Modelling sleep-wake regulation

The dynamics, bifurcations and applications of the two process model

Matthew Bailey

UNIVERSITY OF SURREY

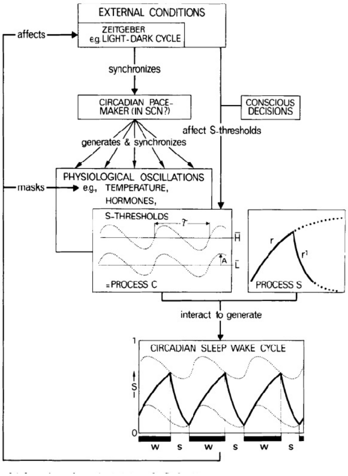
matthew.bailey@surrey.ac.uk

Overview

Why mathematically model sleep?

- Understood that poor sleep can lead to many diseases
- Models can help understand the underlying physiology
- Understanding sleep timing has many practical uses

The two process model



Borbély 1982, Daan et al. 1984

- **Circadian process:** oscillator entrained to 24 hours by external conditions
- **Homeostatic process:** denoting physiological oscillations
- Interaction of these two processes gives switching between sleep and wake

Model equations

Homeostat:

$$H_s(t) = H^+(t_0)e^{\frac{t_0-t}{\chi_s}}.$$

$$H_w(t) = 1 + (H^-(t_0) - 1)e^{\frac{t_0-t}{\chi_w}}.$$

Switching:

$$H^+(t) = H_0^+ + a\sin(2\pi t),$$

$$H^-(t) = H_0^- + a\sin(2\pi t).$$

Assumptions:

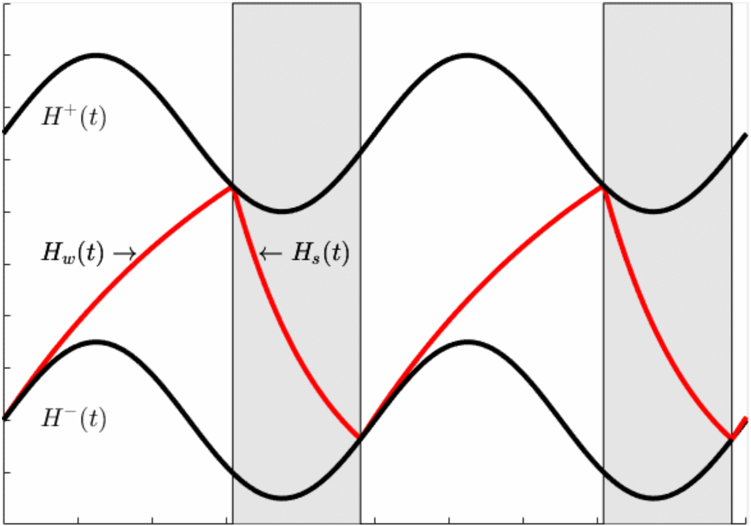
Homeostat increases on wake and decreases on sleep:

$$\chi_{s,w} > 0, \qquad H_0^- + a < 1, \qquad H_0^+ - a > 0$$

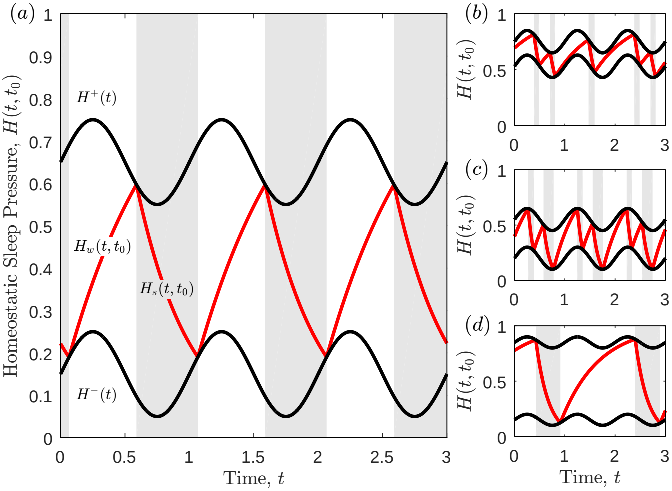
Switching between sleep and wake occurs:

$$H_0^- + a > 0, \qquad H_0^+ - a < 1.$$

Model and assumptions

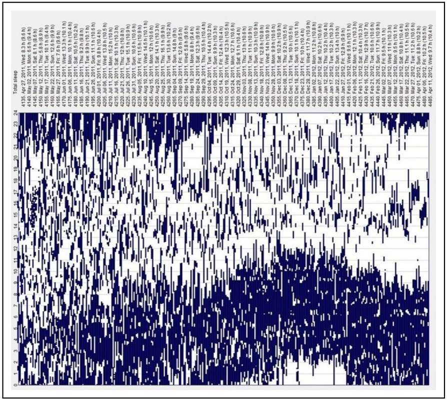


Sleep-wake dynamics



Human sleep

- Monophasic in adults (One sleep per day)
- Changes from birth to adulthood



Down map

$T_d : \mathbb{R} \mapsto \mathbb{R}$ where $T_d(t_0)$ is the first time greater than t_0 such that

$$H_s(T_d(t_0), t_0) = H^-(T_d(t_0)).$$

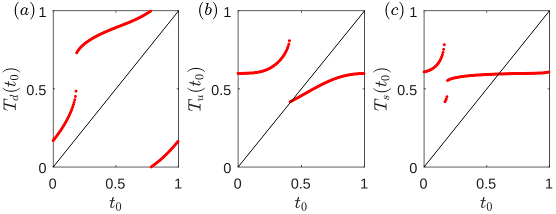
Up map

$T_u : \mathbb{R} \mapsto \mathbb{R}$ where $T_u(t_0)$ is the first time greater than t_0 such that

$$H_w(T_u(t_0), t_0) = H^+(T_u(t_0)).$$

Composite map

$T_s : \mathbb{R} \mapsto \mathbb{R}, \quad T_s(t_0) = T_u(T_d(t_0)).$



All three maps satisfy

$$T_i(t_0 + 1) = T_i(t_0) + 1, \quad i = d, u, s.$$

$T_i(t_0)$ can be seen as the lift of a monotonic circle map on the interval $[0, 1]$.

(p, q) periodic solutions

- Many different types of periodic orbits.
- p sleeps (and hence p wakes) in q days.

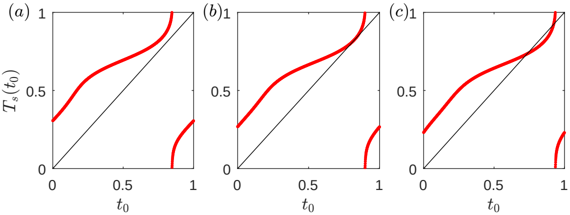
Hence we say that t_0 generates a (p, q) periodic orbit if

$$T_s^p(t_0) = t_0 + q.$$

Interested in the mechanisms which create/ annihilate periodic solutions

Saddle node bifurcations

$$(T_s^p)'(t_0) = 1 \quad \text{and} \quad T_s^p(t_0) = t_0 + q$$



Creates and annihilates periodic solutions

$$0 \to 1 \to 2 \to 1 \to 0$$

Saddle node bifurcations

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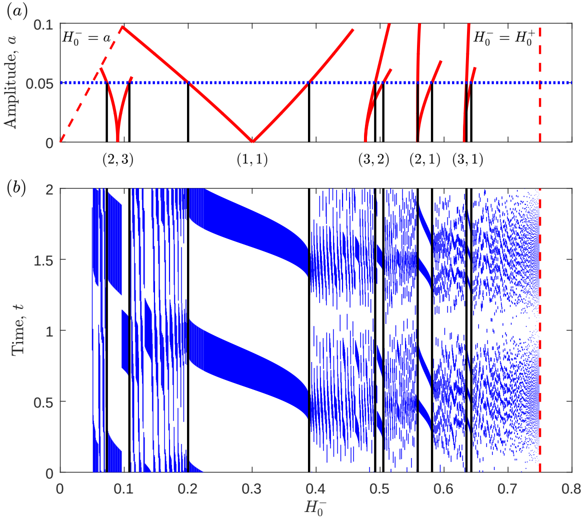
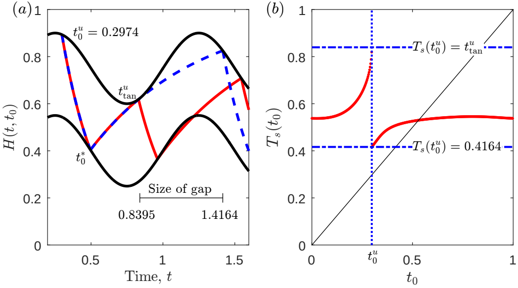
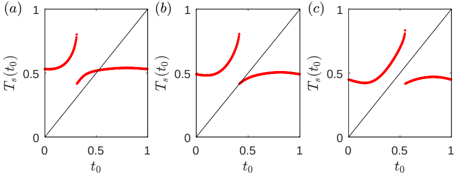


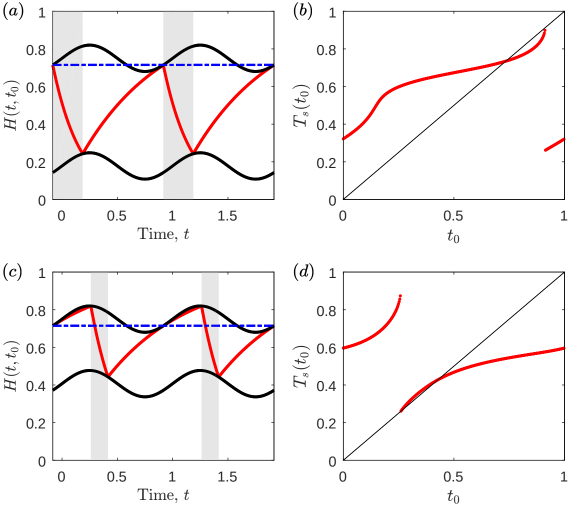
Border collisions



Switch at the tangency point or a near miss



Border collisions



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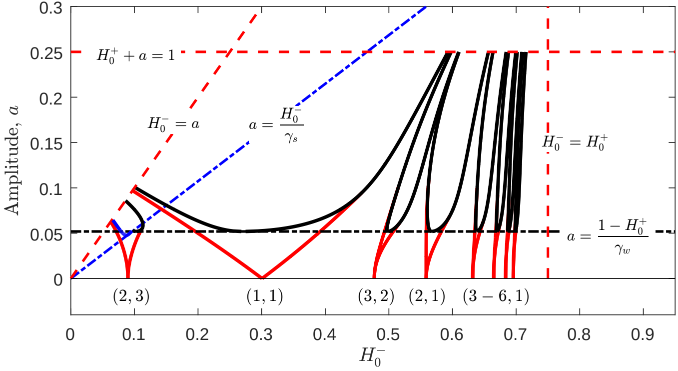
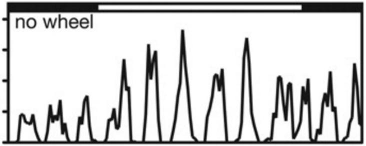
Bifurcation set



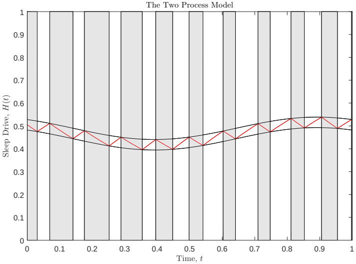
Border collisions take over the Arnold tongue boundaries for larger amplitudes.

The common vole

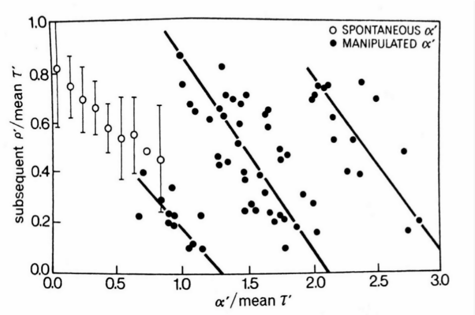
- Polyphasic (many sleeps per day)
- Consolidated sleep and wake
- More sleep during the day



van der Veen et al. 2006



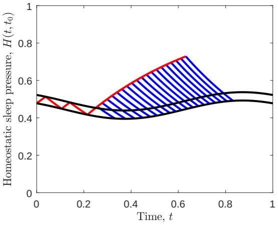
Sleep deprivation

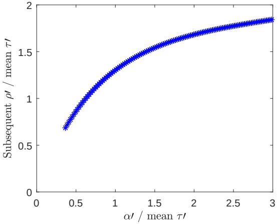


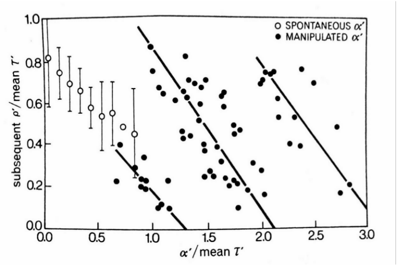
$\alpha\prime$ - Length of wake
$\rho\prime$ - Length of sleep
$\tau\prime$ - Average sleep-wake period length $\left(\frac{1}{8}, \frac{1}{9}, \frac{1}{10}\right)$

Gerkema and Leest, 1991

Sleep deprivation







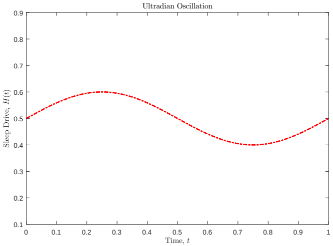
- Jump at each $\tau\prime$ period
- Decreasing sleep length
- Max one $\tau\prime$ sleep length

Ultradian rhythmicity

A recurrent period or cycle repeated throughout a 24-hour circadian day.

$$H^{\pm}(t) = H_0^{\pm} + a\sin(2\pi t) + a_u \sin\left(\frac{2\pi}{\tau'}t\right),$$

where τ' is a divisor of 1 day.



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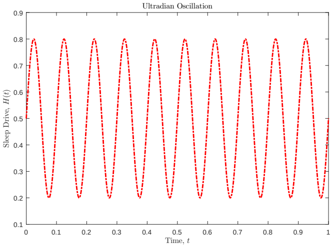

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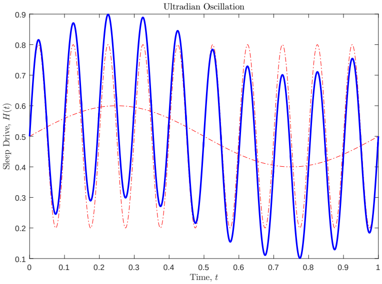

An ultradian solution

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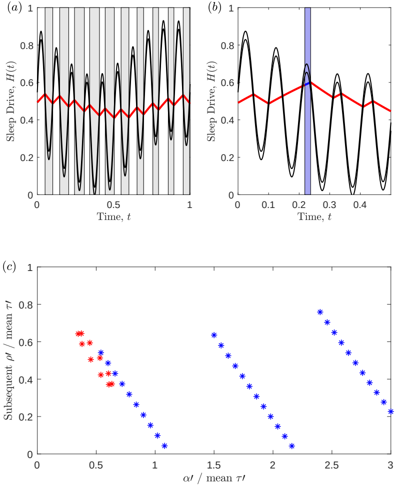
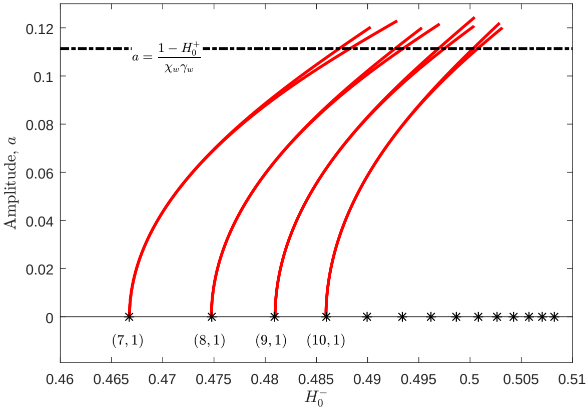


- Periodic
- Hidden ultradian
- a_u creates a barrier
- Decreasing $\frac{\rho'}{\tau'}$ with jumps

The bifurcation diagram

Finite angle decreases as number of sleeps per day or the number of iterations of the map increases.



Points to consider

- Unlikely that TPM parameters for the common vole would lie and remain inside the very narrow tongues.

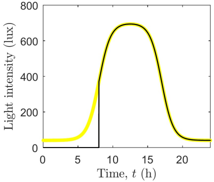
- TPM does not account for individual differences.

In humans, the intrinsic period of the circadian pacemaker is estimated to average 24 hours and 9 minutes ± 12 (SD) minutes and is entrained by external zeitgebers to 24 hours.

- An important zeitgeber in mammals is the light-dark cycle

Human circadian system (cubic van der Pol type oscillator)

Light $\rightarrow$ eye (retina)



$$\frac{dn}{dt} = \gamma\left(\alpha(I)(1-n) - \beta n\right).$$

$\rightarrow$ Forcing term, B

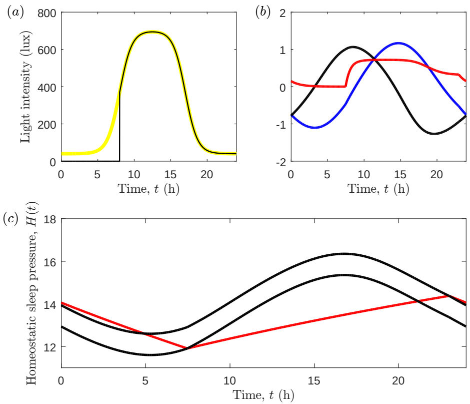
$$\frac{dX}{dt} = \frac{\pi}{12}\left(Y + B\right),$$

$$\frac{dY}{dt} = \frac{\pi}{12}\left(\mu_I\left(Y - \frac{4}{3}Y^3\right) - X\left[\left(\frac{24}{0.99669\tau_c}\right)^2 + kB\right]\right).$$

τ_c intrinsic period

Forger et al. (1999)

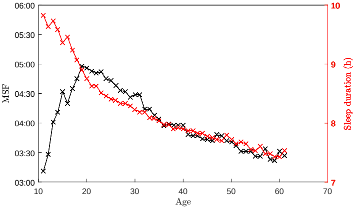
Modified two process model

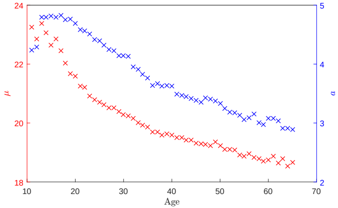


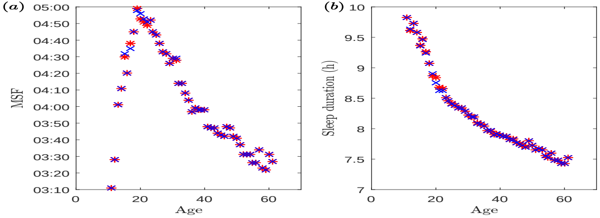
(b) $\frac{dX}{dt}$ (blue), $\frac{dY}{dt}$ (black), $\frac{dn}{dt}$ (red). (c) modified two process $a = 3.37$, $\mu = 20.37$.

Mid-sleep on free days (MSF) and sleep duration data with results

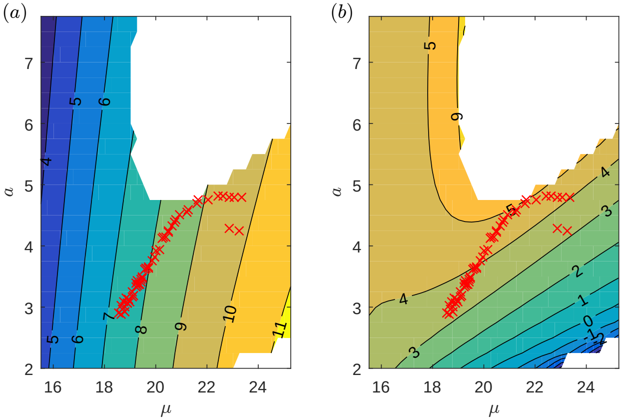
Data from Roenneberg et al. (2004)(2013) as used in Skeldon, Derks, Dijk (2016)







Results



(a) Sleep duration (b) MSF as a function of μ and a. Each red cross represents a (μ, a) pair

Conclusions

- Two process model displays a wide range of dynamics (monophasic and polyphasic sleep - wake patterns)
- Transitions between periodic solutions occur as a result of saddle-node and border collision bifurcations
- Linking the two process model to more complex neuronal models could lead to a better understanding of its parameter values.

Bailey, Derks, Skeldon (2018), *Circle maps with gaps: Understanding the dynamics of the two-process model for sleep-wake regulation* **Eur. J. Appl. Math.**

Acknowledgments

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Pioneering research and skills