Scott D. Bembenek, PhD

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Profile

A 15-year veteran in computer aided drug discovery with expert knowledge in applying these methods to all major drug targets. Expertise in computational modeling, cheminformatics, chemical physics, life science biology, biophysics, biochemistry, and numerical analysis techniques.

Experience

3/2013-Present ***Principal Scientist, Computer-Aided Drug Discovery***
3/2007-3/2013 ***Senior Scientist, Computer-Aided Drug Discovery***
3/2002-3/2007 ***Scientist, Computer-Aided Drug Discovery***

Johnson & Johnson Pharmaceutical Research & Development, San Diego, CA

- Chaired the global kinase initiative to identify and leverage both internal and external technologies/expertise (in chemistry, biology, and computation) for improved support of kinase targets across all therapeutic areas.
- Created a novel computational workflow that resulted in a current clinical candidate for a major kinase target for cancer
- Using internal data and a novel Monte Carlo algorithm, an optimal small number (mini) kinase panel was designed. This mini kinase panel enabled obtaining selectivity data on more compounds early on, more quickly, and at less cost for a given project. In this way, better decisions on those compounds to move forward for optimization has occurred. The mini kinase panel has become a standard panel for global J&J.
- Created our internal master kinase sequence database and analyzer, which leverages a proprietary alignment algorithm. This tool is used globally throughout J&J via the web frontend that was also designed.
- Developed a novel computational platform that resulted in the identification of the small molecule lead series for a major protein-protein interaction target. Served as a project lead for this project, thereby becoming the first computational chemist at J&J to officially co-lead a project alongside the chemistry and biology leads.
- Successfully lead the effort to use data driven analyses to identify target profiles for phenotypic screens.
- Played a major role in the development of and training on the initial cheminformatics platform; received an internal award for and wrote a book chapter on these efforts.
- Successfully maintained an ambitious therapeutic project workload of (on average) five projects at various stages in the drug discovery process.
- Regularly worked closely with medicinal chemists and biologists to support therapeutic projects all the way from lead identification to lead optimization.
- Key contributor to a diverse set of therapeutic targets: enzymes, kinases, ion channels, GPCRs, peptide design, protein-protein interactions, cytokines, nuclear hormone receptors.
- Supported both ligand and structure based projects using a variety of techniques: FEP, conformational analysis, pharmacophore modeling, QSAR, docking (manual, fast, QM/MM), homology modeling, molecular dynamics simulations, free energy perturbation, sequence analysis, virtual screening, combinatorial library design, cheminformatics, clustering, ligand efficiency/fit quality, fragment-based methods, de novo design and ADME/Tox modeling.
- Managed summer interns and postdoctoral associates.

11/1999-2/2002 ***Postdoctoral Research Associate***

Colorado State University, Fort Collins, CO

- Developed a novel analytical theory for dipolar fluids
- Created numerical analysis code to solve nonlinear partial differential equations
- Created numerical analysis code to solve multidimensional integrals using Monte Carlo methods

- Created numerical analysis code to calculate Fourier transforms
- Investigated the use of instantaneous normal modes in time correlation calculations

10/1997-10/1999 ***National Research Council Fellow***
Army Research Laboratory, Weapons & Materials Research Directorate, Aberdeen, MD
- Created molecular dynamics and Monte Carlo simulation code for liquid-vapor interfaces
- Developed new method for parameterizing interaction potentials for complex systems.

9/1993-7/1997 ***Graduate Student Researcher***
University of Kansas, Lawrence, KS
- Developed a novel theory of the glass transition and structural localization
- Investigated the application of density functional theory to glassy systems.
- Created molecular dynamics simulation code for several condensed phase systems
- Performed instantaneous normal mode analysis on a variety of condensed phase systems
- Created code for statistical analysis

Education

9/1993-7/1997 ***PhD, Theoretical Chemical Physics*** (Honors)
University of Kansas, Lawrence, KS
"Localization in Glasses and Supercooled Liquids"

9/1989-5/1993 ***BS, Chemistry, Physics***
Carroll University, Waukesha, WI

Computer Experience

Software: Accelrys, Schrödinger, Scitegic, Pymol, MOE, OpenEye, Gaussian, Tripos
Programming: C/C++, Fortran, Perl, Python, Java, VB, SQL
Platforms: Unix/Linux, Mac, Windows

Honors, Awards, and Fellowships

- J&J Encore Award (leadership skills on a high-profile protein-protein interaction target), 2017
- J&J Encore Award (identification of the lead series for a high-profile protein-protein interaction target), 2016
- J&J Encore Award (identification of a small molecule inhibitor for a high-profile protein-protein interaction target), 2011
- J&J Encore Award (design of novel computational methods for protein-protein interactions), 2011
- J&J Encore Award (risk taking, judgment, and achievements on a kinase project), 2007
- J&J Encore Award (risk taking and achievements on Cathepsin S project), 2007
- J&J Encore Award (role in benchmarking new HTS assay), 2006
- J&J Vision Award (role in the development of the cheminformatics platform), 2003
- National Research Council Postdoctorate Fellowship, 1997-1999
- Final Dissertation Defense completed with Honors, 1997
- Paul Gilles Outstanding Doctoral Candidate Award, 1997
- Oral Examination completed with Honors, 1996
- Argersinger Summer Fellowship for Outstanding First Year Graduate Student, 1994
- KUFS Fellowship for Outstanding Incoming Graduate Student, 1993.
- Bailey-Phillips Fellowship for Outstanding Incoming Graduate Student, 1993

Sessions Chaired

- Fourth Annual Modern Drug Discovery and Development Summit, San Diego, CA, Oct 17, 2008, Combination Therapeutics Section Chair

- Cambridge Healthtech Institute's Second Annual Fragment-Based Drug Discovery, San Diego, CA, May 15, 2007, Round Table Discussion Chair: Computational Tools for Fragment-Based Drug Discovery

- American Physical Society Meeting, Kansas City, MO, March 27, 1997, General Physics Section Chair

Invited Talks

- University of California, San Diego, Chemistry-Biology Interfaces Training Program Career Day, San Diego, CA, June 16, 2017, "Working in Drug Discovery: A Computational Chemistry Perspective"

- Cambridge Healthtech Institute's Eighth Annual Kinase Inhibitor Chemistry, San Diego, CA, April 25, 2017, "Determination of a Focused Mini-Kinase Panel for Early Identification of Selective Kinase Inhibitors"

- Schrodinger User Group Meeting, La Jolla, CA, May 10, 2016, "The Role of Iron Complexation, Strain, and Water in Prolyl Hydroxylase (PHD2) Drug Design"

- University of California, San Diego, Inorganic Chemistry Seminar, San Diego, CA, April 6, 2012, "Computational Approach to HIF Prolyl Hydroxylase (PHD2) Drug Design"

- American Chemical Society Course on Structure Based Drug Design, La Jolla, CA, November 10, 2011, "Computer-Aided Drug Discovery of HIF Prolyl Hydroxylase Inhibitors"

- University of California, San Diego, Michael Gilson Group Meeting, San Diego, CA, August 30, 2011, "Computer-Aided Drug Discovery of HIF Prolyl Hydroxylase Inhibitors"

- Gordon Research Conference on Computer Aided Drug Design, West Dover, VT, July 17-22, 2011, "Computer-Aided Drug Discovery of HIF Prolyl Hydroxylase Inhibitors"

- American Chemical Society Course on Structure Based Drug Design, La Jolla, CA, November 3, 2010, "Docking, Quantum Calculations and Crystal Structure Analysis: Studies of Hypoxia-Inducible Factor Prolyl Hydroxylase"

- Schrodinger User Group Meeting, La Jolla, CA, June 30, 2010, "Docking, Quantum Calculations and Crystal Structure Analysis: Studies of Hypoxia-Inducible Factor Prolyl Hydroxylase"

- American Chemical Society Course on Structure Based Drug Design, La Jolla, CA, November 3, 2009, "Lead Identification of Acetylcholinesterase Inhibitors–Histamine H_3 Receptor Antagonists from Molecular Modeling"

- Accelrys Science Forums 2009, San Diego, CA, June 18, 2009, "Lead Identification of Acetylcholinesterase Inhibitors Histamine H_3 Receptor Antagonists from Molecular Modeling"

- World Pharmaceutical Congress, Targeting Alzheimer's with Novel Therapeutics, Philadelphia, PA, June 11, 2009, "Lead Identification of Acetylcholinesterase Inhibitors–Histamine H_3 Receptor Antagonists from Molecular Modeling"

- Fourth Annual Modern Drug Discovery and Development Summit, San Diego, CA, October 17, 2008, "Lead Identification of Acetylcholinesterase Inhibitors–Histamine H_3 Receptor Antagonists from Molecular Modeling"

- University of Colorado, Colorado Springs, Sigma Xi Scientific Research Society Lecture, September 25, 2008, "Novel Approach to Modeling G-Protein Coupled Receptors: Application to Histamine H_3"

- University of Colorado, Colorado Springs, Senior Chemistry Majors Seminar, September 25, 2008, "Computer Aided Drug Discovery"

- University of Colorado, Colorado Springs, Student Affiliates Meeting, September 25, 2008, "Chemistry in Drug Discovery"

- Accelrys Scientific and Technical Seminar Series, San Diego, CA, June 12, 2008, "Ligand Efficiency: Trends and Physical Interpretation"

- Cambridge Healthtech Institute's Second Annual Fragment-Based Drug Discovery, San Diego, CA, May 14, 2007, "Ligand Efficiency: Trends, Physical Models, and Implications"

- San Diego Bioinformatics Forum, San Diego, CA, April 11, 2006, "Novel Approach to Modeling G-Protein Coupled Receptors: Application to Histamine H_3"

- University of California, Merced, Quantitative Systems Biology Lecture Series, March 8, 2006, "Novel Approach to Modeling G-Protein Coupled Receptors: Application to Histamine H_3"

- Pacifichem 2005, Honolulu, HI, December 16, 2005, "From Distances to Coordinates and Back Again"

- Missouri State University, Chemistry Colloquium, September 19, 2005, "Computer-Aided Drug Discovery"

- SciTegic Cheminformatics Seminar, San Diego, CA, May 21, 2004, "The Role of Pipeline Pilot in Cheminformatics at Johnson & Johnson Pharmaceutical Research & Development, L.L.C"

- U.S. Army Research Laboratory, Aberdeen, MD, Branch Seminar, August 19, 1998, "Localization in Glasses and Supercooled Liquids"

Publications

- "Determination of a Focused Mini Kinase Panel for Early Identification of Selective Kinase Inhibitors", **S.D. Bembenek**, G. Hirst, and T. Mirzadegan, *in progress* (2017).

- "Discovery, Optimization and Evaluation of Potent and Highly Selective PI3Kγ and PI3Kδ Dual Inhibitors", H. Jia, W. Su, G. Dai, K. Xiao, J. Weng, Z. Zhang, Q. Wang, T. Yuan, F. Shi, W. Chen, Y. Sai, J. Wang, X. Li, Y. Cai, J. Yu, J. Venable, **S.D. Bembenek**, T. Rao, submitted to *J. Med. Chem.* (2017).

- "A Prospective Virtual Screening Study: Enriching Hit Rates and Designing Focus Libraries to Find Inhibitors of PI3Kδ and PI3Kγ", K.L. Damm-Ganamet, **S.D. Bembenek**, J.W. Venable, G.G. Castro, L. Mangelschots, D.C.G. Peeters, H.M. Mcallister, J.P. Edwards, D. Disepio, and T. Mirzadegan, *J. Med. Chem.* **59**, 4302 (2016).

- "Extending Kinome Coverage by Analysis of Kinase Inhibitor Broad Profiling Data", E. Jacoby, G. Tresadern, **S.D. Bembenek**, B. Wroblowski, C. Buyck, J. Neefs, D. Rassokhin, A. Poncelet, J. Hunt, H. van Vlijmen, *Drug Discovery Today* **20**, 652 (2015).

- "Functional Studies of Interaction Between Huwentoxin-IV and Voltage-Gated Sodium Channel Nav1.7", A.Y. Shih, **S. Bembenek**, N. Minassian, R. Neff, Y. Liu, M. Flinspach, S. Edavettal, N. Wu, M. Maher, A. Wickenden, T. Mirzadegan, *Biophysical Journal* **102**, 324a (2012).

- "Pharmacological Characterization of 1-(5-Chloro-6-(Trifluoromethoxy)-1H-Benzoimidazol-2-yl)-1H-Pyrazole-4-Carboxylic Acid (JNJ-42041935), A Potent and Selective HIF Prolyl Hydroxylase (PHD) Inhibitor", T.D. Barrett, H.L. Palomino, T.I. Brondstetter, K.C. Kanelakis, X. Wu, P.V. Haug, W. Yan, A. Young, H. Hua, J.C. Hart, D.T. Tran, H. Venkatesan, M.D. Rosen, H.M. Peltier, K. Sepassi, M.C. Rizzolio, **S.D. Bembenek**, T. Mirzadegan, M.H. Rabinowitz, N.P. Shankley, *Mol. Pharmacol.* **79**, 910 (2011).

- "Benzimidazole-2-Pyrazole HIF Prolyl 4-Hydroxylase Inhibitors as Oral Erythropoietin Secretagogues", M.D. Rosen, H. Venkatesan, H.M. Peltier, **S.D. Bembenek**, K.C. Kanelakis, L.X. Zhao, B. Leonard, F.M. Hocutt, X. Wu, H.L. Palomino, T.I. Brondstetter, P.V. Haug, L.Cagnon, W.Yan, L.A. Liotta, A. Young, T. Mirzadegan, N.P. Shankley, T.D. Barrett, M.H. Rabinowitz, *ACS Med. Chem. Lett.* **1**, 526 (2010).

- "Diazinones as P2 Replacements for Pyrazole-Based Cathepsin S Inhibitors", M.K. Ameriks, **S.D. Bembenek**, M.T. Burdett, I.C. Choong, J.P. Edwards, D. Gebauer, Y.Gu, L. Karlsson, H.E. Purkey, B.L. Staker, S. Sun, R.L. Thurmond, J. Zhu, *Bioorg. Med. Chem. Lett.* **20**, 4060 (2010).

- "Thioether Acetamides as P3 Binding Elements for Tetrahydropyrido-Pyrazole Cathepsin S Inhibitors", D.K. Wiener, A. Lee-Dutra, **S. Bembenek**, S. Nguyen, R.L. Thurmond, S. Sun, L. Karlsson, C. A. Grice, T. K. Jones, J.P. Edwards, *Bioorg. Med. Chem. Lett.* **20**, 2379 (2010).

- "Pyrazole-Based Cathepsin S Inhibitors with Arylalkynes as P1 Binding Elements", M.K. Ameriks, F.U. Axe, **S.D. Bembenek**, J.P. Edwards, Y. Gu, L. Karlsson, M. Randal, S. Sun, R.L. Thurmond, J. Zhu, *Bioorg. Med. Chem. Lett.* **19**, 6131 (2009).

- "Ligand Efficiency and Fragment Based Drug Discovery", **S.D. Bembenek**, B.A. Tounge and C.H. Reynolds, *Drug Discovery Today* **14**, 278 (2009).

- "Lead Identification of Acetylcholinesterase Inhibitors–Histamine H_3 Receptor Antagonists from Molecular Modeling", **S. D. Bembenek**, J.M. Keith, M.A. Letavic, R. Apodaca, A.J. Barbier, L. Dvorak, L. Aluisio, K.L. Miller, T.W. Lovenberg and N.I. Carruthers, *Bioorg. Med. Chem.* **16**, 2968 (2008).

- "Dual Binding Site Inhibitors of B-Raf Kinase", R.L. Wolin, **S.D. Bembenek**, J. Wei, S. Crawford, K. Lundeen, A. Brunmark, L. Karlsson, J.P. Edwards and J. Blevitt. *Bioorg. Med. Chem. Lett.* **18**, 2825 (2008).

- "Ligand Binding Efficiency: Trends, Physical Basis, and Implications", C.H. Reynolds, B.A. Tounge and **S.D. Bembenek**, *J. Med. Chem.* **51**, 2432 (2008).

- "The Identification of a Potent, Selective and Orally Active Leukotriene A_4 Hydrolase Inhibitor with Anti-Inflammatory Activity", C.A. Grice, K.L. Tays, B.M. Savall, J. Wei, C.R. Butler, F.U. Axe, **S.D. Bembenek**, A.M. Fourie, P. Dunford, K. Lundeen, F. Coles, X. Xue, J.Riley, K. Williams, L. Karlsson, and J.P. Edwards, *J. Med. Chem.* **15**, 4150 (2008).

- "A Novel B-RAF Inhibitor Blocks Interleukin-8 (IL-8) Synthesis in Human Melanoma Xenografts, Revealing IL-8 as a Potential Pharmacodynamic Biomarker", S. Crawford, D. Belajic, J. Wei, J.P. Riley, P.J. Dunford, **S. Bembenek**, A. Fourie, J.P. Edwards, L.Karlsson, A. Brunmark, R.L. Wolin and J.M. Blevitt, *Mol. Cancer Ther.* **7**, 492 (2008).

- "The Role of Molecular Size in Ligand Efficiency", C.H. Reynolds, **S.D. Bembenek** and B.A. Tounge, *Bioorg. Med. Chem. Lett.* **17**, 4258 (2007).

- "Three-Dimensional Models of Histamine H_3 Receptor Antagonist Complexes and their Pharmacophore", F.U. Axe, **S.D. Bembenek** and S. Szalma, *J. Mol. Graph. Model.* **24**, 456 (2006).

- "Calculation of the Surface Tension of Oxygen using Molecular Dynamics Simulations", **S.D. Bembenek**, *J. Chem. Phys.* **124**, 014709 (2006).

- "A Kinetic Theory for Dilute Dipolar Systems", **S.D. Bembenek** and G. Szamel, *J. Chem. Phys.* **117**, 8886 (2002).

- "Instantaneous Normal Modes Analysis of Amorphous and Supercooled Silica", **S.D. Bembenek** and B.B. Laird, *J. Chem. Phys.* **114**, 2340 (2001).

- "The Role of Attractive Interactions in Self-Diffusion", **S.D. Bembenek** and G. Szamel, *J. Phys. Chem. B* **104**, 10647 (2000).

- "Transitioning Model Potentials to Real Systems. II: Application to Molecular Oxygen", **S.D. Bembenek** and B. M. Rice, *J. Chem. Phys.* **113**, 2354 (2000).

- "Transitioning Model Potentials to Real Systems", **S.D. Bembenek** and B. M. Rice, *Mol. Phys.* **97**, 1085 (1999).

- "Hydrogen Bonding in Tungsten (VI) Salicylate Free Acids", T.E. Baroni, **S.D. Bembenek**, J.A. Heppert, R.R. Hodel, B.B. Laird, M.D. Morton, F. Takusagawa, *Coordination Chemistry Reviews* **174**, 255 (1998).

- "Localization and the Glass Transition", B.B. Laird and **S.D. Bembenek**, *J. Phys.: Condens. Matter* **8**, 9569 (1996).

- "The Role of Localization in Glasses and Supercooled Liquids", **S.D. Bembenek** and B.B. Laird, *J. Chem. Phys.* **104**, 5199 (1996).

- "Instantaneous Normal Modes and the Glass Transition", **S.D. Bembenek** and B.B. Laird, *Phys. Rev. Lett.* **74**, 936 (1995).

Books

- *The Cosmic Machine: The Science That Runs Our Universe and the Story Behind It.* **S. Bembenek**, San Diego: Zoari Press, 2017.

Book Chapters

- "A Web-Based Chemoinformatics System for Drug Discovery", in *Concepts, Methods, and Tools for Drug Discovery*; Methods in Molecular Biology Series 275, **S.D. Bembenek**, B.A. Tounge, S.J. Coats and C.H. Reynolds, Humana Press, NJ, (2004).

Patents

- "Preparation of Novel Heteroaryl and Heterocycle Compounds for Inhibiting the Activity of PI3K", W. Su, G. Dai, H. Jia, Z. Zhang, J. Weng, J.D. Venable, **S.D Bembenek,** W. Chai, S.P. Meduna, J.M. Keith, W. Eccles, A.D. Lebsack, W.M. Jones, R.C. Smith *PCT Int. Appl.*, 195pp., CODEN:PIXXD2; WO 2016119707, A1; 2016:1273788, CAN165:260951 (2016).

- "Preparation of Novel Heteroaryl and Heterocycle Compounds as PI3K inhibitors", W. Su, G. Dai, K. Xiao, H. Jia, J.D. Venable, **S.D Bembenek,** W. Chai, *U.S. Pat. Appl. Publ.*, 206pp., CODEN: USXXCO; US 20150291593, A1; 2015:1651235, CAN163:601761 (2015).

- "Preparation of Heteroaryl and Heterocycle Compounds as Inhibitors of PI3K for Treating Inflammatory and Autoimmune Disorders and Cancer", W. Su, G. Dai, K. Xiao, H. Jia, J.D. Venable, **S.D Bembenek**, *PCT Int. Appl.*, 262pp., CODEN:PIXXD2; WO 2014015675, A1; 2014:152083, CAN160:278937 (2014).

- "Novel Heteroaryl and Heterocycle Compounds as PI3K Inhibitors, Composition and Their Preparation and Use In The Treatment Of Immune-Based Diseases and Cancer", W. Su, G. Dai, K. Xiao, H. Jia, Z. Zhang, J.D. Venable, **S.D Bembenek**, W. Chai, *PCT Int. Appl.*, 270pp., CODEN:PIXXD2; WO 2014015830, A1; 2014:151959, CAN160:278947 (2014).

- "Preparation of Heteroaryl and Heterocycle Compounds as PI3K Inhibitors", W. Su, G. Dai, K. Xiao, H. Jia, J.D. Venable, **S.D Bembenek**, *PCT Int. Appl.*, 153pp., CODEN:PIXXD2; WO 2014015523, A1; 2014:141912, CAN160:265131 (2014).

- "Preparation of Quinazolinones as Prolyl Hydroxylase Inhibitors", **S. D Bembenek**, F. M Hocutt, B.E. Leonard Jr., M. H. Rabinowitz, M.D. Rosen, K.T. Tarantino, H. Venkatesan, *U.S. Pat. Appl. Publ.*, 91pp., CODEN: USXXCO; US 20100204226, A1; 2010:1003346, CAN153:287020 (2010).

- "Preparation of Aryl-Substituted Bridged or Fused Diamines as Therapeutic Modulators of Leukotriene A4 Hydrolase", G.M. Bacani, **S.D. Bembenek,** W. Eccles, J.P. Edwards, M.T. Epperson, L. Gomez, C.A. Grice, A.M. Kearney, A.M. Landry-Bayle, A. Lee-Dutra, K.J. McClure, T. Mirzadegan, A. Santillan, Jr., *U.S. Pat. Appl. Publ.*, 108 pp., CODEN: USXXCO; US 20090111794, A1; 2009:524225, CAN150:472761 (2009).

- "Pyrimidinyl Imidazoles as Inhibitors of B-Raf Kinase", **S. Bembenek**, C. Butler, H. Cui, J. Edwards, D. Gustin, B. Pio, C. Sehon, J. Wei and R. Wolin, *U.S. Provisional Patent Appl.* (2006).

- "Preparation of Benzimidazole, Benzothiazole and Benzoxazole Derivatives and Their Use as LTA4 Hydrolase Modulators", F.U. Axe, **S.D. Bembenek**, C.R. Butler, J.P. Edwards, A.M. Fourie, C.A. Grice, B.M. Savall, K.L. Tays, J. Wei, *PCT Int. Appl.*, 465 pp., CODEN: PIXXD2; WO 2005012297, A1; 2005:120926, CAN142:219286 (2005).

- "Preparation of Benzimidazole, Benzothiazole and Benzoxazole Derivatives and Their Use as LTA4 Hydrolase Modulators", F.U. Axe, **S.D. Bembenek**, C.R. Butler, J.P. Edwards, A.M. Fourie, C.A. Grice, B.M. Savall, K.L. Tays, J. Wei, *PCT Int. Appl.*, 390 pp., CODEN: PIXXD2; WO 2005012296, A1; 2005:120925, CAN142:219285 (2005).