COMMERCIAL RESEARCHER PERSPECTIVE

Presented by Dr. Larry DeLucas
Center for Macromolecular Crystallography
University of Alabama at Birmingham

ABSTRACT

Protein crystallography — a research tool used to study the structure of the complex building blocks of living systems — has a lot to gain from space-based research. In order to know how a protein works in the human body, researchers must understand its molecular structure. Researchers have identified 150,000 different proteins in the body, but they now know the structure of less than a third of them.

The only viable technique for analyzing the structure of these proteins is x-ray diffraction of the proteins in their crystal form. The better the quality of a protein crystal, the more useful it is to researchers who are trying to delineate its structure. The microgravity environment of space allows protein crystals to grow nearly undisturbed by convection and other gravity-driven forces that cause flaws to form in them on the ground. In space, lack of convection enables protein crystals to grow more slowly than they do on Earth, and the slower a protein crystal grows, the fewer flaws it will have.

Protein crystal growth experiments have already flown on 14 Space Shuttle missions. This year’s USML-1 Spacelab mission included protein crystal growth experiments conducted for commercial researchers. The results of protein crystal experiments flown thus far have been larger crystals with more uniform morphologies.

The Center for Macromolecular Crystallography (A NASA-cosponsored CCDS) currently builds flight hardware to meet researchers’ needs and handles sample loading and retrieval for flight experiments.

Protein crystallography enables “rational drug design”: the development of drugs that bind only with the target protein and, hence, do not cause side effects. For example, pharmaceutical companies presently are interested in developing drugs that can inhibit purine nucleoside phosphorylase (PNP), a protein that plays a role in auto-immune diseases. To continue these kinds of investigations, researchers need a constant supply of protein crystals that are as free of flaws as possible.

Space Station Freedom will provide the kind of research environment that will enable the production of such supplies. In addition, Freedom will provide the kind of long-duration facility required by protein crystal researchers: 40 percent of proteins require more than two weeks to crystallize.
Project Organization for
Protein Crystal Growth In Microgravity
University of Alabama in Birmingham / Center for Macromolecular Crystallography

Co-investigators

Principal Investigator and Project Director
Dr. L. DeLucas
Admin. Asst. Mrs. C. Henson

Contract Operations/Management
UAB Research and Grants Administration

Financial Administration (CMC)
Mrs. M. A. Lynch

Quality Control
Dr. B. Andrews

Science Development/Support
- Dr. K. Moore and Mr. J. Stewart, Protein Experiment Coord. and Sample Handling.
- Dr. C. Smith and Dr. M. Carson, X-ray Analysis of Protein Samples
- Dr. W. Rosenblum, Optical Sub-Systems Dev.
- Dr. W. Wilson*, Laser Light Scattering Sub-System Dev.
- Mr. B. Bishop, Fundamental Laser Light Scattering Studies
- Dr. R. Benton**, Control and Data Management Sub-System Dev.
- Mr. T. Bray and To Be Named, N2 and Temperature Control Sub-System Dev.

- Dr. L. DeLucas (P.I.), Sub-Systems Integration and Operation

** Mississippi State University
*** Dial Engineering, Mississippi State University

Need for Microgravity Environment

- 450 protein structures completed

- Molecular biology

- Rational drug design

- Large co-investigator group from universities and industries

- No other technique

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## Morphometry

Number of Crystals Sampled, PCF
STS 37, 43, 49

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<th>SHUTTLE FLIGHT</th>
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<th>GROUND ROSETTE</th>
<th>FLIGHT SINGLE</th>
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<td>405</td>
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<td>1155</td>
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<td>STS 49</td>
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<td>1232</td>
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<td>TOTAL</td>
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Morphometry
Length of Single Crystals
STS 37, 43, 49

![Graph showing the relationship between PCF volume (ml) and millimeters for flight and ground experiments for STS 37, 43, and 49.]
X-Ray Diffraction
Intensity as Function of Crystal Volume
STS-49: 500ml PCF
* GROUND  □ FLIGHT

Intensity: Flight > Ground, 0.0005 level
Volume: Flight = Ground
X-Ray Diffraction
Number of Crystals Sampled, PCF
STS 37, 43, 49

<table>
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<th>SHUTTLE FLIGHT</th>
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<td>12</td>
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<tr>
<td>TOTAL</td>
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Easy Access

- We build hardware to meet science group’s needs
- We handle loading and sample retrieval
- Sample approval process is rapid and can be accomplished late in flow
**Constant Access/Rapid Turnaround**

- Need laboratory around the clock
- Need constant supply of crystals
- Crystals must be harvested frequently
- New protein batches transferred via frequent and consistent shuttle schedule

**Dynamic and Flexible Hardware Program**

- Facility capable of rapidly meeting needs of each corporate partner
- Thermal Enclosure System (TES)
- Protein crystal growth organizational chart
- Hardware development
  - Science objectives
  - Design/analysis
  - Manufacturing
  - Qualification testing (for flight)
  - Functional testing (to meet science objectives)
  - Verification
Consistency/Predictable Schedule

- Corporate/Academic Planning

- Reliability

Real Time Monitoring and Control

- Scientists on board full time

- Observation/Crystal Optimization