Diwakar Shukla

SIMBIOS Distinguished Postdoctoral Fellow
Department of Chemistry, Stanford University
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CONTACT INFORMATION

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EDUCATION

Postdoctoral Fellow, Chemsitry, Stanford University, 2011-Present
- Advisor: **Prof. Vijay S. Pande** and **Prof. Benoît Roux**

Ph.D., Chemical Engineering, Massachusetts Institute of Technology, 2006-2011
- Advisor: **Prof. Bernhardt L. Trout**

M.S., Chemical Engineering Practice, Massachusetts Institute of Technology, 2009
M.Tech., Chemical Engineering, Indian Institute of Technology Bombay, 2006
- Advisor: **Prof. Anurag Mehra**

B.Tech., Chemical Engineering, Indian Institute of Technology, Bombay, 2006

HONORS AND AWARDS

Distinguished Young Scientist Seminar, U. Washington, 2013
SIMBIOS Distinguished Postdoctoral Fellowship, Stanford University, 2011
W. H. Peterson Award, American Chemical Society, 2011
Innovation in Biotechnology Award, AAPS and Genentech, 2011
CoMSEF Graduate Student Award for Outstanding Research Performance, AIChE, 2010
Outstanding Graduate Teaching Assistant Award, MIT, 2010
Keith and Helen Rumbel Fellowship, MIT, 2006-07
Chemical Weekly Best Student Paper Award, IIChE, 2006
R. G. Manudhane Award for Best Master's Thesis, IIT Bombay, 2006
Institute Silver Medal, IIT Bombay, 2006 (top student in graduating class)
Institute Academic Prize, IIT Bombay, 2004, 2005 (top student in chemical eng.)
Young Scientist Award, Department of Science and Technology, India, 2000
- For winning Gold Medal in several categories at Millennium Robot Games, Canada, 2000
- For winning Bronze Medal at International Astronomy Olympiad, Russia, 1998

RESEARCH EXPERIENCE

Postdoctoral Research, Stanford University, July 2011-Present

- **Activation Mechanism of G-Protein Coupled Receptors and Kinases**
  - Investigated activation mechanism of key cellular signaling proteins (GPCRs and Kinases) which are implicated in various diseases including all forms of cancer.
  - Explained the mechanism by which drugs modulate conformational landscape of GPCRs.
  - Predicted presence of novel intermediate states along kinase activation pathway and drug molecules that can block kinase activation.
  - Demonstrated that long-timescale MD simulations (in milliseconds) could be performed using cloud computing platforms such as Google Exacycle.

Graduate Research, MIT, Aug 2006-June 2011

- **Rational Design of Cosolvents for Inhibition of Protein Aggregation**
  - Discovered the mechanism by which L-arginine inhibits aggregation
  - Demonstrated the novel effects of intra-solvent interactions on protein aggregation.
  - Designed cosolvents that are 30 times more effective at aggregation suppression thereby increasing the shelf-life of unstable protein drugs from few days to a year.
  - Wrote 1 patent and 12 papers in journals *JACS*, *JPC* and *PLoS One*.
  - Won outstanding research awards from AIChE, ACS and AAPS.

Undergraduate Research, IIT Bombay, Jan 05 - Aug 06

- **Modeling Precipitation of Nanoparticles in Reverse Micellar Systems**
  - Developed Monte Carlo models for formation of nanoparticle in reverse micelles.
  - Explained the role of particle coagulation and Ostwald ripening in particle growth.
  - Wrote 6 papers in journals *Langmuir* and *Nanotechnology*.
  - Won best student paper award from Indian Institute of Chemical Engineers.

TEACHING EXPERIENCE

- Instructor, BioCore Explorations Program, Fall 2011, Stanford University.
- Teaching Assistant, Transport Phenomena, Fall 2009, MIT.
  - Won outstanding TA award and nominated for institute teaching award.
- Teaching Assistant, Modeling and Simulation, Spring 2006, IIT Bombay.
- Teaching Assistant, Chemical Processes, Fall 2005, IIT Bombay.

INDUSTRIAL EXPERIENCE

- Summer 2007, Cabot Corporation (Billerica, MA). Developed models for the formation of nanoparticles in a flame reactor.
- Summer 2007, Novartis Pharmaceuticals (East Hanover, NJ). Led a team of 3 to investigate and propose innovative solutions for optimization of medication supply process for early clinical trials.

GRANT WRITING EXPERIENCE

INCITE, U.S. Department of Energy Leadership Computing Grant, 2013-2015: 46 million hours of computer time on Oak Ridge National Laboratory's supercomputer TITAN. The main goal of this grant is to use computational methods for design of oxygen tolerant Hydrogenases, the key enzymes involved in H_2 production.

SIMBIOS distinguished postdoctoral fellowship, 2011-2014: To work on biophysical methods for studying protein conformational change in G-protein coupled receptors at NIH center for biomedical computation, Stanford University.

Applied for Burroughs Welcome Fund Career Awards at the Scientific Interface for understanding the origin and modulation of biased signaling in G-Protein Coupled Receptors.

PUBLICATIONS

first/co-first author: 21* | *published/In press: 23* | *h-index: 10

More details can be found on my website.

[30] **D. Shukla**, Yilin Meng, Benoît Roux and V. S. Pande, Activation pathway of Src kinase reveals intermediate states as novel targets for drug design. **Nature Comm.**, Accepted, 2013.

[29] Kai Kohlhoff*, **D. Shukla***, Morgan Lawrenz, Gregory R. Bowman, David E. Konerding, Dan Belov, Russ B. Altman and V. S. Pande, Cloud-based simulations on Google Exacycle reveal ligand-modulation of GPCR activation pathways. **Nature Chem.**, In Press, 2013. * denotes co-first author

[28] T. J. Lane, **D. Shukla**, K. A. Beauchamp and V. S. Pande, To Milliseconds and Beyond: Challenges in the Simulation of Protein Folding. **Curr. Opin. Struc. Bio.**, Vol. 23, No. 1, 58-65, 2013.

[27] **D. Shukla**, and B. L. Trout, Understanding the Role of Arginine and Citrate as Eluents in Affinity Chromatography, Developments in Biotechnology and Bioprocessing, ACS Symposium Series, 2013.

[26] **D. Shukla**, C. P. Schneider and B. L. Trout, Complex Interactions between Molecular Ions in Solution and Their Effect on Protein Stability, **J. Am. Chem. Soc.**, Vol. 113, No. 46, 18713-18718, 2011.

[25] P. Eastman, M. S. Friedrichs, J. D. Chodera, R. J. Radmer, C. M. Bruns, J. P. Ku, K. A. Beauchamp, T. J. Lane, L.-P. Wang, **D. Shukla**, T. Tye, M. Houston, T. Stich, C. Klein, M. R. Shirts, V. S. Pande, OpenMM 4.0: A Reusable, Extensible, Hardware Independent Library for High Performance Molecular Simulation. **J. Chem. Theory Comput.**, Vol. 9, No. 1, 461-469, 2013.

[24] C. P. Schneider*, **D. Shukla*** and B. L. Trout, Effects of Solute-Solute Interactions on Protein Stability Studied Using Various Counterions and Dendrimers. **PLoS One**, Vol. 6 No. 11, e27665, 2011.

[23] **D. Shukla**, C. P. Schneider and B. L. Trout, Effect of PAMAM Dendrimer Salts on Protein Stability. **J. Phys. Chem. Lett.**, Vol. 2, No. 114, 1782-1788, 2011.

[22] **D. Shukla**, C. P. Schneider and B. L. Trout, Molecular Level Insight Into Intra-Solvent Interaction Effects on Protein Stability and Aggregation, **Adv. Drug Deliver. Rev.**, Vol. 63, No. 13, 1074-1085, 2011.

[21] **D. Shukla**, and B. L. Trout, Understanding the Synergistic Effect of L-Arg and L-Glu Mixtures on Protein Solubility. **J. Phys. Chem. B**, Vol. 115, No. 41, 11831-11839, 2011.

[20] C. P. Schneider*, **D. Shukla*** and B. L. Trout, Arginine and the Hofmeister Series: The Role of Ion-Ion Interactions in Protein Aggregation Suppression. **J. Phys. Chem. B**, Vol. 115, No. 22, 7447-7458, 2011.

[19] **D. Shukla**, L. Zamolo, C. Cavallotti and B. L. Trout, Understanding the Role of Arginine as an Eluent in Affinity Chromatography via Molecular Computations. **J. Phys. Chem. B**, Vol. 115, No. 11, 2645-2654, 2011.

[18] **D. Shukla** and B. L. Trout, Preferential Interaction Coefficients of Proteins in Aqueous Arginine solutions and its molecular origins. **J. Phys. Chem. B**, Vol. 115, No. 5, 1243-1253, 2011.

[17] **D. Shukla** and B. L. Trout, On the Interaction of Arginine with Proteins and the Mechanism by Which it Inhibits Aggregation **J. Phys. Chem. B**, Vol. 114, No. 42, Pages 13426-13438, 2010.

[16] **D. Shukla**, C. Shinde and B. L. Trout, Molecular Computations of Preferential Interaction Coefficients of Proteins. **J. Phys. Chem. B**, Vol. 113, No. 37, Pages 12456-12554, 2009.

[15] **D. Shukla**, A. A. Joshi and A. Mehra, Modeling of Formation of Nanoparticles in Reverse Micellar Systems: Ostwald Ripening of Silver Halide Particles. **Langmuir**, Vol. 25, No. 6, pages 3786-3793, 2009.

[14] A. K. Sugih, **D. Shukla**, H. J. Heeres and A. Mehra, $CaCO_3$ Nanoparticle Synthesis by Carbonation of Lime Solution in Microemulsion Systems, **Nanotechnology**, Vol. 18, 035607, 2007.

[13] **D. Shukla** and A. Mehra, Modeling the Formation of Shell in Core-Shell Nanocrystals in Reverse Micellar Systems. **Langmuir**, Vol. 1, No. 22, pages 9500-9506, 2006.

[12] R. Jain, **D. Shukla** and A. Mehra, A Monte Carlo Model for the Formation of Core-Shell Nanocrystals in Reverse Micellar Systems. **Ind. Eng. Chem. Res.**, Vol. 45, No. 1, pages 2249-2254, 2006.

[11] **D. Shukla** and A. Mehra, A Model for Particle Coagulation in Reverse Micelles with a Size Dependent Coagulation Rate. **Nanotechnology**, Vol. 17, pages 261-267, 2006.

[10] **D. Shukla**, and A. Mehra, Modeling of the Formation of Nanoparticles in Reverse Micellar Systems. Proceeding of the 17th International Congress of Chemical and Process Engineering, Prague, Czech Republic, 2006.

[9] R. Jain, **D. Shukla** and A. Mehra, Coagulation of Nanoparticles in Reverse Micellar Systems: A Monte Carlo Model. **Langmuir**, Vol. 21, No. 1, pages 11528-11533, 2005.

Submitted/ In Preparation

[8] C. Schwantes, **D. Shukla** and V. S. Pande, Markov State Model Reveals Slow Folding Phase of NuG2. Submitted, 2013.

[7] D. Vanatta, **D. Shukla**, M. Lawrenz, F. Pontiggia, D. Kern and V. S. Pande, A Network of Molecular-Switches Control the Activation of a Key Bacterial Signaling Protein. Submitted, 2013.

[6] L. J. Lapidus, S. Acharya, C. Schwantes, L. Wu, **D. Shukla**, M. King, S. J. DeCamp, V. S. Pande Complex Pathways in Folding of Protein G Explored by Simulation and Experiment. Submitted, 2013.

[5] **D. Shukla** and V. S. Pande, Huntingtin Headpiece fragment N17 could acts as a template for PolyQ Aggregation. Submitted, 2013.

[4] **D. Shukla** and V. S. Pande, Atomistic View of the Conformational Landscape of Apo- and Holo- Calmodulin. In preparation, 2013.

[3] **D. Shukla**, Benoit Roux, and V. S. Pande, Kinetics of DFG-flip in Src and Abl Kinase. In preparation, 2013.

[2] **D. Shukla*** , K. Kohlhoff* , M. Lawrenz* , D. E. Konerding, D. Belov, R. B. Altman and V. S. Pande, Role of lipid-receptor interactions in conformational dynamics of GPCRs. In preparation, 2013. * denotes co-first author

Manuscripts under review and in preparation can be shared on request.

Patents

[1] B. L. Trout, C. P. Schneider and **D. Shukla**, Dendrimer-based Excipients for the Attenuation of Protein Aggregation, U.S. Patent Application No. 61/412, 600, 2010.

Invited Talks

[5] GPU computing and novel sampling algorithms for atomistic simulations of large biophysical systems, Nvidia Cuda Day, Institute for Computational and Mathematical Engineering, Stanford University, Stanford, CA, 2013.

[4] Proteus Among Proteins: A collection of short stories about conformational chnages in GPCRs and Kinases. ACS Western Regional Meeting, Santa Clara, CA, 2013.

[3] Cloud-based simulations on Google Exacycle provide novel mechanistic insights into conformational transitions in GPCRs and Kinases. Distinguished Young Scientist Seminar Series, University of Washington, Seattle, WA, 2013.

[2] Studying Conformational Changes in Kinases Using Markov State Models, Biophysics Seminar, Stanford University, Stanford, CA, 2013.

[1] Additives for Inhibiting Protein Aggregation. AAPS National Biotechnology Conference, San Francisco, CA, 2011. Invited Talk in the Innovation in Biotechnology Award Session

Conference Presentation

[21] D. Shukla, Elucidating the Role of N-Terminal Huntingtin Fragment in Polyglutamine Aggregation. AIChE Annual Meeting, San Francisco, CA, 2013.

[20] D. Shukla, Benoît Roux, and V. S. Pande, Activation Mechanism of c-Src Tyrosine Kinase. AIChE Annual Meeting, AIChE Annual Meeting, San Francisco, CA, 2013.

[19] D. Shukla, Benoit Roux, and V. S. Pande, Activation Mechanism of c-Src Tyrosine Kinase. ACS Fall Meeting, Indianapolis, 2013.

[18] D. Shukla and V. S. Pande, Elucidating General Principles Guiding Protein Conformational Change Using Multiscale Simulation, ACS Fall Meeting, Indianapolis, 2013.

[17] D. Shukla, M. Lawrenz, and V. S. Pande, Ligand Modulated Conformational Landscape of G-Protein Coupled Receptors. AIChE Annual Meeting, Pittsburgh, PA, 2012.

[16] D. Shukla, and V. S. Pande, Studying the Folding of Multi-domain Proteins. Gordon Research Conference on Protein Dynamics, Ventura, CA, 2012.

[15] D. Shukla and V. S. Pande, Elucidating the Role of N-Terminal Huntingtin Fragment in Polyglutamine Aggregation. AIChE Annual Meeting, Pittsburgh, PA, 2012.

[14] D. Shukla, and B. L. Trout, Preferential Interaction Coefficients of Proteins In Mixed Solvents. AIChE Annual Meeting, Minneapolis, MN, 2011.

[13] D. Shukla, and B. L. Trout, Estimating the Free Energy of the Association of Amyloid Fibril Forming Peptides. AIChE Annual Meeting, Minneapolis, MN, 2011.

[12] D. Shukla, and B. L. Trout, Molecular Modeling of Complex Biological Systems. AIChE Annual Meeting, Minneapolis, MN, 2011.

[11] D. Shukla, C. P. Schneider, and B. L. Trout, Additives for Inhibiting Protein Aggregation. AAPS National Biotechnology Conference, San Francisco, CA, 2011.

[10] D. Shukla, C. P. Schneider, and B. L. Trout, Additives for Inhibiting Protein Aggregation. AAPS National Biotechnology Conference, San Francisco, CA, 2011.

[9] D. Shukla, C. P. Schneider, and B. L. Trout, Rational Design of Additives for Inhibition of Protein Aggregation. ACS National Meeting, Anaheim, CA, 2011.

[8] D. Shukla, and B. L. Trout, A Molecular Perspective on the Role of Eluents in Affinity Chromatography. ACS National Meeting, Anaheim, CA, 2011.

[7] D. Shukla, and B. L. Trout, Effect of Co-Solutes On the Thermodynamics of the Aggregation of Peptides. AIChE Annual Meeting, Salt Lake City, UT, 2010.

[6] D. Shukla, and B. L. Trout, Rational Design of Additives for Inhibition of Protein Aggregation. AIChE Annual Meeting, Salt Lake City, UT, 2010.

[5] D. Shukla, and B. L. Trout, Additives for Inhibiting Protein Aggregation: Mechanistic Understanding, Rational Design, and Performance Prediction. AIChE Annual Meeting, Salt Lake City, UT, 2010.

[4] D. Shukla, C. P. Schneider and B. L. Trout, Rational Design of Additives for Inhibition of Protein Aggregation. ACS National Meeting, Boston, MA, 2010.

[3] D. Shukla, C. P. Schneider and B. L. Trout, Mechanism by Which Arginine Inhibits Protein Aggregation. ACS National Meeting, San Francisco, CA, 2010.

[2] D. Shukla, and B. L. Trout, Preferential Interaction of Arginine With Proteins. ACS National Meeting, San Francisco, CA, 2010.

[1] D. Shukla, and B. L. Trout, Preferential Interaction Parameters of Proteins in Mixed Solvents. AIChE Annual Meeting, Philadelphia, PA, 2008.

AFFILIATIONS American Institute of Chemical Engineers (AIChE)
American Chemical Society (ACS)
American Association of Pharmaceutical Scientists (AAPS)
Biophysical Society

REFERENCES

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