

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Salemme, F Raymond

eRA COMMONS USER NAME (agency login): fsalemme1

POSITION TITLE: Founder & President

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Yale University, New Haven, CT	BA	1967	Molecular Biophysics
University of California, San Diego, CA	MS	1970	Protein Crystallography
University of California, San Diego, CA	PHD	1972	Protein Crystallography
University of California, San Diego, CA	Postdoctoral Fellow	1973	Electron Transport Mechanisms

A. Personal Statement

The PI is a structural biologist-entrepreneur with over 35 years experience in academia, biotechnology and the drug discovery industry. The PI has been a pioneer in the application of both new experimental and computational tools for protein engineering and drug discovery. The PI founded Imiplex LLC (imiplex.com) to develop protein-based nanotechnology for biomedical and biomaterials applications. The company has built an extensive engineered protein technology and intellectual property base, with 3 US patents issued in 2015-2016.

My scientific career began with academic research in structural biology and protein structural theory, and later evolved into pioneering work on the application of structure-based design, computational, and biophysical methods for protein engineering and drug discovery (beta-sheet.org). I have built several successful multidisciplinary R&D organizations, including 3-Dimensional Pharmaceuticals (3DP). 3DP was a drug discovery company I founded that integrated combinatorial chemistry, structure-based drug design, high throughput screening, and cheminformatics within a comprehensive IT infrastructure. 3DP went public in 2000, was acquired by J&J in 2003, and subsequently became a key component of the J&J (now Janssen) R&D organization. As the technology founder of the company, I invented and commercially developed ThermoFluor (aka differential scanning fluorimetry or DSF), a widely used thermodynamic method for protein characterization and HTS, as well as other drug discovery technologies that were successfully licensed to pharma development partners. I have always been a hands-on scientist and am an author of 41 issued US patents (including 3 recently issued to Imiplex LLC) on engineered proteins, computational methods for drug design, biophysical assay methods, and instrumentation, as well as ~100 research articles. As a successful entrepreneur and technological innovator, I have been effective in organizing and leading scientific and business teams in the development and commercialization of new technology and pharmaceutical products. I have raised over \$150 Million in biotech company financing through both venture rounds and public stock offerings, and structured technology licensing and collaborative R&D deals worth over \$50 Million.

Some highly cited publications are listed below. See also scientific contributions below and my website www.beta-sheet.org.

1. Weber PC, Ohlendorf DH, Wendoloski JJ, Salemme FR. Structural origins of high-affinity biotin binding to streptavidin. *Science*. 1989 Jan 6;243(4887):85-8. PubMed PMID: [2911722](https://pubmed.ncbi.nlm.nih.gov/2911722/). (1063 Citations 04/01/16)
2. Howard AJ, Gilliland GL, Finzel BC, Poulos TL, Ohlendorf DH, and Salemme FR. Use of an Imaging Proportional Counter in Macromolecular Crystallography. *J. Appl. Cryst.* 1987; 20: 383-387 (543 citations 04/01/16)

3. Pantoliano MW, Petrella EC, Kwasnoski JD, Lobanov VS, Myslik J, Graf E, Carver T, Asel E, Springer BA, Lane P, Salemme FR. High-density miniaturized thermal shift assays as a general strategy for drug discovery. *J Biomol Screen*. 2001 Dec;6(6):429-40. PubMed PMID: [11788061](#). (519 citations 04/01/16)
4. Salemme FR. An hypothetical structure for an intermolecular electron transfer complex of cytochromes c and b5. *J Mol Biol* 1976 Apr 15;102(3):563-8. PubMed PMID: [178879](#). (348 citations 04/01/16)

B. Positions and Honors

Positions and Employment

1973 - 1983	Assistant, Associate and Full Professor, University of Arizona, Department of Chemistry & Biochemistry, Tucson, AZ
1983 - 1984	Director of Protein Engineering, Genex Corp, Gaithersburg, MD
1985 - 1990	Research Leader, E.I. DuPont Central Research & Development Department, Wilmington, DE
1990 - 1991	Director, DuPont Merck Pharmaceuticals, Wilmington, DE
1991 - 1993	Senior Director, Sterling Winthrop Pharmaceuticals, Collegeville, PA
1993 - 2003	Founder & Chief Executive Officer, 3 Dimensional Pharmaceuticals, Exton, PA
2004 - 2011	President & CEO, RedPoint Bio, Ewing, NJ
2004 - present	Founder & President, Imiplex LLC, Yardley, PA

Other Experience and Professional Memberships

1980 - 1996	Member, NIH Special Study Section on Large-Scale Computer and Synchrotron Resources
1981 - 1993	Special Reviewer, Biological Synchrotrons SLAC (Stanford), CHESS (Cornell), NSLS (Brookhaven National Labs)
1982 - 1982	Member, NIH Study Section, Biochemistry and Biophysics
1982 - 1983	Sabbatical, Yale University
1983 - 1986	Member, NSF Biophysics Review Panel
1985 - 1985	Co-Organizer, Gordon Research Conference on Diffraction Methods in Molecular Biology
1985 - 1993	Advisory Board Member, NASA Macromolecular Crystallography Center UAB Birmingham
1985 - 1996	Member, Brookhaven Protein Data Bank Advisory Committee
1986 - 1987	Member, NASA Space Science Applications Committee
1987 - 1987	Member, NIH Review Committee Structural Biology for Targeted Drug Design for AIDS
1990 - 1993	Member, Keck Center for Computational Biology Rice University Scientific Advisory Board
1991 - 1996	Editorial Board Member, PROTEINS: Structure, Function, Genetics
1992 - 1992	Member, Chemical Science and Technology Panel, NIST NAS/NRC Board of Assessment
1992 - 1992	Member, NIH Review Committee Structural Biology for Targeted Drug Design for AIDS
1992 - 1994	Editorial Board Member, Structure
1992 - 1995	Member, North Carolina Supercomputing Center Resource Advisory Committee
1996 - 1996	Member, NIH Special Study Section on Large-Scale Computer and Synchrotron Resources
1999 - 1999	Member, NIH Special Study Section on the Protein Structure Initiative
1999 - 2005	Member, NIST Visiting Committee (VACT)
2001 - 2008	Advisory Board Member, Penn State Nanofabrication Manufacturing Partnership
2002 - 2008	Member, Biophysical Society Finance Committee
2004 - 2009	Editorial Board Member, Assay and Drug Development Technologies
2004 - 2004	Member, National Cancer Institute Special Review Committee for Chemical Genomics
2004 - 2008	Board of Scientific Counselors, NIH NCBI
2004 - 2008	PubChem Advisory Board, NIH NCBI
2005 - 2005	Member, NIH Special Study Section on the Protein Structure Initiative
2007 - 2007	Guest Lecturer, Rutgers University
2008 - 2015	Board of Advisors, Hauptman Woodward Medical Research Institute
2008 - 2008	Chair, NIH Special Study Section on Drug Docking and Screening Data Resource
2009 - 2009	Chair, NIH Special Study Section on Structural Genomics Knowledge Bases

Honors

1967	Predocctoral Fellow, US Public Health Service
1967	Scholar of the House & Devane Prize, Yale University
1978	Teacher-Scholar Award, Camille and Henry Dreyfus Foundation
1991	US National US-USSR Workshop on Proteins and Glasses, US National Academy of Sciences
1998	Ernst & Young Entrepreneur of the Year Award, Philadelphia Area Biotechnology
2000	Adjunct Faculty, Princeton University Department of Chemistry
2005	Guest Lecturer, Yale University & Yale University School of Medicine

C. Contribution to Science

1. Structural Properties of Proteins

Summary: These papers describe pioneering studies defining the origins of the major structural classifications of proteins, the factors that are responsible for their structural stability, and some of the first applications of structural heuristics to protein modeling.

- Wendoloski JJ, Salemme FR. PROBIT: a statistical approach to modeling proteins from partial coordinate data using substructure libraries. *J Mol Graph.* 1992 Jun;10(2):124-6. PubMed PMID: [1637750](#).
- Finzel BC, Kimatian S, Ohlendorf DH, Wendoloski JJ, Levitt M, Salemme FR. Crystallographic and Modeling Methods in Molecular Design. Ealick S, Bugg CE, editors. New York: Springer Verlag; 1990. FRAGLE: Modeling with Substructure Libraries Derived from Known Protein Structures; p.175-189.
- Salemme FR. Structural properties of protein beta-sheets. *Prog Biophys Mol Biol.* 1983;42(2-3):95-133. PubMed PMID: [6359272](#).
- Weber PC, Salemme FR. Structural and functional diversity in 4-alpha-helical proteins. *Nature.* 1980 Sep 4;287(5777):82-4. PubMed PMID: [6251384](#).

2. Computer Modeling & Molecular Dynamics Simulations of Complex Biological Systems

Summary: These papers describe pioneering studies in the molecular dynamics of large systems of biological and materials science interest.

- Wasserman ZR, Salemme FR. A molecular dynamics investigation of the elastomeric restoring force in elastin. *Biopolymers.* 1990 Oct-Nov;29(12-13):1613-31. PubMed PMID: [2386809](#).
- Wendoloski JJ, Kimatian SJ, Schutt CE, Salemme FR. Molecular dynamics simulation of a phospholipid micelle. *Science.* 1989 Feb 3;243(4891):636-8. PubMed PMID: [2916118](#).
- Wendoloski JJ, Matthew JB, Weber PC, Salemme FR. Molecular dynamics of a cytochrome c-cytochrome b5 electron transfer complex. *Science.* 1987 Nov 6;238(4828):794-7. PubMed PMID: [2823387](#).
- Salemme FR. Cooperative motion and hydrogen exchange stability in protein beta-sheets. *Nature.* 1982 Oct 21;299(5885):754-6. PubMed PMID: [7121607](#).

3. Biological Electron Transfer, Biomaterials, & Protein Engineering

Summary: My work in the structure of electron transfer proteins established fundamental principles of biological electron transfer, including specifically, 1) the role of complementary electrostatic interactions in the facilitation of most biological transfer interactions between reversibly interacting electron transfer proteins, and 2) that biological electron transfer took place by facilitated electron tunneling, as opposed to classical outer sphere electron transfer mechanisms common for non-biological metal complexes in solution. I was also instrumental in the development of novel methods for the production of engineered proteins for improved biopharmaceuticals as well as for new technological applications in advanced materials and molecular electronics.

- a. O'Brien JP, Hoess RH, Gardner KH, Locke RL, Wasserman ZR, Weber PC, Salemme FR. Silk Polymers: Materials Science and Biotechnology. Kaplan D, Adams WW, Farmer B, Vines C, editors. New York: American Chemical Society; 1994. Design, Synthesis and Fabrication of a Novel, Self-Assembling Fibrillar Protein; p.104-117.
- b. Sligar SL, Salemme FR. Protein Engineering for Molecular electronics. Current opinion in structural biology. 1992; 2:587.
- c. Matthew JB, Weber PC, Salemme FR, Richards FM. Electrostatic orientation during electron transfer between flavodoxin and cytochrome c. Nature. 1983 Jan 13;301(5896):169-71. PubMed PMID: [6296691](#).
- d. Salemme FR. An hypothetical structure for an intermolecular electron transfer complex of cytochromes c and b5. J Mol Biol. 1976 Apr 15;102(3):563-8. PubMed PMID: [178879](#).

4. Protein Structure Determination by X-ray Crystallography

Summary: Throughout my career, I have been an active practitioner and innovator of methods of structure determination using protein crystallography. I have helped develop and use X-ray crystallography to investigate protein structure and function, and as a key component for protein engineering and drug discovery.

- a. Weber PC, Ohlendorf DH, Wendoloski JJ, Salemme FR. Structural origins of high-affinity biotin binding to streptavidin. Science. 1989 Jan 6;243(4887):85-8. PubMed PMID: [2911722](#).
- b. Salemme FR, Genieser L, Finzel BC, Hilmer RM, Wendoloski JJ. Molecular Factors Stabilizing Protein Crystals. Journal of crystal growth. 1988; 90:273.
- c. Howard AJ, Gilliland GL, Finzel BC, Poulos TL, Ohlendorf DH, Salemme FR. Use of an Imaging Proportional Counter in Macromolecular Crystallography. Journal of applied crystallography. 1987; 20:383.
- d. Finzel BC, Salemme FR. Lattice mobility and anomalous temperature factor behaviour in cytochrome c'. Nature. 1985 Jun 20-26;315(6021):686-8. PubMed PMID: [2989701](#).

5. Drug Discovery: Structure-Based Drug Design, Computer-Directed Combinatorial Chemistry, Biophysical Drug Screening

Summary: These papers represent the evolution of scientific understanding and technology for integration of biophysical methods, computer-directed combinatorial chemistry and protein 3D structure for drug discovery.

- a. Carver TE, Bordeau B, Cummings MD, Petrella EC, Pucci MJ, Zawadzke LE, Dougherty BA, Tredup JA, Bryson JW, Yanchunas J Jr, Doyle ML, Witmer MR, Nelen MI, DesJarlais RL, Jaeger EP, Devine H, Asel ED, Springer BA, Bone R, Salemme FR, Todd MJ. Decrypting the biochemical function of an essential gene from Streptococcus pneumoniae using ThermoFluor technology. J Biol Chem. 2005 Mar 25;280(12):11704-12. PubMed PMID: [15634672](#).
- b. Pantoliano MW, Petrella EC, Kwasnoski JD, Lobanov VS, Myslik J, Graf E, Carver T, Asel E, Springer BA, Lane P, Salemme FR. High-density miniaturized thermal shift assays as a general strategy for drug discovery. J Biomol Screen. 2001 Dec;6(6):429-40. PubMed PMID: [11788061](#).
- c. Salemme FR, Spurlino J, Bone R. Serendipity meets precision: the integration of structure-based drug design and combinatorial chemistry for efficient drug discovery. Structure. 1997 Mar 15;5(3):319-24. PubMed PMID: [9083110](#).
- d. Weber PC, Wendoloski JJ, Pantoliano MW, Salemme FR. Crystallographic and Thermodynamic Comparison of Natural and Synthetic Ligands Bound to Streptavidin. Journal of the American Chemical Society. 1992; 114:3197.

D. Research Support

Completed Research Support

2012, PA BioAdvance

Salemme, F Raymond (PI)

06/01/12-12/01/12

NanoStructure Assembly

This is a convertible debt equity investment from the Biotechnology Greenhouse of Pennsylvania/.

Role: PI