

Project Title:

Parameterization of a mammalian circadian clock model

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I have been using a mathematical model of the mammalian circadian clock to explore new methodologies for parameter fitting of systems biology models. To be specific, our (simplified) model of the mammalian clock consists of a system of coupled ordinary differential equations (ODEs) with 23 different parameters representing reaction rates, binding constants, etc. The output of the model depends strongly, of course, on the values of these parameters. We have compiled a large amount of experimental data from the literature and used it to formulate a score function that quantifies the agreement between the model output and the available experimental data. In order to evaluate the shape of the parameter landscape and the robustness of the model outputs with respect to different parameter perturbations, we have identified a near-global optimum using an evolutionary algorithm and explored the score function basin using a Metropolis Monte Carlo algorithm.

All calculations used code that was written in C++, with parallelization using MPI.

We submitted a manuscript describing our results to *Biophysical Journal* in early January 2014, and received reviewer comments near the end of February 2014. The reviews were generally positive, but addressing their concerns may require some additional calculations. We plan to carry out these calculations on RICC during the early portion of FY2014, using the same software that we developed during FY2013. The submitted manuscript will be attached along with this document.

RICC Usage Report for Fiscal Year 2013

Fiscal Year 2013 List of Publications Resulting from the Use of RICC

[Publication]

Jolley CC, Ukai-Tadenuma M, Perrin D, Ueda HR (2014). "A statistical-mechanical approach to the mammalian circadian clock." *Biophys. J.*, *in revision*.

[Oral presentation at an international symposium]

American Physical Society March Meeting 2013, Baltimore, MD, USA

14th International Conference on Systems Biology, Copenhagen, Denmark