# Modeling the Effects of Sleep-Wake Cycle on Circadian HPA Rhythms

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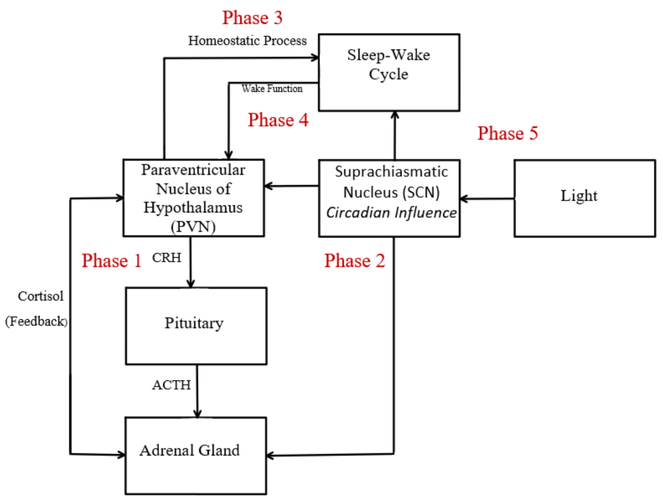
## Introduction

- To maintain homeostasis, body has preprogrammed clocks
- Clocks create innate rhythms for hormone regulation, metabolism, hunger, and others
- Common rhythm is Circadian: light-sensitive, 24-hr period rhythm
- Circadian rhythm governs timing of processes like stress hormone secretion and Sleep-Wake Cycle as shown in model
- Because Sleep-Wake Cycle and Stress center (hypothalamic-pituitary-adrenal axis or HPA axis) both influenced by Circadian rhythm, the processes are related and impact each other

## Methodology

- **Phase 1:** High frequency cortisol secretion
  *Used Runge-Kutta method to solve convoluted differential equations associated with Phase 1.*
- **Phase 2:** Circadian influence
- **Phase 3:** Homeostatic influence
  *Used piecewise function*
- **Phase 4:** Sleep vs. Awake
- **Phase 5:** REM vs. non-REM
  *Used piecewise function*




## Equations

### Circadian process

$$C = 0.5(\cos(\omega(t - t_0)) + 1)$$

### Homeostatic process

$$\frac{dH}{dt} = \frac{\mu W - H}{\tau_H}$$

### ACTH Conc. (y)

$$\frac{dy}{dt} = \nu_{yx} x - \frac{y}{\tau_y}$$

### Wake Step Function

$$W = \frac{1}{1 + \exp(-s_w(C - C_{thr}))}$$

### CRH Conc. (x)

$$\frac{dx}{dt} = aFW\frac{C}{H} - \frac{y}{\tau_x}$$

### Cortisol Conc. (z)

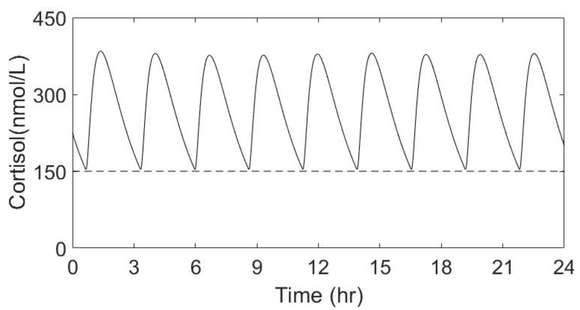
$$\frac{dz}{dt} = \nu_{zy} y + bC - \frac{z}{\tau_z}$$

### CRH Inhibition

$$F = \frac{1}{1 + \exp(s_{GR}(z - z_{GR}))}$$

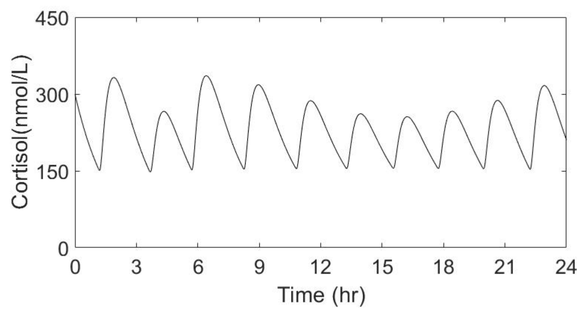
## Results

### Phase 1



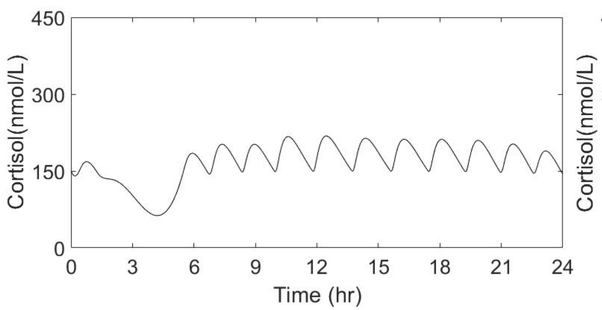

- Bursts of cortisol secretion in 3-hr period

### Phase 2



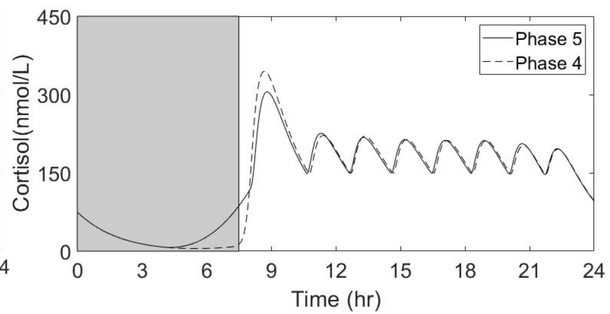

- Varying amplitudes when adding circadian influence

### Phase 3




- Dips in concentration due to homeostatic influence
- Cortisol secretion seen for people with hippocampal damage [1]

### Phase 4 vs. Phase 5




- Phase 4 (dashed line) shows elongated Cortisol deficit and high peak (cortisol-awakening-response)
- Phase 5 (solid line) shows less extreme deficit and lower peak

## Conclusions

- Phase 5 plot aligns with average cortisol concentration profile
- Can be used as a predictive model by changing parameters and assumptions
- The contributions of Sleep-Wake Cycle significantly change the modulation of cortisol concentrations

## Significance & Innovation

- Model provides foundation for understanding processes governed by circadian rhythm
- Introduction of light effects making the model more comparable to experimental results (better predictor)
- With the technology age, new stresses experienced by body with unknown effects, but model can help predict possible outcome of lifestyle changes

## Future Work

- Introduce external stresses
- Different light schedules
- Melatonin effects (blue light exposure)
- Differentiate between non-REM stages
- Include other biological processes governed by circadian rhythm

## References

[1] Postnova, S., Fulcher, R., Braun, H.A. and Robinson, P.A. (2013) A Minimal Physiologically Based Model of the HPA Axis under Influence of the Sleep-Wake Cycles. *Pharmacopsychiatry, 46:* 536-543.

## Acknowledgments

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