ELECTRON-CONFORMATIONAL TRANSFORMATIONS EXPLAIN BOTH THERMAL REGULATION AND ACTIVATION OF ION CHANNELS

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Temperature influences all biochemical processes and ion channels' activity is not a special case. Temperature activates TRP channels, which are the molecular basis of hot and cold sensation in sensory neurons [1]. Some TRP channels can be activated by heat (for example TRPV1); some can be activated by cold (for example, TRPM8). But temperature doesn't activate some channels, it just regulates their activity (for example, RyR [2], temperature just regulates channel's activity by decreasing mean open time and increasing ion current amplitude). There is no model, which can provide a biophysically reasonable explanation of temperature effects for both thermo regulated and thermo activated ion channels yet.

We address a simple physically clear electron-conformational model [3] to describe temperature effects for different ion channels. The model starts with the channel's energy depending on its electronic and conformational state. The ion channel dynamics includes fast electronic transitions triggered by ligands, tunneling effects and slow conformational Langevin dynamics which implies both internal friction(caused by interaction between ion channel residues, channel – membrane and channel – solvent interactions) [4] and conventional thermal fluctuation forces (Gaussian–Markovian noise). We argue that a synergetic effect of external thermal fluctuation forces and internal friction via the temperature stimulation/suppression of the ion channel tunneling probability in case of RyR and via the temperature stimulation/suppression of the ion channel barrier escape probability in case of TRP channels can be considered as a main contributor to the temperature effects on the ion channel's gating. Results of computer modeling allowed us to reproduce temperature effects of RyR [2] and both heat- and cold- activated TRP channels [1].

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References

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