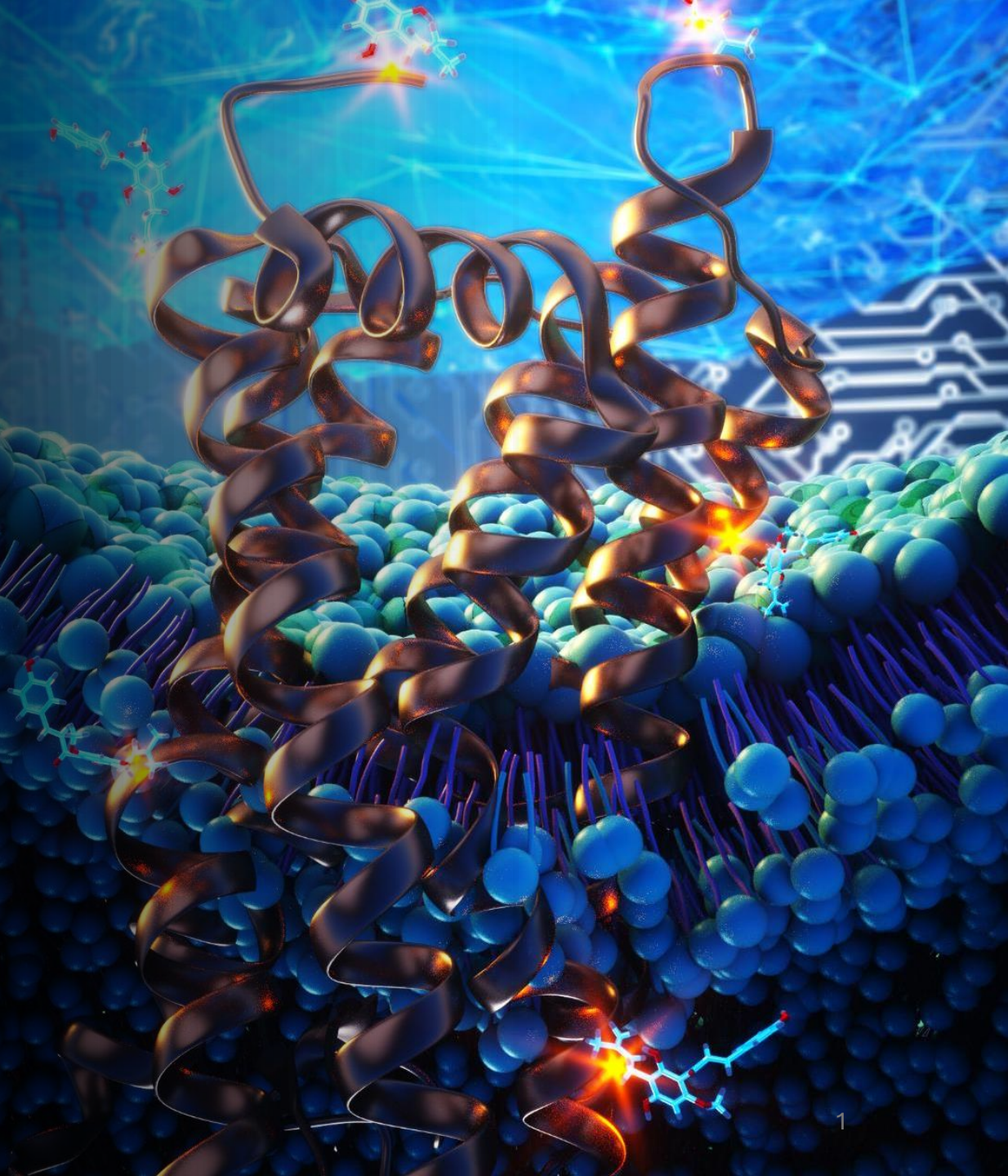
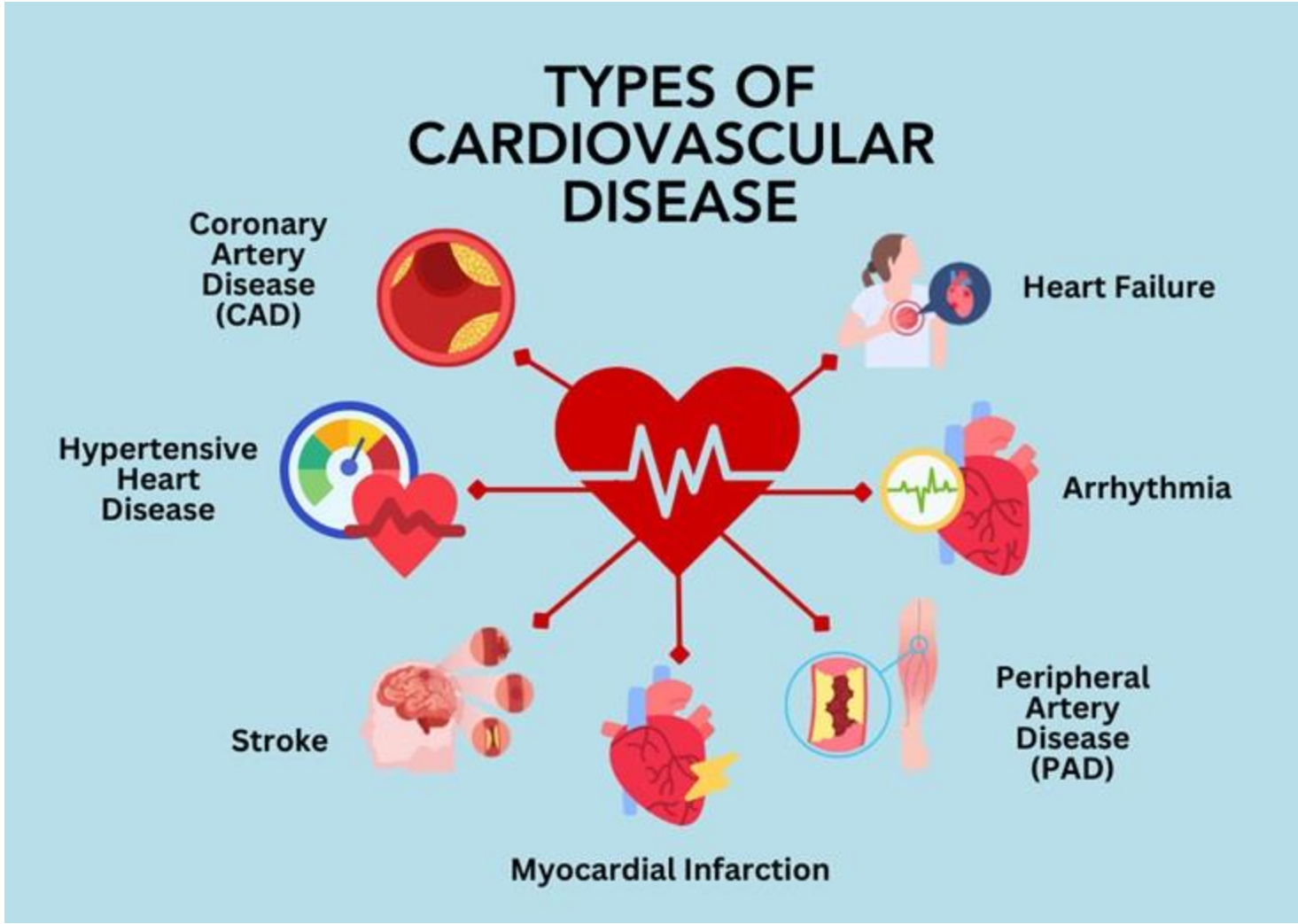
Cardiovascular desease prevention

Small molecule - protein interaction a quantum perspective

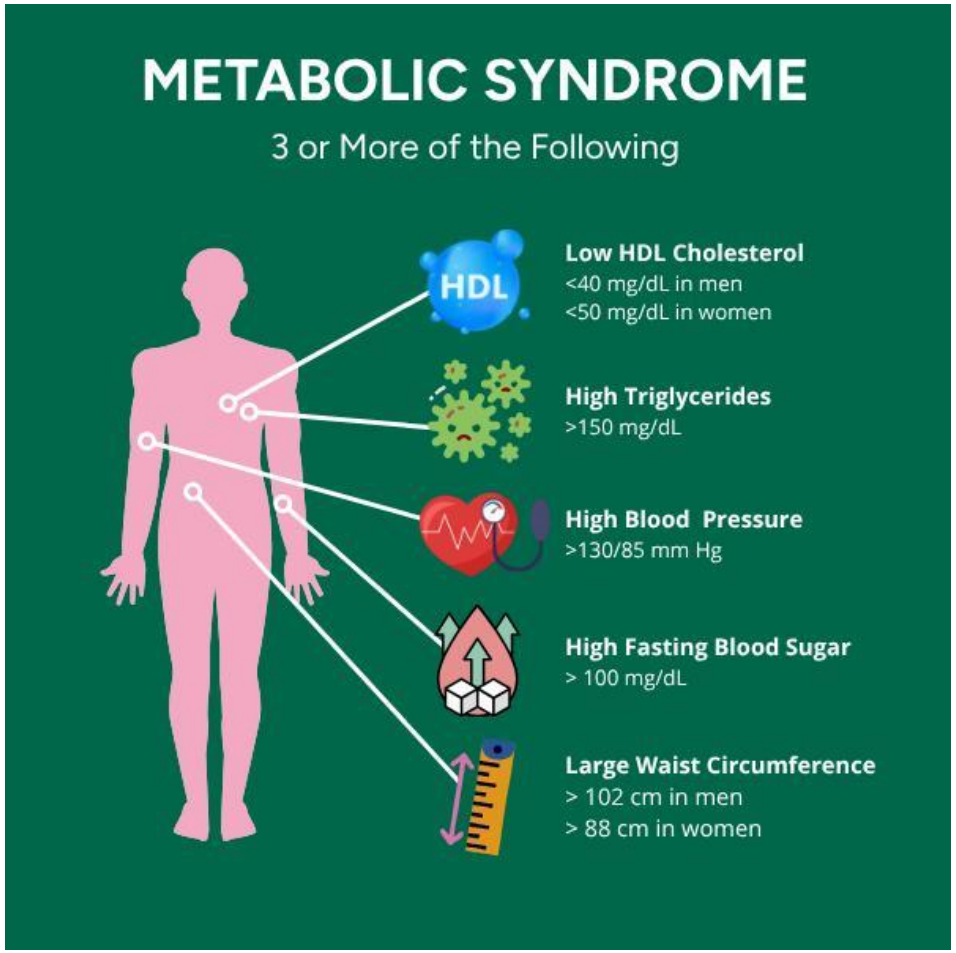
Mariamo Mussa Juane, CESGA postDoc researcher

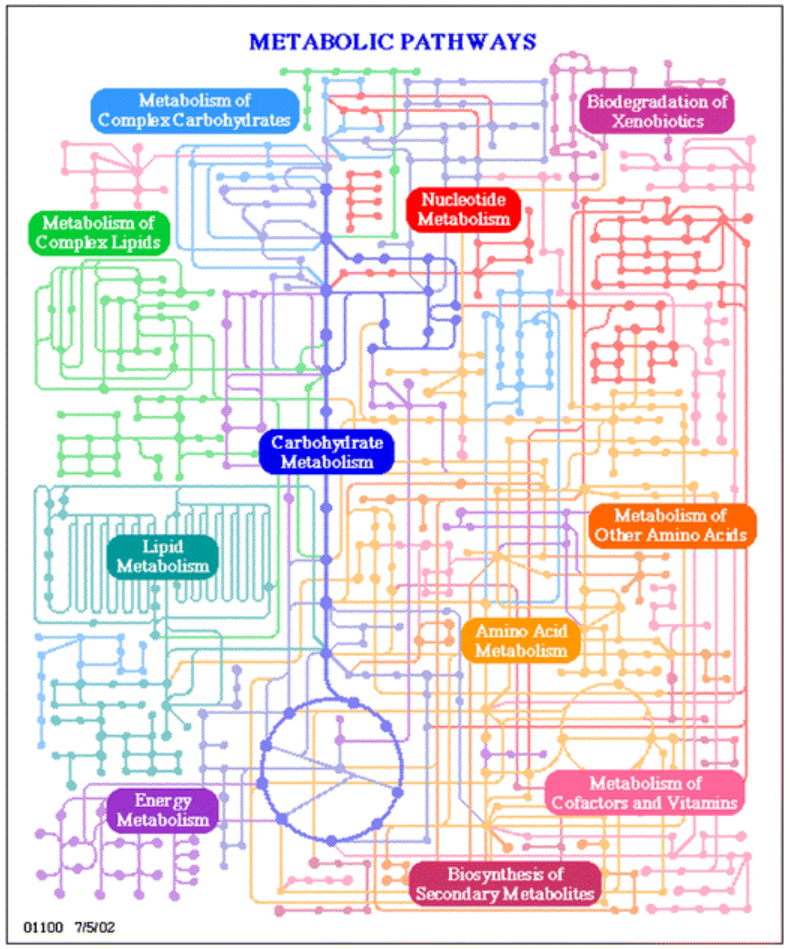
María Paredes, R&D scientist Hijos de Rivera SAU




TYPES OF CARDIOVASCULAR DISEASE
Coronary Artery Disease (CAD)
Heart Failure
Hypertensive Heart Disease
Arrhythmia
Stroke
Peripheral Artery Disease (PAD)
Myocardial Infarction

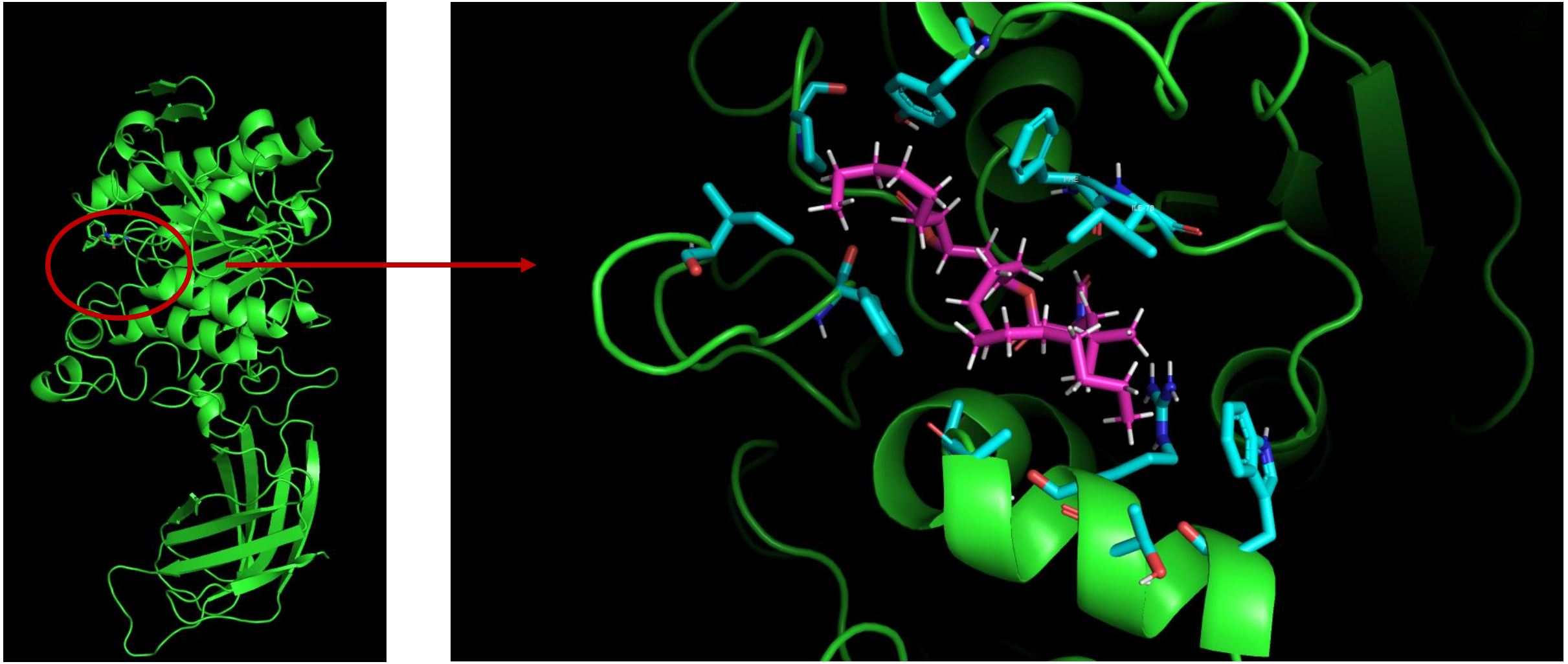
Cardiovascular deseases and metabolic malfunctioning





FOCUS: Lipids metabolism: Lipoprotein Lipase (LPL)

Lipoprotein Lipase (LPL)+small molecule



Dual otimisation: Geometry, charges

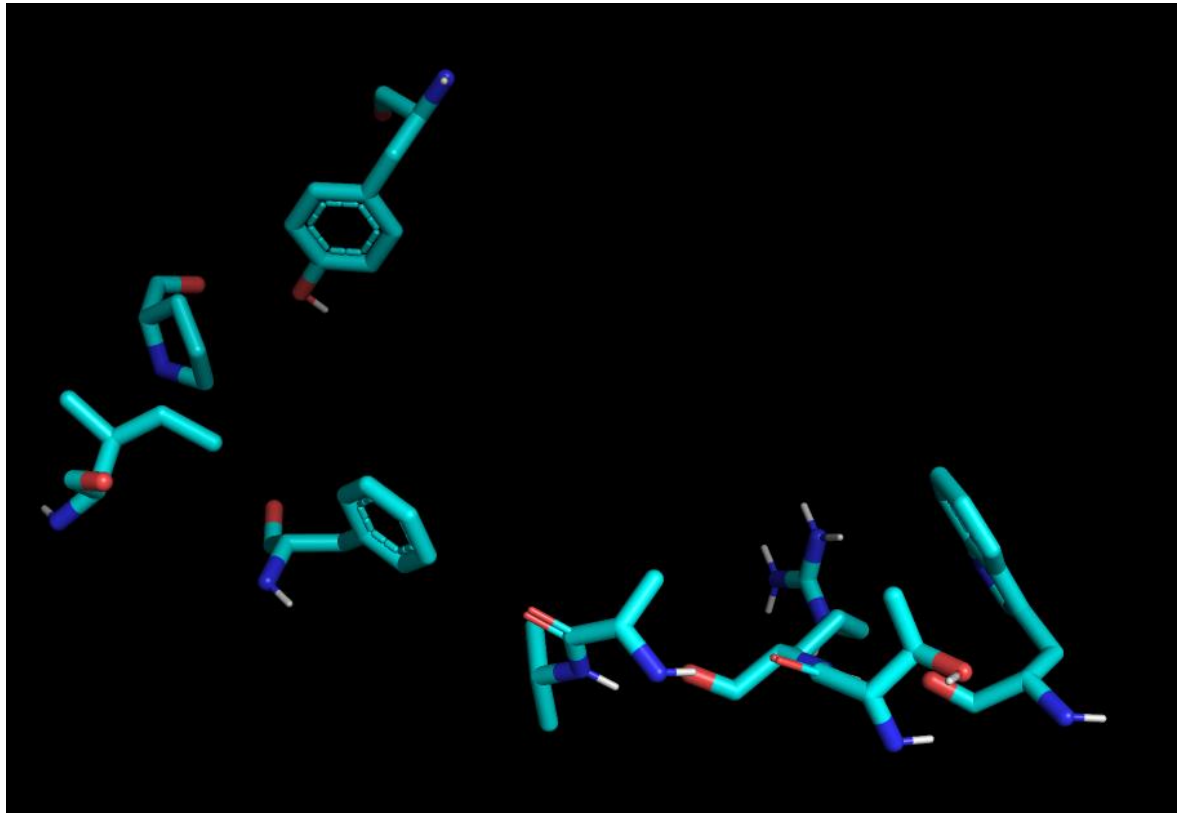
C:\Users\maria\OneDrive\Escritorio\HR\lipase\receptor_finais_pdb\combined_all_fragments_last.pdb - Sublime Text (UNREGISTERED)

File Edit Selection Find View Goto Tools Project Preferences Help

orlistat_bs.pdb | combined_all_fragments_last.pdb

```
HEADER    combined_all_fragments_last
HETATM    1  N   UNK     0      15.446  23.265  57.842  0.0   -0.673042        N1-
HETATM    2  C   UNK     0      14.374  24.254  57.741  0.0   -0.143931        C
HETATM    3  C   UNK     0      14.316  25.302  58.863  0.0   -0.152339        C
HETATM    4  O   UNK     0      14.097  26.480  58.604  0.0   -0.851478        O1-
HETATM    5      UNK     0      13.028  23.553  57.602  0.00  -0.016449        C
HETATM    6      UNK     0      11.888  24.499  57.462  0.00  -0.001821        C
HETATM    7      UNK     0      11.665  25.160  56.255  0.00   0.000593        C
HETATM    8      UNK     0      11.070  24.305  58.562  0.00   0.000593        C
HETATM    9      UNK     0      10.661  26.115  56.143  0.00   0.029551        C
HETATM   10      UNK     0      10.062  25.758  58.461  0.00   0.029551        C
HETATM   11      UNK     0       9.869  26.407  57.243  0.00   0.109616        C
HETATM   12      UNK     0       8.890  27.348  57.113  0.00  -0.385517        O
HETATM   13      UNK     0      15.226  22.312  57.809  0.00  -0.150594        H
HETATM   14      UNK     0       8.986  27.312  56.285  0.00   0.211061        H
HETATM   15      UNK     0       4.757  26.308  58.649  0.00  -0.653828        N
HETATM   16      UNK     0       5.542  26.482  59.857  0.00  -0.141314        C
HETATM   17      UNK     0       6.471  27.505  60.289  0.00  -0.152130        C
HETATM   18      UNK     0       7.191  28.164  59.478  0.00  -0.851473        O
HETATM   19      UNK     0       6.364  25.250  59.440  0.00  -0.028341        C
HETATM   20      UNK     0       5.692  24.743  58.206  0.00  -0.028689        C
HETATM   21      UNK     0       5.221  25.983  57.518  0.00  -0.144224        C
HETATM   22      UNK     0       9.250  16.338  38.821  0.00  -0.669918        N1-
HETATM   23      UNK     0       9.739  15.943  40.133  0.00  -0.099649        C
HETATM   24      UNK     0       9.412  16.990  41.213  0.00  -0.070824        C
HETATM   25      UNK     0       8.953  16.561  42.315  0.00  -0.838669        O1-
HETATM   26      UNK     0      11.245  15.712  40.022  0.00   0.086581        C
HETATM   27      UNK     0      11.855  15.395  41.374  0.00   0.030181        C
```

atoms coordinates partial charges

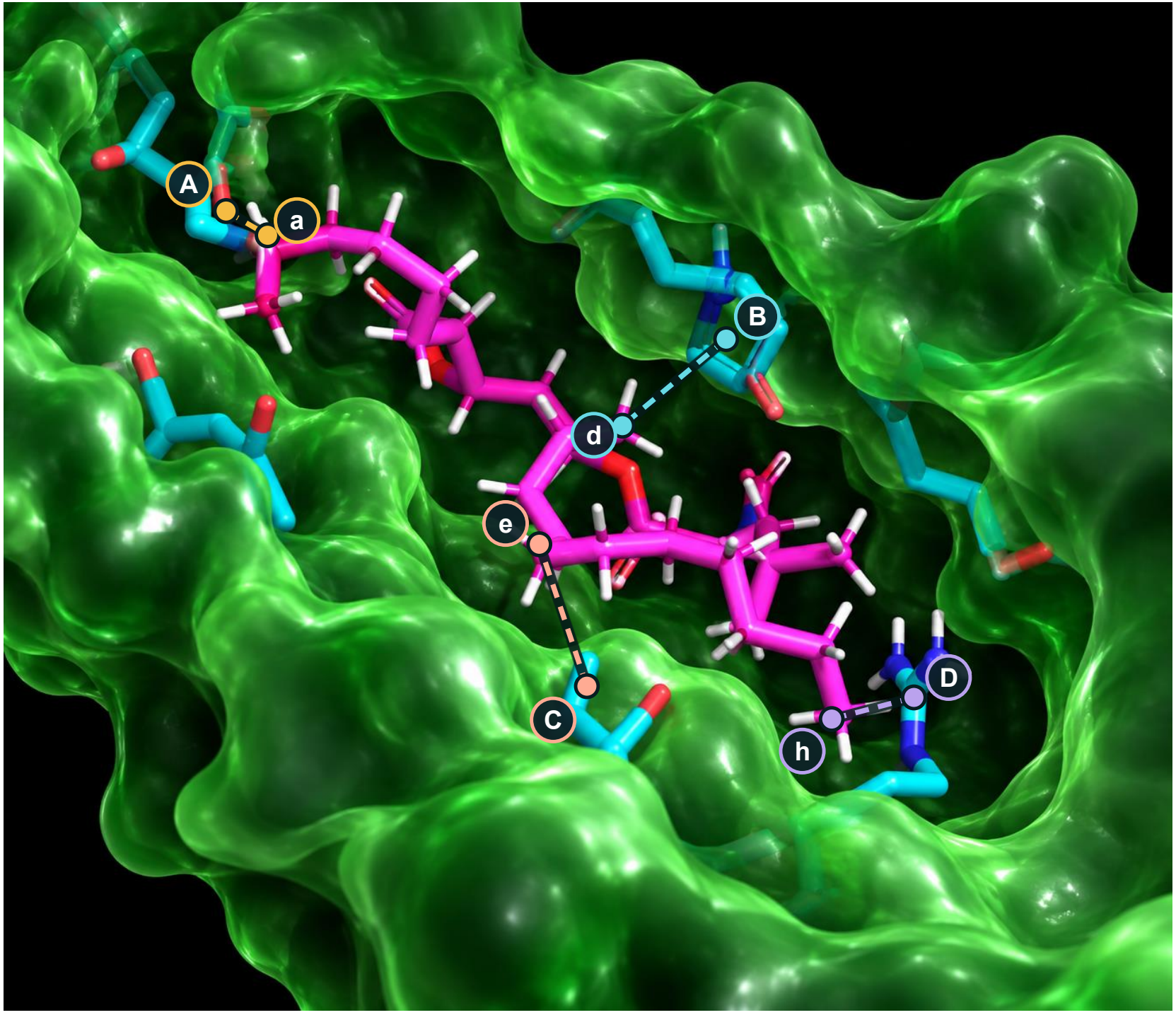


LPL

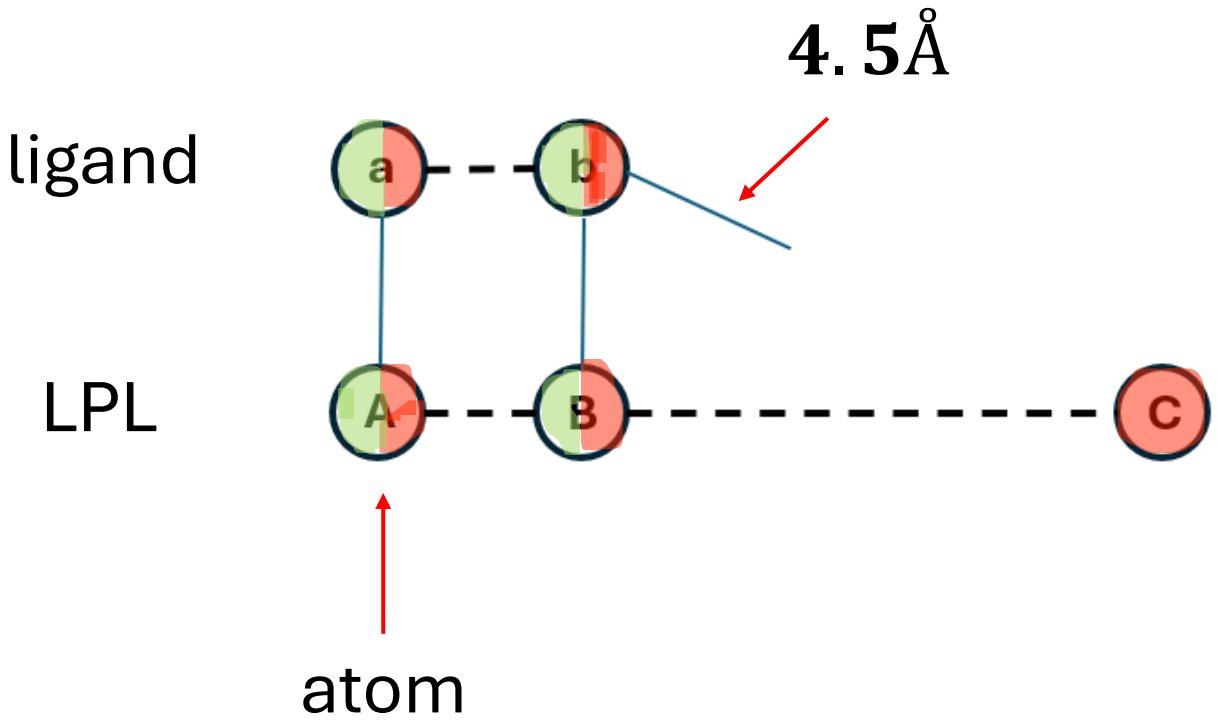


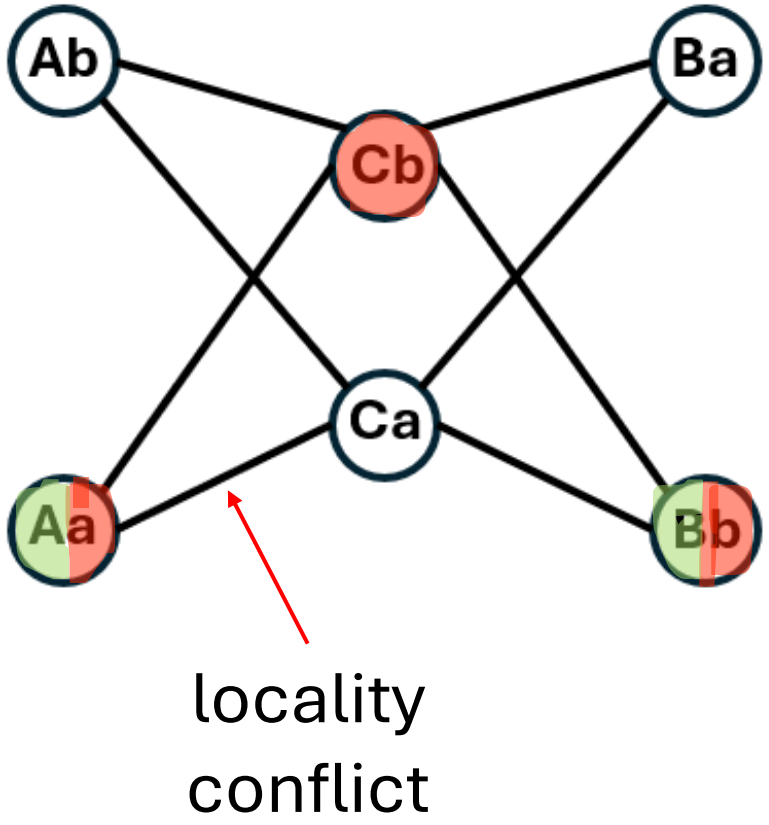





A
a
B
d
e
C
D
h

Graph construction

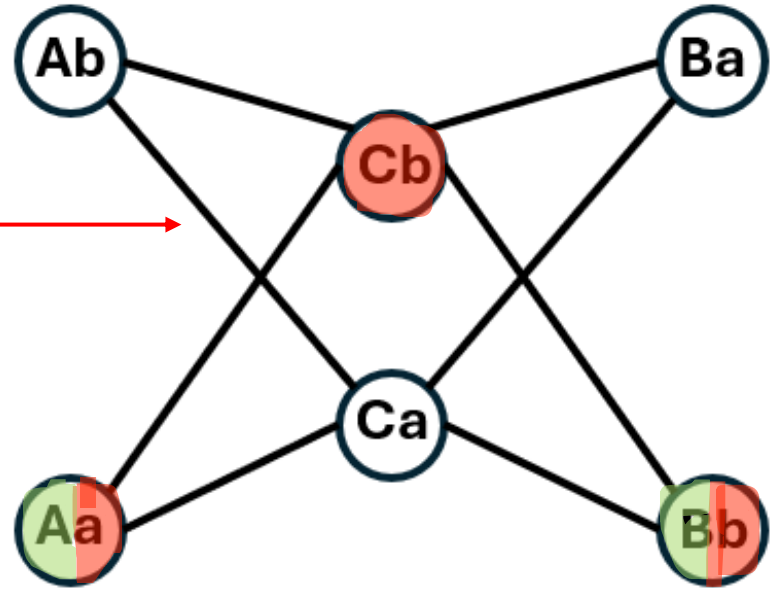




Maximum Weighted Independent Set

Minimise conflicts

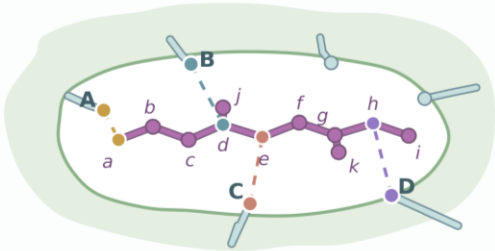
Maximise Coulombian interactions



DATA EXTRACTION

Extract partial charges
(Gasteiger/RDKit)

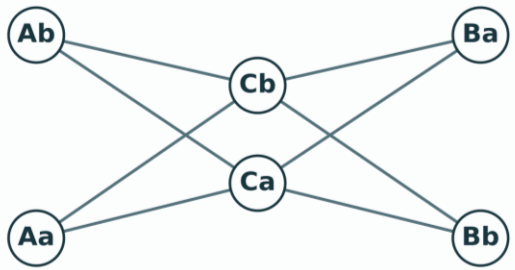
Extract 3D coordinates
(LPL pocket & 8 ligands)



GRAPH CONSTRUCTION

Apply locality condition
(intra- vs intermolecular dist.)

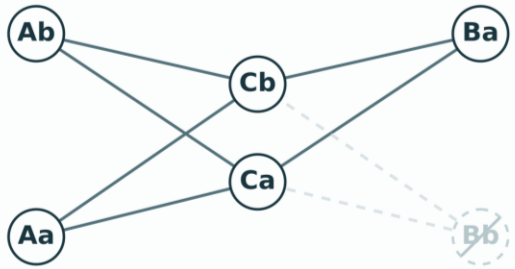
Build conflicto graph
(V: pairs; E: clashes)



VARIABLE REDUCTION

Filter out null & negative interactions

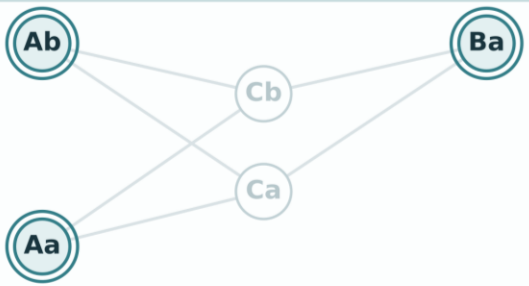
Remove weak interactions ($\omega_v < 0.001$)



OPTIMISATION

Formulate as QUBO / MWIS

Solver Digital annealing (D-wave)



Ligand	MWIS Weight $\alpha_\omega(G)$	Interaction Profile
1	19.18	Baseline
2	21.67	Standard
3	**29.66**	**High energy, low conflict density**
4	25.04	Standard
5	26.87	Standard
6	33.41	High energy (largest size)
7	**13.86**	**Low energy, high conflict density**
8	37.30	Highest energy

Table 2: Cumulative weights of the MWIS representing the interaction energy between the LPL and ligands.

Conclusions

Formulation: Molecular docking was mapped to a QUBO/MWIS problem using the concept of steric impedance (geometry+charges).
Scalability: Resolved conflict graphs of up to $N = 3958$ vertices using quantum-inspired Digital Annealing.
Ligand Ranking: Established a clear classification of molecules with favourable interaction capabilities with the LPL enzyme.

Future

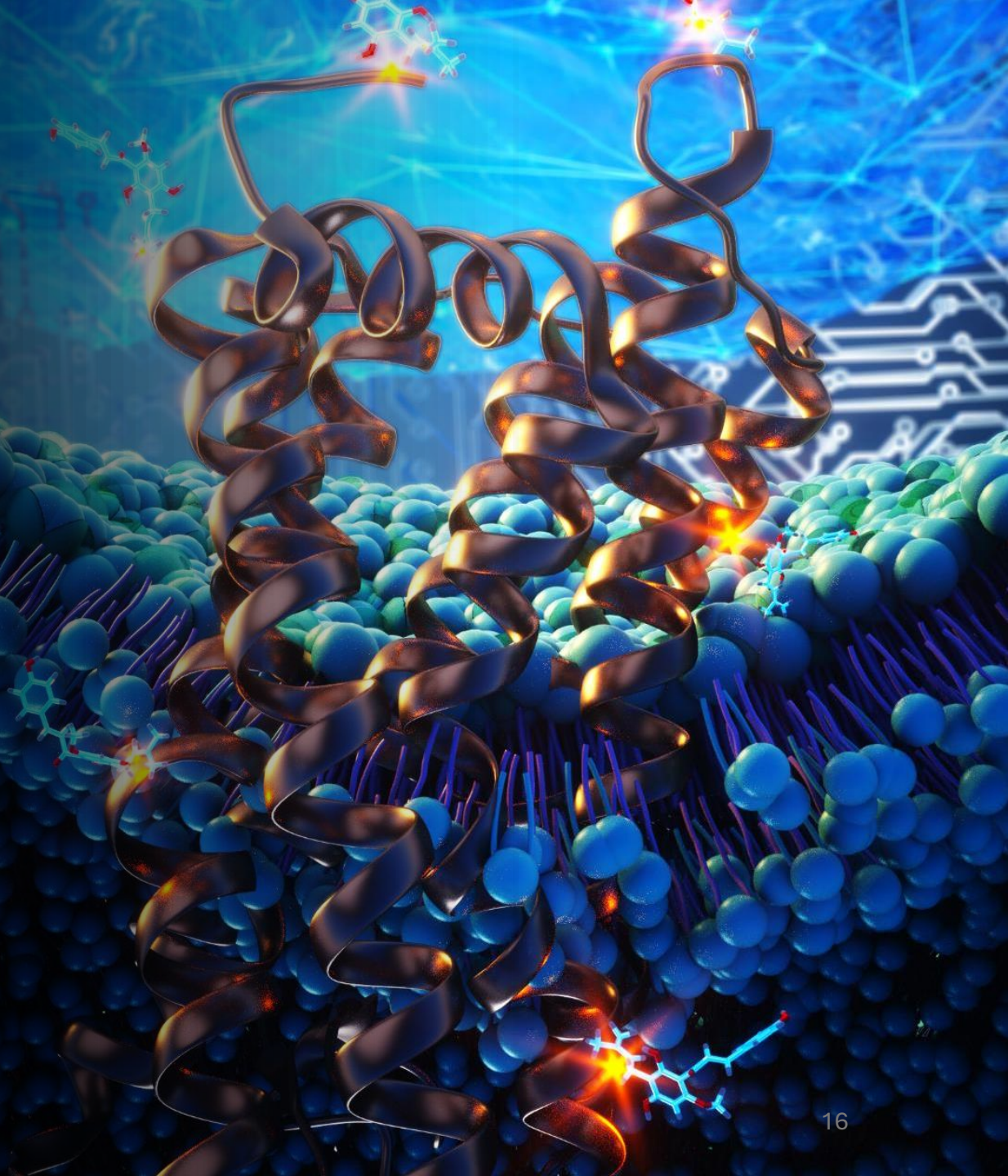
Spatial Reconstruction: Post-processing to map the MWIS solution back to 3D space to determine the final ligand pose.
Pharmacophore Grouping: Reducing variables by grouping atoms into pharmacophores.
Quantum Hardware: Execution on D-Wave Quantum Annealers (LeapHybridBQMSampler).
Digital Quantum Algorithms: Implementing techniques like Pauli Correlation Encoding to compress variables.
Lab tests

Cardiovascular desease prevention

Small molecule - protein interaction a quantum perspective

Mariamo Mussa Juane, CESGA postDoc researcher

María Paredes, R&D scientist Hijos de Rivera SAU



QUBO problem:
Maximum Weighted Independent Set

$$max\left\{\sum_{v\epsilon V}\omega_v x_v - \lambda \sum_{\{u,v\}\epsilon E} x_u x_v\right\}$$

Ligand	Initial Pairs (N_0)	Reduced Vertices (N)	Reduction(%)
1	4992	2197	56
2	6624	2894	56
3	6912	3212	54
4	7584	3477	54
5	8064	3461	57
6	8256	3709	55
7	8448	3429	59
8	8736	3958	55

Table 1: Reduction of the combinatorial search space (2^n) by filtering weak interactions.