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Education

Ph.D. in Biomedical Engineering, **2011**
Texas A&M University, College Station, TX

M.S. in Biomedical Engineering, **2008**
Texas A&M University, College Station, TX

B.E. in Electronics & Instrumentation Engineering, **2003**
University of Madras, India

Work Experience

Post-doctoral Fellow **2015-2016**
Pfizer, Inc., Cambridge, MA

Post-doctoral Fellow **2011-**
Computer Aided-Drug Design Center, University of Maryland Baltimore

Graduate Research Assistant **2005-2011**
Molecular Biomechanics Lab, Texas A&M University, College Station, TX

Software Engineer **2004-2005**
Communications & Embedded Systems, Larsen & Toubro Ltd, Mumbai, India.

Research Intern **2002-2003**
Vehicle Assembly & Static Test Facility, Indian Space Research Organization, Sriharikota, India.

Research Summary

Method Development

- DIRECT-ID: Developed a covariance-matrix based method that automatically identifies structural features with significant differences in conformational dynamics.
- GCMC/MD: Developed a Grand-Canonical Monte-Carlo (GCMC) and Molecular Dynamics (MD) based simulation strategy to drive ligand sampling of proteins in condensed phase. GCMC code was written in C++ and parallelized using *OpenMP*.
- SILCS: Involved in development of SILCS suite of programs, used in rational ligand design and optimization.
- ForceMap: Developed a computational ligand efficacy calculation method using forces generated in a macromolecule through an MD simulation.
- Developed and implemented *normal modes*, *principle component analysis* (PCA) and *geometric triad* based biofilament stiffness measurement methods.
- Developed and implemented a wavelets based algorithm for analyzing signals from non-destructive testing of rocket booster casings.

Drug Design

- Disease: Asthma; Target: β_2-adrenergic G-protein Coupled Receptors (GPCRs). Agonists were identified using virtual screening and docking studies guided by SILCS-GCMC/MD and ForceMaps. *Tanimoto coefficient* based chemical clustering was performed using candidates' MACC fingerprints.

- Disease: Traumatic Brain Injury (TBI); Target: metabotropic Glutamate Receptors (mGluR5). Acyl-2-amino benzimidazoles and cyclopropyl based Positive Allosteric Modulators (PAMs) developed using SILCS-GCMC/MD.

Key Findings

- Identified structural elements involved in the directed and cooperative motility of kinesin-14 Ncd motor protein.
- Identified mechanical inhomogeneity in tropomyosin coiled-coil that could modulate its function.
- Identified conformational dependent ligand functional group requirement changes in GPCR binding pockets.

Publications

- **SK Lakkaraju**, JA Lemkul, J Huang, AD MacKerell, "An Automated Method to Identify and Quantify Conformational Variations - Application to β2-adrenergic GPCR", **J Comp. Chem. 2015**; 37(4):416.
- **SK Lakkaraju**, H Mbatia, M Hanscom, Z Zhao, J Wu, B Stoica, AD MacKerell, Alan I Faden, F Xue, "Cyclopropyl-containing positive allosteric modulators of metabotropic glutamate receptor subtype 5", **Bioorg. Med. Chem. Lett.**, **2015**; 25(11): 2275.
- X He, **SK Lakkaraju**, M Hanscom, Z Zhao, J Wu, B Stoica, AD MacKerell, Alan I Faden, F Xue, "Acyl-2-aminobenzimidazoles: A novel class of neuroprotective agents targeting mGluR5", **Bioorg. Med. Chem.**, **2015**; 23(9): 2211.
- **SK Lakkaraju**, W Yu, EP Raman, AV Hershfeld, L Fang, DA Deshpande, AD MacKerell, "Mapping Functional Group Free Energy Patterns at Protein Occluded Sites: Nuclear Receptors and G-protein Coupled Receptors", **J Chem. Inf. Model.**, **2015**; 55(3):700.
- W Yu, **SK Lakkaraju**, EP Raman, L Fang, AD MacKerell, "Pharmacophore modeling using Site-Identification by Ligand Competitive Saturation with multiple probe molecules", **J Chem. Inf. Model., 2015**; 55(2):407. *(Cover story)*
- **SK Lakkaraju**, EP Raman, W Yu, AD MacKerell, " Sampling of organic solutes in Aqueous and Heterogeneous environments using oscillating chemical potentials in Grand Canonical-like Monte Carlo-Molecular Dynamics Simulations", **J Chem. Theory Comput.**, **2014**; 10(6):2281. *(Cover story)*
- W Yu, **SK Lakkaraju**, EP Raman, AD MacKerell, "Site-Identification by Ligand Competitive Saturation (SILCS) assisted pharmacophore modeling", **J Comput Aid Mol Des.**, **2014**; 28(5):491.
- EP Raman, W Yu, **SK Lakkaraju**, AD MacKerell, "Inclusion of multiple fragment types in Site Identification by Ligand Competitive Saturation (SILCS) approach", **J Chem Inf. Model.**, **2013**; 53(12):3384.
- **SK Lakkaraju**, F Xue, AI Faden, AD MacKerell, "Estimation of ligand efficacies of metabotropic glutamate receptors from conformational forces obtained from molecular dynamics simulations", **J Chem. Inf. Model.**, **2013**; 53(6):1337.
- **SK Lakkaraju**, W Hwang, "Hysteresis-based mechanism for the directed motility of the Ncd motor", **Biophys. J.**, **2011**; 101:1105.
- **SK Lakkaraju**, W Hwang, "Critical buckling length versus persistence length: What governs a biofilament conformation?", **Phys. Rev. Lett.**, **2009**; 102:118102. (selected for the Virtual Journal of Biophysical Research)
- **SK Lakkaraju**, W Hwang, "Modulation of elasticity in functionally distinct domains of the tropomyosin coiled-coil", **Cell. Mol. Bioeng.**, **2009**; 2:57. (Invited contribution)

Conference Publications

- **SK Lakkaraju**, W Yu, EP Raman, AD MacKerell, "Mapping Functional Group Requirements of Ligands at the Occluded Binding pocket of β2-Adrenergic G-Protein Coupled Receptor using Site-Identification by Ligand Competitive Saturation Simulations", **Biophysical Society**, **2015**. (poster)
- W Yu, EP Raman, **SK Lakkaraju**, Lei Fang, AD MacKerell, "Pharmacophore modeling using Site-Identification by Ligand Competitive Saturation with multiple probe molecules", **Biophysical Society**, **2015**. **(platform)**
- MC Small, **SK Lakkaraju**, EP Raman, RB Andrade, AD MacKerell, "Molecular understanding of the binding of macrolide antibiotics to the Ribosome using Site-Identification by Ligand Competitive Saturation", **Biophysical Society**, **2015**. (poster)
- R Rai, F Xue, AD MacKerell, **SK Lakkaraju**, "Synthesis and Evaluation of Protein Tyrosine Phosphatase inhibitors by targeting a novel allosteric site", **American Chemical Society**, Fall National Meeting, **2014**. (poster)
- AD MacKerell, EP Raman, W Yu, **SK Lakkaraju**, O Guvench, "Site Identification by Ligand Competitive Saturation (SILCS): Mapping fragment binding sites including consideration of protein flexibility and fragment desolvation using explicit solvent representation", **American Chemical Society**, Spring National Meeting, **2013**. **(platform)**
- **SK Lakkaraju**, Ashley R McDonald, AD MacKerell, "Quantum Mechanical/Molecular Mechanical simulations: An efficient strategy to calculate vibrational stark shift", **American Chemical Society**, Fall National Meeting, **2012**. (poster)
- **SK Lakkaraju**, Ashley R McDonald, AD MacKerell, "Vibrational Stark Effect calculations using quantum mechanical/molecular mechanical simulations", **American Chemical Society**, Mid-Atlantic Regional Meeting, **2012**. (poster)
- **SK Lakkaraju**, W Hwang, "Mechanical coupling of the motor protein Ncd in the microtubule minus-end directed motion", **Biomedical Engineering Society** Annual Meeting, 2011. **(platform)**
- **SK Lakkaraju**, W Hwang, "Atomistic basis for the directionality and cooperativity of the Ncd motor", The 1st **KIAS Conference** on Subcellular Dynamics: Emergent behaviors of the mechanical elements in the cell, **2011**. **(platform)**
- **SK Lakkaraju**, W Hwang, "Role of non-specific attractions in conformational behavior of biofilaments: A case study of alpha-helices and coiled-coils", 6th **World Congress on Biomechanics**, **2010**. **(platform)**
- **SK Lakkaraju**, W Hwang, "Possible intermediate states in the microtubule minus-end directed movement of the Ncd stalk", **Biophysical Society**, **2010**. **(platform)**
- **SK Lakkaraju**, W Hwang,"Transition Pathway of the minus end directed movement of Kinesin-14 Ncd", **ASME** First Congress of Nanotechnology in Medicine and Biology, **2010**. **(platform)**
- **SK Lakkaraju**, W Hwang, "Length and sequence dependence of elasticity of α-helices and coiled-coils", **ASME**, Summer BioConference, **2009**. (poster)
- **SK Lakkaraju**, W Hwang, "Regional variations in flexibilities limit continuum rod description of long coiled-coils" **Biophysical Society**, **2009**. (poster)
- **SK Lakkaraju**, W Hwang, "Limits in application of linear elasticity theory in characterization of α-helices and filamentous proteins", **Biophysical Society**, **2008**. (poster)

- **SK Lakkaraju**, W Hwang, "Breakdown of linear elasticity in α-helices", **Society of Engineering Science**, **2007**. **(platform)**
- **SK Lakkaraju**, W Hwang, "Molecular mechanics of α-helices", **Cardiovascular Research Institute**, **2006**. **(poster, 3rd prize)**
- **SK Lakkaraju**, Anant Joshi, "Supporting mobility using CAMEL-Location Based Services, a case study", Avionics and Communication Engineering, **2004**. **(platform)**
- **SK Lakkaraju**, R Gopalakrishnan, S V S Rao, "Acoustic Emission Analysis-A Wavelet Transport Approach", Asia Pacific Conference of Non-Destructive Testing, **2003**. **(platform)**

Patents

- US Patent application #: **62/109,141**; **SK Lakkaraju**, DA Deshpande, AD MacKerell, "Novel Agonists for the Beta2-Adrenergic G-Protein Coupled Receptor".
- US Patent application #: **61/932,890**; **SK Lakkaraju**, EP Raman, AD MacKerell, "Methods and Systems for Organic Solute Sampling of Aqueous and Heterogeneous Environments".

Invited Lectures/Speaking Engagements

- "Site Identification by Ligand Competitive Saturation (SILCS) applied to G-protein Coupled Receptors (GPCR)", Computer Aided Drug Design Day, Univ of Maryland, Baltimore, 2016.
- "Lead Optimization through Rapid Estimation of Relative Binding Affinities: Multiple Gene Family Evaluations", Science in the Age of Experience, BioVia User Group Meeting, Boston, MA, 2016.
- "VMD Workshop in Drug-Design", Lady Doak College, Madurai, India, 2016.
- "Mapping functional group requirements, efficacies and ligand-modulated conformational variations in GPCRs", Biotechnology Seminar Series, Indian Institute of Technology, Hyderabad, India, 2016.
- "Drug design challenges for GPCRs", Molecular Modeling Seminar Series, Indian Institute of Chemical Technology, Hyderabad, India, 2016.
- "Free energy patterns in binding pockets, ligand efficacies and mechanics from conformational dynamics", Applied Mechanics Seminar Series, Indian Institute of Technology-Madras, Chennai, India, 2016.
- "Novel computational methodologies in drug design for GPCRs", Center for Computational Natural Sciences and Bioinformatics Seminar, International Institute of Information Technology, Hyderabad, India, 2015.
- "Mapping functional group requirements and ligand modulated conformational variations in β_2-adrenergenic GPCR", Conference on Trend Setting Innovations in Pharmaceutical Industry, Jawaharlal Nehru Technological University, Hyderabad, India, 2015.
- "Elasticity of α-helices and coiled-coils: Role in tropomyosin and stalk of kinesin-14 Ncd", NSF Seminar Series, Material Research Science & Engineering Center, Brandeis University, Waltham, MS, 2010.
- "Mechanics of Tropomyosin in muscle physiology", Molecular Modeling Seminar Series, Indian Institute of Chemical Technology, Hyderabad, India, 2010.

Professional Memberships & Activities

- Reviewer: PLOS One, PLOS Computational Biology; Proteins: Structure, Function & Bioinformatics; Molecular Informatics; Journal of Molecular Graphics and Modeling; Drug Design Development and Therapy.
- Memberships: American Chemical Society (ACS), Biophysical Society, Biomedical Engineering Honors society- Alpha Eta Mu Beta (AEMB), Society for Engineering Science (SES).
- Activities: Chaired Material Sciences subgroup sessions in the ACS National Meeting, Philadelphia, Aug, 2012.

Skills

Languages: C, C++, VC++, MFC, Java, Fortran.

Scripting: shell, awk, perl, python, VB, LateX.

Numerical, plotting & visualization: MATLAB, octave, Armadillo, LAPACK, xmgrace, gnuplot, matplotlib, VMD, pymol, gOpenMol, Molden.

Molecular dynamics: CHARMM, GROMACS, NAMD, ACEMD, Desmond.

QM: Gaussian, QChem, NWChem, GAMESS-UK.

Docking/Virtual Screening: Glide, AUTODOCK-Vina, MOE, Situs.

Project design & data handling: Git, Rational rose, VSS, CVS.

DBMS: MySQL.

OS: Linux, UNIX, Solaris 5.8, Windows.

References

Alexander D MacKerell, Jr.	**Wonmuk Hwang**	**Deepak Deshpande**
Grollman-Glick Professor of Pharmaceutical Sciences,	Associate Professor, Biomedical Engineering,	Associate Professor, Department of Medicine,
20 Penn St, Rm 633, University of Maryland, Baltimore, MD 21201	5060 ETB, Texas A&M University, College Station, TX 77843	1020 Locust St, Rm 543B Thomas Jefferson University, Philadelphia, PA 19107
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