Performance Analysis Cluster Computing Environments on Molecular Dynamic Simulation of RAD GTPase and LOX-Curcumin Molecules with AMBER

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Abstract

Implementation of virtual laboratory on scientific research has produced huge acceleration. One of the virtual scientific research activity is molecular dynamic simulation. The virtual experiments need high computing resources to solve the problem. AMBER is one of the software that provides molecular dynamic simulation that can utilize the parallel computing facilities. In this paper, we conduct the molecular dynamic experiments in order to know reliability of cluster computing environment. The results show that an implicit solvent simulation takes longer time than that in vacuum scenario since one has to consider existence of solvent surround the molecules so the computation is much longer than in vacuum; that the speed up will likely to remain constant on certain additional number of processors; and that there is no significant speed up for case in the LOX-Curcumin explicit solvent simulation.

Keywords: *Performance Analysis, Molecular Dynamic, Cluster Computing, AMBER.*

1. Introduction

Drug design is a research field that comprises many disciplines including chemistry, biology, pharmacy, and computer science. Research on drug design has the characteristics which need huge computing resources, it takes supercomputer as one of high performance computing infrastructure to fulfill the requirement. Establishing supercomputer as primary high performance computing resources become special problems in the research community, especially for the researchers coming from a limited research budget institution or some third world country that does not provide sufficient budget for research on their national budget revenues and expenditure. One of the alternatives is to use cluster and grid computing environment. This technology is one of the finest solutions for every researchers in providing high performance computing resources for drug design experiments.

There are already success reports of drug design that have been produced which is based on computational based drug design. McCammon has produced antiretroviral raltegravir for HIV-1 using AutoDock [1]. Merck already released the product since it has been legalized by U.S. Food and Drug Administration on 12 October 2007. Another successful one is the production of schistomiasis drug that was released by Chen Yuzong. He used InvDock on his drug design research [2].

Molecular dynamics (MD) is a drug design research part that takes important role in the whole drug design research. Researchers do MD to study the molecular structures and its nature, protein folding, and protein structural analysis [3-4]. Previous work have been able to conduct MD on supercomputer with multicore systems [3], other used dedicated cluster with MD-Engine II [4], and

one quite popular similar projects is a volunteer distributed computing of Folding@HOME from University of Stanford, USA [5].

Previously, we have done MD research using GROMACS on our cluster computing environment which gives significant result on five nodes experiments [6]. We also conducted MD in GROMACS using another cluster computing environment, named Cluster05 and computing facility that equipped by GPU (graphical processing unit) which gives speed up until 11-12 times [7]. In this paper we present our MD experiments using AMBER. We would like to study the AMBER performance on cluster computing environment in order to have more comprehensive study on MD simulation using open source software. In the future, this study will result recommendation for establishing suitable high performance computing infrastructure to support MD research on drug design.

2. Molecular Dynamics

Molecular Dynamic (MD) has several functions to show molecule structures, movement and function of molecules. MD performs the computation of atom movement in molecular system using molecular mechanics. The dynamic movement of a protein molecule is a reaction that is produced by protein structure and it is an important element of special function that belongs to the molecules and also represented the general function of the protein. The knowledge of relation between the dynamical 3D structures of a protein is very important to know in order to understand how a protein works. However, real laboratory experiment of protein dynamic movement is very difficult and costly to be done. Thus, people develop molecular dynamic simulation as a virtual experimental method which is able to analyze the relation between structure and protein dynamic movement. The simulation explores conformation energy of a protein molecule itself. Up recently, the development of MD simulation is still in progress. In general, MD simulation is used to gain information on the dynamic movement and the changes of structure conformation of a protein as well as other biological macromolecules. Through this simulation, thermodynamic and kinetic information of a protein can be explored [8].

In this work, we use AMBER [15] as a MD software simulation. This software has several functions that can be used for tuning different parameter of MD simulation. MD module on AMBER uses SANDER, and as for force field computation, it uses LEaP (detail force field parameter can be seen in table (1)). AMBER can be set by several environment model that represent different environment on protein dynamic movement. Those different environment condition are in vacuum, implicit solvent, and explicit solvent that should give different trajectory output and different consumed time of experiments [9].

TABLE 1. FORCE FIELD PARAMETERS ON LEAP [9].

Force field files	Topology	Parameters
leaprc.ff99SB	Hornak & Simmerling	parm99.dat+frcmod.ff99SB
leaprc.ff99bsc0	Hornak & Simmerling	parm99.dat+frcmod.ff99SB+frcmod.parmbsc0
leaprc.ff03.r1	Duan et al. 2003	parm99.dat+frcmod.ff03
leaprc.ff03ua	Yang et al. 2003	parm99.dat+frcmod.ff03+frcmod.ff03ua
leaprc.ff02	*reduced charges*	parm99.dat+frcmod.ff02pol.r1
leaprc.gaff	N/A	gaff.dat
leaprc.GLYCAM_06	Woods et al.	GLYCAM_06c.dat
leaprc.GLYCAM_04EP	Woods et al.	GLYCAM_04EP.dat
leaprc.amoeba	Ren & Ponder	Ren & Ponder

3. The Cluster Computing Environment.

We built two cluster computing environment with different hardware specification. The intention is to see whether there is a significant difference between these two cluster particularly the one that depend on dual core PCs and on quad core PCs. Both cluster computing environment hardware specification can be seen in the table (2).

Table 2. The Hardware specification of cluster computing environment.

Hastinapura	Cluster05
• Sun Fire X2 100	• Assemblies machine
• AMD Opteron 2.2 GHz (dual core)	• Quad Core 2.8GHz
• 1 GB RAM	• 2x2GB RAM
• HDD 80 GB	• HDD 640GB

Hastinapura - one of two cluster computing environments built from 16 server machines of Sun Fire X2 100 with AMD Opteron 2.2 GHz processors, this cluster system can provide 32 logical cores and is quite old, established at 2006 and still used for certain scientific computing. Another cluster, Cluster05, built from four quad core machine hence providing 16 logical cores with better hardware specification. Cluster05 built from 4 PC desktops with quadcore 2.8 GHz in each machine. It provides 16 logical cores to utilize.

Each cluster computing environment uses Linux as operating system, Hastinapura uses Debian and Cuslter05

uses Ubuntu. MPICH 2.0 as a parallel execution platform is installed in both systems. We do not yet use middleware or scheduler application for managing jobs such as SGE (Sun Grid Engine) or PBS scheduler. We utilize this cluster computing environment environment using SANDER from AMBER that can be compiled as a parallel application using SANDER.MPI.

4. Experiments and Results

We use two primary molecules in this experiments. the first molecule is RAD GTPase. RAD (Ras Associated with Diabetes) is of the RGK family small GTPase located in skeletal muscle in humans with type 2 diabetes. Crystalline form of the GTPase RAD has a resolution of 1.8 Angstroms. The crystal structure of the GTPase RAD created by Yanuar, et al. in Structural Biology Laboratory, Nara Institute of Science and Technology [10].

The second molecule used is LOX-Curcumin. This molecule is one of the enzymes that play an important role in inflammatory reactions or inflammation. Many studies on LOX (Lipoxygenase) inhibitors attempted to investigate the anti-cancer properties. The majority of the risk / activators stimulate cancer cell proliferation in carcinogenesis and metastasis through inflammatory mechanisms [11]. LOX inhibition mechanism of anti-inflammatory drugs lipoxygenase is interesting to study, one of it, is inhibition by compounds from medicinal plants. One of the medicinal plants that work synergistic reduce chronic inflammation is curcumin [12]. Curcumin has proven beneficial in the prevention and treatment of a number of inflammatory diseases associated with its anti-inflammatory activity [13]. Curcumin has anti-inflammatory effects via non-immunological mechanisms of inhibition of cyclooxygenase activity and lipoxygenase [14].

We use three different simulation scenario applied to the molecules. In vacuum and Implicit solvent scenario models applied to RAD GTPase and explicit solvent scenario model applied to LOX-Curcumin. Preliminary experiments has been done on the Hastinapura cluster computing environment by using RAD GTPase molecule with in vacuum and implicit solvent as environment scenario models. The other ones are done on Cluster05 cluster computing environment. Here, we used two molecules at the same experiments with three scenario simultaneously. The first scenario is RAD GTPase with in vacuum and implicit solvent scenario models and the second is LOX-Curcumin with explicit solvent scenario model.

The objective of this experiments is to study the effect of incremental of time steps and incremental of processors number on the execution time; to study whether there is a significant difference between two cluster computing environments built and to know the size of MD simulation output. The latter is necessary to see how big the storage is needed in a simulation prior to the execution of the code. This is information is useful to prevent hardware failures. From these three aspects of evaluation, we hope to have enough information on strategic plan on doing reliable MD simulation research on cluster computing environment.

We present the result of our experiments on Hastinapura and the experiments on Cluster05 cluster computing environment. In the table (3), we provide the experiments result of RAD GTPase with in-vacuum scenario model on Hastinapura cluster computing environment. The entries in the table indicate the time (in thousand seconds) required for the simulation to finish. The entries in brackets indicate the speed up gained. The time steps TS are the time required in simulation in Pico seconds, the longer of time steps are expected to provide a good results in term of simulation values. The number of processors NP is the number processors used in the simulation.

TABLE 3. EXECUTION TIME OF MD SIMULATION OF RAD GTPASE WITH IN VACUUM SCENARIO MODEL ON HASTINAPURA

TS	NP			
	1	2	4	8
100	6.69	3.76 (1.8)	3.31 (2.02)	1.51 (4.42)
200	13.41	7.22 (1.8)	4.53 (2.96)	3.04 (4.41)
300	20.25	11.38 (1.7)	6.9 2 (2.93)	4.59 (4.41)
400	27.11	14.93 (1.8)	9.11 (2.98)	5.98 (4.53)

It is obvious to see that increasing timesteps from 100 ps to 400 will almost double the execution time. The fastest process is when executing molecule with 100 ps timestep with 8 processors (25 minutes) and the longest one is executing molecule with 400 ps timestep with 1 processor (7.5 hours). Relative speed up on this cluster computing environment (ratio of fastest and longest execution time on the same timesteps) is 4.44 times on the average. In general, it is also obvious that the speed gained is between 1.7 at two processors to 4.53 at eight processors.

Next, we provide the result that comes from the experiments with different scenario on RAD GTPase. In the table (4), we provide the experiments result of RAD GTPase with implicit solvent scenario model in Hastinapura cluster computing environment

As the previous table (3), we can also see from table (4) that timesteps take effect on execution time. The fastest process is when executing molecule with 100 ps timestep with 8 processors (4.3 hours) and the longest one is executing molecule with 400 ps timestep with 1 processor

(5 days). Relative speed up on this cluster computing environment (ratio of fastest and longest on the same timesteps) is 7.38 times on the average. It takes approximately 2 times better speed up than the first scenario (in vacuum scenario model). It is also obvious that in this case the running the simulation with more processors will gain significant speed up from around 2.0 at two processors to 7.5 at eight processors. The speed up gain in this case is much better than that of table (3).

TABLE 4. EXECUTION TIME OF MD SIMULATION OF RAD GTPASE WITH IMPLICIT SOLVENT SCENARIO MODEL ON HASTINAPURA

TS	NP			
	1	2	4	8
100	112.67	57.01 (1.98)	29.08 (3.87)	15.31 (7.36)
200	225.54	114.73 (1.97)	58.37 (3.86)	31.24 (7.22)
300	337.96	172.03 (1.96)	87.78 (3.85)	45.28 (7.46)
400	452.49	233.12 (1.94)	116.71 (3.88)	60.38 (7.49)

Observing the table (3) and (4) ,we see that the implicit solvent scenario model takes more time on processing MD simulation. In the implicit solvent simulations, the free energy of the solution requires computing ΔG_{lar} long enough because of the free energy calculation of the electrical charges of atoms and solvent electrical charge. Since in a molecule there are huge numbers of atoms so it takes a long time in calculating the free energy of solution.

Now, we compare the previous experiments on Hastinapura with the same scenario on Cluster05. There is a different result as for both of cluster computing environment have different spesification. We provide this in the following table (5)

TABLE 5. EXECUTION TIME OF MD SIMULATION OF RAD GTPASE WITH IN VACUUM SCENARIO MODEL IN CLUSTER05

	NP			
TS	1	2	4	8
100	3.96	2.48 (1.60)	1.74 (2.27)	1.57 (2.51)
200	7.56	4.32 (1.75)	3.49 (2.17)	3.13 (2.41)
300	11.52	6.48 (1.78)	5.15 (2.24)	4.71 (2.45)
400	15.48	8.64 (1.79)	6.72 (2.30)	6.34 (2.44)

The table (5) shows the similar phenomena to the one on the previous experiments. The fastest process is when executing molecule with 100 ps timestep with 8 processors and the longest one is executing molecule with 400 ps timestep with 1 processor . The execution time is almost linear to the increasing of time steps TS.

Next in the table (6) we can see the result of MD experiments with implicit solvent scenario model on Cluster05 cluster computing environment.

TABLE 6. EXECUTION TIME OF MD SIMULATION OF RAD GTPASE WITH IMPLICIT SOLVENT SCENARIO MODEL ON CLUSTER05

	NP			
TS	1	2	4	8
100	55.800	28.080 (2.0)	15.601 (3.6)	9.402 (5.9)
200	113.040	56.520 (2.0)	31.213 (3.6)	19023 (5.9)
300	168.120	84.600 (2.0)	46.828 (3.6)	27.379 (6.1)
400	223.290	113.400 (2.0)	62.296 (3.6)	37.826 (5.9)

Even though it is obvious that the speed up gained is from 2 to 6.1 which is lower than that of on Hastinapura but the one on Cluster05 run much faster.

Table 7.A the running time comparison of In vacuum experiments between those on Hastinapura and Cluster05.

	NP			
TS	1	2	4	8
100	1.7	1.5	1.9	1.0
200	1.8	1.7	1.3	1.0
300	1.8	1.8	1.3	1.0
400	1.8	1.7	1.4	0.9

Table 7.B the running time comparison of implicit solvent experiment between those on Hastinapura and Cluster05

	NP			
TS	1	2	4	8
100	2.0	2.0	1.9	1.6
200	2.0	2.0	1.9	1.6
300	2.0	2.0	1.9	1.7
400	2.0	2.1	1.9	1.6

Next, comparing the time spent on Cluster05 relative to those on Hastinapura on the same set of parameters data experiments on Rad GTPase. Table (7.A) is for the comparison on In vacuum experiments, while Table (7.B) is for implicit solvent case. Both of the entries of these two tables are obtained by dividing the entries of table 3 with entries of table 5 then, entries of table 4 with entries of table 6, respectively.

Observing these two tables, it is obvious that in general Cluster05 is much faster than Hastinapura. This result caused by different computational type on in-vacuum and

implicit solvent scenario model. Molecules computation for in-vacuum scenario model occured very fast, adding node of parallelization on the cluster computing environment will be hampered by its communication delay.

Both in-vacuum and implicit solvent of RAD GTPase molecules produced the same size MD simulation output. We would like to study the effect of the output size when the timesteps are increased. It is obvious that adding timesteps will increase the size of MD simulation output almost linearly. These results is provided in the table 8.

TABLE 8. MD SIMULATION OUTPUT FILE SIZE OF RAD GTPASE MOLECULES

	100 ps	200 ps	300 ps	400 ps	500 ps
Output file size (kb)	6.148	12.292	18.440	24.584	30.727
Conversion to MB	5,86	11,72	17,59	23,45	29,3

Next we present the results of the scenario using LOX-Curcumin only on Cluster05 using more processors up to 16. In this, the objective is to experiment LOX-Curcumin simulation until the longest timesteps that can be reached. While first scenario on RAD GTPase measured using real time execution, this second scenario used an estimated time execution which is a feature that is provided by AMBER in order to measure estimated process time on MD. The result of MD simulation with explicit solvent scenario model on LOX-Curcumin molecule presented in the table (9) and table (10), running with time steps TS 100—500 ps and TS 1-5 ns, respectively. The table entries indicate the simulation time needed in thousands of seconds, while the entries in brackets indicate the speed relative to the sequential process.

Table (9) and (10) show that the fastest process is when executing molecule with 100 ps timestep with 16 processors (28.5 hours) and the longest one is executing molecule with 5 ns timestep with 1 processor (81 days). Relative speed up gained on this cluster computing environment (ratio of fastest and longest on the timestep) is approximately 1.22 times.

It is obvious that still there is no signifcant speed up on this LOX-Curcumin experiments. Now if we do MD until 5 ns timestep then the longest estimated execution time occurred on 5 ns with 1 processor simulation is 7 millions second which is about 81 days. It is quite long for scientific experiment. Using 16 processors, it is reduced to about 5 millions seconds or or about 58 days, which is also still too long for a scientific experiment. Further investigation is needed as whether one should perform a simulation on a certain long timesteps TS.

TABLE 9. EXECUTION TIME OF MD SIMULATION OF LOX-CURCUMIN WITH EXPLICIT SOLVENT IN CLUSTER05 (100-500 PS)

TS (ps)	Processors Number				
	1	2	4	8	16
100	140.04	125.64 (1.11)	111.60 (1.25)	110.16 (1.27)	102.60 (1.36)
200	280.80	250.92 (1.12)	231.12 (1.21)	220.68 (1.27)	205.20 (1.37)
300	420.48	376.92 (1.12)	345.60 (1.22)	342.36 (1.23)	314.28 (1.34)
400	565.92	501.48 (1.13)	454.32 (1.25)	450.72 (1.26)	411.84 (1.37)
500	700.92	627.48 (1.12)	570.24 (1.23)	565.20 (1.24)	541.44 (1.29)

TABLE 10. EXECUTION TIME OF MD SIMULATION OF LOX-CURCUMIN WITH EXPLICIT SOLVENT IN CLUSTER05 (1-5 NS)

TS	Processors Number				
	1	2	4	8	16
1	1402.6	1256.4 (1.120	1122.48 (1.25)	1110.24 (1.26)	1035.36 (1.35)
2	2805.5	2514.2 (1.12)	2217.24 (1.27)	2211.84 (1.27)	2059.56 (1.36)
3	4207.7	3768.1 (1.12)	3374.64 (1.25)	3311.28 (1.27)	3049.20 (1.38)
4	5659.6	5026.3 (1.13)	4490.28 (1.26)	4455.00 (1.27)	4075.92 (1.39)
5	7009.6	6273.0 (1.12)	5639.76 (1.24)	5594.04 (1.25)	5054.04 (1.39)

5. Conclusion

From the results of experiments on RAD GTPase with in vacuum and implicit solvent scenario on two different cluster computing environment we can conclude that implicit solvent takes longer time than in-vacuum scenario because one has to consider existence of solvent surround the molecules so the computation is much bigger than in vacuum.

We can also conclude that the overhead communication still become the bottleneck problem on cluster computing environment. From implicit solvent scenario model provided on the Figure (1) we can see that the speed up will likely to remain constant on certain additional number of processors. In this experiment, this happened when we use 16 logical processors where we can see the trends of its bottleneck.

The last conclusion is that we do not have a significant speed up for case in the LOX-Curcumin explicit solvent simulation. These are shown on the speed up entries in Table 9 which only gain 1.11 speed up at two processors and 1.37 at six teen processors; in Table 10 which gain 1.12 at two processors and 1.39 at six teen processors. Then one may expect that for certain molecules using more logical processors will not speed up the execution time. This will be a challenge in MD simulation but this

will also be justified in our future works.

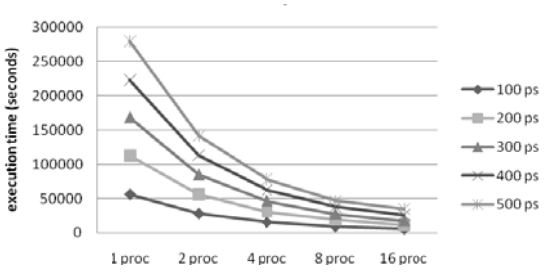

Figure 1. Execution time of MD simulation of RAD GTPase with implicit solvent scenario in Cluster05

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References

[1] Morris. "AutoDock's role in Developing the First Clinically-Approved HIV Integrase Inhibitor", 17 December 2007, [Online]. http://autodock.scripps.edu/news/autodocks-role-in-developing-the-first-clinically-approved-hiv-integrase-inhibitor. [accessed 20 July 2010].

[2] Anonym, "Customizing drugs to suit individuals", 20 January 2009, [Online]. http://www.nus.edu.sg/research/rg100.php. [Accessed 20 July 2010].

[3] S. R. Alam et.al., "Experimental evaluation of molecular dynamics simulations on multi-core systems," in *Proceeding of the 15th International Conference on High Performance Computing*. Bangalore, India, 17-20 December, 2008.

[4] T. Amisaki and S. Fujiwara., "Grid-enabled applications in molecular dynamics simulations using a cluster of dedicated computers, " in *Proceeding of Applications and the Internet Workshops*, pp. 616-622, 26-30 January, 2004.

[5] V. Pande, "Folding@HOME", 2010, Internet: http://folding.stanford.edu.

[6] A. Wibisono et.al., "Performance Analysis of Curcumin Molecular Dynamics Simulation using GROMACS on Cluster Computing Environment" , in *Proceeding of International Conference on Advanced Computer Science and Information System*, Bali, 2010.

[7] H. Suhartanto et.al., "Performance Analysis Cluster and GPU Computing Environment on Molecular Dynamic Simulation of BRV-1 and REM2 with GROMACS", *International Journal of Computer Science Issues*, vol. 8, no. 3, May 2011.

[8] A.H. de Vries et.al., "Molecular Dynamics Simulation of the Spontaneous Formation of a Small DPPC Vesicle in Water in Atomistic Detail, " *Journal of American Chemical Society*, vol. 126, pp. 4488-448, 2004.

[9] P. Lin, "Introduction to the AMBER Molecular Dynamics Package", *Tutorials from Materials Simulation Center, The Pennsylvania State University*, 30 April 2008. [Online]. http://msc.psu.edu/tutorials/IntroAmber_course.pdf. [Accessed, 17 Juni 2010].

[10] A. Yanuar, S. Sakurai, K. Kitano, Hakoshima, and Toshio, "Crystal structure of human rad gtpase of the rgk-family," *Genes to Cells*, vol. 11, no. 8, pp. 961-968, Agustus 2006.

[11] C.A. Hyde and S. Missailidis, "Inhibition of arachidonic acid metabolism and its implication on cell proliferation and tumour-angiogenesis, " *International Immunopharmacology*. 2009.

[12] Z. Ikawati et.al., "Pengaruh senyawa heksagamavunon-1 (HGV-1) terhadap inflamasi akut akibat reaksi Anafilaksis kutaneus aktif pada tikus Wistar jantan terinduksi ovalbumin, " B.S. Thesis, Faculty of Pharmacy, Gadjah Mada University, 2007.

[13] B. Aggarwal, et.al., "Curcumin: The Indian solid gold, " ETO. 2006.

[14] C.A. Utami, "Screening aktivitas anti inflamasi senyawa aktif yang terkandung pada beberapa tanaman obat indonesia melalui penghambatan enzim 12-Lipoksigenase secara in silico, " B.S. Thesis, Department of Pharmacy, Universitas Indonesia, 2009

[15] D.A. Case, T.A. Darden, T.E. Cheatham, III, C.L. Simmerling, J. Wang, R.E. Duke, R. Luo, R.C. Walker, W. Zhang, K.M. Merz, B.P. Roberts, B. Wang, S. Hayik, A. Roitberg, G. Seabra, I. Kolossváry, K.F. Wong, F. Paesani, J. Vanicek, J. Liu, X. Wu, S.R. Brozell, T. Steinbrecher, H. Gohlke, Q. Cai, X. Ye, J. Wang, M.-J. Hsieh, G. Cui, D.R. Roe, D.H. Mathews, M.G. Seetin, C. Sagui, V. Babin, T. Luchko, S. Gusarov, A. Kovalenko, and P.A. Kollman (2010), AMBER 11, University of California, San Francisco.

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