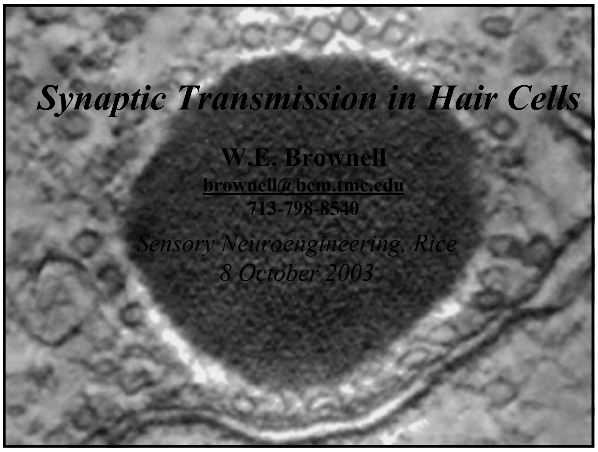
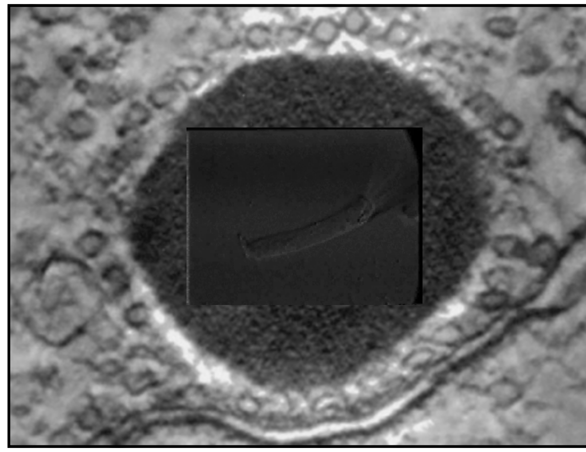


Synaptic Transmission in Hair Cells

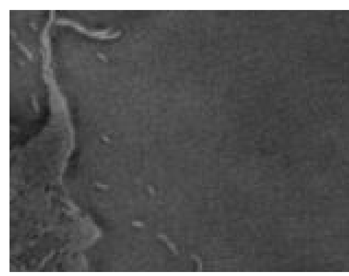
W.E. Brownell
brownell@bcm.tmc.edu
713-798-8540

Sensory Neuroengineering, Rice
8 October 2003



Hypothesis:
OHC electromotility evolved from hair cell synaptic mechanisms.

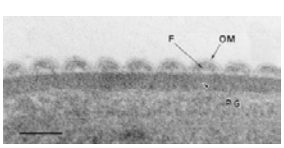
Adventurous Motility



Edge of a *Myxococcus xanthus* colony - individual bacteria showing adventurous gliding motility, time lapse 600x speed (Kaiser lab website - Stanford).

Outer membrane ripples on motile cells: Coincidence or functional roles?

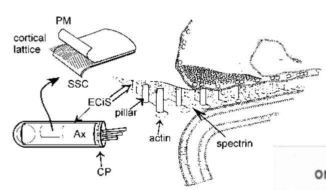
OHC - Dieler et al. 1991



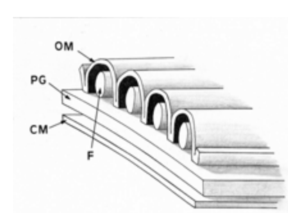
Oscillatoria - Adams et al. 1999

Flexibacter BH3 - Dickson et al. 1980

Trilaminate Walls



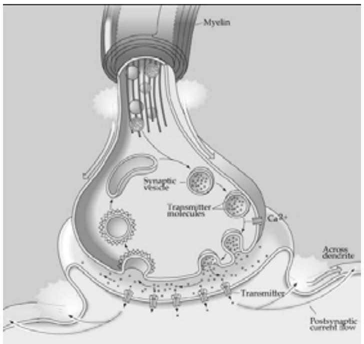
OHC



Oscillatoria –

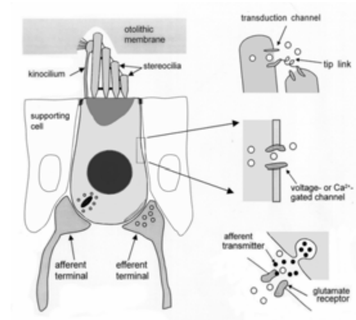
Adams et al. 1999

Neural membrane curvature



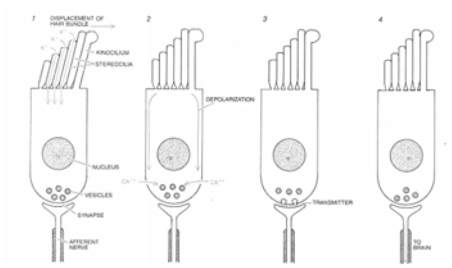
Hair Cells Have Two Functions

Mechano-Electrical Transduction



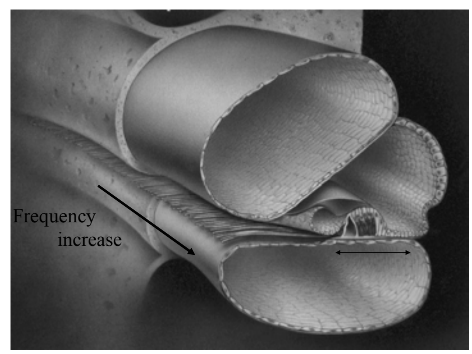
Neurotransmission

Hair Cell Neurotransmission



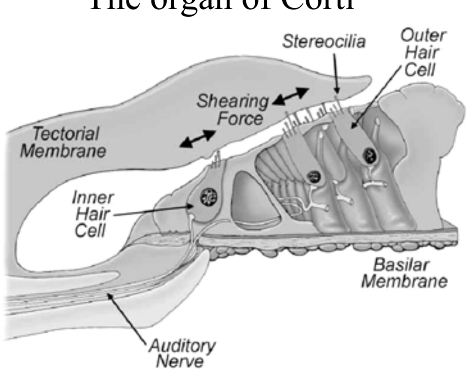
Hudspeth, 1983

The output is neural



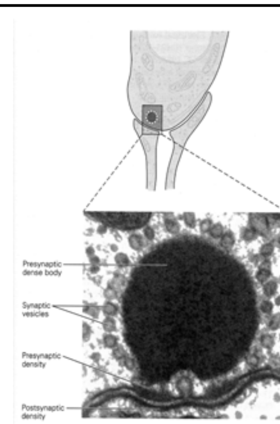
Compton's Interactive Encyclopedia, 1997

The organ of Corti

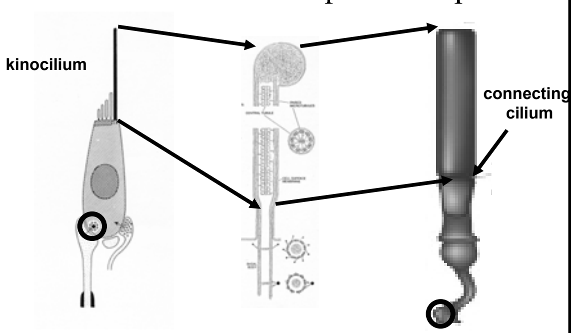


Sensitive Synapse

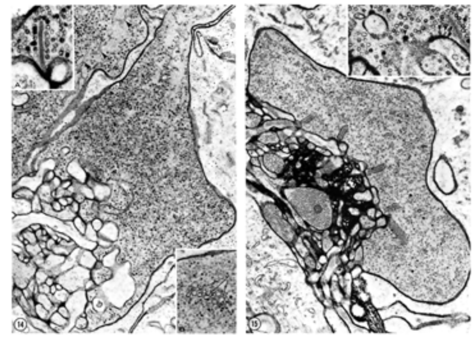
- Continuous release of neurotransmitter
- Rate of release modulated by < mV changes in membrane potential



Patterns - hair cells & photoreceptors



Light dependent transmitter release



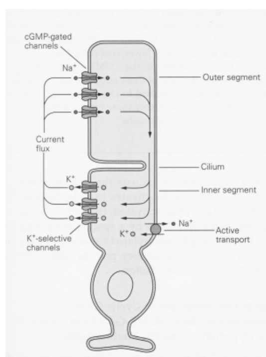
Dark – more release

Light – less release

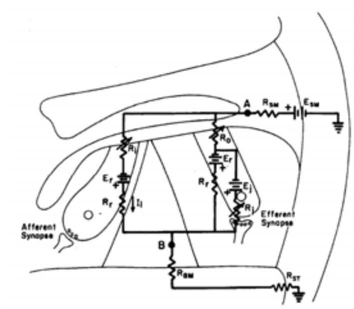
Schaeffer & Raveola, 1978

Phototransduction - dark current

The dark current depolarizes the membrane potential resulting in maximal neurotransmitter release. Light blocks the depolarizing current and decreases neurotransmitter release.

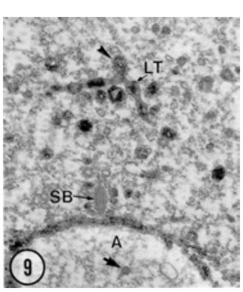


Visualizing the silent current



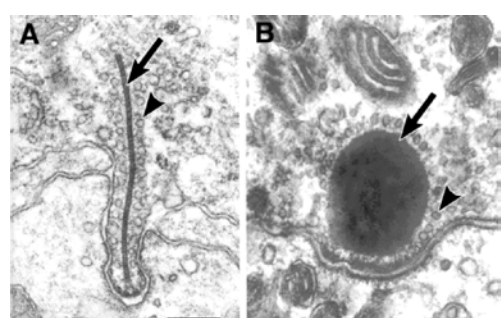
Geisler, 1974

Inner hair cell afferent synapse



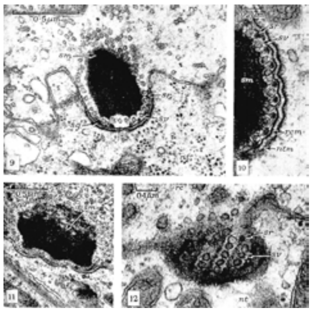
Siegel & Brownell - 1986

Ribbon synapses



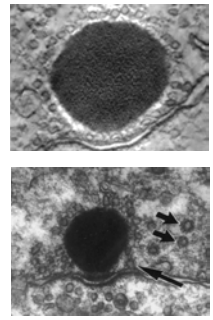
Lenzi & von Gersdorff, 2001

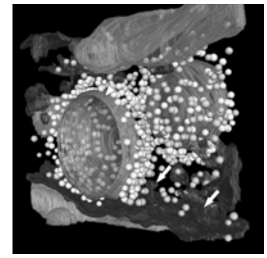
Ampullary organ of the North American Catfish



Mullinger, 1964

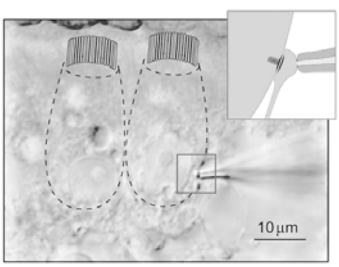
3-D reconstruction of frog hair cell synaptic ribbon





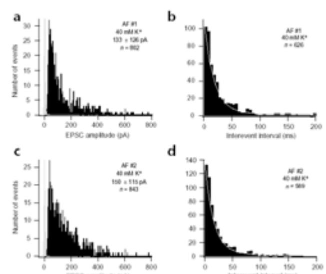
Lenzi et al. 1999

Recording from the synapse



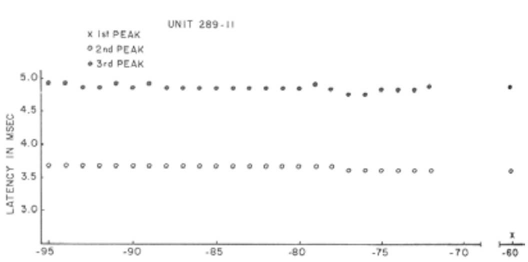
Glowatzki & Fuchs, 2002

Interval between neurotransmitter release is Poisson



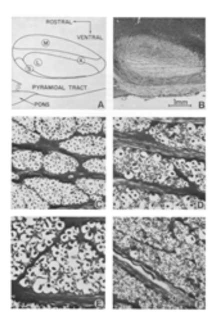
Glowatzki & Fuchs, 2002

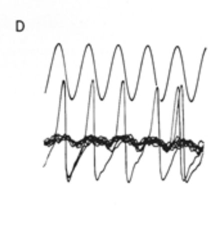
Temporal precision



Kiang et al., 1965

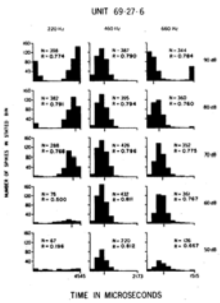
Phase locking





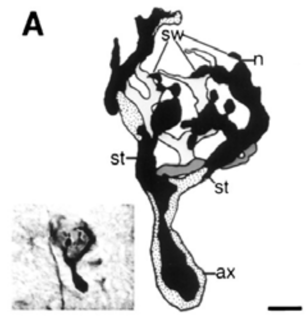
Brownell, 1975

Intensity - invariance



Anderson, 1971

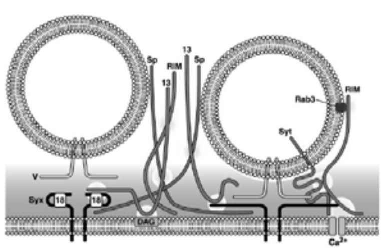
Specialized CNS synapses



Preserve temporal coding

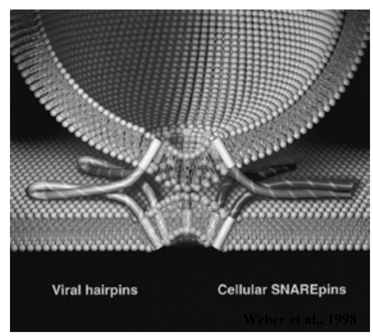
Rowland et al., 2000

Protein-Protein Interactions in the Active Zone Matrix

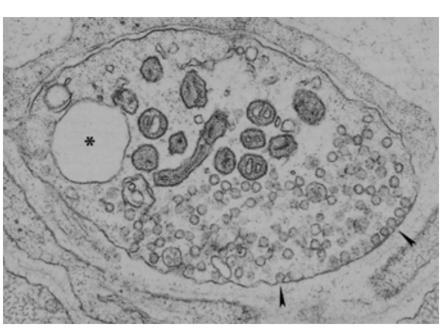


Martin, 2002

Proteins bring membranes together

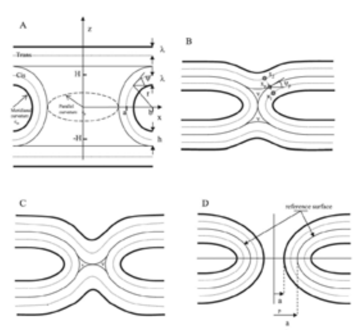


Vesicle fusion



Torri-Tarelli et al., 1985

Membrane fusion



(A) Parameters of the stalk.

(B) Hemifusion,
- initial stage.

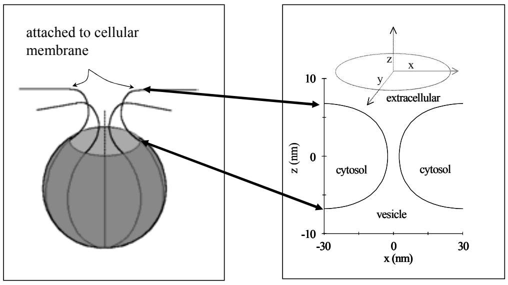
(C) Hemifusion,
- transmonolayers contact.

(D) Complete fusion
- fusion pore.

Markin & Albanesi, 2002

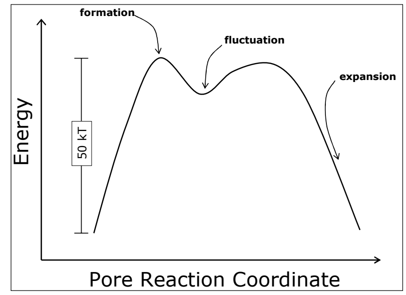
The fusion pore

Geometry | **Model**

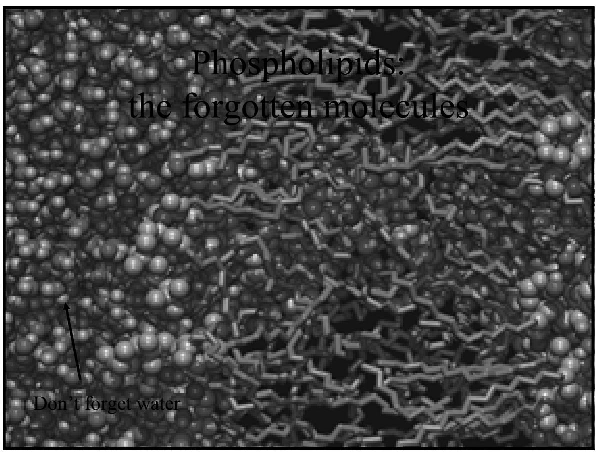


Farrell & Cox, 2002

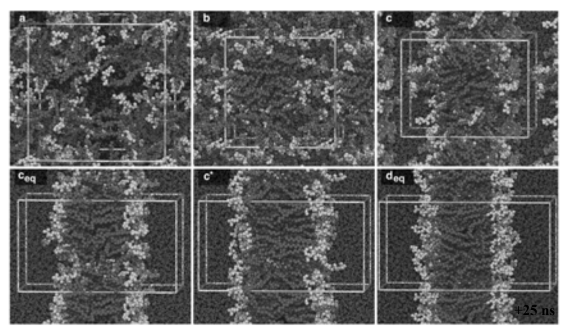
Where do we get the energy to bend the membranes?



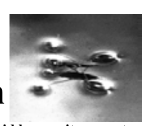
Phospholipids: the forgotten molecules



Membrane self assembly

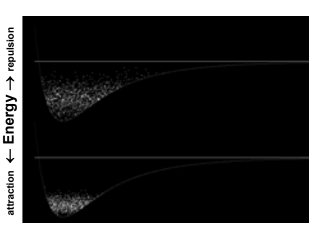


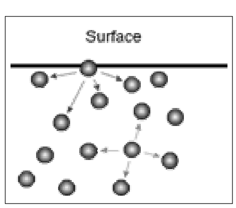
Marrink, Lindahl, Edholm & Mark, 2001



Surface tension

the energy required to increase the surface area of a liquid by a unit amount

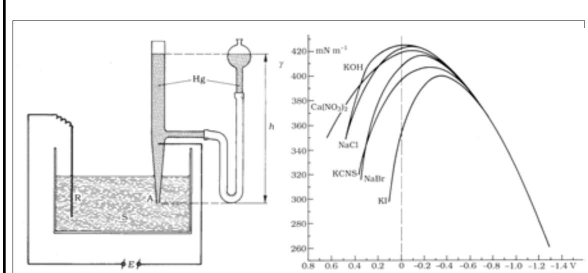




$$\gamma = -\left(\frac{\partial G}{\partial A}\right)_{(\mu, T)}$$

Electrical potential changes γ:

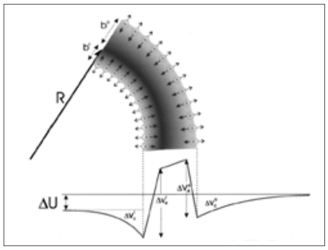
Lippmann mercury voltmeter



G. Lippmann, Ann. Phys. 149 (1873) | **DC Grahame (1947)**

Voltage dependent membrane tension

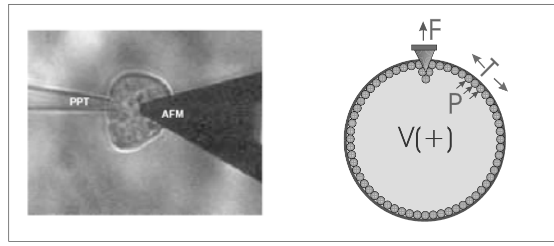
Includes a differential change in surface tension at the two membrane interfaces



Petrov & Sachs, 2002

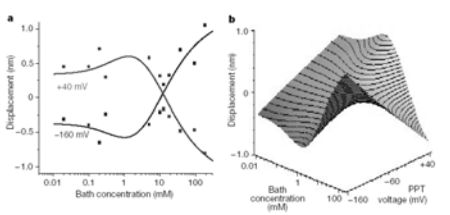
HEK electromotility

measured under voltage clamp with AFM



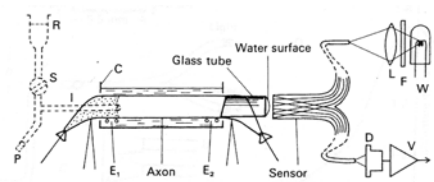
Zhang et al., 2001
Mosbacher et al., 1998

Voltage dependent membrane motion

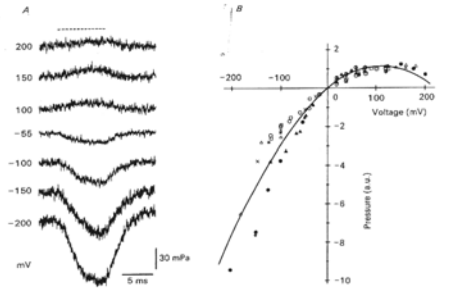


Zhang et al., 2001

Voltage dependent pressure changes in squid axon

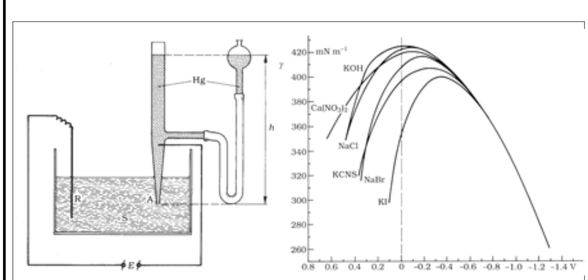


Terakawa, 1984



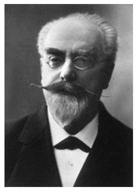
Electrical potential changes γ:

Lippmann mercury voltmeter



G. Lippmann, Ann. Phys. 149 (1873) **DC Grahame (1947)**

Lippmann equation



Gabriel Lippmann
Nobel Prize,
physics 1908

A Gibbs adsorption equation for a polarizable interface,

$$\partial\gamma = -S_A\partial T - \Gamma\partial\mu - \sigma^o\partial E$$

contains the observed relation between surface charge and the ratio of the change in surface tension to the change in electrical potential,

$$\sigma^o = -\left(\frac{\partial\gamma}{\partial E}\right)_{(\mu,T)}$$

σ^o: surface charge (Cm^{-2})
γ: surface tension (Nm^{-1})
E: electrical potential difference (V)
μ: chemical potential (V)
T: temperature (^oK)
Γ: surface concentration one component (moles m^{-2})
S_A: interfacial entropy per unit area ($JK^{-1}m^{-2}$)

Voltage Dependent Tension

$$\sigma^o = -\left(\frac{\partial\gamma}{\partial E}\right)_{(\mu,T)}$$

Integrate the Lippmann under these boundary conditions:

1. $C = \varepsilon\varepsilon_o\kappa_i$ $\qquad \kappa^2 = F^2\sum_j\left[\frac{n_j z_j^2}{\varepsilon\varepsilon_o RT}\right]$

2. At voltage V^o
$\sigma_i^o = -\sigma_i^d$ *when* $\gamma_i=\gamma_i(V^o)$ *and* $\sigma_e^o = -\sigma_e^d$ *when* $\gamma_e=\gamma_e(V^o)$
Upon polarization to voltage V_m
$\sigma_i^o = -(\sigma_i^d - q_p)$ $\gamma_i=\gamma_i(V_m)$ *and* $\sigma_e^o = -(\sigma_e^d + q_p)$ *when* $\gamma_e=\gamma_e(V_m)$

F: Faraday's constant; n_j: concentration of species, j; z_j valency of species, j; R: gas constant; ε_o: permittivity of free space; ε_w: dielectric constant of water; C: capacitance of double layer

Tension is a linear function of voltage under physiological conditions (ΔV< 100 mV)

$$T_V \approx \frac{(C_m)^2}{2}(B_e+B_i)(\Delta V)^2 + C_m(-B_e\sigma_e^o + B_i\sigma_i^o)\Delta V$$

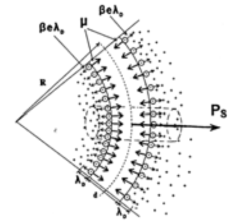
T_V: voltage dependent tension; C_m: membrane capacitance

$$B_e = \pm\frac{1}{\kappa_e\varepsilon\varepsilon_o} \qquad B_i = \pm\frac{1}{\kappa_i\varepsilon\varepsilon_o}$$

Assume:
Physiological medium 0.14 M
External and internal surface charge -0.025 and -0.015 C/m^2
Charging occurs by ions adsorbing onto or desorbing from
ΔV = 100 mV
Energy ≅ Pore Area * T_V
1000-5000 nm^2 * 46μN/m
10-50 kT

Flexoelectricity:

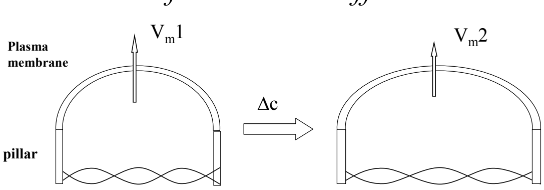
coupling of membrane curvature of with the electric field



Todorov, 1993

characterized in biological membranes by Petrov

The flexoelectric effect

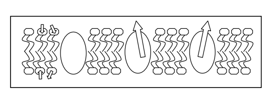


$$U_f \approx \frac{c_b}{\varepsilon_0}\left(\frac{f^C}{\varepsilon_W} + \frac{f^D}{\varepsilon_L}\right)$$

c^b: membrane curvature; f^D: flexoelectric coefficient (dipole); f^C: flexoelectric coefficient (charge); ε_o: permittivity of free space; ε_w: dielectric constant of water; ε_L: dielectric constant of membrane

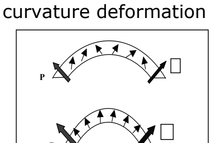
Liquid Crystal Nature of Biomembranes

Protein and lipid molecules comprising biomembranes possess dipole moments



Dipoles contribute to the flexoelectric effect

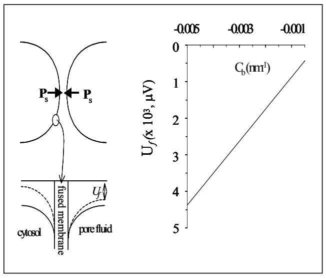
- curvature deformation changes membrane polarization



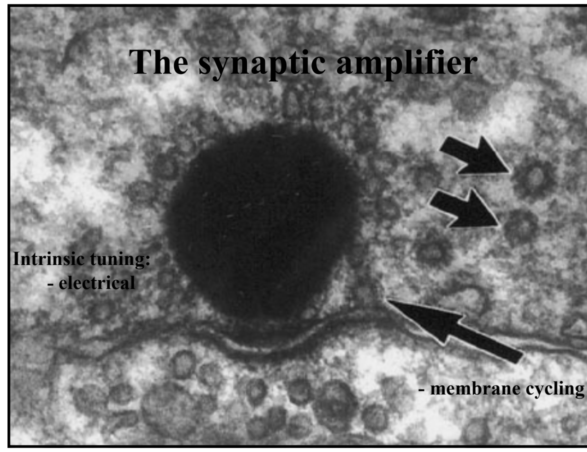
As c is increased, dipoles become more aligned increasing the polarization of the membrane

Direct flexoelectric effect

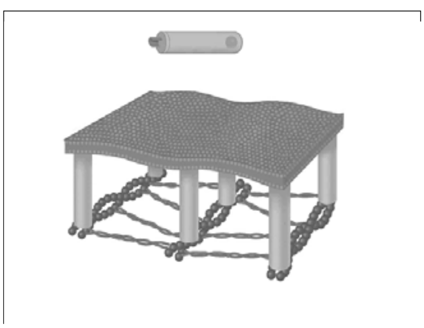
$$U_f \approx \frac{c_b}{\varepsilon_0}\left(\frac{f^C}{\varepsilon_W} + \frac{f^D}{\varepsilon_L}\right)$$



The synaptic amplifier



OHC electromotility – the other membrane based motor



Collaborators

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Rice:
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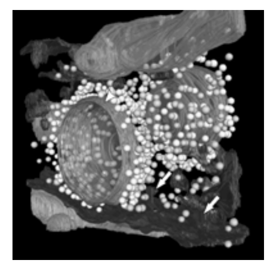
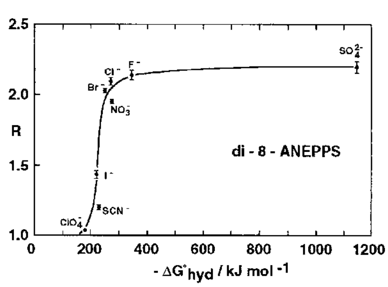


URLs: http://www.bcm.tmc.edu/oto/research/cochlea/
http://www.bioflexoelectricity.org

Hofmeister effect

anion adsorption at membrane interface

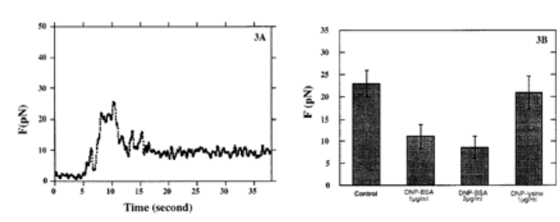


Clarke & Lüpfert, 1999

ClO_4 > SCN > I > NO_3 > Br > Cl > F > SO_4

I > Br > NO_3 > Cl > HCO_3 > F > SO_4 Oliver et al., 2001

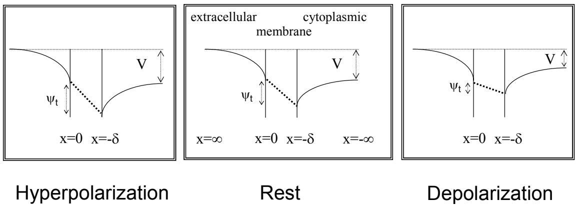
Tension affects vesicle recycling



Dai et al., 1997

Hyperpolarization & depolarization

affect the charge on each interface



Ψ_t : potential difference across the membrane

V : transmembrane potential difference

$\psi_t = \psi(-\delta) - \psi(0)$

$V = \psi(-\infty) - \psi(\infty) = \psi(-\infty)$