« Plenty of room at the bottom »

- Feynman questions on molecular biology (1959-1960)
- How the structure of DNA was discovered (1953)

an accelerated course of molecular biology
for physicists, chemists,…

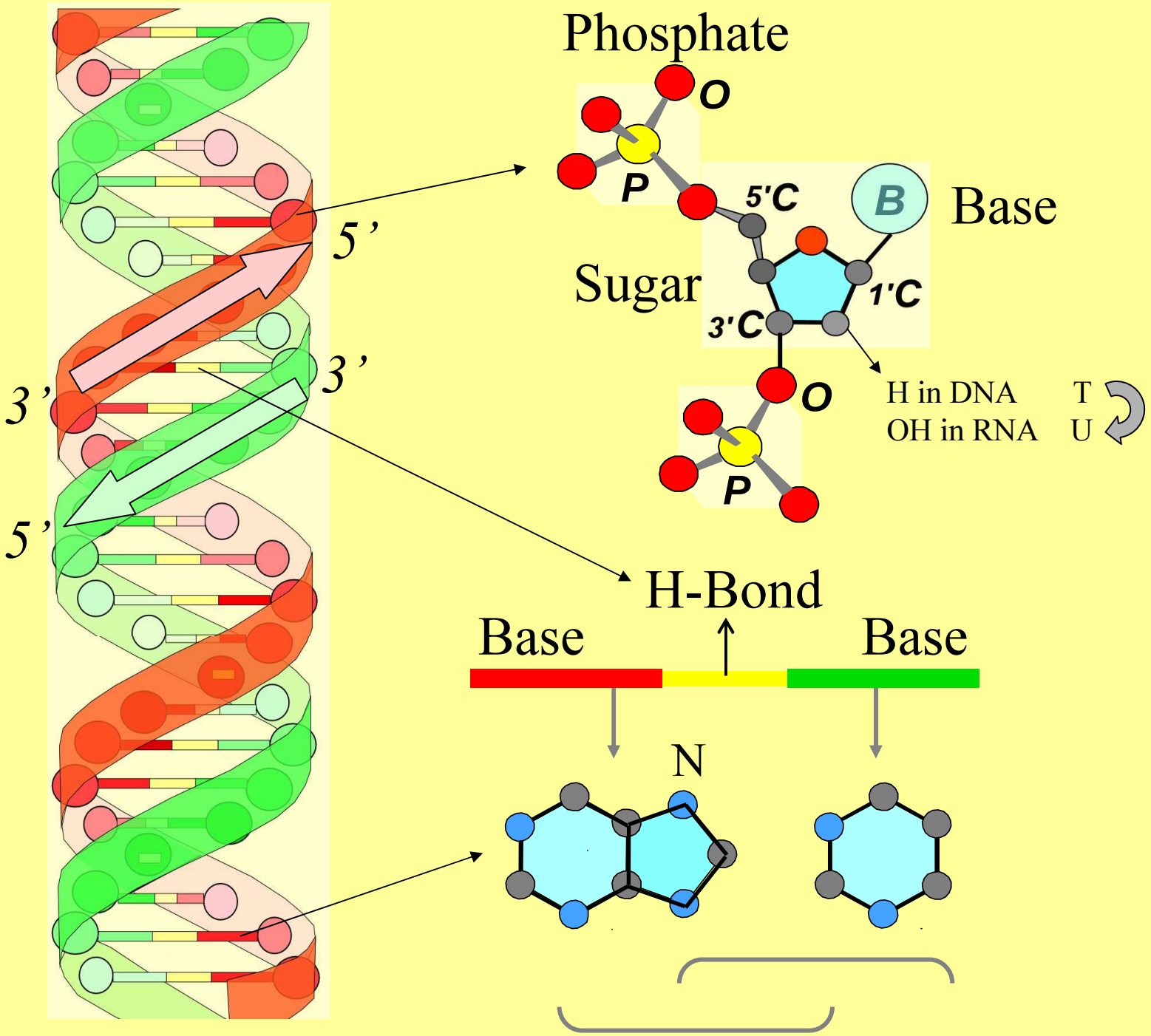
Amand A. LUCAS, Univ. of Namur, Belgium
San Sebastian, October 2007

Feynman questions

- *What is the sequence of bases in DNA ?*
- *What happens when there is a mutation ?*
- *How is the base order in the DNA connected to the order of aminoacids in the protein ?*
- *What is the structure of RNA ?*
- *What is the organisation of the « microsomes » ?*
- *How are proteins synthesized ?*
- *Where does the (m)RNA go ?*
- *How does it sit ?*
- *Where does the protein sit?*
- *Where does the amino acid go in ?*

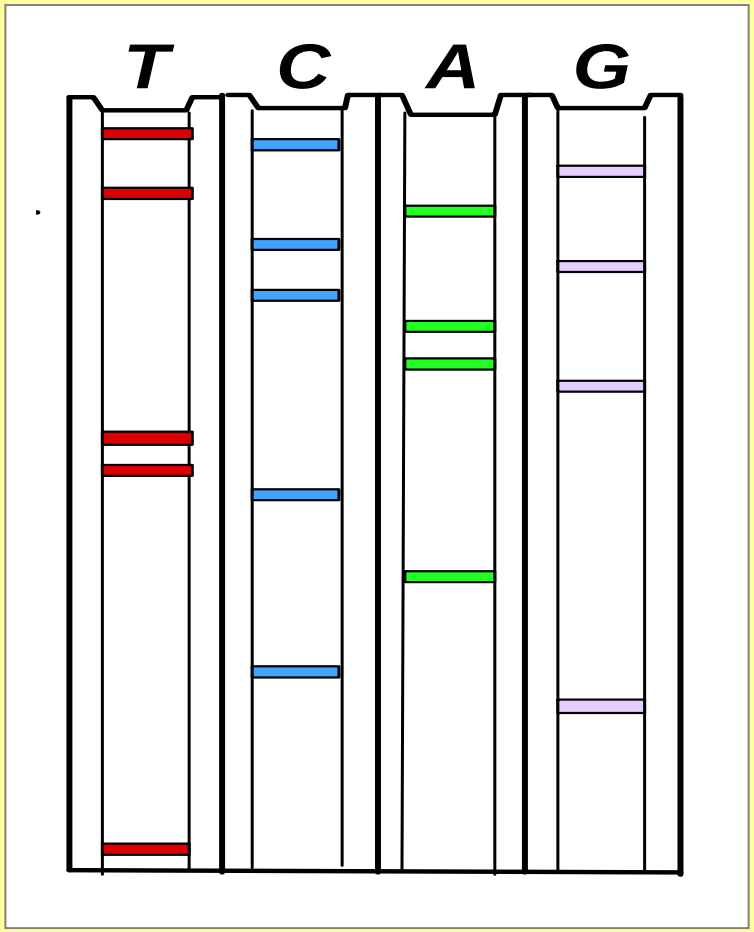
Feynman question 1

- *What is the sequence of bases in DNA ?*


Phosphate
O
P
5'C
B
Base
Sugar
1'C
3'C
O
P
H in DNA
T
OH in RNA
U
5 ’
3 ’
3 ’
5 ’
H-Bond
Base
Base
N

1975-77

F. Sanger - W. Gilbert



TGCACTTGAACGCATGCT

Feynman question

- *What happens when there is a mutation ?*

Error in replication DNA →DNA

or

in retro-transcription RNA →DNA

(RNA viruses)

http://ghr.nlm.nih.gov/handbook/mutationsanddisorders/possiblemutations

What kinds of gene mutations are possible?

Missense mutation

Nonsense mutation

Insertion

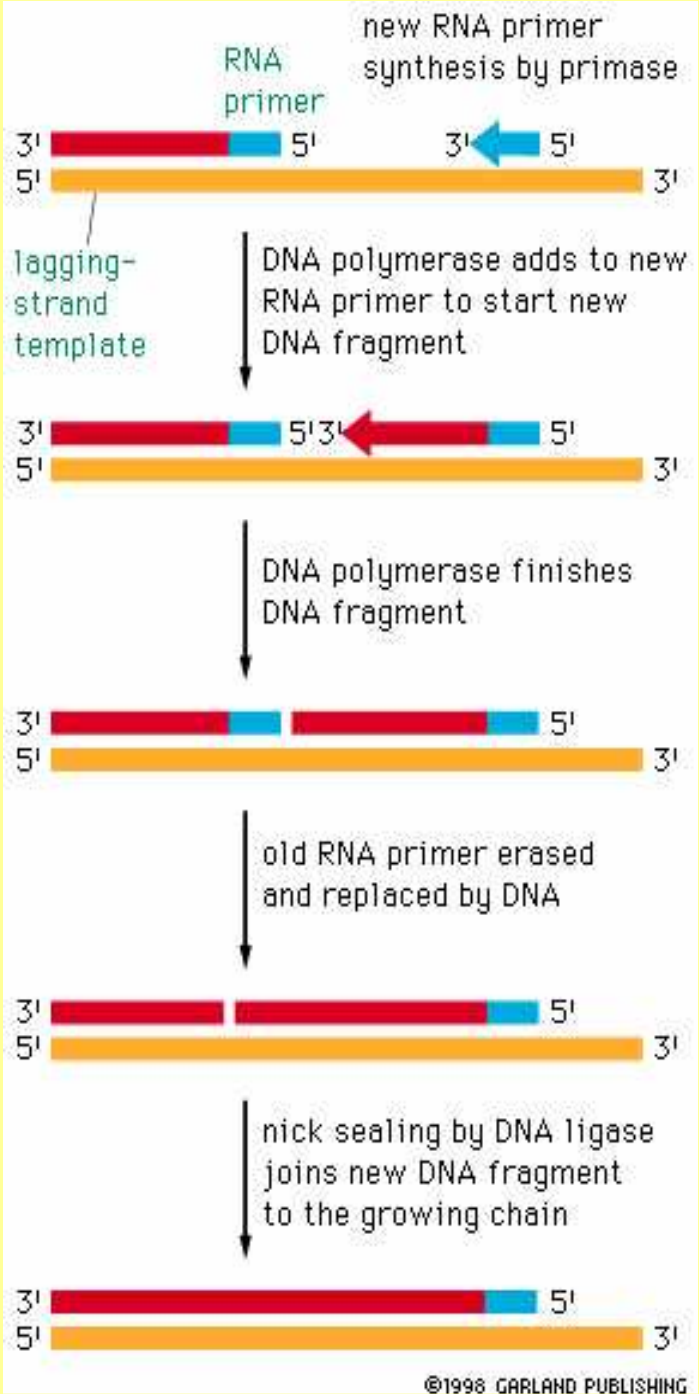
Deletion

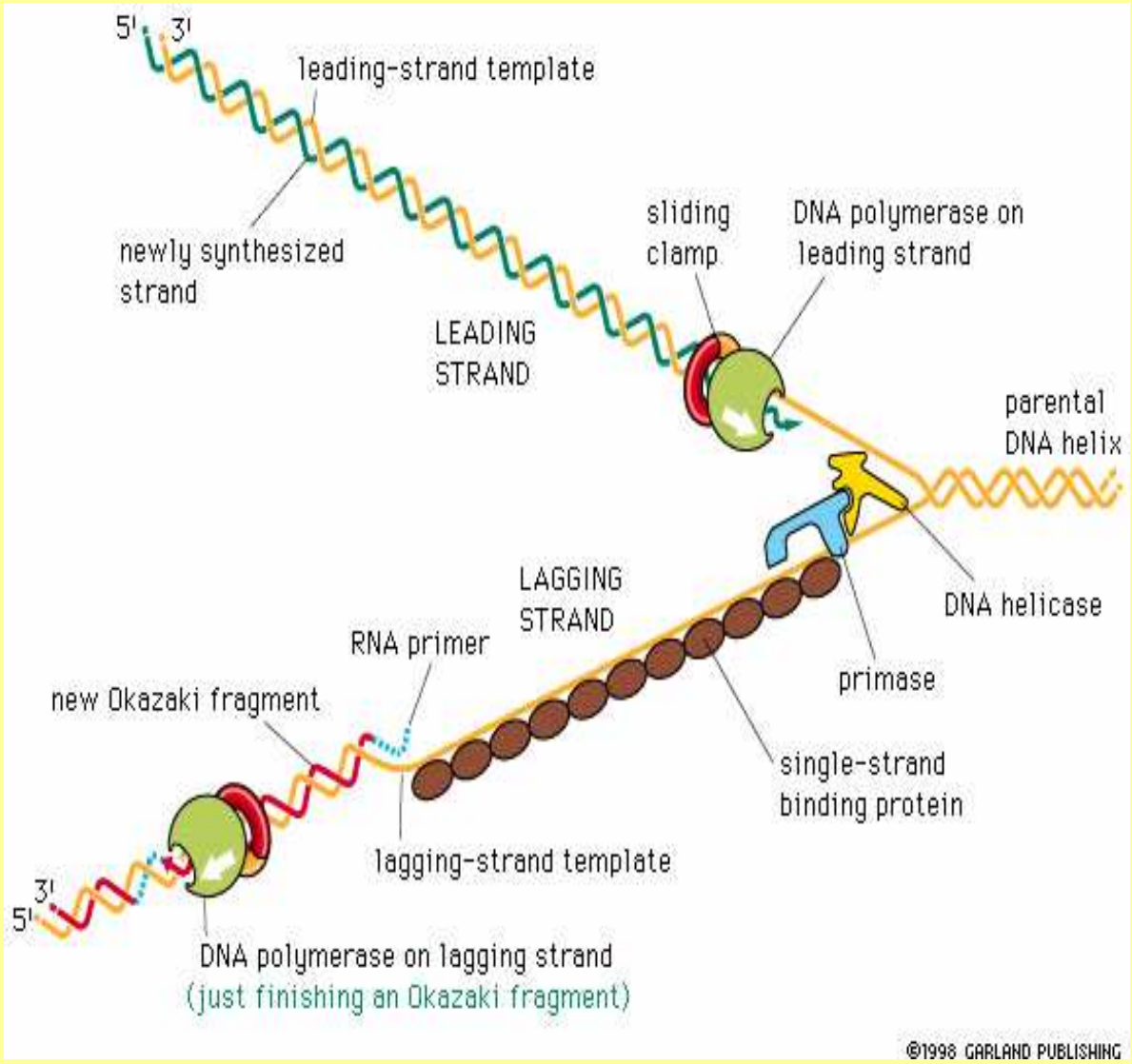
Duplication

Frameshift mutation

Repeat expansion

epli ation b the pol merase robot





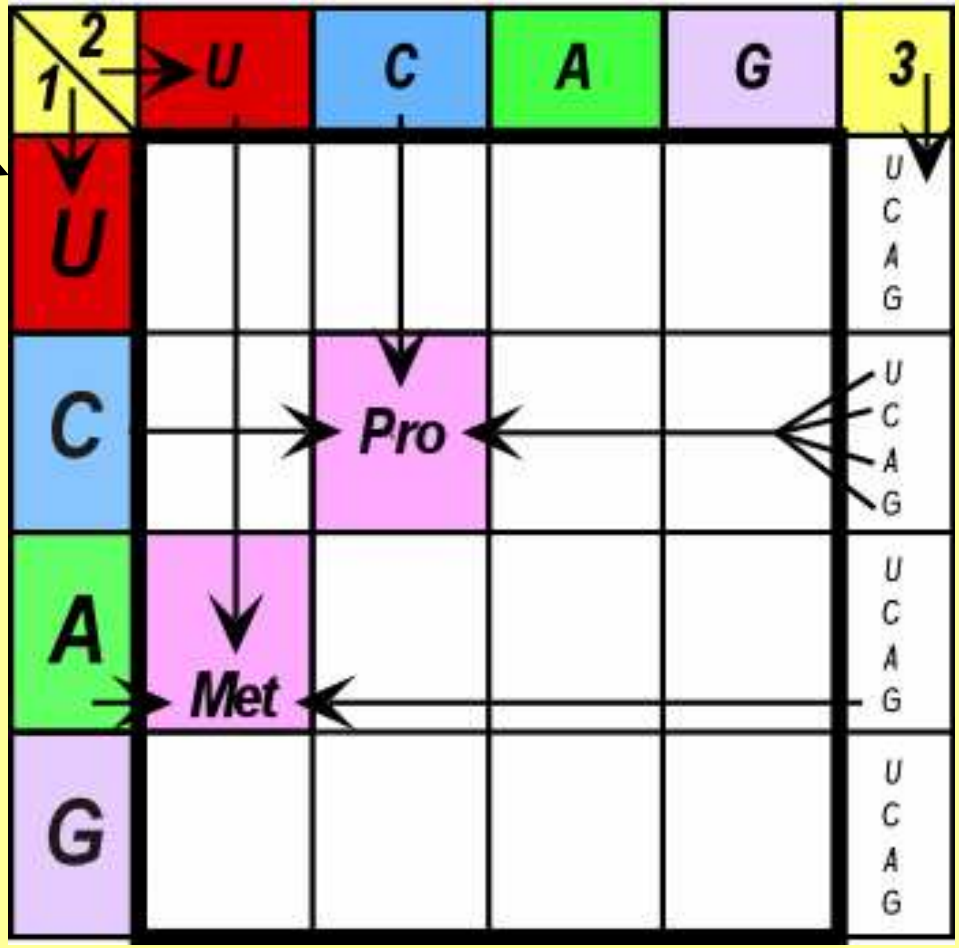
Feynman question

- *o is the base o e in the DNA connecte to the o e of a inoaci s in the otein ?*

19 1-

in DNA
in NA

The *degenerate* Triplet Code



	AGA									UUA					AGC				
	AGG									UUG					AGU				
GCA	CGA						GGA			CUA			CCA	UCA	ACA			GUA	
GCC	CGC						GGC		AUA	CUC			CCC	UCC	ACC			GUC	UAA
GCG	CGG	GAC	AAC	UGC	GAA	CAA	GGG	CAC	AUC	CUG	AAA		CCG	UCG	ACG		UAC	GUG	UAG
GCU	CGU	GAU	AAU	UGU	GAG	CAG	GGU	CAU	AUU	CUU	AAG	AUG	CCU	UCU	ACU	UGG	UAU	GUU	UGA
Ala	Arg	Asp	Asn	Cys	Glu	Gln	Gly	His	Ile	Leu	Lys	Met	Phe	Pro	Ser	Thr	Trp	Tyr	Val	stop
A	R	D	N	C	E	Q	G	H	I	L	K	M	F	P	S	T	W	Y	V	

Start codon

Stop codons

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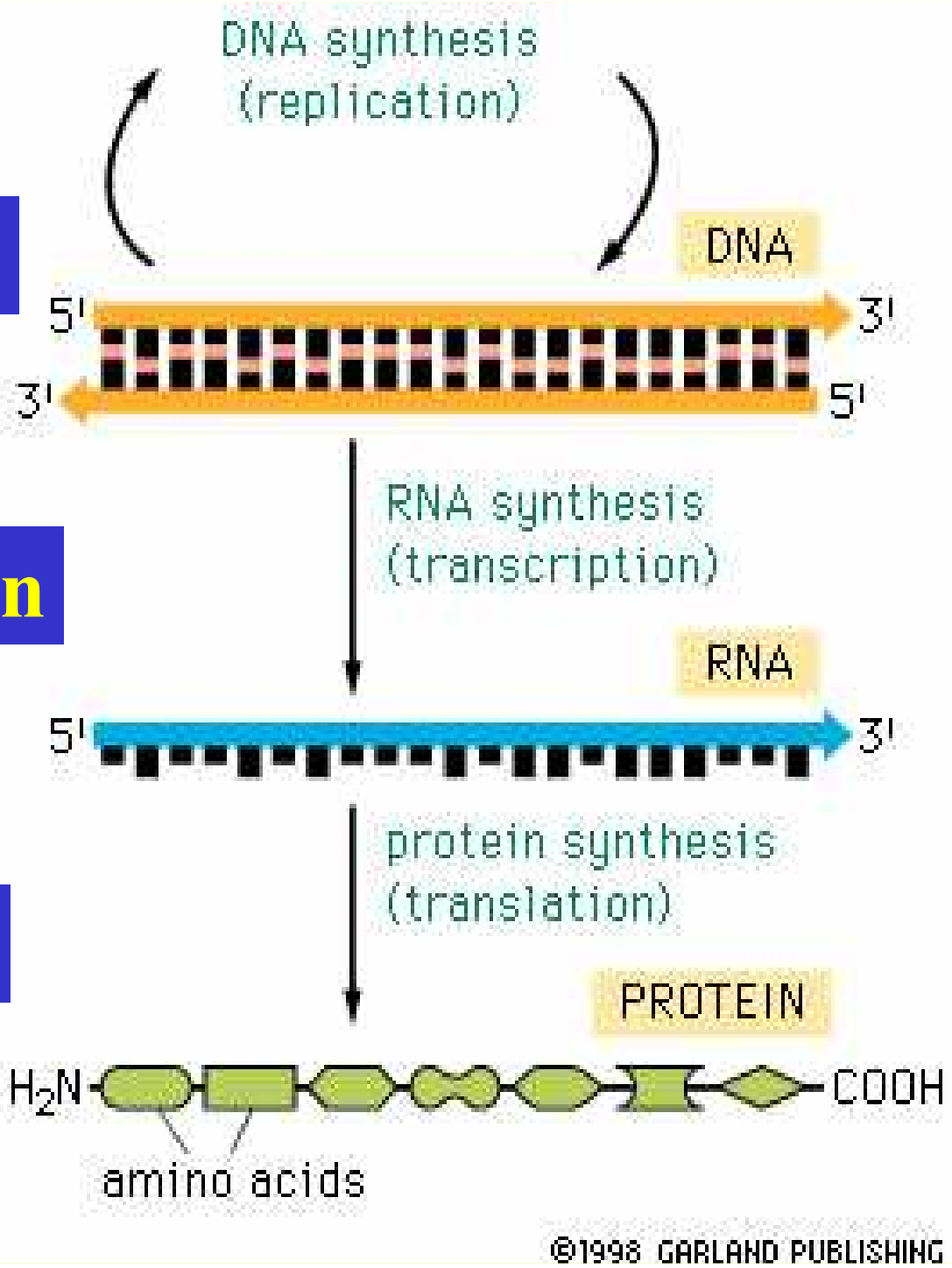
e entra d g a

Replication

Transcription

Translation



Feynman question

- *What is the stru ture o ?*

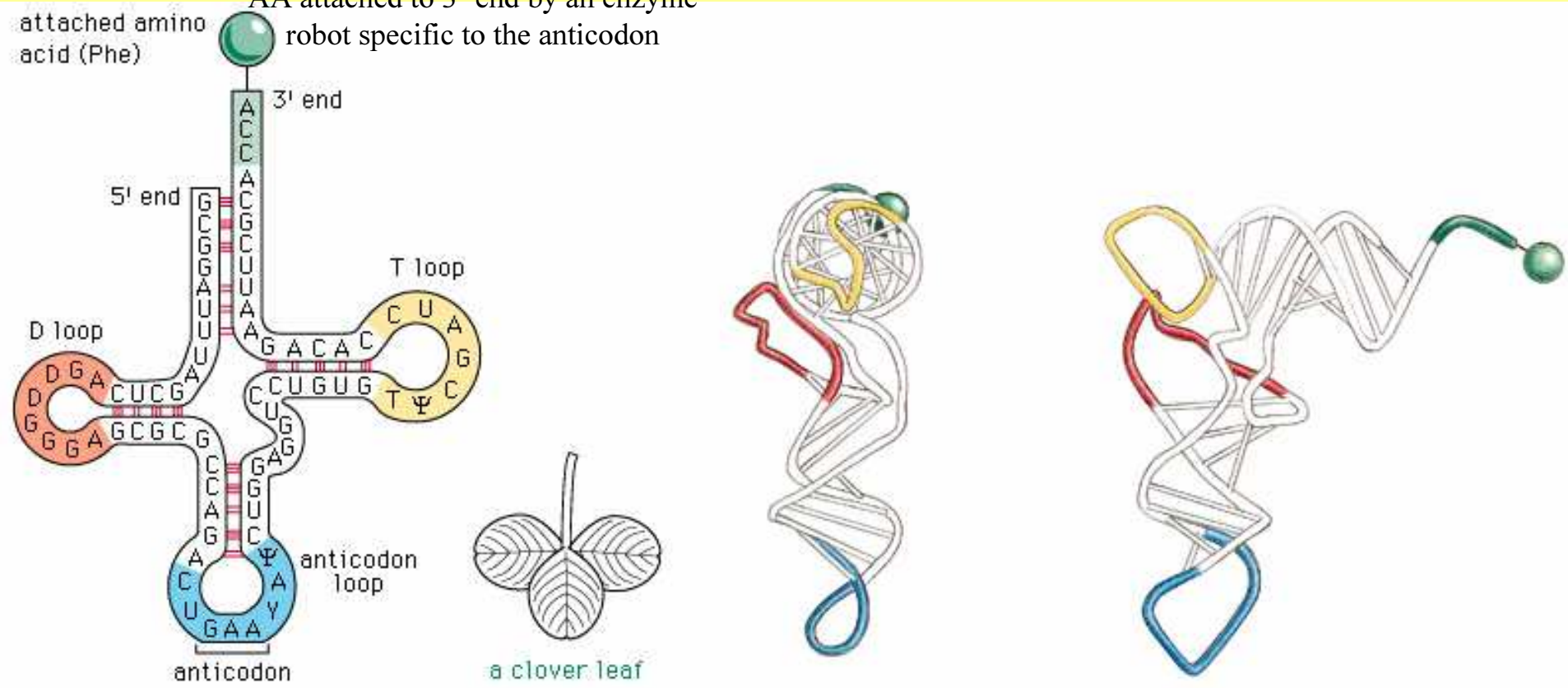
arious single strand RNA(le i le)
olded tRNA (i ed)
ri oso e rRNA (i ed)
ri o es (i ed)

- *ow is the or er in re ate to ?*

ranscription DNA → RNA

ase paired segments of tRNA
(distinct one for each AA) ha e a
spatia structure simi ar to A DNA

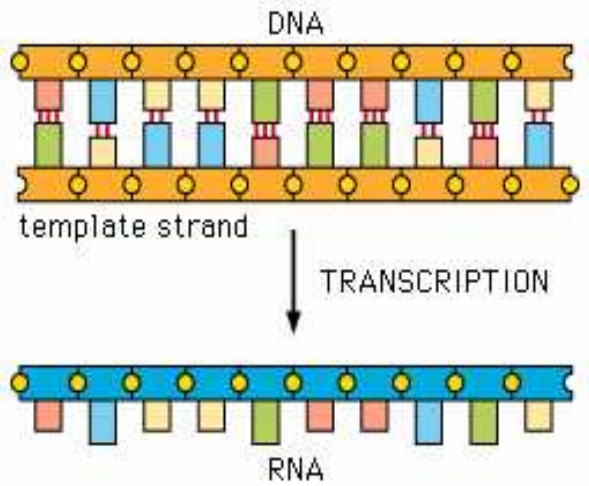
AA attached to 3' end by an enzyme
robot specific to the anticodon



5' GCGGAUUUAGCUCAGDDGGGAGAGCGCCAGACUGAAYAΨCUGGAGGUCCUGUGTΨCGAUCCACAGAAUUCGCACCA 3'

anticodon

(D)



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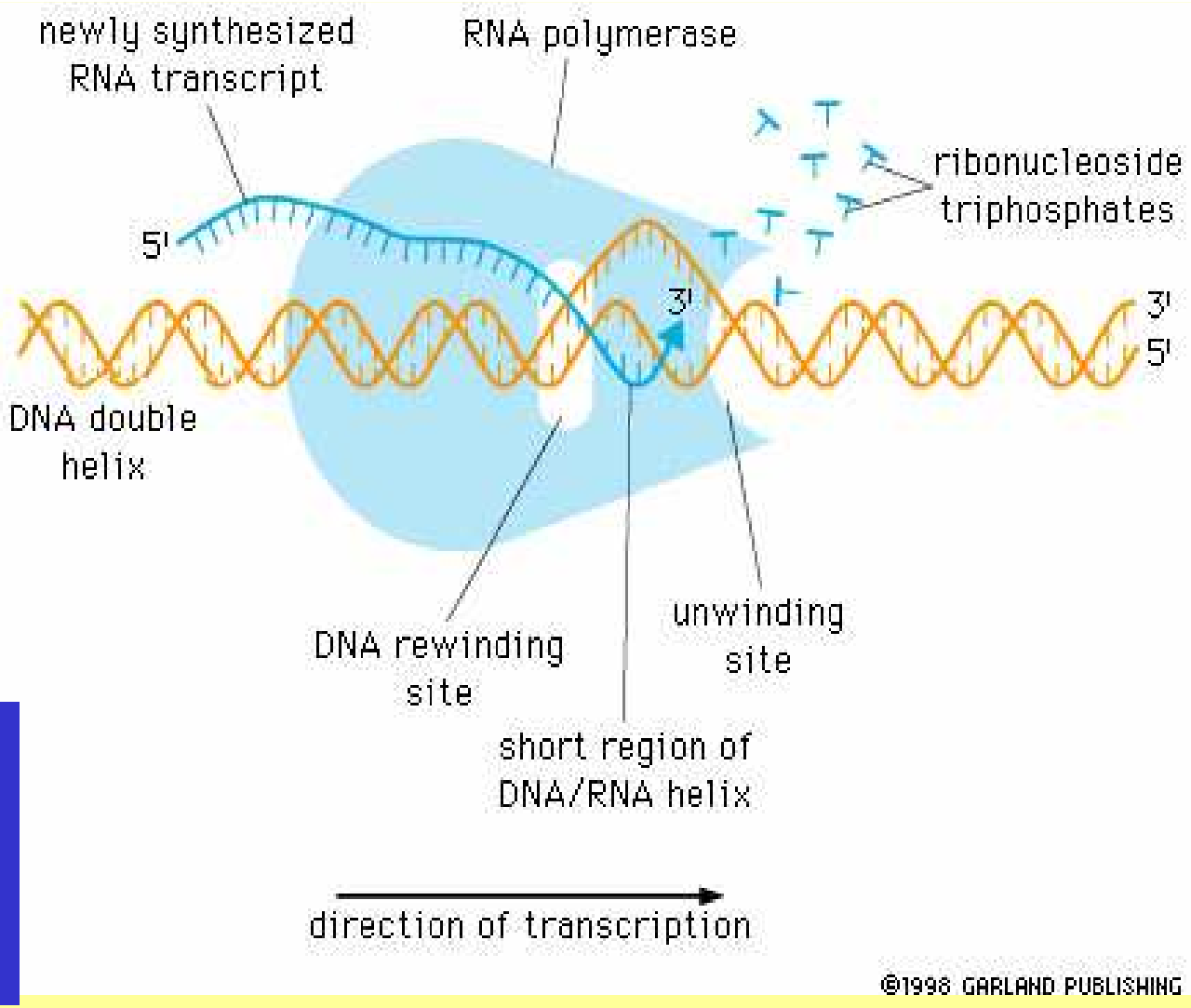
omplementar
to oding
strand



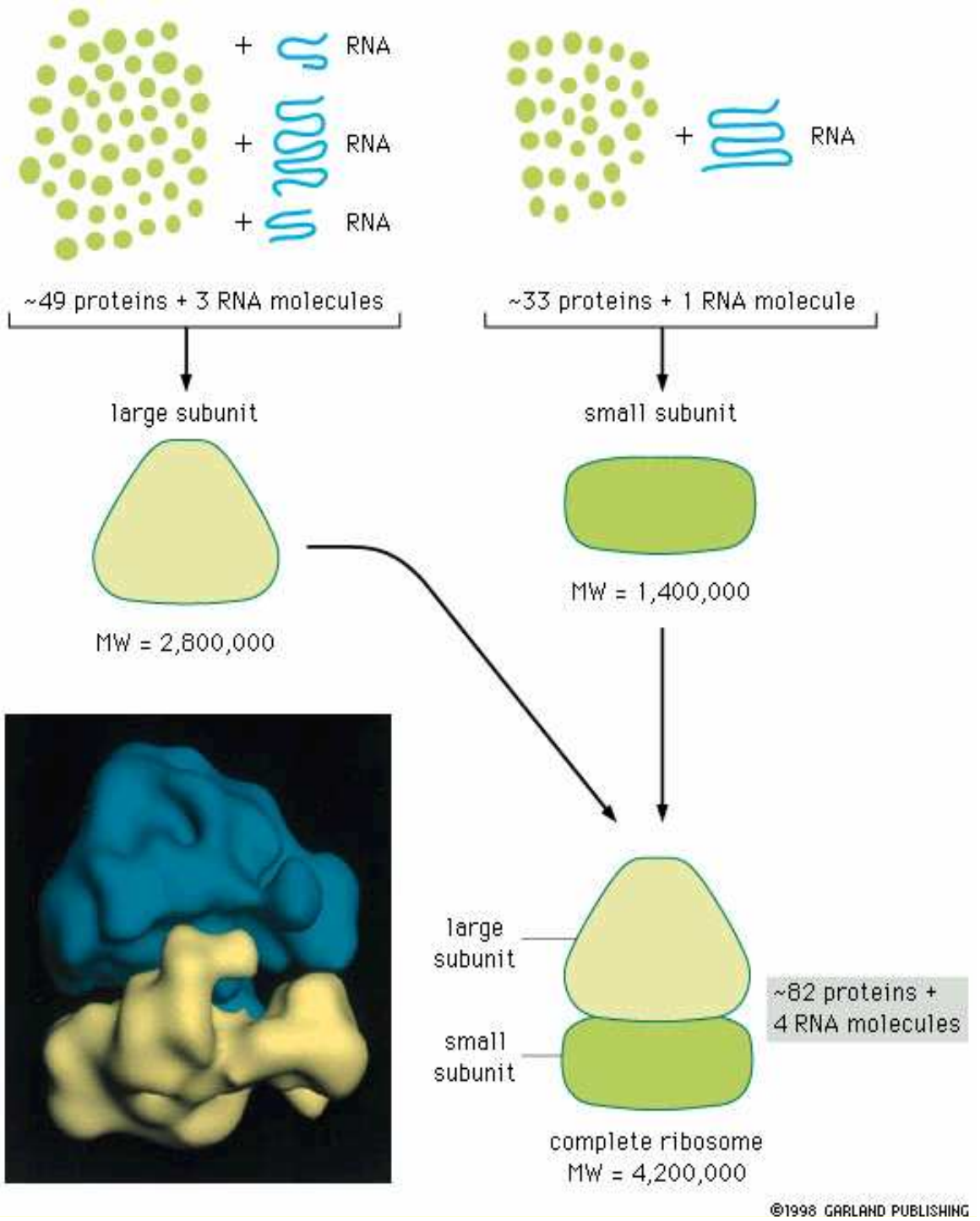
rans ription a hiner
pol merase robot

Feynman questions 5-10
Protein synthesis?

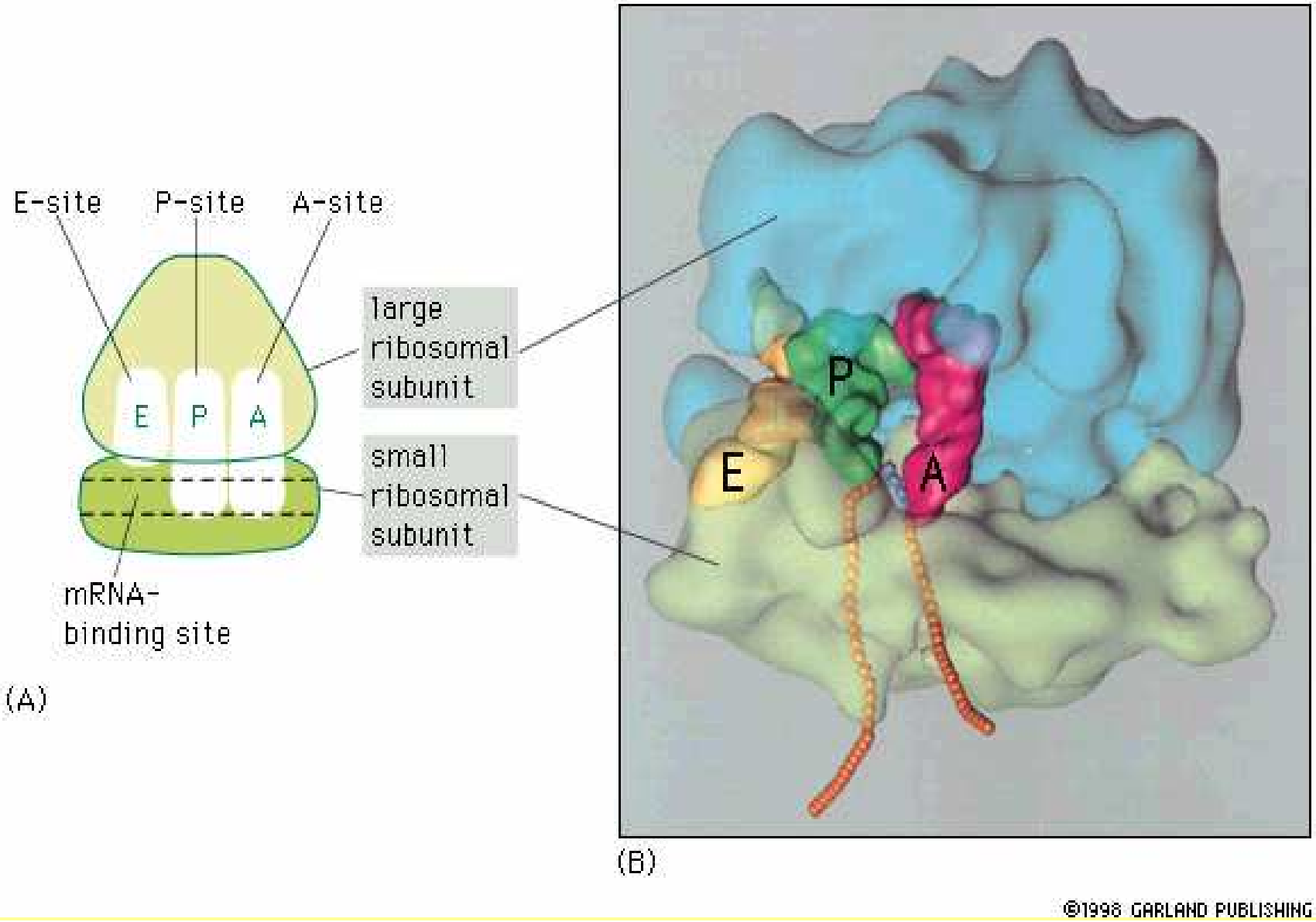
- *What is the o anisation of the ic oso es ?*
- *o a e oteins s nthesi e ?*
- *Whe e oes the NA o ?*
- *o oes it sit ?*
- *Whe e oes the otein sit*
- *Whe e oes the a ino aci o in ?*

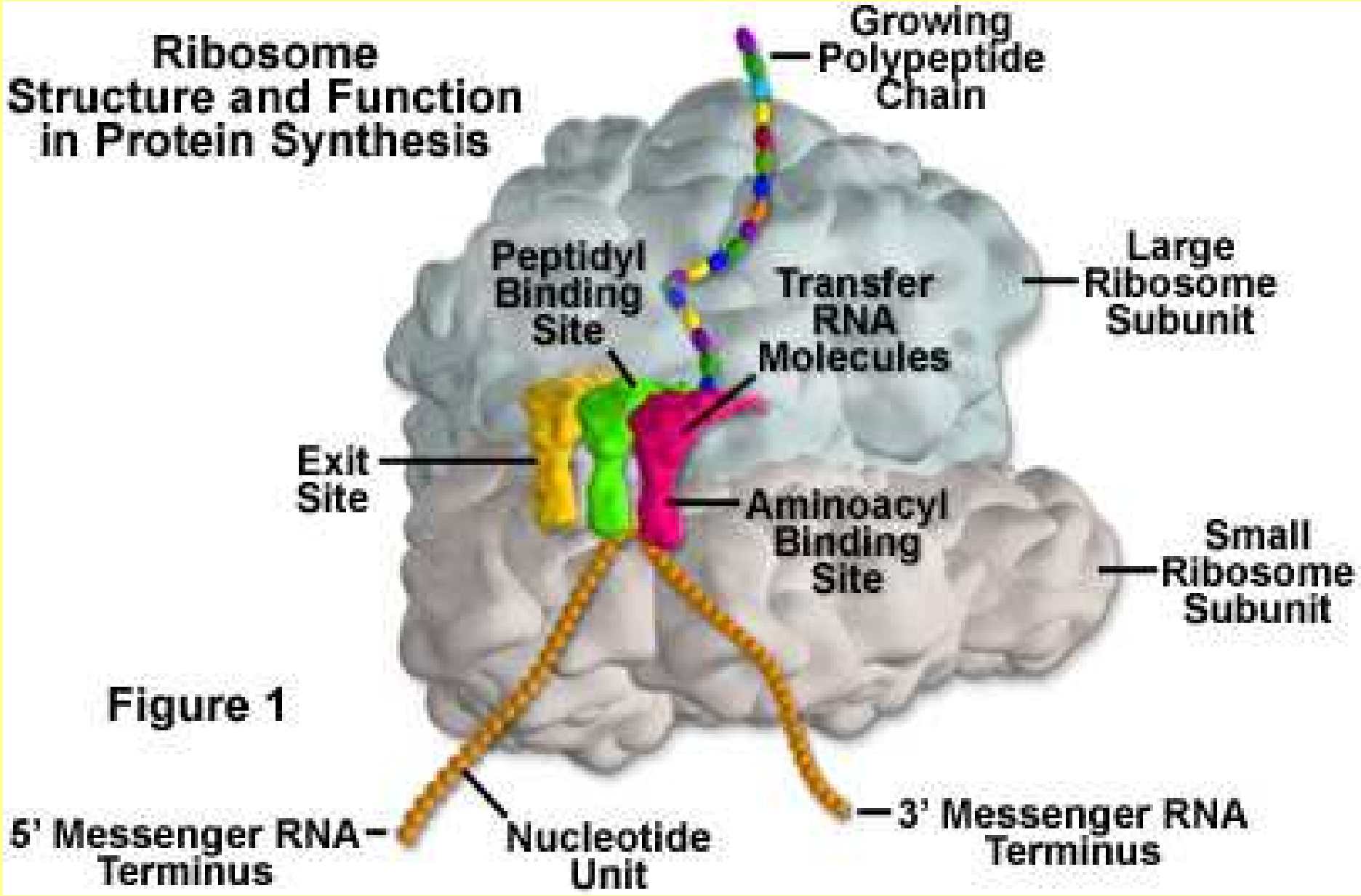
The ri o o e ro ot

u ar oti ribosome omponents



binding sites in ribosome




Ribosome
Structure and Function
in Protein Synthesis
Growing
Polypeptide
Chain
Peptidyl
Binding
Site
Transfer
RNA
Molecules
Large
Ribosome
Subunit
Exit
Site
Aminoacyl
Binding
Site
Small
Ribosome
Subunit
Figure 1
5' Messenger RNA
Terminus
Nucleotide
Unit
3' Messenger RNA
Terminus

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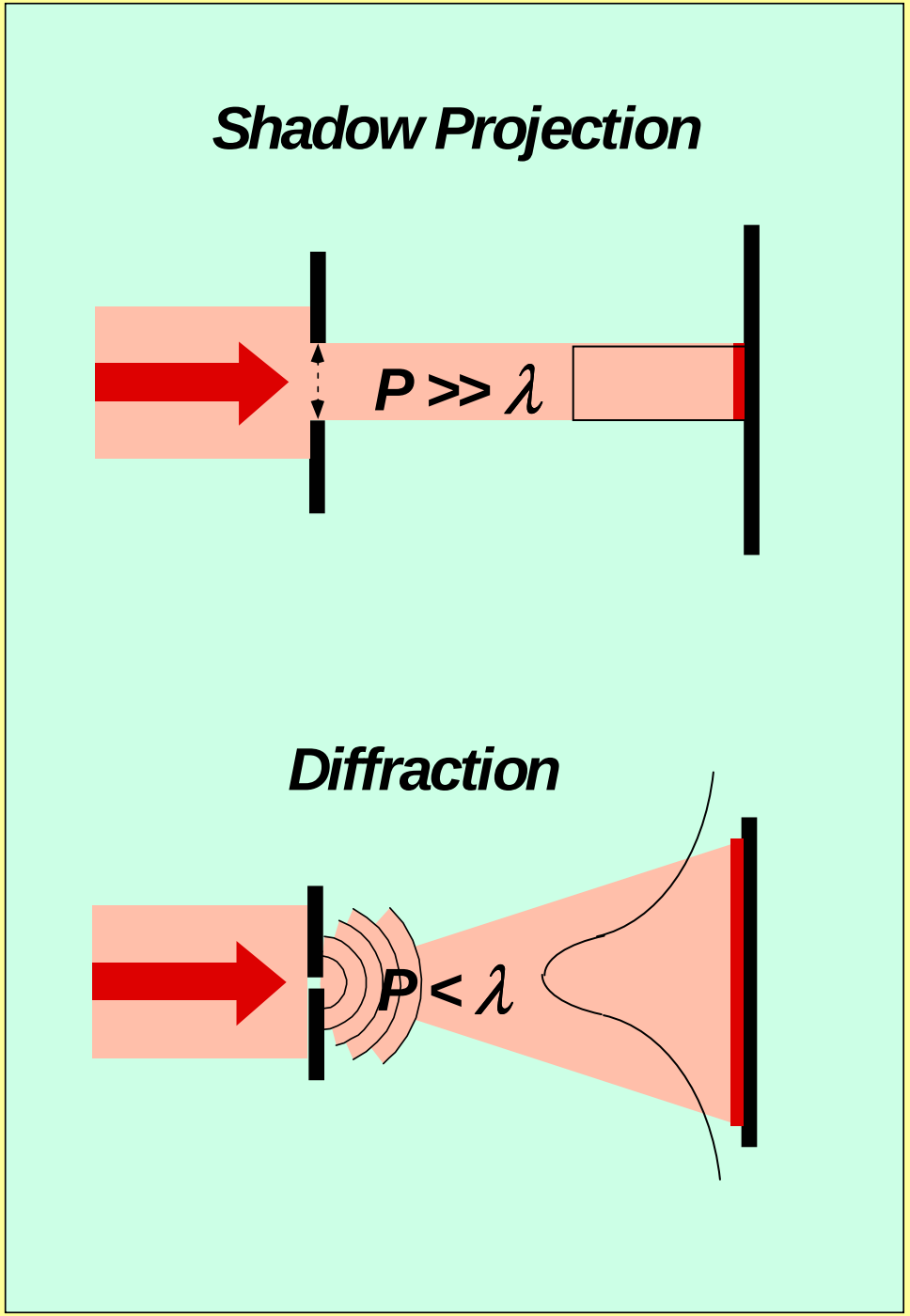
Diffraction



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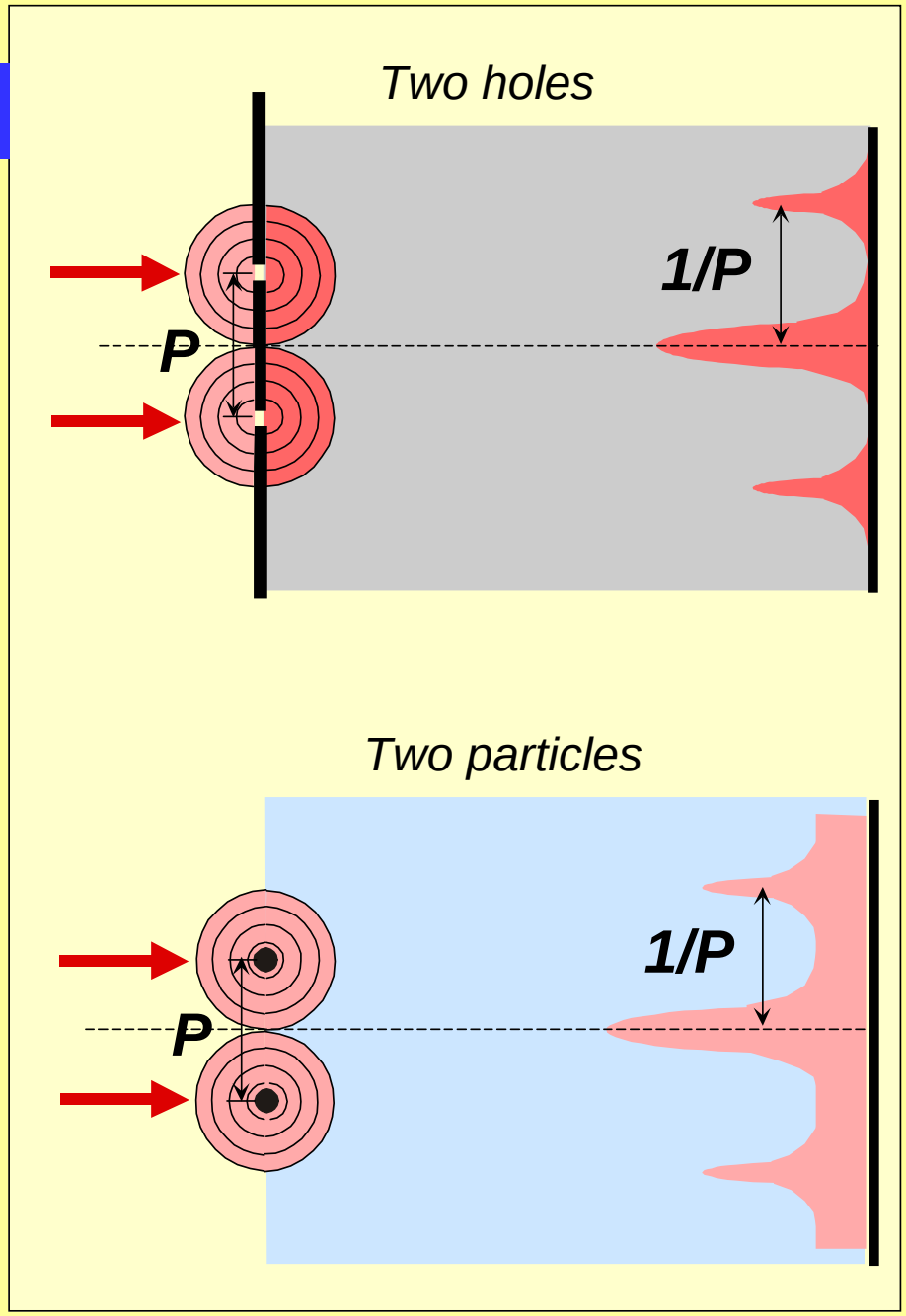

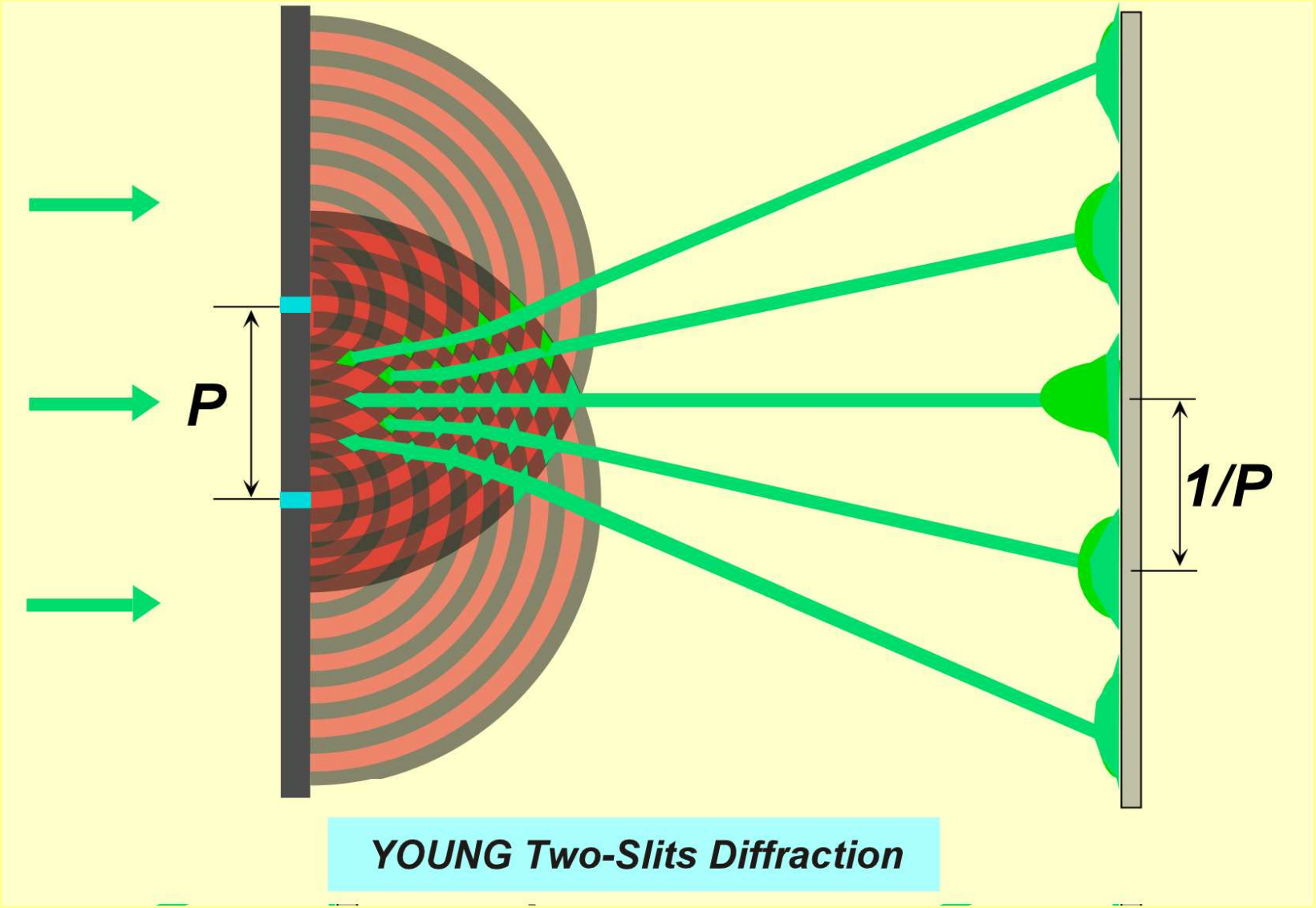
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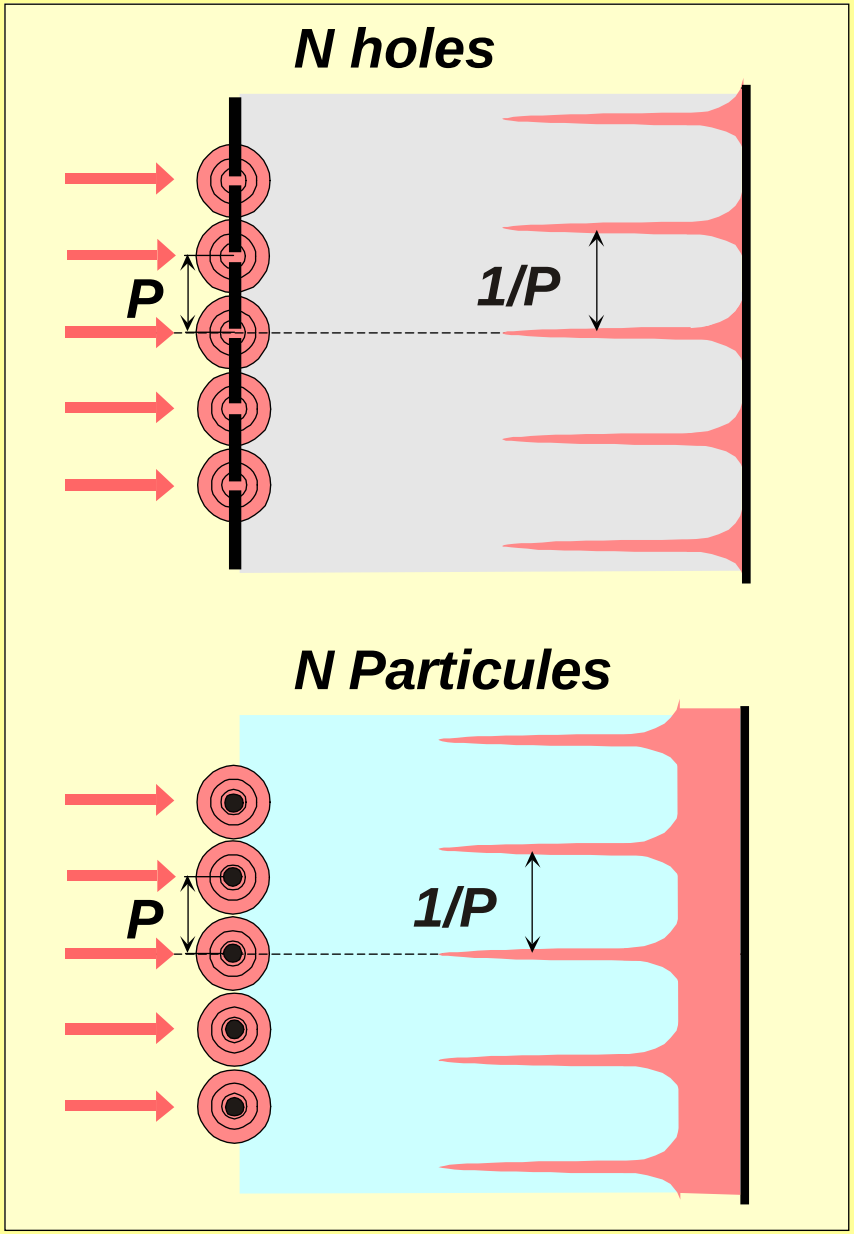
N holes
P
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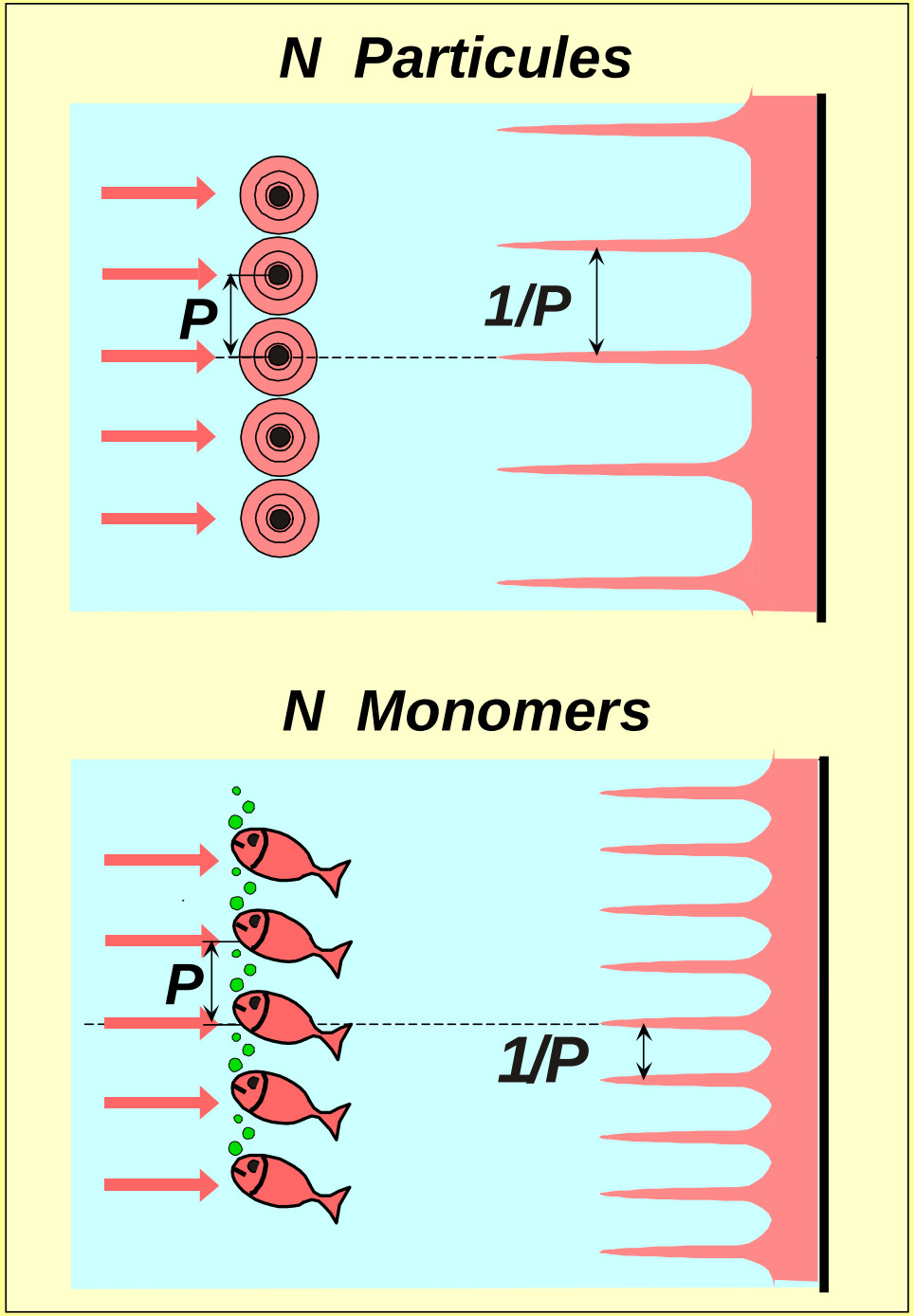
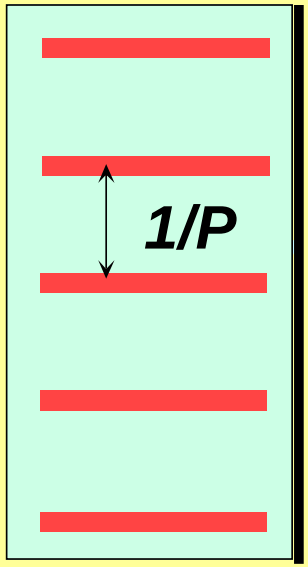
N Particules
P
1/P





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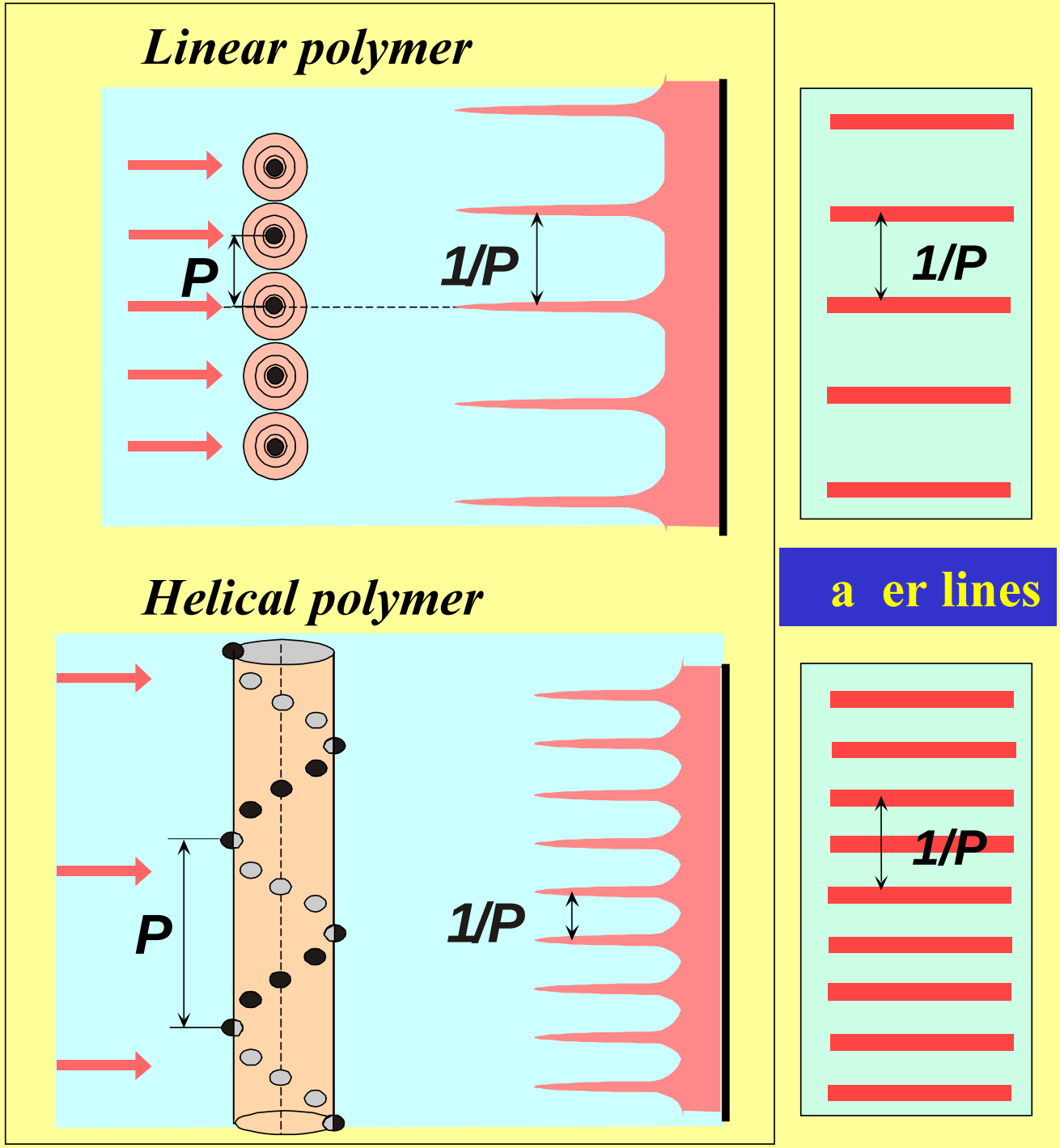
Linear polymer
P
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Helical polymer
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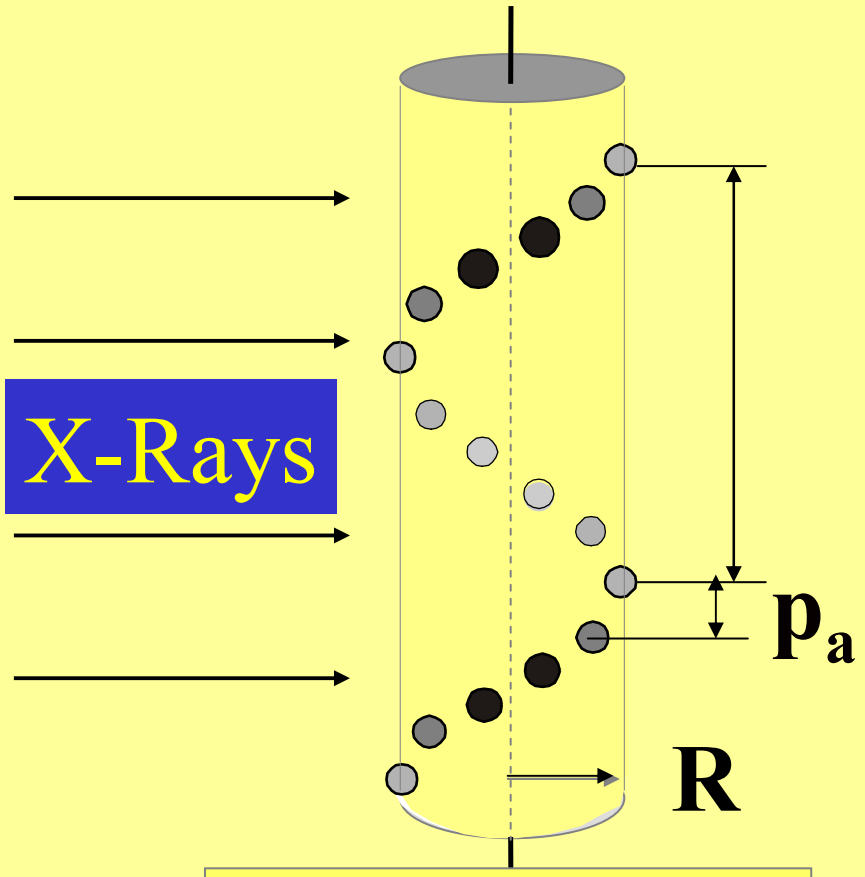
ourier-Bessel trans or o an ato ic heli



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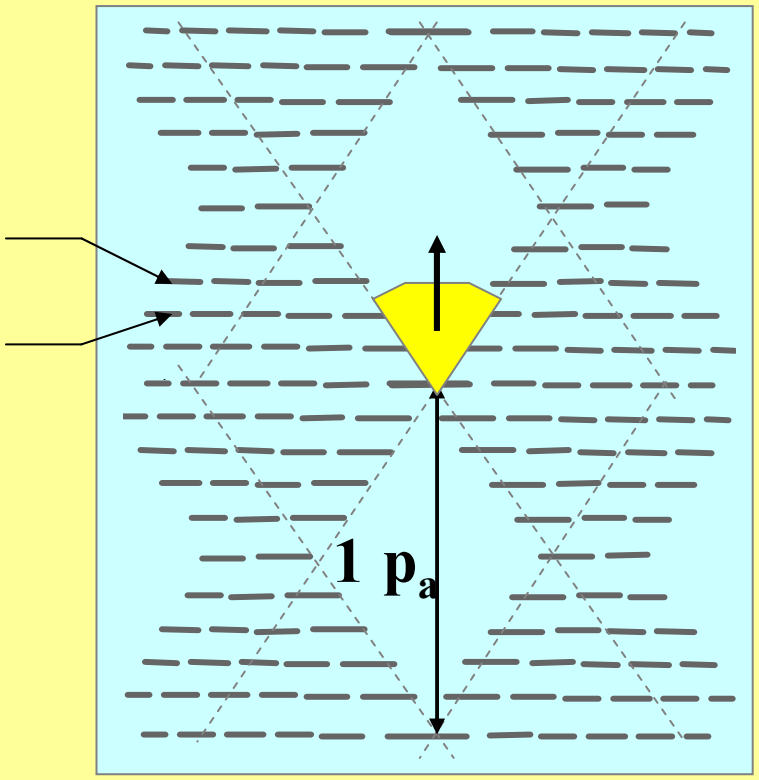
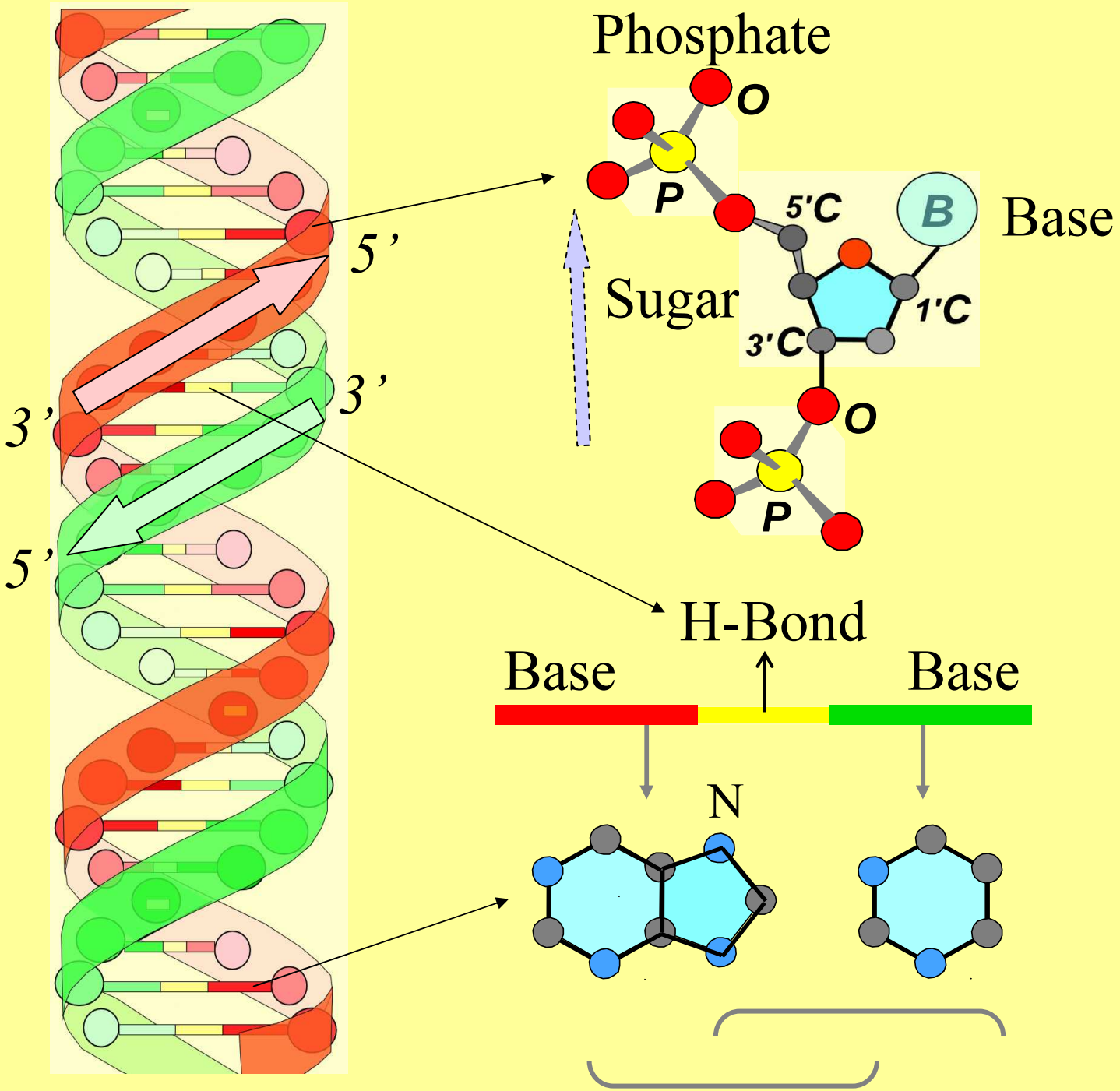


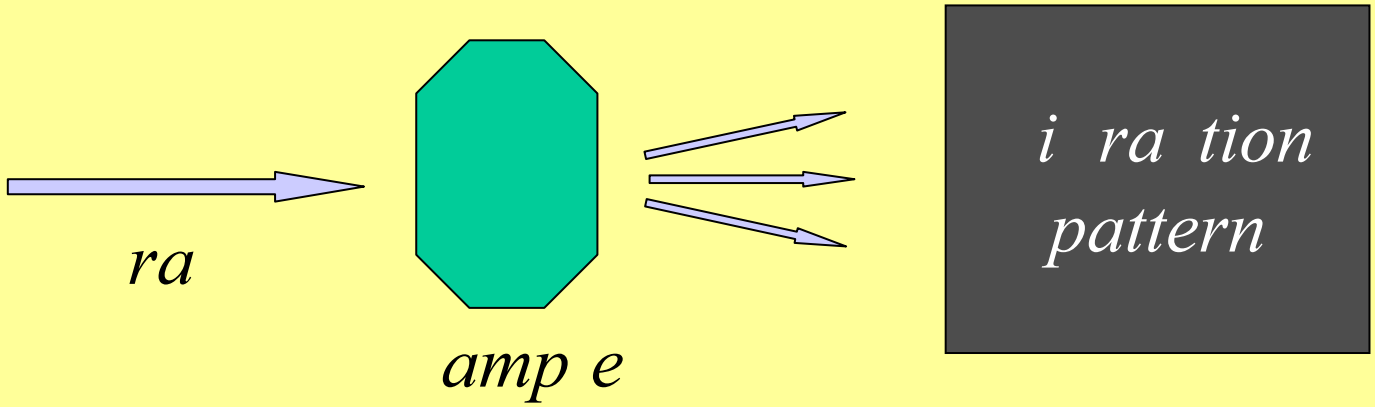
Di raction Pattern

o t e str ct re o as isco ere

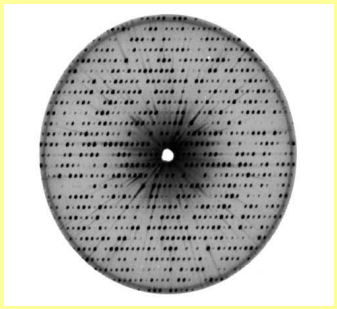

Phosphate
O
P
5'C
B
Base
Sugar
1'C
3'C
O
P
5 ’
3 ’
3 ’
5 ’
H-Bond
Base
Base
N

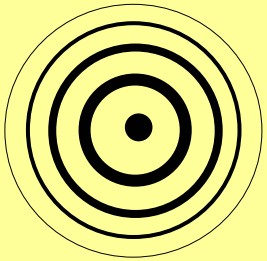
o t e str ct re o as isco ere

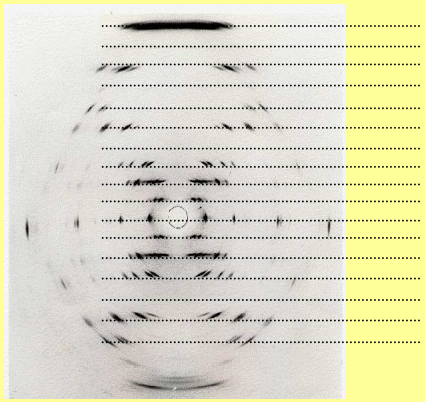
ra i raction i ers



Sa ple	*ing e crysta*	*a owder*	***Fiber***	*Amorphous*
Pattern	*harp spots*	*Rings*	***Layer lines***	*Diffuse*







Too deep for tears: Rosalind in a pensive mood.

he ourth man o
was a woman

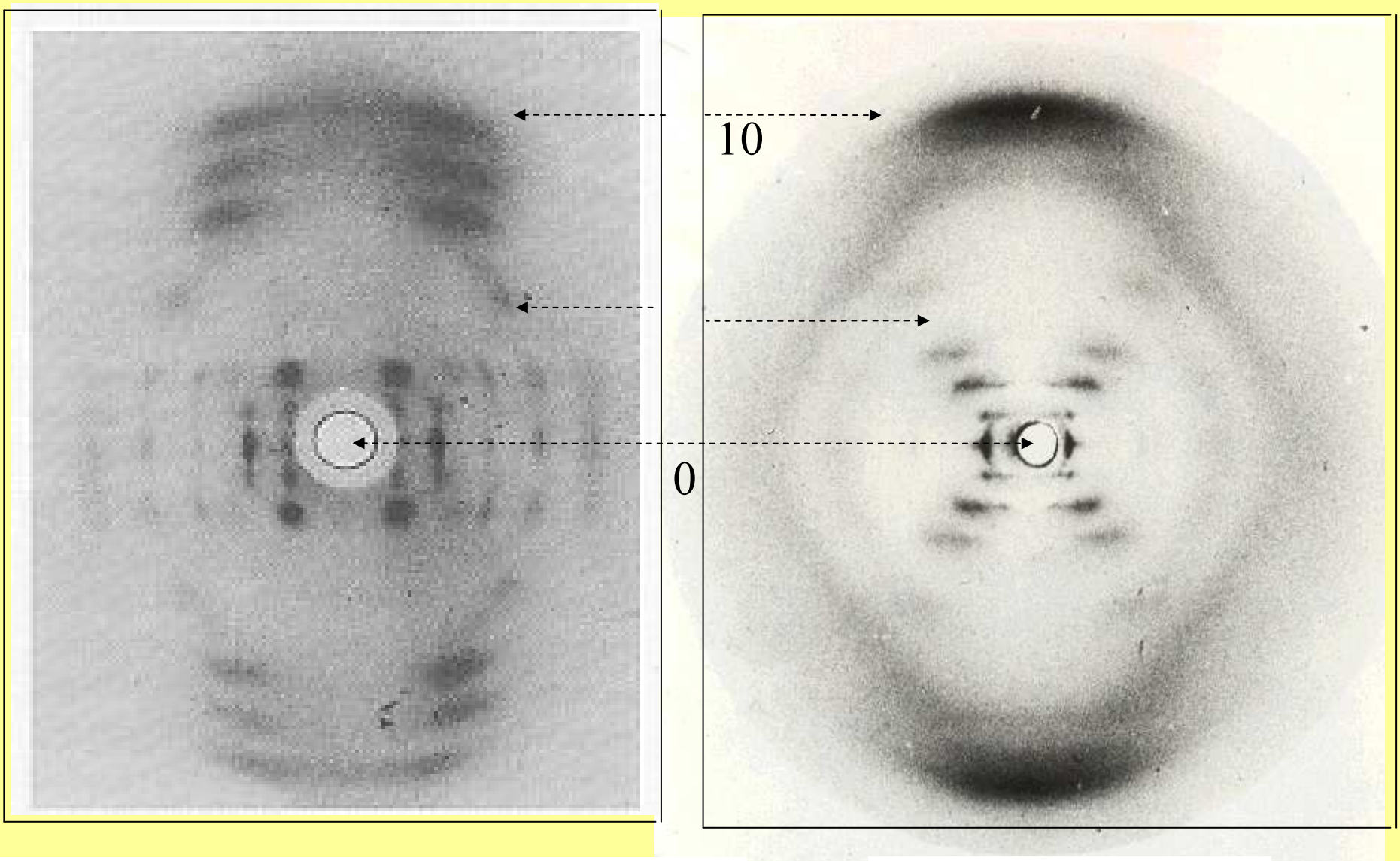
osa in ran in
5

« Her photographs are among the most beautiful X-ray photographs of any substance ever taken. »
J.D. Bernal.

See Brenda Maddox : *Rosalind Franklin, the Dark Lady of DNA*, Harper Collins 2002

Re e ation

Re e ation



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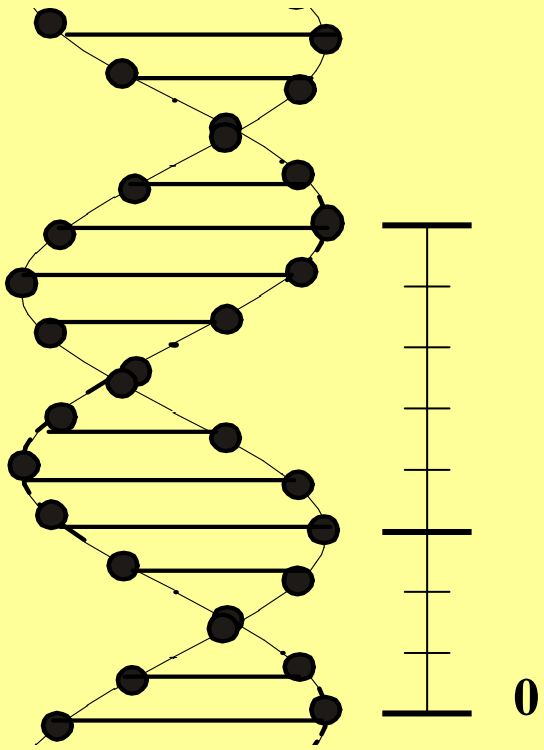

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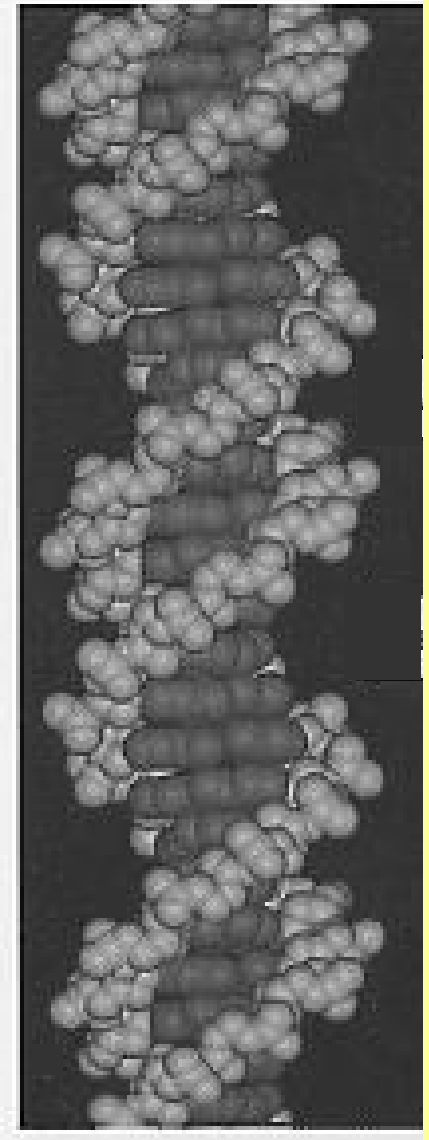

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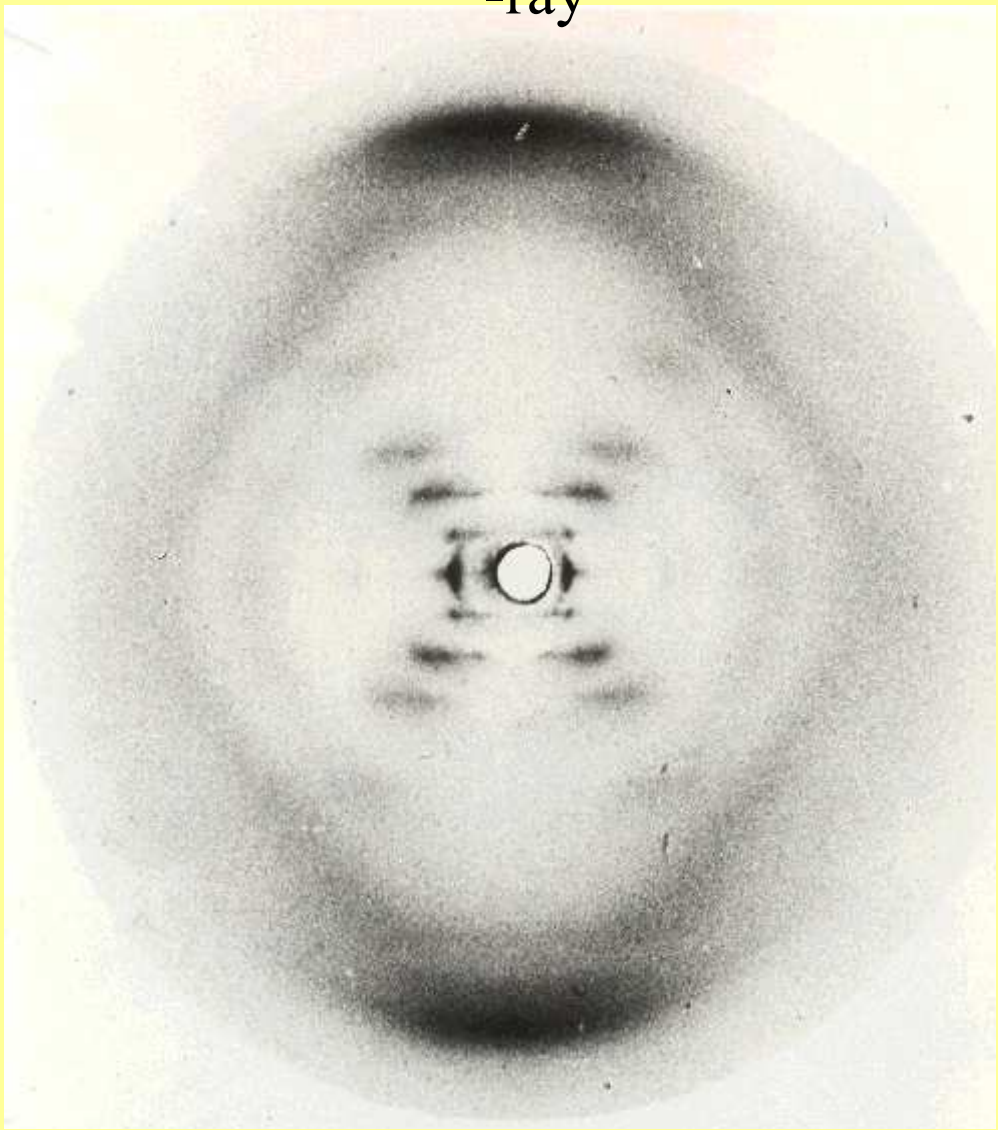
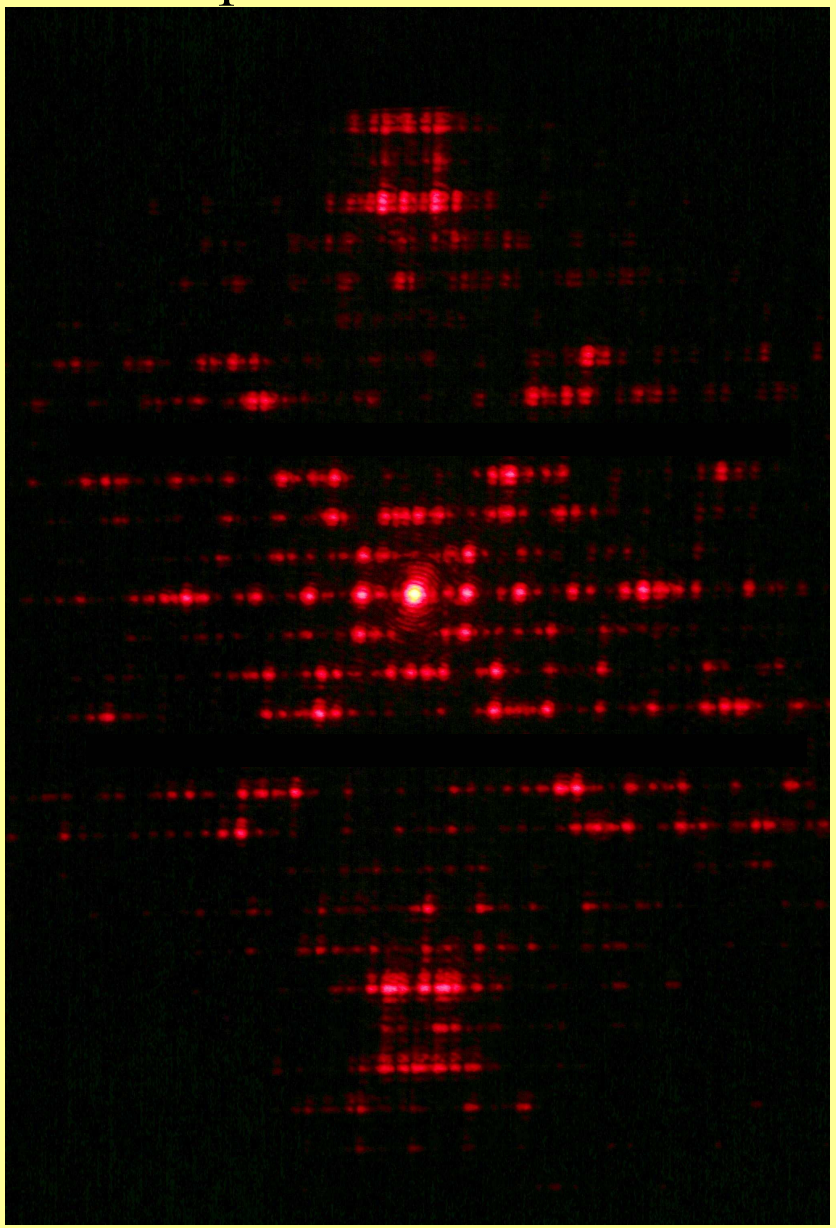


ptical simulation



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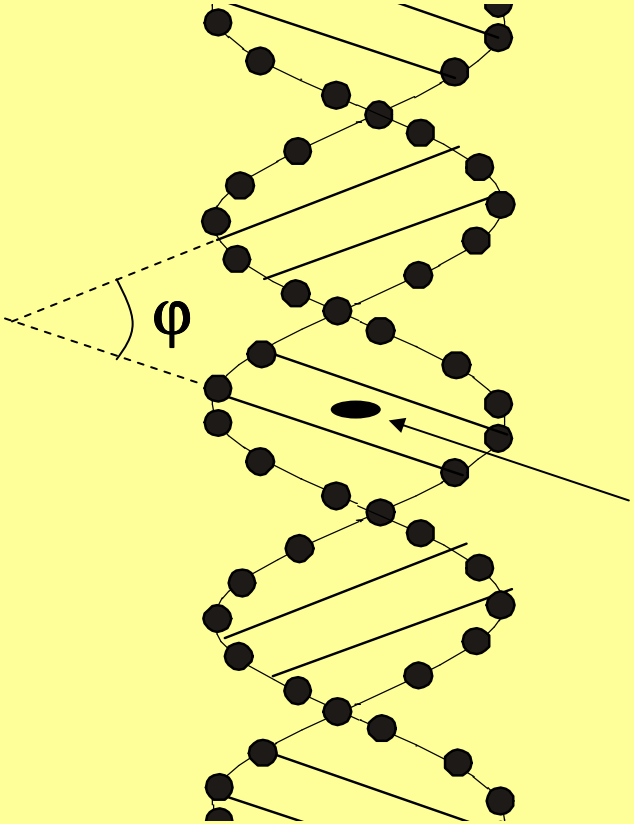

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S mmetr 11
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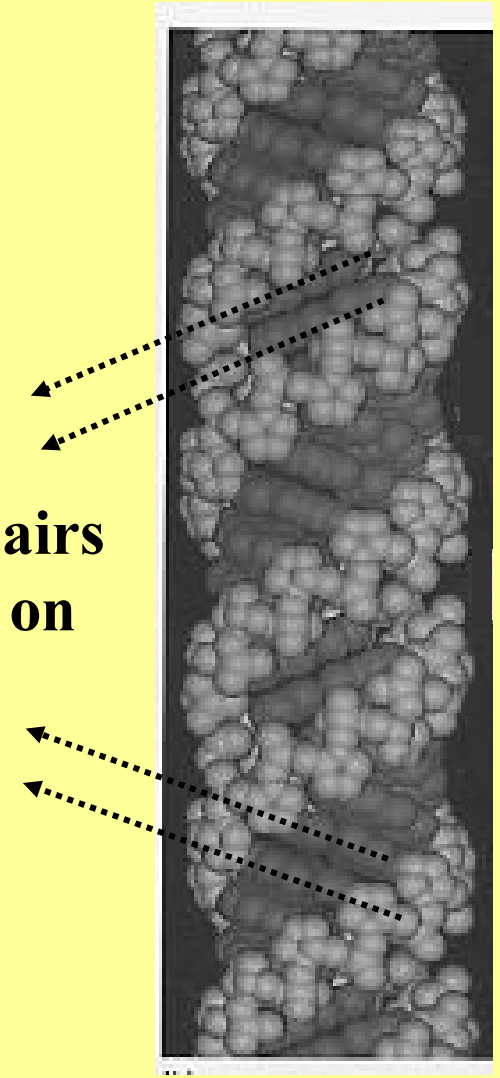
ole ular model



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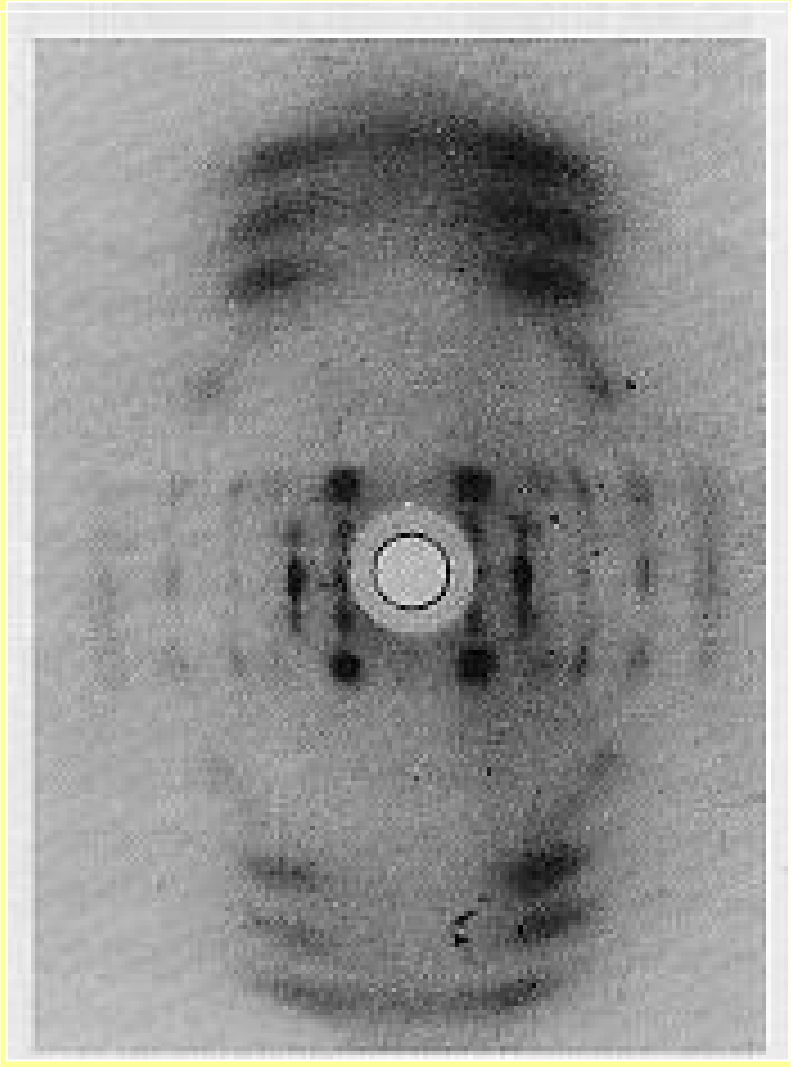
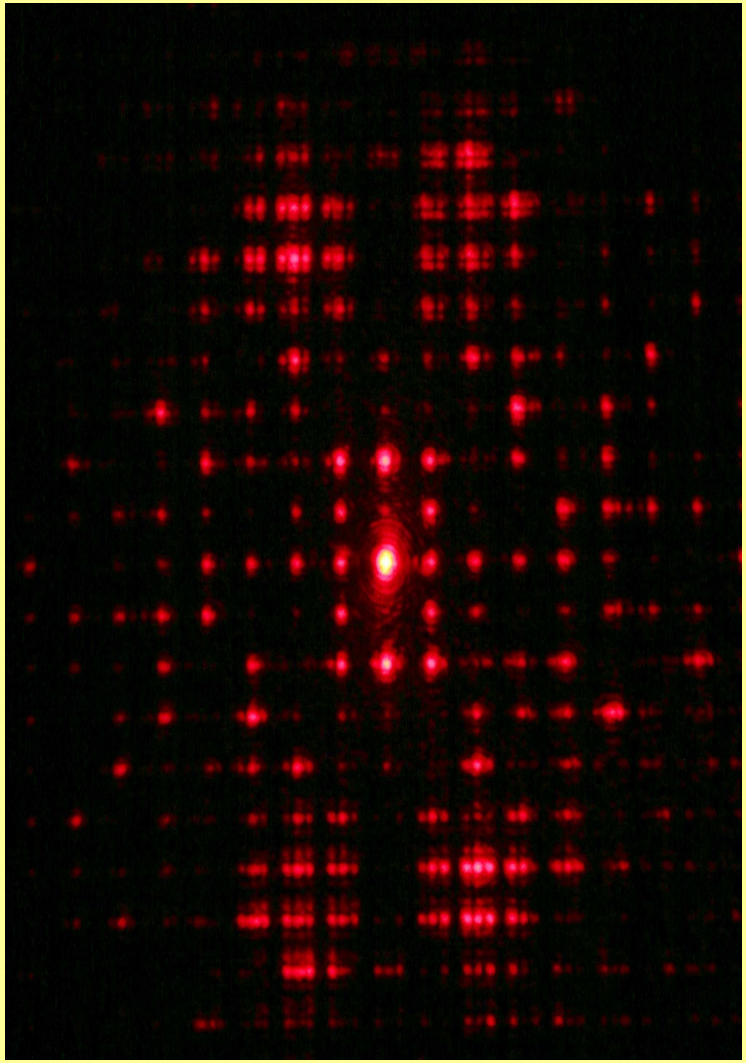


ptical simulation



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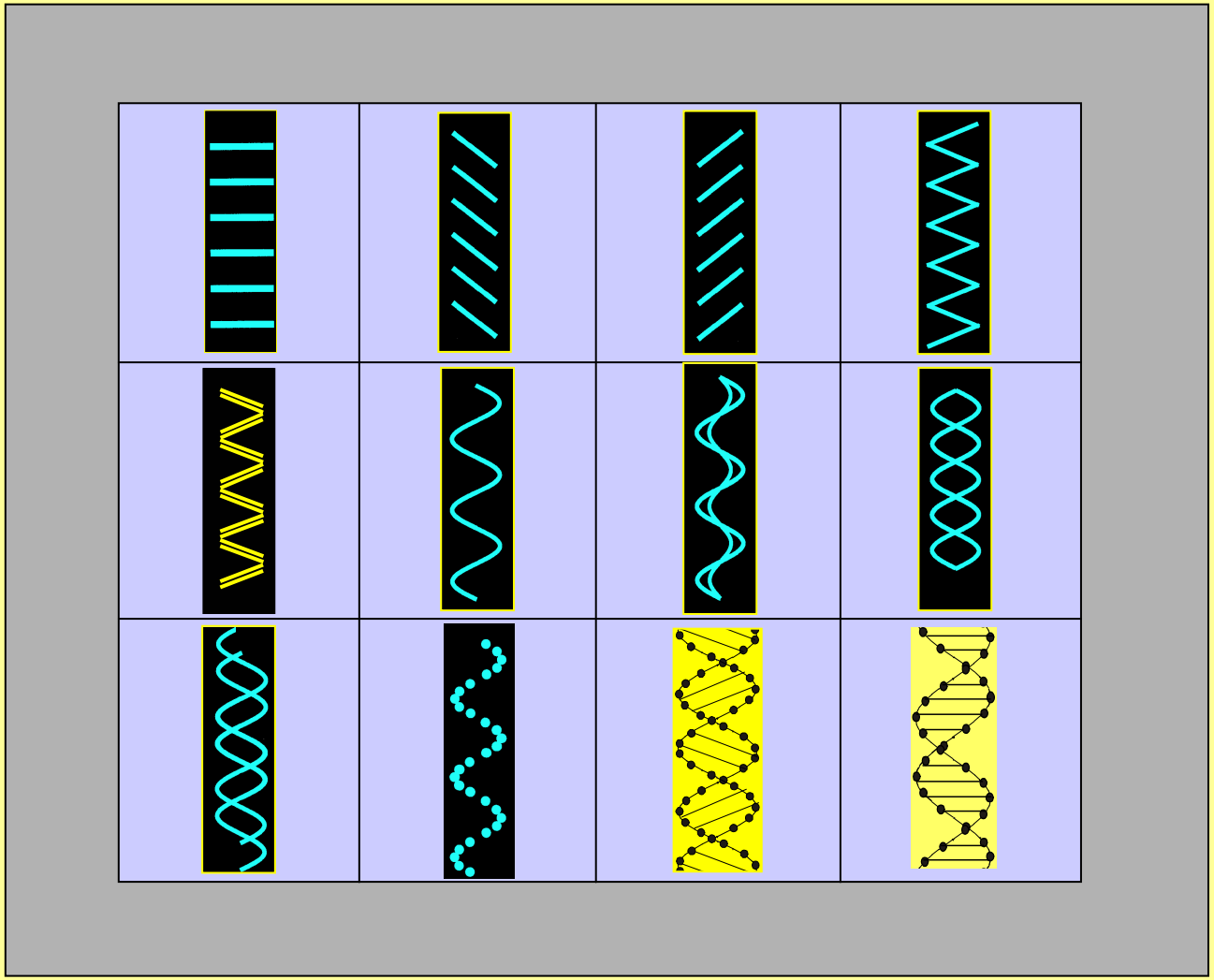
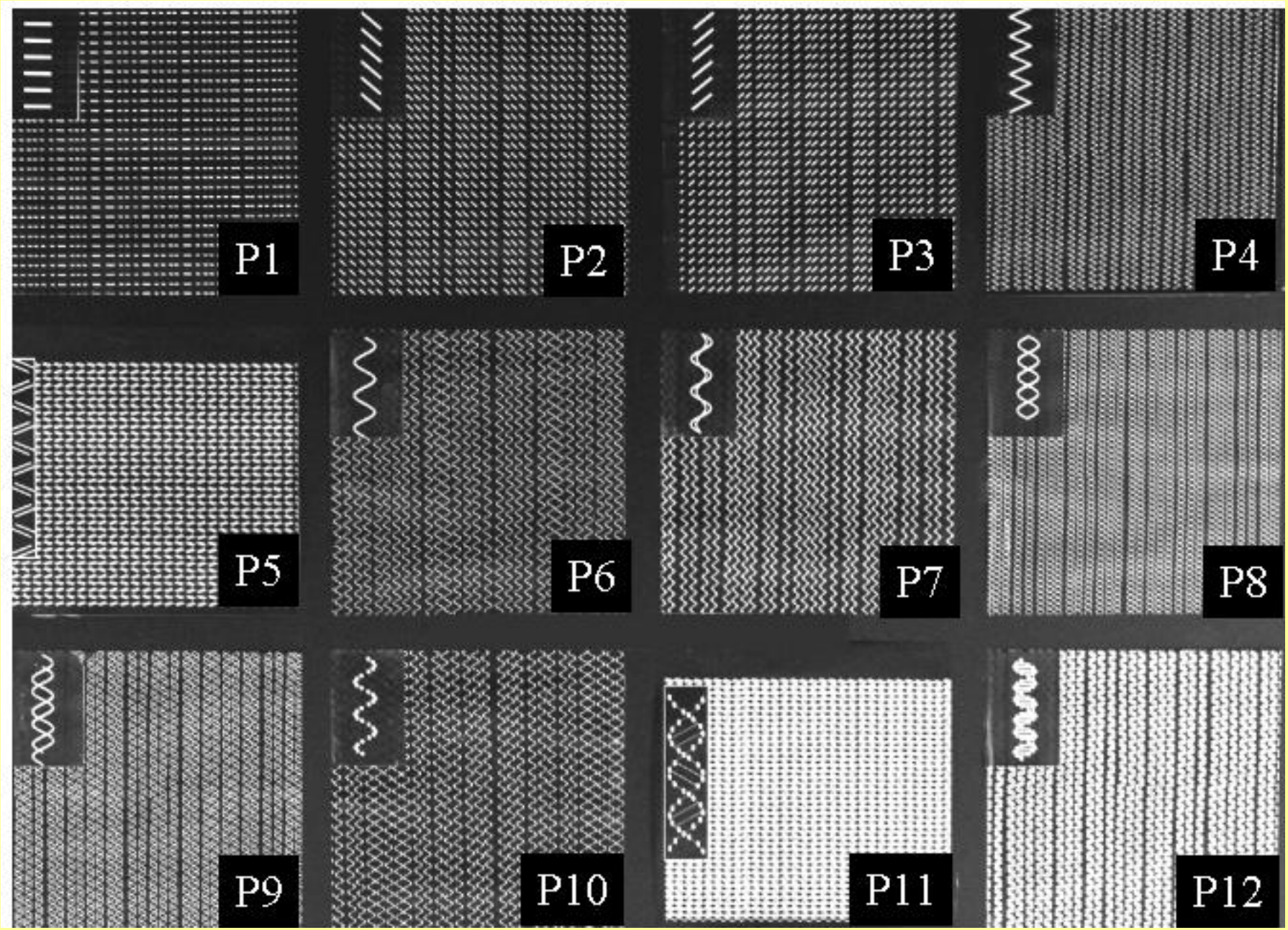
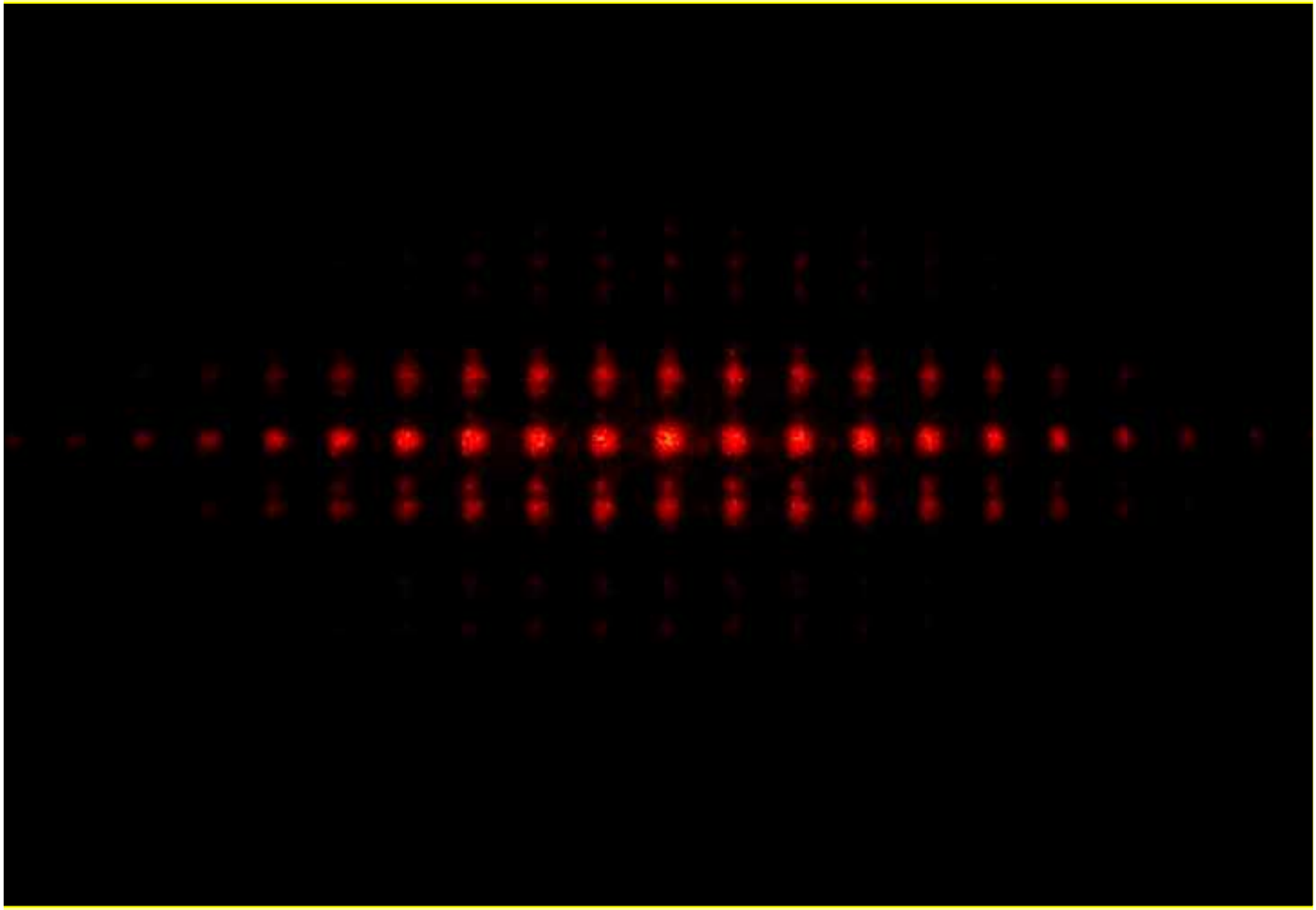
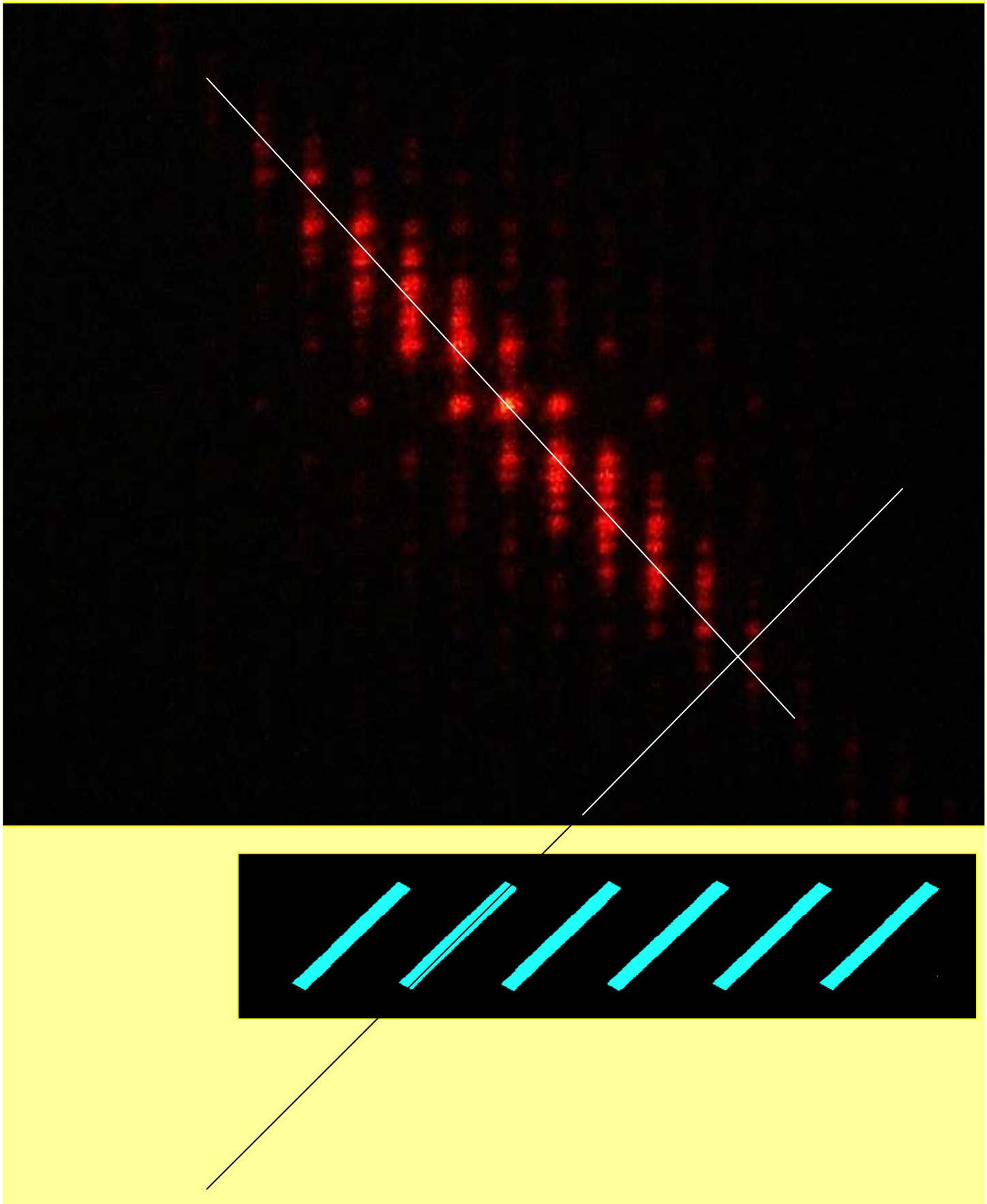
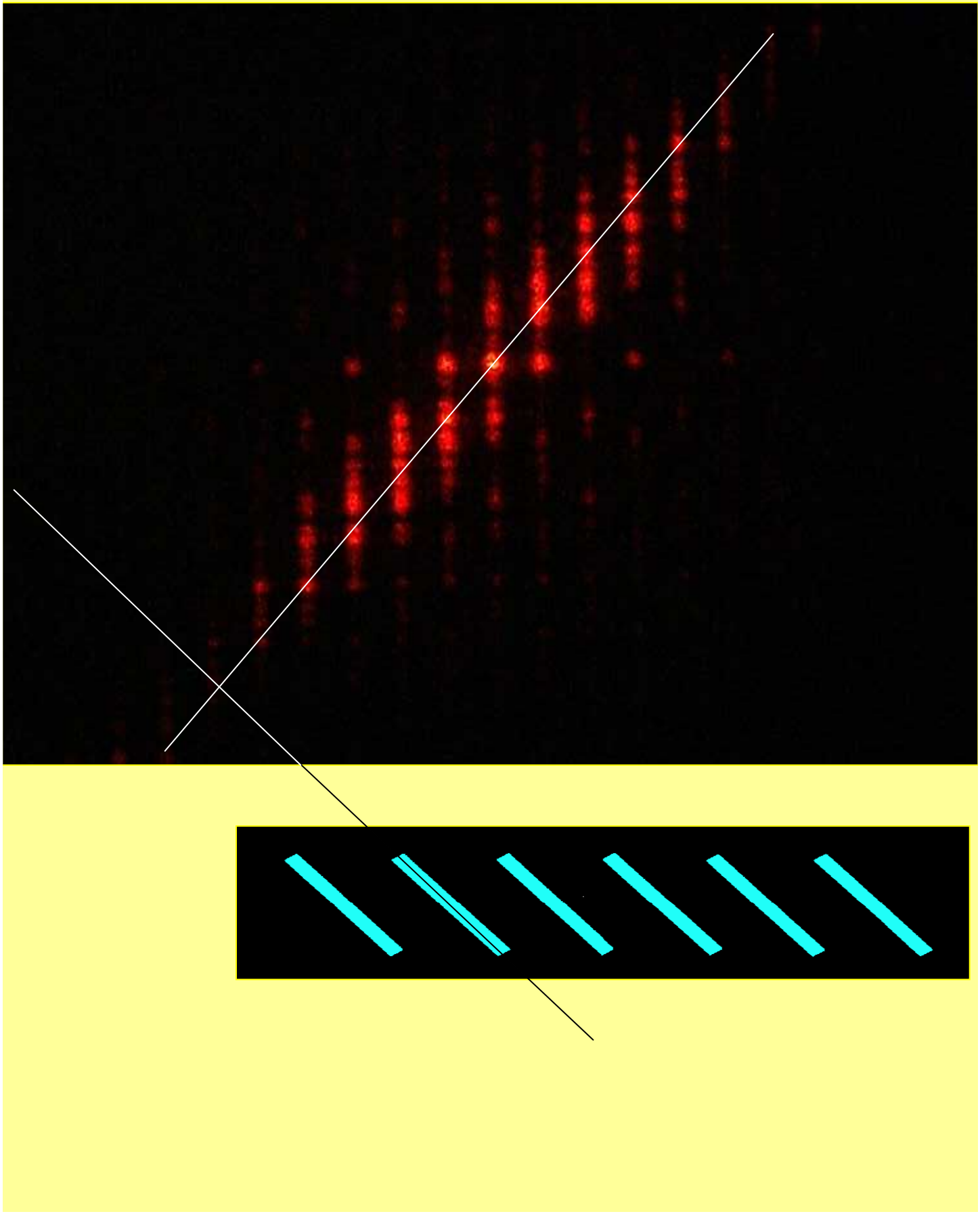


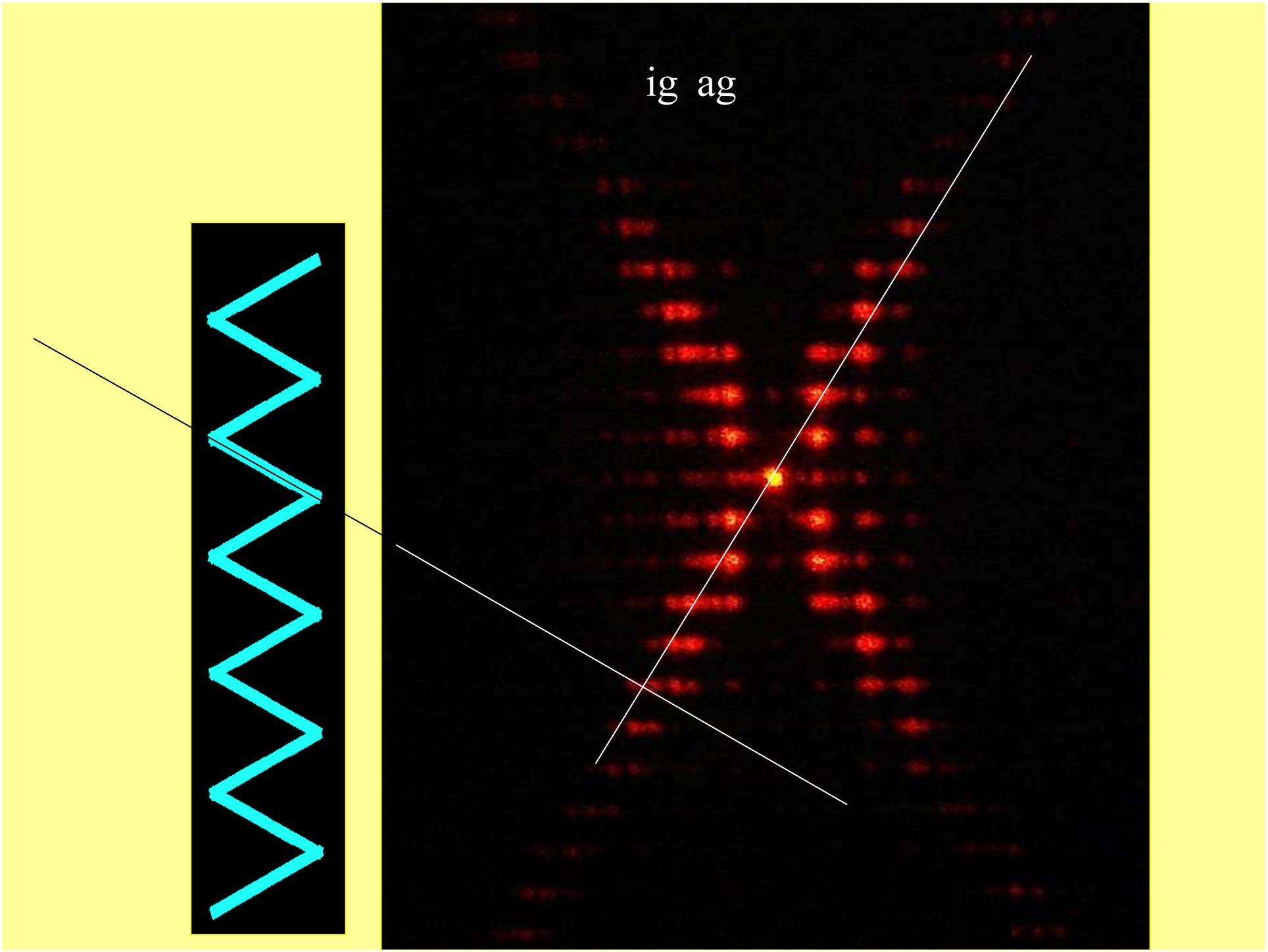
Di raction slide







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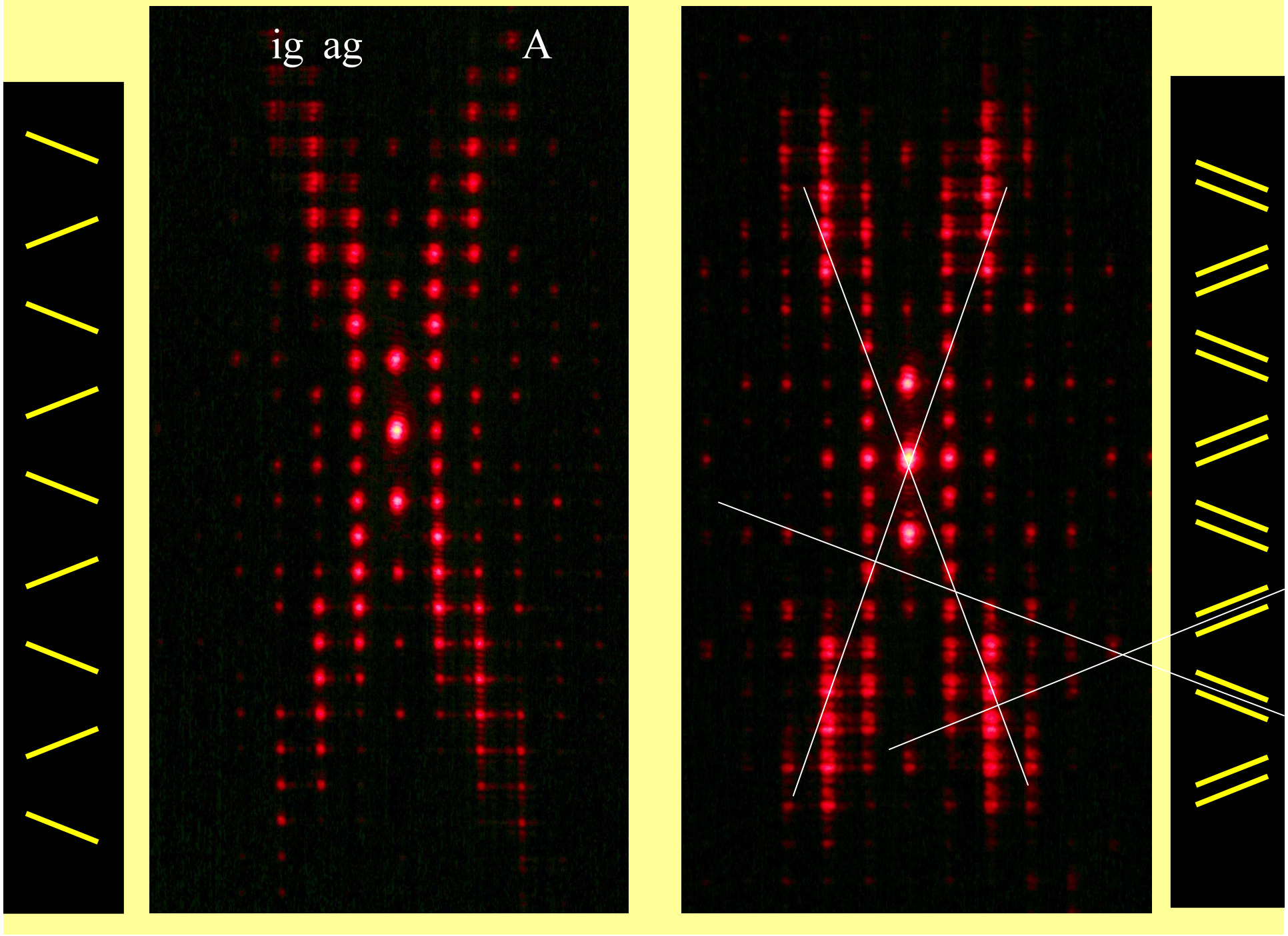
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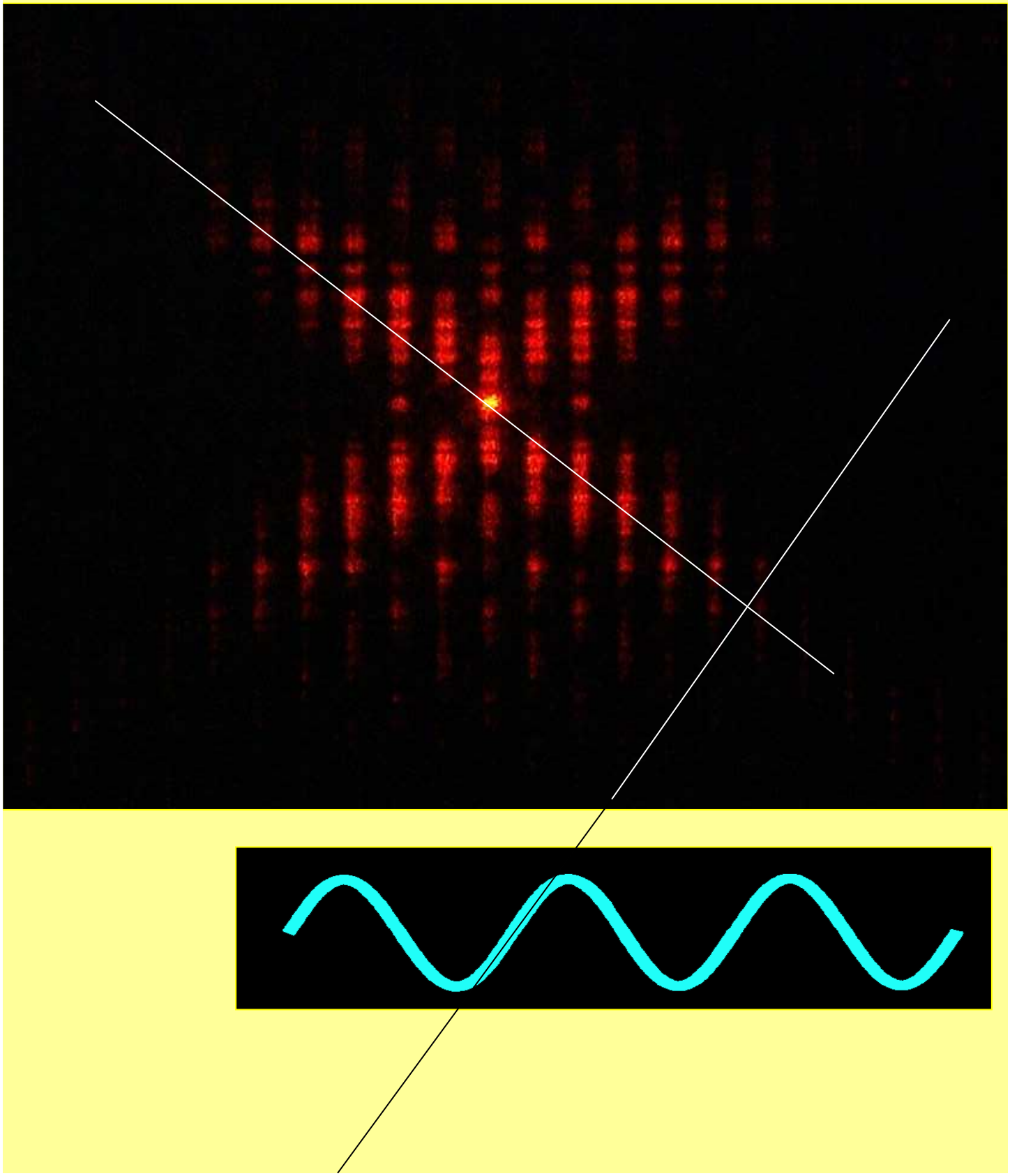

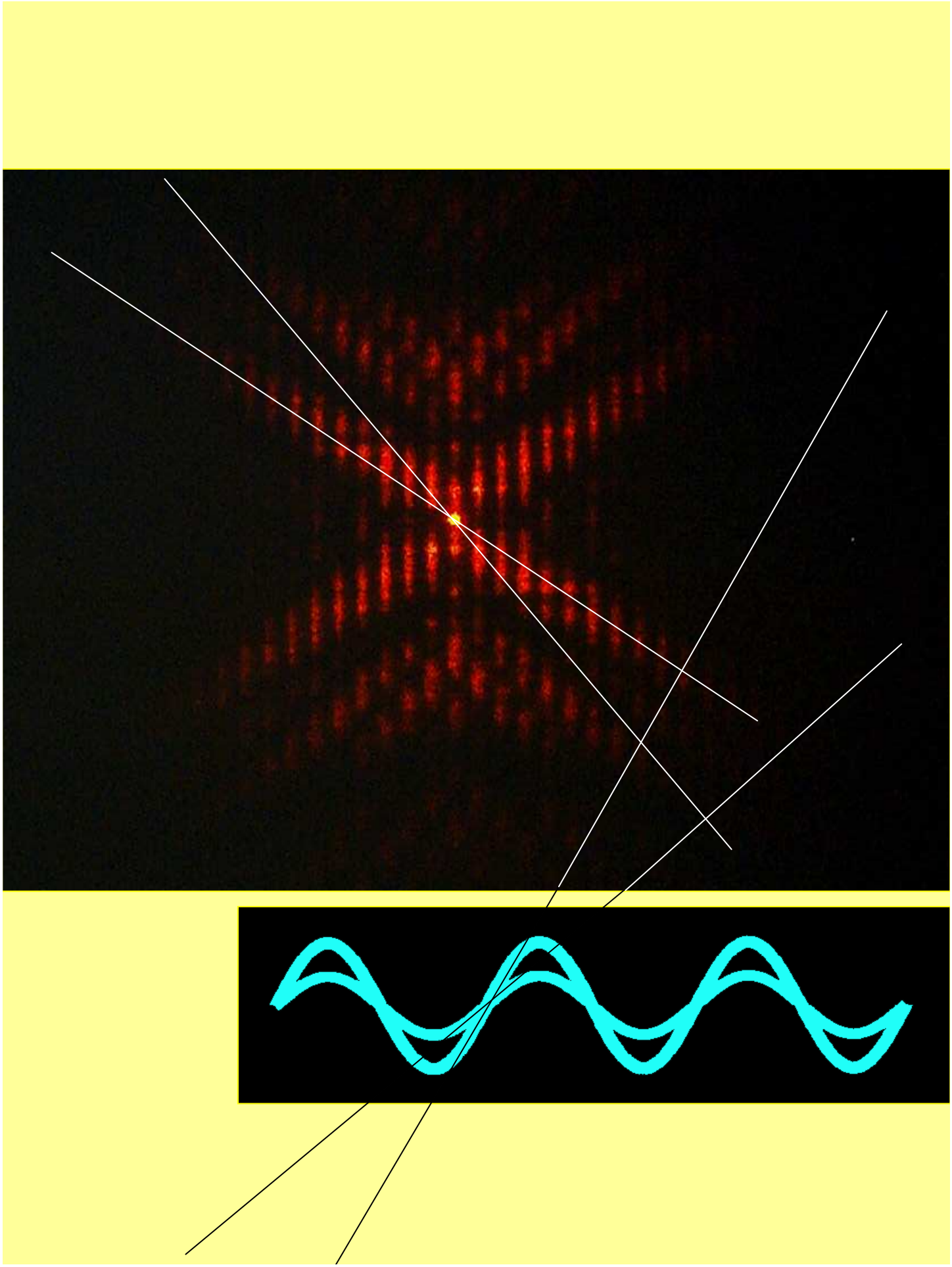

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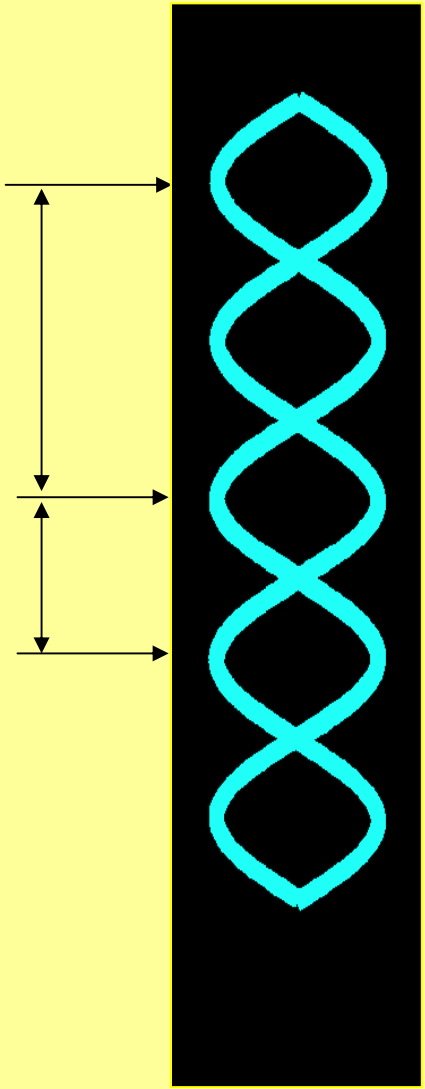
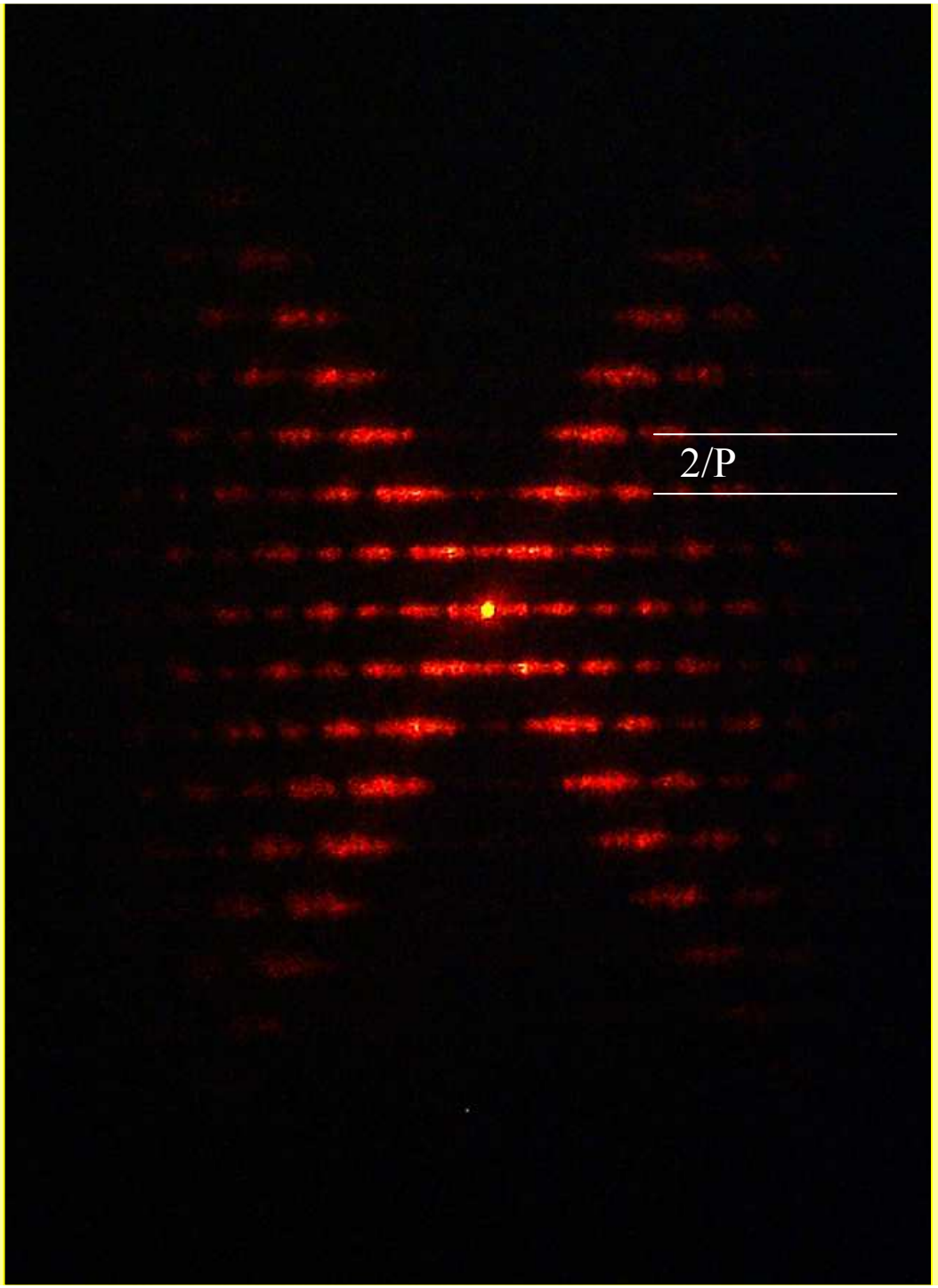
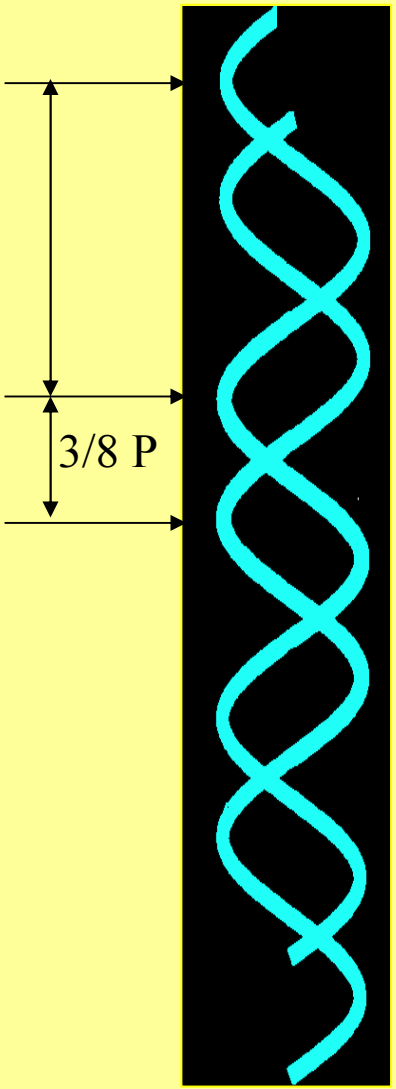
aborted model



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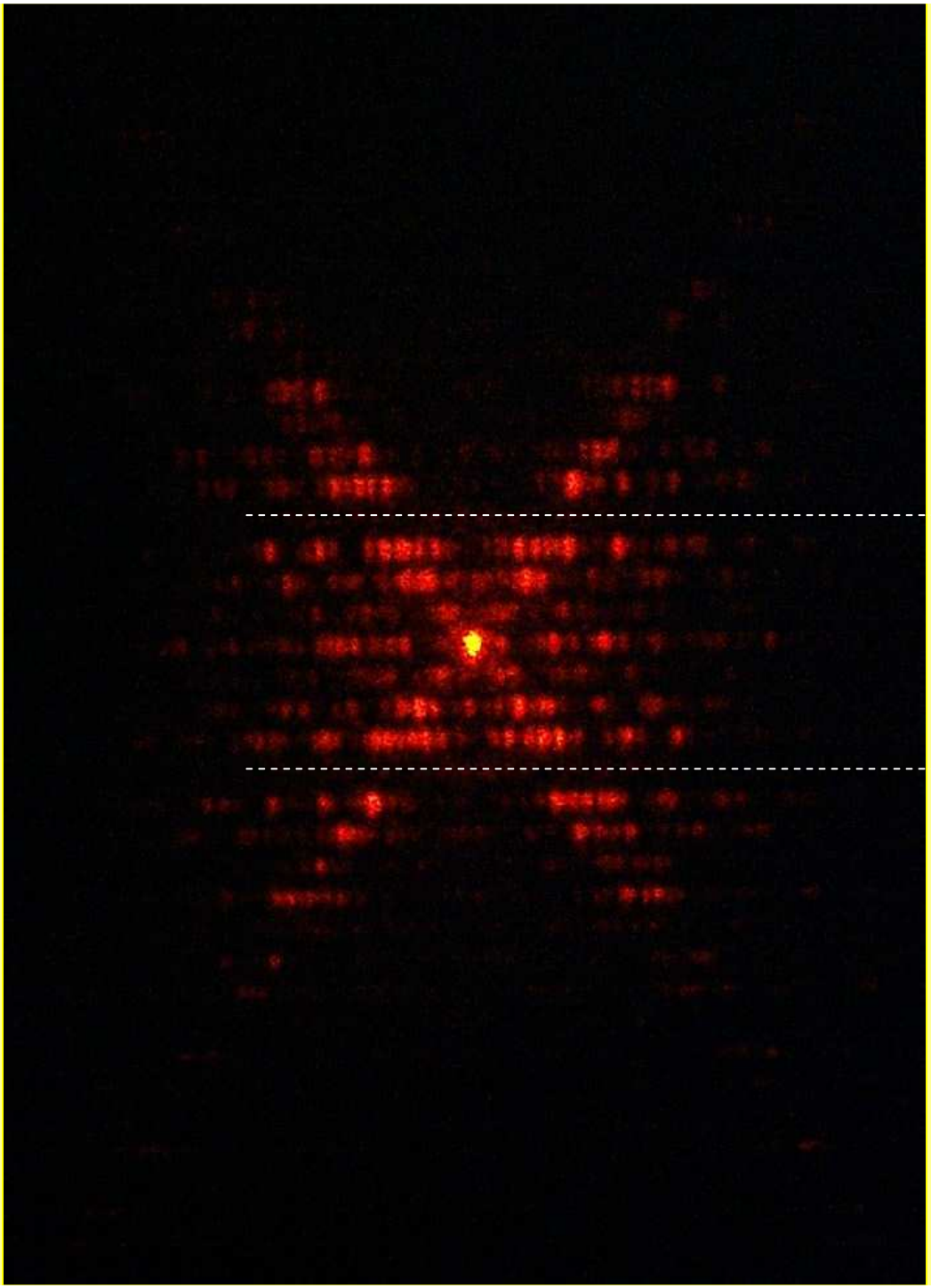
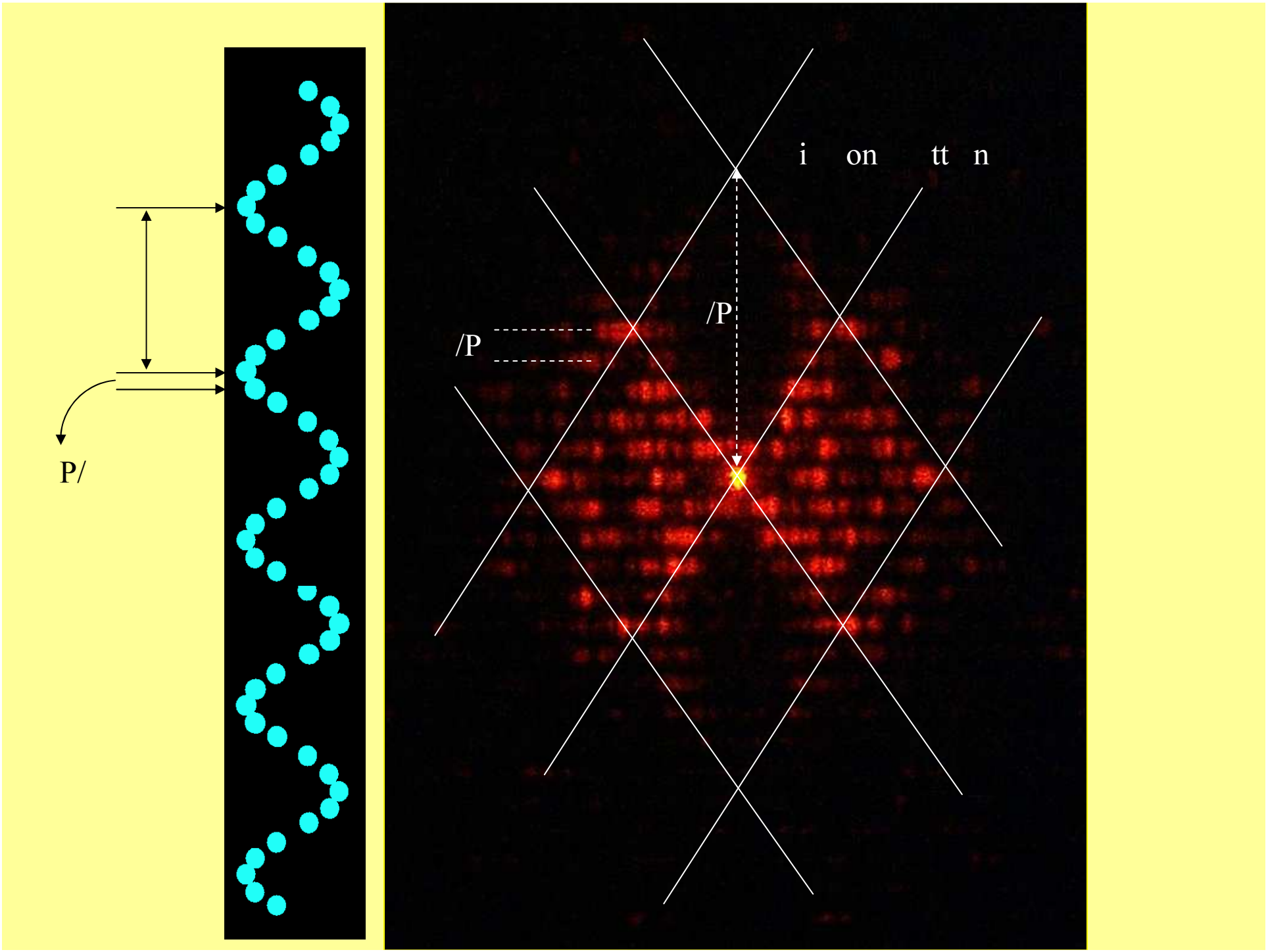

Extinction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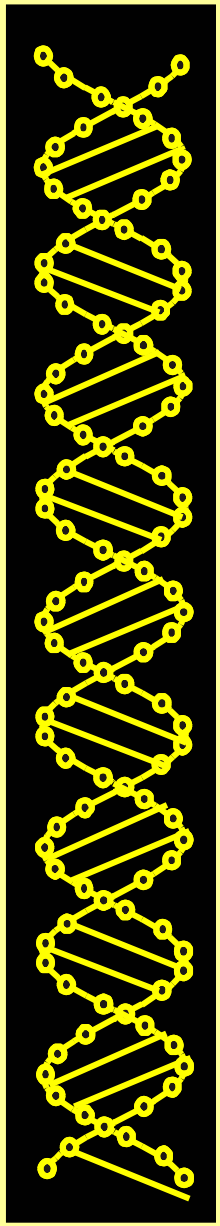
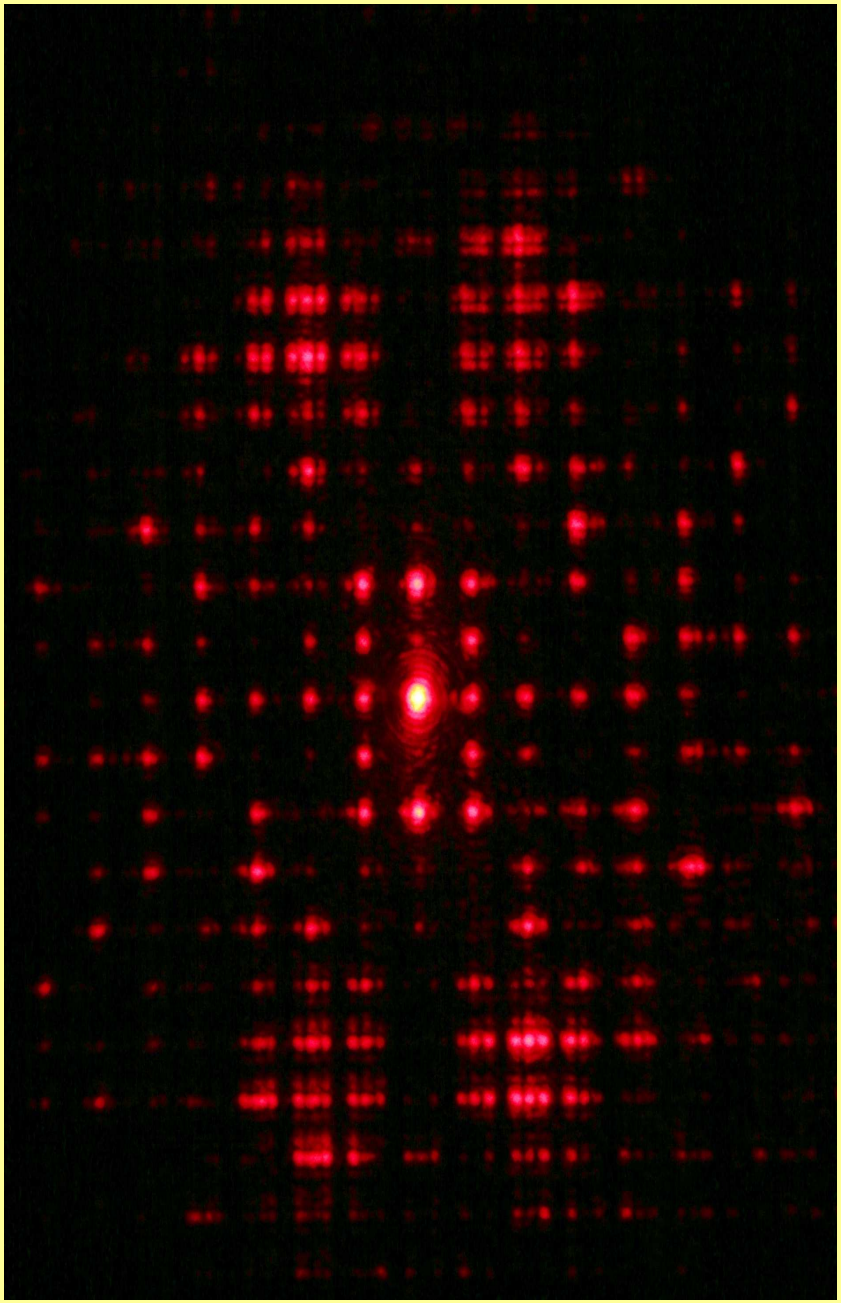
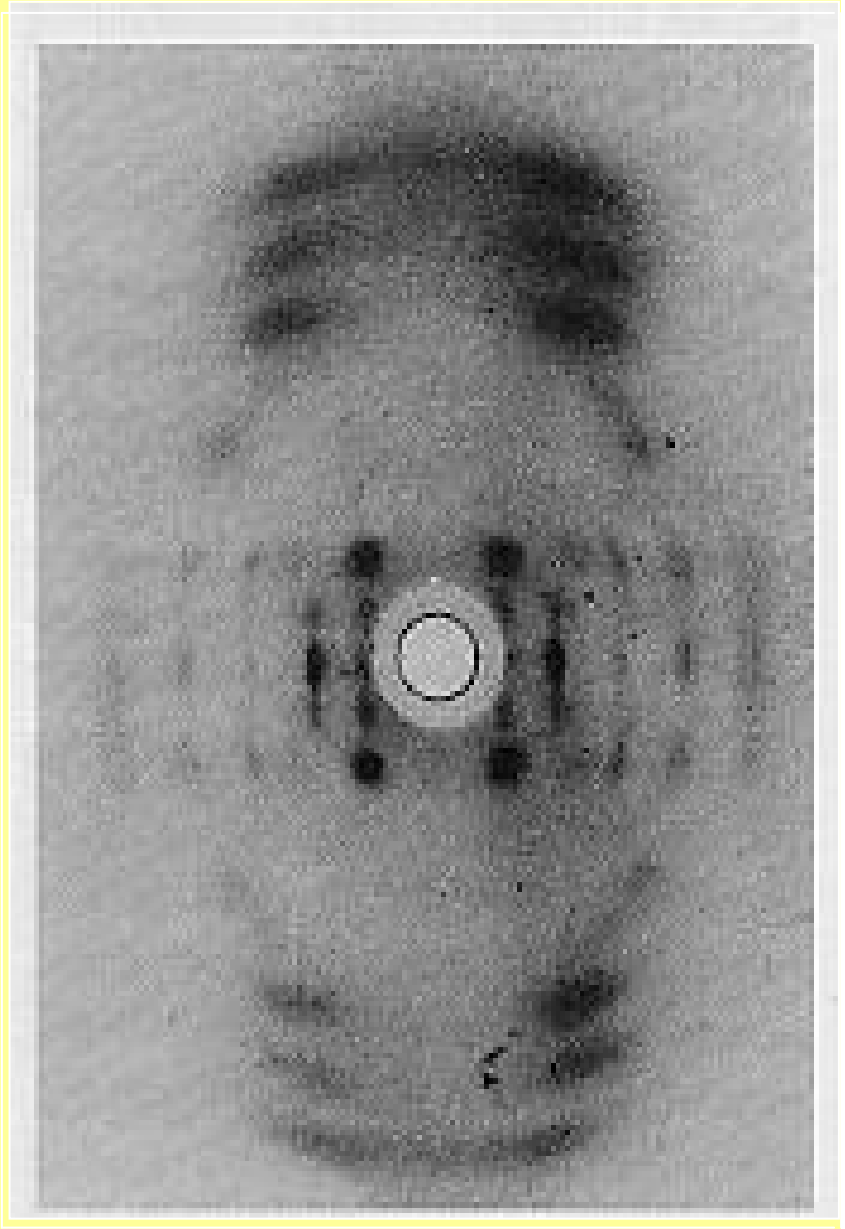
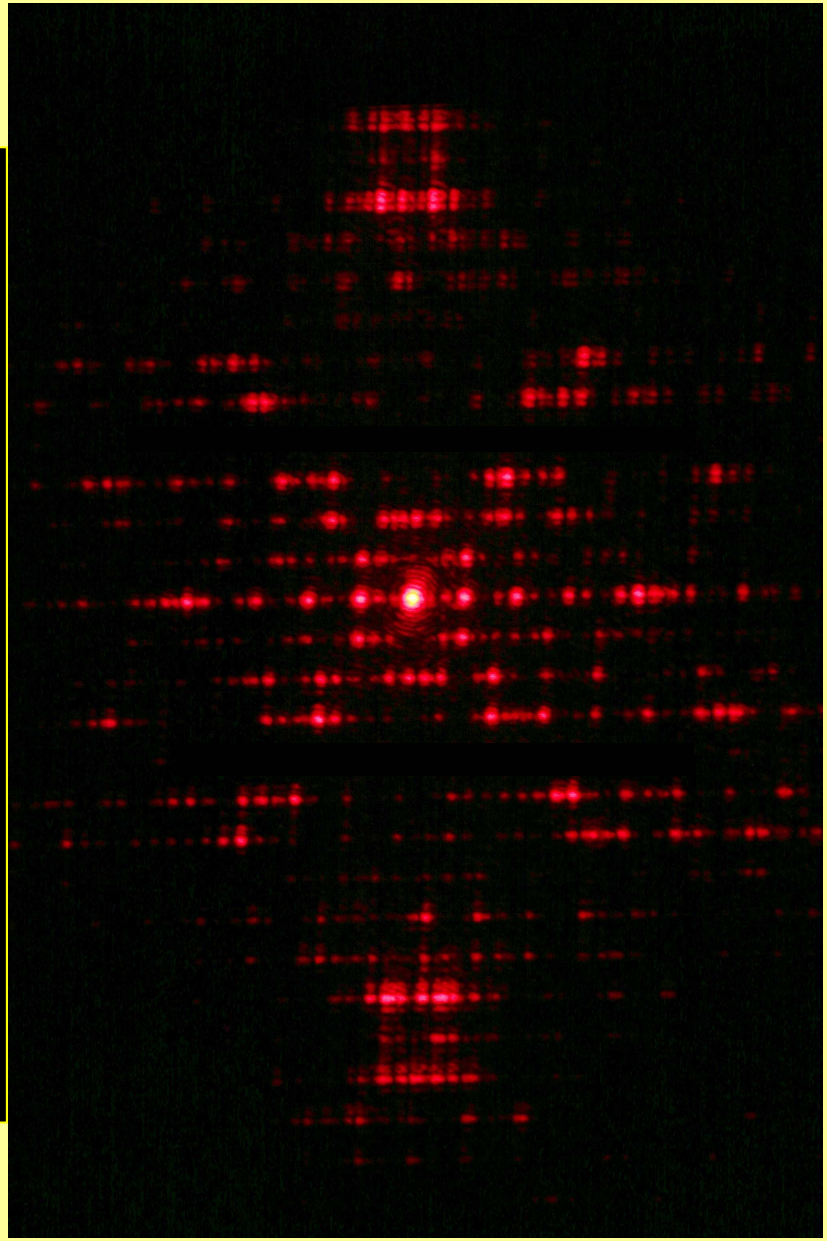
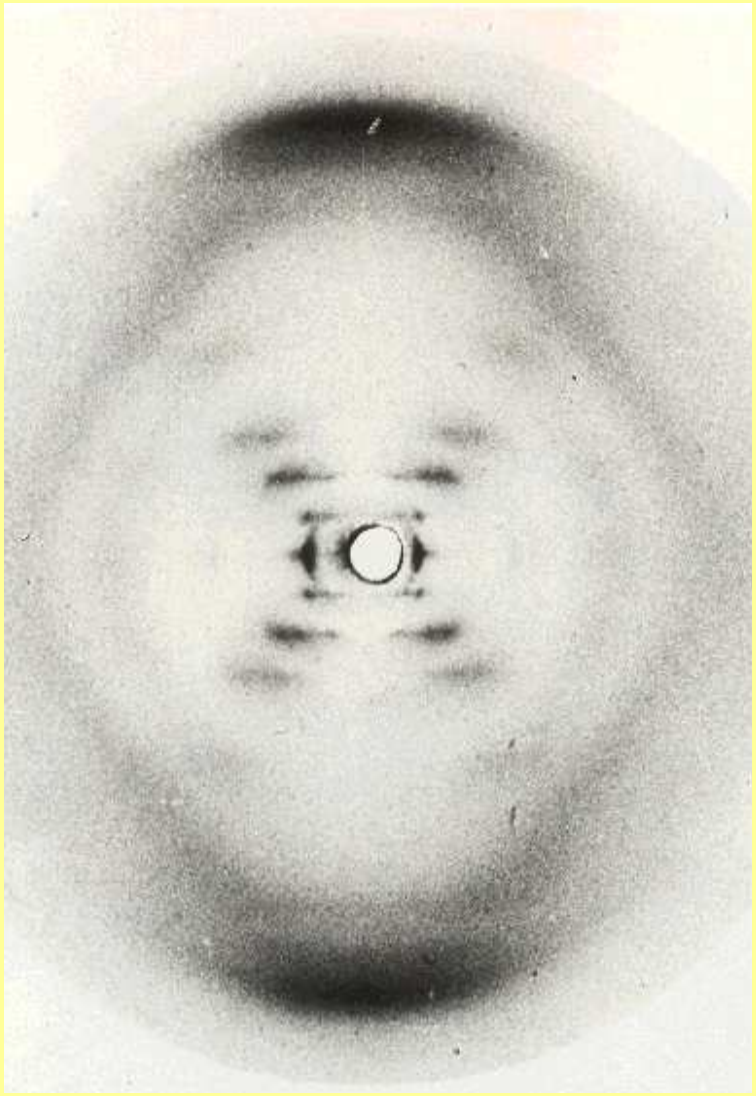






A-DNA Fraunhofer





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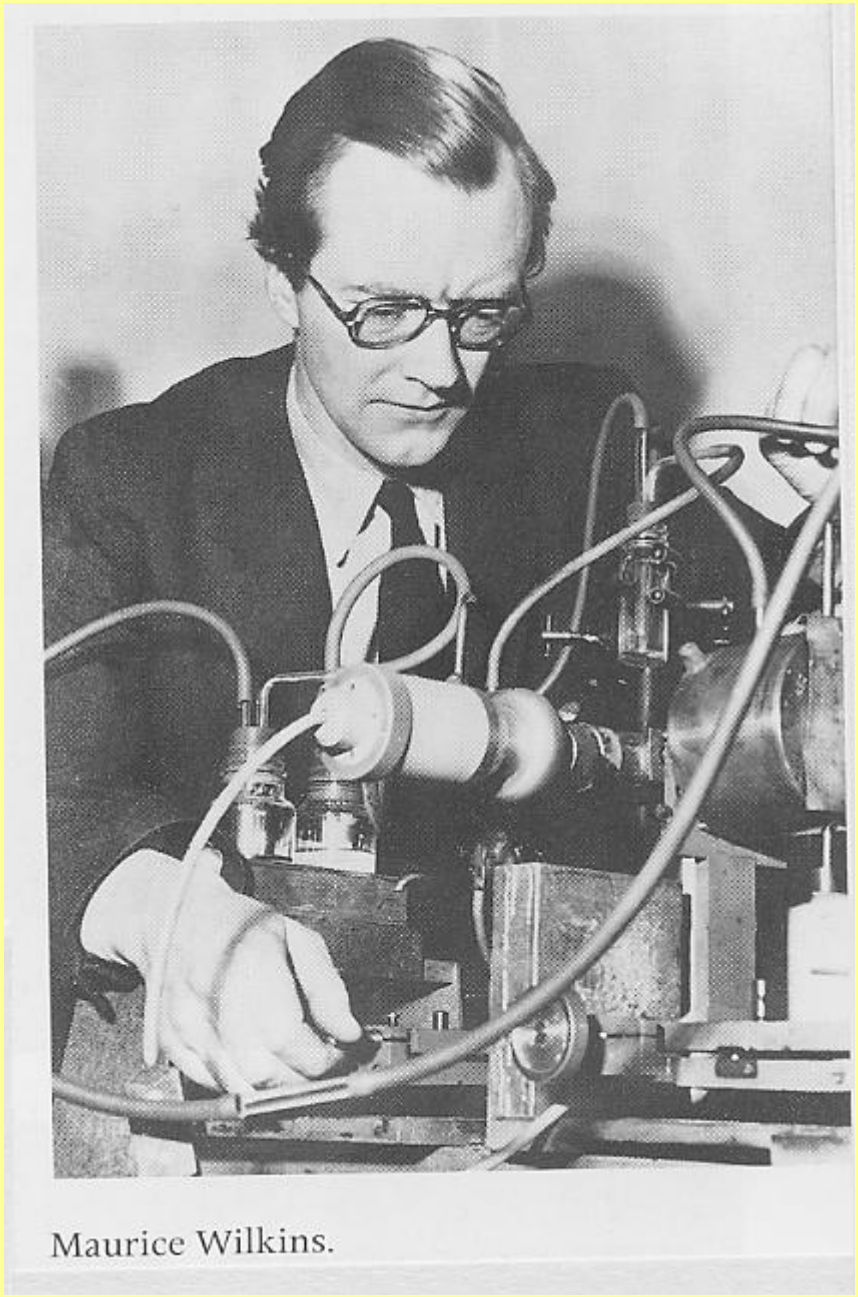
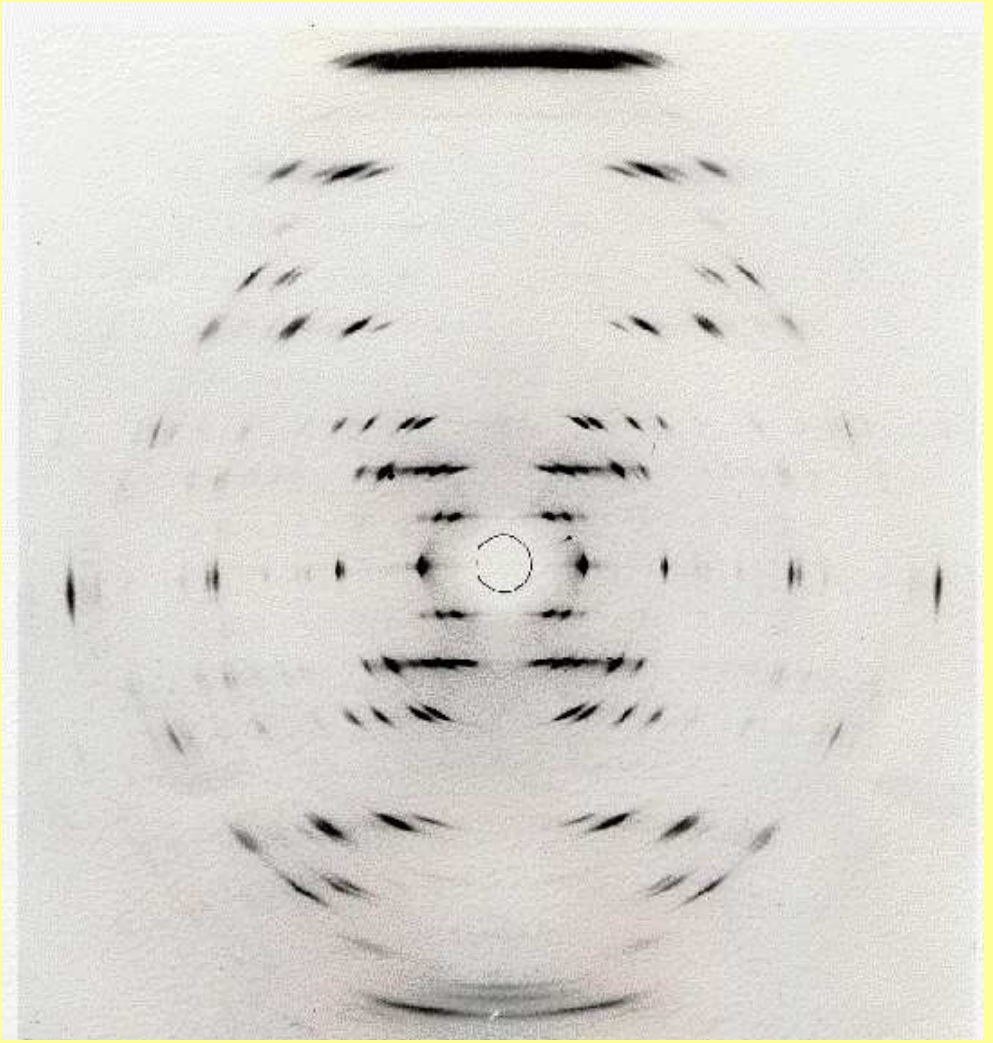


Maurice Wilkins.

M. Wilkins 1957



i -DNA

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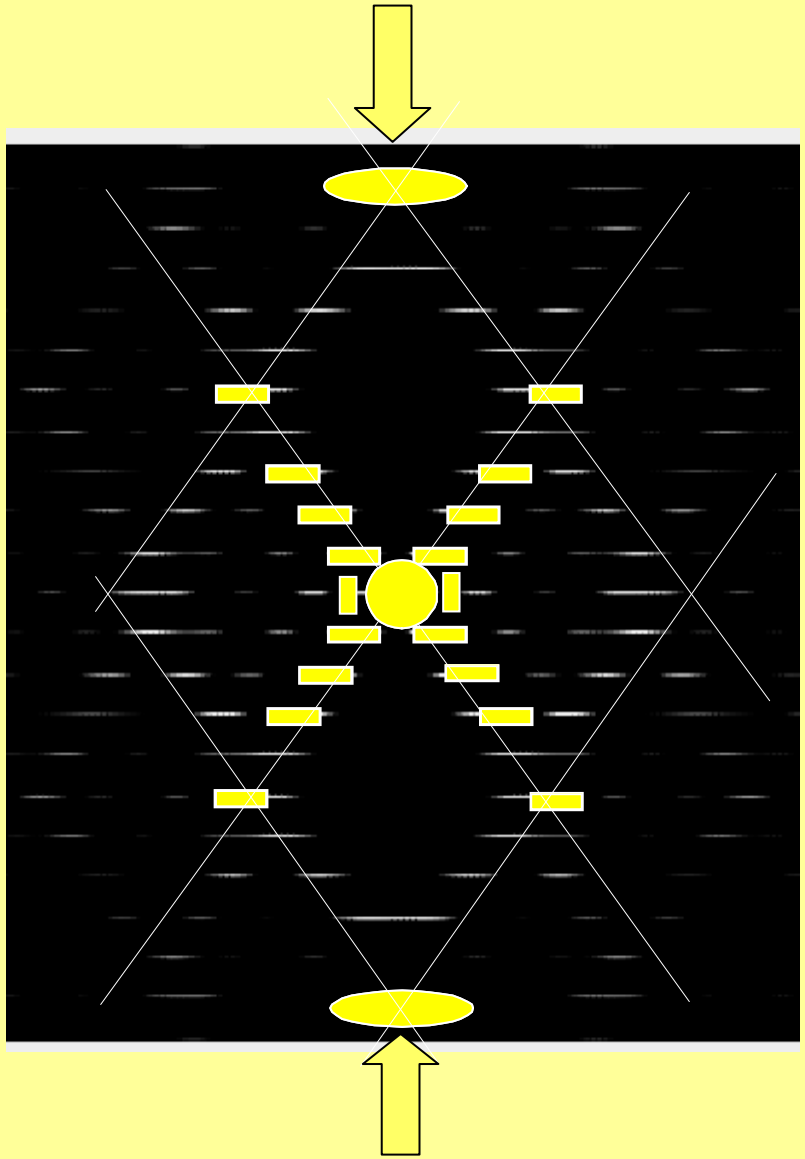

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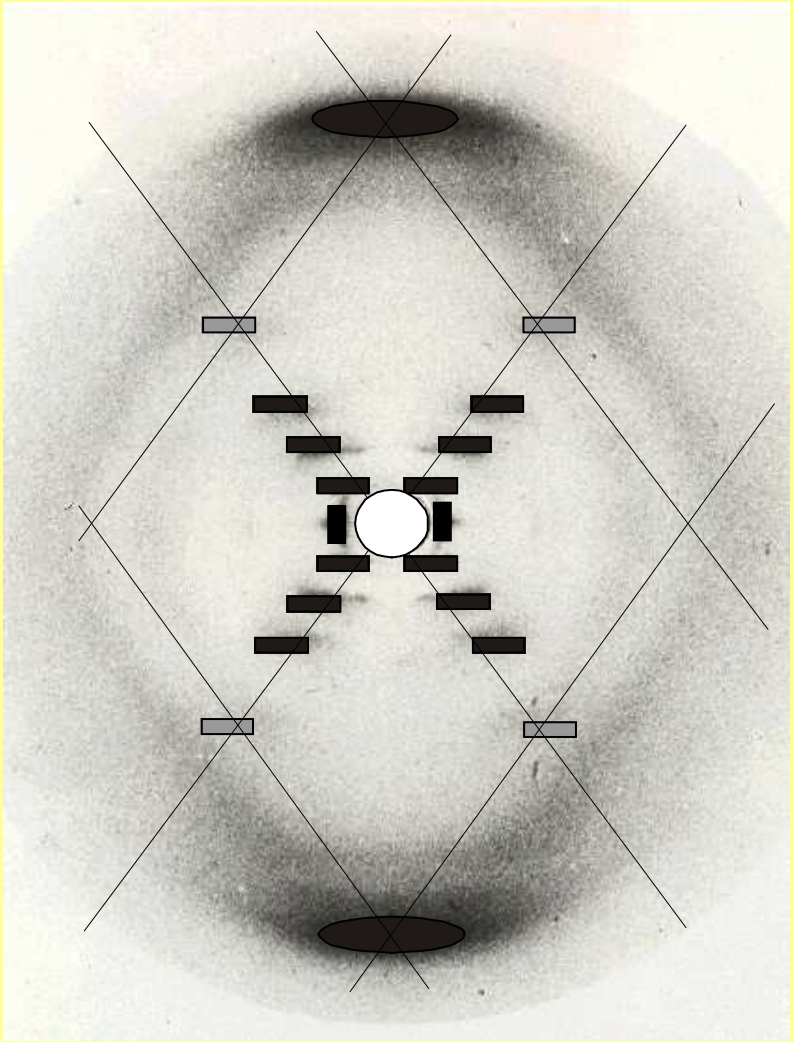

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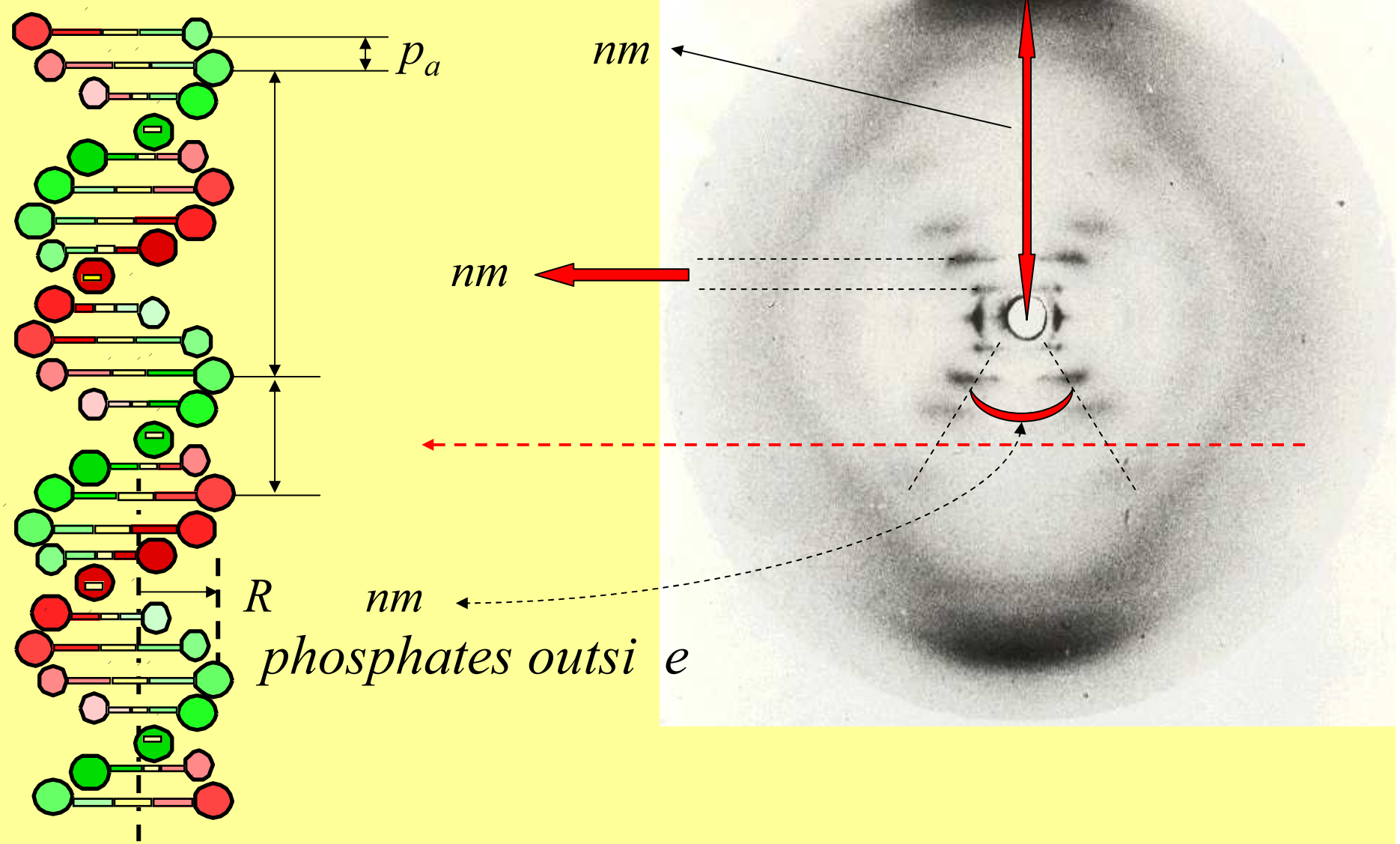
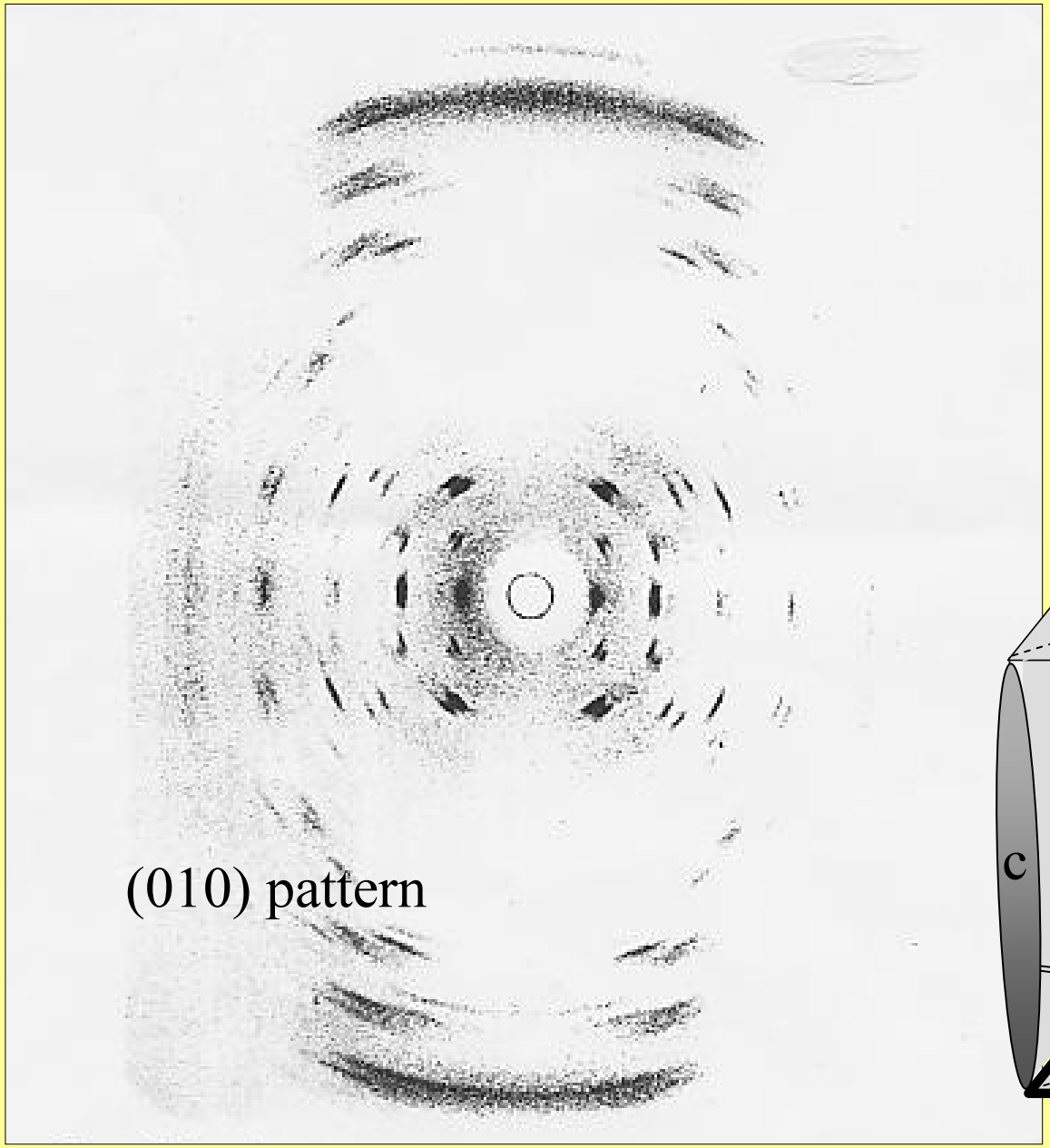
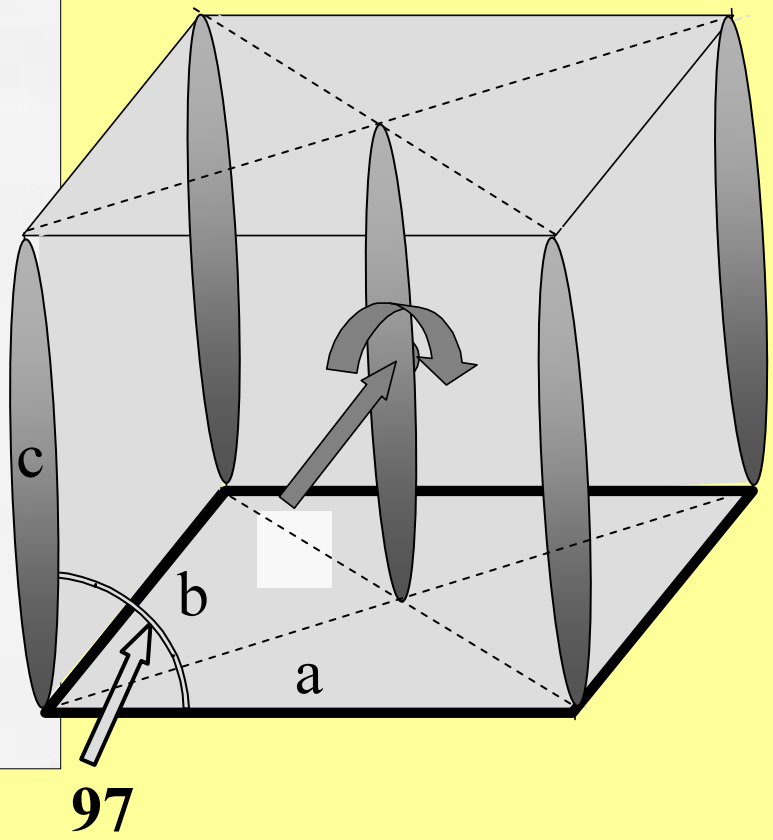




Fran lin, osling
A-DNA rystal fiber

Revelation II:

-face centered
onoclinic unit cell



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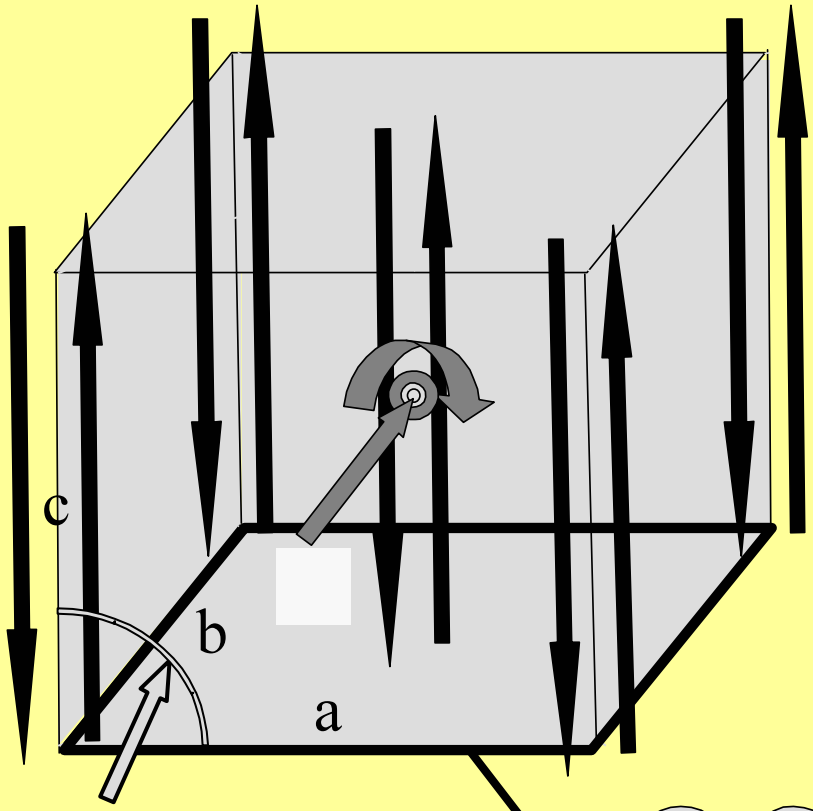

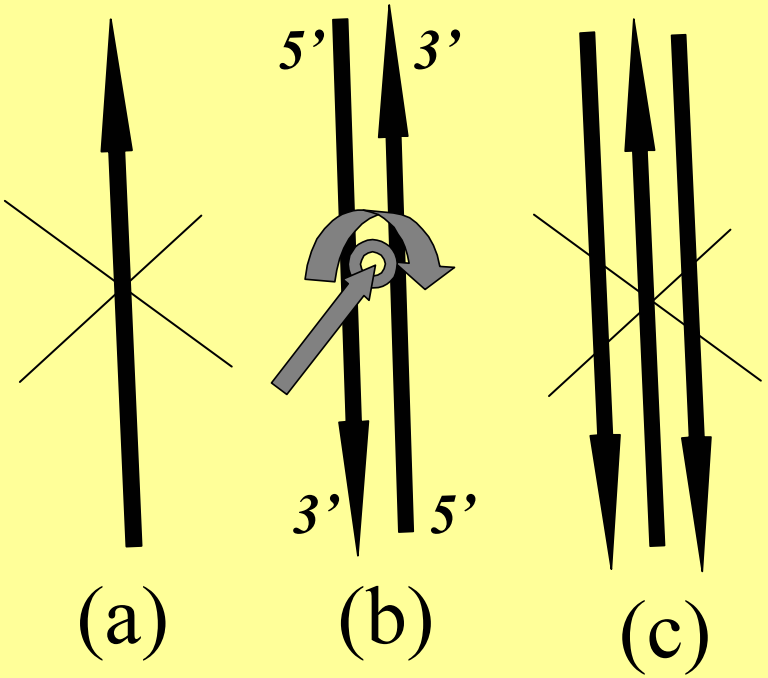

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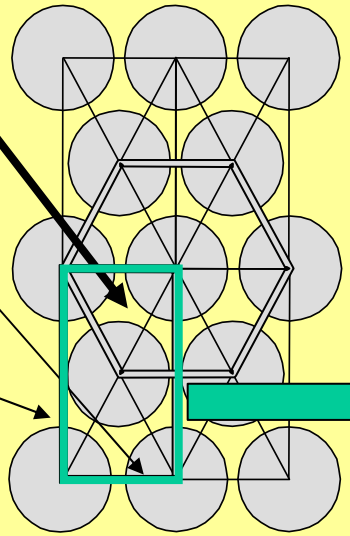

F. Crick

Revelation II

-face-centered monoclinic unit cell of A-DNA

R. Franklin