2003 Molecular Biophysics III

Dynamics and Kinetics of Biomacromolecules

Tuesday and Thursday, 2:00 – 3:30pm,

January 6 - April 28

W1395, BST, University of Pittsburgh

A few points

- **Definitions of dynamics and kinetics**
- **Significance of dynamics and kinetics in biomacromolecules (Dr. Bahar)**
- **Course syllabus**
- **Tips for doing well in this course**

Dynamics and Kinetics

http://dictionary.cambridge.org/

- **Dynamics**: the scientific study of the forces that produce movement
- **Kinetics**: the scientific study of forces on things that are moving

The American Heritage® Dictionary of the English Language: Fourth Edition. 2000

- **Dynamics** *(used with a sing. verb)* The branch of mechanics that is concerned with the effects of forces on the motion of a body or system of bodies, especially of forces that do not originate within the system itself. Also called *kinetics*
- **Kinetics**: *(used with a sing. verb)* **1.** See dynamics (sense 1a). **2.** The branch of chemistry that is concerned with the rates of change in the concentration of reactants in a chemical reaction.

Dynamics and Kinetics

WEBSTER'S THIRD NEW INTERNATIONAL DICTIONARY

Dynamics: a branch of mechanics that deals with forces and their relation primarily to the motion but sometimes also to the equilibrium of bodies of matter

Kinetics:

1. a branch of dynamics that deals with the effects of forces upon the motions of material bodies

2a. a branch of physical science that deals with the rate of change in a physical or chemical system

2b. the rate of change or reaction in such a system

2c. the mechanism by which a physical or chemical change is effected

Dynamics and Kinetics

- **Oxford English Dictionary, 2d edition**

Dynamics: 1. **a**. **The branch of Physics which treats of the action of Force**: in earlier use restricted to the action of force in producing or varying motion, and thus opposed to *Statics* (which treats of rest or equilibrium under the action of forces); more recently (see quots. 1863-67), the name *Kinetics* has been introduced for the former, **Dynamics** being taken in a more comprehensive (and more etymological) sense, to include **Statics** and **Kinetics**. But the earlier usage, in which Statics and Dynamics are treated as co-ordinate, is still retained by some physicists, and has largely influenced the popular and transferred applications of the word and its derivatives. Also called dynamic. **b. That branch of any science in which force or forces are considered**.

Dynamics and Kinetics

Oxford English Dictionary, 2d edition

Kinetics

- 1. **The branch of dynamics which investigates the relations between the motions of bodies and the forces acting upon them**; opposed to *Statics*, which treats of bodies in equilibrium.
- **2a.** A field of study concerned with the mechanisms and rates of chemical reactions or other kinds of process; see also gas kinetics.
- **2b.** Those aspects of a particular process that relate to the rate at which it occurs; the details of the way a process occurs, esp. as regards its rate.

Significance of dynamics and kinetics in biomacromolecules

Motions are essential for living things

. . . everything that living things do can be understood in terms of the jigglings and wigglings of atoms.

Feynman, R. P. (1963) *Six Easy Pieces* (Addison–Wesley, Reading, MA), p. 59.

Motion at different levels

At macroscopic level:

- Heartbeats, eye-blinks, electrical brain waves…

At microscopic level:

- Cell division, DNA transcription and replication, metabolic cycles, membrane channel opening, the processing of substrates by enzymes

At atomic level:

- Residuals in proteins, base pair opening in nucleic acids, …

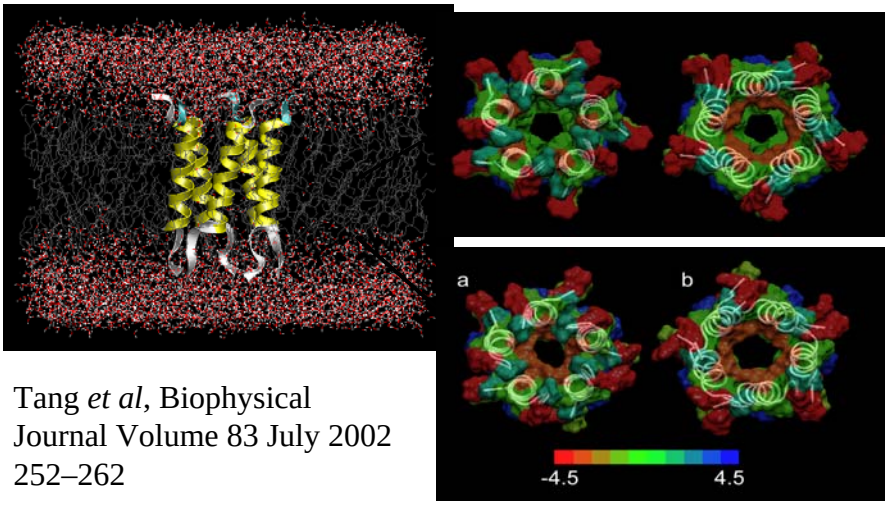
Protein motions are essential for functions

- **P**roteins perform most of the functions of living things, from metabolism to thinking
- 3D static structures provide descriptions of the ground states of proteins and often do not completely explain results from functional biological assays, nor do they necessarily illuminate the path for protein engineering or rational drug design
- Macromolecular function is, in many cases, highly dependent on excursions to excited molecular states and hence intimately coupled to flexibility.

Protein motions are essential for functions

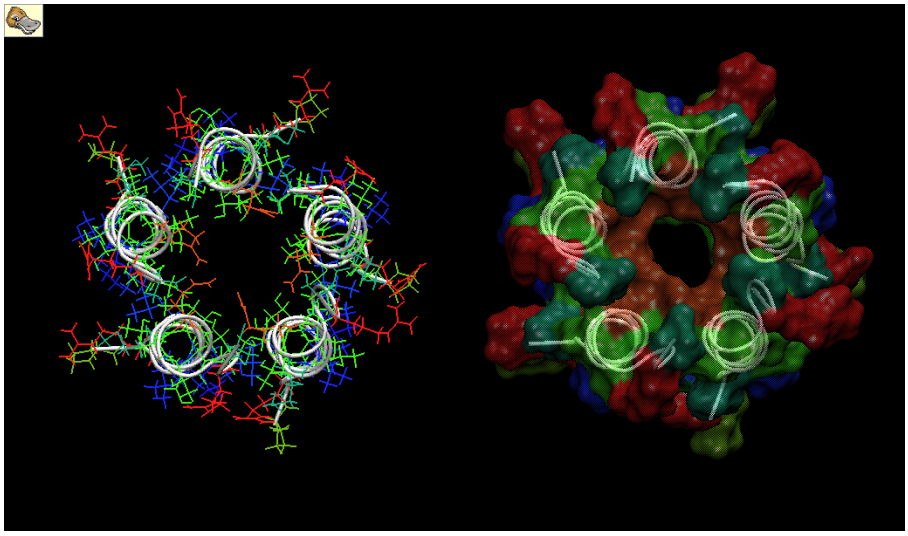
- Moreover, in terms of bioenergetics, a significant component of molecular stability derives from motion, even in the context of folded states of molecules
- Therefore, a complete and much more useful description of the structure of a molecule will require an understanding of how the structure changes with time.

NMR Structures of the Second Transmembrane Domain of the Human Glycine Receptor α1 Subunit:Model of Pore Architecture and Channel Gating



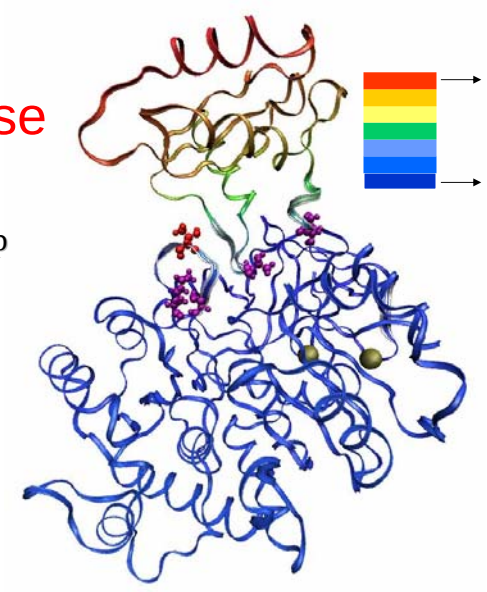
Tang *et al*, Biophysical Journal Volume 83 July 2002 252–262

A possible explanation of the channel gating

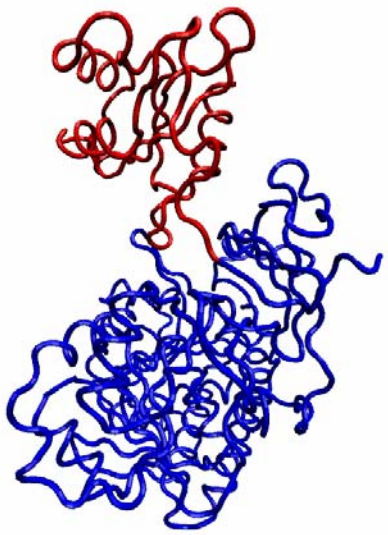


Firefly Luciferase

Belongs to a group of enzymes catalyzing oxidation reaction



Luciferase

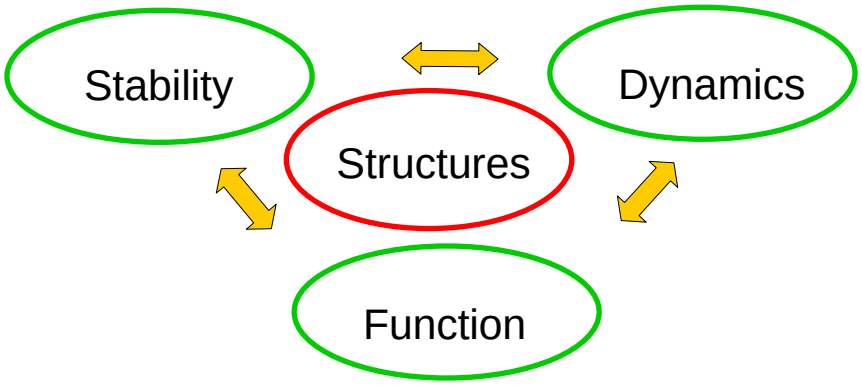


January 1, 2005

The ultimate goal of dynamics studies

- To bridge the gap between static and dynamic pictures of molecular structure and to demonstrate how motion relates to function.

Significance of dynamics and kinetics in biomacromolecules



Course Syllabus

Syllabus

	Date	Topics	Lecturer
1	01/06	General Introduction – Plan	Bahar, Tang
2	01/11	Fluctuations vs. Rotational Isomeric Transitions in Macromolecules (Chapt 6 in Daune) + Chapt 19 in Fersht)	Bahar
3	01/13	MD simulations (Leach)	Hagai
4	01/18	Folding Kinetics, Protein Engineering (Chapt 19 in Fersht)	Camacho
5	01/20	Conformational Changes (Chapt 8 in Daune) + Chapt 10 in Fersht	Zuckerman
6	01/25	Chemical Kinetics – Enzyme Kinetics- Michaelis Menten (Chapt 3 in Fersht)	Bahar
7	01/27	Introduction of Experimental methods + Proton exchange (Chapt 9 in Daune)	Tang
8	02/1	Inelastic Neutron and Light Scattering for dynamics (Chapt7 in Holde +	Tang
9	02/03	NMR fo	Tang
10	02/08	NMR fo	Tang
11	02/10	NMR for protei	Tang
12	02/15	Review	Tang
13	**02/17**	**1st exam**	Tang

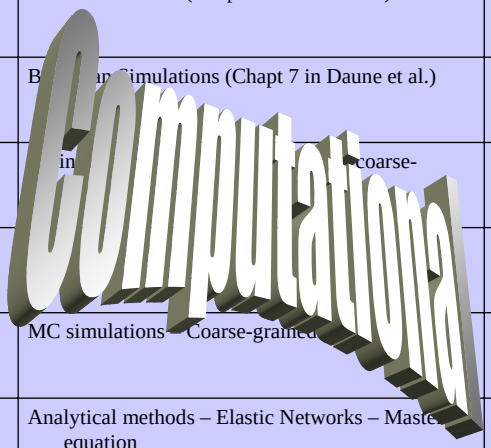
Foundations

Experimental

14	02/22	Folding of soluble protein model system lysozyme	Klein-Seetharaman
15	02/24	Folding of membrane protein model system rhodopsin and bacteriorhodopsin	Klein-Seetharaman
16	03/01	Equilibrium fluctuations of protein coupled receptors	Klein-Seetharaman
17	03/03	Functional conformations of protein coupled receptors	Klein-Seetharaman
18	03/08	Spring Break	
19	03/10	Spring Break	
20	03/15	Single-molecule	
21	03/17	Single-molecule dynamics II	Leuba
22	03/22	Ion channels and electrophysiology I	Levitan
23	03/24	Ion channels and electrophysiology II	Levitan
24	03/29	Motions from EPR (I)	Saxena
25	03/31	Motions from EPR (II)	Saxena
26	**04/05**	**Problem Review – 2nd exam**	Klein-Seetharaman

Experimental

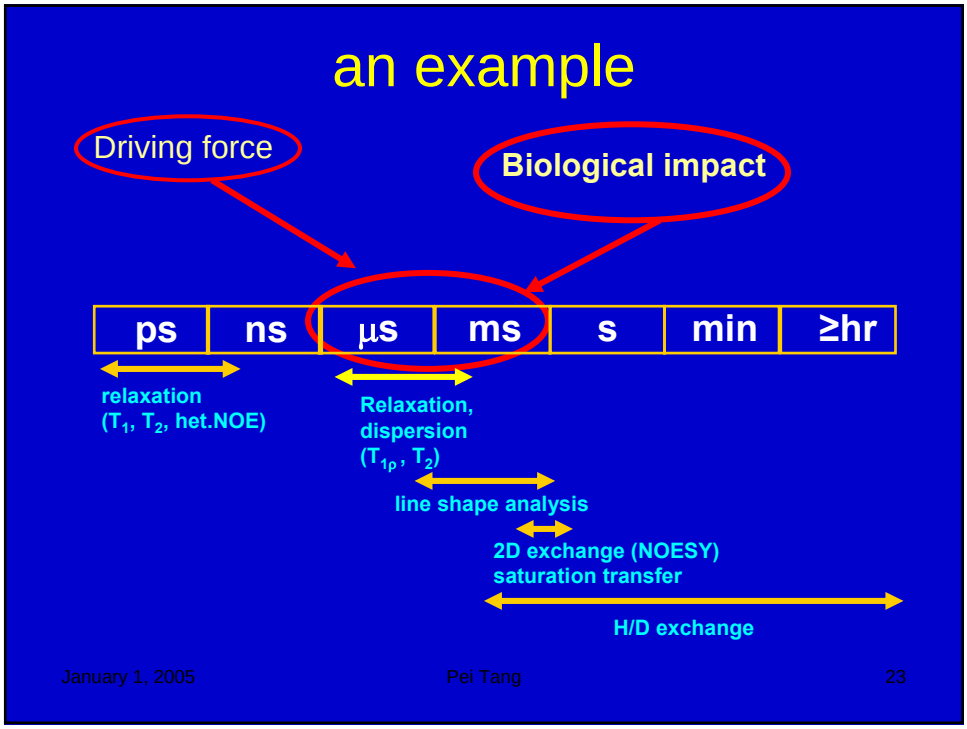
27	04/07	Brownian Motion (Chapt 7 in Daune et al)	Camacho
28	04/12	B[illegible]imulations (Chapt 7 in Daune et al.)	Hagai
29	04/14	in[illegible]coarse-	Hagai
30	04/19		Bahar
31	04/21	MC simulations – Coarse-grained	Zuckerman
32	04/26	Analytical methods – Elastic Networks – Master equation	Bahar
33	**04/28**	**Final exam**	



Tips for doing well in this course

Ask questions:

- What forces drive the motions
- on What time scales
- affect What type of functions
- How to characterize the motion
- …



Exams / Homework / Grades

Exam 1:	30%
Exam 2:	30%
Exam 3:	20%
Homework and participation:	20%

	100%

Additional information

- **Course coordinators:**

Ivet Bahar (bahar@ccbb.pitt.edu)

Pei Tang (tangp@anes.upmc.edu)

- **Web page with class notes**: http://www.biophysics.pitt.edu/student/

- **Office Hours**: by appointment

Homework 1

(optional)

- Give definitions of dynamics and kinetics, either your own definitions on the basis of your understanding or citations from other scientific literatures (please provide the original sources).

- Due day: Tuesday, Jan. 11, 2005