Can Membrane Proteins Drive a Cell?

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Unlike motilities in most cells, in which chemical energy is used by molecules associated with cytoskeletal proteins, the outer hair cell in the mammalian cochlea has a fast motility (Brownell et al. 1985) which is independent of ATP. This motility is membrane potential-dependent, a hyperpolarization being associated with an elongation. This cell is cylinder-shaped and is held at the two ends by other cells. The lateral wall has an extensive submembranous cisternae system, and distribution of actin is concentrated near the plasma membrane. It has been widely accepted that this cell serves as a feedback motor for the vibration of the basilar membrane, enhancing the sharpness of the tuning (de Boer 1991). The question of how this cell can play this role is being hotly debated.

Because the cisternae system is thought to be a Ca^{2+} store and is located next to the motile mechanism in the lateral wall, it is of interest how a change in the intracellular concentration of Ca^{2+}, a ubiquitous second messenger, affects this motility. We examined the sensitivity of this motility to $[Ca^{2+}]_{in}$ by applying ionomycin to the cell while monitoring both current and length changes elicited by square voltage pulses under whole-cell voltage clamp condition (Fig. 1). The membrane resistance serves as a good indicator of $[Ca^{2+}]_{in}$ because of the presence of Ca^{2+}-activated channels (Iwasa et al., 1991). A reduction in the membrane resistance is expected to reduce the amplitude of the voltage drop across the membrane during square pulses due to the presence of pipette resistance. If the motility is not affected by a rise in $[Ca^{2+}]_{in}$, the amplitude of the length change should thus decrease together with the voltage drop (Fig. 1, *solid line*). Although the amplitude of the length change decreases more than the amplitude of the voltage drop as the membrane resistance decreases, this motility does not show a sharp transition with respect to $[Ca^{2+}]_{in}$. Thus, we do not expect a significant direct effect of Ca^{2+} on this motility in the physiological range.

This membrane potential-dependent motility can be characterized by two kinds of experimental observations, observations on membrane elasticity and on the membrane motor. This is clarified further by constructing a biophysical model and examining whether this model can predict other properties of this motility. The elastic property of the cell is described by a membrane model with the cylindrical geometry and area- and shear moduli (Iwasa and Chadwick, 1992). A charge of the motor, which is transferred across the membrane, is determined by the voltage-dependent capacitance of the cell (Ashmore, 1990; Santos-Sacchi, 1991; Iwasa, 1993). An upper bound of the membrane area change of this motile element is determined, because the membrane capacitance decreased when a positive pressure was applied to the cell (Iwasa, 1993). It can be shown that the elastic element and the motor element are connected in series. Thus, apparent strains of the cell are represented by a sum of true elastic strains applied to the elastic element and changes due to motor molecules. With this model, it is possible to obtain isometric force and isotonic displacements of the cell (Iwasa, 1994). The model can predict the correct amplitude (up to 4% of the cell length) of the movement at load-free condition. The predicted value for isometric force, which is between 0.1 and 0.2 nN/mV, is also consistent with in vivo data. The number of these motor units per cell is consistent with the number of densely packed particles in the lateral plasma membrane. These observations indicate that the membrane potential-dependent motility of the outer hair cell is based on membrane motors that use electrical energy.

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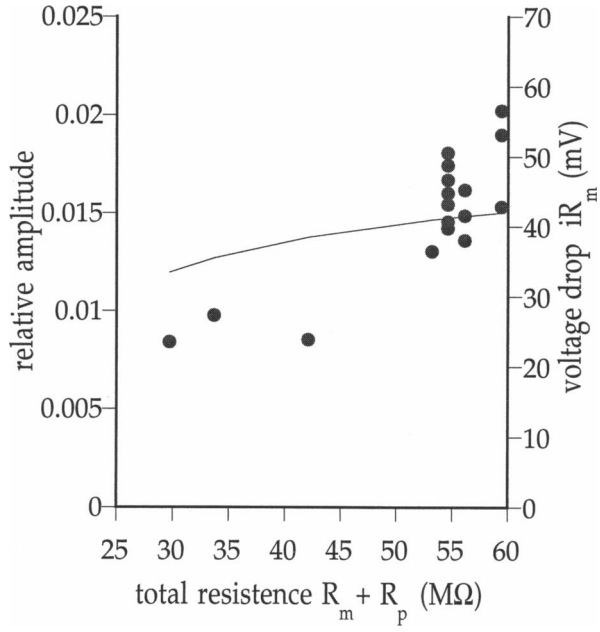

FIGURE 1 Dependence of length change amplitude on the membrane resistance. An outer hair cell was brought into the whole-cell recording mode with a patch pipette, and a train of hyperpolarizing pulses with 50.5 mV amplitude were applied under voltage-clamp condition. While ionomycin, a calcium ionophore, was applied to the bath, length change and membrane current i elicited by these pulses were recorded. A reduction in the membrane resistance was used as an indicator of the intracellular Ca^{2+} concentration because Ca^{2+}-activated currents are present in the cell. Because of the appreciable pipette resistance R_p (around 10 MΩ), the voltage drop $R_m \cdot i$ due to the constant voltage pulses reduced with decreasing membrane resistance R_m. The voltage drop across the membrane (——) and the amplitude of the length change (●) are plotted together. The bath medium was Na^+-rich and had 1.5 mM Ca^{2+}. Holding potential was −30 mV.

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