Biomodelling & Bioinformatica

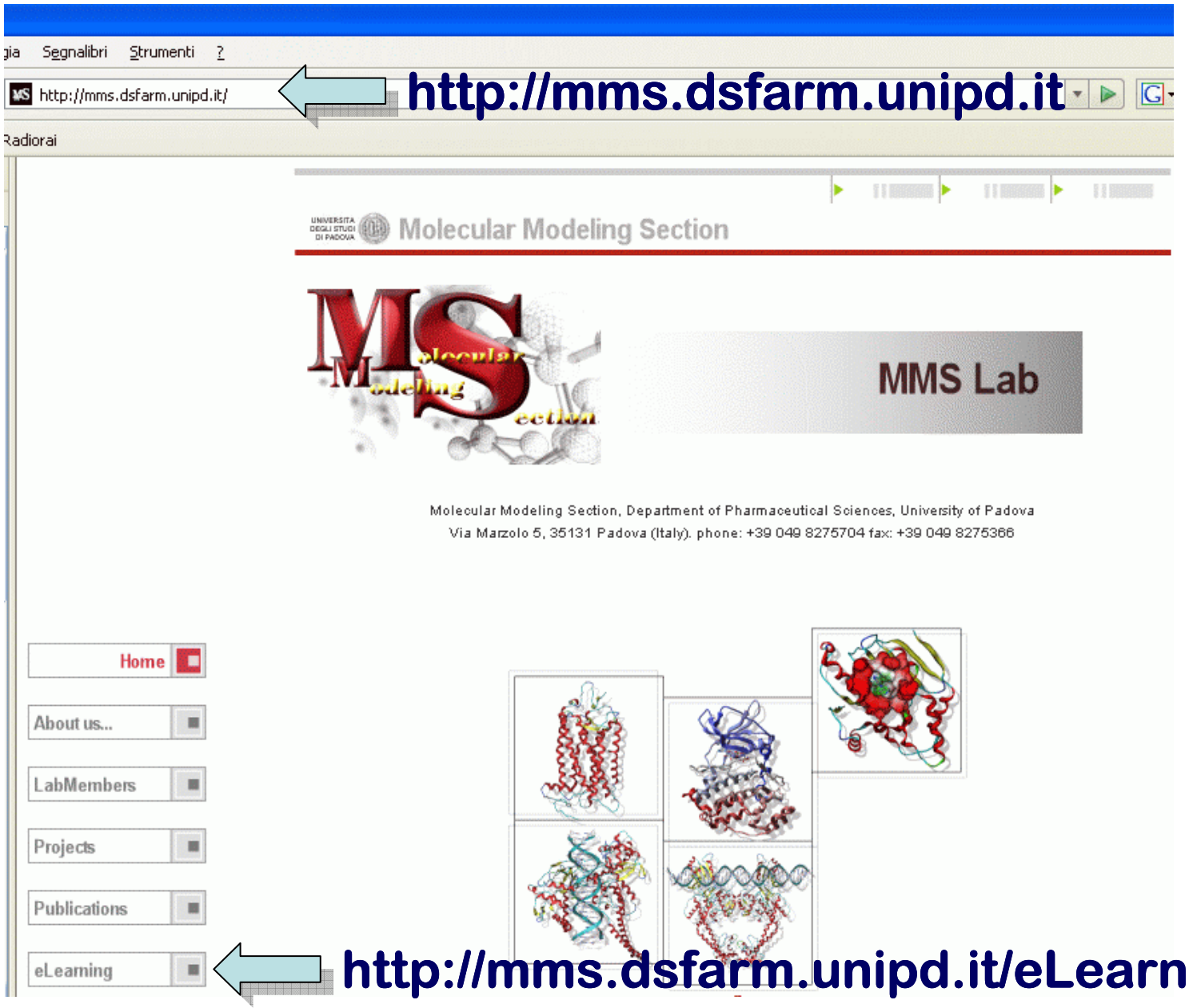
Biotech

by Stefano Moro

Molecular Modeling Section

Department of Pharmaceutical Sciences

University of Padova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eLearning

"Stiamo lavorando ad una sperimentazione di un modello di didattica a distanza sviluppato nell'ambito degli insegnamenti inerenti alla Chimica Farmaceutica Computazionale." Per saperne di più... visitaci!

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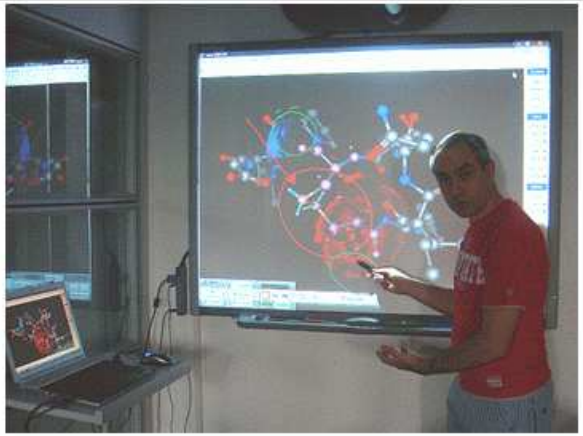


We love SMART teaching... we use SMART Technologies

Chimica Farmaceutica e Tossicologica II

corso per gli studenti di Chimica e Tecnologia Farmaceutiche:

Metodologie Avanzate in Chimica Farmaceutica

corso per gli studenti di Chimica e Tecnologia Farmaceutiche:

Biomodeling & Bioinfomatica

corso per gli studenti di Biotecnologie Indutriali:

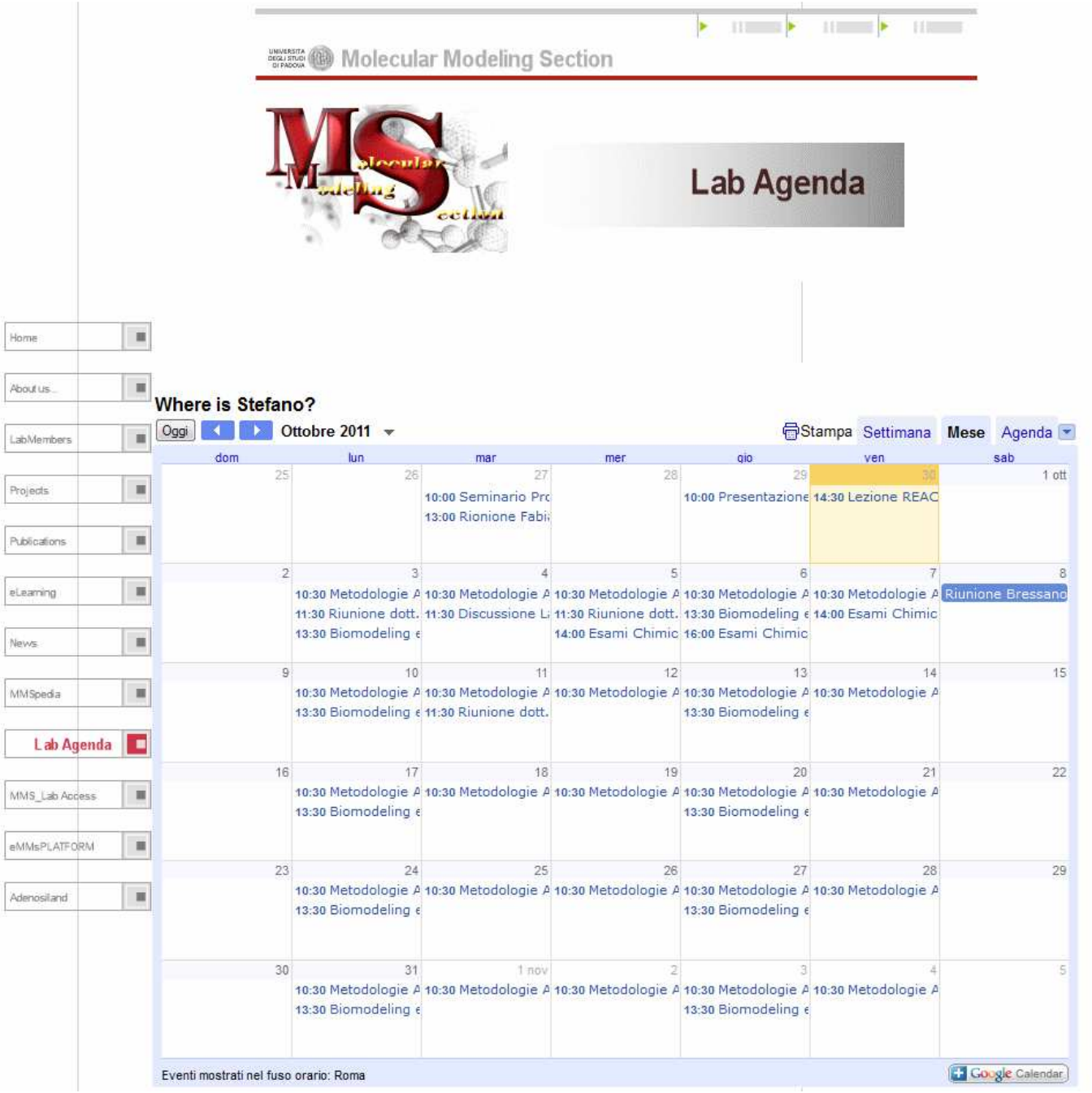
go!!!

Metodologie Avanzate in Chimica Farmaceutica

corso per gli studenti di Biotecnologie Farmaceutiche:

Chemoinformatica

corso per gli studenti di Informazione Scientifica sul Farmaco... e non solo: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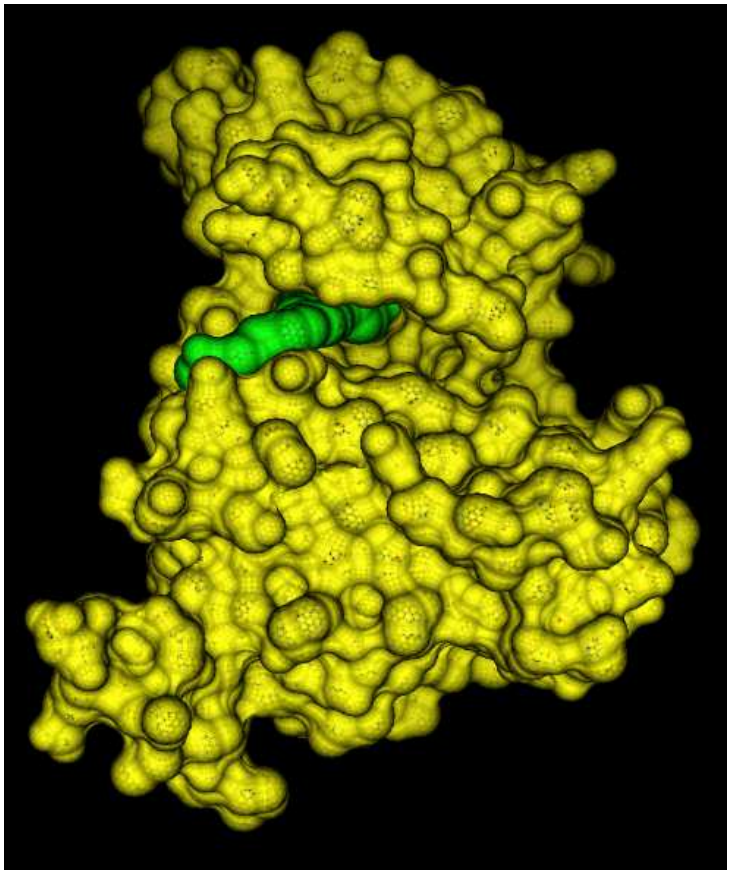
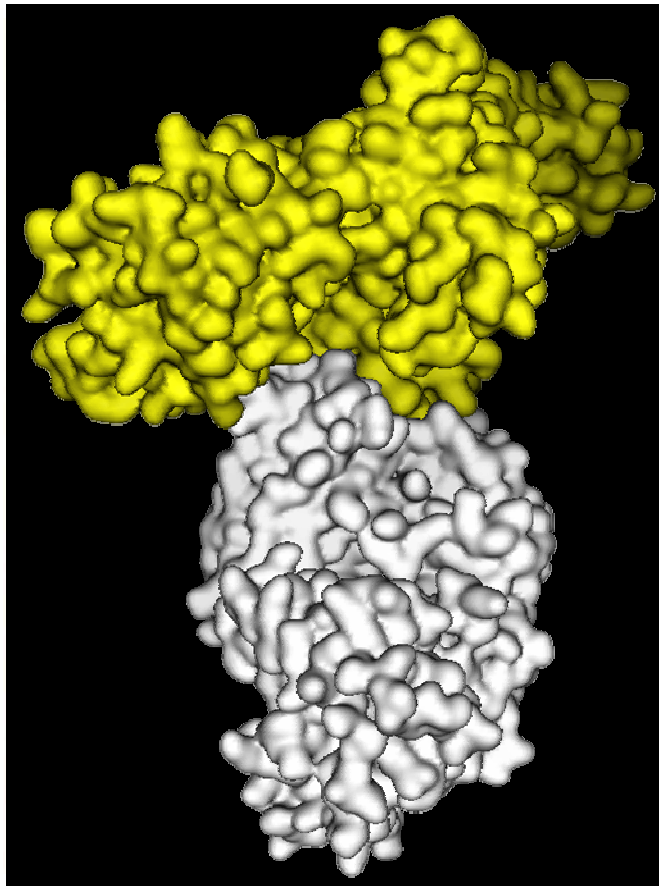
Obbiettivi del corso di *Biomodelina*





Logica e Riconoscimento Molecolare

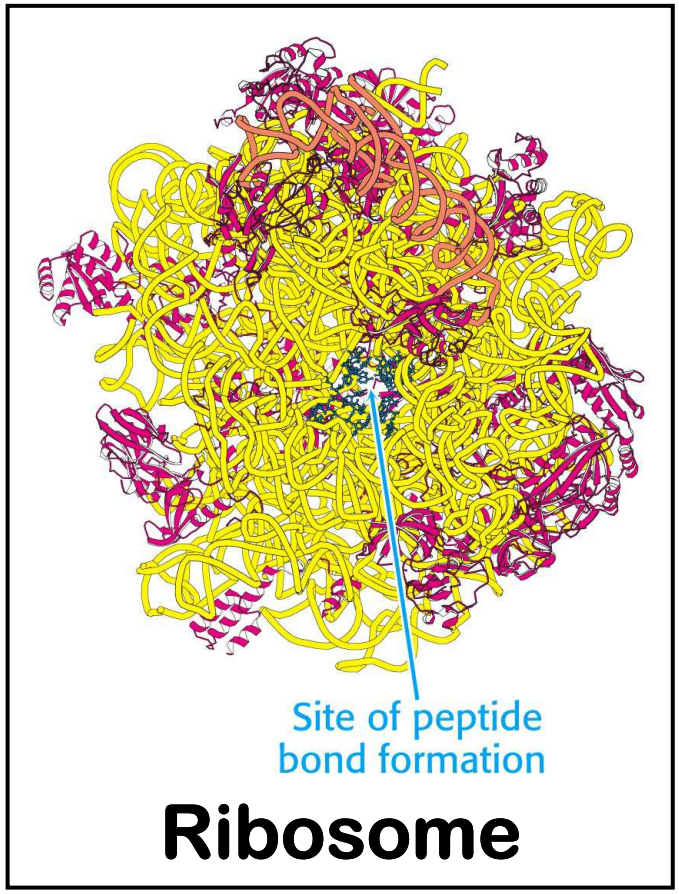
Siamo cacciatori di coordinate:

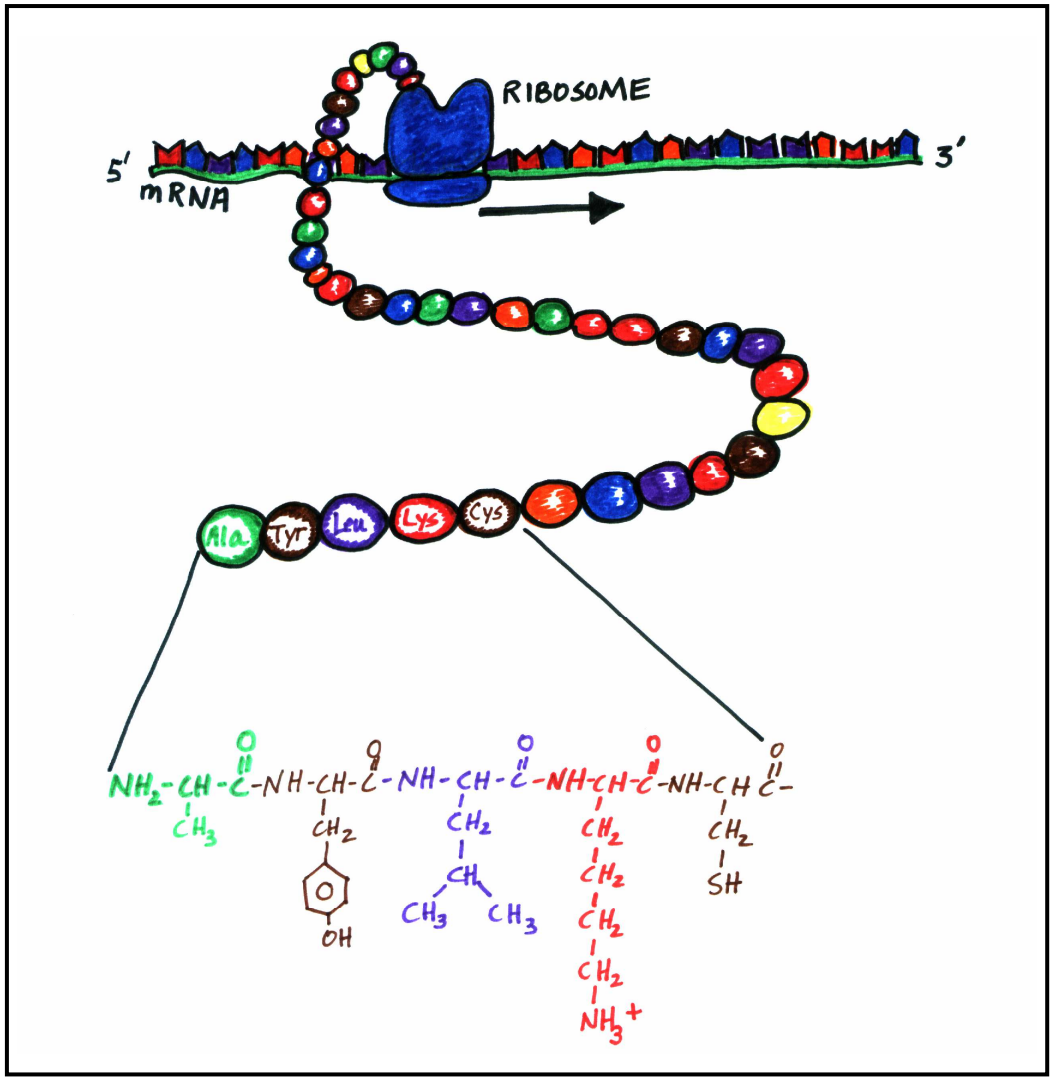
Posso dare per scontato che....

le prossime *n*- (9) diapositive siano già patrimonio comune?

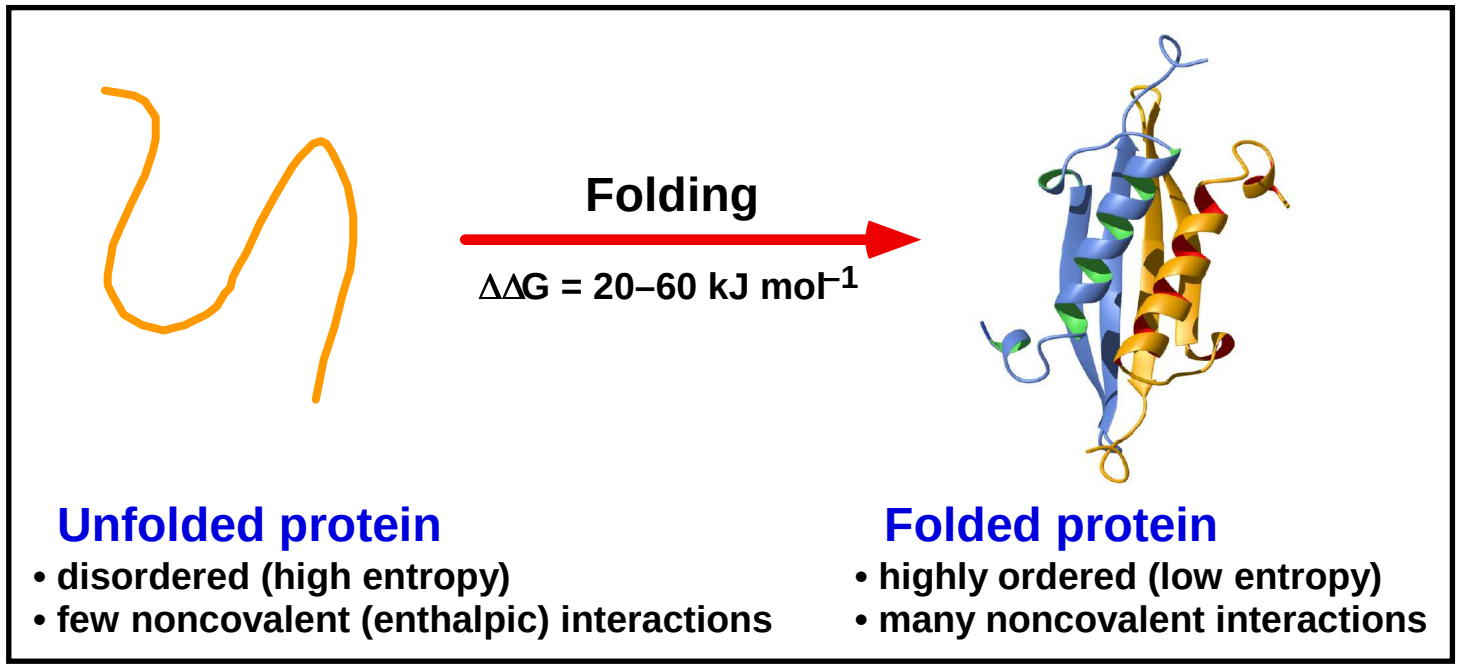
....verifichiamolo velocemente insieme:

Proteins are synthesized as linear polymers





Why do proteins fold into compact structures?



- Folded protein is only marginally more stable than denatured form
- Enthalpic contributions barely overcome the loss of entropy

Hydrophobic effect drives protein folding

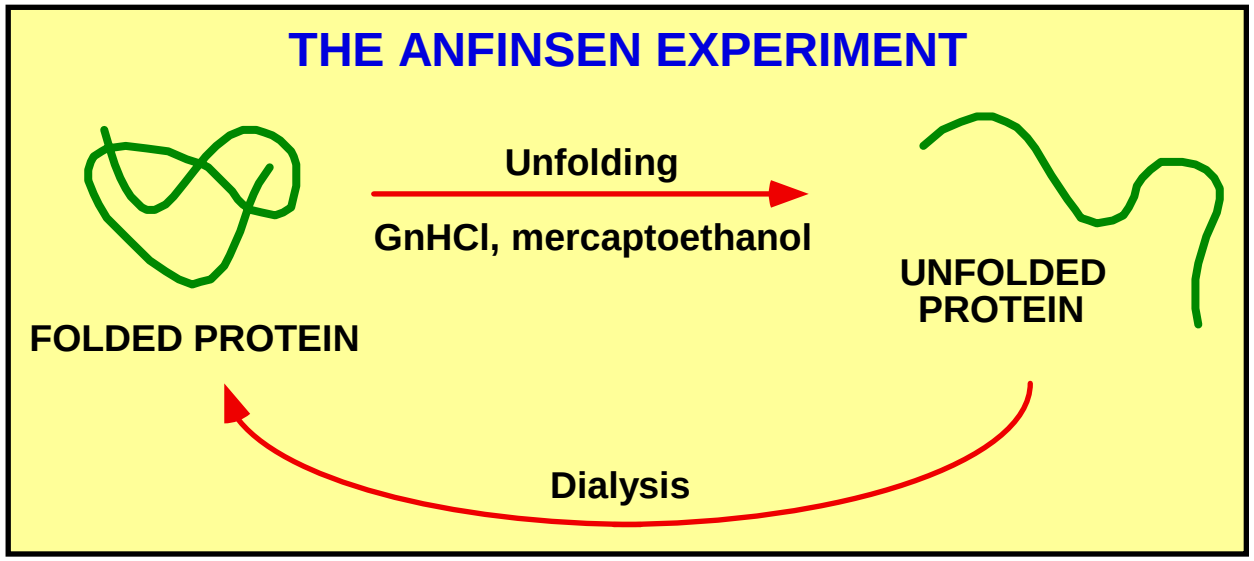
- Proteins fold in a manner that minimizes the solvent exposure of the hydrophobic amino acid residues.

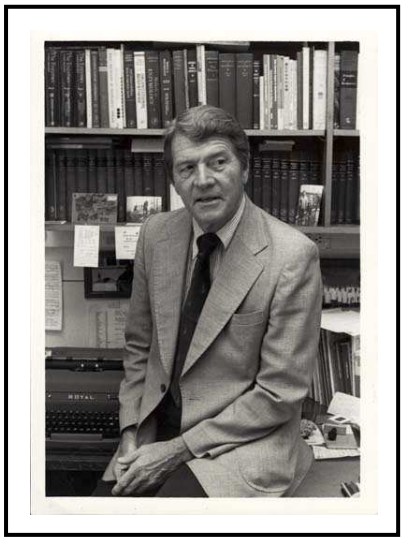
The loss in entropy suffered by the protein when it folds into a compact structure is compensated for by:

(i) the increase in entropy of water molecules which occurs when non-polar sidechains become buried in protein interior.

(ii) a small number of noncovalent interactions (H-bonds and electrostatic interactions) that occur in folded state of protein.

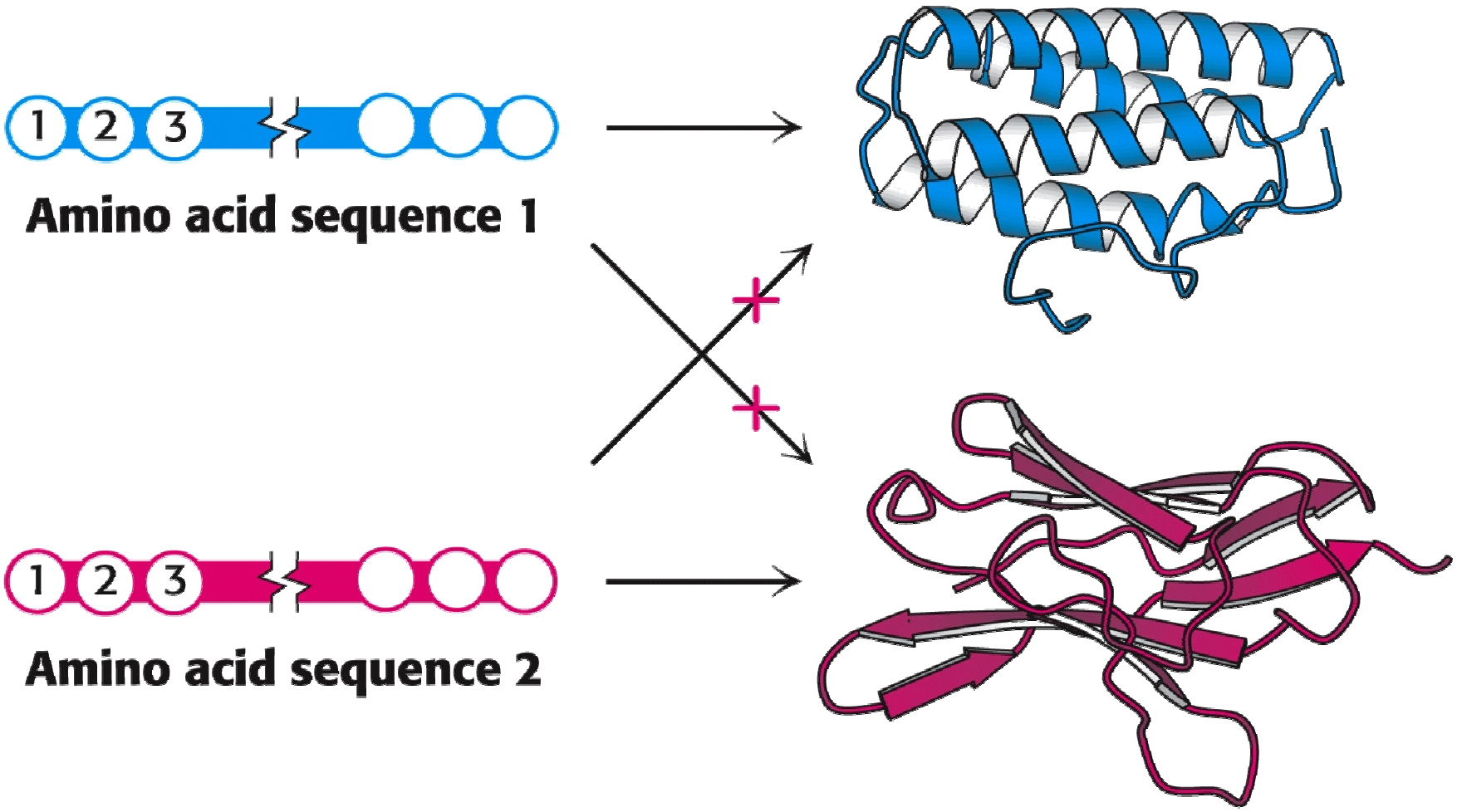
What determines fold? The Anfinsen paradigm



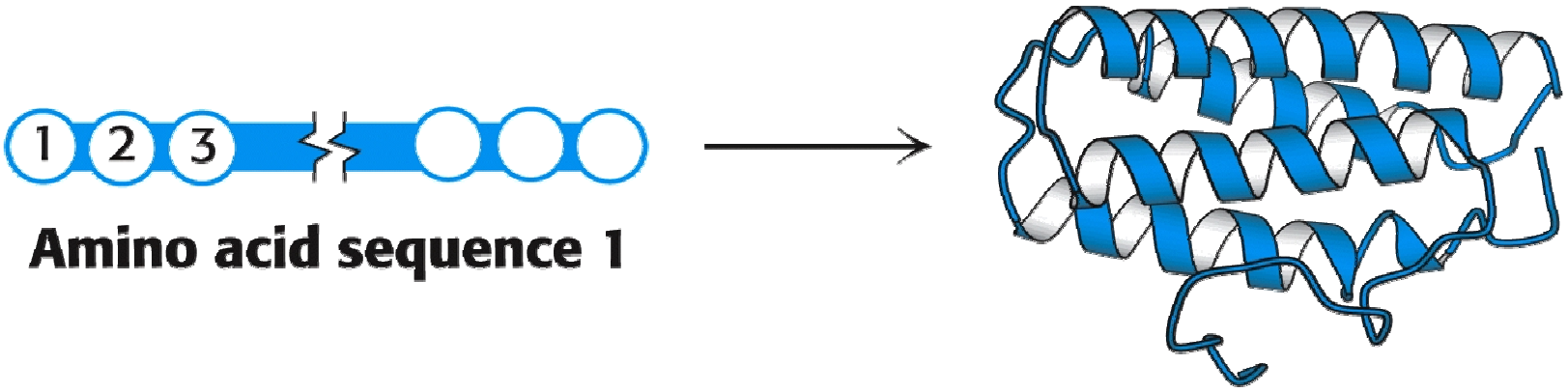


- **Anfinsen paradigm:** the information required for correct folding of the protein is contained within the amino acid sequence
- Christian Anfinsen was awarded the Nobel Prize in 1972

The Anfinsen paradigm



Why is prediction of protein fold difficult?



1D

3D

Why is prediction of protein fold difficult?

Each polypeptide chain can potentially adopt an "astronomical" number of conformations:

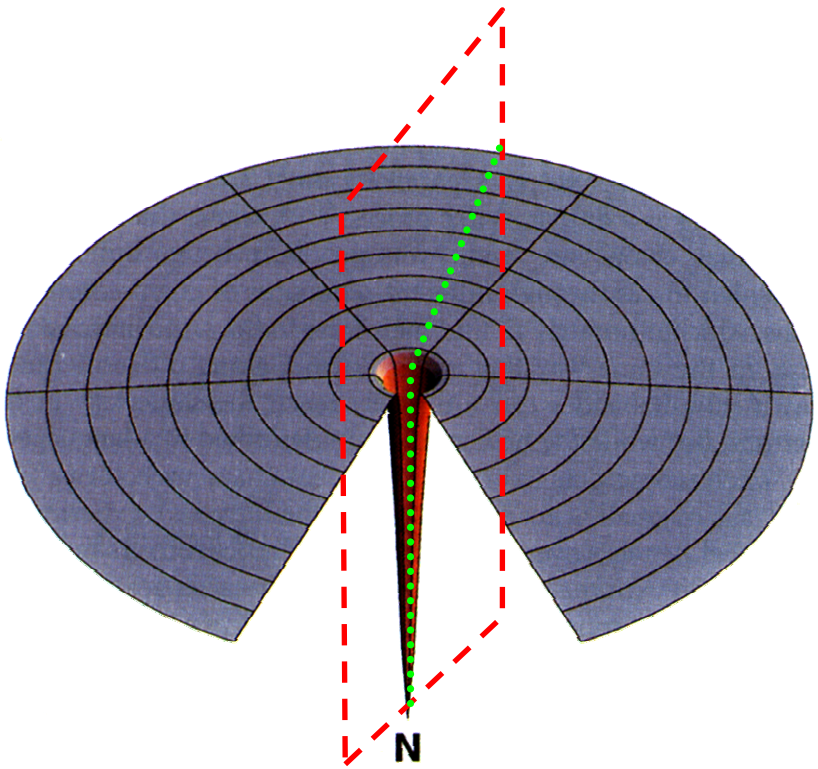
the Levinthal paradox

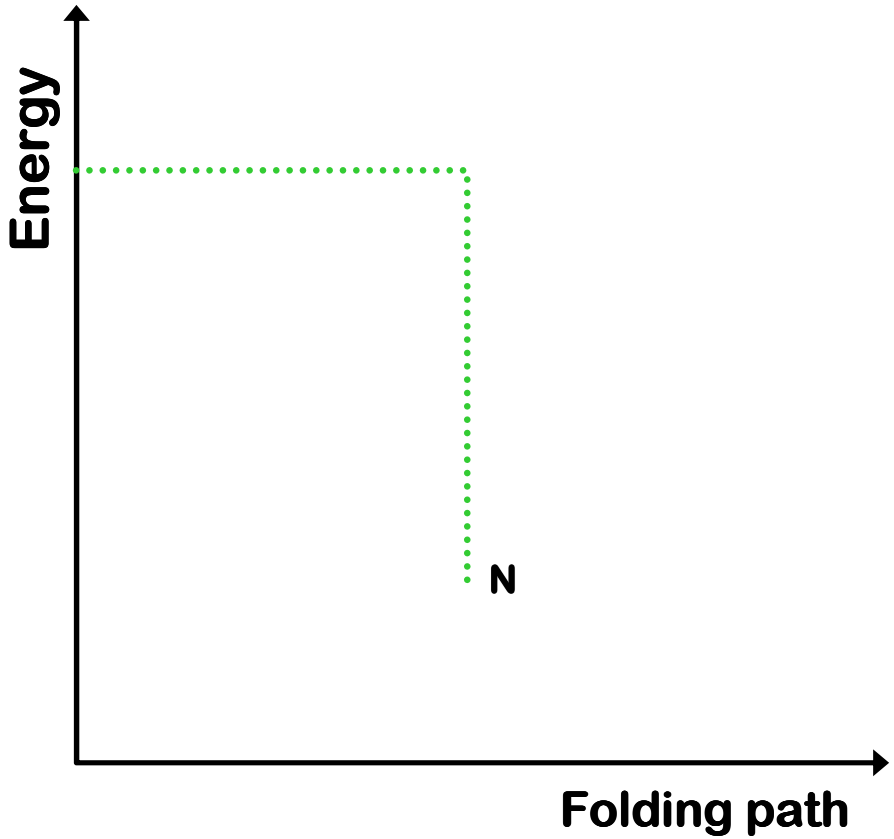
J. Chim. Phys. PCB 65, 44-45 (1968).

The Levinthal paradox

- Many proteins fold in seconds or less: how is this possible?
- Cyrus Levinthal tried to estimate how long it would take a protein to do a random search of conformational space for the native fold.
- Imagine a 100-residue protein (that means 99 peptide bonds, and therefore 198 different phi and psi bond angles) with ONLY three possible conformations per residue. Thus, the number of possible folds = $3^{100} = 5 \times 10^{47}$.
- Let us assume that protein can explore new conformations at the same rate that bonds can reorient (10^{13} structures/second).
- Thus, the time to explore all of conformational space = $5 \times 10^{47}/10^{13} = 5 \times 10^{34}$ seconds = 1.6×10^{27} years >> age of universe

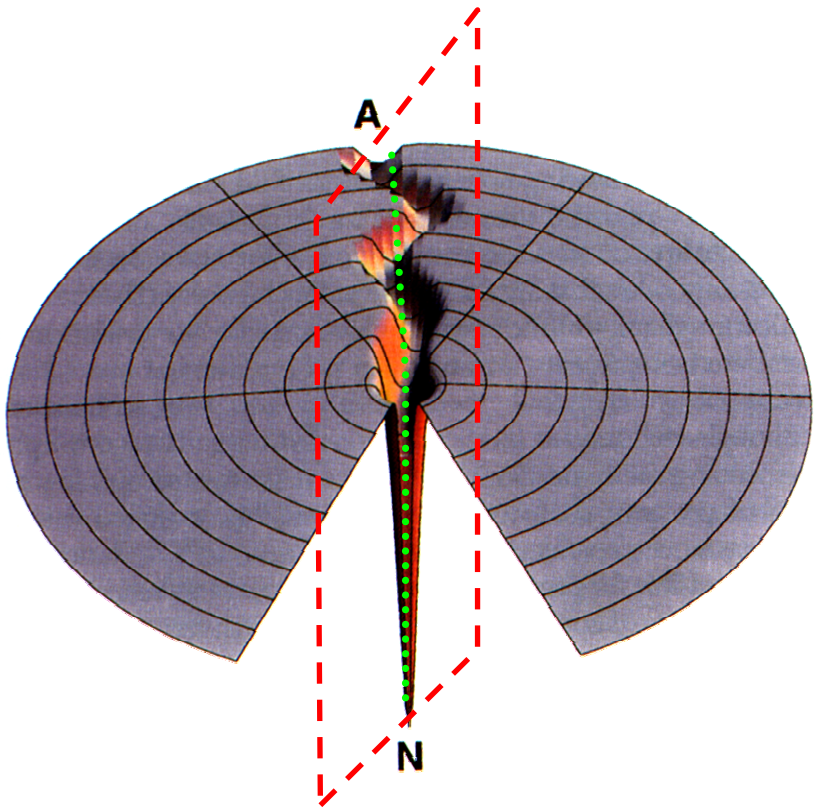
Folding landscapes and the Levinthal paradox

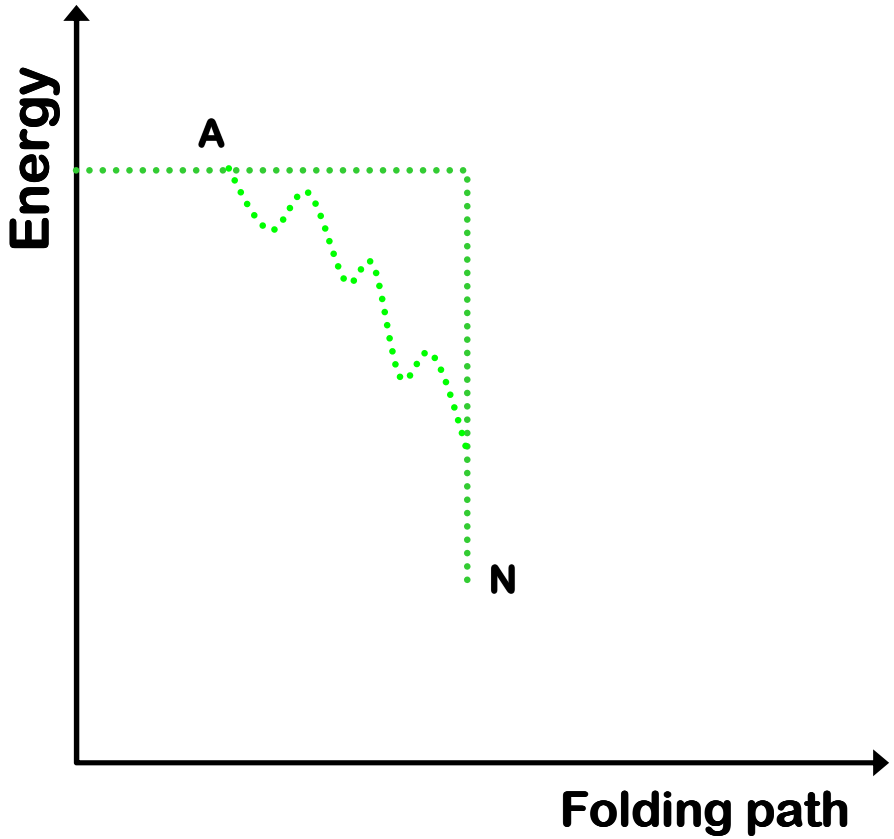




Flat landscape
(Levinthal paradox)

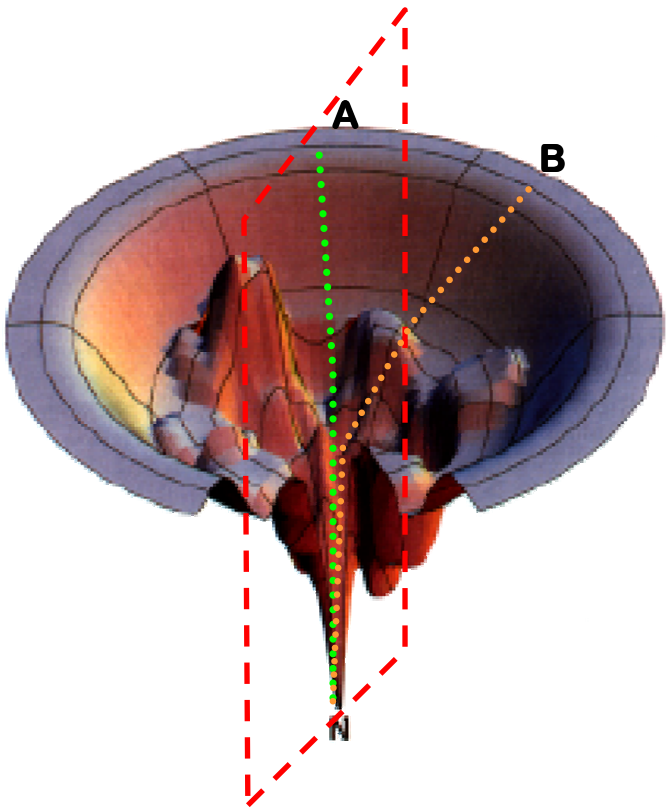
Folding landscapes and the Levinthal paradox

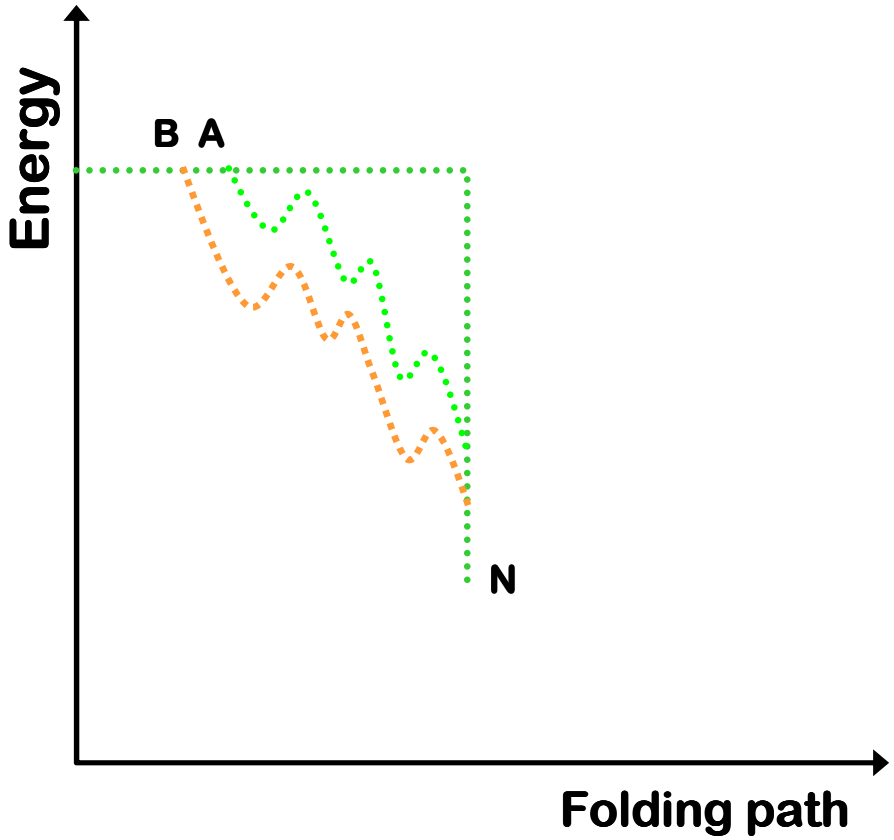




Tunnel landscape
(discrete pathways)

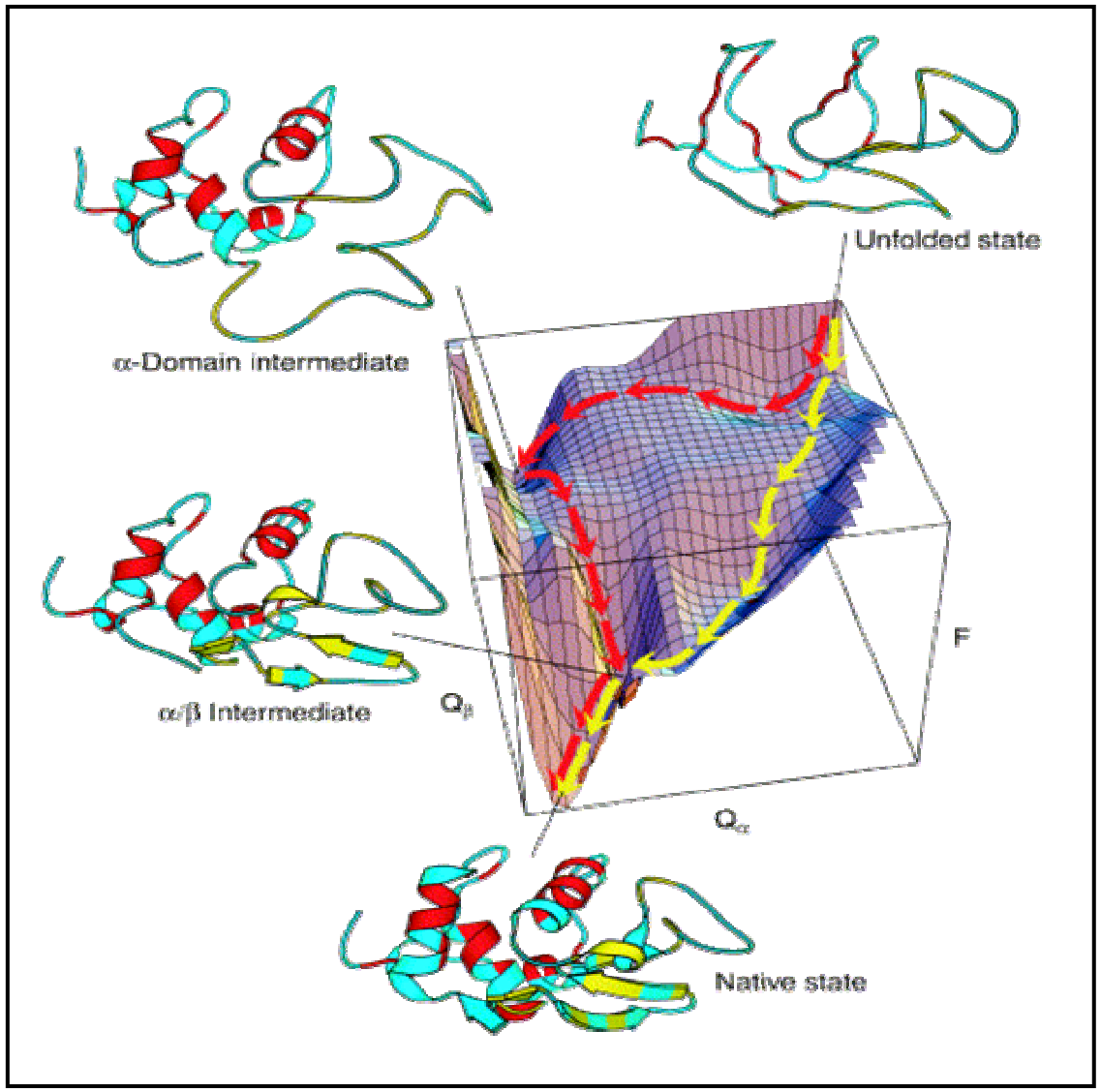
Folding landscapes and the Levinthal paradox





Realistic landscape ("folding funnel")

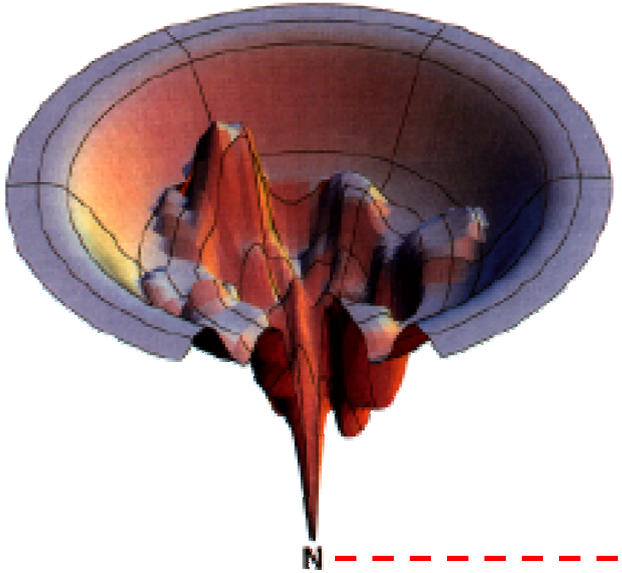
The Folding Funnel: where geometry meets energy.

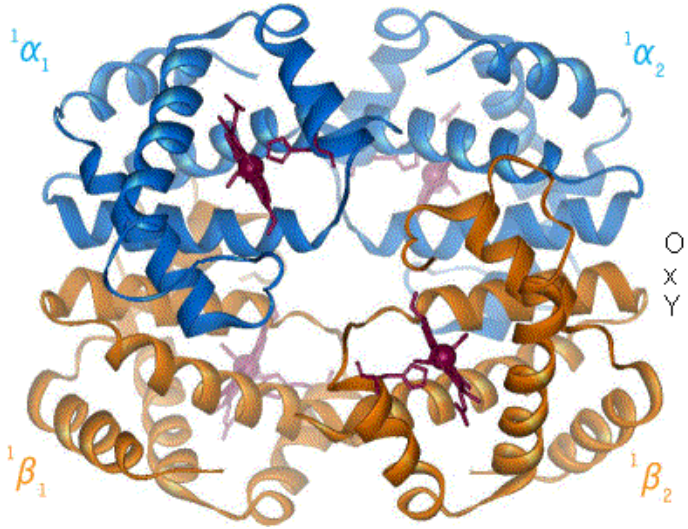


Typically, proteins fold by progressive formation of native-like structures.

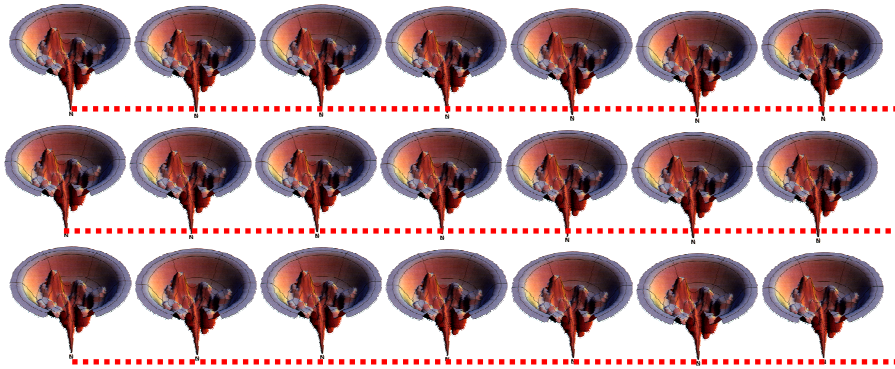
Folding energy surface is highly connected with many different routes to final folded state.

Thermodynamics and Molecular Structure:





Structure & Function



… 6 x 10^{23}

Determinazione della struttura delle proteine

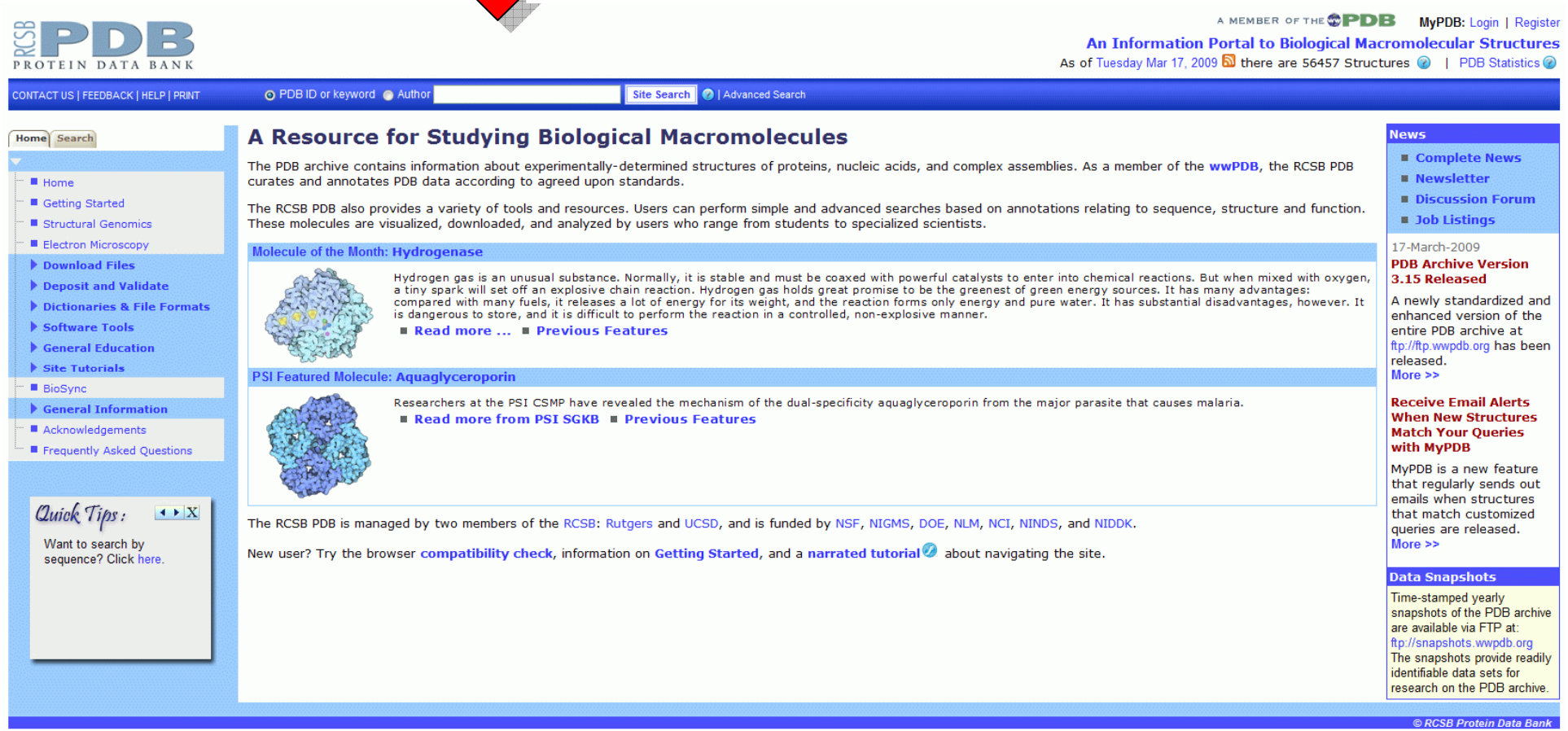
Due tecniche sperimentali (principalmente):

- Cristallografia X-ray (1961 - Kendrew & Perutz)

- Spettroscopia NMR (1986 - Wuethrich)

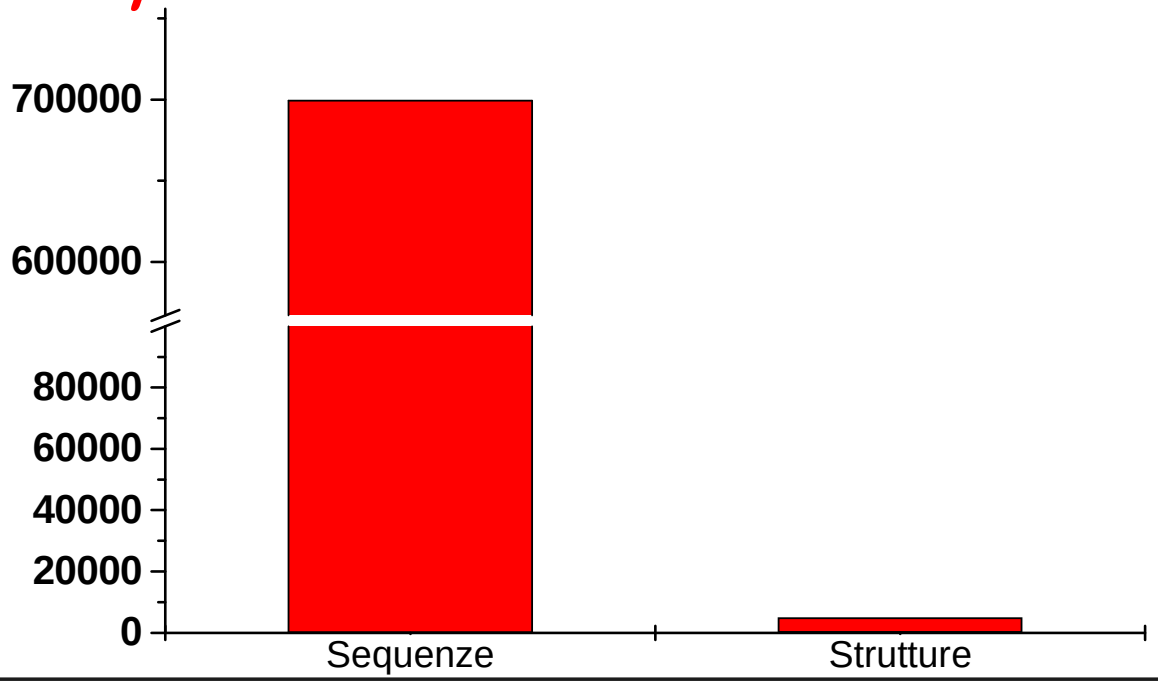
La banca dati Protein Data Bank (PDB)

www.rcsb.org



Allora perché potrebbe essere strategico predire *strutture*?

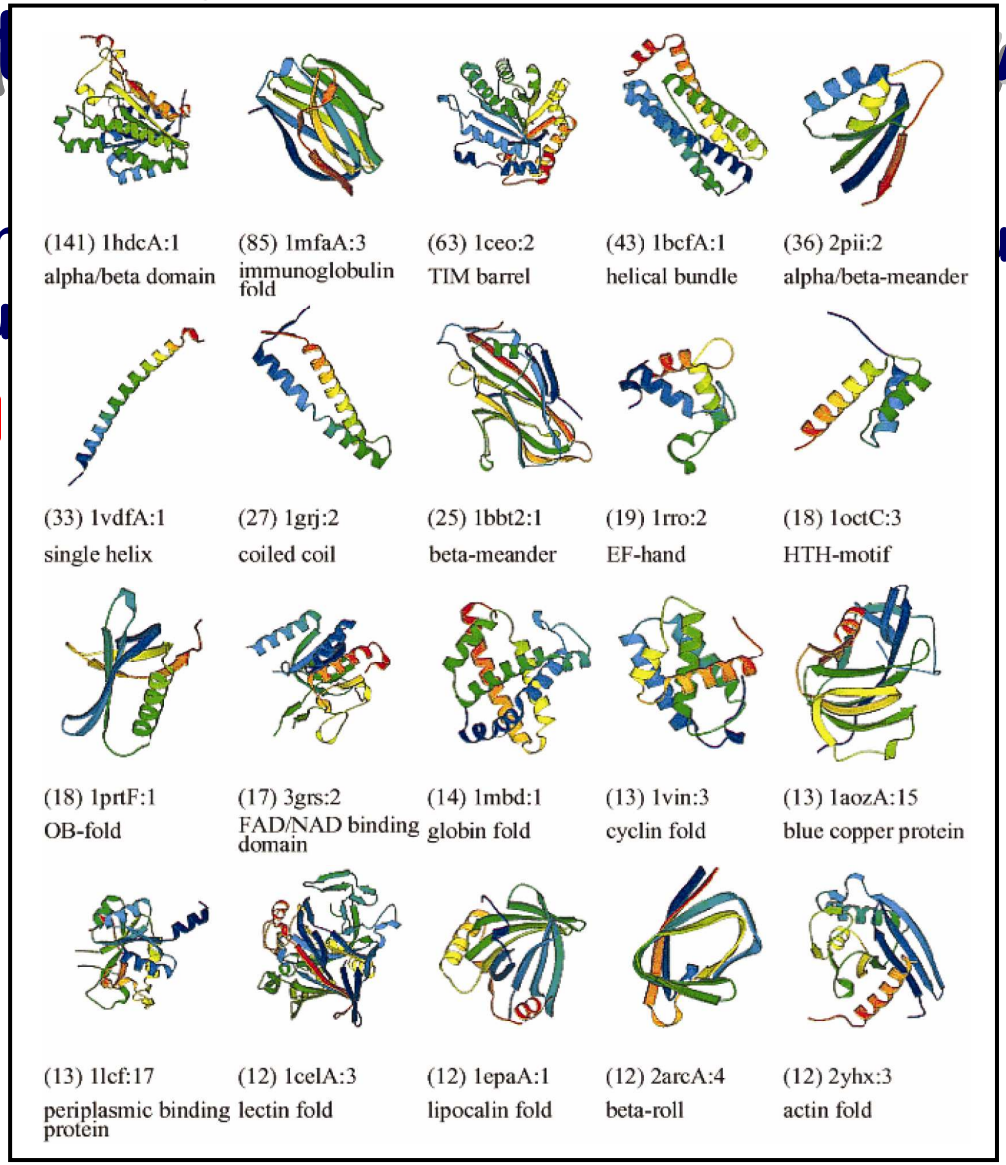
- **Vediamolo in cifre:**
  - ⇨ **700,000+ sequenze proteiche**
  - ⇨ **~ 20,000 strutture, ~ 5,000 uniche**
  - ⇨ ***La distanza tra sequenze e strutture note si sta allargando.***



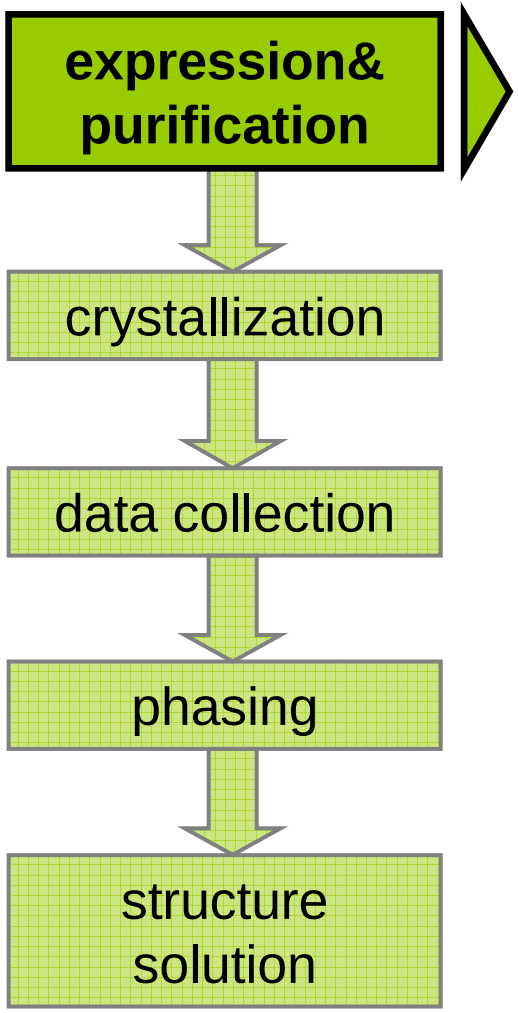
Allora perché potrebbe essere strat re?

- Osservazion rapidamente della struttu

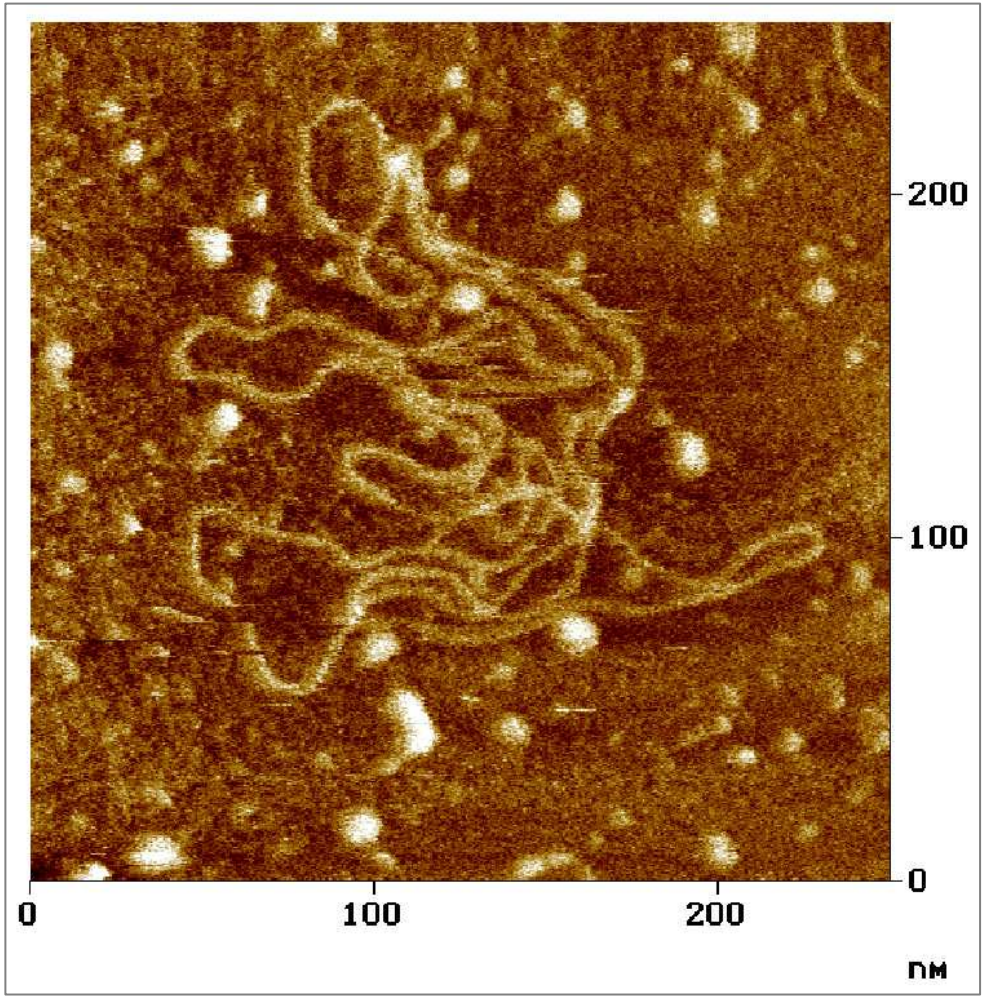
  ⇨ Numero l



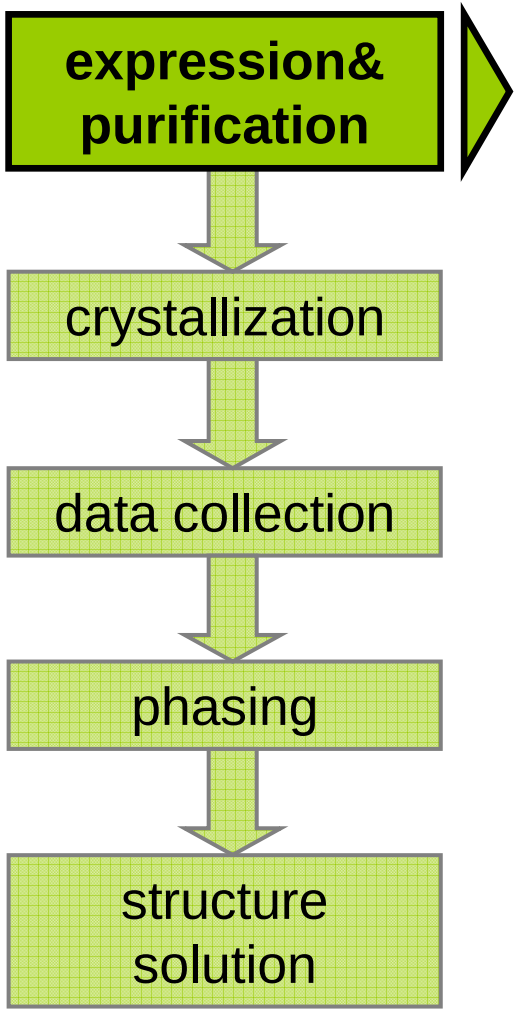
Protein crystallography workflow



protein (DNA, RNA) solution



Protein crystallography workflow



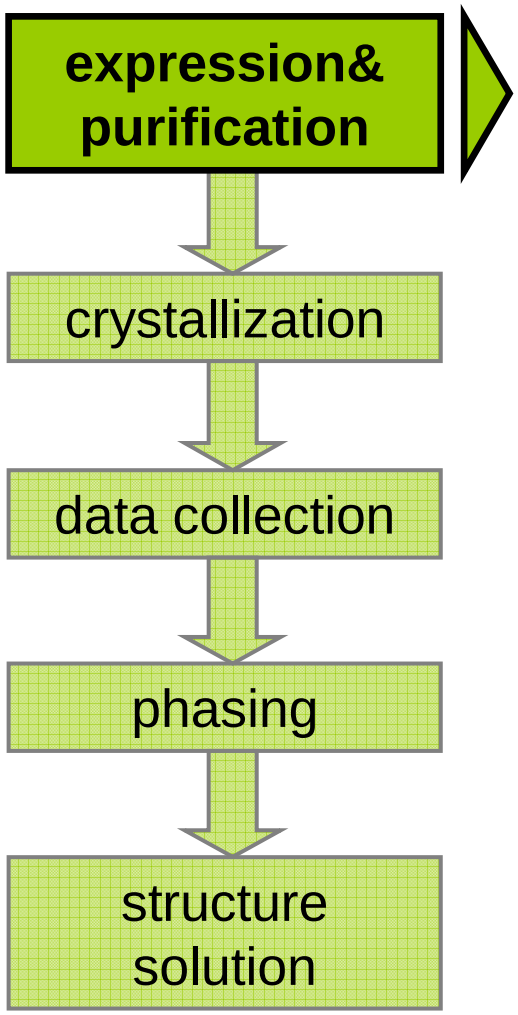
Easy case:

0.1 mg of protein to obtain 10-20 drops in which at least 5-6 generate "good" crystal; usually, if you need to set up the appropriate crystallographic condition for the first time you need at least 1 mg of purified protein.

Taft case:

you need at least 5-6 mg of purified protein… and a lot of lucky!!!

Protein crystallography workflow

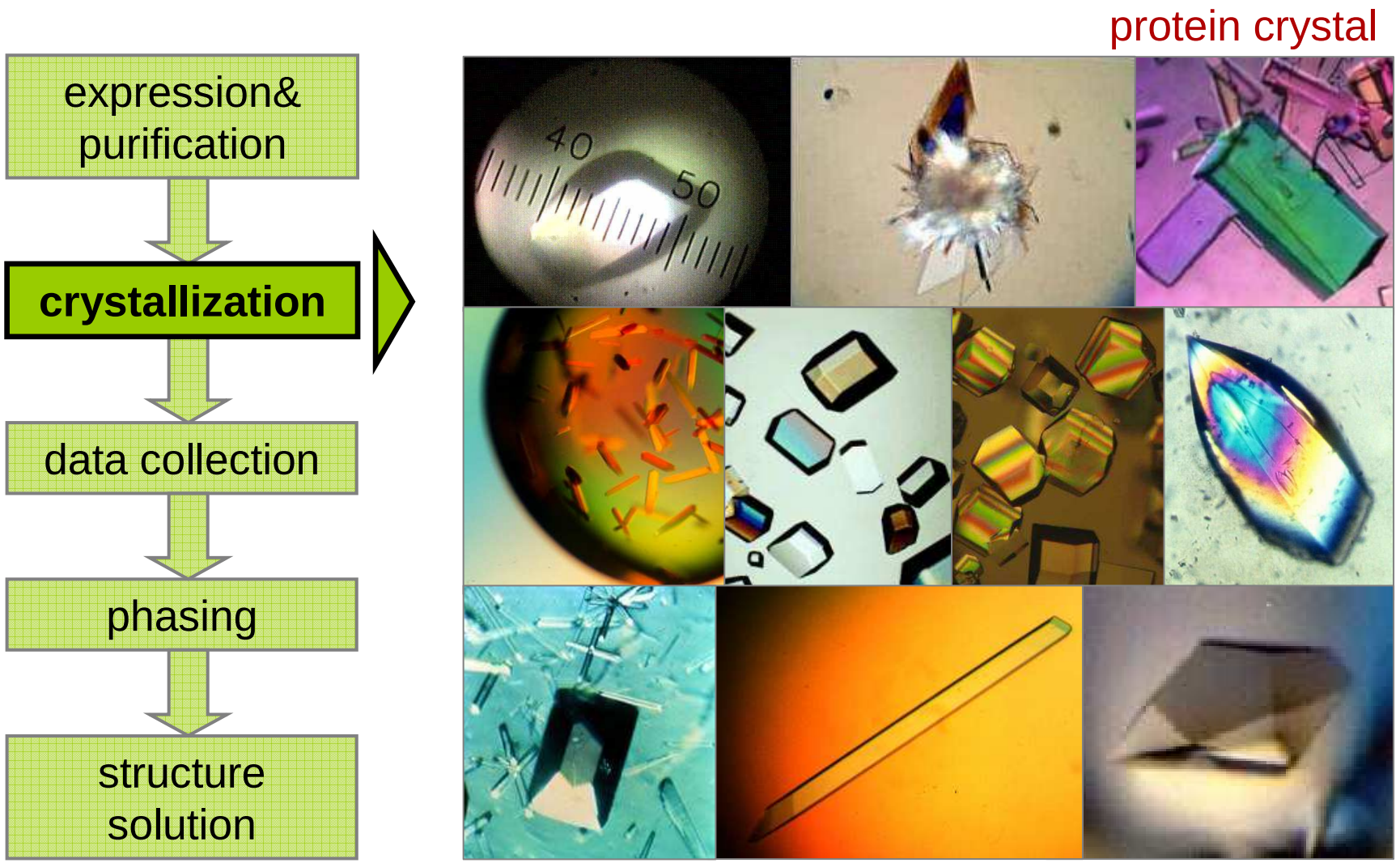


Time scale:

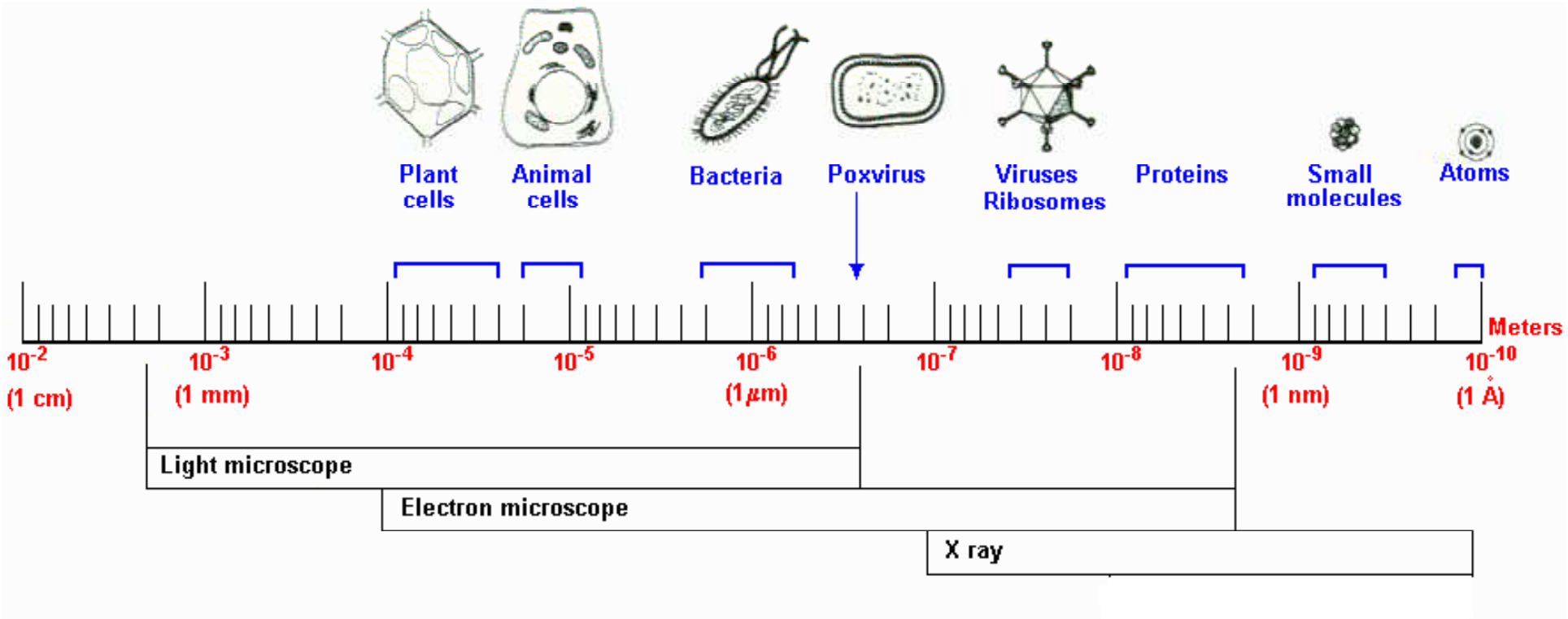
After plasmid cloning and its insertion to bacteria, to obtain 2-5 mg/lt of protein you need 2-4 weeks; moreover, you need other 2-3 weeks to perform the purification step.

If you already have an optimized protocol, you can get the same amount of protein in 7-10 days.

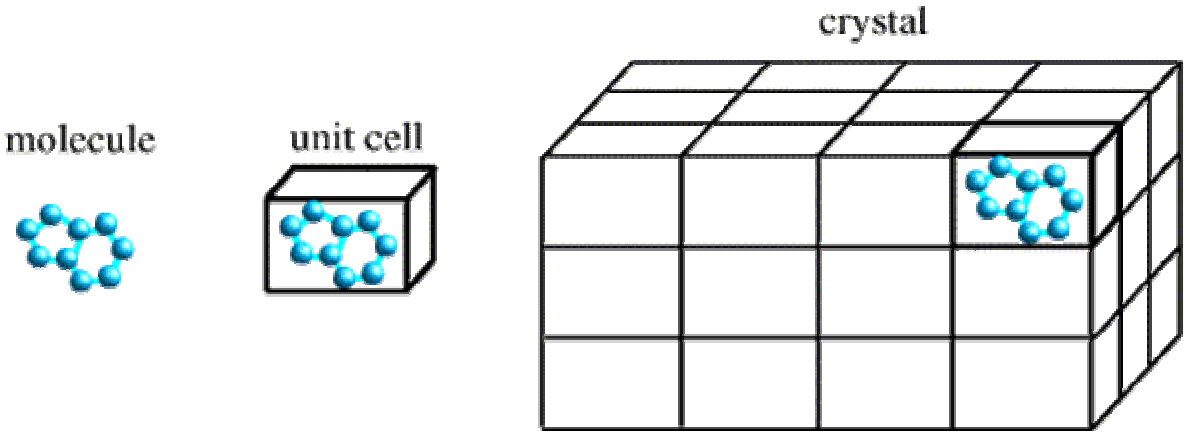
Protein crystallography workflow



Occhio alle dimensioni:



Cristallo: dal greco κρύσταλλος, *krýstallos*, ghiaccio!



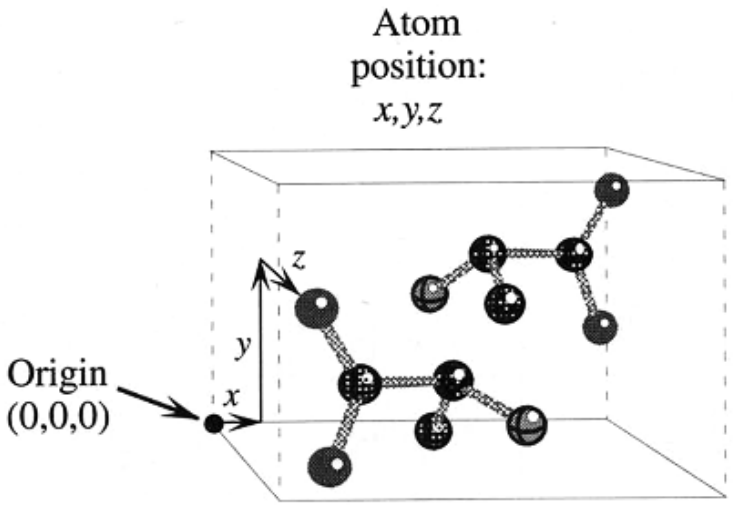
protein crystal

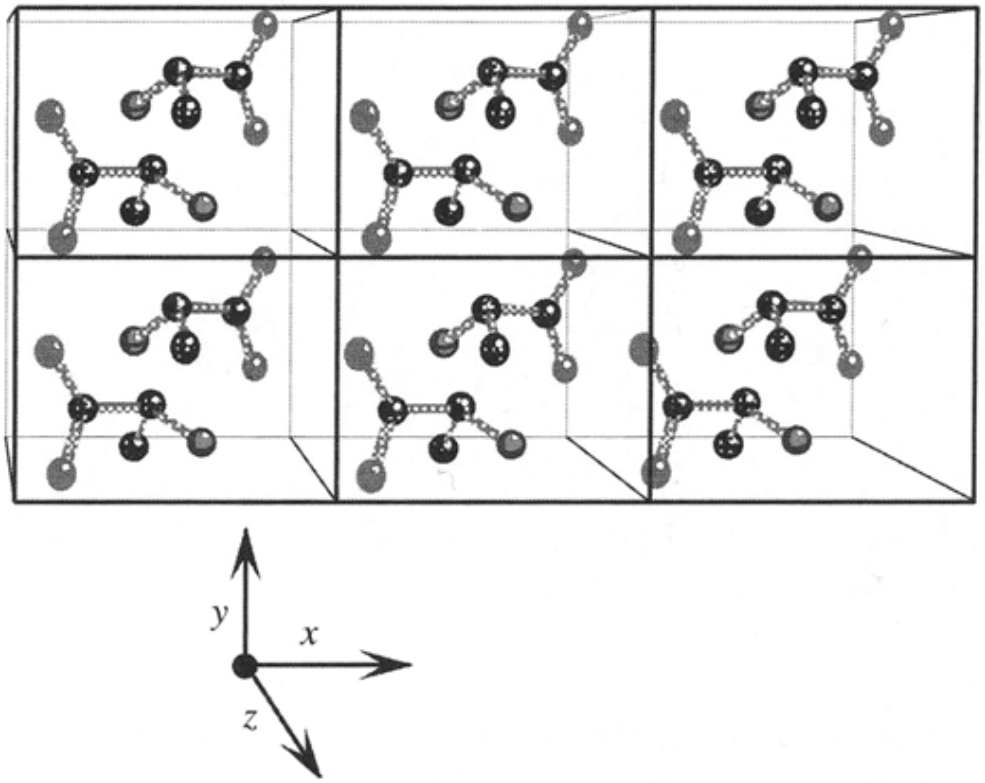
Although this might seem like a rather unnatural state for the protein, most crystals contain 40–60% water by volume, which is not that different to the crowded interior of a cell.

Why crystals?

X-ray scattering from a single molecule would be incredibly weak and extremely difficult to detect above the noise level, which would include scattering from air and water. A crystal arranges huge numbers of molecules in the same orientation, so that scattered waves can add up in phase and raise the signal to a measurable level. In a sense, a crystal acts as an amplifier.

Proprietà geometriche della cella e del cristallo:





Individuare ed ottimizzare le condizioni di cristallizzazione… un arte!

Elevato numero di parametri variabili:

- pH
- Tampone
- Concentrazione della proteina
- Temperatura
- Precipitante
- …

Sono stati messi a punto diversi "crystallization screens", che possono essere acquistati o preparati in laboratorio, che consentono di fare uno screening della proteina di interesse a diverse concentrazioni e "contro" diverse centinaia di condizioni di cristallizzazione.

Una volta individuate le condizioni di cristallizzazione queste devono essere ottimizzate per migliorare le dimensioni e la qualità dei cristalli.

Tecnica di cristallizzazione a goccia pendente

Goccia: $V_t \approx 6$ µl

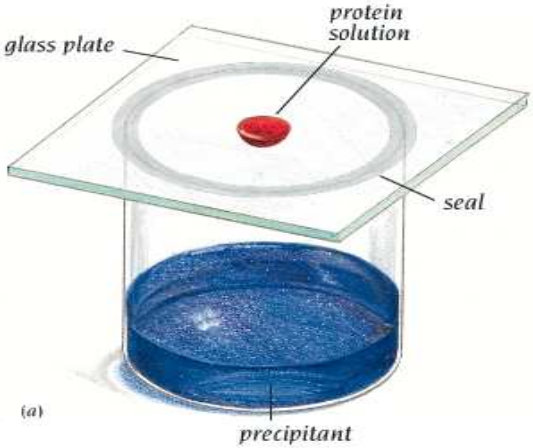
proteina ≈ 4mg/ml

tampone fosfato 1M

pH 8.7

Soluzione:

1 ml di tampone fosfato 1.7 M pH 8.7



Si lascia equilibrare il sistema a 23°, i cristalli appaiono in circa 7 giorni

In generale: una goccia di una soluzione proteica contenente precipitante (circa 5-20 µl) viene sospesa sopra un recipiente contenente una quantità maggiore (0,5-1 ml) di una soluzione più concentrata di precipitante e la goccia viene lasciata equilibrare con la soluzione contenuta nel recipiente.

L' acqua evaporando passa dalla goccia di proteina, meno concentrata, alla soluzione contenuta nel recipiente, più concentrata, causando una contrazione della goccia. (**Diffusione di vapore**)

La concentrazione di proteina e precipitante nella goccia aumenta fino a che raggiunta la saturazione, la proteina comincia a precipitare lentamente.

Se le condizioni di cristallizzazione sono "corrette" il precipitato non sarà amorfo ma cristallino!!

Preparazioni di complessi proteina-ligando

1) Soaking: consiste nell'immergere i cristalli della proteina nativa in una soluzione madre contenente l'inibitore. I cristalli di proteina contengono di solito canali di solvente sufficientemente larghi da permettere all'inibitore di diffondere all'interno dei cristalli

Vantaggi:

è relativamente rapida

richiede piccole quantità di composto

non causa variazioni nelle condizioni di cristallizzazione

Svantaggi:

il ligando deve essere un molecola relativamente piccola

possibili cambiamenti conformazionali indotti dal *binding* del ligando potrebbero essere impediti dall'impacchettamento cristallino e passare quindi inosservati

il reticolo cristallino potrebbe essere incompatibile con il binding del ligando, provocando rottura e/o dissoluzione dei cristalli a seguito di impregnazione, oppure non legare affatto il ligando.

Preparazioni di complessi proteina-ligando

2) Co-cristallizzazione: il complesso si forma in soluzione addizionando il ligando (conc ≈ 1mM) alla soluzione della proteina e successivamente il complesso viene cristallizzato

Vantaggi:

Si possono ottenere cristalli del complesso per ligandi ad alto peso molecolare

eventuali variazioni conformazionali indotte dal ligando non sono ostacolate e si evidenzieranno nella struttura cristallina, poiché il complesso si forma in soluzione

la qualità di diffrazione dei cristalli non è compromessa dalla procedura di soaking

Svantaggi:

A volte le condizioni di cristallizzazione sono leggermente diverse o perfino completamente diverse dalle condizioni di cristallizzazione dei composti puri (proteina, ligando), costringendo a ricominciare daccapo la ricerca delle condizioni di cristallizzazione

La co-cristallizzazione dei complessi impiega da alcune settimane ad alcuni mesi e non tutti i ligandi sono stabili per tempi cosi lunghi

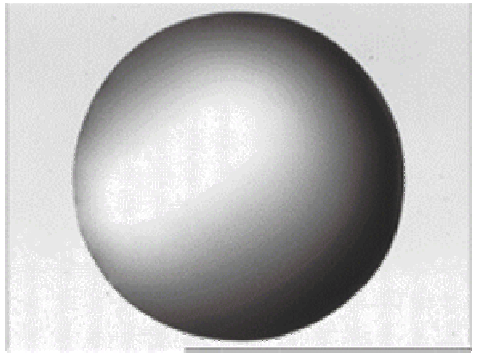
e ricordate:

A watched crystal never grows

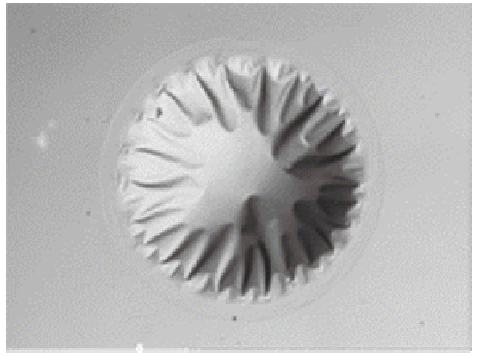
Crystallographer's fortune cookie

che cosa possiamo osservare al microscopio dopo aver pazientato:

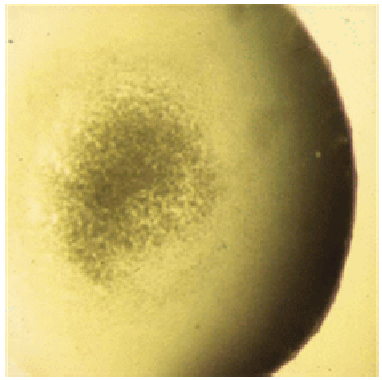
Gocce limpide



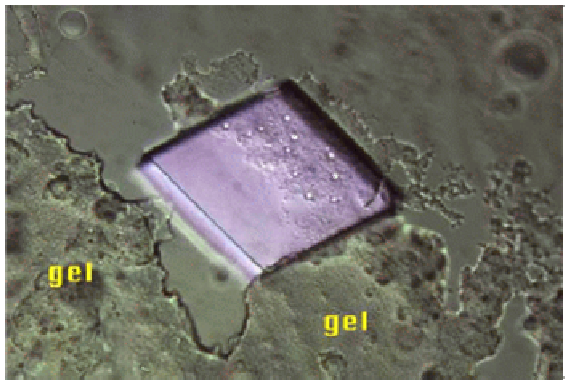
Skin



Precipitati

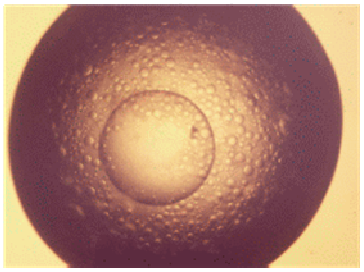


Gels



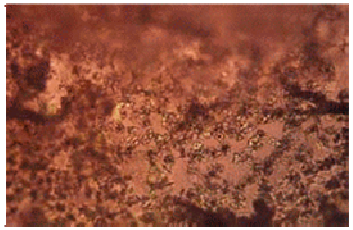
Uummm:

Separazioni di fase

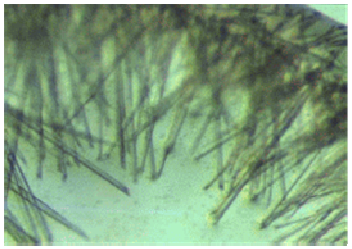


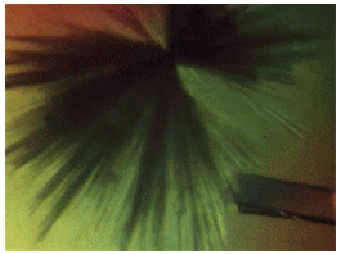
Cristalli:

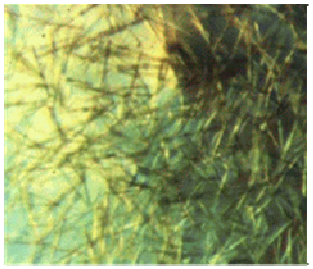
Precipitati microcristallini



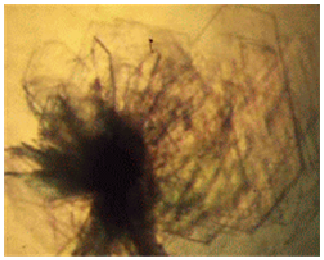
Needles

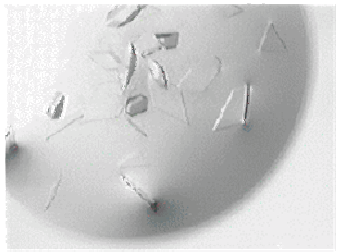






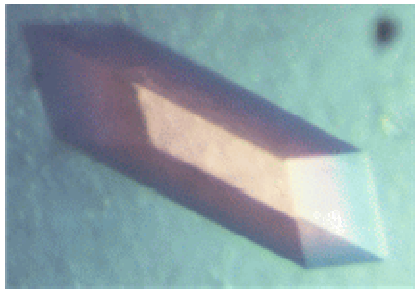
Plates

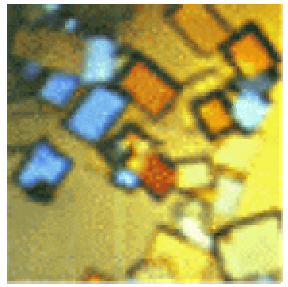




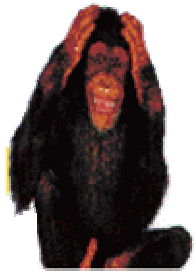
ma ricordate:

If you see a crystal:





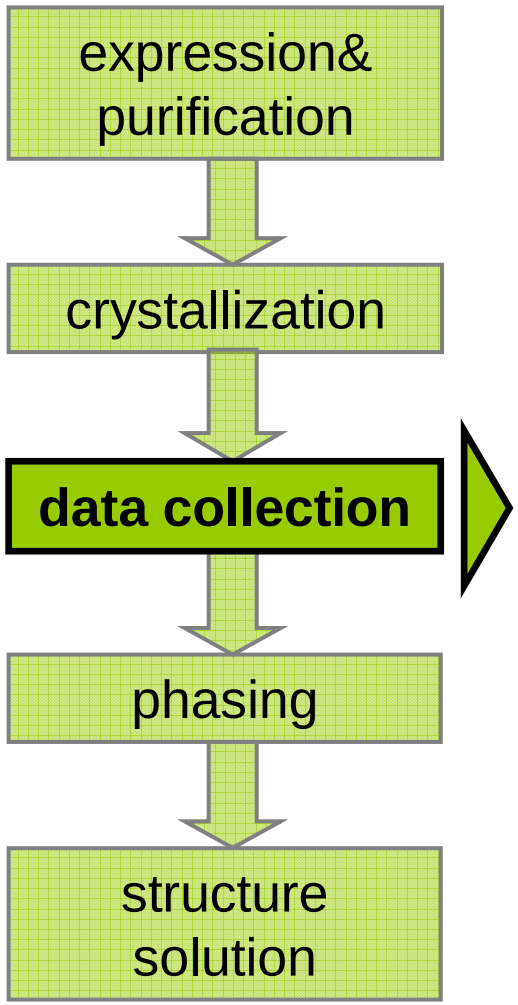
don't go running down the corridor screaming "URRA!!!" until...



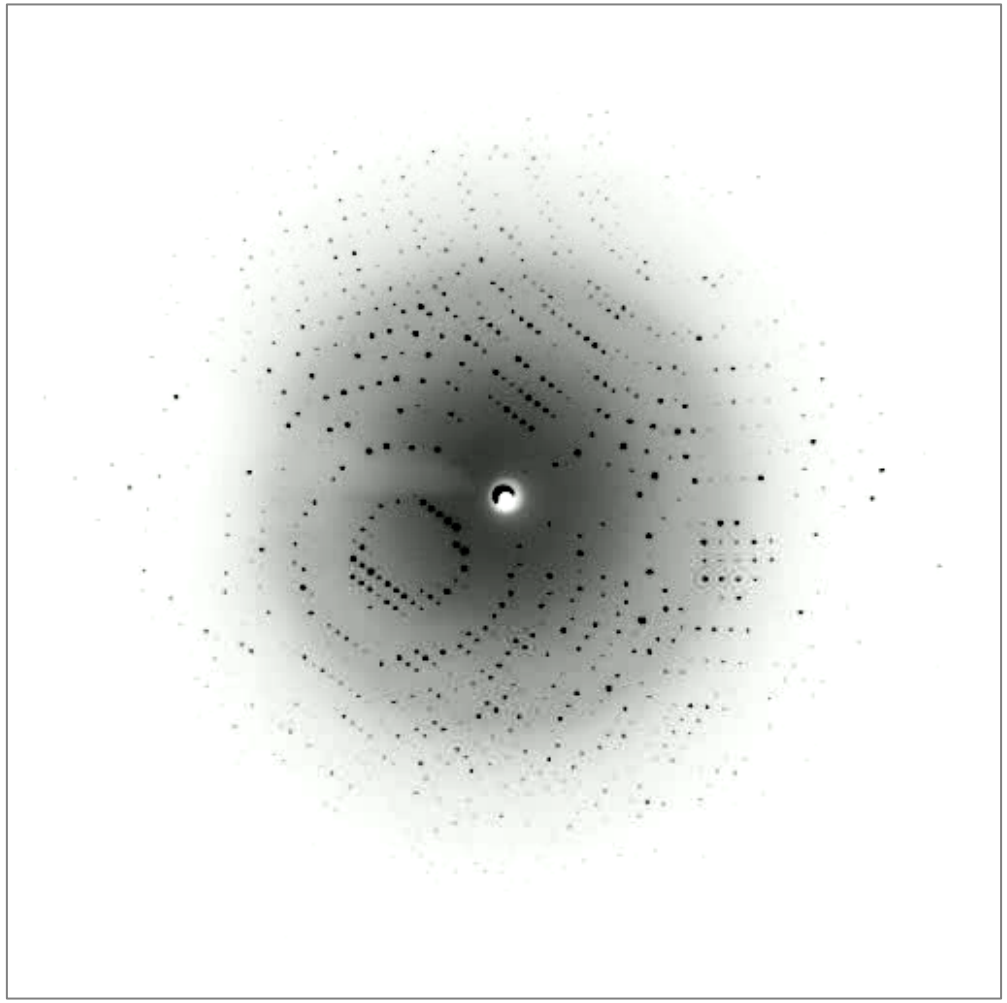
you know your crystal isn't salt...

and that it diffracts

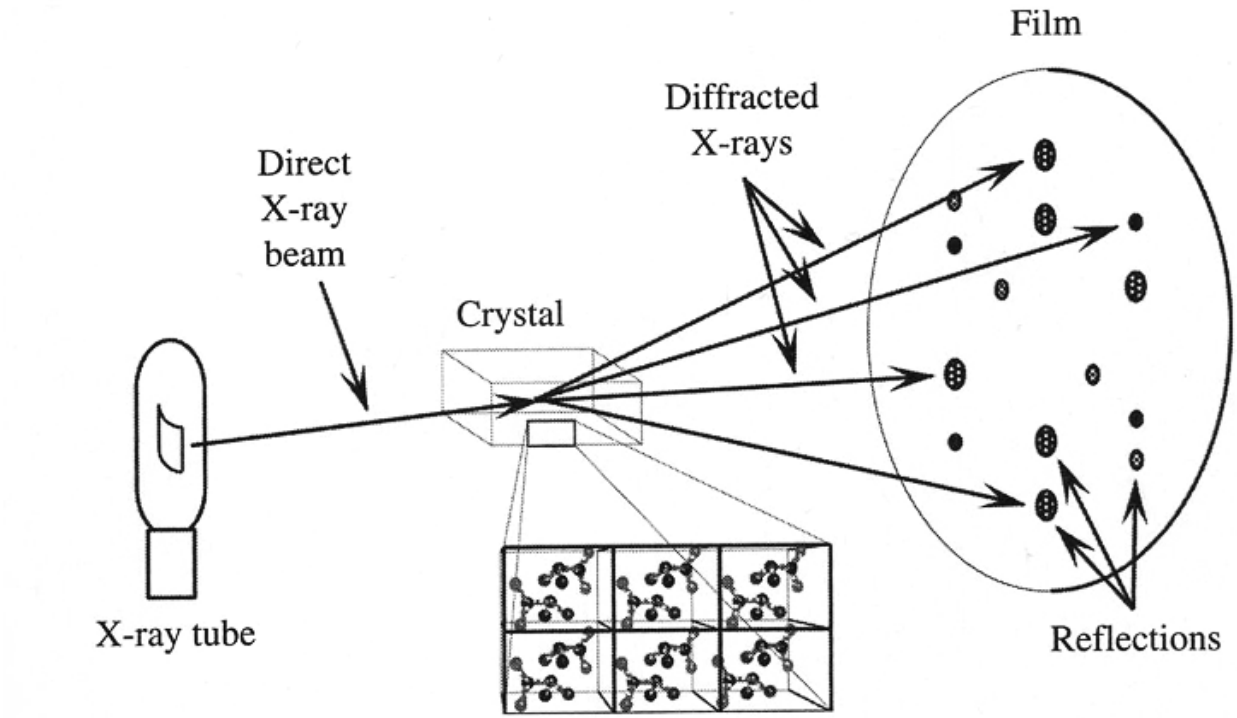
Protein crystallography workflow

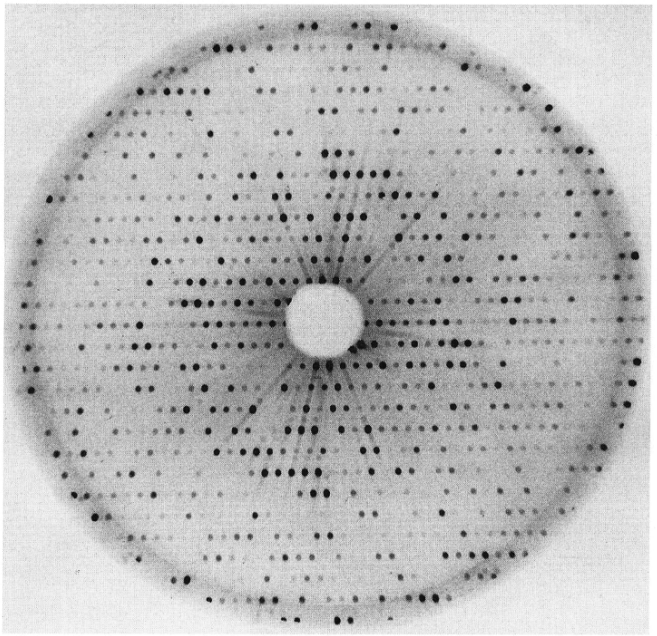


diffraction pattern



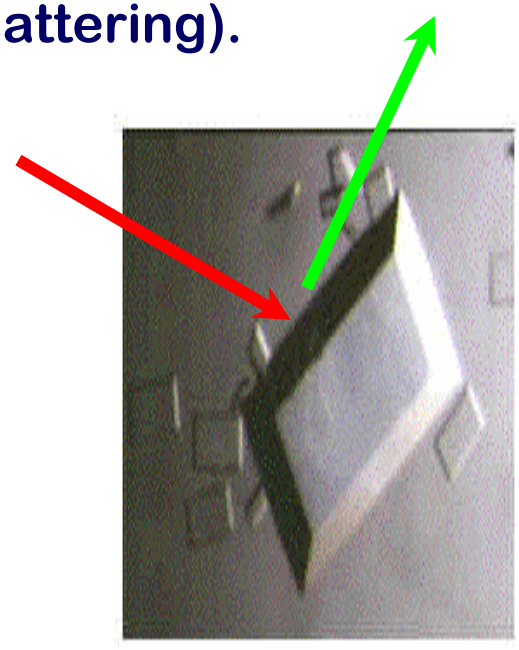
Eccoci alla raccolta dei dati di diffrazione:



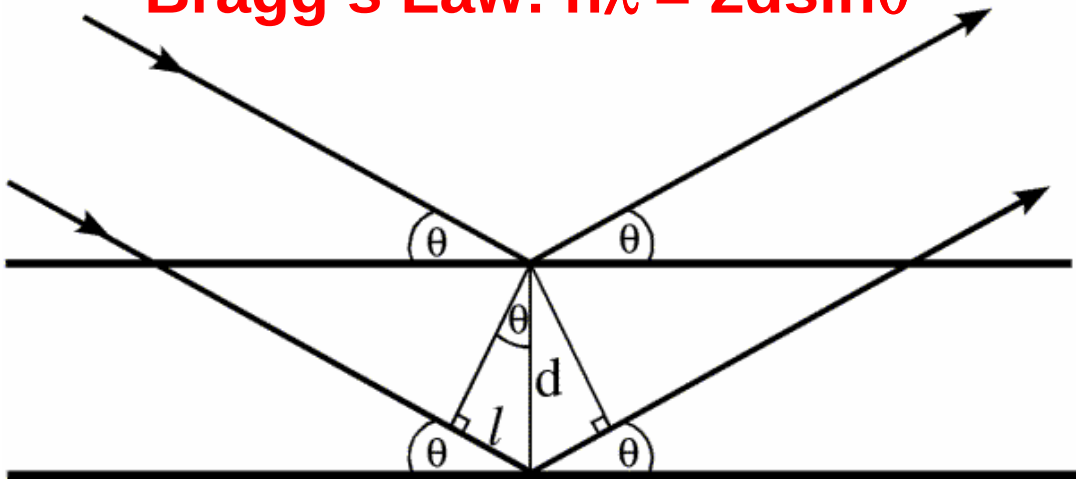


Diffraction Principles

X-ray diffraction is essentially an imaging technique in which X-rays are scattered by atoms in the crystal without loss of energy (elastic scattering).

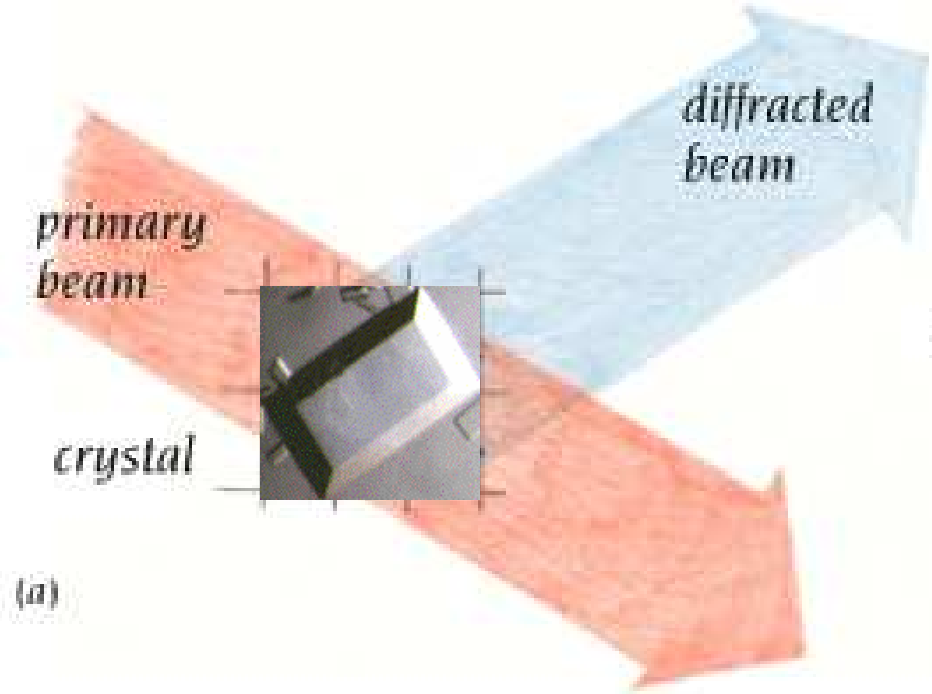


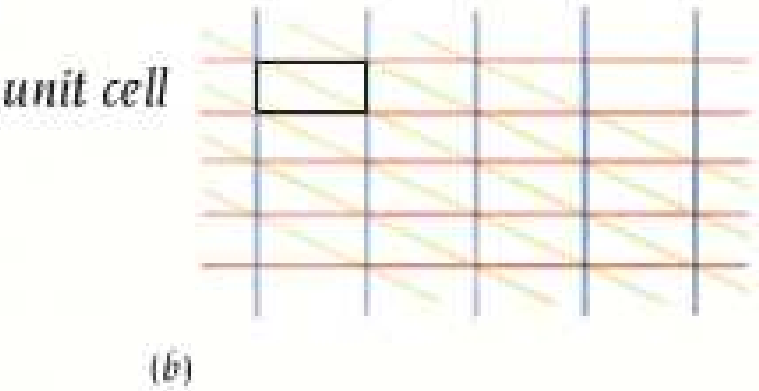
Bragg's Law: $n\lambda = 2d\sin\theta$

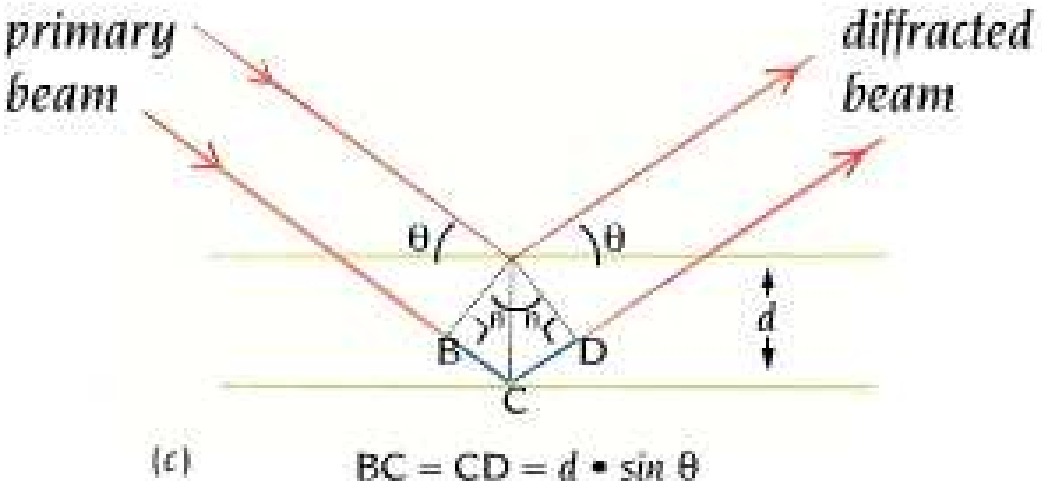


Why X-rays?

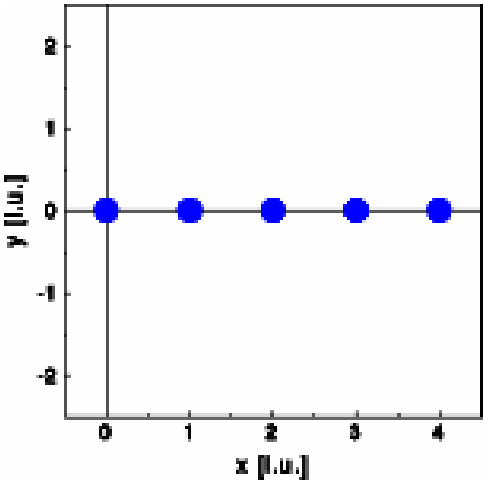
As noted above, the use of electromagnetic radiation to visualize objects requires the radiation to have a wavelength comparable to the smallest features that you wish to resolve. We often use X-rays emitted from copper targets bombarded with high energy electrons, which emit at several characteristic wavelengths: the one we use is called CuKα, which has a wavelength of 1.5418Å. This is very similar to the distance between bonded carbon atoms, so it is well suited to the study of molecular structure.

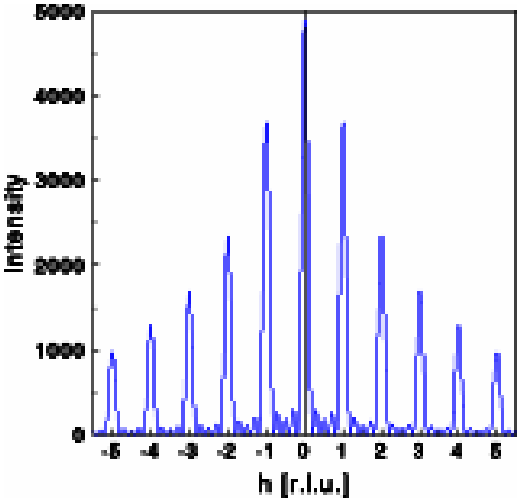

diffracted
beam
primary
beam
crystal
(a)

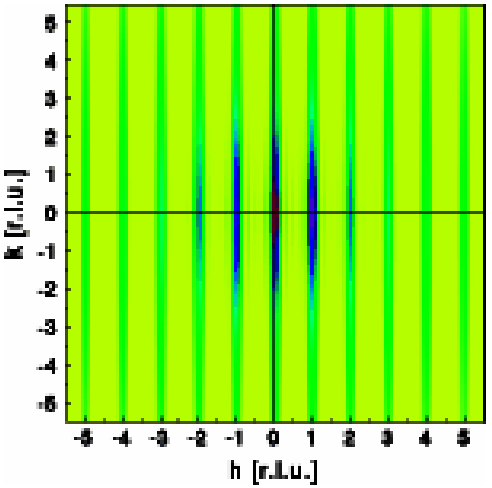

unit cell
(b)


primary
beam
diffracted
beam
θ
θ
B
D
C
d
(c)
BC = CD = d • sin θ

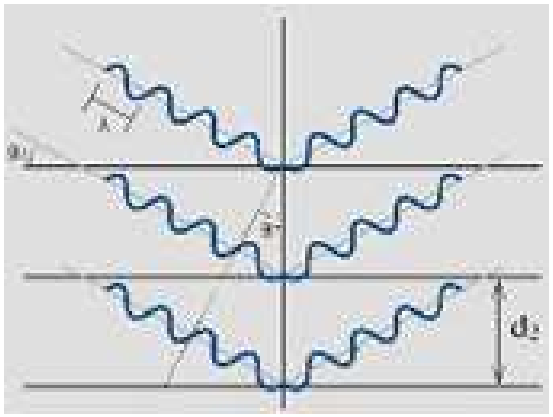
Diffraction Principles





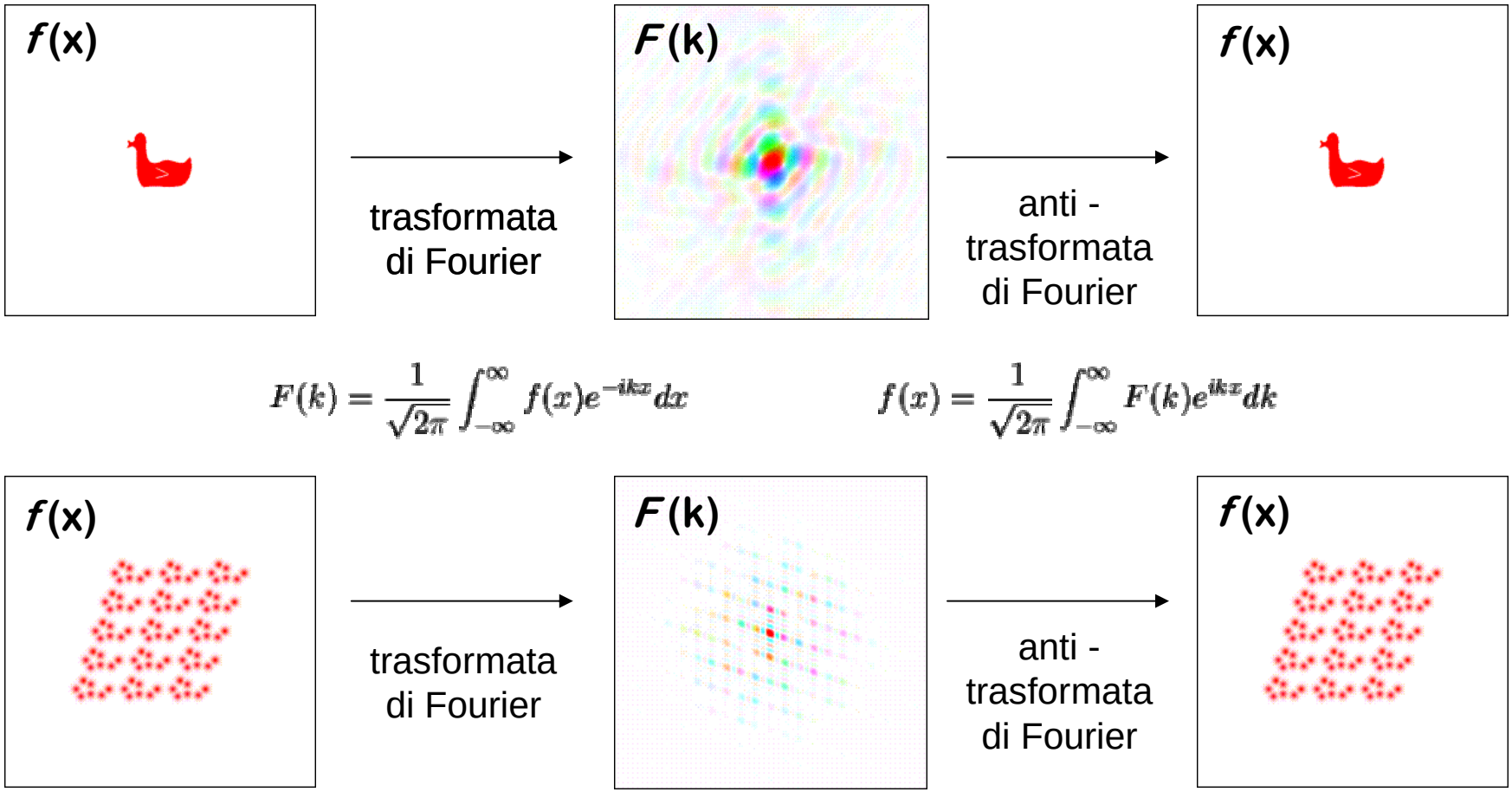


A string of atoms



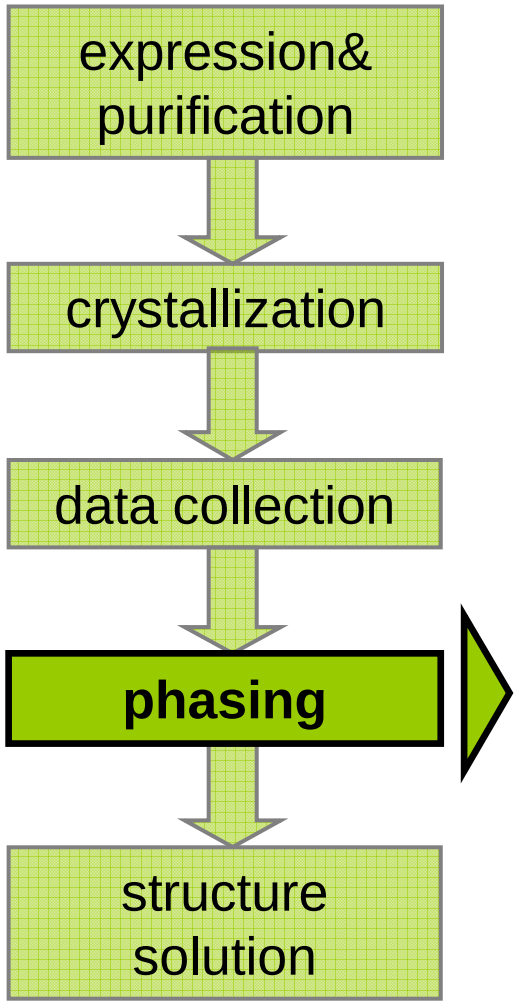
Corresponding Diffraction Pattern

Diffrazione e trasformate di Fourier:

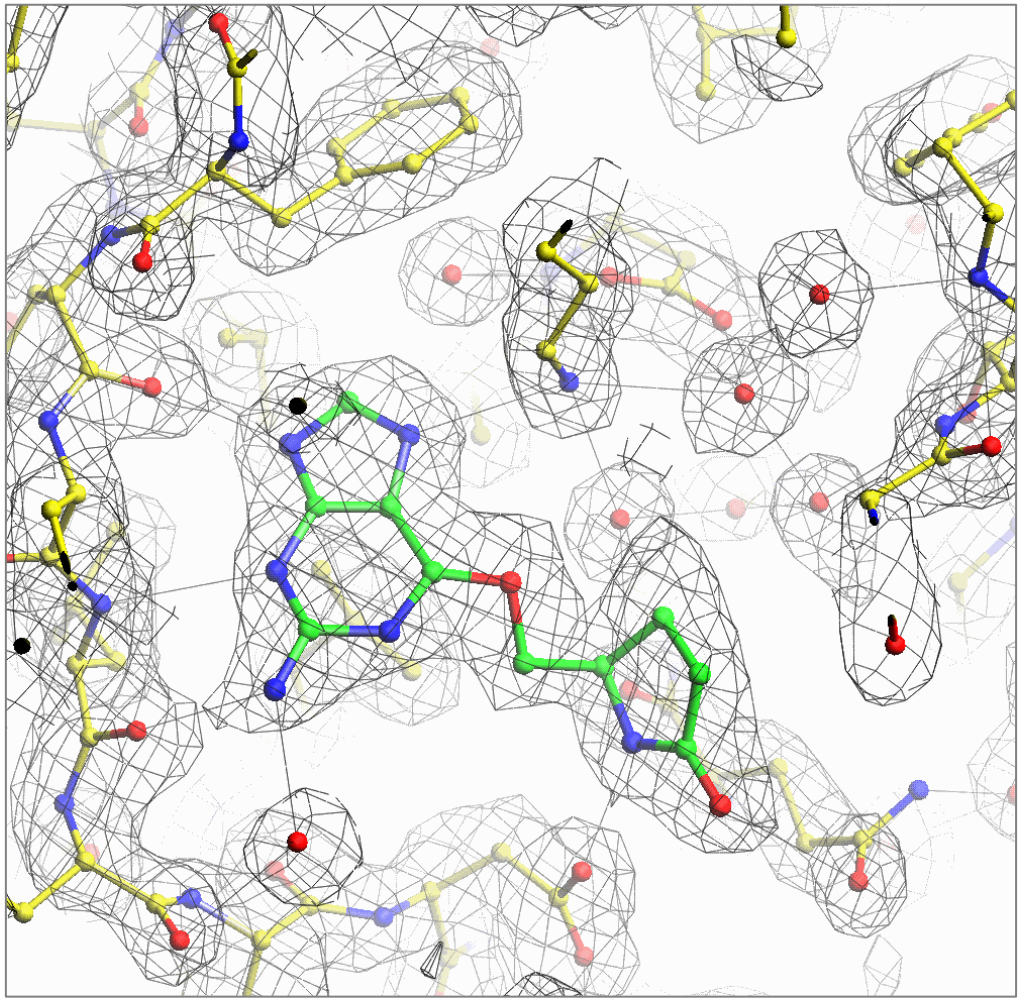


$$F(k) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} f(x) e^{-ikx} dx \qquad f(x) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} F(k) e^{ikx} dk$$

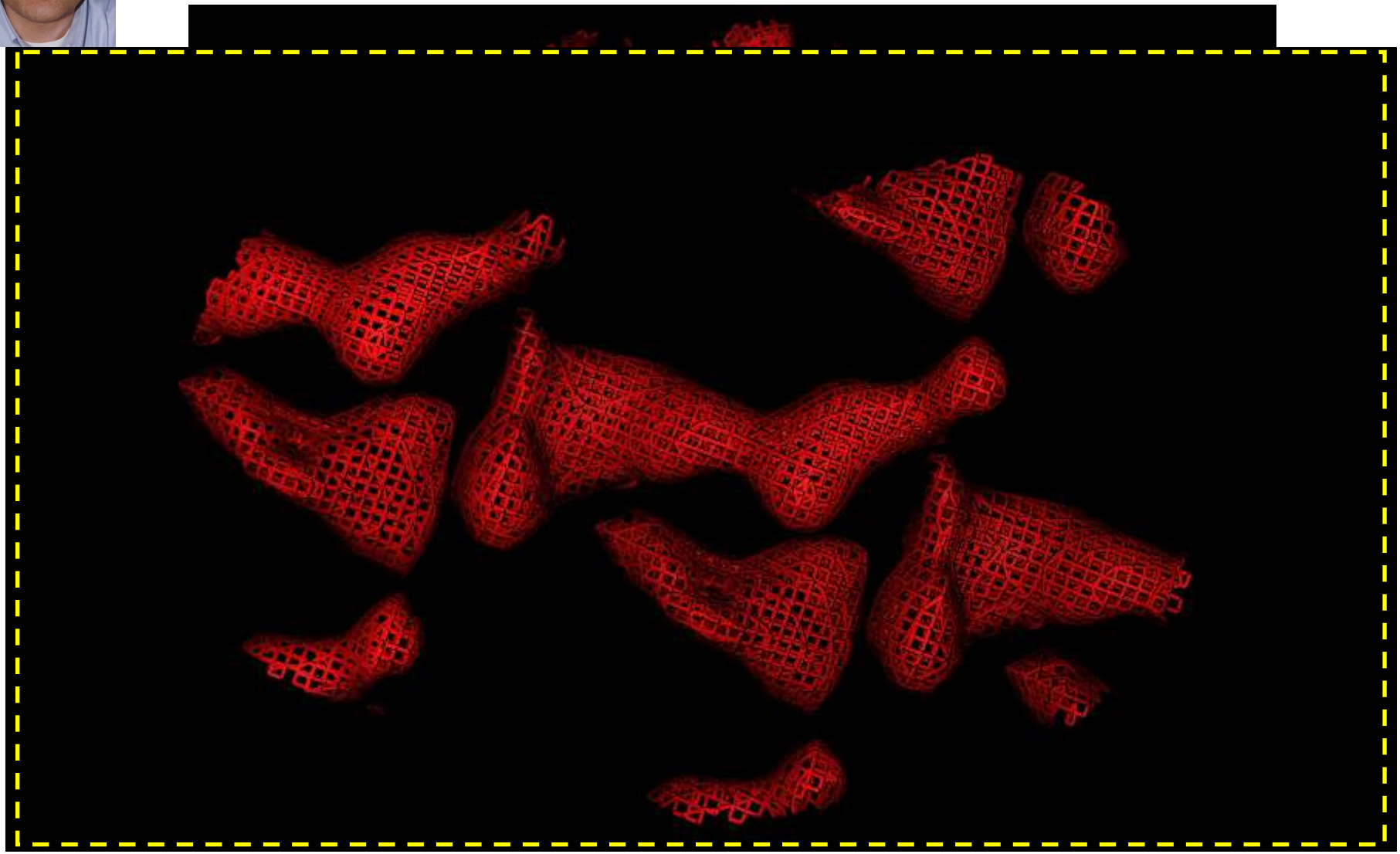
Protein crystallography workflow



electron density map



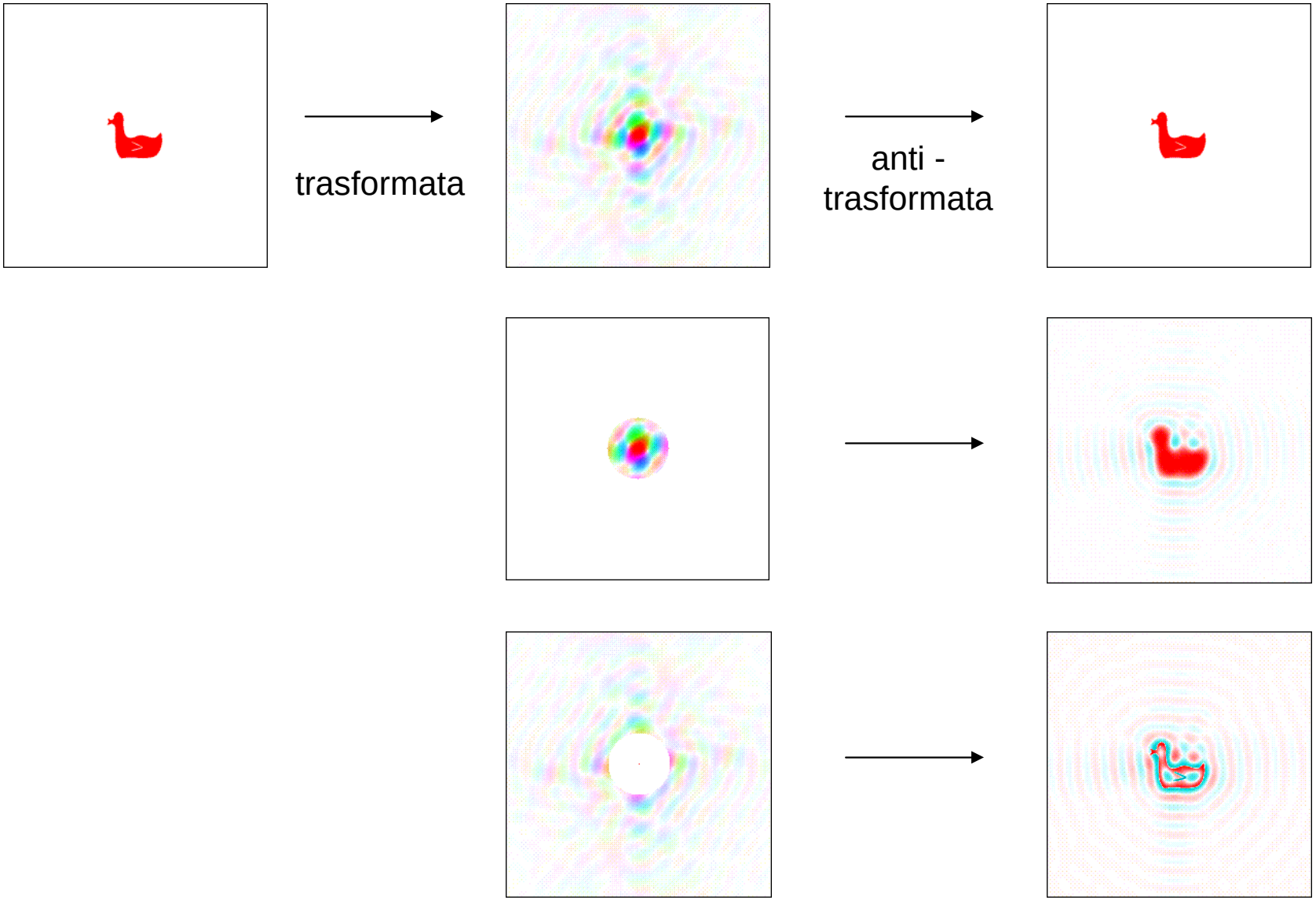
Ecco che cosa vede il cristallografo dopo l'applicazione della sua antitrasformata:



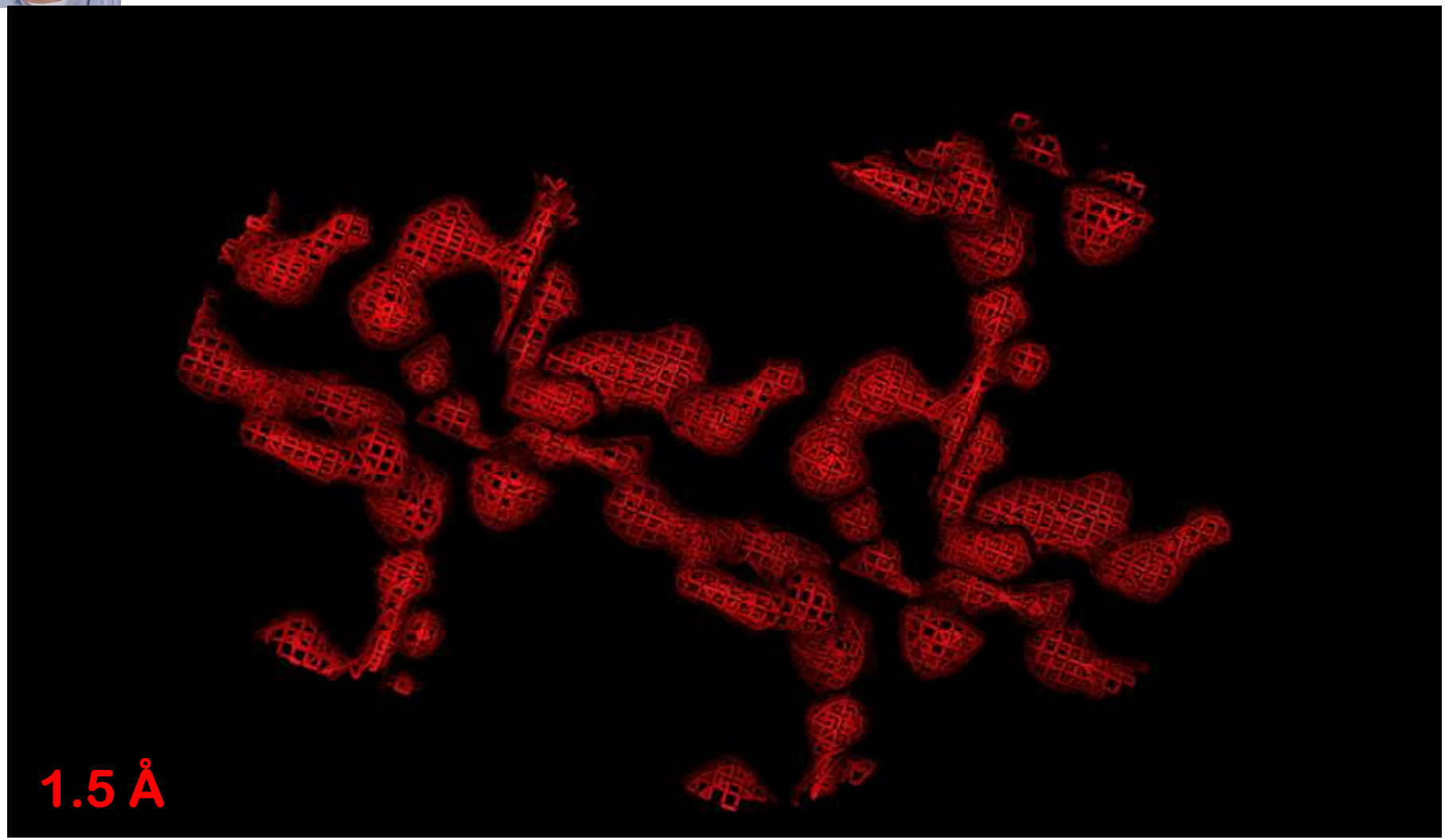
Il problema della risoluzione:

I cristalli proteici presentano un certo grado di disordine: molecole o parti di molecole in diverse celle elementari non occupano esattamente la stessa posizione e non hanno esattamente la stessa orientazione (le proteine non sono completamente rigide).
Tale disordine fa sì che i cristalli abbiano un limite di risoluzione nella loro diffrazione da raggi X. Se i cristalli proteici diffrangono a bassa risoluzione allora la densità elettronica che si otterrà dai dati sperimentali non sarà in grado di rivelare i dettagli strutturali più minuti della proteina.
Poiché la mappa di densità elettronica di una proteina deve essere interpretata, cioè devono essere definite le posizioni degli atomi di ciascun aminoacido, l'accuratezza dell'analisi strutturale dipende dal limite di risoluzione del cristallo.

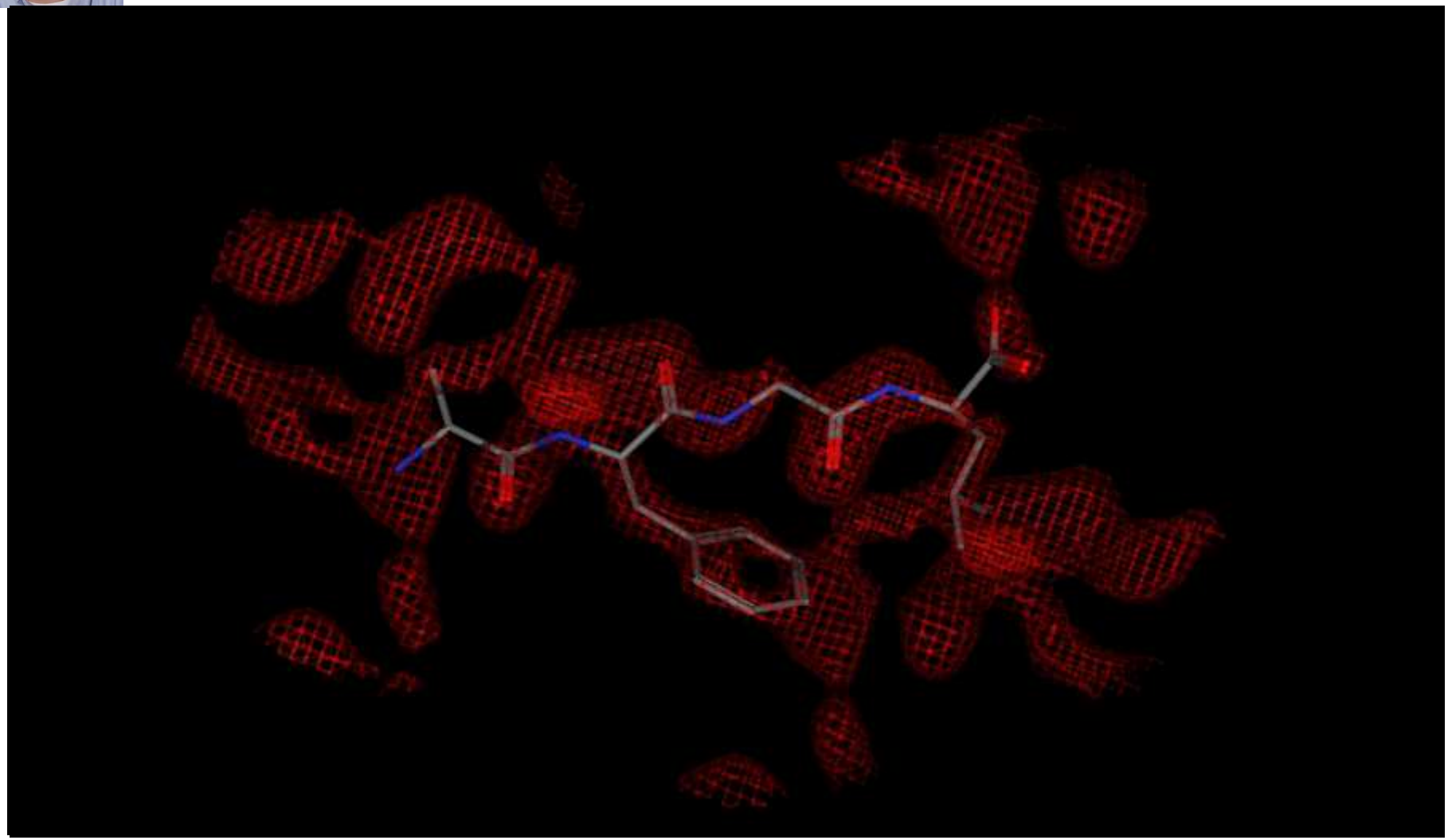
Il problema della risoluzione:



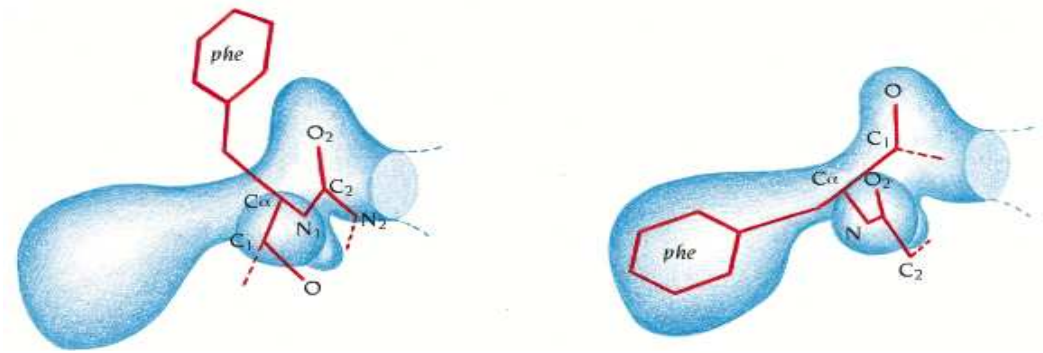
Notate la differenza?



Fitting….



La bontà del fit è espressa dal fattore R (R factor):



$$R = \frac{\Sigma \left| \left| Fo \right| - \left| Fc \right| \right|}{\Sigma \left| Fo \right|}$$

Fo = densità osservata
Fc = densità calcolata

Il modello viene sopposto a continue rifiniture fino a quando non si riscontrano ulteriori miglioramenti nell' R factor ($0 < R < 0.59$).

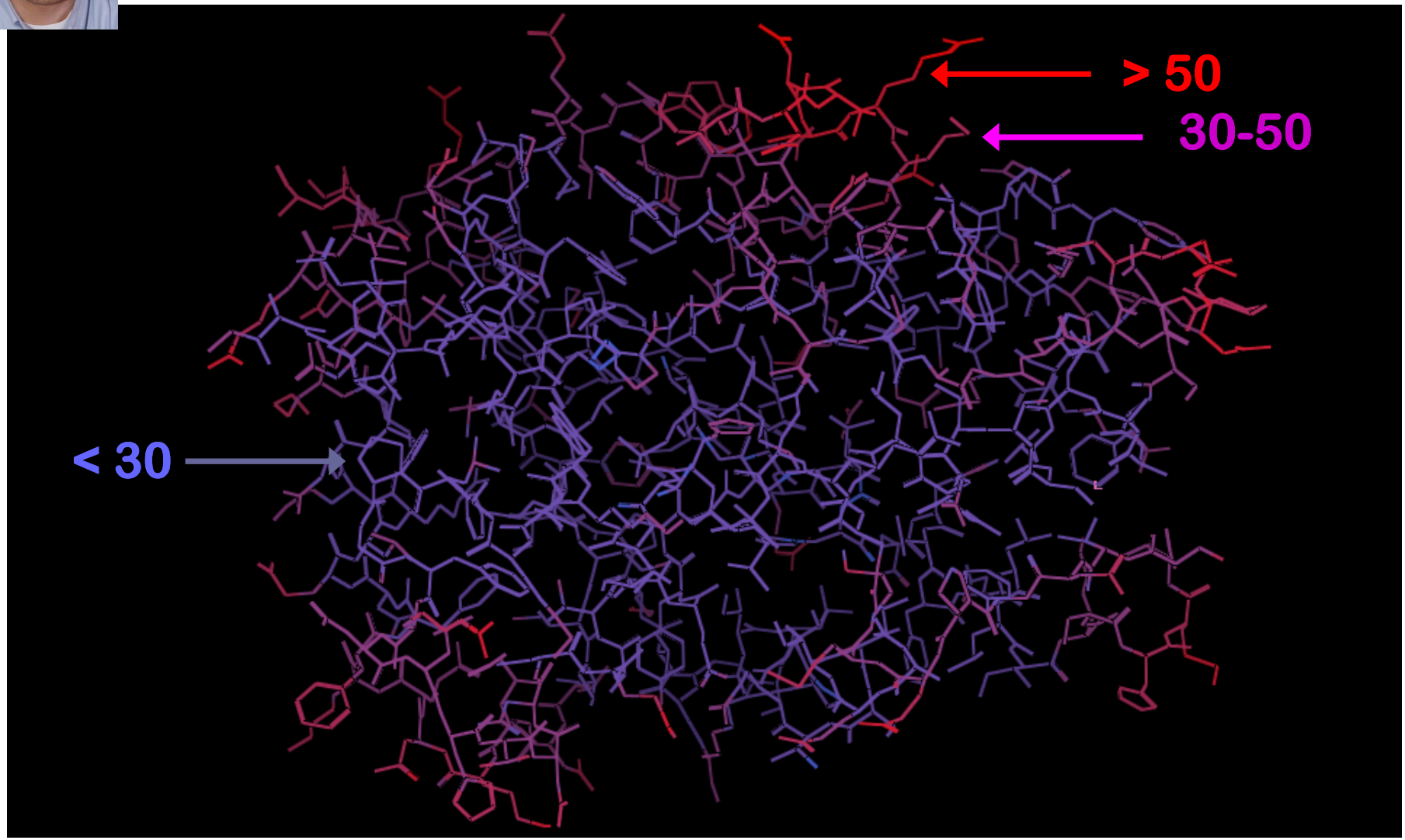
In generale $R = 0.15 \div 0.20$ per una struttura ben determinata.

Un R factor maggiore di 0.30 per una struttura a risoluzione media (3 Å) significa che si possono essere errori anche grossolani nella struttura.

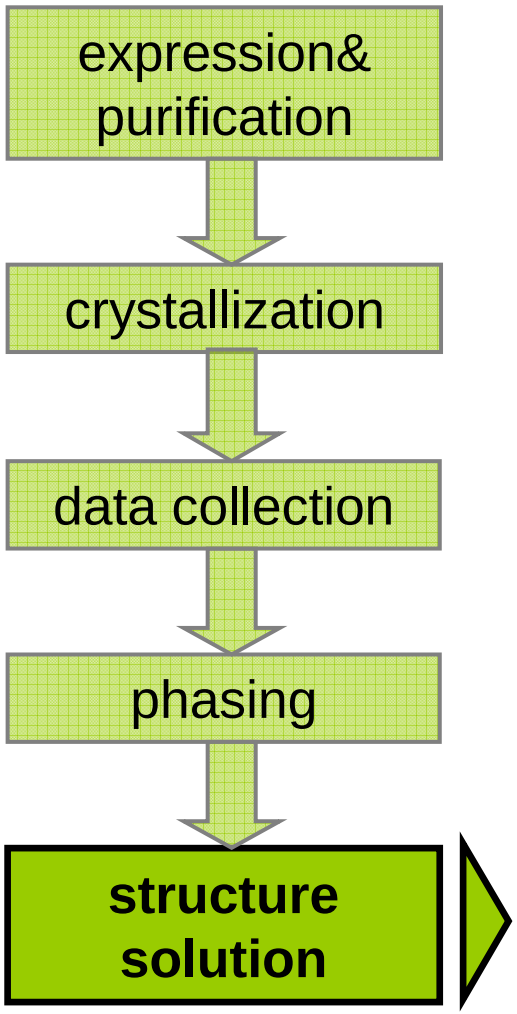
E poi non dimentichiamo il fattore B o fattore di temperatura (B factor):

La mobilità degli atomi in un cristallo è espressa in termini di fattori di temperatura, o fattori B, i quali vengono ottimizzati durante le fasi di affinamento. Lo spostamento medio di atomi con fattori B maggiori di 60 $Å^2$ supera 1.5 Å. Questi atomi sono generalmente poco definiti nelle mappe di densità elettronica.

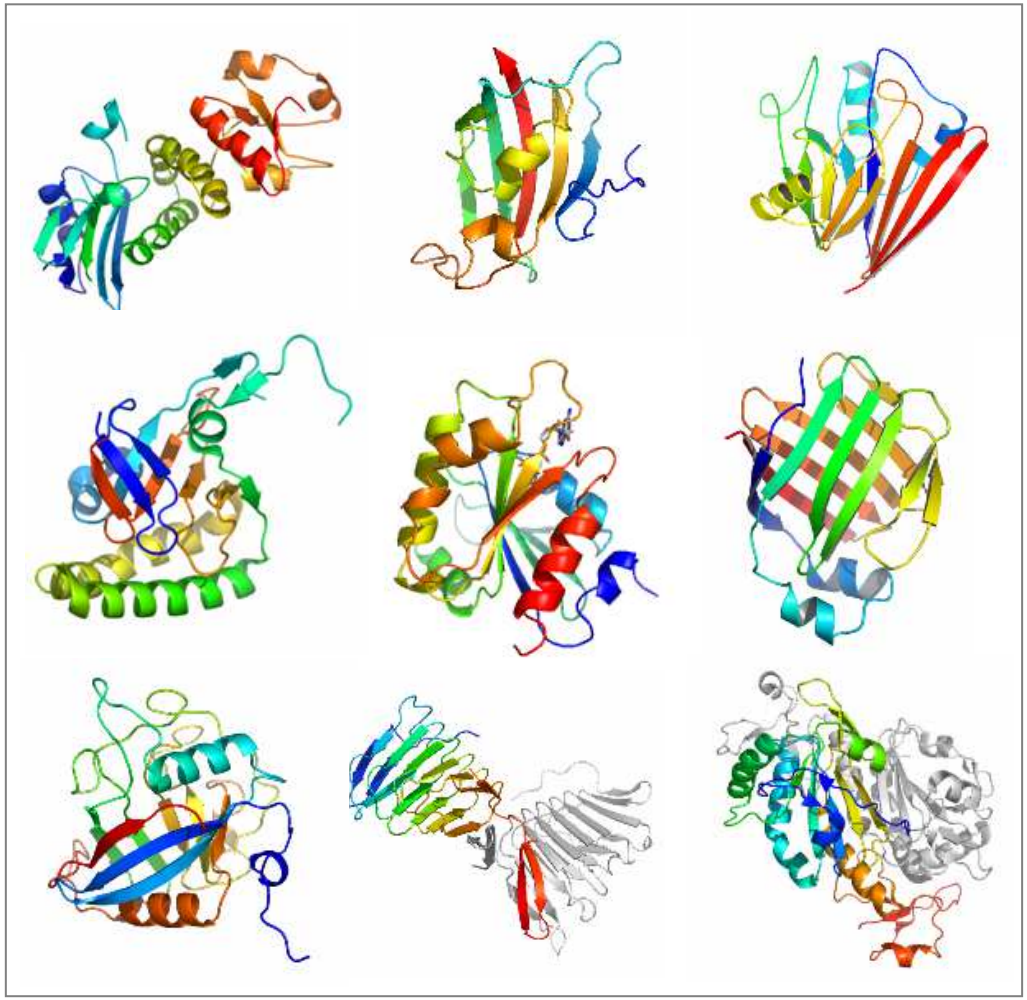
E poi non dimentichiamo il fattore B o fattore di temperatura (B factor):



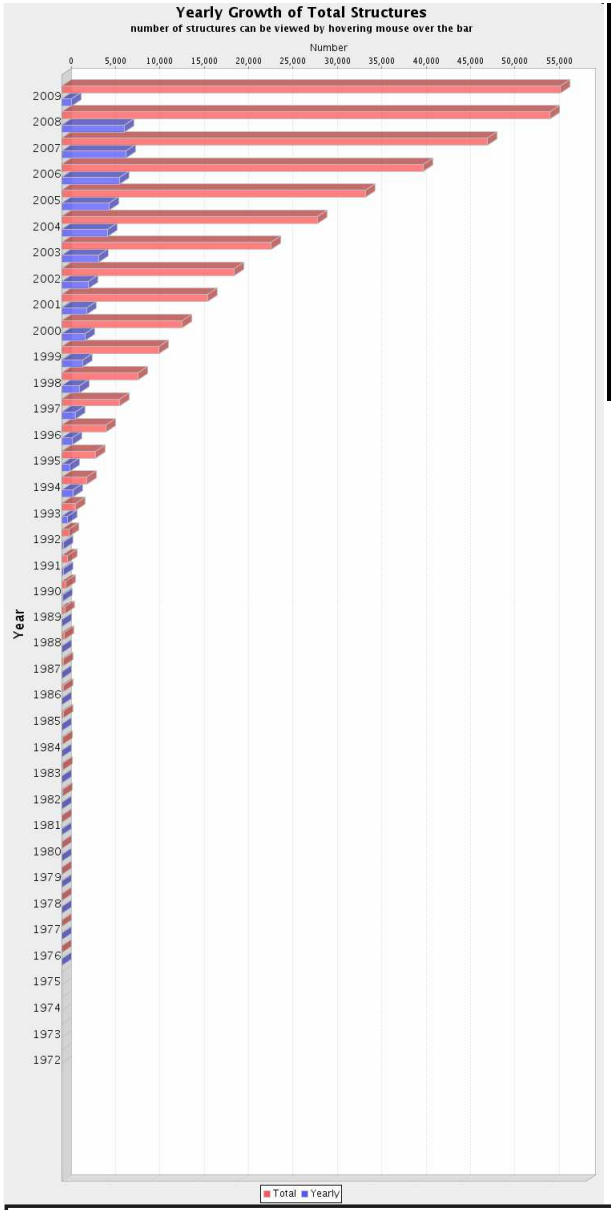
Protein crystallography workflow



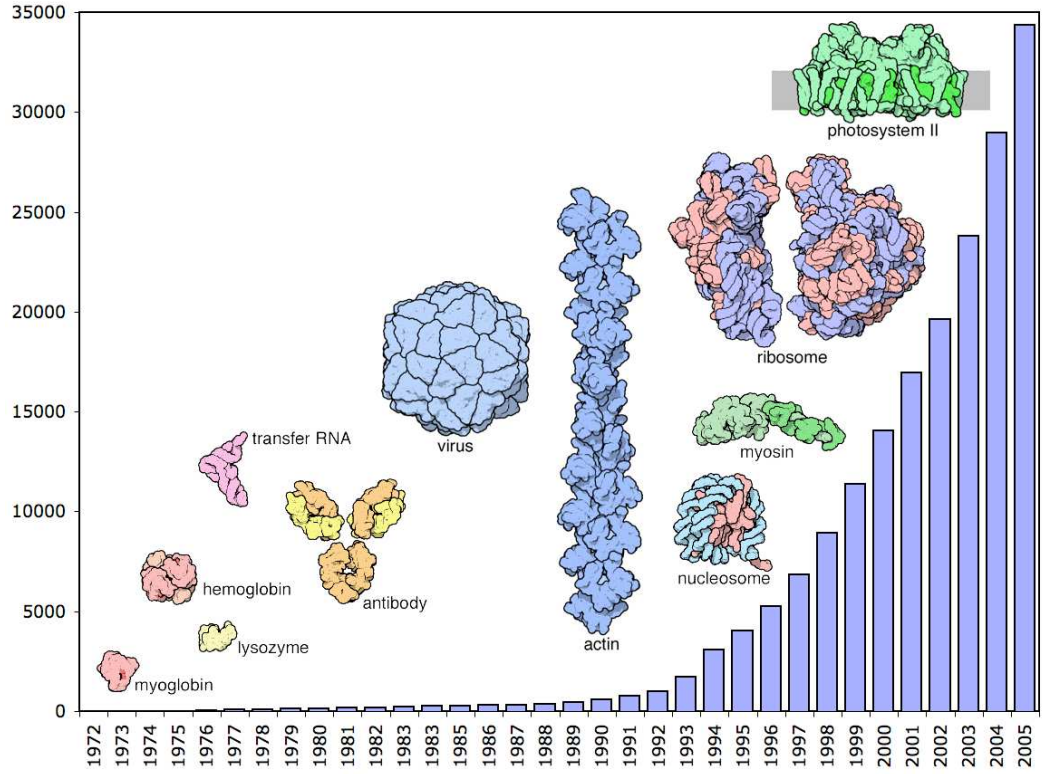
3D structure

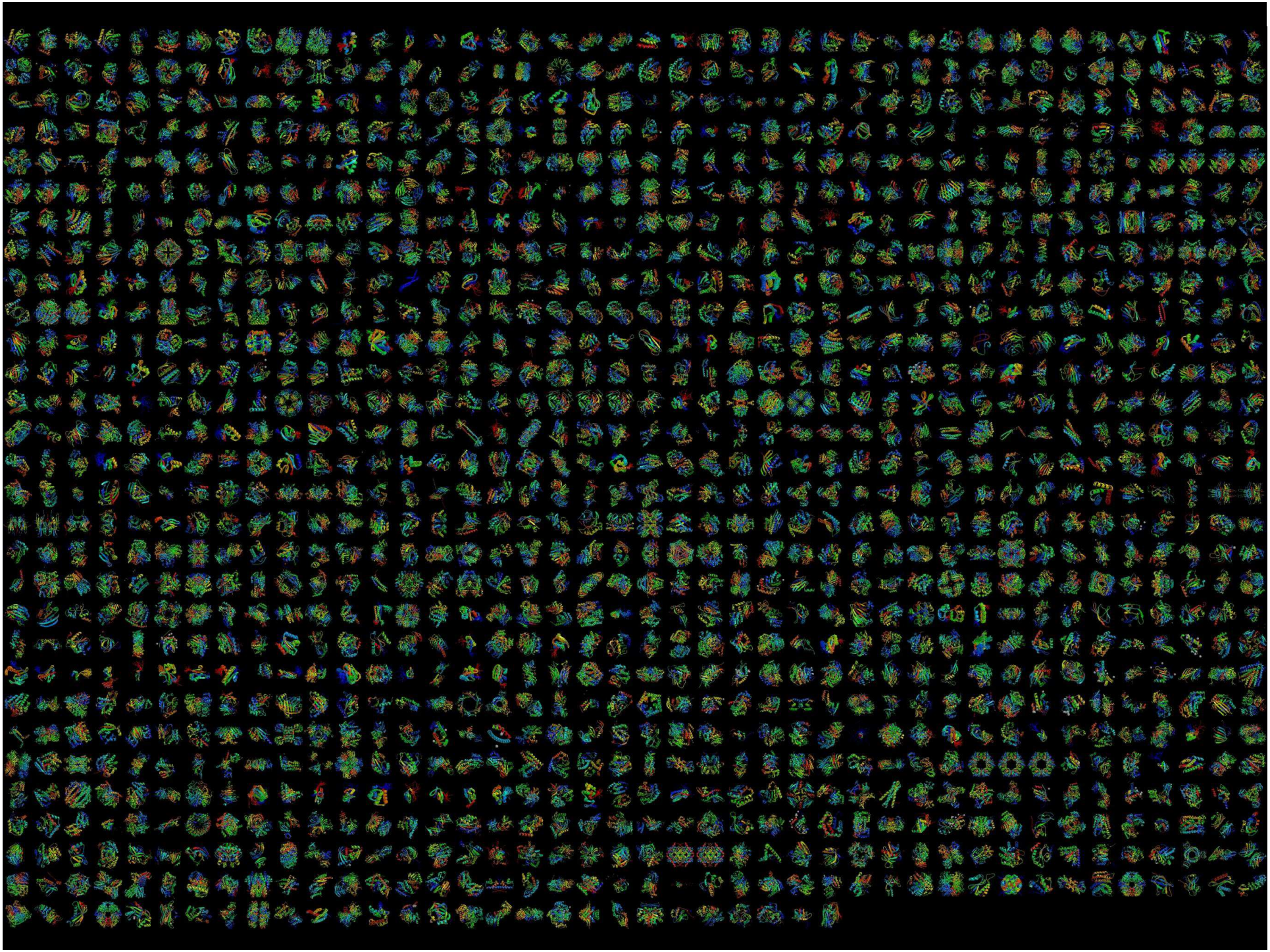


Protein Data Bank (PDB)



Method	Molecule Type				
	Proteins	NA	Complexes	Other	Total
X-ray	27335	807	1270	85	**29497**
NMR	4421	674	118	17	**5230**
El. Microsc.	77	9	27	0	**113**
Other	70	4	3	0	**77**
Total	**31903**	**1494**	**1418**	**102**	**34917**





Anatomia di un file PDB:

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HEADER    ELECTRON TRANSPORT                      19-MAR-90   2TRX       2TRXA  1
COMPND    THIOREDOXIN                                                    2TRXA  2
SOURCE    (ESCHERICHIA $COLI)                                            2TRX   4
AUTHOR    S.K.KATTI,D.M.LE*MASTER,H.EKLUND                               2TRX   5
REVDAT   2   15-JAN-93 2TRXA   1       HEADER COMPND                      2TRXA  3
REVDAT   1   15-OCT-91 2TRX    0                                          2TRX   6
JRNL        AUTH   S.K.KATTI,D.M.LE*MASTER,H.EKLUND                      2TRX   7
JRNL        TITL   CRYSTAL STRUCTURE OF THIOREDOXIN FROM ESCHERICHIA     2TRX   8
JRNL        TITL 2 $COLI AT 1.68 ANGSTROMS RESOLUTION                    2TRX   9
JRNL        REF    J.MOL.BIOL.                  V. 212   167 1990       2TRX  10
JRNL        REFN   ASTM JMOBAK  UK ISSN 0022-2836                  070   2TRX  11
REMARK   1
```

HEADER - PDB accession, date, function
CMPND - name of molecule or compound
SOURCE - origin or source of molecule (species)
REVDAT - revision dates
JRNL - primary reference (journal) describing structure
REMARK - a comment made by depositor

Anatomia di un file PDB:

```
FORMUL   3   CU    2(CU1 ++)                                                 2TRX 110
FORMUL   4  MPD    8(C6 H14 O2)                                              2TRX 111
FORMUL   5  HOH   *140(H2 O1)                                                2TRX 112
HELIX    1 A1A SER A   11  LEU A   17  1 DISORDERED IN MOLECULE B            2TRX 113
HELIX    2 A2A CYS A   32  TYR A   49  1 BENT BY 30 DEGREES AT RES 39        2TRX 114
HELIX    3 A3A ASN A   59  ASN A   63  1                                     2TRX 115
HELIX    4 31A THR A   66  TYR A   70  5 DISTORTED H-BONDING C-TERMINS       2TRX 116
HELIX    5 A4A SER A   95  LEU A  107  1                                     2TRX 117
SHEET    1 B1A 5 LYS A   3  THR A   8  0                                   2TRX 123
SHEET    2 B1A 5 LEU A  53  ASN A  59  1  O  VAL A  55   N  ILE A   5      2TRX 124
SHEET    3 B1A 5 GLY A  21  TRP A  28  1  N  TRP A  28   O  LEU A  58      2TRX 125
SHEET    4 B1A 5 PRO A  76  LYS A  82 -1  O  THR A  77   N  PHE A  27      2TRX 126
SHEET    5 B1A 5 VAL A  86  GLY A  92 -1  N  GLY A  92   O  LYS A  82      2TRX 127
SSBOND   1 CYS A   32    CYS A   35                                         2TRX 143
```

FORMUL - chemical formula of heteroatoms
HELIX - location of helices as identified by depositor
SHEET location of beta sheets as identified by depositor
SSBOND - location and exisitence of disulfide bond

Anatomia di un file PDB:

```
ORIGX1      1.000000  0.000000  0.000000        0.00000                      2TRX 146
ORIGX2      0.000000  1.000000  0.000000        0.00000                      2TRX 147
ORIGX3      0.000000  0.000000  1.000000        0.00000                      2TRX 148
SCALE1      0.011173  0.000000  0.004858        0.00000                      2TRX 149
SCALE2      0.000000  0.019585  0.000000        0.00000                      2TRX 150
SCALE3      0.000000  0.000000  0.018039        0.00000                      2TRX 151
ATOM      1  N   SER A   1      21.389  25.406  -4.628  1.00 23.22           2TRX 152
ATOM      2  CA  SER A   1      21.628  26.691  -3.983  1.00 24.42           2TRX 153
ATOM      3  C   SER A   1      20.937  26.944  -2.679  1.00 24.21           2TRX 154
ATOM      4  O   SER A   1      21.072  28.079  -2.093  1.00 24.97           2TRX 155
ATOM      5  CB  SER A   1      21.117  27.770  -5.002  1.00 28.27           2TRX 156
ATOM      6  OG  SER A   1      22.276  27.925  -5.861  1.00 32.61           2TRX 157
ATOM      7  N   ASP A   2      20.173  26.028  -2.163  1.00 21.39           2TRX 158
ATOM      8  CA  ASP A   2      19.395  26.125  -0.949  1.00 21.57           2TRX 159
ATOM      9  C   ASP A   2      20.264  26.214   0.297  1.00 20.89           2TRX 160
ATOM     10  O   ASP A   2      19.760  26.575   1.371  1.00 21.49           2TRX 161
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ORIGXn - scaling factors to transform from orthogonal coords.
SCALEn - scaling factors to transform to fractional cryst. Coords.
ATOM - atomic coordinates of molecule

Anatomia di un file PDB:

Residue Name

Atom #

X coord (Å)

Z coord (Å)

B-factor

Atom Name

Residue #

Y coord (Å)

Occupancy

```
ATOM      1  N   SER A   1      21.389  25.406  -4.628  1.00 23.22      2TRX 152
ATOM      2  CA  SER A   1      21.628  26.691  -3.983  1.00 24.42      2TRX 153
ATOM      3  C   SER A   1      20.937  26.944  -2.679  1.00 24.21      2TRX 154
ATOM      4  O   SER A   1      21.072  28.079  -2.093  1.00 24.97      2TRX 155
ATOM      5  CB  SER A   1      21.117  27.770  -5.002  1.00 28.27      2TRX 156
ATOM      6  OG  SER A   1      22.276  27.925  -5.861  1.00 32.61      2TRX 157
ATOM      7  N   ASP A   2      20.173  26.028  -2.163  1.00 21.39      2TRX 158
ATOM      8  CA  ASP A   2      19.395  26.125  -0.949  1.00 21.57      2TRX 159
ATOM      9  C   ASP A   2      20.264  26.214   0.297  1.00 20.89      2TRX 160
ATOM     10  O   ASP A   2      19.760  26.575   1.371  1.00 21.49      2TRX 161
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Anatomia di un file PDB:

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REMARK    6  REMOVE E.C. CODE.  15-JAN-93.                              2TRXA  6
SEQRES    1 A  108  SER ASP LYS ILE ILE HIS LEU THR ASP ASP SER PHE ASP  2TRX  74
SEQRES    2 A  108  THR ASP VAL LEU LYS ALA ASP GLY ALA ILE LEU VAL ASP  2TRX  75
SEQRES    3 A  108  PHE TRP ALA GLU TRP CYS GLY PRO CYS LYS MET ILE ALA  2TRX  76
SEQRES    4 A  108  PRO ILE LEU ASP GLU ILE ALA ASP GLU TYR GLN GLY LYS  2TRX  77
SEQRES    5 A  108  LEU THR VAL ALA LYS LEU ASN ILE ASP GLN ASN PRO GLY  2TRX  78
SEQRES    6 A  108  THR ALA PRO LYS TYR GLY ILE ARG GLY ILE PRO THR LEU  2TRX  79
SEQRES    7 A  108  LEU LEU PHE LYS ASN GLY GLU VAL ALA ALA THR LYS VAL  2TRX  80
SEQRES    8 A  108  GLY ALA LEU SER LYS GLY GLN LEU LYS GLU PHE LEU ASP  2TRX  81
SEQRES    9 A  108  ALA ASN LEU ALA                                      2TRX  82
HET     CU    109        1      COPPER ++ ION                            2TRX 100
HET     CU    109        1      COPPER ++ ION                            2TRX 101
HET    MPD    601        8      2-METHYL-2,4-PENTANEDIOL                 2TRX 102
HET    MPD    602        8      2-METHYL-2,4-PENTANEDIOL                 2TRX 103
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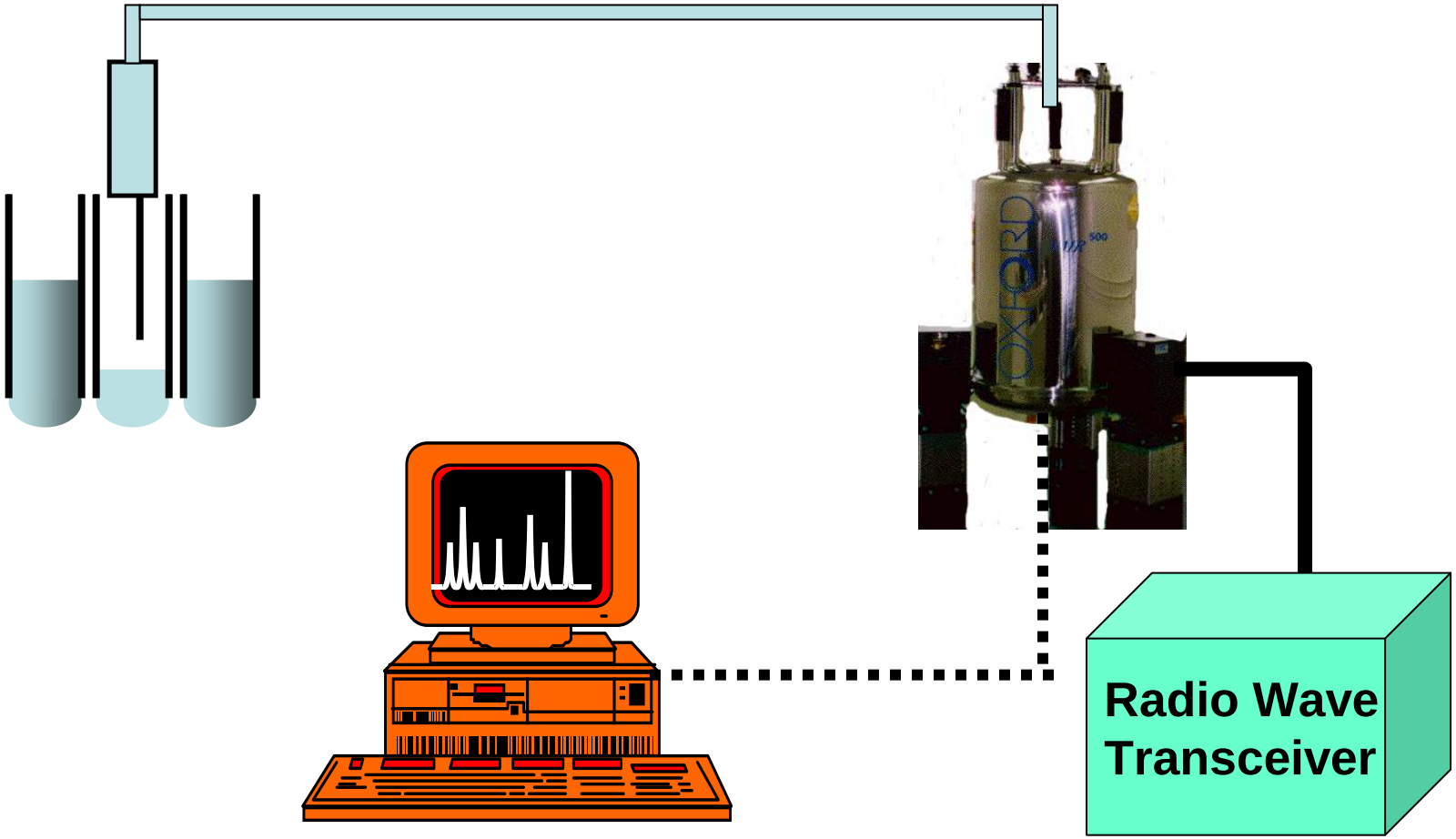
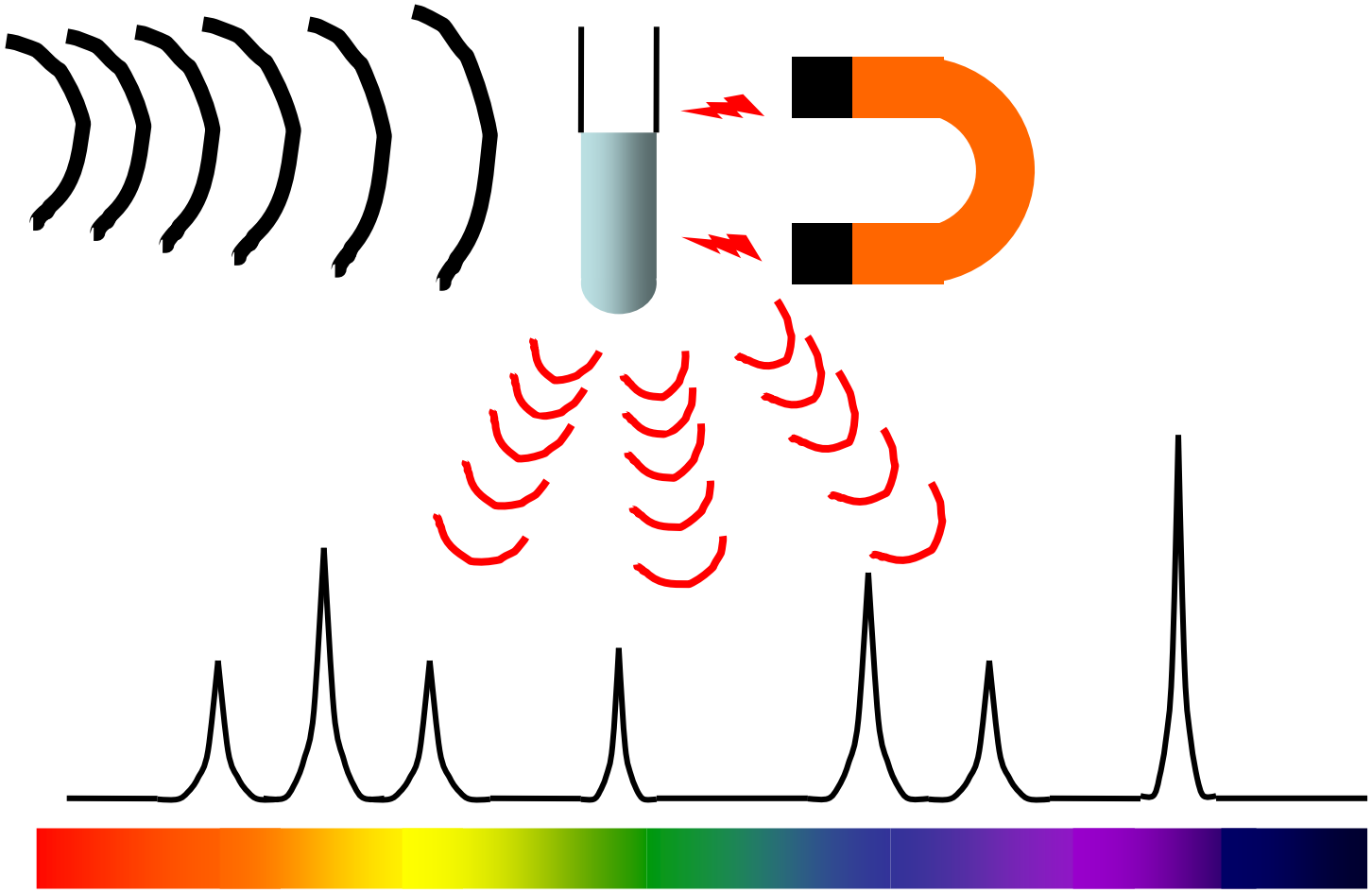
REMARK - a comment made by depositor
SEQRES - sequence of protein in 3 letter code
HET - names of heteroatoms

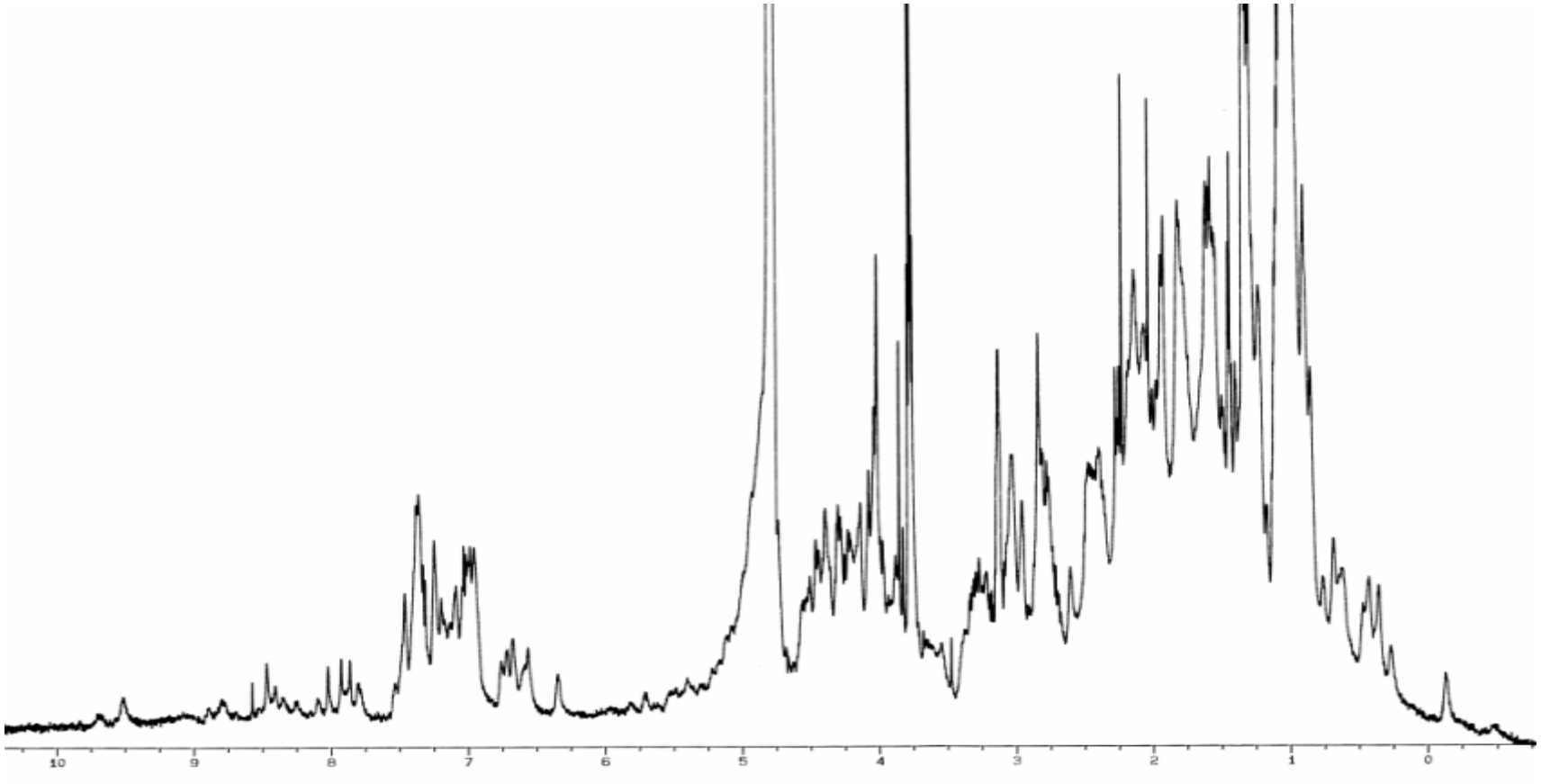
Spettroscopia di Risonanza Magnetica Nucleare (NMR)



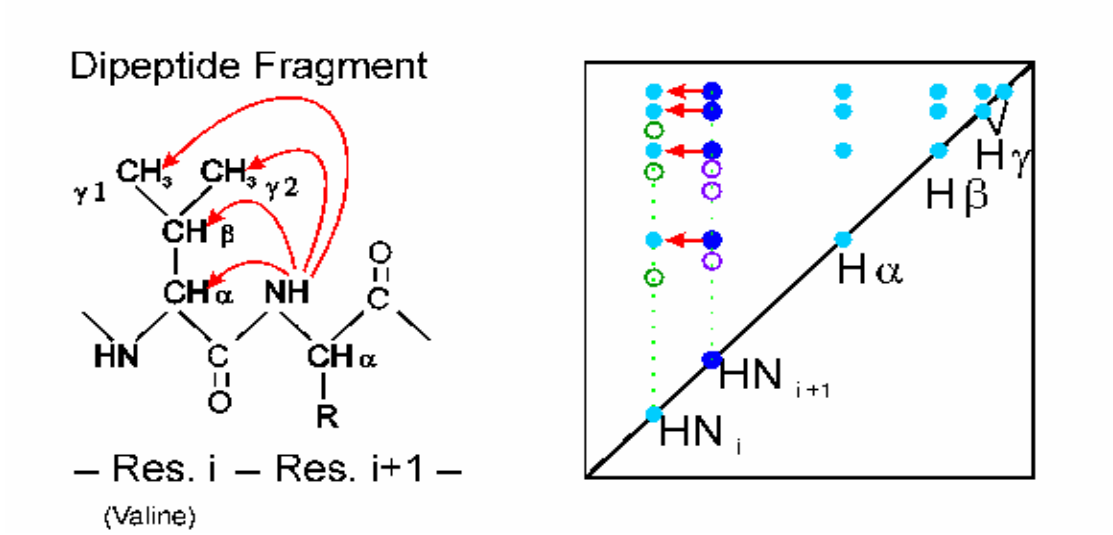
Spettroscopia di Risonanza Magnetica Nucleare (NMR): principi.

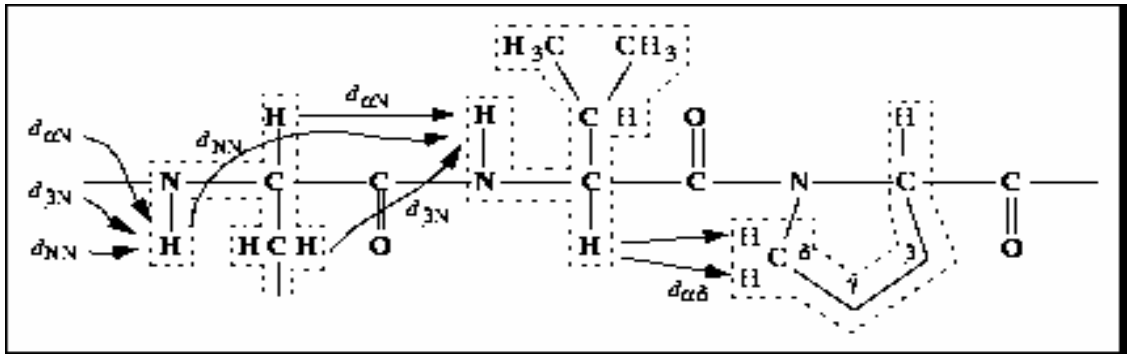


Spettro 1H-NMR di una proteina:



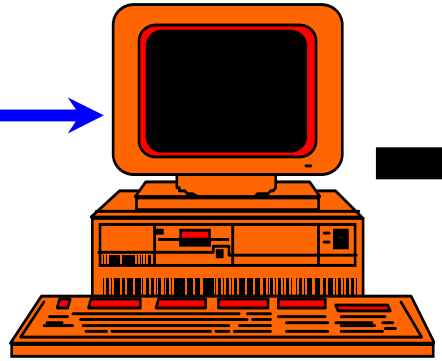
Misurare distanze inter-nucleari (NOEs)



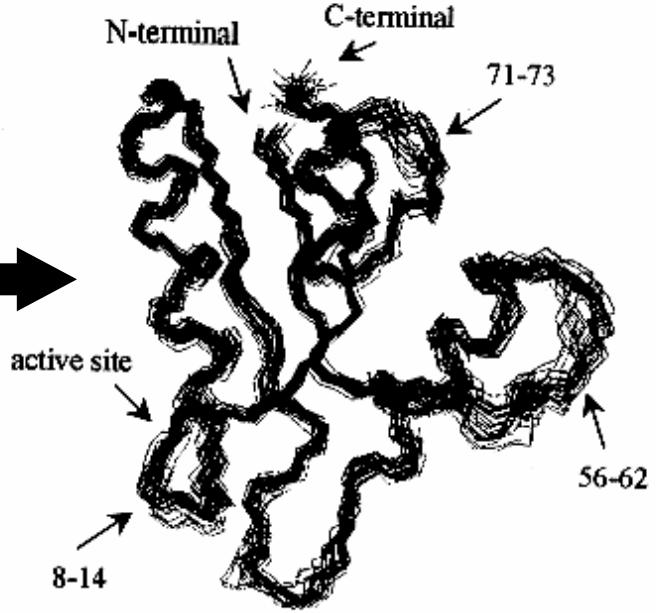


Dalle distanze internucleari alla struttura proteica:

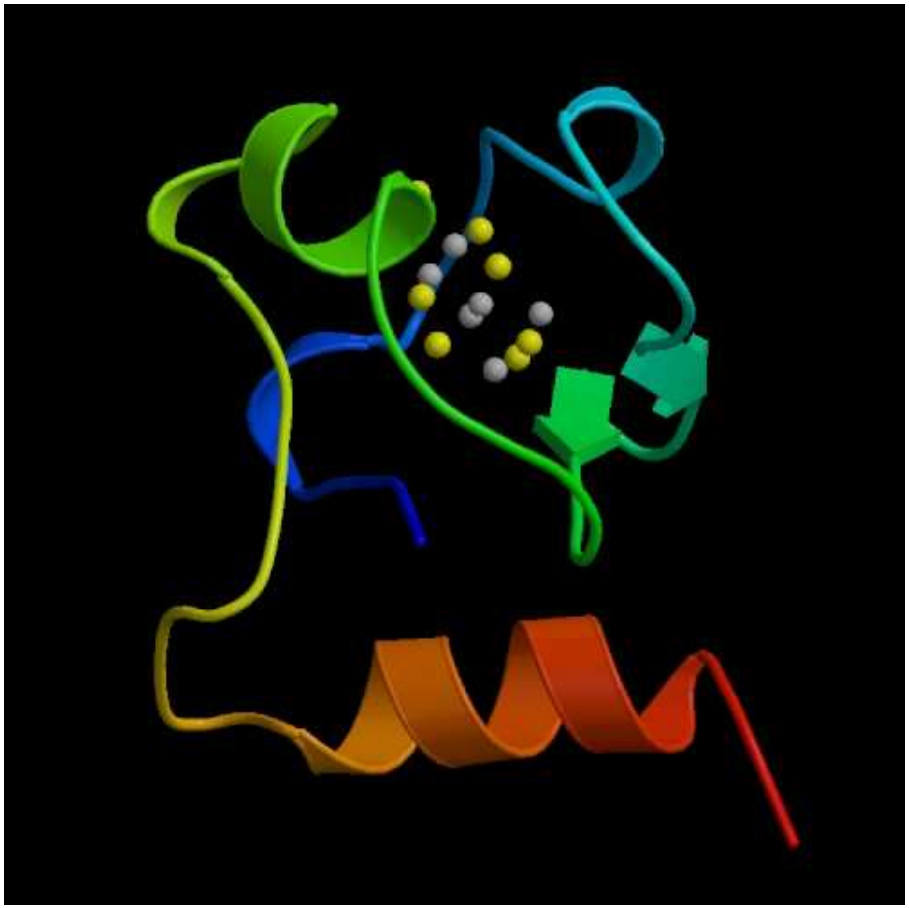
Distanze internucleari



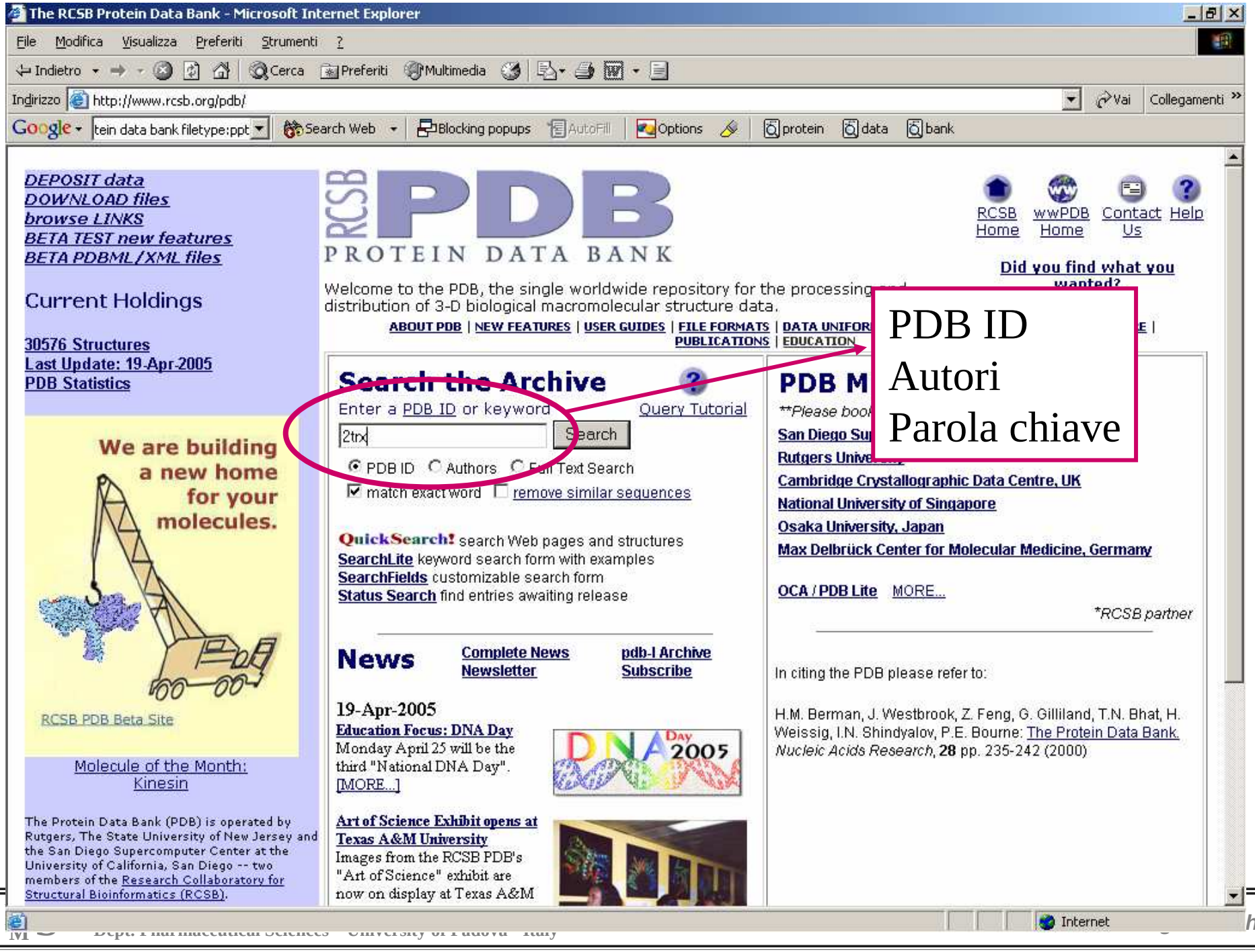
Distance Geometry Simulated Annealing



Struttura NMR (20 conformeri)



Struttura media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Monday April 25 will be the third "National DNA Day". [MORE...]
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Autori
Parola chiave

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Title: **Crystal structure of thioredoxin from Escherichia coli at 1.68 A resolution.**
Compound: **Thioredoxin**
Authors: **S. K. Katti, D. M. LeMaster, H. Eklund**
Exp. Method: **X-ray Diffraction**
Classification: **Electron Transport**
Source: **Escherichia coli**
Primary Citation: **Katti, S. K., LeMaster, D. M., Eklund, H.: Crystal structure of thioredoxin from Escherichia coli at 1.68 A resolution. *J Mol Biol* 212 *pp.* 167 (1990)**

Deposition Date: **19-Mar-1990** *Release Date:* **15-Oct-1991**

Resolution [Å]: **1.68** *R-Value:* **0.165**
Space Group: **C 2**
Unit Cell: *dim [Å]:* *a* **89.50** *b* **51.06** *c* **60.45**
angles [°]: *alpha* **90.00** *beta* **113.50** *gamma* **90.00**

Polymer Chains: **A, B** *Residues:* **216**
Atoms: **1842**

Chemical Components: ("HET" groups)

ID (needs Rasmol)	*Name*	*Formula*	*Retrieve All PDB IDs Containing*
CU	COPPER (II) ION	2(Cu)	CU

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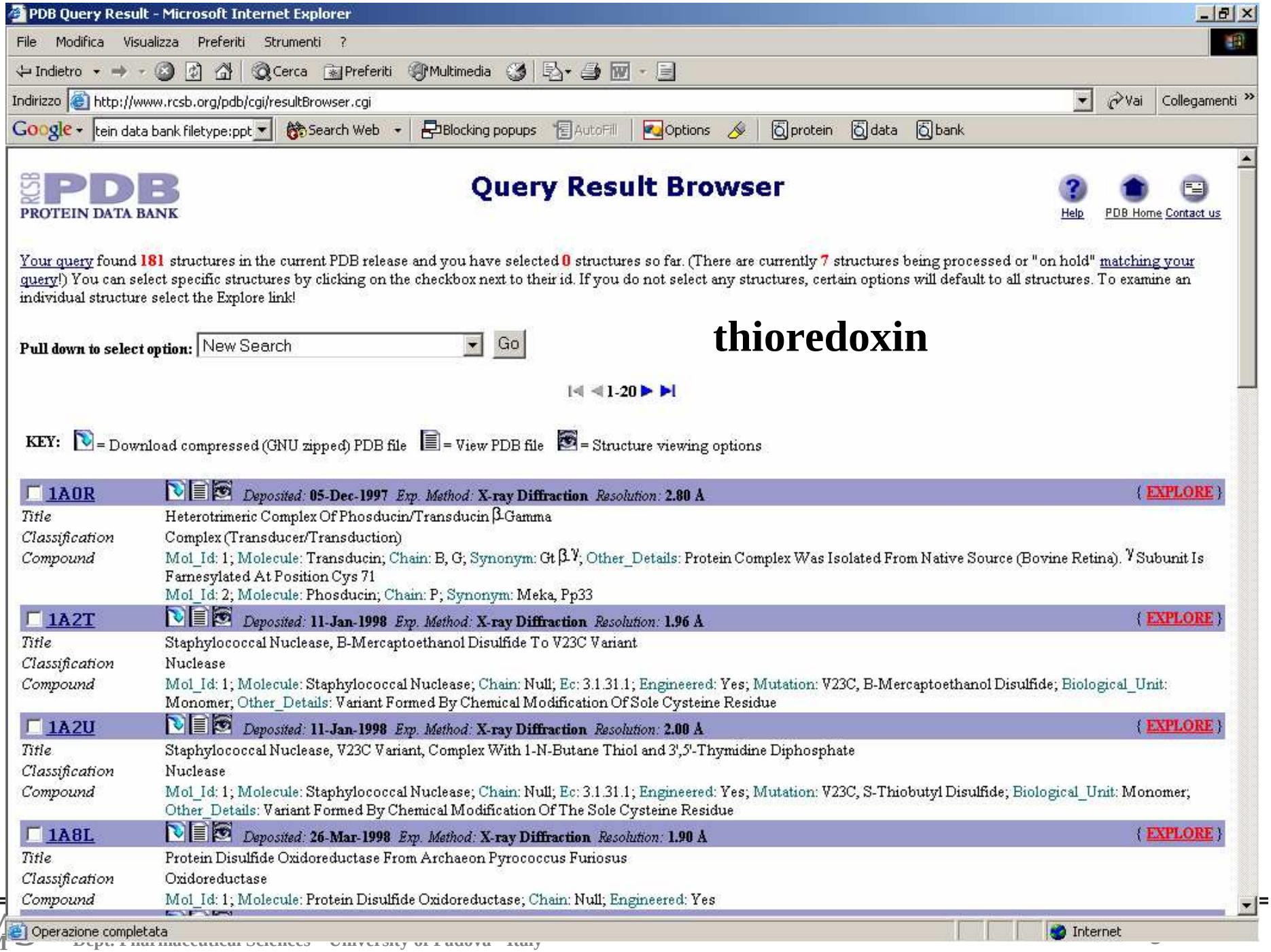
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Pull down to select option: New Search Go
thioredoxin
1-20
KEY: = Download compressed (GNU zipped) PDB file = View PDB file = Structure viewing options
1A0R Deposited: 05-Dec-1997 Exp. Method: X-ray Diffraction Resolution: 2.80 Å { EXPLORE }
Title Heterotrimeric Complex Of Phosducin/Transducin β-Gamma
Classification Complex (Transducer/Transduction)
Compound Mol_Id: 1; Molecule: Transducin; Chain: B, G; Synonym: Gt β.γ; Other_Details: Protein Complex Was Isolated From Native Source (Bovine Retina). γ Subunit Is Farnesylated At Position Cys 71
Mol_Id: 2; Molecule: Phosducin; Chain: P; Synonym: Meka, Pp33
1A2T Deposited: 11-Jan-1998 Exp. Method: X-ray Diffraction Resolution: 1.96 Å { EXPLORE }
Title Staphylococcal Nuclease, B-Mercaptoethanol Disulfide To V23C Variant
Classification Nuclease
Compound Mol_Id: 1; Molecule: Staphylococcal Nuclease; Chain: Null; Ec: 3.1.31.1; Engineered: Yes; Mutation: V23C, B-Mercaptoethanol Disulfide; Biological_Unit: Monomer; Other_Details: Variant Formed By Chemical Modification Of Sole Cysteine Residue
1A2U Deposited: 11-Jan-1998 Exp. Method: X-ray Diffraction Resolution: 2.00 Å { EXPLORE }
Title Staphylococcal Nuclease, V23C Variant, Complex With 1-N-Butane Thiol and 3',5'-Thymidine Diphosphate
Classification Nuclease
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Title Protein Disulfide Oxidoreductase From Archaeon Pyrococcus Furiosus
Classification Oxidoreductase
Compound Mol_Id: 1; Molecule: Protein Disulfide Oxidoreductase; Chain: Null; Engineered: Yes
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Classification **Electron Transport**
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Exp. Method **X-ray Diffraction**

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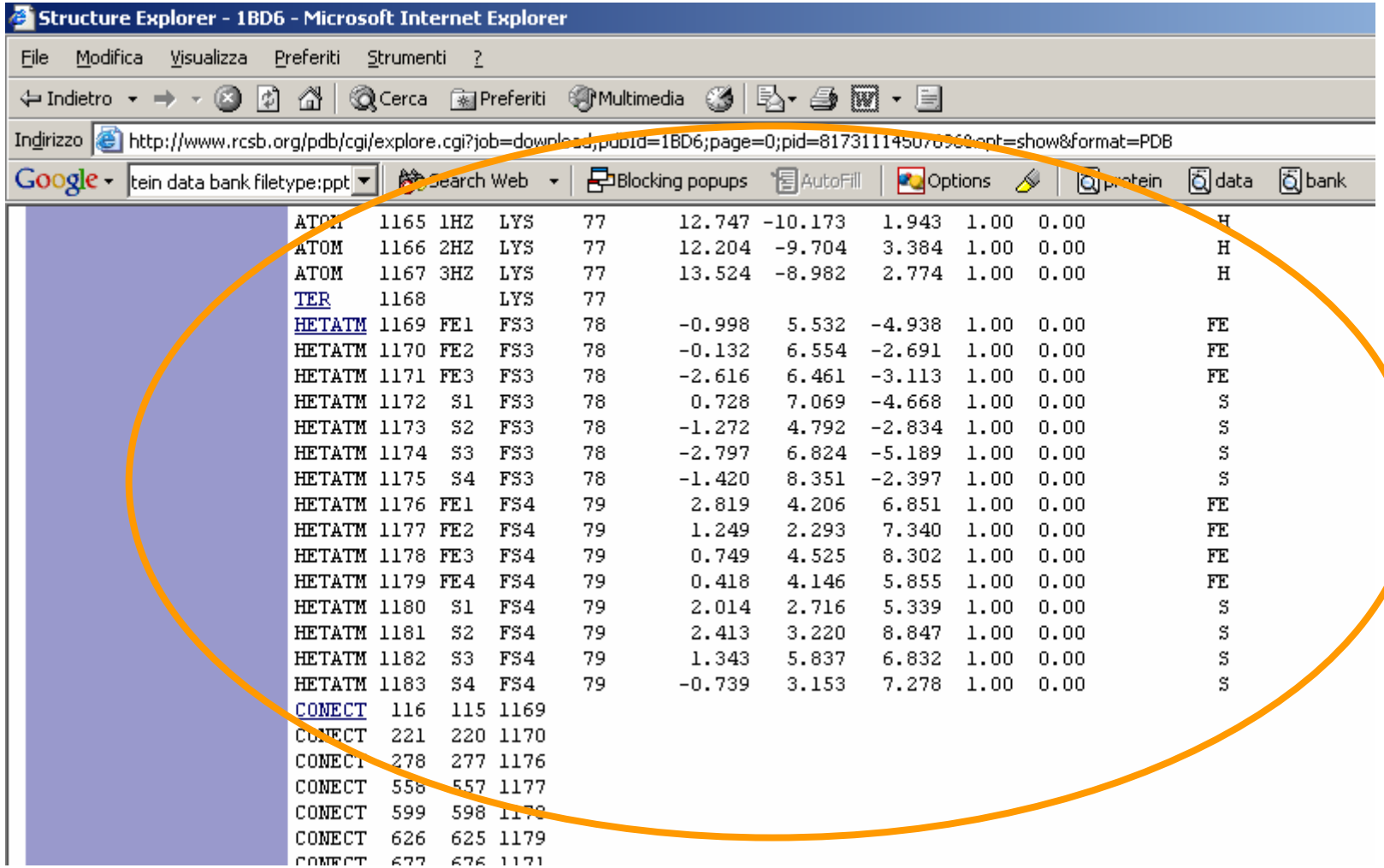

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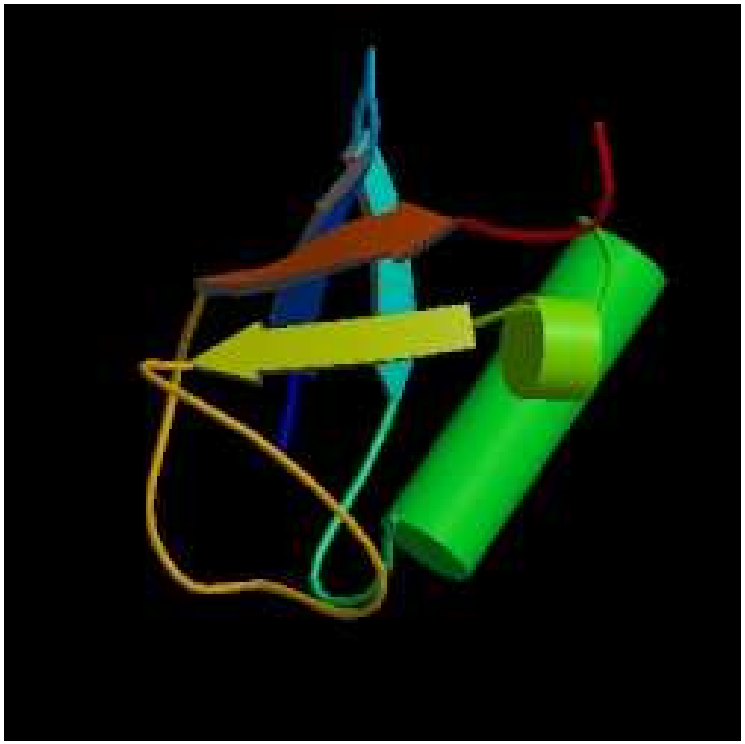

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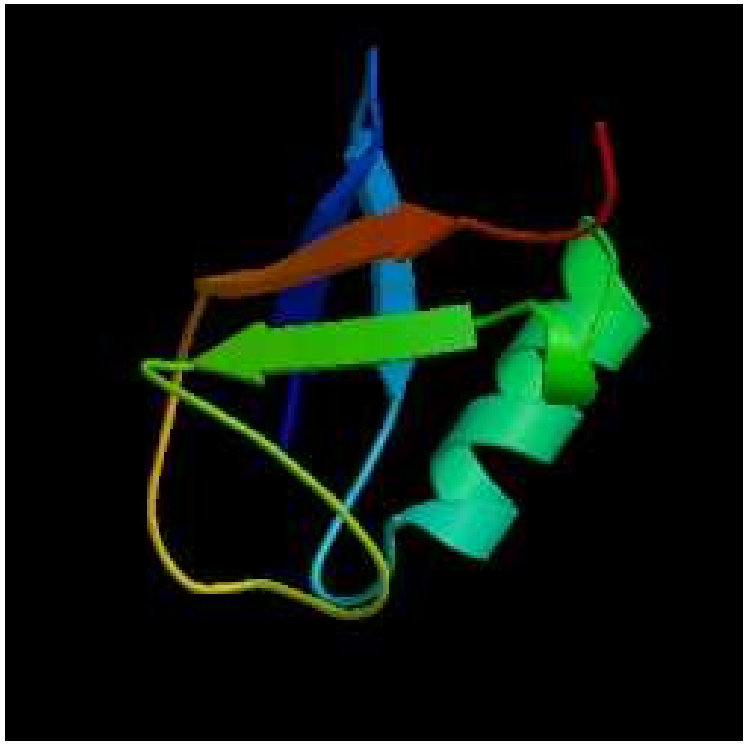
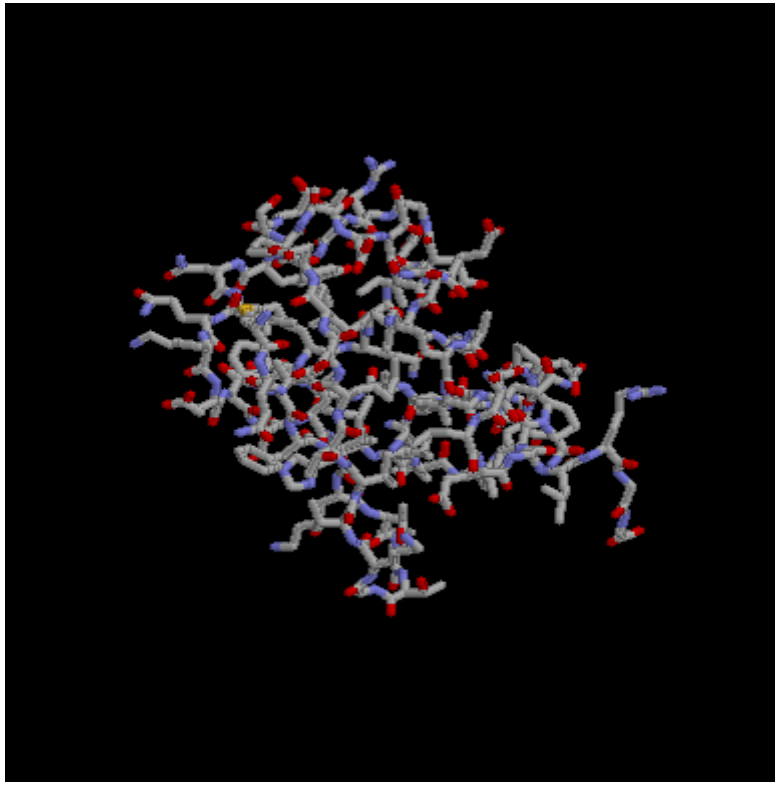


Ribbon (N-C gradient)

Rendering

Ribbon (2º structure)



Stick

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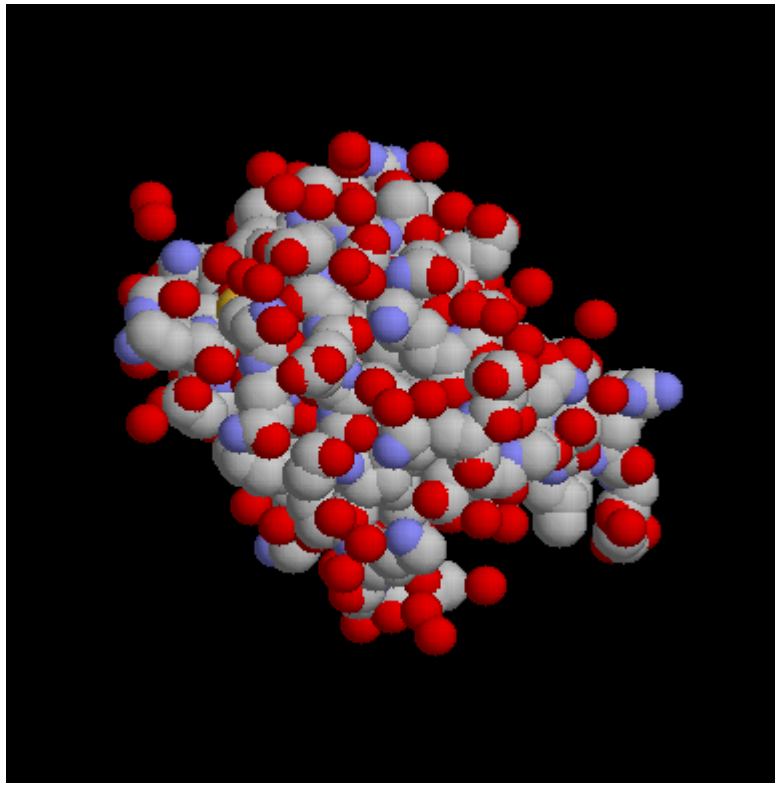

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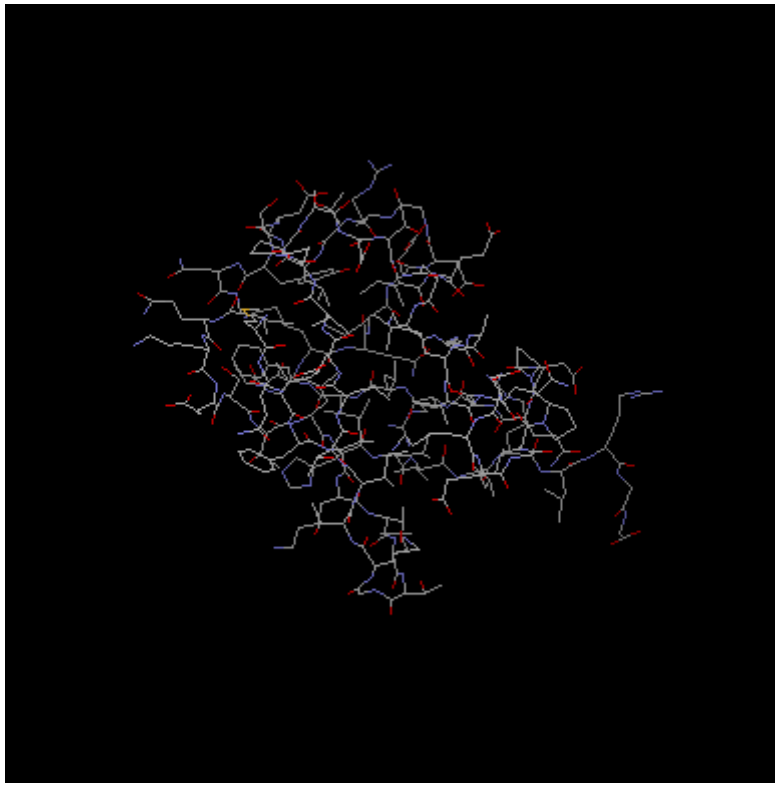

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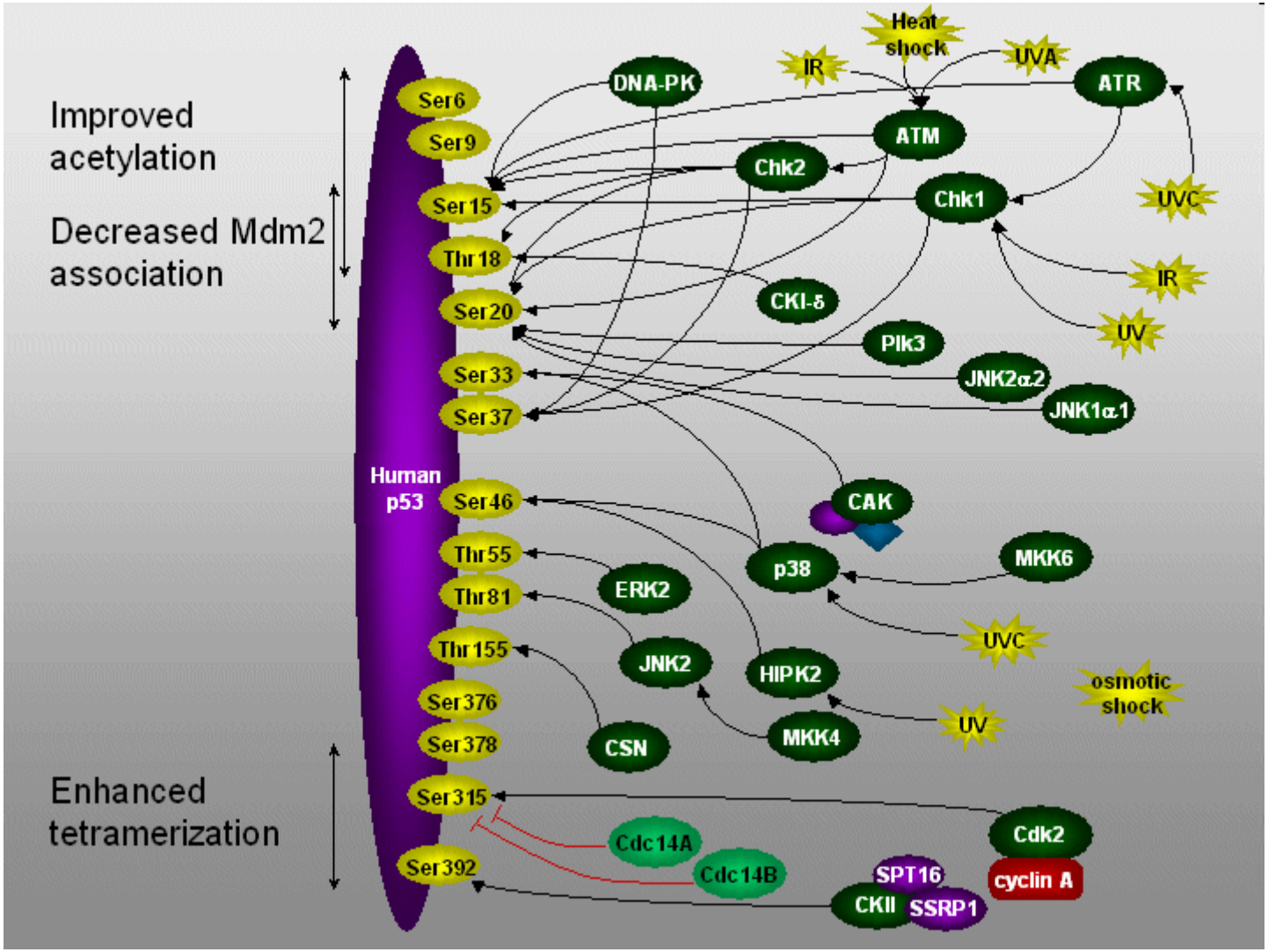
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Ser15
Thr18
Ser20
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Ser46
Thr55
Thr81
Thr155
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Ser378
Ser315
Ser392
DNA-PK
ATM
Chk2
Chk1
CKI-δ
Plk3
JNK2α2
JNK1α1
CAK
p38
MKK6
ERK2
JNK2
HIPK2
MKK4
CSN
Cdc14A
Cdc14B
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