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Accurate Quantum Chemistry in Single Precision Arithmetic: Correlation Energy

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Abstract: In the present work, we show the feasibility of using single precision in quantum chemistry, especially regarding the computation of electron correlation energy. On the example of the MP2 method, we clearly demonstrate that single precision arithmetic is sufficient for evaluating the molecular two-electron integrals by the use of the Cholesky decomposition method. The evaluation of integrals with single precision arithmetic introduces a negligible error into the computed MP2 correlation energy. In particular, the corresponding error in the MP2 correlation energy amounts to only $10^{-7} E_h$ for the 113-atom taxol molecule in double-valence basis set (1099 basis functions). The practical relevance of our result is that 50% performance gain and 50% reduction in memory demands can be achieved by only minor changes in the existing codes. Our finding opens intriguing perspectives for doing accurate correlated quantum chemistry on specialized floating-point mathematical coprocessors.

1. Introduction

The use of double precision is the most common convention in quantum chemistry.[1] This programming rule is biased by the believed paradigm that higher precision automatically yields more accurate results. The interrelation between the precision and the accuracy of the final results is not straightforward, however.[2,3] Indeed, the accuracy of the final results depends not only on the precision used but also on many factors like, e.g., the algorithm utilized, intermediate data generated, compilers and math libraries employed, the hardware architecture, and so forth.

In computational quantum chemistry, the use of double precision is essential at the stages of the implementation and validation of a new theoretical method or computational scheme. Once the method is approved and the code is verified, usually by examples of small and medium-sized systems, further modifications are necessary to enable large scale (many atoms and many basis functions) *ab initio* calculations. At the present time, there exists a wide choice of powerfull methods which can help here: three-index factorization of two-electron repulsion integrals (ERIs), local schemes, the fragmented molecular orbital (FMO) method, and many others.[4–7] These accelerating methods have to provide an optimal balance between the accuracy of the computed quantities and the computational effort required.

Since the formal scaling of the number of ERIs is quartic with respect to the number of basis functions, the evaluation of ERIs is the major computational obstacle in all advanced quantum chemistry calculations. A three-index factorization of the ERIs is known to be a very efficient technique for reducing the computational prefactor and to speed up ab initio calculation. Such a factorization is the cornerstone of the Density Fitting or Resolution of Identity (DF/RI) and Cholesky Decomposition (CD) methods.[8–14] In the framework of this factorization, an ERI is approximated by the inner product of two intermediate vectors (ERI is expressed in terms of three-indexed intermediates). According to published results, the absolute error in an ERI caused by the approximation lies within the range of 10^{-2} to 10^{-16} E_h, depending on the method used.[13,15–17]

By applying the DF/RI and CD methods, one can accelerate ab initio calculations up to a few hundred times and thereby simulate large quantum systems in a reasonable time.[18,19] This acceleration comes, of course, at the cost of accuracy: using approximated ERIs leads to deterioration of the numerical accuracy of the final results (energies, proper-

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Accurate Quantum Chemistry

J. Chem. Theory Comput., Vol. 7, No. 2, 2011 **321**

ties), even though calculations are carried out using double precision. In other words, all of the above-mentioned approximation methods introduce a systematic error to the computed quantities. According to the present standard, this *approximation* error must not exceed the so-called *chemical accuracy*, which is defined to be 1 kcal/mol or, equivalently, 1.593×10^{-3} E_h.[20,21]

From the numerical point of view, the factorization might be effectively interpreted as rounding an exact ERI from double to some intermediate precision. The loss of numerical accuracy resulting from integral approximation opens up the possibility for the use of single precision during the internal intermediate calculations. One might speculate that an energy error caused by working with three-index intermediates in single precision mode (storage and computation) is comparable to the approximation error or is even smaller. The computational benefits of using single precision are enormous. First of all, it automatically halves the memory demands and doubles memory and network bandwidths. Second, single precision arithmetic (32-bit arithmetic) is at least $2\times$ times faster on conventional processors (x86, x86−64, Intel 64, IA-64, IBM Power) and $10\times$ times faster (!) on specially designed mathematical coprocessors (Nvidia's and AMD/ATI's General Purpose Graphics Processing Unit, IBM's Cell BE) than double precision arithmetic (64-bit arithmetic).[22−24]

It is thus not surprising that in recent years the use of single precision in quantum chemistry has attracted considerable attention, especially regarding the evaluation of ERIs. Two computational schemes have been already implemented and assessed: computation of ERIs in an atomic orbital basis for direct HF and DFT calculations[25−30] and evaluation of ERIs in a molecular orbital basis with the DF/RI method for calculating the so-called RI-MP2 correlation energy.[31−33] At present, the prevailing opinion concerning the evaluation of ERIs in single precision arithmetic is that "single precision is generally insufficient to achieve 'chemical accuracy' of 1 kcal/mol in calculations on anything but the smallest and simplest systems, since the errors quickly accumulate for large molecules."[33]

Indeed, the accumulated error in the total Hartree−Fock (HF) and correlation energies grows rapidly with system size and becomes unacceptable ($\geq 1.593 \times 10^{-3}$ E_h) for moderate-sized molecules ($\sim 10^2$ atoms and $\sim 10^3$ basis functions).[26,31] In order to overcome this problem, a mixed precision computational model was developed. This model utilizes both the host CPU (for evaluating large ERIs with 64-bit arithmetic) and an attached GPGPU (for the evaluation of the remaining of ERIs with 32-bit arithmetic).[28,32] By using this CPU−GPU heterogeneous model, the required accuracy of 1 kcal/mol has been achieved.[27,33] In particular, Aspuru-Guzik and co-workers, by using this mixed-precision computational model, have reduced the absolute error in the RI-MP2 correlation energy from 9.980×10^{-3} to 7.986×10^{-4} E_h for the 113-atom taxol molecule in a double-ζ valence basis set (1123 basis functions).[32,33]

The aim of the present study is to demonstrate the particular feasibility and practicability of using single precision in conjunction with three-indexed intermediates gener-

ated via the CD method. In contrast to the DF/RI method, the potential of the CD method for generating ERIs within single precision arithmetic has never been investigated before. Our computational strategy is to focus here on the correlated level of theory.

2. Theoretical Background

2.1. The Three-Index Factorization of Two-Electron Repulsion Integrals.
Generally, an ERI in the framework of a three-index factorization can be represented as the inner product of two intermediate vectors:

$$(\mu\nu|\lambda\sigma) \approx (\overline{\mu\nu|\lambda\sigma}) = \mathbf{L}_{\mu\nu} \cdot \mathbf{L}_{\lambda\sigma} = \sum_{K=1}^{M} L_{\mu\nu}^{K} L_{\lambda\sigma}^{K} \quad (1)$$

where μ, ν, λ, and σ label atomic orbitals; $(\mu\nu|\lambda\sigma)$ and $(\overline{\mu\nu|\lambda\sigma})$ are the exact ERI and its approximation in Mulliken notation, respectively; $L_{\lambda\sigma}^{K}$ are three-indexed intermediates. In the particular case of the CD method, $\mathbf{L}_{\mu\nu}$ is called the *Cholesky vector* in the AO basis and M is the number of Cholesky vectors.

The main advantage of the CD method is that the accuracy of the approximation (eq 1) can be rigorously controlled. By construction, the accuracy control is accomplished by varying only one parameter, the so-called CD threshold δ:

$$\Delta = |(\mu\nu|\lambda\sigma) - (\overline{\mu\nu|\lambda\sigma})| \leq \delta \quad (2)$$

where Δ is the approximation error of an ERI. Depending on the decomposition scheme, the strict error bound (eq 2) holds for all ERIs or only for certain types. In the case of the full-CD scheme, the introduced error can be made as small as needed for all ERIs:

$$\lim_{\delta \to \infty} \Delta = \varepsilon$$

or equivalently

$$\lim_{\delta \to \infty} (\overline{\mu\nu|\lambda\sigma}) = (\mu\nu|\lambda\sigma) \quad (3)$$

where ε is the machine epsilon (2.220×10^{-16}). In finite precision arithmetic, this limit is reached when $\delta \leq 10^{-10}$. In the case of the recently developed *atomic CD* (aCD) or its compact form (acCD), this inequality (eq 2) is valid only for the one-center and two-center "Coulomb" ERIs, but three- and four-center integrals as well as "exchange" two-center integrals may be subject to large errors.[15,16,34] In other words, within the framework of the aCD/acCD schemes, the accuracy of the approximation (eq 1) for a part of ERIs cannot be improved beyond a certain limit no matter what CD threshold is used.

In practice, a CD threshold in the range of 10^{-4} to 10^{-6} is being used in most applications, and the corresponding number of the Cholesky vectors (M) is $5−7$ times larger than the number of the basis functions (N). These CD thresholds guarantee the chemical accuracy of the final results and accelerate the calculation up to a few hundred times. By taking into account eq 2 and these CD thresholds, one might claim that the actual precision of the approximated ERIs used is numerically close to single

(8 significant decimal digits) rather than double (16 significant decimal digits) precision.

Another concern related to using the CD method is the final error in the computed energies. As rule of thumb, the absolute error of computed total energies and other properties caused by using the CD method is proportional to δ and becomes virtually equal to zero for $\delta \leq 10^{-10}$. Relative energies like, e.g., electron propagator poles (ionization potentials and electron affinities) or excitation energies are very robust with respect to the CD threshold and converge rapidly to the numerically exact ones ($\delta \geq 10^{-5}$ is more than enough to achieve millielectronvolt accuracy).[35,36]

Before we leave this section, let us briefly discuss some technical aspects of the factorization. For correlated methods, an important feature of this factorization is that it holds also in the case of the molecular orbital (MO) representation. If **C** is the MO expansion coefficients matrix, then an ERI in MO representation can be calculated by exploiting the same factorization (eq 1):

$$(pq|rs) = \sum_{K=1}^{M} L_{pq}^{K} L_{rs}^{K} \qquad (4)$$

where p, q, r, and s denote MO indices and a MO transformed Cholesky vector L_{pq}^{K}:

$$L_{pq}^{K} = \sum_{\mu} \sum_{\nu} C_{\mu p} L_{\mu\nu}^{K} C_{\nu q} \qquad (5)$$

reduces the scaling of the atomic orbital (AO) to molecular orbital (MO) transformation from $\mathcal{O}(N^5)$ to $\mathcal{O}(N^4)$. The CD factorization substantially reduces storage demands (by factor $\sim N^2/M$) and I/O overheads and thus converts the problem of determining electron correlation energies from a memory-bound one to a compute-bound one.[37,38] The time needed to complete a compute-bound task depends mostly on the performance of an execution unit (CPUs core, GPUs core) and can be significally reduced by using single precision arithmetic.

2.2. A Priori Error Estimation Caused by Using Single Precision Arithmetic. In MP2 theory, only the ($ov|ov$) class of molecular ERIs is needed to compute the electron correlation energy $E^{(2)}$:

$$E^{(2)} = \sum_{\substack{i \\ j \geq i}}^{N_o} \sum_{\substack{a \\ b}}^{N_v} \frac{(2 - \delta_{ij})[2(ai|bj) - (aj|bi)](ai|bj)}{\varepsilon_i - \varepsilon_a + \varepsilon_j - \varepsilon_b} \qquad (6)$$

where a and b denote virtual orbitals, and i and j denote occupied HF orbitals; N_o and N_v are the total number of ocuppied and virtual orbitals, respectively. Let us estimate the error introduced by using single precision arithmetic for generating an approximated ERI via formula eq 4.

The error introduced in the inner product due to single precision arithmetic can be estimated as follows:[39,40]

$$|fl(\widetilde{ai|bj}) - (\widetilde{ai|bj})| \leq \gamma_M \sqrt{(\widetilde{ai|ai})(\widetilde{bj|bj})} \qquad (7)$$

where

$$\gamma_M = \frac{Mu}{1 - Mu} \qquad (8)$$

$fl(\widetilde{ai|bj})$ means that an approximated ERI is computed with single precision arithmetic via eq 4, and $u = 2^{-24} \approx 5.960 \times 10^{-8}$ is named *unit roundoff*.[41] The prefactor γ_M depends hyperbolically on M. However, as long as $M \leq 10^6$, this dependency is essentially linear. Since the number of Cholesky vectors M typically grows linearly with system size, the prefactor γ_M should scale linearly with the system size. By looking at the square root in eq 7, one can easily recognize the so-called Schwarz upper bound to an ERI. Figure 1 shows the distribution of the upper bounds of the ERIs relevant to the MP2 correlation energy for the illustrative example of the water dimer $(H_2O)_2$ according to eq 7. We notice that this distribution is in the range from 10^{-5} to 10^{-8} and peaks at 10^{-6}.

According to our empirical experience, this is a typical distribution. A relevant reason for this well behaved distribution is that the Cholesky vectors are free from large components (see Figure S1 in the Supporting Information). The CD method is numerically well conditioned, and available implementations are very robust.[14,19,42] CD methods have other appealing features related to the structure of the Cholesky vectors which we do not discuss here, and we refer the interested reader to refs 16, 34, and 43 for more details.

A particularly relevant point is that the upper bounds of the ERIs shown in Figure 1 significantly overestimate the true error induced by the use of single precision arithmetic. For this purpose, we also show in Figure 1 the distribution of the true errors of the ERIs, i.e., of $|fl(\widetilde{ai|bj}) - (\widetilde{ai|bj})|$. As clearly seen, the true errors range from 10^{-8} to 10^{-14}, and the distribution peaks at about 10^{-11}.

In summary, we expect that the evaluation of the ERIs in single precision arithmetic has only a slight impact on the MP2 correlation energies. To be more precise, we claim that the error caused by single-precision arithmetic is expected to be comparable to the error introduced by the CD method in common practical computations.

3. Computational Details

For test calculations, we used a set of water clusters $(H_2O)_n$ ($n = 2, ..., 20$)[44,45] and the taxol molecule $(C_{47}H_{51}NO_{14})$.[46] In the present study, we employed Roos's ANO-L-VXZP (X = D, T) basis sets.[47,48]

The MP2 method in single precision was implemented in the development version of the P-RICDΣ program.[35] As input data, P-RICDΣ uses the integral tables in the AO representation ($\mathbf{L}_{\mu\nu}$) and the SCF MO LCAO coefficients which are generated with the MOLCAS ab initio package.[19,49]

Within P-RICDΣ, the computation of the MP2 correlation energy proceeds in two steps: a stepwise parallel transformation of integral tables from the AO to MO representation and subsequent calculation of the $E^{(2)}$ energy correction via eq 6. The transformed Cholesky vectors in the MO basis ($\mathbf{L}_{ai}$) are stored in single precision (each number occupies 32 bits rather than 64 bits). The approximated ERIs are
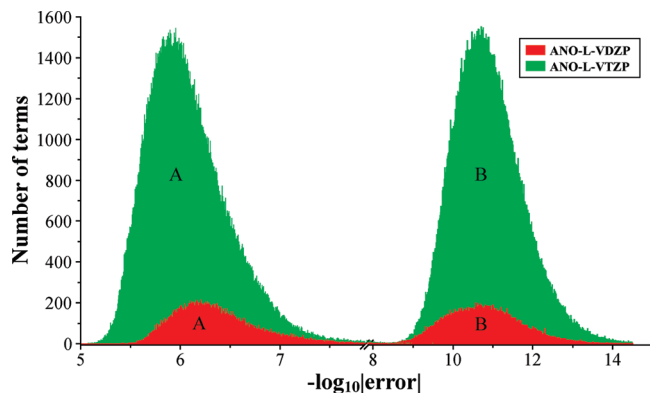
Accurate Quantum Chemistry

J. Chem. Theory Comput., Vol. 7, No. 2, 2011 **323**

Figure 1. Distributions of the errors of the $(ai|bj)$ ERIs for the water dimer using ANO-L-VDZP and ANO-L-VTZP atomic basis sets: (A) The distribution of the upper bounds according to inequality 7, i.e., $\gamma_M \sqrt{(ai|ai)(bj|bj)}$. (B) The distribution of the true error, i.e., $|fl(\widetilde{ai|bj}) - (\widetilde{ai|bj})|$. Note the logarithmic scale used.

Figure 2. The normalized absolute error (Δ_{64-32}/n) in the all-electron MP2 energy caused by single precision for a series of water clusters $(H_2O)_n$ ($n = 2-20$) employing the ANO-L-VDZP and ANO-L-VTZP basis sets. The dash horizontal lines display the average normalized error. Those are 3.55×10^{-9} (red color) and 8.65×10^{-9} E_h (green color) in the VDZP and VTZP basis sets, respectively. The solid horizontal line (black) indicates chemical accuracy (1.593×10^{-3} E_h). Note the logarithmic scale used.

computed in single precision arithmetic by calling an appropriate *sdot* BLAS function (single precision inner product). The above-described utilization of single precision (type casting and using the *sdot* function) automatically reduces the memory demands and execution time by a factor of 2. In order to accumulate the $E^{(2)}$ energy corrections, double precision was used because this yields a substantial gain in the final accuracy. Summation in double precision which scales as $\mathcal{O}(N_o^2 N_v^2)$ does not lead to any performance degradation because it only constitutes less than 1% ($\propto 1/M$) of the total number of floating point operations required. The most computationally demanding step of the entire algorithm is by far the generation of the $(\widetilde{ai|bj})$ ERIs, which scales as $\mathcal{O}(N_o^2 N_v^2 M)$.[31,50]

For comparison, standard MP2 energy calculations (in double precision) were carried out within the MOLCAS 7 program using a CD-based implementation.[51] It should be particularly emphasized that the single precision MP2 calculations were done over exactly the same data and in the same runtime environment that were used for the double precision ones.

All programs used in this work were compiled within Intel Cluster Toolkit 4.0. All calculations were done on Intel Xeon E5440 (2.83 GHz) processors.

In all calculations, a CD threshold of 10^{-10} was used unless otherwise specified.

4. Results and Discussion

4.1. Water Clusters. The key results of our work are displayed in Figure 2 (see also Figure S2 and Tables S3 and S4 in the Supporting Information). The figure shows the absolute error in the $E^{(2)}$ energy correction (Δ_{64-32}) normalized to the size of the cluster (i.e., divided by the number of water molecules) caused by the evaluation of ERIs in single precision. The error is determined as the absolute difference between the MP2 energy computed using the P-RICDΣ (single precision) and MOLCAS 7 (double precision) programs and the $\delta = 10^{-10}$ CD threshold. As predicted in section 2, single precision arithmetic introduces a negligible
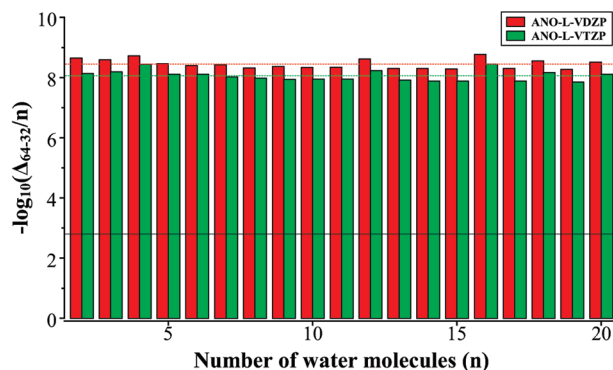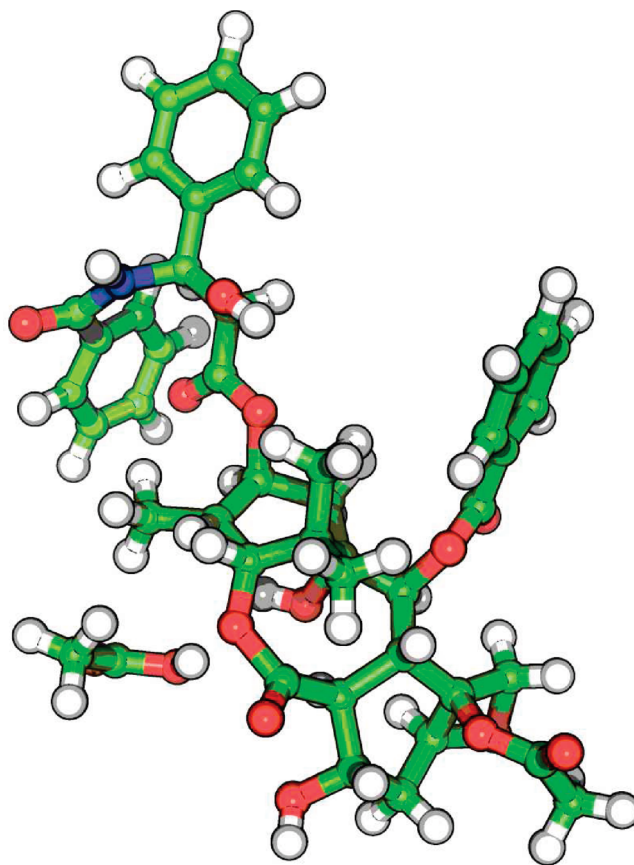

Figure 3. The taxol molecule ($C_{47}H_{51}NO_{14}$). The total number of basis functions in the ANO-L-VDZP basis set is 1099.

error into the computed MP2 correlation energy. The actual error encountered in the correlation energies amounts to 100 nHartree (1 nHartree = 10^{-9} E_h) only. In particular, the maximal (mean) absolute errors in the $E^{(2)}$ energy correction are 100 (43.7) and 269 (107) nHartree in the ANO-L-VDZP and ANO-L-VTZP basis sets, respectively.

It is clearly seen from Figure 2 that the normalized error only slightly depends on the cluster size and mostly depends

Table 1. The $E^{(2)}$ Correlation Energies for the Taxol Molecule Computed in Double ($E_{64}^{(2)}$) and Single Precision ($E_{32}^{(2)}$) by Employing Different CD Schemes and the ANO-L-VDZP Valence Basis Set[a]

method[b]	$E_{64}^{(2)}$	$E_{32}^{(2)}$	Δ_{CD}	Δ_{64-32}
CD-4	−9.399108640	−9.399108549	1.906×10^{-3}	9.100×10^{-8}
acCD-4*	−9.400377074	−9.400377031	6.373×10^{-4}	4.300×10^{-8}
acCD-4	−9.396719436	−9.396719405	4.295×10^{-3}	3.100×10^{-8}
CD-6	−9.400953079	−9.400952911	6.128×10^{-5}	1.680×10^{-7}
acCD-6*	−9.400673749	−9.400673704	3.406×10^{-4}	4.500×10^{-8}
acCD-6	−9.397581736	−9.397581697	3.433×10^{-3}	3.900×10^{-8}
CD-9	−9.401014359	−9.401013997	0.000	3.620×10^{-7}

[a] The CD-9 scheme is highly accurate and provides the reference value. The basis set contains 1099 basis functions; the number of the doubly occupied orbitals is 223. Shown also are the absolute errors of the correlation energies caused by using single precision arithmetic (Δ_{64-32}) and the errors of the various approximate CD schemes (Δ_{CD}). All energies in au. [b] CD-n refers to the full-CD decomposition threshold $\delta = 10^{-n}$. acCD-n* means "*atomic compact CD*", and acCD-n auxiliary basis sets have been formed from the original acCD-n* ones by removing the highest angular momentum functions. See refs 15, 16 for details.

on the atomic basis set used. By going from the ANO-L-VDZP to the ANO-L-VTZP basis set, the averaged normalized error changes from 3.6 to 8.7 nHartree, i.e., becomes only 2.42 times larger. At the same time, the number of floating point operations needed to compute $E^{(2)}$ increases by a factor of ∼18.62 (the generation of the $(\overline{ai}\overline{bj})$ ERIs). This difference by about one order of magnitude is due to the cancellation of errors when summing up the contributions from the individual integrals in eq 6. By taking into account the information that the corresponding number of Cholesky vectors increased by a factor of 2.43, in average, over the set of water clusters (see Table S5 in the Supporting Information), we can claim that the Δ_{64-32} error varies linearly with the number of Cholesky vectors, i.e., with the system size. This observation is in complete agreement with the error model considered in the section 2.2 (see eqs 7 and 8).

Let us make a rough estimate of the critical size which a system must have in order to cross the limit of chemical accuracy. By taking the value 10 nHartree (10^{-8} E_h) as averaged error per water molecule, the critical size is estimated to be 160 000 water molecules or, equally, 500 000 atoms. This critical size is currently much beyond reach for correlated quantum chemistry.

4.2. Taxol Molecule. In order to demonstrate that the numerical results reported above are general and are not biased to the water clusters set only, let us consider another example, namely, the taxol molecule (see Figure 3). Table 1 reports the MP2 correlation energies computed in double and single precision by employing various CD schemes. As in the case of the water clusters, the single precision errors (Δ_{64-32}) are negligibly small: the error lies in the range from 31 to 362 nHartree. It is clearly seen from the Table 1 that the error caused by the use of single precision (Δ_{64-32}) is a few orders of magnitude smaller than the corresponding approximation error Δ_{CD} of the CD scheme.

5. Future Prospect and Perspectives

The high-end floating-point mathematical coprocessors available on the market offer teraflop (10^{12} floating point operations per second) single-precision performance. For example, the performance of Nvidia's Tesla S2050 GPGPU and IBM's PowerXCell 8i based solutions are 4.1 and 6.4 teraflops, respectively.[52,53] Such performances are roughly

equivalent to the total performance of 200 Intel Xeon 54xx (Harpertown) cores. But the current price of either Nvidia's or IBM's solution is only a 1/10th of the corresponding CPUs. With respect to the results we have obtained, we consider coprocessors as very promising computational platforms for performing accurate large-scale correlated calculations. With particular emphasis on electron propagator calculations, which are our primary goal, we plan to extend the capabilities of our P-RICDΣ program accordingly (transfer Cholesky vectors to coprocessors and generate the needed molecular integrals via a BLAS library provided by vendor).

6. Conclusions

In the present work, we clearly demonstrate by the illustrative example of MP2 theory that single precision is sufficient for post Hartree−Fock methods relying on the Cholesky decomposition of the two-electron integrals. The key advantage of the proposed scheme is that 50% performance gain and 50% reduction in memory demands can be achieved by only minor changes in the existing codes. Our results open intriguing perspectives for future developments and trends in the computational quantum chemistry.

Supporting Information Available: Graphical representation of the distrubution of the components of Cholesky vectors in molecular orbital basis sets. The graphical representation of the absolute error (Δ_{64-32}) in the all-electron MP2 energy caused by single precision, tables containing total Hartree−Fock energies, MP2 correlation energies (computed with double and single precision), number of cholesky vectors for a set of $(H_2O)_n$ ($n = 2, ..., 20$) water clusters employing the CD threshold of $\delta = 10^{-10}$ and the ANO-L-VDZP and ANO-L-VTZP atomic basis sets. This material is available free of charge via the Internet at http://pubs.acs.org/.

References

(1) In the source codes of the most widely used ab initio packages such as Molcas, Molpro, and ACES-III, one can easily detect

Accurate Quantum Chemistry

J. Chem. Theory Comput., Vol. 7, No. 2, 2011 **325**

that each function or subroutine explicitly declares all variables in double precision.

(2) Boisvert, R. F.; Cools, F.; Einarsson, B. Precision, Accuracy and Reliability. In *Accuracy and Reliability in Scientific Computing (Software, Environments, Tools)*; Einarsson, B., Ed.; SIAM Press: Philadelphia, PA, 2005; Vol. SE-18, p 21.

(3) Loh, E.; Walster, G. W. *Reliab. Comput.* **2002**, *8*, 245–248.

(4) Martinez, T. J.; Carter, E. A. Pseudospectral methods applied to the electron correlation problem. In *Modern Electronic Structure Theory. Part II*, 2nd ed.; Yarkony, D. R., Ed.; World Scientific: Singapore, 1995; Vol. 2, pp 1132−1165.

(5) Pulay, P. *Chem. Phys. Lett.* **1983**, *100*, 151–154.

(6) Saebø, S.; Pulay, P. *Annu. Rev. Phys. Chem.* **1993**, *44*, 213–236.

(7) Fedorov, D. G.; Ishimura, K.; Ishida, T.; Kitaura, K.; Pulay, P.; Nagase, S. *J. Comput. Chem.* **2007**, *28*, 1476–1484.

(8) Harris, F. E.; Rein, R. *Theor. Chim. Acta* **1966**, *6*, 73–82.

(9) Billingsley, F. P.; Bloor, J. E. *J. Chem. Phys.* **1971**, *55*, 5178–5190.

(10) Whitten, J. L. *J. Chem. Phys.* **1973**, *58*, 4496–4501.

(11) Vahtras, O.; Almlöf, J.; Feyereisen, M. W. *Chem. Phys. Lett.* **1993**, *213*, 514–518.

(12) Linderberg, J. *Int. J. Quant. Symp.* **1977**, *S11*, 353–357.

(13) Beebe, N. H. F.; Linderberg, J. *Int. J. Quantum Chem.* **1977**, *12*, 683–705.

(14) Koch, H.; Sánchez de Merás, A.; Pedersen, T. B. *J. Chem. Phys.* **2003**, *118*, 9481–9484.

(15) Aquilante, F.; Lindh, R.; Pedersen, T. B. *J. Chem. Phys.* **2007**, *127*, 114107.

(16) Aquilante, F.; Gagliardi, L.; Pedersen, T. B.; Lindh, R. *J. Chem. Phys.* **2009**, *130*, 154107. We note that the Supplementary Material corresponding to this article contains important information.

(17) Aquilante, F.; Pedersen, T. B.; Lindh, R.; Roos, B. O.; Sánchez de Merás, A.; Koch, H. *J. Chem. Phys.* **2008**, *129*, 024113.

(18) Hättig, C. Beyond Hartree-Fock: MP2 and Coupled Cluster Methods for Large Systems. In *Computational Nanoscience: Do It Yourself!*; Grotendorst, J., Blügel, S., Marx, D., Eds.; John von Neumann Institute for Computing: Jülich, Germany, 2006; Vol. 31, pp 245−278.

(19) Aquilante, F.; De Vico, L.; Ferré, N.; Ghigo, G.; Malmqvist, P.-Å.; Neogrády, P.; Pedersen, T. B.; Pitoñák, M.; Reiher, M.; Roos, B. O.; Serrano-Andrés, L.; Urban, M.; Veryazov, V.; Lindh, R. *J. Comput. Chem.* **2010**, *31*, 224–247.

(20) Pople, J. A. *Rev. Mod. Phys.* **1999**, *71*, 1267–1274.

(21) Hoffmann, R.; Schleyer, P. V. R.; Schaefer, H. F., III. *Angew. Chem.* **2008**, *47*, 7164–7167.

(22) Tesla C2050/C2070 GPU Computing Processor. http://www.nvidia.com/object/product_tesla_C2050_C2070_us.html (accessed Sep 17, 2010).

(23) AMD FireStream Technology, see for example: AMD FireStream 9270 GPU Compute Accelerator. http://www.amd.com/us/products/workstation/firestream/firestream-9270/ Pages/firestream-9270.aspx (accessed Sep 17, 2010).

(24) The Cell project at IBM Research. http://www.research.ibm./cell/cell_chip.html (accessed Sep 17, 2010).

(25) Ufimtsev, I. S.; Martinez, T. J. *J. Chem. Theory Comput.* **2008**, *4*, 222–231.

(26) Ufimtsev, I. S.; Martinez, T. J. *Comput. Sci. Eng.* **2008**, *10*, 26–34.

(27) Ufimtsev, I. S.; Martinez, T. J. *J. Chem. Theory Comput.* **2009**, *5*, 1004–1015.

(28) Yasuda, K. *J. Comput. Chem.* **2007**, *29*, 334–342.

(29) Yasuda, K. *J. Chem. Theory Comput.* **2008**, *4*, 1230–1236.

(30) Asadchev, A.; Allada, V.; Felder, J.; Bode, B. M.; Gordon, M. S.; Windus, T. L. *J. Chem. Theory Comput.* **2010**, *6*, 696–704.

(31) Vogt, L.; Olivares-Amaya, R.; Kermes, S.; Shao, Y.; Amador-Bedolla, C.; Aspuru-Guzik, A. *J. Phys. Chem. A* **2008**, *112*, 2049–2057.

(32) Olivares-Amaya, R.; Watson, M. A.; Edgar, R. G.; Vogt, L.; Shao, Y.; Aspuru-Guzik, A. *J. Chem. Theory Comput.* **2010**, *6*, 135–144.

(33) Watson, M.; Olivares-Amaya, R.; Edgar, R. G.; Aspuru-Guzik, A. *Comput. Sci. Eng.* **2010**, *12*, 40–51.

(34) Pedersen, T. B.; Aquilante, F.; Lindh, R. *Theor. Chem. Acc.* **2009**, *124*, 1–10.

(35) Vysotskiy, V. P.; Cederbaum, L. S. *J. Chem. Phys.* **2010**, *132*, 044110.

(36) Böstrom, J.; Delcey, M. G.; Aquilante, F.; Serrano-Andrés, L.; Pedersen, T. B.; Lindh, R. *J. Chem. Theory Comput.* **2010**, *6*, 747–754.

(37) Memory bound refers to a situation in which the time to complete a given computational problem is decided primarily by the amount of available memory to hold data. In other words, the limiting factor of solving a given problem is the memory access speed.

(38) CPU bound (or compute bound) is when the time for a computer to complete a task is determined principally by the speed of the central processor.

(39) Higham, N. J. Basics. In *Accuracy and Stability of Numerical Algorithms*, 2nd ed.; SIAM Press: Philadelphia, PA, 2002; pp 62−65.

(40) Golub, G. H.; Van Loan, C. F. Matrix analysis. In *Matrix Computations*, 3rd ed.; The Johns Hopkins University Press: Baltimore, MD, 1996; pp 62−64.

(41) IEEE standard for binary floating-point arithmetic. ANSI/IEEE Standard, Std 754−1985, New York, 1985.

(42) Røeggen, I.; Johansen, T. *J. Chem. Phys.* **2008**, *128*, 194107.

(43) Jung, Y.; Sodt, A.; Gill, P. M. W.; Head-Gordon, M. *Proc. Natl. Acad. Sci. U. S. A.* **2005**, *102*, 6692–6697.

(44) Maheshwary, S.; Patel, N.; Sathyamurthy, N.; Kulkarni, A. D.; Gadre, S. R. *J. Phys. Chem. A* **2001**, *105*, 10525–10357.

(45) The Cambridge Cluster Database, Ab initio Optimized (H2O)$_N$ Clusters. http://www-wales.ch.cam.ac.uk/wales/CCD/anant-watcl.html (accessed Sep 17, 2010).

(46) The cartesian coordinates are available on the Web: http://www.petachem.com/data/taxol.xyz (accessed Sep 17, 2010).

(47) Widmark, P.-O.; Malmqvist, P.-Å.; Roos, B. O. *Theor. Chim. Acta.* **1990**, *77*, 291–306.

(48) Widmark, P.-O.; Persson, B. J.; Roos, B. O. *Theor. Chim. Acta.* **1991**, *79*, 419–432.

(49) Karlström, G.; Lindh, R.; Malmqvist, P.-Å.; Roos, B. O.; Ryde, U.; Veryazov, V.; Widmark, P.-O.; Cossi, M.; Schimmelpfennig, B.; Neogrady, P.; Seijo, L. *Comput. Mater. Sci.* **2003**, *28*, 222–239.

(50) Katouda, M.; Nagase, S. *Int. J. Quantum Chem.* **2009**, *109*, 2121–2130.

(51) Aquilante, F.; Pedersen, T. B. *Chem. Phys. Lett.* **2007**, *449*, 354–357.

(52) The Tesla S2050 1U Computing System. http://www.nvidi-a.com/object/product-tesla-S2050-us.html (accessed Sep 17, 2010).

(53) IBM BladeCenter QS22. http://www-03.ibm.com/systems/bladecenter/hardware/servers/qs22/ (accessed Sep 17, 2010).

(54) bwGRiD, member of the German D-Grid initiative, funded by the Ministry for Education and Research (Bundesministerium für Bildung und Forschung) and the Ministry for Science, Research and Arts Baden-Wuerttemberg (Ministerium für Wissenschaft, Forschung und Kunst Baden-Württemberg). http://www.bw-grid.de (accessed Sep 17, 2010).