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Deciphering intermolecular interactions in complex heterogeneous systems

Many biological systems contain complex mixtures of filaments, such as actin containing and myosin containing filaments and the cytoskeleton. The properties of the interacting partners are keys to understanding how the systems function. In muscle, the filament systems are composed of multiple proteins that modify the basic filament. In the case of actin, the troponin-tropomyosin system provides a mechanism for regulating attachment by the myosin motors and thus muscle contraction. During muscle contraction, myosin motors attach the thin filament in multiple ways producing a heterogeneous system that is difficult to dissect. Many proteins interact with F-actin to form cross-linked bundles. Among these are fimbrin, villin, α-actinin and several glycolytic enzymes and even elevated concentrations of magnesium and polylysine. An important characteristic of these cross-linkers is an ability to form 2-D rafts on positively charged lipid monolayers. Actin rafts should be ideal for structure determination by electron microscopy (EM) but several problems exist, in particular heterogeneity. All raft cross-linkers produce polymorphic rafts that are either polar or have mixed polarity. Even bundles of defined polarity can have heterogeneous cross linkers. We have developed a strategy for obtaining information from these heterogeneous systems using sub-volume alignment and classification that will be applicable to this type of problem and perhaps many others where there is difficulty obtaining large populations of homogeneous entities, be they filament segments or single particles.

Biography

Kenneth A Taylor has completed his PhD in 1975 from University of California Berkeley on the topic of Electron Microscopy and Electron Diffraction of Frozen Hydrated Biological Specimens, widely regarded at the start of the field of cryo-electron microscopy. He has spent 4 years as a Post doctorate at the MRC Laboratory of Molecular Biology and 15 years on the faculty at Duke University Medical Center. He is currently the Donald L. D. Caspar Professor of Biological Science. He studies the structure of macromolecular assemblies in muscle, the cytoskeleton and viruses using cryo-electron microscopy and cryo-electron tomography.

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