BIOL 200 (Section 921)
Lecture # 11
July 4, 2006

UNIT 8: Cytoskeleton

Reading:
ECB, 2nd ed. **Chap 17**. pp 573-606; Questions 17-1, 17-2, 17-12 to 17-23.
ECB, 1st ed. **Chap 16**. pp 513-542; Questions 16-1, 16-2, 16-10 to 16-21.

I. Cytoskeleton - Introduction, Intermediate Filaments, Microtubules basic structure

Learning objectives

- Two major roles for cytoskeleton - skeletal support and motility
- Distinguish between three major cytoskeletal systems - intermediate filaments, microtubules and actin filaments (microfilaments).
- Be able to describe how intermediate filaments are assembled from polypeptides to form a microscopically visible fibre.
- Know major cell function of intermediate filaments
- Know structure of microtubules, their process of assembly, the meaning of plus and minus ends, and the role of MTOCs.

Three major cytoskeletal systems and their general properties

a) **Intermediate Filaments** - a system of elastic fibers - used to strengthen cells and to transmit mechanical strain across cells in a tissue. These filaments are purely skeletal in nature.

b) **Microtubules** - rigid protein tubules. These are involved in generation of cell shape and provide substrate for two different types of motor systems, dyneins and kinesins. The mitotic spindle is a variant form of the microtubular cytoskeleton.

c) **Microfilaments** (actin filaments) - this is the most complex system. Occurs in many forms, bundles of fibers or networks. Interacts with many types of molecules including its own class of motor proteins, the myosins. Its most elaborate form occurs in striated muscle. Microfilaments are responsible for cytoplasmic streaming and amoeboid motion.

II. Microtubules and microtubule-based motors, flagella

Study Objectives

- Understand dynamic instability and how it may be applied to microtubules and microtubule containing structures.
- Understand the role of GTP in the generation and control of dynamic instability of microtubules.
- Understand how motor proteins work and how their movement relates to the polarity of their molecular substrates
- Be able to describe the structure of flagella and the molecular basis of flagellar bending

Microtubules, dynamic instability. Microtubules may elongate, remain at a stable length, or may shorten by disassembling, usually from the plus end. Thus, some microtubules may be extending, while

others, arising from the same MTOC, may be contracting. To understand this we need to look at how the process of MT growth occurs:

- Tubulin dimers are present in two forms, active and inactive. The inactive dimers have bound GDP, while the active dimers bind ATP.
- Inactive dimers can be activated by having the bound GDP phosphorylated by ATP to produce bound GTP.
- The active dimer with GTP can then bind to the plus end of the microtubule. GTP bearing tubulin dimers bind avidly to GTP bearing dimers at the plus end of MTs.
- With time the bound GDP is hydrolyzed. This is presumably an enzymatic reaction as the GTP molecule is, itself stable. This GTP hydrolysis reduces the affinity of binding tubulin dimers to each other in the microtubule.
- A growing microtubule thus consists of a GTP/tubulin dimer containing cap, and a shaft composed mostly of subunits with bound GDP.
- These GDP binding units are more readily disassembled.

III. Microfilaments and related systems

Learning Objectives

Understand the

- assembly of actin filaments,
- dynamic instability of actin filaments; comparison with that of microtubules.
- role of actin filaments in formation of the cell cortex, and regulation of cell structure and movement,
- myosins and the myosin activity cycle as it relates to muscle.

Be able to compare the role and activity of myosin and dynein motor systems

Actin microfilaments are structures that arise from self-assembly of subunits (monomer – actin)

Actin microfilament polymerization

- Monomers of actin in has ATP bound to it
- Monomers assemble into two stranded helix=7 nm filament, with "polarity"
- After incorporation of actin into microfilament, ATP hydrolyzed to ADP
- This reduces the affinity between monomers, reducing polymer stability
- Thus one end of the microfilament is inherently less stable than the other
- End where assembly greater, actin with ATP bound="plus end"
- End where actin with ADP bound inherently less stable="minus end"
- Polarity is not just structural, also polymer dynamics at each end differ.

That assembly/dissasembly is essential to the function of actin can be seen by action of drugs called cytochalasins, prevent assembly or phalloidin which artificially stabilizes actin Assembly/disassembly in cell cortex important for changes in cell shape and migration.

CYTOSKELETON: IMPORTANT POINTS

Cytoskeletal Element	**Diameter, nm**	**Monomers**	**Function**	**Example cell type that this element is prominent in***
Microtubule (MT)	Largest, 25 nm	tubulins	Dynamic structural elements, mitosis	Sperm-flagella Dividing cell-pull chromosomes apart
Actin microfilaments (Mf)	Smallest, 7 nm	Actin	Movement	Muscle
Intermediate filaments	Intermediate between MT and Mf	Family of related proteins	Strength, mechanical support	Skin

*all of these elements are found in all mammalian cells, these cells just have prominent (lots).