Année de publication : 2009

P-Y Plaçais, M Balland, T Guérin, J-F Joanny, P Martin (2009 Jun 23)

Spontaneous oscillations of a minimal actomyosin system under elastic loading.

Physical review letters : 158102

Résumé

Spontaneous mechanical oscillations occur in various types of biological systems where groups of motor molecules are elastically coupled to their environment. By using an optical trap to oppose the gliding motion of a single bead-tailed actin filament over a substrate densely coated with myosin motors, we mimicked this condition in vitro. We show that this minimal actomyosin system can oscillate spontaneously. Our finding accords quantitatively with a general theoretical framework where oscillatory instabilities emerge generically from the collective dynamics of molecular motors under load.

Année de publication : 2007

Jean-Yves Tinevez, Frank Jülicher, Pascal Martin (2007 Aug 17)

Unifying the various incarnations of active hair-bundle motility by the vertebrate hair cell.

Biophysical journal : 4053-67

Résumé

The dazzling sensitivity and frequency selectivity of the vertebrate ear rely on mechanical amplification of the hair cells’ responsiveness to small stimuli. As revealed by spontaneous oscillations and forms of mechanical excitability in response to force steps, the hair bundle that adorns each hair cell is both a mechanosensory antenna and a force generator that might participate in the amplificatory process. To study the various incarnations of active hair-bundle motility, we combined Ca(2+) iontophoresis with mechanical stimulation of single hair bundles from the bullfrog’s sacculus. We identified three classes of active hair-bundle movements: a hair bundle could be quiescent but display nonmonotonic twitches in response to either excitatory or inhibitory force steps, or oscillate spontaneously. Extracellular Ca(2+) changes could affect the kinetics of motion and, when large enough, evoke transitions between the three classes of motility. We found that the Ca(2+)-dependent location of a bundle’s operating point within its force-displacement relation controlled the type of movement observed. In response to an iontophoretic pulse of Ca(2+) or of a Ca(2+) chelator, a hair bundle displayed a movement whose polarity could be reversed by applying a static bias to the bundle’s position at rest. Moreover, such polarity reversal was accompanied by a 10-fold change in the kinetics of the Ca(2+)-evoked hair-bundle movement. A unified theoretical description, in which mechanical activity stems solely from myosin-based adaptation, could account for the fast and slow manifestations of active hair-bundle motility observed in frog, as well as in auditory organs of the turtle and the rat.

Année de publication : 2004

Björn Nadrowski, Pascal Martin, Frank Jülicher (2004 Aug 11)

Active hair-bundle motility harnesses noise to operate near an optimum of mechanosensitivity.

Proceedings of the National Academy of Sciences of the United States of America : 12195-200

Résumé

The ear relies on nonlinear amplification to enhance its sensitivity and frequency selectivity to oscillatory mechanical stimuli. It has been suggested that this active process results from the operation of dynamical systems that operate in the vicinity of an oscillatory instability, a Hopf bifurcation. In the bullfrog’s sacculus, a hair cell can display spontaneous oscillations of its mechanosensory hair bundle. The behavior of an oscillatory hair bundle resembles that of a critical oscillator. We present here a theoretical description of the effects of intrinsic noise on active hair-bundle motility. An oscillatory instability can result from the interplay between a region of negative stiffness in the bundle’s force-displacement relation and the Ca(2+)-regulated activity of molecular motors. We calculate a state diagram that describes the possible dynamical states of the hair bundle in the absence of fluctuations. Taking into account thermal fluctuations, the stochastic nature of transduction channels’ gating, and of the forces generated by molecular motors, we discuss conditions that yield a response function and spontaneous noisy movements of the hair bundle in quantitative agreement with previously published experiments. We find that the magnitude of the fluctuations resulting from the active processes that mediate mechanical amplification remains just below that of thermal fluctuations. Fluctuations destroy the phase coherence of spontaneous oscillations and restrict the bundle’s sensitivity as well as frequency selectivity to small oscillatory stimuli. We show, however, that a hair bundle studied experimentally operates near an optimum of mechanosensitivity in our state diagram.

Année de publication : 2003

Pascal Martin, D Bozovic, Y Choe, A J Hudspeth (2003 Jun 14)

Spontaneous oscillation by hair bundles of the bullfrog’s sacculus.

The Journal of neuroscience : the official journal of the Society for Neuroscience : 4533-48

Résumé

One prominent manifestation of mechanical activity in hair cells is spontaneous otoacoustic emission, the unprovoked emanation of sound by an internal ear. Because active hair bundle motility probably constitutes the active process of nonmammalian hair cells, we investigated the ability of hair bundles in the bullfrog’s sacculus to produce oscillations that might underlie spontaneous otoacoustic emissions. When maintained in the normal ionic milieu of the ear, many bundles oscillated spontaneously through distances as great as 80 nm at frequencies of 5-50 Hz. Whole-cell recording disclosed that the positive phase of movement was associated with the opening of transduction channels. Gentamicin, which blocks transduction channels, reversibly arrested oscillation; drugs that affect the cAMP phosphorylation pathway and might influence the activity of myosin altered the rate of oscillation. Increasing the Ca 2+ concentration rendered oscillations faster and smaller until they were suppressed; lowering the Ca 2+ concentration moderately with chelators had the opposite effect. When a bundle was offset with a stimulus fiber, oscillations were transiently suppressed but gradually resumed. Loading a bundle by partial displacement clamping, which simulated the presence of the accessory structures to which a bundle is ordinarily attached, increased the frequency and diminished the magnitude of oscillation. These observations accord with a model in which oscillations arise from the interplay of the hair bundle’s negative stiffness with the activity of adaptation motors and with Ca 2+-dependent relaxation of gating springs.

Année de publication : 2001

P Martin, A J Hudspeth (2001 Nov 29)

Compressive nonlinearity in the hair bundle’s active response to mechanical stimulation.

Proceedings of the National Academy of Sciences of the United States of America : 14386-91

Résumé

The auditory system’s ability to interpret sounds over a wide range of amplitudes rests on the nonlinear responsiveness of the ear. Whether measured by basilar-membrane vibration, nerve-fiber activity, or perceived loudness, the ear is most sensitive to small signals and grows progressively less responsive as stimulation becomes stronger. Seeking a correlate of this behavior at the level of mechanoelectrical transduction, we examined the responses of hair bundles to direct mechanical stimulation. As reported by the motion of an attached glass fiber, an active hair bundle from the bullfrog’s sacculus oscillates spontaneously. Sinusoidal movement of the fiber’s base by as little as +/-1 nm, corresponding to the application at the bundle’s top of a force of +/-0.3 pN, causes detectable phase-locking of the bundle’s oscillations to the stimulus. Although entrainment increases as the stimulus grows, the amplitude of the hair-bundle movement does not rise until phase-locking is nearly complete. A bundle is most sensitive to stimulation at its frequency of spontaneous oscillation. Far from that frequency, the sensitivity of an active hair bundle resembles that of a passive bundle. Over most of its range, an active hair bundle’s response grows as the one-third power of the stimulus amplitude; the bundle’s sensitivity declines accordingly in proportion to the negative two-thirds power of the excitation. This scaling behavior, also found in the response of the mammalian basilar membrane to sound, signals the operation of an amplificatory process at the brink of an oscillatory instability, a Hopf bifurcation.

P Martin, A J Hudspeth, F Jülicher (2001 Nov 29)

Comparison of a hair bundle’s spontaneous oscillations with its response to mechanical stimulation reveals the underlying active process.

Proceedings of the National Academy of Sciences of the United States of America : 14380-5

Résumé

Hearing relies on active filtering to achieve exquisite sensitivity and sharp frequency selectivity. In a quiet environment, the ears of many vertebrates become unstable and emit one to several tones. These spontaneous otoacoustic emissions, the most striking manifestation of the inner ear’s active process, must result from self-sustained mechanical oscillations of aural constituents. The mechanoreceptive hair bundles of hair cells in the bullfrog’s sacculus have the ability to amplify mechanical stimuli and oscillate spontaneously. By comparing a hair bundle’s spontaneous oscillations with its response to small mechanical stimuli, we demonstrate a breakdown in a general principle of equilibrium thermodynamics, the fluctuation-dissipation theorem. We thus confirm that a hair bundle’s spontaneous movements are produced by energy-consuming elements within the hair cell. To characterize the dynamical behavior of the active process, we introduce an effective temperature that, for each frequency component, quantifies a hair bundle’s deviation from thermal equilibrium. The effective temperature diverges near the bundle’s frequency of spontaneous oscillation. This behavior, which is not generic for active oscillators, can be accommodated by a simple model that characterizes quantitatively the fluctuations of the spontaneous movements as well as the hair bundle’s linear response function.

Année de publication : 2000

A J Hudspeth, Y Choe, A D Mehta, P Martin (2000 Oct 26)

Putting ion channels to work: mechanoelectrical transduction, adaptation, and amplification by hair cells.

Proceedings of the National Academy of Sciences of the United States of America : 11765-72

Résumé

As in other excitable cells, the ion channels of sensory receptors produce electrical signals that constitute the cellular response to stimulation. In photoreceptors, olfactory neurons, and some gustatory receptors, these channels essentially report the results of antecedent events in a cascade of chemical reactions. The mechanoelectrical transduction channels of hair cells, by contrast, are coupled directly to the stimulus. As a consequence, the mechanical properties of these channels shape our hearing process from the outset of transduction. Channel gating introduces nonlinearities prominent enough to be measured and even heard. Channels provide a feedback signal that controls the transducer’s adaptation to large stimuli. Finally, transduction channels participate in an amplificatory process that sensitizes and sharpens hearing.

P Martin, A D Mehta, A J Hudspeth (2000 Oct 12)

Negative hair-bundle stiffness betrays a mechanism for mechanical amplification by the hair cell.

Proceedings of the National Academy of Sciences of the United States of America : 12026-31

Résumé

Hearing and balance rely on the ability of hair cells in the inner ear to sense miniscule mechanical stimuli. In each cell, sound or acceleration deflects the mechanosensitive hair bundle, a tuft of rigid stereocilia protruding from the cell’s apical surface. By altering the tension in gating springs linked to mechanically sensitive transduction channels, this deflection changes the channels’ open probability and elicits an electrical response. To detect weak stimuli despite energy losses caused by viscous dissipation, a hair cell can use active hair-bundle movement to amplify its mechanical inputs. This amplificatory process also yields spontaneous bundle oscillations. Using a displacement-clamp system to measure the mechanical properties of individual hair bundles from the bullfrog’s ear, we found that an oscillatory bundle displays negative slope stiffness at the heart of its region of mechanosensitivity. Offsetting the hair bundle’s position activates an adaptation process that shifts the region of negative stiffness along the displacement axis. Modeling indicates that the interplay between negative bundle stiffness and the motor responsible for mechanical adaptation produces bundle oscillation similar to that observed. Just as the negative resistance of electrically excitable cells and of tunnel diodes can be embedded in a biasing circuit to amplify electrical signals, negative stiffness can be harnessed to amplify mechanical stimuli in the ear.

Année de publication : 1999

P Martin, A J Hudspeth (1999 Dec 10)

Active hair-bundle movements can amplify a hair cell’s response to oscillatory mechanical stimuli.

Proceedings of the National Academy of Sciences of the United States of America : 14306-11

Résumé

To enhance their mechanical sensitivity and frequency selectivity, hair cells amplify the mechanical stimuli to which they respond. Although cell-body contractions of outer hair cells are thought to mediate the active process in the mammalian cochlea, vertebrates without outer hair cells display highly sensitive, sharply tuned hearing and spontaneous otoacoustic emissions. In these animals the amplifier must reside elsewhere. We report physiological evidence that amplification can stem from active movement of the hair bundle, the hair cell’s mechanosensitive organelle. We performed experiments on hair cells from the sacculus of the bullfrog. Using a two-compartment recording chamber that permits exposure of the hair cell’s apical and basolateral surfaces to different solutions, we examined active hair-bundle motion in circumstances similar to those in vivo. When the apical surface was bathed in artificial endolymph, many hair bundles exhibited spontaneous oscillations of amplitudes as great as 50 nm and frequencies in the range 5 to 40 Hz. We stimulated hair bundles with a flexible glass probe and recorded their mechanical responses with a photometric system. When the stimulus frequency lay within a band enclosing a hair cell’s frequency of spontaneous oscillation, mechanical stimuli as small as +/-5 nm entrained the hair-bundle oscillations. For small stimuli, the bundle movement was larger than the stimulus. Because the energy dissipated by viscous drag exceeded the work provided by the stimulus probe,

the hair bundles powered their motion and therefore amplified it.