NMX – A Macromolecular Diffractometer at the ESS

Esko Oksanen
Scientific Project Leader

ESS Science Symposium on Crystallography for Soft Matter, Prague 2015-09-08

Outline

- **Introduction to neutron macromolecular crystallography – a scientific case for NMX**
- Functional requirements
- Layout and components overview
- Expected performance

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NMX Instrument team

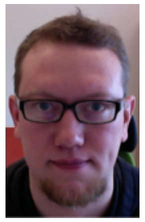
Partners

Institut de Biologie Structurale

Centre for Structural Biology · Aarhus University ·

WIGNER

Scientific Project Leader



Esko Oksane n

Lead Instrument Engineer

Giuseppe Aprigliano

Neutron Optics and Shielding

Valentin a Santoro

Phillip Bentley

Damian Martin-Rodriguez

Neutron Choppers

Iain Sutton

Markus Olsson

Motion Control & Automation

Thomas Gahl

Paul Barron

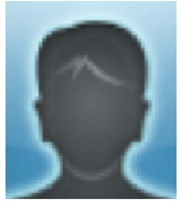
Neutron Detectors

Richard Hall-Wilton

Dorothea Pfeiffer

Data Management & Software Center

Thomas Holm Rod

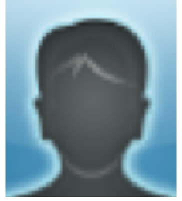


Jonathan Taylor

Planning office

Magnus Israelsson

Systems Engineering Support



Peter Sångberg

Scientific and Technical Advisory Panel (STAP) for Macromolecular Crystallography

John Helliwell, University of Manchester, UK Chair

Paul Langan, ORNL, TN, USA

Sean McSweeney, BNL, NY, USA

Derek Logan, Lund University, Sweden

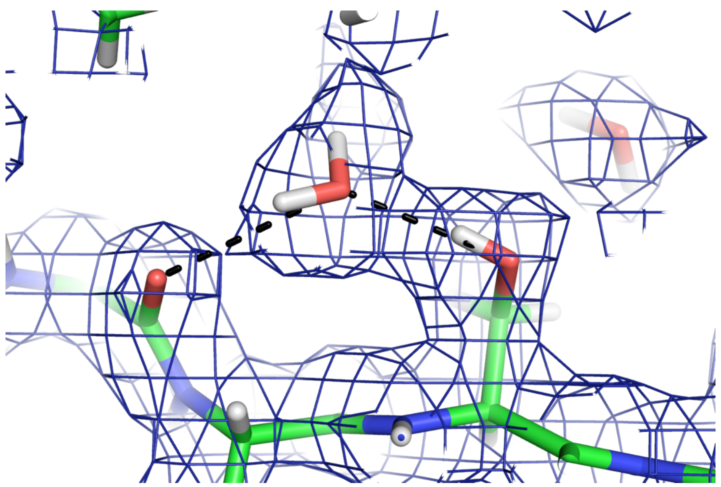
Matthew Blakeley, ILL, France

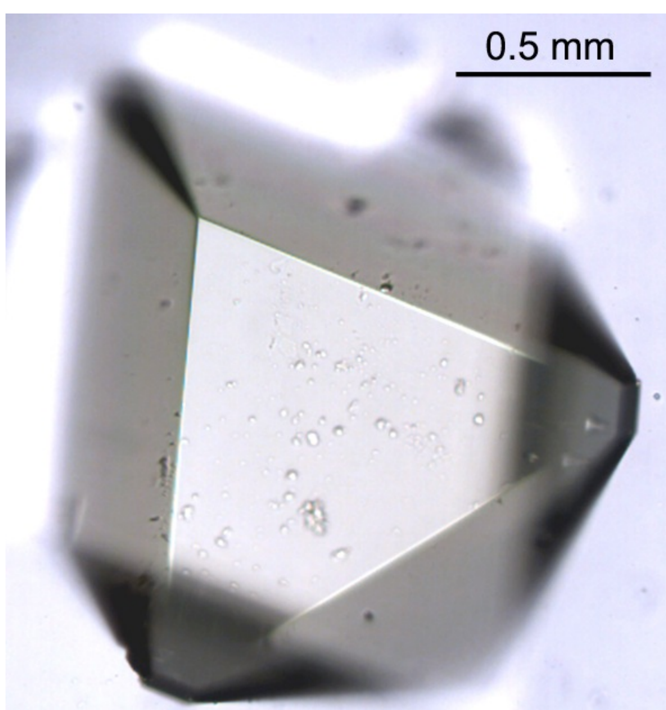
Nobuo Niimura, Ibaraki University, Japan

Manuel Angst, FZJ, Germany

Structural biology with neutrons

Crystallography





Oksanen, E *et al. J. R. Soc. Interface* **2009**, *6 Suppl 5*, S599-610.

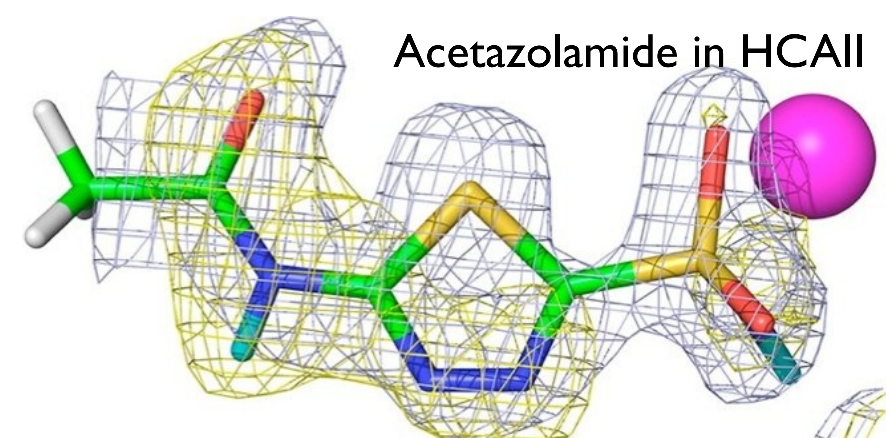
- ☺ Hydrogens are visible
- ☺ No radiation damage
- ☹ Large crystals needed
- ☹ Data collection takes weeks
- ☹ Few instruments available

Where are hydrogens important?

Enzyme mechanisms

Protein-ligand interactions

Proton transport across membranes



Fisher SZ et al. JACS 2012;134:14726-14729

Scientific drivers - Locating hydrogens in bio-macromolecules

Key advantages of ESS Macromolecular Diffractometer

Smaller crystals needed (200 μm vs. 1 mm)

Data collection faster (days vs. weeks)

Larger unit cells possible (300 Å vs. 150 Å)

The Nobel Prize in Chemistry 2009
Venkatraman Ramakrishnan, Thomas A. Steitz, Ada E. Yonath

Venkatraman Ramakrishnan - Facts

Photo: U. Montan

Venkatraman Ramakrishnan

Born: 1952, Chidambaram, Tamil Nadu, India

Affiliation at the time of the award: MRC Laboratory of Molecular Biology, Cambridge, United Kingdom

Prize motivation: "for studies of the structure and function of the ribosome"

Field: Biochemistry, structural chemistry

"Hydrogens represent nearly half of the atoms in biomolecules. Hydrogen bonding and proton transfer play a critical role in biological structure and in catalytic mechanisms." V. Ramakrishnan, University of Cambridge

The Nobel Prize in Chemistry 1988
Johann Deisenhofer, Robert Huber, Hartmut Michel

Hartmut Michel - Facts

Hartmut Michel

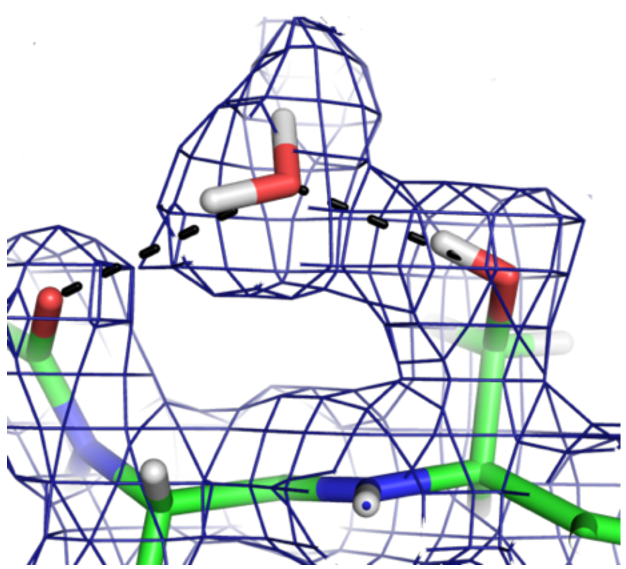
Born: 18 July 1948, Ludwigsburg, West Germany

Affiliation at the time of the award: Max-Planck-Institut für Biophysik, Frankfurt-on-the-Main, Federal Republic of Germany

Prize motivation: "for the determination of the three-dimensional structure of a photosynthetic reaction centre"

Field: biochemistry, structural chemistry

"There is no alternative to neutron crystallography in order to uniquely identify the location of protons, which is of particular importance when dealing with proton translocating proteins" H. Michel, MPI of Biophysics



ASTBURY CENTRE — UNIVERSITY OF LEEDS

"-One of our first questions using the ESS MX beamline will be to understand the protonation states of the reactive site aspartate acids, which will help us understand the mechanism and so lead to novel drug molecules. This, given the size of the protein, is impossible with any current technology." A. Goldman, University of Leeds

Outline

- Introduction to neutron macromolecular crystallography – a scientific case for NMX
- **Functional requirements**
- Layout and components overview
- Expected performance

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Requirements

Table 4.2-2 Requirements Metadata

Item	Function
Requirement ID	Provides a unique numbering system for sorting and tracking.
Rationale	Provides additional information to help clarify the intent of the requirements at the time they were written. (See "Rationale" box below on what should be captured.)
Traced from	Captures the bidirectional traceability between parent requirements and lower level (derived) requirements and the relationships between requirements.
Owner	Person or group responsible for writing, managing, and/or approving changes to this requirement.
Verification method	Captures the method of verification (test, inspection, analysis, demonstration) and should be determined as the requirements are developed.
Verification lead	Person or group assigned responsibility for verifying the requirement.
Verification level	Specifies the level in the hierarchy at which the requirements will be verified (e.g., system, subsystem, element).

Rationale

The rationale should be kept up to date and include the following information:

- **Reason for the Requirement:** Often the reason for the requirement is not obvious, and it may be lost if not recorded as the requirement is being documented. The reason may point to a constraint or concept of operations. If there is a clear parent requirement or trade study that explains the reason, then reference it.
- **Document Assumptions:** If a requirement was written assuming the completion of a technology development program or a successful technology mission, document the assumption.
- **Document Relationships:** The relationships with the product's expected operations (e.g., expectations about how stakeholders will use a product). This may be done with a link to the ConOps.
- **Document Design Constraints:** Imposed by the results from decisions made as the design evolves. If the requirement states a method of implementation, the rationale should state why the decision was made to limit the solution to this one method of implementation.

NMX

1. System requirements

High level scientific requirements for the instrument (13.6.4)

1. The instrument shall allow data collection from crystals with unit cell repeats > 300 Å.
2. The instrument shall allow data to be collected to a d_{min} of 1.5 Å.
3. The instrument shall match the size of the neutron beam to the size of the sample.
4. The instrument shall match the divergence of the neutron beam to the mosaicity of the sample.
5. The instrument should maximise the signal-to-background (S/B) ratio of the Bragg reflections.
6. The instrument should allow data collection from crystals of < 0.01 mm^3 volume

General notes

Instrument parameters that are defined as user selectable should be selectable with < 15 min delay (ref ConOps).

1.1 Functional Requirements for NMX subsystems

1.1.1 Beam transport system (BTS) (13.6.4.1)

1. **Wavelength resolution**
   1.1. The BTS shall transport from the moderator a beam of neutrons to the sample at a distance that leads to a maximal wavelength uncertainty of 5% (Δ/) for the detected neutrons using the full ESS pulse
   1.2. Rationale: A moderate wavelength resolution allows the full pulse to be used while conserving the advantage of TOF for the S/B (see 13.6.4 (5))
   1.3. Verification: Measurement of the pulse length at sample
2. **Beam size**
   2.1. The BTS shall transport from the moderator to the sample a beam of neutrons with maximum size (full width half maximum) of 5 ± 0.1 mm and minimum size of 0.2 ± 0.02 mm.
   2.2. Rationale: Matching the beam size to the sample size maximises the S/B (see 13.6.4 (3,5-6))
   2.3. Verification: Measurement of the beam intensity profile at sample

Esko Oksanen, European Spallation Source

High-level Scientific Requirements

- 1. The instrument shall allow data collection from crystals with unit cell repeats > 300 Å.
- 2. The instrument shall allow data to be collected to a d_{min} of 1.5 Å.
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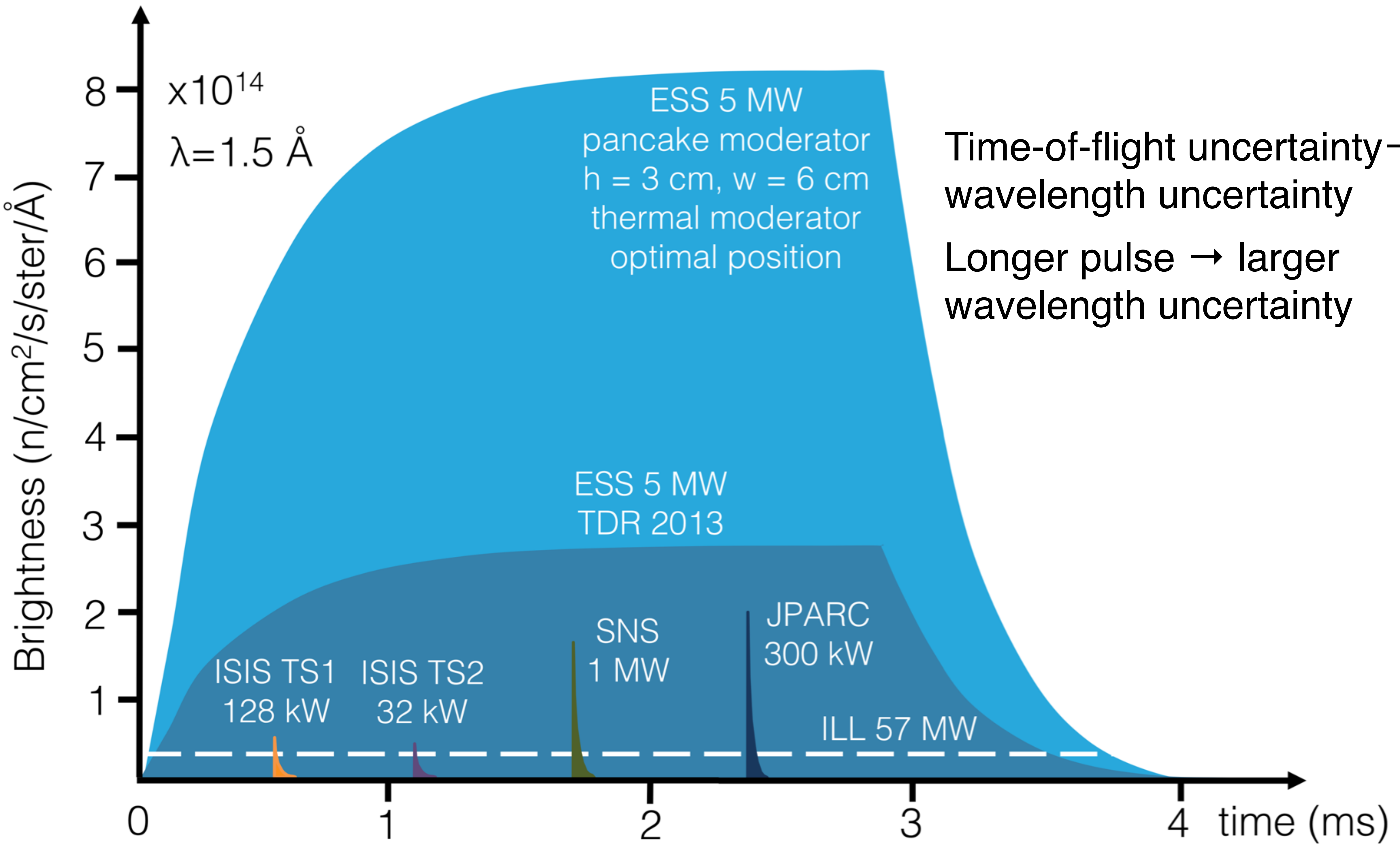
ESS Long-Pulse



Time-of-flight uncertainty → wavelength uncertainty

Longer pulse → larger wavelength uncertainty

NMX – A quasi-Laue time-of-flight diffractometer with high **q**-resolution

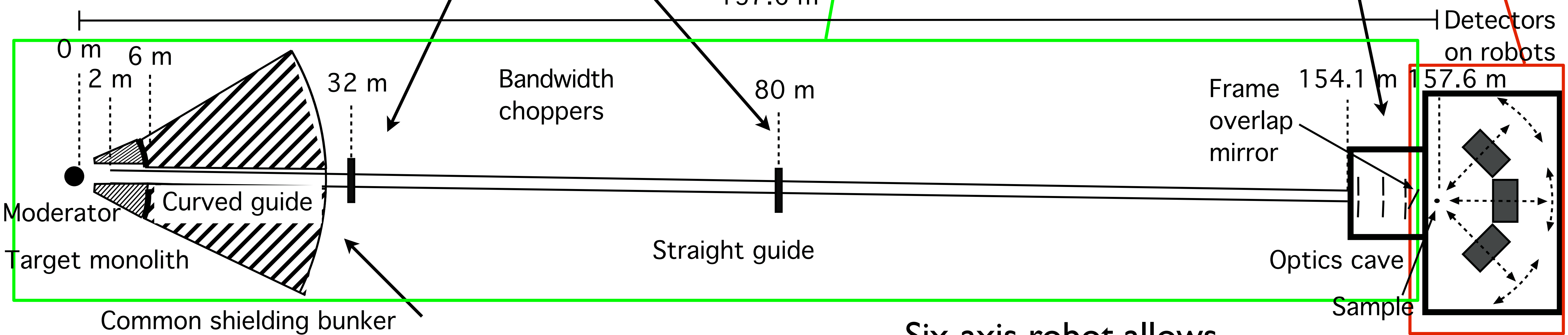
Existing technology

Needs R&D

Adjustable opening chopper allows flexible bandwidth selection.

Collimation section giving flexibility in beam size and divergence

Cold moderator



1.74 Å wavelength band (1.8-3.55 Å)

m=1 is sufficient on three sides, m=2.2 for curving

Six-axis robot allows selecting crystal orientation

Three 60 x 60 cm detectors with 0.2 mm spatial resolution
Variable sample-detector distance (0.2-1.0 m)
Variable 2θ angle (0-110°)

- Match beam size to sample size (max 5 x 5 mm)
- Match beam divergence to sample mosaicity (max. ±0.2°)
- Maximize (useful) flux at sample!

BTS Subsystem Requirements

Functional requirements

1. Wavelength resolution

1.1. The BTS shall transport from the moderator a beam of neutrons to the sample at a distance that leads to a maximal wavelength uncertainty of 5% ($\Delta\lambda/\lambda$) for the detected neutrons using the full ESS pulse

→ ~150 m flight path

1.2. Rationale: A moderate wavelength resolution allows the full pulse to be used while conserving the advantage of TOF for the S/B (see 13.6.4 (5))

1.3. Verification: Measurement of the pulse length at sample

2. Beam size

2.1. The BTS shall transport from the moderator to the sample a beam of neutrons with maximum size (full width half maximum) of 5 ± 0.1 mm and minimum size of 0.2 ± 0.02 mm.

→ ~ 3 cm guide

2.2. Rationale: Matching the beam size to the sample size maximises the S/B (see 13.6.4 (3,5-6))

→ ±0.1 K temperature stability

2.3. Verification: Measurement of the beam intensity profile at sample

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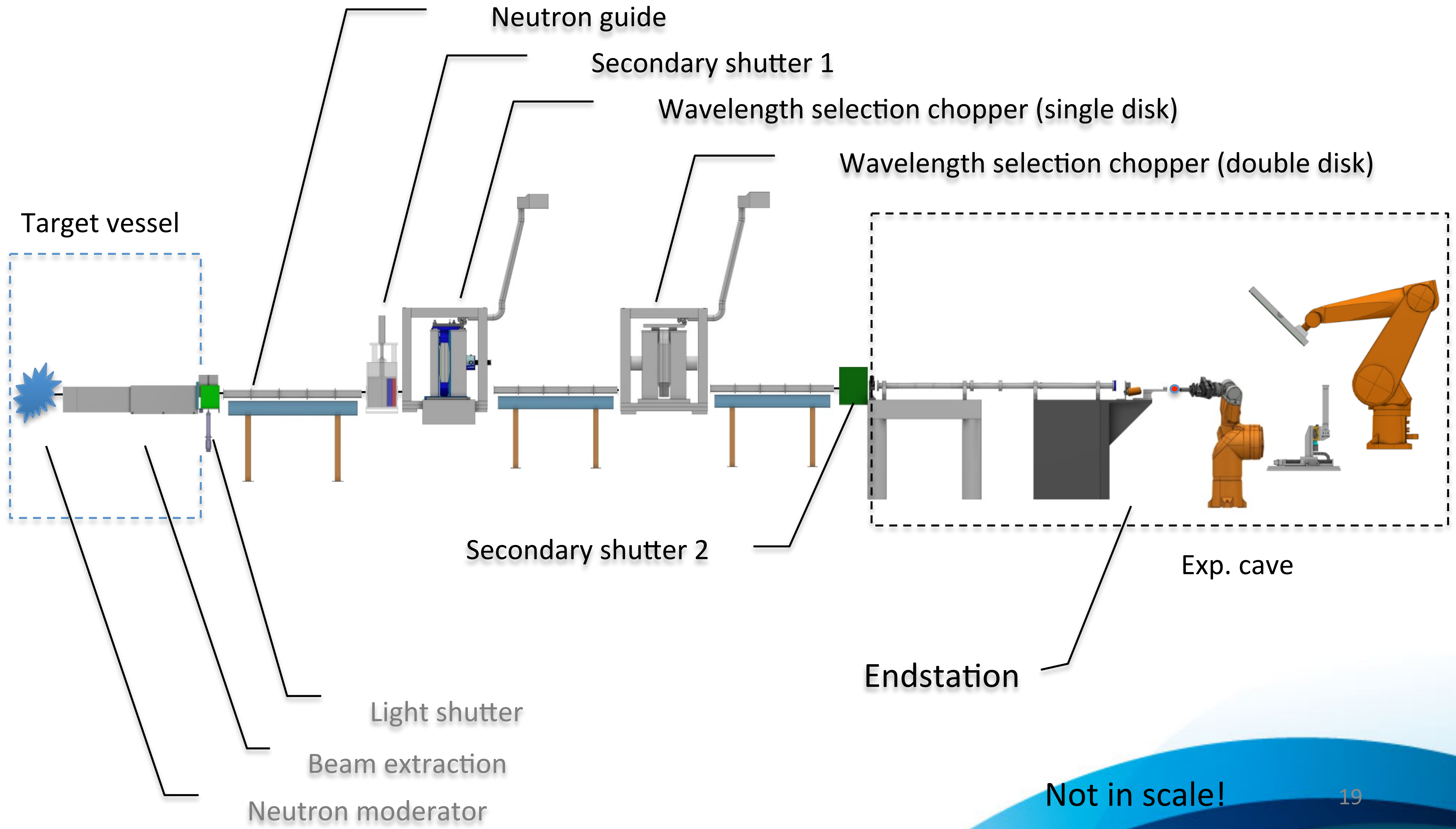
- **Layout and components overview**
- Expected performance

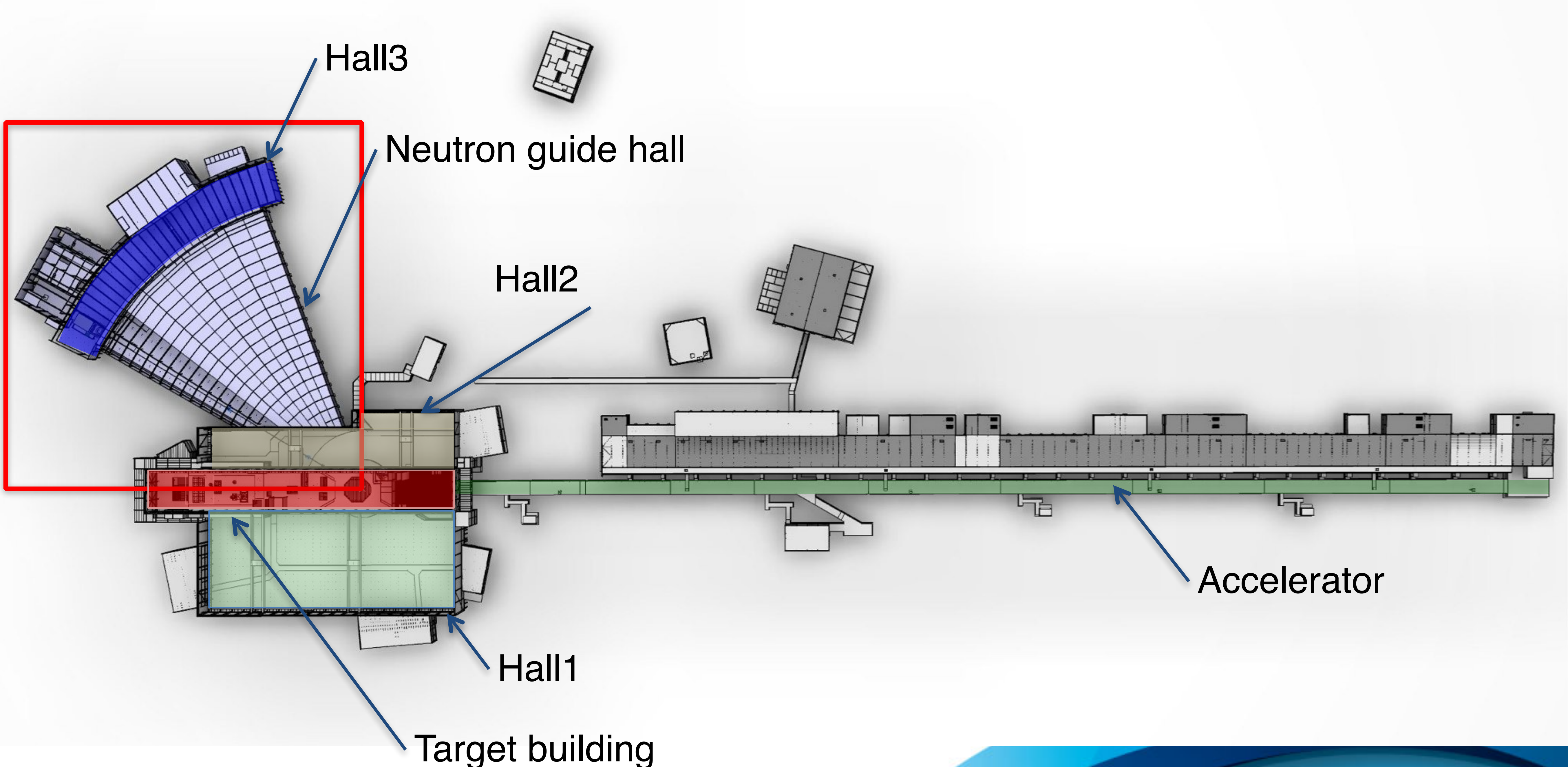
NMX Overview



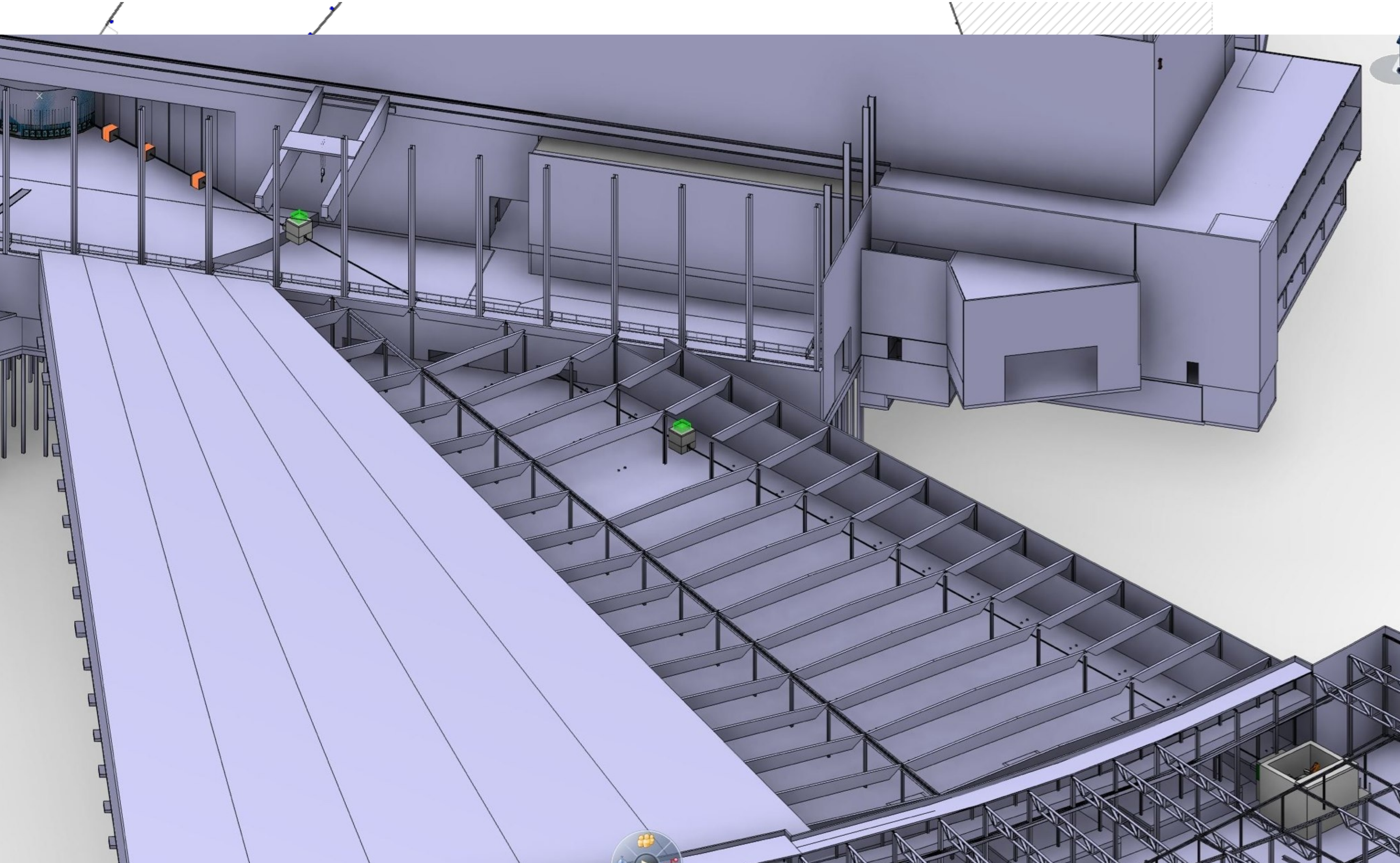
Not in scale!

Esko Oksanen, European Spallation Source

ESS Layout


Hall3
Neutron guide hall
Hall2
Accelerator
Hall1
Target building

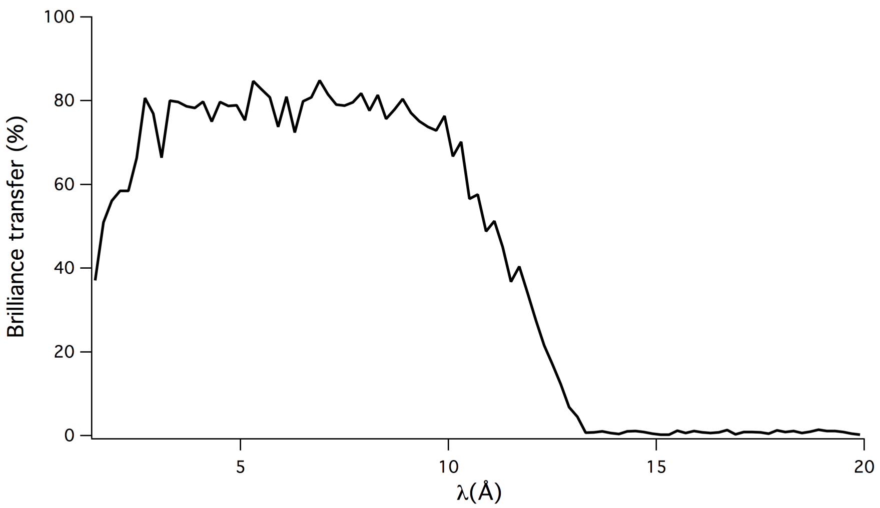
NMX layout



Damian Martin Rodriguez

Optics overview

Curved inside bunker, optimised for maximum brilliance transfer at 2Å



- Monolith insert horizontally straight, vertically tapers from 31 mm to 46 mm, m =2 horizontal, m = 1 vertical
- 1.2 km curvature radius within bunker
- m = 2.2 on the curve, otherwise m = 1
- Line of sight lost at 31.5 m from the moderator
- Straight guide up to 154.1 m from the moderator, m = 1
- Frame overlap mirror for λ > 10 Å

Optics concept choice - pros

Damian Martin Rodriguez

Option 4: Curved inside bunker, optimised for maximum brilliance transfer at 2Å

- Acceptable performance for ±0.2° divergence at < 2 Å
- Good performance all round for ±0.1° divergence – this range is more typical for experiments
- Loss of line-of-sight almost within bunker – lower shielding cost & easier component maintenance
- Deflects the beam far enough from the sector centreline to allow two beams to be extracted from the same beamport

Choppers

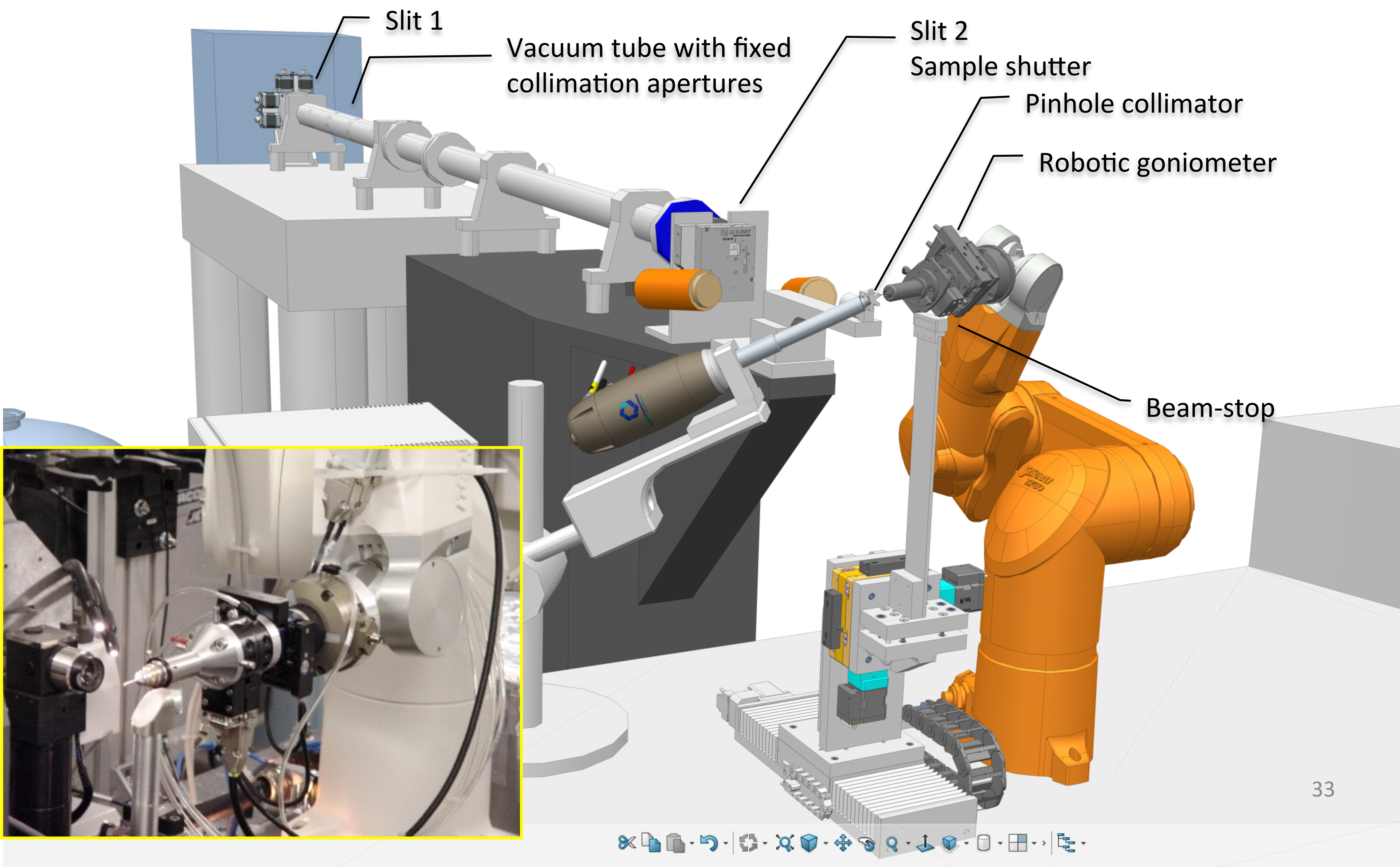
Markus Olsson

- Choppers are for wavelength selection
- Single disc chopper at 32 m, co-rotating double disc chopper at 80 m
- Transmission has priority
- Frame overlap suppressed for $\lambda < 12.4$ Å
- Penumbra should be minimized
- No choppers in common bunker

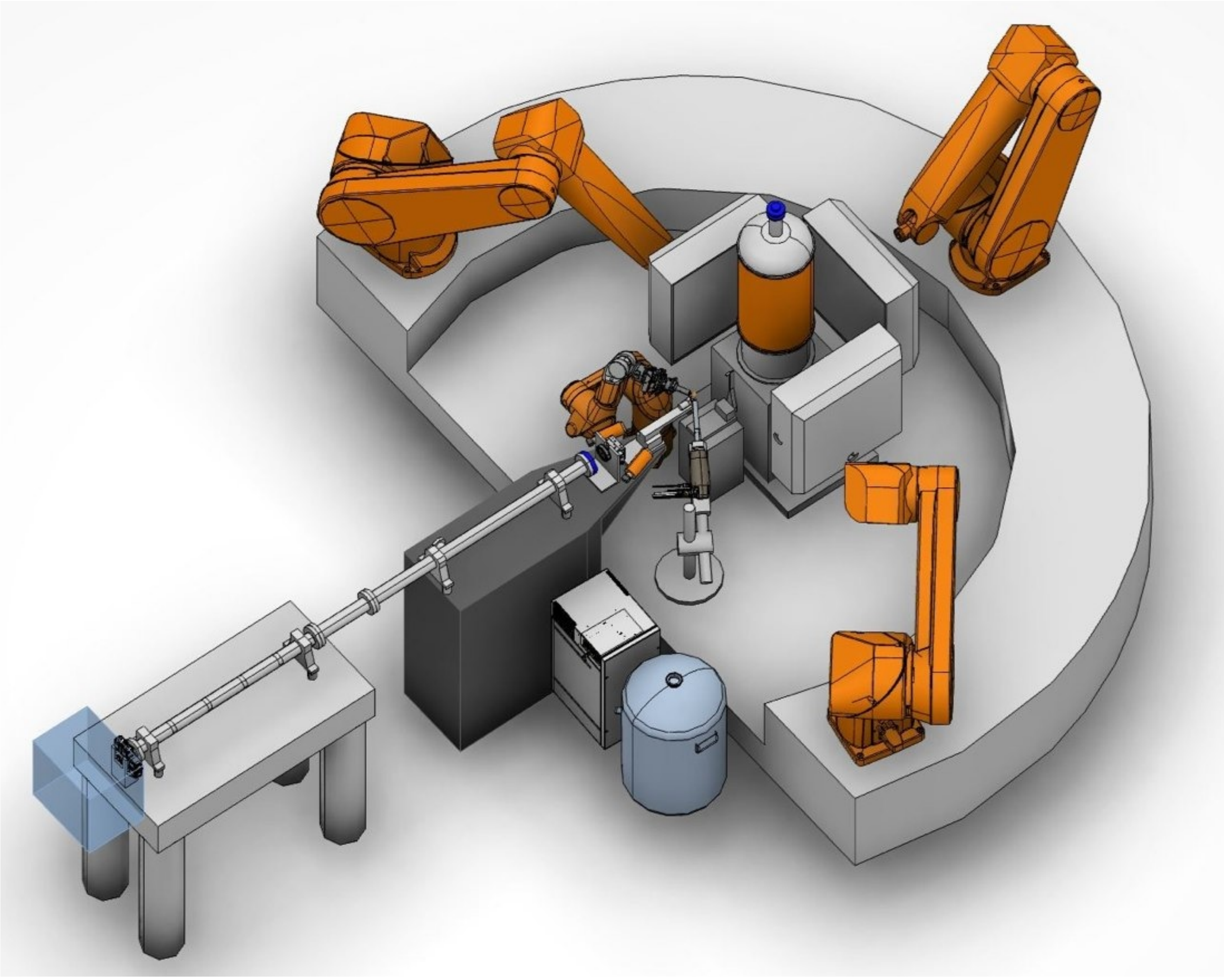
Always 14Hz

Control bandwidth by change of phase and variable openings

Endstation design



Detector geometry

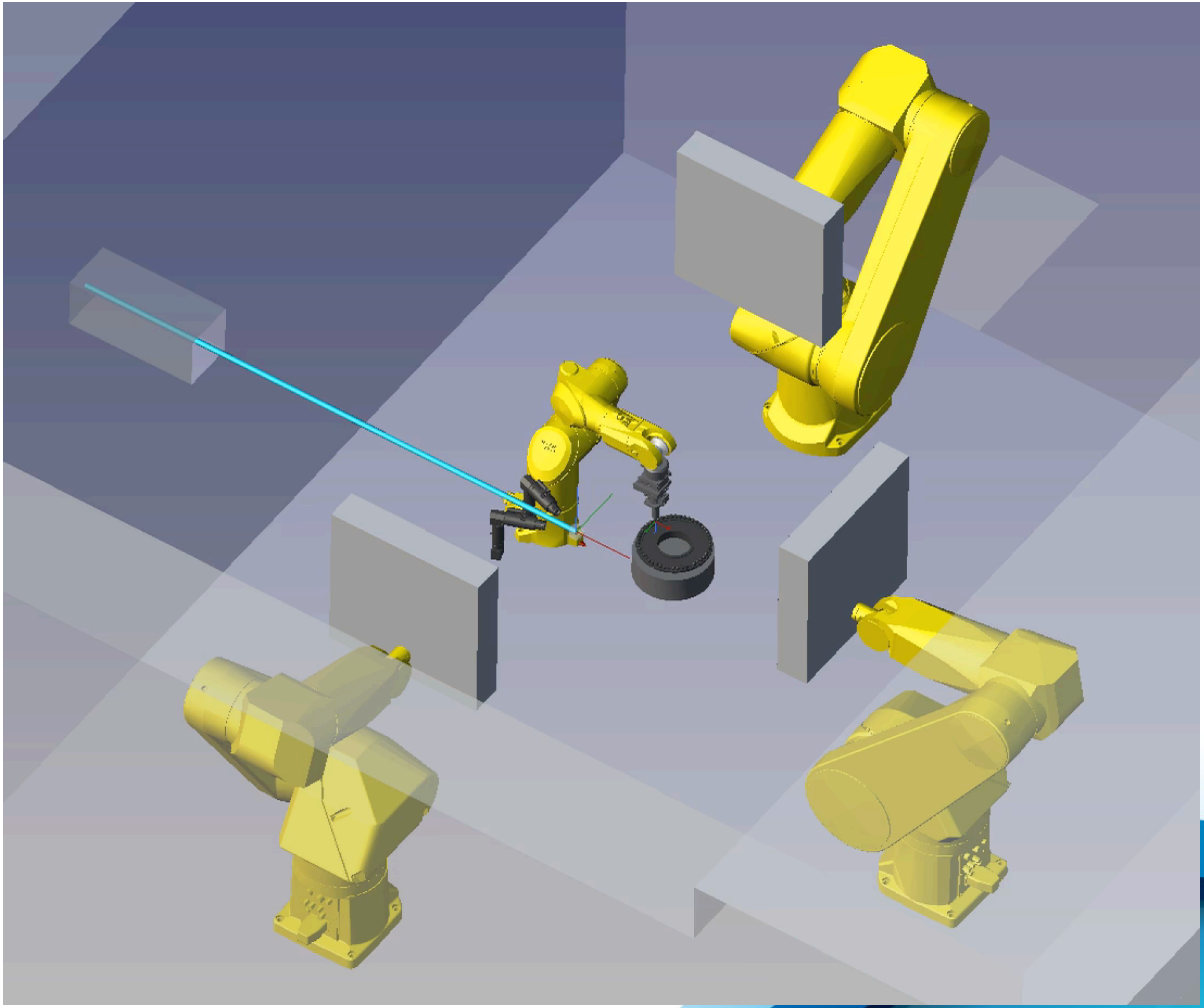


Robotic goniometer allows choice of sample rotation axis direction

Three 60 x 60 cm detectors with 0.2 mm spatial resolution
Sample-detector distance (0.2-1.0 m) and 2θ angle (0-110°) variable by robotic positioning

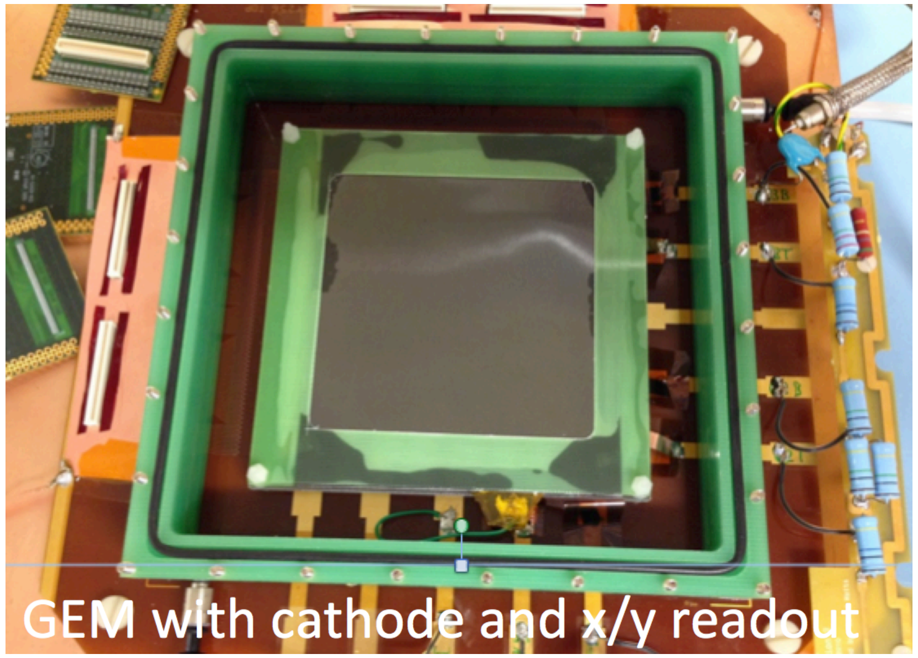
- Solid angle coverage can be traded for unit cell size
- Large unit cells will take longer to collect

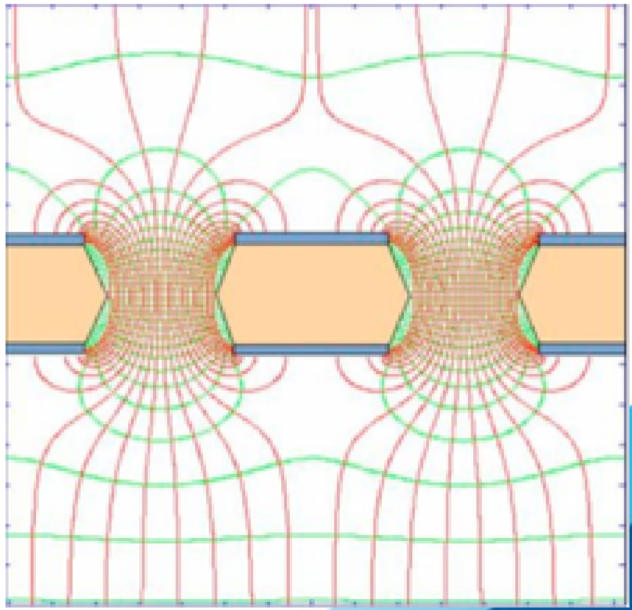
Detector geometry

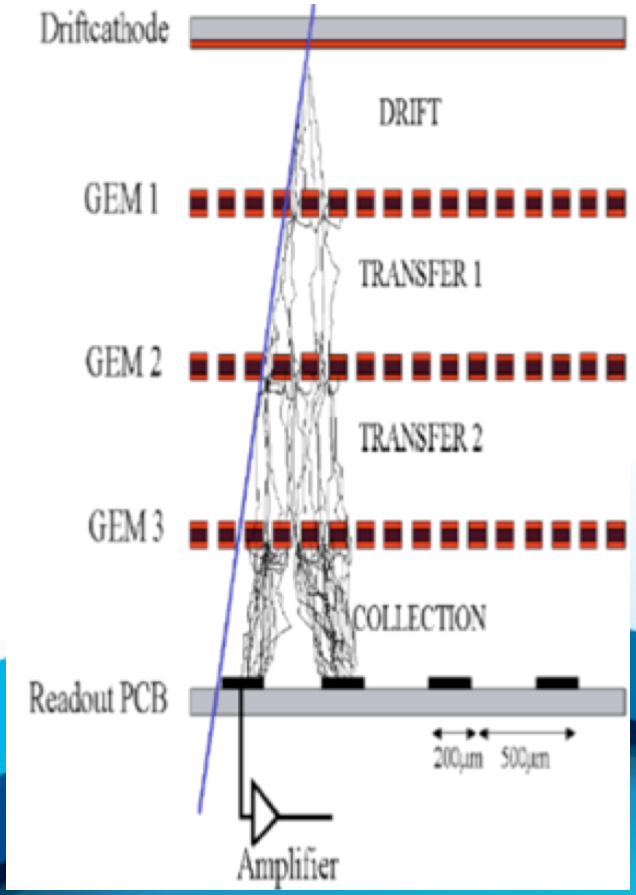


Detectors - technological risk and mitigation strategy

- R&D required to reach 0.2 mm spatial resolution with reasonable area and efficiency
- Gd coated micropattern (GEM) detectors promising - prototypes developed at CERN
- GEM detectors widely used in particle physics
- Large areas readily available

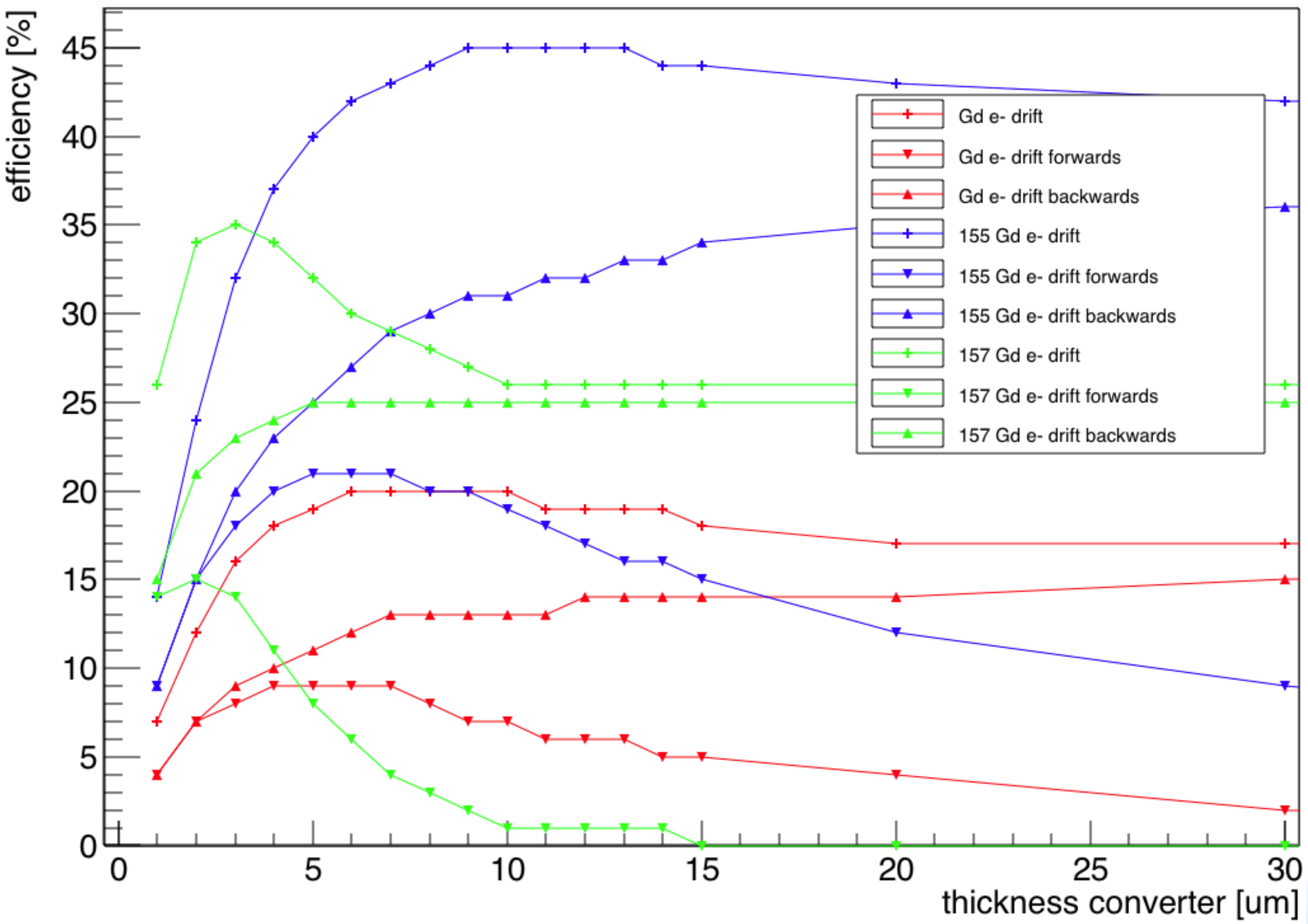

GEM with cathode and x/y readout



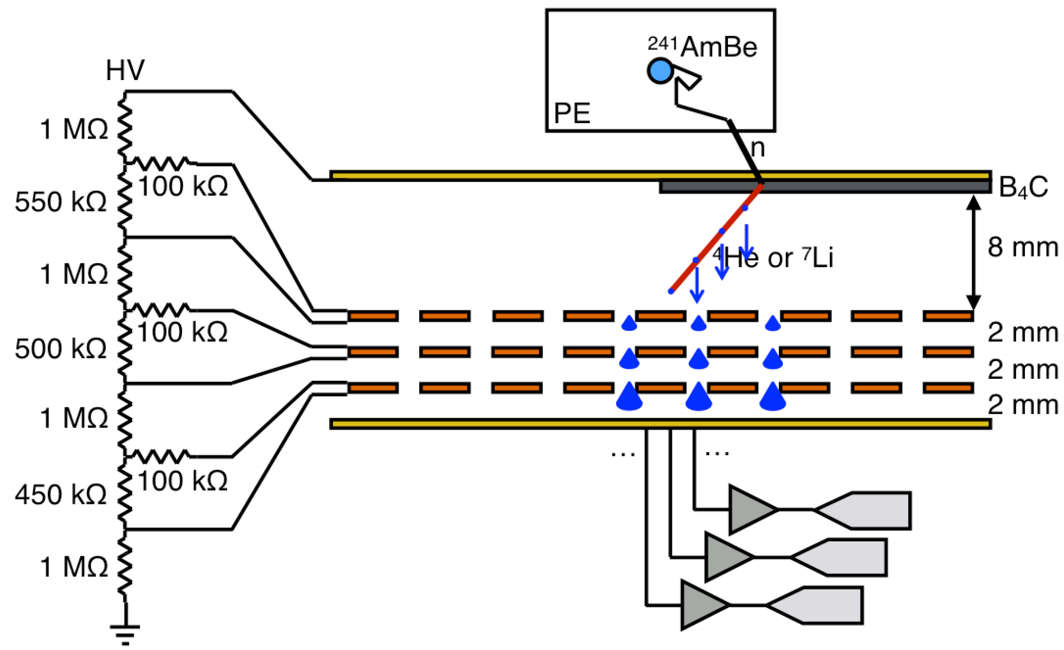


How detect neutrons with a GEM?

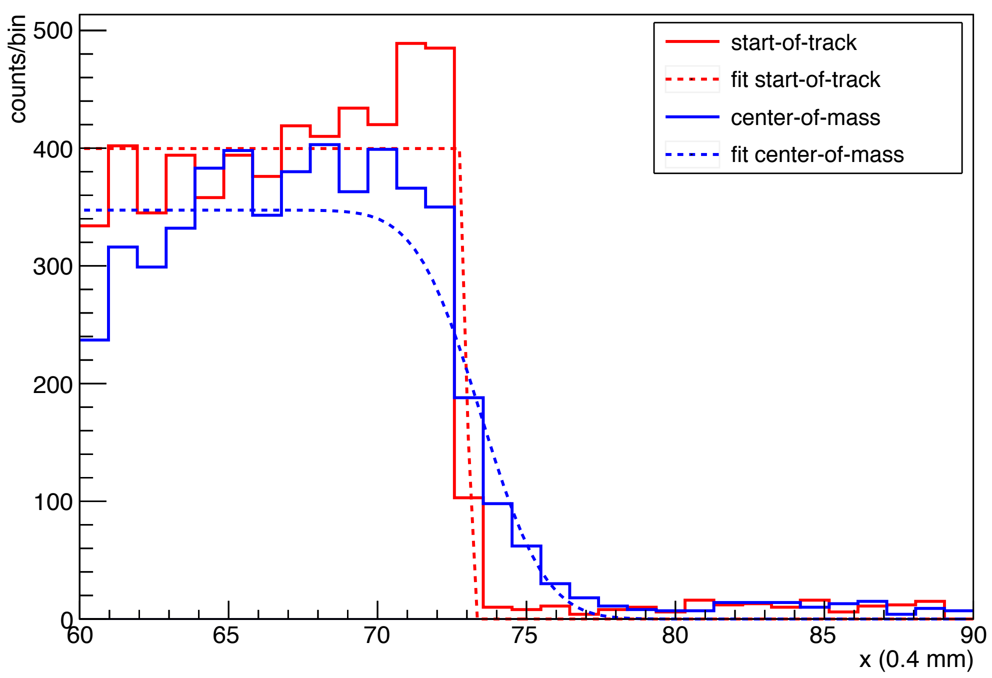
- Neutron converter on cathode
- ^{10}B has been demonstrated to deliver spatial resolution, but low efficiency
- Gd has much higher absorption cross section, but conversion electrons are more difficult to detect
- Enriched ^{155}Gd would improve efficiency significantly



Spatial resolution – μTPC



(a)



(b)

- Spatial resolution of < 100 μm was achieved with a ^{10}B-GEM
- Based on the μTPC concept (algoritms from CERN)

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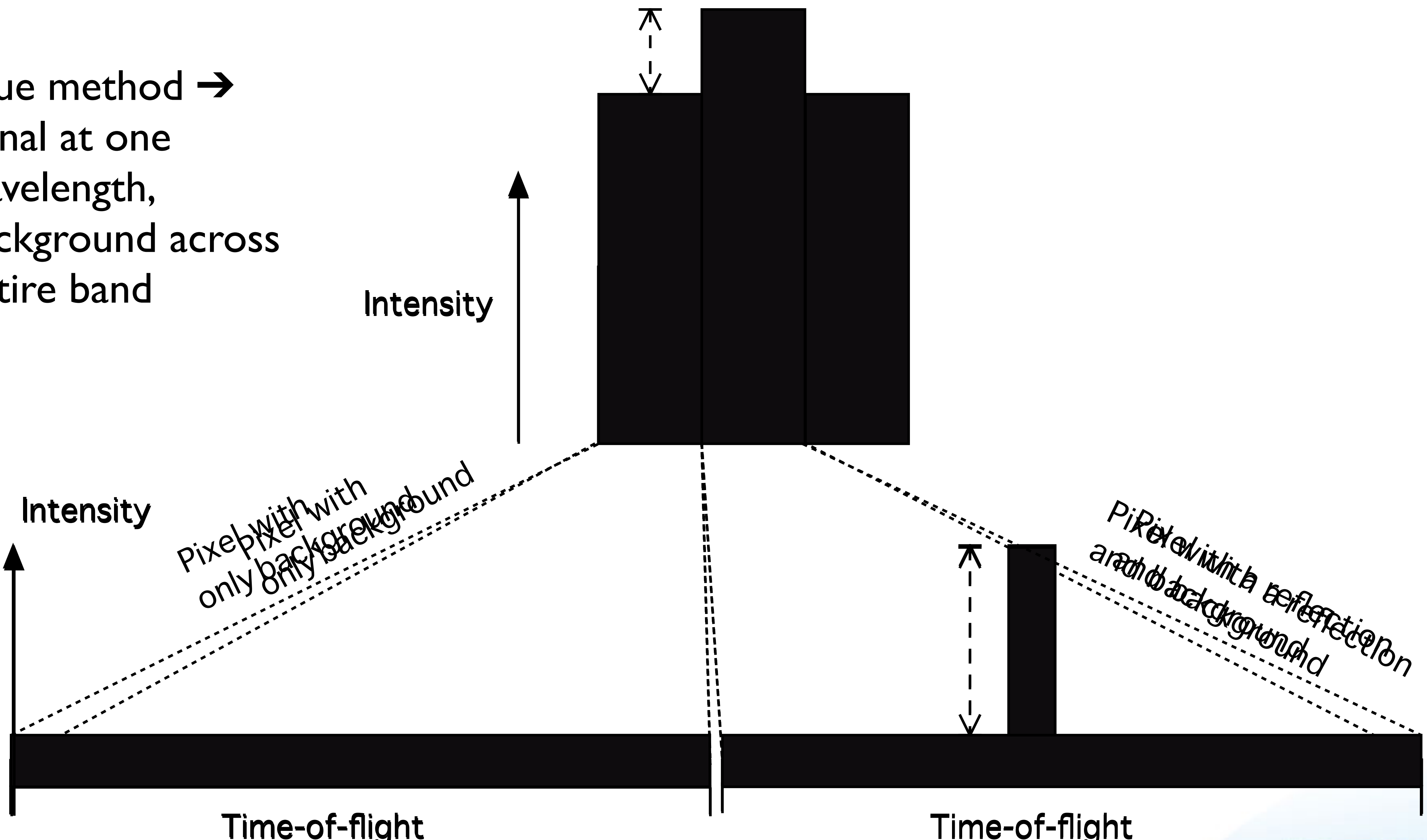
Spreading background over time-of-flight

Laue method → signal at one wavelength, background across entire band



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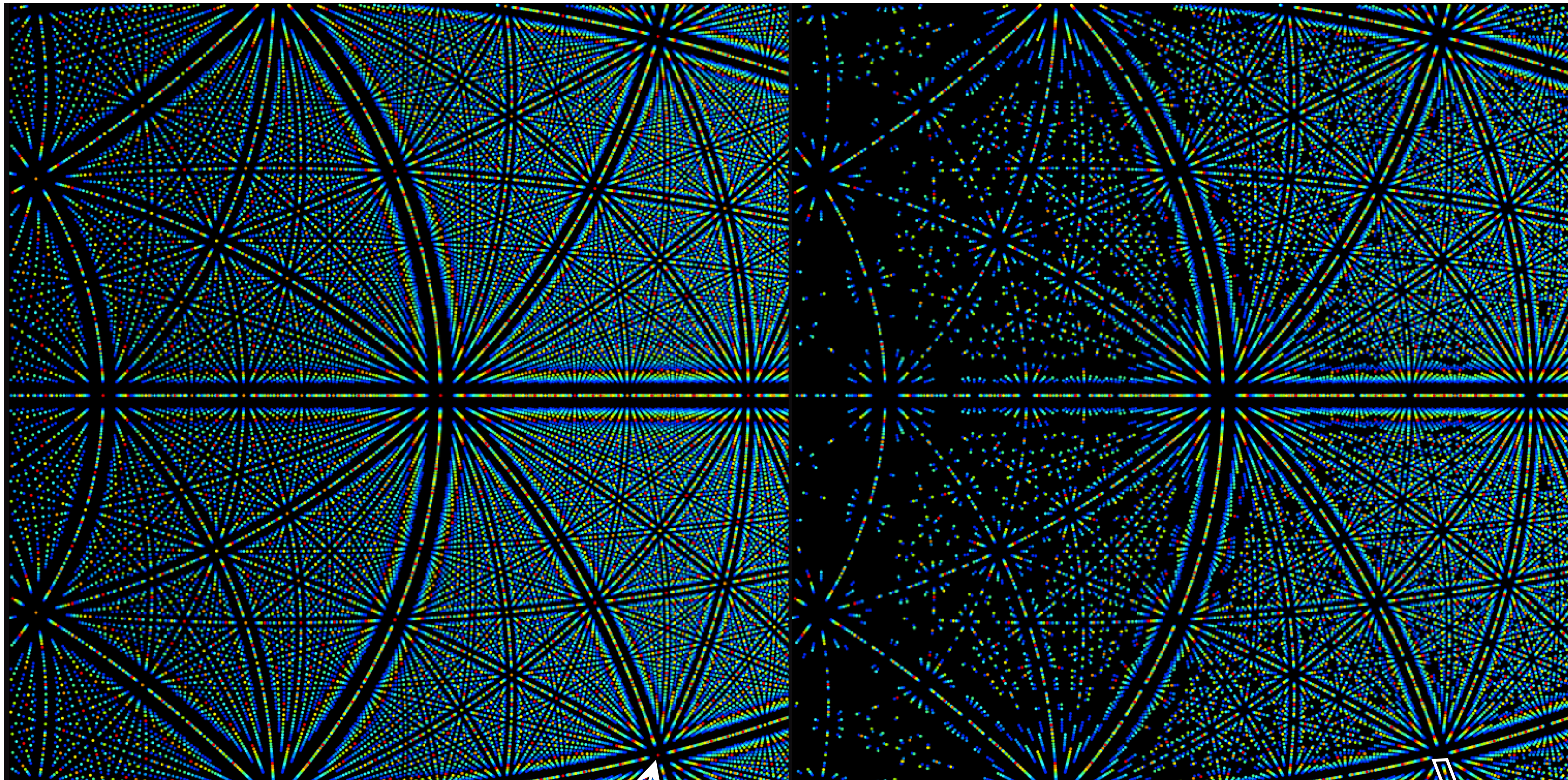
Bovine heart cytochrome c oxidase
$P2_12_12_1$
a = 182.59 Å
b = 205.40 Å
c = 178.25 A
Detector distance 1 m



All reflections

14 28 42 (3.409 Å, 134.4 ms) 21 35 49 (2.809 Å, 110.8 ms)
15 29 43 (3.309 Å, 130.5 ms) 22 36 50 (2.739 Å, 108.0 ms)
16 30 44 (3.215 Å, 126.8 ms) 23 37 51 (2.672 Å, 105.4 ms)
17 31 45 (3.124 Å, 123.2 ms) 24 38 52 (2.608 Å, 102.9 ms)
18 32 46 (3.040 Å, 119.9 ms) 25 39 53 (2.548 Å, 100.5 ms)
19 33 47 (2.959 Å, 116.7 ms) 26 40 54 (2.489 Å, 98.2 ms)
20 34 48 (2.882 Å, 113.6 ms)

Spatial overlaps only

27 53 79 (1.812 Å, 71.4 ms)
22 43 64 (2.236 Å, 88.2 ms)
18 35 52 (2.752 Å, 108.5 ms)
17 33 49 (2.920 Å, 115.1 ms)
19 37 55 (2.602 Å, 102.6 ms)
15 29 43 (3.327 Å, 131.2 ms)
27 52 77 (1.856 Å, 96.4 ms)
26 50 74 (1.933 Å, 76.2 ms)
24 46 68 (2.103 Å, 82.9 ms)
22 42 62 (2.306 Å, 90.9 ms)
21 40 59 (2.424 Å, 95.6 ms)
20 38 56 (2.553 Å, 100.7 ms)
28 53 78 (1.833 Å, 72.3 ms)

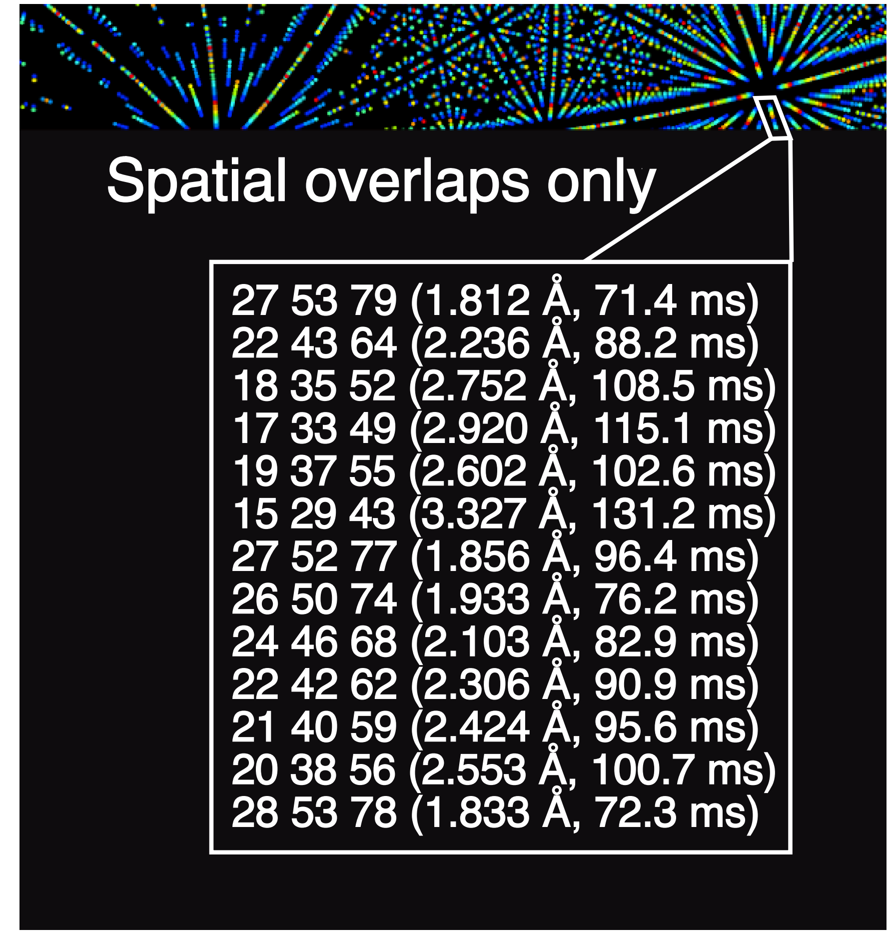
1.800 to 2.019 Angstroms
2.019 to 2.237 Angstroms
2.237 to 2.456 Angstroms
2.456 to 2.675 Angstroms
2.675 to 2.894 Angstroms
2.894 to 3.112 Angstroms
3.112 to 3.331 Angstroms
3.331 to 3.550 Angstroms

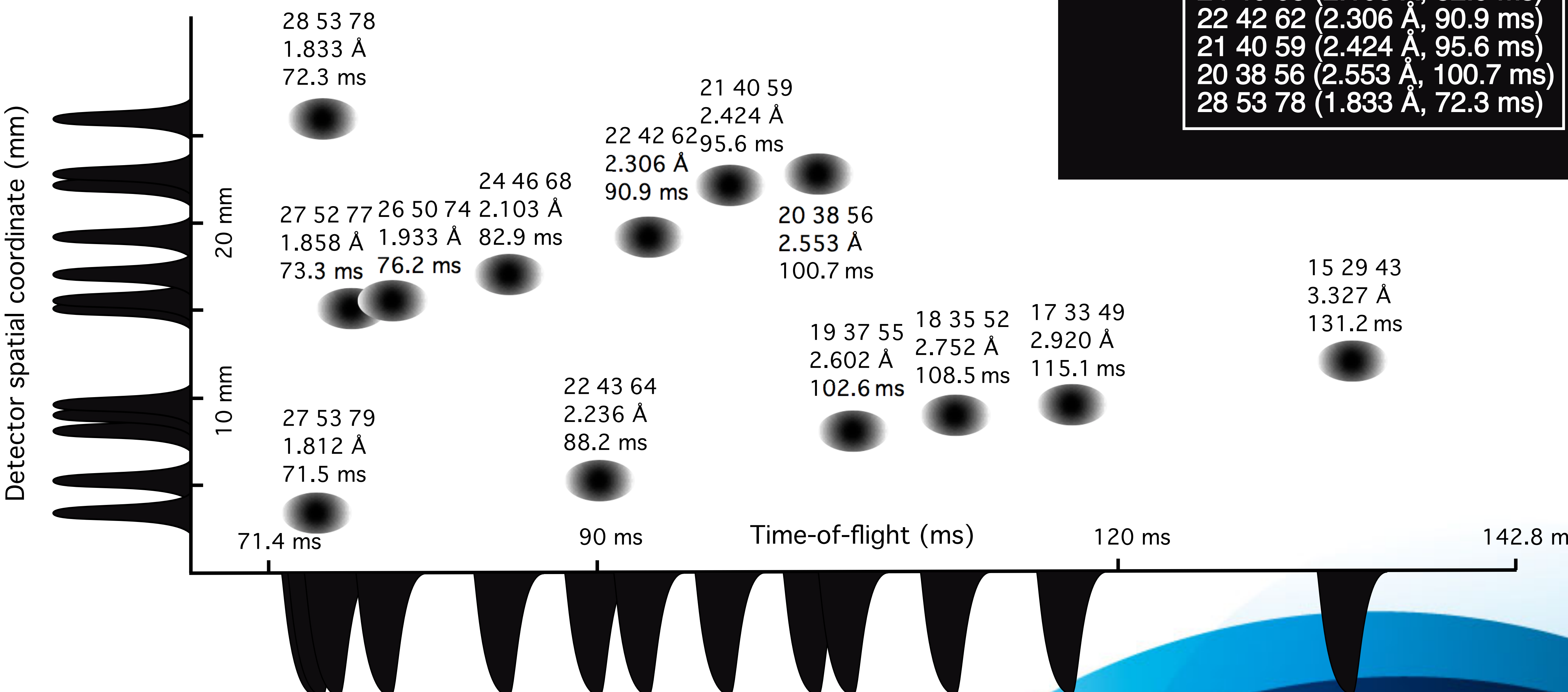
Generated using the Daresbury Laue Suite

Campbell et al. J. Appl. Cryst. (1998). 31, 496-502
Artz et al. J. Appl. Cryst. (1999). 32, 554-562
Helliwell, J.R. et al. J. Appl. Cryst. (1989) 22, 483–497

Overlap separation with TOF

Bovine heart cytochrome c oxidase
$P2_12_12_1$
a = 182.59 Å
b = 205.40 Å
c = 178.25 A
Detector distance 1 m





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Flux at sample – time averaged

- By Monte Carlo simulation 1.8 x 10^9 n/s/cm^2 at ±0.2° divergence
- By Monte Carlo simulation 9.4 x 10^8 n/s/cm^2 at ±0.1° divergence
- In proposal analytically 3 x 10^8 n/s/cm^2 at ±0.1° divergence (simulations agree)
- LADI-III 5 x 10^7 n/s/cm^2, divergence unclear
- PCS 9.7 x 10^6 n/s/cm^2 at ±0.1° divergence

Factor 3

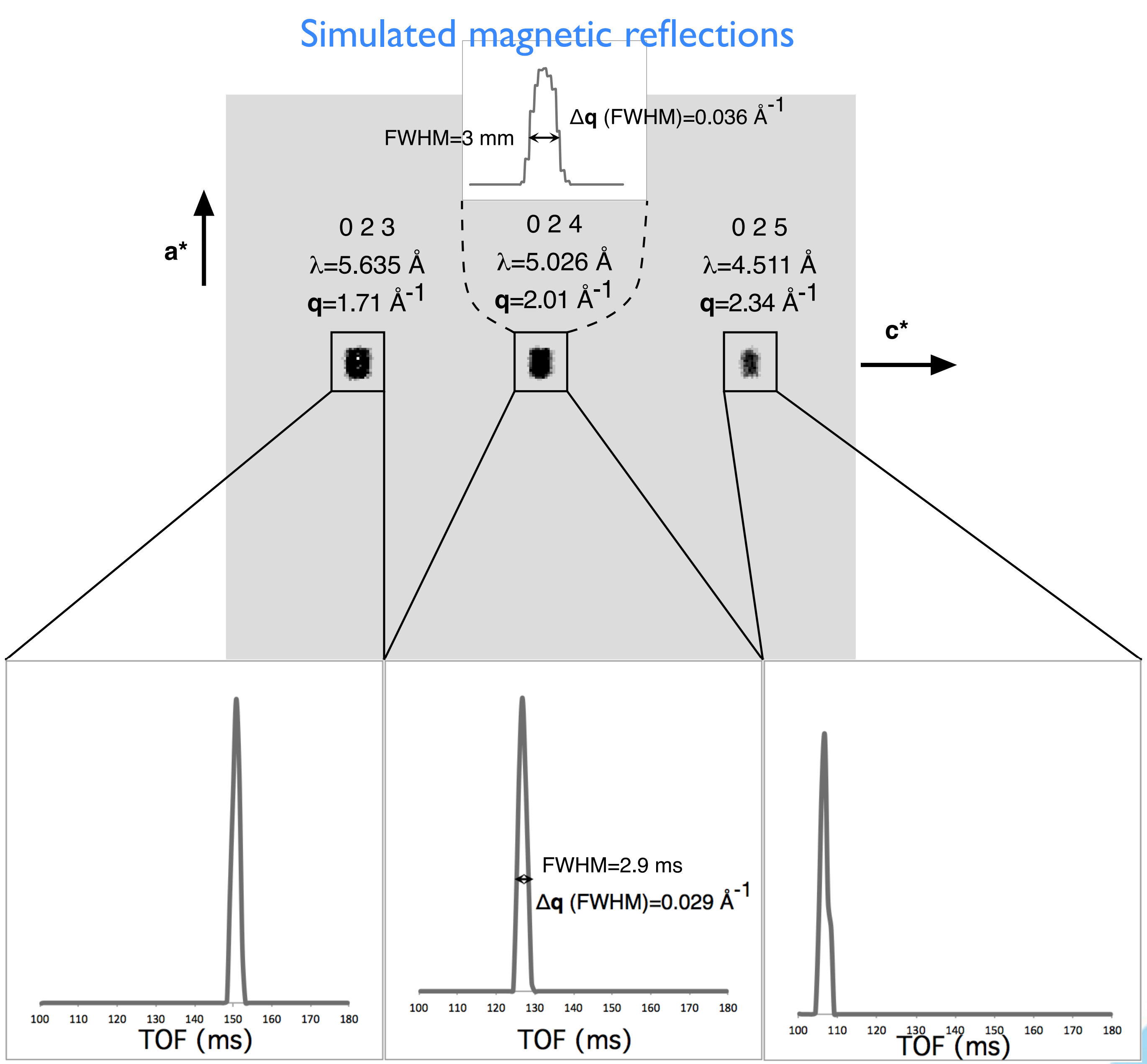
Factor 18

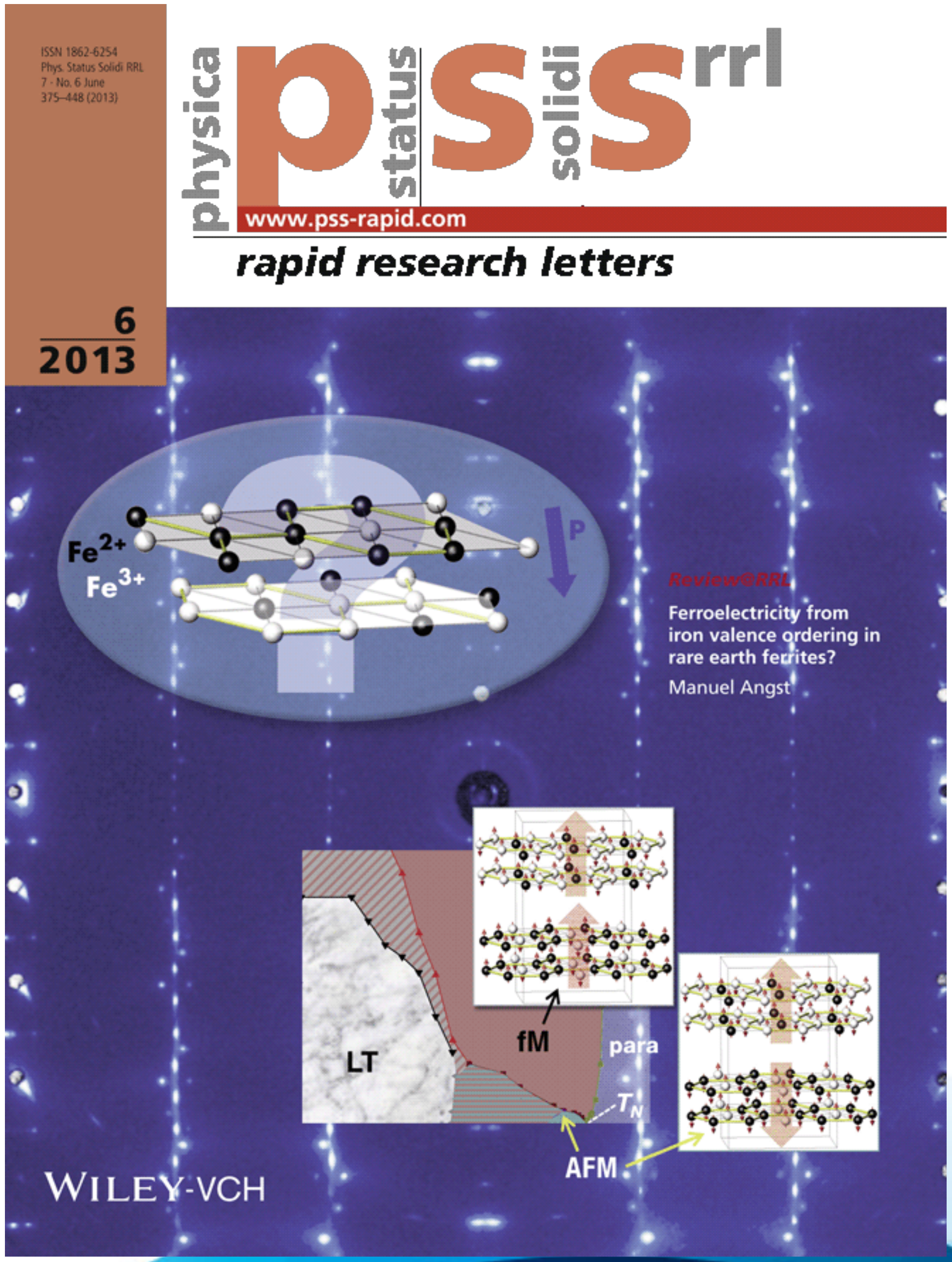
Factor 100

Should be realistic to collect 0.1 mm^3 crystal in < 1 day

Magnetic structures at ESS NMX

- Magnetic ordering in a proposed charge-ordered ferroelectric ($LuFe_2O_4$)
- Magnetic superstructure peaks easily integrateable
- **q**-resolution allows peak splitting to be observed





Manuel Angst (FZJ)

Questions?