Wearables: non-functional approaches

ENAR 2021

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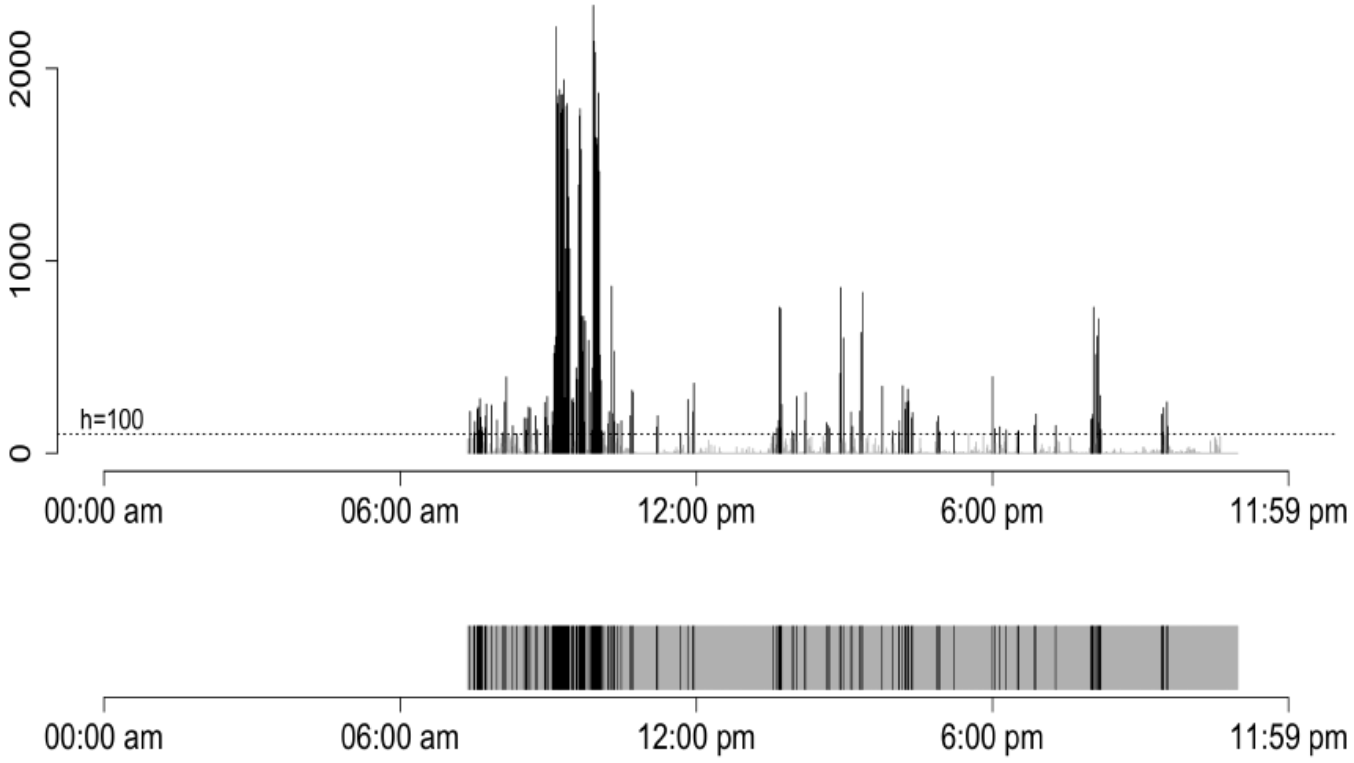
Overview

- Review of PA, SL, CR
- PA: Fragmentation
- SL: Review, summary measures, mid-point
- CR: parametric and non-parametric approaches
- JIVE for PA, SL, CR
- Empirical Mode Decomposition

Fragmentation



Fragmentation

Nonparametric

Metrics	Interpretation	Definition	Estimation
AAC (μ)	average duration	Ed_i	$\frac{T}{n}$
nAAC ($^*\mu$)	normalized average	$\frac{Ed_i}{^*d}$	$\frac{T}{^*dn}$
Gini (g)	normalized variability	$\frac{E\lvert d_i - d_j\rvert}{2\mu}$	$\frac{\sum_{ij}\lvert d_i - d_j\rvert}{2n\sum_t d_t}$
AH ($\bar{h}$)	average hazard	$h(t) = \frac{F'(t)}{1-F(t)}$	$\bar{h} = \frac{1}{m}\sum_{t\in\mathcal{D}}\hat{h}(t)$

Systematic Derivation $\quad I_\psi(\hat{F}) = \int_0^{^*d} \psi(\hat{F}(t))dt$

AAC	$\hat{\mu} = \int_0^{^*d}(1-\hat{F}(t))dt$
nAAC	$^*\hat{\mu} = \frac{1}{^*d}\int_0^{^*d}(1-\hat{F}(t))dt$
Gini	$\hat{g} = \frac{1}{\hat{\mu}}\int_0^{^*d}\hat{F}(t)(1-\hat{F}(t))dt$
AH	$\bar{h} = \frac{1}{^*d}\int_0^{^*d}\frac{\hat{F}(t)-\hat{F}(t-1)}{1-\hat{F}(t-1)}dt$

Between-State Transition Probabilities

- Assumption: two state system (sedentary (S) and active (A))

  $P_S = \Pr(x_t = 0)$: proportion of time spent sedentary

  $P_A = \Pr(x_t = 1)$: proportion of time spent active

  0, 1 for sedentary and active bout respectively, x_t is the type of bout

- Between-state transition probabilities

$$ASTP = \Pr(x_{t+1} = 0 | x_t = 1)$$
$$SATP = \Pr(x_{t+1} = 1 | x_t = 0)$$

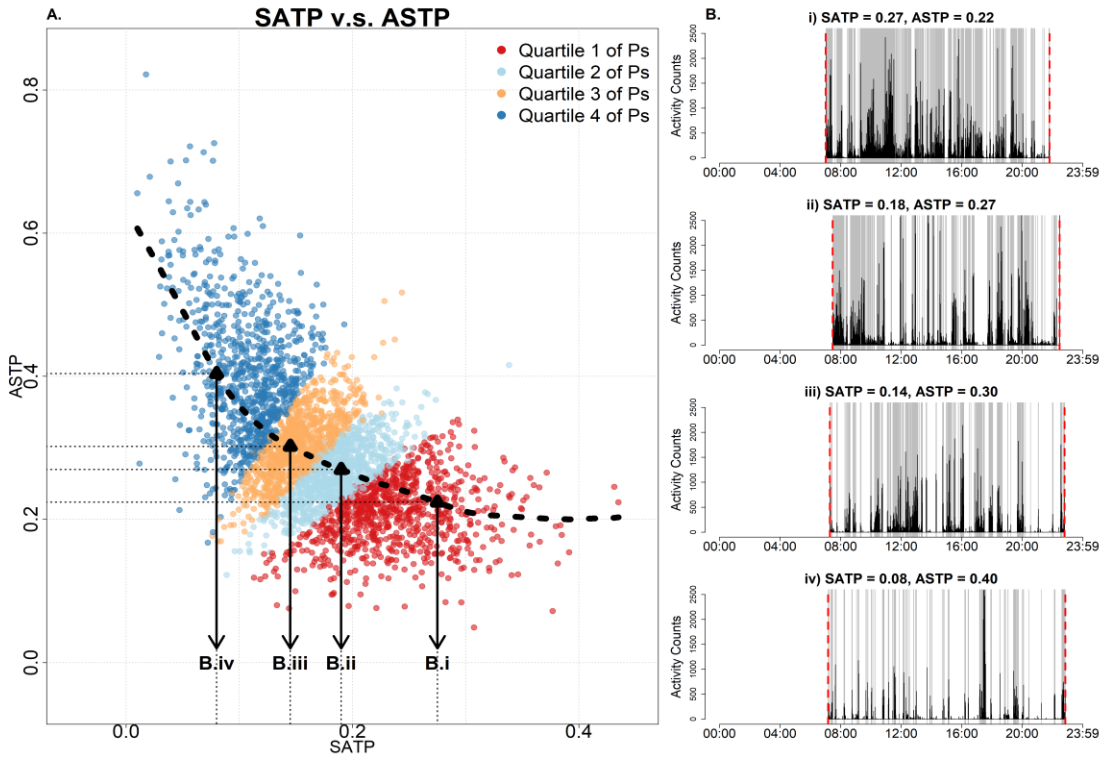
- Estimation

$$\widehat{ASTP} = \frac{n_A}{T_A} = 1/\text{average active bout}$$
$$\widehat{SATP} = \frac{n_S}{T_S} = 1/\text{average sedentary bout}$$

n_A, n_S: total number of active and sedentary bouts

T_A, T_S: total number of active and sedentary time

Properties and Intuitions for ASTP and SATP



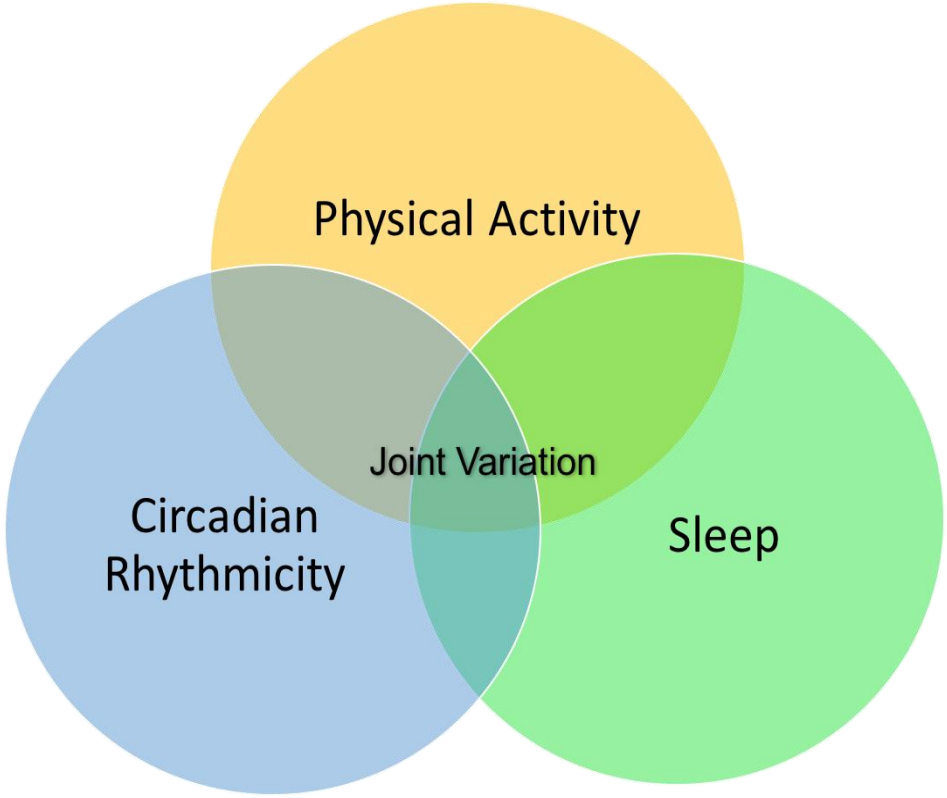
Grey background: active state
White background: sedentary state

Figure 2. ASTP and SATP stratified by quartiles of total daily sedentary proportions (P_S).

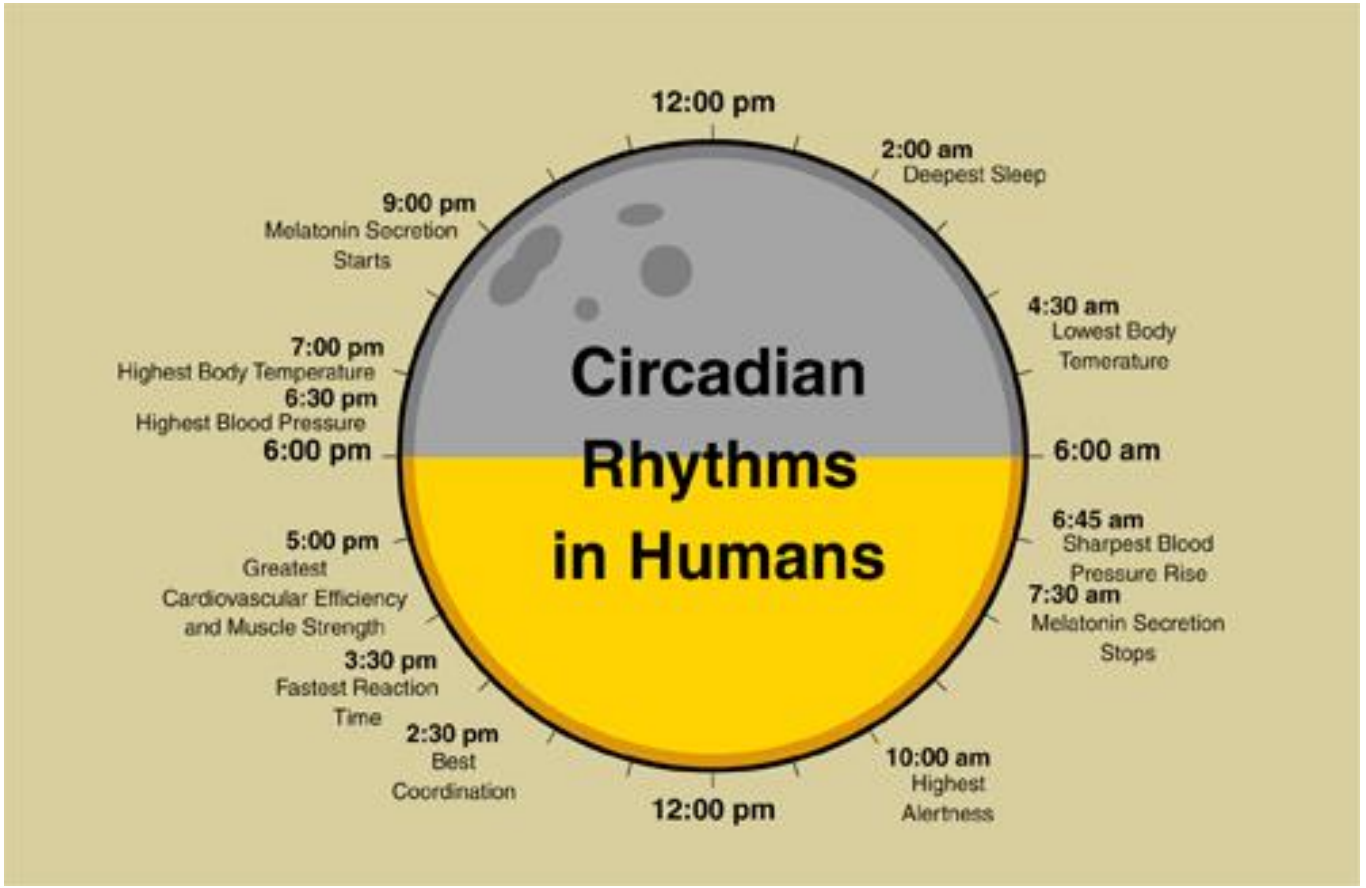
- Di, J., Leroux, A., Urbanek, J., Varadhan, R., Spira, A., Schrack, J., Zipunnikov, V. Patterns of Sedentary and Active Time Accumulation Are Associated with Mortality in US adults: The NHANES Study https://www.biorxiv.org/content/biorxiv/early/2017/08/31/182337.full.pdf

Three domain approach

- Interdependency: same 24-hour cycles from the same group of subjects.
- Domains represent different physiological systems.

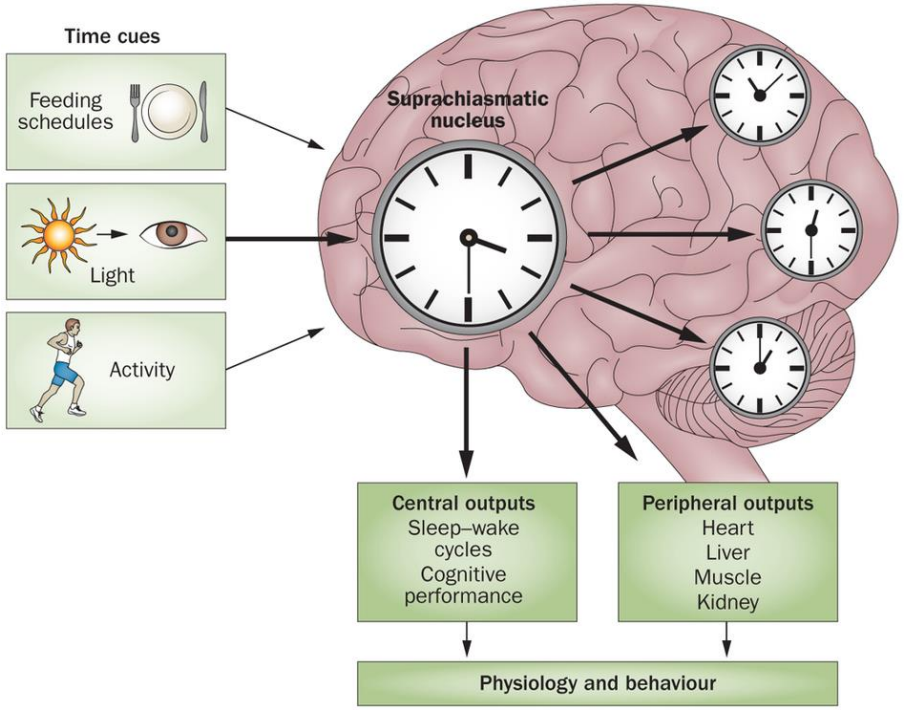


Circadian Clock



Circadian Clock

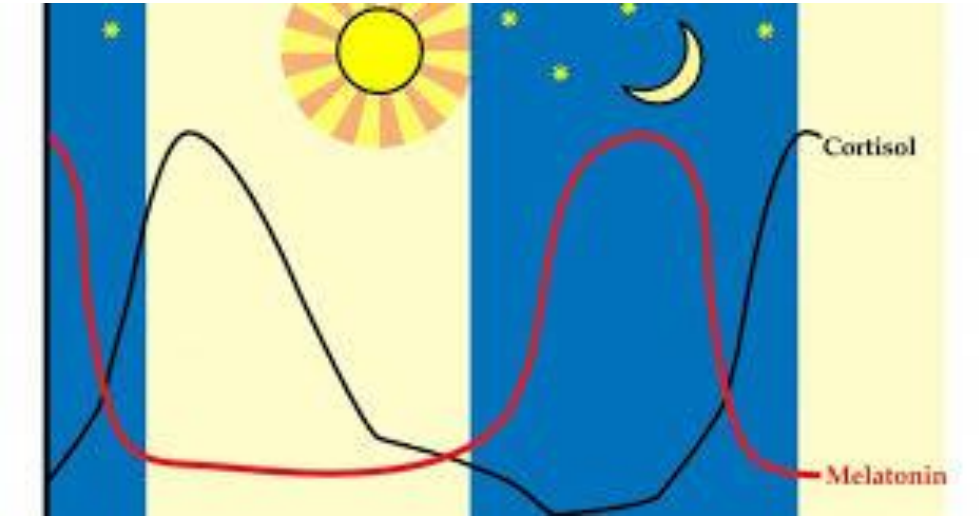
- **Suprachiasmatic nucleus** (SCN) is a small region hypothalamus
- SCN receives input from melanopsin-containing ganglion cells in retina
- SCN modulates core body temperature and production of hormones (cortisol and melatonin)
- SCN allows entrainment of daily rhythms to the 24-hour cycles in nature
- Circadian dysregulation leads to circadian rhythm sleep disorders



Circadian Rhythmicity and Disregulation

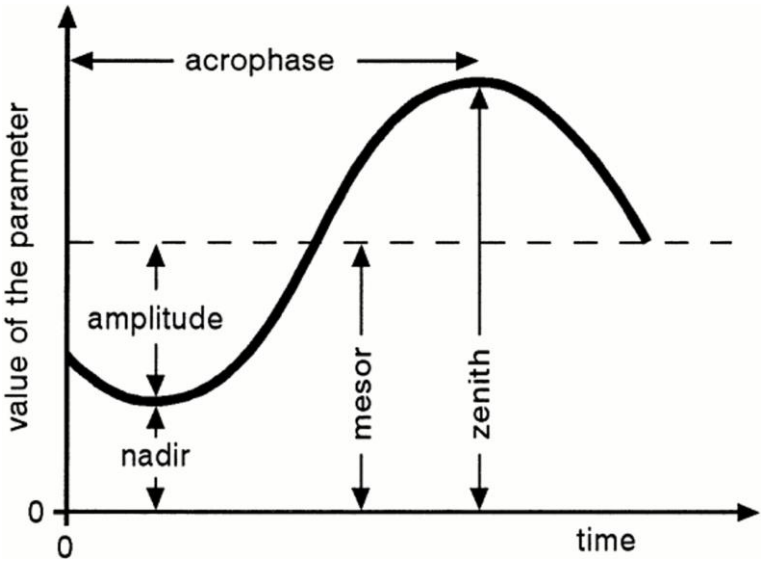
Circadian markers (hard to measure)

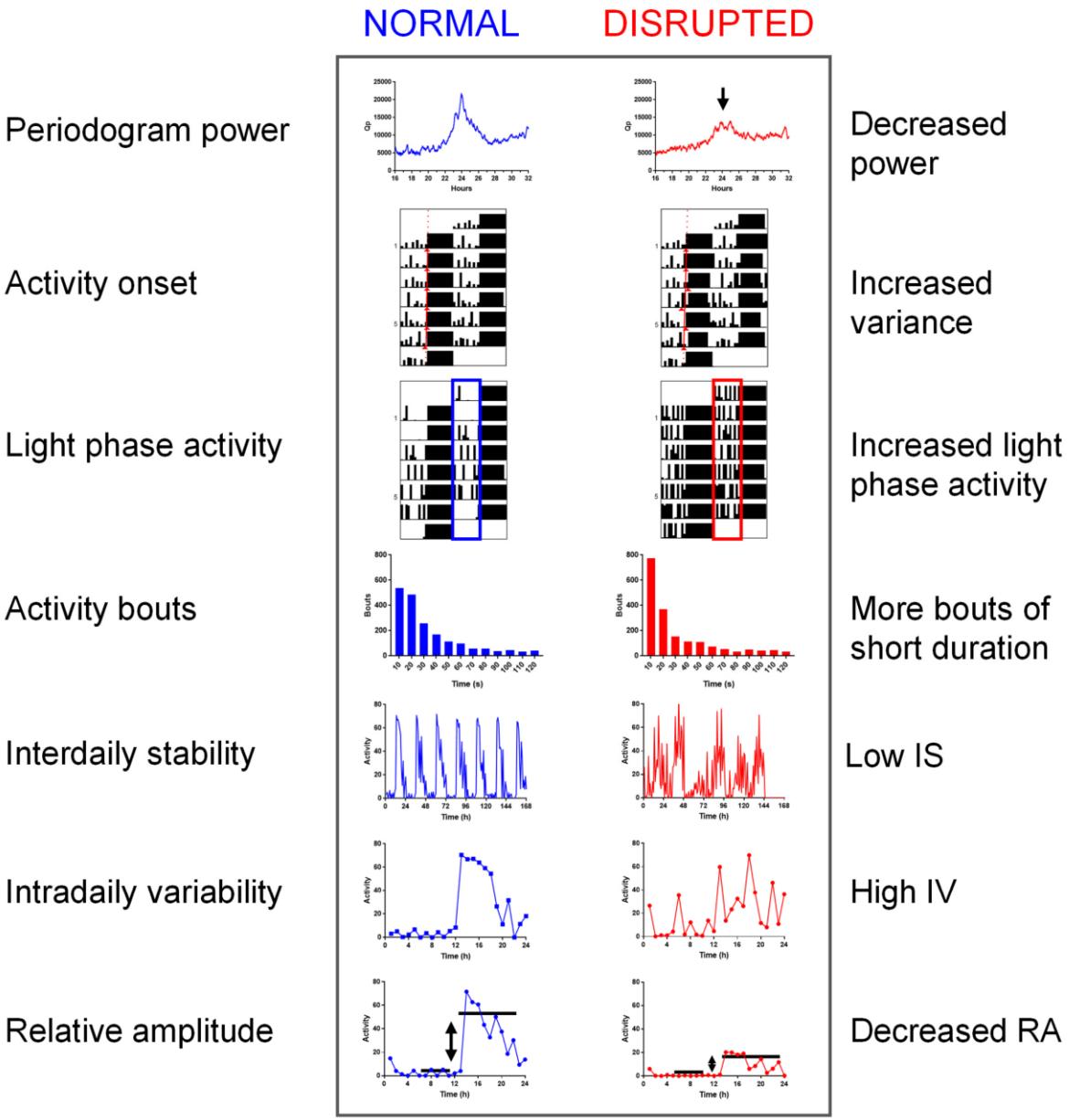
- Melatonin
- Cortisol
- Core body temperature



Circadian Rhythmicity (Actigraphy)

- Cosinor-based models (period, amplitude, phase, phase-shifts)
- Wavelet-based methods (time-frequency transformations)
- Nonparametric methods: IV, IS, RA;

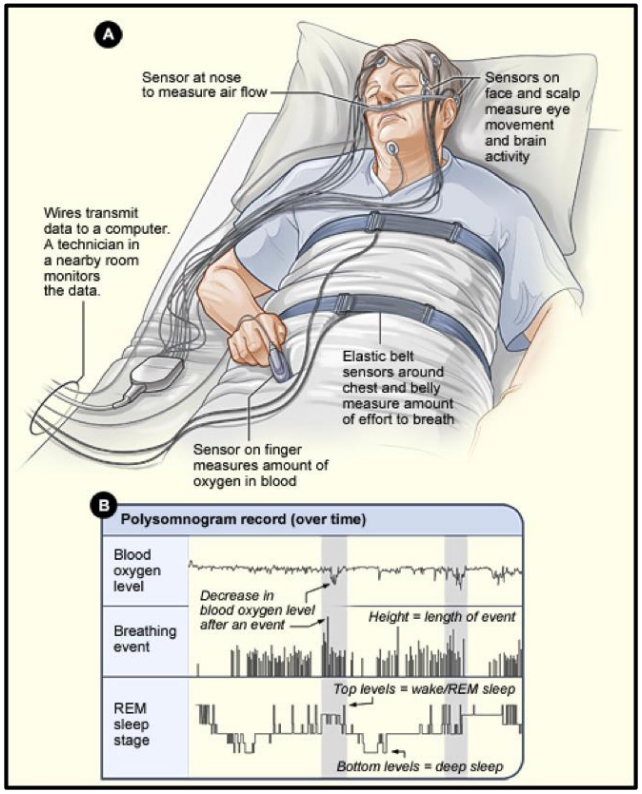




Telling the Time with a Broken Clock: Quantifying Circadian Disruption in Animal Models
Laurence A. Brown † , Angus S. Fisk †, Carina A. Pothecary and Stuart N. Peirson; Biology (MDPI)

Sleep (PSG)

- Polysomnography (golden standard)



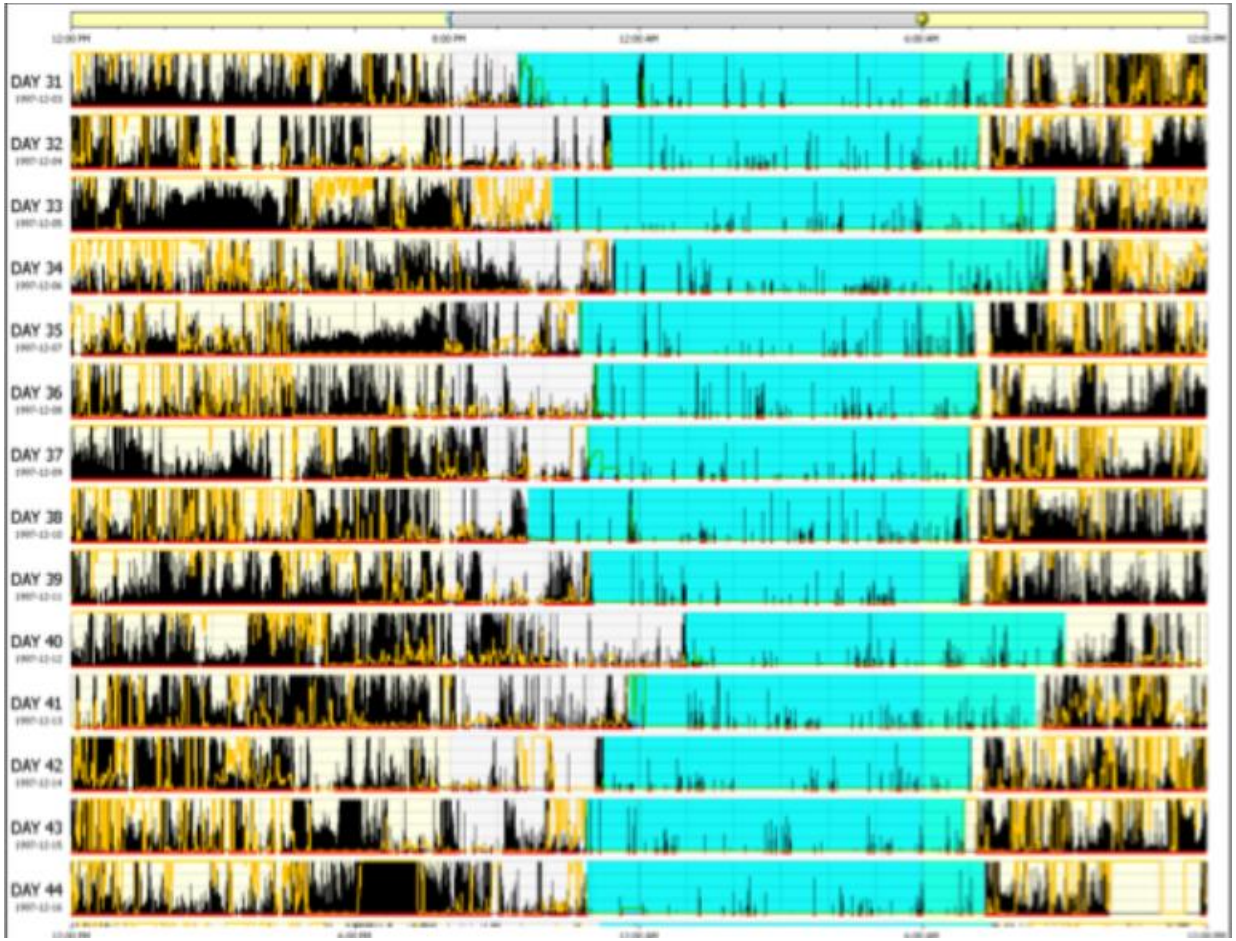
Clinical Report:

- Time in REM, NREM (1,2,3)
- Desaturation summaries
- Fragmentation

Limitations:

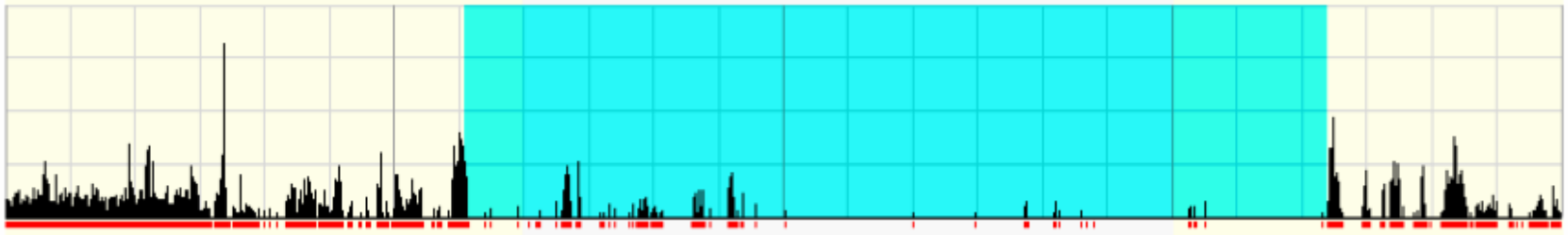
- Invasive
- Impractical for ambulatory applications

Sleep (Actigraphy)

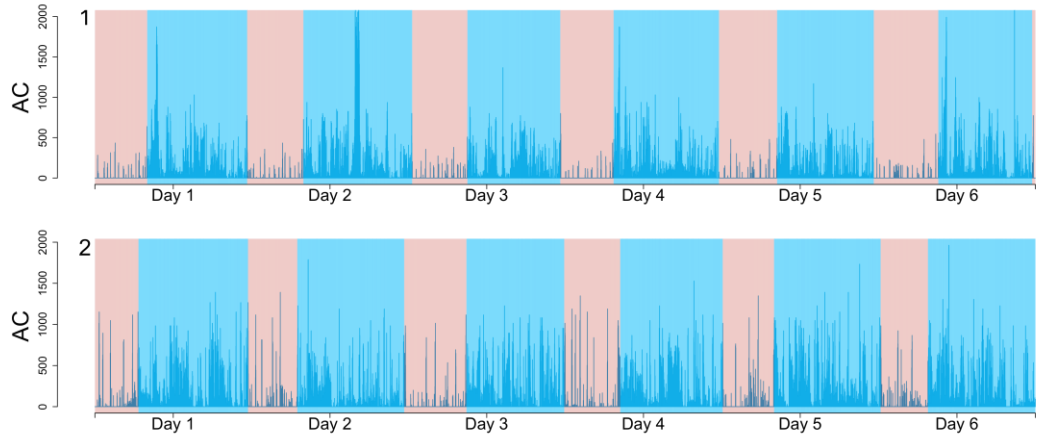


Actigraphy-Measured Sleep Quality

- Summaries
  - Total Sleep Time (TST)
  - Wake After Sleep Onset (WASO)
  - Number of Wake Bouts
  - Sleep Efficiency (SEFF)
  - Sleep Onset Latency
- Major Limitations
  - cannot discriminate between sleep stages
  - No oxygenation information

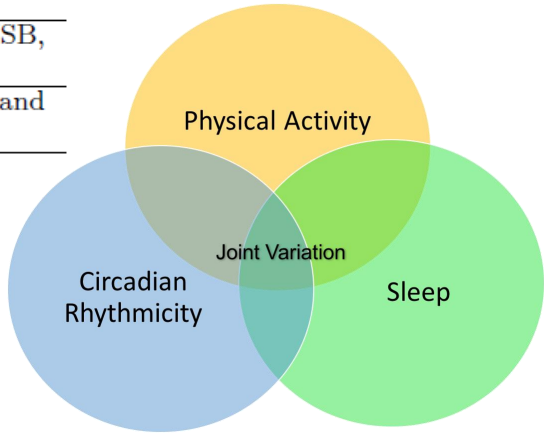


Joint and Individual Modelling of Sleep, Physical activity, Circadian Rhythmicity



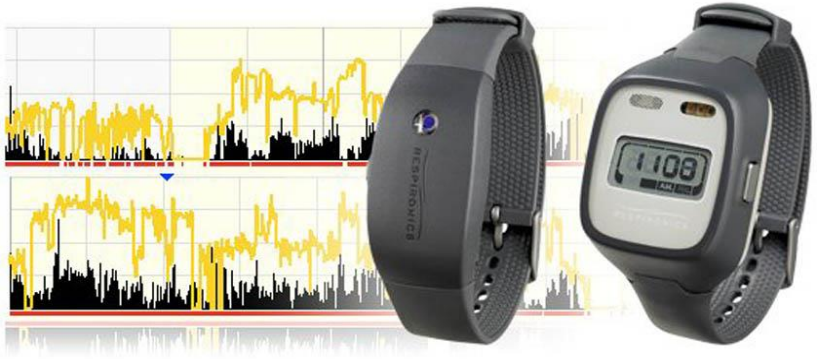
Domain-specific Features

Domains	Thresholds	Features
PA	50,100	TAC, TLAC, LTAC, TST, pST, μ, λ, g, α
SL	20,40	SOL, SEFF, WASO, pWT, NWB, AWB, TSLT, pSLT, NSB, WSTP
CR	-	min, mesor, amplitude, α, β, ϕ, RA, IV (at both minute and hourly level), fPC_1, fPC_2,..., fPC_{10}



Baltimore Longitudinal Study of Aging

- 415 BLSA participants (aged 24 – 96 y.o.)
- 7 consecutive 24-hour periods measured with Actiwatch-2
- Days with more than 5% daily missing data (72) were excluded. Subjects with fewer than 3 days of valid days were excluded
- Features were averaged across days



Multi-Domain Data

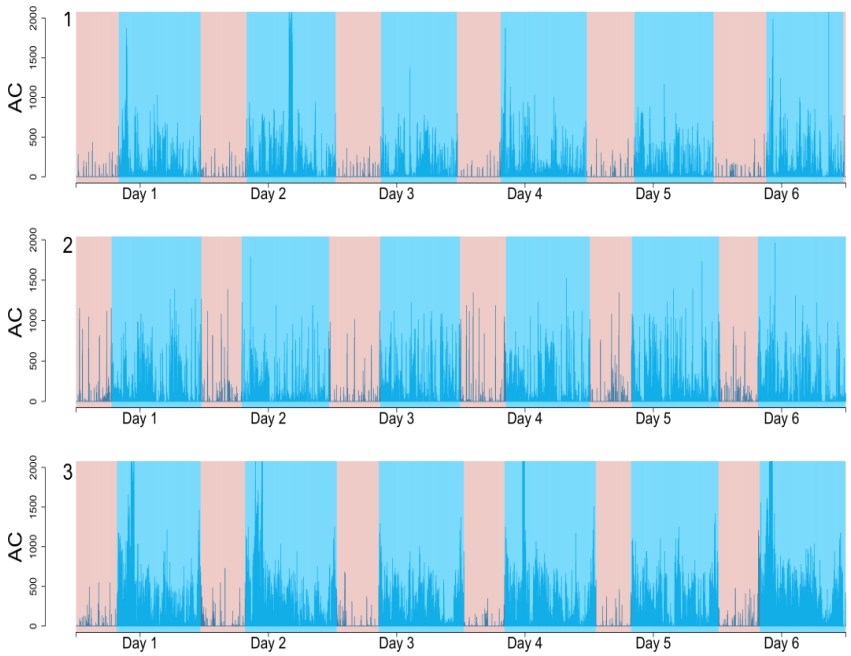


Figure 9. 24-hour measurement for 6 days from BLSA

- Continuous actigraphy measurement enables us to study
  - Physical activity (PA): waking period

    e.g. sedentary behavior and its accumulation patterns are risk factors for a wide range of diseases and mortality.
  - Sleep (SL): night time sleeping period

    e.g. sleep has been shown to be associated with cognitive function and neurodegenerative disease.
  - Circadian rhythms: 24 hour oscillation

    e.g. misalignment of circadian rhythm is associated with adverse metabolic and cardiovascular consequences.
- Guided by specific questions, researches typically focus on one of the three domains without considering the joint dependence of features within and between the domains.
- It becomes crucial to understand the joint effect of all three domains

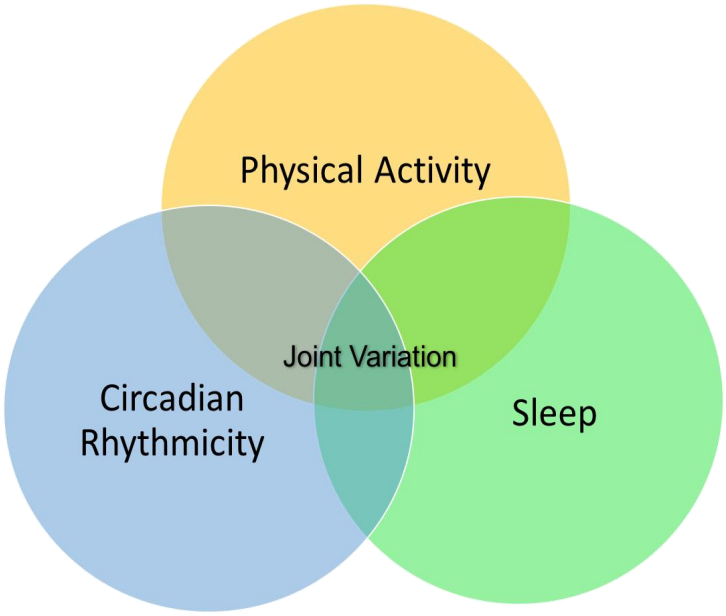
Multivariate within Each Domain

Domains	Threshold	Features
PA	50, 100	TAC, TLAC, LTAC, TST, WT, pST, μ, λ, g, α, $\bar{h}$
SL		TiB, SOL, SEFF, WASO, pWT, NWB, AWB, TSLT, pSLT, NSB, ImmbT, pImmb, NImmbB, AImmbB, TMT, pMT, NMB, AMB, N1ImmbB, p1ImmbB, Fragment
CR	Original scale Log-transformed	mesor, amp, acrophase, fPC1-6, IV, RA

- The list of features can be easily expanded with new summaries or by applying different thresholds.
- For multivariate data, dimension reduction can eliminate redundancy and capture most of relevant information.

Interdependency and Heterogeneity

- Interdependency: same 24-hour cycles from the same group of subjects.
- Heterogeneity: domains represent different physiological systems.



Joint and Individual Variation Explained (JIVE)

$$\mathbf{Y}^1 = J^1 + A^1 + \epsilon^1 = \Phi_J^1 \Gamma_J + \Phi_A^1 \Gamma_A^1 + \epsilon^1$$
$$\vdots$$
$$\mathbf{Y}^{\mathbf{D}} = J^D + A^D + \epsilon^D = \Phi_J^D \Gamma_J + \Phi_A^D \Gamma_A^D + \epsilon^D$$

- Joint Structure: $\mathbf{J} = \begin{bmatrix} J^1 \\ \vdots \\ J^D \end{bmatrix}$, with score Γ_J and loading Φ_J, rank(**J**) = r
- Individual structures: A^d, with scores Γ_A^d and loading Φ_A^d, rank(A^d) =r_d
- Orthogonality constraint: $\mathbf{J}A^{d^T} = 0$ (joint pattern unrelated to the individual pattern)

Lock, E.F., Hoadley, K.A., Marron, J.S. and Nobel, A.B., 2013. Joint and individual variation explained (JIVE) for integrated analysis of multiple data types. *The annals of applied statistics*, *7*(1), p.523.

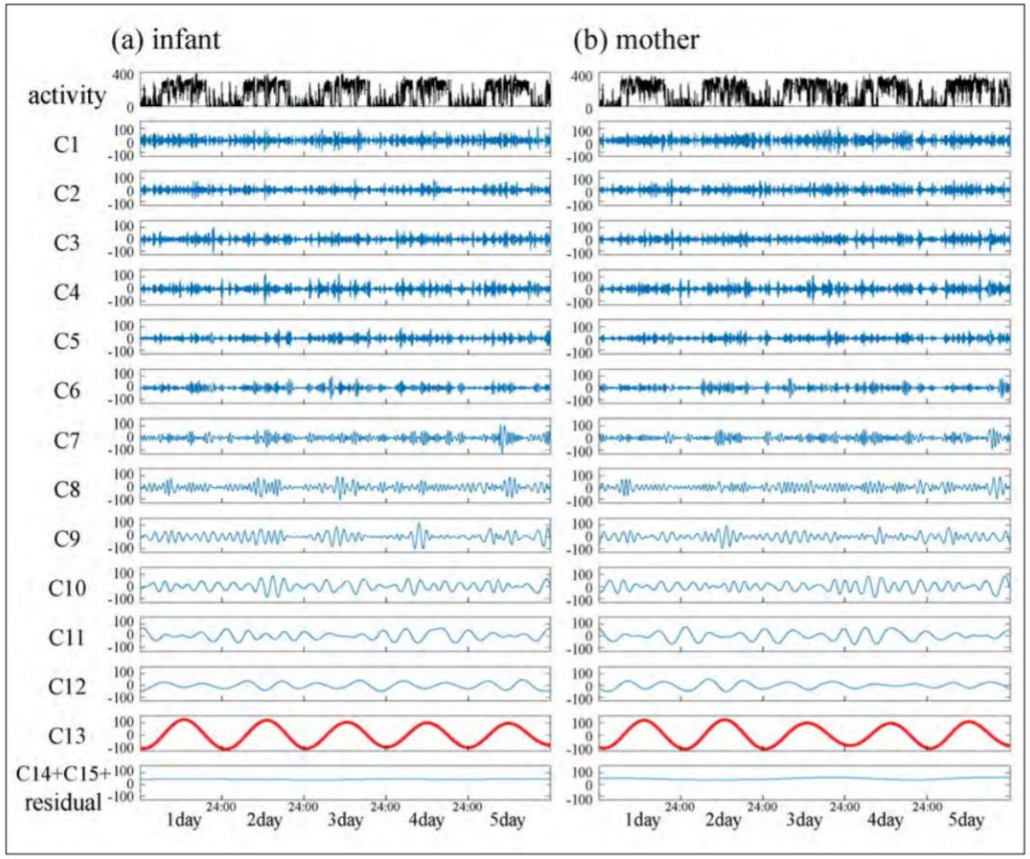
Scientific Applications: Model Gait Speed with Scores

Predictors	Beta	95% CI	P Values	Predictors	Beta	95% CI	P Values
JT-PC1	**0.13**	**(0.04, 0.22)**	**0.0048**	SL-PC3	-0.141	(-0.32, 0.04)	0.13
JT-PC2	0.084	(-0.002, 0.17)	0.056	SL-PC4	-0.178	(-0.47, 0.11)	0.23
JT-PC3	-0.04	(-0.13, 0.05)	0.37	CR-PC1	-0.003	(-0.09, 0.08)	0.93
PA-PC1	-0.035	(-0.12, 0.05)	0.41	CR-PC2	-0.07	(-0.15, 0.02)	0.11
PA-PC2	**0.155**	**(0.07, 0.24)**	**0.0006**	CR-PC3	0.023	(-0.06, 0.11)	0.59
PA-PC3	-0.07	(-0.16, 0.016)	0.11	CR-PC4	0.03	(-0.05, 0.11)	0.48
SL-PC1	**-0.203**	**(-0.33, -0.08)**	**0.0012**	CR-PC5	-0.01	(-0.1, 0.08)	0.82
SL-PC2	0.043	(-0.04, 0.13)	0.32				

- The model is adjusted by age, gender, and BMI (adj-R2 = 0.24)
- PA-PC2 and SL-PC1 are highly loaded on activity and sleep fragmentation. (adj-R2 = 0.34)

- Di, J., Spira, A., Bai, J., Urbanek, J., Leroux, A., Wu, M., Resnick, S., Simonsick, E., Ferrucci, L., Schrack, J. and Zipunnikov, V., 2019. Joint and Individual Representation of Domains of Physical Activity, Sleep, and Circadian Rhythmicity. *Statistics in Biosciences*, pp.1-32.

Empirical Mode Decomposition



Focus Theme – Original Articles

Application of Empirical Mode Decomposition to Mother and Infant Physical Activity

Synchronization of Circadian Rhythms is Associated with Maternal Mental Health

Etsuko Shimizu[1]; Toru Nakamura[2]; Jinhyuk Kim[3]; Kazuhiro Yoshiuchi[4]; Yoshiharu Yamamoto[1]

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[4]Graduate School of Medicine, The University of Tokyo, Tokyo, Japan