ALERTNESS SAFETY AND PRODUCTIVITY

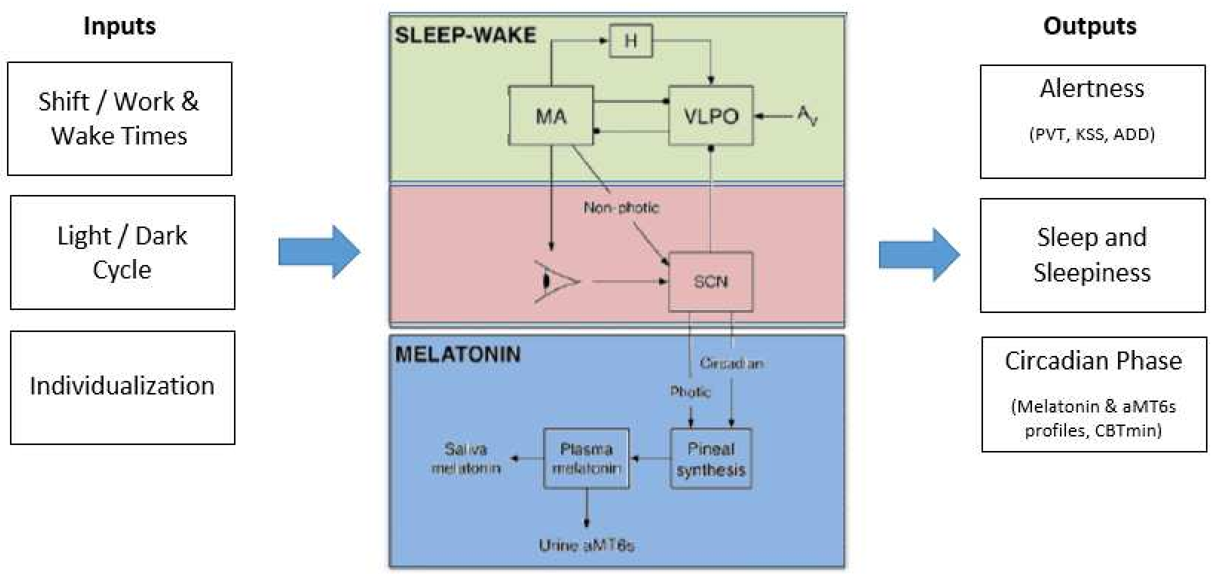
Australian Government
Department of Industry, Innovation and Science

Business Cooperative Research Centres Programme

Project Output Profile: Biophysical Model of Arousal Dynamics

The Alertness CRC model of arousal dynamics (MAD) predicts alertness, sleep, and circadian dynamics under a variety of conditions, including normal daytime activities, shiftwork, and jetlag. It is comprised of a system of ordinary differential equations, which were developed based on neurobiological mechanisms of sleep and circadian regulation. The model has been validated against more than sixty experimental studies, including sleep deprivation, forced desynchrony, shiftwork[1-3] and chronic sleep restriction (unpublished) and was tested against real-world data in a hospital shift work setting. The model is calibrated to predict dynamics for a standard individual (or group average) but can be personalized for individuals by adjusting model parameters.

<u>A model based on sleep and circadian neurobiology</u>



Model Functionality

The MAD is a mathematical model that captures the biological dynamics underlying the sleep-wake cycle, circadian rhythms, and alertness in humans. It captures the dynamics of the build-up of a need for sleep with time spent awake, the recovery that occurs during sleep, and the associated effects on alertness and interactions with circadian rhythms.

The model's predictions correspond to the biological dynamics of an average or typical person. When evaluated without any additional constraints, the model will predict sleep of approximately 8 hours per night, starting near midnight. These predictions of sleep are based on the times when the biological need for sleep exceeds a certain threshold.

It is important to note that the model does not capture the behavioural decisions that result from work, social or environmental constraints. However, the model can incorporate and respond to such constraints. Such constraints on the model's evaluation must be provided as inputs. These constraints take two main forms:

- forced-wake; and
- specific light exposure.

For the model to make interesting "real world" predictions it is necessary to evaluate the model in the context of a specific set of environmental and behavioural constraints. For example, for a given shift-schedule and commute times the model can be used to predict potential disturbances to sleep patterns and the effect on alertness during shift.

Available Inputs

A number of inputs can be provided to the model depending on a use case:

- Work schedule (if not provided, days off are assumed);
- Times when must be awake but not at work; e.g., social commitments. (If not provided, sleep is allowed at any non-work time according to sleep need);
- Sleep times, actual or desired (customize sleep opportunities. If not provided, sleep is predicted according to sleep need and other inputs);
- Light profile, can be given in photopic lux, melanopic lux, or irradiance + spectral power density (if not provided, ambient daylight is assumed and constant office lighting during work);
- Personalized parameters; e.g. chronotype (if not provided, standard individual is assumed);
- Caffeine intake* (can be added if required but is not included in the generic version).

Available Outputs

- Alertness measures at 1 minute resolution (KSS, PVT lapses, ADD) and variety of quantities calculated from them; e.g., mean/max/min alertness on shifts or commute and high/medium/low risk times;
- Sleep times (unless provided as an input);
- Circadian phase markers; e.g., DLMO in plasma/saliva, aMT6s acrophase in urine, and core body temperature minimum;
- Melatonin profile in plasma and saliva; and
- aMT6s profile in urine

References

1) Postnova S, Postnov DD, Seneviratne M, Robinson PA (2014) Effects of rotation interval on sleepiness and circadian dynamics on forward rotating 3-shift systems. J Biological Rhythms 2014 29:60–70.

2) Postnova S, Lockley SW, Robinson PA. Sleep Propensity under Forced Desynchrony in a Model of Arousal State Dynamics. J Biol Rhythms. 2016 Oct;31 (5):498-508. doi:10.1177/0748730416658806. Epub 2016 Jul 17. https://www.ncbi.nlm.nih.gov/pubmed/27432116

3) Postnova S, Lockley SW, Robinson PA. Prediction of Cognitive Performance and Subjective Sleepiness Using a Model of Arousal Dynamics. J Biol Rhythms. 2018 Apr;33(2):203-218. doi: 10.1177/0748730418758454. https://www.ncbi.nlm.nih.gov/pubmed/29671707

4) Abeysuriya RG, Lockley SW, Robinson PA, Postnova S. A unified model of melatonin, 6-sulfatoxymelatonin, and sleep dynamics. J Pineal Res. 2018 May;64(4):e12474. doi: 10.1111/jpi.12474. Epub 2018 Mar 8. https://www.ncbi.nlm.nih.gov/pubmed/29437238

5) Postnova, S. “Physiologically-based modelling of Alertness”, WIMSIG: Celebration of Women in Australian Mathematical Sciences, Adelaide, Australia, 24-26 September 2017.

6) Physiology-Based Modeling of Sleep and Wake Phenomena in the Human Brain A Thesis Submitted for the Degree of Doctor of Philosophy by M S ZOBAER January 2018. Chapter 4 Quantitative modelling of the effects of the light spectrum on the human circadian rhythm M S Zobaer, P A Robinson, S W Lockley, S Postnova.

7) Tahereh Tekieh, Stephen McCloskey, Steven W Lockley, Peter A Robinson, Svetlana Postnova: Quantitative modelling of the direct alerting effects of light. 24th Congress of the European Sleep Research Society.

Alertness CRC is exploring a range of options to further the use of its research, technology and products and is open to speaking with a range of interested entities from investors to licensees and commercialization partners. Additional public information is available at: https://mjkpartners.com/opportunities/alertnesscrc/ or contact Myron Kassaraba, MJK Partners, LLC, Tel. 617-902-0639, myron@mjkpartners.com.

