Unwinding nature's clocks, with $14 million from DARPA

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From the time we eat breakfast to when we leave work, mechanical clocks control a large part of our lives. But we, and other creatures, also have biological clocks that regulate just about every function in our bodies.

Scientists know our biological clocks are coordinated – from our daily rhythms to our metabolism, and the growth, development and death of cells – but they aren't sure how. Using a $14 million grant from DARPA, the Defense Advanced Research Projects Agency, a team of biologists and mathematicians at Duke and other universities will be looking more closely at the timepieces that drive life.

"Biological systems have amazing timing capabilities," says Duke mathematician John Harer, the lead investigator on the new grant. The body and its individual cells form an intricate machine, with complex timing mechanisms, which often work flawlessly and usually repair themselves when they don't, he says.

Harer and his collaborators want to unwind the variety of biological clocks found in cells, looking closely at their pieces to see how they work individually and how they work together. Scientists have studied how day and night affects animals' and plants' circadian rhythms, how cells divide, live and die and how they control their own metabolism and growth, Harer says.

But, it's been much more challenging to understand how these and other processes in cells relate to one another and how they work within life's larger rhythms. The researchers wonder whether there are universal rules controlling such cyclic behavior.

With the DARPA grant, Harer has assembled some of the world's leading experts on the cell cycle, the circadian clock, the metabolism of yeast, root growth in plants and pulsing processes in bacteria, to deconstruct the molecular and genetic rhythms that keep these organisms alive.

One of the most challenging goals is to identify the specific genes that turn each type of biological clock on and off and what signals those genes send with each on-off switch, Harer says. The other challenge is to identify what role each gene plays in the clock and whether it would be a good indicator of the position of that clock in its cycle. They might, for example, find a gene that controls the circadian clock, and then study it further to find out whether it's six in the morning or six at night, according to that organism's clock.

If scientists can isolate the genes, molecules and signals of these different biological clocks, they could find ways to control and repair them if they are broken or damaged, Harer says. They could then use that information to better understand and control specific groups of cells, organisms and possibly even systems within our bodies. Harer says scientists may also be better able to explain a variety of other observations, such as the connection between sleep problems and cancer.

One specific DARPA application would be to adjust soldiers' biological clocks when they travel, to speed recovery from jetlag or slow down their metabolism after an injury. There's also interest in the signals that genes and cells send to each other, despite a lot of noise from their surroundings. If scientists can figure out how timing signals are sent, that could be useful for improving the way we send, receive and decipher our own communication signals, Harer says.

Under the new grant, he and his colleagues have four years to investigate the diverse rhythms of life. DARPA will be checking in along the way, but ultimately the agency is looking for the scientists to write the equivalent of sheet music for life's rhythms and then be able to use the notes to identify the clocks of previously unstudied organisms.

Provided by Duke University

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