Hackathon Prompt: Protein Structure Prediction with Quantum Computing

# Background and motivation:

Predicting a protein’s three-dimensional structure from its amino acid sequence remains a central challenge in molecular biology. While AI-based methods such as AlphaFold have achieved remarkable success, they often struggle with sequences lacking known structural homologs. Physics-based free modeling approaches offer greater accuracy in principle but are computationally prohibitive on classical hardware.

Quantum computing offers a fundamentally different approach. By combining quantum algorithms with coarse-grained lattice models, which discretize protein structures into simplified representations, quantum processors can efficiently sample the vast conformational landscape of proteins. However, the choice of lattice model significantly impacts accuracy and resource demands. Tetrahedral lattices are efficient but too rigid to model key secondary structures. In contrast, face-centered cubic (FCC) lattices provide higher geometric fidelity, enabling more realistic folding patterns such as α-helices and β-sheets, though at increased quantum resource cost.

Your challenge is to go further: design a quantum algorithm for protein structure prediction using a 3D lattice model of your choice, with a focus on leveraging the capabilities of current IBM quantum hardware (Eagle R3, Heron R2). Go beyond the tetrahedral and FCC lattices, explore possibilities such as body-centered cubic (BCC), custom hybrid lattices, and others to balance biological realism with quantum efficiency.

# Getting started:

Create a quantum algorithm that predicts the folded structure of a short protein (5–10 amino acids) by minimizing a Hamiltonian that encodes energy terms and structural constraints on your chosen 3D lattice. Use Qiskit to:

* Encode the protein’s fold using turn-based or coordinate-based lattice encodings.
* Construct Hamiltonians that account for interaction energies (e.g., hydrophobic-polar, Miyazawa-Jernigan) and constraints like self-avoidance and non-backtracking.
* Implement and optimize your algorithm using variational methods (QAOA, CVaR-VQE, VQEC, etc.), optionally incorporating error mitigation and hybrid workflows.

# Tips:

* FCC offers 12 directions and multiple 3-body bond angles (60°, 90°, 120°, 180°), improving modeling accuracy but increasing qubit and Hamiltonian complexity.
* Tetrahedral lattices require fewer qubits but underperform when modeling helices due to fixed 3-body angles (only 109.5° is permitted).
* Consider novel lattices like Body-centered cubic (BCC) or others for tunable flexibility versus encoding overhead.
* Try to avoid slack variables when enforcing constraints; instead, try polynomial fitting or Lagrangian duality (with VQEC) for more scalable encodings.
* Compare your results to a known, ground-truth structure, using root mean square deviation (RMSD) or radius of gyration metrics if possible.

# Deeper Questions:

* How does your chosen lattice affect the biological fidelity and quantum circuit depth?
* Can your encoding recover native-like structures on real hardware?
* How would you scale your approach to longer peptides or more complex scoring functions?

# Suggested resources:

* Doga H, Raubenolt B, Cumbo F, Joshi J, DiFilippo FP, Qin J, Blankenberg D, Shehab O. A Perspective on Protein Structure Prediction Using Quantum Computers. J Chem Theory Comput. 2024 May 14;20(9):3359-3378. doi: 10.1021/acs.jctc.4c00067. Epub 2024 May 4. PMID: 38703105; PMCID: PMC11099973. <https://pubs.acs.org/doi/10.1021/acs.jctc.4c00067>
* Robert A, Barkoutsos PK, Woerner S, et al. Resource-efficient quantum algorithm for protein folding. npj Quantum Inf 7, 38 (2021). <https://doi.org/10.1038/s41534-021-00368-4>
* Li R, Doga H, Raubenolt R, et al. Quantum Algorithm for Protein Structure Prediction Using the Face-Centered Cubic Lattice. arXiv (2025).