Detection of painful stimuli in the periphery is mediated by temperature-sensitive transient receptor potential (TRP) channels which are expressed in primary afferent endings of free sensory neurons called nociceptors. TRP channels in nociceptors are involved in the detection of thermal, but also mechanical and chemical stimuli. Out of seven known types of temperature-sensitive TRP channels, three are responsible for detecting painful temperatures: vanilloid receptors TRPV1 (> 42 ^{o}C) and TRPV2 (> 52 ^{o}C) detect noxious heat, and ankyrin receptor TRPA1 detects noxious cold (< 17 ^{o}C). Better knowledge of TRP channel mechanisms of action is essential for understanding TRP channel functions and ultimately for the design of potential analgesics. New findings presented in this thesis clarify mechanisms of action of TRPV1 and TRPA1 receptors, focusing on camphor and voltage sensitivity of TRPV1 channels and calcium modulation of TRPA1 channels.

The first topic discussed in this thesis is the mechanism of camphor sensitivity of TRPV1 receptor. Camphor is a naturally occurring substance known since time immemorial for its effective analgesic properties, yet its mechanism of action is not understood. Camphor is known to be a partial agonist of TRPV1 channel, a full agonist of TRPV3 channel, but also an inhibitor of TRPA1 channel. In this study we investigated the effects of camphor on TRPV1 activity, as well as camphor-induced changes in the properties of plasma membrane. We found that camphor is able to quickly activate TRPV1 channels through conformational changes in a short helix located inside the channel pore. This helix is proposed as the site of camphor interaction with the receptor. Moreover, camphor induced changes in the distribution of phosphatidylinositol-4,5-bisphosphate, a minor phospholipid component of the plasma membrane and an important TRPV1 modulator. This mechanism of action can be also important for camphor-induced modulation of other PIP_2-sensitive membrane receptors.

In addition to camphor sensitivity of TRPV1, we have studied the function of the S4-S5 region of TRPV1. The results were compared with the function of corresponding amino acids in two other vanilloid channels, TRPV2 and TRPV3. Although the residues within the S4-S5 region are strongly conserved among TRPV channels, some of the conserved charged residues serve distinct functions in thermal, voltage, and chemical sensitivity of the different members of the TRPV family.

The final topic discussed in this thesis is the role of the distal part of the C-terminal end of the TRPA1 channel in calcium-dependent modulation. TRPA1 is an ion channel whose function is strongly modulated by Ca^{2+} ions, but the mechanism of this modulation has not been identified. Our experimental data suggest that the C terminus of the TRPA1 receptor

serves as a calcium sensor. Amino acid substitutions in this area have demonstrated the role of these residues in Ca^{2+}-induced potentiation and inactivation. These results contribute to a better understanding of TRPA1 channel function in chemical nociception.