



# Ab initio study of Hyperfine Interactions in Metal Binding Site in Biological Systems: Cd in DNA Bases.

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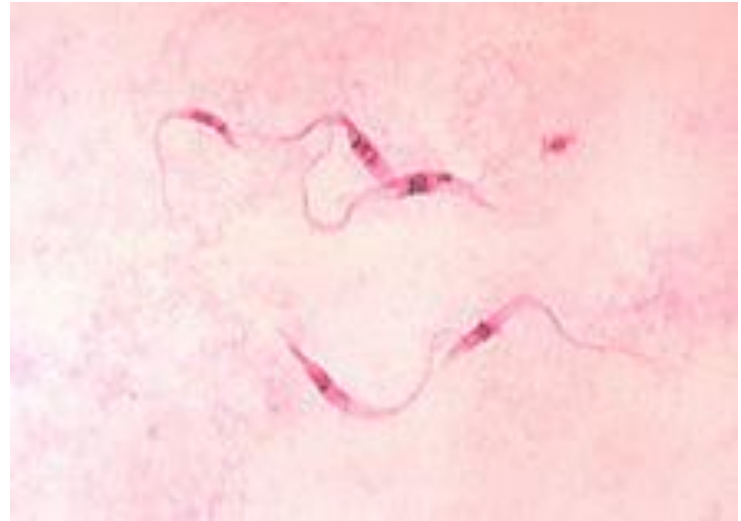
# Motivation

# 1 Chagas disease

Chagas disease, also known as American trypanosomiasis, is a potentially life-threatening illness caused by the protozoan parasite, *Trypanosoma cruzi* (*T. cruzi*).

It is mostly transmitted to humans by the faeces of triatomine bugs, known as “kissing bugs”.

An estimated 10 million people are infected worldwide, mostly in Latin America where Chagas disease is endemic. More than 25 million people are at risk of the disease. It is estimated that in 2008 Chagas disease killed more than 10 000 people.



“The kissing bug” or “the assassin bug”. In Brazil is called “barbeiro”

# Chagas disease

<sup>1</sup>The observation of the difference in the resistance of the people infected with the *T. cruzi* led us to the hypothesis that the host's genetic may influence disease development and survival of patients.

Different species of mice were challenged with different doses of *T. cruzi*.



<sup>1</sup>The objective is to evaluate the pattern of immunoglobulins response present by resistant and susceptible mice to *T. cruzi* as well as lineages developed from the mating between them.

# Work Hypothesis

Hyperfine Interactions can be a powerful tool to identify local environments in many different systems.

The group of prof. Saxena and prof. Carbonari at the Instituto de Pesquisas Energéticas e Nucleares (IPEN), São Paulo, Brazil, used the Time Differential Perturbed Angular Correlation (TDPAC) measurement to investigate the mouse DNA infected with the *Trypanosoma cruzi*.

The  $^{111}\text{In} \rightarrow ^{111}\text{Cd}$  decay can be used in a TDPAC measurement to investigate the Cd metal binding to DNA.

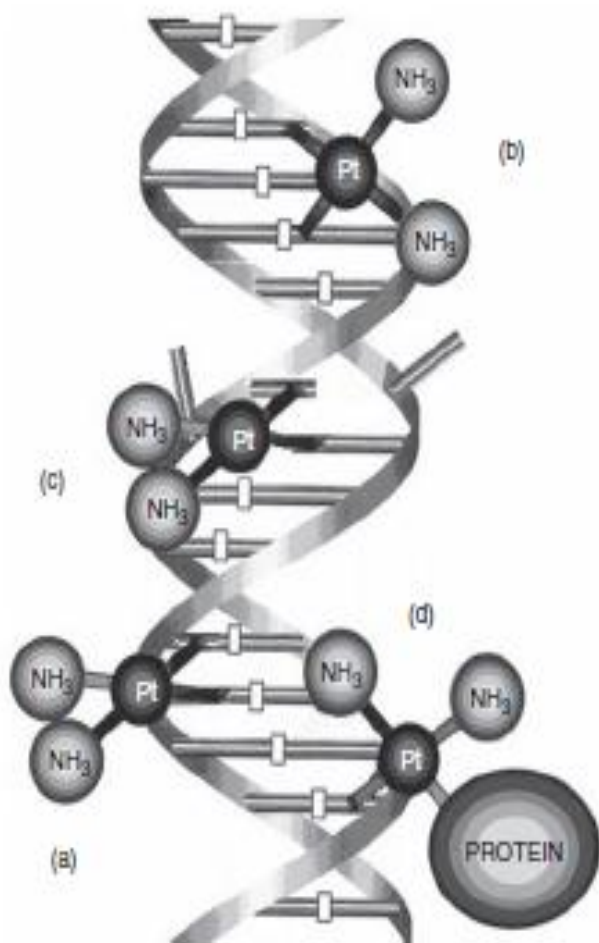
The investigation of Electric Field Gradient (EFG) is interesting because it can help both in interpreting experimental results and to estimate the adequacy of structural models.

See 03 poster

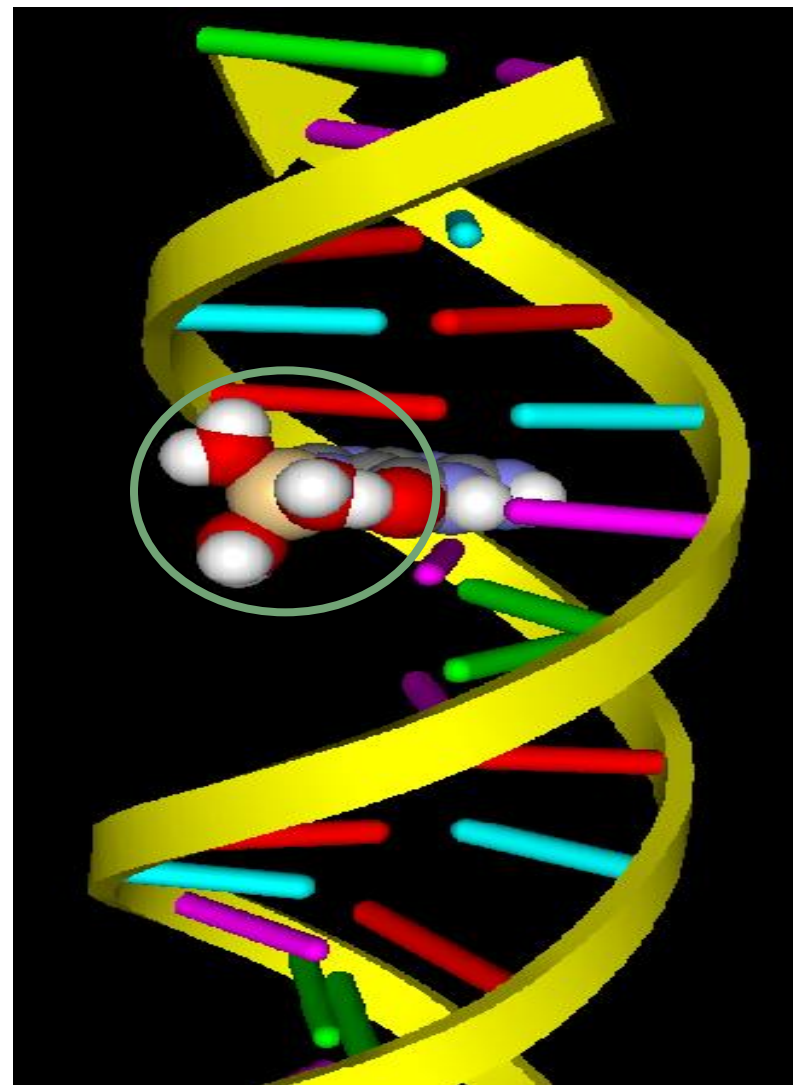
# Objective

Where is the Cd probe in the DNA????

To build a model to explain the interaction of the DNA with the Cd probe.



Scheme proposed for Metal – DNA in literature<sup>1</sup>.



Cd attached to guanine base at DNA.

<sup>1</sup> N. Hadjiliadis, E. Sletten, et. al *Metal Complex- DNA interactions*, Ed. Wiley, United Kingdom, 2009.

# Work Hypotesis

Biological systems are often difficult to study.

DNA is a very large molecule.

And also very **complicated** and **computationally expensive**

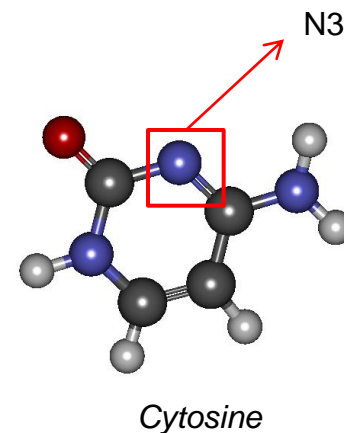
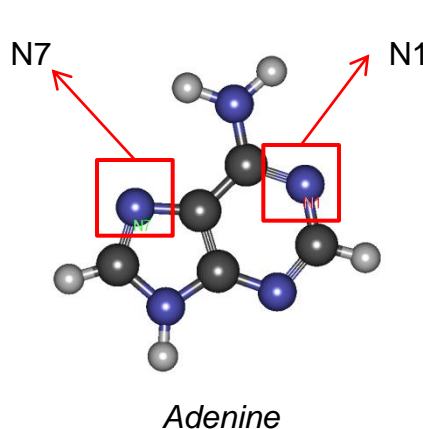
As a first step we study the interactions of Cd with the DNA bases by ab initio electronic structure calculations



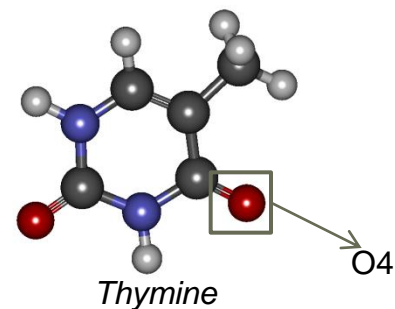
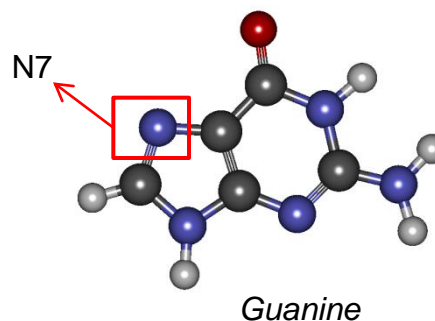
# Work Hypothesis



<sup>1</sup>Metal binding sites on the purine and pyrimidine nucleobases are: guanine N7, adenine N1 and/or N7, cytosine N3 and thymine O4.



<sup>1</sup>The order of stability of 3d transition metal ion – nucleobase complexes are: G > A, C > T.



# Methodology

# Electronic structure calculations :

Calculations is based on the <sup>2</sup>Kohn-Sham scheme of the Density Functional Theory (DFT)

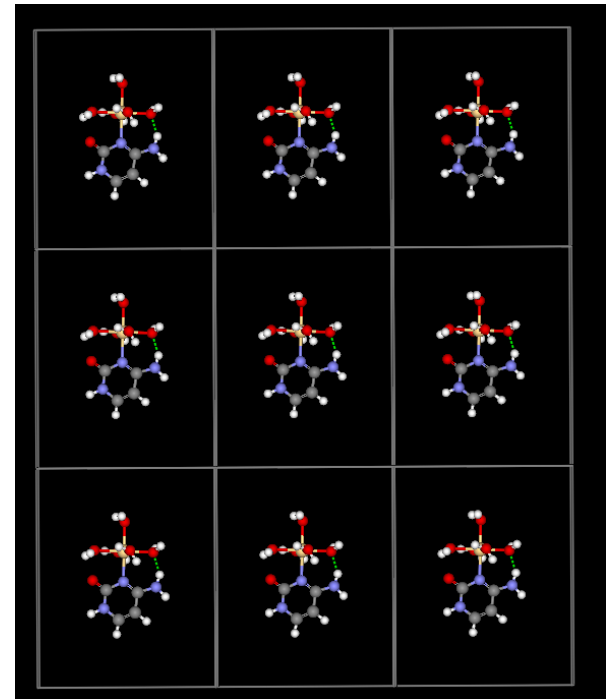
<sup>1</sup>Projector Augmented-Wave Method + Car Parrinello (CP-PAW) code

Periodic unit cells



Calculation parameters:

- Plane Wave cut off: 30Ry
- Non-Spin Polarized (LDA) functional.
- <sup>3</sup>Perdew-Burke-Ernzerhof (PBE) GGA for exchange and correlation



1- P. Blöchl, *Phys. Rev. B.*, **50**, 17953 (1994)

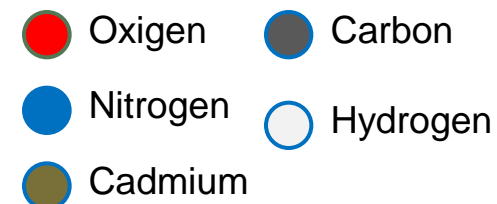
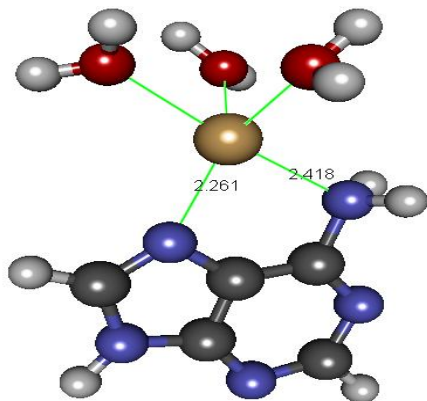
2 - W. Kohn, L. J. Sham, *Phys. Rev. B.*, **140**, 1133 (1965)

3 - *Phys.Rev.Lett* **77**, 3865 (1996)

# Results

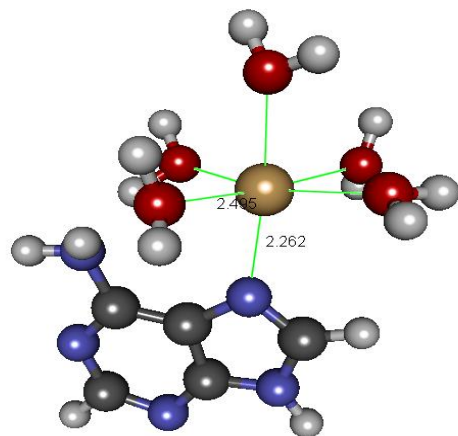
Cd + DNA bases:  
Optimization of the molecular  
structure and EFG results.

# Adenine



## Theoretical Results (CP-PAW)

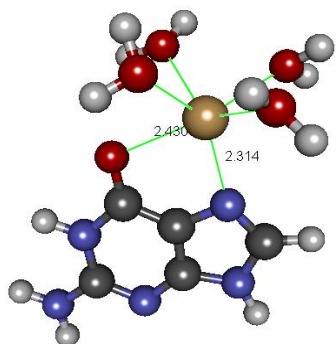
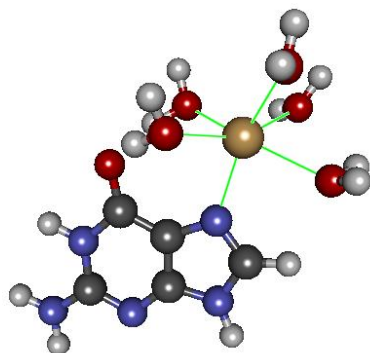
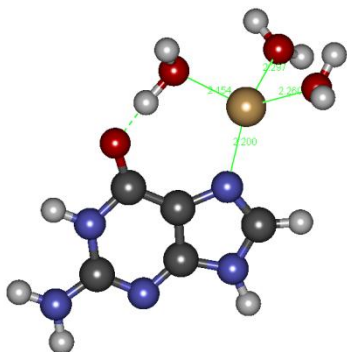
Coordination (ligands with Cd <sup>2+</sup> )	EFG (CP-PAW) [10 <sup>21</sup> V/m <sup>2</sup> ]	Assimetry Parameter (η)	Temperature [K]
5	9,56	0,48	0
6	7,41	0,94	0



## <sup>1</sup>Measurements Results (TDPAC)

EFG (TDPAC) [10 <sup>21</sup> V/m <sup>2</sup> ]	Assimetry Parameter (η)	Temperature [K]
7,14	0,55	77

# Guanine



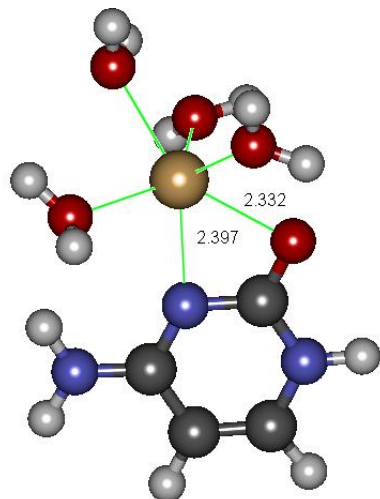
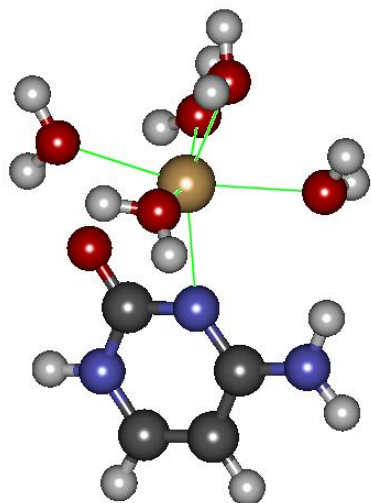
## Theoretical Results (CP-PAW)

Cd coordination	EFG (CP-PAW) [ $10^{21}$ V/m $^2$ ]	Assimetry Parameter ( $\eta$ )	Temperature [K]
4	11,74	0,61	0
6	4,83	0,52	0
6 (with the oxigen)	5,80	0,9	0

## <sup>1</sup>Measurements Results (TDPAC)

EFG (TDPAC) [ $10^{21}$ V/m $^2$ ]	Assimetry Parameter ( $\eta$ )	Temperature [K]
7,55	0,61	77

# Cytosine



## Theoretical Results (CP-PAW)

Coordination (ligands with Cd <sup>2+</sup> )	EFG (CP-PAW) [10 <sup>21</sup> V/m <sup>2</sup> ]	Assimetry Parameter (η)	Temperature [K]
6	5,22	0,14	0
6	8,33	0,50	0

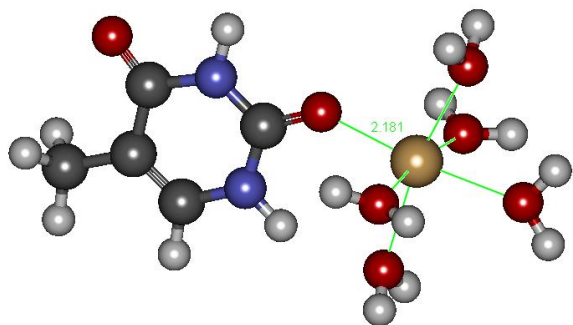
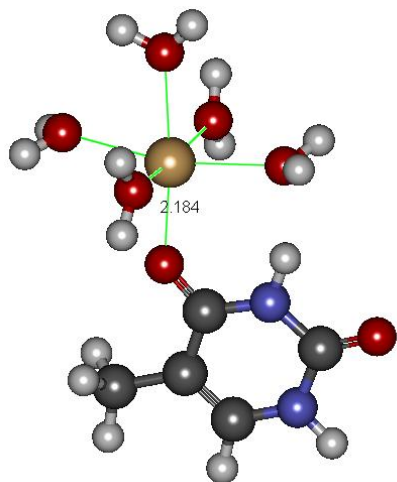
## <sup>1</sup>Measurements Results (TDPAC)

EFG (TDPAC) [10 <sup>21</sup> V/m <sup>2</sup> ]	Assimetry Parameter (η)	Temperature [K]
7,32	0,55	77

# Thymine

## Theoretical Results (CP-PAW)

Coordination (ligands with Cd <sup>2+</sup> )	EFG (CP-PAW) [10 <sup>21</sup> V/m <sup>2</sup> ]	Assimetry Parameter (η)	Temperature [K]
6 (with the oxigen O4)	7,08	0,29	0
6 (with the oxigen O2)	6,17	0,32	0



## <sup>1</sup>Measurements Results (TDPAC)

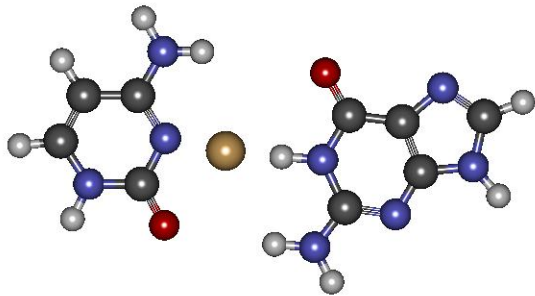
EFG (TDPAC) [10 <sup>21</sup> V/m <sup>2</sup> ]	Assimetry Parameter (η)	Temperature [K]
6,99	0,60	77



# Results

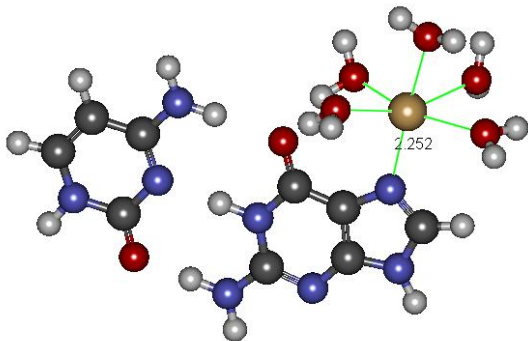
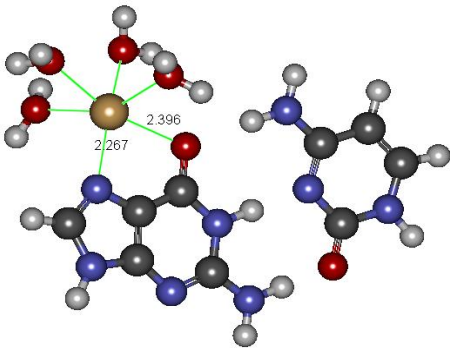
Cd + DNA pair-bases:  
Optimization of the molecule  
structure and EFG results.

# Guanine - Cytosine pair:

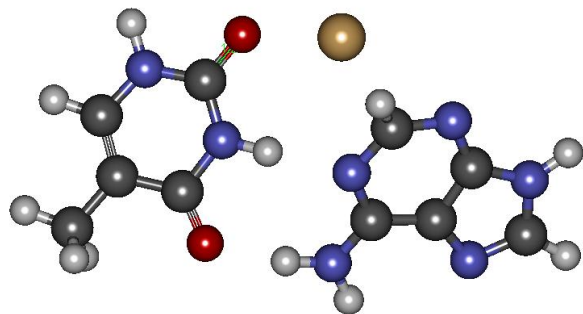


## Theoretical Results (CP-PAW)

Coordination (ligands with Cd <sup>2+</sup> )	EFG (CP-PAW) [10 <sup>21</sup> V/m <sup>2</sup> ]	Assimetry Parameter (η)	Temperature [K]
3	66,80	0,02	0
6 ( with 4 H <sub>2</sub> O)	7,57	0,85	0
6 (with 5 H <sub>2</sub> O)	8.40	0,35	0

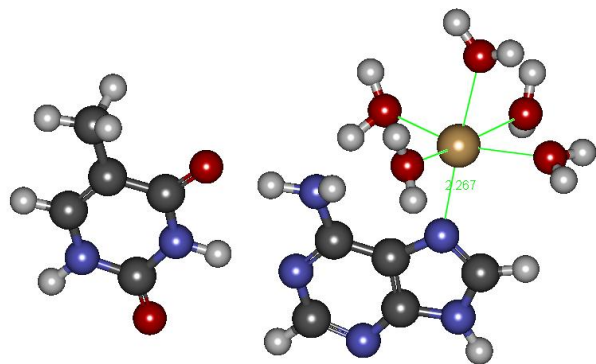


# Thymine-Adenine pair



## Theoretical Results (CP-PAW)

Coordination (ligands with Cd <sup>2+</sup> )	EFG (CP-PAW) [10 <sup>21</sup> V/m <sup>2</sup> ]	Assimetry Parameter (η)	Temperature [K]
2	16,80	0,5	0
6 (with 5 H <sub>2</sub> O)	7.16	0,98	0



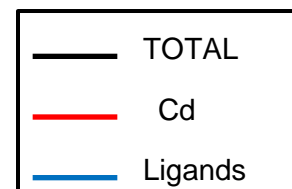
Molecule	Coordination	EFG (CP-PAW) [10 <sup>21</sup> V/m <sup>2</sup> ]	EFG (TDPAC) [10 <sup>21</sup> V/m <sup>2</sup> ]	Assymetry Parameter (η) CP-PAW	Assymetry Parameter (η) TDPAC
Adenine	5	9,56	7,14	0,48	0,55
	6	7,41		0,94	
Thymine	6 (with the oxygen O4)	7,08	6,99	0,29	0,60
	6 (with the oxygen O2)	6,17		0,32	
Thymine - Adenine	2	16,80	-	0,5	-
	6 (with 5 H2O)	7.16		0,98	
Guanine	4	11,74	7,55	0,61	0,61
	6	4,83		0,52	
	6 (with the oxigen)	5,80		0,9	
Cytosine	6	5,22	7,32	0,14	0,55
	6 (with the oxigen	8,33		0,50	
Guanine – Cytosine	3	66,80	-	0,02	-
	6 ( with 4 H2O)	7,57		0,85	
	6 (with 5 H2O)	8.40		0,35	

# Results

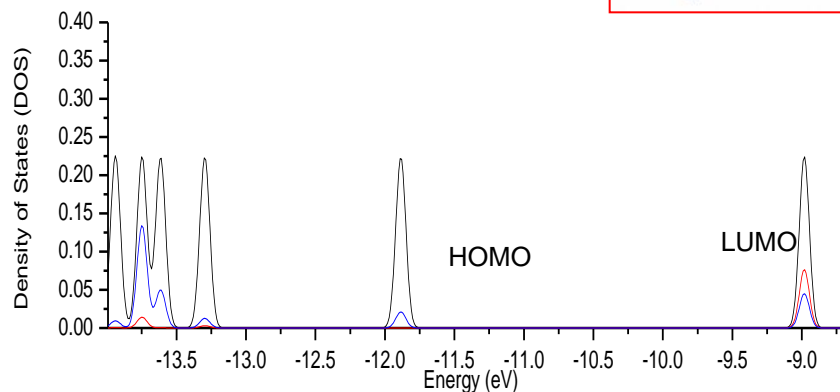
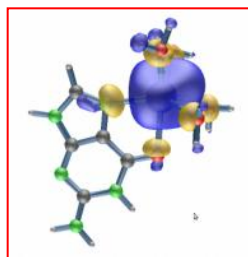
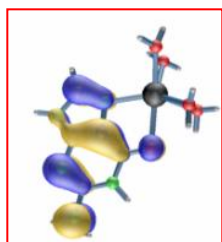
Cd + DNA bases and pair of DNA bases:  
Density of States (DOS) and Kohn-Sham  
orbital's.

# Guanine and Guanine - Cytosine: DOS analysis

4 H<sub>2</sub>O

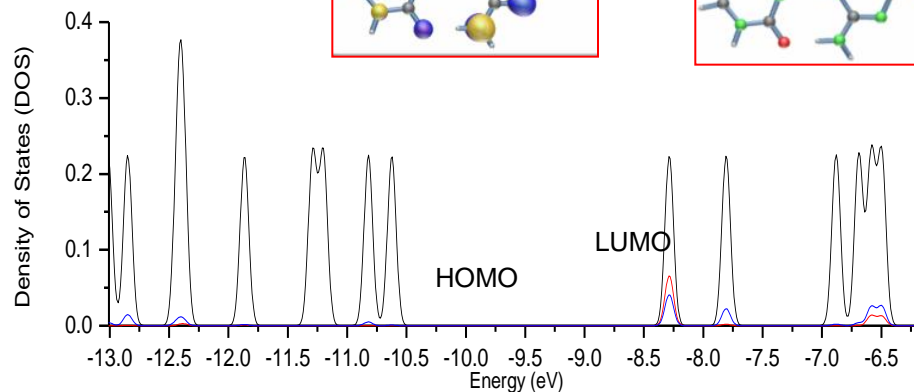
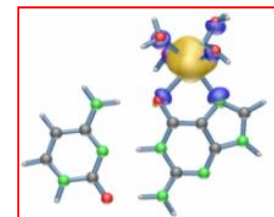
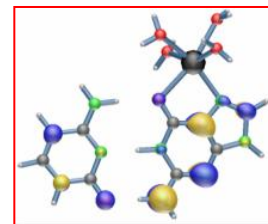


EFG [10 <sup>21</sup> V/m <sup>2</sup> ]	Assimetry Parameter ( $\eta$ )
5,8	0,9



Guanine

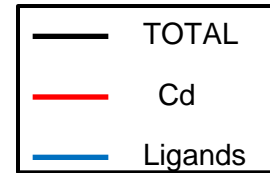
EFG [10 <sup>21</sup> V/m <sup>2</sup> ]	Assimetry Parameter ( $\eta$ )
7,57	0,85



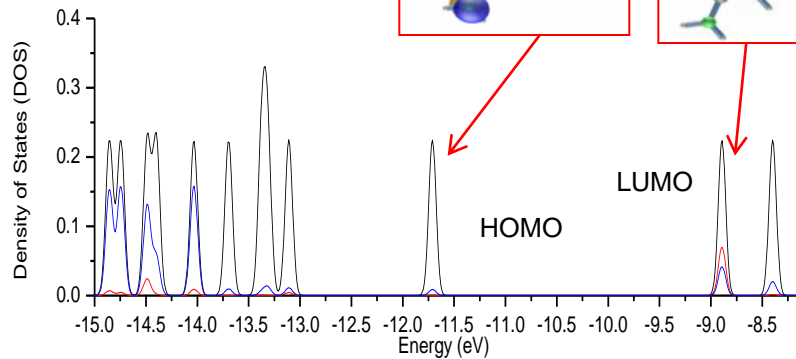
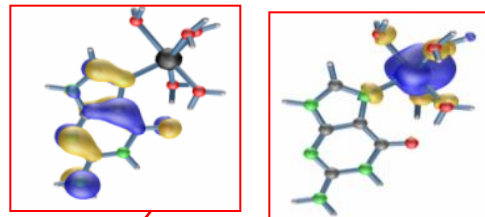
Guanine – Cytosine

# Guanine and Guanine - Cytosine: DOS analysis

5 H<sub>2</sub>O

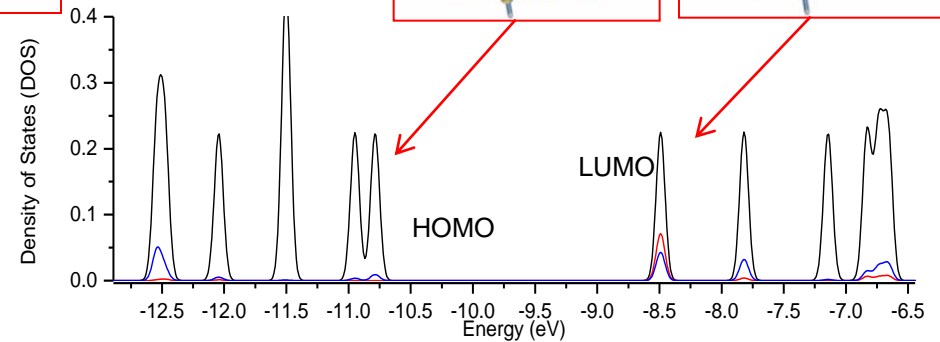
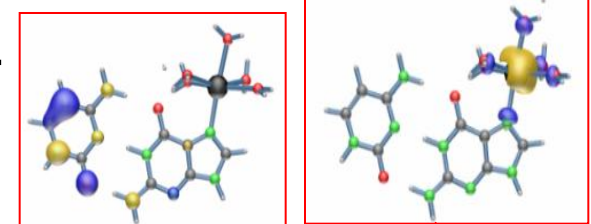


EFG [10 <sup>21</sup> V/m <sup>2</sup> ]	Assimetry Parameter ( $\eta$ )
4,83	0,52



Guanine

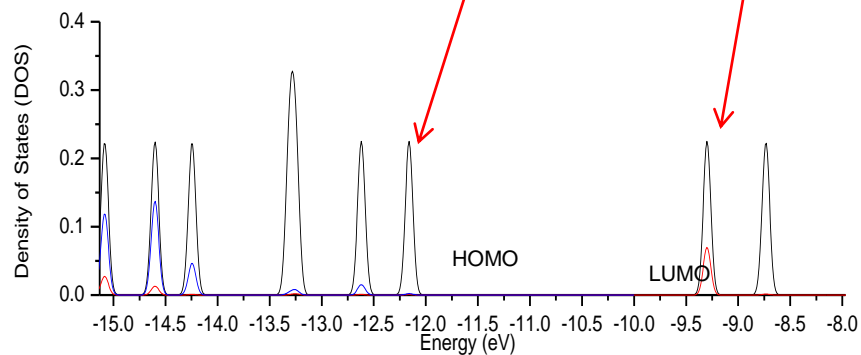
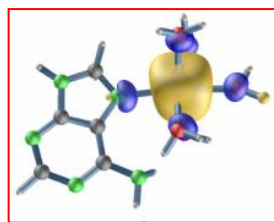
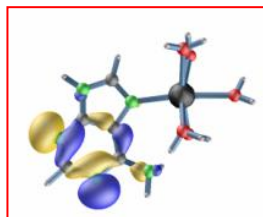
EFG [10 <sup>21</sup> V/m <sup>2</sup> ]	Assimetry Parameter ( $\eta$ )
8,4	0,35



Guanine – Cytosine

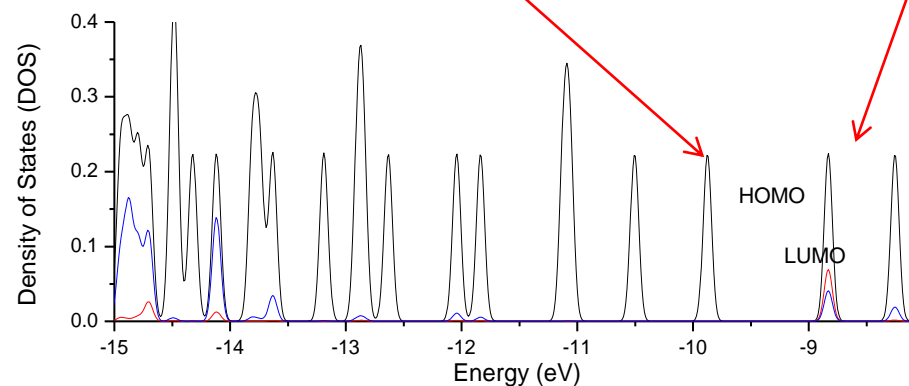
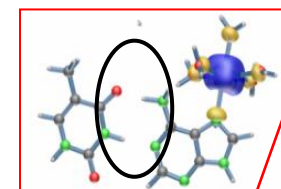
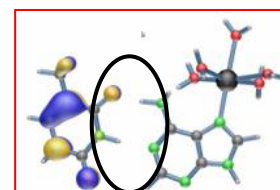
# DOS Analysis of the Guanine and Adenine bases:

EFG [ $10^{21}$ V/m <sup>2</sup> ]	Assimetry Parameter ( $\eta$ )
7,41	0,94

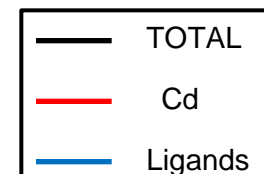


Adenine

EFG [ $10^{21}$ V/m <sup>2</sup> ]	Assimetry Parameter ( $\eta$ )
7,16	0,98



Adenine – Thymine





# Final remarks:

The EFG varies significantly with the coordination of the Cd

We can consider the possibility of the Cd with others coordinations as for example 4 or 5 coordinations.

With the values obtained of the EFG we can say that  $\text{Cd}^{2+}$  is binding in the DNA.

However, further investigation need to be done in order to distinguish the exact Cd location in the DNA.

# Acknowledgements

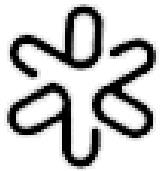


*Grupo Nanomol*



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de ALTO DESEMPENHO EM SÃO PAULO





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Departamento de Física dos Materiais e Mecânica

*Grupo Nanomol*



THANK YOU !!!!!