2017 CAP LECTURE TOUR

The Canadian Association of Physicists (CAP)
and the
Department of Physics and Engineering Physics of
the
University of Saskatchewan
present

The Physics of Folding: Watching Structures Self-Assemble in Single Biological Molecules using Laser Tweezers

by

Dr. Michael Woodside
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Time: [3:30-4:30 PM Tuesday, March. 21st, 2017]

Room: [Rm. 103 Physics Building]

Abstract: Biological molecules like proteins, DNA, and RNA form a great variety of complex structures that are linked intimately to their biological function. These structures self-assemble in a process known as folding, whereby the linear chain of the molecule changes from a random coil to a specific structure. Folding is a critical process, because if the wrong structure forms then the molecule won't function correctly, leading in many cases to disease. However, for over 50 years experimentalists were unable to observe the structural changes directly during folding as they actually occurred, because such measurements required the previously unattainable ability to monitor a single molecule with near-atomic precision and us-scale time resolution. As a result, only indirect characterisation of the energy barriers that define the folding mechanism was possible. We have now succeeded in directly observing single molecules during the fleeting moments when they change structure. By using laser tweezers to apply tension to the ends of single protein and nucleic acid molecules, we induce the molecular structure to unravel and refold, monitoring the length change that occurs when unfolded parts of the molecule are stretched out under the applied tension. By measuring the properties of the "transition paths" between the folded and unfolded states, we can test the fundamental physical theory of folding and gain new insight into folding mechanisms. The distribution of times required to cross the transition paths and velocities along the paths prove that folding is fundamentally a random walk, a diffusive search for the correct structure. For the first time, the unstable transition states dominating the dynamics can be visualised, via brief pauses during the the transition paths, and the constant transient explorations of 'incorrect' structures expected theoretically can be detected. This work provides the first fully experimental validation of the basic physical picture of folding.

Short Bio: Michael Woodside is an Associate Professor in the Department of Physics at the University of Alberta, and a Senior Research Officer in Nanobiology at the National Institute for Nanotechnology in Edmonton. He obtained a BSc in Physics and Music at the University of Toronto, followed by a PhD in Physics from UC Berkeley, where he studied electron transport in nanostructures with scanned probe microscopy. He trained in biophysics during a postdoc in the Department of Biological Sciences at Stanford University before moving to Edmonton in 2006. His research centres on the question of how structures form in biological molecules, focusing on four themes: the fundamental physics of folding, novel experimental methods and analytical tools, folding in RNA as it relates to gene regulation in pathogens, and protein misfolding that causes disease. His work has led to new methods for measuring the energy landscapes that govern folding, the first direct observation of misfolding in the protein that causes mad-cow disease, and new approaches to discovering drugs that prevent misfolding disease and determining how they work at the molecular level.