

# Lecture 6: Diffraction, part 2: The core theory

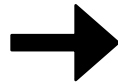
**R. Ranganathan**

Green Center for Systems Biology, ND11.120E

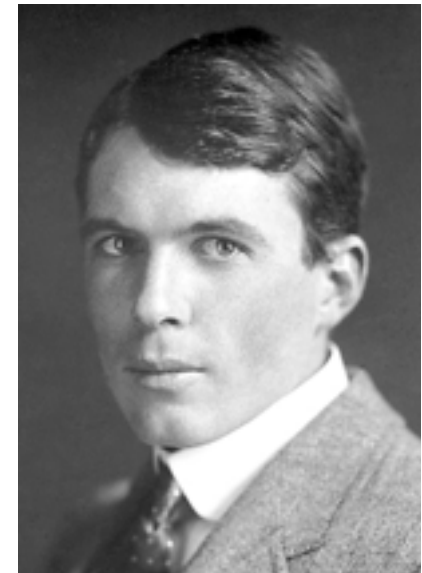
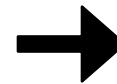
The theory of scattering of light by matter....the basis for x-ray crystallography



Christiaan Huygens  
1629 - 1695



Thomas Young  
1773 - 1829



William Lawrence  
Bragg  
1890 - 1971

## The theory of diffraction

- a. Light as waves ... basic properties
- b. An optical diffraction experiment to build our intuition.
- c. Wave addition and the Argand diagram.
- d. x-ray scattering ... simple to complex structures.
- e. The molecular transform.
- f. x-ray scattering from a crystal of molecules.
- g. The crystal transform.

## The theory of diffraction

Let's start with a quick review of the core concepts from yesterday.

# The theory of diffraction

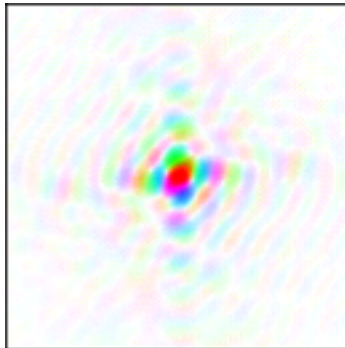
Let's start with a quick review of the core concepts from yesterday.

- ① The goal is to understand how the diffraction pattern stores the information about the object that is scattering photons. We want a general theory that relates the diffraction pattern and the object.

A duck

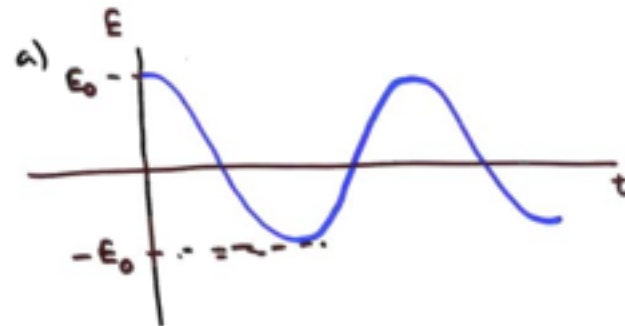


Its diffraction pattern

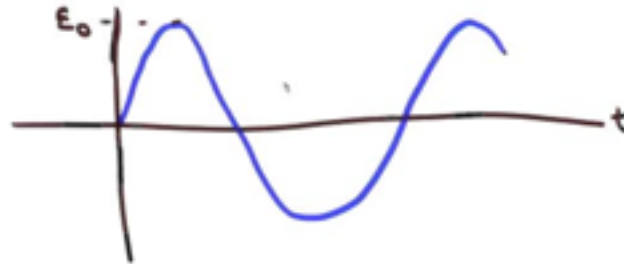


## The theory of diffraction

- (2) Step 1 of understanding scattering of light: Light waves can be represented in several ways:

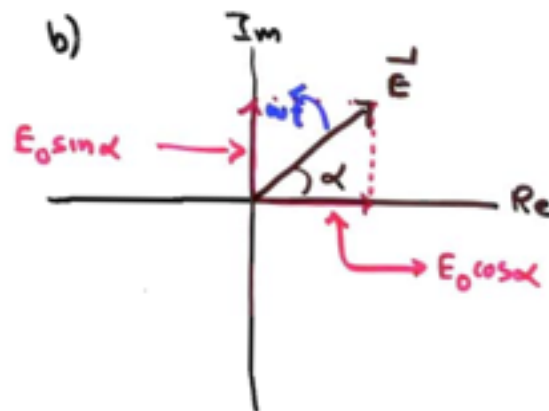
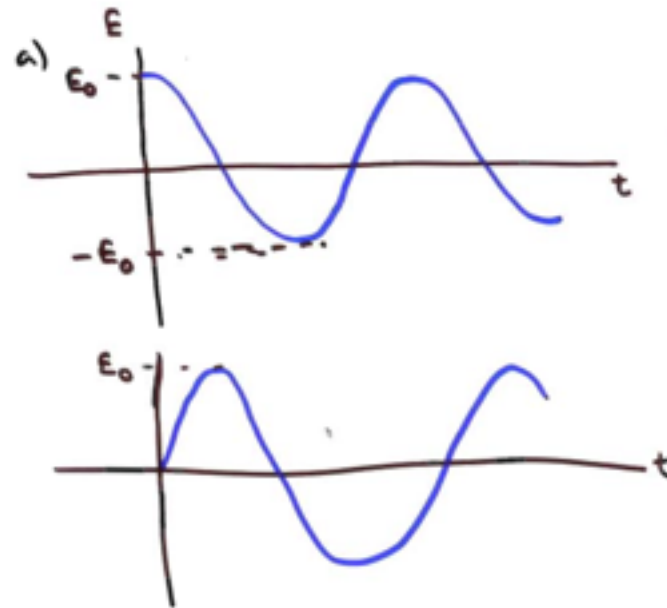


$$E(t) = E_0 \cos(\omega t + \alpha)$$



## The theory of diffraction

- (2) Step 1 of understanding scattering of light: Light waves can be represented in several ways:



The Argand diagram...

## The theory of diffraction

③ Using Euler's theorem:

$$A \cos \alpha + A i \sin \alpha = A e^{+i\alpha}$$

So... a wave of amplitude A and phase angle  $\alpha$  with angular velocity  $\omega t$  is written as:

$$\vec{A} = A e^{i\alpha}$$

....where the angular velocity is represented implicitly

## The theory of diffraction

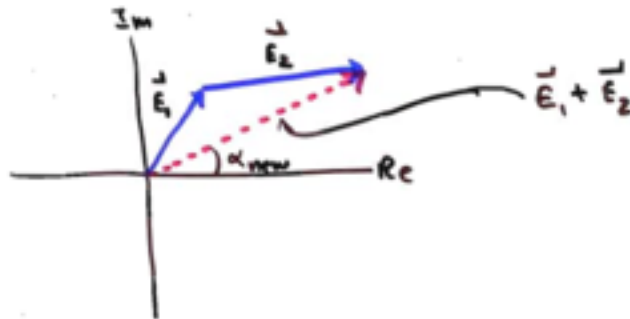
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## The theory of diffraction

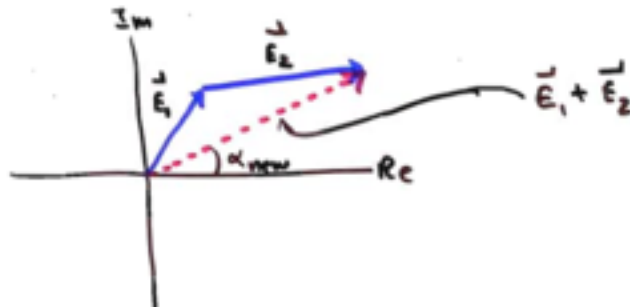
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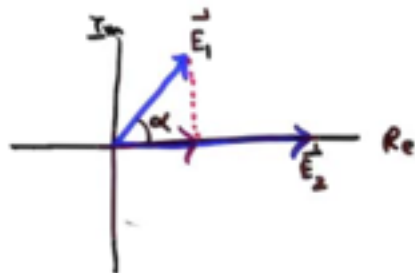
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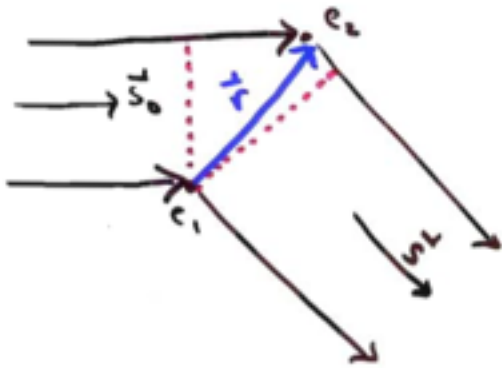
⑤ The projection of one vector onto another ... the dot product.



$$\vec{E}_1 \cdot \vec{E}_2 = |\vec{E}_1| |\vec{E}_2| \cos \alpha$$

## The theory of diffraction

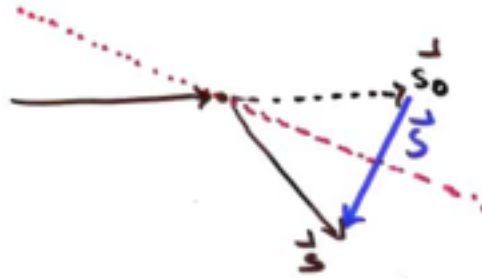
⑥ For a simple system of 2  $e^-$ :



Extra pathlength of wave scattered from  $e_2$  relative to  $e_1$  causes a phase shift:

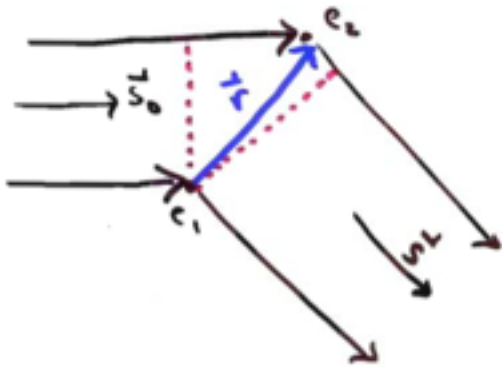
$$\alpha = +2\pi \vec{r} \cdot \vec{S}$$

where  $\vec{S}$  is the scattering vector.



## The theory of diffraction

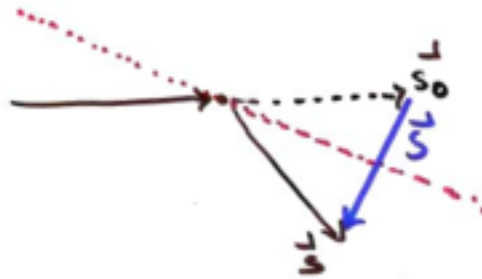
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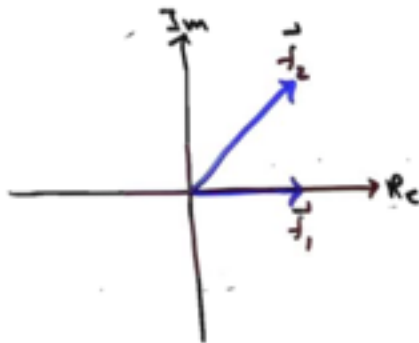
Extra pathlength of wave scattered from  $e_2$  relative to  $e_1$  causes a phase shift:

$$\alpha = +2\pi \vec{r} \cdot \vec{S}$$

where  $\vec{S}$  is the scattering vector.



⑦ From this we conclude that the total scattering in direction  $\vec{S}$  is the addition of the x-ray scattered by  $e_1$  and that scattered by  $e_2$ :



$$\vec{F}(s) = f_1 e^{+2\pi i \vec{r}_1 \cdot \vec{S}} + f_2 e^{+2\pi i \vec{r}_2 \cdot \vec{S}}$$

This is the so-called structure factor equation for this little structure of two electrons.

## The theory of diffraction

⑧ for  $n$  electrons:

$$\vec{F}(s) = \sum_n f_n e^{+2\pi i \cdot \vec{r}_n \cdot \vec{S}}$$

The structure factor depends on two things for <sup>each</sup> electron:  $\vec{r}$ , the distance and direction from the origin, and  $\vec{S}$ , the scattering angle. These go into changing the phase of the scattered ray.

## The theory of diffraction

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What about the structure factor amplitude?

## The theory of diffraction

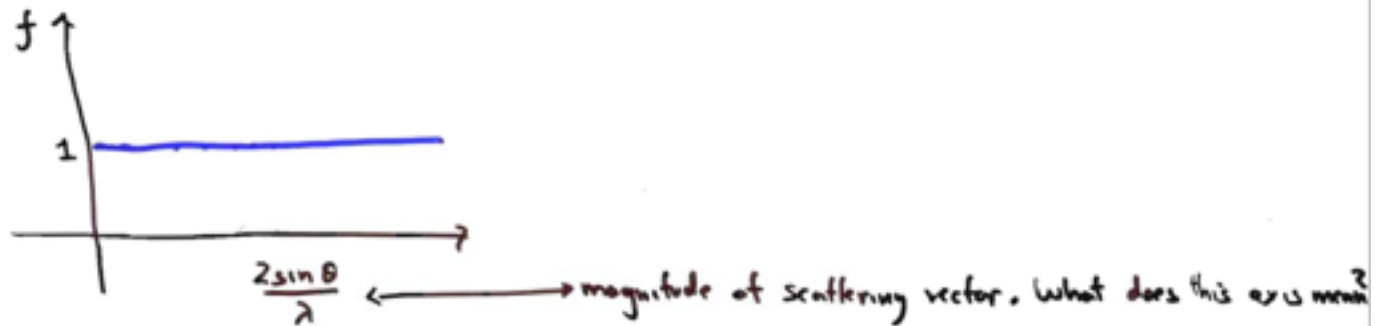
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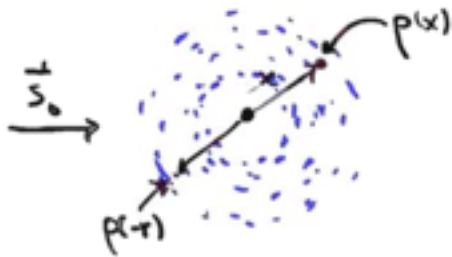
What about the structure factor amplitude?

Well... for a free electron, it is constant ... that is scattering is equal in intensity at all angles.



## The theory of diffraction

Of course ... atoms are more complex. They have clouds of  $e^-$  density surrounding the nucleus ... and have different numbers of  $e^-$  if different types of atoms.



So ... scattering from an atom is more complicated in only one way we need to worry about now ... that is the scattering intensity is not constant with scattering angle. It depends like this ...

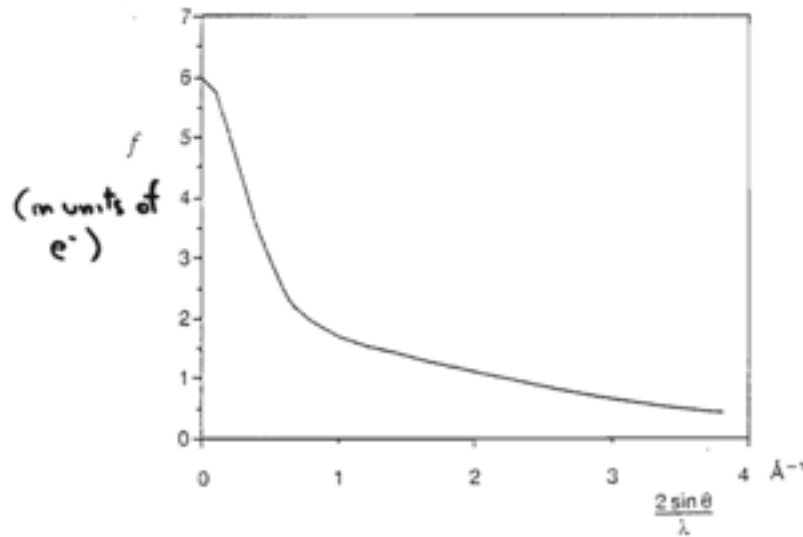


Figure 4.11. The scattering factor  $f$  for a carbon atom as a function of  $2(\sin \theta/\lambda)$ .  $f$  is expressed as electron number and for the beam with  $\theta = 0$ ,  $f = 6$ .

## The theory of diffraction

Such graphs are available for all atoms in standard tables.

So for atom  $i$ :

$$\vec{F}_i(s) = f_i e^{+2\pi i \vec{r}_i \cdot \vec{S}}$$

where now  $f_i$  itself depends on the scattering vector  $\vec{S}$ .



# The theory of diffraction

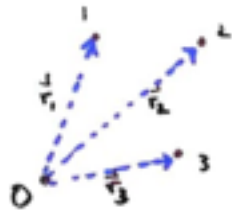
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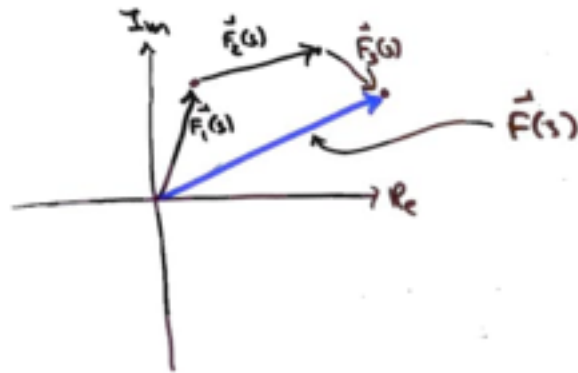
What about a more complex molecule of 3 atoms?



well, each atom will scatter as above, and the net result is:

$$\vec{F}(s) = f_1 e^{+2\pi i \vec{r}_1 \cdot \vec{S}} + f_2 e^{+2\pi i \vec{r}_2 \cdot \vec{S}} + f_3 e^{+2\pi i \vec{r}_3 \cdot \vec{S}}$$

In an Argand diagram:



$$\vec{F}(s) = \sum_i f_i e^{+2\pi i \vec{r}_i \cdot \vec{S}}$$

This is the molecular structure factor

## The theory of diffraction

$$\vec{F}(s) = \sum_i f_i e^{+2\pi i \vec{r}_i \cdot \vec{s}}$$

This is the molecular structure factor

...the relationship between real space (defined by  $r$ ) and the diffraction pattern (Fourier space, reciprocal space,  $S$  space).

This is the **spatial Fourier transform**, and its inverse gives us the basis of reconstructing the object from the diffraction pattern...

## The theory of diffraction

To see this ... we write the structure factor equation in a slightly different way:

$$\vec{F}(s) = \sum_{\substack{\text{points } j \\ \text{in space}}} \rho(j) e^{2\pi i \vec{r}_j \cdot \vec{s}}$$

$\rho(j)$  is the electron density at the  $j^{\text{th}}$  point in space.

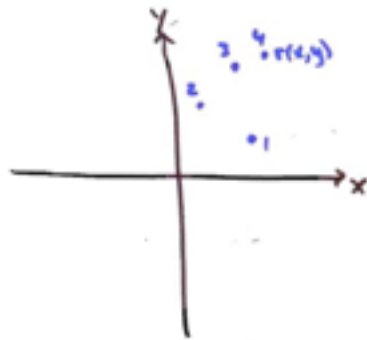
Then the inverse relationship is this:

$$\rho(j) = \sum_{\substack{\text{points } k \\ \text{in } S \text{ space}}} F_k(s) e^{-2\pi i \vec{r}_k \cdot \vec{s}}$$

So... if we know the amplitude of scattering at every point in "S space", and if we know each associated phase angle, then we can reconstruct the electron density at every point  $j$  in real space.

# The theory of diffraction

So now we can understand the diffraction pattern space (or S space, <sup>?</sup>  
or Fourier space,  
or reciprocal space)



[real space]  
dimensions are distance



[reciprocal space]  
dimensions are spatial frequency

# The theory of diffraction

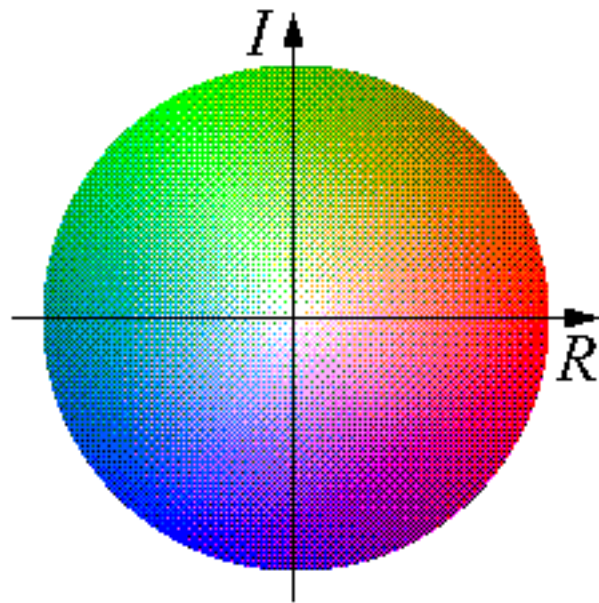
forward...

$$\vec{F}(s) = \sum_{\substack{\text{points } j \\ \text{in space}}} p(j) e^{2\pi i \vec{r}_j \cdot \vec{s}}$$

reverse...

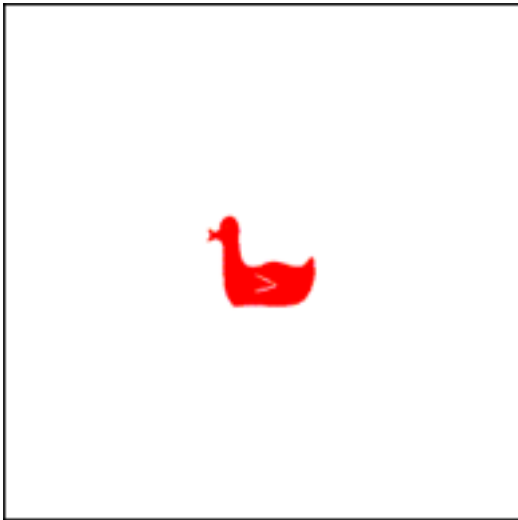
$$p(j) = \sum_{\substack{\text{points } k \\ \text{in } S \text{ space}}} F_k(s) e^{-2\pi i \vec{r}_k \cdot \vec{s}}$$

# Reciprocal Space

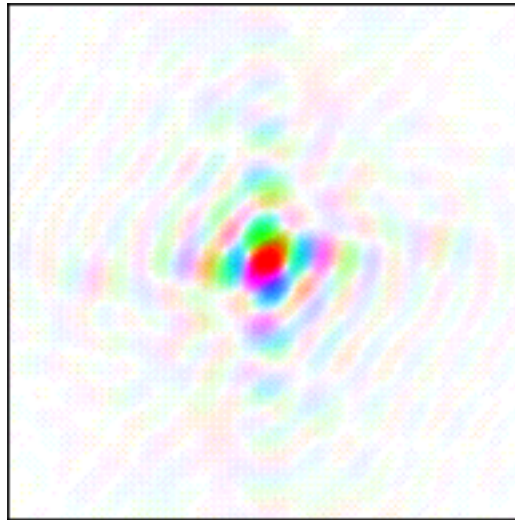


A duck....

Real space



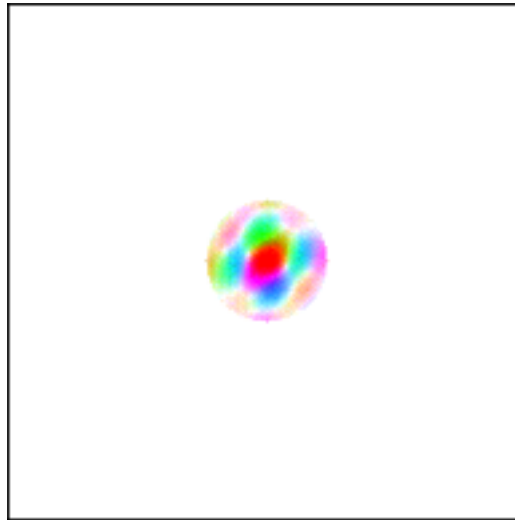
Fourier space



The low scattering angle information from the duck....

Real space

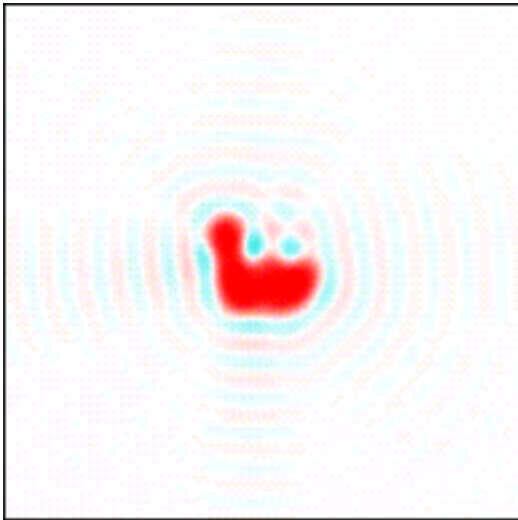
Fourier space



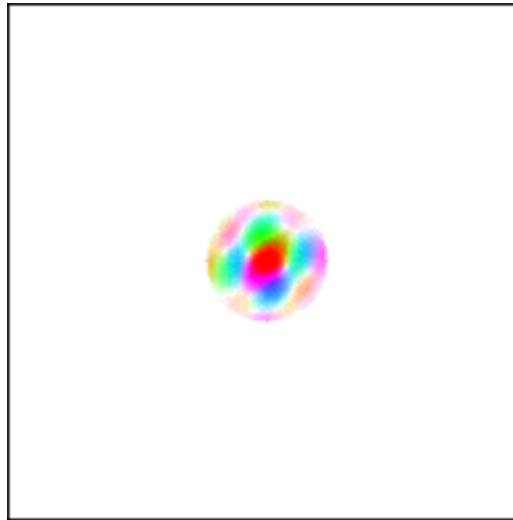


A low-resolution duck....

Real space



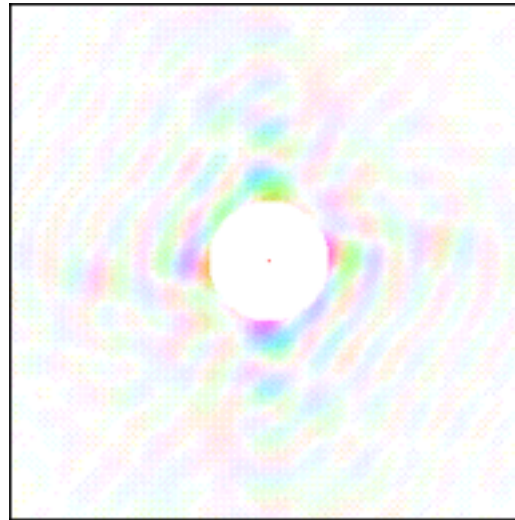
Fourier space



The high scattering angle information from the duck....

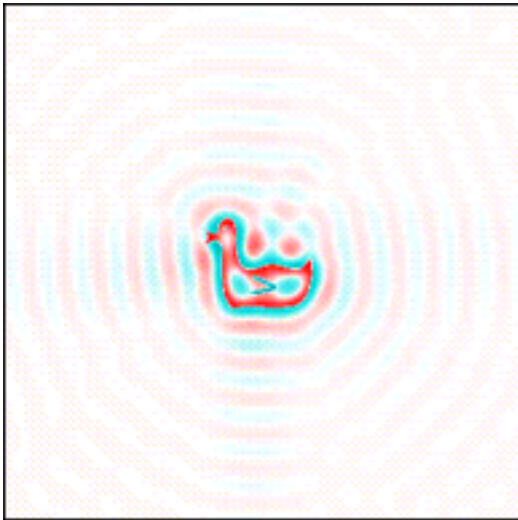
Real space

Fourier space

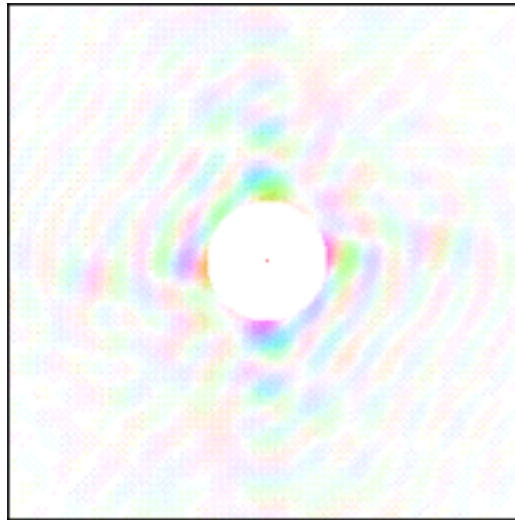


High spatial frequency duck....

Real space



Fourier space



Now ... for two big depressing problems ...

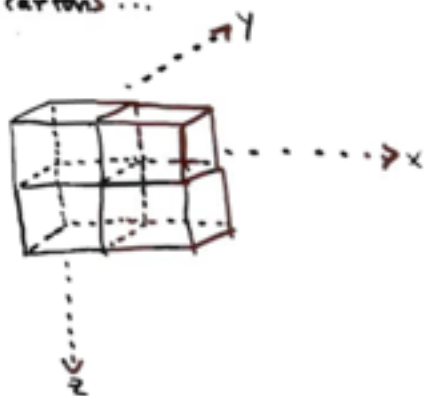
- ① we cannot practically collect the diffraction pattern of a single molecule.  
Too weak ... so how can we solve structures?
- ② we do not directly get any phases in protein crystallography. All we get are amplitudes!

So... crystals.

If we grow an ordered array of molecules (i.e. a crystal) we can measure the diffraction pattern of the crystal! Why? And how can we get the molecular structure out of it?

A crystal is a 3-D array of molecules. But let's think of it as a 3-D array of unit cells, each of which contains one molecule (or molecules).

Like egg cartons...



One unit cell :



The unit cell (in the most general case) is defined by a maximum of 6 parameters :

$a, b, c$  [unit cell dimensions]

$\alpha, \beta, \gamma$  [unit cell angles]

Translation of the unit cell by distance  $a, b, \text{ or } c$ , in directions  $a, b, \text{ or } c$  respectively causes the unit cell and its contents to be exactly repeated.

This is the simplest case of crystallographic symmetry.

Very often there is more symmetry in crystals ... but not important for now.

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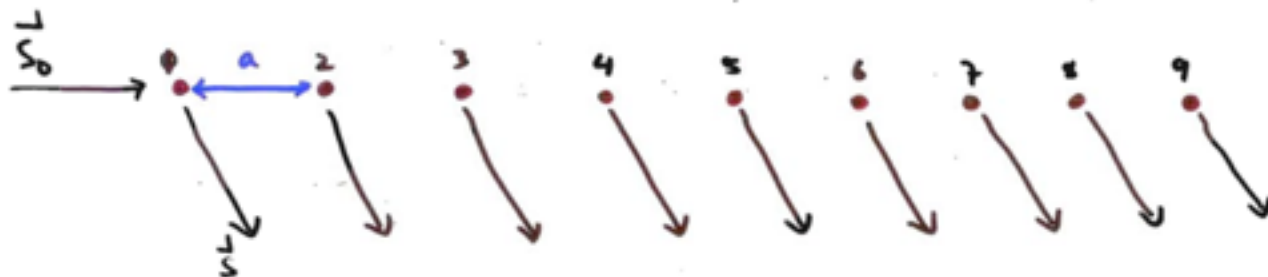
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How does the crystal amplify the diffraction pattern? And what are the rules of this?

# The Laue diffraction condition...

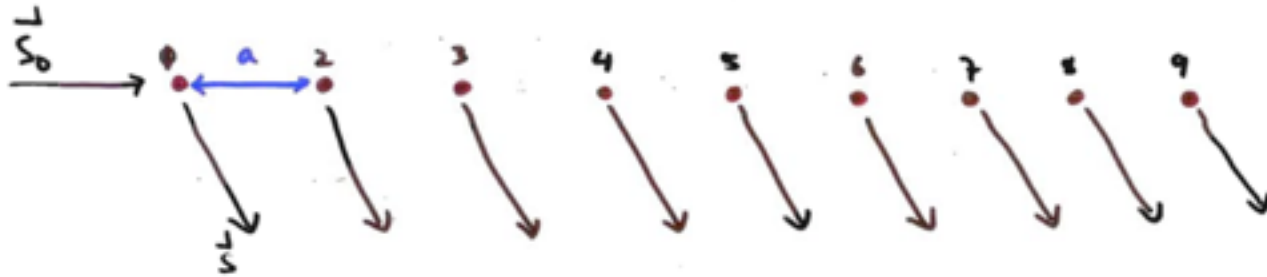
lets consider a one-dimensional crystal to start with. The unit cell dimension is  $a$ ; there is one scattering object in each unit cell (the dot)





## The Laue diffraction condition...

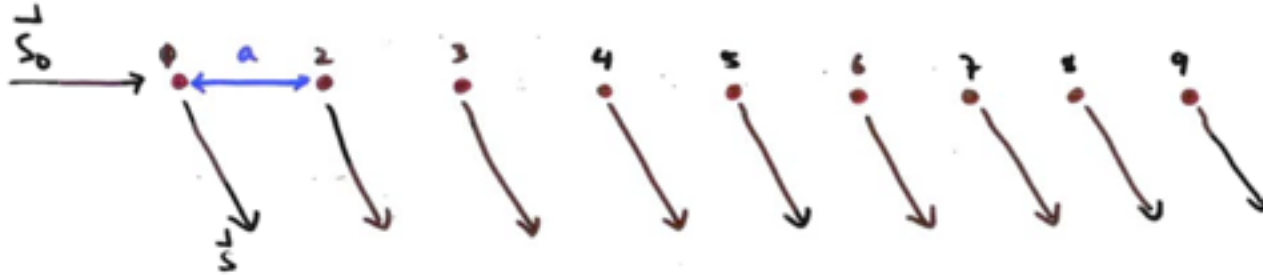
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## The Laue diffraction condition...

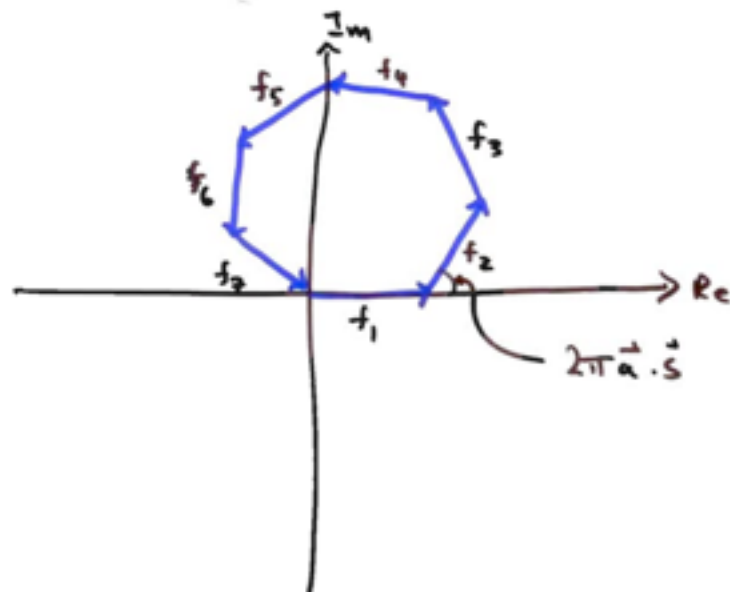
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- ① The first unit cell is taken as the origin. Each scattering direction  $\vec{S}$  will contain an intensity of diffraction equal to the sum of all diffracted rays from each unit cell.
- ② Each unit cell is displaced by distance  $a$ . So ... the diffracted ray is phase shifted by  $2\pi \vec{a} \cdot \vec{S}$

Let's look at the consequence using the Argand diagram...

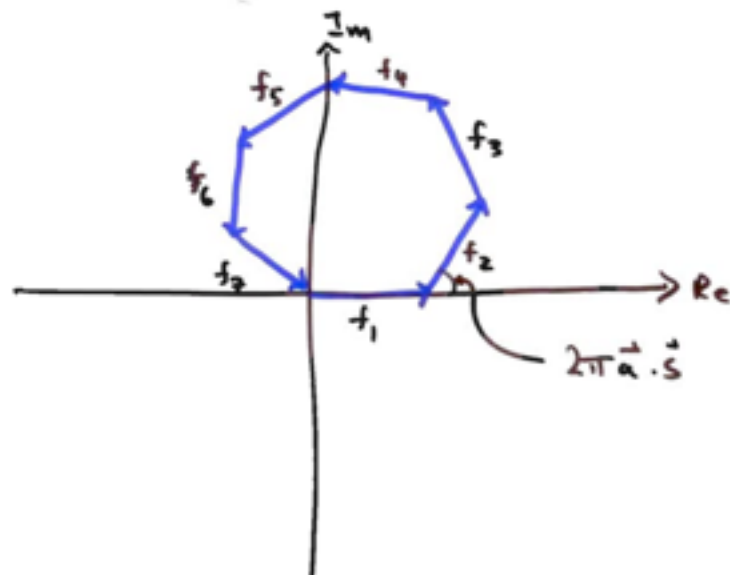
In the Argand diagram:



Do you see that for nearly every direction  $\vec{S}$ , the net diffraction is close to zero?

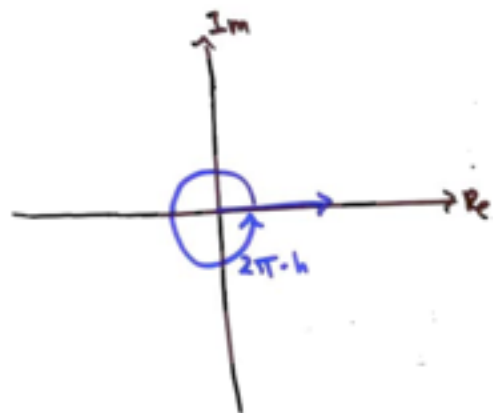
But at what special condition of phase will the scattering from unit cells constructively add up?

In the Argand diagram:



Do you see that for nearly every direction  $\vec{S}$ , the net diffraction is close to zero?

But at what special condition of phase will the scattering from unit cells constructively add up?



Well, when the phase is integer multiple of  $2\pi$ ! ...  $h = 1, 2, 3, \dots$

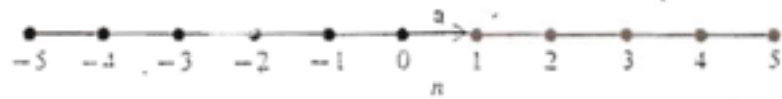
So... the condition for constructive addition is when

$$h \cdot 2\pi = 2\pi \vec{a} \cdot \vec{S}$$

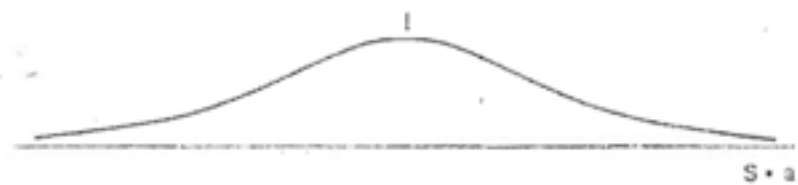
or...

$$\vec{a} \cdot \vec{S} = h$$

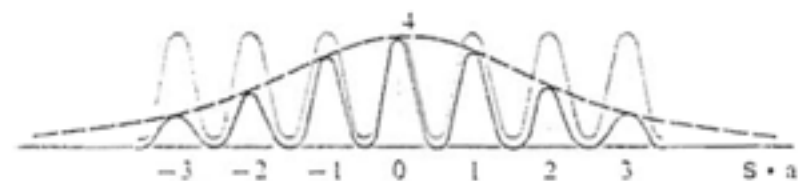
This is a fundamental result called the Laue diffraction condition for a crystal.



(a)

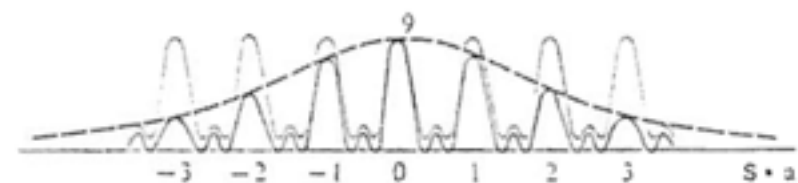


1 atom at origin

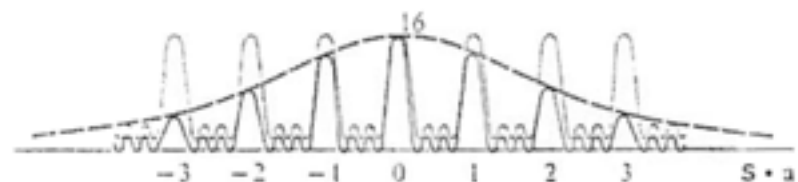


2 atoms, at  $-a/2$  and  $+a/2$

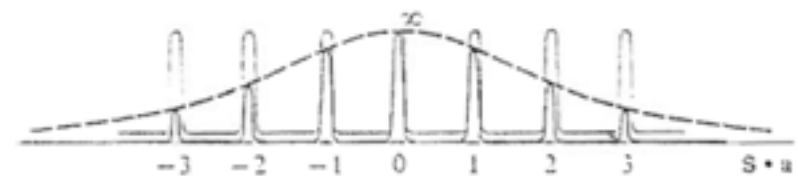
Intensity  $\uparrow$



3 atoms, at  $-a, 0,$  and  $+a$

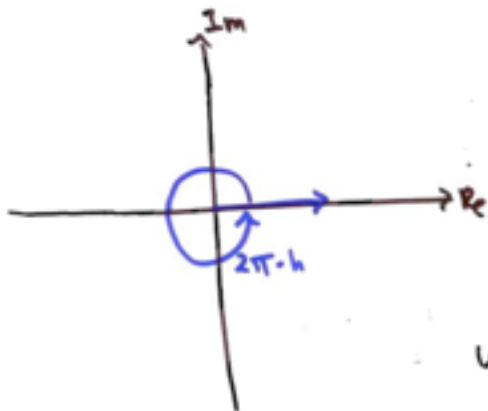
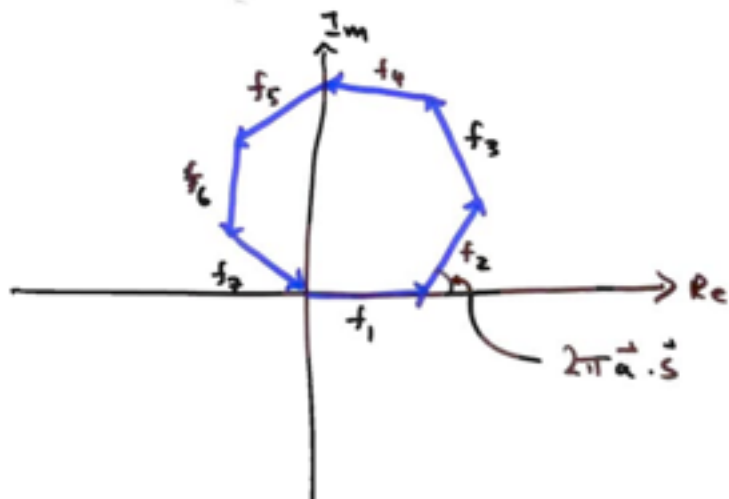


4 atoms, at  $-(3/2)a, -(1/2)a,$   
 $+(1/2)a,$  and  $+(3/2)a$



An infinite row of atoms

(b)



What does it mean?

- ① Diffraction in most scattering directions is close to zero for a periodic crystal.
- ② Diffraction is strong at the Bragg condition, and only strong there.

For a 3-D crystal ... the Laue conditions are:

$$\begin{array}{l} \vec{a} \cdot \vec{S} = h \\ \vec{b} \cdot \vec{S} = k \\ \vec{c} \cdot \vec{S} = l \end{array}$$

where  $\vec{a}$ ,  $\vec{b}$ , and  $\vec{c}$  are the unit cell vectors, and  $\vec{S}$  is a scattering vector.

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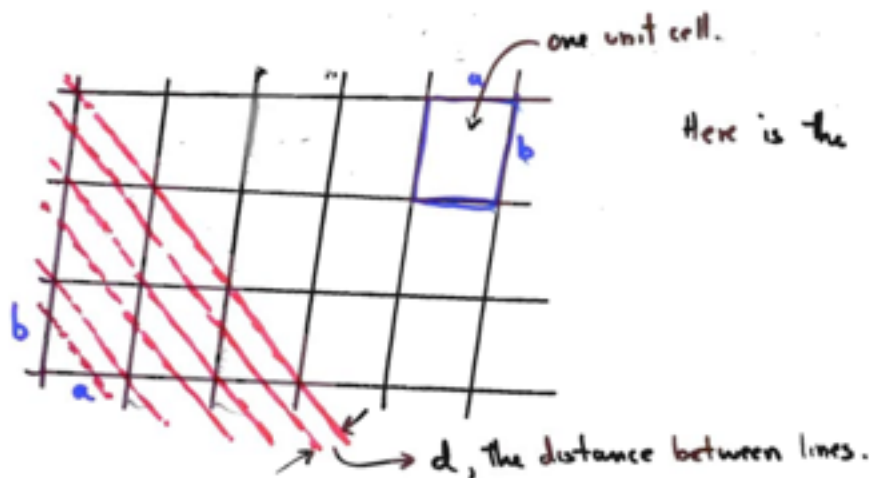
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where  $\vec{a}$ ,  $\vec{b}$ , and  $\vec{c}$  are the unit cell vectors, and  $\vec{S}$  is a scattering vector.

Another way to write the Laue conditions is:

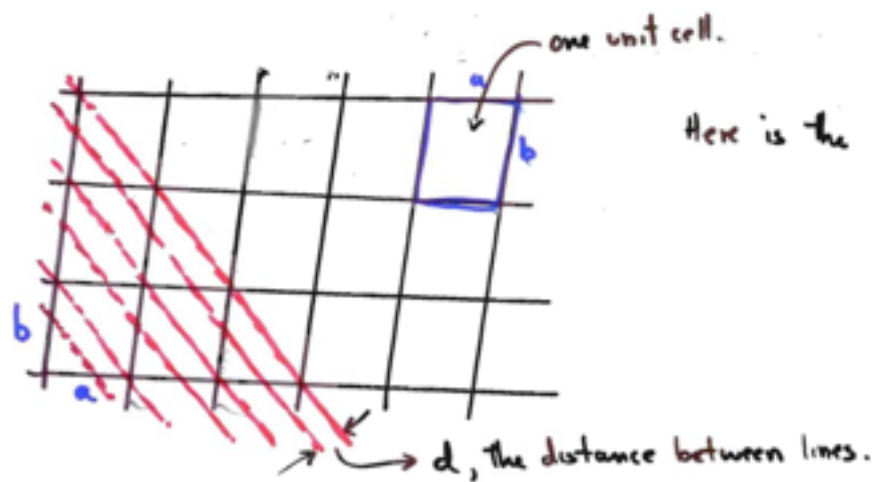
$$\frac{\vec{a}}{h} \cdot \vec{S} = 1 \quad \frac{\vec{b}}{k} \cdot \vec{S} = 1 \quad \frac{\vec{c}}{l} \cdot \vec{S} = 1$$

So ...  $h$ ,  $k$ , and  $l$  are integer divisions of each unit cell dimension. In 2-D:



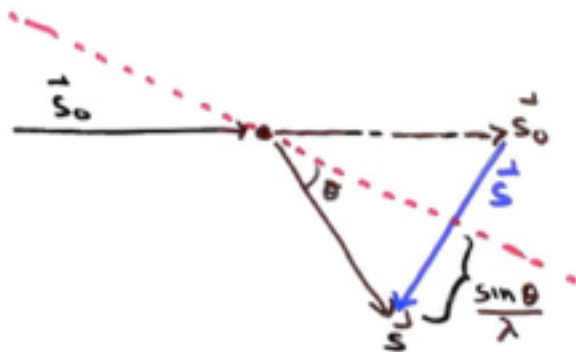
Here is the case of  $h=2$ ,  $k=2$





Lets look at diffraction as if it were reflections coming from these parallel planes ...

Remember we said that diffraction could be seen this way?



where  $\theta$  is the scattering angle. Thus,

$$|\vec{s}'| = \frac{2 \sin \theta}{\lambda}$$

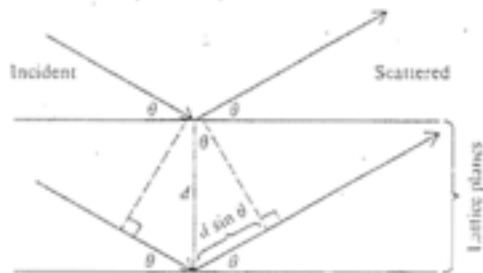
Lets' look at two adjacent planes...



The bottom ray travels an extra distance of  $2d \sin \theta$ . When this distance is equal to one wavelength of x-ray, they will constructively interact and add up. So...

$$2d \sin \theta = \lambda \quad \text{Bragg's Law.}$$

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or...

$$\frac{2 \sin \theta}{\lambda} = \frac{1}{d}$$

or...

$$|\vec{S}| = \frac{1}{d}$$

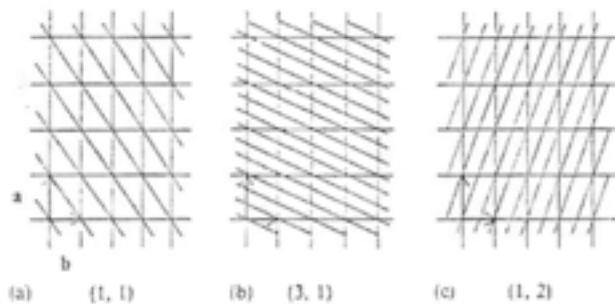
... this demonstrates what we said earlier. Smaller spacings with the unit cell, which have smaller  $d$  and higher resolution, are associated with larger  $|\vec{S}|$  ... that is greater angle of scattering.

Consistency with Laue conditions (in just one dimension, for clarity...)

$\vec{a} \cdot \vec{S} = h$  or ... that conditions for constructive interference from a crystal are ...

$$d = \frac{a}{h}$$

In fact, there are many (an infinite) number of such planes that can be created.



Note: As  $h, k, l$  increase, we are cutting each unit cell into more divisions, and ~~the~~ thus into finer spatial resolution.

$h, k, l$  are called Miller indices.

So... the crystal is an amplifier of the molecular transform. What we get is the molecular transform sampled at all the places in reciprocal space that satisfy the Laue diffraction conditions.

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This diffraction pattern allows us to solve the structure of the unit cell (and its contents). What we must know is the intensity of diffraction at each spot (the amplitude) and the phase of every spot.

The crystal transform:

$$F(hkl) = \sum_{\substack{\text{real space} \\ x, y, z}} \rho(x, y, z) e^{2\pi i(hx + ky + lz)}$$

The inverse transform

$$\rho(x, y, z) = \sum_{h, k, l} F(h, k, l) e^{-2\pi i(hx + ky + lz)}$$

Now ... for two big depressing problems ...

- ① we cannot practically collect the diffraction pattern of a single molecule.  
Too weak.... so how can we solve structures?
- ② we do not directly get any phases in protein crystallography. All we get are amplitudes!

---

$$P(\mathbf{s}) = \sum_{\substack{\text{points } \mathbf{k} \\ \text{in } S \text{ space}}} F_{\mathbf{k}}(\mathbf{s}) \cdot e^{-2\pi i \mathbf{r}_{\mathbf{k}} \cdot \mathbf{s}}$$

The famous "phase problem"....

## The phase problem...

$$P(x, y, z) = \frac{1}{V} \sum_{hke} |F(hke)| e^{-2\pi i (hx + ky + ez) + i \alpha(hke)}$$

So... we need  $|F(hke)|$  and  $\alpha(hke)$  to compute the structure.  
We only get  $|F(hke)|$ !

Why not  $\alpha(hke)$ ?



## The phase problem...

well let's see ... what kind of time resolution do we need to directly measure phases? well, to accurately measure some fraction of  $2\pi$  radians, we need sub- $\lambda$  time resolution.

For a Cu K $\alpha$  photon ...  $\lambda = 1.542 \text{ \AA} \Rightarrow \nu \sim 2 \times 10^{18} \text{ Hz}$

So we would need time resolution around  $10^{-19} \text{ s}$ !

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So... how can we do this?

- (1) The **Patterson** synthesis
- (2) The technique of **isomorphous replacement**
- (3) The technique of **multi wavelength anomalous dispersion**

Next, we consider the general analysis of systems with many parameters....

	$n = 1$	$n = 2$ or $3$	$n \gg 1$	continuum
Linear	exponential growth and decay	second order reaction kinetics	electrical circuits	Diffusion
	single step conformational change	linear harmonic oscillators	molecular dynamics	Wave propagation
	fluorescence emission	simple feedback control	systems of coupled harmonic oscillators	quantum mechanics
	pseudo first order kinetics	sequences of conformational change	equilibrium thermodynamics	viscoelastic systems
Nonlinear	fixed points	anharmonic oscillators	systems of non-linear oscillators	Nonlinear wave propagation
	bifurcations, multi stability	relaxation oscillations	non-equilibrium thermodynamics	Reaction-diffusion in dissipative systems
	irreversible hysteresis	predator-prey models	protein structure/function	Turbulent/chaotic flows
	overdamped oscillators	van der Pol systems	neural networks	
		Chaotic systems	the cell	
			ecosystems	