Crystallography

Topics:

1. **Image Formation** *(what we see is not always accurate)*
   - **Resolution / Wavelength (Amplitude, Phase) / Diffraction & Interference**
   - **Light Microscopy / EM / X-ray / (NMR)**
2. **Protein Data Bank (PDB)**
   - **Data mining and Protein Structure Analysis Tools**
3. **IYCr 2014 - Celebrating 100 years of X-ray Crystallography**

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4. **X-Ray Crystallography – practical aspects**
   - **a) Crystal Growth – Materials / Methods**
   - **c) Crystal Lattices - Lattice Constants / Space Groups / Asymmetric Unit**
   - **d) X-ray Sources – Sealed Tube / Rotation Anode / Synchrotron**
   - **e)Theory of Diffraction – Bragg's Law / Reciprocal Space**
   - **f) Data Collection – Methods / Detectors / Structure Factors**
   - **g) Structure Solution – Phase Problem: MIR / MR / MAD**
   - **h) Refinements and Models / Analysis and presentation of results**

Five common human senses

iClicker Question

Sight: rods / cones

Smell

Taste: sweet, salty, sour, bitter, and umami (savory)

Touch: pressure, temperature, pain, itch

Name your favorite sense?

A) Taste B) Sight C) Hearing D) Smell E) Touch

"No Highway in the Sky" **(1951)**

"No Highway in the Sky"

(1951) –

James

Stew

Crystallography – Worlds of Wonder

⟹ • **Crystallography - What is it?**
How does it Work? Why should I care?

- Early Years – historical overview
- Demonstration of diffraction / image formation
- Crystals + X-rays → *record of Nobel Prizes*

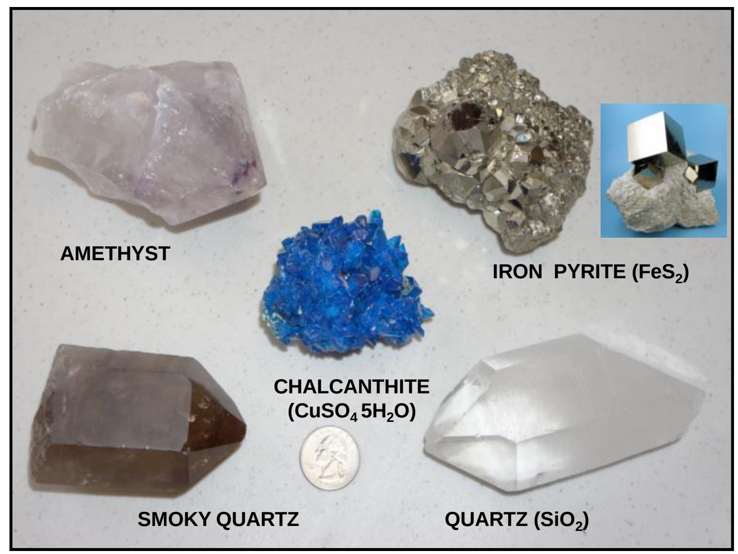
• **Advances in X-ray crystallography (last 50 years)**

sources / computers / detectors

• **Benefits of Crystallography to Society / IYCr 2014**

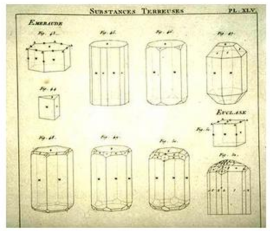
Crystallographic Awareness / Celebration / Training

IYCr: Summits (Africa / Asia / Latin America)
Crystal growth contests / Exhibits / etc.
Crystallography Discovery Kit for teachers & museums
symmetry / crystal growth / diffraction



The Law of Constancy of Angles

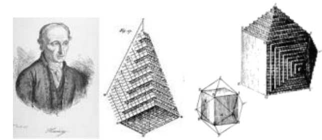
1669 The Danish physician Nicholas Steno was the first to notice that in quartz crystals the angles between the faces are constant - the Law of Constancy of the Angles. He made enlightened hypotheses concerning the mechanism of crystal growth. His work marks the beginning of crystallography as an independent discipline.



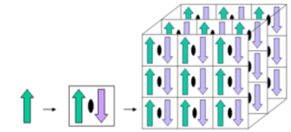
1801 In *Traité de Minéralogie*, *René-Just Haüy described how The Law of Rational Indices relates the orientations of crystal faces, and explained how crystalline solids consist of replicas of a unit cell.*

Crystallography - What is it?

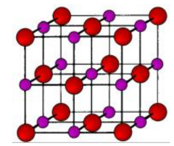
Crystals – (Strabo ~7 BC; used Greek word *krustallos* describing quartz crystals*)* *a body that is formed by the solidification of a chemical element, a compound, or a mixture and has a regularly repeating internal arrangement of its atoms and often external* plane faces



René Just Haüy (1743-1822)



X-ray Crystallography - a method used for determining the atomic and molecular structure of a crystal.



Sodium Chloride (NaCl)
(a.k.a. Table salt)

Words

Trees
BY JOYCE KILMER

I think that I shall never see
A poem lovely as a tree.

A tree whose hungry mouth is prest
Against the earth's sweet flowing breast;

A tree that looks at God all day,
And lifts her leafy arms to pray;

A tree that may in Summer wear
A nest of robins in her hair;

Upon whose bosom snow has lain;
Who intimately lives with rain.

Poems are made by fools like me,
But only God can make a tree.

Images

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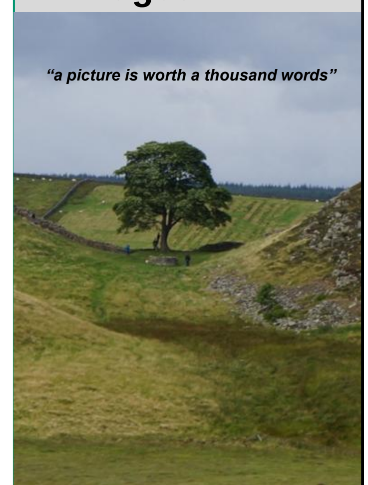
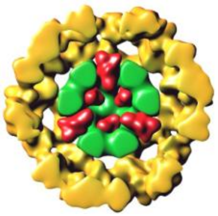


3

"If a picture is worth a thousand words, then a macromolecular structure is priceless to a physical biochemist." – van Holde

- Light Photography
  λ ~ 400 - 700 nm

- Electron Microscopy
  λ ~ 0.001 - 0.1 nm



- X-Ray or NMR
  λ ~ 0.1 nm

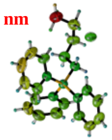


Image Formation

Abbe (~1873):

Limit Res. ~ wavelength/2

Resolution Limit

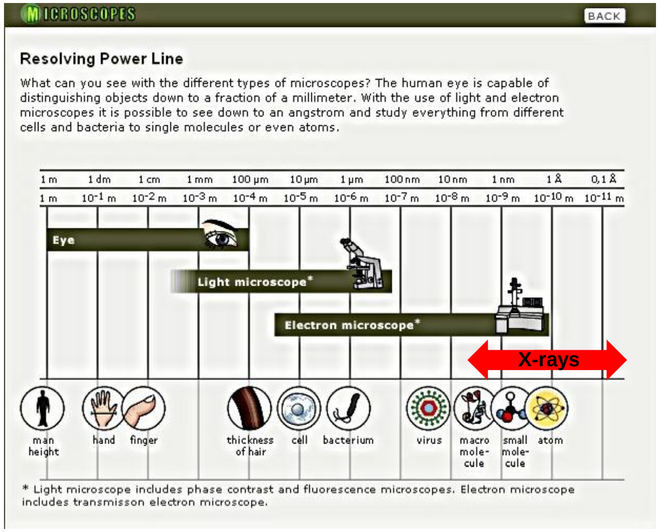
The diffraction limit of a microscope is,

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

where d is the resolvable feature size, λ is the wavelength of light, n is the index of refraction of the medium being imaged in, and θ (depicted as α in the inscription) is the half-angle subtended by the optical objective lens.

Memorial to Ernst Abbe
University of Jena

Secondary school named Ernst Abbe Gymnasium



Superman's X-ray Vision

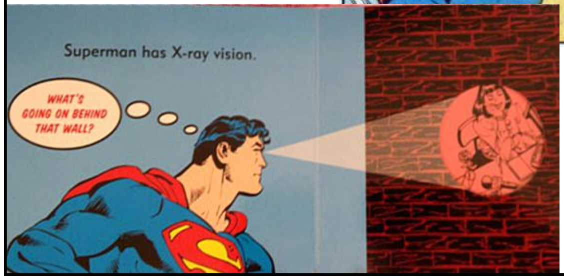
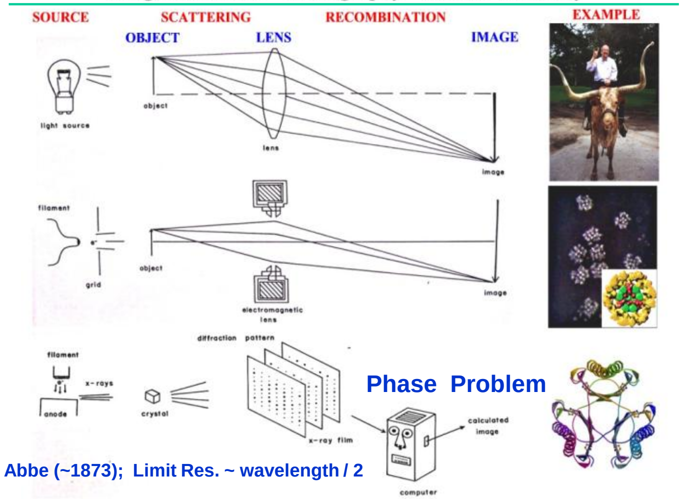


Image Formation - "Photography" vs. EM vs. X-ray



Abbe (~1873); Limit Res. ~ wavelength / 2

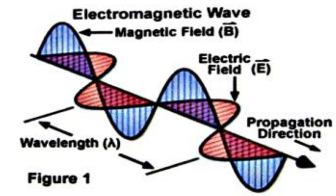
To understand the beginnings of X-ray crystallography, one needs to understand three key properties of waves – **wavelength**, ***diffraction*** and ***interference***.

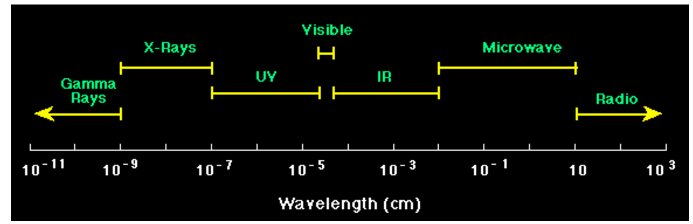
Wavelength

Radio: 100 MHz (300 cm)

Visible light: 600 nm = 6 x 10^{-5} cm

X-rays: 0.1 nm = 1 x 10^{-8} cm





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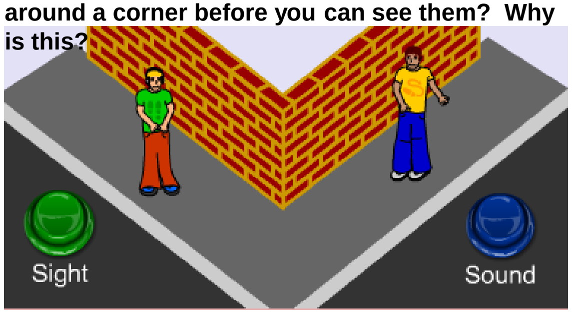
Diffraction

Have you noticed how you can hear someone around a corner before you can see them? Why is this?



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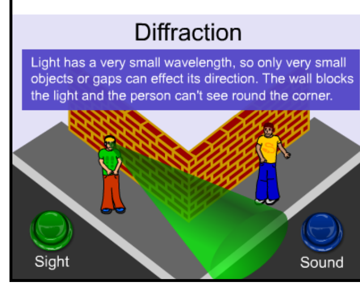
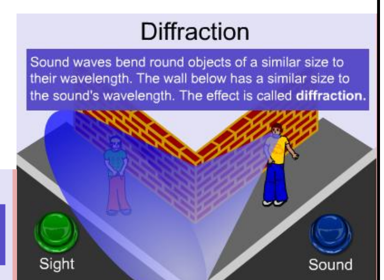
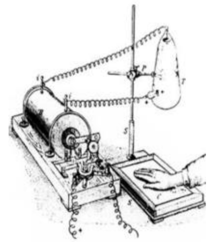


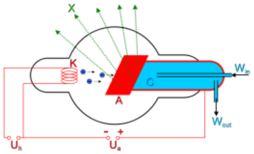


The Nobel Prize in Physics 1901
Wilhelm Conrad Röntgen

The Nobel Prize in Physics 1901

Wilhelm Conrad Röntgen



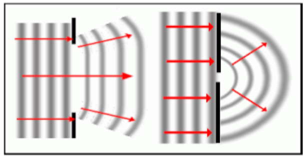


The Nobel Prize in Physics 1901 was awarded to Wilhelm Conrad Röntgen *"in recognition of the extraordinary services he has rendered by the discovery of the remarkable rays subsequently named after him".*

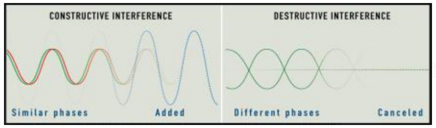
To understand the beginnings of X-ray crystallography, one needs to understand three key properties of waves – **wavelength**, ***diffraction*** and ***interference***.

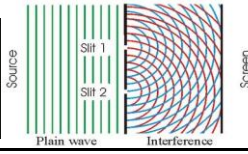
Diffraction: When a wave encounters an obstacle, such as the apparent bending of waves around small obstacles and the spreading out of waves past small openings. Diffraction occurs with all waves, including sound waves, water waves, and electromagnetic waves such as visible light, X-rays, and radio waves.

Diffraction effects are most pronounced for waves where the wavelength is roughly similar to the dimensions of the diffracting objects.

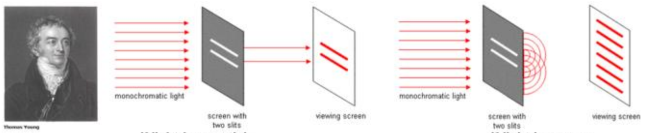


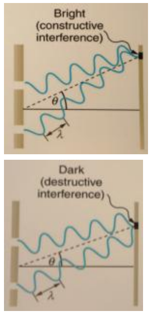
Interference: Interference is a phenomenon in which two waves superimpose to form a resultant wave of greater (***constructive interference***) or lower (**destructive interference**) amplitude.

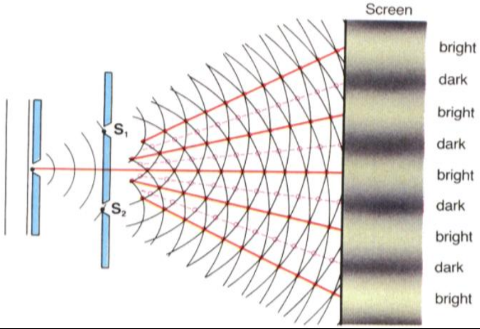




Young (1801) used a 2-slit experiment to show that light was made of waves instead of particles.
Von Laue (1912) proposed that the concept could be applied to X-rays using crystals.

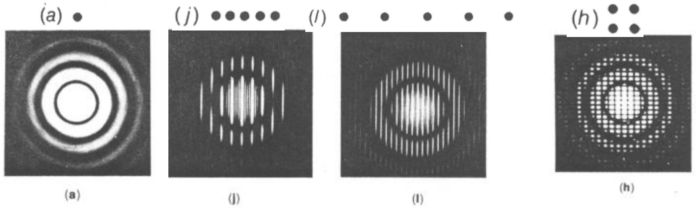




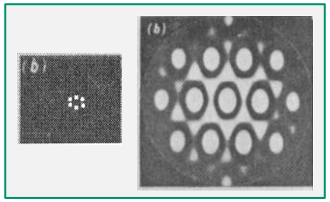


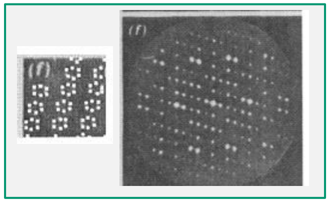
Wave Properties: Diffraction / Interference

Interference: 1D crystal - 5 identical "objects" with but different spacings (unit cells)



Diffraction + **Interference**: **2D Crystal**





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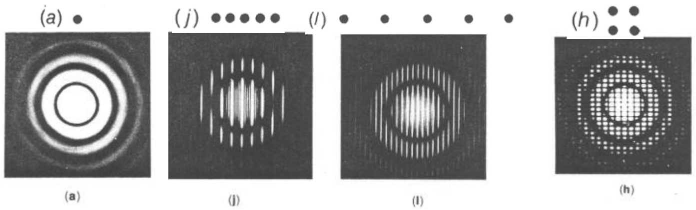
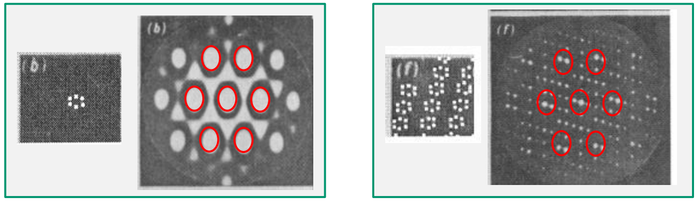
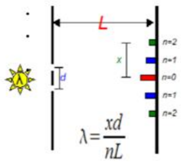


Diffraction + Interference: 2D Crystal



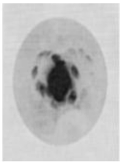
In 1912 Max von Laue proposed that if X-rays were short wavelength waves, then if a crystal were exposed to short wavelength X-ray waves, the small spacings in crystals should result in a "diffraction / interference" pattern of "spots". If the wavelength is known, then the spacings of the spots can be used to calculate the spacings of the atoms in the crystals (e.g. unit cell lengths)!



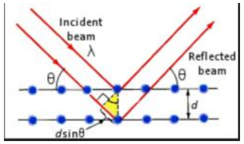
$$\lambda = \frac{xd}{nL}$$

λ = wavelength of light used (m)
x = distance from central fringe (m)
d = distance between the slits (m)
n = the order of the fringe
L = length from the screen with slits to the viewing screen (m)

$$\lambda = \frac{d \sin\theta}{n}$$



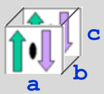
William Lawrence Bragg realized that the intensity of the "spots" could be combined with the distance information to determine the structural arrangement of the atoms in the crystals. In 1913, young Bragg and his father determined the first crystal structures of NaCl, diamond, etc. Note the reciprocal relationship of "d" and "sinθ" in Bragg's Law.



Bragg's Law ($n\lambda = 2d \sin\theta$)

Spacings of spots → size of unit cell

a b c

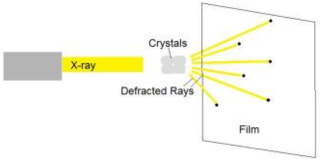


Intensity of spots → location of atoms

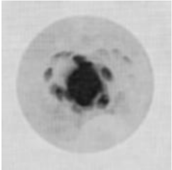
The Nobel Prize in Physics 1914
Max von Laue

2014 international year of crystallography IUCr

The Nobel Prize in Physics 1914



Max von Laue

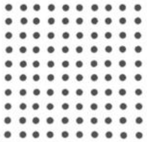


Friedrich & Knipping's first diffraction photograph - 1912.

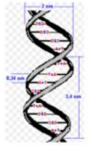
The Nobel Prize in Physics 1914 was awarded to Max von Laue *"for his discovery of the diffraction of X-rays by crystals".*

Optical Transforms (iClicker Question)

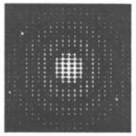
Below are four objects (e, f, g, h) and four transforms. Match the objects with their corresponding optical transforms by placing the appropriate letter on the blank provided.

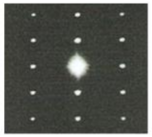
e) 

f) 

g) 

h) 

__ 

__ 

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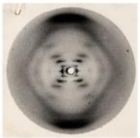
__ 

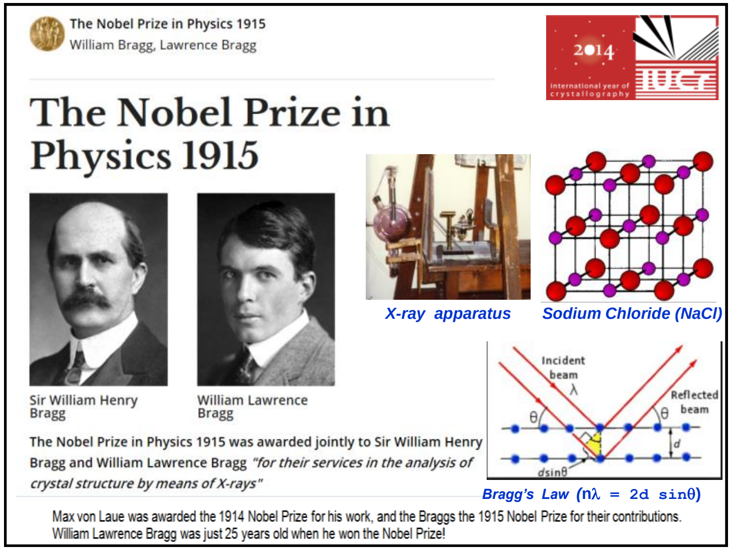
A) e f / h g

B) e h / f g

C) h e / f g

D) g f / e h

E) h f / e g


The Nobel Prize in Physics 1915
William Bragg, Lawrence Bragg
2014 international year of crystallography
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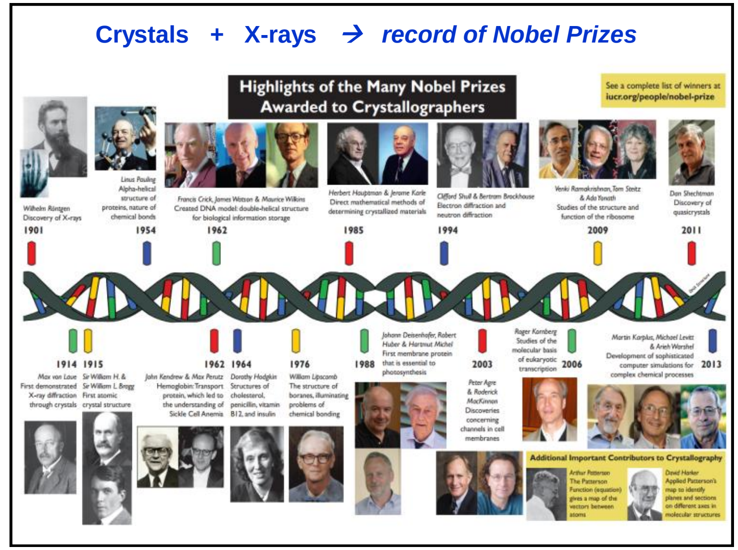
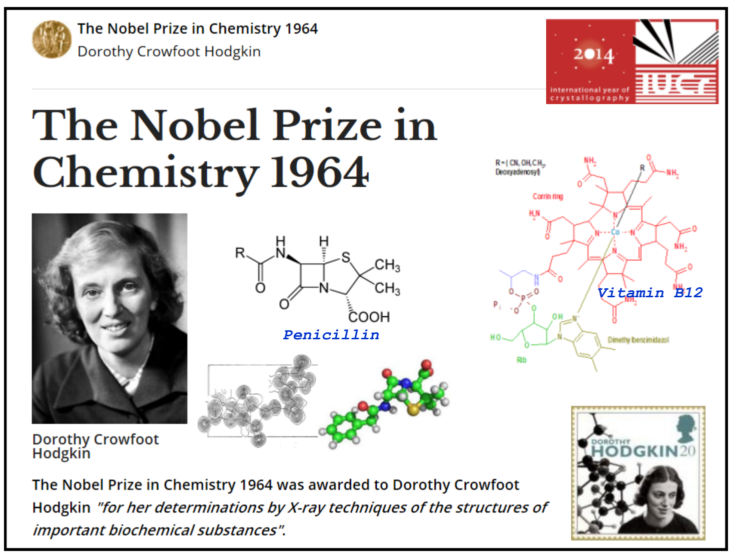
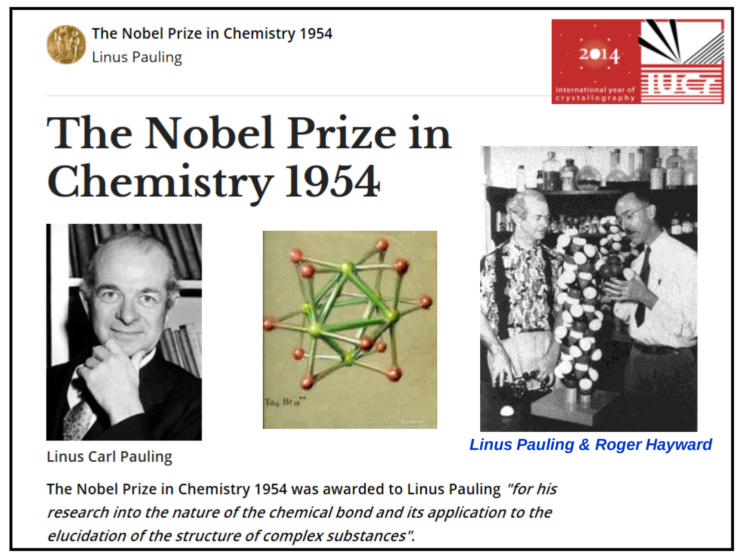
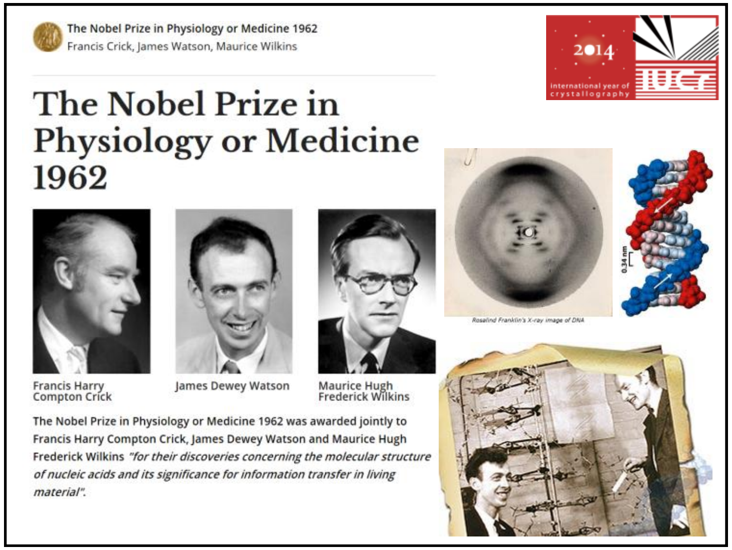
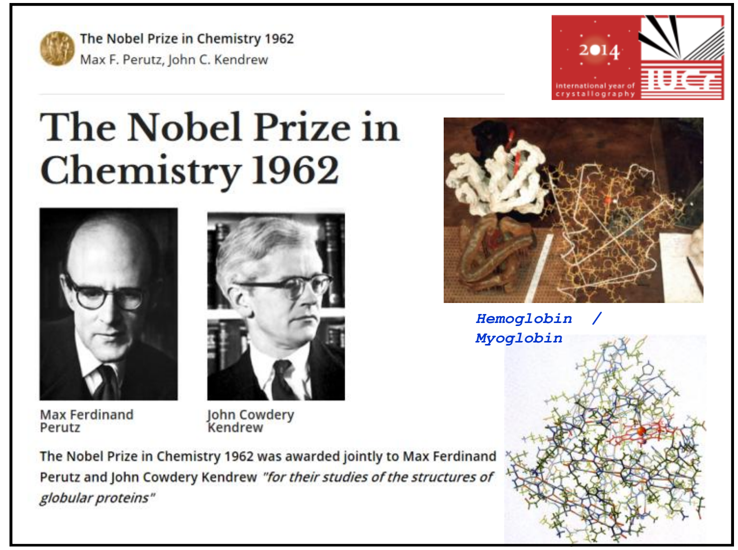
The Nobel Prize in Physics 1915
Sir William Henry Bragg
William Lawrence Bragg
X-ray apparatus
Sodium Chloride (NaCl)
Incident beam
Reflected beam
λ
θ
d
dsinθ
The Nobel Prize in Physics 1915 was awarded jointly to Sir William Henry Bragg and William Lawrence Bragg "for their services in the analysis of crystal structure by means of X-rays"
Bragg's Law (nλ = 2d sinθ)
Max von Laue was awarded the 1914 Nobel Prize for his work, and the Braggs the 1915 Nobel Prize for their contributions.
William Lawrence Bragg was just 25 years old when he won the Nobel Prize!

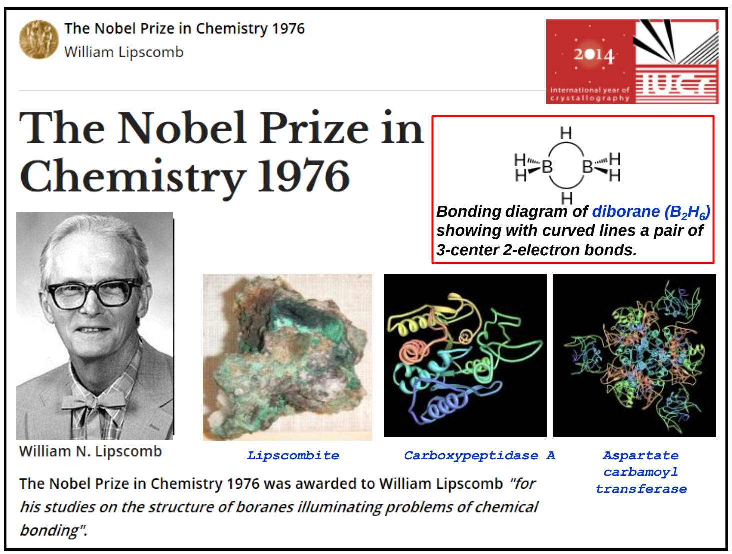

Crystals + X-rays → record of Nobel Prizes
Highlights of the Many Nobel Prizes Awarded to Crystallographers
See a complete list of winners at iucr.org/people/nobel-prize
1901
1954
1962
1985
1994
2009
2011
1914 1915
1962 1964
1976
1988
2003
2006
2013
Additional Important Contributors to Crystallography

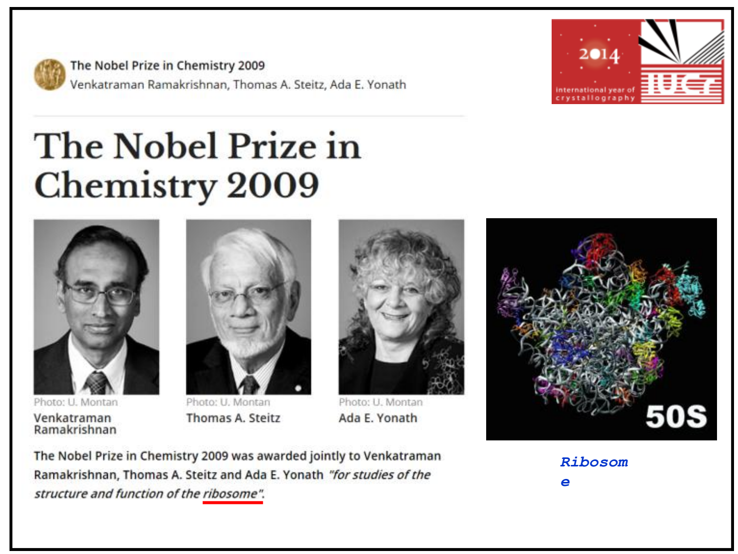

The Nobel Prize in Chemistry 1964
Dorothy Crowfoot Hodgkin
2014 international year of crystallography
IUCr
The Nobel Prize in Chemistry 1964
Dorothy Crowfoot Hodgkin
Penicillin
Vitamin B12
DOROTHY HODGKIN 20
The Nobel Prize in Chemistry 1964 was awarded to Dorothy Crowfoot Hodgkin "for her determinations by X-ray techniques of the structures of important biochemical substances".


The Nobel Prize in Chemistry 1954
Linus Pauling
2014 international year of crystallography
IUCr
The Nobel Prize in Chemistry 1954
Linus Carl Pauling
Linus Pauling & Roger Hayward
The Nobel Prize in Chemistry 1954 was awarded to Linus Pauling "for his research into the nature of the chemical bond and its application to the elucidation of the structure of complex substances".


The Nobel Prize in Physiology or Medicine 1962
Francis Crick, James Watson, Maurice Wilkins
2014
international year of crystallography
IUCr
The Nobel Prize in Physiology or Medicine 1962
Francis Harry Compton Crick
James Dewey Watson
Maurice Hugh Frederick Wilkins
Rosalind Franklin's X-ray image of DNA
The Nobel Prize in Physiology or Medicine 1962 was awarded jointly to Francis Harry Compton Crick, James Dewey Watson and Maurice Hugh Frederick Wilkins "for their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material".


The Nobel Prize in Chemistry 1962
Max F. Perutz, John C. Kendrew
2014
international year of crystallography
IUCr
The Nobel Prize in Chemistry 1962
Max Ferdinand Perutz
John Cowdery Kendrew
Hemoglobin / Myoglobin
The Nobel Prize in Chemistry 1962 was awarded jointly to Max Ferdinand Perutz and John Cowdery Kendrew "for their studies of the structures of globular proteins"


The Nobel Prize in Chemistry 1976
William Lipscomb
2014
international year of crystallography
IUCr
The Nobel Prize in Chemistry 1976
Bonding diagram of diborane (B_2H_6) showing with curved lines a pair of 3-center 2-electron bonds.
William N. Lipscomb
Lipscombite
Carboxypeptidase A
Aspartate carbamoyl transferase
The Nobel Prize in Chemistry 1976 was awarded to William Lipscomb "for his studies on the structure of boranes illuminating problems of chemical bonding".


The Nobel Prize in Chemistry 2009
Venkatraman Ramakrishnan, Thomas A. Steitz, Ada E. Yonath
2014
international year of crystallography
IUCr
The Nobel Prize in Chemistry 2009
Photo: U. Montan
Venkatraman Ramakrishnan
Photo: U. Montan
Thomas A. Steitz
Photo: U. Montan
Ada E. Yonath
50S
Ribosome
The Nobel Prize in Chemistry 2009 was awarded jointly to Venkatraman Ramakrishnan, Thomas A. Steitz and Ada E. Yonath "for studies of the structure and function of the ribosome".

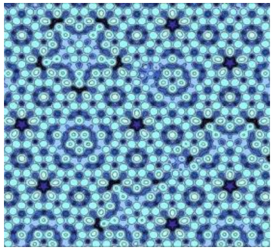
The Nobel Prize in Chemistry 2011
Dan Shechtman

The Nobel Prize in Chemistry 2011

Dan Shechtman

Linus Pauling –
"There is no such thing as quasicrystals, only quasi-scientists."

Quasicrystals have low thermal and electrical conductivity, while possessing high structural stability – ideal for non-stick insulation for electrical wires and cooking equipment.



Quasicrystals - ordered crystalline materials lacking repeating structures, such as this Al-Pd-Mn alloy.

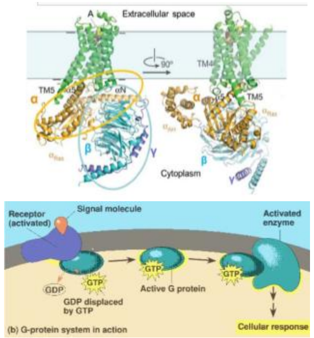
The Nobel Prize in Chemistry 2011 was awarded to Dan Shechtman *"for the discovery of quasicrystals".*

The Nobel Prize in Chemistry 2012
Robert J. Lefkowitz, Brian K. Kobilka

The Nobel Prize in Chemistry 2012

Photo: U. Montan
Robert J. Lefkowitz

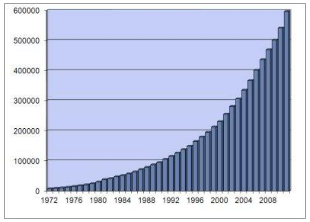
Photo: U. Montan
Brian K. Kobilka

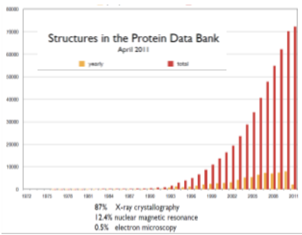


The Nobel Prize in Chemistry 2012 was awarded jointly to Robert J. Lefkowitz and Brian K. Kobilka *"for studies of G-protein-coupled receptors"*

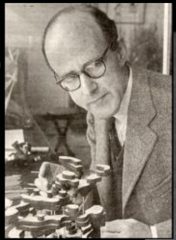
A Half Century of Advances in Small Molecule Crystallography

Decade	1950's	1960's	1970's	1980's	1990's	2000's
Size	30 atoms	<100 non-H atoms	<200 non-H atoms	<400 non-H atoms	<600 non-H atoms	<1000 non-H atoms
Time / Structure	~ 1year	3-6 months	1 month	1 week	Few days	Few hours
# Structures	<500	~8300	32,000	95,000	229,000	528,000

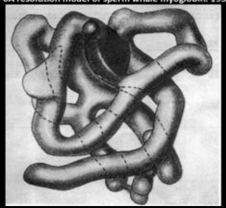


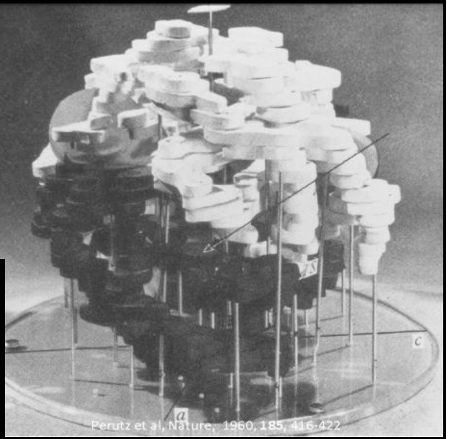


Max
circa 1959

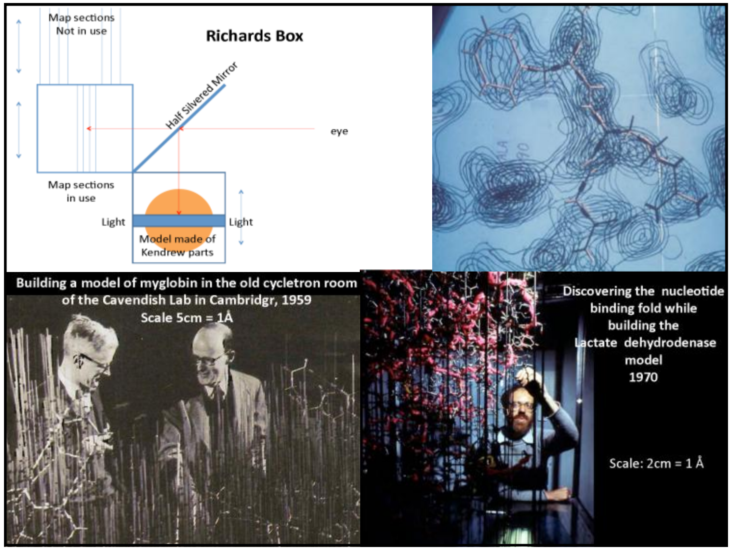


The 6Å resolution model of sperm whale myoglobin. 1957

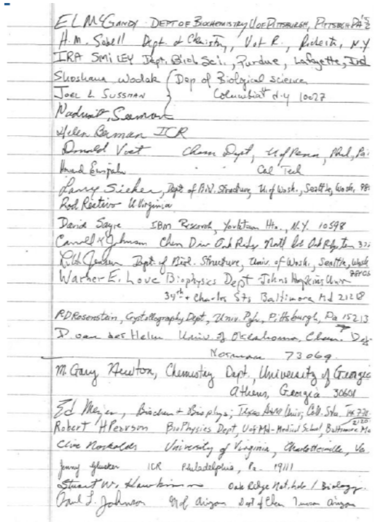




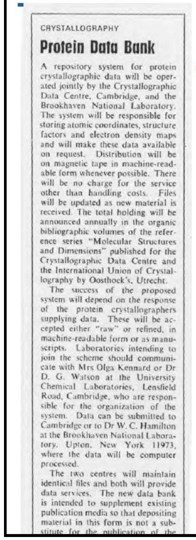
Perutz et al, Nature, 1960, **185**, 416-422



A petition to establish a central repository for atomic coordinate data of protein structures was written at the American Crystallographic Association Winter Meeting, Columbia, SC, February 1971



Michael Rossmann – PDB40 address



CRYSTALLOGRAPHY

Protein Data Bank

A repository system for protein crystallographic data will be operated jointly by the Crystallographic Data Centre, Cambridge, and the Brookhaven National Laboratory. The system will be responsible for storing atomic coordinates, structure factors and electron density maps and will make these data available on request. Distribution will be on magnetic tape in machine-readable form whenever possible. There will be no charge for the service other than handling costs. Files will be updated as new material is received. The total holding will be announced annually in the organic bibliographic volumes of the reference series "Molecular Structures and Dimensions" published for the Crystallographic Data Centre and the International Union of Crystallography by Oosthoek's, Utrecht.

The success of the proposed system will depend on the response of the protein crystallographers supplying data. These will be accepted either "raw" or refined, in machine-readable form or as manuscripts. Laboratories intending to join the scheme should communicate with Mrs Olga Kennard or Dr D. G. Watson at the University Chemical Laboratories, Lensfield Road, Cambridge, who are responsible for the organization of the system. Data can be submitted to Cambridge or to Dr W. C. Hamilton at the Brookhaven National Laboratory, Upton, New York 11973, where the data will be computer processed.

The two centres will maintain identical files and both will provide data services. The new data bank is intended to supplement existing publication media so that depositing material in this form is not a substitute for the publication of the

Creation of PDB announced in 1971 (*Nature New Biology* 1971, 233, 223)

Walter Hamilton, Helen Berman, Tom Koetzle in 1972

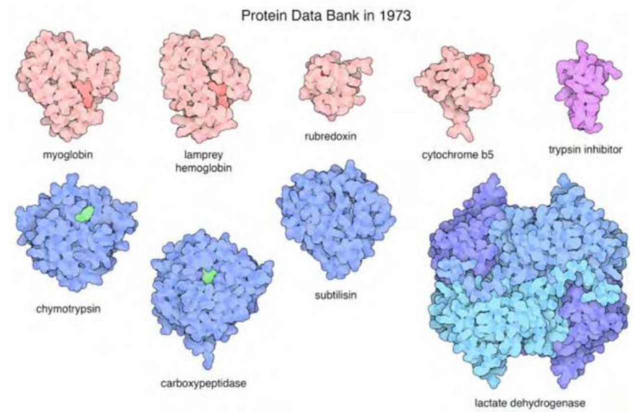
Walter Hamilton and Harold W. Wyckoff at the CSHL meeting in 1971

The First protein structures

1958	6.0 Å Myoglobin	Cambridge	John Kendrew
1959	5.5 Å oxy-Haemogbin	Cambridge	Max Perutz
1959	2.0 Å Myglobin	Cambridge	John Kendrew
1965	HEW lysozyme	RI London	David Phillips
1967	Carboxypeptidase	Harvard	Bill Lipscomb
1968	Ribonuclease	Yale	Fred Richards
1968	Chymotrypsin	Cambridge	David Blow
1968	Papain	Groningen	Jan Drenth
1970	2.8 Å oxy Haemogbin	Cambridge	Max Perutz
1970	De-oxy Haemoglobin	Cambridge	Max Perutz
1970	Lactate dehydrognase	Purdue	Michael Rossmann
1971	Staphylococcal nuclease	MIT	Al Cotton
1971	Carbonic anhydrase	Uppsala	Anders Liljas
1972	Subtilisin	Gronignen	Wim Hol
1972	Lamprey Haemoglobin	Johns Hopkins	Werner Love
1972	Rubridoxin	U of Washington	Lyle Jensen
1972	Trypsin inhibitor	Max Plank	Robert Huber
1973	Cytochrome b5	Washington U	Scott Matthews

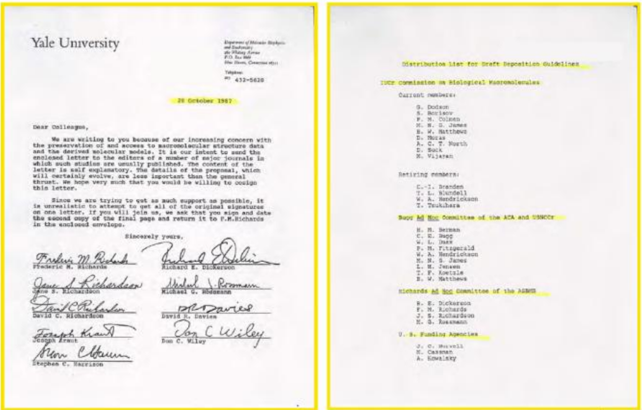
1973 PDB holdings in red

Michael Rossmann – PDB40 address



Michael Rossmann – PDB40 address

1987: Users Compel Deposition



Yale University

432-5620

28 October 1987

Dear Colleagues,

We are writing to you because of our increasing concern with the preservation of and access to macromolecular structure data and the derived molecular models. It is our intent to send the enclosed letter to the editors of a number of major journals in which such studies are usually published. The content of the letter is self explanatory. The details of the proposal, which will certainly evolve, are less important than the general thrust. We hope very much that you would be willing to cosign this letter.

Since we are trying to get as much support as possible, it is unrealistic to attempt to get all of the original signatures on one letter. If you will join us, we ask that you sign and date the second copy of the final page and return it to F.M.Richards in the enclosed envelope.

Sincerely yours,

Frederic M. Richards — Richard E. Dickerson
Jane S. Richardson — Michael G. Rossmann
David C. Richardson — David R. Davies
Joseph Kraut — Don C. Wiley
Stephen C. Harrison

Distribution List for Draft Deposition Guidelines

IUCr commission on Biological Macromolecules

Current members:

G. Dodson
S. Borisov
P. M. Colman
M. N. G. James
B. W. Matthews
D. Moras
A. C. T. North
D. Suck
M. Vijayan

Retiring members:

C.-I. Branden
T. L. Blundell
W. A. Hendrickson
T. Tsukihara

Bugg Ad Hoc Committee of the ACA and USNCCr

H. M. Berman
C. E. Bugg
W. L. Duax
P. M. Fitzgerald
W. A. Hendrickson
M. N. G. James
L. H. Jensen
T. F. Koetzle
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Richards Ad Hoc Committee of the ASBMB

R. E. Dickerson
F. M. Richards
J. S. Richardson
M. G. Rossmann

U. S. Funding Agencies

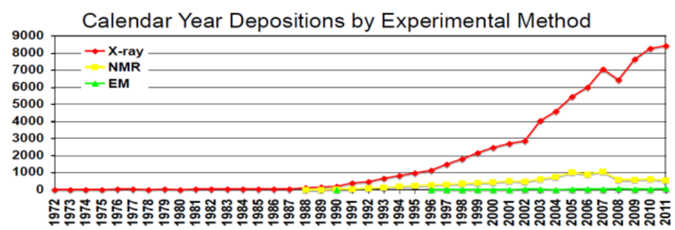
J. C. Norvell
M. Cassman
A. Kowalsky

Stephen K. Burley – PDB40 address

10,000-Fold Growth in Four Decades

http://www.wwpdb.org/PDB40.html

- 7→>76,000 entries
- 2011 will see ~9,000 depositions
- Electron Microscopy is beginning to hit its stride



Stephen K. Burley – PDB40 address

RCSB PDB PROTEIN DATA BANK → PDB-101

A MEMBER OF THE wwPDB

An Information Portal to Biological Macromolecular Structures

As of Tuesday Nov 06, 2012 at 4 PM PST there are 86008 Structures | PDB Statistics

All Categories | Author | Macromolecule | Sequence | Ligand

Search | All Categories: e.g., PDB ID, molecule name, author | Browse | Advanced

PDB Current Holdings Breakdown

Exp.Method	Proteins	Nucleic Acids	Protein/NA Complexes	Other	Total
X-RAY	70690	1400	3562	3	75655
NMR	8463	1010	191	7	9671
ELECTRON MICROSCOPY	322	23	120	0	465
HYBRID	45	3	2	1	51
other	144	4	5	13	166
Total	79664	2440	3880	24	86008

(Click on any number to retrieve the results from that category.)

65078 structures in the PDB have a structure factor file.

6978 structures in the PDB have an NMR restraint file.

737 structures in the PDB have a chemical shifts file.

RCSB Protein Data Bank

Statistics For PDB Structures That Are Deposited And Processed By Year And Site

Year	Total Depositions	Deposited To			Processed By		
		RCSB PDB	PDBj	PDBe	RCSB PDB	PDBj	PDBe
2000	2983	2445	10	528	2297	158	528
2001	3287	2673	118	496	2408	383	496
2002	3565	2769	289	507	2401	657	507
2003	4830	3488	673	669	3135	1026	669
2004	5508	3796	900	812	3082	1614	812
2005	6678	4507	1166	1005	3563	2110	1005
2006	7282	5145	1052	1085	4252	1945	1085
2007	8130	5399	1603	1128	4703	2299	1128
2008	7073	5452	648	973	4106	1994	973
2009	8300	6715	527	1058	5069	2173	1058
2010	8878	6912	593	1373	5464	2041	1373
2011	9250	7172	582	1496	5938	1816	1496
2012	9972	7695	601	1676	6409	1887	1676
2013	9010	6856	607	1547	5774	1689	1547
TOTAL	94746	71024	9369	14353	58601	21792	14353

Note: Includes theoretical models and entries later withdrawn or obsoleted

Last Updated: 6 Nov 2013

PDB

20 Person Years→20 Person Days

- Faster and Faster Computing
- Graphical Display (Geis→Frodo→O→COOT→…)
- Simulated Annealing Refinement
- Gene Cloning/Protein Expression Systems
- Protein Purification/Engineering
- Crystallization Strategies (Factorial, LCP, …)
- Data Collection: Cryogenics/Area Detectors
- Synchrotron Beamlines→MAD/SAD Phasing
- Automated Map Interpretation/Model Building
- Micro Focus X-ray Beamlines

Stephen K. Burley – PDB40 address

Analyze – structure (Ramachandran Plot) and biochemistry

Publish in leading biochemical or structural biology journal

Contribute results (coordinates, etc.) to PDB

****

Data Mining

Visualization programs (Cn3D / RasMol / SwissPDBV / etc)

SCOP – Structural Classification of Proteins

CATH – Classification / Arch / Topology

SCOP Structural Classification of Proteins

Structural Classification of Proteins

Root: scop

Classes:

1. All alpha proteins (151)
2. All beta proteins (111)
3. Alpha and beta proteins (a/b) (117)
   Mainly parallel beta sheets (beta-alpha-beta units)
4. Alpha and beta proteins (a+b) (212)
   Mainly antiparallel beta sheets (segregated alpha and beta regions)
5. Multi-domain proteins (alpha and beta) (39)
   Folds consisting of two or more domains belonging to different classes
6. Membrane and cell surface proteins and peptides (12)
   Does not include proteins in the immune system
7. Small proteins (59)
   Usually dominated by metal ligand, heme, and/or disulfide bridges
8. Coiled coil proteins (5)
   Not a true class
9. Low resolution protein structures (17)
   Not a true class
10. Peptides (95)
    Peptides and fragments. Not a true class
11. Designed proteins (36)
    Experimental structures of proteins with essentially non-natural sequences. Not a true class

CATH - Protein Structure Classification

CATH is a novel hierarchical classification of protein domain structures, which clusters proteins at four major levels: Class (C), Architecture (A), Topology (T), and Homologous (H) Superfamily

Class, derived from secondary structure content, is assigned for more than 90% of protein structures automatically. **Architecture**, which describes the gross orientation of secondary structures, independent of connectivities, is currently assigned manually. The **topology** level clusters structures according to their topological connections and numbers of secondary structures. The **homologous superfamilies** cluster proteins with highly similar structures and functions. The assignments of structures to toplogy families and homologous superfamilies are made by sequence and structure comparisons.

CATH