John D. Chodera

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Education and positions

2019–2021	**BIH Einstein Visiting Professor, Charité, Berlin**
2018–	**Associate Member, Memorial Sloan-Kettering Cancer Center**
2018–	**Associate Professor, Physiology, Biophysics, and Systems Biology Program, Weill Cornell Graduate School of Medical Sciences**
2013–2018	**Assistant Professor, Physiology, Biophysics, and Systems Biology Program, Weill Cornell Graduate School of Medical Sciences**
2012–2018	**Assistant Member, Memorial Sloan-Kettering Cancer Center**
2008–2012	**Independent Distinguished Postdoctoral Fellow, California Institute for Quantitative Biosciences (QB3), University of California, Berkeley** Independent research funding, sponsors Phillip L. Geissler and Susan Marqusee
2007–2008	**Postdoctoral researcher, Department of Chemistry, Stanford University** With Vijay S. Pande (head of Folding@Home distributed computing project)
1999–2006	**PH.D. in Biophysics, University of California, San Francisco** Committee: Ken A. Dill, Matthew P. Jacobson, Vijay S. Pande
1995–1999	**B.S. in Biology, California Institute of Technology** Undergraduate research with Paul H. Patterson (*experimental molecular neurobiology*) and Jerry E. Solomon (*computational chemistry*)

Fellowships and awards

2019–2021	BIH Einstein Visiting Fellowship
2017	Silicon Therapeutics Open Science Fellowship
2013–2016	Louis V. Gerstner Young Investigator Award
2013–2014	Google Exacycle for External Faculty
2008–2012	QB3-Berkeley Distinguished Postdoctoral Fellowship, University of California, Berkeley
2005–2006	IBM Predoctoral Fellowship
2000–2005	Howard Hughes Medical Institute Predoctoral Fellowship

Research overview

My research focuses on **bringing physical modeling into the high-throughput biology and genomics era** and **reimagining the way we develop small molecules for chemical biology and drug discovery**. By combining novel algorithmic advances to achieve orders-of-magnitude efficiency gains with powerful but inexpensive GPU hardware, machine learning, and distributed computing technologies, my lab is developing next-generation approaches and open source software for predicting small molecule binding affinities, designing small molecules with desired properties, predicting the drug sensitivity or resistance of clinical mutations, and understanding the detailed structural mechanisms underlying oncogenic mutations. We co-develop the OpenMM GPU-powered molecular simulation framework, which powers numerous biomolecular modeling and simulation applications. As a core member of the Folding@home Consortium, my lab harnesses the computing power of hundreds of thousands of volunteers around the world to study functional implications of mutations and new opportunities for therapeutic design against cancer targets. Using automated biophysical measurements, we collect new experimental data targeted to advance the quantitative accuracy of our methodologies, and gather new insight into drug susceptibility and resistance in kinases and other cancer targets. My work makes extensive use of scalable Bayesian statistical inference, machine learning via probabilistic programming, and information theoretic principles for designing experiments and quantifying error. I am passionate about open science, disseminating scientific best practices, and maximizing research reproducibility.

Software

Major codes developed by our lab can be found at `http://choderalab.org/code`
All software is licensed under permissive OSI-approved open source licenses and available on GitHub

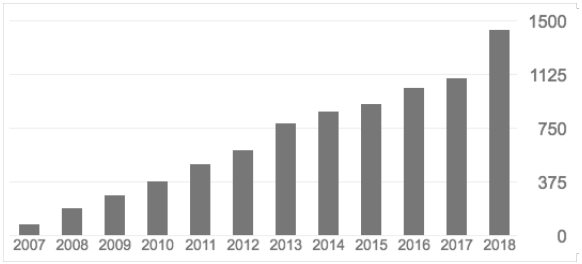
Publications

All publications: http://choderalab.org/publications
Google Scholar statistics: http://goo.gl/qO0JW
MyNCBI Bibliography: http://goo.gl/e3kjgK
bioRχiv preprints: https://bit.ly/2LHGwxJ
arχiv preprints: https://bit.ly/2Rp2Y3T
Open source software: http://choderalab.org/code Major datasets: http://choderalab.org/data
h-index: 40 / i10-index: 63 / citations: 9278 (27 Aug 2019)

* denotes co-first-authors

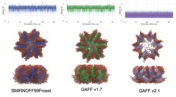
† denotes co-second-authors

‡ denotes co-corresponding authors



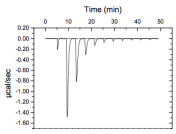
annual citation counts (Google Scholar) – 31 Dec 2018

Submitted and Under Review

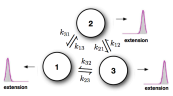


Submitted · manubot
Slochower DR, Hendrikson NM, Wang LP, **Chodera JD**, Mobley DL, and Gilson MK
Binding thermodynamics of host-guest systems with SMIRNOFF99Frosst 1.0.5 from the Open Force Field Initiative
We assess the accuracy of the SMIRNOFF99Frosst 1.0.5 force field in reproducing host-guest binding thermodynamics in comparison with the GAFF force field, demonstrating how the SMIRNOFF format for compactly specifying force fields provide comparable accuracy with 20x fewer parameters.

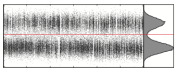
Preprints ahead of submission



Preprint ahead of submission · bioRχiv
Boyce SE, Tellinghuisen JT, and **Chodera JD**
Avoiding accuracy-limiting pitfalls in the study of protein-ligand interactions with isothermal titration calorimetry
We demonstrate how to avoid accuracy-limiting problems in standard isothermal calorimetry experiments as well as capture the primary sources of uncertainty in thermodynamic parameters.

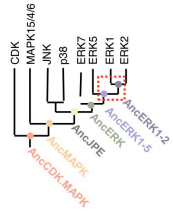


Preprint ahead of submission · arχiv
Chodera JD, Noé F, Hinrichs NS, Keller B, Elms PJ, Kaiser CM, Ewall-Wice A, Marqusee S, and Bustamante C
Bayesian hidden Markov model analysis of single-molecule biophysical experiments
We present a Bayesian hidden Markov model analysis scheme that allows biomolecular conformational dynamics—and the corresponding uncertainty due to limited data—to be inferred from single-molecule trajectories. This approach was developed for a single-molecule study examining folding dynamics of nascent proteins exiting the ribosome [Science 334:1723, 2011 · DOI].

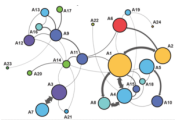


Preprint ahead of submission · arχiv
Chodera JD, Elms PJ, Swope WC, Prinz J-H, Marqusee S, Bustamante C, Noé F, and Pande VS
A robust approach to estimating rates from time-correlation functions
We present a simple, robust approach to estimating two-state rate constants from experimental or simulation data.

Published and In Press

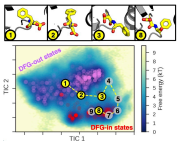


eLife, 2019;8:e38805 · DOI
Sang D, Pinglay S, Wiewiora RP, Selvan ME, Lou HJ, **Chodera JD**, Turk B, Gümüş Z, and Holt LJ.
Ancestral reconstruction reveals mechanisms of ERK regulatory evolution
To understand how kinase regulation by phosphorylation emerged, we reconstruct the common ancestor of CDKs and MAPKs, using biochemical experiments and massively parallel molecular simulations to study how a few mutations were sufficient to switch ERK-family kinases from high- to low-autophosphorylation.

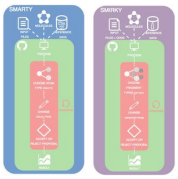


eLife 8:e45403, 2019 · DOI
Rafal P. Wiewiora†, Shi Chen†, Fanwang Meng, Nicolas Babault, Anqi Ma, Wenyu Yu, Kun Qian, Hao Hu, Hua Zou, Junyi Wang, Shijie Fan, Gil Blum, Fabio Pittella-Silva, Kyle A. Beauchamp, Wolfram Tempel, Hualing Jiang, Kaixian Chen, Robert Skene, Y. George Zheng, Peter J. Brown, Jian Jin, **Chodera JD** ‡, and Minkui Luo‡
The dynamic conformational landscapes of the protein methyltransferase SETD8
In this work, we show how targeted X-ray crystallography using covalent inhibitors and depletion of native ligands to reveal structures of low-population hidden conformations can be combined with massively distributed molecular simulation to resolve the functional dynamic landscape of the protein methyltransferase SETD8 in unprecedented atomistic detail. Using an aggregate of six milliseconds of fully atomistic simulation from Foldinghome, we use Markov state models to illuminate the conformational dynamics of this important epigenetic protein.

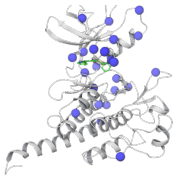
Nature Communications 10:2691, 2019 · DOI
Minuesa G, Albanese SK, Chow A, Schurer A, Park SM, Rotsides CZ, Taggart J, Rizzi A, Naden LN, Chou T, Gourkanti S, Cappel D, Passarelli MC, Fairchild L, Adura C, Glickman FJ, Schulman J, Famulare C, Patel M, Eibl JK, Ross GM, Tan DS, Leslie CS, Beeming T, Golgur Y, **Chodera JD** , and Kharas MG.
Small-molecule targeting of MUSASHI RNA-binding activity in acute myeloid leukemia
We use absolute alchemical free energy calculations to identify the likely interaction site for a small hydrophobic ligand that shows activity against MUSASHI in AML.



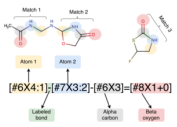
Cell Chemical Biology 26:390, 2019 · DOI
Hanson SM*, Georghiou G*, Miller WT, Rest JS, **Chodera JD** ‡, and Seeliger MA‡
What makes a kinase promiscuous for inhibitors?
Using a combination of chemogenomics, structural biology, and molecular simulation approaches, we identify a set of human kinases that are especially promiscuous binders of small molecule kinase inhibitors, and show that a prototypical member of this class, DDR1, achieves this promiscuity by virtue of its more stable Asp-DFG-out conformation.



Journal of Chemical Theory and Computation 15:402, 2019 · DOI
Zanette C, Bannan CC, Bayly CI, Fass J, Gilson MK, Shirts MR, **Chodera JD** , Mobley DL
Toward learned chemical perception of force field typing rules
We show how machine learning can learn typing rules for molecular mechanics force fields within a Bayesian statistical framework.



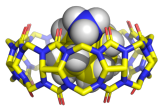
Communications Biology 1:70, 2018 · DOI
Hauser K, Negron C, Albanese SK, Ray S, Steinbrecher T, Abel R, and **Chodera JD** , and Wang L
Predicting resistance of clinical Abl mutations to targeted kinase inhibitors using alchemical free-energy calculations
We show how alchemical free energy calculations can be used to predict whether clinical point mutations in human kinase domains confer resistance or susceptibility to targeted kinase inhibitors.



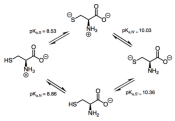
Journal of Chemical Theory and Computation 14:6076, 2018 · DOI
Mobley DL‡, Bannan CC, Rizzi A, Bayly CI, **Chodera JD** , Lim VT, Lim NM, Beauchamp KA, Shirts MR, Gilson MK, and Eastman PK
Escaping atom types using direct chemical perception with SMIRNOFF v0.1
We describe the philosophy behind a modern approach to molecular mechanics forcefield parameterization, and present initial results for the first SMIRNOFF-encoded forcefield: SMIRNOFF99Frosst.

Journal of Chemical Theory and Computation, in press · DOI
Swenson DWH, Prinz JH, Noé F, **Chodera JD** , and Bolhuis PG
OpenPathSampling: A Python framework for path sampling simulations. I. Basics
To make powerful path sampling techniques broadly accessible and efficient, we have produced a new Python framework for easily implementing path sampling strategies (such as transition path and interface sampling) in Python. This first publication describes some of the theory and capabilities behind the approach.

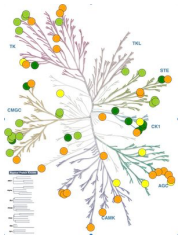
Journal of Chemical Theory and Computation, in press · DOI
Swenson DWH, Prinz JH, Noé F, **Chodera JD** , and Bolhuis PG
OpenPathSampling: A Python framework for path sampling simulations. II. Building and customizing path ensembles and sample schemes
To make powerful path sampling techniques broadly accessible and efficient, we have produced a new Python framework for easily implementing path sampling strategies (such as transition path and interface sampling) in Python. This second publication describes advanced aspects of the theory and details of how to customize path ensembles.



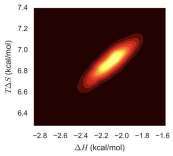
Journal of Computer Aided Molecular Design 32:937, 2018. · DOI
Rizzi A, Murkli S, McNeill J, Yao W, Sullivan M, Gilson MK, Chiu MW, Isaacs L, Gibb BC, Mobley DL‡, and **Chodera JD** ‡
Overview of the SAMPL6 host-guest binding affinity prediction challenge
We present an overview of the host-guest systems and participant performance for the SAMPL6 host-guest blind affinity prediction challenges, assessing how well various physical modeling approaches were able to predict ligand binding affinities for simple ligand recognition problems where receptor sampling and protonation state effects are eliminated due to the simplicity of supramolecular hosts. We find that progress is now stagnated likely due to force field limitations.



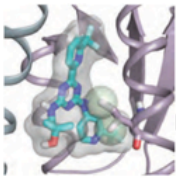
Journal of Computer Aided Molecular Design 32:1117, 2018 · DOI
Isik M, Levorse D, Rustenburg AS, Ndukwe IE, Wang H, Reibarkh M, Martin GE, Makarov AA, Mobley DL, Rhodes T‡, and **Chodera JD** ‡
pKa measurements for the SAMPL6 prediction challenge for a set of kinase inhibitor-like fragments
The SAMPL5 blind challenge exercises identified neglect of protonation state effects as a major accuracy-limiting factor in physical modeling of biomolecular interactions. In this study, we report the experimental measurements behind a SAMPL6 blind challenges in which we assess the ability of community codes to predict small molecule pKas for small molecule resembling fragments of selective kinase inhibitors.



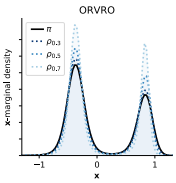
Biochemistry 57:4675, 2018 · DOI
Albanese SK*, Parton DL*, Isik M†, Rodríguez-Laureano L†, Hanson SM, Gradia S, Jeans C, Levinson NM, Seeliger M, and **Chodera JD**
An open library of human kinase domain constructs for automated bacterial expression
To establish a tractable experimental system for studying the biophysical determinants of selective kinase inhibitor resistance in clinical cancer mutations, we engineer a library of human kinase domains with useful bacterial expression with phosphatase coexpression.



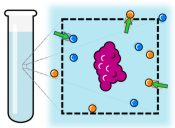
PLOS ONE 3(9): e0203224, 2018 · DOI
Nguyen TH, Rustenburg AS, Krimmer SG, Zhang H, Clark JD, Novick PA, Branson K, Pande VS, **Chodera JD** ‡, MinH DDL‡
Bayesian analysis of isothermal titration calorimetry for binding thermodynamics
We show how Bayesian inference can produce greatly improved estimates of statistical uncertainty from isothermal titration calorimetry (ITC) experiments, allowing the joint distribution of thermodynamic parameter uncertainties to be inferred.



Nature 559:125, 2018 · DOI
Intlekofer AM*, Shih AH*, Wang B, Nazir A, Rustenburg AS, Albanese SK, Patel M, Famulare C, Correa FM, Arcila ME, Taylor J, Tallman MS, Roshal M, Petsko GA, **Chodera JD** , Thompson CB‡, Levine RL‡, Stein, EM‡
Acquired resistance to IDH inhibition through trans or cis dimer-interface mutations
Clinical double mutations acting in trans in cancer patients receiving IDH2 inhibitors act through a novel biophysical mechanism.

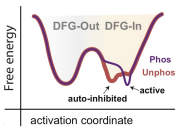


Entropy 20:318, 2018 · DOI
Fass J, Sivak DA, Crooks GE, Beauchamp KA, Leimkuhler B, and **Chodera JD**
Quantifying configuration-sampling error in Langvevin simulations of complex molecular systems
We address a fundamental question regarding why molecular dynamics simulation works despite the fact that the use of finite timesteps leads to error in the sampled probability densities and populations, demonstrating how to measure configuration-space sampling error for an important class of Langevin integrators widely used in biomolecular simulation.

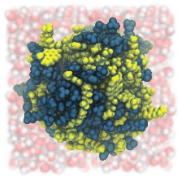


Journal of Physical Chemistry B 122:5466, 2018 · DOI
Ross GA, Rustenburg AS, Grinaway PB, Fass J, and **Chodera JD**
Biomolecular simulations under realistic salt conditions
We show how NCMC can be used to implement an efficient osmostat in molecular dynamics simulations to model realistic fluctuations in ion environments around biomolecules, and illustrate how the local salt environment around biological macromolecules can differ substantially from bulk.

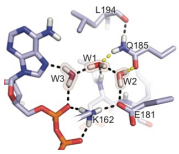
Journal of Physical Chemistry 122:5579, 2018 · DOI
Gill SC, Lim NM, Grinaway PB, Rustenburg AS, Fass J, Ross GA, **Chodera JD** , and Mobley DL
Binding Modes of Ligands Using Enhanced Sampling (BLUES): Rapid Decorrelation of Ligand Binding Modes Using Nonequilibrium Candidate Monte Carlo
Nonequilibrium candidate Monte Carlo can be used to accelerate the sampling of ligand binding modes by orders of magnitude over instantaneous Monte Carlo.



eLife 7:e32766, 2018 · DOI
Ruff EF, Muretta JM, Thompson A, Lake E, Cyphers S, Albanese SK, Hanson SM, Behr JM, Thomas DT, **Chodera JD**, and Levinson NM
A dynamic mechanism for allosteric activation of Aurora kinase A by activation loop phosphorylation
Through a combination of FRET, IR, and EPR labeling and large-scale molecular dynamics simulations, we show that phorphorylation activates Aurora kinase by a novel mechanism that does not simply correspond to a DFG-out to DFG-in population shift, but rather reorganization of DFG-in subpopulations.

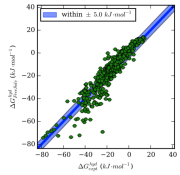


Nature Materials 17:361, 2018 · DOI
Shamay Y, Shah J, Tschaharganeh DF, Roxbury D, Budhathoki-Uprety J, Işik M, Mizrachi A, Nawaly K, Sugarman JL, Baut E, Neiman MR, Johnson DC, Sridharan R, Chu KL, Rajasekhar VK, **Chodera JD**, Lowe SW, and Heller DA
Quantitative self-assembly prediction yields targeted nanoparticles
A decision tree based on predicted physical properties and and molecular descriptors is capable of predicting the assembly of drug/dye nanoparticles that can be used in tumor-targeted selective kinase inhibitor therapy to minimize on- and off-pathway toxicity.



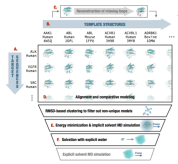
Nature Chemical Biology 13:402, 2017 · DOI
Cyphers S, Ruff E, Behr JM, **Chodera JD**, and Levinson NM
A conserved water-mediated hydrogen bond network governs allosteric activation in Aurora kinase A
Over 50 microseconds of aggregate simulation data on Folding@home reveal a surprisingly stable hydrogen bond network underlies allosteric activation by Tpx2.

Nature Chemical Biology 13:494, 2017 · DOI
Intlekofer A, Wang B, Liu H, Shah H, Carmona-Fontaine C, Rustenburg AS, Salah S, Gunner MR, **Chodera JD**, Cross JR, and Thompson CB
Acidification enhances production of L-2-hydroxyglutarate through alternative substrate use by dehydrogenase enzymes
At low pH, metabolic enzymes lactate dehydrogenase and malate dehydrogenase undergo shifts in substrate utilization that have high relevance to cancer metabolism due to surprisingly simple protonation state effects.



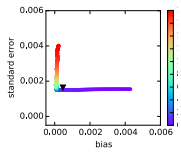
Journal of Chemical & Engineering Data 62:1559, 2017 · DOI
Matos GDR, Kyu DY, Loeffler HH, **Chodera JD**, Shirts MR, and Mobley DL
Approaches for calculating solvation free energies and enthalpies demonstrated with an update of the FreeSolv database
We review alchemical approaches to computing solvation free energies and update FreeSolv—the most popular database of hydration free energies of neutral molecules—with more computed and experimental properties.

PLoS Computational Biology 13:e1005659, 2017 · DOI
Eastman P, Swails J, **Chodera JD**, McGibbon RT, Zhao Y, Beauchamp KA, Wang LP, Simmonett AC, Harrigan MP, Brooks BR, and Pande VS
OpenMM 7: Rapid development of high performance algorithms for molecular dynamics
The latest version of the GPU-accelerated molecular simulation OpenMM features a variety of incredibly flexible but fast tools for rapidly prototyping, evaluating, and deploying new simulation algorithms.

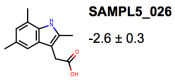


PLoS Computational Biology 12:e1004728, 2016 · DOI
Parton DL, Grinaway PB, Hanson SM, Beauchamp KA, and **Chodera JD**
Ensembler: Enabling high-throughput molecular simulations at the superfamily scale
We demonstrate a new tool that enables—for the first time—massively parallel molecular simulation studies of biomolecular dynamics at the superfamily scale, illustrating its application to protein tyrosine kinases, an important class of drug targets in cancer.

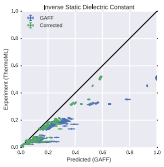
Journal of Clinical Investigation 126:3529, 2016 · DOI
Xu J, Pham CG, Albanese SK, Dong Y, Oyama T, Lee CH, Rodrik-Outmezguine V, Yao Z, Han S, Chen D, Parton DL, **Chodera JD**, Rosen N, Cheng EH, and Hsieh JJ
Mechanistically distinct cancer-associated mTOR activation clusters predict sensitivity to rapamycin
We use massively parallel distributed molecular simulations on Folding@home to probe the mechanism activating mutations of the mTOR kinase identified in clinical populations.



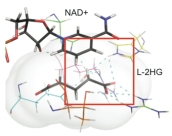
Journal of Chemical Theory and Computation 12:1799, 2016 · DOI
Chodera JD
A simple method for automated equilibration detection in molecular simulations
We present a simple approach to automatically determining the equilibrated region of a molecular simulation, a longstanding challenge formerly without a good solution.



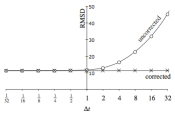
Journal of Computer Aided Molecular Design, 30:945, 2016 · DOI
Rusteburg AS, Dancer J, Lin B, Ortwine D, Mobley DL, and **Chodera JD**
Measuring cyclohexane-water distribution coefficients for the SAMPL5 challenge
To test the accuracy of physical modeling techniques in predicting free energies of transfer between aqueous and nonpolar solvents, we worked with Genentech to develop a new protocol to measure cyclohexane-water distribution coefficients for 53 druglike compounds at pH 7.4, fielding a blind community challenge as part of the SAMPL5 exercise. A special issue of JCAMD was published with 16 papers describing various approaches used by participants to predict this data and understand their failures.



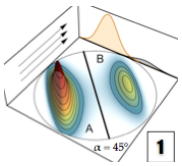
Journal of Physical Chemistry B 199:12912, 2015 · DOI
Beauchamp KA, Behr JM, Rustenburg AS, Bayly CI, Kroenlein K, and **Chodera JD** .
Towards automated benchmarking of atomistic forcefields: Neat liquid densities and static dielectric constants from the ThermoML data archive
Molecular mechanics forcefields are critical to computer-guide drug design, but the benchmarking and improvement of these forcefields has been hindered by the lack of high-quality machine-readable physical property datasets. We show how the NIST-curated ThemoML Archive, which stores physical property data in an IUPAC-standard XML format, can eliminate these roadblocks and reveal issues with current generation forcefields.



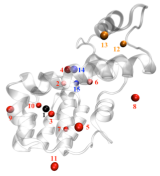
Cell Metabolism 22:1–8, 2015 · DOI
Intlekofer AM, Dematteo RG, Venetti S, Finley LWS, Lu Chao, Judkins AR, Rutenburg AS, Grinaway PB, **Chodera JD** , Cross JR, and Thompson CB
Hypoxia introduces production of L-2-Hydroxyglutarate
Molecular docking is used to demonstrate the potential for alternative substrate usage by isocitrate dehydrogenases under hypoxic conditions in cancer.



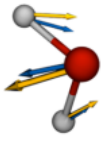
Journal of Physical Chemistry B, 118:6466–6474, 2014. William C. Swope Festschrift · DOI
Sivak DA, **Chodera JD** , and Crooks GE
Time step rescaling recovers continuous-time dynamical properties for discrete-time Langevin integration of nonequilibrium systems
We derive a simple, easy-to-implement Langevin integrator that has universally useful properties in molecular simulations.



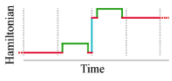
Physical Review X 4:011020, 2014 · DOI
Prinz J-H, **Chodera JD** , and Noé F
Spectral rate theory for two-state kinetics
We present a new mathematical framework for unifying various two-state rate theories presented in the physical chemistry literature over many decades, and provide a quantitative way to measure reaction coordinate quality.



Journal of Computer Aided Molecular Design 27:989–1007, 2013 · DOI
Wang K, **Chodera JD** , Yang Y, and Shirts MR
Identifying ligand binding sites and poses using GPU-accelerated Hamiltonian replica exchange molecular dynamics
We show how bound ligand poses can be identified even when the location of the binding sites are unknown using the machinery of alchemical modern free energy calculations on graphics processors.

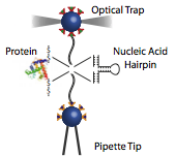


Journal of Physical Chemistry B 117:9956–9972, 2013 · DOI
Wang L-P, Head-Gordon TL, Ponder JW, Ren P, **Chodera JD** , Eastman PK, Martinez TJ, and Pande VS
Systematic improvement of a classical molecular model of water
Water is the most important molecule in biology, and accurate treatment of its interactions is critical to accurate modeling for drug discovery. While polarizable models of water can achieve very high accuracies, they are both difficult to parameterize and expensive to employ. Here, we show how a high quality inexpensive polarizable model of liquid water can be derived using an automated parameterization engine.

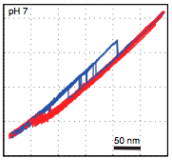


Physical Review X 3:011007, 2013 · DOI
Sivak DA, **Chodera JD** , and Crooks GE
Using nonequilibrium fluctuation theorems to understand and correct errors in equilibrium and nonequilibrium discrete Langevin dynamics simulations
All molecular dynamics simulations introduce error into the sampled distribution by virtue of the finite timestep used to integrate the equations of motion on a digital computer. While traditional approaches to analyzing this error are extremely complicated, we show how interpreting finite-timestep integrators as a form of nonequilibrium driving leads to simple, straightforward schemes for assessing the impact of these errors, as well as correcting for them.

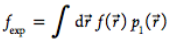
Journal of Chemical Theory and Computation 9:461, 2012 · DOI
Eastman P, Friedrichs MS, **Chodera JD**, Radmer RJ, Bruns CM, Ku JP, Beauchamp KA, Lane TJ, Wang L, Shukla D, Tye T, Houston M, Stich T, Klein C, Shirts MR, and Pande VS
OpenMM 4: A reusable, extensible, hardware independent library for high performance molecular simulation
Inexpensive consumer GPUs promise a 100-fold increase in simulation power by problems that can effectively exploit their highly specialized structure. Here, we describe the latest advances in an extremely high performance, open-source, extensible GPU-accelerated library and toolkit for molecular simulation.



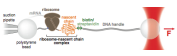
Biophysical Journal 103:1490, 2012 · DOI
Elms PJ, **Chodera JD**, Bustamante CJ, Marqusee S
The limitations of constant-force-feedback experiments
Popular constant-force-feedback single-molecule experiments can cause severe artifacts in single-molecule force spectroscopy data. We demonstrate a simple alternative that eliminates these artifacts.



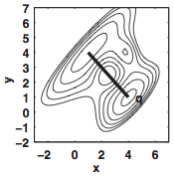
Proceedings of the National Academy of Sciences 109:3796, 2012 · DOI
Elms PJ, **Chodera JD**, Bustamante C, Marqusee S
The molten globule state is unusually deformable under mechanical force
We measure the physical properties of the molten globule state of apo-myoglobin, and show that it is unusually deformable compared to typical protein native states.



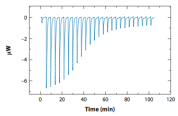
Journal of Chemical Theory and Computation 8:3445, 2012 · DOI
Pitera JW and **Chodera JD**
On the use of experimental observations to bias simulated ensembles
We show how the concept of maximum entropy can be used to recover unbiased conformational distributions from experimental data, and how this concept relates to the popular 'ensemble refinement' schemes for NMR data analysis.



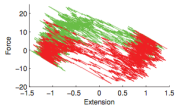
Science 334:1723, 2011 · DOI
Kaiser CM, Goldman DH, **Chodera JD**, Tinoco I, Jr., and Bustamante C
The ribosome modulates nascent protein folding
Using single-molecule force spectroscopy, we show how the ribosome itself modulates the folding dynamics of nascent protein chains emerging from the exit tunnel.



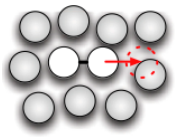
Physical Review Letters 107:098102, 2011 · DOI
Chodera JD and Pande VS
Splitting probabilities as a test of reaction coordinate choice in single-molecule experiments
We demonstrate a simple test for identifying poor reaction coordinates in single-molecule experiments.



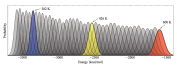
Analytical Biochemistry 414:297, 2011 · DOI
Tellinghuisen JT and **Chodera JD**
Systematic errors in isothermal titration calorimetry: Concentrations and baselines
A word of caution about large errors in isothermal titration calorimetry measurements arising from ligand concentration errors.



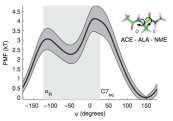
Journal of Chemical Physics 134:024111, 2011 · DOI
Minh DDL, **Chodera JD**
Estimating equilibrium ensemble averages using multiple time slices from driven nonequilibrium processes: Theory and application to free energies, moments, and thermodynamic length in single-molecule pulling experiments
We derive a new estimator for estimating equilibrium expectations from nonequilibrium experiments, and show how it can be used to estimate a variety of useful quantities in simulated single-molecule force spectroscopy experiments.



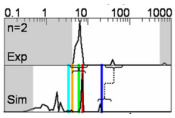
Proceedings of the National Academy of Sciences 108:E1009, 2011 · DOI
Nilmeier JP, Crooks GE, Minh DDL, and **Chodera JD**
Nonequilibrium candidate Monte Carlo is an efficient tool for equilibrium simulation
We present a significant generalization of Monte Carlo methods that provide an enormously useful tool for enhancing the efficiency of molecular simulations and enabling molecular design.



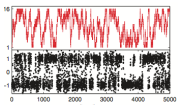
Journal of Chemical Physics 134:244108, 2011 · DOI
Prinz J-H, **Chodera JD**, Pande VS, Smith JC, and Noé F
Optimal use of data in parallel tempering simulations for the construction of discrete-state Markov models of biomolecular dynamics
We demonstrate how multitemperature data from parallel tempering simulations can be used to construct fully temperature-dependent models of the dynamics of biomolecular systems.



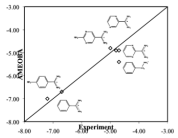
Journal of Chemical Physics 134:244107, 2011 · DOI
Chodera JD, Swope WC, Noé F, Prinz J-H, Shirts MR, and Pande VS
Dynamical reweighting: Improved estimates for dynamical properties from simulations at multiple temperatures
We describe how reweighing techniques can provide optimal estimates of temperature-dependent dynamical properties from simulations conducted at multiple temperatures.



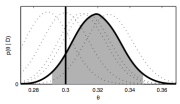
Proceedings of the National Academy of Sciences 108:4822, 2011 · DOI
Noé F, Doose S, Daidone I, Löllmann M, Sauer M, **Chodera JD**, and Smith JC
Dynamical fingerprints: A theoretical framework for understanding biomolecular processes by combination of simulation and kinetic experiments
We present a new framework for comparing essential features of the dynamics between experiment and simulation to identify the kinetics processes contributing to individual relaxation timescales in perturbation-response or correlation spectroscopy experiments.



Journal of Chemical Physics 135:194110, 2011 · DOI
Chodera JD and Shirts MR
Replica exchange and expanded ensemble simulations as Gibbs sampling:
Simple improvements for enhanced mixing
We show how a simple change to the way exchanges are handled in the popular replica-exchange simulation methodology can astronomically increase efficiency at no increase in computational cost.

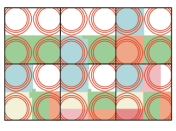


Journal of Physical Chemistry B 114:2549, 2010 · DOI
Ponder JW, Wu C, Ren P, Pande VS, **Chodera JD**, Mobley DL, Schnieders MJ, Haque I, Lambrecht DS, DiStasio RA Jr., Head-Gordon M, Clark GNI, Johnson ME, and Head-Gordon T
Current status of the AMOEBA polarizable force field
The AMOEBA polarizable force field is able to reproduce a diverse set of physical chemical phenomenon to high accuracy.

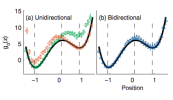


Journal of Chemical Physics 133:105102, 2010 · DOI
Chodera JD and Noé F
Probability distributions of molecular observables computed from Markov models.
II. Uncertainties in observables and their time-evolution
A simple Bayesian approach for the modeling of statistical uncertainties in kinetic and equilibrium quantities computed from Markov state models of biomolecular dynamics.

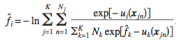
Biophysical Journal 98:3062, 2010 · DOI
Adelman JL, **Chodera JD**, Kuo IW, Miller TF, and Barsky D
The mechanical properties of PCNA: Implications for the loading and function of a DNA sliding clamp
Molecular simulations of the PCNA clamp responsible for DNA polymerase processivity show a surprisingly small energetic penalty for the deformation required for clamp loading. Featured on issue cover.



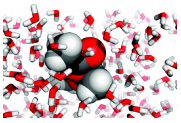
Journal of Chemical Physics 131:045106, 2009 · DOI
Bacallado S, **Chodera JD**, and Pande VS
Bayesian comparison of Markov models of molecular dynamics with detailed balance constraint
A Bayesian scheme for comparing state space decompositions for Markov state models of biomolecular dynamics that incorporates the fact that physical systems must obey detailed balance. This paper utilizes recent results from Markov chain theory on edge-reinforced random walks.



Journal of Chemical Physics 131:134110, 2009 · DOI
Minh DDL, **Chodera JD**
Optimal estimators and asymptotic variances for nonequilibrium path-ensemble averages
We derive an optimal estimator and corresponding statistical uncertainties for inferring expectations of bidirectional nonequilibrium processes. These estimators have widespread applicability in single-molecule biophysical force-spectroscopy experiments and nonequilibrium molecular simulations.

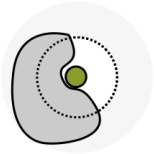


Journal of Chemical Physics 129:124105, 2008 · DOI
Shirts MR, **Chodera JD**
Statistically optimal analysis of samples from multiple equilibrium states
We present a highly general, statistically optimal approach for producing estimates of free energies and equilibrium expectations from multiple simulations that provably extracts all useful information from the data.

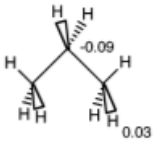


Journal of Medicinal Chemistry 51:769, 2008 · DOI
Nicholls A*, Mobley DL*, Guthrie JP, **Chodera JD**, and Pande VS
Predicting small-molecule solvation free energies: A blind challenge test for computational chemistry
A blind evaluation of the accuracy of alchemical free energy methods for computing gas-to-water transfer free energies (solvation free energies) of small molecules demonstrates that modern forcefields are likely sufficiently accurate to be useful in drug design.

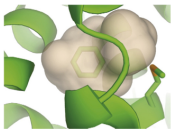
Journal of Physical Chemistry B 112:938, 2008 · DOI
Mobley DL, Dill KA, and **Chodera JD**
Treating entropy and conformational changes in implicit solvent simulations of small molecules
An quantitative examination of how much conformational entropy contributes to hydration free energies of small molecules, with implications for ligand binding.



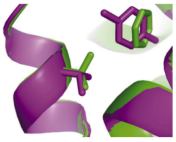
Journal of Physical Chemistry B 111:13052, 2007 · DOI
Shirts MR*, Mobley DL*, **Chodera JD**, and Pande VS
Accurate and efficient corrections for missing dispersion interactions in molecular simulations
We identify a major source of systematic error in absolute alchemical free energy calculations of ligand binding and show how a simple procedure can inexpensively and accurately eliminate it.



Journal of Physical Chem B 111:2242, 2007 · DOI
Mobley DL, Dumont E, **Chodera JD**, Bayly CI, Cooper MD, and Dill KA
Comparison of charge models for fixed-charge force fields: Small-molecule hydration free energies in explicit solvent
We compare a number of popular methods for deriving charge models for small molecules, deriving lessons about best practices for accurate simulations.



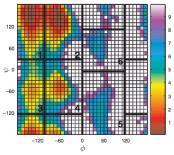
Journal of Molecular Biology 371:1118, 2007 · DOI
Mobley DL, Graves AP, **Chodera JD**, McReynolds AC, Shoichet BK, and Dill KA
Predicting absolute ligand binding free energies to a simple model site
We show how alchemical free energy calculations are capable of accurate blind prediction of small-molecule binding affinities to a simple model protein binding site.



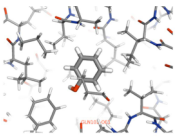
Journal of Chemical and Theoretical Computation 3:1231, 2007 · DOI
Mobley DL, **Chodera JD**, and Dill KA
Confine-and-release method: Obtaining correct binding free energies in the presence of protein conformational change
We present a general scheme for obtaining correct ligand binding affinities when protein conformational change is implicated in ligand binding.

Journal of Chemical Physics 126:155101, 2007 · DOI
Chodera JD *, Singhal N*, Swope WC, Pitera JW, Pande VS, and Dill KA
Automatic discovery of metastable states for the construction of Markov models of macromolecular conformational dynamics
Proposing one of the first automated algorithms for discovering kinetically metastable states of biomolecules from molecular simulations, this paper shows how many biomolecules can possess numerous distinct long-lived conformational states even though the the equilibrium populations of these states may too small for standard structural biology techniques to detect.

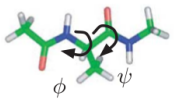
Proceedings of the National Academy of Sciences 104:11987, 2007 · DOI
Ozkan SB, Wu GA, **Chodera JD**, and Dill KA
Protein Folding by Zipping and Assembly
A review of the utility of the proposed zipping and assembly mechanism for the concomitant formation of secondary and tertiary structure in protein folding for predicting folding pathways and native structures.



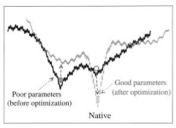
Journal of Chemical Theory and Computation 3:26, 2007 · DOI
Chodera JD, W. C. Swope, J. W. Pitera, C. Seok, and K. A. Dill
Use of the weighted histogram analysis method for the analysis of simulated and parallel tempering simulations
The weighted histogram analysis method (WHAM), a mainstay of molecular dynamics simulation analysis, is thoroughly explained and modernized for the analysis of simulated and parallel tempering simulation data.



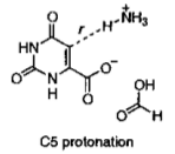
Journal of Chemical Physics 125:084902, 2006 · DOI
Mobley DL, **Chodera JD**, and Dill KA
On the use of orientational restraints and symmetry corrections in alchemical free energy calculations
We illustrate how orientational restraints can be used to greatly reduce the computational effort in alchemical calculations of ligand binding free energies, and clarify how symmetry corrections are necessary when molecules contain symmetric or pseudosymmetric substituents.



Multiscale Modeling and Simulation 5:1214, 2006 · DOI
Chodera JD, Swope WC, Pitera JW, and Dill KA
Long-time protein folding dynamics from short-time molecular dynamics simulations
We show how the long-time dynamics of biomolecular systems can be recapitulated from statistics collected from short molecular simulations sampling transitions between kinetically metastable states.

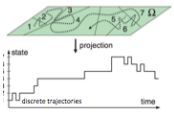


Journal of Computational Chemistry 24:89, 2003 · DOI
Seok C, Rosen JB, **Chodera JD**, Dill KA
MOPED: Method for optimizing physical energy parameters using decoys
We propose a new way to optimize parameters for a physical energy function using decoy structures for protein folding studies.

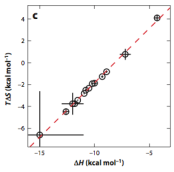


Journal of the American Chemical Society 123:12837, 2001 · DOI
Lee TS*, Chong LT*, **Chodera JD**, and Kollman PA
An alternative explanation for the catalytic proficiency of orotidine 5'-phosphate decarboxylase
A combined QM and MD analysis of potential plausible mechanisms to explain the enormous catalytic acceleration of one of the most proficient enzymes known.

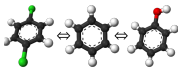
Reviews and Commentaries



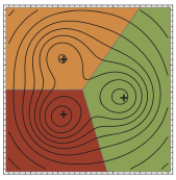
Current Opinion in Structural Biology 25:135, 2014 · DOI
Chodera JD and Noé F
Markov state models of biomolecular conformational dynamics
A review of exciting recent developments in the stochastic modeling of biomolecular dynamics using techniques I originally co-developed to study protein folding.



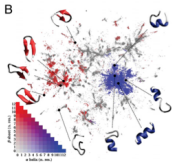
Annual Reviews in Biophysics 42:121, 2013 · DOI
Chodera JD and Mobley DL
Entropy-enthalpy compensation: Role and ramifications for rational ligand design
Entropy-enthalpy compensation is likely a universal phenomena, but not as severe as widely thought, and irrelevant for drug discovery and ligand design.



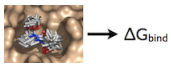
Current Opinion in Structural Biology 21:150, 2011 · DOI
Chodera JD, Mobley DL, Shirts MR, Dixon RW, Branson KM, and Pande VS
Free energy methods in drug discovery and design: Progress and challenges
A review of current opportunities and challenges for alchemical free energy calculations in drug discovery and design.



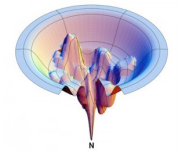
Journal of Chemical Physics 134:174105, 2011 · DOI
Prinz JH, Wu H, Sarich M, Keller B, Fischbach M, Held M, **Chodera JD**, Schütte, and Noé F
Markov models of molecular kinetics: Generation and validation
Current best practices for the generation and validation of Markov state models for describing the stochastic dynamics of biomolecular systems.



Proceedings of the National Academy of Sciences 108:12969, 2011 · DOI
Chodera JD and Pande VS
The Social Network (of protein conformations)
A new methodology for mapping protein conformational spaces is reminiscent of how we use two-dimensional maps to navigate a three-dimensional world.



Annual Reports in Computational Chemistry 3:41, 2007 · DOI
Shirts MR, Mobley DL, **Chodera JD**
Alchemical free energy calculations: Ready for prime time?
A review of current alchemical free energy methodologies and their potential for use in drug discovery and ligand design.



Current Opinion in Structural Biology 17(3):342, 2007 · DOI
Dill KA, Ozkan SB, Weikl TR, **Chodera JD**, and Voelz VA
The protein folding problem: When will it be solved?
A review of the current state of the protein folding problem.

Scientific Advisory Boards

2013–2018 Schrödinger, LLC
2018– OpenEye Scientific

Peer reviewer for scientific journals

Bioinformatics, Biopolymers, Chemical Physics, Computation, Drug Discovery Today, European Biophysics Journal, Entropy, International Journal of Molecular Sciences, Journal of the American Chemical Society, Journal of Chemical Theory and Computation, Journal of Computer-Aided Molecular Design, Journal of Computational Chemistry, Journal of Computational Physics, Journal of Physical Chemistry, Journal of Physical Chemistry Letters, Molecular Physics, Multiscale Modeling & Simulation, Nature Chemistry, Nature Communications, Nature Physics, Pacific Symposium in Biocomputing, PLoS Computational Biology, PLoS One, Proceedings of the National Academy of Sciences, Science, Scientific Reports, Structure

Service

2018– Open Force Field Consortium Governing Board
http://openforcefield.org/consortium

2012–2015 MSKCC High Performance Computing Steering Committee
Member, Co-founder

Graduate Programs

2013– Program in Physiology, Biophysics, and Systems Biology (PBSB)

2013– Tri-Institutional PhD Program in Chemical Biology (TPCB)

2013– Tri-Institutional Program in Computational Biology and Medicine (CBM)

2015– Gerstner Sloan Kettering Graduate Program (GSK)

Teaching

Virginia Tech Summer 2017	MolSSI Software Summer School Instructor Molecular Software Sciences Institute
Tri-I 2015–2018	CBM Journal Club Moderator Tri-I Computational Biology and Medicine Program
WCMC 2018–	BCMB Biochemistry WCMC Graduate School of Medical Sciences (statistical mechanics and thermodynamics unit)

Grant Reviews and Study Sections

NIH

Macromolecular Structure and Function B [MSFB] (*early career reviewer*)

NSF

Ad hoc reviewer and virtual panel member for Chemical Theory, Models, and Computational Methods (CTMC)

Conferences organized

London, UK Sep 2019	CompBioMed 2019 IET London
Berlin, Germany May 2019	MolKin 2019: Molecular Kinetics: Sampling, Design and Machine Learning Freie Universität Berlin, Germany
Göttingen, Germany May 2019	Alchemical Free Energy Methods Workshop Novartis, Cambridge, MA
Boston, MA May 2018	Free Energy Methods and Molecular Kinetics in Drug Design Workshop Novartis, Cambridge, MA
San Francisco, CA Sep 2017	MolSSI Workshop on Workflows in Biomolecular Simulation Autodesk
Berkeley, CA Jan 2017	SMML//2017: Statistical Mechanics // Machine Learning University of California, Berkeley
Boston, MA May 2016	Free Energy Methods in Drug Design Workshop Vertex Pharmaceuticals, Boston, MA
Cambridge, MA May 2016	Markov State Models in Drug Design Workshop Novartis, Cambridge, MA
Berlin, Germany Sep 2015	World Molecular Kinetics Workshop 2015 Freie Universität Berlin, Germany
Boston, MA May 2014	Free Energy Methods in Drug Design Workshop Vertex Pharmaceuticals, Boston, MA
Berlin, Germany Sep 2013	World Molecular Kinetics Workshop 2013 Freie Universität Berlin, Germany
Cambridge, MA May 2012	Free Energy Methods in Drug Design Workshop Vertex Pharmaceuticals, Cambridge, MA
Berlin, Germany Sep 2011	World Molecular Kinetics Workshop 2011 Freie Universität Berlin, Germany
Cambridge, MA May 2010	Free Energy Methods in Drug Design Workshop Vertex Pharmaceuticals, Cambridge, MA
Berlin, Germany May 2009	World Molecular Kinetics Workshop 2009 Freie Universität Berlin, Germany

Recent Invited Talks

Seminars

Bethesda, MD 15 Nov 2018	Advancing quantitative biophysical predictions: How can we move things forward? National Institute for Advancing Translational Sciences (NIH NCATS)
Philadelphia, PA 4 Oct 2018	What will it take to predict kinase inhibitor selectivity and resistance using computational physical modeling? Fox Chase Cancer Center
Waltham, MA 15 Aug 2018	Predicting porin permeation for antimicrobial drug development Entasis Therapeutics
Göttingen, Germany 18 Jul 2018	Redesigning drug design Max Planck Institute for Biophysical Chemistry
Berlin, Germany 17 Jul 2018	Redesigning drug design: Selectively targeting the kinome and beyond Charité
Darmstadt, Germany 8 Jul 2018	Can free energy really be free? The state of open source absolute and relative free energy calculations Merck KGaA
Cambridge, MA 22 May 2018	What will it take to predict kinase inhibitor selectivity and resistance using computational physical modeling? Blueprint Medicines
Cambridge, MA 21 May 2018	Redesigning drug design: Selectively targeting the kinome and beyond Pfizer
San Francisco, CA 12 Apr 2018	Redesigning drug design: Selectively targeting the kinome and beyond Pharmaceutical Chemistry Departmental Seminar, UCSF
Portland, OR 9 Feb 2018	Selective kinase inhibition and emergence of resistance mutations in cancer: Probing driving forces with physical modeling and automated biophysical experiments Biomedical Engineering Seminar, OHSU
Minneapolis, MN 14 Dec 2017	What will it take to predict kinase inhibitor selectivity and resistance using computational physical modeling? Department of Pharmacology, University of Minnesota
Stanford, CA 27 Oct 2017	How can physical modeling play a major role in drug discovery and biomedicine? Vijay Pande group, Stanford University
New York, NY 13 Oct 2017	Markov chain Monte Carlo and nonequilibrium statistical mechanics in drug discovery Applied Math Seminar, NYU Courant
Darmstadt, Germany 18 Sep 2017	Advancing drug design with alchemical free energy calculations Merck Darmstadt
Mountain View, CA 16 Jun 2017	Redesigning drug design Google Advanced Sciences
Rahway, NJ 9 May 2017	Advancing quantitative biophysical predictions with blind challenges Merck Formulations
San Francisco, CA 10 Apr 2017	Redesigning drug design Diane Barber lab, UCSF
Boston, MA 14 Feb 2017	Is there a use for nonequilibrium statistical mechanics in drug design? Harvard Widely Applied Math Seminar
Collegeville, PA 15 Dec 2016	Redesigning drug design GlaxoSmithKline
Bethesda, MD 8 Dec 2016	Redesigning drug design Bernie Brooks group, NHLBI National Institutes of Health
Stanford, CA 28 Oct 2016	Redesigning drug design Vijay Pande group, Stanford University
Barcelona, Spain 15 Sep 2016	Redesigning drug design Universitat Pompeu Fabra
Slough, UK 13 Sep 2016	Redesigning drug design UCB Pharma
Darmstadt, Germany 6 Sep 2016	Alchemical free energy calculations for drug discovery Merck KGaA
San Francisco, CA 29 Oct 2015	Redesigning drug design Autodesk
Rahway, NJ 8 Oct 2015	Redesigning drug design Merck
Cambridge, MA 24 Jul 2015	Redesigning drug design Novartis
Tokyo, Japan 3 Jun 2015	Redesigning drug design University of Tokyo / RCAST

Waltham, MA 15 May 2015	Redesigning drug design AstraZeneca
New Haven, CT 13 May 2015	Redesigning drug design Yale Theoretical Chemistry Seminar
Chicago, IL 15 Apr 2015	Redesigning drug design Illinois Institute of Technology
New Brunswick, NJ 8 Apr 2015	Making the most of limited data in biophysics: Challenges in single-molecule biophysics, nonequilibrium statistical mechanics, and drug discovery Rutgers — Department of Statistics and Biostatistics Seminar

Meetings and Conferences

Baltimore, MD 5 Mar 2019	Closing the loop in automated design and measurement: Scalable inference for biophysical experiments Biophysical Society Meeting: Symposium on Bayesian methods in biophysics
Stockholm 27 Nov 2018	Streamlining molecular simulation data BioExcel Workshop on Interoperability and Reproducibility in Molecular Simulations
Berlin 11 Nov 2018	Redesigning drug design Future Medicine Berlin
Tempe, AZ 7 Oct 2018	What can protein folding teach us about drug discovery? Statistical Physics in Biology
Vienna, Austria 2 Oct 2018	Rare events and large-scale conformational changes in drug discovery ECAM Workshop: Large scale activated event simulations
Biddeford, ME 12 Jun 2018	What can physical modeling tell us about mutational mechanisms of kinase inhibitor resistance? Human Genetic Variation GRC
Santa Fe, NM 8 Mar 2018	Testing the Friesner Conjecture: Are relative free energy calculations always more efficient than absolute? OpenEye CUP XVIII
San Diego, CA 22 Feb 2018	The SAMPL6 Challenges: Advancing molecular modeling accuracy with targeted blind challenges Drug Design Data Resource (D3R) Workshop
New York, MA 13 Nov 2017	Bridging scales in cancer Simons MPS Conference
Cambridge, MA 9 Nov 2017	Building next-generation forcefields and moving free energy calculations to the cloud OpenEye MiniCUP
Berlin, Germany 20 Sep 2017	Next-generation small molecule forcefields RDKit User Group Meeting
Gaithersberg, MD 24 Aug 2017	Challenges and opportunities for reproducibility and reliability in molecular simulations MolSSI Best Practices Workshop, NIST
Leiden, Netherlands 15 Aug 2017	Developing GPU-accelerated molecular simulation tools with OpenMM and the Omnia ecosystem ECAM Software Workshop on Path Sampling
Telluride, CO 14 Jul 2017	Toward realizing the dream of free-energy based small molecule design Telluride Free Energy Workshop
New York, NY 2 Jun 2017	What can physical modeling tell us about mutational mechanisms of kinase inhibitor resistance? NYU Genomics Symposium
Toronto, Canada 29 May 2017	The statistical mechanics of drug discovery Canadian Society of Chemistry 100th Anniversary National Meeting
Waltham, MA 3 May 2017	What can physical modeling tell us about mutational mechanisms of kinase inhibitor resistance? EMBL-EBI Informatics and -omics for Oncology Drug Resistance
Santa Fe, NM 8 Mar 2017	Can free energies really be free? Alchemical free energy calculations in the cloud OpenEye CUP XVII
Houston, TX 8 Oct 2016	Advancing Quantitative Biophysical Predictions Molecular Software Sciences Institute — Biomolecular Simulation
London, UK 14 Sep 2016	Redesigning drug design CCPBioSim — Kings College London
Philadelphia, PA 23 Aug 2016	What is required for alchemical free energy calculations to be useful for predicting drug polypharmacology? ACS Fall National Meeting
Philadelphia, PA 22 Aug 2016	Advancing quantitative biophysical predictions: What can be gained from industry-academic data sharing? ACS Fall National Meeting
Boston, MA 17 May 2016	How can we combine computation and experiment to move the field forward?

	Free Energy Calculations in Drug Discovery, Vertex
San Diego, CA 16 May 2016	Redesigning drug design ACS San Diego
Edinburgh, UK 4 Mar 2016	Redesigning drug design International Centre for Mathematical Sciences (ICMS)
La Jolla, CA 1 Mar 2016	What will it take to design kinase inhibitors with desired selectivity and resistance profiles? GTC 11th Protein Kinases in Drug Discovery Meeting
Edinburgh, UK 19 Oct 2015	Biomolecular software interoperability CECAM Software Interoperability Workshop
Vienna, Austria 18 Sep 2015	Reaction coordinates in drug discovery ESI Insight from Molecular Simulations
Berlin, Germany 8 Sep 2015	Redesigning drug design World Molecular Kinetics Meeting
Tokyo, Japan 5 Jun 2015	Redesigning drug design OpenEye JCUP VI
New York, NY 21 Jan 2015	Redesigning drug design New York Structural Biology Discussion Group

Funding

All funding sources are publicly available online at http://choderalab.org/funding

ACTIVE

Single-Investigator Grants

NIH R01 GM121505
The role of reorganization energy in achieving selective kinase inhibition
The goal of this project is to probe the role of protein reorganization energy in achieving selectivity in targeted kinase inhibition with small molecules.
9/1/2017 – 8/31/2022
$196,250 annual direct costs

Vir Biosciences Collaboration
Development of alchemical free energy methods for predicting the impact of point mutations
The goal of this project is to develop alchemical free energy methods for predicting the impact of point mutations on antibody:antigen affinities.
7/25/19 – 7/24/2021
$55,556 annual direct costs to the Chodera lab

Collaborative Grants

NIH R01 GM124270 (PI: David Mobley, UCI)
Advancing predictive physical modeling through focused development of model systems to drive new modeling innovations
The goal of this project is to enable blind community challenges that drive progress toward quantitative accuracy in the field of computational physical modeling of drug-receptor interactions.
9/10/2018 – 8/31/2022
$57,588 annual direct costs to the Chodera lab

NSF CHI 1904822 (PI: David Minh, IIT)
Collaborative Research: CDS&E: Elucidating Binding using Bayesian Inference to Integrate Multiple Data Sources
The goal of this project is to develop a scalable approach to Bayesian inference from biophysical experiments
9/1/2019 – 8/31/2022
$47,237 annual direct costs to the Chodera lab

Functional Genomics Initiative (FGI)
Integrated Approaches Annotate Functions of Cancer-associated H3K36 Methyltransferases
The goal of this project is to develop approaches for using large-scale physical modeling and biochemical experiments to annotate the functions of clinical cancer mutations.
1/1/2019 – 12/31/2020
co-PI: Minkui Luo
$125,000 annual direct costs to the Chodera lab

BIH Einstein Visiting Professorship at the Charité Berlin
Computational polypharmacology: A new paradigm for selectively promiscuous kinase inhibitors
The goal of this project is to develop structure-informed machine learning approaches to predicting kinase inhibitor polypharmacology for computer-guided small molecule design.
1/1/2019 – 12/31/2021
EUR150,000 annual direct costs to Chodera (via Charité) for Berlin working group

The Open Force Field Consortium
An academic-industry consortium to develop open biomolecular force fields
http://openforcefield.org/consortium
10/1/2018 – (renewed annually)
$600,000 annual total costs to the Consortium

Fellowships

Hannah Bruce Macdonald
MolSSI Investment Fellowship
7/1/2019 – 12/31/2020
direct costs: $50K/year stipend support

Chaya Stern, TPCB Graduate Student
MolSSI Phase II Fellowship
1/1/2019 – 6/30/2020
direct costs: $40,000/year stipend

Marcus Wieder, Postdoctoral Research Fellow
Austrian Schrödinger Stipendium
10/1/2018 – 9/30/2019
direct costs: Fellowship recipient direct paid

Simon Boothroyd, Postdoctoral Research Fellow
XtalPi / Open Force Field Consortium Distinguished Postdoctoral Fellowship
10/1/2018 – 9/30/2019
direct costs: Fellowship recipient direct paid

Andrea Rizzi, CBM Graduate Student
MolSSI Open Force Field Predoctoral Fellowship
1/1/2019 – 6/30/2019
direct costs: $20,000/six months stipend support

PENDING

Single-Investigator Grants and Contracts

None

Collaborative Grants

NIH Focused Technology Development R01 1R01GM132386
Open data-driven infrastructure for building biomolecular force fields for predictive biophysics and drug design
co-PI: Michael Shirts (University of Colorado)
co-Is: David Mobley (UCI), Lee-Ping Wang (UC Davis), Michael Gilson (UCSD)
The goal of this project is to develop a modern open infrastructure for building fully consistent biopolymer and small molecule force fields for drug design and predictive biophysical modeling.
6/1/2019 – 5/30/2023
$105,000 annual direct costs to the Chodera lab

NIH R01 (PI: Daniel Heller, MSKCC)
Targeted delivery of kinase inhibitors to RAS-driven GI tumors
The goal of this project is to develop predictive computational models for the design and optimization of nanoparticles for the targeted delivery of selective kinase inhibitors.
4/1/2020 – 3/31/2025
$471,771 annual direct costs / $98,218 annual direct costs to Chodera lab

Wellcome Trust UNS95190 (PI: Frank von Delft, Oxford/DiamondMX)
Effecting a transformation in compound discovery through open, experiment-coupled AI-led drug design
The goal of this proposal is to develop computational techniques for autonomously designing small molecules and interpreting experimental assays utilizing the DiamondMX high-throughput beamline.
3/1/2020 – 2/28/2025
$955,159 annual direct costs / $91,980 annual direct costs to Chodera lab

Chan Zuckerberg Initiative – Essential Open Source Software for Science (PI: John Chodera, MSKCC)
co-I: Gianni de Fabritiis (Universitat de Pompeu Fabra, Barcelona)
OpenMM: Scalable biomolecular modeling, simulation, and machine learning
The goal of this project is to support continued development of OpenMM, transition to a community governance and distributed development model, and extension to integrate physical and machine learning models to enable genomic-scale biomolecular modeling, simulation, and prediction.
12/1/2019 – 11/30/2020
$100,000 annual direct costs to the Chodera lab

Fellowships

None

COMPLETED

Single-Investigator Grants and Contracts

Relay Therapeutics Collaboration
Development of efficient open source cloud-enabled free energy based lead optimization algorithms and integrative Bayesian model of experimental biophysical and molecular simulation data
The goal of this project is to develop open source scalable cloud workflows for lead optimization using relative and absolute alchemical free energy calculations, as well as Bayesian integrative modeling techniques for experimental biophysical data and molecular simulations.
4/5/2018 – 4/5/2019
$74,074 annual direct costs

Entasis Therapeutics Collaboration
Development of efficient equilibrium and nonequilibrium algorithms for predicting small molecule porin permeation with potential of mean force methods
The goal of this project is to develop algorithms and open source tools for efficient equilibrium and nonequilibrium potential of mean force calculations for bacterial porins.
4/5/2018 – 4/5/2019
$74,074 annual direct costs

Parker Institute for Cancer Immunotherapy Pilot Grant
Physics-based computational prediction of cancer-associated mutant MHC class II epitopes
The goal of this project is to develop algorithms and open source tools for efficient computation of MHC class II epitope binding affinities.
4/2/2018 – 4/1/2019
$75,000 annual direct costs

NSF D3SC EAGER CTMC
A probabilistic framework for automated forcefield parameterization from experimental datasets
The goal of this project is to develop a scalable Bayesian inference infrastructure to parameterize molecular mechanics forcefields using experimental datasets.
9/1/2017 – 8/31/2019
$52,030 annual direct costs

Silicon Therapeutics Collaboration
Development of efficient open source free energy based lead optimization algorithms
The goal of this project is to develop open source scalable parallel workflows for lead optimization using relative alchemical free energy calculations.
5/17/2017 – 11/17/2018
$48,655 annual direct costs

Merck KGaA Collaboration
Developing automated workflows for absolute alchemical free energy calculations
The goal of this project is to develop open source automated workflows using absolute alchemical free energy calculations for use in prioritizing compounds for synthesis in drug discovery applications.
7/26/2016 – 1/25/2019
$90,273 annual direct costs

Astra-Zeneca iMed Collaboration
Evaluating the potential for Markov state models of conformational dynamics to advance quantitative prediction of thermodynamics and kinetics of selective kinase inhibitors
The goal of this project is to evaluate the potential for Markov state models of conformational dynamics to quantitatively predict the thermodynamics and kinetics of selective kinase inhibitors to CK2 and SYK.
7/30/2015 – 1/30/2017
$117,505 annual direct costs

Gerstner Family Foundation
Louis V. Gerstner, Jr. Young Investigator Award
Dates: 2/1/2013 – 1/30/2016
$75,000 annual direct costs

MSKCC Functional Genomics Initiative (FGI) Rapid Response Grant
Biophysical characterization of clinically-identified kinase mutations
The goal of this project is to quantify the impact of clinically-identified kinase domain mutations on FDA-approved selective kinase inhibitor binding.

4/1/2016 – 3/31/2016
$25,000 annual direct costs

MSKCC Functional Genomics Initiative (FGI) Rapid Response Grant
Biophysical characterization of clincally-identified K-Ras mutants
The goal of this project is to biophysically characterize clinically-identified K-Ras mutants.
7/1/2016 – 6/30/2016
$25,000 annual direct costs

Fellowships

Rafal P. Wiewiora, TPCB Graduate Student
DOD Peer-Reviewed Cancer Research Program Award
8/15/2017 – 8/14/2019
direct costs: $75,000/year for stipend and supplies

Karmen Čondić-Jurkić, Postdoctoral Research Fellow
Open Force Field Consortium Postdoctoral Fellowship
1/1/2019 – 6/30/2019
direct costs: $60,628 stipend and travel support

Chaya Stern, TPCB Graduate Student
MolSSI Phase I Fellowship
7/1/2018 – 12/31/2018
direct costs: $40,000/year stipend

Chaya Stern, TPCB Graduate Student
NSF Graduate Research Fellowship
8/1/2015 – 7/30/2018
direct costs: $32,000/year stipend support

Mehtap Isik, TPCB Graduate Student
Doris J. Hutchison Fellowship
7/1/2017 – 6/30/2018
direct costs: $38,668/year stipend support

Gregory A. Ross, Postdoctoral Fellow
Molecular Software Sciences Institute (MolSSI) Graduate Research Fellowship
direct costs: $50,000/year stipend support

Steven Albanese, GSK Graduate Student
Summer Internship, Schrödinger
Summer 2017

Ariën S. Rustenburg, PBSB Graduate Student
Summer Internship, Genentech
Summer 2015

Andrea Rizzi, CBM Graduate Student
Tri-I CBM Student Stipend Assistance
direct costs: $13,500/year stipend support

Collaborative Grants

2014 Functional Genomics Initiative (PI: James Hsieh, MSKCC)
Characterization of Cancer-derived mTOR Mutations for Precision Therapeutics
The goal of this project is to understand the mechanism underlying clinically-identified mTOR activating mutants and evaluate the potential for rapalog therapy to aid the 2% of cancer patients harboring mTOR mutations.
5/1/2015 – 4/30/2017
$118,000

2014 STARR Cancer Consortium (PI: Minkui Luo, MSKCC)
Designing sinefungin scaffolds as specific protein methyltransferase inhibitors
The goal of this project is to use computational techniques that explicitly incorporate protein flexibility to design selective inhibitors for protein lysine methyltransferases.
1/1/2015 – 6/30/2017
$125,000

Personnel

CURRENT MEMBERS

Postdocs

- Karmen Čondić-Jurkić, PhD Friedrich Alexander University, Erlangen (4/6/2019–)
  Biomolecular force fields; open science; interoperability in molecular simulations
- Ana Silveira, PhD Federal University of Rio de Janeiro (8/1/2018–)
  Integrative modeling of allosteric inhibition; modeling antimicrobial permeation of bacterial porins
- Marcus Wieder, PhD University of Vienna (9/1/2018–)
  Modeling tautomer shifts upon binding of small druglike molecules
- Hannah Bruce Macdonald, PhD University of Southampton (10/1/2018–)
  Advanced alchemical free energy methods for drug discovery
- Jiaye Guo, PhD Stony Brook University (10/1/2018–)
  Design of selective kinase inhibitors and emergence of resistance
- Simon Boothroyd, PhD Lancaster University (11/1/2018–)
  Development of advanced biomolecular force fields for drug discovery
- Jaime Rodríguez-Guerra, PhD Autonomous University of Barcelona (4/1/2019–) **(Berlin group)**
  Scalable machine learning and alchemical free energy calculations for drug discovery

Graduate Students

- Ariën Sebastian Rustenburg (10/1/2013–*9/30/2018 anticipated*)
  Program in Physiology, Biophysics, and Systems Biology (PBSB)
  Constant-pH dynamics; protonation states effects in kinase inhibitors via experiment and theory
- Andrea Rizzi (9/1/2015–*12/31/2019 anticipated*)
  Tri-Institutional Program in Computational Biology and Medicine (CBM)
  Quantitatively accurate alchemical free energy calculations for kinase inhibitor design
- Chaya Stern (4/01/2014–*12/31/2019 anticipated*)
  Tri-Institutional Training Program in Chemical Biology (TPCB)
  Analysis of single-molecule biophysical experiments; Bayesian inference for forcefield parameterization
- Joshua Fass (9/1/2015–*12/31/2019 anticipated*)
  Tri-Institutional Program in Computational Biology and Medicine (CBM)
  Machine learning and statistical inference for biomolecular dynamics and forcefield parameterization
- Rafal Wiewiora (6/1/2015–*3/31/2020 anticipated*)
  Tri-Institutional Training Program in Chemical Biology (TPCB)
  Design of selective inhibitors for protein methyltransferases; Markov state modeling
- Mehtap Isik (6/1/2015–*6/30/2020 anticipated*)
  Tri-Institutional Training Program in Chemical Biology (TPCB)
  Model experiemntal systems for protein-small molecule recognition; targeted nanoparticle design
- Ivy Zhang (8/1/2018–)
  Program in Physiology, Biophysics, and Systems Biology (PBSB)
  Scalable free energy calculations for predicting the impact of clinical mutations in antibodies and kinases
- Yuanqing Wang (7/1/2018–)
  Program in Physiology, Biophysics, and Systems Biology (PBSB)
  Machine learning of physical models for drug discovery
- Dominic Rufa (4/1/2019–)
  Tri-Institutional Program in Computational Biology and Medicine (CBM)
  Small molecule multi-objective design by free energy methods
- Talia Kimber (4/1/2019–) (**Berlin group)**
  Charité Universitätmedizin (supervisor: Andrea Volkamer)
  Freie Universität Berlin, Computer Science PhD program (supervisor: Frank Noé)
  Machine learning for optimizing affinity/selectivity and predicting resistance

Technicians

- Erica Goldberger (7/1/2019–)
  Automated human kinase expression and measurements of small molecule kinase inhibitor affinities to mutant kinases
- Binisha Karki (8/1/2019–)
  Scalable biophysical measurements of model protein-ligand systems for advancing computational chemistry

PAST TRAINEES

Postdocs

- Levi N. Naden (until 8/10/2018)
  Current position: *Software Scientist* at the NSF **Molecular Sciences Software Institute (MolSSI)**
- Sonya M. Hanson (until 6/30/2017)
  Current position: *Postdoctoral Researcher with Joachim Frank*, **Columbia University**
- Gregory Ross (until 6/30/2017)
  Current position: *Senior Scientist*, Free Energy Methods, **Schrödinger**
- David W. H. Swenson (until 12/30/2015)
  Current position: *Postdoctoral Researcher*, **Universiteit von Amsterdam**
- Daniel L. Parton (until 8/31/2015)
  Current position: *Lead Data Scientist*, **Bardess Group**
- Kyle A. Beauchamp (until 6/12/2015)
  Current position: *Computational Research Scientist*, **Counsyl**
- Jan-Hendrik Prinz (until 1/30/2015)
  Current position: *Digital Solutions Architect*, **Keylight GmbH**
- Sarah E. Boyce (until 10/31/2013)
  Current position: *Senior Scientist, Drug Discovery Group*, **Schrödinger**

Graduate Students

- Steven Albanese (6/1/2015–3/31/2019)
  Gerstner Graduate Program (GSK)
  Free energy calculations to predict kinase inhibitor selectivity and resistance; Biophysics of kinase activation
- Patrick B. Grinaway (7/1/2013–12/31/2018)
  Program in Physiology, Biophysics, and Systems Biology (PBSB)
  Current position: *Scientist*, **Onai**
- Julie M. Behr (1/10/2014–12/31/2016)
  Tri-Institutional Program in Computational Biology and Medicine (CBM)
  Current position: *Transferred to Imielinski lab after publishing three papers with the Chodera lab*

Technicians

- Lucelenie Rodriguez (7/1/2015–12/31/2016; 12/4/2017–7/20/2018)
  Current position: *Medical student*, **NYU School of Medicine**
- Erin Grundy (6/1/18–7/31/2019)
  Current position: *Graduate student*, **George Washington University**

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  Co-Director, Molecular Sciences Software Institute (MolSSI)
  Senior Scientist, Center for Theoretical Biological Physics
  Einstein Visiting Fellow, Freie Universität Berlin
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