N93-22615

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.

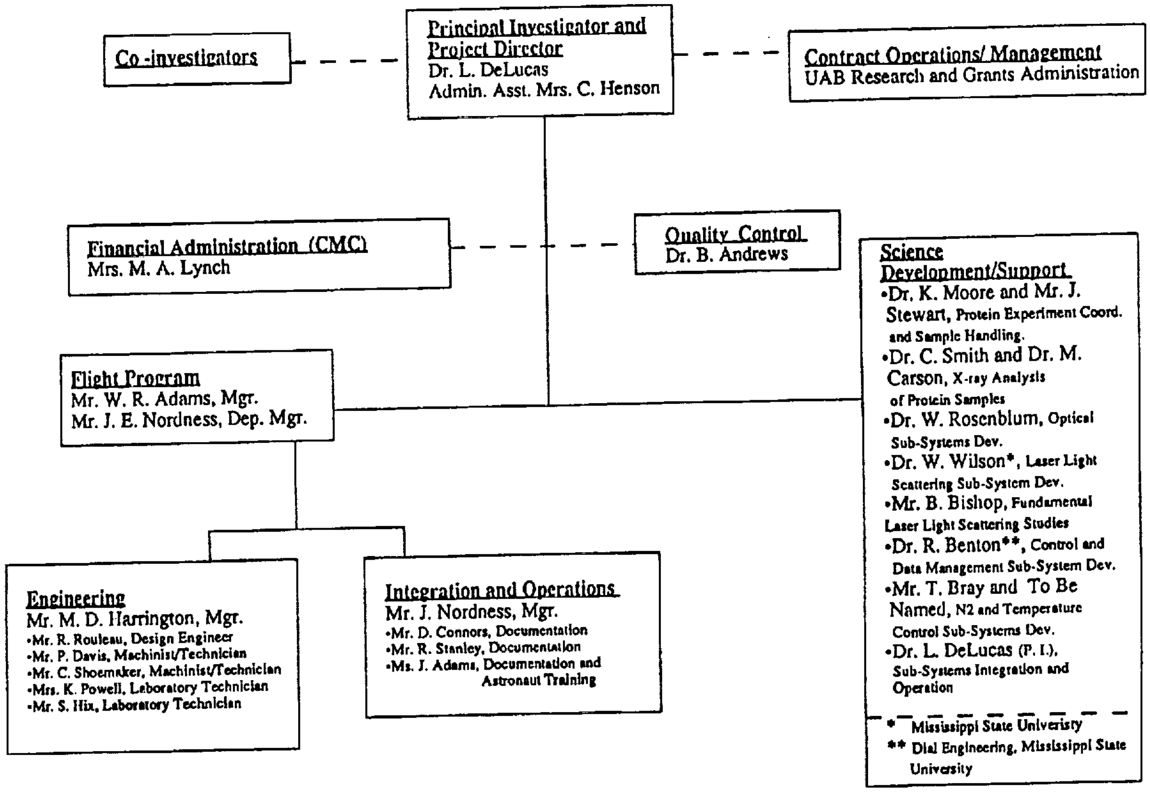
Protein crystallography enables "rational drug design": the development of drugs that bind only with the target protein and, hence, do not cause side effects. For example, pharmaceutical companies presently are interested in developing drugs that can inhibit purine nucleoside phosphorylase (PNP), a protein 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 at Birmingham / Center for Macromolecular Crystallography



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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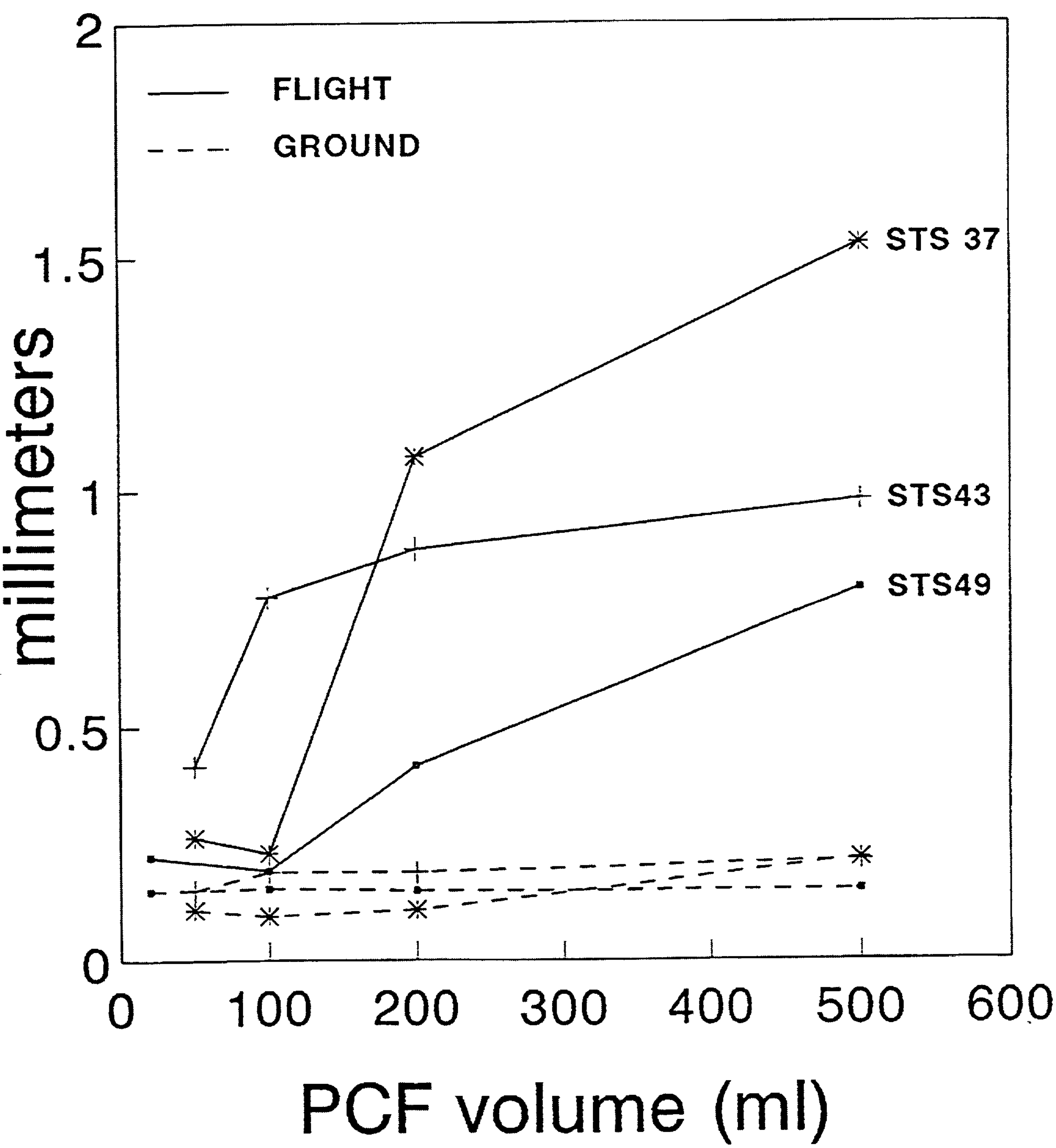
Morphometry

Number of Crystals Sampled, PCF

STS 37, 43, 49

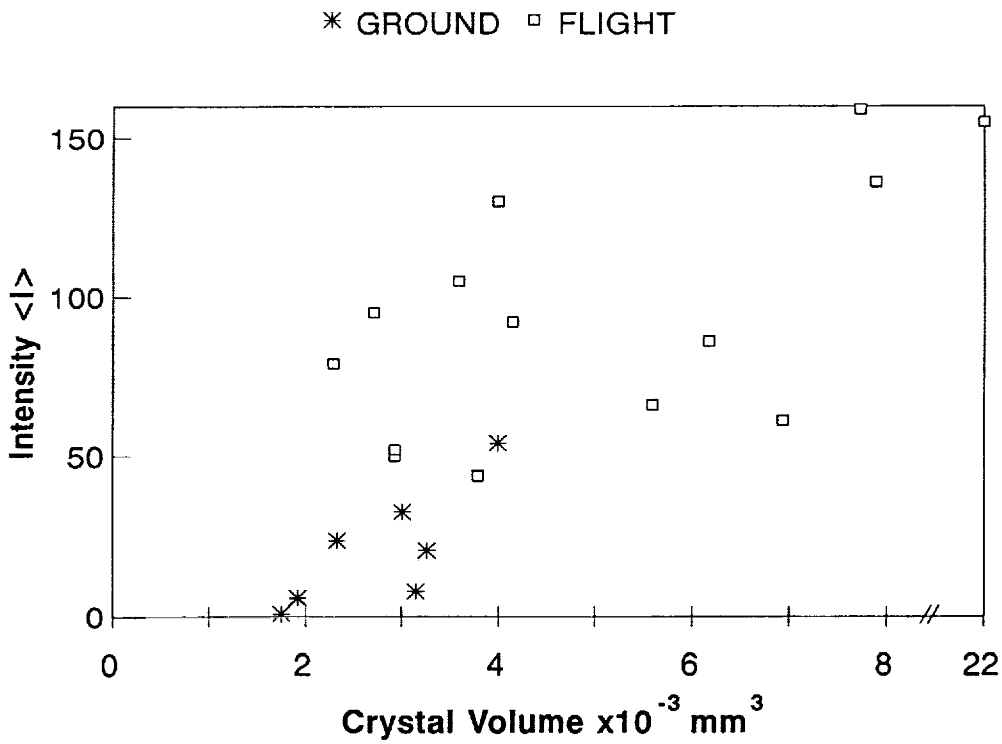
SHUTTLE FLIGHT	GROUND SINGLE	GROUND ROSETTE	FLIGHT SINGLE	FLIGHT ROSETTE
STS 37	700	600	405	550
STS 43	458	na	1155	na
STS 49	1220	1232	328	530
TOTAL	7178			

Morphometry
Length of Single Crystals
STS 37, 43, 49



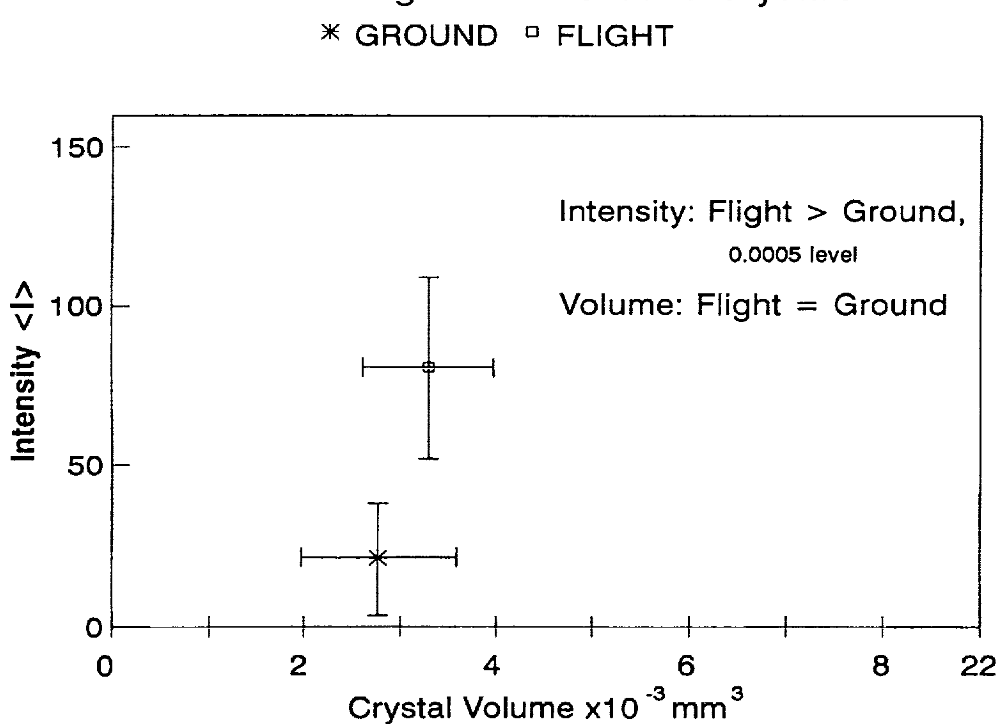
X-Ray Diffraction

Intensity as Function of Crystal Volume
STS-49: 500ml PCF



X-Ray Diffraction

Intensity as Function of Crystal Volume
STS-49: 500ml PCF
Means for 8 Flight and 7 Ground Crystals



X-Ray Diffraction

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

SHUTTLE FLIGHT	GROUND	FLIGHT
STS 37	7	5
STS 43	10	10
STS 49	9	12
TOTAL	53	

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