

BIOINFORMATICS-DRIVEN PROTEIN DESIGN

By

Philippa Jane Reeder

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Examining Committee:

Jonathan S. Dordick, Thesis Advisor

Christopher Bystroff, Thesis Advisor

Steven Cramer, Member

Susan Sharfstein, Member

Rensselaer Polytechnic Institute

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ABSTRACT

The focus of this thesis is the development of bioinformatics - and rational design-based methods for stabilization and optimization of proteins for use under industrial conditions, as well as in aid of unique design applications. To this end, two approaches are described: the consensus approach, which is used to determine thermostabilizing mutations in the Subtilase superfamily based on protein sequence data mining and rational design, and the re-wire approach, a novel protein redesign methodology under development by our research groups. The primary focus of this thesis, the re-wire method allows direct manipulation of protein structures for optimization of protein folding rates, stability and specificity. In particular, we focus on how changing the topology of a model protein, Green Fluorescent Protein (GFP), without altering core intramolecular contacts effects successful protein folding and stability. In addition, we developed self-reporting polymer-enzyme composite materials for biosensing devices based of the leave-one-out GFP biosensor complementation system.