Introducing the Viewpoint

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With the publication of the article by Benoit Roux and colleagues in this issue (Vargas et al.), the JGP introduces a new type of article, the Viewpoint. A Viewpoint shares features with two other article types, Perspectives and Reviews, but is distinct from them. Like the Perspective, a Viewpoint will present a summary and critical analysis of a scientific issue of strong current interest to the readership. But a Viewpoint, unlike a Perspective, is initiated by the authors and needs not be accompanied by other Perspectives that provide differing views of the topic. A Viewpoint, like a Review, is expected to present a scholarly and accurate summary of the topic, but like a Perspective is expected to be sharply focused rather than comprehensive. A Viewpoint may be up to 20 pages in length and contain up to five figures—sufficient space for presenting the kind of carefully reasoned arguments and conclusions expected in primary research articles. It is recommended that authors considering submitting a Viewpoint send a preliminary inquiry to the editors first. A Viewpoint submission will be evaluated by the editors for suitability and reviewed by outside reviewers. Letters to the editor submitted in response to a Viewpoint within three months of its publication will be entertained.

The article by Vargas et al., “An emerging consensus on voltage-dependent gating from computational modeling and molecular dynamics (MD) simulations,” is an exemplar of the Viewpoint, and indeed should serve as a template for authors considering developing and submitting such a manuscript to the JGP. Although x-ray structures of crystallized ion channels have become almost commonplace, it has not been possible to use crystallography to directly determine channel structure under the constraints that are present in the living cell membrane, nor to determine the movements of the distinctive domains of channels that govern gating, permeation, and selectivity. Such constraints include those imposed by the transmembrane voltage as well as those imposed by cytoskeletal elements that interact mechanically with channels. This lack of crystal structures for different physiological states has been particularly acute in the case of voltage-gated channels. A K channel in a hyperpolarized neuron at rest (−70 to −90 mV) is subject to a very powerful inward-directed electric field that forces the voltage-sensing domains (VSDs) inward, driving the channel into a configuration that closes the pore. But precisely how does this resting structure differ from the known crystal structures, which represent the activated channel with the pore open? An even more difficult question arises in defining the dynamically changing structures of a K channel when the membrane is suddenly depolarized, the VSDs move, and the gate opens. The answer to these questions has wide implications for understanding how voltage-gated channels operate, and for how they malfunction in disease states. In their Viewpoint, Vargas et al. summarize the case that computational modeling and MD simulations provide a molecular structure of the rest state of K channels accurate to within a few angstroms, and also of the movements of the VSDs during the gating process. The general agreement in the work from several different investigators on the molecular structure of the rest state of K channels is notable, as are consensus insights into how the electric field is concentrated in a region much smaller than the full bilayer thickness. In contrast, while revealing new details about permeation, simulations have not yet yielded model K channels with conductivities close to the unitary conductances measured in single-channel recordings, suggesting that the model force field calculations need to undergo considerable refinement.

Computational methods such as all-atom MD simulations are making increasingly important contributions to our understanding of membrane physiology. Good simulations can capture the current state of knowledge of the molecular structure and dynamics of membrane proteins, visually enhance our understanding of the underlying processes, and help to focus questions and experiments. The JGP welcomes research with novel mechanistic insight that incorporates such simulations, and is delighted to present the important Viewpoint (Vargas et al.) in this rapidly advancing area.

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