Ambulatory assessment of human circadian phase and related sleep disorders from heart rate variability and other non-invasive physiological measurements
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Figure 1.1 The suprachiasmatic nuclei (SCN) located in the anterior hypothalamus is the master circadian clock. It relies on input from the eyes via the optic nerve and is able to relay timing information to other slave oscillators in the body.

Figure 1.2 Schematic of entrainment and free-run of a circadian rhythm. Black represents the main sleep interval, gray represents wake time. In natural conditions, subjects were entrained to the 24 hours light:dark cycle showing consistent sleep timing. In temporal isolation, subjects began drifting and became delayed every day. When they were returned to natural lighting conditions, the subjects were able to re-entrain to the 24 hour light:dark cycle. The timing of the dark:light cycle plays a major role in the entrainment of the circadian clock to the external clock.

Figure 1.3 Depiction of the normal sleep timing versus delayed sleep phase disorder versus advanced sleep phase disorder. The black bars represent the sleep intervals. The DSPD situation would present an issue when trying to adhere to conventional work schedules, or would result in sleep deprivation and lack of alertness. The ASPD situation could interfere with social or familial interactions or obligations in the evenings. Note that the extent of these misalignments can be larger or smaller than depicted here.

Figure 1.4 Phase response curve (PRC) for short light pulses during constant darkness at different times of the circadian cycle (below) and the corresponding shifts in the circadian clock (above) where black lines represent the subjective night. A pulse at (A) has no shifting effect, at (B) and (C) causes delays of different magnitudes, at (D) and (E) causes advances of different magnitudes. Figure from Moore-Ede et al. [24].

Figure 1.5 Core body temperature (CBT) measured via a rectal thermometer over 30.5 hours. The thick center line shows the mean, while the thinner lines are plus or minus one SE. Adapted from Kräuchi et al. [27].

Figure 1.6 Schematic of typical melatonin profile over one night. Melatonin production starts in the evening and usually reaches a plateau during the night before decreasing by morning. Melatonin, specifically DLMO, is the most commonly used biomarker for circadian phase.

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Figure 5.1 Mio Alpha wrist-worn PPG-based heart rate monitor.

Figure 5.2 Protocol for the second part of the study. Time intervals shown are not representative of the schedule of all participants. On average, the data consisted of 48 hours of actigraphy, 40 hours of PPG, 32 hours of ECG, 2 PSG recordings, and 5 saliva samples for melatonin analysis.

Figure 5.3 RR intervals from an ECG compared to the pulse-to-pulse intervals from a PPG signal. Since the PPG signal is a mechanical signal while the ECG is electrical, there is a delay in the measurement of the pulse in the PPG as it reaches the sensor location at the wrist.

Figure 5.4 Flowchart of circadian phase estimation model. The RR intervals from the 3 separate recordings are first stitched together. All signals are then median filtered with a window of 15 minutes and normalized. Signal combinations are then used as inputs into the ARMAX model which then outputs an estimated cosine wave. The cosine is then fitted using a cosinor fitting. The maximum of the newly created cosine is determined and this is the estimated DLMO surrogate.

Figure 6.1 RR intervals of sleep onset insomnia patients. Error bars show the standard error of the measurements.

Figure 6.2 Spectral HRV features from 24 hour ECG recordings from sleep onset insomnia patients. The vertical line shows the sleep onset time. Error bars represent the standard errors of the measurements.

Figure 6.3 Temporal HRV features from 24 hour ECG recordings from sleep onset insomnia patients. The vertical line shows the sleep onset time. Error bars represent the standard errors of the measurements.

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