**Q1** 10 ps

**Q2** 5 ns

**Q3** One atom leaves the protein environment and dissociates into solution. It is a potassium ion, hence this represents one of the steps in the ion transport process.

**Q4** Step 130| the potassium ion leaves its biding site and jumps to the end of the selectivity filter

Step 130-250| the potassium ion is diffusing through the protein toward solvent.

Step 250| onwards, the potassium ion is diffusing in free solution.

Step 440 the potassium ion jumps across the upper Z face of the periodic boundary box, reappearing through the lower Z face.

**Q5** The jump in distance of about 7.5 Å from 84.48 Å to 91.95 Å between frames 441 and 442 is an artefact caused by the jump across the periodic boundary box.

**Q6** It is unusual to have many charged residues either in the interior of a protein (usually a hydrophobic core) or buried in a membrane. The hERG voltage sensor domains have a line of positively charged residues along on helix, opposed to a line of negatively charged residues on a neighbouring parallel helix. Furthermore, the former helix is connected to the vestibule region of the channel structure where open and closed conformations of the channel have been reported in homologous structures. It is thought that an electrostatic charge across the membrane will induce a conformational change in the voltage sensing domain which is transmitted to the vestibule region of the channel. MD simulations like this one are beginning to disclose this effect.

**Q7** Aligning each frame to the initial structure removes the effects of translation and rotation of the whole protein in the bilayer, Hence, the remaining RMSD is the average of the flexibility of the protein itself, over this time period. Correspondingly, the non aligned structures yield the combined effects of the proteins flexibility and movement in the bilayer.