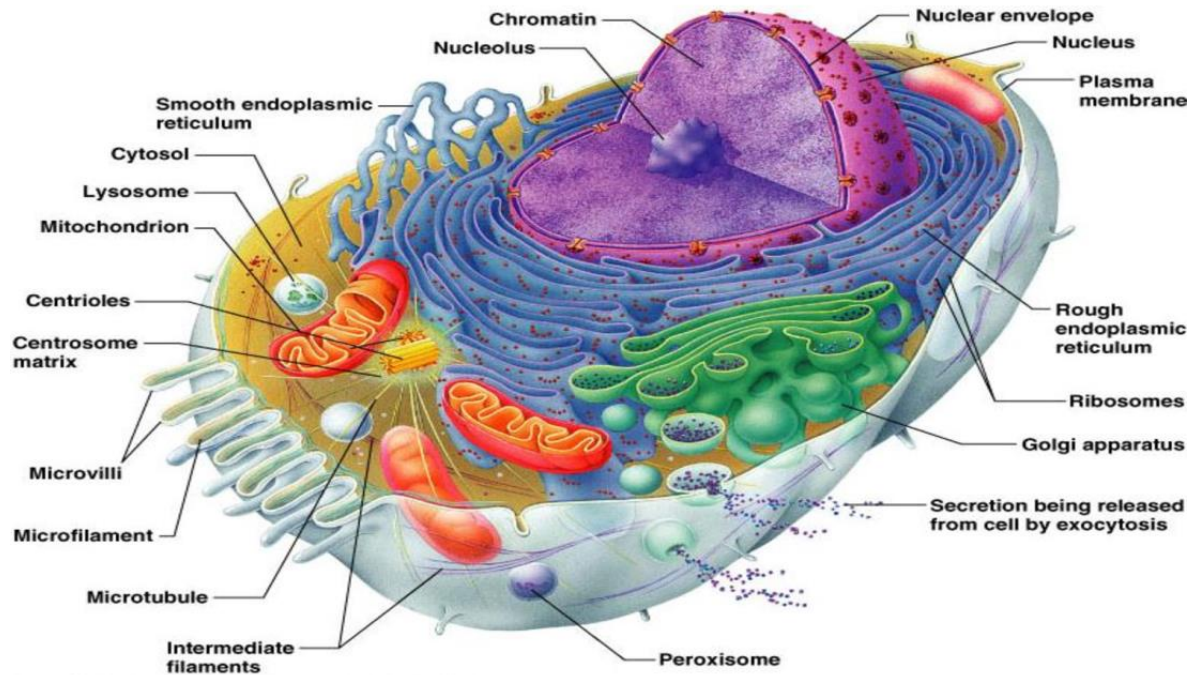


Smaller instrumentation projects – smaller science?

Stefan Fiedler
EMBL Hamburg

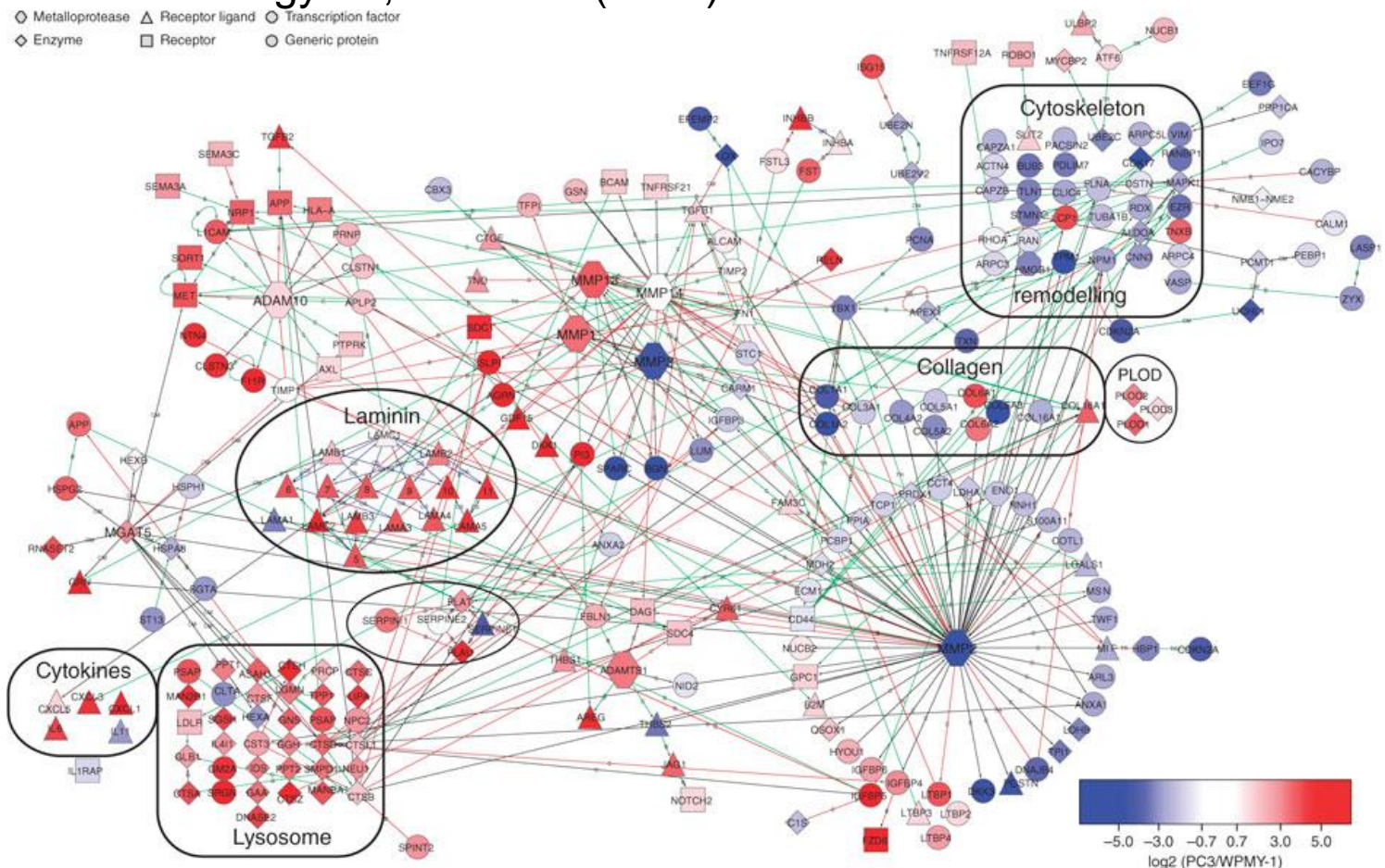
Central research object of EMBL

Structure of a Generalized Cell



Investigation of protein interaction networks (interactomes)

Selective enrichment of newly synthesized proteins for quantitative secretome analysis
 Katrin Eichelbaum, Markus Winter, Mauricio Berriel Diaz, Stephan Herzig & Jeroen Krijgsveld; Nature Biotechnology 30, 984–990 (2012)



Structure of EMBL and consequences for projects

- EMBL has many independent research groups (~100) following different different research directions.

2006-9

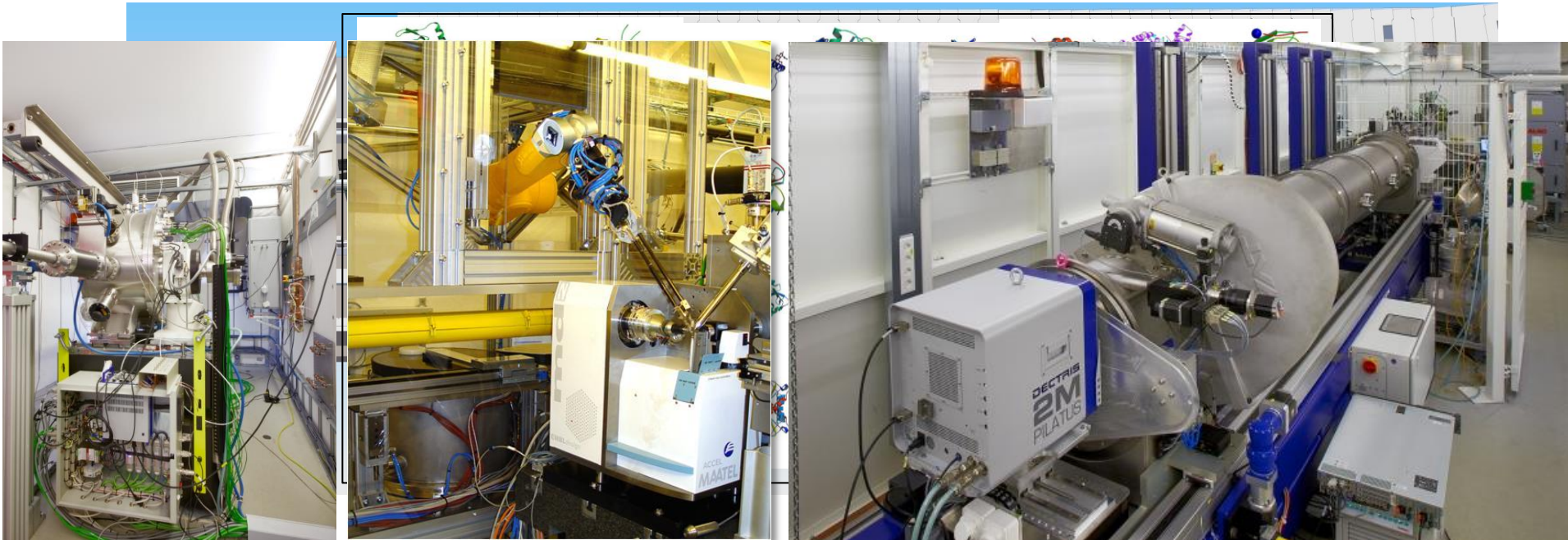


Structure of EMBL and consequences for projects

- EMBL has many independent research groups (~100) following different research directions.
- No common 'big' instrument.
- Central research infrastructure provided through 'Core Facilities' (Advanced Light microscopy, (Cryo) electron microscopy, Chemical Biology, Flow Cytometry, Protein Expression & Purification, Genomics, Proteomics, Transgenics).
- Major instrumentation projects take place in core facilities.
- Synchrotron based structural biology performed in Grenoble & Hamburg Unit.

Synchrotron beamlines for structural biology

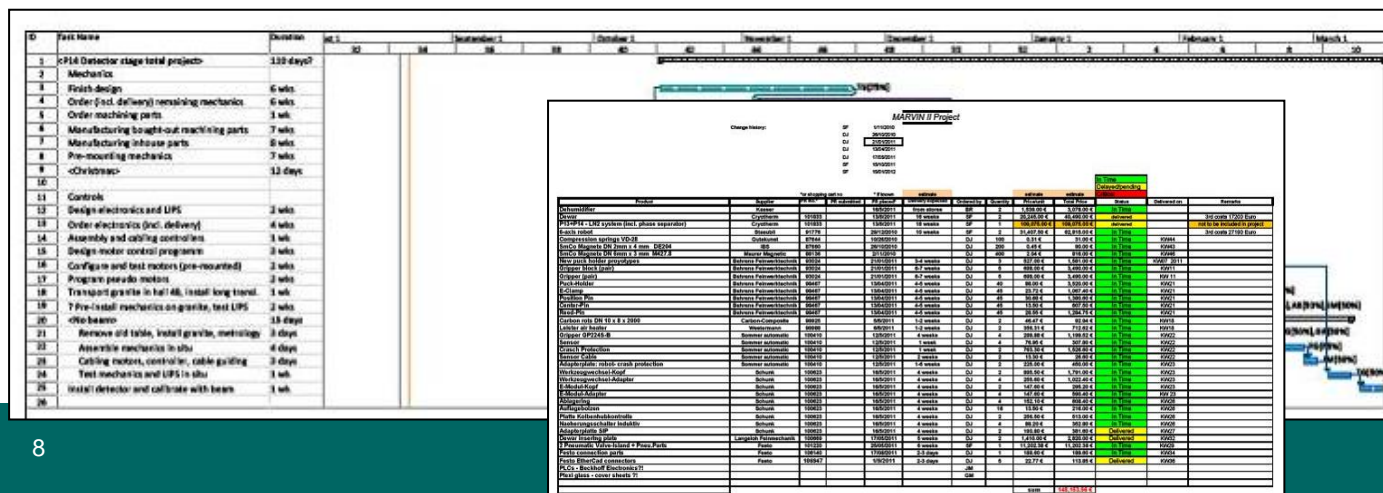
- User facilities for in-house and external research.
- Synchrotron beamlines are highly productive – more than 100000 protein structures deposited in PDB databank and 90% are determined from synchrotron data.
- Beamlines are multi-component facilities. To each instrument a project is related.



General approach:

- ## Use of simple planning tools:

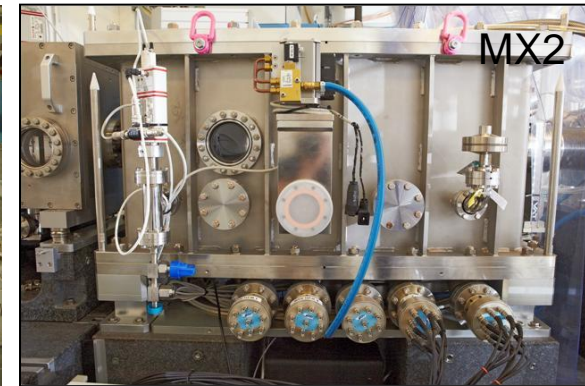
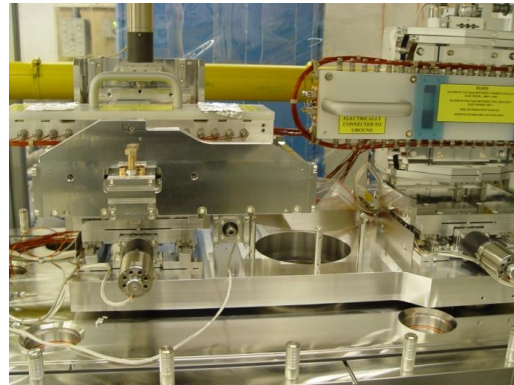
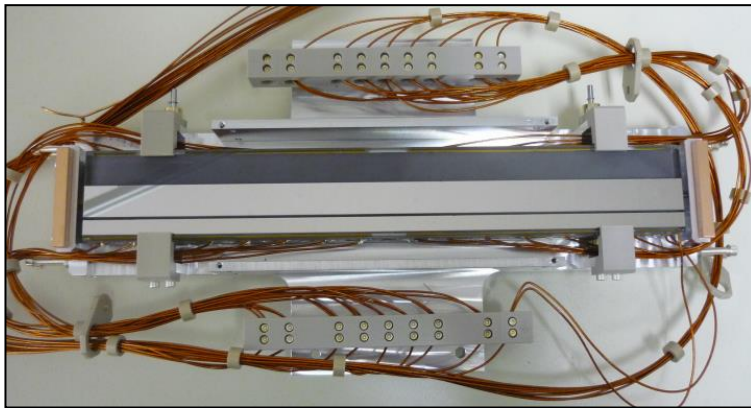
- | No | Duration | Work | Assigned to | Status / Comment |
|----|--------------------|--|-----------------------------------|--|
| | | Week 4 (Schedule) | | |
| 13 | Week 22 | Finish construction P13 & P14 stages | Thomas | In-progress |
| | Week 21 – P14 | Manufacture of in-house probeable parts for P13 & P14 | George + Boris | Started |
| 14 | Week 25 | Ordering, and delivery of all materials/parts for P12 | Thomas | In-progress, parts ordered in progress |
| 15 | Week 25 | P14 intermediate solution: Construction of interface + protective protection shield | Thomas | In-progress |
| 16 | Week 25 | P14 intermediate solution: Ordering + delivery mechanical parts, pneumatics | Thomas | In-progress |
| 17 | Week 24 | P14 temporary solution: Machining | George | |
| 18 | Week 23 | P14 temporary solution: Off-line installation of shroud | George (Thomas on hold) | |
| 19 | Week 24-26 | P14 temporary solution: software integration and off-line test | Anastasi + Uwe | |
| 20 | Week 26 (Shutdown) | Delivery + installation of P14 PLATUS detector | Uwe + Thomas | |
| 21 | Week 26/27 | P14 temporary solution: Off-line tests | Anastasi + Uwe | |
| 22 | Week 27 – 31 of 44 | Operation with temporary solution until September 15 (scheduled as October 15 th currently) | Uwe | |
| 23 | Week 28 | Prepare Redshift control electronics with P13 | Isichen | Started |
| 24 | Week 24 | Clean up P13-3 hatch, prepare storage on waste | All, Matt (orders placed) | Started |
| 25 | Week 26 – 29 | Mechanical installation P13 stage off-line in P14-3 | Thomas | |
| 26 | Week 23 – 28 | Prepare control software and safety logic and test installation of large BOSCH translation off-line | Uwe + Anastasi | Started |
| 27 | Week 29-31 | Implement control software and test P13 stage off-line including safety logic | Anastasi + Thomas + Isichen | |
| 28 | Week 30 (Shutdown) | De-install preliminary table and install P13 detector | Thomas + George | |
| 29 | Week 30/31 | Transfer/Install mechanically stage electronics and cabling of motion control on P13 baseframe | Thomas + George | P13 down |
| 30 | Week 31 – 32 | Implement and on-line test of control software and safety logic on P13 baseframe | Anastasi + Thomas + Uwe + Isichen | P13 down |
| 31 | Week 32/33 | Cells and commission P13 stage with Rayonix detector | Michael + Anastasi | |
| 32 | Week 33-36 | Operation with Rayonix detector | Michael | |
| 33 | Week 37 (Shutdown) | Delivery P13 PLATUS and installation on detector stage and test on-line | Thomas + Anastasi + Michael | |
| 34 | Week 21 | Ordering, and delivery of all materials/parts for P14 | Thomas | In-progress |
| 35 | Week 23 | Prepare Redshift control electronics rack for P14 | Isichen | |



Example project: focusing mirrors

Technical background

- Adaptive X-ray optics based on piezo actuators sandwiched between highly polished SiO_2 substrates (bimorph mirror).
- Similar layout for 3 beamlines (6 mirrors in KB geometry).
- System consists out of several principal components:
Bimorph mirrors; mirror HVBPS; precision positioning mechanics; UHV vessels and supports; mirror electronics; motion control (electronics).



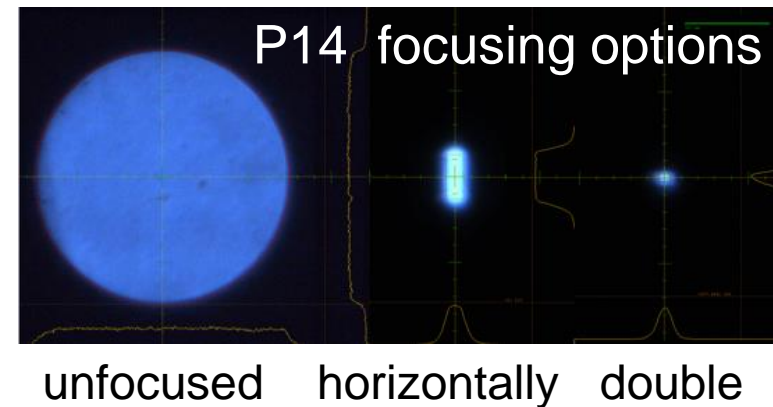
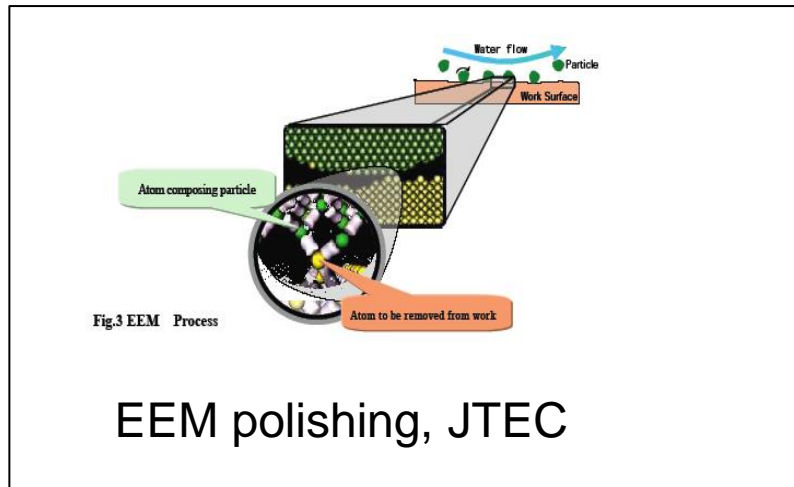
Focusing mirrors project

Project parameters

- Costs: 1.6 M€ estimation; 1.7 € (actual).
- Duration: 2 a (planned); 3.5 a (last mirror in operation).
- FTEs (in-house): 30 person months.

Strong points, challenges and risks

- High flexibility for modification in technology.
- Staggering of projects as a function of needs and resources possible.
- Small administrative overhead.

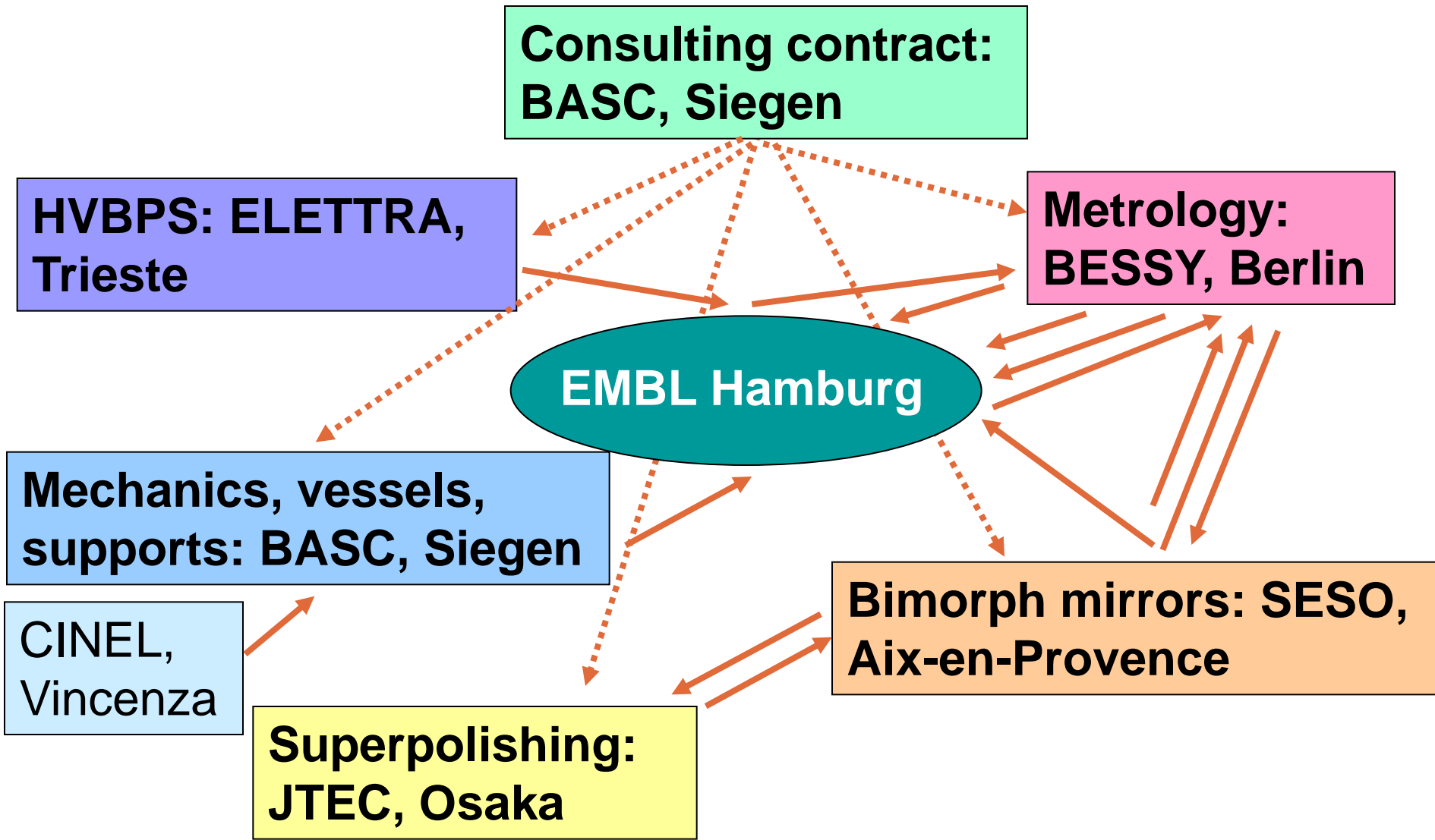


Challenges

General and human resource related

- Technology risks: deliveries not in specs; loops between metrology and manufacturer.
- Late deliveries by suppliers, availability of supplier.
- In particular in case of delay: Crossfire from projects that compete for resources or are dependent on availability of primary project or resources become necessary for standard operation.
- Limited possibilities to put pressure on suppliers ('small' customers with respect to overall business).
- High turnover of personnel (time limited contracts).
- General risks like transport, currency ...
- Limitations in apparatus to follow up complex contracts.

KB Mirrors: traffic of outsourced components



Challenges

Grant related

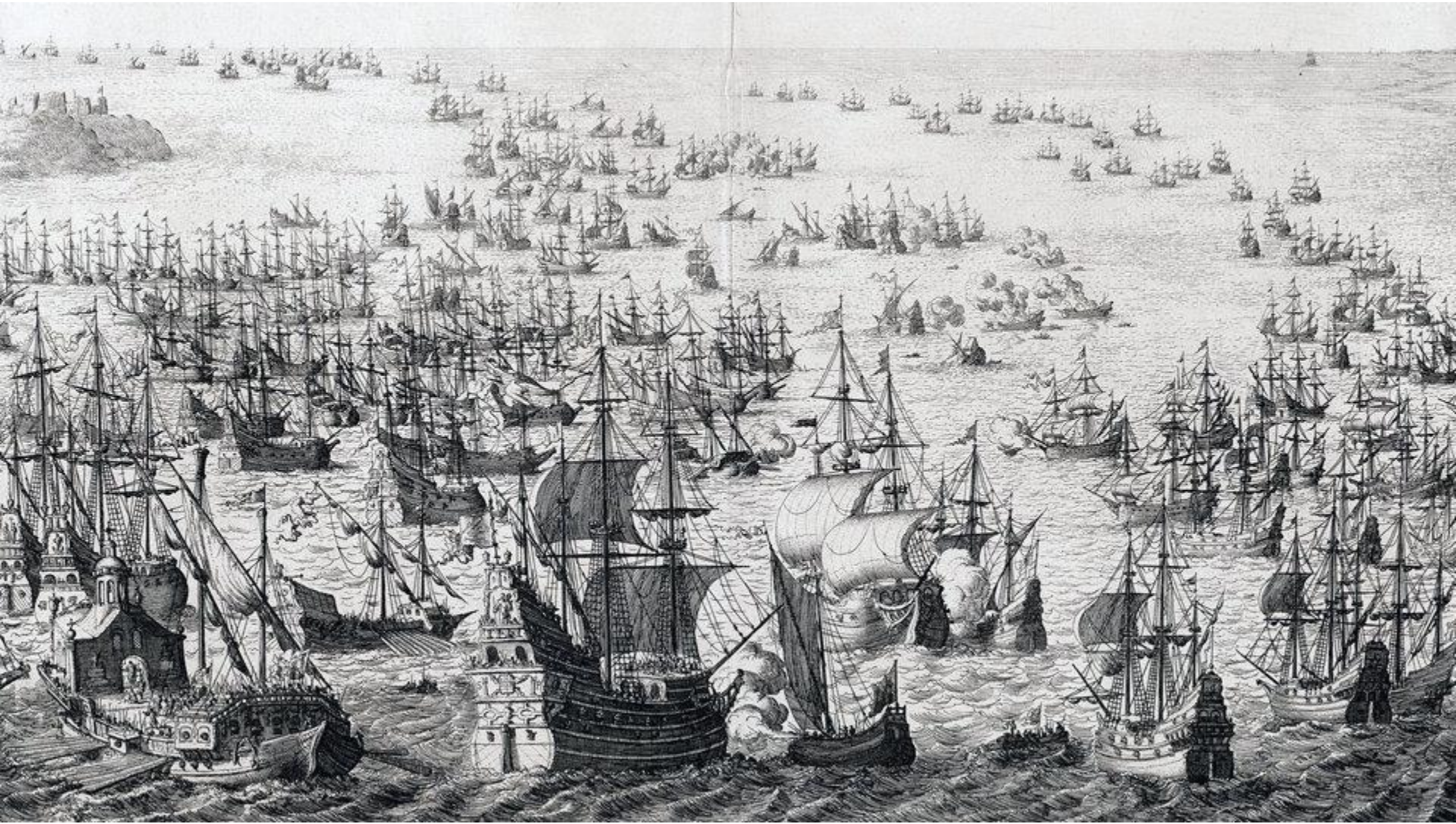
- Unrealistic timelines and spending profiles imposed by grants.
- ‘Politically’ motivated project budgets with unrealistic deliverables within available budget; insufficient planning period.
- Most grants don’t include contingencies.
- Work-around: list of features that can be canceled or postponed and financed by follow-up grants.
- ...



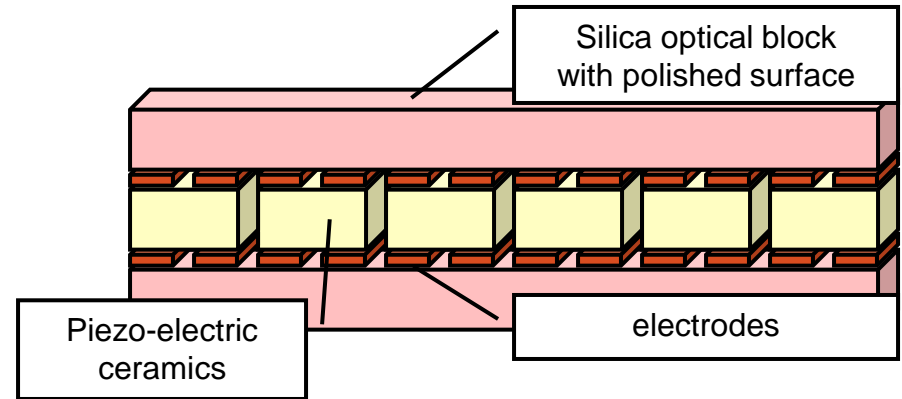
Cost explosion:
From 70M€ to 700 M€.

Hamburg; Elbphilharmonie

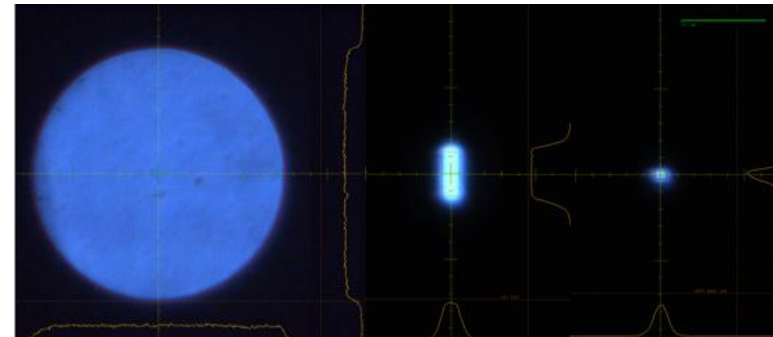
Thank you for your attention!



The galleons of the Spanish armada attacked by the English fleet

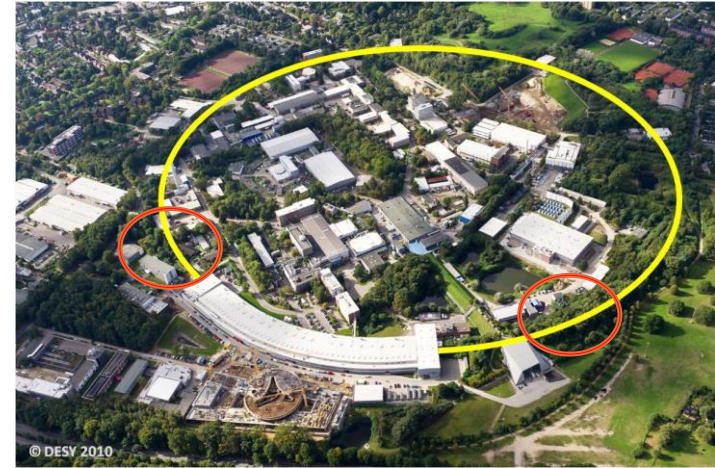


Beam size at focus	Vertical [μm] FWHM	Horizontal [μm] FWHM
BioSAXS/P12	113	200
MX1/P13	23	29
MX2/P14	5	7



PETRA III shutdown in 2014 & new facilities

- Storage ring shutdown 02/14 – 04/15
- PETRA III extension halls



East hall

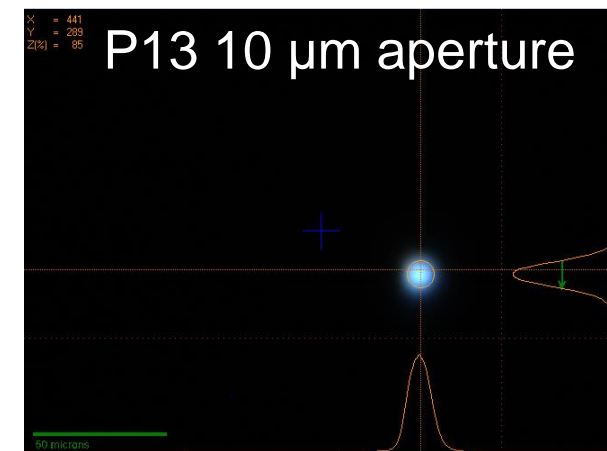
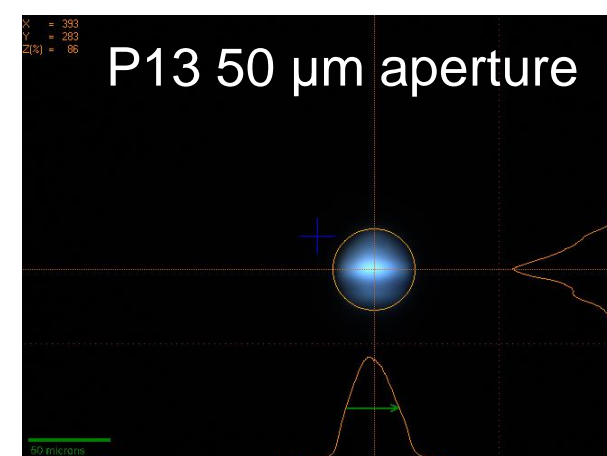


North hall

KB mirrors: Focusing results

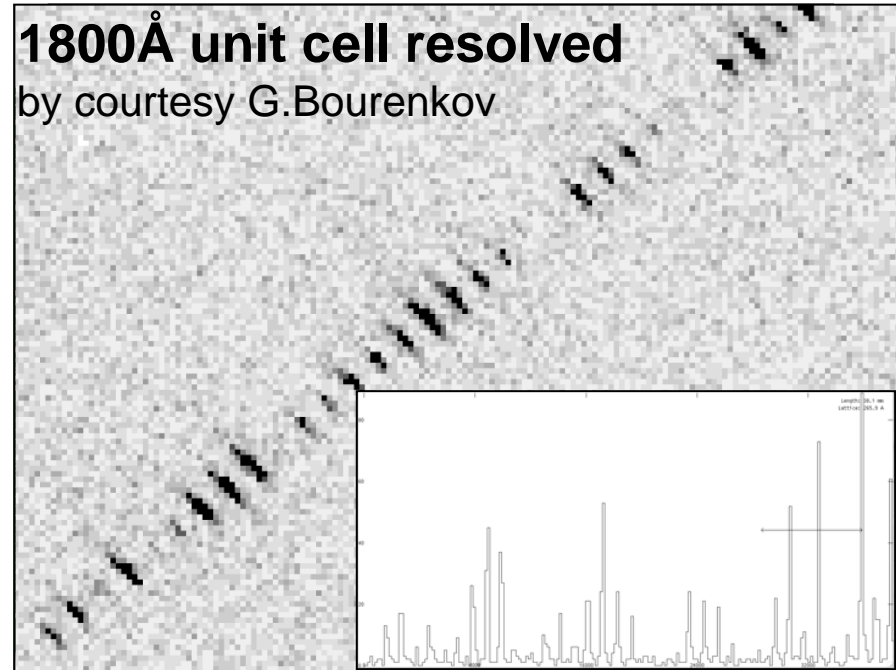
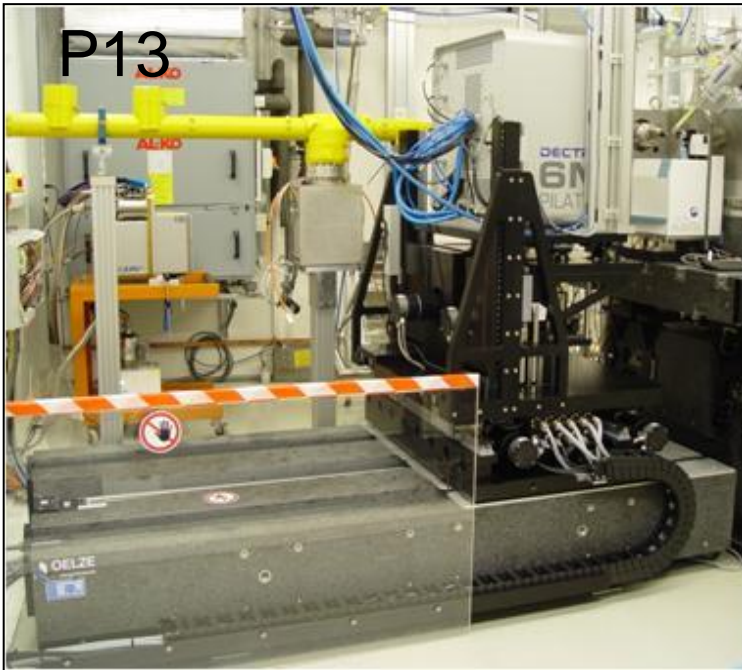
Beam size at focus	Vertical [μm] FWHM	Horizontal [μm] FWHM
BioSAXS/P12	113	200
MX1/P13	23	29
MX2/P14	5	7

- Intensity in focus: beamline dependent, varies between 5×10^{12} ph/s – 2×10^{13} ph/s.
- Residual vertical beam structure in focus.
- Homogeneous part can be selected with pinhole.
- (Automatic) toggling between focused and unfocused beam possible (P14, P13).

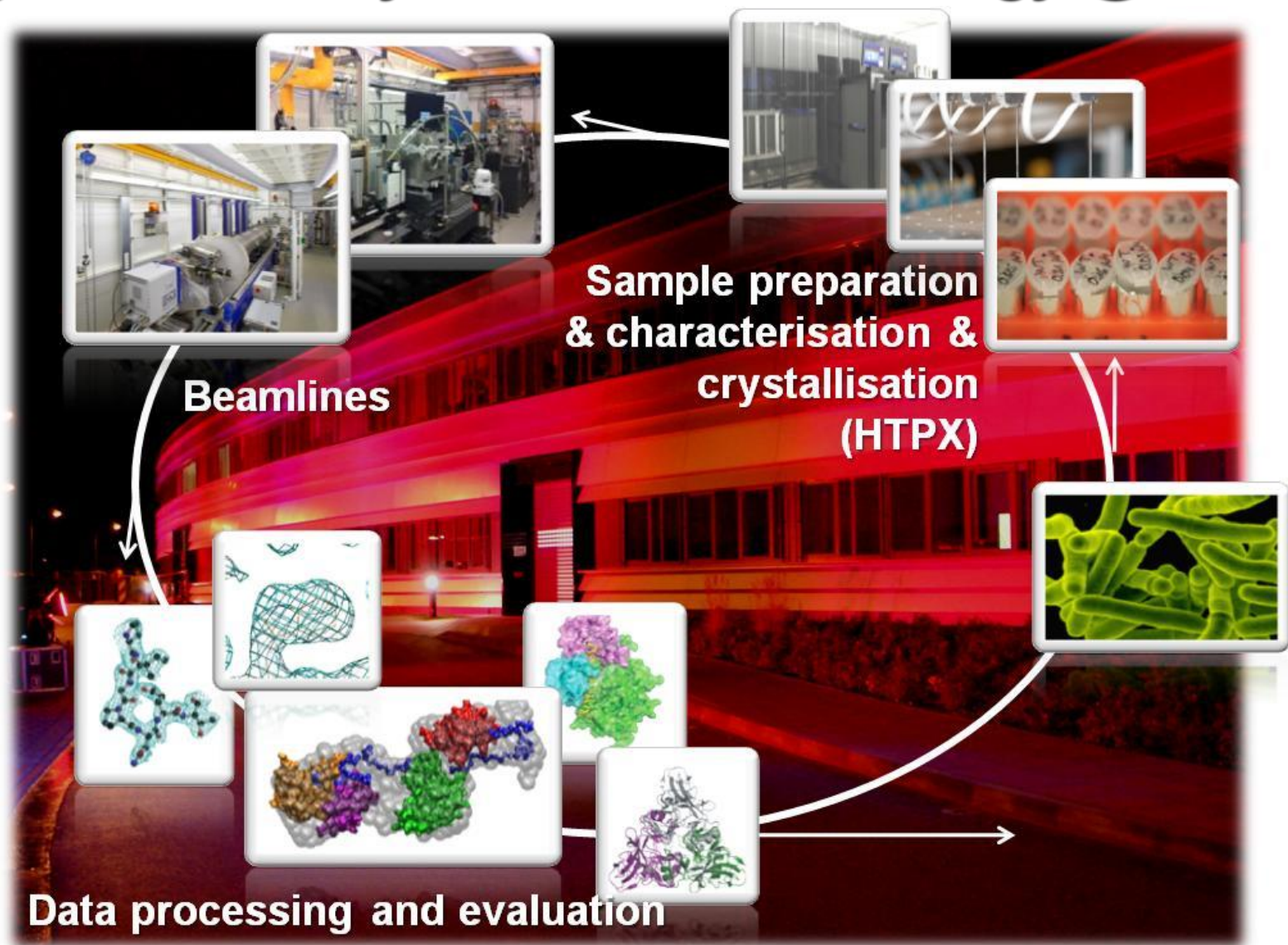


Detectors (supports) for MX

- PILATUS 6M pixel detectors (direct conversion)
- Detector stages with 4(5) motorized and encoded degrees of freedom mounted on long granite supports (1.5m P13; 4m P14).
- Large 2θ inclination (P13).
- Long lateral detector translation for swapping between detectors (P14).

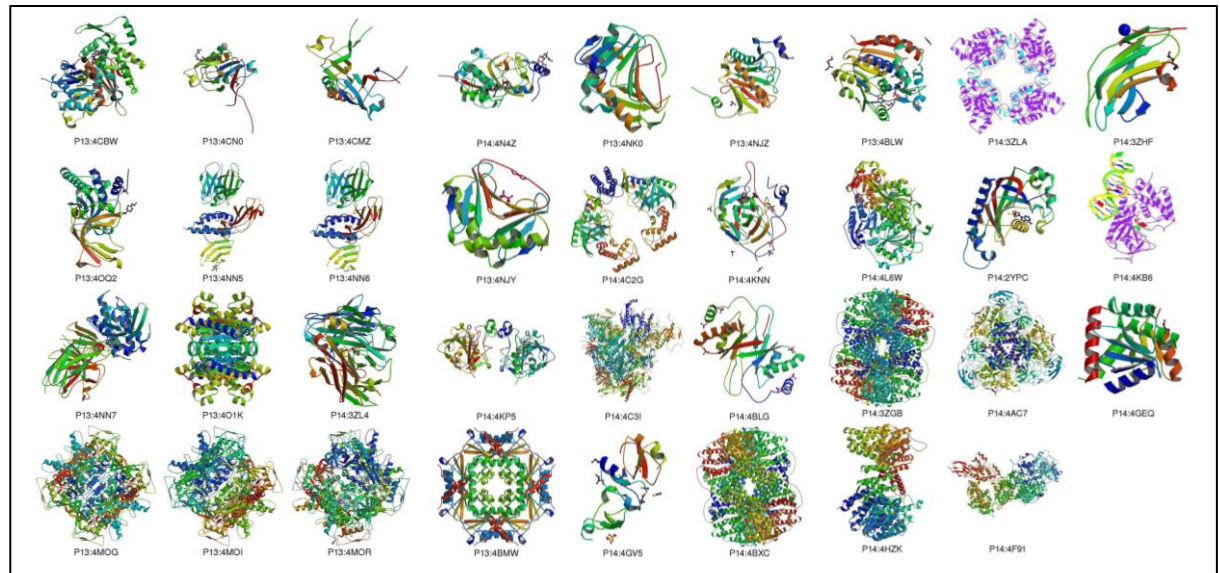
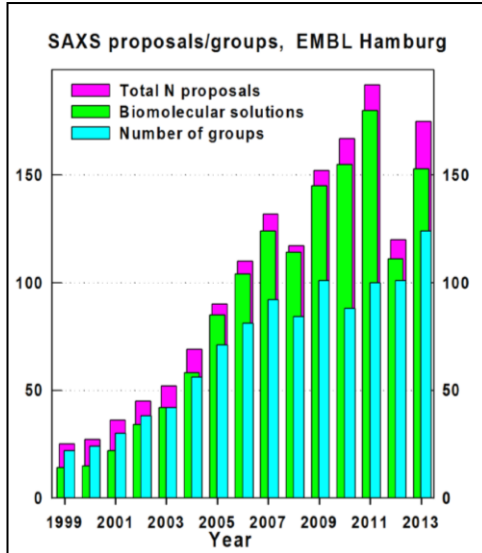


Integrated Facility for Structural Biology @PETRA III



User operation

- All beamlines in regular user operation.
- P12 (09/12 – 02/14)
No of User visits: 491
No experiments: 225 (incl. HZG) +16 (remote)
- No of PDB depositions (P13+P14) > 35.
- No of publications for all beamlines > 50 (including Nature, Cell, PNAS).



Summary

- Beamlines equipped with (nearly) all instruments from original design and performing excellently.
- Most of technical problems solved.
- Successful user operation on all beamlines.
- New projects under way to keep facilities at the cutting edge.

Acknowledgments

Thomas Schneider and group
Gleb Bourenkov,
Michele Cianci

Dmitri Svergun and group
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Spilotros, Ursula Tietze (HZG)

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EMBL Grenoble
Florent Cipriani and group

DESY
Horst Schulte-Schrepping
Ilya Sergeev, Ralf Doehrmann



EMBL Hamburg instrumentation team

+



Thank you !



Hamburg construction sites



