Lecture #6: Mechanotransduction

What is mechanotransduction?

What questions do we answer when we study mechanotransduction?

Disease	Dysfunctional Cell Type
Deafness	Hair cells in the inner ear
Glaucoma (Loss of Vision)	Optical neurons
Muscular Dystrophy	Myocytes, Endothelial Cells, Fibroblasts
Cardiomyopathy	Cardiomyocytes
Osteoporosis	Bone Cells
Arteriosclerosis	Endothelial Cells, Smooth Muscle Cells
Immune System Disorders	White Blood Cells
Central Nervous System Disorders	Neurons

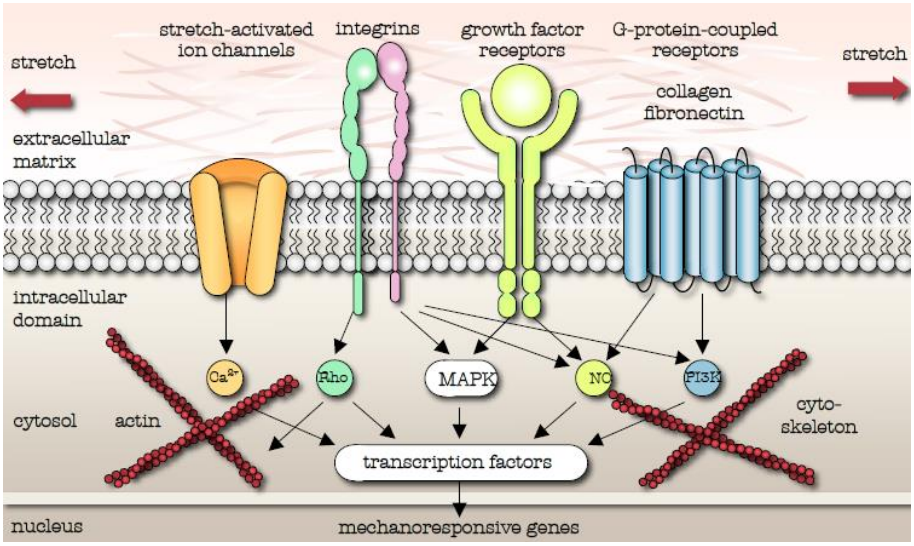
Example: Skin Growth

Three Stages of Mechanotransduction

(i.) Mechanoreception

(ii.) Intracellular Signal Transduction

(iii.) Target Activation



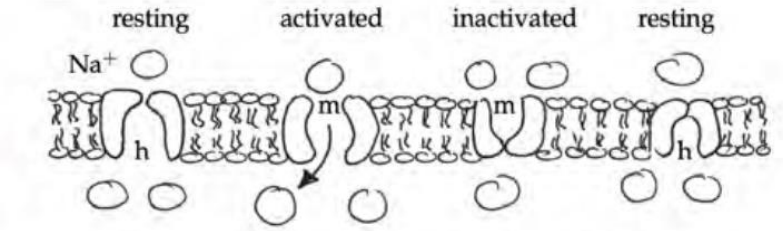
Probing Mechanotranduction

- Mechanotransduction probed in living cells in three major ways:

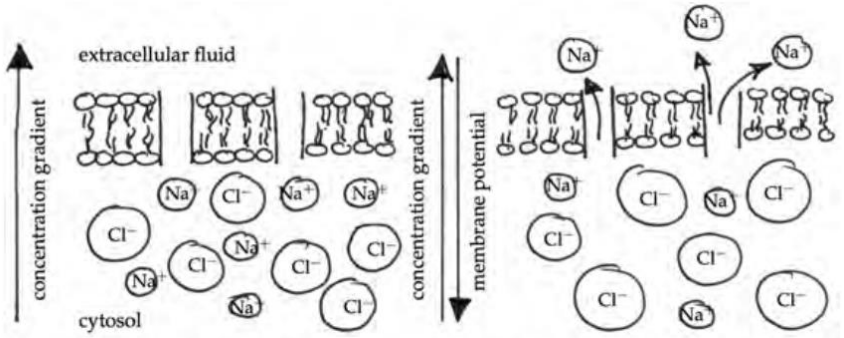
Some history…

- From 1948-1952: Hodkin and Huxley conducted patch clamp experiments on a giant squid axon and used this to develop a model.
  - They manipulated ionic concentration and controlled membrane potential
- From the mid-1950s: FitzHugh simplified Hodkin-Huxley work to a two variable model.

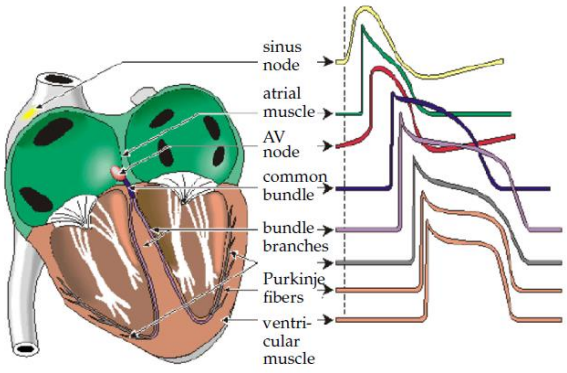
Electrophysiology (Father of the field is Luigi Galvani)



Cell	Na^+_{int} (mM)	Na^+_{ext} (mM)	K^+_{int} (mM)	K^+_{ext} (mM)	Cl^-_{int} (mM)	Cl^-_{ext} (mM)	Resting pot. (mV)
Nerve	50	437	397	20	40	556	-65
Skeletal Muscle	13	110	138	2.5	3	90	-99
Cardiac Muscle	10	145	135	4	25	140	-90
Red Blood	19	155	136	5	78	112	-8



Problem: Cardiomyocyte [Heart cell] and Neuron action potential upstroke



There are two different categories for models: ionic and phenomenological models. We will focus on the later – specifically: **FitzHugh-Nagumo Model**
We start with the following:

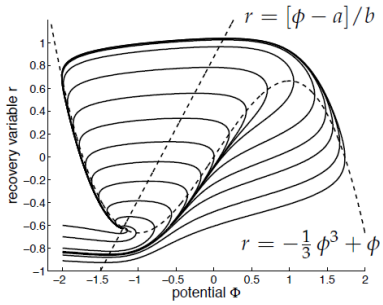
With the help of Lienard's transformation, you state

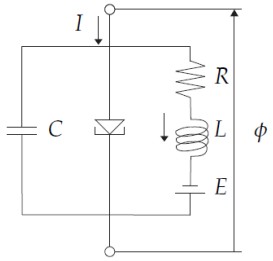
so

and use this to turn our original 2nd order differential equation into two 1st order equations.

What is r? It is something like a phenomenological representation of the influences of all ionic fluxes.
We now want to add some sort of stimulus and this will result in the classical FitzHugh-Nagumo model.

Now, FitzHugh did this entire math part of this model but Nagumo's contribution was creating an electrical circuit interpretation. Additionally, when you plot these two equations, you can create a 2-d phase space plot as shown below. For homework 3, I have given you code for coupled neurons and you will play around with the parameters.





Now what do these results exactly mean?