PRATUL K. AGARWAL http://www.agarwal-lab.org/

Summary

Over 15 years of experience as independent researcher (PI) resulting in 3 patents and >50 publications. Currently have 3 active grants as PI (NIH R01 and 2 industry grants), with >$4 million received in funding over career. On Editorial Board of 3 international journals. Mentored several young staff scientists and post-docs.

Areas of Expertise/Interest

- Protein structure, dynamics and function; Enzyme dynamics
- Structural systems biology; Allosteric modulator discovery
- Large and multi-variate data analysis, computational infrastructure, heterogeneous computing
- Theoretical and computational modeling of bio-molecules; Multi-scale methods
- High performance computing; Parallel computing for scientific applications

Education

B. Tech./M.Tech., Biochemical Engineering and Biotechnology (1995/97)
Indian Institute of Technology-Delhi, New Delhi, India (GPA: 9.05/10.00)
Thesis Title: Computational studies of protein-DNA interactions in m^5C-methyltransferase M. *Hha*I

Ph.D., Chemistry (2002)
University of Notre Dame, Notre Dame, IN (1997-2000), and
The Pennsylvania State University, University Park, PA (2000-2002) (GPA: 4.00/4.00)
Thesis Title: Quantum Effects and Protein Motion in Enzymatic Catalysis
Thesis Advisor: Prof. Sharon Hammes-Schiffer (*Member, National Academy of Sciences USA*)

Current Positions

Senior R&D Staff Scientist (Jan 2012 – present)
Computer Science and Mathematics Division, Computational Biology Institute
Oak Ridge National Laboratory (ORNL), Oak Ridge, Tennessee

Joint Faculty (July 2011 – present)
Department of Biochemistry, Cellular and Molecular Biology (BCMB)
University of Tennessee, Knoxville (UTK), Knoxville, Tennessee

Past Positions

Computational Biology Acting Group Leader (Oct 2012 – Feb 2014)
Computer Science and Mathematics Division, ORNL

Adjunct Faculty (Jan 2007 – Jun 2011)
Department of Biochemistry, Cellular and Molecular Biology, UTK

R&D Staff Scientist (Jan 2008 – Dec 2011)
Computational Biology Institute & Computer Science and Mathematics Division, ORNL

Associate R&D Staff Scientist (Apr 2005 – Dec 2007)
Computational Biology Institute & Computer Science and Mathematics Division, ORNL

Post-doctoral Research Associate (May 2002 – Apr 2005)
Computer Science and Mathematics Division, ORNL

Professional Services

Currently being vetted for Editorial Board, *Journal of Biological Chemistry*
Academic Editor, *PLoS ONE*, 2012–present
Editorial Board Member, *Microbial Cell Factories*, 2006–present
Lead, High Performance Computing (HPC) Working Group, NIH/IMAG and MSM Consortium, 2012–2014
Graduate Student Thesis Committees:
Genome Science and Technology Program, University of Tennessee, Knoxville
Biochemistry, Cellular and Molecular Biology Department, University of Tennessee, Knoxville

Panelist and Proposal Reviewer:

NIH (including Study Section MSFD *ad-hoc*, Study Sections on Biological Data, BD2K centers, and SBIR/STTR), NSF (Panel for OCI/Track 2 supercomputer), EPA, DTRA, Petroleum Research Fund, Swiss National Supercomputing Centre, Swiss High Performance and High Productivity Computing (HP2C), Italian Ministry of Health, National Science Centre Poland

Manuscript Reviewer (including *Journals* and Conferences):

Amino Acids, Biochemical Engineering Journal, *Biochemistry*, *Biomacromolecules, Biophysical Journal, Chemical Physics Letters*, *International Journal of Biological Macromolecules, Journal of the American Chemical Society, The Journal of Biochemistry, Journal of Chemical Information and Modeling, Journal of Chemical Physics, Journal of Chemical Theory and Computation*, *Journal of Parallel and Distributed Computing, Journal of Physical Chemistry*, *Microbial Cell Factories*, *The Journal of Physical Chemistry Letters, PLoS Computational Biology*, *PLoS ONE*, *Proteins (Proteins: Structure, Function and Bioinformatics), Protein Science*, *Spectroscopy Letters*, *Systems Biology and Medicine*
HiBB (High Performance Bioinformatics and Biomedicine)
HiCOMB (International Workshop on High Performance Computational Biology)
HPCS (International Conference on High Performance Computing and Simulation)

Honors and Awards

- Research *"Protein Dynamics and Function"* featured in US President's Information Technology Advisory Committee's (PITAC) Report to the President (George W. Bush), "Computational Sciences: Ensuring America's Competitiveness" (2005) [See #1 in Reports below.]
- Research Featured on cover of Journal *IEEE Computer* (2007) [#15 in Publications below.]
- Research Featured on cover of *Journal of Physical Chemistry B* (2009) [#23 in Publications below.]
- Outstanding Paper Award at the *International Conference on High Performance Computing and Simulation (HPCS) 2010, Caen, France.* (2010) [#26 in Publications below.]
- Key Contributor Award, UT-Battelle Partnerships Awards (2010)
- Research Featured on cover of *Journal of Physical Chemistry B* (2011) [#30 in Publications below.]
- Distinguished Contributor Award (June 2011), Computing & Computational Science Directorate, ORNL
- Research/Image featured on the cover of *PLoS Biology* (2011) [#34 in Publications below.]
- ORNL Press Release (Sept. 2011) *ORNL invention unravels mystery of protein folding,* http://www.ornl.gov/ornlhome/print/press_release_print.cfm?ReleaseNumber=mr20110914-00
- ORNL Press Release (Nov. 2011) *ORNL fundamental discovery casts enzymes in new light,* http://www.ornl.gov/ornlhome/print/press_release_print.cfm?ReleaseNumber=mr20111108-00
- ORNL Press Release (Apr. 2012) *ORNL process improves catalytic rate of enzymes by 3,000 percent* http://www.ornl.gov/ornlhome/print/press_release_print.cfm?ReleaseNumber=mr20120417-00
- Best Poster Award, GRC Medicinal Chemistry 2012

Lead Software Developer

1. VigyaanCD, bio/chemical software workbench (>250,000 downloads) http://www.vigyaancd.org/
2. GPU-LAMMPS for biomolecular simulations

Teaching Experience

- **BCMB 530** (Experimental Design and Analysis) Spring 2015, University of Tennessee, Knoxville *Full graduate level course co-taught with Dr. Liz Howell.* Fundamentals of hypothesis development, experimental design, data analysis, report writing, and grant writing and peer-review process.
- **BCMB 511** (Advanced Protein Chemistry and Cellular Biology) Fall 2014-Fall 2016, University of Tennessee, Knoxville**.** Guest lectures on Enzyme kinetics and Enzyme dynamics.

Graduate (Ph.D.) Students Advised

- **Dr. Arvind Ramanathan**, Carnegie Mellon University (with Dr. Chris Langmead, graduated 05/2010)
- **Khushboo Bafna**, University of Tennessee, Current student (started August 2014)
- **Shantanu Shukla** University of Tennessee, Current student (started August 2015), with Dr. Dean Myles.

Past Group Members at ORNL

- **Dr. Scott Hampton** (Post-doc, 2006-2010). Currently Research Faculty at University of Notre Dame.
- **Dave Rogers** (Masters student, 2007)
- **Phillip Martin** (Masters student, 2007)
- **Dr. Jose Borreguero** (Post-doc, 2008-2011). Currently Staff Scientist at ORNL
- **Dr. Ganesh Kamath** (Post-doc, 2009-2011). Currently Post-doc at University of Missouri, Columbia.
- **Dr. Arvind Ramanathan** (Post-doc, 2010-2012). Currently Staff Scientist at ORNL
- **Dr. Chitra Narayanan** (Visiting Post-doc, 2014). Currently Post-doc at University of Quebec.

Graduate Student Thesis Committee served

- Brian Erickson (Genome Science and Technology Program, UTK)
- Zixing Wang (Genome Science and Technology Program, UTK)
- Nicole Edwards (Genome Science and Technology Program, UTK)
- Chandrasegaran Narasimhan (Genome Science and Technology Program, UTK)
- Benjamin Lindner (Genome Science and Technology Program, UTK)
- Roland Schulz (Genome Science and Technology Program, UTK)
- Sarah Wisecarver (Biochemistry, Cellular and Molecular Biology Dept., UTK)
- Timkhite-Kulu Berhane (Biochemistry, Cellular and Molecular Biology Dept., UTK)
- Arvind Ramanathan (CMU-UPitt PhD Program in Computational Biology, Carnegie Mellon University)
- Deepika Nambiar (Biochemistry, Cellular and Molecular Biology Dept., UTK)
- Gabriel Fuente Gomez (Biochemistry, Cellular and Molecular Biology Dept., UTK)

Funding Profile

Current

Agency:	National Institutes of Health (NIH), NIGMS
Title:	Conformational sub-states in enzyme catalysis: Applications to ribonuclease.
Role:	PI (Multi-PI R01)
Amount:	$ 2,576,912 ($ 953,870 to P.K.A.)
Period:	04/01/2014 - 03/31/2019
Description:	Development and application of multi-scale modeling framework and strategies for enabling identification and characterization of rare intermediates and conformational transitions associated with protein function. Applications to ribonuclease A.

Agency:	BASF Enzymes LLC
Title:	Investigating novel approaches to enzyme engineering
Role, Amount:	PI, $250,000 (actual amount being negotiated)
Period:	10/01/2016 - 09/30/2019
Description:	Using our pioneering computational approaches to develop new solutions for improving the catalytic activity and stability of modified enzymes. This activity is funded through the BASF's research alliance activity with UC Berkeley (CARA).

Agency:	Amano Enzymes LLC
Title:	Enzyme activity improvement
Role, Amount:	PI, $100,000 (actual amount being negotiated)
Period:	10/01/2016 - 09/30/2018
Description:	Using our pioneering computational approaches to develop new solutions for improving the catalytic activity and stability of modified enzymes.

Pending

Agency: Defense Threat Reduction Agency (DTRA)
Title: Enhancing Bioscavenger Catalysis and Efficacy
Role: Co-PI (PI: Carey Pope, Oklahoma State University)
Amount: $ 2.6 million ($ 800,000 to P.K.A.)
Period: 04/01/2017 - 03/31/2021
Description: Using our enzyme engineering approach to develop engineered human butyryl-cholinesterase G117H that shows enhanced activity against organo-phosphates. Long term goal is to develop treatment against nerve gas agents.

Agency: National Science Foundation (NSF)
Title: Hyper-catalytic Enzyme Engineering Approach for Renewable Energy
Role: PI
Amount: $466,123
Period: 04/01/2017 - 03/31/2020
Description: Applying computational approaches to investigate cellulase and RuBisCO enzymes to develop biocatalyst engineering approaches for application in renewable energy.

Completed

Agency: Battelle Memorial Institute
Title: A Novel Approach to Enzyme Engineering
Role: PI
Amount: $160,000
Period: 03/01/2007 – 06/30/2009
Description: Developing technology for a novel approach for enzyme engineering.

Agency: Department of Energy (DOE), Advanced Scientific Computing Research (ASCR)
Title: Investigation of Cellulose Degrading Protein Machines:
Enabling Technologies for Petascale Biomolecular Simulations
Role: PI
Amount: $819,623
Period: 01/01/2007 - 12/31/2009
Description: Development of high performance computing software and simulation strategies for large biomolecular complexes.

Agency: Laboratory Directed Research and Development (LDRD), ORNL
(selected after Peer-Review and Oral Interview, Success Rate about 20%)
Title: Mapping the Protein Structure, Dynamics and Function Landscape
Role: PI
Amount: $391,000
Period: 10/01/2007 - 09/30/2010
Description: Joint computational-neutron scattering to explore protein structure, dynamics and function (with Dr. Dean Myles and Dr. Ken Herwig).

Agency:	National Institute of Health, NIGMS
Title:	Accelerating Biomolecular Simulations on Reconfigurable Computing Hardware (R21GM083946)
Role:	PI
Amount:	$409,447
Period:	08/15/2008 - 06/30/2011 (with 1 year no cost extension)
Description:	Biomolecular simulations software development for graphical processing units (GPUs) and Field-Programmable Gate Arrays (FPGAs).

Agency:	Laboratory Directed Research and Development (LDRD), ORNL
Title:	High Throughput Computational Screening Approach for Systems Medicine *(selected after Peer-Review and Oral Interview, Success Rate about 20%)*
Role:	PI
Amount:	$610,000
Period:	10/01/2008 - 09/30/2011
Description:	Developing high throughput computational approach for allosteric site prediction and chemical compound library screening against the discovered targets.

Agency:	Department of Energy, Office of Science
Title:	Improvement of Fault Tolerance in Systems (CIFTS)
Role:	Investigator (PI: Pete Beckman, Argonne National Laboratory)
Amount	$10.5 million ($2,750,000 to ORNL)
Period:	10/01/2006 – 09/30/2012
Description:	The major goals of this project are to develop fault tolerant software for next generation HPC architecture.

Agency:	ORNL/DOE (National Center for Computational Sciences)
Title:	Application porting and optimization for Titan supercomputer
Role:	Investigator
Amount:	$350,000 to P.K.A.
Period:	02/01/2011 - 09/30/2012
Description:	Characterizing and developing strategies to overcome the impact of OS jitter on science applications on the Cray XK7 supercomputer.

Agency:	ORNL Technology Transfer Program
Title:	Maturation funds for optimizing enzyme engineering approach
Role:	PI
Amount:	$60,000
Period:	02/21/2012 - 12/31/2012
Description:	Optimization of the enzyme engineering approach through conformational modulation.

Peer-reviewed Publications (* denotes corresponding author)
(Please click on the icon to follow external link to the article)

1. **Agarwal P.K.**; Bhattacharya S.K. "Construction of a multi RE module: Exploitation of mechano-chemistry of restriction endonucleases", *Biotechnology & Bioengineering* (1999) **65**, 233-239.
2. **Agarwal, P.K.**; Webb, S.P.; Hammes-Schiffer, S. "Computational studies of the mechanism for proton and hydride transfer in liver alcohol dehydrogenase", *J. Am. Chem. Soc.* (2000) **122**, 4803-4812.
3. Webb, S.P.; **Agarwal, P.K.**; Hammes-Schiffer, S. "Combining electronic structure methods with calculation of hydrogen vibrational wavefunctions: application to hydride transfer catalyzed by liver alcohol dehydrogenase", *J. Phys. Chem. B* (2000) **104**, 8884-8894.
4. Billeter, S.R.; Webb, S.P.; Iordanov, T.; **Agarwal, P.K.**; Hammes-Schiffer, S. "Hybrid approach for including electronic and nuclear quantum effects in molecular dynamics simulations of hydrogen transfer reactions in enzymes", *J. Chem. Phys.* (2001) **114**, 6925-6936.
5. Billeter, S.R.; Webb, S.P.; **Agarwal, P.K.**; Iordanov, T.; Hammes-Schiffer, S. "Hydride transfer in liver alcohol dehydrogenase: quantum dynamics, kinetic isotope effects, and the role of enzyme motion", *J. Am. Chem. Soc.* (2001) **123**, 11262-11272.
6. **Agarwal, P.K.**; Billeter, S.R.; Rajagopalan, P.T.R.; Benkovic, S.J.; Hammes-Schiffer, S. "Network of coupled promoting motions in enzyme catalysis", *Proc. Natl. Acad. Sci. USA* (2002) **99**, 2794-2799.
7. **Agarwal, P.K.**; Billeter, S.R.; Hammes-Schiffer, S. "Nuclear quantum effects and enzyme dynamics in dihydrofolate reductase catalysis", *J. Phys. Chem. B* (2002) **106**, 3283-3293.
8. Watney, J. B.; **Agarwal, P. K.**; Hammes-Schiffer, S. "Effect of mutation on enzyme motion in dihydrofolate reductase", *J. Am. Chem. Soc.* (2003) **125**, 3745-3750.
9. **Agarwal, P. K.*** "Computational studies of the mechanism of cis/trans isomerization in HIV-1 catalyzed by cyclophilin A", *Proteins: Struct. Funct. Bioinformatics* (2004) **56**, 449-463.
10. **Agarwal, P. K.*** Geist A.; Gorin A. "Protein dynamics and enzymatic catalysis: Investigating the peptidyl-prolyl cis-trans isomerization activity of cyclophilin A", *Biochemistry* (2004) **43**, 10605-18.
11. **Agarwal, P. K.*** "Role of protein dynamics in reaction rate enhancement by enzymes", *J. Am. Chem. Soc.* (2005) **127**, 15248-15246.
12. **Agarwal, P. K.*** "Enzymes: An integrated view of structure, dynamics and function", *Invited Review Article: Microbial Cell Factories.* (2006) **5**:2.
13. Alam, S. R.*; **Agarwal, P. K.*;** Vetter, J. S.; Geist A. "Performance characterization of bio-molecular simulations using molecular dynamics", *Proceedings of the eleventh ACM SIGPLAN symposium on Principles and practice of parallel programming*. (2006) 59-68.
14. **Agarwal, P. K.*;** Alam, S. R. "Biomolecular simulations on Petascale: Promises and challenges", *J. Physics Conference Series* (2006) **46**, 327-333.
15. Alam, S. R.; **Agarwal, P. K.;** Smith, M. C.; Vetter, J. S.; Calliga, D. "Using FPGA devices to accelerate biomolecular simulations", Cover Feature, *IEEE Computers* (2007) **40**, 66-73.
16. **Agarwal, P. K**.*; Alam, S. R.; Geist A. "Simulating Biomolecules on Petascale Supercomputers". Invited book chapter. *Petascale Computing: Algorithms and Applications*, Edited by David A. Bader, CRC Press (2007).
17. Alam, S. R.; **Agarwal, P. K.** "On the path to enable multi-scale biomolecular simulations on PetaFLOPS supercomputer with multi-core processors", *Proceedings of the IEEE International Workshop on High Performance Computational Biology (HiCOMB 2007), in conjunction with IPDPS*, (2007), 1-8
18. Alam, S. R.; **Agarwal, P. K.;** Vetter, J. S.; Smith, M. C. "Throughput improvement of molecular dynamics simulations using reconfigurable computing", *Scalable Computing: Practice and Experience* (2007) **8(4)**, 395-410.
19. Alam, S. R.; **Agarwal, P. K.;** Kuehn, J. A. "Performance evaluation of a scalable molecular dynamics simulation framework on a massively-parallel system", *In Proceedings of the 7th IEEE International Conference on Bioinformatics and Bioengineering, BIBE,* (2007), 1459-1466.
20. Alam, S. R.; **Agarwal, P. K.;** Vetter, J. S. "Performance characteristics of biomolecular simulations on high-end systems with multi-core processors", *Parallel Computing* (2008) **34,** 640-651.

21. Alam, S. R.; **Agarwal, P. K.;** Hampton, S. S.; Ong H. "Experimental evaluation of molecular dynamics simulations on multi-core systems", *Proceedings of the annual IEEE International Conference on High Performance Computing (HiPC)* (2008) 1-11.
22. Alam, S. R.; **Agarwal, P. K.;** Hampton, S. S.; Ong. H.; Vetter, J. S. "Impact of multicores on large-scale molecular dynamics simulations", *Proceedings of the IEEE International Symposium on Parallel and Distributed Processing (IPDPS)* (2008) 1-7.
23. Ramanathan, A.; **Agarwal, P. K.*** "Computational identification of slow conformational fluctuations in proteins", Journal Cover, *J. Phys. Chem. B* (2009) **113 (52)**, 16669-16680.
24. Ramanathan, A.; **Agarwal, P. K.;** Kurnikova, M.; Langmead, C.J. "An online approach for mining collective behaviors from molecular dynamics simulations", *J. Comput. Biol.* (2010) **17(3)**, 309-324.
25. Nallamuthu, A.; Smith, M. C.; Hampton, S. S.; **Agarwal, P. K.;** Alam, S. R. "Energy efficient biomolecular simulations with FPGA-based reconfigurable computing", *Proceedings of the 7th ACM international conference on Computing frontiers* (2010) 83-84.
26. Hampton, S. S.; **Agarwal, P. K.*;** Alam, S. R.; Crozier, P. S. "Towards microsecond biological molecular dynamics simulations on hybrid processors", Outstanding Paper Award, *Proceedings of International Conference on High Performance Computing and Simulation* (2010) 98-107.
27. Hampton, S. S.; Alam, S. R.; Crozier, P. S.; **Agarwal, P. K.*** "Optimal utilization of heterogeneous resources for biomolecular simulations" *In the Proceedings of International Conference for High Performance Computing, Networking, Storage and Analysis (SC' 10), New Orleans, LA* (2010). 1-11.
28. Kamath, G.; Howell, E. E.; **Agarwal, P. K.*** "The tail wagging the dog: Insights into catalysis in R67 dihydrofolate reductase", *Biochemistry* (2010) **49**, 9078-9088.
29. Ramanathan, A.; Savol, A.; Langmead, C. J.; **Agarwal, P. K.*;** Chennubhotla, C. S.* "Discovering conformational sub-states relevant to protein function", *PLoS ONE* (2011) **6(1):** e15827.
30. Borreguero, J. M.; He, J.; Meilleur, F.; Weiss, K.; Brown, C. M.; Myles, D. A. A.; Herwig, K. W.; **Agarwal, P. K.** "Redox-promoting protein motions in rubredoxin", Journal Cover. *J. Phys. Chem. B.* (2011) **115 (28)**, 8925-8936.
31. Park, B. H.; Naughton, T. J.; **Agarwal, P. K.;** Bernholdt, D. E.; Geist, A.; Tippens., J. L. "Realization of user level fault tolerant policy management through a holistic approach for fault correlation", *In the Proceedings of IEEE International Symposium on Policies for Distributed Systems and Networks (POLICY 2011)* (2011).
32. Savol, A. J.; Burger, V. M.; **Agarwal, P. K.;** Ramanathan, A. R.; Chennubhotla, C. S. "QAARM: Quasi-anharmonic auto-regressive model reveals molecular recognition pathways in ubiquitin", *Bioinformatics* (2011) **27(13)**, i52-i60.
33. Burger, V. M.; Ramanathan, A. R.; Savol, A. J.; Stanley, C.; **Agarwal, P. K.;** Chennubhotla, C. S. "Quasi-anharmonic analysis reveals intermediate states in the nuclear co-activator receptor binding domain ensemble", *Pacific Symposium on Biocomputing 2012* (2012).
34. Ramanathan, A.; **Agarwal, P. K.*** "Evolutionarily conserved linkage between enzyme fold, flexibility, and catalysis", Featured Image *PLoS Biology* (2011), **9(11)**, e1001193. (Impact Factor: 11.771)
35. **Agarwal, P. K.***; Schultz, C.; Kalivreteno, A.; Ghosh, B.; Sheldon, B. "Engineering a hyper-catalytic enzyme by photo-activated conformation modulation", *J. Phys. Chem. Lett.* (2012), **3**, 1142-1146. (Journal Impact Factor: 6.687)
36. Heredia, A.; Meunier, V.; Bdikin, I. K.; Gracio, J.; Balke, N.; Jesse, S.; Tselev, A.; **Agarwal, P. K.**; Sumpter, B. G.; Kalinin, S. V.; Kholkin, A. L. "Nanoscale ferroelectricity in crystalline gamma-glycine", *Advanced Functional Materials* (2012) **22**, 2996-3003. (Journal Impact Factor: 10.439)
37. Ramanathan, A.; Savol, A. J.; **Agarwal, P. K.**; Chennubhotla, C. S. "Event detection and sub-state discovery from bio-molecular simulations using higher-order statistics: application to enzyme adynelate kinase", *Proteins: Structure, Function and Bioinformatics,* (2012) **80 (11),** 2536.2551.
38. **Agarwal, P. K.***; Hampton S. S.; Poznanovic, J.; Ramanathan, A.; Alam, S. R; Crozier, P. S. "Performance modeling of microsecond scale biological molecular dynamics simulations on heterogeneous architectures", *Concurrency and Computation: Practice and Experience* (2012) **25 (10),** 1356-75.

39. Ramanathan, A.; Savol, A.; Burger, V.; Quinn S.; **Agarwal, P. K.**; Chennubhotla, C. "Statistical inference for big data problems in molecular biophysics", *In Proceedings of Big Learning 2012*
40. **Agarwal, P. K.*** "Role of protein motions in function", *Physics of Life Reviews* (2013) **10 (1)**, 35-36.
41. Ramanathan, A.; Savol, A.; Burger, V.; Chennubhotla, C. S.*; **Agarwal, P. K.*** "Protein conformational populations and functionally relevant sub-states", *Accounts of Chemical Research* (2014) **47 (1)**, 149-156. (Journal Impact Factor: 24.348)
42. Gange, D.; French, R. L.; Narayanan, C.; Simonovi, M.; **Agarwal, P. K.**; Doucet, N., "Perturbation of the conformational dynamics of an active-site loop alters enzyme activity", (2015), *Structure,* **23 (12)**, 2256-2266.
43. Duff Jr., M. R.; Chopra, S.; Strader, B. D.; **Agarwal, P. K.**; Howell, E. E., "Tales of Dihydrofolate Binding to R67 Dihydrofolate Reductase", *Biochemistry* (2016), **55**, 133-145.
44. **Agarwal, P. K.***; Doucet, N.; Chennubhotla, C. S.; Ramanathan, A.; Narayanan, C., "Conformational sub-states and populations in enzyme catalysis" (2016)**,** Invited article, *Methods in Enzymology***, 578**, 273-297.
45. Gagné, D.; Nhung, T. N.; Narayanan, C.; Roux, L.; Brunzelle, J. S.; Couture, J.-F.; **Agarwal, P. K.**; Doucet, N. "Ligand Binding Induces Enhanced Conformational Exchange in Xylanase B2 from *Streptomyces lividans*", *Biochemistry* (2016), **55**, 4184-4196.
46. Bhojane, P.; Duff Jr., M. R.; Bafna, K.; Rimmer, G.; **Agarwal, P. K.**; Howell, E. E., "Aspects of Weak Interaction between Folate and Glycine Betaine" *Biochemistry* (2016)*,* **55**, 6282-6294.
47. O'Dell, W.B.; **Agarwal, P. K;** Meilleur, F. "Oxygen activation at the active site of a fungal lytic polysaccharide monooxygenase", *Angewandte Chemie* (2017), **56**, 767-770.
48. Norris, V.; Krylov, S. N.; **Agarwal, P. K.**.; White, G. J., "Synthetic, switchable enzymes", *J. Mol. Microb. Biotech.* (2017), **12**, 117-127.
49. Narayanan, C.; Bafna, K..; Roux, L.D.; **Agarwal, P. K.**; Doucet, N. "Applications of NMR and computational methodologies to study protein dynamics", *Archives of Biochemistry and Biophysics* (2017), In Press.
50. Gagné, D.; Narayanan, C.; Bafna, K..; Charest, L.-A.; **Agarwal, P. K.**; Doucet, N. "Sequence-specific backbone resonance assignments and microsecond timescale molecular dynamics simulation of human eosinophil-derived neurotoxin", *Biomolecular NMR Assignments* (2017). In Press.
51. **Agarwal, P. K.***; Naughton, T. J.; Alam, S. R.; Park, B. H.; Bernholdt, D. E.; Hursey, J. J.; Geist, A. "Application self-health monitoring for extreme-scale resiliency using cooperative fault management", *Concurrency and Computation: Practice and Experience* (2017) In Revision.
52. Duff, M.; Borreguero, J. M.; Cuneo, M.; Ramanathan, A.; He, J.; Kamath, G.; Chennubhotla, C.; Meilleur, F.; Howell, E. E.; Herwig, K. W.; Myles, D. A. A.; **Agarwal, P. K.*** "Intertwining of solvent and dynamics affects enzyme catalysis", *Nature Communications* (2017), Submitted.
53. **Agarwal, P. K.*** "A biophysical model of enzyme catalysis", Invited Current Topics Article, *Biochemistry* (2017). Submitted.
54. Narayanan, C.; Bernard, D. N.; Bafna, K..; Gagné, D.; Chennubhotla, C.; Doucet, N.*; **Agarwal, P. K.*** "Conservation of dynamics associated with biological function in an enzyme superfamily", *PLoS Computational Biology* (2017), Submitted.
55. Li, L.; Ghimire-Rijal, S.; Lucas S. L.; Stanley, C. B.; Wright, E.; **Agarwal, P. K.**; Myles, D. A. A.; Cuneo, M. "A second allosteric switch in periplasmic binding protein mediated ABC transport", *Biochemistry* (2017), Submitted.

Patents

1. Fast computational methods for mechanism of protein folding and prediction of protein structure from primary sequence, *Pratul K. Agarwal*, US Patent # 7,983,887, Issued 07/19/2011.
2. Identification and Modification of Dynamically Active Protein Residues, *Pratul K. Agarwal*, US Patent # 8,417,461, Issued 04/09/2013.
3. Identification and Modification of Dynamically Active Protein Residues (Divisional), *Pratul K. Agarwal*, US Patent # US 9,195,795, Issued 11/24/2015.

Reports

1. Protein Dynamics and Function: *PITAC Report to the President of United States on Computational Science: Ensuring America's Competitiveness* (June 2005), page 83.
2. Vibrations may be Key to Protein Functions: *DOE Advanced Scientific Computing Research FY 2004* Accomplishment.
3. Evaluation of the SGI Altix 3700 at Oak Ridge National Laboratory.
4. Cray X1 Evaluation Status Report, *Proceedings of the 46th Cray User Group Conference*, Knoxville TN, May 17-20, 2004.

Contributed and Invited Talks

1. **Invited Seminar:** University of Tennessee (Genome Science and Technology program seminar), Knoxville TN, Jan. 18th, 2006, *Enzymes: An integrated view of structure, dynamics and function.*
2. **Invited Seminar:** NIST (Physics Division Seminar) Gaithersburg MD, April 18th, 2006, *Protein Vibrations Promoting Enzyme Catalysis.*
3. University of Minnesota (Supercomputing Institute and Department of Chemistry seminar), Minneapolis MN, May 31st and Jun. 2nd 2006, *Protein Vibrations Promoting Enzyme Catalysis.*
4. **Invited Seminar:** IBM Inc., Rochester MN, Jun 1st 2006, *Next generation simulations in biology.*
5. **Invited Talk:** NanoFocUL workshop, ORNL, Oak Ridge TN, Aug. 29th 2006, *Multi-scale modeling of enzymes.*
6. **Invited Seminar:** Vanderbilt University, (Dept. Chemical Engineering seminar), Nashville, TN, Sep. 4th 2006, *Multi-scale modeling of enzyme catalysis.*
7. Workshop on the Future of BioMolecular Simulations: From Ab Initio to Nano-molecular Machine, Oak Ridge TN, Dec. 11th 2006, *Biomolecular Simulations on Petascale: Promises and challenges.*
8. **Invited Seminar:** University of Cincinnati, Cincinnati, OH, 15th March 2007, *Protein vibrations promote enzyme catalysis: An integrated view of enzyme structure, dynamics and function.*
9. CERMACS 2007 (ACS regional meeting), Covington KY, 23rd May 2007, *Evolution of enzyme fold: Role of protein dynamics in enzyme catalysis.*
10. VII European Symposium of the Protein Society, Stockholm (Sweden), 15th May 2007, *Protein vibrations promote enzyme catalysis: An integrated view of enzyme structure, dynamics and function.*
11. Argonne National Laboratory, Argonne, IL, 30th Aug. 2007, *Towards A Fault Tolerant Molecular Dynamics Application.*
12. **Invited Seminar:** Carnegie Mellon University, Pittsburgh, PA, 17th September, 2007, *Evolutionary linkage between enzyme structure, dynamics and function.*
13. **Invited Seminar:** HPC user's forum, Santa Fe 27th Sept. 2007, *Biomolecular Simulations with HPC: Implications for Bio-ethanol.*
14. **Invited Talk:** DOE BER, Germantown MD, Dec 17th 2007, *Multi-scale Modeling of Enzymes: Implications of low cost ethanol.*
15. **Invited Talk:** Protein Dynamics Workshop, Tarrytown NY, May 2nd 2008, *Evolution of Enzyme Fold: Linking Protein Dynamics and Catalysis.*
16. **Invited Talk:** Workshop in Trend, Technologies and Collaborative Opportunities (WTTC) 2008, Bangkok Thailand, June 9th 2008, *High Performance Simulations in Biology: Implications for Health, Energy and Environment.*
17. **Invited Talk:** Workshop in Trend, Technologies and Collaborative Opportunities (WTTC) 2008, Phuket Thailand, June 11th 2008, *High Performance Simulations in Biology: Implications for Health, Energy and Environment.*
18. 236th Annual Meeting of the American Chemical Society, Philadelphia PA, August 19th 2008, *An Integrated View of Enzyme Structure, Dynamics and Function.*
19. 236th Annual Meeting of the American Chemical Society, Philadelphia PA, August 20th 2008, *Evolution of Enzyme Fold: Linking Protein Dynamics and Catalysis*
20. **Invited Seminar:** St. Jude Children's Research Hospital, Memphis, TN, November 25th, 2008, *Evolution of enzyme fold: Linking protein dynamics and catalysis.*

21. Biophysical Society 53rd Annual Meeting, Boston, MA, March 3rd, 2009, *Evolution of enzyme fold: Linking protein dynamics and catalysis.*
22. ACS 238th National Meeting, Washington, DC, August 17, 2009, *Linking enzyme structure, dynamics, and catalysis.*
23. LAMMPS Users Workshop, Sandia National Laboratories, Albuquerque, NM, Feb 26th 2010, *GPU-enabled biomolecular simulations with LAMMPS.*
24. **Outstanding Paper Award:** International Conference on High Performance Computing and Simulation (HPCS) 2010, Caen, France, July 1st 2010, *Towards Microsecond Biological Molecular Dynamics Simulations on Hybrid Processors.*
25. **Invited Talk:** University of Tennessee, Knoxville, Department of Biochemistry, Cellular and Molecular Biology (BCMB) Retreat, Knoxville, 20th August 2010, *The Tail Wagging the Dog: Insights into Catalysis in R67 Dihydrofolate Reductase.*
26. American Chemical Society 240th National Meeting, Boston, MA, August 22nd 2010, *Biomolecular simulations in heterogeneous computing architectures.*
27. **Invited Talk:** Workshop on force field development, CNMS, ORNL, Oak Ridge, TN, Sept. 15th 2010, *Linking Protein Flexibility to Enzyme Catalysis.*
28. Bio-molecular Simulations on Future Computing Architectures, ORNL, Oak Ridge, TN, Sept. 15th 2010, *Optimal biomolecular simulations on future computing architectures.*
29. SC10, Intl. Conf. for High Performance Computing, Networking, Storage and Analysis, New Orleans, LA., November 14th 2010, *Molecular Biophysics in Cloud: Promises and Challenges.*
30. SC10, Intl. Conf. for High Performance Computing, Networking, Storage and Analysis, New Orleans, LA., November 18th 2010, *Optimal utilization of heterogeneous resources for biomolecular simulations.*
31. Zing Conference on Biocatalysis, Puerto Morelos, Mexico, December 11th 2010, *Evolutionary Conserved Linkage Between Enzyme Fold, Flexibility, and Catalysis.*
32. ACS 241st National Meeting, Anaheim, CA, March 31, 2011, *Non-homologous enzymes catalyzing same chemistry: Insights into linkage between enzyme fold, flexibility and catalysis*
33. Workshop on Biocatalysis, Denver, CO, May 26th, 2011, *Computational Bio-catalysis for Renewable Energy and Environmental Research*
34. Zing Conference on Enzymes, Coenzymes and Metabolic Pathways, Xcaret, Mexico, November 20th 2011, *Role of enzyme dynamics: Engineering hypercatalytic enzymes by conformation modulation.*
35. Next-Gen Kinase Inhibitors, Boston, MA, June 5th 2012, *Discovering and characterizing allosteric sites for novel drug design.*
36. **Best Poster Award:** GRC Medicinal Chemistry, New London, NH, August 9th 2012, *Discovering and characterizing allosteric sites for novel drug design.*
37. ACS 244th National Meeting, Philadelphia, PA, August 19 2012, *Learning from and manipulating enzymes for better catalysis.*
38. ACS 244th National Meeting, Philadelphia, PA, August 19 2012, *Unraveling the mystery of solvent-protein thermodynamical coupling: Insights from enzyme catalysis in organic solvents.*
39. ACS 244th National Meeting, Philadelphia, PA, August 20 2012, *Engineering hyper-catalytic enzyme by photo-activated conformation modulation.*
40. **Invited Seminar:** BiG Seminar Series, University of North Carolina, Charlotte, September 21 2012, *Using Computations to Understand and Manipulate the Working of Biomolecules.*
41. Drug Design 2012 Conference, Oxford, United Kingdom, September 28th, 2012, *Discovering and Characterizing Allosteric Sites for Novel Drug Design.*
42. **Invited Talk:** 10th Discovery on Target, Allosteric Modulators Series, Boston MA, October 3rd, 2012. *Biophysical Approach to Allosteric Site Discovery and Characterization of Kinases.*
43. **Invited Talk:** Novartis Institutes for BioMedical Research, Cambridge MA, October 4th, 2012. *Biophysical Approach to Allosteric Site Discovery and Characterization of Kinases.*
44. **Invited Talk:** Zing Conference on Mathematical and Computational Medicine, Xcaret, Mexico, December 4th 2012, *Biophysical Approach to Allosteric Site Discovery and Characterization of Kinases.*
45. Zing Conference on Biocatalysis, Xcaret, Mexico, December 6th 2012, *Engineering Hyper-catalytic Enzymes through Conformation Modulation.*

46. **Invited Speaker:** 13th Annual Symposium of PROTEO, the Quebec Network for Research on Protein Structure, Function and Engineering. Montreal, Canada, May 17th 2013. *Protein Dynamics and Conformational Sub-states in Enzyme Catalysis.*
47. **Invited Speaker:** 2nd Conference on Dynamics in Enzymatic Catalysis, Telluride, CO, July 29th-August 2nd, 2013. *Conformational sub-states and Conformational Modulation in Enzyme Catalysis.*
48. **Invited Speaker:** Modeling and Computational Design Symposium, Society for Industrial Microbiology and Biotechnology (SIMB) Conference 2013, San Diego, CA, August 11-15th 2013.
49. **Invited Speaker:** CBE Graduate Seminar, University of Tennessee, January 23, 2014. *A Biophysical Model of Enzyme Catalysis: Applications for Rational Biomolecular Design.*
50. **Invited Speaker:** Northeastern University, January 28, 2014. *Understanding and Manipulating How Enzymes Work*
51. **Invited Speaker:** Univ. of Massachusetts Lovell, April 29, 2014. *The Fascinating World of Enzymes.*
52. **Invited Seminar:** Biology and Soft Matter Division Seminar, Spallation Neutron Source Directorate, ORNL, June 12, 2014. *Protein Dynamics and Conformational Sub-states in Enzyme Catalysis.*
53. **Invited Talk:** Workshop on Intrinsically Disordered Proteins, July 16, 2014. *Protein Dynamics and Conformational Sub-states in Enzyme Catalysis.*
54. **Invited Talk:** University of Montreal, Montreal, Canada, November 6, 2014. *Conformational Diversity and its Role in Enzyme Catalysis.*
55. **Invited Talk:** Workshop on Frontiers in Data, Modeling, and Simulation, Argonne National Laboratory, March 31, 2015. "*Neutrons, Simulations and Models in Biology".*
56. **Invited Seminar:** Department of Computational & Systems Biology, School of Medicine, University of Pittsburgh, May 12, 2015. *Conformational sub-states and allosteric modulation in drug discovery.*
57. **Invited Talk:** 3rd Conference on Role of Protein Dynamics in Enzyme Catalysis, Telluride, CO, August 3-7, 2015. *Role of conformational sub-states and solvent in enzyme catalysis.*
58. **Invited Talk:** Enzyme Engineering Conference, St. Petersburg, FL, September 9, 2015. *Designing Hyper-Catalytic Enzymes using Conformational Modulation.*
59. **Invited Seminar:** Department of Physics, University of South Florida, Tampa, FL, February 16, 2016. *Enzymes: Nature's highly efficient molecular machines.*
60. **Invited Seminar:** Department of Toxicology, Oklahoma State University, Stillwater, OK, March 3, 2016. *Enzymes as Biophysical Machines: Applications for Engineering and Drug Discovery.*
61. **Invited Seminar:** IALS, University of Massachusetts, Amherst, MA, April 7, 2016. *Enzyme Catalysis: Following nature's footsteps for designing better enzymes and novel allosteric modulators.*
62. **Invited Talk:** College of Chemistry, University of California, Berkeley, CA, April 25, 2016. *Enzymes as Biophysical Machines: Designing Faster and Better Biocatalysts.*
63. **Invited Talk:** CNLS Workshop, Santa Fe, May 10 2016. *Riding through the conformational landscapes of enzymes: Relating dynamics and activity.*
64. **Invited Seminar:** Computational Science Division, Argonne National Laboratory, Argonne, IL, August 10, 2016, *Improving Human Health with Predictive Computational Models.*
65. **Invited Special Seminar:** BASF Enzymes LLC, February 22, 2017, *A Dreamer's View of Rational Enzyme Engineering.*
66. **Invited Talk:** Biomolecular Machines Conference, May 21 2017, Banff, Canada. *Solvent Dynamics and Conformational Sub-states in Enzyme Catalysis.*

Research Program Development Experience

1. **Biomolecular Structure, Dynamics and Function:** In 2002, started developing theoretical models and computational simulations for investigating the link between protein dynamics and enzyme catalysis. Developed high quality validated models of over a dozen enzyme systems. This research has already led to understanding the mechanisms of enzyme catalyzed reactions and development of an engineering approach for hyper-catalytic enzymes through conformational modulation. (1 patents and >20 papers)
2. **Enzyme engineering and rational protein design:** In 2007, started rational protein and enzyme design based on the understanding of role of protein dynamics in enzyme catalysis. Assembled a computational and experimental team that could isolate functionally relevant conformations associated with promoting

catalysis and modulate them using photo-activatable ligand linkers. Results show ~3000% increase in enzyme activity. Other approaches including rational biomolecular design for improved catalytic activity as well as new catalyzing new chemical reactions are currently underway. (2 patents and 1 papers)

3. **Open Source Software for Scientific Computing.** In 2004, started the development of VigyaanCD, an open source bio/chemical software workbench. This distribution provides a list of open-source modeling and simulation tools as "ready to go" Linux CD. This software became extremely popular world-wide with over 250,000 copies downloaded and several international magazines distributed copies of the developed software. (1 distributable Linux Live image)
4. **Heterogeneous Architectures for Computational Biology.** In 2007, conceptualized, developed and implemented a research program for the use of non-traditional (heterogeneous) computing architecture for use in computational molecular biophysics. Developed relationships outside laboratory including Clemson University, Swiss National Supercomputing Centre, and San Diego Supercomputing Center as well as with vendors (IBM, NVIDIA, ClearSpeed and others) for strategic partnerships. Applied and received funding from National Institutes of Health (NIH) for porting and optimizing biology codes on FPGA and GPUs. (>10 papers)
5. **Role of cyclophilins in retroviral infection:** Human cyclophilin A is required for infectious activity of HIV-1 and cyclophilin B is required for infectious activity of HCV. We have developed detailed models of the interaction between human and viral proteins. Currently exploring the development of allosteric modulators for these systems. (>10 papers)
6. **Development of Allosteric Modulators.** Starting in 2010, as an interesting application of the developed *Biophysical Model of Catalysis*, I started discussions with several pharmaceutical companies regarding the development of new allosteric modulators. Based on the feed-back, my group has developed a new computational approach through identification of true allosteric sites and discovery of allosteric ligands that modulate the target. This approach has been validated and is being applied to several kinases. The preliminary results have received extremely positive feed-back from the pharmaceutical companies.

Current Collaborative Activities

1. With **BASF Enzymes and Amano Enzymes LLC**. We are currently funded by these two separate companies for creating novel engineered enzymes. Using our new computations driven approach to engineering of enzymes, we are working with them to develop more efficient version of enzymes. The work consists of both fundamental research (developing new engineering strategies) as well as applied research for improving the activity of commercially valuable enzymes.
2. With **Dr. Nicolas Doucet** (INRS, University of Quebec) and **Dr. Chakra Chennubhotla** (University of Pittsburgh). In the joint project (multi-PI R01), we have combined NMR (Dr. Doucet's lab), with simulations (my lab) and statistical analysis (Dr. Chennubhotla lab) for identifying and characterizing conformational sub-states in protein/enzyme function. Have already jointly developed computational methodologies and software infrastructure for identifying multi-scale motions, named *Quasi-Anharmonic Analysis (QAA)* based on the higher-order statistics of protein motions. Application of QAA has allowed the identification of functionally relevant protein motions and conformational sub-states. Currently applying it to ribonucleases and other enzyme systems.
3. With **Dr. Kenneth Herwig** (Instrument and Source Division, Spallation Neutron Source, ORNL) and **Dr. Dean Myles** (Biology and Soft Matter Division, Spallation Neutron Source, ORNL). This collaboration focuses on joint computational-experimental investigation of protein structure, dynamics and function. Neutron scattering, X-ray crystallography and biophysical simulations are being used to investigate the protein motions at various time-scales. For the protein Rubredoxin, this strategy provided unique insights into the onset of function promoting motions. More recently, we are also using other strategies (including enzyme catalysis in organic solvents) to investigate the role of protein function promoting motions.
4. With **Dr. Elizabeth Howell** (University of Tennessee, Knoxville). We are using joint experimental-computational strategy to understand the similarities and differences between the same enzyme reaction catalyzed by non-homologous protein fold that do not share sequence or structural similarity. We are investigating the hydride transfer reaction catalyzed by the plasmid encoded dihydrofolate reductase (R67 DHFR). Based on our computational models of R67 dihydrofolate reductase enzyme, Dr. Howell's lab is

designing mutation and experimentally verifying the role of protein and solvent motions in the enzyme kinetics. The comparison of the mechanism of R67 DHFR with the non-homologous chromosomal DHFR (*E. coli* DHFR) is providing new insights into the role of structure and flexibility in enzyme catalysis. Recently, we are also jointly exploring the impact of osmolytes and inactive proteins on enzyme function.

5. With **Dr. Sadaf Alam** (Swiss National Supercomputing Centre, Switzerland), **Dr. Melissa Smith** (Clemson University), **Dr. Paul Crozier** (Sandia National Laboratories), **Duncan Poole** (NVIDIA), and **Carlos Sosa** (Cray, Inc.). The future computing architectures, particularly the heterogeneous platforms, are posing new challenges for the scientific computing. We are working with several academic groups and hardware vendors for porting molecular dynamics simulations and molecular docking codes on graphical processing units (GPUs), many-core processors, low power ARM processors, Field-Programmable Gate Arrays (FPGAs). Our emphasis is on developing performance models that will allow optimal utilization of the heterogeneous computing resources for best scientific productivity. Codes including LAMMPS, AMBER and AutoDock are being optimized for heterogeneous architectures.