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Structural analysis and ion translocation mechanisms of the muscle-type acetylcholine receptor channel

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The aim of this work is to analyze the conformational changes in the acetylcholine receptor caused by channel opening and to investigate the electrostatic profile during ion translocation through the channel. A computational model of the human muscle-type acetylcholine receptor (AChR) was built and used to analyze channel structure and its interactions with different ions. Using the Torpedo AChR crystal structure as a homologous template, the 3D structure of the human muscle-type AChR was reconstructed. This first model was optimized and an open structure of the channel was generated using Normal Mode Analysis in order to assess morphologic and energetic differences between open and closed structures. In addition, the issue of ion translocation was investigated in further detail. Results elucidate different aspects of the channel: channel gate structure, channel interactions with translocating ions, differences between muscle-type AChR and previous neuronal-type AChR models. The model here reconstructed is ideal for further computational studies on muscle-type AChR and its pathologic mutations.