Project Title:

Role of Epigenetic Mechanisms in Circadian Clock Mechanisms

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Our project involves the development of computational models and the application of theoretical concepts from Complexity Science and Artificial Intelligence to Systems Biology, with a particular focus on mechanisms related to the circadian clock.

One of the challenges is to explain how the clock system makes a transition from a steady state in embryonic stem cells to an oscillatory behavior in all differentiated cells. Our intuition is that epigenetic mechanisms play a crucial role, and may be part of this missing link.

To assist model development, we rely on theoretical concepts such as reinforcement learning, (where an "agent" takes "actions" in an environment so as to maximize some notion of cumulative "reward"), in the sense that cells try to minimize the stress associated with being out of phase with the cues received from the environment.

Complementary wet experiments and advanced data analysis are required to both develop and validate this model. This means that the project also involves adapting techniques from Operations Research (e.g. evolutionary optimization) to the analysis of large biomedical datasets such genome-wide DNA methylation information obtained through next-generation sequencing.

The modeling approaches require large resources, and it was anticipated that access to RICC would significantly accelerate their development.

However, shortly after our "Quick User" proposal was accepted, it was necessary to postpone this work on new computational methods. The motivations were two-fold.

First, we initially had to focus on analyzing the results of complementary experiments, based on next-generation sequencing. Such analysis is not suited to RICC jobs, because of the type and size of data, as well as because of the software used for analysis. This analysis is taking longer than expected (in part due to the results), and is still ongoing.

Second, in the second half of FY2013, priority had to be given to another aspect of the data analysis, namely the registration, alignment and analysis of high-resolution 3D images. Again, the software tools we had to use for this analysis (whose results are to be published shortly) are not compatible with parallel computing and RICC execution.

As a result, it was unfortunately not possible to use the account as expected.

In the future, our focus will switch back to reinforcement learning, and code suitable for parallelization will be developed. It is also possible that implementation (and parallelization) of new registration techniques will be considered.

At this stage, it remains unclear exactly when this will occur, and no application has therefore been submitted for FY2014.