Hypothesis:
OHC electromotility evolved from hair cell synaptic mechanisms.

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

- **Oscillatoria**
  - Adams et al. 1999
Neural membrane curvature

Hair Cells Have Two Functions
Mechano-Electrical Transduction

Hair Cell Neurotransmission

The output is neural

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

Schaeffer & Raveola, 1978

Dark – more release
Light – less release

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

Ribbon synapses

Siegel & Brownell - 1986

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

Intensity - invariance

Anderson, 1971

Specialized CNS synapses

Specialized CNS synapses

Preserve temporal coding

Rowland et al., 2000

Protein-Protein Interactions in the Active Zone Matrix

Protein-Protein Interactions in the Active Zone Matrix

Proteins bring membranes together

Proteins bring membranes together

Martin, 2002

Viral hairpins

Cellular SNAREpins

Webber et al., 1998

Vesicle fusion

Vesicle fusion

Torelli-Tarelli et al., 1985

Membrane fusion

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

Where do we get the energy to bend the membranes?

Geometry

x

y

z

Model

Energy

Pore Reaction Coordinate

Phospholipids:
the forgotten molecules

Membrane self assembly

Surface tension

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

Electrical potential changes \( \gamma \):
Lippmann mercury voltmeter

\[ \gamma = \frac{\delta G}{\delta A/k_B T} \]
Voltage dependent membrane tension

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

Petvar & 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 $\gamma$:
Lippmann mercury voltmeter

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

A Gibbs adsorption equation for a polarizable interface,

\[ \gamma = -S \partial T - \Gamma \partial \mu - \sigma \partial E \]

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

\[ \sigma = \left( \frac{\partial \gamma}{\partial E} \right) \}

\[ \text{surface charge (C/m²)} \]  
\[ \text{surface tension (Nm)} \]  
\[ \text{electrical potential difference (V)} \]  
\[ \text{chemical potential (V)} \]  
\[ \text{temperature (K)} \]  
\[ \text{surface concentration one component (moles/m²)} \]  
\[ \text{interfacial entropy per unit area (JK/m²)} \]

-2

\[ \text{o} \]

\[ -2 \]

\[ \text{surface charge (C/m²)} \]

\[ -1 \]

\[ \text{surface tension (Nm)} \]

\[ \text{electrical potential difference (V)} \]

\[ \text{chemical potential (V)} \]

\[ \text{temperature (K)} \]

\[ \text{surface concentration one component (moles/m²)} \]

\[ \text{interfacial entropy per unit area (JK/m²)} \]

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\[ \text{chemical potential (V)} \]

\[ \text{temperature (K)} \]

\[ \text{surface concentration one component (moles/m²)} \]

\[ \text{interfacial entropy per unit area (JK/m²)} \]

Tension is a linear function of voltage under physiological conditions (\( \Delta V < 100 \text{ mV} \))

\[ T_V \approx \frac{(C_w) B_1 + B_2 (\Delta V)}{2} + C_{\sigma -} \Delta \sigma \]

Assume:

Physiological medium 0.14 M
External and internal surface charge -0.025 and -0.015 C/m²
Charging occurs by ions adsorbing onto or desorbing from
\( \Delta V = 100 \text{ mV} \)
Energy \( \approx \) Pore Area \( \times \) \( T_V \)
1000-5000 nm² \( \times \) 46 \( \mu \text{N/m} \)
10-50 kT

**Voltage Dependent Tension**

\[ \sigma = \frac{\partial \gamma}{\partial E} (\mu, T) \]

Integrate the Lippmann under these boundary conditions:

1. \( \sigma = \varepsilon \kappa, \kappa_1 \)
   \[ \kappa^2 = F \sum \frac{n_i^2}{ek RT} \]

2. At voltage \( \Delta V \)
   \[ \sigma = \gamma (\Delta V) \text{ and } \sigma = -\gamma (\Delta V) \text{ when } \gamma = \gamma (\Delta V) \]
   Upon polarization to voltage \( V_p \)
   \[ \sigma = -(\sigma_1 + q_1) \text{ and } \sigma = -(\sigma_2 + q_2) \text{ when } \gamma = \gamma (V_p) \]

\( \varepsilon \) Faraday’s constant; \( \kappa_1 \) concentration of species; \( \varepsilon \) valency of species; \( e \) gas constant;
\( \varepsilon \) permittivity of free space; \( \varepsilon \) dielectric constant of water; \( \varepsilon \) capacitance of double layer.

**Flexoelectricity:**

Coupling of membrane curvature with the electric field

characterized in biological membranes by Petrov

**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**

\[ U_f = \frac{e_0}{e_s} \left( \frac{f'}{e_s} - \frac{f''}{e_s} \right) \]

**OHC electromotility – the other membrane based motor**

**Collaborators**

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  Robert M. Raphael, Ph.D.

**Hofmeister effect**

Anion adsorption at membrane interface

\[ \text{di} - 8 - \text{ANEPPS} \]

Clarke & Lüpfert, 1999

\[ \text{SO}_4 > \text{SCN} > \text{I} > \text{NO}_3 > \text{Br} > \text{Cl} > \text{F} > \text{SO}_4 \]

Oliver et al., 2001

**Tension affects vesicle recycling**

Dai et al., 1997

**The synaptic amplifier**

Intrinsic tuning:
- electrical
- membrane cycling
Hyperpolarization & depolarization affect the charge on each interface

$$V(x) = \psi(-\infty) - \psi(0)$$
$$V = \psi(-\infty) - \psi(\infty) = \psi(-\infty)$$

$\Psi_t$: potential difference across the membrane
$V$: transmembrane potential difference

Hyperpolarization | Rest | Depolarization

- $\psi = \psi(-\delta) - \psi(0)$
- $V = \psi(-\infty) - \psi(\infty) = \psi(-\infty)$