Toward construction of a neutron diffractometer for protein crystal with large unit cell at J-PARC
～trial for improving data accuracy～

Quantum Beam Science Center
Japan Atomic Energy Agency

Geant4 Space User's Workshop

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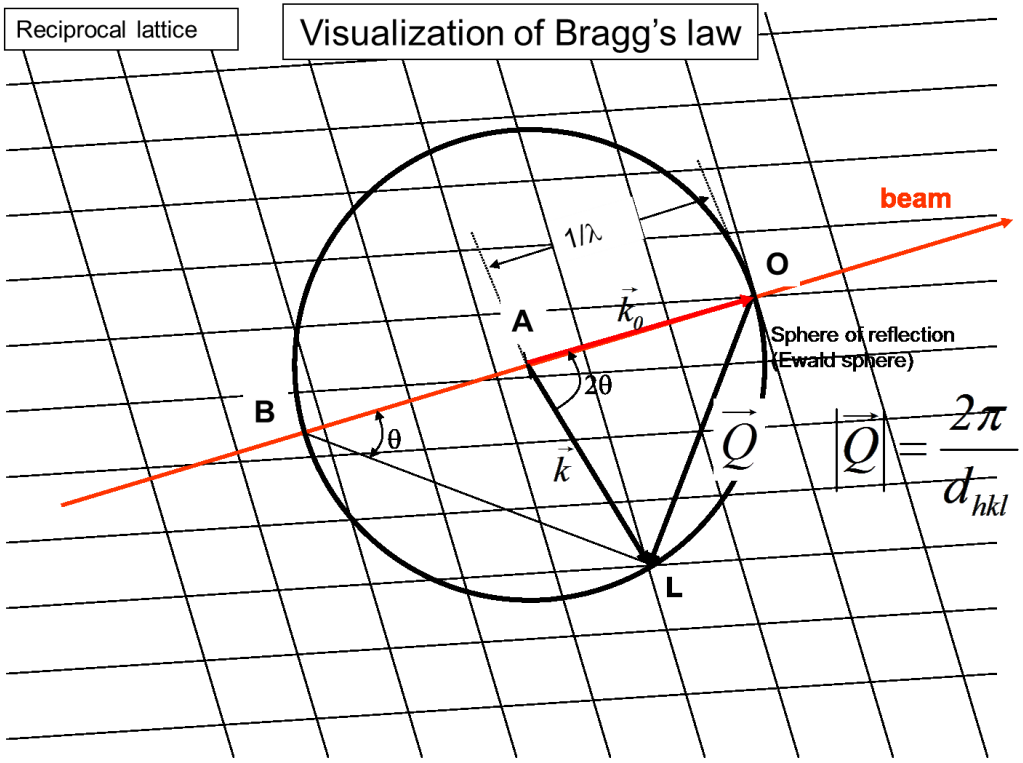
Elastic Scattering: Diffraction

$$\left(\frac{d\sigma}{d\Omega}\right)_{coh} = \frac{N(2\pi)^3}{v_0}\sum_{\tau}\delta(\vec{Q}-\vec{\tau})\left|F_N(\vec{Q})\right|^2$$

Where v_0 is the unit cell volume and τ a reciprocal lattice vector



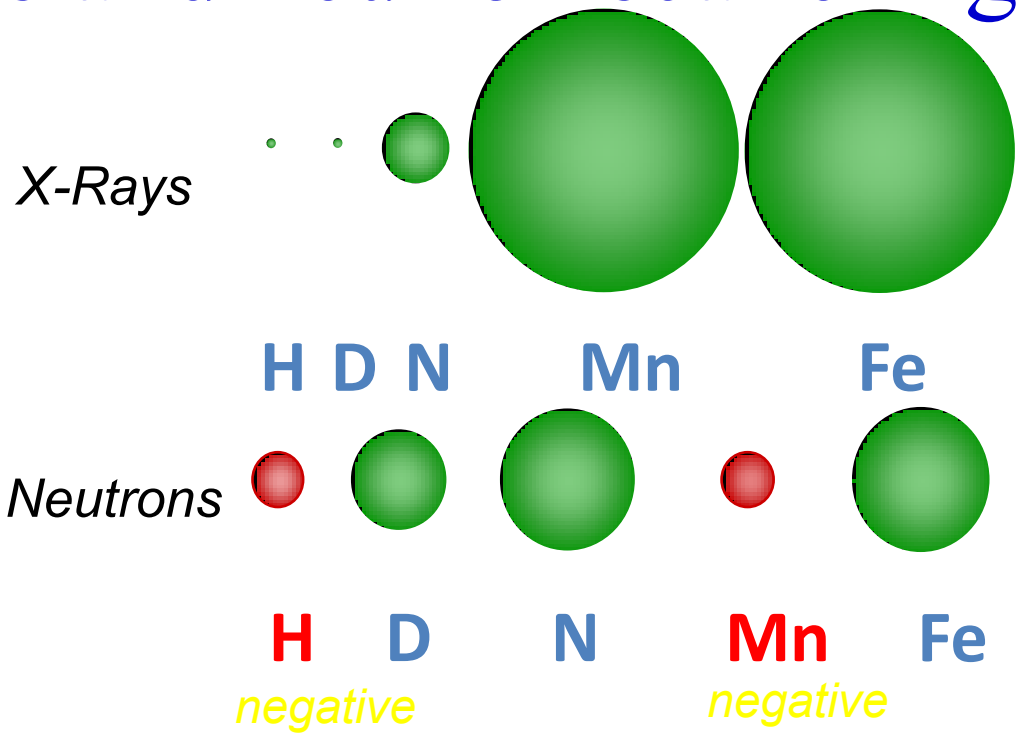
$$\vec{k} - \vec{k}_0 = \vec{Q} = \vec{\tau}$$

$$\left|\vec{\tau}\right| = \left|\vec{k} - \vec{k}_0\right| = Q = 2k\sin(\theta)$$

Bragg Law

$$\lambda = 2d\sin\theta$$

X-rays and neutron scattering lengths

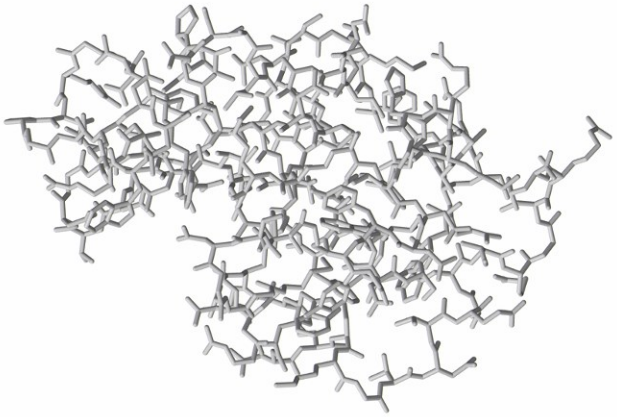


	%	b_c	b_i	σ_c	σ_i	σ_s	σ_a
H	99.985	-3.741	25.27	1.758	80.27	82.03	0.3326
D	0.015	6.671	4.04	5.592	2.051	7.643	0.000519

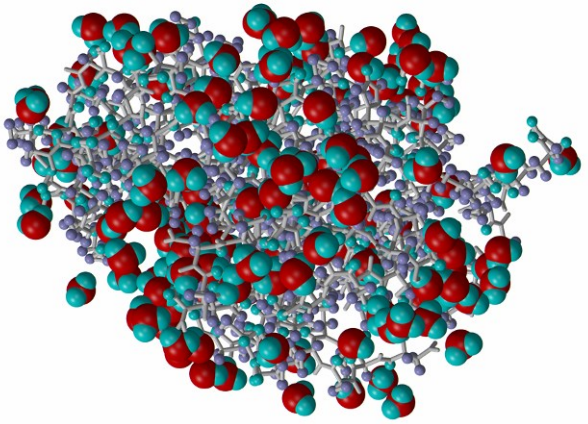
Unit of b is fm. Unit of cross-section σ is $4\pi b^2$ in barns (100 fm^2). $\sigma_s = \sigma_i + \sigma_c$

- Neutrons see hydrogen well – perhaps too well.
- Neutron incoherent scattering is an isotropic "random" scattering of neutrons. This is the basis of some techniques (quasi-elastic neutron scattering) but is a killer for neutron, at least diffraction

Elucidation of structure-function relationship of biological macromolecules



X-ray: structure of main and side chains



Neutrons: locations of hydrogen atoms and hydration structures

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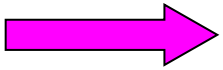
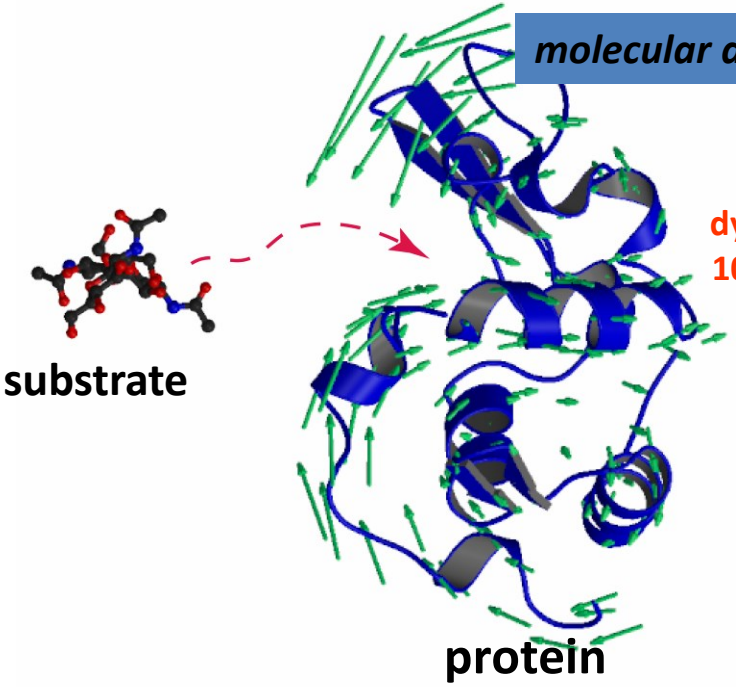
Dynamics of proteins

Elucidation of molecular mechanisms how the protein recognizes and takes substrates



contribute to elucidate mechanisms of diseases and drug design



Diffraction Peak Intensities:

Structure Factor:

X-ray case:

$$F_{(hkl)} = \sum_j f_j \exp\left[2\pi i\left(hx_j + ky_j + lz_j\right)\right]\exp\left[-B_j \sin^2\theta/\lambda^2\right]$$

Neutron case:

$$F_{(hkl)} = \sum_j b_j \exp\left[2\pi i\left(hx_j + ky_j + lz_j\right)\right]\exp\left[-B_j \sin^2\theta/\lambda^2\right]$$

Peak Intensities:

$$I_{(hkl)} = s\, p_{(hkl)}\, L_\theta\, A_\theta\, P_{(hkl)} \left|F_{(hkl)}\right|^2$$

$$I_{(hkl)} \propto \left|F_{(hkl)}\right|^2$$

$F_{(hkl)}$ = structure factor
f_j = X-ray form factor
b = neutron scatt. length
h,k,l = Miller indices
x_j, y_j, z_j = atomic coordinates of atom j
B_j = thermal parameter
θ = diffraction angle
λ = wavelength
Σ over entire unit cell
$I(hkl)$ = intensity

Correction factors:
s = scale factor
L = Lorentz-polarization
p = multiplicity
A = absorption correction
P = preferred orientation

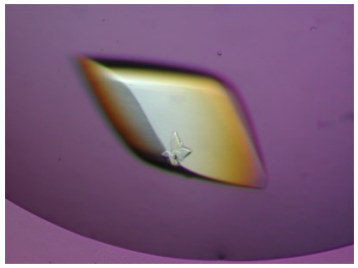
Structure Determination

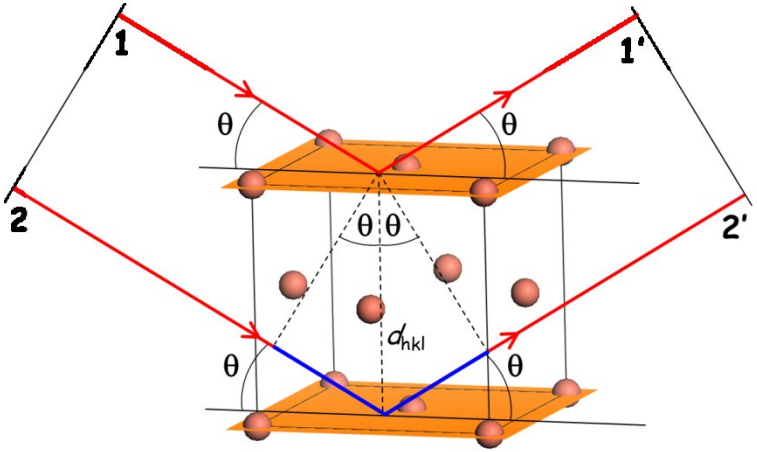
- Experiment ➔ I_{hkl} ➔ $|F_{hkl}| = \mathrm{Sqrt}(I_{hkl})$
- Needed for 3D structure (approximate)

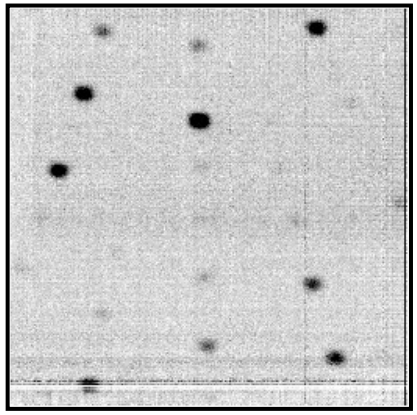
  Phases: ϕ_{hkl}

$|F_{hkl}| + \phi_{hkl} = F_{hkl}$ ➔ 3D-Fourier Synthesis

$$\rho(x,y,z) = [\ \Sigma_{hkl}\ F_{hkl}\ \exp\{-2\pi i(hx + ky + lz)\}] / Vc$$

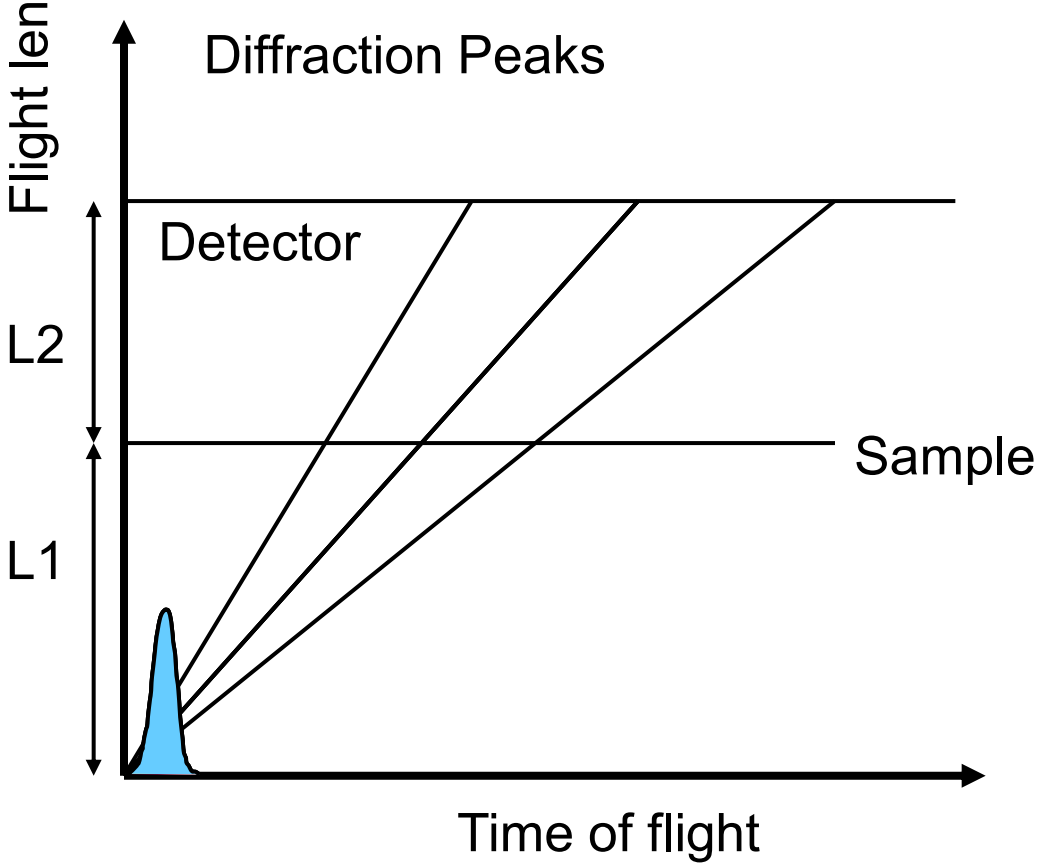


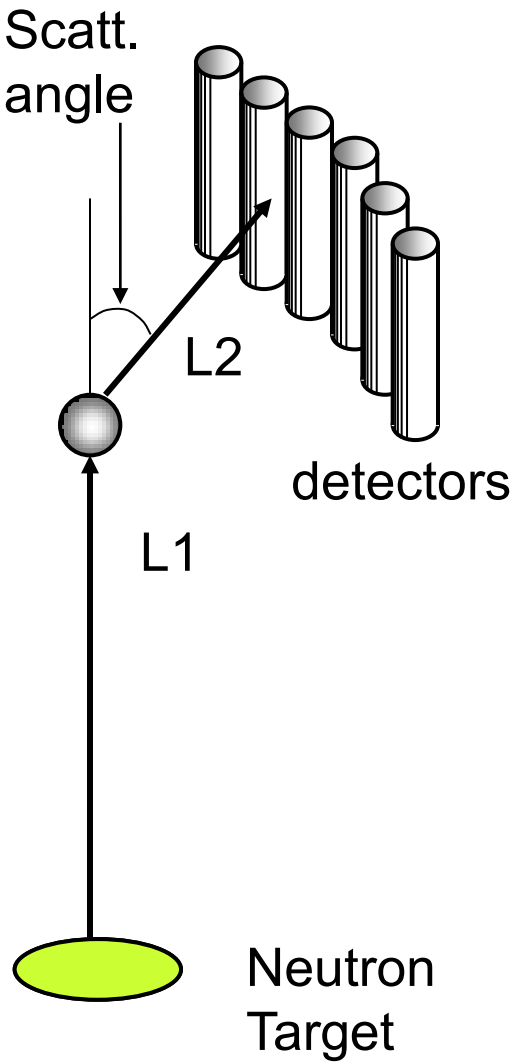




Time-of-flight single-crystal diffraction

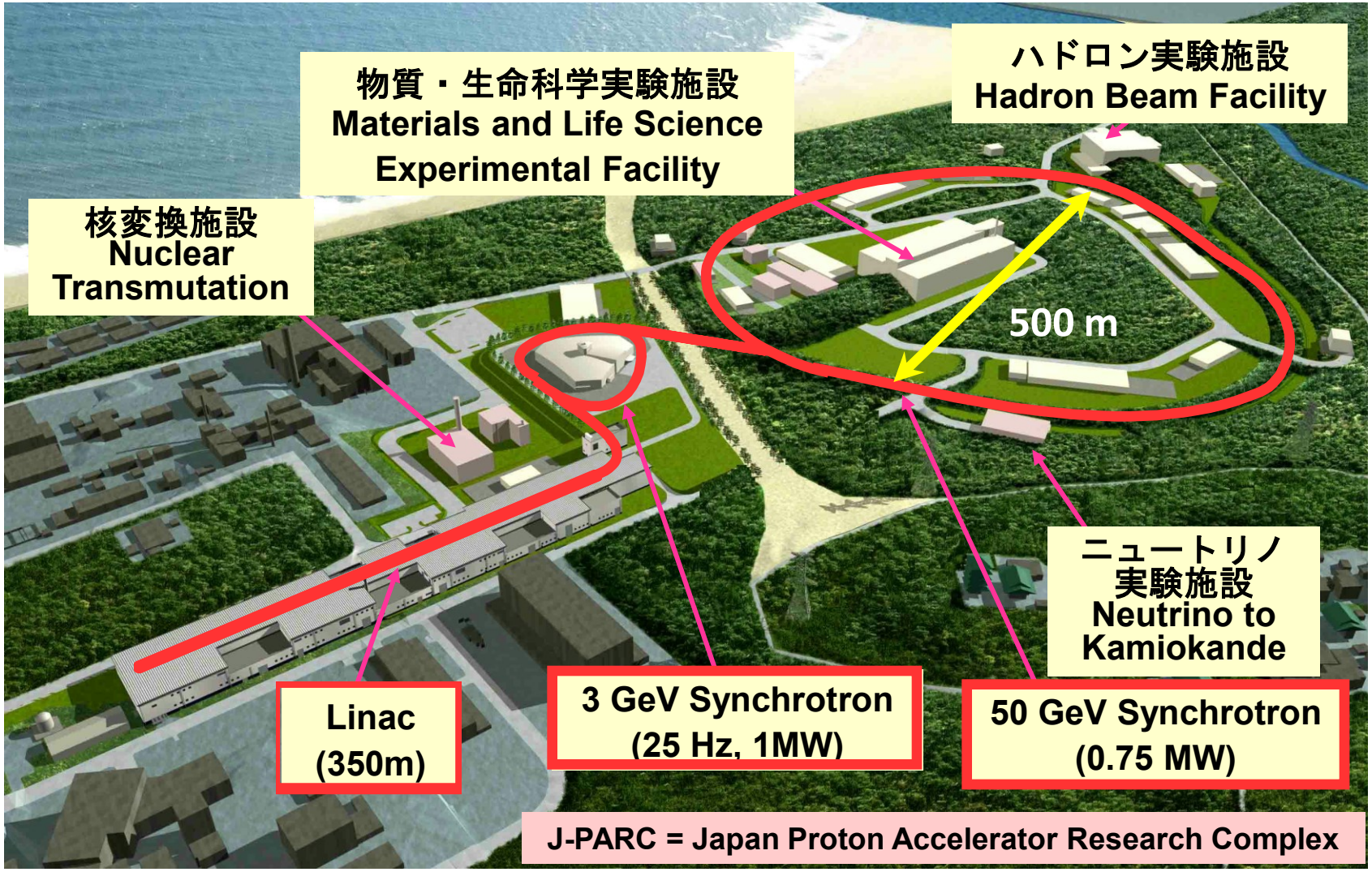
Time of Flight method
(analyze neutron energy/wave-length)





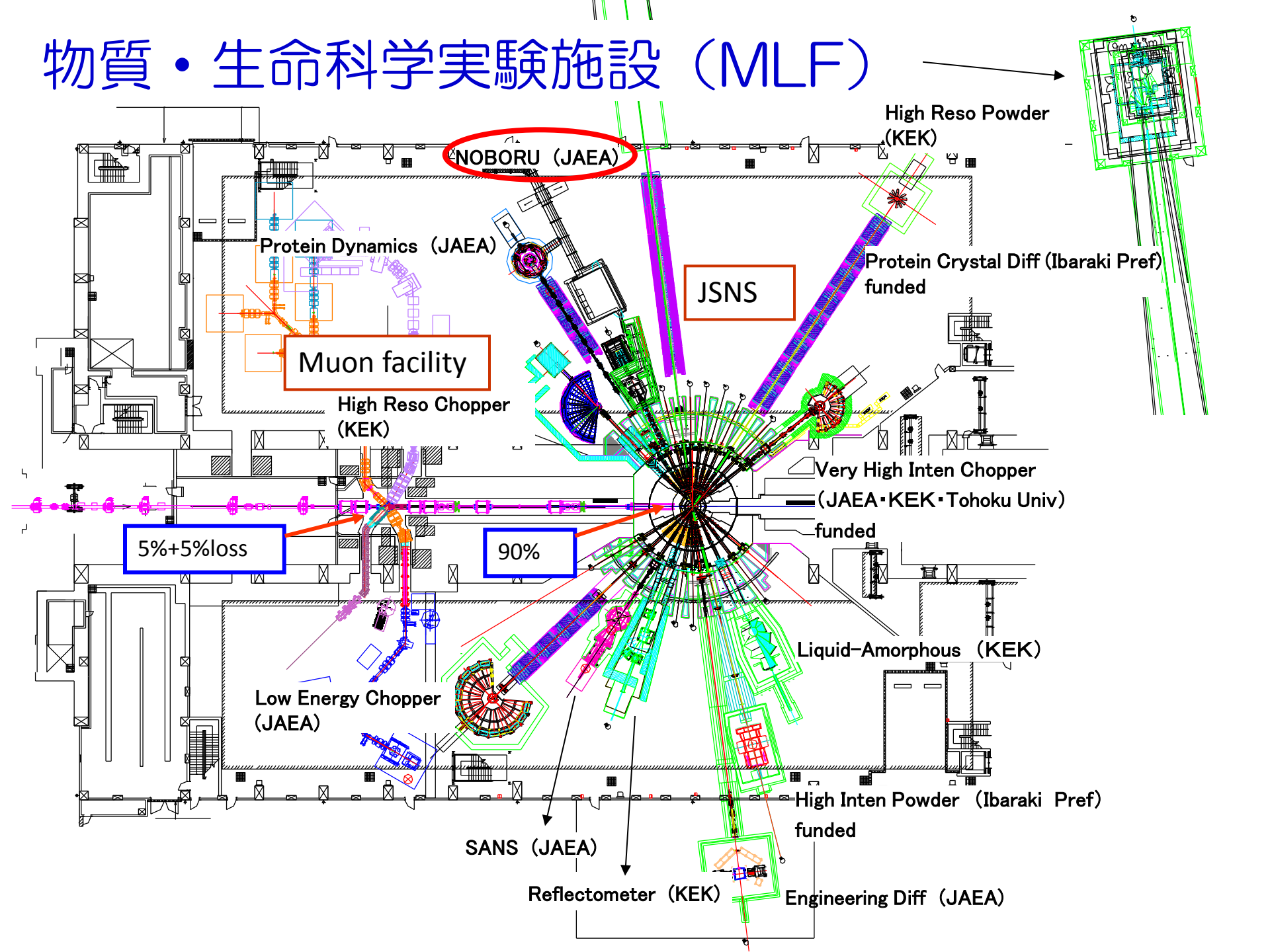
Sharper pulse or longer flight pass
gives higher resolution

Japan Proton Accelerated Research Complex (J-PARC)

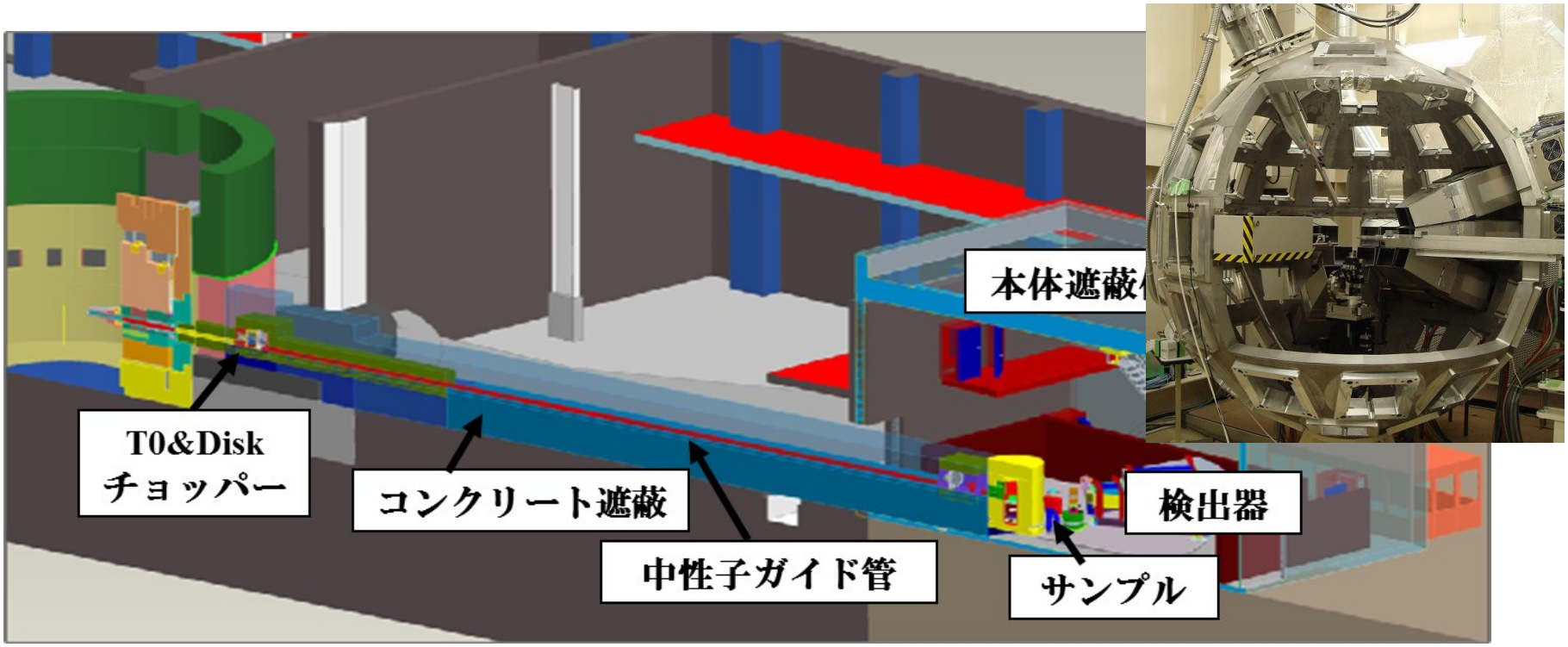


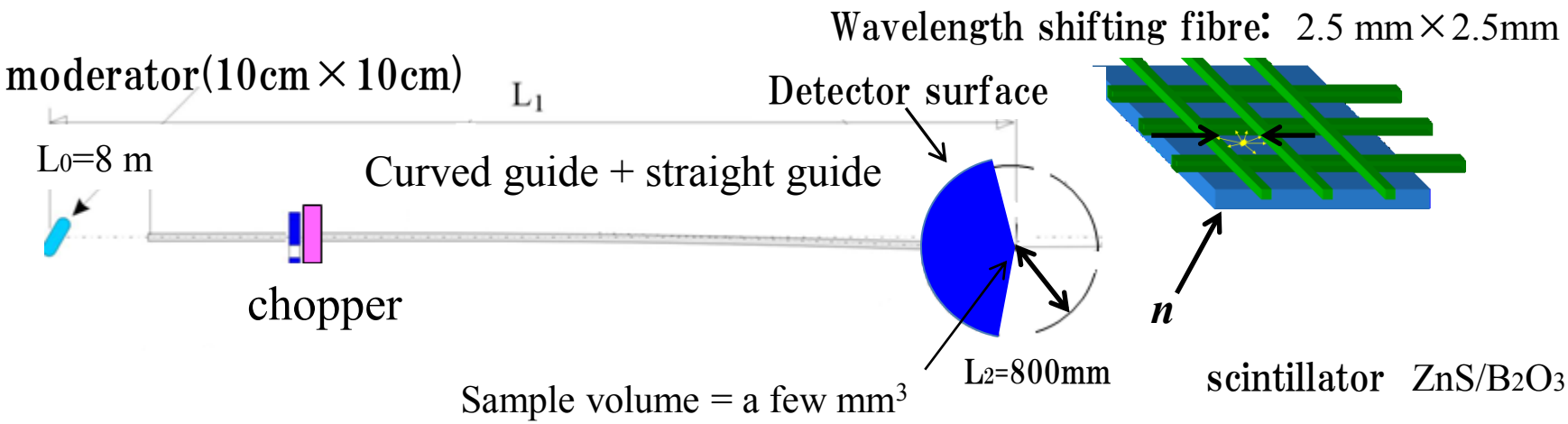
Joint Project between KEK and JAEA (former JAERI)

物質・生命科学実験施設（MLF）



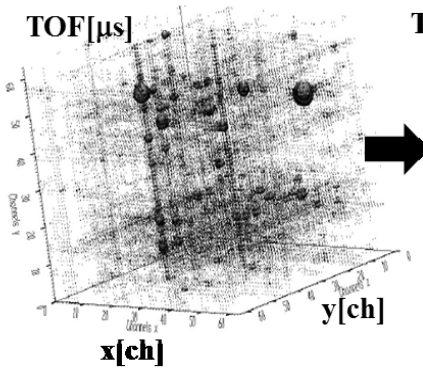
Concept of single-crystal pulsed neutron diffractometer



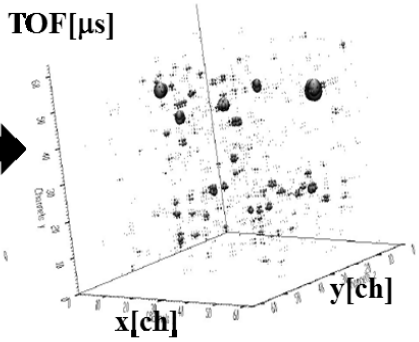


Trial for data reduction to improve S/N

Raw data

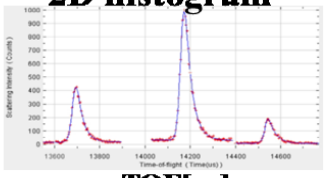


SNIP background elimination

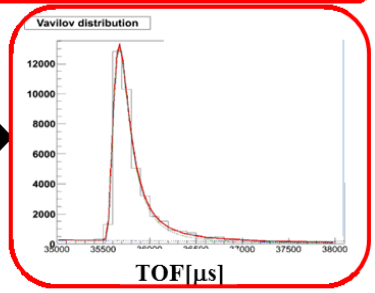


Projection Ex.

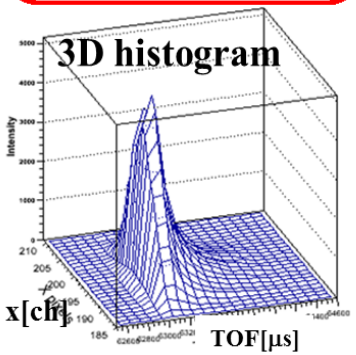
2D histogram

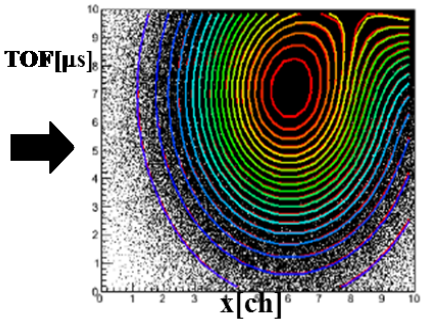


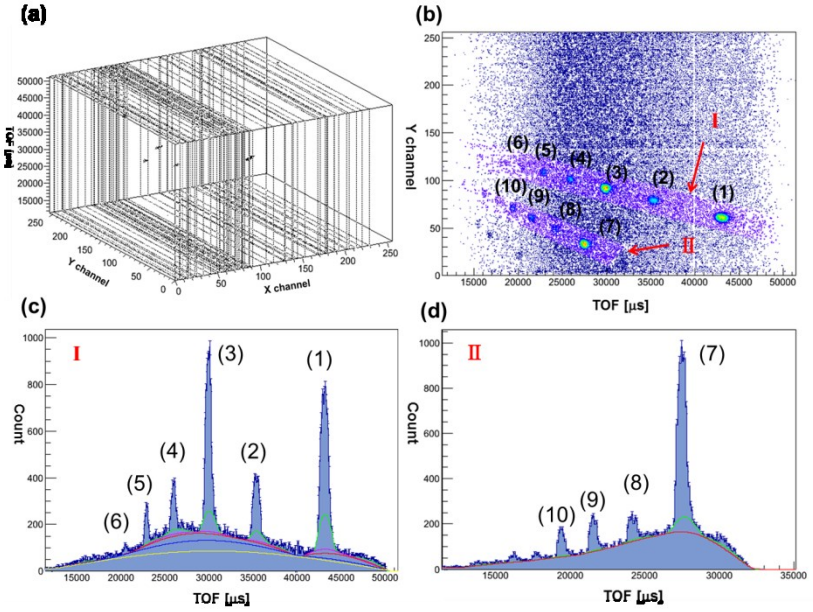
Profile integration: Landau/Vavilov Fitting

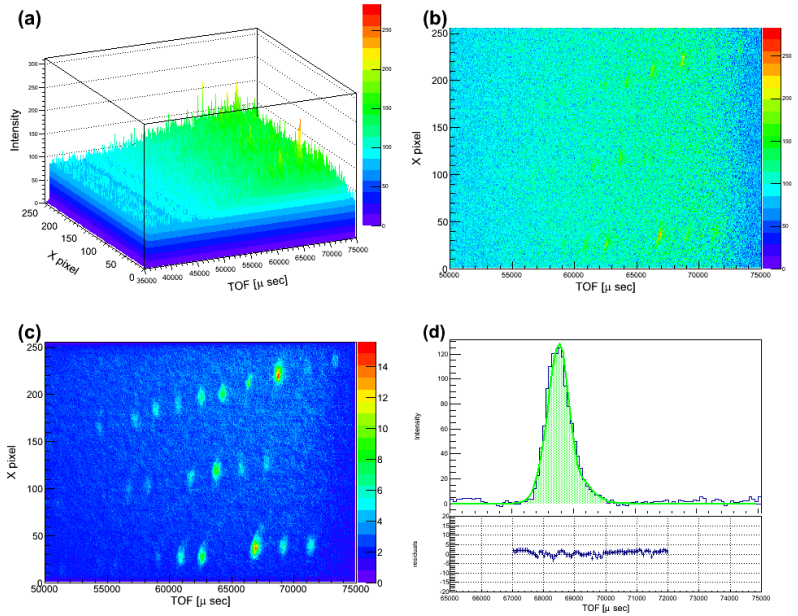


3D histogram





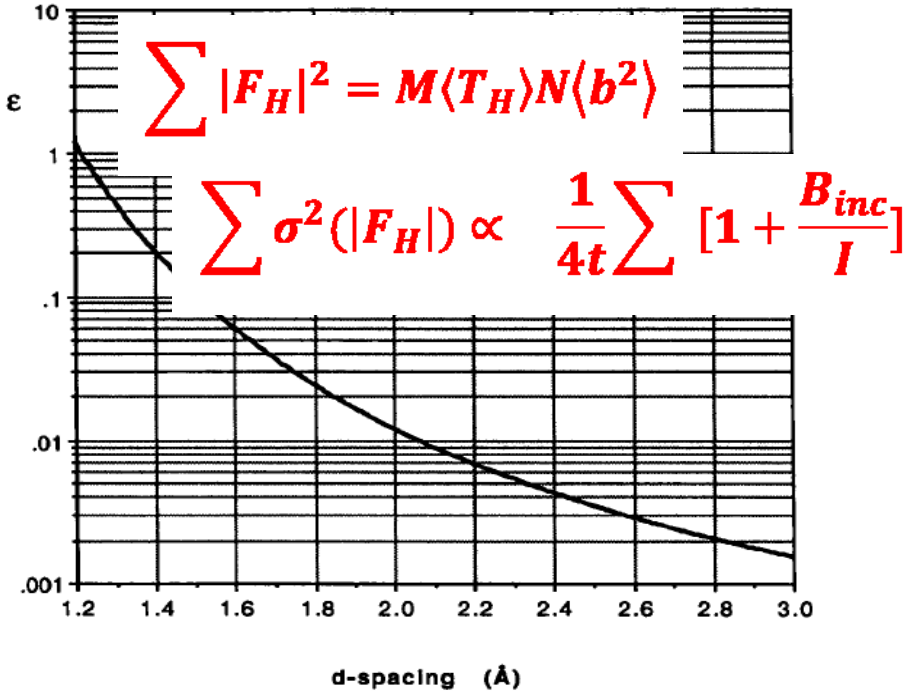




Evaluation of measurement time

W. Jauch, J Neutron Rsearch **6** (1997), 161-171

$$\varepsilon^2 = \frac{\sum \sigma^2(|F_H|)}{\sum |F_H|^2}$$

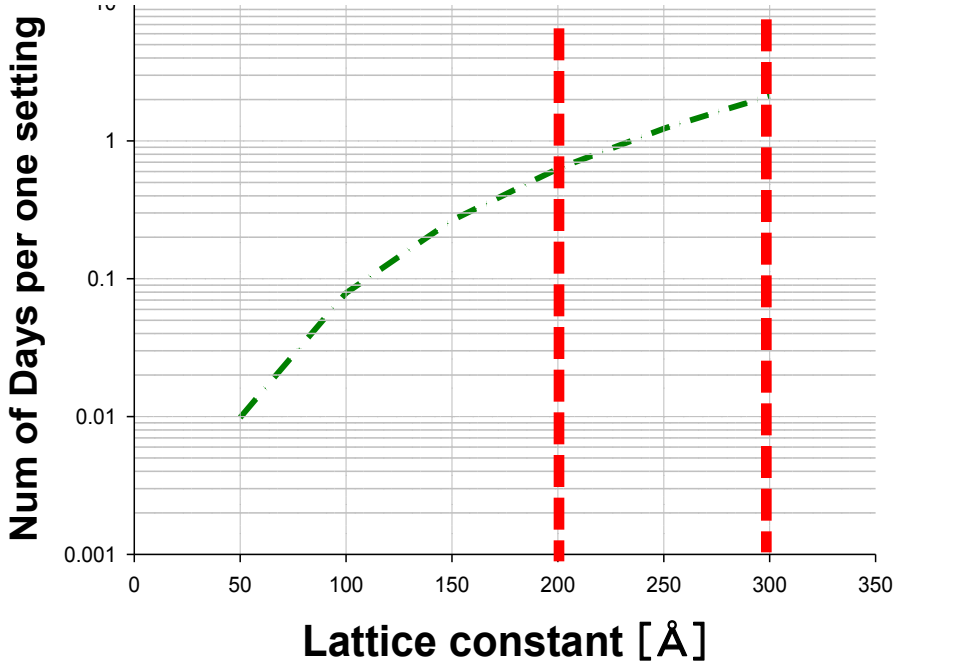


$$\sum |F_H|^2 = M\langle T_H \rangle N \langle b^2 \rangle$$

$$\sum \sigma^2(|F_H|) \propto \frac{1}{4t} \sum \left[1 + \frac{B_{inc}}{I}\right]$$

Crystal system: Cubic, Solvent content:50%

$V = 3.0mm^3$ $d_{min} = 2.0Å$ $B = 20\,[Å^2]$



Full dataset (20 setting) more than 40 days required for the measurement of ～ 250 unit cell crystal of DM

Summary

- Designing TOF neutron diffractometer targeted for biomacromolecules crystals with large unit cells.
  - Moderator choice
  - Shielding
  - Neutron guide
- Developing of integration method on weak Bragg reflections to improve S/N.
  - Appropriate profile function and background evaluation method
- Precise estimation of measurement time to improve S/N.
  - Coherent / incoherent scattering
  - Crystallographic unit cell definition & Orientation of crystals
- Effects of radiation damage of protein crystal sample inside experimental cave
  - Capture gamma→ electromagnetic shower → characteristic X-ray etc
  - The effect on water molecules and protonation state of acidic amino residue