*Learning Goal ii_* Understand the various roles that non-covalent interactions may play in the structure and function of an enzyme
Malate Dehydrogenase CUREs Community: Hypothesis Development and Proposal Module

Learning Objective	*Excellent*	*Acceptabl*	*Poor*	*Unacceptable*
Compare and contrast the physical basis for coulombic interactions and Hydrophobic interactions	Coulombic interactions: charge - charge interactions, Coulomb's law, attractive, repulsive, depend upon magnitude of charge, full, partial charges, depends upon surrounding dielectric, distance. .Hydrophobic interactions- only favorable, need polar solvent, depend upon entropy of the system, solvent cages around individual hydrophobes decrease entropy, hydrophobic interactions minimize entropy loss	Misses 1-2 points of excellent	Misses 3-4 points of excellent	Minimal or no aspects of answer
Briefly outline the types of non covalent interactions you would expect to stabilize secondary structure in a protein	Hydrogen bonds- in helix between C=O and N-H in i to i+4 relationship- in beta sheets: between strands, C=O to N-H May get charge or hydrophobic stabilization between side chains in helices (helix wheel, ridges and grooves) but not necessary for formation.	Misses 1-2 points of excellent	Misses 3-4 points of excellent	Minimal or no aspects of answer
Briefly outline the types of non covalent interactions you would expect to be involved in maintaining a functional tertiary structure in a protein	Hydrophobic core (solvent exclusion), hydrogen bonds and charge - charge interactions, van der Waals interactions. Attractive and repulsive: importance of dynamic structure, intrinsically disordered regions/proteins. For folded proteins attractive > repulsive, but not by much . Usually greater in extremophile proteins	Misses 1-2 points of excellent	Misses 3-4 points of excellent	Minimal or no aspects of answer
Proteins like malate dehydrogenase have quaternary structure. What types of non covalent interactions might you expect to see across the subunit interface? What functions might these interactions play?	Wide variety of attractive and repulsive interactions- Coulombic, Hydrophobic, van der Waals: govern stability of interface: attractive > repulsive: Functions: govern symmetry, homo and hetero-oligomers, Allosteric regulation, Protein-Protein Interactions	Misses 1-2 points of excellent	Misses 3-4 points of excellent	Minimal or no aspects of answer
What types of non covalent interactions would you anticipate are involved in substrate binding to an enzyme?- compare the relative strengths of the interactions you suggest	Van der Waals (steric) – size, Charge-Charge attractions (full and partial), Hydrophobic. Full charges > partial charges and hydrogen bonds- affected by polarity of local environment. Important for specificity as well as affinity- 3 point attachment theory etc. Any given ligand may have repulsive as well as attractive interactions.	Misses 1-2 points of excellent	Misses 3-4 points of excellent	Minimal or no aspects of answer
How might non covalent interactions in a protein-substrate complex promote catalysis?	Catalysis promoted by orientation (correct orientation increases number of productive collisions) and by strain of bonds involved in reaction. Strain may be physical or electronic (strained bonds more reactive-higher energy, less stable, better nucleophile, electrophile	Misses 1-2 points of excellent	Misses 3-4 points of excellent	Minimal or no aspects of answer

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What types of mutations at nearby residues would you predict alter the pKa of a protonatable group on a protein?	Ones that change the local environment of the protonatable group: mutations that lower polarity promote protonation, raising the pKa, mutations that increase polarity have opposite effect. Mutations that remove or create formal like charge impact pKa to favor the lower energy (more stable) state: eg two adjacent carboxyl groups- one will be protonated, one unprotonated	Misses 1-2 points of excellent	Misses 3-4 points of excellent Minimal aspects	Minimal or no aspects of answer