Biophysical Journal 94:1040a (2008)

3107-Pos
Board B410

Bubbles, Gating, and Anesthetics in Ion Channels

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We suggest that bubbles are the bistable hydrophobic gates responsible for the on-off transitions of single channel currents. In this view, many types of channels gate by the same physical mechanism—dewetting by capillary evaporation—but different types of channels use different sensors to modulate hydrophobic properties of the channel wall and thereby trigger and control bubbles and gating. Bubbles nearly exist in bulk water. Experiments show thin gas layers on hydrophobic surfaces in water. Spontaneous emptying of channels has been seen in many simulations. Because of the physics involved, such (pseudo) phase transitions are inherently sensitive, unstable threshold phenomena difficult to simulate reproducibly and thus convincingly.

We present a thermodynamic analysis of a bubble gate using morphometric density functional theory of classical (not quantum) mechanics. Thermodynamic analysis of phase transitions is generally more reproducible and less sensitive to details than simulations. Anesthetic actions of inert gases – and their interactions with hydrostatic pressure (e.g., nitrogen narcosis) – can be easily understood by actions on bubbles. A general theory of gas anesthesia may involve bubbles in channels. Only experiments can show whether, or when, or which channels actually use bubbles as hydrophobic gates: direct observation of bubbles in channels are needed.