SESSION # 8

GEM 4 - AUGUST 2006 8/9/06

INTRODUCTION TO CELL BIOLOGY

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I CELL CYTOSKELETAL FUNCTION

FUNCTIONS OF CELL ⇒ APPROACH PROBLEM AS ENGINEER

PHYSICAL FACTORS ⇒ INTEGRATED WITH BIOCHEMICAL ACTIVITY IN MANY CELL FUNCTIONS

CELL ROBUSTNESS ⇒ ADAPT THEIR BEHAVIOR TO ENVIRONMENTAL FACTOR IN ORDER TO SURVIVE

(15 μm DIAMETER)

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

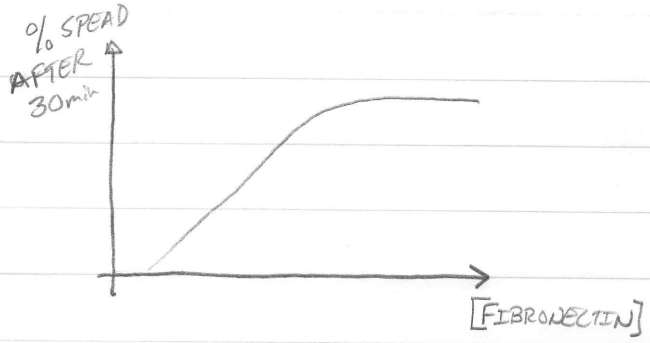
(ENGINEERING) PRINCIPLES FOR ROBUST FUNCTIONS:

- 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

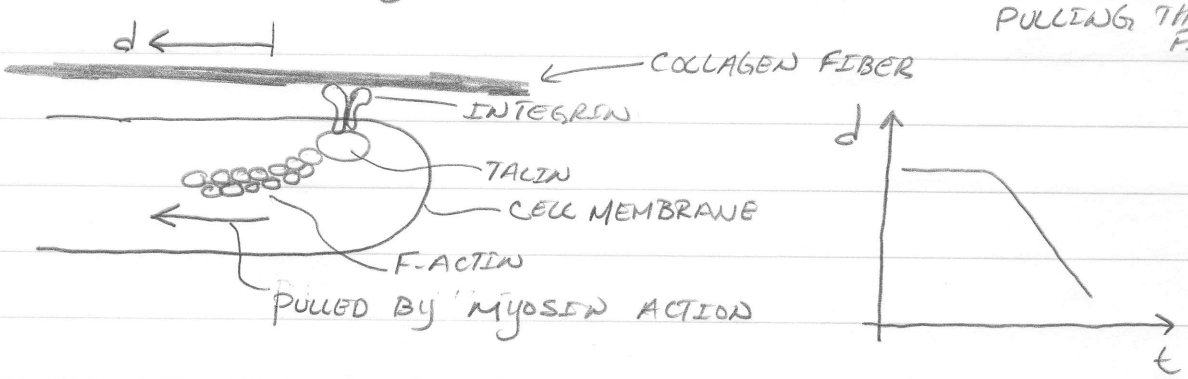
CELL CYTOSKELETON: μ-TUBULES, F-ACTIN, INTERMEDIATE FILAMENTS

(NO MOTOR PROTEINS ASSOCIATED WITH THESE)

CELL SPREADING:



CELL-ECM ⇒ FIBROBLAST WILL "GRAB" ON TO A COLLAGEN FIBER AND PULL USING MYOSIN IIb (SEE MOVIE) ~ 2nN OF FORCE PULLING THE FIBER



SURFACE COATING AFFECTS CELL MOTILE BEHAVIOR

GLASS VS. COLLAGEN
(RIGID) (FLEXIBLE)

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

IN GONORHEA, 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 CAMELLIPOD EXTENSION

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

II BIOLOGY OF RED BLOOD CELL

DR. NARLA MOHANDAS (NEW YORK BLOOD CENTER)

RED BLOOD CELL ⇒ ALL PLASMA MEMBRANE, INSIDE OF CELL IS A HIGH CONCENTRATION OF HEMOGLOBIN (~30g/dL)

↑ FROM BONE MARROW

120 DAYS → LIFETIME OF RBC

RBC ⇒ HIGHLY DEFORMABLE, WHY?

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

SOME DISEASES AFFECT RBC PROPERTIES:

HEREDITARY HYDROCYTOSIS ⇒ INCREASE H_2O CONTENT

" XEROCYTOSIS ⇒ DECREASE " "

" SPHEROCYTOSES ⇒ MORE SPHERICAL SHAPE

SICKLE CELL ANEMIA ⇒ SINGLE AA SUBSTITUTION IN β-GLOBIN
↳ 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 ⇒ MEASURE MECHANICAL PROPERTIES OF RBC
TEST EFFECTS OF DEFFICIENCY 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
PHOSPHATIDYLSERINE (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