A Perspective from NIH on Light Source Facilities

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NIGMS

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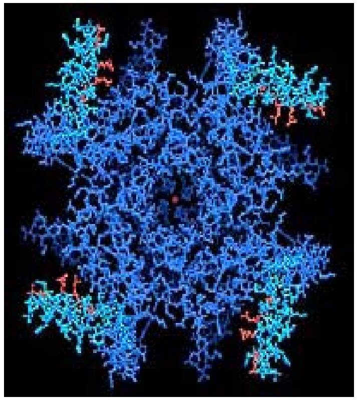
NIGMS

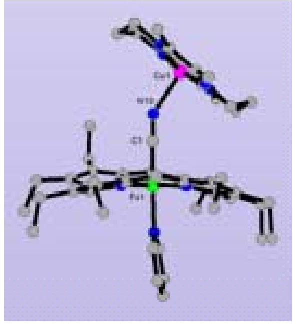
Summary

- The Cooperative Stewardship Funding model has served the biomedical research community well
- Advances in structural biology are crucial to the NIH mission
- NIH has made substantial investments in light source development and operation
- NIH is current analyzing needs for the future

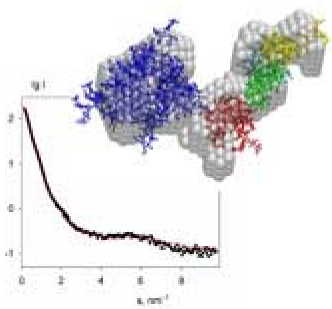
Synchrotron X-rays are needed for many different molecular biology applications



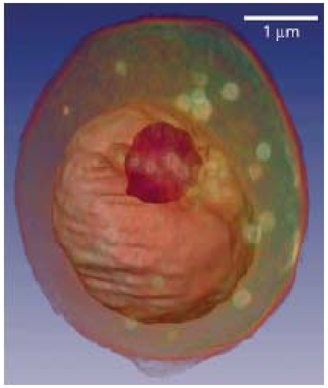
Crystallography yields 3-D atomic structures



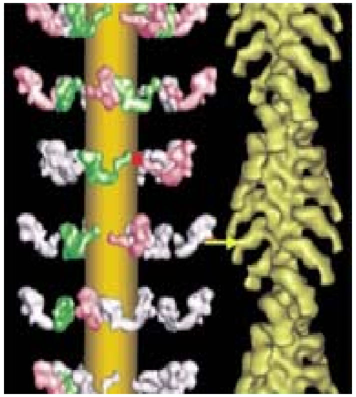
X-ray Spectroscopy yields information about metals in proteins



X-ray scattering provides information about proteins in solution



X-ray microscopy can image a cell in its natural hydration state



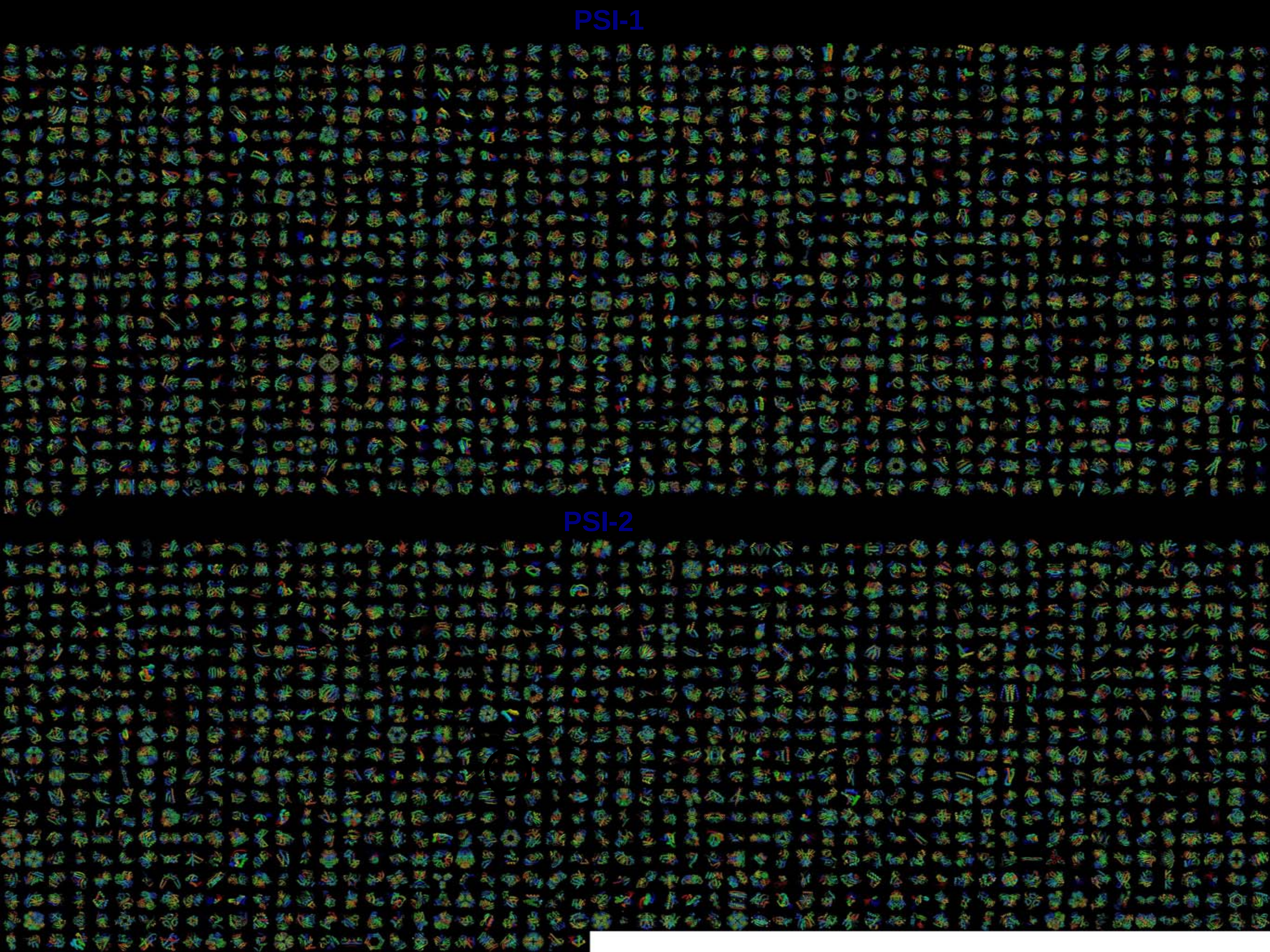
Fiber diffraction reveals detailed structures of fibrous molecules such as myosin and actin

Protein Structure Initiative (PSI)

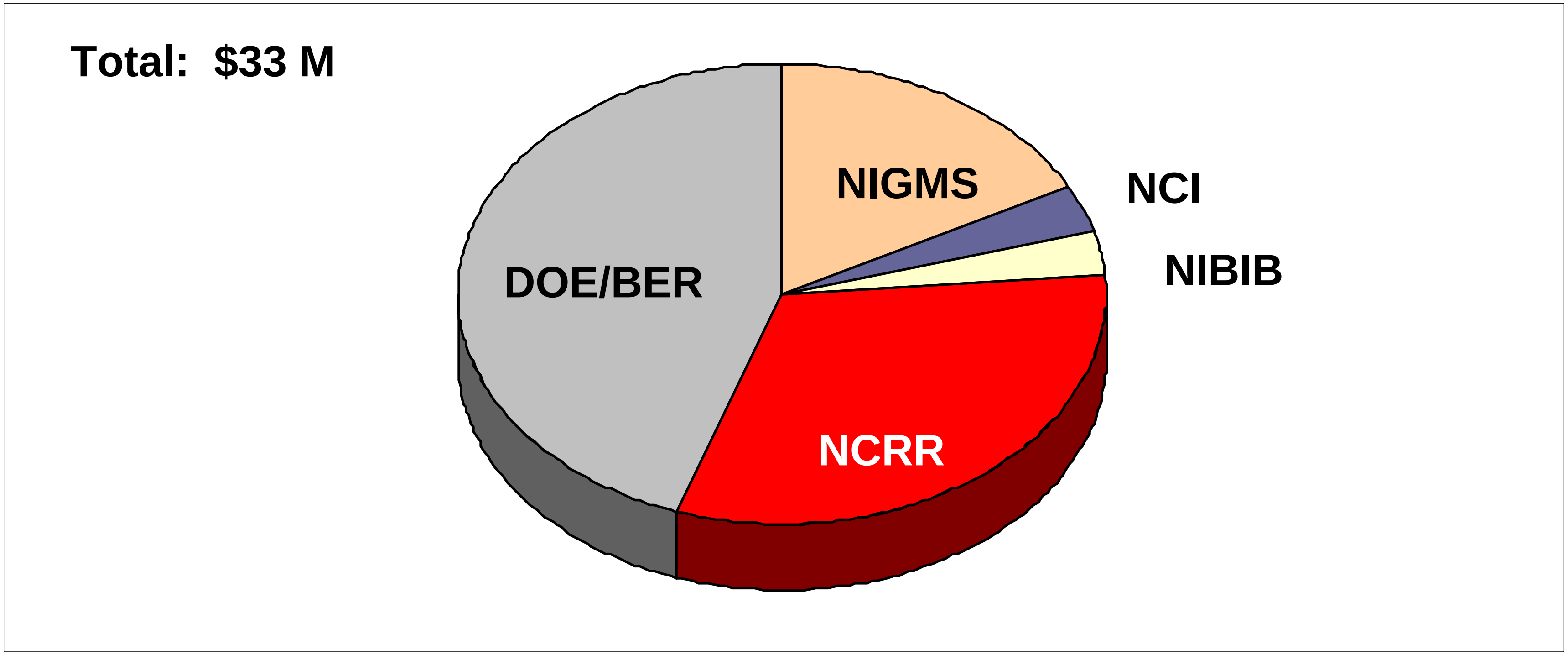
- **PSI-1 (2000-2005)**
  - Organized following three workshops and Council discussions
  - Pilot phase
- **PSI-2 (2005-2010)**
  - Organized based on PSI-1 outcomes and following PSIAC and Council discussions
  - Production phase

PSI-2 Research Network

- **Large-scale research centers**
- **Specialized research centers for technology development for challenging proteins (co-funded by NCRR)**
- **Homology modeling program**
- **Materials Repository**
- **Knowledge Base**


PSI-1
PSI-2

Federal Funding of Life Sciences Beamlines, FY2006



NIGMS Synchrotron User Enhancement Equipment

Synchrotron Facility	Equipment
SSRL	Detector, beamline equipment, computer, support laboratory
NSLS	Complete beamline and endstation, detector
CHESS	Mirror, monochrometer, endstation
ALS	Mirror system, endstation equipment, detector
CAMD	Complete beamline, detector

GM/CA CAT

National Institute of General Medical Sciences

National Cancer Institute

GM/CA CAT

National Institutes of Health

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

NATIONAL INSTITUTES OF HEALTH

GM/CA CAT Scientific Goals

- MAD capability in all stations (high energy resolution)
- Rapid tunability over a wide energy range
  U M_V edge to Xe K edge 3.5-35 keV 3.54-0.35 Å
- Beam size appropriate for small crystals, *i.e*. < 50 μm
- Parallel beam for large unit cells
- Robust, reliable optics
- Automation
  beamline alignment
  sample mounting
  sample alignment
- Robust, user-friendly beamline operation

A Tunable, Tabletop, Synchrotron Light Source
5-R44-GM066511-03, Jeffrey Rifkin, PI

TECHNOLOGY
TOOLS & TECH

Shrinking the Synchrotron

New laser-based technology could provide laboratory-scale synchrotron source

Advanced synchrotron radiation sources have revolutionized structural biology, allowing X-ray crystallographers to solve complex macromolecular structures. But as few of these soccer field-sized facilities exist worldwide, researchers have only limited access to them. Now researcher Ronald Ruth at the Stanford University Linear Accelerator Center has designed and is currently building a new desktop-sized synchrotron source called the Compact Light Source (CLS) that could permit universities and corporations to set up their own structural biology facilities. "Assuming it takes off, it is really going to change the way people are doing their X-ray crystallography research at home," says Bill Weis, professor of structural biology, Stanford University School of Medicine.

Conventional synchrotrons use large magnetic rings (roughly 305 m in diameter) to store high-energy electron beams. Undulating magnetic fields bend or "wiggle" the beams to produce X-ray radiation whose wavelength is proportional to the period of the magnets and the energy of the electron beam. A 5-GeV beam combined with a 2-cm undulator can produce 1-Å radiation, the wavelength required for biological applications.

The CLS will instead use a laser pulse to bend the electrons. A 25-MeV electron beam, which can be stored in a desktop-sized ring, produces 1-Å radiation when undulated by a 1-μm laser. "It's straight physics," says structural proteomics researcher Peter Kuhn, professor of cell biology at the Scripps Research Institute, La Jolla, Calif.

Weis notes several advantages to the CLS over the rotating anode generators found in most X-ray crystallography laboratories. The generators emit monochromatic light that is too weak to probe complex structures, whereas the CLS is designed to be tunable, allowing users to select wavelengths. It also emits more intense light and is probably easier to maintain than rotating anodes, which contain many moving mechanical parts, Weis adds.

Ruth has founded Palo Alto-based Lyncean Technologies (www.lynceantech.com) to develop and market the device. He says the ongoing prototype development, funded by the National Institutes of Health, is addressing practical issues, and full system tests are slated for 2005.

According to Ruth, the Lyncean system "complements the major facilities with a source that can do a good fraction of what can be done at the large synchrotron, and in an individual station." But don't expect synchrotrons to become extinct, says Weis: Cutting-edge experiments will still require a trip to an advanced photon source.

—Aileen Constans

The Scientist, June 7, 2004, p. 46.

Current Questions/Issues

- Capacity and utilization of existing synchrotron resources
- Next phase of Protein Structure Initiative
- Potential impact of emerging technologies