Integrating Diurnal Cycles into the HPA axis in an Integrative Computational Model

Bucknell University

Susquehanna Valley Undergraduate Research Symposium

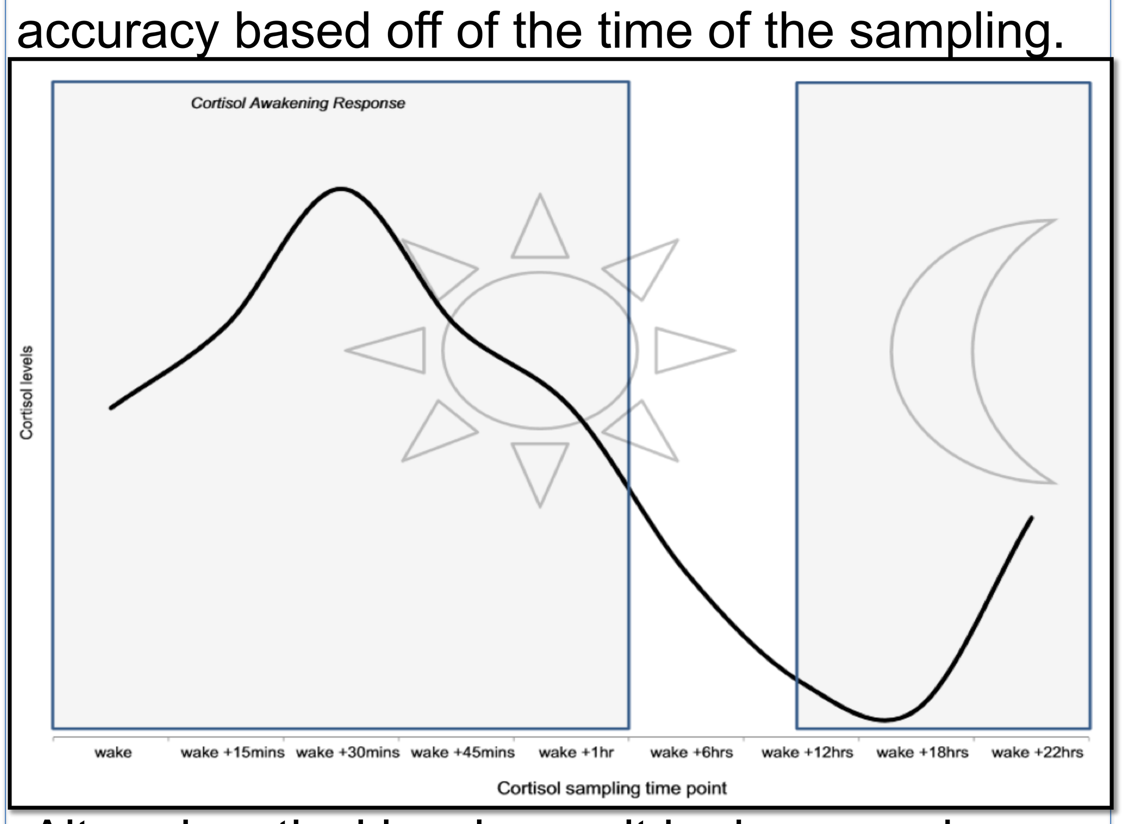
Department of Computer Science, Bucknell University, Lewisburg, Pa.

Abstract

With intelligent software, computational simulations of the human body have the capability of replacing certain physical experiments, easing the ethical and financial burden on the scientific community. HumMod is an integrative biological model of the human body, composed of thousands of variables that all together create a system that interacts and adapts in a way that simulates the human body [1]. This project integrates the well-studied daily changes of Cortisol in to HumMod. Cortisol levels fluctuate greatly over the day, with elevated levels just before and just after waking that deplete during the day to reach a minimum several hours into sleep. We chose to integrate a two-part model of cortisol secretion into HumMod in order to better model these daily changes, as their current model lacks diurnal changes. One part of the model focuses on the effects that sleep, or lack has on cortisol secretion. The second part of the model focuses on the secretion as a function of circadian rhythms, our internal clock. The result is an integrative model capable of altering cortisol output based off of time of day as well as sleeping patterns.

Introduction

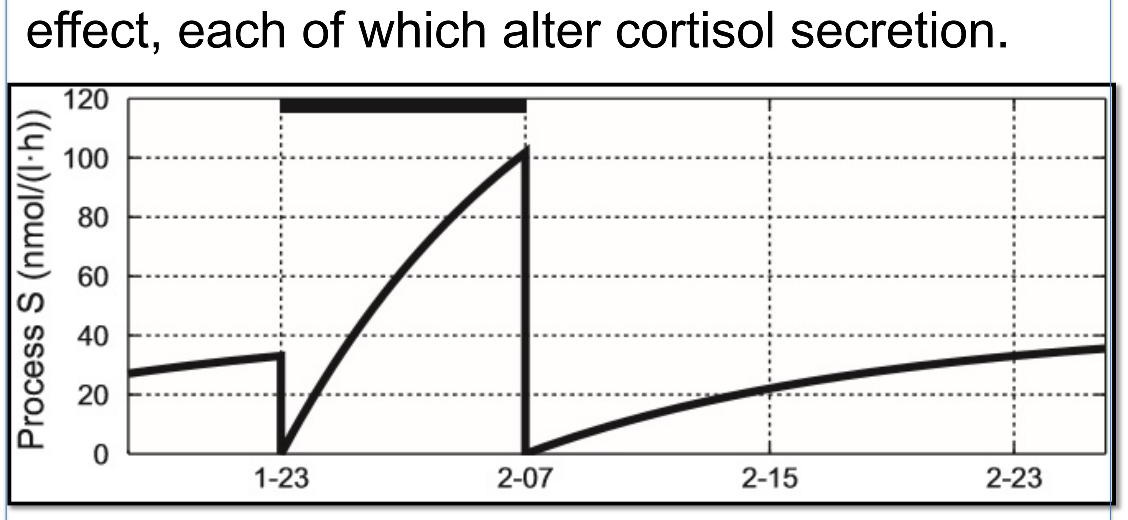
Cortisol has a number of factors that contribute to its secretion. What this project focuses on is sleep, circadian rhythms, and stress. Total and partial sleep deprivation can cause flattened cortisol profiles, lower secretion levels in the morning [4]. By integrating sleep deprivation and diurnal rhythms in to cortisol's structure in HumMod, we can improve its accuracy based off of the time of the sampling.



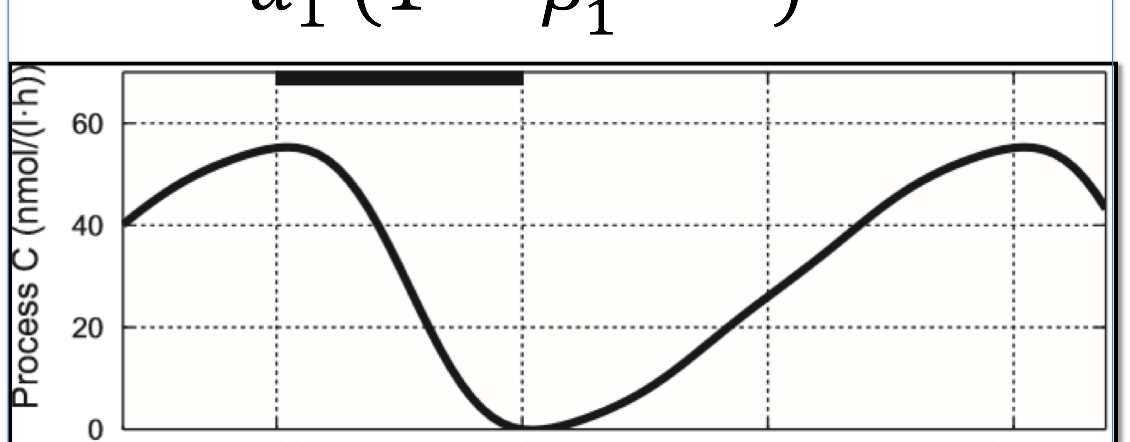
Altered cortisol levels result in decreased performance in declarative memory tests when induced by stress and when raised medically by an oral dose [3]. This means that cortisol affects memory directly, and thus memory effects can be modeled directly from it. This will be modeled in the cognitive structure ACT-R. with this we can model daily changes to declarative memory, and discern those differences within ACT-R/ϕ.

Implementation

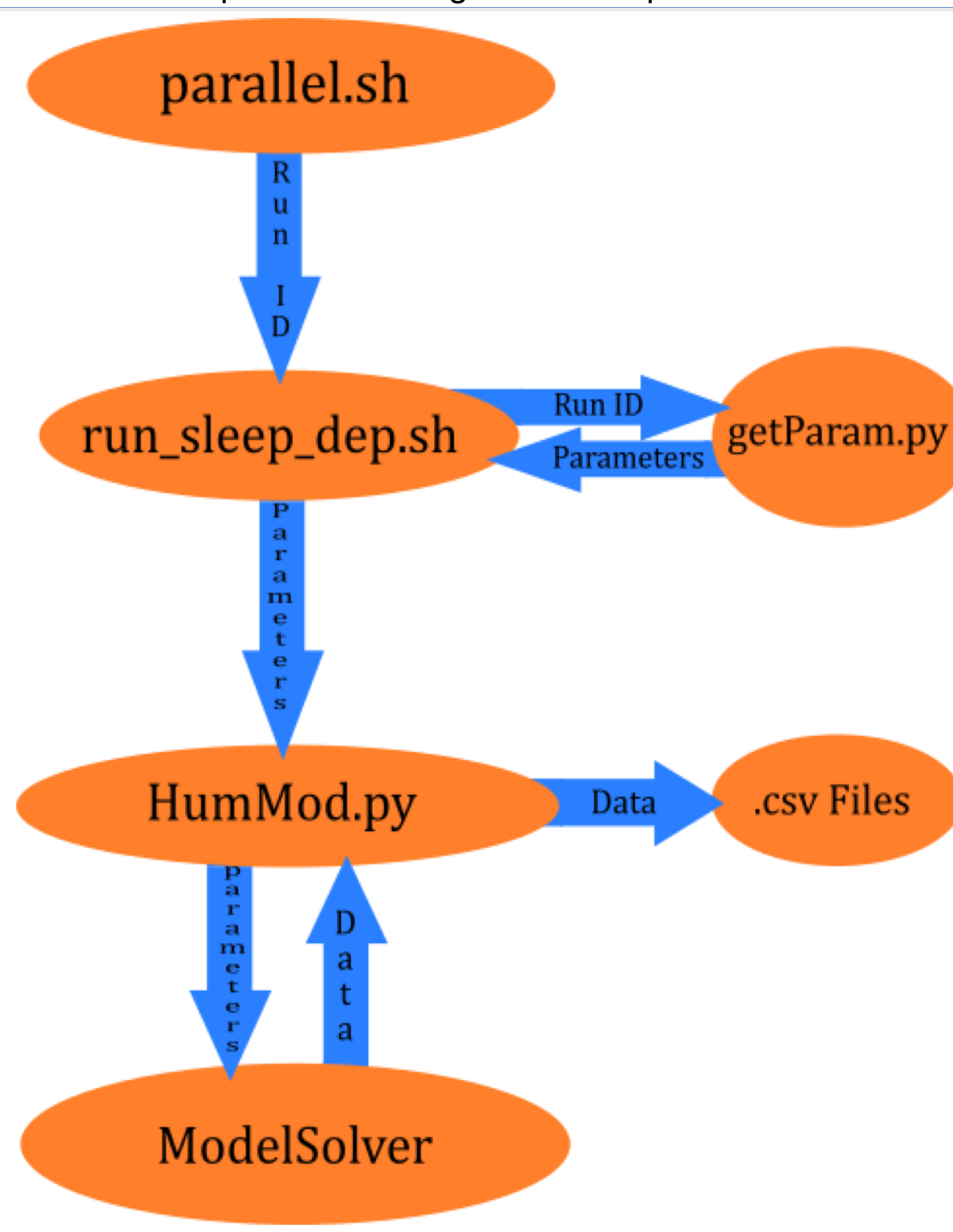
We chose to base the structure of our model on that of Thorsley [2]. This consists of two different parts, a sleep effect and a circadian effect, each of which alter cortisol secretion.



$$\alpha_1\left(1-\beta_1^{(t-t_0)}\right)$$



$$\alpha_2 \sin\left(\frac{\pi(t+\phi)}{12}\right)+\beta_2 \sin\left(\frac{\pi(t+\phi)}{24}\right)$$



Testing Methods

In order to ensure that we have an accurate model, we need to test many different parameters. To do this we needed to run HumMod many different times with different parameters to see what their effects were.

The top layer is our parallel.sh script. It parallelizes the different runs, allowing multiple different parameter sets to be tested at the same time.

The second layer is the run_sleep_dep.sh script. It receives the unique parameter set from the getParam.py python script. It then starts the HumMod.py script and passes the parameters and other information to it.

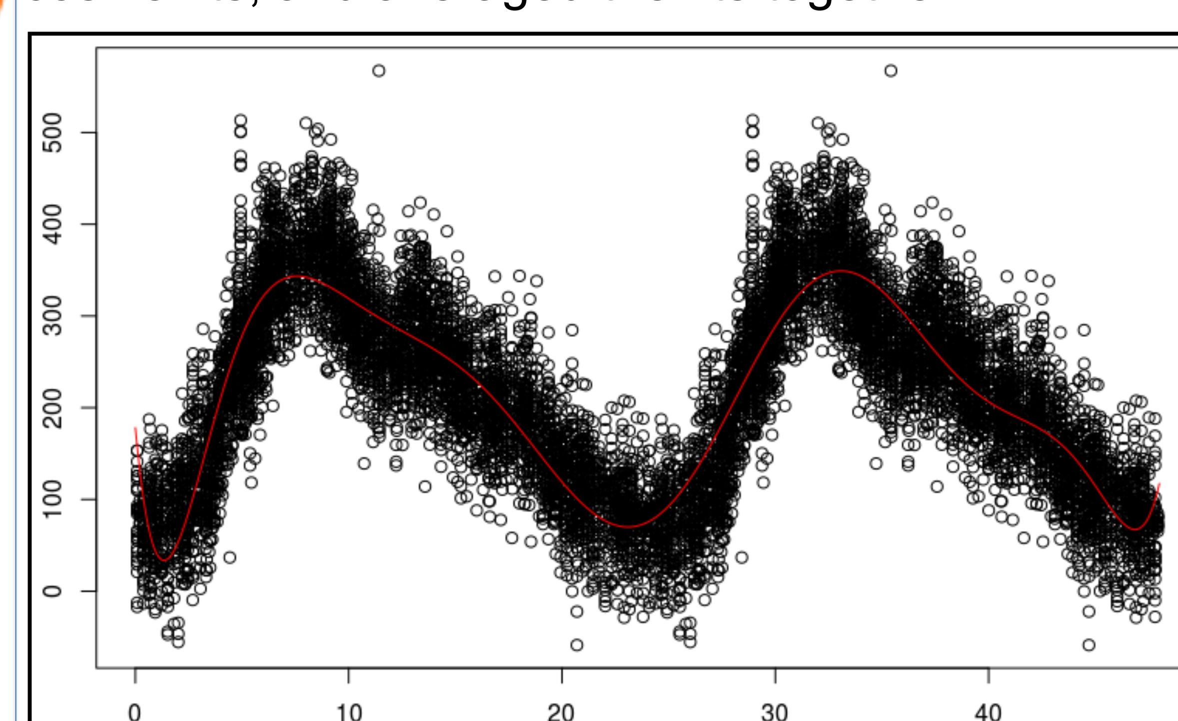
The third layer is the HumMod.py script. This starts the ModelSolver with the given parameters, and keeps inputting data as it is needed. When the ModelSolver is finished, it saves all of the data for the variables that we need to measure in csv files for later analysis.

The final level of our sweep system is the HumMod ModelSolver. This takes in information from the python script, and performs the calculations we need within HumMod's architecture to solve for the required variables.

Funding for this project was provided by Bucknell University's Program for Undergraduate Research Through the James L.D. and Rebecca Roser Research Fund, as well as by Bucknell University's Presidential Fellowship through the John C. Hoover Scholarship All computations were completed in the statistical programming language R.

Analysis

Once the sweep is finished, we begin analyzing all of the data in the csv files. We first had to get cortisol profiles to compare to. Since we lacked our own data set, we pulled several profiles from summary data of different studies. We then created many simulated samples from those studies, linearized sin and cosine fits, and averaged the fits together.



After we had data in a form we could compare it to, we have to measure our comparison against the different parameter's runs in the csv files. For each run, we fit the data using the same fitting method as we did for the comparative data. Then we compared the array of points from the parameter's fit to the array of points from the profiles using the Pearson test to asses the similarity of the vectors. From there we are able to select the best fits for further analysis, and further refine our search.

References

1. Hester, R. L., Brown, A. J., Husband, L., Iliescu, R., Pruett, D., Summers, R., & Coleman, T. G. HumMod: A Modeling Environment for the Simulation of Integrative Human Physiology. Frontiers in Physiology, 2. (2011).
2. Thorsley, D., Leproult, R., Spiegel, K., & Reifman, J. A Phenomenological Model for Circadian and Sleep Allostatic Modulation of Plasma Cortisol Concentration. AJP: Endocrinology and Metabolism, 303(10). (2012).
3. 3. Kirschbaum, C., O.t Wolf, M. May, W. Wippich, and D.h Hellhammer. "Stress- and Treatment-induced Elevations of Cortisol Levels Associated with Impaired Declarative Memory in Healthy Adults." Life Sciences 58.17 (1996): 1475-483. Web.
4. Elder, Greg J., et al. "The Cortisol Awakening Response: Applications and Implications for Sleep Medicine." Sleep Medicine Reviews, vol. 18, no. 3, 2014, pp. 215–224., doi:10.1016/j.smrv.2013.05.001.

Future Work

The future of the project is to integrate our cortisol model into an existing system: ACT-R/ϕ, that couples HumMod with ACT-R, a computational model of the way we think. The negative effects of altered cortisol levels on memory will then be able to be modeled in this coupled system in relation to sleep deprivation and time of day. With this work we may one day be able to accurately model the cognitive effects of sleep and circadian rhythms under a variety of different physiological and psychological conditions.