Project Abstract Approved for Public Release

Systems-Based Design of Biomolecular Modalities and Materials

Bioinspired nanotechnology seeks to mimic the ability of life forms to use a similar set of building blocks and chemical reactions to achieve a bewildering array of functions. Through over a decade of DoD funded research, we elucidated design principles for short peptide-based nanomaterials with properties such as self-assembly, recognition, catalysis, and actuation. The proposed VBFF project will build on this strong foundation, and approach the far greater challenge of systems-level design to access complex functions that normally differentiate living and non-living matter and that emerge when multiple reactions and interactions are coordinated and integrated. Critically, our approach is not constrained by known biological designs, but instead is based on unbiased and rational searching and mapping of the sequence space for function. This approach gives rise to solutions that are typically much simpler compared to biological solutions and allows us to optimize them for technical applications.

To achieve this systems-level understanding, we will: (i) develop integrated experimental and computational methods to search, map and reduce the multi-faceted biomolecular interaction space to isolate a specific design space; (ii) use experimental optimization processes to enable the integration of multiple features, such as induced-fit, molecular recognition, shape shifting in materials made from sets of interacting peptides; and (iii) compare our laboratory-optimized designs with biologically evolved solutions, in order to create insights into the molecular origins of complex functions of living systems.

Our approach has the potential to be transformative and lead to new bottom-up approaches for understanding, enhancing and engineering the molecular processes of life in order to create unprecedented synthetic materials with adaptive functions. The approaches we propose here collectively represent a paradigm shift, with a realistic potential of making groundbreaking advances in several areas of primary relevance for the DoD and society in general, including autonomous sensing modalities, reconfigurable systems and materials that respond to specific molecular signals, insights into seamless interfacing and integrating biomolecular structures with abiotic systems, and repurposing of biochemical processes, which may, in the long term, be relevant to maintaining or enhancing warfighter resilience and performance.

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