UCRL-TR-209715

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Development of a Fast Microfluidic Mixer for Studies of Protein Folding KineticsFinal Report Cover Page

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February 15, 2005

This work was performed under the auspices of the U.S. Department of Energy by University of California, Lawrence Livermore National Laboratory under Contract W-7405-Eng-48.

FY04 LDRD Final Report
Development of a Fast Microfluidic Mixer for Studies of Protein Folding Kinetics
LDRD Project Tracking Code: 02-ERD-040
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We designed and fabricated mixing devices that will help us elucidate the mechanisms of protein folding through measurements of folding reaction rates. These devices can be used in studying of other biological systems and are compatible with various spectroscopic observation methods. The project involved development of fabrication processes and setup of a laboratory for assembly and characterization of microfluidic devices, as well as measurements of protein folding kinetics.

We produced three variants of the mixer:

1) The ultra fast mixer for Foerster Resonance Energy Transfer measurements (described by Anal. Chem. Article (UCRL-JRNL-206676) and MicroTAS Conference Proceedings article (UCRL-JC-153057) included in the report
2) The ultra fast mixer for UV measurements (described by the poster presented at MicroTAS conference (UCRL-POST-207476) included in the report)
3) The mixer for single molecule measurements (described by the Science article (UCRL-JC-153057) included in the report

In these mixers, the channels are narrow, ranging from a few to hundreds of μm, so that the flow is laminar and all of the mixing is achieved through diffusion. Our goal is to develop robust microfluidic mixer with at least 100 times lower consumption rate, shorter dead time and time resolution than commercially available mixers that would be compatible with most commonly used spectroscopic methods. We are also developing mixers that can be used in combination with single molecule spectroscopy. The mixers are used to study kinetics of fast protein folding reactions using bulk fluorescence and single molecule fluorescence resonance energy transfer techniques. Capabilities for microfluidic have been developed at BSNL that will be useful for studies of interactions of DNA with proteins and other projects such as the single molecule detector for detection of low concentration of toxins.

Return on Investment

This work is contributing to high visibility of the science done at LLNL. Considerable interest in the scientific community has been generated by the publications that were produced through this project. The Science article was highlited by CAS Science Spotlight as one of the most intriguing documents of the quarter. CAS scientists analyze over 200,000 documents per quarter among articles from over 9,000 journals, and patents from 50 active patent-issuing authorities from around the world. Document is selected as "intriguing" if it contains new, novel or trendsetting scientific research that is likely to be of growing interest over time. The Analytical Chemistry article was featured on the cover of the December 15 issue and was featured in the Analytical Chemistry A-Page Magazine from January 2005 (included in the report).

Several collaborations have been established through this work: with Bill Eaton’s group at the NIH, leaders in the protein folding field, with Juan Santiago’s group at Stanford, leaders in microfluidic research, and with Shimon Weiss’s group at UCLA, leaders in single molecule spectroscopy field.

This research is positioning us, via the demonstration of robust and high performance devices, to successfully compete for external funding. So far we have obtained funding through Human Frontiers Science Program for development of microfluidic mixers for synchrotron circular dichroism. This project is currently funding a graduate student through UC Davis Center for Biophotonics Science and Technology to work at LLNL.

Strategic Alignment-

This project has developed capabilities for design and assembly of microfluidic devices at the CMS. This work is aligned with CMS strategic interests is developing new capabilities in the areas of bioscience and heath care and is serving as a conduit for attracting the next generation of scientific staff to carry out the future mission of LLNL/DOE.