BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Michael LEVITT	Professor
eRA COMMONS USER NAME (credential, e.g., agency login) LEVITT.MICHAEL	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
King's College, London, England	B.Sc.	06/1967	Physics
Royal Society Fellow, Weizmann Institute Israel	N/A	09/1968	Conformation Analysis
Cambridge University, England	Ph.D.	12/1971	Computational Biology

A. Personal Statement

I pioneered of computational biology setting up the conceptual and theoretical framework for a field that I am still actively involved in at all levels. More specifically, I still write and maintain computer programs of all types including large simulation packages and molecular graphics interfaces. I have also developed a high-level of expertise in Perl scripting, as well as in the advanced use of the Office Suite of programs (Word, Excel and PowerPoint), which is more important and rare than it may seem. My research focuses on three different but inter-related areas of research. First, we are interested in predicting the folding of a polypeptide chain into a protein with a unique native-structure with particular emphasis on how the hydrophobic forces affect the pathway. We expect hydrophobic interactions to energetically favor structure that are more native-like. In this way, the same stabilizing interactions that exist in the final folded state the search tractable. Second we are interested in predicting protein structure from sequence without regard for the process of folding. Such prediction relies on the well-established paradigms that similar protein sequences imply similar three-dimensional structures. We have focused on the hardest problem in homology modeling: the refinement of a near-native structure to make it more precisely like the actual native structure of protein. We have also focused on how the general similarity of all protein sequences resulting from their evolution from common ancestor sequence affects the nature of the protein universe. Third, we are focusing on mesoscale modeling of large macromolecular complexes such as RNA polymerase and the mammalian chaperonin. In this work, done in close collaboration with experimentalists, we use new morphing strategies combined with normal mode analysis in torsion angle space to overcome problems caused by the size and complexity of these critical, biomedically important systems. All this work depends on the way a molecular structure is represented in terms of the force-field that allows calculation of the potential energy of the system. We employ a very wide variety of such energy functions that extend from knowledge-based statistical potentials for a single interaction center per residue to quantum-mechanical force-fields that include inductive effects as well as polarization.

B. Positions, Honors and Review Service:

Positions and Employment

1972-1974 EMBO Postdoctoral Fellow with Shneior Lifson Weizmann Institute, Rehovot, Israel.
1974-1979 Staff Scientist, MRC Laboratory Molecular Biology, Cambridge, England.
1977-1979 Visiting Scientist with Francis Crick, Salk Institute, La Jolla, California.
1979-1987 Associate & Full Professor of Chemical Physics, Department of Chemical Physics, Weizmann Institute, Israel. Chair from 1980-1983, Full Professor from 1984.
1987- Professor of Structural Biology, Department of Structural Biology, Stanford University School of Medicine, Stanford. Chair from July 1993 till 2004.

1989- Ad Hoc reviewer for NIH, NSF and DOE, British MRC & Swedish National Research Foundation.
1995-1999 Charter Member BBCA Study Section.
1998-2003 Reviewer of Sloan-DOE fellowships in Computation Biology.

Other Experience and Professional Memberships

1989- Ad Hoc reviewer British, Israeli & Swedish National Research Councils.
1995-1999 Charter Member BBCA Study Section.
1998-2003 Reviewer of Sloan-DOE fellowships in Computation Biology.
2000- Editor for J. Mol. Biol.
2002- Editor for PLoS Compuational Biology.
2007- PNAS Editorial Board Member.
2010- Reviewer for NIH College of Reviewers
2010- Reviewer for NIH Pioneer Awards

Honors

1983- Member of European Molecular Biology Organization.
1982-1987 Scientific Advisory Board, European Molecular Biology Laboratory, Heidelberg.
1986 Federation of European Biochemical Societies Anniversary Prize (protein folding).
2001- Fellow of the Royal Society, London, UK.
2002- Member of the US National Academy of Science.
2010- Member of the American Academy of Arts & Sciences.

C. Selected Peer-reviewed Publications (Selected from 160 peer-reviewed publications)

Five most relevant to the current application

146. Sykes, M.T. and **M**. **Levitt**. Simulations of RNA base pairs in a nanodroplet reveal solvation-dependent stability. *Proc. Natl. Acad. Sci. USA*. **104**: 12336-12340 (2007).

151. Chopra, G., Summa C. and **M. Levitt**. Solvent Dramatically Affects Protein Structure Refinement. *Proc Natl. Acad. Sci USA*, **105**, 20239-20244 (2008).

152. Weiss, D. R. and **M**. **Levitt**. Can Morphing Methods Predict Intermediate Structures? *J. Mol. Biol.* **385**, 665-674 (2009).

159. Zhang, J., Baker, M. L., Schröder, G., Douglas, N. R., Reissmann, S., Jakana, J., Dougherty, M., Fu, C. J, **Levitt, M**., Ludtke, S. J., Frydman, J., and W. Chiu. Mechanism of Folding Chamber Closure in a Group II Chaperonin. *Nature*, **463**, 379-384 (2010).

160. Schröder, G., Brunger, A. and **M. Levitt**. Super-Resolution Biomolecular Crystallography with Low-Resolution Data. *Nature* **464**, 1218-1222 (2010).

Ten additional recent publications of importance to the field (in chronological order)

1. **Levitt**, **M**. and S. Lifson. Refinement of Protein Conformations Using a Macromolecular Energy Minimization Procedure. *J. Mol. Biol*. **46**: 269-279 (1969).

11. **M**. **Levitt**. A Simplified Representation of Protein Conformations for Rapid Simulation of Protein Folding. *J. Mol. Biol.* **104**: 59-107 (1976).

19. Jack, A. and **M**. **Levitt**. Refinement of Large Structures by Simultaneous Minimization of Energy and R Factor. *Acta Crystallogr*. **A34**: 931-935 (1978).

35. **M**. **Levitt**. Protein Folding by Restrained Energy Minimization and Molecular Dynamics. *J. Mol. Biol*.**170**:723-764 (1983).

45. **Levitt**, **M**. and R. Sharon. Accurate Simulation of Protein Dynamics in Solution. *Proc. Natl. Acad. Sci. USA*. **85**: 7557-7561 (1988).

113. **M**. **Levitt**. The Birth of Computational Structural Biology, *Nature Structural Biol*., **8**: 392-393 (2001).

121. Xia, Y. and **M**. **Levitt**. Roles of Mutation and Recombination in the Evolution of Protein Thermodynamics. *Proc Natl. Acad. Sci U S A*. **99**: 10382-10387 (2002).

145. **M**. **Levitt**. Growth of Novel Protein Structural Data. *Proc. Natl. Acad. Sci. USA*. **104**: 3183-3188 (2007).

156. Wang, D., Bushnell, D.A., Huang, X, Westover, K.D., **Levitt, M**. and R.D. Kornberg. Structural Basis of Transcription: Backtracked RNA Polymerase II at 3.4 Å Resolution. *Science* **324**, 1203-1206 (2009).

157. **Levitt, M**. Nature of the Protein Universe. *Proc. Natl. Acad. Sci USA*. **106**, 11078-11084 (2009).

D. Research Support

Ongoing Research Support

5R37GM041455-17 (PI: Levitt) 7/1/07 - 6/30/12

Simulation and Prediction of Protein Folding

The major goals of this project are to consider in detail the stability, dynamics and folding of proteins. It includes our work on the *ab initio* prediction of protein structure from sequence.

R01 GM63817-05 (PI: Levitt) 8/1/09 - 7/31/13

Accurate Molecular Modeling in Structural Genomics

The major goals of this project are to develop new methods for accurate, rapid and automatic homology modeling. Emphasis is placed on better energy functions for refinement and on automatic multiple structure alignment.

R01 GM081712-01 (PI: Koehl); UC Davis RA06-002708-STAN (PI: Levitt) 08/15/07 - 07/31/10

Alignments and Improved Refinements for High-Accuracy Protein Structure Modeling

The major goals of this project are (a) get crystal structure quality models for close homologs (>30% sequence identity) and (b) build high accuracy models for remote homologs (~10% sequence identity). The project involves a group of three PI's: Koehl, Levitt & Keasar.

1U54GM072970-01 (PI's: Russ Altman & Scott Delp)09/15/04 - 08/31/09

Physics Based Simulation of Biological Structures

The major goals of this Center are to develop, disseminate, and support a simulation tool kit (SimTK) that will enable biomedical scientists to develop and share accurate models and simulations of biological structures from atoms to organisms. 16 labs at Stanford are involved.

2PN2EY016525-02 (PI: Wah Chui) 09/30/04 - 09/30/10

Center for Protein Folding Machinery

The major goals of this project, which involves a group of 15 PI's working on experimental and theoretical aspects of *in vivo* protein folding machinery, is to modulate protein folding pathways and chaperone function for therapeutic and biomedical applications.

CNS-0619926 (PI: Levitt) 08/30/06 - 07/31/10

Acquisition of a Hybrid Shared-Memory/Massively-Parallel Commodity Cluster for Cost-Effective Super-Computing at Stanford

The major goal of this project, which involves a group of 21 PI's is to acquire a new super-computer for use by all Stanford Bio-X faculty (about 400 in all).

RGPOO2412008-C (PI: Michael Kiebler) 07/01/08 - 06/30/11
Human Frontier Science Program Organization 0.0 cal mos. $99,970
Structure and Dynamics of Neuronal Granules that Regulate RNA Localization
The major goal of this project, which involves an international group of 4 PI's is to study RNA in Neuronal Granules.

Pending Research Support
None

Past Research Support (past five years)
None