Complex Questions about Protein Structure:

Q1. How do hydrogen bond contribute to protein stability?

Need to Knows:

What are the energetic contributions of hydrogen bonds within the protein's secondary and tertiary structures?

How can we detect and quantify the number and strength of hydrogen bonds in a protein using computational tools?

What role do solvent interactions play in the formation and stability of hydrogen bonds in proteins?

Can we correlate the pattern of hydrogen bonding with thermodynamic stability measures obtained from empirical data?

How do mutations or post-translational modifications affect hydrogen bonding patterns within a protein?

Q2. Are there amino-acid composition variation between classes of protein folds?

Need to Knows:

How can we classify and compare the amino acid compositions of different protein folds using bioinformatics databases?

What statistical methods or algorithms can be used to detect significant variations in amino acid composition between protein classes?

Can we employ machine learning techniques to predict protein fold class based on amino acid composition?

What evolutionary factors might explain the observed variations in amino acid composition between protein folds?

Complex Questions about Protein Function:

Q1. How can we predict the impact of protein-protein interactions on cellular signaling pathways?

Need to Knows:

What bioinformatics resources are available to identify known protein-protein interactions relevant to a particular signaling pathway?

How can we simulate the dynamic aspects of protein-protein interactions affecting signal transduction using systems biology models?

What computational methods can be used to predict unknown protein-protein interactions based on structural complementarity and surface properties?

How do changes in protein conformation influence their interaction affinity and specificity within signaling pathways?

Q2. How can we predict mutational hotspots within proteins that are critical for stability or activity?

Need to Knows:

What computational tools can identify conserved regions within a protein sequence that are likely to be sensitive to mutations?

How can molecular dynamics simulations contribute to understanding the effects of mutations on protein stability or function?

Can we use evolutionary conservation data to predict which mutations are likely to be deleterious?

What are the common features of known mutational hotspots that can be used to develop predictive models?

Annotation:

The "Need to Knows" related to hydrogen bonding and amino acid composition variations can be addressed through the analysis of protein structures found in databases such as the PDB. We can use PyMol, VMD, and UCSF Chimera to detect and quantify the number and strength of hydrogen bonds. We can use Python with BioPython library as computational tools for amino acid composition analysis. Use heat maps, bar charts, or principal component analysis to visualize the differences in amino acid composition. However, predicting unknown protein-protein interactions and developing new predictive models for mutational hotspots will likely need additional outside information.