1. (8 Pts) What are the requirements for biological nitrogen fixation in terms of electrons/nitrogen molecule and ATP consumed/nitrogen molecule fixed. Does the reaction require the same amount of electrons as chemical fixation? If not, how do these numbers differ and why are they different?

$$\begin{align*}
N_2 + 8 H^+ + 16 ATP + 8 Fd_{red} (n 8 e^-) + 16 H_2O & \rightarrow 2 NH_3 + H_2 + 16 ADP + 16 P_i + 8 Fd_{ox} (n 8 Oe^-) \quad \text{[biological]} \\
N_2 + 6 H^+ + 6 e^- & \rightarrow 2 NH_3 \quad \text{[chemical]} \\
\end{align*}$$

Nitrogenase needs 2 extra electrons because it produces a byproduct H₂.

2. (10 pts) Threonine deaminase (the enzyme that degrades threonine) is allosterically regulated. It is inhibited by isoleucine and activated by valine. Why does this make sense in light of the biosynthetic pathways for valine and isoleucine biosynthesis?

3. (14 pts) Outline the biosynthetic pathway for lysine (structures). In this pathway, a one carbon piece is lost. What is this piece, and what cofactor assists in this reaction? Draw a general mechanism for this transformation (structures and curly arrows please).
4. (8 pts) Draw the mechanism for the first step in the biosynthesis of valine (structures and curly arrows, please).

5. (10 pts) All of the heavy atoms of methionine are derived from other amino acids. Draw the structure of methionine, numbering each heavy atom. Draw the amino acids from which methionine is derived, showing which atom in methionine corresponds to the atom from its precursor.

6. (12 pts) The conversion of UDP to dUDP is catalyzed by which enzyme? Draw a mechanism for this transformation. What provides the ultimate reducing power for this process. How is this reducing power transferred to the enzyme?
7. (10 pts) There are two different pathways that are used for the synthesis of glu in the liver. Please show them. (Do not use transamination.) What are the energetic requirements of these reactions? Why are there two pathways?

1) [Chemical structure diagram]

Pathway 1 occurs when [NH₃] is high. Km is too high for this enzyme & it's reversible.

Pathway 2 occurs when [NH₃] is low. Km is low so it binds to ammonia well & it is not reversible.

8. (16 pts) Thymidilate synthase (TS) and dihydrofolate reductase are important cancer targets. Why? Draw the mechanism of TS and explain (using structures and words) how fluorouracil inhibits this enzyme.

[Chemical structure diagrams]

THF must be regenerated from DHF by DHFReductase so THF can be reused to synthesize more TMP.

Thymidilate Synthase produces TMP which is ultimately needed for DNA synthesis.

Targeting either has downstream effects on DNA synthesis which is needed by cancer cells.
9. (12 Pts). Draw and number the structures of tryptophan and histidine. Using your labeling system, draw the precursor molecules for their biosynthesis and show where the heavy atoms of these two amino acids are derived from.

10. (8pts) Describe the general mechanism used by cells to replace a carbonyl group with an amino group in nucleotide biosynthesis. Please use structures to illustrate your point. What are the nitrogen donors used in nucleotide biosynthesis?

11. (6 pts) What are the carbon donors for synthesis of the purine base in nucleotide biosynthesis? (name(s) or structure(s))

12. (6 pts) What are the carbon donors for synthesis of the pyrimidine base in nucleotide biosynthesis? (Name(s) or structure(s))