OMB No. 3145-0279 (Expiration Date 10/31/2026)

NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: Levitt, Michael

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-8414-7397

Position Title: Professor of Structural Biology, Department of Structural Biology, Stanford University School of Medicine

Organization and Location: Stanford University, Stanford, California, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
Weizmann Institute, Rehovot, Not Applicable, N/A, Israel	Postdoctoral Fellow	09/1972	08/1974	Computational Biology
Cambridge University, Cambridge, Not Applicable, N/A, United Kingdom	Doctor of Philosophy (PHD)	09/1968	01/1972	Computational Biology
Weizmann Institute, Rehovot, Not Applicable, N/A, Israel	Fellow	10/1967	09/1968	Computational Biology
King's College, London, Not Applicable, N/A, United Kingdom	Bachelor of Science (BS)	09/1964	06/1967	Physics

Appointments and Positions

1987 - present	Professor of Structural Biology, Department of Structural Biology, Stanford University School of Medicine, Stanford University, Stanford, California, United States
2026 - present	Scientific Advisory Board Member, Human Longevity Inc., San Diego, California, United States
2025 - present	Consultant, Conquest Technologies Corporation, Palo Alto, California, United States
2025 - present	Consultant, AoBo (OPUSBio), Wuhan, Not Applicable, N/A, China
2025 - present	Consultant, Prisma Labs, Palo Alto, California, United States
2024 - present	Consultant, FreeCurve, Berkeley, California, United States
2022 - present	Consultant, Harvest Biotech, Jiaxing, Not Applicable, N/A, China
2021 - present	Member Academic Committee, The Starry Night Foundation, Hangzhou, Not Applicable, N/A, China
2021 - present	Consultant, Zhejiang Mebolo Biotechnology, Jinhua, Not Applicable, N/A, China
2020 - present	Consultant, Fondin Biotech, Shanghai, Not Applicable, N/A, China
2018 - present	Honorary dean and Consultant to the Multiscale Research Institute of Complex Systems, Fudan University, Shanghai, Not Applicable, N/A, China
2018 - present	Member of Executive Committee, World Laureates Association, Shanghai, Not Applicable, N/A, China
2014 - present	Scientific Advisory Board member, Insilico Medicine, George Town, Not Applicable, N/A, Cayman Islands
2014 - 2024	Consultant, InterX Inc, Berkeley, California, United States

Products

Products Closely Related to the Proposed Project

1. Levitt M, Marten B, Oren G, Ioannidis J. Reclassification and Weighting of Multiple Causes of Death: US Death Certificates 2003-2023. medRxiv. 2026 Apr 19; PubMed Central PMCID: PMC12889793.
2. Butin O, Pereyaslavets L, Kamath G, Illarionov A, Sakipov S, Kurnikov IV, Voronina E, Ivahnenko I, Leontyev I, Nawrocki G, Darkhovskiy M, Olevanov M, Cherniavskyi YK, Lock C, Greenslade S, Kornberg RD, Levitt M, Fain B. The Determination of Free Energy of Hydration of Water Ions from First Principles. J Chem Theory Comput. 2024 Jun 25;20(12):5215-5224. PubMed Central PMCID: PMC11881599.
3. Levitt M, Sander C, Stern PS. Protein normal-mode dynamics: trypsin inhibitor, crambin, ribonuclease and lysozyme. J Mol Biol. 1985 Feb 5;181(3):423-47. PubMed PMID: 2580101.

4. Mitsikosta S, Westerfield JM, Pardo-Avila F, Levitt M, von Heijne G, Metola A. Quasi-continuous cotranslational compaction and folding of a multidomain protein. bioRxiv. 2026 Feb 6; PubMed Central PMCID: PMC12889668.
5. Rosenwasser Z, Cohen-Fultheim R, Levitt M, Levanon EY, Oren G. ADAR-GPT: A continually fine-tuned language model for predicting A-to-I RNA editing sites. Proc Natl Acad Sci U S A. 2026 Jan 13;123(2):e2529073123. PubMed Central PMCID: PMC12798952.

Other Significant Products Highlighting Contributions to Science

1. Levitt M, Lifson S. Refinement of protein conformations using a macromolecular energy minimization procedure. J Mol Biol. 1969 Dec 14;46(2):269-79. PubMed PMID: 5360040.
2. Warshel A, Levitt M. Theoretical studies of enzymic reactions: dielectric, electrostatic and steric stabilization of the carbonium ion in the reaction of lysozyme. J Mol Biol. 1976 May 15;103(2):227-49. PubMed PMID: 985660.
3. Levitt M. A simplified representation of protein conformations for rapid simulation of protein folding. J Mol Biol. 1976 Jun 14;104(1):59-107. PubMed PMID: 957439.
4. Kalisman N, Adams CM, Levitt M. Subunit order of eukaryotic TRiC/CCT chaperonin by cross-linking, mass spectrometry, and combinatorial homology modeling. Proc Natl Acad Sci U S A. 2012 Feb 21;109(8):2884-9. PubMed Central PMCID: PMC3287007.
5. Levitt M. Detailed molecular model for transfer ribonucleic acid. Nature. 1969 Nov 22;224(5221):759-63. PubMed PMID: 5361649.

Certification:

I certify that the information provided is current, accurate, and complete. This includes, but is not limited to, information related to current, pending, and other support (both foreign and domestic) as defined in 42 U.S.C. § 6605.

In accordance with Section 10632 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19232), each individual identified as a senior/key person must certify that they are not a party to a malign foreign talent recruitment program.

Research Security Training Requirement for Federal Award Personnel: In accordance with Section 10634 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19234), each individual identified as a senior/key person must certify that they have completed the requisite research security training that meets the requirements specified in Item 2 of Important Notice No. 149 within 12 months prior to proposal submission.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§287, 1001, 1031 and 31 U.S.C. §§3729-3733 and 3802.

Certified by Levitt, Michael in SciENcv on 2026-09-09 19:04:41

NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: Levitt, Michael

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-8414-7397

Position Title: Professor of Structural Biology, Department of Structural Biology, Stanford University School of Medicine

Organization and Location: Stanford University, Stanford, California, United States

Personal Statement

I was one of the first to work in computational biology, and I built much of the conceptual, theoretical and computational framework of a field in which I am still active. I still write the programs myself, in Fortran, C and Python. That matters here, because the work proposed needs code that does not yet exist.

Physics-based simulation is where I started and where this project returns. In 1967 Shneior Lifson, at the Weizmann Institute in Rehovot, set me to refine protein conformations by energy minimization, and the force fields and simplified representations that followed are still in use (PMID 957439, PMID 985660). The energy function has kept improving: with Boris Fain and Roger Kornberg we computed the free energy of hydration of water ions from first principles, with no fitted parameters (PMC11881599). The proposed study of motion in large assemblies uses a real force field, ENCAD, rather than an elastic network. It is the calculation I published with Chris Sander and Peter Stern in 1985 (PMID 2580101), now attempted on assemblies a hundred times larger. Every published normal-mode analysis of the ribosome uses an elastic network, so the comparison has never been made.

Structures carrying too little data to be solved conventionally are the second thread. With Nir Kalisman I ordered the subunits of the eukaryotic chaperonin TRiC/CCT, a problem that had defeated both cryogenic electron microscopy and X-ray crystallography, by generating more than a million possible arrangements and asking which fitted a handful of cross-links (PMC3287007). The same habit, treat the model as a hypothesis and let sparse data falsify it, drives the proposed work with Gunnar von Heijne on cotranslational folding, where the force on the nascent chain is almost the only observable (PMC12889668).

Heterogeneity in human populations is the third. With John Ioannidis and Francesco Zonta I showed that published estimates of pandemic excess death disagree by factors of two or more, and why (PMC9225924). With Ben Marten and Gal Oren we then went to the death certificates themselves, reclassifying and reweighting United States records from 2003 to 2023 by every cause listed rather than one (PMC12889793). Both papers make the same point: an aggregate curve hides the spread in the population underneath it.

Mentoring is what I am proudest of. From 1967 to 1986 I had no group and worked alone or with peers. Since coming to Stanford in 1987 I have supervised 50 young people, 15 of them doctoral students. Of the 42 who have left, 24 are in academia and 17 of those hold tenure. I give them as much independence as they will take: 53 of my publications are sole-author and 158 have three or fewer co-authors, so a name on one of my papers means something.

All my research products are published under the name Michael Levitt.

Honors

2024	Reverend Joseph Carrier Medal, University of Notre Dame
2014	DeLano Award for Computational Biosciences, American Society for Biochemistry and Molecular Biology
2014	Honorary Fellow, Royal Society of Chemistry, London, United Kingdom
2014 - 2024	Honorary doctorates: Bar-Ilan University 2014, King's College London 2014, Technion 2015, Cambridge University 2019, Hong Kong University of Science and Technology 2024, Five universities, as listed
2014 - 2017	Honorary professorships: Zhejiang University 2014, Xi'an Jiaotong University 2017, Northwest University 2017, Northwestern Polytechnical University 2017, Fudan University 2017, Five universities in China, as listed
2013	Nobel Prize in Chemistry, shared with Martin Karplus and Arieh Warshel, Royal Swedish Academy of Sciences
2010	Member, American Academy of Arts and Sciences
2010	Robert W. and Vivian K. Cahill Endowed Professor in Cancer Research, Stanford University
2003 - 2004	Blaise Pascal Professor of Research, Fondation de l'Ecole Normale Superieure, Paris, France
2002	Member, National Academy of Sciences, United States
2001	Fellow, Royal Society, London, United Kingdom
1986	Anniversary Prize, for protein folding, Federation of European Biochemical Societies
1981	Member, European Molecular Biology Organization

1972 - 1974	Fellowship, European Molecular Biology Organization
1970 - 1974	Research Fellowship, Gonville and Caius College, Cambridge, United Kingdom

Contributions to Science

1. Force fields and methods for simulating biological macromolecules
   In the late 1960s there was no way to compute the energy of a protein. With Shneior Lifson at the Weizmann Institute I built the first force field able to refine a protein conformation by energy minimization, and from the start the programs were given away: QCFF/PI and EREF in 1974, ENCAD in 1982.
   With Arieh Warshel I then did two things that became the two halves of the field. We simulated the folding of a small protein using one point per residue, the ancestor of every coarse-grained model now in use (PMID 957439). And we treated an enzyme reaction quantum mechanically inside a classically modeled protein, showing that lysozyme works by electrostatic stabilization of the carbonium ion rather than by strain (PMID 985660). That second paper is the origin of the hybrid quantum-classical methods standard in enzymology today, and it is the work recognized by the 2013 Nobel Prize in Chemistry, shared with Martin Karplus and Arieh Warshel.
   The energy function is not finished. With Boris Fain, Roger Kornberg and colleagues at InterX we computed the free energy of hydration of water ions from first principles, fitting nothing to experiment, and matched the measured values (PMC11881599).
   Role: I conceived and coded the early work, alone or with one collaborator, and in the recent collaborations I am the person who insists the physics be real rather than fitted.

2. Motion and structure of large molecular assemblies.
   Proteins are not static, and the motions that matter for function are the slowest and the largest. In 1985, with Chris Sander and Peter Stern, I computed the normal modes of four proteins from a full atomic force field and showed that a few low-frequency modes account for most of the observed flexibility (PMID 2580101). Monica Tirion made that calculation cheap in 1996 by replacing the chemistry with identical springs, and almost everything since, including every published normal-mode study of the ribosome, has used a network rather than a force field. Whether the chemistry matters at ribosome scale has therefore never been tested.
   The companion problem is getting a structure at all when the data are thin. With Nir Kalisman and Christopher Adams I determined the subunit order of the eukaryotic chaperonin TRiC/CCT by enumerating over a million candidate arrangements and scoring each against a small set of chemical cross-links (PMC3287007). The enumeration is its own statistical control, which is what lets the right answer be picked when the signal is too weak to falsify any single model. Earlier versions of the same idea are the simultaneous energy and R-factor refinement I published with Alan Jack in 1978, now standard in crystallography, and the deformable elastic network method with Gunnar Schroeder and Axel Brunger in 2007.
   With Gunnar von Heijne in Stockholm and Fatima Pardo-Avila we now apply this logic to a chain that is still on the ribosome, where compaction and folding are read out from the force on the nascent chain (PMC12889668).
   Role: I devised the combinatorial approach and co-wrote the code with Kalisman.

3. Sequence, structure and function: from the protein universe to language models
   The known protein sequences and structures are a compact catalog of all life on earth, and I have spent forty years asking what its shape means. With Cyrus Chothia in 1976 I classified globular proteins into four structural classes, which is the scheme still taught. With Joel Janin and Shoshana Wodak in 1978 we showed side-chain conformations are strongly preferred, the basis of every rotamer library. In 2009 I measured how the set of folds itself grew and saturated, and with Rachel Kolodny we asked in 2013 whether folds are discrete at all.
   Attention then moved from structure to sequence. With Andrea Scaiewicz in 2018 we found that genomes are distinguished by their rare short words rather than their common ones, treating proteomes as text.
   That line now runs into language models. With Gal Oren, Erez Levanon and Ziv Rosenwasser we built ADAR-GPT, a continually fine-tuned model that predicts which adenosines are edited to inosine in human RNA (PMC12798952). Editing sites are the sharpest available test of such models, because the substrate is a single base in a long transcript and the ground truth is measured.
   Role: I raised the linguistic and structural question; and also co-supervised the analysis. Oren and Levanon led ADAR-GPT, and I am proud that the group now produces first-rate papers on which I am neither first nor last author.

4. Antibody modeling and humanized antibody therapeutics
   Mouse antibodies are useless as human drugs because patients reject them. Making them human means moving six loops onto a human framework without losing the binding site, which cannot be done by hand.
   AbMod, the program I wrote in the 1980s, models the loops of any antibody from its sequence. With Cyrus Chothia and Arthur Lesk we first predicted the structure of an immunoglobulin fragment and then saw the crystal structure confirm it (1986), and we then showed the hypervariable loops take a small number of canonical conformations (1989), which is why the

modeling works at all.
Cary Queen at Protein Design Labs in Palo Alto applied the method to the anti-TAC antibody, producing the first humanized therapeutic antibody against the interleukin 2 receptor (PMC298637). The patents that followed underpin humanized antibody therapeutics at Genentech and elsewhere, in a market now worth about 200 billion dollars a year. The path from a loop-modeling program to an approved drug took forty years and needed academia, a startup, large pharmaceutical companies and patent lawyers, none of which could have done it alone.
Role: I wrote AbMod, and provided the models Queen worked from.

5. Heterogeneity and depletion in human populations
In January 2020 I began analyzing the outbreak in China, and I have worked on COVID-19 since. Two findings have lasted. The first is that outbreaks do not grow exponentially. Every early outbreak we examined followed the Gompertz law, decelerating from the beginning rather than after saturation, and with Francesco Zonta we showed that virus spread on a scale-free contact network reproduces this without any intervention. A skewed distribution of contacts is enough: the most connected people are infected first and removed first, so the effective transmission rate falls as the epidemic proceeds.
The second is that excess death is much less certain than published figures suggest. With John Ioannidis and Zonta I showed that reasonable choices of baseline, age adjustment and population denominator move national excess-death estimates by factors of two or more (PMC9225924). With Ben Marten, Gal Oren and Ioannidis we went to the primary records, reclassifying and reweighting United States death certificates from 2003 to 2023 so that every cause listed counts, not just the underlying one (PMC12889793).
These now converge on one mechanism. Selective depletion of the most exposed or frailest members makes an aggregate decelerate relative to a uniform population, and the controlling quantity is the variance over the mean of activity or frailty among those still at risk. This is the spine of the proposed renewal, tested in epidemic spread and in late-life mortality at once.
Role: I did the original analyses and wrote the code, and I am first or last author on the primary papers.

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