Analysis of time series data measured with wearable devices

Eder Zavala

E.Zavala@bham.ac.uk

@ederzavala

Slides, Python code and demo files at:
https://shorturl.at/hDps9

Other useful resources:

pyBOAT - Wavelet analysis
https://github.com/tensionhead/pyBOAT

CosinorPy - Rhythmometry analysis
https://github.com/mmoskon/CosinorPy

UNIVERSITY OF BIRMINGHAM

Centre for Systems Modelling & Quantitative Biomedicine

Menu

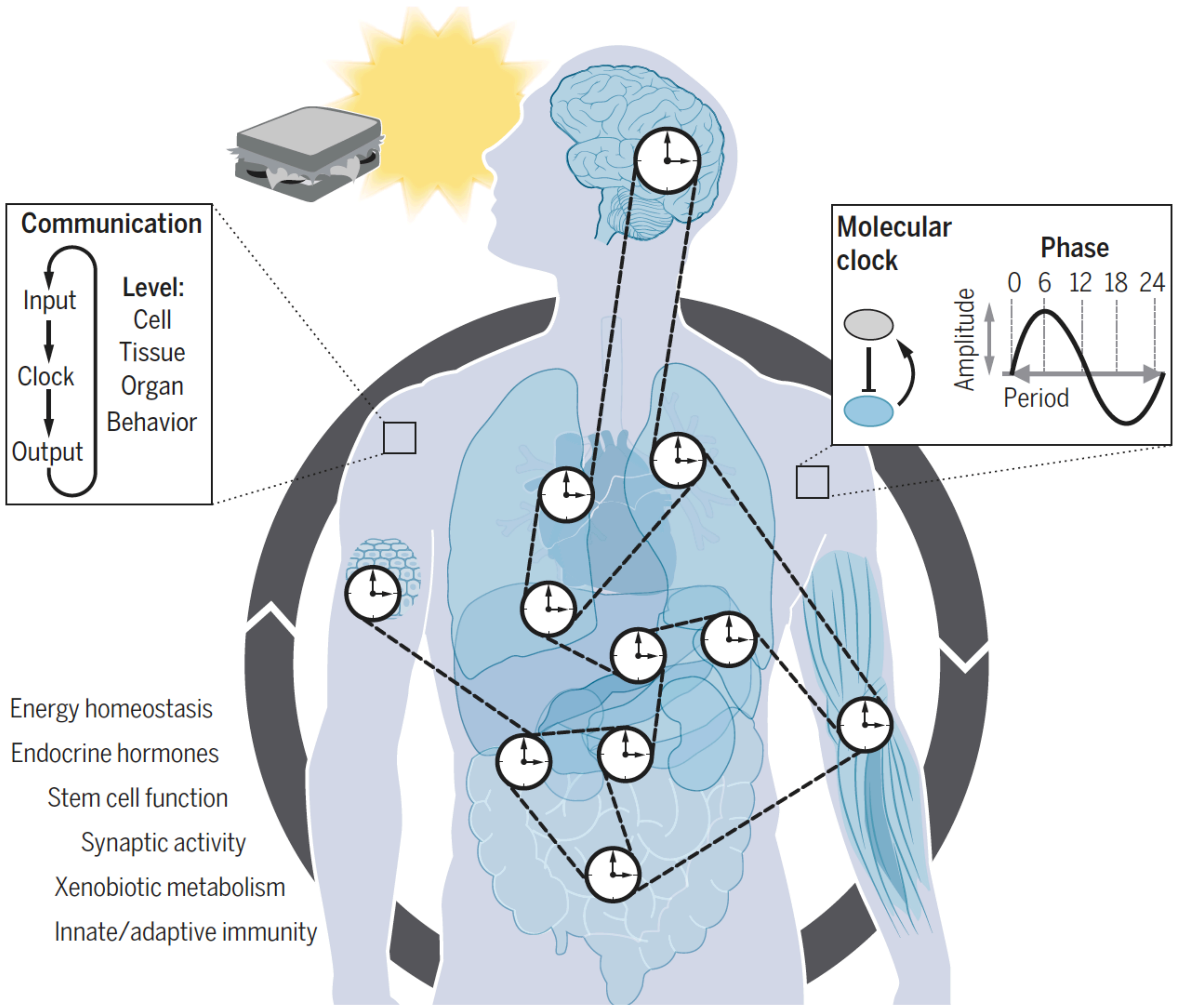
Why do we need to analyse time series data from wearables?

- **Characterise body rhythms.** Quantitatively, at multiple time scales (not just circadian), and at adequate time resolutions.
- **Quantifying variability.** Endogenous, behavioural, environmental. Inter- vs intra-individual.
- **Understanding the effects of chrono-disruptions.** Quantifying fast dynamic responses to perturbations and slow transitions to diseased states.

How do we analyse time series data from wearables?

A dynamical systems view of physiology

Sustaining healthy homeostasis requires the coordination of body rhythms

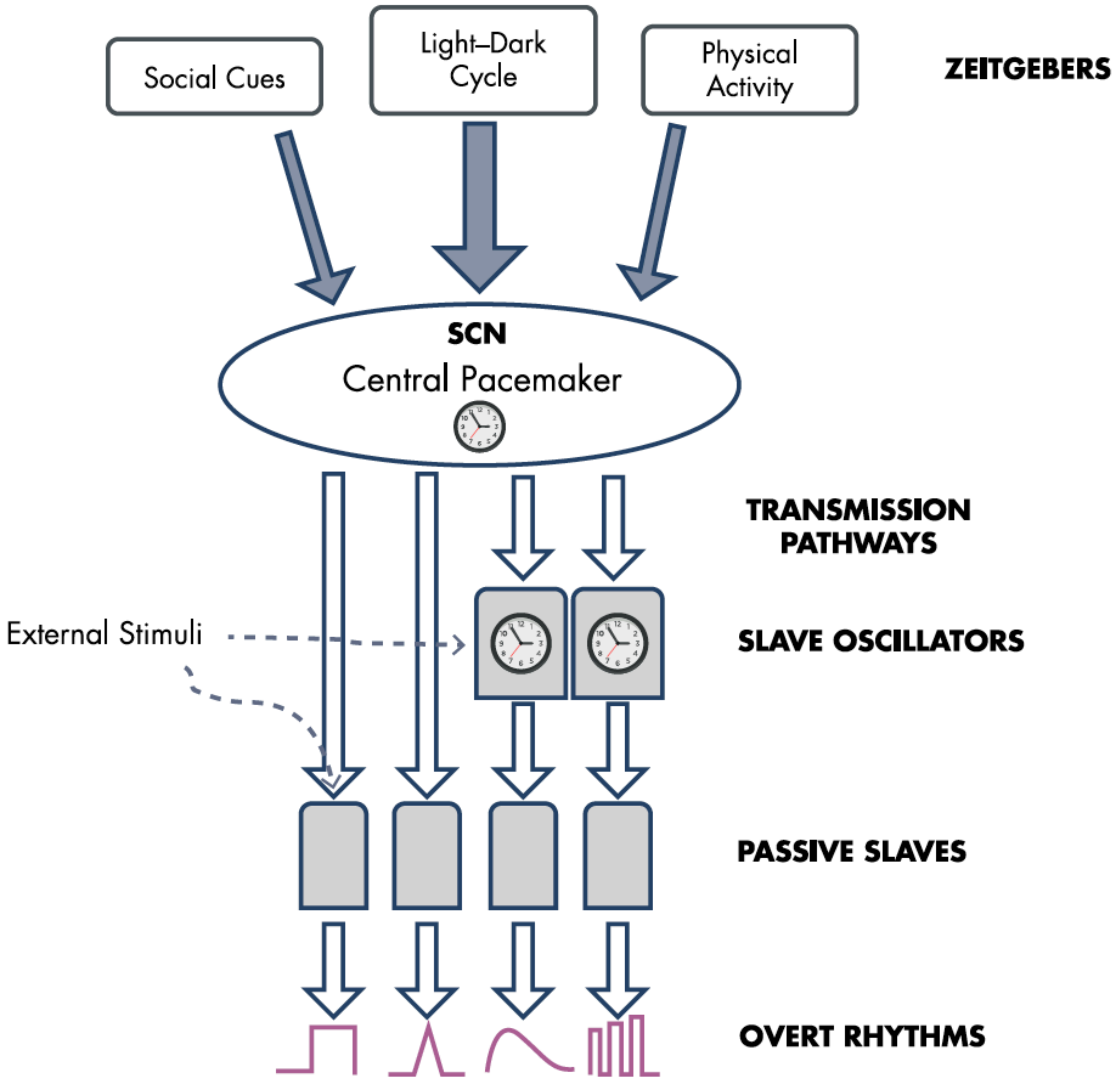


*Chrono*disruption
*Chrono*diagnosis
*Chrono*therapy

Understanding

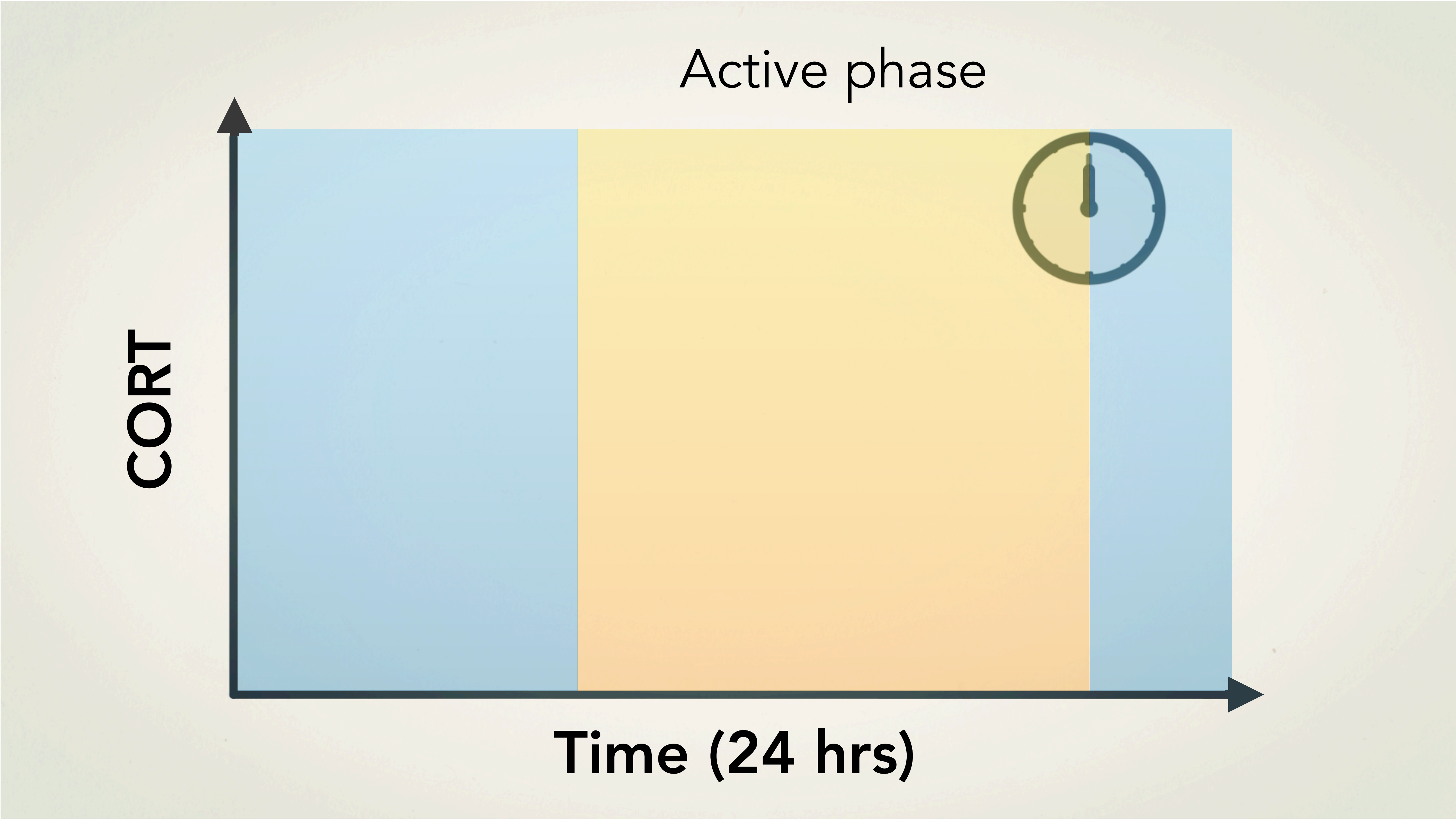
Mathematics, computer science, & clinical expertise.

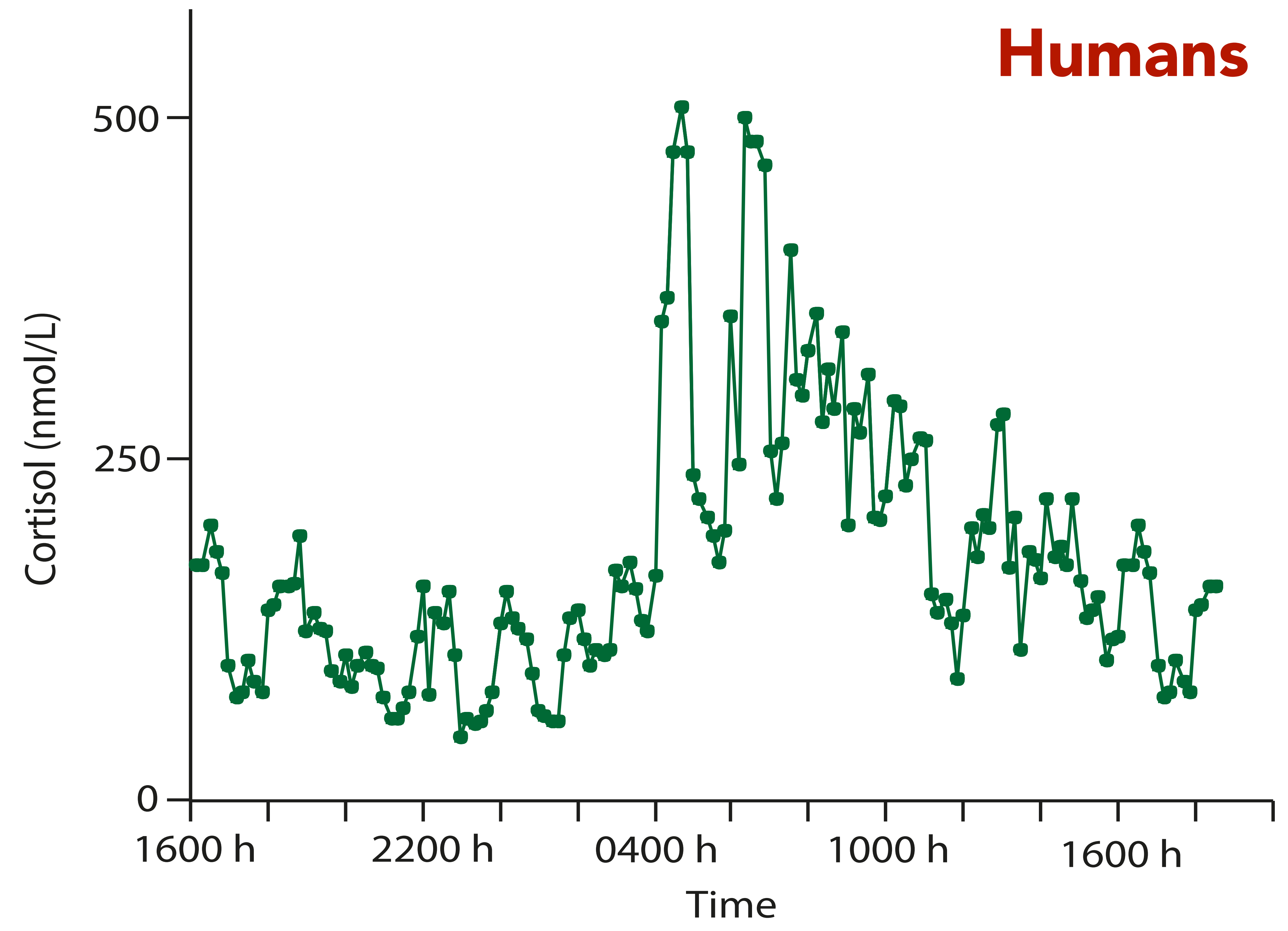
A systems-level view of body rhythms



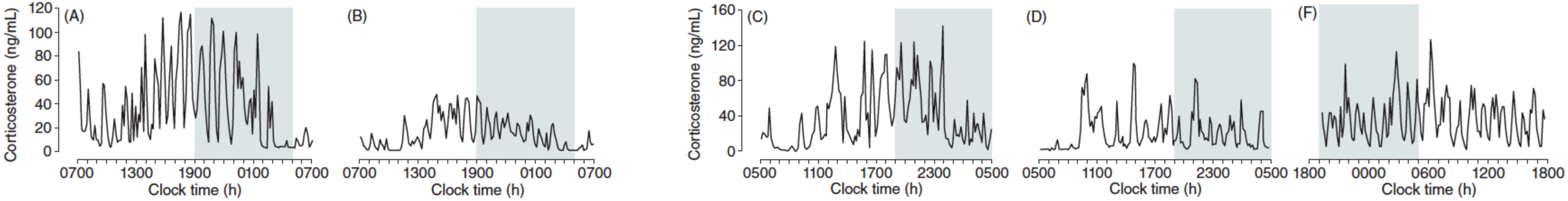
Koronowsky & Sassone-Corsi 2021 *Science* **371**:690 / Oster et al. 2017 *EndoRevs* **38**(1):3-45

Plasma cortisol levels are dynamic





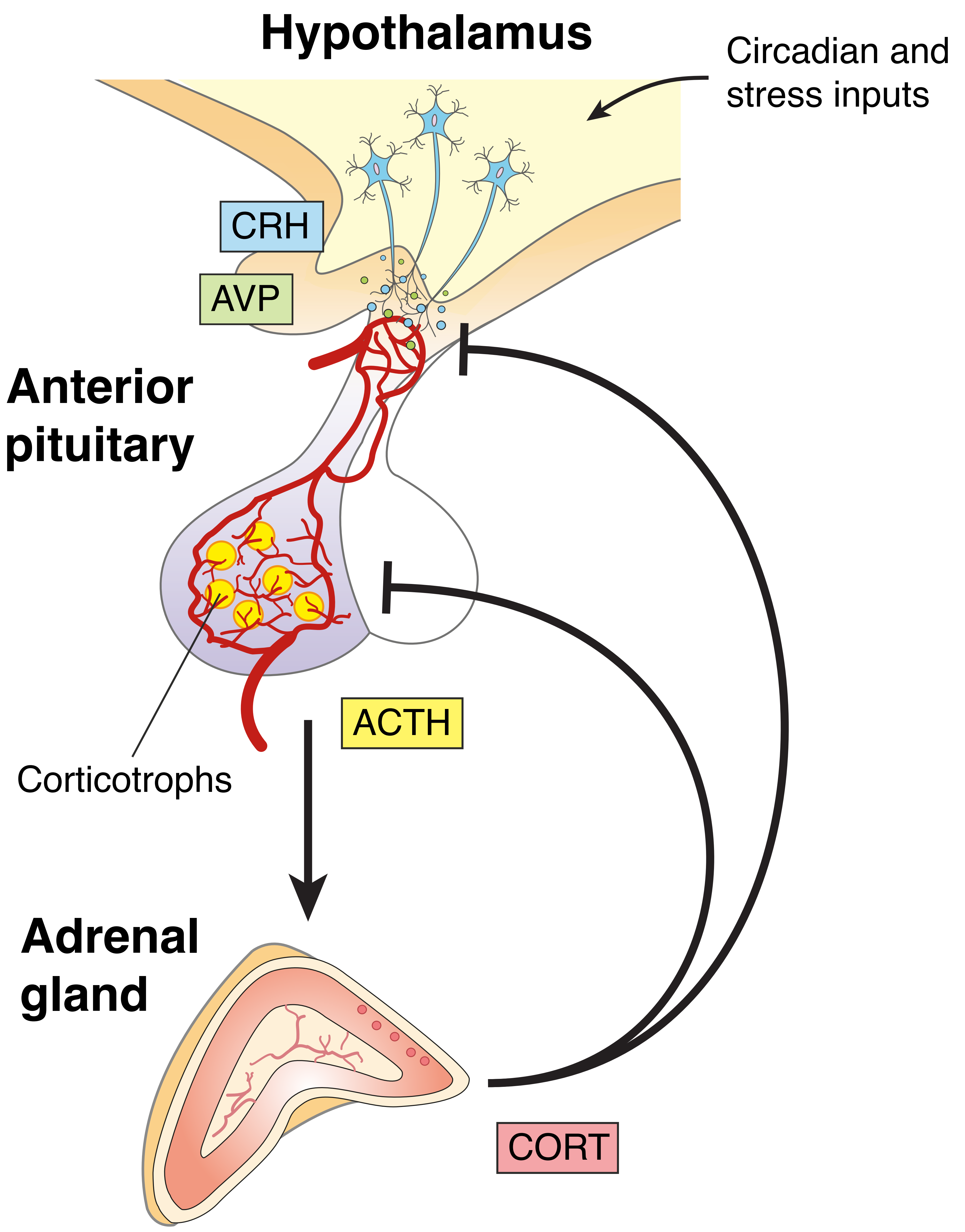
Rats

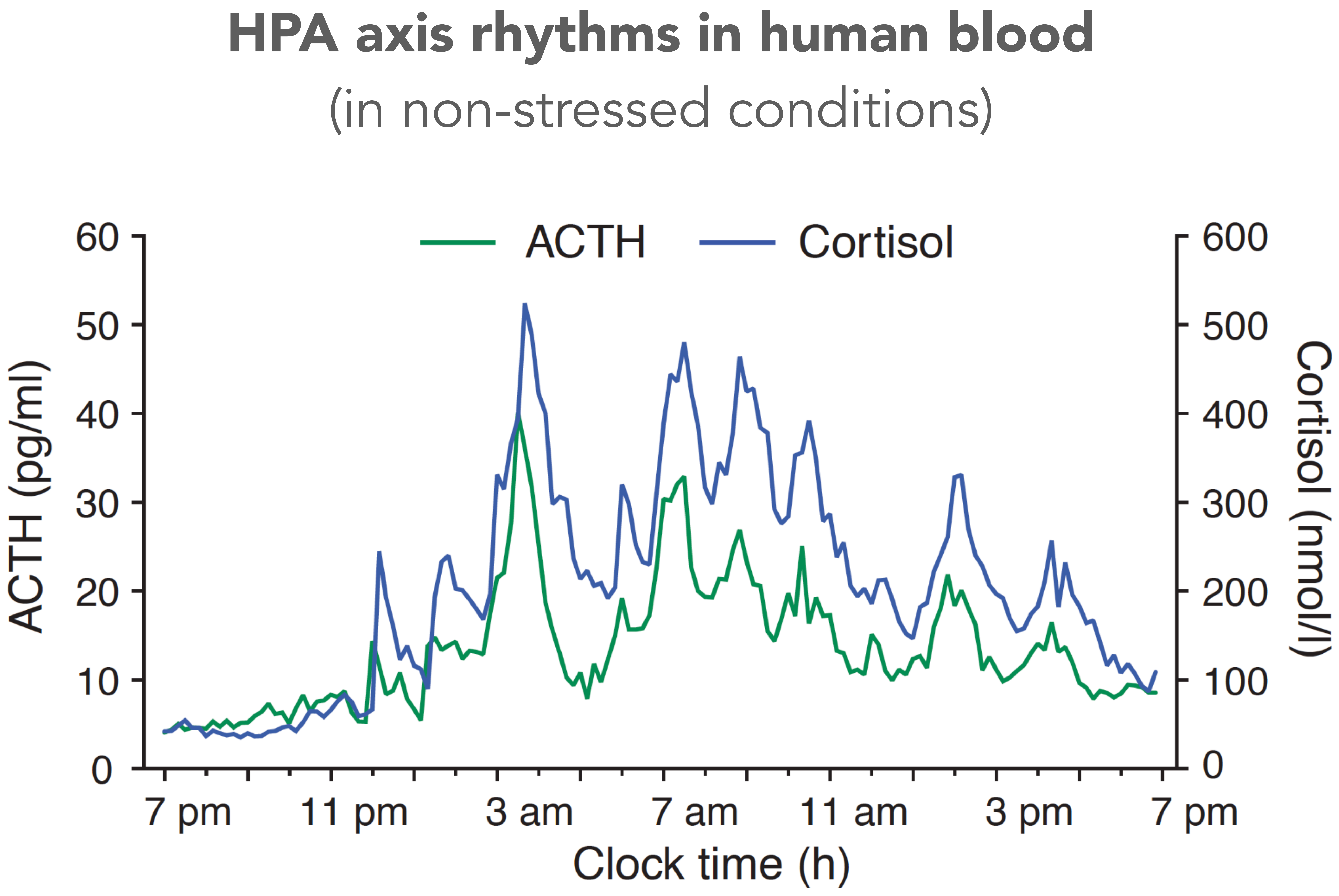


Female | Male | Juvenile | Old | Arthritis

Lightman & Terry 2014 *Lancet* **2**:593-99 / Spiga et al. 2014 *ComprPhys* **4**:1273-98

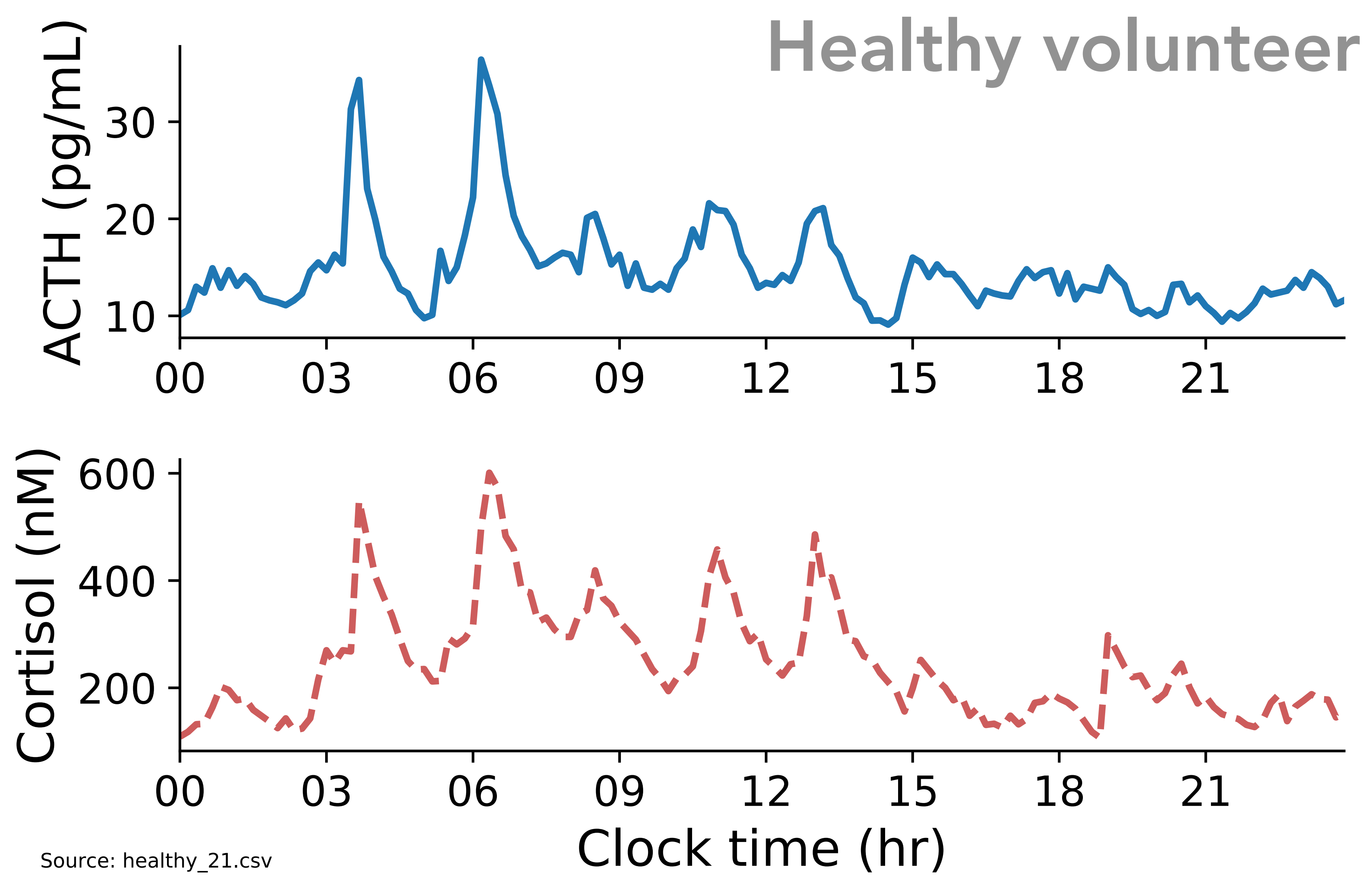
The HPA axis governs dynamic cortisol secretion

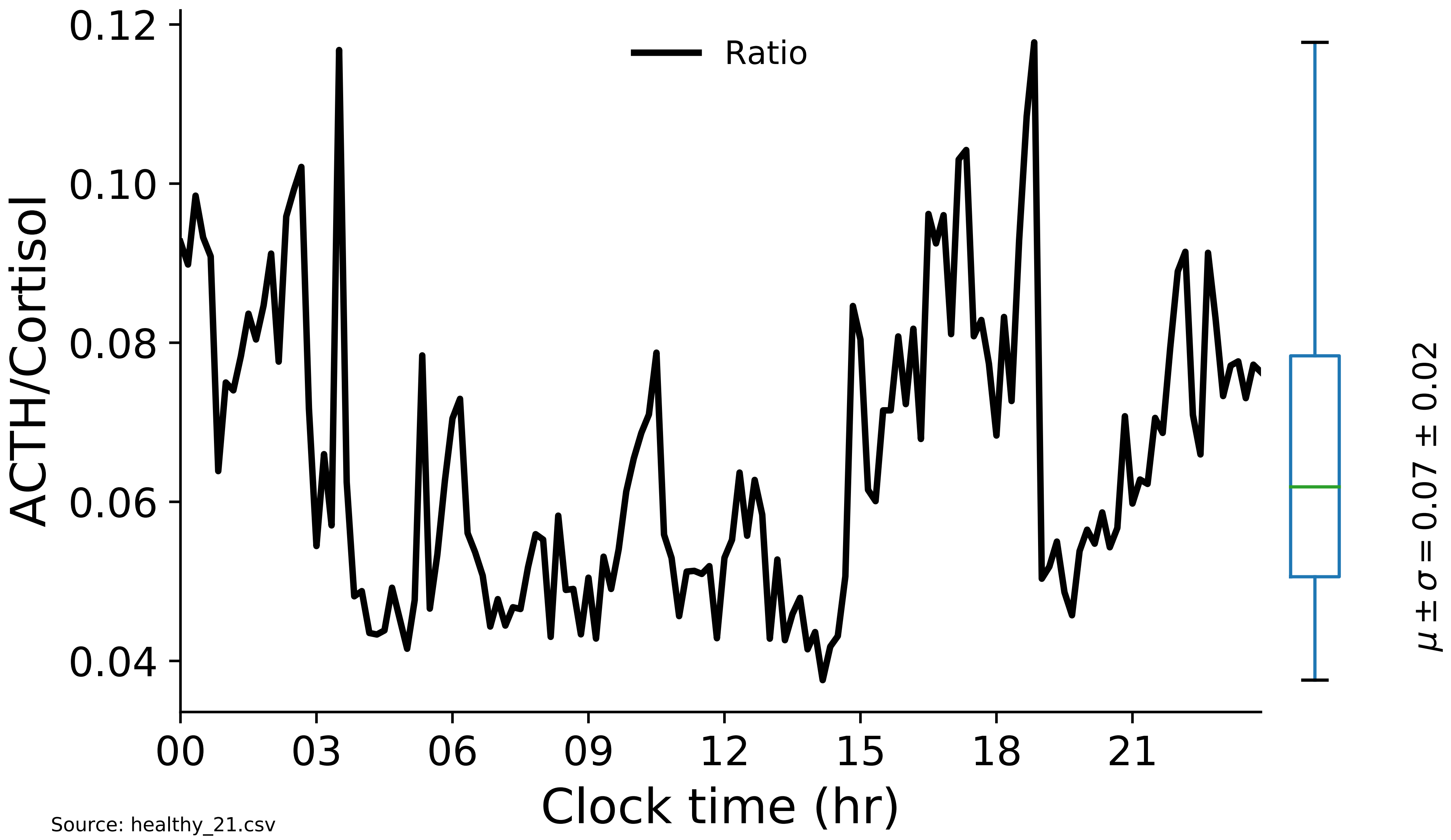


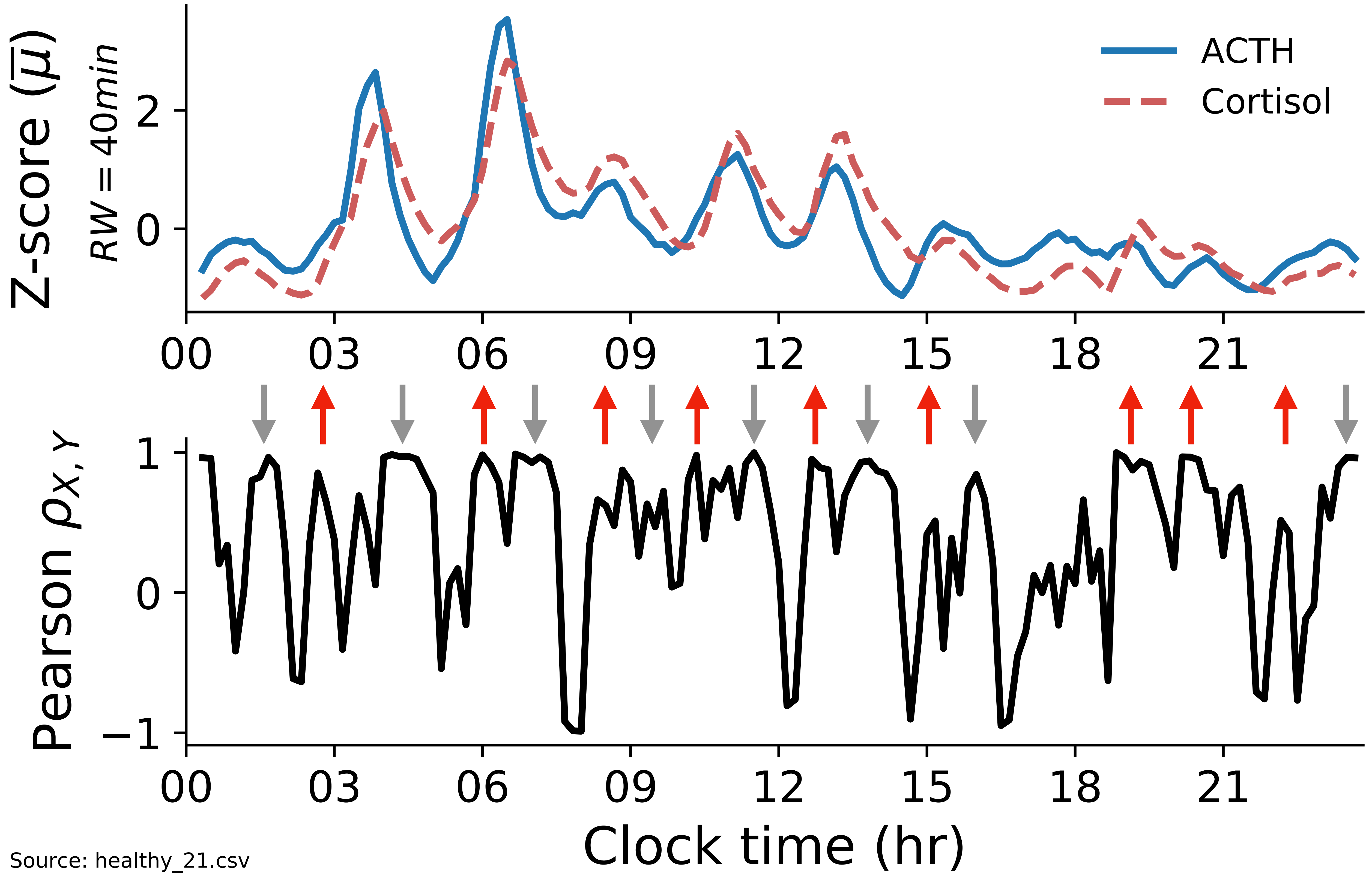


Zavala et al. 2019 *TrendsEndoMetab* **30**(4):244-57

Dynamic relationship between ACTH & cortisol



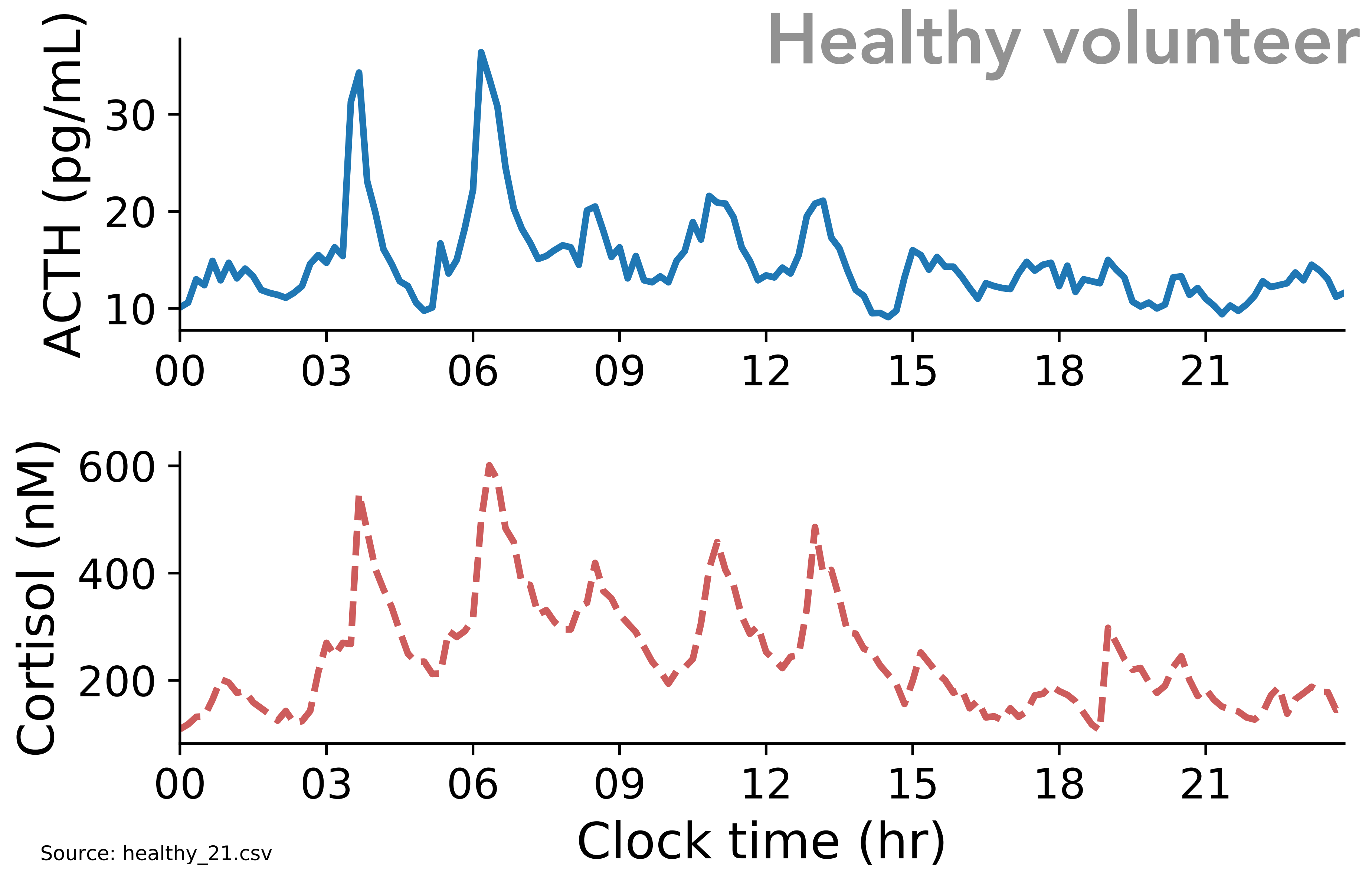


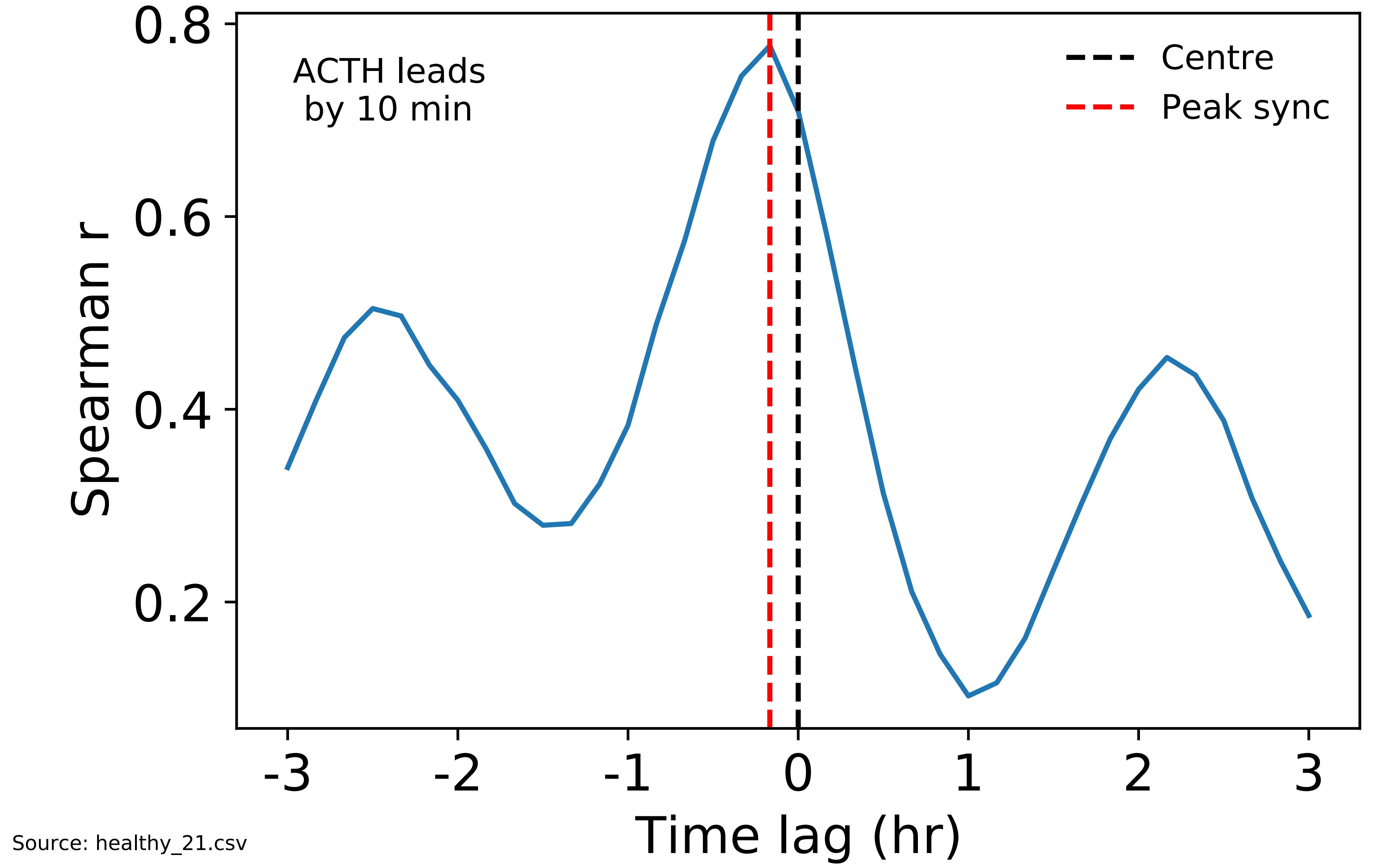


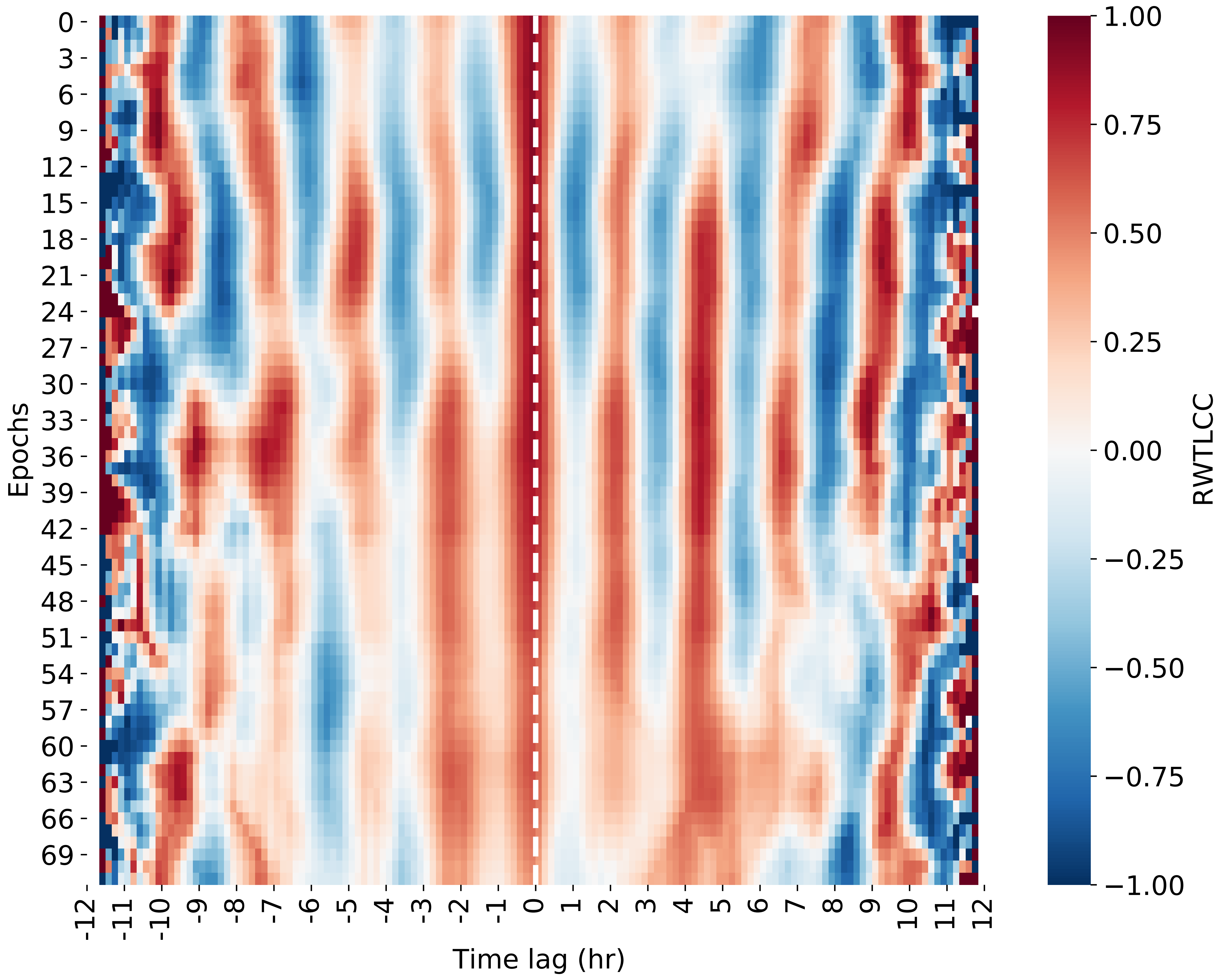
Ultradian period: ~2.5

Galvis, Zavala et al. 2022 *JRoySocInterface* **19**:20210925

Dynamic relationship between ACTH & cortisol

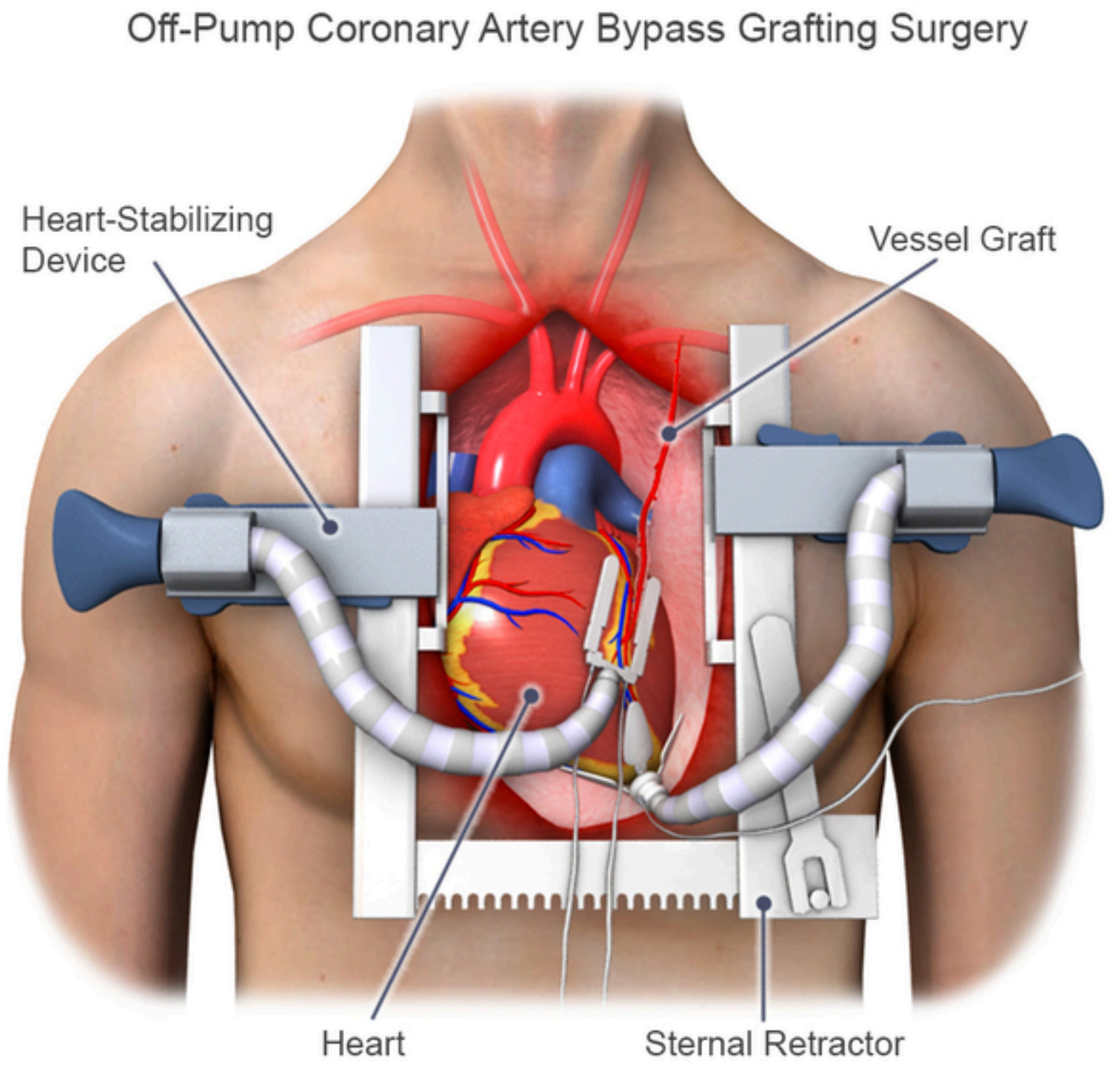




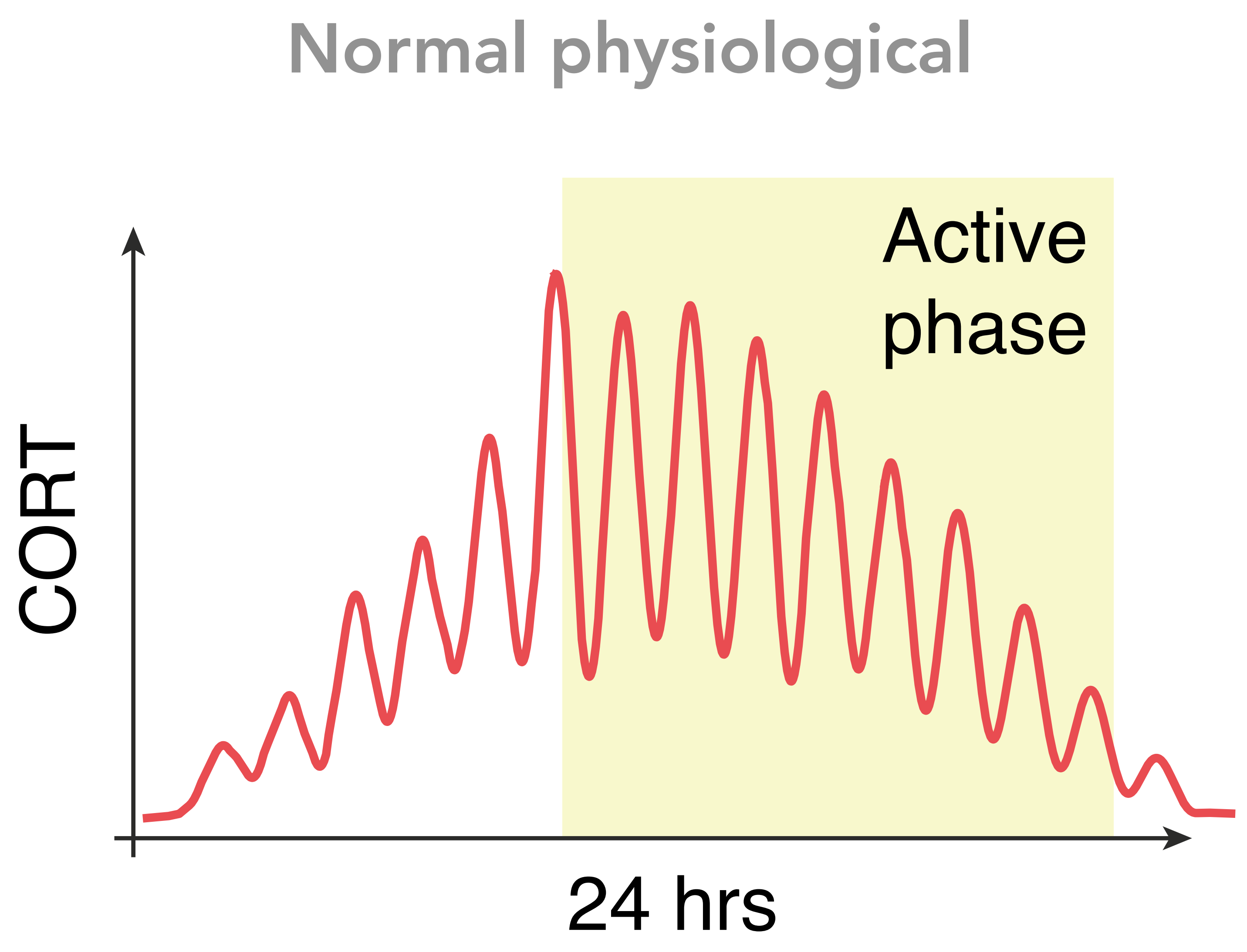


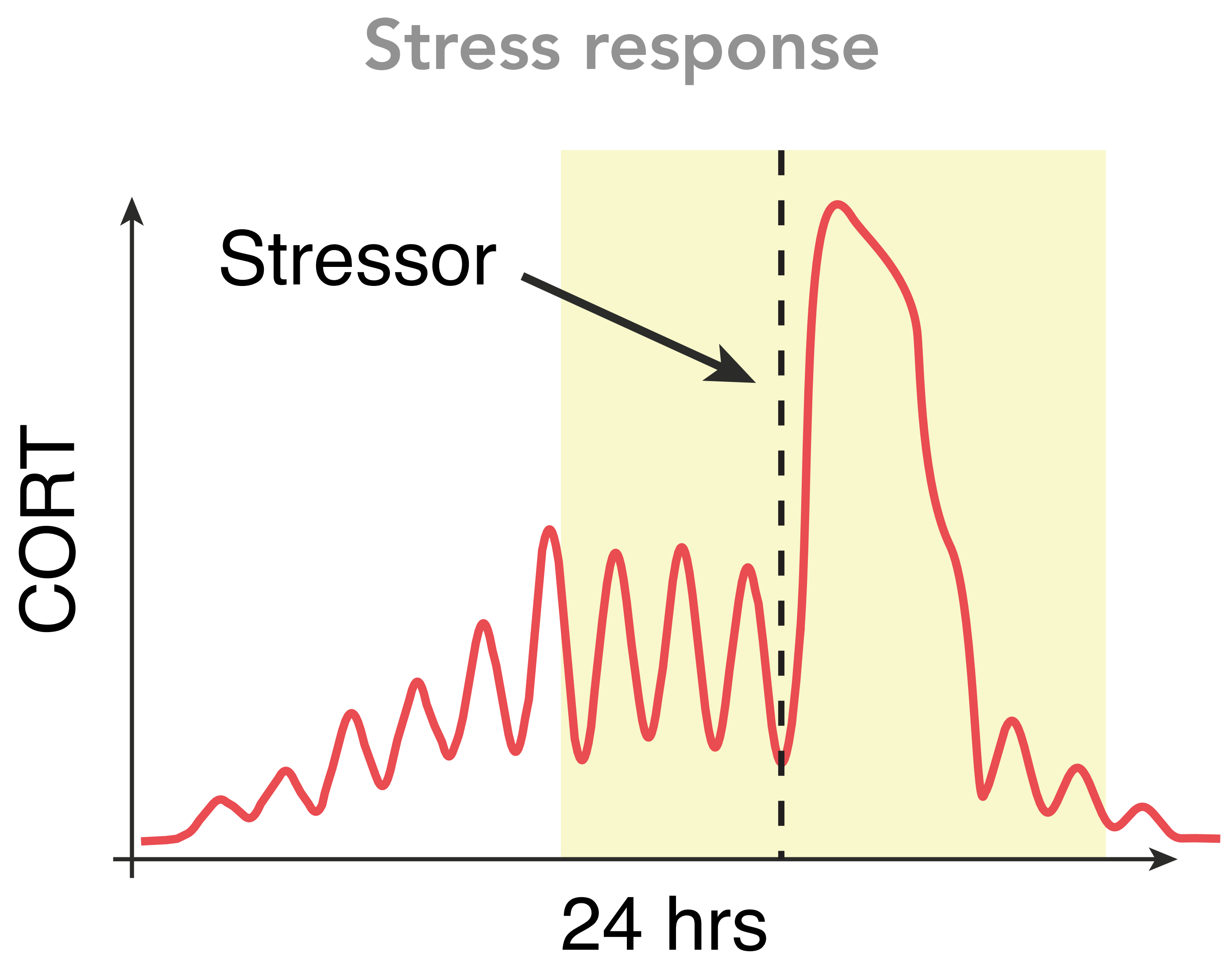
Galvis, Zavala et al. 2022 *JRoySocInterface* **19**:20210925

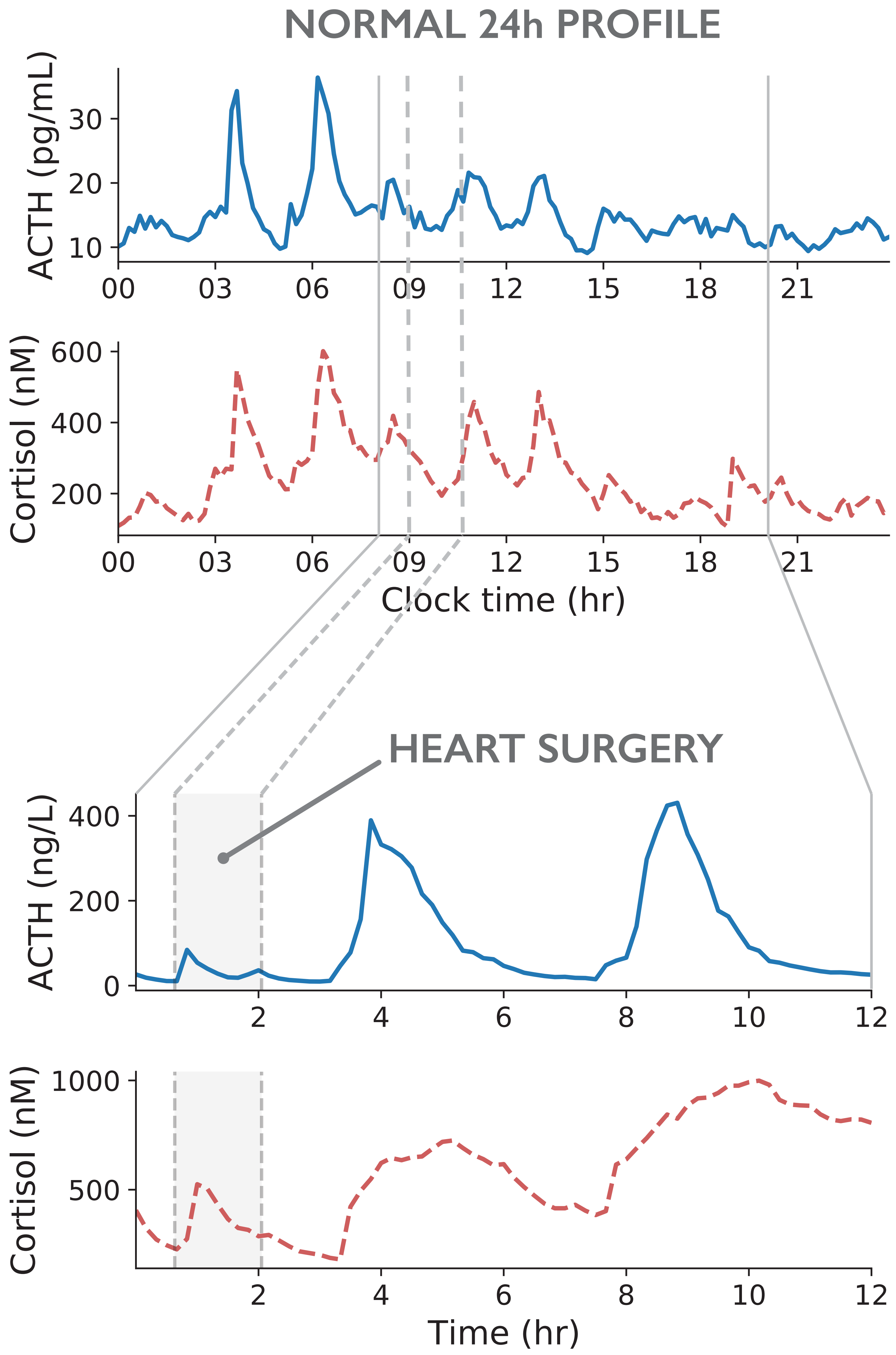
Case study: stress induced by heart surgery



	controls ($n = 3$)	patients ($n = 10$)
age	54 ± 13.8 years	65 ± 6.2 years
height	180 ± 6.7 cm	173 ± 6.4 cm
weight	87.5 ± 13.7 kg	83 ± 10.7 kg
BMI	26.9 ± 2.1 kg m^{-2}	27.8 ± 4.1 kg m^{-2}
sampling duration	24 h	12 h
anaesthesia start time	—	8.26 h (± 22 min)
surgery start time	—	9.19 h (± 22 min)
surgery end time	—	12.15 h (± 60 min)
surgery duration	—	176 ± 58.2 min
critical care stay	—	3 (range 2–7) days
hospital stay	—	5 (range 4–8) days

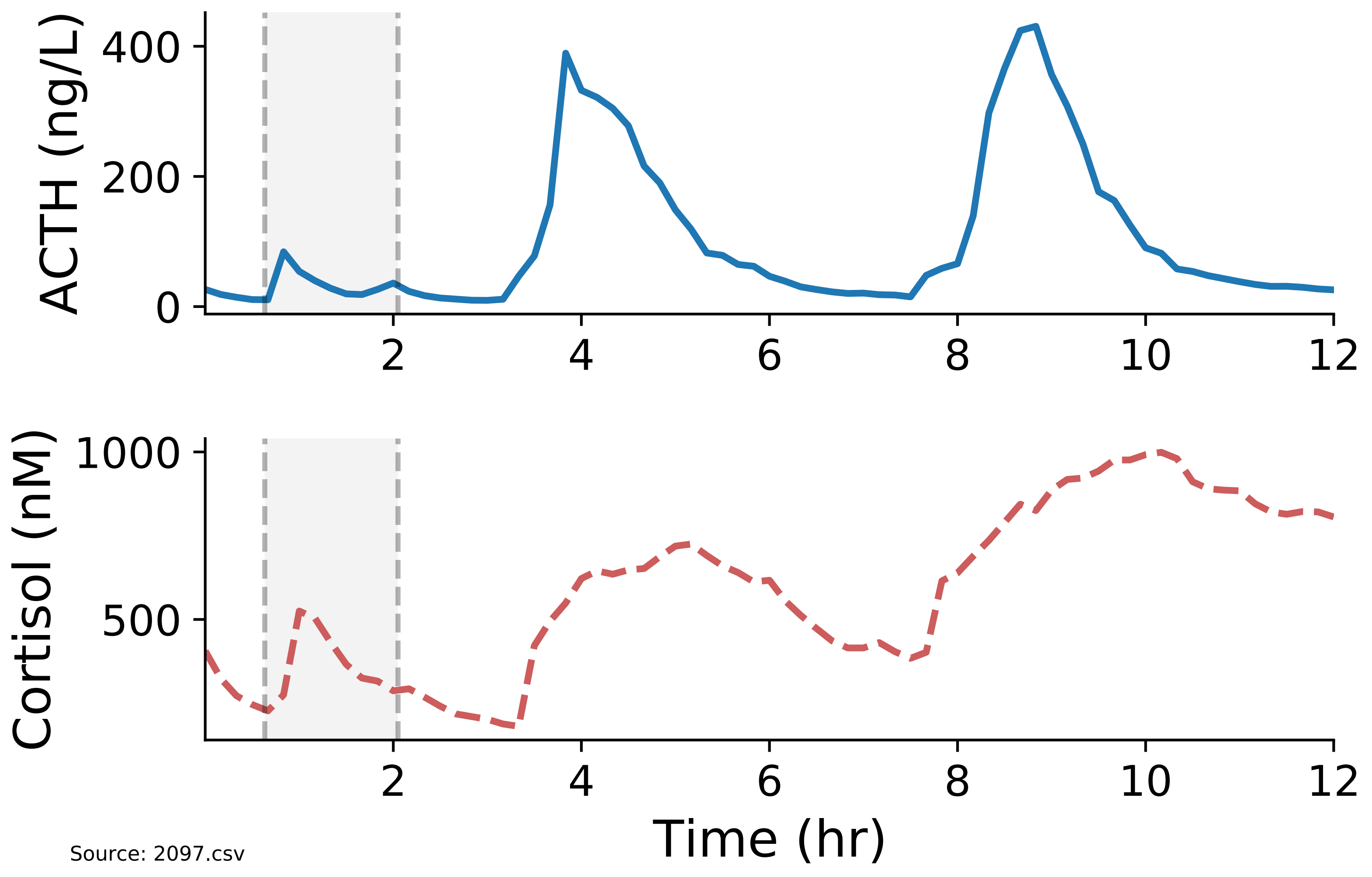


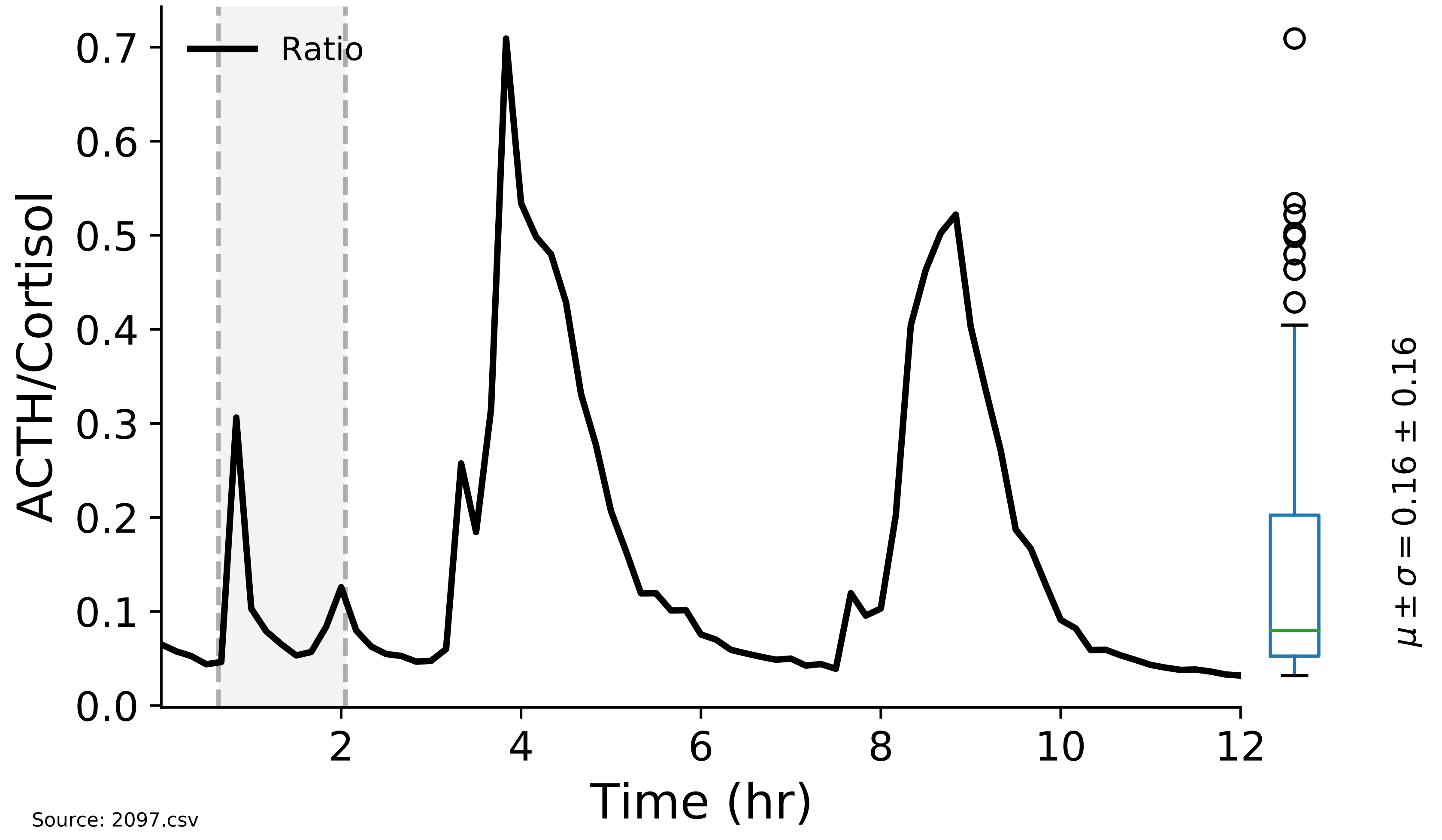


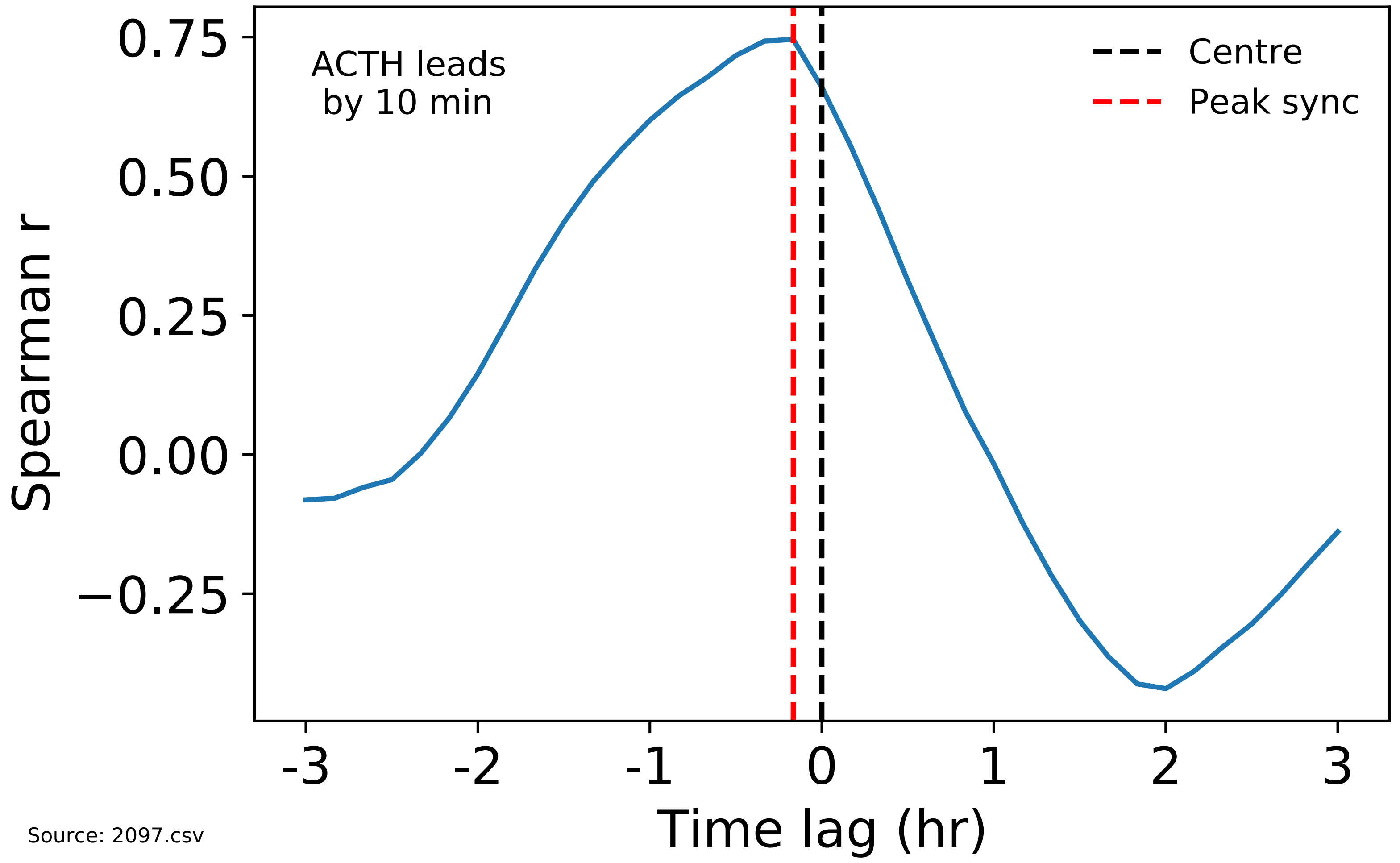


Galvis, Zavala et al. 2022 *JRoySocInterface* **19**:20210925

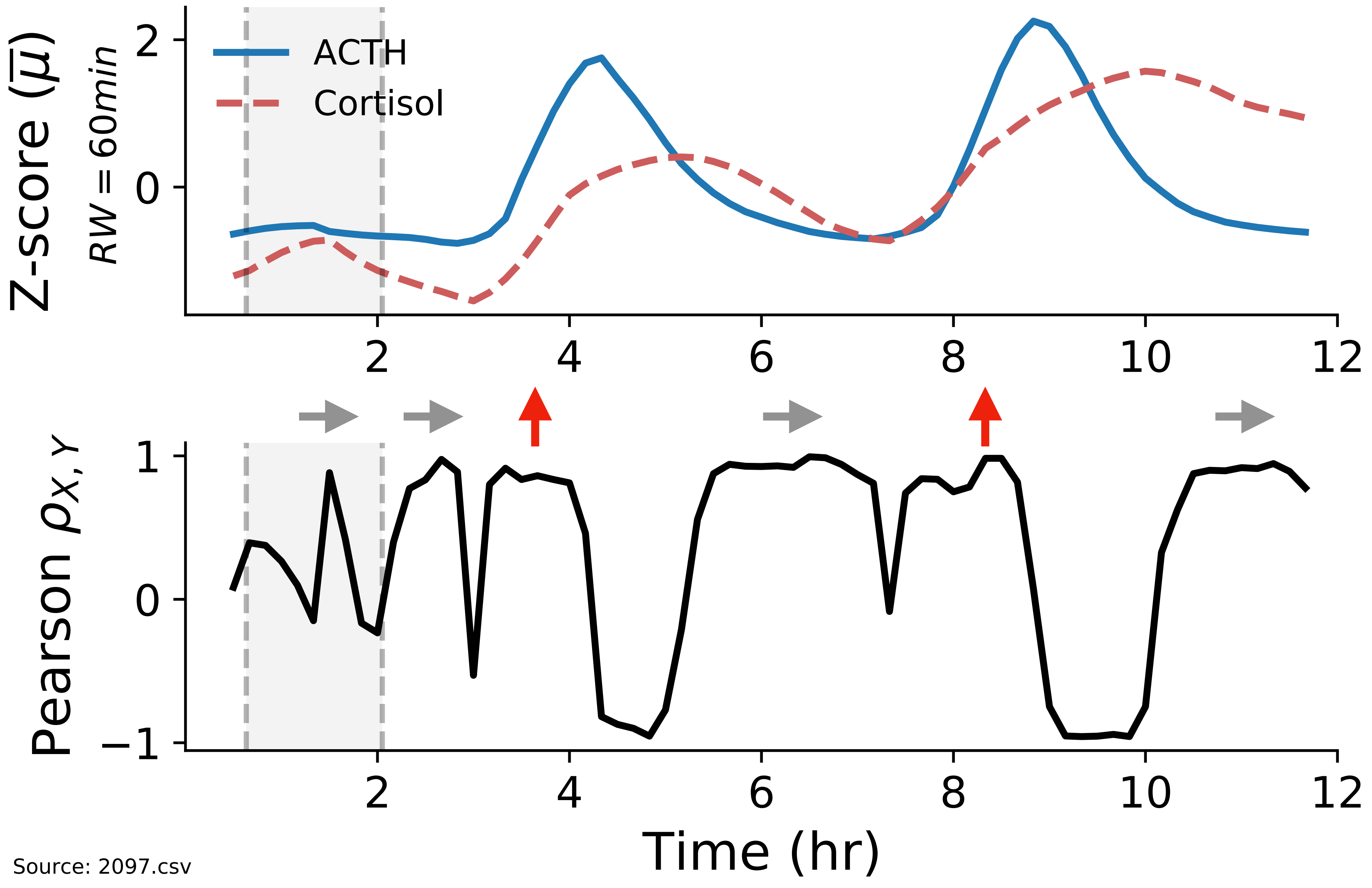
ACTH/CORT dynamic dissociation following CABG

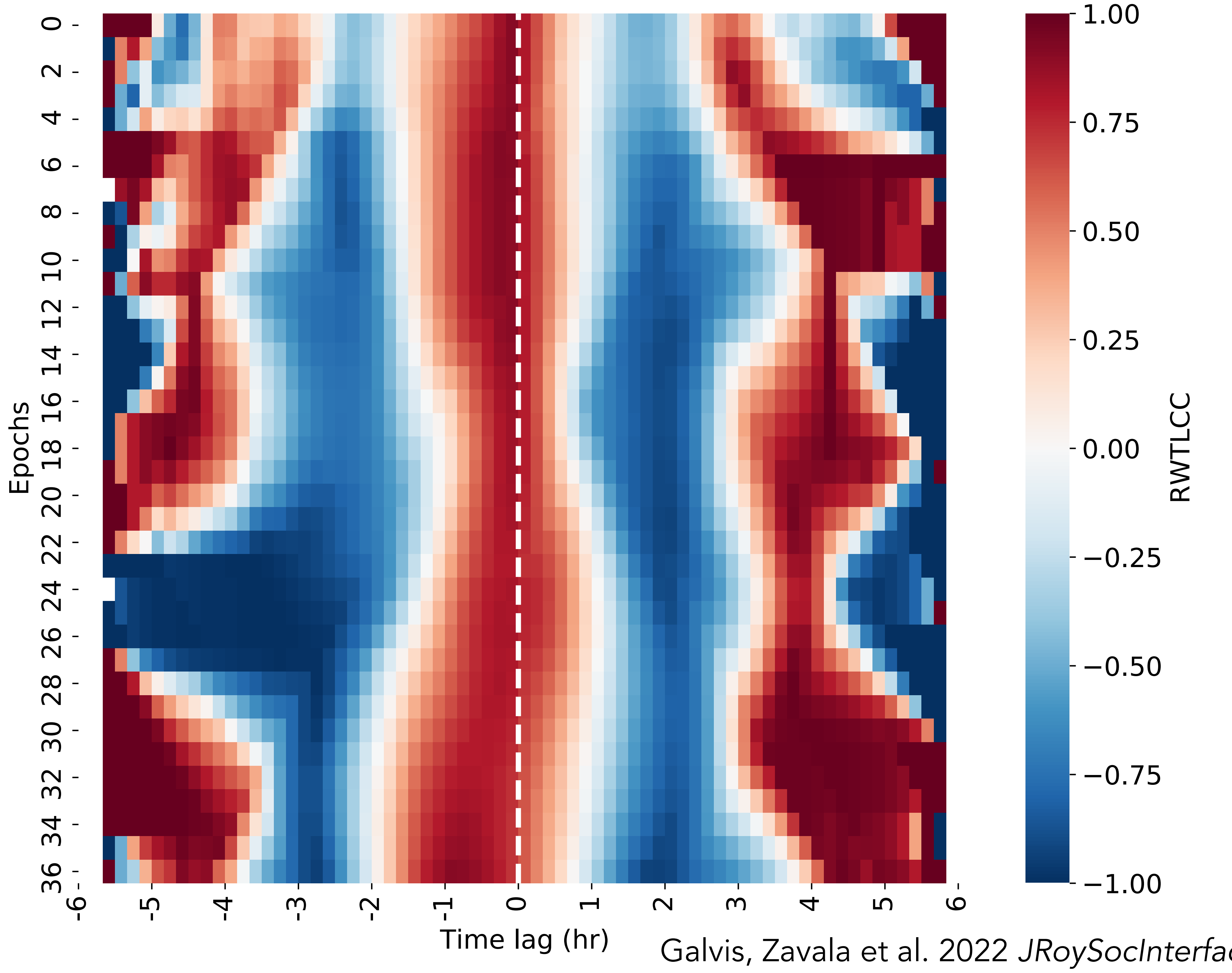






Ultradian period
5 hrs





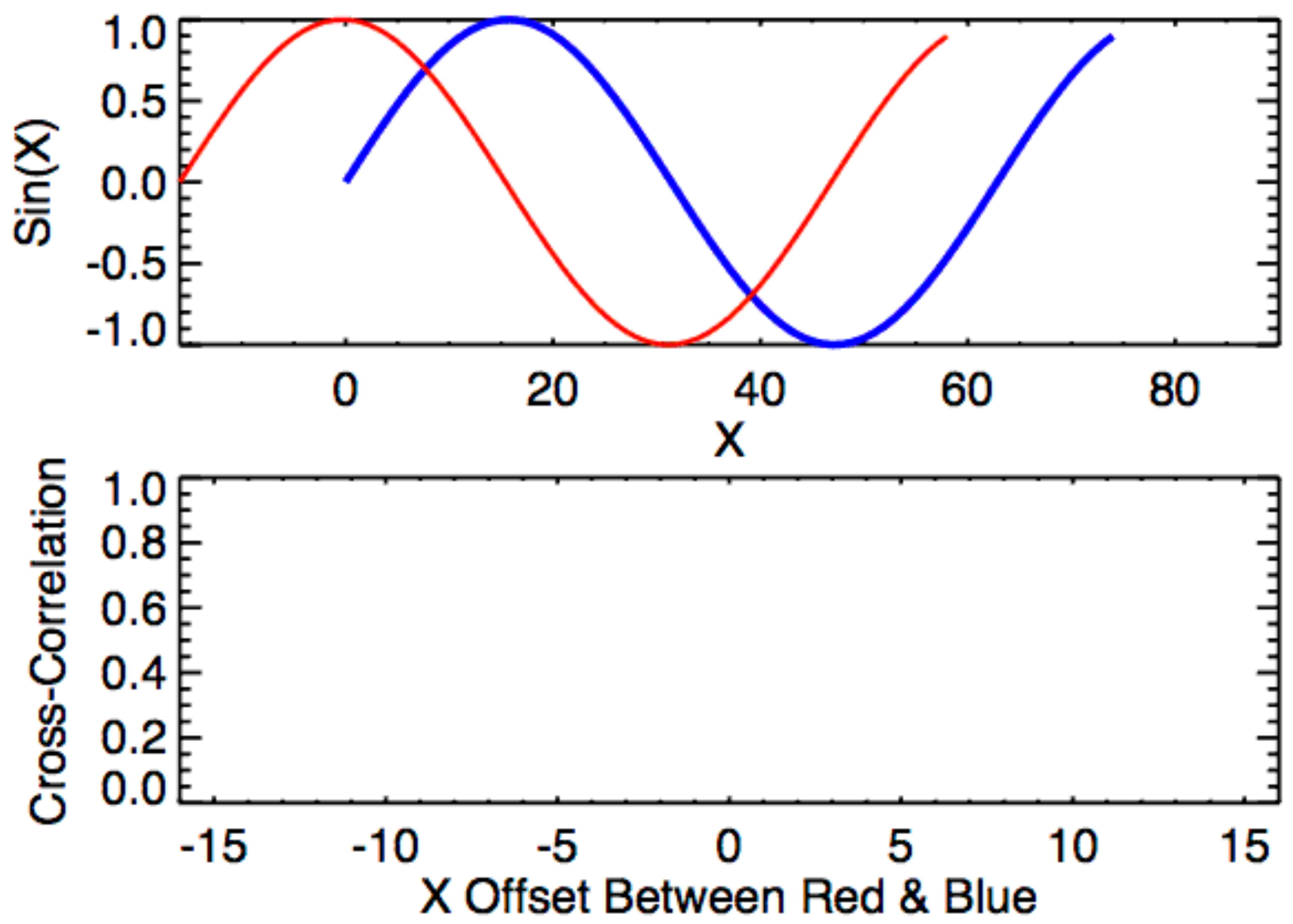
Galvis, Zavala et al. 2022 *JRoySocInterface* **19**:20210925

Let's look at some code!

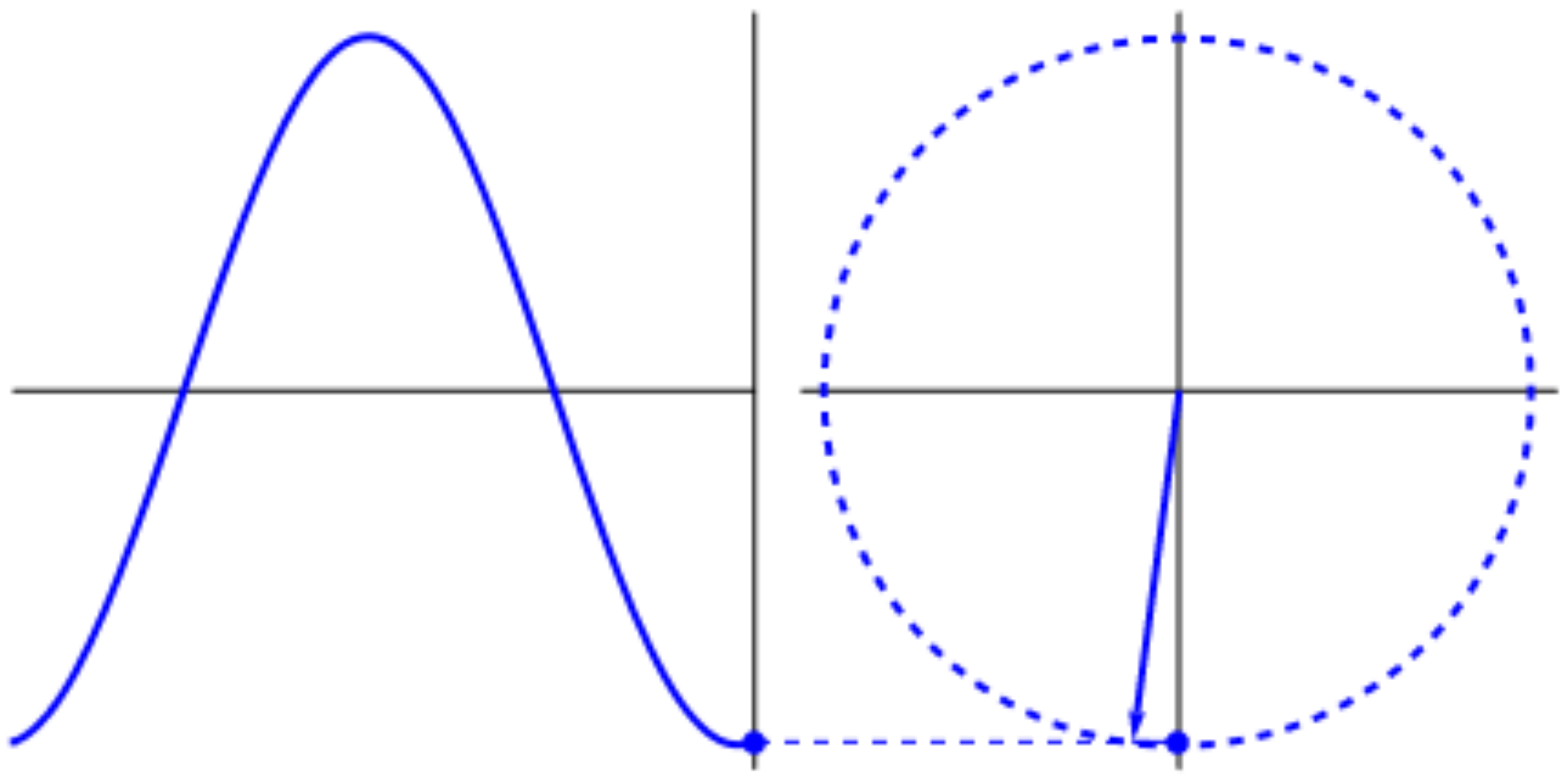
pip install *module_name*

Pearson correlation. The Pearson correlation measures how two continuous signals co-vary over time and indicate the linear relationship as a number between -1 (negatively correlated) to 0 (not correlated) to 1 (perfectly correlated). Two things to be cautious when using Pearson correlation is that 1) outliers can skew the results of the correlation estimation and 2) it assumes the data are homoscedastic such that the variance of your data is homogenous across the data range. Generally, the correlation is a snapshot measure of global synchrony. Therefore it does not provide information about directionality between the two signals such as which signal leads and which follows.

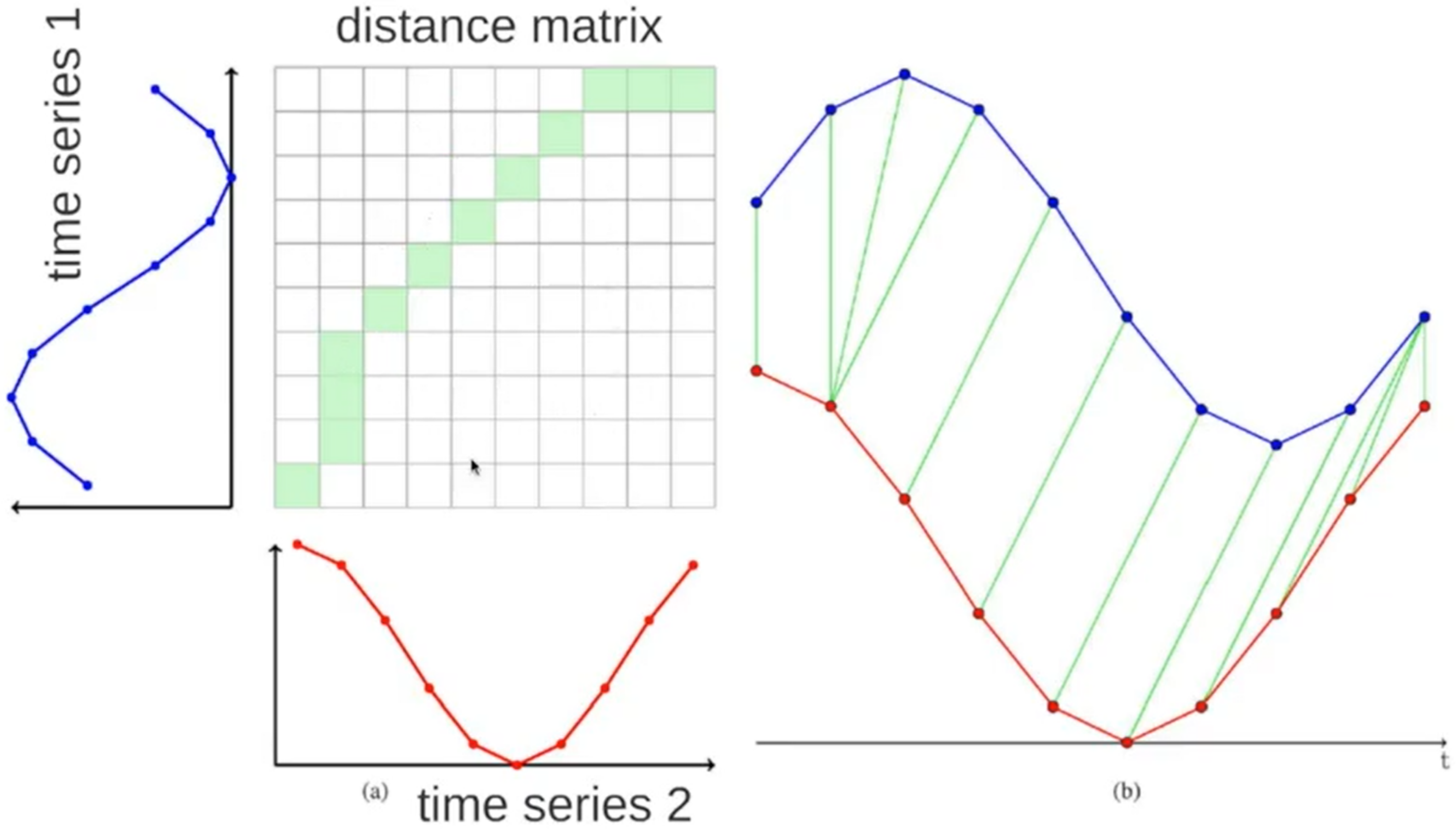
Time Lagged Cross Correlation. The TLCC can identify directionality between two signals such as a leader-follower relationship in which the leader initiates a response which is repeated by the follower.

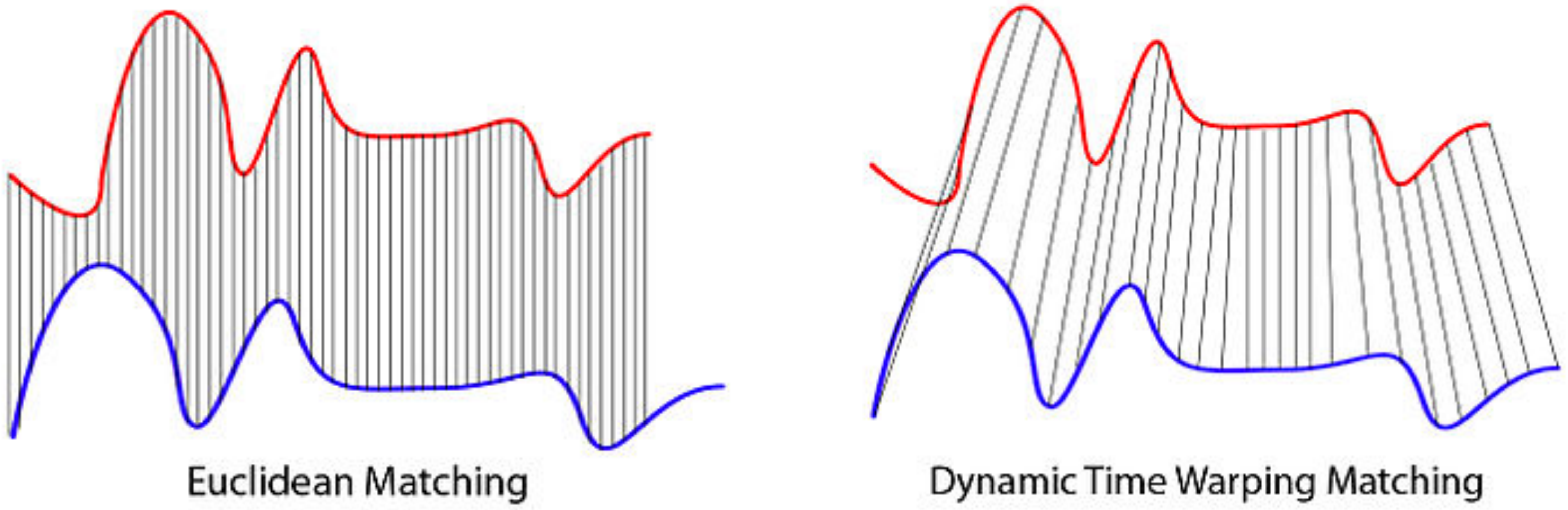


Instantaneous Phase Synchrony. The IPS measures moment-to-moment synchrony between two signals. It can be somewhat subjective because you need to filter the data to the wavelength of interest but you might have theoretical reasons for determining such bands. To calculate phase synchrony, we need to extract the phase of the signal which can be done by using the Hilbert transform which splits the signal into its phase and power. This allows us to assess if two signals are in phase (moving up and down together) or out of phase.

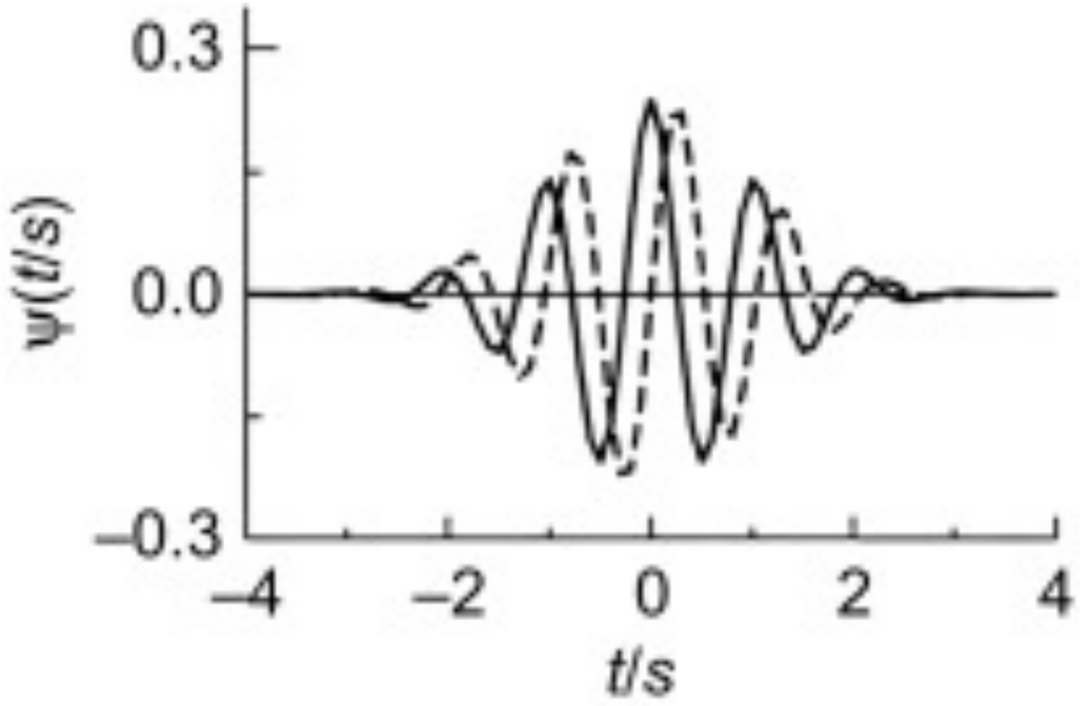


Dynamic Time Warping. DTW is a method that computes the (euclidean) path between two signals that minimize the distance between the two signals. One downside is that it cannot deal with missing values so you would need to interpolate beforehand if you have missing data points.

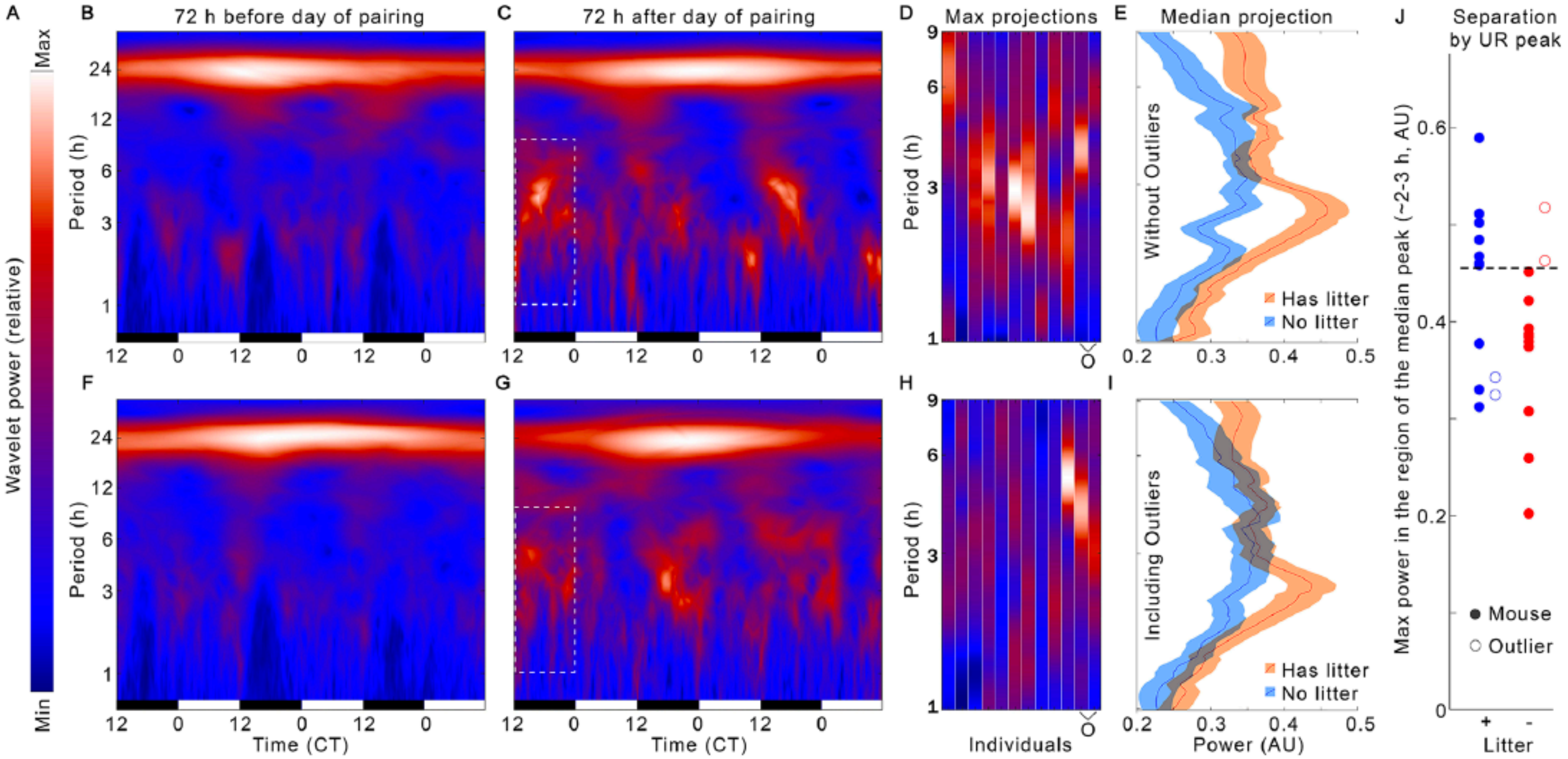




Wavelet analysis. An alternative to windowed Fourier transforms that also yields a two-dimensional plot showing strengths of variations as a function of both period (or frequency) and time. Unlike Fourier analysis, which characterizes similarities between time series and trigonometric functions of infinite extent, wavelet analysis addresses similarities, over limited portions of the time series, to waves of limited time extent called wavelets.



PLOS | ONE



RESEARCH ARTICLE

Detection of Successful and Unsuccessful Pregnancies in Mice within Hours of Pairing through Frequency Analysis of High Temporal Resolution Core Body Temperature Data

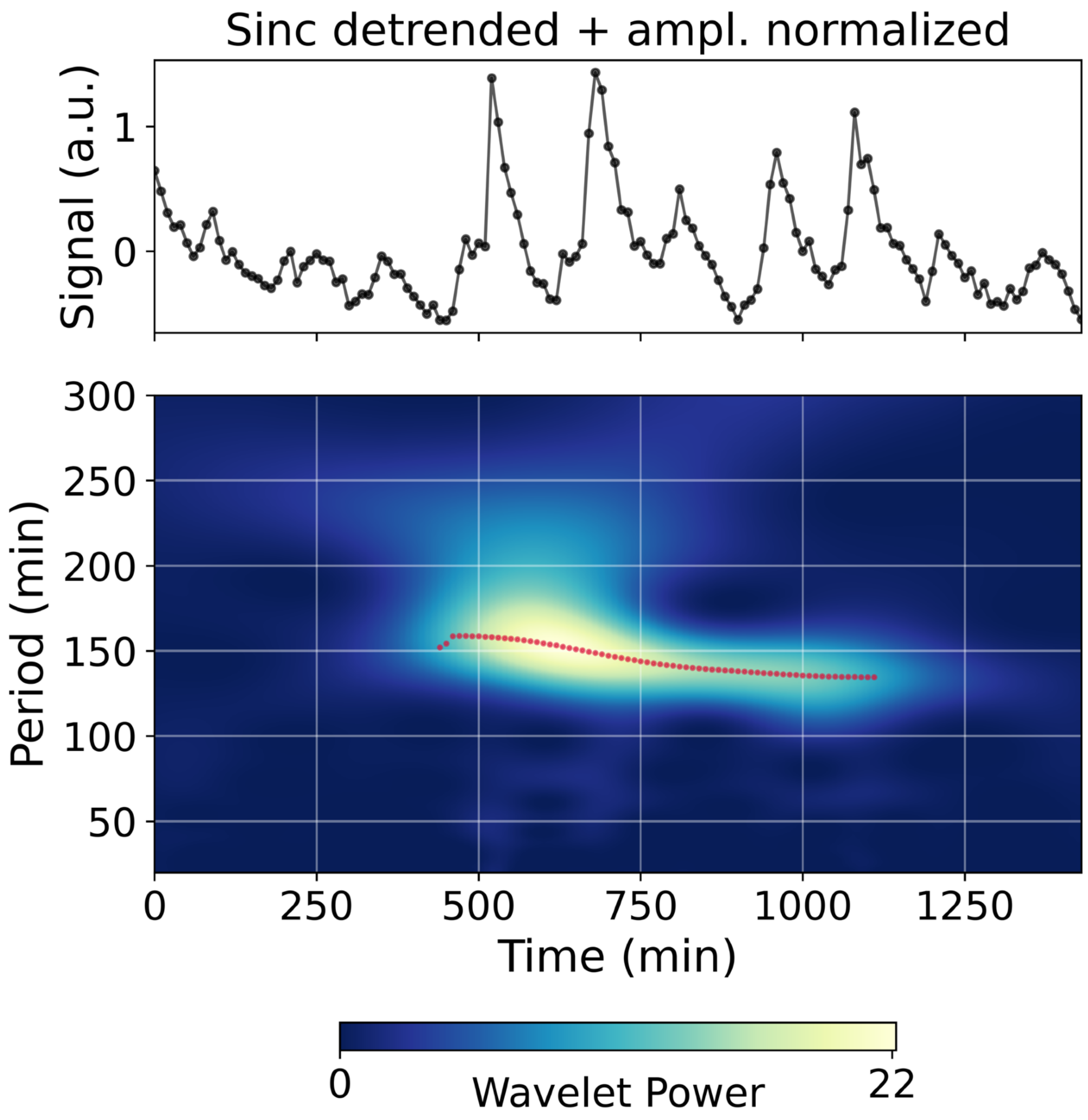
Benjamin L. Smarr[1], Irving Zucker[1,2], Lance J. Kriegsfeld[1,3]*

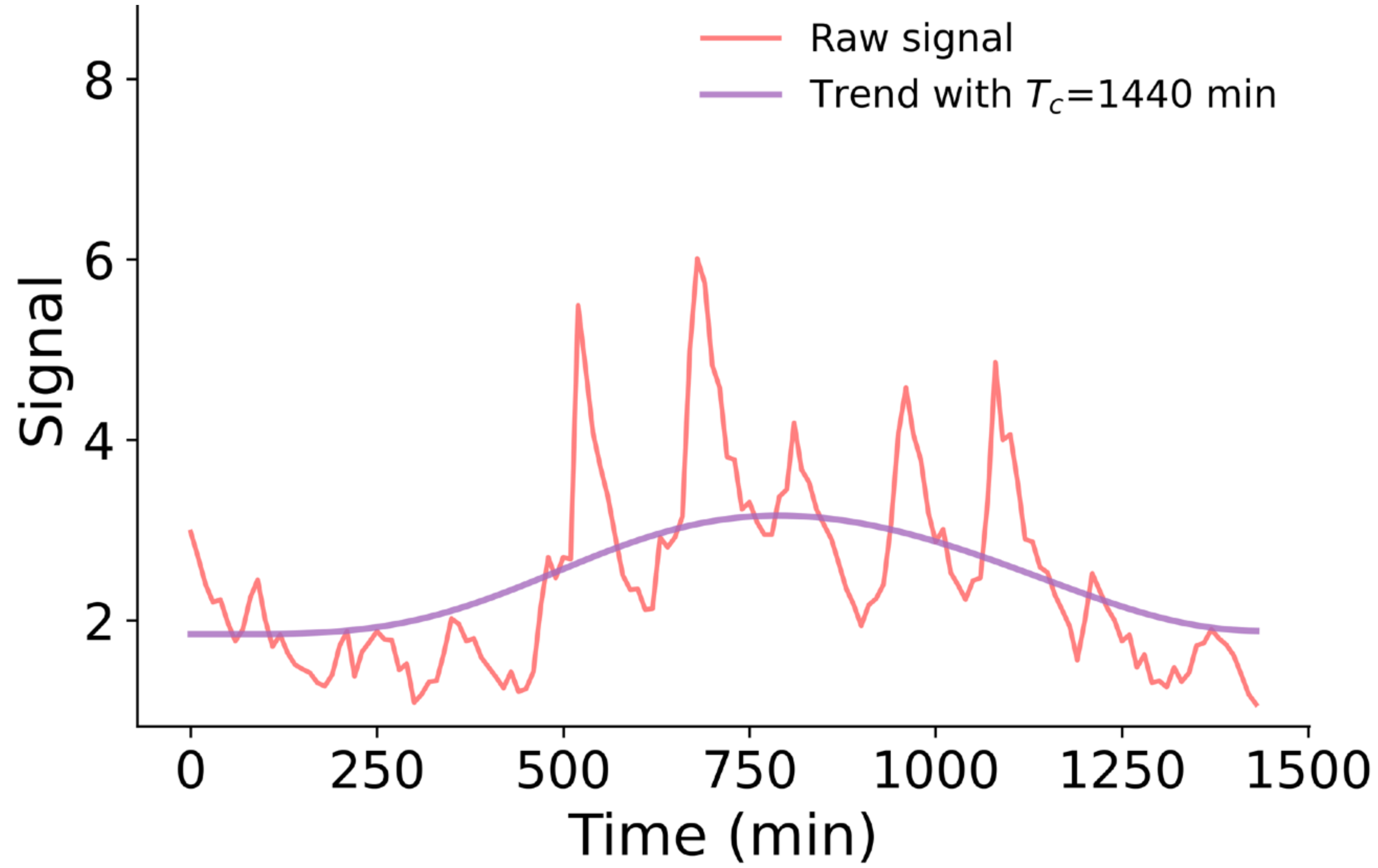
1 Department of Psychology, University of California, Berkeley, United States of America, 2 Department of Integrative Biology, University of California, Berkeley, United States of America, 3 The Helen Wills Neuroscience Institute, University of California, Berkeley, United States of America

* kriegsfeld@berkeley.edu

Wavelet analysis of cortisol rhythms

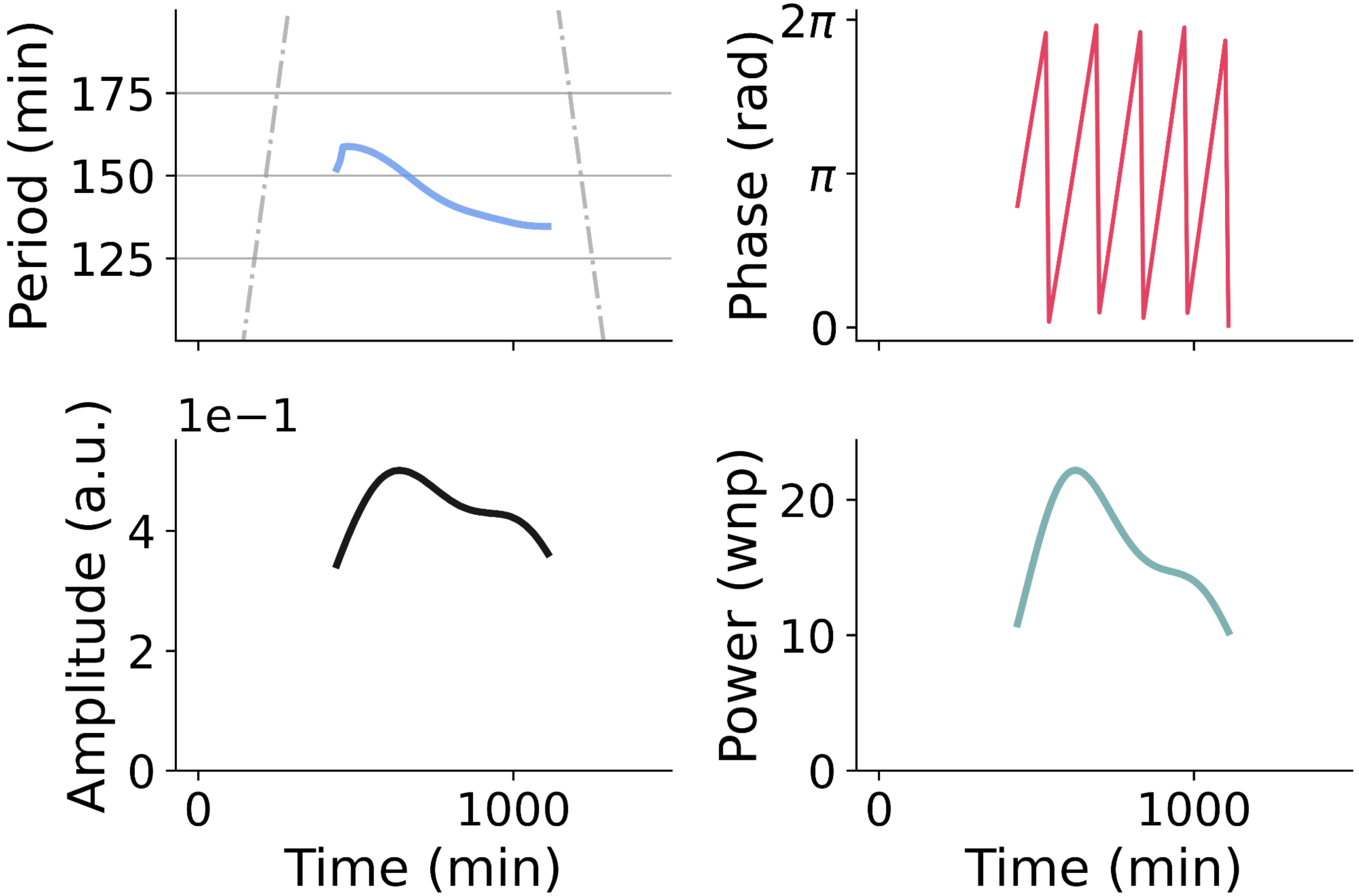
pyBOAT





Belinda Lombard

University of Birmingham



Measuring cortisol in different compartments

Pros and Cons

Saliva and urine

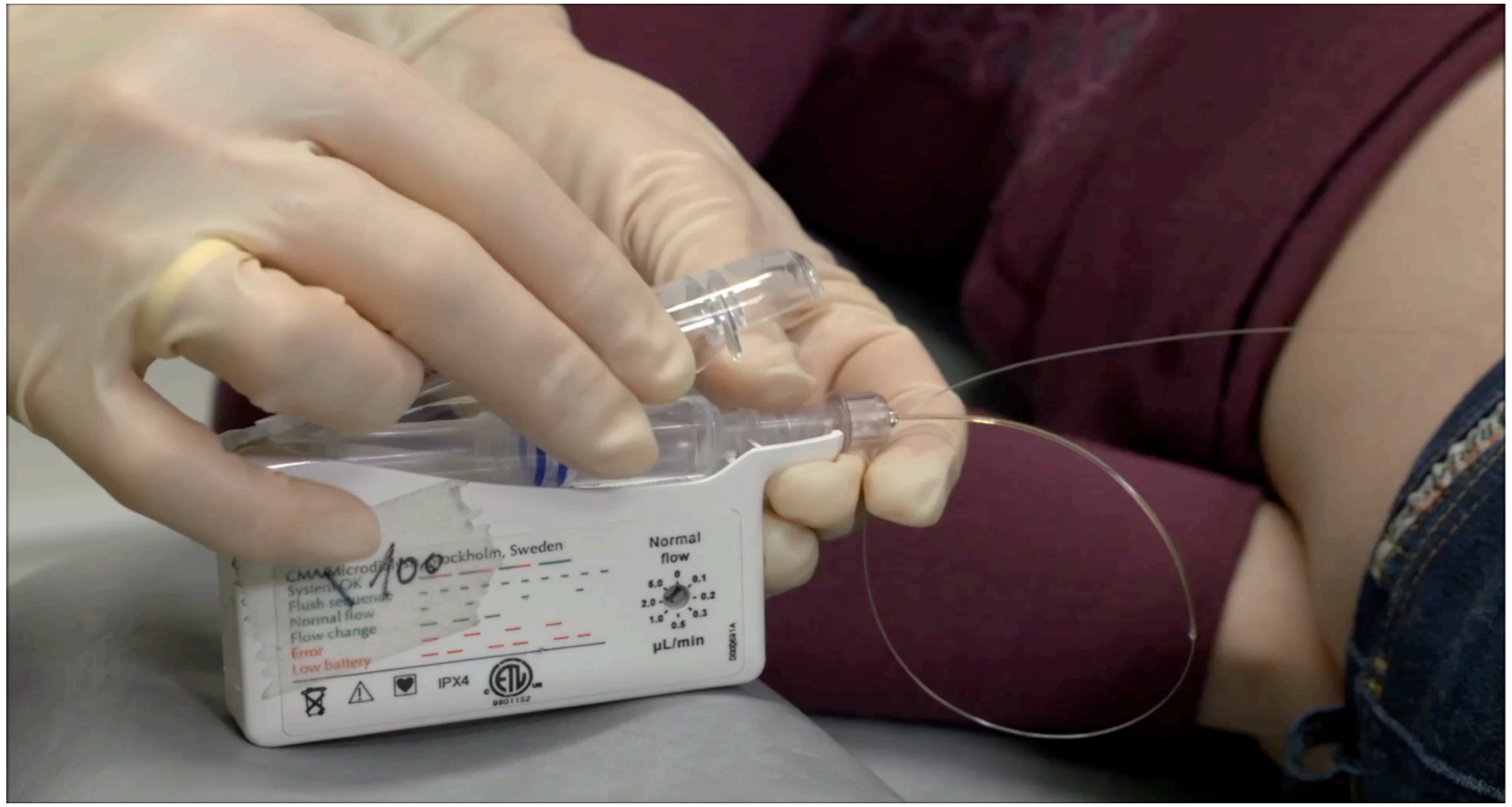
Easy, cheap, widely available. However, it does not capture rapid cortisol dynamics.

Plasma

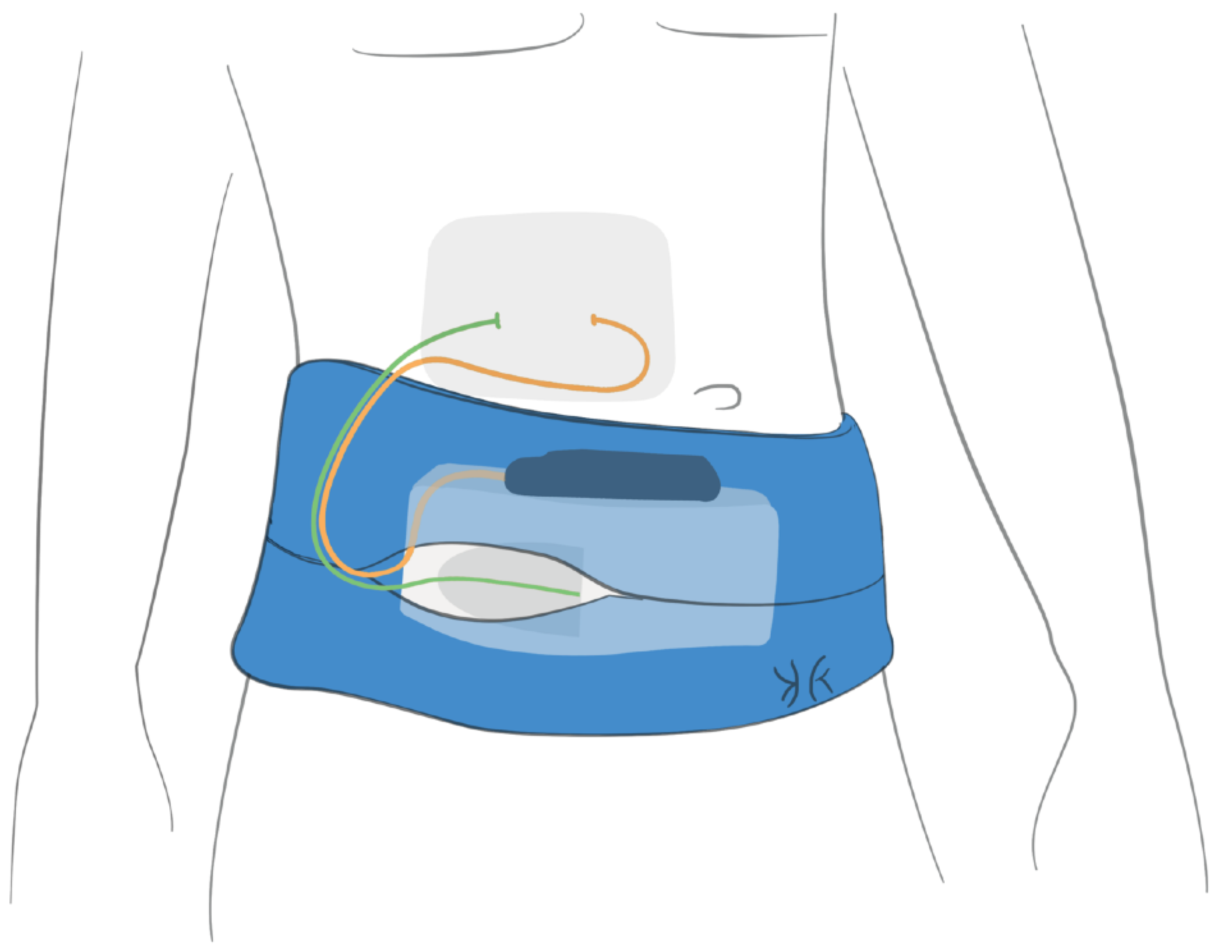
The gold standard. Difficult, expensive, limited to some labs.

Interstitial fluid (ISF)

Continuous, high-resolution ambulatory micro-dialysis now possible. Easier, versatile, limited availability. Highly correlated with plasma.



U-RHYTHM ambulatory micro-dialysis



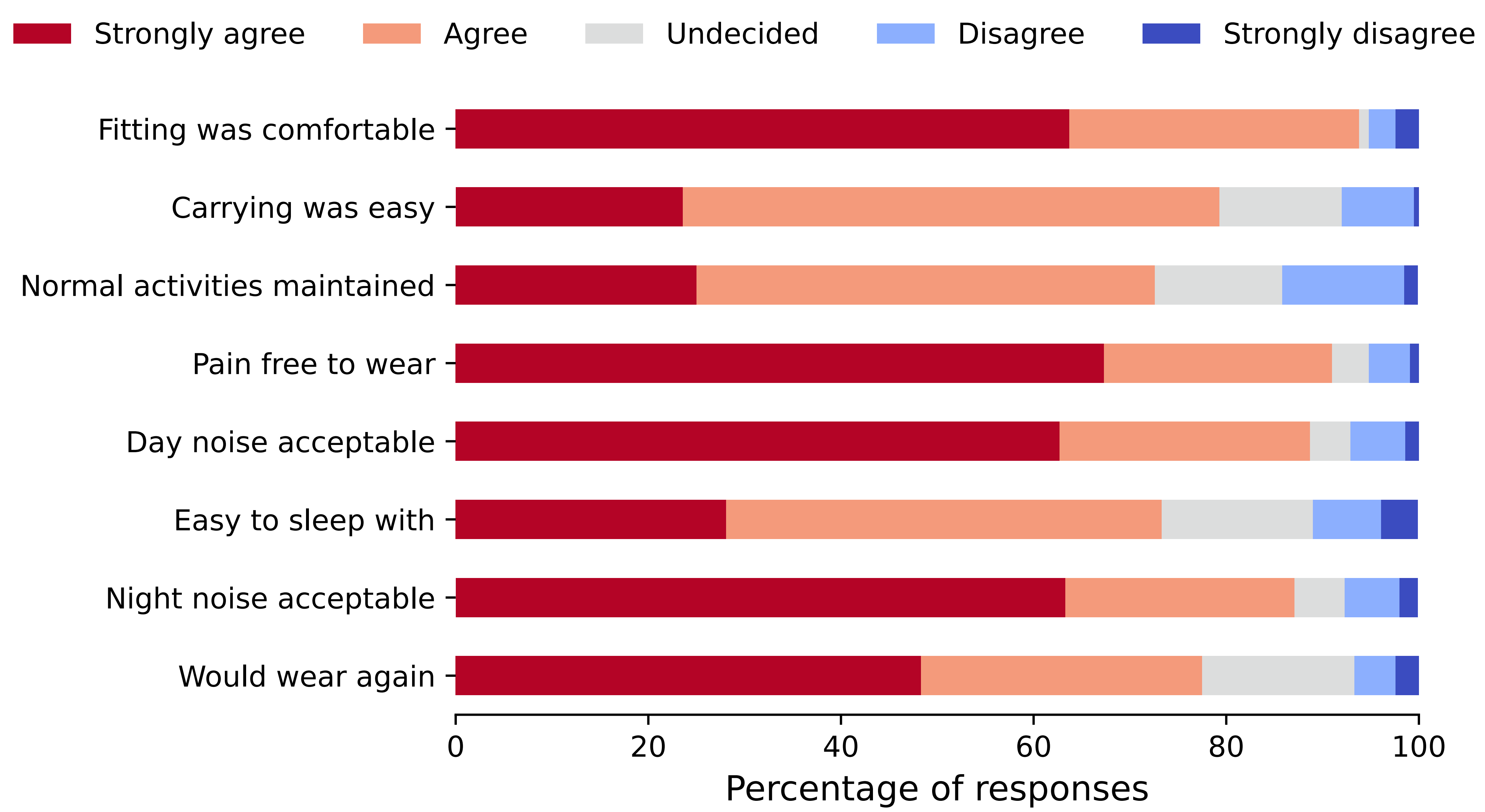
Horizon 2020 Programme

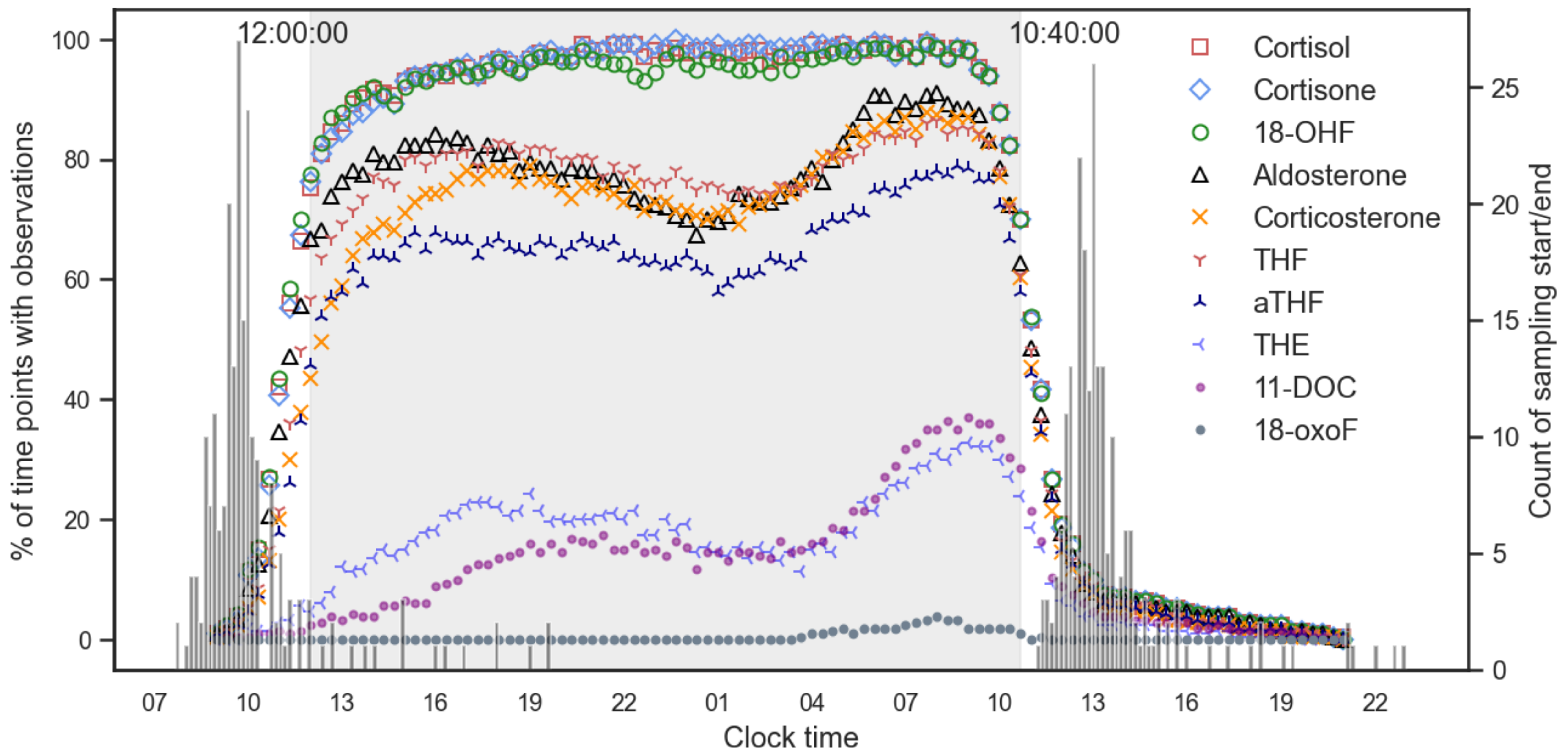
ULTRADIAN

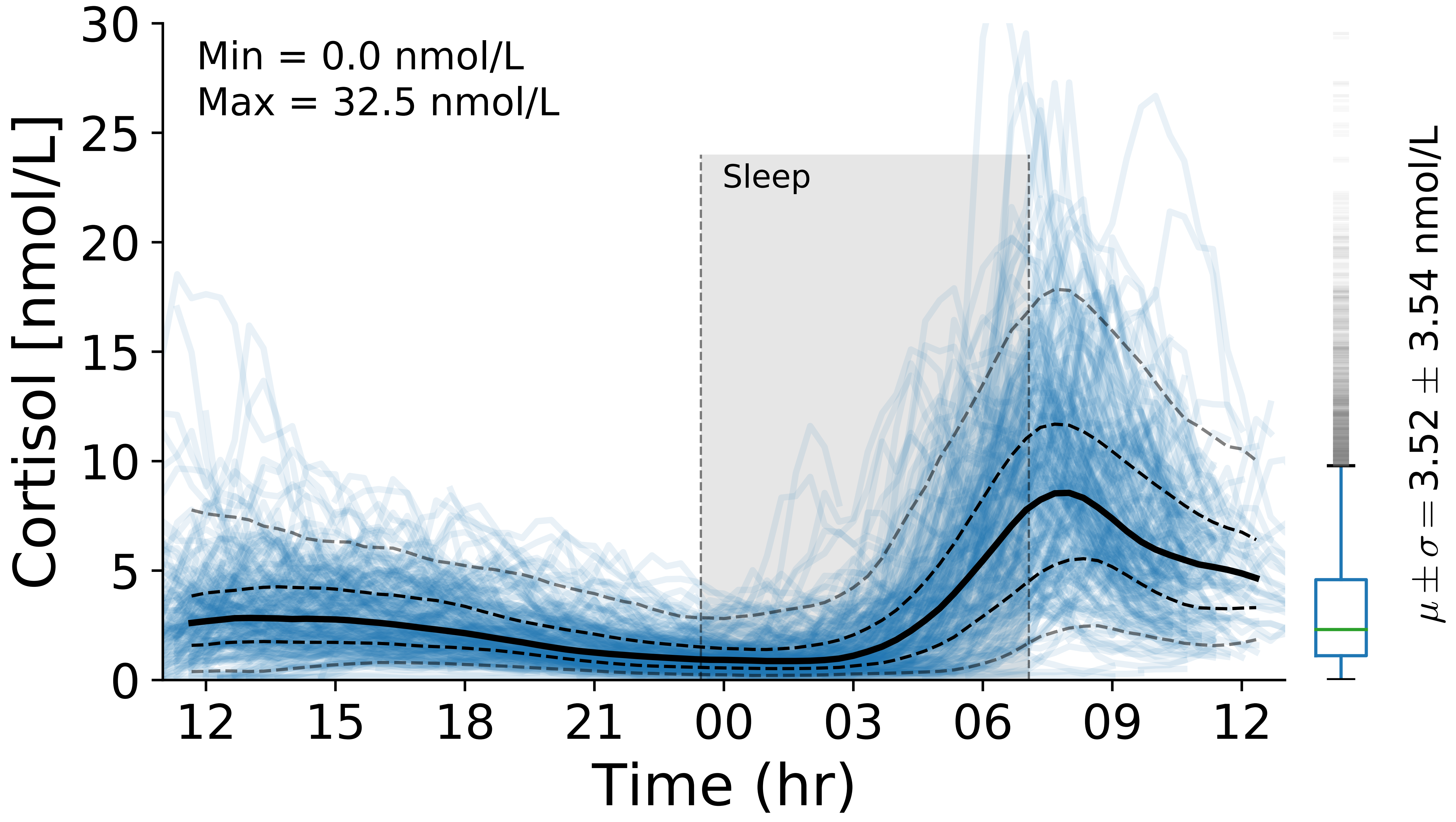
Bhake et al. 2019 *JClinEndoMetab* **104**(12):5935-47 / Bhake et al. 2020 *JClinEndoMetab* **105**(4):e1749-61 / https://www.u-rhythm.co.uk/

Inter-individual variability in healthy volunteers

- n = 214 healthy volunteers (98 M, 116 F)
- Age: 20 to 68 years old (42.5 ±14.1)
- BMI: 16 to 30 kg/m² (23.5 ±2.7)
- Sleep onset: 23:28 hrs ± 58 min
- Final wake: 7:04 hrs ± 76 min
- Samples collected every 20 min (72 samples in 24 hrs)
- Sleep and food diaries





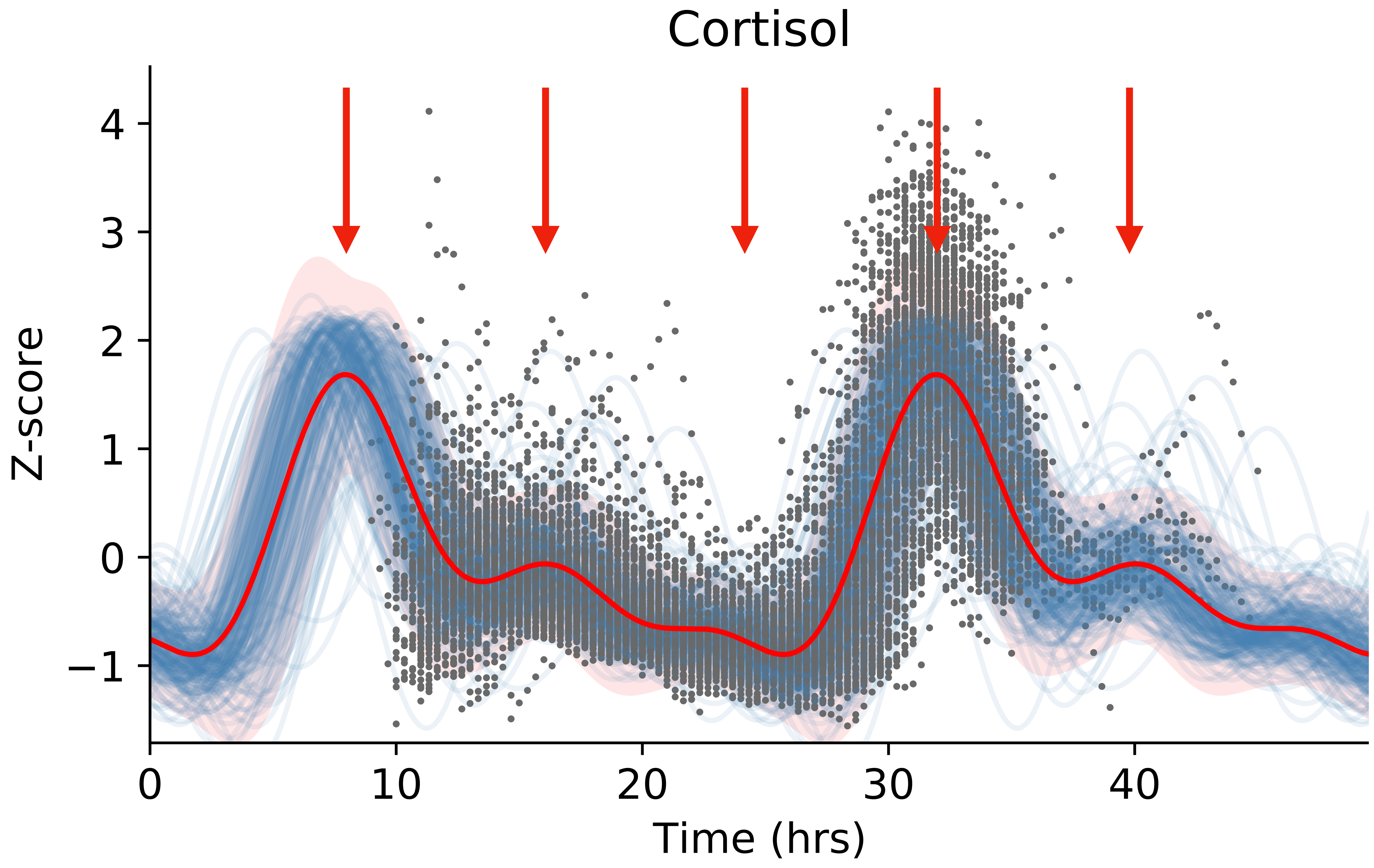


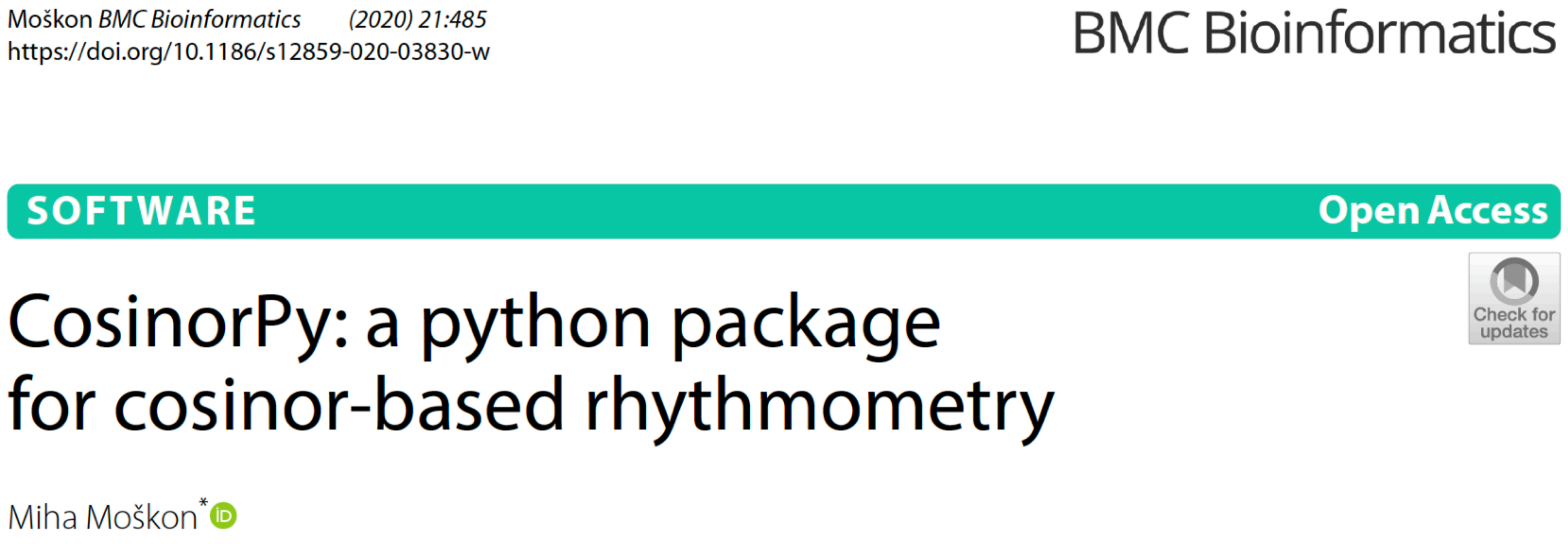
Upton, Zavala, Methlie et al. 2023 *ScienceTransMed* **15**:eadg8464

Rhythmic secretion of 7 tissue-free adrenal steroids *(n=214)*

Upton, Zavala, Methlie et al. 2023 *ScienceTransMed* **15**:eadg8464

Tissue-free adrenal steroids exhibit circadian and ultradian rhythmicity




Moškon *BMC Bioinformatics* (2020) 21:485
https://doi.org/10.1186/s12859-020-03830-w

BMC Bioinformatics

SOFTWARE Open Access

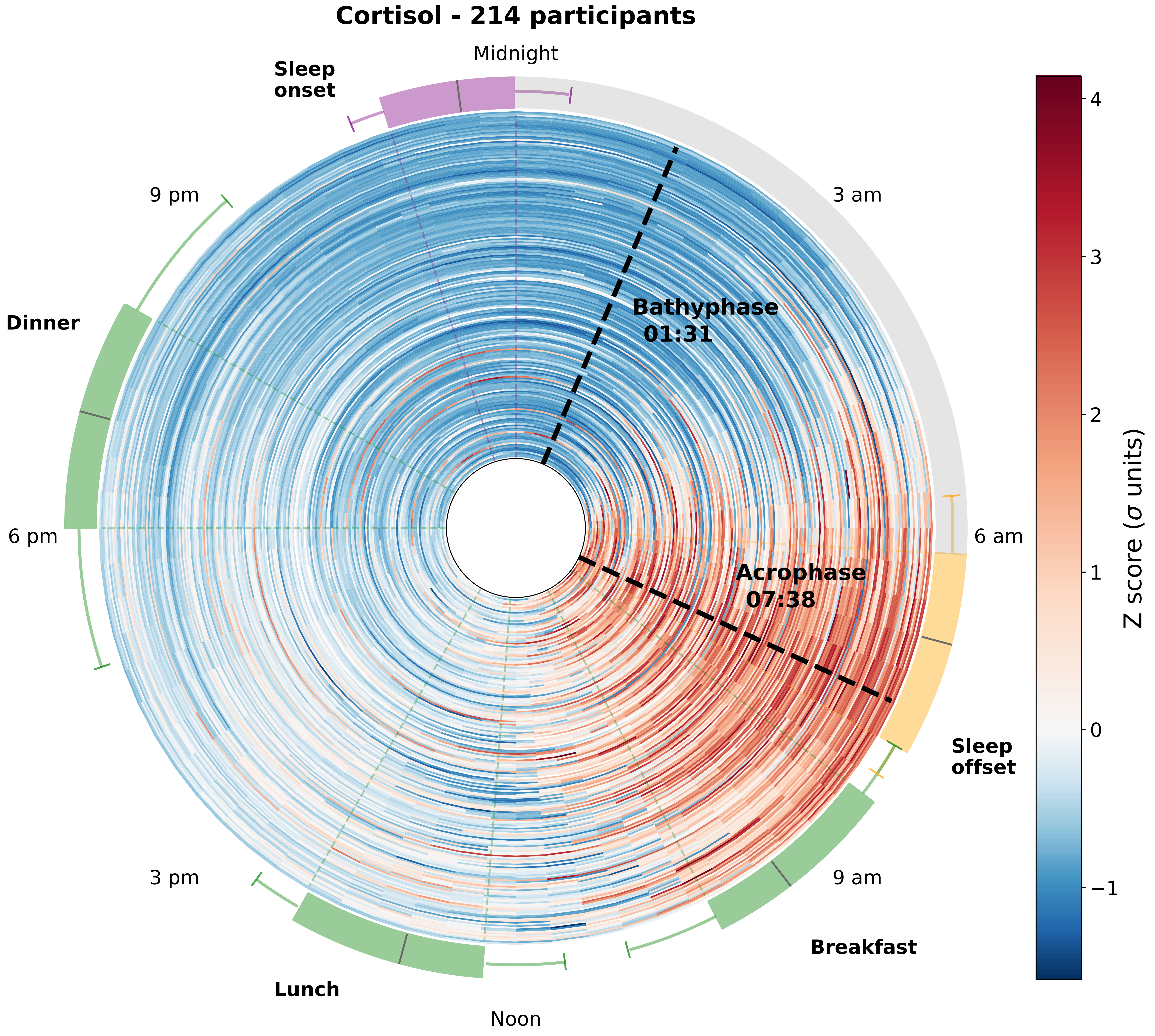
CosinorPy: a python package for cosinor-based rhythmometry

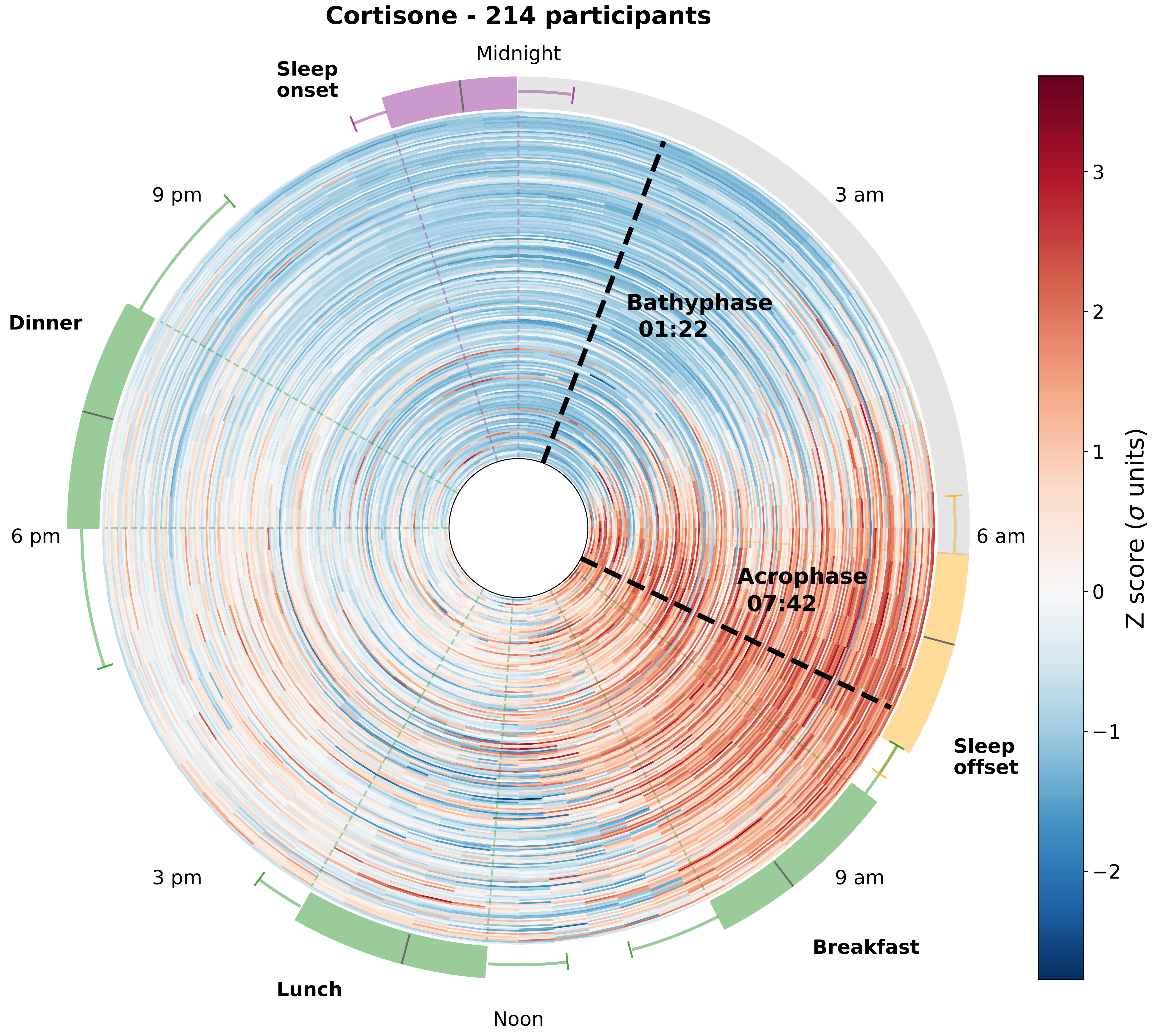
Miha Moškon*

$$y(t) = \sum_{i=1}^{N} \left(A_{i,1} \cdot \sin\left(\frac{t}{P/i} \cdot 2\pi\right) + A_{i,2} \cdot \cos\left(\frac{t}{P/i} \cdot 2\pi\right)\right) + M + e(t)$$

Upton, Zavala, Methlie et al. 2023 *ScienceTransMed* **15**:eadg8464 / Moškon 2020 *BMCBioinf* **21**:485

Inter-individual variability in healthy volunteers *(n=214)*

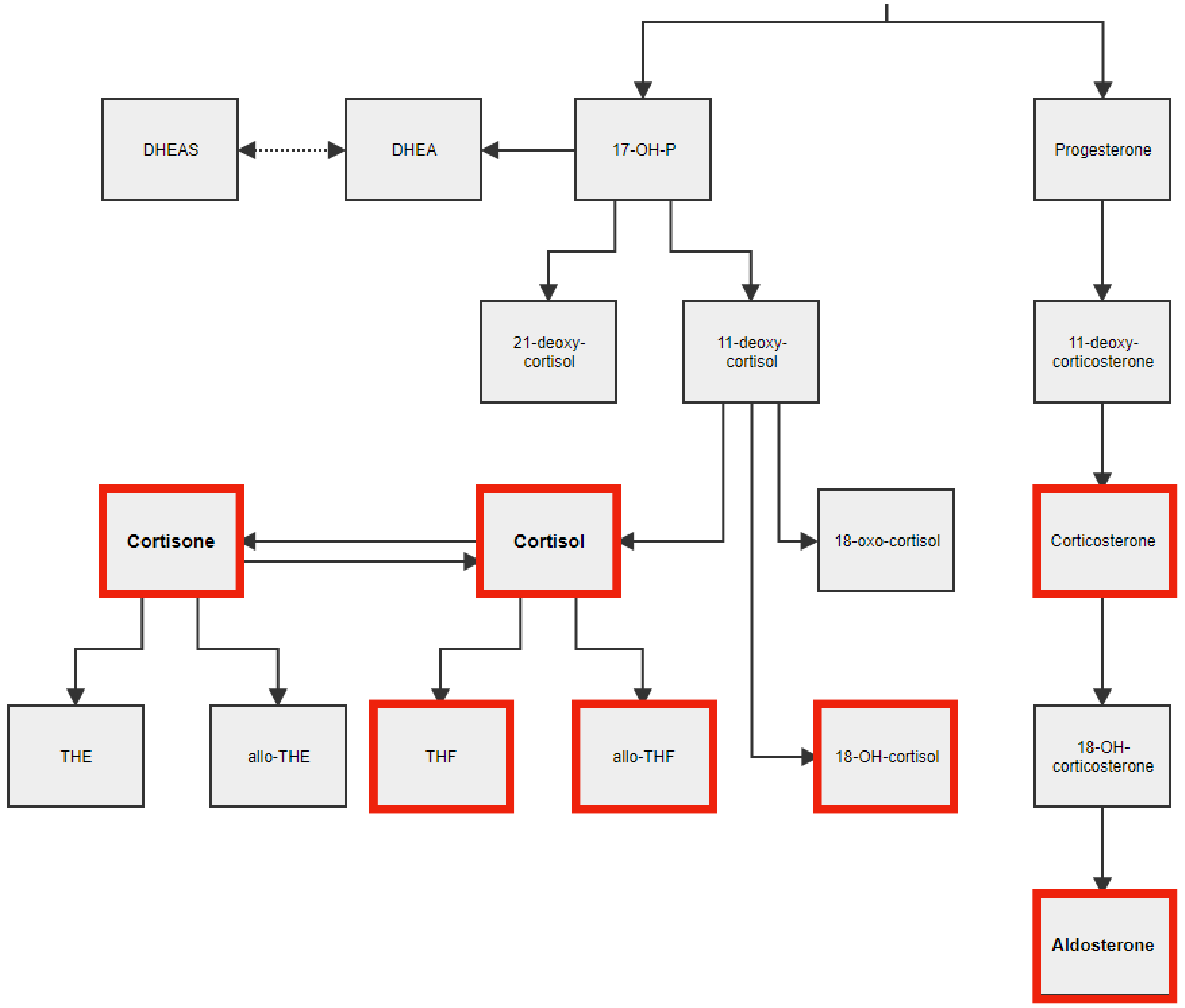


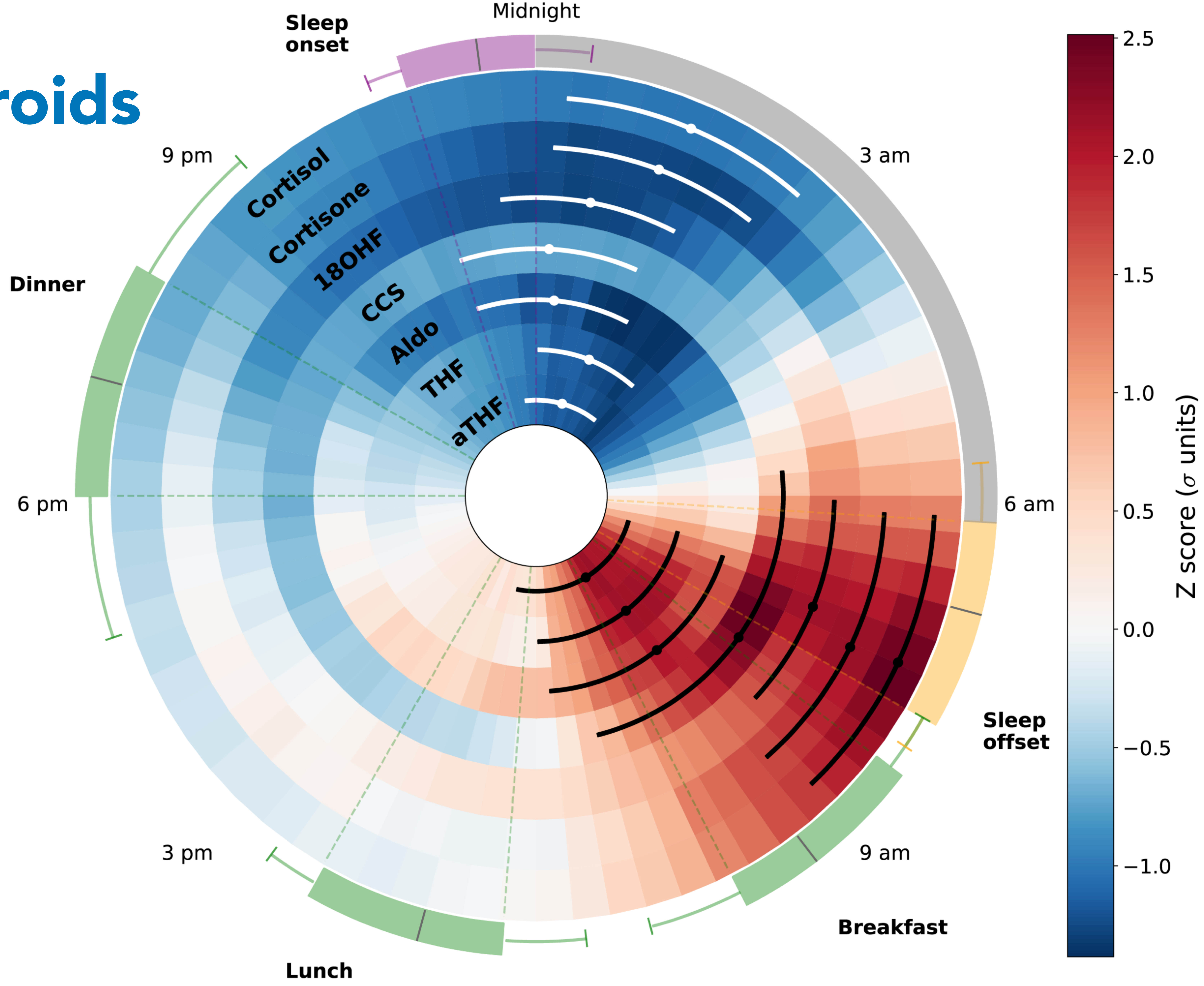


Upton, Zavala, Methlie et al. 2023 *ScienceTransMed* **15**:eadg8464

Diurnal dynamics of 7 tissue-free adrenal steroids

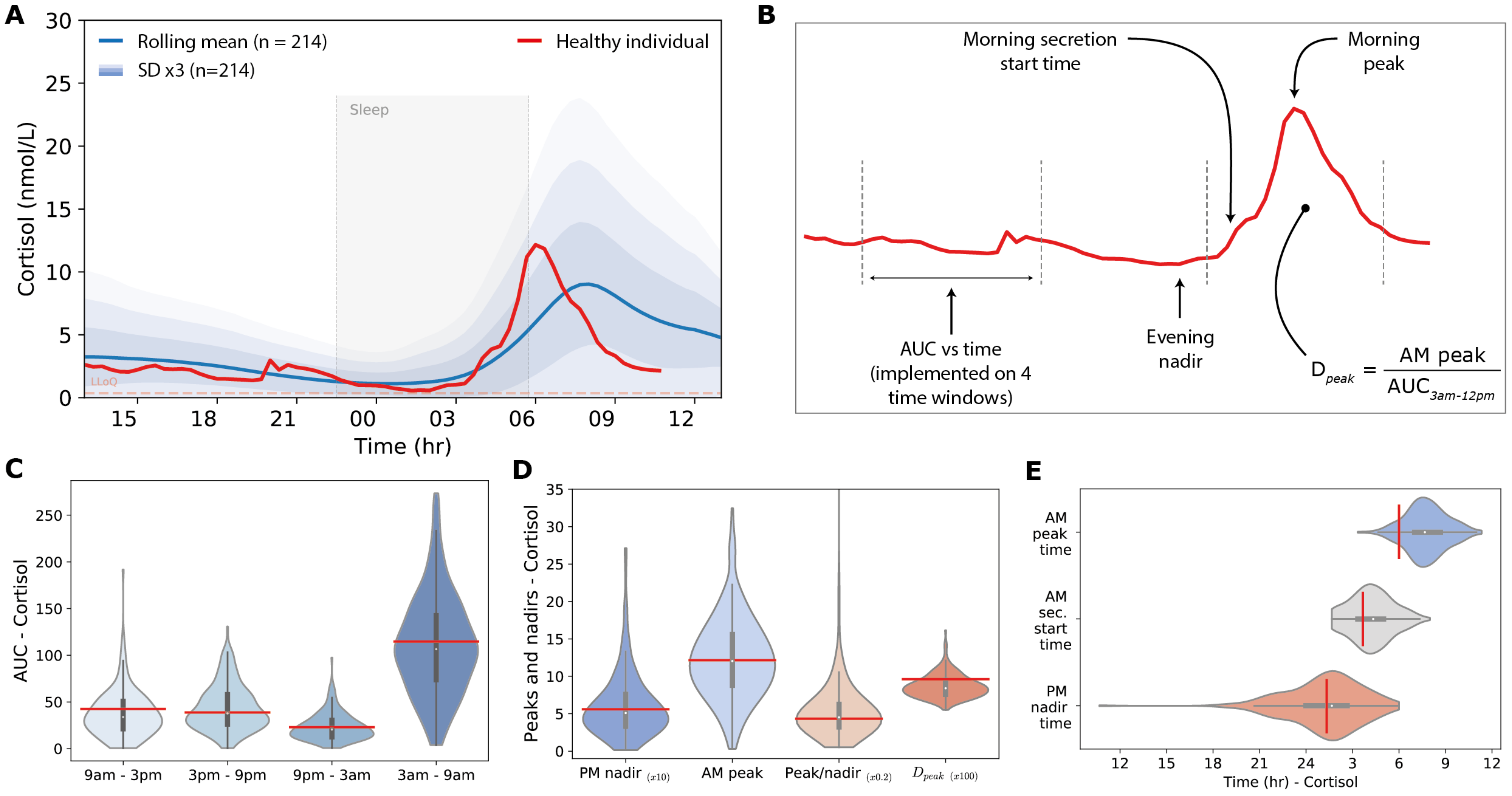
(averaged over 214 healthy volunteers)



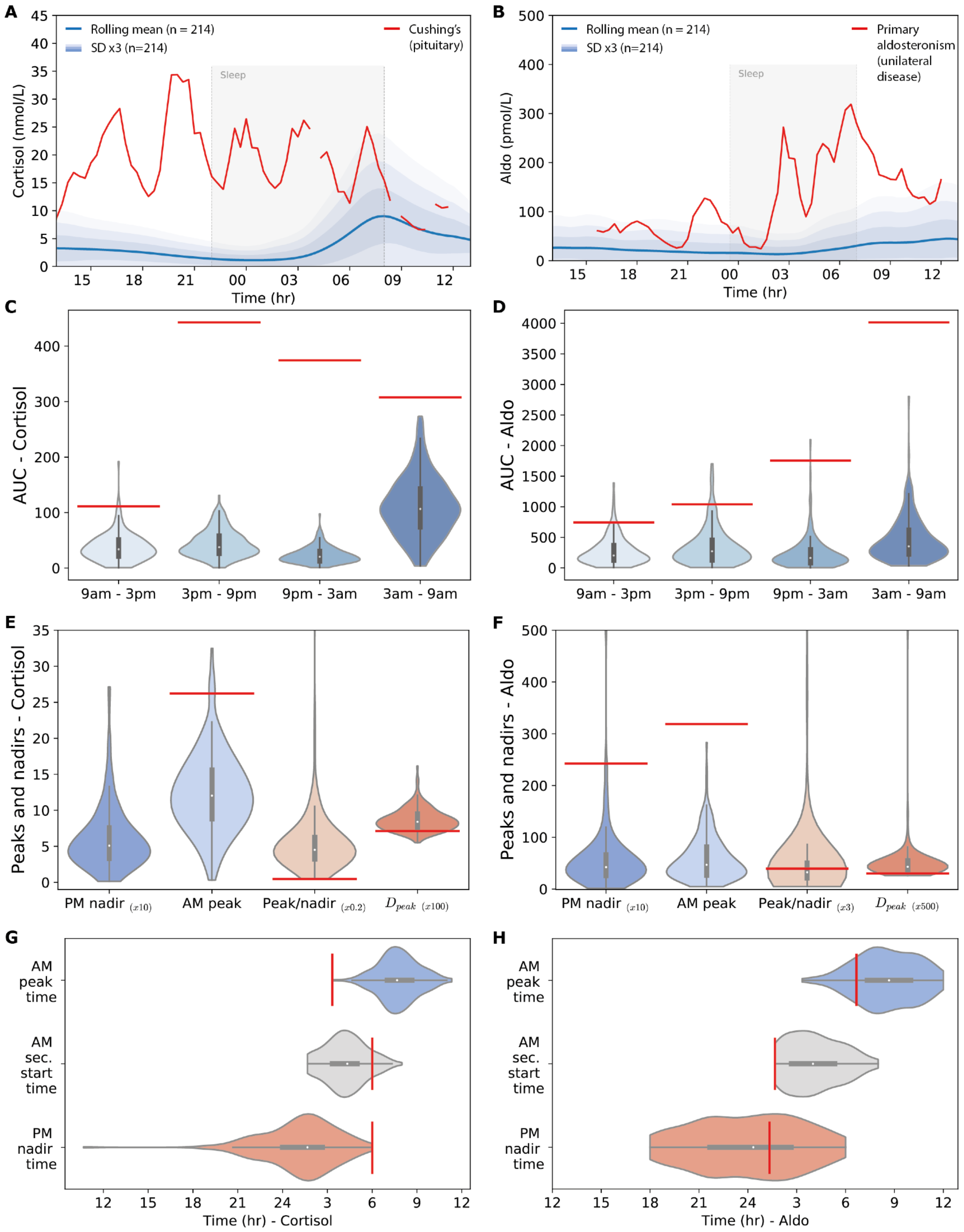


Upton, Zavala, Methlie et al. 2023 *ScienceTransMed* **15**:eadg8464

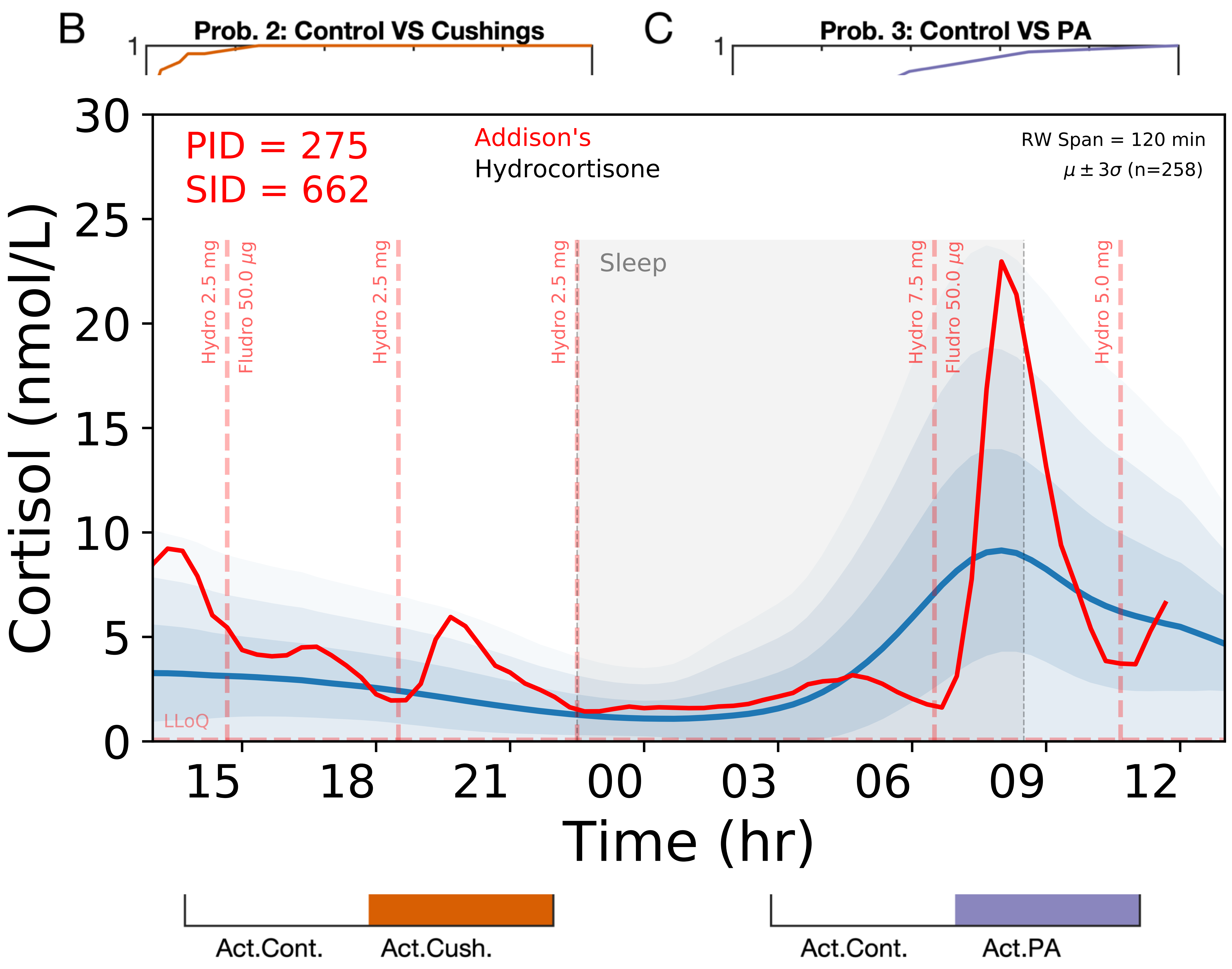
Dynamic biomarkers to quantify variability



Upton, Zavala, Methlie et al. 2023 *ScienceTransMed* **15**:eadg8464



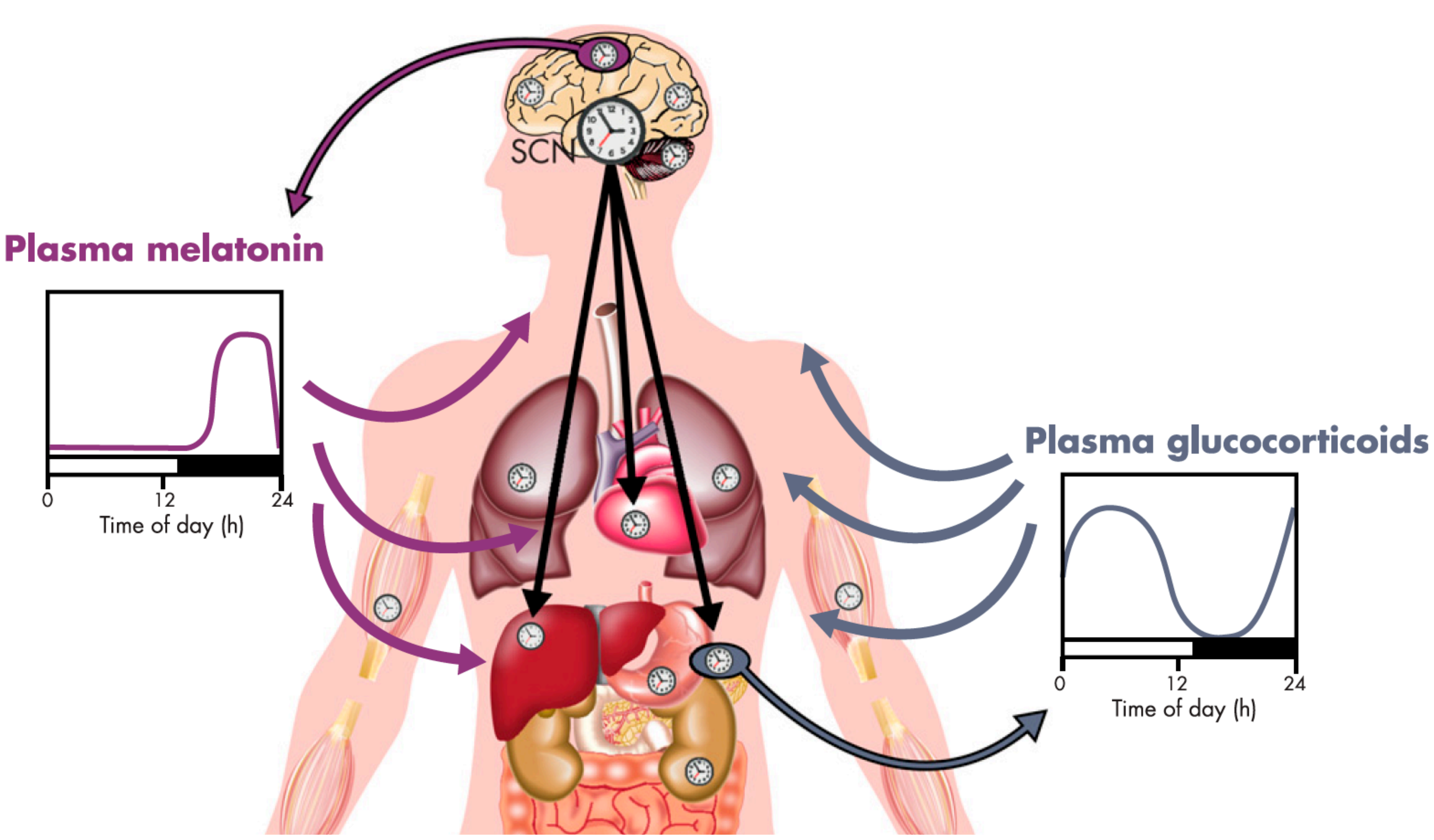
Dynamic biomarkers to support diagnosis and disease mgmt



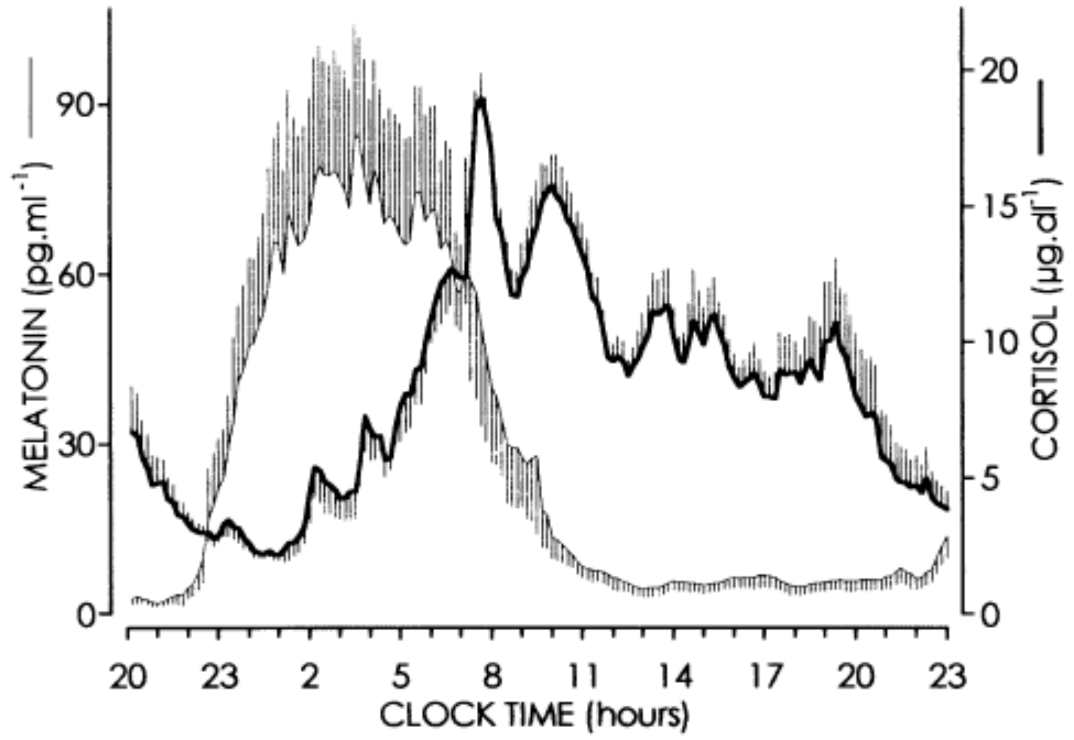
Upton, Zavala, Methlie et al. 2023 *ScienceTransMed* **15**:eadg8464

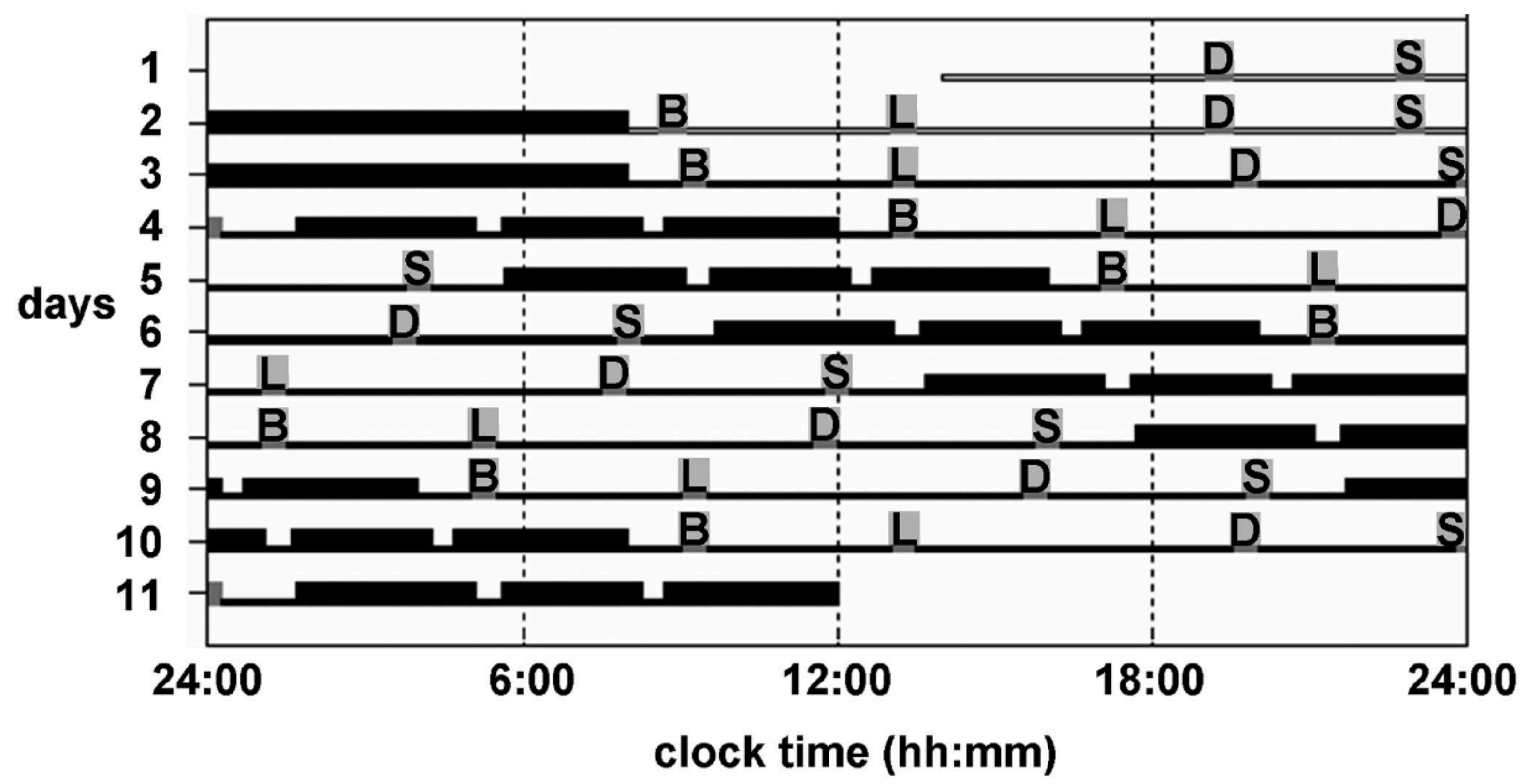
Misalignment of endocrine axes

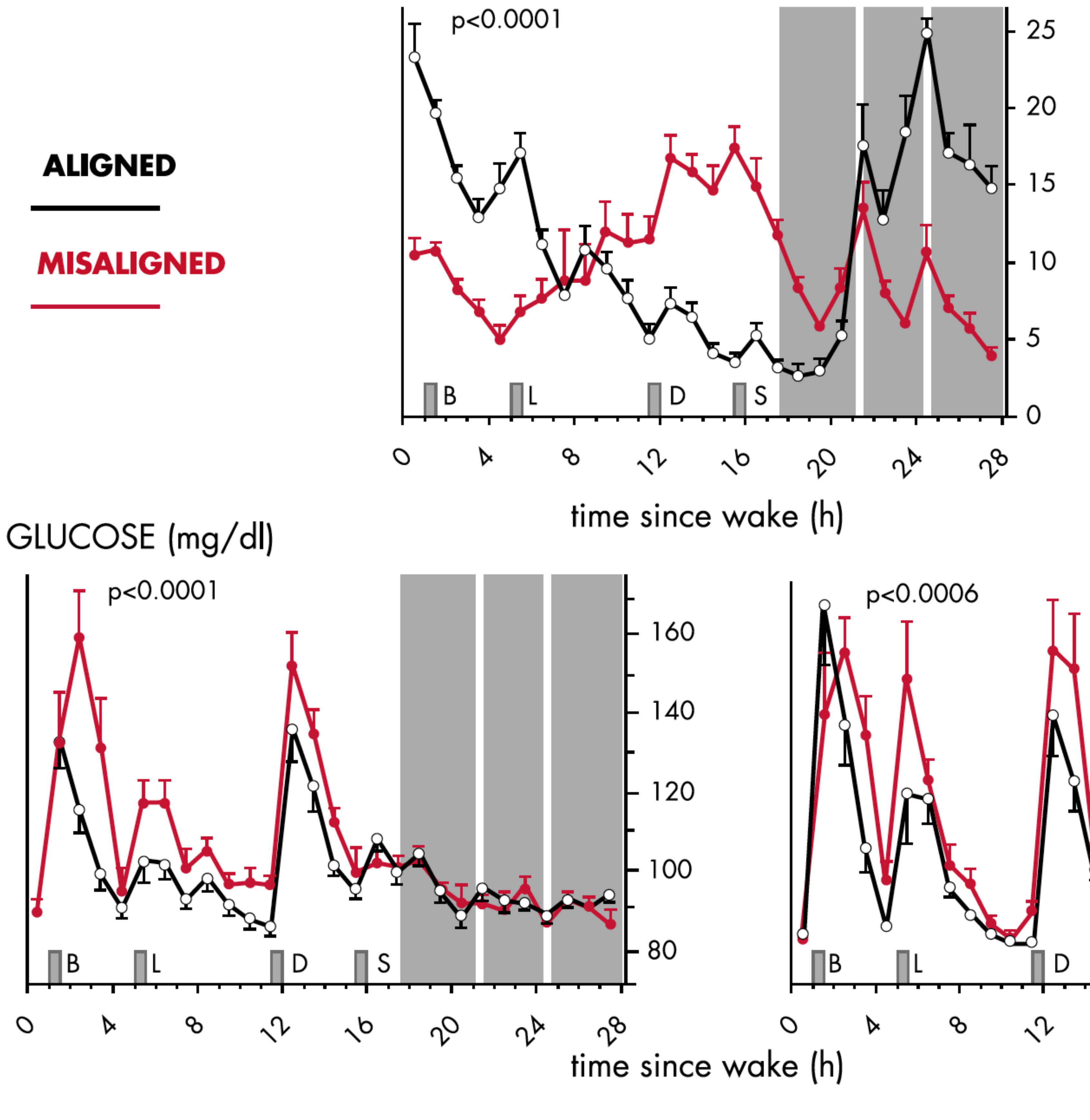
CORT, sleep & metabolism



N = 8 day-active individuals



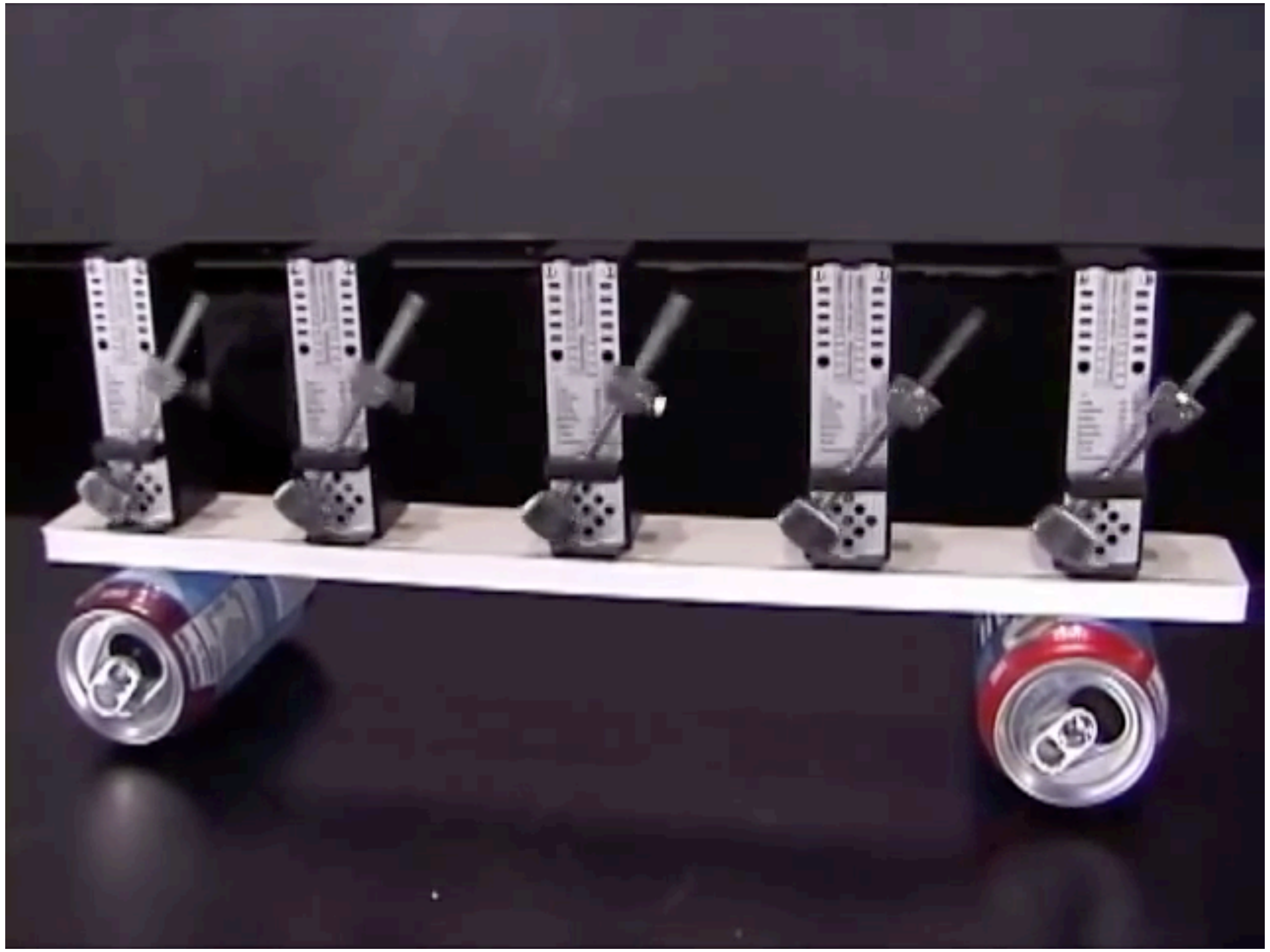


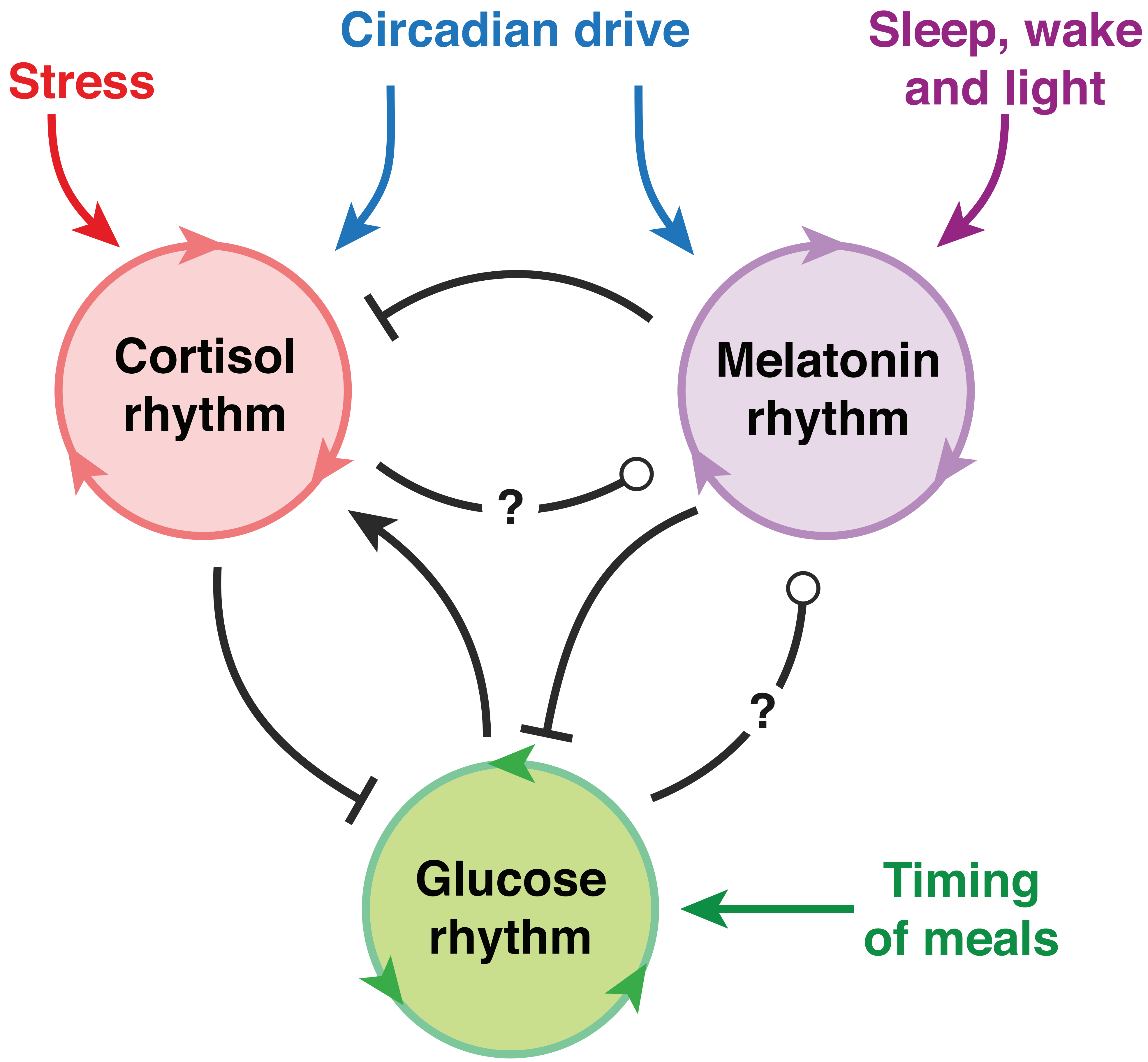


N = 10 individuals under desynchrony protocol

Scheer et al. 2009 *PNAS* **106**(11):4453-8 / Weibel & Brandenberger 2002 *NeurosciLetters* **318**:89-92

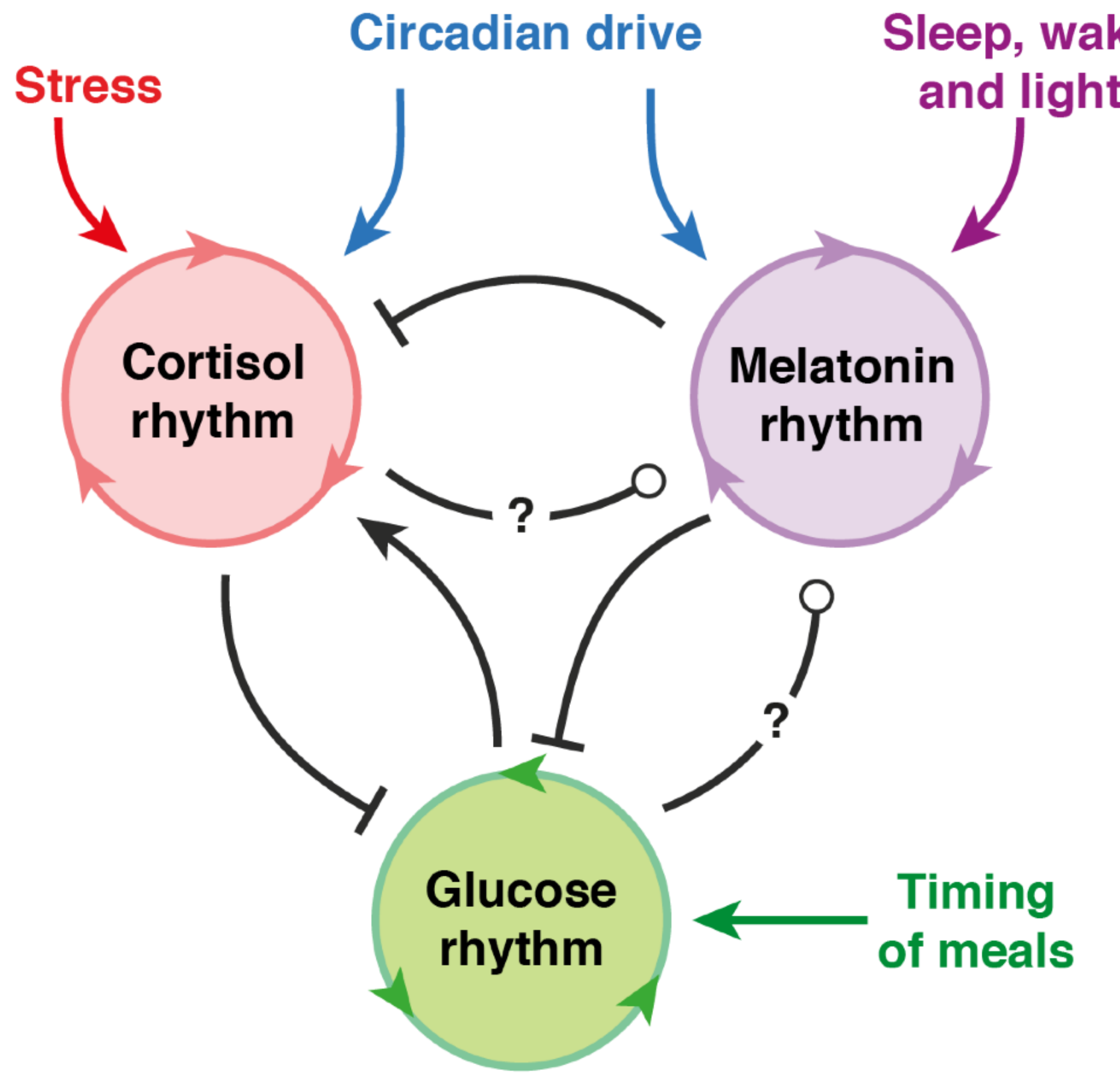
Coupling mechanisms allow the exchange of information



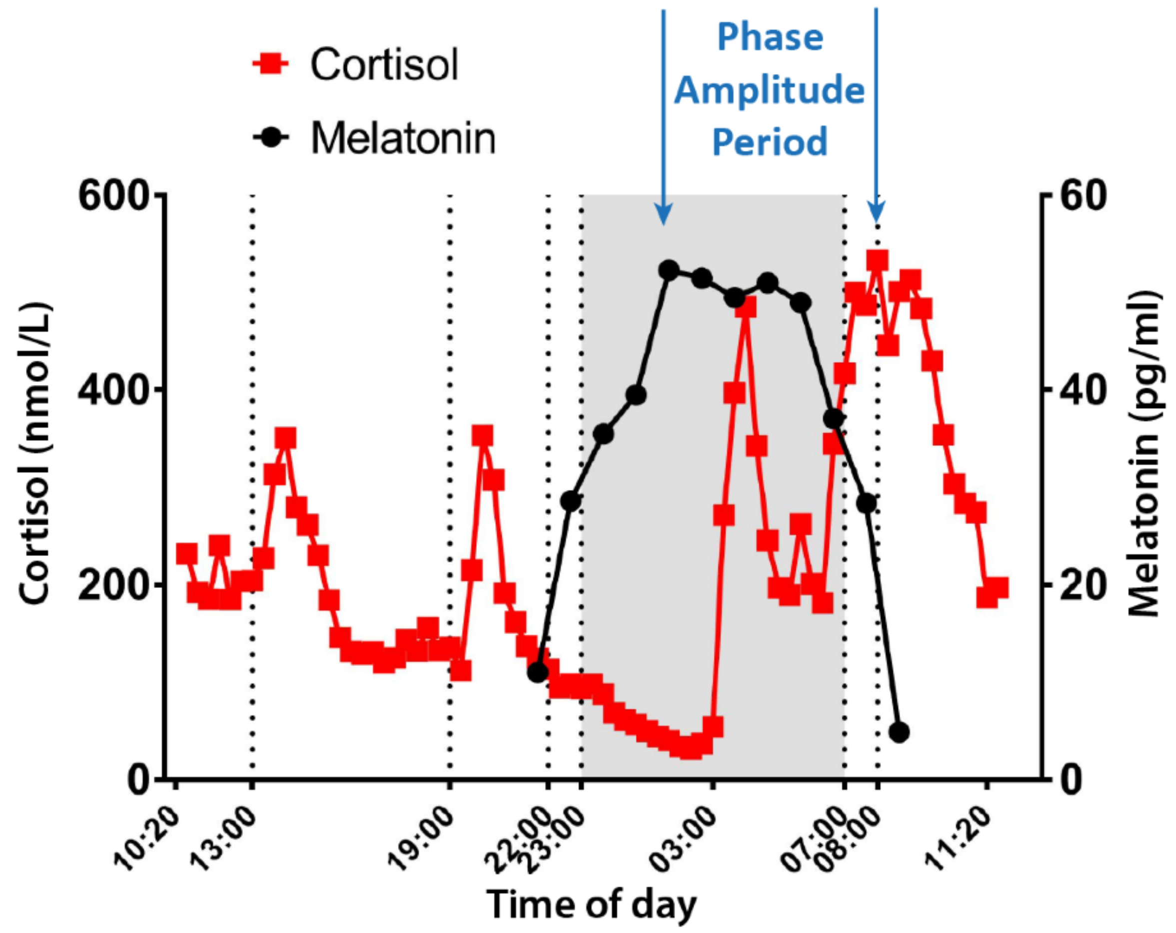


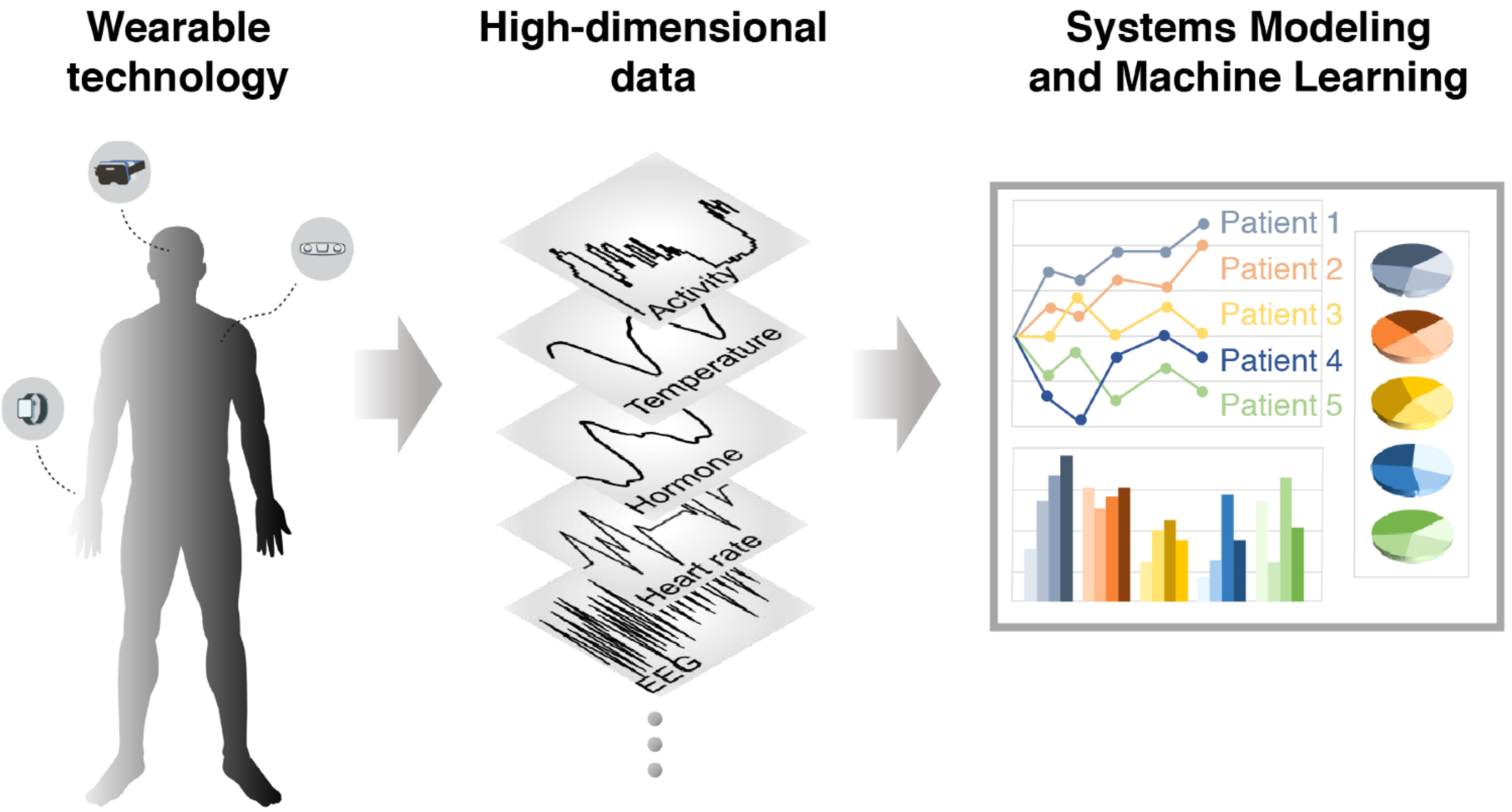
https://www.youtube.com/watch?v=Aaxw4zbULMs / Zavala 2022 *JNeuroEndo* **e13144**

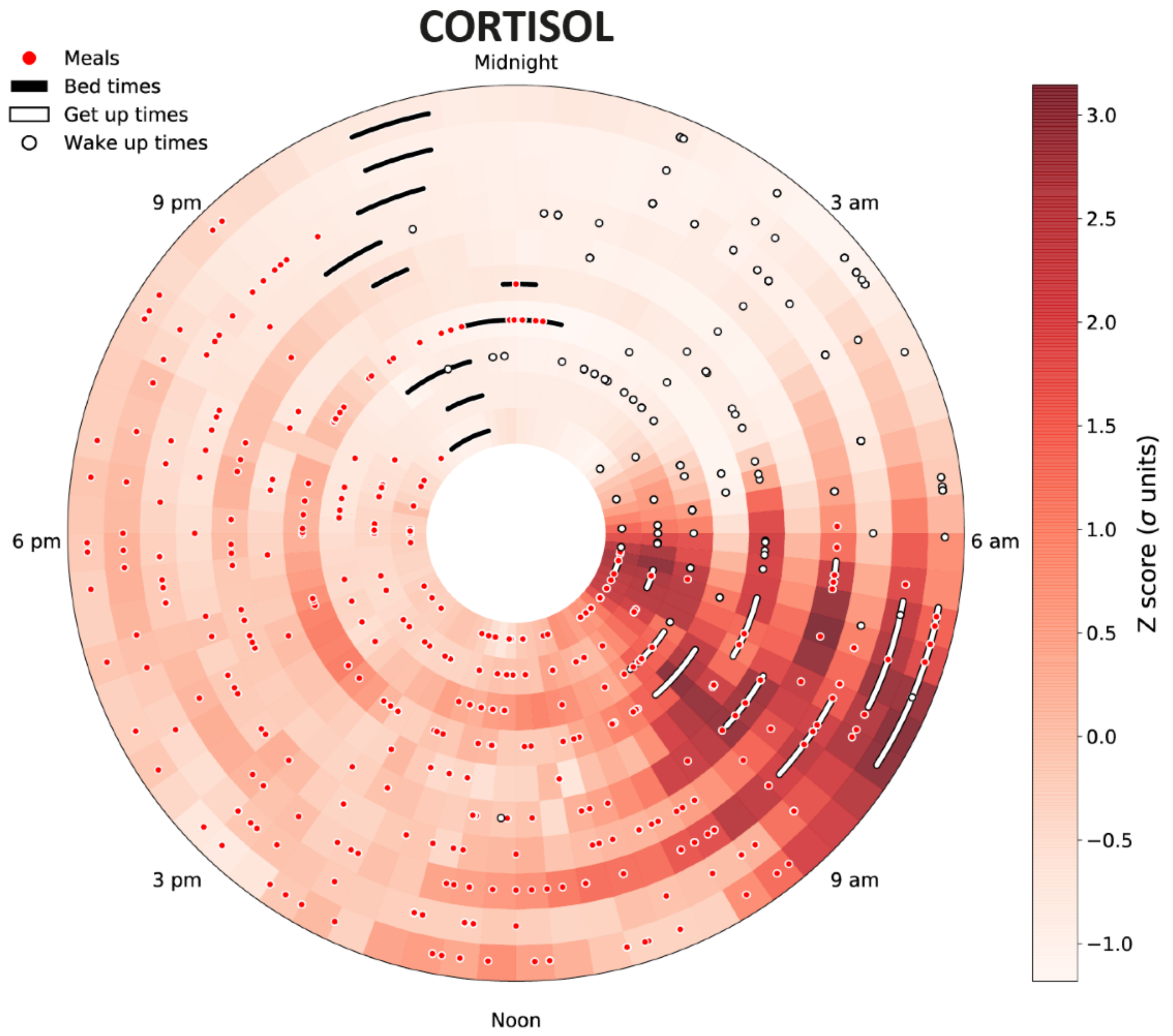
Understanding coupling between endocrine systems

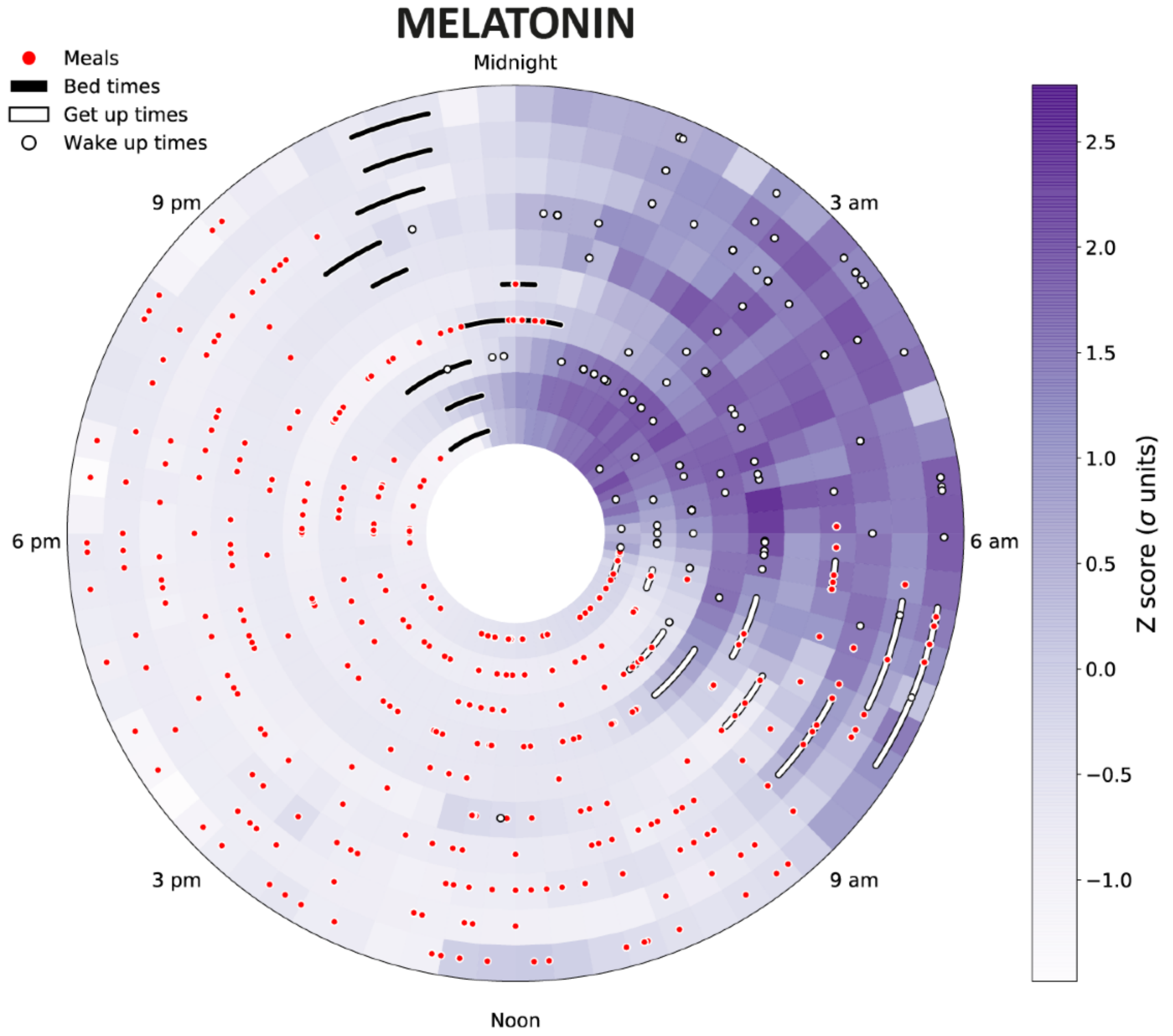


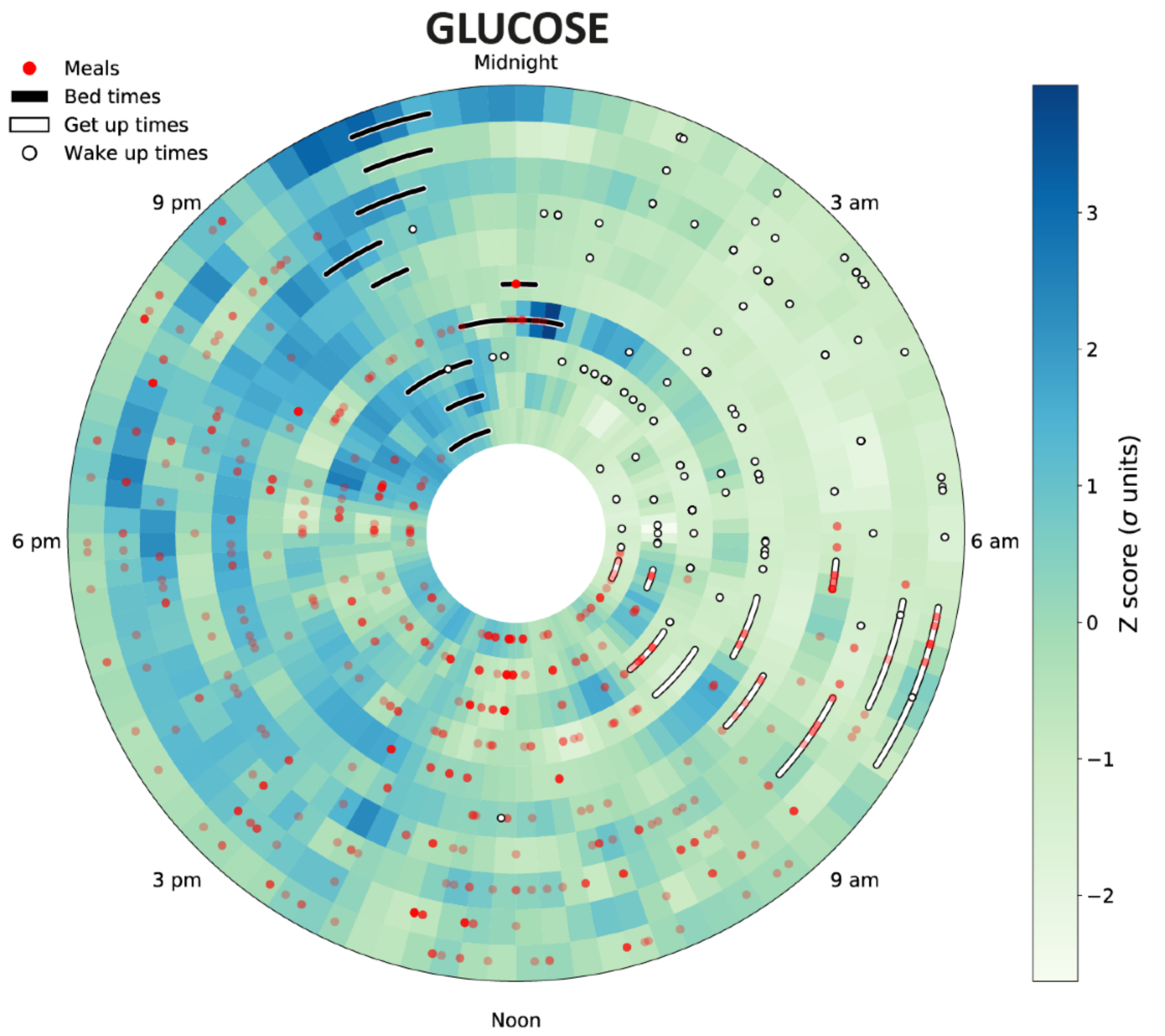
Coupled oscillator modelling
Considers endocrine axes as coupled oscillators subject to perturbations











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University of Birmingham

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University of Birmingham

University of Birmingham
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