

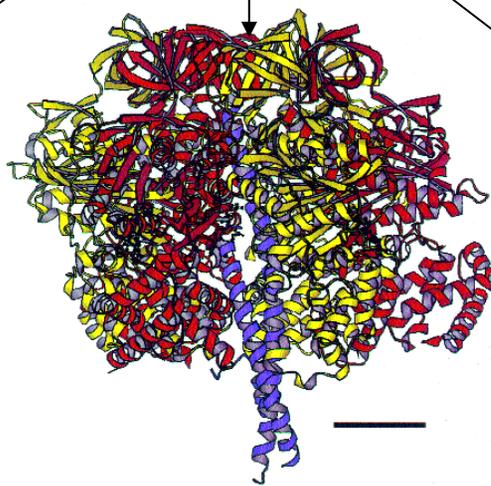
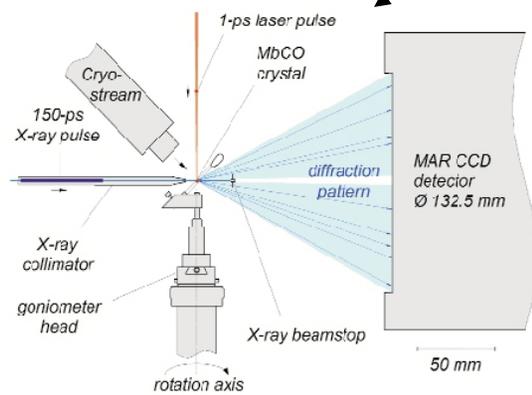
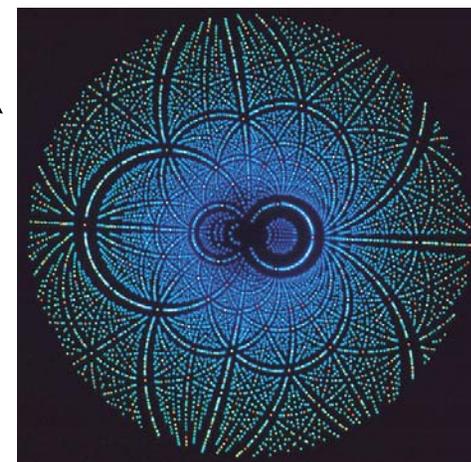
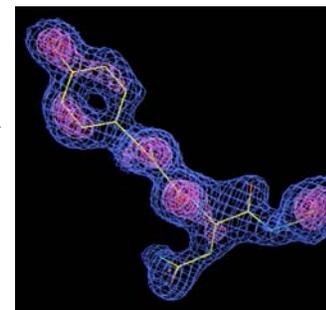
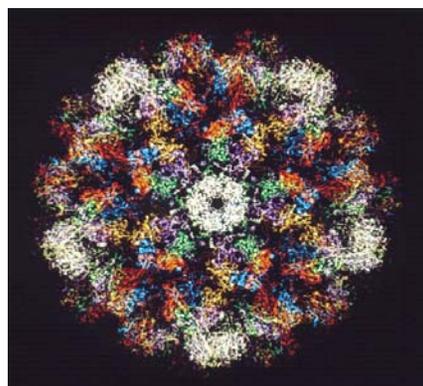
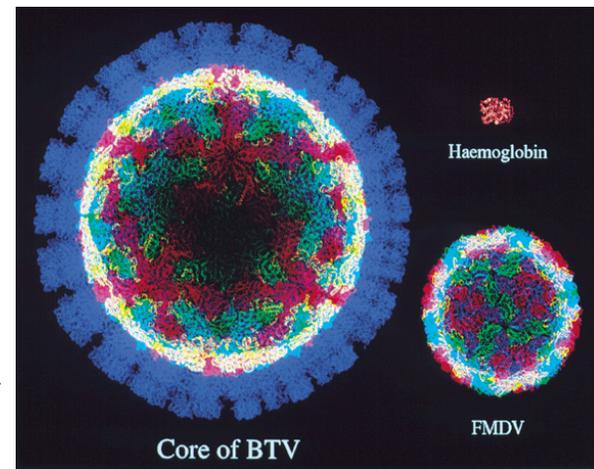
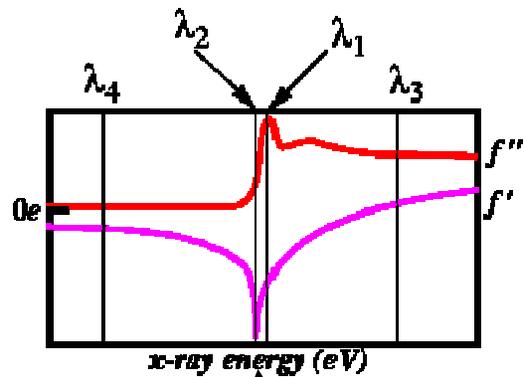
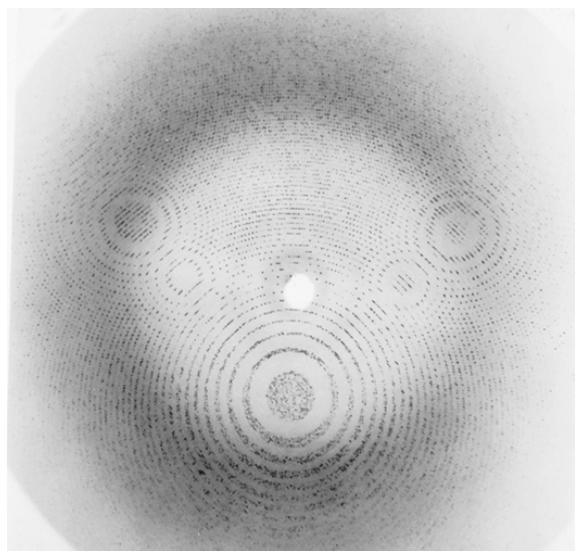
*Overview: Structural Biology on  
the World Scene—  
What it Means to the APS*

Prof John R Helliwell,  
APS Cross-cut Review of Chair,  
Member of APS Science Advisory Committee  
Wednesday January 24<sup>th</sup> 2007

# Areas to address

- Other large scale facilities around the world: plans for structural biology
- Plans of major molecular biology institutes and agencies
- Achievements in SR structural biology
- Examples of SR and neutron facility instrument plans
- The big expansion of SR facilities for protein crystallography

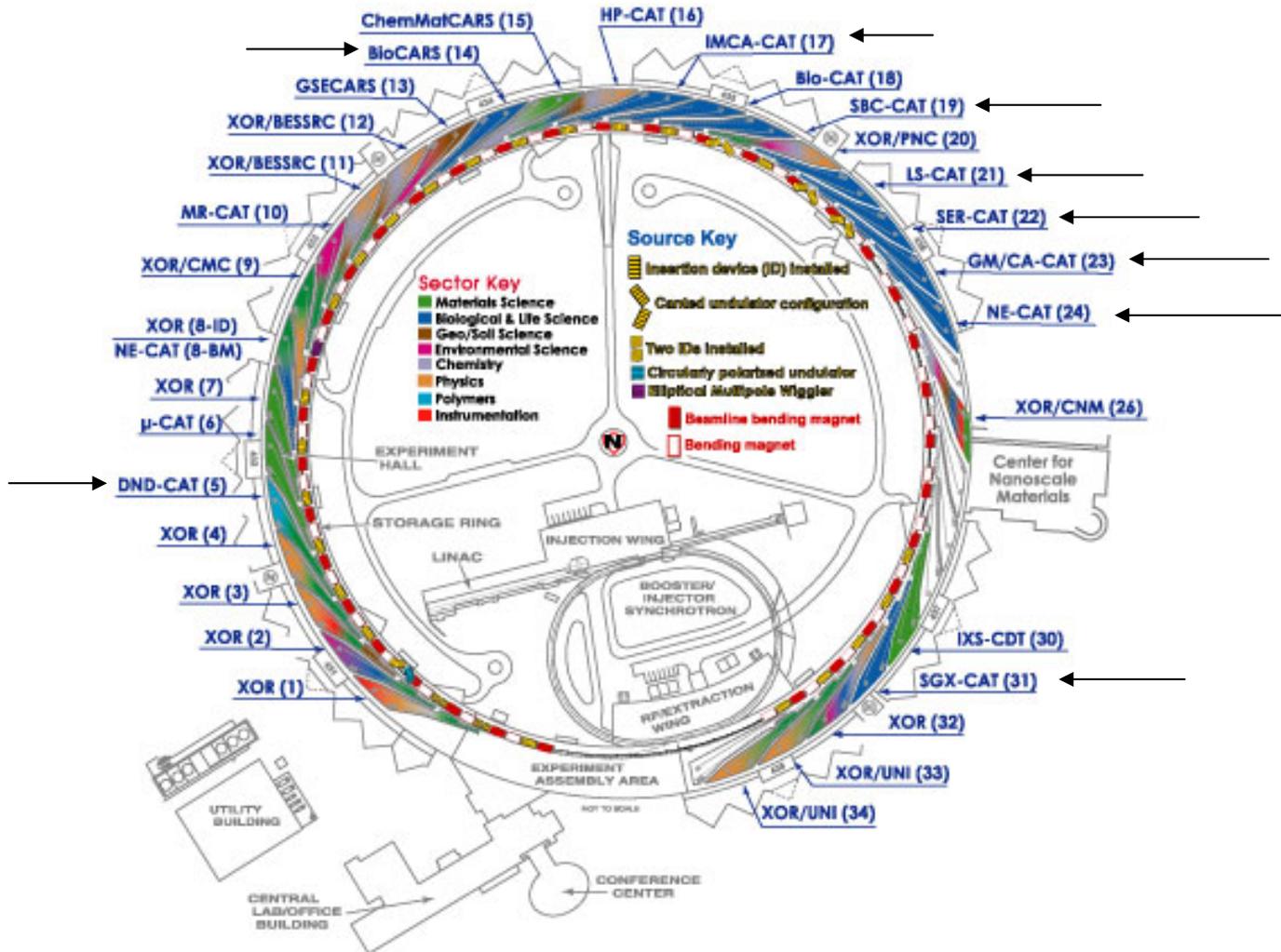
*What constitutes this field of  
research?>>>*



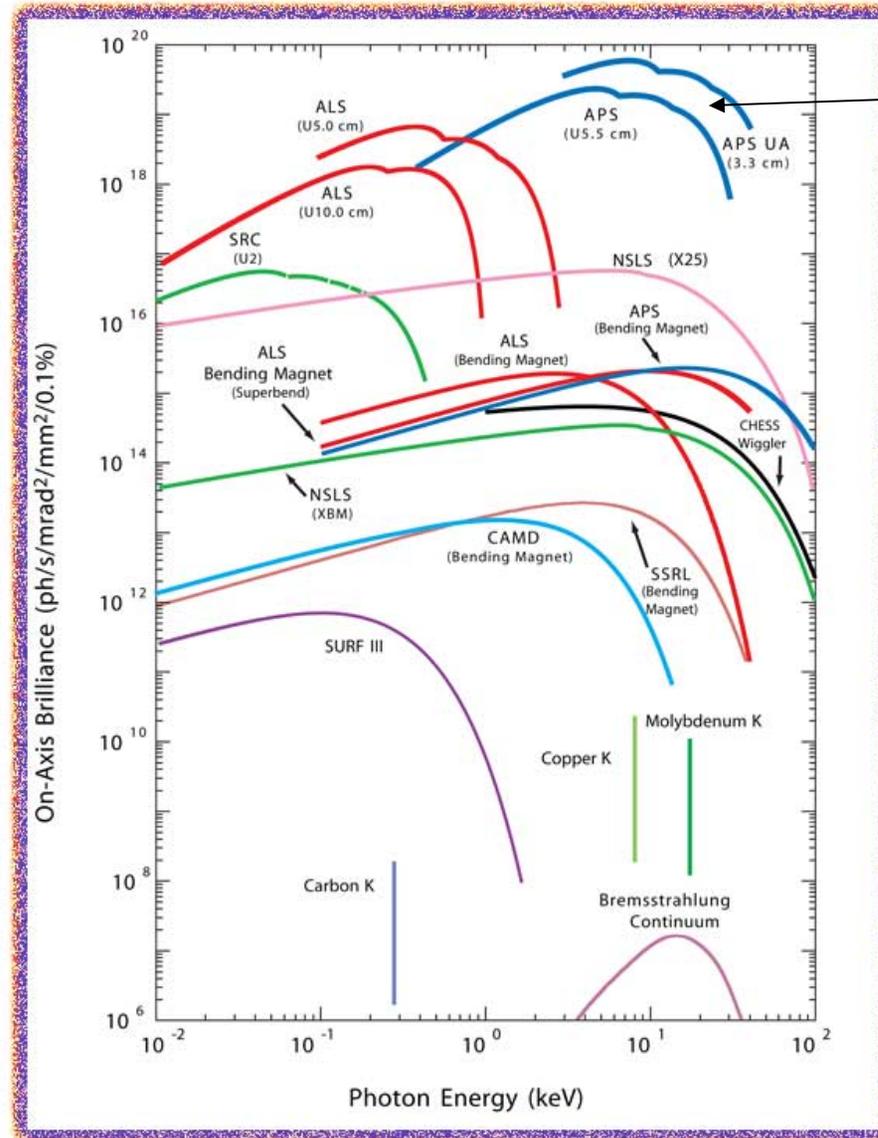
# THE ADVANCED PHOTON SOURCE

## Sector Allocations & Disciplines

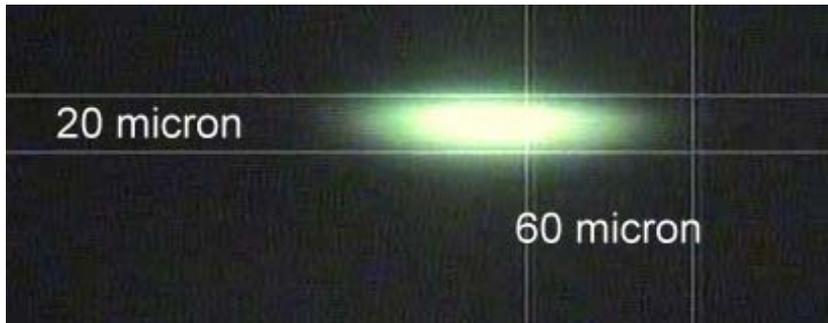
### Source Configuration



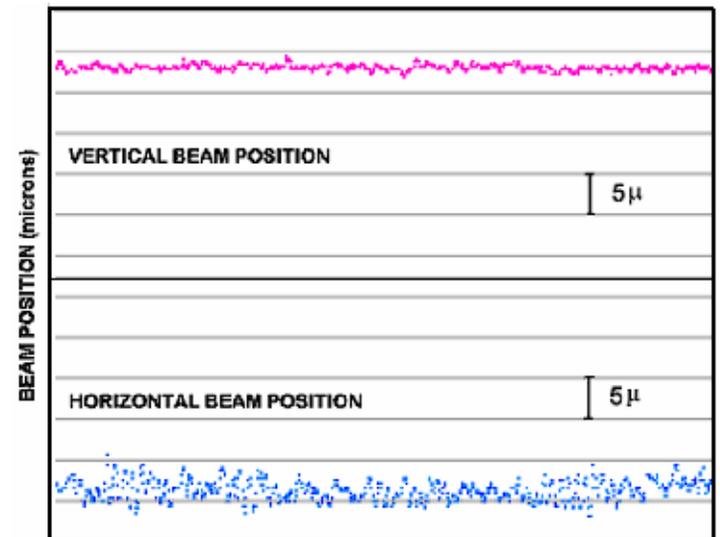
# APS brilliance curves comparison



# APS is a high reputation source



Small beam size



Exceptional stability

Decisions involving APS's development are very important

# SR Facilities with structural biology

- APS, ESRF, SPRing8<<<<the 'big 3'
- New national sources & third-generation sources: Diamond, Soleil, Australian SR Source, Canadian SR source
- The special case of PETRA III in Germany (brilliance up by 10 to 100 on APS, ESRF, SPRing8)
- Planned:- NSLS-II
- Also SSRL, NSLS-I, MacCHESS, ALS, SLS, Elettra...
- TRISTAN at KEK Tsukuba for single bunch time-resolved
- Apologies to those I forgot!

# Lets compare with ESRF plans

- A detailed upgrade plan aiming at 'nano-focus' beamline developments
- Also expects UK usage of its MX beamlines to decrease overall due to Diamond coming on line but expects its MX programme to be sustained by new categories of expt specifically >>>
- membrane proteins and complexes where screening of even thousands of crystals will be likely be done (to find a good crystal) >>>
- and or exceptionally small crystals only will be available
- Also new member countries are expected to join the ESRF partnership

# Also upcoming the '4GLSs': XFELs and FELs with structural biology

- LCLS, Stanford
- XFEL, DESY Hamburg
- 4GLS, Daresbury UK

# Neutron Facilities with structural biology

- The Institut Laue Langevin
- SNS, Oak Ridge
- JPARC, Japan
- Europe's new proposal; a 1MW short pulse spallation source 'probably at ISIS' and a 1 to 5 MW long pulse source 'probably on a green field site'
- ISIS, Rutherford Lab (planned)

# The Users' view

## EMBL as an example

- Five sites with 1345 staff
- EMBL's Strategic Forward Look 2006-2015, <http://www.embl.org/aboutus/news/publications/index.html>
- *“European molecular biology’s scientific challenge, is not Europe specific....the life sciences are moving into a phase where reductionist studies will be complemented by integrative systems biology. This will require a commitment to interdisciplinary collaborative research and critical mass in a variety of disciplines.”*

# EMBL's report on its "Programme for 2007 to 2011"

- This expands on the 10 year strategy
- The EMBL will design and build new beamlines for structural biology on the upgraded PETRA-III thus enhancing its support of X-ray and neutron beamlines for structural biology researchers in Europe (at Hamburg and Grenoble)
- The EMBL will participate in XFEL in Hamburg
- In house research at its Outstations are vital for recruitment

# EMBL's approach also to promote...

- “areas seen to be crucial for systems biology... *computational biology, imaging and high throughput technology... chemical biology.*”
- “its Mouse Biology Outstation activity in support of understanding the molecular biology of disease and its support of the EBI (European Bioinformatics Institute)”

# USA NIH PSI



- The **Protein Structure Initiative (PSI)** is a federal, university, and industry effort to dramatically reduce costs and lessen the time to determine a three-dimensional protein structure
- PSI has the goal to make the three-dimensional atomic-level structures of most proteins easily obtainable from their DNA sequences

## Protein Structure Initiative Centres

- **Four Large-Scale Centers** (of which the **Midwest Center for Structural Genomics** is led by Dr A Joachimiak here at Argonne)
- **Six Specialized Centers**

# Structural biology progress analysed by enzyme classification

Table 1. Genome Coverage

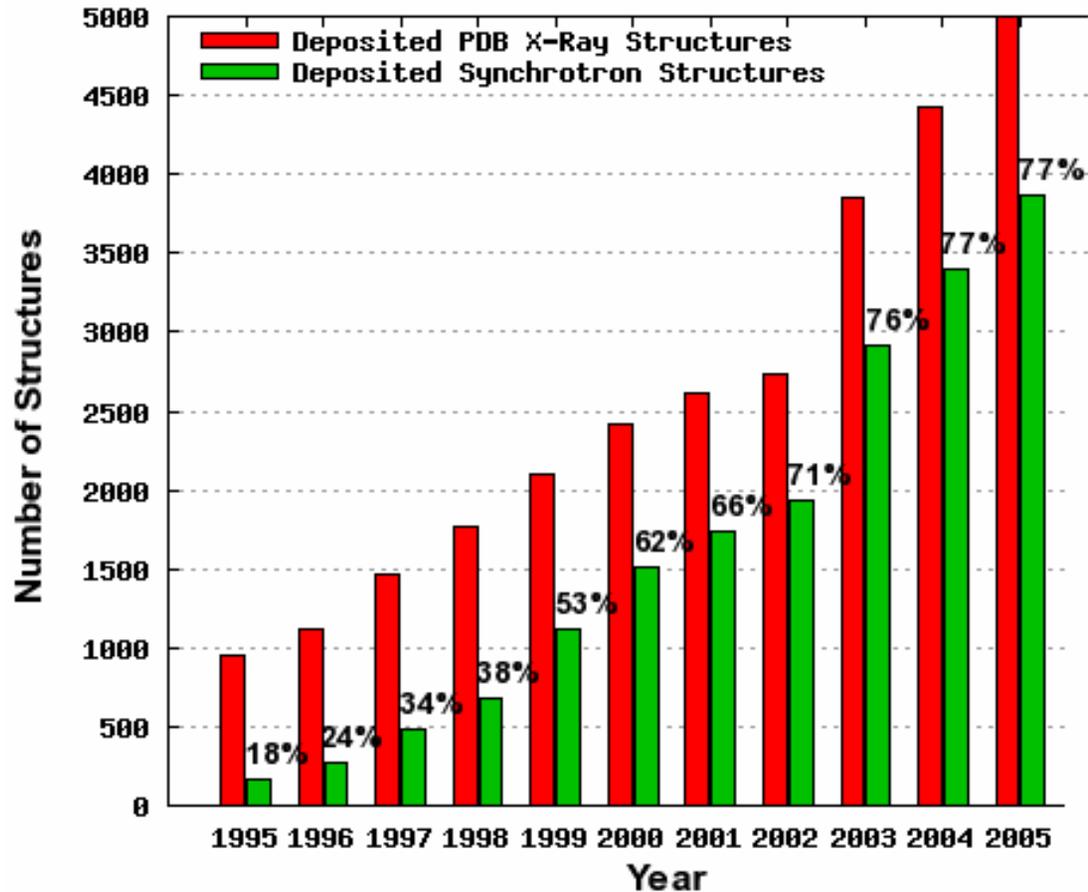
	<u>Function Coverage</u>
GENOME SEQUENCES	1.000
PDB STRUCTURES	0.418
SG TARGETS	0.385
HOMOLOGY MODELS	0.546
PDB STRUCTURES+SG TARGETS	0.601
PDB STRUCTURES+HOMOLOGY MODELS	0.627
SG TARGETS+HOMOLOGY MODELS	0.698
PDB STRUCTURES+SG TARGETS+HOMOLOGY MODELS	0.741

*Increasing coverage*



Summaries also available by biological process, cell component, molecular function and disease at [http://function.rcsb.org:8080/pdb/function\\_distribution/index.html](http://function.rcsb.org:8080/pdb/function_distribution/index.html)

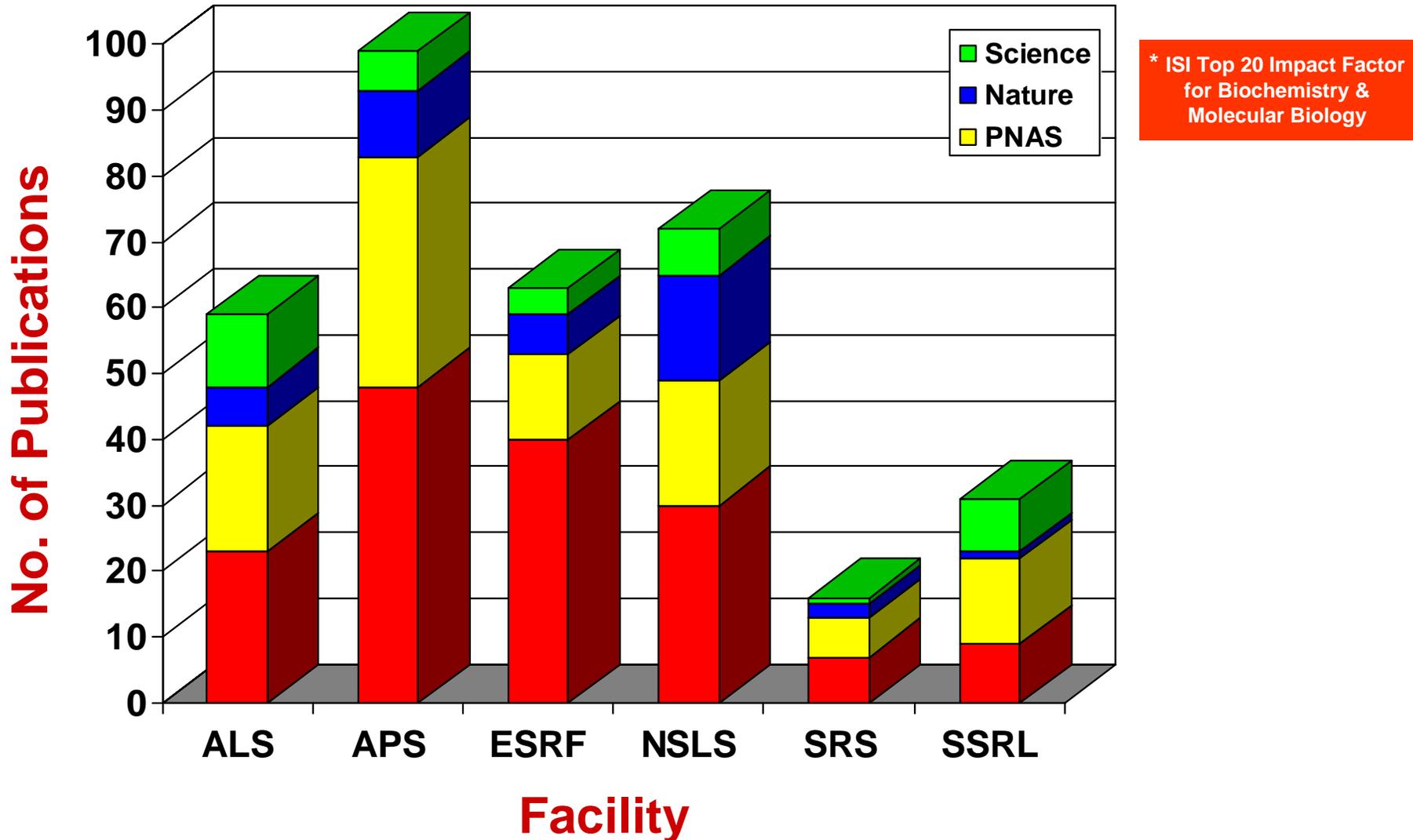
# SR Facilities MX productivity log



SR Facilities are big players in PDB depositions and growing

<http://rcsb-biosync-beta.rutgers.edu/usbeam.html>

# 2005 High-Impact\* SB Papers from Light Source Facilities



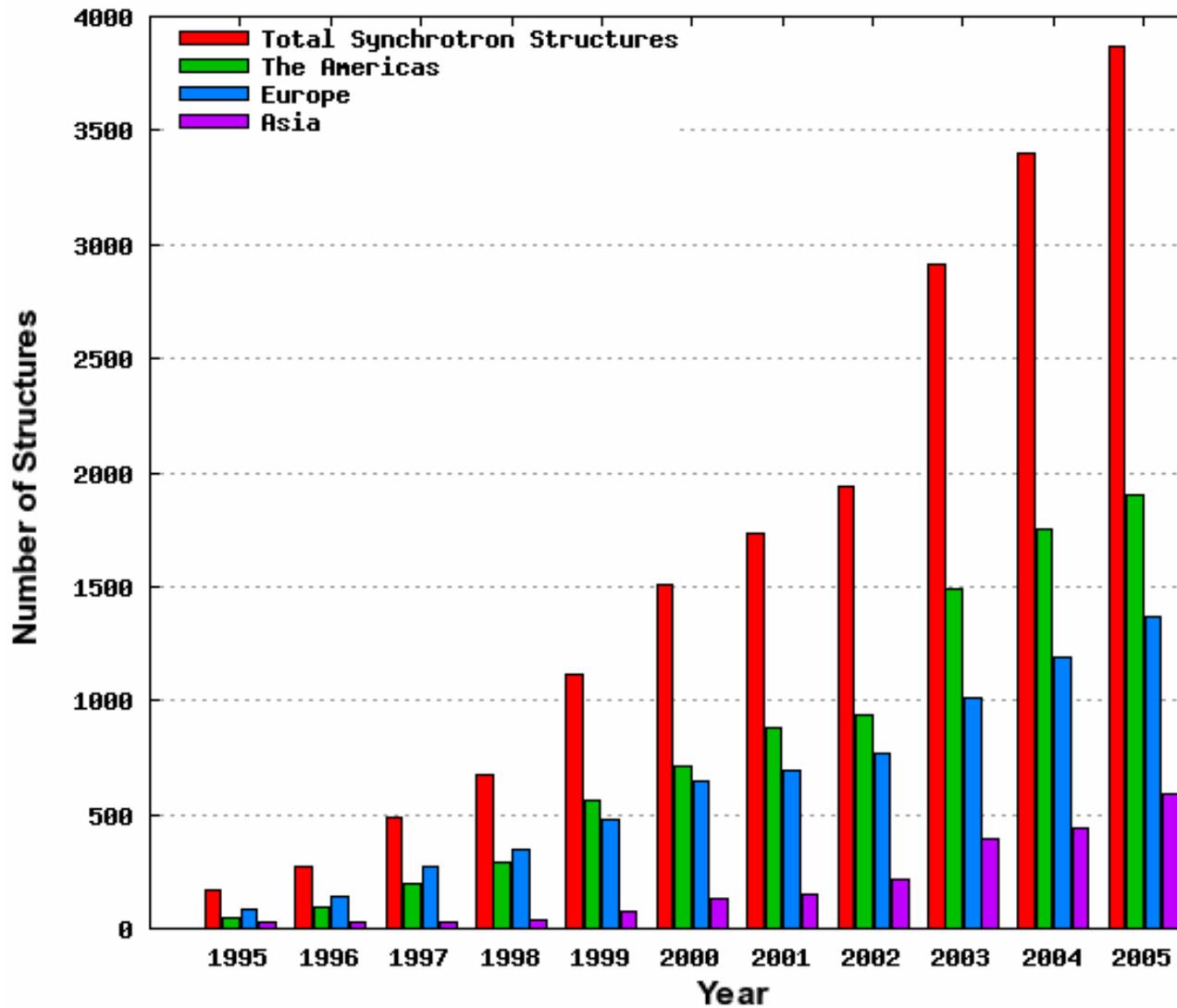
Kindly prepared by Rick Fenner, APS.

\*Hi-impact journals as listed in ISI Journal Citation Reports "Biochemistry & Molecular Biology" category (<http://portal.isiknowledge.com/?DestApp=JCR&Func=Frame>), sorted by Impact Factor. Papers with no hits in any facility publications database were excluded, as were non-SB papers..

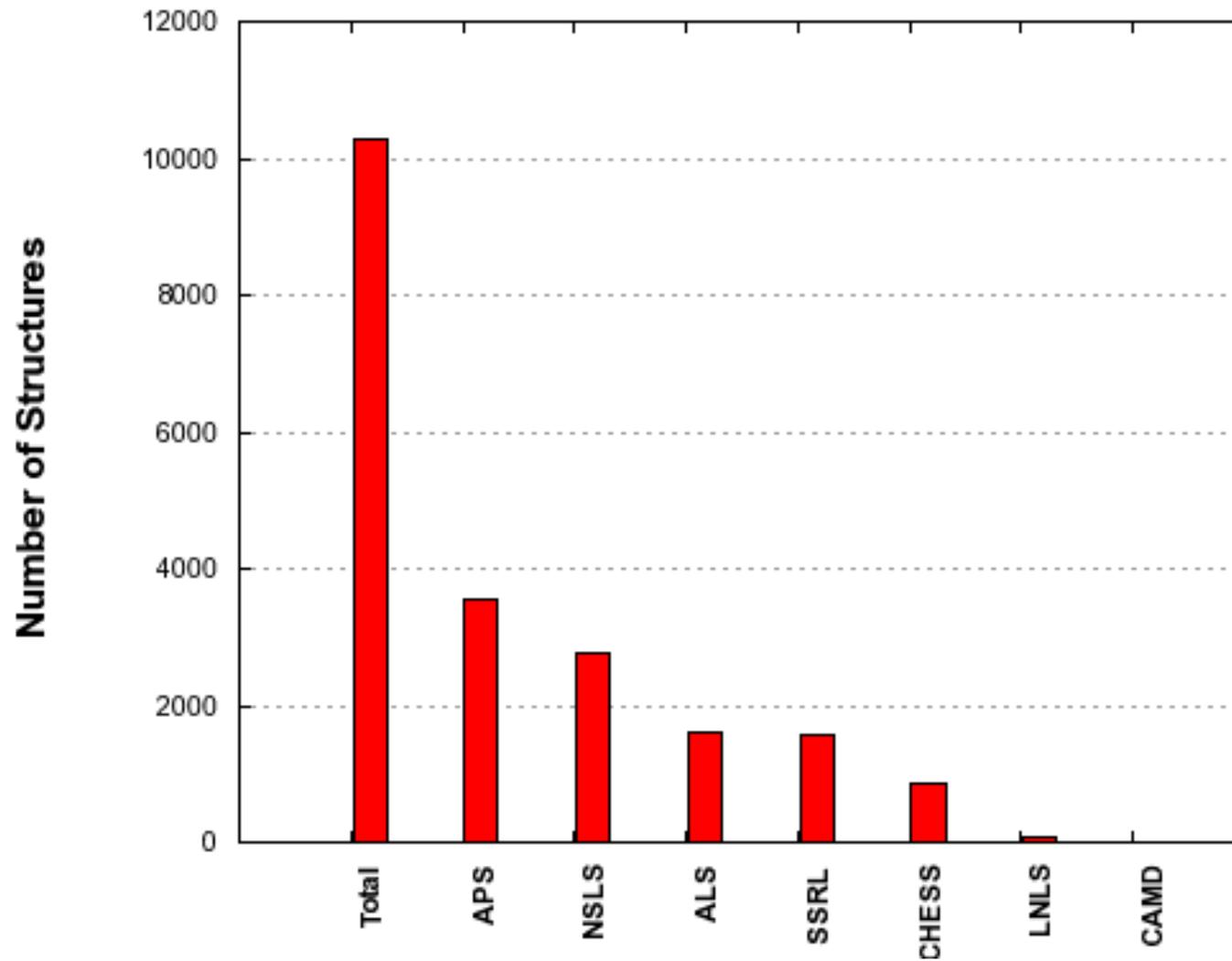
In addition to publications a considerable quantity of proprietary research takes place notably at

- IMCA CAT
- SGX CAT

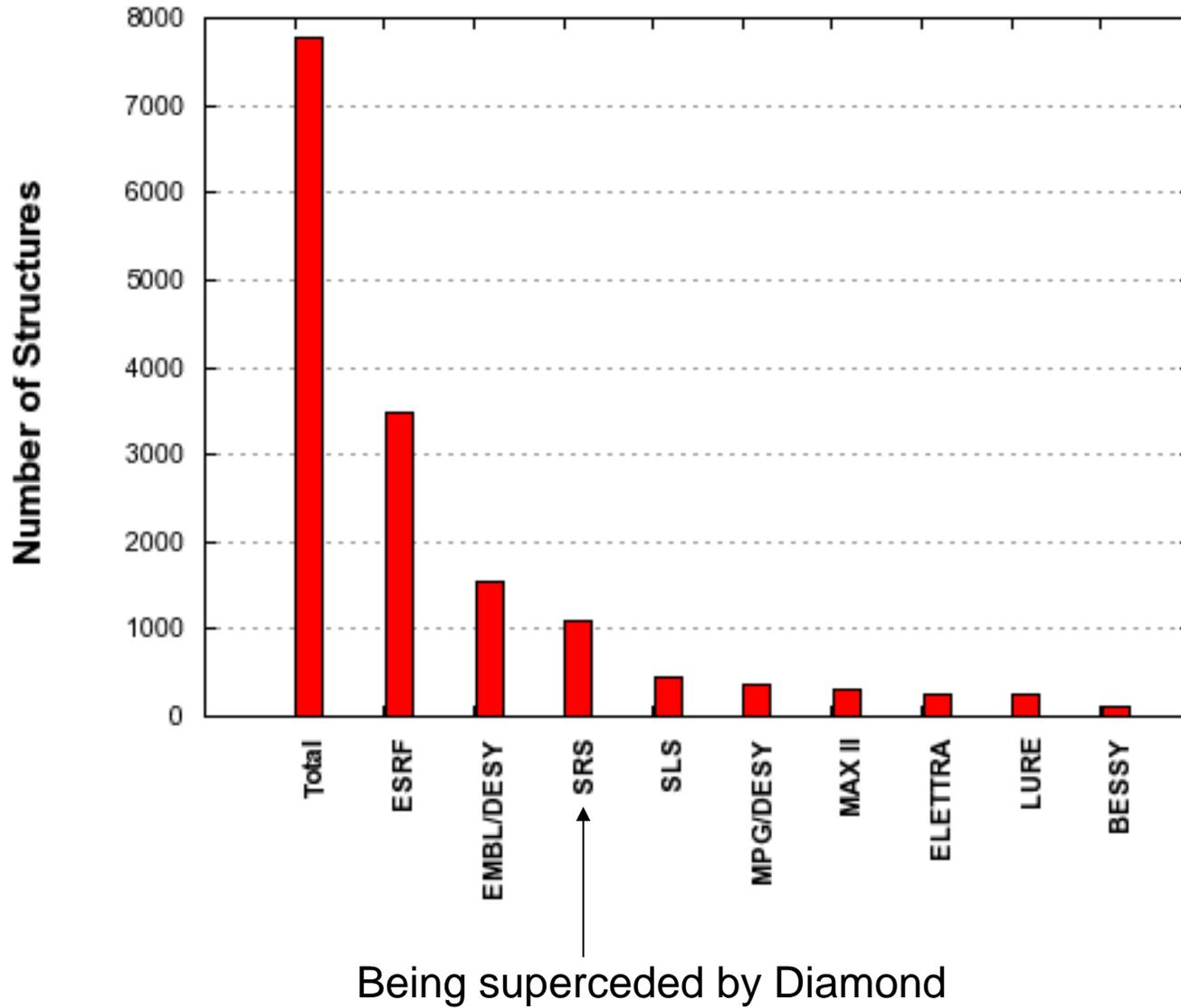
# SR Facilities by region



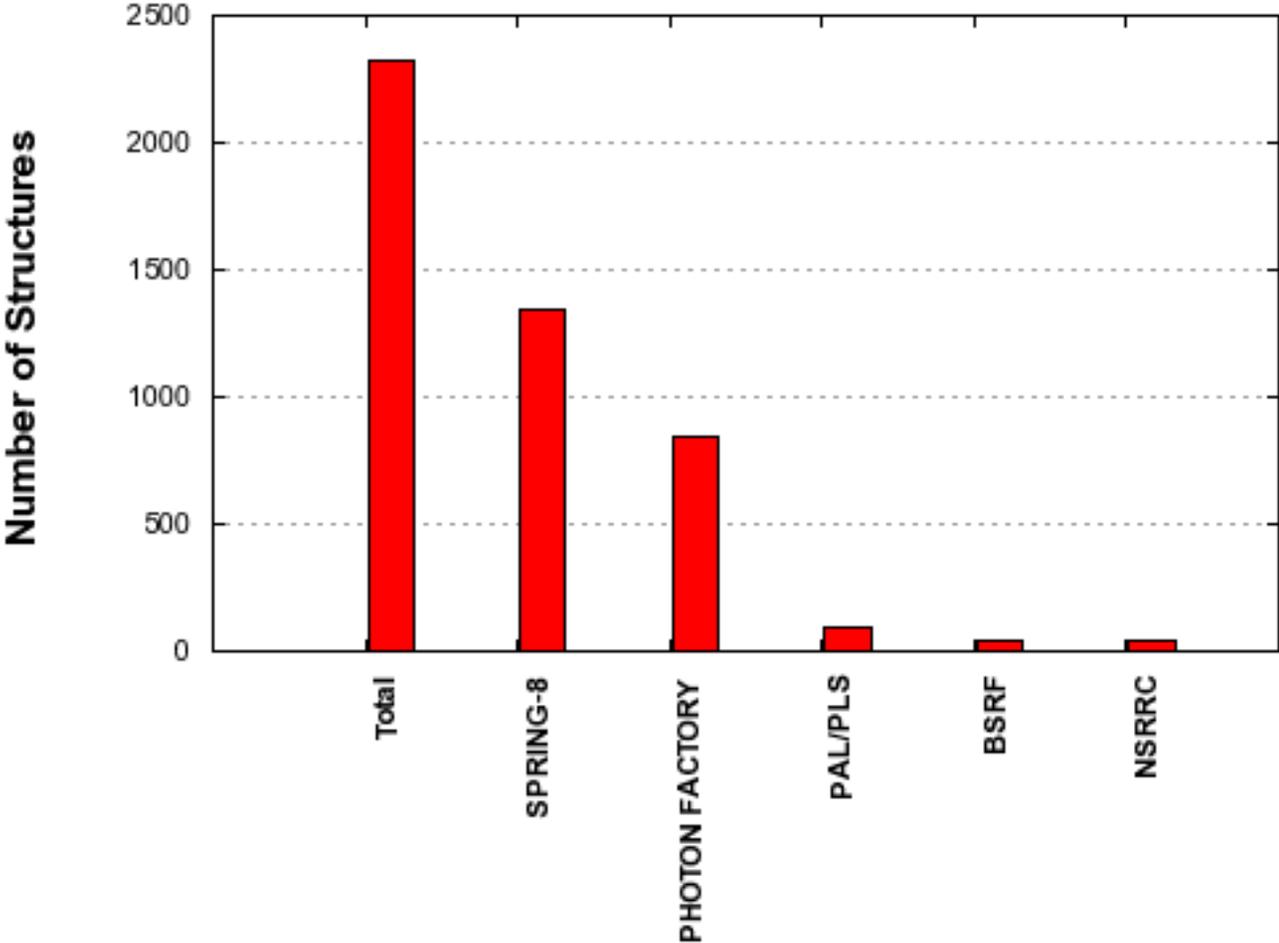
# Within the Americas



# Within Europe



# Within Asia



# SR instrumentation advances impact on throughput

- robotics
- higher flux beamlines
- fast read-out detectors
- auto-alignment
- *These have implications for total capacity*

# Structures throughput

- Increases are evident from 2<sup>nd</sup> generation to 3<sup>rd</sup> and from BM to ID
- In addition Jiang and Sweet (2004)\* analysis indicates that SR yields larger molecular weight structures
- IDs deliver higher molecular weights than BMs or 2GLS machines.

*J. Synchrotron Rad.* (2004). 11, 319-327

**Protein Data Bank depositions from synchrotron sources**

# There are also some difficult to predict possibilities

- Wide availability of compact SR sources in home institutes/Universities
- NMR expands further than expected
- Microscopy developments expand further than expected
- Single molecule imaging structure determination expands further than expected

# The scale of the challenge to APS's structural biology sectors

- The older facilities must reinvent or refurbish themselves in terms of experimental capabilities or simply fade away from lack of use
- Progress in the development of synchrotron capabilities has been so rapid and so extensive that new and better facilities are being built before old facilities exceed their useful lifetimes
- This is healthy because this is the stuff of progress
- Scientists are also making rapid and extensive progress and are demanding newer and better facilities
- A guiding maxim about beamline usage is that *'users vote with their feet'*
- Be popular or perish

# The diversity of APS CATs for data collection and experiments coverage

- high-throughput operations
- quality data collection
- industrial usage
- automation development
- ‘mini-focus’ (~10 microns) aiming towards ‘microfocus’
- very large unit cells
- time-resolved
- wide wavelength range for SAD, MAD, MIROAS etc

Robert Browning >>*aim high*>>

**“...our reach should exceed our grasp, or  
what's a heaven for?”**

# The menu of presentations coming up

**8.30 Sector 14**

*Vukija Srajer, BioCARS*

**8:55 Sector 17**

*Lisa Keefe, IMCA-CAT Director*

**9:20 Sector 19**

*Andrzej Joachimiak, SBC-CAT Director*

**9:45 Sector 22**

*J Chrzas, SER-CAT Sector Manager*

**10:10 Break**

**10:30 Sector 23**

*Robert Fischetti, GM/CA-CAT Associate Director*

**10:55 Sector 24**

*Malcolm Capel, NE-CAT Deputy Director*

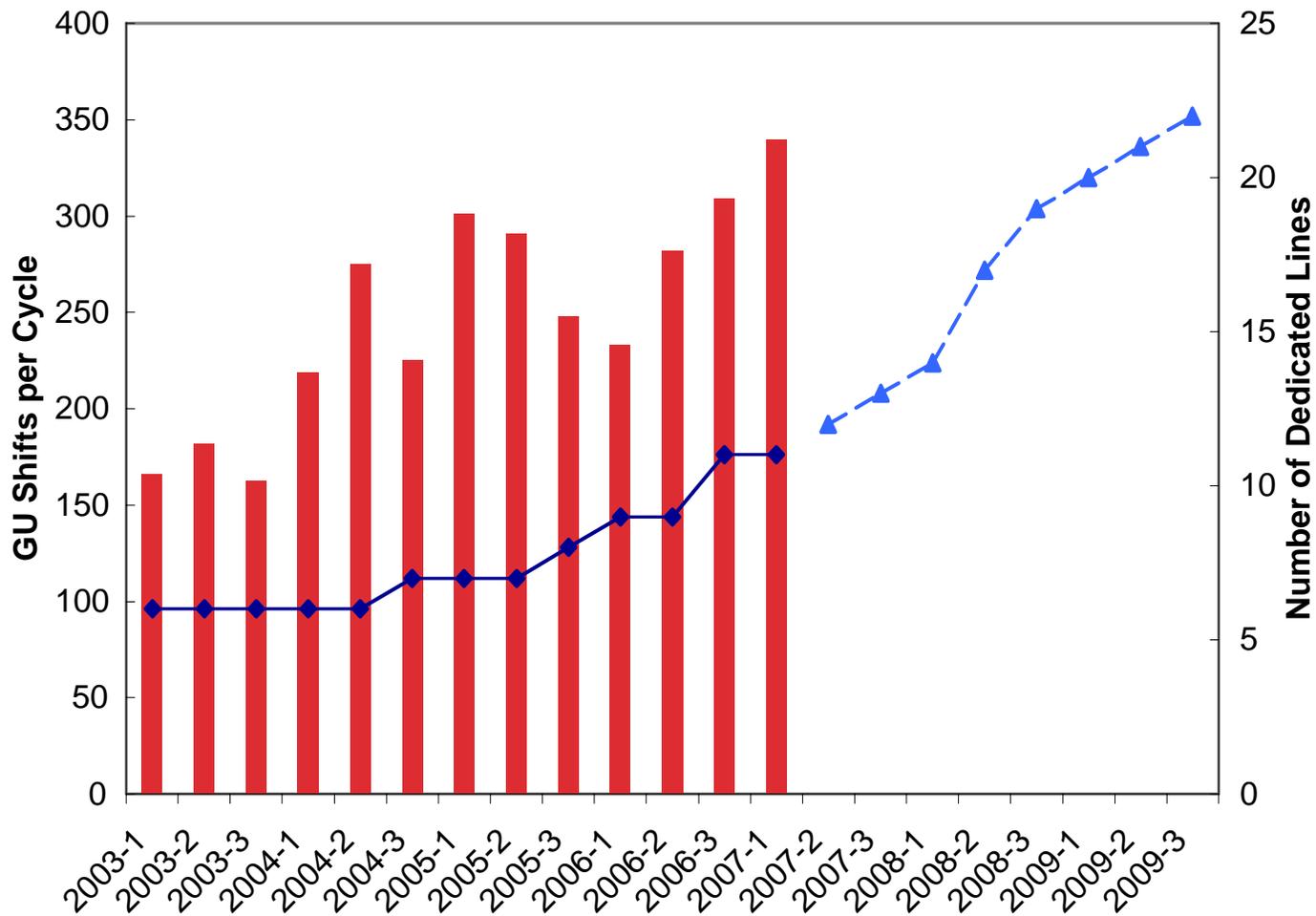
**11:20 Sector 31**

*Kevin D'Amico, SGX-CAT Director*

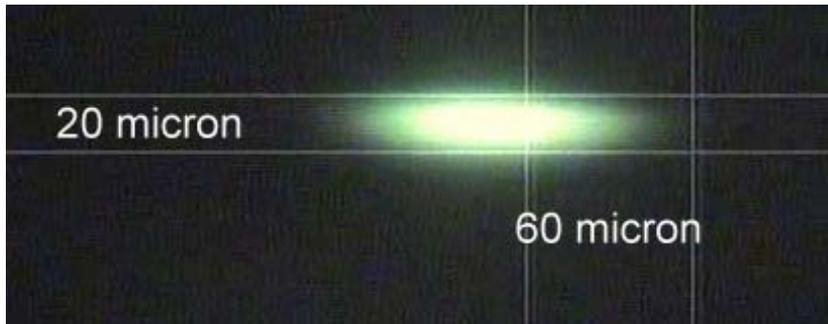
**11:45 Sectors 5 and 21**

*Denis Keane/Wayne Anderson, DND-CAT and LS-CAT Directors*

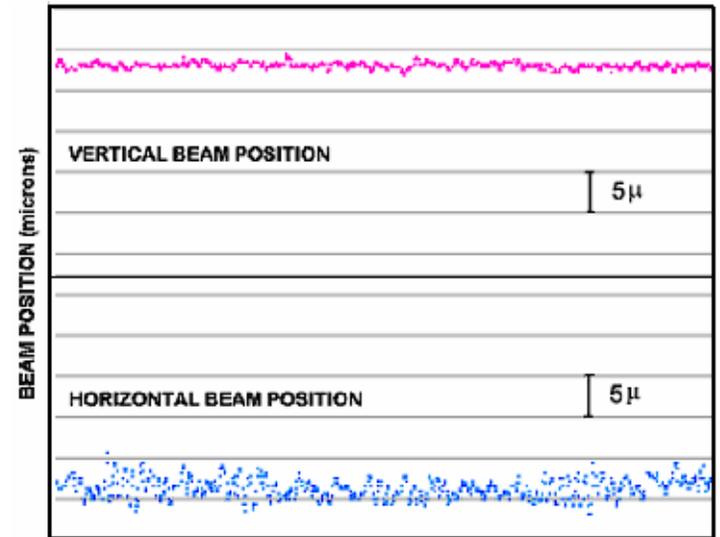
# MC Capacity at the AF



# Decisions involving APS's development are very important



Small beam size



Exceptional stability

APS is a high reputation source

*Thank you and let's enjoy a fruitful  
day of discussion and vision*

