Institution: Cardiff University

Unit of Assessment: Chemistry 8

Title of case study:
Transforming quantitative prediction of molecular properties through software - Molpro

1. Summary of the impact

Research in quantum-mechanical methods, conducted at the School of Chemistry at Cardiff University, has resulted in the creation of an innovative software package called Molpro. Molpro provides the ability to calculate from first principles (ab initio) the properties of molecular matter. It is unique and differs from other quantum chemistry packages because, using local electron correlation methods, it significantly reduces the increase of the computational cost with molecular size. This means highly accurate computations can be performed for much larger molecules than with most other programs, and the screening of far wider libraries of potential new materials is enabled. Consequently, Molpro is extremely valuable to the global chemical and pharmaceutical industries and has been endorsed and applied by major international corporations that manufacture products that are used by a wide range of industries (including cosmetics, automotive and construction). Examples are BASF, Mitsubishi Chemical Group, Sasol and Nissan Chemical Industries.

The software is distributed under licence through Cardiff University and resellers, operating in China, Japan, Brazil, Taiwan, Russia, Poland and the USA. During the REF period, it has generated over £1.75M in revenue, and is used by over 650 organisations worldwide. Accordingly the impact claimed is extensive economic gain and impact on practitioners and professional services.

2. Underpinning research

The research that has generated the Molpro software has been carried out over a long time period by a number of collaborating researchers, led by Peter Knowles (Professor of Theoretical Chemistry, Cardiff University, since 2004) and Hans-Joachim Werner (Stuttgart). Some of the computational methods that have been invented and then embodied in the software have been very extensively used, reflected, for example, in the heavy citation of http://dx.doi.org/10.1016/0009-2614(94)00815-9, http://dx.doi.org/10.1063/1.465990 and http://dx.doi.org/10.1063/1.1564816. An overview can be found in reference 3.1.

Three specific research advances made at Cardiff University have been major contributors to the impact.

A. Linear-scaling Hartree-Fock methodology using local orbitals [3.2]. This 2004 paper showed for the first time how to compute molecular orbitals for large molecules, including the exchange interaction exactly, with effort that scales linearly with the size of the molecule. This was a key step in making more accurate correlated linear-scaling methods feasible, **since before this work was done, Hartree-Fock was the computational bottleneck.** The distinctive feature of the Cardiff contribution, **essential to the success of the project**, was the **use of innovative basis sets based on the solutions of Poisson's equation, which provides a speed-up by a factor of approximately two.**

B. Portable one-sided remote memory access in parallel scientific computing [3.3]. This work, conducted in Cardiff between 2007 and 2011, addressed an important challenge in the use of parallel computers for computations involving large intermediate data structures. In most of the electronic structure methods embodied in Molpro, very large matrices are distributed across the processors of a parallel machine, and data must sometimes be accessed by a process that is remote from the node on which the data are stored. The MPI parallelisation standard does not provide properly for this, and until this work it was necessary to use non-standard libraries to achieve this function. In this work, new algorithms for managing data

were designed, implemented completely portably within the MPI standard, and performance-analysed. This research and its deployment is crucial for the operation of the whole Molpro software system on the high-performance computers of today and tomorrow, where parallelism becomes more and more important, **and all Molpro calculations on large machines now depend on this work.**

C. New theories and approximations for breaking chemical bonds [3.4, 3.5]. This work, started in 2008, **brings new capabilities to predict the energetics of covalent bond breaking, crucial for the simulation of chemical reactions**. The new methods allow 'black-box' calculations that ultimately will scale linearly with system size.

3. References to the research

[3.1] Molpro: a general-purpose quantum chemistry program package. H-J. Werner, **P.J. Knowles,** G. Knizia, F.R. Manby, and M. Schütz, *Wiley Interdisciplinary Reviews: Computational Molecular Science*, 2012, 2, 242-253. ISSN 1759-0876 (http://dx.doi.org/10.1002/wcms.82)

[3.2] Fast Hartree-Fock theory using local density fitting approximations.
R. Polly, H.-J. Werner, F.R. Manby, and **P.J. Knowles,** *Molecular Physics*, 2004, 102 (21-22). pp. 2311-2321. ISSN 0026-8976 (http://dx.doi.org/10.1080/00268970420002748O1).

[3.3] Improved version of parallel programming interface for distributed data with multiple helper servers. **M. Wang, A.J. May** and **P.J. Knowles,**
Computer Physics Communications, 2011, 182 (7). pp. 1502-1506. ISSN 0010-4655
(http://dx.doi.org/10.1016/j.cpc.2011.03.020)

[3.4] *Breaking Multiple Covalent Bonds with Hartree-Fock-based Quantum Chemistry: Quasi-Variational Coupled Cluster Theory with Perturbative Treatment of Triple Excitations*.
J.B. Robinson and **P.J. Knowles,**
Phys. Chem. Chem. Phys., 2012, 14(19). pp. 6729-6732. ISSN 0021-9606
(http://dx.doi.org/10.1039/C2CP40698E)

[3.5] *A linked electron pair functional*. **P.J. Knowles** and **B. Cooper,**
Journal of Chemical Physics, 2010, 133 (22) 224106. ISSN 00219606
(http://dx.doi.org/10.1063/1.3507876)

4. Details of the impact

The research outcomes above and the related body of research (see reference 3.1) have been embodied in the Molpro software (http://www.molpro.net), which has been developed, supported and distributed under licence since 2004. Since 2008, there have been three major releases of the software (2008, 2010 and 2012) at which new capabilities have been added as a result of research in theory and methods.

Impact on Practitioners and Professional Services

The value of Molpro is that it offers key functionality (in particular local correlation for large molecules; multireference methods for chemical reactions and excited states) that are not available in Gaussian (the industry-standard general purpose code) or any other code [5.1]. A wide range of companies, each operating on an international basis, has opted to use Molpro, as a new process that offers enhanced capabilities, to enable the development and production of a plethora of products that are marketed to industries including agriculture, aerospace, construction, automotive, pharmaceutical, packaging and personal care. The list includes BASF, Sasol, Schrödinger, Bristol-Myers-Squibb, Mitsubishi Chemical Group and Nissan Chemical Industries. BASF, for example (an organisation that has over 380 production sites worldwide and produces a range of products

for eight industries), purchased Molpro in 2011. Ansgar Schäfer, the Group Leader in Quantum Chemistry at BASF, states that "Molpro, and in particular its capability for very accurate computations on large molecules, has become a valuable tool for estimating thermochemical and kinetic data for substances and reactions involved in our development of new materials and processes" [5.2]. Similarly, Bristol-Myers-Squibb (BMS), which has 26 facilities in 10 countries and manufactures prescription drugs to treat diseases such as cancer, HIV/AIDS, cardiovascular disease, diabetes, hepatitis and rheumatoid arthritis, acquired Molpro in 2008. Dan Cheney, Group Leader at BMS, commented that "In the Bristol-Myers Squibb CADD group, we believe that effective drug design rests on an affordable and acceptable level of scientific rigor. Among quantum chemistry programs, Molpro is unique in enabling us to do this by offering coupled cluster code that can be applied to drug-like systems using reasonable computational resources" [5.3]. No other package is competitive on this basis. Molpro has significantly progressed industrial knowledge and capabilities.

Economic Gain

Molpro has resulted in significant economic gain, manifested in a) the number of licences sold, and b) the augmentation of corporations authorised to resell the software.

a) Licences sold

Between 1/1/2008 and 31/7/2013, 780 paid-for Molpro licences were issued. Total sales, including those effected by sales agents and net of their commission, amounted to £1,783,714. As a result of this, several posts have been created in Cardiff to support the work, to achieve further sales and to develop activities in Stuttgart, Lund, Regensburg, Bristol and Uppsala. Sales are continuing to increase, as demonstrated by the six monthly income figures; in October 2012, the amount was £179,535, but by April 2013 this had risen to £290,132 [5.4].

b) Companies reselling the software

There are presently twelve authorised resellers of the software that have reaped considerable financial gain from the sale of Molpro. Examples are Beijing Hongcam Software Technologies Co. and Ryoka Systems, Inc. Ryoka Systems have stated that, during the REF period, sales of Molpro amounted to £145,143 [5.5]. Molpro sales have continued to increase; there was a 19% increase for the period 2008-2010 compared to 2005-2007, while in the last two and a half years the software has remained a source of ongoing profit for Ryoka. Similarly, Beijing Hongcam Software Technologies has accumulated sizeable financial benefit from distributing Molpro; during the REF period, sales amounted to £82,705 [5.4].

5. Sources to corroborate the impact (indicative maximum of 10 references)

[5.1] *Molpro User's Manual*, version 2012.1, http://www.molpro.net/info/2012.1/doc/manual.pdf, *Describes the functionality of the software.*

[5.2] Group Leader in Quantum Chemistry, BASF. *Corroborates the use of the research by BASF and resulting impact. Letter on file at UoA.*

[5.3] Group Leader at BMS. *Corroborates the use of the research by BMS and resulting impact. Letter on file at UoA.*

[5.4] Digests of company accounts, University College Cardiff Consultants Ltd. *Corroborates the*

sales and financial data connected to Molpro. On file at UoA.

[5.5] Ryoka Systems, Inc, Science and Technology System Division. *Corroborates the impact of Molpro on this company. Letter on file at UoA.*

[5.6] Vice President of Business Development, Beijing Hongcam Software Technologies Co. *Corroborates the impact of Molpro on this corporation. Letter on file at UoA.*