Universidade Federal da Paraíba

Departamento de Química

Laboratório de Química Quântica Computacional

Grupo de Química Computacional mais Oriental das Américas

L.Q.Q.C. - UFPB - João Pessoa - PB

Aplicação de Métodos de Química-Quântica no Tratamento de Sistemas Biológicos

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Não pulem os capítulos da química quântica !!!!!

Em especial o cap. 2

Métodos·Semi-empíricos·de·Estrutura·Eletrônica·em¶
Química·Quântica¶

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1·Introdução¶

¶

→ A·expressão·"semi-empírico"·foi·utilizada·pela·primeira·vez·em·química·teórica·em·1931·por·Michael·Polanyi·(1891-1976)·e·Henry·Eyring·(1901-1981)**Erro!·Fonte·de·referência·não·encontrada.**[2]·em·sua·tentativa·de·unir·cinética·química,·termodinâmica,·mecânica·quântica·e·a·teoria·da·ligação·de·elétrons·de·valência.·Um·dos·sub-títulos·do·trabalho·era:·"*Halbempirisches·verfahren·zur·schliesslichen·berechnung·der·reaktion*·H·+·H_2·→·H_2·+·H"[1].·A·história·e·os·debates·relacionados·ao·chamado·"método·semi-empírico"·de·London-Eyring-Polanyi·estão·relatados·em·

Chemistry of Complex Systems

Current challenge in quantum chemistry

- **Full quantum chemical treatment of large molecular systems**
  - Bio-molecules (carbohydrates, DNA, proteins, lipids, membranes, etc.)
  - Material (glasses, amorphous solids, crystals, minerals, etc.)
  - Polymers
  - Metal surfaces

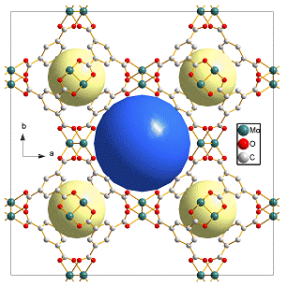
CHEMISTRY

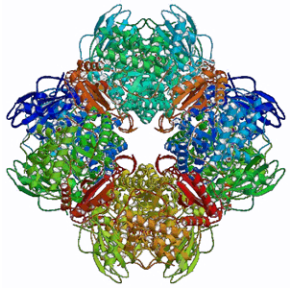
Quantum Chemistry of Complex Systems

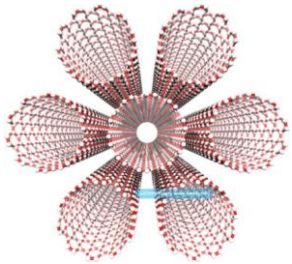
David C. Clary

Progress in developing quantum chemical calculations that describe complex atomic systems has applications in molecular biology, materials science, and chemistry.

www.sciencemag.org SCIENCE VOL 314 13 OCTOBER 2006







The Nobel Prize in Chemistry 2013
Martin Karplus, Michael Levitt, Arieh Warshel

The Nobel Prize in Chemistry 2013

© Harvard University
Martin Karplus

Photo: © S. Fisch
Michael Levitt

Photo: Wikimedia Commons
Arieh Warshel

The Nobel Prize in Chemistry 2013 was awarded jointly to Martin Karplus, Michael Levitt and Arieh Warshel *"for the development of multiscale models for complex chemical systems"*.

Estratégias

1. Novas estratégias teóricas (parametrização e métodos) ;
2. Algoritmos que escalonem linearmente na CPU e na memória;
3. Computadores rápidos e em paralelo.

Novos métodos e Parametrizações

Métodos de estrutura eletrônica

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

The Schrodinger equation was discovered in 1926 by Erwin Schrodinger, an Austrian theoretical physicist. It is an important equation that is fundamental to quantum mechanics.

- Hamiltoniano para um sistema com N-partículas

$$\hat{H} = \hat{T} + \hat{V}$$

Soma das energias cinética (T) e potencial (V)

$$\hat{T} = \sum_{i=1}^{N} \hat{T}_i = -\sum_{i=1}^{N} \frac{\hbar^2}{2m_i} \nabla_i^2 = -\sum_{i=1}^{N} \frac{\hbar^2}{2m_i} \left(\frac{\partial^2}{\partial x_i^2} + \frac{\partial^2}{\partial y_i^2} + \frac{\partial^2}{\partial z_i^2} \right)$$

Energia cinética

$$\nabla_i^2 = \left(\frac{\partial^2}{\partial x_i^2} + \frac{\partial^2}{\partial y_i^2} + \frac{\partial^2}{\partial z_i^2} \right)$$

Operador Laplaciano

$$\hat{V} = -\sum_{A=1}^{NA} \sum_{j=1}^{N} \frac{Z_A}{r_{Aj}} + \sum_{i=1}^{N} \sum_{j>1}^{N} \frac{1}{r_{ij}}$$

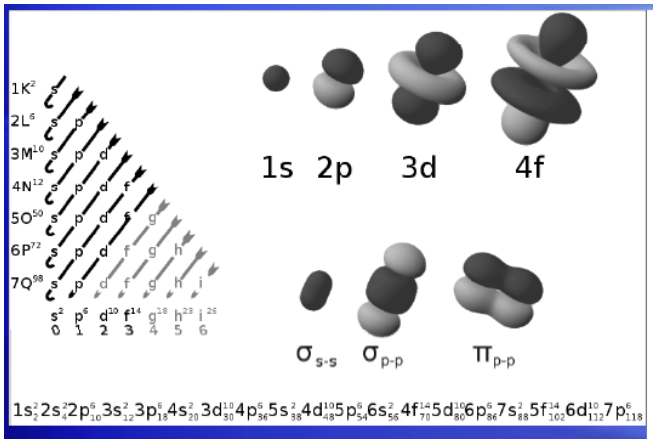
Energia potencial

Métodos de estrutura eletrônica

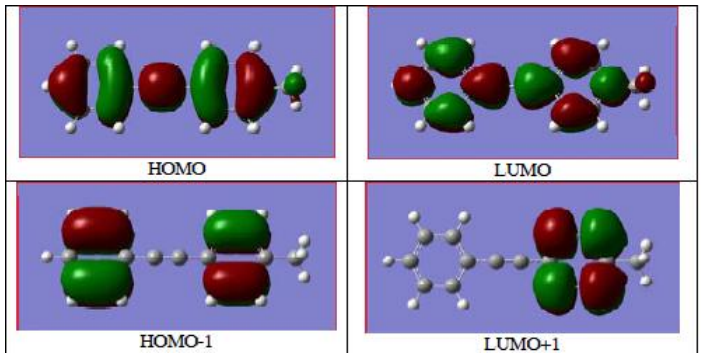
- Função de onda

$$\Phi_{SD} = \begin{vmatrix} \phi_1(1) & \phi_2(1) & \cdots & \phi_N(1) \\ \phi_1(2) & \phi_2(2) & \cdots & \phi_N(2) \\ \cdots & \cdots & \cdots & \cdots \\ \phi_1(N) & \phi_2(N) & \cdots & \phi_N(N) \end{vmatrix}, \quad \langle \phi_i | \phi_j \rangle = \delta_{ij}$$

Orbitais Atômicos



$$\phi_\mu = \sum_{i=1}^{n} c_{i\mu}\varphi_i$$



Orbitais Moleculares

Mono-determinantal → Hartree-Fock

Multi-determinantal → Métodos pós-Hartree-Fock

Combinação linear de determinantes $\Psi = \sum \Phi_{SD}$

Modelo de Hartree-Fock-Roothaan

A expressão da energia será:

$$E = 2\sum_{i}^{n}\sum_{\mu}\sum_{\nu} c_{\mu}^{(i)} c_{\nu}^{(i)} h_{\mu\nu} + \sum_{i}^{n}\sum_{j}^{n}\sum_{\mu\nu\lambda\sigma} c_{\mu}^{(i)} c_{\nu}^{(j)} c_{\lambda}^{(i)} c_{\sigma}^{(j)} \left(2(\mu\nu\,|\,\lambda\sigma) - (\mu\sigma\,|\,\nu\lambda)\right)$$

Vamos definir a quantidade:

$$P_{\mu\nu} = 2\sum_{i}^{n} c_{\mu}^{(i)} c_{\nu}^{(i)}$$

⇒ **Matriz densidade**

Teremos assim:

$$E = \sum_{\mu\nu} P_{\mu\nu} h_{\mu\nu} + \frac{1}{2}\sum_{\mu\nu\lambda\sigma} P_{\mu\nu} P_{\lambda\sigma} \left((\mu\nu\,|\,\lambda\sigma) - \frac{1}{2}(\mu\sigma\,|\,\nu\lambda) \right)$$

$$\sum_{\nu} \left(F_{\mu\nu} - \varepsilon_i S_{\mu\nu}\right) c_{\nu}^{(i)} = 0 \therefore \mu = 1,2,3,\cdots$$

$$F_{\mu\nu} = h_{\mu\nu} + \sum_{\lambda\sigma} P_{\lambda\sigma} \left((\mu\nu\,|\,\lambda\sigma) - \frac{1}{2}(\mu\sigma\,|\,\nu\lambda) \right)$$

Forma matricial

$$\mathbf{FC} = \mathbf{SC}\varepsilon$$

Equação de autovalores generalizada

Semiempirical Theory

Zero differential overlap - ZDO

$$\int \varphi^{*}_{\mu_A}(1)\varphi_{\nu_B}(1)d\tau_1 = 0 \quad \mu_A \neq \nu_B$$

Integral approximations

CNDO

$$(\mu_A\nu_B \mid \lambda_C\sigma_D) = (\mu_A\mu_A \mid \lambda_C\lambda_C)\delta_{\mu\nu}\delta_{\lambda\sigma}\delta_{AB}\delta_{CD}$$

INDO

$$(\mu_A\nu_B \mid \lambda_C\sigma_D) = (\mu_A\nu_A \mid \lambda_C\sigma_C)\delta_{\mu_A\nu_B}\delta_{\lambda_C\sigma_D}$$

NDDO

$$(\mu_A\nu_B \mid \lambda_C\sigma_D) = (\mu_A\nu_A \mid \lambda_C\sigma_C)\delta_{AB}\delta_{CD}$$

Parameterization procedure:

Adjusted using numerical procedures

From experiments or high level calculations

Parametrization procedure

Define o poder preditivo dos métodos semi-empíricos

Temos que decidir sobre :

- Função custo;
- Molecular data set;
- Propriedades moleculares;
- Algoritmos de otimização (busca de mínimo global);

$$F^{resp} = \sum_{i=1}^{n} \left(X_i^{Calc} - X_i^{Exp} \right)^2 \cdot w_i^2$$

Property	Weight
Heat of formation (ΔH_f)	1 kcal^{-1} mol
Ionization Potential (IP)	10 eV^{-1}
Dipole Moment (μ)	20 D^{-1}
Bond Length (R_{ab})	100 Å^{-1}
Angle (θ_l)	2/3 degree^{-1}
Torsion angle (θ_d)	1/3 degree^{-1}

Recife Model 1 (RM1)

Formalismo – NDDO/AM1

- Átomos
  - **C, H, N, O** ← **Organic Chemistry**
  - **P, S** ← **Biochemistry**
  - **F, Cl, Br, I** ← **Drugs**
  - **Lantanídeos** ← **Photonics and Medicine**
- 191 + 252 = 443 parâmetros

WILEY InterScience® DISCOVER SOMETHING GREAT

RM1: A Reparameterization of AM1 for H, C, N, O, P, S, F, Cl, Br, and I

GERD B. ROCHA,[1] RICARDO O. FREIRE,[1] ALFREDO M. SIMAS,[1] JAMES J. P. STEWART[2]
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 J Comput Chem 27: 1101–1111, 2006

271 citações 19.07.2014 (web of Science)

www.rm1.sparkle.pro.br

RM1 Semiempirical Molecular Orbital Model - Windows Internet Explorer

http://www.rm1.sparkle.pro.br/

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RM1 Semiempirical Molecular Orbital Model

Página | Segurança | Ferramentas

RM1 Semiempirical Molecular Orbital Model

中文 | 日本語 | 한국어 | ไทย

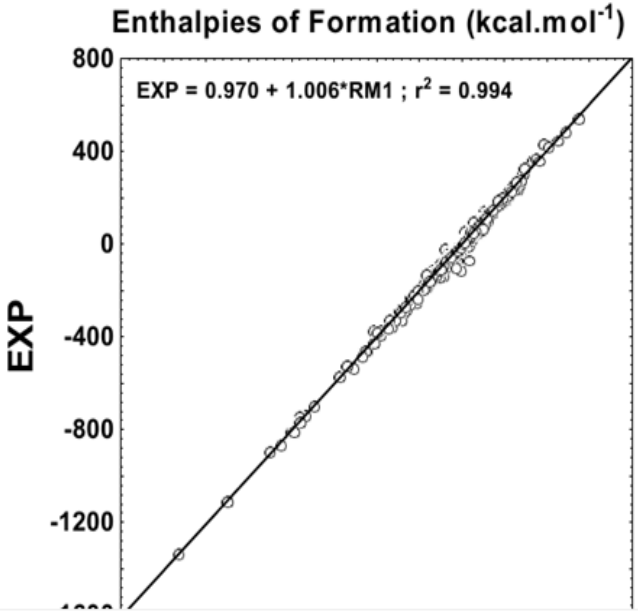
- RM1 x AM1, PM3, PM5
- RM1 software
  - MOPAC2009
  - MOPAC - earlier
  - Spartan'08
  - AMPAC
  - AMBER
  - HyperChem
  - PCGAMESS/Firefly
  - pDynamo
  - Phenix eLBOW
  - ConGENER
  - GAMESS-US
  - Gaussian 09
  - Gaussian - earlier
  - GROMACS
  - Ghemical
  - CambridgeSoft
  - WebMO
  - Winmostar
  - MATEO
  - SimuPac
- Recent articles
- Books
- RM1 research topics
  - QSAR
  - ADME-Tox
  - Barrier height
  - Calixarene
  - Cavitand
  - CI

Scholarly article

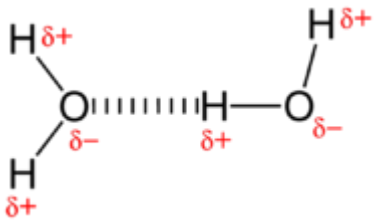
RM1: a Reparameterization of AM1 for H, C, N, O, P, S, F, Cl, Br, and I

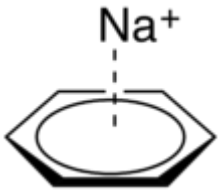
Gerd Bruno Rocha, Ricardo Oliveira Freire, Alfredo Mayall Simas*, and James J. P. Stewart.

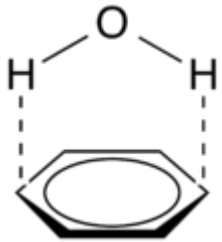
Journal of Computational Chemistry 27(10), 1101-1111, 2006

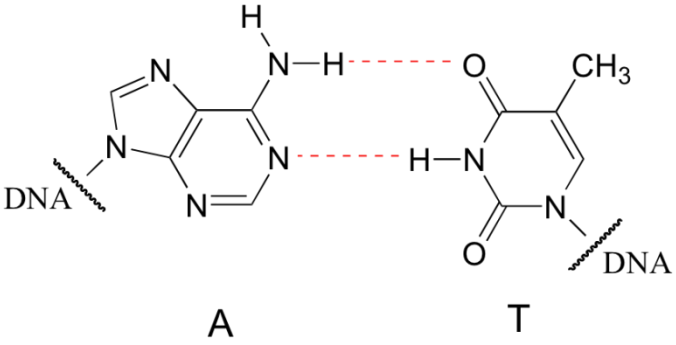


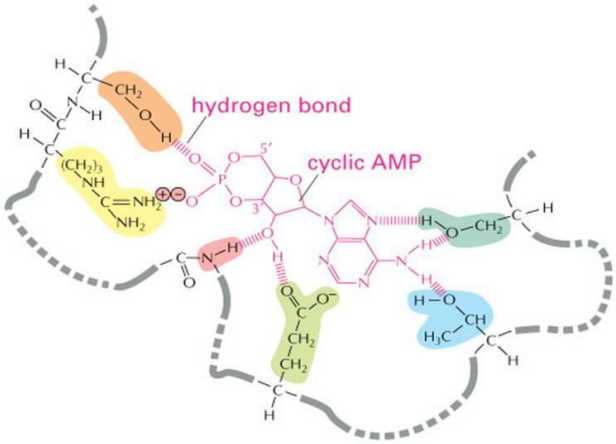
Non-covalent interactions

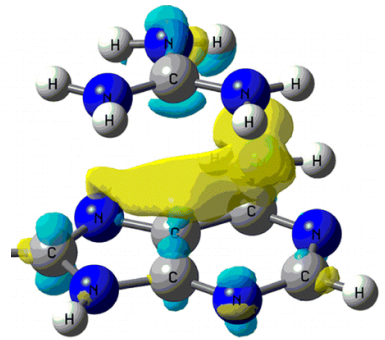












DOI: 10.1021/jp407339v

- Em geral os métodos quânticos de baixo custo falham em descrever essas interações: semiempiricos, DFT, RHF, etc..

Métodos com correção de ligações não covalentes

A idéia principal por parte do método DFT-D [Grimme, S., *J. Comput. Chem.*, **25** (2004) 1463.] é adicionar correções de dispersão após o cálculo da energia total convergida.

$$E_{DFT-D} = E_{DFT} + E_{disp}$$

$$E_{disp} = -s_6 \sum_{i=1}^{N_{at}-1} \sum_{j=i+1}^{N_{at}} \frac{C_6^{ij}}{R_{ij}^6} f_{dump}(R_{ij}) \qquad C_6^{ij} = 2 \cdot \frac{C_6^i C_6^j}{C_6^i + C_6^j}$$

Aqui, N_{at} é o número de átomos no sistema, C_6 denota coeficientes de dispersão para o par de átomos *ij*, s_6 é um parâmetro multiplicativo global e R_{ij} é a distância interatômica. Uma função, f_{dump}, é adicionada para evitar singularidades.

$$f_{dump}(R_{ij}) = \frac{1}{1 + e^{-\alpha\left(\frac{R}{R_0} - 1\right)}}$$

Essa função introduz mais um parâmetro ajustável, o α. E a quantidade R_0 é obtida a partir da soma dos raios de van der Waals do par atômico envolvido.

Non-covalent corrections for many Semiempirical Hamiltonians

Advanced Corrections of Hydrogen Bonding and Dispersion for Semiempirical Quantum Mechanical Methods

Jan Řezáč *† and Pavel Hobza †‡
† Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic and Center for Biomolecules and Complex Molecular Systems, 166 10 Prague, Czech Republic
‡ Regional Centre of Advanced Technologies and Materials, Department of Physical Chemistry, Palacky University, 771 46 Olomouc, Czech Republic

J. Chem. Theory Comput., **2012**, *8* (1), pp 141-151
DOI: 10.1021/ct200751e

$$E_{SM-D} = E_{SM} + E_{disp}$$

SM = AM1-D, PM3-D, PM6-DH2, PM6-DH+, OMx-D or PM7

Semi-empírico X campos de força

Are Current Semiempirical Methods Better Than Force Fields? A Study from the Thermodynamics Perspective†

Gustavo de M. Seabra,‡ Ross C. Walker,§ and Adrian E. Roitberg*,‡

The semiempirical Hamiltonians MNDO, AM1, PM3, RM1, PDDG/MNDO, PDDG/PM3, and SCC-DFTB, when used as part of a hybrid QM/MM scheme for the simulation of biological molecules, were compared on their abilities to reproduce experimental ensemble averages at or near room temperatures for the model system alanine dipeptide in water. Free energy surfaces in the (ϕ, ψ) dihedral angle space, $^3J(H_N,H_\alpha)$ NMR dipolar coupling constants, basin populations, and peptide−water radial distribution functions (RDF) were calculated from replica exchange simulations and compared to both experiment and fully classical force field calculations using the Amber ff99SB force field. In contrast with the computational chemist's intuitive idea that the more expensive a method the better its accuracy, the ff99SB force field results were more accurate than most of the semiempirical methods, with the exception of RM1. None of the methods, however, was able to accurately reproduce the experimental data. Analysis of the results indicate that the specific QM/MM interactions have little influence on the sampling of free energy surfaces, and the differences are well explained simply by the intrinsic properties of the various QM methods.

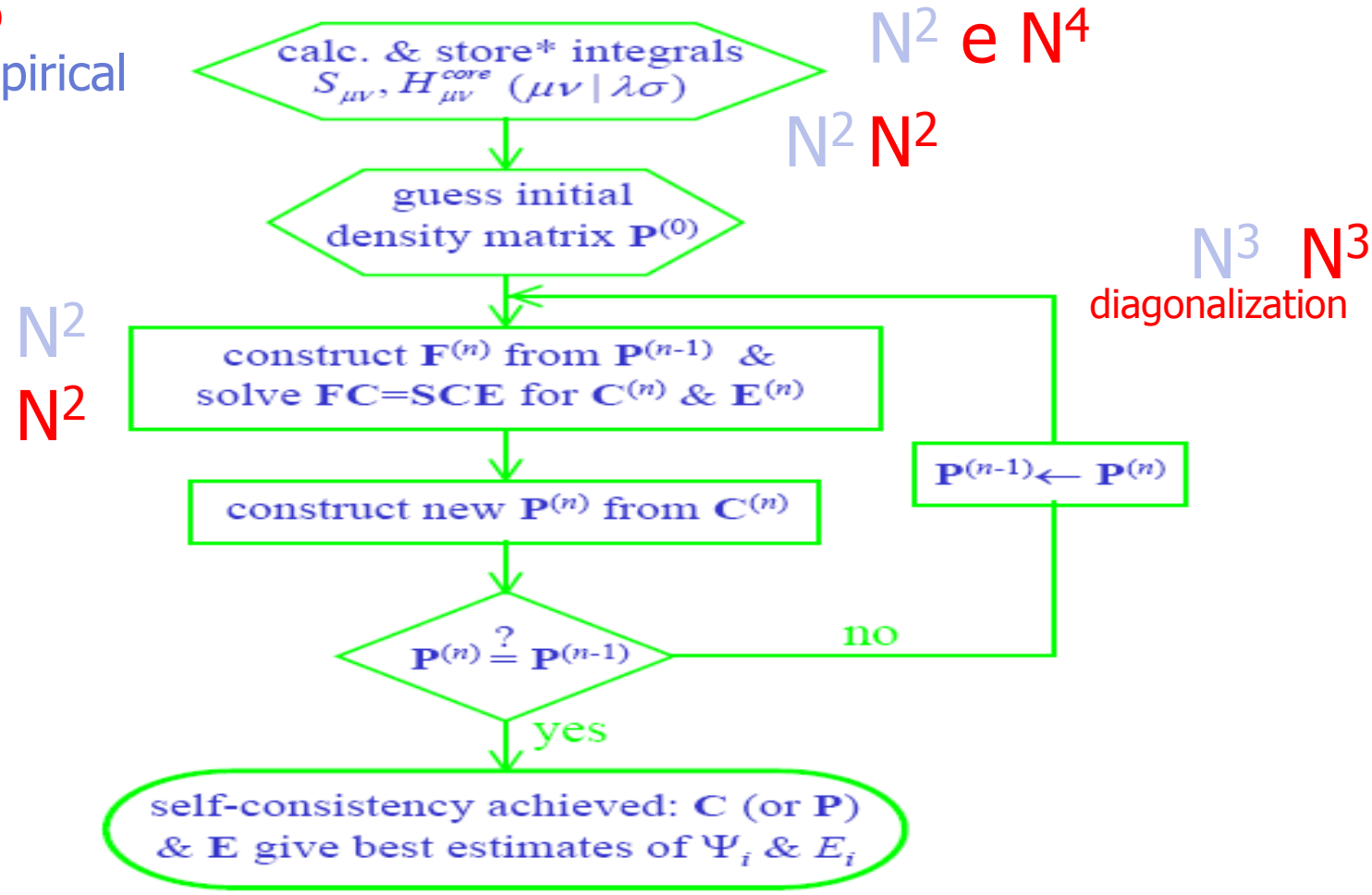
Os campos de força são muito bons para a dinâmica de proteínas.

Algoritmos de linear scaling na CPU e na memória

Where is the bottleneck?

Complexities for some parts of conventional single point energy calculation (SCF algorithm)

Ab initio
Semiempirical



Natureza do problema (localidade em química quântica)

A interação Coulômbica depende de: r^{-1}

Em se tratando de matrizes densidade:

$$\rho(r,r') = \exp[-\sqrt{E_{gap}}\,|r-r'|]$$

Apenas os elementos da matriz densidade que pertencem a átomos próximos possuem valor significativo.

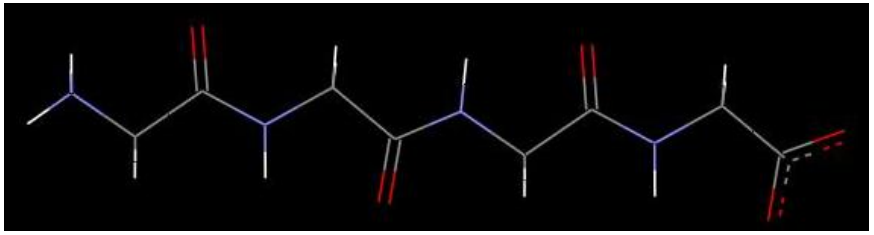
- Raios de corte
- Gera matrizes esparsas

Uso de raios de corte

TABLE I
Bond-orders between terminal nitrogen and backbone atoms in GLY – GLY – GLY – GLY.

Bond to	Order
C_2	1.017090
C_3	0.015249
N_4	0.004989
C_5	0.001219
C_6	0.000086
N_7	0.000031 → 7.2Å
C_8	0 000009
C_9	0.000001
N_{10}	0.000000
C_{11}	0.000000
C_{12}	0.000000

GLY–GLY–GLY–GLY has the structure H_2N–CH_2–CO–NH–CH_2–CO–NH–CH(–CH_3)–$COOH$



7-9 Å → Valor comumente usado

TABLE IV
Effect of varying cutoff.

Cutoff (Å)	ΔH_f (kcal / mol)	Diff.[a]	Gradient[b] (kcal / mol / Å)	Time (s)
3.0	−2071.41	+72.99	3.629	570
4.0	−2152.08	−7.68	1.146	1078
5.0	−2135.00	+9.40	0.689	1493
6.0	−2141.87	+2.53	0.596	1955
7.0	−2143.56	+0.84	0.723	2267
8.0	−2143.51	+0.89	0.351	2360
9.0	−2144.13	+0.27	0.230	2583
10.0	−2144.33	+0.07	0.250	2840
12.0	−2144.16	+0.24	0.170	2882
14.0	−2144.33	+0.07	0.131	3056
16.0	−2144.40	0.00	0.084	3157
18.0	−2144.40	0.00	0.061	3198
20.0	−2144.41	−0.01	0.038	3219
22.0	−2144.39	+0.01	0.026	3257
24.0	−2144.40	0.00	0.014	3277
26.0	−2144.40	0.00	0.000	3273

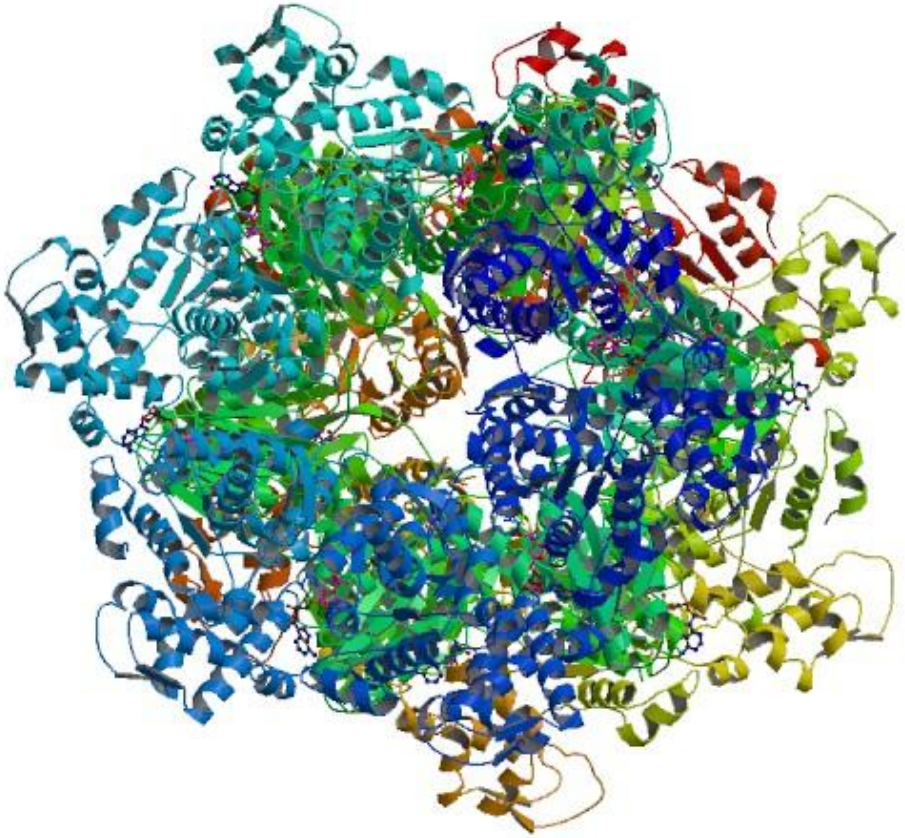
[a] Difference between ΔH_f at given cutoff and ΔH_f at 26 Å.
[b] Root-mean-square difference of gradient components at given cutoff and gradient at 26 Å.

Definido o raio de corte a esparsidade da matriz densidade está praticamente determinada

Mozyme (Stewart 1996)

Esparsidade das matrizes que surgem em cálculos de macroloméculas

Crystal Structure of the HSLUV Protease-chaperone Complex, **91.510** atoms, PDB: 1G3I



Using a cutoff of 9Å, non-zero elements < 1% .

Sparse Matrices

$$A = \begin{pmatrix} 10 & 0 & 0 & 0 & -2 & 0 \\ 3 & 9 & 0 & 0 & 0 & 3 \\ 0 & 7 & 8 & 7 & 0 & 0 \\ 3 & 0 & 8 & 7 & 5 & 0 \\ 0 & 8 & 0 & 9 & 9 & 13 \\ 0 & 4 & 0 & 0 & 2 & -1 \end{pmatrix}$$

CSR format: Compressed Sparse

val	10	-2	3	9	3	7	8	7	$3 \cdots 9$	13	4	2	-1
col_ind	0	4	0	1	5	1	2	3	$0 \cdots 4$	5	1	4	5

row_ptr	0	2	5	8	12	16	19

.

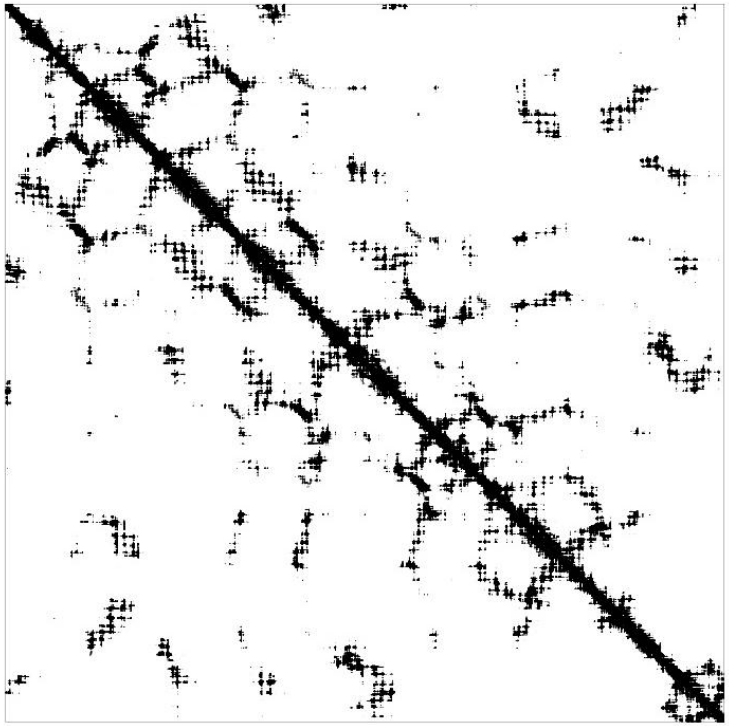
Padrão de esparsidade da Matriz de Fock para uma proteína com 4626 atoms

Sparse libraries for CPU

SPARSKIT

A basic tool-kit for sparse matrix computations (Version 2)

Sparse BLAS from Intel MKL



Localized Molecular Orbitals and MOZYME

$$\mathbf{FC} = \mathbf{SC}\varepsilon$$

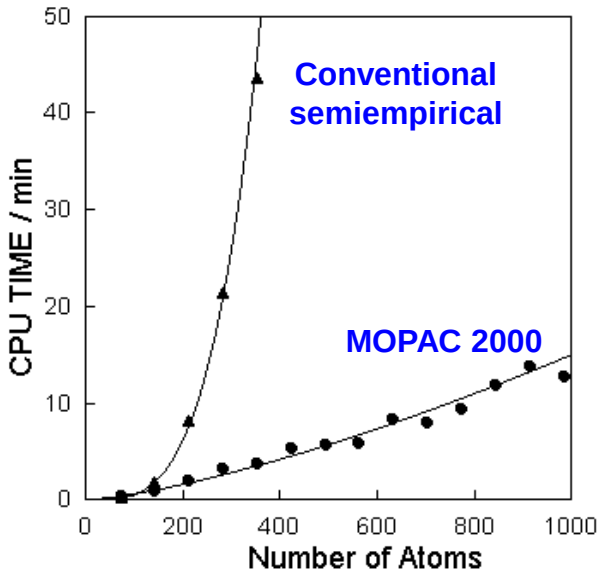
Canonical molecular orbitals are delocalized solutions to the HFR equation.

The canonical MOs are not suitable for the calculation of large molecular systems. → They do not reflect the local nature of the problem.

To circumvent such difficulty we have to use localized molecular orbitals as initial guess (Lewis based MOs) to solve the HFR equations.

MOZYME

Application of Localized Molecular Orbitals to the Solution of Semiempirical Self-Consistent Field Equations. J. J. P. Stewart. Int. J. Quantum Chem., 58, 1996, 133-146.



Scales as N^2

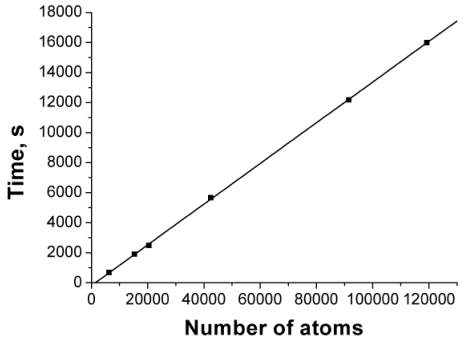
Cálculo de Bio-moléculas ultra grandes

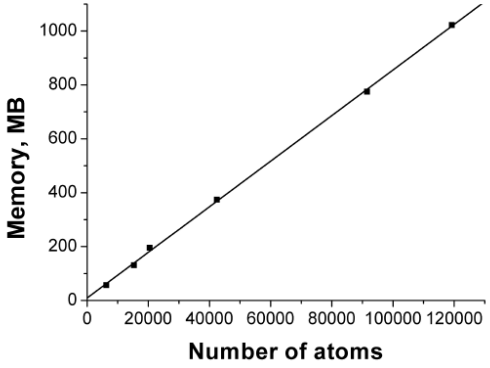
LocalSCF – linear scaling method

Escalonamento do Tempo de Cálculo e uso da memória com o Tamanho do Sistema

Table 1. Computer time and memory requirement of LocalSCF total energy calculation of proteins at the fixed geometry

Protein	N atoms	PDB id	CPU Time, sec	Memory, Mb
Dismutase	6254	1AVM	684	57
HIV-1 Reverse Transcriptase	15329	1FK9	1911	131
HIV-1 Antibody	20462	1HZH	2489	196
RNA Polymerase	42470	1I6V	5670	374
Protease-Chaperone Complex	91510	1G3I	12174	774
GroEL-GroES Chaperonin	119273	1AON	15988	1022





Pentium IV – 2.4GHz – 1Gb RAM

N.A. Anikin, V.M. Anisimov, V.L Bugaenko, V.V Bobrikov e A.M. Andreyev, *J. Chem. Phys.*, 121 (2004) 1266

Charge Transfer Effects in the GroEL–GroES Chaperonin Tetramer in Solution

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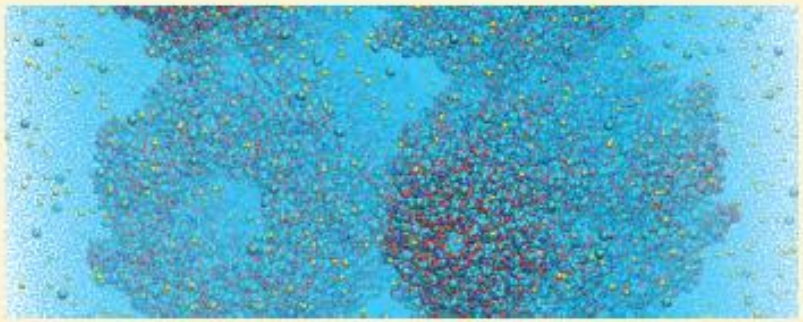
†National Center for Supercomputing Applications, University of Illinois at Urbana—Champaign, 1205 West Clark Street, Urbana, Illinois 61801, United States

‡Australian National University, Supercomputer Facility, Leonard Huxley Bld. (#56), Canberra, ACT 0200, Australia

Supporting Information

ABSTRACT: In this work, we present the results of a large-scale, semiempirical LocalSCF quantum mechanical study of GroEL–GroES chaperonin in solution containing 2 481 723 atoms. We find that large biological systems exhibit strong quantum mechanical character, the extent of which was not previously known. Our data show that protein transfers −743 electron units of charge to solvent, which is not described by classical force fields. Contrary to the commonly held belief, which is based on classical mechanics, our computational data suggest that the quantum mechanical effects of charge transfer increase with the size of biological systems. We show that the neglect of charge transfer in classical force fields leads to significant error in the electrostatic potential of the macromolecule. These findings illustrate that a quantum mechanical framework is necessary for a realistic description of electrostatic interactions in large biological systems.



dx.doi.org/10.1021/jp211385e | J. Phys. Chem. B XXXX, XXX, XXX–XXX

PC Intel octa-core com 48GB de RAM.

Sparse Projetced-Gradient Method

JCTC Journal of Chemical Theory and Computation — Article
pubs.acs.org/JCTC

Sparse Projected-Gradient Method As a Linear-Scaling Low-Memory Alternative to Diagonalization in Self-Consistent Field Electronic Structure Calculations

Ernesto G. Birgin,[†] J. M. Martínez,[‡] Leandro Martínez,*[,§] and Gerd B. Rocha[∥]

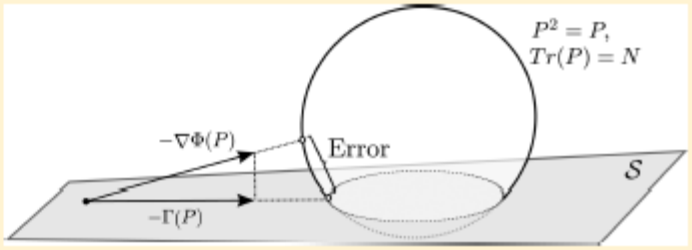
[†]Department of Computer Science, Institute of Mathematics and Statistics, University of São Paulo, SP, Brazil

[‡]Department of Applied Mathematics, Institute of Mathematics, Statistics and Scientfic Computing, State University of Campinas, Campinas, SP, Brazil

[§]Institute of Chemistry, State University of Campinas, Campinas, SP, Brazil

[∥]Department of Chemistry, Federal University of Paraíba, João Pessoa, Paraíba, Brazil

ABSTRACT: Large-scale electronic structure calculations usually involve huge nonlinear eigenvalue problems. A method for solving these problems without employing expensive eigenvalue decompositions of the Fock matrix is presented in this work. The sparsity of the input and output matrices is preserved at every iteration, and the memory required by the algorithm scales linearly with the number of atoms of the system. The algorithm is based on a projected gradient iteration applied to the constraint fulfillment problem. The computer time required by the algorithm also scales approximately linearly with the number of atoms (or non-null elements of the matrices), and the algorithm is faster than standard implementations of modern eigenvalue decomposition methods for sparse matrices containing more than 50 000 non-null elements. The new method reproduces the sequence of semiempirical SCF iterations obtained by standard eigenvalue decomposition algorithms to good precision.



Sparse Projetced-Gradient Method

Table 1. Performance of Bisalfa and Lapack for the Eigenvalue Decomposition of Single Real Fock Matrices Obtained from Low-Density Water Clusters

				computer time/s	
N_{water}	K	N	$N_{non\text{-}null}$	Bisalfa	Lapack
80	480	320	25 354	0.51	0.17
120	720	480	39 367	0.91	0.53
160	960	640	52 142	1.21	1.17
300	1800	1200	108 907	3.06	8.52
1000	6000	4000	391 946	13.40	451.39
5000	30 000	20 000	2 112 571	79.37	43415.64

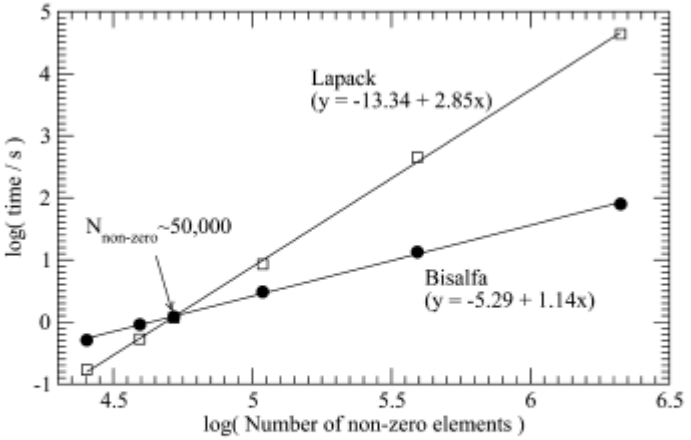


Figure 1. Scaling of Lapack and Bisalfa for systems of up to 2 million non-null elements. Bisalfa is nearly linear-scaling in practice, and it is faster than Lapack for sparse systems with more than 50 000 non-null matrix elements and ~99.5% sparsity.

Table 2. Details of the SCF Calculations on Water Clusters of up to 6000 Water Molecules Using Bisalfa or Lapack

		iterations[a]		time		final energy/kcal mol^{-1}	
N_{waters}	sparsity (%)	Bisalfa	Lapack	Bisalfa	Lapack	Bisalfa	Lapack
350	89.9	19(19)	16	7.0 min	4.6 min	−18878.2084	−18879.1351
1500	97.2	18(22)	17	56.5 min	6.0 h	−80772.7671	−80777.4152
3000	98.6	20(21)	18	2.2 h	61 h	−161353.3016	−161358.2292
3500	98.8	17(24)	16	4.3 h	84 h	−187935.4158	−187940.7421
3500 parallel MKL using 12 cores					29 h		−187940.7421
4000	98.9	16(20)	16	3.3 h	122 h	−214526.6706	−214532.6311
6000	99.3	22(25)		6.4 h	*b*	−321889.2913	

[a]Total number of calls to algorithm 2.1 from Bisalfa in parentheses. [b]Unable to run problem due to lack of memory.

Parallel version is under construction

High Performance Computing em Modelagem Molecular: Estratégias computacionais

High performance computing in chemistry

Important themes

- Parallelization of codes
- Efficient Algorithms
- Programming languages
- High performance architectures
- Benchmarks
- Numerical libraries
- Communication libraries

Clusters, GRIDs, Supercomputers, GPUs, etc.

PERSPECTIVE www.rsc.org/pccp | Physical Chemistry Chemical Physics

Utilizing high performance computing for chemistry: parallel computational chemistry

Wibe A. de Jong,*[a] Eric Bylaska,[a] Niranjan Govind,[a] Curtis L. Janssen,[c] Karol Kowalski,[a] Thomas Müller,[d] Ida M. B. Nielsen,[c] Hubertus J. J. van Dam,[a] Valera Veryazov[b] and Roland Lindh*[e]

Received 10th February 2010, Accepted 4th May 2010
First published as an Advance Article on the web 8th June 2010
DOI: 10.1039/c002859b

Parallel hardware has become readily available to the computational chemistry research community. This perspective will review the current state of parallel computational chemistry software utilizing high-performance parallel computing platforms. Hardware and software trends and their effect on quantum chemistry methodologies, algorithms, and software development will also be discussed.

Accelerating computational chemistry using GPGPU

NOVEL ARCHITECTURES

Graphical Processing Units for Quantum Chemistry

The authors provide a brief overview of electronic structure theory and detail their experiences implementing quantum chemistry methods on a graphical processing unit. They also analyze algorithm performance in terms of floating-point operations and memory bandwidth, and assess the adequacy of single-precision accuracy for quantum chemistry applications.

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Accelerating Molecular Dynamic Simulation on Graphics Processing Units

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[1]*Department of Bioengineering, Stanford University, Stanford, California 94305*
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[4]*NVIDIA Corporation, Santa Clara, California*
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Received 19 September 2008; Revised 12 December 2008; Accepted 13 December 2008
DOI 10.1002/jcc.21209
Published online in Wiley InterScience (www.interscience.wiley.com).

Abstract: We describe a complete implementation of all-atom protein molecular dynamics running entirely on a graphics processing unit (GPU), including all standard force field terms, integration, constraints, and implicit solvent. We discuss the design of our algorithms and important optimizations needed to fully take advantage of a GPU. We evaluate its performance, and show that it can be more than 700 times faster than a conventional implementation running on a single CPU core.

 J Comput Chem 00: 000–000, 2009

JCTC Journal of Chemical Theory and Computation

Article

Accelerating Density Functional Calculations with Graphics Processing Unit

Koji Yasuda

J. Chem. Theory Comput., **2008**, 4 (8), 1230-1236• DOI: 10.1021/ct8001046 • Publication Date (Web): 04 July 2008

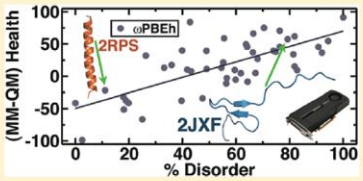
Ab Initio Quantum Chemistry for Protein Structures

Heather J. Kulik,[†,‡] Nathan Luehr,[†,‡] Ivan S. Ufimtsev,[†,‡] and Todd J. Martinez*[,†,‡]

[†]Department of Chemistry and PULSE Institute, Stanford University, Stanford, California, 94305, United States
[‡]SLAC National Accelerator Laboratory, Menlo Park, California 94025, United States

Supporting Information

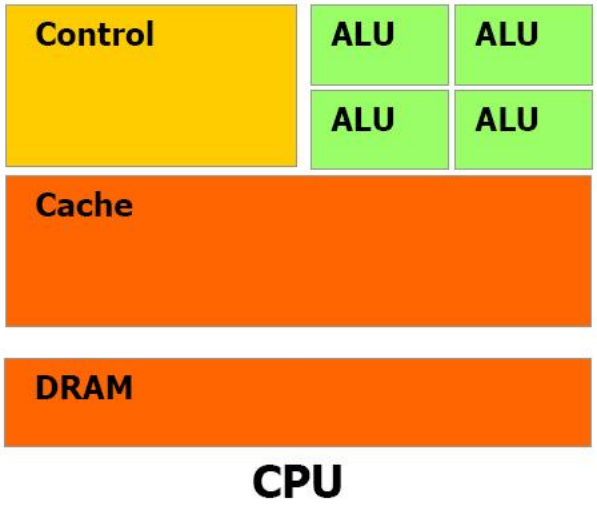
ABSTRACT: Structural properties of over 55 small proteins have been determined using both density-based and wave-function-based electronic structure methods in order to assess the ability of ab initio "force fields" to retain the properties described by experimental structures measured with crystallography or nuclear magnetic resonance. The efficiency of the GPU-based quantum chemistry algorithms implemented in our TeraChem program enables us to carry out systematic optimization of ab initio protein structures, which we compare against experimental and molecular mechanics force field references. We show that the quality of the ab initio optimized structures, as judged by conventional protein health metrics, increases with increasing basis set size. On the other hand, there is little evidence for a significant improvement of predicted structures using density functional theory as compared to Hartree–Fock methods. Although occasional pathologies of minimal basis sets are observed, these are easily alleviated with even the smallest double-ζ basis sets.



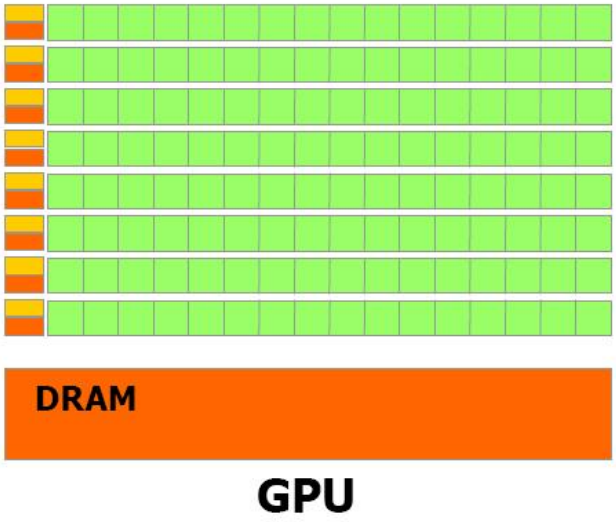
and many others ...

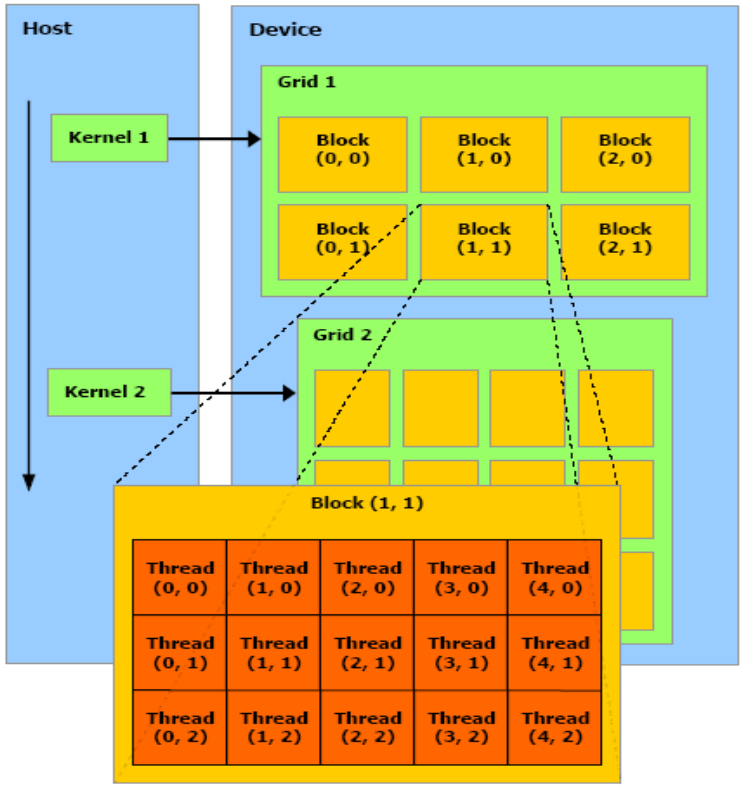
CPU x GPU

GPUs have many transistors dedicated to data processing



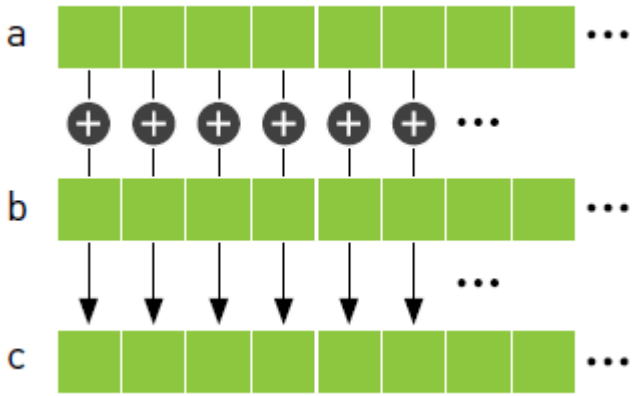
High parallelism





The host issues a succession of kernel invocations to the device. Each kernel is executed as a batch of threads organized as a grid of thread blocks

C++ code for GPUs




```
void add( int *a, int *b, int *c ) {
    for (i=0; i < N; i++) {
        c[i] = a[i] + b[i];
    }
}
```

C++ code for summing two vectors in CPU

```
__global__ void add( int *a, int *b, int *c ) {
    int tid = blockIdx.x;    // handle the data at this index
    if (tid < N)
        c[tid] = a[tid] + b[tid];
}
```

CUDA code for summing two vectors in GPU

http://openmopac.net

MOPAC®

What MOPAC is

MOPAC (Molecular Orbital PACkage) is a semiempirical quantum chemistry program based on Dewar and Thiel's NDDO approximation. Most users use MOPAC with a Graphical User Interface.

MOPAC2012

MOPAC2012 is MOPAC2009 plus the PM7 and PM7-TS methods. If a bug is detected, please send a message by E-mail to MrMOPAC@OpenMOPAC.net, along with an example illustrating the bug. If you qualify for Academic not-for-profit use and already have a password for MOPAC 2009, go straight to download, otherwise request a password and download. For commercial and governmental prices, see Prices.

Commercial users in Europe and America, please contact CAChe Research (see Resellers)
Commercial users in Japan, please contact Ryoka Systems
Commercial users in Korea, please contact KREIS I&C

PM7

PM7 is a modified form of PM6. A few errors in NDDO theory that affect large systems have been removed. All atomic and diatomic parameters were re-optimized. Average errors in organic compounds have been reduced by ~10%, and errors in large organics and solids have been significantly reduced, see PM7 Accuracy.

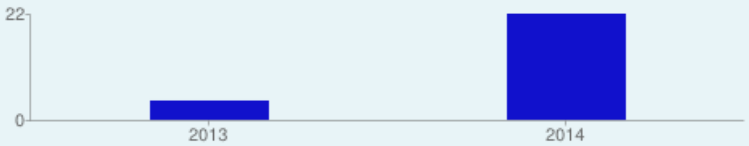
MOPAC calculation using CPU-GPU hybrid computational systems

« Voltar à lista | Editar | Exportar | Excluir

Título	GPU linear algebra libraries and GPGPU programming for accelerating MOPAC semiempirical quantum chemistry calculations [PDF] de researchgate.net
Autores	Julio Daniel Carvalho Maia, Gabriel Aires Urquiza Carvalho, Carlos Peixoto Mangueira Jr, Sidney Ramos Santana, Lucidio Anjos Formiga Cabral, Gerd B Rocha
Data de publicação	2012/8/13
Nome da publicação	Journal of Chemical Theory and Computation
Volume	8
Edição	9
Páginas	3072-3081
Editora	American Chemical Society
Descrição	In this study, we present some modifications in the semiempirical quantum chemistry MOPAC2009 code that accelerate single-point energy calculations (1SCF) of medium-size (up to 2500 atoms) molecular systems using GPU coprocessors and multithreaded shared-memory CPUs. Our modifications consisted of using a combination of highly optimized linear algebra libraries for both CPU (LAPACK and BLAS from Intel MKL) and GPU (MAGMA and CUBLAS) to hasten time-consuming parts of MOPAC such as the pseudodiagonalization, ...

Total de citações: Citado por 26

Citações por ano:



Artigos do Google Acadêmico:
GPU linear algebra libraries and GPGPU programming for accelerating MOPAC semiempirical quantum chemistry calculations
JDC Maia, GA Urquiza Carvalho, CP Mangueira Jr... - Journal of Chemical Theory and Computation, 2012
Citado por 26 - Artigos relacionados - Todas as 3 versões

« Voltar à lista | Editar | Exportar | Excluir

As contagens de datas e citações são aproximadas e são determinadas automaticamente por um programa de computador.

J. Chem. Theory Comput., 2012, 8 (9), pp 3072–3081 DOI: 10.1021/ct3004645

Where is the bottleneck in MOPAC code?

Time profiling analysis: 1SCF calculation (level shift)

Hotspots - Hotspots

Analysis Target | Analysis Type | Summary | **Bottom-up** | Top-down Tree | Module Timeline

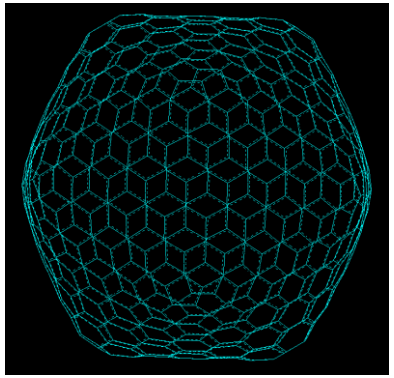
Grouping: Function / Call Stack

Function / Call Stack	CPU Time	Module	Function (Full)
+diag	55.2%	M71_linux	diag
+densit	36.3%	M71_linux	densit
+ddot	3.2%	M71_linux	ddot
+daxpy	2.3%	M71_linux	daxpy
+elau	1.4%	M71_linux	elau
+freda	0.9%	M71_linux	freda
+charmo	0.4%	M71_linux	charmo
+jab	0.1%	M71_linux	jab
+kab	0.1%	M71_linux	kab
+fock2	0.0%	M71_linux	fock2
+iter	0.0%	M71_linux	iter
+einvit	0.0%	M71_linux	einvit
+cnvg	0.0%	M71_linux	cnvg
+helect	0.0%	M71_linux	helect
+eqlrat	0.0%	M71_linux	eqlrat
+diat	0.0%	M71_linux	diat
Selected 1 row(s):	55.2%	[Unknow ...	[Unknown]

Total time ~ 1h

~91.5%

C540 fullerene



Diag.F90 → Pseudo-diagonalization procedure

Desnsit.F90 → Density matrix from MO coefficients

Pseudo-diagonalization method (PD)

PD is based in:

"To have a self-consistent density matrix is sufficient to have annihilated all Fock matrix elements connecting the occupied and virtual molecular orbitals". (Stewart, J.J.P., JCC, 3, 2 227, 1982).

Equations for PD:

$$\mathcal{F}_{o-v} = C_o^T F C_v$$

$$C_i^{new} = cC_i - sC_\alpha \quad and \quad C_\alpha^{new} = sC_i + cC_\alpha$$

$$s = \frac{\mathcal{F}_{i\alpha}}{\varepsilon_i - \varepsilon_\alpha} \quad and \quad c = \sqrt{1 - s^2}$$

Our GPU implementation:

CUBLAS Library DGEMM

Plane rotation of two vectors

Equation for density matrix:

$$P = C_o^T C_o$$

Our GPU implementation:

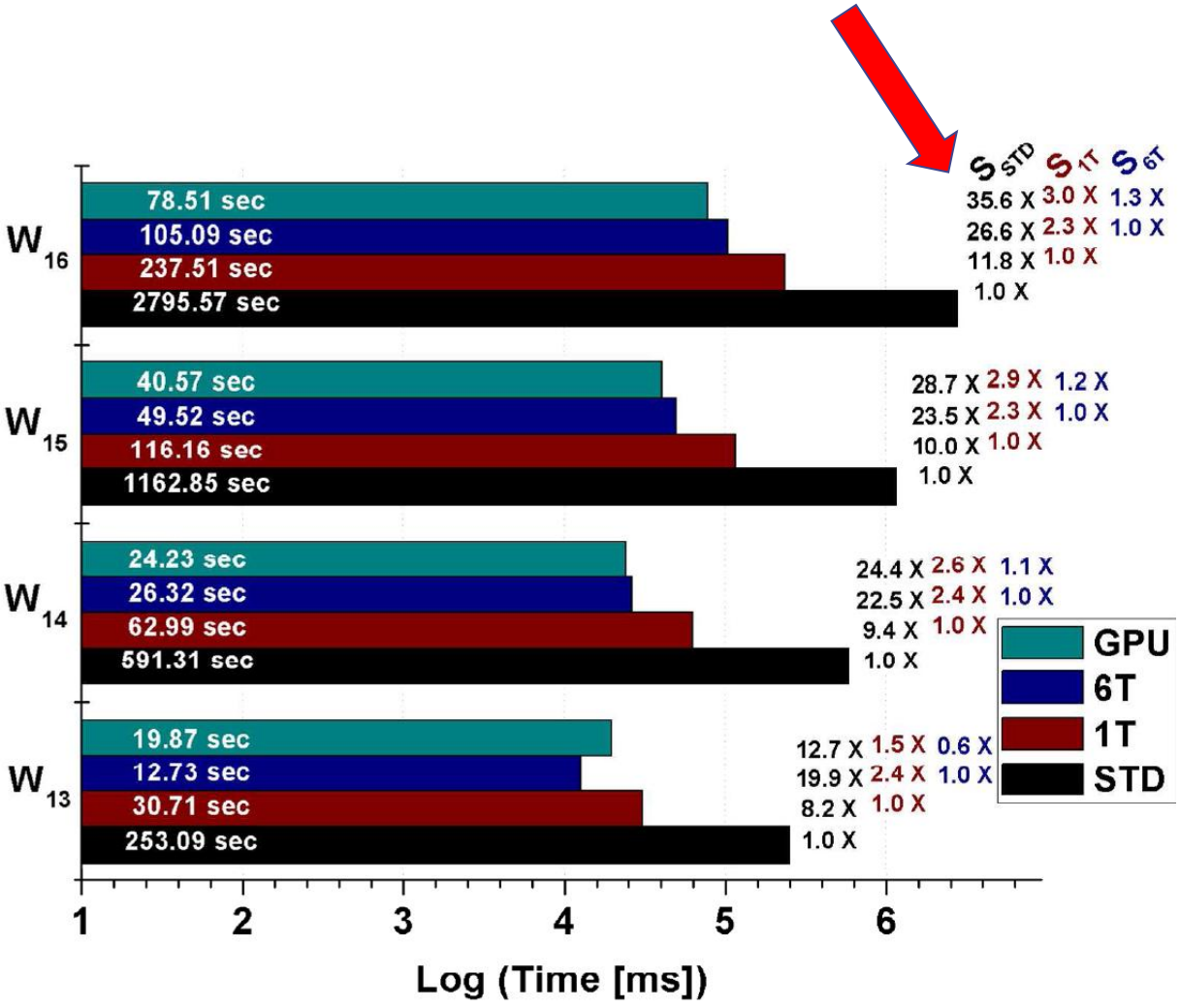
CUBLAS Library DSYRK

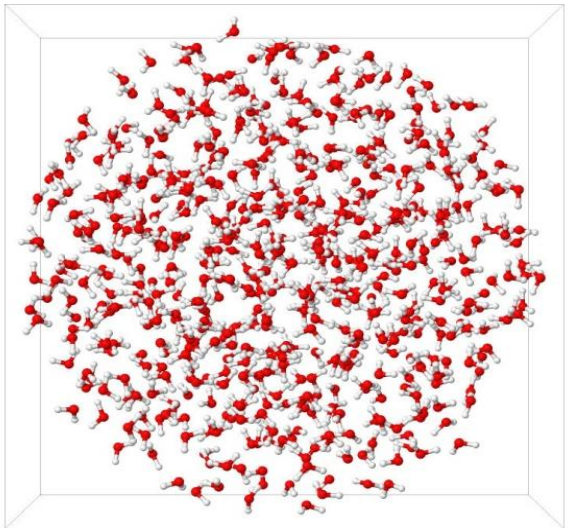
Full diagonalization

Our GPU implementation:

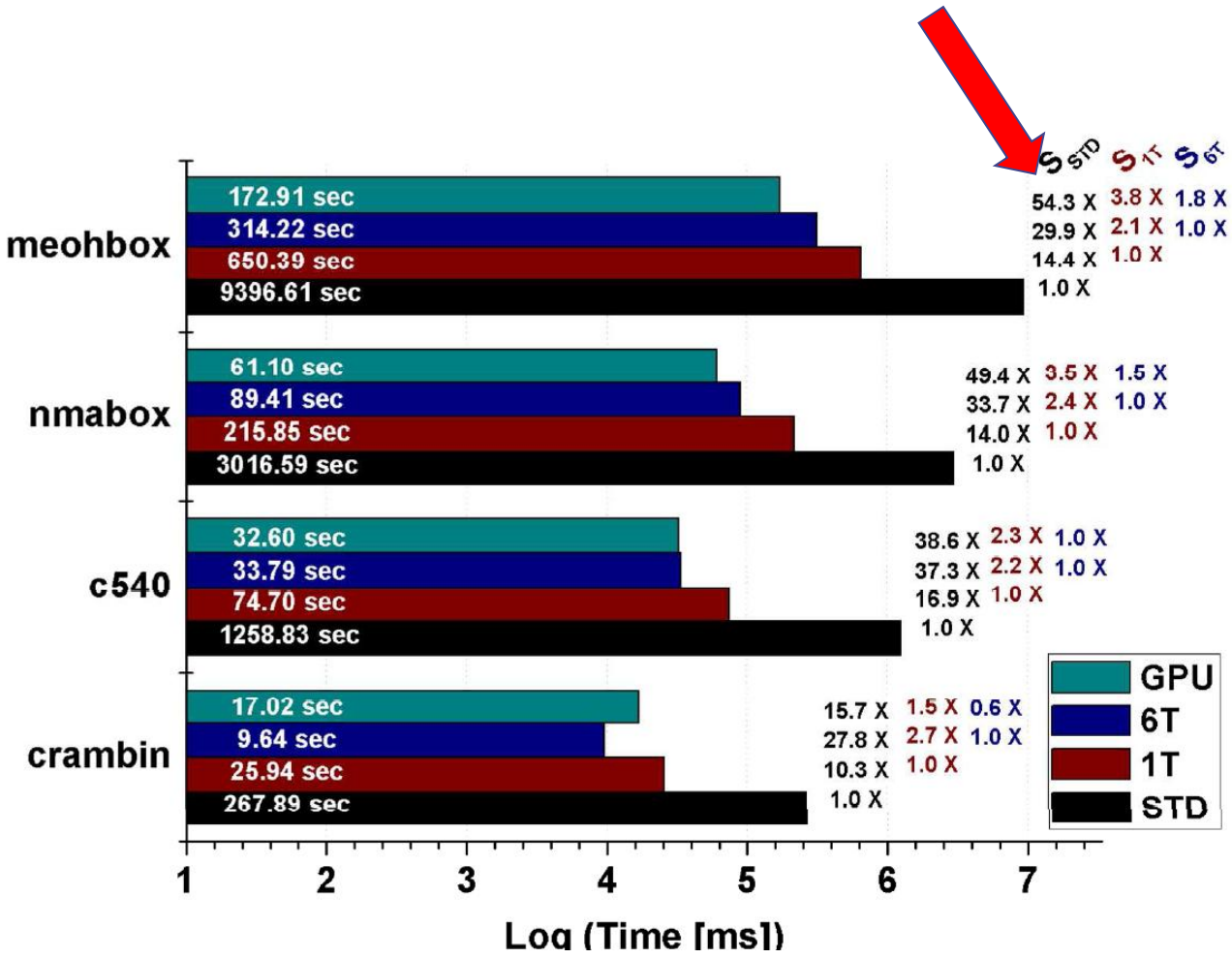
MAGMA Library and Intel MKL

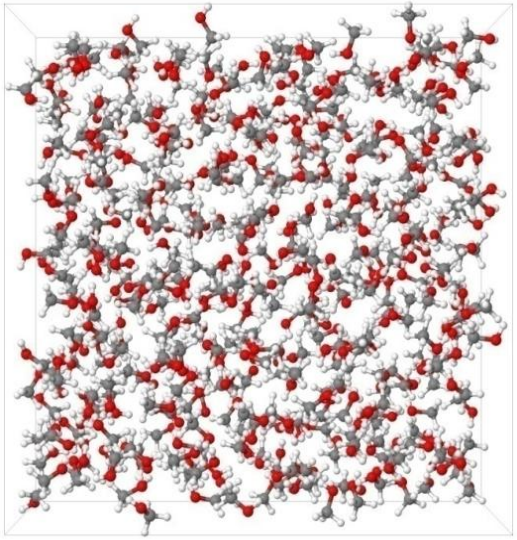
Speedups for Water clusters

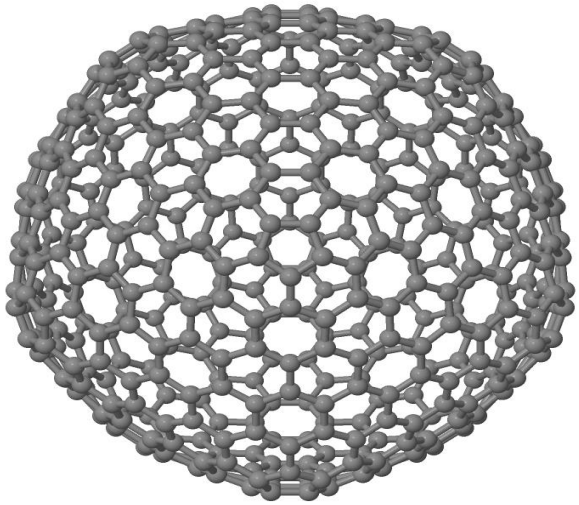




Speedups for simulation boxes, fullerenes and proteins

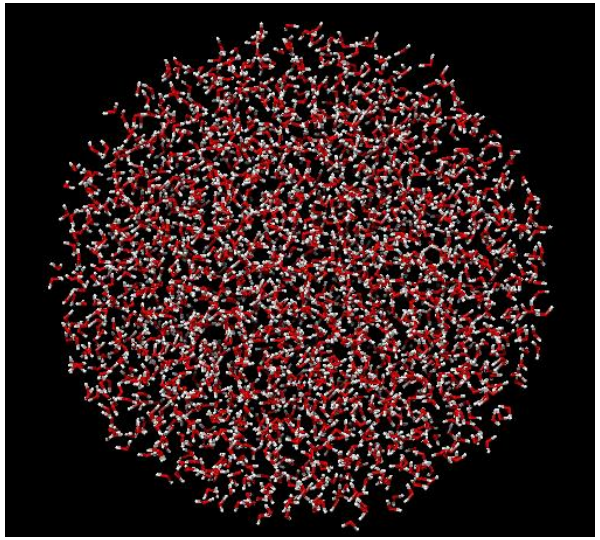


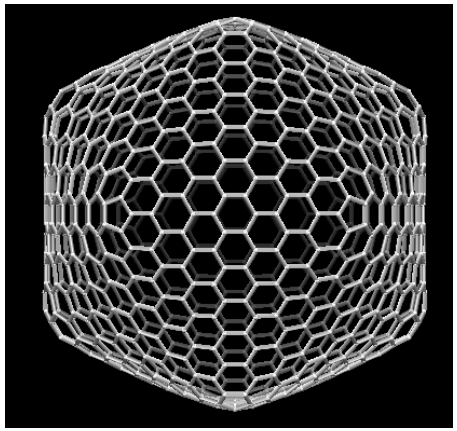


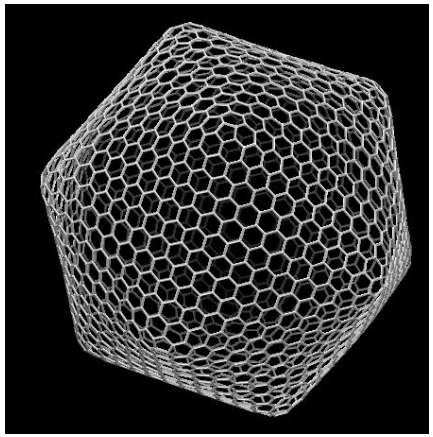


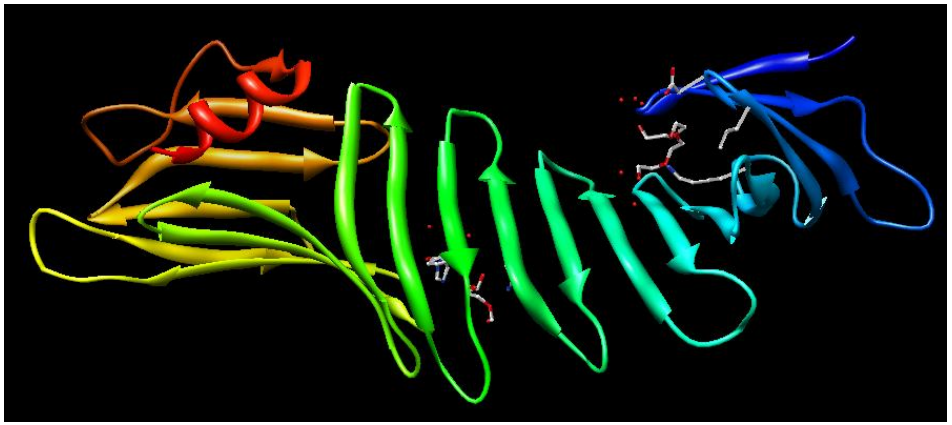
Larger Molecular Systems

Modelo	Descrição	Átomos	Orbitais
water25	Caixa esférica de simulação de raio 25Å, com 2165 moléculas de água.	6594	12990
2G8C	Proteína extraida da bactéria Borrelia burgdorferi.	4934	11545
C2160	Fulereno	2160	8640
C960	Fulereno	960	3840

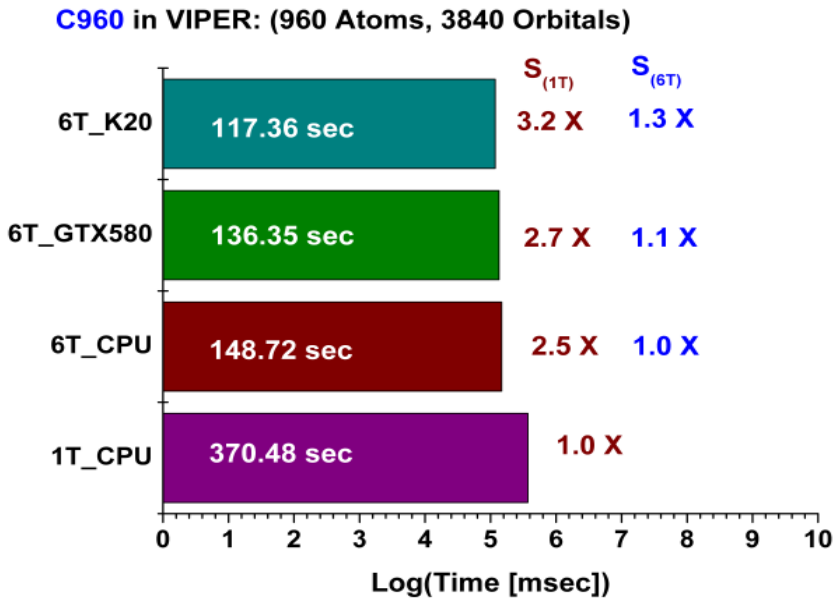


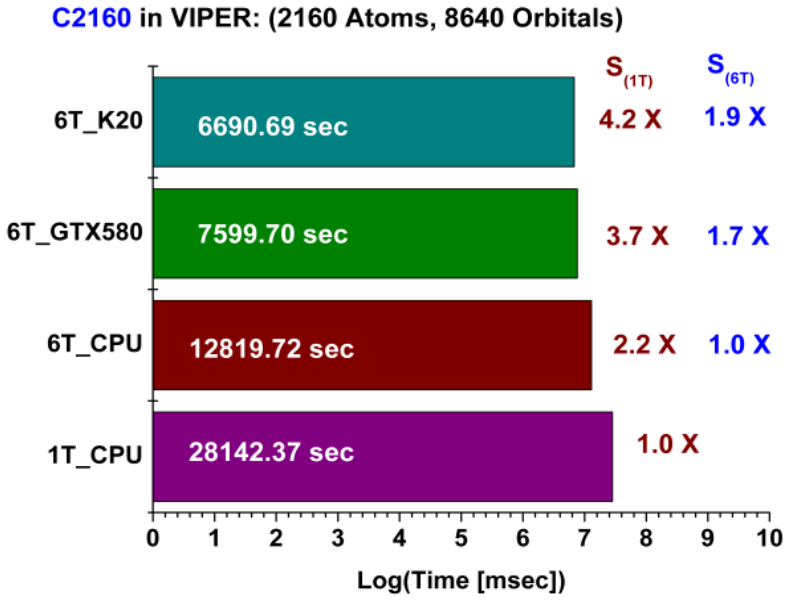


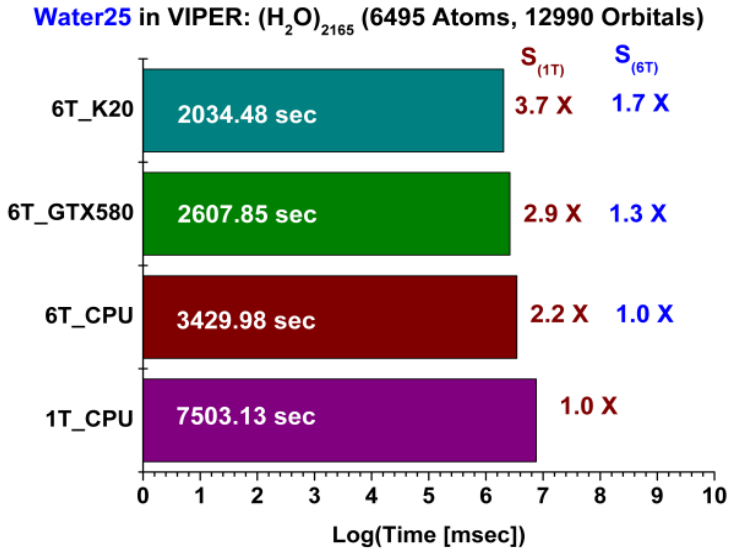


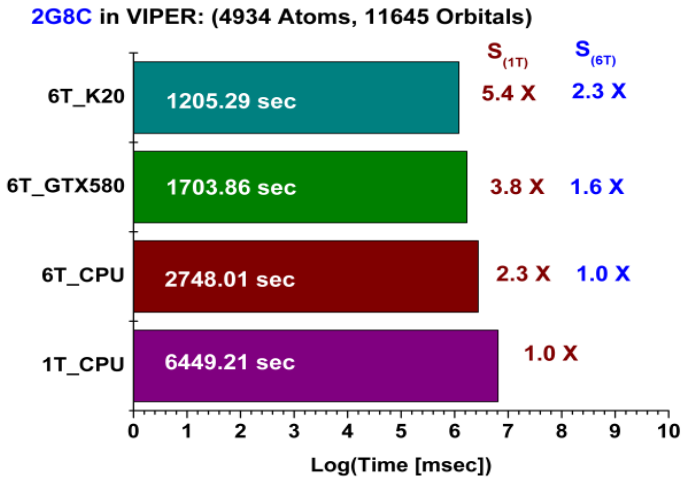


Larger Molecular Systems

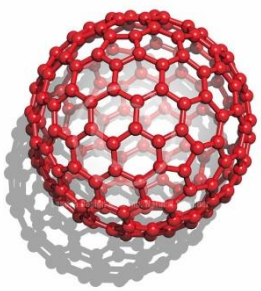


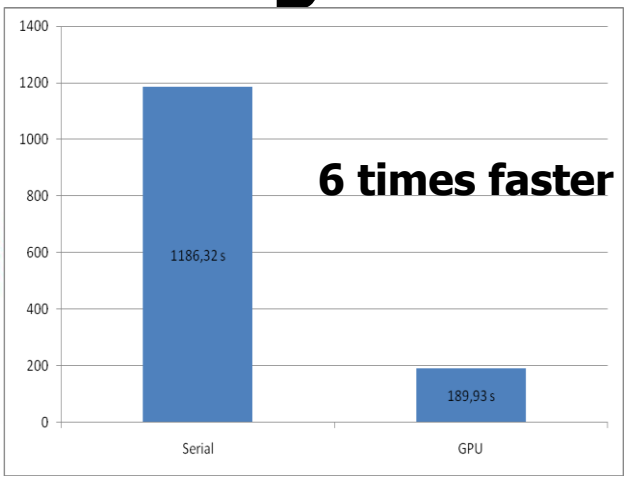




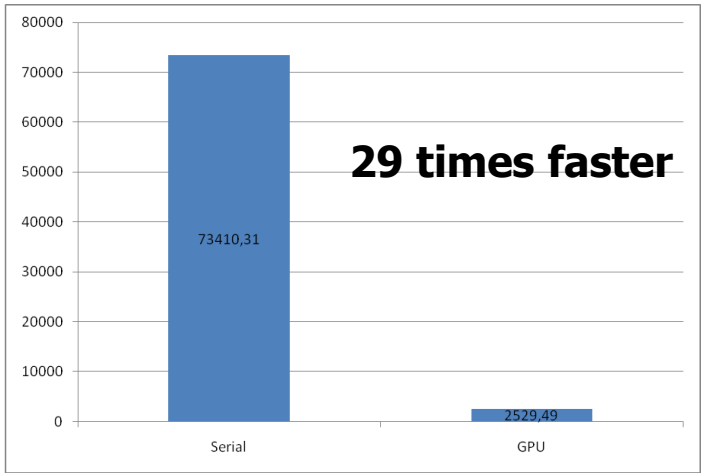


Geometry Optimization of large molecules on GPUs

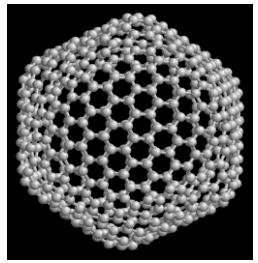


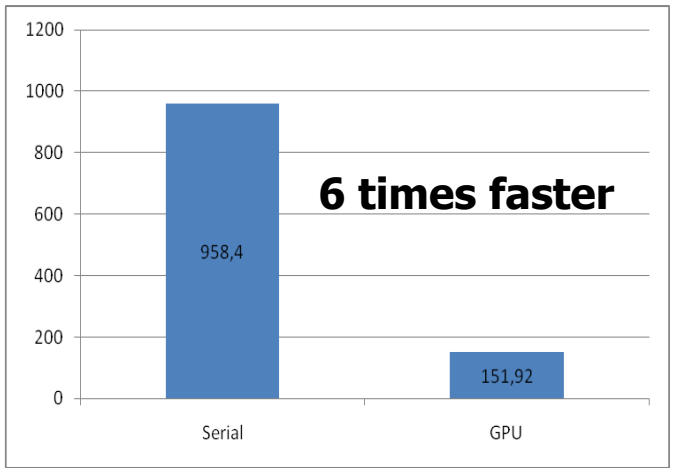


Times (s) for geometry optimization (only 100 cycles) of C180.

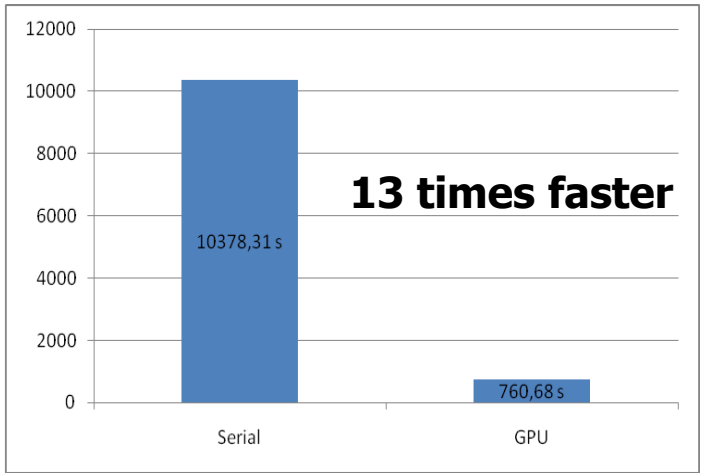


Times (s) for geometry optimization (only 100 cycles) of C540.

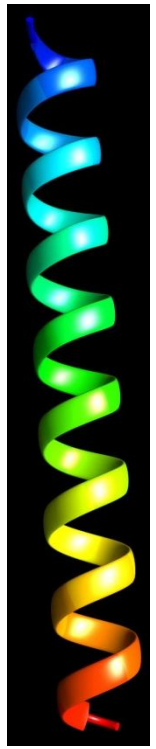




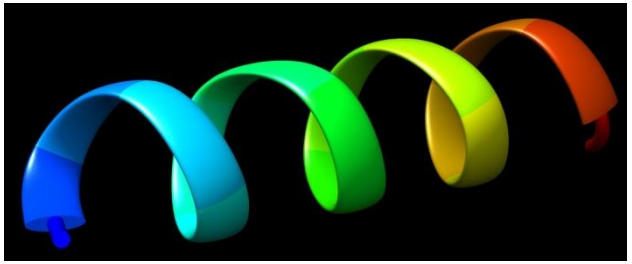
Times (s) for geometry optimization (only 100 cycles) of $(Glu\text{-}Ala)_8$.

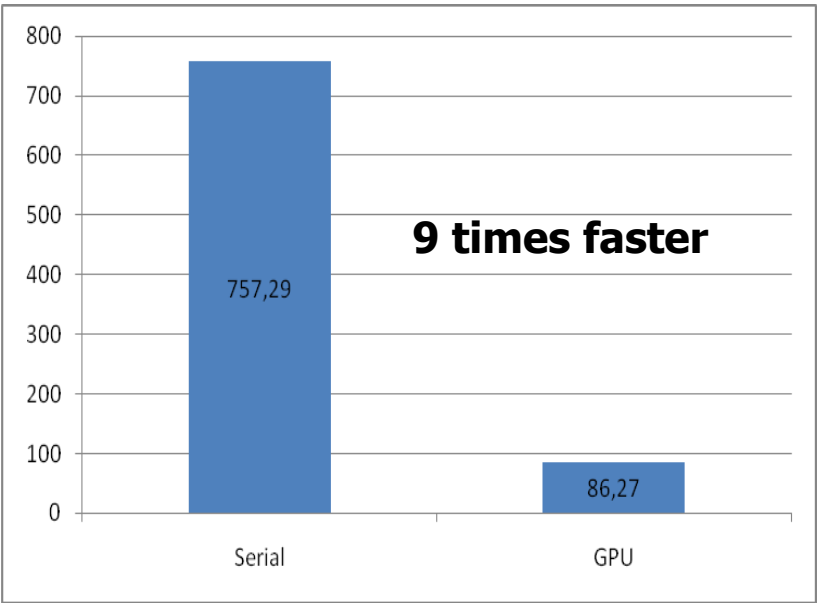


Times (s) for geometry optimization (only 100 cycles) of $(Glu\text{-}Ala)_{16}$.

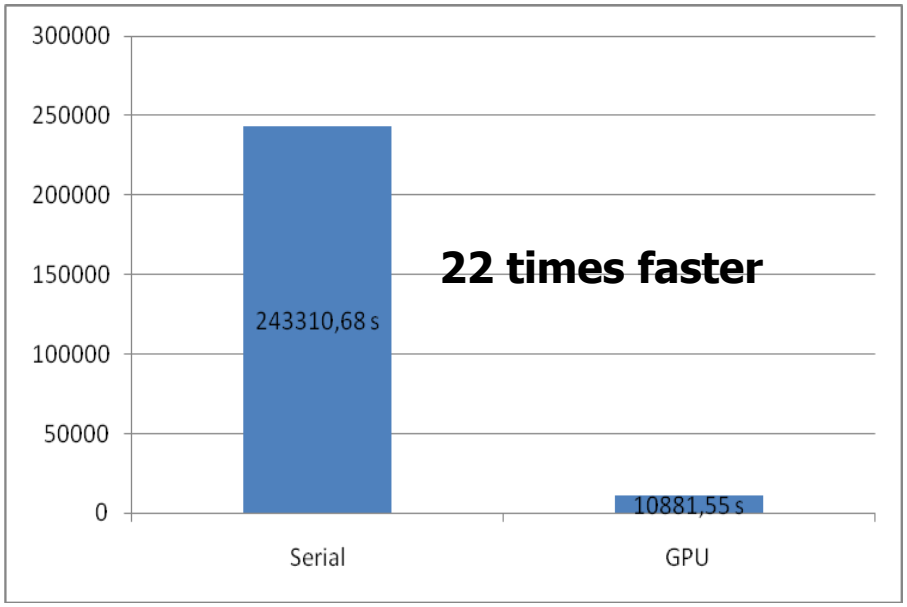


Vibrational frequencies of large molecules on GPUs

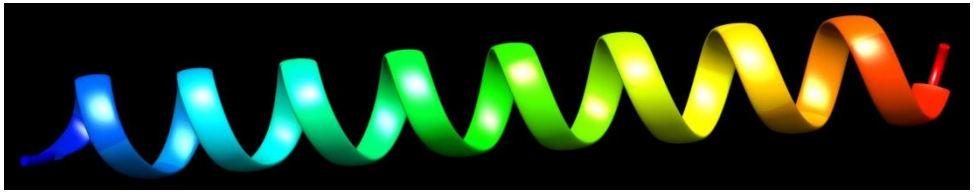




Times (s) for calculation of vibrational frequencies of $(Glu\text{-}Ala)_8$.



Times (s) for calculation of vibrational frequencies of $(Glu\text{-}Ala)_{16}$.



Accelerating Semiempirical Quantum Chemical Calculation by Using Multi-GPU Platforms

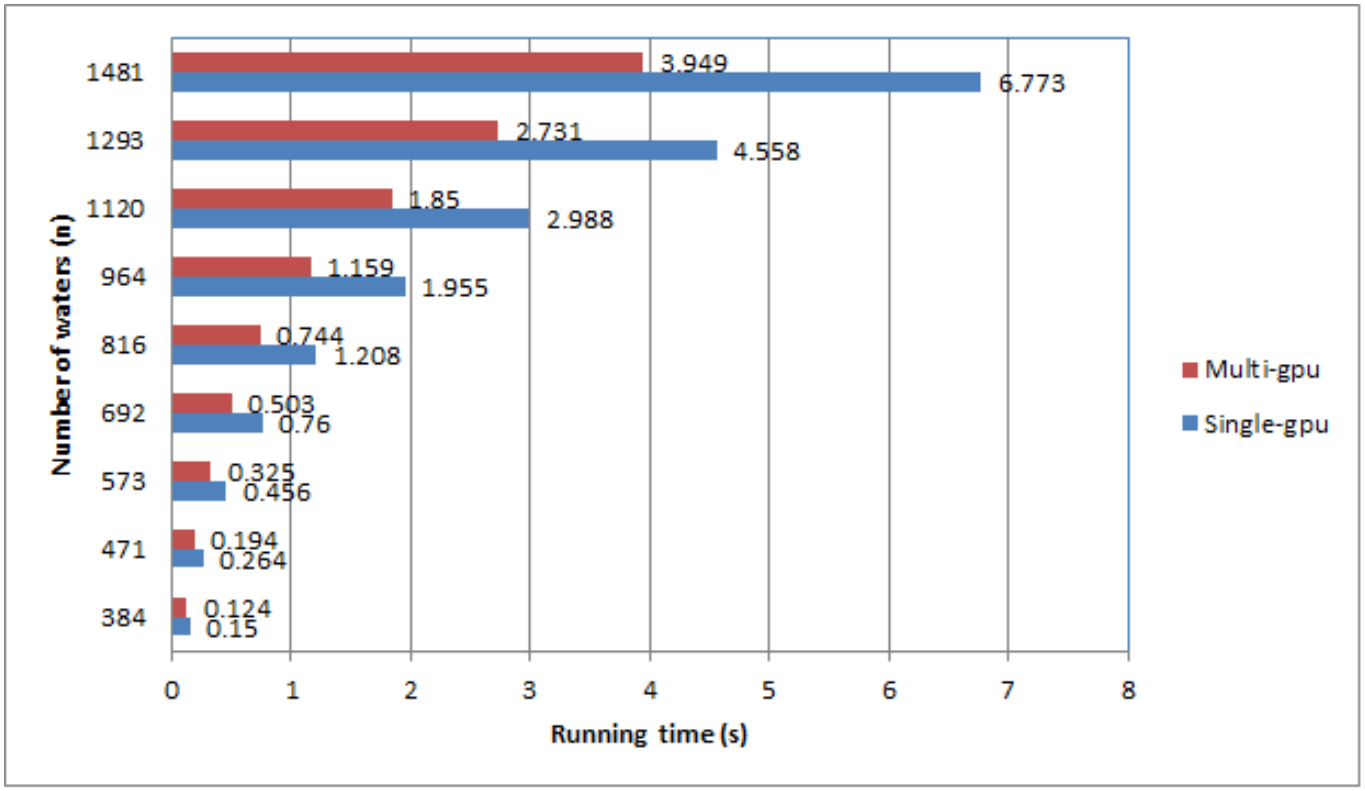


Figure 1: Runtimes (s) of the 1st part of PD for Water simulation boxes $(H_2O)_n$, n = 384 – 1481.

• Our main effort was to replace simple CUBLAS invocations with its Multi-GPU version, CUBLAS-XT. The CUBLAS-XT library presents a series of new features that makes Multi-GPU computing easier, such as not having explicitly to make memory transfers from host to device and device to host. CUBLAS-XT can also perform hybrid steps, dividing the workload across many GPUs and shared memory CPUs as well, using matrix-tiling techniques;

• All calculations were carried out in an Intel Core i7 920 @2.6GHz with 16GB RAM memory and 2 NVIDIA GTX 580 GPU cards;

Accelerating Semiempirical Quantum Chemical Calculation by Using Multi-GPU Platforms: Implementations and Benchmarks, Rocha e Maia (WATOC 2014).

http://openmopac.net

MOPAC®

What MOPAC is

MOPAC (Molecular Orbital PACkage) is a semiempirical quantum chemistry program based on Dewar and Thiel's NDDO approximation. Most users use MOPAC with a Graphical User Interface.

MOPAC2012

MOPAC2012 is MOPAC2009 plus the PM7 and PM7-TS methods. If a bug is detected, please send a message by E-mail to MrMOPAC@OpenMOPAC.net, along with an example illustrating the bug. If you qualify for Academic not-for-profit use and already have a password for MOPAC 2009, go straight to download, otherwise request a password and download. For commercial and governmental prices, see Prices.

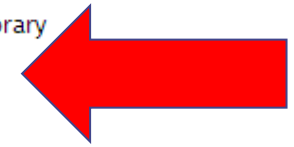
Commercial users in Europe and America, please contact CAChe Research (see Resellers)
Commercial users in Japan, please contact Ryoka Systems
Commercial users in Korea, please contact KREIS I&C

PM7

PM7 is a modified form of PM6. A few errors in NDDO theory that affect large systems have been removed. All atomic and diatomic parameters were re-optimized. Average errors in organic compounds have been reduced by ~10%, and errors in large organics and solids have been significantly reduced, see PM7 Accuracy.

Reducing Computation Time

Computation time has been reduced, in some cases by over 99%, as a result of using the Intel Math Kernel Library (MKL) and by parallelizing parts of the code. For details, see MKL and HTTP://www.quantum-chem.pro.br



References and Citations

MOPAC2012 MOPAC2009, PM6, PM7

Instructions and Manual

A manual is available for MOPAC2012. Please try finding answers to questions there before sending an E-mail message requesting help. For individual topics of interest, see Discussion Topics.

Maintenance record

MOPAC2012 is under constant maintenance. If your copy of MOPAC2012 does not work correctly, check the maintenance record to see if there is a more up-to-date version.

PM6

PM6 is a re-parameterization of the NDDO method. Three modifications to the approximations were made, these mainly affect the way the core-core interaction was defined. Parameters were optimized for most elements, the exceptions being 12 of the lanthanides and all of the actinides. The lanthanides can be represented by sparkles. For details, see the on-line PM6 journal article, and its supplementary material.

Downloads

Downloads of source and binaries for the various older versions of MOPAC are available.

http://www.nvidia.com/object/computational_chemistry.html

Quantum Chemistry Applications

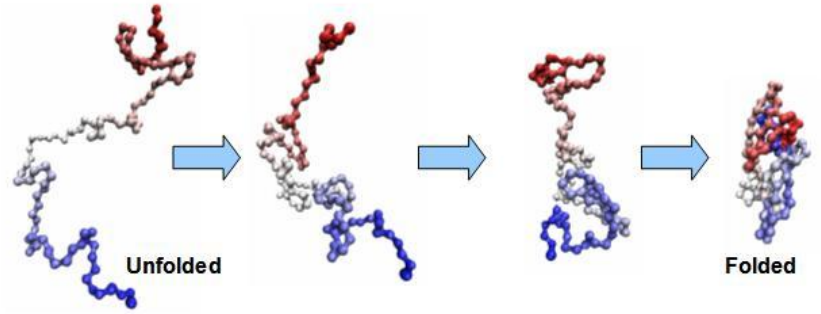
Application	Features Supported	GPU Perf	Release Status	Notes
MOPAC2012	Pseudodiagonalization, full diagonalization, and density matrix assembling	3.8-14X	Released MOPAC2013 available Q1 2014 Single GPU	Academic port. http://openmopac.net
NWChem	Triples part of Reg-CCSD(T), CCSD & EOMCCSD task schedulers	7-8X	Released, Version 6.3 Multiple GPUs	Development GPGPU benchmarks: www.nwchem-sw.org And http://www.olcf.ornl.gov/wp-content/training/electronic-structure-2012/Krishnamoorthy-ESCMA12.pdf
Octopus	Full GPU support for ground-state, real-time calculations; Kohn-Sham Hamiltonian, orthogonalization, subspace diagonalization, poisson solver, time propagation	1.5-8X	Released, Version 4.1.0	http://www.tddft.org/programs/octopus/

Gaussian (In Development)	Predicts energies, molecular structures, and vibrational frequencies of molecular systems	Joint NVIDIA, PGI and Gaussian collaboration	Yes
GPAW	Real-space grid DFT code written in C and Python	Electrostatic poisson equation, orthonormalizing of vectors, residual minimization method (rmm-diis)	Yes
LATTE	Density matrix computations	CU_BLAS, SP2 Algorithm	Yes
MOLCAS	Methods for calculating general electronic structures in molecular systems in both ground and excited states	CU_BLAS	Single only Additional GPU support coming in Version 8
MOPAC2013	Semiempirical Quantum Chemistry	Pseudodiagonalization, full diagonalization, and density matrix assembling	Single only
NWChem	Calculations	Triples part of Reg-CCSD(T), CCSD and EOMCCSD task schedulers	Yes
Octopus	Used for ab initio virtual experimentation and quantum chemistry calculations	Full GPU support for ground-state, real-time calculations; Kohn-Sham Hamiltonian, orthogonalization, subspace diagonalization, poisson solver, time propagation	TBD
Q-CHEM	Computational chemistry package designed for HPC clusters	Various features including RI-MP2	TBD

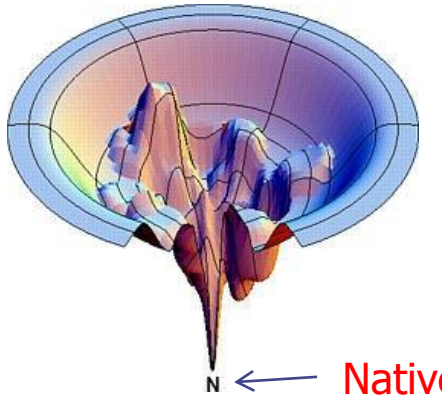
Protein folding Problem

In its most fundamental form, the folding problem can be separated into two distinct parts:

1. To find an efficient and accurate way of sampling the very large conformational space of a protein.
2. To find an energy function that can discriminate accurately between the native and non-native forms of the protein geometry.



Free energy



Native structure

The accuracy of these functions is determined by their ability to correctly guess the native function from among the many other misfolded conformations.

Behind the folding funnel diagram

Martin Karplus

This Commentary clarifies the meaning of the funnel diagram, which has been widely cited in papers on protein folding. To aid in the analysis of the funnel diagram, this Commentary reviews historical approaches to understanding the mechanism of protein folding. The primary role of free energy in protein folding is discussed, and it is pointed out that the decrease in the configurational entropy as the native state is approached hinders folding, rather than guiding it. Diagrams are introduced that provide a less ambiguous representation of the factors governing the protein folding reaction than the funnel diagram.

Protein folding

Assessment of Semiempirical Quantum Mechanical Methods for the Evaluation of Protein Structures

Andrew M. Wollacott† and Kenneth M. Merz, Jr.*

Abstract: The ability to discriminate native structures from computer-generated misfolded ones is key to predicting the three-dimensional structure of a protein from its amino acid sequence. Here we describe an assessment of semiempirical methods for discriminating native protein structures from decoy models. The discrimination of decoys entails an analysis of a large number of protein structures and provides a large-scale validation of quantum mechanical methods and their ability to accurately model proteins. We combine our analysis of semiempirical methods with a comparison of an AMBER force field to discriminate decoys in conjunction with a continuum solvent model. Protein decoys provide a rigorous and reliable benchmark for the evaluation of scoring functions, not only in their ability to accurately identify native structures but also to be computationally tractable to sample a large set of non-native models.

J. Chem. Theory Comput. **2007**, *3*, 1609−1619

In that paper, the authors have designed score functions based in semiempirical Hamiltonians to discerning between decoys and the native structure.

Protein Folding

Table 1. Select Decoy Sets Used

decoy set	PDB	description	type	N_{decoys}	N_{res}	N_{atoms}	rmsd range (Å)	%H/%E[b]
4-state-reduced	1ctf	C-terminal domain of ribosomal protein L7/L12	X-ray	630	68	1005	2.1−9.8	53/26
	1r69	N-terminal domain of phage 434 repressor	X-ray	675	63	997	2.2−9.4	70/0
	1sn3	scorpion toxin variant 3	X-ray	660	65	948	2.5−10.3	12/22
	2cro	phage 434 Cro protein	X-ray	674	65	1081	2.0−9.5	66/0
	4pti	trypsin inhibitor	X-ray	687	58	892	2.8−10.7	16/24
	4rxn	rubredoxin	X-ray	677	54	794	2.5−9.2	0/20
Rosetta	1gb1	immunoglobulin binding domain of streptococcal protein G	NMR	999	54	823	3.1−18.0	28/33
	1hsn	high mobility group protein I box	NMR	999	62	1014	4.1−17.6	79/0
	1orc	Cro repressor (mutant)	X-ray	999	56	877	4.0−14.1	46/27
	1pgx	protein G (B2 domain)	X-ray	999	57	873	3.4−20.4	26/46
	1uxd	fructose repressor DNA-binding domain	NMR	999	43	690	2.2−12.5	81/0
	2fow	RNA binding domain of ribosomal protein LII	NMR	999	66	1009	4.0−21.6	52/9
	1hc8[a]	RNA binding domain of ribosomal protein LII	X-ray	999	66	1009	4.0−21.6	53/9
	1r69	N-terminal domain of phage 434-repressor	X-ray	999	61	976	3.1−15.5	70/0

[a] 1hc8 is the X-ray structure for the 2fow decoy set. [b] Percentage of helices and sheets in the native.

Table 5. Energy Decomposition for All-Atom Minimized Decoy Sets as Calculated with DivScore Using the PM3 Hamiltonian

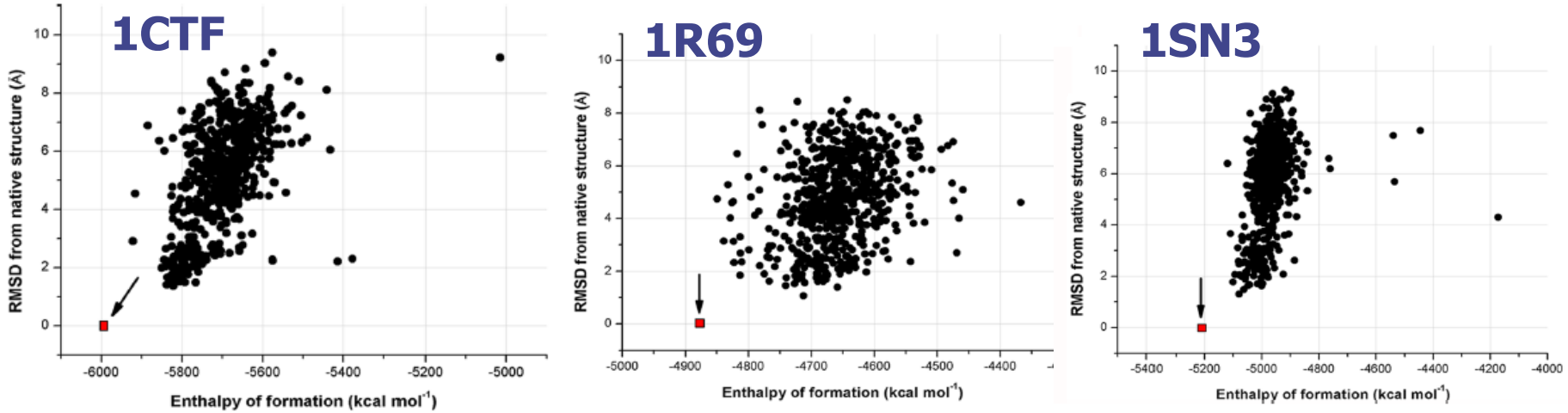
decoy type	system	$rank_{tot}$	$rank_{Hf}$[a]	gap_{Hf}[d]	$rank_{solv}$[b]	gap_{solv}[d]	$rank_{LJ6}$[c]	gap_{LJ6}[d]
4-state-reduced	1ctf	1	4	44.62	471	570.51	1	−22.04
	1r69	1	2	19.53	594	559.40	1	−58.94
	1sn3	1	1	−63.47	569	613.26	5	22.06
	2cro	1	16	72.01	524	515.20	1	−59.28
	4pti	1	16	95.99	440	455.73	25	58.75
	4rxn	1	1	−32.07	646	925.86	10	34.17
Rosetta	1gb1	1	3	4.07	976	677.13	1	−13.66
	1hsn	15	154	152.73	857	447.77	1	−1.42
	1orc	1	64	183.35	812	570.97	7	6.07
	1pgx	1	1	−10.12	978	627.83	1	−60.63
	1uxd	45	21	118.11	972	343.64	1	−23.04
	2fow	5	56	173.82	894	618.72	4	16.15
	1hc8	1	24	124.08	920	644.35	1	−12.19
	1r69	1	1	−10.07	977	828.78	1	−141.21

[a] Heat of formation. [b] Solvation energy. [c] Dispersive term of the classic LJ6−12 potential. [d] Energy gaps are reported as the energetic difference between the native structure and the decoy with the lowest value for the given energetic term.

Protein folding problem as an application of GPGPU computing in chemistry

Our contribution:

We demonstrated that the ΔH_f predicted using PM6-DH+ can be used as a good score function to discriminate higher-energy conformers from native protein structure



J. Chem. Theory Comput., 2012, 8 (9), pp 3072–3081

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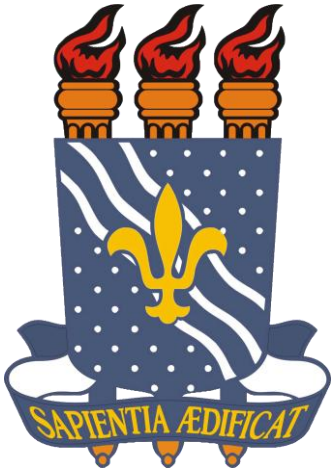
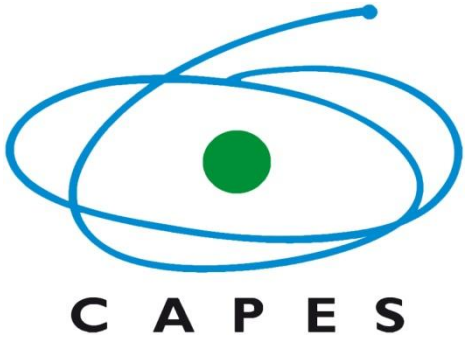
UG., Julio Daniel de Carvalho Maia

UG., Jessé Nóbrega

Venha fazer parte desse time.

Acknowledgements





Rede de Porfirinas

FIM