



Comp Chem Communiqué

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Introduction

Welcome to the Computational Chemistry Communiqué! If you have information that you would like to post or topics you would like to see addressed, please contact Merry Ambos. The Computational Chemistry Communiqué is published quarterly by Molecular Solutions. If you would like to receive C³ via email as a pdf file or you would like to have your name removed from our mailing list, please email Merry at mambos@molsol.com.

As this issue of C³ went to press, we were saddened to learn of the death of a friend and fellow computational chemist, Jim Kaminski (Schering-Plough). We will miss Jim's contributions to our craft, but even more, we will miss his booming laugh and sense of humor that made many ACS meetings and symposia memorable events.

People on the Move

Pat Brady has moved from Bristol Myers Squibb to GlaxoSmithKline as an Investigator in the Structural Chemistry group.

Michelle Lamb, formerly with DeltaGen, has accepted the position of Computational Chemist at AstraZeneca, Waltham.

Ramkumar Rajamani has joined the computational chemistry group at the R. W. Johnson Pharmaceutical Research Institute as a postdoctoral fellow. Ram received his Ph.D. at the University of Minnesota under the direction of Jiali Gao.

Robert Stanton recently has accepted the position of Project Leader, Computational Chemistry, at the Pfizer Discovery Technology Center in Cambridge.

Weifan Zheng, formerly with GlaxoSmithKline, has joined Eli Lilly & Company in Research Triangle Park as a Senior Computational Chemist. He also serves as an Adjunct Assistant Professor in Medicinal Chemistry at UNC-Chapel Hill.

New Technology

MDL Information Systems, Inc. (<http://www.mdli.com>) and Current Drugs Ltd. announced that they are formalizing an agreement to index the Investigational Drugs Database (IDdb) into DiscoveryGate™, MDL's Web-based service that integrates, indexes, and links the essential content sources required for effective drug discovery. IDdb provides R&D profiles on approximately 15,970 companies and institutions involved in pharmaceutical and biotechnology research, data on over 19,000 investigational drugs, and information on approximately 85,000 therapeutic patents and over 56,000 chemical structures.

ChemAxon (<http://www.chemaxon.com>) has released Marvin Applets and Marvin Beans 3.0. The packages contain software development tools and applications for chemistry. Marvin Applets and JavaBeans support drawing/displaying chemical structures and handling molecule objects. The company provides free access to the following:

- Marvin Applets (limited to free web sites)
- MarvinSketch and MarvinView applications accessed from ChemAxon's web site
- Locally installed MarvinSketch, MarvinView, and MolConverter applications.

Integrated DNA Technologies' (<http://www.idtdna.com>) Biotools provides freely usable Internet access to software for oligonucleotide design for the PCR, secondary structure prediction, sequence similarity, and several other biophysical properties of nucleotide sequences.

The Career Corner

In this issue of C³, we will skip ahead in the interview process. Let us assume that you have submitted your resume, passed the phone screen, and completed the on-site interview. You are excited about the opportunities at the company and they seem to be interested in you. How do you increase your chances of receiving an offer?

One of the most important steps after the on-site interview is to keep your qualifications in front of the company and to express continued interest in the opportunity. Thank you letters are an excellent vehicle to accomplish this goal.

While you are returning from the interview, take the time to note the people you talked with and what was discussed. Use this information to write an individual thank you note to each of the people who interviewed you. These notes do not have to be lengthy, but they should convey your interest in their work, your ability to contribute to the company's goals, and your desire to join the organization. If you have made a commitment to locate information (i.e., a reference to a paper, etc.) for someone you met during the interview, this is also a good time to include it.

Avoid the temptation to use email as the medium for these notes. Since your objective is to impress a potential employer and stand out from other candidates, a written thank you letter conveys a higher level of interest and signifies that you are willing to "go the extra mile" to impress your future manager and colleagues.

However, a formal thank you letter also can be a disaster - if it contains incorrect grammar or misspelled words. Above all, make sure that you have the full, correct spelling of the recipient's name and title before you send your letter. Since this is a business letter, you also want to keep it brief and personal, but not overly familiar.

The final thought on thank you letters is timing. In the south, we are taught that thank you letters for gifts must be mailed before you can use the gift. Many southerners have note cards and stamped addressed envelopes in the car when they go to a party. They use these to write a brief thank you note and mail it on the way home (we are not making this up). While you do not need to be this punctual, you should mail your letters the day you return from your interview trip. If you arrive home late in the evening, make your letters the first activity for the next day. When you mail your letter, make sure that you use a personal envelope and a stamp rather than company/university stationary and a meter label. We recommended that candidates start their interview process by purchasing a box of note cards with their name imprinted. These make a personal impression at a minimal cost.

BioBriefs

With the first 2003 issue of *C³*, we introduce a new column - Biographical Briefs (BioBriefs). This quarter's profile looks at Mike Cory, who recently retired from GlaxoSmithKline after a career spanning

over thirty years. Mike received his Ph.D. in 1971 from The University of California, Santa Barbara in bioorganic chemistry. His thesis, under the direction of B. R. Baker, was focused on irreversible enzyme inhibitors found in the complement system. After completing his degree, Mike found that the market for new graduate students "was impossible, no one was hiring in the pharmaceutical industry. Baker tried very hard to find me and my fellow graduate students jobs, but we couldn't even get interview trips."

Through a previous connection with Stanford Research Institute (SRI), Mike was able to secure a postdoctoral position under the direction of David W. Henry. During this period, he worked on synthetic anti-parasitic agents for animals and on other anti-parasitic drugs for humans. "A lot of the work was under contract to Walter Reed Medical Institute and was motivated by concern for the health of the soldiers in Vietnam" Mike explained. While at SRI, Mike co-wrote a grant application to continue the complement work that had been started at Santa Barbara. The grant was funded and it allowed Mike to continue at SRI as a full time staff member.

It was at SRI that Mike first encountered computational chemistry. Corwin Hansch published a paper in which he utilized QSAR to analyze the compounds published in Mike's thesis. "It showed that I could have obtained just as much enzyme data with many fewer compounds. This was about the time that sigma and pi were becoming widely used for QSAR work. Log P was a new concept. A colleague at SRI, Howard Johnson, went to Corwin's lab to learn how to use his multiple regression program and to bring it back to SRI.

In 1975 Karl Kuhlman Howard and Mike submitted a grant to the NIH for access to the Prophet system, a project that offered computer resources for medicinal chemistry. This was one of the first programs to provide drawing capabilities using a Tektronix 4010 graphics tablet and refresh screen. According to Mike, "you could draw a molecule and compute a 3D model using a molecular mechanics program from Todd Wipke. The program also provided facilities for creating and manipulating tables and graphs; similar to Excel today and long before Visicalc. The software was also extensible, in that users could contribute to the system." Mike used the system to extend his work on complement inhibitors and published his first papers that contained 3D structures.

Mike has a unique historical perspective on computational chemistry. "We dialed in at 1200 baud to a DEC 10 computer in Boston; we were the first to dial coast to coast on a regular basis for this type of application. Because of the potential impact that

Prophet could have on our research, I decided to spend time with it and learned to write code for it. We developed a program to take a Prophet molecule and compute Log P and MR from the structure. It was interesting that our efforts overlapped with the work that Al Leo was conducting independently at Pomona College. However, our program was only available to Prophet users.”

When Mike moved to Burroughs Wellcome (now GlaxoSmithKline) in 1977 it was understood that the company would obtain access to Prophet. He wrote a request to NIH and proposed the first commercial access to Prophet where the company would pay for connect time and CPU usage. “We mainly worked on DNA binding compounds but some protein modeling also was done. Our use of the Protein Data Bank also started at this time; it was a new resource and each file was transferred from tapes to Prophet. To run a molecular mechanics minimization of an intercalator and 2 base pairs was a 2-hour job. As a result, we ran them overnight on the Prophet computer. Comparing this to the fact that you can now run 20 base pairs interactively on a PC really gives a perspective to how things have changed during my career.”

The difference in hardware and software that has occurred over twenty years is not the only change that Mike has noticed. “The biggest change has been the acceptance of molecular modeling as a useful approach by ‘bench’ chemists. Well-known synthetic chemists used to consider computational chemistry to be “TV chemistry” not too long ago. As a result, they resisted all suggestions about target molecules. Now that the pace and pressure of large scale discovery projects demands rapid well thought out experiments, many chemists view computational chemistry as a contribution to project ideas.”

As for the skills needed in computational chemistry today, Mike feels that “the hardest skill for the computational chemist to master is communication of his/her results. We must communicate results, warts and all, to the non-computational chemist who may be skeptical. The current ‘big pharma’ paradigm is to have large teams work on a drug target. These teams range from the geneticist through to the computational chemist, medicinal chemist, biologist, enzymologist.... Many of these people have to be convinced that the computational chemist has something to contribute, more than just pretty pictures. It has gotten easier over the years as more people use computers, and as more have experience with macromolecular structures. But the personal interactions are still the important ones. Very arrogant or very passive team members will not succeed as computational chemists.”

Mike and Sheila are currently dividing their time between Chapel Hill and Seattle and Mike is active within the Triangle Orchid Society where he is Vice President and Webmaster.

About Molecular Solutions

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