INSTITUTE FOR CELLULAR ENGINEERING

Mathematical Modeling of the Circadian Cycle in Humans

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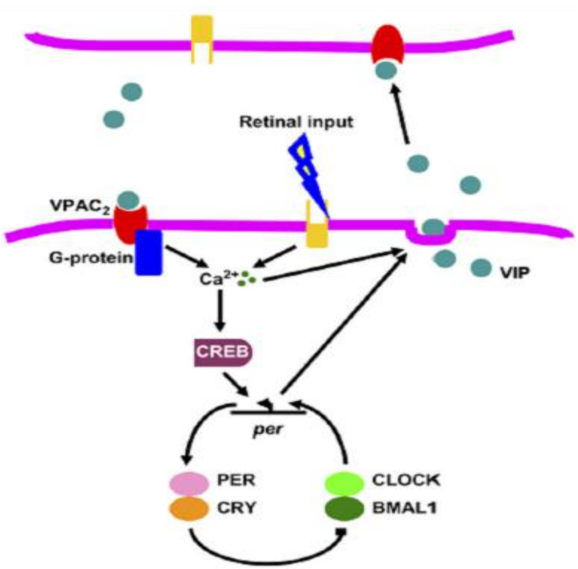
The ability of the human body to autonomously maintain internal rhythms that adapt to its natural environment is critical to human survival. Organ systems, specializing in functions ranging from respiration and circulation to inflammation and hormone release, rely on signals sent from a part of the brain known as the Suprachiasmatic Nucleus (SCN). In its computer models, the Henson laboratory attempts to model all of the factors inducing expression of the *Per* gene, as is manifested through the transcription of *Per* mRNA. By monitoring this transcription, our research is capable of determining the ability of the SCN to adapt to environmental cues through the coordination of its constituent neurons, as *Per* transcription is induced by the production of the main chemical responsible for neuronal coordination, Vasoactive Intestinal Peptide (VIP). (*To et al., Biophysical Journal 2007)*



The circadian cycle, at the molecular level, is initiated by Per gene expression, which is derived from a retinal input (light) and the release of calcium. Through a complex set of reactions, Per expression enables VIP synthesis, which again increases calcium levels and perpetuates this cycle.

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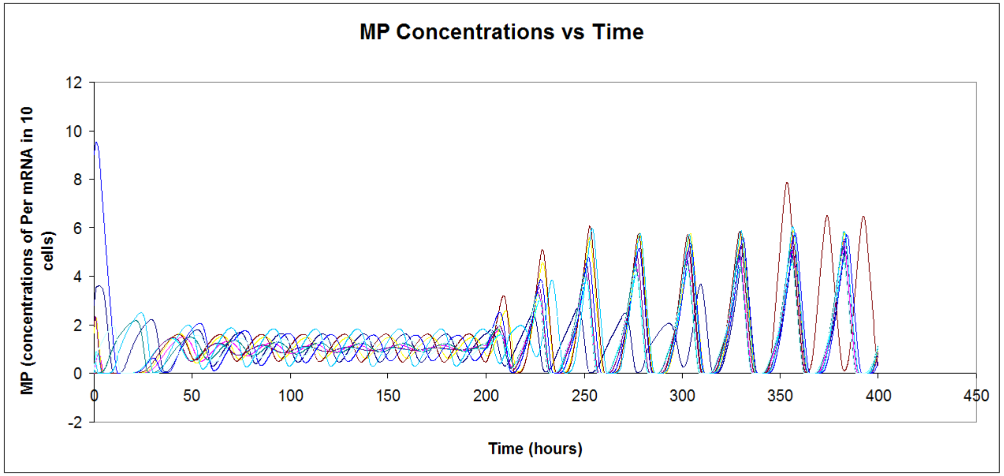
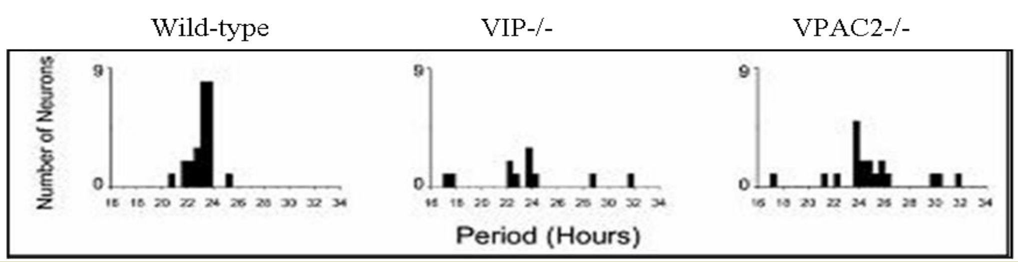


Our research (top) has, using a FORTRAN computational algorithm, demonstrated the ability to more efficiently model Per gene expression than have previous models presented in the MATLAB language. Considering the intricacy of the model, it is imperative to use the most efficient language possible when analyzing cell populations of significant size (over 400 cells). Eventually, our model could be applied to discern differences in rhythm generation between normal and abnormal subjects (bottom; Aton et al., Nature Neuroscience 2005), leading to the treatment of certain disorders.



As of 2008, a firm quantitative understanding of the molecular mechanisms that generate circadian rhythms has not been conceived of by biologists. More importantly, the pharmaceutical industry will not be able to effectively individualize drug administration regiments until this firm understanding is possessed. With such an understanding, problems ranging from jet lag and insomnia to bipolar disorder and cardiovascular disease could be remedied with more effective medicinal regimentation rather than simply more powerful drugs. Moreover, the design of pharmaceutical products that more aptly mimic the way in which chemicals are naturally distributed throughout the body will improve the standards of living for time-sensitive medication users while reducing the risks and costs for pharmaceutical companies associated with the experimentation and testing of new, potentially dangerous drugs. (*Liu et al., Nature Chemical Biology 2006)*

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