

# Study shows more genes are controlled by biological clocks

August 29 2008

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The tick-tock of your biological clock may have just gotten a little louder. Researchers at the University of Georgia report that the number of genes under control of in living things than suspected only a few years ago. The biological clock in a much-studied model organism is dramatically higher than previously reported. The new study implies that the clock may be much more important.

"This new finding may help to explain why the clock is so far-reaching in its effects on the organism," said Jonathan Arnold, a professor in the UGA department of genetics and director of the research project. "We found that some 25 percent of the genes in our model organism appear to be under clock control. I wasn't suspecting anything remotely like that."

The new research, just published in the *Public Library of Science One*, also shows how Arnold's team used a new methodology called Computing Life to yield these new discoveries about biological clocks. And this tool of systems biology was the key to showing what makes a biological clock tick.

In addition to Arnold, authors of the paper include Wubei Dong, James Griffith, Roger Nielsen and Rosemary Kim in the department of genetics, and Xiaojia Tang, Yihai Yu and Bernd Schuttler of the department of physics and astronomy. Griffith also has an appointment in the College of Environmental and Agricultural Sciences. The department of genetics is in the Franklin College of Arts and Sciences.

The team's new discoveries about the extent of genes under the control of the biological clock and the utility of Computing Life came from studying genes in *Neurospora crassa*—bread mold. In fact, much of what science knows about biological clocks has come from studying *Neurospora*.

Before the current research, only 16 clock-controlled genes had been discovered in *Neurospora* in more than 40 years of research. Arnold's team uncovered a remarkable 295 genes that are influenced by the biological clock—and that number could be dramatically higher, given the conservative controls the researchers put on their work.

"It appears the clock influences a number of biological processes, including cell cycling, protein metabolism and varied signaling processes," said Arnold. "But perhaps the most important role we've seen so far is the clock's role in ribosome biogenesis."

Ribosomes assemble individual amino acids into polypeptide chains by binding a messenger RNA and then using this as a template to connect the correct sequence of amino acids. Ribosome biogenesis is the process of making ribosomes, so knowledge that the process is under clock control adds a dramatic new dimension to the clock's inherent biological value as an adaptation.

The new Computing Life technology, refined in the Arnold and Schuttler labs, integrates several cycles of modeling and experiments to yield discoveries about a genetic network. Using Computing Life, the scientists were able to unravel how a network of genes and their products tell time, thereby demonstrating the solution of one of the key problems in systems biology.

"The resulting molecular mechanism or genetic network for the clock identified by this mode-guided discovery process will have a broad

appeal to geneticists, physiologists and those with an interest in signaling pathways," said Arnold. "The methods used to characterize what makes a biological clock tick will have numerous applications in finding genetic networks describing other complex traits in many biological systems."

Computing Life will also allow researchers to design a sequence of genomics experiments that will winnow the field of competing hypotheses and to move experiments in directions where new discoveries are likely to arise.

Biological clocks hold the key to much of life and disease processes. In February 2007, Arnold's team reported in the *Proceedings of the National Academy of Sciences* the first working model that explains how biological clocks operate. The UGA scientists discovered how three genes in *Neurospora* make such a clock tick at the molecular level.

That discovery also had broad implications for understanding biochemical signaling and other regulatory processes in cells, Arnold said.

Source: University of Georgia

Citation: Study shows more genes are controlled by biological clocks (2008, August 29) retrieved 10 April 2024 from <https://phys.org/news/2008-08-genes-biological-clocks.html>

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