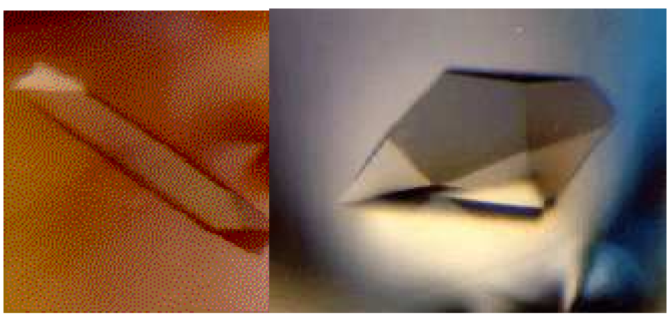
PROTEIN CRYSTAL GROWTH

ACTUAL CRYSTALS FROM PCG



INTRODUCTION

The human body contains thousands of different proteins, which play essential roles in maintaining life. A protein's structure determines the specific role that protein plays in the human body; however, researchers lack detailed knowledge about the structures of many proteins. Crystallography allows scientists, through the study of protein crystals, to determine the three-dimensional molecular structures of proteins, other large molecules, and some viruses. With an improved understanding of the molecular structures and interactions of proteins, drug designers may be able to develop new drug treatments that target specific human, animal, and plant diseases.

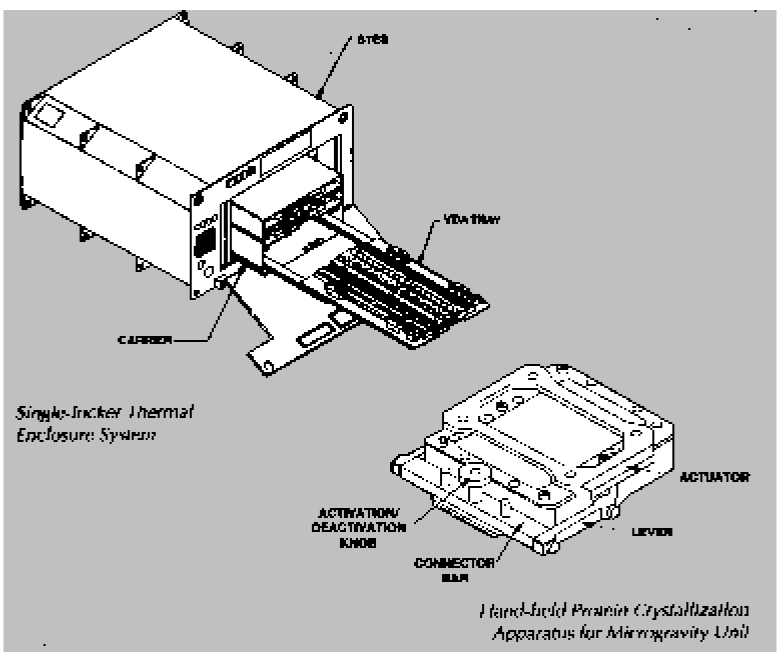
To learn how various proteins function, scientists construct computer models that reveal the complex three-dimensional structures of these large biological molecules. To solve a protein's structure, scientists known as protein crystallographers must first crystallize the protein and analyze the resulting crystals by a process called X-ray diffraction. Precise measurements of thousands of diffracted intensities from each crystal help scientists map the probable positions of the atoms within each protein molecule. This complex process requires from several months to several years to complete.

The structures of many important proteins remain a mystery simply because researchers are unable to obtain crystals of high enough quality or large enough size. Generally, crystals must have dimensions of approximately 0.3 mm to 1.0 mm, and the protein molecules must be arranged in an orderly, repeating pattern.

The National Aeronautics and Space Administration's (NASA's) Protein Crystal Growth (PCG) program has been developed to learn how protein crystals grow in space and how to optimize the growth process, while producing large, high-quality crystals of selected proteins. The microgravity conditions inside an orbiting spacecraft, being relatively free from the gravitational effects of sedimentation and convection, provide an exceptional environment for studying this process. Since 1985, NASA has flown multiple PCG experiments on the Space Shuttle and produced diffraction-quality crystals of many proteins. Data derived from each crystal analyzed provide an additional piece of the puzzle leading researchers closer to the desired high-resolution of a particular protein.

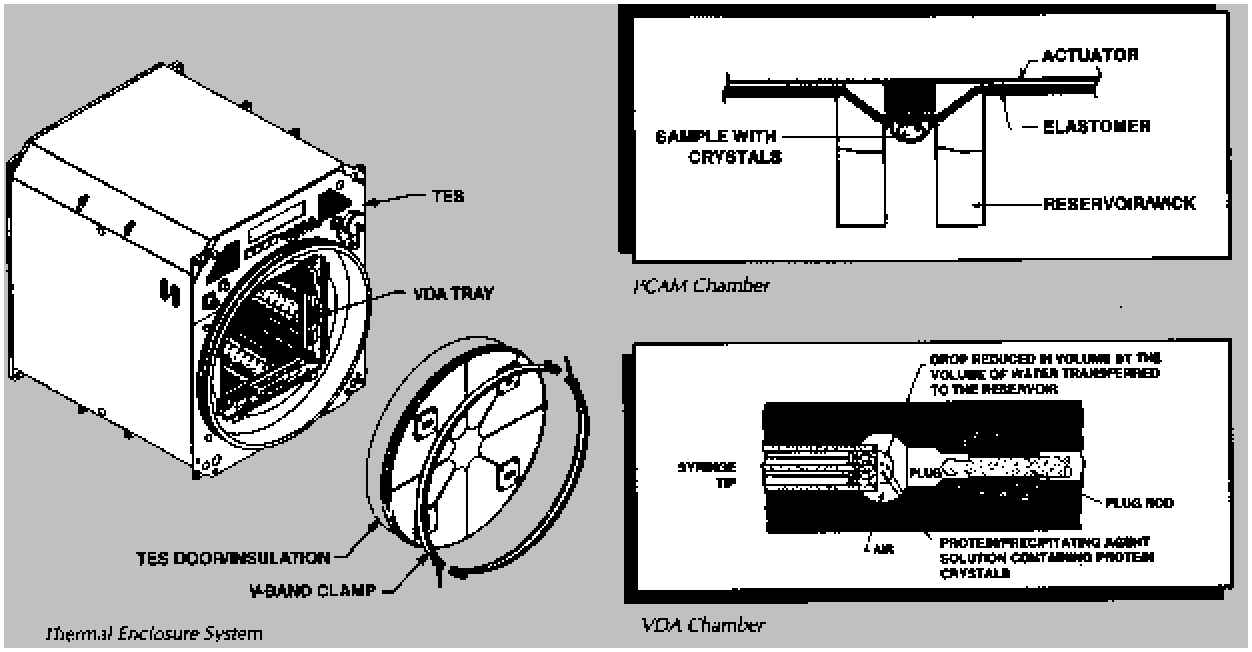
New PCG hardware, consisting of enclosures, advanced diagnostics, and experiment apparatus, will enable scientists to enhance and expand this important space-based research.

HARDWARE DESCRIPTION



The new PCG hardware consists of a variety of experiment equipment including improved Vapor Diffusion Apparatus (VDA) trays, hand-held Protein Crystallization Apparatus for Microgravity (PCAM) units, the Crystallization Observation System

(COS), and the Advanced Crystallization Observation System (A/COS). This equipment is inserted in special thermal enclosures that are installed in place of lockers in the Orbiter middeck. The two configurations available are the dual-locker Thermal Enclosure System (TES) and the Single-locker Thermal Enclosure System (STES).



Thermal Enclosure System

PCAM Chamber

VDA Chamber

The TES can be operated as a refrigerator, with a minimum set point temperature of 4.0øC, or as an incubator, with a maximum set point temperature of 40.0 øC. It can maintain the temperature at the controlling sensor location within +0.2 øC of the set point. The TES can be set to maintain a constant temperature or pro- grammed to change temperature settings over time. Internal temperature measurements are recorded by a data logger. Larger equipment, such as the COS and A/COS, must fly in the TES.

The STES, a commercially derived refrigerator incubator module, provides many of the same features as the TES. Its temperature control range is from 1.0 øC to 40.0 øC, and the unit can maintain the temperature at the controlling sensor location within +0.5 øC of the set point.

OPERATIONS

The most often employed method of growing protein crystals is vapor diffusion. The VDA trays, PCAMS, COS and A/COS use this process, which relies on water vapor pressure differences within a chamber, to create optimum growth conditions.

Each vapor diffusion device has a number of experiment chambers, and each chamber contains a protein solution and a precipitating (or crystallizing) agent. Various methods--from a double-barreled syringe (VDA tray) to a pedestal in the center of a circular chamber (PCAM)--are used to contain the solutions. In each case, the surrounding chamber holds an absorbent reservoir that contains a solution of the precipitant. Vapor pressure differences between the protein solution and the reservoir solution force water to move from the protein solution to the reservoir. As protein concentrations increase, protein crystals begin to nucleate and grow.

Other equipment, such as the COS and A/COS, will increase our understanding of the crystal growth process by allowing scientists to monitor the crystal growth in each chamber of the experiment apparatus. The COS consists of a specially designed VDA tray with six chambers, a video camera for each chamber, a lighting system, and associated hardware. By observing the crystal growth in each chamber, researchers can identify which conditions and concentrations of proteins and precipitants are best for promoting the crystal growth of a particular protein. The A/COS provides a similar function, incorporating a moveable camera to view 20-chamber VDA trays.

The scope of NASA's PCG program continues to expand as PCG experiment results indicate the need for continual, long-term access to the microgravity environment. Extended stays in space will allow longer periods of crystal growth for slow-growing and hard-to-grow proteins and permit more repetitive testing. Longer Shuttle flights and research on the space station will play a vital role during this next phase of protein crystal research.