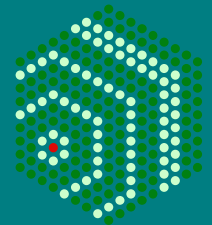


EMBL Grenoble

Structural biology
Instrumentation-wise

EMBL Grenoble outstation
F. Cipriani Instrumentation Group



EMBL European Molecular Biology Laboratory



- EMBL is a non-profit organization, publicly-funded
- 20 European member states, Israel and Australia
- 1,700 people, including 200 visitors
- Main laboratory in Heidelberg (800), 4 outstations with specific activities
- Total budget 170 M€
 - 50% from the member states, 25% Grants, 25% other
 - Netherlands 4.6% (2011)*

EMBL Member States:



Associate Member:



EMBL European Molecular Biology Laboratory



MISSIONS

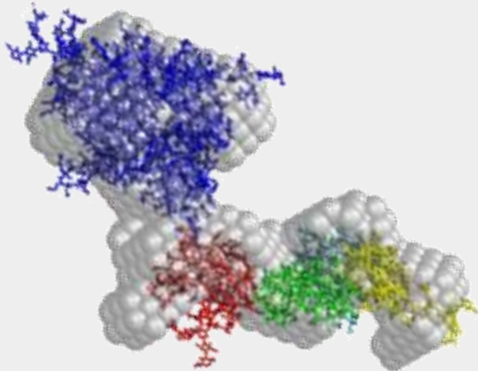
- Perform **basic research** in molecular and system biology
To understand mechanisms of life and diseases
- **Train** scientists, students and visitors at all levels
International PhD program (200 students)
- Offer **technical platforms and services** to scientists
E.g. Structural biology service in Grenoble
- Develop **new instruments** and methods
E.g. Instrumentation for X-ray diffraction experiments in Grenoble
- **Transfer** knowledge & technologies to industry



Structural Biology at **EMBL**



- Determine the Nature and Position of the **ATOMS** in biological **MOLECULES**
- Understand the function of biological **MOLECULES** and **COMPLEXES**
- Develop new **DRUGS**



3D Structure of a macromolecular complex composed of 4 proteins

Preferred technique is X-ray scattering

Macromolecular X-ray Crystallography (MX, high resolution)

Small angle X-ray scattering (SAXS, low resolution)

Data is collected at SYNCHROTRON beamlines

Structural Biology at **EMBL Grenoble**



90 people, 10 research groups/teams

3 groups focus on X-ray diffraction methods,
in close collaboration with the ESRF

- High-throughput crystallisation Team **J.A. Marquez**
Provides crystallization services
- Synchrotron crystallography Team **A. McCarthy**
Operates 5 beamlines at the ESRF
Supports external beamline users
- **Instrumentation** Team **F. Cipriani**
Develops instruments for diffraction experiments
with expertise in sample environment



www.psb-grenoble.eu

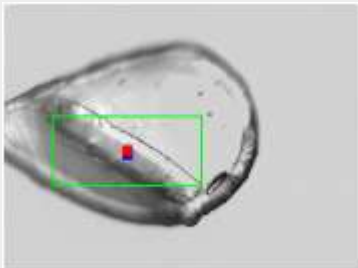
Partnership for Structural Biology

Provides scientists with an *integrated environment*
for structural biology

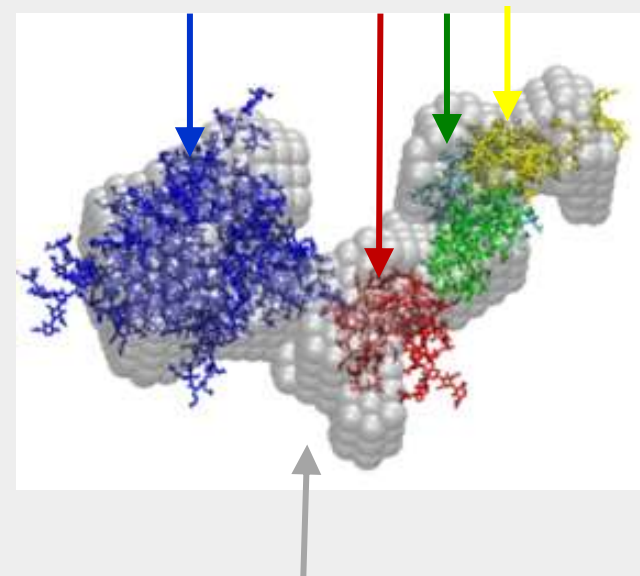


X-ray scattering *Our main tools*

1 – Macromolecular crystallography (MX)



- Atomic resolution (0.8 Å -50 nm)
- Crystallised form
- Size of molecules is limited



2 – Small Angle X-ray Scattering (SAXS)



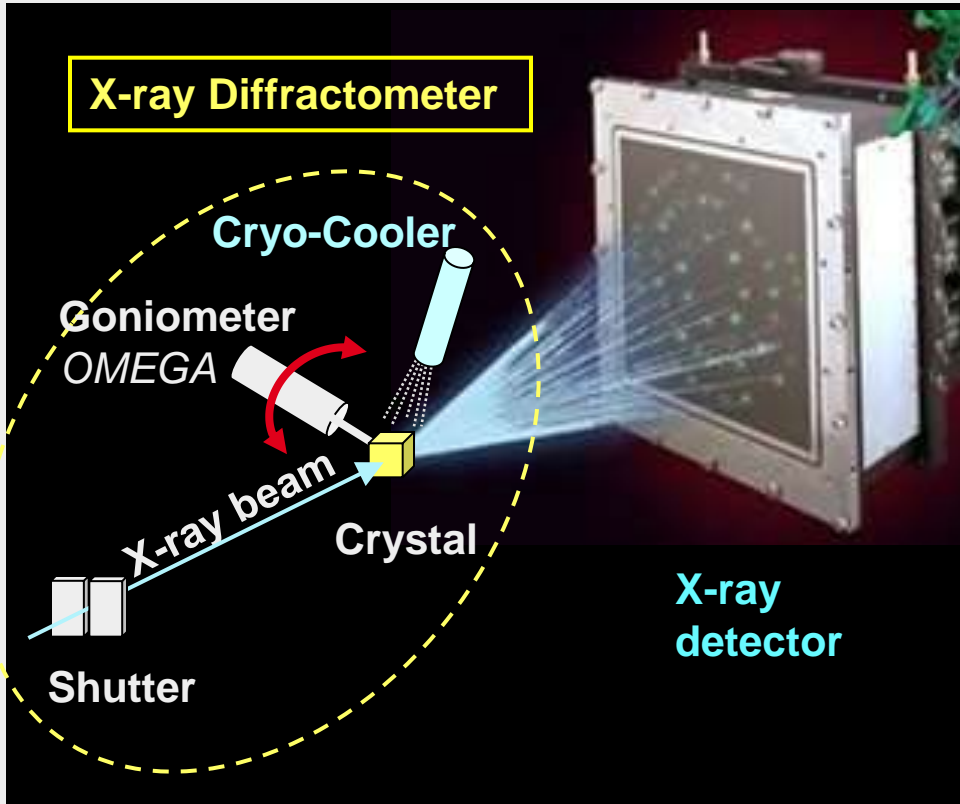
- Resolution is limited to 10 Å (Up to 500 nm)
- Sample in solution
- Large macromolecules, assemblies (**complexes**)
- Kinetics

Other low resolutions techniques used

Light microscopy, electron microscopy
NMR (Nuclear Magnetic Resonance)
Neutron diffraction

Macromolecular X-ray crystallography (MX)

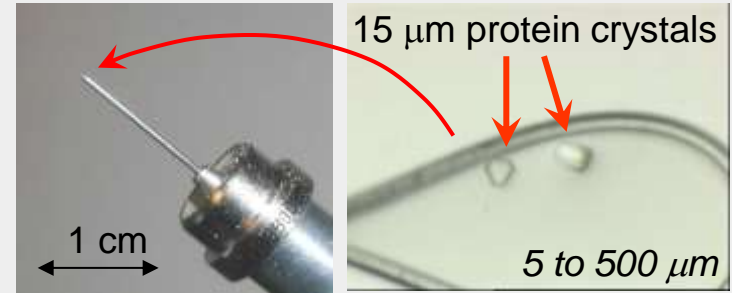
Typical Experimental setup



Collecting a diffraction data set

Several hundred images collected during angular Scans
Typical **scan**: 1 degree in 0.1 to 5 sec

Crystals mounted in a “cryo-loop”

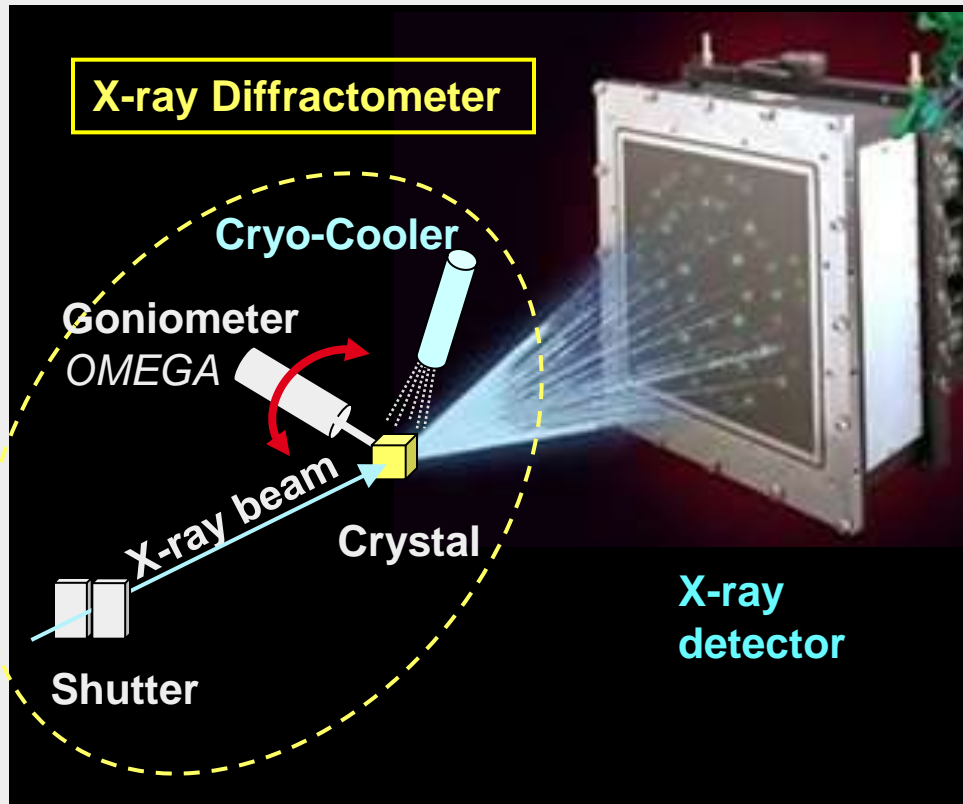


Challenges

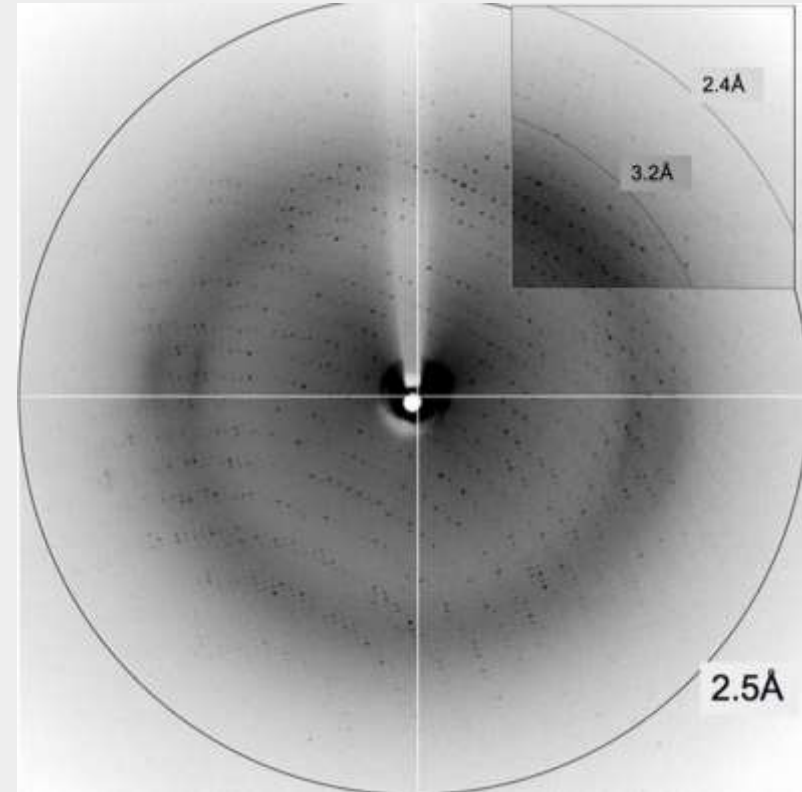
- **Precision of the goniometer spindle**
- **Mount frozen crystals on the goniometer**
- **Alignment of the crystal with the X-ray beam**

Macromolecular X-ray crystallography (MX)

Typical Experimental setup



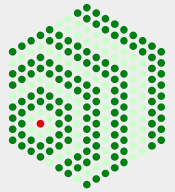
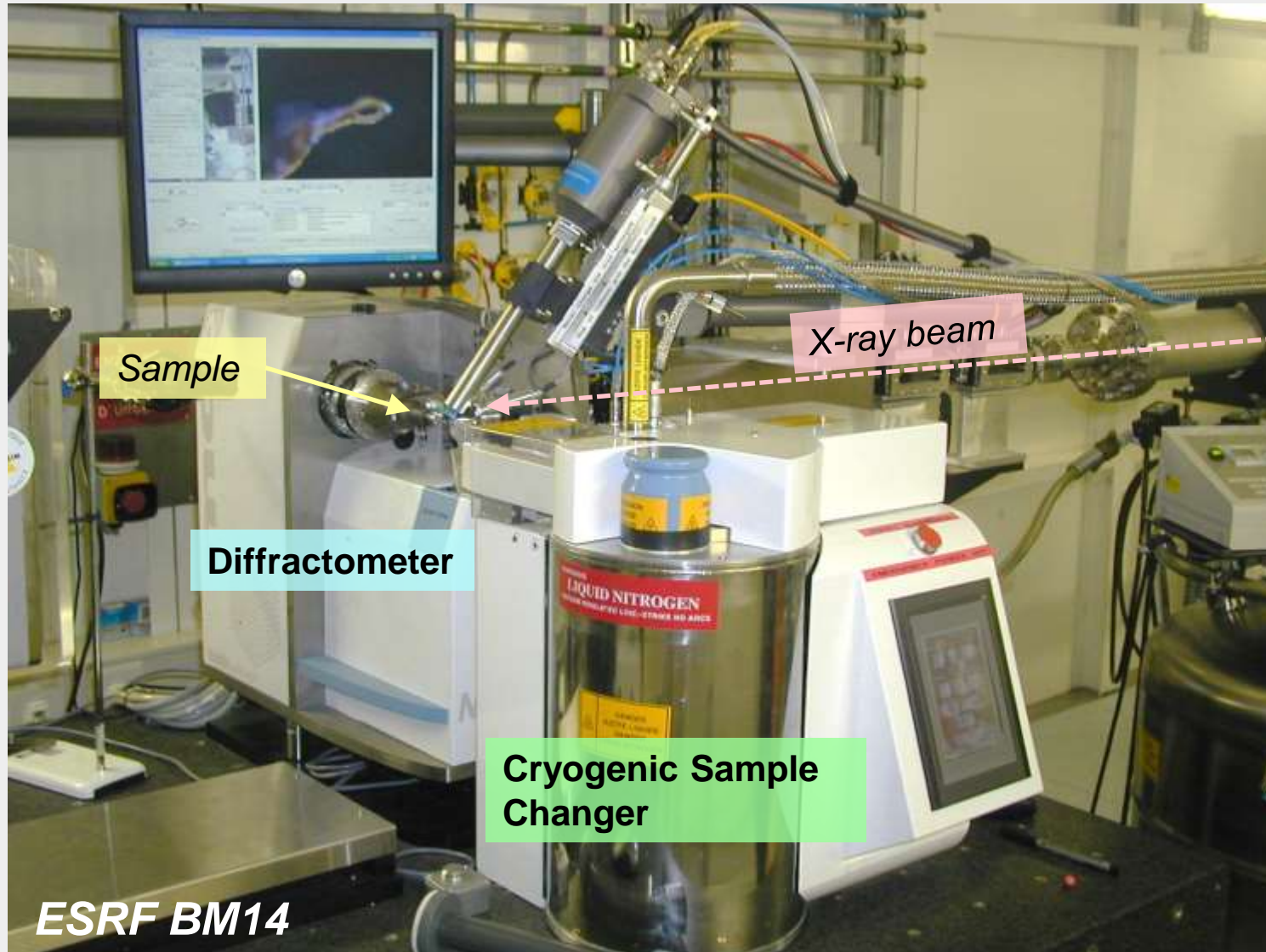
Crystals mounted in a "cryo-loop"



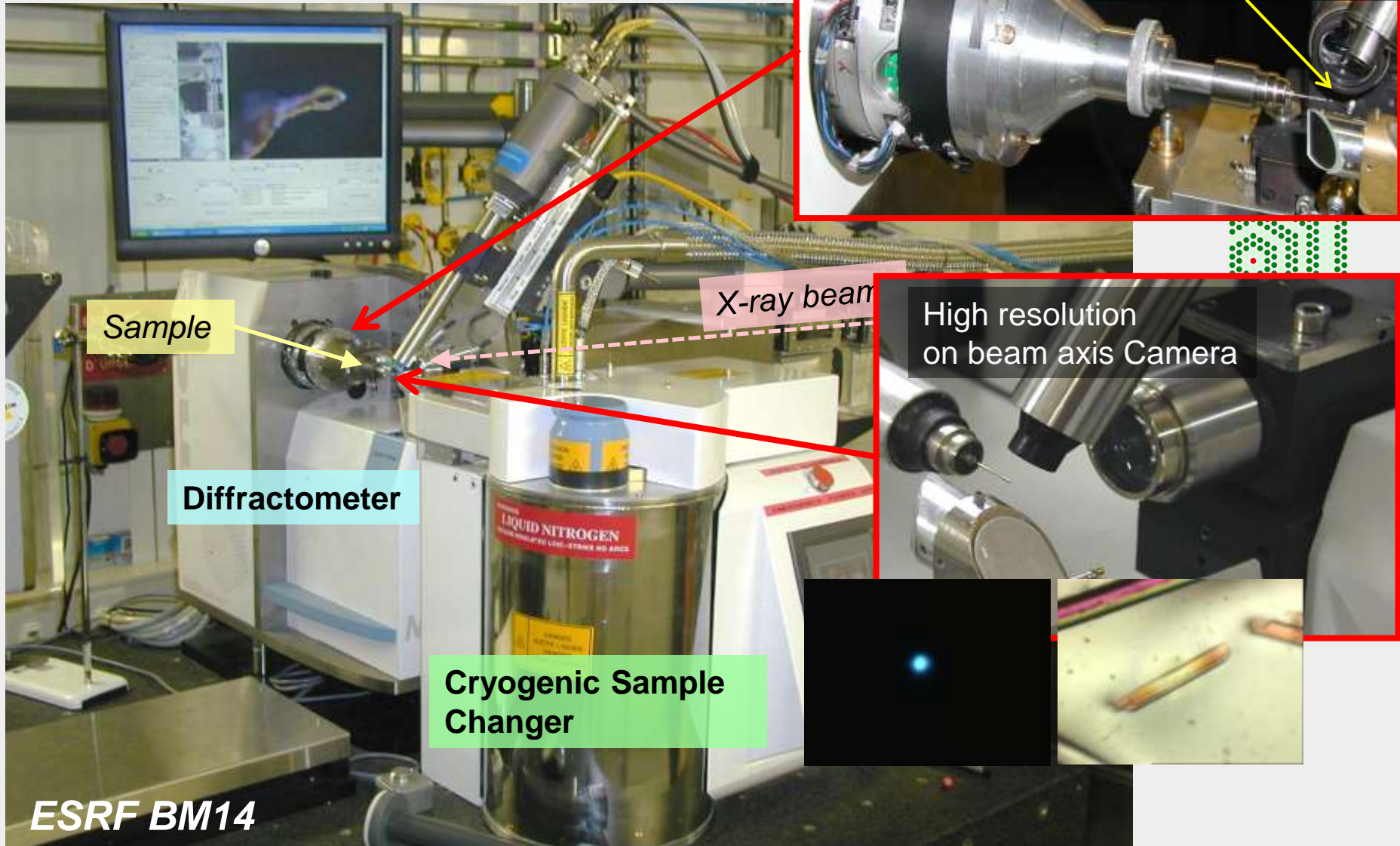
Collecting a diffraction data set

Several hundred images collected during angular Scans
Typical *scan*: 1 degree in 0.1 to 5 sec

Typical sample environment developed for MX



Typical sample environment of



Screening crystals *Before automation!*

An ordinary day on a beamline...



Changing a Crystal:

...Open the experimental hutch

Unmount the previous crystal

Mount the new one

Align it

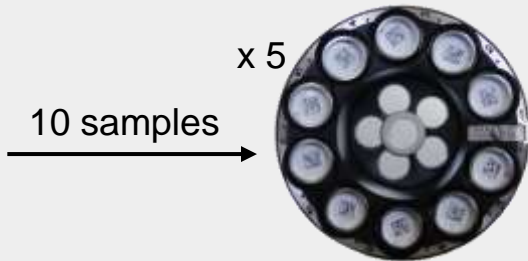
Close the hutch

Start data collection...



Since 2005

An “extra”ordinary day on a beamline! ...**Screening** crystals...



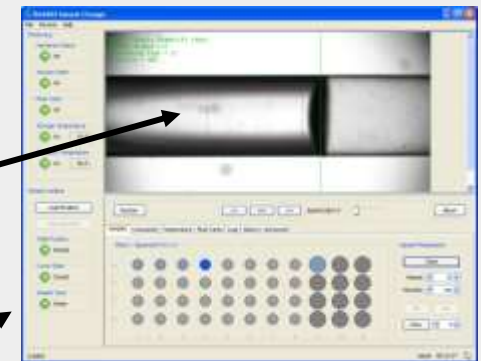
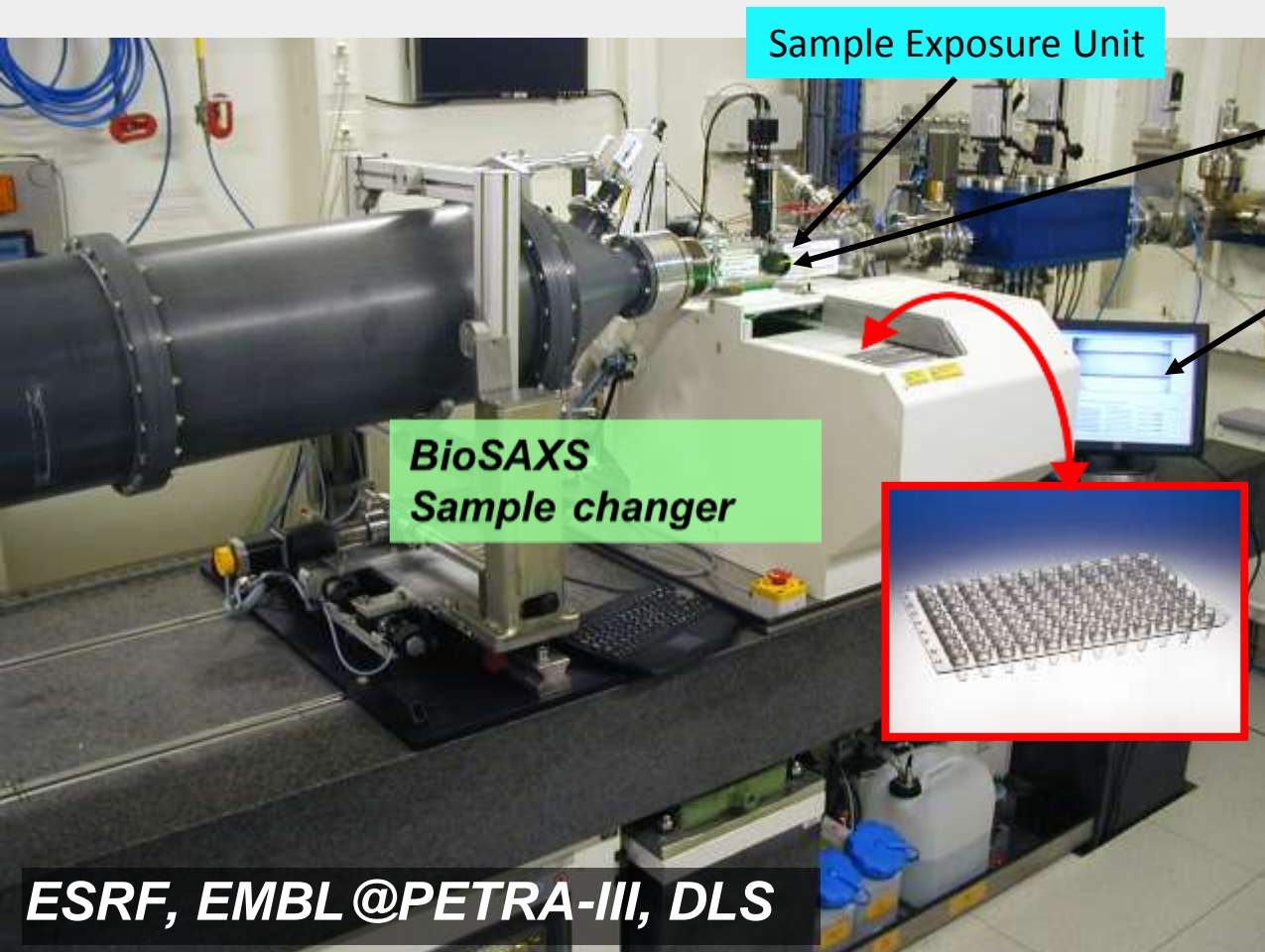
Automatic screening
■ 50 samples in 2H00'



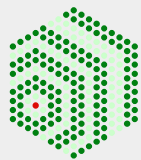
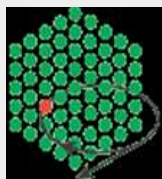
Second generation of robotics under developm^t
→ based on 6 axes industrial robots
→ Increased capacity



BioSAXS sample changer

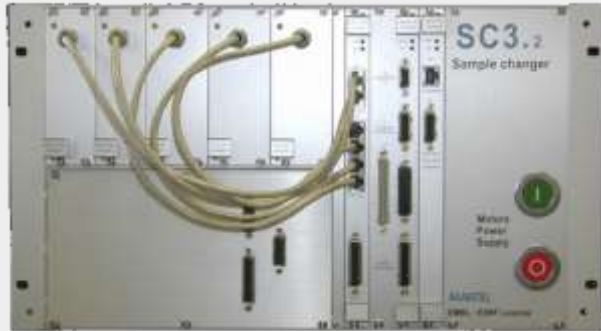


- Samples **stored** in 96 wells Microplates
- **Exposed** in a 10 μm walls cell, in vacuum (2-60 $^{\circ}\text{C}$)
- **Transfers** down to 5 μl of solution
- **Cycle time** 40 sec
- Exposure in flow mode



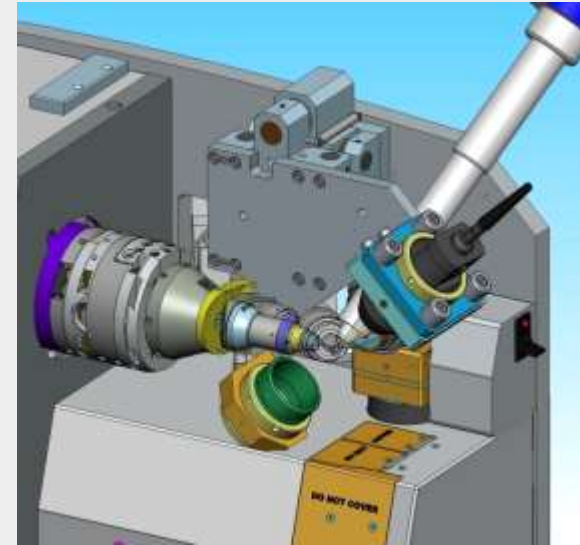
Instrumentation at EMBL

Our expertise: **System engineering**



Precision mechanics ■
Optics ■
Cryogenics ■

■ **Analog/digital Electronics**
Motion control

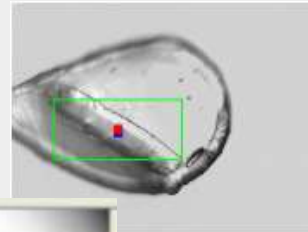


■ **Software**

← **Instrument control**

Image processing →

Crystal alignment



Liquid positioning



Industry → EMBL → Industry

■ EMBL customer

■ Buy components

- Mechanics, electro mechanics
- Optics
- cryogenics
- Electronics (motion control, PLCs...)

■ Buy services

- Precision machining, welding...
- Electronic CAD
- Specific developments (RFID tags...)

■ EMBL supplier

■ Technology transfers

- X-ray diffractometers
- Neutron diffractometers
- Crystal dehydration devices
- BioSAXS sample changers
- Piezoelectric shutters
- Consumables
- ... under development



EMBL-GR Instruments installed today

- **MD2** Diffractometer/OAV/C3D - 30 units
- **HC1** Dehydration device - 11 units
- **BioSAXS** sample Changer - 3 units
- **QLD** Neutron IP Diffractometer - 5 units

23 sites
50 instruments

12 M€

CANADA
CLS (MD2, HC1)

USA
APS (7x MD2, HC1)
ALS (2xMD2, HC1)
SSRL (OAV, C3D)
NSLS (C3D)
SNS (QLD)

EUROPE
EMBL/ ESRF (6xMD2, 2xHC1)
SOLEIL (MD2)
SLS (MD2)
BESSY (MD2, HC1)
PETRA3 (MD2, MD3)
DLS (MD2, 2xHC1)
MRC (HC1)
MAX-lab (MD2, HC1)
ALBA (MD2)
Virchow Institute (HC1)
ILL (2xQLD)
FRM-II (QLD)

KOREA
PLS (MD2)
KAERI (QLD)

CHINA
SSRF (3xMD2)

TAIWAN
NSRRC (2xMD2)

AUSTRALIA
ANSTO (QLD)

February 2013

People involved

Head of EMBL Grenoble
Stephen Cusack



Diffraction Instrumentation Team

Franck Felisaz
Alexandre Gobbo
Christophe Landret
Gergely Papp
Ulrich Zander
Clement Sorez
Raphael Moya
Anthony Astruc
Florent Cipriani

High Throughput Crystallography Team

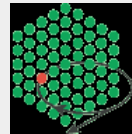
José Antonio Marquez
Ulrich Zander
Martin Roewer
Guillaume Hoffmann
Gael Seroul
Vincent Mariaule

Synchrotron Crystallography Team

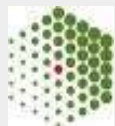
Andrew McCarthy
Hassan Belrhali (BM14)
Max Nanao



S. McSweeney
MX group



EMBL Hamburg *G. Bourenkov MD3*
D. Svergun. M. Roessle BioSAXS



EMBLEM



MAATEL



BioStruct

