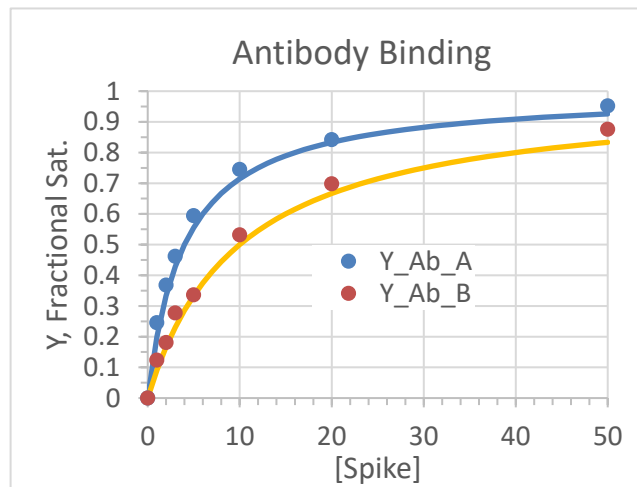
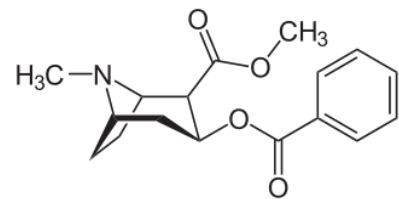


1. Two different antibodies (Ab_A, Ab_B) are being tested as treatments for Covid-19 infection. Both of these antibodies bind to a surface protein on the virus, the spike protein, preventing the virus from entering the cell (physical blocking). A plot of fractional saturation versus the concentration of the spike protein (in nM) is shown on the right. Please answer the following questions.



- What is the K_D for each antibody?
- Which of these antibodies will be more effective against Covid-19? You can assume that the concentration of spike protein is 10 nM during an infection. Justify your answer.

2. The Jmol page associated with this problem set contains the structure of a complex between an immunoglobulin (antibody) and cocaine. The chemical structure of cocaine is shown on the right. Only the very top part of the immunoglobulin (Fv region) is shown on the Jmol page.



- Describe the energetics of the interaction between Tryptophan33H and the bound cocaine. Your answer should discuss what stabilizes the bound cocaine, e.g. H-bonds, electrostatics, van der Waals, or the hydrophobic effect.
- Describe the interaction(s) between Tyrosine32L and the bound cocaine. Your answer should discuss what stabilizes the bound cocaine, e.g. H-bonds, electrostatics, van der Waals, or the hydrophobic effect.
- How would changing tyrosine32L to phenylalanine affect the affinity of cocaine to the antibody? Would the cocaine binding be stronger or weaker? Justify your answer. Note that the N is in a non-aromatic ring, so its properties would be similar to ammonia in terms of hydrogen bonding.

https://www.andrew.cmu.edu/user/rule/03_131/Pset/PS03/ps03_jmol_b.html

3. Determine how mutations in trypsin will affect substrate binding or the ability to cleave the peptide bond.

Navigate to the Jmol page:

https://www.andrew.cmu.edu/user/rule/bc_oli/Pset/PS06/jmol_trypsin_mutants.html

The two panels are identical, allowing you to make a side-by-side comparison. You can load the unmodified (non-mutant) by clicking on the "Unmodified" button. You can load the mutant enzymes by clicking on the "Trp1" through "Trp7" buttons. Each mutant has a single amino acid change that effects either specificity (binding of lysine containing peptides) or catalytic efficiency (ability to cleave peptide bonds).

i) Complete the following table for two of the mutants:

	Residue Altered	Changed to	Affects Specificity (Y/N)	Affects Catalytic efficiency (Y/N)
Trp1				
Trp6				

ii) For the mutation that affects specificity, suggest how the specificity of the mutant enzyme would be different from the wild-type. Recall that the wild-type likes to bind substrates with lysine sidechains.

Important hints:

- Be sure to click on "SimpleView" – it will display the backbone and only the important sidechain.
- When you hover over an atom a label will appear that will tell you the position of the amino acid in the chain and the name of that amino acid, e.g. [ASP]102 = aspartic acid is the 102 amino acid in the protein.

4. What disease is the drug Trastuzumab used to treat? Briefly describe how it works to cure the patient (*please use the web and provide the appropriate citation*).
5. Write a short paragraph on Hers' disease. Your essay should discuss:
 - i) The normal function of the enzyme that is affected by this genetic disease.
 - ii) The consequence of loss of function to the individual.(*please use the web and provide the appropriate citation*).