



| The European Synchrotron



PIONEERING SYNCHROTRON SCIENCE



2019

BEST WISHES FOR THE NEW YEAR



The Pan African Conference on Crystallography (PCCR2) and

The African Light Source Conference (AfLS2)



The Extremely Brilliant Source at the ESRF

31 January 2019

F. Sette, Director
General of the ESRF

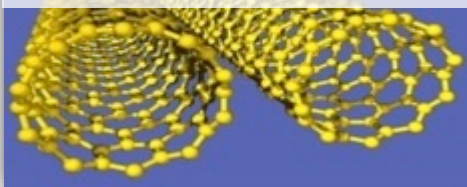


SYNCHROTRON X-RAY SCIENCE AND APPLICATIONS

Fundamental, applied and industrial research

Large variety of a applications for a common goal: link Function to Atomic Structure

ADVANCED MATERIALS



ENERGY & ENVIRONMENT



HEALTH & FOOD



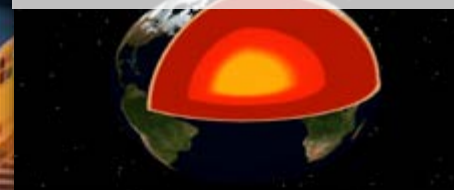
MICROELECTRONICS



CONSUMER PRODUCTS



EXTREME CONDITIONS



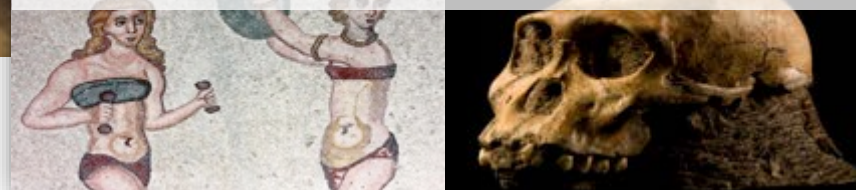
METALLURGY



PETROCHEMICALS



CULTURAL HERITAGE



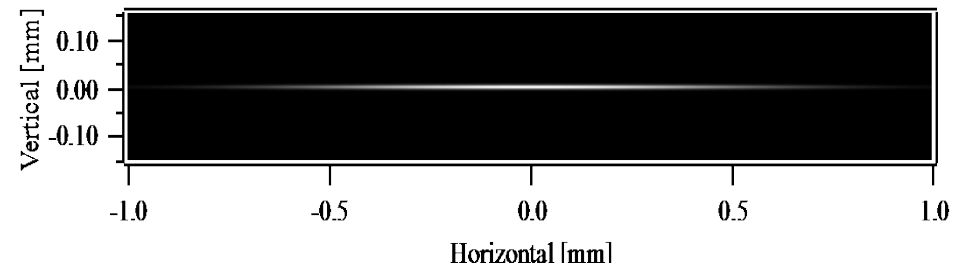
Major synchrotrons in the world



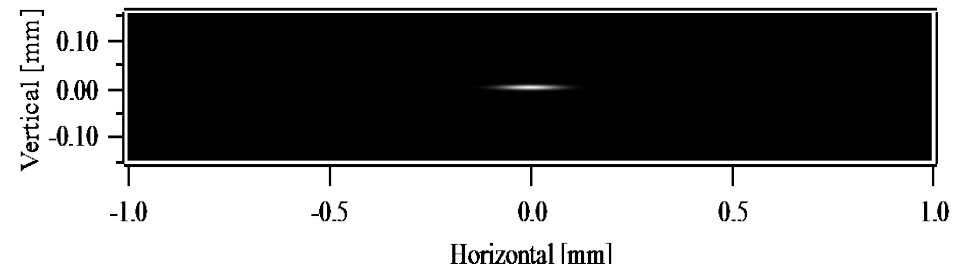
Present

Middle of ID straight

High Beta ~ parallel beam and large source size



Low Beta : large horizontal divergence and small source size





ESRF 2017 beamtime allocation breaks all records



2409
proposals
submitted



1022
proposals
allocated
(first time over 1000)



14752
shifts
allocated
118 016 hours

13.5 years of beam time every year

A world landmark for Science

- 44 beamlines
- Leader in scientific output: almost 2 000 publications/year and more than 32 500 publications since 1994
- Leader in number of users: ~7 000 user visits/year, more than 10 000 individual users in the last three years
- 4 Nobel Prizes for 5 ESRF users



Brian Kobilka,
Shared 2012 GPCR

**ESRF today: the world's most
performing and brilliant
“third-generation” light source**

EPN SCIENCE CAMPUS : A UNIQUE SITE FOR RESEARCH AND INNOVATION



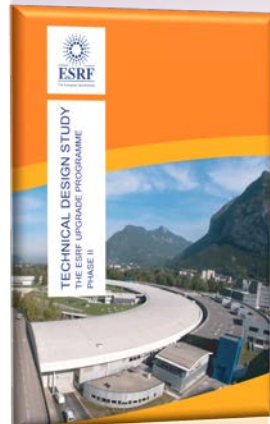
- +500 scientists in the Campus
- 3 European Organisations, Members of EIROFORUM, and IBS – a French Institute for Structural Biology (CEA-CNRS-University Grenoble-Alpes)



ESRF SCIENCE Programme: New and better Science



Purple
Book
January
2008

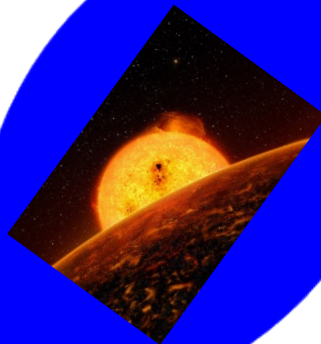


Orange
Book
January
2015

Pump-and-Probe
Experiments and
Time-resolved
Science



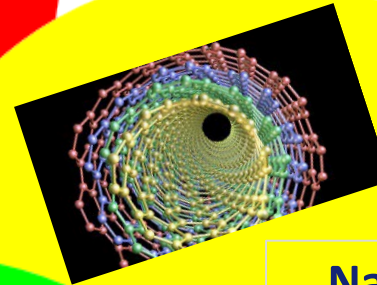
Science
at Extreme
Conditions



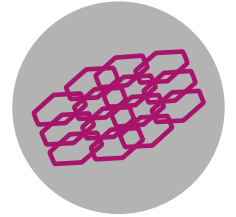
X-ray Imaging
Science



Nano-Science
And
Nano-Technology



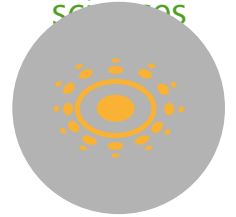
Structural and
Functional Biology
And Soft Matter



New and
innovative
materials



Health &
life
sciences



Energy and
Environment

Purple
Book
January
2008



ESRF UPGRADE PHASE I
180 M€ (2009-2015):
ESFRI ROADMAP 2006-2016

- 19 new beamlines, many specialised on *nano-science*
- New user support facilities
- Study for a revolutionary new storage ring

➤ **Constructing a suite of new and upgraded instruments dedicated to explore matter with nanometric resolution**



THE NEW HIGH THROUGHPUT MX BEAMLINES – A NEW LEVEL OF AUTOMATION

ExiMX Extended ISPyB for MX_{BETA}

Version: 5.5.0.7
Released: 20180426

Home Shipment Prepare Experiment Data Explorer Manager Help SMIS search by protein acronym Log out MX415@leonard

MX415

15-05-2018 21:23:29
/data/visitor/mx415/d29/20180515/RAV/VMTON/VMTON-MtOnpos2

Summary Beamline Parameters Data Collections 1 Sample Last Collect Results 20 Workflow

Workflow	Res. (corner)	2.50 Å (1.81 Å)	P 41 21 2	Completeness	Res.	Rmerge
Protein	VMTON	En. (Wave.)	12.800 keV (0.9686 Å)	Overall	100.0-3.1	15.7
Sample	MtOnpos2	Omega range	0.05 °	Inner	100.0-13.8	3.7
Prefix	VMTON-MtOnpos2_vr1	Omega start (total)	116.00 ° (100°)	Outer	3.17-3.08	104.5
Run #	1	Exposure Time	0.037 s			
# Images (Total)	2000 (2000)	Flux start	1.25e+11 ph/sec			
Transmission	12.0 %	Flux end	7.97e+10 ph/sec			

Comments:

Characterization 15-05-2018 21:20:45
/data/visitor/mx415/d29/20180515/RAV/VMTON/VMTON-MtOnpos2

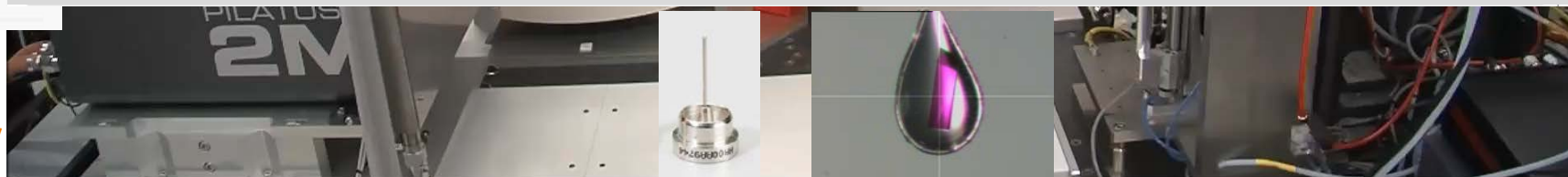
Summary Beamline Parameters Data Collections 1 Sample Last Collect Results Workflow 1

Workflow	Res. (corner)	1.70 Å (1.31 Å)	Indexed	Mosaicity	2.15
Protein	VMTON	En. (Wave.)	12.800 keV (0.9686 Å)	Space Group	P4
Sample	MtOnpos2	Omega range	1.00 °	Rank. Res.	2.69 Å
Prefix	ref-VMTON-MtOnpos2	Omega start	100.15 °	Osc. start (total)	° (73 °)
Run #	2	Exposure Time	0.037 s	Images	1460
# Images (Total)	2 (2)	Flux start	1.67e+12 ph/sec	Osc. range	0.05 °
Transmission	100.0 %	Flux end	1.67e+12 ph/sec	Transmission	12.0 %

3D View: Structure | Electron Density | Ligand Interaction

Standalone Viewers
Protein Workshop | Ligand Explorer

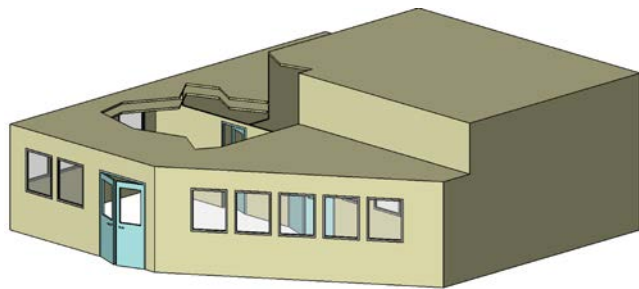
~12% of academic data collection done remotely or by mail-in, and ~90% for industry



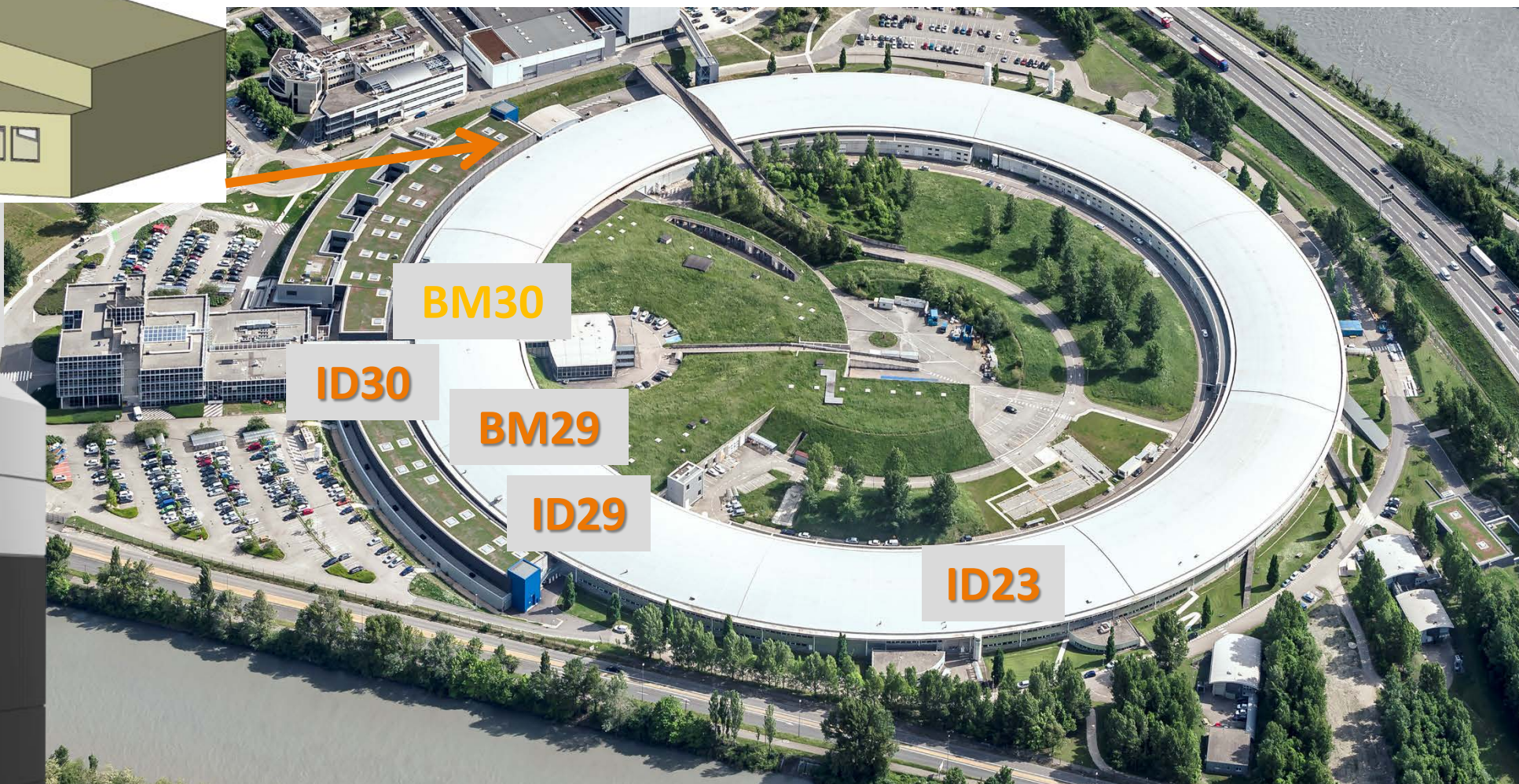
Over the last ~3 years, structural biology activity at the ESRF has seen:

- > 8300 users (>800 proprietary research)
- > 500 high impact factor (IF > 9) peer-review publications
- > 2600 PDB depositions

THE MX BEAMLINES AND NEW HIGH CRYO-ELECTRON MICROSCOPY PLATFORM AT THE ESRF



CM01
cryoEM



Titan Krios G2 – Open to
users since November 2017

Cryo-EM at the ESRF

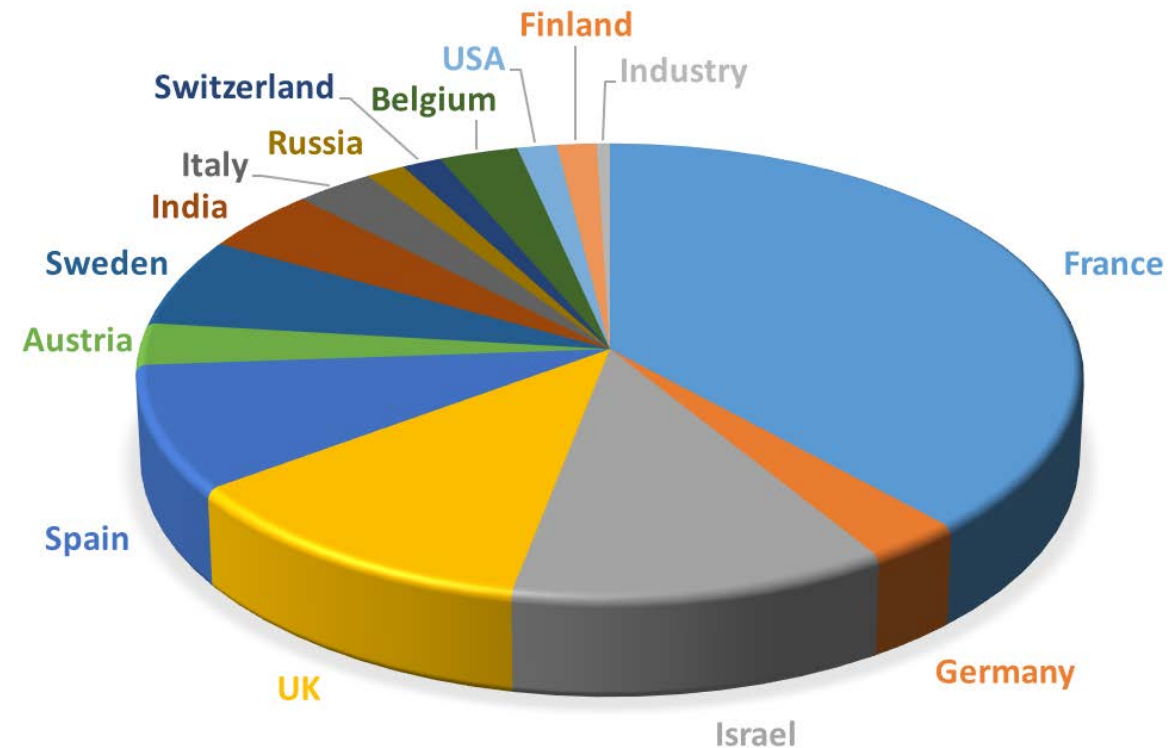


Excellent science being published



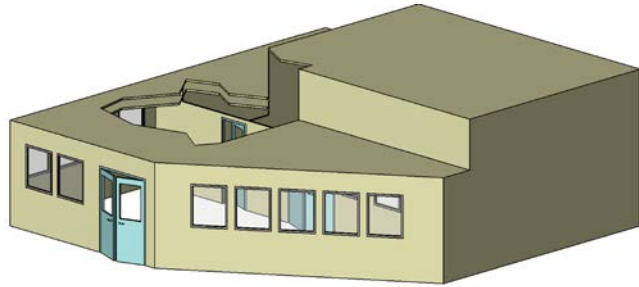
66 user experiments (602 shifts – 200 days – 3 day/exp)
1 industrial mail-in experiment

- A state-of-the-art cryo-EM platform open to structural biology scientists from all over the world
- Time provided on *Scientific Excellence* basis by the ESRF Peer-Review System
- ~5 000 hours/year
- Full ESRF access programme applies:
OPEN TO USERS SINCE 11 – 2017



24/11/2017 – 09/12/2018

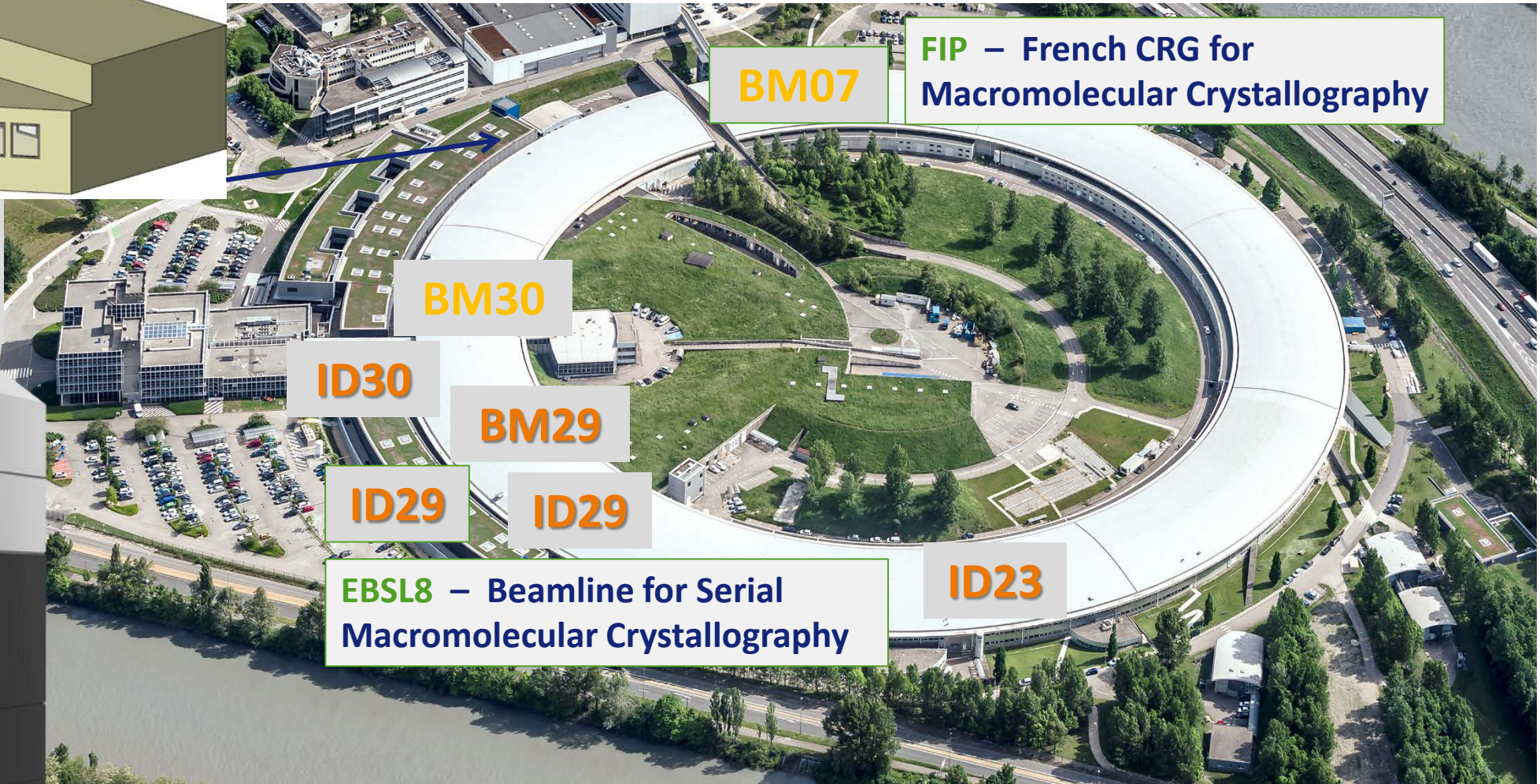
THE MX BEAMLINES AND NEW HIGH CRYO-ELECTRON MICROSCOPY PLATFORM AT THE ESRF



CM01
cryoEM



Titan Krios G2 – Open to
users since November 2017



BM07

FIP – French CRG for
Macromolecular Crystallography

BM30

ID30

BM29

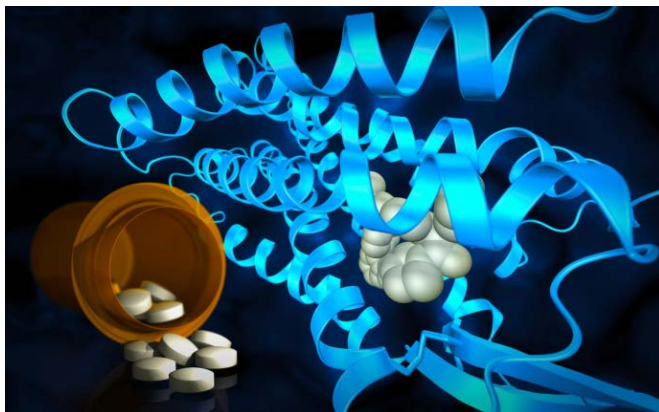
ID29

ID29

EBSL8 – Beamline for Serial
Macromolecular Crystallography

ID23

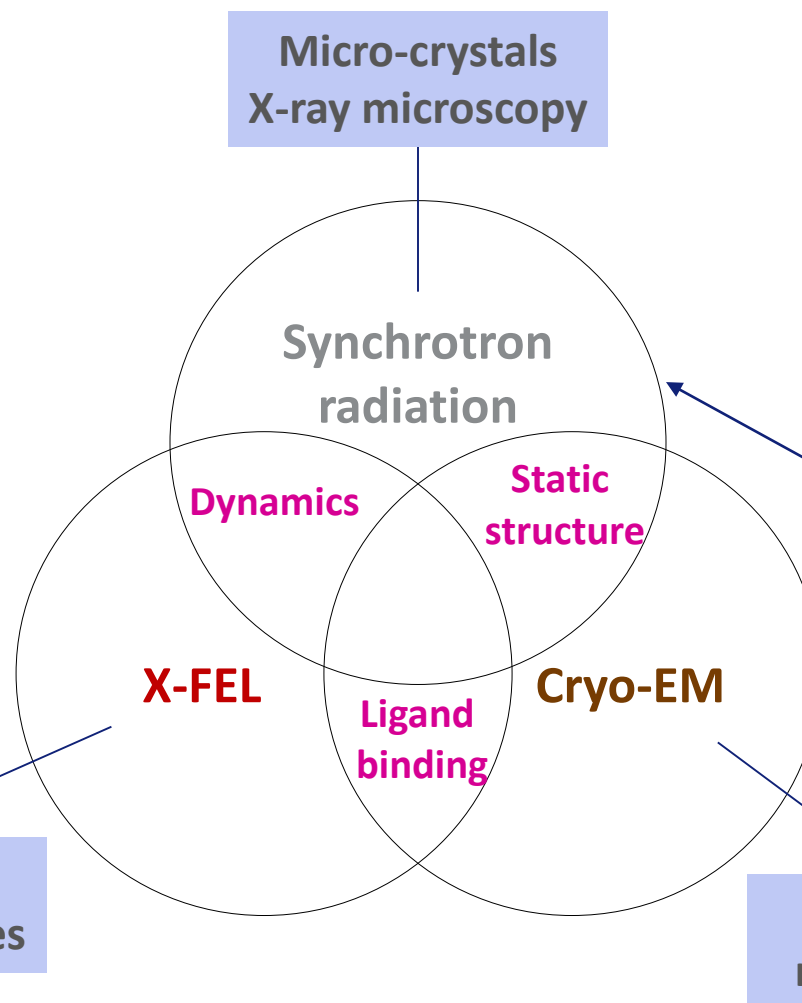
Structural Biology with X-rays and electrons



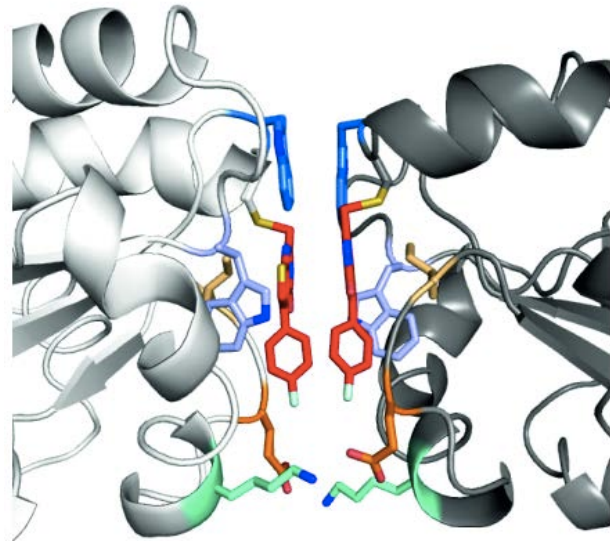
“Revealing molecular structures can show where drugs interact with receptors. These help in designing medicines of the future.”

Greg Stewart/SLAC National Accelerator Laboratory;
<https://phys.org/news/2017-04-x-ray-reveals-long-sought-insights-potential.html>

From molecules to drugs



ESRF Strategy:
State-of-the-art
Facilities for
High throughput and
serial-crystallography
Cryo-microscopy
User Platform



The perfect dimer:
Crystallographically
observed inhibitor-
mediated dimerization
interface.

Credits: Wagner, A.

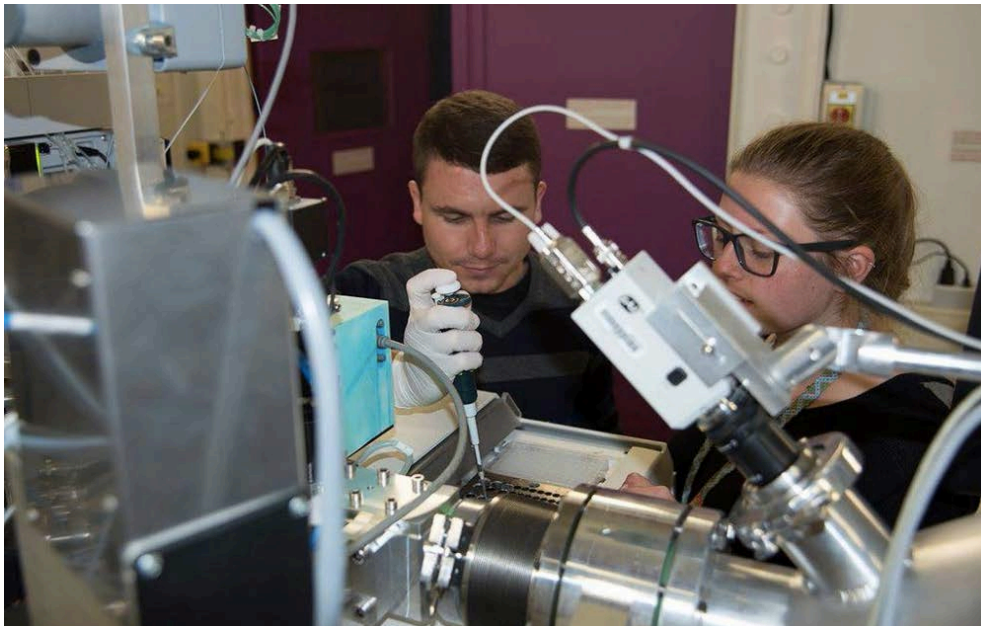
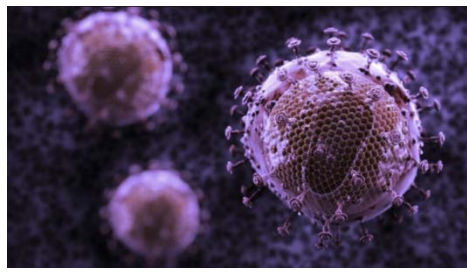
MX + bioSAXS

Structural biology: how synchrotron techniques help to address health diseases

- **As an example: studies on sleeping sickness**
- Human African trypanosomiasis (HAT), also known as sleeping sickness, is a major cause of mortality in Africa. Current therapy has unacceptable side-effects with an overall mortality of 5%.
- **Several teams of scientists have used ESRF MX beamlines to discover how inhibitors against essential proteins of the parasite which causes African sleeping sickness works.**
- **These studies could help in the future design of drugs combatting this disease.**
- *Inhibitor-induced dimerization of an essential oxidoreductase from African Trypanosomes, Angew. Chem. Int. Ed. Engl. (2019) (ESRF ID29).*
- *Inhibitors of PEX14 disrupt protein import into glycosomes and kill Trypanosoma parasites, Science (2017) (ID30B)*

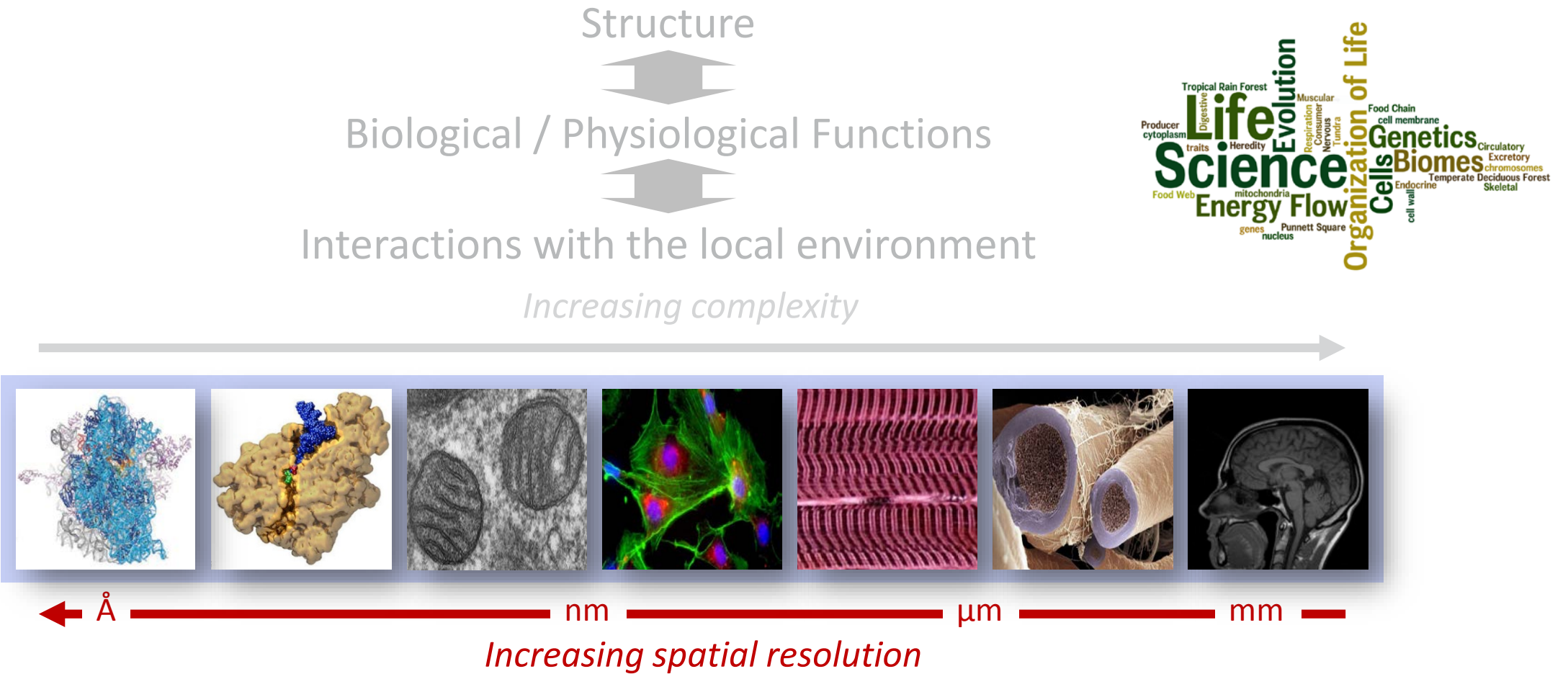


PROTEA
support



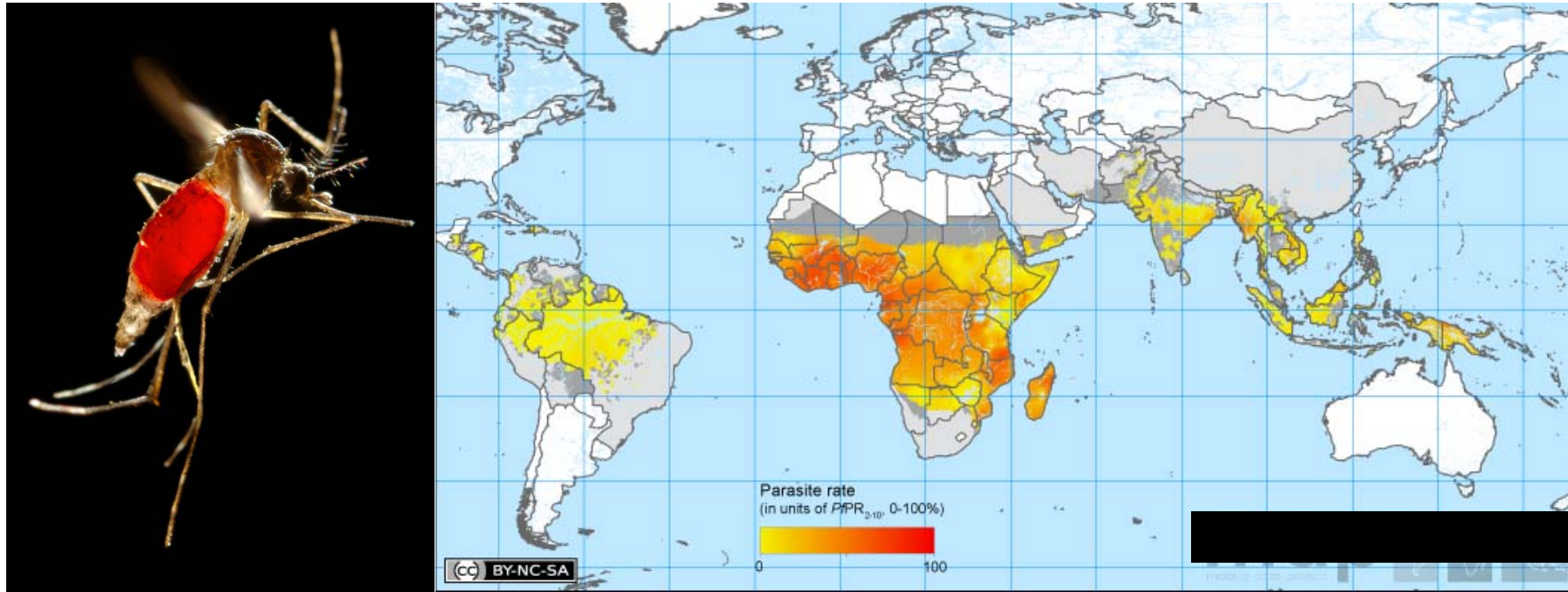
2015-2016: a fruitful collaboration on Health through the PROTEA grant

- The South Africa/France Protea joint call were created to develop relationship between French and South African scientific communities through joint research.
- **Topic: “Structural characterisation of macromolecular protein and DNA complexes in Malaria and HIV”**
 - **Malaria: research on life cycle and infection**
 - **HIV: research on infection mechanisms**
- 20k€ dedicated to researcher mobility between ESRF, ILL and Wits University
- **The results:** the mobility of 7 young researchers (3 from France, 4 from South Africa) and 5 senior staff



- Structure & morphology
- Elemental & chemical composition
- Dynamics

Sub-cellular label-free localisation of anti-malarian drugs



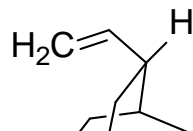
Malaria:

CJL Murray et al., Lancet 2012; 379: 413

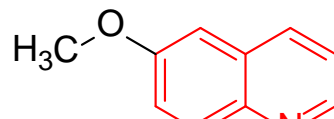
- ~ 400 million clinical cases per year
- ~ 1.2 million deaths (mostly children under five)
- Resistance of main parasite to existing drugs
- Essential to constantly develop new anti-malarial drugs



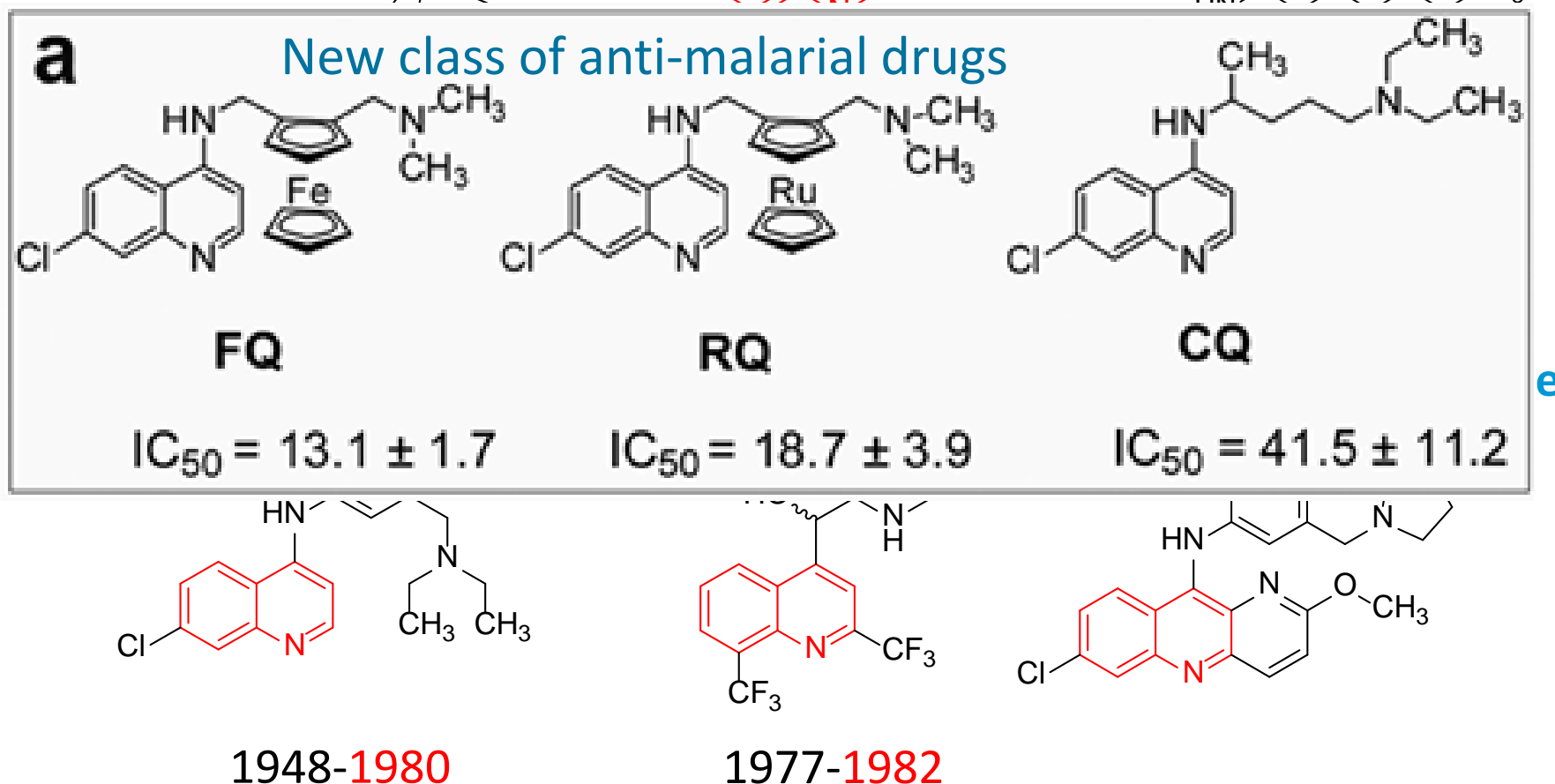
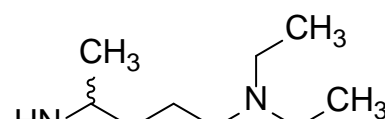
Quinine



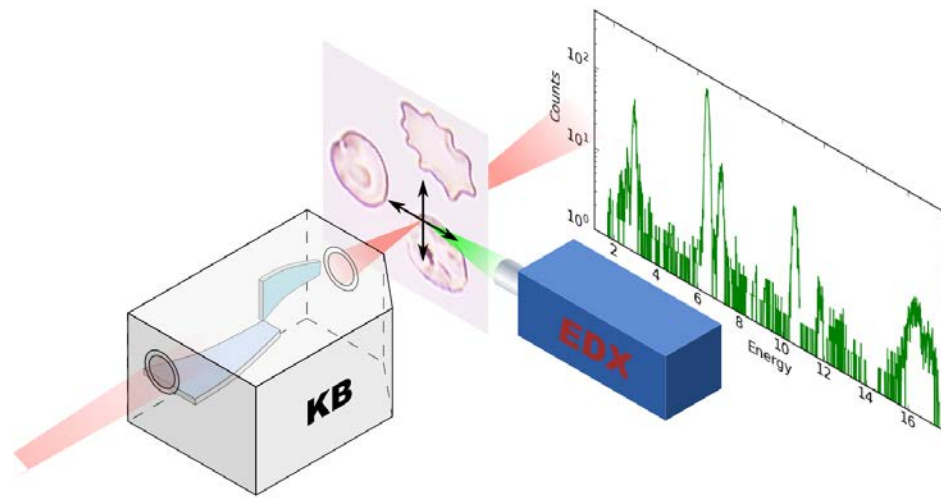
Primaquine



Chloroquine



Synchrotron *nano*-probe techniques contribute to the localisation of new drugs and to the elucidation of their action mechanisms.



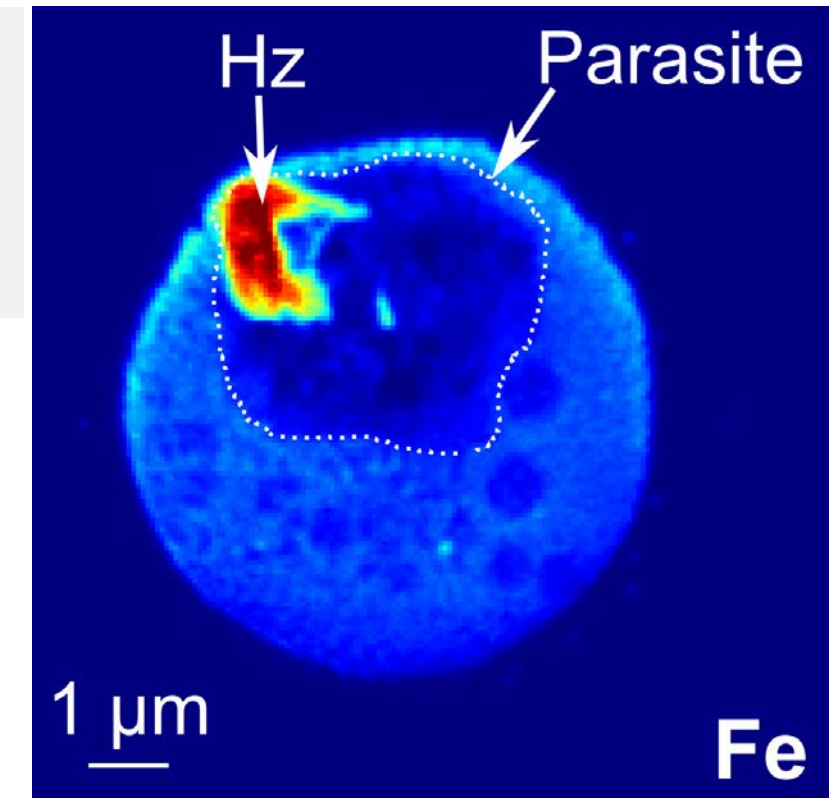
Iron from haem groups sequestered as an in-vivo Haemozoin (Hz) crystal

ESRF *nano*-probe ID16B

50 nm pixel, flux $\sim 5 \cdot 10^{11}$ ph/s, $E_0 = 17$ keV,

Simultaneous acquisition of the **fluorescence signature of most elements of biological interest**

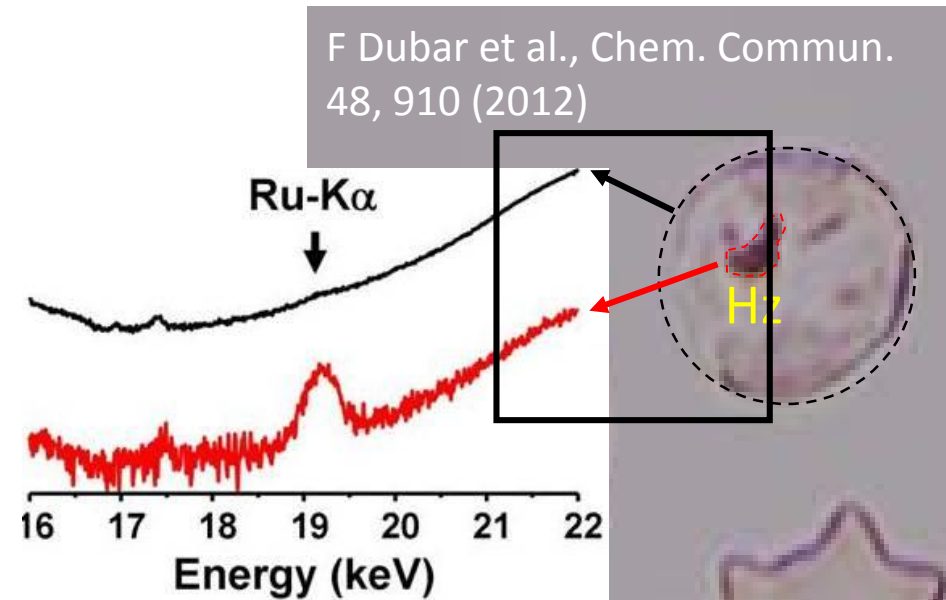
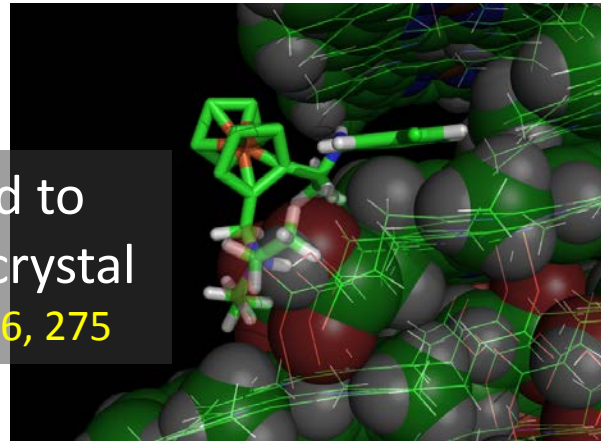
Fe fluorescence
in malaria infected red blood cell



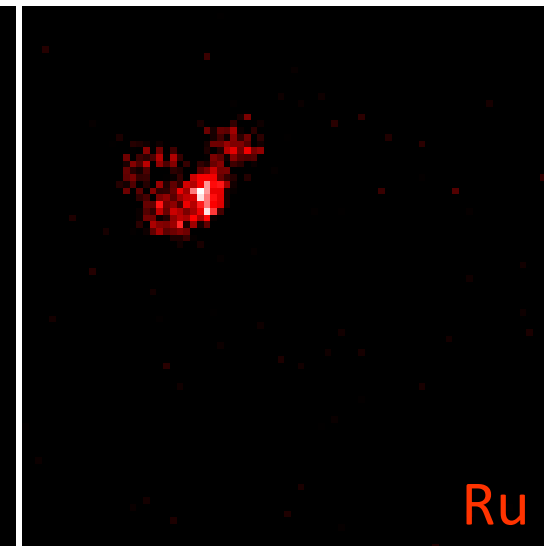
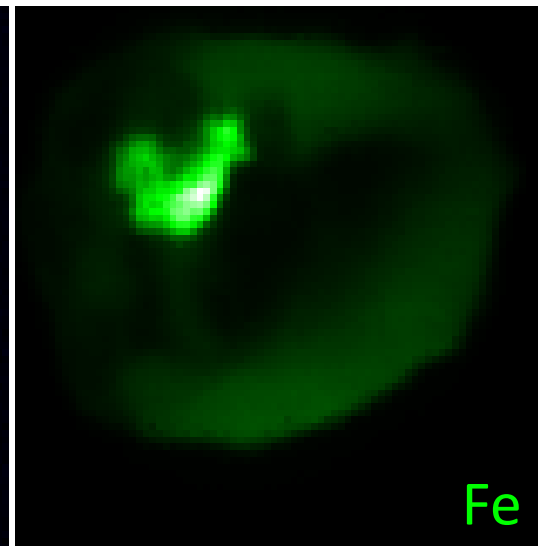
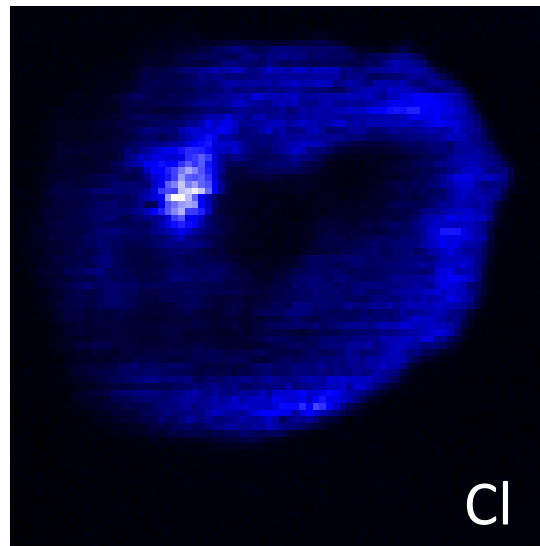
F Dubar et al., Chem. Comm. 48, 910 (2012)

Localisation of a new drug candidate Ruthenoquine (Ferroquine equivalent)

Ferroquine bound to
Haemozoin (Hz) crystal
ACS Chem Biol, 2011, 6, 275



$E_0 = 29$ keV





**AM processes are poorly understood
and simulation models are limited**

Manufacture of complex, high value added components:

- AM built Ti-alloy aerofoils in a aircraft engine XWB-97k test bed engine
- knee replacements



Simulation courtesy
H. Basalto, U.Birm.

High-speed
optical imaging

AM build
chamber

X-ray imaging



Photron



ultra-fast (<10ms) process



optimisation (Ti64 at 50,000fps)

Peter D. Lee et al.
(peter.lee@ucl.ac.uk)

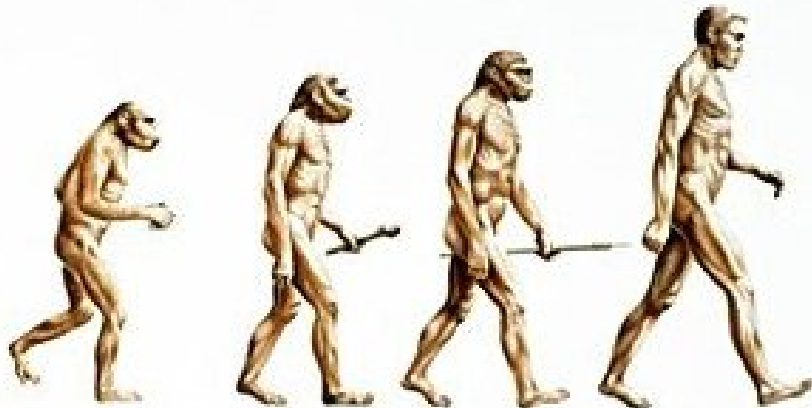
The European Synchrotron



New hominid species (age 1.9 million years) have been discovered in August 2008 in South Africa by Pr. Lee Berger and colleagues.

“Transition” species showing intermediate character between *Australopithecus* and *Homo-Genus*.

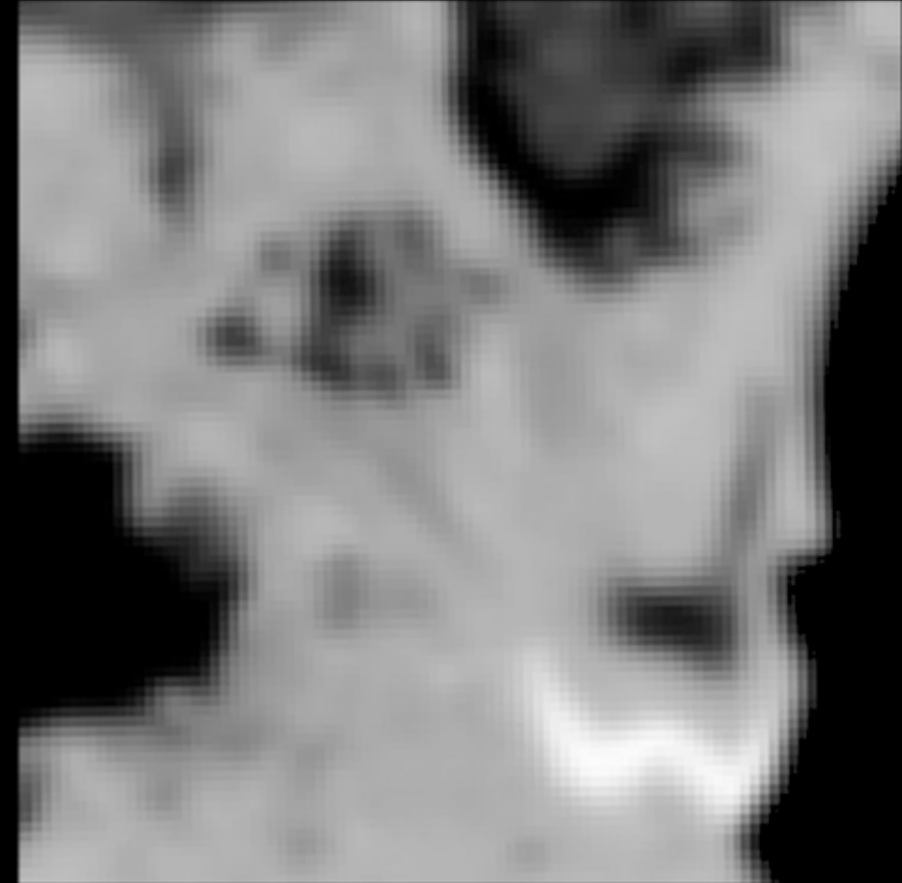
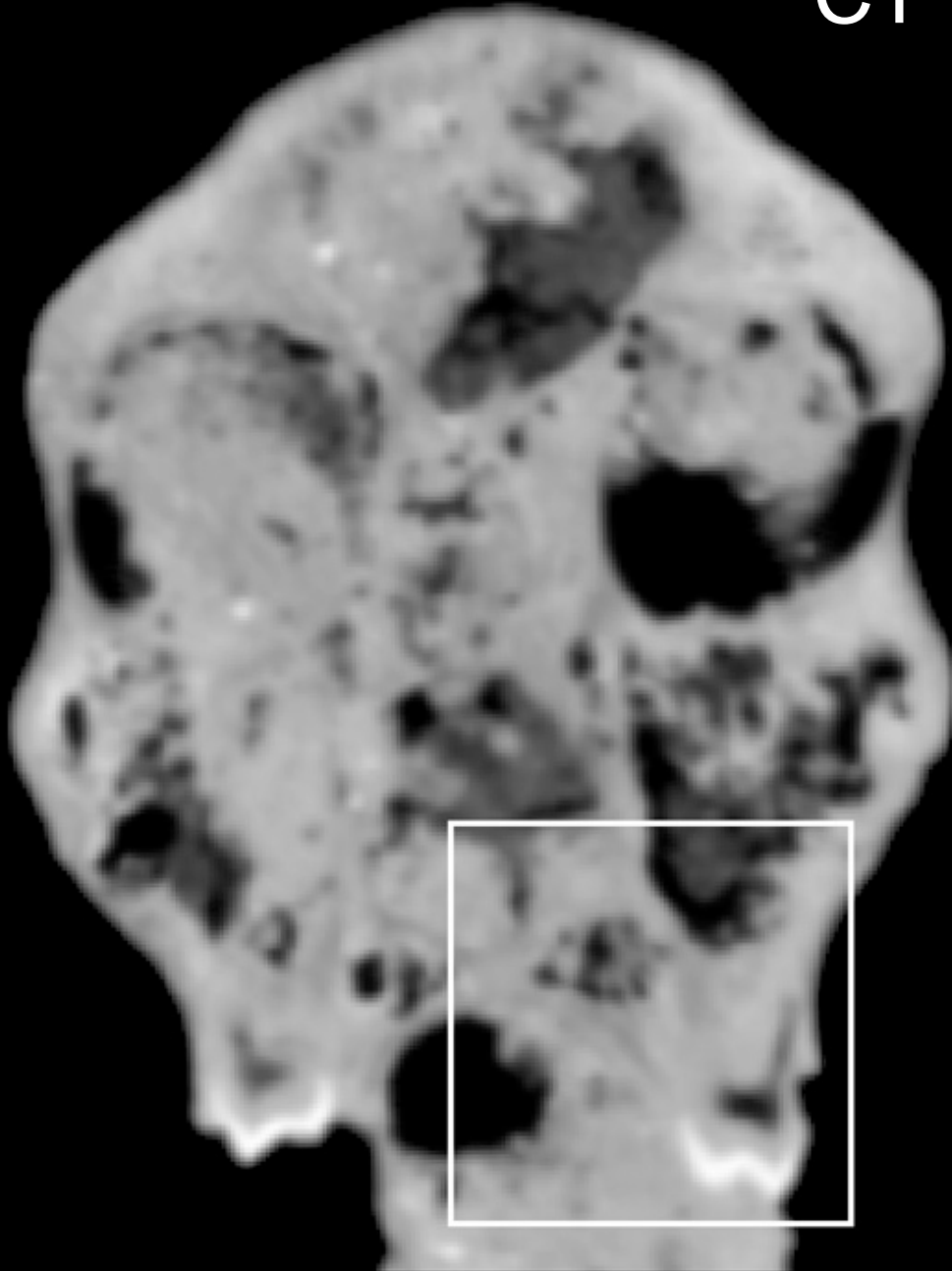
Sediba means "natural spring" or "well" in the Sotho language



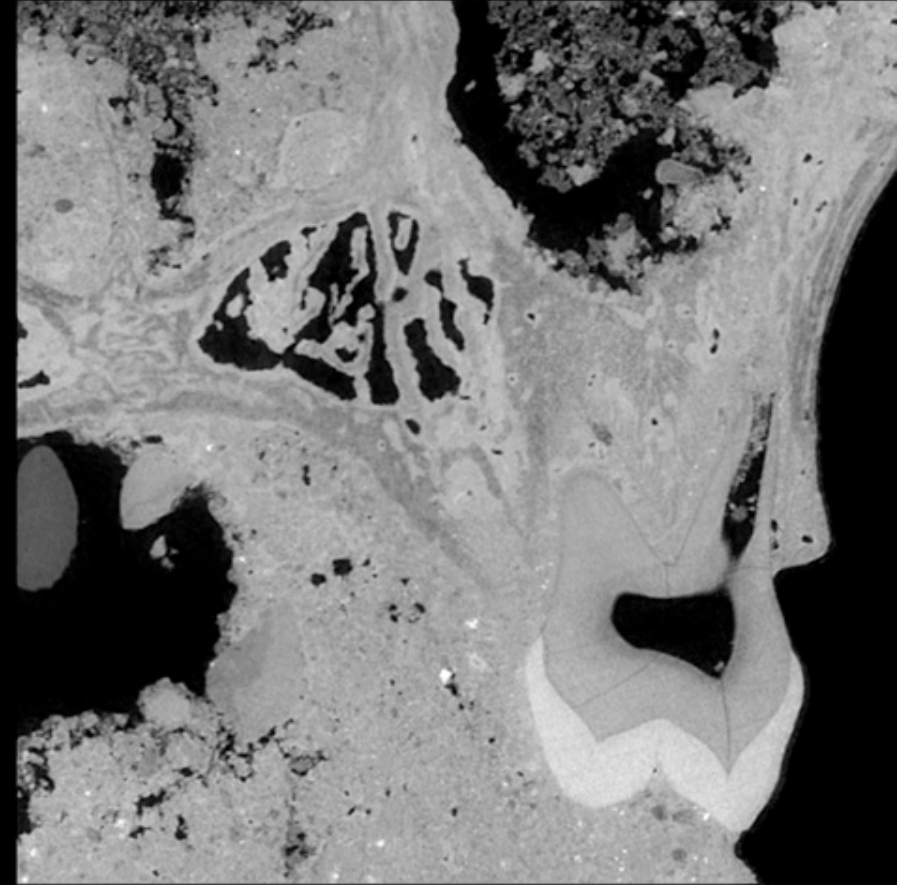
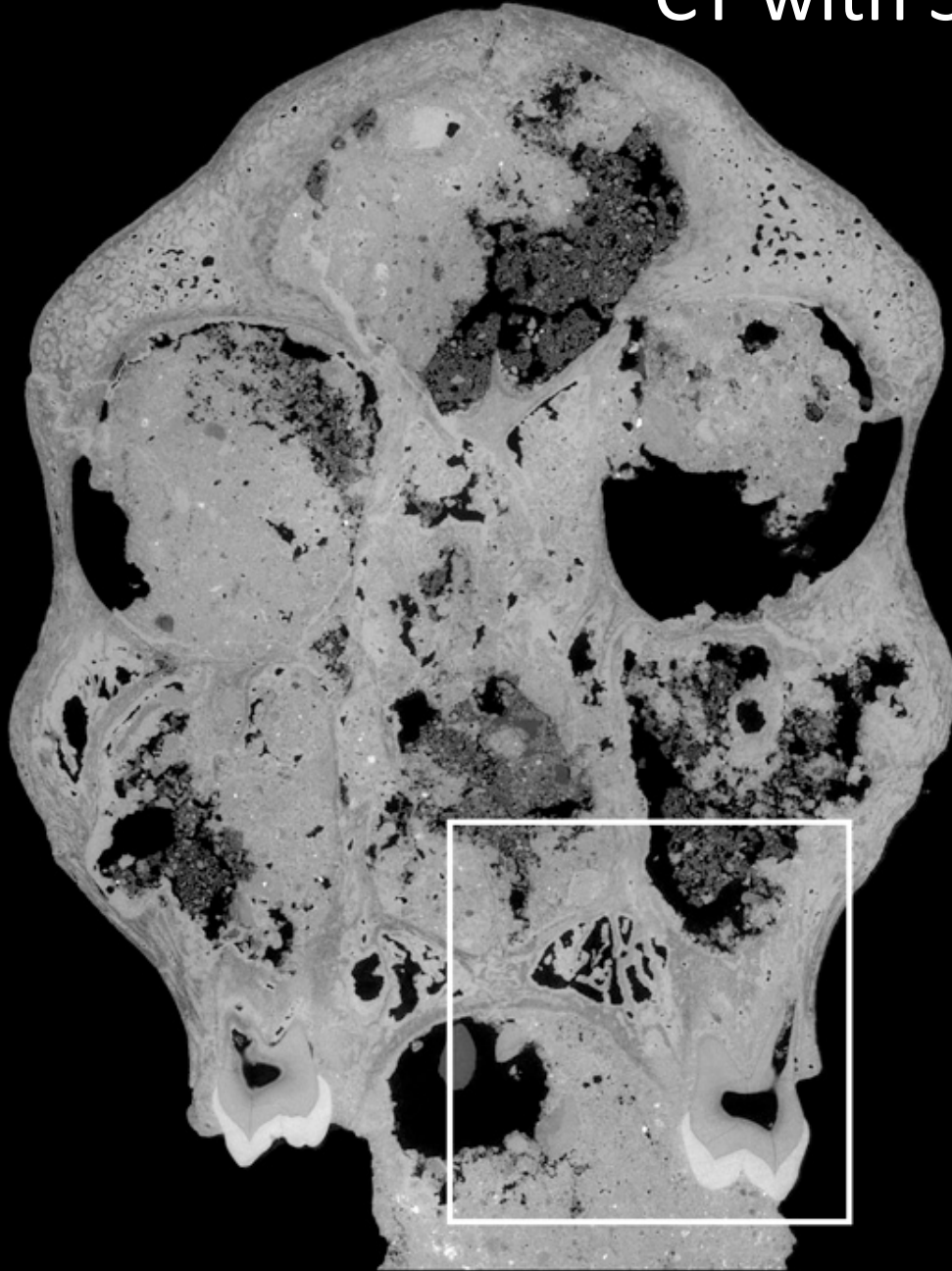
9 April 2010: Four papers in SCIENCE describe the discovery of a new hominid species

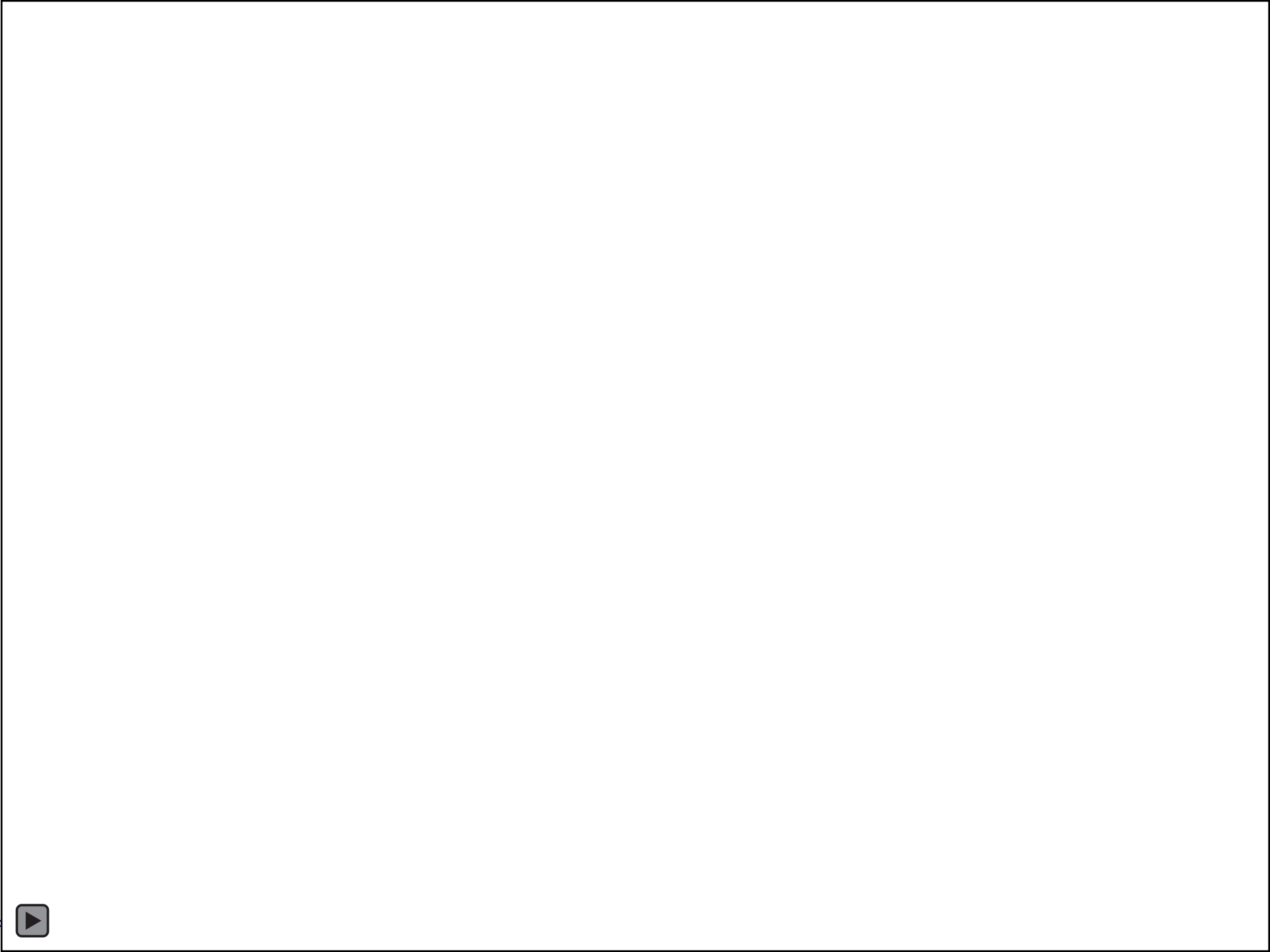


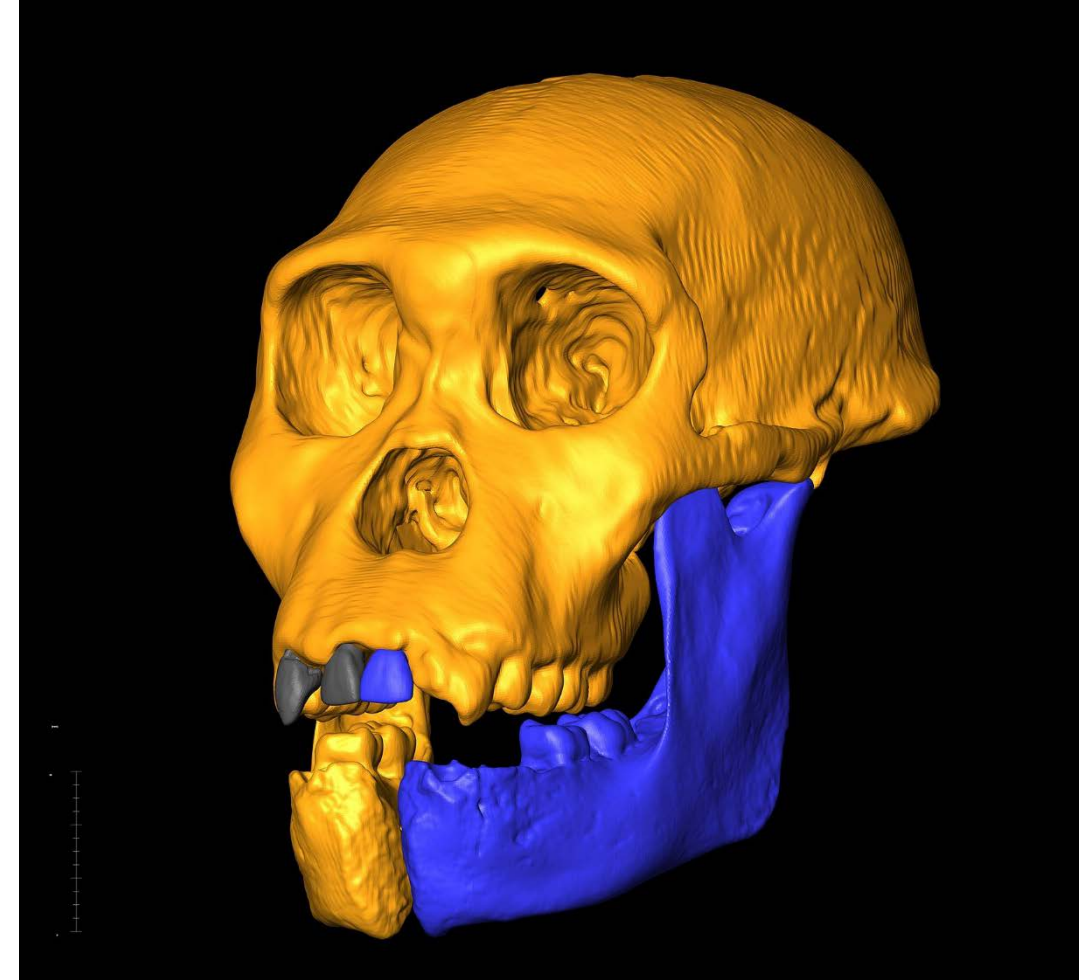
CT with a Hospital Machine



CT with Synchrotron Light at ESRF

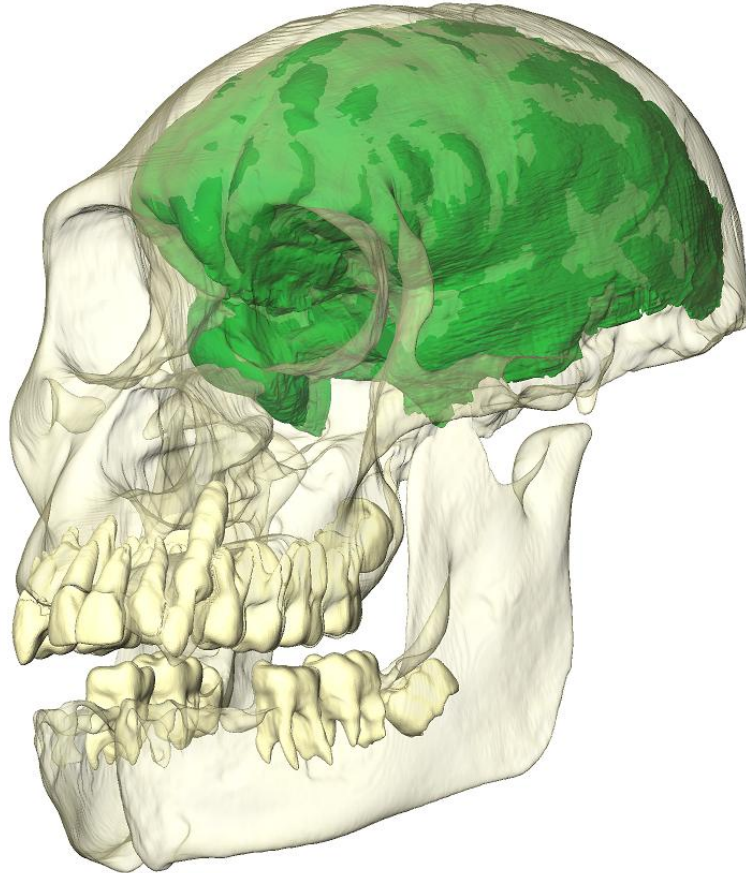






Among many interesting results from a 3D-virtual rendering of the precious fossil: a quantitative measure of brain dimensions and features and a precise reconstruction of missing parts (in blue)

Australopithecus Sediba at the ESRF



9 Sept 2011
Five papers on:
Brain (ESRF)
Hand
Hip bone (pelvis)
Foot and ankle
Exact age



<http://www.esrf.eu/UsersAndScience/Publications/Highlights/2011/imaging/ima7>

"The many very advanced features found in the brain and body ...make it possibly the best candidate ancestor for our genus, the genus Homo."
Lee Berger, Wits U, Johannesburg



Original skeleton of the *A. sediba* holotype MH1,
on display at Maropeng, CRADLE OF HUMANKIND,
South Africa



Purple
Book
January
2008



ESRF UPGRADE PHASE I 180 M€ (2009-2015): ESFRI LANDMARK (2016) IN TIME – WITHIN BUDGET

- 19 new beamlines, many specialised on *nano*-science
- New user support facilities
- Study for a revolutionary new storage ring

- Studying the possibility to construct a new X-ray source with qualitatively increased performances:
- Discovery of a new revolutionary storage ring

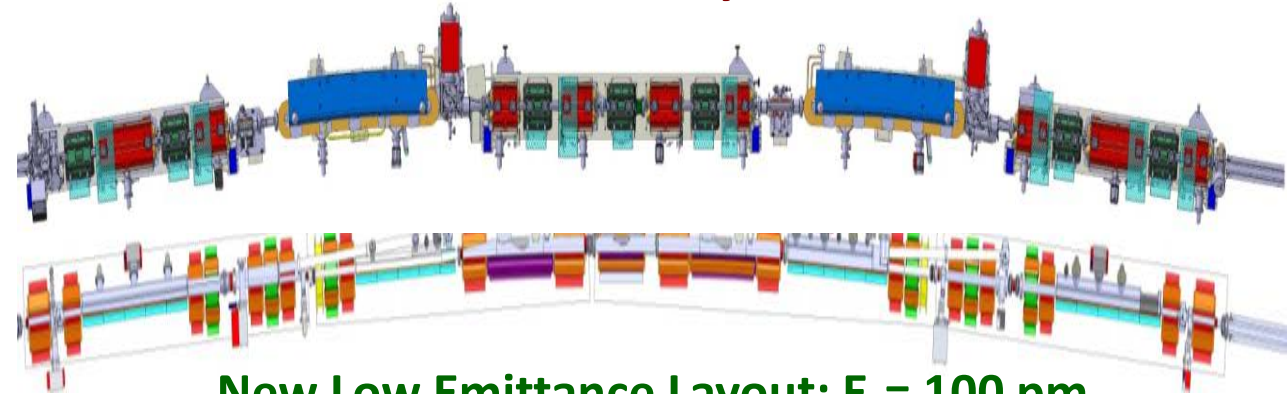


A QUEST FOR A NEW AMBITIOUS STANDARD FOR X-RAY SYNCHROTRON SOURCES

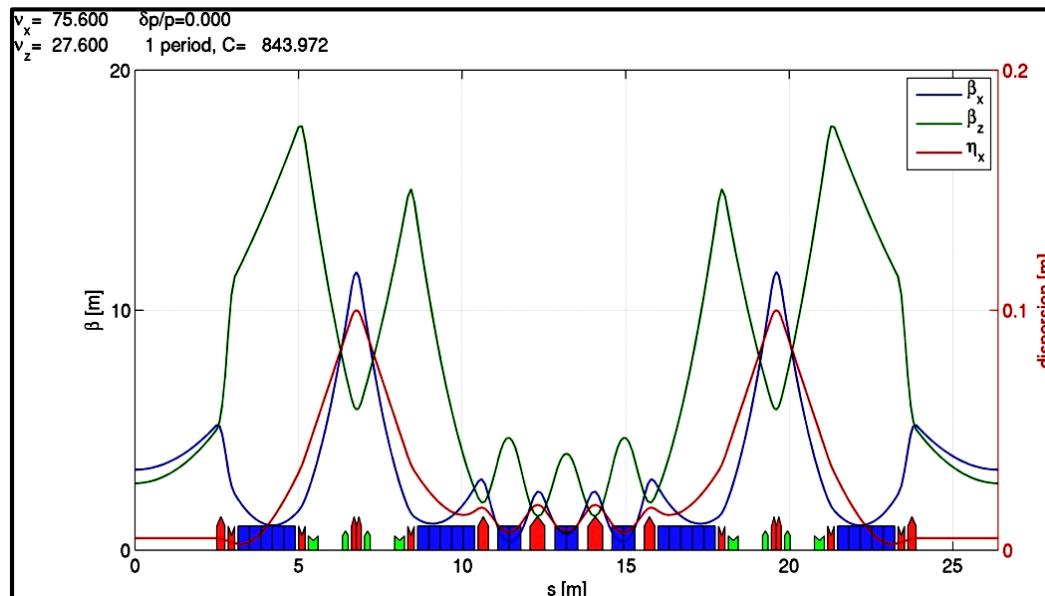
Key Parameters

H7BA lattice
Energy 6 GeV
Current 200 mA
 ε_x 100 pm rad
 ε_z 4 pm rad

Present ESRF Arc Layout: $\varepsilon_x=4\text{nm}$



New Low Emittance Layout: $\varepsilon_x=100\text{pm}$



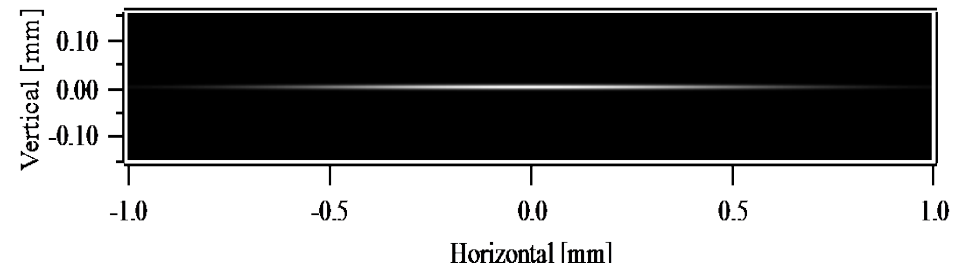
- **Drastic reduction of the horizontal equilibrium emittance**
- Maintain the existing ID straights for the beamlines
- Maintain the existing bending magnet beamline ports
- Preserve time-structure and multibunch - 200 mA Operation Modes
- Keep the present injector complex
- Reuse, as much as possible, the existing hardware (~80%)
- Minimise the energy lost in synchrotron radiation
- Minimise operation costs, particularly wall-plug power
- Limit downtime for installation and commissioning to 20 months

ELECTRON BEAM SIZE AT THE ESRF AND THIRD GENERATION SYNCHROTRON SOURCES

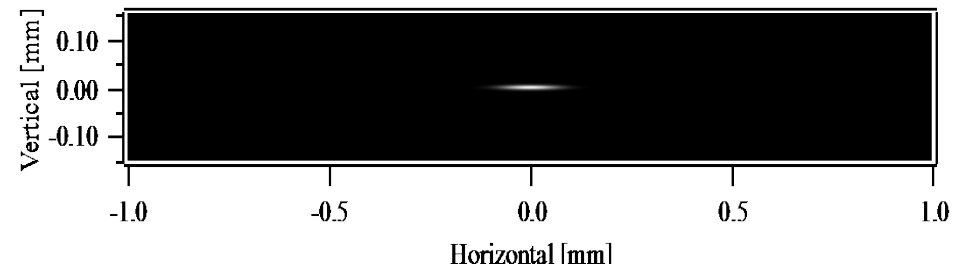
Present

Middle of ID straight

High Beta ~ parallel beam and large source size

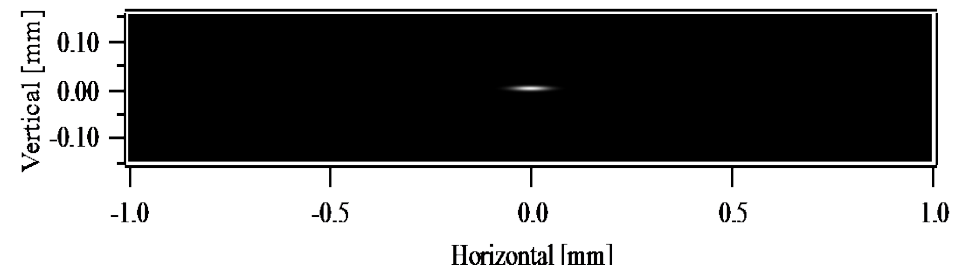


Low Beta : large horizontal divergence and small source size



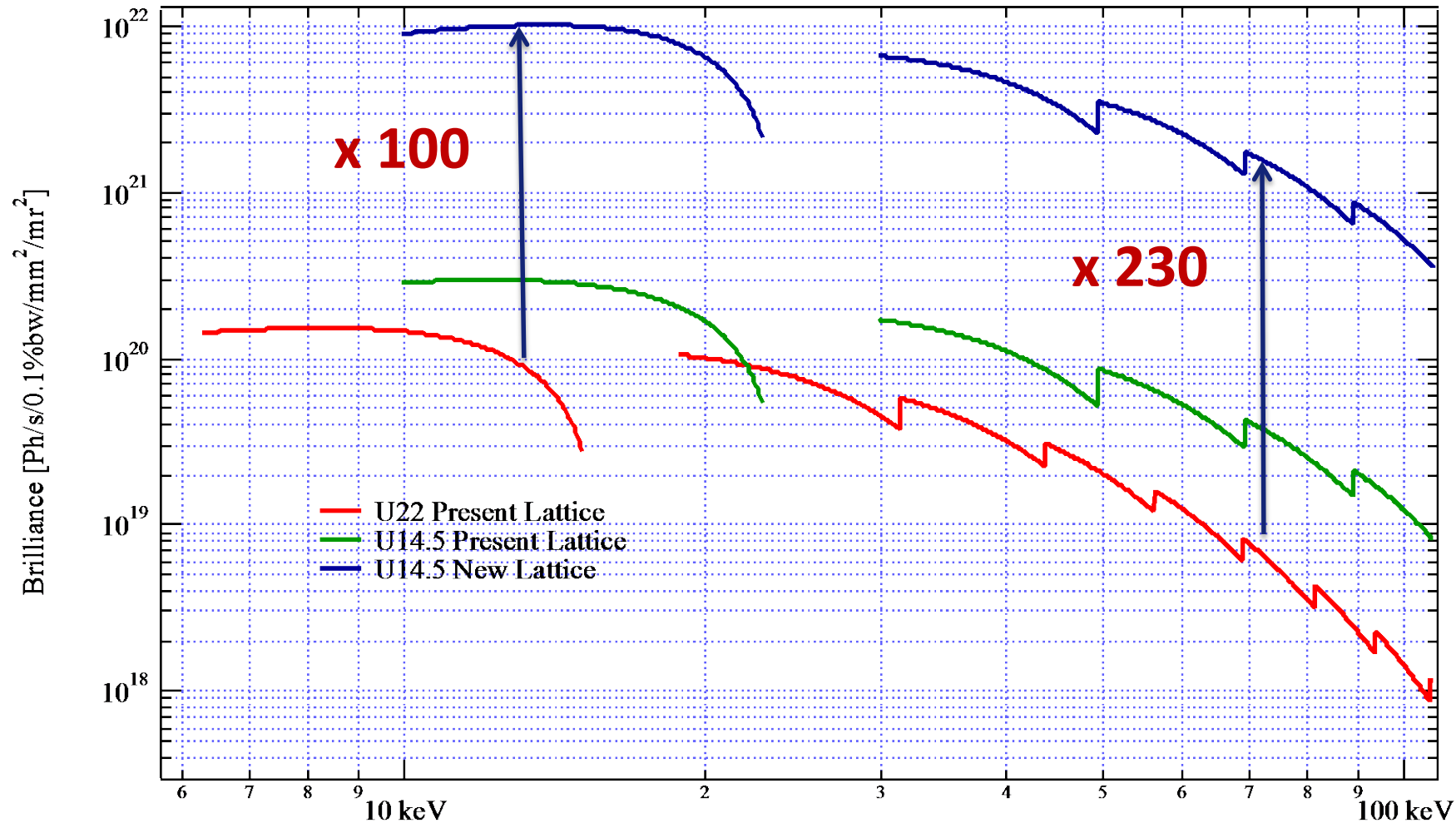
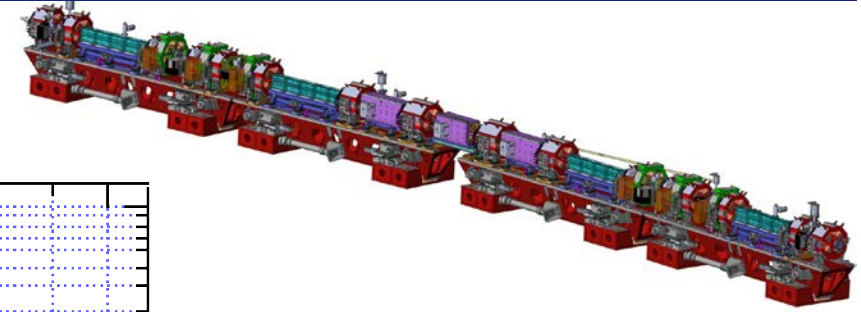
Future

ESRF EBS ~ an even more parallel beam and smaller source size



H7BA LATTICE – SOURCE BRILLIANCE

IVUN22 min. gap 6 mm, $K_{\max}=1.7$
CPMU14.5 min. gap 4 mm, $K_{\max}=1.7$



Key Parameters

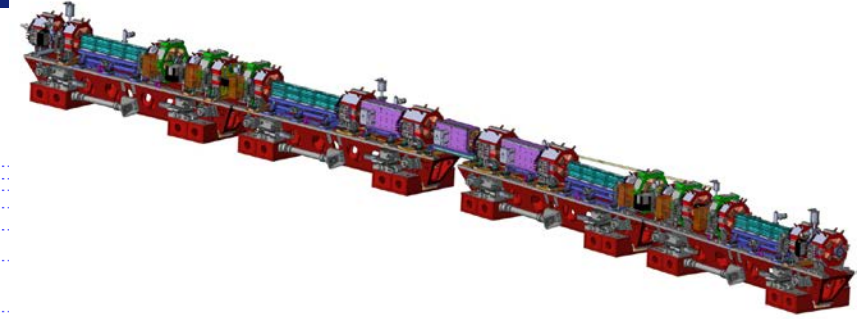
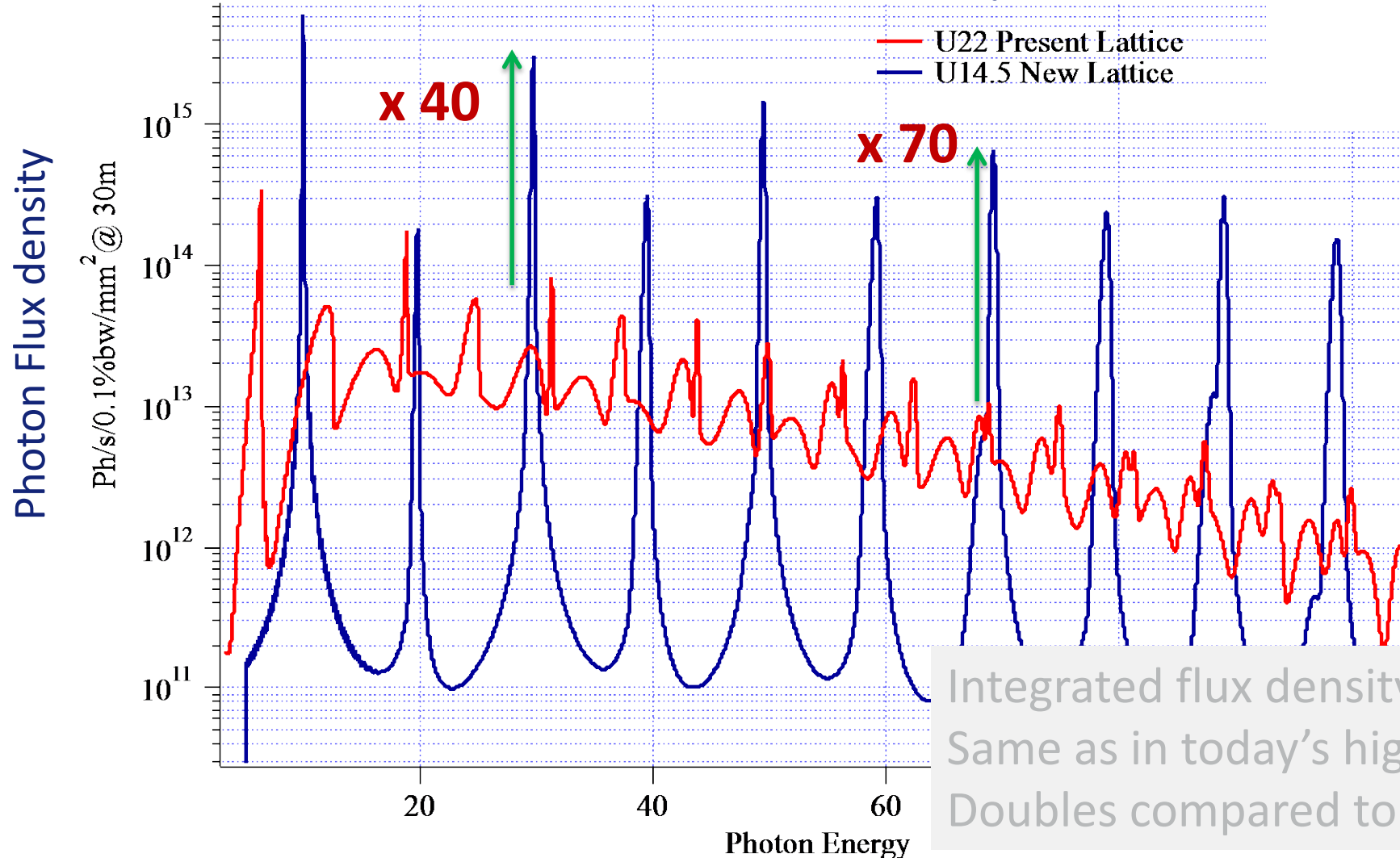
H7BA lattice
Energy 6 GeV
Current 200 mA
 ε_x 100 pm rad
 ε_z 4 pm rad

Photon Energy

H7BA LATTICE – SOURCE PHOTON FLUX DENSITY

IVUN22 min. gap 6 mm, $K_{\max}=1.7$

CPMU14.5 min. gap 4 mm, $K_{\max}=1.7$

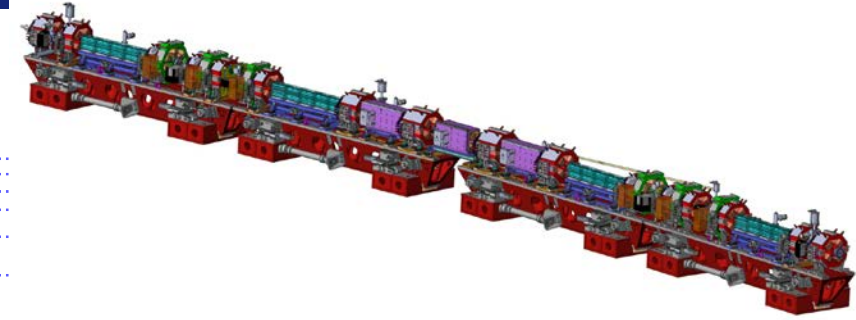
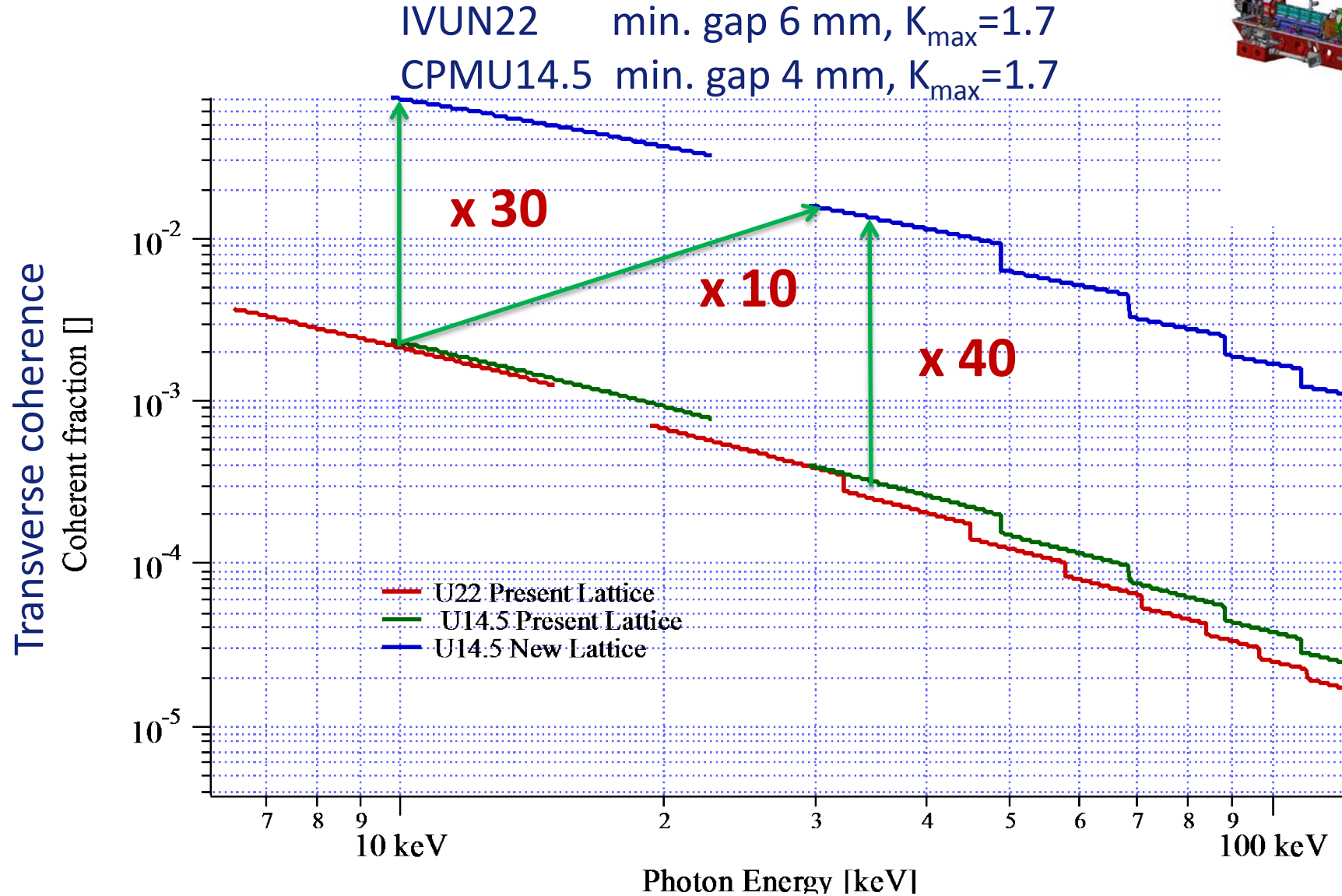


Key Parameters

H7BA lattice
Energy 6 GeV
Current 200 mA
 ϵ_x 100 pm rad
 ϵ_z 4 pm rad

Integrated flux density:
Same as in today's high-beta sections
Doubles compared to today's low beta sections

H7BA LATTICE – SOURCE PHOTON COHERENT FLUX FRACTION



Key Parameters

H7BA lattice
Energy 6 GeV
Current 200 mA
 ε_x 100 pm rad
 ε_z 4 pm rad

ESRF Extremely Brilliant Source

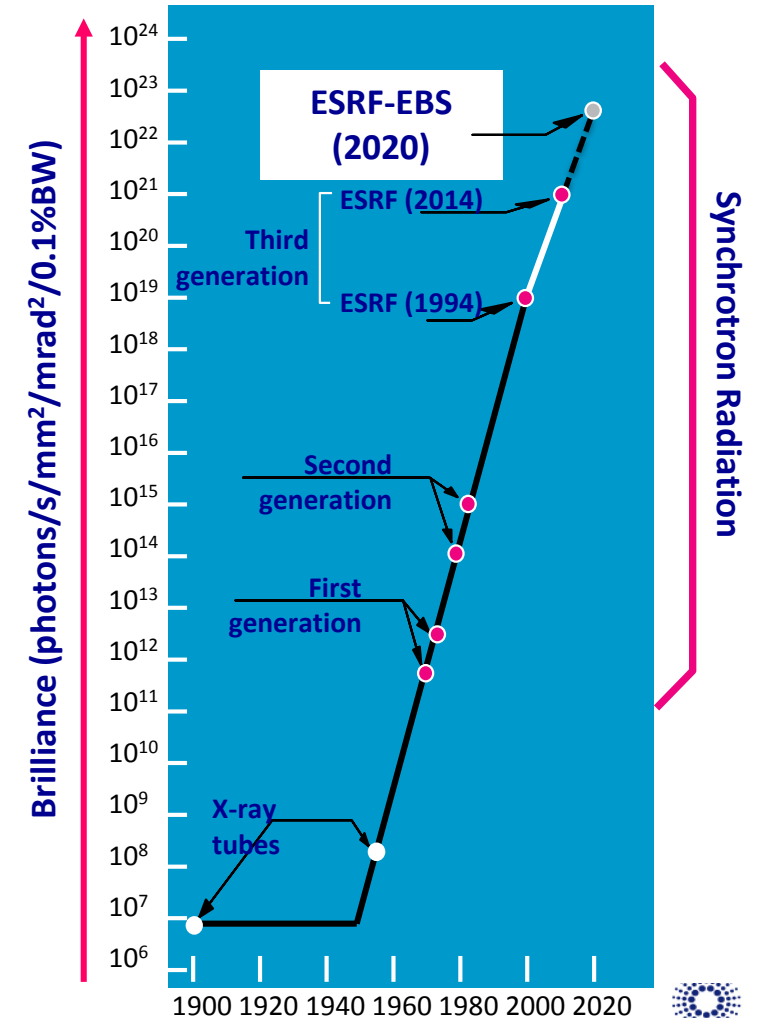
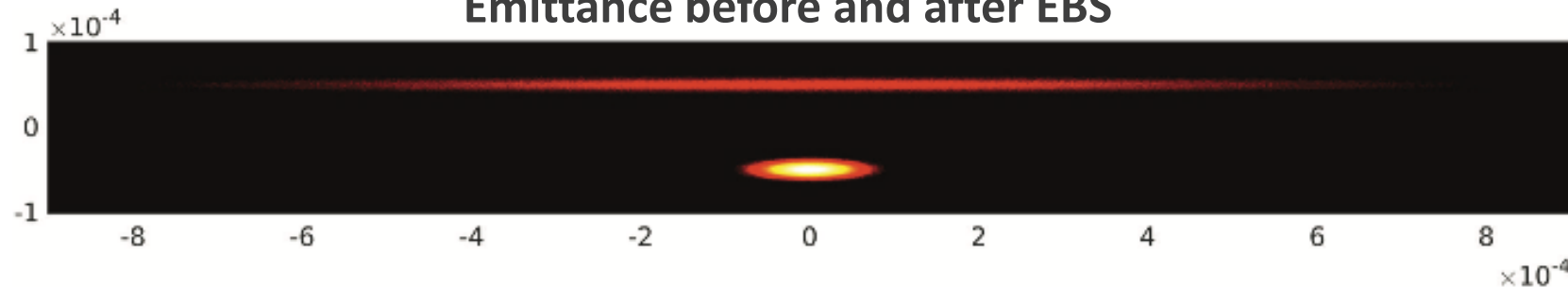
The 1st high-energy 4th-generation synchrotron light source



Pantaleo Raimondi wins the Gersch Budker IPAC17 Prize

For his invention of the “Hybrid Multi Bend Achromat” (HMBA) lattice, which has become the design basis of most future “fourth generation” synchrotron sources in the world

Emittance before and after EBS



ESRF EBS: AN AMBITIOUS NEW STANDARD FOR SYNCHROTRON STORAGE RINGS

Purple
Book
January
2008



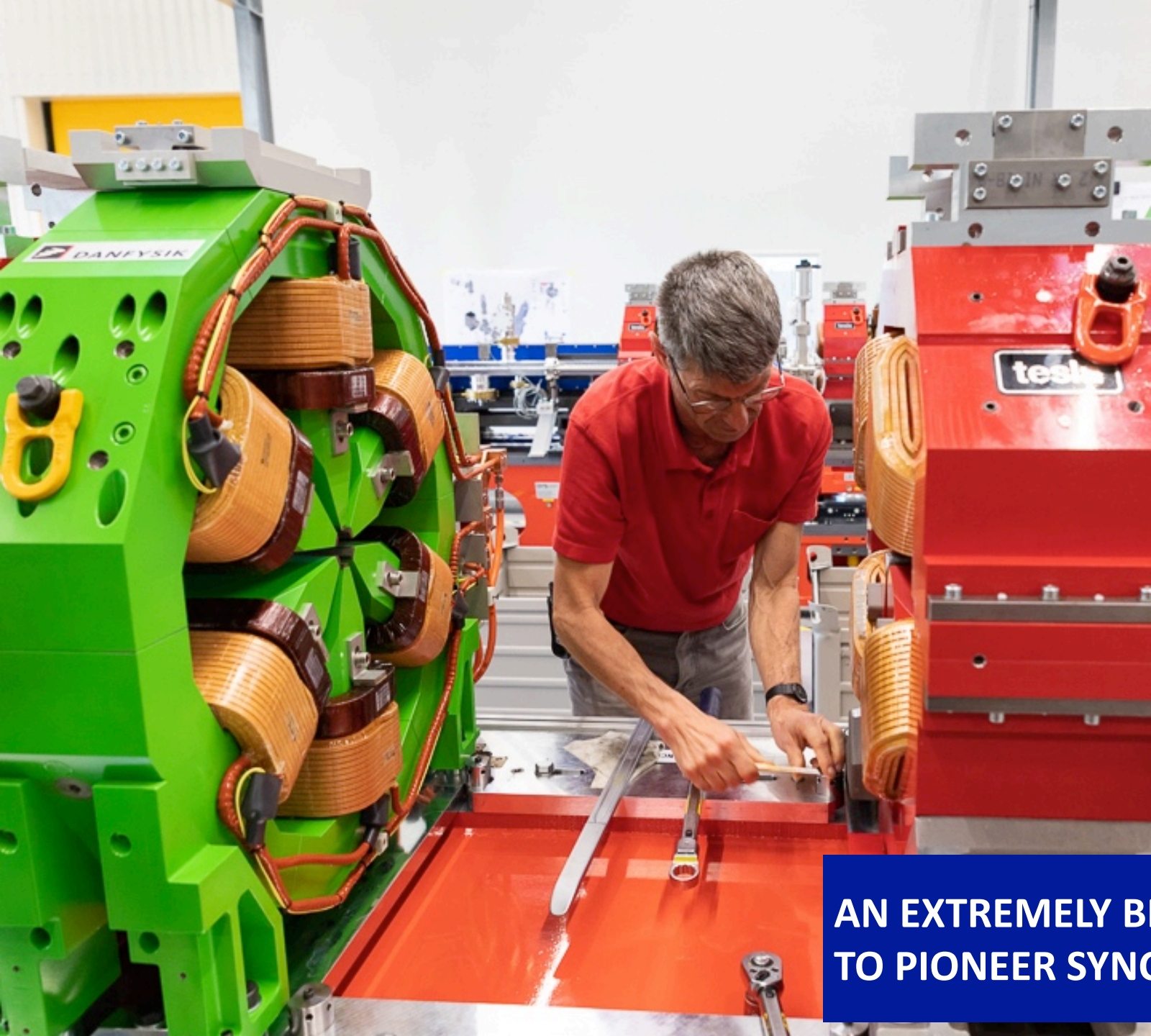
Orange
Book
January
2015

ESRF UPGRADE PHASE I
180 M€ (2009-2015):
ESFRI ROADMAP 2006-2016
ESFRI LANDMARK (2016)
In time – within the budget
- **19 new beamlines**
specialised on nano-science
- Study for a revolutionary
storage ring

ESRF-EBS
Extremely Brilliant Source
150M€ (2015-2022)
ESFRI LANDMARK (2016):

- The 1st high-energy fourth-generation synchrotron
- 4 new flagship beamlines
- Detectors, Instrumentation and Data As A Service

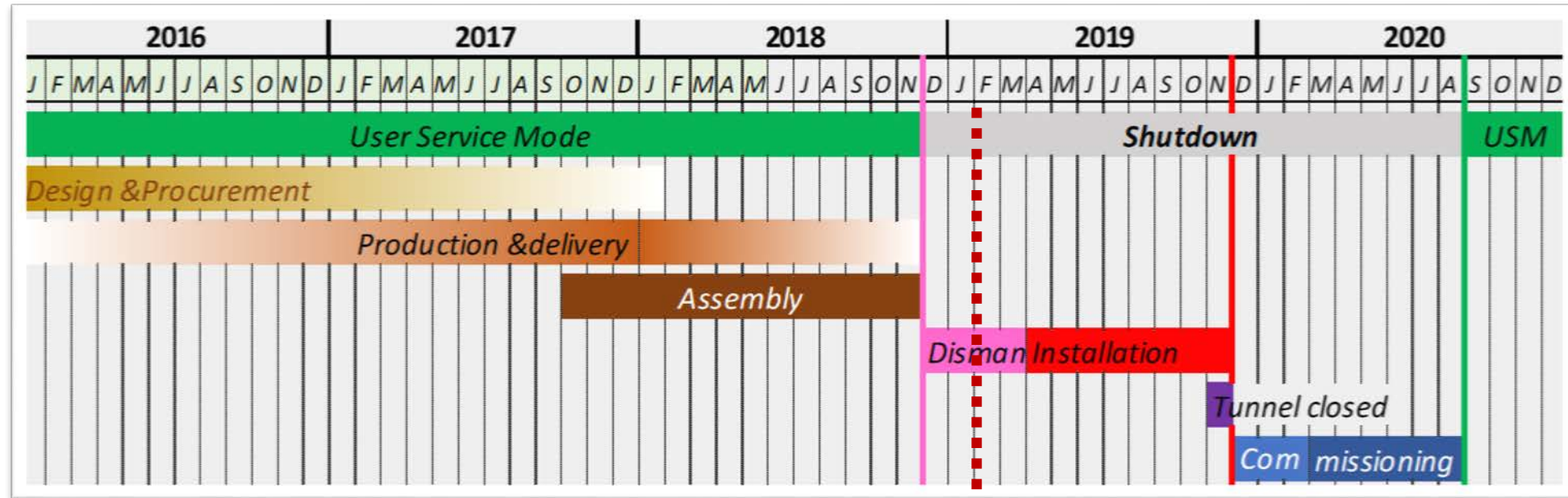




**AN EXTREMELY BRILLIANT SOURCE, EBS,
TO PIONEER SYNCHROTRON SCIENCE**

EBS STORAGE RING: CONSTRUCTION MASTER SCHEDULE

EBS storage ring implementation schedule and beamlines restart



20 October	2017	Start girder assembly (12 months)
10 December	2018	End of USM and Start of Shutdown (20 months)
		Dismantling (3 months) and Installation (8 months)
8 November	2019	Tunnel closed
2 December	2019	Accelerator commissioning (4 months)
March	2020	Beamlines and Accelerator commissioning (5 months)
25 August	2020	Back to USM

EBS STORAGE RING: GIRDER ASSEMBLY IN THE ESRF-01 BUILDING



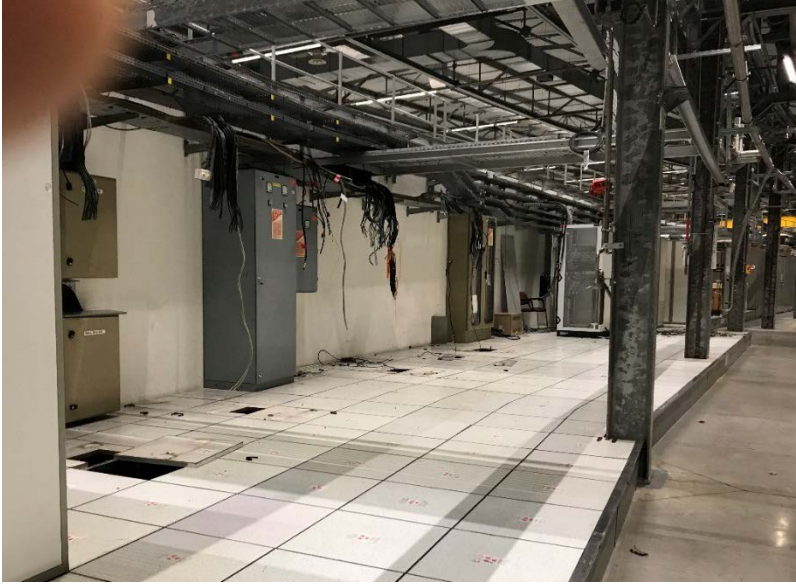
BINP and ESRF colleagues working together in the ESRF-01 building: BINP contract ended 31-10-2018

Assembly of the 129 girders composing the 32 arcs of the new EBS storage ring started in Autumn 2017

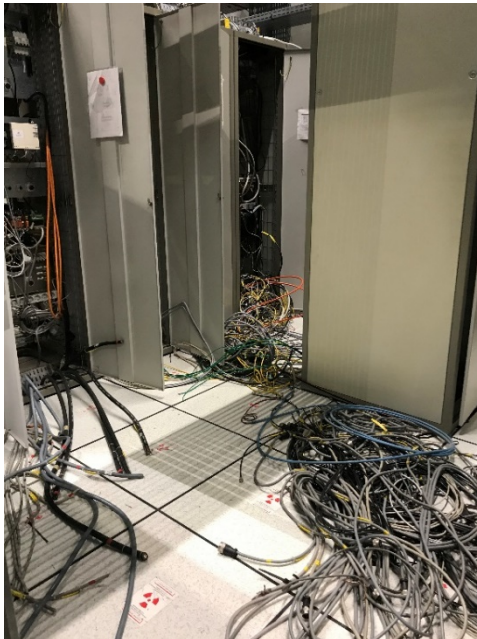
GIRDERS ARE NOW ASSEMBLED AND READY TO BE INSTALLED IN THE TUNNEL



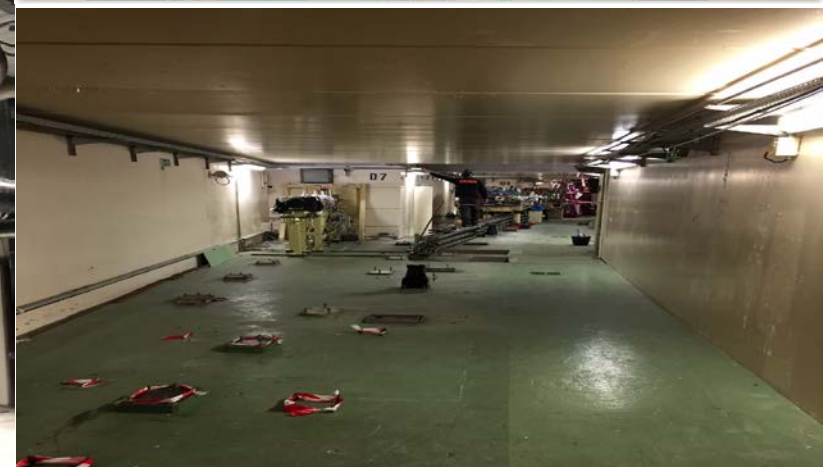
WORKS IN PROGRESS



Technical Gallery



RF Zone



Removal of Sector 23:

- Straight section
- Girder G10, G15, G20 & VLM Chs.



EBS STORAGE RING INSTALLATION IS BEING PREPARED IN ALL ITS "INFINITE" DETAILS TO START IN APRIL 2019



- ✓ Material for the installation of the EBS storage ring is continuously arriving on site, or stored in adapted areas close to the ESRF
- ✓ The vast majority (+95%) of the new storage ring components have been procured
- ✓ Gantry assembly tests and vacuum system preparation activities
- ✓ Alignment of thousands of components on the girders with $\sim 20\mu\text{m}$ tolerances on a 1 km length scale (~ 20 ppb)
- ✓ New timing system commissioned
- ✓ Etc.



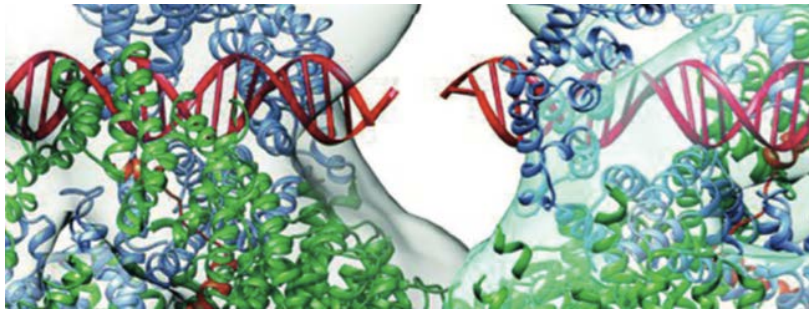
New and
innovative
materials



Health and
life science



Energy and
environment



EBS will enable scientists to write a new chapter in X-ray science by providing new tools for the investigation of materials and living matter

Construction of 4 flagships beamlines: ESRF Council on 26-27 June 2017

- **EBSL1** – Beamline for Coherent X-rays Dynamics and Imaging Applications
- **EBSL2** – Beamline for Hard X-ray Diffraction Microscopy
- **EBSL3** – Beamline for High throughput Large Field Phase-Contrast Tomography
- **EBSL8** – Beamline for Serial Macromolecular Crystallography

New and better science unveiling the secrets of nature

Down to the single atom

Go to extreme conditions

Detect new phenomena

Higher throughput and faster dynamics

IMPACT OF SYNCHROTRON LIGHT SOURCES IN EUROPE AND WORLDWIDE

1963: Europe – Pioneer of synchrotron science with the invention of the storage ring electron accelerator in Frascati: learning on particle physics machines – 1st generation

1970s to 90s: Powerful programme at 2nd generation synchrotrons: BESSY – Berlin, HASYLab – Hamburg, LURE – Paris, MAX – Lund; NINA – Daresbury; PULS – Frascati

1994: Inauguration of the ESRF, the first 3rd generation synchrotron, and opening of a new page in X-ray science

1990s to nowadays: the ESRF success and technology drives the construction of eleven very performing synchrotron facilities in Europe, and the building up of a European Users Community of 24 000 scientists

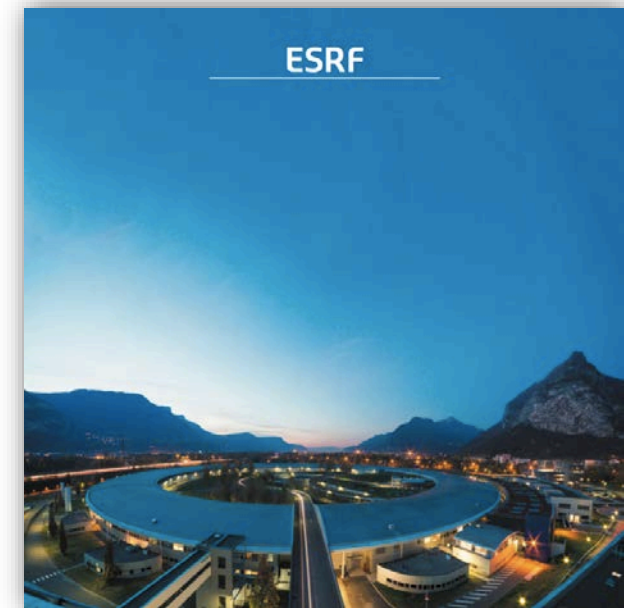
2013: ESRF-EBS storage ring lattice concept opens a new horizon for future 4th generation synchrotron sources, which mobilizes the SR world

2016: Inauguration of MAX IV, the first multi-bend synchrotron source

2020: The ESRF will open a new page in X-ray science with the inauguration of the EBS storage ring, fulfilling its mission of pioneering synchrotron science worldwide

B. Touschek
INFN-Frascati

R. Chasman, G.K.Green
Brookhaven National
Laboratories



P. Raimondi
INFN-Frascati and ESRF

ESRF EBS IN THE INTERNATIONAL CONTEXT

Major new projects in X-ray science

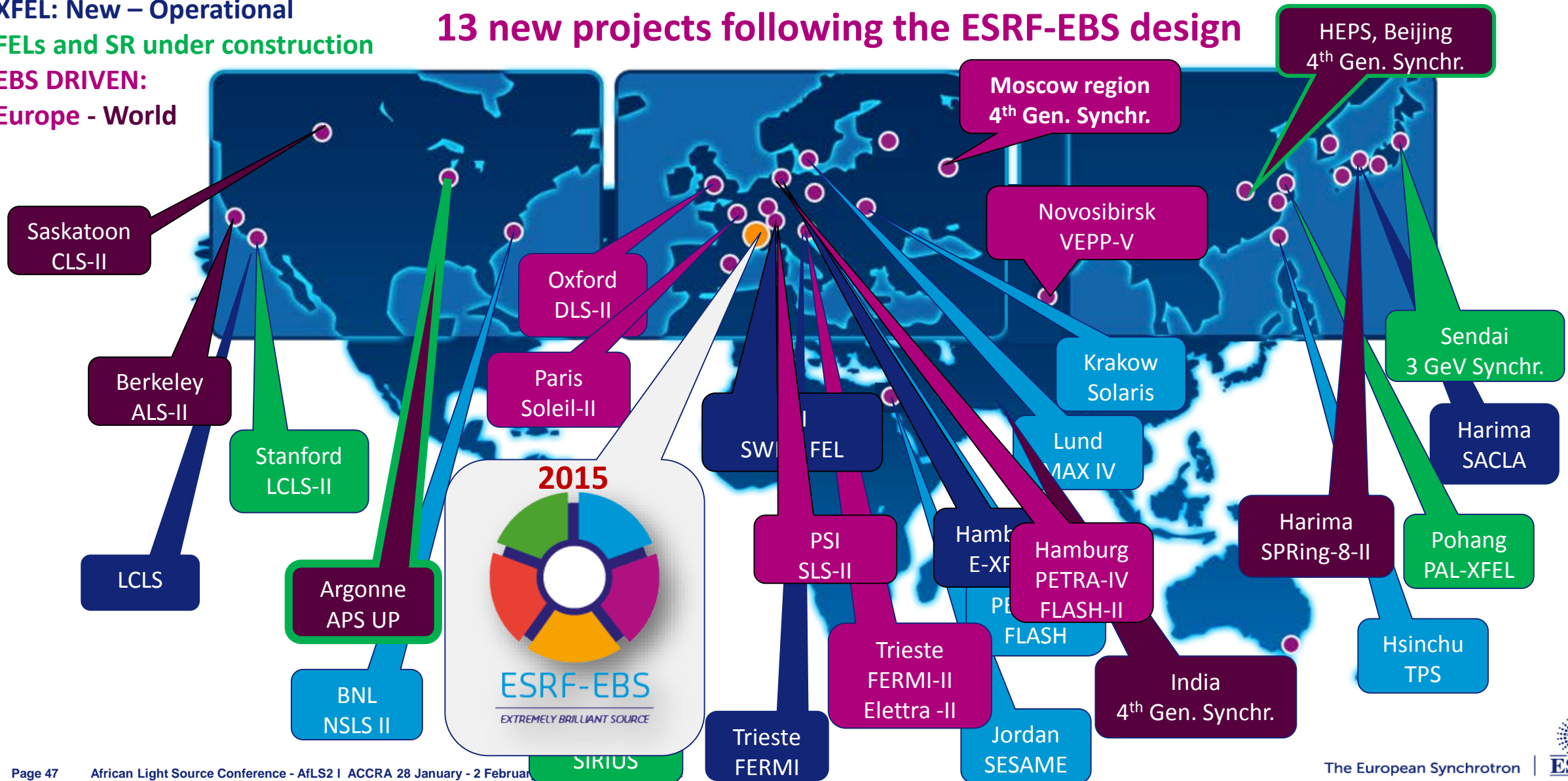
13 new projects following the ESRF-EBS design

SR: New – Operational

XFEL: New – Operational

FELs and SR under construction

EBS DRIVEN:
Europe - World



ESRF objective is enabling scientific excellence in the the domain of synchrotron science:

- To serve advancement of knowledge
- To address global societal challenges, enabling key research in areas as: health – energy – food – environment
- To support education and training programmes for the next generation
- To foster innovation
- To contribute shaping a sustainable future
- To support the European strategy for: open-science – open-data – open to the world
- **Ready to discuss cooperation and association programmes with African Countries in the context of building up the African Light Source**



Thanks for your attention! @esrfsynchrotron