RESEARCH PAPER
Communicative & Integrative Biology 6:6, e26763; November/December; © 2013 Landes Bioscience

Falsification of the ionic channel theory of hair cell transduction

Michelangelo Rossetto*

New York, NY USA

Keywords: hair cell, transduction, ion channel, Nernst equation

The hair cell provides the transduction of mechanical vibrations in the balance and acoustic sense of all vertebrates that swim, walk, or fly. The current theory places hair cell transduction in a mechanically controlled ion channel. Although the theory of a mechanical input modulating the flow of ions through an ion pore has been a useful tool, it is falsified by experimental data in the literature and can be definitively falsified by a proposed experiment.

Presentation of the hypotheses

An ionic channel, or pore, in a membrane allows ions to flow from the more concentrated to the less concentrated side of the membrane. The Nernst equation rigorously describes the equilibrium state of 2 similar solutions of different concentrations separated by a barrier with ionic pores. We show how data in the literature is not compatible with transduction through an ion pore as defined by the Nernst equation. An experiment is proposed to definitively demonstrate the falsification of the concept of transduction through a mechanically controlled ion channel.

Testing the hypothesis

We propose a test that will definitively show the falsification of the current theory of hair cell transduction through an ion channel by comparing the reversal potential with the Nernst equilibrium potential with 2 different ionic concentrations in the cells environment.

Implications of the hypothesis

The falsification of the ionic theory of hair cell transduction will reopen the long-settled search for the hair cell mechanism underlying the sense of balance and the acoustic sense.

Background

In a sensory cell the equilibrium potential for a given ion can be determined experimentally by finding the reversal potential of transduction. The reversal potential is the membrane voltage where the transduction current is zero. That is, the voltage whose electrostatic repulsive force just balances the force driving ions through a membrane pore, which results from the concentration gradient across the membrane.[1] **Figure 1** is an illustration of such a measurement. The transduction current produced by a fixed mechanical vibration is plotted vs. the membrane potential, which is controlled and slowly scanned through a range of values.

In 1979, this first measurement of the reversal potential of a hair cell showed that the reversal potential of transduction of a hair cell was zero.[2] This measurement was made with 129 mM Na^+ in the external medium.

An ionic channel, or pore, in a membrane allows ions to flow from the more concentrated to the less concentrated side of the membrane. The Nernst equation, which can be derived from the Boltzman equation of statistical mechanics, rigorously describes the equilibrium state of 2 similar solutions of different concentrations separated by a barrier with ionic pores. Ions will flow down the concentration gradient until sufficient charge has passed to develop a voltage whose electrostatic repulsive force inhibits the ion from flowing down its gradient. This voltage, which stops the further flow of ions by means of electrostatic repulsion, is the equilibrium potential given by the Nernst Equation.[3] The measured reversal potential of a transducing cell is the Equilibrium Potential for that cell. The reversal potential must equal the computed equilibrium potential based on the opposing concentrations across the membrane.

Presentation of the hypothesis

The contradiction presented in this paper is found in the difference between the measured reversal potential and the computed equilibrium potential using the Nernst equation.

The Nernst equation describes the equilibrium state of 2 similar solutions of different concentrations separated by a barrier with ionic pores. The ions flow from the more concentrated to the less concentrated side. They flow down the concentration gradient until the charge that has passed develops a voltage inside the cell whose electrostatic repulsive force stops the ion from flowing down its gradient. This voltage, which stops the further flow of ions by means of electrostatic repulsion is the Equilibrium Potential, Es, given by the Nernst Equation:[3]

*Correspondence to: Michelangelo Rossetto; Email: marossetto@yahoo.com
Submitted: 09/26/2013; Accepted: 10/09/2013
Citation: Rossetto M. Falsification of the ionic channel theory of hair cell transduction. Communicative & Integrative Biology 2013; 6:e26763; http://dx.doi.org/10.4161/cib.26763

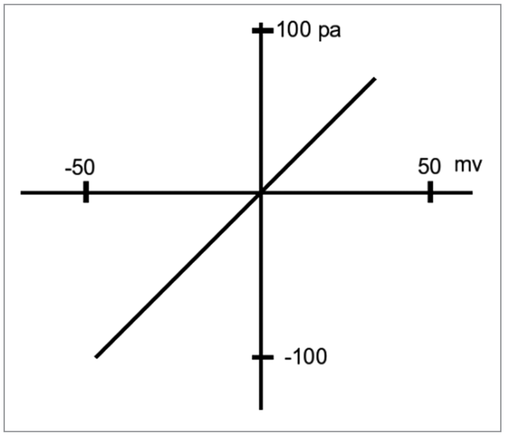

Figure 1. Transduction current vs. membrane voltage while a fixed mechanical input is applied to the hair cell. It is abstracted from Figure 2 of Reference 1, and it shows that the reversal potential of the hair cell is zero.

$$Es = \frac{RT}{ZF} \ln \frac{So}{Si}$$

Where for a cell:

So is the concentration of the ion outside the membrane of the cell

Si is the concentration of the ion inside the cell

R is the gas constant: 8.15 J/k/mol

T is temp in kelvin

T(K) = 273.16 + t (Celsius)

Z is the charge of the ion (valence)

F is the Faraday Constant: 9.648 × 10 exp4 Coulombs/ Mole

Ln is the natural log function

For a monovalent ion at 37 C

The term

(Eqn. 2)

$$\frac{RT}{ZF}$$

= 0.026 J/coulomb = 0.026 V

The ionic conditions of the hair cell measurements that revealed a reversal potential of zero were:

Na^+ outside the cell = 129 mM

Na^+ inside the cell = 12 mM

Applying the Nernst equation to the example listed above yields:

(Eqn. 3)

The Nernst equation predicts a reversal potential of 61 mV.

$$E_s = 26mv \ln \frac{124mMNa}{12mMNa} = 61mv$$

The measurement shows a reversal potential of 0 mV.

Testing the hypothesis

The question of whether or not an ion channel is involved in hair cell transduction can be easily and definitively addressed by repeating the Corey and Hudspeth 1979 experiment under 2 different conditions: first, with the original 124 mM Na^+ in the external fluid, which should give the same zero voltage reversal potential, and second: doubling the Na^+ concentration. Two-hundred-forty-eight mM Na^+ is placed in the external fluid, which should give different reversal voltage if the Nernst equation holds.

If the 2 measurements of reversal potential are the same, transduction cannot come from the action of an ion channel.

My prediction is that the reversal potential will remain at zero in violation of the Nernst equation and require a reevaluation of current transduction theory.[1]

Implications of the hypothesis

The failure of the hair cell to behave in the manner predicted by the Nernst equation presents a contradiction between theory and experiment that has remained unaddressed and unresolved for over a quarter century. The experimental data of zero reversal potential comes from highly respected sources and has been replicated.[4] The Nernst equation stems from basic scientific principles and is accepted as completely describing the behavior of ionic pores in a biological membrane. It is important to revisit this contradiction because it addresses the foundation of our understanding of ion channels on which the current theory of transduction through a nonspecific mechanically controlled ion pore is based.

There currently is a lot of active work being pursued in trying to understand the basic biophysical mechanisms that allow hair cells in some phyla to regenerate while others do not. If sensory problems at this level are ever to be unraveled it will be necessary to have a true understanding of all the biophysical processes involved.

The goal of this communication is succinctly expressed by a quote of Agatha Christie's fictional investigator Hercules Poirot:

> "Method, you comprehend! Method!
> Arrange your facts. Arrange your ideas.
> And if some little fact will not fit in-
> do not reject it but consider it closely.
> Though its significance escapes you,
> be sure that it is significant."[5]

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

References

1. Hill B. Ionic Channels of Excitable Membranes. Sunderland, MA: Sinaur Press, 1992
2. Corey DP, Hudspeth AJ. Ionic basis of the receptor potential in a vertebrate hair cell. Nature 1979; 281:675-7; PMID:45121; http://dx.doi.org/10.1038/281675a0
3. Alberts B. Molecular Biology of the Cell. New York: Garland Sciences, 2002:634
4. Holton T, Hudspeth AJ. The transduction channel of hair cells from the bull-frog characterized by noise analysis. J Physiol 1986; 375:195-227; PMID:2432221
5. Christie A. The Murder on the Links. New York: Dodd Mead, 1923