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EDITORIAL

Biophysics of Mechanotransduction

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Mechanosensory transduction is ancient, paralleling the appearance of the first primordial cells on the surface of the Earth some 3.8 billion years ago. These primal organisms experienced osmotic pressure as the first likely mechanical stimulus resulting from the inherent role that water plays in the existence of all life forms. Mechanical stimuli acting on the variety of living organisms existing today include, for example, sound and direct contact, for which these organisms developed specialized mechanoreceptors serving as transducers of these mechanical stimuli into senses of hearing and touch, respectively. Other forms of mechanotransduction range from turgor pressure regulation in microorganisms such as bacteria and yeasts to gravitropism in plants or blood flow regulation in humans (Hamill and Martinac 2001). Central to mechanotransduction is the cellular membrane surrounding every living cell. The cell membrane provides a separation between the extracellular and intracellular compartments and serves as a highly dynamic functional barrier composed of membrane proteins and lipid bilayer, controlling the traffic of ions, water and nutrients between these compartments (Singer and Nicolson 1972). As a physical barrier it presents a major target of mechanical forces stretching, compressing, bending or even breaking it, if an excessive force is acting on it.

As a composite of a large variety of lipid molecules such as phospholipids, sphingolipids, cholesterol and many others, the lipid bilayer of the cell membrane presents, mechanistically speaking, a supporting matrix for a great variety of membrane-associated proteins. To strengthen its mechanical properties, the lipid bilayer can in different types of cells be supported by a cell wall as in bacterial and plant cells or can associate with extracellular (EC) matrix and cytoskeletal (CSK) proteins as in animal and human cells (Hamill and Martinac 2001). Membrane proteins embedded in the lipid bilayer of the cell membrane are functional units performing a range of functions enabling the survival of biological cells. A class of membrane proteins functioning as biological force-sensing systems are mechanosensitive (MS) ion channels, which together with cytoskeleton and muscles represent firmly established biological mechanosensors (Martinac 2014). MS channels have over the last two decades entered into the focus of the mechanobiology research area and are, together with the lipid bilayer, also the focus of this issue of the *European Biophysics Journal*.

This special issue on the biophysics of mechanotransduction assembles nine papers from a number of leading scientists interested in mechanical properties of cell membrane and its components, which play a role in mechanosensory transduction in living cells. The papers in this issue are based on several presentations given at the Mechanotransduction Satellite Symposium, which took place last year in Broadbeach on the Gold Coast in conjunction with the 2014 IUPAB International Biophysics Congress in Brisbane, Australia.

Special Issue: Biophysics of Mechanotransduction.

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Two of the papers deal with the lipid bilayer from the perspective of lipid–protein interactions. Herrmann and coworkers describe that insertion of an outer membrane phospholipase (OmpLA) into the lipid bilayer can be achieved by controlled destabilisation of the barrier function of the membrane through the use of detergents (Herrmann et al. 2015), while Svetina discusses how mismatch between protein surface and curvature of the lipid bilayer influences binding between the two surfaces (Svetina 2015). The remaining seven papers focus on MS channels and their interaction with the lipid bilayer as a modulator of their function. Five of them focus on MscL, the bacterial channel of large conductance (Martinac 2011; Sukharev et al. 1994; Chang et al. 1998), which has served as a model for studies of MS channel gating according to the force from lipids (FFL) principle (Teng et al. 2015). Foo and colleagues show that release of particulates through MscL in liposomes is dependent on both detergent and acyl chain length of lyso-lipids (Foo et al. 2015). In a molecular modelling study, Sawada and Sokabe examine interaction of water with residues at the MscL gate, showing that water interaction weakens the hydrophobic lock around the gate, facilitating opening (Sawada and Sokabe 2015). Using a hidden Markov analysis study, in addition to the five subconducting states, Almanjahie et al. show that MscL has two conformational states at the closed level (Almanjahie et al. 2015). Chi et al. (2015) developed a new homogeneously expressing MscL construct, enabling more accurate protein concentration measurements than before. Importantly, the channel gating properties are indistinguishable with the heterogeneously expressed MscL constructs. Yilmaz et al. use a multidisciplinary experimental approach based on partial-denature-reassembling, double labeling and electron paramagnetic resonance (EPR) spectroscopy, to reveal the conformational states of MscL leading to the channel opening by precisely controlling the number of subunits in open configuration (Yilmaz et al. 2015). Their results should provide valuable insights into the functioning of MS channels. The remaining two papers describe MscS and MscCG, the two bacterial MS channels of small conductance belonging to the family of MscS-like channels (Cox et al. 2015). Ridone and colleagues demonstrate that cardiolipin modulates the activation threshold and gating behaviour of *Escherichia coli* MscS in both azolectin and mixtures of pure liposomes (Ridone 2015). Finally, Becker and Krämer review the functional significance of the C-terminal domain of the MscCG channel from *Corynebacterium glutamicum*, an industrially important soil bacterium, for glutamate efflux (Becker and Krämer 2015).

The limited selection of papers showcased in this issue is definitely not representative of the great achievements that many scientists have contributed to the mechanobiology field over the past 30 years. It nevertheless represents a small section of recent very valuable contributions advancing our understanding of the structure and function of bacterial MS channels and their intimate interactions with the lipid bilayer as an essential component modulating their function in mechanotransduction processes in living cells. We believe that these recent lessons learned from bacterial MS channels may be applicable to studies of many other MS channels found in cells of all life forms.

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References

Almanjahie IM, Kahn RN, Milne RK, Nomura T, Martinac B (2015) Hidden Markov analysis of improved bandwidth mechanosensitive ion channel data. Eur Biophys J. doi:10.1007/s00249-015-1060-7

Becker M, Krämer R (2015) MscCG from *Corynebacterium glutamicum*: functional significance of the C-terminal domain. Eur Biophys J. doi:10.1007/s00249-015-1041-x

Chang G, Spencer RH, Lee AT, Barclay MT, Rees DC (1998) Structure of the MscL homolog from *Mycobacterium tuberculosis*: a gated mechanosensitive ion channel. Science 282:2220–2226

Chi G, Rohde PR, Ridone P, Hankamer B, Martinac B, Landsberg M (2015) Functional similarities between heterogeneously and homogenously expressed MscL constructs. Eur Biophys J. doi:10.1007/s00249-015-1062-5

Cox CD, Nakayama Y, Nomura T, Martinac B (2015) The evolutionary 'tinkering' of MscS-like channels: generation of structural and functional diversity. Pflugers Arch 467:3–13

Foo A, Battle AR, Chi G, Hankamer B, Landsberg MJ, Martinac B (2015) Inducible release of particulates from liposomes using the mechanosensitive channel of large conductance and l-alpha-lysophosphatidylcholine. Eur Biophys J. doi:10.1007/s00249-015-1055-4

Hamill OP, Martinac B (2001) Molecular basis of mechanotransduction in living cells. Physiol Rev 81:685–740

Herrmann M, Danielczak B, Textor M, Klement J, Keller S (2015) Modulating bilayer mechanical properties to promote the coupled folding and insertion of an integral membrane protein. Eur Biophys J. doi:10.1007/s00249-015-1032-y

Martinac B (2011) Bacterial mechanosensitive channels as a paradigm for mechanosensory transduction. Cell Physiol Biochem 28:1051–1060

Martinac B (2014) The ion channels to cytoskeleton connection as potential mechanism of mechanosensitivity. Biochim Biophys Acta 1838:682–691

Ridone P, Nakayama Y, Martinac B, Battle AR (2015) Patch clamp characterization of the effect of cardiolipin on MscS of *E. coli*. Eur Biophys J. doi:10.1007/s00249-015-1020-2

Sawada Y, Sokabe M (2015) Molecular dynamics study on protein–water interplay in the mechanogating of the bacterial mechanosensitive channel MscL. Eur Biophys J. doi:10.1007/s00249-015-1065-2

Singer SJ, Nicolson GL (1972) The fluid mosaic model of the structure of cell membranes. Science 175:720–731

Sukharev SI, Blount P, Martinac B, Blattner FR, Kung C (1994) A large-conductance mechanosensitive channel in *E. coli* encoded by MscL alone. Nature 368:265–268

Svetina S (2015) Curvature-dependent protein–lipid bilayer interaction and cell mechanosensitivity. Eur Biophys J. doi:10.1007/s00249-015-1046-5

Teng J, Loukin S, Anishkin A, Kung C (2015) The force-from-lipid (FFL) principle of mechanosensitivity, at large and in elements. Pflugers Arch 467:27–37

Yilmaz D, Dimitrova AI, Walko M Koçer A (2015) Study of light-induced MscL gating by EPR spectroscopy. Eur Biophys J. doi:10.1007/s00249-015-1063-4