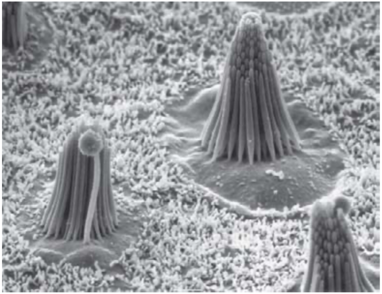
# Hearing

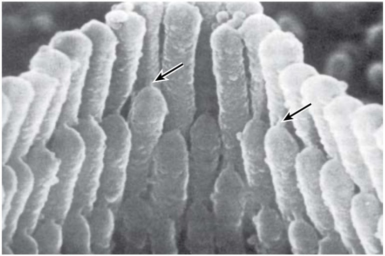
## Gating compliance during mechanoelectrical transduction

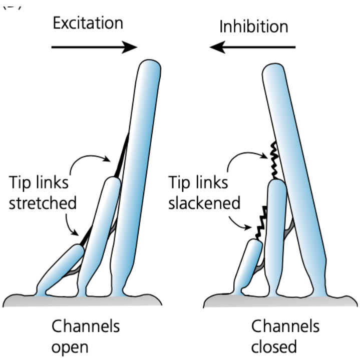
Aravi Samuel
David Zimmerman

Physics 141
Harvard University

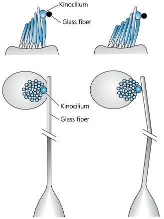
Week 10

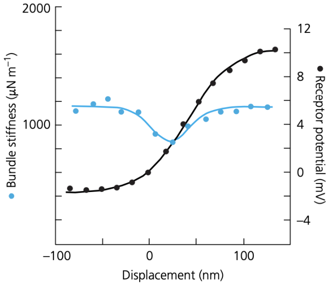







Do tip links transduce hair cell into force and displacement of mechanoelectrical channels?



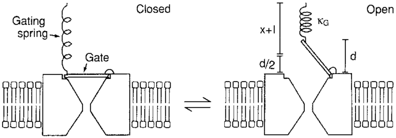

The stiffness of the hair bundle ($\mathbf{K_B}$ includes the stiffness of the stereociliary pivots ($\mathbf{K_S}$, the stiffness of the gating springs ($\mathbf{K_G}$, and a term that depends on the probability of the channel's being open:

$$\mathbf{K_B} = \mathbf{K_S} + \mathbf{K_G} - \frac{Nz^2 p(1-p)}{kT}$$

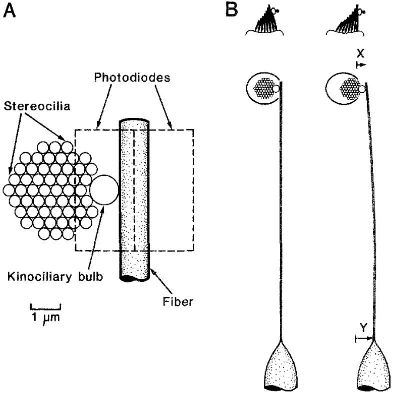
where $N$ is the number of channels and $z$ is the gating force of a single channel.

The steady-state probability of the channels' being open is a sigmoidal function of bundle displacement ($X$) and of the single-channel gating force:

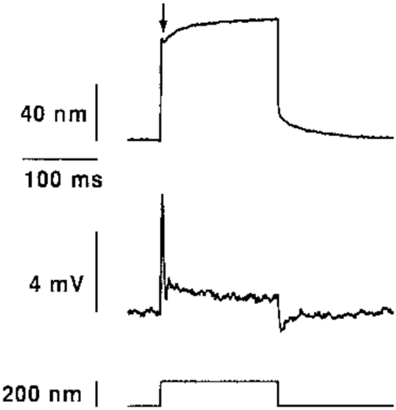
$$p = \frac{1}{1 + \exp\left[-\frac{z(X - X_O)}{kT}\right]}$$



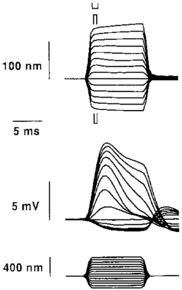

- The conductance of a transduction channel is regulated by a molecular gate that can assume only two positions, *open* and *closed*.
- Positive displacement of the hair bundle increases the tension in the gating spring, of stiffness $\boldsymbol{\kappa_G}$, which is attached to the gate.
- When the channel is closed, the spring is extended by a distance $x + d/2$ beyond its natural length, $l$. Opening of the channel shortens the spring by a distance $d$

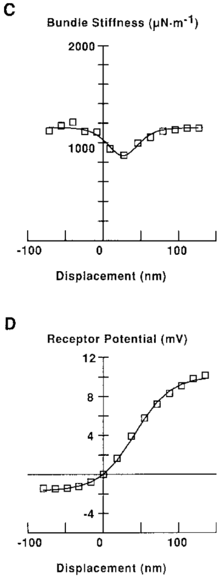



- A hair cell from the bullfrog was stimulated by displacing a fine glass fiber adhering to the tip of the kinocilium about 6.7 $\mu$m above the bundle's base.
- Displacement of the fiber base by $Y$ led to a displacement of the hair bundle by a distance $X$. The extent to which the calibrated fiber was bent ($Y - X$) provided a measure of stiffness

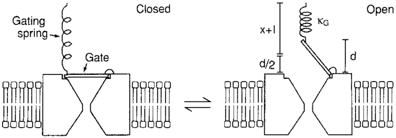



- Apply a force of about 70 nm
- Bundle moves rapidly about 74 nm
- A transient reversal or rebound quickly occurs
- Bundle relaxes to a new steady state with a time constant of 43 ms
- After force pulse, bundle relaxes to old steady state with a time constant of 43 ms






- Stiffness smaller over a roughly 125 nm range of displacements and was minimal at 26 nm positive to resting position
- Minimal stiffness was 290 $\mu$N/m smaller than the stiffness of 1150 $\mu$N/m when pushed far negative or far positive
- A transient reversal or rebound quickly occurs
- Displacement dependence of the peak of the simultaneously recorded receptor potential indicated that the transducer was most sensitive over the range of deflections for which the bundle was least stiff

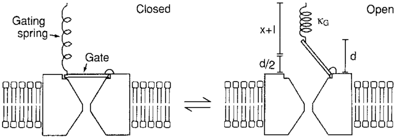



- Suppose that the gating spring has a stiffness $\kappa_G$. At a given displacement of the hair bundle, $x$ is the extension of the gating spring midway between the open and closed states
- When the channel is closed, the energy of the transduction element comprising the spring and channel is

$$g_c^0 = \frac{1}{2}\boldsymbol{\kappa_G}(x + d/2)^2 + \mu_c^0$$

- When the channel is open, the energy of the transduction element comprising the spring and channel is

$$g_o^0 = \frac{1}{2}\boldsymbol{\kappa_G}(x - d/2)^2 + \mu_o^0$$




- The energy difference between the open and closed states is

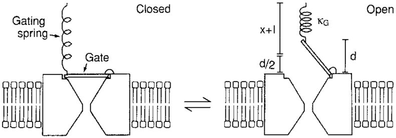
$$\Delta g^{o} = g^{o}_{o} - g^{o}_{c} = -\boldsymbol{\kappa_G} \times d \times x + \mu^{o}_{o} - \mu^{o}_{c}$$

- The probability ($p$) of finding the channel in the open state when the system is in equilibrium is given by the Bolzmann law:

$$p = \frac{1}{1 + \exp\left[-z(X - X_o)/kT\right]}$$

  where the single channel gating force is $z = \boldsymbol{\kappa_G} \times d \times \gamma$

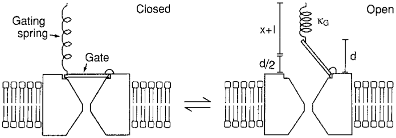
- The steady-state transduction current will be proportional to $p$




- The force exerted by a gating spring on its insertions is $f_c = \boldsymbol{\kappa_G}(x - d/2)$ when the channel is open and $f_o = \boldsymbol{\kappa_G}(x + d/2)$ when the channel is closed.
- The time average of the force exerted by one transduction element is thus

$$
\begin{aligned}
f &= pf_o + (1 - p)f_c \\
&= \boldsymbol{\kappa_G}(x + d/2) - \boldsymbol{\kappa_G} d \times p
\end{aligned}
$$

- Because of the lever ratio ($\gamma$) between spring elongation and bundle displacement, the force exerted at the tip of the bundle (and in the direction of bundle displacement) is $N\gamma f$

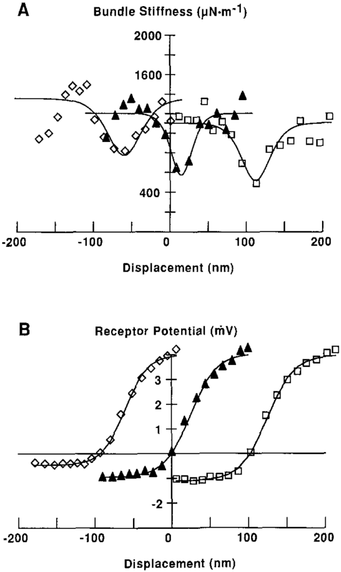



- The steady-state force required to hold the hair bundle at position $X$

  $$F = \mathbf{K_S}(X - X_S) + N\kappa_G\gamma(\gamma X + x_r + d/2) - Nzp$$

  in which $\mathbf{K_S}$ is the stiffness of the elastic components in parallel with the transduction elements such as the basal tapers and $X_s$ is the steady-state position in the absence of gating springs.
- Differentiation of $F$ with respect to $X$ gives the bundle stiffness:

  $$\mathbf{K_B} = \mathbf{K_S} + N\kappa_G\gamma^2 - Nz^2 p(1-p)/kT$$




- the position of the bundle's increased compliance should shift with the region of mechanosensitivity.
- a hair cell was stimulated by a family of force pulses to the hair cell's tip
- the experiment was repeated while the bundle was offset by positively or negatively directed stimuli that produced steady displacements of 103 nm and -93 nm
- gating compliance changes its position during adaptation