

MODELS OF HAIR CELL BUNDLE FUNCTIONING

Alexander V. Kondrachuk, Vasyl P. Lukomsky, Ivan S. Gandzha,
Institute of Physics, National Academy of Sciences, Kyiv, Ukraine;
kondr@kondr.kiev.ua / Fax: 38–044–2651589

Summary The model of the mechanoreceptor hair cell bundle (HCB) interaction with the moving viscoelastic gel was considered for two extreme cases: 1) the HCBs exactly follow the gel displacement; 2) stiff stereocilia and weak surrounding gel allow the motion of the bundle relative to the gel. The results suggest that the HCB structure is designed to reconstruct the temporal pattern of external acceleration from nonhomogeneous displacement (or its velocity) of the gel in the form of temporal pattern of cell depolarization.

Animals utilize sensory (vestibular, lateral-line, auditory) systems with hair cells to detect a variety of mechanical stimuli from their environment. The forces exerted on the hair cell (cilia) bundle (HCB) due to its interaction with the moving environment result in deformation of the HCB and stretching or shortening of the special fine strands located between stereocilia and called "tip-links". It leads to cell polarization that modulates neural activity of the afferent. The moving medium may be viscoelastic gel or viscous fluid. The HCB interaction with the moving environment is a key problem of sensory organs utilizing the HCBs. Three features of this system are common for all sensory organs with the HCBs: 1) there is a surface bordering the moving medium that results in spatial dependence of displacements (gel) or velocity (fluid) on the distance from the surface; 2) the HCBs protruding from this surface are embedded in this medium, 3) the heights of cilia are monotone varying. The present modeling is focused on the vestibular system, in particular, on an otolith organ that is responsible for perceiving linear accelerations. Transformation of the mechanical input in the chain: acceleration of otolithic membrane (OM)-displacement of the OM gel layer relative to macular surface-deflection of hair cell bundles located on this surface-deformation of the system of tip-links- formation of temporal pattern of polarization was studied using the simplified analytical models of these stages of conversion of mechanical stimulus into the HCB electrical response. The dynamic behavior of an otolithic membrane (OM) was considered using homogeneous viscoelastic (Kelvin-Voight) model of the OM (Fig.1). Let the acceleration vector (A) be parallel to the macular plane (x -axis). The dynamic equation for the displacements $U_x(z)$ of the OM gel may be written as [5]:

$$\rho_{om} \frac{\partial^2 U_x}{\partial t^2} = \frac{E}{2(1+\sigma)} \frac{\partial^2 U_x}{\partial z^2} + \mu \frac{\partial^3 U_x}{\partial t \partial z^2} + \Delta \rho A_x a(t/T); \quad U_x(z=0,t)=0, \quad dU_x/dz|_{z=h}=0 \quad (1)$$

where $\Delta \rho = \rho_{om} - \rho_{endolymph}$, σ is Poisson's ratio, E and μ are the Young's modulus and dynamical viscosity of the OM gel substance. $A(t) = A_0 a(t)$, A_0 is the magnitude of the OM acceleration.

Two alternative models of an "HCB-surrounding gel" interaction corresponding to extreme types of functioning of the HCB-gel system were analyzed [3,4]. In the Model 1 the HCBs passively follow gel deformation. This model suggests that: stereocilia are absolutely flexible and non-stretchable structures, the deformations of each stereocilium are independent, an existence of tip-links does not influence the deformation of the HCB, the structure of the HCB in a resting position may be approximated by a set of parallel stereocilia (Figs.1A, 1B); the result of mechanical stimulation of the OM is the change of lengths of the tip-links (l_i) corresponding to neighboring stereocilia. In this case, the time-dependent change of the tip-link lengths due to displacement of the gel will be determined by the trajectories of the points of gel corresponding to the ends of the tip-links between the neighboring stereocilia. Therefore, to find the dynamics of tip-links of stereocilia in the framework of this model, we have to determine the dependence of OM displacements ($U_x(z)$, Eq.1) on the distance from the macular plane, and then, to find the trajectories of the ends of tip-links between i - and $(i+1)$ - stereocilia.

Model 2 suggests that: the HCBs are rather stiff cylinders that can be bent only at the place of their fixation to the surface; their deflection due to the motion of viscous surrounding gel corresponds to the behavior of straight cylinders pivoting around their bases in the moving fluid [1], an existence of tip-links does not influence the deformation of the HCB. Thus due to the stiffness of HCB their deformation is controlled by viscous forces integrated over the length of cylinders and may not follow local deformation of surrounding gel. The deflection of this structure caused by viscous interaction with moving surrounding gel results in deformation of the HCB due to the shift of stereocilia rows relative to each other. Since the heights of the rows are different, their interaction with viscous gel and thus the angles of deflection will be different for these rows. Although the results of application of the model of the action of viscous fluid on straight cylinder (stereocilia) to the HCB-OM gel interaction are mainly qualitative, this simplified model discloses major frequency sensitive features of such interaction. The viscous force exerted on the bundle from surrounding gel is proportional to the velocity of gel displacement relative to the stereocilia. Assuming that the motion of the HCBs does not influence the motion of the OM, we can use the solution of Eq.1 to determine the viscous force deflecting the HCB. Since the velocity of gel is proportional to the time derivative of external acceleration, it implies that depending on mechanical properties of the HCB the system of the HCB-OM gel may record either external acceleration or time variation of this acceleration, if the mechanism of depolarization formation in these two types of the HCBs is the same.

It is assumed [3] that in mechanoelectrical transduction process tip-link tensions produce cell depolarization, which is proportional to the number of open channels. We formulated the following simplified model of cell depolarization kinetics: the elongation of tip-links occurs due to stereocilia deflection; the critical (threshold) elongation triggers the

opening of ion-channel that results in generating cell depolarization (signal) of unit amplitude; the signal remains constant until the elongation exceeds the threshold value a_c ; the cell depolarization $F(t)$ is proportional to the sum of signals produced by all ion channels open at the time t . Figs.1C,1D illustrate the result of calculations corresponding to Model 1 in the case of periodic stimulation of the OM. This is simplified imitation of the experiment [2].

The results of modeling show that: 1) depending on its parameters the system "HCB-OM gel" may function as an accelerometer (Model 1-the case of strong gel-HCB interaction) or measures the time derivative of external acceleration (Model 2-the case of weak gel-HCB interaction); 2) the following hypothesis may be proposed: the HCB structure with stereocilia of varying heights is designed to transform the temporal pattern of external acceleration (or its time derivative) to temporal pattern of cell depolarization by measuring spatial distribution of displacements (or velocities) of gel caused by this acceleration near the surface.

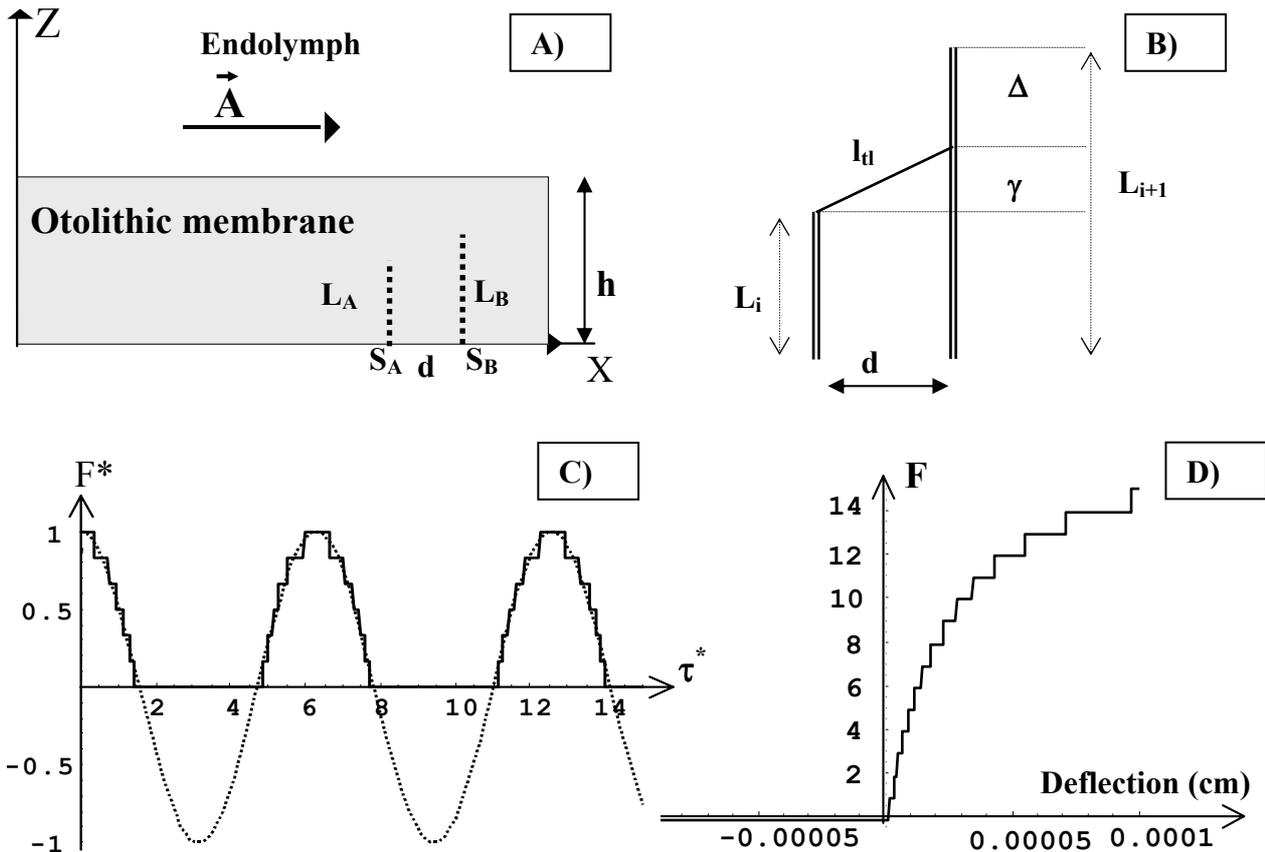


Fig.1. A) Model structure of otolithic membrane: h is the thickness of gel layer ($\sim 30\mu\text{m}$), d is the distance ($\sim 1\mu\text{m}$) between the bases of stereocilia (S_A and S_B), L is stereocilia length ($\sim 5\text{-}20\mu\text{m}$). B) Simplified structure of the hair cell bundle; l_{ti} is the tip-link length. C) Kinetics of depolarization F^* in Model 1 (F^* denotes $F(t)$ normalized to 1). Dotted lines are for gel displacements $\varphi(\tau^*) = \cos(\tau^*)$, $\tau^* = t/T_2$. Firm lines are for depolarization when the thresholds of tip-links triggering are linear function of stereocilium number i : $a_c = a_0(1 + \nu i)$ ($a_0 = 10^{-9}\text{m}$, $\nu = 3$, $L_0/h = 0.5$, number of stereocilia $k = 20$). D) The dependence of the number of activated tip-links (F) on the deflection of longest stereocilia if $\varphi(\tau^*) = \cos(\tau^*)$.

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