Protein Modeling Event

Part 1: Pre-Build (40% of total score)

Your Pre-Build Model should have been impounded the morning of the competition. You may pick up your Pre-Build model at the end of the competition after all models have been scored. Unclaimed models will be thrown away.

Part 2: On-Site-Build (30% of total score)

The workstation should have the On-Site Model Competition Environment open on the computer. Using the 240 cm Mini-Toober provided, construct a model of amino acids 116-235 of chain A of 2HU4.pdb. The scale should be 2 cm per amino acid. A meter stick/ruler has been provided for you. Your Mini-Toober model of amino acids 116-235 of chain A of 2HU4.pdb should include the following:

A: Two amino acids: Asp151 and Arg224 (use metal clips to connect amino acids to your Mini-Toober)
B: Blue end cap indicating the amino terminus (N-terminal end) of this region (amino acids 116-235) of the protein
C: Red end cap indicating the carboxylic acid terminus (C-terminal end) of this region (amino acids 116-235) of the protein

Part 3: On-Site Exam (30% of total score)

The On-Site Exam consists of both multiple choice and short answer questions. You may use any materials provided at your work station as well as the ten sheets you brought with you to answer these questions. You may NOT use the Internet to answer these questions.

There are ten multiple choice questions in the On-Site Exam (each worth 1 point for a total of 10 points). Clearly print the letter of the one BEST answer to each question in the blank provided for that question. Illegible answers will be incorrect.

There are also five short answer questions in the On-Site Exam. The point value for each question is given in parentheses at the end of the question (20 pts total). The points for the tie-breaker questions (identified with ★ Tie Breaker) will be included in the final score but may be used to determine team placement in case of a tie.
Multiple Choice Questions:

1. Which of the following amino acids is involved in disulfide bonds?
   A. Cysteine
   B. Histidine
   C. Tyrosine
   D. Methionine

2. Which of the following bonds is the strongest?
   A. Hydrogen bond
   B. Covalent bond
   C. Ionic bond
   D. Electrostatic bond

3. On your onsite model, you positioned amino acid Asp151. Which of the following statements is an accurate description of the significance of this amino acid?
   A. Asp151 is involved in binding Tamiflu, an antibiotic used to treat influenza.
   B. Asp151 plays a role in creating the tertiary structure necessary for the function of neuraminidase.
   C. Asp151 is one of the important amino acids necessary to dock the influenza virus on the host cell.
   D. Asp151 is an amino acid that is essential to the catalytic activity of the enzyme.

4. Which of the following two amino acids are involved in a “salt bridge” or “electrostatic interaction”?
   A. Alanine and Aspartic Acid
   B. Tryptophan and Proline
   C. Lysine and Tyrosine
   D. Glutamic Acid and Arginine

5. Which class of amino acids will most likely be located on the surface of a protein that is embedded in the phospholipid cell membrane?
   A. Acidic Amino Acids
   B. Hydrophilic Amino Acids
   C. Basic Amino Acids
   D. Hydrophobic Amino Acids
6. Which of the following statements best describes neuraminidase?

A. Neuraminidase is primarily a binding protein and, like hemagglutinin, neuraminidase binds to sialic acid receptors on the host cell surface.
B. Neuraminidase is responsible for docking the virus on the host cell membrane.
C. Neuraminidase cleaves sialic acid residues, enabling newly budded viruses to dissociate from the host cell membrane.
D. Neuraminidase plays a role in releasing the viral genetic contents into the host cell.

7. In spring 2009, the world heard about a novel H1N1 flu strain that was quite virulent. Which of the following past influenza outbreaks is also associated with a strain of the H1N1 virus?

A. The 1957 Asian Flu
B. The 1968 Hong Kong Flu
C. The 1918 Spanish Flu
D. The 2005 Avian Flu

8. Alpha helices represent which level of protein structure?

A. Primary
B. Secondary
C. Tertiary
D. Quarternary

9. Hemagglutinin facilitates viral entry into the host cell by first:

A. Binding to antibodies on the surface of the host cell.
B. Binding to sialic acid residues on the surface of the host cell.
C. Entering the host cell through a receptor-mediated channel.
D. Hemagglutinin bores a hole through the host cell membrane to allow entry.

10. Hemagglutinin consists of two chains, HA1 and HA2, yet they are coded on a single segment of RNA. How can this be?

A. The two subunits are coded by alternate splicing of multiple exons in the gene.
B. Viral genes are arranged in operons, in which a single promoter regulates the transcription of multiple consecutive genes.
C. Influenza A is a segmented RNA virus, and the two proteins are encoded on the same segment.
D. A single polypeptide precursor is cleaved after translation to produce HA1 and HA2.
1. Since our body develops immunity to the bacteria and viruses we are exposed to, whether through illness or vaccine, why do we need to get a flu shot every year? (4 pts)

Influenza is an RNA virus and the RNA polymerase made by the virus is error-prone (1 pt). Therefore, viral proteins mutate frequently (1 pt). As a result, the strains of influenza virus circulating each year are slightly different from the previous year (1 pt). Getting a vaccine each year exposes us to the new strains of influenza that are circulating (1 pt).

2. Influenza strains that are resistant to the antiviral, Tamiflu, have been emerging, which means that treating patients with Tamiflu is becoming less effective against the viral infection. What is the key mutation in neuraminidase that leads to resistance to the antiviral? What is significant about this mutation that prevents Tamiflu from working effectively? (4 pts; ★ Tie Breaker )

His274 has been found to be mutated to Tyr274 in strains of influenza that are resistant to Tamiflu (1 pt). When the drug Tamiflu binds in the active site of neuraminidase, Glu276 is pushed upward toward His274 (1 pt). If His274 has been mutated to Tyr274, the larger sidechain of tyrosine pushes Glu276 back toward the active site (1 pt). This shift in amino acid position reduces the space needed by Tamiflu to bind effectively in the neuraminidase active site. In the mutated form of neuraminidase, Tamiflu cannot bind strongly to the active site, and it thus easily displaced (1 pt). It is important to note that this mutation does not inhibit sialic acid from binding, thus still allowing for neuraminidase to function normally.

3. Hemagglutinin undergoes a major conformational change after the virus has been taken into the host cell through endocytosis. What triggers this conformational change and why is this change so essential to the function of hemagglutinin? (4 pts; ★ Tie Breaker )

Hemagglutinin is located on the surface of the virus capsid and serves as the docking agent to allow the virus to bind to the host cell. Once docked, the virus is taken into the host cell via endocytosis, and the virus is now located within an endosome, which has a lower pH than the extracellular environment (1 pt). This lowered pH causes hemagglutinin to undergo a conformational change (1 pt). This conformational change is essential to the function of the protein because it moves the fusion peptide, which is buried within the structure at pH7, to an exposed position, allowing the fusion peptide (which is hydrophobic in nature) to be embedded into the endosome membrane (1 pt). This change in structure allows for membrane fusion between the endosome and virus, enabling genetic material to be transferred to the host (1 pt).
4. Explain how antigenic shift and antigenic drift contribute to the appearance of novel strains of influenza viruses. (4pts; ★ Tie Breaker)

Antigenic shift refers to the abrupt changes in influenza viruses to produce novel subtypes not currently in circulation (0.5 pt). Antigenic shifts can occur from direct transmission of an animal virus to human, or a mixing of animal and human viruses to create a new subtype. (1 pt)

Antigenic drift refers to the gradual changes in the genetic sequence of the antigens, HA and NA (0.5 pt), that occur through point mutations (0.5 pt). These minor changes may alter the binding pocket of the HA (0.5 pt), but do not affect the overall function of the protein.

Through minor genetic changes (drift) and through reassortment (shift), the genetic make-up of influenza viruses could change in such a way that circulating antibodies do not recognize the new strain of the virus, thus potentially leading to illness. (1 pt)

5. Explain why influenza vaccines are used to prevent the spread of influenza and antiviral medications are used to treat infections. (4 pts)

The goal of immunization is to expose the immune system to a latent version of the virus, which triggers the expression of antibodies (1 pt), allowing the body to be primed to fight off an infection. The vaccine enables the body to fight off an invading virus before infection sets in. This is a preventive measure. (1 pt)

Antiviral medications are used to treat a patient who has a viral infection. The antiviral targets a specific protein necessary for the replication of the virus (1 pt), thus preventing further infection within the host organism. The antiviral medications are to be used to treat an infection, as this medicine does not prevent infection (1 pt), but rather prevents the further replication of the virus.