

EPFL Physical Chemistry Seminar (PCHEM) Thursday 20th May 2021
Guest Speaker: Prof. Kenneth Taylor, Florida State University, USA

Title:

How a flight muscle thick filament from the giant water bug informs on muscle structure and function across species

Abstract:

Since Hugh Huxley first reported the isolation of the thick myosin containing filaments from the striated muscles of vertebrates in 1963, their structure has been an object of intense if not always successful study. Thick filaments from invertebrate striated muscles are favorable objects for study by cryoEM because most filaments are helical in structure in the region where myosin heads project. The first major breakthrough definitively described the arrangement of the myosin head, a molecular motor, in its “switched off” state, now called super-relaxed state due to its very low rate of ATP consumption. The filament backbone, which played a significant part in the description of both the α -helix and the coiled coil remained pretty intractable. Partly, this is because it was thought to be little more than a scaffold for positioning the myosin motors and hence not worthy of much effort. With the advent of the “resolution revolution” in cryoEM, it is now possible to obtain subnanometer and even near atomic resolution reconstructions from invertebrate thick filament backbones. These reconstructions have shown some surprising variation among even a fairly well-defined set of insects that use asynchronous flight muscle for flight. Even more surprising is the agreement with crystal structures of human cardiac muscle myosin tail fragments. Thus, similar to the muscle thin filament, whose structure is highly conserved across muscle types and species, varying mostly in the actin associated proteins, thick filaments have an underlying structural feature, the “curved molecular crystalline layers” and also vary most in the thick filament associated proteins. This lecture will explore just how seemingly very different thick filaments can be similar in their tail arrangement, but vary significantly in other features. The thick filament is not just a scaffold for projecting myosin heads, but plays significant role in the regulation of muscle contraction, potentially explaining the large number of mutations in the myosin tail that lead to various human diseases.