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Biol 555
Final Exam

1. Structure Math
    a.
    b.

2. Crystallography
    a. Orthorhombic, because the descriptors following the lattice descriptor, in this case P(Primitive) indicate that there are screw axes
    b.
    c.

3. Multiple Methods

2LGB has an additional amino acid at the C-terminus of the insulin A-chain. While the A-chain is not of pharmaceutical interest, this additional amino acid interactions with the B-chain which is of interest. These interactions takes place at the β-turn in the B-chain and causes it have greater flexibility at its own C-terminus. This novel insulin was also found to have an additional Arg at the C-terminus of the B-chain. These modifications, together cause the isoelectric point to shift lower than normal, which decreases the solubility of the insulin. This could be of importance because it would make the release of insulin into the blood stream from the injection site slower offering greater glucose control.

3U4N discusses insulin as part of a system and how to offer stability to this protein during storage. The insulin discussed in this paper was typical and the paper focused on stabilizing it by creating a system of covalently linked dimers. This insulin has six cys residues that form disulfide bonds that create links between the A-chain and B-chain. The weakness of the insulin dimer is what allows it to be broken down into monomers in the circulation, but finding ways to give stability to it and prevent it from degrading too quickly is key to providing better and constant glucose levels.

References

Borowicz, Piotr, Elzbieta Bednarek, et al. "Recombinant A22G -B31R-human insulin. A22 addition introduces conformational mobility in B chain C-terminus." *Journal of Biomolecular NMR*. 52. (2012): 365-370. Print.

Vinther, Tine, Mathias Norrman, et al. "Novel Covently Linked Insulin Dimer Engineered to Investigate the Function of Insulin Dimerization." *PLoS ONE*. 7.2 (2012): 1-8. Print.

4. Structure Refinement
    a. Yes, this would affect the calculated structure amplitudes. They would be slightly wrong, the structure amplitude is determined from the structure factor and the structure factor's sum covers all atoms in the unit cell, so an incorrectly placed side chain would affect the comparison between the calculated structure factors and what was experimentally observed.
    b. The error would be noticed when the comparison between calculated data and what was observed is performed. The Rice distribution is used to account for model error and would help locate the misplaced side chain.

5. Crystallographic structure determination

The majority of structures are determined by using molecular replacement. It is easier to perform than experimental phasing, as long as a similar structure has been solved previously. As data bases grow larger this method becomes easier and the chances of finding a good structure to serve as a model increase. At the very least a partial match is most likely going to be found using molecular replacement. This method also gives a starting point to begin work as it is based off another model. Having another model be the initial starting point can cause problems as it can lead to a biased final result. This problem is more likely to happen at lower resolutions. The computations for molecular replacement are also time consuming because this is a 6-dimensional problem solving for an unknown. Experimental phasing is the only way to determine genuine new structures and is based on the scattering of heavy atoms (MIR), electron absorption of certain wavelengths (MAD) and the use of single wavelength absorption (SAD). There are programs to perform the computations for these methods as well, but there are cases of difficult examples that require additional calculations. The advantage to SAD is that the crystal spends the least amount of time in the beam which reduces the chance of radiation damage.

6. Nucleic Acid Structure
7. Muscle Diffraction

If the muscle was contracting the diffraction pattern would have more space because as the sarcomere shortens to contract the muscle the lattice space increases in x-ray diffractions.

8. Computational structural biology
9. X-ray scattering