

## MS8. Molecular machines and motors

Chairs: Nenad Ban, Leonid Sazanov

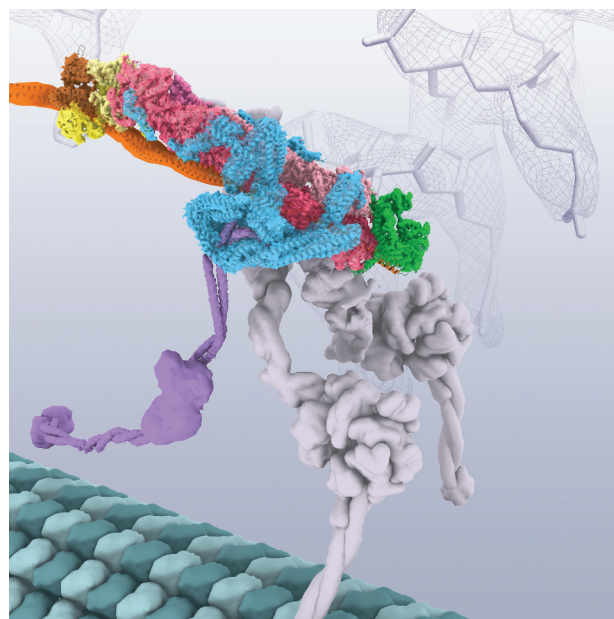
### MS8-O1 Transporting cargo over long distances: insight from dynein/dynactin structures

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Cells depend on components being moved to the correct place at the correct time. My group is interested in cytoplasmic dynein-1 (dynein-1), a motor which delivers many different cargos via the microtubule network. When dynein-1 is mutated it leads to neurodegeneration and it is susceptible to hijack by viruses which use it to travel into the cell. We have determined X-ray crystal structures of the dynein motor before and after it binds and hydrolyses ATP. We subsequently used single molecule fluorescence assays to show how a cofactor, dynactin, activates the full length 1.4MDa dynein complex to move long distances along microtubules. A high resolution (4.0Å) cryo-electron microscopy (cryo-EM) structure of dynactin explained how this 23 subunit complex is assembled. We also used a combination of cryo-EM and X-ray crystallography to show how dynactin binds to dynein. The two complexes are only brought together in the presence of an adaptor protein, Bicaudal-D2, that links them to the cargo they will carry. This suggests the large and intricate dynein/dynactin transport machine only assembles when a cargo is ready to move.



**Figure 1.** Model of the structure of cytoplasmic dynein (grey) bound to dynactin (multicolor) via the Golgi vesicle cargo adaptor BICD2 (orange). Dynein is reaching down towards its microtubule track.

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