

Please return to Xin Zhang before 12:00pm on June 1st at Braun 180.

- (1) High-affinity *E. coli* methionine ABC transporter. (Kadaba, *et al.*)
 - a. Describe where and how ABC transporters bind ATP, including the role of the Walker A motif (P-loop), Walker B motif, and the ABC signature motif (LSGGQ) in nucleotide binding and hydrolysis
 - b. Please describe the allosteric regulatory mechanism proposed for the MetNI transporter. In addition, briefly summarize what structural properties are responsible for this mechanism.

- (2) The open state of the mechanosensitive channel MscS. (Wang, *et al.*)
 - a. Why is the MscS mutant A106V believed to represent an open state or “conducting” conformation in the reported crystal structure?
 - b. What are the key conformational changes that drive the switch from between “nonconducting” and “conducting” states, according to the authors?
 - c. The data in this paper provide valuable information on the conformational features of “conducting” versus “nonconducting” mechanosensitive channels. However, the conformational properties of the native “conducting” state and the dynamic process of channel switch still remain ambiguous. Please propose a series of experiments based on what you have learnt in this course (other than crystallography) to answer at least two of the following questions: (1) what does the native “conducting” state look like in a membrane system? (2) how does MscS sense a change in membrane tension and how is this coupled to channel opening? (3) how does MscS close the channel to resume a “nonconducting” state? You only need to briefly describe what approaches you would take to solve those questions and state what results you would expect and how you would interpret them. Students who answer more than two questions would receive bonus credits accordingly if the answer were plausible.

- (3) How lipids shape membrane-protein function. (Philips *et al.*)
 - a. In Fig. 3c and d, the indicated curves illustrate the variation in energy density (free energy of deformation per unit area of membrane) with changes in membrane distortion. Explain the difference in the “red”, “yellow”, and “green” dots on the curves according to the molecular presentations. Briefly discuss what is meant by “hydrophobic mismatch” and “bilayer midplane slope” and why these effects increase the energy density of the membrane.
 - b. Briefly describe the four situations in Fig. 4 in your own words.
 - c. The authors discuss their perspectives about the field summarized in this review. If you were appointed as the chairperson of the study board in NIH and were about to fund labs to solve questions related to the content in this review, what is the most important question in your mind? Please describe this question briefly. (answer is expected to be clear and plausible.)