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The solution structure of the pentameric ligand-gated ion channel GLIC probed by small-angle neutron scattering

Content

Pentameric ligand-gated ion channels undergo subtle conformational cycling to control electrochemical signal transduction in many kingdoms of life. Several crystal structures have now been reported in this family, but the functional relevance of such models remains unclear. We used small-angle neutron scattering (SANS) to probe ambient solution-phase properties of the pH-gated bacterial ion channel GLIC under resting and activating conditions. Data collection was optimized by inline paused-flow size-exclusion chromatography, and exchanging into deuterated detergent to hide the micelle contribution. Resting-state GLIC was the best-fit crystal structure to SANS curves, with no evidence for divergent mechanisms. Moreover, enhanced-sampling molecular dynamics simulations enabled differential modeling in resting versus activating conditions, with the latter corresponding to an intermediate ensemble of both the extracellular and transmembrane domains. This work demonstrates state-dependent changes in a pentameric ion channel by SANS, an increasingly applicable method for macromolecular characterization as neutron source brilliance increases and inline SEC-SANS set-ups become increasingly accessible.

Primary author(s) : LYCKSELL, Marie (Stockholm University)

Co-author(s) : ROVSNIK, Urska (Stockholm University); BERGH, Cathrine (KTH Royal Institute of Technology); JOHANSEN, Nicolai T (Niels Bohr Institute); MARTEL, Anne (Institut Laue-Langevin); PORCAR, Lionel (Institut Laue-Langevin); ARLETH, Lise (Niels Bohr Institute); HOWARD, Rebecca J (Stockholm University); LINDAHL, Erik (Stockholm Univesity)

Presenter(s) : LYCKSELL, Marie (Stockholm University)

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