Année de publication : 2020

R G Alonso, M Tobin, P Martin, A J Hudspeth (2020 Nov 17)

Fast recovery of disrupted tip links induced by mechanical displacement of hair bundles.

Proceedings of the National Academy of Sciences of the United States of America : 30722-30727 : DOI : 10.1073/pnas.2016858117

Résumé

Hearing and balance rely on the capacity of mechanically sensitive hair bundles to transduce vibrations into electrical signals that are forwarded to the brain. Hair bundles possess tip links that interconnect the mechanosensitive stereocilia and convey force to the transduction channels. A dimer of dimers, each of these links comprises two molecules of protocadherin 15 (PCDH15) joined to two of cadherin 23 (CDH23). The « handshake » that conjoins the four molecules can be disrupted in vivo by intense stimulation and in vitro by exposure to Ca chelators. Using hair bundles from the rat's cochlea and the bullfrog's sacculus, we observed that extensive recovery of mechanoelectrical transduction, hair bundle stiffness, and spontaneous bundle oscillation can occur within seconds after Ca chelation, especially if hair bundles are deflected toward their short edges. Investigating the phenomenon in a two-compartment ionic environment that mimics natural conditions, we combined iontophoretic application of a Ca chelator to selectively disrupt the tip links of individual frog hair bundles with displacement clamping to control hair bundle motion and measure forces. Our observations suggest that, after the normal Ca concentration has been restored, mechanical stimulation facilitates the reconstitution of functional tip links.

Année de publication : 2019

Mathieu Richard, Carles Blanch-Mercader, Hajer Ennomani, Wenxiang Cao, Enrique M De La Cruz, Jean-François Joanny, Frank Jülicher, Laurent Blanchoin, Pascal Martin (2019 Jul 11)

Active cargo positioning in antiparallel transport networks.

Proceedings of the National Academy of Sciences of the United States of America : DOI : 10.1073/pnas.1900416116

Résumé

Cytoskeletal filaments assemble into dense parallel, antiparallel, or disordered networks, providing a complex environment for active cargo transport and positioning by molecular motors. The interplay between the network architecture and intrinsic motor properties clearly affects transport properties but remains poorly understood. Here, by using surface micropatterns of actin polymerization, we investigate stochastic transport properties of colloidal beads in antiparallel networks of overlapping actin filaments. We found that 200-nm beads coated with myosin Va motors displayed directed movements toward positions where the net polarity of the actin network vanished, accumulating there. The bead distribution was dictated by the spatial profiles of local bead velocity and diffusion coefficient, indicating that a diffusion-drift process was at work. Remarkably, beads coated with heavy-mero-myosin II motors showed a similar behavior. However, although velocity gradients were steeper with myosin II, the much larger bead diffusion observed with this motor resulted in less precise positioning. Our observations are well described by a 3-state model, in which active beads locally sense the net polarity of the network by frequently detaching from and reattaching to the filaments. A stochastic sequence of processive runs and diffusive searches results in a biased random walk. The precision of bead positioning is set by the gradient of net actin polarity in the network and by the run length of the cargo in an attached state. Our results unveiled physical rules for cargo transport and positioning in networks of mixed polarity.

Mélanie Tobin, Atitheb Chaiyasitdhi, Vincent Michel, Nicolas Michalski, Pascal Martin (2019 Apr 2)

Stiffness and tension gradients of the hair cell's tip-link complex in the mammalian cochlea.

eLife : DOI : 10.7554/eLife.43473

Résumé

Sound analysis by the cochlea relies on frequency tuning of mechanosensory hair cells along a tonotopic axis. To clarify the underlying biophysical mechanism, we have investigated the micromechanical properties of the hair cell's mechanoreceptive hair bundle within the apical half of the rat cochlea. We studied both inner and outer hair cells, which send nervous signals to the brain and amplify cochlear vibrations, respectively. We find that tonotopy is associated with gradients of stiffness and resting mechanical tension, with steeper gradients for outer hair cells, emphasizing the division of labor between the two hair-cell types. We demonstrate that tension in the tip links that convey force to the mechano-electrical transduction channels increases at reduced Ca. Finally, we reveal gradients in stiffness and tension at the level of a single tip link. We conclude that mechanical gradients of the tip-link complex may help specify the characteristic frequency of the hair cell.

Année de publication : 2018

Jérémie Barral, Frank Jülicher, Pascal Martin (2018 Feb 6)

Friction from Transduction Channels' Gating Affects Spontaneous Hair-Bundle Oscillations.

Biophysical journal : 425-436 : DOI : S0006-3495(17)31251-1

Résumé

Hair cells of the inner ear can power spontaneous oscillations of their mechanosensory hair bundle, resulting in amplification of weak inputs near the characteristic frequency of oscillation. Recently, dynamic force measurements have revealed that delayed gating of the mechanosensitive ion channels responsible for mechanoelectrical transduction produces a friction force on the hair bundle. The significance of this intrinsic source of dissipation for the dynamical process underlying active hair-bundle motility has remained elusive. The aim of this work is to determine the role of friction in spontaneous hair-bundle oscillations. To this end, we characterized key oscillation properties over a large ensemble of individual hair cells and measured how viscosity of the endolymph that bathes the hair bundles affects these properties. We found that hair-bundle movements were too slow to be impeded by viscous drag only. Moreover, the oscillation frequency was only marginally affected by increasing endolymph viscosity by up to 30-fold. Stochastic simulations could capture the observed behaviors by adding a contribution to friction that was 3-8-fold larger than viscous drag. The extra friction could be attributed to delayed changes in tip-link tension as the result of the finite activation kinetics of the transduction channels. We exploited our analysis of hair-bundle dynamics to infer the channel activation time, which was ~1 ms. This timescale was two orders-of-magnitude shorter than the oscillation period. However, because the channel activation time was significantly longer than the timescale of mechanical relaxation of the hair bundle, channel kinetics affected hair-bundle dynamics. Our results suggest that friction from channel gating affects the waveform of oscillation and that the channel activation time can tune the characteristic frequency of the hair cell. We conclude that the kinetics of transduction channels' gating plays a fundamental role in the dynamic process that shapes spontaneous hair-bundle oscillations.

Année de publication : 2014

Pascal Martin (2014 Aug 21)

All that jazz coming out of my ears.

Biophysical journal : 800-2 : DOI : 10.1016/j.bpj.2014.07.011

Résumé

Volker Bormuth, Jérémie Barral, Jean-François Joanny, Frank Jülicher, Pascal Martin (2014 May 5)

Transduction channels' gating can control friction on vibrating hair-cell bundles in the ear.

Proceedings of the National Academy of Sciences of the United States of America : 7185-90 : DOI : 10.1073/pnas.1402556111

Résumé

Hearing starts when sound-evoked mechanical vibrations of the hair-cell bundle activate mechanosensitive ion channels, giving birth to an electrical signal. As for any mechanical system, friction impedes movements of the hair bundle and thus constrains the sensitivity and frequency selectivity of auditory transduction. Friction is generally thought to result mainly from viscous drag by the surrounding fluid. We demonstrate here that the opening and closing of the transduction channels produce internal frictional forces that can dominate viscous drag on the micrometer-sized hair bundle. We characterized friction by analyzing hysteresis in the force-displacement relation of single hair-cell bundles in response to periodic triangular stimuli. For bundle velocities high enough to outrun adaptation, we found that frictional forces were maximal within the narrow region of deflections that elicited significant channel gating, plummeted upon application of a channel blocker, and displayed a sublinear growth for increasing bundle velocity. At low velocity, the slope of the relation between the frictional force and velocity was nearly fivefold larger than the hydrodynamic friction coefficient that was measured when the transduction machinery was decoupled from bundle motion by severing tip links. A theoretical analysis reveals that channel friction arises from coupling the dynamics of the conformational change associated with channel gating to tip-link tension. Varying channel properties affects friction, with faster channels producing smaller friction. We propose that this intrinsic source of friction may contribute to the process that sets the hair cell's characteristic frequency of responsiveness.

Année de publication : 2012

L Dinis, P Martin, J Barral, J Prost, J F Joanny (2012 Dec 11)

Fluctuation-response theorem for the active noisy oscillator of the hair-cell bundle.

Physical review letters : 160602

Résumé

The hair bundle of sensory cells in the vertebrate ear provides an example of a noisy oscillator close to a Hopf bifurcation. The analysis of the data from both spontaneous and forced oscillations shows a strong violation of the fluctuation-dissipation theorem, revealing the presence of an underlying active process that keeps the system out of equilibrium. Nevertheless, we show that a generalized fluctuation-dissipation theorem, valid for nonequilibrium steady states, is fulfilled within the limits of our experimental accuracy and computational approximations, when the adequate conjugate degrees of freedom are chosen.

Jérémie Barral, Pascal Martin (2012 May 3)

Phantom tones and suppressive masking by active nonlinear oscillation of the hair-cell bundle.

Proceedings of the National Academy of Sciences of the United States of America : E1344-51 :

DOI : 10.1073/pnas.1202426109

Résumé

Processing of two-tone stimuli by the auditory system introduces prominent masking of one frequency component by the other as well as additional « phantom » tones that are absent in the sound input. Mechanical correlates of these psychophysical phenomena have been observed in sound-evoked mechanical vibrations of the mammalian cochlea and are thought to originate in sensory hair cells from the intrinsic nonlinearity associated with mechano-electrical transduction by ion channels. However, nonlinearity of the transducer is not sufficient to explain the rich phenomenology of two-tone interferences in hearing. Here we show that active oscillatory movements of single hair-cell bundles elicit two-tone suppression and distortions that are shaped by nonlinear amplification of periodic stimuli near the characteristic frequency of spontaneous oscillations. When both stimulus frequencies enter the bandwidth of the hair-bundle amplifier, two-tone interferences display level functions that are characteristic both of human psychoacoustics and of in vivo mechanical measurements in auditory organs. Our work distinguishes the frequency-dependent nonlinearity that emerges from the active process that drives the hair bundle into spontaneous oscillations from the passive nonlinear compliance associated with the direct gating of transduction channels by mechanical force. Numerical simulations based on a generic description of an active dynamical system poised near an oscillatory instability–a Hopf bifurcation–account quantitatively for our experimental observations. In return, we conclude that the properties of two-tone interferences in hearing betray the workings of self-sustained « critical » oscillators, which function as nonlinear amplifying elements in the inner ear.

Année de publication : 2011

Jérémie Barral, Pascal Martin (2011 Aug 10)

The physical basis of active mechanosensitivity by the hair-cell bundle.

Current opinion in otolaryngology & head and neck surgery : 369-75 : DOI : 10.1097/MOO.0b013e32834a8c33

Résumé

Hearing starts with the deflection of the hair bundle that sits on top of each mechanosensory hair cell. Recent advances indicate that the hair bundle mechanically amplifies its inputs to participate in the active process that boosts the ear's technical specifications. This review integrates experimental and modeling studies to dissect the mechanisms of active mechanosensation by the hair-cell bundle.

Année de publication : 2010

J Ashmore, P Avan, W E Brownell, P Dallos, K Dierkes, R Fettiplace, K Grosh, C M Hackney, A J Hudspeth, F Jülicher, B Lindner, P Martin, J Meaud, C Petit, J Santos-Sacchi, J R Santos Sacchi, B Canlon (2010 Jun 15)

The remarkable cochlear amplifier.

Hearing research : 1-17 : DOI : 10.1016/j.heares.2010.05.001

Résumé

This composite article is intended to give the experts in the field of cochlear mechanics an opportunity to voice their personal opinion on the one mechanism they believe dominates cochlear amplification in mammals. A collection of these ideas are presented here for the auditory community and others interested in the cochlear amplifier. Each expert has given their own personal view on the topic and at the end of their commentary they have suggested several experiments that would be required for the decisive mechanism underlying the cochlear amplifier. These experiments are presently lacking but if successfully performed would have an enormous impact on our understanding of the cochlear amplifier.

A J Hudspeth, Frank Jülicher, Pascal Martin (2010 Jun 10)

A critique of the critical cochlea: Hopf–a bifurcation–is better than none.

Journal of neurophysiology : 1219-29 : DOI : 10.1152/jn.00437.2010

Résumé

The sense of hearing achieves its striking sensitivity, frequency selectivity, and dynamic range through an active process mediated by the inner ear’s mechanoreceptive hair cells. Although the active process renders hearing highly nonlinear and produces a wealth of complex behaviors, these various characteristics may be understood as consequences of a simple phenomenon: the Hopf bifurcation. Any critical oscillator operating near this dynamic instability manifests the properties demonstrated for hearing: amplification with a specific form of compressive nonlinearity and frequency tuning whose sharpness depends on the degree of amplification. Critical oscillation also explains spontaneous otoacoustic emissions as well as the spectrum and level dependence of the ear’s distortion products. Although this has not been realized, several valuable theories of cochlear function have achieved their success by incorporating critical oscillators.

Jérémie Barral, Kai Dierkes, Benjamin Lindner, Frank Jülicher, Pascal Martin (2010 Apr 19)

Coupling a sensory hair-cell bundle to cyber clones enhances nonlinear amplification.

Proceedings of the National Academy of Sciences of the United States of America : 8079-84 : DOI : 10.1073/pnas.0913657107

Résumé

The vertebrate ear benefits from nonlinear mechanical amplification to operate over a vast range of sound intensities. The amplificatory process is thought to emerge from active force production by sensory hair cells. The mechano-sensory hair bundle that protrudes from the apical surface of each hair cell can oscillate spontaneously and function as a frequency-selective, nonlinear amplifier. Intrinsic fluctuations, however, jostle the response of a single hair bundle to weak stimuli and seriously limit amplification. Most hair bundles are mechanically coupled by overlying gelatinous structures. Here, we assayed the effects of mechanical coupling on the hair-bundle amplifier by combining dynamic force clamp of a hair bundle from the bullfrog’s saccule with real-time stochastic simulations of hair-bundle mechanics. This setup couples the hair bundle to two virtual hair bundles, called cyber clones, and mimics a situation in which the hair bundle is elastically linked to two neighbors with similar characteristics. We found that coupling increased the coherence of spontaneous hair-bundle oscillations. By effectively reducing noise, the synergic interplay between the hair bundle and its cyber clones also enhanced amplification of sinusoidal stimuli. All observed effects of coupling were in quantitative agreement with simulations. We argue that the auditory amplifier relies on hair-bundle cooperation to overcome intrinsic noise limitations and achieve high sensitivity and sharp frequency selectivity.

Thomas Guérin, Jacques Prost, Pascal Martin, Jean-François Joanny (2010 Jan 16)

Coordination and collective properties of molecular motors: theory.

Current opinion in cell biology : 14-20 : DOI : 10.1016/j.ceb.2009.12.012

Résumé

Many cellular processes require molecular motors to produce motion and forces. Single molecule experiments have led to a precise description of how a motor works. Under most physiological conditions, however, molecular motors operate in groups. Interactions between motors yield collective behaviors that cannot be explained only from single molecule properties. The aim of this paper is to review the various theoretical descriptions that explain the emergence of collective effects in molecular motor assemblies. These include bidirectional motion, hysteretic behavior, spontaneous oscillations, and self-organization into dynamical structures. We discuss motors acting on the cytoskeleton both in a prescribed geometry such as in muscles or flagella and in the cytoplasm.

Année de publication : 2009

Nicolas Michalski, Vincent Michel, Elisa Caberlotto, Gaelle M Lefèvre, Alexander F J van Aken, Jean-Yves Tinevez, Emilie Bizard, Christophe Houbron, Dominique Weil, Jean-Pierre Hardelin, Guy P Richardson, Corné J Kros, Pascal Martin, Christine Petit (2009 Sep 17)

Harmonin-b, an actin-binding scaffold protein, is involved in the adaptation of mechanoelectrical transduction by sensory hair cells.

Pflügers Archiv : European journal of physiology : 115-30 : DOI : 10.1007/s00424-009-0711-x

Résumé

We assessed the involvement of harmonin-b, a submembranous protein containing PDZ domains, in the mechanoelectrical transduction machinery of inner ear hair cells. Harmonin-b is located in the region of the upper insertion point of the tip link that joins adjacent stereocilia from different rows and that is believed to gate transducer channel(s) located in the region of the tip link's lower insertion point. In Ush1c (dfcr-2J/dfcr-2J) mutant mice defective for harmonin-b, step deflections of the hair bundle evoked transduction currents with altered speed and extent of adaptation. In utricular hair cells, hair bundle morphology and maximal transduction currents were similar to those observed in wild-type mice, but adaptation was faster and more complete. Cochlear outer hair cells displayed reduced maximal transduction currents, which may be the consequence of moderate structural anomalies of their hair bundles. Their adaptation was slower and displayed a variable extent. The latter was positively correlated with the magnitude of the maximal transduction current, but the cells that showed the largest currents could be either hyperadaptive or hypoadaptive. To interpret our observations, we used a theoretical description of mechanoelectrical transduction based on the gating spring theory and a motor model of adaptation. Simulations could account for the characteristics of transduction currents in wild-type and mutant hair cells, both vestibular and cochlear. They led us to conclude that harmonin-b operates as an intracellular link that limits adaptation and engages adaptation motors, a dual role consistent with the scaffolding property of the protein and its binding to both actin filaments and the tip link component cadherin-23.

F Jülicher, K Dierkes, B Lindner, J Prost, P Martin (2009 Aug 25)

Spontaneous movements and linear response of a noisy oscillator.

The European physical journal. E, Soft matter : 449-60 : DOI : 10.1140/epje/i2009-10487-5

Résumé

A deterministic system that operates in the vicinity of a Hopf bifurcation can be described by a single equation of a complex variable, called the normal form. Proximity to the bifurcation ensures that on the stable side of the bifurcation (i.e. on the side where a stable fixed point exists), the linear-response function of the system is peaked at the frequency that is characteristic of the oscillatory instability. Fluctuations, which are present in many systems, conceal the Hopf bifurcation and lead to noisy oscillations. Spontaneous hair bundle oscillations by sensory hair cells from the vertebrate ear provide an instructive example of such noisy oscillations. By starting from a simplified description of hair bundle motility based on two degrees of freedom, we discuss the interplay of nonlinearity and noise in the supercritical Hopf normal form. Specifically, we show here that the linear-response function obeys the same functional form as for the noiseless system on the stable side of the bifurcation but with effective, renormalized parameters. Moreover, we demonstrate in specific cases how to relate analytically the parameters of the normal form with added noise to effective parameters. The latter parameters can be measured experimentally in the power spectrum of spontaneous activity and linear-response function to external stimuli. In other cases, numerical solutions were used to determine the effects of noise and nonlinearities on these effective parameters. Finally, we relate our results to experimentally observed spontaneous hair bundle oscillations and responses to periodic stimuli.