

# Relation between K<sup>+</sup> channel gating and sequence specific helix distortions by a joint experimental and molecular dynamics simulation approach

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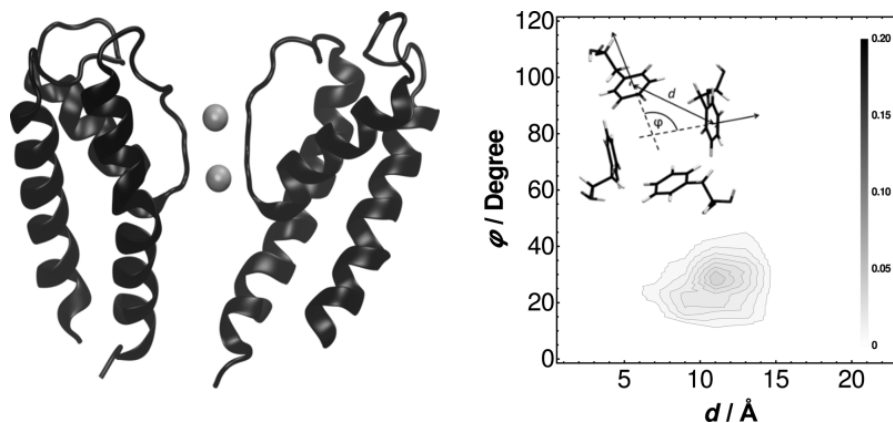
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Ion channels fluctuate stochastically between “open” and “closed” states, which determine the ion flux through biological membranes, also known as “gating”. This crucial feature of ion channels is necessary in cellular, biological systems to regulate the ion concentration level, which is essential for the processes of homeostasis or second messaging. Yet the origin of gating is not fully understood. A suitable ion channel model for investigations of gating is the tetrameric potassium-selective ion channel KcV<sub>ATCV-1</sub>. This minimalistic channel is found in *chlorella* viruses, and comprised of only 82 amino acids per monomer [1-3]. While electrophysiological experiments have already identified two gates in the wild-type channel, an additional 3<sup>rd</sup> gating state is found in the related channel KcV<sub>ATCV-“Smith”</sub> (KcV<sub>S</sub>). This 3<sup>rd</sup> gate leads to a predominantly closed channel (over 70%) in comparison with the wild-type KcV<sub>ATCV-1</sub> and the related KcV<sub>ATCV-“next to Smith”</sub> (KcV<sub>N<sub>T</sub>S</sub>) channel, which both lack this additional gate.



Site directed mutagenesis experiments revealed a significant dependency of this gate on the presence of phenylalanine at position 78 and serine at position 77. To investigate the characteristics of this 3<sup>rd</sup> gate by molecular dynamics (MD) simulations, initial homology models were created for KcV<sub>ATCV-1</sub> and for the two related channels KcV<sub>S</sub> and KcV<sub>N<sub>T</sub>S</sub>. For the description of the different behaviour in gating, potential  $\pi$ - $\pi$ -interactions of the Phe78 residues were analysed in terms of angle/distance probabilities, considering also interactions between different monomers as well as probably interactions of the Ser77 which lead to a channel gating. The results allow for a microscopic interpretation of the gating states in KcV<sub>ATCV</sub> variants.

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