Richard Humfry Henchman

CURRICULUM VITAE

CONTACT INFORMATION:

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EMPLOYMENT:

2002 – present: Research Associate, Howard Hughes Medical Institute in the Department of Chemistry and Biochemistry, Center for Theoretical Biological Physics, University of California, San Diego, working for Prof. J. A. McCammon.

2000 – 2002: Postdoctoral Fellow in the Department of Chemistry and Biochemistry, University of California, San Diego, working for Prof. J. A. McCammon.

EDUCATION:

1996 – 99: Ph.D. in Physical Chemistry, University of Southampton, UK. Awarded February 21, 2000. Funded by a Commonwealth Scholarship. Supervisor: Dr. J. W. Essex.

1992 – 95: Bachelor of Science. Awarded the University Medal and First Class Honours in Theoretical Chemistry, University of Sydney, Australia.

PUBLICATIONS:

1. Revisiting free energy calculations: a theoretical connection to MM/PBSA and direct calculation of the association free energy, J. M. J. Swanson, R. H. Henchman, J. A. McCammon, *Biophys. J.* accepted for publication.

2. Discovery of a novel binding trench in HIV integrase. J. R. Schames, R. H. Henchman, J. S. Siegel, C. A. Sotriffer, H. Ni, J. A. McCammon, submitted for publication.

3. Conformational and enantioselectivity in host-guest chemistry: the selective binding of *cis* amides examined by free energy calculations. R. H. Henchman, J. D. Kilburn, D. L. Turner, J. W. Essex, submitted for publication.

4. Asymmetric structural motions of the homomeric $\alpha 7$ nicotinic receptor ligand binding domain revealed by molecular dynamics simulation. R. H. Henchman, H. Wang, S. M. Sine, P. Taylor, J. A. McCammon, *Biophys. J.*, 2003, 85, 3007-3018.

5. The dynamics of ligand barrier crossing inside the acetylcholinesterase gorge. J. M. Bui, R. H. Henchman, J. A. McCammon, *Biophys. J.*, 2003, 85, 2267-2272.

6. From model complexes to metalloprotein inhibition: a synergistic approach to structure-based drug design. D. T. Puerta, J. R. Schames, R. H. Henchman, J. A. McCammon, S. M. Cohen, *Angew. Chem. Int. Ed.*, 2003, 42, 3772-3774.

7. Partition function for a simple liquid using cell theory parametrized by computer simulation. R. H. Henchman, *J. Chem. Phys.* 2003, 119, 400-406.

8. Mathematical and molecular neurobiology. N. Baker, K. Tai, R. Henchman, D. Sept, A. Elcock, M. Holst, J. A. McCammon in *Methods for Macromolecular Modeling*, T. Schlick and H. H. Gan, Eds., Springer-Verlag, 2002, 24, 31-60.

9. Structural and dynamic properties of water around acetylcholinesterase. R. H. Henchman and J. A. McCammon, *Protein Sci.*, 2002, 11, 2080-2090 (cited by Chemistry Nobel Laureate Ahmed Zewail in *Proc. Natl. Acad. Sci. U.S.A.*, 2002, 99, 15297-15302).

10. Molecular dynamics of acetylcholinesterase. T. Shen, K. Tai, R. H. Henchman, J. A. McCammon, *Acc. Chem. Res.*, 2002, 35, 332-340.

11. Mechanism of acetylcholinesterase inhibition by fasciculin: a 5 ns molecular dynamics simulation. K. Tai, T. Shen, R. H. Henchman, Y. Bourne, P. Marchot, J. A. McCammon, *J. Am. Chem. Soc.* 2002, 124, 6153-6161.

12. Extracting hydration sites around proteins from explicit water simulations. R. H. Henchman, J. A. McCammon, *J. Comput. Chem.*, 2002, 23, 861-869.

13. Properties of water molecules in the active site gorge of acetylcholinesterase from computer simulation. R. H. Henchman, K. Tai, T. Shen, J. A. McCammon, *Biophys. J.*, 2002, 82, 2671-2682.

14. Free energies of hydration using restrained electrostatic potential derived charges via free energy perturbations and linear response. R. H. Henchman, J. W. Essex, *J. Comput. Chem.*, 1999, 20, 499-510.

15. Generation of OPLS-like charges from molecular electrostatic potential using restraints. R. H. Henchman, J. W. Essex, *J. Comput. Chem.*, 1999, 20, 483-498.

16. Transition-state theory model for the diffusion coefficients of small penetrants in glassy polymers. A. A. Gray-Weale, R. H. Henchman, R. G. Gilbert, M. L. Greenfield, D. N. Theodorou, *Macromolecules*, 1997, 30, 7296-7306.

PH.D. THESIS:

Simulation Studies of the Structure and Energetics of a Host-Guest System, 1999. Supervisor: Dr. J. W. Essex.

The aim was to determine the conformational, side chain, and enantioselectivity of the host molecule, macrobicycle 12, for amino acids using free energy perturbation calculations. The techniques learned were force field parametrization for charges and dihedrals; development of the REPD method for deriving OPLS-like charges by fitting to electrostatic potentials; parametrization and implementation of the implicit solvent GB/SA method for chloroform; Monte Carlo simulations and move selection to achieve comprehensive sampling; free energy perturbation and the linear interaction energy method; various analysis methods to examine binding modes.

AWARDS:

1996 – 99	Commonwealth Scholarship in the United Kingdom.
1998	MGMS Young Modellers' Forum, 3rd Prize.
1996	Australian Postgraduate Award.
	University Medal in Theoretical Chemistry for B. Sc.
	Henry Bertie and Florence Mabel Gritton Medal.
	George Harris Scholarship (University of Sydney).
	St Paul's College Foundation Postgraduate Scholarship.
	Council Prize (St Paul's College).
1995	NSW Polymer Group Royal Australia Chemical Institute Prize.
	Hush Prize in Theoretical Chemistry (University of Sydney).
	GS Caird Scholarship in Chemistry, Major (University of Sydney).
	Grainger Scholarship (St Paul's College).
1994	Dean's Honours List (3rd in Science, University of Sydney).
	Grainger Scholarship (St Paul's College).

1993	Science Foundation for Physics, Scholarship No. 1 (University of Sydney).
	Levey Scholarship No. 2 in Chemistry (University of Sydney).
	Aspinall-Kemp Scholarship (St Paul's College).
1992	Liversidge Scholarship in Chemistry (University of Sydney).
	Canon Stephen Scholarship (St Paul's College).
	Premier's Certificate in Excellence in 4 Unit Science (1st in NSW).
	BHP Medal in Mathematics and Science (1st in NSW in combined Mathematics/Science).
	Australian Students Prize for Excellence (TER Score 99.95).
1990, 1991	General Merit Prize (Sydney Grammar School).
1986 – 91	Sir Leslie Herron Scholarship (Sydney Grammar School).
1986	Prox. Ac. (2nd in school, Sydney Grammar School).
1985 – 86	Sir Charles Mackerras Scholarship (cello, Sydney Grammar School).
1985	Open External Student Tuition Scholarship (cello, Conservatorium High School).
1982, 1983	Dux of School (Sydney Grammar Edgecliff Preparatory School).

TEACHING EXPERIENCE:

- Mentored four graduate students during my postdoctoral research at the University of California, San Diego.
- Teaching Assistant in laboratory and tutorials during my Ph.D. at the University of Southampton.
- Laboratory and workshop demonstrator in my final undergraduate year at the University of Sydney.

REVIEWS PERFORMED FOR THE FOLLOWING JOURNALS:

- Journal of Medicinal Chemistry, Biophysical Journal, Proteins — Structure, Function and Genetics, Molecular Pharmacology.

PRESENTATIONS:

1. The ARC/TAP hydration site method for studying water molecules around proteins. Invited presentation in Prof. W. F. van Gunsteren's laboratory, ETH Zentrum, Zurich, Switzerland, 2002.
2. Conformational stabilisation of amino acid derivatives by a macrobicycle host, CECAM Workshop on Free Energy Calculations, Lyon, France, 2000.
3. Conformational stabilisation of amino acid derivatives by a macrobicycle host. Invited presentation in Prof. J. C. Smith's laboratory, University of Heidelberg, Germany, 2000.
4. Generation of OPLS-like charges from the molecular electrostatic potential using restraints. MGMS Young Modellers' Forum, London, UK, 1998.
5. Diffusion of small molecules in glassy polymers. Australian Polymer Symposium, Adelaide, Australia, 1996.

POSTERS:

1. Ligand induced allosteric change in the $\alpha 7$ nicotinic receptor. Protein Society Symposium, Boston, Massachusetts, 2003.
2. Ligand induced allosteric change in the $\alpha 7$ nicotinic receptor. Gordon Conference: Computer Aided Drug Design, Tilton, New Hampshire, 2003.
3. Correlated motions in the human $\alpha 7$ nicotinic receptor ligand binding domain from computer simulation. Biophysical Society Symposium, San Antonio, Texas, 2003.

4. Correlated motions in the human $\alpha 7$ receptor ligand binding domain from computer simulation. Protein Society Symposium, San Diego, California, 2002.

5. Influence of water on the function of acetylcholinesterase. XIth International Symposium on Cholinergic Mechanisms, St Moritz, Switzerland, 2002.

6. Kinetics of acetylcholine binding to acetylcholine binding protein. Biophysical Society Symposium, San Francisco, California, 2002.

7. Kinetics of acetylcholine binding to acetylcholine binding protein. Keystone Meeting: Frontiers in Molecular Biology, Breckenridge, Colorado, 2002.

8. A structural and dynamical analysis of water in acetylcholinesterase. ACS Meeting, San Diego, California, 2001.

9. A structural and dynamical analysis of water in acetylcholinesterase. Methods in Molecular Modeling, New York City, New York, 2000.

10. Conformational stabilisation of amino acid derivatives by a macrobicycle host, MGMS Conference, York, UK, 2000.

UNDERGRADUATE RESEARCH PROJECTS:

- 1996: Calculated and examined the thermodynamic properties of a particular water model, and potentials of mean force in Ne-Xe solutions using integral equation theory under the supervision of Prof. A. D. J. Haymet.

- 1995 – 96 : Developed a model to describe the diffusion of small molecules in glassy polymers under the supervision of Prof. R. G. Gilbert and in collaboration with Prof. D. N. Theodorou at U. C. Berkeley (published in *Macromolecules*, 1997, 30, 7296-7306).

- 1995 – 96 : Developed a model and carried out computer simulations of muscle contraction under the supervision of Dr. P. Harrowell.

- 1993 – 95 : Designed equipment and computer software and carried out experiments examining the crystallization of supercooled water and anti-freeze properties of proteins under the supervision of Prof. A. D. J. Haymet (published in *J. Chem. Phys.*, 2001, 115, 7599-7608).

- 1993 : In a team of undergraduates, designed a heat conductivity experiment for first year students under the supervision of Dr. I. D. Johnston (published in *ANZP* Jan/Feb Supplement, 1994, 31, 1-6).

PROFESSIONAL MEMBERSHIPS:

- American Chemical Society, Biophysical Society, Protein Society.

REFEREES:

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