

Jim Werner

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EDUCATION **Cornell University** (Ithaca, NY)
1998 Ph.D. in Applied Physics
1994 M.S. in Applied Physics

1992 **California Institute of Technology** (Pasadena, CA)
BS in Applied Physics

SELECTED AWARDS

R&D 100 Award- "*3D Tracking Microscope*" (2008)
Hertz Foundation Fellowship (1992-1998)
Caltech Carnation Merit Award (1990-92)

RESEARCH INTERESTS

Analytic and biophysical applications of single molecule detection by laser induced fluorescence, instrument development, protein folding, and laser spectroscopy.

RESEARCH EXPERIENCE

Los Alamos National Laboratory, Technical Staff Member (2002-present)

Recent efforts include leading a team in the design and construction of a novel fluorescence microscope design capable of tracking single molecules in 3 dimensions (patent pending) and leading a team effort to use single molecule fluorescence microscopy to observe individual antigen-antibody binding dynamics. General job responsibilities include postdoctoral supervision, responding to external (NIH, DTRA, DARPA) and internal (LDRD) proposal calls, running and maintaining several laser spectroscopic instruments (home built and commercial) and communicating results to the scientific community. Have supervised a total of 5 postdoctoral research associates and a number of undergraduate summer students. Primary Collaborators: Peter Goodwin, Andy Shreve, Andrew Bradbury, and Jennifer Martinez

Los Alamos National Laboratory, Postdoctoral Research Associate (1998-2002)

2000-2002: Probed the folding and unfolding kinetics of protein secondary structure by laser-initiated temperature jumps and time resolved vibrational spectroscopy. Advisor: R. Brian Dyer.

1998-2000: Designed and implemented experiments in single molecule detection using laser-induced fluorescence and time correlated single photon counting in efforts to sequence single DNA molecules. Advisors: Peter Goodwin and Richard Keller.

Cornell University, Hertz Foundation Fellow (1992-1998)

Set up a four-wave mixing experiment to generate tunable vacuum ultra violet (120-160 nm) radiation from visible laser sources. Used this VUV light as an ionization source to perform time of flight mass spectrometry on radicals extracted by a molecular beam from a flame front. Dissertation title: "*VUV Photoionization Studies of Selected Flames,*" Advisor: Terrill Cool.

SKILLS

- **LASER SPECTROSCOPY**

Single molecule fluorescence spectroscopy, time correlated single photon counting, fluorescence correlation spectroscopy, four-wave mixing and nonlinear optics, optical trapping and manipulation, CW and pulsed laser sources from the vacuum ultra-violet to the mid IR.

- **OPTICAL MICROSCOPY**

Confocal and wide field fluorescence microscopy, including the full instrument development of a new confocal microscope design (Patent Pending) that uses a unique spatial filter geometry and active feed-back to follow individual fluorescent molecules in 3 spatial dimensions.

- **COMPUTER PROGRAMMING**

C/C++, Labview, Fortran, and Igor Pro. Instrument control using real-time operating systems. Experience with the writing and use of simple Monte Carlo simulations for data interpretation and instrument design.

- **PROGRAM DEVELOPMENT**

Have grown internal seed funding into award-winning programs now supported through external sponsors, such as the National Institutes of Health. Submit, organize, and participate in a number of multi-investigator research proposal efforts each year.

CURRENT FUNDING

"Tracking the intracellular spatial trajectory of an individual IgE molecule," National Institutes of Health, R21AI07707. Work uses novel instrumentation developed in our lab (a confocal microscope that uses active feedback to follow single molecules in 3 dimensions) to study receptor mediated endocytosis and 3D intracellular transport of individual IgE-FcεR1 receptors. Ends 12/2009. Role: PI.

"Tracking single quantum dots in 3 dimensions" National Nanotechnology Enterprise Development Center (NNEDC). Work supports efforts to commercialize 3D single molecule tracking instrumentation developed in our laboratory. Ends 10/2008. Role: PI.

"Understanding the Mechanism of Plant Virus-Vector Interaction through the use of new Imaging Technologies." Office of Research, UC Riverside, UCR-LANL Collaborative program in pathogen-induced plant disease. Work aims to use advanced imaging methods developed in our lab to better understand virion spread and sequestration in plant and vector hosts. Ends 10/2009. Role: co-PI. Other PI: James Ng, UCR.

"Center for Integrated Nanotechnologies," (DOE sponsored nanoscience center) Work involves helping external users acquire and interpret data using conventional and home-built fluorescence microscopes. Role: Co-Investigator. PI: Antoinette Taylor

"Predictive Design of Noble Metal Nanoclusters" Los Alamos Directed Research and Development (LDRD), 20090017DR. Work aims to develop and exploit, from first-principles, noble metal nanoclusters for applications in biological imaging and sensing. My role lies primarily in helping with single-molecule photophysical characterization methods. Ends 10/2011. Role: Co-Investigator., PI: Jen Martinez.

SERVICE

- Chaired a session on *Biological and Non-Biological Optical Microscopy* for the National OSA meeting (Frontiers in Optics XIX) San Jose, CA, September 20, 2007.
- Reviewer for *Nature Methods*, *Biophysical Journal*, *Analytical Chemistry*, *Journal of Biotechnology*, *Cytometry*, and *Journal of Physical Chemistry*.
- Served on Laboratory Directed Research and Development (LDRD) proposal review panels in Biology, Biochemistry & Biophysics (BBB) for FY2005, as well as Atomic and Molecular Optical Physics (AMOP) for FY2004.

SUBMITTED MANUSCRIPTS

- [31] Temirov, J., Bradbury A. and Werner J. H., "*Measuring an Antibody Affinity Distribution Molecule by Molecule*," submitted July 2008 to **Analytical Chemistry**.
- [30] Werner, J. H., Montano G.A., Garcia A.L., Zurek N.A., Akhadov E.A., Lopez G.P. and Shreve A.P., "*Formation and dynamics of supported phospholipid membranes on a periodic nanotextured substrate*," submitted July 2008 to **Langmuir**.
- [29] Wells, N. P., Lessard G.A. and Werner J. H., "*Confocal, 3-Dimensional Tracking of Individual Quantum-Dots in High Background Environments*," submitted June 2008 to **Optics Letters**.

PUBLICATIONS

- [28] Lessard, G.A., Habuchi S, Werner J.H., Goodwin P. M., De Schryver F.C., Hofkens J. and Cotlet M., "*Probing dimerization and Intraprotein fluorescence resonance energy transfer in a far red fluorescent protein from the sea anemone *Heteractis crispa**," **Journal of Biomedical Optics** 031212-1 to 031212-7 (2008).
- [27] Dai, M., Temirov J., Emanuele P., Kiss C., Pavlik P., Werner J. H. and Bradbury A., "*Using T7 phage display to select GFP-based binders*," **Protein Engineering Design and Selection** (2008).
- [26] Lessard, G.A., Goodwin P. M. and Werner J. H., "*Three dimensional tracking of individual quantum dots*," **Applied Physics Letters** 2224106 (2007).
- [25] Werner, J. H., McCarney E. R., Keller R. A., Plaxco K. W. and Goodwin P. M., "*Increasing the resolution of single pair fluorescence resonance energy transfer measurements in solution via molecular cytometry*," **Analytical Chemistry** 3509-3513 (2007).
- [24] Dai, M, Fisher H, Temirov J, Kiss C, Phipps M.E., Pavlik P., Werner J.H. and Bradbury A, "*The creation of a novel fluorescent protein by guided consensus engineering*," **Protein Engineering Design and Selection** 69-79 (2007).
- [23] Werner, J. H., Joggerst R, Dyer R.B. and Goodwin P. M., "*A two dimensional view of the folding energy landscape of cytochrome c*," **Proceedings of the National Academy of Sciences (USA)** 11130-11135 (2006).
- [22] Temirov, J, Bradbury A and Werner J.H., "*Surface-immobilized antibody-antigen binding affinity studies by single molecule fluorescence imaging*," **Proceedings of the SPIE** 6092001 to 60920010 (2006).
- [21] Lessard, G. , Goodwin P.M. and Werner J.H., "*Three dimensional tracking of single fluorescent particles*," **Proceedings of the SPIE** 609205-1 to 609205-8 (2006).
- [20] Cotlet, M. , Habuchi S., Whitier J. E., Werner J. H., De Schryver F. C., Hofkens J. and Goodwin P. M., "*Single Molecule Spectroscopic Characterization of a Far-Red Fluorescent protein (HcRed) from the Anthozoa Coral *Heteractis Crispa**," **Proc. of the SPIE** 609804-1 to 690804-11 (2006).
- [19] Cotlet, M., Goodwin P.M., Waldo G. S. and Werner J. H., "*Time-resolved Detection of the One- and Two-Photon Excited Fluorescence of Single Molecules of a Folding Enhanced Green Fluorescent Protein*," **Proc. of the SPIE** 609204-1 to 609204-10 (2006).
- [18] Cotlet, M., Goodwin P.M., Waldo G. S. and Werner J. H., "*A comparison of the fluorescence dynamics of single molecules of a green fluorescent protein: one- vs two-photon excitation*," **ChemPhysChem** 250-260 (2006).
- [17] Werner, J.H., Cai H., Keller R.A. and Goodwin P.M., "*Exonuclease I hydrolyzes DNA with a distribution of rates*," **Biophysical Journal** 1403-1412 (2005).

PUBLICATIONS (continued)

- [16] McCarney, E.R., Werner J.H., Bernstein S.L., Ruczinski I., Makarov D.E., Goodwin P.M. and Plaxco K.W., "*Site-specific dimensions across a highly denatured protein; a single molecule study*," **Journal of Molecular Biology** 672-682 (2005).
- [15] Werner, J.H., Cai H., Jett J.H., Reha-Krantz L., Keller R.A. and Goodwin P.M., "*Progress towards single-molecule DNA sequencing: A one color demonstration*," **Journal of Biotechnology** 1-14 (2003).
- [14] Ambrose, W.P., Cai H., Goodwin P.M., Grace K.G., Habbersett R.C., Jett J.H., Larson E.J., Werner J.H. and Keller R.A., "*DNA Fragment Sizing by Flow Cytometry*," **Topics in Fluorescence VI: DNA Technology** (2003). JR Lakowicz, Editor.
- [13] Baker, G.A., Baker S.N., McCleskey T.M. and Werner J.H., "*Aspects of chemical recognition and biosolvation within room temperature ionic liquids*," **ACS Symposium Series: Ionic Liquids as Green Solvents** 212-224 (2003).
- [12] Werner, J.H., Baker S.N. and Baker G.A., "*Fluorescence correlation spectroscopic studies of diffusion within the ionic liquid 1-butyl-3-methylimidazolium hexafluorophosphate*," **Analyst** 786-789 (2003).
- [11] Werner, J.H., Dyer R.B., Fesinmeyer R.M. and Andersen N.H., "*Dynamics of the primary processes of protein folding: Helix nucleation*," **Journal of Physical Chemistry B** 487-494 (2002).
- [10] Goodwin, P.M., Ambrose W.P., Cai H., Grace W.K., Larson E.J., Marrone B.L., Jett J.H., Werner J.H. and Keller R. A., "*Single molecule nucleic acid analysis by fluorescence flow cytometry*," **NATO Advanced Research Workshop on Biological, Biophysical and Theoretical Aspects of Polymer Structure and Transport** 351-370 (2002).
- [9] Werner, J.H., Larson E.J., Goodwin P.M., Ambrose W.P. and Keller R.A., "*Effects of fluorescence excitation geometry on the accuracy of DNA fragment sizing by flow cytometry*," **Applied Optics** 2831-9 (2000).
- [8] Werner, J.H. and Cool T.A., "*Kinetics of the combustion of trichloroethylene for low Cl/H ratios*," **Combustion and Flame** 125-142 (2000).
- [7] Werner, J.H. and Cool T.A., "*Kinetic model for the decomposition of DMMP in a hydrogen/oxygen flame*," **Combustion and Flame** 78-98 (1999).
- [6] Werner, J.H., Cai H., Goodwin P.M. and Keller R.A., "*Current status of DNA sequencing by single molecule detection*," **Proceedings of the SPIE** 355-366 (1999).
- [5] Ambrose, W.P., Goodwin P.M., Jett J.H., Van Orden A., Werner J.H. and Keller R.A., "*Single molecule fluorescence spectroscopy at ambient temperature*," **Chemical Reviews** 2929-2956 (1999).
- [4] Werner, J.H. and Cool T.A., "*The combustion of trichloroethylene studied with vacuum ultraviolet photoionization mass spectrometry*," **27th International Symposium on Combustion** 413-423 (1998).
- [3] Werner, J.H. and Cool T.A., "*Flame sampling photoionization mass spectrometry of dichloroethanol*," **Chemical Physics Letters** 81-7 (1998).
- [2] Werner, J.H. and Cool T.A., "*Flame sampling photoionization mass spectrometry of CH₃PO₂ and CH₃OPO₂*," **Chemical Physics Letters** 278-82 (1997).
- [1] Satyapal, S., Werner J.H. and Cool T.A., "*An extended flame zone in the combustion of CH₃Cl*," **Combustion Science and Technology** 229-238 (1995).

SELECTED ORAL PRESENTATIONS

- "Tracking single quantum dots in 3 dimensions," *Frontiers in Optics: Laser Science XIX*, San Jose, CA, September 20, 2007. (Invited)
- "Three dimensional tracking of single quantum dots," *Nanotechnology in Cellular Biology*, University of New Mexico IGERT symposium, Albuquerque, NM, August 14, 2007. (Invited)
- "Three dimensional tracking of individual quantum dots," *27th Annual Meeting of the Center for Nonlinear Studies*, Santa Fe, NM, May 2007. (Invited)
- "Tracking single quantum dots in 3 dimensions" Aspen Center for Physics, *Single Molecule Biophysics*, Aspen, CO, February 2007.
- "An approach to tracking single fluorophores in 3-D" Portland State University, Portland, OR, October 2005. (Invited)
- "An approach to tracking single molecules in 3-D" delivered at *Pittcon*, Orlando, FL, March 2005. (Invited)
- "Single molecule tracking," Sandia National Laboratories, Albuquerque, NM, August 2004. (Invited)
- "Energy transfer distributions measured by single molecule fluorescence flow cytometry," Aspen Center for Physics, *Single Molecule Biophysics*, Aspen, CO, January 2003
- "Dynamics of the primary processes in protein folding: Helix nucleation." *American Chemical Society Annual Meeting*, San Diego, CA, April 2002. (Invited)
- "Current status of DNA sequencing by single molecule detection," *Photonics West*, San Jose, CA, January 1999.

PATENTS & INVENTION DISCLOSURES

- Werner, J. H., Reed S.M. and Swanson B. I., "*Screening of libraries using fluorescently reactive lipids and fluorescence correlation spectroscopy*," **US Patent Application 20050191705** (Filed internally 4/2003.).
- Werner, J.H., Goodwin P. M. and Lessard G., "*Apparatus and method for tracking a molecule or particle in three dimensions*," **US Patent Application 20080085550** (2008).
- Werner, J.H., Temirov J and Bradbury A., "*Single-molecule antibody arrays*," **LANL invention disclosure S-109,108** (Filed internally 6/2005).
- Werner, J. H., Shreve A.P. and Goodwin P. M., "*Method and Apparatus for 3D imaging on nanometer length scales*," **S112966/L2008060** (2008).