

More Problems

1. In the text, you should consider the problems at the end of chapter 13. There's lots of good ones, but minimally, you should be happy with your answers to...

- 13.1
- 13.3
- 13.5
- 13.17

13.18 is also worth giving some serious thought.

2. In the paper by Doyle et al on the structure of potassium channel, consider the following:

a) In the first paragraph of the last column on p. 69, the authors claim that "there are two closely related varieties of K⁺ channels, those containing two membrane-spanning segments per subunit and those containing six"

1) This conclusion was arrived at before there were any structures. Describe the analysis that gave rise to this conclusion.

2) Explain why this analysis apparently failed to predict the existence of the pore helix.

3) On p. 70, beginning at the bottom of the second column, the authors note that sequence conservation is strongest for the amino acids corresponding to the pore region, and, interestingly, the inner helix. Inspection of Figure 1 shows that in the inner helix, residues 93, 97, 99, and 110 are particularly conserved. Bring up this structure in Protein Explorer, and make those amino acids visible (for example by displaying the whole molecule as a backbone representation, and then selecting the individual amino acids - [Enter: **select 93** in the command window to select residue 93] - and displaying them as ball and stick structures so you can see them.

1) Are the side chains of these amino acids all located on the same side of the inner helix?

2) The location of these side chains suggests that these sequences are not conserved in order to preserve their interactions with potassium ions passing through the channel. Explain.

3) The location of these side chains does suggest a reason for their conservation through evolution. What is that reason?

c) In the first column on p. 74, the authors explain the hydrophobicity of the pore lining by suggesting that "it would be counterproductive to achieving a high throughput of K⁺ ions were

the lining of the channel to interact strongly with ions outside of the selectivity filter”.

1) Why would it be counterproductive?

2) This argument should apply to the selectivity filter as well. Explain what makes the selectivity filter different.

d) In the authors' discussion of Figure 8c (which actually appears in the second column on p. 75), the network of Val, Tyr, and Trp side chains is described as “like a layer of springs stretched radially outward to hold the pore open”. This language makes it sound as if keeping the pore diameter from becoming smaller is at least as, if not more, important than keeping the pore diameter from becoming larger. Explain why keeping the pore from becoming smaller is so important.

3) A bright-eyed molecular biologist had an idea for a project. Having noted that the GTPase of transducin molecule is so very slow, she thought she would improve the efficiency of the response of the visual system to light by engineering a new transducin with a much more active (faster) GTPase activity. Is this change likely to produce a better system for seeing in the dark?

4) Speaking of seeing in the dark, somebody, somewhere, noted that in rhodopsin, mutation of a glu residue to an ala close to the Schiff base linkage with retinal results in night blindness in humans. Why might this be so?