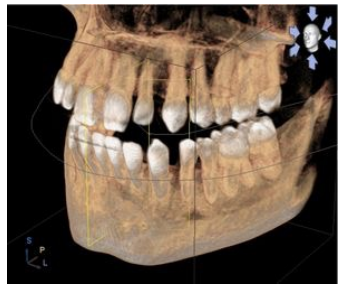
Structural Analysis
Part III - X-ray tools

Session 2:

X-ray scattering and diffraction

Discovery of X-rays triggered many technological and scientific developments



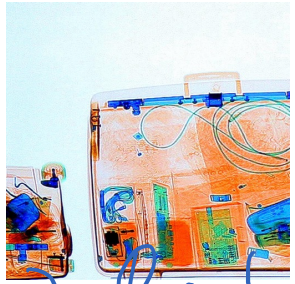
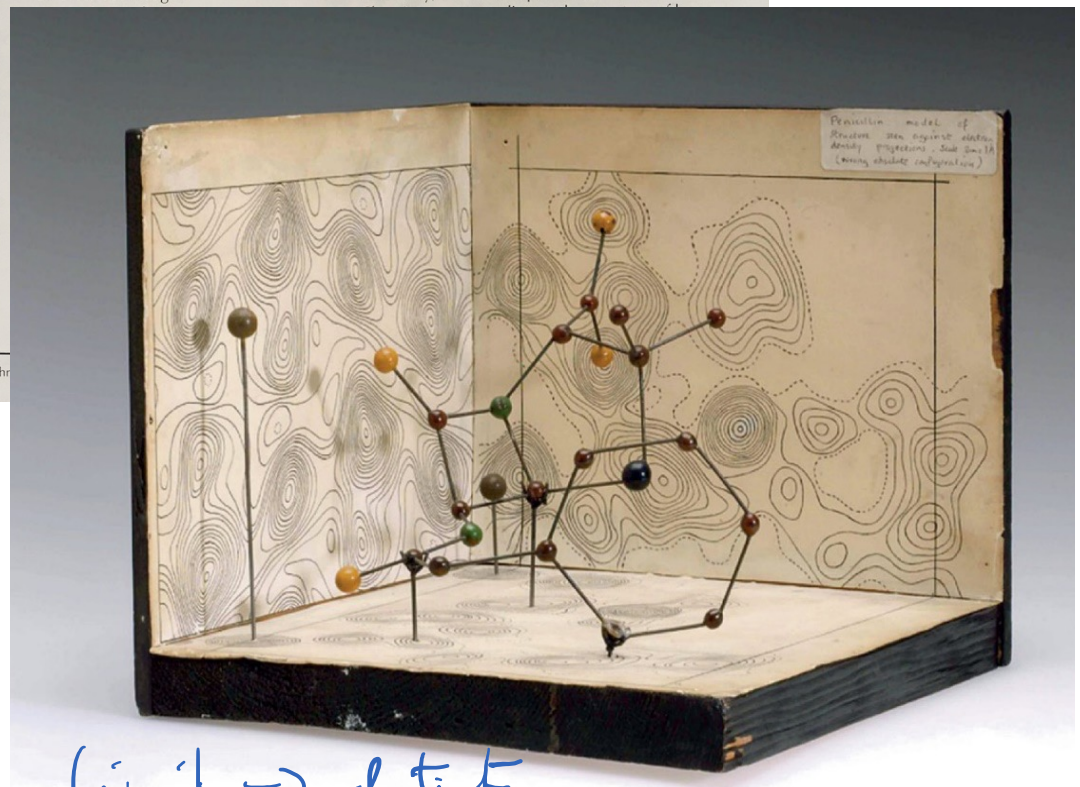
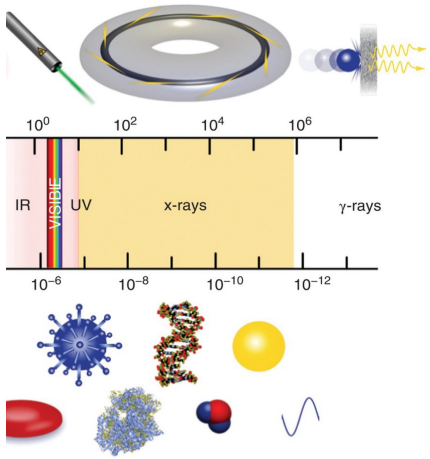


Table 1.1 Nobel Prizes awarded in the field of x-ray research.

Year	Recipient(s)	Research discipline
1901	W. C. Röntgen	Physics; discovery of x-rays
1914	M. von Laue	Physics; x-ray diffraction from crystals
1915	W. H. Bragg and W. L. Bragg	Physics; crystal structure derived from x-ray diffraction
1917	C. G. Barkla	Physics; characteristic radiation of elements
1924	K. M. G. Siegbahn	Physics; x-ray spectroscopy
1927	A. H. Compton	Physics; scattering of x-rays by electrons
1936	P. Debye	Chemistry; diffraction of x-rays and electrons in gases
1946	H. J. Muller	Medicine; discovery of x-ray-induced mutations
1962	M. Perutz and J. Kendrew	Chemistry; structures of myoglobin and haemoglobin
1962	J. Watson, M. Wilkins, and F. Crick	Medicine; structure of DNA
1964	D. Crowfoot-Hodgkin	Chemistry; structure of penicillin
1976		
1979		
1981		
1985		
1988		
1997		
2003		
2006		
2009		
2012		
2018		

†Work using synchr





↳ Resolution limit → detector

λ matched to size of molecule structures

+

diffraction

⇓

atomic resolution

Why care about x-ray diffraction of crystals?

Why should we care about x-rays, crystals, lattices, etc?

Source:
The Cambridge Structural Database (CSD)

Organic
43%

Metal-Organic
57%
At least one transition metal, lanthanide, actinide or any of Al, Ga, In, Tl, Ge, Sn, Pb, Sb, Bi, Po

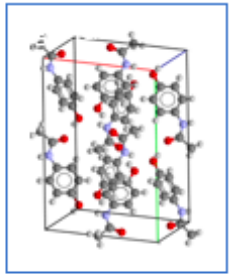
Not Polymeric
89%

Polymeric: 11%

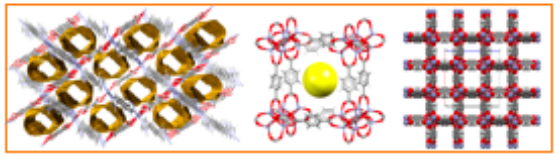
Single Component
56%

Multi Component
44%

Organic
- Drugs
- Agrochemicals
- Pigments
- Explosives
- Protein ligands

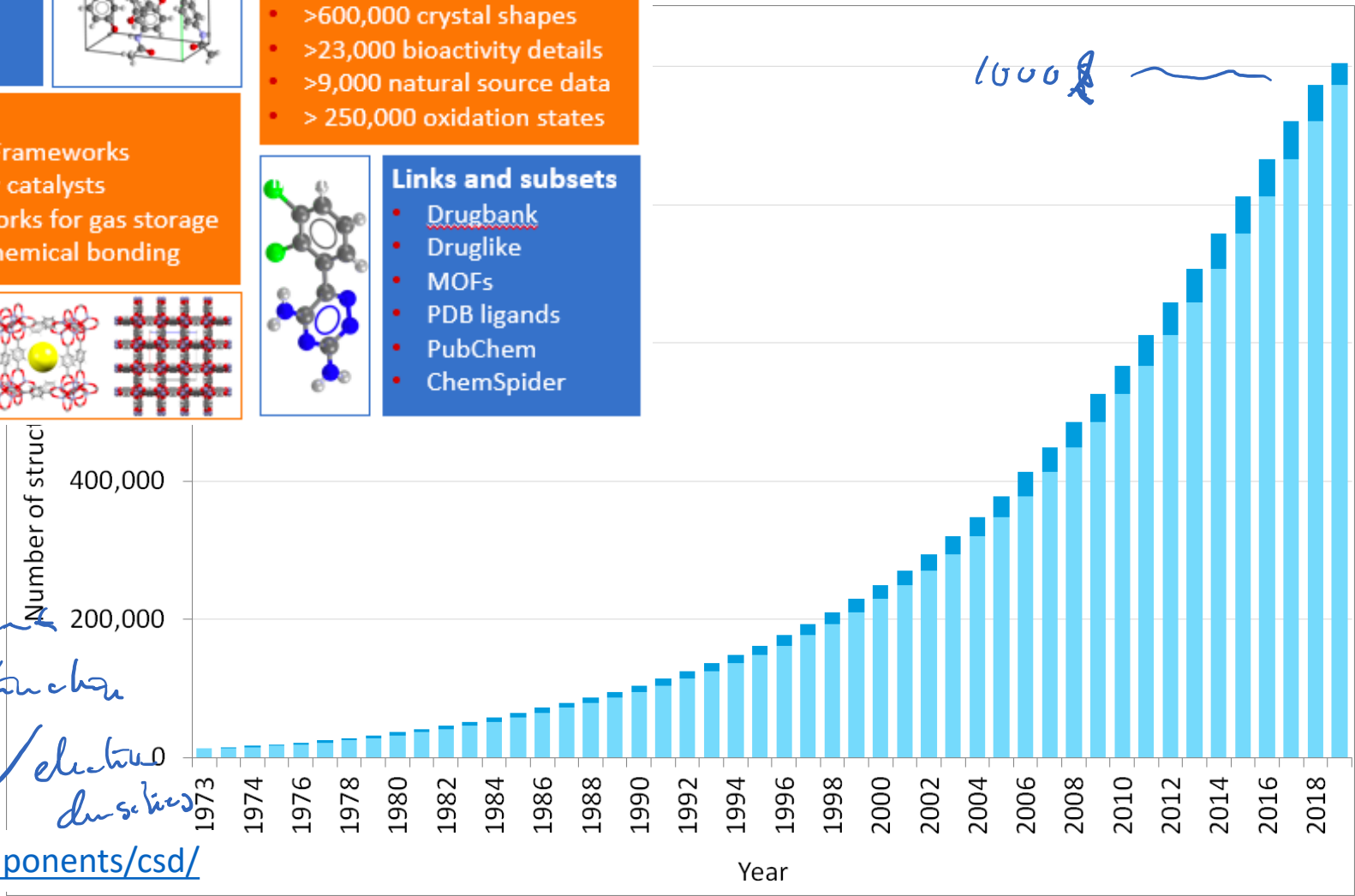


Metal-Organic
- Metal Organic Frameworks
- Models for new catalysts
- Porous frameworks for gas storage
- Fundamental chemical bonding



Additional data
- >10,000 polymorph families
- >160,000 melting points
- >700,000 crystal colours
- >600,000 crystal shapes
- >23,000 bioactivity details
- >9,000 natural source data
- > 250,000 oxidation states

Links and subsets
- Drugbank
- Druglike
- MOFs
- PDB ligands
- PubChem
- ChemSpider



⇒ one of the most important structural analysis tools

⇒ combine with MS → constituents
NMR → local structure

⇒ large molecule backbone / electron density

https://www.ccdc.cam.ac.uk/solutions/csd-system/components/csd/

Example: Diamondoids – Diamond Molecules

REPORT

Isolation and Structure of Higher Diamondoids, Nanometer-Sized Diamond Molecules

J. E. Dahl, S. G. Liu, R. M. K. Carlson*
+ See all authors and affiliations

Science 03 Jan 2003:
Vol. 299, Issue 5603, pp. 96-99
DOI: 10.1126/science.1078239

Example: diamondoids

Question: how to figure out that this is not just another hydrocarbon

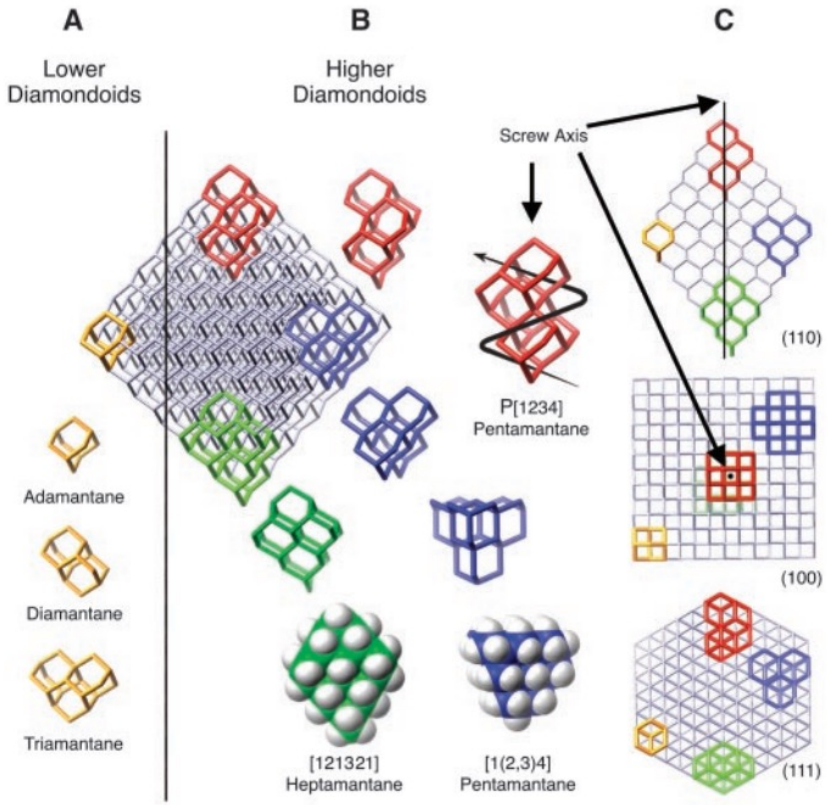


Fig. 1. The relation between the face-centered cubic diamond lattice and diamondoid structures. (**A**) Adamantane (yellow) is shown superimposed upon the lattice of a 455-carbon octaghedral diamond (some carbons removed for clarity). Adamantane, diamantane, and triamantane (all in yellow) are also shown separate from the diamond lattice. (**B**) Screw-shaped higher diamondoid P [1234] pentamantane (red), pyramidal [1(2,3)4] pentamantane (blue), and rhombus-shaped [121321] heptamantane (green) superimposed upon the diamond lattice and also separate from the lattice. (**C**) The 455-carbon diamond with superimposed diamondoid structures viewed along the (110), (100), and (111) lattice planes showing the diamond lattice faces of the pentamantanes and heptamantane. Views of the P [1234] pentamantane screw axis are indicated by straight arrows. The clockwise helical arrow indicates the groove in the red P [1234] pentamantane molecule.

Supplemental Material: Crystallization for XRD

Crystallization

We crystallized specific higher diamondoids from Hypercarb HPLC fractions by preparing super-saturated solutions in acetone. Crystallization vials (standard GC-MS autosampler vials) were sealed for approximately one to two weeks after which a small hole was made in the caps and the solvent allowed to evaporate. The crystals were harvested and submitted for structural determination by X-ray crystallography. Fig. S1

2

shows [1(2,3)4] pentamantane (structure 7 in Fig. 3 in the paper) grown using this method.

⇒ Remember general LS class

⇒ Super saturation, drip growth, ...

Fig. S1. Photomicrographs of [1(2,3)4] pentamantane crystals used for X-ray crystallography. Field of view, approx. 3.5 mm. Photograph, Marilyn Olmstead, U. C. Davis.

Can apply x-ray techniques

Cambridge Structural Database entry

CCDC FIZ Karlsruhe Leibniz Institute for Information Infrastructure

CSD Entry: GUTDAA

Sign In

Licensed to: Paul Scherrer Institute (PSI)

Simple Search | Structure Search | Unit Cell Search | Formula Search

Your query was: Compound name: pentamantane and the search returned 6 records.

Back to Search List | Modify Search | New Search

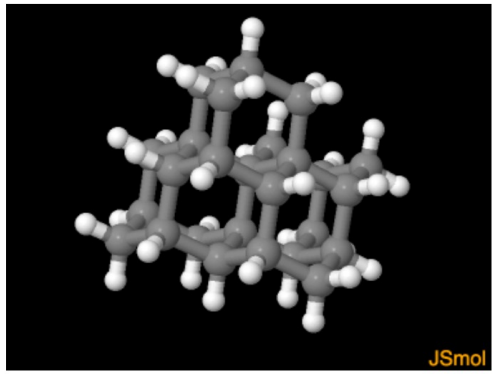
Results

Database Identifier	Deposition Number
GUTDAA	198851

Download

GUTDAA : (12(3)4)Pentamantane
Space Group: P 2_1/n (14), **Cell:** *a* 7.7105(9)Å *b* 27.040(3)Å *c* 8.9375(10)Å, *α* 90° *β* 115.121(4)° *γ* 90°

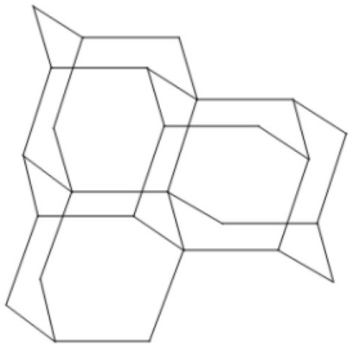
3D viewer



H | Disorder | Menu | Open

Style	Labels	Packing	Measure
Ball and Stick	No Labels	None	None

Chemical diagram



View group symbols key

files to use

Additional details

Deposition Number	198851
Data Citation	J.E.Dahl, S.G.Liu, R.M.K.Carlson CCDC 198851: Experimental Crystal Structure Determination, 2003, DOI: 10.5517/cc6nxk9
Deposited on	29/11/2002

Associated publications

J.E.Dahl, S.G.Liu, R.M.K.Carlson, *Science*, 2003, 299, 96, DOI: 10.1126/science.1078239

Chemical details

Formula	$C_{26}H_{32}$

Crystal details

Space group	P 2_1/n (14)
Unit cell	***a*** 7.7105(9)Å ***b*** 27.040(3)Å ***c*** 8.9375(10)Å ***α*** 90° ***β*** 115.121(4)° ***γ*** 90°
Cell volume	1687.14
Reduced cell	***a*** 7.711Å ***b*** 8.938Å ***c*** 27.040Å ***α*** 90.000° ***β*** 90.000° ***γ*** 115.121°
Z, Z'	4, 1
Habit	needle
Colour	colorless

Symmetry
unit cell
dimensions

Experimental details

R-factor (%)	5.23
Temperature (K)	[illegible]
Density (CCDC)	1.056
Radiation probe	x-ray
Experiment type	single crystal

→ confidence

how structure
was determined

https://www.ccdc.cam.ac.uk/structures/Search?Compound=pentamantane&DatabaseToSearch=Published

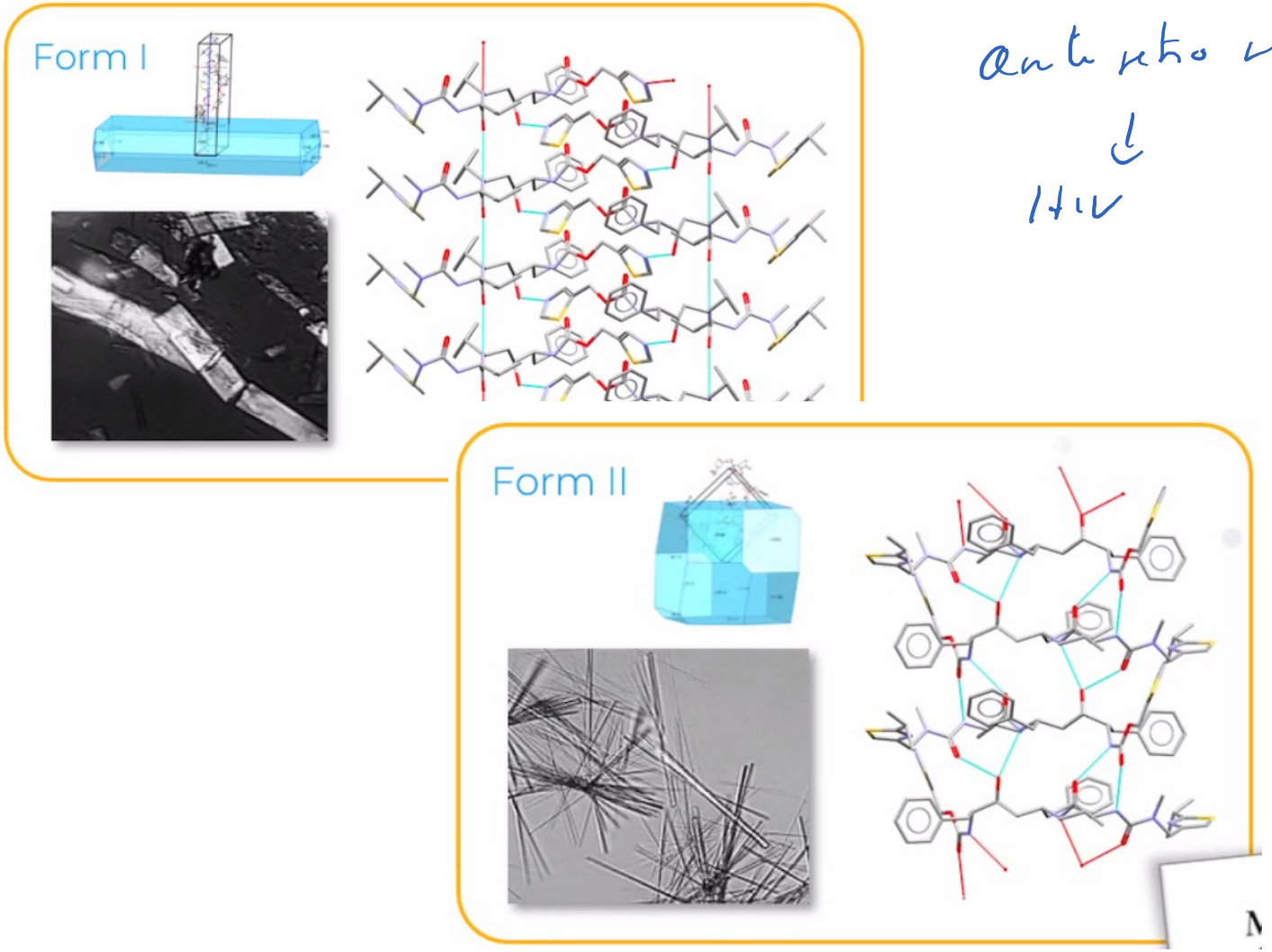
A real world example: Crystal structure of the Novir Drug → Ritonavir

antiretroviral

HIV

Crystalline structure of (drug) compounds determines

- Melting properties
- Hygroscopicity
- Hydrate formation
- Soluablility
- And other properites



Acknowledgement: Susan Reutzel-Edens, CCDC – EPFL PChem Seminar Fall 2021

A real world example: Crystal structure of the Novir Drug

Science news:

> Pharm Res. 2001 Jun;18(6):859-66. doi: 10.1023/a:1011052932607.

Ritonavir: an extraordinary example of conformational polymorphism

J Bauer [1], S Spanton, R Henry, J Quick, W Dziki, W Porter, J Morris

Affiliations + expand

PMID: 11474792 DOI: 10.1023/a:1011052932607

Abstract

Purpose: In the summer of 1998, Norvir semi-solid capsules supplies were threatened as a result of a new much less soluble crystal form of ritonavir. This report provides characterization of the two polymorphs and the structures and hydrogen bonding network for each form.

Methods: Ritonavir polymorphism was investigated using solid state spectroscopy and microscopy techniques including solid state NMR, Near Infrared Spectroscopy, powder X-ray Diffraction and Single crystal X-ray. A sensitive seed detection test was developed.

Results: Ritonavir polymorphs were thoroughly characterized and the structures determined. An unusual conformation was found for form II that results in a strong hydrogen bonding network A possible mechanism for heterogeneous nucleation of form II was investigated.

Conclusions: Ritonavir was found to exhibit conformational polymorphism with two unique crystal lattices having significantly different solubility properties. Although the polymorph (form II) corresponding to the "cis" conformation is a more stable packing arrangement, nucleation, even in the presence of form II seeds, is energetically unfavored except in highly supersaturated solutions. The coincidence of a highly supersaturated solution and a probable heterogeneous nucleation by a degradation product resulted in the sudden appearance of the more stable form II polymorph.

Similar articles

Business news:

thepharmaletter

* Up to date news for the Pharmaceutical and Biotechnology industries

Abbott Reports Production Problems For Norvir

27-07-1998

Abbott Laboratories has reported that it is having difficultiesmaintaining production of its HIV protease inhibitor Norvir (ritonavir). The problems are related to its capsule formulation of the antiretroviral.

"We have encountered an undesired formation of a Norvir crystalline structure that affects how the capsule form of Norvir dissolves," commented Arthur Higgins, senior vice president for pharmaceutical operations at Abbott. Although the problem has been identified, to date the company has been unable to come up with a solution.

Abbott stressed that capsules already in circulation are not affected, but there will be shortages and an interruption in supply of the product. Given the seriousness of interrupting treatment in highly-active antiretroviral therapy (which could be associated with the development of resistance and ultimately treatment failure), Abbott is planning to manufacture Norvir in a substitute oral solution so that patients on the drug can maintain their supply. It is estimated that 60,000-70,000 people with HIV are taking the drug.

Effect On Full-Year Sales? Abbott had been projecting sales of around $250 million for Norvir in 1998, and as yet it is unclear whether the supply problems will impact this figure. Sales of the drug last year were around $170 million, less than the performance seen with the other protease inhibitors in 1997. Datamonitor says that Merck & Co's Crixivan (indinavir) had sales of $240 million last year, while Agouron's Viracept (nelfinavir) made around $190 million last year, and Roche's Invirase (saquinavir) made over $200 million.

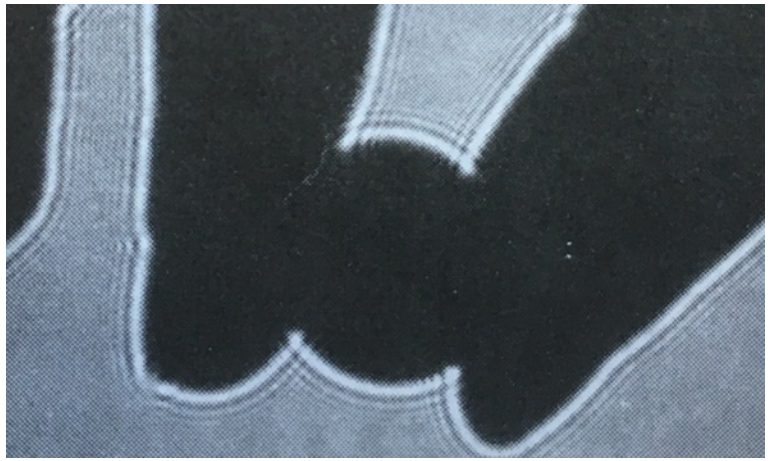
Analyst Hemant Shah of HKS & Co told Reuters that the other protease inhibitors would definitely gain market share at the expense of Norvir, adding that the impact on Abbott's bottom line will depend greatly on the duration of the problem.

Some very basics about diffraction and scattering

Diffraction, a short review

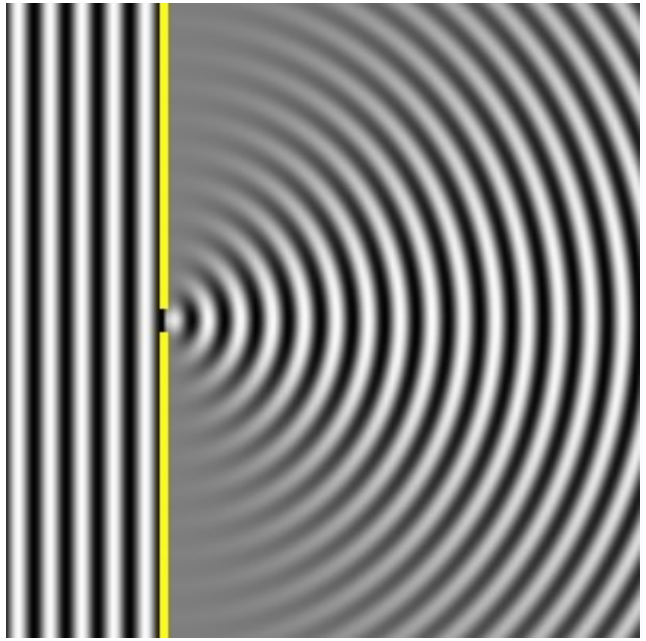
https://physicsforme.com/2012/01/04/teaching-waves-with-google-earth/

- Should be familiar concept
- A wave encountering an object changes its wavefront. Note that this can also be a density change (later more)
- Fundamental properties of all waves with relevant effects from electron microscopy to shaping coastal landscapes
- In optics most commonly known for limiting resolution in optical setups (microscopes)
- But there is much more!

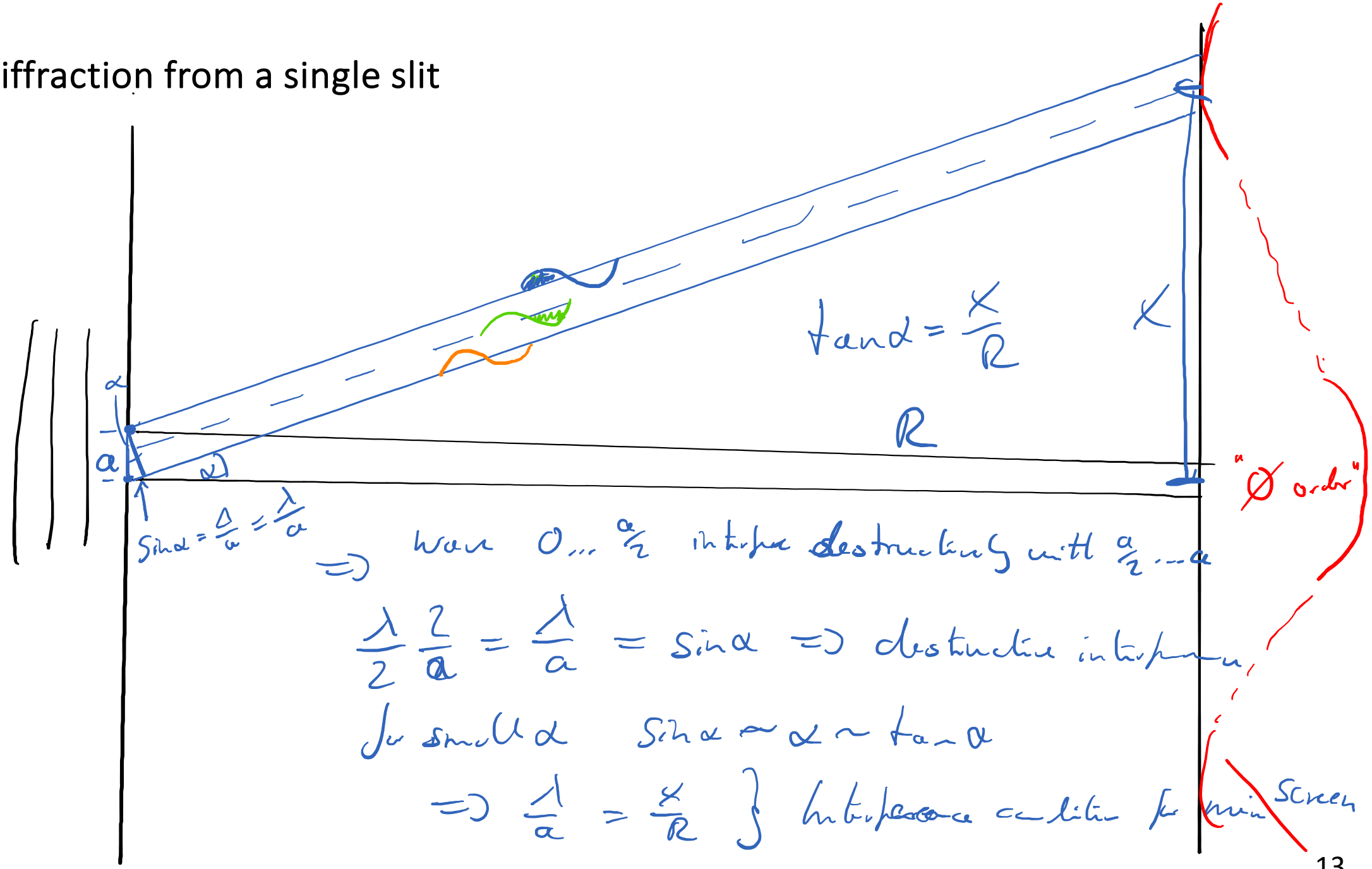


The Huygens-Fresnel Principle

- Hugens: every point a wave (a luminous disturbance) reaches becomes a source of a spherical wave; the sum of these secondary waves determines the form of the wave at any subsequent time.
- Huygens-Fresnel: every unobstructed point of a wavefront serves as a source of spherical secondary wavelets. The amplitude of the wave beyond is the superposition of all these wavelets. (includes amplitude and relative phase)



Diffraction from a single slit



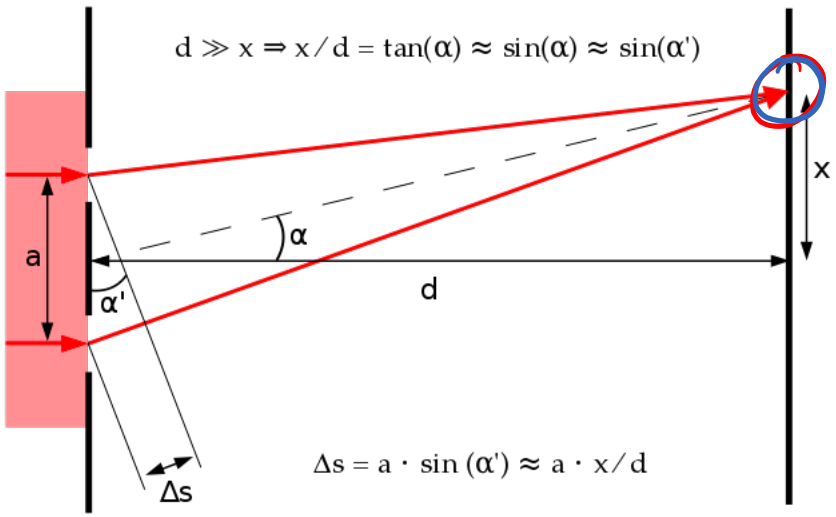
$\Rightarrow$ wave $0 \ldots \frac{a}{2}$ interfere destructively with $\frac{a}{2} \ldots a$

$$\frac{\lambda}{2}\frac{2}{a} = \frac{\lambda}{a} = \sin\alpha \Rightarrow \text{destructive interference}$$

for small α $\quad \sin\alpha \sim \alpha \sim \tan\alpha$

$$\Rightarrow \frac{\lambda}{a} = \frac{x}{R} \Big\} \text{ interference condition for min}$$

The double slit



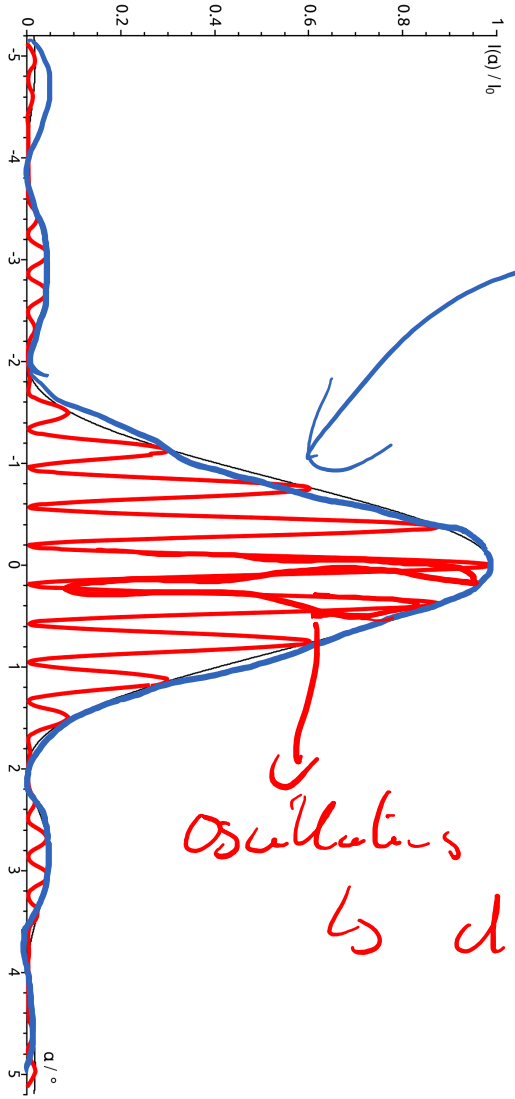
interference condition

↑

geometry

↳ two infinitesimal slits, separated by a distance

⇒ Fourier space



envelope

↓

slit size / single slit

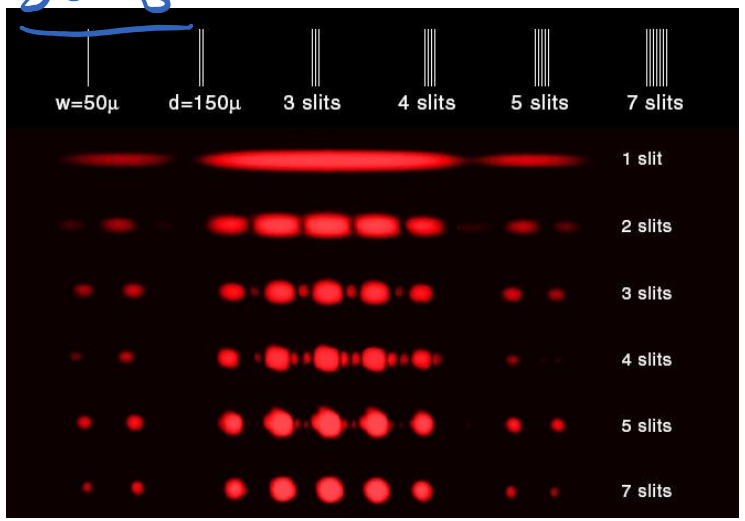
oscillations

↳ double slit

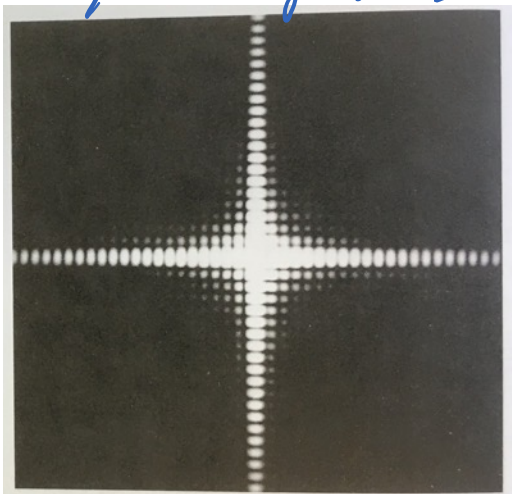
Image source: wikipedia

Diffraction examples

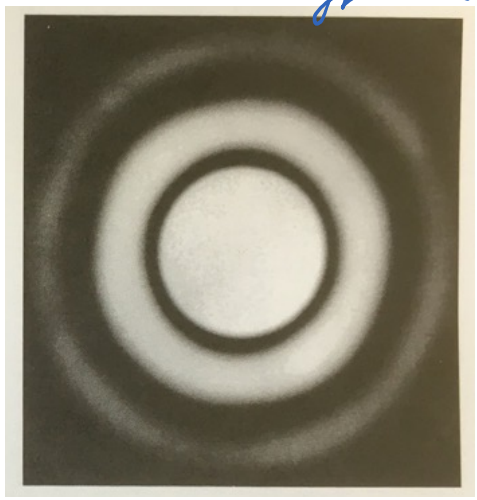
Slits



Square apertures

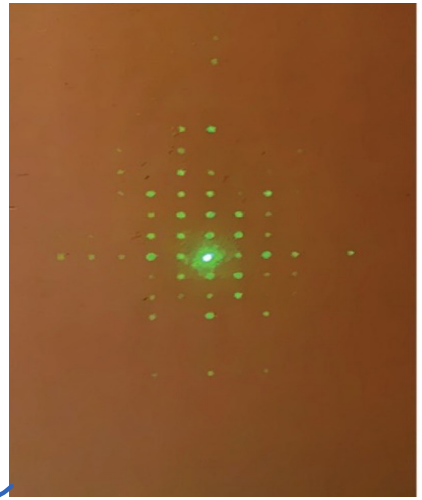


Circular apertures



Pixel pattern

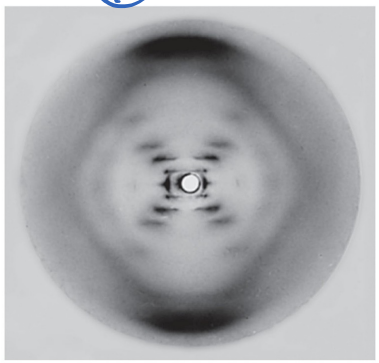
Again
Scattering approach
overcomes
resolution limit
of detectors



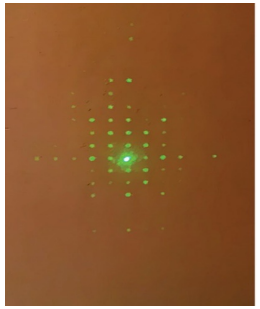
Watson Crick
DNA

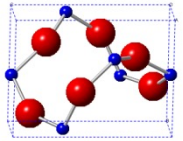
Rosalind
Franklin

X-ray diffraction
data of DNA



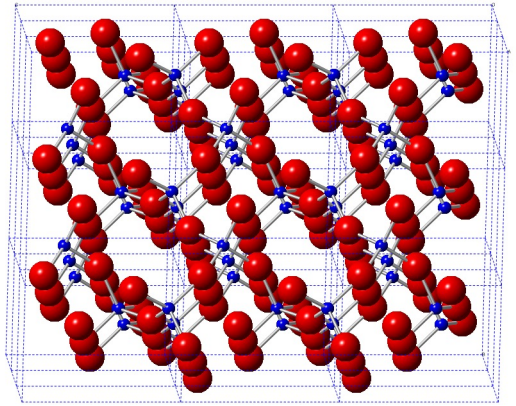
Crystaline materials are characterized by the long-range order





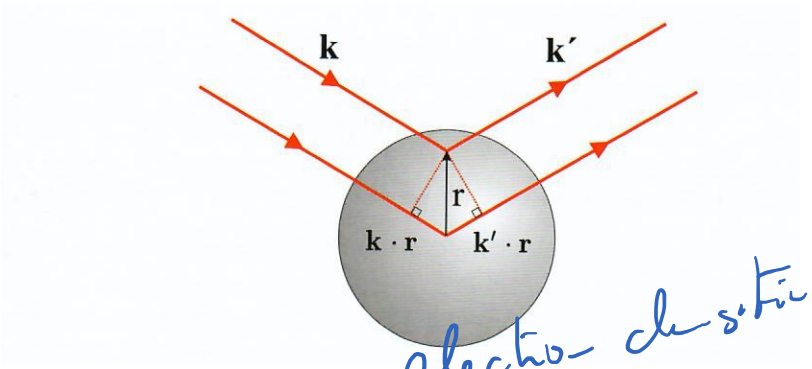
unit cell

lattice

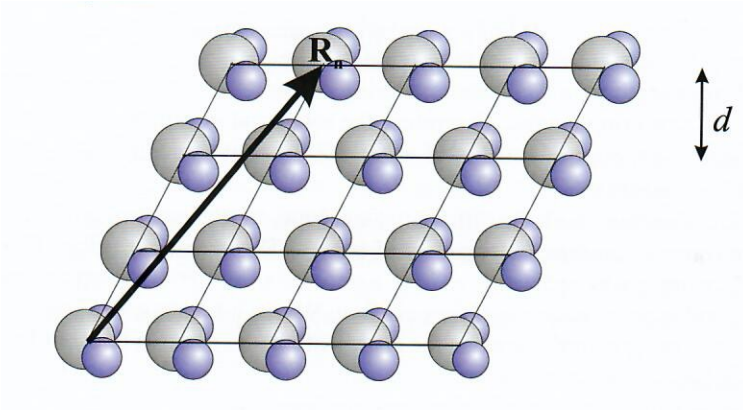


macroscopic properties

atom



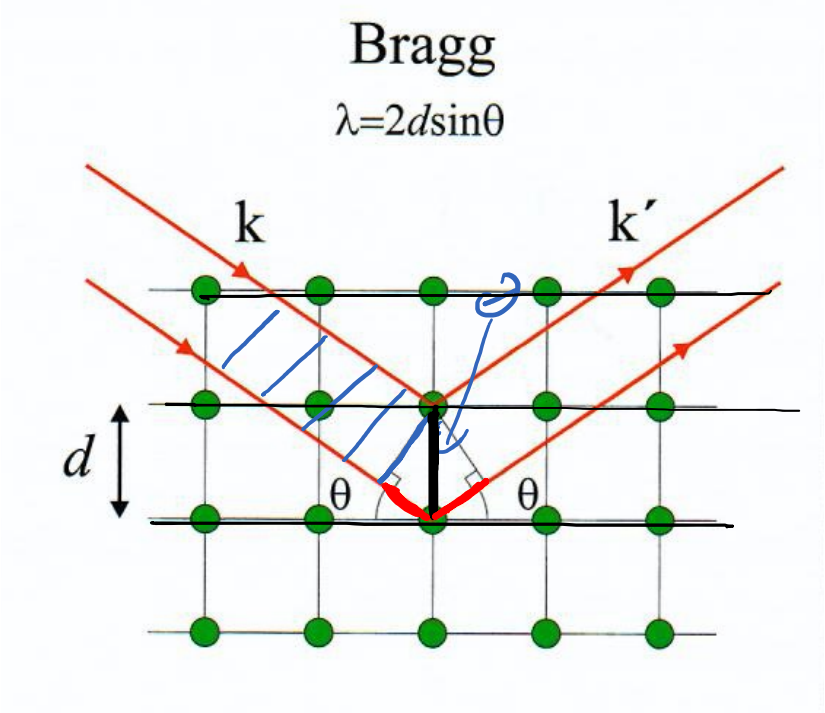
electron density

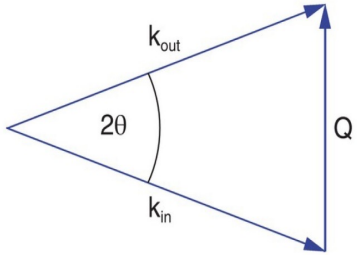


→ electrons are localized at atoms

in periodic arrangement

Bragg scattering





→ atoms in defined positions

→ defined crystal planes

→ x-rays can "reflect" from these planes

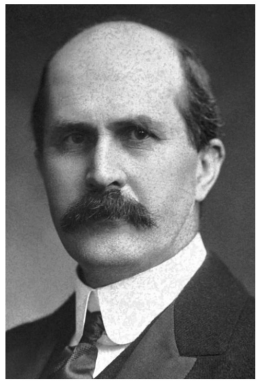


Photo from the Nobel Foundation archive.
Sir William Henry Bragg
Prize share: 1/2

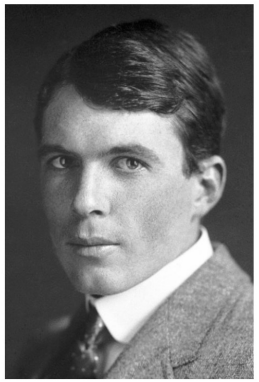


Photo from the Nobel Foundation archive.
William Lawrence Bragg
Prize share: 1/2

The Nobel Prize in Physics 1915

Main idea: exploit interference phenomena

constructive interference

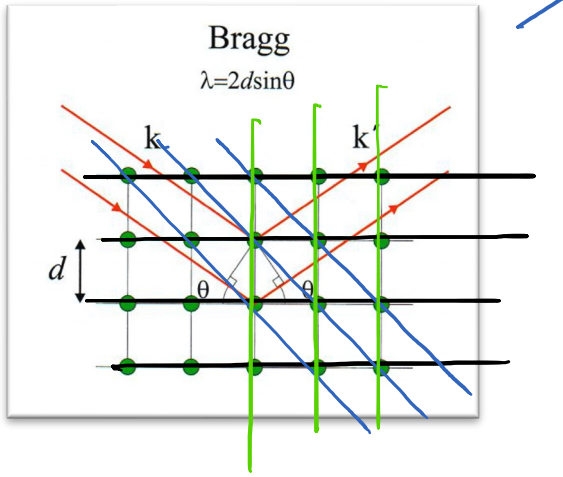
$$\Rightarrow \lambda = 2 \cdot d \sin\theta$$

$$\sin\theta = \frac{n\lambda}{2d} \Rightarrow \boxed{2d\sin\theta = n\lambda}$$

$n = 1, 2, 3, \ldots$

Bragg law

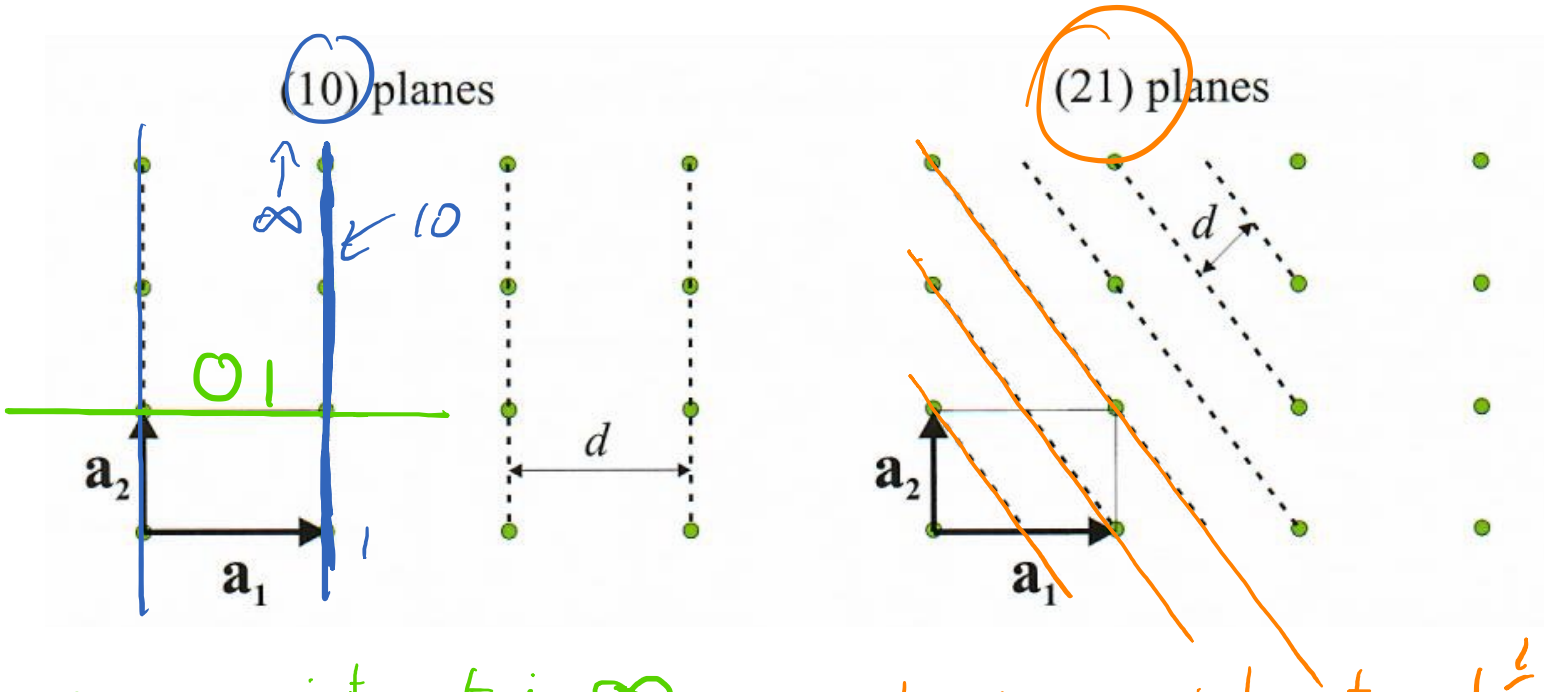
Lattice planes



Formal way of describing lattice planes

1) Look where plane intersects axes

2) Take the inverse number & reduce to smallest number



Step ① a_1, intersects in ∞
a_2, intersects in 1

Step ② $\frac{1}{\infty}$ and $\frac{1}{1}$

Step 1: a_1 intersects at $\frac{1}{2}$
a_2 intersects at 1

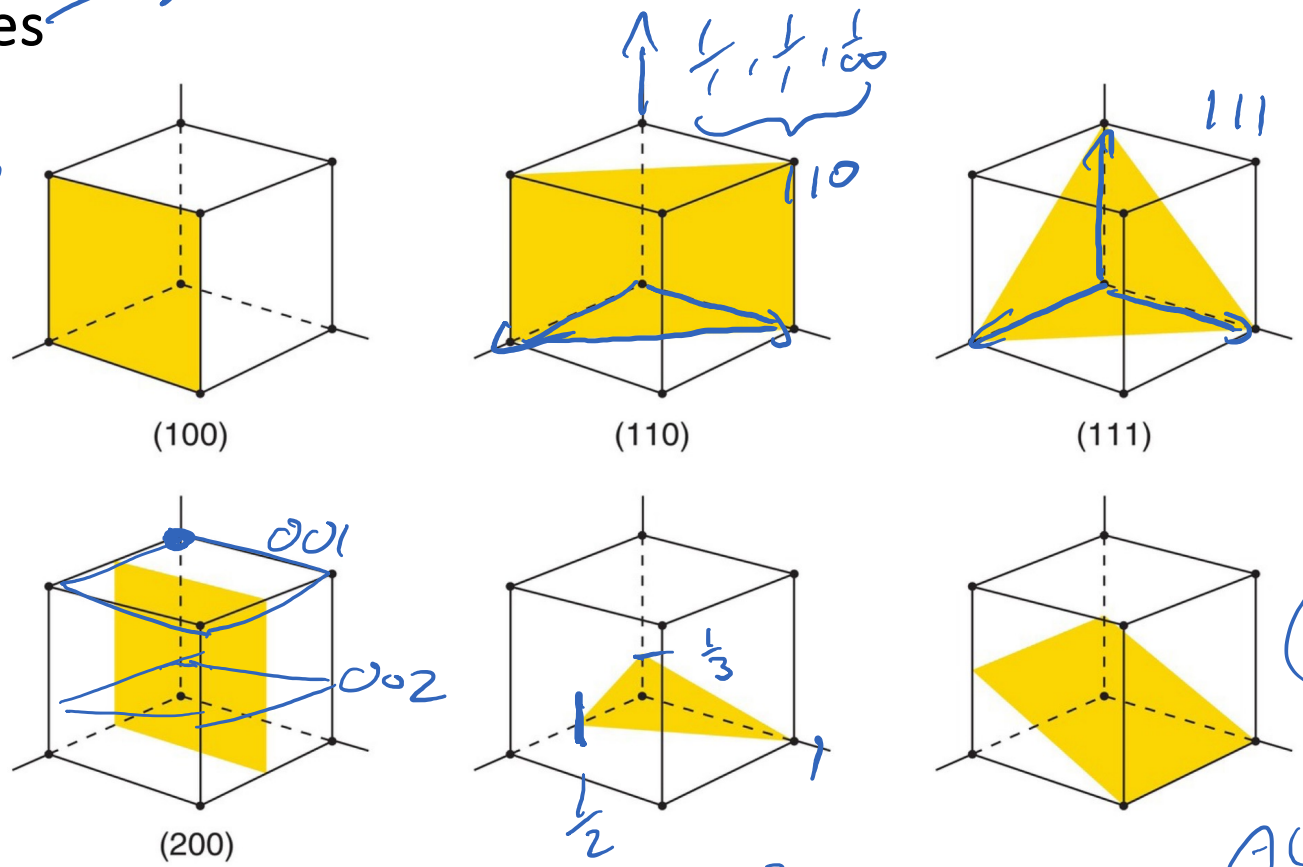
Step 2: $\frac{1}{1/2}$ and $\frac{1}{1}$ ⇒ 21

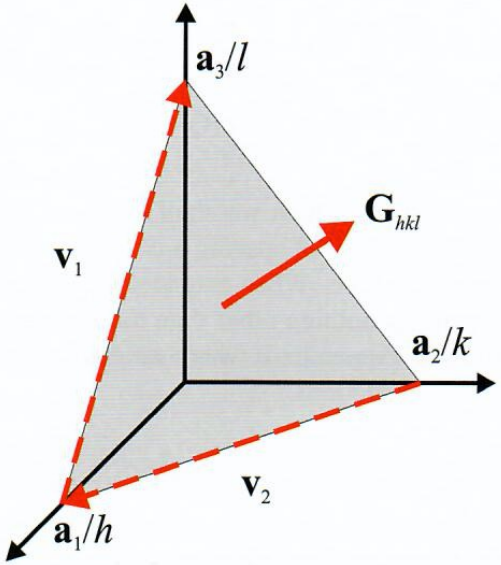
Miller indices

Common way to describe lattice planes

$\frac{1}{1}, \frac{1}{\infty}, \frac{1}{\infty}$

100





(012)

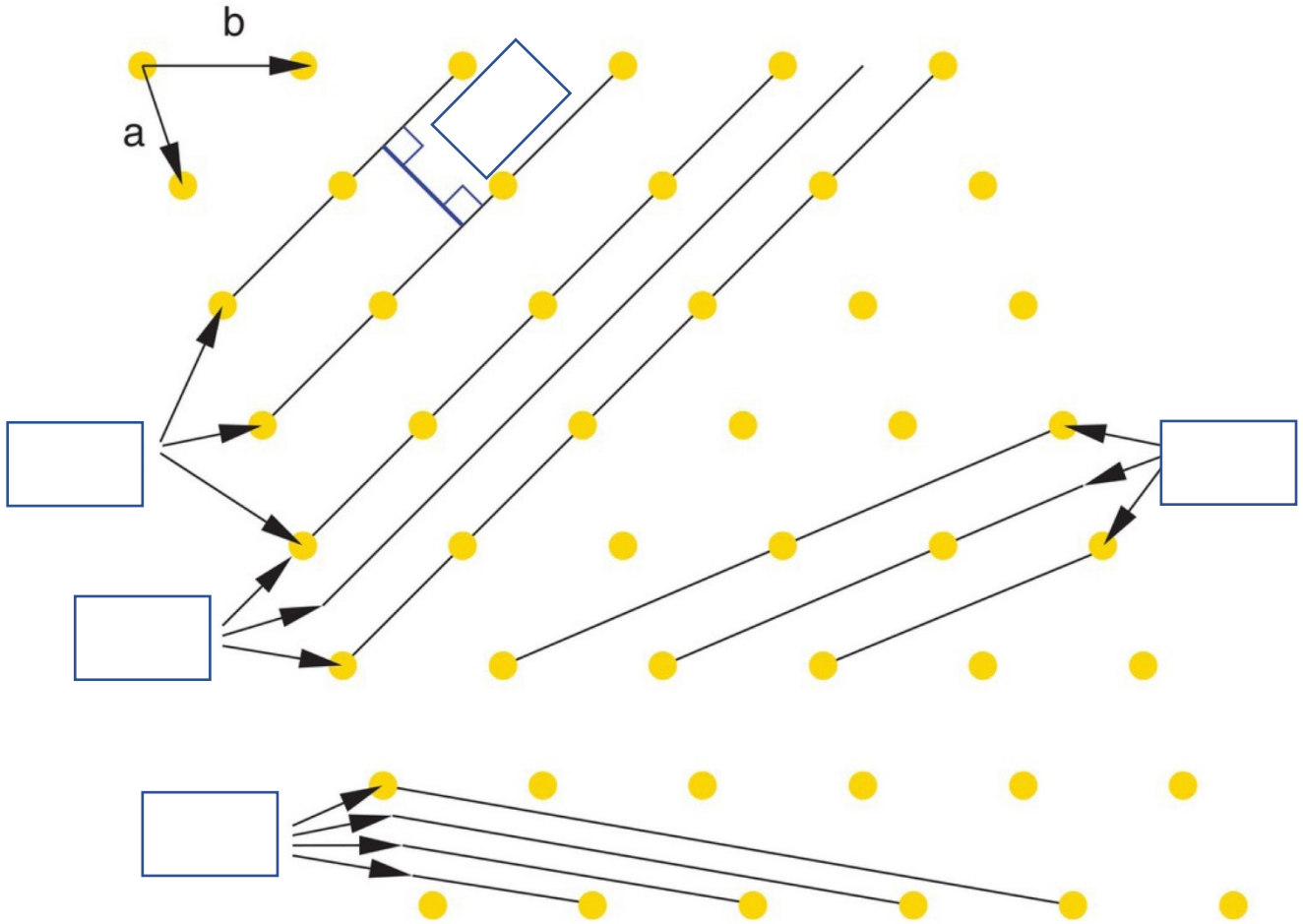
x	y	z
$\frac{1}{\frac{1}{2}}$	$\frac{1}{1}$	$\frac{1}{\frac{1}{3}}$

(2 1 3)

Algorithm

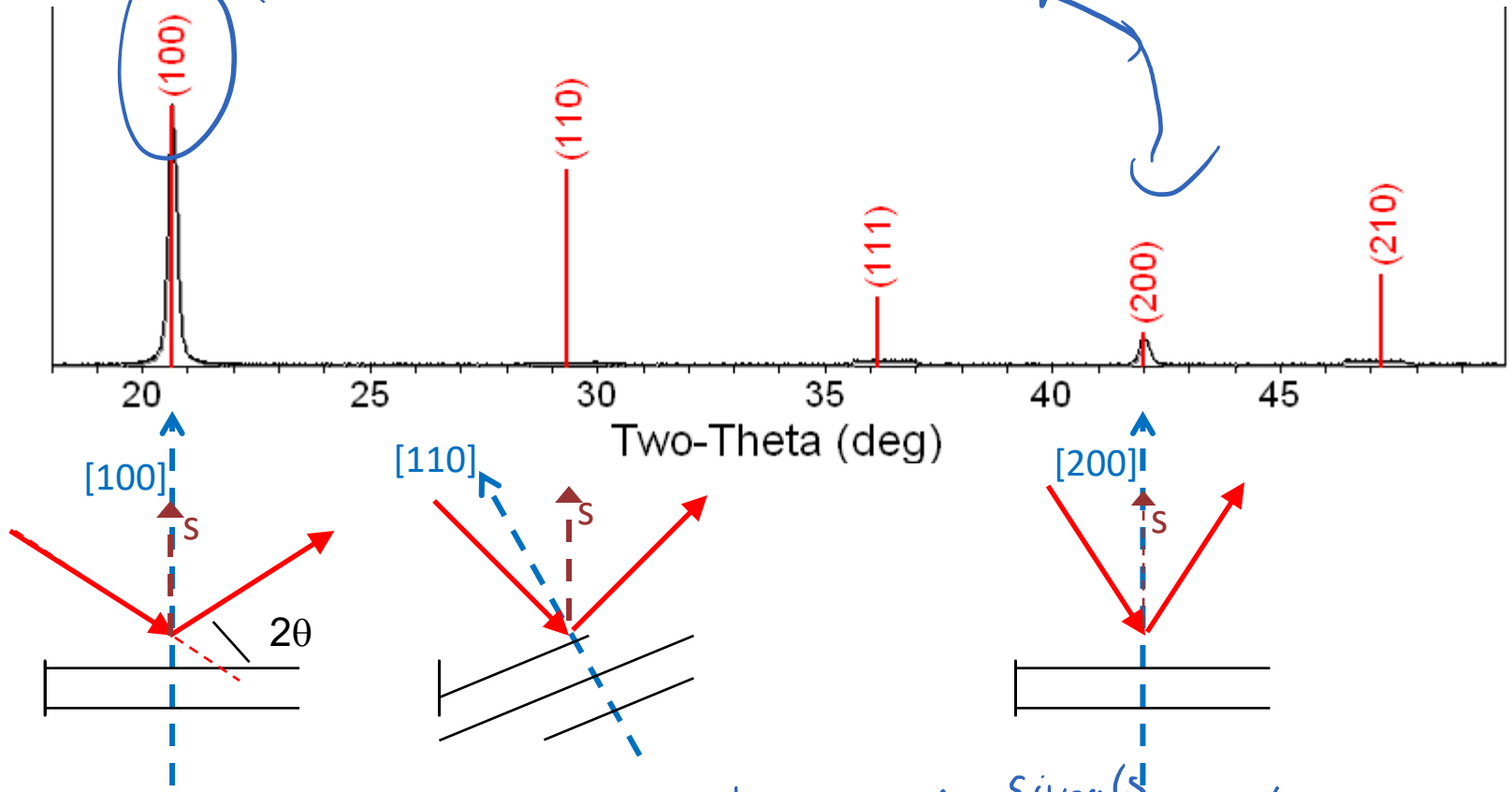
- find the intercepts of the plane on respective axis
- take the reciprocal of these numbers, reduce to smallest ones

Exercise: Identify lattice planes



A single crystal (typically) produces one family of Bragg peaks for fixed geometry and λ

parallel

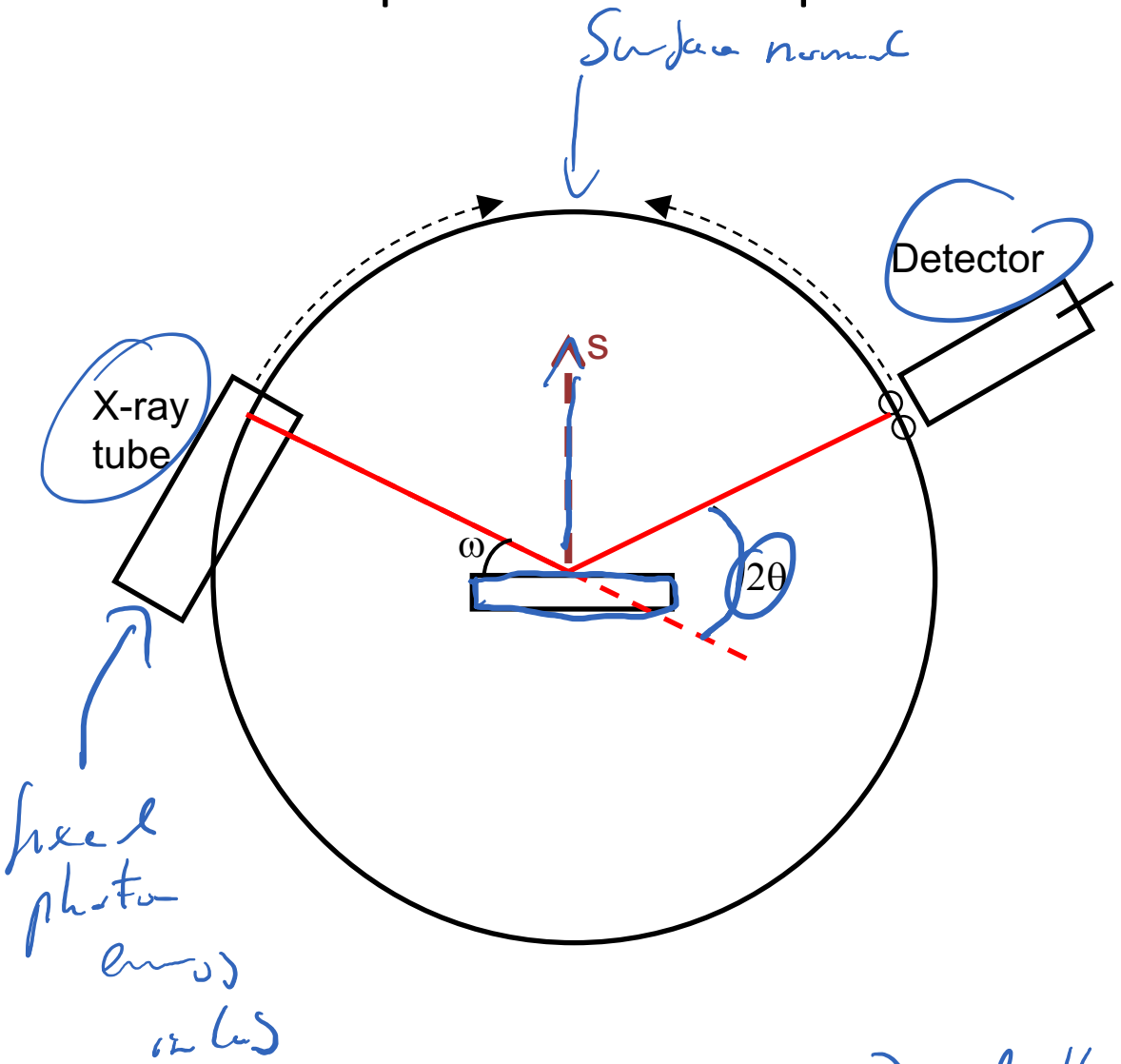


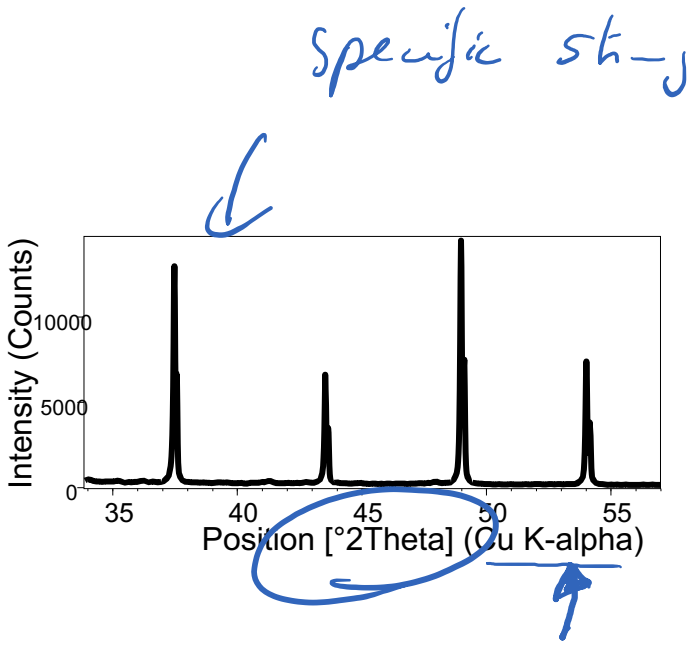
100, 200 parallel, both yield ~~signals~~ signals at different angles

If Bragg condition is not met → no constructive interference (no signal)

Diffraction examples

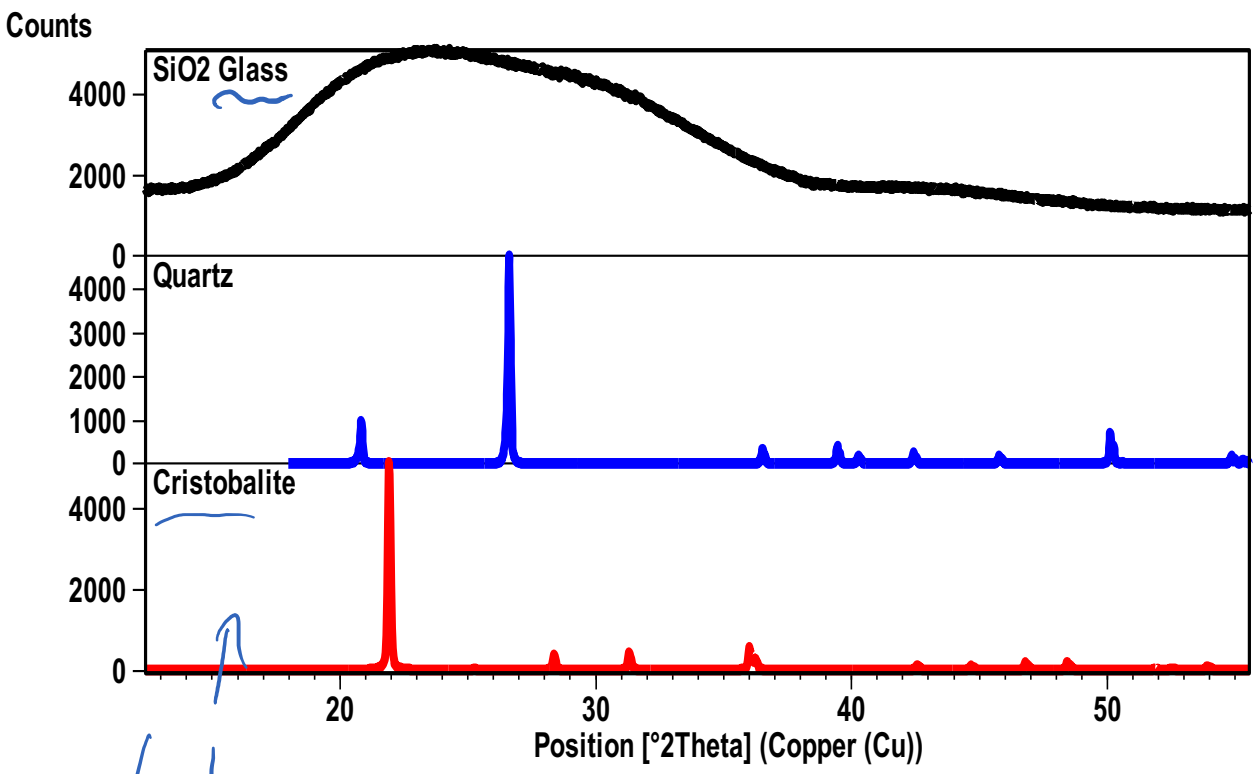
Diffraction experiment - example



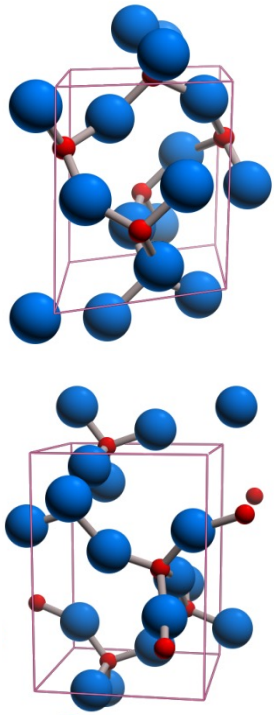


⟹ diffraction signal ⟺ structure of your sample

Characteristic signals from different – chemically identical – samples



high pressure phase



all SiO_2 samples but different phases

all structures are chemically identical

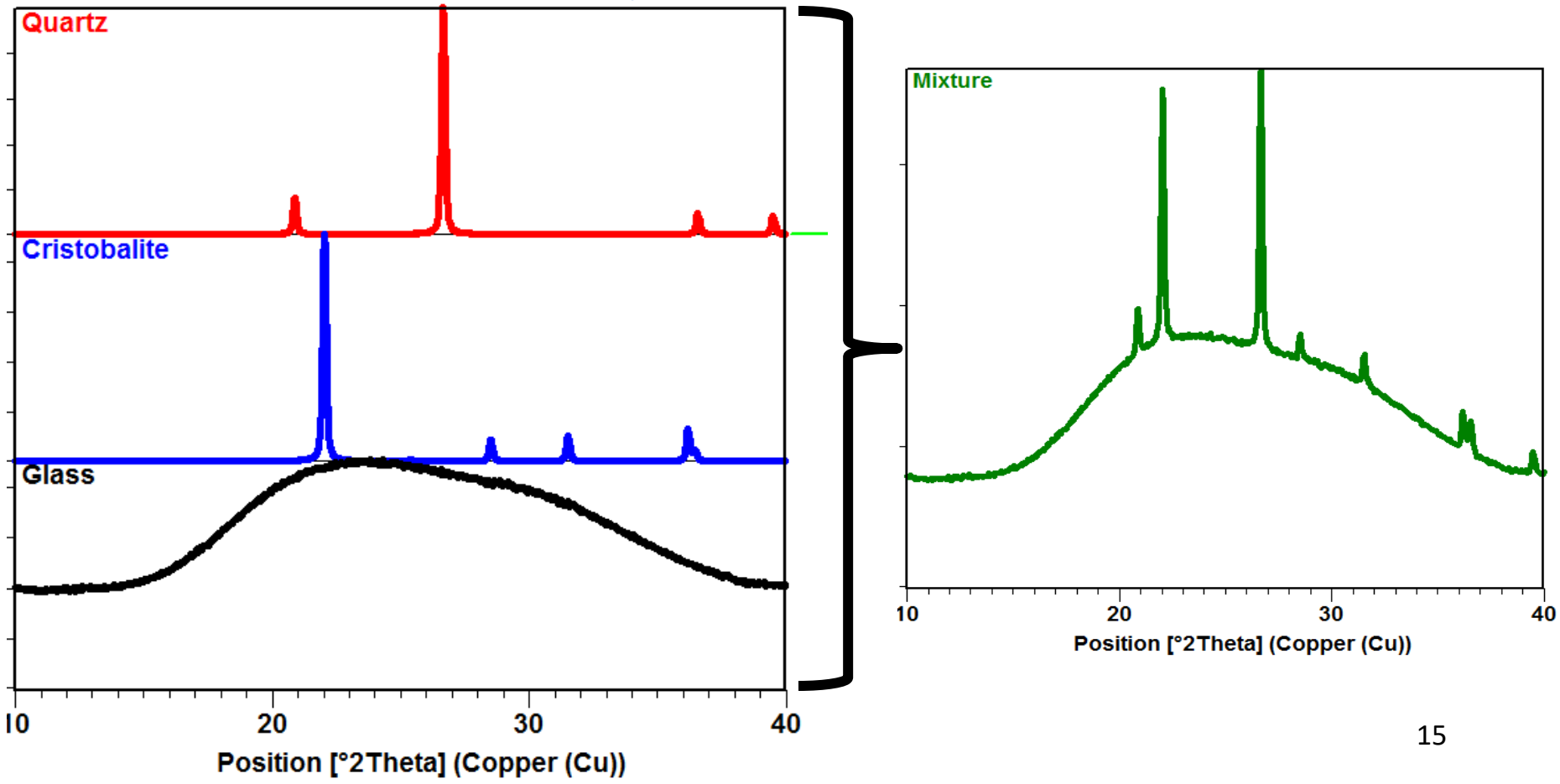
but their structures different

⇓

XRD yield info atomic arrangements

The diffraction pattern of a mixture is a simple sum from each component phase

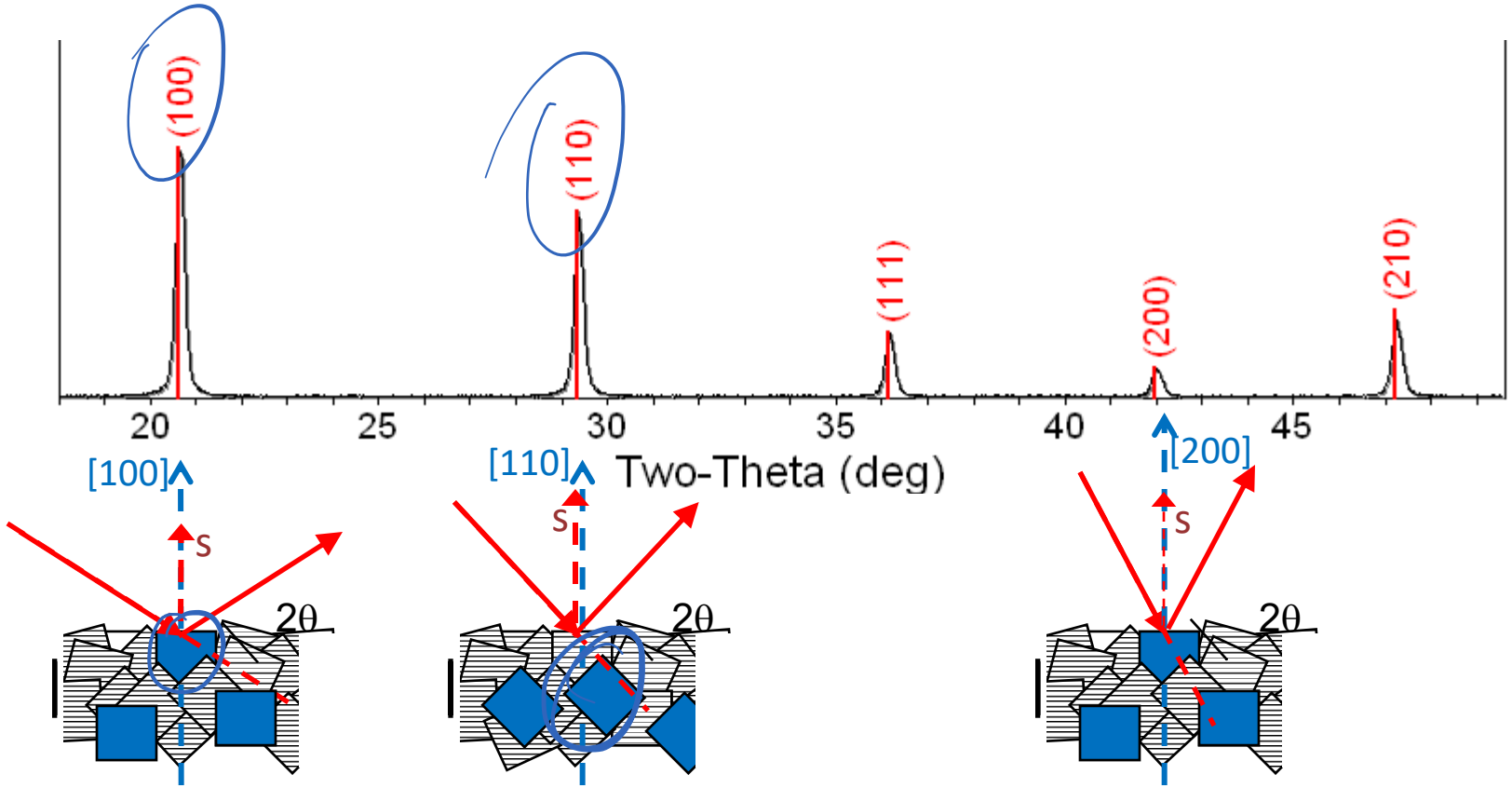
⟹ good analysis tools



15

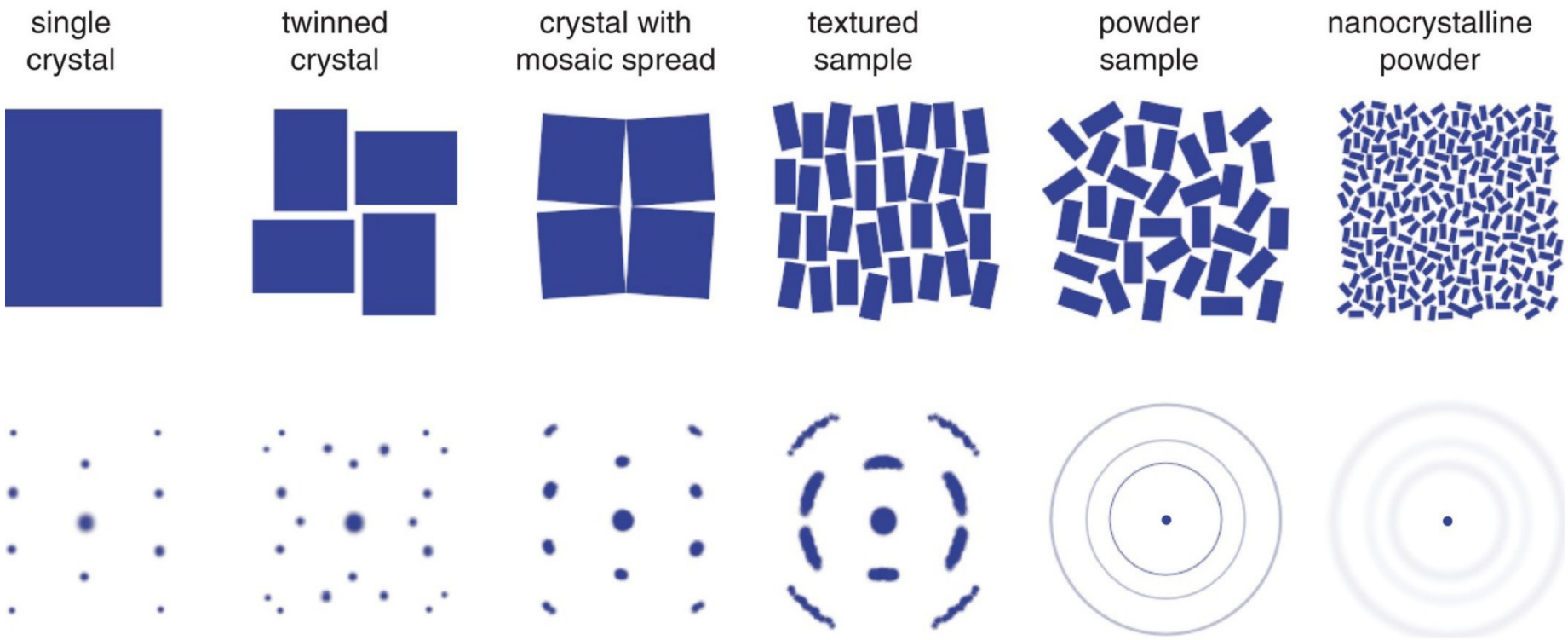
Powder diffraction

Diffraction of a polycrystalline sample

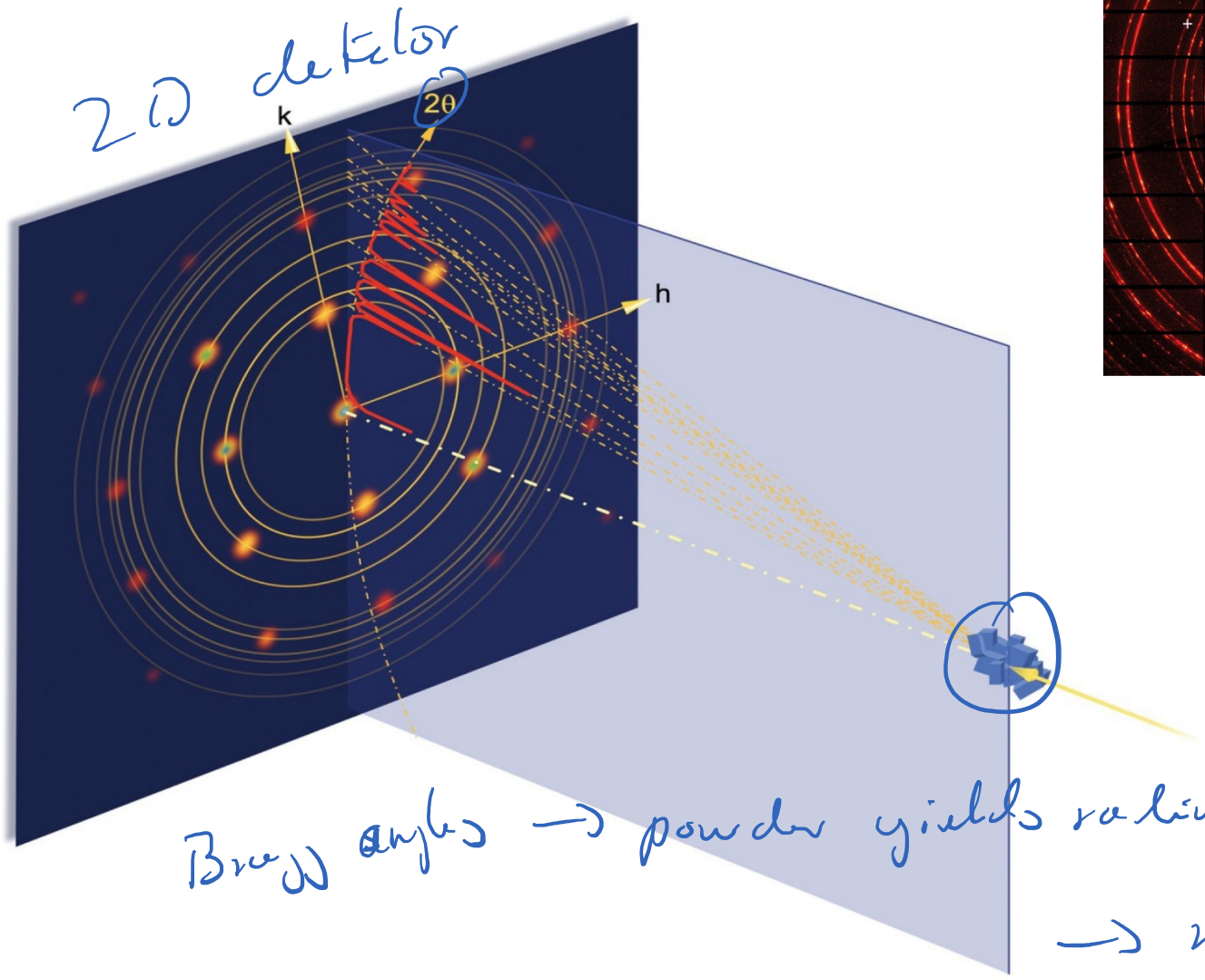


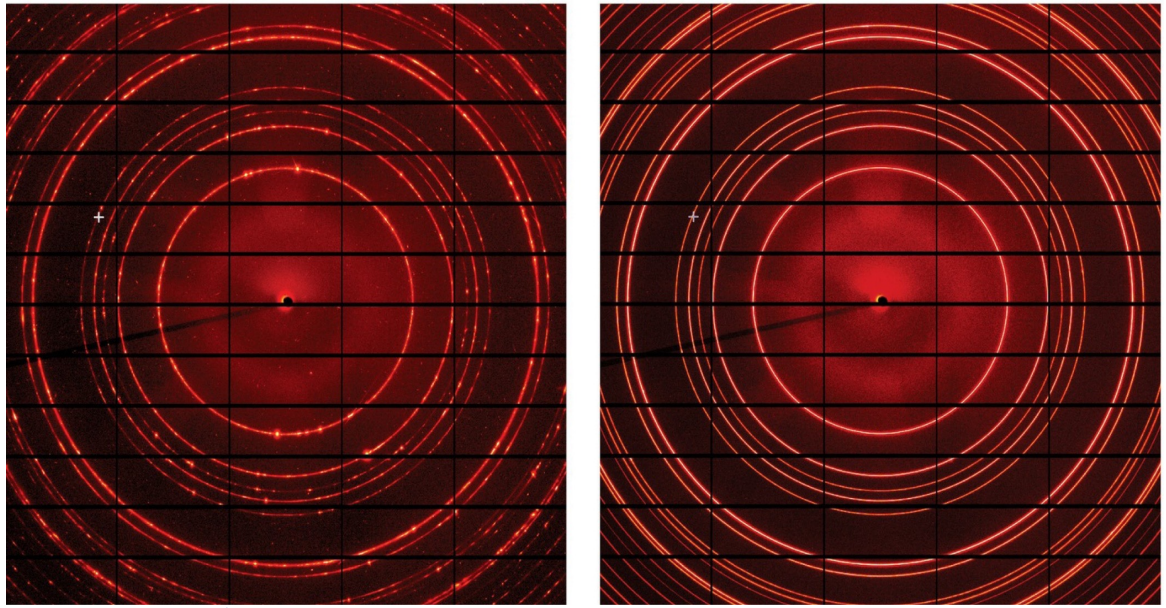
⇒ measure all possible orientations in a statistical average

Diffraction signal of different sample types



Powder diffraction experiments





crystallites sizes

average

⟹ 2D pixel detectors

Bragg angles → powder yields radial average – 2θ

→ rings

Powder diffraction geometry → Laue diffraction

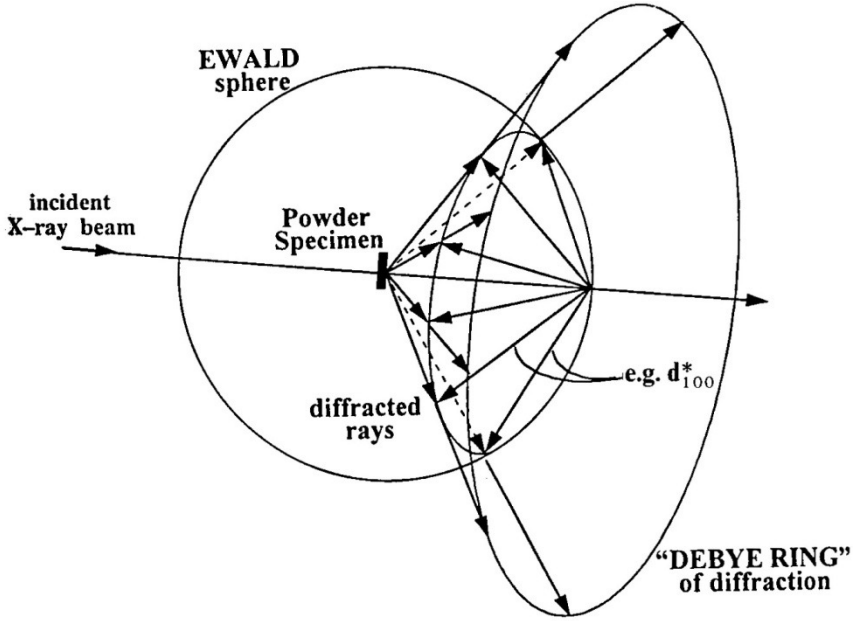
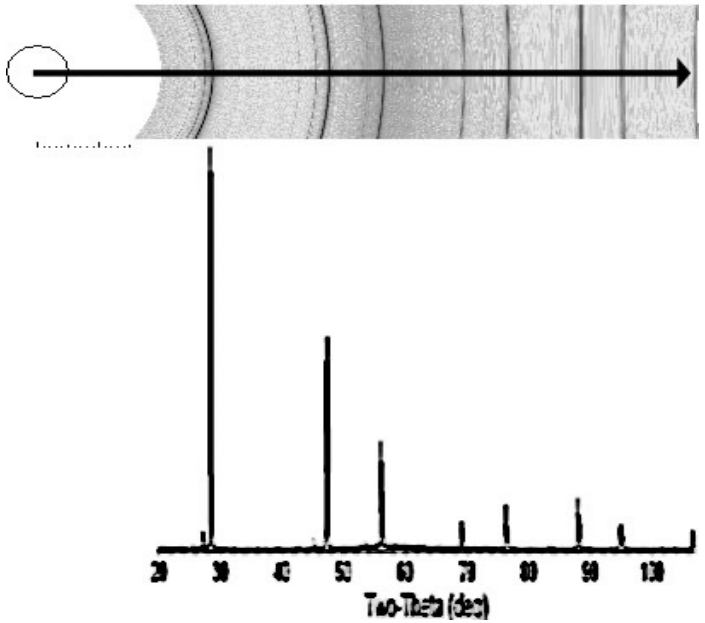


Figure 3.9. The intersection of $\mathbf{d}^*_{100}$ vectors from a powder with the Ewald sphere.

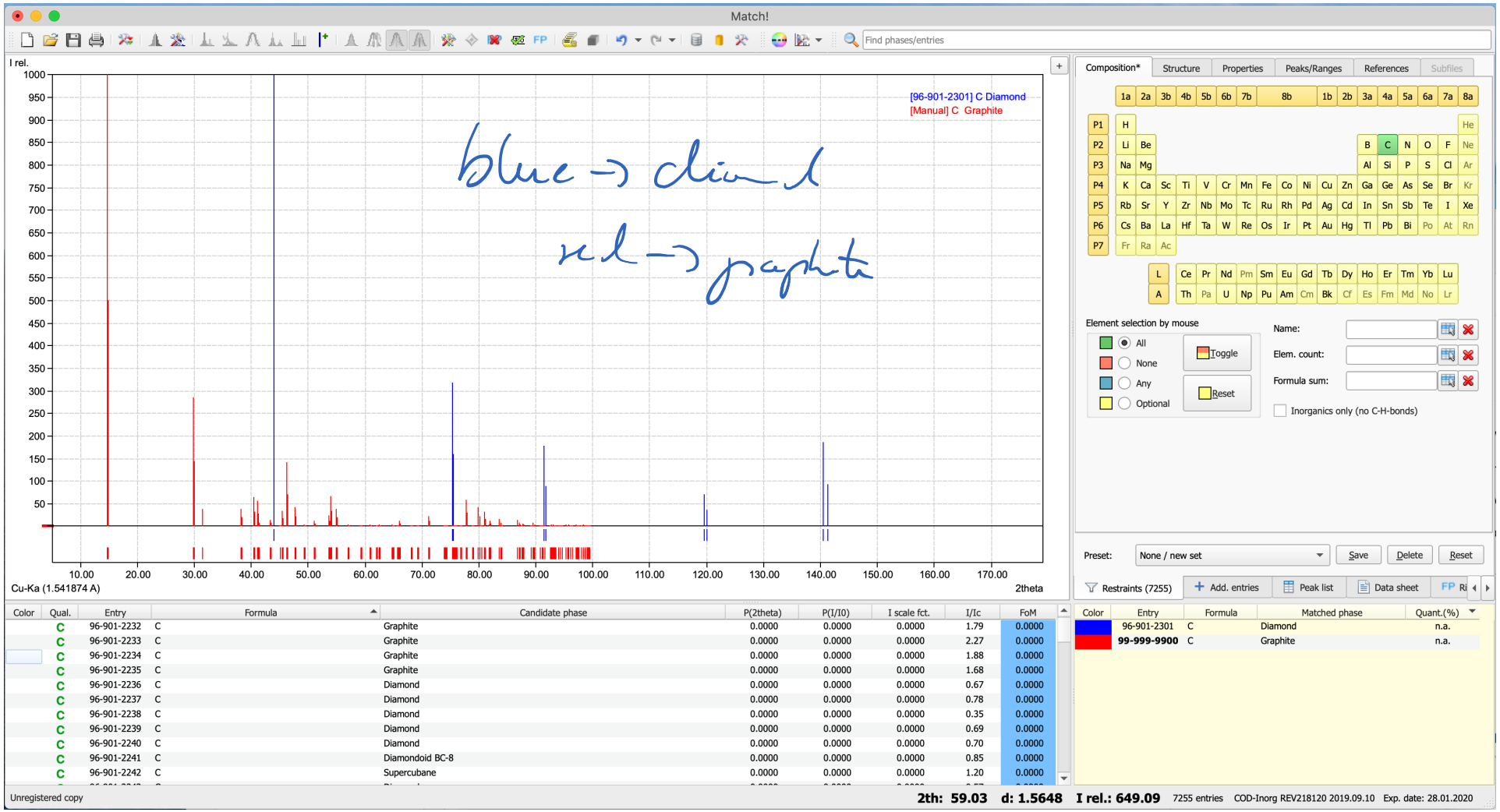


↑ transmission geometry

↑ rings in detector plane

↑ earlier strip/film detectors, today 2D pixel detectors

Powder diffraction data bases for elemental analysis

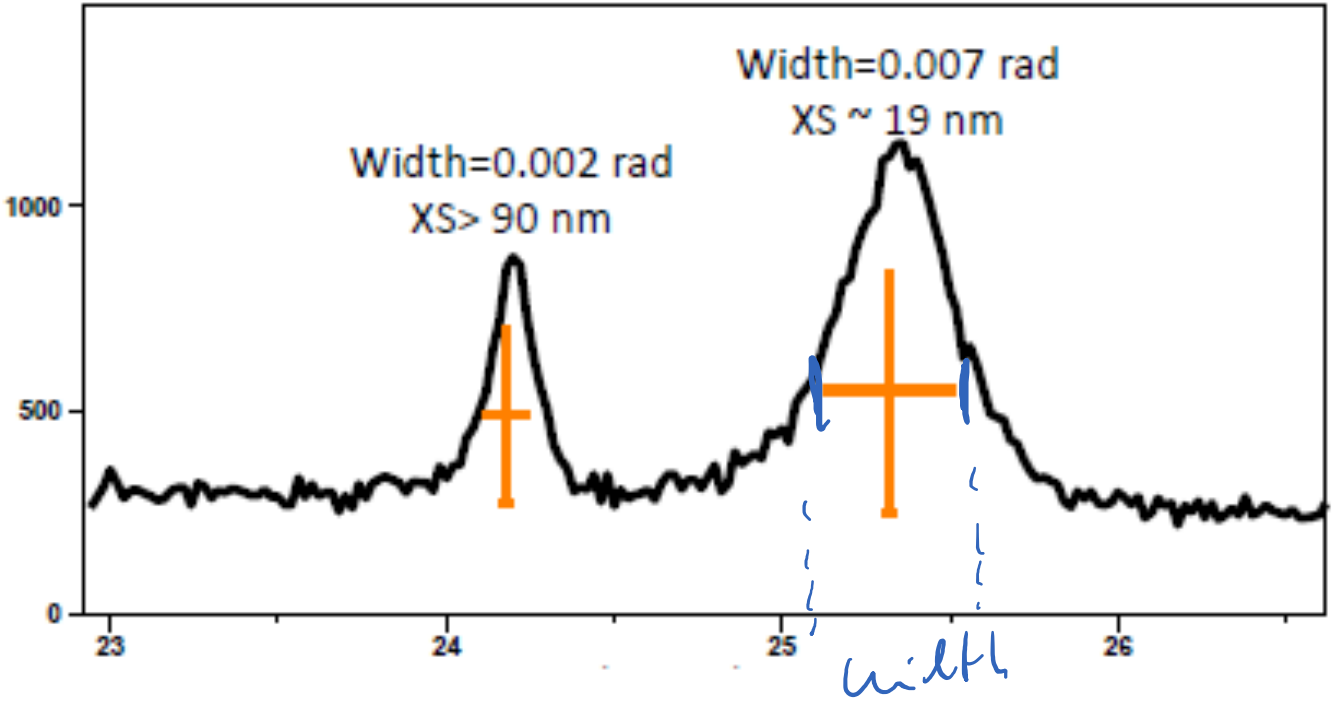


Commonly used for structure & phase analysis

feed in your pattern, → spits out structure

Debye-Scherrer Formula

The diffraction peak width may contain microstructural information



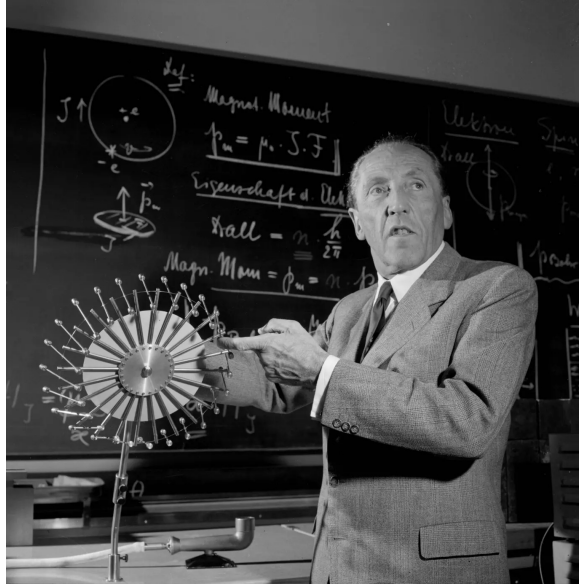
roughly < 100nm

K~0.9

$$\text{Size} = \frac{K\lambda}{Width * \cos\theta}$$

Relates width of diffraction peak with particle size

for small samples with-l infinite translational symmetry

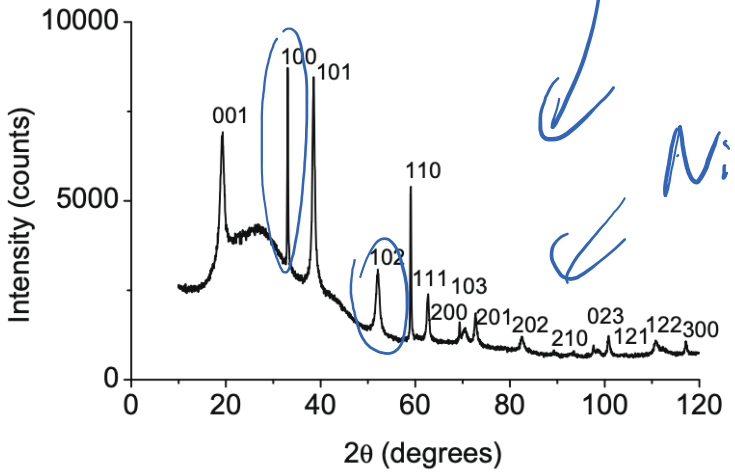


Paul Scherrer
Swiss Physicist (1890-1969)

Exercise: Colloidal nanoparticles

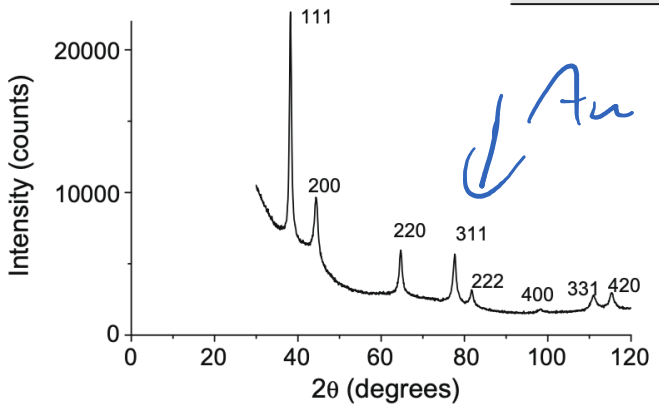
→ Debye Scherrer

The diffraction experiments were carried out with a Stoe STADI-P X-ray powder diffractometer at University College London with a Ge(111) monochromator before the sample. A Cu $K\alpha_1$ X-ray beam of wavelength 0.154056 nm was used. The samples were measured in 0.35 mm diameter glass capillaries at room temperature. Capillary diameters were checked to be equal with a micrometer. The diffraction patterns were collected using a position-sensitive



$Ni(OH)_2$

Fig. 1. X-ray diffraction pattern from $Ni(OH)_2$ dispersion ($c = 4.610(3)$ Å) with diffraction peaks labeled with *hkl* indices



Au

Fig. 2. X-ray diffraction patterns from dispersed Au particles ($a = 4.067(3)$ Å) with diffraction peaks are labeled with *hkl* indices.

Journal of Colloid and Interface Science 338 (2009) 105–110

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Use of wide-angle X-ray diffraction to measure shape and size of dispersed colloidal particles

S. Junaid S. Qazi [a,*], Adrian R. Rennie [a], Jeremy K. Cockcroft [b], Martin Vickers [b]

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[b] *Applied Crystallography Group, Department of Chemistry, University College London, 20 Gordon Street, London WC1H 0AJ, UK*

Table 1
Results from the pseudo-Voigt function fit to the $Ni(OH)_2$ sample. 2θ is the peak position for the Cu $K\alpha_1$ radiation wavelength (0.154056 nm).

hkl	Bragg angle 2θ (°)	Peak width 'β' (°)	Instrument resolution (°)	Corrected β (°)
001	19.25	1.140	0.121	1.02
100	33.06	0.197	0.115	0.08
101	38.52	0.593	0.114	0.48
102	52.06	0.876	0.117	0.76
110	59.05	0.248	0.120	0.13
111	62.67	0.550	0.122	0.43

fill in

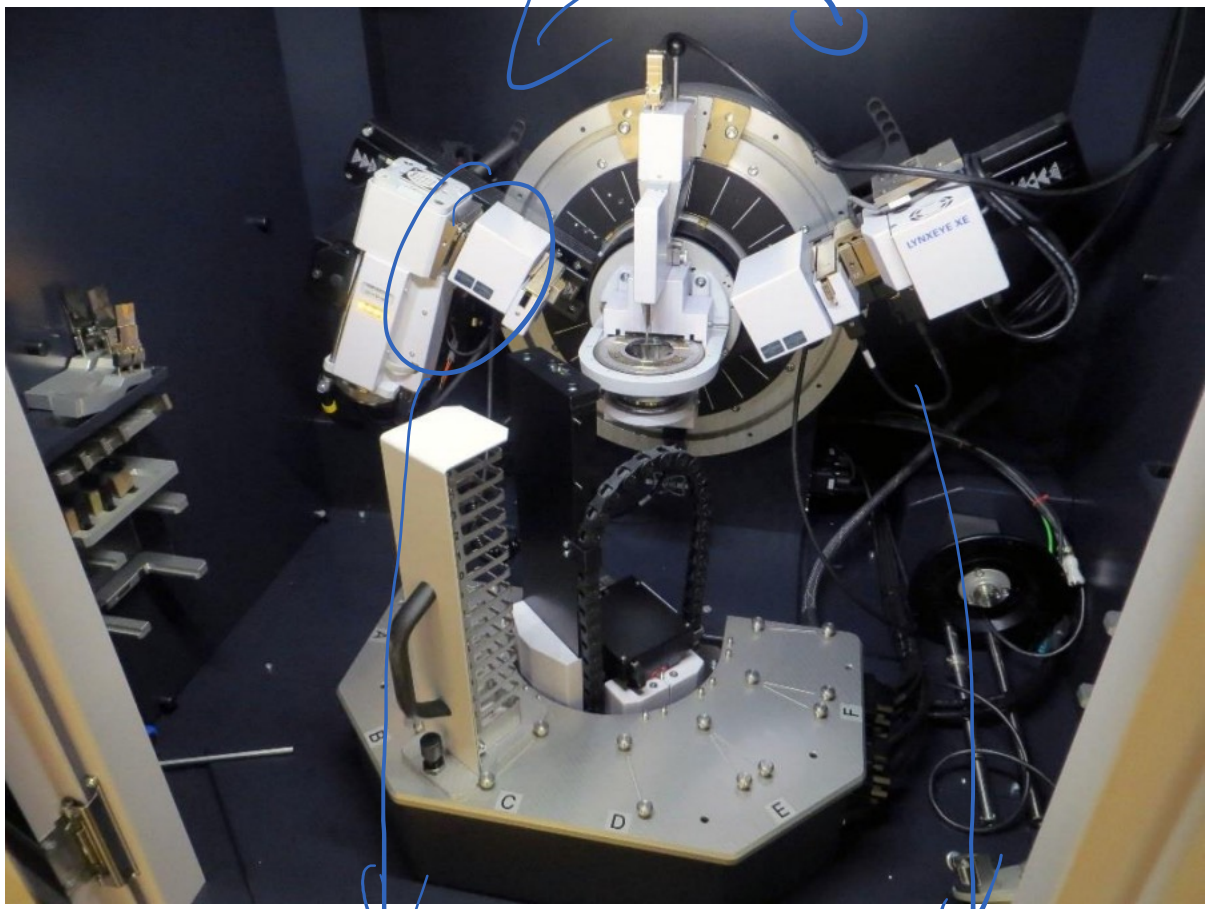
Table 2
Results from the pseudo-Voigt fit to the Au particles. 2θ is the peak position for the Cu $K\alpha_1$ radiation wavelength (0.154056 nm).

hkl	Bragg angle 2θ (°)	Peak width 'β' (°)	Instrument resolution (°)	Corrected β (°)
111	38.21	0.580	0.114	0.47
200	44.34	0.822	0.115	0.71
220	64.69	0.810	0.123	0.68
311	77.63	0.905	0.135	0.77
420	115.34	1.194	0.119	1.07

A few examples and case studies

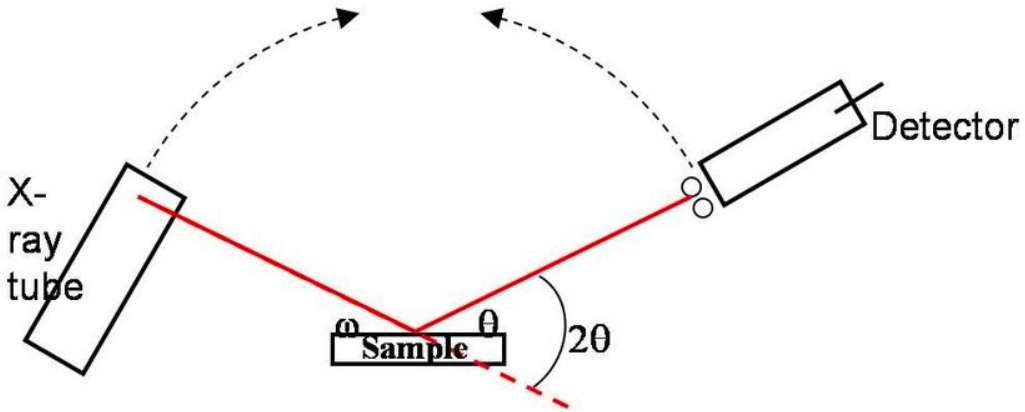
Example: EPFL XRD instrument

2D



Source

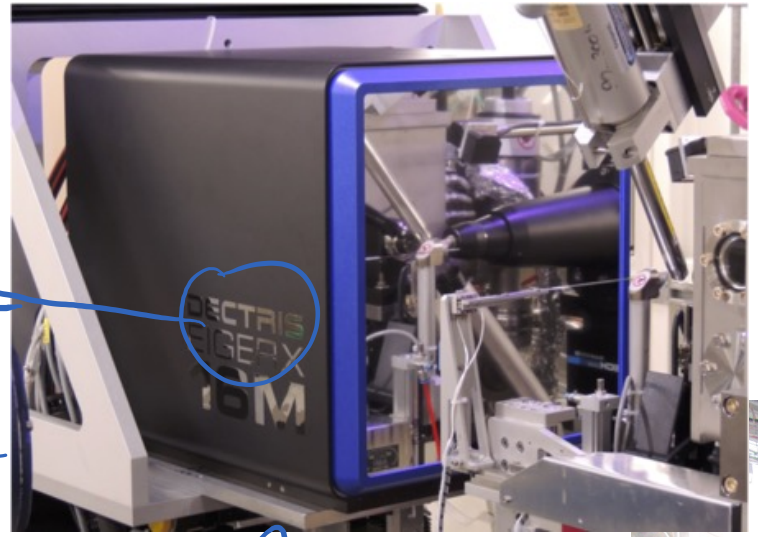
detector



→ accessible as tool

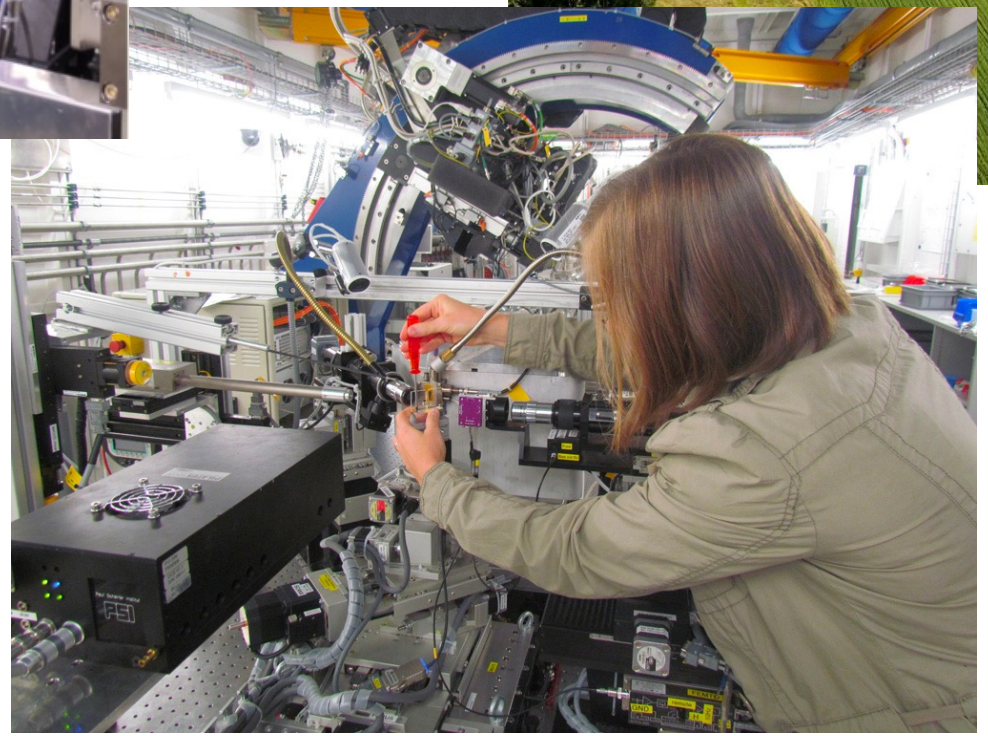
→ elective course about XRD

Example Synchrotron Source



Spin off PSI

(expensive) area detectors



delicated beamlines for different approaches

Villigen

Some beamlines delicated to powder diff.

Example: In-operando battery research

JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Article
pubs.acs.org/JACS

In Operando X-ray Diffraction and Transmission X-ray Microscopy of Lithium Sulfur Batteries

Johanna Nelson,[†,‡,⊥] Sumohan Misra,[†,⊥] Yuan Yang,[§,⊥] Ariel Jackson,[§] Yijin Liu,[†] Hailiang Wang,[∥] Hongjie Dai,[∥] Joy C. Andrews,[†] Yi Cui,*[,‡,§] and Michael F. Toney*[,†,‡]

[†]Stanford Synchrotron Radiation Lightsource, and [‡]Stanford Institute for Materials and Energy Science, SLAC National Accelerator Laboratory, 2575 Sand Hill Road, Menlo Park, California 94025, United States

[§]Department of Materials Science and Engineering, and [∥]Department of Chemistry, Stanford University, Stanford, California 94305, United States

→ new/alternative battery designs

→ structural/morphological changes at cathode

→ Exp showed recrystallization of S during charging

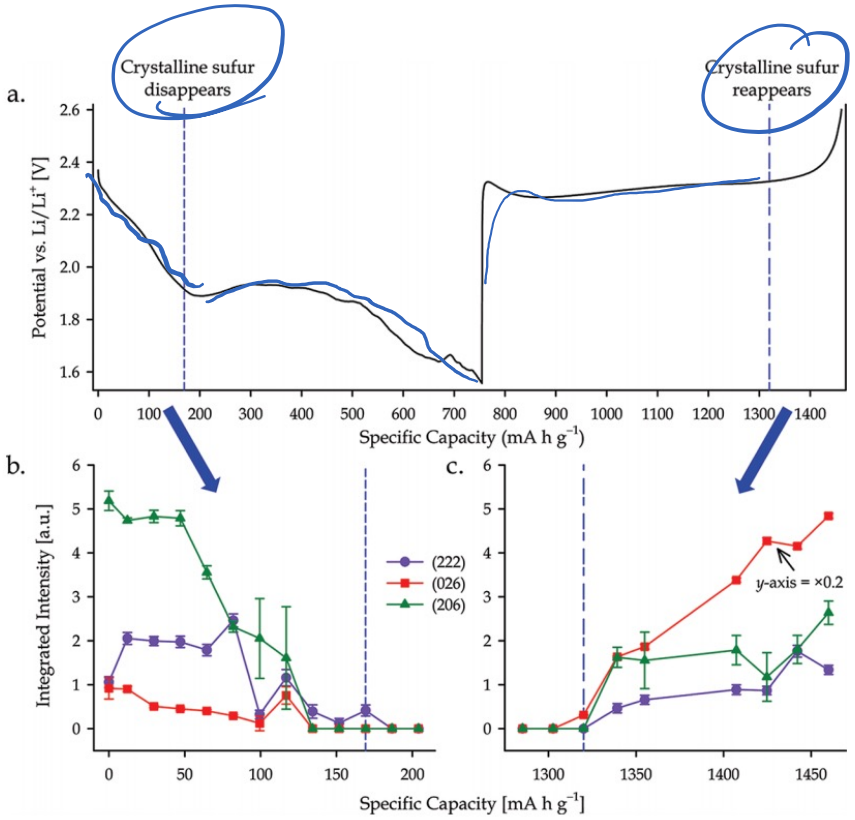


Figure 3. Integrated diffraction intensities of sulfur peaks for a Li–S cell cycled at C/8 and with a cathode prepared as a sulfur/Super P composite: (a) electrochemical plot showing the first cycle of the Li–S cell; (b and c) integrated intensity plots for (222), (026) ,and (206) Bragg peaks, which show the disappearance of crystalline sulfur by the end of the first discharge plateau and its reappearance by the end of the charge cycle. The blue arrows indicate the specific capacity regions over which the integrated intensities are plotted. The dashed lines emphasize where sulfur peaks disappear and reappear. The total discharge capacity is 755 mA h g^{-1}, and the total charge capacity is 707 mA h g^{-1}. Error bars on the integrated intensities were determined using Levenberg–Marquardt minimization.

Example: In operando – laser printing PSI

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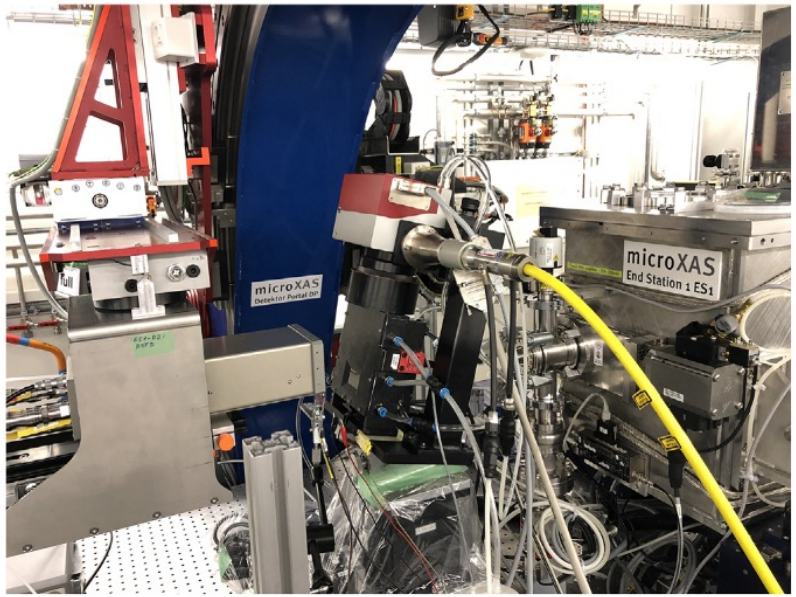
Operando X-ray diffraction during laser 3D printing

Samy Hocine [1,2], Helena Van Swygenhoven [1,2,*], Steven Van Petegem [1], Cynthia Sin Ting Chang [1], Tuerdi Maimaitiyili [1], Gemma Tinti [3], Dario Ferreira Sanchez [4], Daniel Grolimund [4], Nicola Casati [5]



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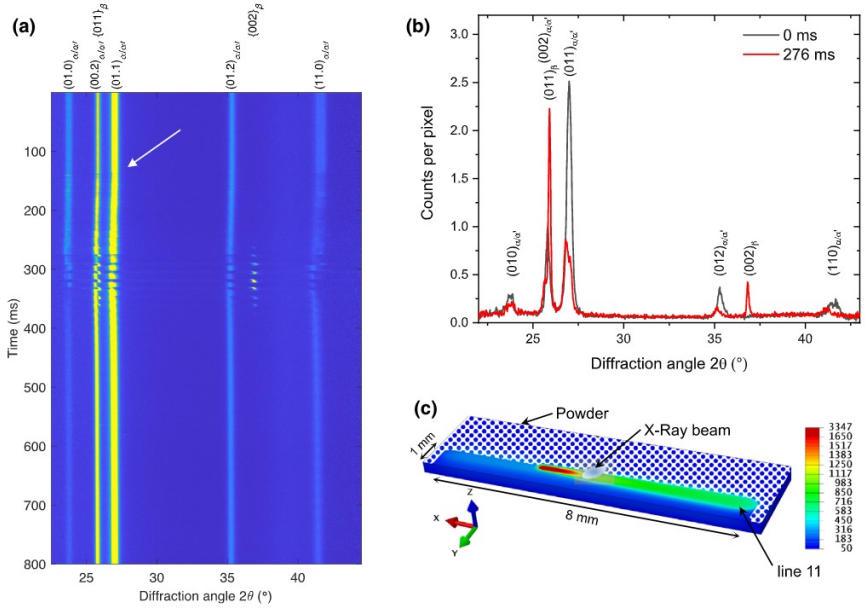


FIGURE 3

(a) Phase evolution during printing of a single layer, shown as an intensity vs. diffraction angle and time by stacking 16,000 individual diffraction patterns. The white arrow indicates the start of the printing process, (b) diffraction patterns recorded prior to printing and during printing of the 11th line at $t = 276$ ms, (c) schematic representation of the relative position of laser, X-ray beam and HAZ at $t = 276$ ms. (Temperature scale in degree Celsius).

Outlook

Diffraction as Fourier Transform

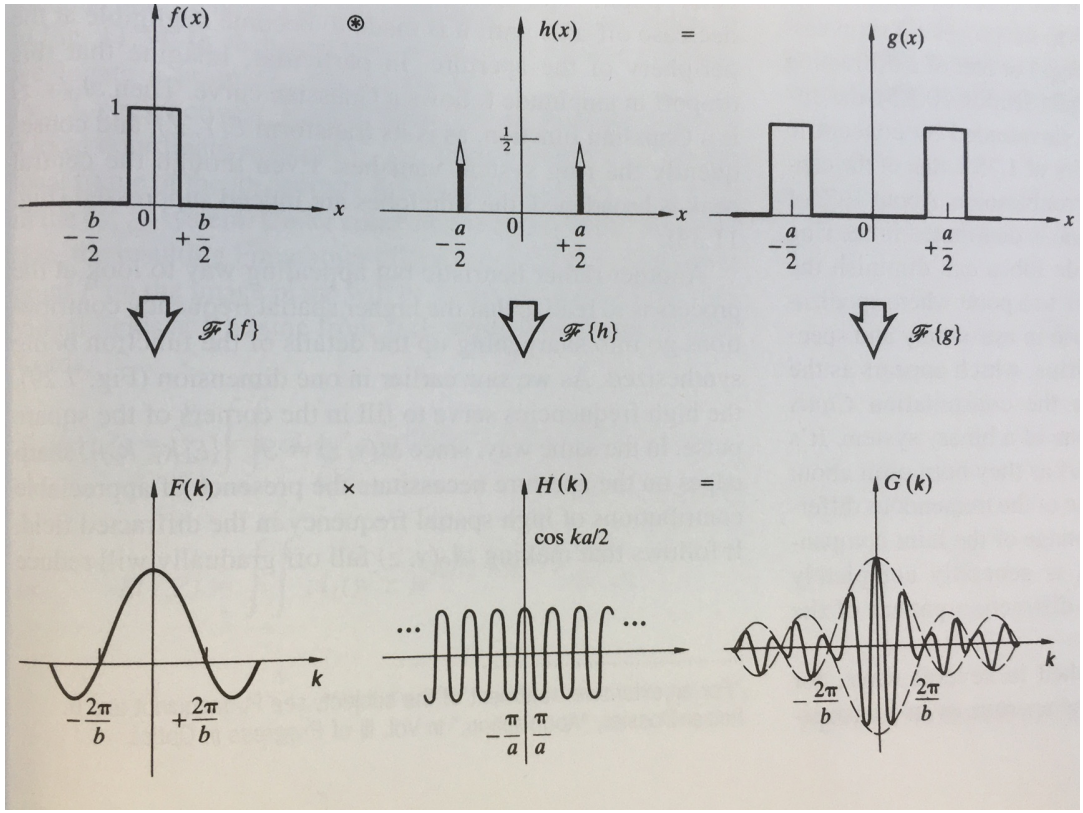
Reciprocal Lattice

Bragg and Laue Diffraction

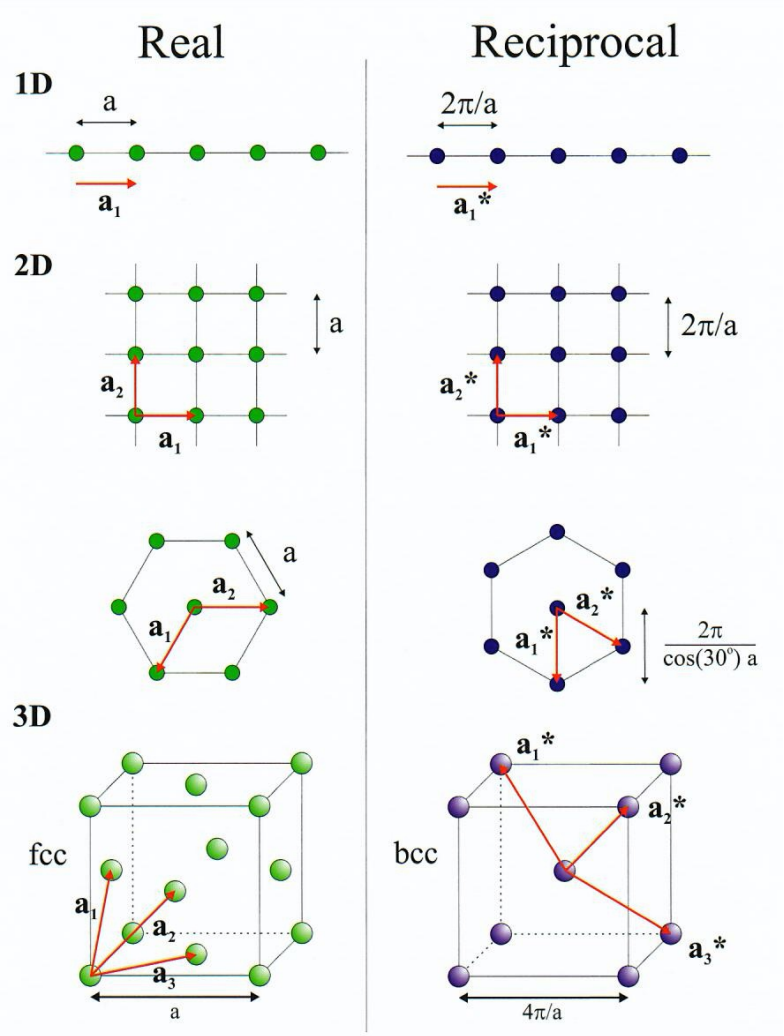
Structure Factor

Detailed Electronic Structure Maps

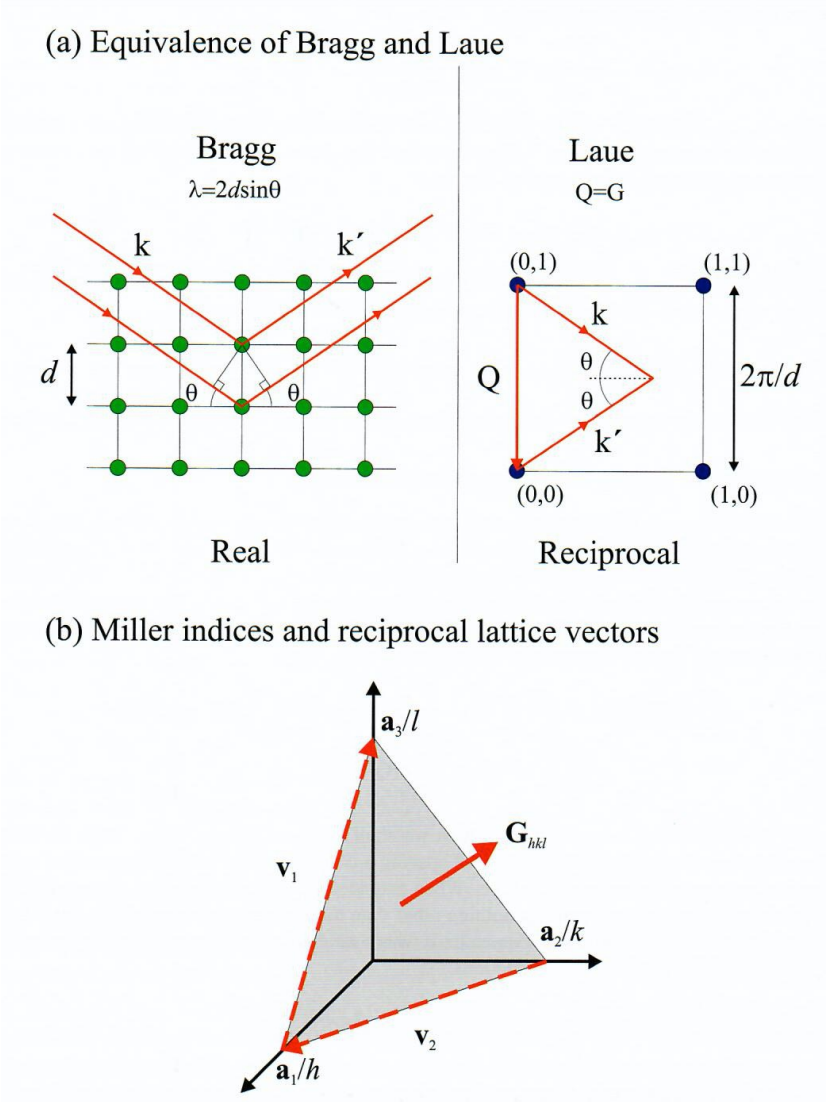
Diffraction as Fourier transform:



For each lattice a reciprocal lattice can be defined



Bargg and Laue conditions



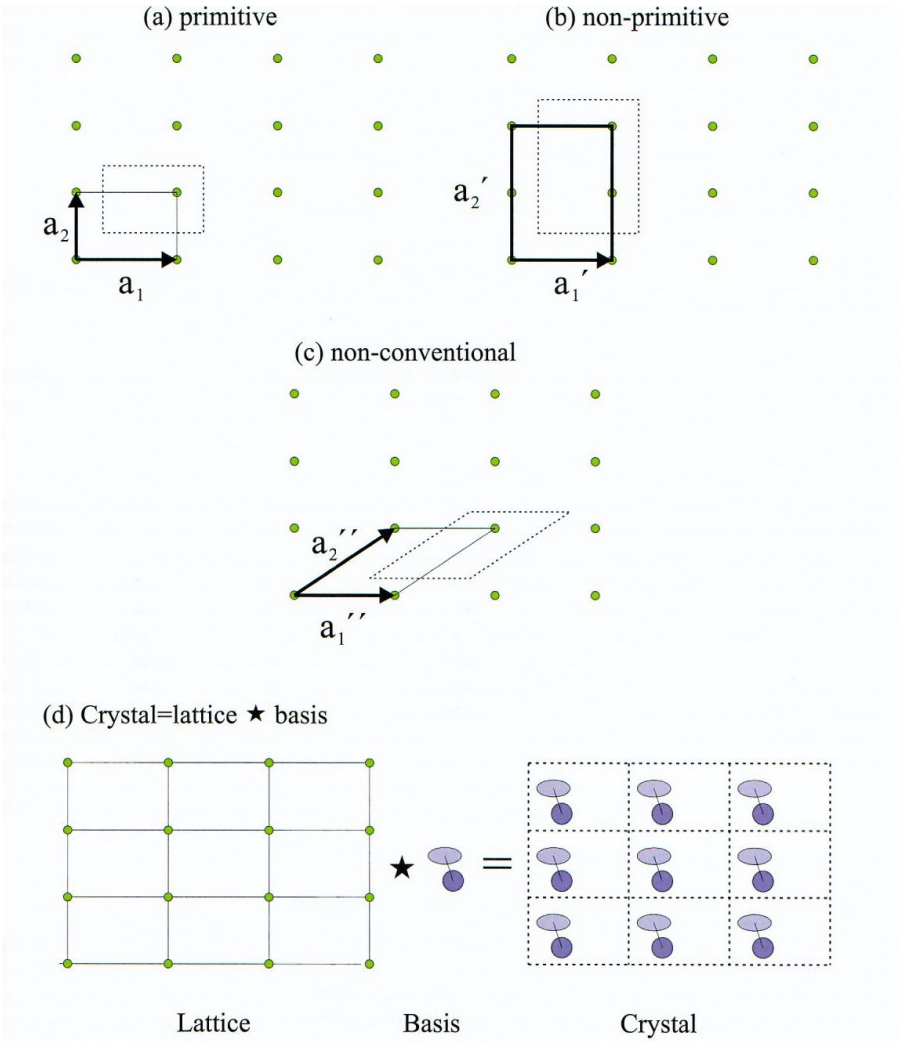
The Nobel Prize in Physics 1914

Photo from the Nobel Foundation archive.

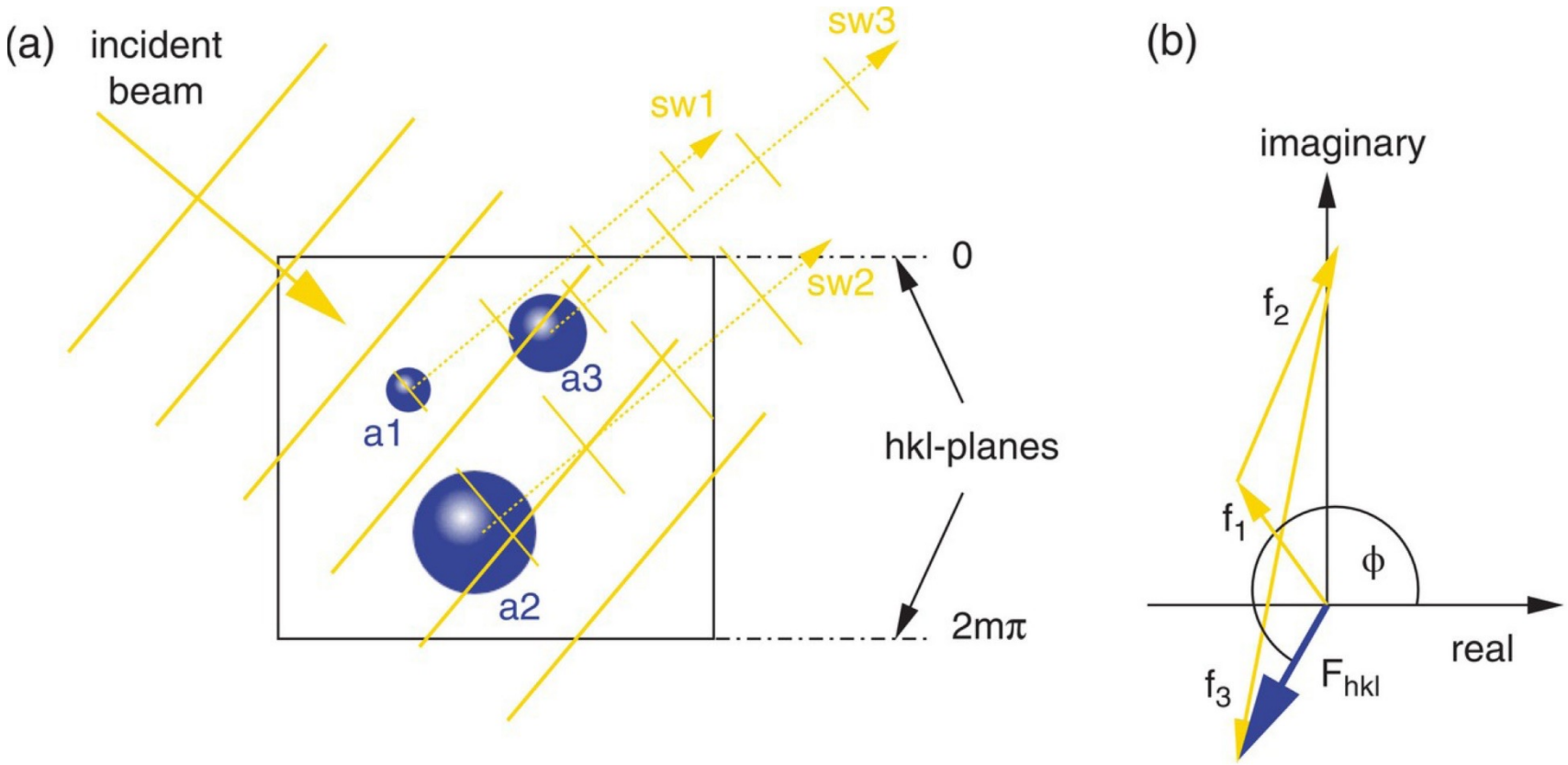
Max von Laue

Prize share: 1/1

A crystal is defined by ist lattice and basis



The structure factor



The end