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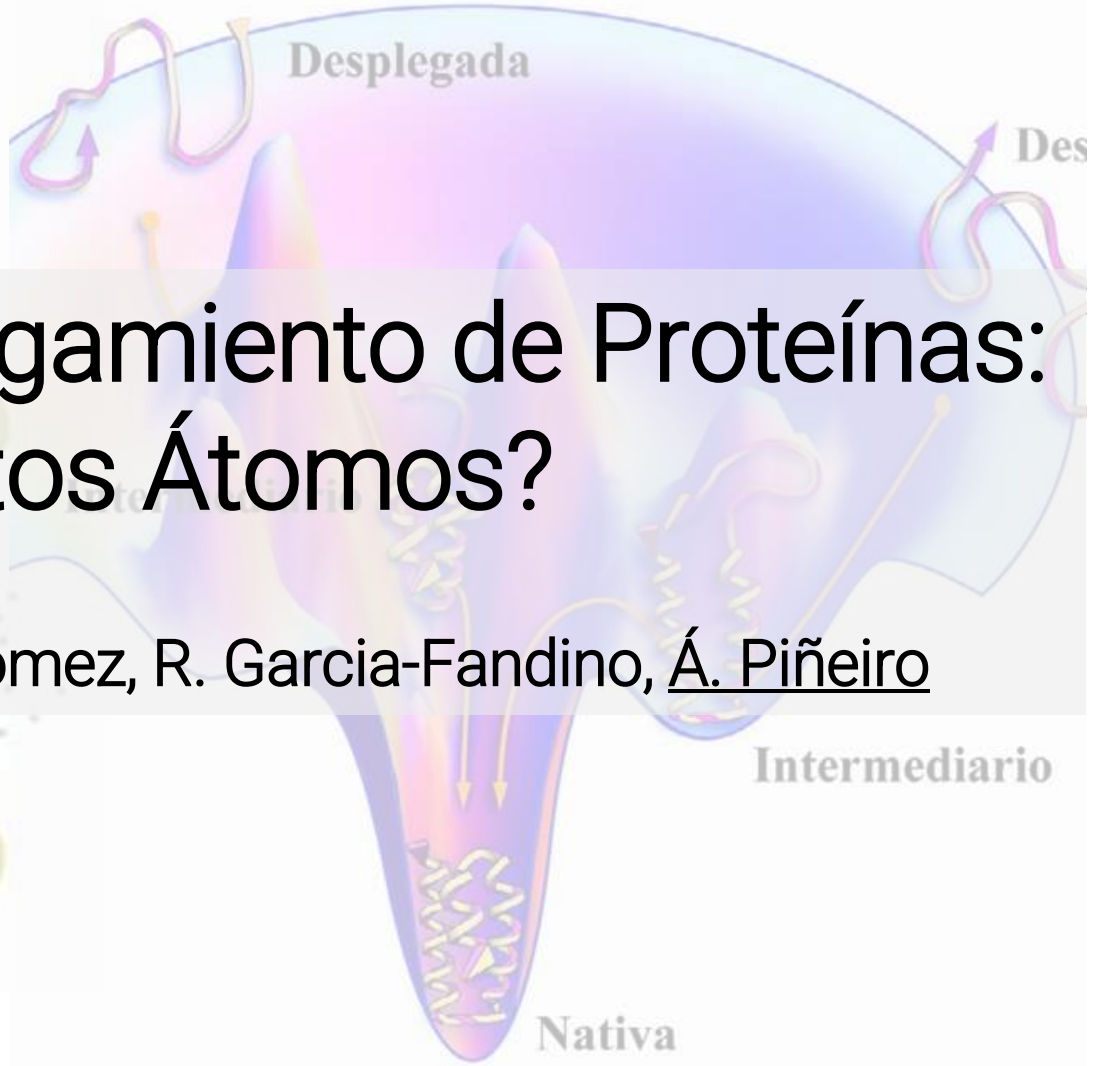
USC UNIVERSIDADE DE SANTIAGO DE COMPOSTELA

CESGA Centro de Supercomputación de Galicia

JORNADA TÉCNICA COMPUTACIÓN CUÁNTICA

Qmio



Computación Cuántica en Plegamiento de Proteínas: ¿ Suficientes Qubits para Tantos Átomos?

D. Conde-Torres, M. Mussa-Juane, D. Faílde, A. Gómez, R. Garcia-Fandino, Á. Piñeiro

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¿ Quiénes somos y qué hacemos?

Rebeca García
CSO

Ángel Piñeiro
CEO

Amelia Anderson
PhD student CyTx

Alexandre Blanco
PhD student DI Xunta

Fabián Suárez
PhD student DI Xunta

Caracterización de interacciones moleculares a partir de simulaciones computacionales → diseño/optimización de moléculas

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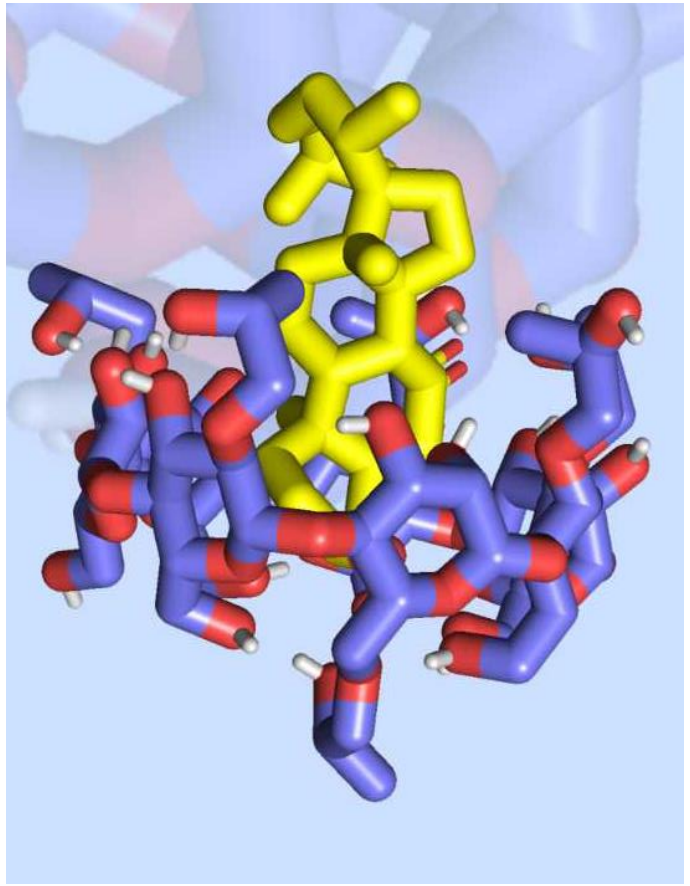
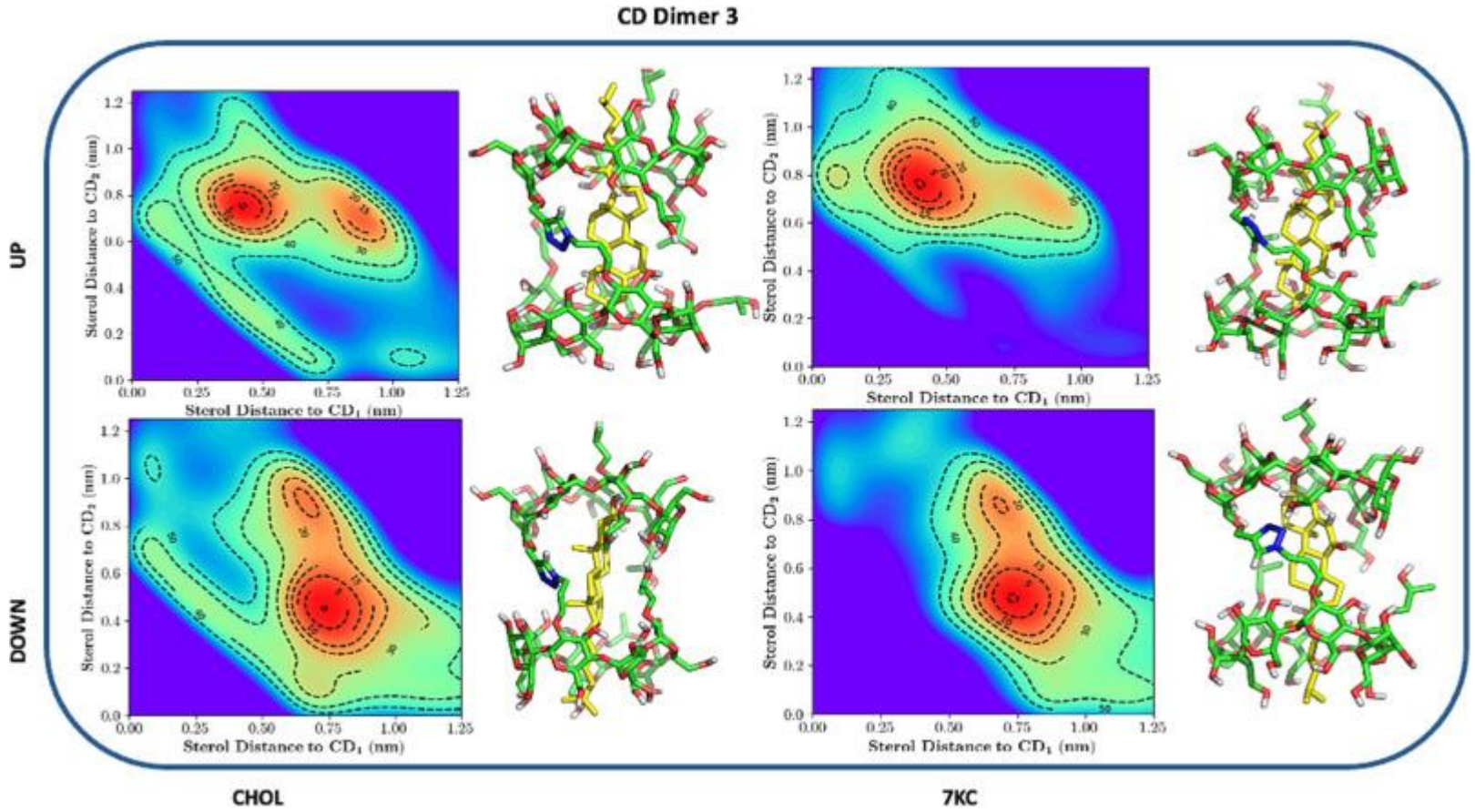
Ejemplos (en producción)





CYCLARITY THERAPEUTICS

Ligand

Oculis

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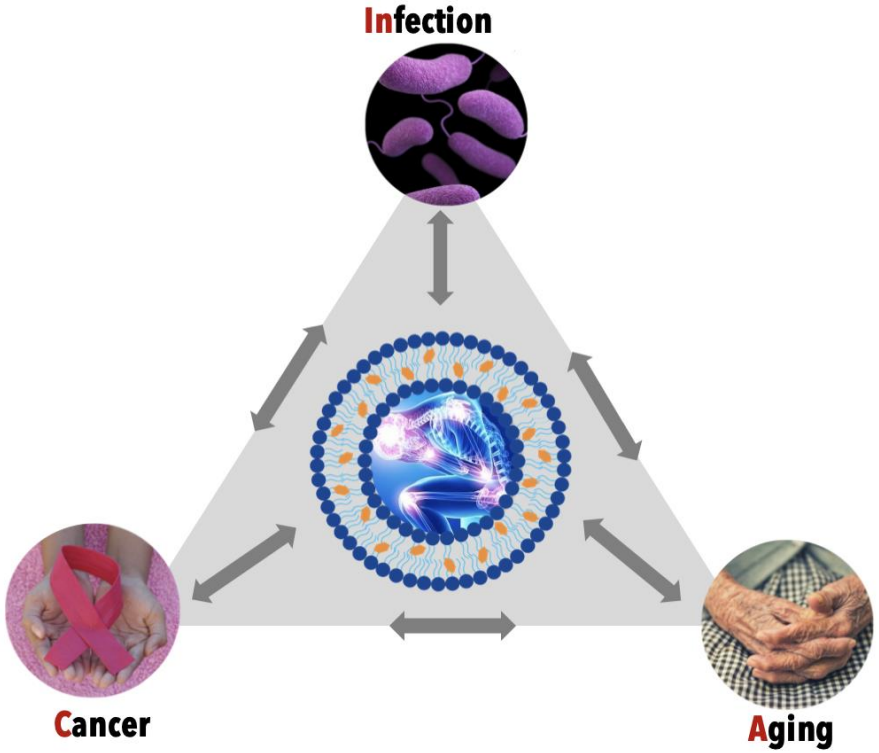
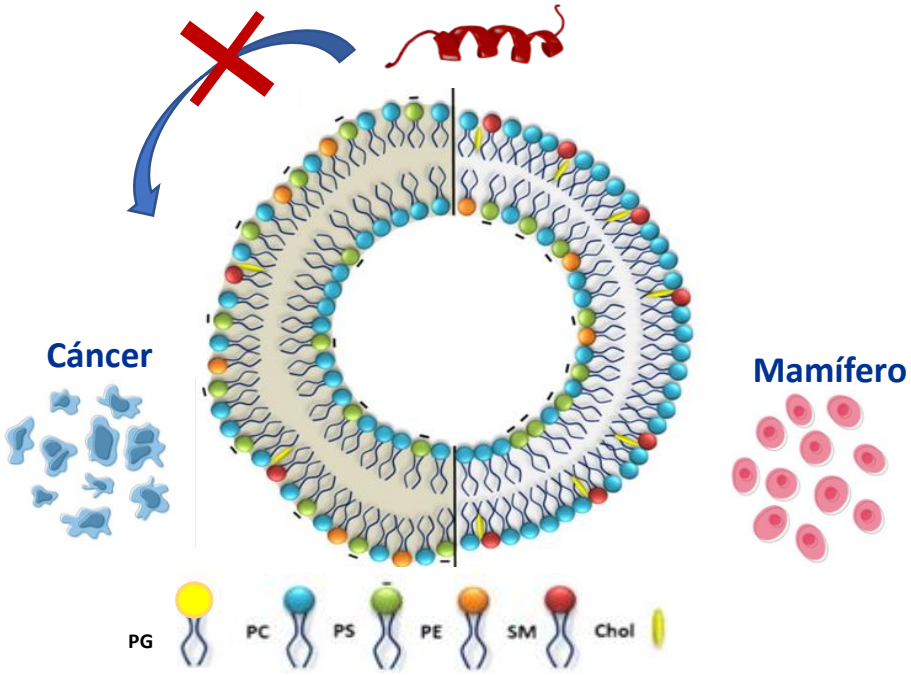
Ejemplos (en desarrollo)



Triángulo de CAIn

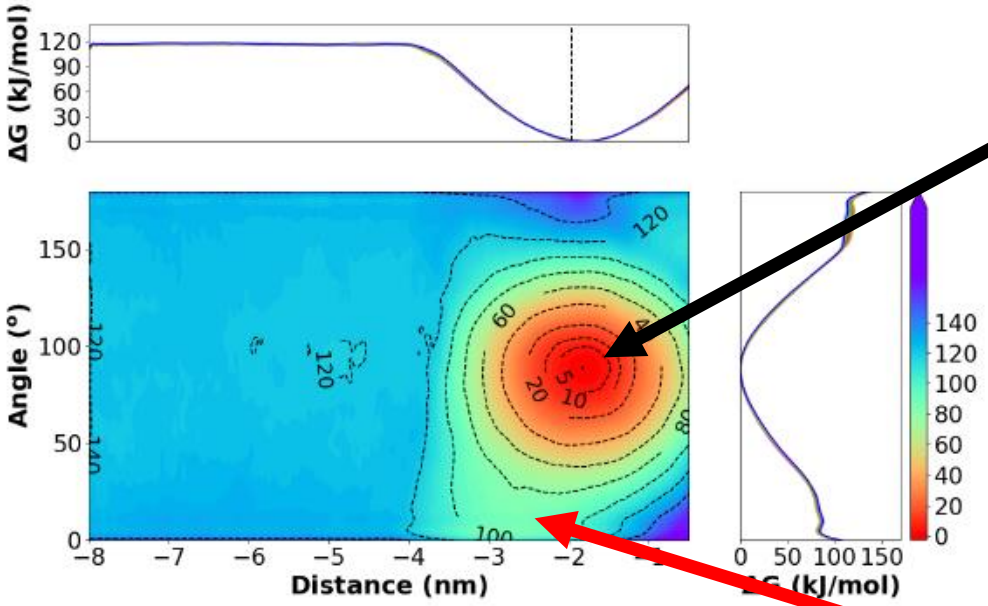
(Cancer-Aging-Infection)

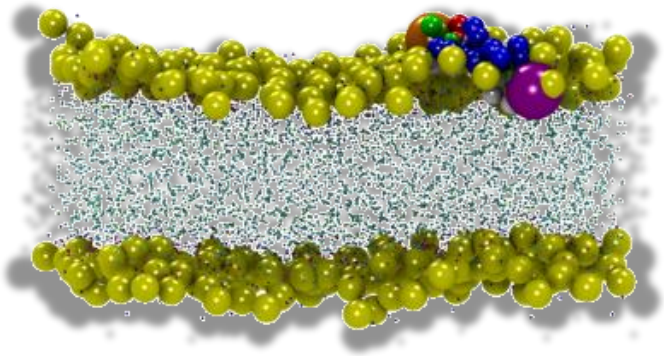


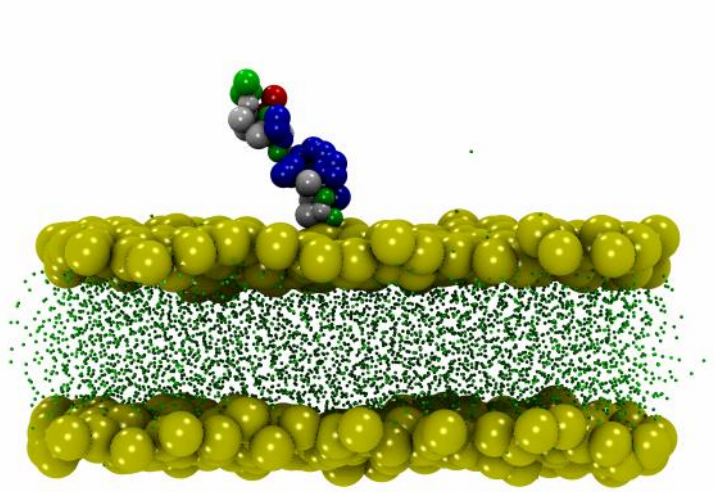
Problema: estructura de los péptidos

Ejemplos (en desarrollo)

Aproximación(es)







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El problema del plegamiento

nature

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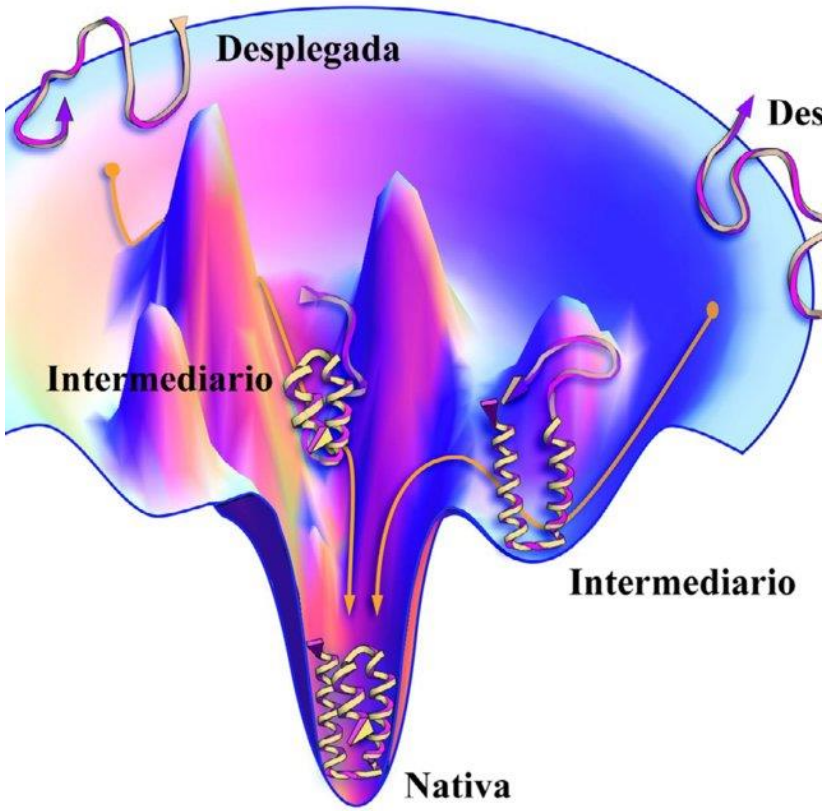
Article | Open access | Published: 15 July 2021

Highly accurate protein structure prediction with AlphaFold

John Jumper ✉, Richard Evans, Alexander Pritzel, Tim Green, Michael Figurnov, Olaf Ronneberger, Kathryn Tunyasuvunakool, Russ Bates, Augustin Žídek, Anna Potapenko, Alex Bridgland, Clemens Meyer, Simon A. A. Kohl, Andrew J. Ballard, Andrew Cowie, Bernardino Romera-Paredes, Stanislav Nikolov, Rishub Jain, Jonas Adler, Trevor Back, Stig Petersen, David Reiman, Ellen Clancy, Michal Zielinski, Martin Steinegger, Michalina Pacholska, Tamas Berghammer, Sebastian Bodenstein, David Silver, Oriol Vinyals, Andrew W. Senior, Koray Kavukcuoglu, Pushmeet Kohli & Demis Hassabis ✉ — Show fewer authors

Nature **596**, 583–589 (2021) | Cite this article



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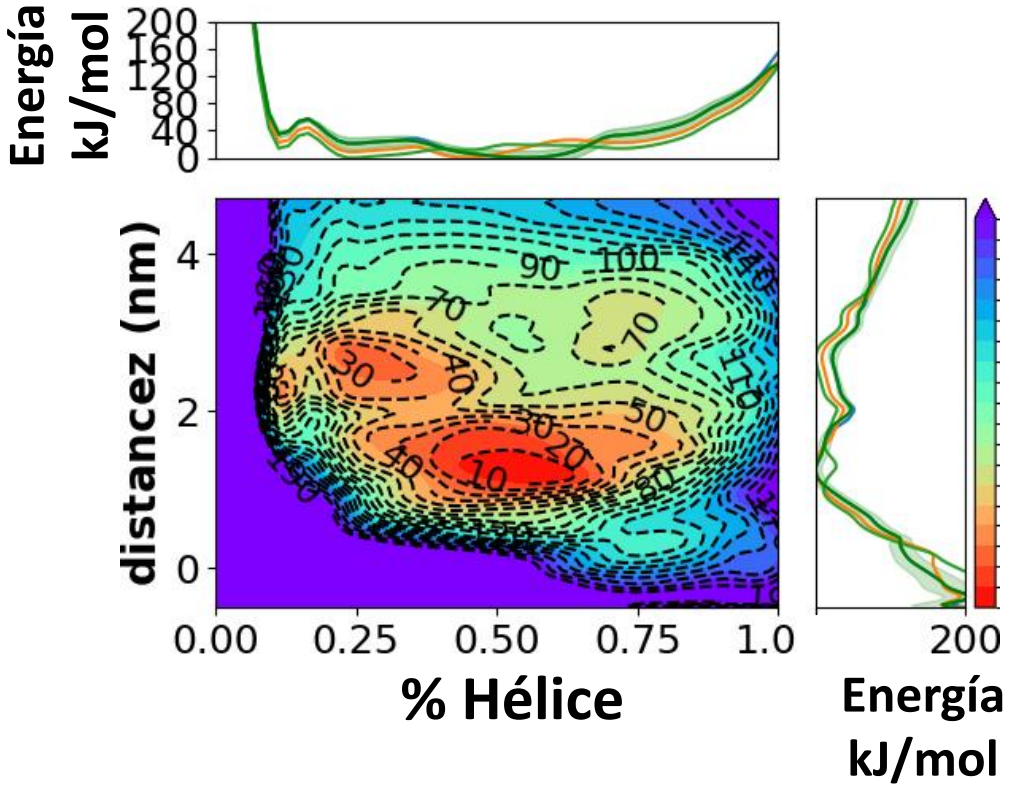
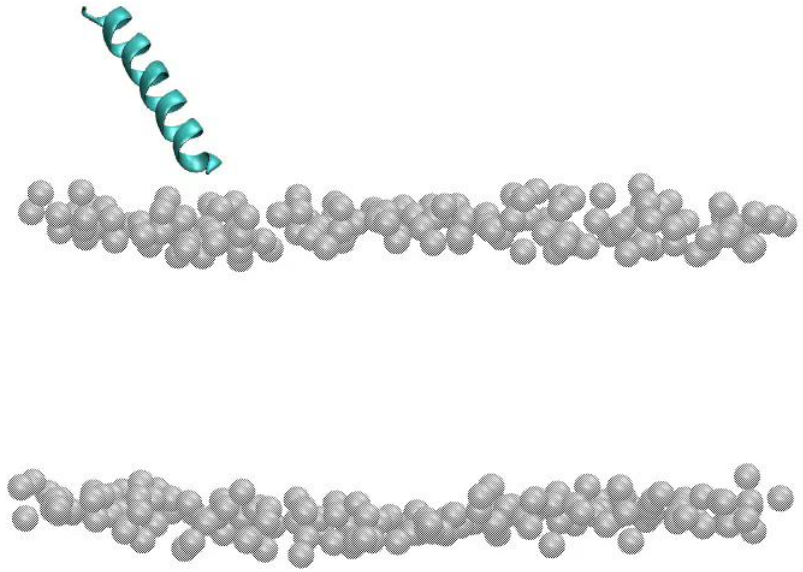
El problema del plegamiento





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Aproximación con computación cuántica

https://github.com/qiskit-community/qiskit-research/blob/main/docs/protein_folding/protein_folding.ipynb

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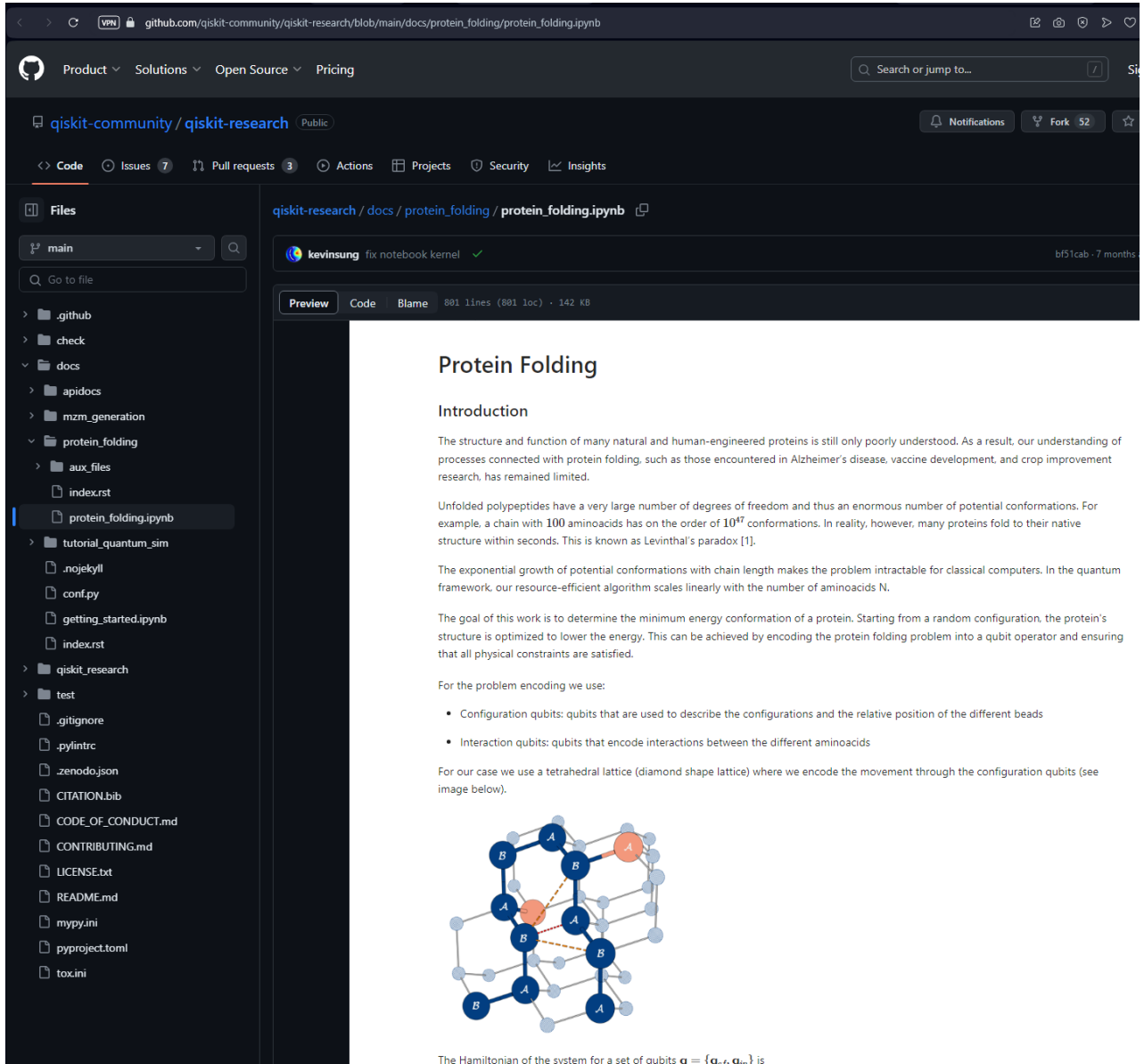
Article | Open access | Published: 17 February 2021

Resource-efficient quantum algorithm for protein folding

Anton Robert, Panagiotis Kl. Barkoutsos, Stefan Woerner & Ivano Tavernelli

npj Quantum Information **7**, Article number: 38 (2021) | Cite this article

23k Accesses | **49** Citations | **54** Altmetric | Metrics



Aproximación con computación cuántica

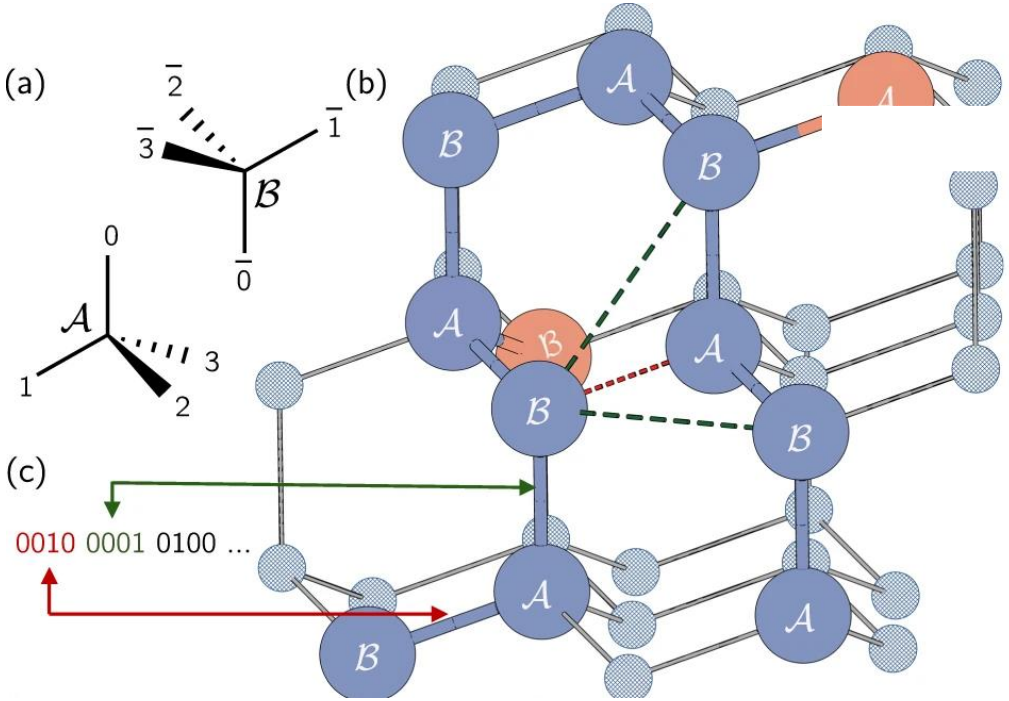
The configuration qubits

As for the previous models in literature, a polymer configuration is grown on the lattice by adding the different beads one after the other and encoding, in the qubit register the different "turn" t_i that defines the position of the bead $i+1$ relatively to the previous bead i. Using a tetrahedral lattice, we distinguish two sets of non-equivalent lattice points $\mathcal{A}$ and $\mathcal{B}$ (see Fig. 1). At the $\mathcal{A}$ sites, the polymer can only grow along the directions $t_i \in \{0, 1, 2, 3\}$ while at site $\mathcal{B}$ the possible directions are $t_i \in \{\bar{0}, \bar{1}, \bar{2}, \bar{3}\}$. Along the sequence, the $\mathcal{A}$ and $\mathcal{B}$ sites are alternated so that we can use the convention that $\mathcal{A}$ (respectively $\mathcal{B}$) sites correspond to even (odd) *is*. Without loss of generality, the first two turns can be set to $t_1 = \bar{1}$ and $t_2 = 0$ due to symmetry degeneracy. To encode the turns, we assign one qubit per axis $t_i = q_{4i-3}q_{4i-2}q_{4i-1}q_{4i}$ (Fig. 1(c)). Therefore, the total number of qubits required to encode a conformation $\mathbf{q}_{cf}$ corresponds to $N_{cf} = 4(N-3)$.

The interaction qubits

To describe the interactions, we introduce a new qubit register $\mathbf{q}_{in}$, composed of $\mathbf{q}_{i,j}^{(l)}$ for each l^{th} nearest neighbor (l-NN) interaction on the lattice (see red and green dashed lines for $l = 1$ and $l = 2$ in Fig. 1, b) between beads i and j.

pairwise interaction energies $\epsilon_{i,j}^{(l)}$ between the beads at distance l can be arbitrarily defined to reproduce a fold of interest or it can be adapted from pre-existing models, like the one proposed by Miyazawa and Jernigan (MJ) for 1-NN interactions[17].



$$\mathbf{q} = \{\mathbf{q}_{cf}, \mathbf{q}_{in}\}),$$

$$H(\mathbf{q}) = H_{gc}(\mathbf{q}_{cf}) + H_{ch}(\mathbf{q}_{cf}) + H_{in}(\mathbf{q})$$

Aproximación con computación cuántica

JMB

J. Mol. Biol. (1996) **256**, 623–644

Residue–Residue Potentials with a Favorable Contact Pair Term and an Unfavorable High Packing Density Term, for Simulation and Threading

Sanzo Miyazawa[1] and Robert L. Jernigan[2]*

e_{ij}

	CYS	MET	PHE	ILE	LEU	VAL	TRP	TYR	ALA	GLY	THR	SER	GLN	ASN	GLU	ASP	HIS	ARG	LYS	PRO
CYS	-5.44	-5.05	-5.63	-5.03	-5.03	-4.46	-4.76	-3.89	-3.38	-3.16	-2.88	-2.86	-2.73	-2.59	-2.08	-2.66	-3.63	-2.70	-1.54	-2.92
MET	0.70	-6.06	-6.68	-6.33	-6.01	-5.52	-6.37	-4.92	-3.99	-3.75	-3.73	-3.55	-3.17	-3.50	-3.19	-2.90	-3.31	-3.49	-3.11	-4.11
PHE	0.52	-0.22	-6.85	-6.39	-6.26	-5.75	-6.02	-4.95	-4.36	-3.72	-3.76	-3.56	-3.30	-3.55	-3.51	-3.31	-4.61	-3.54	-2.83	-3.73
ILE	0.80	-0.18	0.14	-6.22	-6.17	-5.58	-5.64	-4.63	-4.41	-3.65	-3.74	-3.43	-3.22	-2.99	-3.23	-2.91	-3.76	-3.33	-2.70	-3.47
LEU	0.59	-0.09	0.06	-0.16	-5.79	-5.38	-5.50	-4.26	-3.96	-3.43	-3.43	-3.16	-3.09	-2.99	-2.91	-2.59	-3.84	-3.15	-2.63	-3.06
VAL	0.73	-0.02	0.14	0.00	-0.01	-4.94	-5.05	-4.05	-3.62	-3.06	-2.95	-2.79	-2.67	-2.36	-2.56	-2.25	-3.38	-2.78	-1.95	-2.96
TRP	0.67	-0.63	0.12	0.19	0.11	0.13	-5.42	-4.44	-3.93	-3.37	-3.31	-2.95	-3.16	-3.11	-2.94	-2.91	-4.02	-3.56	-2.49	-3.66
TYR	0.60	-0.12	0.25	0.25	0.41	0.19	0.04	-3.55	-2.85	-2.50	-2.48	-2.30	-2.53	-2.47	-2.42	-2.25	-3.33	-2.75	-2.01	-2.80
ALA	0.59	0.29	0.31	-0.05	0.19	0.10	0.03	0.18	-2.51	-2.15	-2.15	-1.89	-1.70	-1.44	-1.51	-1.57	-2.09	-1.50	-1.10	-1.81
GLY	0.64	0.37	0.79	0.55	0.56	0.50	0.43	0.36	0.19	-2.17	-2.03	-1.70	-1.54	-1.56	-1.22	-1.62	-1.94	-1.68	-0.84	-1.72
THR	0.70	0.16	0.52	0.23	0.33	0.38	0.26	0.15	-0.04	-0.09	-1.72	-1.59	-1.59	-1.51	-1.45	-1.66	-2.31	-1.97	-1.02	-1.66
SER	0.61	0.22	0.61	0.42	0.48	0.42	0.50	0.21	0.11	0.13	0.00	-1.48	-1.37	-1.31	-1.48	-1.46	-1.94	-1.22	-0.83	-1.35
GLN	0.43	0.30	0.56	0.33	0.25	0.24	-0.01	-0.31	0.00	-0.01	-0.29	-0.18	-0.89	-1.36	-1.33	-1.26	-1.85	-1.85	-1.02	-1.73
ASN	0.93	0.33	0.67	0.91	0.70	0.91	0.39	0.10	0.61	0.32	0.14	0.23	-0.13	-1.59	-1.43	-1.33	-2.01	-1.41	-0.91	-1.43
GLU	1.23	0.43	0.50	0.47	0.58	0.49	0.36	-0.06	0.34	0.45	0.00	-0.15	-0.30	-0.04	-1.18	-1.23	-2.27	-2.07	-1.60	-1.40
ASP	0.54	0.61	0.59	0.68	0.79	0.71	0.28	0.01	0.16	-0.05	-0.32	-0.23	-0.33	-0.06	-0.16	-0.96	-2.14	-1.98	-1.32	-1.19
HIS	0.48	1.11	0.21	0.75	0.44	0.48	0.08	-0.17	0.55	0.53	-0.06	0.19	-0.02	0.18	-0.29	-0.26	-2.78	-2.12	-1.09	-2.17
ARG	0.71	0.23	0.58	0.48	0.43	0.38	-0.16	-0.28	0.44	0.10	-0.42	0.21	-0.72	0.07	-0.79	-0.80	-0.04	-1.39	-0.06	-1.85
LYS	1.11	-0.15	0.53	0.34	0.20	0.45	0.15	-0.31	0.08	0.18	-0.23	-0.15	-0.65	-0.19	-1.08	-0.90	0.24	0.57	0.13	-0.67
PRO	0.40	-0.49	0.29	0.23	0.42	0.10	-0.36	-0.43	0.03	-0.04	-0.21	-0.02	-0.69	-0.04	-0.22	-0.11	-0.19	-0.56	-0.15	-1.18

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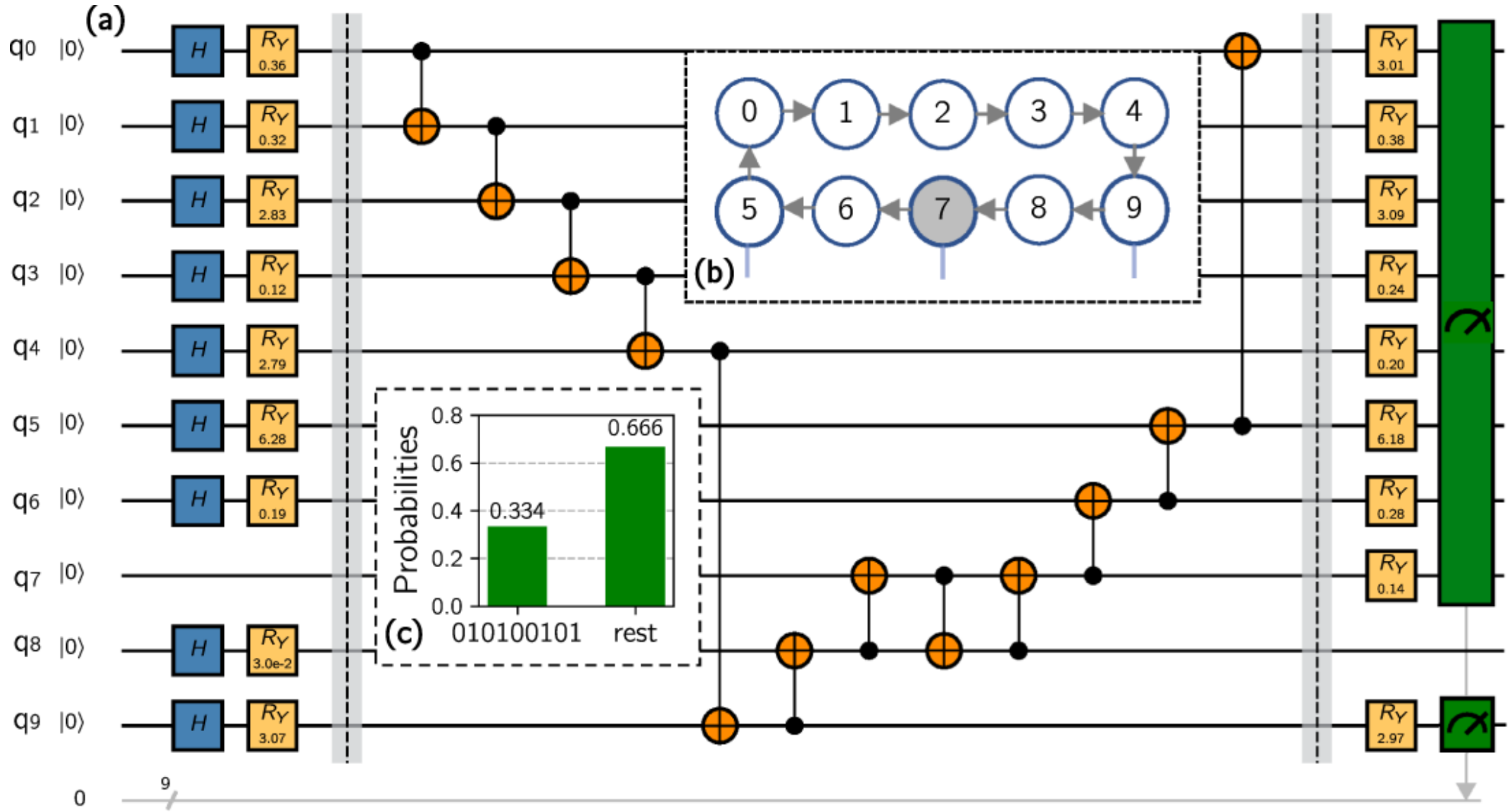
Aproximación con computación cuántica



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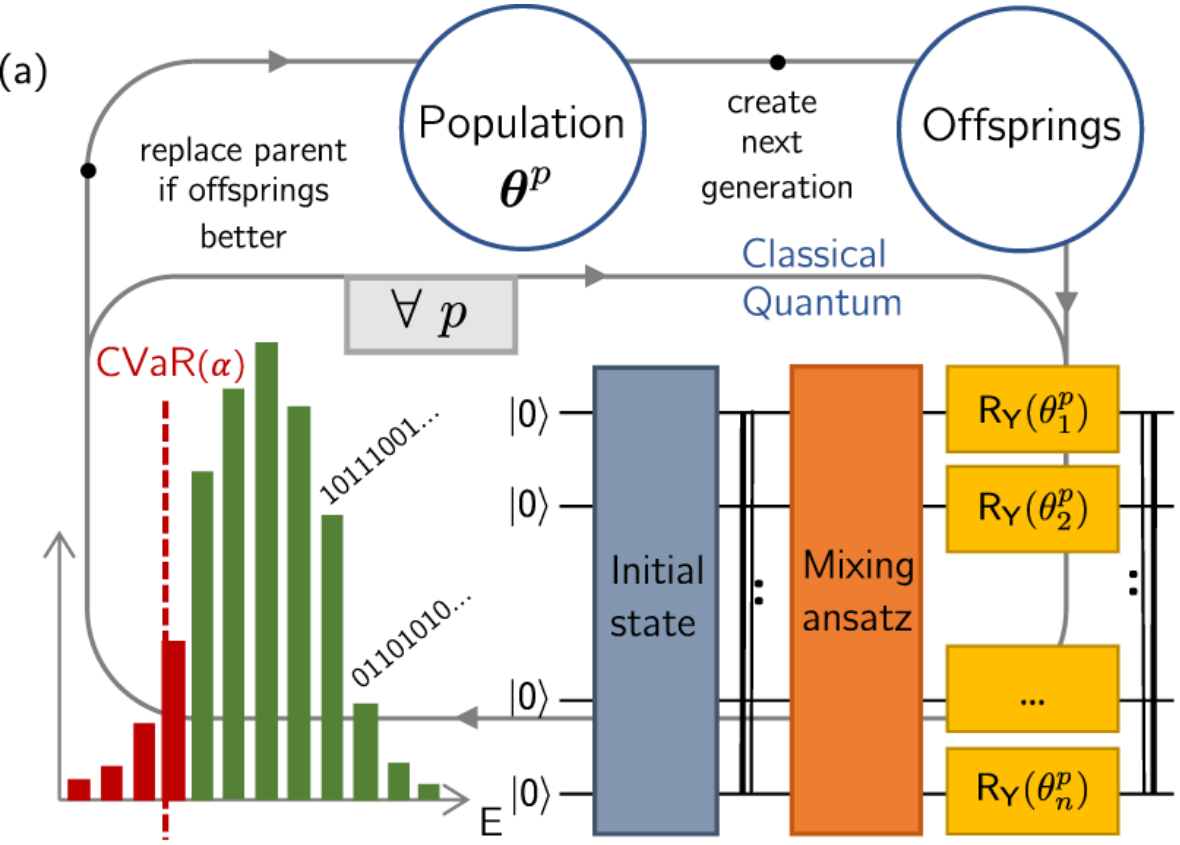
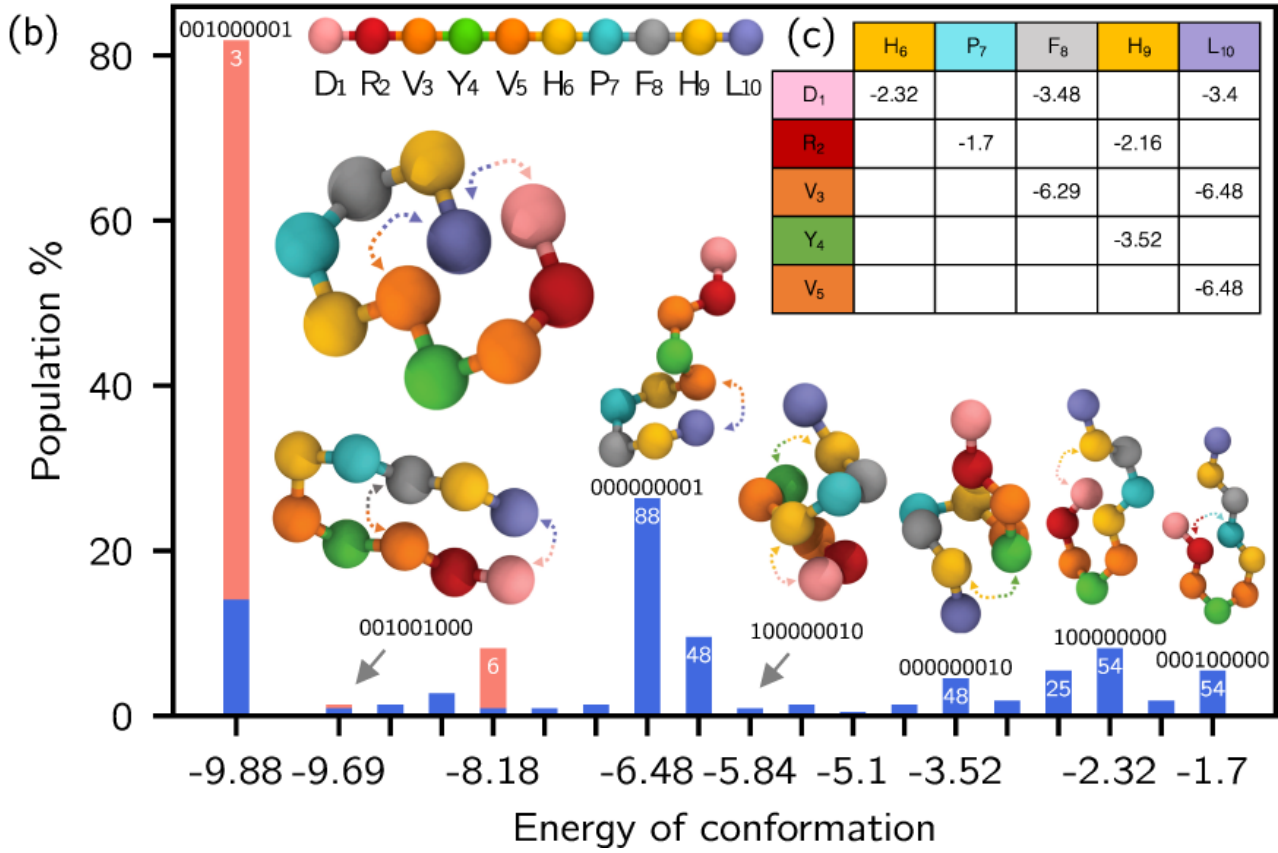
Aproximación con computación cuántica





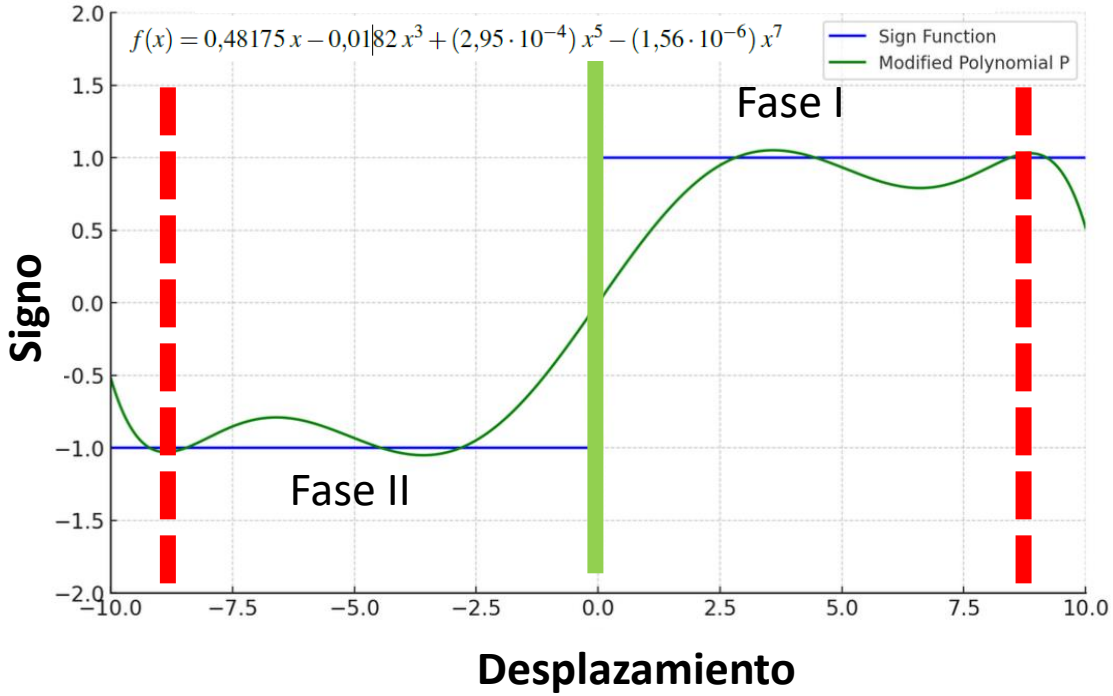
	H_6	P_7	F_8	H_9	L_{10}
D_1	-2.32		-3.48		-3.4
R_2		-1.7		-2.16	
V_3			-6.29		-6.48
Y_4				-3.52	
V_5					-6.48

Implementación de una interfase

Fauchère, J., and Pliska, V. **1983**. Hydrophobic parameters of amino-acid side chains from the partitioning of N-acetyl-amino-acid amides. *Eur. J. Med. Chem*. 8: 369–375

Nomenclatura, grado de hidrofobicidad y comportamiento en disolución de los aminoácidos naturales			
Código de 3 letras	Código de 1 letra	Hidrofobicidad	Comportamiento
ASP	D	-0.77	ácido
GLU	E	-0.64	ácido
LYS	K	-0.99	básico
ARG	R	-1.01	básico
HIS	H	0.13	básico
HISH	H	0.13	básico
GLY	G	0.00	hidrofóbico
ALA	A	0.31	hidrofóbico
VAL	V	1.22	hidrofóbico
LEU	L	1.70	hidrofóbico
ILE	I	1.80	hidrofóbico
PRO	P	0.72	hidrofóbico
PHE	F	1.79	hidrofóbico
MET	M	1.23	hidrofóbico
TRP	W	2.25	hidrofóbico
SER	S	-0.04	polar
THR	T	0.26	polar
CYS	C	1.54	polar
TYR	Y	0.96	polar
ASN	N	-0.60	polar
GLN	Q	-0.22	polar

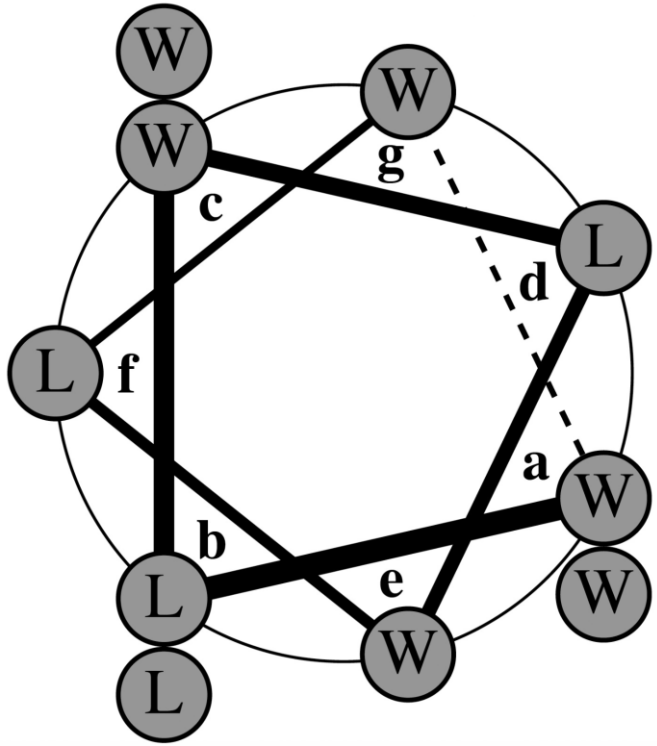
Aproximación de Chebyshev



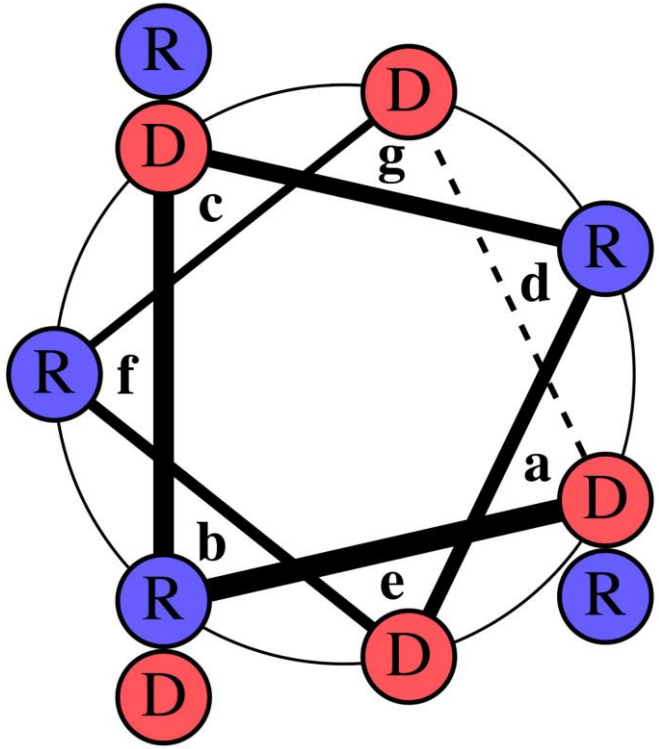
$$H(\mathbf{q}) = H_{\mathrm{gc}}(\mathbf{q}_{\mathrm{cf}}) + H_{\mathrm{ch}}(\mathbf{q}_{\mathrm{cf}}) + H_{\mathrm{in}}(\mathbf{q}) + H_{\mathrm{fase}}(\mathbf{q})$$

$$H_{\mathrm{fase}}(\mathbf{q}) = \sum (\Delta\text{polaridad} \cdot \text{signo} \cdot \mathrm{K})_a$$

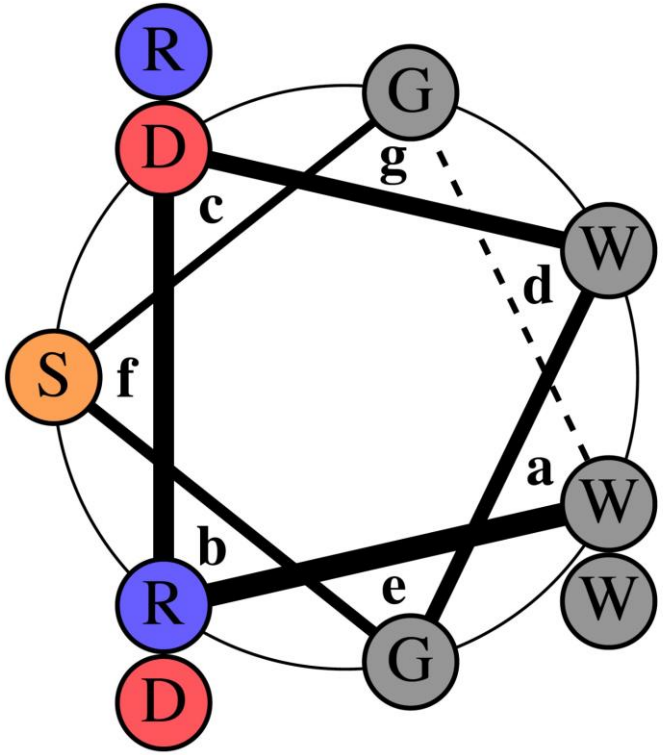
Sistemas de prueba



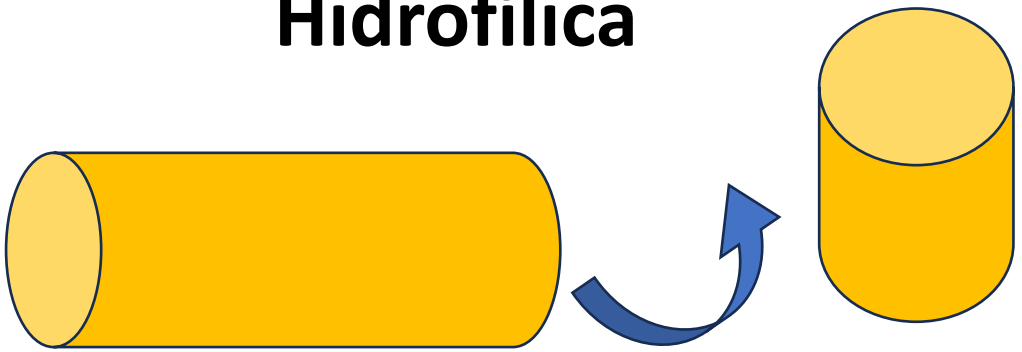
Hidrofóbica



Hidrofílica



Anfifílica



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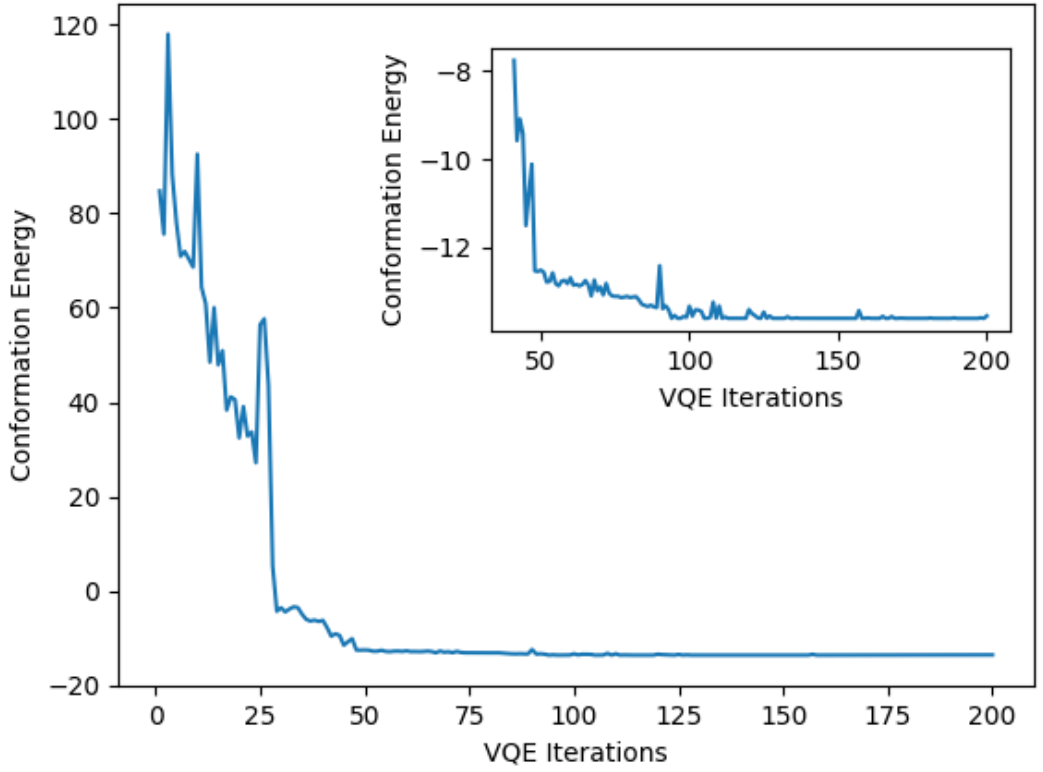
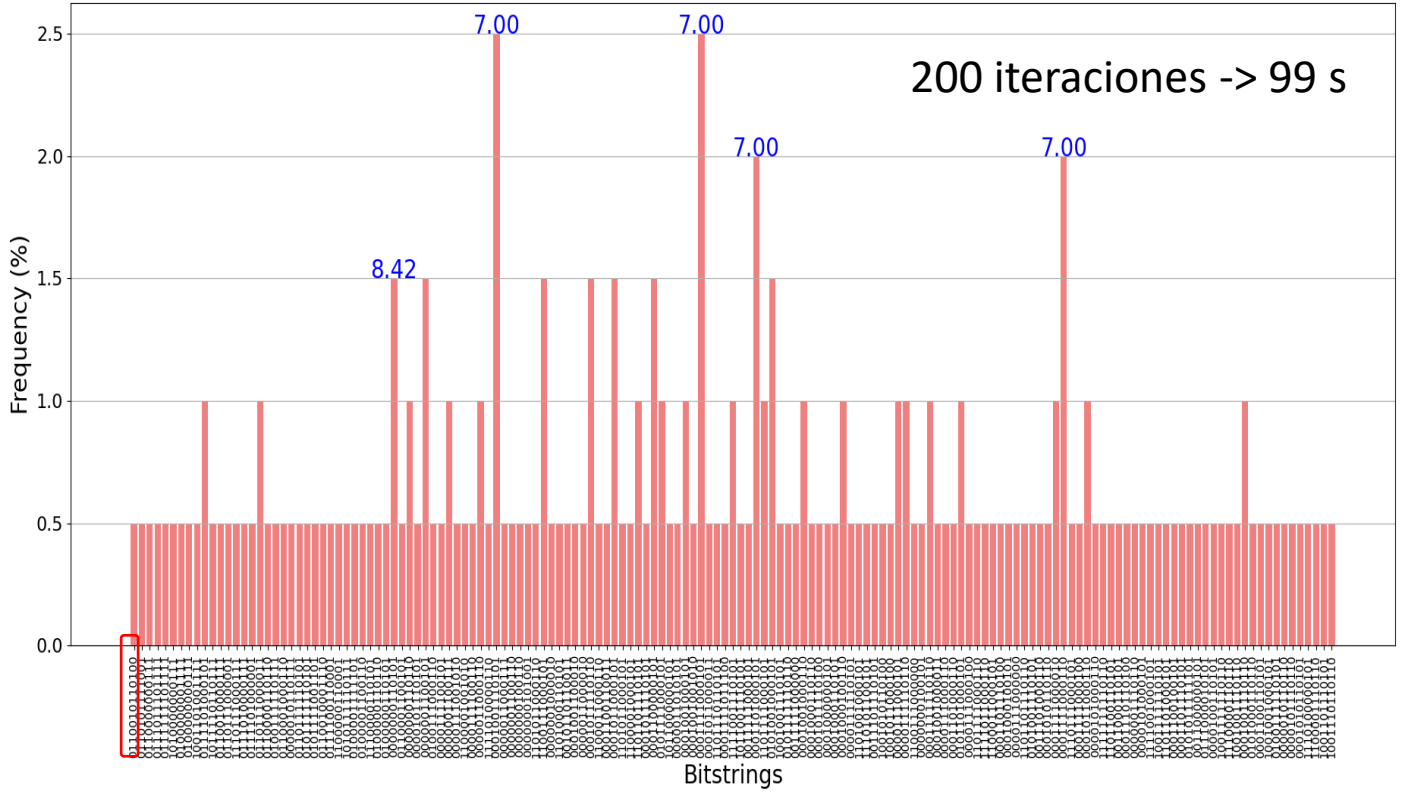
Resultados





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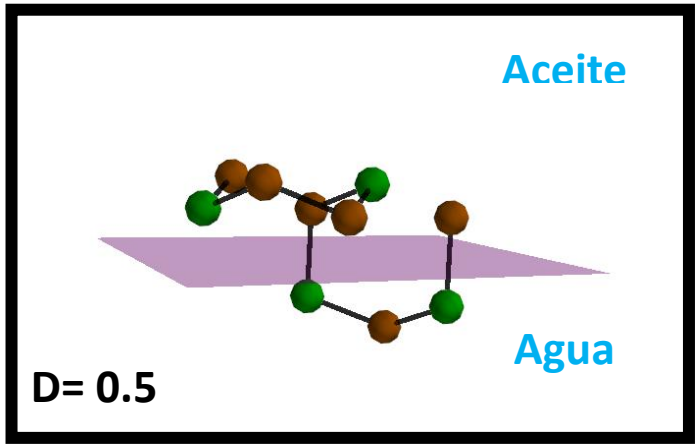
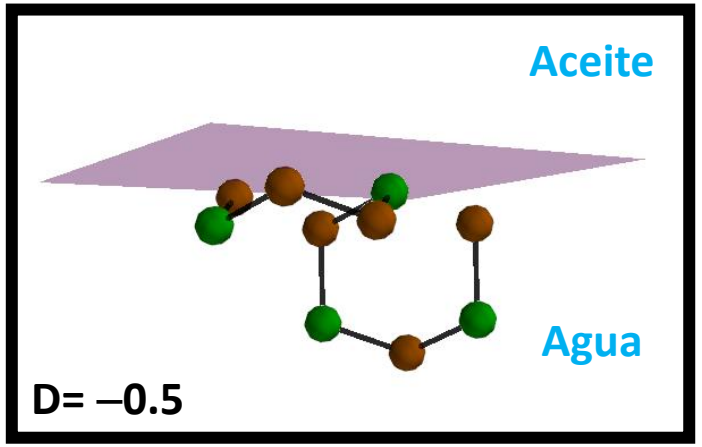
Resultados

Hidrofóbica





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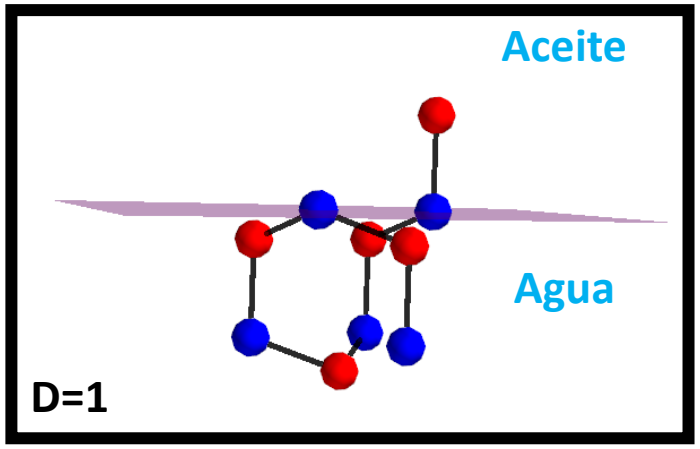

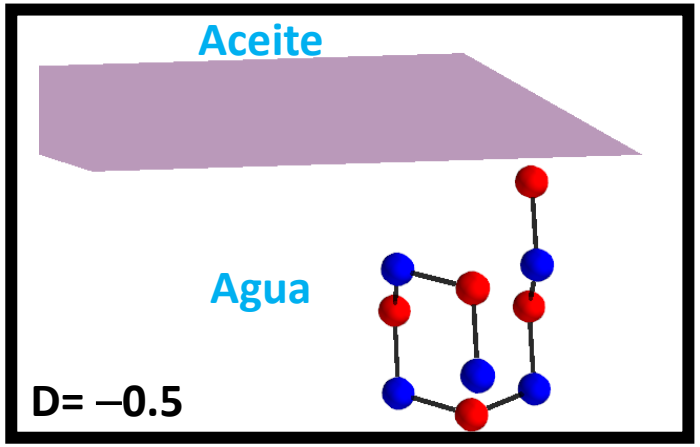

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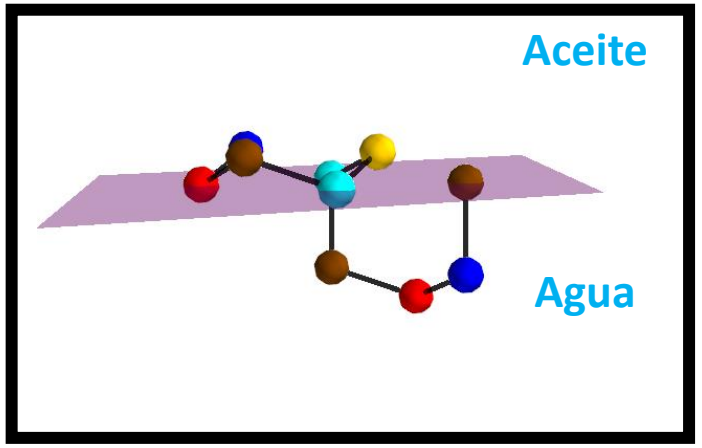

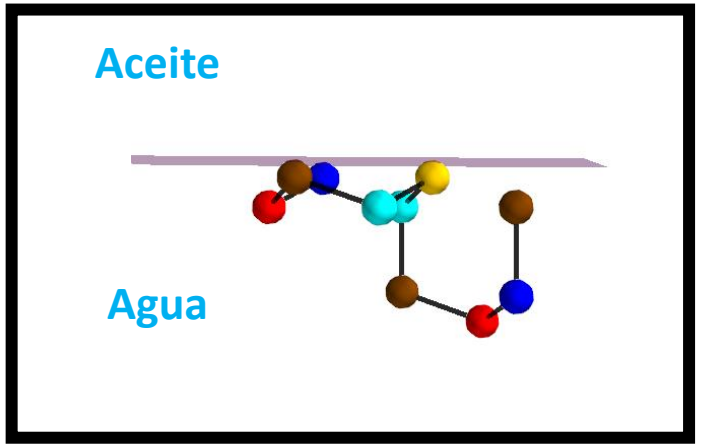

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Conclusiones

- **Ventaja cuántica** en problemas de plegamiento de péptidos → **eficiencia de muestreo**, principalmente cuando crece el número de aminoácidos ya que el espacio de posibles soluciones crece exponencialmente.

- **Hemos conseguido implementar el efecto de una interfase** que separa dos medios de diferente polaridad, para modelar la superficie de una membrana.

- Nuestra **implementación de la interfase es eficiente**, ya que no precisa aumentar el número de qubits.

- El modelo tiene **muchas aproximaciones** que hacen que los resultados todavía no sean útiles desde el punto de vista práctico, principalmente por el **reducido número de partículas** que se pueden modelar y por la **aproximación discreta** de las posiciones de estas partículas.

- **Muchas oportunidades de optimización** utilizando nuevos algoritmos de computación cuántica y grandes expectativas en mejora de hardware.

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XUNTA DE GALICIA

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CESGA
Centro de Supercomputación de Galicia

USC UNIVERSIDADE DE SANTIAGO DE COMPOSTELA

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