

# Computer simulations of the kinetics of peptide-HLA detachment

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## Abstract

Peptide - HLA complex is widely studied from different points of view. Due to disposing of structural and binding data (IC50), the system is ideal to set up new methods to study the detachment process with computational techniques. In this project we want to set up a technique able to obtain similar information than MD but using less computational resources by using pyrosett<sup>1</sup> to study the detachment of the HLA complex with simulated annealing and Montecarlo<sup>2</sup> techniques. Up to date promising results have been obtained using 100000 steps simulations. The method allows us to describe the path of detachment for each peptide, suggesting that the method could be used to our objective but a larger dynamics is needed.

HLA	SEQ	pIC50	PDB	Ressolution	interval
H2-Db	KAVYNFATC	5.32	1FG2	2.75	3
HLA-B*35:01	LPFEKSTVM	5.96	3LKS	1.90	4
HLA-A*02:01	RQISQDVKL	5.72	4NO5	2.10	4
HLA-A*02:01	SLYNTVATL	5.78	5NME	2.94	4
HLA-B*40:02	REFSKEPEL	6.10	5IEK	1.80	5
HLA-A*68:01	AIFQSSMTK	6.84	4HWZ	2.40	6
HLA-B*07:02	RPPIFIRRL	6.72	5WMO	1.62	6
HLA-A*01:01	EVDPIGHLY	7.58	5BRZ	2.62	8
HLA-A*02:01	SLFNITAVL	7.37	5NMG	2.75	8
HLA-A*03:01	AIFQSSMTK	8.03	3RL1	2.00	9

Set of peptides used to perform the simulations

## Material and methods

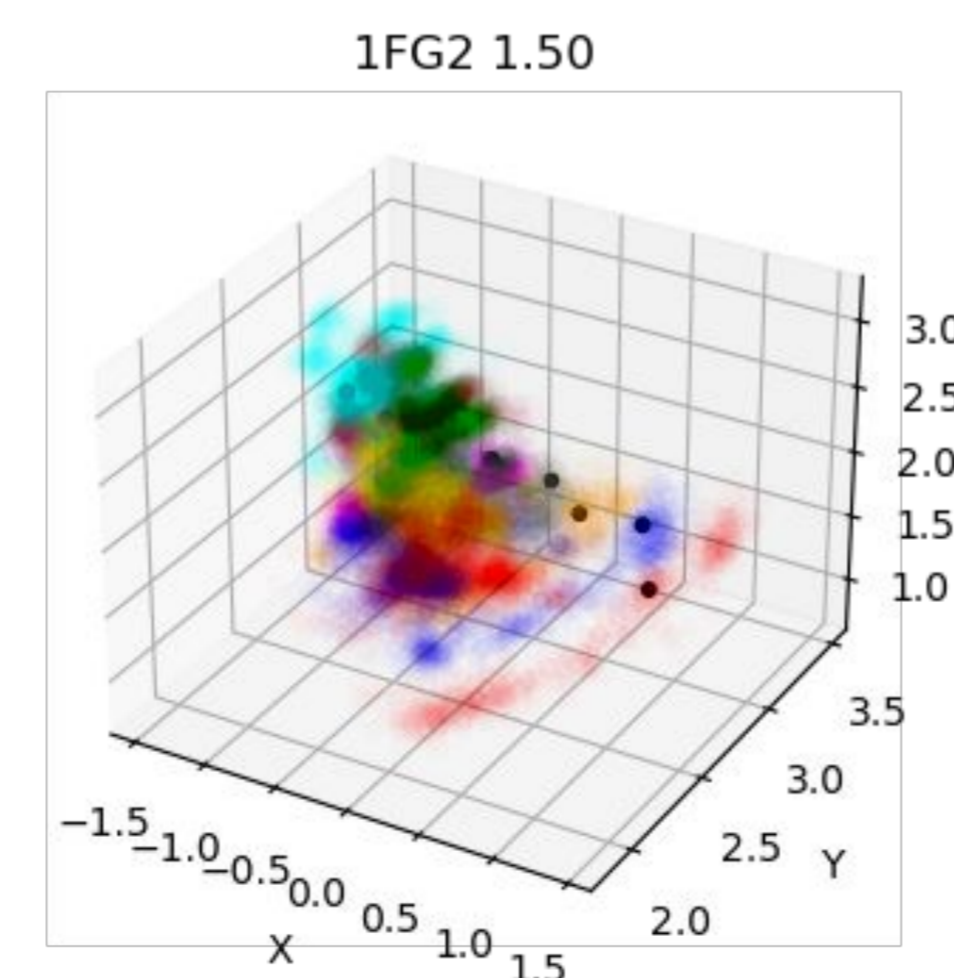
### Peptide Selection

All peptide - HLA complexes annotated at the Immune Epitope database<sup>3</sup> (IEDB) with the IC50 measurement and with crystallographic structures at the PDB. The IC50 values were divided into 10 ranges. Finally, one representant of each range was chosen randomly.

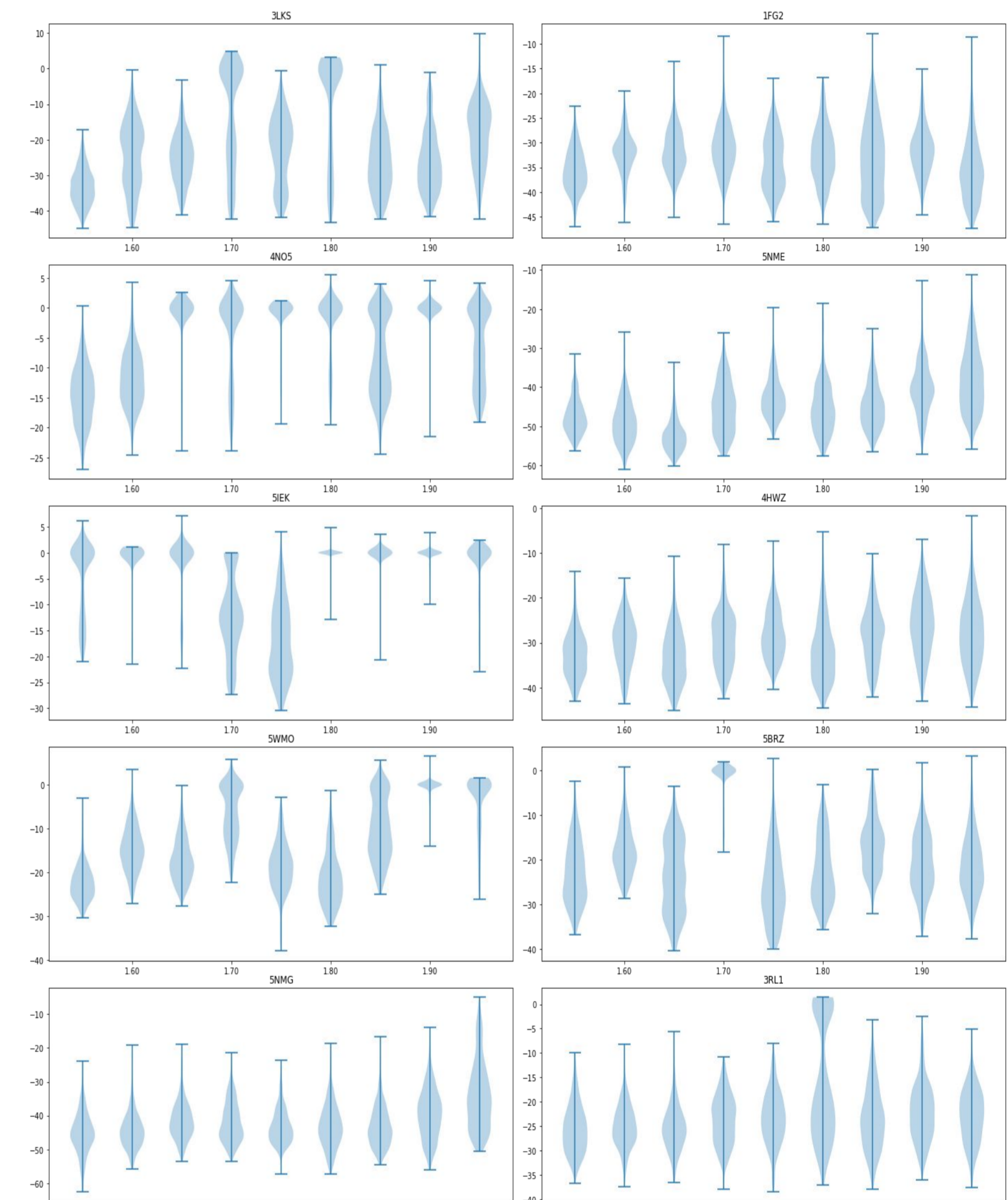
### Annealing simulation

Simulations were performed using the coarse-grain model with the Montecarlo protocol implemented in pyrosetta. A total of 90 simulations, 9 for each peptide. Each of the 9 runs was performed at a different temperature. Each temperature was constant for all the run.

## Results



Representacion of the movement of the peptide inside the HLA pocket



Change of the distribution of the interaction energy between the peptide and the receptor at different increasing temperatures

<sup>1</sup> S. Chaudhury, S. Lyskov & J. J. Gray, "PyRosetta: a script-based interface for implementing molecular modeling algorithms using Rosetta," *Bioinformatics*, **26**(5), 689-691 (2010).

<sup>2</sup> Bernhard Knapp, Samuel Demharer, Charlotte M. Deane, Peter Minary, Exploring peptide/MHC detachment processes using hierarchical natural move Monte Carlo, *Bioinformatics*, Volume 32, Issue 2, 15 January 2016, Pages 181–186.

<sup>3</sup> Vita R, Mahajan S, Overton JA, Dhanda SK, Martini S, Cantrell JR, Wheeler DK, Sette A, Peters B. The Immune Epitope Database (IEDB): 2018 update. *Nucleic Acids Res.* 2018 Oct 24. doi: 10.1093/nar/gky1006