PHYS-804

Principles of Single Molecule Biophysics and its Applications

Bustamante Carlos

Cursus	Sem.	Type
Physics		Obl.

Language of teaching	English
Credits	1
Session	
Exam	Oral presentation
Workload	30h
Hours	**14**
Courses	14
Number of positions	**50**

Frequency

Only this year

Remark

Next time: From 08.10.2018 to 11.10.2018

Summary

This course will present the basic principles underlying single molecule biophysics and its multiple applications to biology. It is intended for students of the degree in physics, biophysics and bioengeneering. It will be given at the level of an upper division undergraduate course in Berkeley.

Content

This course will start with an introduction to the methods of single molecule manipulation in biophysics and the challenges and possibliities that arise from using force and torques as directly observable variables in these experiments. We will then discuss how forces and /or torques change the main equations of thermodynamics and kinetics illustrating how to extract information of the system in mechanical manipulation experiments.
Next we will consider a number of applications of biological interest. This part of the course will start with a review of the main theories of polymer elasticity, the freely jointed chain and several variants of this model that involve increasing restrictions on the polymer joints. The idea is to describe average polymer dimensions such as mean square end-to-end distance and radius of gyration of the polymer molecule. We will then discuss the central ideas of coarse-graning introduced by Kuhn and derive the distribution of polymer conformations for a given end-to-end distance of the molecule. We will treat then the worm-like chain that treats the molecule as made up of an elastic continuum, and discuss the meaning of the persistence length and its experimental determination.
We next will derived the force extension expressions for a freely jointed chaind and a worm-like chain under tension and compare the predictions with those obtained via experiment. Specifically, we will discuss single molecule DNA extensional and torsional elasticity as revealed by experiments that have been performed to extract the constant of bending rigidity of double stranded DNA and the constant of torsional rigidity.Finally, we will discuss the torsion-stretch coupling of double stranded DNA. The validity of the worm-like chain model to other biopolymers (double stranded RNA, single stranded RNA and DNA, polysacharides and unfolded polypeptides).
We will next discuss some of the most important methods of single molecule manipulation: the atomic force microscope, magnetic tweezers and optical tweezers. In particular, optical tweezers will be described in some detail including their physical principle of operation, their spatial and temporal resolution and the factors that limit them in practice.
The next subject will be discussion of the mechanical folding/unfoldinng of proteins and RNA. We will illustrate the type of data that can be obtain with modern optical tweezers instrumentation how to extract important parameters from the data, and we will present two case studies: a small globular protein and a small 2-domain protein. Using the latter we will illustrate how to extract equilibrium iformation from non-equlibrium measurements.
In the following section of the course, we will describe the use of single molecule mechanical manipulation experiments to investigate the operation of molecular motors. We will first discuss some of the common properties of molecular motors. their force-dependent velocity, their stall force, the step size of the motor, their processivity, the coordination between various parts of the motor, their mechanism of operation as Brownian Ratchets or Power Stroke machines, etc. We will discuss what do we want to learn from the single molecule studies of molecular motors and how to extract this

information from the data.
We will then study in great deatail a couple of motors: the DNA packaging motor of bacteriophage Phi29 as an example of a oligomeric ring ATPase, and RNA polymerase. We will also compare the operation of these two motors to those that are being unravelled by single molecule studies of the ribosome, of the unfoldase ClpXP and others.

Keywords

Single Molecule
Biophysics

Learning Prerequisites

Required courses

Basic Physical Chemistry
Basic Statistical Mechanics

Resources

Notes/Handbook

Read the current literature