Neuroscience 201A Reading (2015)

Topic (Structure-Function of Ion Channels)

Books/Book Chapters

Fain G (2014) *Molecular and Cellular Physiology of Neurons*, 2nd edition, Harvard University Press, Chapters 6 and 7; Pages 192-278.

Hille B (2001) *Ion Channels of Excitable Membranes*, 3rd edition, Sinauer

Review Articles:

Gouaux, E. & Mackinnon, R. Principles of selective ion transport in channels and pumps. *Science* **310**, 1461-1465, doi:10.1126/science.1113666 (2005)

Minor, D. L., Jr. The neurobiologist's guide to structural biology: a primer on why macromolecular structure matters and how to evaluate structural data. *Neuron* **54**, 511-533, doi:10.1016/j.neuron.2007.04.026 (2007)

Swartz, K. J. Sensing voltage across lipid membranes. *Nature* **456**, 891-897, doi:10.1038/nature07620 (2008)

Assigned Paper(s) for Discussion:

Payandeh, J., Scheuer, T., Zheng, N. & Catterall, W. A. The crystal structure of a voltage-gated sodium channel. *Nature* **475**, 353-358, doi:10.1038/nature10238 (2011)

Tang, L. *et al.* Structural basis for Ca2+ selectivity of a voltage-gated calcium channel. *Nature* **505**, 56-61, doi:10.1038/nature12775 (2014)

Study Questions for Discussion:

1. Why do you think Na_vAb was crystallized, rather than a regular mammalian Na_v? Do you think the structure represent a good model for Na_v?
2. Why do you think the voltage sensor of the channel is in the activated state? How does this relate to the aqueous cleft and the focused membrane electric field?
3. How might the S4 domain be stabilized within the membrane? What kind of motion does it do for channel gating?
4. What is the gating pore? What does it conduct and what ions cannot go through the gating pore?

5. Is the pore of the channel open or closed in the Na_vAb structure? Does it correspond to the state of the voltage sensor? How might this pore conformation be reconciled with the voltage sensor placement?
6. What happens with Na^+ ions in the central cavity of the channel? Do Na^+ ions permeate through the activation gate with or without the hydration shell?
7. What is the difference between selectivity filters of Na_v and K_v channels? What is the reason for this difference?
8. What is a possible role for the lateral fenestration of the Na_vAb?
9. How could the gating motion of Na_vAb be determined? Is the mechanism of pore opening for Na_vAb different from that proposed for K_v?
10. What is different between the selectivity filter of Na_vAb and Ca_vAb? How does it account for their different ion selectivity?
11. What is your overall perception of the papers?