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Comp Chem Communiqué

Fall 2004

Introduction

Welcome to this issue of 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 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.

People on the Move

Wendy Cornell has moved from the Novartis Institutes for BioMedical Research to accept the position of Director in the Molecular Systems group at Merck Research Laboratories.

Bill Egan has moved from Vertex to the Computational Chemistry group at the Novartis Institutes for BioMedical Research.

Steve Gallion, formerly with ArQule, has joined Cellular Genomics as the Associate Director, Computational Chemistry.

Edward E. Hodgkin, formerly with Tripos, has joined BrainCells, Inc. as the Company's President and Chief Business Officer.

Richard Lewis, formerly with Eli Lilly, will assume the position of Global Head, Computer Aided Molecular Modeling within Global Discovery Chemistry (GDC) at the Novartis Institutes for BioMedical Research (NIBR). Richard joined NIBR in October and is located in Basel.

Rebecca Perlow-Poehnelt has joined the Basic Chemistry group at Merck Research Laboratories as a Senior Research Chemist.

Daniel Severance has moved from Neurogen to Kalypsys as the Associate Director of Computational Chemistry.

Dennis Sprous has recently joined the computational chemistry group at CytRx Labs as a Senior Principal Investigator in CADD.

Terry Stouch, formerly with Bristol Myers Squibb, has joined Lexicon Pharmaceuticals as the Head of Computational Chemistry.

John van Drie, formerly with Vertex, has joined the Novartis Institutes for BioMedical Research as the Head of the Cambridge Computational Chemistry Group.

New Technology

In an effort to keep the community up to date with new approaches to computational tools, Molecular Solutions has invited two companies to briefly describe their latest products.

Cabinet: **Chemical And Biological Informatics NETwork** has recently been announced by **Metaphorics, LLC** (<http://www.metaphorics.com>).

Large amounts of data continue to be generated from genomics, high throughput screening, combinatorial chemistry, structural biology, systems biology, proteomics and other increasingly high throughput techniques. Thus it is crucial for scientists and decision makers to see connections between disparate data sets. In this diverse scientific world, no one can be an expert in all the relevant areas. So there is a great need for informatics systems which help users to navigate and query unfamiliar domains. Cabinet is such a system.

Cabinet comprises a set of tools to generate federated chemical and biological informatics servers and a federation of servers built upon these tools. The Cabinet tool set includes tools for handling chemical structures (built upon the Daylight CIS toolkits) as well as protein sequences, Enzyme Commission numbers, protein and ligand structures, images, enzyme networks and other biological and genomics data types. The servers built with Cabinet tools speak HTTP protocol and so can interact with web browsers. They also communicate with each other to exchange queries.

Each Cabinet server provides access to a certain type of information. For example, the QSAR server provides access to Quantitative Structure Activity Relationships while the Empath server provides access to information about metabolic pathways. Each server has a data model that is appropriate to the data that it serves and the data models can be quite different from one another. In a federated system there is no need to have a unified overall data model. Instead, Cabinet servers share a set of common languages that they use to exchange queries with one another. For example, the servers use the SMILES language (<http://www.daylight.com/smiles>) to define chemical structures. Thus, one Cabinet server might send a SMILES to the other servers to find out what they know about that molecule or similar molecules. Each Cabinet server is free to answer that query based on its own data model. The answers from that query are collected and presented to the user as new hyperlinks that can be followed. Each page of information presented by a Cabinet server typically has one or more hyperlinks that will cause such queries to be sent to the other servers to find related information. The rule in Cabinet is to click on a hyperlink if you want more information about an item or related items. Thus, there is typically no complicated query system to learn and no need to understand complex data schema before one can use Cabinet.

Recent additions to the Cabinet suite of servers are CARD (Cabinet Access to Relational Databases) and Postage (a report and image generation server). CARD allows users to generate new Cabinet servers using simple HTML templates to control the page appearance and SQL and simple scripting to retrieve the data from a back end RDBMS. This allows users to integrate their own data, typically stored in Oracle or other relational systems, into the Cabinet federation with the ability to exchange information and queries with all the other Cabinet servers. CARD provides a powerful new way to explore internal databases and visualize the connections between those data and other Cabinet servers with a wide variety of other data. Postage provides the ability to generate nicely formatted reports formatted for browsing or (in PDF format) for high quality printed reports, including chemical structures.

More information on Cabinet is available at the Metaphorics web site and free web access to functioning Cabinet servers can be obtained by signing up at <http://cabinet.metaphorics.com>.

Optive Research, Inc.
(<http://www.optive.com>), a life sciences software company providing innovative solutions for computer-assisted molecular

discovery, has announced the availability of its latest software for *in silico* drug and agrochemical discovery:

EA-Inventor breaks the paradigm of traditional *de novo* molecular design programs. Its novel technology makes it both faster and easier for chemists to "invent" new compounds for *in silico* lead discovery, to modify R-groups around a fixed scaffold for lead exploration, or to invent new scaffolds for increasingly important "lead-hopping" strategies.

EA-Inventor employs a novel Evolutionary Algorithm to "invent" or evolve new compounds by modifying (mutating) the structures of an initial set of compounds. The mutated structures evolve via a "survival of the fittest" process.

One of the most unique aspects of EA-Inventor is the ease with which it can work with whatever fitness function (or multi-component fitness function) best describes the user's specific constraints and discovery objectives. Another unique aspect is the broad palette of mutation operators which provides further control, leading to the faster evolution of desired, chemically sensible structures.

Unlike other *de novo* design products which require use of built-in, proprietary, "black box" scoring functions, EA-Inventor works with literally any external scoring function, including 3rd-party or user-developed scoring functions. In addition, users are not restricted to only structure-based scoring functions, as with other *de novo* packages, but can also use ligand-based scoring functions to guide the evolutionary process.

Available on the Linux and SGI® IRIX® platforms, EA-Inventor can be used with any 3rd-party scoring functions (regardless of whether they require 2D or 3D structures) and ships with several unique scoring functions developed by Optive Research. Significantly, EA-Inventor is designed to leverage the power of distributed processing on Linux clusters, multi-processor SGI IRIX servers, or across a heterogeneous network of IRIX and Linux workstations. More information about EA-Inventor can be found by visiting <http://www.optive.com/invent>.

Career Corner

One of the essential aspects of a career in science is the ability to present findings to colleagues both in reports and at meetings. As your career advances however, the scope of this activity will grow and you will find yourself responsible for editing books and/or journals and arranging meetings. In this edition of the

Computational Chemistry Communiqué, Georgia McGaughey, Neysa Nevins and Gregory Warren describe their experience setting up and moderating the Docking and Scoring Symposium at the Fall 2004 meeting of the American Chemical Society.

Docking and Scoring Symposium: Lessons Learned.

None of us had ever organized a symposium at this level (37 speakers). Sure, we had orchestrated our weddings, parties and company-wide meetings, but this was a new task. One issue was clear – we all had a vested interest in Docking and Scoring. We think that was the real key: enlightened self-interest was an important driver in the success of this symposium.

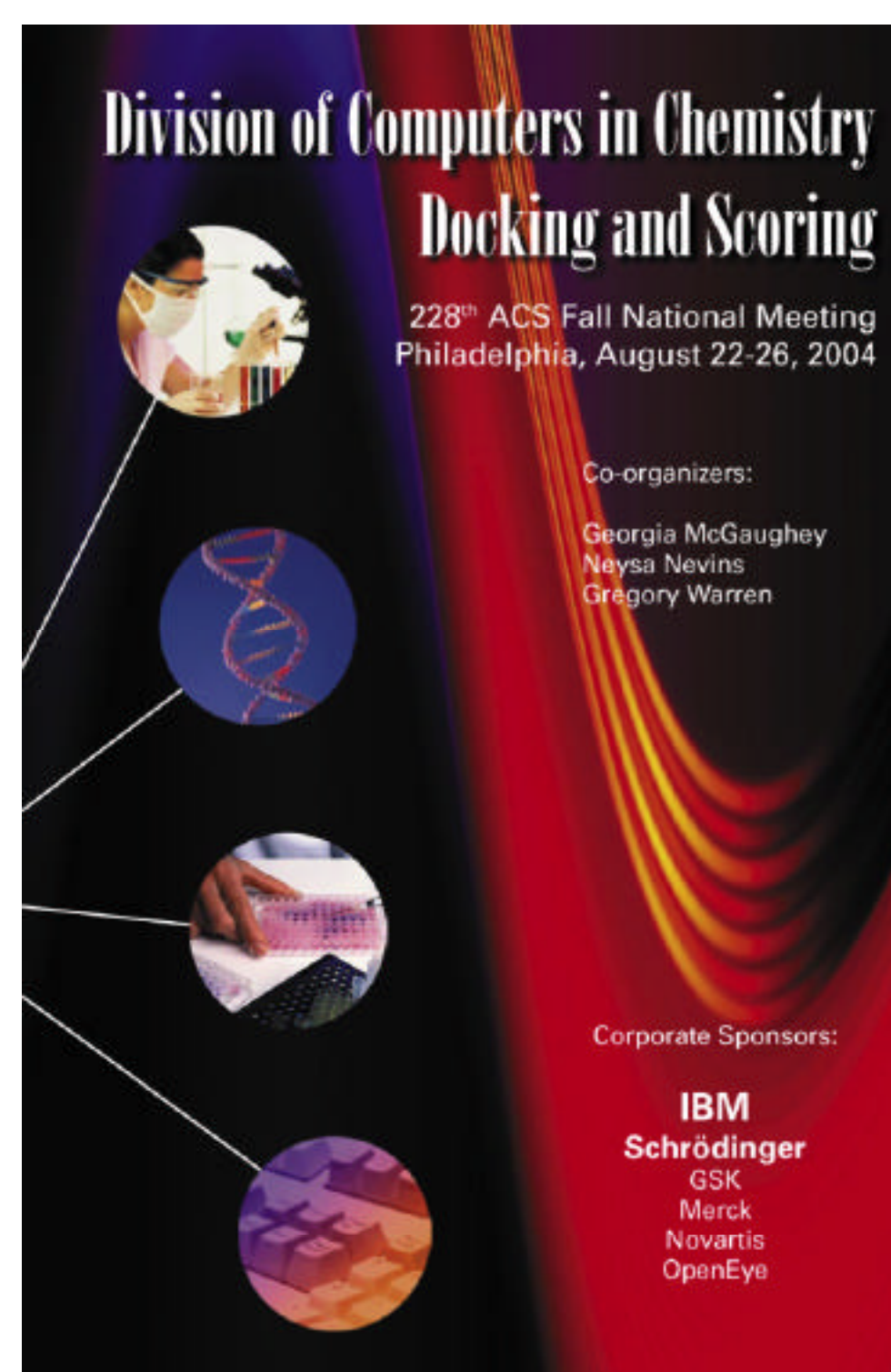
All of us had attended numerous ACS meetings before. We knew what typical expectations were from the attendees and conference organizers (keep the meetings running smoothly and on time). We also knew that at times, ACS sessions can be a hodgepodge of divergent variations on a theme. Furthermore, we were all at large pharmaceutical companies – and wanted a fair representation of science at universities, software companies and biotechnology centers.

We started thinking about the symposium approximately 8 months in advance. We divided the speakers into 3 categories: 1) academics 2) industry and 3) software companies. We literally generated lists where we ranked potential speakers. Since we were all very familiar with the topics, this wasn't such a difficult task. However, in cases where we weren't clear or there was some lively discussion amongst us, we searched relevant journals to see who had recently published manuscripts in the area of Docking and Scoring. We strove to be as fair as possible!

The three of us were basically at the same point in our careers. We think that worked to our advantage as none of us had the upper hand – and we all felt comfortable asking questions and disagreeing at times with one another. We did ask our respective bosses and the COMP chair for advice. The three of us held teleconferences bimonthly and when necessary, invited our line management and/or the COMP chair.

Based on advice from management, we began exploring the possibility of corporate sponsors for the symposium. This was only after it became clear that we would have at least 20 speakers. The physical location (Philadelphia, PA) of the meeting helped as there are so many people on the East Coast – most people said 'yes'

to the invitation. We asked our respective companies for money and then asked the hardware and software people for additional funding. We didn't ask for a specific amount, but companies suggested amounts between \$300 and \$10,000. We said 'yes' to any amount and always sent a note (two of us are from the South – we can't help but write thank you notes) thanking the respective organization for the 'generous' support regardless of the amount. We also had posters (depicted in Figure 1) created which were placed outside of the conference room (and one inside) 'thanking' the sponsors. This was the only time we were a bit more explicit, or should we say, subtle, regarding the difference in funding: the font size for the companies was larger for those funding a larger amount of money.



Due to a large amount of money raised, we were able to reimburse the academic speakers for their ACS registration in full (providing that they registered early and were ACS members to get necessary discounts). Any remaining money would be then used to assist in travel expenses. In addition, we were able to host a MIXER which consisted of an open bar and dinner food for two hours. This MIXER was held after the second day of the Symposium and we planned the exact date months in advance after discussion with the COMP chair. We cannot stress enough the benefit of keeping in close contact with your chair!

In the weeks leading up to the meeting, we wrote approximately three emails to the speakers reminding them of the location of the room, the date and time they were to speak and

the duration of their seminar. We also updated them on the hardware in the rooms (what they should expect) in the hopes of mitigating incompatibilities with hardware and software. Only one person was not able to make it to the meeting and we were warned a few weeks in advance.

Finally, after the symposium was over (within the week), we sent an email thanking all of our speakers (remember, we're from the South!). The *Journal of Medicinal Chemistry* was interested in creating a special issue on Docking and Scoring and we used the opportunity to ask our speakers if they would be interested in contributing to such an issue.

Above all, try and have fun! We think we all stressed over the Symposium more than the speakers. One also has to realize things will happen beyond our control (not all USB adaptors are universal) – and that one can never have too many backup plans.

Note: For people interested in organizing symposia at future ACS meetings, Wendy Cornell, Chairperson of the Comp Division Program Committee has forwarded the following information. Small symposia can be organized up to 7 months in advance but larger symposia may require up to 10-12 months. Anyone interested in organizing a symposium for the Spring 2006 meeting in Atlanta should contact Wendy. The schedule for the Fall 2005 meeting in Washington D.C. is already more full than usual. Symposia that have been scheduled for upcoming meetings can be found at the National Meetings link on the COMP Web site <http://membership.acs.org/C/COMP/>.