Brigita Urbanc

Boston University, Physics Department
Center for Polymer Studies
590 Commonwealth Avenue
Boston, MA 02215
e-mail: brigita@.bu.edu
TEL: (617) 353-3411
FAX: (617) 353-9393
web site: polymer.bu.edu/~brigita

EDUCATION:

- B.S., 1987 - Physics, University in Ljubljana, Slovenia.
- M.S., 1990 - Physics, University in Ljubljana, Jožef Stefan Institute, Slovenia.
- Ph.D., 1994 - Physics, Soft Condensed Matter; University in Ljubljana, Jožef Stefan Institute, Jamova 39, 1001 Ljubljana, Slovenia. Thesis title: **Ferroelectric liquid crystals in external fields**.

ACADEMIC APPOINTMENTS:

- Research Associate, Theoretical Physics Department, J. Stefan Institute, Ljubljana, Slovenia. 1993–1999.
- Visiting Scientist, Boston University, Center for Polymer Studies, Boston, USA. 1994–1996.
- Research Associate, Boston University, Center for Polymer Studies, Boston, USA. 1999–2005.
- Senior Research Associate, Boston University, Center for Polymer Studies, Boston, USA. 2005–2007.
- Research Associate Professor, pending approval by Boston University. 2007.

GRANTS, HONORS AND AWARDS:

- Postdoctoral award from the Slovenian Ministry of Science. Duration: 1993–1995. Personal award.
- Adler Foundation Fellowship for research on Alzheimer Disease. Duration: 1997–2000. Personal award.
- Award from the Fidelity foundation for research on Alzheimer's disease. Duration: 1997–2003. Personal role: collaborator (H. E. Stanley, Principal Investigator). Personal contribution: research, writing, and oral presentations at three site visits.
- NIH R03 grant "Methods for Spatial Analysis of Microcolumns in Cortex." Duration: July 2004–June 2006. Personal role: co-investigator (H. E. Stanley, Principal Investigator). Personal contribution: preparation of scientific communications and grant applications, research.
- NIH R21 grant "Molecular Modeling of Amyloid-β Oligomer Formation". Duration: December 2004–November 2006. Personal role: co-investigator (H. E. Stanley, Principal Investigator). Personal contribution: preparation of scientific communications and grant applications, research.
- Alzheimer's Association Zenith Fellows Award "Understanding Formation of Neurotoxic Oligomers in Alzheimer's Disease". Duration: December 2005–November 2007. Personal role: co-investigator (H. E. Stanley, Principal Investigator). Personal contribution: preparation of scientific communications and grant applications, research.
- Bechtel Postdoctoral Fellowship Award for the research on Alzheimer's disease. Duration: May 2005–April 2006. Personal award.
- NIH R01 grant "Spatial Analysis of Cerebral Cortex in Aging Monkeys." Duration: Sept 2005 - May 2008. Personal role: co-investigator (H. E. Stanley, Principal Investigator). Personal contribution: research and writing.
- NIH PPG grant "Pathologic protein folding in human disease", Project 4 "*Ab initio* Molecular Dynamics Simulations of Aβ Folding and Assembly." Duration: April 2006–March 2011. Personal role:

co-investigator (David B. Teplow, Principal Investigator; H. Eugene Stanley, Project Leader). Personal contribution: spearheaded the application of discrete molecular dynamics to amyloid β-protein folding and aggregation, preparation of all scientific communications, including the grant application.

- Inclusion in the 60^{th} Diamond Edition of MARQUIS Who's Who in America, 2006.
- Editorial Board Member of *The Open Biochemistry Journal* (http://www.bentham.org/open/tobiocj), 2007.

TEACHING EXPERIENCE:

- Teaching Assistant, University of Ljubljana, Slovenia, Physics Department, 1987–1996.
- Coordinator of the hands–on experiments for the "Water and Molecular Networks" education project. Duties included the development of curriculum materials for chemistry, physics, and biology high school courses using simple hands–on activities, including wet–lab experiments. Topics ranging from percolation to granular materials are introduced in a very intuitive and visual way in order to bridge the gap between the microscopic and the macroscopic. Boston University, summer 1994 - summer 1996.
- Coordinator of the "Water and Molecular Networks" education project. Duties included the development of a written manual for high school and college students, which accompanies the molecular dynamics simulation software, visualizing random motion phenomena. The project gives a cutting edge approach to teaching science on high school and undergraduate levels via the use of computers. Boston University, 1996–1998.
- Instructor, PY-313 Elementary Modern Physics Course, Summer I, Boston University, 2006.
- Instructor, PY-482 Seminar "Statistical Physics Approach to Understanding Alzheimer's Disease", Boston University, October 2006.
- Instructor, PY-105 Guest Lecture "Applications of Newtonian Mechanics to Understand Molecular Basis of Alzheimer's Disease: A Molecular Dynamics Study of Protein Folding and Aggregation", Boston University, March 2007.

DIRECTING GRADUATE STUDENTS RESEARCH ACTIVITY:

- Jožef Stefan Institute, University in Ljubljana, Slovenia: Barbara Rovšek (Ph.D. 1996).
- Boston University, Physics Department, Center for Polymer Studies, USA: Jose M. Borreguero (Ph.D. January 2005), Shouyong Peng (Ph.D. July 2005), Sijung Yun, Alfonso Lam, Andrew Inglis, Jiayuan Luo.

MAJOR RESEARCH INTERESTS:

- Discrete Molecular dynamics studies of protein folding and aggregation in general and in particular related to the origin of neurodegenerative diseases linked to protein misfolding and/or aggregation, such as Alzheimer's disease.
- Develop and Generalize Discrete Molecular Dynamics Approach to study interactions between proteins and biological membranes, between proteins and DNA, and to study protein folding and aggregation in the presence of obstacles.
- Developing and adapting statistical physics approaches to the neuroanatomy of aging and neurological disorders, such as Alzheimer's disease, schizophrenia, and others.
- Discrete Molecular dynamics simulations of liquid crystal molecules to study their behavior at a molecular level.

PUBLICATIONS:

[1] B. Žekš, T. Carlsson, C. Filipič, **B. Urbanc**, *Thermodynamic model of ferroelectric liquid crystals and its microscopic basis*, Ferroelectrics **84**, 3–14 (1988). [*Times Cited:* **37**]

[2] **B. Urbanc**, B. Žekš, *Microscopic model of the spontaneous polarization in ferroelectric liquid crystals*, Liq. Cryst. **5**, 1075–1082 (1989). [*Times Cited:* **42**]

[3] **B. Urbanc**, B. Žekš, T. Carlsson, *Nonlinear effects in the dielectric response of ferroelectric liquid crystals*, Ferroelectrics **113**, 219–230 (1991).

[4] B. Žekš, **B. Urbanc**, *The microscopic model of polar and quadrupolar ordering in ferroelectric smectic C^* liquid crystals*, Ferroelectrics **113**, 151–162 (1991).

[5] **B. Kutnjak-Urbanc**, B. Žekš, in *Phase transitions in Liquid Crystals*, edited by S. Martellucci and A. N. Chester, *The phase transition from the SmC^* to the SmC phase induced by an external magnetic field* (Plenum, New York, 1992), Chap.23.

[6] **B. Kutnjak-Urbanc**, B. Žekš, *Theoretical investigation of the behavior of ferroelectric liquid crystals in a magnetic or in a high-frequency electric field*, Phys. Rev. E **48**, 455–464 (1993). [*Times Cited:* **7**]

[7] **B. Kutnjak-Urbanc**, B. Žekš, B. Rovšek, *The influence of finite dimensions on the static ordering of the SmC^* phase in an electric field*, Liq. Cryst. **14**, 999–1005 (1993).

[8] B. Žekš, T. Carlsson, I. Muševič, **B. Kutnjak-Urbanc**, *Dielectric response of ferroelectric liquid crystals in bias electric field*, Liq. Cryst. **15**, 103–111 (1993). [*Times Cited:* **8**]

[9] **B. Kutnjak-Urbanc**, B. Žekš, *Microscopic origin of spontaneous polarization in ferroelectric SmC^* liquid crystals*, Liq. Cryst. **18**, 483–488 (1995). [*Times Cited:* **8**]

[10] **B. Kutnjak-Urbanc**, B. Žekš, *Behavior of ferroelectric liquid crystals in external fields*, Phys. Rev. E **51**, 1569–1572 (1995).

[11] **B. Kutnjak-Urbanc**, B. Žekš, *Phase excitation spectrum of ferroelectric liquid crystals in an external static electric field*, Phys. Rev. E **52**, 3892–3903 (1995).

[12] **B. Kutnjak-Urbanc**, S. Zapperi, S. Milošević, H. E. Stanley, *Sandpile model on the Sierpinski gasket fractal*, Phys. Rev. E **54**, 272–277 (1996). [*Times Cited:* **9**]

[13] **B. Kutnjak-Urbanc**, S. Havlin, H. E. Stanley, *Temporal correlations in a one–dimensional sandpile model*, Phys. Rev. E **54**, 6109–6113 (1996). [*Times Cited:* **6**]

[14] L. Cruz, **B. Urbanc**, S. V. Buldyrev, R. Christie, T. Gómez-Isla, S. Havlin, M. McNamara, H. E. Stanley, and B. T. Hyman, *Aggregation and disaggregation of Senile Plaques in Alzheimer Disease*, Proc. Natl. Acad. Sci. **94**, 7612–7616 (1997). [*Times Cited:* **38**]

[15] **B. Urbanc** and L. Cruz, *Order Parameter and Segregated Phases in a Sandpile Model with Two Particle Sizes*, Phys. Rev. E **56**, 1571–1579 (1997).

[16] H. E. Stanley, S. V. Buldyrev, L. Cruz, T. Gomez-Isla, S. Havlin, B. T. Hyman, R. Knowles, **B. Urbanc** and C. Wyart, *Statistical Physics and Alzheimer's Disease* [Proc. Bar-Ilan Conf], Physica A **249**, 460–471 (1998).

[17] **B. Urbanc**, L. Cruz, S. V. Buldyrev, S. Havlin, M. C. Irizarry, H. E. Stanley, and B. T. Hyman, *Dynamics of Plaque Formation in Alzheimer Disease*, Biophys. J. **76**, 1330–1334, (1999). [*Times Cited:* **22**]

[18] **B. Urbanc**, L. Cruz, S. V. Buldyrev, S. Havlin, B. T. Hyman, and H. E. Stanley, *Dynamic Feedback in an Aggregation–Disaggregation Model*, Phys. Rev. E **60**, 2120–2126 (1999). [*Times Cited:* **6**]

[19] R. B. Knowles, C. Wyart, S. V. Buldyrev, L. Cruz, **B. Urbanc**, M. E. Hasselmo, H. E. Stanley, and B. T. Hyman, *Plaque–Induced Neural Network Disruption in Alzheimer's Disease* Proc. Natl. Acad. Sci. **96**, 5274–5279 (1999). [*Times Cited:* **56**]

[20] S. V. Buldyrev, L. Cruz, T. Gomez-Isla, E. Gomez-Tortosa, S. Havlin, R. Le, H. E. Stanley, **B. Urbanc** and B. T. Hyman, *Description of microcolumnar ensembles in association cortex and their disruption in Alzheimer and Lewy body dementias*, Proc. Natl. Acad. Sci. **97**, 5039–5043 (2000). [*Times Cited:* **30**]

[20a] E. G. Jones, "Microcolumns in the cerebral cortex" Proc. Natl. Acad. of Sci. **97**, 5019–5021 (2000) [3 page "Invited Commentary" accompanying Ref. 20].

[21] R. Le, L. Cruz, **B. Urbanc**, R. B. Knowles, K. Hsiao-Ashe, K. Duff, M. Irizarry H. E. Stanley, and B. T. Hyman, *Plaque-induced abnormalities in neurite geometry in transgenic models of Alzheimer's disease: implications for neural system disruption*, J. Neuropath. Exp. Neurol. **60**, 763–758 (2001). [*Times Cited:* **32**]

[22] **B. Urbanc**, L. Cruz, R. Le, J. Sanders, K. Hsiao-Ashe, K. Duff, H. E. Stanley, M. C. Irizarry and B. T. Hyman, *Neurotoxic Effects of Thioflavin S Positive Amyloid Deposits*, Proc. Natl. Acad. Sci. **99**, 13990–13995 (2002). [*Times Cited:* **45**]

[23] S. Peng, **B. Urbanc**, L. Cruz, B. T. Hyman, and H. E. Stanley, *Neuron Recognition by Parallel Potts Segmentation*, Proc. Natl. Acad. Sci. **100**, 3847–3852 (2003).

[24] S. Peng, F. Ding, **B. Urbanc**, S. V. Buldyrev, L. Cruz, H. E. Stanley, and N. V. Dokholyan, *Discrete molecular dynamics simulations of peptide aggregation*, Phys. Rev. E **69**, 041908 (2004). [*Times Cited:* **13**]

[25] **B. Urbanc**, L. Cruz, F. Ding, D. Sammond, S. Khare, S. V. Buldyrev, H. E. Stanley, and N. V. Dokholyan, *Molecular Dynamics Simulation of Amyloid-β Dimer Formation*, Biophys. J. **87**, 2310–2321 (2004). [*Times Cited:* **36**]

[26] L. Cruz, D. L. Roe, **B. Urbanc**, H. Cabral, H. E. Stanley, and D. L. Rosene, *Age-related reduction in microcolumnar structure in area 46 of the rhesus monkey correlates with behavioral decline*, Proc. Natl. Acad. Sci. **101**, 15846–15851 (2004).

[27] **B. Urbanc**, L. Cruz, S. Yun, S. V. Buldyrev, G. Bitan, D. B. Teplow, and H. E. Stanley, *In silico study of amyloid β-protein folding and oligomerization*, Proc. Natl. Acad. Sci. **101**, 17345–17350 (2004). [*Times Cited:* **31**]

[28] L. Cruz, S. V. Buldyrev, S. Peng, D. L. Roe, **B. Urbanc**, H. E. Stanley, and D. L. Rosene, *A Statistically Based Density Map Method for Identification and Quantification of Regional Differences in Microcolumnarity in the Monkey Brain*, J. Neurosci. Methods **141**, 321–332 (2005).

[29] J. M. Borreguero, **B. Urbanc**, N. D. Lazo, S. V. Buldyrev, D. B. Teplow, and H. E. Stanley, *Folding events in the 21-30 region of amyloid β-protein (Aβ) studied in silico*, Proc. Natl. Acad. Sci. **102**, 6015–6020 (2005). [*Times Cited:* **13**]

[30] **B. Urbanc**, J. M. Borreguero, L. Cruz, and H. E. Stanley, *Ab initio discrete molecular dynamics approach to protein folding and aggregation*, invited review, Methods in Enzymology **412**, Ch. 19, 314–338 (2006).

[31] L. Cruz, **B. Urbanc**, J. M. Borreguero, N. D. Lazo, D. B. Teplow, and H. E. Stanley, *Solvent and mutation effects on the nucleation of amyloid β-protein folding*, Proc. Natl. Acad. Sci. **102**, 18258–18263 (2005). [*Times Cited:* **11**]

[32] **B. Urbanc** and M. Čepič, *Possible Isostructural Transitions in the Ferroelectric Liquid Crystals in High External Electric Fields*, presented at the 20th International Liquid Crystal Conference, 4-9 July, 2004, Ljubljana (Slovenia), Mol. Cryst. Liq. Cryst. **438**, 41(1605)–46(1610) (2005).

[33] **B. Urbanc**, L. Cruz, D. B. Teplow, and H. E. Stanley, *Computer simulations of Alzheimer's amyloid β-protein folding and assembly*, invited review, Current Alzheimer Research **3**, 493–504 (2006).

[34] A. Lam, **B. Urbanc**, J. M. Borreguero, N. D. Lazo, D. B. Teplow, and H. E. Stanley, *Discrete Molecular Dynamics Study of Alzheimer Amyloid β-protein (Aβ) Folding. Proceedings of The 2006 International Conference on Bioinformatics & Computational Biology*, CSREA Press, Las Vegas, Nevada, 322–328 (2006).

[35] D. B. Teplow, N. D. Lazo, G. Bitan, S. Bernstein, T. Wyttenbach, M. T. Bowers, A. Baumketner, J.-E. Shea, **B. Urbanc**, L. Cruz, J. Borreguero, and H. E. Stanley, *Elucidating Amyloid β-protein Folding and Assembly: A Multidisciplinary Approach. Account of Chemical Research* **39**, 635–645 (2006).

[36] S. Yun, **B. Urbanc**, L. Cruz, G. Bitan, D. B. Teplow, and H. E. Stanley, *Role of electrostatic interactions in amyloid β-protein oligomer formation: A discrete molecular dynamics study.*, *Biophys. J.* **92**, 4064–4077 (2007).

[37] A. Inglis, L. Cruz, D. L. Roe, H. E. Stanley, D. L. Rosene, and **B. Urbanc**, *Automated retrieval of neuron location from Nissl-stained tissue*, submitted to *Journal of Microscopy* (2007).

[38] L. Cruz, **B. Urbanc**, N. D. Lazo, D. B. Teplow, and H. E. Stanley, *Comparative analysis of the Dutch and Iowa mutations on the nucleation of the amyloid β-protein: a molecular dynamics study. in preparation* (2007).

[39] L. Cruz, D. L. Roe, **B. Urbanc**, A. Inglis, H. E. Stanley, and D. L. Rosene, *Age-dependence of the strength of microcolumns in area 46 of the rhesus monkey brain. in preparation* (2007).

[40] L. Cruz, **B. Urbanc**, D. L. Roe, A. Inglis, H. E. Stanley, and D. L. Rosene, *Computer simulations of the effects of aging in the brain*, *in preparation* (2007).

[41] **B. Urbanc**, L. Cruz, and G. Bitan, *In silico study of amyloid β-protein aggregation in the presence of peptide inhibitors*, *in preparation* (2007).

[42] **B. Urbanc**, L. Cruz, and G. Bitan, *Oligomerization of amyloid β-protein with oxidized Met35: A discrete molecular dynamics study*, *in preparation* (2007).

[43] **B. Urbanc**, R. Bansil, and B.S. Turner, *Folding of Mucin Domains: A discrete molecular dynamics study*, *in preparation* (2007).

CONFERENCE PRESENTATIONS AND TALKS:

[1] **B. Kutnjak-Urbanc**, B. Žekš: *The Microscopic Origin of the Polarization in Ferroelectric Liquid Crystals*, oral presentation, "The Molecular Dynamics of Liquid Crystals," NATO Advanced Study Institute, Il Ciocco, Italy, 1989.

[2] **B. Kutnjak-Urbanc**, B. Žekš: *Influence of Static Electric and Magnetic Fields on Optical Properties of Ferroelectric Liquid Crystals*, III. International Topical Meeting on Optics of Liquid Crystals, Cetraro, Italy, 1990.

[3] **B. Kutnjak-Urbanc**, B. Žekš: *The Phase Diagram of Ferroelectric Liquid Crystals in the External Magnetic Field*, poster presentation, European Conference on Liquid Crystals, Courmayeur, Italy, 1991.

[4] **B. Kutnjak-Urbanc**, B. Žekš, B. Rovšek: *Unwinding of the helical structure of the SmC* phase in external magnetic and electric fields*, poster presentation, 14th International Liquid Crystal Conference, Pisa, Italy, 1992.

[5] I. Drevenšek, M. Čopič, **B. Kutnjak-Urbanc**, B. Žekš: *Nonlinear optical susceptibility of ferroelectric liquid crystals*, poster presentation, 14th International Liquid Crystal Conference, Pisa, Italy, 1992.

[6] **B. Kutnjak-Urbanc**, B. Žekš: *Phason Spectrum of Ferroelectric Liquid Crystals in an External Electric Field*, poster presentation, European Conference on Liquid Crystals, Flims, Switzerland, 1993.

[7] **B. Kutnjak-Urbanc**, B. Žekš: *Phase Transition in Ferroelectric Liquid Crystals Induced by an Electric Field*, poster presentation, NATO Advanced Study Institute "Phase Transitions and Relaxation in Systems with Competing Energy Scales," Geilo, Norway, 1993.

[8] **B. Kutnjak-Urbanc**, B. Žekš, *Microscopic origin of spontaneous polarization in ferroelectric SmC* liquid crystals*, poster presentation, 15th International Conference on Liquid Crystals, Budapest, Hungary, 1994.

[9] **B. Kutnjak-Urbanc**, S. Zapperi, S. Milošević and H. E. Stanley, *Sandpile model on Sierpinski gasket fractal*, oral presentation, Gordon Conference "Condensed Matter Physics," Brewster Academy, New Hampshire, 1995.

[10] **B. Kutnjak-Urbanc**, S. Havlin and H. E. Stanley, *Temporal correlations in a one–dimensional sandpile model*, 20–minute talk on Material Research Science (MRS) Fall Meeting, Boston (Abstract M11.8), 1995.

[11] **Brigita Urbanc** and Boštjan Žekš, *Microscopic model for spontaneous polarization in ferroelectric liquid crystals*, invited talk at Rio Piedras, San Juan, Puerto Rico, 1997.

[12] R. B. Knowles, L. Cruz, **B. Kutnjak-Urbanc**, R. H. Christie, H. E. Stanley, and B. T. Hyman, meeting abstract, *The effect of senile plaques and neuropil threads on neurite morphology in Alzheimer's disease*, *Neurology* **48**, 3045–3045 Suppl. 2, 1997.

[13] B. T. Hyman, R. B. Knowles, C. Wyart, S. V. Buldyrev, L. Cruz, **B. Urbanc**, M. E. Hasselmo, and H. E. Stanley, meeting abstract *Plaque-induced neurite abnormalities: Implications for disruption of neural networks in Alzheimer's disease*, J. Neuropath. Exp. Neurol. **58** 557-557, 1999.

[14] **Brigita Urbanc**, *Molecular Dynamics Simulation of Amyloid-β Dimer Formation*, invited talk, Second ICAM Workshop on Physical Principles of Amyloid Diseases: "Protein Misaggregation: From Molecules To Neurodegeneration," Lenox Hotel, Boston, Massachusetts, 2004.

[15] **Brigita Urbanc**, *In silico study of amyloid-β folding and oligomer formation*, invited talk at the session "Biophysical Aspects of Protein and Peptide Aggregation: Experiment and Theory," American Chemical Society Meeting, Convention Center, San Diego, California, 2005.

[16] S. M. Spring, S. L. Bernstein, N. D. Lazo, **B. Urbanc**, H. E. Stanley, M. T. Bowers, D. B. Teplow, and G. Bitan, *Towards inhibition of amyloid β-protein oligomerization*, Understanding Biology Using Peptides, Sylvie E. Blondelle (Ed.), 19th American Peptide Society Symposium, San Diego, California, Proceedings, 515–516 (2005).

[17] **B. Urbanc**, *Statistical Physics Approach to Understanding Alzheimer's Disease*, an invited seminar, 12 December 2005, California State University Northridge, Physics Department, Los Angeles, California.

[18] **B. Urbanc**, In vitro *driven computer simulations of relevance to Alzheimer's disease*, an invited talk at *A Society for Neuroscience 2006 Satellite Symposium* (13 October, 2006), Atlanta.

[19] **B. Urbanc**, L. Cruz, E. Fradinger, G. Bitan, D. B. Teplow, and H. E. Stanley, *Computational study of amyloid β-protein oligomerization in the presence of C-terminal fragments*, a poster presentation (**168.15**) at *A Society for Neuroscience 2006 Annual Meeting* (15 October, 2006), Atlanta.

[20] **B. Urbanc**, In vitro *driven computer simulations of relevance to Alzheimer's disease*, an invited talk at *Biophysical Society Meeting* (6 March, 2007), Baltimore.

RESEARCH IMPACT:

- The mathematical model with the corresponding clinical consequences contained in "Publications" (Ref. [14]) published in the *Proceedings of the National Academy of Science*, Vol. 94, in 1997 were reviewed on the fall edition of *Bostonia* in 1997. The feature article was entitled "Unraveling Alzheimer's" and was written by their managing editor, Taylor McNeil.
- The findings contained in "Publications" (Ref. [20]), that appeared in the *Proceedings of the National Academy of Science* on May 9, 2000 were reviewed on a column in *BioWorld Today*, **11** No. 76 , April 20, 2000, under the title "Physicists Correlate Neuronal Die–Off in Alzheimer's Patients with Cortical Columnar Damage," by their science editor, David N. Leff. *BioWorld Today* is a newspaper for the biotechnology industry. It is faxed every day to leading biotechnology professionals and investors with high impact in Wall Street and the business world in general. In addition, the main figure illustrating the findings of the microcolumnar organization of neurons in the brain won the honor to be featured on the cover of the May 9th issue of the *Proceedings of the National Academy of Science* with an invited commentary, (see "Publications", Ref. [20a]).
- The findings contained in "Publications" (Ref. [26]) that appeared in the *Proceedings of the National Academy of Science* on November 9, 2004, regarding the loss of microcolumnar strength as a function of age in area 46 of rhesus monkey brains, were reviewed in the AAAS Science online publication *Science of Aging Knowledge Environment*, **2004** Iss. 45, pp. nf100, November 10, 2004. The review article was entitled "Out of Whack, Out of Mind" and was written by M. Leslie. In addition, these scientific findings were reviewed in an article that appeared in the *NCRR Reporter* **XXVIII**, No. 4 (2004), a quarterly magazine of the National Center for Research Resources of the NIH. The article was entitled "Aging Neurons on the Move," and was written by Tina Adler.

REVIEWER FOR THE FOLLOWING JOURNALS:

- Cell Biology and Biophysics.
- European Physical Journal B.
- Journal of American Chemical Society
- New Journal of Chemistry.
- Physica A.
- Physical Review E.
- Physical Review Letters.
- Proteins: Structure, Function, and Bioinformatics.

INVITED COMMENTARIES ON THE WEB:

- **Urbanc B.** on LIVE DISCUSSION: Messing with the Membrane: An Alternative Interpretation of the Amyloid-β Hypothesis, Comment of 1 Nov 2006, Alzheimer Research Forum (www.alzforum.org).
- **Urbanc B.** on PAPER: Lim KH. et al., "Characterizations of distinct amyloidogenic conformations of the Aβ(1-40) and (1-42) peptides." Biochem. Biophys. Res. Commun. **353**, 443–449 (2007), Comment of 9 Jan. 2007, Alzheimer Research Forum (www.alzforum.org).
- **Urbanc B.** on PAPER: Sawaya MR. *et al.*, "Atomic structures of amyloid cross-β spines reveal varied steric zippers." Nature, ahead of print (29 April 2007), Comment of 14 May 2007, Alzheimer Research Forum (www.alzforum.org).

COMPUTER SKILLS:

- Programming in Fortran;
- Programming in C++, using OpenGl and Tk/Tcl for graphical user interface plus 3D Visualization;
- Experience in Unix, Linux and Microsoft Windows operating systems.

LANGUAGES:

Slovenian (native), English (proficient), Serbo-Croatian (conversant), French (conversant), German (read), Spanish (read).

STATEMENT OF RESEARCH INTERESTS

I am experienced in a hierarchy of computational approaches to study Aβ folding and assembly. The most coarse-grain approach I use is a cellular-automaton model of amyloid deposition ("Publications", Refs. [14,17,18]). The intermediate level of complexity which is most appropriate to study aggregation of many proteins consists of a four-bead or united-atom protein model with amino acid-specific interactions in combination with an efficient discrete molecular dynamics method, DMD ("Publications", Refs. [27,29]). The highest level of complexity which is appropriate to study folding of protein fragments is all-atom molecular dynamics approach in an explicit solvent ("Publications", Refs. [32]). Of the three approaches, I am currently focused on the intermediate level due to a powerful compromise between the computer efficiency and the degree of details that these protein models offer.

My major research interest is the **DMD approach to study folding and assembly of proteins** associated with neurological disorders, such as Alzheimer's disease (recent reviews in "Publications", Refs. [33,35]), and other proteins such as gastric mucin protein domains ("Publications", Ref.[44]). The advantage of the DMD method over a more conventional all-atom molecular dynamics in explicit solvent is in its efficiency: DMD can span about 10^7 longer times, i. e. times needed to study biologically relevant processes (recent review in "Publications", Ref.[30]). Currently the DMD method relies on a "home-made" software package written by a variety of researchers. From a method-development point of view I will **unify the algorithms into a professional package with an open access** that will be available to other research groups. As a "gold standard" I will use GROMACS or NAMD all-atom molecular dynamics packages. I will **generalize the DMD approach to allow for studies of interactions between proteins or protein assemblies with a lipid bilayer or with DNA molecules**. An important part of this project will be **development of water models** to allow for explicit interactions between the water and protein molecules.

Alzheimer's disease (AD) is the most prevalent age-dependent dementia. Compelling evidence supports a central role of the amyloid β-protein (Aβ) in AD. Research both *in vitro* and *in vivo* has revealed that early aggregates of Aβ, called oligomers, are the earliest and the most potent neurotoxic structures in the brain. Due to these discoveries current research efforts are focused towards understanding early steps in Aβ monomer folding and aggregation. To produce therapeutic agents targeting toxic oligomers, we need to understand the mechanism of oligomerization and resolve the structure of oligomers. From an experimental standpoint, resolving the structure of oligomers is very challenging because unlike fibrils and proteins with stable folds, oligomers are metastable and cannot be crystallized for X-ray diffraction studies nor can they be studied easily using solution phase NMR. My recent work demonstrates that the DMD method combined with a coarse–grain protein model is especially suitable for the reconstruction of the three-dimensional structure of Aβ oligomers and the study of their aggregation pathways ("Publications", Refs. [25,27]). Moreover, a more detailed united-atom model of proteins can be used to study atomic details of Aβ folding ("Publications", Ref. [29]). These three studies yielded results in agreement with *in vitro* findings and predicted new structural features amenable to *in vitro* testing.

In my most recent work I am investigating the **structure-toxicity relationship** of oligomeric aggregates of Aβ and its mutants (in collaboration with Gal Bitan's lab at UCLA). While the origin of toxicity of these aggregates is still unknown there are several hypothesis that link their three-dimensional structure to their toxic properties. The DMD approach provides a powerful method to test these structure-toxicity hypothesis as demonstrated in my recent studies ("Publications", Refs. [42,43]). These studies also demonstrate how the DMD approach can be used to **study oligomer formation in the presence of peptide inhibitors**, such as C-terminal Aβ fragments ("Publications", Ref. [42]). The DMD approach used in all these studies is *ab initio*. When combined with physical intuition, these recent studies indicate that it can provide essential structural information needed to speed up the search for cures. This approach can be extended to **study interaction between the potentially toxic protein assemblies and a lipid bilayer (membrane)** and thereby test their potential membrane damaging effects at atomic level.

STATEMENT OF TEACHING INTERESTS AND PHILOSOPHY

My teaching interests include teaching general and intermediate physics as well as more specialized topics, such as thermodynamics, statistical physics, mathematical physics, polymer physics, biophysics, medical physics, and physics of liquid crystals.

My general teaching approach is to engage the students as much as possible to stimulate active learning. During a typical course, I will present a question or phenomenon related to the topic under study and then ask students to discuss it for a short period of time in small groups of 2-4 students (depending upon the size of the class). I will emphasize that the wrong answer at this point is much better than no answer at all because it helps build creativity. Whenever possible, I will use either a hands–on activity or another kind of visualization tool to illustrate the molecular basis of the phenomena and to develop intuition that otherwise is difficult to attain. No matter how complex the topics under study I will end the class with a simple take–home message to help students remember the main points.

Depending on the course I will be teaching, I will implement the existing materials as well as develop new visualization tools to facilitate the understanding of different physical (biophysical) principles and phenomena. An example can be taken from the principles of statistical physics: concepts such as temperature, ideal gas, states of matter can all be visualized on a computer using existing visualization tools combined with simple molecular dynamics models that allow for adjustment of temperature, number of particles, and interparticle interactions. Such a tool will help understand phenomena such as phase transitions, condensation, sublimation, deposition, and critical points. Moreover, computer models can be developed to visualize protein folding and assembly. The idea is to find new approaches to teaching science that would engage students more actively and that would enable them to learn in a more research–oriented way, thus increasing their motivation and deepen the level of understanding.

Depending upon the interest of the department, discrete molecular dynamics can be developed into a visualization teaching tool at an undergraduate or graduate level. Many basic thermodynamic properties of proteins and/or polymers, for example, can be visualized using simplified coarse-grain models and implicit solvent.

PERSONAL REFERENCES

H. Eugene Stanley, PhD
Professor of Physics & Physiology
Director of the Center for Polymer Studies
Boston University
590 Commonwealth Av.
Boston, MA 02215.
phone: (617) 353-2617
fax: (617) 353-3783
e-mail: hes@buphy.bu.edu

David B. Teplow, Ph.D.
Professor in Residence
Department of Neurology
David Geffen School of Medicine at UCLA
Neuroscience Research Building 1, Room 445
635 Charles E. Young Drive South (Mail Code 733422)
Los Angeles, CA 90095-7334
phone: (310) 206-2030
fax: (310) 206-1700
e-mail: dteplow@ucla.edu

Rama Bansil, PhD
Professor of Physics
Physics Department, Room SCI-216
Boston University
590 Commonwealth Av.
phone: (617) 353-2969
fax: (617) 353-9393
e-mail: rb@bu.edu

Douglas L. Rosene, Ph.D.
Professor of Neurology
Department of Anatomy and Neurobiology
715 Albany St., W701
Boston University School of Medicine
Boston, MA 02118
phone: (617) 638-4061
fax: (617) 638-4922
e-mail: drosene@bu.edu

Shlomo Havlin, PhD
Professor of Physics
Gonda-Goldschmied Center and Dept. of Phys.
Bar-Ilan University
Ramat-Gan 52900
Israel
phone: 972 (3) 6777-505
fax: 972 (3) 535-3298
e-mail: havlin@ophir.ph.biu.ac.il

Brad T. Hyman, MD, PhD
Professor of Neurology
Harvard Medical School
Massachusetts General Hospital
114 16th Street Room 2009
Charlestown, MA 02129
phone: (617) 726-2299
fax: (617) 724-1480
e-mail: b_hyman@helix.mgh.harvard.edu