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Introduction to Cell Biology notes

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SESSION # 8

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INTRODUCTION TO CELL BIOLOGY

DR. MICHAEL SHEETZ (COLUMBIA UNIVERSITY)

I CELL CYTOSKELETAL FUNCTION

FUNCTIONS OF CELL \Rightarrow APPROACH PROBLEM AS ENGINEERPHYSICAL FACTORS \Rightarrow INTEGRATED WITH BIOCHEMICAL

ACTIVITY IN MANY CELL FUNCTIONS

CELL ROBUSTNESS \Rightarrow ADAPT THEIR BEHAVIOR TO ENVIRONMENTAL FACTOR IN ORDER TO SURVIVE(15 μ m DIAMETER)

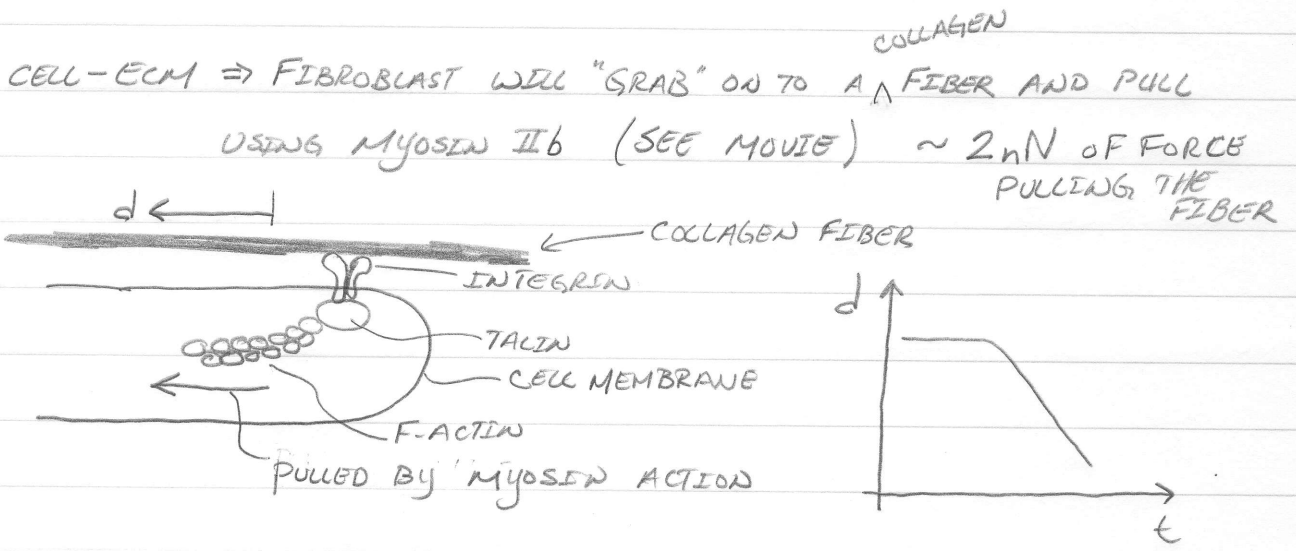
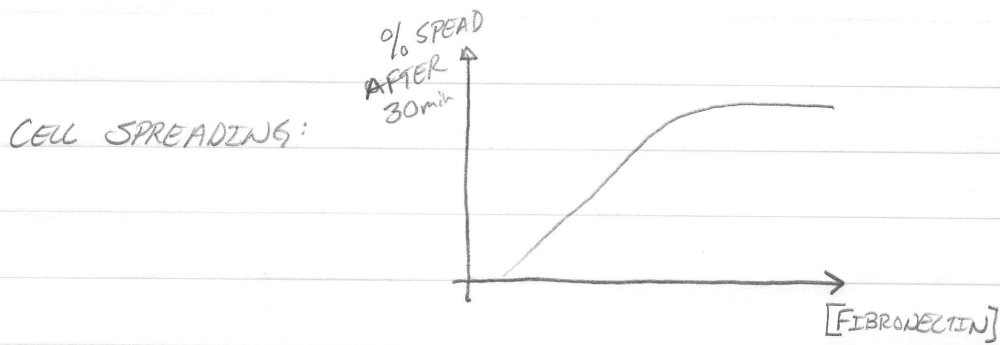
- CELL VOLUME $\sim 2 \times 10^{-9} \text{ cm}^3$ VS. BACTERIUM $\sim 1 \times 10^{-12} \text{ cm}^3$
- PROTEIN CONCENTRATION $\sim 180 \text{ mg/mL}$ (50% AVERAGE)
- NO. PROTEINS/CELL $\sim 4 \times 10^9$ PER EUKARYOTIC (10,000 DIFFERENT PROTEINS)
 $\sim 2 \times 10^6$ PER PROKARYOTIC (2,000 " ")
 $\sim 10^3 - 10^5$ MOLECULES OF A PROTEIN PER CELL

(ENGINEERING) PRINCIPLES FOR ROBUST FUNCTIONS:

- FUNCTIONAL MODULES (RIBOSOMES, FOCAL CONTACT)
- COMPARTMENTALIZATION OF FUNCTION (NUCLEUS, LAMELLIPODIUM)
- TERM LIMITS (FUNCTION STOPS AFTER SHORT PERIOD)
- BASIC TOOL KIT (COMPLEX PROCESSES REQUIRE LINKING SEVERAL MODULES)
- PHASE BEHAVIOR WITH SHARP TRANSITIONS

CELL CYTOSKELETON: μ -TUBULES, F-ACTIN, INTERMEDIATE FILAMENTS

NO MOTOR PROTEINS ASSOCIATED WITH THESE



SURFACE COATING AFFECTS CELL MOTILE BEHAVIOR

GLASS VS. COLLAGEN
 (RIGID) (FLEXIBLE)

IF YOU CUT THE CELL SEPARATING THE CAPELLIPODIUM FROM THE REST OF THE CELL, FOR THE SHORT TERM, THE CAPELLIPOD WILL CONTINUE MIGRATING. IT IS A "SELF-CONTAINED MODULE".

IN GONORRHEA, IT MOVES RANDOMLY BY EXTENDING A PILUS A FEW MICRONS AND THEN PULLING.

CELL MIGRATION IS A CYCLIC PROCESS OF FORCE GENERATION
 EXTENSION → ATTACHMENT → CONTRACTION → RELEASE → RECYCLE
 (LEADING EDGE) (LEADING EDGE) (CELL BODY) (TRAILING EDGE)

ASSEMBLY OF ACTIN FILAMENTS AT THE LEADING EDGE
PROMOTES AMEUBIPOD EXTENSION

- PROFILIN PROMOTES ACTIN POLYMERIZATION
- THE FORMATION OF FILAMENTS IS DEPENDENT TO THE CONCENTRATION OF FREE MONOMERS
- AMEUBIPODIUM GROWTH IS ALSO REGULATED BY MEMBRANE TENSION

II BIOLOGY OF RED BLOOD CELL

DR. NARLA MOHANDAS (NEW YORK BLOOD CENTER)

RED BLOOD CELL \Rightarrow ALL PLASMA MEMBRANE, INSIDE OF CELL
 \uparrow IS A HIGH CONCENTRATION OF HEMOGLOBIN
 FROM BONE MARROW ($\sim 30\text{g/dL}$)

120 DAYS \rightarrow LIFETIME OF RBC

RBC \Rightarrow HIGHLY DEFORMABLE, WHY?

- CELL GEOMETRY \Rightarrow FAVORABLE SURFACE AREA TO VOLUME RATIO
- STATE OF HYDRATION \Rightarrow REGULATION CELL HEMOGLOBIN CONCENTRATION
- MEMBRANE DEFORMABILITY AND ITS MECHANICAL STABILITY

SOME DISEASES AFFECT RBC PROPERTIES:

HEREDITARY HYDROCYTOSIS \Rightarrow INCREASE H_2O CONTENT

" XEROCYTOSIS \Rightarrow DECREASE " "

" SPHEROCYTOSIS \Rightarrow MORE SPHERICAL SHAPE

SICKLE CELL ANEMIA \Rightarrow SINGLE AA SUBSTITUTION IN β -GLOBIN
 \hookrightarrow LEADS TO MULTI-ORGAN DAMAGE

RBC PLASMA MEMBRANE

- SPECTRIN (α, β)
- ACTIN (SHORT FILAMENTS), TROPOMYOSIN, TROPOMODULIN
- ANKYRIN (LINKS SPECTRIN WITH TRANSMEMBRANE PROTEINS)
- AQUAPORIN (H_2O CHANNEL)

μ -PIPETTE ASPIRATION \Rightarrow MEASURES MECHANICAL PROPERTIES OF RBC
 TEST EFFECTS OF DEFICIENCY OF DIFFERENT PROTEINS
 TO IDENTIFY WHICH ONES CONTRIBUTE TO THE MECHANICAL
 RESPONSE OF CELL.

SELF-ASSOCIATION SITE

α AND β SPECTRIN FORM A HETERODIMER DUE
 TO α -HELICES INTERACTIONS (ONE IN α , TWO IN β).
 THIS FORMS A HIGHLY STABLE TETRAMER

REVERSIBLE UNFOLDING OF SPECTRIN REPEATS CAN
 ACCOUNT FOR THE FLEXIBILITY OF RBCs.

αI -SPECTRIN IS UNIQUE TO MAMMALS

MEMBRANE-PROTEIN INTERACTIONS

PHOSPHATIDYL SERINE (PS) ASSOCIATES WITH PEPTIDES
 TO STABILIZE MEMBRANE

MANY OF THE DISEASES CAN BE LINKED TO DIFFERENT MUTATIONS ON THE COMPONENTS OF RBC, MAINLY SPECTRIN. (SEE SLIDES FOR EXAMPLES)

MALARIA → MODIFIES ORGANIZATION OF CYTOPLASMIC PROTEINS