SB and the ESRF-EBS Project
MX BAG Meeting
February 2017

Gordon Leonard

ESRF UPGRADE PROGRAMME PHASE I: A NEW GENERATION OF BEAMLINES

Purple Book January 2008

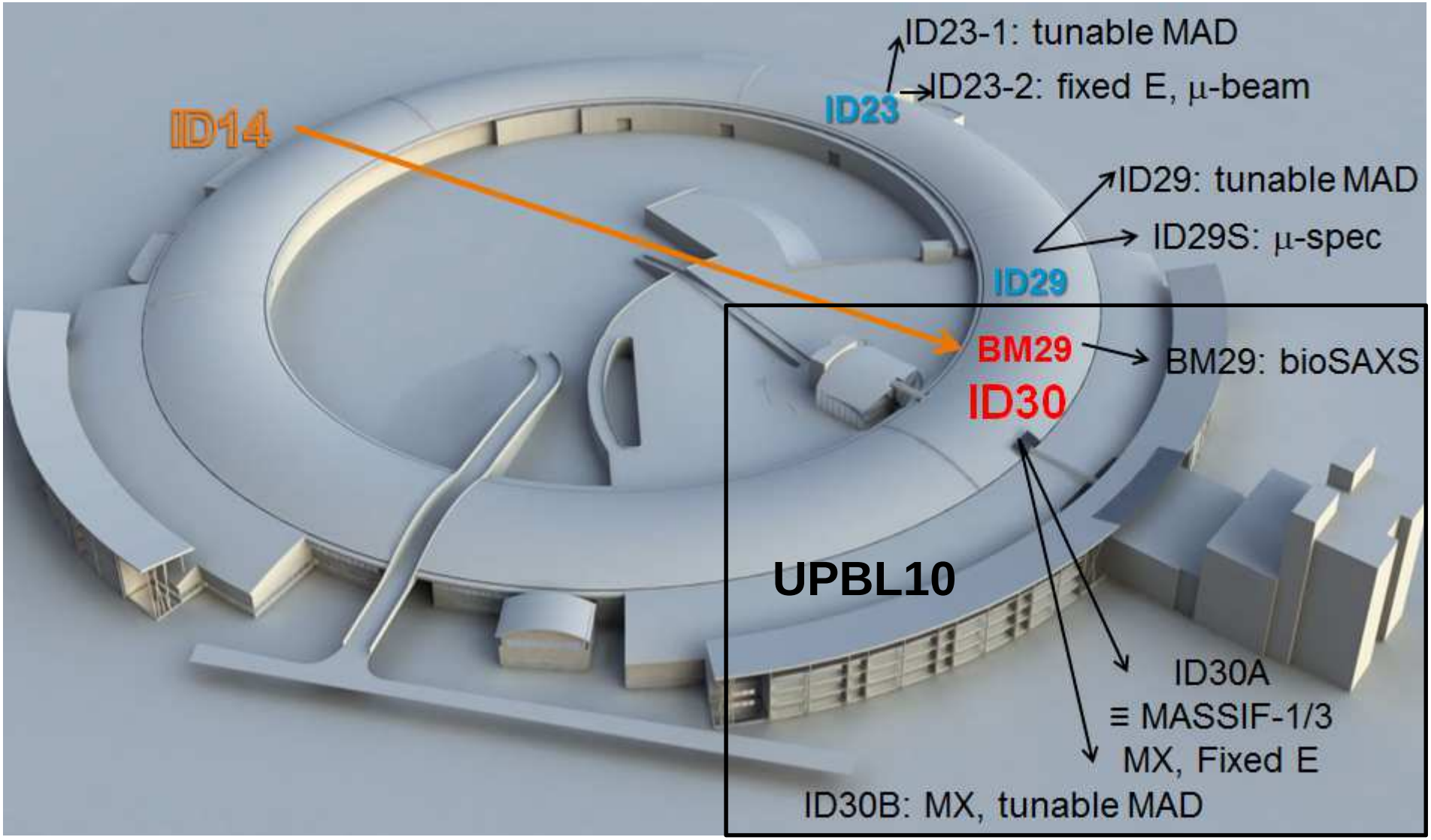
ESRF UPGRADE PHASE I
180 M€ (2009-2015):
ESFRI ROADMAP 2006-2016
IN TIME – WITHIN BUDGET

- **19 new beamlines, many specialised on *nano*-beam science**
- **Upgrade and renewal of facilities and support laboratories**

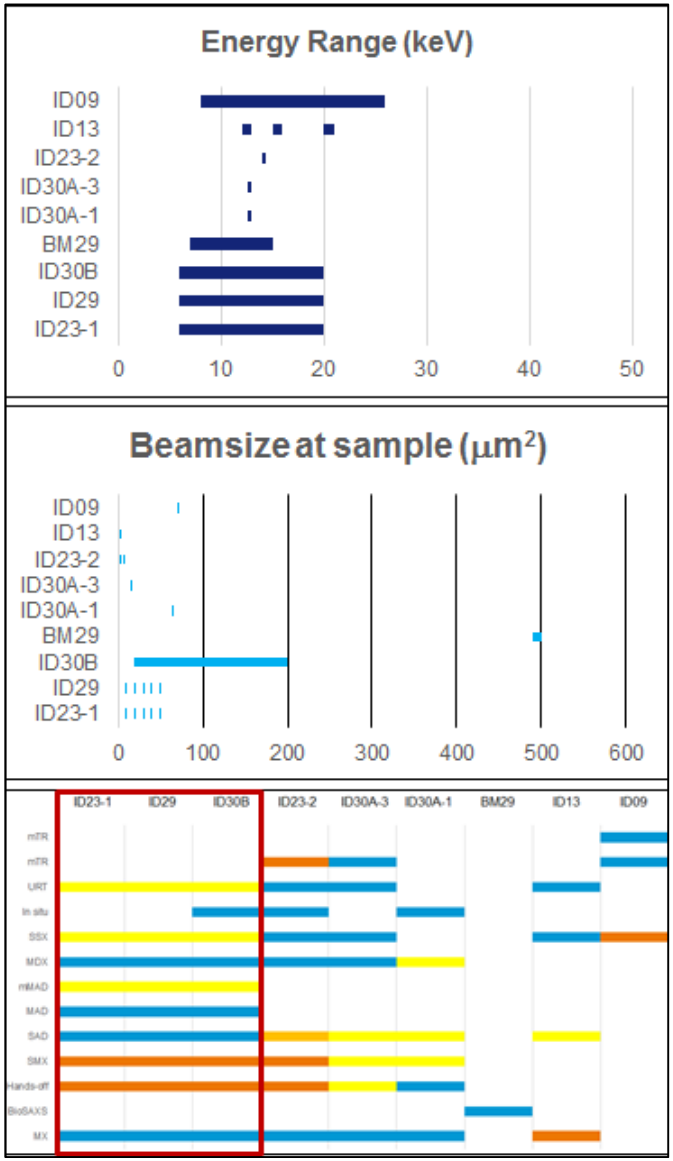
ESFRI

European Commission

STRUCTURAL BIOLOGY AT ESRF: 2016

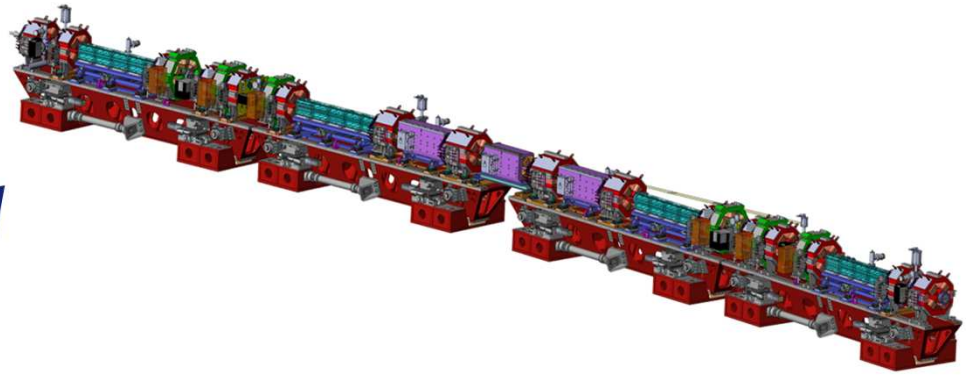


CURRENT STATUS ESRF, SB GROUP BEAMLINES

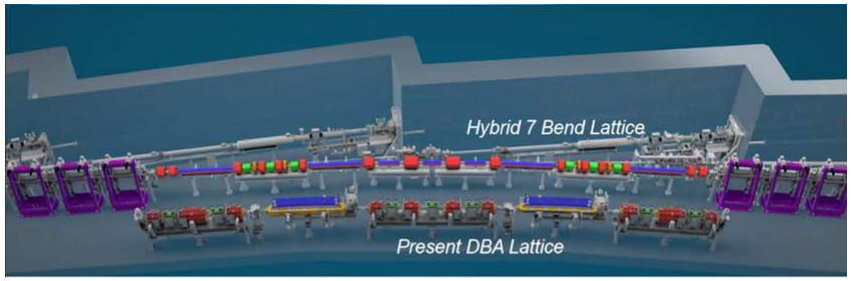


BL	Comments
MASSIF-1	*High throughput hands-off data (fragment/ligand screening) and initial stages of projects.*
MASSIF-3	*High throughput data collection from smaller/μcrystals. Multi-crystal, multi-position data collection. Fixed wavelength SSX.*
ID30B	*'Standard' MAD/SAD data collection. In situ data collection/phasing. Multi-crystal, multi-position data collection.*
BM29	*High throughput BioSAXS.*
ID23-1	*Standard' MAD/SAD data collection. In situ data collection/phasing. Multi-crystal, multi-position data collection.*
ID23-2	*Nano-/μfocus end-station. 'Standard' data collection from μcrystals. Fixed wavelength SSX. Multi-crystal, multi-position data collection.*
ID29	*Standard' MAD/SAD data collection. In situ data collection/phasing. Multi-crystal, multi-position data collection. On-line spectroscopy (raman)*
ID29-S	*Cryobench: in crystallo spectroscopy*

ESRF Extremely Brilliant Source
ESRF-EBS – 150 M€ (2015-2022)



- FIRST of a new generation of synchrotron storage rings
- ~100 times more brilliant and coherent X-rays
- Programme to exploit the qualities of this new and so far unique extremely brilliant X-ray source:
  - Creation of new beamlines
  - Innovative detector programme
  - « Data as a Service » strategy

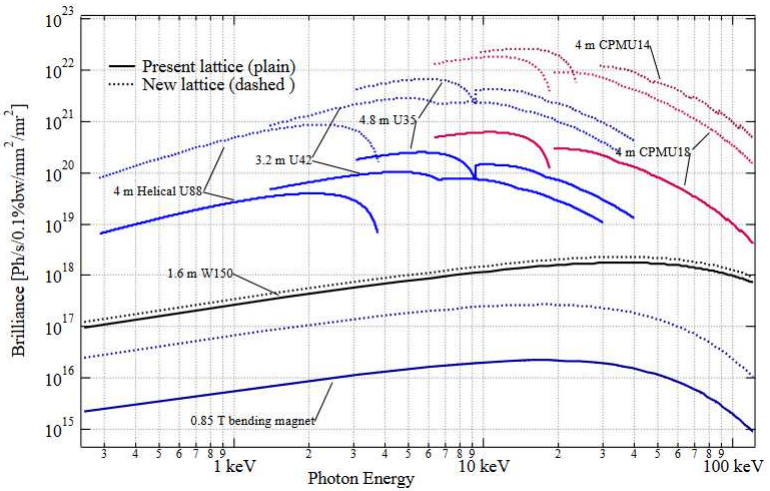


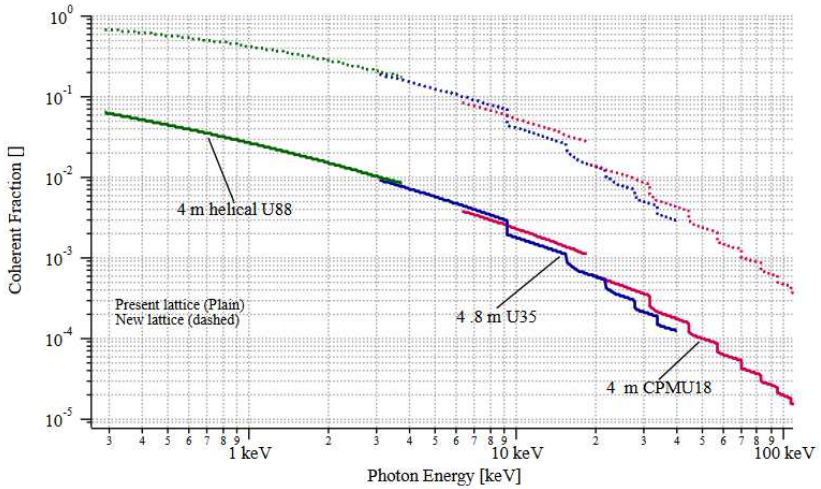
The source properties of the current and ESRF-EBS storage ring lattices.

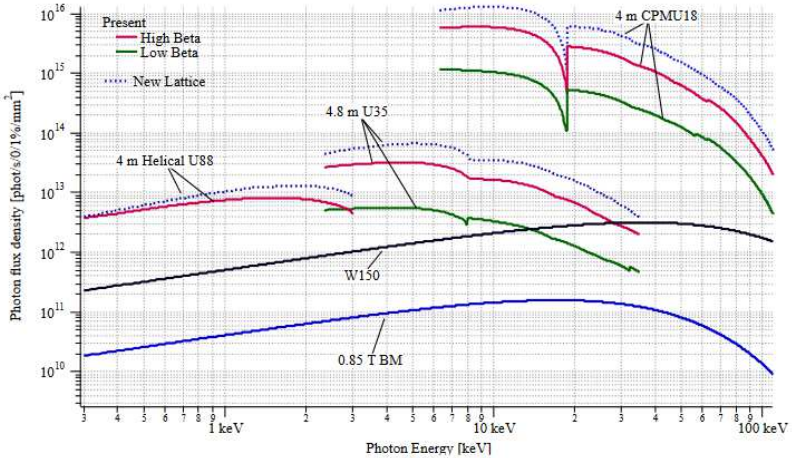
	Emittance		Beta [m]		λ [Å]	L [m]	r.m.s. size [μm]		Divergence [μrad]	
	H [nm]	V [pm]	H	V			H	V	H	V
High β	4	5	37.2	3	6.2	3.2	409	10.8	14.5	10.3
					1	3.2	409	5.6	11.9	6.1
					0.2	4	409	4.7	11.3	4.7
Low β	4	5	0.37	3	6.2	3.2	50	10.8	104	10.3
					1	3.2	49	5.6	104	6.1
					0.2	4	49	4.7	104	4.7
ESRF-EBS	0.13	2	4.7	2.7	6.2	3.2	26.7	10.3	11.4	10.2

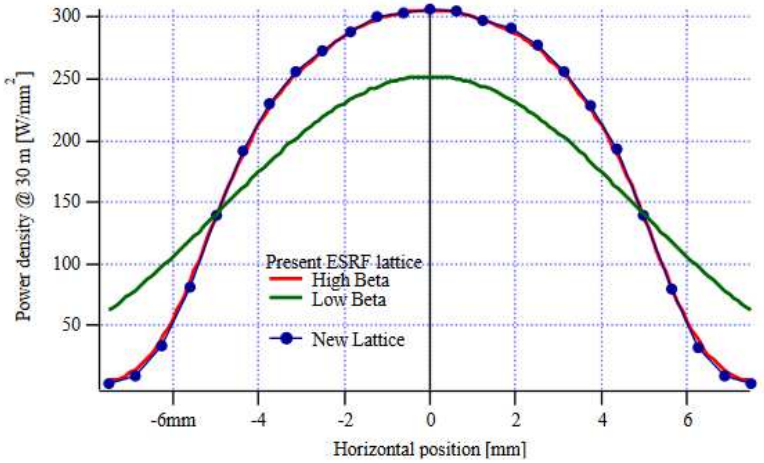
- Smaller source size
- Lower divergence
- Smaller X-ray beams
- Much brighter beams
- All straight sections equal
- Higher coherence fraction

ESRF-EBS; HIGHER BRILLIANCE & COHERENCE





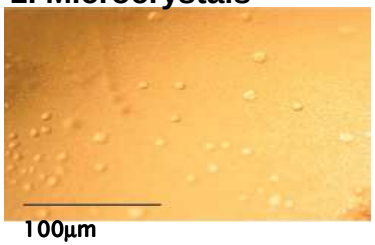


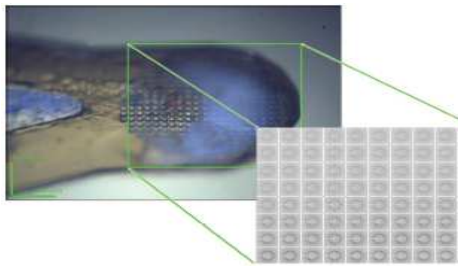


http://www.esrf.fr/files/live/sites/www/files/about/upgrade/documentation/whitepaper-upgrade-phaseII.pdf

DOING ‘STANDARD’ THINGS (AUTOMATICALLY) FASTER & BETTER

1. Microcrystals





- Where? – What? – Optimise? – Trash?
- Smaller beam = finer sampling

EIGER 4M@MASSIF-3

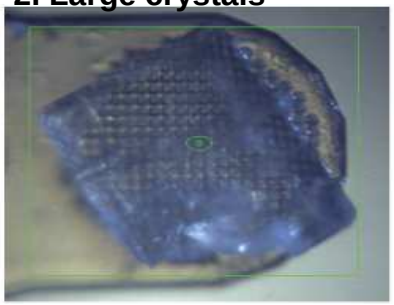
0.5 s — 750 Hz

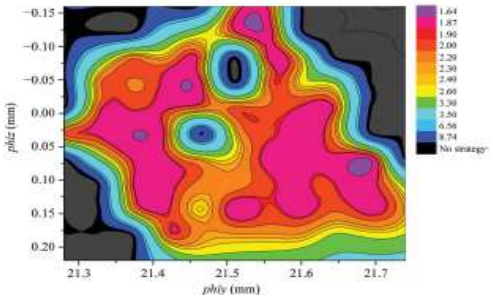
1.7 s — 750 Hz

Image Prefix	Run No	# images	Exp. Param.	Status	Space Group	Completeness	Resolution	Rsymm Inner / Outer / Overall	Unit_cell a, b, c / alpha, beta, gamma	Exp. Type
insulin1_750Hz_w1	3	400			I 2 3		31.72 - 5.66 1.51 - 1.46 31.72 - 1.46	2.7 104.0 5.7	77.70, 77.70, 77.70 90.00, 90.00, 90.00	OSC
insulin1_500Hz_w1	2	400			I 2 3		31.72 - 5.66 1.51 - 1.46 31.72 - 1.46	2.4 98.2 5.4	77.69, 77.69, 77.69 90.00, 90.00, 90.00	OSC
insulin1_100Hz_w1	1	400			I 2 3		31.71 - 5.66 1.51 - 1.46 31.71 - 1.46	1.9 102.0 5.1	77.68, 77.68, 77.68 90.00, 90.00, 90.00	OSC
ref-insulin1	1	2			I23		1.85		76.74, 76.74, 76.74 90.00, 90.00, 90.00	Char...
thaumatin1_750Hz_w1	3	1300			P 41 21 2		45.78 - 5.23 1.4 - 1.35 45.78 - 1.35	3.5 81.3 10.5	57.76, 57.76, 150.16 90.00, 90.00, 90.00	OSC
thaumatin1_500Hz_w1	2	1300			P 41 21 2		45.77 - 5.23 1.4 - 1.35 45.77 - 1.35	3.5 82.1 10.4	57.75, 57.75, 150.12 90.00, 90.00, 90.00	OSC
thaumatin1_100Hz_w1	1	1300			P 41 21 2		45.76 - 5.23 1.4 - 1.35 45.76 - 1.35	3.5 79.1 10.4	57.73, 57.73, 150.07 90.00, 90.00, 90.00	OSC
ref-thaumatin1	1	2			P4		1.54		57.05, 57.05, 148.51 90.00, 90.00, 90.00	Char...

David von Stetten, MASSIF-3

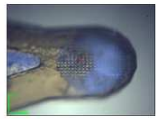
2. Large crystals



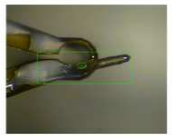


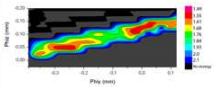
- Where is ‘sweet spot’?
- Smaller beam = finer sampling

- **Where is my sample**
- **Is it my sample?**

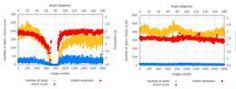


- **Where is the best part of my sample**

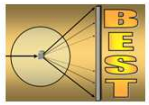


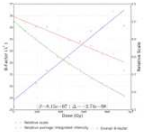


- **For small crystals – X-ray centring in the beam (full rotation)**



- **How to avoid (too much) radiation damage?**
- **How to best collect diffraction data?**





Bowler *et al.* & Leonard , Diffraction cartography. *Acta Cryst.* (2010). **D66,** 855–864

EBS: PRODUCTION OF VERY SMALL, VERY HIGHLY INTENSE X-RAY BEAMS

	Emittance		Beta [m]		λ [Å]	Rms size [μm]		Divergence [μrad]	
	H [nm]	V [pm]	H	V		H	V	H	V
High beta	4	5	37.2	3	6.2	409	10.8	14.5	10.3
					1	409	5.6	11.9	6.1
					0.2	409	4.7	11.3	4.7
Low beta	4	5	0.37	3	6.2	50	10.8	104	10.3
					1	49	5.6	104	6.1
					0.2	49	4.7	104	4.7
New lattice	0.13	2	4.7	2.7	6.2	26.7	10.3	11.4	10.2
					1	25	4.7	7.4	5.3
					0.2	25	3.5	6.8	4.4

ID23-2 in 2017 and beyond

Solution	Beam size (μm², H x V)	Flux (ph/s)	Beam size (μm², H x V)	Flux (ph/s)
CRL (V) CRL (H)	3.8 x 5.6	4×10^{12}	3.9 x 1.3	2.1×10^{12}
CRL (V) Mirror (H)	6.8 x 5.1	1.7×10^{13}	1.0 x 1.2	1.2×10^{13}
KB mirrors	5.5 x 3.8	9×10^{12}	2.0 x 1.6	8.4×10^{12}
Solution	**Beam size (μm², H x V)**	**Flux (ph/s)**	**Beam size (μm², H x V)**	**Flux (ph/s)**
CRL (V) CRL (H)	3.7 x 5.6	4.8×10^{12}	4.1 x 1.5	2.5×10^{13}
CRL (V) Mirror (H)	5.4 x 5.3	5.6×10^{13}	0.75 x 1.3	4.9×10^{13}
KB mirrors	4.3 x 3.7	4×10^{13}	1.6 x 1.6	4.1×10^{13}

ESRF ID29			
	Current	New lattice	New Lattice (50:1)
Source size (FWHM; H × V; μm²)	49 × 5.6	59 x 11	**59 x 11**
Divergence (r.m.s. H × V; μm²)	104 × 6.1	7.4 x 5.3	**7.4 x 5.3**
Demagnification ratio	3:1	3:1	**50:1**
Beamsize @ sample (μm²)	~60 x 30	20 x 4	**1.2 x 0.2**
Flux @ sample (ph/sec)	~1 x 10^{13}	~1 x 10^{14}	**~1 x 10^{14}**
Flux density @ sample (ph/sec/μm²)	**1.7 x 10^{9}**	2.1 x 10^{12}	**2.4 x 10^{14}**
Absorbed dose rate (Gy/sec)	**7.8 x 10^{5}**	9.6 x 10^{8}	**1.2 x 10^{11}**
Time to Henderson Limit (sec)	**26**	0.021	**0.0002**

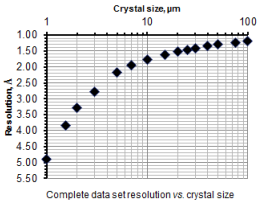
- **Smaller beams (**micro, nano);
- **Increase in flux density**
  - 2.5 orders of magnitude
  - 5 orders of magnitude

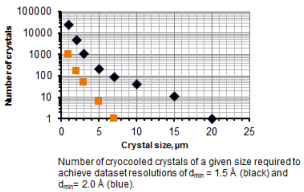
WHAT DO OUR USERS WANT? EBS EXPRESSIONS OF INTEREST SB GROUP

no	proposer	Title	Techniques	Comments
1	Jegorov	Pharma industry	SMX; determination of absolute configuration. Crystal size ~ 1 μm in smallest dimension.	Needs combination of characteristics hard to achieve on MX BL
15	Caliandro	Heavy atoms speciation in protein crystals	MX, XAS	Should be relatively straightforward to implement on MX tuneable BL. Does not depend on EBS.
40	M. Czjzek	EBS for macromolecular structural biology of original proteins and complexes	MX, MDX *in situ* screening (i.e. crystallisation plates, or microfluidic devices) at cryo-conditions but also at ambient temperature	Smaller and/or higher flux density beams on post-EBS MX BLs should make this straightforward to implement (i.e. MASSIF-3, ID23-2, ID30B).
41	**Sulzenbacher**	**Extremely brilliant source for the investigation of challenging biological systems**	**SSX (nano-size crystals) combined with spectroscopic experiments**	**Requires nano-/μbeam). Will address dynamics in biological systems, not amenable for the moment.**
42	Marquez	Macromolecular crystallography and structure guided drug design	MX, MDX, SSX Accelerate analysis of small molecule-protein interactions by x-ray crystallography for drug design programs.	Post-EBS MASSIF-1, MASSIF-3, ID30B will be ideally suited for this purpose
43	**Cusack**	**Serial synchrotron crystallography for structural biology**	**SSX**	**1 – 10 μm beamsize on both a tuneable and a fixed wavelength BL.**

- **Relatively few Expressions of Interest suggests that most ESRF MX users want more of the same, but better.**
- **Clear ideas for ambient temperature/SSX.**
- **So, what should we do?**

CDR8 – A SERIAL CRYSTALLOGRAPHY BEAMLINE

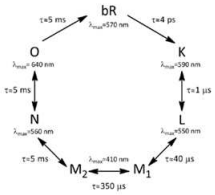


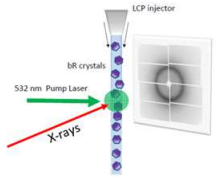


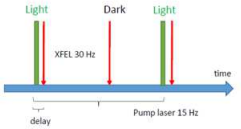
Science Case

Andrew Leslie

9th December 2016







- A SSX beamline with large bandwidth (~1%), very high flux 10^{16}ph/s
- Focus beam to 0.5 – 10 μm
- Tuneable from 10-30 keV

Expert panel
Andrew Leslie, MRC-LMB, Cambridge, UK
Robert Fischetti, APS, Argonne, USA
Martin Weik, IBS, Grenoble, France
Gwyndaf Evans, DLS, Didcot, UK
Alke Meents, Hasylab at DESY, Hamburg, Germany

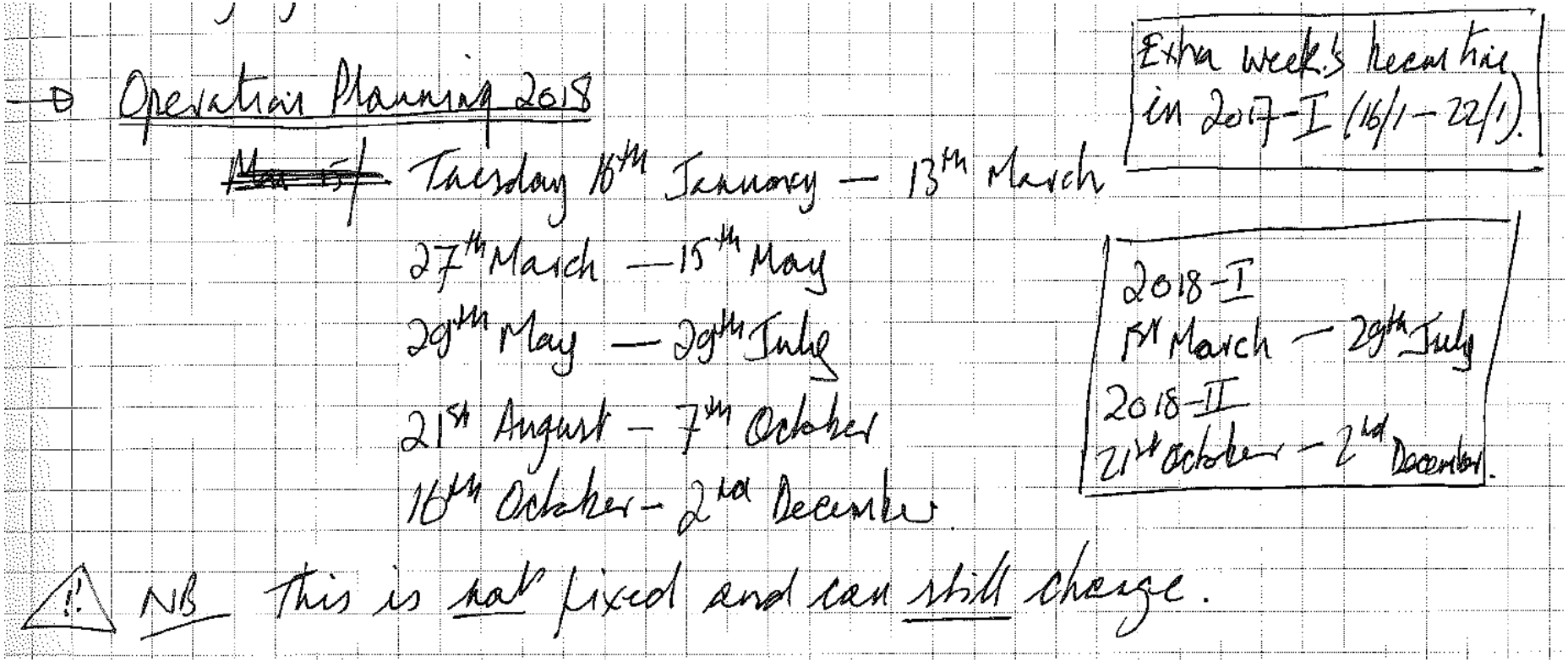
SAC observer
Frithjof Nolting: PSI, Villigen, Switzerland

ESRF coordinators
Daniele de Sanctis
Gordon Leonard, Head of Structural Biology Group

THE FUTURE OF MX/BIOSAXS AT THE ESRF?

BL	Comments
MASSIF-1	Fixed wavelength. Very high throughput hands-off data collection (fragment/ligand screening ; initial stages of projects). In situ screening/data collection. Hands-off dehydration experiments.
MASSIF-3	High throughput data collection from smaller/µcrystals. Multi-crystal, multi-position data collection. Fixed wavelength SSX. msec/µsec time resolution (with ID29S).
ID30B	Variable focus [20 – 200 μm^2]. High throughput data collection [smaller crystals]. 'Standard' MAD/SAD data collection. Multi-crystal, multi-position , multi-temperature data collection. In situ data collection/phasing. Extend to lower energies?
BM29	Higher throughput [remote access?], improved pipelines, microfluidic chips. TR-BioSAXS?
ID23-1	'Standard' MAD/SAD data collection. In situ data collection/phasing. Multi-crystal, multi-position multi-temperature data collection. Variable focus [5 – 300 μm^2]? Extended energy range [higher energies]? Low resolution data collection?
ID23-2	Nano-/µfocus end-station. 'Standard' data collection from µcrystals. Fixed wavelength SSX. Multi-crystal, multi-position data collection.
ID29	Tunable (TR-SSX)
ID29-S	Cryobench: in crystallo spectroscopy. Support for TR-SSX experiments.
Cryo Electron Microscopy	

THE EBS-SHUTDOWN BE?



EBS-Shutdown: December 2018 – September 2020 (not definitive)

Thanks for your attention