Curriculum Vitae **ROBERT CALLENDER** Date: July 1, 2016
Department of Biochemistry
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DEGREES

University of Minnesota	1960-1964	B.A. Mathematics, M.S. Physics
Harvard University	1964-1969	Ph.D. Applied Physics

APPOINTMENTS

University of Paris	10/69-9/70	Postdoctoral Research Associate
The Hebrew University	1/77-7/77	Visiting Associate Professor
Columbia University	9/85-6/86	Visiting Professor
The City College of The City University	9/70-9/1996	Ph.D. program faculty in Physics (1970) & Biochemistry (1980)
The City University	7/89-9/1996	Distinguished Professor of Biophysics
Albert Einstein College of Medicine	9/96-present	Professor of Biochemistry

VISITING APPOINTMENTS/CONSULTING

The GoodYear Rubber & Tire Co.	1986-1987	Consultant
The Eli Lilly and Company	1992-1993	Consultant
Los Alamos National Labs	1992-2005	Visiting Scientist/Consultant
Emisphere Corporation	1998-2000	Consultant
TPP Global Development Ltd	2012-present	Consultant

PROFESSIONAL ACTIVITIES

Publishing:

Editorial Board Member, *Basic and Applied Biological Physics* series (AIP Press), 1994-1996; Editorial Board, *Israel Journal of Chemistry*, 1995;
Editorial Advisory Board, *Biospectroscopy*, 1994-1998;
Editorial Board, Biological Physics Series, AIP press, 1997-present;
Editorial Board Member and Associate Editor of *Biophysical Journal*, 1985-1991, 1998-2002.
Editor-in-Chief, *Biophysical J*., 2002-2007

Advisory Boards:

Biological Physics Study Group, Div. Physics, NSF;
Los Alamos Physics Division Advisory Committee (1997-2002)
Member, FASEB Publications Committee.

American Physical Society:

Fellow; Division of Biological Physics
Executive Committee Member, 1988-1991
Division of Biological Physics, vice-Chair elect, vice Chair, Chair, 1991-1993
Member of Society Nominating Committee, 1993-1995
Centennial Speaker, Am. Physical Soc, 1998-1999
Member of Council, Am. Phys. Soc., 1997-2000.

Peer Review Boards:

NSF Biophysics review panel, 1987-1990, 2001
NIH reviewers reserve, 1995-1999; numerous times member various study sections

PROFESSIONAL SOCIETY MEMBERSHIP

American Physical Society (fellow) Biophysical Society
American Chemical Society Protein Society

COURSES TAUGHT

Physics (and Some Math)

Remedial Math
Freshman Physics
Computer Interfacing (grad & undergraduate)
Optics (undergraduate)
Biophysics (grad & undergraduate)
Advanced Physics Laboratory (grad and undergraduate)
Classical Mechanics (graduate level)
Quantum Mechanics (undergraduate)
Thermodynamics (undergraduate)

Biology

Physical Biochemistry (graduate level)
Molecular Biophysics (graduate)
Protein Folding: Disease and Design (graduate): last taught Spring 2012 (with Profs. Jon Lai and Marion Schmidt)
Physics & Biology of Vision (graduate level)
Biochemistry (graduate level)

Science and Religion

Science and Religion: pillars of human experience. Undergrad level.

CITY UNIVERSITY AND CITY COLLEGE RELATED ACTIVITIES

Graduate Committee on Admission and Awards;
Development of Computer Interfacing Course;
Member, City University Committee on Research (1985-1987);
Science Division Computer Committee Chairman;
Member, City University's Chancellor's Advisory Committee on Academic Program Planning, 1992;
Chair, committee to develop applied physics degree in materials science, optics/photonics and biomedical physics (1993-1996).

ALBERT EINSTEIN

Awards Committee
Faculty Senate
Promotions Committee

TEACHING, LOCAL AND NATIONAL INVOLVEMENT (recent)

Participated in the summer course to prepare graduate students for studies at Einstein. Summer, 2016.
Emergence and the Evolving 'Becoming' Universe. Lectures given at Westchester Community College, Jan. 20116.
Organized 2015 Telluride Conference on the 'Role of Dynamics in Enzyme Catalysis", summer 2015.

TEACHING

I have had the wonderful privilege of mentoring a group of just very talented of scientists.

Primary mentor for 20 Ph. D. graduates.
Primary mentor for 34 Postdoctoral research fellows.

PUBLICATIONS
(www.bioc.aecom.yu.edu/labs/calllab/PPpapers/callender/bobPubs.pdf)
148 scientific articles in Peer Reviewed Journals
20 Invited Reviews

Recent INVITED TALKS (NATIONAL AND INTERNATIONAL MEETINGS):
"Mechanisms of thermal adaptation: a look at how nature adopts protein flexibility", Telluride Conference on The Role of Dynamics in Enzyme Catalyzed Reactions, Telluride, CO, Aug. 3 – Aug. 7, 2015.
"Atomic Motion Encoding Function in lactate dehydrogenase", Telluride Conference on The Role of Dynamics in Enzyme Catalyzed Reactions, Telluride, CO, July 29 – August 2, 2013.
"The Energy Landscape of the Michaelis Complex of Lactate Dehydrogenase: relationship to catalytic mechanism", American Chemical Society fall meeting, September 8-14, 2013.

GRANTS
Closed
"Protein Dynamics in Enzymatic Catalysis", NIH, P01GM068036. 5/1/2004-4/30/2009, $5,922,836 (total direct costs); 5/1/2004-4/30/20014, $6,971,653 (total direct costs). The goal of this Program Project is to study atomic motion in enzymes. We are trying to understand how the dynamical nature of proteins affect enzymic function and the energy landscape of enzymes from enzyme-substrate to on-enzyme transition state formation.

Current
"Protein Dynamics in Enzymatic Catalysis", NIH, P01GM068036. 5/1/2014-4/30/2019. $9,005,090 total costs awarded. Callender overall PI and PI for Project 1. This Program consists of four Projects with, collectively, two overall Aims:

(1) To determine, via integrated application of experiment and theory, the elements of protein structure that create specific dynamics that are part of enzymatic catalysis on all relevant timescales. We will study how protein dynamics, particularly focused on the energy landscape of the Michaelis complex and motion of the promoting vibrations, is coupled to allostery and how this concept can be expanded to fully elucidate allosteric regulation of proteins. This presents a potential paradigm shift for protein and enzyme regulation via new drug action. In addition, a deeper understanding of transition state passage leaves us with the view that transition state inhibitors often do not function by "locking in" a specific structure, but rather by preserving dynamics at the transition state. We will investigate this new principle of strong inhibitor binding via dynamic preservation as a paradigm for enzyme function and inhibition.
(2) To use the understanding of how important functional dynamics are coded into the protein structure gained in (1) as a means to manipulate them in order to modify protein function. This objective comprises several parts. One is to design active site inhibitors against the dynamical nature of the enzyme. Another is to design small molecules to modify the dynamical nature through an 'allosteric' action which will either down or up-regulate activity and/or binding of substrate. The third is to develop methods to design rate controlling dynamics on a variety of timescales into engineered enzymes.

RESEARCH INTERESTS
Our work is centered on studying the structural and dynamical properties of proteins in order to understand the molecular mechanisms of protein function. We have developed new spectroscopic methods to obtain the vibrational spectra of specific protein groups and/or bound ligands, even within large proteins. With these techniques, it is possible to determine bond lengths with an accuracy of better than 0.01 Å. We also have developed techniques to monitor atomic motion in proteins on multiple time scales, as fast as picoseconds and out to minutes.

The primary problem of the lab is to understand the dynamics of enzymatic catalysis at a molecular level. This involves measurement of (1) static structures of enzymes complexes with their ligands and (2) how atomic motion evolves during the catalytic event. Structure is probed with vibrational spectroscopic tools that are capable of determining the Raman and IR spectra of bound substrates and specific protein molecular moieties. Vibrational spectroscopy yields a very high resolution of structure (better than 0.01 Å), and changes on this order are key to understanding enzymatic catalysis.

Modern paradigms for enzymatic catalysis all include atomic motion of the catalyst and reactants, either implicitly or explicitly. Binding of a substrate to form the Michaelis complex involves motions: formation of encounter complex(es), movement of the substrate towards the enzyme active site, desolvation of substrate, and often loop or flap closure or domain motion. Once the Michaelis complex is formed, movement of atoms and groups at the binding site occur to bring about the proper catalyzed chemistry and achieve these catalytic states with the incredible rate enhancements approaching 10^{18} relative to uncatalyzed reactions. We have recently developed kinetic approaches that can measure molecular motions in proteins on fast time scales (down to 10 ps), here-to-fore inaccessible to measurement, based on initiating chemical and structural changes via a laser induced temperature jump. Measurements of evolving structure is probed using optical and vibrational spectroscopies.

We also wish to understand how proteins arrive at their three dimensional structure (the protein folding problem). A number of studies are underway to understand the thermodynamics of folding. In addition, the crucial kinetic events of protein folding occur faster than the conventional millisecond time scale of stopped-flow mixing techniques. These early kinetic events in the folding process are being studied using our fast advanced initiation techniques. Our work in this area is currently focused on the folding/unfolding of enzymes near their functional structure(s) and how the so-called energy landscape of a folded and near folded protein affects function.

BRIEF RESEARCH HIGHLIGHTS

- Our results suggest a physical mechanism to understand LDH catalyzed chemistry in which the bulk of the rate enhancement can be viewed as arising from a stochastic search through an available phase space that, in the enzyme system, involves a restricted ensemble of more reactive conformational sub-states as compared to the same chemistry in solution. "Direct Evidence of Catalytic Heterogeneity in Lactate Dehydrogenase by Temperature Jump Infrared Spectroscopy", Michael Reddish", Huo-Lei Peng, Hua Deng, Kunal Panwar, Robert Callender, R. Brian Dyer, J. Phys. Chem. B 118, 10854-10862 (2014).

- T-jump kinetic studies of NADH emission reveal that the most important parameter affecting thermal adaptation appears to be enzyme control of the specific kinetics and dynamics of protein motions that lie along the catalytic pathway. "On the Mechanism of Thermal Adaptation in the Lactate Dehydrogenases", Huo-Lei Peng, Tsuyoshi Egawa, Eric Chang, Hua Deng, Robert Callender, J. Phys. Chem. B 119, 15256-15262 (2015).

See: www.callenderlab.org and/or www.proteindynamics.org.