

THE UNIVERSITY OF BRITISH COLUMBIA
Curriculum Vitae for Faculty Members

Date: Dec. 2009

1. **SURNAME:** Plotkin **FIRST NAME:** Steven
MIDDLE NAME(s): Samuel
2. **DEPARTMENT/SCHOOL:** Physics
3. **FACULTY:** Science
4. **PRESENT RANK:** Assistant Professor

5. POST-SECONDARY EDUCATION

University or Institution	Degree	Subject Area	Dates
University of Illinois,Urbana-Champaign	Ph. D.	Physics, Advisor: Peter G. Wolynes	Oct. 1998
University of Illinois,Urbana-Champaign	M. Sc.	Physics	Sept. 1994
Rensselaer Polytechnic Institute	B.Sc.	Physics Advisor: Charles P. Bean	Aug. 1990

6. EMPLOYMENT RECORD

(a) Prior to coming to UBC

University, Company or Organization	Rank or Title	Dates
University of California at San Diego	Post-Doctoral Fellow	Aug 99 – Aug 01
University of California at San Diego	Post-Doctoral Researcher, Advisor: Jose N. Onuchic	Oct 98 – Aug 99
University of Illinois at Urbana-Champaign	Summer research assistant on CLEO project	Jun-Aug 1994
Rensselaer Polytechnic Institute	Summer research fellow in High energy theory	Jun-Aug 1992

(b) At UBC

Rank or Title	Dates
Assistant Professor	Aug. 2001
Associate member applied mathematics	March 2006

7. TEACHING

(a) Areas of special interest and accomplishments

Biological physics, Statistical physics, Phase transitions and renormalization group,
 Mechanics.

8. SCHOLARLY AND PROFESSIONAL ACTIVITIES

(a) Areas of special interest and accomplishments

My research contributions include the following: The quantitative development of the energy landscape theory of protein folding, including Non-Markovian reaction dynamics, structural and energetic heterogeneity in folding, and the general prediction of “noise-assisted” folding by non-native interactions; The theory of three-body interactions in protein folding models, and the demonstration that many-body interactions improve predictive accuracy; Original development of the equations describing the generalization of Euclidean distance to higher dimensional objects, and the application of these equations to protein conformational dynamics; The first theory of a spatially varying, anisotropic dielectric function in proteins, and its application to electrostatic stability and ion channel permeability; The first computational

model of DNA with rigid-body ellipsoidal constituents, and its predictions of new structural transitions in single and double-stranded DNA; The development of an algorithm capable of predicting misfolding nuclei in proteins, and its application of predicting targets for rational immunotherapy in neurodegenerative diseases.

(b) Invited Presentations

Invited Symposia Lectures

- Telluride Science Research Center Workshop on Protein and Peptide Interactions in Cellular Environments, Telluride, CO July 19-23, 2010.
- Telluride Science Research Center Workshop on Characterizing Landscapes: From Biomolecules to Cellular Networks, Telluride, CO June 14th-18th, 2010.
- Complex Energy Landscapes Symposium, German physical society meeting, Regensburg, Germany, March 21-26, 2010.
- “Frontiers in Biomolecular Physics”, March 17, 2009, APS March meeting, Pittsburgh, PA.
- First Annual Protein and Peptide conference (PepCon-2008), April 22-24, 2008 Shenzhen, China
- “Research Day on Protein Misfolding Diseases”, March 8, 2008, UBC Vancouver.
- “New Frontiers in Biological Physics” 2008 APS March meeting, New Orleans, LA.
- “Soft Surfaces and Interfaces: from Proteins and Lipids to Cells” Symposium in honor of Myer Bloom Sept 13-14, 2007.
- “Mechanical Behavior of Glassy Materials” PITP conference, Vancouver, July 21-23, 2007.
- US-Japan Symposium on Folding and Design, University of Pennsylvania, PA (May 2005).
- CAP Congress, Quebec City. Symposium in honor of Dr. John Harrison (June 2002).
- Invited introduction at the Quantitative Challenges in the Post-Genomic Sequence Era Workshop and Symposium, San Diego, CA (January 2000).

Invited Lectures

- University of California, Santa Barbara (Aug 2009), Computational Biology group seminar, Department of Chemistry.
- The 6th Congress of the International Society for Theoretical Chemical Physics (ISTCP-VI) Vancouver, Canada (July 2008).
- University of British Columbia (Mar 2008) Department of Physics colloquium.
- Kyoto University, Japan (Dec 2007) Department of Biophysics Seminar
- McMaster University (Dec 2007), Department of Physics Colloquium.
- SUNY Stony Brook (Dec 2007), Department of Physics seminar.
- U Toronto (Nov 2007), Department of Biochemistry seminar for the CIHR Training Program in Protein Folding: Principles & Diseases.
- U. Western Ontario (Nov 2007), Department of Applied Mathematics Colloquium.
- University of California Los Angeles (Oct 2007), Department of Bio-Mathematics Seminar.
- Theoretical Biophysics session (DPT/DTP) CAP conference, Brock University, St. Catharines (June 12, 2006)
- Simon Fraser University (April 2006), Biological Physics and Soft condensed matter seminar.
- University of British Columbia, (March 2006), Institute for Applied Mathematics Invited seminar
- University of British Columbia (November 2005), Physical Chemistry Seminar.
- University of British Columbia (September 2005), Mathematical Biology Seminar.
- IPAM Workshop, “MA2005 Workshop I: Multiscale Modeling in Soft Matter and Bio-Physics” Los Angeles (Sept 2005).
- Congress of the CAP Conference, Vancouver BC (June 2005)
- Rice University (Feb 2005), Keck Seminar.
- University of Victoria (Feb 2005), Colloquium at the Department of Physics.
- University of British Columbia Vancouver, BC (Sept 2004), Theory Seminar, Department of Physics and Astronomy.

- Gordon Research Conference on Protein Folding Dynamics, Ventura, CA (Jan 2004).
- University of British Columbia, Vancouver, BC (March 2003), Theory seminar, Department of Physics and Astronomy.
- University of British Columbia, Vancouver, BC (November 2002), Physics Society seminar at the Department of Physics.
- Simon Fraser University, Burnaby, BC (December 2001), Seminar at the Department of Physics.
- University of California at San Diego, La Jolla, CA (April 2001), Non-linear Dynamics seminar at the Department of Physics.
- American Chemical Society, San Diego, CA (April 2001).
- University of British Columbia, Vancouver, British Columbia (March 2001), Biophysics seminar at the Department of Physics.
- Brown University, Providence, RI (March 2001), Department of Applied Mathematics.
- Purdue University, West Lafayette, IN (February 2001), Department of Physics Colloquium.
- Rice University, Houston, TX (February 2001), Department of Physics Colloquium.
- Wake Forest University, Winston-Salem NC (February 2001), Department of Physics Colloquium.
- University of IA, Ames, IA (February 2001), Department of Physics Colloquium.
- University of California at San Diego, La Jolla, CA (January 1998), Non-linear dynamics seminar, Department of Physics.

(c) Students Supervised

Postdoctoral Fellows

Researchers Name	Program Type	Year		Principal Supervisor	Projects	Current Position
		Start	Finish			
Erik Abrahamsson	PDF (Sweden -America Foundation)	Jan 2008	Jan 2010	Steven Plotkin	Development of molecular visualization, Nanopore translocation.	

Postdoctoral Research Associates

Researchers Name	Program Type	Year		Principal Supervisor	Projects	Current Position
		Start	Finish			
Reza Ejtehadi	PDRA	Oct-2002	Oct 2004	Steven Plotkin	Reaction coordinates in protein folding. Nano-pore transport problems.	Assistant Professor, Sharif U. Tehran
Yuri Gusev	PDRA	May-2003	May 2004	Steven Plotkin	Gene location and transcription. Steiner trees and phylogeny.	IRMACS Post doctoral researcher, SFU, B.C.

Graduate Students

Student Name	Program Type	Year		Principal Supervisor	Co-Supervisor(s)	Current Position/Awards
		Start	Finish			
Baris Oztop ¹	MSc	Sept 2002	July 2004	Steven Plotkin		PhD student, Bilkent U., Turkey
Alena Shmygelska ²	PhD	Sept 2002	Sept 2006	Holger Hoos (Comp-Sci)	Steven Plotkin	Post-doc fellow, Stanford
Alex Morriss-Andrews ³	MSc	Sept 2007	Aug 2009	Steven Plotkin (co-supervised)	Joerg Rottler (co-supervised)	Ph.D. student, UCLA Applied Math
Shirin Hadizadeh ⁴	PhD	Sept 2005		Steven Plotkin		
Ali Reza Mohazab ⁵	PhD	Feb 2007		Steven Plotkin		
William Guest ⁶	M.D./Ph.D.	Sept 2007		Steven Plotkin (co-supervised)	Neil Cashman (co-supervised)	

¹**Thesis title:** "Effects of heterogeneity on protein folding rates"

²**Thesis title:** "Novel heuristic search methods for protein folding and identification of folding pathways" **Awards:** NSERC Graduate Scholarship, NSERC Post-doctoral fellowship.

³**Thesis title:** "Coarse-grained molecular dynamics simulations of DNA representing bases as ellipsoids" **Awards:** NSERC Graduate Scholarship.

⁴**Awards:** University Graduate Fellowship.

⁵**Awards:** University Graduate Fellowship.

⁶**Awards:** Michael Smith Foundation for Health Research Trainee Award.

Undergraduate Students

Student Name	Program Type	Year		Principal Supervisor	Project
		Start	Finish		
Philip Edgecumbe	Eng Phys coop work-study	Sept 2009		Steven Plotkin	Computational models of DNA under force.
Gene Polovy	Phys 449 thesis	Sept 2009		Steven Plotkin	Protein unfolding and misfolding
Alvin Cheung	Phys 449 thesis	Sept 2008	May 2009	Steven Plotkin	Osmolytes and protein stability
Sebastian Ohse	ISCI (Integrated Sciences) 448B Directed Studies	May 2008	August 2008	Steven Plotkin	Effects of confinement and osmolyte concentration on protein stability.
Christopher Yearwood	summer co-op research, Phys 449 thesis	Summer 2006, Fall 2006	Summer 2007	Steven Plotkin	Simulations of coarse-grained DNA with rigid-body molecular dynamics.
Johanna Hansen	summer co-op research	Summer 2005	Summer 2005	Steven Plotkin/ Andre Marziali	Single molecule gene sequencing by nano-pore translocation.

Benjamin Lindler	Phys 449 Thesis	Fall 2003	Spring 2004	Steven Plotkin	Interaction potentials for protein structure prediction
Justin Hsu	Phys 449 Thesis	Fall 2003	Spring 2004	Steven Plotkin	Simulation tests of protein folding mechanisms
David Rudko	Phys 349	Summer 2004	Summer 2004	Steven Plotkin	Protein-DNA binding; Gene finding
Stefan Avall	Phys 449 Thesis	Fall 2002	Spring 2003	Steven Plotkin	Large- scale simulations of protein folding with implicit many-body Hamiltonians.
Sebastian Cogswell	Phys 449 Thesis	Fall 2002	Spring 2003	Steven Plotkin	Many-variable analysis of determinants of protein folding rates.
Brian Ng	Phys 449 Thesis	Fall 2001	Spring 2002	Steven Plotkin	Gene search problems in transcription.

Visitors

Researchers Name	Program Type	Year		Principal Supervisor	Projects
		Start	Finish		
Matthias Huber	Rotary Scholar	June 2004	April 2005	Steven Plotkin	Mechanisms of protein folding.
Brent Wathen	Summer research assistant	May 2005	May 2005	Steven Plotkin	Protein structure prediction
Apichart Linhananta	Sabbatical visitor, Lakehead University	January 2009	June 2009	--	Osmolyte-Induced Protein Stability

(d) Conference Participation (Organizer, Keynote Speaker, etc.)

Organized or Co-organized Workshops/Conferences

<i>Organizer, "New Frontiers in Molecular Biophysics" (Invited speakers A.Grosberg, A. Dunn, D. Astumian, S. Plotkin, J. Saven) 2009 APS March Meeting Symposium.</i>
<i>Organizer, "New Frontiers for Biological Physics" (Invited speakers Z. Bryant, E. Evans, K.C. Huang, E. Kussell, S. Plotkin) 2008 APS March Meeting Symposium.</i>
<i>Co-organizer (with Nancy Forde, Eldon Emberly (SFU Physics), Eric Cytrynbaum (UBC Math)) of joint UBC/SFU Biophysics Retreat, October 13-15, 2006. http://www.sfu.ca/biophysics/frontiers/</i>
<i>Organizer, Theoretical Biophysics session (DPT/DTP) CAP conference June 2006, Brock University (Invited speakers J. Banavar, R. Bundschuh, B. Ingalls, S. Plotkin, J. Portman).</i>

9. SERVICE TO THE UNIVERSITY

University

- Pacific Institute for the Mathematical Sciences (PIMS) UBC Steering Committee 2008-09
- Institute for Applied Mathematics (IAM) associate membership 2006.
- PITP Complex systems division membership.
- Guest lecturer, Science One program at UBC. (2003)

10. SERVICE TO THE COMMUNITY

(a) Memberships on scholarly societies, including offices held and dates

- Protein Society (April 2009)
- PrioNet Canada (Jul 2008-)
- American Physical Society (Lifetime member)
- Canadian Association of Physicists
- Biophysical Society

(f) Reviewer (journal, agency, etc. including dates)

Reviewer for the following research journals: Science, Biophysical Journal, Journal of Chemical Physics, Journal of Physical Chemistry, Macromolecular Theory and Simulations, Physical Review Letters, Physical Review E, Proceedings of the National Academy of Sciences USA, Proteins: Structure, Function and Genetics, Europhysics Letters.

11. AWARDS AND DISTINCTIONS

- UBC Killam Faculty Research Fellowship, 2010.
- Renewal, Tier II Canada Research Chair in Theoretical Biomolecular Physics, University of British Columbia, May 2006-2010.
- Alfred P. Sloan Research Fellow, 2005.
- Tier II Canada Research Chair in Theoretical Biomolecular Physics, University of British Columbia, Nov 2001-Nov 2005.
- National Science Foundation Post-Doctoral Fellowship in Bio-Informatics, University of California at San Diego 2000-2001
- Sigma Xi Student Paper Award for "Correlated Energy Landscape Model for Finite, Random Heteropolymers", Sigma Xi, Scientific Research Society, University of Illinois Chapter, Oct. 1996
- Department of Energy Graduate Fellow, Rensselaer Polytechnic Institute, Aug 1990-Aug 1991

THE UNIVERSITY OF BRITISH COLUMBIA
Publications Record

SURNAME: Plotkin

FIRST NAME: Steven

MIDDLE NAME(s): Samuel

Date: Dec. 2009

1. REFEREED PUBLICATIONS

(a) Journals

1. **Plotkin, S. S**, Wang, J, & Wolynes, P.G. "Correlated Energy Landscape Model for Finite, Random Heteropolymers", *Phys. Rev. E* **53** (6) 6271-6296 (1996).
2. ***Plotkin, S. S**, Wang, J, & Wolynes, P. G. "Statistical mechanics of a correlated energy landscape model for protein folding funnels". *J Chem Phys* **106**, 2932-2948 (1997).
3. Wang, J, **Plotkin, S. S**, & Wolynes, P.G. "Configurational Diffusion on a Locally Connected Correlated Energy Landscape; Application to Finite, Random, Heteropolymers", *J. Phys I France* **7** 395-421 (1997).
4. **Plotkin, S. S** & Wolynes, P. G. "Non-Markovian configurational diffusion and reaction coordinates for protein folding". *Phys Rev Lett* **80**, 5015-5018 (1998).
5. ***Plotkin, S. S** & Onuchic, J. N. "Investigation of routes and funnels in protein folding by free energy functional methods". *Proc Nat Acad Sci USA* **97**, 6509-6514 (2000).
6. **Plotkin, S. S**. "Speeding Protein Folding Beyond the Go Model: How a Little Frustration Sometimes Helps". *PROTEINS: Structure, Function, and Genetics* **45**, 337-345 (2001).
7. **Plotkin, S. S**. and Onuchic, J. N. "Structural and Energetic Heterogeneity in Protein Folding I: Theory", *J. Chem. Phys.* **116** (12) 5263-5283 (2002).
8. **Plotkin, S. S**, Onuchic, J. N. "Understanding Protein Folding with Energy Landscape Theory, Part I: Basic Concepts", *Quart. Rev. Biophys* **35** (2) 111-167, (2002).
9. **Plotkin, S. S**, Onuchic, J. N. "Understanding Protein Folding with Energy Landscape Theory, Part II: Quantitative Aspects", *Quart. Rev. Biophys* **35** (3) 205-286 (2002).
10. **Plotkin, S. S**, Wolynes, P. G. "Buffed energy landscapes: Another solution to the kinetic paradoxes of protein folding", *Proc Nat Acad Sci USA* **100** (8), 4417-4422 (2003).
11. *Clementi, C. and **Plotkin, S. S**. "The effects of nonnative interactions on protein folding rates: Theory and simulation", *Protein Science* **13**, 1750-1766 (2004).

12. *Ejtehadi, M. R., Avall, S. A. and **Plotkin, S. S.** "Three-body interactions improve the prediction of rate and mechanism in protein folding models", *Proc Nat Acad Sci USA* **101**, 15088-15093 (2004).
13. Oztop, B., Ejtehadi, M. R. and **Plotkin S. S.** "Protein folding rates correlate with heterogeneity of folding mechanism" *Phys. Rev. Lett.* **93**, 208105 (4pp) (2004).
14. **Plotkin, S. S.** "Determination of barrier heights and prefactors from protein folding rate data" *Biophys. J.* **88** (6) 3762-3769 (2005).
15. ***Plotkin, S. S.** "Generalization of distance to higher dimensional objects", *Proc Nat Acad Sci USA.* **104** 14899-14904 (2007).
16. Mohazab, A. R. and **Plotkin, S. S.** "Minimal distance transformations between links and polymers: Principles and applications" *J Phys Condens Matter* **20** 244133 (24pp) (2008).
17. Mohazab, A. R. and **Plotkin, S. S.** "Minimal folding pathways for coarse-grained biopolymer fragments" *Biophysical Journal*, **95** (12) 5496-5507 (2008).
18. Li Li, Huang, A., Guest, W., **Plotkin S. S.**, Cashman N. "Immunological mimicry of PrPc-PrPSc interactions: Antibody-induced PrP misfolding" *Protein Engineering, Design, and Selection*, **22** (8) 523-529 (August 2009)
19. Mohazab, A. R. and **Plotkin, S. S.** "Structural alignment using the generalized Euclidean distance between conformations" *Int J Quant Chem*, Vol 109, 3217–3228 (2009).
20. Abrahamsson, E. and **Plotkin, S. S.**, "BioVEC: A program for Biomolecule Visualization with Ellipsoidal Coarse-graining", *J. Mol. Graph. Model* **28**, 140-145 (2009).
21. Guest W, Cashman N, **Plotkin SS**, "Electrostatics in the Stability and Misfolding of the Prion Protein: Salt Bridges, Self-Energy, and Solvation" *Biochem Cell Biol* (in press).
22. Morriss-Andrews, A, Rottler J, **Plotkin SS**, "A systematically coarse-grained model for DNA, and its predictions for persistence length, stacking, twist, and chirality" *J. Chem. Phys.* (in press).

(b) Conference Proceedings

1. **Plotkin, S. S.**, Wang, J., and Wolynes, P. G. "Statistical Mechanics of Correlated Energy Landscape Models for Random Heteropolymers and Proteins", in *Landscape Paradigms in Physics and Biology: Concepts, Structures and Dynamics*, Elsevier Press ©1997, special edition of *Physica D.* **107**, 322-325 (1997).

2. PATENTS

“Protein unfolding algorithm for identification of stable and unstable protein structural elements”
US Provisional 61/136,815

LICENSEE

Amorfix Life Sciences Ltd., a corporation continued under the laws of Canada, with a registered office at 3403 American Drive, Mississauga, Ontario, L4V 1T4

FIELD OF THE INVENTION

The present invention provides a fast, accurate and efficient means for identifying epitopes present in proteins implicated in protein misfolding diseases or present on the surface of cancerous cells that are selectively exposed for binding when these proteins have assumed a misfolded conformation. In a novel approach, the present invention identifies such disease specific epitopes in proteins by means of a computer method that uses an energy function to compute the free energy of unfolding for all or several subsequences in a protein of interest, identifies the candidate epitopes corresponding to the minima in free energy, and screens these epitopes for immunogenicity, uniqueness in the proteome, and degree of exposure in the native structure of the protein. The present invention further provides misfolding-specific monoclonal or polyclonal antibodies raised against a free peptide with the same sequence as the identified epitopes.. In an alternative embodiment of the present invention, non-antibody agents capable of binding the selected epitopes may also be used, including low molecular weight functionalized organic molecules. The present invention is thus adaptable as a tool for describing conformations of many disease specific peptide epitopes as a result of misfolded proteins, and is especially suitable for use in the design of drugs, and the discovery of targets for the design of drugs.

3. OTHER WORKS

Plotkin, S. S. “Physical models of protein folding within the energy landscape theory” Ph.D. thesis, University of Illinois, Urbana-Champaign with Prof. Peter Wolynes, 1998.

4. WORK SUBMITTED

- Guest W, Cashman N, **Plotkin SS**, "On the Anisotropic and Inhomogenous Dielectric Properties of Proteins" (submitted August 2009).
- Grad LI, Yanai A, Guest W, O'Neill MA, Pokrishevsky E, Yousefi M, Plotkin SS, Cashman NR, "Prion-like propagation of misfolded superoxide dismutase-1" (submitted November 2009).