Engineering and Physical Sciences Research Council Doctoral Landscape Award

PROJECT TITLE: Protein Quantum Logic Gates

Lead Supervisor: Dr Jonathan Phillips

Co-Supervisors:
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Project details: Protein Quantum Logic Gates. Nature computes efficiently using dynamic molecular interactions between proteins and their environment. Living organisms utilise interactions between proteins and other biomolecules to perform complex computations while dissipating tiny amounts of free energy (100 kBT is the typical potential energy barrier) per operation. We want to learn how these dynamic interactions result in logical outputs and ultimately build bio-molecular computers. Nature has evolved an impressive ability to sense the weak (20-50 μT) geomagnetic field. This is transduced by quantum mechanical means, exploiting pairs of radical ions formed within cryptochrome proteins, which act as a 'molecular compass'. We have developed assays to quantitatively measure magnetosensation at the radical pair and at a transduced downstream site in a given protein. We are, therefore, in an exciting position to measure how changes to the composition of a protein, or changes in its environment, impact its ability to sense – by quantum mechanical means – an applied magnetic field and to transduce that into a classical biochemical signal. Generative AI protein design tools enable us to engineer molecules with new properties. Since 2020, new tools (AlphaFold; RF Diffusion; ProteinMPNN) have been created which, coupled with scalable dynamical network models, enable us to engineer a protein to gain a defined ligand-binding response. Recent advances such as Genie 2, which introduces multi-motif scaffolding in diffusion models, ProT-GFDM, which employs fractional diffusion dynamics to capture long-range dependencies, and SAGE-Prot, which combines generative modeling with iterative scoring for multi-objective optimization, further strengthen our ability to design proteins with both structural precision and functional versatility. We propose to couple this to the magnetosensitive response in a target protein whereby both stimuli together will produce a unique output state. This will result in a protein logical AND gate. We will aim to establish a proof of principle for a unit of protein computation with quantum control over one of the inputs. Ultimately, this will form the basis of

(i) new understanding for how noisy biological systems combine quantum and classical control elements to transduce a signal and

(ii) (ii) biocompatible and genetically encoded quantum logic gates that could be used to build larger circuits in order to do computation using proteins.

This project aligns with the EPSRC Quantum Technologies Theme to "support world-leading research into novel quantum technologies" and "develop high level skills," opening a new avenue of quantum biology. The student will gain experience in optical biophysics, analytical chemistry, and time-resolved mass spectrometry, alongside quantum simulation and generative AI protein design, in collaboration with world leading laboratories. The work also supports "translation of quantum technology research towards potential application," with outputs forming the basis for genetically encoded protein computing and magnetogenetic biotechnology.

This studentship will therefore train a postgraduate in cutting-edge protein design and biophysics, equipping them with cross-disciplinary expertise and excellent career prospects in both research and industry.

References:

Kish. 2023. https://doi.org/10.1021/JACS.3C08934
Kish. 2023. https://doi.org/10.1021/ACS.BIOCHEM.2C00671
Guo. 2022. https://doi.org/10.1038/s41467-022-28425-2
Smith. 2022. https://doi.org/10.1038/S41598-022-09901-7

Project specific entry requirements: Bachelor degree in a natural sciences (or closely related) discipline

Potential PhD programme of study: PhD in Biological Sciences

Department: Biosciences

Location: Living Systems Institute

Please direct project specific enquiries to: Dr Jonathan Phillips (jj.phillips@exeter.ac.uk), Prof. Daniel Kattnig (D.R.Kattnig@exeter.ac.uk) or Prof. Marc Goodfellow (M.Goodfellow@exeter.ac.uk)

Please ensure you read the entry requirements for the potential programme you are applying for.

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