# Sleep, dreams, and bifurcations: REM sleep and nonsmooth maps for sleep/wake dynamics

Cecilia Diniz Behn

Department of Applied Mathematics and Statistics, Colorado School of Mines
Department of Pediatrics, University of Colorado Anschutz Medical Campus

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# Introduction

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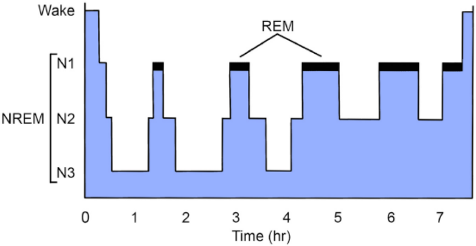
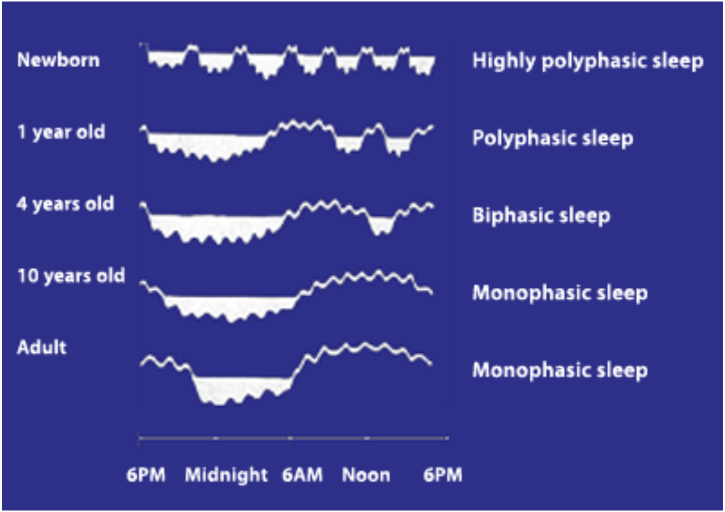
- Normal adult human sleep occurs in a consolidated nighttime period
- Sleep includes both rapid-eye movement (REM) sleep and non-REM (NREM) sleep
- Over the course of the night, people cycle between NREM and REM sleep approximately every 90 minutes




Scammell et al., Neuron, 2017

# Sleep across the lifespan



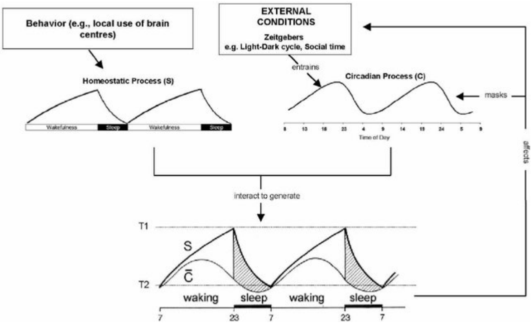
# Goal

Use mathematical modeling and analysis to investigate the role of REM sleep in sleep/wake dynamics during the transition from polyphasic to monophasic sleep and gain insight into physiology during development.

# Two-process model

# Two-process model

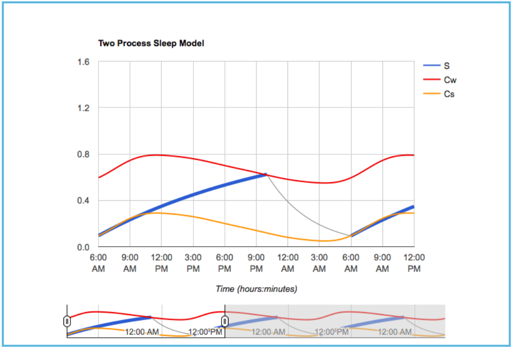
- Circadian rhythm (Process C): propensity to sleep that changes over 24 h day
- Homeostatic sleep drive (Process S): propensity to sleep that increases with time in prior wakefulness

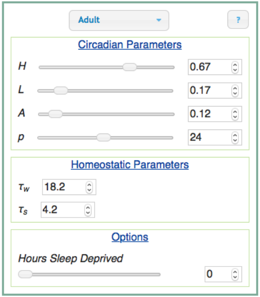



Borbély, 1982

# Web-based simulator of two-process model

Developed in collaboration with Victoria Booth, U. Michigan




http://twoprocessmodel.math.lsa.umich.edu

# Two-process model equations

- Circadian rhythm (Process C) represented with sinusoid (may include higher harmonics):

$$C^+(t) = H_0^+ + a\sin(2\pi t);\ \ C^-(t) = H_0^- + a\sin(2\pi t)$$

- Homeostatic sleep drive (Process S) represented by
  - Exponential growth during wake:

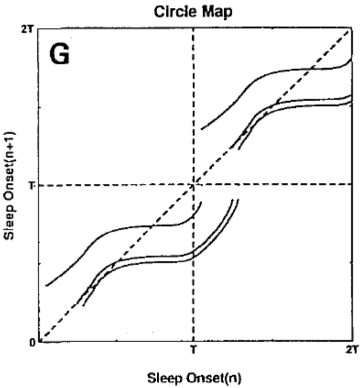
$$H_s(t, t_0) = H^+(t_0)\exp((t_0 - t)/\chi_s)$$

  - Exponential decay during sleep:

$$H_w(t, t_0) = 1 - (1 - H^-(t_0))\exp((t_0 - t)/\chi_w)$$

# Circle map for two-process model

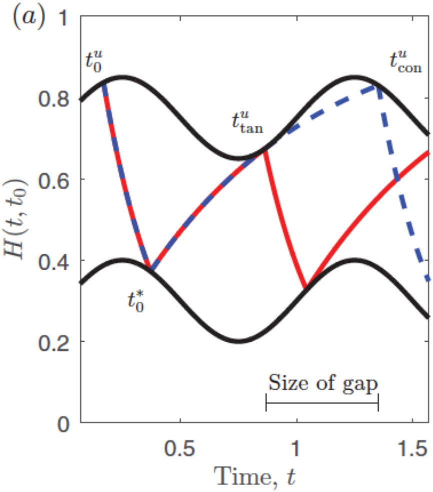
- Compute map describing successive phases of sleep onset
- Stable fixed point of map = entrained sleep-wake behavior
- Map monotonic with a vertical gap




Nakao et al., 1997

# Gap in map

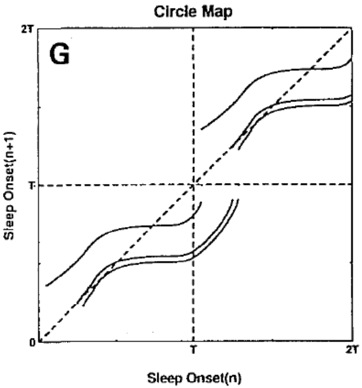
- Vertical gap comes from tangency of homeostat with upper or lower threshold
- Nearby initial phases of transition to wake onset can produce large differences in phase of next sleep onset
- This feature plays a role in the observed patterns in recovery sleep following sleep deprivation




Bailey et al., 2018

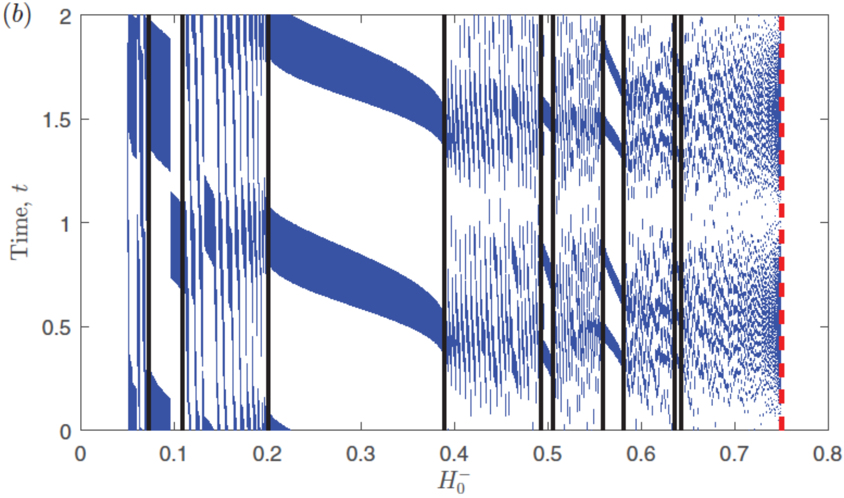
# Circle map for two-process model

- Existence and stability of fixed points changes with $H_0^-$
- System may undergo a border collision bifurcation
- Period-adding sequences observed in the number of sleep episodes/day




Nakao et al., 1997

# Number of daily sleep episodes changes with $H_0^-$

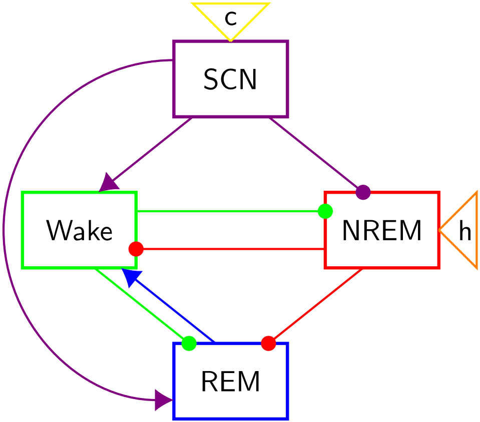



Bailey et al., 2018

# Three-state network model

# Three-state sleep/wake network model

- Represents neuronal network in brainstem and hypothalamus
  - Arrows = excitatory projections
  - Circles = inhibitory projections
- Circadian modulation *C* relayed by suprachiasmatic nucleus (SCN)
- Homeostatic modulation *h* on NREM-promoting population



# Model equations - firing rates for neuronal populations

$$F'_X = \frac{F_{X\infty}\left(\sum_i g_{i,X} C_{i\infty}(F_{Yi})\right) - F_X}{\tau_X}$$

$$F_{X\infty}(c) = X_{max}(0.5(1 + \tanh((c - \beta_X)/\alpha_X)))$$

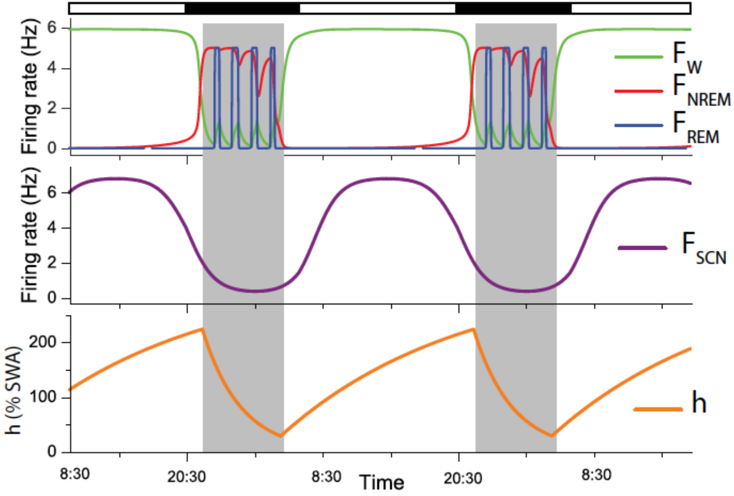
$$C_{i\infty}(f) = \tanh(f/\gamma_i)$$

for $X = W, N, R, SCN$.

**Elements of Two-process model also present here:**

- Forger circadian pacemaker model produces 24 h variation in $F_{SCN}$
- Homeostatic sleep drive modulates activation threshold of $F_{NREM}$

# Typical model behavior



# Model equations - homeostatic sleep drive

$$\frac{dh}{dt} = \frac{h_{max} - h}{\chi\tau_{hw}} H[F_W - \theta_W] - \frac{h}{\chi\tau_{hs}} H[\theta_W - F_W]$$

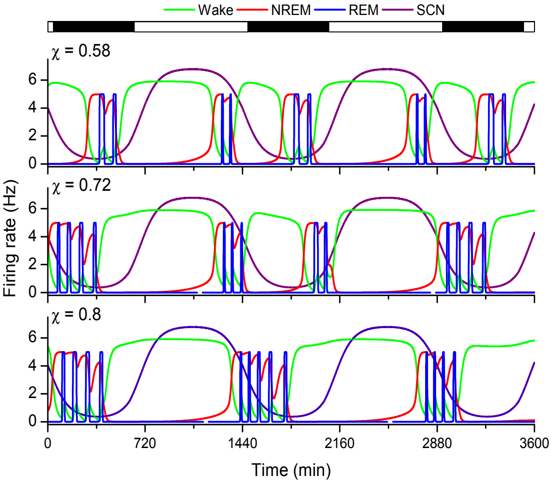
- Initial time constants fit to experimental measurements in adults.
- Parameter $\tau_{hw}$ controls growth of homeostatic sleep drive
- Parameter $\tau_{hs}$ controls decay of homeostatic sleep drive
- Decreasing the scaling parameter $\chi$ below 1 causes both growth and decay to occur more quickly

# Three-state model dynamics change with $\chi$

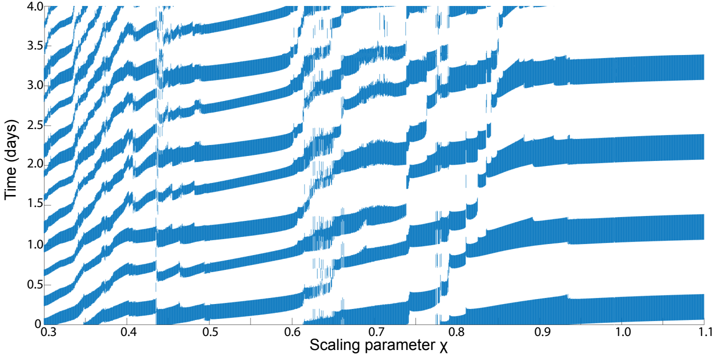
As $\chi$ decreases, it affects both

- Number of sleep episodes per day
- Number of REM bouts per sleep episode

Notation:
$\{1_{[4]}, \ldots\}$,
$\{1_{[4]}, 1_{[5]}, \ldots\}$

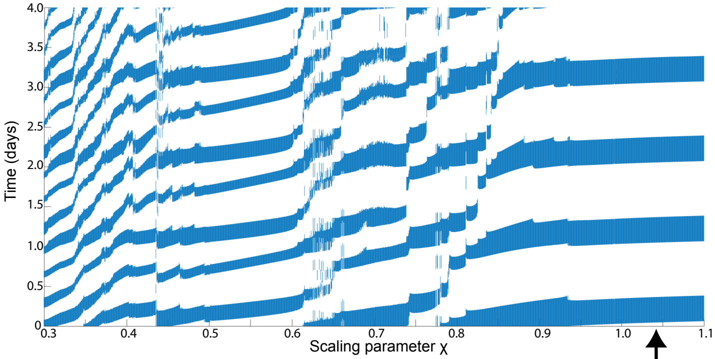


# Three-state model dynamics change with $\chi$




Time spent in sleep over 4 day period as $\chi$ is decreased. Blue areas represent sleep; white areas represent wake.

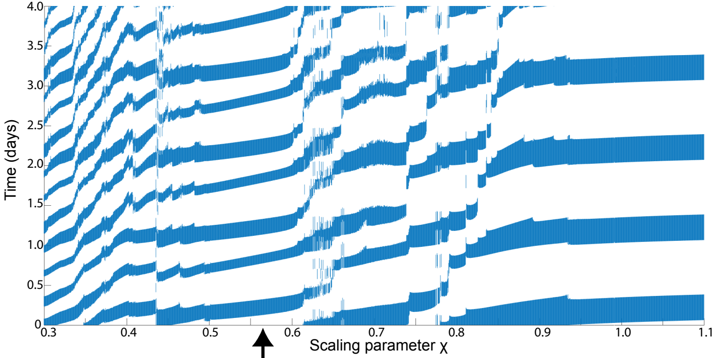
# Three-state model dynamics change with $\chi$




1 sleep episode per day

Time spent in sleep over 4 day period as $\chi$ is decreased. Blue areas represent sleep; white areas represent wake.

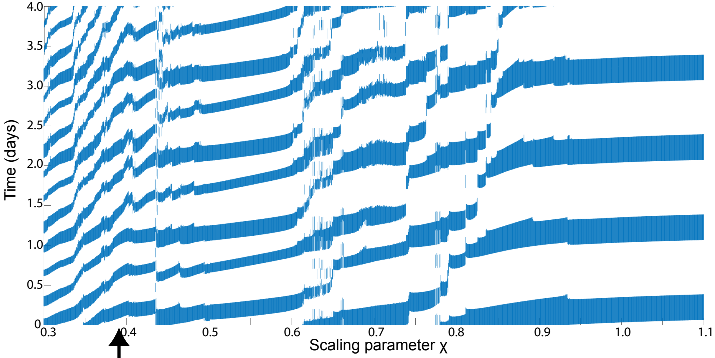
# Three-state model dynamics change with $\chi$




2 sleep episodes per day

Time spent in sleep over 4 day period as $\chi$ is decreased. Blue areas represent sleep; white areas represent wake.

# Three-state model dynamics change with $\chi$

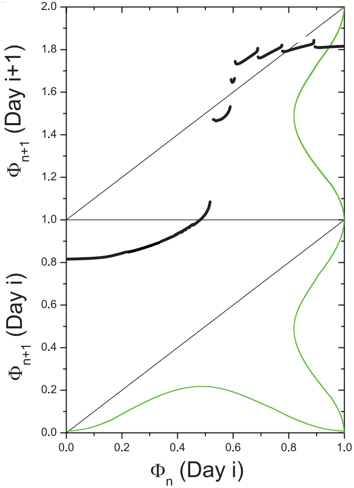



3 sleep episodes per day

Time spent in sleep over 4 day period as $\chi$ is decreased. Blue areas represent sleep; white areas represent wake.

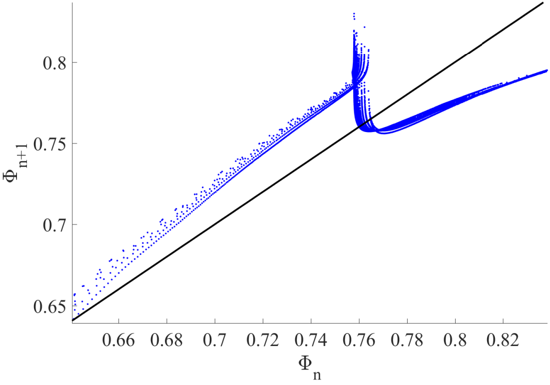
# Map of three-state model

- Numerically compute map to describe the sleep onset phase, $\Phi_{i+1}$, as a function of the previous sleep onset phase, $\Phi_i$
- Determining appropriate initial conditions was key step in algorithm for computing map
- For $\chi = 1$, map has one stable fixed point and multiple gaps




Booth, Xique, CDB, SIADS, 2017

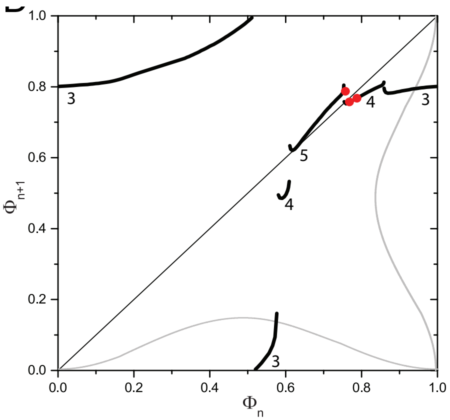
# Map dynamics near fixed point - $\chi = 0.92$




Cusp-like behavior of map near fixed point causes fixed point to lose stability near $\chi = 0.92$ in a putative period-doubling bifurcation.

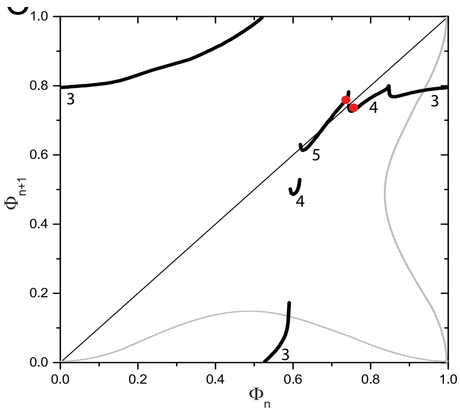
# Map - $\chi = 0.92$

- For $\chi = 0.92$, the fixed points goes unstable, and REM occurs in a $\{1_{[4]}, 1_{[4]}, 1_{[5]}, \ldots\}$ pattern.
- Sleep onsets (red dots) plotted on the map show two on the branch associated with 4 REM bouts/sleep period and one on the branch with 5 REM bouts/sleep period



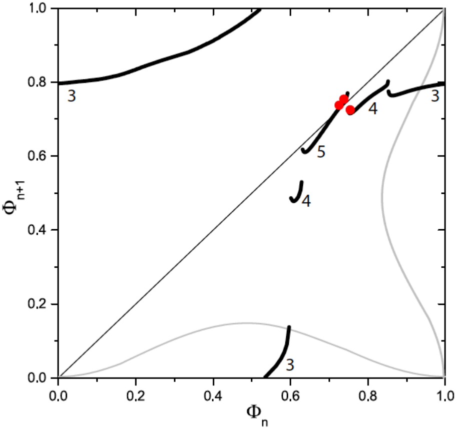
# Map - $\chi = 0.89$

- For $\chi = 0.89$, unstable fixed point associated with one sleep episode per day
- The number of REM bouts in each sleep episode alternates in a $\{1_{[5]}, 1_{[4]}, \ldots\}$ pattern
- One sleep onset (red dots) mapped to each branch

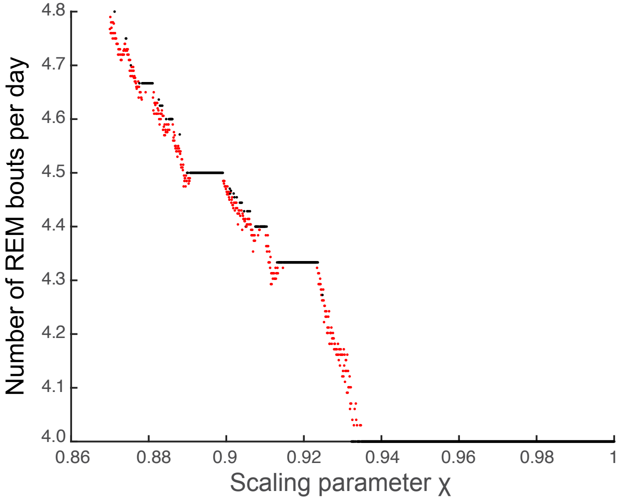


# Map - $\chi = 0.88$

- For $\chi = 0.88$ REM bouts occur in a $\{1_{[5]}, 1_{[5]}, 1_{[4]} \ldots\}$ pattern
- Two sleep onsets (red dots) mapped to branch associated with 5 REM bouts and one mapped to branch associated with 4 REM bouts



# Summary of REM bouts/sleep episode changing with $\chi$



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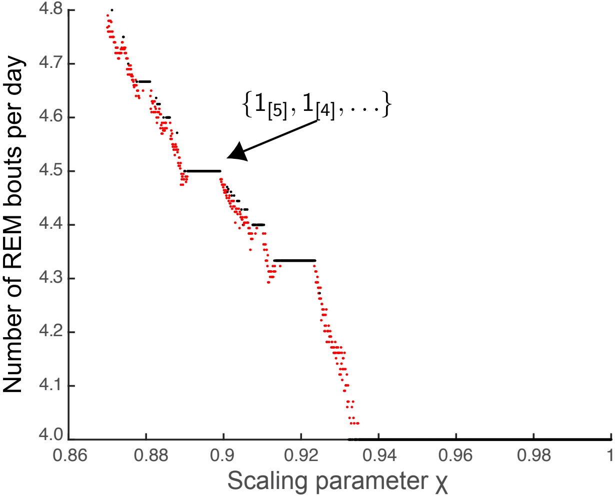

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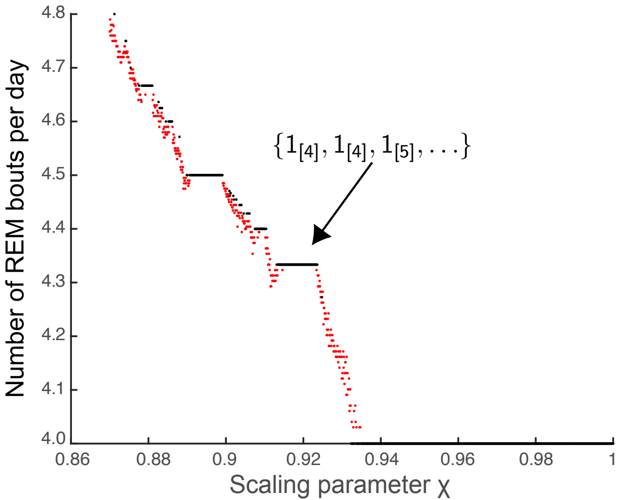
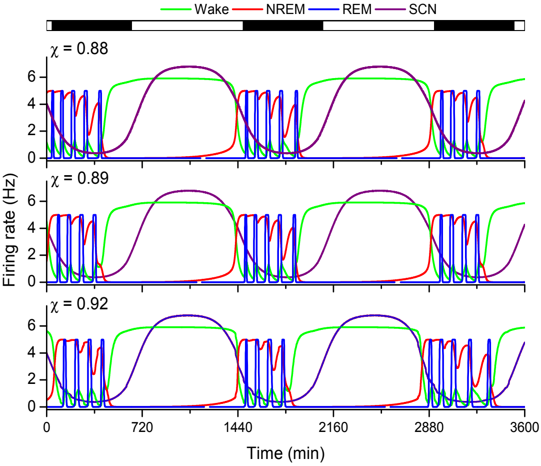


# REM sleep dynamics also change with $\chi$

- For $\chi = 1$, there are 4 REM bouts per sleep episode.
- As $\chi$ decreases, 4 or 5 REM bouts occur in successive sleep episodes.



# Conclusions

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- Border collision bifurcations involved in the transition from one to two sleep cycles per day in both two-process model and our physiologically-based three-state model
- Period-doubling bifurcations may contribute to changes in the number of REM bouts/sleep cycle
- REM sleep contributes to stabilizing and destabilizing sleep/wake patterns and should be considered when analyzing sleep/wake dynamics, particularly during transition periods
- Results suggest that during the transition from napping to not napping in early childhood, physiology may promote higher order patterns of sleep-wake behavior

# Acknowledgements


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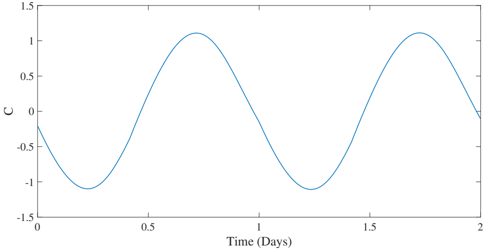
# Model equations - circadian oscillator

Forger circadian pacemaker model produces oscillation with $\sim$ 24 h rhythm is entrained to 14:10 light/dark cycle [6]:

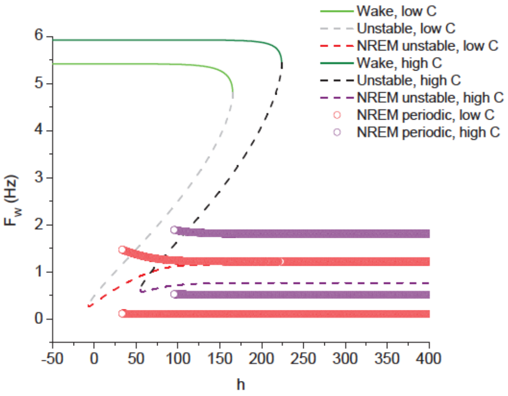
$$\frac{dC}{dt} = \frac{\pi}{720}(x_c + B(t))$$

$$\frac{dx_c}{dt} = \frac{\pi}{720}\left[\mu\left(x_c - \frac{4x_c^3}{3} - C\left(\frac{24}{0.99669\tau_c}\right) + kB(t)\right)\right]$$



# Fast-slow analysis of model dynamics

- Taking homeostatic and circadian variables to be slow, we have z-shaped surface
- Hysteresis loop with respect to *h* is common feature of many sleep models
- REM sleep → hysteresis loop interacting with limit cycle




Booth, Xique, CDB, SIADS, 2017