1. Carboxypeptidase hydrolyzes the C-terminal peptide bonds of peptides. A mechanism for this enzyme is shown below. What are the roles of the Zn$^{2+}$ ion and Glu-270 in this mechanism?

Zn ion acts by electrostatic catalysis – helps to stabilize the negative charges on the intermediates by coordinating with the oxygens. The Zn also orients the attacking OH group so that it can properly attack the peptide bond.

Glu-270 acts as a general base in the reaction, pulling a proton from the water molecule.
2. Glycogen phosphorylase is an enzyme that adds phosphate to glycogen to make glucose-1-phosphate (see the picture below). The reaction takes place by nucleophilic attack of a phosphate oxygen onto C-1 of glucose, with concurrent breaking of the C-O bond to yield the final product. Suppose that glycogen phosphorylase uses general acid catalysis to weaken the scissile C-O bond. Draw the structure of an amino acid side chain (in its correct ionization state) that could act as a general acid catalyst in this reaction. Which atom on the phosphate or glycogen might be protonated by the general acid to aid in the reaction? Is water involved in this reaction? Why or why not?

Many amino acids could act as a general acid here – the most likely candidates are his or cys. But any protonated amino acid capable of donating its proton could act as a general acid. The oxygen involved in the glycosidic bond would be protonated by the general acid. Water is not involved in this mechanism – the mechanism is similar to that seen for lysozyme, but in this case, phosphate acts as the nucleophile, not water.
3. Glycogen phosphorylase is an allosteric enzyme, activated by AMP and inhibited by ATP. Sketch out three curves relating \( \frac{v}{V_{\text{max}}} \) and [phosphate], indicating the unaffected glycogen phosphorylase, glycogen phosphorylase in the presence of AMP, and glycogen phosphorylase in the presence of ATP.

Top curve = + AMP
Center curve = no effector
Bottom curve = + ATP
4. Suppose that a hypothetical enzyme requires general acid catalysis by two different amino acids, one histidine (pK = 7.0) and aspartic acid (pK = 4.0). Sketch the pH profile for this enzyme; that is, the measured enzyme velocity as a function of pH.

Since both amino acids have to be protonated, the pH profile for the enzyme will mirror the pH behavior of the amino acid with the lower pK, namely, aspartic acid. Once aspartic acid is deprotonated, the enzyme will not work. The curve has 50% activity at the pK of the amino acid, which I estimate at 4.0.