生体分子構造解析学特論

シンクロトロン光研究センター
渡邉 信久

第5回

講義スケジュール

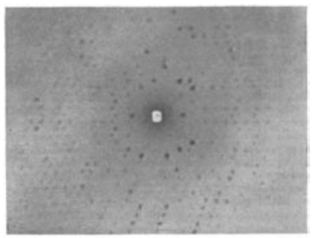
- 1：混沌の時代から繊維写真の時代
- 2：サイクロール説
- 3：二次構造の解明
- 4：DNAの構造
- 5：結晶構造解析法の発展
- 6：高分解能構造解析の始まり

蛋白質結晶学の胎動

1926
urease の結晶
JB Sumner

1930's
消化酵素群 の結晶
J Northrop

ヘモグロビンの結晶の回折写真



Bernal, Fankuchen & Perutz, Nature (1938) 141, 523

JD Bernal の決断
@ Cavendish

"X線で結晶中の蛋白質を観察する"

→ 3人の若手

D. Crowfoot (Hodgkin)
Max Perutz
Isidor Fankuchen

→ ブレークスルー

蛋白質結晶の
キャピラリー封入

How to solve a protein structure

history of the MIR phasing method

key paper

hemoglobin sagaの一報目

An X-ray study of horse methaemoglobin. I

By Joy Boyes-Watson, Edna Davidson and M. F. Perutz

Cavendish Laboratory and Molteno Institute, University of Cambridge

(*Communicated by Sir Lawrence Bragg, F.R.S.—Received 3 February* 1947)

Proc. Roy. Soc. London (1947) A191, 83-132

myoglobin の3次元構造速報

A THREE-DIMENSIONAL MODEL OF THE MYOGLOBIN MOLECULE OBTAINED BY X-RAY ANALYSIS

By Drs. J. C. KENDREW, G. BODO, H. M. DINTZIS, R. G. PARRISH and H. WYCKOFF

Medical Research Council Unit for Molecular Biology, Cavendish Laboratory, Cambridge

AND

D. C. PHILLIPS

Davy Faraday Laboratory, The Royal Institution, London

Nature (1958) 181, 662-666

myoglobin の3次元構造解析

The crystal structure of myoglobin

V. A low-resolution three-dimensional Fourier synthesis of sperm-whale myoglobin crystals

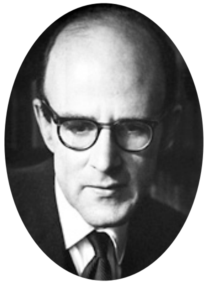
By G. Bodo, H. M. Dintzis, J. C. Kendrew and H. W. Wyckoff

Medical Research Council Unit for Molecular Biology, Cavendish Laboratory, University of Cambridge

(*Communicated by Sir Lawrence Bragg, F.R.S.—Received 22 April* 1959)

Proc. Roy. Soc. London (1959) A253, 70-102

Perutz and Kendrew



〜1938 M. Perutz

hemoglobin @1959

〜1947 JC Kendrew

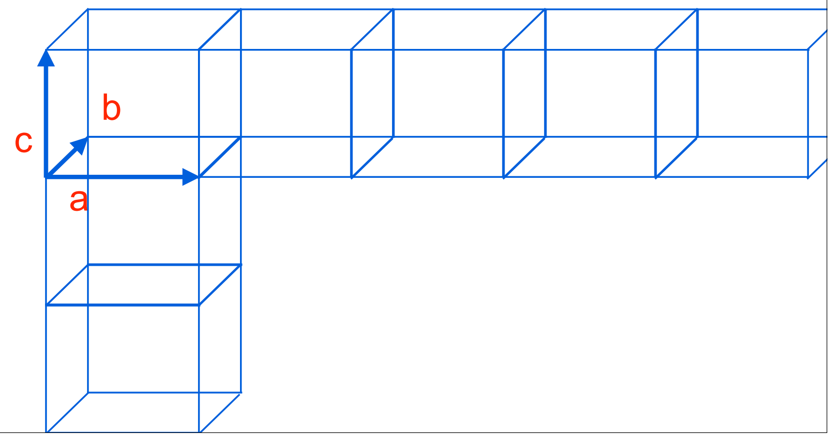
@1957 myoglobin

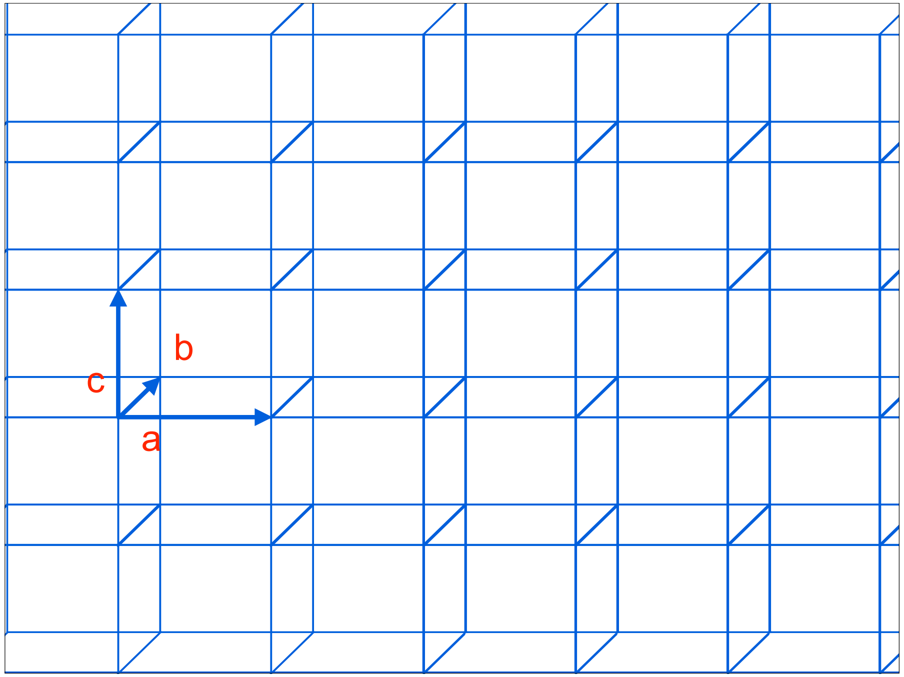
the diffraction pattern of a crystal is its Fourier transform

three-dimensional image of the crystal has been broken down into component sinusoidal waves

crystal & diffraction pattern

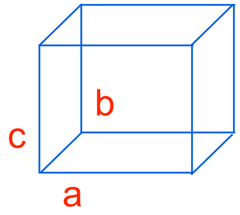
unit cell: a, b and c

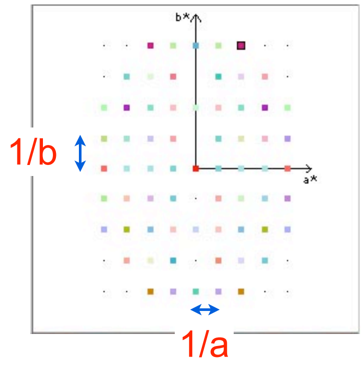




crystal & diffraction pattern

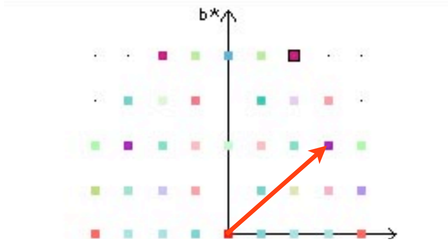
unit cell: a, b and c





diffraction pattern: 1/a, 1/b and 1/c

diffraction spots & waves in the Fourier synthesis



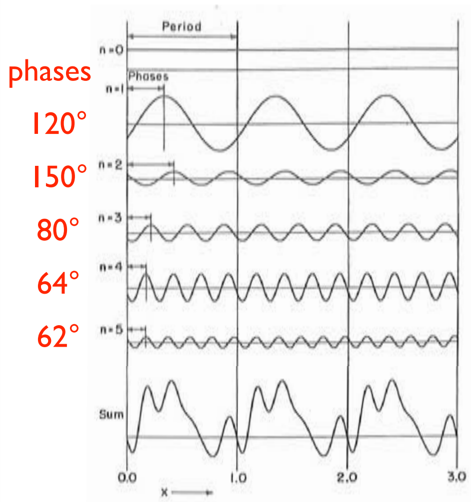
vector to the spot ⟷ direction of the wave

distance to the spot ⟷ wavelength of the wave

intensity of the spot ⟷ amplitude of the wave

no information... ⟷ phase shift of the wave

diffraction spots & waves in the Fourier synthesis



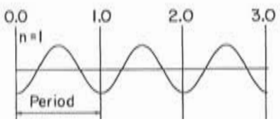
(direction of the wave)

wavelength of the wave

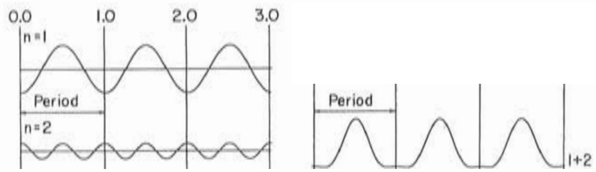
amplitude of the wave

phase shift of the wave

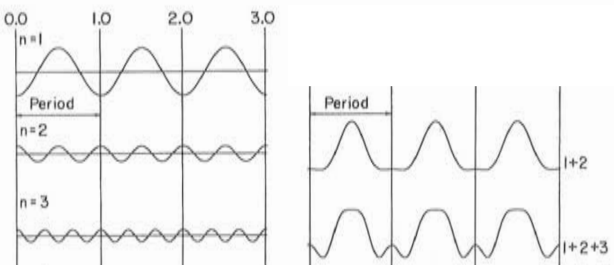
Fourier synthesis & resolution



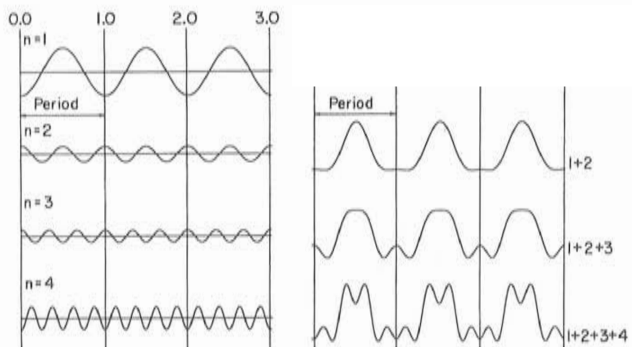
Fourier synthesis & resolution



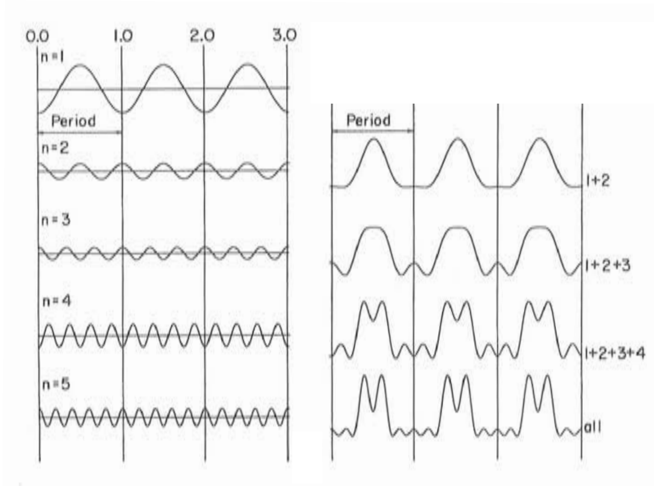
Fourier synthesis & resolution



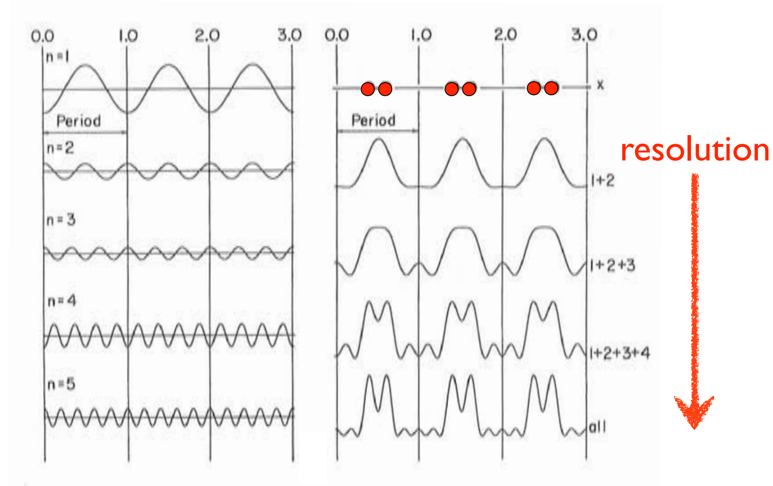
Fourier synthesis & resolution



Fourier synthesis & resolution

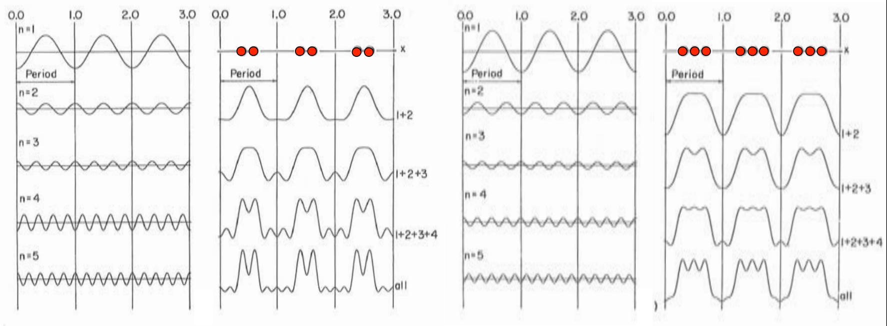


Fourier synthesis & resolution

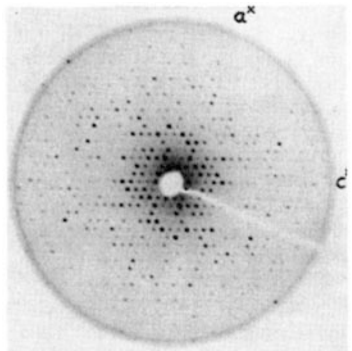


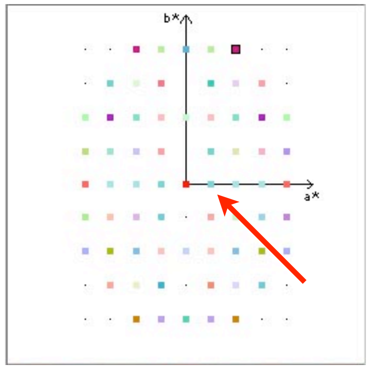
Fourier synthesis

amplitude & phases

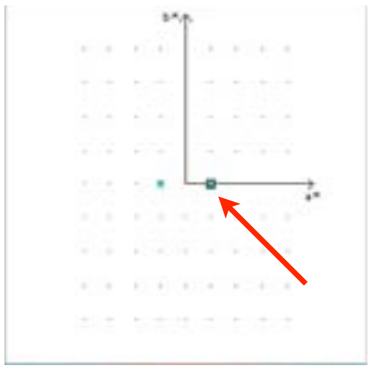


diffraction pattern & Fourier component

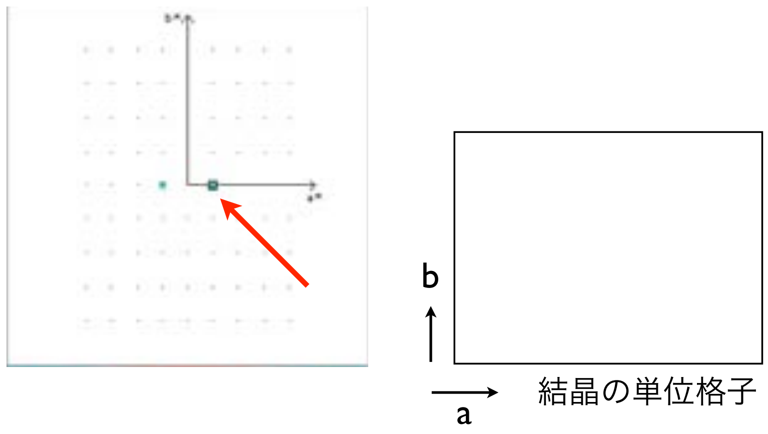




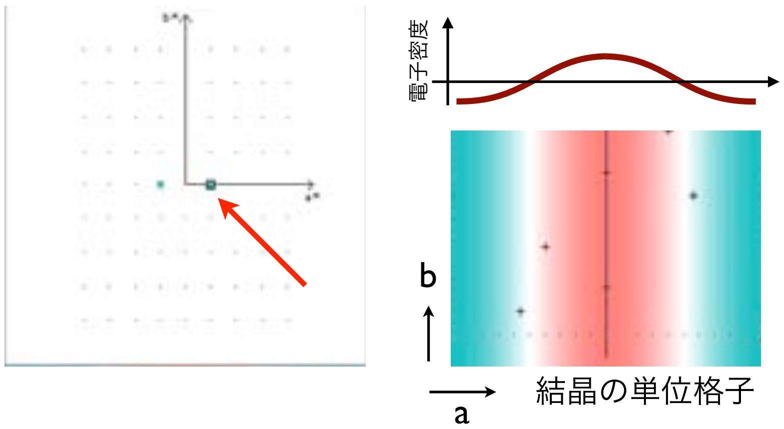
diffraction pattern & Fourier component



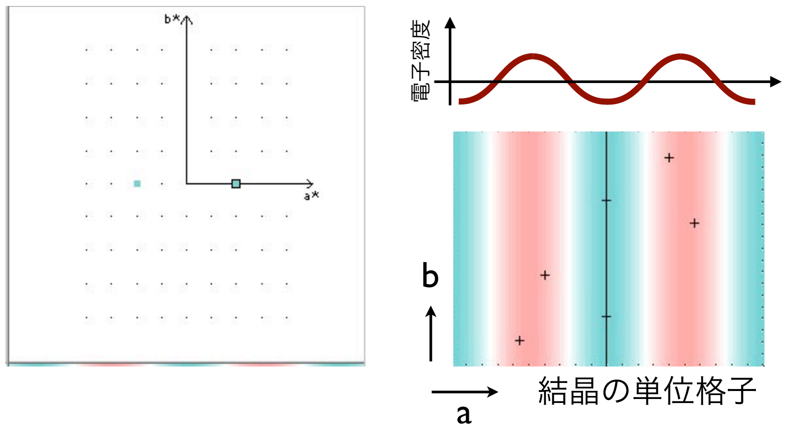
diffraction pattern & Fourier component



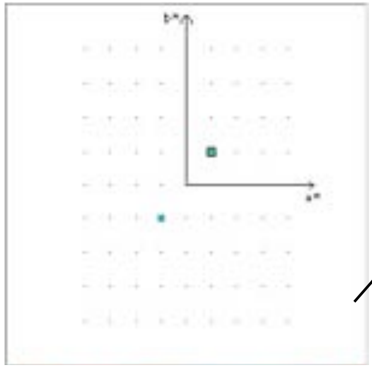
diffraction pattern & Fourier component

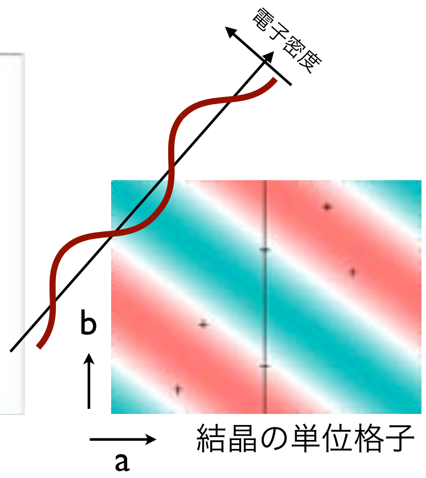


diffraction pattern & Fourier component

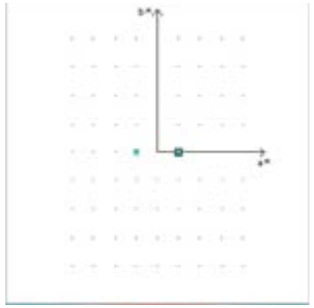


diffraction pattern & Fourier component

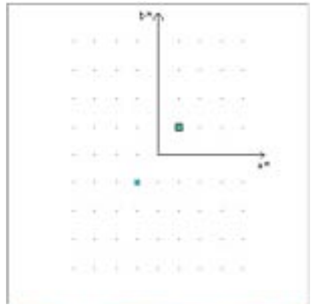




Fourier synthesis

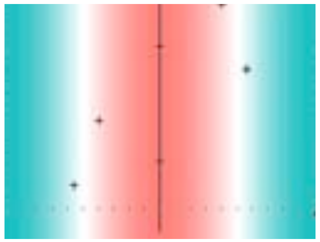


+

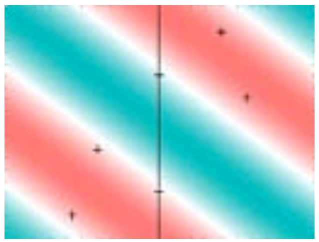


=

Fourier synthesis



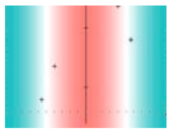
+



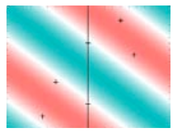
=

電子密度分布の周期成分の足し算

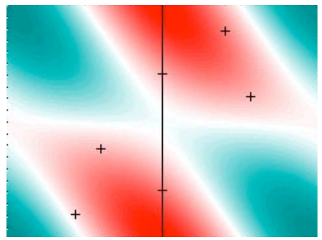
Fourier synthesis



+

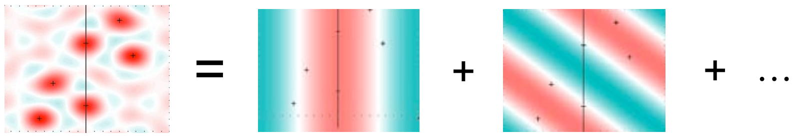


=



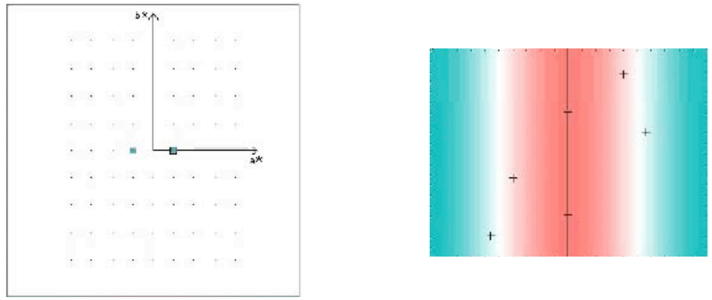
Fourier synthesis

$$\rho(x,y,z) = \sum_h \sum_k \sum_l \mathbb{F}_{hkl} e^{-2\pi i(hx+ky+lz)}$$

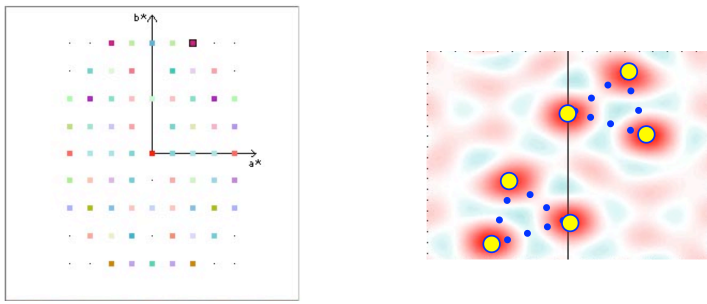


$\mathbb{F}_{10}$ $\mathbb{F}_{11}$

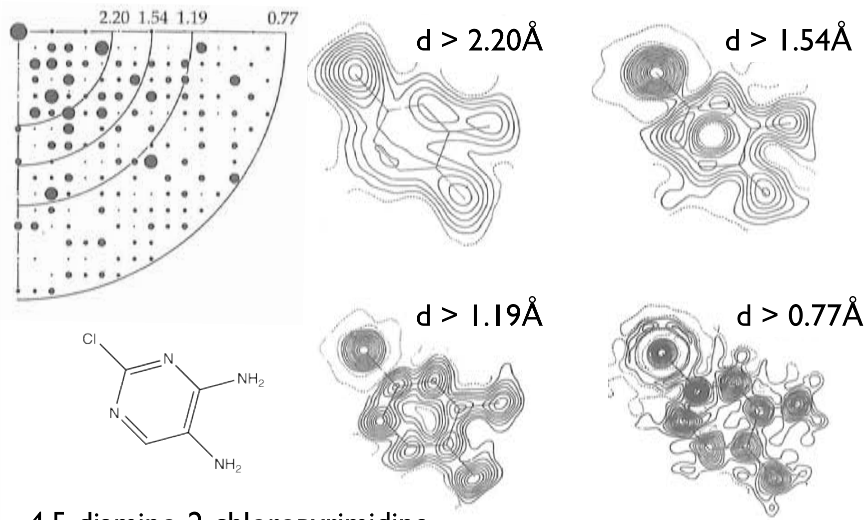
Fourier synthesis



Fourier synthesis



resolution & electron density map

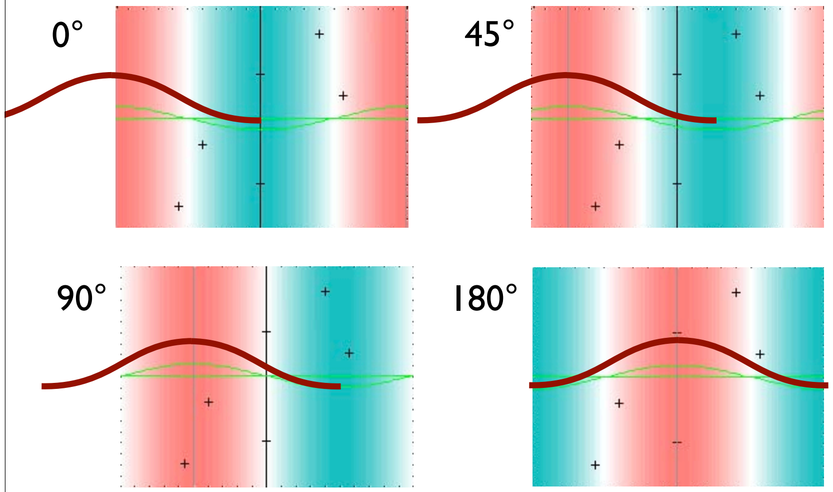


4,5-diamino-2-chloropyrimidine

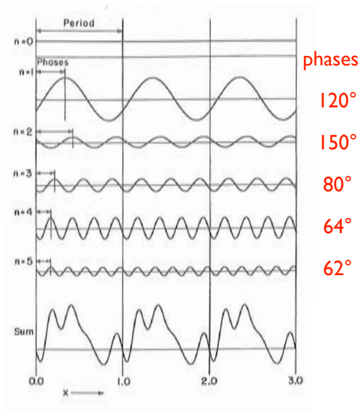
phase problem

the phase angle of each Fourier wave is lost in the diffraction pattern

phase

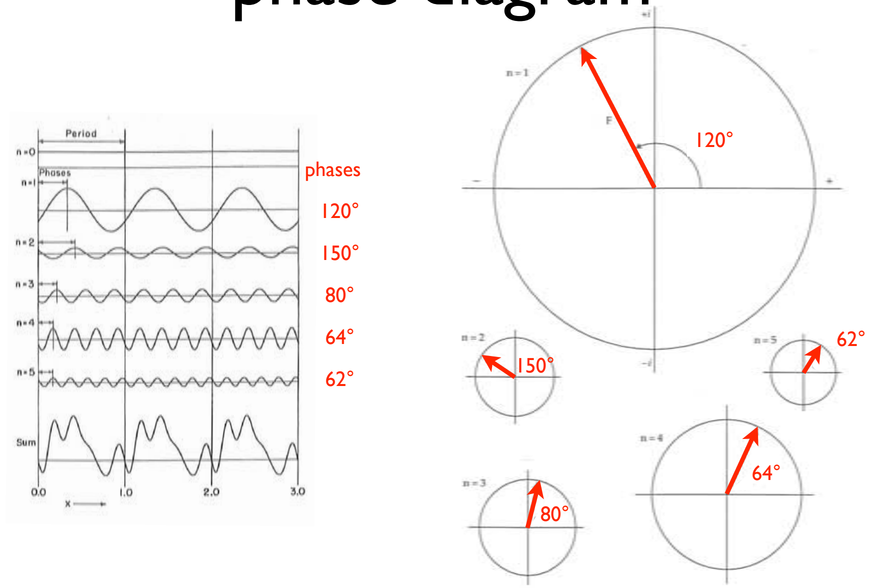


phase diagram



$$\mathbb{F} = Fe^{-i\phi}$$
$$= F(cos\phi + isin\phi)$$

phase diagram



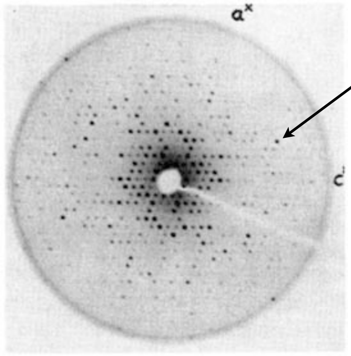
electron density

$$\rho(x,y,z) = \sum_h \sum_k \sum_l \mathbb{F}_{hkl} e^{-2\pi i(hx+ky+lz)}$$

$$= \sum_h \sum_k \sum_l (F_{hkl} e^{-i\phi}) e^{-2\pi i(hx+ky+lz)}$$

phase angle

phase problem



$$I_{hkl} \propto |\mathbb{F}_{hkl}|^2$$

$$= F_{hkl} e^{-i\phi} \times F_{hkl} e^{+i\phi}$$

$$= F_{hkl}^2$$

phase problem

$$\mathbb{F}_{hkl} = F_{hkl} e^{-i\phi}$$

$$= \sum_j f_j e^{2\pi i(hx_j+ky_j+lz_j)}$$

f_j : the scattering power of atom j

depends on the positions of atoms (x_j, y_j, z_j)

how to solve...

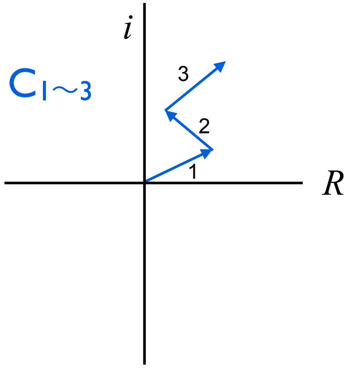
for smaller molecules

(a) Guess & trial-and-error

(b) heavy atom phasing

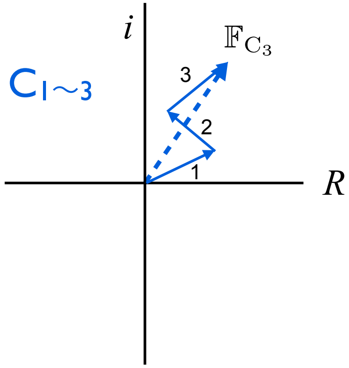
example: C_3Br molecule

$$\mathbb{F}_{hkl} = \sum_{j=1}^{3} f_C e^{2\pi i(hx_j+ky_j+lz_j)} + f_{Br} e^{2\pi i(hx_{Br}+ky_{Br}+lz_{Br})}$$



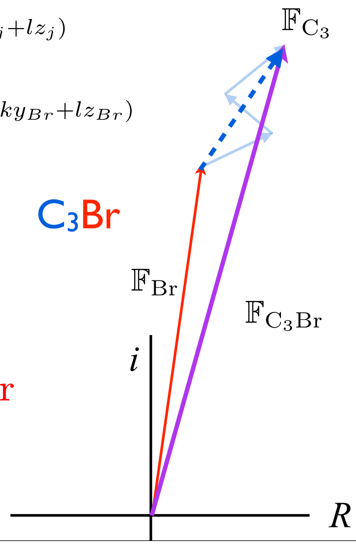
example: C_3Br molecule

$$\mathbb{F}_{hkl} = \sum_{j=1}^{3} f_C e^{2\pi i(hx_j+ky_j+lz_j)} + f_{Br} e^{2\pi i(hx_{Br}+ky_{Br}+lz_{Br})}$$



example: C_3Br molecule

$$\mathbb{F}_{hkl} = \sum_{j=1}^{3} f_C e^{2\pi i(hx_j+ky_j+lz_j)} + f_{Br} e^{2\pi i(hx_{Br}+ky_{Br}+lz_{Br})}$$



$$\mathbb{F}_{Br} \approx \mathbb{F}_{C_3Br}$$

but... our target is a protein molecule

for example

myoglobin

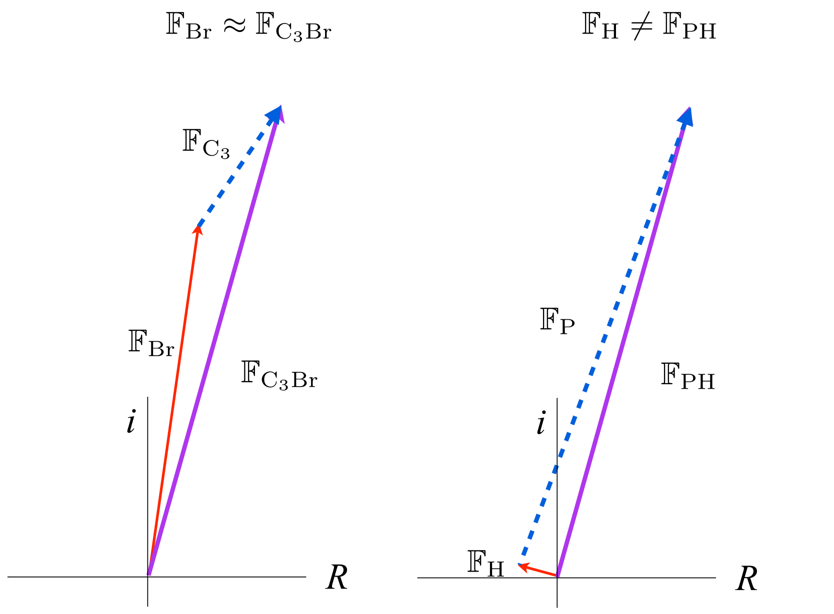
molecular weight: 17,184

1,200 non-hydrogen atoms

more than 9,000 electrons

Hg

only 80 electrons



key paper

myoglobin の
2Åの構造解析

STRUCTURE OF MYOGLOBIN
A THREE-DIMENSIONAL FOURIER SYNTHESIS AT 2 Å. RESOLUTION
By DRS. J. C. KENDREW, R. E. DICKERSON, B. E. STRANDBERG, R. G. HART and D. R. DAVIES*
Medical Research Council Unit for Molecular Biology, Cavendish Laboratory, Cambridge
AND
D. C. PHILLIPS and V. C. SHORE
Davy Faraday Laboratory, The Royal Institution, London

Nature (1960) 185, 422-427

Virus の構造予測

Structure of Bushy Stunt Virus
D. L. D. CASPAR*
Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems,
Cavendish Laboratory,
Cambridge.
Jan. 23.

Nature (1956) 177, 476-477

ここで時間切れ...

MIR法の説明以降は次週