Research Roundup

Does the Kai clock rotate?

Jiemin Wang (Yale University, New Haven, CT) suggests that an ancient circadian clock rotates much like a hand on an analogue clock. His analysis of cyanobacterial clock protein structures reveals a similarity with the F$_1$-ATPase rotary motor.

The cyanobacterial clock is controlled by the KaiA, KaiB, and KaiC proteins, which form a complex at night that falls apart in the day. Mutations causing more stable complexes correspond to a longer periodicity. But little is known about how the timing of complex formation is controlled. Wang analyzed the recently solved structures of the Kai proteins to suggest a mechanism.

When KaiC is ATP-bound, the Kai complex is stable. But when ATP is bumped off by autophosphorylation near the ATP-binding site, the complex falls apart. Autophosphorylation is stimulated in vitro by KaiA.

Wang realized that the ATP-binding domains of KaiC hexamers resemble the F$_1$-ATPase ring. He proposes that KaiA fits inside the ring much like the γ subunits fit inside the F$_1$-ATPase ring. Based on previous structures, KaiA dimers are too large to fit inside the ring. But Wang proposes that KaiA dimers must first be activated by the extension of helical domains. This proposed extension makes KaiA dimers resemble γ subunits. The need for KaiA activation would also explain the two-hour delay between the rise in KaiA and KaiC levels at dusk and complex formation. The stimulus for such KaiA activation is unclear.

In Wang’s model, KaiA is expected to contact at most two KaiC monomers at a time and stimulate their autokinase activity. Autophosphorylation would both displace ATP and provide energy for the rotation of KaiA to new KaiC subunits. This cycle would repeat until the KaiC hexamer lacks ATP completely and the complex falls apart.

The rotation of KaiA might be hindered by KaiB, which Wang predicts bridges KaiA and KaiC below the ring. This suggestion fits with previous in vitro data showing that KaiB slows KaiC autophosphorylation. In fact, says Wang, “the autophosphorylation rate of KaiC is very slow, about three to four hours per [dimer].” Thus, one round of KaiA rotation should be approximately equivalent to the span of a night, or one rotation of an average wall clock.

Reference: Wang, J. 2005. JCB. 169:735-741.

Stiffening under pressure

Natural networks, such as collagen gels or cytoskeletal webs, have the ability to increase their stiffness with increasing strain. This unique feature is an advantage over most synthetic fibers. If blood vessels were made of rubber tubing, for example, the pressure from a heart beat would vastly increase vessel diameter. But collagen’s nonlinear elasticity prevents such a drastic endothelial deformation.

This ability is usually explained by the heterogeneous nature of biological gels—perhaps tauter filaments take over at increasing strains. But in vitro measurements by Storm et al. now show that uniform biopolymer gels also exhibit nonlinear elasticity. The authors then produced a mathematical model that explains this behavior based on the characteristics of the individual polymer filaments within a cross-linked network.

“We show that strain stiffening comes about automatically because of the semiflexible nature of the chains in the biomaterials,” says Janmey. “They’re not exactly straight, but they’re not randomly highly coiled either. That flexibility allows for short range movement under mild strain, but under greater strain the filaments reach the end of their leash and stop extending. Slightly stiffer polymers [actin, collagen], with shorter leashes, stop extending at lower strains. Softer gels, such as intermediate filaments, take larger deformations before they stiffen.

The model makes certain assumptions that might not hold true in vivo. For one, networks were assumed to form randomly. But Arp2/3 complexes, for instance, bias actin filament branching at specific angles. Additionally, cross-links were assumed to stay put under strain, although they are probably labile in cells. Determining the effects of these variations on strain stiffening will require further modeling.

Beyond biological interests, the findings might also prove useful to engineers. “If you wanted to make a material that stiffens as you deform it,” says Janmey, “filaments as stiff as intermediate filaments would create a new type of [synthetic] polymer.”

Reference: Storm, C., et al. 2005. Nature. 435:191-194.