

Laurence Richard Brewer
Curriculum Vitae

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Education

Postdoctoral National Bureau of Standards, Boulder, CO (1987).
Ph.D Massachusetts Institute of Technology, Department of Physics, (1985).
B.S. Yale University, Department of Physics, (1978).

Research Experience

1998-2005 Biophysicist, (LLNL) Topics studied using “single molecule” techniques include:

- ♦ DNA condensation by spermatid proteins using fluorescence and force spectroscopy.
- ♦ Compaction of DNA by the yeast mitochondrial protein Abf2p.
- ♦ Unwinding of duplex DNA by the helicase RecBCD.
- ♦ Design and construction of microfluidic flow cells for single molecule studies.

1993-1998 Human Genome Program (LLNL) Designed and built confocal detection optics for large array DNA sequencers.

1992-1993 Physics Program (LLNL) Designed experiment for trapping and laser-cooling highly-charged ions.

1987-1992 Laser Program, Lawrence Livermore National Lab (LLNL), Livermore, CA. Frequency-locked laser diode arrays and measured their coherence properties.

1985-1987 National Bureau of Standards, Time and Frequency Division, Boulder, CO. Laser cooled atomic ions to create and study strongly-coupled plasmas.

1978-1985 Massachusetts Institute of Technology, Physics Department, Cambridge, MA. Ph.D Thesis – “Resonant Multiphoton Ionization of Atomic Hydrogen”, Prof. Daniel Kleppner, thesis supervisor.

Teaching Experience

1978 Tutor in the Department of Physics, Yale University, New Haven, CT.

Honors

- ♦ Biology & Biotechnology Research Program Achievement Award, LLNL, 2001.
- ♦ Electronics Engineering Technologies Div. National Recognition Award, LLNL 1999.
- ♦ H. Schultz award in undergraduate experimental physics, Yale University, 1978.

Research Interests

Dr. Brewer studies chromatin remodeling during spermiogenesis using biophysical, “single molecule” techniques to understand the higher order structure of genomic DNA within the sperm cell. He uses dual laser optical traps (“tweezers”) to measure changes in the tension of a single DNA molecule held at fixed extension as it is reeled into 50-nm diameter structures called “toroids” due to the binding of spermatid proteins. The DNA appears to be reeled in via a thermal “ratchet and pawl” mechanism, after which it is locked into place (via an unknown mechanism) resisting attempts to unwind it with forces greater than 100 pN. Fluorescence and force microscopy are used in conjunction with novel microfluidic, multichannel flow cells to observe kinetic and structural changes in individual DNA molecules as they are exposed to proteins in the

same order as that in the cell. This research is important for understanding both male fertility and abnormal embryo development.

Dr. Brewer is also interested in understanding the role that the helical state of the DNA molecule plays in fundamental biological processes such as transcription and replication. He is currently building an instrument that measures changes in the twist, writhe, and tension of a single DNA molecule as it is exposed to proteins or enzymes.

Funding

- ◆ “DNA-Protein Interactions in Sperm Chromatin” NIH, HD01387 (**Brewer**), 2000–2005, \$157,000/year.
- ◆ “Single Assembly of Protein-DNA Complexes” NIH, GM64745-01 (Kowalczykowski) 2002–2005, (\$30,000/year for Brewer).
- ◆ “Manipulation of Individual DNA Molecules Using Optical Traps: Application to DNA Mapping by AFM and Single Molecule Force Measurements” DOE/LLNL LDRD, 96-LW-045 (Balhorn), 1996-2000, \$180,000/year.
- ◆ “Coherent Combination of Laser Diode Arrays by Injection-Locking” DOE/LLNL Laboratory Directed Research and Development (LDRD), 91-LW-009 (**Brewer**) 1991, \$116,000.

Patents

- ◆ **Brewer, L.R.**, Kimbrough, J., Balch, J., Davidson, J.C., “System and Method for Optically Locating Microchannel Positions”. U.S. Patent 6,225,635, May 1, 2001.
- ◆ Balch, J.W., **Brewer, L.R.**, Davidson, J.C., Kimbrough, J.R. “System and Method for Chromatography and Electrophoresis Using Circular Optical Scanning”. U.S. Patent 6,296,749, Oct. 2, 2001.

Professional Organizations and Service

- ◆ Biophysical Society (2005)
- ◆ Ad-hoc reviewer for the 2003 NIH, BCB (Biophysical Chemistry) study section.
- ◆ Reviewer for the journal “Reproduction, Fertility, and Development” (2004)

Recent Talks and Presentations (2004-2005)

1. “New Techniques for Understanding How DNA is Packaged in Cells”, St. Andrews University Physics Department, Scotland, July 5, 2005.
2. “The mechano-elastic properties of DNA toroids” (poster), Science Day, LLNL, May 23, 2005.
3. “LLNL-UCSB Joint Research Workshop on Biosensing Nanosystems”, April 19th, 2005
4. “Single molecule study of spermiogenesis” (poster), Biophysical Society Annual Meeting, Long Beach, CA, Feb.11-15, 2005.
5. “Single molecule studies of chromatin remodeling during spermiogenesis”, U.C. Santa Cruz, Department of Molecular, Cellular, and Developmental Biology, Nov. 22, 2004.
6. “Single molecule studies of chromatin remodeling during spermiogenesis”, Biology & Biotechnology Research Program, LLNL, Nov. 18, 2004.
7. “Chromatin Remodeling During Spermiogenesis”, U.C. Irvine Physics Department, March 4, 2004.

Publications

1. **Brewer, L.**, Corzett, M., Lau, E.Y., Balhorn, R. Dynamics of Protamine 1 Binding to Single DNA Molecules (2003) *J Biol Chem* **278**, 42403–42408.

2. **Brewer, L.R.**, Friddle, R., Noy, A., Baldwin, E., Martin, S.S., Corzett, M., Balhorn, R., Baskin, R.J. Packaging of Single DNA Molecules by the Yeast Mitochondrial Protein Abf2p (2003) *Biophys J* **85**, 2519-2524.
3. **Brewer, L.**, Corzett, M. & Balhorn, R. Condensation of DNA by spermatid basic nuclear proteins (2002). *J Biol Chem* **277**, 38895-900.
4. Bianco, P. R., **Brewer, L.R.**, Corzett, M., Balhorn, R., Yeh, Y., Kowalczykowski, S.C., Baskin, R.J. Processive translocation and DNA unwinding by individual RecBCD enzyme molecules (2001) *Nature* **409**, 374-8.
5. Balhorn, R., **Brewer, L.**, Corzett, M. DNA condensation by protamine and arginine-rich peptides: analysis of toroid stability using single DNA molecules (2000) *Mol Reprod Dev* **56**, 230-4.
6. **Brewer, L. R.**, Corzett, M. & Balhorn, R. Protamine-induced condensation and decondensation of the same DNA molecule (1999) *Science* **286**, 120-3.
7. **Brewer, L. R.**, Davidson, J. C., Balch, J. W. & Carrano, A. V. Three-dimensional imaging of DNA fragments during electrophoresis using a confocal detector (1995) *Electrophoresis* **16**, 1846-50.
8. **Brewer, L. R.**, Davidson, J. C., Balch, J. W. Three-dimensional imaging of DNA fragments during electrophoresis using a confocal detector (1995) *Ultrasensitive Instrumentation for DNA Sequencing and Biochemical Diagnostics*, Gerald E. Cohn et.al. Editors, SPIE **2386**, 86-96.
9. **Brewer, L. R.** Suppression of Beam Steering in an Injection-Locked Laser Diode Array. *Applied Physics Letters* **59**, 3078-3080 (1991).
10. **Brewer, L. R.** Highly Coherent Injection-Locked Laser Diode Arrays (1991) *Applied Optics* **30**, 317-320.
11. **Brewer, L. R.**, Buchinger, F., Ligare, M. & Kelleher, D. E. Resonance-enhanced multiphoton ionization of atomic hydrogen (1989). *Physical Review. A* **39**, 3912-3923.
12. Itano, W. M., **Brewer, L. R.**, et. al. Quantitative study of laser cooling in a Penning trap in *Proceedings of the 4th Symposium on Frequency Standards and Metrology* (Springer Verlag, Ancona, Italy, 1988).
13. Itano, W. M., **Brewer, L. R.**, Larson, D. J. & Wineland, D. J. Perpendicular laser cooling of a rotating ion plasma in a Penning trap (1988) *Physical Review. A* **38**, 5698-5706.
14. **Brewer, L. R.** et al. Static properties of a non-neutral ${}^9\text{Be}^+$ -ion plasma (1988). *Physical Review. A* **38**, 859-873.
15. Bollinger, J. J., **Brewer, L. R.**, et. al. Ion trapping techniques: laser cooling and sympathetic cooling in *Intense Positron Beams* (ed. E.H. Ottewitte, W. Kells) (World Scientific Press, Singapore, 1988).
16. **Brewer, L. R.**, Prestage, J. D., Bollinger, J. J., Wineland, D. J. A High G, strongly coupled, nonneutral ion plasma. In *Strongly Coupled Plasmas* (ed. Rogers, F., DeWitt, D) (Plenum Press, 1987).
17. Kelleher, D. E., Ligare, M. & **Brewer, L. R.** Resonant four-photon ionization of atomic hydrogen (1985) *Physical Review. A* **31**, 2747-2749.

Publications in Preparation

18. **Brewer, L.R.**, Corzett, M., Balhorn, R. A Force-Exerting Nanomachine Coils DNA in Sperm (2005).

Website: <http://scienceday.llnl.gov/Bios/brewer.htm>

References

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