UK in SFX @ the EU XFEL

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On behalf of the UK Structural Biology Community

Who am I?

- Trained as a chemist, work as a structural biologist, been in St Andrews since 1995
  - google scholar naismith
  - ResearcherID H-3408-2012
  - SCOPUS_ID 7005691850
- Led CCP4 (UK structural biology community software effort) for 7 years, prior member of its executive
- Previous member of MX beamline planning, Diamond SAC and now non-Exec Diamond Board

History of UK MX

- The UK has a proud history in structural biology
  - Perutz/Kendrew first protein
  - Hodgkin first hormone
  - Philips first enzyme
  - Walker & Ramakrishnan recent Chemistry Nobel
- The UK structural biology community has been at the forefront of innovation, often working together
  - SRS – early synchrotron for MX
  - CCP4 – collaborative effort
  - INSTRUCT – EU wide community, UK engaged
  - BM14 – MX beamline run by UK community

Genome revolution

- Structural biology was recognized by Whitesides in his EPRSC report as a particular strength in the UK
- The genome revolution demands much higher throughput on all downstream approaches
- Biology as a system requires integrating information to really understand process, hence predict and modify it (lots more data)
- Next generation enzyme chemistry will move to shorter timescales to understand bond breaking and making

Challenges for MX

- The most important biological systems - complexes, membrane proteins - are barely tractable to current technologies
- Crystals are often too small or poorly ordered
- Current 3rd generation sources destroy samples, we are limited by radiation damage
- Either we catch up or face irrelevance in biomedical science
- Our belief is more photons, more resolution, more information

XFEL potential

- See Henry Chapman's talk
- Communityopen day in November, over 40 group leaders (talks from Henry, Richard Neutze and Ilme Schlichting); science focused
- The UK structural community decided
  - XFEL remains an unproven but promising technology for MX
  - Plausible it could transform structural biology
  - The UK cannot afford to sit out
  - The UK could help drive its development

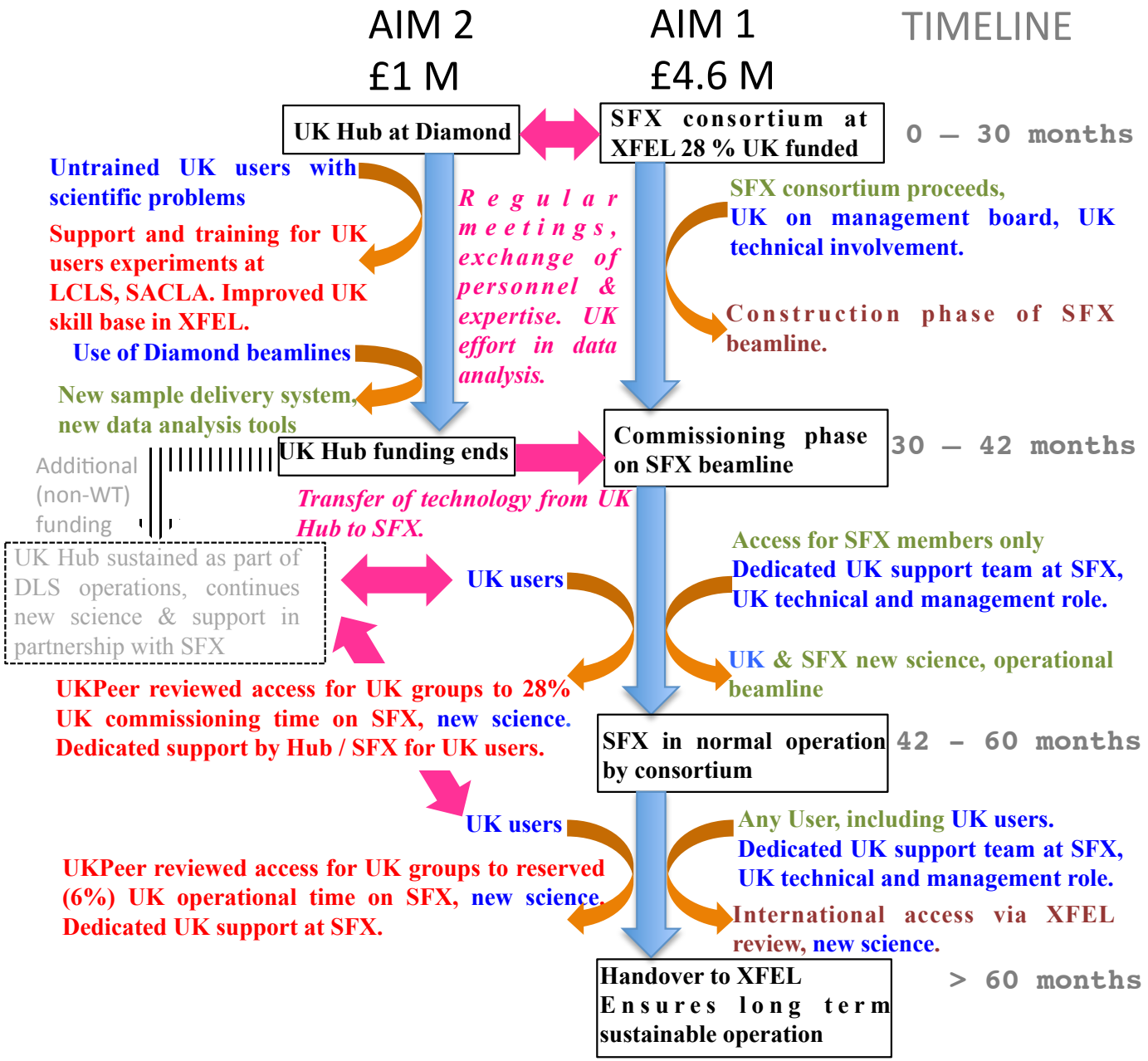
Opportunity

- Henry Chapman and Professor Massimo Altarelli (letter) made the UK MX community an offer
  - Join the SFX consortium despite the UK as a whole sitting out the XFEL
  - The SFX model guarantees UK access to XFEL; thus precompetitive access to develop expertise
  - SFX works by shareholder, total cost approx £16.5M
  - UK community decided to bid to become the major shareholder of SFX, 28% (depends on exchange rate)

The UK plan

- UK MX groups are not doing well at securing XFEL time at SACLA or LCLS
- A serious risk is that UK fails to capitalize on the new technologies because we lack expertise
- We decided therefore to adopt a two pronged strategy
  - Create a UK HUB at Diamond
  - Join SFX, offering our expertise as a consortium member

The concept


AIM 2
£1 M
AIM 1
£4.6 M
TIMELINE
UK Hub at Diamond
SFX consortium at XFEL 28 % UK funded
0 – 30 months
Untrained UK users with scientific problems
Support and training for UK users experiments at LCLS, SACLA. Improved UK skill base in XFEL.
Use of Diamond beamlines
New sample delivery system, new data analysis tools
Regular meetings, exchange of personnel & expertise. UK effort in data analysis.
SFX consortium proceeds, UK on management board, UK technical involvement.
Construction phase of SFX beamline.
UK Hub funding ends
Commissioning phase on SFX beamline
30 – 42 months
Additional (non-WT) funding
Transfer of technology from UK Hub to SFX.
UK Hub sustained as part of DLS operations, continues new science & support in partnership with SFX
UK users
Access for SFX members only
Dedicated UK support team at SFX, UK technical and management role.
UK & SFX new science, operational beamline
UKPeer reviewed access for UK groups to 28% UK commissioning time on SFX, new science. Dedicated support by Hub / SFX for UK users.
SFX in normal operation by consortium
42 – 60 months
UK users
Any User, including UK users.
Dedicated UK support team at SFX, UK technical and management role.
UKPeer reviewed access for UK groups to reserved (6%) UK operational time on SFX, new science. Dedicated UK support at SFX.
International access via XFEL review, new science.
Handover to XFEL
Ensures long term sustainable operation
> 60 months

Mechanics

- At open meeting all interested life science RC's present (STFC, BBSRC, MRC) and Wellcome Trust
- Dialogue with and between possible funders began before meeting, but crucially funders took note of attendees and discussion at meeting
- At end of meeting, funders discussed options for bids
- Colin Miles "BBSRC never rejects good ideas. It rejects grants but not good ideas."

Just a FECing minute

- BM14 funded in part by BBSRC was old model
- RCUK pay 80 % of FEC
- No UK university could afford or would contemplate paying 20 % of capital cost of a beamline in Germany
- DESY has no overhead; this helps
- RCUK & WT solved problem, thanks to Tom (WT), Colin (BBSRC) and Adam (MRC)
- Highlights huge advantage of our history of community engagement with RCUK and WT; BM14

Back on track

- Wellcome and RCUK agreed that WT would lead the peer review process; no double jeopardy
- Preliminary strategic award submitted 17th February; approved for full application April
- Full application submitted June 3rd
- RCUK potential funders (BBSRC and MRC), now carry out their evaluation of strategic fit with their portfolios. STFC fully engaged
- Decision point Autumn 2013

Community bid

- 60 group leaders wrote letters of support
  - Critical are letters from world leaders in the UK
  - Large labs York, LMB-Cambridge, Oxford, IC all strong supported bid
- All group leaders received copies of preliminary application before asking for LoS
- Final application put on semi public website for all group leaders to download
- JHN writes to all group leaders to keep them informed

Aim 1

- Science largely covered by Henry Chapman
- UK will fund costs at DESY; managed by SFX board, not managed day to day directly by UK
- UK will sit on management board (JHN) and propose technical board membership
  - Crucially management board is by share but technical board is by merit / ability
  - See real synergies between Diamond and XFEL at technical level
- Some partners already in, UK would be financial tipping point (as penguins all jump together)

- 6 months: Recruitment of personnel
- 12 months: Optical design choice finalised, full technical review completed, construction underway.
- 18 months: Detailed plan for commissioning, construction of hutches.
- 24 months: Front end in operation, first beam (not refocused), begin installation of sample delivery system.
- 30 months: First detector element in place, refocused beam in hutch, commissioning of SFX begins, UK users arrive
- 36 months: Sample delivery commissioning completed, DAQ system fully operational, additional detector module installed.
- 42 months: Full detector installed, SFX in operational mode, preparation made for laser installation.
- 48 months: Design begins of next generation of sample delivery system.
  54 months: Second generation of data analysis software (partnership with Diamond)
- 60 months: Grant ends, XFEL takes over beamline, long term sustainability

Staffing (UK's 28%)

Post 3	SFX Senior Beamline Scientist, DESY employee

Post 4	SFX Beamline Scientist 2, DESY employee

Post 5	SFX Engineer, DESY employee

Post 6	SFX PDRA Scientist, DESY employee

Post 7	SFX PDRA Scientist 2, DESY employee

£1.7M UK cost

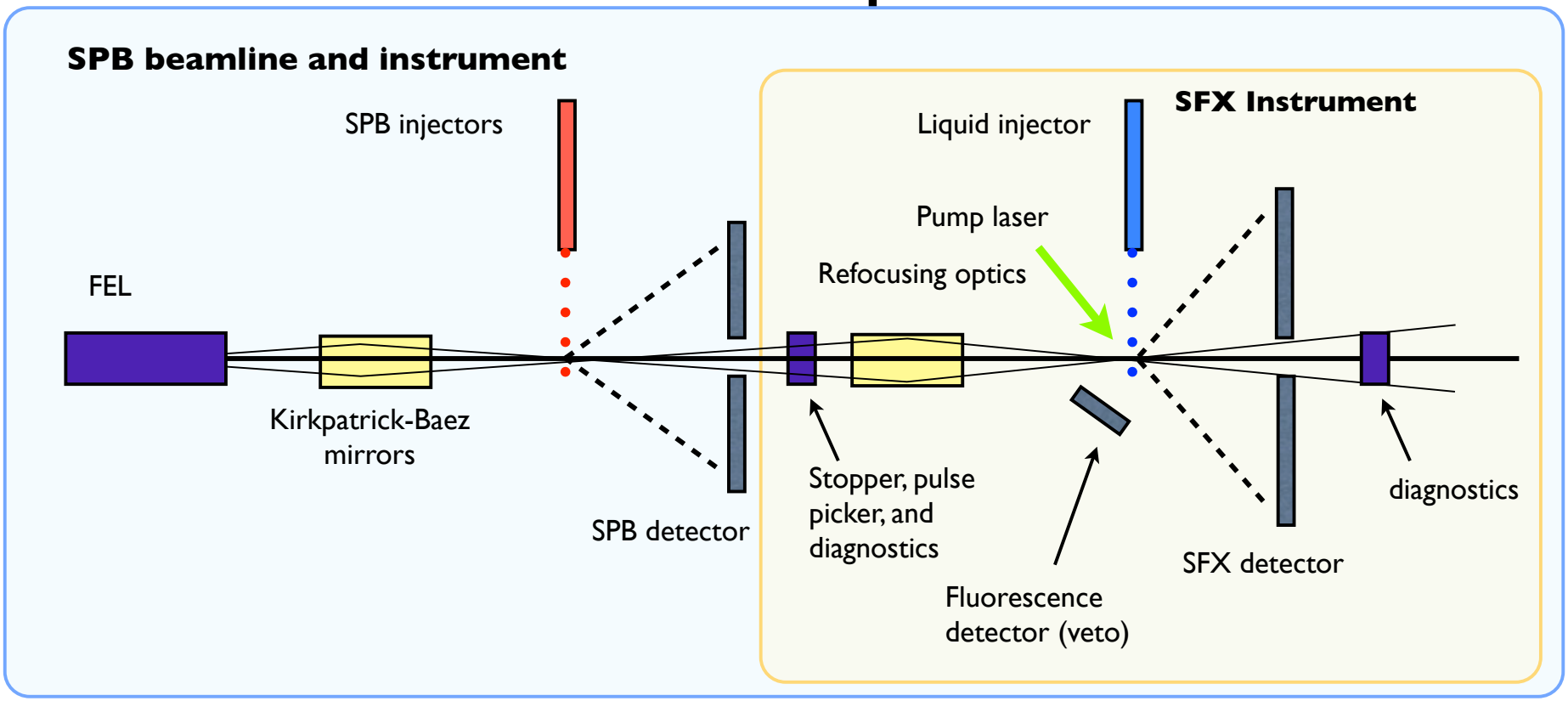
(b) Materials and consumables (description)	Costs
Commissioning costs of beamline (28% UK share)	255000
Operation costs of beamline (28% UK share)	666000

£0.9M UK

Type of equipment	Equipment specification	Preferred manufacturer/ supplier (if known)	Maintenance contract duration (months)	Cost of maintenance contract	Number of items	Cost per item	**Total cost**	**Contribution from other sources**	**Amount requested**
XFEL AGIPD X-ray detector	This is the UK share (28%) of the cost of the detector for the beamline	AGIP consortium	60	0	1	1350000	**1350000**	**973000**	**377000**
XFEL Data acquisition rig	This is the UK share (28%) of the cost of the detector for the beamline	DESY	60	0	1	835000	**835000**	**601000**	**234000**
XFEL Data storage	This is the UK share (28%) of the cost of the detector for the beamline	XFEL	60	0	1	1020000	**1020000**	**733000**	**287000**
XFEL Hutch for SFX	This is the UK share (28%) of the cost of the detector for the beamline	XFEL	60	0	1	561000	**561000**	**404000**	**157000**
XFEL Beamline components	This is the UK share (28%) of the cost of the detector for the beamline	DESY	60	0	1	564000	**564000**	**405000**	**159000**
XFEL Beamline optics	This is the UK share (28%) of the cost of the detector for the beamline	DESY	60	0	1	386000	**386000**	**278000**	**108000**
XFEL Sample and	This is the UK	DESY	60	0	1	736000	**736000**	**530000**	**206000**
XFEL Compatibility with pumping laser	This is the UK share (28%) of the cost of the detector for the beamline	XFEL	60	0	1	475000	**475000**	**342000**	**133000**
XFEL Beamline diagnostics	This is the UK share (28%) of the cost of the detector for the beamline	XFEL	60	0	1	425000	**425000**	**306000**	**119000**
XFEL Sample delivery robot	This is the UK share (28%) of the cost of the detector for the beamline	DESY	60	0	1	775000	**775000**	**558000**	**217000**
Equipment total							7100000	5100000	2000000

£2M UK

SFX dedicated and parasitic modes



- SFX energy range is 3 to 16keV; suitable for molecular replacement or refinement
- The detector will accept scattering angles 2θ up to about 60^0 at 5cm from sample (4 Å at 3keV, < 1Å at 16keV)

UK access arrangements to SFX

- Peer review; no sweetheart deals for applicants
- Peer review process will be run through Diamond on BM14 model
- We are contemplating a UK BAG model for access to other X-FELS
- Commissioning: 18 days dedicated, 18 days parasitic
- Operational time: 6 days dedicated and 6 days of parasitic

Operational mode

- In addition to reserved time, UK can bid for X-FEL peer review time (80 % of instrument time)
- SFX supports users, still to be defined
- Jan 2019 X-FEL will take over operation – long term sustainability
- Costs are SFX risk, X-FEL have validated estimates but careful assessment is needed throughout

The UK HUB

- Funded for three years in first instance
- Continuity plan involves Diamond taking over UK Hub
- Community supported
  - Facilitate the use of XFELs by the UK community, especially the SFX instrument when it comes on-line. XFEL time limited we need to use it well.
  - provide a development centre for sample-related hardware and data handling software developments.

Costs of UK Hub

Post 1	UK XFEL Hub PDRA scientist, 3 yrs at Diamond

£370K staff costs 3 years

Post 2	UK XFEL Hub Beamline scientist, 3 yrs at Diamond

UK Hub Liquid stream injector	This injects sample for test and preparation at UK hub	Arizona State University and LBL	60	0	1	100000	**100000**		**100000**
UK Hub computing storage	Store data from UK experiments		60	0	1	100000	**100000**		**100000**
UK Hub Computer cluster	Process data		60	0	1	100000	**100000**		**100000**
UK Hub High bandwidth networking	Transmit data		60	0	1	100000	**100000**		**100000**

£400K equipment cost

Consumable of UK test injector	125000
General lab consumables UK hub	5000
Travel of UK beamline scientist, post-doc and UK users to XFEL for three years, over 20 trips	100000
Travel of UK applicants to XFEL	10000

£230K consumable cost

UK Hub data processing

- Focus on getting better data out of images as quickly as possible
  - Many images cannot be processed
  - Statistics are problematic, due to partiality, intensity or sigma are currently mis-estimated
    - Typical of cutting edge technology
  - Processing is currently far from real time
    - We know this is often crucial for good experiments and efficient use of beamlines

UK Hub sample preparation

- Sample preparation and loading, currently need very high volumes of crystal slurry, challenging often clogs
  - Purchase current state of the art and start work with it
  - Evaluate competing approaches
  - Load up UK samples for shipment
- Provide collaborative support to UK groups to use SACLA and LCLS; then SFX when onstream
- Focal point for UK expertise, critical to ensure we use scare time efficiently

Synergies with Diamond

- Key to have support of Diamond
  - CEO very supportive of UK community
  - Run peer review, 'trusted brand'
  - Provides access to microfocus beamline, upcoming VMX beamline will handle too small to see xtals
  - Hub of EU funded data processing effort, pipelining well established
- Leverages significant UK investment in high volume data handling required for SFX AGIP output of 24 GBs^{-1}
  - (from CERN) RAL is point of presence
  - Diamond detectors already generate > 1GBs^{-1}

Timeline and milestones

- 3 months: Peer review process implemented, first call for proposals.
- 6 months: Recruitment of personnel, set up lab space; start building sample jet delivery system.
- 12 months: 6 month trial allocation period completed. Processes reviewed and improved, UK XFEL Block Allocation Group (BAG) system implemented.
- 18 months: UK sample jet in routine use, improved delivery system in development.
- 18 months: Beta testing of data analysis pipelines, using UK data from first allocation periods. 24 months: Data reduction and analysis pipelines released.
- 30 months: Coordinate first user visit to SFX.
- 36 months: Second generation sample delivery system implemented at UK hub.
- > 36 months: Technology transfer to SFX, Hub integrated into Diamond.