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Extension of a genetic network model by iterative experimentation and mathematical analysis.

Locke JCW, Southern MM, ... , Turner MS, Millar AJ

Mol Syst Biol 2005 **Jun 28**:Featured Article [order article] WebBridge

Selected by | Charles Auffray
Evaluated 27 Jul 2005

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Faculty Member	Comments
Charles Auffray Centre National de la Recherche Scientifique (CNRS), France PHYSIOLOGY Hypothesis Tech Advance	**This is, in my view, a milestone paper for the emerging field of systems biology, demonstrating the power of an iterative process combining modeling and simulation of experimental data to generate and test hypotheses on the functioning of biological systems.** The authors went two cycles of model buiding and refinement based on existing and newly designed experiments on circadian clocks in Arabidopsis. As an initial feedback loop failed to account for some of the known features of the circadian rythms, including control of time delays, they first introduced an additional unknown component X in their model, which had a better but incomplete fit with observations. In the second iteration, they introduced a second unknown component Y and an interlocked feedback loop, resulting in a much better fit of the model, which also accounts for the robustness of the circadian clock. They further identified GIGANTEA as a likely candidate for the Y component, and proposed novel experiments for further refinement of their model. This is an example which should inspire systems biologists in other research areas. See also comments by Lee Sweetlove [nonpub113939]. For the abstract of this paper, please see http://www.nature.com/msb/journal/v1/n1/full/msb4100018.html Evaluated 27 Jul 2005

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