

1 Andre Kamkin • Irina Kiseleva
2 Editors
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8 **Mechanosensitivity**
9 **of the Nervous System**
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21 Forewords by Nektarios Tavernarakis
22 and Pontus Persson
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Foreword

Mechanotransduction, the conversion of a mechanical stimulus into a biological response constitutes the basis for a plethora of fundamental biological processes such as the senses of touch, balance and hearing and contributes critically to development and homeostasis in all organisms. Perception of incident mechanical stimuli is critically important for interfacing with the physical world. Naturally, the mechanisms underlying the capability of living cells to receive and act in response to mechanical inputs are among the most ancient, implemented during evolution. Proteins with mechanosensitive properties are ubiquitously present in eubacteria, archaea and eukarya, and are postulated to have been an essential part of the physiology of the Last Universal Ancestor. The first mechanosensitive processes may have evolved as backup mechanisms for cell protection, e.g. to reduce intracellular pressure and membrane tension during osmotic swelling. Subsequent organismal diversification and specialization resulted in variable requirements for mechanotransduction in different organisms. Hence, evolutionary pressure has shaped a large repertoire of mechanotransducers, optimized for a great assortment of tasks that range from maintenance of intracellular osmotic balance and pressure to our impressive ability of hearing and discriminating sounds, and reading Braille code with our fingertips.

Elegant genetic and electrophysiological studies have shown that specialized macromolecular complexes, encompassing mechanically gated ion channels, play a central role in the transformation of mechanical forces into a cellular signal, which takes place in mechanosensory organs of diverse organisms. These complexes are highly efficient sensors, closely entangled with their surrounding environment. Such association appears essential for proper channel gating, and provides proximity of the mechanosensory apparatus to the source of triggering mechanical energy. In addition to the core channel proteins, several other potentially interacting molecules have in some cases been identified, which are likely parts of the mechanotransducing apparatus. Based on cumulative data, a model of the sensory mechanotransducer has emerged that encompasses our current understanding of the process and fulfills the structural requirements dictated by its dedicated function. It remains to be seen how general this model is, and whether it will withstand the impetuous test of time.

1 Mechanotransduction in living organisms can operationally be categorized
2 as sensory or regulatory. Sensory mechanotransduction or mechanosensation
3 alerts the organism to mechanical inputs in the form of touch, pressure, stretch,
4 sound, vibration and acceleration. Such stimuli provide vital awareness of the
5 environment, and information with regard to the organism's relative position
6 and movement. This prowess is important in negotiating with the physical
7 world and is based on highly adapted mechanotransducers that have evolved
8 to optimally carry out the task.

9 Both cellular and organismal homeostasis often requires adjustment to mechan-
10 ical forces generated by environmental sources or internal processes. For example,
11 osmotic balance, ion concentration homeostasis, cell volume and shape regulation,
12 blood pressure and turgor control all depend on appropriately responding to
13 mechanical stretch or shearing forces. Dedicated mechanotransducers in these
14 paradigms serve as regulatory valves that initiate a cascade of events towards
15 adjusting to or counteracting any substantial deviation from normal conditions.
16 The requirement for regulatory mechanotransduction is probably as ancient as life
17 itself. Cells constantly need to fight shearing and stretch forces they encounter, and
18 the faculty of mechanotransduction was most likely decisive for the survival of the
19 first cell. The universal occurrence of mechanotransduction capabilities in all living
20 organisms argues for such early emergence of mechanotransducers.

21 Sensory and regulatory mechanotransducers obey similar principles and it is
22 likely that the first derived from the second by refinement towards acquiring
23 dedicated functions. In higher organisms, specific neurons, the mechanorecep-
24 tors are equipped with a mechanotransducing apparatus and signal upon
25 reception of a stimulus. Frequently, these cells are implanted within accessory
26 structures that serve to filter and amplify an incoming stimulus. For example
27 skin touch receptor neurons are occasionally associated with hair shafts, while
28 hair cells of the inner ear are enclosed in elaborate anatomical structures that
29 greatly facilitate capture and tunneling of sound wave energy.

30 This book, edited by Andre Kamkin and Irina Kiseleva, provides an excel-
31 lent point of reference for the current state of the art in the field of mechan-
32 otransduction, encompassing authoritative essays on a series of diverse,
33 relevant topics. The articles are properly organized into four parts, with the
34 first part focusing on the mechanosensitivity of nerve cells, the second on
35 mechanoreceptors, the third on the biomechanics of the nervous system and
36 the fourth on the mechanosensitivity of the neurovascular system. Thus, the
37 book provides much needed coverage on key themes of modern mechanotrans-
38 duction research and is a timely undertaking, which nicely complements the
39 current body of the literature in the field.
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42 Professor Nektarios Tavernarakis
43 Institute of Molecular Biology and Biotechnology
44 Foundation for Research and Technology – Hellas
45 Crete, March 18, 2008 Heraklion, Crete, Greece