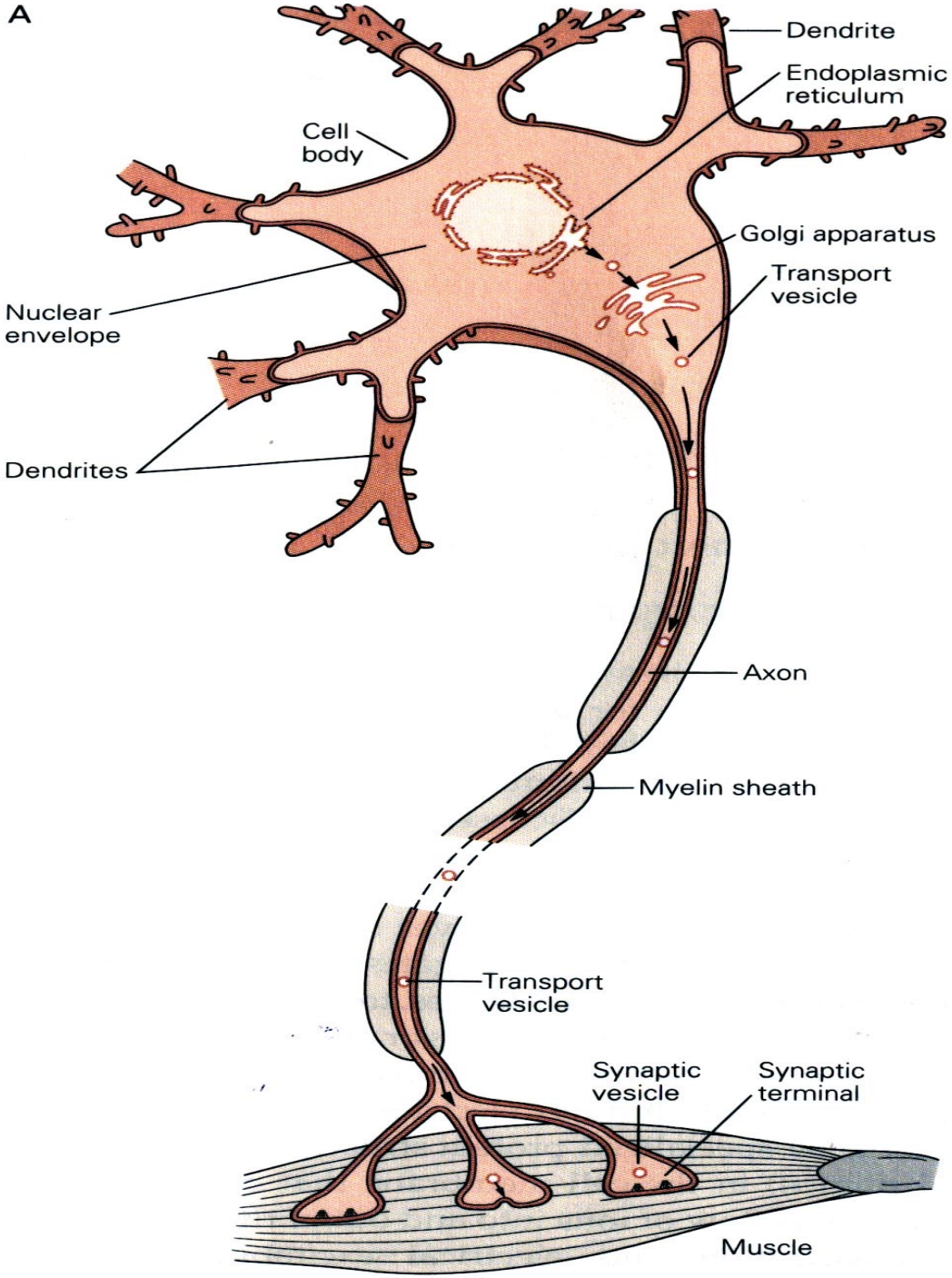
BHARATHIDASAN UNIVERSITY

Program: M.Sc., Biomedical Science

Course Title: Neurobiology

Axonal transport

Prof. Narkunaraja Shanmugam
Dept. of Biomedical Science



(Proximal)

Neurons have proximal-distal (=basal-apical) polarity

(Distal)

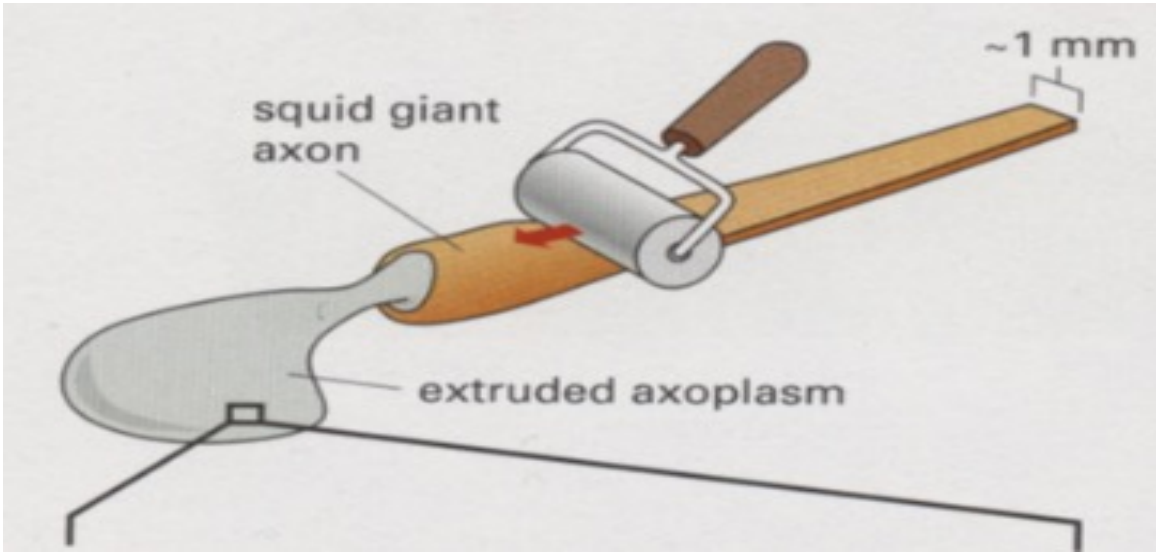
(Kandel/Schwartz)

Axonal transport does not require an intact cell

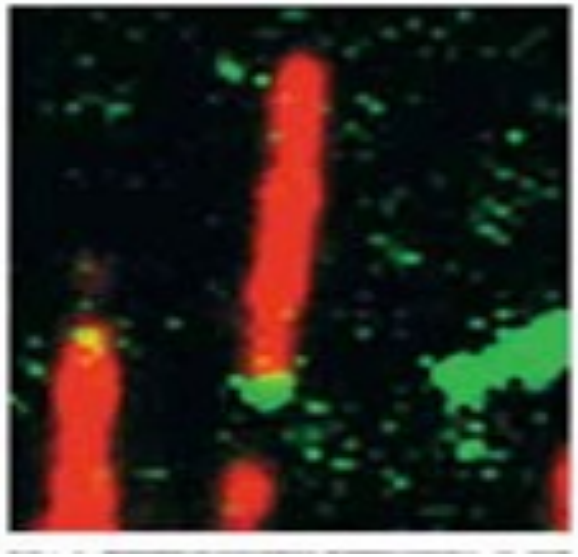
Extruded axoplasm assays - Cytosol is squeezed from the axon with a roller onto a glass coverslip.

Addition of ATP shows movement by videomicroscopy

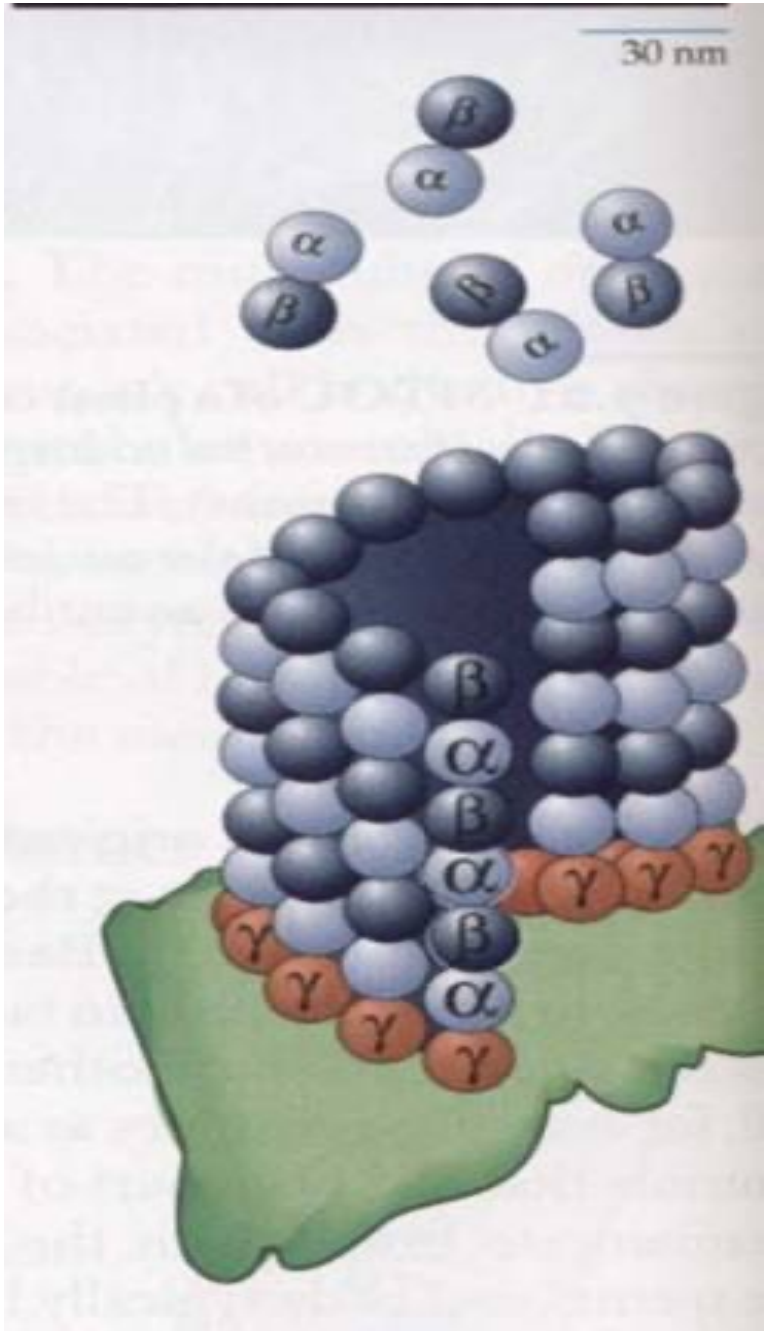
Vesicle movement in this system is about 1-2um/s similar to fast axonal transport.



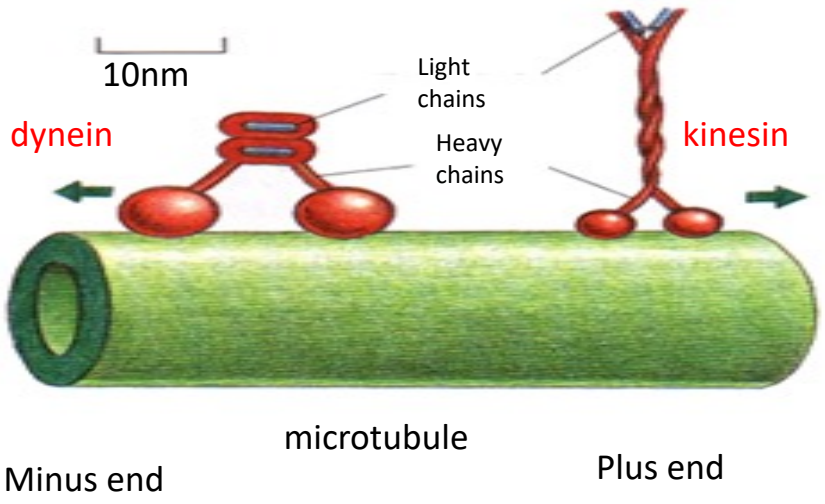
Intracellular transport requires microtubules

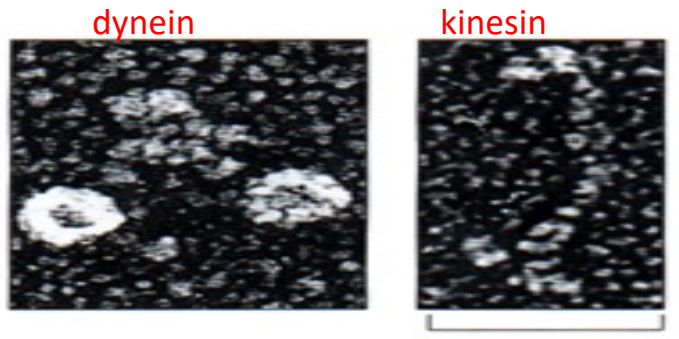


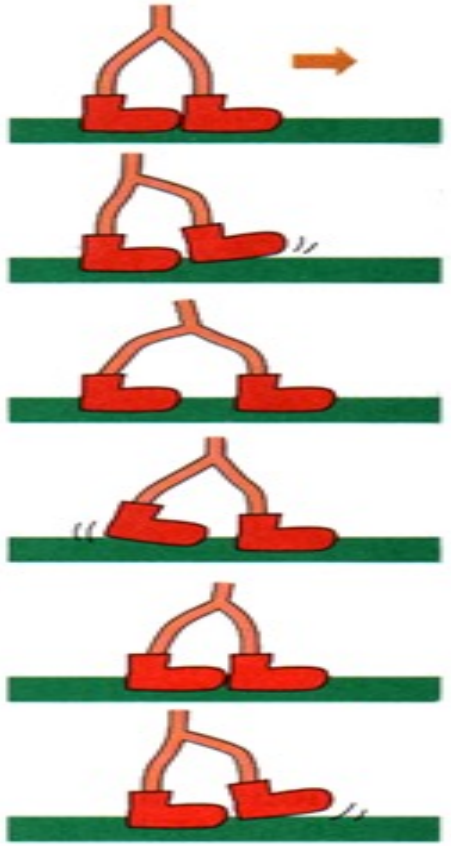
Stain with an anti-gamma tubulin antibody (red). Gamma-tubulin at initiates synthesis at one end (-) (green)



Molecular structure of dyneins and kinesins







Dyneins - composed of 2-3 heavy chains with a total Mr of 1,000kD
- interact with microtubules indirectly through microtubule- binding proteins

Kinesin

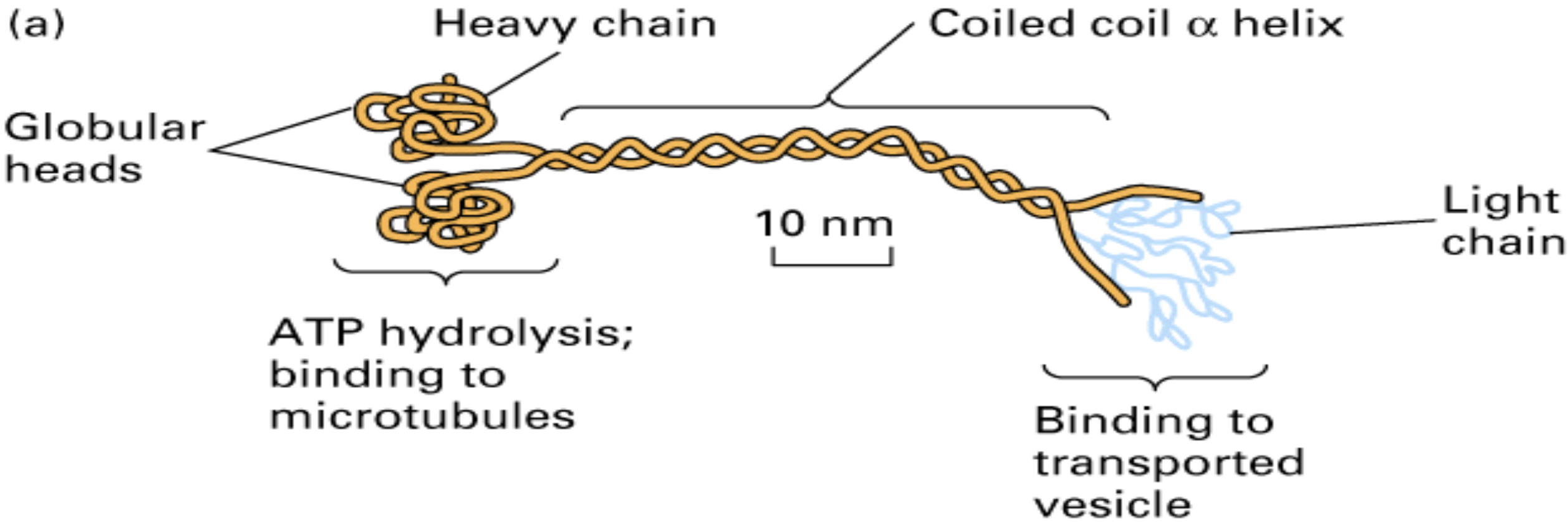
Dimer of a heavy chain complexed to a light chain

Mr= 380kD

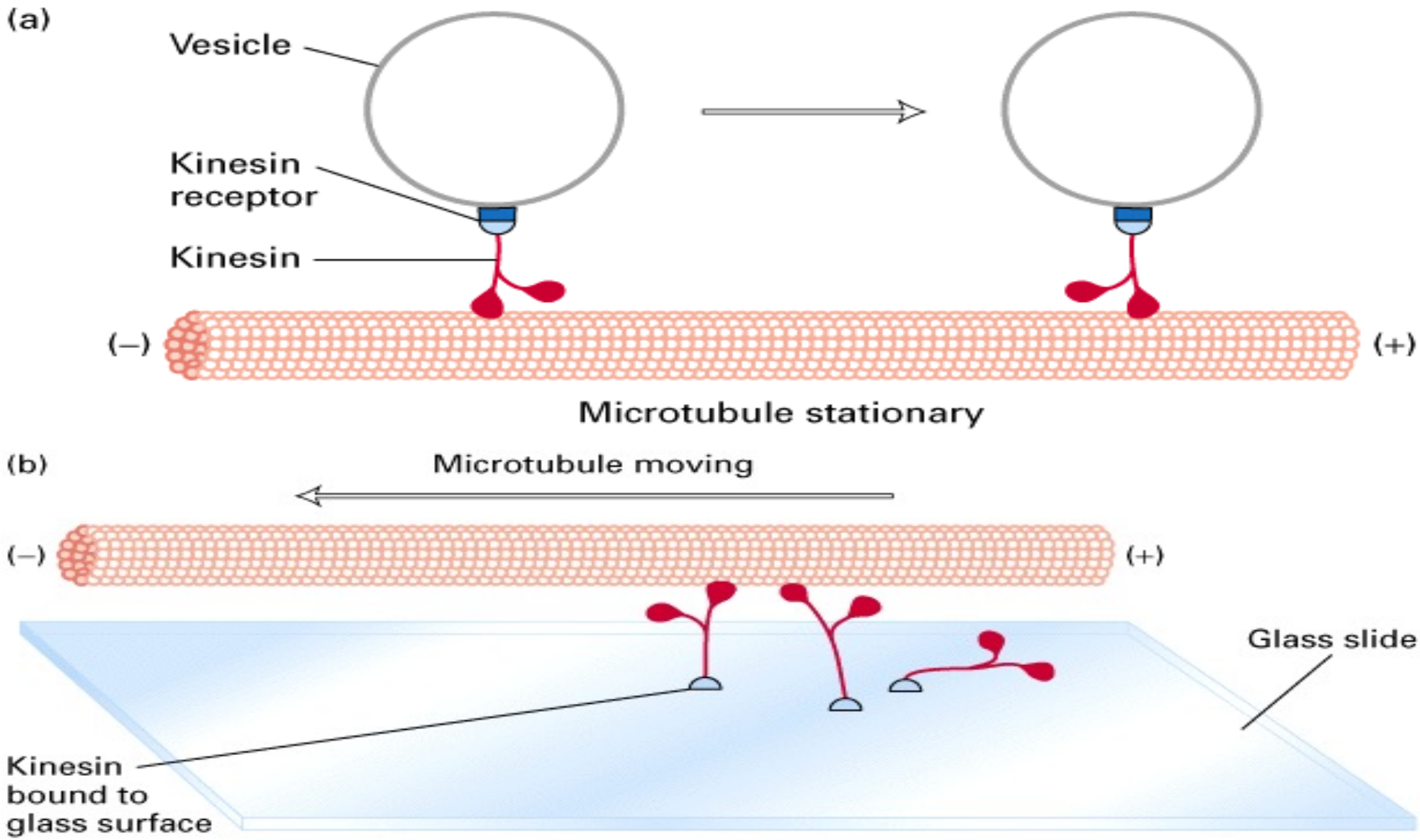
Three domains:
1) Large globular head
Binds microtubules and ATP
2) Stalk
3) Small globular head
Binds to vesicles

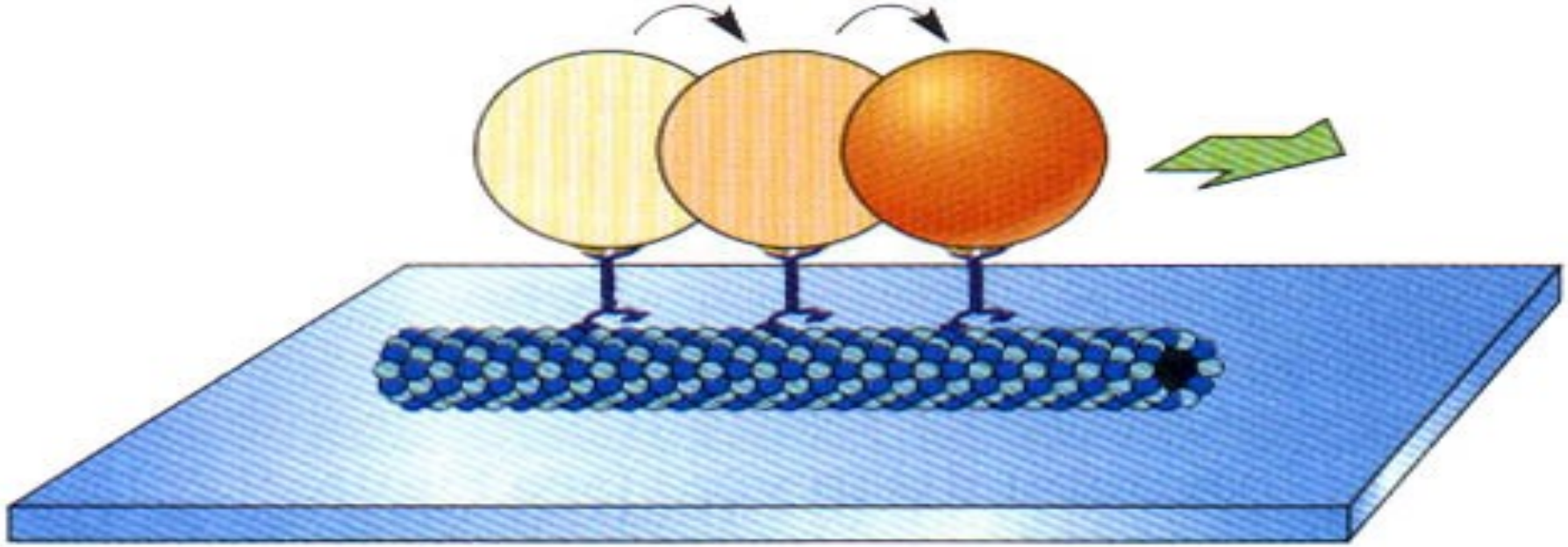
To date 12 different family
Members have been identified

Structure of Kinesin



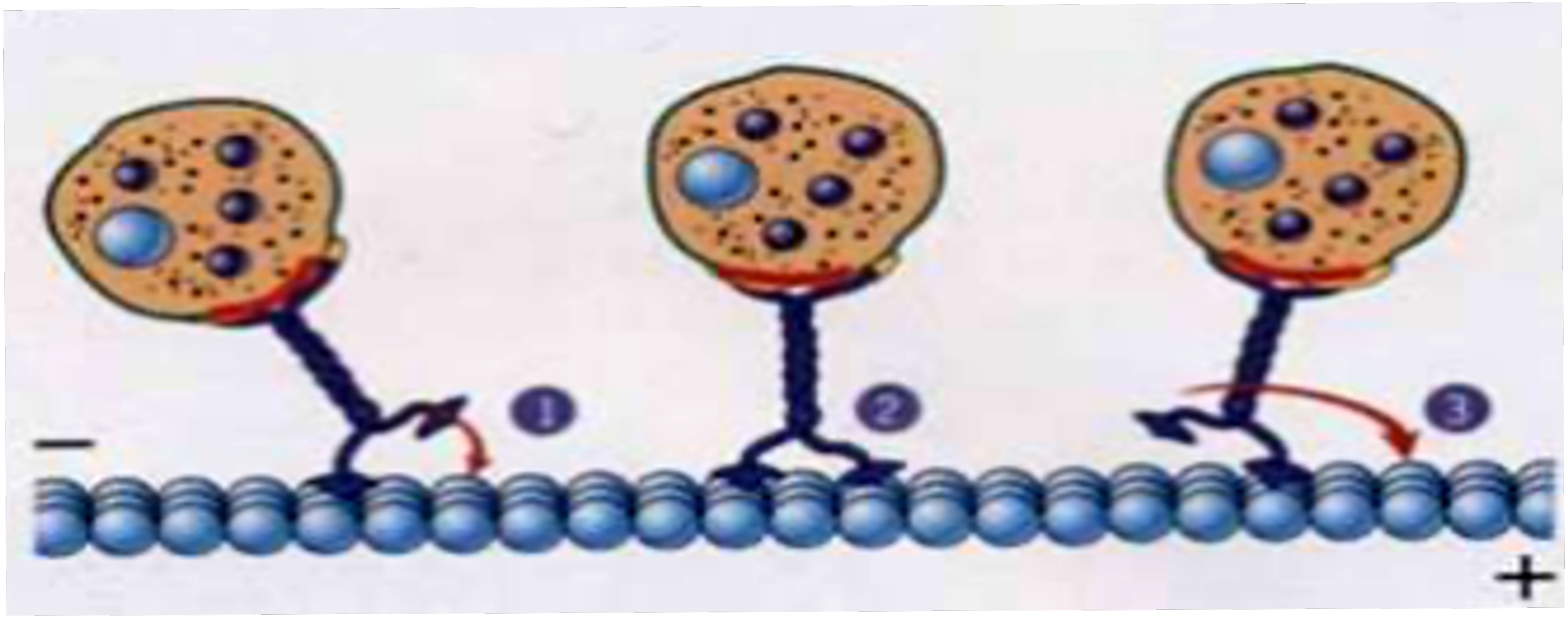
How does Kinesin catalyze transport?

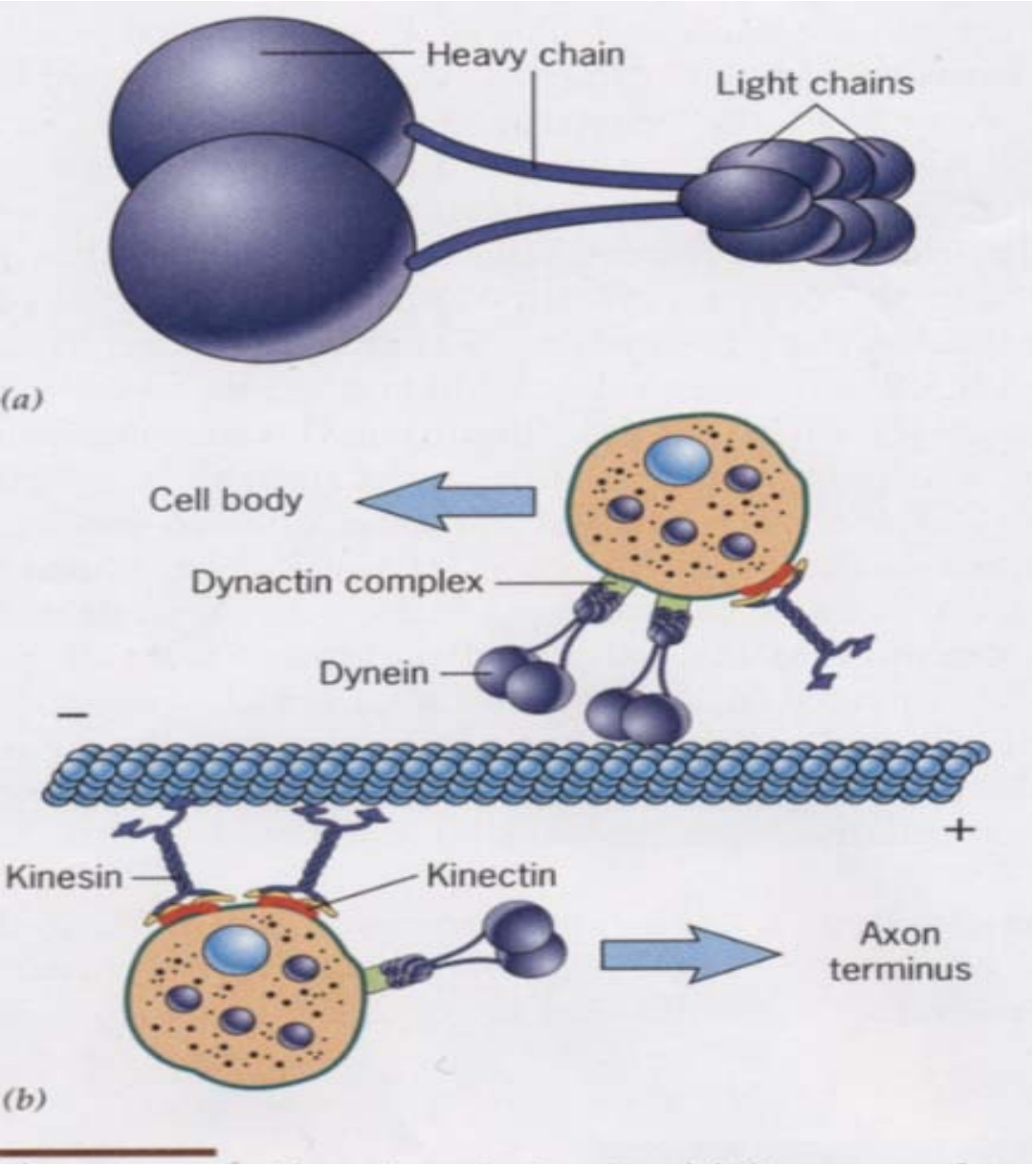




- Beads coated with kinesin binds to microtubules and move along
- Dynein promotes movement in the opposite direction

How does Kinesin catalyze transport?





How to build directionality and specificity?

- Multiple motor proteins can bind to a given cargo
- Each kinesin/dynein transports a specific cargo