Joint Fujitsu-A*STAR Computational Bio-Medicine Forum

Date: 25th August 2009 **Venue:** M-Hotel, 81 Anson Road

Program:

MORNING

9:00 – 9:10 Welcome speech by **Dr Raj Thampuran,** Executive Director, Institute of High Performance Computing, A*STAR

Part I: Heart in the computer

9:10 – 10:00 **Prof Kadooka,** Fujitsu, **"**Challenges towards realization of tailor-made medical treatment by Heart Simulator"

10:00 – 10:15 **Coffee break**

10:15 – 11:00 **Dr Su Yi,** IHPC, A*STAR, "Geometrically-driven approach for monitoring left ventricular remodeling" and "4D patient-specific modeling of the left heart"

11:00 – 11:45 **Mr Huang Su,** SBIC, A*STAR, "A comprehensive approach for automatic segmentation of the left ventricle from cine magnetic resonance images "

11:45 – 12:15 **Panel Discussion**

12:15 – 1:30 **Lunch**

AFTERNOON

Part II: In–Silico drug design

1:30 – 2:10 **Mr Matsumoto,** Fujitsu, "Overview Fujitsu in-silico drug discovery technologies"

2:10 – 3:10 **Dr Fujitani,** Fujitsu, "MAPLE-CAFEE: Predictive computation of pharmaceutical protein-ligand affinity"

3:10 – 3:30 **Coffee break**

Part III: DNA Aptamers

3:30 – 4:15 **Dr Shozo FUJITA,** Fujitsu Laboratories Ltd. "Modified DNA Aptamer development service"

Part IV: Nature inspired therapeutic devices and computational biology

4:15 – 5:00 **Prof Andrew C. McIntosh**, University of Leeds, "Pharmaceutical sprays inspired by the bombardier beetle"

5:00 – 5:30 **Dr Chandra Verma**, BII, A*STAR, "Computer simulations in understanding molecular mechanisms in biology"

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Abstracts and Biographies of Speakers

Prof Y. Kadooka, Fujitsu, "Challenges towards realization of tailor-made medical treatment by Heart Simulator"

Abstract: Collaboratively with Profs Toshiaki Hisada and Sugiura Seiryo in the University of Tokyo (http://www.sml.k.u-tokyo.ac.jp/) we are now developing the Heart Simulator. On the other hand, Fujitsu is developing the Peta-Scale Computer (PSC) system whose capacity exceeds 10 PFLOPS and will be released on 2012. It is indispensable for the Heart Simulator, which realizes multi-scale phenomena, from cell to organ level, and multi-physics simulation, to run on such supercomputer system as the PSC.

In this presentation, the outline of PSC is introduced. Next, the functions of the Heart Simulator and some medical applications such as a development of Implantable Cardioverter-Defibrillator, Planning of Surgery for Dilatative Cardiomyopathy and a contribution to drug discovery are explained. Finally, the target of our research, namely tailor-made medical treatment system by the Heart Simulator is introduced.

After this presentation, I would like to hear your frank opinions, problems or issues to be overcome for us towards the realization and utilization of the Heart Simulator in clinical practice and to seek collaborations based on the Heart Simulator.

Biography:

Dr. Yoshimasa Kadooka has worked for Fujitsu Limited for the past 16 years. He began work as a Telecommunication Engineer and then was appointed Manager, Research and Development of Multimedia System. In 1997 he was appointed Director, Planning and Development of new Network Services for Fujitsu Business Systems Ltd. In 2002 he became a Research Fellow, IT Core Research Laboratories at Laboratories Ltd. In 2006 he was appointed General Manager and Senior Research Fellow, Peta-Scale Computing Research Center.

In 2004 he was awarded a Doctor of Science from the Graduate School of Natural Science and Technology, at Kanazawa-University. Since 2004 he has been Professor, Visiting Faculty, Kansai University and since 2007 he has been the Invited Professor at the Center for Advanced Medical Engineering and Informatics in Osaka University,

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Dr Su Yi, IHPC, A*STAR, "Geometrically-driven approach for monitoring left ventricular remodeling and 4D Patient-Specific Modeling of the Left Heart"

Abstract: There are two objectives we are trying to achieve in the 4D Heart Modeling Project. This first question is on "How to quickly extract a patient-specific geometrical model from medical image?" This includes the mitral valve and the other portions above the left ventricle.

This is a very common bottleneck faced by almost everyone trying to simulate the heart, because the geometry is the starting point. To have any clinical value, the geometric model must be patient-specific. This is the problem studied and solved by my team.

The second objective is to study the hemodynamic pattern, which is essentially a clinical question. This portion is to be done by the CFD team. We are using existing CFD codes and are currently exploring FLITE (from Swansea), FEFLO (embedded mesh approach) and a modified Peskin's approach developed by IHPC staff in the IHPC Biophysics group.

In summary, we are trying to answer other questions than how to do the CFD simulation. First, is on automatic geometrical modeling. Second, is related to clinical physiology. This method will also provide surgeons with 4D models for pre-operative study and preparation. The keywords are perhaps "automatic" and "patient-specific".

Biography:

Dr. Su Yi received his Mechanical Engineering degrees, B.Eng. with honors in 1997 and PhD in 2002 from National University of Singapore. Since 2006 he has been a Research Scientist cum Assistant Programme Manager at A8STAR's Advanced Computing, Institute of High Performance Computing, and Team Leader, Digital Modeling and Visualisation, Between 2003-2006 he was Senior Research Engineer, Software and Computing, IHPC, and from 2000 to 2003 a Research Engineer, Micro Electro-Mechanical Systems, IHPC.

His research expertise is in the areas of Automatic quadrilateral and hexahedral mesh generation, Non-manifold and mixed-dimensional mesh generation, Mesh enrichment and adaptive mesh generation, Computational geometry, and Scientific visualization.

Su Yi received the Outstanding Reviewer Award, 2005 IEEE/ASME International Conference on Advanced Intelligent Mechatronics. Between 1997-2000 he was a recipient of Research Scholarship, NUS. In 1997 and 1994 he was on the Dean's List, Mechanical and Production Engineering, NUS and in 1996-96 received Industrial Attachment Award from Motorola Electronics Pte Ltd.

Dr Su Yi serves in review and editorial boards of many international conferences and journals and program committees of international conferences. He has been publishing widely in high impact journals and invited conference publications and books.

Mr Huang Su, SBIC, A*STAR, " A comprehensive approach for automatic segmentation of the left ventricle from cine magnetic resonance images"

Abstract: Segmentation of the left ventricle is important in assessment of cardiac functional parameters. Manual segmentation for acquiring these parameters is time-consuming. Hence, automated and accurate segmentation methods are needed by cardiac clinicians. We propose a comprehensive approach for automatic segmentation of the left ventricle from cine cardiac images. This segmentation method has achieved good accuracy. We believe this could provide

cardiac radiologists a practical measure for automatic left ventricle segmentation from 4 dimensional cardiac images.

Biography:

Mr. Huang Su obtained Master of Science degree in Computer Application from Beijing University, China, in 1989. He has been working in medical image research for more than 10 years since joining A*STAR, Singapore. He has contributed more than 30 papers to medical and engineering journals and conferences, and received several awards from clinical societies. He is a research project manager in Biomedical Imaging Lab in Singapore Bio-imaging Consortium. His research interests include medical image analysis, modeling and visualization methods, and clinical application development.

Mr S. Matsumoto, Fujitsu, "Overview Fujitsu in-silico drug discovery technologies"

Abstract: Fujitsu provides in-silico drug discovery technologies to get novel bio-active chemical structures for targets of interest. OPMF, abstract fragment based de-novo drug design system, and MAPLE CAFEE, precise affinity prediction system, are the core components of these technologies. The power of HPC enables them to become practical and effective tools of drug discovery, based on molecular simulations with fine-tuned parameters and efficient exhaustive search in the vast space of novel drug candidates. Some cases of drug design with OPMF and datasheets of IL-6, IgE-R antagonists will be shown.

Biography:

Mr Shunji Matsumoto begun work at Fujitsu Industries in 1983 on Artificial Intelligence Research and Applications. In 1995 he became the Manager of Intelligent Systems Laboratories. In 2002 he was appointed the Director of Bio Software Division, Life Sciences Business Group and in 2004 became the General Manager of Bio-Chemical Information Research Division, BioIT Business Development Unit. In 2006 he was appointed the General Manager of In-silico Drug Discovery Research Division, Fujitsu's BioIT Business Development Unit.

Dr H. Fujitani, Fujitsu, "MAPLE-CAFEE: Predictive Computation of Pharmaceutical Protein-Ligand Affinity"

Abstract: Massively parallel computation is used to calculate an absolute binding free energy of a ligand for a pharmaceutical target protein, based on the equality of non-equilibrium work distribution with the free energy difference between two thermodynamic states. There are important requirements for accurate calculations. The first is a well-equilibrated bound structure including the conformational change of the protein induced by the binding of the ligand. The second requirement is the convergence of the work distribution in the massively parallel computation. Finally, the most important requirement is the accurate force field parametrization.

Biography:

Dr Hideaki Fujitani has been working at Fujitsu Laboratories Ltd for the past 25 years. He has been a visiting scientist at Oxford, Beijing and Stanford Universities and since 2007 has been a part-time lecturer at University of Tokyo. He is also a member of Japanese Physical Society, American Physical Society, American Chemical Society.

Dr Shozo FUJITA, Nanoelectronics Research Center, Fujitsu Laboratories Ltd., Fujitsu Laboratories Ltd., "Modified DNA Aptamer development service"

Abstract: Oligonucleotide with affinity to a target molecule comparable with monoclonal antibody is called an aptamer. Though RNA aptamer is very unstable in vivo and in vitro compared with DNA aptamer, but is well known by its high efficacy. We established a unique platform, A-Daptamer, to develop high affinity DNA aptamer at high success rate. You can get a unique DNA aptamer of its dissociation constant of several nM using our technology. A-Daptamer can incorporate various chemical residues such as amino acids along a DNA backbone.

In my talk, I would like to introduce you our technology and show some examples of developed aptamer molecules.

Biography:

Dr. Shozo Fujita is the Director, Nano-Bio Research Organization: Nanoelectronics Research Center, Fujitsu Laboratories Limited. He studied Chemistry at Niigata University ('74); received his M.Sc. in 1976 and Doctorate of Medical Sciences in 1980 from Niigata University. He was a Postdoctoral Researcher at the Brain Research Institute, Niigata University in 1981 and at Division of Biological Membranes, National Institute of Physiology, Okazaki, 1983. In 1985 he became a Research Assistant at Department of Anesthesia, School of Medicine, Niigata University. In 1985 Dr Fujita joined Fujitsu Laboratories Limited. Between '85–'98 he was involved in "Protein crystal growth under microgravity environment" and between '90–'96 in development of a miniature oxygen sensor. He was the organizer of ISO14001 activities in Fujitsu laboratories Ltd. In 2000 he became a Senior Research Fellow, Nanotechnology Research Center and in 2009 its Director.

Professor Andrew Charles McIntosh, University of Leeds, "Pharmaceutical sprays inspired by the bombardier beetle"

Abstract: The innocuous looking bombardier beetle is one of the most remarkable creatures around. This tiny insect is able to fight off any spider, frog, ant or bird that comes too close by blasting the attacker with a powerful jet of hot, toxic fluid. Furthermore, the beetle can aim its

weapon in any direction (even over its head) with pinpoint accuracy, and can reach distances of up to 20 cm with its spray. The bombardier beetle, which is rare in Europe but common in Africa, Asia and warmer parts of the US, forms a noxious spray by reacting small amounts of hydroquinone with hydrogen peroxide in the presence of the catalysts catalase and peroxidase in a pair of combustion chambers in its abdomen.

This exothermic reaction produces a toxic solution of benzoquinone, other chemicals and water, and heats the solution (which is mainly water) to above its boiling point. Although some details of the chemical process have been known for years, until recently scientists did not understand how the beetle managed to eject this solution so powerfully. The answer to this puzzle, has led to building an experimental rig mimicking the major physics of the beetle ejection system and that knowledge could revolutionize industrial spray technology.

The technology has led to much interest from industry in using the remarkable spray system for fuel injectors, pharmaceutical drug delivery systems such as nebulisers and also fire extinguishers.

Biography:

Professor Andrew Charles McIntosh, DSc., FIMA, C. Math., FEI, C. Eng., FinstP, MIGEM, FRAeS**,** School of Process, Environmental and Materials Engineering, University of Leeds LEEDS, LS2 9JT, UK.

Graduated 1st Class Hons. in Applied Mathematics, University of Wales (1973), with PhD "Unsteady Premixed Laminar Flames" from Cranfield University (1981), and has DSc "Mathematical modelling of unsteady combustion processes within gases, fluids and solids" from University of Wales (1998).

Professor Andrew C. McIntosh DSc, FIMA, C.Math, FInstE, CEng FInstP, MIGEM, FRAeS holds a chair in Thermodynamics and Combustion Theory in the Energy and Resources Research Institute at the University of Leeds, where he lectures and researches in the field of Combustion and Explosions. His research has included investigations involving fluids (the interaction of pressure waves with flames) as well as solids. In the area of heterogeneous combustion he is interested in the safety of reactive substances, which can include traditional fuels such as coal, but also may include agrochemicals some of which are now being used widely to increase crop yields, but in bulk can have unusual ignition properties. At present he is investigating the ignition of explosives where a double combustion wave phenomenon is apparent. This work is in collaboration with Orica Ltd (ex ICI company based in Canada and Australia). He has over 150 publications in Journals and Conferences on these subjects.

In the last few years he has been involved in research in the area of biomimetics where the minute combustion chamber of the bombardier beetle is being studied. This has led to research first sponsored by the Engineering and Physical Sciences Research Council followed by extensive funding from industry to apply the technology discovered to a number of aerospace and pharmaceutical uses. He is a trained mathematician and has worked in aerodynamics at Cranfield University and the Royal Aircraft Establishment (Bedford) before coming to Leeds where he gained a DSc in 1998 and a personal chair in 2000. He became a Fellow of the Institute of Physics in 2002 and in 2003 was elected a Fellow of the Royal Aeronautical Society.

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Dr Chandra Verma, BII, A*STAR, "Computer simulations in understanding molecular mechanisms in biology"

Abstract: Computer simulations of atomic level processes in biology is increasingly becoming a part of the regular toolkit of investigative technologies. Examples will be given of the novel insights that have been provided and also where developments are needed both in terms of concepts and technological limitations.

Biography:

Dr Chandra Verma is currently the head of the division of biomolecular modelling and design at the A-STAR Bioinformatics Institute. The division focuses on structural and mechanistic understanding of biomolecular processes. Chandra carried out his PhD at York University, UK and then was working with the structural biology group at York. He joined A*STAR in 2003. His group uses atomistic computer simulations extensively and works in close collaboration with experimentalists and clinicians in Singapore and abroad. A major goal of the group is towards the development of novel therapeutics.

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