ACS SyntheticBiology

In This Issue

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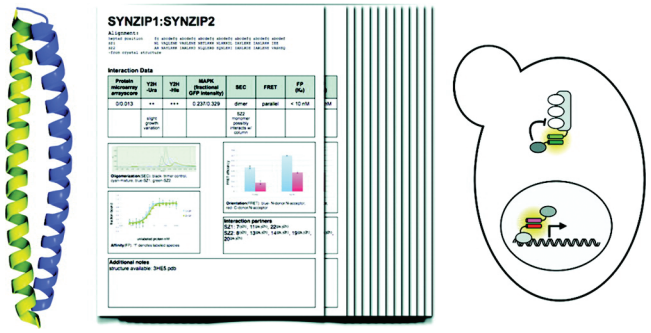
A PROTEIN INTERACTION TOOLBOX FOR SYNTHETIC PEPTIDES

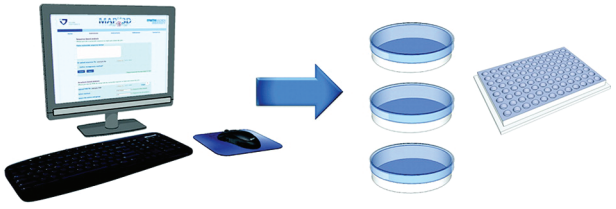
Alpha helices intertwine to form superhelical bundles, coiled-coils, which function as protein interaction domains. These have a rich history of use in fields ranging from structural biology to materials science to synthetic biology. Coiled-coils can be appended to other domains to make fusion proteins that, in turn, can be used to oligomerize molecules or mediate scaffold recruitment events. However, the number of currently available, well-characterized coiled-coil peptides and other protein interaction domains is very limited. Thompson *et al.* (DOI: 10.1021/sb200015u) now provide a very detailed description of interaction characteristics of 22 previously published synthetic coiled-coil peptides called SYNZIP.



The authors provide elaborate specification sheets for peptide interactions *in vitro*, in the yeast nucleus, and in the yeast cytoplasm. They describe oligomerization states, helix orientations, and affinities of each interacting pair of peptides. This protein interaction toolbox greatly enhances the number of interaction parts available for synthetic biology, facilitating a variety of molecular engineering applications.

A SEQUENCE BASED SERVER FOR PROTEIN ENGINEERING

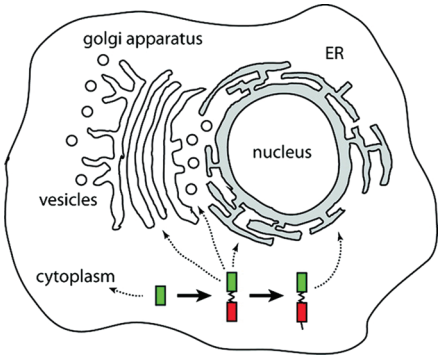
The Mutagenesis Assistant Program (MAP) is a web-based tool that provides statistical analyses of the effects of different mutagenesis methods on the level of amino acid substitutions for a given sequence of protein. While this method could be used to predict the type, extent, and chemical nature of the diversity generated by different mutagenesis methods, it lacked the ability to correlate the MAP indicators to the structural properties of the protein. Verma *et al.* (DOI: 10.1021/sb200019x) now describe a new server, MAP$^{2.0}$3D, which combines the MAP sequence-based analyses with structural information from the crystallographic or theoretical structure of the target protein.



Using three different examples of engineered proteins from literature, the authors illustrate the improved analytical capabilities of the MAP$^{2.0}$3D server by comparing previously reported experimental results with those from the MAP$^{2.0}$3D analysis. The new server with improved functionalities could prove to be a useful tool in protein engineering.

ASSEMBLY OF SYNTHETIC TRANSMEMBRANE PROTEINS

Transmembrane proteins span cellular membranes, regulating intercellular and intracellular interactions. Traditionally, the N-terminal peptide facilitates recruitment of the protein to the endoplasmic reticulum, while the transmembrane helix is responsible for integration of the protein into the membrane. Here, Nagaraj *et al.* (DOI: 10.1021/sb200007r) describe the use of a parts-based assembly approach to confirm that the minimum requirement for the development of a transmembrane protein is a transmembrane helix.



Using this method, the authors were also able to determine the orientation of each synthetic transmembrane protein. Together, this method can prove to be a critical tool in the development of synthetic transmembrane proteins with varied functions and biological applications.

DE NOVO PROTEINS BIND TO SMALL MOLECULES

The availability of large collections of *de novo* designed proteins present new opportunities to devise functional macromolecules for applications in synthetic biology. For many of these applications, proper function will depend on the ability of a novel protein to recognize and bind to a small molecule. Small molecules can contribute to protein function by acting as substrates or cofactors or can enable functions ranging from enzyme catalysis to gene regulation. Here, Cherny *et al.* (DOI: 10.1021/sb200018e) present the first experimental assessment of the ability of *de novo* proteins to recognize and bind a range of small molecules.

The authors show that although their *de novo* proteins were not explicitly engineered to recognize particular targets, they are able to bind various compounds with moderate affinity and specificity. These results suggest new approaches for the design

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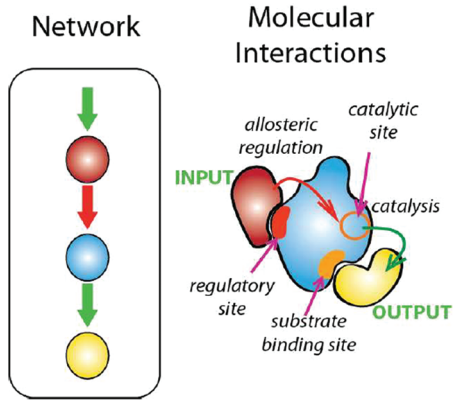
and use of novel binding proteins for use in synthetic biological applications.

EVOLUTIONARY SYNTHETIC BIOLOGY

This review focuses primarily on synthetic biology studies that have attempted to elucidate the molecular mechanisms behind how signaling networks evolve. It discusses work that determines how mutations, ranging from the substitution of single amino acids to the shuffling of modular domains, result in varied evolutionary trajectories and, therefore, diverse network rewiring.



Here, Peisajovich (DOI: 10.1021/sb300012g) suggests that it is the intrinsic evolutionary properties of signaling proteins that regulate the evolution of signaling networks. Directed evolution together with synthetic biology promises to greatly advance our knowledge of the evolutionary processes that govern complex biological systems.

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