DAVID A PEARLMAN

Lexington MA 02421
DAPearlman [AT] gmail.com

SUMMARY

Uniquely qualified computational science pioneer with multiple Product Management successes seeks challenging new leadership opportunities
Pioneering computational chemist who has repeatedly taken early stage ideas from germination to success ■ The only person who can claim primary contributions to three of the biggest computational molecular modeling platforms (AMBER, Schrodinger, Discovery Studio) ■ Vision to see both big picture and deal with details ■ Exemplary communications and writing skills, including ability to present technical material to non-technical audiences ■ Out-of-box thinker able to manage multiple clients in dotted line relationships

CAREER HIGHLIGHTS

- ☑ Product Manager: Developed BioLuminate biologics structure design platform for Schrödinger, from ground up. Most successful product launch in their history. First biologics-focused package on market.
- ☑ Product manager of the very first commercialized molecular modeling package, Discover; Helped launch Biosym Techologies (now Accelrys/Biovia);
- ☑ Product Manager & Director Customer Experience for Cyrus Biotechnology: Providing first commercialization of Rosetta Protein Design as Google based SaaS
- ☑ First author of several versions of Amber (most used molecular modeling package in the world)
- ☑ String of early, seminal publications in field of Free Energy Perturbation (FEP)
- ☑ Nearly 70 publications, majority as primary author, widely cited (ResearchGate score 35)
- ☑ First degree from UC Berkeley in modern computational chemistry
- ☑ First person to provide formal avenue for music promotion on the Internet
- ☑ Helped establish Vertex Pharmaceuticals' reputation in drug design through prolific publication

PROFESSIONAL EXPERIENCE

DIRECTOR/PRODUCT MANAGER PROTEIN DESIGN PLATFORM – Cyrus Biotechnology – 2017 to 2019
Both product manager and director of customer experience for Cyrus Bench

- First successful commercialization of academic Rosetta protein design platform
- Modern SaaS tool using Google Cloud on the backend
- Bridged customer and developer clients, pre-sales, post-sales
- Project management of milestone-based collaborative science with customers
- As member of executive team, helped lead corporate strategy
- Managed customer support team

DIRECTOR/PRODUCT MANAGER BIOLOGICS SOFTWARE PLATFORM – Schrödinger Inc – 2010 to 2017
Successfully created structure-based design platform for biologics/biopharmaceuticals from scratch/vision to market

- Most successful new product launch in Schrödinger history
- Duties include: Overall product strategy; poll customers; write internal white papers; create feature specs; design GUI interfaces; oversee implementation; oversee beta testing and refinement; create internal and external marketing documents; external pre-sales presentations; work closely with sales account managers; triage improvement/bug requests; create roadmaps for new features.
- Adept at generating cross-team internal buy-in, and balancing team, internal and external stakeholders.
- Provide direction for new biologics-related basic research
- Speak at 6-8 relevant conferences per year, dozens pre- and post- sales presentations per year

- Create impactful story at appropriate level that helped open a new market for this product
- Collaborate and publish on basic research related to biologics, including antibody prediction and FEP
- Project management of collaborative science with customers
- Develop collaborative ties to academic laboratories

COMPUTATIONAL CHEMIST III – Broad Institute of MIT & Harvard/Stanley Center – 2007 to 2010
Provide direction and support for all aspects of computational chemistry / molecular modeling for Stanley Center for Psychiatric Research

- Molecular docking campaigns
- Structure-based ligand design
- Develop new methodologies and paradigms to improve efficiency of drug design

CEO – Dapper Research – 2004 to 2007
Development and characterization of high-throughput ligand scoring functions

- FURMASA (simplified function based on an MD grid and a surface area term)
- ZIPAP (molecular scoring function derived from experimental potential of mean force data)
- MM-PBSA (combined molecular mechanics and Poisson-Boltzmann energies)

PRINCIPAL INVESTIGATOR – Vertex Pharmaceuticals – 1991 to 2004
Early employee, hired to be "scientist in residence", i.e. to publish quality research at a substantial rate, speak publicly, etc. to prove the now-successful company was serious about their new paradigm that elevated the importance of computational chemistry to drug discovery

- Develop new methods for theoretical free energy calculations (FEP/TI)
- Develop new scoring methods for high throughput data mining
- Develop new methods for *de novo* drug design
- Develop new methods for NMR refinement
- Contribute to internal drug discovery projects
- Contribute as first author to AMBER software package in collaboration with UCSF

POST DOCTORAL ASSOC / ASST RESEARCH CHEMIST – University of California San Francisco – 1987 to 1991
Worked with Peter Kollman. Computational chemistry: Methodology development and application

- First author / primary developer of the AMBER software package, versions 4-5
- Numerous early, defining, methodology papers on free energy calculations (FEP, TI)
- Determination of NMR structures from NOE data, including time-averaged restraints

DISCOVER PROGRAM LEADER– Biosym Technologies (now Accelrys/Biovia) – 1985 to 1986
Helped launch company (employee #7). In charge of primary product: Simulation platform Discover. This was the first commercialization of structure-based modeling software.

- Lead commercialization efforts of platform
- Interface with customers, triage requests, road mapping, pre-sales presentations, installations
- Biosym is now Accelrys, acquired by Dassault in 2014 for $750M.

EDUCATION

GRADUATE SCHOOL (PH.D.) from University of California, Berkeley (1980-1985)

Advisor: Sung-Hou Kim
Research: Computational studies of DNA systems. Small molecule crystallography to determine charges from high resolution x-ray density. Predict effects of photodamage on DNA. First person to graduate from UC-Berkeley with focus on computational chemistry.

UNDERGRADUATE (B.S.) from Stanford University, Stanford, California (1977-1980)
With distinction, in three years.

PUBLICATIONS

1) David A. Pearlman, Stephen R. Holbrook, David H. Pirkle and Sung-Hou Kim (1985) ``Molecular Models for DNA Damaged by Photoreaction.'' *Science* **227**, 1304-1308.

2) David A. Pearlman and Sung-Hou Kim (1985) ``Determinations of Atomic Partial Charges for Nucleic Acid Constituents from X-ray Diffraction Data. I. 2'-Deoxycytidine 5'-Monophosphate.'' *Biopolymers* **24**, 327-357.

3) David A. Pearlman and Sung-Hou Kim (1985) ``The Conformations and Energetics of Photodamaged DNA.'' *Proceedings of the International Symposium on Biomolecular Structure and Interactions* (Supplement to *Journal of Biosciences*), **8**, 579-592.

4) Sung-Hou Kim, David A. Pearlman, Stephen R. Holbrook and David H. Pirkle (1985) ``Structures of DNA Containing Psoralen Crosslink and Thymine Dimer.'' In: *Molecular Basis of Cancer* (R. Rein, ed.), pp. 143-152, Alan R. Liss, Inc., New York.

5) David A. Pearlman and Sung-Hou Kim (1985) ``Conformational Studies of Nucleic Acids. I. A Rapid and Direct Method for Generating Furanose Coordinates from the Pseudorotation Angle.'' *Journal of Biomolecular Structure and Dynamics* **3**, 81-98.

6) David A. Pearlman and Sung-Hou Kim (1985) ``Conformational Studies of Nucleic Acids. II. The Conformational Energetics of Commonly Occurring Nucleosides.'' *Journal of Biomolecular Structure and Dynamics* **3**, 99-126.

7) David A. Pearlman, Stephen R. Holbrook and Sung-Hou Kim (1985) ``The Conformational Effects of UV Induced Damage on DNA.'' In: *Proceedings of the 18th Jerusalem Symposium on the Interrelationship Among Aging, Cancer and Differentiation* (B. Pullman, P.O.P. Ts'o, and E.L. Schneider, eds.), pp. 163-172, D. Reidel Publishing Company, Boston.

8) David A. Pearlman and Sung-Hou Kim (1986) ``Conformational Studies of Nucleic Acids. III. Empirical Multiple Correlation Functions for Nucleic Acid Torsion Angles.'' *Journal of Biomolecular Structure and Dynamics* **4**, 49-68.

9) David A. Pearlman and Sung-Hou Kim (1986) ``Conformational Studies of Nucleic Acids. IV. The Conformational Energetics of Oligonucleotides: d(ApApApA) and ApApApA.'' *Journal of Biomolecular Structure and Dynamics* **4**, 69-98.

10) David A. Pearlman and Sung-Hou Kim, (1988) ``Conformational Studies of Nucleic Acids. V. Sequence Specificities in the Conformational Energetics of Oligonucleotides: The Homo-Tetramers.'' *Biopolymers* **27**, 59-77.

11) Stephen R. Holbrook, David A. Pearlman and Sung-Hou Kim (1988) ``Molecular Models of Photodamaged DNA.'' *Reviews of Chemical Intermediates* **10**, 71-100.

12) Sung-Hou Kim, Milan T. Tomic, David E. Wemmer, David Pearlman and Stephen Holbrook (1988) ``Structure of DNA damaged by UV and psoralen'' *Biochemical Pharmacology* **37**, 1791.

13) David A. Pearlman and Peter A. Kollman (1989) ``A New Method for Carrying Out Free Energy Perturbation Calculations: Dynamically Modified Windows.'' *Journal of Chemical Physics* **90**, 2460-2470.

14) David A. Pearlman and Peter A. Kollman (1989) ``Free Energy Perturbation Calculations: Problems and Pitfalls Along the Gilded Road.'' In: *Computer Simulation of Biomolecular Systems: Theoretical and Experimental Applications* (W. van Gunsteren and P.K. Weiner, eds.), pp. 101-119, Escom Science Publishers, Netherlands.

15) Wilson S. Ross, Charles C. Hardin, Ignacio Tinoco, Jr., Shashidar N. Rao, David A. Pearlman and Peter A. Kollman (1989) ``Effects of Nucleotide Bromination on the Stabilities of Z-RNA and Z-DNA: A Molecular Mechanics / Thermodynamic Perturbation Study.'' *Biopolymers* **28**, 1939-1958.

16) David A. Pearlman and Peter A. Kollman (1989) ``The Lag Between the Hamiltonian and the System Configuration in Free Energy Perturbation Calculations.'' *Journal of Chemical Physics* **91**, 7831-7839.

17) David A. Pearlman and Sung-Hou Kim (1990) ``Atomic Charges for DNA Constituents Derived from Single-Crystal X-Ray Diffraction Data.'' *Journal of Molecular Biology* **211**, 171-187.

18) David A. Pearlman and Peter A. Kollman (1990) ``The Calculated Free Energy Effects of 5-Methyl Cytosine on the B to Z Transition in DNA.'' *Biopolymers* **29**, 1193-1209.

19) Liem X. Dang, David A. Pearlman and Peter A. Kollman (1990) ``Why Do AT Base Pairs Inhibit Z-DNA Formation?'' *Proceedings of the National Academy of Sciences, USA* **87**, 4630-4634.

20) David A. Pearlman and Sung-Hou Kim (1990) ``Atomic Partial Charges For Nucleic Acids From X-Ray Diffraction Data.'' In: *Theoretical Chemistry and Molecular Biophysics* (D.L. Beveridge and R.L. Lavery, eds.), pp. 259-270, Adenine Press, New York.

21) David A. Pearlman and Peter A. Kollman (1990) ``Are Free Energy Calculations Necessary? A Comparison of DNA Modeling Studies.'' In: *Theoretical Chemistry and Molecular Biophysics* (D.L. Beveridge and R.L. Lavery, eds.), pp. 139-152, Adenine Press, New York.

22) David A. Pearlman and Peter A. Kollman (1991) ``The Overlooked Bond-Stretching Contribution in Free Energy Perturbation Calculations.'' *Journal of Chemical Physics* **94**, 4532-4545.

23) Thomas L. James, Miriam Gochin, Deborah J. Kerwood, David A. Pearlman, Uli Schmitz and Paul D. Thomas (1991) ``Refinement of Three-Dimensional Protein and DNA Structures from NMR Data.'' In: *Computational Aspects of the Study of Biological Macromolecules by Nuclear Magnetic Resonance Spectrsocopy* (J.C. Hoch, F.M. Poulsen and C. Redfield, eds.), pp. 331-347, Plenum Press, New York.

24) David A. Pearlman and Peter A. Kollman (1991) ``Evaluating the Assumptions Underlying Force Field Development and Application, Using Free Energy Conformational Maps for Nucleosides.'' *Journal of the American Chemical Society* **113**, 7167-7177.

25) David A. Pearlman and Peter A. Kollman (1991) ``Are Time-Averaged Restraints Necessary for NMR Refinement? A Model Study for DNA.'' *Journal of Molecular Biology* **220**, 457-479.

26) Naoki Mizushima, David Spellmeyer, Suichi Hirono, David Pearlman and Peter A. Kollman (1991) ``Free Energy Perturbation Calculations on Binding and Catalysis After Mutating Threonine-220 in Subtilisin.'' *Journal of Biological Chemistry* **266**, 11801-11809.

27) Uli Schmitz, David A. Pearlman and Thomas L. James (1991) ``Solution Structure of d(GTATATAC)$_2$ via Restrained Molecular Dynamics Simulations with NMR Constraints Derived from Relaxation Matrix Analysis of 2D NOE Experiments.'' *Journal of Molecular Biology* **221**, 271-292.

28) Mark R. Hurle, Charles D. Eads, David A. Pearlman, George L. Seibel, John Thomason, Phyllis A. Kosen, Peter Kollman, Stephen Anderson and Irwin D. Kuntz (1992) ``Comparison of Solution Structures of Mutant Bovine Pancreatic Trypsin Inhibitor Proteins Using Two-Dimensional Nuclear Magnetic Resonance.'' *Protein Science* **1**, 91-106.

29) David M. Ferguson, David A. Pearlman, William C. Swope and Peter A. Kollman (1992) ``Free Energy Perturbation Calculations Involving Potential Function Changes'' *Journal of Computational Chemistry* **13**, 362-370.

30) Yaxiong Sun, David Spellmeyer, David A. Pearlman and Peter Kollman (1992) ``Simulation of the Solvation Free Energies for Methane, Ethane, and Propane and Corresponding Amino Acid Dipeptides: A Critical Test of the "Bond-PMF" Correction, a New Set of Hydrocarbon Parameters, and the Gas Phase-Water Hyrdophobicity Scale'' *Journal of the American Chemical Society* **114**, 6798-6801.

31) David A. Pearlman (1993) ``Determining the Contributions of Constraints in Free Energy Calculations: Development, Characterization, and Recommendations'' *Journal of Chemical Physics* **98**, 8946-8957.

32) David A. Pearlman and Mark A. Murcko (1993) ``CONCEPTS: A New Dynamic Algorithm for *de Novo* Drug Suggestion'' *Journal of Computational Chemistry* **14**, 1184-1193.

33) Suresh B. Singh, David A. Pearlman and Peter A. Kollman (1993) ``Free Energy Component Analysis: Application to the "Z-Phobicity" of A*T Base Pairs'' *Journal of Biomolecular Structure & Dynamics* **11**, 303-312.

34) Craig A. Gough, David A. Pearlman and Peter Kollman (1993) ``Calculations of the Relative Free Energies of Aqueous Solvation of Several Fluorocarbons: A Test of the Bond-Potential of Mean Force Correction.'' *Journal of Chemical Physics* **99**, 9103-9110.

35) David A. Pearlman (1994) ``How is an NMR Structure Best Defined? An Analysis of Molecular Dynamics Distance-Based Approaches.'' *Journal of Biomolecular NMR* **4**, 1-16.

36) David A. Pearlman (1994) ``Free Energy Derivatives: A New Method for Probing the Convergence Problem in Free Energy Calculations.'' *Journal of Computational Chemistry* **15**, 105-123.

37) David A. Pearlman (1994) ``A Comparison of Alternative Approaches to Free Energy Calculations'' *Journal of Physical Chemistry* **98**, 1487-1493.

38) Stephen E. Debolt, David A. Pearlman and Peter A. Kollman (1994) ``Free Energy Perturbation Calculations on Parallel Computers – Demonstrations of Scalable Linear Speedup'' *Journal of Computational Chemistry* **15**, 351-373.

39) David A. Pearlman (1994) ``How Well do Time-Averaged J-Coupling Restraints Work?'' *Journal of Biomolecular NMR* **4**, 279-299.

40) Piotr Cieplak, David A. Pearlman and Peter A. Kollman (1994) ``Walking on the Free Energy Hyperspace of the 18-Crown-6 Ion System Using Free Energy Derivatives'' *Journal of Chemical Physics* **101**, 627-633.

41) Christopher A. Lepre, David A. Pearlman, Jya-Wei Cheng, Maureen T. DeCenzo, Robert A. Aldape, David J. Livingston and Jonathon M. Moore (1994) ``Solution structure of FK506 bound to the R42K, H87V double mutant of FKBP-12'' *Biochemistry* **33**, 13571-13580.

42) Susumu Itoh, Maureen T. DeCenzo, David J. Livingston, David A. Pearlman and Manuel A. Navia (1995) ``Conformation of FK506 in X-Ray Structures of its Complexes with Human Recombinant FKBP12 Mutants'' *Bioorganic & Medicinal Chemistry Letters* **5**, 1983-1988.

43) David A Pearlman, David A Case, James W Caldwell, William S Ross, Thomas C Cheatham, Stephen E DeBolt, David M Ferguson, George L Seibel and Peter A Kollman (1995) ``AMBER, a Package of Computer Programs for Applying Molecular Mechanics, Molecular Dynamics and Free Energy Calculations to Simulate the Structural and Energetic Properties of Molecules'' *Computer Physics Communications* **91**, 1-41.

44) Christophe Chipot, Bernard Maigret, David A. Pearlman and Peter A. Kollman (1996) ``Molecular Dynamics Potential of Mean Force Calculations: A Study of the Toluene-Ammonium π-Cation Interactions'' *Journal of the American Chemical Society* **118**, 2998-3005.

45) David A. Pearlman and Patrick Connelly (1995) ``Determination of the Differential Effects of Hydrogen Bonding and Water Release on the Binding of FK506 to Native and Tyr82→Phe82 FKBP-12 Proteins Using Free Energy Simulations'' *Journal of Molecular Biology* **248**, 696-717.

46) David A. Pearlman and Mark A. Murcko (1996) ``CONCERTS: Dynamic connection of fragments as an approach to de novo drug design'' *Journal of Medicinal Chemistry* **39**, 1651-1663.

47) Christophe Chipot, Peter A. Kollman and David A. Pearlman (1996) ``Alternative Approaches to Potential of Mean Force Calculations: Free Energy Perturbation Versus Thermodynamic Integrations--Case Study of some Representative Nonpolar Interactions'' *Journal of Computational Chemistry* **17**, 1112-1131.

48) David A. Pearlman (1996) ``FINGAR: A new genetic algorithm-based method for fitting NMR data'' *Journal of Biomolecular NMR* **8**, 49-66.

49) Christopher A. Lepre, David A. Pearlman, Olga Futer, David J. Livingston and Jonathan M. Moore (1996) ``Practical applications of time-averaged restrained molecular dynamics to ligand-receptor systems: FK506 bound to the Q50R, A95H, K98I triple mutant of FKBP-13 *Journal of Biomolecular NMR* **8**, 67-76.

50) Christophe Chipot, R. Jaffe, Bernard Maigret, David A. Pearlman and Peter A. Kollman (1996) ``Benzene Dimer: A good model for Pi-Pi interactions in proteins. A comparison between the benzene and the toluene dimmers in the CAS phase and in an aqueous solution.'' *Journal of the American Chemical Society* **118**, 11217-11224.

51) David A. Pearlman (1997) ``Applications of Free Energy Calculations to Drug Design.'' In: *Thermodynamics and Structure-Based Drug Design* (J. Ladbury, P.R. Connelly, eds.), pp. 1-17, R.G. Landes Co., London.

52) Johan Kordel, David A. Pearlman and Walter J. Chazin (1997) ``Protein solution structure calculations in solution: Solvated molecular dynamics refinement of calbindin D-9k.'' *Journal of Biomolecular NMR* **10**, 231-243.

53) David A. Pearlman and B. Govinda Rao (1998) ``Free Energy Calculations: Methods and Applications'' In: *The Encyclopedia of Computational Chemistry* (P von Rague Schleyer, N L Allinger, T Clark J Gasteiger, P A Kollman, H F Schaefer III and R P Schreiner eds.), John Wiley & Sons, NY, pp. 1036-1061.

54) Thomas Darden, David A. Pearlman and Lee Pederson (1998) ``Ionic charging free energies: Spherical vs. periodic boundary conditions'' *Journal of Chemical Physics* **109,** 10921-10935.

55) David A. Pearlman (1999) ``Automated Detection of Error Restraints in NMR Data Sets Using the FINGAR Genetic Algorithm Method.'' *Journal of Biomolecular NMR* **13**, 325-335.

56) David A. Pearlman (1999) ``Free energy grids: A practical qualitative application of free energy perturbation to ligand design using the the OWFEG method.'' *Journal of Medicinal Chemistry* **42**, 4313-4324.

57) David A. Pearlman and Paul S. Charifson (2001) ``Improved scoring of ligand-protein interactions using OWFEG free energy grids'' *Journal of Medicinal Chemistry* **44**, 502-511.

58) David A. Pearlman and Paul S. Charifson (2001) ``Are free energy calculations useful in practice? A comparison with rapid scoring functions for the p38 MAP kinase protein system'' *Journal of Medicinal Chemistry* **44**, 3417-3423.

59) David A. Pearlman (2001) ``Free Energy Calculations: Methods for Estimating Ligand Binding Affinities'' In: *Free Energy Calculations in Rational Drug Design* (M. Rami Reddy and Mark D. Erion eds.) Kluwer Academic/Plenum Publishers, 2001, pp. 9-35.

60) Chris Chipot and David A. Pearlman (2002) ``Free energy calculations. The long and winding gilded road'' *Molecular Simulations* **28,** 1-12.

61) David A. Pearlman (2005) ``Evaluating the Molecular Mechanics Poisson-Boltzmann Surface Area Method Using a Congeneric Series of Ligands to p38 MAP Kinase'' *Journal of Medicinal Chemistry* **48**, 7796-7807.

62) David A. Pearlman, B. Govinda Rao and Paul S. Charifson (2008) ``FURSMASA: A new rapid scoring function that uses a MD-averaged potential energy grid and a solvent accessible area term with parameters GA fit to experimental data*'' Proteins: Structure, Function and Bioinformatics* **71**, 1519-1538.

63) Letian Kuai, Shao-En Ong, Jon M Madison, Xiang Wang, Jeremy R Duvall, Timothy A Lewis, Catherine J Luce, Sean D Conner, David A Pearlman, John L Wood, Stuart L Schreiber, Steven A Carr, Edward M Scolnick and Stephen J

Haggarty (2011) ``AAK1 Identified as an Inhibitor of Neuregulin-1/ErbB4-Dependent Neurotrophic Factor Signaling Using Integrative Chemical Genomics and Proteomics'' *Chemistry & Biology* **18**, 891-906.

64) Hege Beard, Anuradha Cholleti, David Pearlman, Woody Sherman and Kathryn A Loving (2013) ``Applying Physics-Based Scoring to Calculate Free Energies of Binding for Single Amino Acid Mutations in Protein-Protein Complexes'' *PLoS ONE* **8**, e82849.

65) Noeris K Salam, Matvey Adzhigirey, Woody Sherman and David A Pearlman (2014) ``Structure-based approach to the prediction of disulfide bonds in proteins'' *Protein Engineering Design and Selection* **10**, 365-374.

66) Kai Zhu, Tyler Day, Dora Warshaviak, Colleen Murrett, Richard Friesner and David Pearlman (2014) ``Antibody Structure Determination Using a Combination of Homology Modeling, Energy-Based Refinement and Loop Prediction'' *Proteins Structure Function and Bioinformatics* **82**, 1646-1655.

67) Sarah Sirin, David A. Pearlman, Woody Sherman (2014) ``Physics-Based Enzyme Design: Predicting Binding Affinity and Catalytic Activity'' *Proteins Structure Function and Bioinformatics* **82**, 3397-3409.

68) Thomas Steinbrecher, Chongkai Zhu, Lingle Wang, Robert Abel, Christopher Negron, David Pearlman, Eric Feyfant, Jianxin Duan, Woody Sherman (2016) `` Predicting the Effect of Amino Acid Single Point Mutations on Protein Stability–Large Scale Validation of MD-based Relative Free Energy Calculations'' *Journal of Molecular Biology* **429**, 948-963.

69) Christopher Negron, David A Pearlman, Guillermo del Angel (2019) ``Predicting mutations deleterious to function in beta-lacatamase TEM1 using MM-GBSA'' *PLoS ONE* 14 e0214015

70) David A. Pearlman (2019) Ligand binding to Histone Deacetylase HDAC2: using the FURSMASA approach to predict binding efficacy and to probe the assay time dependence of benzamide class ligands (in preparation).