Determination of crystal structure by single crystal X-ray diffraction

Mestrado em Química e Mestrado em Química Tecnológica
2020/2021

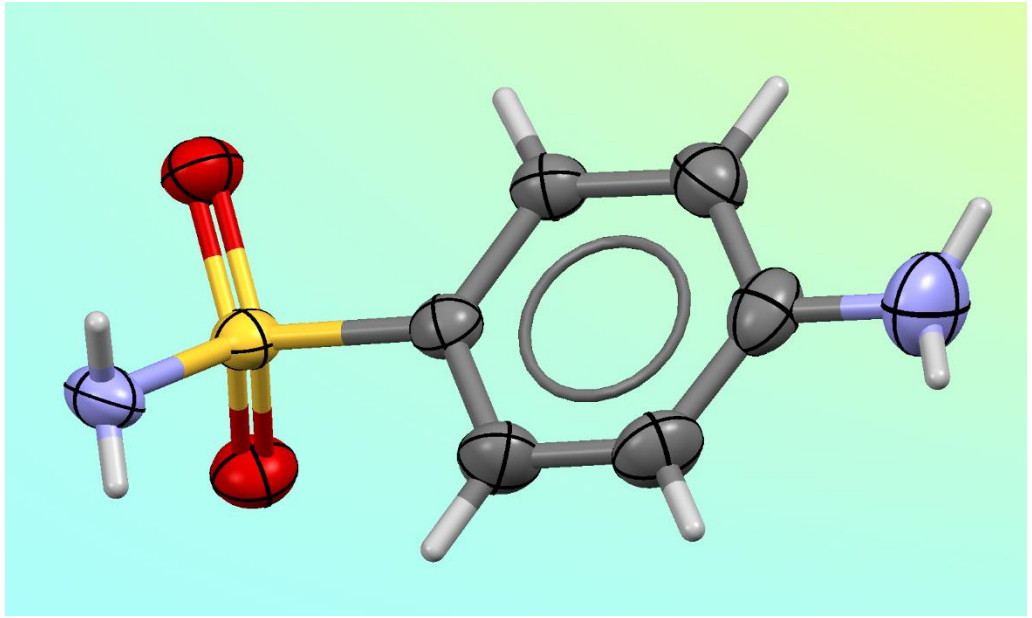
Fátima Piedade

mdpiedade@fc.ul.pt

Why this class on structural analysis of single crystal

- One of the most common and more accurate methods for determining the three-dimensional structure of crystalline compounds

SULFONAMIDE



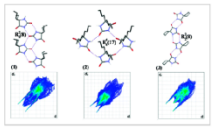
Why this class on structural analysis of single crystal

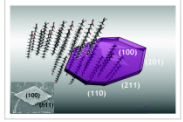
- One of the most common and more accurate methods for determining the three-dimensional structure of crystalline compounds
- There is virtually no scientific publication of a new compound, without its crystalline structure.

Toward Controlled Nucleation: Balancing Monolayer Chemistry with Monolayer Fluidity
Conrad Lendrum and Kathryn M. McGrath
pp 4463–4470
Publication Date (Web): September 13, 2010 (Article)
DOI: 10.1021/cg1006764
Abstract | Supporting Info
Full Text HTML | Hi-Res PDF [2081K] | PDF w/ Links [977K]

Environmentally Friendly Growth of Well-Developed $LiCoO_2$ Crystals for Lithium-Ion Rechargeable Batteries Using a NaCl Flux
Katsuya Teshima, SunHyung Lee, Yusuke Mizuno, Hikaru Inagaki, Masato Hozumi, Keiichi Kohama, Kunio Yubuta, Toetsu Shishido, and Shuji Oishi
pp 4471–4475
Publication Date (Web): August 27, 2010 (Article)
DOI: 10.1021/cg100705d
Abstract | Supporting Info
Full Text HTML | Hi-Res PDF [2076K] | PDF w/ Links [916K]

Supramolecular Architectures in 5,5′-Substituted Hydantoins: Crystal Structures and Hirshfeld Surface Analyses
Basab Chattopadhyay, Alok K. Mukherjee, N. Narendra, H. P. Hemantha, Vommina V. Sureshbabu, Madeliene Hellwell, and Monika Mukherjee
pp 4476–4484
Publication Date (Web): August 30, 2010 (Article)
DOI: 10.1021/cg100706n
Abstract | Supporting Info
Full Text HTML | Hi-Res PDF [4219K] | PDF w/ Links [1125K]





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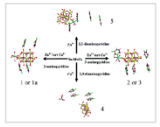
Polyoxometalate Supported Transition Metal Complexes: Synthesis, Crystal Structures, and Supramolecular Chemistry
T. Arumuganathan, A. Srinivasa Rao, and Samar K. Das
pp 4272–4284
Publication Date (Web): September 21, 2010 (Article)
DOI: 10.1021/cg901507z
Abstract | Supporting Info
Full Text HTML | Hi-Res PDF [5669K] | PDF w/ Links [1453K]



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Formation and Self-Assembly of Cadmium Hydroxide Nanoplates in Molten Composite-Hydroxide Solution
Jing Zhang, Yonghao Wang, Zhang Lin, and Feng Huang
pp 4285–4291
Publication Date (Web): September 15, 2010 (Article)
DOI: 10.1021/cg901559y
Abstract
Full Text HTML | Hi-Res PDF [3829K] | PDF w/ Links [1080K]

First Principles Simulations of the Structural and Dynamical Properties of Hydrated Metal Ions Me^{2+} and Solvated Metal Carbonates (Me = Ca, Mg, and Sr)
Devis Di Tommaso and Nora H. de Leeuw
pp 4292–4302
Publication Date (Web): September 1, 2010 (Article)
DOI: 10.1021/cg100059p
Abstract | Supporting Info
Full Text HTML | Hi-Res PDF [2051K] | PDF w/ Links [1174K]

Crystal Polymorphs and Transformations of 2-Iodo-4-nitroaniline
Dawn M. Kelly, Kevin S. Eccles, Curtis J. Elcoate, Simon E. Lawrence, and Humphrey A. Moynihan
pp 4303–4309
Publication Date (Web): September 21, 2010 (Article)
DOI: 10.1021/cg1001418
Abstract | Supporting Info
Full Text HTML | Hi-Res PDF [4778K] | PDF w/ Links [969K]

Lanthanide Contraction and Temperature-Dependent Structures of Lanthanide Coordination Polymers with Imidazole-4,5-Dicarboxylate and Oxalate
Wen-Guan Lu, Long Jiang, and Tong-Bu Lu
pp 4310–4318
Publication Date (Web): September 13, 2010 (Article)
DOI: 10.1021/cg100196j
Abstract | Supporting Info
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Larger Cover

October 6, 2010
Volume 10, Issue 10
Pages 4203–4670

In this issue:

About the Cover:
The first systematic crystallographic study of the whole family of nonplanar polyaromatic hydrocarbons having a stepwise increase in surface area, curvature, and strain is presented (*Cryst. Growth Des.* **2010**, *10*, 4607–4621). The effect of controlled extension of π-aromatic surfaces on the solid state structures of the resulting crystalline solids and their implications for molecular electronics are discussed. Cover art image produced by Alexander Filatov. View the article.

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EDITORIAL

Virtual Special Issue on British Association for Crystal Growth 40th Anniversary Conference 2009
Fiona C. Meldrum, Radoljub I. Ristic
pp 4203–4205
Publication Date (Web): September 9, 2010 (Editorial)
DOI: 10.1021/cg1010727
Abstract
Full Text HTML | Hi-Res PDF [627K] | PDF w/ Links [636K]
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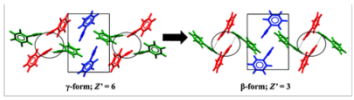
COMMUNICATIONS



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ARTICLES

Fluorobenzonitriles: Influence of the Substitution Pattern on Melting and Crystallization Properties
Vera Vasylyeva and Klaus Merz
pp 4250–4255
Publication Date (Web): September 15, 2010 (Article)
DOI: 10.1021/cg100794s
Abstract | Supporting Info
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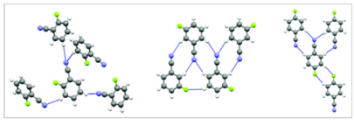

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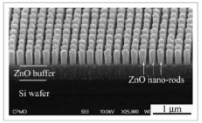
Creation of Nanoscale Two-Dimensional Patterns of ZnO Nanorods using Laser Interference Lithography Followed by Hydrothermal Synthesis at 90 °C
Tae-Un Kim, Jin-A Kim, S. M. Pawar, Jong-Ha Moon, and Jin Hyeok Kim
pp 4256–4261
Publication Date (Web): August 30, 2010 (Article)
DOI: 10.1021/cg901223t
Abstract
Full Text HTML | Hi-Res PDF [3668K] | PDF w/ Links [1046K]



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Relationship between the Crystal Structure and Morphology of Carboxylic Acid Polymorphs. Predicted and Experimental Morphologies
Evelyn Moreno-Calvo, Teresa Calvet, Miguel Angel Cuevas-Diarte, and Dino Aquilano
pp 4262–4271
Publication Date (Web): September 10, 2010 (Article)
DOI: 10.1021/cg901436p
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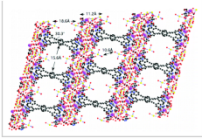

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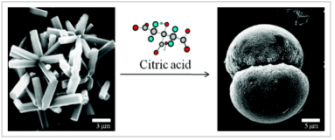
Morphology Control of Fluorapatite Crystallites by Citrate Ions
Yu-Ju Wu, Yao-Hung Tseng, and Jerry C. C. Chan
pp 4240–4242
Publication Date (Web): August 23, 2010 (Communication)
DOI: 10.1021/cg100859m
Abstract | Supporting Info
Full Text HTML | Hi-Res PDF [2659K] | PDF w/ Links [821K]



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Sulfoxides: Potent Co-Crystal Formers
Kevin S. Eccles, Curtis J. Elcoate, Stephen P. Stokes, Anita R. Maguire, and Simon E. Lawrence
pp 4243–4245
Publication Date (Web): August 23, 2010 (Communication)
DOI: 10.1021/cg1010192
Abstract | Supporting Info
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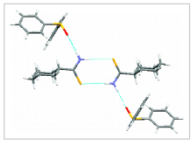

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pp 4501–4508
Publication Date (Web): August 30, 2010 (Article)
DOI: 10.1021/cg100760t
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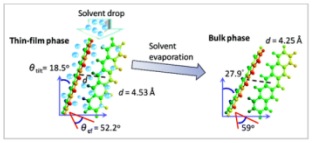

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Use of Silver(I) and Copper(II) Ions to Assist the Self-Assembly of Polyrotaxanes Incorporating Symmetrical α,α′,δ,δ′-Tetramethyl-cucurbit[6]uril
Jin-Ping Zeng, Shi-Min Zhang, Yun-Qian Zhang, Zhu Tao, Qian-Jiang Zhu, Sai-Feng Xue, and Gang Wei
pp 4509–4515
Publication Date (Web): September 9, 2010 (Article)
DOI: 10.1021/cg1007796
Abstract | Supporting Info
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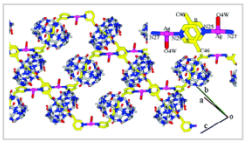

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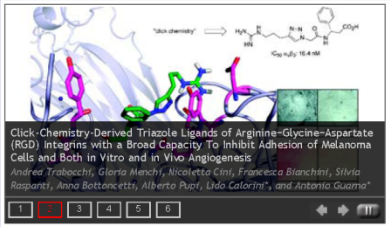
A Racemic Conglomerate Nipped in the Bud: A Molecular View of Enantiomer Cross-Inhibition of Conglomerate Nucleation at a Surface
Abel Robin, Patrizia Iavicoli, Klaus Wurst, Matthew S. Dyer, Sam Haq, David B. Amabilino, and Rasmita Raval
pp 4516–4525
Publication Date (Web): September 3, 2010 (Article)
Abstract | Supporting Info
Full Text HTML | Hi-Res PDF [7540K] | PDF w/ Links [1488K]

Journal of Medicinal Chemistry



Click-Chemistry-Derived Triazole Ligands of Arginine–Glycine–Aspartate (RGD) Integrins with a Broad Capacity To Inhibit Adhesion of Melanoma Cells and Both in Vitro and in Vivo Angiogenesis

Andrea Trabocchi, Gloria Menchi, Nicoletta Cini, Francesca Bianchini, Silvia Raspanti, Anna Bottarcetti, Alberto Pupi, Lido Calorini, and Antonio Guarna**

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About the Journal

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The most cited journal in Medicinal Chemistry, publishing original research on the correlation of molecular structure to biological activity with a focus on the relationships of chemistry to biological activity.

Editor-in-Chief: Philip S. Portoghese

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4-Oxo-1,4-dihydropyridines as Selective CB_2 Cannabinoid Receptor Ligands: Structural Insights into the Design of a Novel Inverse Agonist Series

Abstract | Full Text HTML | Hi-Res PDF [2902K] | PDF w/ Links [1090K]

Jamal El Bakali, Giulio G. Muccioli, Nicolas Renault, Delphine Pradal, Mathilde Body-Malapel, Madjid Djouina, Laurie Hamtiaux, Virginie Andrzejak, Pierre Desreumaux, Philippe Chavatte, Didier M. Lambert, and Régis Millet

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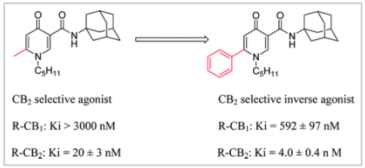
Publication Date (Web): October 27, 2010 (Article)



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Novel α3β4 Nicotinic Acetylcholine Receptor-Selective Ligands. Discovery, Structure–Activity Studies, and Pharmacological Evaluation

Abstract | Supporting Info | Full Text HTML | Hi-Res PDF [1253K] | PDF w/ Links [802K]

Nurulain Zaveri, Faming Jiang, Cris Olsen, Willma Polgar, and Lawrence Toll

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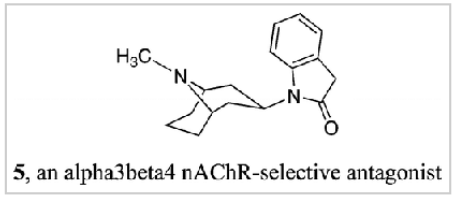
Journal of Medicinal Chemistry (ACS Publications)

Publication Date (Web): October 27, 2010 (Brief Article)



5, an alpha3beta4 nAChR-selective antagonist

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Essential Structural Features of TNF-α Lectin-like Domain Derived Peptides for Activation of Amiloride-Sensitive Sodium Current in A549 Cells

Abstract | Full Text HTML | Hi-Res PDF [1931K] | PDF w/ Links [914K]

Parastoo Hazemi, Susan J. Tzotzos, Bernhard Fischer, Gowri Shankar Bagavananthem Andavan, Hendrik Fischer, Helmut Pietschmann, Rudolf Lucas, and Rosa Lemmens-Gruber

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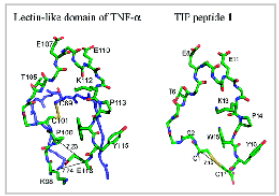
Publication Date (Web): October 27, 2010 (Article)



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Endoperoxide Carbonyl Falcipain 2/3 Inhibitor Hybrids: Toward Combination Chemotherapy of Malaria through a Single Chemical Entity

Abstract | Supporting Info | Full Text HTML | Hi-Res PDF [2971K] | PDF w/ Links [852K]

Peter Gibbons, Edite Verissimo, Victoria Barton, Gemma L. Nixon, Richard K. Amewu, James Chadwick, Paul A. Stocks, Giancarlo A. Biagini, Abhishek Srivastava, Philip J. Rosenthal, Jiri Gut, Rita C. Guedes, Rui Moreira, Raman Sharma, Neil Berry, M. Lurdes S. Cristiano, Alison E. Shone, Stephen A. Ward, and Paul M. O'Neill

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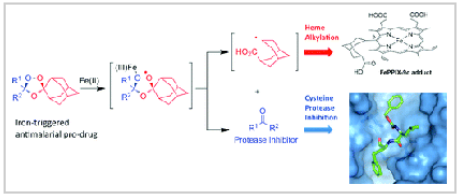
Publication Date (Web): October 27, 2010 (Brief Article)



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Organometallic Osmium Arene Complexes with Potent Cancer Cell Cytotoxicity

Abstract | Supporting Info | Full Text HTML | Hi-Res PDF [1960K] | PDF w/ Links [798K]

Ying Fu, Abraha Habtemariam, Ana M. Pizarro, Sabine H. van Rijt, David J. Healey, Patricia A. Cooper, Steven D. Shnyder, Guy J. Clarkson, and Peter J. Sadler

Articles ASAP (As Soon As Publishable)
Publication Date (Web): October 26, 2010 (Brief Article)
DOI: 10.1021/jm100560f

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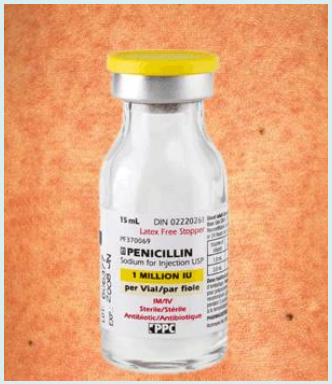
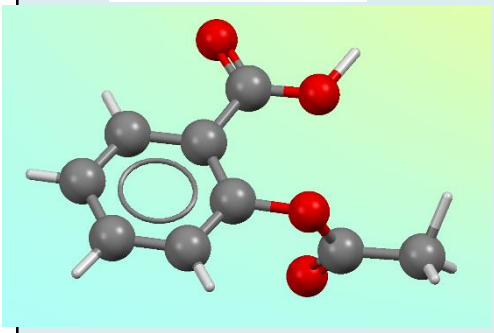
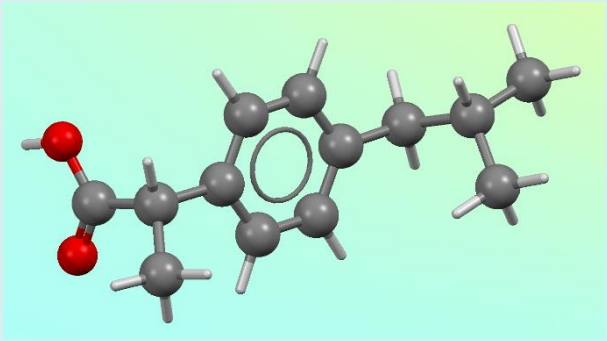
Why this class on structural analysis of single crystal

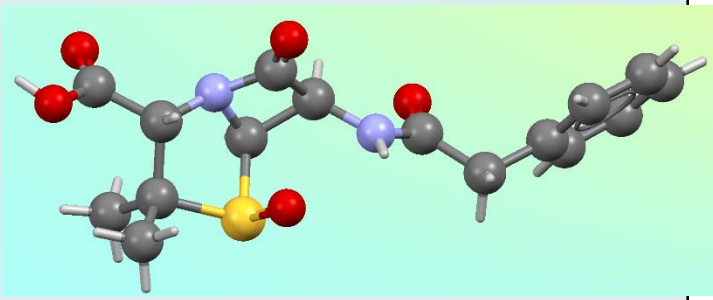
- One of the most common and more accurate methods for determining the three-dimensional structure of crystalline compounds
- There is virtually no scientific publication of a new compound, without its crystalline structure.
- Much information about molecular and non-molecular crystals.
- Most of the students come in contact with this method during their degree, or postgraduate courses.

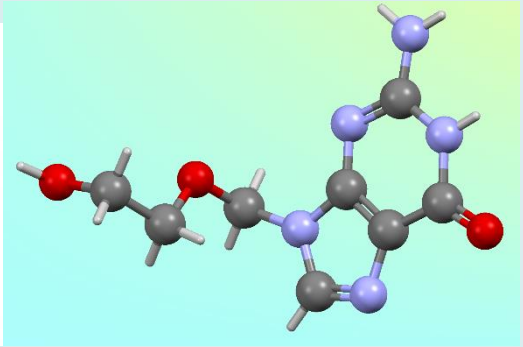
Examples of organic compounds

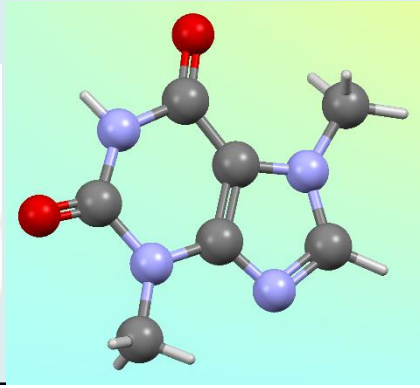






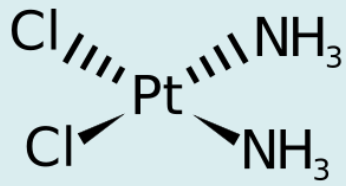


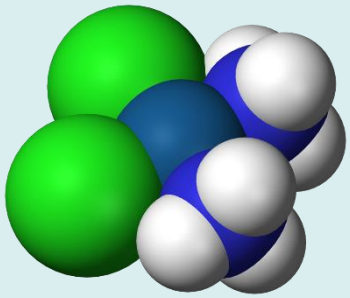




Examples of inorganic compounds

cisplatin





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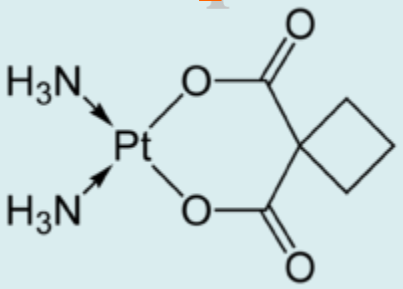
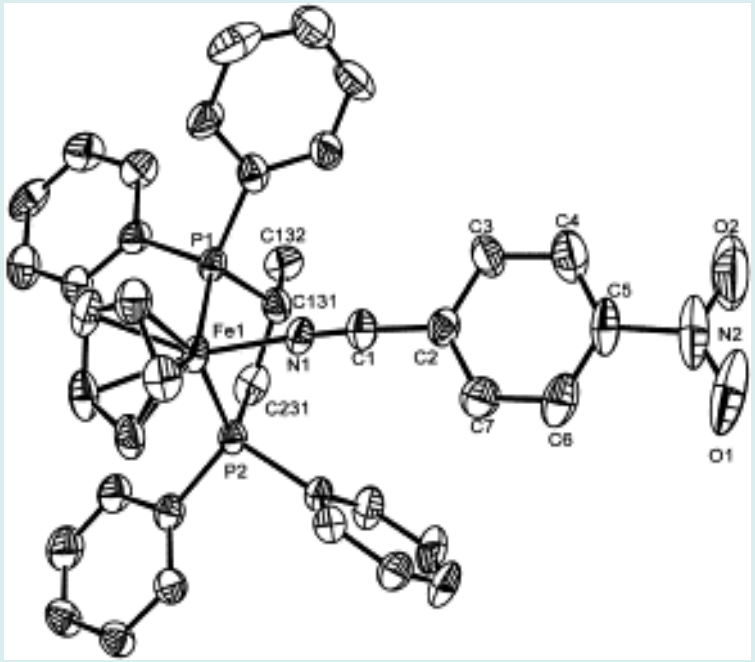
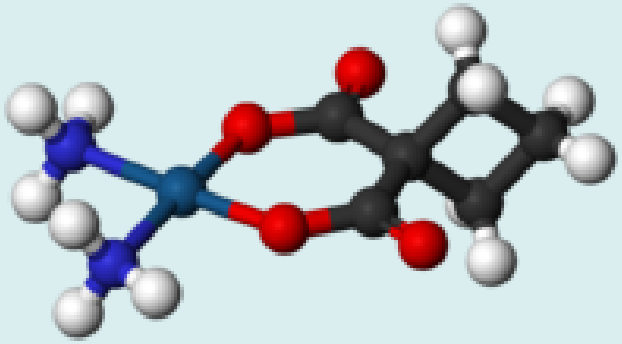
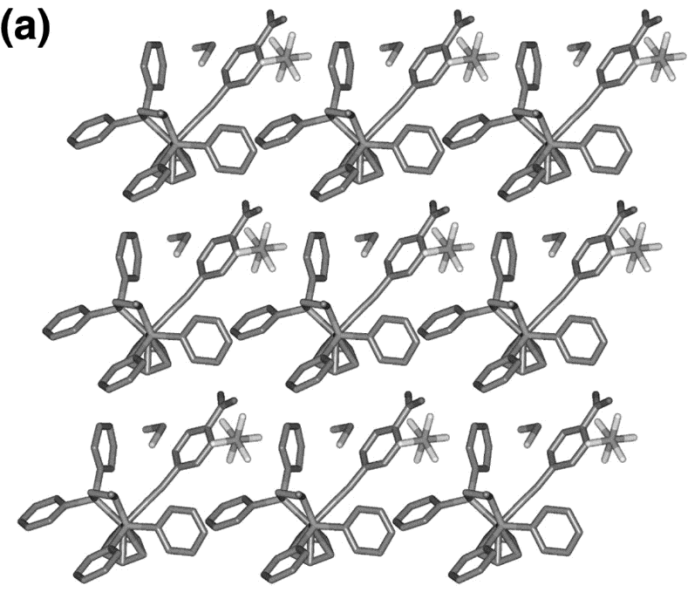
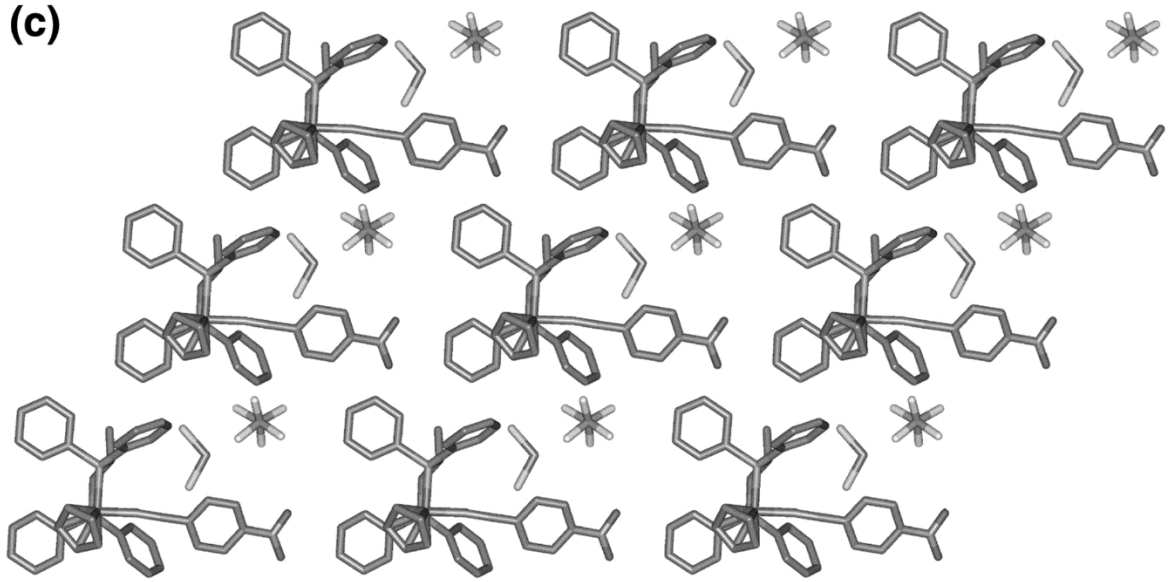







(a)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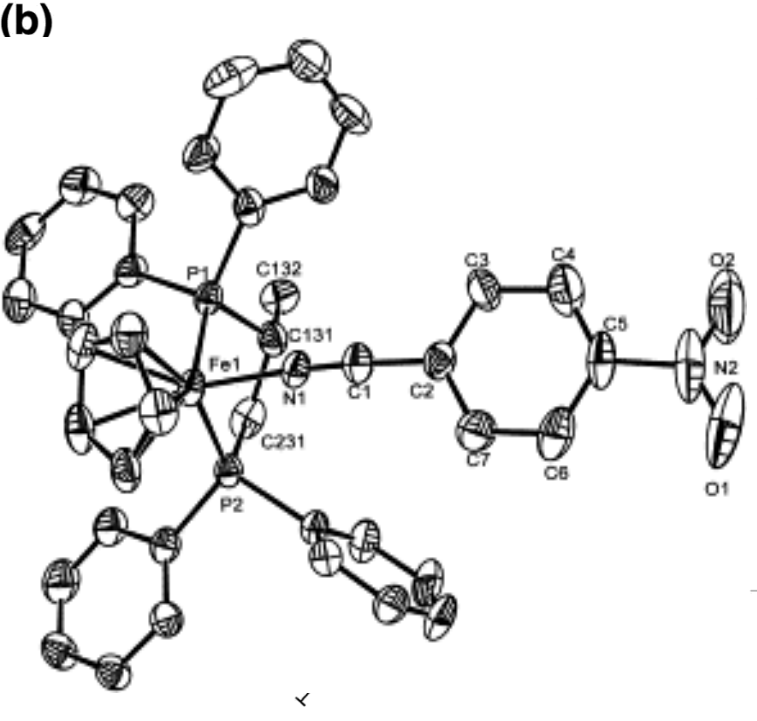
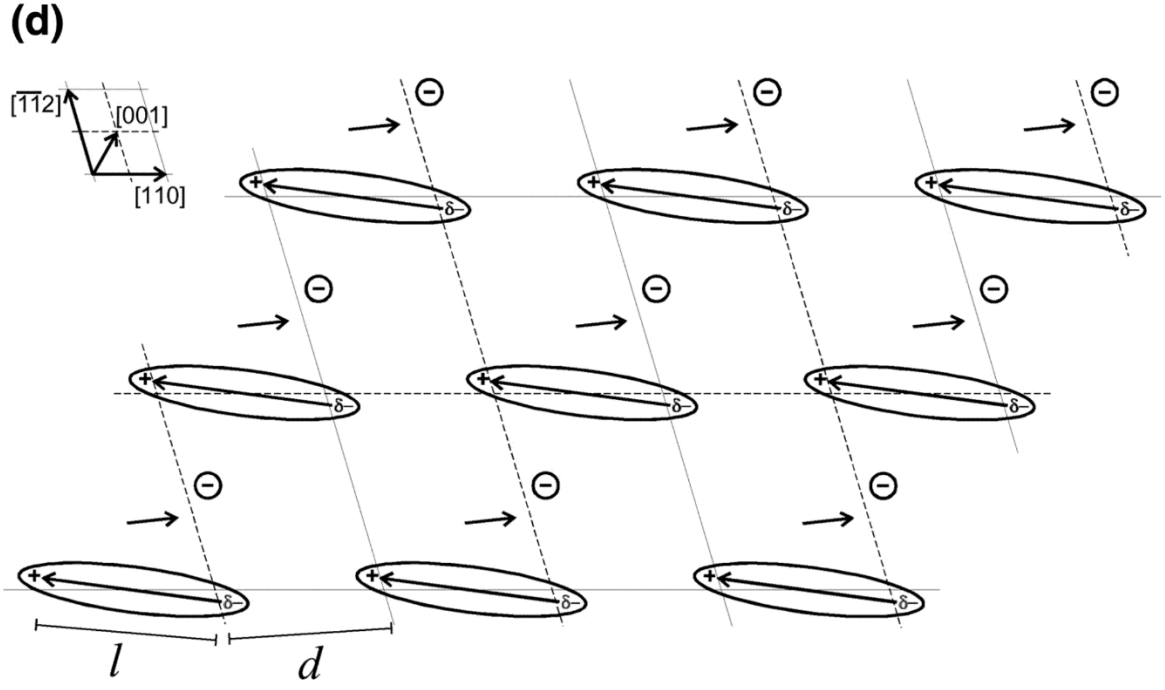
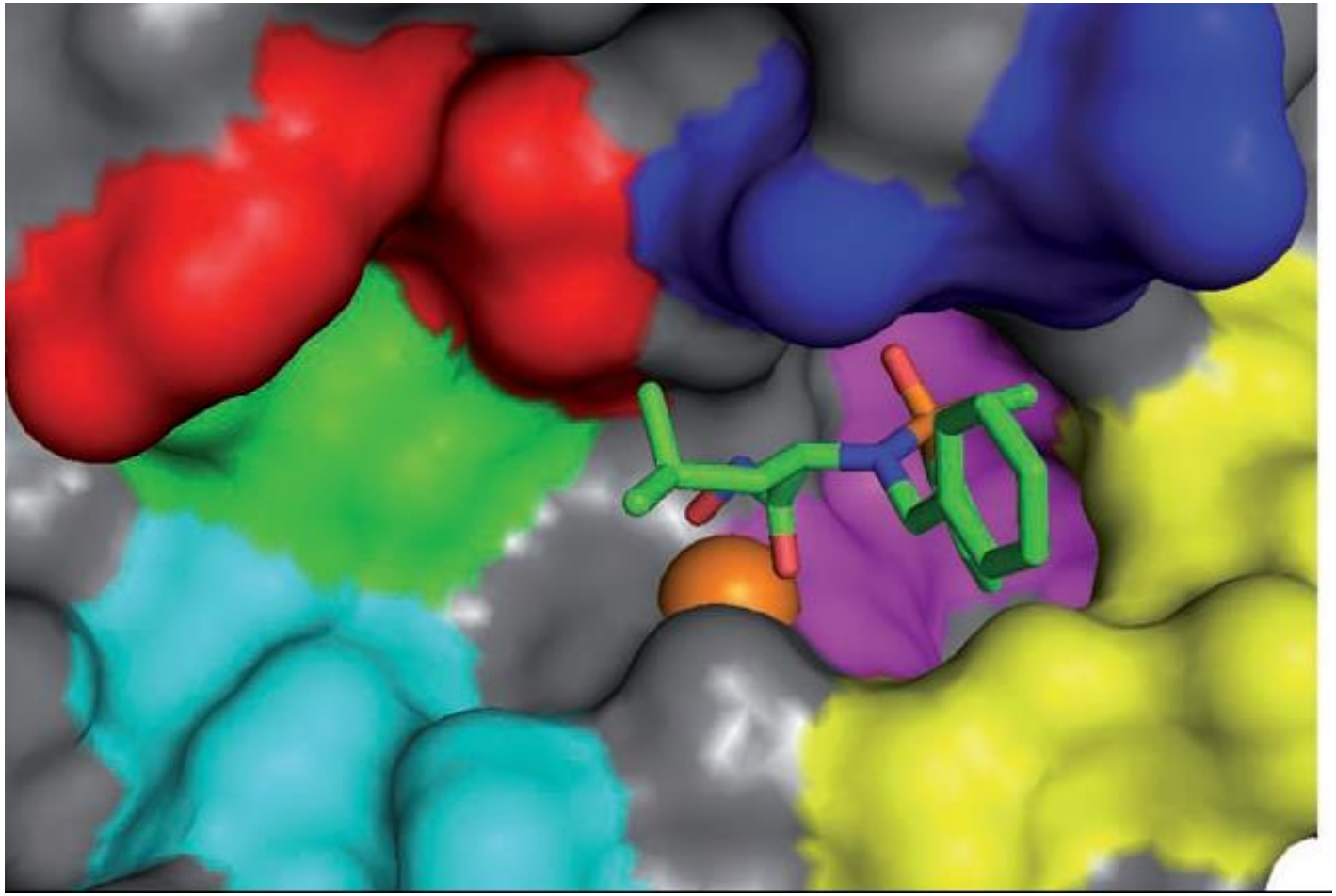
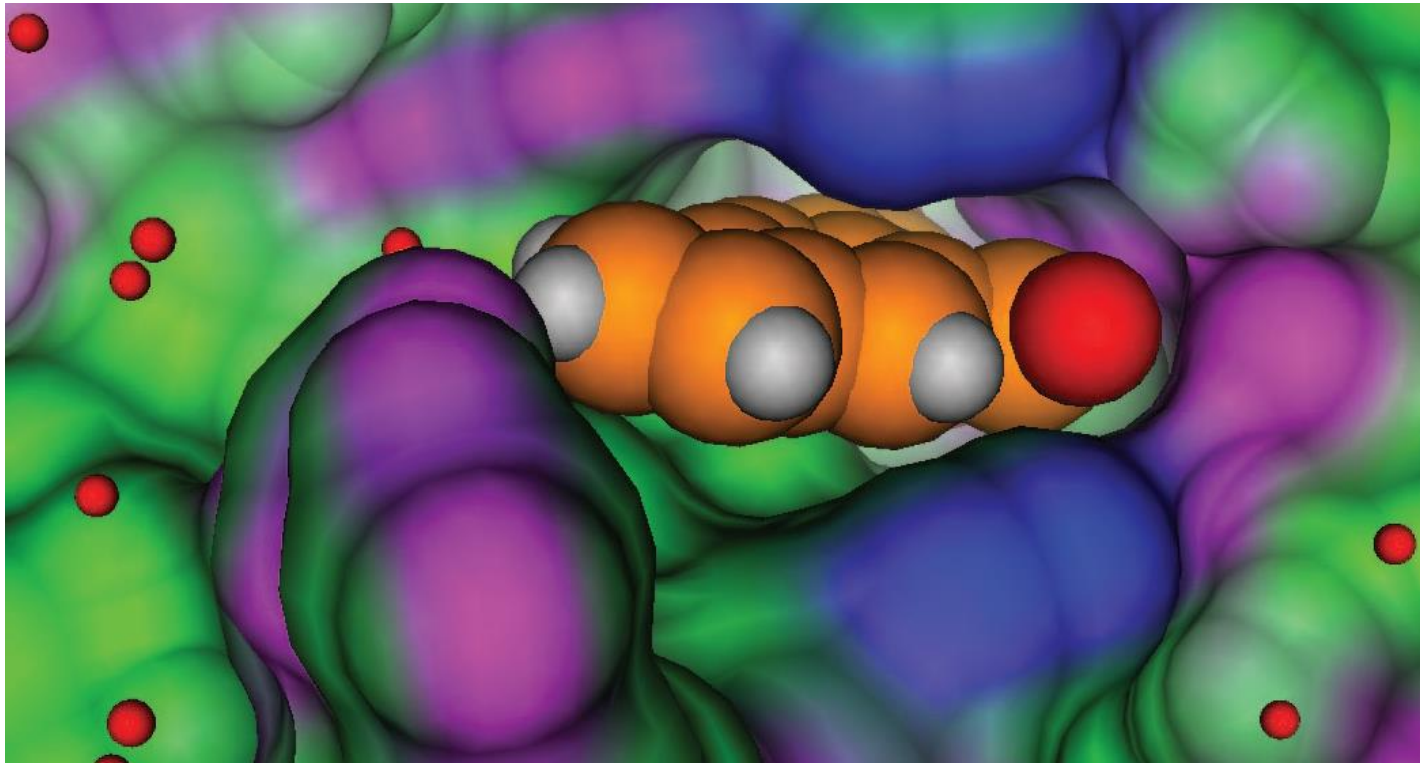

(b)
P1
C132
C131
Fe1
N1
C1
C2
C3
C4
C5
C6
C7
O2
N2
O1
C231
P2


(d)
[1̄1̄2]
[001]
[1̄10]
δ+
δ−
l
d



In the design of a new molecule in chemistry the crystalline structure is very important because one can visualize the way it binds to the receptor.

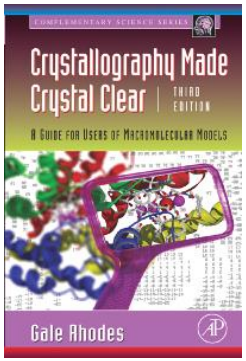


Using this information the chemist can synthesize analogous compounds, making changes to increase the interaction with the receptor molecule and / or alter the properties of the drug without decreasing the affinity of the parent compound to the target compound.

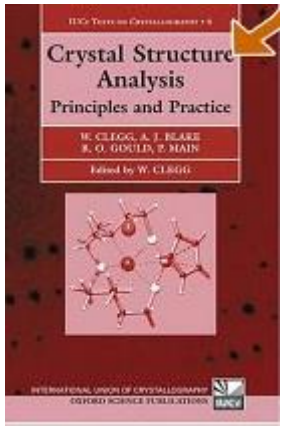
Why this class on structural analysis of single crystal

- **One of the most common and more accurate methods for determining the three-dimensional structure of crystalline compounds**
- **There is virtually no scientific publication of a new compound, without its crystalline structure.**
- **Much information about molecular and non-molecular crystals.**
- **Most of the students come in contact with this method during their degree, or postgraduate courses.**
- **Knowledge of the crystal structure of a compound is absolutely necessary for a deeper understanding of their physical properties.**

BIBLIOGRAFIA



Crystallography Made Crystal Clear
A Guide for Users of Macromolecular Models
Gale Rhodes
Elsevier



Crystal Structure Analysis: Principles and Practice
William Clegg, A. J. Blake, R. O. Gould and P. Main
Oxford University Press

Website

http://www.iucr.org/

Objectives that must learn in this lesson on structural analysis of single crystal

- Theoretical basis of this method
- How to make the structural determination?
- Possibilities: What can be learned in a single crystal structure?
- Limitations: How precise and accurate is this method? What can be determined?
- Critical view of the results in a structural determination?
- How can analyze the result and the quality of a structural determination?
- How can detect possible errors in structural analysis?

What is X-ray diffraction useful for?

- **Gives information about the molecule: relative position of the atoms, bond lengths and angles, torsion angles, conformation and flexibility of the molecule.**

- **Allows the understanding of the non-bonded interactions and therefore the 3D structure – supramolecular arrangement**

Is a non-destructive method

Is an **essential** tool for the design of new compounds.

STRUCTURE ⟶ FUNCTION

X-ray diffraction analysis

- Crystals! How to obtain them? Crystallization techniques
- What are X-rays? How are they generated? X-ray tubes and synchroton radiation
- Difraction X-rays interact with electrons (van Laue equations; Bragg's law)

- Real /reciprocal spaces

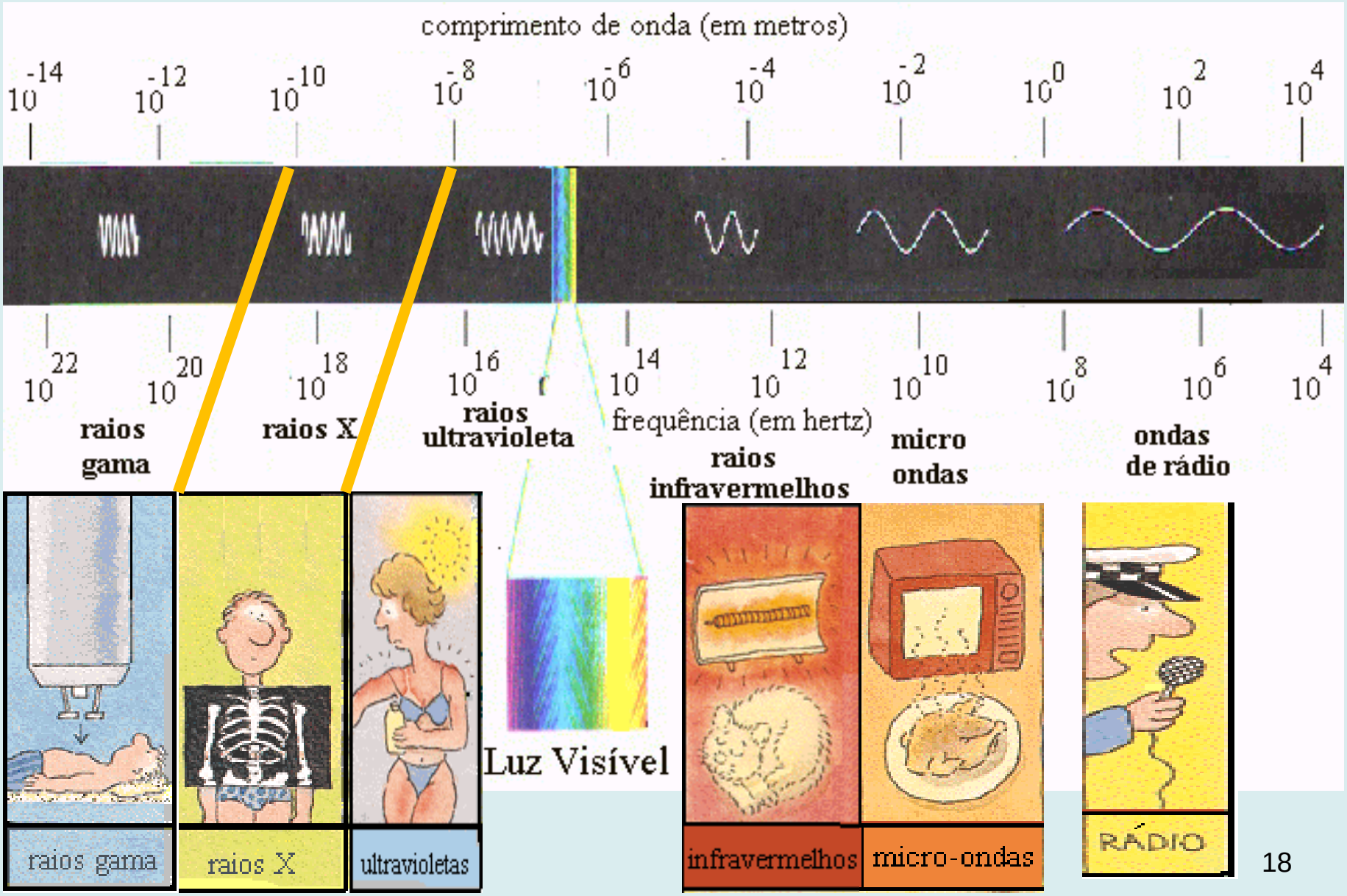
  (electronic density, atomic positions / structure factors, Miller indices)
- Real space versus reciprocal space FOURIER Transform
- Phase: Model >> fitting >> refinement

  (model – experimental electronic density)

•Structural Information

Design

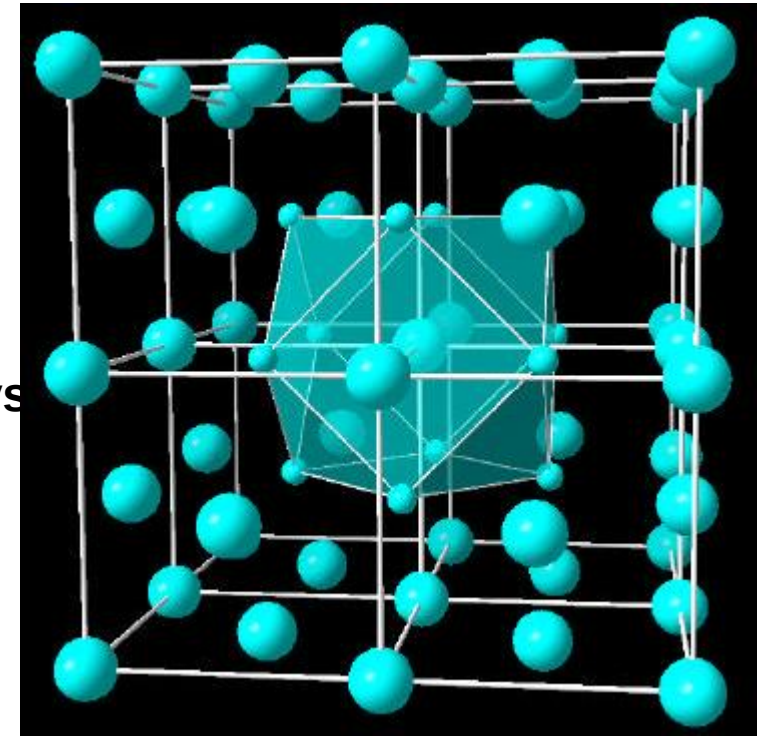
Electromagnetic spectrum



Definition of single crystal structure made by X-ray diffraction

Determination of the exact three-dimensional arrangement of blocks (atoms, ions, molecules) using a compound of X-ray radiation.
Analysis of a single crystal structure by X-ray diffraction

Wilhelm Conrad Röntgen
1845-1923
Physics teacher
Discovered the X-rays on 08/11/1895
1st Physics Nobel Prize in 1901

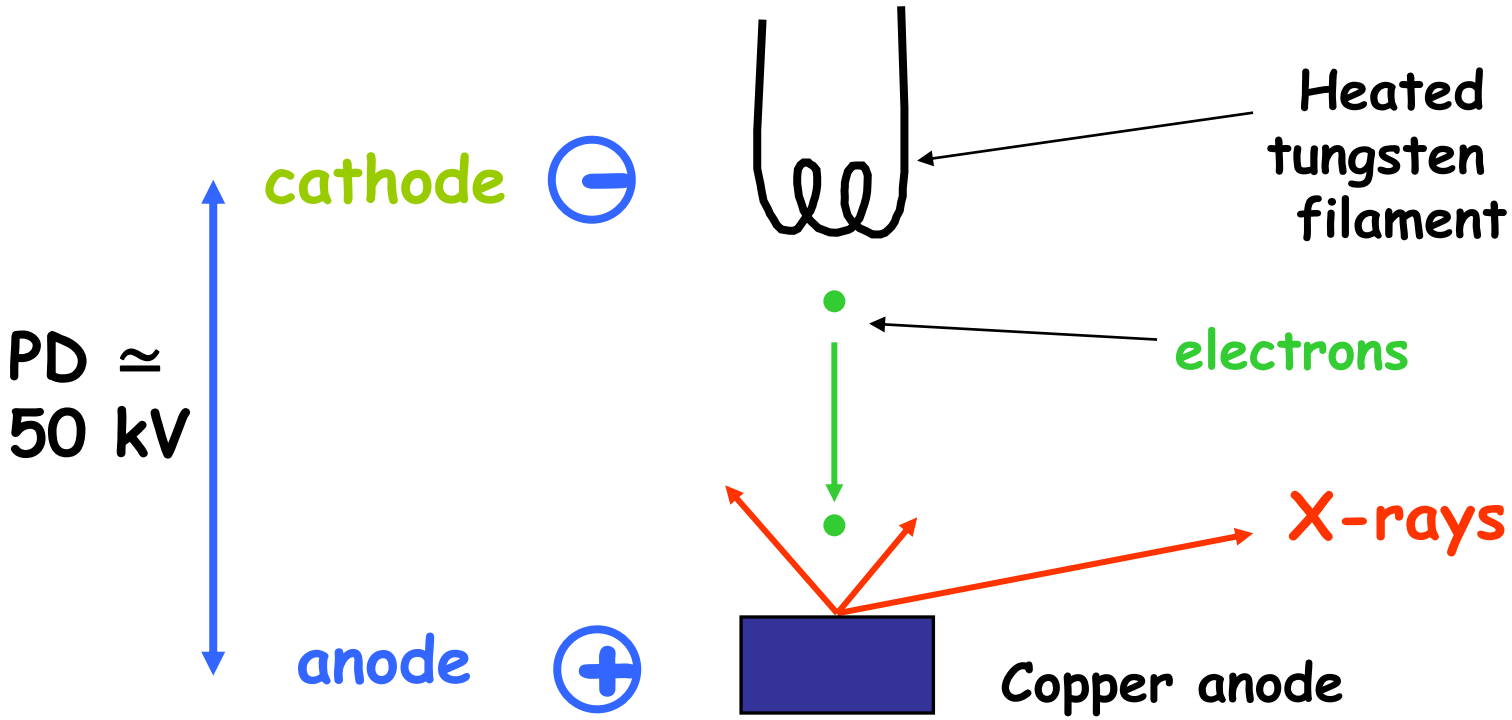


X-Rays

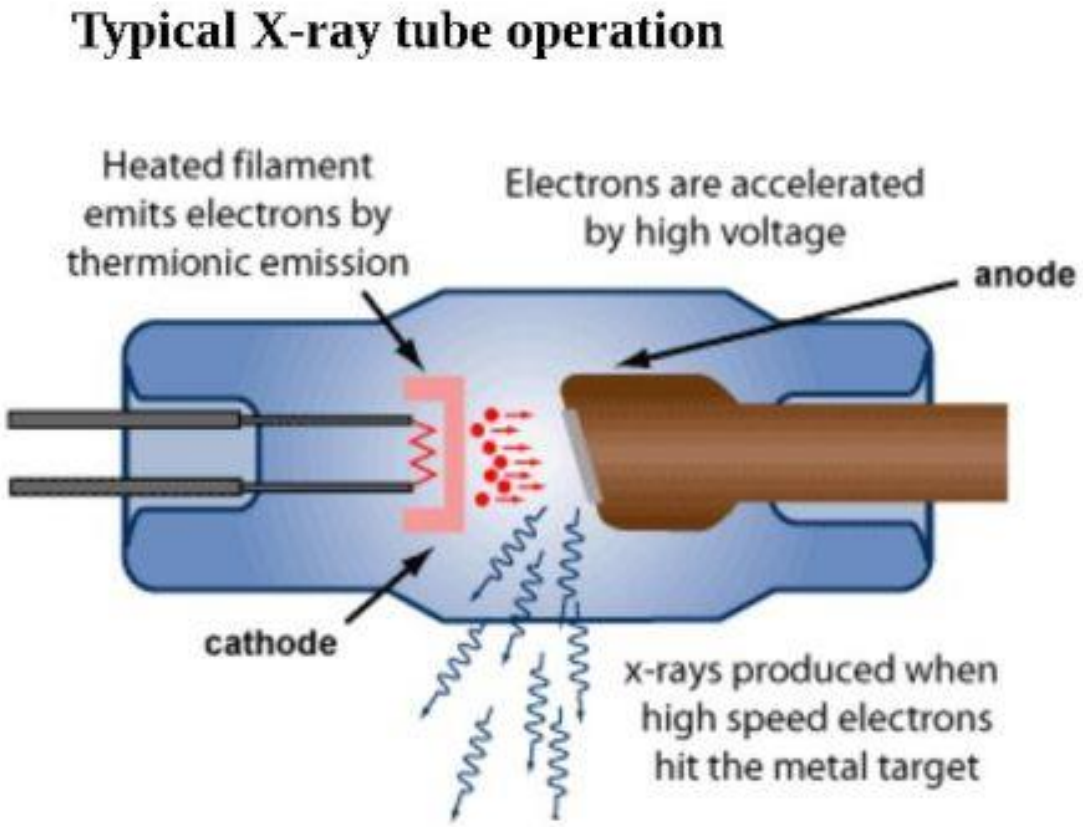
- **Radiation obtained when electrons produced by termoionic emission from a W filament are accelerated by potential difference towards the anode.**

- **High energy electrons (≃ 50 keV) hit the metallic target (e.g. Cu ou Mo)**

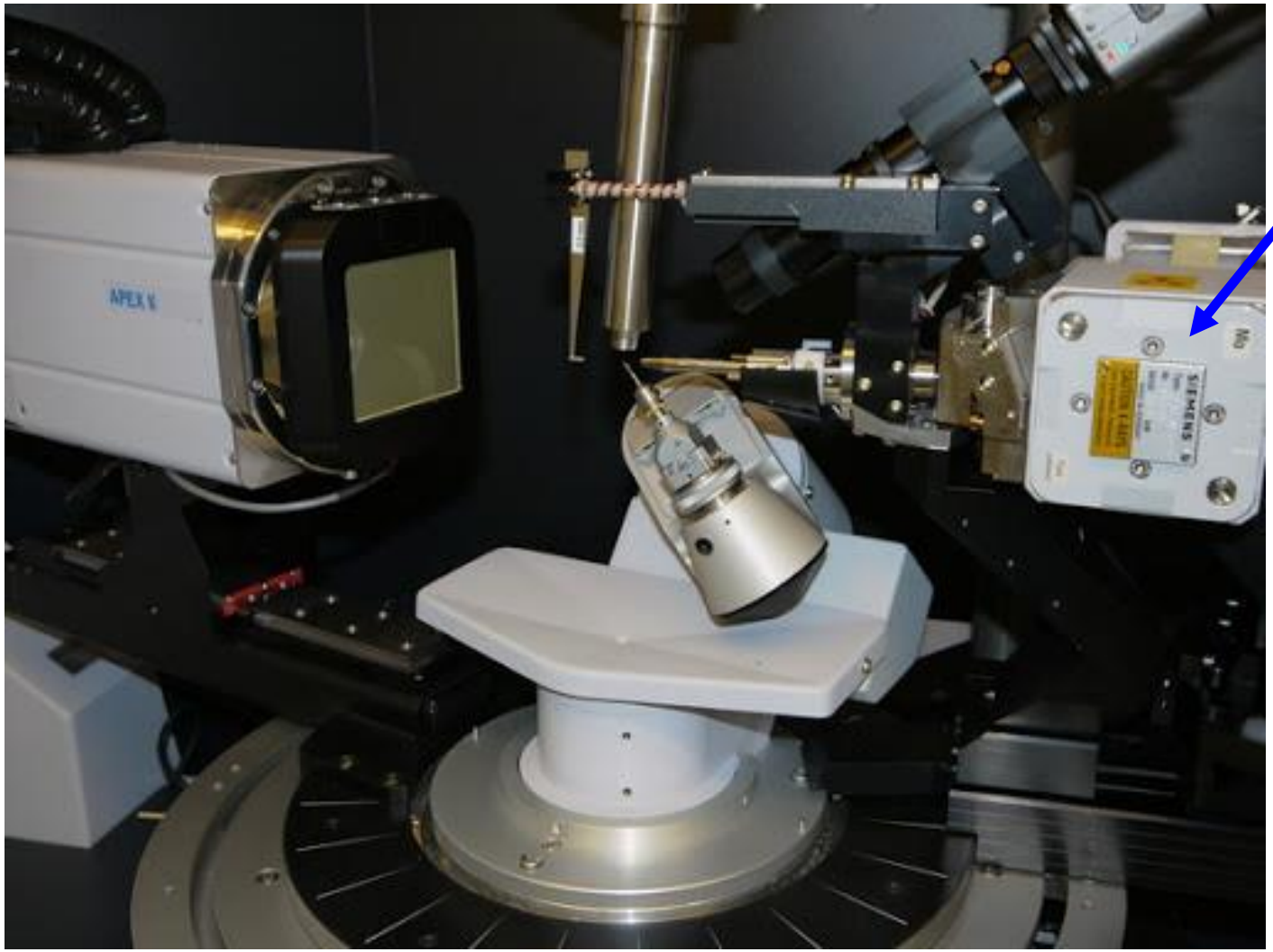
- **X-rays are generated by the interaction between the electrons and the target**



HOW ARE X-RAYS PRODUCED ?



X- RAY TUBE


X-ray tube

How a Synchrotron Works

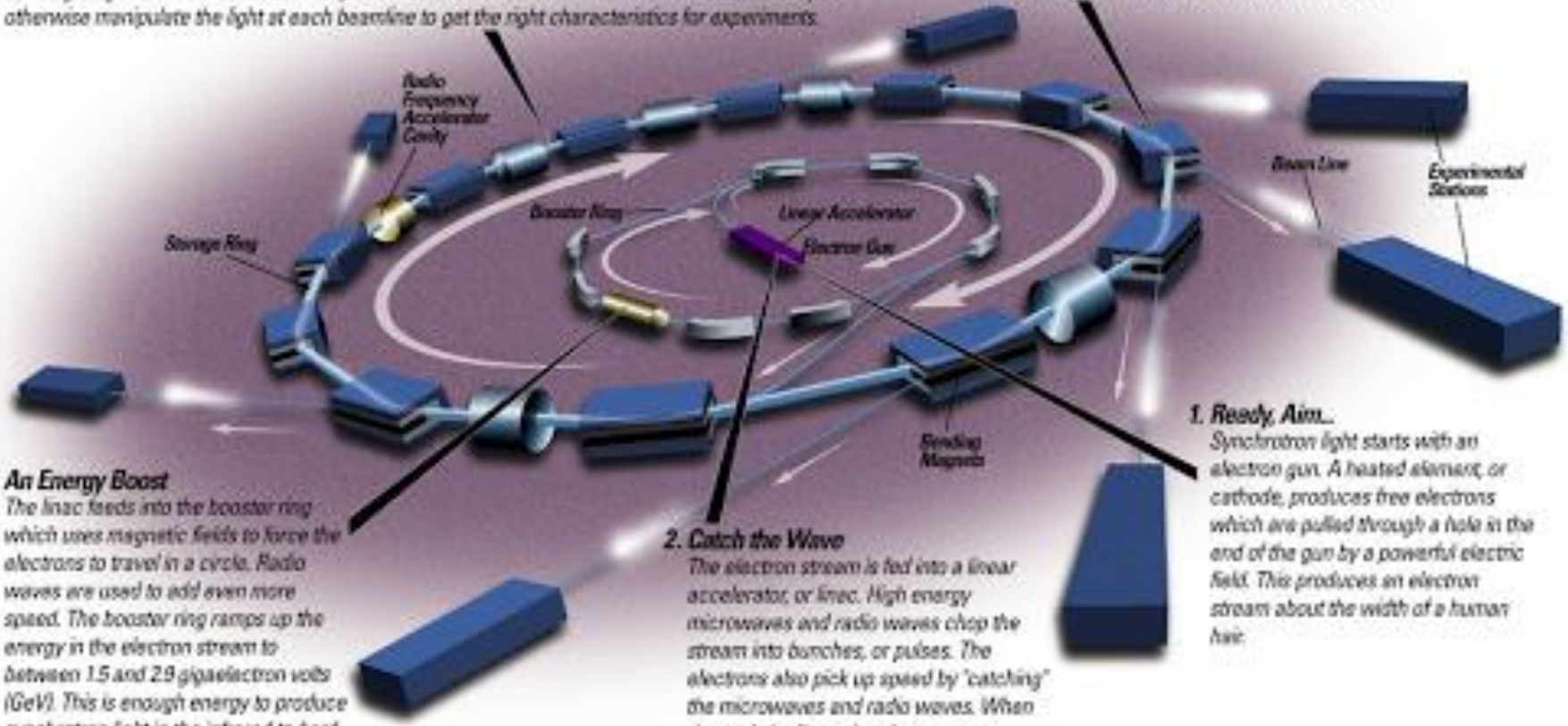
4. Storage Ring

The booster ring feeds electrons into the storage ring, a many-sided donut-shaped tube. The tube is maintained under vacuum, as free as possible of air or other stray atoms that could deflect the electron beam. Computer-controlled magnets keep the beam absolutely true.

Synchrotron light is produced when the bending magnets deflect the electron beam; each set of bending magnets is connected to an experimental station or beamline. Machines filter, intensify, or otherwise manipulate the light at each beamline to get the right characteristics for experiments.

5. Focusing the Beam

Keeping the electron beam absolutely true is vital when the material you're studying is measured in billionths of a metre. This precise control is accomplished with computer-controlled quadrupole (four pole) and sextupole (six pole) magnets. Small adjustments with these magnets act to focus the electron beam.



1. Ready, Aim...

Synchrotron light starts with an electron gun. A heated element, or cathode, produces free electrons which are pulled through a hole in the end of the gun by a powerful electric field. This produces an electron stream about the width of a human hair.

2. Catch the Wave

The electron stream is fed into a linear accelerator, or linac. High energy microwaves and radio waves chop the stream into bunches, or pulses. The electrons also pick up speed by "catching" the microwaves and radio waves. When they exit the linac, the electrons are travelling at 99.99986 per cent of the speed of light and carry about 300 million electron

3. An Energy Boost

The linac feeds into the booster ring which uses magnetic fields to force the electrons to travel in a circle. Radio waves are used to add even more speed. The booster ring ramps up the energy in the electron stream to between 1.5 and 2.9 gigaelectron volts (GeV). This is enough energy to produce synchrotron light in the infrared to hard X-ray range.

Source: University of Saskatchewan / Paradigm Media Group Inc.

A SYNCHROTON X-RAY SOURCE @ GRENOBLE - ESRF

ESRF

Why use the X-rays?

You can not view objects that are not separated by at least half the wavelength of the radiation used (resolution).

$$\lambda/2$$

In a molecule the atoms are separated by distances on the order of 1 Å = 0.1 nm = $1x10^{-10}$ m.

.

Why do you use the X-rays?

You can not view objects that are not separated by at least half the wavelength of the radiation used (resolution).

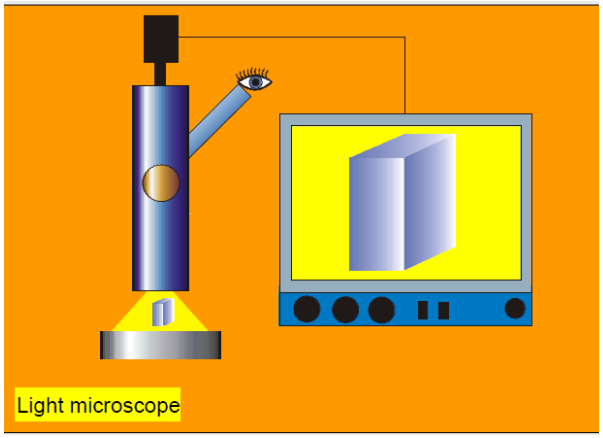
$\lambda/2$

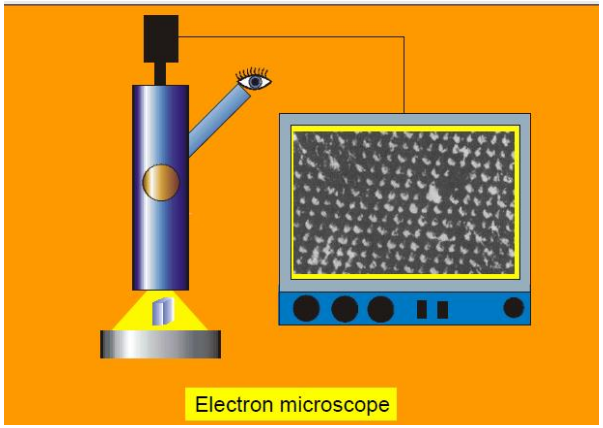
In a molecule the atoms are separated by distances on the order of 1 Å = 0.1 nm = $1x10^{-10}$ m. $1\ Å = 10^{-8}\ cm$

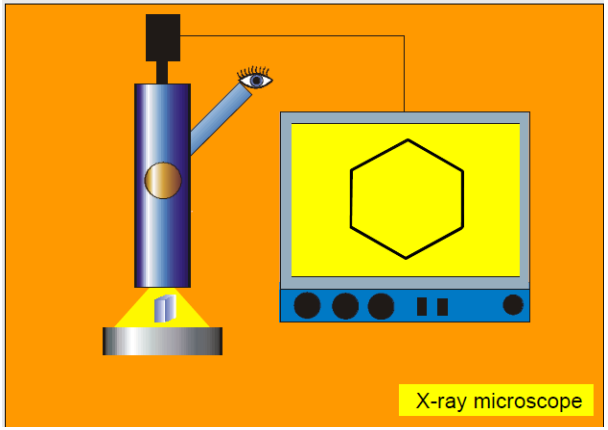
Visible light λ = **4 a 8** $x10^{-5}$ **cm**

X-ray $\lambda = 10^{-8}$ **cm**

This is the range of right wavelength?





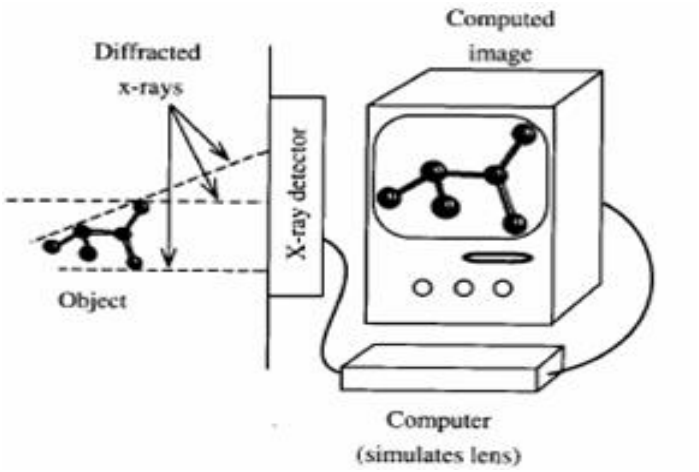


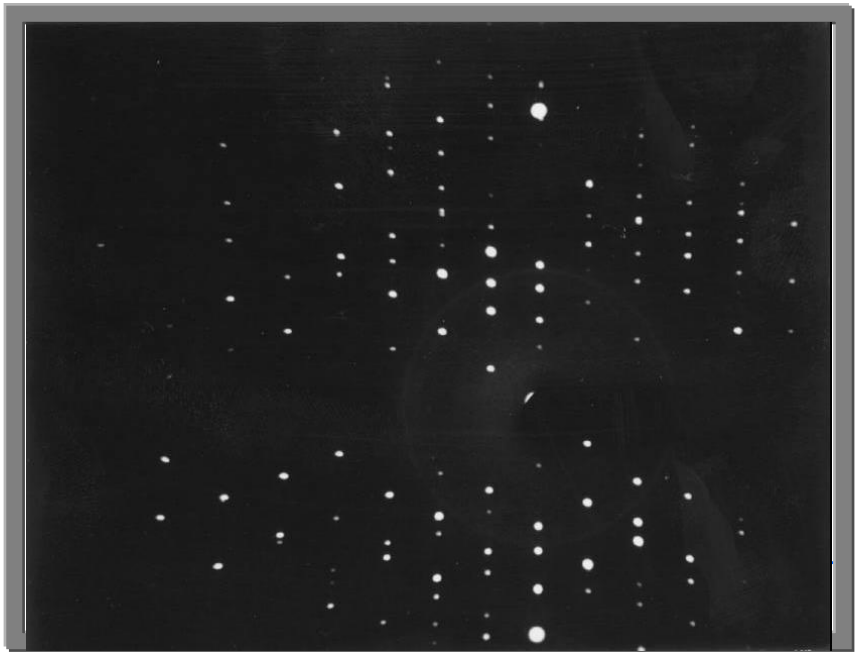
However . . .

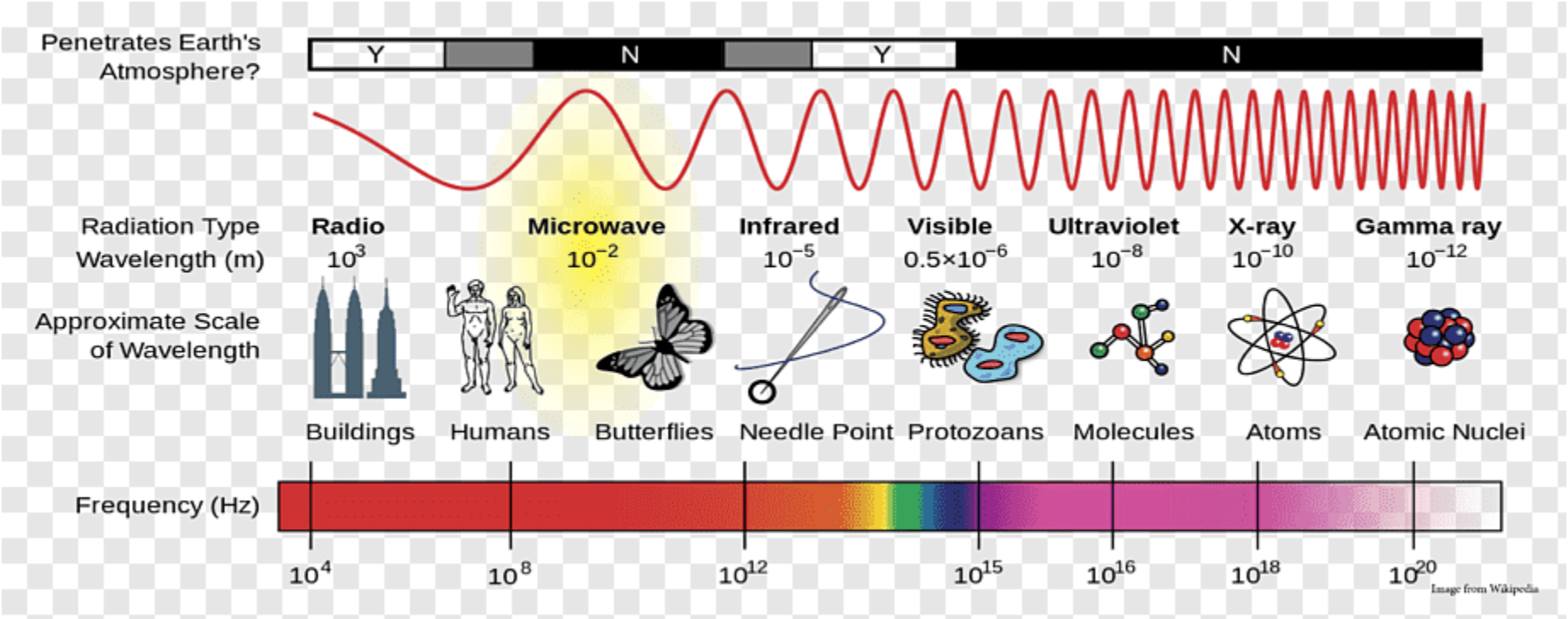
- Unlike to what happens in microscope, there is no way to focus X-rays diffracted.

- Alternatively collect the diffraction pattern (spots) or a list of intensities of the diffracted reflections.

Determination of the crystal structure







IMPOSSIBLE TO SEE THE MOLECULES USING A MICROSCOPE – NO LENS CAN BE USED

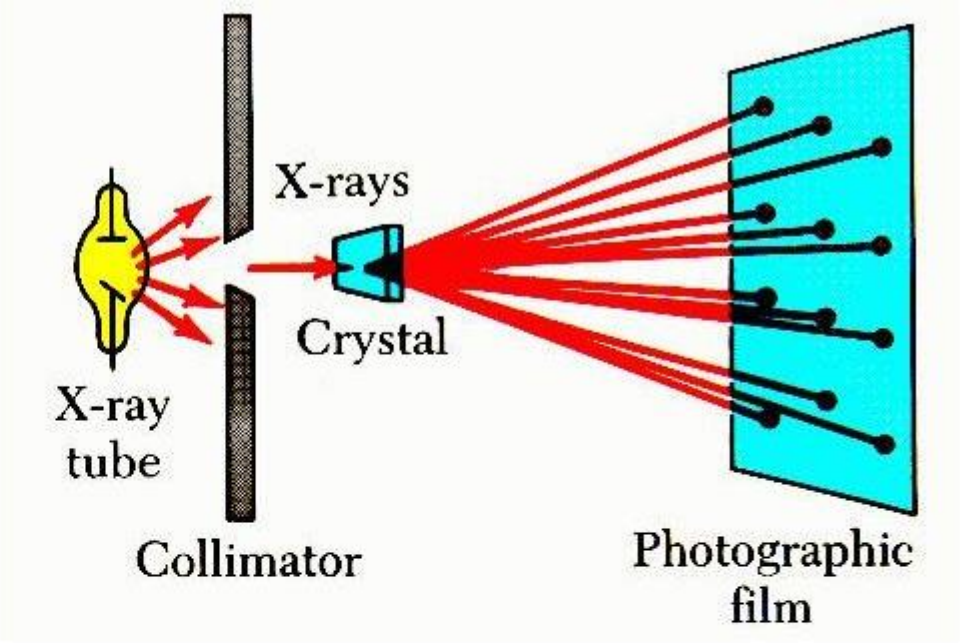
Discover of X-ray diffraction by a crystal

Max Felix Theodor von Laue

1879-1960

Professor for physics

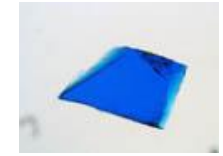
Von Laue discovered X-ray interference at crystal lattices and proved the wave nature of X-rays in 1912 together with Walther Friedrich and Paul Knipping. For this he became a Nobel prize winner in physics in 1914.

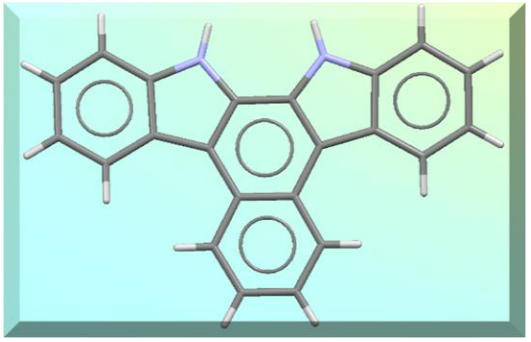


What is X-Ray Crystallography?

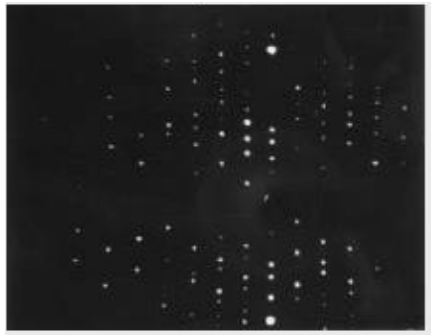
It's a process of:

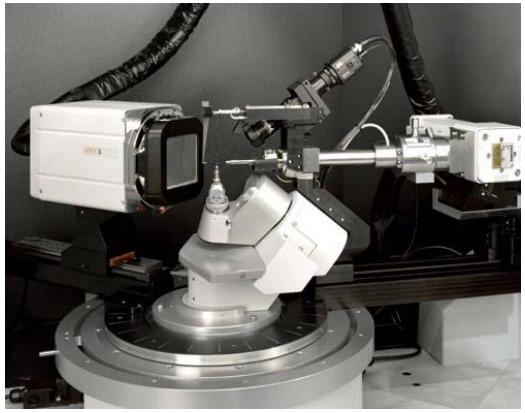
- **Measure the diffraction produced by a X - ray beam passing through a single crystal.**
- **Calculate the electron density corresponding to each reflected X - ray.**
- **Determine the molecular model that best fits the experimental data.**

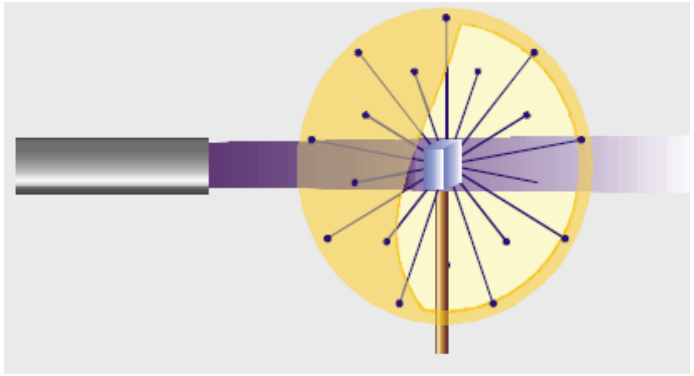




$$F_{hkl} = \sum_{j=1}^{N} N_j \cdot f_j \cdot \exp\left(-B \cdot \frac{\sin^2\theta}{\lambda^2}\right) \cdot \exp\left[2\pi i \left(hx_j + ky_j + lz_j\right)\right]$$

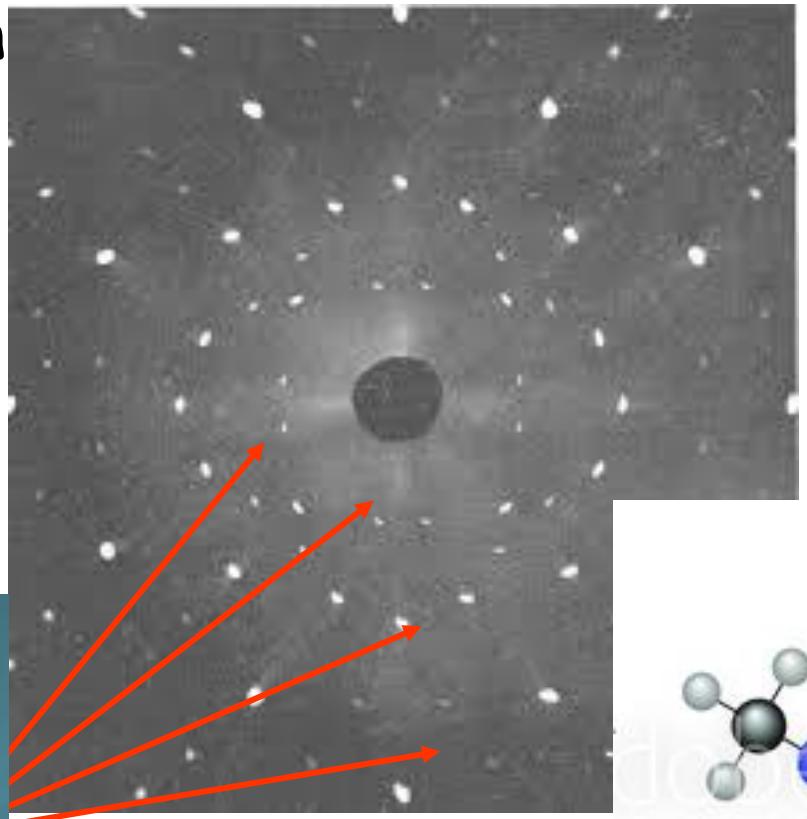






Diffraction pattern

Reciprocal space

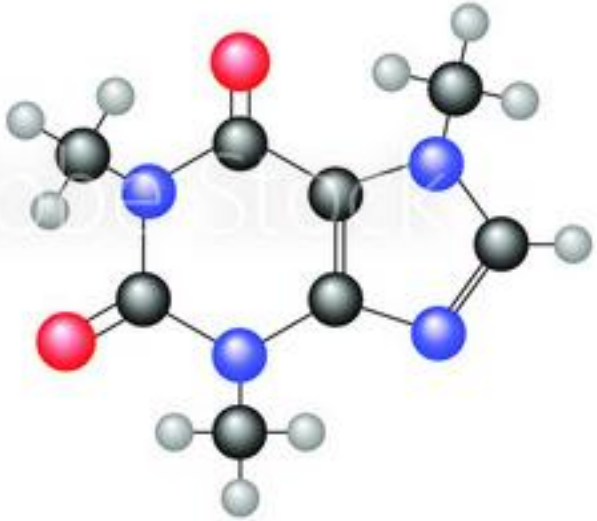


Fourier Transform

Crystal

Real space

Diffracted beam



X- Rays

Structure

Real space

Basic concepts

CRYSTALS – CRYSTALLINE SYMMETRY

SYMMETRY OPERATION

UNIT CELL

CRYSTALLINE CLASSE

SPACE GROUP

ASSYMETRIC UNIT

X-RAY DIFFRACTION – BRAGG'S LAW

RECIPROCAL SPACE

Fourier Transforms

INTENSITY of REFLECTION – Electronic density (ρ(xyz))

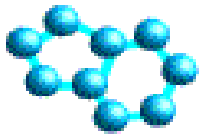
STRUCTURE FACTOR

What is F(hkl) and how is it obtained??

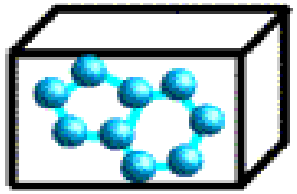
Crystals

What is a crystal? It is a homogeneous solid that exhibits a high degree of internal order

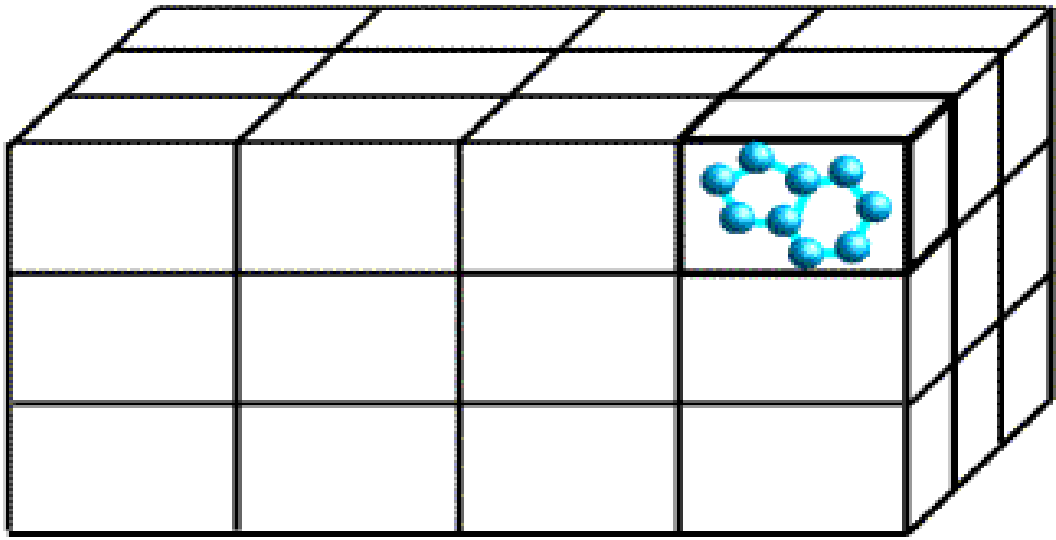
molecule

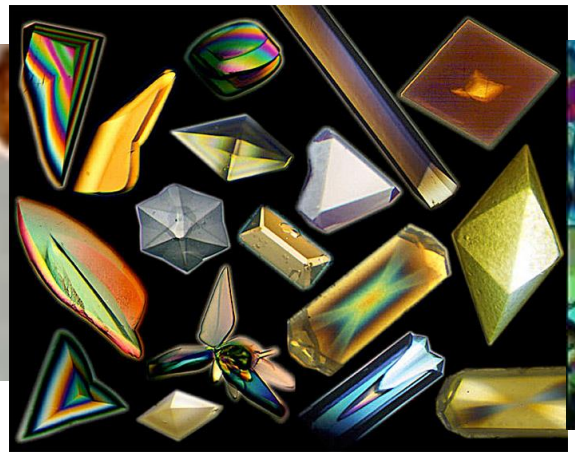


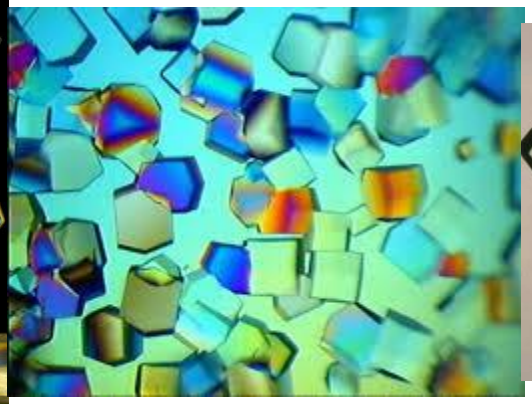
Repetitive motif

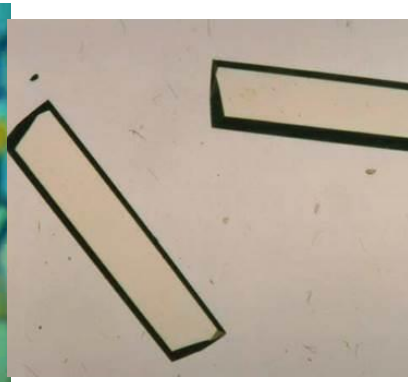


crystal









Crystals

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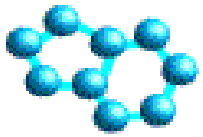
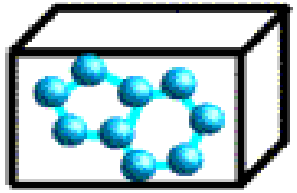
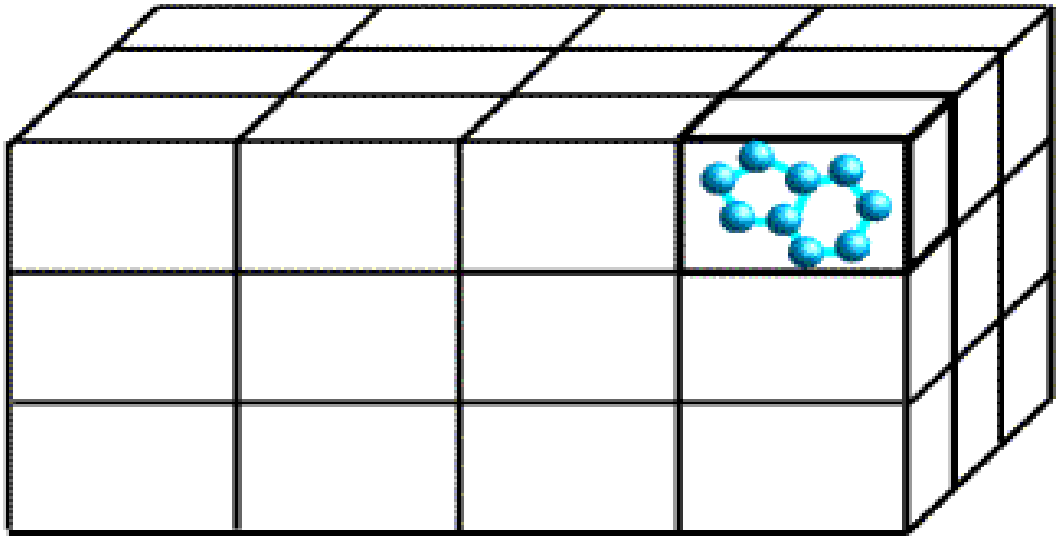
molecule



Repetitive motif



crystal

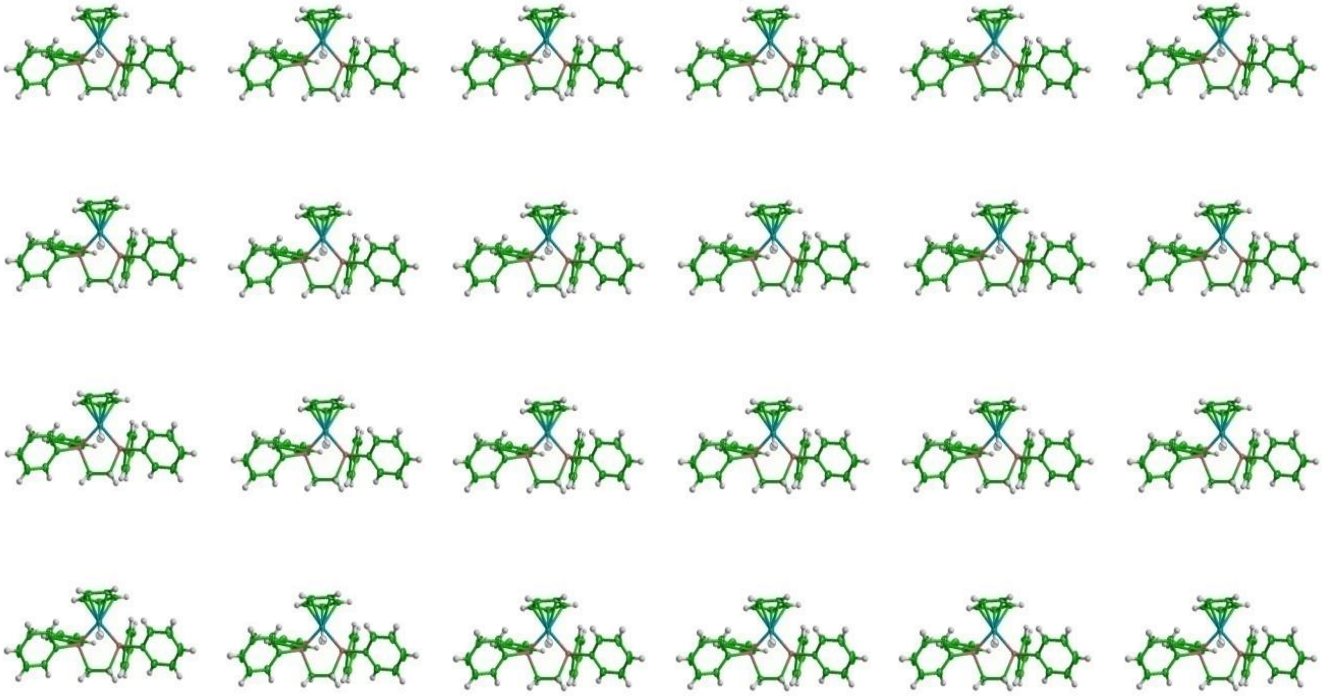


- In the crystalline state, the molecules adopt one or more orientations producing a repetitive three-dimensional structure of molecules
- The unit cell is the smallest possible volume that, when repeated, represents the entire crystal.
- The unit cell therefore contains multiple copies of the same molecule whose positions are governed by rules of symmetry.

One molecule is not enough to obtain a X-ray diffraction pattern

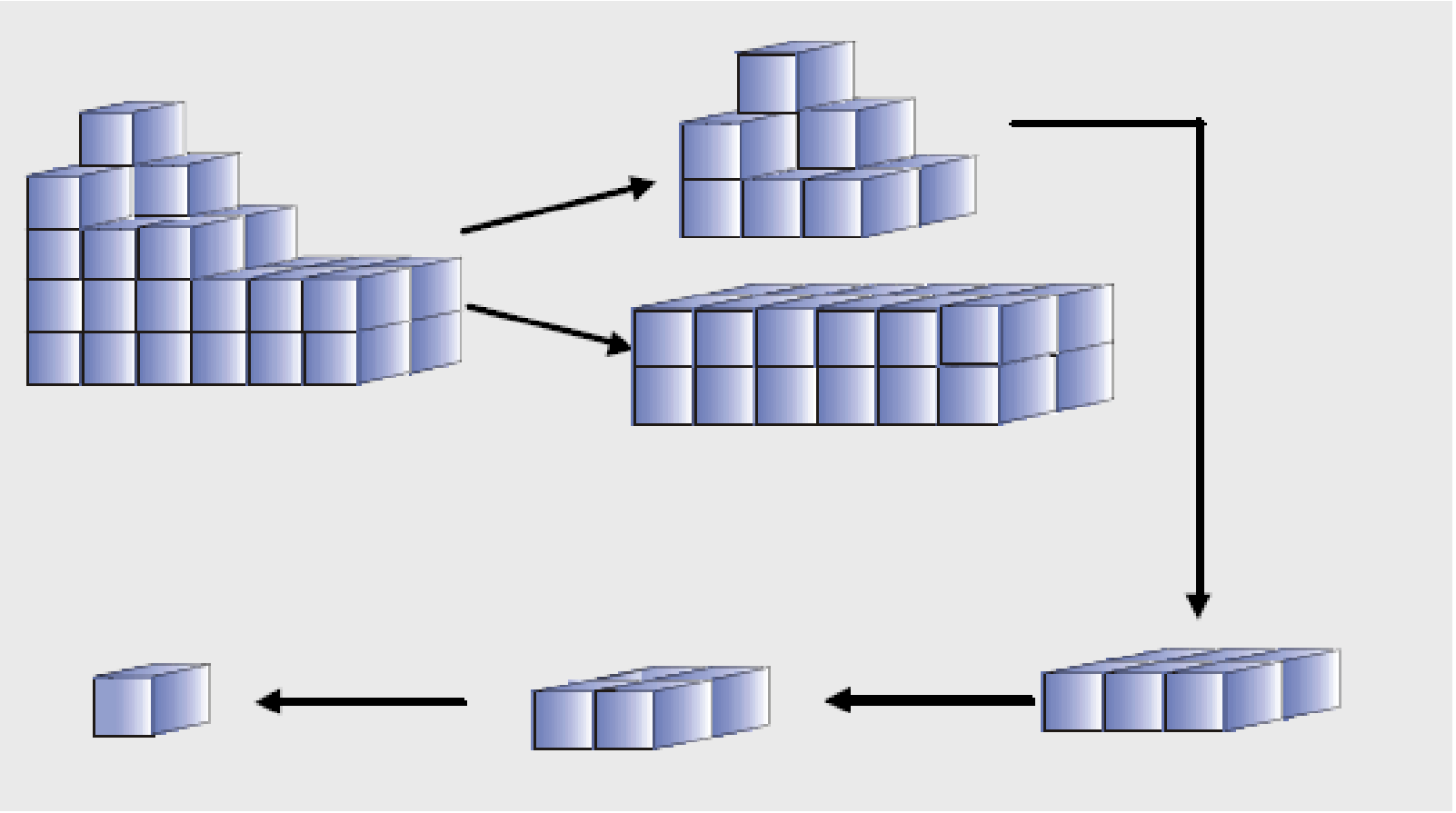
The X-rays are diffracted by the electronic density

The solution for this problem is to use many molecules arranged in a **3D** regular pattern: ***A crystal***



The crystal acts as an amplifier

The unit cell concept



Numbers of unit cells in a crystal of 1 mm^3 (10^6 $Å^3$):

NaCl	10^{19} unit cells
D-xylose-isomerase	10^{15} unit cells

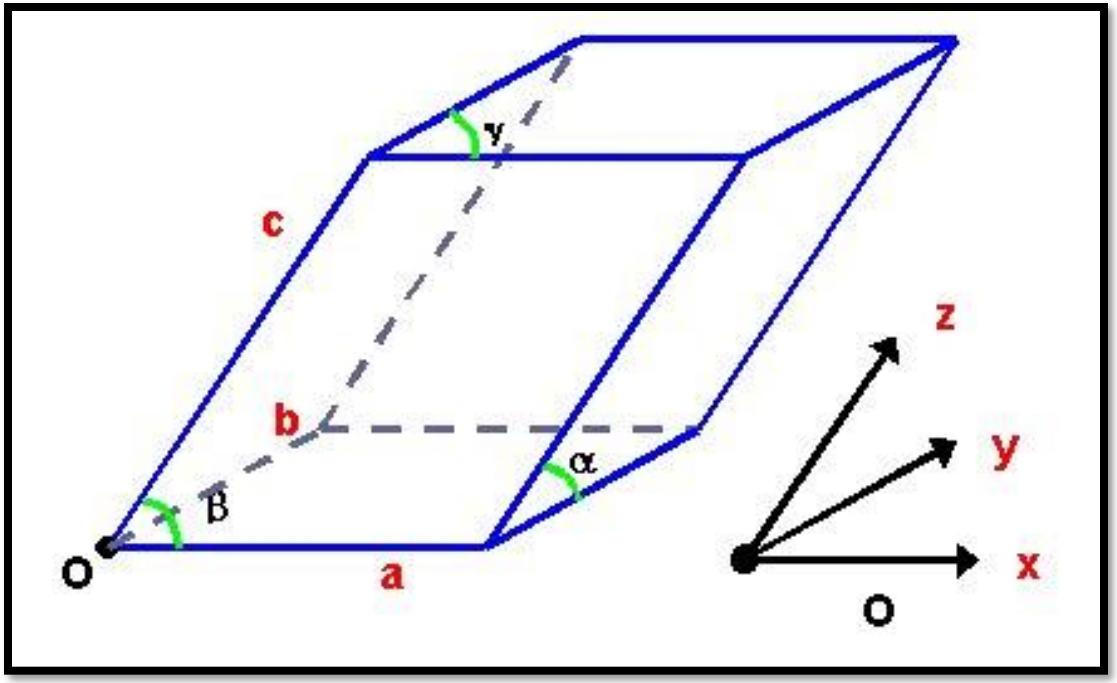
Definitions

Unit Cell

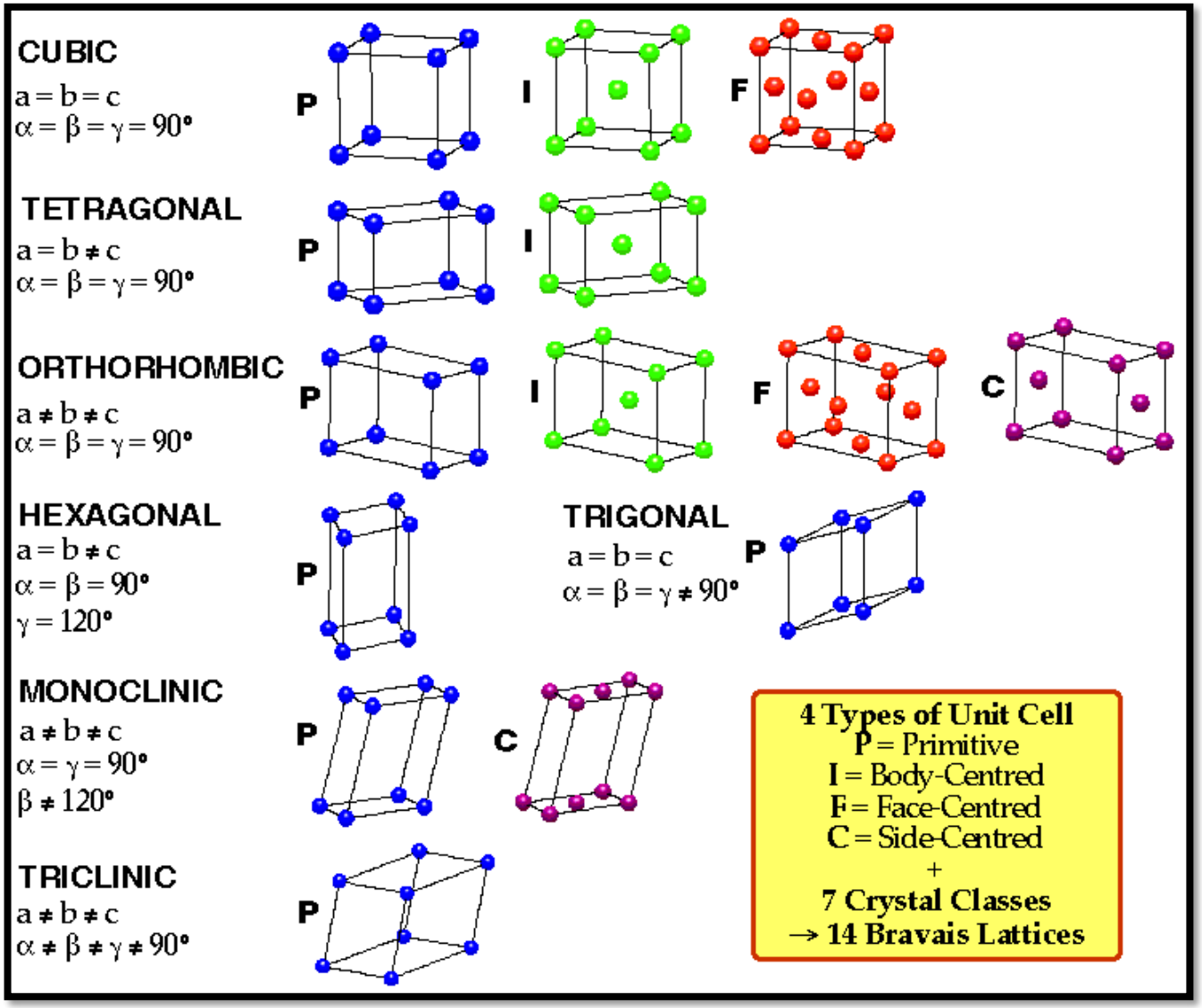
"The smallest repeat unit of a crystal structure, in 3D, which shows the full symmetry of the structure"

Unit cell is defined by:

- 3 axis - *a*, *b*, *c*
- 3 angles - α, β, γ



Bravais lattices and Space groups



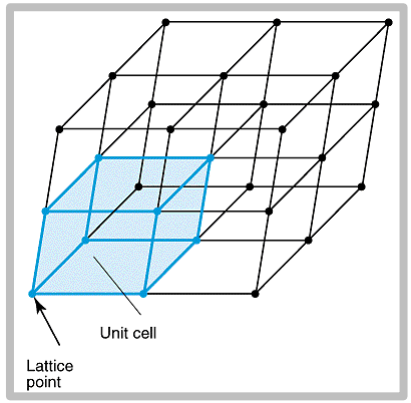
32 point groups, 14 Bravais lattices, each of the latter belonging to one of the 7 lattice systems

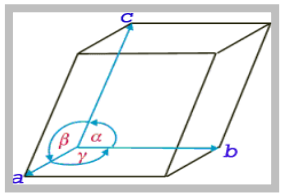
230 space

Unit Cell, the Atomic Planes and the Lattice

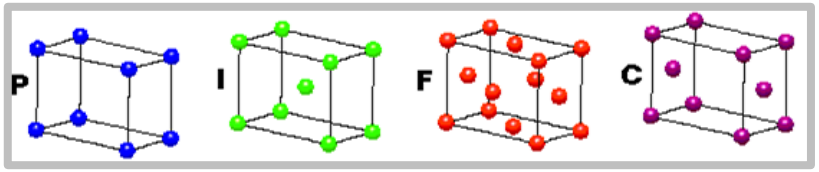
Large number of identical molecules arranged in a regular way → Repeated in all directions to give a highly ordered tri-dimensional structure

Symmetry in the Unit Cell





- 7 Lattice Systems
- 14 Bravais Lattices
- 32 Point Groups
- 230 Space Groups



Primitive unit cell

Centred unit cells

Non-translational:

- ✓ Rotation
- ✓ Reflection
- ✓ Inversion
- ✓ Improper rotation

Translational:

- ✓ Screw axes
- ✓ Glide planes

Most commons:

- Triclinic system - No restrictions
- Monoclinic system - α = γ = 90°
- Orthorhombic system - α = β = γ= 90°

Space groups: construction plan of crystals

The combination of all symmetry elements including the translation symmetry elements yields only 230 combination.

These combinations are called "**space groups**".

The correct determination of the space group is absolutely necessary for the determination of the crystal structure.

Space groups	Symmetry elements
Centrosymmetric	Translation, rotational axis, mirror planes center of inversion and combinations
Non-centrosymmetric	Translation, rotational axis, mirror planes and combinations
Chiral	Translation, rotational axis and combinations

Characteristics and advantages of the unit cell concept

Characteristics of the unit cell:

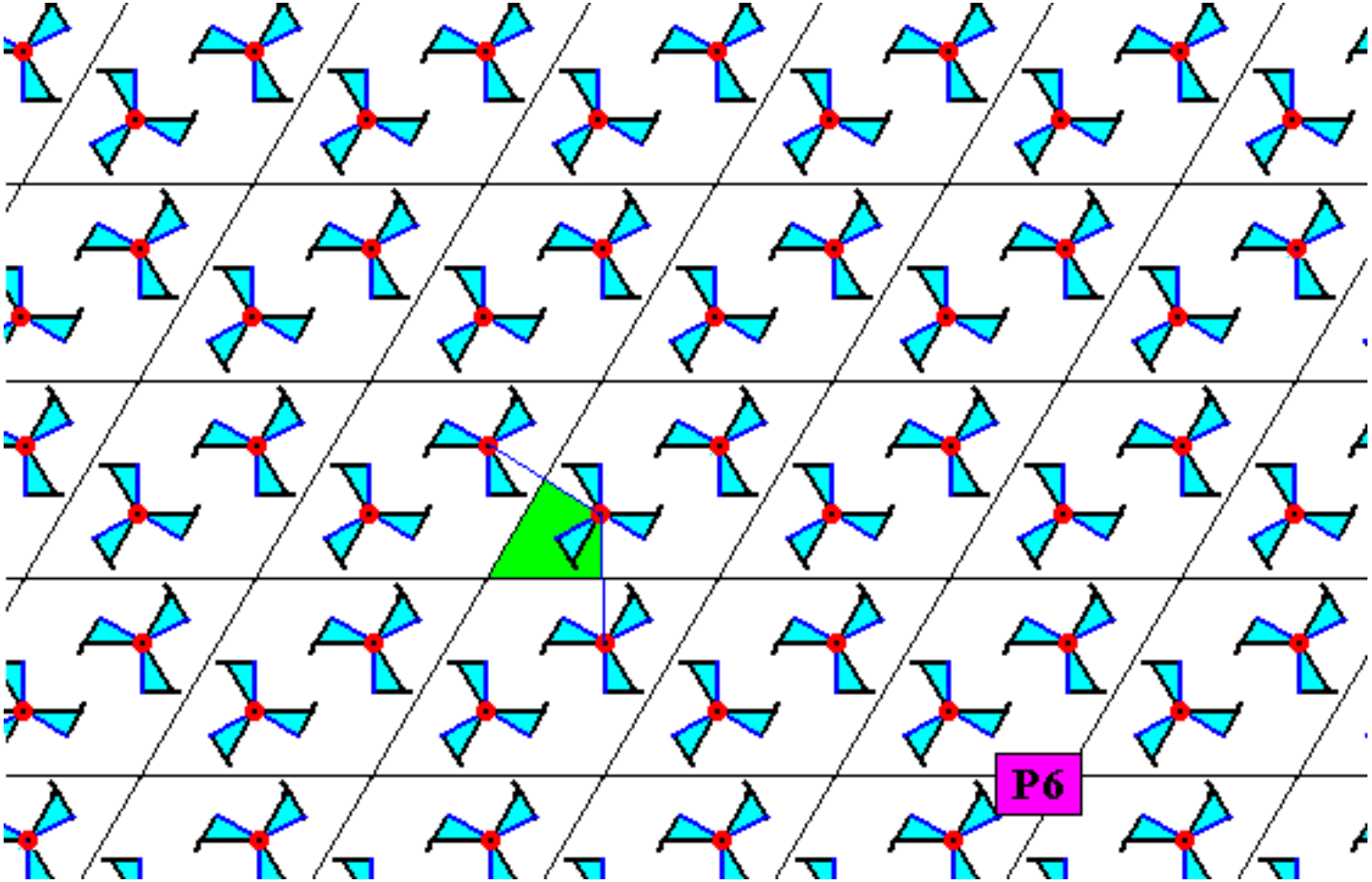
- Imaginary building block that helps to appreciate the internal periodicity of crystals (that contains atoms or molecules, not unit cells)
- is usefull for an easier description of the periodicity in crystals

Advantages of the unit cell concept:

- The crystal is divided into small identical units
- For the description of the whole structure only a few parameters are needed
- The problem of determining the structure is reduced to that of determining the structure of the content of only one unit cell; any other unit cell will be like the first.
- Only the positioning of the atoms in the unit cell must be determined.

Which atomic positions must be determined ?

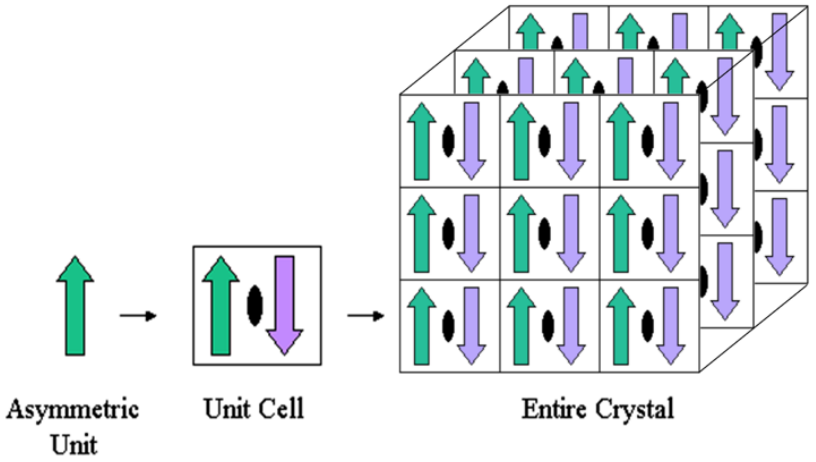
The content of one unit cell or something less ?



Asymetric unit

•The asymmetric unit contains a number of atoms whose positions have to be determined in a crystal structure determination.

•These atoms together with the symmetry operations giving by the space group are sufficient to describe the content of the unit cell and therefore the whole crystal structure.



In a crystal structure analysis only the positions of the atoms of the asymmetric unit have to be determined.

Basic concepts

CRYSTALS – CRYSTALLINE SYMMETRY

SYMMETRY OPERATION

UNIT CELL

CRYSTALLINE CLASSE

SPACE GROUP

ASSYMETRIC UNIT

X-RAY DIFFRACTION – BRAGG'S LAW

RECIPROCAL SPACE

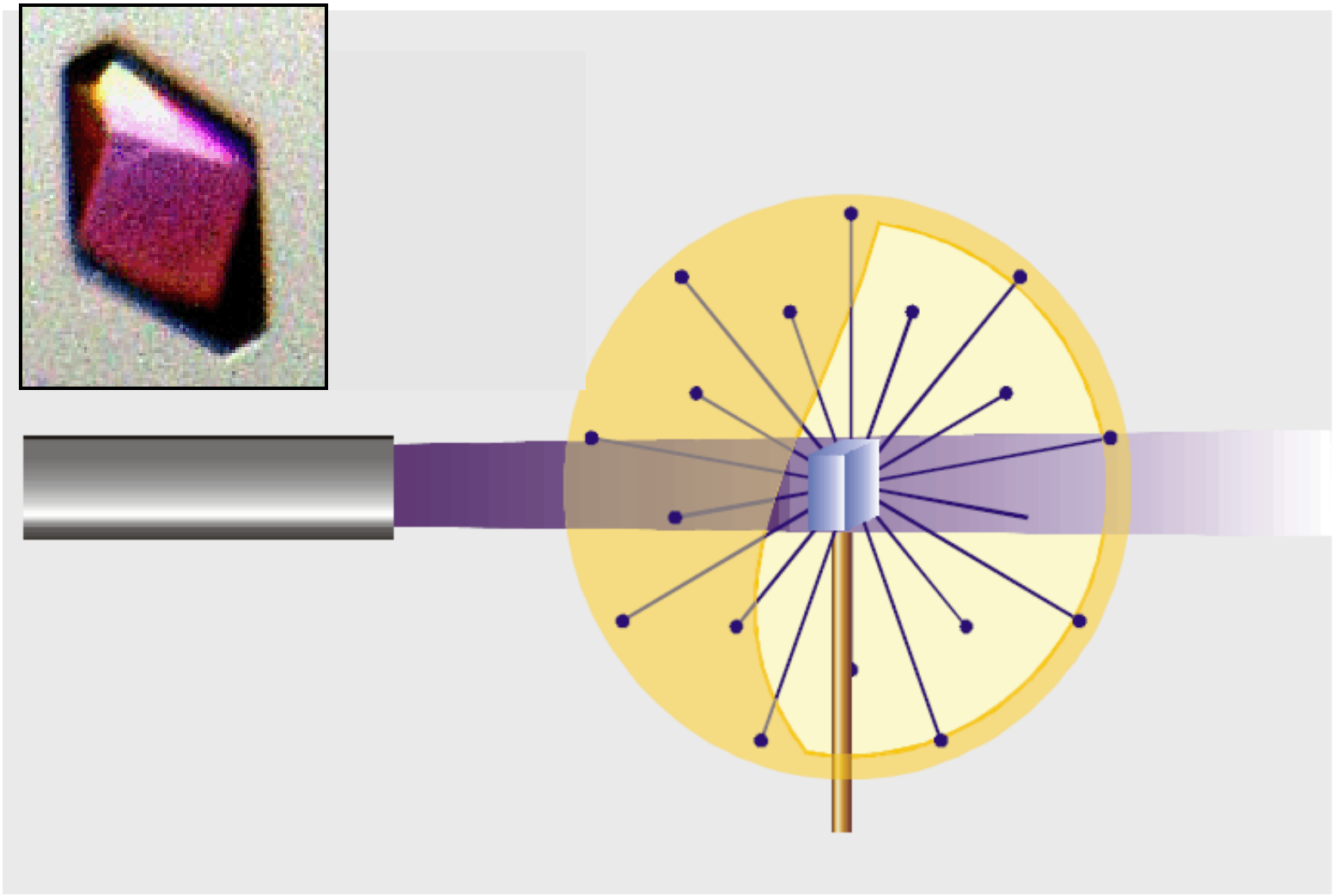
Fourier Transforms

INTENSITY of REFLECTION – Electronic density (ρ(xyz))

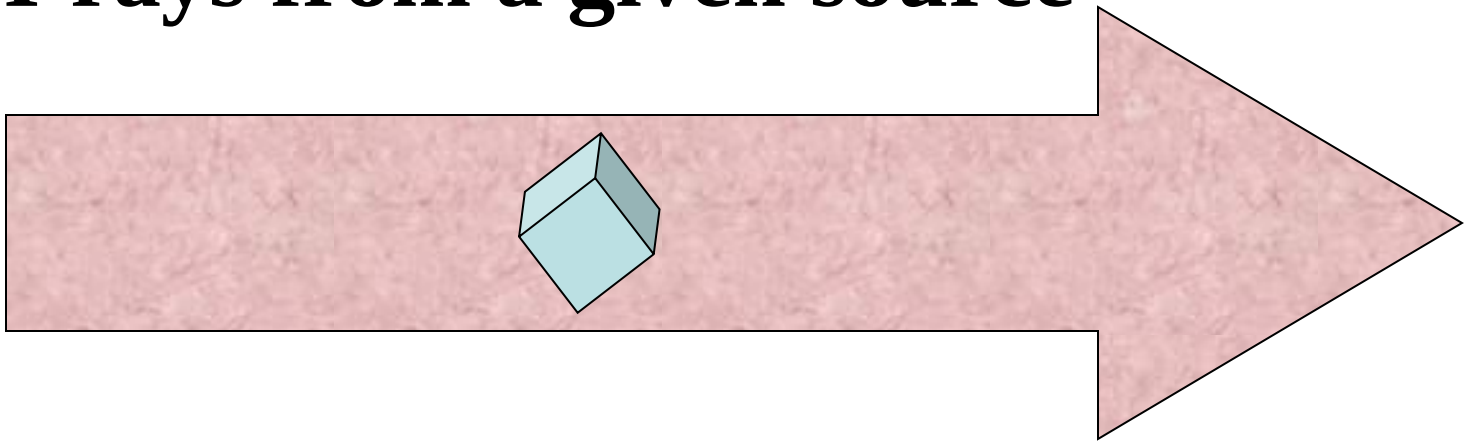
STRUCTURE FACTOR

What is F(hkl) and how is it obtained??

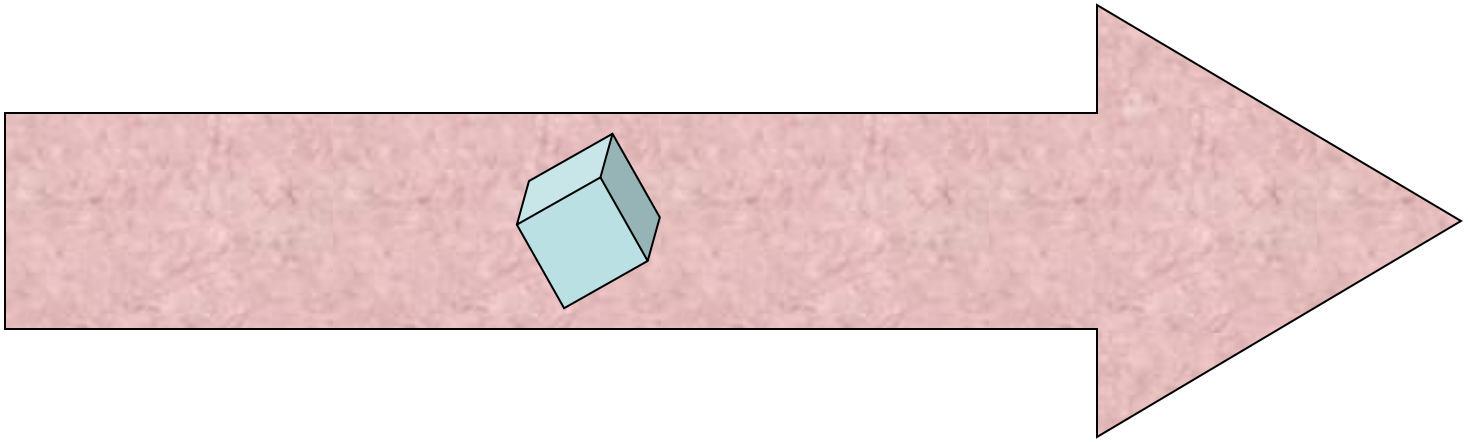
DIFFRACTION: What positions can be expected to diffraction points?

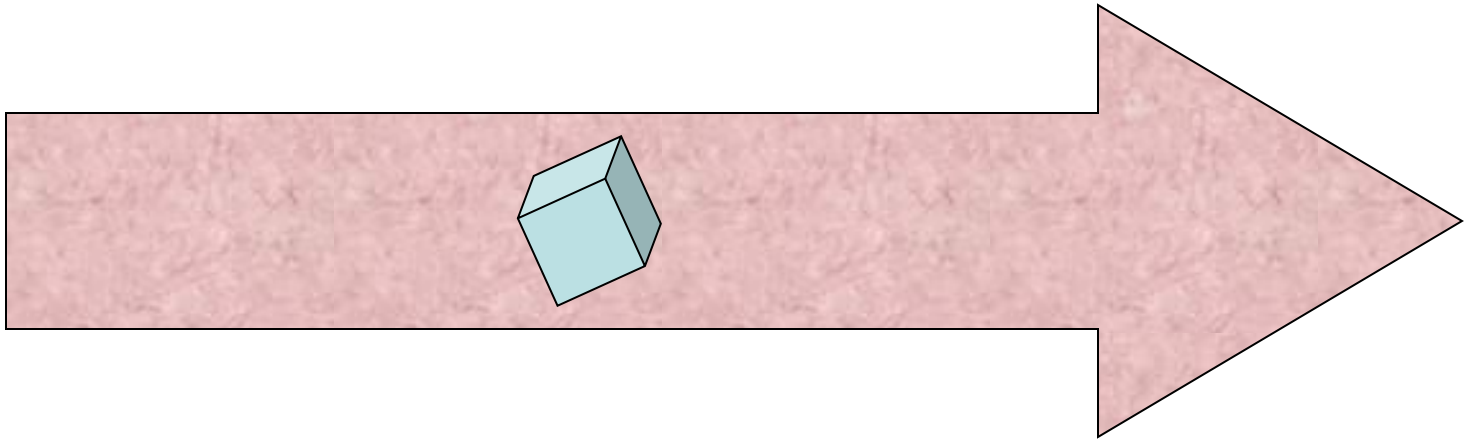


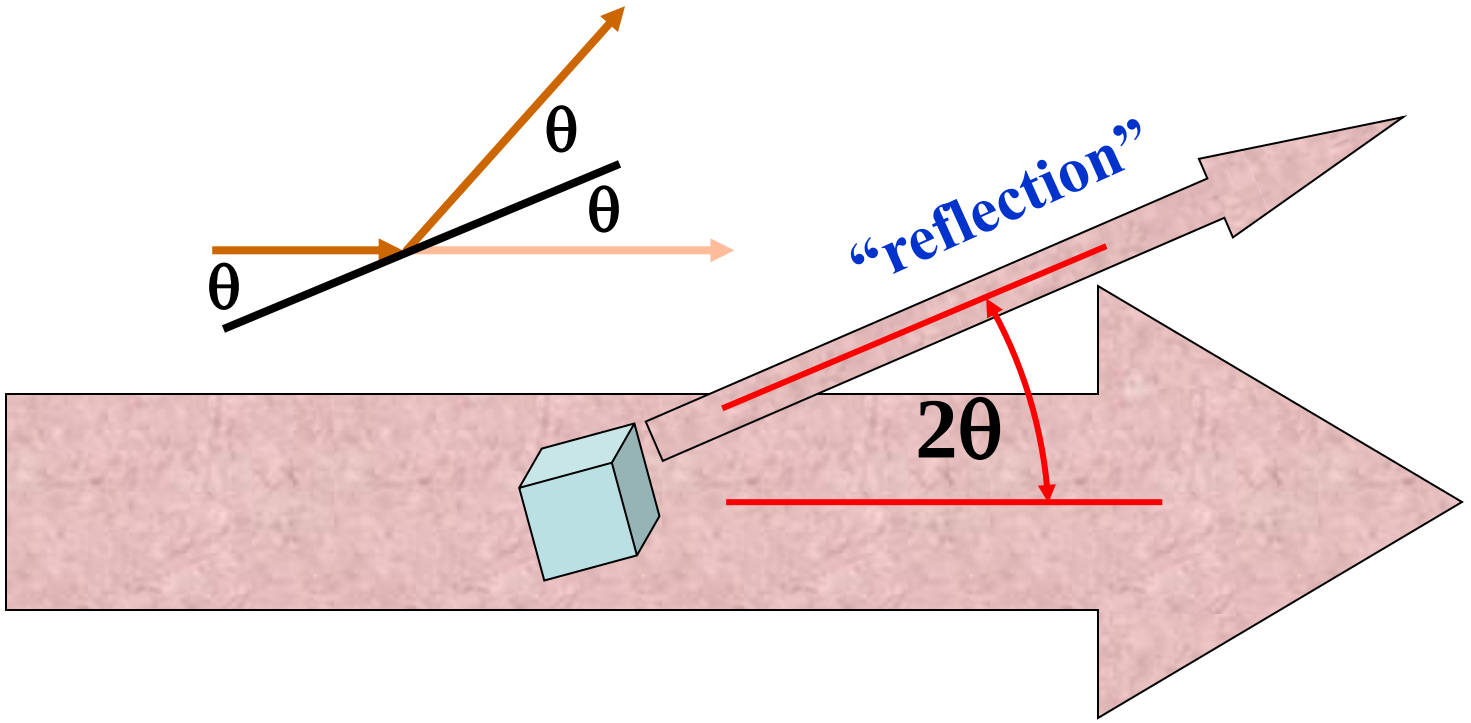
X-rays from a given source



The crystal is kept in the incident beam during the rotation





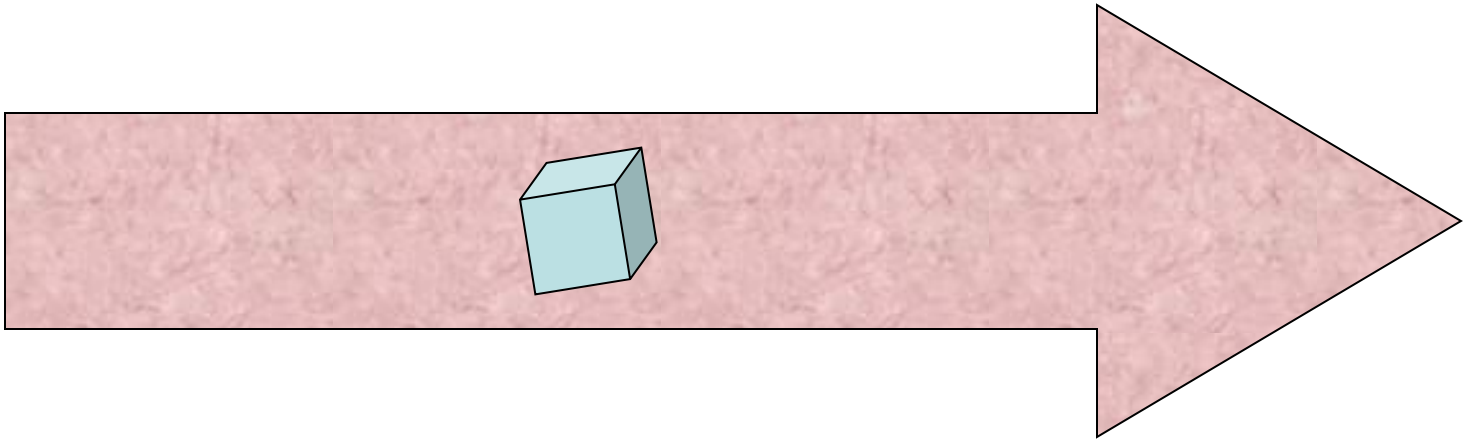


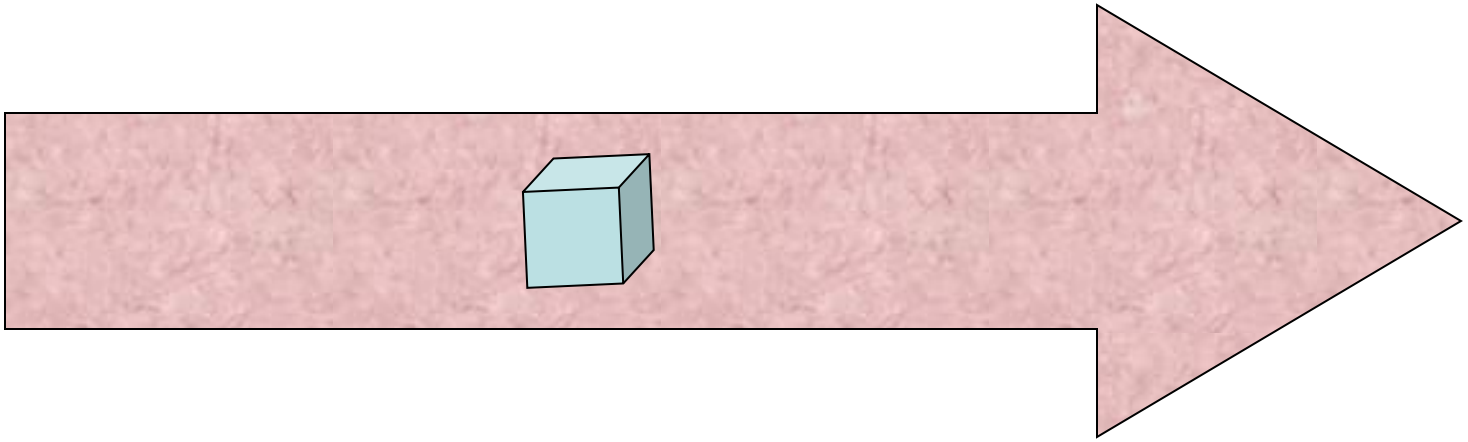
θ = Bragg angle, 2θ = scattering angle

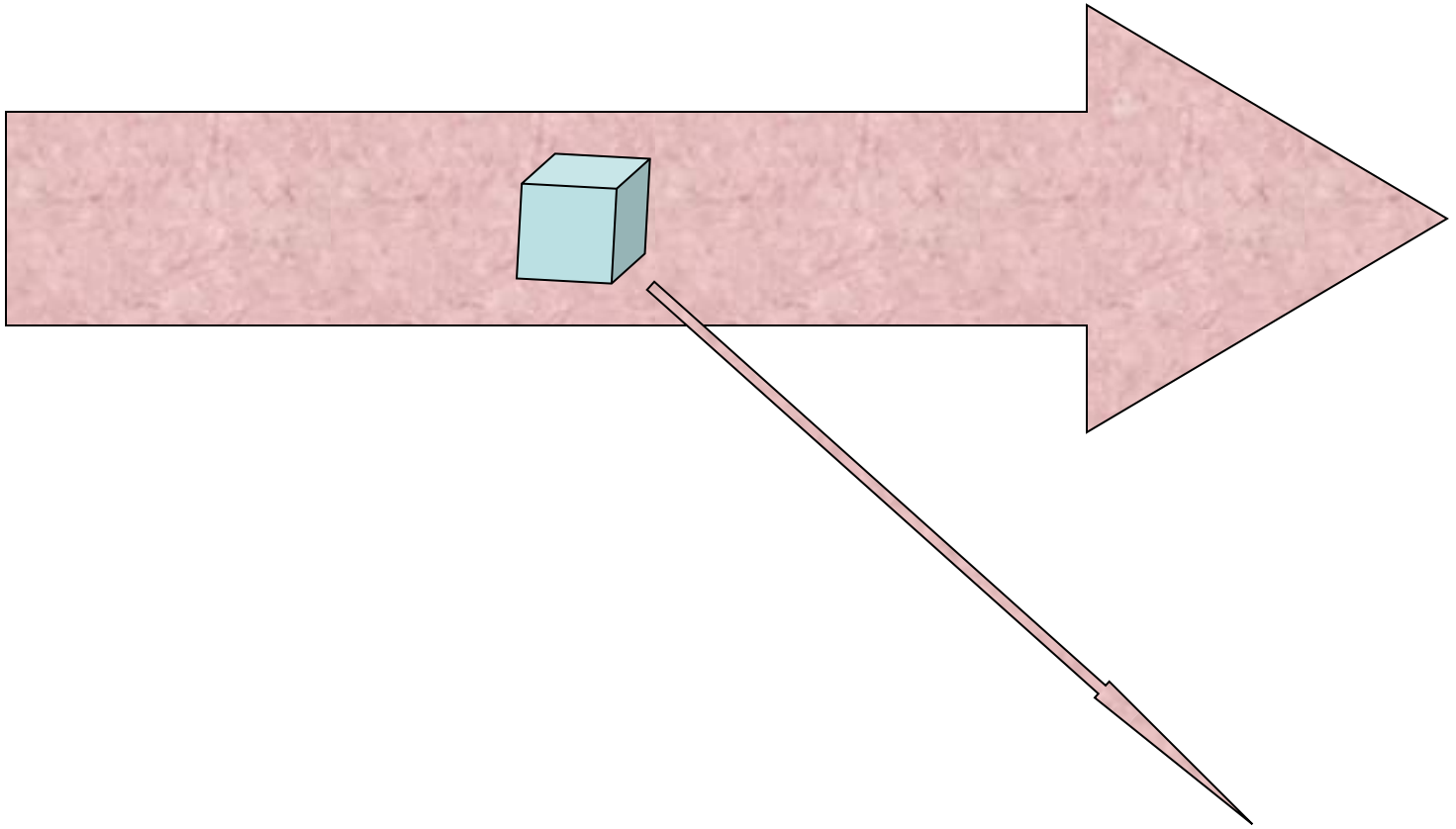
$\lambda = 2d_{hkl} \sin \theta$ (Bragg's law)

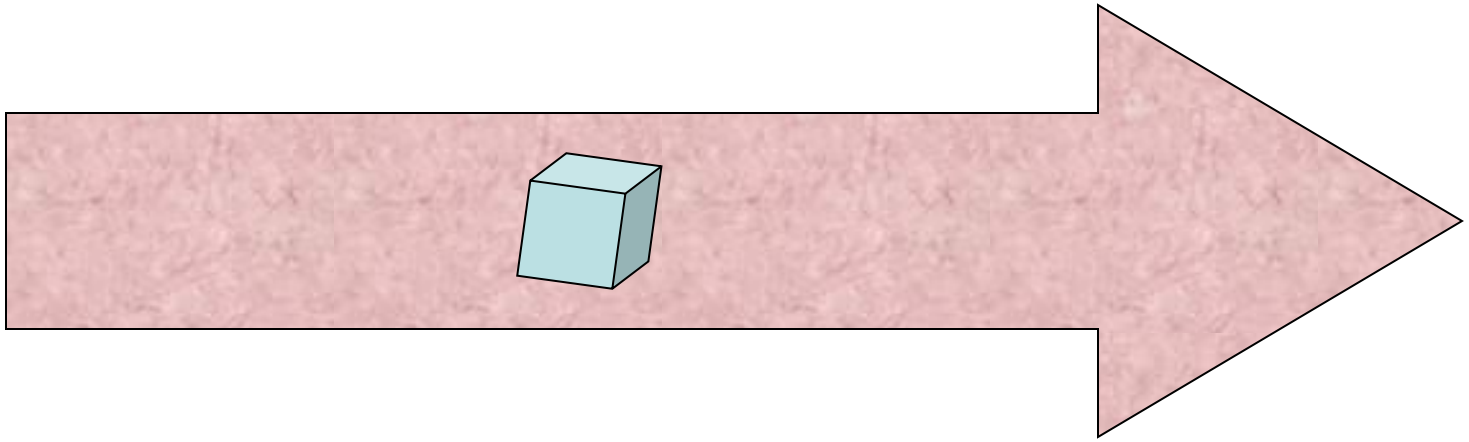
λ = X-ray wavelength

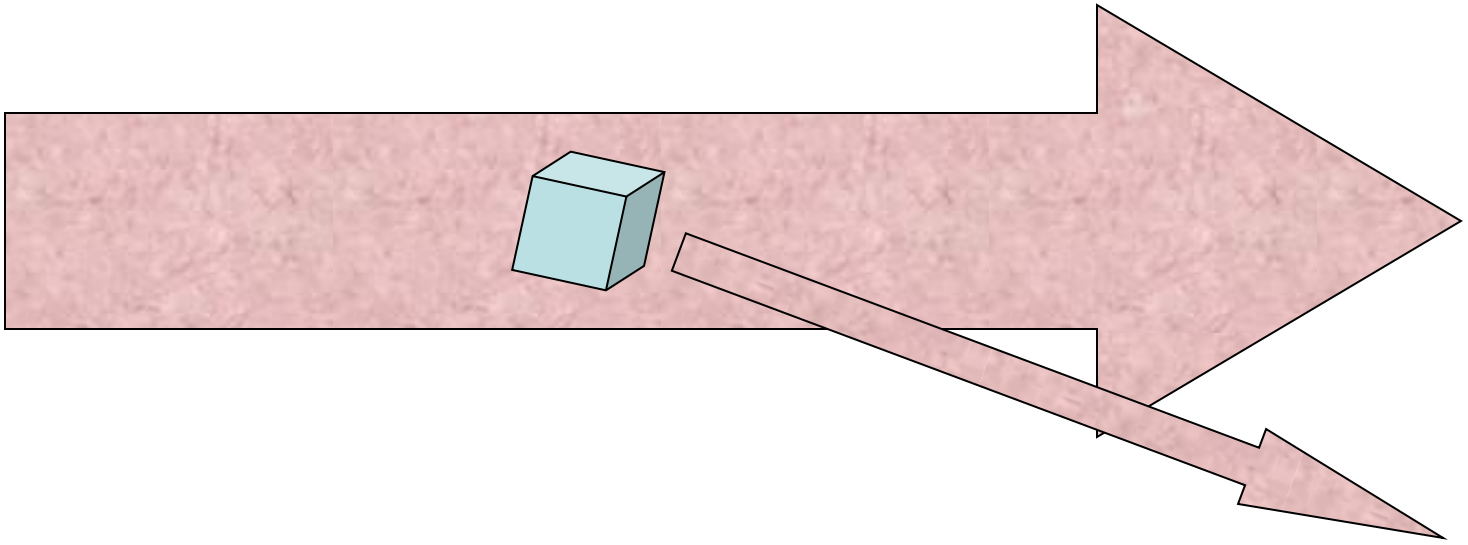
d_{hkl} = interplanar spacings in the crystal

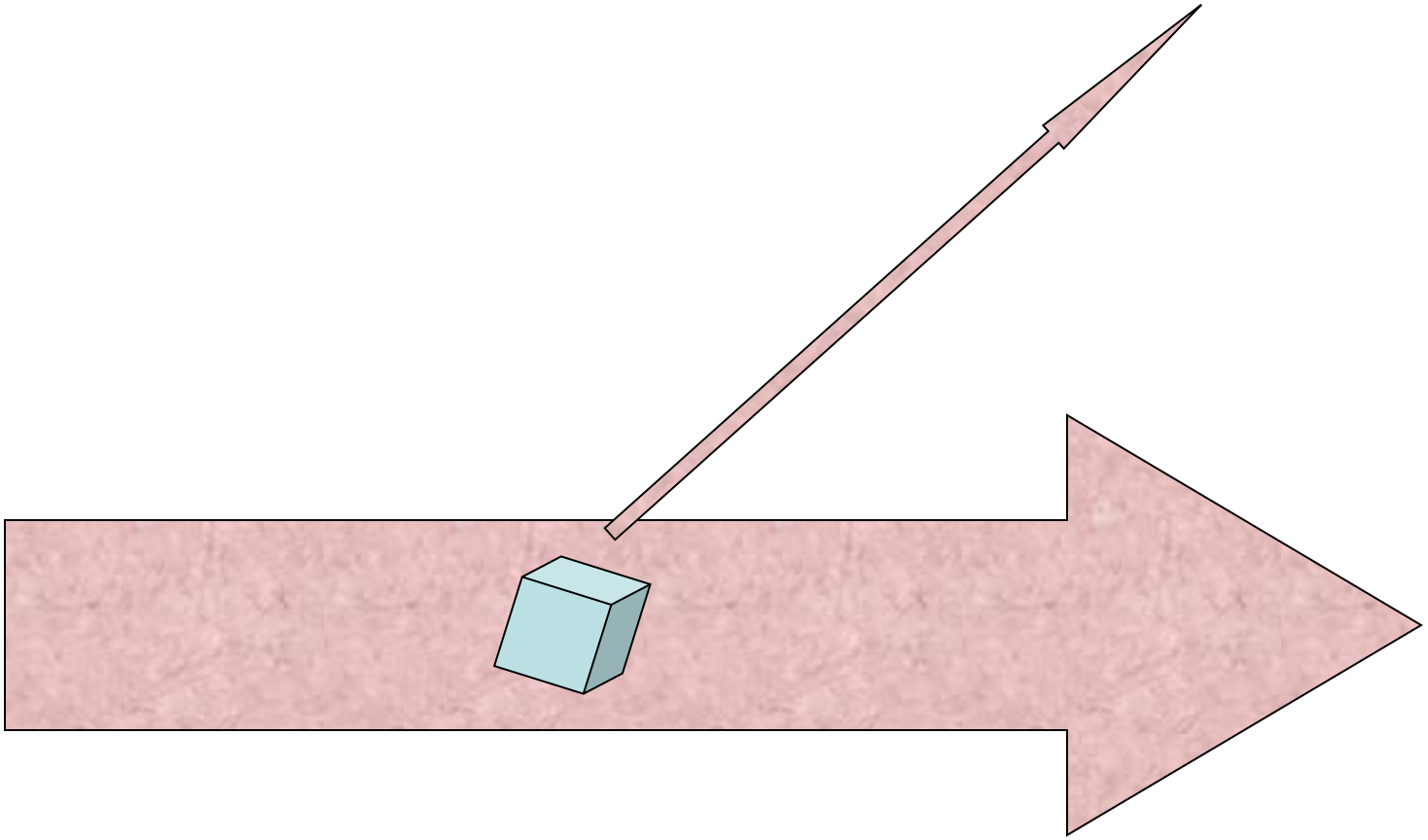


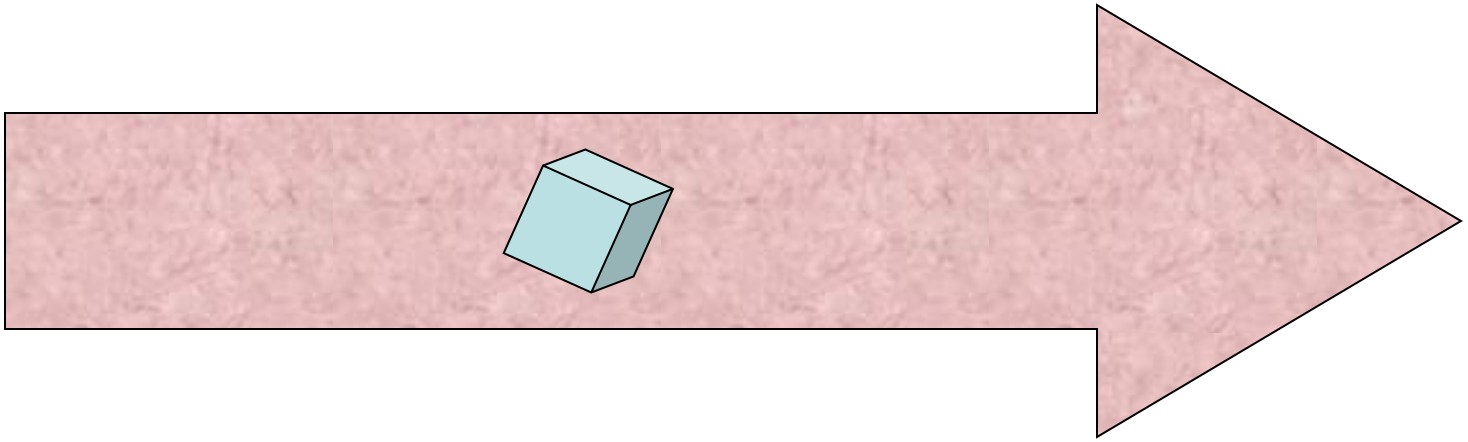


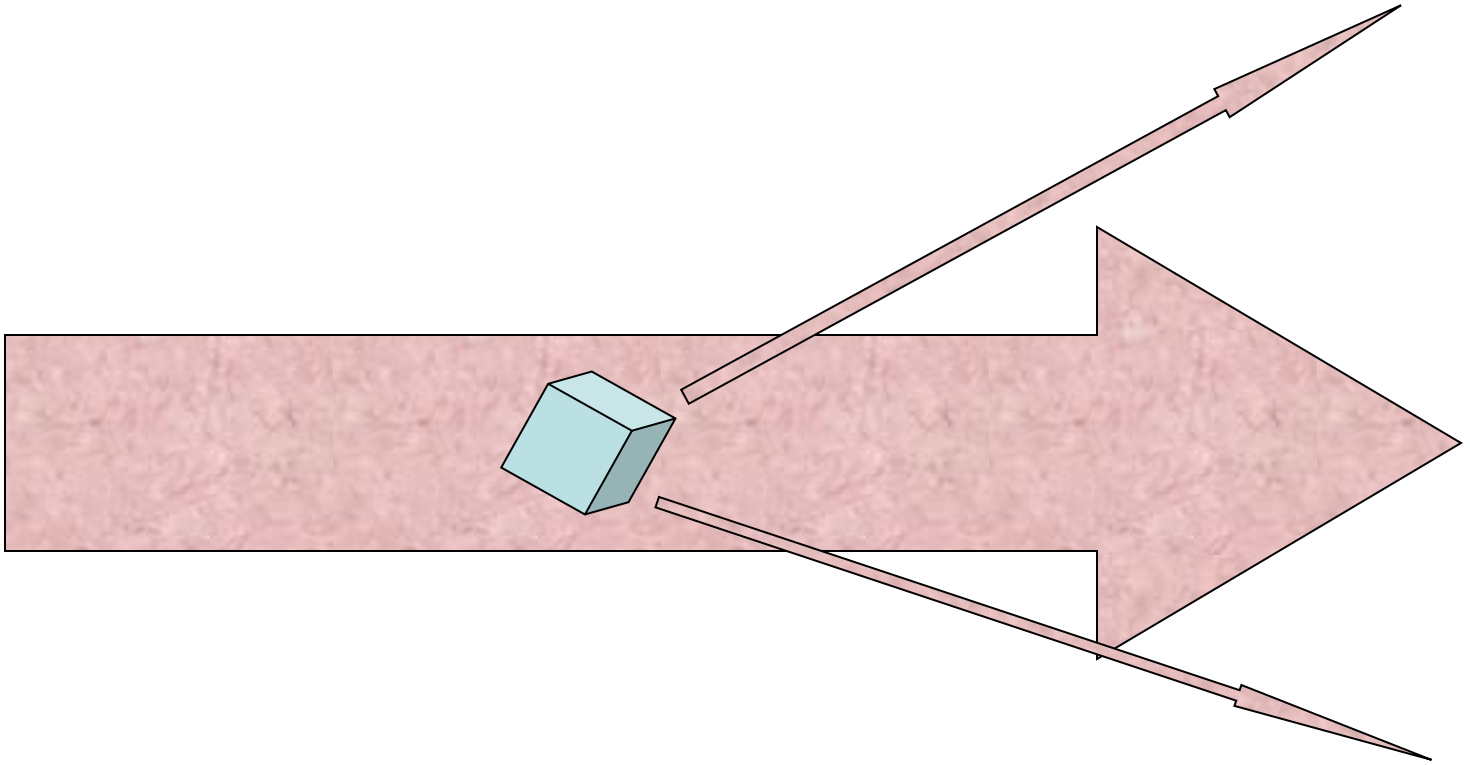




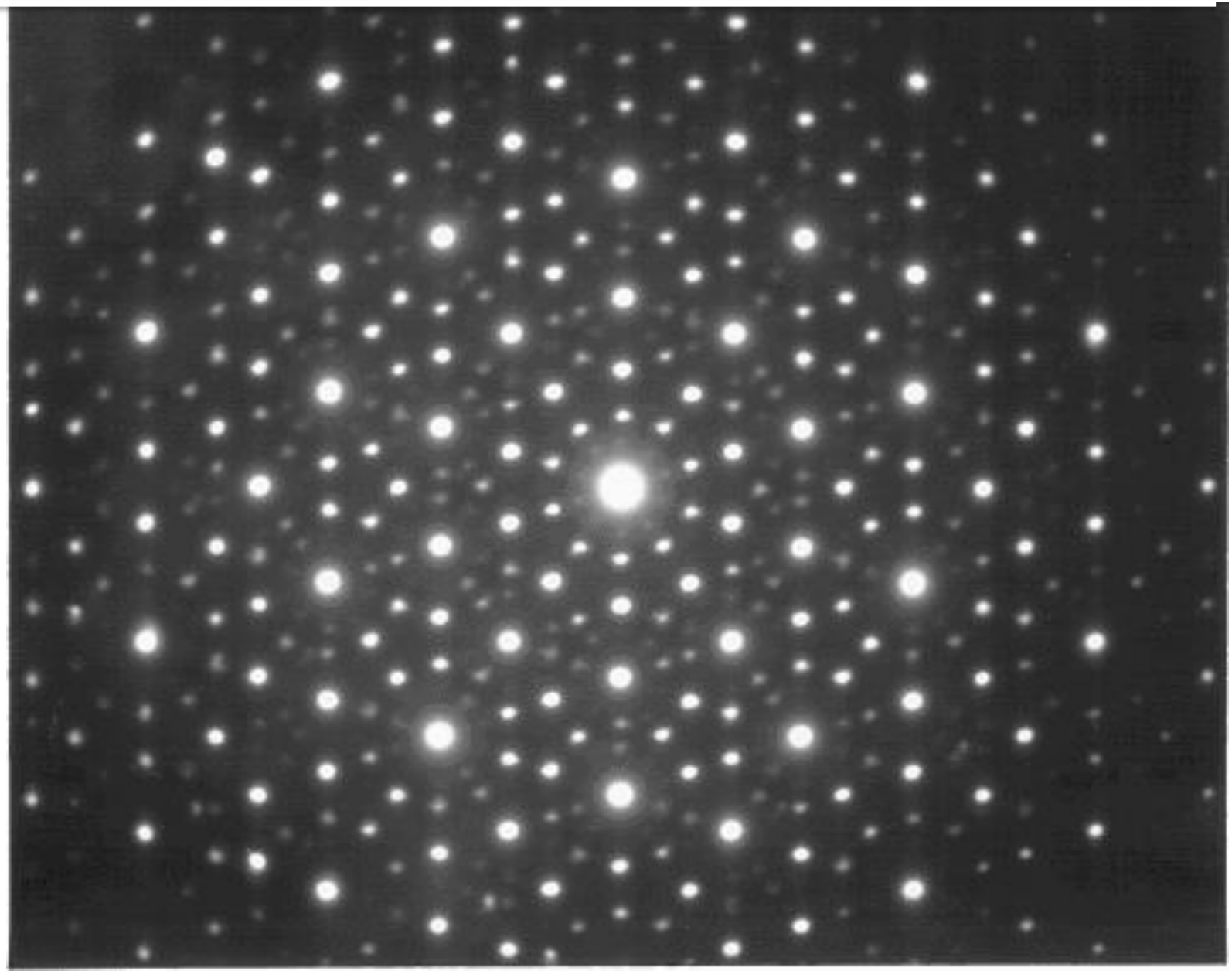


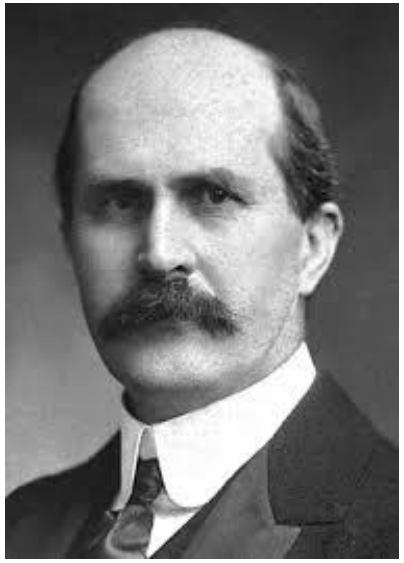


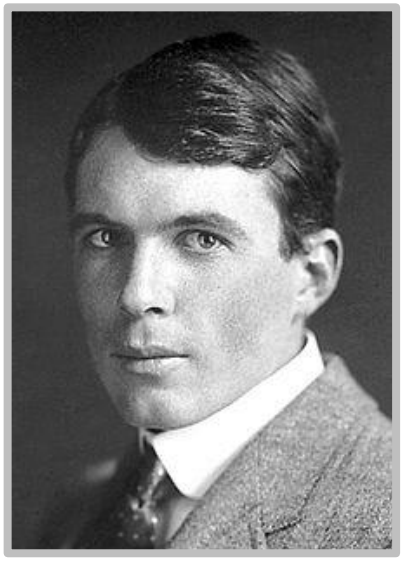




DIFFRACTION: Examples of diffraction patterns







In 1912, Sir William Henry Bragg and William Lawrence Bragg developed the **Bragg's Law**

The Nobel Prize in Physics 1915 was awarded jointly to Sir William Henry Bragg and William Lawrence Bragg "for their services in the analysis of crystal structure by means of X-rays"

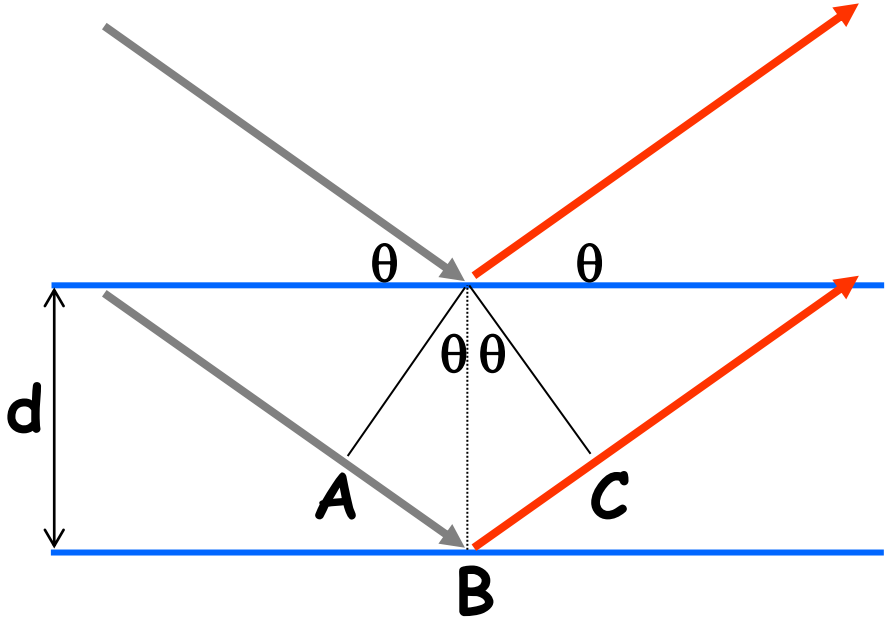
$$2d_{hkl}\sin\theta = n\lambda$$

Diffraction ≈ Reflection from planes in the lattice

Basis for X-ray diffraction

Diffraction: Bragg's Law

A simple way to describe the diffraction conditions established by Bragg in 1912, is to consider the diffraction as a reflection of the X radiation by adjacent planes in the crystal lattice



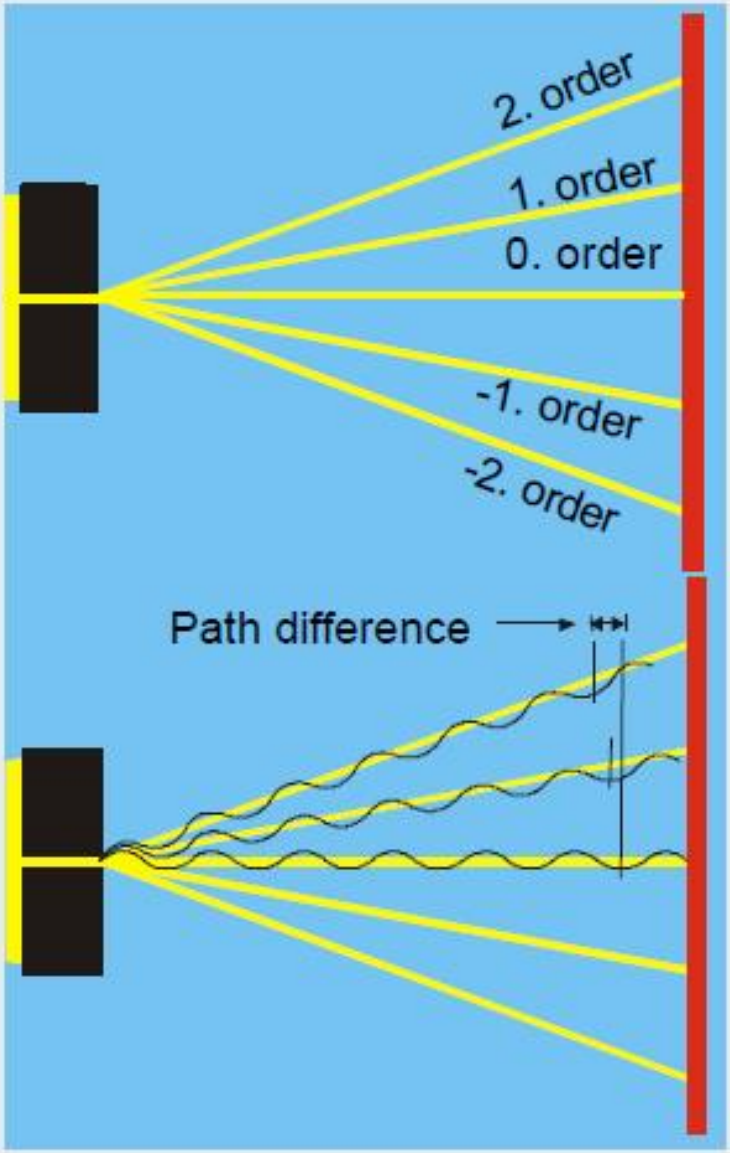
Difference in the pathway
= AB + BC
= d*sin*θ + d*sin*θ
= 2d*sin*θ

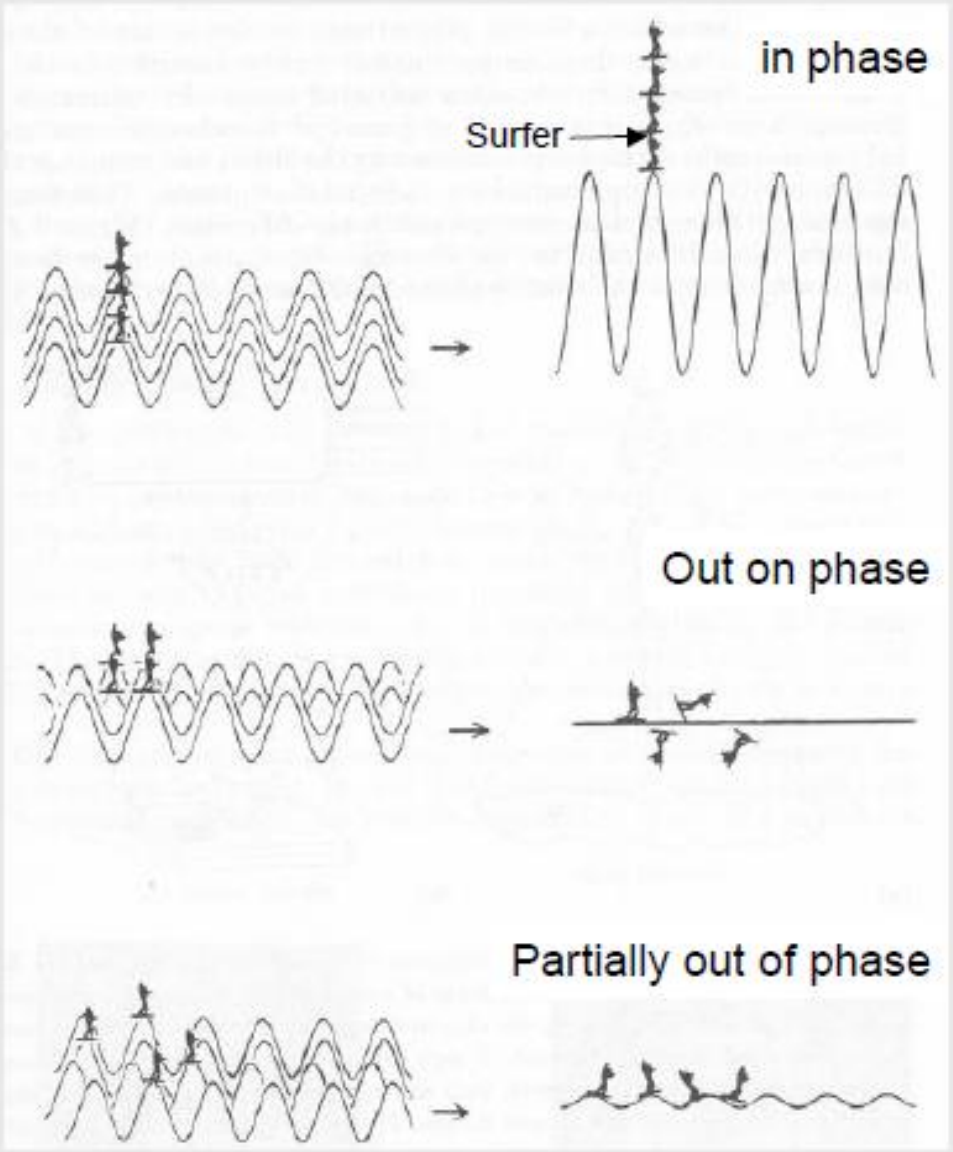
Condition for a constructive interference:

Difference in the pathway = nλ => nλ= 2d*sin*θ (n = 0,1,2,...)

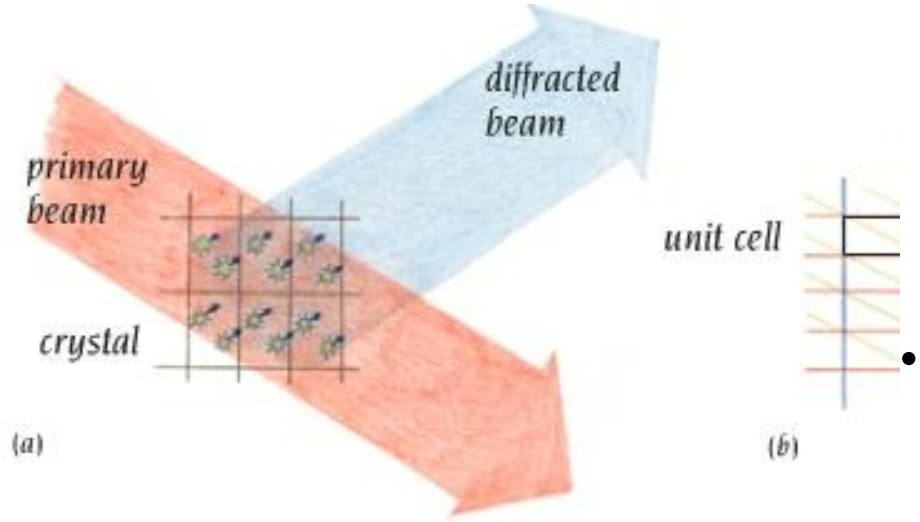
1/d=2*sin*θ/ λ = |s|

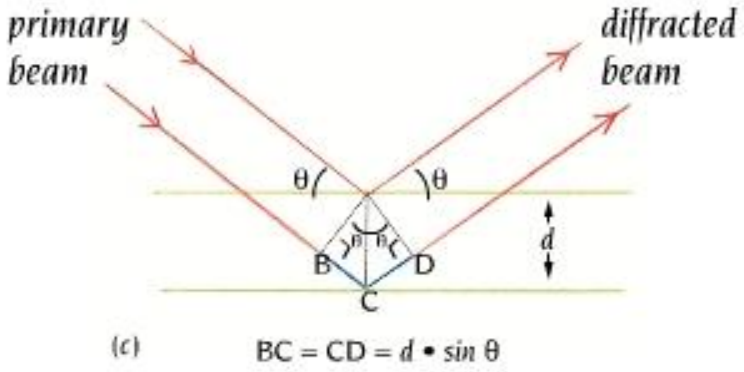
INTERFERENCE

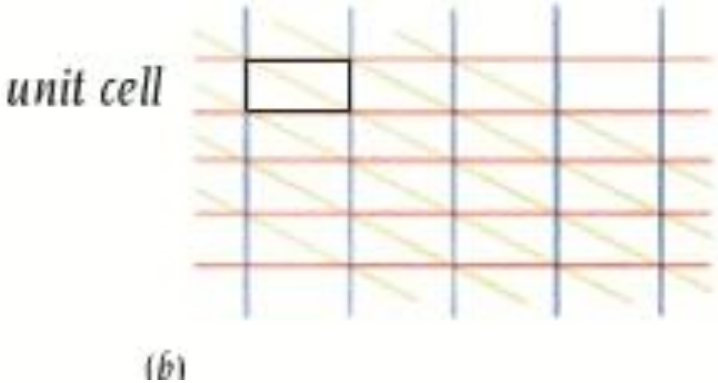




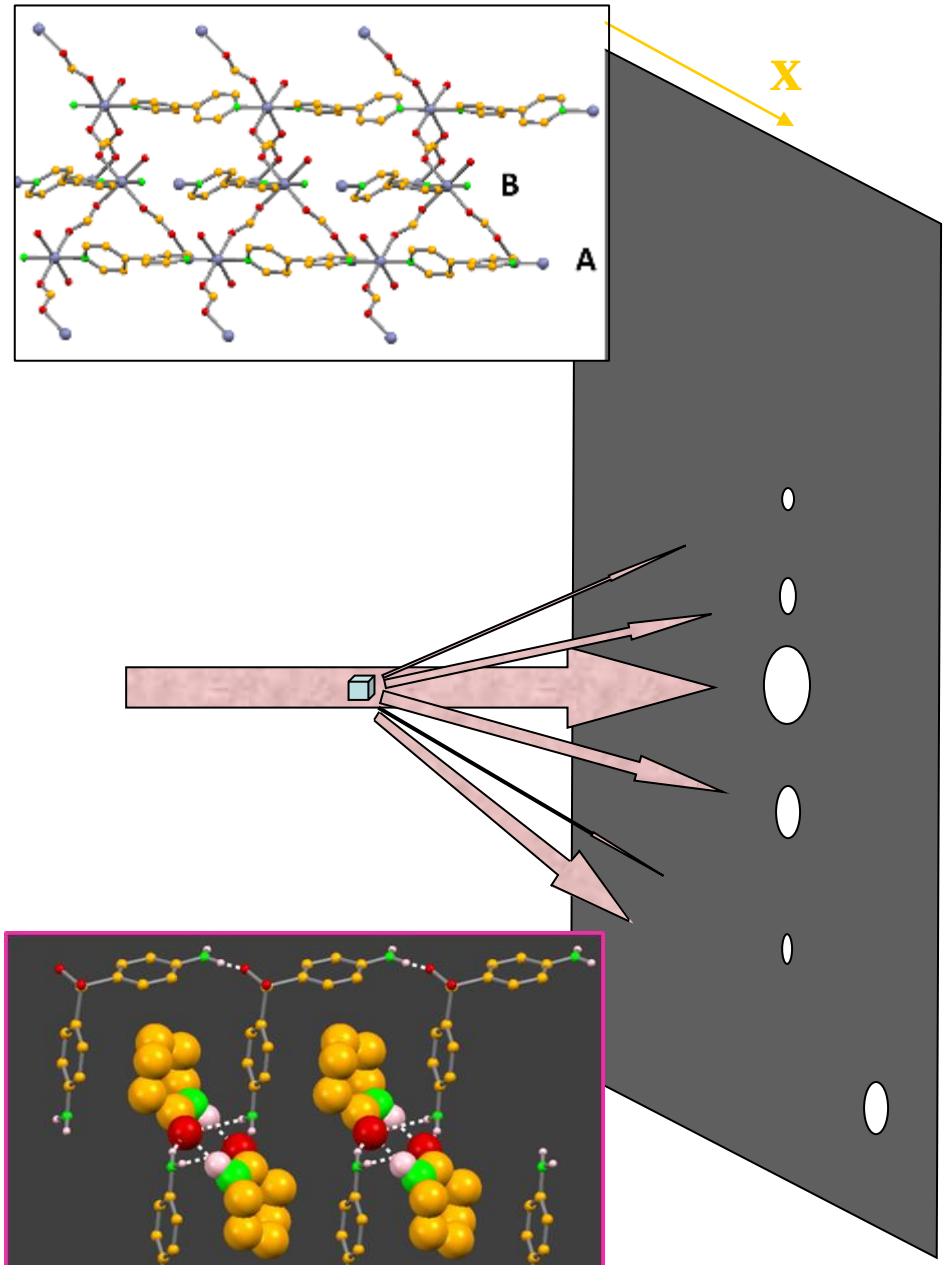
Diffraction by a Crystal







- When the X-ray beam hits a crystal, all the atoms in the crystal disperse the radiation in all the directions. In most cases, the radiation is cancelled, but in a certain direction it is added and forms a diffracted beam.
- Different planes disperse the radiation in such a way that each diffracted beam can be visualized as a reflection of the incident beam by a system of parallel planes separated by a distance *d*.



Crystals produce 10^2-10^5 reflections.

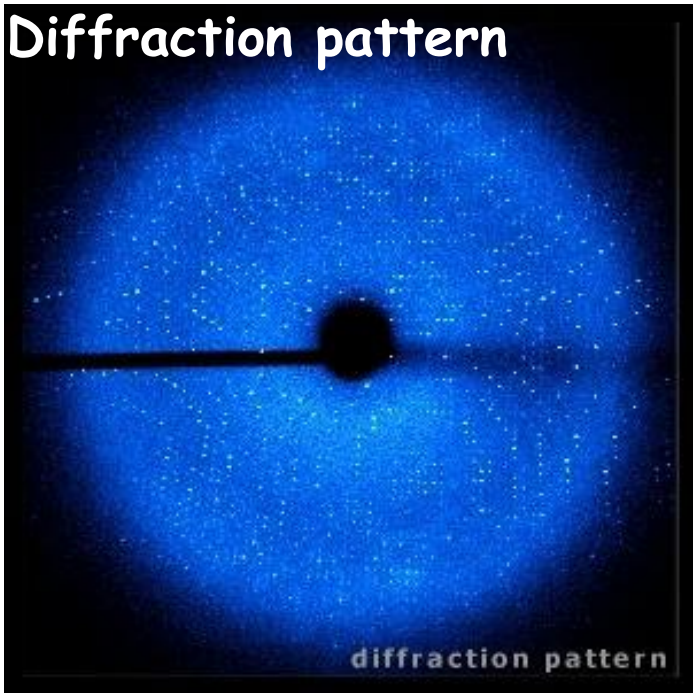
Each crystal produces a unique pattern of reflections, as a finger print.

The interpretation of the pattern leads to the crystalline and molecular structure.

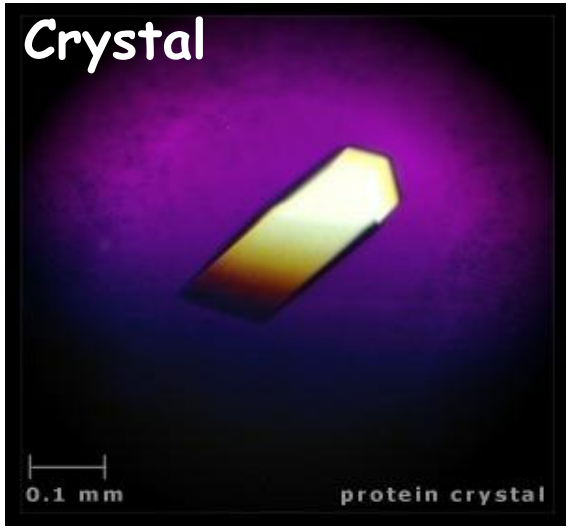
Real and Reciprocal Spaces

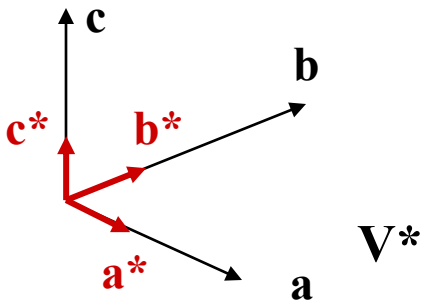
Reciprocal space

Real space



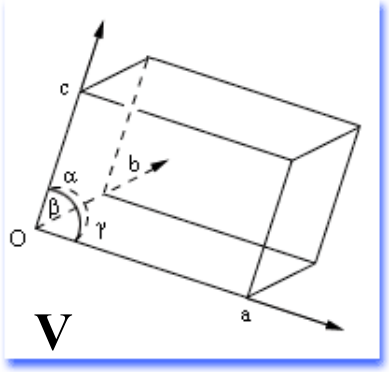
FT





$V^* = 1/V$

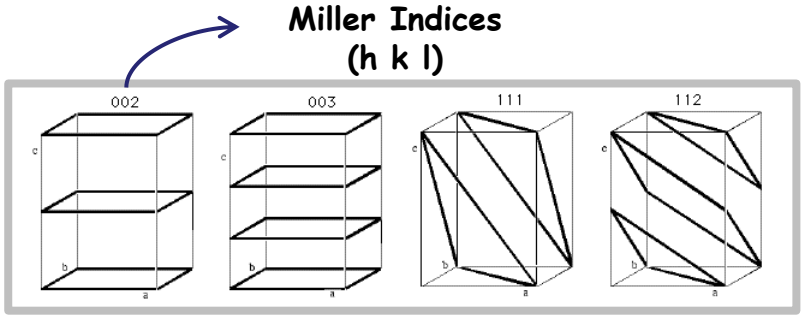
$a^* = 1/a;\ b^* = 1/b;\ c^* = 1/c$

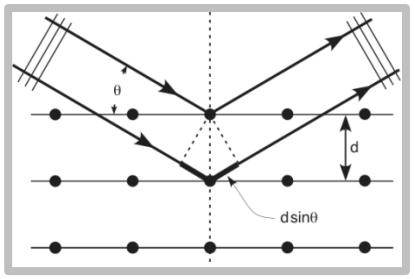


The symmetry is kept.

The dimensions are inverted.

Diffraction - The Bragg's Law



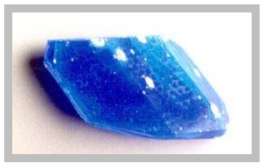


⇨ Diffraction occurs when a X-ray (with λ wavelength) focus into the set of parallel planes (with d_{hkl} distance) with θ angle and is reflected at the same angle

$$2d_{hkl}\sin\theta = n\lambda$$

Real Space and Reciprocal Space

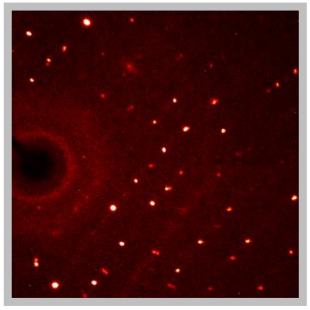
Real space
The crystal



FT of the electron density

Experimental

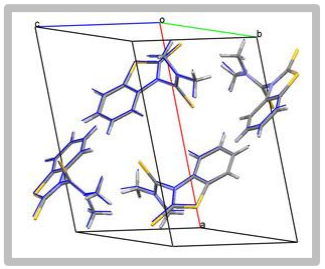
Reciprocal space
Diffraction Pattern



FT of the diffraction pattern

Calculated

Real space
Internal structure of the crystal



$$\rho(xyz) = \frac{1}{V}\sum_{hkl} F(hkl).e^{-2\pi i(hx+ky+lz)} \qquad F(hkl) = \int_{V} \rho(xyz).e^{2\pi(hx+ky+lz)}\,dV \qquad F(hkl) = |F(hkl)|.e^{i\Phi(hkl)} \qquad |F(hkl)| = \sqrt{I(hkl)}$$

Phase Problem For small molecules (<1000 non-H atoms) - Direct Methods

Basic concepts

CRYSTALS – CRYSTALLINE SYMMETRY

SYMMETRY OPERATION

UNIT CELL

CRYSTALLINE CLASSE

SPACE GROUP

ASSYMETRIC UNIT

X-RAY DIFFRACTION – BRAGG'S LAW

RECIPROCAL SPACE

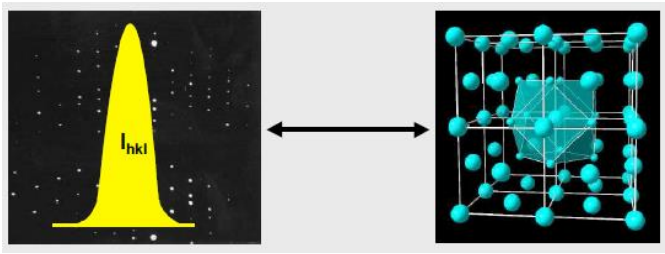
Fourier Transforms

INTENSITY of REFLECTION – Electronic density (ρ(xyz))

STRUCTURE FACTOR

What is F(hkl) and how is it obtained??

Electronic density = Fourier Transform
FT is reversible, thus: $\rho \leftrightarrow F$



Electronic density

Unit cell volume

phase

$$\rho(x,y,z,) = 1/V \sum_{h,k,l} \sum \sum | F(h,k,l) | e^{i\alpha(h,k,l)} e^{-2\pi i(hx,ky,lz)}$$

$$|F(hkl)| = \sqrt{I(hkl)}$$

Structure factor amplitude

Average intensities

The angle α is unknown... PHASE PROBLEM!!

Electronic density

Unit cell volume

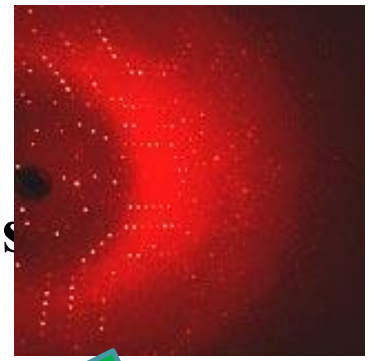
phase

$$\rho(x,y,z,) = 1/V \sum_{h,k,l} \sum \sum | F(h,k,l) | e^{i\alpha(h,k,l)} e^{-2\pi i(hx,ky,lz)}$$

$$|F(hkl)| = \sqrt{I(hkl)}$$

Structure factor amplitude

Average intensities



Those we have

So, an approximate model for the structure, the position parameters (x,y,z) are needed to determined $|F_{calc}|$ e α_{calc}

It is assumed that each reflection can be described by a Fourier series:

$$F(hkl) = \sum f(j) \exp 2\pi i (hxj+kyj+lzj)$$

in which f(j) is the contribution of atom j for F(hkl)

Methods for the phase determination

1- Heavy atom method (Patterson):

Considers that the diffraction is mostly due to the heavy atoms (mostly used in coordination compounds)

2 – Direct Methods

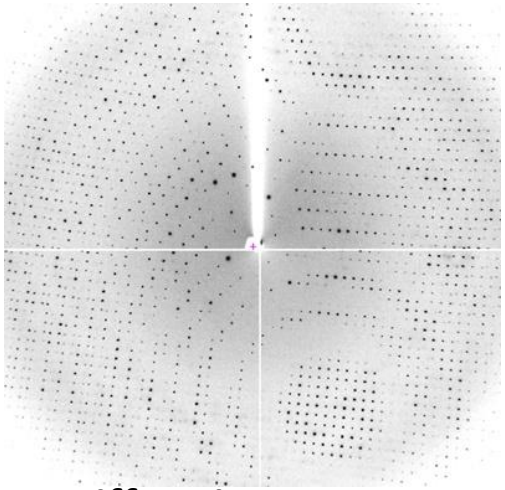
Probability methods, purely based on mathematical relations (organic molecules)

Diffraction and Fourier synthesis

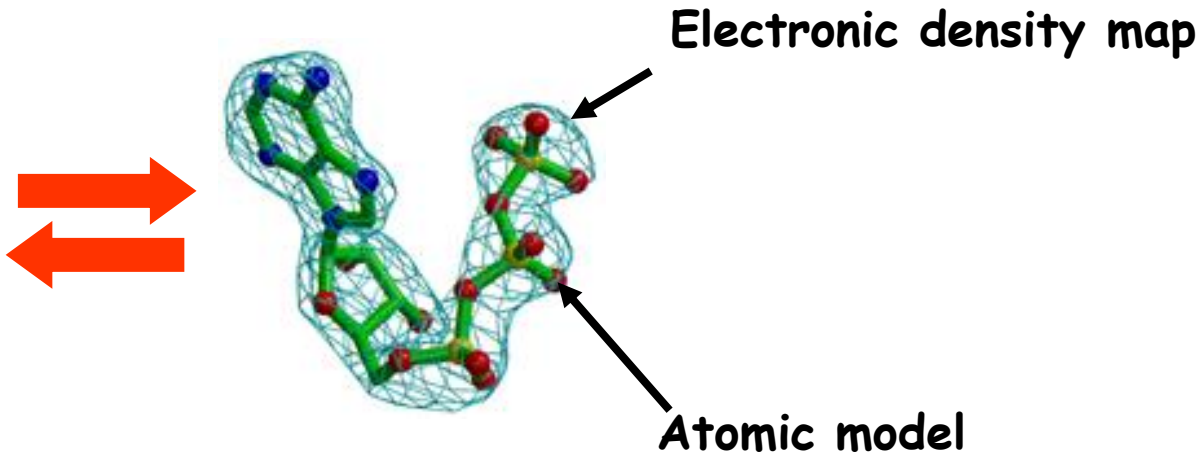
For a crystal:

$F(s) = T\,[r(r)]$ diffraction pattern = TF of electronic density

$r(r) = T^{-1}[F(s)]$ electronic density = TF of diffraction pattern



Diffraction pattern



We can always go back and forth with the TF:

- from the electronic density calculate the diffraction pattern
- from the diffraction pattern calculated the electronic density

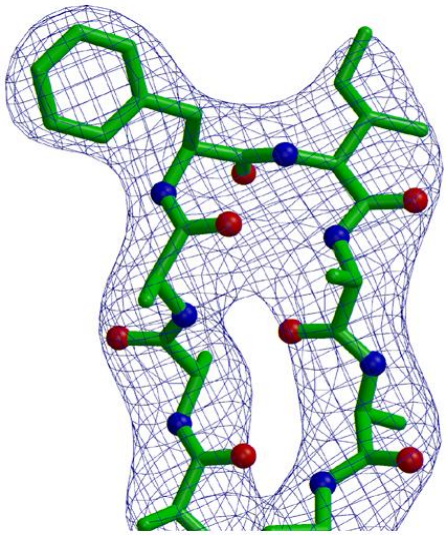
Resolution: why is it important?

"Resolution" is related with the level of detailed that can be obtained: a high resolution map gives more detailed image of the atomic structure

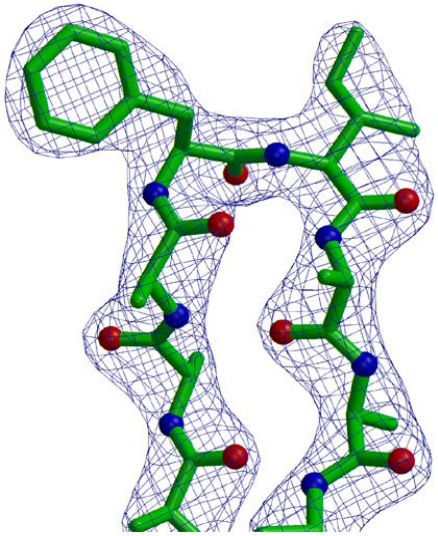
Resolution: $\sin\theta / \lambda$

Low resolution
low θ, high d

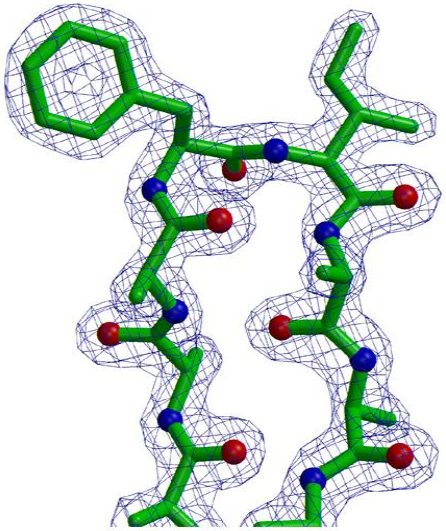
High resolution
high θ, low d



Map at 4 Å
Diffuse



Map at 2.9 Å



Map at 2 Å
Almost contains the atomic detail

Refinement & Errors

- **Refinement removes the initial errors in the model by optimizing the model with experimental measures**

- **The difference between the model and the experimental parameters is expressed by the R factor:**

$$R = \frac{\sum_{hkl} ||F_{obs}| - k|F_{calc}||}{\Sigma |F_{obs}|}$$

A good quality structure determination should have R-factor ~ 5 (10)% and small standard deviations

- **Error sources:**
  - **Error in the intensity measures**
  - **Slight variations in conformation of the molecules**

Steps of a structure determination

1. Obtain crystals
2. Selecting a crystal using a microscope
3. Collect diffraction data
4. Data collection, data reduction and absorption correction
5. Solve structure
6. Refinement - accurate determination of atomic coordinates and temperature factors
7. Validate and check structure
10. Structural analysis - Distances, angles, graphics and confidence factors

1. **Obtain crystals**

2. **Selecting a crystal using a microscope**

- ✓ Transfer the crystals to inert oil
- ✓ Select one crystal under a microscope
- ✓ Mount in the X-ray apparatus

Crystallization techniques
Small molecules

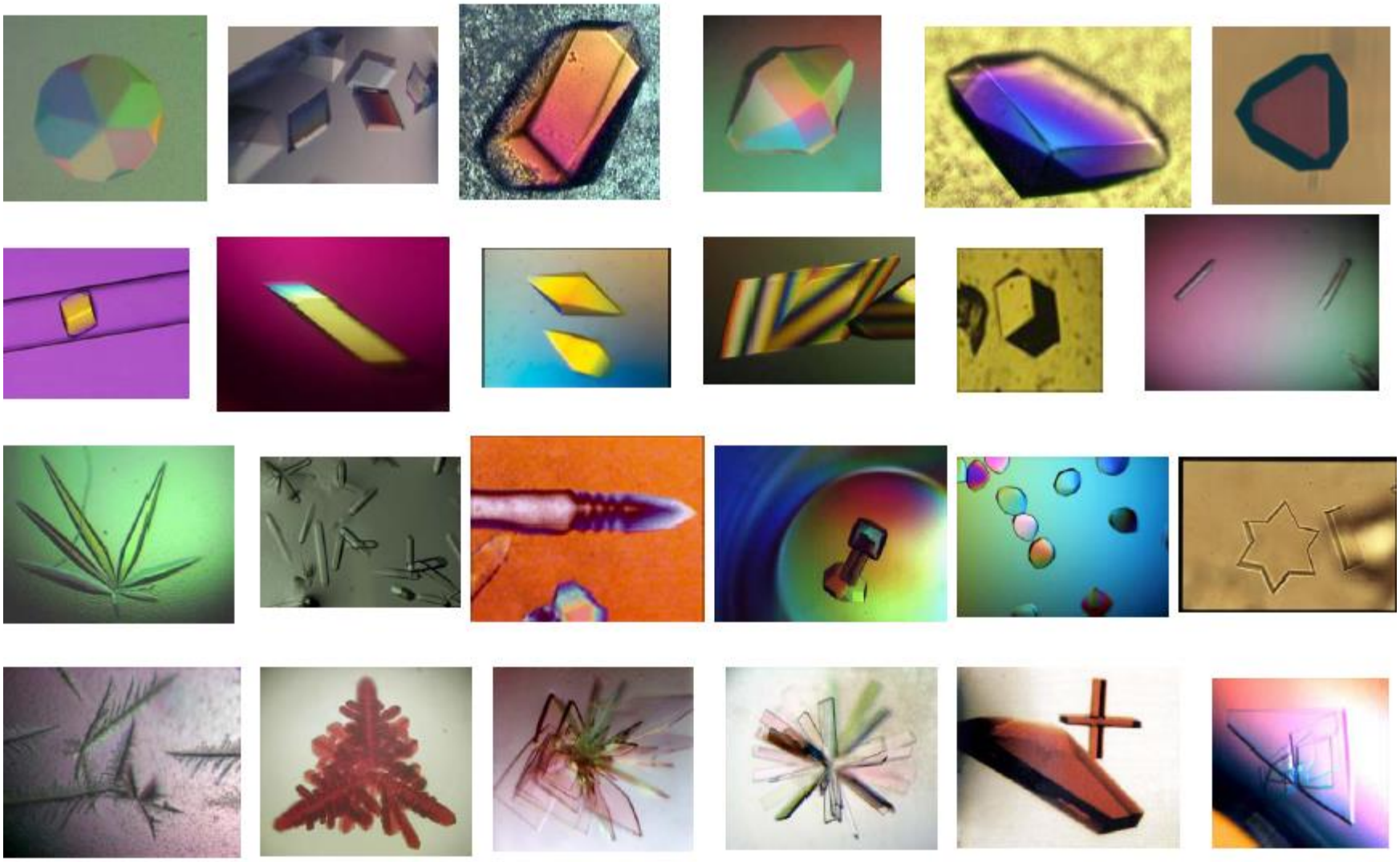
- Slow evaporation from the solvente
- Slow vapor diffusion
- Mixture of miscible and non-miscible solvents (several techniques: direct, gel permeation, evaporation…)
- Slow diffusion of solventes (porous plates, gel..)
- Slow precipitation
- Use of low temperature

Getting good crystals is o major importance!

– Well organized molecules: Stronger diffraction

Better results!

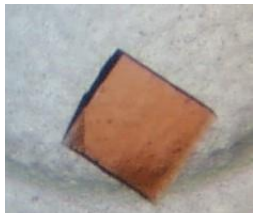
CRYSTALS

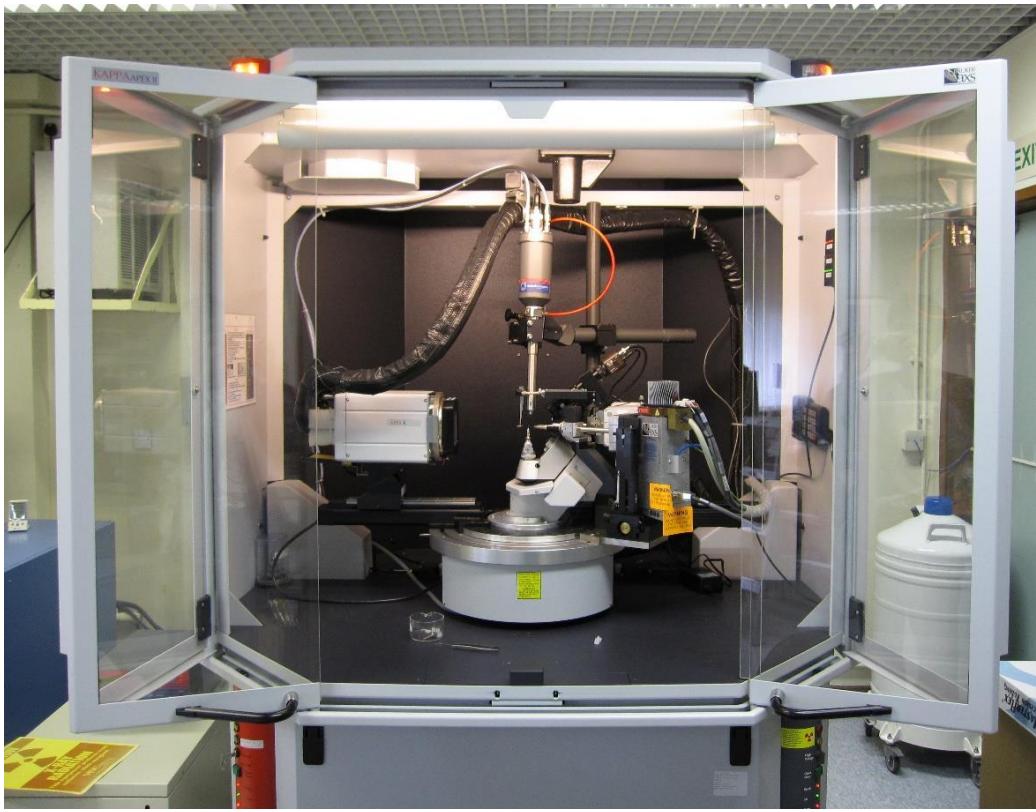


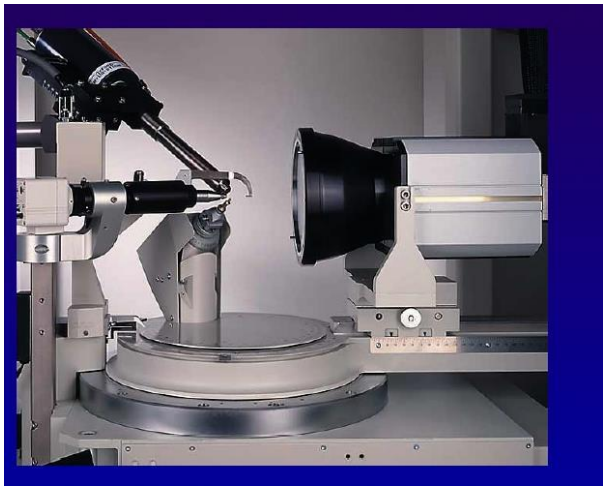
The second step for determining the molecular structure by crystallography is to get the **diffraction data**.

1.Select and mount the crystal on goniometer head.

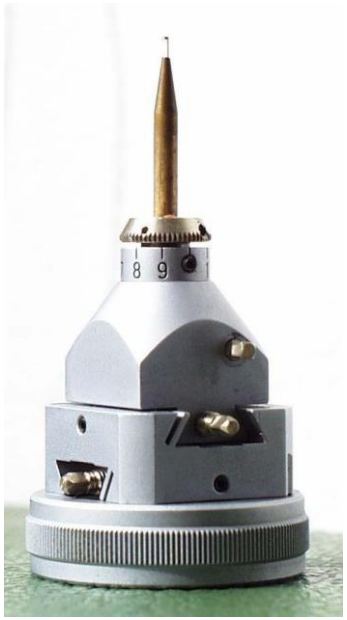
2.Set the goniometer head in the goniometer of the diffractometer

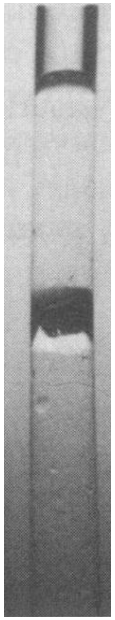


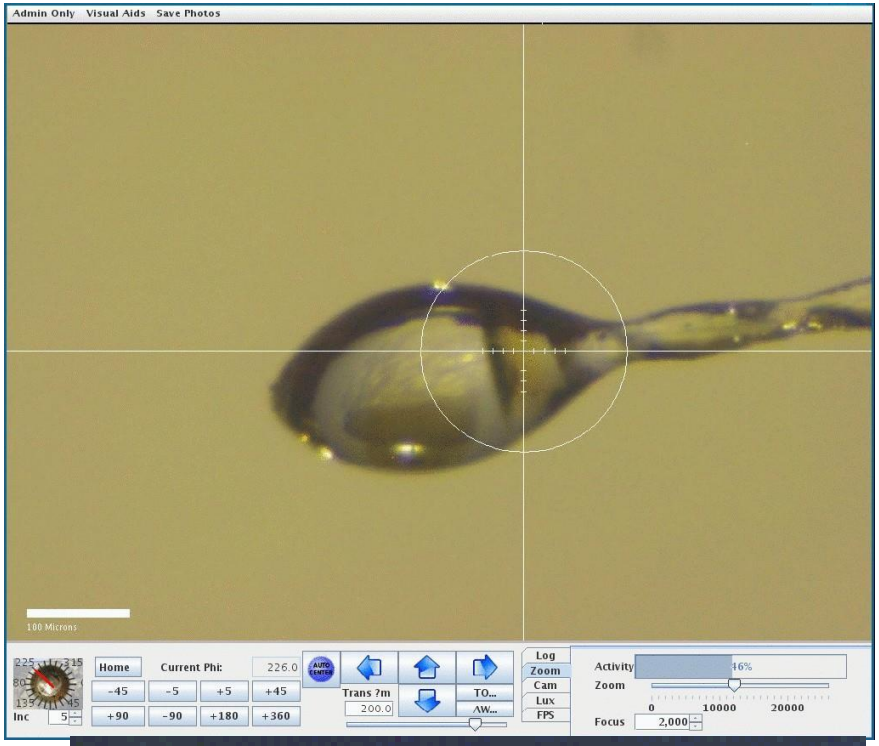


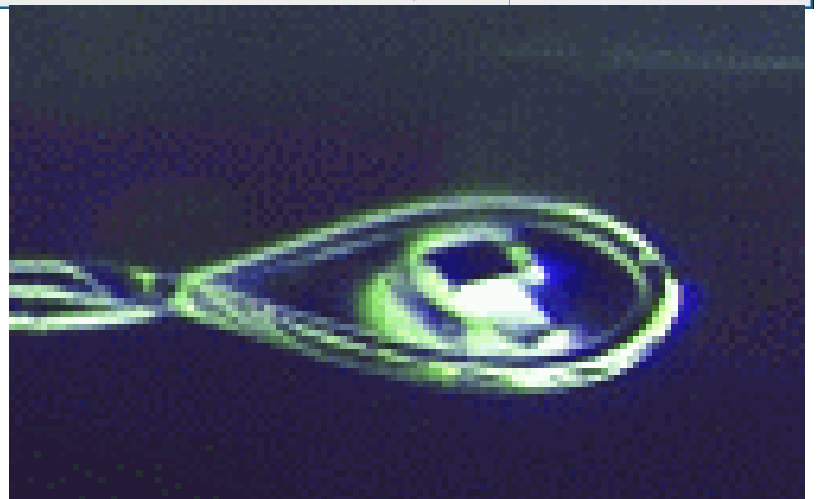


Crystal Mount

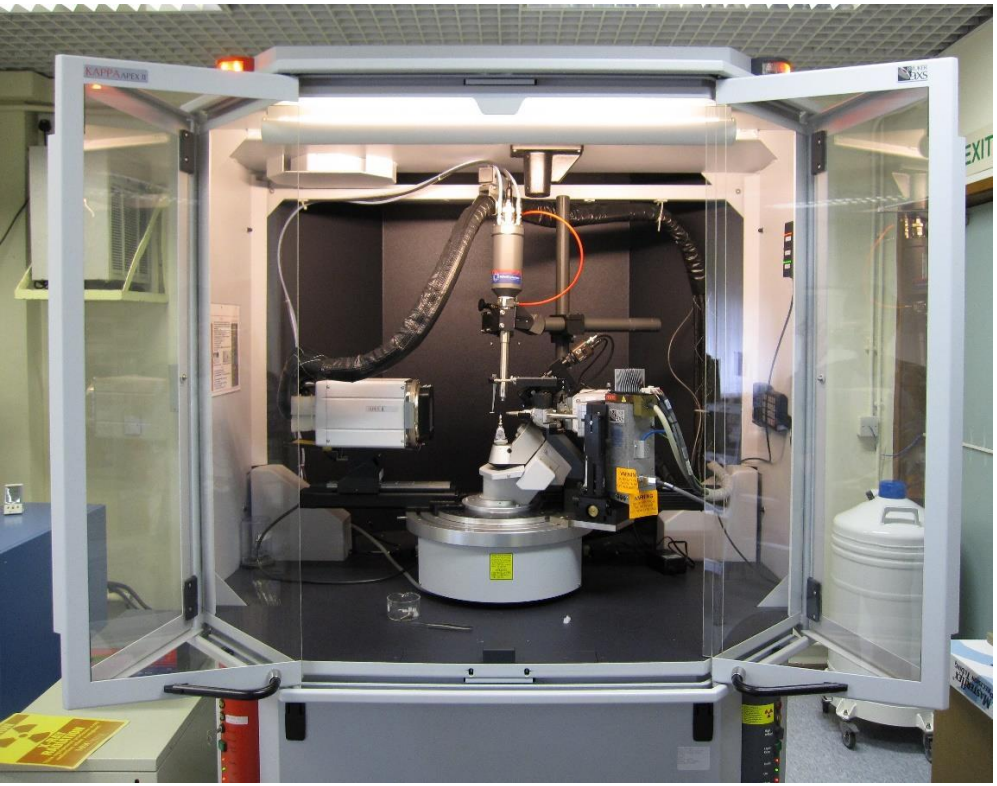


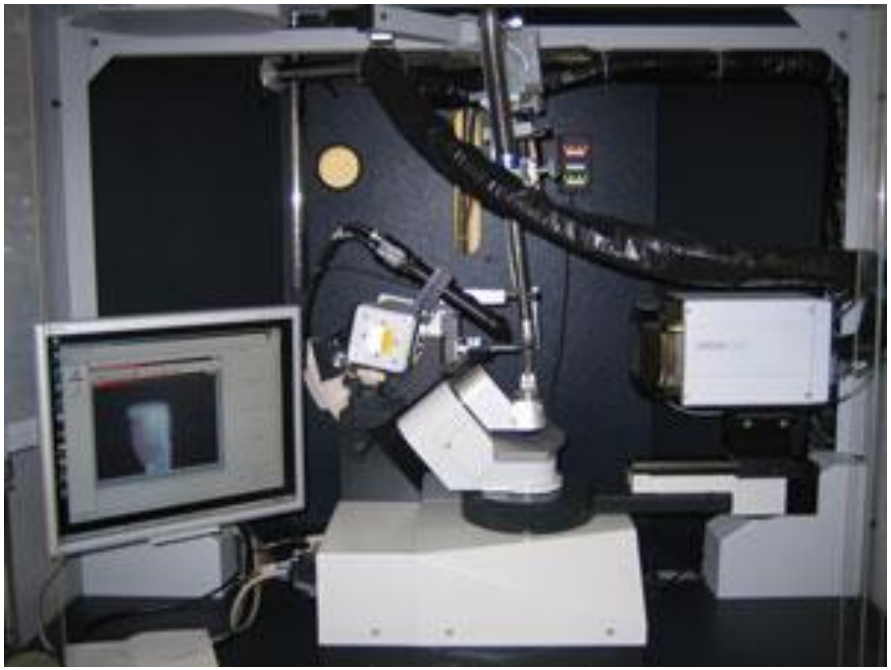






Instruments for measuring intensity: diffractometers with area detector





The complete diffraction pattern is measured and stored as a photographic film

Advantages:

- Fast measurement (simultaneous measurement of multiple reflections)
- smaller crystals (highest sensitivity)
- Weak crystals measurement (twinned crystals)
- Super structures can be easily detected

Collect diffraction data

- ✓ Collect:
  1) An image: Screen the sample quality
  2) A preliminary set of frames: Determine the unit cell
- ✓ Index the reflections, refine and convert to crystal system
- ✓ Perform the intensity data collection

Reflections:

Adequate intensity

Good shape(sharp and not split)

Incremental scan method:

Crystal moves through small angles (0.1-0.3°) with an image recorded at each step

Data collection, data reduction and absorption correction

Diffractometer software package

- ✓ **Integrate the images into a single file (list of intensities)**
- ✓ **Merge (identify same peaks in two or more images)**
- ✓ **Scale the relative images**

5. Solve structure

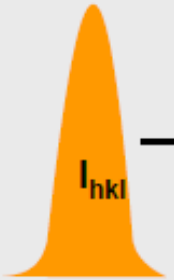
Atom assignments

✓ **Transfer final data to structure determination software package – WINGX and SHELXL program suites**
✓ **Perform the Direct Methods calculations: programs SIR92, SIR97 or SIR2004**

Assignment process:

Heavier elements are associated to higher intensities
Distances and angles between intensity centres

Structure solution: Introduction



$$F_{hkl} = \sum_{j=1}^{N} f_j \cdot \exp\left(-B \cdot \frac{\sin^2\theta}{\lambda^2}\right) \cdot \exp\left[2\pi i \left(hx_j + ky_j + lz_j\right)\right]$$

What is needed for a structure determination?

- The intensity of each reflection (from intensity measurement)

- The phase of each reflection (Get lost in the intensity measurement (called "Phase problem" ?)

- The phase of each reflection is determined by structure solution

Phase determination

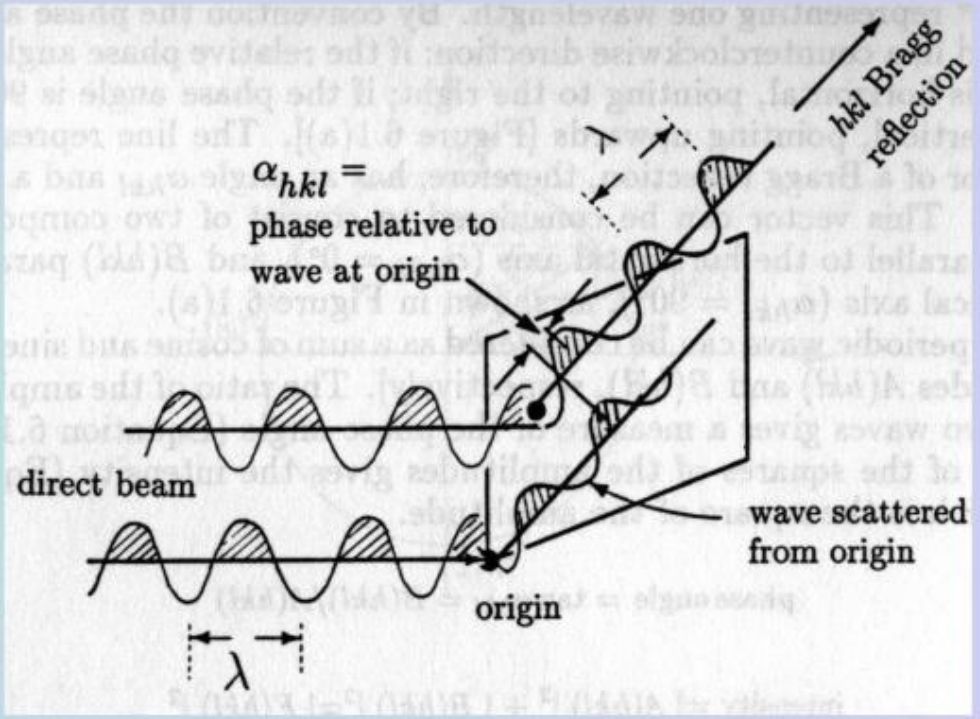
This is the famous "phase problem" of crystallography

Each reflection (diffraction point) is described mathematically by a vector designated by a design factor (F) which may be represented by:

$$\mathbf{F} = |F|\, e^{i\alpha}$$

$|F|$: amplitude

$e^{i\alpha}$: phase



The reflection intensity is proportional to the square of the amplitude factor of the structure: $I = |F|^2$

Thus, although the scale of the structure factor can be directly calculated intensity of reflection, the phase can not.

Phase determination

The next step for the determination of molecular structure is to solve the crystallography **Phase Problem**

- To reconstruct the image you need phases (even if approximate). Therefore is necessary to build a model; we use this model to calculate the reciprocal lattice and compare with the true diffraction data.

There are several methods for solving the structures:

- Direct methods (the most used) - statistical method for determining the phase angles
  - Works in general for all atoms
  - The phase angles are estimated with some probability
- Patterson methods (when there is a heavy atom)
  - Interpretation of interatomic vectors for the determination of the phase angles
  - heavy atoms must be present in the structure

Electronic density ρ

X-rays are scattered by the electrons of the atoms; therefore the result of a determination of structure is the distribution of electrons in the crystal (asymmetric unit)

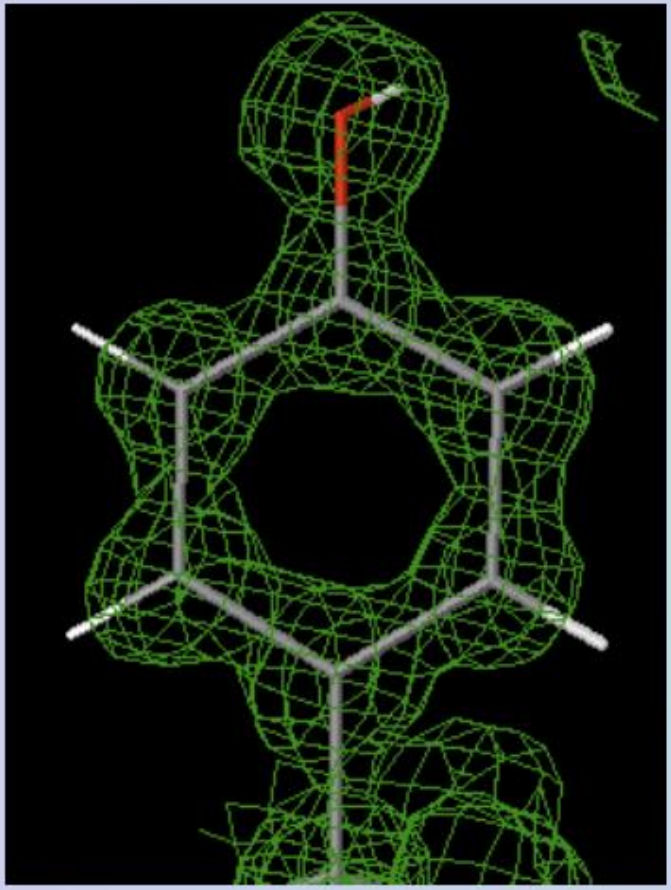
The electron density in a crystal is a periodic function.

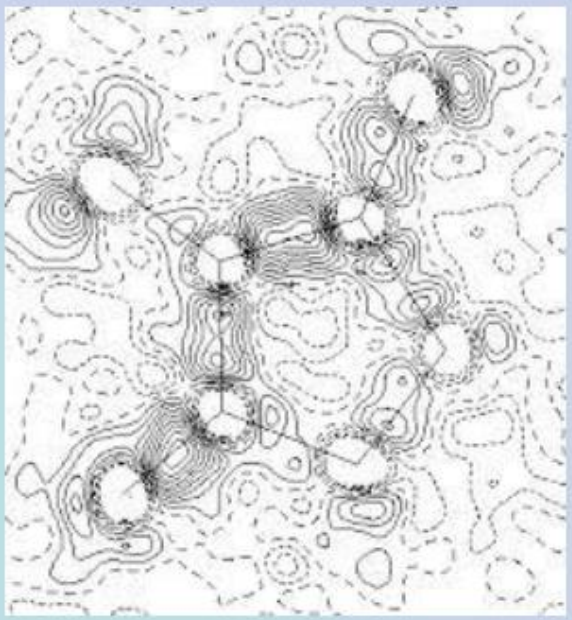
The electron density map is calculated by a Fourier synthesis:
If the intensity and the phase angle of each (structure factor) reflection is known, th
E-map means that the crystal structure can be calculated.

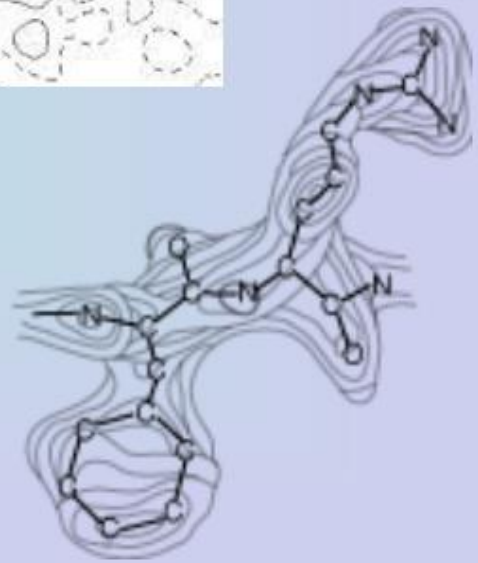
$$\rho_{xyz} = (1/V)\Sigma_{hkl}|F_{hkl}|\exp[2\pi i(hx+ky+lz)+i\alpha hkl]$$

The electron density (e/Å^3) can be calculated at each point in the asymmetric unit

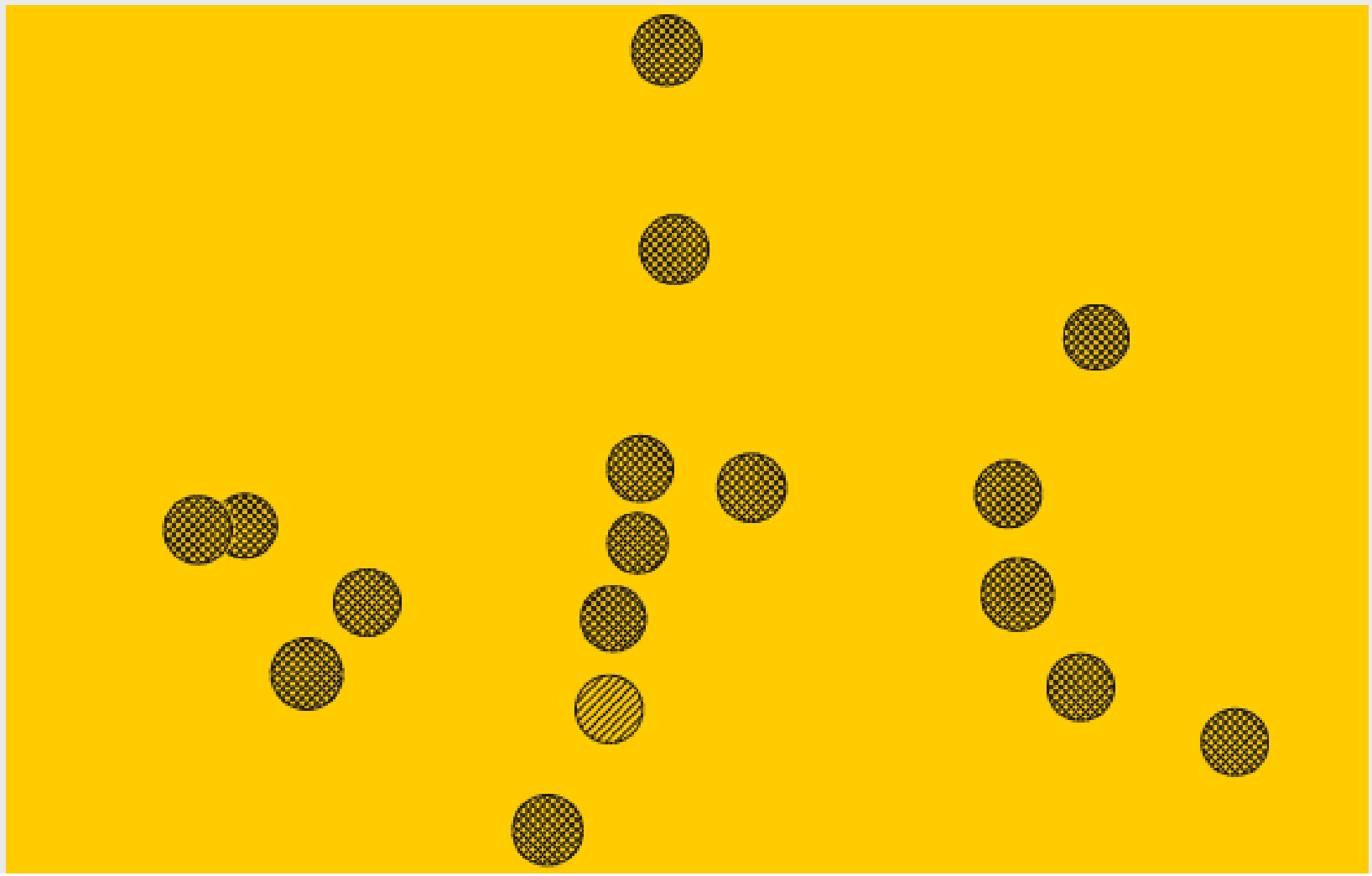
Electron density maps







Assignment of atoms to the maxima in the electron density map



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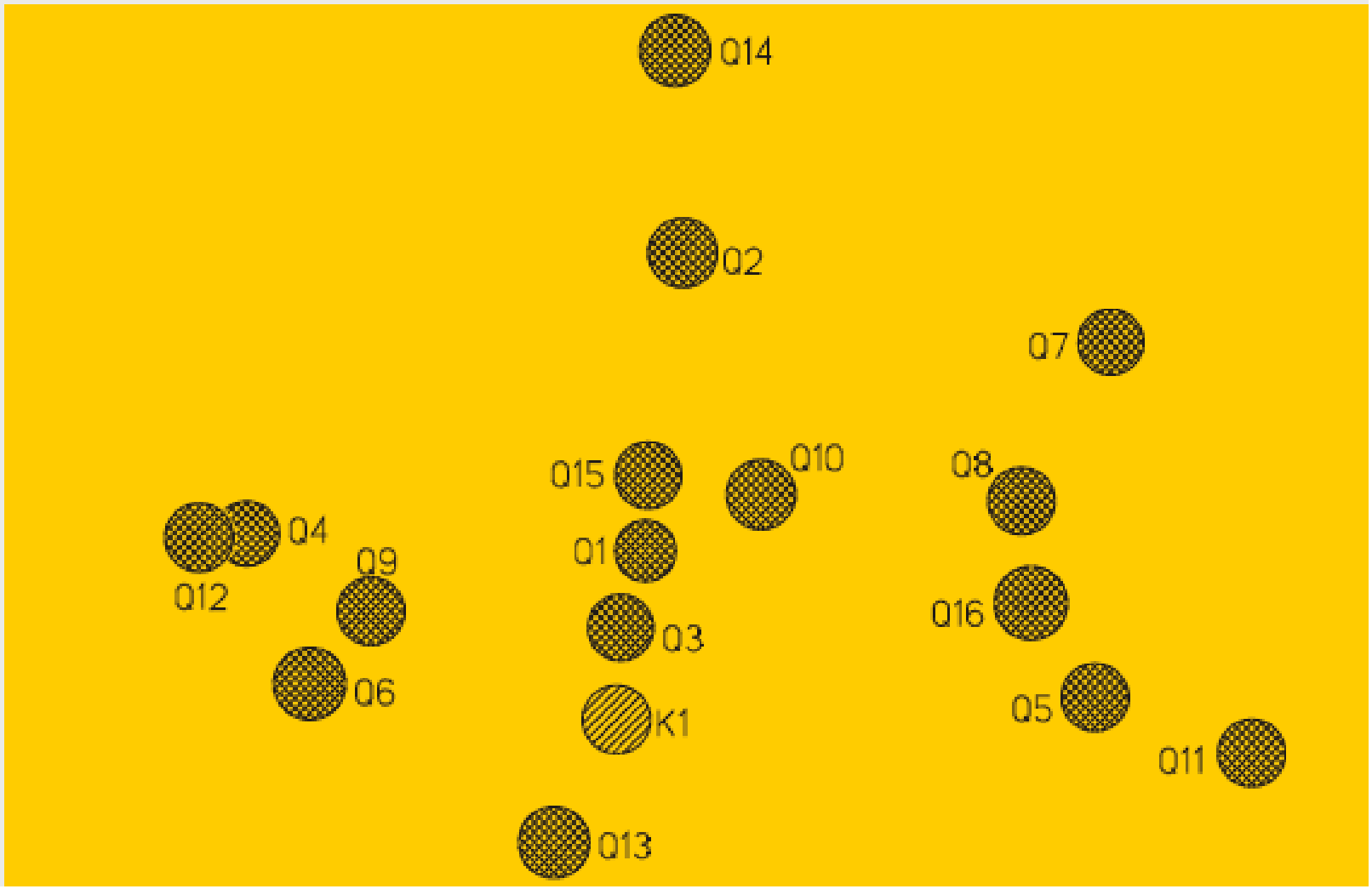

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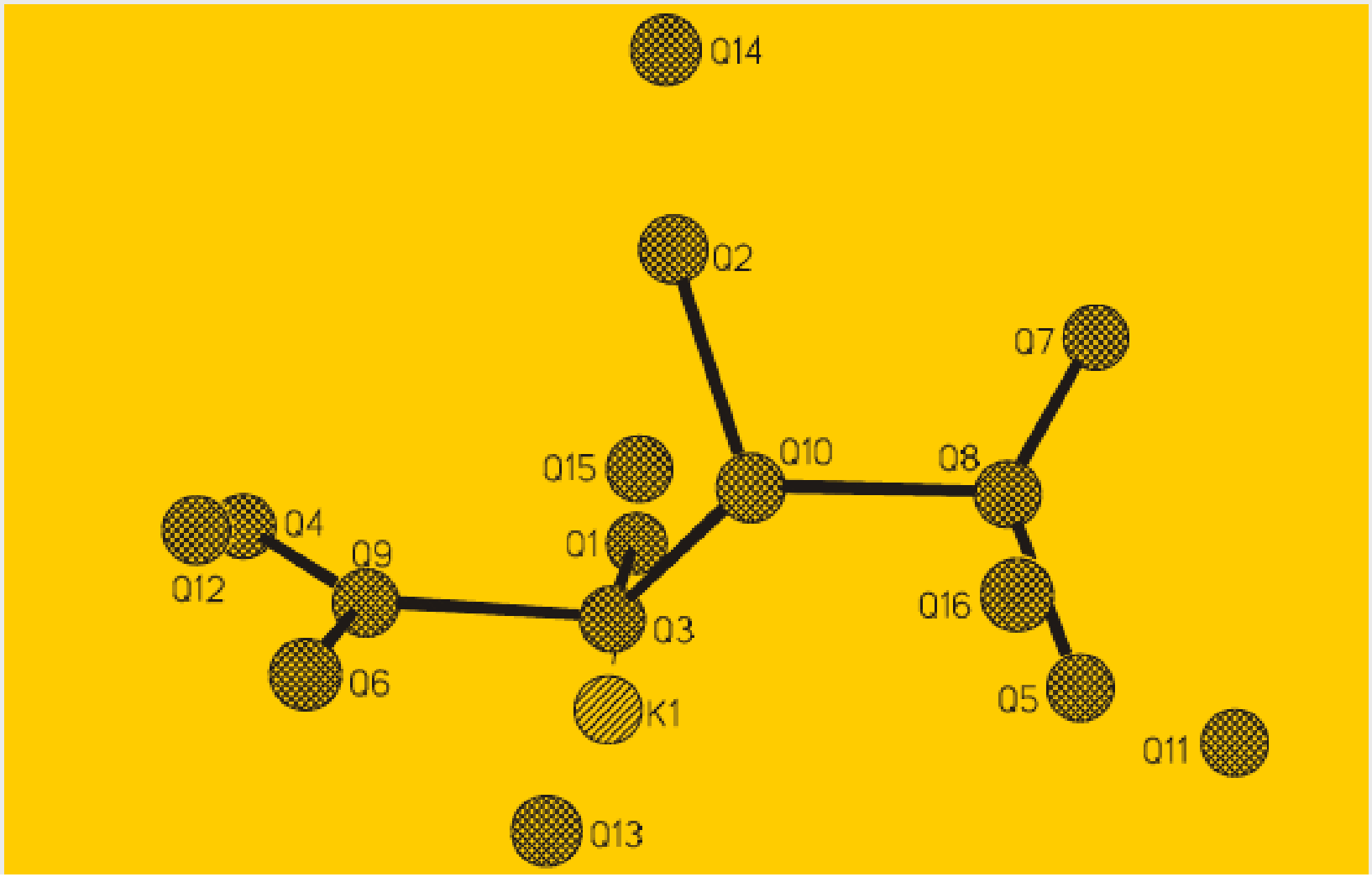
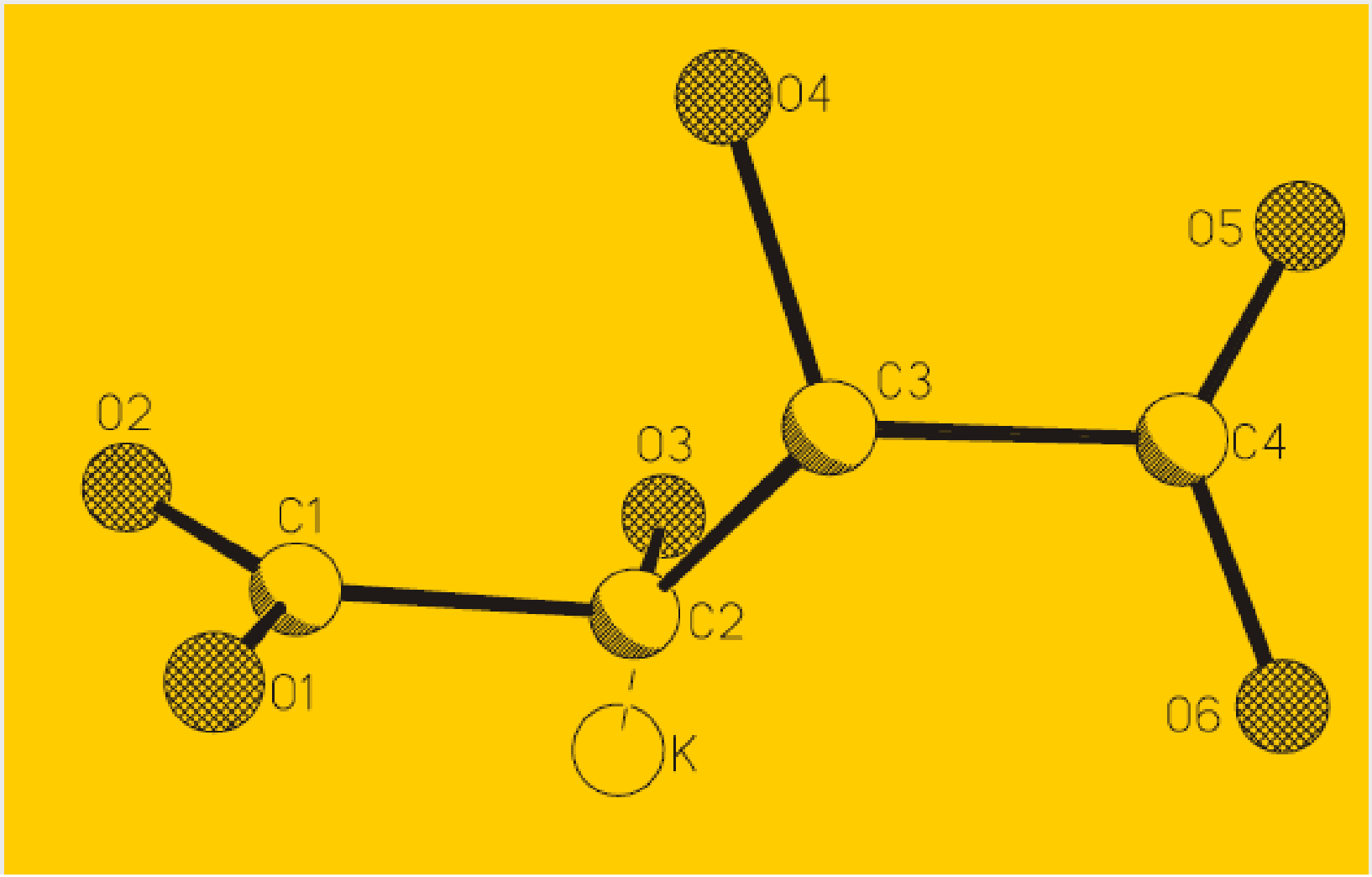


Assignment of atoms to the maxima in the electron density map



6. Refinement - accurate determination of atomic coordinates and temperature factors

Remove some errors in the model through least-squares

- ✓ Atoms are allowed to move slightly from previous positions
- ✓ Thermal factors are applied to each atom

Diffraction pattern calculated

=

Experimental diffraction pattern

Structure refinement

- Problem:
- The structure model obtained from the E-map contains some errors in the atomic
- coordinates and therefore, the position of the atoms is inaccurate
- Solution:
- Variation of the parameters in a way that the difference between the experimental
- structure factors and those calculated becomes smaller
- Method:
- Method of Least-squares
- Structure refinement
- Which parameters must be refined ?
- 1. Atomic coordinates x, y, z
- 2. Isotropic and anisotropic displacement parameters (A measure for the electron
- distribution of an atom which depends on thermal motion, disorder and the atomic
- number)

The model is therefore improved to give a better concordance between the structure factors observed and calculated.

Currently, this is done by computer, however the role of the crystallographer is to interpret the result and decide if the changes made are the right ones or if the model got worse!

R factor

- The process of refinement of the structure is followed by the agreement between observed data (data which is acquired in the diffractometer) and calculated data (data calculated from the model). =

Factor R

$$R = \frac{\sum | (|Fobs| - |Fcalc|) |}{\sum (|Fobs|}$$

- R=0% => Perfect agreement between observed and calculated intensities.
- In practice this is not achieved due to random errors in the experimental measurements.
- A good structure should have a factor R smaller than 8%.

Other statistical factors

wR_2 - R is a weighted factor that uses all the diffraction data and allows the crystallographer follow the refining process. The numerator of wR_2 equation is the function that is minimized in refining.

$$wR_2 = \{ \sum [w (Fo^2 - Fc^2)^2] / \sum [w (Fo^2)^2] \}^{1/2}$$

S - Another statistical factor that is known as the goodness of fit. Theoretically, goodness of fit is "the standard deviation of a observation with a weight 1." In practice the goodness of fit shows how reliable are the deviations of the positional and thermal parameters of atoms. This factor ranges from 0 to 1. For a refinement on F2 the goodness of fit is determined by:

$$GoF = S = \{\sum [w(Fo^2 - Fc^2)^2] / (n-p)\}^{1/2}$$

where n = is the number of measured data,
and
p = is the number of parameters.

The structure is completed when ...

1. The bonds in the model must make sense chemically. Similar bonds should have similar geometries, and all distances and bond angles, etc., should have similar values in the literature.

2. There can be no atoms with temperature factors with values too high or too low. Values should range between 00:03 and 00:15 depending on the type of atom.

2. R1 and end wR2 The structure must be refined to convergence, i.e., the ratio shift / error should be <0.05.
4. The goodness of fit, S, must have a value close to 1.0.
5. The final difference Fourier map should not be very large or very small peaks.

6. Final R_1 ad wR_2 values should be reasonably low compared to data quality.

7. Validate and check structure

Online service available by the International Union of Crystallography

- ✓ **Reports the consistency and integrity of the crystal structure**

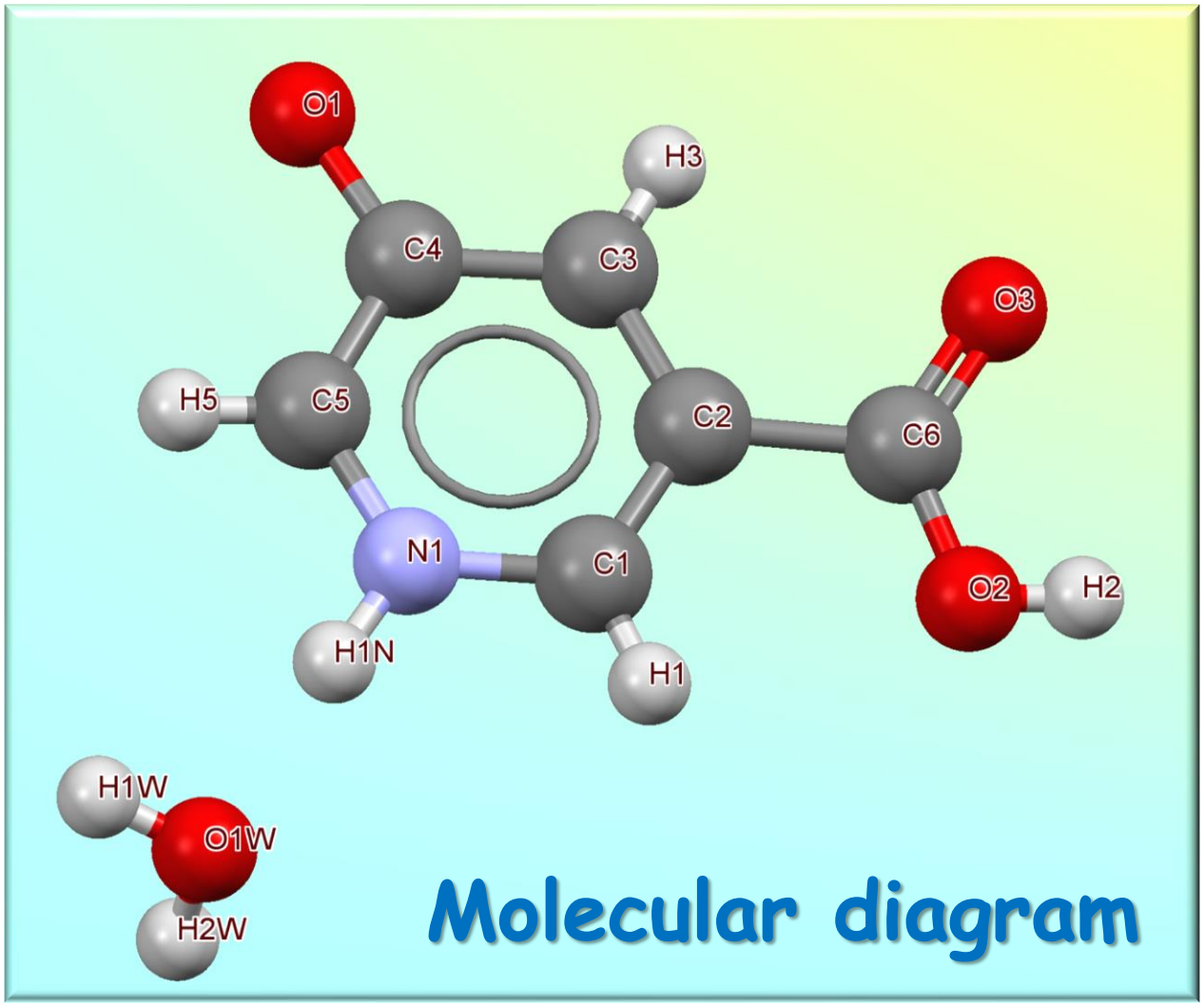
Structural analysis

What are actually the results of crystal structure determination?

- Atomic coordinates
- Temperature Factors
- Unit cell geometry
- Unit cell symmetry
- Bond lengths
- Bond angles
- Torsion angles
- Ring conformation
- Association degree
- Intermoleculares Interactions (ex: hydrogen bond)

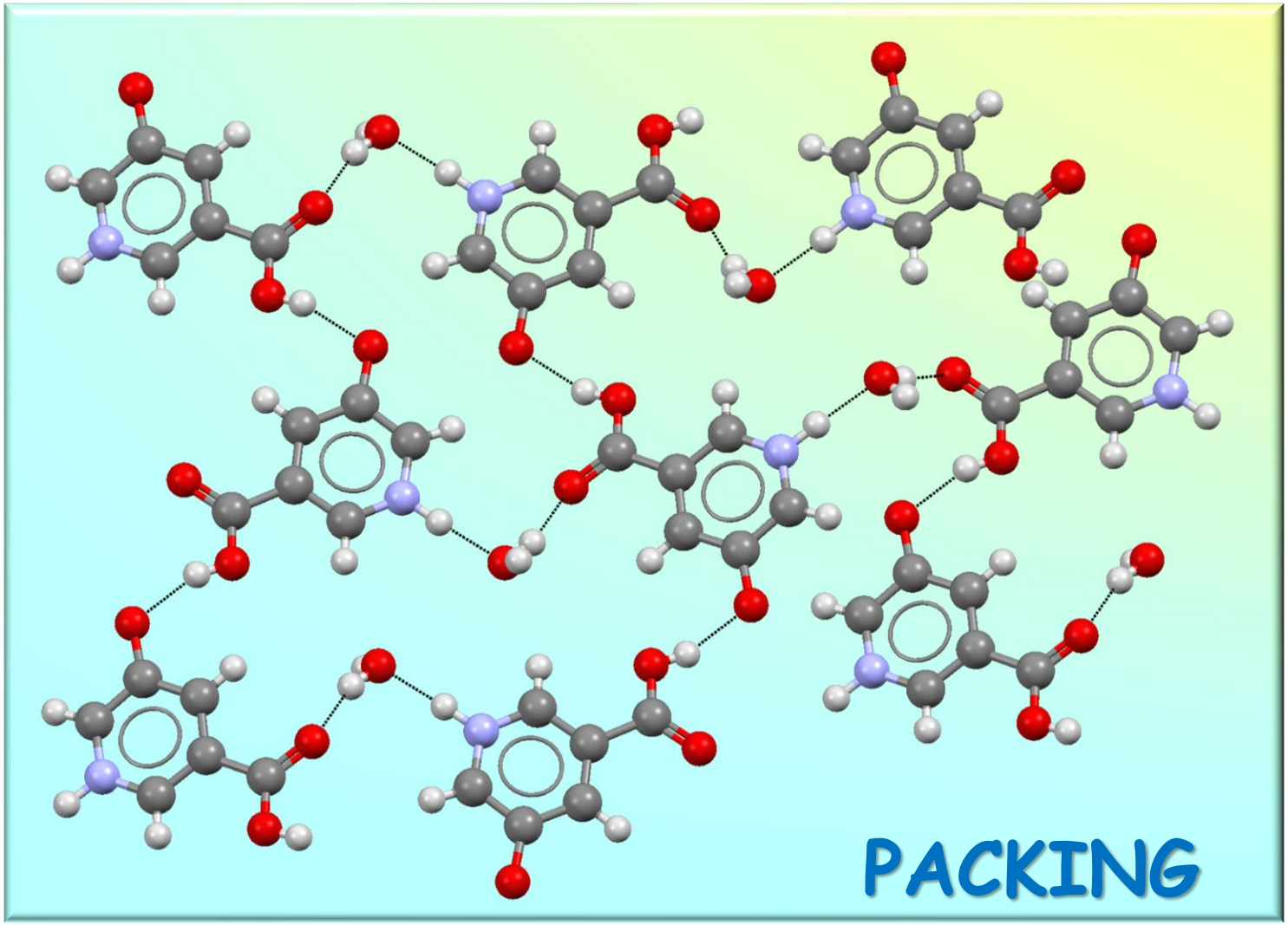
Structural analysis

What are actually the results of crystal structure determination?



Structural analysis

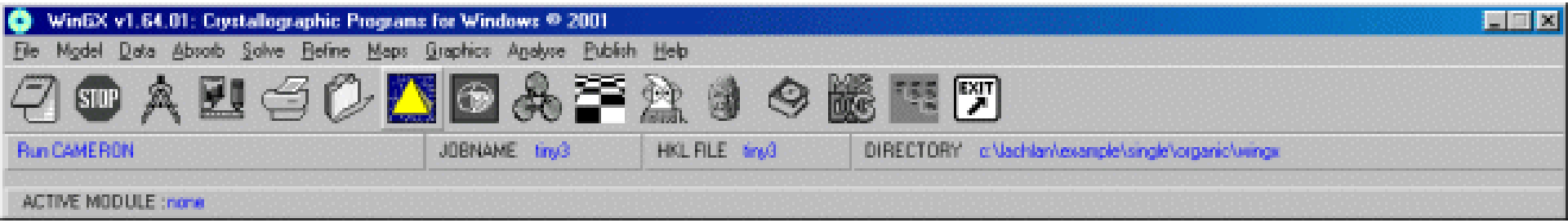
What are actually the results of crystal structure determination?



Computer programs used in structures determinations

The most used GUI is :

WinGX – An Integrated System of Windows Programs for the Solution, Refinement and Analysis of Single Crystal X-Ray Diffraction Data de Louis Farrugia, Dept. Of Chemistry, University of Glasgow.



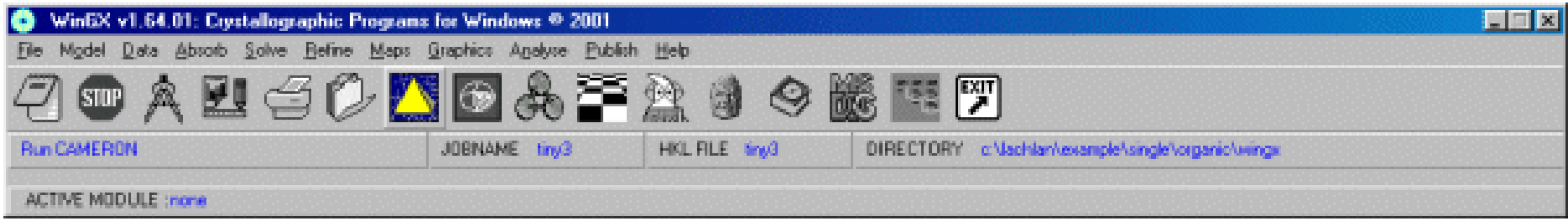
✓**WinGX** is a system of programs to solve and analyze data refine X-ray diffraction of single crystal, for small molecules.
It provides a consistent graphical user interface and easy to use for some of the best crystallography programs available to the public, and has interfaces with other popular programs such as SIR-97 / SIR-2002.

http://www.chem.gla.ac.uk/~louis/software/wingx

Computer programs used in structures determinations

A interface gráfica mais utilizada é:

WinGX – An Integrated System of Windows Programs for the Solution, Refinement and Analysis of Single Crystal X-Ray Diffraction Data de Louis Farrugia, Dept. Of Chemistry, University of Glasgow.

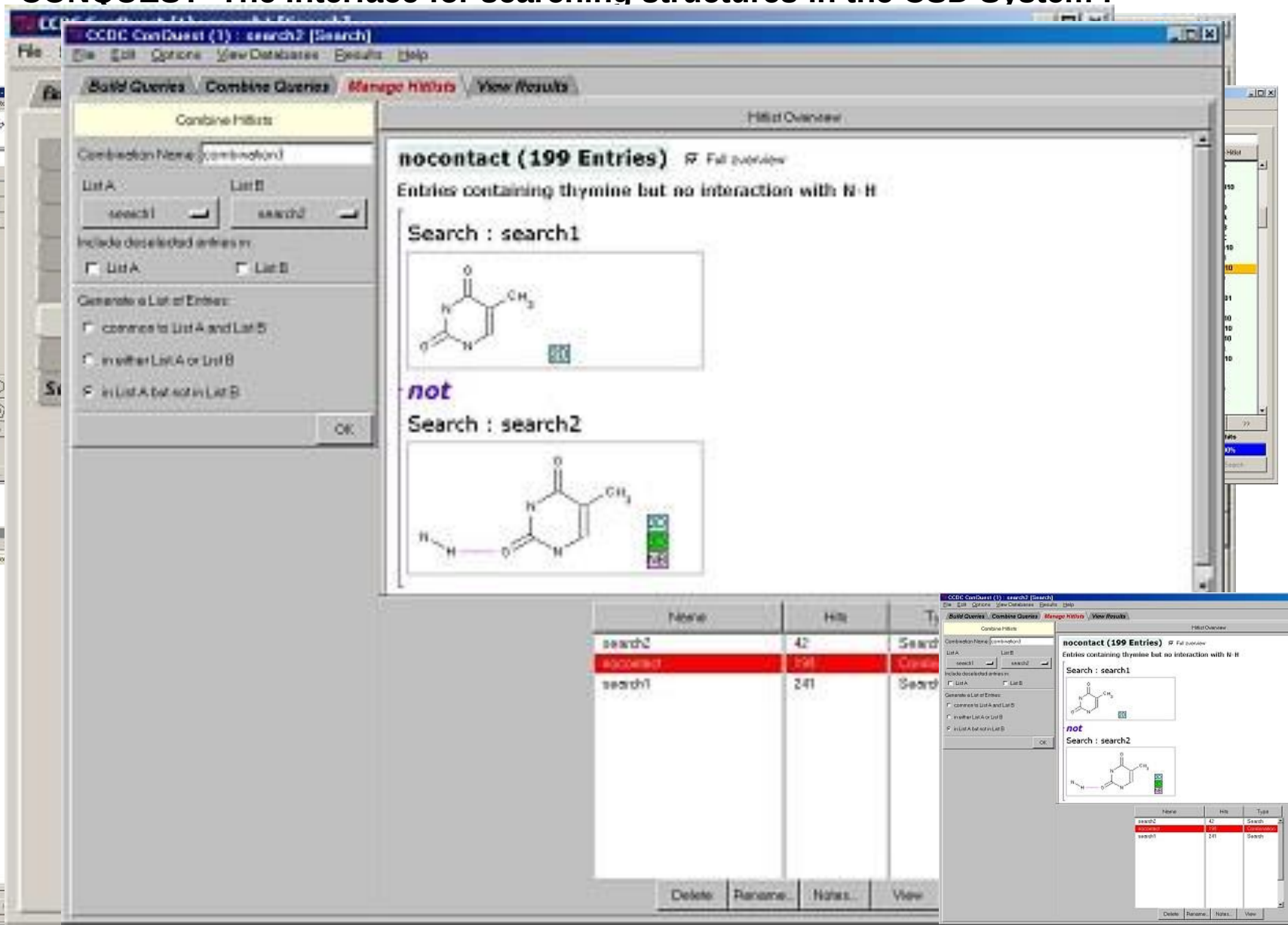


✓**It provides a consistent graphical user interface and easy to use for some of the best publicly available crystallographic programs, Such As:**

- **Data reduction - (CAD4 /Siemens P4/ *KappaCCD/ SMART*)**
- **Data Analysis - Graphics reciprocal network, peak profiles**
- **Absorption correction (analytical, semi-empirical, ref-DELF)**
- **Structure resolution - SHELXS Programs, DIRDIF, SIR**
- **Refinement structure - SHELXL-97 (CRYSTALS / Jana2000)**
- **Analysis of results - THMA, PLATON, PARST, GEOM**
- **Graphics - ORTEP, CAMERON (Schakal, RasMol, POV-Ray ...)**
- **Publication - CIF creation, validation (CIFtbx tools)**

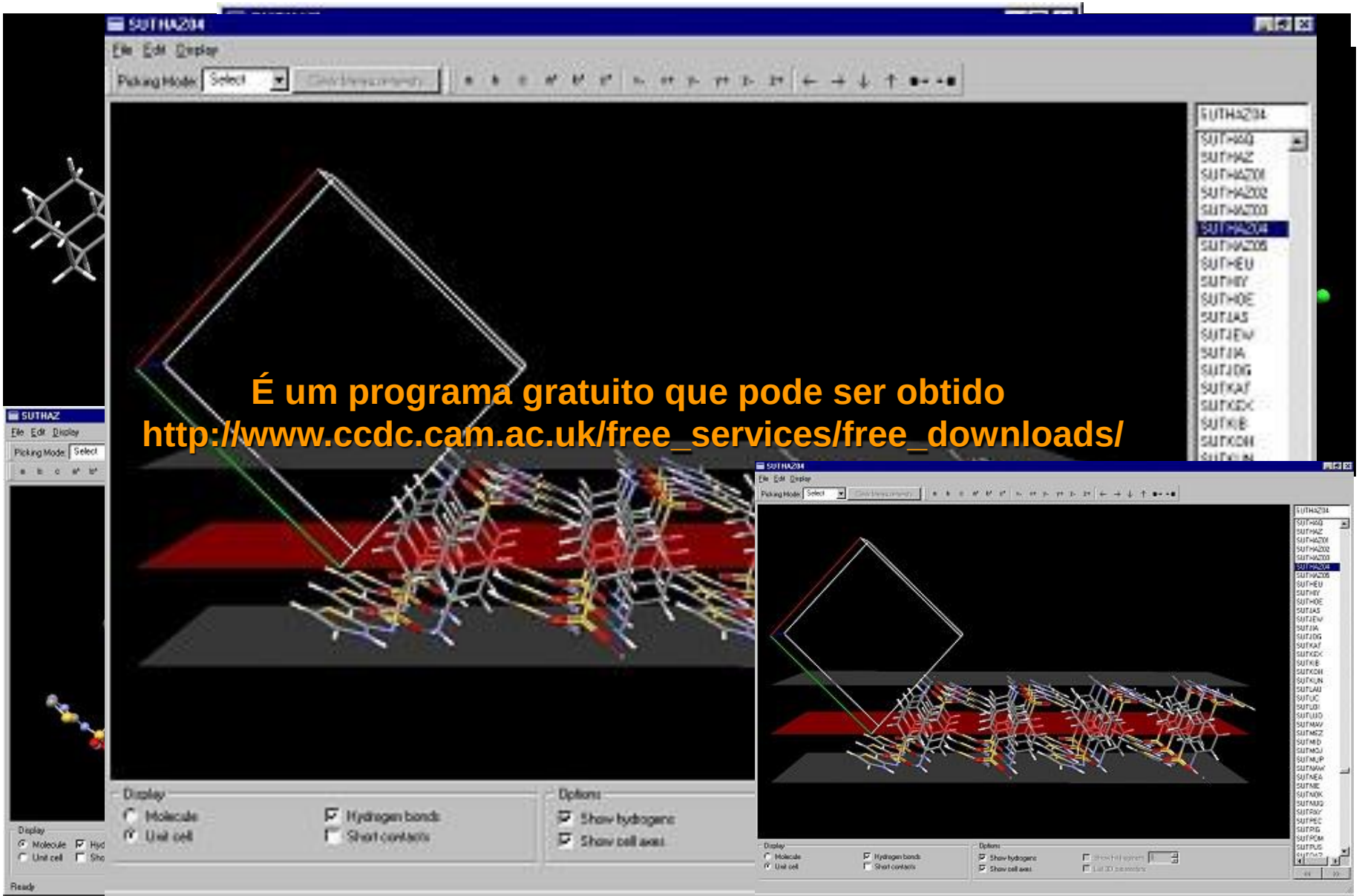
Crystallographic database - Cambridge DataBase

CONQUEST- The Interface for searching structures in the CSD System .



Crystallographic database - Cambridge DataBase

MERCURY- Crystal Structure Visualisation and Exploration Made Easy.



Information in a single crystal structure determination

- Crystal system, Bravais symmetry, space group, lattice parameters
- Electronic density and "chemistry composition"
- Symmetry of the molecules
- Constitution and absolute configuration of the compound
- Three-dimensional structure and crystal packing
- Precise and sometimes accurate lengths and bond angles
- Conformation of molecules (torsion angles)
- Intermolecular and intramolecular interactions
- Van der Waals Radius
- Volume of molecules
- Electronic Distribution
- Dynamics in crystalline solids
- Static and dynamic disorder in crystalline solids

Exercise:

The spacing of one set of crystal planes in NaCl (table salt) is d = 0.282 nm. A monochromatic beam of X-rays produces a Bragg maximum when its glancing angle with these planes is θ = 7º . Assuming that this is a first order maximum (n = 1), find the wavelength of the X-rays.

The Bragg law is

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

$$\lambda = 2d \sin \theta = 2 \times (0.282 \text{ nm}) \times \sin 7^{o} = 0.069 \text{ nm}$$

Powder X-ray diffraction

Allows :

- Do phase identification
- To detect phase transition
- Follow a reaction path
- Identify and compare molecular and crystal structures
- Study polymorphism
- Study micro and mesoporous materials

And sometimes

to determine the molecular structure

(need synchrotron source; accurate equipment)