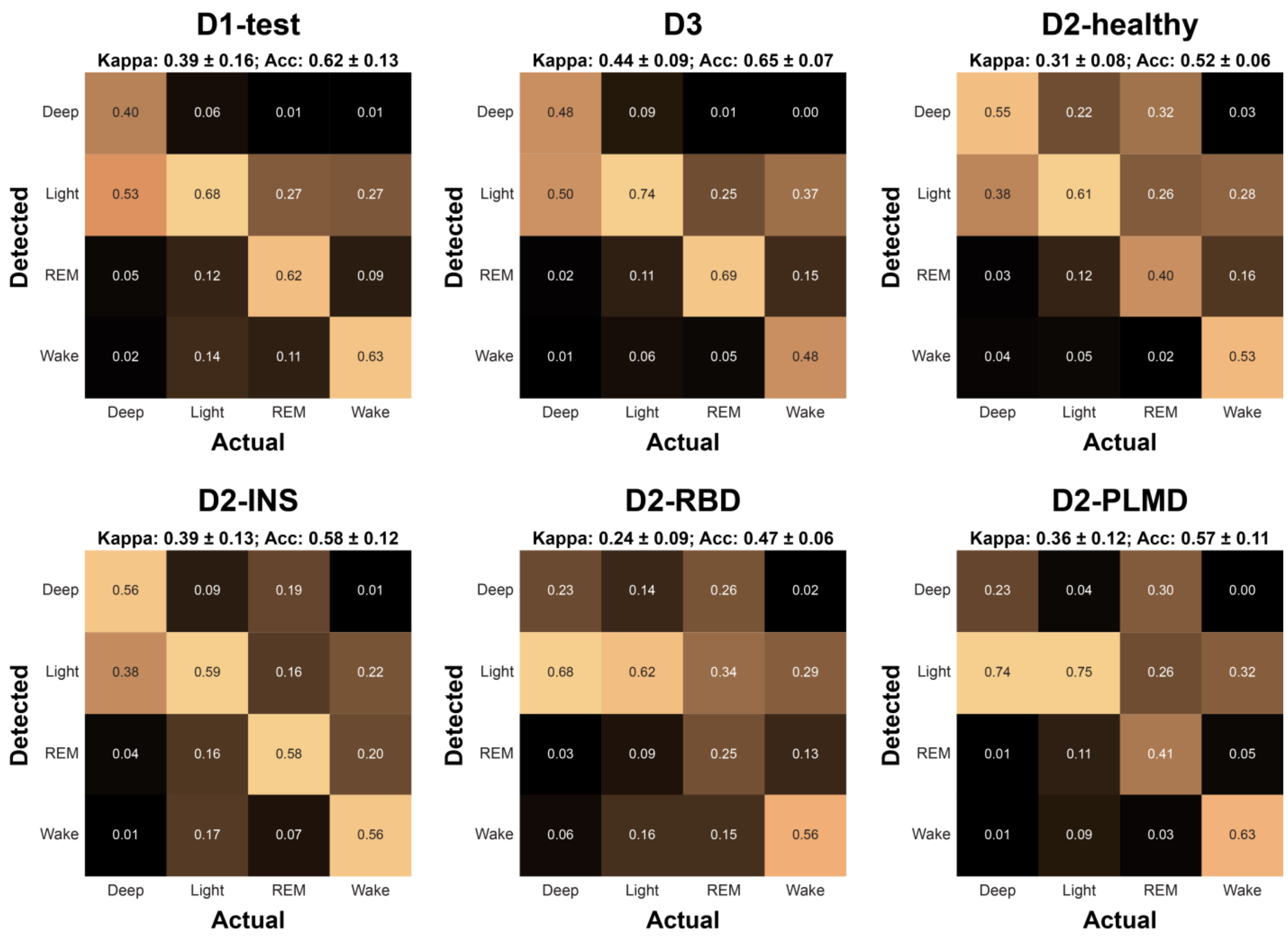
Sleep staging accuracy for all datasets using probability thresholds

Stage	Sensitivity						Specificity					
	D1-test	D2-healthy	D2-INS	D2-RBD	D2-PLMD	D3	D1-test	D2-healthy	D2-INS	D2-RBD	D2-PLMD	D3
Deep	0.37 (0.33)	0.57 (0.23)	0.51 (0.36)	0.25 (0.28)*	0.22 (0.22)	0.46 (0.33)	0.96 (0.06)	0.76 (0.08)***	0.93 (0.07)	0.86 (0.12)***	0.89 (0.06)**	0.94 (0.06)
Light	0.68 (0.16)	0.62 (0.13)	0.58 (0.11)	0.65 (0.15)*	0.74 (0.10)	0.74 (0.13)*	0.67 (0.16)	0.72 (0.09)	0.77 (0.11)	0.63 (0.11)	0.63 (0.13)	0.64 (0.12)
REM	0.58 (0.30)	0.41 (0.08)	0.50 (0.34)	0.23 (0.17)***	0.38 (0.17)*	0.67 (0.26)*	0.90 (0.09)	0.89 (0.09)	0.85 (0.12)	0.91 (0.07)	0.92 (0.05)	0.90 (0.06)
Wake	0.65 (0.21)	0.63 (0.26)	0.57 (0.21)	0.54 (0.26)**	0.57 (0.23)	0.49 (0.17)***	0.88 (0.12)	0.96 (0.01)*	0.86 (0.15)	0.86 (0.15)	0.93 (0.11)	0.95 (0.07)***

*P < 0.05 vs D1-test
**P < 0.01 vs D1-test
***P < 0.001 vs D1-test
All data presented as mean (SD)

INS, insomnia; PLMD, periodic limb movement disorder; RBD, REM behavior disorder; REM, rapid eye movement; SD, standard deviation.

The confusion matrices show a diagonal dominance, with lower Kappa values associated with the D2 datasets



Acc, accuracy; INS, insomnia; PLMD, periodic limb movement disorder; RBD, REM behavior disorder; REM, rapid eye movement sleep.