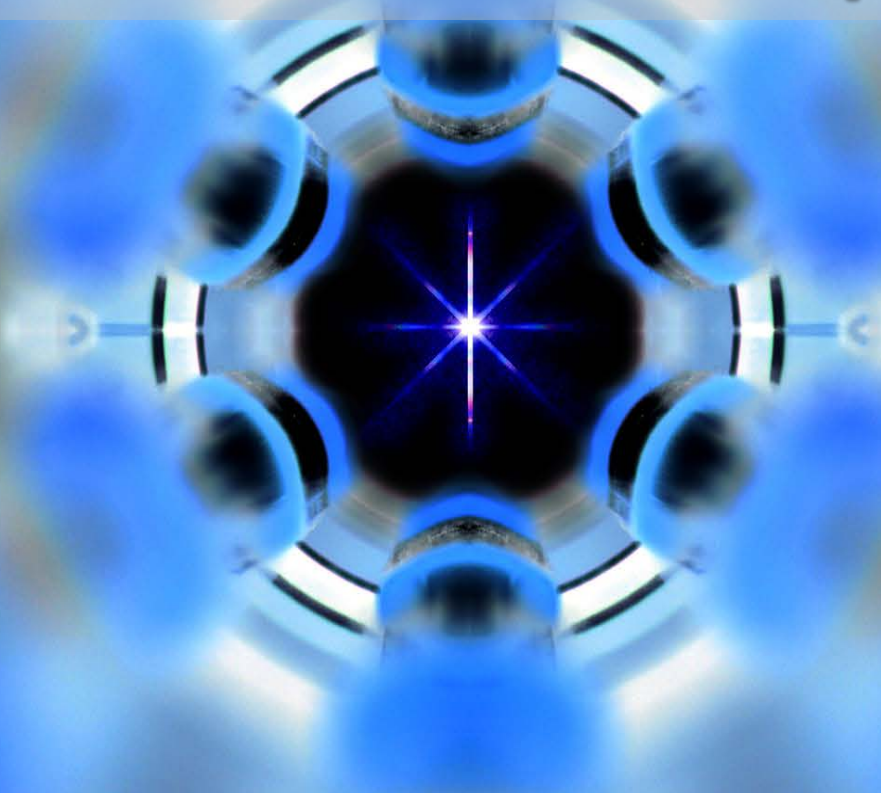


# An Introduction to Diamond and the Harwell Campus



*Martin Walsh*

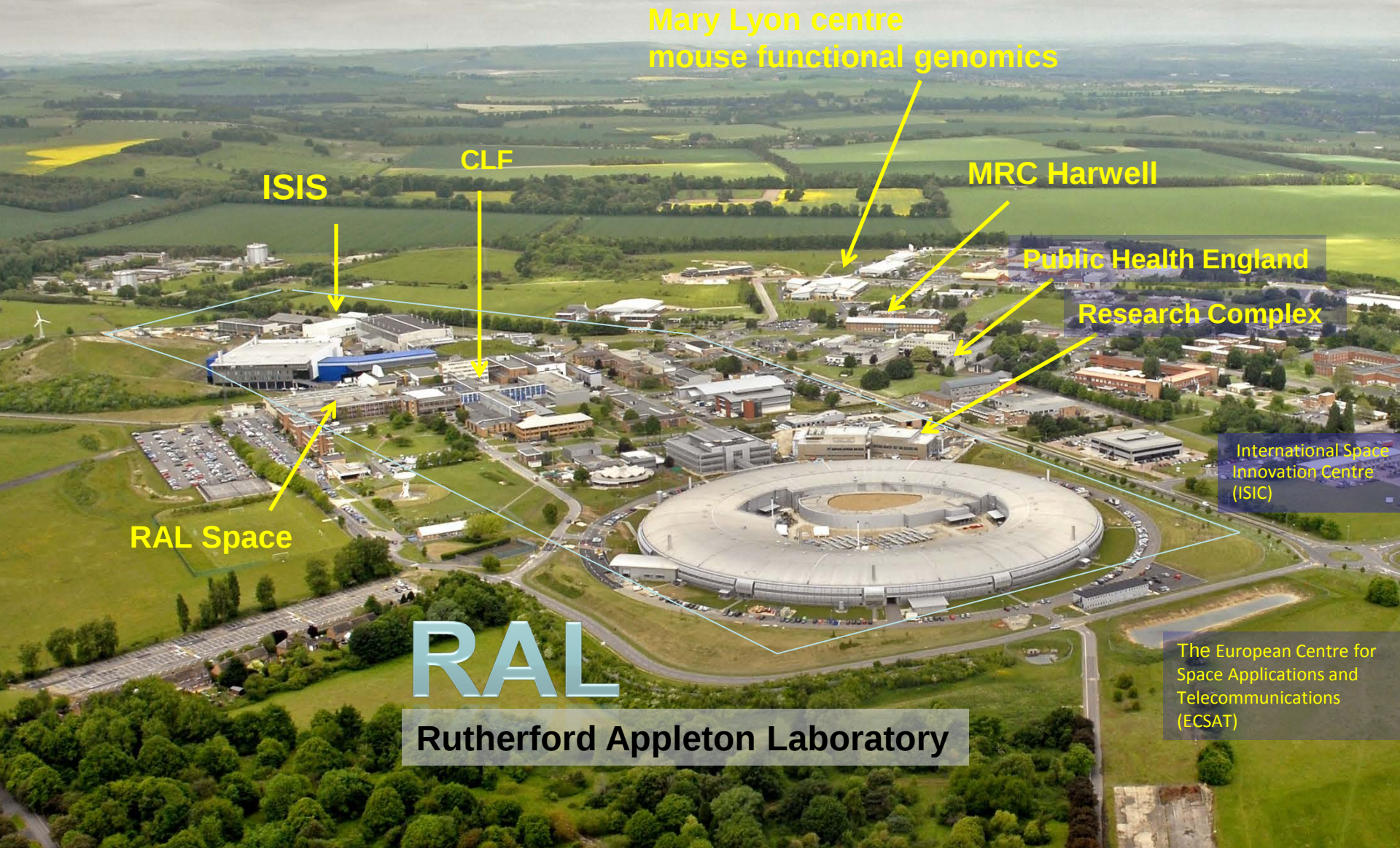
# The Diamond Project



- Diamond Light Source Ltd set up in April 2002 and created through a Joint Venture Agreement (JVA) between the UK Government and the Wellcome Trust;
- Construction completed 2006;
- Machine commissioned from June 2006
- First Users Jan 2007

|                        |              |
|------------------------|--------------|
| Electron Beam Energy   | 3 GeV        |
| Circumference          | 561.6 m      |
| Diameter of outer wall | 235 m        |
| Beam current           | 300 (500) mA |

# Harwell Campus



Mary Lyon centre  
mouse functional genomics

ISIS

CLF

MRC Harwell

Public Health England

Research Complex

International Space  
Innovation Centre  
(ISIC)

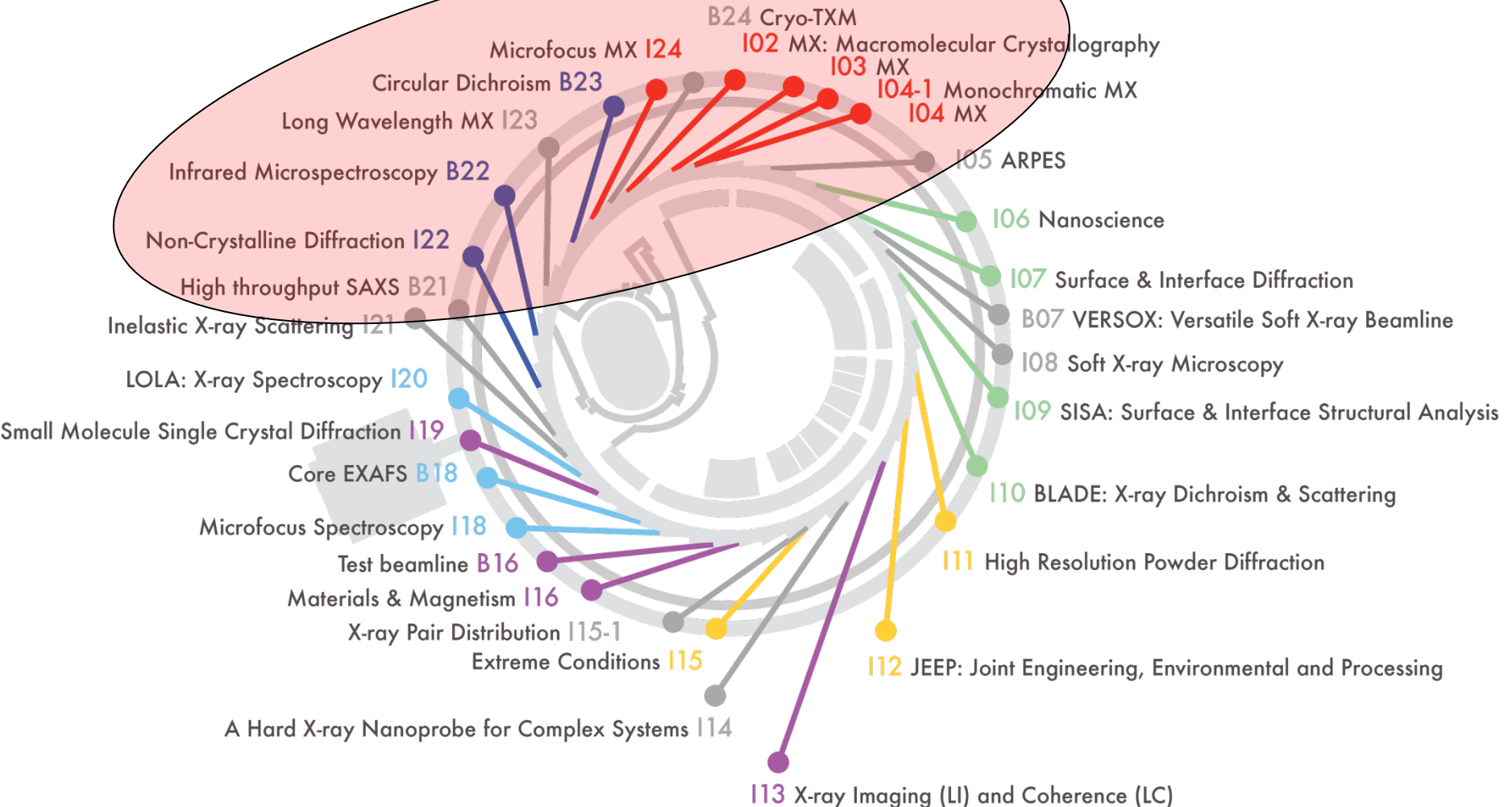
The European Centre for  
Space Applications and  
Telecommunications  
(ECSAT)

RAL Space

**RAL**

Rutherford Appleton Laboratory

# Beamlines by Village



● **Macromolecular Crystallography**

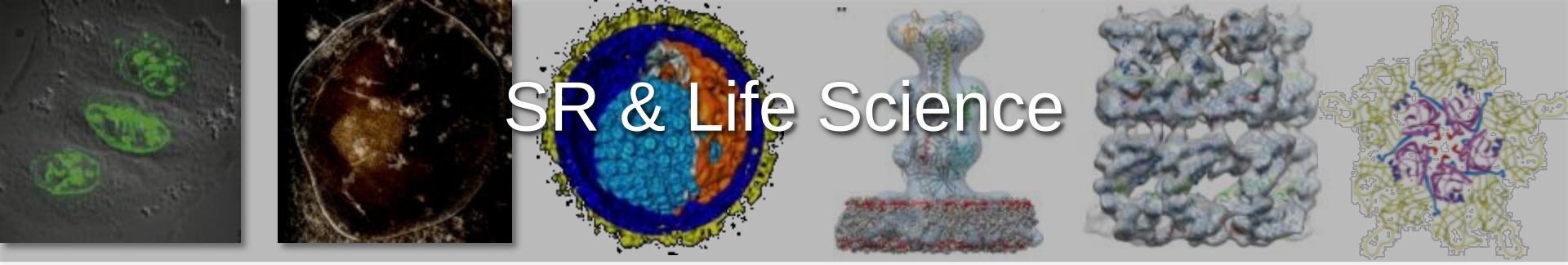
● **Soft Condensed Matter**

● **Spectroscopy**

● **Materials**

● **Engineering and Environment**

● **Surfaces and Interfaces**



# SR & Life Science

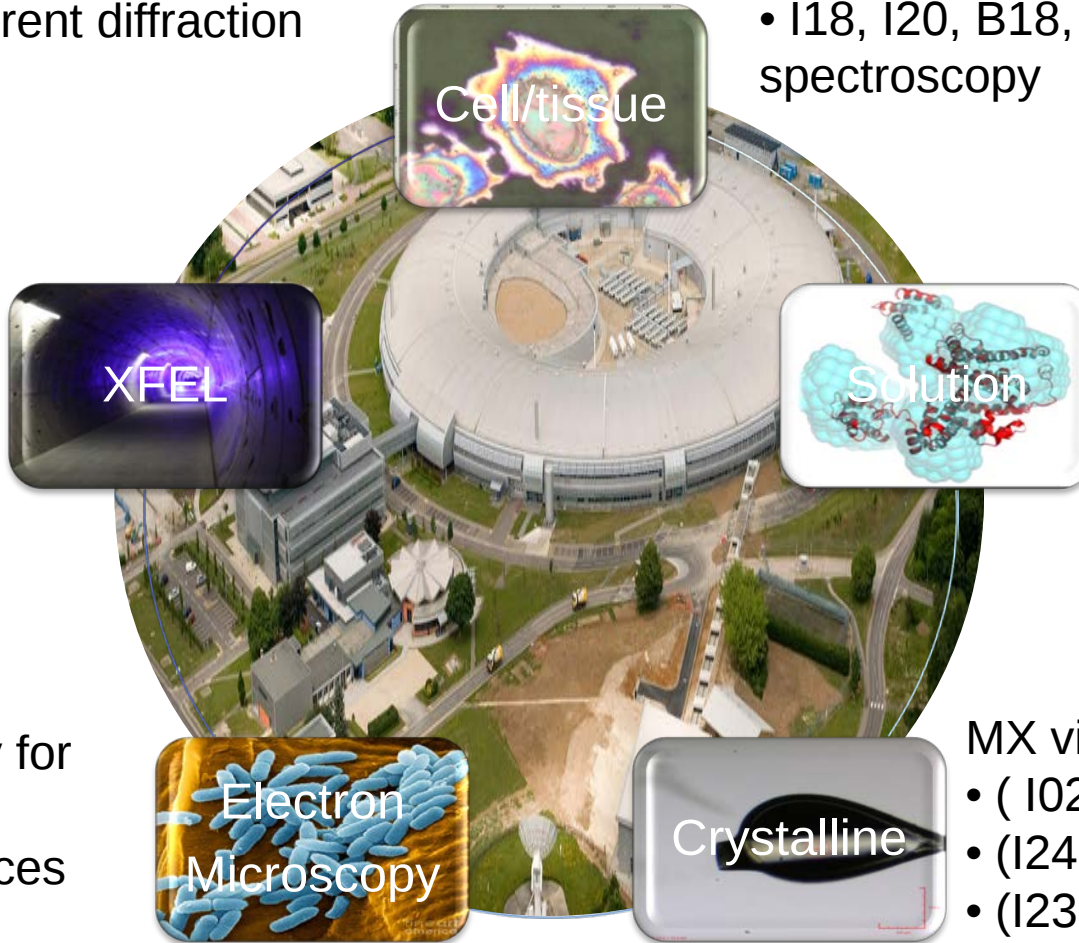
- Provision of state of the art technologies for structural and cellular biology
- Challenge now is to understand how proteins function dynamically within
  - Multi-complex macromolecular assemblies
  - Cellular pathways
  - ...ultimately at the organism level
- **Requires a multifaceted approach across different resolutions scales to achieve:**
  - X-ray diffraction, SAXS, X-ray microscopy, X-ray spectroscopy, X-ray fluorescence, CD, IR imaging etc..
  - Harwell campus infrastructure – a unique resource: RC@H, OPPF-UK, CCP4, MPL@DLS, Central Laser Facility, ISIS...

# Life Science & DLS

- I08 X-ray STXM
- I13 X-ray tomography & coherent diffraction

- B22 Infrared
- B24 Cryo X-ray microscopy
- I18, I20, B18, I14 X-ray spectroscopy

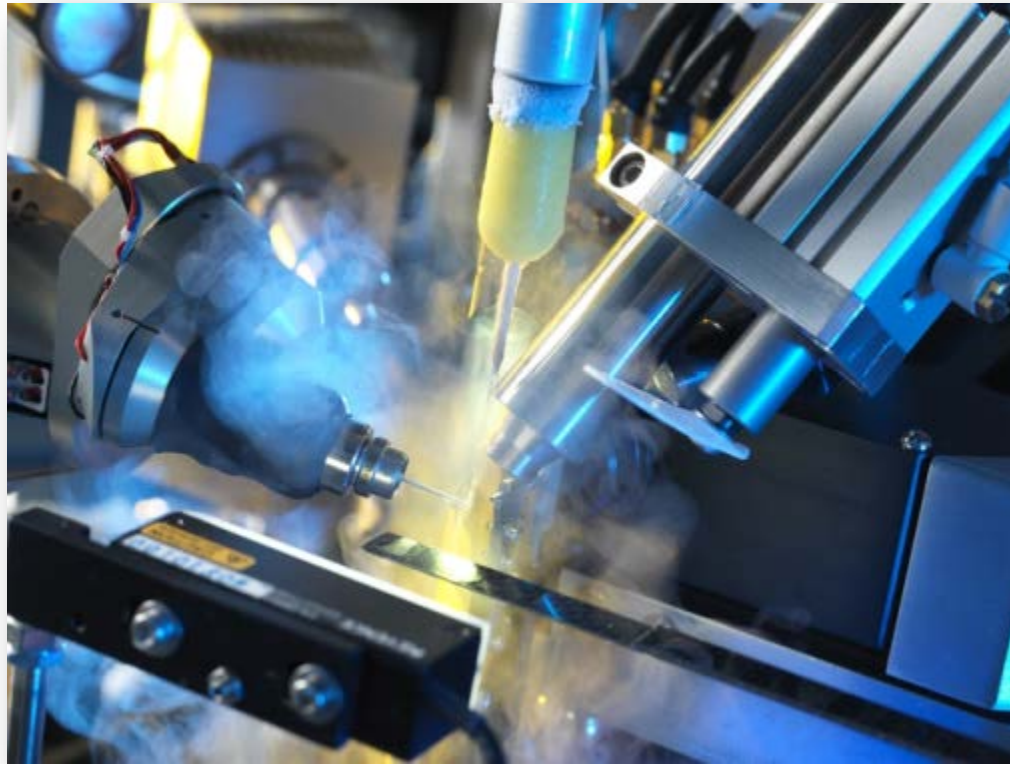
UK Hub for  
XFEL sample  
and software  
developments



- I22/B21 SAXS
- B23 CD
- Spectroscopy

National facility for  
EM in life &  
Physical Sciences

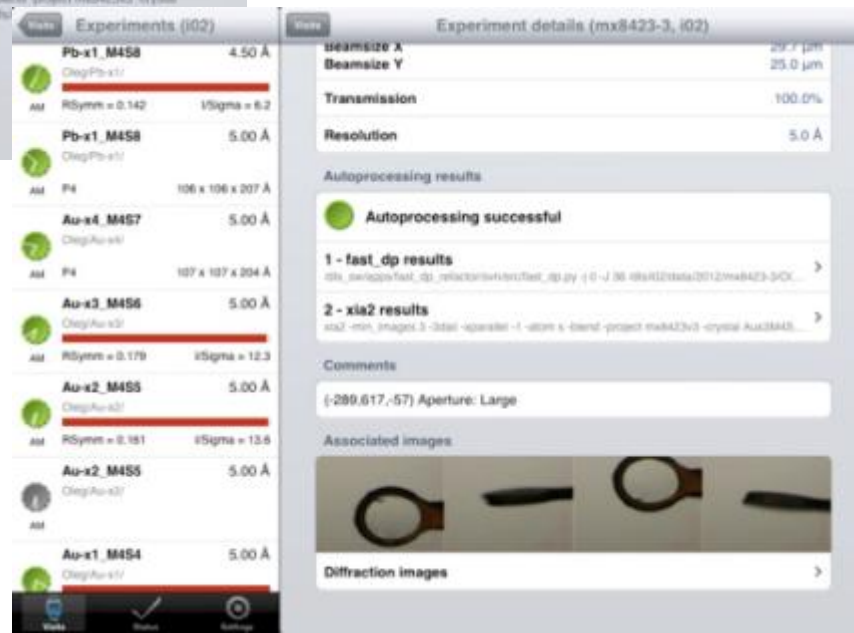
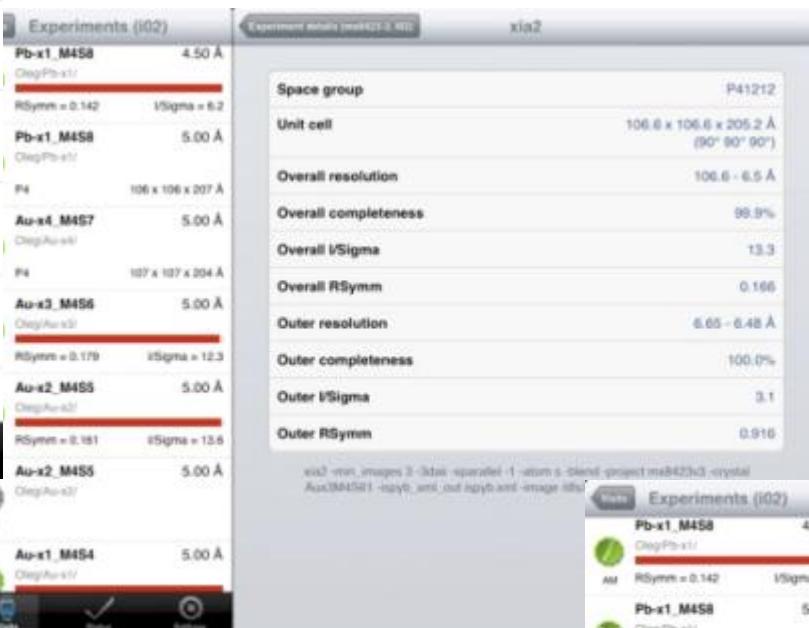
- MX village
- ( I02, I03, I04)
  - (I24, I04-1)
  - (I23, VMX)



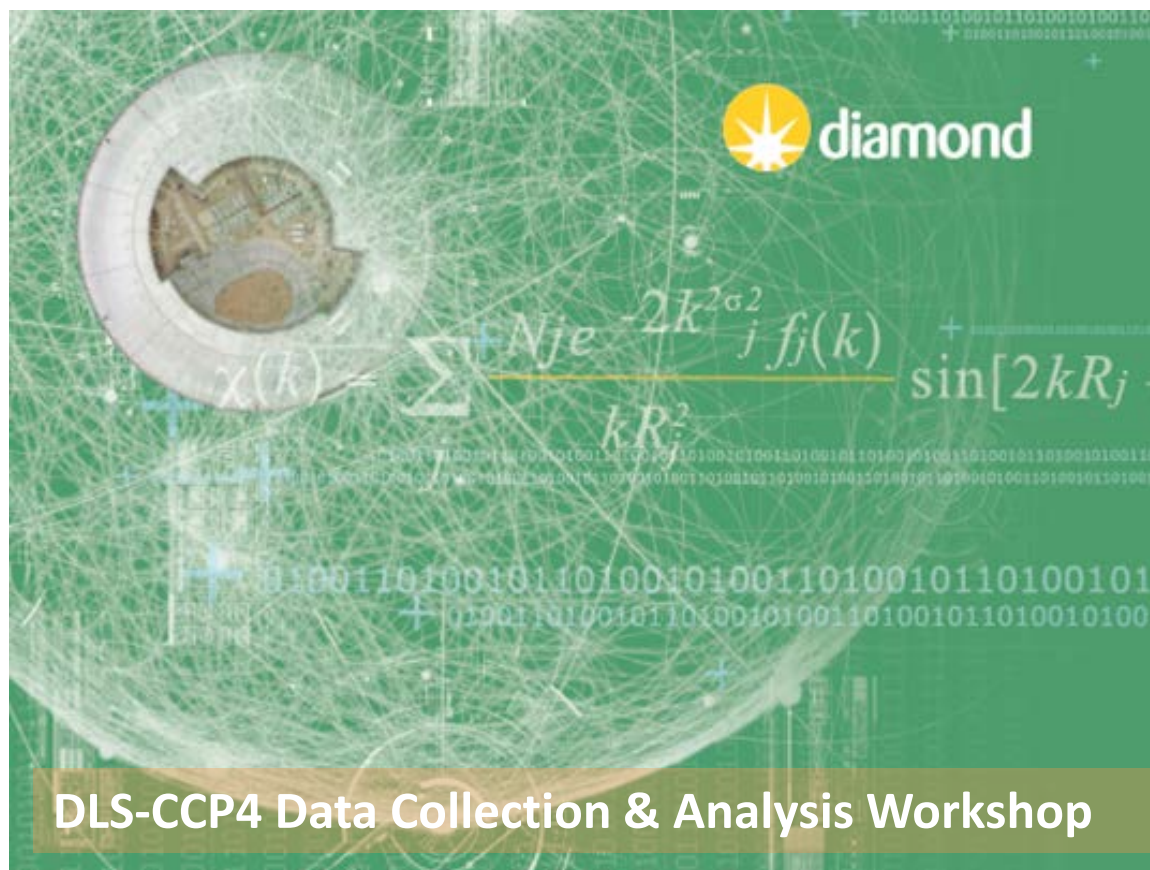
## MX@DLS

I02 & VMXi Thomas Sorensen I03 Katherine McAuley  
I04 Dave Hall I04-1 Frank von Delft I24 Robin Owen  
I23 Armin Wagner & VMXm Gwyndaf Evans

# Synchlink - IOS app for ISPyB



Ginn et al J. Appl. Cryst. 47, 1781-3 (2014)



## **A note on potential success of participants projects....**

If you publish results that stem directly from work done during this workshop we would very much appreciate an appropriate acknowledgement in the paper. Please also inform the organisers of the publication of your papers. These will be listed on the CCP4 website for the workshop and will help to ensure that CCP4 can keep funding future workshops like this



## **BIOSAXS B21**

B21 HATSAXS Rob Rambo Katsuaki Inoue,  
James Douth Mark Tully

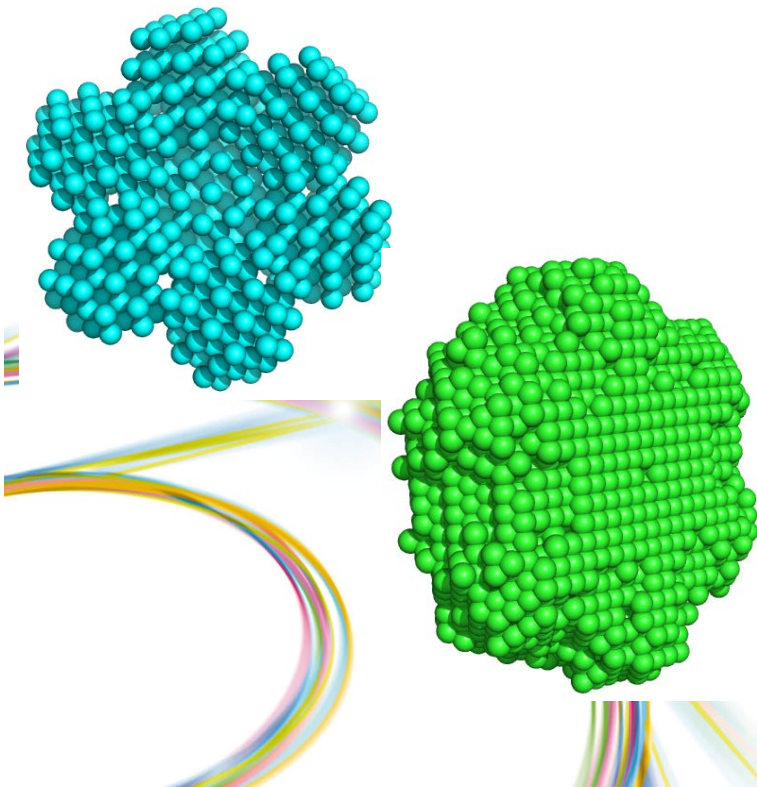
# What is solution SAXS?

- Small-angle x-ray scattering offers the ability to build low resolution models of macromolecular structures in solution ( $\sim 20$  Å resolution)
- Gives us information on shape and quaternary structure
- Samples can be studied under a variety of conditions

- first user December 2013
- range  $0.004$  to  $0.42$  Å<sup>-1</sup> ( $1570$  Å) at 4 m
- implementing bioSAXS training workshops
- developing software:

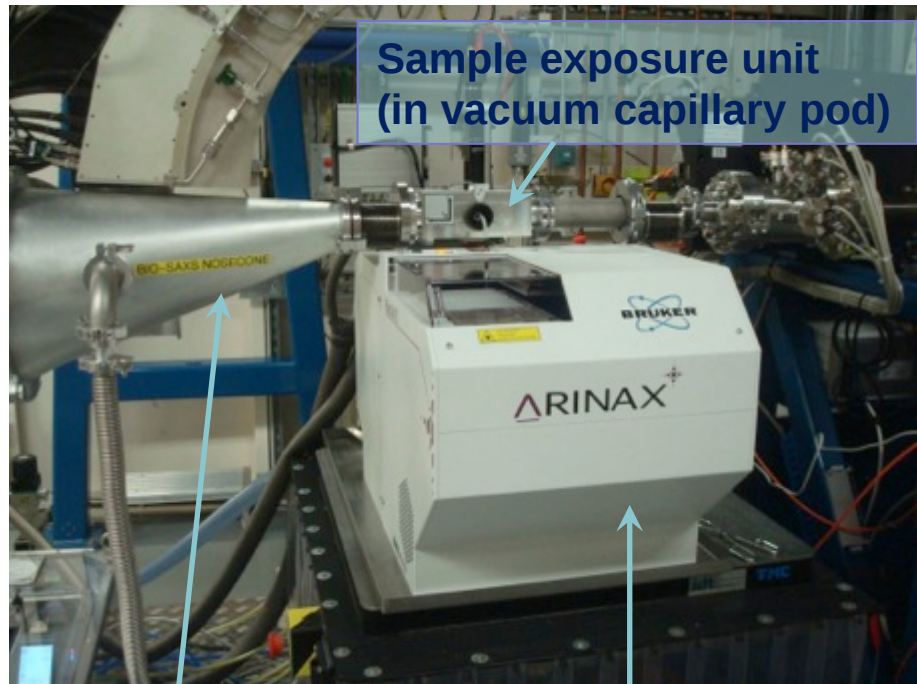


- piloting mail-in SAXS Services
  - 1) plate screening
  - 2) size-Exclusion Coupled SAXS



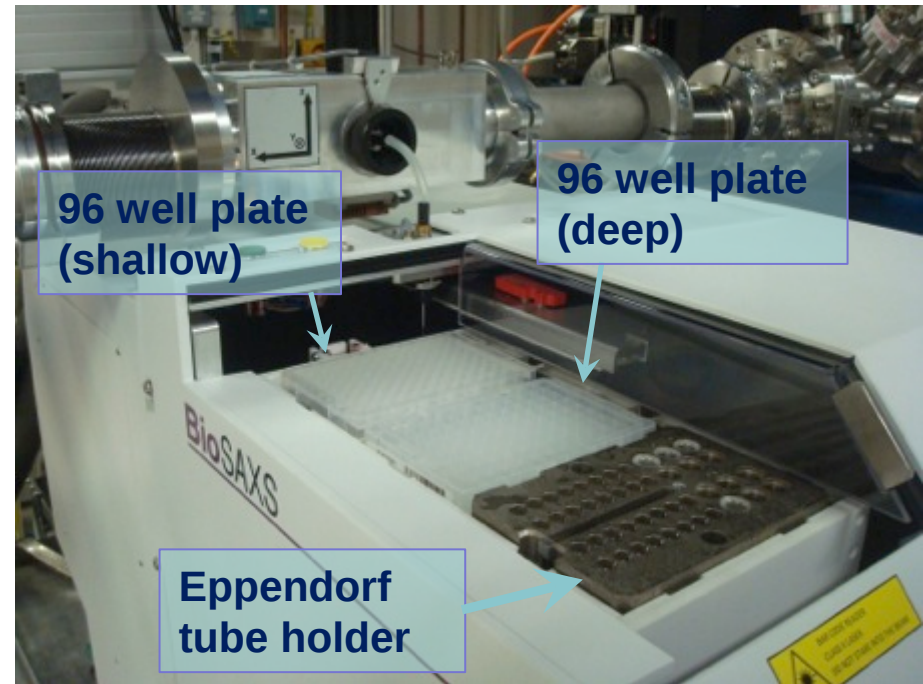


# BIOSAXS automation – EMBL robot



## SAXS flight tube

**Sample storage unit  
(temperature controlled)**

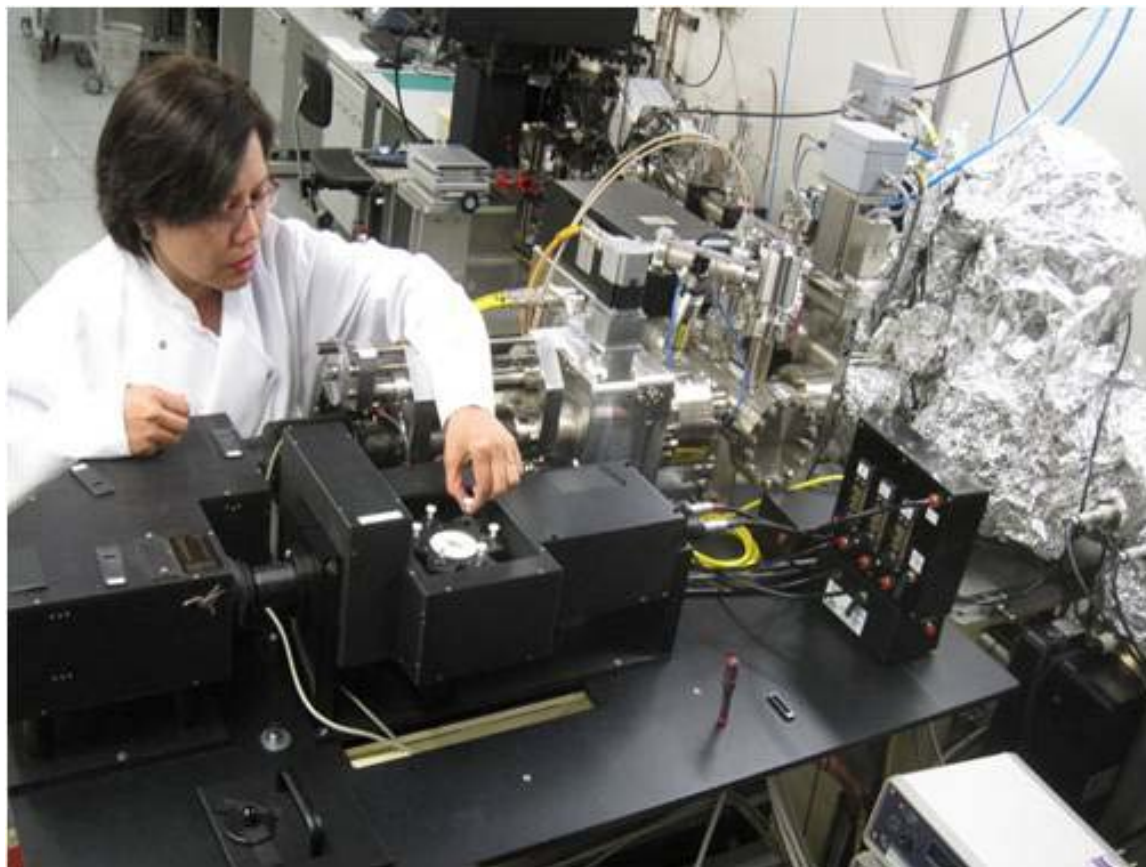


## Fully automated routines;

**inject → exposure → flush → wash → dry → inject → exposure .....**  
 | ← 1 minute → |

**Maximum number of measurements: 55 /hour!!**

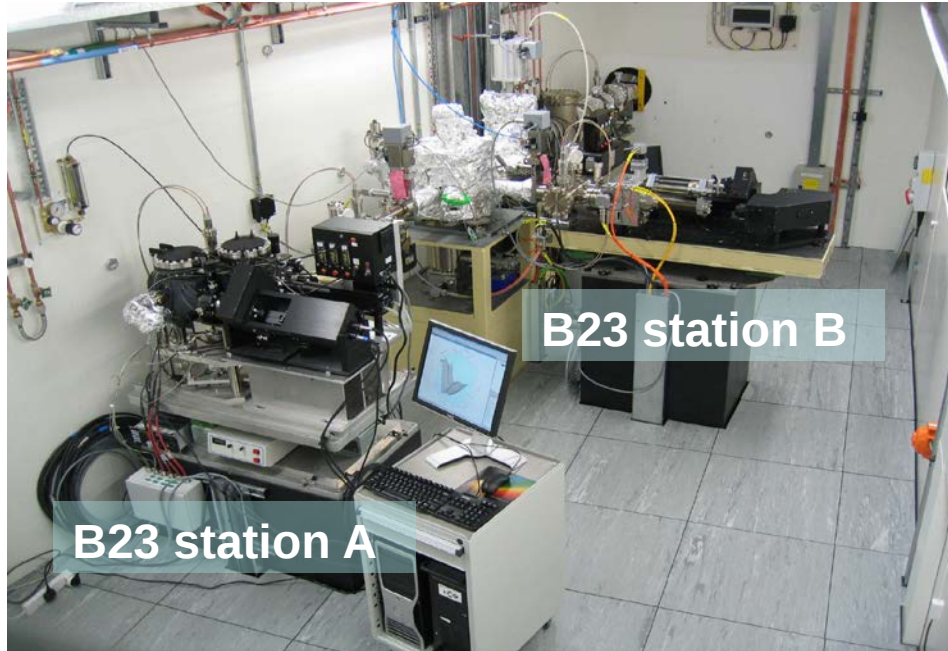




## **B23 Circular Dichroism**

Giuliano Siligardi @diamond.ac.uk

# B23 - applications



- Qualitative and quantitative analysis of protein-protein and protein-ligand interactions
- Characterisation of IMP's
- Protein stability
- Quality control /drug formulations and delivery

***Experimental cabin of B23 beamline. B23 consists of two stations with wavelength range of 125-550nm for B23-A, and 170-650nm for B23-B. Insert) Beam profile of the light beam of B23 module B at the sample in the sample house compartment measured with beam profile monitor Beamage USB.***



## Cryo transmission X-ray microscopy

B24 Liz Duke @diamond.ac.uk

# B24: Soft X-ray Microscope

- Soft X-ray tomography allows to image whole hydrated cells in 3-D to resolutions of 50 nm or better.
- Provides for imaging of thick samples ~up to 10  $\mu\text{m}$
- Contrast provided by the differential absorption of X-rays hence imaging of cells in a close-to-native state possible
- Amiable to high-throughput
- Correlated imaging possible with light microscopy - allowing tagged molecules to be localized in the high resolution 3-D image of a cell
- Visualisation of 3D structural details
  - Complementary to cryo-EM
  - Correlative light microscopy

# B24 Cryo soft x-ray tomography

From data collected in-house with plasma source

**N: Nucleus**

**C: Cytoplasm**

Nuclear envelope

Nucleoli

**N**

**C**

Cell membrane

Cytoskeleton

Endoplasmic reticulum

Mitochondria

Lysosomes

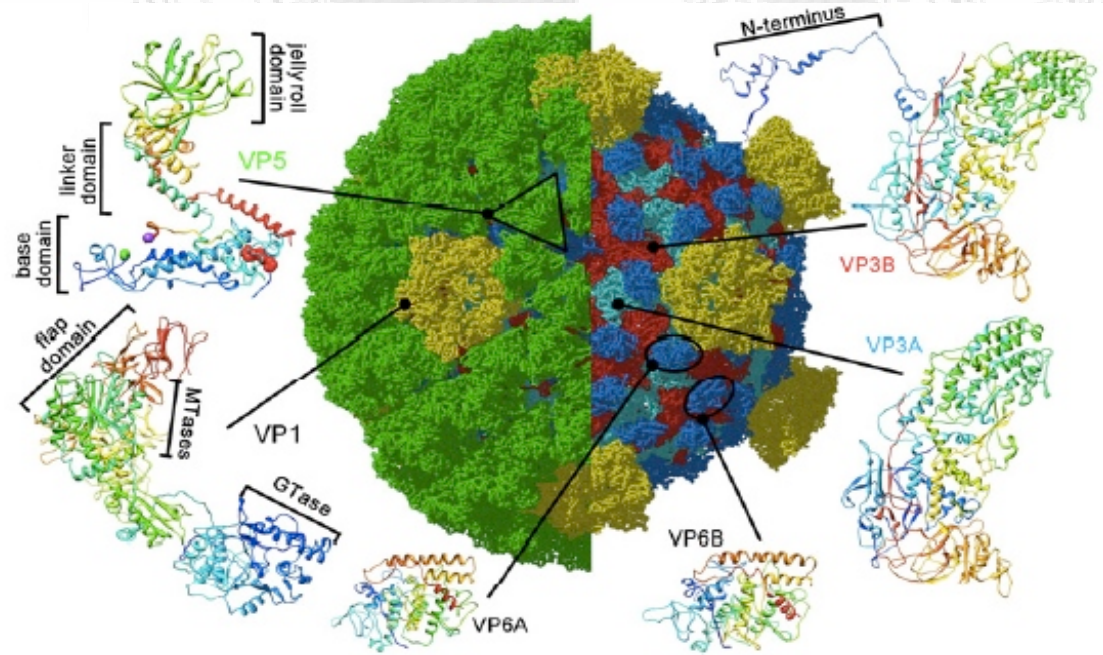
# A National User Facility for Biological Electron Cryo-microscopy

Wellcome Trust Strategic Award/MRC/BBSRC, applicants:

Helen Saibil, Kay Grünewald, David Stuart, Gerhard Materlik

- Funded by the Wellcome Trust, MRC and BBSRC at level of £15.6 M over 5 years

### 3.3 Å Cryo-EM Structure of a Nonenveloped Virus



### Aims:

- Establish state-of-the art facilities for single particle analysis and cryo-tomography
- Uniquely provide these via a beamline-like access programme
- Provide ancillary facilities to increase the ambitions of the UK community
- Grow/train the user community, especially structural biologists and cell biologists
- Foster the development of Integrated Structural Biology in the UK, linking with other developments

# The EM-synchrotron concept

**Direct electron detectors – a revolution**

**Major microscopes ordered – 2015 delivery**

**Dual-beam machine (milling) – now commissioning**

**Beamtime via Oxford, offered in 2014**

**Building:**







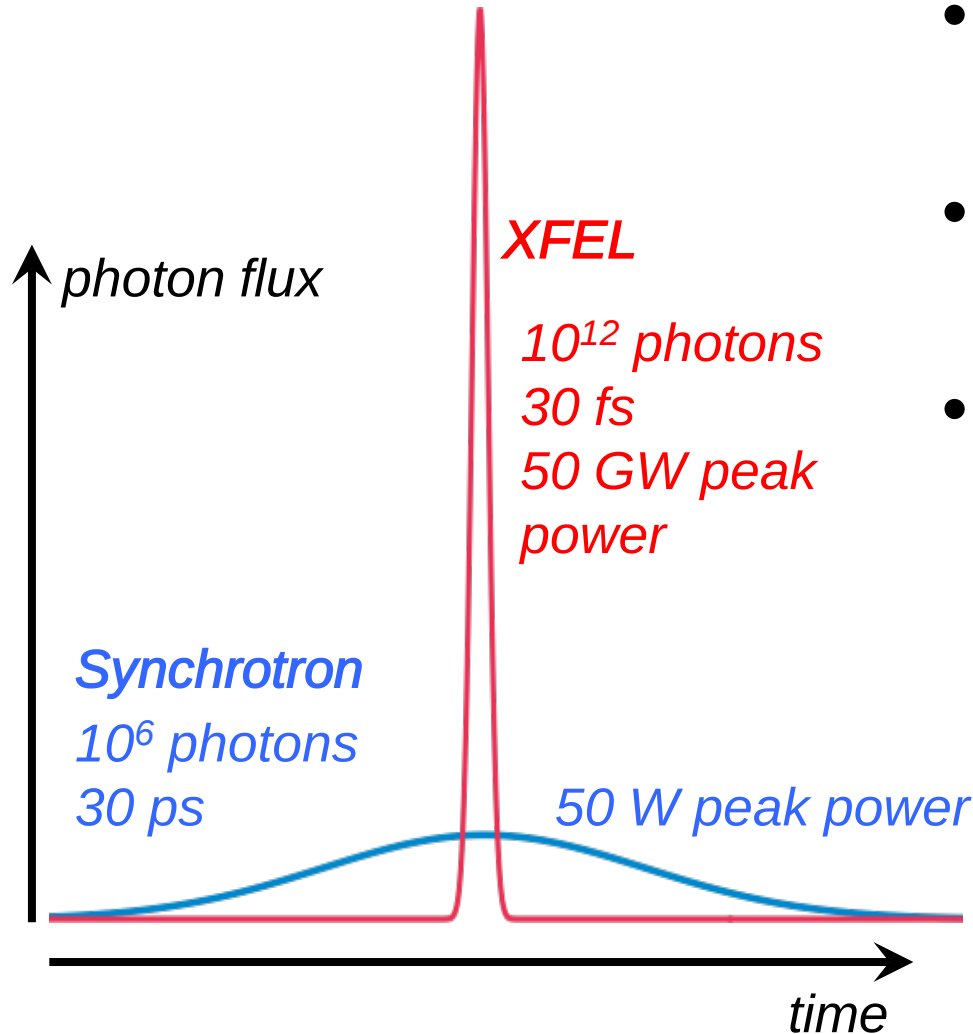
## UK and femtosecond crystallography at the European X-FEL - SFX

James Naismith David I Stuart Jan Löwe Martin A Walsh  
Henry N Chapman

On behalf of the UK Structural Biology Community  
via Instruct & CCP4

- Funded by Wellcome Trust, BBSRC and MRC to make the UK the largest partner in the consortium at the European XFEL (<http://www.xfel.eu>) for this dedicated crystallography instrument
- Enable diffraction from nanocrystals...time resolved experiments...ultimate goal image single particles...

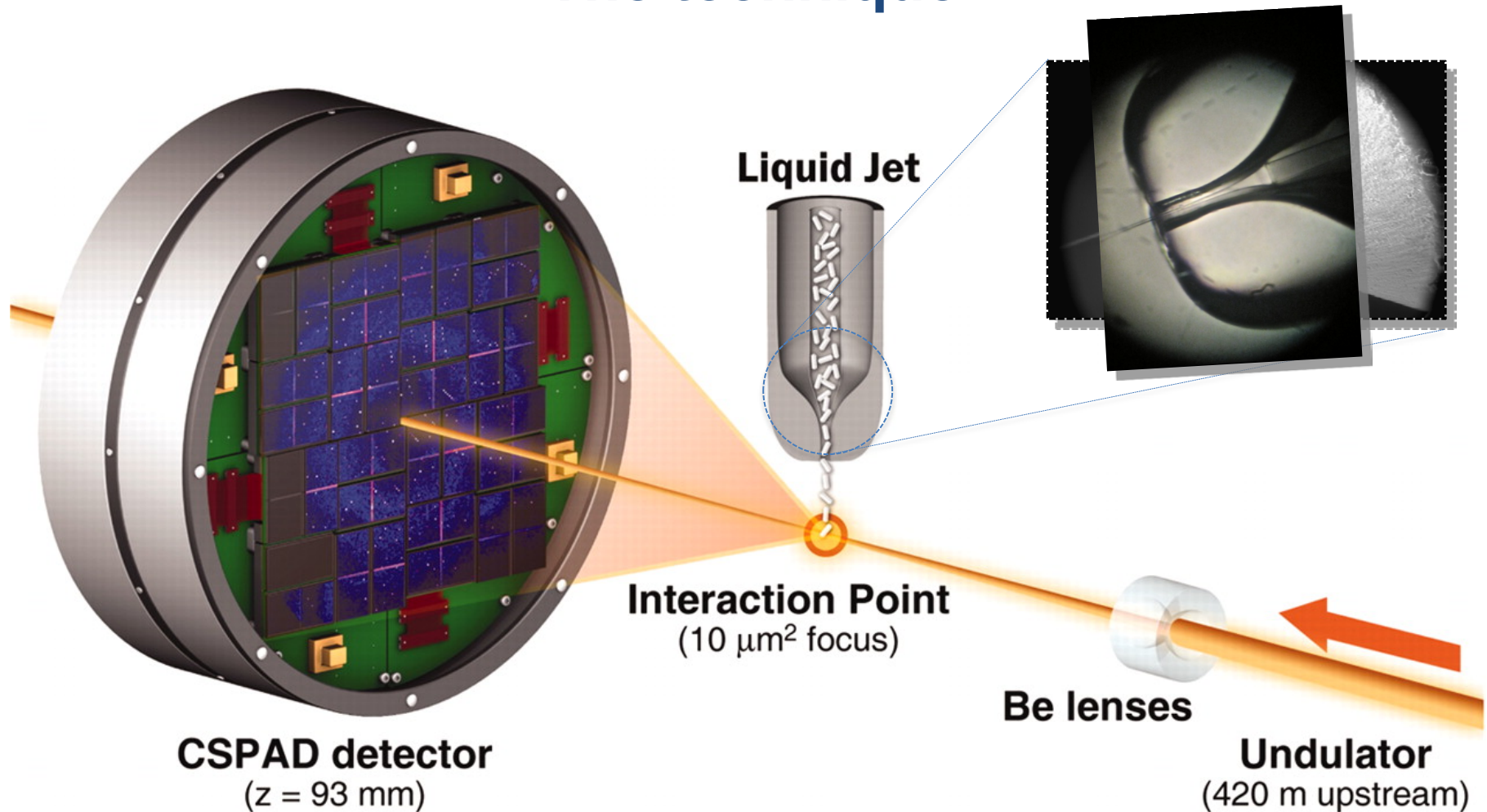
# Potential of XFEL



- 30 fs pulse, X-ray doses exceeding 1 GGy
- **Unique: diffraction before sample destruction**
- Structures from smaller & sensitive crystals not currently tractable: paradigm shift for
  - Membrane proteins
  - Protein protein complexes

# Serial Femtosecond Crystallography

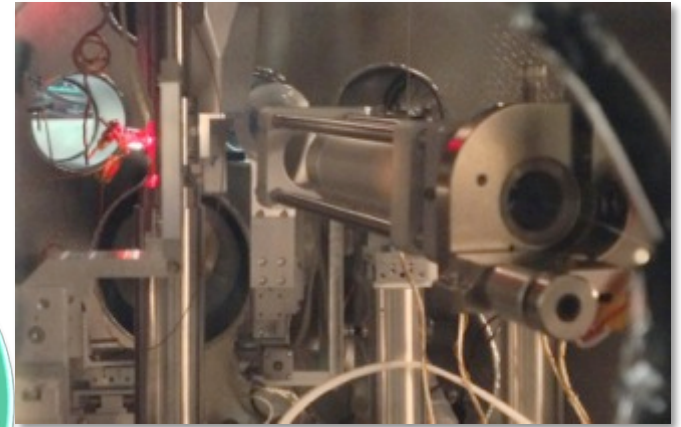
## The technique



Single shot diffraction patterns are obtained from a stream of fully hydrated nano-crystals injected at room temperature into the intense X-ray pulses from the XFEL source. Each intense pulse lasts for ~30 Femtoseconds and allows the diffraction data to be collected before the crystal is destroyed

# UK Hub at Diamond

- establishing an open XFEL user programme



Software Developments for automated data analysis

Development of Sample delivery & Environments

High Performance Computing and Data curation

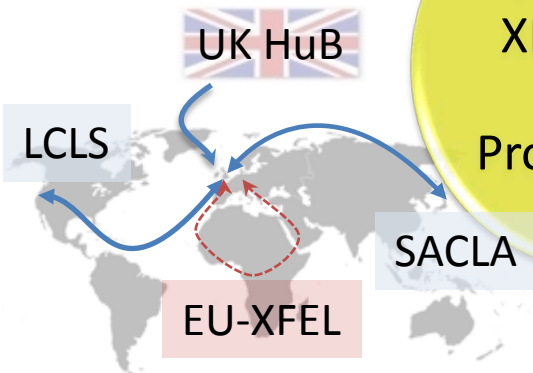


UK XFEL HuB

Facilitate access to XFELS/UK User Program for SFX

Integrated Structural Biology Infrastructure @RAL

Users





## **Research Complex at Harwell**

Funded by Research Councils UK and  
Diamond

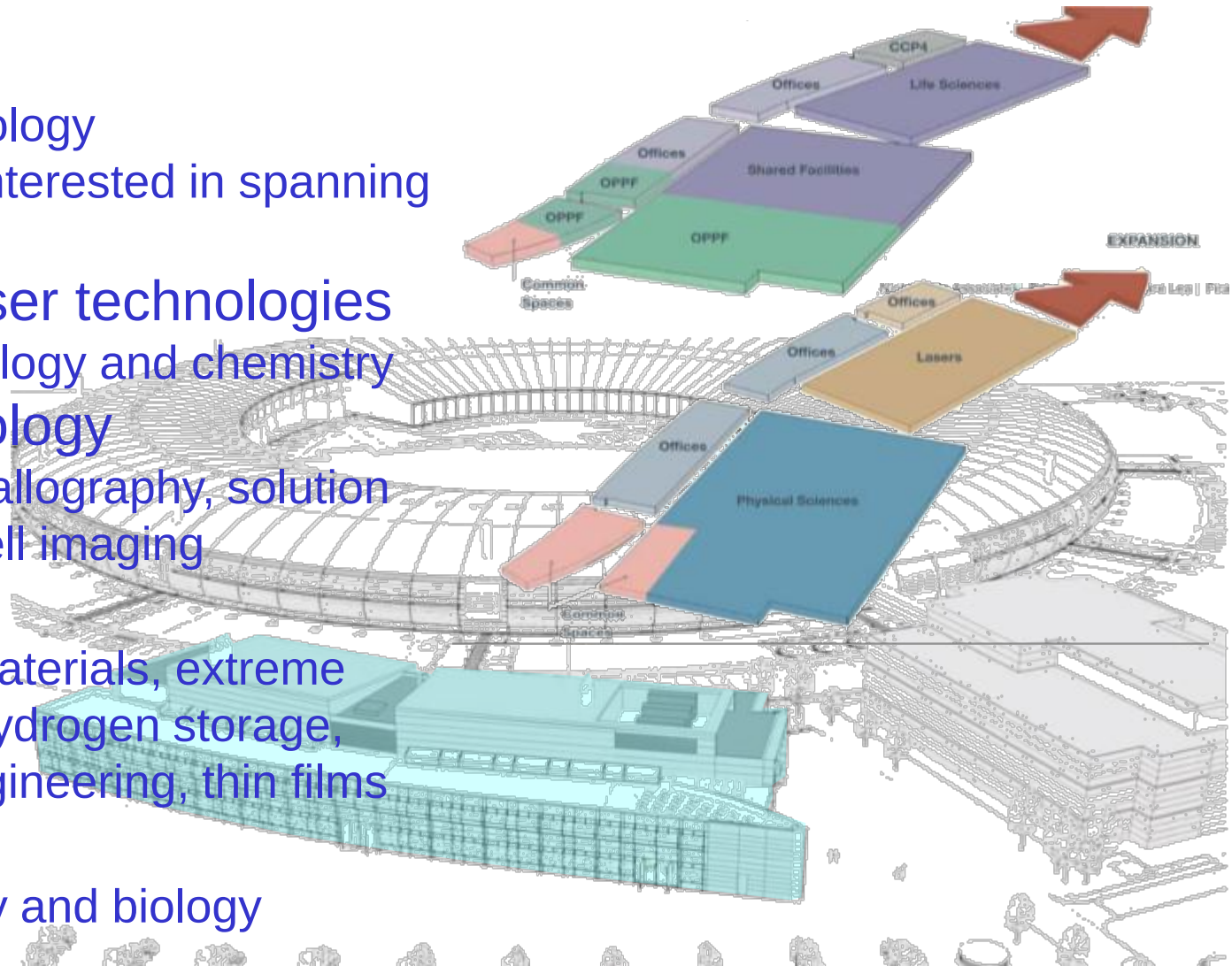
# The Research Complex (RCaH)



- Joint venture of UK research councils (RCUK) and Diamond
  - A multidisciplinary laboratory in the life and physical sciences
- Mission
  - To carry out research optimising use of the combination of large facilities at RAL
  - To encourage scientists from different subjects to work together

# Research Themes in RCaH

- Imaging
  - Materials
  - Nanotechnology
  - Biologists interested in spanning length scales
- Ultra Fast laser technologies  
LSF, both biology and chemistry
- Structural biology  
Protein crystallography, solution scattering, cell imaging
- Materials
  - Magnetic materials, extreme conditions, hydrogen storage, materials engineering, thin films
- Catalysis
  - In chemistry and biology



# Central Laser Facility

ASTRA GEMINI

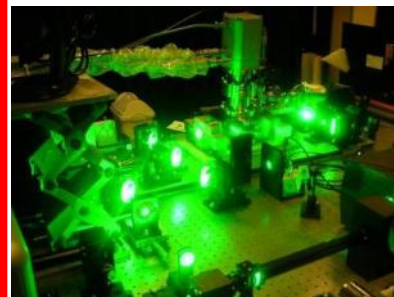
VULCAN

ARTEMIS

ULTRA

OCTOPUS

- High Power Lasers



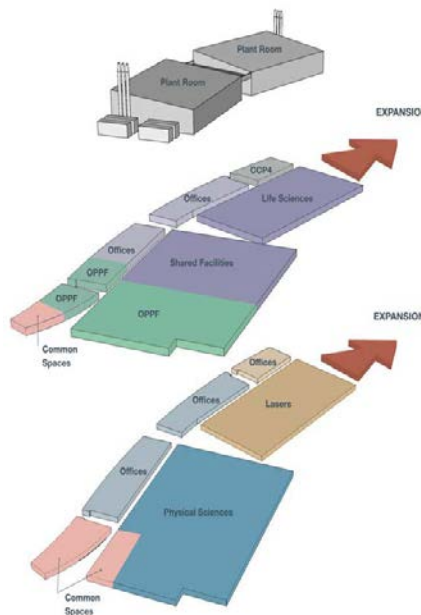
- Ultrafast vibrational spectroscopy

- Imaging, laser tweezers and microscopy

“Lasers for Science Facility” in the Research Complex at Harwell

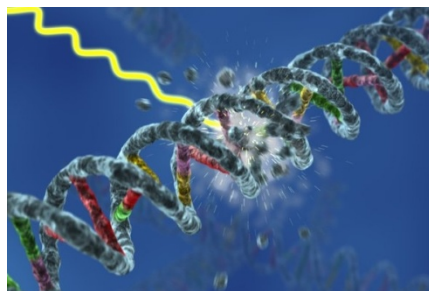
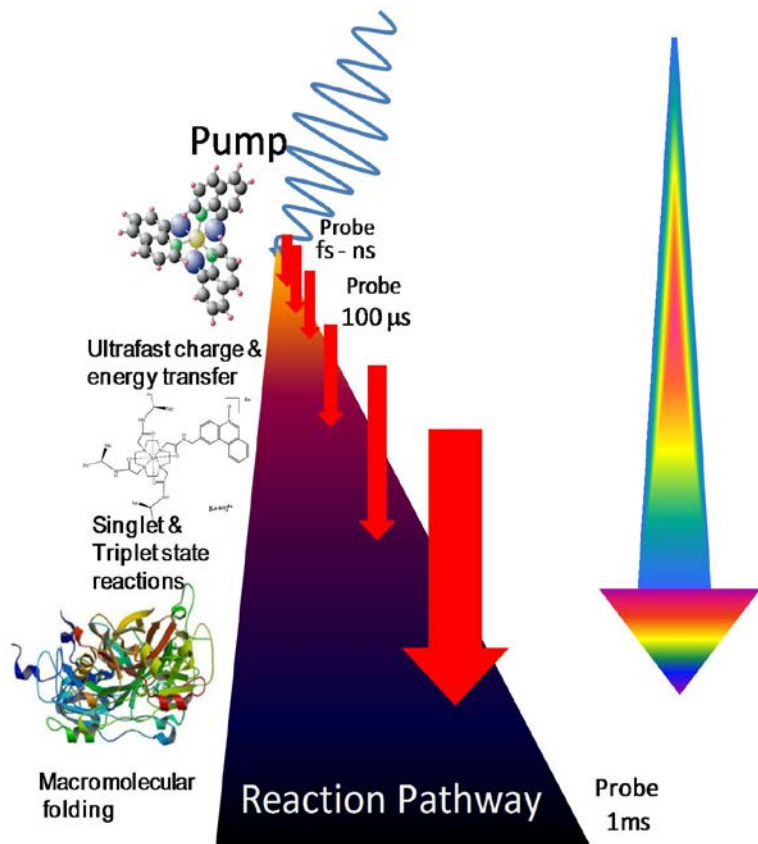


A multidisciplinary laboratory that provides facilities for researchers to undertake new and cutting edge scientific research in both life and physical sciences and the interface between them.

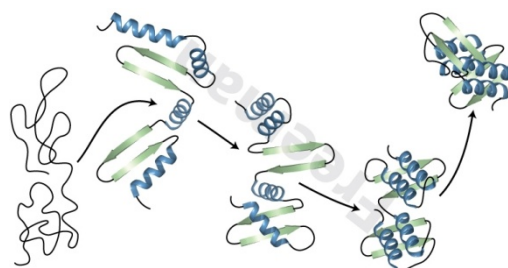


# ULTRA to investigate Molecular Dynamics

Ultrafast spectroscopy techniques to probe the links between molecular structure and function, in the “real world” environment.

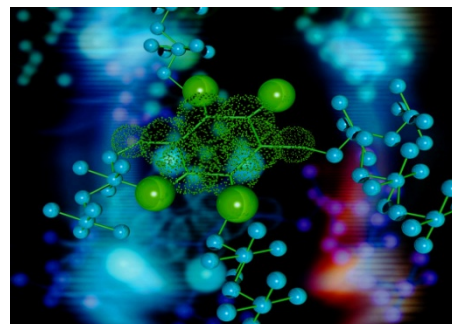


**DNA damage.** DNA is chemically very stable but is still subject to damage by UV light, leading to genetic mutation and skin cancer. ULTRA UV lasers can be used to initiate changes, which are then monitored using time-resolved infrared spectroscopy (*picoseconds to milliseconds*).



**Protein folding and dynamics.** The function of proteins is determined by their 3-dimensional structures. ULTRA is able to investigate how these structures form by initiating folding using laser temperature-jump, and following the process with infrared or UV probes (*nanoseconds to milliseconds*).

 **BBSRC**



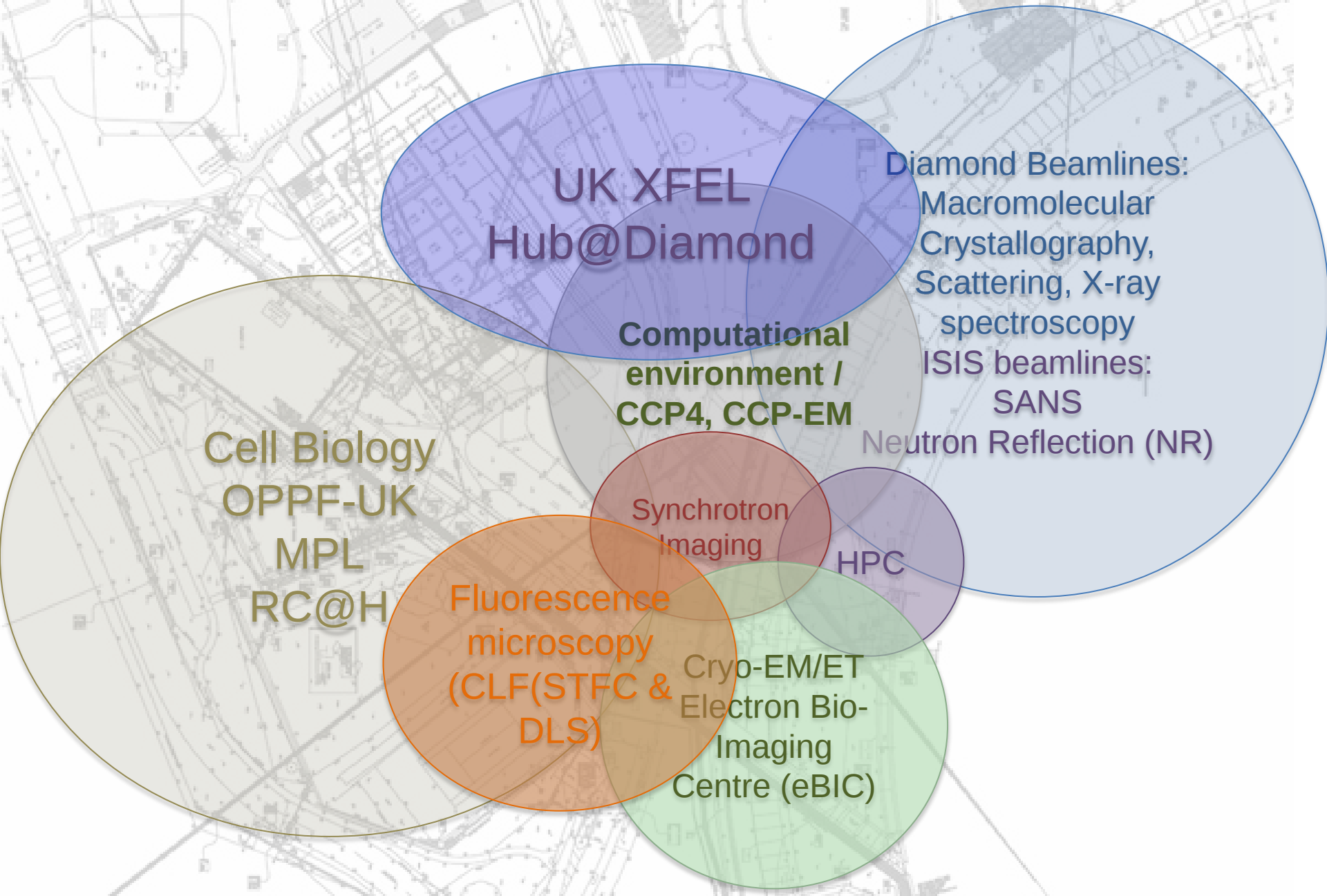
**Chemical reactions in solution.** Most industrially and biologically relevant chemical reactions occur in the solution phase. The very high sensitivity of ULTRA allows reactions to be investigated in these “real life” conditions (*femtoseconds to nanoseconds*).

 **EPSRC**  
Pioneering research and skills

ULTRA's combination of tunable laser sources allows processes to be initiated “with one pulse (pump), and monitored with another (probe).

Processes can be monitored on the femtosecond to millisecond timescale.

# An integrated Approach to Structural Biology



Thanks for your  
attention

And thanks to our  
course sponsors:

**DECTRIS**®

 **Rigaku**

*MiTeGen* 