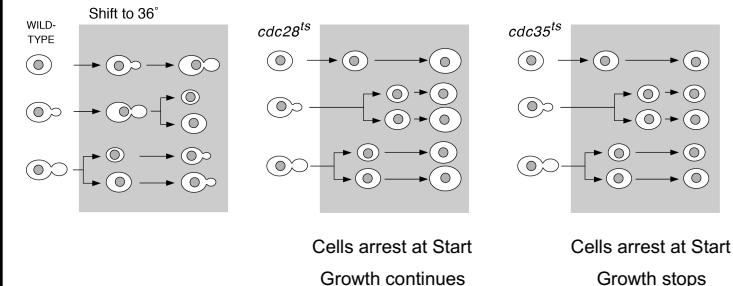


Enzymology 2: Learning goals

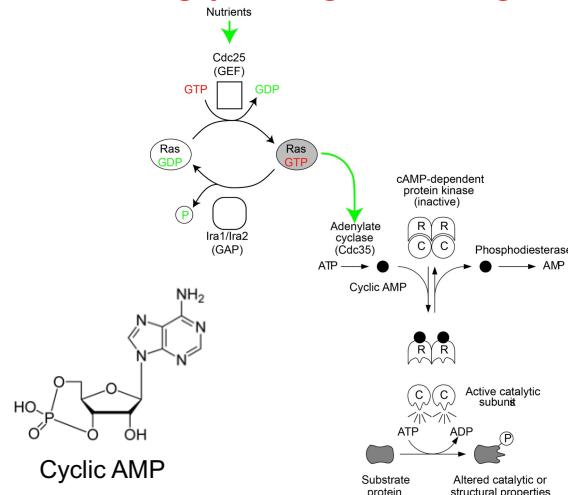
Protein kinases control many biological processes
 Metal ions orient and catalyze reactions
 Side chain positioning favors chemical reactions
 Protein phosphorylation regulates conformation & activity
 Motors couple ATP hydrolysis to mechanical movement

Two types of mutants block Start

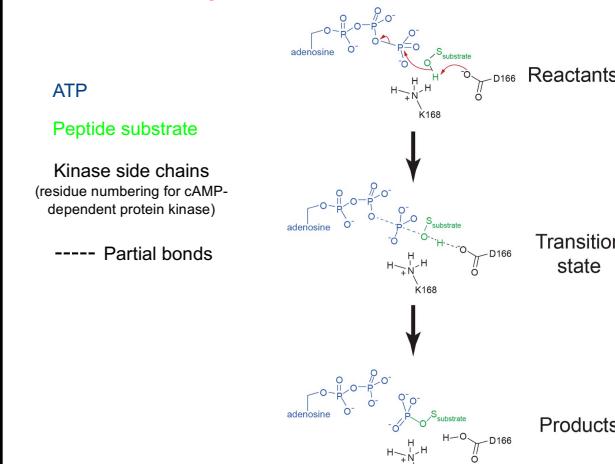
cdc mutants block arrest the cell cycle
 Two *cdc* classes prevent passage through Start



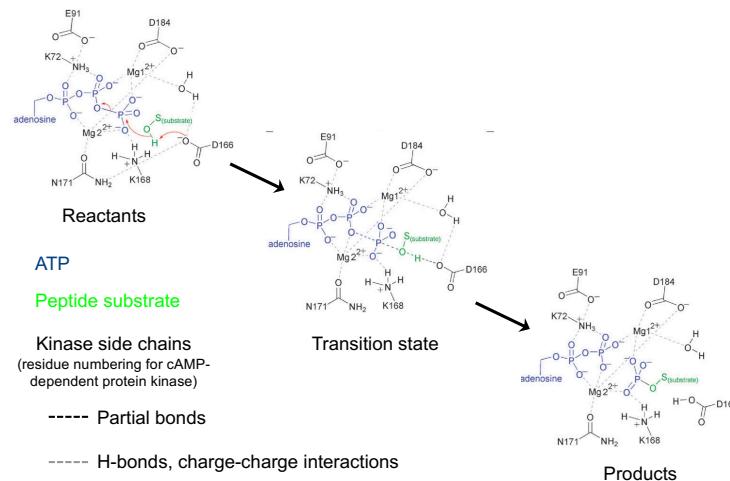
Budding yeast growth regulation



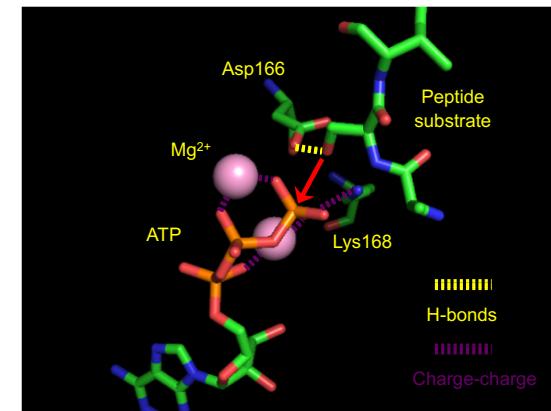
Ser/Thr protein kinase mechanism



Ser/Thr protein kinase mechanism

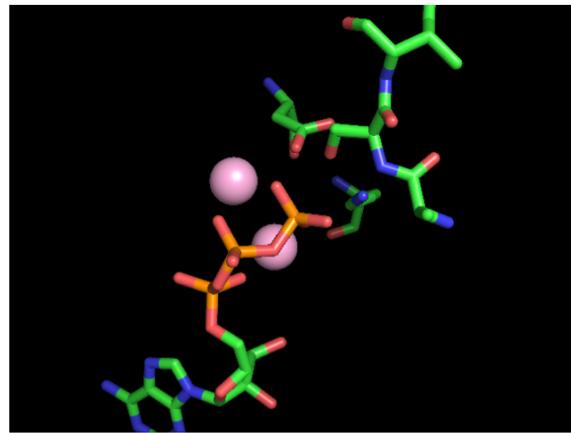


Protein kinase catalytic details

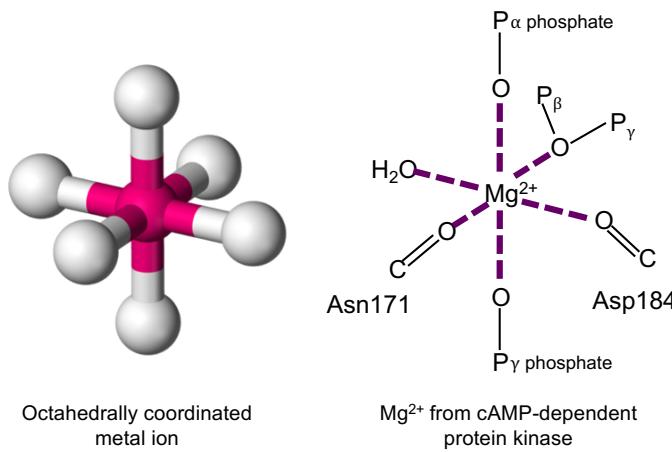


Amino acids numbered for cAMP-dependent protein kinase, mechanism conserved

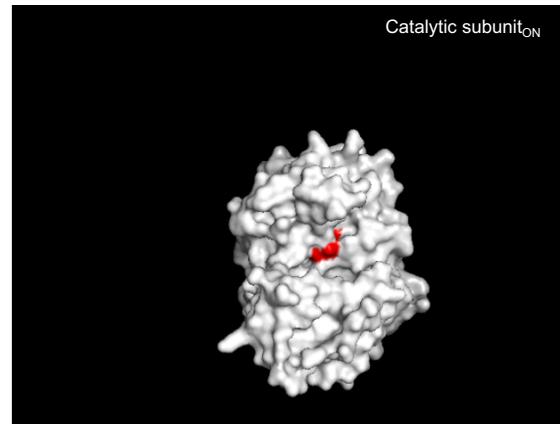
Protein kinase catalysis: the movie



Metal ions enforce geometry

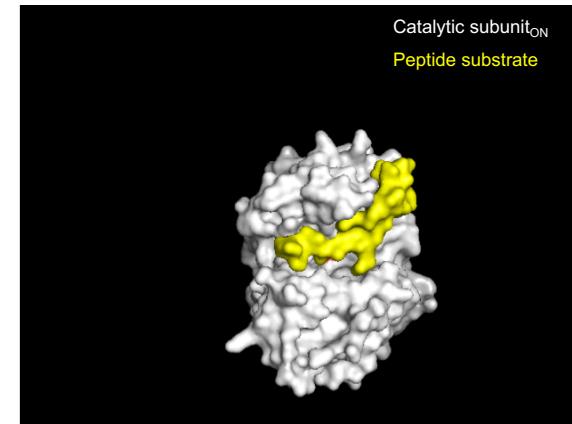


Naked, the kinase is active



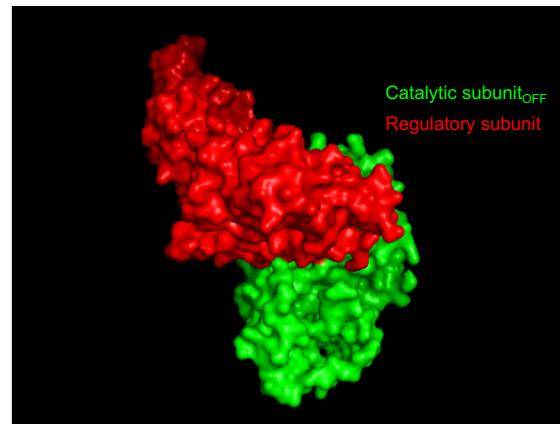
Surface exposed parts of catalytic amino acids (D166, K168)

The peptide binds a groove on the kinase

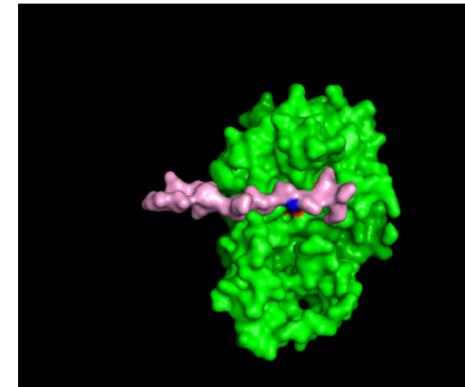


Catalytic subunit_{ON}
Peptide substrate

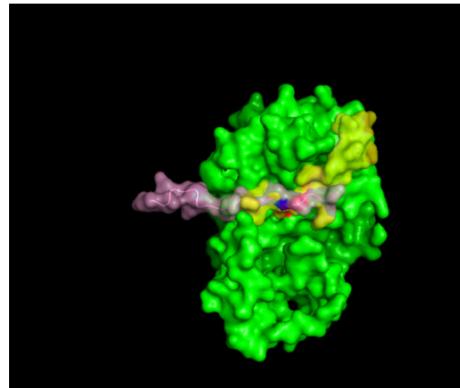
Regulatory subunit binds, inhibits catalysis



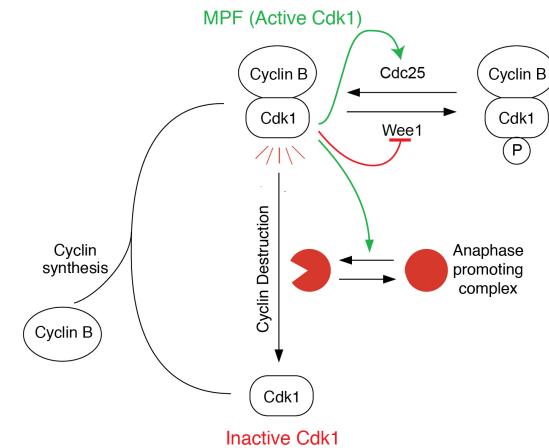
Regulatory subunit occupies peptide site



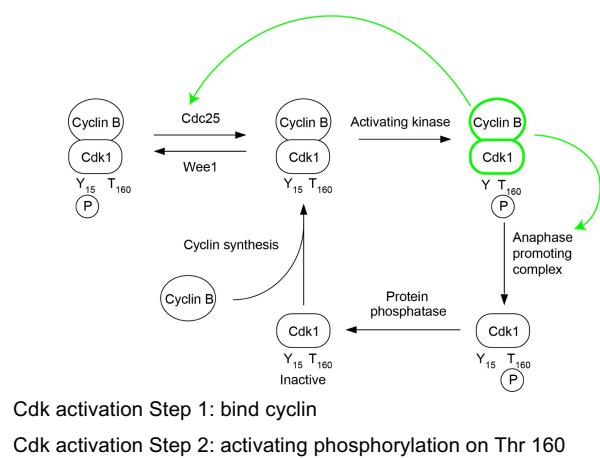
Inhibitory and substrate peptides clash



The (over)simplified cell cycle engine



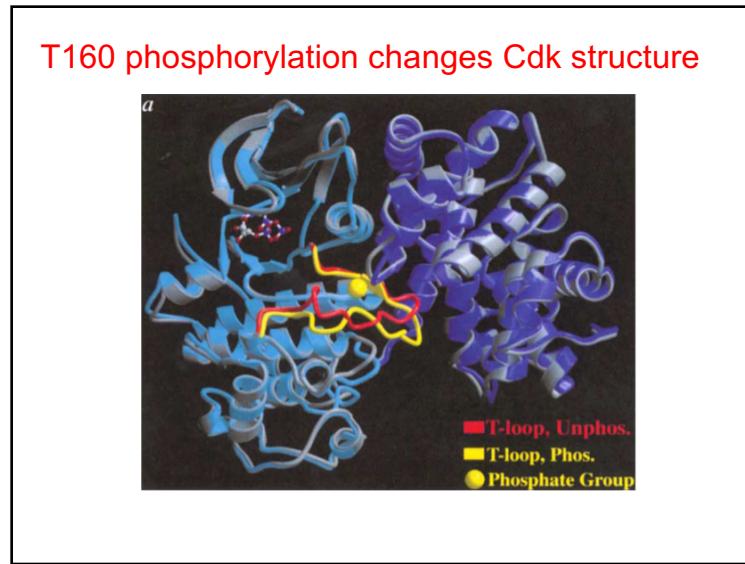
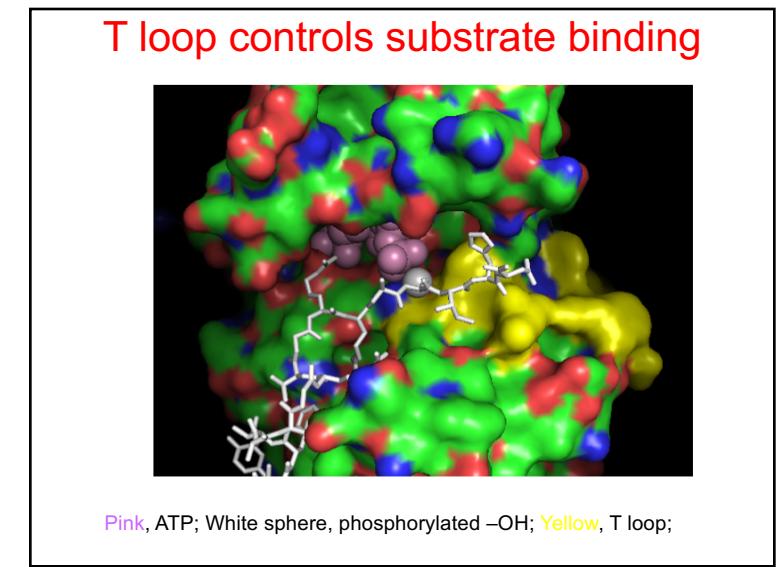
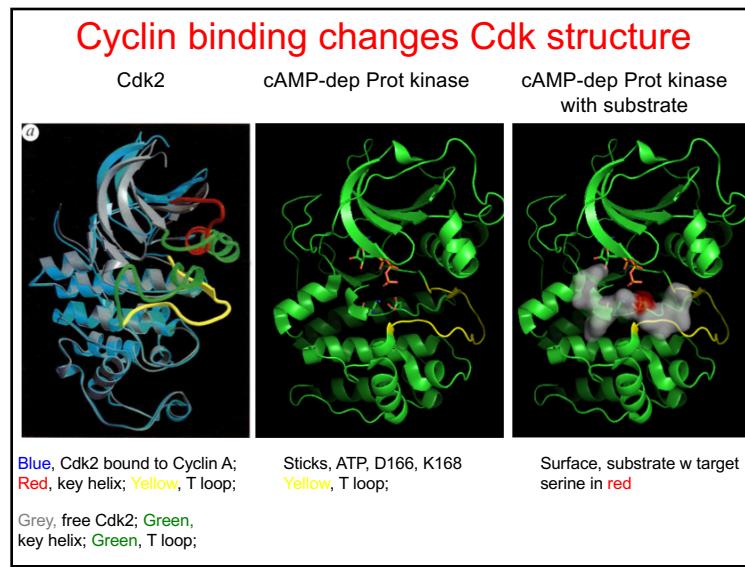
A more realistic cell cycle engine



Unphosphorylated Cdk-Cyclin complex



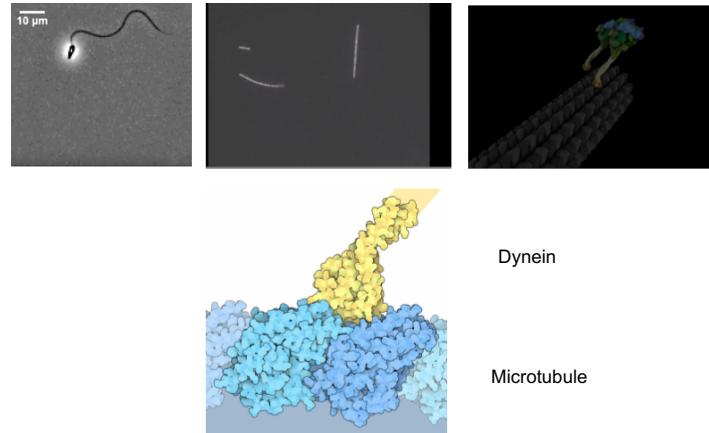
Blue, Cdk2; Purple, Cyclin A; Red, key helix; Yellow, T loop; Sticks, ATP



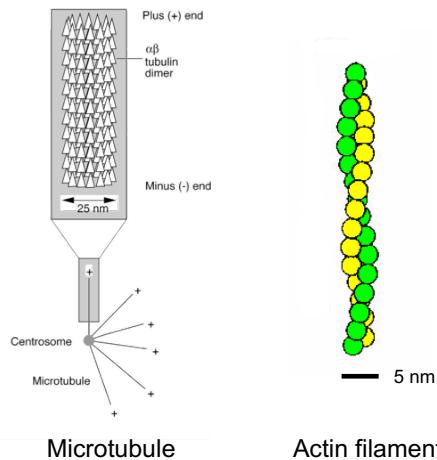
The movement of motors

Chemical → Mechanical energy

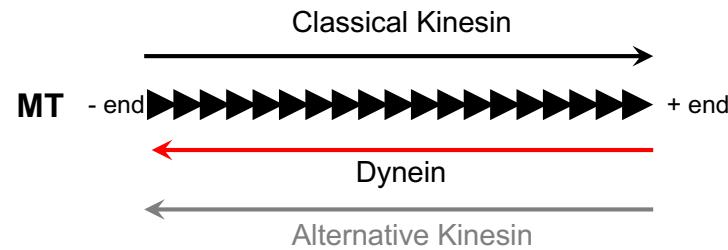
Biology: levels of abstraction



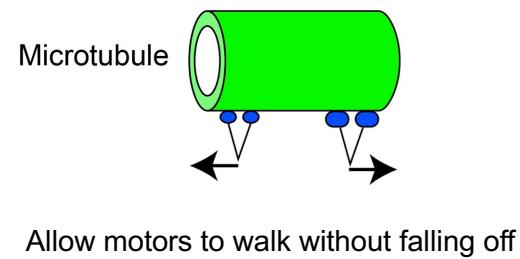
Motors move along actin or microtubules



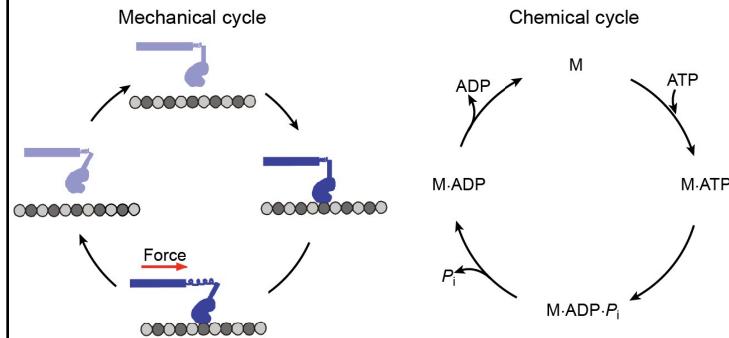
Motors can move up or down filaments



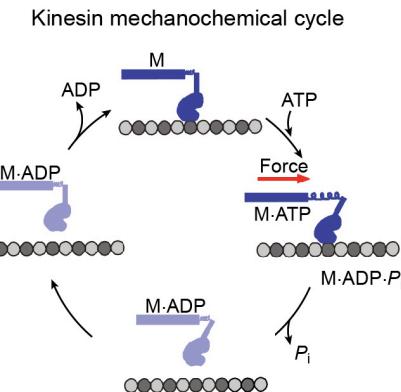
Two-legged motors



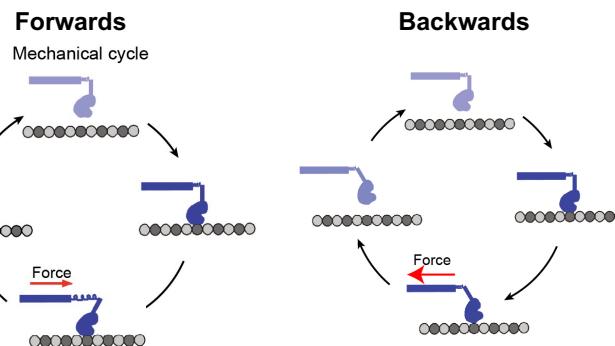
Motors have mechanical & chemical cycles



Coupling mechanical & chemical cycles



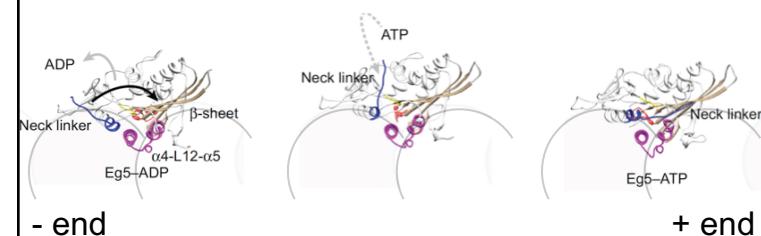
Swing direction sets motor direction



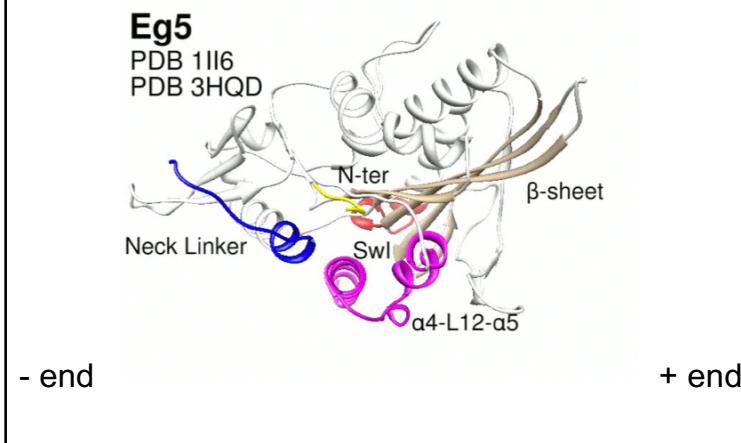
Conformational change depends on presence of γP_i

Moving a plus end-directed kinesin

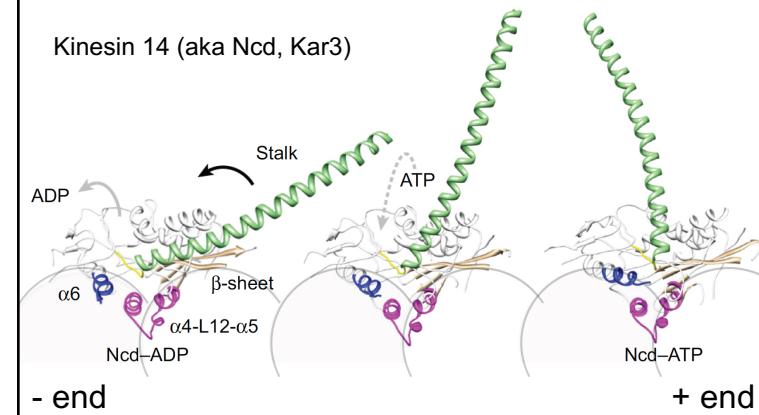
Kinesin 5 (aka Eg5, Cin8, Cut7)



Moving a plus end-directed kinesin



Moving a minus end-directed kinesin



Moving a minus end-directed kinesin

