

Special Bioinformatics Faculty Search Seminar

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Understanding cotranslational protein folding at the molecular and cellular levels

Understanding and manipulating protein folding in living cells is one of the great challenges in biology. It requires that we understand the concomitant folding of proteins with their biosynthesis by the ribosome molecular machine, a factor shown to be important in determining the cellular concentration of successfully folded proteins. I will discuss my efforts to understand the physical principles of such cotranslational folding at the molecular and cellular length scales through the development of coarse-grained simulation force-fields, chemical kinetic modeling, bioinformatics techniques and systems biology methods. I will show how these tools have allowed us to gain novel insights into fundamental issues of in vivo folding, including the impact of variable translation rates and synonymous codon usage, the effect of chaperones, and, at the cellular level, the co-translational folding properties of the *E. coli* proteome. These methods are opening up new avenues of research in the areas of synthetic biology, biomedicine and biotechnology and providing a quantitative theoretical framework for addressing key questions in nascent protein behavior.