Special Joint Lecture of the
CENTRE FOR RESEARCH IN MOLECULAR MODELING
MERCK FROSST and the
DEPARTMENT OF CHEMISTRY AND BIOCHEMISTRY

April 25, 2008, 5:00 pm - Concordia University SP-S110

Quantum Mechanics and Molecular Mechanics: Could They/Should They Play a Key Role in Systems Biology? What's Possible? What's Not?

Dennis R. Salahub
Department of Chemistry, Institute for Biocomplexity and Informatics, and Institute for Sustainable Energy, Environment and Economy
University of Calgary

One viewpoint of the still emerging field of systems biology sees integration along one axis involving system size (and perhaps some dynamics) going from macromolecules (proteins, DNA, RNA, etc) to cells, to tissues, to organs, to organisms, etc. This is sometimes called computational biology. Another axis looks at kinetic models at growing levels of complexity going from pathways, to modules to full genetic regulatory networks. This is taken to lie in the general field of bioinformatics. There is an almost unpopulated chasm between the two communities pursuing these two approaches.

In this lecture I will argue that a starting point at even a finer level of resolution is necessary if one is to fill the gap between the two axes. I will attempt to describe the state-of-the-art of atomistic multi-scale approaches including those that use quantum mechanics to describe chemical reactions. I will review the pertinent molecular dynamics literature. Following that I will give a few results for nano-bio systems that are now being calculated using Density Functional Theory (DFT). Although modern DFT is fast, it is still not fast enough for applications in biology so we are paying attention to so-called reactive force fields (ReaxFF) which try to capture the essence of quantum mechanical calculations through parametrization against DFT calculations on full chemical reaction paths.

Turning to the other axis, I will summarize recent results on protein production regulated by genetic networks that incorporate the main steps in the transcription and translation processes. The Gillespie (Kinetic Monte Carlo) algorithm is used to solve the (effective) chemical master equation.

The seminar will finish with our first (baby-step) attempts to fill the gap by looking at the mechanism of transcription involving metallo-proteins with Mg ions in the active site. The project uses both DFT and the ReaxFF force field. We hope, in the fullness of time, to be able to feed calculated information on reaction rates into the Gillespie (or other) algorithm and, hence, have the behavior of the regulatory network guided by the underlying atomistic and electronic mechanisms.

Dr. Salahub joined the University of Calgary on July 1, 2002 as Vice-President (Research). On July 1, 2003 his mandate was expanded to include internationalization and international relations and he was named Vice-President (Research & International). At the end of his term in June, 2007 he was named Vice-President (Research and International), Emeritus. Dr. Salahub also holds appointments as professor in the Department of Chemistry at the University of Calgary, as a Senior Fellow of the Institute for Biocomplexity and Informatics and as a Senior Fellow of the Institute for Sustainable Energy, Environment and Economy.

Prior to joining the University of Calgary, Dr. Salahub served as the Director General of the Steacie Institute for Molecular Sciences at the National Research Council of Canada in Ottawa from 1999 -2002. From 1976-1999, he was a Professor of Chemistry at the Université de Montreal, holding a

McConnell Chair from 1990. A native of Alberta, Dr Salahub has been interested in theoretical and computational chemistry since his undergraduate days in Edmonton, and completed his doctorate in the field at the Université de Montreal. He has published over 250 research papers and four edited books, and has delivered more than 300 invited lectures nationally and internationally.

Dr. Salahub has served the science and innovation communities on a broad front. He was the Program Leader of the Centers of Excellence in Molecular and Interfacial Dynamics (CEMAID) from 1991 to 1994 and a founding member of the Centre de Recherche en Calcul Appliqué (CERCA) in 1991. He has served on NSERC's Grant Selection Committee and twice on the Reallocation Steering Committee for Chemistry (1997, 2001, Chair). As Vice-President (Research and International) he served on more than 50 Boards and governing committees, including University Technologies, International, iCORE, Calgary Technologies Inc., the Alberta Ingenuity Centre for In-Situ Energy, the Alberta Ingenuity Centre for Water Research, the Alberta Ingenuity Centre for Carbohydrate Science, and the Canadian Space Agency. He contributed to the establishment of the National Institute for NanoTechnology, the Alberta Nano strategy, the emerging Alberta strategy for Integrated Life Sciences/Systems Biology and to the vision and strategic business plan for the University Innovation Park. He developed strong strategies for internationalization at the UofC with particular emphasis on China and Mexico and emerging strategies for India, Africa and the Middle East.

In 1998 he was named as a Fellow of the Royal Society of Canada, and in 2006 he was named a Fellow of the American Association for the Advancement of Science.

This lecture is part of the joint seminar series of the Centre for Research in Molecular Modeling (CERMM), Merck Frosst, and the Department of Chemistry and Biochemistry. It is also the plenary lecture of the 8th Annual CERMM Symposium, which is generously sponsored by Aid to Research-Related Events grants from the Faculty of Arts & Science and the Office of the Vice-President, Research and Graduate Studies.