Mechanotransduction and the crayfish stretch receptor

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Abstract

Mechanotransduction or mechanosensitivity is found in almost every cell in all organisms from bacteria to vertebrates. Mechanosensitivity covers a wide spectrum of functions from osmosensing, cell attachment, classical sensory mechanisms like tactile senses in the skin, detection of sound in hair cells of the hearing apparatus, proprioceptive functions like recording of muscle length and tension in the muscle spindle and tendon organ, respectively, and pressure detection in the circulation etc. Since most development regarding the molecular aspects of the mechanosensitive channel has been made in nonsensory systems it is important to focus on mechanosensitivity of sensory organs where the functional importance is undisputed. The stretch receptor organ of the crustaceans is a suitable preparation for such studies. The receptor organ is experimentally accessible to mechanical manipulation and electrophysiological recordings from the sensory neuron using intracellular microelectrode or patch clamp techniques. It is also relatively easy to inject substances into the neuron, which also makes the neuron accessible to measurements with fluorescent techniques. The aim of the present paper is to give an up to date summary of observations made on the transducer properties of the crayfish stretch receptor (Astacus astacus and Pacifastacus leniusculus) including some recent unpublished findings. Finally some aspects on future line of research will be presented.

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1. Introduction

The crayfish stretch receptor is a classical model for the study of mechanosensory transduction. The organ is an invertebrate analogue to the human muscle spindle and was first described in 1951 by the Polish-British zoologist Alexandrowicz working in Plymouth [1]. However already Retzius in the late 19th century had been interested in the crayfish nervous system but in this preparation he devoted most of his scientific efforts to the microscopic anatomy of the central nervous system of the crayfish [2]. His detailed and beautifully lithographed microscopic observations are amazingly detailed despite the relatively primitive instruments that he used (see cover picture of a leech ganglion similar to the one in crayfish). He might also have observed the stretch receptor organ since he studied in some detail the skeletal muscles of the crayfish.

Soon after its discovery the stretch receptor organ and its neurons were subjected to a number of neurophysiological studies to determine the transducer properties of the sensory neurons. In particular studies were initiated in the laboratory of Stephen Kuffler in the early 1950s with co-workers Carlos Eyzaguirre and Charles Edwards. In 1957 the late Professor David Ottoson, as a postdoc in Kufflers laboratory, worked with the stretch receptor organ resulting in an important paper together with Charles Edwards in which they showed that the impulse generation in the sensory neuron started in the axon hillock region [3]. This work inspired him to set up the model at the department of Physiology at the Karolinska Institute.

The interest in the stretch receptor has been due to the following factors: (i) the obvious analogy to the human muscle spindle, (ii) the availability of the sensory neurons for electrophysiological investigations of the transducer properties and (iii) the possibility of analysing experimentally the mechanical properties of the receptor muscle fibres (i.e., the viscoelastic properties).

The functional studies in the 1950s started with extracellular recordings soon followed by intracellular recordings. However,
using intracellular micropipettes it was difficult to keep them inside the cell while pulling the receptor muscle. During the last decade’s development in techniques for mechanical stimulation, development in electrophysiological techniques like the two electrode voltage clamp and the patch clamp technique and optical investigations using fluorescence and absorption spectroscopy have opened up new pathways for the investigation of this receptor. This has made it possible to study the sensory neurons down to the ion channel level.

This article will review some old and recent findings on the structure and function of the stretch receptor organ of the crayfish mainly performed at the Karolinska Institute but will also briefly touch upon ongoing projects and clinical importance.

2. Structure of the receptor organ

Each abdominal segment of the crayfish contains two receptor organs, one on each side. The organ is located in the extensor muscles and contains a slowly adapting and a rapidly adapting receptor. Each receptor is made up of a receptor muscle and a sensory neuron whose dendrites intermingle with the central part (intercalated tendon) of the receptor muscle (Fig. 1). The receptor muscle attaches to consecutive segments of the abdominal cuticle. The axons from the sensory neurons follow the dorsal segmental nerve to the ventral ganglion. The receptors also receive efferent innervation: i) one or two motor neurons to the receptor muscle and ii) inhibitory GABA-ergic innervation to the sensory neurons and the muscle[1,4–6].

In the crayfish both the slowly and rapidly adapting receptor muscles consist of a single muscle fibre. The central part (intercalated tendon) is made up mainly of collagen but with some myofibrils inserting into or passing the region. The slowly receptor muscle is thinner (30–80 μm) and has thick filaments and long sarcomeres (6.5 μm) compared to the rapidly receptor muscle which is courser (70–150 μm) and has shorter sarcomeres (3.3 μm) [7]. The rapidly receptor muscle resembles fast arthropod muscle.

The sensory neurons are large (30–100 μm) multipolar neurons of pyramidal to fusiform shape (Fig. 1c). They contain a large nucleus (10 μm) with a clear and easily visible nucleolus. The dendrites branch about 5 times, the first branch being 20–30 μm in diameter and 50 to 100 μm long and with final terminal branches about 2 μm long and 0.1 μm in diameter [8]. The axon from the sensory neuron is 20–30 μm in diameter. The sensory neurons are covered by several layers of sheet (glial) cells.

3. Functional properties

3.1. General behavior

The receptors are activated, i.e., stretched, by flexion of the abdomen or contraction of the receptor muscle, basically in the same way as the human muscle spindle, and are involved in the motor control of the abdomen. The first experiments were done by Wiersma et al. [9] and Kuffler [10] and subsequent studies by Eyzaguirre and Kuffler [11,12] and Edwards and Ottoson [3] on lobster and crayfish showed that stretching the receptor organs gave rise to impulse discharge from the neurons. It was found that the firing properties of the two neurons were clearly different, one neuron maintained firing as long as the stretch was applied (slowly adapting) whereas the other neuron generated a short high frequency discharge (rapidly adapting) at the onset of the stretch (see Fig. 1a and [13,14]).

The chain of events that leads from extension of the receptor muscle to impulse discharge in the stretch receptor is represented by the steps outlined in Fig. 1d. In the first step the extension of the receptor muscle is converted to tension in

![Fig. 1. (a and b) Abdominal stretch receptor organ from one side with typical impulse responses from the slowly and the rapidly adapting neuron. (c) Typical neuron with different ion channel populations. (d) Different responses from receptor muscle and receptor neuron as a result of extension of the receptor muscle (modified after [15]).](image-url)
the muscle, which leads to deformation of the dendritic membrane of the sensory neuron. This will open mechanosensitive (gated) ion channels (MSC) permeable to Na⁺, K⁺ and Ca²⁺ ions resulting in an inward receptor (or generator) current. The transformation from receptor current to impulse response is a complex process determined by passive membrane properties, capacitance \( (c_m) \), and membrane resistance \( (r_m) \) or leak conductance \( (g_L) \), and the voltage-gated ion conductances \( (g_{ion}) \) present in the neuron, mainly from K⁺ and Na⁺ channels. In addition the geometry of the cell and the spatial distribution of the different ion channels will contribute to the type of impulse response seen in the cell. Fig. 1d shows the receptor potential after block by TTX, 4-aminopyridine and tetraethylammonium chloride and the receptor potential after block with TTX only. The difference in responses reflects the relativity of the concept of receptor potential [15].

3.2. Methods

The methods used in the study of the crayfish stretch receptor are measurement of tension in the receptor muscle [16], intracellular two electrode voltage and current clamp techniques [14,17] and the patch clamp technique [18,19]. It has to be stressed that voltage clamp is used in this context in two different ways: (i) holding the potential constant during stretch eliminates the influence of voltage-gated currents and the injected current is equal to the receptor current through the mechanosensitive channels. (ii) In the traditional voltage clamp mode no stretch is applied and voltage-gated currents are studied with potential steps.

By using a balanced stretch for the two ends of the receptor muscle the movements of the cell body during stretch can be minimized [20].

3.3. Viscoelastic properties of the receptor muscles

The viscoelastic properties of the receptor muscles in the slowly and rapidly adapting receptors were investigated by extending the muscles while measuring the resulting force in one end of the muscle fibre. It was found that the viscoelastic properties of the two muscles differed considerably, the rapidly adapting receptor muscle having more dynamic characteristics (Fig. 2a). The muscles could be reasonably well described by a viscoelastic model consisting of a Voigt element (parallel spring and damping element) in series with a non-linear spring [16], (Fig. 2a inset). The difference in viscoelastic properties is probably related to the morphological differences mentioned above. It is concluded that part of the difference in adaptive properties between the slowly and rapidly adapting receptors can be accounted for by the different viscoelastic properties of the muscle fibres [21].

3.4. The transducer properties and the nature of the mechanosensitive channels

Considerable advances of the nature and function of mechanosensitive ion channels (MSCs) or stretch-activated (SA) ion channels have been made over the last 20 years since the first recording of MSCs from cells were published by Guharay and Sachs [22]. There is little doubt today that mechanotransduction is due to the opening of MSCs. However, it has also become clear that the molecular substrate of mechanosensitive channels differ between different systems and that mechanosensitive channels is

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Fig. 2. (a) Tension responses from a slowly and rapidly adapting receptor muscle from the same receptor organ. The muscles were subjected to extension from 3% to 30% with increment of 3%. Slope of ramp 1500% s⁻¹. Inset shows a viscoelastic model (from [16]). (b) Receptor currents from a slowly and a rapidly adapting sensory neuron from the same organ exposed to extensions of 6, 12, and 18% (bottom trace) (from [14]). (c) Peak amplitude of receptor current from a rapidly adapting neuron from an experiment similar to (b) TEA + 4-AP did not affect the receptor current.
not a homogenous molecular species and there is still some controversy regarding the gating mechanism(s) of MSCs [23].

If the sensory neuron of the stretch receptor is subjected to voltage clamp it is possible to observe the receptor current generated by extending the receptor muscle without interference of voltage-gated ion channels. This means that the receptor current reflects the assemble activation of the MSCs of the neuron (Fig. 2b). The response mirrors the tension response of the muscle for the same type of stimulus but the dynamic part is more prominent.

The stimulus–response relation for both the slowly and rapidly adapting receptor is not linear but typically sigmoid in character [14,24] and the amplitude of the receptor current reaches a maximum determined by the number of MSCs being simultaneously open, Fig. 2c. The sigmoid character of the stimulus–response relation for the receptor current suggests that there is no simple relation between the tension in the muscle and current. The time course of the receptor current of the slowly and rapidly adapting stretch receptors differs, the rapidly receptor current having a more typical dynamic character (Fig. 2b and [14]).

The permeabilities underlying the receptor currents is \( P_{Na^+}, P_{K}, \) and \( P_{Ca^{2+}}, \) the permeability for \( Na^+ \) being dominant with \( P_{Na^+}/P_{K} = 1.6 [17,25] \). This is somewhat different from the results by Erxleben for the MSC (or SA channel) in the stretch receptor neurons [26]. He determined the conductance for the MSC to be 71 pS for \( K^+ \), 50 pS for \( Na^+ \) and 23 pS for \( Ca^{2+} \). The permeability of the MSC to \( Ca^{2+} \) is of special interest. When the \( Ca^{2+} \) concentration outside the preparation was lowered the receptor current increased [17]. This could be due to direct effects on the MSC facilitating gating when \( Ca^{2+} \) is decreased presumably on the inside of the membrane. In the normal situation opening of MSC leading to influx of \( Ca^{2+} \) the channel will as a result close, thus contributing to the adaptation of the receptor current.

It is possible to model the receptor current and the resulting stimulus–response relations taking into account the viscoelastic model of the receptor muscle and the properties of the MSCs in the sensory neurons including an inactivating parameter possibly resulting from the \( Ca^{2+} \) influx as mentioned above [27].

The receptor current is not affected by TTX, 4-aminopyridine (4-AP) or tetraethylammoniumchloride (TEA) (see [14], Fig. 2c) consistent with the findings on the MSC [26]. Since a molecular characterisation of the MSC in the crustacean stretch receptor has not been successful so far, despite several attempts, pharmacological characterisation has given some clues to the molecular nature of the MSC. The trivalent lanthanide Gadolinium (Gd\(^{3+}\)) was found to block the MSC in the stretch receptor neuron. The MSCs were more sensitive to Gd\(^{3+}\) when \( Ca^{2+} \) was lowered indicating some competitive action between these two ions [28].

Several local anaesthetics were found to affect the receptor current in the stretch receptor neuron. Lidocaine at low concentration facilitated the receptor current whereas tetracaine, bupivacaine and an analogue to lidocaine (LL33) partially blocked the receptor current [29]. In an earlier study it was shown that several nonionic detergents in the Triton series could also block the receptor current [30]. In a recent study it was found that a calmodulin inhibitor CGS 9343B (zaldarine maleate) reversibly blocked the receptor current [31]. These results indicate that the effect on this particular MSC is through the lipid phase and further indicates that the gating mechanism could be similar to what is found for bacterial MSCs (see [23]).

Since some TRP (transient receptor potential) ion channels have been suggested to be mechanosensitive [32], e.g., the TRPV4, we have recently been using ruthenium red, known to block TRP channels, to investigate possible effects on the stretch receptor neuron. This is an attractive possibility since the TRP channel family was shown to be responsible for mechanosensitivity in Drosophila — an invertebrate relative. However, no effect on the receptor current in the stretch receptor neuron has been observed (Fernström and Rydqvist, unpublished observations). This indicates that a TRP protein (channel) might not be the MSC in the crayfish. A spider toxin from the spider Grammestola spatulata (GsMTx4) has been shown to block some mechanosensitive ion channels in the heart and astrocytes [33]. In preliminary experiments we have studied the effects on the receptor current of the purified fraction GsMTx4 at concentrations up to 10 \( \mu M \). No effect was found using this toxin (unpublished observations).

Also, in a similar type of experiment the stretch receptor preparation was exposed to 1 mM amiloride, a substance known to block mechanosensitive channels of the ENaC type (epithelial Na\(^+\) channel), responsible for mechanotransduction in C. elegans and hair cells (see [23,34]). The result clearly shows that this substance has very small effects on stretch-activated currents. In three experiments no significant effect could be demonstrated (unpublished observations).

It is thus an open question what kind of molecule that constitutes the MSC in the crayfish stretch receptor neuron. It is observed in experiments using local anaesthetics and detergents on the stretch receptor that substances that are interfering with the lipid phase have an increased tendency to affect mechanotransduction. Further, the more hydrophobic the substance is the larger the blocking effect. This indicates tentatively that the MSC in the sensory neuron is gated through the lipid phase and not through the cytoskeleton or extracellular matrix. This is supported by the fact that part of the local anaesthetic effect was a shift in the stimulus–response curve indicating an effect on gating (see [29]). In addition, the relatively slow onset of the effect in these experiments, similar to what was found by Martinac [35] could be explained by diffusion of the anaesthetics into the lipid bilayer.

3.5. Passive membrane properties and space clamp considerations

The passive membrane properties are important since it determines the accuracy of the voltage clamp when the receptor current is recorded. The whole cell leak conductance, \( g_L \), is typically between 0.25 and 1 \( \mu S \) and the whole cell capacitance, \( C_m \), is 4–5 nF [36,37].

Voltage clamping of the neuron depends on good clamping of all parts of the neuron. This is normally difficult in particular
when long axons are present. When recording receptor currents it must be kept in mind that they are set up in the dendrites but the clamping is performed in the soma. We have previously made calculations according to [38] and found that the 95% of a potential change generated in the dendritic tips are seen in the soma [20]. This is consistent with recent recalculations [39] using a detailed analysis of the dendritic tree, soma and axon to make the geometry fit whole cell resistance (1.8 MΩ). A specific membrane resistance \( R_m \) of 2000 Ω cm\(^2\) and an internal resistance of 70 Ω cm gave an attenuation of 1.4% using \( L = l/\lambda = 0.2 \) (\( \lambda \) is length constant, \( l \) length of equivalent cylinder and \( L \) is dimensionless electrotonic length). Using the methods advised by Rall and Segev [40] under the same conditions as above a receptor-like current generated in the dendritic tips was calculated to be recorded with amplitude of 97% in a soma voltage clamp. A 50% reduction of \( R_m \) to 1000 Ω cm\(^2\) decreased the current amplitude in the soma to about 95%.

On the other hand care must be taken when voltage-gated currents are analysed since such currents are present in high density in the axon of the sensory neuron. It is clear that axons several mm long cannot be tolerated. It is important to cut the axon 200–300 μm from the soma to avoid regenerative current signals when clamping the neuron. This is possible without the cell being damaged.

3.6. Action potentials and voltage-gated ion channels

The action potentials in the slowly and rapidly adapting neuron differ to some extent. In the rapidly adapting receptor the amplitude is around 55 mV whereas in the slowly adapting neuron the amplitude is around 80 mV. It was also found that the duration was longer in the slowly adapting receptor mainly due to a slower repolarisation [41]. This is consistent with the difference in properties of the Na\(^+\) and K\(^+\) channels. Na\(^+\) currents generate the action potential in both the slowly and rapidly adapting neuron. In the slowly adapting neuron the sodium current is larger and the inactivation (\( \tau_i \)) is slower and takes place at more negative potentials compared to that in the rapidly adapting neuron, consistent with the properties of the action potentials. It was also observed that pinching the axon of the rapidly adapting neuron close to the soma totally abolished the action potentials. This was not the case in the slowly adapting neuron. Further, in the rapidly adapting neuron the action potentials in the axon were larger and had slightly faster rise time than those in the soma [41]. Taken together these observations point towards a distribution of Na\(^+\) channels illustrated in Fig. 3b with Na\(^+\) channels located further out in the axon of the rapidly adapting neuron.

It was also observed that in the slowly adapting neuron the Na\(^+\) currents, as recorded using the two electrode voltage clamp technique, indicated the presence of two channel populations differing in kinetic properties [41,42]. Since this was not the case using macropatch clamp recordings in the soma of the slowly adapting neuron [18] the observations point towards a specific spatial distribution of at least two different sets of Na\(^+\) channels. As a result of these observations we recorded soma Na\(^+\) currents from the slowly and rapidly adapting neurons after cutting the axons at different positions from about 350 μm to about 100 μm from the soma. The interesting finding was that in the rapidly adapting neuron the Na\(^+\) current was completely abolished when the axon was cut at about 150 μm from the soma whereas in the slowly adapting neuron most of the sodium current was preserved even if the axon was cut up to 100 μm from the axon.

This indicates that in the slowly adapting neuron Na\(^+\) channels are present in the axon and the soma, and that one of the suggested channels is dominating in the soma and that both may be present in the axon. In the rapidly adapting neuron the results so far indicate a single Na\(^+\) channel population located at least 150 to 200 μm out in the axon. The difference in spatial distribution of the Na\(^+\) channels between the two neurons suggests that it might have importance for the difference in adaptation.

A calculation using a compartmental model is under way, and this should give some hints whether this is conceivable or not.

There are presently over 100 genes coding for potassium channel subunits including the number of beta-units modulating K\(^+\) channels and many neurons and other cells contain a large number of different K\(^+\) channels. In the stretch receptor neuron of the crayfish 3 types of voltage-gated K\(^+\) channels and a Ca\(^{2+}\) activated K\(^+\) channel have been defined up to date.

The whole cell potassium currents in the slowly [17,43] and the rapidly adapting neuron [37] was initially characterised by a transient and an outwardly rectifying component. The activation time constant for the rapidly K\(^+\) current was smaller and the activation took place at more negative potentials as compared to the slowly adapting receptor. The results were supported by macropatch recordings from the soma of the slowly adapting neuron that gave almost identical results [18]. The inactivation as derived from whole cell currents had two time constants in both receptors, a fast component about 0.5 ms and a slow component ranging from 2 to 8 s. Pharmacological dissection of the K\(^+\) currents in the slowly and rapidly adapting neurons using 4-AP and TEA revealed two different populations of ionic channels one channel having high affinity to TEA and the other low affinity to TEA [44].

Later experiments using patch clamp recordings from the SA soma have demonstrated the existence of 3 different types of K\(^+\) channels in this neuron.

First, an outward delayed rectifier has been analysed in detail having a single channel conductance of 13 pS and a \( P_C = 6.5 \times 10^{-14} \) cm\(^2\)/s with little inactivation (Fig. 3d). First latency analysis suggested a two closed states preceding two open states. The channel displays properties similar to Kv1.2 [19]. Second, a K\(^+\) channel with large conductance (53 pS) has properties suggesting a delayed outward rectifier with very little inactivation as seen from cell-attached recordings (Fig. 3e). The third K\(^+\) channel is clearly a transient K\(^+\) channel (Fig. 3f) with fast inactivation (estimated time constant in the order of 20–50 ms). This channel has a conductance of 23 pS. The 23 pS and 53 pS K\(^+\) channels are difficult to detect at resting membrane potential but could be activated at a depolarisation 10–20 mV. Other K\(^+\) channels with single channel conductance of less than
10 pS have also been observed but further experiments are necessary to analyse these currents.

The spatial distribution and density of the potassium channels have been difficult to define but experiments using macropatch recordings from different locations in the soma have given some clues [18]. The experiments show that the K+ current density is higher close to the axon hillock area as compared to current densities in the dendritic part of the soma. This suggests that K+ channel distribution is different over the neuronal surface and it can be anticipated that the slowly and rapidly neurons differ in their K+ channel set up.

Finally, a Ca2+ activated potassium channel was suggested by Ottoson and Swerup [45–47], who injected EGTA and TEA into the slowly adapting sensory neuron and found changes in adaptation consistent with effects on a K+ channel. This was supported by Erxleben [48], who recorded simultaneously from stretch-activated and K+ channels. He observed that when stretch-activated channels were stimulated by suction in the patch pipette, the K+ channel in the same patch increased its activity. He concluded that Ca2+ entering through the stretch-activated channel activated the potassium channel thus being a Ca2+ activated channel. Ottoson and Swerup [45–47] concluded that this channel contributed to the early adaptation in the receptor potential.

4. Adaptation

From Fig. 1a it is clear that there is a distinct difference in adaptation of impulse response between the rapidly and slowly adapting receptor. The rapidly adapting receptor gives a brief impulse discharge in response to a ramp and hold extension whereas the slowly adapting receptor gives a sustained impulse discharge for the same stimulus. Somewhat surprising almost the same difference is seen when the neurons are electrically stimulated. Adaptation is therefore a consequence of several processes in the receptor organs.

Viscoelastic properties of the receptor muscle contribute to adaptation as is seen in Figs. 1d and 2a. A distinct difference can
be seen between the tension response in the rapidly receptor muscle and the slowly receptor muscle (Fig. 2a, [21]). The transient peak is more pronounced in the rapid muscle compared to that in the slow muscle. This correlates well with the difference in receptor current seen in Fig. 2b. The receptor current of the rapidly adapting neuron has a dynamic phase that is more pronounced as compared to the slowly adapting neuron. The decay phase of the rapidly receptor current is also considerably faster as compared to the slowly adapting current [14]. From the studies of viscoelastic properties and the properties of the mechanosensitive ion channels (MSC) it was possible to model the receptor potential responses for the stretch receptor [27].

However, since electrical stimulation gave the same principal type of impulse discharge adaptation non-mechanical factors must contribute to adaptation. Analysis of both Na\(^+\) and K\(^+\) currents in the slowly and rapidly adaptive neurons as outlined above have revealed small differences in kinetic properties between the two neurons. Some of these kinetic changes are consistent with the adaptive properties seen in the two neurons but the spatial distribution of the Na\(^+\) and K\(^+\) channels might turn out to be of additional importance. So far, it has only been possible to define tentatively the spatial distribution of the sodium channel but the exact distribution and density of K\(^+\) channels are probably even more important. However, so far this has not been possible to achieve. Even so, a complete tentative model including viscoelastic properties, MSC proper-

ties and kinetic properties of the whole cell Na\(^+\) and K\(^+\) currents has been derived and found to be successful in predicting the impulse response due to extension of receptor muscle [24,27]. It has also been possible to predict the difference in impulse discharge due to electrical stimulation between the rapidly and slowly adapting neuron [49].

Presently we are in the process of developing a compartmental model to be able to better study how different densities and distribution of channels might influence impulse discharge in these receptor neurons. It will also be necessary to develop more efficient methods to determine experimentally the location of ion channels on the cell membrane.

5. Concluding remarks

The stretch receptor organ is a very useful preparation for the study of mechanotransduction in all its aspects. It is also a muscle receptor analogous to the human muscle spindle and participates in the motor control of the crayfish abdominal extensor muscles. To understand fully the proprioceptive contribution to motor control it is necessary to have detailed knowledge of the transducer process in the receptor organs. This includes knowledge on receptor muscle function, specific knowledge on functional and structural properties of the mechanosensitive channel (MSC), and better knowledge of the voltage-gated ion channels and how they are distributed over the cell surface. Further, this knowledge can be used to modify the function of the muscle receptors affecting the tone of the muscle. In particular it should be of some interest to find clinically useful therapies to release spastic conditions.

Theoretically this is possible through the muscle receptors since many spastic conditions are generated through reflexes, which include these organs. One interesting possibility should be to block the mechanosensitive ion channels selectively. As presented above this has not been possible so far and until the molecular details of the MSCs are known, this will be difficult. Another possible way to modify the receptor function is to affect with precision the voltage-gated ion channels or in some way their density or distribution over the cell surface. We have found that very small changes in voltage-gated kinetic properties can profoundly change the excitability properties of the stretch receptor neuron.

We thus believe that experimental and model studies of this invertebrate receptor can help considerably to propose ways in which certain motor problems can be improved. The results from these investigations are also of fundamental importance for the general understanding of generation of signals in sensory receptors.

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References
