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Molecular Modelling: Advances in Biomolecular and Materials Modelling

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The conference 'Molecular Modelling – 2010: Advances in Biomolecular and Materials Modelling' (MM2010) was held in Melbourne, Australia from the 28th November to 1st December, 2010. The meeting was organized by AMMA, the Association of Molecular Modellers of Australasia (www.mgms.org.au), the Asia/Pacific Chapter of the Molecular Graphics and Modelling Society (MGMS), and was held at the Monash Institute of Pharmaceutical Sciences (MIPS). The conference was organized and chaired by Elizabeth Yuriev, David Manallack and David Chalmers, who were amply helped by other members of the organizing committee (Brian Smith (current AMMA president), Amanda Barnard, Nathan Hall and Irene Yarovsky). MM2010 was the 5th AMMA meeting and the 14th in the series of initial workshops and then conferences that originated in Melbourne in 1994.

This meeting focused on the latest developments in molecular modelling in both the life sciences and materials sciences, particularly in the areas of drug development, nanotechnology, biophysical modelling and methods and algorithms. The conference was well attended by representatives from 17 countries, from Europe, South and North America and Australasia. The two and a half day discourse included cutting edge plenary and invited presentations by world leaders in molecular modelling, as well as excellent and exciting contributed talks by Australian and international researchers. The highlights of the meeting were the presentation of the inaugural AMMA Medal and the Young Modellers Forum.

The AMMA medal (Fig. 1) is awarded in recognition of eminent services to the field of molecular modelling in the Australasian region in the broadest sense. The award is made for activities that include research, service to the molecular modelling community, and leadership. The inaugural AMMA medal was awarded to Leo Radom, Professor of Chemistry at the University of Sydney, a chief investigator in the ARC Centre of Excellence in Free Radical Chemistry and Biotechnology, and the current President of the World Association of Theoretical and Computational Chemists. Leo's influence on the computational chemistry community, both nationally and internationally, is apparent by his publication record, the number of personal invitations to meetings, the award of numerous prizes, and the success of current and past members of his group. He is a most deserving recipient of the inaugural AMMA medal.

The Young Modellers Forum showed the amazing breadth and depth of molecular modelling research carried out by graduate students and young postdocs. The topics ranged from investigations of zinc-sulfide nanoparticles and functionalized porous graphene to modelling of carbohydrates, disease-specific

Professor Michelle Coote is a graduate of the University of New South Wales, where she completed a B.Sc. (Hons) in industrial chemistry (1995), followed by a Ph.D. in polymer chemistry (2000). Following postdoctoral work at the University of Durham, UK, she joined the Research School of Chemistry, Australian National University in 2001, initially as a postdoctoral fellow with Professor Leo Radom. She established her own research group in 2004 and has recently taken up an ARC Future Fellowship. She has published extensively in the fields of polymer chemistry, radical chemistry and computational quantum chemistry, and is a member of the ARC Centre of Excellence for Free-Radical Chemistry and Biotechnology. She has received many awards, including the 2001 IUPAC prize for young scientists, the RACI Cornforth medal (2000), Rennie medal (2006) and David Sangster Polymer Science and Technology Achievement Award (2010), and the Le Fevre Memorial Prize of the Australian Academy of Science (2010).

Elizabeth Yuriev is a Senior Lecturer at the Monash Institute of Pharmaceutical Sciences, Monash University. Her research interests include molecular modelling of protein-carbohydrate interactions and G Protein-Coupled Receptors. She is a Secretary of the Association of Molecular Modellers of Australasia (AMMA).

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Fig. 1. The Association of Molecular Modellers of Australasia Medal

proteins and poliovirus virions. The quality of young modellers' research and their presentation skills were very impressive and were rewarded with student prizes, selected by international judges.

This Research Front comprises a selection of papers, contributed by MM2010 attendees and representing a wide scope of molecular modelling research 'from bio to nano'.

Two contributions deal with drug design issues for HIV, looking at it from therapeutics[1] and vaccine[2] development points of view. The former of these two papers came from Renate Griffith and co-workers (University of New South Wales and University of Wollongong, Australia).[1] In the short communication, they report on a recent discovery of an under-used binding area, which allows access to the active site of HIV reverse transcriptase (RT) and may lend itself to the design of new inhibitors with a better resistance profile. They have used molecular docking to investigate this little-used expansion of the very well known RT binding pocket and have shown that the studied compounds can potentially access this novel binding space.

In the second HIV-related contribution, researchers from the University of Natural Resources and Life Sciences, Austria, report on molecular dynamics (MD) simulations carried out to rationalize the activity of humanized antibody (Ab2/3H6), directed against the human 2F5 antibody, which is capable of neutralizing HIV-1.[2] Ab2/3H6 is an interesting vaccine candidate with framework regions expected to trigger an immunogenic response when administered to humans. In this study, Chris Oostenbrink and co-workers have applied MD and free energy calculations to rationalize the effect of different humanization techniques (methods affecting the sequence of the framework regions) on the structures of antibody binding sites. They found that although the sequences of the complementarity determining region (CDR) loops in four antibodies were completely identical for all models, the structural orientations were quite different, and could explain the experimentally determined binding affinity profiles of four humanized antibodies. Their results have demonstrated the influence of specific residues on the binding affinities of the humanized antibodies and emphasized that humanization processes should not only preserve the sequences of the CDRs but also the structure and dynamic behaviour in these regions.

Lifeng Yang and colleagues from the National University of Singapore have also applied MD simulations to a biological problem, this one being the interactions between human ficolin and the pathogen *N*-acetylglucosamine (GlcNAc).[3] This infection- or inflammation-mediated interaction is associated with local acidosis. Therefore, they have performed constant-pH MD simulations on L-ficolin fibrinogen-like domain over a wide pH range and established an existence of an unusual *cis*-peptide bond in a specific ficolin binding site, which is likely to be indispensable for biological action.

The other two papers in this Research Front, while also focusing on biological systems, use a different set of computational methods. Kai Yang from Soochow University and Yu-qiang Ma from Nanjing University[4] applied dissipative particle dynamics to study the wrapping and internalization processes of different particles (e.g. spheres and ellipsoids) by a lipid vesicle. They found rotation to be possibly an important mechanism in the particle internalization process under strong adhesive interaction. Their simulations provided interesting insights into the possible mechanisms of endocytosis.

Finally, Jóhannes Reynisson and co-workers from the University of Auckland used Mulliken and Natural Bond Orbital (NBO) methods based on the density functional theory (DFT) to calculate partial charges of exocyclic nitrogen atoms for nitrenium ions formed from 201 known drugs and 50 mutagenic compounds containing aryl amine and nitro moieties.[5] Their work was based on the hypothesis that the mutagens have a more negative charge on their exocyclic nitrogen atoms resulting in stable nitrenium ions, and thus a longer lifetime to react selectively with DNA. However, their results have indicated that other physical properties, besides the stability of the nitrenium ions, are likely to be important for determining the mutagenic potential of aryl amine and nitro containing compounds.

It is our pleasure to recommend to the reader this collection of papers, associated with MM2010.

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