Modular design and construction of de novo protein nanowires and light harvesting arrays

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Project description:

Electron and captured energy flow within proteins is essential to life; these phenomena underpin cellular respiration and photosynthesis, both of which are dependent on complex protein machinery that support chains of redox active cofactors or chromophores. Despite the apparent complexity of these proteins and multi-protein assemblies, simple engineering rules are evident and can inform the design and construction of completely artificial proteins exhibiting sophisticated functions intrinsic to the respiratory and photosynthetic protein machinery. For instance, by minimising intermolecular distances between cofactors or chromophores, highly efficient and rapid energy and electron transfer can potentially be achieved in a de novo protein scaffold. The natural proteins and enzymes are also clearly modular in design, and this can also inform the construction of de novo proteins that can transfer electrons for tens of nanometers, and deliver captured light energy to photosynthetic reaction centres. It is therefore the goal of the laboratory to design and construct de novo proteins equipped with chains of redox-active cofactors and chromophores to gain both a deeper understanding of of processes fundamental to life, while providing a framework for exploiting such exceptional properties as efficient photon capture and energy transduction, long range and directional electron transfer, multi-electron redox catalysis, and transmembrane proton translocation.

The aims of this project are to use powerful computational and iterative approaches to the de novo design of multi-heme, and subsequently multi-chromophore, proteins. We will employ a combination of the Rosetta protein design package and atomistic biomolecular simulations, alongside electrostatic calculations, thereby facilitating an unparalleled control and precision over the protein sequence, structure and biophysical characteristics. This will enable directionality to be imprinted on the electron transfer through the proteins, a feat which has yet to be achieved. Given the similarity between heme and photosynthetic pigments, we will adapt our designs to accommodate multiple chromophores within the binding sites, thus creating soluble light harvesting units to study energy capture and transfer. We also aim to implement electrostatic calculations within our VR design framework which already includes the Rosetta protein design package. All designed proteins will be subjected to an array of biophysical techniques and spectroscopies (e.g. CD and ultrafast multidimensional pump-probe spectroscopy, electrochemistry), and where appropriate, directed evolution will be employed to improve characteristics such as cofactor binding.