ESF Science Meeting
Reference Number: 4582

ESF Activity
Unit(s): PESC
Activity Title: Advanced Concepts in Ab Initio Simulations of Materials
Activity Acronym: Psi-K2

PROJECT
Science Meeting: School
Title of Science Meeting: "Summer school on ab initio Molecular Dynamics for Biomolecules"
Location: S. Stefano di Sessanio (Italy)
Date of Science Meeting: 9/6/2013 – 14/6/2013
Convenors' Names: Prof. Leonardo Guidoni (University of L'Aquila, Italy), Dr Carla Molteni, King's College London (UK), Dr Daniele Varsano (CNR Institute of Nanoscience, Modena)

SUMMARY

Understanding how biological systems function at the atomistic level is becoming increasingly important in a variety of fields and disciplines (from bioenergetics to drug and nanomaterials design). Atomistic simulations are proving very useful tools to complement and expand the experimental information with the help of more and more powerful computers. In particular, ab initio simulations, based largely on density functional theory (DFT), are needed for phenomena where the electronic structure plays an essential role, such as in electron transfer of photo-activated processes, a prototypical example of which is photosynthesis.
The Summer School, attended by 36 students, provided an overview of the theoretical and computational methods necessary for performing ab initio molecular dynamics (MD) simulations of biological systems, supplemented by computer tutorials to put the theory into practice and by experimental lectures to illustrate open questions and areas of potential applications, such as X-ray crystallography and optical and vibrational spectroscopy. The School was conceived to fulfil the growing need to train early stage researchers (PhD students and postdocs) in the multi-disciplinary area of biological (ab initio) simulations, which is not usually included in the academic curriculum. Topics that were covered included how to select and validate an experimental structure from the protein data bank, how to set up a protein simulations and how to perform a quantum mechanical/molecular mechanical (QMMM) calculations (taking as examples the implementations in the CPMD and CP2K codes). Direct links with the experimental talks were assured by lectures focused on calculations of excited states and vibrational properties. Accuracy issues and the need to go beyond DFT were discussed for metallo-enzymes. Electron transfer calculations were also presented as well as an introduction to metadynamics, a method to accelerate rare events and sample free energy. Evening lectures focused on an historical introduction to the development of molecular biology and on state-of-the-art applications and future perspectives of ab initio molecular dynamics for biological systems.

SCIENTIFIC CONTENTS AND DISCUSSION

The School focussed on the practical use of ab initio electronic structure methods, in particular based on DFT, to enhance the scope of classical molecular dynamics (MD) simulations for biomolecules. It was attended by 36 students, mostly PhD students, from 11 countries, with backgrounds in physics, chemistry and materials science. 12 scientists, of which 3 experimentalists, gave lectures over 6 days. The location, a small medieval village within the Gran Sasso and Monti della Laga National Park, provided an ideal setting for the School, allowing the establishment of an engaged and interacting group of students. The School consisted of lectures and computer tutorials; students brought their own laptops and were provided guest accounts on a server at the University of L'Aquila which they could access for running calculations. Electronic

copies of the lecture notes and tutorial material were made available.
The School started on Sunday evening with an historical review of the development of molecular biology through the advancements of x-ray crystallography that allows the determination of protein and nucleic acids structures at the atomic level. The review, from Roentgen to the latest results with free electron lasers, was presented by **Doriano Lamba**, a crystallographer from the CNR Institute of Crystallography in Trieste (Italy) who, on Monday, gave a very instructive lecture and tutorial, with many notions theoreticians would not be aware of, on how to read, interpret and validate protein data bank (pdb) structure files, which are the starting point of MD simulations. **Leonardo Guidoni**, one of the School organizers from the University of L'Aquila, gave an introduction on the motivations and needs of ab initio molecular dynamics for biological systems, illustrating in particular the case of photosynthesis and the challenges that this complex poses to simulations. He presented the steps that are needed to set up a model for simulations starting from a pdb structure, with a focus on the peridinin-chlorophyll-a-protein which was analyzed in the computer tutorial. Students presented high quality posters about their research under the porch in the late afternoon, showing a range of knowledge and expertise and creating opportunities for lively discussions. The prize for the best poster presentation was awarded to **Anna Muszkiewicz** (Oxford University) for the poster entitled *"Allostery in the PDZ3 domain: a computational study*"; she was invited to give a talk about her work on the last day of the school.
Tuesday was entirely dedicated to QMMM simulations with lectures in the morning by **Carme Rovira** from the University of Barcelona (Spain) and **Teodoro Laino** from IBM Zurich (Switzerland), on the motivations for using a QMMM approach and a guide on how to set up QMMM simulations the CPMD and CP2K codes. This was illustrated by several biological examples (e.g. heme proteins and aquaporin) and followed by afternoon tutorials scrutinizing and discussing selected input files for the CPMD and CP2K codes (related to ATPase and urease biomolecules).
On Wednesday two experimental talks by **Tullio Scopigno** and **Simonetta Fornarini** (both from the University of Rome, La Sapienza, Italy) on ultra-fast optical spectroscopy and vibrational spectroscopy for biomolecules presented overviews of what these techniques can measure, providing ideas and challenges for ab initio simulations. **Daniele Varsano** (one of the School organizers from the University of Modena and Reggio Emilia, Italy) reviewed methods for electronic excitations in biomolecules, with an emphasis on time-dependent density functional theory and calculations of optical spectra, with examples including natural dyes, retinal and carotenoids. Challenges with charge transfer excitations were also discussed. **Adam Kubas**, from University College London (UK), focused on problems related to accuracy for calculations of metal cofactors in metallo-enzymes, where DFT is useful for exploratory studies but should be used with care and supplemented by more accurate quantum chemistry methods, such as CASSCF.
Thursday started with an introduction to metadynamics by **Carla Molteni** (one of the school organizers from King's College London, UK) as an example of an efficient technique for accelerating rare events and sample free energy surfaces. She illustrated its usefulness for biological systems by presenting simulations of trans-cis isomerisation in proline dipeptide, which are relevant for investigating mechanisms of ion channel gating and HIV-infection. **Jochen Blumberger** (University College London, UK) reviewed the theory, simulation methods, challenges and examples of electron transfer in biological systems; he then exemplified what can be practically achieved showing recent calculations in a complex bacterial deca-heme nanowire protein. In the afternoon a round table with the students was organized in order to have feedback on the content and organization of the School; further feedback was collected with an anonymous survey form. Rodolphe Vuilleumier (UPMC, Paris, France) then provided an overview of ab initio MD simulations of vibrational properties and IR spectra, followed by a computer tutorial on water and peridinin. After dinner, **Paolo Carloni** (German Research School for Simulation Sciences in Juelich, Germany) discussed the role and perspectives of ab initio molecular dynamics for multiscale modeling of biological systems, with examples of applications from bioenergetics to medicine.
On Friday, Rodolphe Vuilleumier concluded the tutorial on vibrational properties. Anna Muszkiewicz, winner of best poster presentation, gave a talk on her research on allostery in the PDZ3 domain. The School ended with concluding remarks by Leonardo Guidoni and acknowledgements to the local team that provided an excellent organization for a smooth running

of the School.

RESULTS AND IMPACT ON FUTURE DIRECTIONS

The School stems from the Psik working group 7 *"From Molecules to Biological Systems"*, of which Leonardo Guidoni is spokesperson and Carla Molteni a member of the coordination committee, and was meant to equip early stage researchers from different disciplines and expertise with knowledge of a range of state-of-the-art techniques and ideas for performing ab initio calculations of systems of biological interests. The School was advertised as a Psik-School though the Psik-mailing list, other mailing lists like the UK National Service for Computational Chemistry Software mailing list and websites, and personal contacts. 58 applications were received, although only 36 students could be accepted due to the capability of the lecture room. This demonstrates that there was a clear interest in the School. The contribution of the ESF "Advanced Concepts in Ab Initio Simulations of Materials" programme was acknowledged during the School and in the advertising materials. Together with contributions from the regional government, local University and foundations, it was possible to cover accommodation and subsistence for 20 students; lecturers were also reimbursed their travel expenses.
The location was particularly suited for a summer School with an excellent quality/price ratio in a region which is still recovering from a devastating earthquake in 2009.
Overall the School was very successful and contributed to train the next generation of scientists interested in ab initio simulations of biological systems. The students were satisfied with the contents, location and organization as evident from the verbal and written feedback and the lecturers were impressed by the students' interest and engagement. The average overall score of the feedback papers distributed at the end od the school and anonymously filled by the students was 4.3/5, indicating a good success of the event. The weakest point, emerged both by the organizer's feeling and by the student's feedback concerns the computer tutorials. These tutorial were limited due to time constraints and to the wide variety of topics covered and were intended to give a flavour of practical activities. If the School is re-run in the future they can be either removed to give more space to lectures or re-developed so to focus on a single system. The students actively participated in the lectures and activities of the School, networking and exchanging ideas with the lecturers and among themselves. The presence of experimentalists was appreciated and proved very useful. Given the interest registered in the application stage and then during the School, a similar School organized in a couple of years from now would be welcome and appropriate.

FINAL PROGRAMME OF THE MEETING

Sunday 9/6/2013

17:00 -19:00 Registration
19:30 Dinner
21:00 – 22:00 Opening Lecture
"Structural Biology: a historical perspective" - Doriano Lamba

Monday 10/6/2013

Building up the bio-systems and the classical setup
9:00 – 10:45 X-ray crystallography and protein data bases - Doriano Lamba
10:45 Coffee-Break
11:15 – 12:15 From the PDB to a reliable atomistic model I – Leonardo Guidoni
12:45 Lunch
(Computer Tutorials)
15:00 – 15:30 – From the PDB to a reliable atomistic model II – Leonardo Guidoni
15:30 – 16:00 – From the PDB to a reliable atomistic model III - Doriano Lamba
16:00 – 17:30 – Practical exercises – Doriano Lamba & Leonardo Guidoni

18:00 – 19:30 Poster session with aperitif
20:00 - Dinner

Tuesday 11/6/2013

Quantum Mechanics / Molecular Mechanics methods
9:00 – 10:30 - Why using a QM/MM approach and how to set up a QM/MM simulation – Carme Rovira
10:30 Coffee Break
11:00 – 12:30 General QM/MM methods and multigrid techniques - Teodoro Laino
12:45 Lunch
(Computer Tutorials)
15:00 – 18:00 –QMMM implementation in CPMD and CP2K. – Teodoro Laino & Carme Rovira
18:00 – *Guided tour of S. Stefano di Sessanio*
19:30 - Dinner

Wednesday 12/6/2013

Spectroscopy, properties and applications I
9:00 – 11:00 Optical biospectroscopy – Tullio Scopigno
11:00 Coffee Break
11:30 – 12:45 Excited states in biomolecules – Daniele Varsano
13:00 Lunch
14:30 – 15:45 Infra-red spectroscopy of biomolecules – Simonetta Fornarini
15:45 – 16:45 Electronic structure of transition metal compounds: the case of metalloenzymes – Adam Kubas
17:30 – 22:00 – Social Excursion to Rocca Calascio with Social Dinner

Thursday 13/6/2013

Spectroscopy, properties and applications II
9:00 – 11:00 Metadynamics – Carla Molteni
11:00 Coffee Break
11:30 – 12:30 Electron transfer in proteins - Jochen Blumberger
12:30 School Photograph
13:00 Lunch
16:00 Roundtable with Coffee
17:15 - 18:15 Vibrational spectroscopy by ab initio molecular dynamics – Rodolphe Vuilleumier
(Computer tutorial)
18:15 - 19:15 Effective normal modes I - Rodolphe Vuilleumier
19:30 - Dinner
21:00 – 22:30 Ab initio molecular dynamics applications for biomolecules – Paolo Carloni

Friday 14/6/2013

Spectroscopy, properties and applications III
(Computer tutorial)
9:00 - 10:45 Effective normal modes II - Rodolphe Vuilleumier
10:45 – 11:00 Presentation from the winner of the Poster Award
11:00 – 11:15 Concluding remarks
12:30 Lunch

LIST OF PARTICIPANTS

Organisers

Leonardo Guidoni (Università degli Studi de L'Aquila, Italy)
Carla Molteni (King's College, London, United Kingdom)
Daniele Varsano (Centro S3, CNR Istituto di Nanoscienze, Modena, Italy)

Local Organisers
Leonardo Guidoni (Università degli Studi de L'Aquila)
Emanuele Coccia (Università degli Studi de L'Aquila)
Daniele Narzi (Sapienza – Università di Roma)

Lecturers
Jochen Blumberger (University College London, United Kingdom)
Paolo Carloni (German Research School for Simulation Sciences, Jülich, Germany)
Simonetta Fornarini (Sapienza - Università di Roma, Italy)
Leonardo Guidoni (Università degli Studi dell'Aquila, Italy)
Adam Kubas (University College London, United Kingdom)
Teodoro Laino (IBM Zurich Research Laboratory, Switzerland)
Doriano Lamba (IC-CNR, Trieste, Italy)
Carla Molteni (King's College London, United Kingdom)
Carme Rovira (ICREA, Universitat de Barcelona, Spain)
Tullio Scopigno (Sapienza - Università di Roma, Italy)
Daniele Varsano (Centro S3, CNR Istituto di Nanoscienze, Modena, Italy)
Rodolphe Vuilleumier (UPMC, Paris, France)

Students

Italy
Matteo Barborini, Università degli Studi de L'Aquila
Alberto De Petris, Sapienza – Università di Roma
Marco Micciarelli, Sapienza – Università di Roma
Maria Montagna, Università degli Studi de L'Aquila
Fabio Pitari, Università degli Studi de L'Aquila
Daniele Bovi, Sapienza – Università di Roma
Daniele Narzi, Sapienza – Università di Roma
Chiara Pasquini, Sapienza – Università di Roma
Andrea Zen, Sapienza – Università di Roma
Roberto Paciotti, Università "G. d'Annunzio" Chieti-Pescara
Claudia Violante, University of Rome Tor Vergata

Germany
Vera Krewald - Max Planck Institute for Chemical Energy Conversion, Mulheim an der Ruhr
Xiaoqing Wang - Max Planck Institute for for the Physics of complex systems, Dresden

Norway
Siv Aalbergsjo - University of Oslo

Peru
Adolfo Poma - Universidad Nacional Mayor de San Marcos

Poland
Wictor Beker - Wroclaw University of Technology
Wictoria Giedroyc-Piasecka - Wroclaw University of Technology
Rafal Roszak - Wroclaw University of Technology

Serbia
Lidija Zivanovic - University of Belgrade

Spain
Jorge Gonzalez Rodriguez - University of the Basque Country UPV/EHU

Sweden
Hakkim Vovusha - Uppsala University

Switzerland
Sandra Luber - University of Zurich
Gabriele Sosso - ETH Zurich, Lugano

United Kingdom
Antoniya Aleksandrova - University of Cambridge
Dominic Botten - King's College London
Christopher Cave-Ayland - University of Southampton
Federico Comitani - King's College London
Pablo Garcia Jambrina - King's College London
Leo Holroyd - University of St Andrews
Sam Mulholland - University of Nottingham
Anna Muszkiewicz - University of Oxford
Peter Repiscak - Heriot-Watt University, Edinburgh
Chen Song - University of Oxford
Eleanor Turpin - University of Nottingham
Valerie Vaissier - Imperial College London

United States of America
Christoph Kreisbeck - Harvard University, Cambridge

Breakdown of costs

Travel	2300
Meals (social dinner)	1250
Accommodation with full pension	
- Speakers	2200
- Students	9750
Other Costs (stationary)	500
Total	16000

Total Finantial contributions

ESF	9000
Carispaq Fundation	2500
Università de L'Aquila	1000
Regione Abruzzo	3500
Total	16000

Name of head of Finantial Department

Antonio Mecozzi

Email of Financial Officer approving the Financial Report

antonio.mecozzi@univaq.it