

Making sense of protein structure with computers

Interpretarea structurilor proteinelor prin intermediul computerelor

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Intalnire AARD 19/06/22



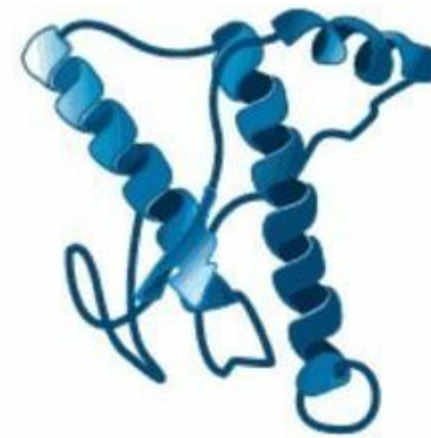
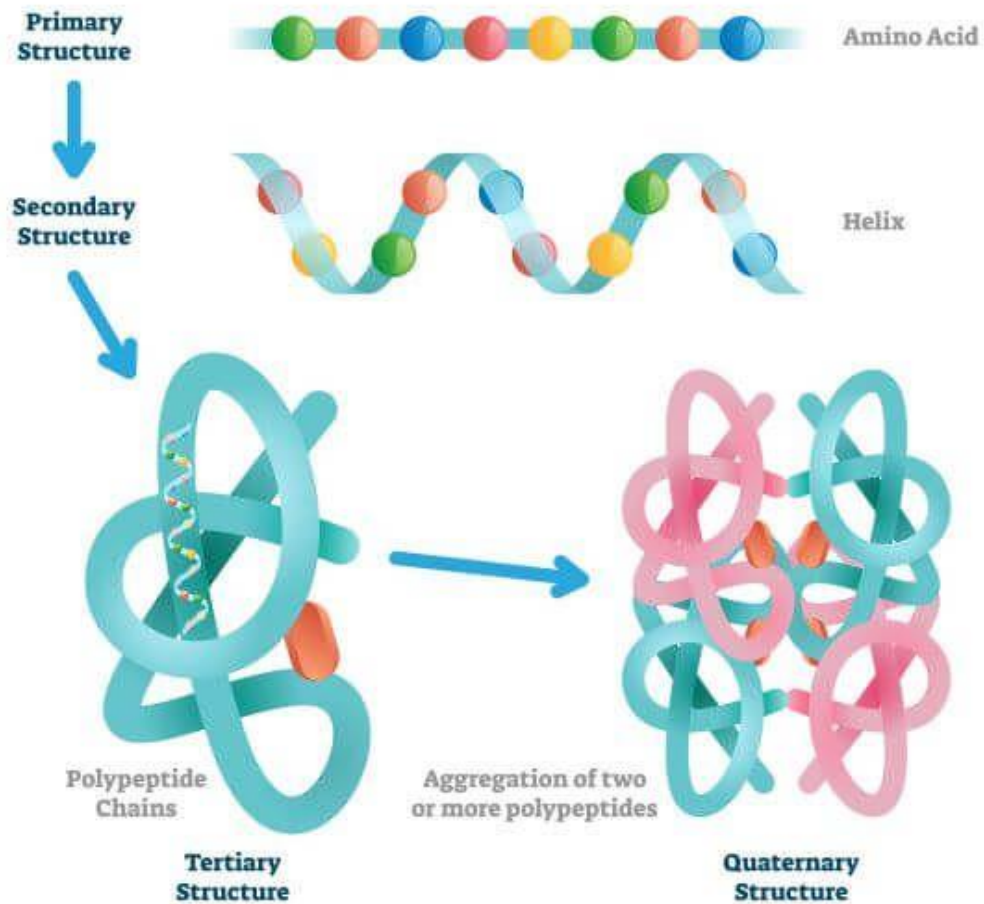
ZEALAND PHARMA

About me

- Licenta in Chimie, 2013, Universitatea din Bucuresti
- Master in Chimia Medicamentelor, 2015, Universitatea din Bucuresti
- Doctorat in Chimie Teoretica, 2019, Lunds Universitet
- Postdoc 2020, DTU
- Computational Chemistry Scientist, present, Zealand Pharma



PROTEIN STRUCTURE

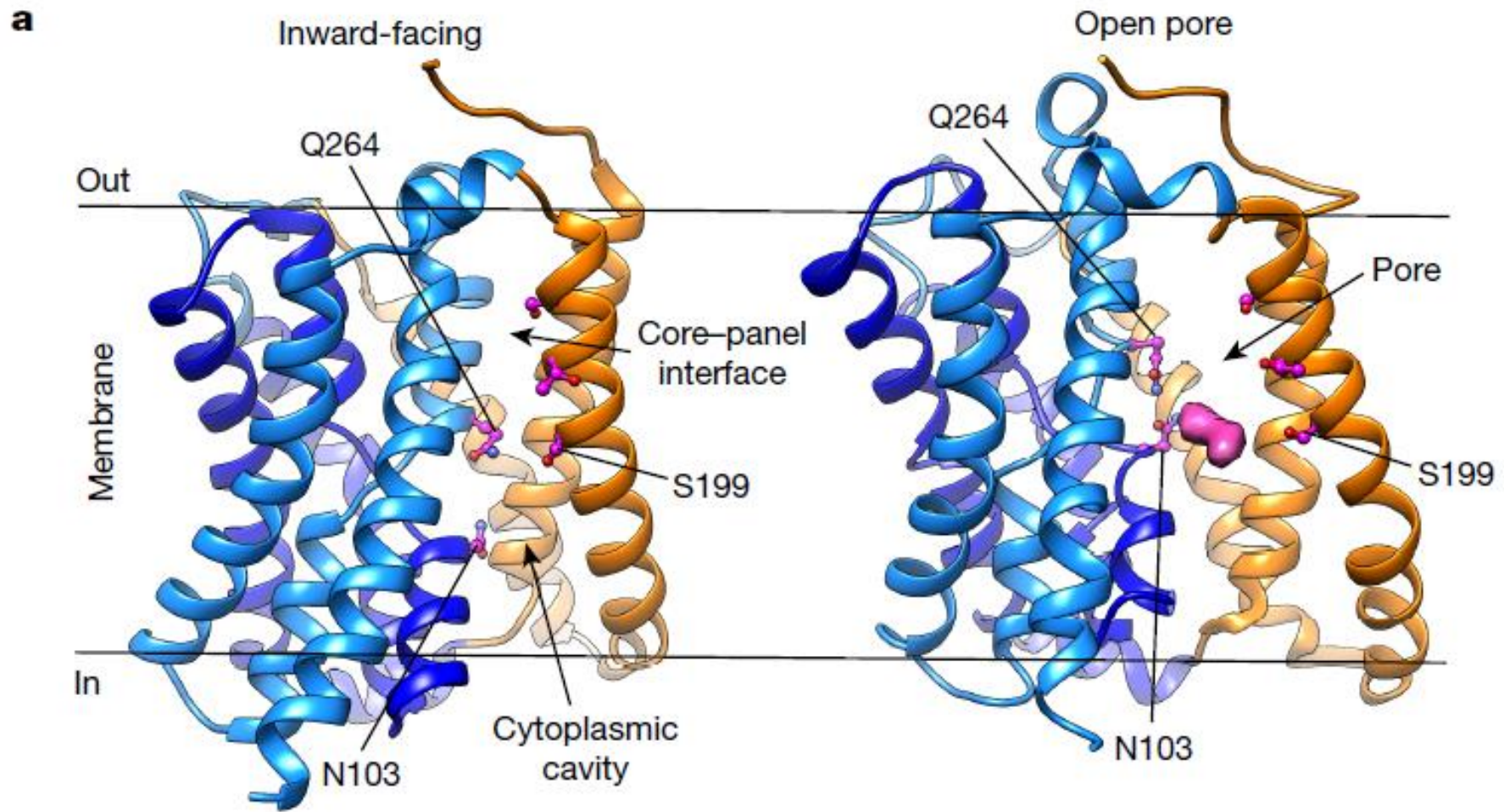


NORMAL PRION PROTEIN (PrP^C)



DISEASE-CAUSING PRION (PrP^{Sc})

Prima structura tridimensională a unei proteine (mioglobina) determinată în 1958 (Premiu Nobel 1962)



Forma închisa (inward-facing) a NTCP nu este recunoscuta de virusul hepatitei B

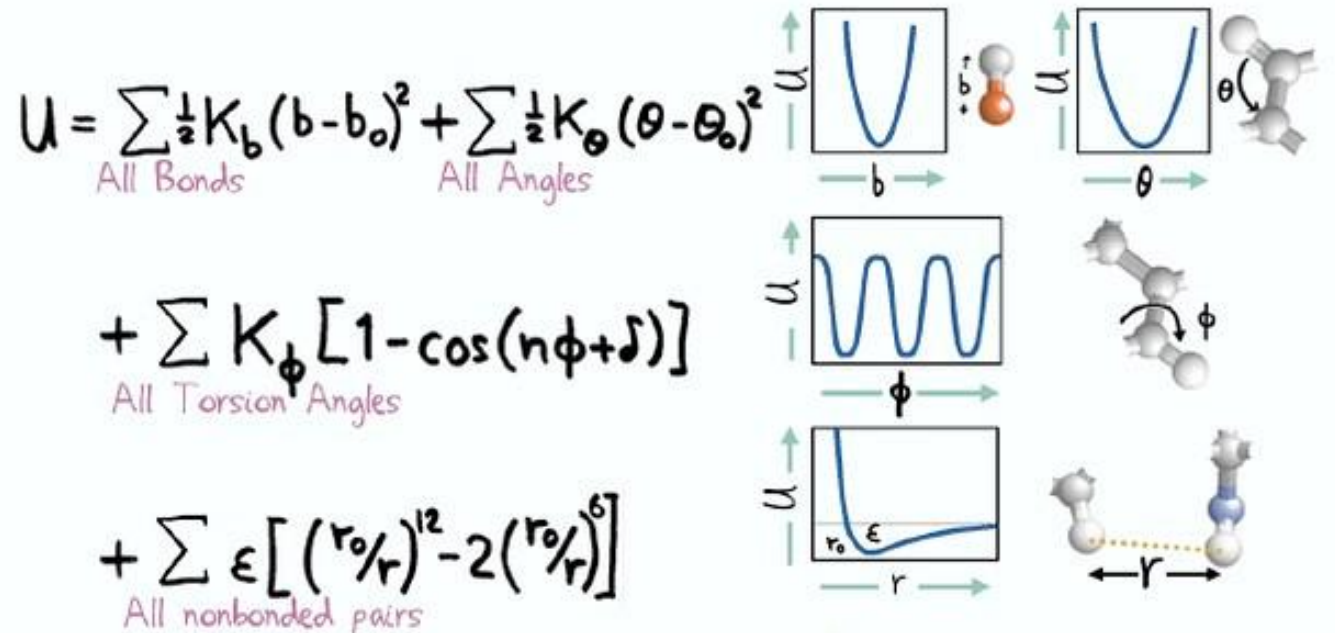
Ce pot sa faca computerele?

Rezolvare de ecuatii complicate (rapid)

$$\hat{H}\Psi = E\Psi$$



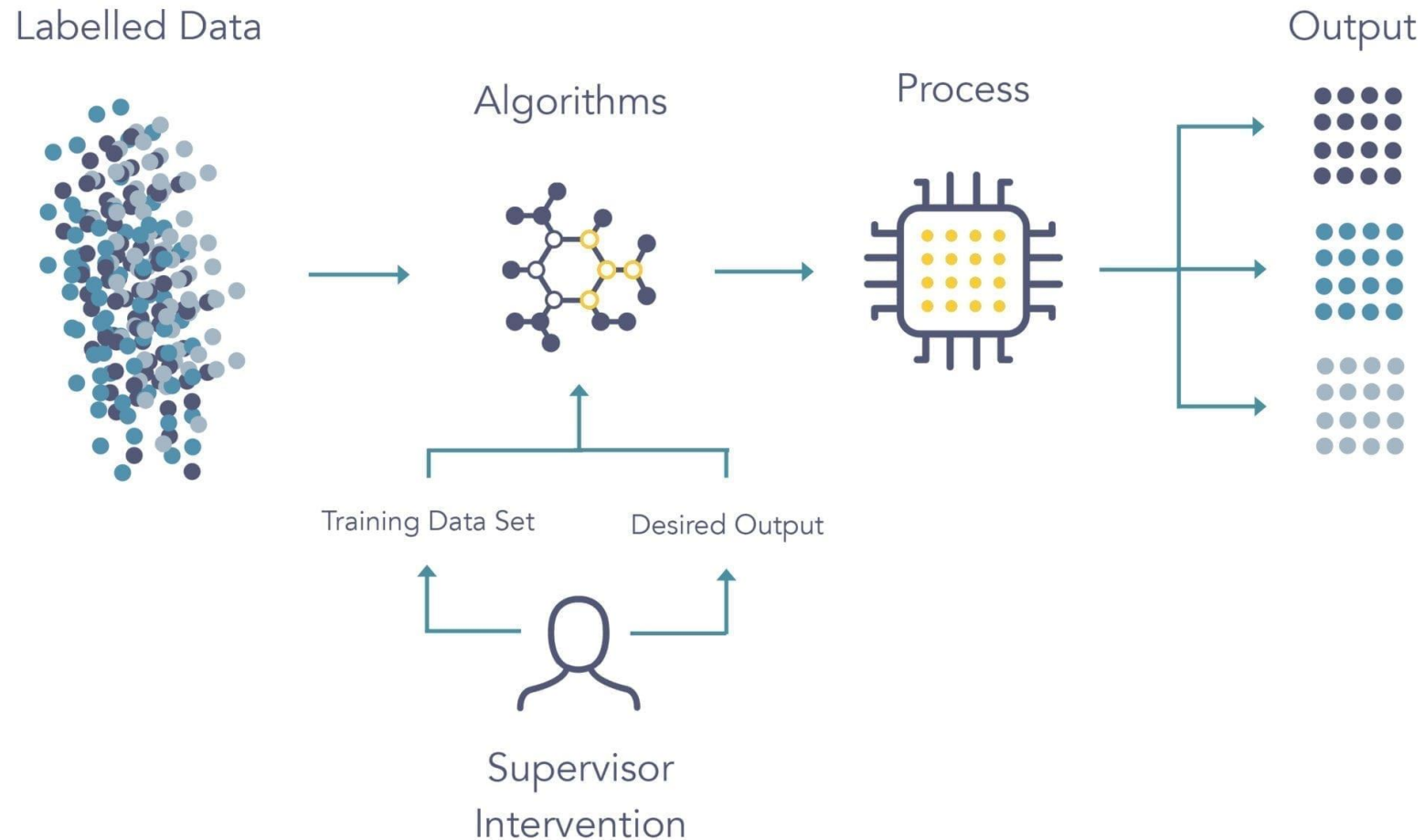
Mecanica cuantica



Mecanica moleculara

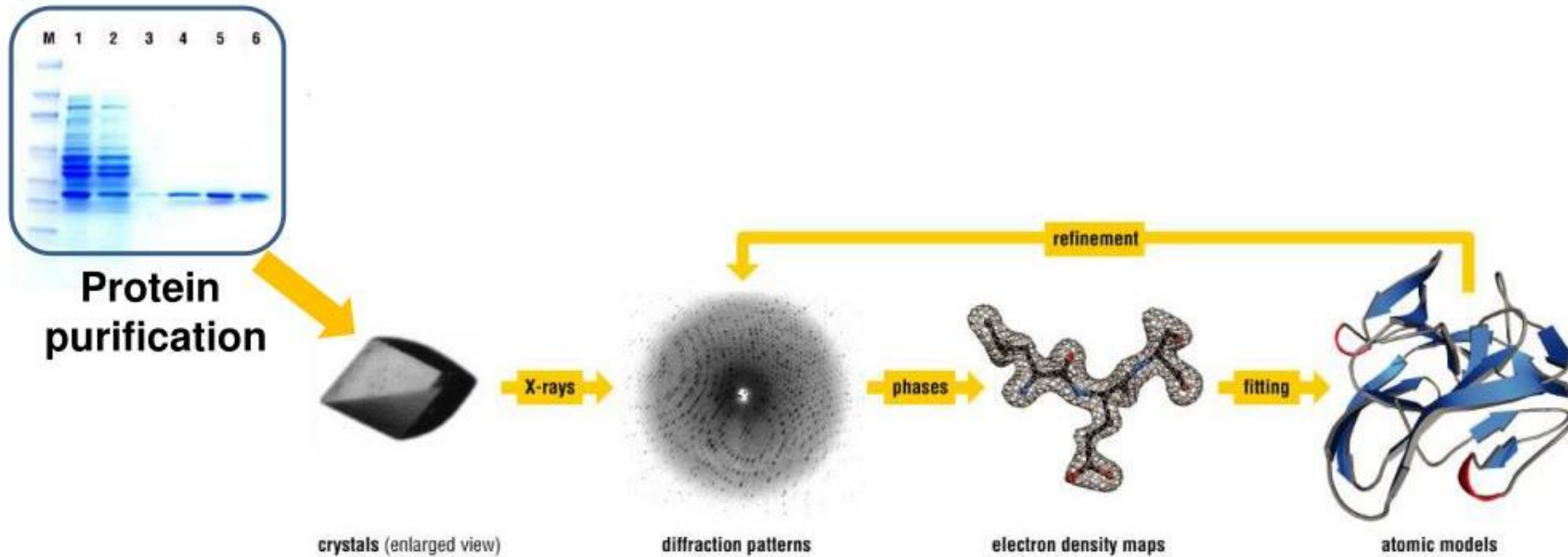
Ce pot sa faca computerele?

Corelatii intre (multe) date

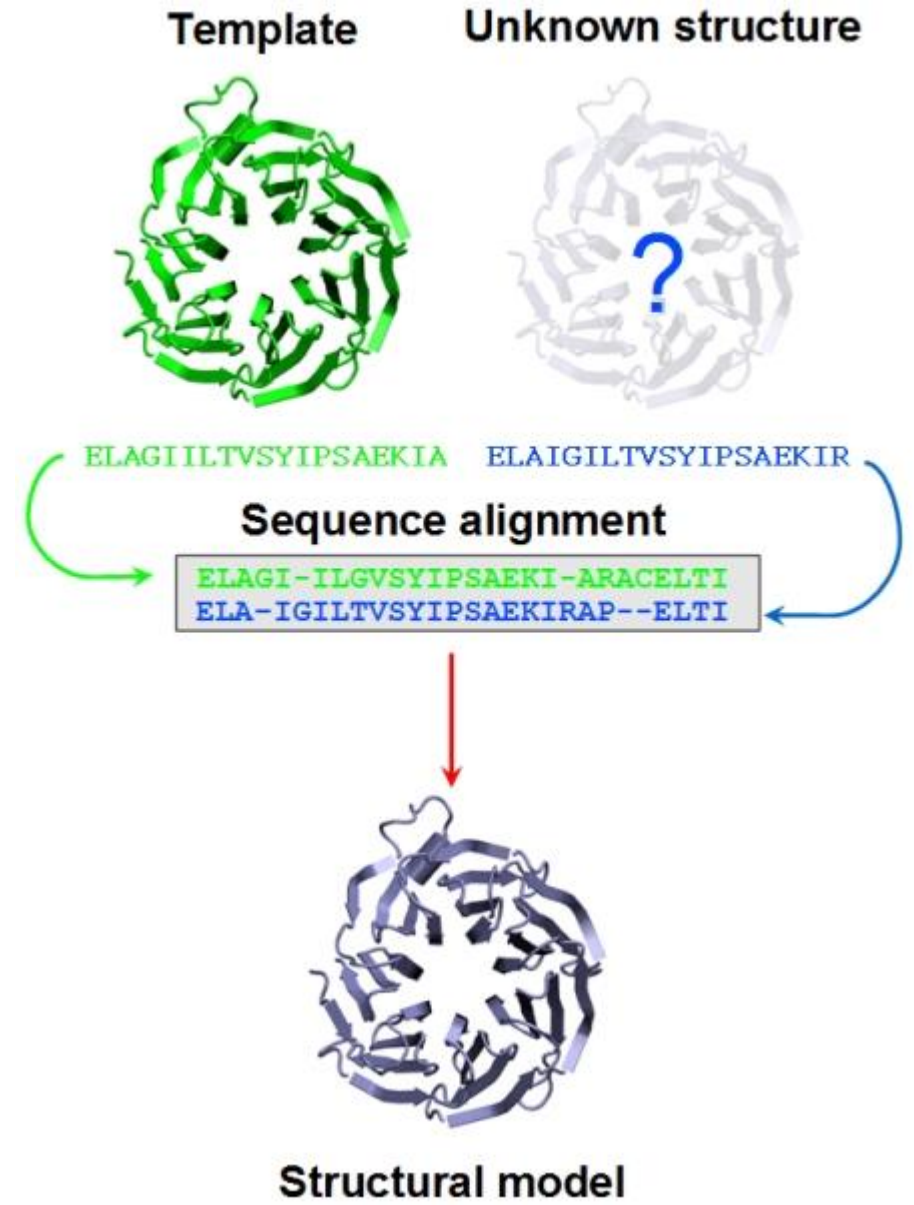
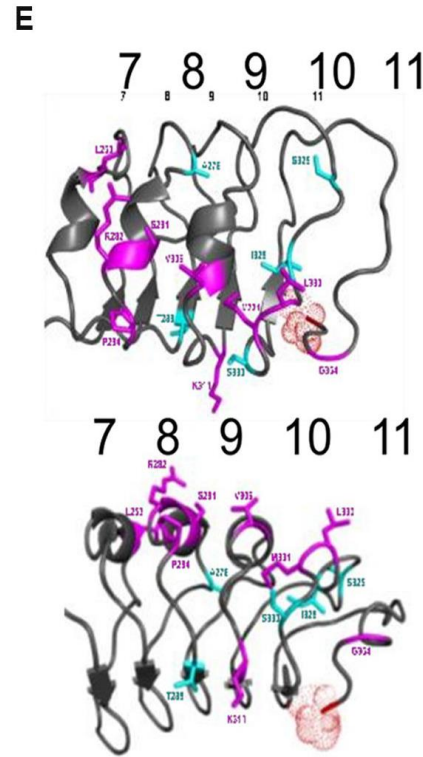
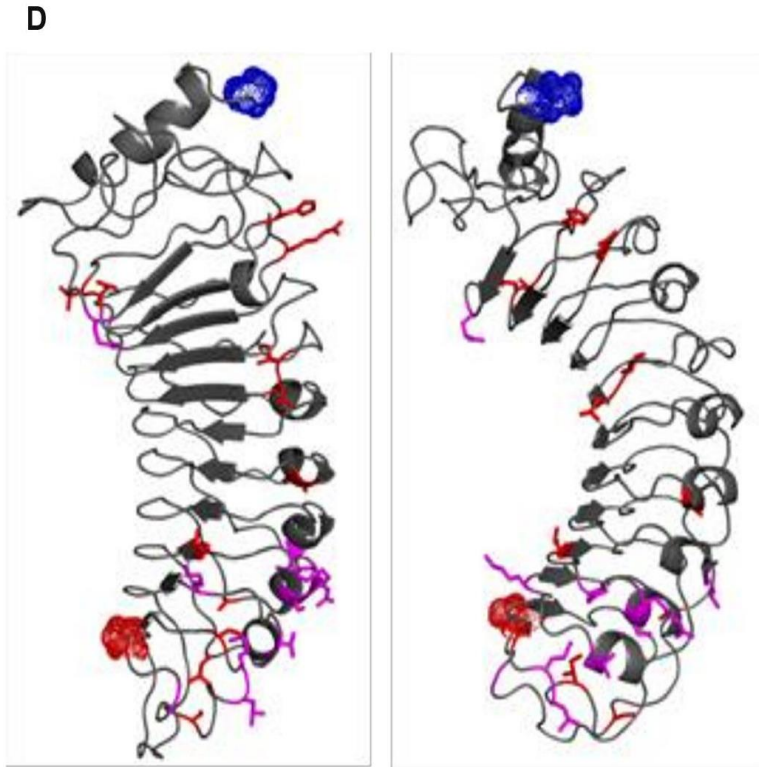


De ce computere?

I. Experimentele sunt scumpe



Homology modelling

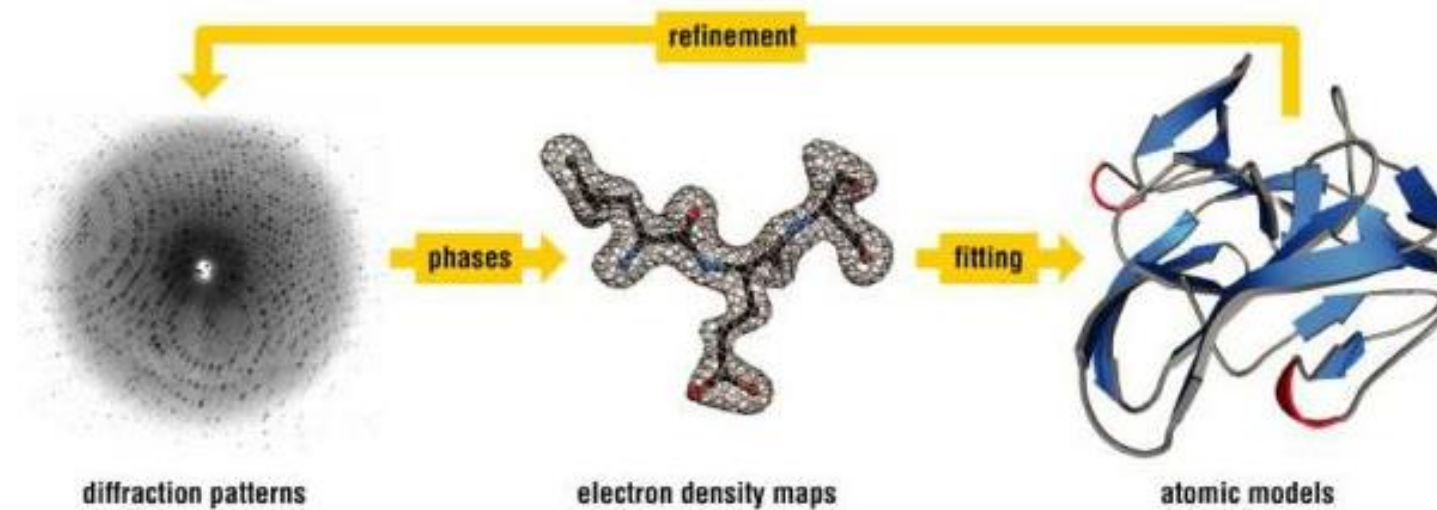


Prezicerea structurii LRR a proteinelor de imunitate in plante

Octav Caldararu et al., Frontiers in Plant Science, 2016

De ce computere?

II. Experimentele nu sunt destul de bune



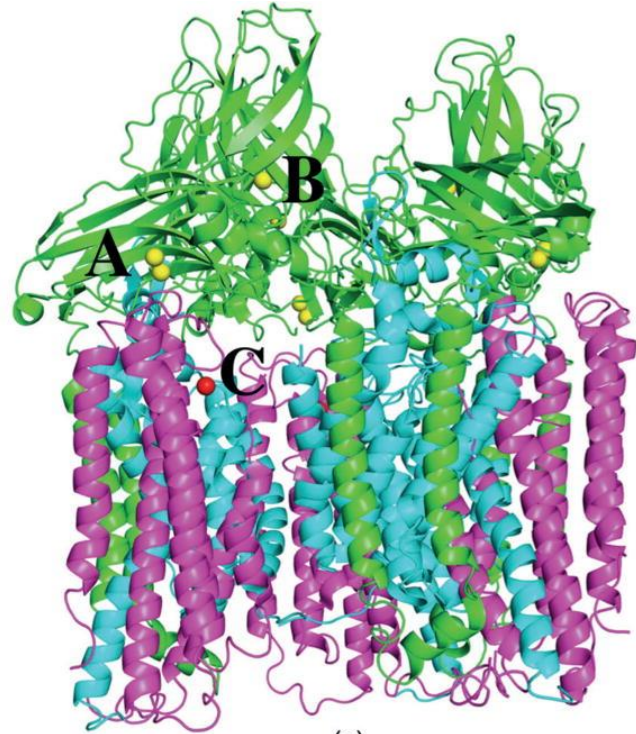
~5000 date la rezolutia de 2.5 Å

2000 atomi x 3 coordonate
+ 2000 "erori" (B-factors)
= 8000 parametri

Crystallographic refinement

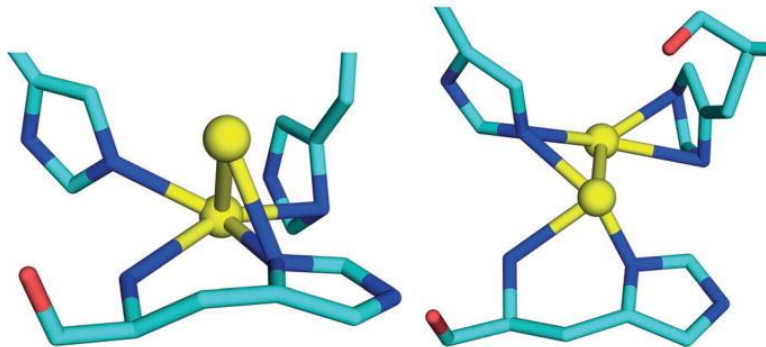
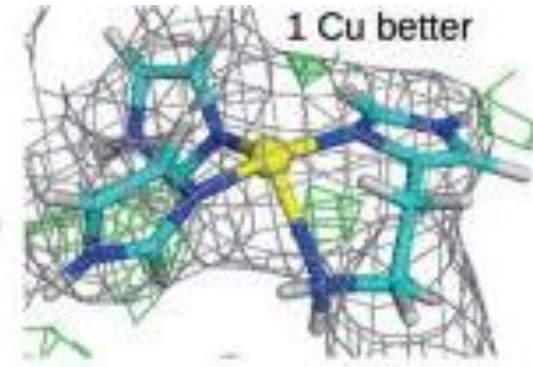
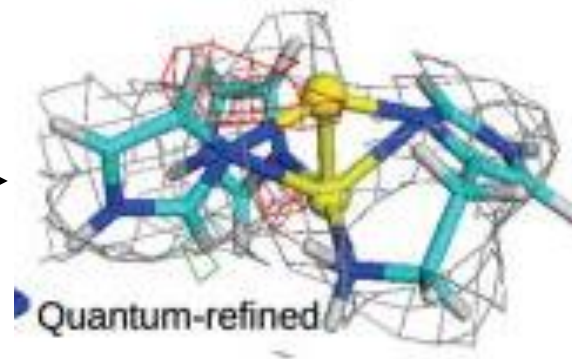


LUNDS
UNIVERSITET



(a)

$$\hat{H}\Psi = E\Psi$$



(b)

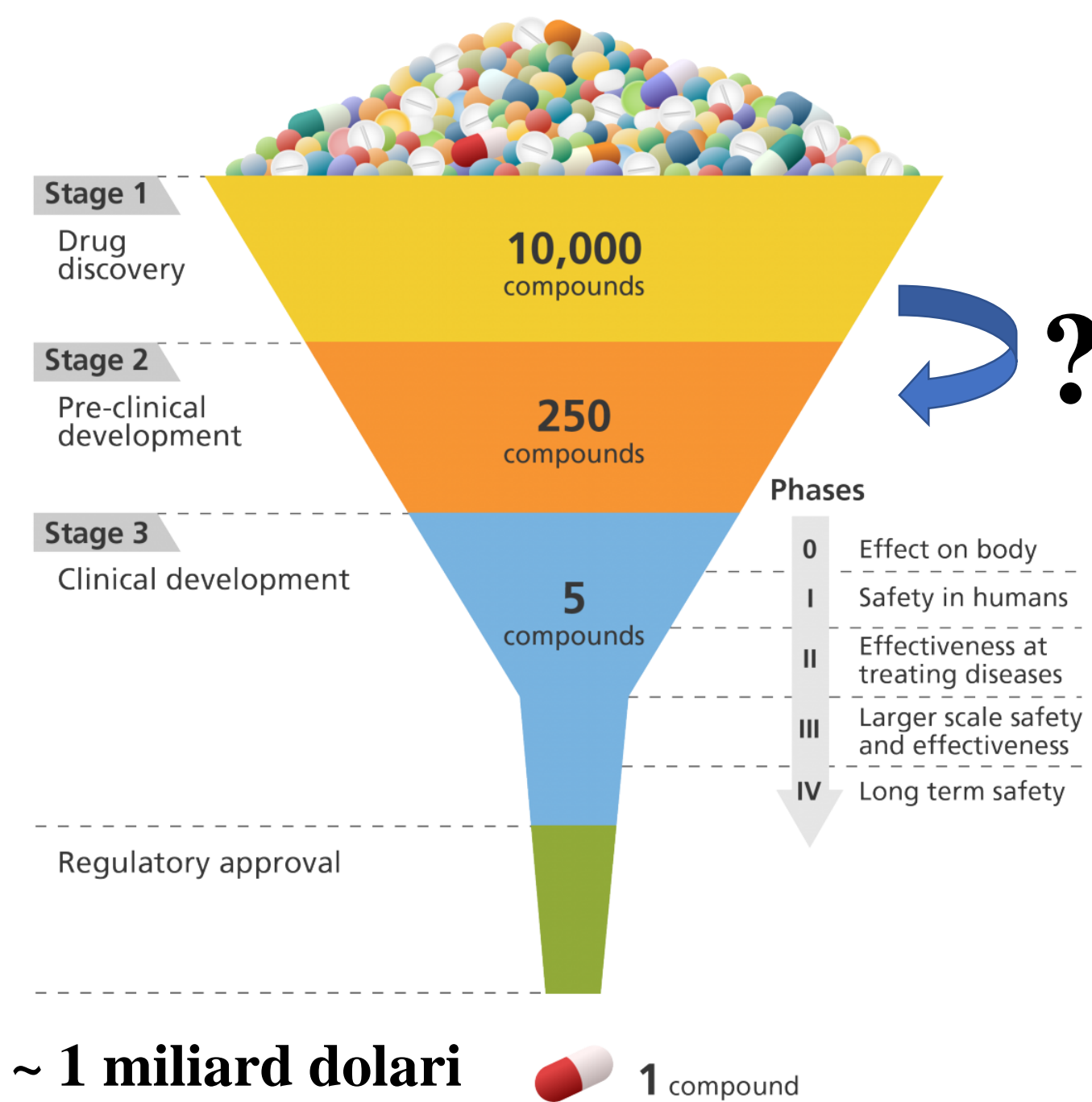
(c)

Quantum Refinement Does Not Support Dinuclear Copper Sites in Crystal Structures of Particulate Methane Monooxygenase

Octav Caldararu et al., Angewandte Chemie, 2018

De ce computere?

III. Experimentele sunt SCUMPE



Thank you!



$$\frac{a}{b} + \frac{c}{d} = \frac{ad+bc}{bd}$$
$$\frac{a}{\frac{b}{c}} = \frac{ac}{b}$$
$$\frac{\frac{a}{b}}{c} = \frac{a}{bc}$$

$$n(B \cap C) = 22$$
$$n(B) = 68$$
$$n(C) = 84$$

$$n(B \cup C) = n(B) + n(C) - n(B \cap C)$$

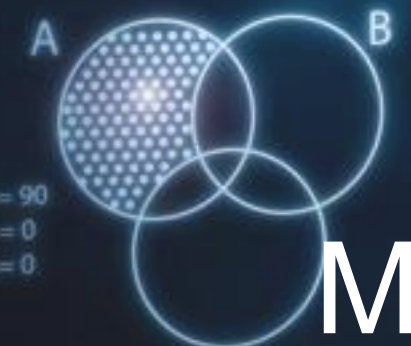
He = 4.002602
Na = 22.989769
Ar = 39.948



$$\bar{x}_1 = \frac{1+3+3+6+8+9}{6} = 5$$
$$\bar{x}_2 = 2+4+4+8+12 = 30$$
$$\bar{x}_3 = 4+7+1+6 = 18$$



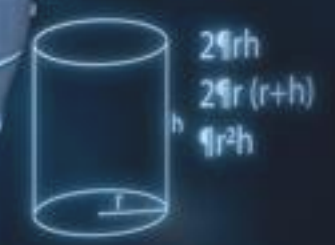
$$\log_b b^x = x$$
$$\log_a x = \frac{\log_b x}{\log_b a}$$
$$\log_b (x^r) = r \log_b x$$
$$\log_b (xy) = \log_b x + \log_b y$$
$$\log_b \left(\frac{x}{y}\right) = \log_b x - \log_b y$$



$$a(bc) = (ab)c$$
$$a+b = b+a$$
$$a(b+c) = ab+ac$$
$$126 = 6xy$$
$$2x + 2y = 20$$

$$(x)(2x+3) = 90$$
$$2x^2+3x-90 = 0$$
$$(2x+15)(x-6) = 0$$

Mulțumesc!



$$|a| = |-a|$$
$$|a| \geq 0$$
$$|ab| = |a||b|$$
$$ab+ac = a(b+c)$$
$$\frac{a}{\frac{b}{c}} = \frac{ac}{b}$$
$$\frac{\frac{a}{b}}{c} = \frac{a}{bc}$$