What makes circadian clocks tick?

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Circadian clocks are found within microbes and bacteria, plants and insects, animals and humans. These clocks arose as an adaptation to dramatic swings in daylight hours and temperature caused by the Earth's rotation. But we still don't fully understand how these tiny biological clocks work.

During the 62nd Biophysical Society Annual Meeting, held Feb. 17-21, in San Francisco, California, Andy LiWang at the University of California, Merced will present his lab's work studying the circadian clock of blue-green colored cyanobacteria. One type of cyanobacteria, called spirulina, is high in vitamins and minerals and is used as a natural food dye for candy and gum.

LiWang's group discovered that how the proteins move hour by hour is central to cyanobacteria's circadian clock function. "And now it's becoming clear that the same is true for eukaryotic [animal] clocks," LiWang said.

Cyanobacterial circadian clock proteins are unique because they can be reconstituted within a test tube in the absence of live cells. Researchers made a solution of these proteins and adenosine triphosphate (ATP), food for the proteins, to create a circadian clock that functioned for weeks.

LiWang's structural biology lab uses nuclear magnetic resonance (NMR) spectroscopy, the parent technology for MRI, to study the protein structure and dynamics of biological molecules and then uses the structures to gain insights into their function. "We also examine how the proteins wiggle, flex, and shape-shift, because these motions ... are also critical to their biological function," LiWang said.

LiWang's lab also collaborates with X-ray crystallographers like Carrie Partch at the University of California, Santa Cruz, because X-ray crystallography is a powerful technique to capture static structures of proteins and their complexes at atomic and near-atomic resolution.

"A big surprise for us was the extent to which internal motions of circadian clock proteins dictate ... their function," LiWang said. "Static X-ray crystal structures of individual proteins, mostly solved by other labs, were invaluable to our work but told only part of the story."

Cyanobacterial clock proteins aren't exactly the same as the clock proteins of animals or human clocks, but proteins serve as the cogs, gears and springs of all circadian clockworks and the overall function of the proteins is similar.

"Because clock proteins need to keep time, there should be some basic principles of biological timekeeping shared between all clocks regardless of whether the proteins are the same or not," LiWang said. "Our structures of the complexes of the circadian clock proteins of cyanobacteria provided important mechanistic insights, but are static snapshots of a system that's continuously moving and changing hour by hour," said LiWang.

More information: 231-Pos, Board B1 "Ticking mechanism of a biological clock" is authored by Andy LiWang. It will be displayed at 1:45 p.m. PST, Sunday, Feb. 18, 2018, in the South Hall ABC of the Moscone Center South. Abstract: plan.core-apps.com/bpsam2018/a … 1290aae09439cc42e19d