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Small-Angle Neutron Scattering of a Pentameric Ligand-Gated Ion Channel Reveals a Dynamic Regulatory Domain

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Pentameric ligand-gated ion channels (pLGICs) perform electrochemical signal transduction in organisms ranging from bacteria to humans. Among the prokaryotic pLGICs there is an architectural diversity involving N-terminal domains (NTDs) not found for the eukaryotic relatives, exemplified by the calcium-sensitive channel DeCLIC. Here, we characterized DeCLIC structure using cryogenic electron microscopy (cryo-EM), small-angle neutron scattering (SANS), and molecular dynamics (MD) simulations. In both the presence and absence of calcium, cryo-EM reconstructions were similar to a previously reported calcium-bound X-ray structure. The NTD exhibited lower local resolution than the canonical unit, consistent with this domain being relatively mobile. The small-angle scattering profile revealed a feature not explained by the available structures, indicating that further conformational diversity is available to DeCLIC. MD simulations indicated that this profile is largely attributable to rigid-body motions of the NTD relative to the protein core, including conformations similar to those in experimental structures, as well as more expanded and asymmetric conformations. Using these expanded conformations, it was possible to fit the previously unexplained SANS feature, indicating the presence of such conformations under solution conditions. This work reveals the range of motion available to the DeCLIC NTD, expanding the conformational landscape of the pLGIC family; and demonstrates the power of combining low-resolution, high-resolution, and simulations data in the study of protein structure.

Session

Structural biology

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