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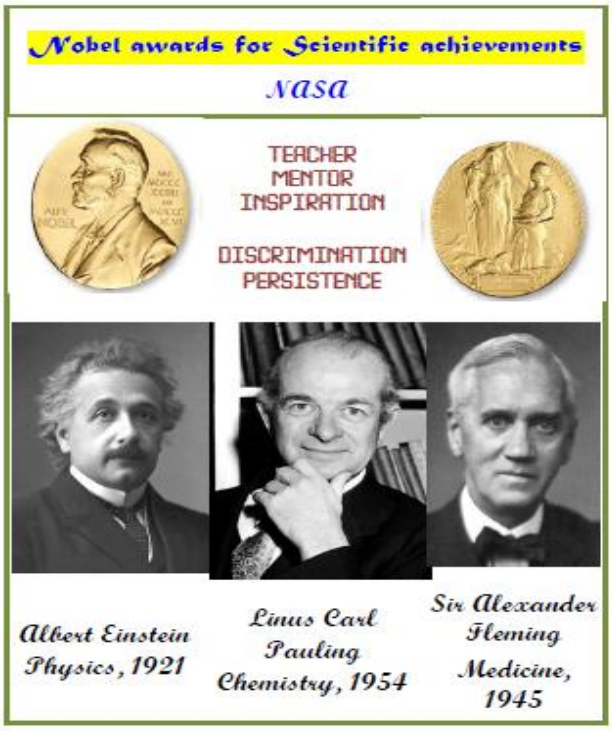

NASA

Part I: Chemistry at Harvard Macromolecular Mechanics (CHARMM)

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Nobel Prize in Chemistry (NPic) – CHARMM

In 2013, Nobel Prize in chemistry was shared by Martin Karplus, Michael Levitt and Arieh Warshel for "Multiscale models for complex Chemical systems" [1]. These studies, since early nineteen seventies, were around combination of molecular mechanics/ force fields/ Quantum chemistry/ molecular dynamics and application to chemical/ bio-chemical reactions/interactions of macro-molecules, proteins and enzymes in presence/absence of water/ solvent/ small-molecules including drugs. CHARMM, software package, was initiated and nurtured by Martin Karplus with inputs from other colleagues. The select publications of the Nobel laureates are in Table 1.

Physics, mathematics and/or chemistry are science windows at nature (Swans) to probe, understand visible and invisible universe (nature) with human eyes/third eye (knowledge) and/or state-of-art-instruments. These three powerful disciplines mutually influence the study of inanimate and life processes on all scales.

The four pillars of science are experiments, instruments, computations and simulations. The fifth paradigm is knowledge coupled with intelligence sparkles bringing renaissance in rational approach of correlated stochastic/ multi-variable dynamic fuzzy systems monitored by multi-channel multi-response fused probes. The inspiration from nature of 13.7 billion years young for the expert humans (of 200K years old) in development/ advancement of scientists' physics, mathematics and chemistry is perineal in bringing out nanoscopic science windows in nature's evolution (Swine).

Table 1a: Select research publications of

M. Levitt,

2013 Nobel Laureate in chemistry

School of Medicine
Stanford University,
Stanford, CA 94085

Refinement of Protein Conformations Using a Macromolecular Energy Minimization Procedure
M. Levitt, S. Lifson, *J. Mol. Biol.* **1969**, 46, 269–79.

Computer Simulation of Protein Folding
M. Levitt, A. Warshel, *Nature* **1975**, 253,694–698.

A Simplified Representation of Protein Conformations for Rapid Simulation of Protein Folding
M. Levitt, *J. Mol. Biol.* **1976**, 104, 59–107.

Conformation Analysis of Proteins
M. Levitt, PhD Thesis,
Cambridge University,Cambridge, UK, 1971.
http://csb.stanford.edu/levitt/Levitt_Thesis_1971/Levitt_Thesis_1971.html

On the Nature of the Binding of Hexa-N-Acetyl Glucosamine Substrate to Lysozyme
M. Levitt, In *Peptides, Polypeptides and Proteins*,
Wiley, New York, 1974, pp.99–113.

Theoretical Studies of Enzymic Reactions: Dielectric, Electrostatic and Steric Stabilization of the Carbonium Ion in the Reaction of Lysozyme
A. Warshel, M. Levitt,*J. Mol. Biol.* **1976**, 103, 227–249.

Accurate Simulation of Protein Dynamics in Solution
M. Levitt, R. Sharon, *Proc. Natl. Acad. Sci. USA* **1988**, 85, 7557–7561.

Molecular Dynamics Simulation of Helix Denaturation
V. Daggett, M. Levitt, *J. Mol. Biol.* **1992**, 223, 1121–1138.

Can Morphing Methods Predict Intermediate Structures?
D. Weiss, D. and M.Levitt, *J. Mol. Biol.* **2009**, 385, 665–674.

Millisecond Dynamics of RNA Polymerase II Translocation at Atomic Resolution
D-A, Silva, D. Weiss, F. Pardo, L-T. Da1, M. Levitt., D. Wang., X. Huang,
Proc. Natl. Acad. Sci. USA **2014**.

Protein Normal-Mode Dynamics: Trypsin Inhibitor, Crambin, Ribonuclease and Lysozyme
M. Levitt, C. Sander, P.S. Stern, *J. Mol. Biol.* **1985**, 181, 423–447.

Conformational Optimization with Natural Degrees of Freedom: A Novel Stochastic Chain Closure Algorithm
P. Minary, M. Levitt, *J. Comp. Chem.* **2010**, 17,993–1010.

Modeling and Design by Hierarchical Natural Moves
A. Y. L. Sim, M. Levitt, P. Minary,
B. *Proc. Natl. Acad. Sci. USA* **2012**, 109: 2890–2895.

Training-free atomistic prediction of nucleosome occupancy
P. Minary, M. Levitt,*Proc. Natl. Acad. Sci. USA* **2014**.

Subunit Order of Eukaryotic TRiC/CCT Chaperonin by Cross-linking, Mass Spectrometry and Combinatorial Homology Modeling
N. Kalisman, C. M. Adams, M.Levitt,
Proc. Natl. Acad. Sci. USA **2012**, 109, 2884–2889.

Architecture of an RNA polymerase II transcription pre-initiation complex
K.Murakami, H. Elmlund, N. Kalisman, D. A. Bushnell, C. M. Adams, M. Azubel, D. Elmlund, Y. Levi-Kalisman, X. Liu, B. J. Gibbons, M. Levitt, R. D Kornberg, *Science* **2013**, 342, 1238724.

The Predicted Structure of Immunoglobulin D1.3 and its Comparison with the Crystal Structure
C. Chothia, A. M.Lesk, M. Levitt, A. G. Amit, R. A. Mariuzza, S.E. V. Phillips, R. J. Poljak, *Science* **1986**, 233: 755–758.

The Conformations of Immunoglobulin Hypervariable Regions
C. Chothia, A.M. Lesk, M. Levitt, A., Tramontano, S. J. Smith-Gill, G, Air, S. Sheriff, E. A. Padlan, D. Davies, W. R. Tulip, P.M. Colman, *Nature* **1989**, 342, 877–883.

A Humanized Antibody that Binds to the IL-2 Receptor
C. Queen, W. P. Schneider,H.E. Selick, P. W. Payne, N. F. Landolfi, J. F. Duncan, A. M. Avdalovic, M. Levitt,R. P. Junghans, T. A. Waldmann, *Proc. Natl. Acad. Sci. USA* **1989**, 86, 10029–10033.

Life-Long Influence of Max Perutz and the Laboratory of Molecular Biology
M.Levitt,
in *Memories and Consequences*, edited by H. Huxley, **2013**. http://www2.mrc-lmb.cam.ac.uk/ebooks/Memories_and_consequences-Hugh_Huxley.epub

WeFold: A coopetition for protein structure prediction
George A. Khoury, Adam Liwo, Firas Khatib,Hongyi Zhou, Gaurav Chopra, Jaume Bacardit, Leandro O. Bortot, Rodrigo A. Faccioli, Xin Deng, Yi He, Pawel Krupa, Jilong Li, Magdalena A. Mozolewska, Adam K. Sieradzan, James Smadbeck, Tomasz Wirecki, Seth Cooper, Jeff Flatten, Kefan Xu, David Baker, Jianlin Cheng, Alexandre C. B. Delbem, Christodoulos A. Floudas, Chen Keasar,Michael Levitt,Zoran Popovic, Harold A. Scheraga, Jeffrey Skolnick, Silvia N. Crivelli, and Foldit Players
Proteins 2014; 82:1850–1868.

Millisecond dynamics of RNA polymerase II translocation at atomic resolution
Daniel-Adriano Silva, Dahlia R. Weiss, Fátima Pardo Avila, Lin-Tai Da, Michael Levitt, Dong Wang,and Xuhui Huang
PNAS,May 27, 2014,vol. 111, no. 21, 7665–7670

Redundancy-weighting for better inference of protein structural features
Chen Yanover, Natalia Vanetik, Michael Levitt, Rachel Kolodny, and Chen Keasar
Bioinformatics · April 2014

Table 1b: Research publications of Martin Karplus, 2013 Nobel Laureate in chemistry

Université de Strasbourg, Strasbourg, France, Harvard University, Cambridge, MA, USA

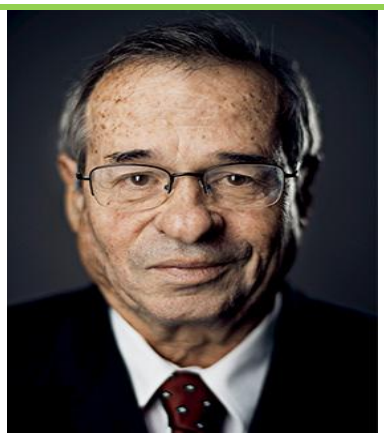
B. Honig, A. Warshel, M. Karplus	Acc. Chem. Res. 8, 92–100 (1975).
C. M. Dobson, A. Sali, M. Karplus	Angew. Chem. Int. Ed. 37, 868–893 (1998).
M. Karplus D. L. Weaver	Biopolymers 18, 1421–1437 (1979).
P. J. Rossky, M. Karplus A. Rahman,	Biopolymers 18, 825–854 (1979).
Y. Q. Gao, W. Yang, M. Karplus	Cell 123, 195–205 (2005).
A. Warshel M. Karplus	Chem. Phys. Letters 32, 11–17 (1975).
P. J. Rossky M. Karplus	J. Am. Chem. Soc. 101, 1913–1937 (1979).
A. Warshel M. Karplus	J. Am. Chem. Soc. 94, 5612–5625 (1972).
W. Yang, R. Bitetti-Putzer, M. Karplus	J. Chem. Phys. 120, 2618–2628 (2004).
M. Karplus R. N. Porter, R. D. Sharma,	J. Chem. Phys. 45, 3871–3873 (1966).
V. Ovchinnikov, B. L. Trout, M. Karplus	J. Mol. Biol. 395, 815–833 2010).
B. Honig M. Karplus	Nature 229, 558–560 (1971).
M. Karplus D. L. Weaver,	Nature 260, 404–406 (1976).
J. A. McCammon, B. R. Gelin, M. Karplus	Nature 267, 585–590 (1977).
K. A. Henzler-Wildman, V.Thai, M. Lei, M. Ott, M. Wolf-Watz, T. Fenn, E. Pozharski, M. A. Wilson, G. A. Petsko, M. Karplus C. G. Hübner, D. Kern,	Nature 450, 838–844 (2007).
D. Vitkup, D. Ringe, G. A. Petsko, M. Karplus	Nature Struc. Biol. 7, 34–38 (2000).
K. A. Henzler-Wildman, M. Lei, V. Thai, S. J. Kerns, M. Karplus D. Kern,	Nature450, 913–916 (2007).
M. Cecchini, A. Houdusse, M. Karplus	PLoS Computational Biology 4, e1000129:1–19 (2008).
W. Yang, Y. Q. Gao, Q. Cui, J. Ma, M. Karplus	Proc. Natl. Acad. Sci. USA 100, 874–879 (2003).
W. Hwang, S. Zhang, R. D. Kamm, M. Karplus	Proc. Natl. Acad. Sci. USA 101, 12916–12921 (2004).
J. Pu M. Karplus	Proc. Natl. Acad. Sci. USA 105, 1192–1197 (2008).

A. S. Khalil, D. C. Appleyard, A. K. Labno, A. Georges, M. Karplus A. M. Belcher, W. Hwang, M. J. Lang	Proc. Natl. Acad. Sci. USA 105, 19246–19251 (2008
B. R. Gelin M. Karplus	Proc. Natl. Acad. Sci. USA 72, 2002–2006 (1975).
M. Karplus D. L. Weaver,	Protein Science 3, 650–668 (1994).
M. Garcia-Viloca, J. Gao, M. Karplus D. G. Truhlar	Science 303, 186–195(2004).

Table 1c: Typical research publications of

A Warshel,

2013 Nobel Laureate in chemistry



University of Southern California, Los Angeles, CA, USA

Computer Modeling of Chemical Reactions in Enzymes and Solutions

Warshel, A.,1997, Wiley-Interscience Imprint John Wiley & Sons: Hoboken. 256 p. ill.

Abstract of the 34th meeting: On the interaction of Chymotrypsin with ionized substrates,

Warshel. A. and Y. Shalitin, Israel J. Chemistry, 1966. **4**: p. 85.

Consistent Force Field for Calculations of Conformations Vibrational Spectra and Enthalpies of Cycloalkane and N-Alkane Molecules

Lifson, S. and A. Warshel, J. Chemical Physics, 1968. **49**(11): p. 5116.

Consistent Force Field Calculations .2. Crystal Structures, Sublimation Energies, Molecular and Lattice Vibrations, Molecular Conformations, and Enthalpies of Alkanes,

Warshel, A. and S. Lifson J. Chemical Physics, 1970. **53**(2): p.582–&.

Oxidation of 4a,4b-Dihydrophenanthrenes .3. A Theoretical Study of Large Kinetic Isotope Effect of Deuterium in Initiation Step of Thermal Reaction with Oxygen

Warshel, A. and A. Bromberg, J. Chemical Physics, 1970. **52**(3): p.1262.

Calculation of Ground and Excited-State Potential Surfaces of Conjugated Molecules .1. Formulation and Parametrization

Warshel, A. and M. Karplus, J. American Chemical Society, 1972. **94**(16): p. 5612–&.

Quantum-Mechanical Consistent Force-Field (Qcff/Pi) Method—Calculations of Energies, Conformations and Vibronic Interactions of Ground and Excited-States of Conjugated Molecules

. Warshel, A., Israel J. Chemistry, 1973. **11**(5):p. 709–717.

Microscopic Models for Quantum Mechanical Calculations of Chemical Processes in Solutions: LD/AMPAC and SCAAS/AMPAC Calculations of Solvation Energies

Luzhkov, V. and A. Warshel, J. Comp. Chem., 1992. **13**: p. 199–213.

Progress in Ab Initio QM/MM Free-Energy Simulations of Electrostatic Energies in Proteins: Accelerated QM/ MM Studies of pK(a), Redox Reactions and Solvation Free Energies

Kamerlin, S.C.L., M. Haranczyk, and A. Warshel, J. Physical Chemistry B, 2009. **113**(5): p. 1253–1272.

Energetics of Enzyme Catalysis

Warshel, A., Proc. Natl. Acad. Sci. USA., 1978. **75**:p. 5250–5254.

Electrostatic basis for enzyme catalysis

Warshel, A., et al., Chem. Rev., 2006.**106**(8): p. 3210–35.

Calculations of Electrostatic Interactions in Biological Systems and in Solutions

Warshel, A. and S.T. Russell, Q. Rev. Biophys., 1984. **17**: p. 283–421.

Modeling electrostatic effects in proteins .

Warshel, A., et al., Biochimica Et BiophysicaActa-Proteins and Proteomics, 2006. **1764**(11): p. 1647–1676.

Vicatos, S., M. Roca, and A. Warshel, Effective approach for calculations of absolute stability of proteins using focused dielectric constants

Vicatos, S., M. Roca, and A. Warshel, Proteins-Structure Functionand Bioinformatics, 2009. **77**(3): p. 670–684.

An Empirical Valence Bond Approach for Comparing Reactions in Solutions and in Enzymes

Warshel, A. and R.M. Weiss, J. Am. Chem. Soc., 1980. **102**(20): p.6218–6226.

Computer simulations of enzyme catalysis: Methods, progress, and insights

Warshel, A., Ann. Rev. Biophys. Biomol. Struct., 2003. **32**: p. 425–443.

Exploring, Refining, and Validating the Paradynamics QM/MM Sampling

Plotnikov, N.V. and A. Warshel, J. Physical Chemistry B, 2012. **116**(34): 10342–10356.

Frozen Density-Functional Approach for Ab-Initio Calculations of Solvated Molecules

Wesolowski, T.A. and A. Warshel, J. Phys. Chem., 1993. **97**: p. 8050–8053.

Semiclassical Trajectory Approach to Photoisomerization

Warshel, A. and M. Karplus Chemical Physics Letters, 1975. **32**(1): p. 11–17.

Calculation of Pi Pi Excited-State Conformations and Vibronic Structure of Retinal and Related Molecules

Warshel, A. and M. Karplus J. AmericanChemical Society, 1974. **96**(18): p. 5677–5689.

Bicycle-Pedal Model for 1st Step in Vision Process

Nature, 1976. **260**(5553): p. 679–683.

Control of Redox Potential of Cytochrome c and Microscopic Dielectric Effects in Proteins

Churg, A.K. and A. Warshel,

Biochemistry, 1986. **25**: p. 1675.

Energetics of Ion Permeation through Membrane Channels—Solvation of Na+ by Gramicidin-A
Aqvist, J. and A. Warshel,
Biophysical Journal, 1989. **56**(1): p.171–182.

Calculations of Chemical Processes in Solutions
Warshel, A.,
J. Physical Chemistry, 1979. **83**(12): p. 1640–1652.

Dynamics of reactions in polar solvents. Semiclassical trajectory studiesof electron-transfer and proton-transfer reactions
Warshel, A.,
J. Phys. Chem., 1982. **86**: p.2218–2224.

Simulating the Energetics and Dynamics of Enzymatic Reactions, in Specificity in Biological Interactions,
Warshel, A.,
C. Chagas and B. Pullman, Editors. 1984,
Springer Netherlands. p. 59–81.

Molecular dynamics simulations of biological reactions
Warshel, A.,
Accounts of Chemical Research, 2002. **35**(6): p. 385–395.

Renormalizing SMD: The Renormalization Approach and Its Use in Long Time Simulations and Accelerated PAU Calculations of Macromolecules
Dryga, A. and A. Warshel,
J. Physical Chemistry B, 2010. **114**(39): p. 12720–12728.

Renormalizing SMD: The Renormalization Approach and Its Use in Long Time Simulations and Accelerated PMF Calculations of Macromolecules
Dryga, A. and A. Warshel,
J. Phys. Chem. B, 2010. **114**(39): p. 12720–12728.

Electrostatic origin of the mechanochemical rotary mechanism and the catalytic dwell of F1-ATPase
Mukherjee, S. and A. Warshel,
Proc. Natl. Acad. Sci. USA, 2011.**108**(51): p. 20550–5.

Realistic simulations of the coupling between the protomotive force and the mechanical rotation of the F0-ATPase
.Mukherjee, S. and A. Warshel,
Proc. Natl. Acad. Sci. USA, 2012. **109**(37): p. 14876–81.

On the energetics of translocon-assisted insertion of charged transmembrane helices into membranes
Rychkova, A., S. Vicatos, and A. Warshel,
Proc. Natl. Acad. Sci. USA, 2010. **107**(41): p. 17598–17603.

Exploring the nature of the translocon-assisted protein insertion
Rychkova, A. and A. Warshel,
Proc. Natl. Acad. Sci. USA, 2013. **110**(2): p. 495–500.

.Predicting drug-resistant mutations of HIV protease
Ishikita, H. and A. Warshel
Angew. Chem. Int. Ed., 2008. **47**(4): p. 697–700.

Validating the vitality strategy for fighting drug resistance
Singh, N., M.P. Frushicheva, and A. Warshel,
Proteins-Structure Function and Bioinformatics, 2012.**80**(4): p. 1110–1122.

Electrostatic contributions to protein protein binding affinities: Application to Rap/Raf interaction
Muegge, I., T. Schweins, and A. Warshel,
Proteins-Structure,Function and Genetics, 1998. **30**(4): p. 407–423.

REFERENCES

[1] K RamaKrishna, R Sambasiva Rao, *J. Appl. Chem*, 2015, 4(5), 1563-1570.
Chemical education (Ice): 1. Nobel prizes in Chemistry (2000 to 2014)
[2] http://www.nobelprize.org/