Chemical Crystallography and Structural Chemistry

(VO 270287)

Lecture 2

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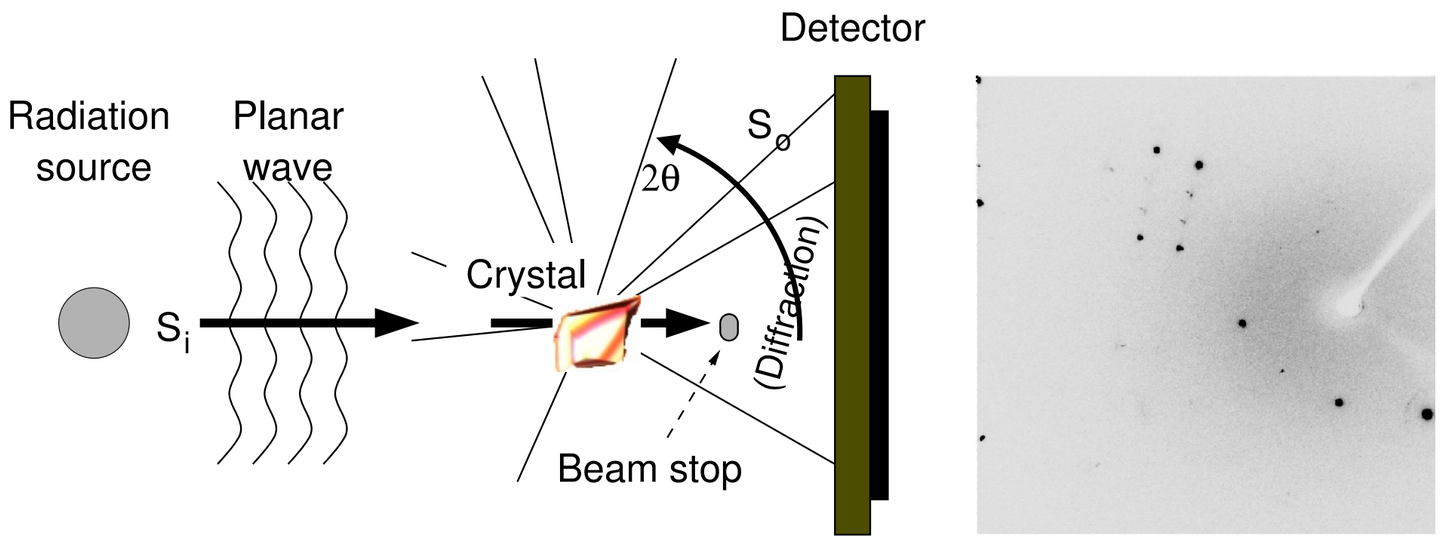
Previous Lecture

1. (Teaching) Resources for crystallography
2. (public) data bases for crystallography
3. what are crystals
4. X-rays and X-ray diffractometers
5. (Conducting a diffraction experiment)

Today's Lecture

1. Conducting a diffraction experiment - cont'd
2. Objectives of a Crystal Structure
3. Diffraction theory
4. Unit Cell and Reflections

Data Collection experiment

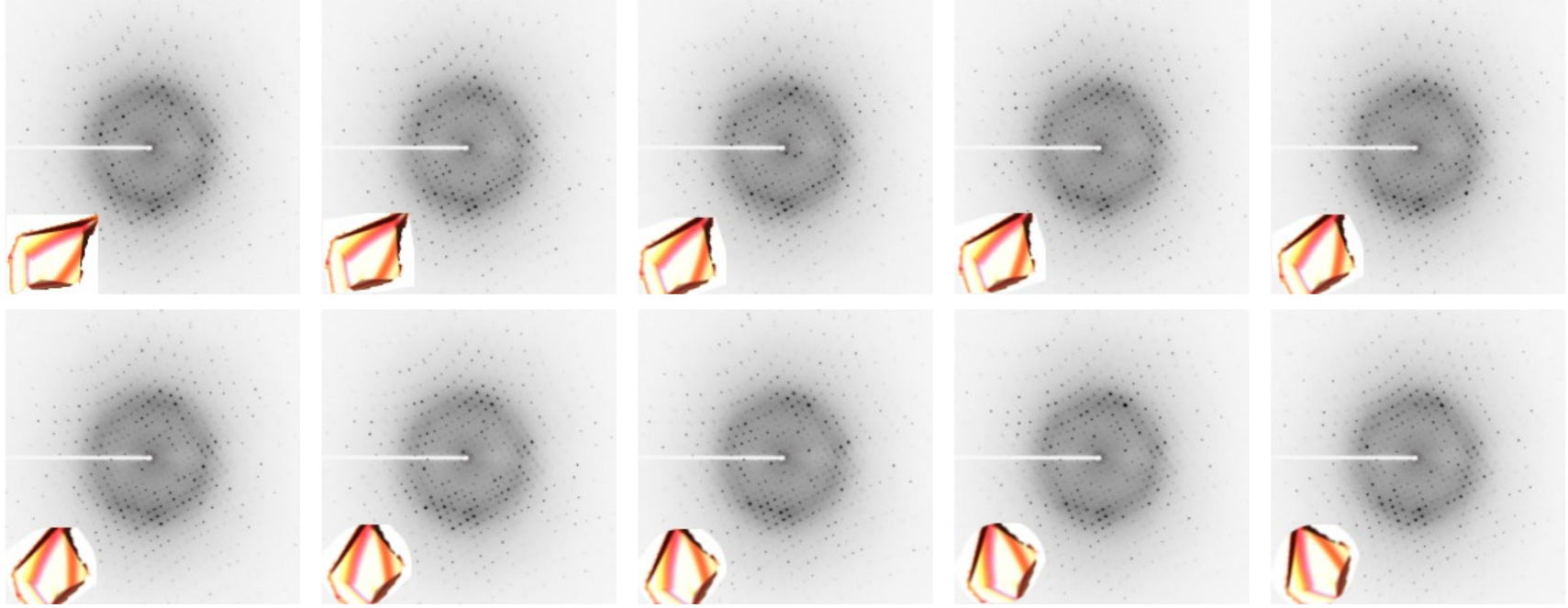


Reflections are data point. Each one contains different information. In order to collect as many data points as possible:

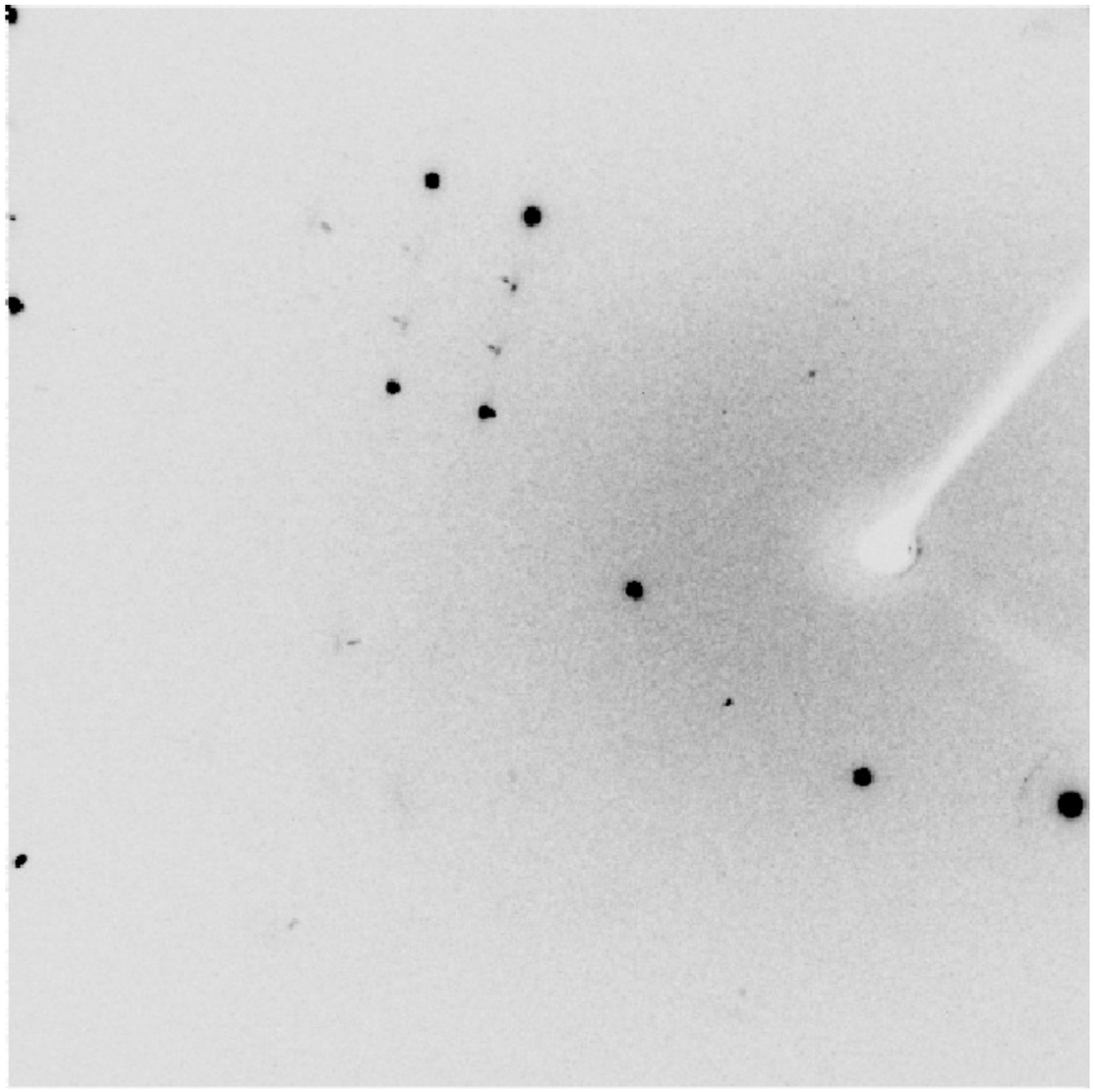
1. Rotation of the crystal (about one of three different axes, called ϕ–, ω–, and χ–circles)).
2. Rotation of the detector around the crystal, called 2θ–circle. This is parallel to the ω–circle).

The Data Set

The reflections can be described as three dimensional **reciprocal lattice**. The two dimensional detector records an intersection of the three dimensional lattice.
The full experiment results in a **data set**.
One data set consists of several runs (1–20). One run is the rotation of the crystal about a single axis. Per run, 180–2,000 **frames** are recorded. One frame corresponds typically to 0.1° – 1° rotation of the crystal.

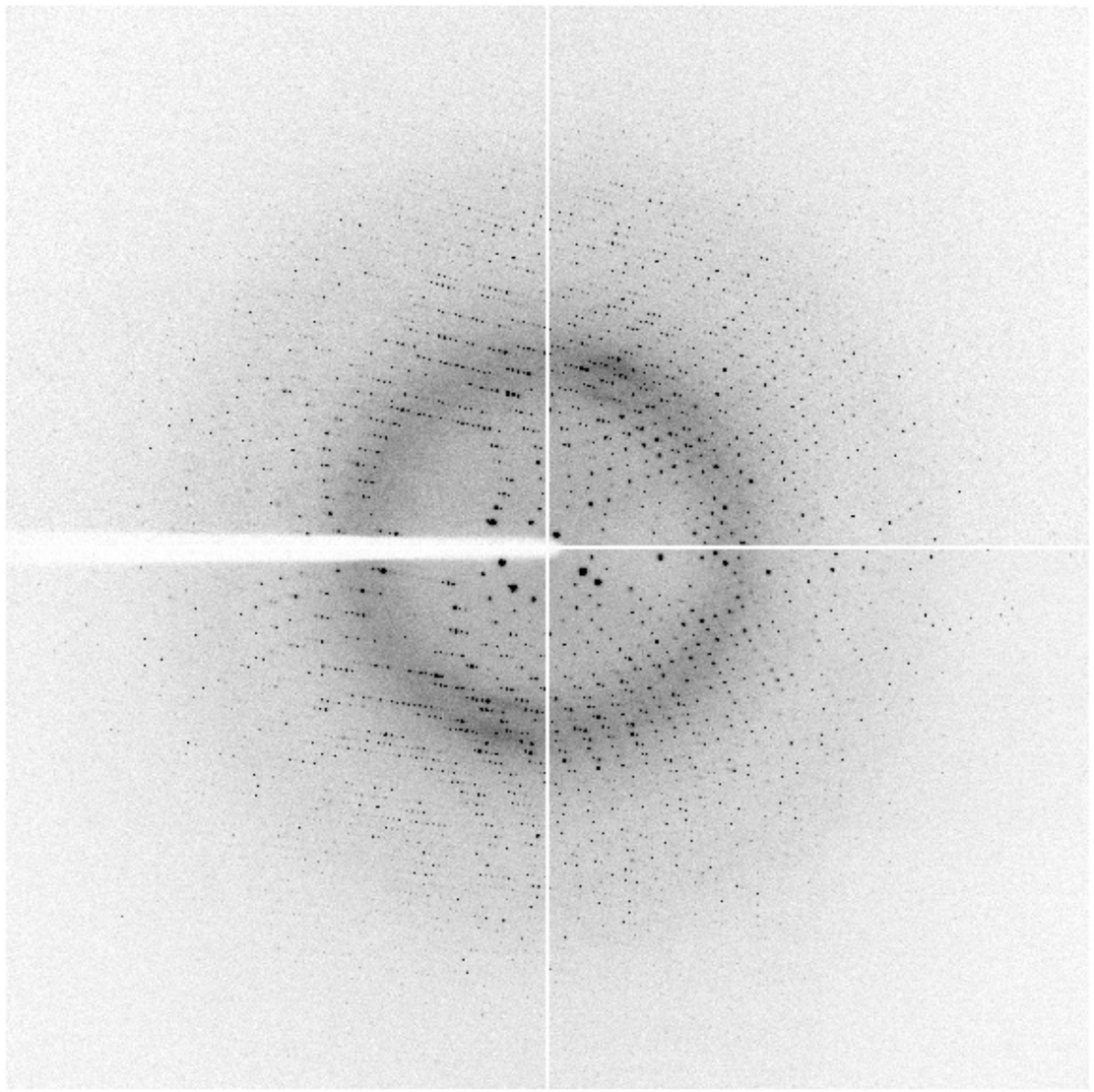


Examples of Data Frames



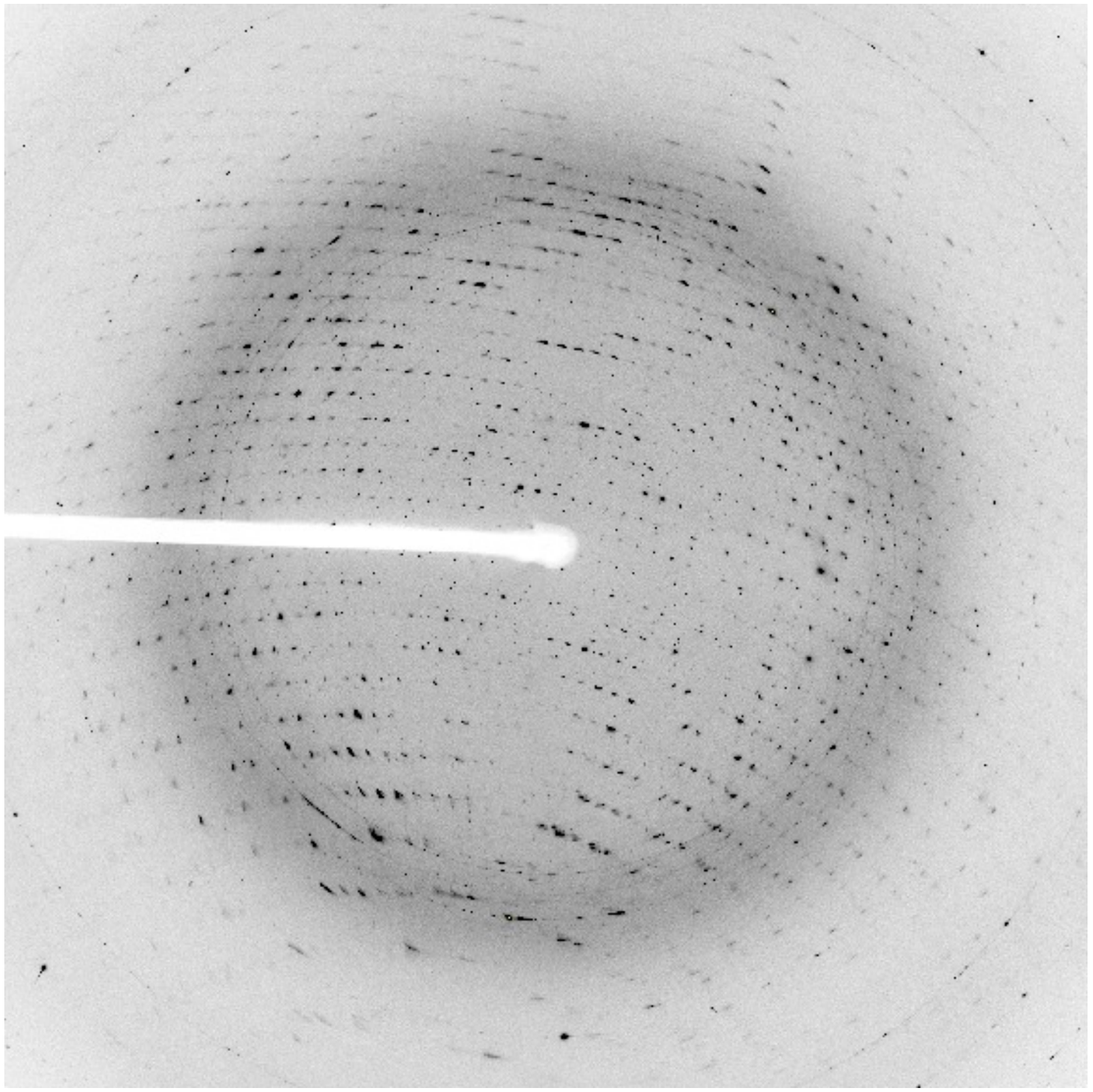
- Small molecule, unit cell dimensions: $a = 10.56$Å, $b = 11.64$Å, $c = 16.14$Å, $\alpha = \beta = \gamma = 90°$
- Small unit cell: $\Rightarrow$ few reflections
- Reflections beyond edge of detector: $\rightarrow 2\theta$ offset of detector necessary
- black reflections = data; grey regions: noise, neglectable

Examples of Data Frames



- Macromolecule. unit cell dimensions: $a = 92.6$Å, $b = 92.6$Å, $c = 128.9$Å, $\alpha = \beta = 90°, \gamma = 120°$
- Many more reflections
- Reflexes form patterns Muster (lunes, “Kugeldreiecke”)
- Intensity reduces towards edge of detector

Examples of Data Frames



- Macromolecule. unit cell dimensions: $a = 111.7$Å, $b = 80.5$Å, $c = 70.3$Å, $\alpha = \gamma = 90°, \beta = 94.2°$
- smeared reflexes
- ice rings (formed during measurement, or due to poor shock-freezing conditions)
- Closer look: small spots between “patterns”: twinned crystal, not a single crystal.

Objectives of a Crystal Structure

Why Crystal Structure Determination?

The Structure provides atom coordinates: arrangement of elements in 3D space

Organic Chemistry:

- Purity of synthesis
- Success (or failure) of synthesis
- Determination of absolute structure

Inorganic Chemistry"

- Bonding geometry, coordination geometry (of metals . . .)

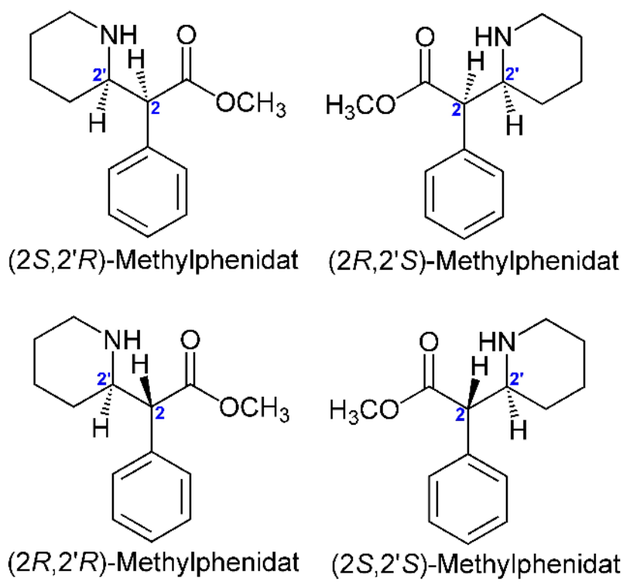
Comparison with other Structural Methods

NMR : chemical environment, sum formula. Not absolute structure

Rotational spectroscopy: (and gas phase electron diffraction): bond distances (**much more precise** than crystal structure)

Crystallography : Virtually no size limit (protein complexes $>$ 1.5 MDa; differentiation of element types

Examples: Absolute structure and degree of purity



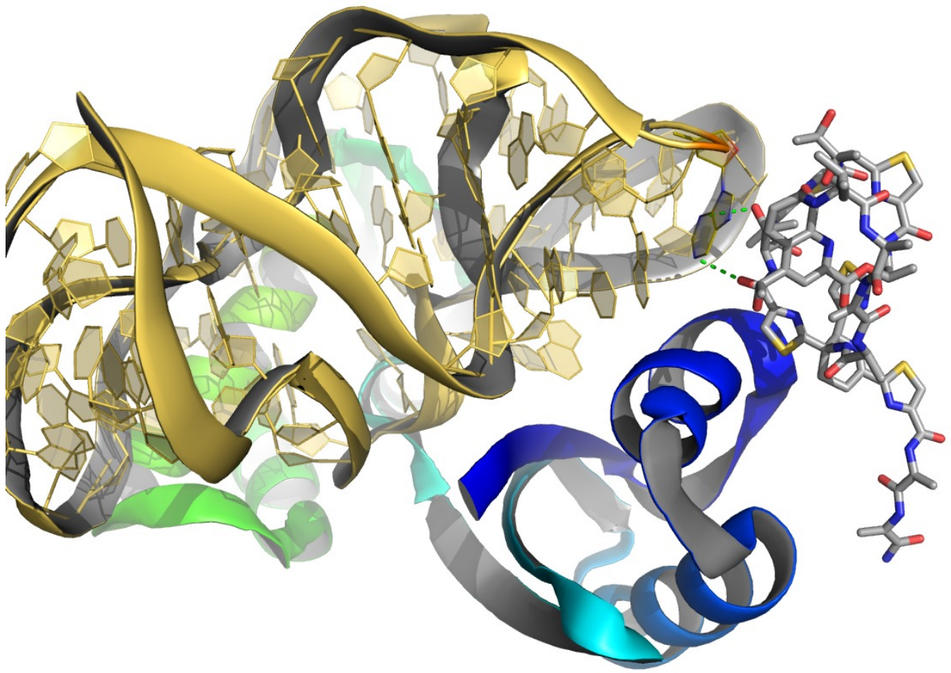
- Methylphenidate (*alias* Ritalin): medication to treat Attention Deficit Hyperactivity Disorder (ADHD).
- Two chiral centres, *four* stereoisomers
- Typical: only one stereoisomer with desired effect.
- Remaining stereoisomers: side effects

(E. J. Ariëns:*Stereochemistry, a basis for sophisticated nonsense in pharmacokinetics and clinical pharmacology*, European Journal of Clinical Pharmacology, **26** (1984), pp. 663–668).

`http://de.wikipedia.org/wiki/Methylphenidat`

The crystal structure is the only method to determine the absolute structure and the degree of purity of mixtures.

Structure based Drug Development



The antibiotic *Thiostrepton* together with its target DNA. Dr. K. Pröpper.

Knowledge of structure of ligand and target:

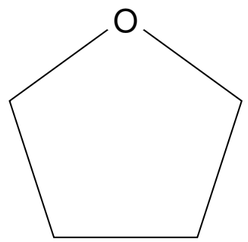
- Improvement of chemical interaction
- Improvement of shape / surface: Functionality and access to cell or nucleus.
- Uptake in body (cf. `http://de.wikipedia.org/wiki/Insulinpräparat`)

Crystal Diffraction: Why do crystals produce reflections?

Independent Atom Model (IAM)

Crystal structure determination is based on the **independent atom model** (IAM):

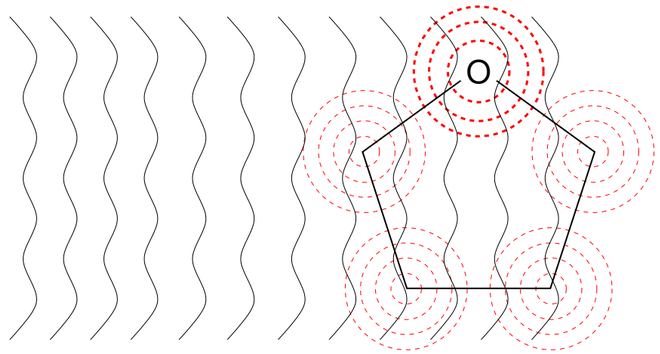
- the molecule consists of spherical atoms



Independent Atom Model (IAM)

Crystal structure determination is based on the **independent atom model** (IAM):

- the molecule consists of spherical atoms
- upon irradiation, each atom re-emits a small spherical wave independently from the others
- the strength depends on the atom type



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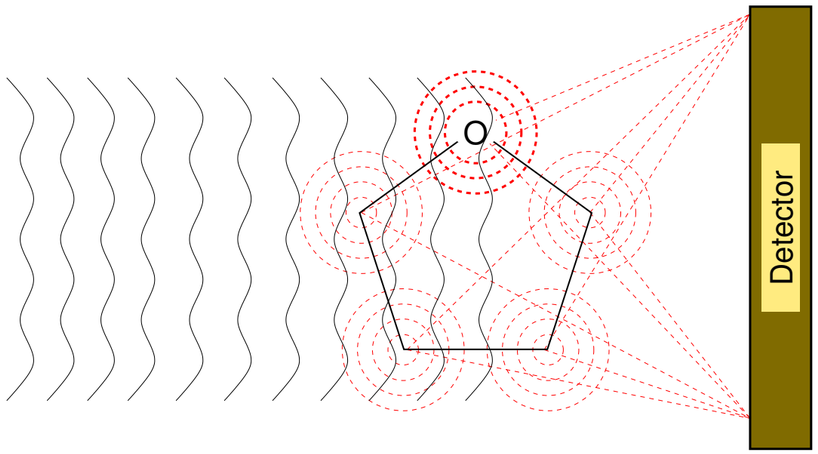
Crystal structure determination is based on the **independent atom model** (IAM):

- the molecule consists of spherical atoms
- upon irradiation, each atom re-emits a small spherical wave independently from the others
- the strength depends on the atom type
- the detector records the overlap of all (tiny) waves



Independent Atom Model (IAM)

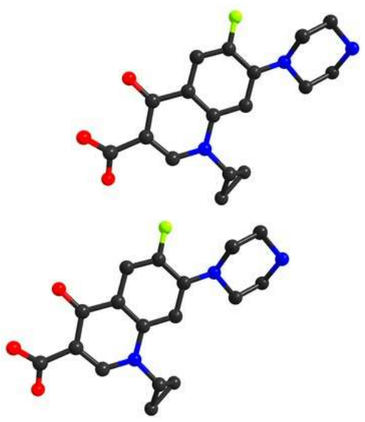
- every atom emits a tiny signal
- individual molecules are too weak to detect
- the crystal **amplifies** the signal

To understand, we introduce the **unit cell** and the **crystal lattice**.

The Unit Cell

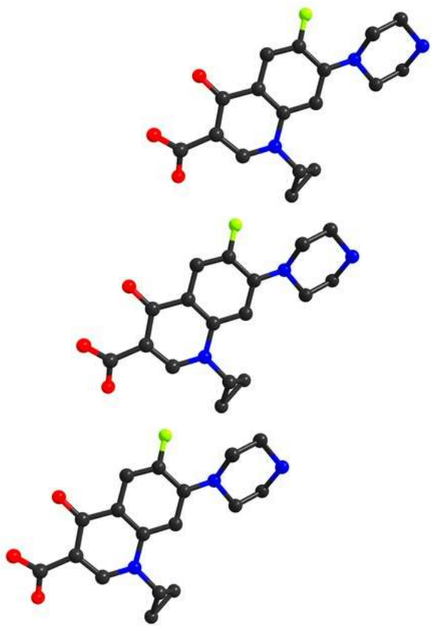
“Periodicity of the unit cell”?

The Unit Cell



“Periodicity of the unit cell”?

The Unit Cell



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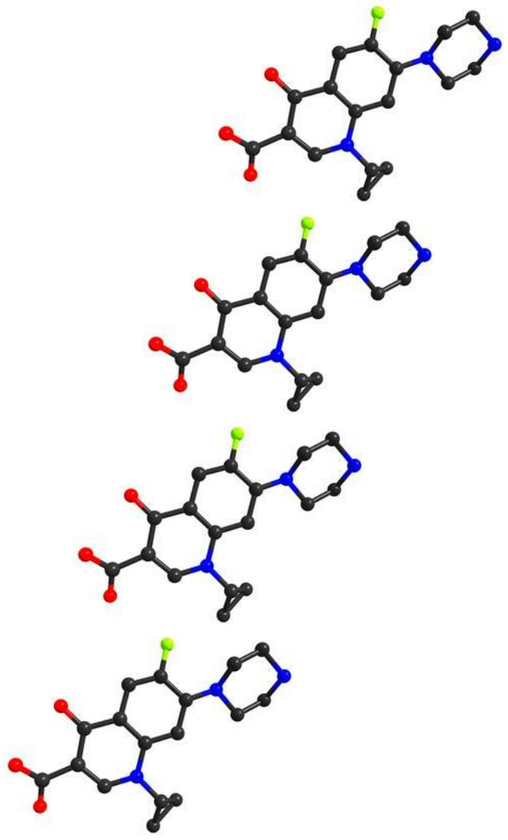

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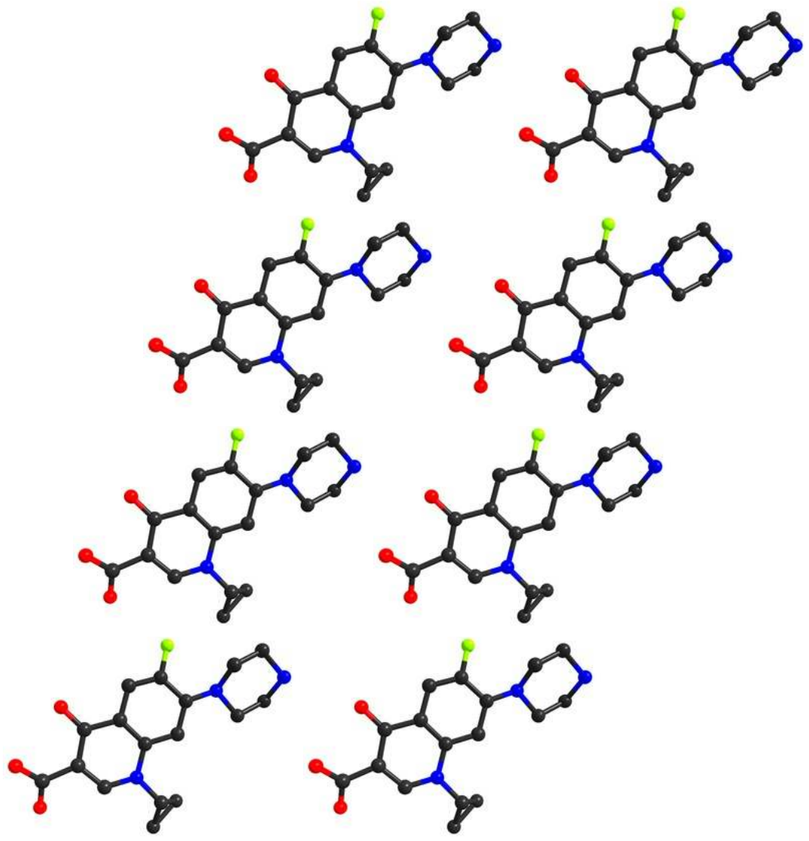

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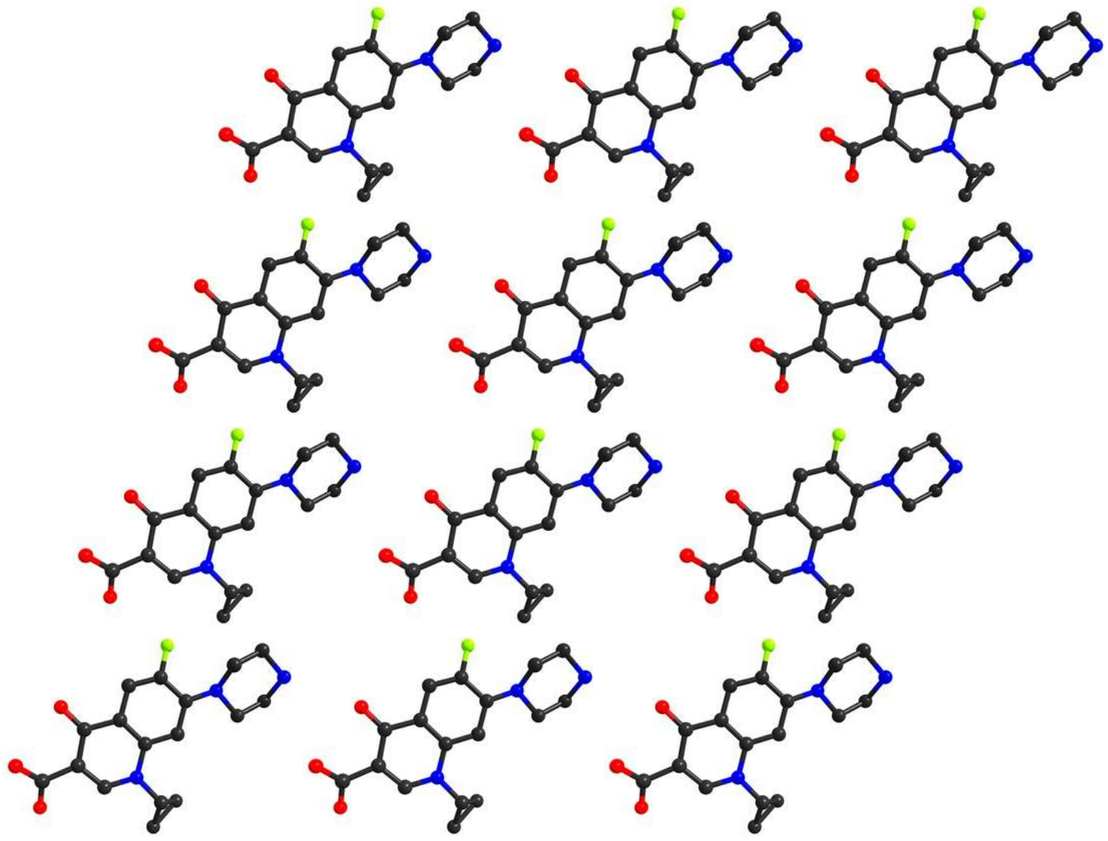

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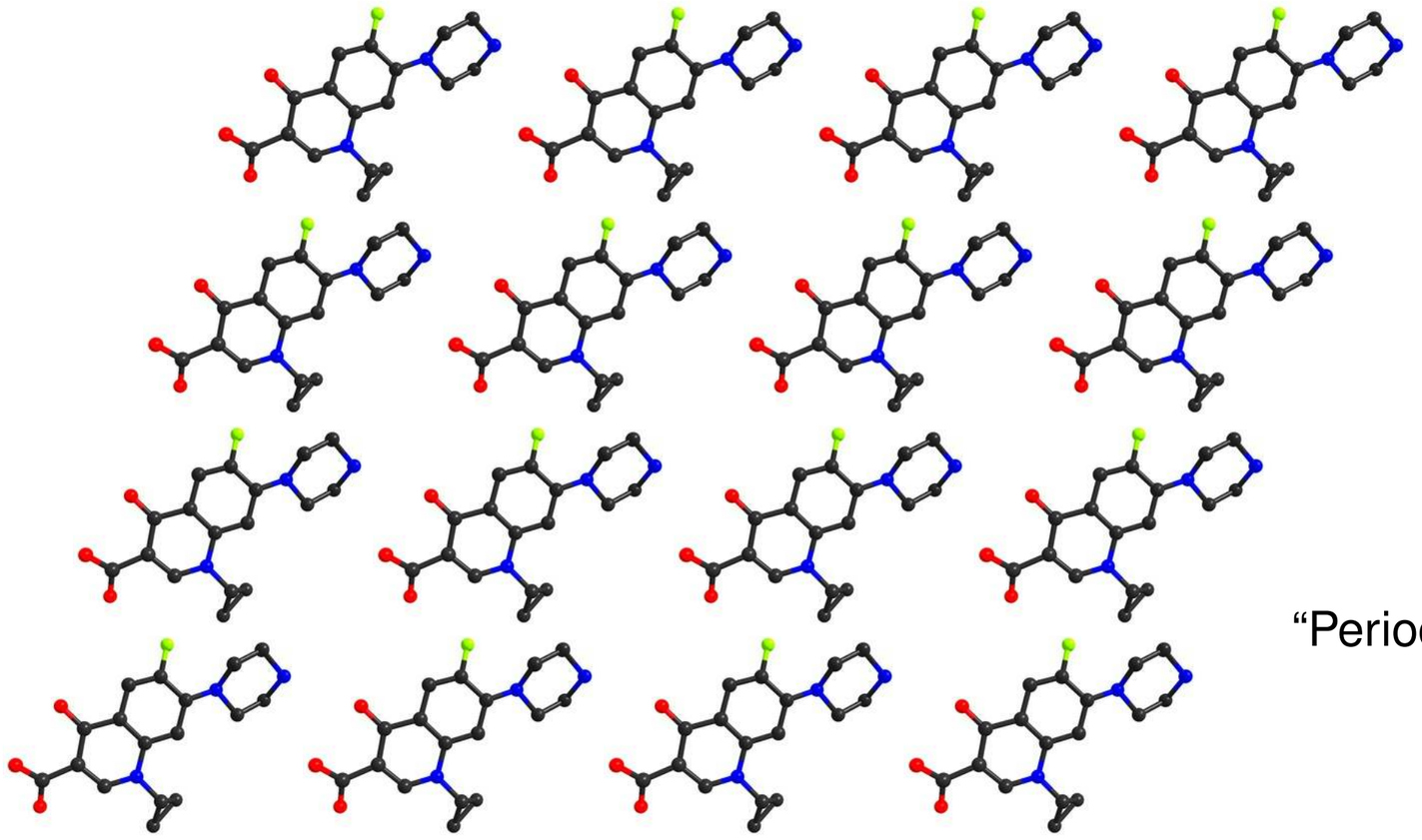

“Periodicity of the unit cell”?

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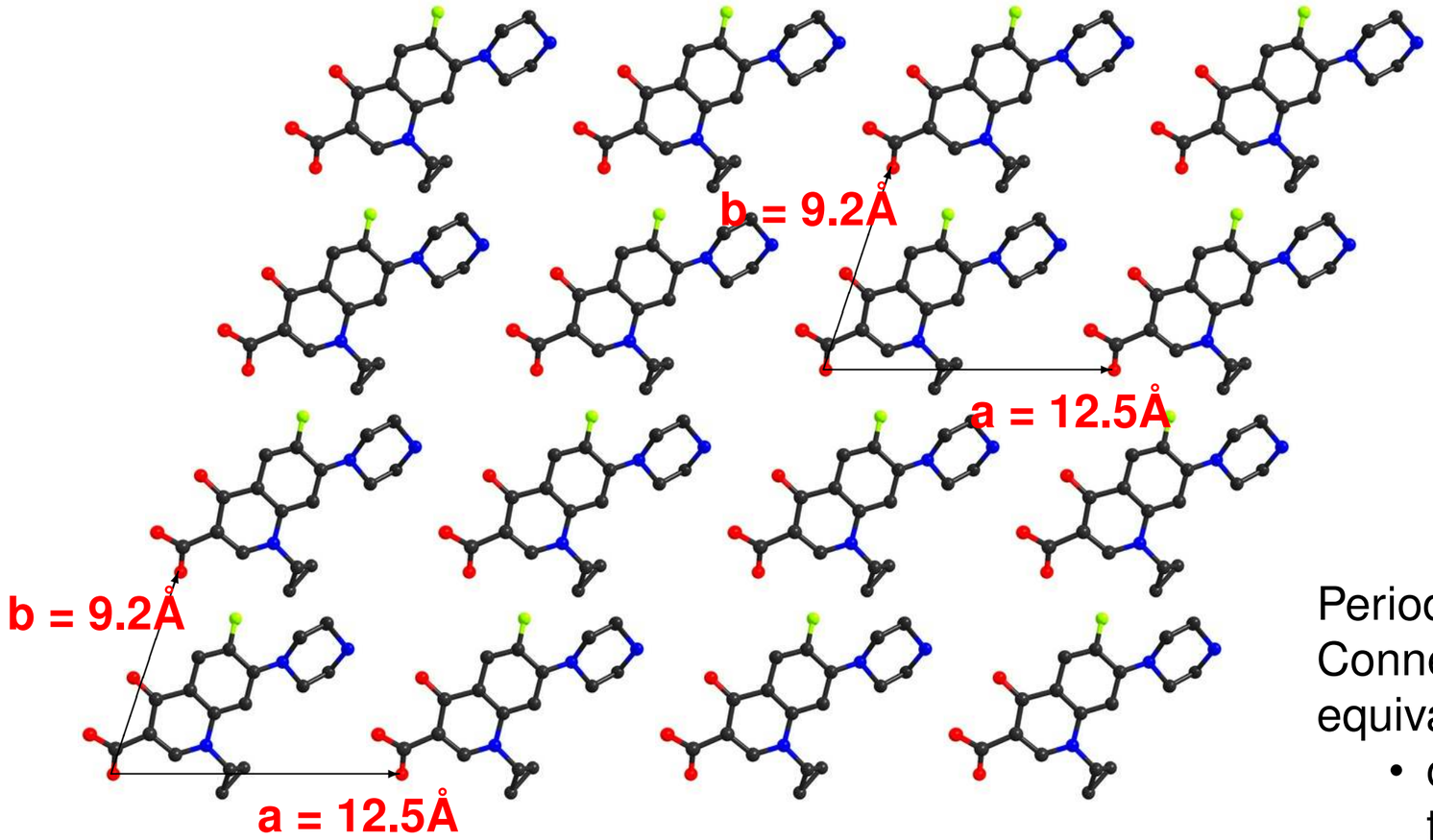
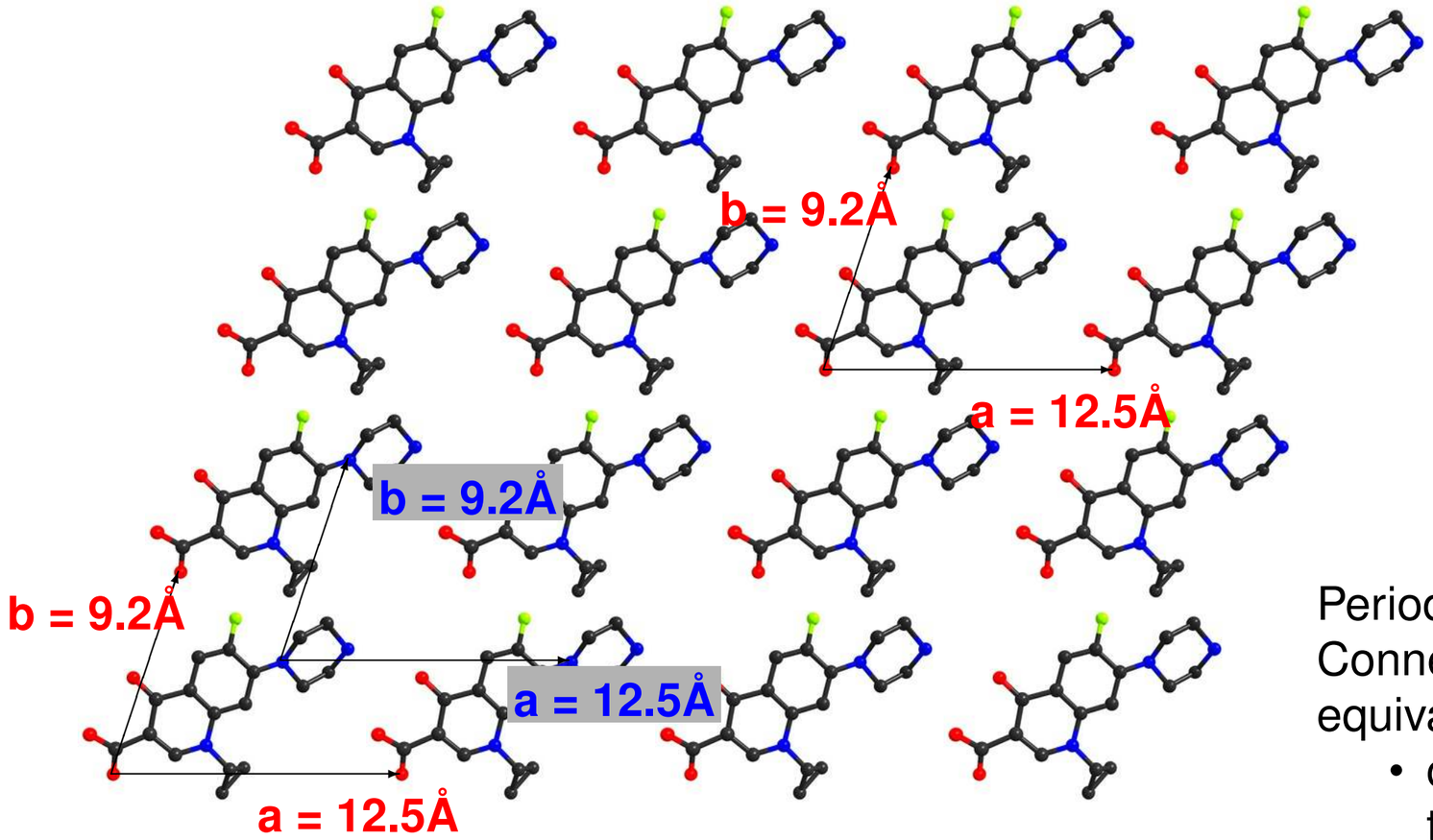


Periodicity of the unit cell:
Connect two equivalent atoms in two equivalent molecules:

- connection can be shifted throughout the crystal

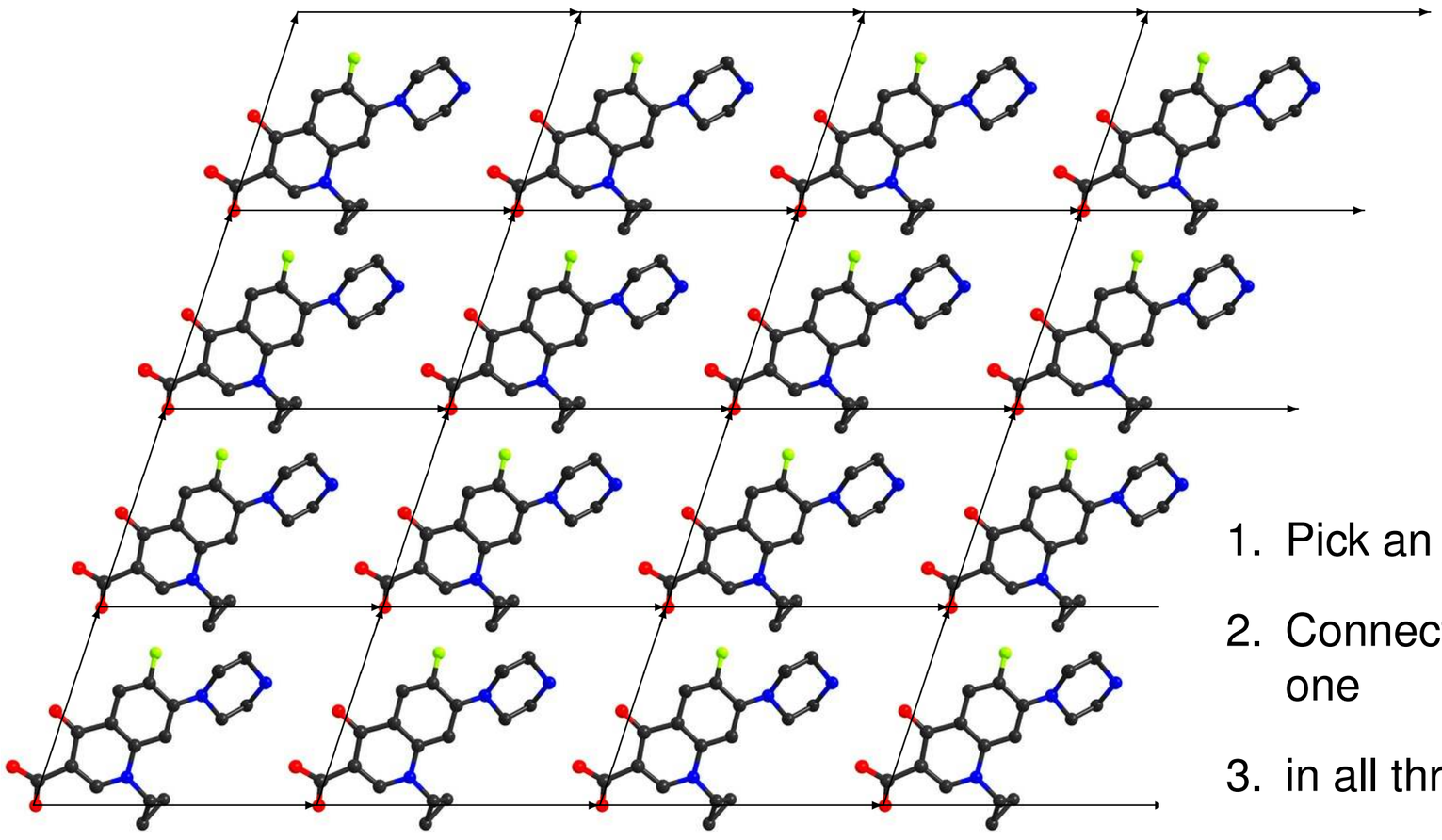
The Unit Cell



Periodicity of the unit cell:
Connect two equivalent atoms in two equivalent molecules:

- connection can be shifted throughout the crystal
- connection **independent of atom**

The Unit Cell



1. Pick an arbitrary reference atom
2. Connect with the next equivalent one
3. in all three directions
4. Continue for all molecules:

This results in the **crystal lattice**
The smallest parallelepiped (smallest “box”) from the **unit cell** of the crystal.

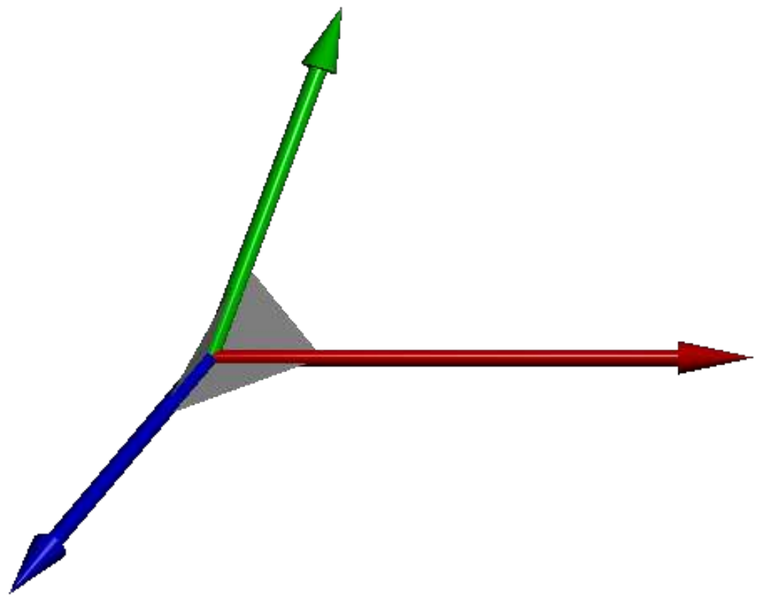
The Unit Cell

A three-dimensional box requires six parameters:

- unit cell constants a, b, c (edge lengths)
- angles between the edges

$$\alpha = \angle(b,c) \qquad \beta = \angle(c,a) \qquad \gamma = \angle(a,b)$$

- constants and angles are independent from the orientation of the crystal
- when written as vectors $\vec{a}$, $\vec{b}$, $\vec{c}$, they also describe the orientation of the crystal with respect to the instrument.



The convention a: red, b: green, c: blue comes from computer graphics, where colours are described as *rgb*.

Fractional Coordinates

Atom coordinates are often described with *fractional coordinates*.
Every position in the crystal has unique coordinates (x, y, z)

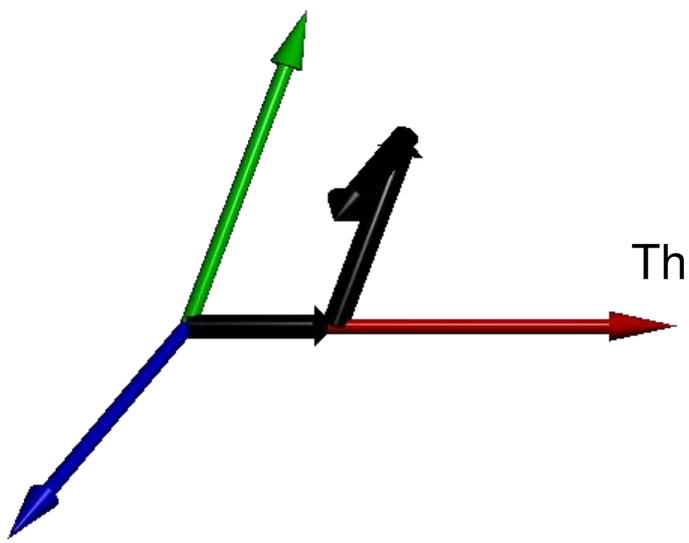
$$x * \vec{a} + y * \vec{b} + z * \vec{c}$$

(x, y, z) are called the **fractional coordinates** of this position.
For any position *inside* the unit cell:

$$0 \leq x, y, z \leq 1.$$

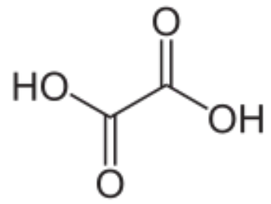
Fraction coordinates facilitate the use of symmetry operators. They are normally used in crystallographic computing.

- SHELXL ins-files always use fractional coordinates.
- Macromolecular PDB-files use orthogonal coordinates.

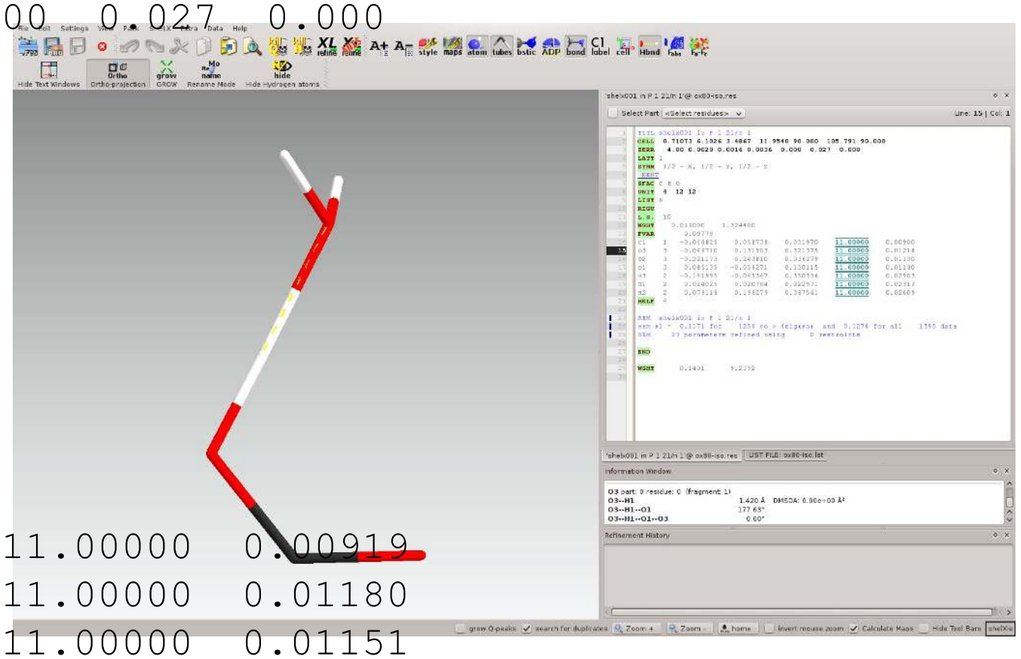


The position (0.3, 0.6, 0.5).

Example: `ins`-file for Oxalic Acid




```
TITL Oxalic Acid in P 1 21/n 1
CELL  0.71073 6.1026 3.4867  11.9540 90.000  105.791 90.000
ZERR   4.00 0.0020 0.0016 0.0036  0.000  0.027  0.000
LATT 1
SYMM  1/2 - X, 1/2 + Y, 1/2 - Z
NEUT
SFAC C H O
UNIT  4  12 12
LIST 6
RIGU
L.S.  10
WGHT  0.0180  1.3244
FVAR   0.09892
C1   1 -0.045033  0.058931  0.051985  11.00000  0.00919
O3   3 -0.048452  0.131974  0.321439  11.00000  0.01180
O2   3 -0.221285  0.243842  0.036277  11.00000  0.01151
O1   3  0.085162 -0.055871  0.150165  11.00000  0.01216
H3   2 -0.142238 -0.045413  0.350385  11.00000  0.02677
H1   2  0.023619  0.022591  0.223012  11.00000  0.02363
H2   2  0.079486  0.197530  0.387391  11.00000  0.02464
HKLF  4
END
```



Summary: The Unit Cell

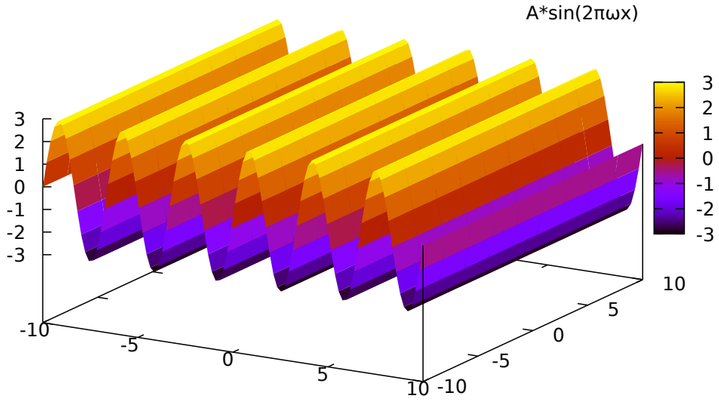
The crystal structure is described by

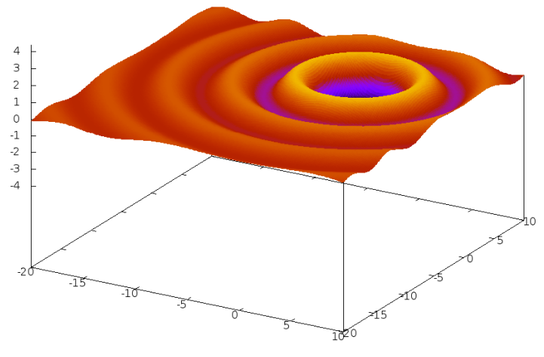
1. the unit cell parameters $a, b, c, \alpha, \beta, \gamma$
2. positions and element types of the atoms inside the unit cell

The whole crystal is the result of integer translations (= shifts without gaps or overlaps) of the unit cell in all three directions.

Diffraction Theory — Atoms and X-rays

Physicists' description of light





Planar wave:

$$A(\vec{x},t) = A_0 \cos(\vec{k}\vec{x} - \omega t)$$

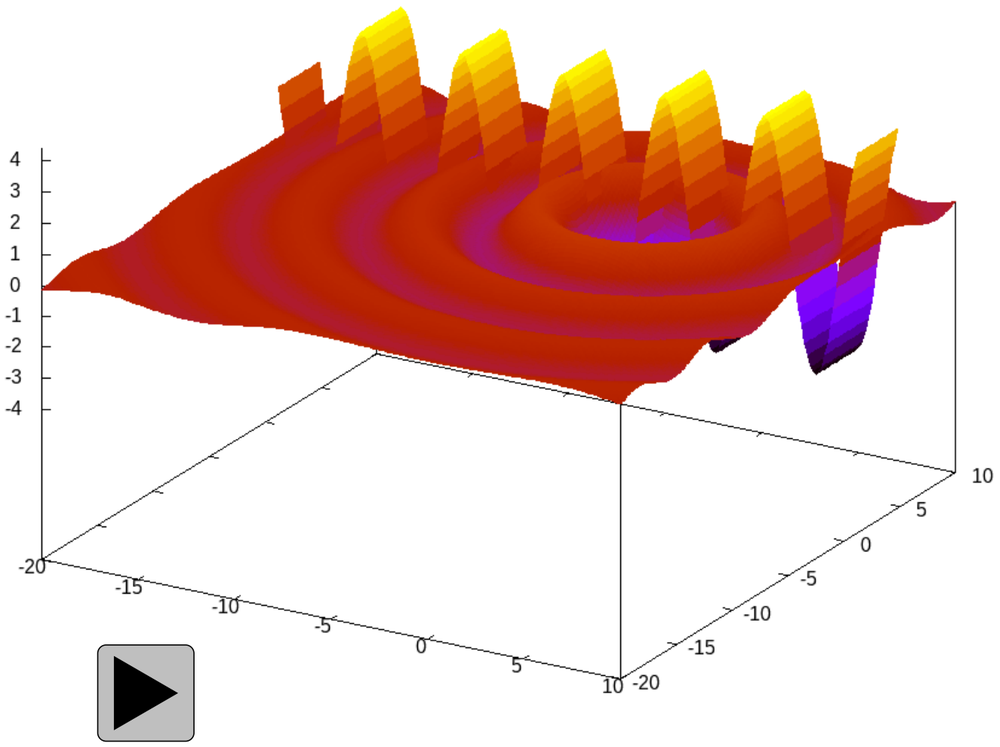
Spherical wave:

$$A(\vec{x},t) = \frac{A_0}{|\vec{x}|} \cos(|k||\vec{x}| - \omega t)$$

- Intensity $I \propto {A_0}^2$ and $I \propto (A_0/|x|)^2$, respectively
- Direction of propagation: $\vec{k}$; $|\vec{k}| = 2\pi/\lambda = \omega/c$

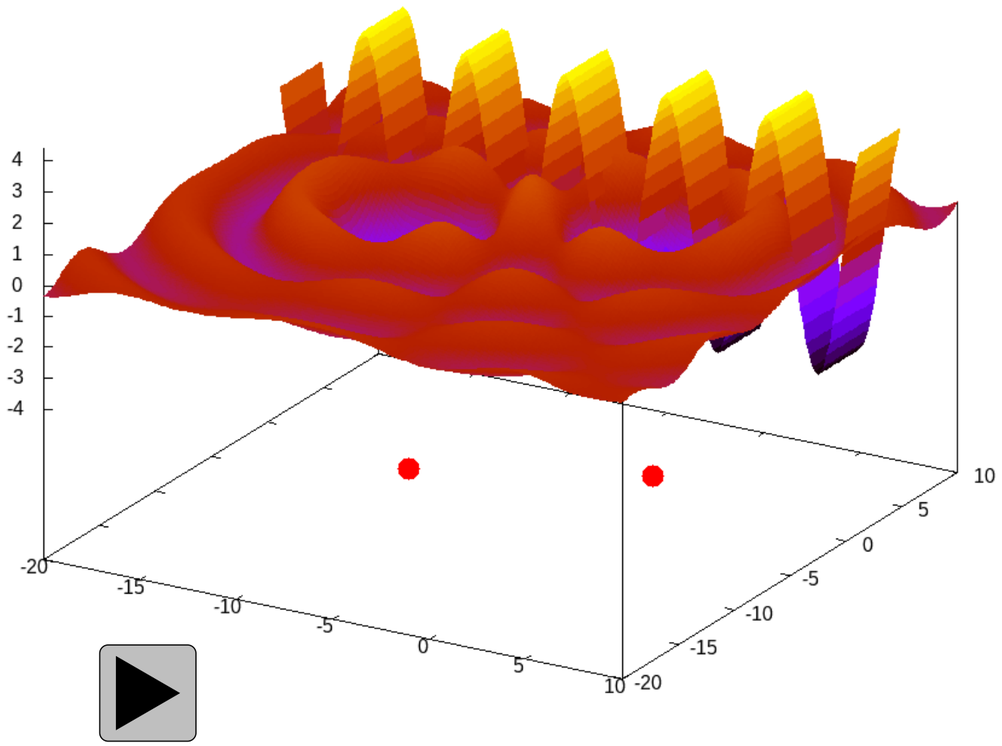
Important features of waves: the sum of two waves result in a wave

One Atom and X-rays

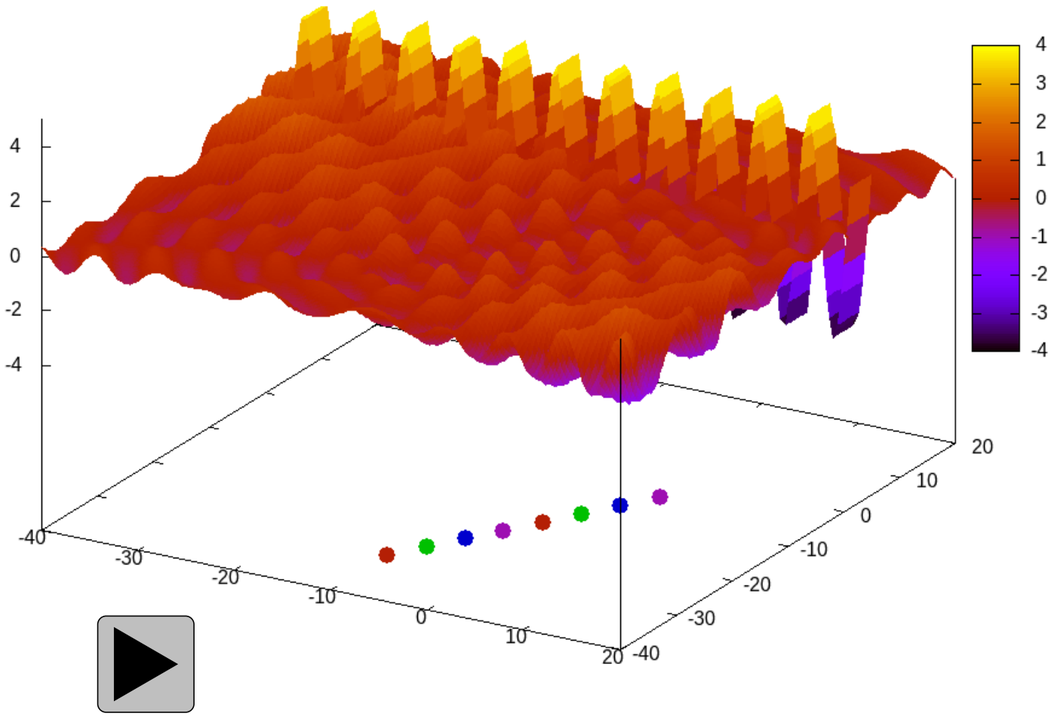


When a planar X-ray wave hits an atom, a spherical wave is emitted.

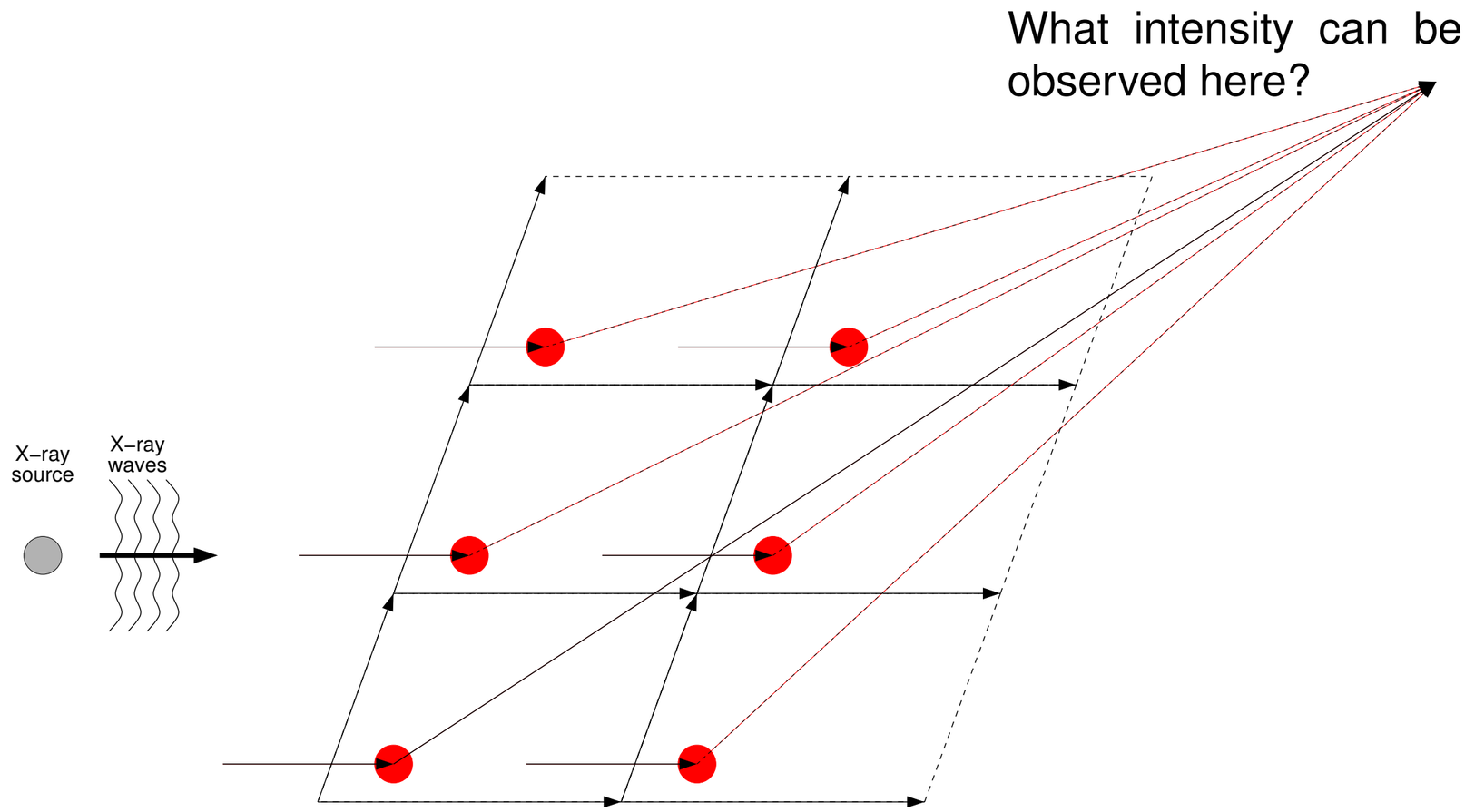
Superposition with two Atoms



Superposition with regular atoms (crystal)



Crystal as amplifier



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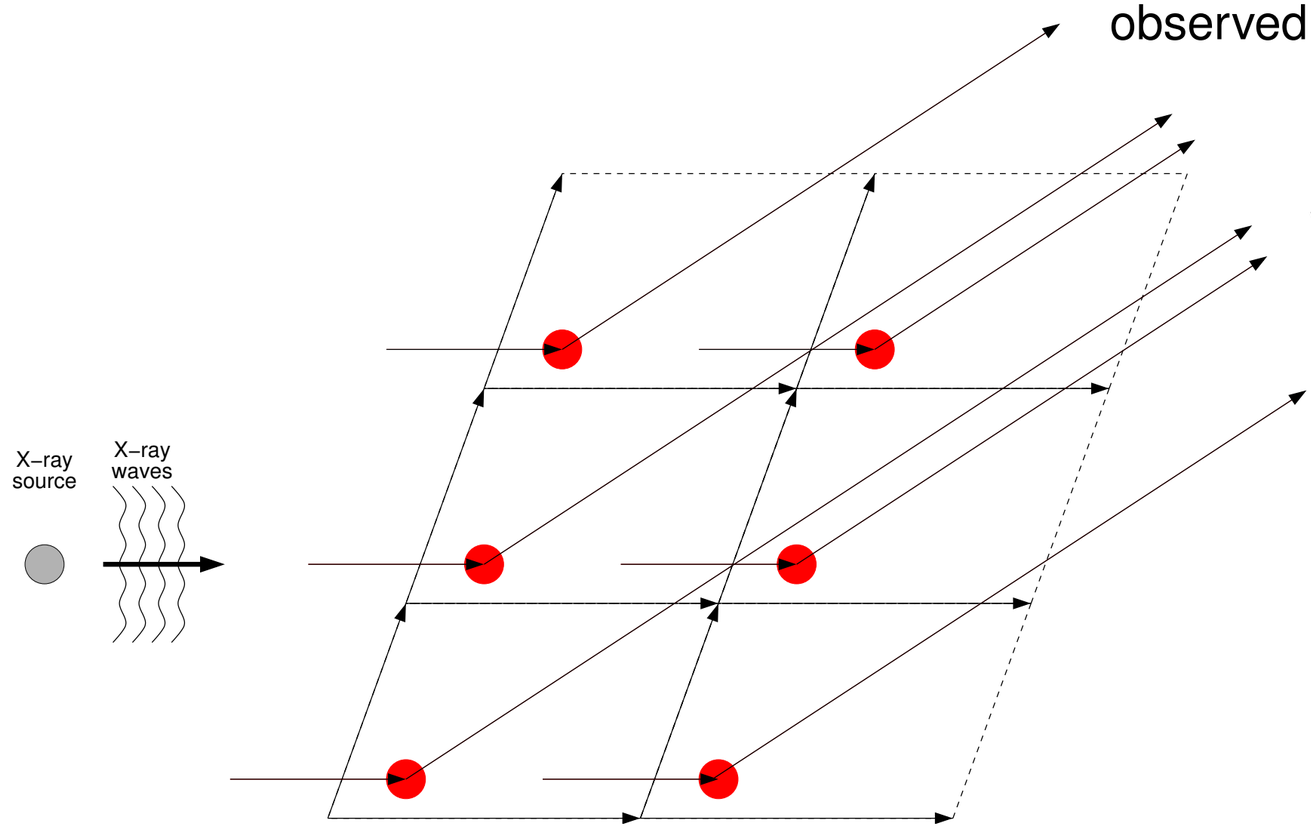
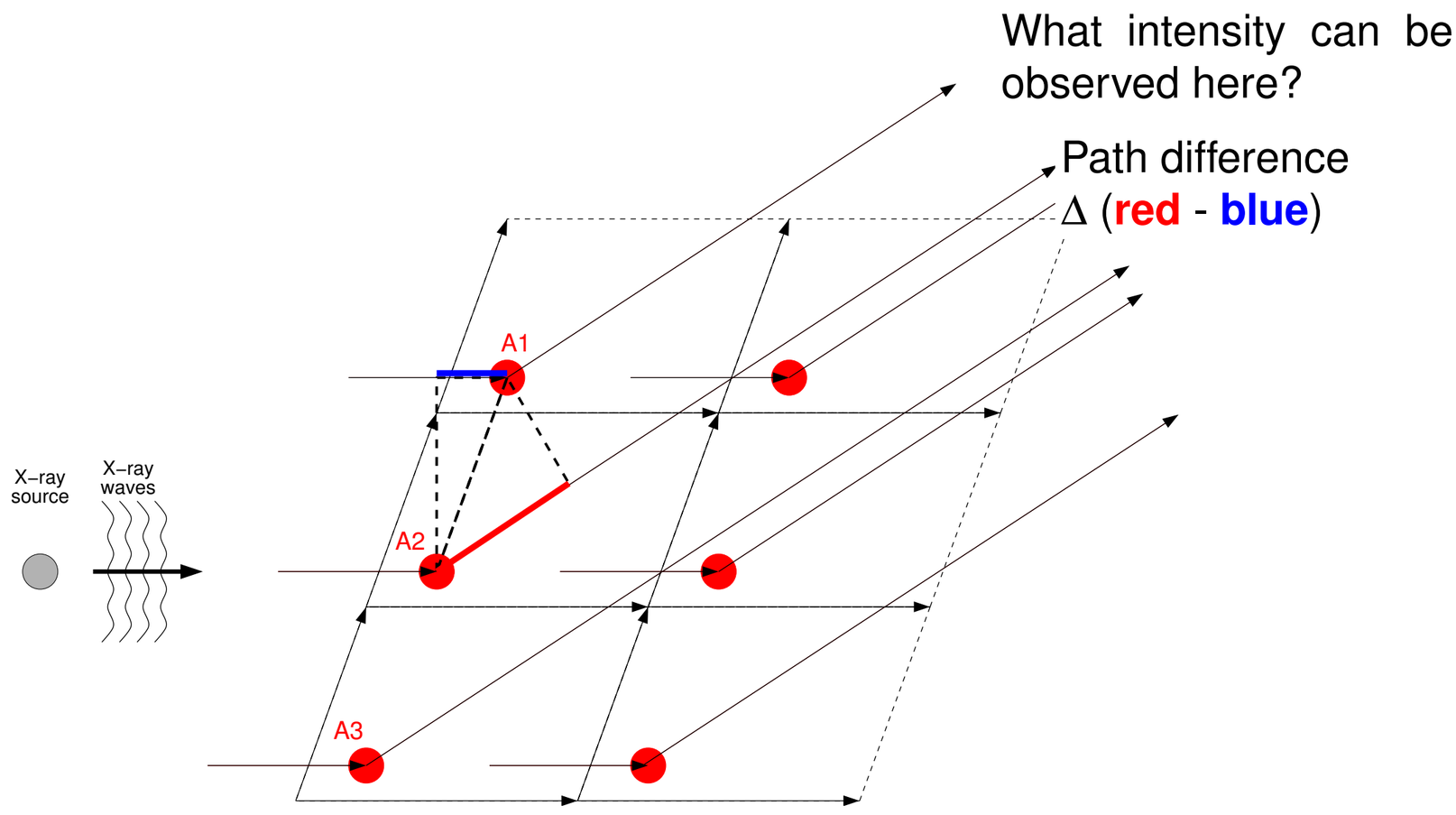


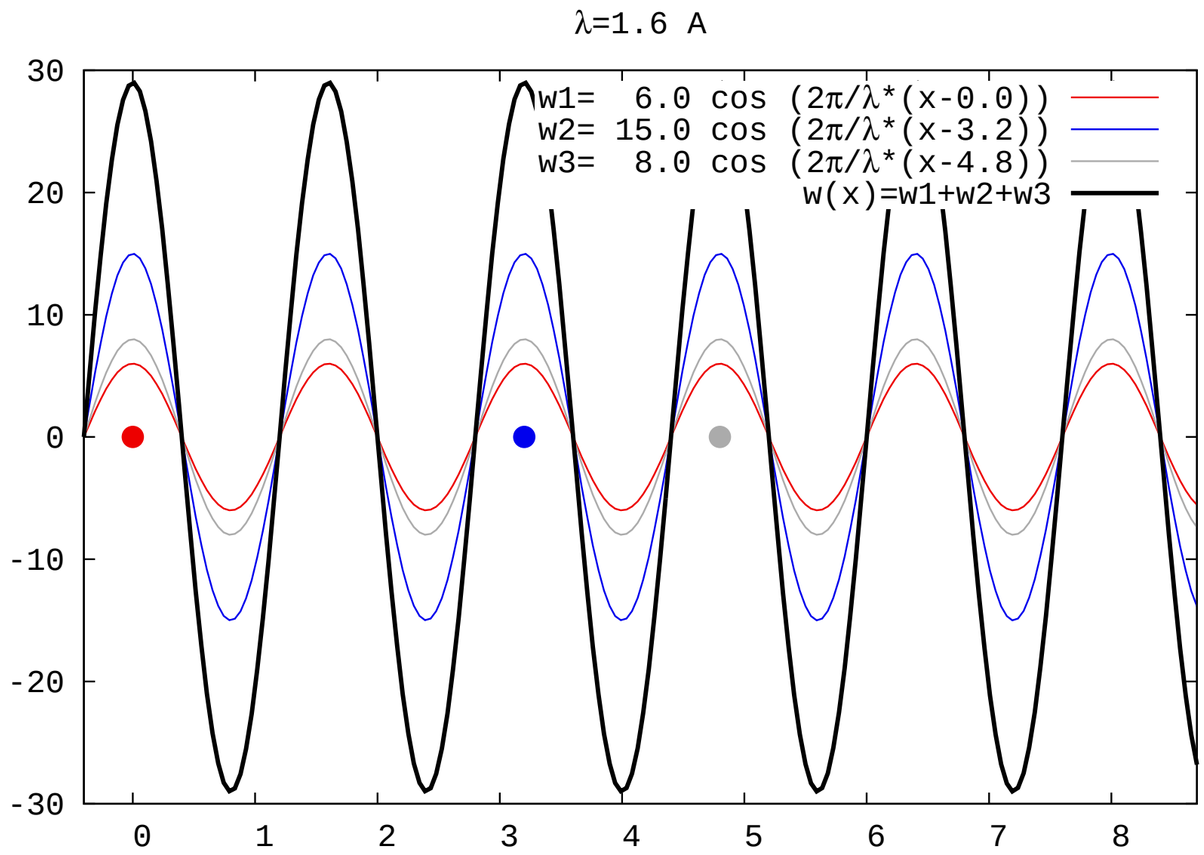
What intensity can be observed here?

Far field approx-imation: Detector very far away, all rays are parallel.

Crystal as amplifier



Constructive interference



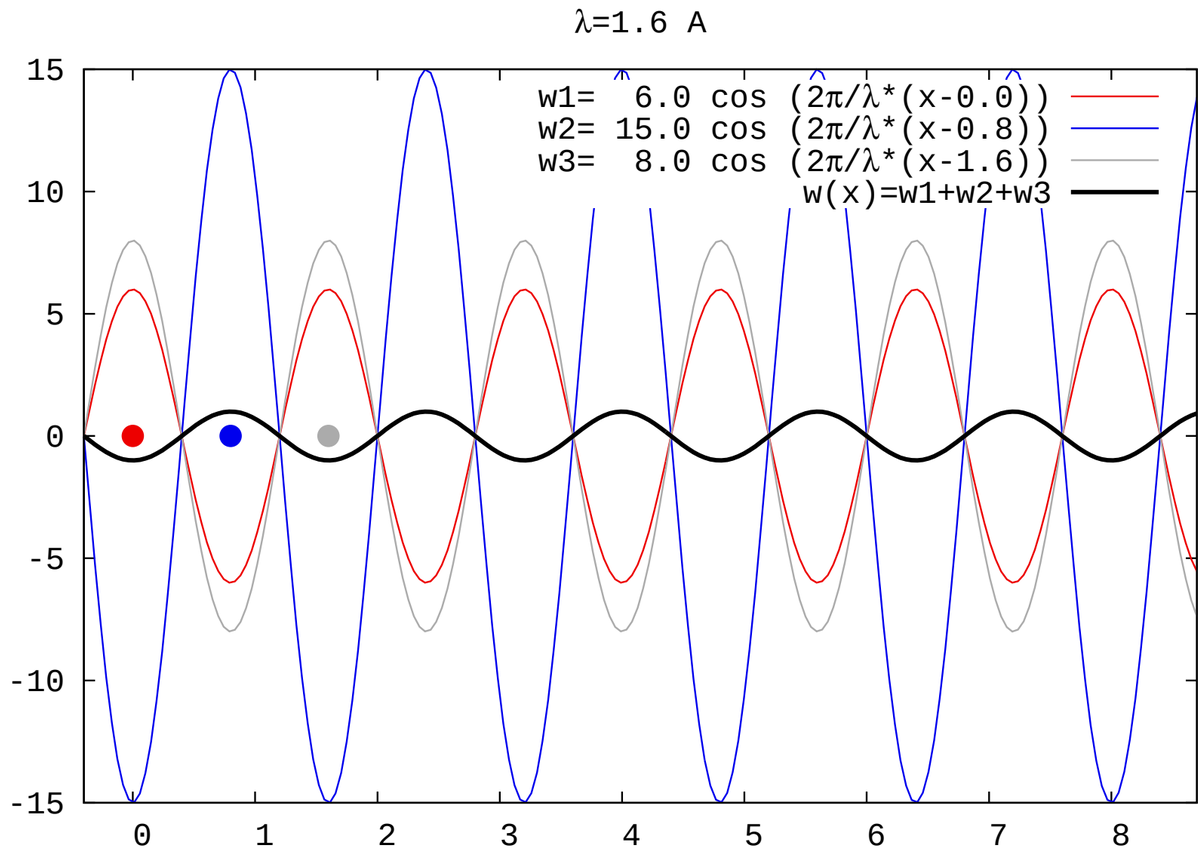
$\Delta = n \cdot \lambda$

Path difference: integer multiple of the wavelength: Maxima superpose with maxima, minima superpose with minima.

$\rightarrow$ Maxima = spots on detector

Total amplitude: 6+15+8=29

Destructive Interference



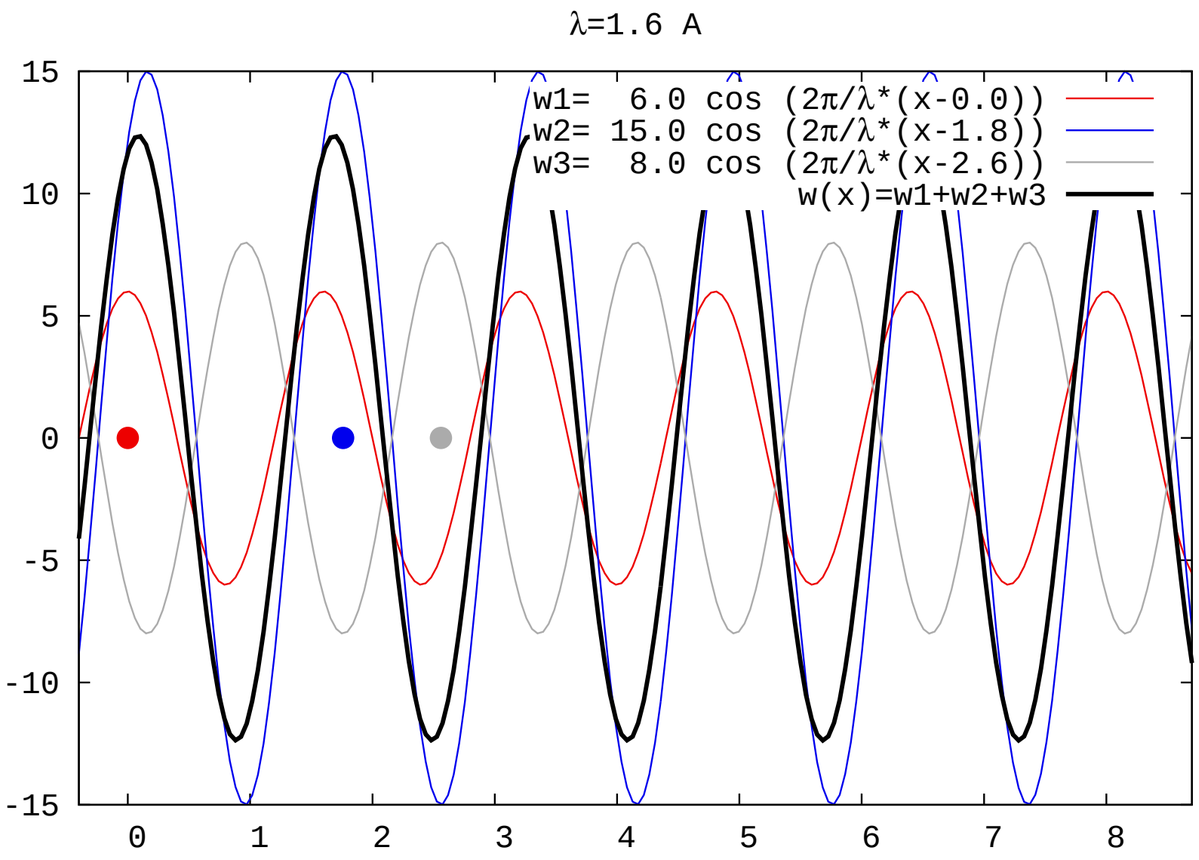
$\Delta = (n + \frac{1}{2}) \cdot \lambda$

Path difference: Shift by half wave length:

Maxima coincide with minima

Total amplitude: (6+8)-15=-1

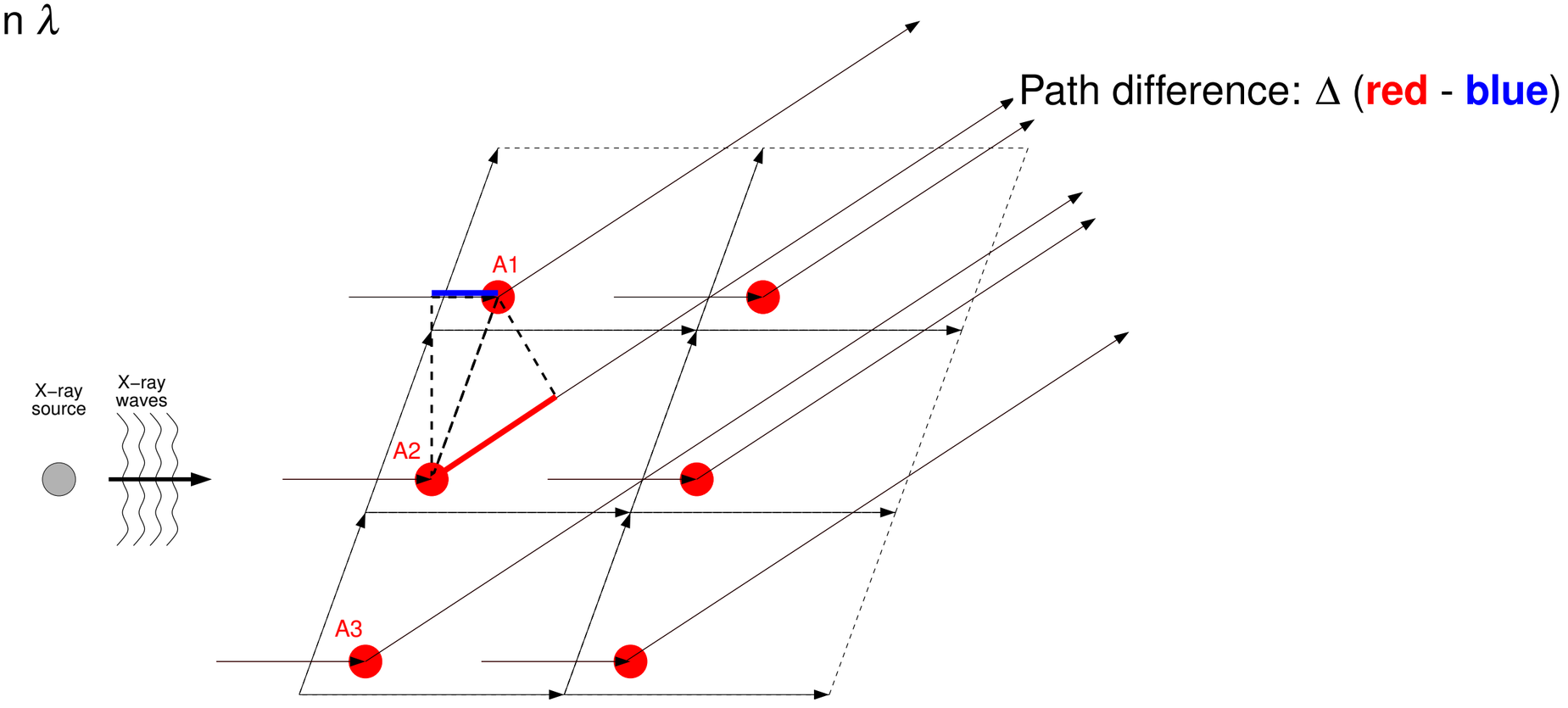
Inbetween maxima and minima



In all other cases:
Total amplitude somewhere between 0 and 29.
With **very many** Atoms:
no detectable signal, just noise

Crystal as amplifier

constructive interference:
$\Delta = n \lambda$

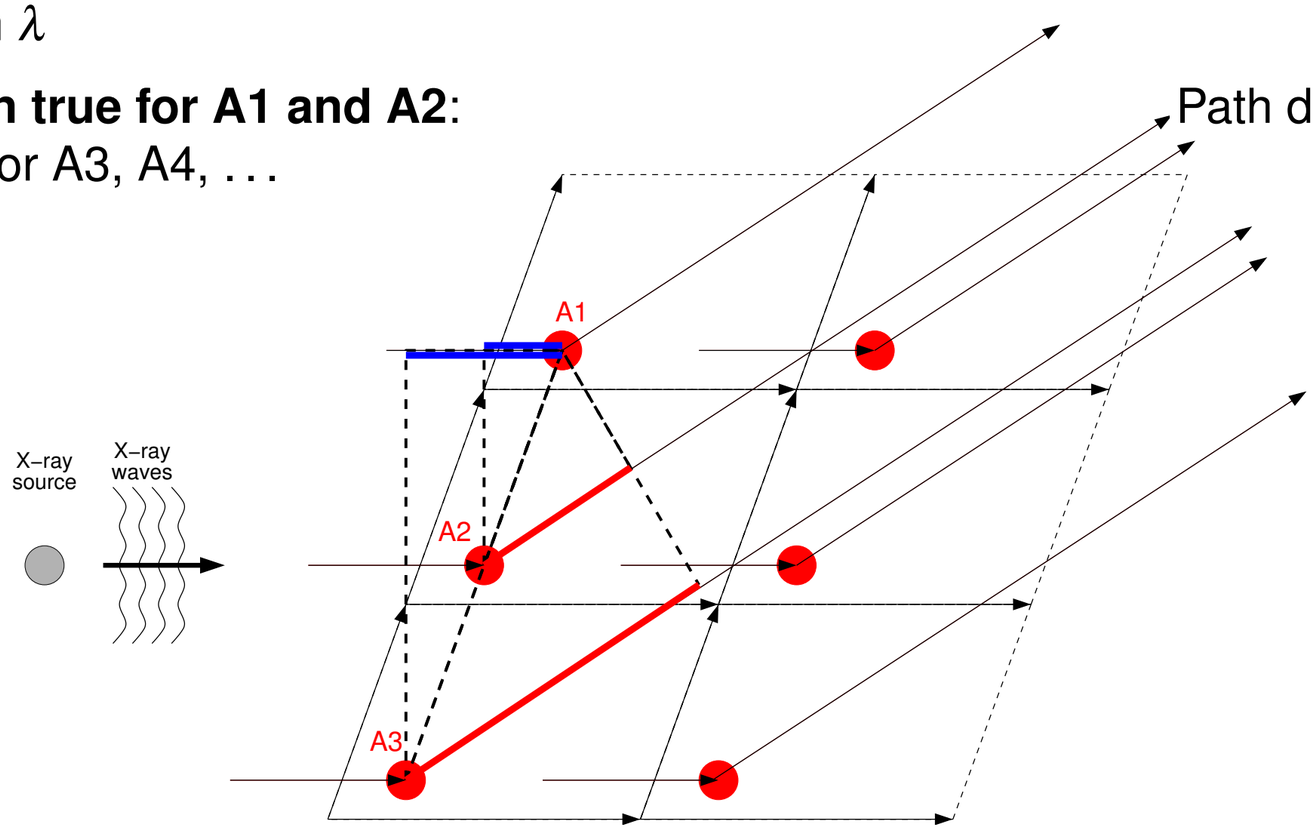


Crystal as amplifier

constructive interference:
$\Delta = n\,\lambda$

When true for A1 and A2:
true for A3, A4, . . .

Path difference: Δ (**red** - **blue**)



Crystal as amplifier

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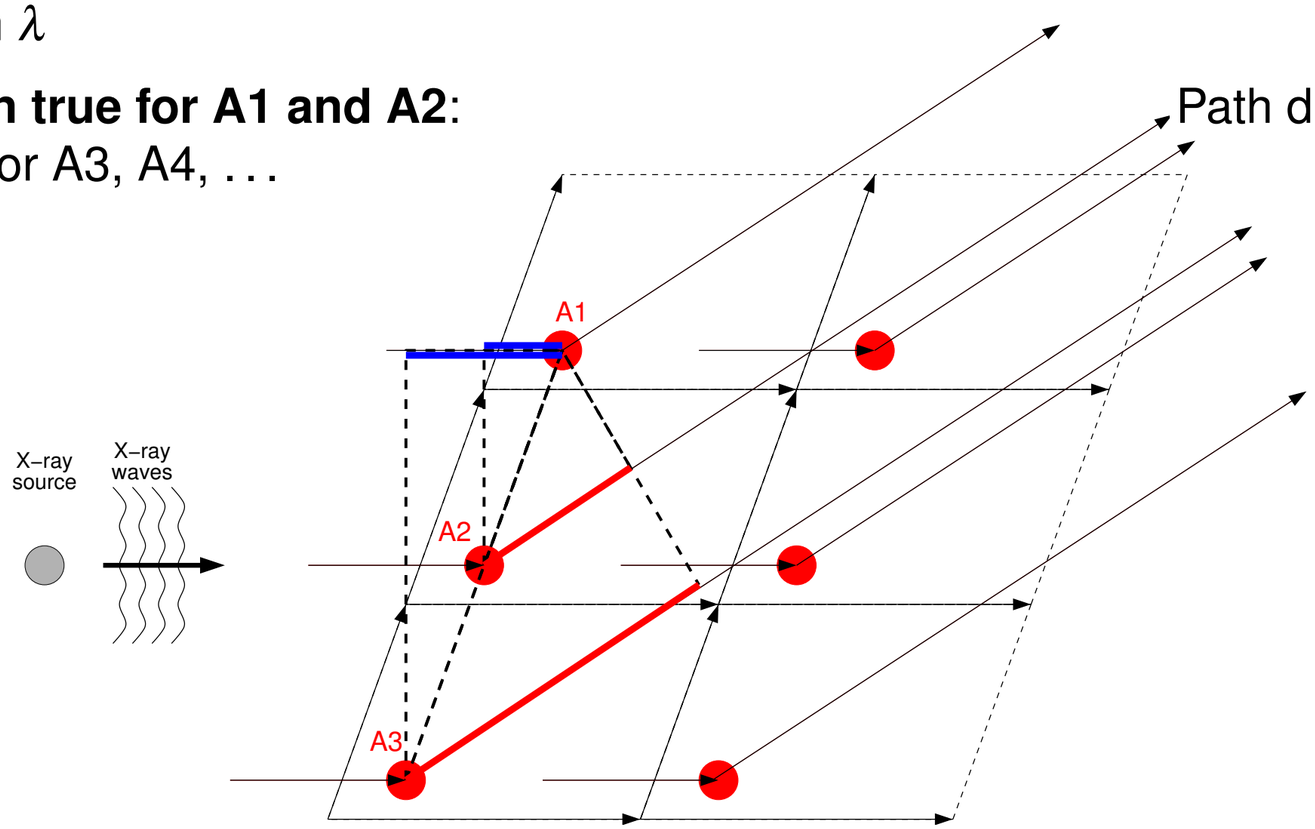


Amplification due to crystal periodicity

The Laue equations

Laue equations

- A reflection occurs at the detector, where the path difference is an integer multiple of the wave length.
- The locations lie on rays coming from the crystal
- The directions depend on unit cell parameters and crystal orientation
- The directions are described by the **Laue equations** (Max von Laue, 1879 - 1960) .

Laue equations

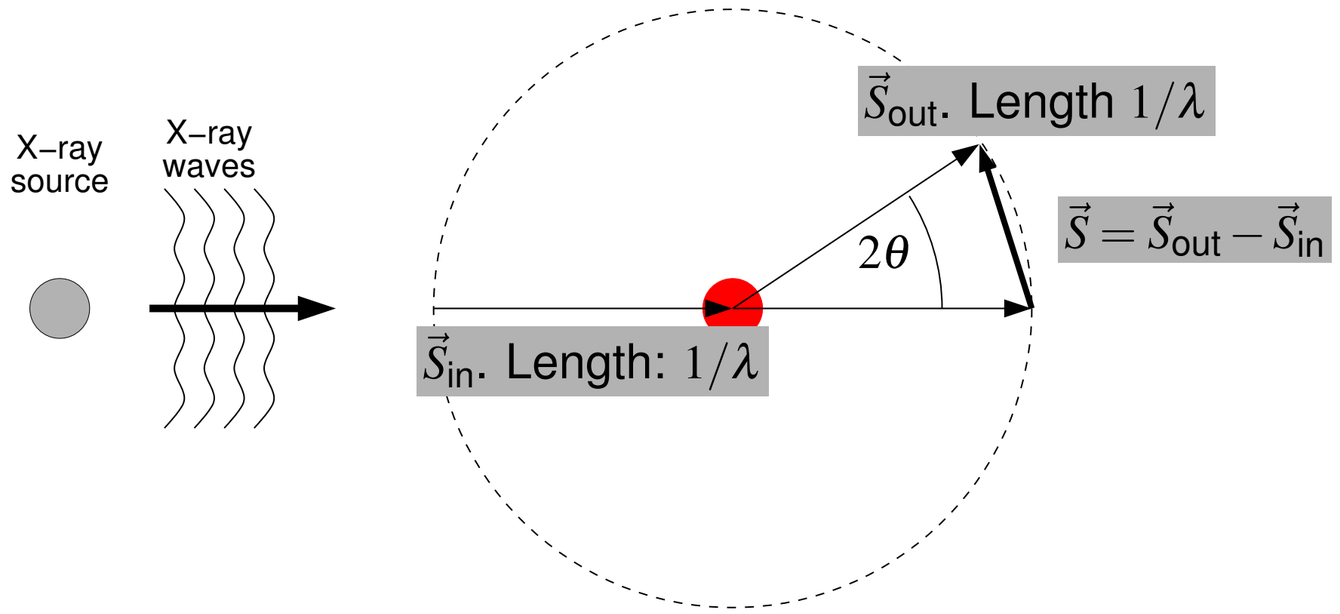
$$\vec{a}\cdot\vec{S} = |\vec{a}||\vec{S}|\cos(\vec{a},\vec{S}) = h$$
$$\vec{b}\cdot\vec{S} = |\vec{b}||\vec{S}|\cos(\vec{b},\vec{S}) = k$$
$$\vec{c}\cdot\vec{S} = |\vec{c}||\vec{S}|\cos(\vec{c},\vec{S}) = l$$

h,k,l: integer numbers ; $\vec{S}$ the *scattering vector*

Laue equations

$$\vec{a}\cdot\vec{S} = |\vec{a}||\vec{S}|\cos(\vec{a},\vec{S}) = h$$
$$\vec{b}\cdot\vec{S} = |\vec{b}||\vec{S}|\cos(\vec{b},\vec{S}) = k$$
$$\vec{c}\cdot\vec{S} = |\vec{c}||\vec{S}|\cos(\vec{c},\vec{S}) = l$$

h,k,l: integer numbers ; $\vec{S}$ the *scattering vector*



Laue equations

$$\vec{a} \cdot \vec{S} = |\vec{a}||\vec{S}| \cos(\vec{a}, \vec{S}) = h$$
$$\vec{b} \cdot \vec{S} = |\vec{b}||\vec{S}| \cos(\vec{b}, \vec{S}) = k$$
$$\vec{c} \cdot \vec{S} = |\vec{c}||\vec{S}| \cos(\vec{c}, \vec{S}) = l$$

The Laue equations describe the geometry of the experiments and reflect the physics of interference:

$\vec{a}, \vec{b}, \vec{c}$**:** Orientation of the crystal

$|\vec{S}_{\mathbf{in}}| = 1/\lambda$**:** wavelength of the experiment

$|\vec{S}_{\mathbf{out}}|$**:** direction, *alias* position at the detector (is there a spot or not?)

h, k, l **integer:** integer multiple of path differences $\Delta = n \cdot \lambda$

Laue equations

- Each scattering vector $\vec{S}$ describes exactly one position on the detector
- Only those positions, that fulfil all three Laue equations at once, will show a reflection
- Each reflection is uniquely described by the triplet of integers (hkl)
- The triplet (h,k,l) is called **the Miller index** of the corresponding reflection (W. H. Miller, 1801–1880)
- The *direct beam* $\vec{S}_{\text{in}}$ coincides with the reflection $(0,0,0)$
- The reflection $(0,0,0)$ cannot be measured!