

SGX-CAT

APS Cross-cut Review

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1/24/07

- Vision
- Implementation
- Overall highlights
- Technology highlights
- Science highlights
- Summary

Vision for SGX-CAT

A high-throughput macromolecular crystallography facility supporting structure-based small-molecule drug discovery

Vision Requires...

- Beamline is means to an end and not an end in itself
- Maximum reliability
- Maximum automation/Minimum staff size
- Commercial hardware and software
- Development projects **only** for specific needs unmet by capabilities in commercial marketplace
- **Information flow is critical**
- Improved efficiency through integration of **automation** with **information management**

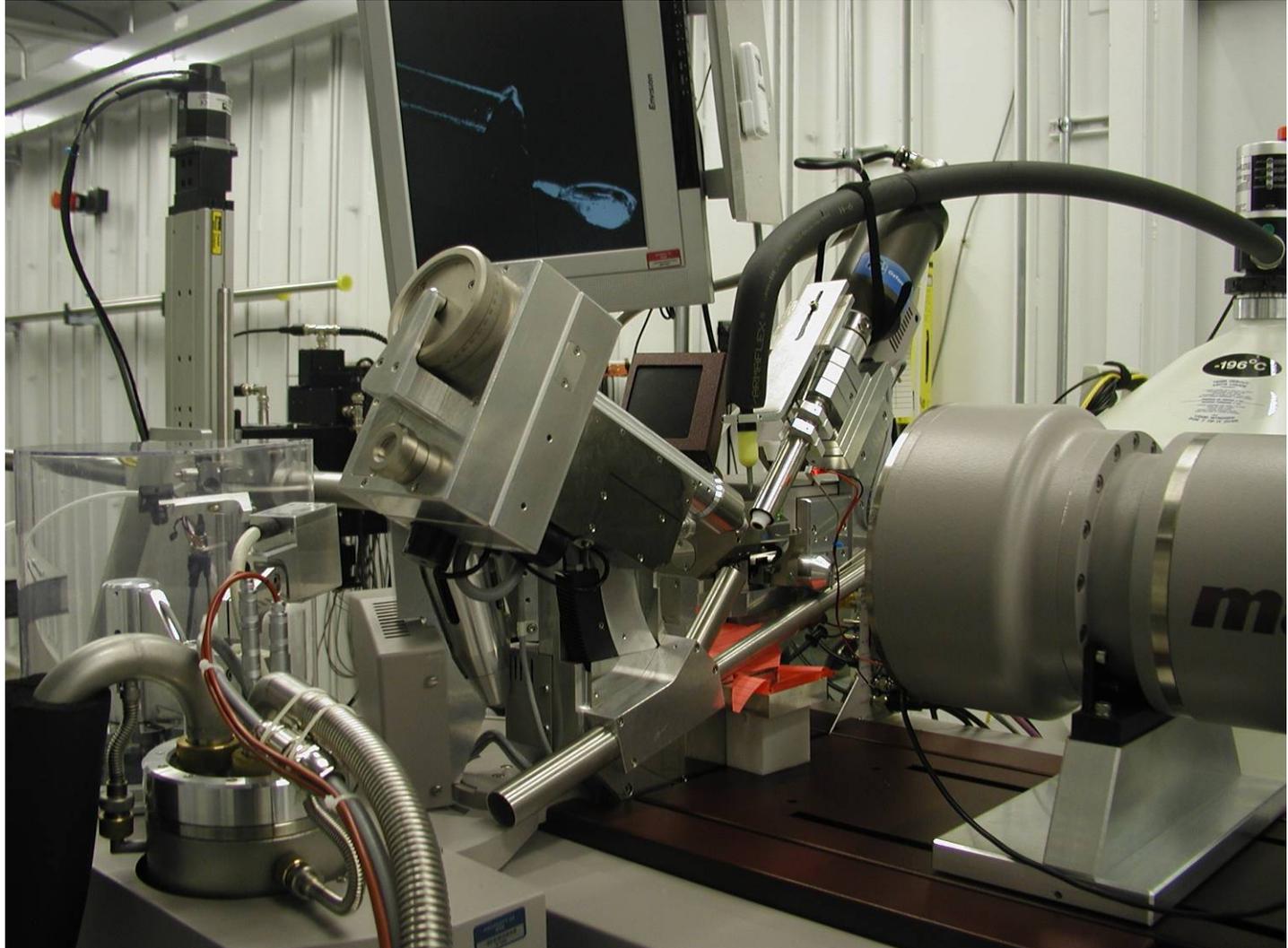
- "FedEx" or "Mail-in" crystallography an oversimplification
- Beamlines have matured to point where they can be part of an integrated facility
- Facility capabilities have evolved over five years
 - Data flow to/from database
 - Automated processing
 - Sample changer
 - Automated centering
 - Automated crystal evaluation
- Group not constrained by traditional data collection procedures

Highlights

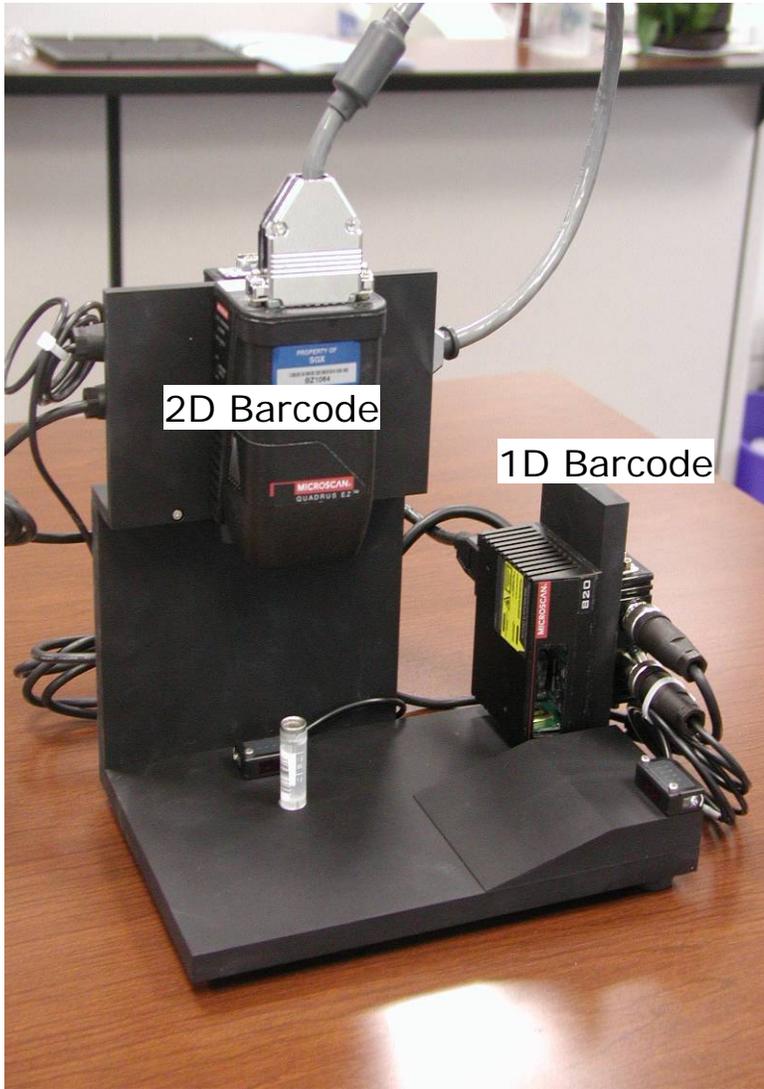
- >\$600,000/annum paid in proprietary charges for 2005 and 2006
- ~100 PDB depositions in 2006 in support of NIH PSI
- >9,300 crystals examined and >4,400 data sets collected in each of 2005 and 2006
- >30,000 crystals examined in five years on SGX-CAT
- Data tracking with SGX LIMS database, crystal-scoring algorithms, and automated management of data collection
- >\$500M drug discovery collaboration with Novartis on SGX compounds for treatment of drug resistant chronic myeloid leukemia
- Progress on cystic fibrosis drug discovery project funded by the CFF

- Sample changer
 - Sample barcoding
 - Autocentering
 - Liquid nitrogen wash
- “Scoring” applied to evaluating crystal quality
 - Automated evaluation of crystal quality
- LIMS status screen
 - Monitor status of up to 380 crystals
- Carousel changer
 - Increase duration of unattended operation

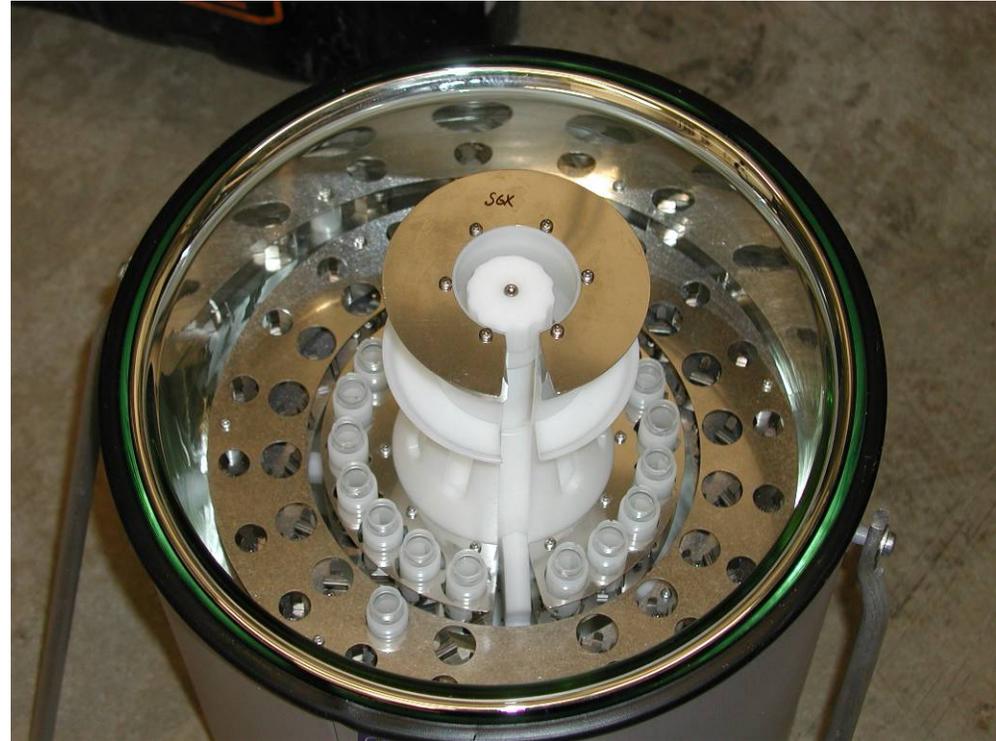
Sample Changer



Crystal Loading



Barcode Reading Station



Carousel Loading Dewar (LN₂ not shown)

Automatic Loop Alignment

Crystal Alignment Software Version 0.0.9

Contrast Error Palette Transmitter Log Image
 Receiver Circle Center

"ALIGN" command in progress Present Crystal Center(mm) X 405 Y 152.000

Operating Mode

- Alignment START
- Blank Image Snapped?
- Loop Detected?
- Offset Detected?
- Alignment Done?

Blank Image 

Elapsed Time 00:01:26

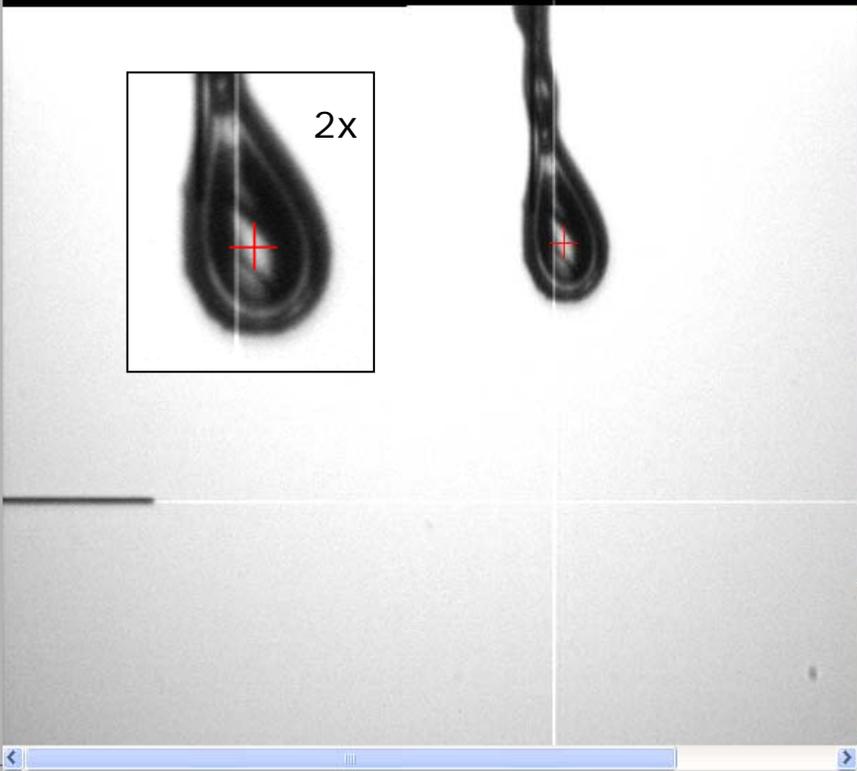
Manual Operation
Motion Axis

Send

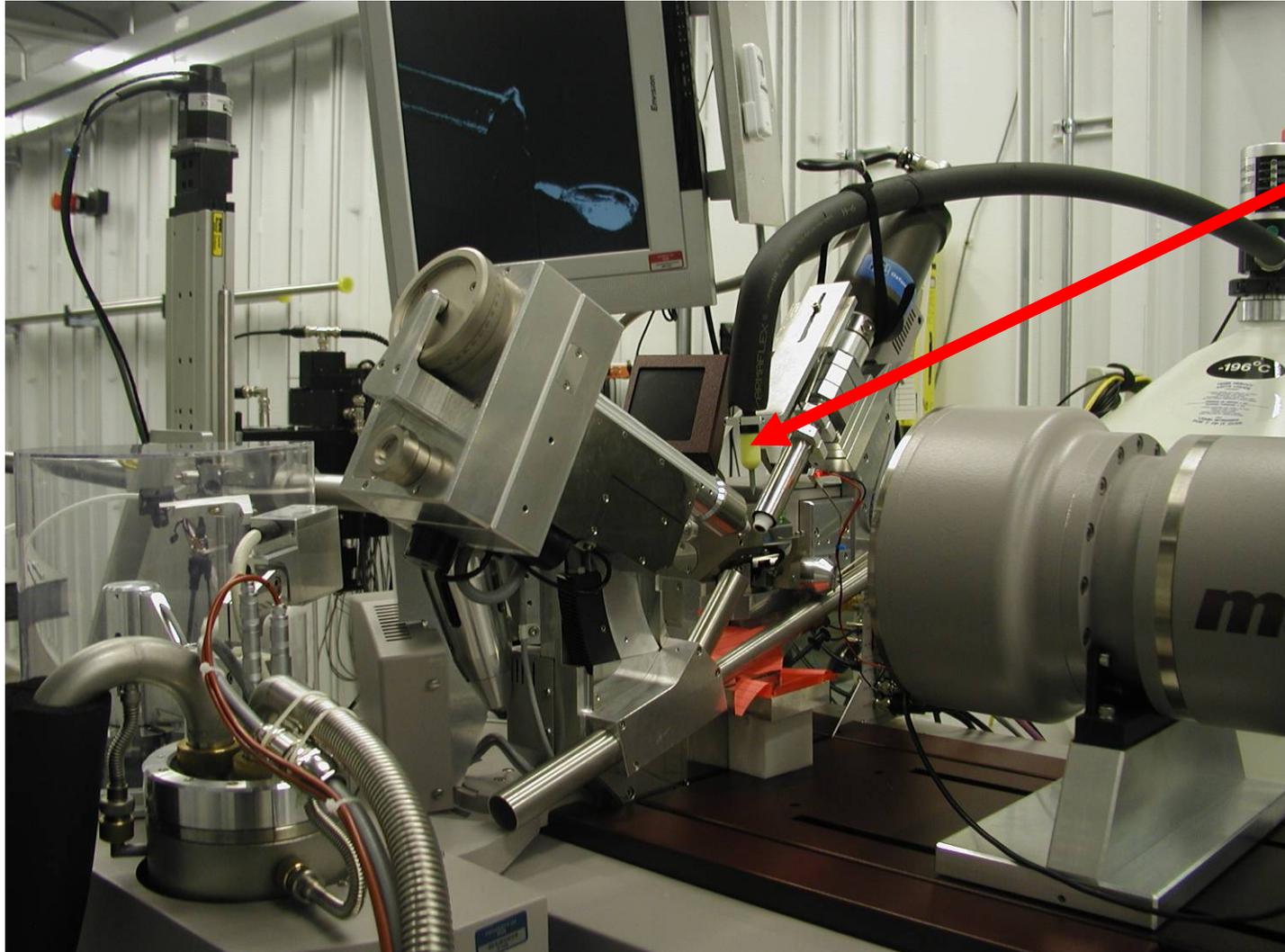
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Receive

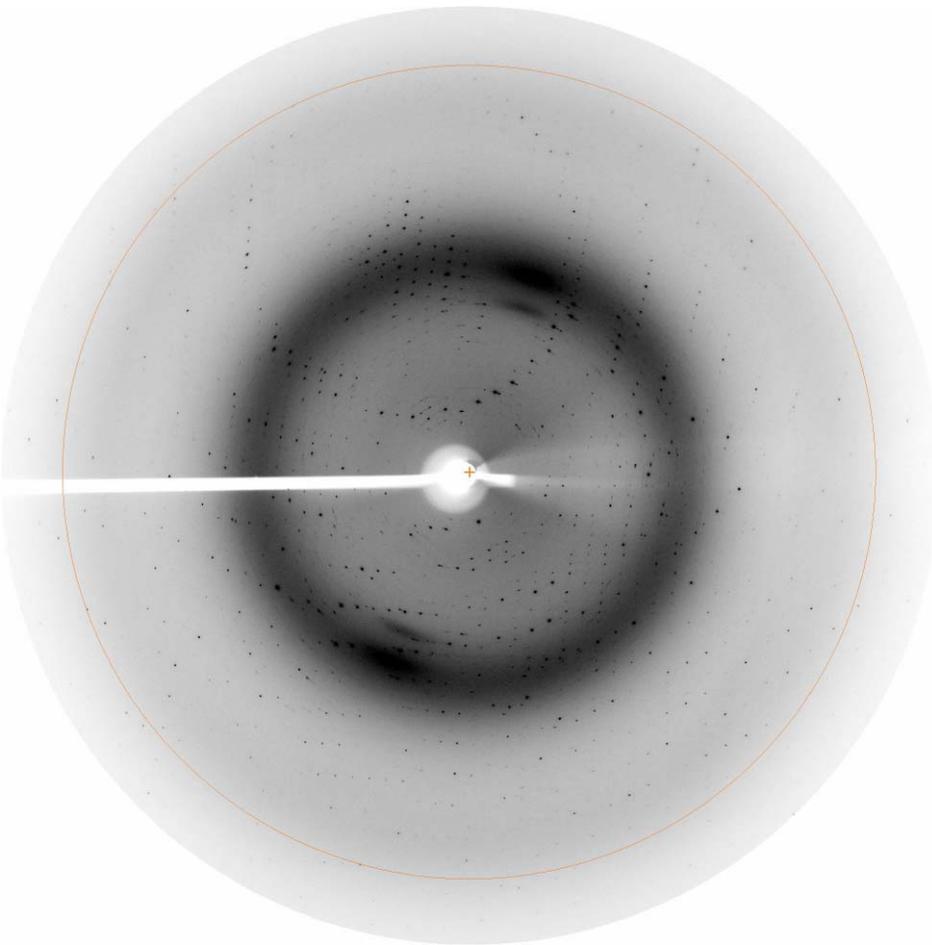
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Liquid Nitrogen Wash



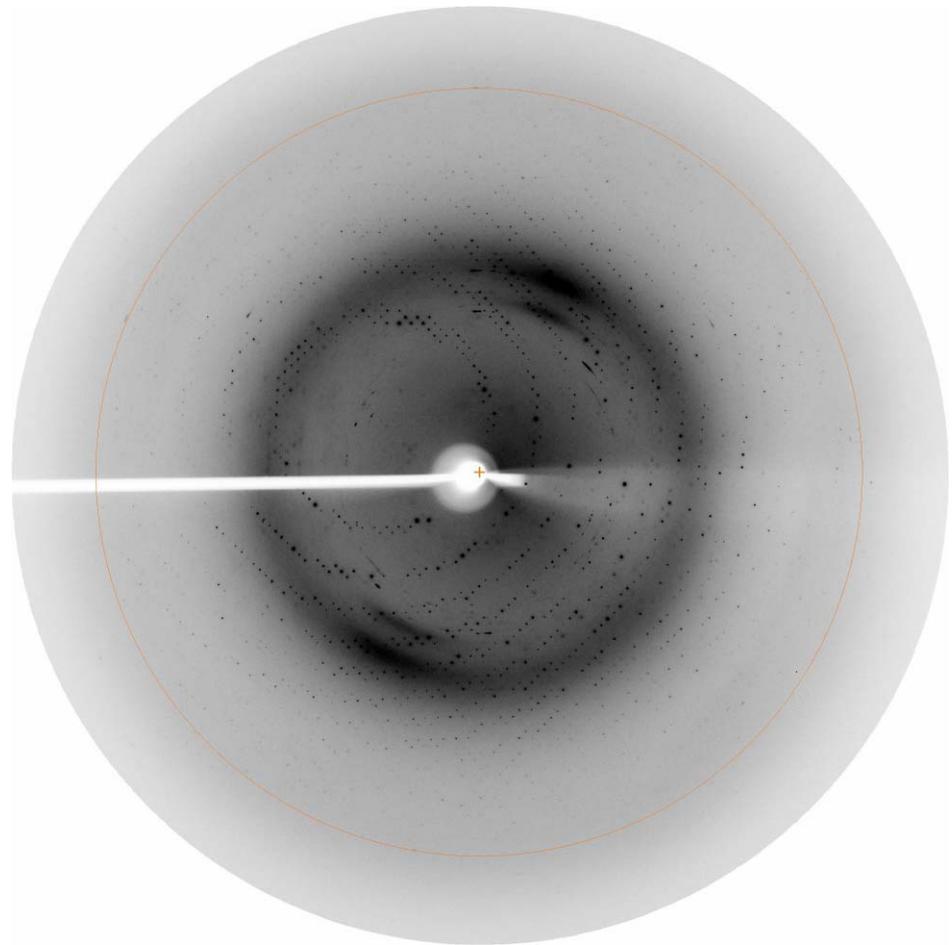
Scoring Examples



Score: 1490

Estimated Resolution: 1.7 Å

Dataset: 2.0 Å

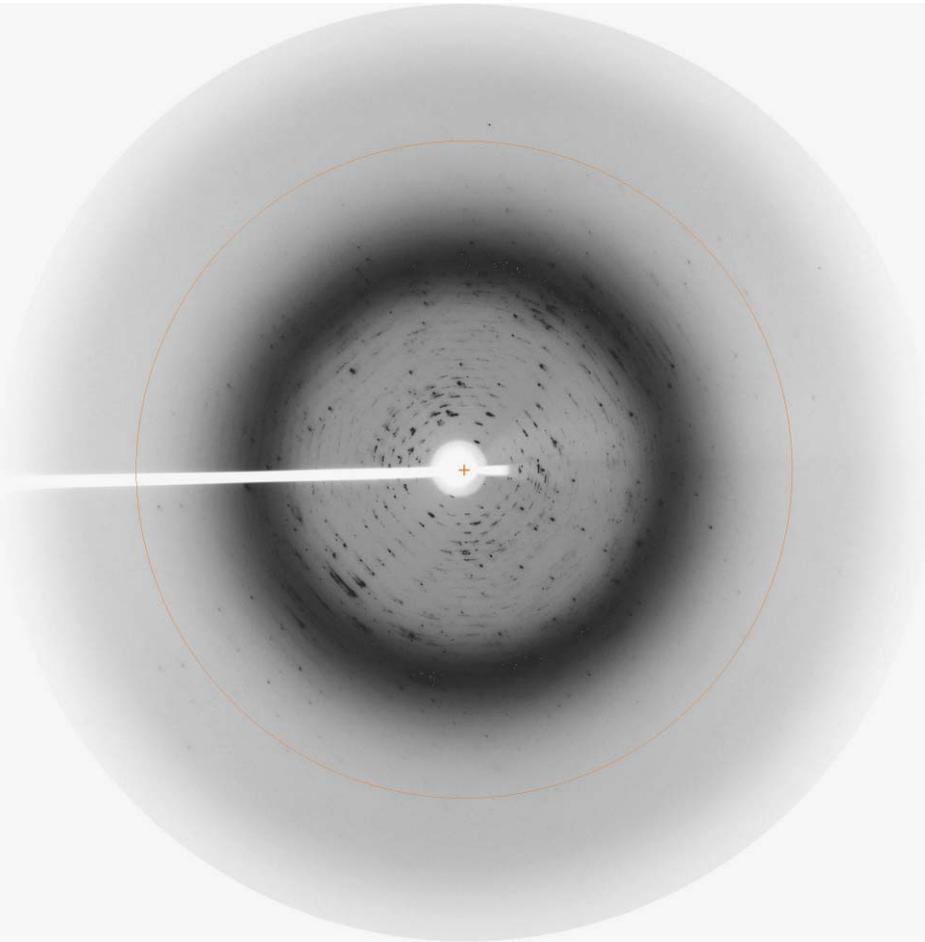


Score: 1044

Estimated Resolution: 2.0 Å

Dataset: 2.1 Å

Scoring Examples



Score: 405

Estimated resolution: 2.1 Å

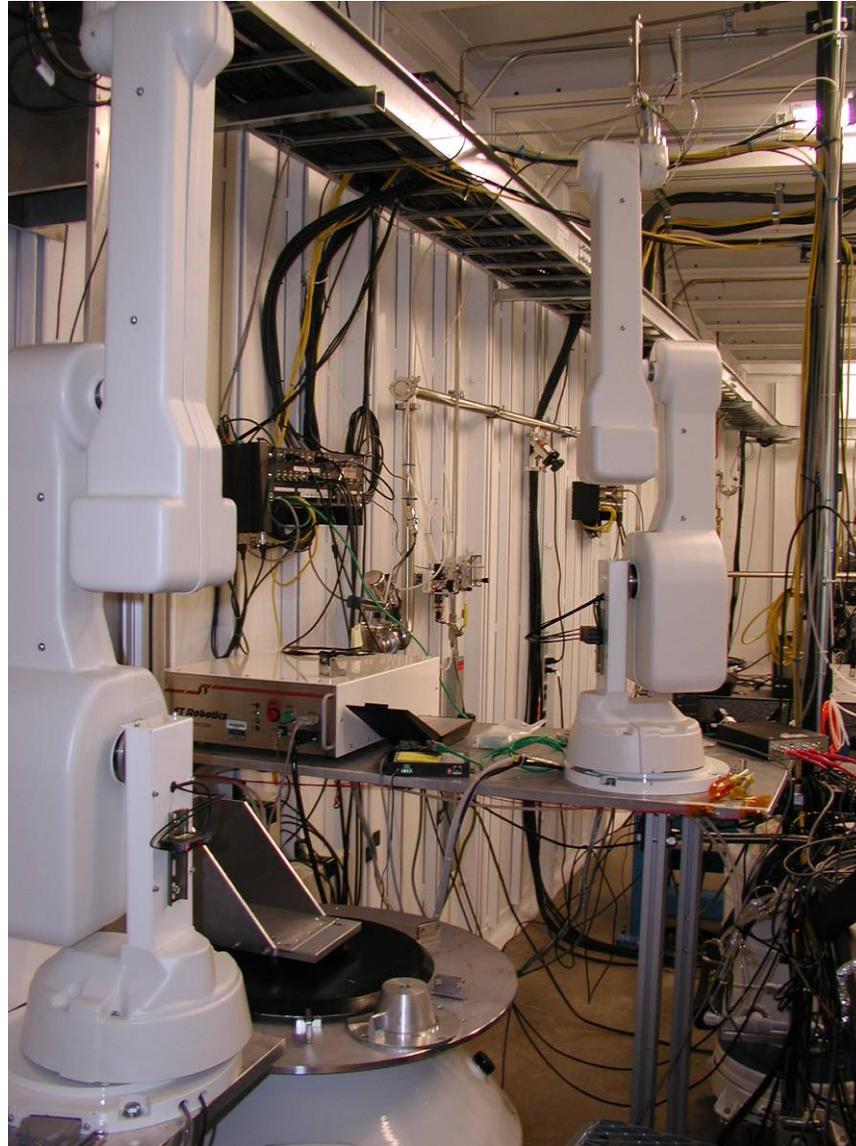
Dataset: 2.4 Å



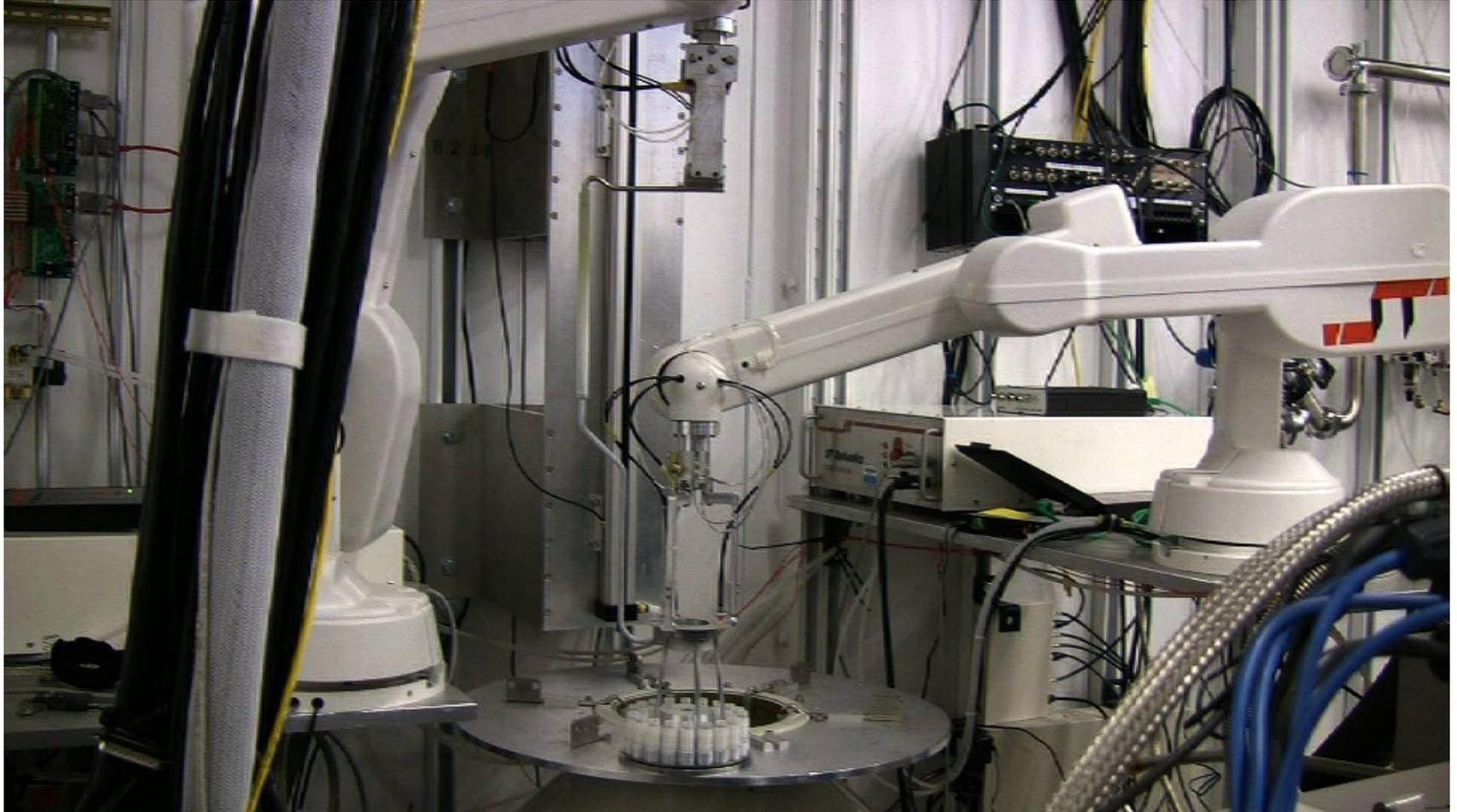
Score: -334

Crystal discarded

Carousel Changer



Carousel Changer



Summary

- SGX operates an efficient facility for macromolecular crystallography
- The facility supports SGX's drug discovery programs
- Efficiency has been achieved by concentrating on commercially-available technology, augmented by customized solutions as appropriate, and information management
- Our operation is unique in its level of automation of mechanical and software systems