BIOGRAPHICAL SKETCH

NAME: Tamar Schlick

POSITION TITLE: Professor of Chemistry, Mathematics, and Computer Science

EDUCATION/TRAINING:

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Wayne State University, Detroit, MI	B.S.	05/1982	Mathematics
New York University, Courant Institute of Mathematical Sciences (CIMS), New York, NY	M.S.	05/1984	Applied Mathematics
New York University, CIMS, New York, NY	Ph.D.	08/1987	Applied Mathematics
Weizmann Institute Postdoctoral Fellow, Weizmann Institute of Science, Rehovot, Israel	Postdoctoral	08/1988	Applied Mathematics
NSF Mathematical Sciences Postdoctoral Fellow, CIMS, NYU, New York, NY	Postdoctoral	08/1989	Applied Mathematics

A. Personal Statement

The study of biomolecular structure, dynamics, and function is a wonderful interdisciplinary field that not only involves huge temporal and spatial scales of biological phenomena, but also applies both experimental and computational methods in new and inventive ways. I am excited about contributing to the growth and enhanced education in our field that has been increasing in importance to society. Trained as an applied mathematics, my work has been devoted to developing innovative mathematical and computational tools for biomolecular modeling and simulation and applying them to fundamental biological problems involving protein/nucleic acid complexes associated with biological regulation such as polymerase mechanisms, chromatin organization, and RNA structure and function. We have addressed fundamental structural and dynamical problems of wide interest to the biomedical community, such as associated with genome organization and transcription control, RNA structure and design, and viral mechanisms. Our novel multiscale models and computational methods (including our graph-theory framework RNA-As-Graphs for RNA) and collaborations with experimentalists have generated structures and mechanisms for gene folding, epigenetic control, and disease progression; and RNA frameshifting mutations and coronavirus landscapes as potential gene-editing approaches for suppression of viral infections. My community activities in many editorial boards and advisory committees in mathematics, computational biology, and chemistry reflect my interdisciplinary and educational interests, particularly to enhance and broaden graduate education in applied mathematics and computational biology. I enjoy training and working with young scientists, including to date 70 postdoctoral fellows/junior faculty and 40 research students, as well as 40 undergraduate and high school students, many of which have continued to successful independent scientific careers. My textbook, Molecular Modeling: An Interdisciplinary Guide (Springer-Verlag, second edition, 2010) is used worldwide. I will continue to promote and enhance research and educational activities in biomolecular structure and biophysics to our next generation of young multidisciplinary scientists, and prepare them for independent innovative careers in the biomedical sciences.

B. Positions and Honors

Positions and Employment:

NSF Mathematical Sciences Postdoc (1987–1989); Asst. (1989–1992) and Assoc. (1992–1996) Professor of Chemistry and Mathematics, Faculty of Arts and Science and Courant Institute of Mathematical Sciences, NYU (1989–1996); Professor of Chemistry, Mathematics, and Computer Sciences, NYU (1996–Present); Affiliate, Biochemistry Dept., NYU School of Medicine (1996–Present); Associate Investigator, Howard Hughes Medical Institute (1994–2003); Director of Graduate Studies, Dept. of Chemistry, NYU (1999–2003); Director of Graduate Program Development, Dept. of Chemistry (2003–2006); Director of new Multidepartmental Computational Biology Doctoral Program, Graduate School of Arts and Science (2003– 2006); Associate Director, Simons Center for Computational Physical Chemistry, NYU (2021–Present).

Honors (Selected):

Wayne State University Merit Scholar (1978–1992); American Cancer Society Postdoctoral Fellow (declined) (1987–1990); Weizmann Institute Postdoctoral Fellow (1987–1989); NSF Mathematical Sciences Postdoctoral Fellow (1987–1989); Jay Krakauer Prize for Outstanding Dissertation in the Sciences, NYU (1988); Kurt O. Friedrichs Prize for Outstanding Dissertation in Mathematics, Courant Institute (1988); Marie Curie American Fellow, American Association for University Women Educational Foundation (1990–1991); Whitehead Presidential Fellow, NYU (1991); Searle Scholar (1991–1994); Whitaker Fellow (1991–1994); NSF Presidential Young Investigator (1991–1996); NYU Distinguished Recent Alumna (1993); Alfred P. Sloan Research Fellow (1993–1995); John Simon Guggenheim Fellow (2000–2001); Burroughs Wellcome Visiting Professor (UNC) (2000–2001); AWIS Outstanding Woman in Science (2000); Agnes Fay Morgan Research Award in Chemistry, Iota Sigma Pi (I Σ Π), National Honor Society for Women in Chemistry (2003); Sri Chinmoy Lifting Up the World Oneness Heart Award (2003); American Association for the Advancement of Science (AAAS) Fellow (2004); American Physical Society (APS) Fellow (2005); Aspen Health Forum Fellow (2007); Weston Visiting Professor, Department of Structural Biology, Weizmann Institute of Science (2011); Biophysical Society Fellow (2012); SIAM (Society of Industrial and Applied Mathematics) Fellow (2012); NYU Global Research Institute Fellow, Tel Aviv University (2013), AMS Keynote Lecture (Oct. 2014); NYU Global Research Institute Fellow, Tel Aviv University and London (2014-2018); Murray and Adylin Rosenblatt Endowed Lecture in Applied Mathematics, UCSD (2017); Distinguished Seminar Speaker of Computational Biology, U. Pittsburgh (2020); Keynote Speaker, Covid-19 Symposium, Biophysical Society (2020); Keynote Speaker, 7th International Conference Algorithms for Computational Biology (2021); Keynote Opening Lecture, Advances and Challenges in Biomolecular Simulations, EMBO and BioExcel (2021); Keynote Lecture, German Conference on Cheminformatics (2021); Pitzer Lecture for Outstanding Research in Theoretical and Computational Chemistry (2022); Plenary Lecture, Foundations of Molecular Modeling and Simulation, AIChE and CAChE (2024).

Community Service

Advisory Committee Member/Panelist (Selected):

NIH Special Review Committee for Structural Biology as Applied to the Problem of Targeted Drug Design for the Treatment of AIDS Initiative (1992); NSF Advanced Scientific Computing Postdoctoral Research Associateship Program (1992–1994); NSF Biophysics Division (1993–1995); NRC, NAS, Report on Mathematical Challenges from; Theoretical/Computational Chemistry, Chair: F. Stillinger (1994–1995); NIH Board of Scientific Counselors, National Library of Medicine (1994–1999); SIAM's representative to the AMS-ASA-AWM-IMS-MAA-NCTM-SIAM Committee on Women in the Mathematical Sciences (1994–2000); Chair of NIH RAC Board for the Parallel Structural Biology Project of the San Diego Supercomputing Center and UCSD (1994–2005); AMS-SIAM Committee on Applied Mathematics (1995–1998); The Burroughs Welcome Fund, Advisory Committee for the Fund's new Interface Program Between the Physical and Biological Sciences (1995–2000); NSF Academic Research Infrastructure Program (1996); NSF/NIH/DOE panel, Next Generation Biology: The Role of Next Generation Computing (1998); NIH BBCA study section (1999); SIAM Life Sciences Activity Group (1999–2005); NIH Site Visit panel, Intramural Review of Computational Applications Program (SAIC), National Cancer Institute (2000); NIH Special Study Section B, National Institute of General Medical Sciences (2001); Philip Morris External Research Program Peer Review (2003); NIH Physical Biochemistry Study Section (2003–2004); NSF with UK (EPSRC) High Speed Computing Postdoctoral Research Program (2004); National Iota Sigma Pi Award Committee (2004); NYAS Women Investigators Network (2004–); NIH Computational Biophysics Study Section (2004); NYU's Center for Teaching Excellence Advisory Board (2004–); DOE Extreme Biology Workshop, Co-Chair (2009); NSF-OCI (OCI, Office of Cyberinfrastructure) Task Force on Grand Challenges and Implications for Cyberscience Communities, NSF (2010–); Simons Foundation Science Series (2010–); Ad Hoc Member, NIH MFSD study section (Biology, Chemistry & Macromol. Biophysics) (2011, 2021); NSF-sponsored National Institute for Mathematical and Biological Synthesis (2013–2016); Ecole Normale Superieure Chemical Sciences Advisory Board (2013–2018); America's Amazing Teen Project (2013–); NIH Directors New Innovator Award (2014); NIH National Biomedical Computation Resource at SDSC Advisory Board (2014–); TSRC Advisory Board (2016-); Univ. Vienna Advisory Board for Professorship in Quantitative Modeling (2019); Founder and Co-Chair, Multiscale Genome Organization BPS Subgroup (2020–2022); NIH MIRA Review Panel (2023–); Biophysical Society Council (2024–2027).

Editorial Boards (Selected):

Springer Verlag, Biophysics for Life Sciences series, Advisory Board (2010–); Intl. J. for Multiscale Computational Engineering (2007–, Assoc. Editor); J. Phys. Chem. B (2007–2012, Advisory Board); J. Theo. Biol. (1995–2005); Springer Verlag Lecture Notes in Comp. Sci. Eng. (1996–); J. Comp. Phys. (1997–); Biophysics J. (2004–2007), Biomedical Computation Review (2005–2015); SIAM Multiscale Modeling and Simulation (2005–2015); SIAM J. Sci. Comp. (2005–2010); Faculty of 1000, Structural Biology (2001–); SIAM Life Science Activity Group (2001–); Ad Hoc Member, F1000 Research (2013–); Frontiers in Molecular Biosciences (2014); PLoS One, Academic Editor (2015–); J. Mol. Biol. Special Volume on Challenges in RNA Modeling and Design, with A. Pyle (2016); Biophys J. Special Volume of RNA Modeling, with A. Pyle (2017); Biophys J. Special Memorial Volume for J.

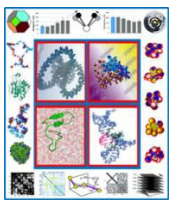
Langowski, with A. Stasiak (2018); Biophys J., Associate Editor, Nucleic Acids and Genome Biophysics Section (2016–2022) and Editor (2022–2025); Biophys J. Special Volume on Covid-19 (2020–2021); PLoS Comp. Biol., Academic Editor (2020–); Biophys J. Special Volume on Innovations in Biophysics (2022); Biophys J. Special Volume on Machine Learning (2024–2024); J. Chem. Phys. Special Volume on Genome Structure and Dynamics (2023–2024).

Organizer/Co-Organizer (Selected):
Program in Mathematical Biology, MSRI Berkeley (1992); Multigrid Techniques with Applications to Molecular Dynamics; Weizmann Institute (1995); Molecular Dynamics Minisymposium, SIAM, Charlotte (1995); IMA Special Year in High Performance Computing, Molecular Structure Workshop, Minneapolis (1997); DIMACS/PMMB Workshop on DNA Topology (1997); International Conference on Multiscale Methods, Weizmann Institute (2000); Third International Symposium on Algorithms for Macromolecular Modeling, New York (2000); SIAM Computational Sciences Meeting, Washington, D.C. (2000); Founder: WoW (Women on Women) Support Group for Women in Science (2001–); First SIAM Life Sciences Conference, Boston (2002); Modeling and Simulation for Materials, Institute of Pure and Applied Mathematics (IPAM), University of California, Los Angeles (2002); Mathematical and Computational Approaches to Biomolecular Simulations, MSRI, Berkeley (2003); Geometric and PDE Modeling Problems in the Life Sciences, PRIMA, Hawaii (2004); Second SIAM Life Sciences Conference, Co-Chair (2004); Fourth International Symposium on Algorithms for Macromolecular Modeling, University of Leicester, England (2004); IMA Year on the Mathematics of Molecular and Cellular Biology, Univ. of Minnesota (2007–2008); IMA Special Year in Computational Chemistry, Univ. of Minnesota (2008–2009); Fifth International Symposium on Algorithms for Macromolecular Modeling, University of Texas, Austin (2009); Macromolecular Proteins and Protein Complexes, Co-Chair of DOE Extreme Biology Workshop (2009); Challenges in RNA Structural Modeling and Design Workshop, Telluride, CO, Organizer with Anna Pyle (2014); RNA Society Meeting Session Chair (2015); Frontiers in Polymer and Biomolecular Chemistry, Tel Aviv, Israel, Organizer with Gil Markovich (2015); Challenges in Large-Scale Biomolecular Simulations Workshop, Telluride, CO, Organizer with K. Schulten (2015) and R. Amaro (2018, 2022); Challenges in RNA Structural Modeling and Design Workshop, Telluride, CO, Organizer with Anna Pyle (2016, 2018, 2022); Tel Aviv University/NYU Second International Symposium in Chemistry: Material Science and Nanochemistry, New York, Co-Organizer with Gil Markovich (2016); Challenges Across Large-Scale Biomolecular and Polymer Simulations CECAM workshop, Co-organizer with I. Coluzza, S. Pasquali, and C. Dellago, Vienna (2017); Modeling and Experimental Approaches to Genome Organization CECAM workshop, Co-organizer with J. Langowski, A. Stasiak, and R. Everaers (2017); International Congress for Structural Mechanics, Chair of Computational Biology and Chemistry, New York (2018); Multiscale Modeling of Chromatin: Bridging Experiment with Theory, BPS Thematic Meeting, with A. Stasiak, L. Nordenskiold, and T. Bishop, Les Houches (2019); CECAM Meeting on Large Scale Biomolecular Simulations, with Pasquali *et. al.*, Cargèse (2019); Chromatin Modeling Thematic Program, Erwin Schrödinger Inst., Vienna, with C. Likos (2023); Structural Genome & Multiscale Simulations, ICTP and SISSA, Trieste, with A. Rosa and others (2023); Multiscale Modeling, CECAM, with G. Voth and S. Pasquali (2023–2025).

C. Contributions to Science (see publications: http://www.biomath.nyu.edu**/)**

With my students and postdocs from mathematics, physics, bioengineering, and chemistry, we have advanced the development and application of innovative modeling and simulation techniques for long-time, large-scale biomolecular processes which have uncovered important features of chromatin structure and dynamics, DNA polymerase mechanisms, and RNA structure prediction and design.

1. **Algorithms for Biomolecular Simulation.** Computational methods are now recognized to be essential for advancing biology and medicine in the 21st century. Prior methods for multivariate minimization and molecular dynamics were limited by slow convergence and instabilities. From pioneering early work on multivariate minimization and long-timestep integration that overcame resonance artifacts in molecular dynamics, we have created successful tailored algorithmic combinations for biological applications.



   a. E. Barth and T. Schlick. Overcoming stability limitations in biomolecular dynamics: I. Combining force splitting via extrapolation with Langevin dynamics in LN. *J. Chem. Phys.*, 109:1617–1632, 1998.
   b. T. Schlick. *Molecular Modeling: An Interdisciplinary Guide*. Springer-Verlag, New York, NY, second edition, 2010.
   c. T. Schlick, *et al*. Biomolecular Modeling and Simulation: A Prospering Multidisciplinary Field. Annu. Rev. Biophys., 50:267–301, 2021.
   d. T. Schlick and S. Portillo-Ledesma. Biomolecular Modeling Thrives in the Age of Technology. Nat. Comput. Sci. 1:321–331, 2021.

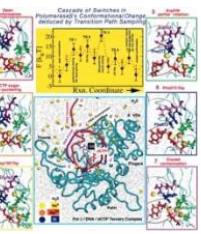
2. **Chromatin Organization.** The tight packaging of genomic DNA influences directly many biological processes, from replication to protein synthesis. While direct visualization is not possible, computational models can help link DNA geometry and topology to DNA's wide-ranging functions in the cell. Our innovative coarse-grained models for DNA supercoiling dynamics were extended to mesoscale chromatin models at nucleosome resolution, including gene systems, revealing chromatin's heterogeneous structure, novel higher-order folding of genes, unfolding mechanisms by histone tail modifications, microdomain formation by protein binding, and linker histone interactions linked to cancer progression. These findings have significant implications on transcription regulation, epigenetic control, and human disease and point to new ways for gene regulation via chromatin modifications.

   a. S. Rao, ..., G. Bascom, …., T. Schlick, …., E. Lander, and Aiden, E. Cohesin loss eliminates all loop domains. *Cell*, 171: 305–320, 2017.
   b. G. D. Bascom, C. G. Myers, and T. Schlick. Mesoscale modeling reveals formation of an epigenetically driven HOXC gene hub. *Proc. Natl. Acad. Sci. USA*., 116: 4955–4962, 2019. With commentary: M. Di Pierro. Inner workings of gene folding, p. 4774.
   c. N. Yusufova, …., S. Portillo-Ledesma, …., T. Schlick, …., E. Cesarman, and A. Melnick. Histone H1 loss drives lymphoma by disrupting 3D chromatin architecture. *Nature*, 589: 299–305, 2021
   d. S. Portillo-Ledesma, Z. Li, and T. Schlick. Genome modeling: From chromatin fibers to genes. *Curr. Opin. Struct. Biol.,* 78: 102506, 2023

3. **RNA Structure and Design.** As with protein structural genomics, a primary goal of ribonomics is to completely catalog distinct RNA folds in different functional RNA classes and to apply this knowledge to RNA design and function. Our RNA-As-Graphs framework has led to a systematic classification of RNA motifs, design of novel RNA motifs, automated scanning of genomes for structural modules, enrichment of new RNA motifs for in vitro selection, and applications to the SARS-CoV-2 frameshifting element: structures, design, and mechanisms. Our most recent coronavirus works designed mutations of frameshifting elements to profoundly alter RNA folds and frameshifting efficiencies, as potential new anti-viral therapeutics.

   a. T. Schlick, Q. Zhu, S. Jain, and S. Yan. Structure-Altering Mutations of the SARS-CoV-2 Frameshifting RNA Element. *Biophys. J.*, 120: 1040–1053, 2021.
   b. T. Schlick, Q. Zhu, A., ….., and A. Laederach. To Knot or Not to Knot: Multiple Conformations of the SARS-CoV-2 Frameshifting RNA Element. *J. Am. Chem. Soc.*, 143*:* 11404–11422*,* 2021
   c. S. Yan, Q. Zhu, S. Jain, and T. Schlick. Length-dependent motions of SARS-CoV-2 frameshifting RNA pseudoknot and alternative conformations suggest avenues for frameshifting suppression. *Nat. Commun*, 13: 4184, 2022.
   d. S. Yan, Q. Zhu, J. Hohl, A. Dong, and T. Schlick. Evolution of Coronavirus Frameshifting Elements: Competing Stem Networks Explain Conservation and Variability. *Proc. Natl. Acad. Sci. USA*, 120: e2221324120, 2023.

4. **DNA Polymerase Mechanisms.** How our instruction book for life is transmitted from one generation to the next and how this process leads to mutations is a fundamental problem in both basic and applied research. As DNA polymerases perform this venerable task of DNA repair, and malfunction can trigger many human diseases like cancer and neurological conditions, significant effort has been expended to understand polymerase repair mechanisms. Our enhanced sampling approaches for DNA polymerases have helped link macroscopic kinetic data and polymerase crystal structures by unraveling conformational pathways that assemble active sites in DNA repair pathways. Our work has revealed how site-specific local motions trigger large-scale enzyme rearrangements, interpreted puzzling experiments on inactive enzyme mutants, and advanced induced-fit/conformational sampling mechanisms for DNA repair processes.



   a. R. Radhakrishnan and T. Schlick. Orchestration of cooperative events in DNA synthesis and repair mechanism unraveled by transition path sampling of DNA polymerase β's closing. Proc. Natl. Acad. Sci. USA, 101:5970–5975, 2004.
   b. Y. Li, C. L. Gridley, J. Jaeger, J. B. Sweasy, and T. Schlick. Unfavorable electrostatic and steric interactions in DNA polymerase β E295K mutant interfere with the enzyme's pathway. *J. Amer. Chem. Soc.*, 134:9999–10010, 2012.
   c. B. D. Freudenthal, W. A. Beard, ……., T. Kim, T. Schlick, and S. H. Wilson. Uncovering the polymerase-induced cytotoxicity of an oxidized nucleotide. *Nature*, 517:635– 639, 2015.
   d. T. Kim, B. D. Freudenthal, W. A. Beard, S. H. Wilson, and T. Schlick. Insertion of Oxidized Nucleotide Triggers Rapid DNA Polymerase Opening. *Nuc. Acids Res.* 44:4409–4424, 2016.

Biophysical Society Activities: Society Member since 1987 and BPS Fellow since 2012. *Biophysical Journal* Associate Editor (2016-2021) and Editorial Board Member (2022-2024); Founding Co-Chair of Multiscale Genome Organization Subgroup (2020-2022); Co-Organizer of BPS Thematic Meeting on "Multiscale Modeling

of Chromatin", Les Houches, France (2019) and "Biophysicists Address Covid-19" Symposium (2020); Editor or Co-Editor of seven *BJ* special volumes on: "Challenges in RNA Modeling"(2016), "Genome Biophysics" (2017), "J. Langowski memorial issue" (2018); "Multiscale Genome Organization" (2020); "Biophysicists Address Covid-19" (two volumes in 2021); and "Innovations in Biophysics", Ned Seeman memorial issue (2022). Keynote Speaker in BPS meetings: "Genome Biophysics" thematic meeting, Santa Cruz (2018), "Biophysicists Address Covid-19" (2020), "Organization of the Nucleus" Symposium, Annual Meeting (2021), "Biophysics at the Dawn of Exascale Computing", Hamburg (2022), and others. Author of many research and editorial articles in *BJ,* and general interest articles in inaugural issues of *The Biophysicist* ("Eight Suggestions for Future Leaders of Science and Technology", 2020) and *The Biophysicist ("*From Butterflies to Bits: A Sweeping Vision for Biology", 2021).