CINF 1

“Chemical Information Instructor” feature: Telling the story of successful faculty-librarian partnerships in the Journal of Chemical Education

A. Twiss-Brooks, atbrooks@uchicago.edu. John Crerar Library, University of Chicago, Chicago, IL, United States

Since 1992 the Chemical Information Instructor (CII) feature has been providing instructors with practical information on a wide range of topics related to teaching information-searching skills to undergraduates, graduate students, and other researchers. The Editors of CII have encouraged the submission of articles featuring creative and successful collaborations between librarians and teaching faculty. Some of these collaborations have included integration of information instruction into one or more chemistry courses, incorporating instruction using specific information tools, and addressing scientific information retrieval in non-science major courses. Information on CII, examples of interesting collaborations reported in the feature, and possible future directions will be presented.

CINF 2

Teaching students to use REAXYS in order to find synthetic methods for making benzylic acid from benzaldehyde

S. K. Cardinal[1], scardinal@library.rochester.edu, and W. D. Jones[2]. [1]Carlson Science and Engineering Library, University of Rochester, Rochester, NY, United States, [2]Department of Chemistry, University of Rochester, Rochester, NY, United States

In Honors Organic Chemistry, second semester sophomores search the chemical literature to find their own experimental procedures: one for oxidizing benzoin to benzil and a second for the conversion of benzil to benzilic acid. Because the literature on these reactions is extensive, they need to evaluate the methods using parameters that are mutually agreed upon in class. Together, a librarian and a faculty member have created a hands-on tutorial that demonstrates how Reaxys (formerly Beilstein CrossFire) may be used to identify relevant articles.

CINF 3

In depth chemical information instruction in a second year organic chemistry course at Indiana University-Purdue University Indianapolis

E. Snajdr, esnajdr@hotmail.com. University Library, Indiana University-Purdue University Indianapolis, Indianapolis, IN, United States

We are embedded librarians in a second semester organic chemistry course at Indiana University-Purdue University Indianapolis. Librarian involvement in this

course consists of approximately six hours of instruction. The chemistry librarians lead the students in six separate modules which encompass the following topics: searching for analytical data, searching for a chemical structure and synthetic procedure, searching for a reagent, searching for an experimental procedure, and finally, searching for scientific papers by a known author. The course was developed in collaboration between the chemistry librarians and instructors of the course and has continued to evolve along with technology and information tools.

CINF 4

Qualitative analysis in the library

J. N. Currano, currano@pobox.upenn.edu. Chemistry Library, University of Pennsylvania, Philadelphia, PA, United States

This paper describes a long-standing collaboration between the University of Pennsylvania's chemistry librarian and the instructors of the advanced undergraduate laboratory course. The chemistry librarian teaches the students two intense lectures, complete with credit-bearing assignments, that teach them to use the chemical information resources. The first lecture and assignment review the structure of the chemical literature and teach the students to find physical properties and preparations of substances. The second lecture teaches students techniques of text and structure searching using truncation, preparing them to use the chemical information resources to answer open-ended questions, exemplified in the accompanying assignment.

CINF 5

Integrating library instruction into SAGES seminars at Case Western Reserve University for undergraduate chemistry students: A strategic plan

S. Guo, shu.guo@case.edu. Kelvin Smith Library, Case Western Reserve University, Cleveland, Ohio, United States

Chemistry is a unique science discipline which requires special searching techniques to locate its enormous collection of information. Systematic library instruction on the chemical literature and specialized search techniques required for chemistry and the related scientific disciplines have long been recognized as important. Case Western Reserve University has had its SAGES program in place for years, offering undergraduate students with a series of seminars to enhance their skills on learning, writing, and scholarly inquiry. Currently our librarians have been teaching general library collection/resources and searching skills in most SAGES First and University seminars. The strategic plan is to integrate library instruction sessions on chemistry resources and searching skills into SAGES's Departmental and Capstone Seminars. Through the joint efforts of science librarians and teaching faculty, undergraduate chemistry students will be systematically exposed to chemical information resources and specialized search techniques. Therefore, the students will be well prepared for their academic classes and professional careers.

CINF 6

USC Chemistry OIL program

N. Xiao, nxiao@usc.edu. Science and Engineering Library, University of Southern California, Los Angeles, CA, United States

With more information available on-line, more technologies available for users to access information virtually, and more interdisciplinary research shaping our collection, librarians are facing more challenges than before. For instance, how can we penetrate users' information search life and help them find what they want in numerous information resources that have ever-changing search interfaces and features? How do we shape our users' chemical information literacy in the e-resources environment? On the other hand, to what degree can we partner with users, especially faculty members, to provide the customized information services and collections that they need? The USC Chemistry Outreach and Information Literacy Program (OIL) serves to reach out to users and to collaborate with faculty members to provide customized, systemic, broad, and in-depth information literacy training (e.g. research group, course-related, project-related). This presentation will answer the questions posed above and offer some best practices in sustainable chemical information education.

CINF 7

Beyond Google: Integrating chemical information into the undergraduate chemistry curriculum

M. C. Peters, mpeters@library.ucla.edu. Science & Engineering Library, UCLA, Los Angeles, CA, United States

At UCLA the focus is on partnering with faculty and teaching assistants in integrating the basics of chemical information into three sequential courses required for chemistry and biochemistry majors. Resources “beyond Google” include many recommended in “Information Competencies for Chemistry Undergraduates: the elements of information literacy” (http://units.sla.org/division/dche/il/cheminfolit.pdf). A multi-faceted approach includes primarily hands-on sessions in small laboratory sections, occasional large group lectures, and a comprehensive Web site, http://www.library.ucla.edu/libraries/sel/12451.cfm. The Instructional Resources Web site, available 24/7, features “Library resources for chemistry and biochemistry, chemical and biomolecular engineering, and materials science and engineering.” Web pages cover hands-on, guided library exercises including the organic “chemystery,” homework assignments, lecture notes, and resources for specific courses, plus general reference sources. Many UCLA sites feature links to “Library Resources” and its pages, including departmental sites, course management systems, the undergraduate Science Learning Center workstations’ “Welcome” screen, and individual course pages.

CINF 8

No chemistry librarian: How chemistry faculty can participate in collection development and its increased use

A. W. Kozlowski, kozlowskia@ccsu.edu. Department of Chemistry, Central Connecticut State University, New Britain, CT, United States

Designating an interested chemistry faculty member as a library liaison can benefit both the department and the library. This person can help faculty make the best use of resources that are already available, assist with instruction, and articulate to librarians the highest needs for the curriculum. This approach helps get the most value for the money available.

CINF 9

Beyond Metlin: Extending metabolite databases to enhance identifications in metabolomics

G. Suizdak, siuzdak@scripps.edu. Center for Mass Spectrometry, The Scripps Research Institute, La Jolla, California, United States

Global (untargeted) metabolite profiling using mass spectrometry has a history dating to 1966 (*Biochemical Journal*, **1966**, 792) and was then limited by both the gas chromatography mass spectrometry technology and the tools used to perform post-experimental analysis. These limitations included comparative analysis capabilities and database searching, largely because neither existed. Over the course of the last 40 years GC/MS has evolved into a very mature technology for performing metabolomics experiments, however, the more comprehensive LC/MS experiments are experiencing the same limitations as did its predecessor, namely a lack of differential analysis tools and a very limited number of known metabolites. The METLIN database currently contains ~;24,000 compounds and over 10,000 high resolution (ESI-QTOF) MS/MS spectra. Data mining and machine learning techniques have been developed to not only identify known metabolites but also to characterize and classify unknowns. Based on known structures, the fragment assignment to MS/MS data of known compounds, and novel fragmentation prediction software, we have been able to identify the structural characteristics for unknown metabolites. Machine learning methods are used to predict functional groups from MS/MS data and subsequently assign unknown metabolites to compound classes. We are developing a web based application where 1) users can upload MS/MS data to perform an automatic database search to identify metabolites, 2) MS/MS based similarity search can be conducted to show structural similarities for unknown metabolites and 3) functional groups are predicted and unknown metabolites are assigned to compound classes.

CINF 10

Stable isotope-resolved metabolomics analysis of UDP-GlcNAc & UDP-GalNAc: Computational resolution and modeling of their converging biosynthetic pathways

H. N. B. Moseley[1,3], hunter.moseley@louisville.edu, A. C. Belshoff[2,3], R. M. Higashi[1,3], T. W.-M. Fan[1,2,3], and A. N. Lane[2,3]. [1]Department of Chemistry, University of Louisville, Louisville, Kentucky, United States, [2]JG Brown Cancer Center, University of Louisville, Louisville, Kentucky, United States, [3]Center for Regulatory and Environmental Analytical Metabolomics (CREAM), University of Louisville, Louisville, Kentucky, United States

Regulation of uridine diphospho-N-acetylglucosamine (UDP-GlcNAc) and uridine diphospho-N-acetylgalactosamine (UDP-GalNAc) levels underlies the control of many biological processes via O-linked glycosylation of proteins, including nutrient sensing, protein degradation, and gene expression. We used FT-ICR-MS to make rapid, high-confidence measurements of ^{13}C incorporation into both UDP-GlcNAc and UDP-GalNAc from [U- ^{13}C]-glucose, in LNCaP-LN3 prostate cancer cells. This incorporation involves the flow of different ^{13}C-labeled functional moieties via parallel, converging metabolic pathways. We developed a simulated annealing and genetic algorithms (SAGA) method to parse all 17 sets of combined UDP-GlcNAc/UDP-GalNAc mass-equivalent isotopomers (isotopologues) into these functional moieties. This revealed the relative contribution of specific metabolic pathways to ^{13}C incorporation and allowed direct confirmation using NMR positional isotopomer data. The rates of synthesis and utilization of UDP-GlcNAc/UDP-GalNAc were substantially decreased by methyl seleninic acid (MSA), suggesting MSA effects homeostatic regulation of these sugar nucleotides.

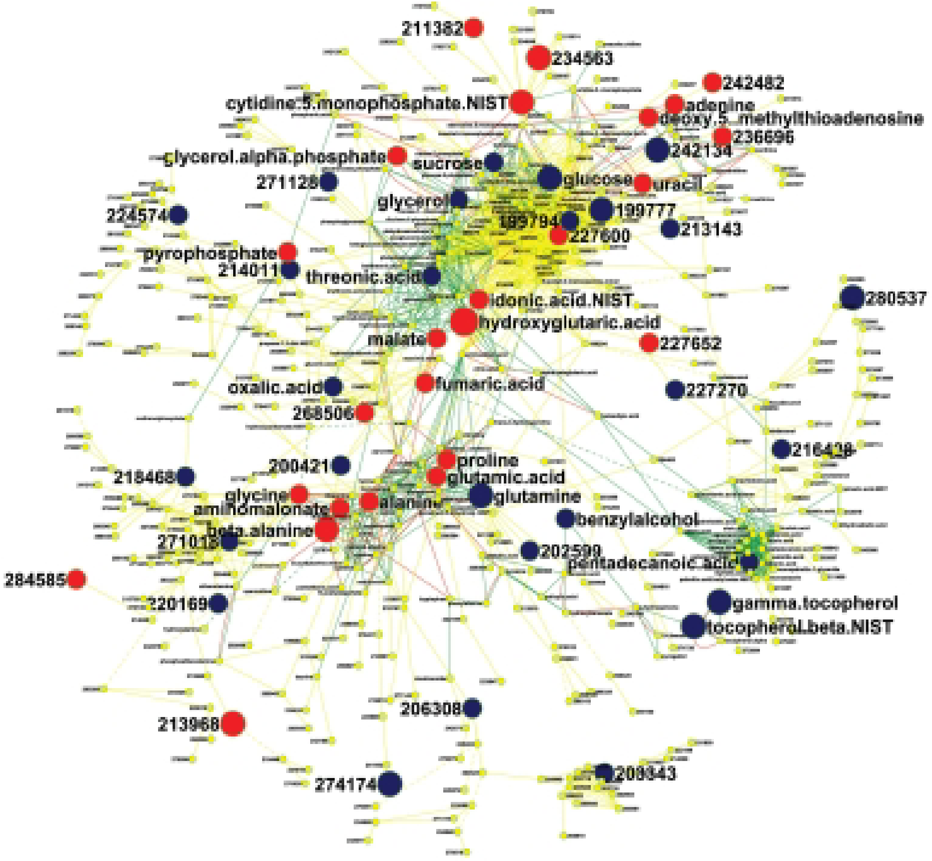
CINF 11

Functional and structural network modeling of metabolomics datasets

D. K. Barupal, dinkumar@ucdavis.edu, G. Wohlgemuth, and O. Fiehn. Genome Center, University of California, Davis, Davis, California, United States

Network approaches facilitate metabolic studies. For mass spectrometry based metabolomics datasets, the BinBase database generated lists of known and unknown metabolites detected in biological matrix. We compared two types of network models, functional and structural. Functional network models were less comprehensive than structural models because biochemical databases such as KEGG and MetaCyc lack pathway and reaction annotation for several known metabolites. Only PubChem has entries for all the known metabolites. By

applying chemical similarity, mass spectral similarity and atomic mapping of reaction pairs, structural networks were constructed which included all known and unknown metabolites. Cytoscape visualization of these models yielded a modular network graph resembling known metabolic modules. Statistical differences in ER+/- breast cancer comparisons were imposed by color grades to highlight differences in biochemical pathways.



CINF 12

Computational aspects of metabolomic Quantitative Trait Locus (mQTL) mapping and metabolome-wide genome-wide association studies

M.-E. Dumas[1], m.dumas@imperial.ac.uk, J.-B. Cazier[2], J. K. Nicholson[1], and D. Gauguier[2,3]. [1]Department of Surgery and Cancer, Biomolecular medicine, Imperial College London, London, United Kingdom, [2]Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, Oxfordshire, United Kingdom, [3]INSERM U872, Centre de Recherche des Cordeliers, Paris, France

The study of human multifactorial diseases, like diabetes, cardiovascular disease, insulin resistance, or complex biological processes such as ageing, represent a major healthcare challenge for the western and developing world. Metabolomic Quantitative Trait Locus (mQTL) mapping consists of the robust and accurate statistical integration of genome-wide genotyping and metabolome-wide profiling, to identify candidate biomarkers and susceptibility genes for disease. Like other QTL mapping approaches, mQTL, relies on the extended Haley-Knott method. To improve the initial mQTL technology, we present a range of computational developments in dataset normalisation, co-factor corrections, automatic peak alignment, statistical recoupling and automatic peak detection and integration, aiming at optimising QTL analysis algorithm efficiency on ^{1}H NMR variables and mQTL discovery rate. We apply this approach to biofluids, aqueous and lipid extracts from both rats and mice, to identify new candidate metabolite biomarkers and loci associated to disease.

CINF 13

Metabolite identification pipeline based on MS fragmentation

M. Rojas-Chertó[1,3], m.rojas@lacdr.leidenuniv.nl, **J. E. Peironcely**[1,2], peironcely@chem.leidenuniv.nl, P. T. Kasper[1,3], A. Bender[4], J.-L. Faulon[5], T. Reijmers[1,3], L. Coulier[2], R. Vreeken[1,3], and T. Hankemeier[1,3]. [1]Department of Netherlands Metabolomics Centre, Leiden University, Leiden, Zuid Holland, The Netherlands, [2]Quality of Life, TNO, Zeist, Utrecht, The Netherlands, [3]Department of Analytical Biosciences, Leiden University, Leiden, Zuid Holland, The Netherlands, [4]Department of Medicinal Chemistry, Leiden University, Leiden, Zuid Holland, The Netherlands, [5]Department of Biology, Evry University, Evry, Île-de-France, France

Here we will show different parts of the metabolite identification pipeline based on MS fragmentation data. **MS^n** spectral trees were acquired on the LTQ-Orbitrap (Thermo) equipped with a Triversa nanoMate (Advion) nanoelectrospray ion source. By using in-house developed software, integrating among others the Chemistry Development Kit (CDK) and XCMS libraries, the spectral data was processed. Application of the Multi-stage Elemental Formula (MEF) tool resolved the elemental composition of the parent compound and its fragment ions. A database containing fragmentation trees of metabolite standards is created, enabling the characterization of fragments from an unknown compound by querying and matching subtrees from known compounds. To be able to elucidate the structure of an unknown compound a structure generator is developed that uses as input the elemental formula and fragments. The generated structures These structures are evaluated and ranked with chemoinformatic models predicting ‘metabolite likeness’.

CINF 14

Consensus-phenotype integration of metabolomic and transcriptomic data enhances the detection of pathways associated with drug response

R. Cavill[1], A. Kamburov[2], M. S. C. Blagrove[1], T. J. Athersuch[1], J. K. Ellis[1], R. Herwig[2], **T. M. D. Ebbels**[1], t.ebbels@imperial.ac.uk, and H. C. Keun[1]. [1]Biomolecular Medicine, Department of Surgery and Cancer, Imperial College London, London, United Kingdom, [2]Max Planck Institute for Molecular Genetics, Berlin, Germany

The successful combination of different types of biological data is a critical challenge in systems biology. In this work, we aim to define pathways predictive of drug sensitivity using publically available drug response, transcriptomic and metabolomic measurements from the NCI60 cell line panel, together with a novel approach to data integration. Initially focusing on platinum-based chemotherapeutics we show that the sets of pathways associated with sensitivity to four platinum drugs are highly coincident. Many significantly altered pathways, covering wide range of metabolic and signaling processes, were consistent with the previously reported molecular determinants of platinum response. The sensitivity for the detection of predictive pathways was improved by ~;85% by combining "-omics" data at the point of pathway analysis. Extending the approach across a wide panel of compounds, we show how consensus-phenotype integration can help to reveal the complex relationships between biological pathways and drug response.

CINF 15

Designing a cyberinfrastructure for metabolomics

M. Arita, arita@k.u-tokyo.ac.jp. Department of Computational Biology, The University of Tokyo, Kashiwa, Chiba, Japan

Most Wiki-based databases do not provide a measure to control vocabulary (ontology) of, or extract statistical information from input data. This is the often overlooked side of community-driven projects: terminology in a wiki environment tends to be heterogeneous and it will be extremely hard to 'manage' data. To overcome this disadvantage, we present an extension to the MediaWiki system, the most popular wiki-based platform. As a proof of principle, a collection of more than 7000 flavonoid structures, over 1700 plant species information, and the information for basic metabolism are linked together using latin names and structural IDs as database keys. In this talk, I will introduce functionality of this approach and describe the difference from conventional systems. The system is available at http://metabolomics.jp/. This mechanism will be supported by several academic societies in Japan to integrate their academic information into a single portal site.

CINF 16

Computational discovery of new zeolite-like materials

M. W. Deem, mwdeem@rice.edu, and D. J. Earl, dearl@pitt.edu. Bioengineering and Physics & Astronomy, Rice University, Houston, TX, United States

We present a database of computationally predicted zeolite-like materials. The materials were identified by a Monte Carlo search of Si atom positions as the number of unique atoms, density, space group, and unit cell of the crystalline material was systematically explored. Over 2.7M unique structures were identified, with roughly 10% within the +30 kJ/mol,Si energetic band above alpha-quartz in which the known zeolites lie. Predicted structures within this band have geometric and topological characteristics similar to that of the known zeolites. Known zeolites are shown to lie on the low-density edge of the distribution of predicted structures. Dielectric constants and X-ray powder diffraction patterns are calculated. Strategies for chemical synthesis of these materials are discussed, a low-density subset of the materials is identified as particularly interesting, and the complementarity of these materials to high-throughput methods is discussed. These structures have been deposited in two publicly available databases.

CINF 17

Using multiple levels of computer modeling to accelerate development of metal organic frameworks materials for membrane applications

D. S. Sholl, david.sholl@chbe.gatech.edu, S. Keskin, T. Watanabe, E. Haldoupis, and S. Nair. School of Chemical & Biomolecular Engineering, Georgia Institute of Technology, United States

Metal-organic frameworks (MOFs) are crystalline nanoporous materials with a variety of potential applications in gas separations and storage. Because thousands of distinct MOFs are known, approaches that can rapidly identify structures with particular promise for specific applications have considerable value. We will describe a hierarchical modeling approach to screen MOFs for membrane-based gas separations, an application that is challenging because it requires information on both adsorption affinity and molecular diffusivities. Our approach uses geometric characterization to screen hundreds of materials, then molecular modeling and quantum chemistry calculations to make detailed predictions about strong candidate materials. We will show examples of using this approach to develop materials for efficient separation of methane and carbon dioxide. We will also describe our progress in fabricating and testing MOF-based membranes based on materials identified via modeling.

CINF 18

Informatics approaches for analyzing zeolites

E. Blaisten-Barojas, blaisten@gmu.edu. Computational Materials Science Center, George Mason University, Fairfax, Virginia, United States

Zeolites are natural and synthetic crystalline materials with interesting microporous framework structures. The framework type of zeolites is traditionally determined from information of coordination sequences, vertex symbols, tiling and transitivity. We developed the Framework-Type-Predictor (FTP), a novel informatics-based model that is very efficient for classifying zeolites according to their framework type. The FTP is built on topological, physical, and chemical features, is able to precisely classify into 41 framework types, achieves accuracies of up to 100%, and is superior for zeolites with crystalline distortions. Additionally, we present an unsupervised clustering model for grouping zeolites into four attractor-classes. Trained with 1300 zeolites from the Inorganic Crystal Structure Database, with an optimal 9-dimensional feature vector, this model yields classification into four attractors with 97% accuracy. Such attractors should be useful for material designers producing computationally generated zeolitic compounds. *(Supported by National Science Foundation CHE-0626111, ICSD data courtesy of NIST).*

CINF 19

Screening tools for identification of porous materials for CO_2 separation

M. Haranczyk[1], mharanczyk@lbl.gov, J. Kloke[2], K. Theisen[3], B. Liu[3], G. Carlsson[2], and B. Smit[3]. [1]Computational Research Division, Lawrence Berkeley National Laboratory, Berkeley, CA, United States, [2]Department of Mathematics, Stanford University, Palo Alto, CA, United States, [3]Department of Chemical Engineering, University of California, Berkeley, Berkeley, CA, United States

Porous materials, e.g. zeolites, have many applications in the chemical industry. They can also be used for gas separations. The number of possible zeolite structures has been estimated to be larger than 2.5 millions. Databases of hypothetical zeolite structures are being developed and they could in principle be screened for best zeolites for the task of CO_2 capture. The current state-of-the-art molecular simulations allow for accurate prediction of zeolite properties but the computational cost of such calculations prohibits their application in the characterization of the entire database of hypothetical structures, which would be required to perform brute-force creening for novel structures with useful properties. Our work focuses on the development of an efficient screening technique that requires such expensive characterization only for carefully selected and statistically relevant subset of a database. Then, the database is screened employing the similarity principle. The developed screening technique, structural descriptors and similarity measures as well as first results will be presented.

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CINF 20

3D-Characterization and modeling of composite materials

O. Wirjadi, wirjadi@itwm.fraunhofer.de. Image Processing Group, Fraunhofer ITWM, Kaiserslautern, Germany

Composites form an important class of functional materials in many industries. Examples include open metal foams used as heat exchangers and carbon fiber-reinforced polymers to reduced the weight of fuselages in aircraft. An important factor that determines these materials' macroscopic properties is their geometry at the micro- and meso-scale. Combining tomographic imaging with image analysis allows to describe their 3D-geometry. We present 3D-image analysis algorithms and stochastic models for automatic characterization and modeling of large batches of specimens. In a first step, we characterize the microstructure in terms of mean values and empirical distributions (e.g. strut lengths and cell geometry for foams, fiber densities and orientation distributions for fiber-reinforced polymers). From these measurements, a second step is to model these materials. Such models allow for "virtual design" of composites, i.e., when combined with finite element-simulation of physical or mechanical properties, geometries with desirable properties can be identified.

CINF 21

Growing focus on green chemistry: What the CAS databases reveal

R. Schenck, rschenck@cas.org. Chemical Abstracts Service, Columbus, OHIO, United States

Green chemistry is a trend that has spiked during recent years. This presentation will focus on specific areas of interest and the nature of the research going on in those areas, as seen from the perspective of the CAS databases. For instance, the fermentation process that yields alcohol from corn is well understood, but the CAS databases contain a wealth of articles on catalysts for optimizing this process in addition to research on the genetic engineering of corn, or the biomass, so that it may be more efficiently converted to ethanol. Features in SciFinder for identifying green reactions will be illustrated, as well as content in the CAS databases that support REACH reporting requirements.

CINF 22

California's green chemistry initiative: Application of life cycle assessment in public policy

B. Boughton, bboughto@dtsc.ca.gov. Department of Toxic Substances Control, California EPA, Sacramento, California, United States

The California Green Chemistry initiative comes at a time of growing concern that the federal Toxic Substances Control Act, passed three decades ago, has failed to control an explosion of hazardous materials. California law passed last fall has jump-started the program. AB 1879 requires the state to identify "chemicals of concern" and to evaluate safer alternatives by implementing a policy option, "Accelerate the Quest for Safer Products, creating a systematic, science-based process to evaluate chemicals of concern and alternatives to ensure product safety and reduce or eliminate the need for chemical-by-chemical bans". The adopted rules will lay out the process for products with chemicals of concern to be compared to alternatives by assessing the "environmental and economic footprint" of each using a life-cycle perspective. This application of life-cycle thinking for assessing environmental impacts and for assessing total costs will be described. The background information on the initiative is at www.dtsc.ca.gov

CINF 23

ChemSpider: How an online resource of chemical compounds, reaction syntheses, and property data can support green chemistry

A. J. Williams, antony.williams@chemspider.com, and V. Tkachenko. ChemSpider, Royal Society of Chemistry, Wake Forest, NC, United States

ChemSpider is an online database containing in excess of 20 million chemical compounds and associated experimental and predicted physicochemical data, reaction synthesis details and analytical data. A significant amount of the data contained within the database has been harvested and collated from a number of inventory systems and integrated to provide a centralized resource for the community. The ChemSpider database has the added benefit of being available for community deposition, annotation and curation. As a result it offers the potential for researchers to share their latest research with the public and participate in the creation of a rich resource of chemistry related information for the Green Chemistry community. This presentation will provide an overview of present capabilities and discuss the future vision for the platform.

CINF 24

From biochemical pathways to retrobiosynthesis

C. H. Schwab, schwab@molecular-networks.com, O. Sacher, sacher@molecular-networks.com, B. Bienfait, bienfait@molecular-networks.com, and J. Gasteiger, gasteiger@molecular-networks.com. Molecular Networks GmbH, Erlangen, Bavaria, Germany

Intracellular transformations as outlined by the Biochemical Pathways wall charts form a high-dimensional space that interconnects many biochemical compounds by a multitude of enzyme-catalyzed reactions. In order to explore (and exploit) this vast information to address challenges in the areas of metabolomics, drug discovery, modeling of biological systems or green chemistry and metabolic

engineering, the wall charts (plus recent literature data) have been converted into the database BioPath of cross-linked chemical structures, reactions and pathways [1].

The paper introduces the BioPath database and its application in the program system BioPath.Design that supports the planning of biotechnological manufacturing of bulk and fine chemicals. Starting with the full target structure, BioPath.Design systematically searches in the BioPath database and suggests new biochemical reaction steps and synthesis routes based on similar known enzyme-catalyzed reactions, even if the target is not present in the database. The method can be used either in a step-wise, interactive or multi-step, fully automatic retrosynthetic manner. Some examples will be demonstrated.

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CINF 25

Green chemistry database and analytical compliance suite (GC-DACS)

G. R. Thompson, georgethompson@chemply.com. Chemical Compliance Systems, Inc., Lake Hopatcong, NJ, United States

Application of “the twelve principles of green chemistry” to complex formulations requires comparison of both efficacy and toxicity data (i.e., standardized criteria) for multiple chemical constituents and/or their alternatives. Thus, “reducing toxicity” or identifying “hazardous substances” must encompass broad ecological, health, and safety measures. How can these parameters be integrated into a quantitative set of “green” criteria for application to chemicals, processes, products, and waste across the entire product lifecycle (i.e., cradle to cradle)? In 2003, Chemical Compliance Systems, Inc. (CCS) developed four web-based, analytical compliance modules for their GC-DACS to help improve product design, manufacturing process comparisons, and “greening” the waste stream while assuring compliance with the national Standard for Green Chemical Products and Processes. Ultimately, these analytical tools enhance the green principles by providing a broad definition and a depth of quantification not previously available in other web-based capabilities.

CINF 26

Importance of benchmarking Green Chemistry

G. Gurau, and **R. D. Rogers**, rdrogers@as.ua.edu. Department of Chemistry, Center for Green Manufacturing, The University of Alabama, Tuscaloosa, AL, United States

Readily searchable and accessible data with which to benchmark ‘improvements’ to chemical or chemical technology are critical to the field of Green Chemistry. Green Chemistry strives to develop chemicals and chemical processes which are non toxic, not harmful to the environment, and sustainable. It is however, often difficult to determine whether improvements in one aspect of a process (e.g., elimination of volatile solvents), might actually be more harmful in another (e.g., greater energy use). Green Chemistry is really about careful decision making in order to balance many, often competing goals. Here we will discuss how extracting benchmarking information from the literature can help in these decision making processes.

CINF 27

Software advancements for performing compound identification QC on large metabolomic datasets

C. DeHaven, lgosselin@metabolon.com. Department of Metabolomics, Metabolon, Research Triangle Park, NC, United States

Traditional collection, sorting and analysis of metabolomic data has generally involved single data files each corresponding to a single biological sample. Data is then individually compared to spectral libraries of known metabolites in order to identify compounds contained in each biological sample. This labor-intensive approach does not lend itself to industrialization of the process; it also presents a problem correlating the analysis of multiple biological samples, including meta-data, with one another to determine trends and population differences. The ability to analyze and perform QC on large-scale, multi-sample metabolomics data on an industrial scale is an important step in the evolution of metabolomics technology as a whole. This presentation will provide an overview of software advancements which provide options for quickly performing rapid quality-control of metabolomic data.

CINF 28

Fold-change analysis and visualization of multispectral datasets in NMR-based metabolomics

S. L. Robinette, slrobin@ufl.edu, and A. S. Edison. Biochemistry and Molecular Biology, University of Florida, Gainesville, FL, United States

Large dataset visualization is a critical component in the analysis and interpretation of metabolomics data. Nuclear magnetic resonance offers particular challenges in terms of visualization as datasets are generally composed of multiple highly complex spectra with hundreds of overlapping signals arising from many small molecules. Here, we explore methods of fold-change based visualization using one- and two-dimensional NMR spectra in order to identify and interpret patterns of differential expression of metabolites. We show that cluster analysis of peak fold-change matrices identifies both structurally related peaks and metabolic coregulation using statistical relationships between signals in 1D ^{1}H NMR spectra and that fold-change analysis of individually aligned two-dimensional spectra provides complementary information. We demonstrate the utility of this methodology using tissue extract and media samples relevant to metabolomics.

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CINF 29

Data mining tool for automated metabolite identification and quantification using *J*-resolved NMR spectroscopy

S. He[1], C. Ludwig[2], J. M. Easton[3], H. Chen[1], S. Tiziani[2], A. Lodi[2], S. Manzoor[4], A. D. Southam[4], T. N. Arvanitis[3], U. L. Guenther[2], and **M. R. Viant**[4], m.viant@bham.ac.uk. [1]School of Computer Science, University of Birmingham, Birmingham, West Midlands, United Kingdom, [2]CR UK Institute for Cancer Studies, Henry Wellcome Building for Biomolecular NMR Spectroscopy (HWB-NMR), University of Birmingham, Birmingham, West Midlands, United Kingdom, [3]School of Engineering, University of Birmingham, Birmingham, West Midlands, United Kingdom, [4]School of Biosciences, University of Birmingham, Birmingham, West Midlands, United Kingdom

Although one-dimensional (1D) nuclear magnetic resonance (NMR) spectroscopy remains one of the leading analytical technologies in metabolomics, it suffers from severe spectral overlap which limits its ability to identify and quantify metabolites. 2D *J*-resolved (JRES) NMR spectroscopy is rapidly gaining in popularity, and benefits from a dispersion of peaks into a second dimension, improving metabolite specificity and potentially the accuracy of quantification. Here we report a freely-available data mining software package for quantitative metabolic profiling based on 2D JRES NMR spectroscopy. It incorporates a novel 2-step screening/quantification algorithm along with a 500 MHz NMR library containing ca. 220 JRES spectra of pure metabolites. The NMR library is housed in a MySQL database, with web accessibility, and is compliant with the Metabolomics Standards Initiative endorsed data standards. Validation of the data mining tool will be demonstrated using simulated as well as real metabolomics datasets comprising of chemically-defined metabolite mixtures.

CINF 30

Identification of parent-fragment pairs via rigorous statistical modeling of LC-MS metabolomic data

A. Ipsen, andreas.ipsen06@imperial.ac.uk, E. Want, J. Lindon, and T. Ebbels. Biomolecular Medicine, Department of Surgery & Cancer, Imperial College London, United Kingdom

The untargeted analysis of metabolic samples by Liquid Chromatography-Mass Spectrometry often generates a large number of signals that are due to unknown compounds and whose identification forms an important challenge in many metabolomic studies. The analysis of a metabolite’s fragmentation pattern following collision induced dissociation provides an important tool for its identification, but one that can be severely impeded by the close chromatographic coelution of distinct metabolites. We propose and validate a statistically rigorous algorithm for identifying clusters of related fragments and for distinguishing these from unrelated compounds. Unlike current techniques the algorithm presented here is derived directly from the statistical distribution of ion arrivals and moreover provides a rigorous probabilistic measure of the uncertainty of the assignment. We argue that many of the central problems that are encountered in the analysis of LC-MS data could potentially be addressed by means of similar ‘ab initio’ methods.

CINF 31

Generation of in-silico MS/MS mass spectra using combinatorial algorithms and reaction prediction expert systems

T. Kind, tkind@ucdavis.edu, K.-H. Liu, D. Y. Lee, and O. Fiehn. Metabolomics, UC Davis Genome Center, Davis, CA, United States

Metabolomic profiling using mass spectrometry suffers from the large number of unidentified compounds and small mass spectral libraries. For certain substance classes like lipids and oligosaccharides that are built from consisting building blocks it is possible to generate fragmentation patterns and to model peak abundances. We discuss methods for mass spectrometric fragmentation prediction. Using combinatorial library enumeration tools like ModLab SMILIB and Markush enumeration tools like ChemAxon Reactor we developed in-silico compound libraries for lipid classes which are not yet found in CAS, PubChem or ChemSpider databases but were already analyzed using mass spectrometric techniques. We used HighChem Mass Frontier and own fragmentation and abundance modeling software to simulate accurate mass tandem mass spectra. We show successful compound identifications using experimental tandem mass spectra from different types of mass analyzers including ion traps, quadrupoles, FT-MS, time-of-flight as well as hybrid ion mobility analyzers and discuss further applications in workflows.

CINF 32

Using aggregative Web Services for drug discovery

Q. Zhu[1], qianzhu@indiana.edu, M. S. Lajiness[2], and D. J. Wild[1]. [1]school of informatics and computing, Indiana Unversity, Bloomington, In, United States, [2]Eli Lilly and Company, Indianapolis, In, United States

Recent years have seen a huge increase in the amount of publicly-available information pertinent to drug discovery, including online databases of compound and bioassay information; scholarly publications linking compounds with genes, targets and diseases; and predictive models that can suggest new links between compounds, genes, targets and diseases. However, there is a distinct lack of data mining tools available to harness this information, and in particular to look for information across multiple sources. At Indiana University we are developing an aggregative web service framework to solve this kind of problems. It offers a new approach to data mining that crosses information source types to look at the "big picture" and to identify corroborating or conflicting information from models, assays, databases and publications.

CINF 33

Semantifying polymer science using ontologies

E. O. Cannon, eoc21@cam.ac.uk, N. Adams, and P. Murray-Rust. Department of Chemistry, University of Cambridge, Cambridge, Cambridgeshire, United Kingdom

Ontologies are graph based, formal representations of information in a domain. Currently, there is a large interest in ontologies for biology and medicine, though little effort has been concentrated in the field of chemistry, let alone polymer science. We have developed a number of ontologies for polymer science: properties, measurement techniques and measurement conditions, using the Web Ontology Language. These ontologies will help facilitate the standardization of data exchange formats in polymer science by providing a common domain of knowledge. The properties ontology contains over 150 properties and has been integrated with the measurement techniques and conditions ontology, to give information on how a property is measured and under what conditions. The ontologies will be of use to polymer scientists wishing to reach a consensus in this area of knowledge. The ontologies also have the advantage that they can be integrated into software applications to leverage this knowledge.

CINF 34

PDZ domain: A computational insight into protein similarity and ligand specificity

C. S. D. Sisu, csds2@cam.ac.uk, and G. H. Grant. Unilever Centre for Molecular Science Informatics, University of Cambridge, Cambridge, Cambridgeshire, United Kingdom

PDZ domain is one of the most common protein interaction modules. We explored its peculiar properties from two perspectives: protein similarity and ligand specificity. Firstly, the protein similarity was studied using reduced dimensionality representations. A two dimensional map was generated for every protein using a Monte Carlo like technique. The similarity between proteins was assessed based on the similarity of their respective maps. The proteins were compared at the level of amino acid side chain conformation and binding induced dynamics. Based on our findings we propose a novel classification of PDZ domains. Secondly, the promiscuous binding properties of PDZ domains were investigated using molecular dynamics simulations. MMPBSA as implemented in Amber 10 was used to calculate the thermodynamic parameters of protein-peptide interactions. We show that PDZ domain proteins capture the subtle differences between potential binding partners dynamically. Even more there is a direct correlation between binding affinity and protein dynamics.

CINF 35

Homology modeling and molecular dynamics of the APJ receptor, a co-receptor for cellular entry of HIV

N. J. M. Macaluso, max.macaluso2@gmail.com, and R. C. Glen, rcg28@cam.ac.uk. Unilever Centre for Molecular Sciences Informatics, Department of Chemistry, University of Cambridge, Cambridge, Cambridgeshire, United Kingdom

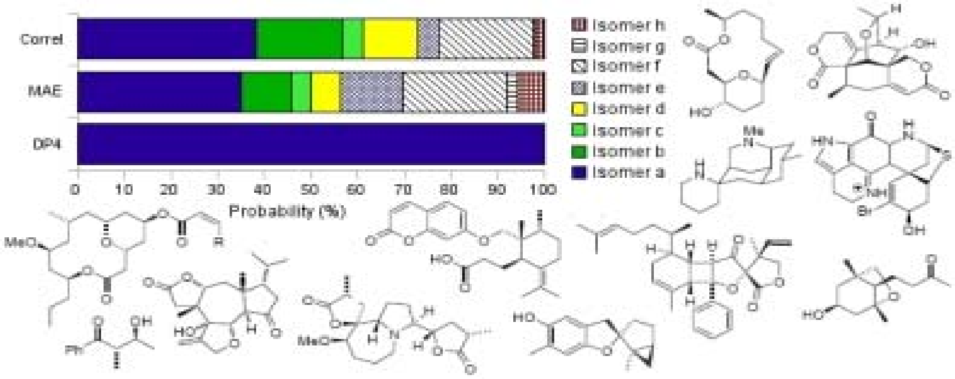
The APJ receptor is a class A GPCR and binds the endogenous ligand apelin-13 (NH_2-QRPRLSHKGPMPF-COOH). This signaling pathway is linked to cardiovascular disease, tumor neoangiogenesis, and HIV infection. The absence of a crystal structure has hampered the identification of a binding site and subsequent design of small molecule antagonists. We have constructed the first homology model of APJ using the backbone coordinates of the recent β2-adrenergic receptor crystal structure. This model was initially refined through extensive molecular dynamics in a solvated POPC lipid bilayer and further simulations were performed with the receptor in complex with the apelin peptide. Sequence information and structure-activity data derived from synthesis and binding affinity evaluation of novel cyclic peptides guided our initial placement of apelin. The resulting simulation is an important step in elucidating the binding mode of apelin.

CINF 36

Assigning stereochemistry using GIAO NMR shift calculation

S. G. Smith, sgs30@cam.ac.uk, and J. M. Goodman. Department of Chemistry, University of Cambridge, Cambridge, United Kingdom

GIAO NMR shift calculation has been applied to the challenging task of assigning stereochemistry to complex molecules such as natural products. Two new approaches, CP3 and DP4, have been developed for quantifying the agreement between calculated and experimental shifts in two different situations. These approaches are significantly more successful at making correct assignments with high confidence than are those based on the correlation coefficient and mean absolute error.



CINF 37

Combination of target-specific pose filters and force field-based scoring functions to improve the structure-based virtual screening

J.-H. Hsieh[1], juihua_hsieh@unc.edu, S. Yin[1], syin@email.unc.edu, X. S. Wang[1], xswang@email.unc.edu, S. Liu[2], shubin@email.unc.edu, N. V. Dokholyan[1], dokh@med.unc.edu, and A. Tropsha[1], alex_tropsha@unc.edu. [1]University of North Carolina at Chapel Hill, Chapel Hill, NC, United States, [2]Renaissance Computing Institute at UNC-CH, United States

Poor performance of scoring functions is currently a bottleneck in structure-based virtual screening (VS). Knowledge-based scoring functions capture subtle physical interactions that are otherwise difficult to model explicitly while force field-based scoring functions are less dependent on training sets. Thus these two approaches are intrinsically complementary to each other. We have combined a cheminformatics-based, target-specific pose filters with a force field-based scoring function, MedusaScore, to score presumed ligand poses during VS. Our results demonstrate that the novel pose filter improves the hit recovery in VS, especially for top-ranked ligands, for 5 out of 6 benchmarking sets retrieved from the Database of Useful Decoys (DUD). The further analysis shows that the improvements result from the elimination of decoy poses with high MedusaScore so these decoys are not ranked. Moreover, the top 10 hits include chemically diverse ligands, which is a highly desired outcome of any biological screening effort.

CINF 38

Toxicity reference database (ToxRefDB) to develop predictive toxicity models and prioritize compounds for future toxicity testing

H. Tang[1,2], tangh@email.unc.edu, H. Zhu[1], L. Zhang[1], A. Sedykh[1], A. Richard[3], I. Rusyn[4], and A. Tropsha[1]. [1]Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States, [2]Department of Biochemistry and Biophysics, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States, [3]National Center for Computational Toxicology, Office of Research & Development, U.S. Environmental Protection Agency, Chapel Hill, NC, United States, [4]Department of Environmental Sciences and Engineering, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States

EPA's ToxCast program aims to use in vitro assays to predict chemical hazards and prioritize chemicals for toxicity testing. We employed the predictive QSAR workflow to develop computational toxicity models for ToxCast compounds with historical animal testing results available from ToxRefDB. To ensure model stability and robustness, multiple classifiers and 5-fold external cross-validation were applied. Results show that for three of the 78 toxicity endpoints, including one chronic and two reproductive endpoints, the Correct Classification Rate for external validation datasets was above 0.6 for all types of QSAR models. Our studies suggest that it is feasible to develop QSAR models for some endpoints, which could be further augmented by in vitro assay measures. The validated toxicity models were used for virtual screening of 50,000 chemicals compiled for the REACH program. The compounds predicted as toxic could be regarded as candidates for future toxicity testing. Abstract does not reflect EPA policy.

CINF 39

Chem2bio2RDF: Semantic systems chemical biology

B. Chen[1], binchen@indiana.edu, X. Dong[1], D. Jiao[1], H. Wang[1], Y. Ding[2], and D. J. Wild[1]. [1]School of Informatics and Computing, Indiana University, Bloomington, IN, United States, [2]School of Liberary and Information Science, Indiana University, Bloomington, IN, United States

Recent advances in high throughput techniques, predictive modeling, and data generation have contributed to the emergence of new chemical & biological disciplines. In particular, systems biology adopts a comprehensive approach to the study of biological systems; chemogenomics studies the impact of small molecules towards biological systems and carries datum description about interaction among chemical entities and protein molecules; and the integration between cheminformatics and bioinformatics within the realm of systems biology leads to a new related discipline of systems chemical biology. These disciplines all involve the processing and data mining of very large amounts of information that come from diverse sources and disciplines, and aggregating and integrating these information sources can be very challenging. The work reported here

addresses this problem using Semantic Web technology. Our focus is on the aggregation of public chemogenomic data distributed around the Web into RDF formats, which enables linking with other biological Semantic Web information resources such as Bio2RDF and LODD. We examine the integrated use of this information in addressing problems in polypharmacology and adverse drug reaction using a variety of cheminformatics and bioinformatics techniques.

CINF 40

Application of novel data mining techniques to improve chemical array design decisions during lead optimisation

G. Papadatos[1], g.papadatos@shef.ac.uk, M. Alkarouri[1], V. Gillet[1], P. Willett[1], V. Kadirkamanathan[2], C. Luscombe[3], G. Bravi[3], N. Richmond[3], S. Pickett[3], J. Pritchard[3], A. Cooper[3], and S. Macdonald[3]. [1]Department of Information Studies, University of Sheffield, Sheffield, United Kingdom, [2]Department of Automatic Control and Systems Engineering, University of Sheffield, Sheffield, United Kingdom, [3]GlaxoSmithKline Medicines Research Centre, Stevenage, United Kingdom

Matched molecular pair analysis (MMPA) studies the effect of specific structural modifications on properties of interest. In modern drug discovery this analytical tool becomes very important, especially during the lead optimisation phase, when medicinal chemists synthesise and test iteratively hundreds of compounds in chemical arrays. In this study, we have developed novel data mining algorithms to assess the extent to which MMPA is valid and informative. To this end, a set of both established and bespoke 2D and 3D descriptors and multiple assay data from several GlaxoSmithKline lead optimisation projects have been used. We have investigated a number of important drug properties such as hERG inhibition, solubility, lipophilicity as well as biological activity. The outcomes are useful as part of a decision support system which enables the medicinal chemists to mine relevant information and to explore systematically the chemical space in the vicinity of the seed structure in each round of chemical array design.

CINF 41

Biological and chemical network construction from linked open data

D. Jiao, djiao@indiana.edu. School of Informatics, Indiana University at Bloomington, Bloomington, IN, United States

Linked open data (LOD) is a joint effort in the Semantic Web community to provide linkages among open data. LOD data sets in the life science domain, such as Bio2RDF and Linked Open Drug Data (LODD), provide a great resource for systematic study of life science. However, the sheer size and heterogeneity of the LOD data sets is daunting, suggesting that studies based on these data sets could benefit substantially from methods that facilitate the retrieval of targeted information. In this poster, we propose a workflow-based method for constructing

biological and chemical networks from the underlying RDF graphs of Linked Open Data, using semantic web technologies and scientific workflow tools. It uses implicit SPARQL queries and generic rule-based reasoning for retrieval and construction of the networks. Using this method, biological and chemical networks, such as protein-proteininteraction networks, drug-target networks, or metabolic networks, could be retrieved from Bio2RDF or LODD.

CINF 42

Novel approach to drug discovery integrating chemogenomics and QSAR modeling: Applications to anti-Alzheimer's agents

R. Hajjo[1], hajjo@email.unc.edu, S. Wang[1], B. L. Roth[2], and A. Tropsha[1]. [1]Department of Medicinal Chemistry and Natural Products, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States, [2]Department of Pharmacology, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States

Chemogenomics is an emerging interdisciplinary field relating the receptorome-wide biological screening to functional or clinical effects of chemicals. We have developed a novel chemogenomics approach combining QSAR modeling, virtual screening (VS), and gene expression profiling for drug discovery. Gene signatures for the Alzheimer's disease (AD) were used to query the Connectivity Map (cmap,http://www.broad.mit.edu/cmap/) to identify potential anti-AD agents. Concurrently, QSAR models were developed for the serotonin, dopamine, muscarinic and sigma receptor families implicated in the AD. The models were used for VS of the World Drug Index database to identify putative ligands. 12 common hits from QSAR/VS and cmap studies were subjected to parallel binding assays against a panel of GPCRs. All compounds were found to bind to at least one receptor with binding affinities between 1.7 - 9000 nM. Thus, our approach afforded novel experimentally confirmed GPCR ligands that may be implied as putative treatments for the AD.

CINF 43

Use of QSAR models to validate the HTS assay data in PubChem: Application to the serotonin receptor 5-HT1A ligands

M. Luo, mluo@email.unc.edu, S. X. Wang, xswang@email.unc.edu, A. Golbraikh, golbraik@email.unc.edu, and A. Tropsha, alex_tropsha@unc.edu. Department of Medicinal Chemistry, University of North Carolina, Chapel Hill, Chapel Hill, NC, United States

PubChem is an open-access data repository system, acting as the portal site for NIH Molecular Libraries and Imaging initiative. To help evaluate the quality of some biological activities deposited in PubChem, we conducted *in silico* modeling studies on 5-Hydroxytryptamine Receptor Subtype 1A (5-HT1A) ligands (PubChem AID:613, 718, 755). The dataset of 105 binders/61 non-binders were retrieved from the NIMH Psychoactive Drug Screening Program Ki database, and three methods, *k*-Nearest Neighbor, Random Forest and Support Vector Machines, were employed for model building using Dragon descriptors. Models were further validated by predicting 69 additional 5-HT1A ligands from the WOMBAT database with Correct Classification Rate of 0.94. However, 25 out of the 46 agonists/antagonists in PubChem bioassays were predicted to be non-binders with high confidence, suggesting that they may be false positives. We propose that rigorously developed QSAR models could be used to identify both false positives and false negatives reported in PubChem.

CINF 44

Speeding up chemical database searches

R. J. Nasr, rnasr@ics.uci.edu, and P. Baldi, pfbaldi@ics.uci.edu. Department of Computer Science, University of California, Irvine, Irvine, CA, United States

In many large chemoinformatics database systems, molecules are represented by long binary fingerprint vectors whose components record the presence or absence of particular functional groups or combinatorial features. To speedup database searches, we develop and validate two new approaches. In the first approach, we compute for each fingerprint a corresponding small count vector containing the sums of hashed subsets of components. From these count vectors, we derive tight bounds on fingerprint similarity measures, such as the Tanimoto measure. During a database search, every time these bounds are unfavorable, the corresponding molecule can be discarded with no need for further inspection. The second approach adapts techniques from text search based on inverted indices to chemical fingerprints. For both approaches we construct probabilistic models that allow us to estimate the level of pruning under different conditions. These theoretical results are corroborated by experimental results obtained on a large set of molecules.

CINF 45

OrbDB: A database of molecular orbital interactions

M. A. Kayala, mkayala@ics.uci.edu, C. A. Azencott, J. H. Chen, and P. F. Baldi. Department of Computer Science, University of California - Irvine, Irvine, CA, United States

The ability to anticipate the course of a reaction is essential to the practice of chemistry. This aptitude relies on the understanding of elementary mechanistic steps, which can be described as the interaction of filled and unfilled molecular orbitals. Here, we create a database of mechanistic steps from previous work on a rule-based expert system (ReactionExplorer). We derive 21,000 priority ordered favorable elementary steps for 7800 distinct reactants or intermediates. All other filled to unfilled molecular orbital interactions yield 106 million unfavorable elementary steps. To predict the course of reactions, one must

recover the relative priority of these elementary steps. Initial cross-validated results for a neural network on several stratified samples indicate we are able to retrieve this ordering with a precision of 98.9%. The quality of our database makes it an invaluable resource for the prediction of elementary reactions, and therefore of full chemical processes.

CINF 46

PropOrb: A frontier molecular orbital interaction proposer

C.-A. Azencott, cazencot@ics.uci.edu, M. A. Kayala, mkayala@ics.uci.edu, and P. Baldi, pfbaldi@ics.uci.edu. Department of Information and Computer Science, UC Irvine, Irvine, CA, United States

Chemoinformatics methods to assist chemists in the essential problem of reaction prediction are highly desirable. Brute force examination of all potentially interacting molecular orbitals (MOs) is computationally intractable. For example, concurrent work to develop a database of MO interactions yields more than 100 million interactions for a few thousand systems. Inspired by human chemists, we leverage the principles of frontier orbital theory to propose a tool that rapidly identifies the most reactive molecular orbitals in a given system. Due to the simplicity of our approach, we aim to identify only a few top candidates. Further resource intensive refinement, such as quantum mechanical or statistical approaches, might then be necessary to differentiate between the proposer’s suggestions. However, our approach significantly reduces the number of possibilities for downstream analysis. The speed, simplicity, and efficacy of our MO interaction proposer make it an essential component of a reaction prediction system.

CINF 47

Dataviz explosion: Considering effectiveness in classrooms and across disciplines

E. Dorland, dorland@wustl.edu. PARC Communications, Washington University, St Louis, MO, United States

Data visualization is exploding. Newspapers and businesses use complex visualizations in stories and reports. Visualizations are valued for their beauty as well as clarity, and the best “go viral” in Facebook, Twitter, and the blogosphere. The popular website “Visual Complexity” has hundreds of examples. But how effective are visualizations? What types are best in which situations? How do we know? The interdisciplinary community of the Gordon Research Conference on Visualization in Science and Education focuses on how students learn from visualizations. When is 3D or video best? When is a simple diagram better than a more complex one? Is 3D always better than 2D? I will discuss findings from collaborative research among scientists, mathematicians, engineers, cognitive psychologists, graphic designers, web and video developers, and the learning

sciences. Examples will come from undergraduate science topics and will include the presentation and display of data in 3D Virtual Worlds.

CINF 48

ASAP: Emphasizing multidimensional drug discovery

W. P. Walters, pat_walters@vrtx.com, Y. Bennani, and T. Kramer. Vertex Pharmaceuticals, Cambridge, MA, United States

One of the biggest challenges facing drug discovery teams is extracting information from the large volume of data generated in the course of a lead optimization effort, and using this information to make decisions. A typical lead optimization project can track between 15 and 30 assays (enzyme, cell, properties, PK, etc), and identifying trends in this data can be difficult. In an effort to address this problem and help scientists to make better decisions, we have developed a new software platform called ASAP. ASAP provides an intuitive overview of the data that also allows scientists to easily “drill down” and examine the details of particular experiments. A combination of “filters” and heat maps allows teams to focus on aspects of the data while remaining aware of the “big picture”.

CINF 49

Visual analyses for guiding compound selection and design

E. Champness, ed.champness@optibrium.com. Optibrium Ltd, Cambridge, United Kingdom

Decision-making in drug discovery is challenging due to the need to simultaneously optimise multiple, often conflicting properties for which the available data have varying degrees of confidence. In this presentation we will present a workflow, supported by appropriate visualisations, to guide decisions on selection and design of compounds in the context of a drug discovery project. This includes approaches to explicitly consider the ability to confidently distinguish between molecules, visualise the trade off between quality and diversity and interpret the relationship between structure and properties for individual molecules. We will demonstrate the integration of these into a dynamic interface that can be intuitively used by discovery scientists of all disciplines. This can significantly reduce the time to factor all information into the decision-making process as a drug discovery project progresses and the volume of data increases.

CINF 50

Contextual visualization of biological and chemical networks using linked open life science data

D. Jiao[1], djiao@indiana.edu, Y. Ding[2], dingying@indiana.edu, and D. J. Wild[1], djwild@indiana.edu. [1]School of Informatics, Indiana University, Bloomington, IN, United States, [2]School of Library and Information Science, Indiana University, Bloomington, IN, United States

Semantic web technologies, such as ontologies and RDF (Resource Description Framework), have played important roles in life science data representation, interchange, and integration. Recently several groups have built RDF networks to integrate open data in life science. The results, which are part of the open linked data, provide great resources for research in life science. For example, Bio2RDF and LODD (Linked Open Drug Data) could be used in the area of systems chemical biology, since they contain structured information in almost every aspect that systems chemical biology requires. However, the sheer size and heterogeneity of the open linked data is daunting, suggesting that studies based on these data could benefit substantially from targeted technologies of visualization and information retrieval. In this talk we will discuss a visualization tool to facilitate the systematic study of chemistry and biology based on open linked data such as Bio2RDF or LODD. This tool aims at the capability of implicit retrieval of biological/chemical networks from Bio2RDF and LODD and integrated nonlinear and contextual visualization of these networks. For example, using this tool, researchers would be able to extract and visualize networks such as drug-target interaction networks, or metabolic networks in the context of Bio2RDF or LODD, which means that they could obtain detailed information, such as biological pathways that contains certain targets or properties of a drug, while viewing and analyzing the networks. This tool is built using Jena, a semantic web framework, and integrated to Cytoscape, a widely used system biology network visualization and analysis software. The many types of view of information are achieved by assembling various semantic lenses, which are tools for context-specific display of data.

CINF 51

iTunes™ for chemistry and biology: Addressing usability in cheminformatics

D.-T. Nguyen, Y. Wang, R. Guha, **N. Southall**, southalln@mail.nih.gov, R. Huang, and **A. Jadhav**, ajadhav@mail.nih.gov. NIH Chemical Genomics Center, National Institutes of Health, Bethesda, MD, United States

Giving scientists access to data through a well-established framework can empower naïve users to perform very complicated tasks. The analysis and interpretation of large datasets from high throughput screening (HTS) is one such task. It involves differentiating bioactives from assay artifacts, rapid identification of chemical series, interpretation of structure-activity-relationships, and the assessment of activity profiles of series in context of related biological assays. The proliferation of available chemical and biological databases in the public domain makes the task even more complicated. Such analysis is often performed in ad-hoc manner using various combinations of commercial and in-house tools.

We have been developing an open-source system that integrates over 70 public databases and makes them available in a user-friendly way, which enables rapid analysis and visualization of chemical libraries and HTS data. In this talk, we highlight some key features of the current platform: data visualization, fragment-based automated analysis, mining of activity databases such as PubChem and StARLite, and the integration of compounds, fragments, genes, targets, pathways, and diseases with minimal user effort.

CINF 52

Interaction Maps: Understanding compound pathway space

Y. Tanrikulu[1], yusuf.tanrikulu@roche.com, M. Weisel[1], R. Kondru[2], and H. M. Bitter[1]. [1]In Silico Sciences, Hoffmann-LaRoche, Nutley, New Jersey, United States, [2]Discovery Chemistry, Hoffmann-LaRoche, Nutley, New Jersey, United States

Traditional efforts in bio- and cheminformatics have utilized sequence identity and structural homology as a way to relate proteins to gain a better understanding of biological pathways and processes. Here, we unveil for the first time an internally developed data representation which allows for linking targets through chemical space, that is by their ligands. Initial efforts have been conducted in academia and thus have been limited by the relatively sparse data available in the public domain. In-depth analysis of our in-house data enabled us to generate mappings of compounds to targets, which may reveal molecules which are being profiled for one target but show greater potency for another. Therefore, our method may provide a fresh perspective on mechanisms of action, potential repurposing of drugs as well as identification of off-target events and novel insights of well-known diseases by integrating chemical and biological space or “ligand-target profiles”.

CINF 53

PubChem: A public cheminformatics system for bioactivity analysis

Y. Wang, ywang@ncbi.nlm.nih.gov. NIH, NCBI/NLM, Bethesda, MD, United States

PubChem (http://pubchem.ncbi.nlm.nih.gov) is a public repository for chemical structures and biological test results hosted by the U.S. National Institutes of Health(NIH). It was created as part of the research program under the NIH Molecular Libraries Program (MLP). PubChem’s contents are currently derived from the voluntary contributions of over 90 commercial, academic and government organizations, with the majority of biological test results contributed by the MLP funded laboratories. PubChem currently contains 61 million chemical substance records, representing more than 25 million unique chemical structures. The PubChem BioAssay component contains 1700 bioassay depositions with more than 50 million bioactivity outcomes involving over 3000

molecular targets. The goal of the PubChem BioAssay system is to optimize the utility of such rich information, and to provide services to make the biological activity data of this large scale collection easily accessible to the public. PubChem can be accessed and searched through the NCBI Entrez information retrieval system. Furthermore, PubChem provides an integrated cheminformatics system to facilitate the utilization of the information. Web-based summary services are provided allowing one to review the deposited substance and bioassay record in detail. A suite of exploratory bioactivity analysis tools are developed to integrate the chemical and biological activity information, and to support the navigation and in-depth data analysis that facilitates identification of chemical probes and biological targets contained within PubChem.

CINF 54

High throughput synthesis and screening system for discovery of improved materials for rechargeable batteries

B. Li, F. Matsumoto, B. Howard, R. Olugbile, D. Greenburg, C. Riley, C. O’Neill, M. S. Bailey, and **S. S. Kaye**, skaye@wildcatdiscovery.com. Wildcat Discovery Technologies, San Diego, CA, United States

Substantial improvement in the energy density of batteries is required to meet the future needs for vehicle electrification, energy storage, consumer electronics, and medical devices. Recent trends highlight the importance of simultaneous optimization of many components, including active material microstructure, electrolyte, binder, conductive diluents and porosity. Historically, these were optimized independently and often years apart in separate laboratories. Wildcat Discovery Technologies has developed a platform for high throughput discovery of battery materials that enables evaluation of thousands of cells per week. Wildcat’s system produces materials in bulk form, enabling high throughput formulation of the electrochemically active material into an electrode and evaluation of its properties in a complete cell. This allows parallel optimization of all aspects of the cell, including active materials, binders, separator, electrolyte and additives. Here, I will discuss the development and validation of Wildcat’s high throughput discovery platform and our initial results from our first discovery libraries.

CINF 55

The Clean Energy Project: Finding new renewable energy materials, one screensaver at a time

A. Aspuru-Guzik, aspuru@chemistry.harvard.edu. Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA, United States

In collaboration with IBM’s World Community Grid, my reserach group and I have embarked on “The Clean Energy Project”, an endeavour to scan the electronic properties of tens of thousands of molecular candidates for organic photovoltaic

materials using computer time from voluntary donors around the world. The users download a distributed computing client that performs calculations to aid in the development of a database of compounds. The project encompasses the combinatorial generation of candidates, the distributed molecular dynamics and electronic structure calculations, and a user-friendly property database. New candidates for high hole and electron mobilities, good light-absorption properties and photoresistance are sought. In this talk, I will provide an overview of the project and discuss our preliminary results.

CINF 56

Compound discovery and design via materials informatics: An “omics” approach to materials science

K. Rajan, krajan@iastate.edu. Department of Materials Science and Engineering, Iowa State University, Ames, IA, United States

One of the fundamental questions in materials crystal chemistry is why do atoms arrange themselves in the way they do? Historically, there have been two primary approaches for addressing this challenge. One is to search, organize and classify homologous compounds from known data. Another approach has been to take advantage of advances in first principles computational modeling and high performance computing methods to explore large numbers of combinations of atomic configurations to search and identify potentially new structures. In this presentation, we describe a new alternative strategy, based on statistical learning. It systematically integrates diverse attributes of chemical and electronic structure descriptors of atoms with descriptors associated with crystal structure of compounds to capture complexity in crystal geometry and bonding. Using informatics, we have been able to discover new compounds with targeted functionalities, the chemical design rules governing the stability of these compounds as well new structure-property relationships.

CINF 57

Organic electronic materials by design: Finding a needle through the haystack

G. R. Hutchison[1], geoffh@pitt.edu, and N. O’Boyle[2]. [1]Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, United States, [2]Analytical & Biological Chemistry Research Facility, University College Cork, Ireland

Organic electronic materials show promise for exciting applications ranging from energy-efficient displays to inexpensive, flexible solar cells. We discuss how to use cheminformatics techniques to efficiently search molecular structures in silico, including developing significant diversity sets, finding efficient, accurate screening methods for electronic structure and charge transport, and using genetic algorithms to find novel photovoltaics.

CINF 58

Searching chemical space by inverse design

B. C. Rinderspacher, berend.rinderspacher@arl.army.mil, J. Andzelm, A. Rawlett, J. Dougherty, and R. Lambeth. Army Research Laboratory, Aberdeen Proving Ground, Maryland, United States

Finding optimal architectures of functional molecules that contain numerous substituents in various conformations is a daunting task. The number of accessible compounds with molecular weight below 850 a.m.u. (a typical size, e.g., of electro-optical chromophores) is staggering at about 10^{200}. More than 20 years of research have established many rules for the optimal design of chromophores, effectively reducing the design space. Nevertheless, surprising new architectures of chromophores are appearing at increased rates with computational chemistry playing an important partnership role in these discoveries. Efficient exploration of enormous molecular spaces requires new optimization schemes that search directly for the property optimum, and in the process discover new molecular architectures. Often the objective is subject to multiple constraints, further complicating the search. We introduce a general optimization algorithm based on an interpolation of property values on a hypercube. The resultant algorithm is related to branch and bound/tree search methods. To demonstrate the broad applicability, we have applied the framework to optimizing electro-optic chromophores under spectral constraints as well as to optimizing organo-metallic clusters for tensile strength.

CINF 59

High-throughout quantum chemistry and virtual screening for materials solutions

M. D. Halls, mhalls@mhalls.com. Materials Science Division, Accelrys, Inc., San Diego, CA, United States

The use of virtual structure libraries for computational screening to identify lead systems for further investigation has become a standard approach in drug discovery. Transferring this paradigm to challenges in material science is a recent possibility due to advances in the speed of computational resources and the efficiency and stability of materials modeling packages. This makes it possible for individual calculation steps to be executed in sequence comprising a high-throughput quantum chemistry workflow, in which material systems of varying structure and composition are analyzed in an automated fashion with the results collected in a growing data record. This record can then be sorted and mined to identify lead candidates and establish critical structure-property limits within a given chemical design space. To-date, only a small number of studies have been reported in which quantum chemical calculations are used in a high-throughput fashion to compute properties and screen for optimal materials solutions. However, with time high-throughput computational screening will

become central to advanced materials research. In this presentation, the use of high-throughput quantum chemistry to analyze and screen a materials structure library, representing a well defined chemical design space, is demonstrated for organic light-emitting diode (OLED) materials and Li-ion battery additives. The OLED case focuses on the chemical design space around the archetype electron-transport and emitting material tris(8-hydroxyquinoline) aluminum(III) (Alq3). The battery additive example explores the property space for derivatives of ethylene carbonate (EC).

CINF 60

Impacts of closing academic branch libraries

S. J. Redalje, curie@u.washington.edu. University of washington, United States

How do you complete a year-long celebration of your branch library’s 20 years in its current location? By closing it, of course. This is what happened to the University of Washington’s Chemistry Library. It, along with two other branches, were closed and merged with the main library at the end of the 2008-2009 school year. Nationally, greatly reduced budgets and the desire to take advantage of new technologies and approaches to better serve the users 24/7 are some of the factors driving the closures and mergers of academic branch libraries. What are the impacts on the students and faculty? What about the librarians whose lives have been turned upside down? These, and other factors will be discussed in the paper.

CINF 61

e-Books and e-references collection in academic libraries: A case study

N. Xiao, nxiao@usc.edu. Science and Engineering Library, University of Southern California, Los Angeles, CA, United States

The nature of publishing and communication in science and technology fields has changed dramatically, and more and more collection are moving on-line and/or digitized. How will librarians select users-need center e-collection to support institution’s education and research mission, especially under challenging economic environment? This presentation will attempt to answer this question. It will overview e-books and e-references collection change at USC Science and Engineering Library, which has space shortage issue and supports a very large S&E information users population, including more and more users from engineering distance education programs (http://mapp.usc.edu/distanceeducation/). Issues of pricing models, e-collection accessibility and flexibility, and benefits to users and the institution in short and long term will be discussed as well.

CINF 62

Future of the liaison in academic libraries

M. Lafferty, mlaffert@umn.edu. University Libraries, University of Minnesota, Minneapolis, Minnesota, United States

The role of the departmental library liaison in colleges and universities has been in flux over the last decade and continues to shift, largely as a result of changes in technology. Over the last couple of years, the University of Minnesota Libraries created a position description framework to capture and describe the new roles liaisons are taking on and clarify what is expected of them. Among other changes, the emphasis of our positions is moving more towards supporting the process of research and away from the end products. I will address where we are currently and where we, as well as liaisons in general, might be headed.

CINF 63

New workspaces: From library facility to online service

L. Solla, LRM1@cornell.edu. Physical Sciences Library, Cornell Unviersity, Ithaca, NY, United States

Local users of the former Physical Sciences Library at Cornell once had a one-stop place for library services: access to journals and books, librarians, computers and quiet & group study. Now the journals and books are online, the librarians and computers are roving and the quiet & group study options are changing with new building spaces. Although the physical facility closed in December 2009, the library's presence continues as a portal for scholarly resources, a virtual collection and service through research specialists. The Edna McConnell Clark Physical Sciences Virtual Library provides 24/7 electronic access to scholarly literature and information sources in astronomy, chemistry, and physics for the Cornell community. Print materials in these subject areas are available at a number of Cornell library facilities and subject librarians are on-site in the physical sciences building cluster to provide research services and support for faculty, staff and students. 9 months of strategic planning by several teams of faculty and students in the physical sciences working with library staff went into gathering input and mapping out the transition process from a facility to an online service model. At press time, anticipated results include enhanced online access to journal backfiles, books, reference databases, online browsing, document delivery, and workflow services delivered from a new local taxonomy based website. This presentation will address the status of these results, the effectiveness for the users and continuing future strategies.

CINF 64

PLoS ONE: A new model for online journal publishing

P. Binfield, pbinfield@plos.org. Public Library of Science, San Francisco, CA, United States

PLoS ONE (www.plosone.org) is an innovative, online-only, Open Access, peer-reviewed journal from the Public Library of Science (www.plos.org). Since launch in December 2006 *PLoS ONE* has grown to be the third largest journal in the world (having published 4,600 articles in 2009) and was the recipient of the 2009 ALPSP Award for Publishing Innovation. This presentation will detail the innovative editorial criteria of the journal (which do not make any subjective judgments about the potential ‘importance’ of any submission); PLoS’s development of post-publication evaluation tools at the article-level (so called ‘article-level metrics, which record citations, online usage, comments, ratings, social bookmark data and so on, on each article); some of the more interesting functionality in the journal; and the use of ‘web 2.0’ social media tools to effectively promote the journal in a cost effective manner.

The presentation will be made by the Publisher of *PLoS ONE*.

CINF 65

Impact of emerging economies on publishing

J. Bhate, jignesh@molecularconnections.com. Corporate & Development Centre, Molecular Connections Private Limited, Basavanagudi, Bangalore, India

Over the next few years, developing economies such as China and India, are expected to continue their dramatic growth. These developments are influencing global companies to realign their businesses and operational planning in order to establish increased presence in these developing markets. This trend is already visible among leading publishers. This talk highlights economic performance indicators as well as other significant market drivers such as the availability of a highly skilled and educated workforce capable of fulfilling a variety of professional jobs, including information and publishing roles. Predictions for the future shape of the primary and secondary publishing industry in the next five to ten years will be made.

CINF 66

Ensuring sustainability of scientific data resources: Technologies and business models for the future

C. R. Groom, edir@ccdc.cam.ac.uk. Cambridge Crystallographic Data Centre, United Kingdom

The Cambridge Crystallographic Data Centre provides the Cambridge Structural Database to scientists in well over 1000 institution, spread over 69 countries. To do this we must balance a number of conflicting requirements; the need for complex processing and curation contrasts with the need to handle large volumes of data. Let’s see how ‘technology’ will help the CCDC. We must also deliver knowledge and data in a way that appeals to users – we can learn a great

deal from other communities. We are changing our organisation to exploit technological advances, but must also respond to the continued challenge to established publishing business models. We are adapting to our new environment, but can also shape this environment ourselves. This presentation will discuss whether the technology we use and business model we have serve us for today. Most importantly we'll look to the years ahead – what must we change?

CINF 67

Vision and strategy for the future of RSC Publishing

R. J. Parker, parkerr@rsc.org, and J. Milne. Royal Society of Chemistry, Cambridge, United Kingdom

RSC Publishing is currently a large small publisher: large compared with many scientific society publishers, but small compared with most commercial publishers. What might the future hold for such an animal, especially during and after a global economic downturn combined with a period of unprecedented disruptive change? How will it evolve and adapt to take advantage of the challenges and opportunities that it faces?

CINF 68

Challenges facing the STM industry

M. O'Malley, m.omalley@elsevier.com. Corporate Markets, Elsevier, Inc., New York, NY, United States

The broad trends of technological advance, globalisation, and information proliferation present threats and opportunities for the STM customer base and the STM industry. In this presentation we discuss the evolution of the STM publishing industry, against the backdrop of historical and near-term change. We conclude that to meet the challenges of a continually evolving market, both large and small players need to transition their role from traditional publishers to information solution providers. This transformation requires a close collaboration with customers, a willingness to partner openly with technology providers and competitors, and new transparent approaches to solution development and deployment.

CINF 69

Vision and strategy for scholarly communication at the ACS

S. King, s_king@acs.org. American Chemical Society, Washington, DC, United States

ACS is uniquely positioned to serve the interdisciplinary communications needs of research professionals as well as foster the education and practice of chemistry and allied sciences. The Society's mission-driven support of scholarly communication encompasses the application of innovative publishing technologies that serve the needs of authors and readers of ACS peer-reviewed journals in traditional and evolving areas and that are among the most highly cited publications in the world; the scientific reporting excellence contained in C&EN, the leading weekly news magazine for the chemical industry; the comprehensive indexing by CAS of the global research and patent literature across chemistry and allied fields; and the overall coordination of the world's largest scientific society, including local chapters and technical divisions and the programming for two national meetings per year. Building on integrated content linking achieved among CAS *SciFinder*® resources and the Web Editions of ACS Journals, as well as the social networking features of the ACS Network, the ACS has just begun to tap the power of Web 2.0 and evolving information technologies to further foster scholarly communication. ACS welcomes its members, authors, readers, customers, and the global scientific community to join with us as we move beyond traditional boundaries, while preserving the quality and integrity of scholarly communication.

CINF 70

Network visualization of structure activity landscapes

R. Guha, guhar@mail.nih.gov. NIH Chemical Genomics Center, Rockville, MD, United States

Lead optimization is an integral part of the drug discovery process. During this stage synthetic programs will generate a number of compounds, generally based on a few chemotypes. A key feature of such programs is identifying small structural changes that lead to significant changes in measured activity - so called 'activity cliffs'. Such cliffs represent interesting regions of the SAR landscape and can be suggestive of specific receptor binding features, as well as suggest new directions for synthesis. In this paper we present a visualization of SAR landscapes, which allows users to highlight activity cliffs. The approach is based on a network representation of a molecular dataset (structures and activities), and employs the Structure Activity Landscape Index (SALI). This metric allows one to quantitate the degree to which a pair of ocmpounds represent an activity cliff. By using the SALI value as a cutoff one can generate multiple network representations that highlight activity cliffs of varying degree. We will show that the structure of the network allows one to explore synthetic programs to identify modifications that lead to improvements in activity. While useful as a retrospective visual summary of a synthetic program we will also highlight the use of this approach in quantitatively charactering the quality of QSAR models that attempt to encode a SAR landscape. This methodology has been implemented in a Java-based tool, which is freely available, allowing users to generate SALI networks with their own data.

CINF 71

Visualization and analysis of bioisosteric analogs generated with BROOD

J. J. Corkery[1], jcorkery@eyesopen.com, A. G. Skillman[2], K. E. Schmidt[1], and B. Kelley[1]. [1]OpenEye Scientific Software, Cambridge, MA, United States, [2]OpenEye Scientific Software, Santa Fe, NM, United States

BROOD is a program developed by OpenEye Scientific Software to generate bioisosteres based on shape and electrostatic similarity. A single BROOD run may generate 1000s of potential ideas for a specified query. Not surprisingly, visualization and analysis of this data can be particularly challenging. To solve this problem, a custom Python extension to facilitate BROOD visualization was developed for VIDA (OpenEye's visualization and data analysis platform). This extension enables the ideas to be easily organized into "Idea Groups" which can quickly and easily be viewed in 2D, 3D, or both simultaneously. In addition, all of the non-structural data generated by BROOD (e.g. synthetic accessibility, similarity to query, etc) can be viewed side-by-side with the structures or in the embedded chemically-aware spreadsheet which can be used to further filter/organize the results. The techniques utilized in this talk can easily be extrapolated to facilitate visualization and analysis of a large variety of other result types including but not limited to clustering output and a wide variety of virtual screening results.

CINF 72

Visualizing polypharmacology in chemical libraries

D. Marcus, david.marcus1@mail.huji.ac.il, D. Barasch, A. Rayan, and A. Goldblum. Institute of Drug Research, The Hebrew University of Jerusalem, Jerusalem, Israel

Modern drug discovery increasingly focuses on drugs that should interact with multiple targets to elicit the desired pharmacological response. Visualizing several SAR models at once may be helpful for easier interpretation when comparing different chemical libraries or for picking new actives. A colored matrix is commonly used to visualize each compound's predictions, however this visualization is highly complex when analyzing large libraries. We developed a ranking method to prioritize compounds by both their activity and their reliability using a single index value. We display these indexes by tag clouds that show each target as a tag and vary by size, color and position, which clarifies better the polypharmacology contents of each library. Visually comparing clouds from different libraries makes comparisons easier to evaluate. We also demonstrate how we use this visualization with huge libraries such as ZINC, to pick molecules that have the desired polypharmacology nature in several cases.

CINF 73

Linear scaling mapping of chemical space

J. S. Delaney, john.delaney@syngenta.com. Chemistry, Syngenta, Bracknell, Berkshire, United Kingdom

A novel method for producing 2D maps of chemical space is presented. Each compound is represented by standard binary substructural fingerprint (Daylight or SciTegic) which is used to produce an integer number in a defined range. This is used to define a 2D coordinate for each compound by mapping the number onto a Hilbert space-filling curve. The key advantages of the method are that it scales linearly with the number of compounds to be mapped (allowing large datasets to be processed) and it produces an absolute coordinate in a well-defined range for each compound, allowing maps of different compound sets to be compared on a like-for-like basis. Examples of the method applied to large compound sets (300k+) and comparisons between maps of sets with different properties (structural and biological activity) will be presented.

CINF 74

Integrated visualization for the interpretation of QSPR and QSAR models

G. D. Purvis[1], gpurvis@us.fujitsu.com, W. D. Laidig[2], and D. T. Stanton[2]. [1]Biosciences Group, Fujitsu America Inc, Beaverton, Oregon, United States, [2]Modeling & Simulation, Miami Valley Innovation Center, The Procter & Gamble Company, Cincinnati, OH, United States

Molecular structure visualization integrated with conventional 2D plots of quantitative structure property relationships (QSPR) and quantative structure activity relationships (QSAR) is shown to speed the analyis and interpertation of QSPR/QSAR models. Identification of outliers is simplified and relationships of specific molecular descriptors to molecular structure are more easily comprehended. Integrated visualization is demonstrated for least squares models, partial least squares (PLS) models and robust regression modeling.

CINF 75

VTK: The visualization toolkit and its applications to the analysis of chemical data

M. D. Hanwell, marcus.hanwell@kitware.com. Department of Scientific Visualization, Kitware, Inc., Clifton Park, NY, United States

The visualization toolkit (VTK) is an open source, cross platform, freely available software library providing a framework for visualization ranging from 3D computer graphics, image processing and data filtering to information visualization and standard 2D plotting. It is written in C++, tested daily on Linux, Mac and Windows, and has bindings for Python, Tcl and Java. VTK has been used in chemical visualization applications such as Molekel (C++) and the CCP1 GUI

(Python). Related applications such as ParaView use VTK to process and visualize very large data sets. Many of the same algorithms and techniques can be used by chemists to create new visual representations of large data sets. This presentation gives an overview of the functionality available in VTK, and ways in which it can be leveraged to rapidly analyze and visualize chemical data.

CINF 76

Molecular similarity characterization of ADME landscapes

R. R. Gupta[1], rishi.gupta@pfizer.com, **B. Chen**[2], binchen@indiana.edu, and E. M. Gifford[1]. [1]Computational Sciences Center of Emphasis, Pfizer Global Research and Development, Groton, CT, United States, [2]School of Informatics and Computing, Indiana University, Bloomington, IN, United States

Activity landscape characterization has been demonstrated to be a valuable tool in screening and lead optimization. In this work, we applied various molecular similarity methods to characterize chemical landscapes for 9 ADME (Absorption, Distribution, Metabolism, and Excretion) endpoints. Our results show that landscapes behave differently among endpoints and the observation can be quantified to prioritize compounds while transforming compound from HIGH risk class to LOW risk class.

CINF 77

Chemical information usage patterns under the microscope: The prospects of GIS-based visualization for libraries

M. P. Brändle, braendle@chem.ethz.ch. Informationszentrum Chemie Biologie Pharmazie, ETH Zürich, Zürich, Switzerland

The utility of geographical information systems (GIS) as decision support tools that provide analysis of geocoded demographic data on maps had been recognized in particular by public libraries in the UK and US. However, GIS can also be used for in-house analysis on library floor plans, as J. Xia had shown in preliminary work (e.g. J. Xia, Library Hi Tech 22(2), 209(2004)). The topic has recently received broad attention since we published interactive visualizations of usage and holding patterns on the Web (www.infochembio.ethz.ch/en/holdings.html). In this presentation, technical and organizational prerequisites for library space-based visualization of library data, its benefits for collection management and user guidance, and novel descriptors for library collection analysis will be discussed.

CINF 78

Scholarly communication in the 21st Century: Changing paradigms of communication and access

R. Schwarzwalder, rns@stanford.edu. Cecil H. Green Library, Stanford University, Stanford, CA, United States

The world of scholarly communication is experiencing a growing identity crisis. While the structure of academic publishing and its role in establishing intellectual property and academic credentials continues to be traditionally defined, the nature of information access and usage is being revolutionized by technical, business and social forces. This presentation will present an overview on the factors that have preserved the traditional model of academic publication and the changing environment that threatens the continued viability of that approach. Ideas will be discussed as to how traditional publishers could respond to the changing nature of scholarship without abandoning their core mission and focus.

CINF 79

oreChem project: Semantic infrastructure and applications for chemistry scholarship

C. Lagoze, clagoze@gmail.com. Information Science Program, Cornell University, Ithaca, NY, United States

The oreChem Project is an international collaboration between chemists and information/computer scientists to design, prototype, and deploy a semantics-aware information infrastructure for chemistry scholarship and applications to demonstrate the utility of that infrastructure. A major component of this work is the development of ontologies to represent in machine-readable form information about scholarly publications, molecular compounds, experiments, and reactions. These ontologies provide the foundation for the representation of information retrospectively extracted from legacy publications and information proactively accumulated in electronic laboratories notebooks and from instruments. A subsequent phase of this work will leverage this data as the basis for innovative applications for searching, browsing, and mining chemical information.

CINF 80

Chemistry: Computation, synthesis and communication

J. M. Goodman, jmg11@cam.ac.uk. Department of Chemistry, University of Cambridge, Cambridge, United Kingdom

My research group has projects in both experimental and computational chemistry. What form of publishing would best help us to communicate our disparate results in a form that is accessible to all our readers without prejudicing the interests of our sponsors? We try to balance between reporting enough to be valuable without eroding the intellectual property we share with everyone involved in the project, using a variety of forms of scholarly publishing. I will explain how I would like to see scholarly publishing develop in the fields of computational and synthetic organic chemistry.

CINF 81

Primary data for chemistry

I. Sens[1], irina.sens@tib.uni-hannover.de, S. Haak[2], Susanne.Haak@thieme.de, J. Brase[1], Jan.Brase@tib-hannover.de, and **G. F. Herrmann**[2], Guido.Herrmann@thieme.de. [1]German National Library of Science and Technology (TIB), Hannover, Germany, [2]Georg Thieme Verlag KG, Stuttgart, Germany

Primary data is scientific data gathered from experimental measurements and predominately available in electronic formats. In the field of chemistry, such data is accumulated by a variety of analytical, spectroscopic or computer simulation methods. Analytical data, from various experiments, is the foundation of research work and scientific papers. Thus far, the vast amount of data lies scattered on the computers of scientists, who have produced the information. As no central repository exists, no accessible archival storage is possible at the moment. Scientific results are solely published in journals – but not the primary data from which those results originate. The German National Library of Science and Technology (TIB) and Thieme Publishers have addressed this problem in collaboration. In this talk we will present a system and a process to systematically make primary chemistry data accessible worldwide. Thieme and TIB have developed a uniform structure for publishing primary data. Through structuring and central data registration, a Germany-wide unique service of TIB, valuable knowledge will be harnessed. From now on, primary data will be registered and made available online via the Thieme eJournals website (www.thieme-connect.com/ejournals) using digital object recognition in the form of Digital Object Identifiers (DOI). The publication of primary data will be implemented into the existing system of publications as well as their citations. The data will be permanently saved and, by assigning them a DOI, made accessible and searchable, as well as citable and linkable. This enhancement to the chemistry publishing process will enable scientists to easily locate research articles, including accompanying data, and make more productive use of the scientific content. Peer review will benefit from access to the original primary data by potential improvements to the process and better validation of the presented research. Primary Data Sample (FREE access):

K. Jarowicki, C. Kilner, P. J. Kocienski*, Z. Komsta, J. E. Milne, A. Wojtasiewicz, V. Coombs Synthesis 2008, 2747-2763:

http://dx.doi.org/10.1055/s-2008-1067226

CINF 82

Papers to papers: The future of reading, storing, and producing chemical literature in an academic environment

J. N. Currano, currano@pobox.upenn.edu. Chemistry Library, University of Pennsylvania, Philadelphia, PA, United States

The proliferation of primary literature in chemistry has created a conundrum for the well-read, well-published chemist. Managing the flow of information from the outside world is challenging, but keeping the useful articles that one finds at one's fingertips is even more daunting. This paper reviews techniques currently used by academic chemists to assemble and manage their own electronic file cabinets, focusing on the needs and desires of the researchers, and closing with a suggested model system extrapolated from requests articulated by scientists during the course of library reference encounters.

CINF 83

Socialized medicine: Medical publishing in the era of the read-write web

K. R. Anderson, kanderson@nejm.org. New England Journal of Medicine, Waltham, MA, United States

Publishers have long been experts in distribution, formatting, packaging, and selling content for distribution. However, as Clay Shirky stated in 2009, "The Internet is the first media that has native capacity to support both groups and conversations at the same time." This digital publishing revolution is forcing publishers from a broadcast distribution paradigm into a conversation paradigm. For established brands, embracing this shift requires a retooling and rethinking, and a test of skills and goals. At the New England Journal of Medicine, the Publishing Division is undertaking an ambitious social media publishing project called CardioExchange, which combines semantically tagged content, editorial curation, community management, and social media tools to create a new value equation around an important and dynamic medical specialty. This presentation will provide an overview of the smaller community experiments that led to this more ambitious pilot, and will cover the rapid, agile development process used to build the pilot, considerations in community creation and definition, measurements and goals, staff roles and work definition changes, and marketing/engagement issues, as well as presenting results from the experiment thus far.

CINF 84

Scholarly communication between chemists and their uptake and use of Web 2.0 and other new technologies

W. G. Town, bill.town@kilmorie.com. Kilmorie Clarke Ltd, London, London, United Kingdom

Web 2.0 and other new technologies potentially can bring beneficial changes in the access to, use and re-use of journal and database content by chemists. However, it is widely believed that chemists are slow in adopting change

although so far there has been little factual evidence to support this This project set out to make a snapshot of scholarly communication practices of chemists by undertaking a series of individual interviews with key decision makers and then conducting an online survey to identify the specific requirements of chemistry researchers and teachers. The defined requirements were then matched to an up-to-date list (also developed as part of the project) of new and recent developments in methods of scholarly communication used by chemists. This presentation will give a summary of the research findings and present ideas for improving the situation. Comparison will be made with a parallel study of economists.

CINF 85

ChemSci3D: An integrated 2D and 3D desktop chemistry interface

T. J. O'Donnell, tjo@gnova.com. gNova, Inc., San Diego, CA, United States

There are many types of 2D and 3D models of chemical information. Some computer applications concentrate on the display of 3D structural information. Others excel at representation of 2D structures, tables and plots. I present here a new application that can display of a variety of 2D and 3D models in a single desktop interface. This is accomplished by integrating a general 3D graphics and animation system (GRAMPS) with tools to display 2D structures, tables of data, plots and other diagrams. Currently under development are techniques to allow interactions among these various graphical components. I will show examples of how this integrated chemistry interface can be used and discuss the underlying software architecture components. I will also show ways in which ChemSci3D can be used to integrate novel chemical models.

CINF 86

Real-time ray-tracing in molecular graphics

M. Keil, mkeil@chemcomp.com. Chemical Computing Group, Inc., Montreal, Quebec, Canada

In recent years a wide variety of new features were added to modern graphics cards. One major enhancement is the ability to directly program parts of the graphics pipeline with the new OpenGL Shading language. It is even possible to perform computations on the graphic processing unit (GPU). This talk will present how one can enhance molecular graphics by ray-tracing basic geometric objects like spheres and cylinders. Due to the highly parallel nature of modern GPUs this ray-tracing can be done in real-time and even outperform traditional triangle based drawing methods. Other molecular graphics improvements using modern graphics card features will be discussed as well.

CINF 87

Avogadro: Framework for chemical structure analysis and visualization

M. D. Hanwell, marcus.hanwell@kitware.com. Department of Scientific Visualization, Kitware, Inc., Clifton Park, NY, United States

Avogadro is an open source, cross platform visualization framework with a well defined C++ API, and Python bindings. It makes use of OpenBabel, and so it is possible to use the functionality of OpenBabel and PyBel within Avogadro's API. The library is plugin based, and can be extended at runtime by both compiled C++ plugins and Python extension scripts. This means that researchers can easily tailor Avogadro to their specialized area by writing a few small scripts and/or plugin classes. Details will be presented on creating custom applications that leverage the Avogadro library, and how to write plugins that can visualize structures using custom techniques without the need to deal with the low level APIs and boilerplate code usually necessary. Several examples of Avogadro's use in industry and research will be presented.

CINF 88

2D graphical depiction of zeolite voidspace topology

K. J. Theisen[1,2], kevin@tfam.us, B. Smit[1], and M. Haranczyk[2]. [1]Department of Chemistry, University of California: Berkeley, Berkeley, CA, United States, [2]Department of Computational Research, Lawrence Berkeley National Laboratory, Berkeley, CA, United States

Zeolite materials contain complex networks of nanopores and channels that can be exploited for industrial applications. Nearly 200 unique embeddings have been synthesized with millions predicted. Researchers perform lengthy simulations on these structures to identify optimal choices for tasks such as adsorbate separation and catalytic conversion. Researchers usually rely on 3D visualization to gain insight about structural features and choose embeddings to investigate, a task that is often hindered by the structure's sheer complexity, especially if an orthographic perspective view is used. We have developed an alternative method to depict the important features of these complex structures, facilitating their visual analysis. Our approach involves reducing these structures based on symmetry and perceived building blocks to a compressed two-dimensional graphical representation that allows for easy and efficient structure analysis and comparison.

CINF 89

Computational methods for 2D-visualization of molecular interaction patterns

K. Stierand[1], **M. Rarey**[1], rarey@zbh.uni-hamburg.de, and C. Lemmen[2]. [1]Center for Bioinformatics, University of Hamburg, Hamburg, Germany, [2]BioSolveIT GmbH, Sankt Augustin, Germany

Chemists are well trained in perceiving 2D molecular sketches. On the side of computer assistance, the automated generation of such sketches becomes very difficult when it comes to multi-molecular arrangements such as protein-ligand complexes in a drug design context. During the last few years we have developed PoseView,[1,2] a tool which displays molecular complexes incorporating a simple, easy-to-perceive arrangement of the ligand and the amino acids to which it forms interactions. Resulting in atomic resolution diagrams, PoseView operates on a fast tree re-arrangement algorithm to minimize crossing lines in the sketches. Due to a de-coupling of interaction perception and the drawing engine, PoseView can draw any interactions, such as hydrogen bonds, metal interactions, pi interactions and undirected hydrophobic contacts, determined by either distance-based rules or the FlexX interaction model. Owing to the small-molecule drawing engine 2Ddraw[3], molecules are drawn in a textbook-like manner following the IUPAC regulations. Besides the novel underlying interaction models, we will present new algorithmic approaches, assess usability issues and a large-scale validation study on the PDB.

Literature:
[1] K. Stierand, M. Rarey, ChemMedChem, **2007**, 2: 853. [2] K. Stierand, P. Maaß, M. Rarey, Bioinformatics **2006**, 22, 1710. [3] P.C. Fricker, M. Gastreich, M. Rarey, J. Chem. Inf. Comput. Sci. **2004**, 44(3): 1065.

CINF 90

Visualizing combinatorial molecular materials research using Avogadro

G. R. Hutchison, geoffh@pitt.edu, and M. D. Hanwell. Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, United States

The open source molecular visualization package Avogadro can be used interactively, or as a scripted viewer. We outline methods to explore combinatorial data sets for organic electronic materials using the Python scripting interface, particularly correlating multi-dimensional data on screen. We explore the use of color to focus on particular molecular structure motifs. In particular, the plugin interfaces in Avogadro allow users to easily change rendering style or color to reflect correlated data.

CINF 91

Visualizing chemistry in Second Life

A. S. I. D. Lang[1], alang@oru.edu, and **J.-C. Bradley**[2], bradlejc@drexel.edu. [1]Department of Computer Science and Mathematics, Oral Roberts University, Tulsa, OK, United States, [2]Department of Chemistry, Drexel University, Philadelphia, PA, United States

This talk will focus on the current level on chemistry research, education, and visualization possible within the multi-user virtual environment of Second Life. We will discuss how Second Life has been used as a platform for the interactive and collaborative visualization of data from molecules and proteins to spectra and experimental data. We then review how these visualizations can be scripted for immersive educational activities and real-life collaborative research. We also discuss the benefits of the social networking within Second Life for both chemists and chemistry students.

CINF 92

Next-generation visualization technologies: How close are we to the Science 2.0?

O. Isayev, olexandr.isayev@case.edu. Department of Chemistry, Case Western Reserve University, Cleveland, OH, United States

A set of technologies called Web 2.0 is transformed the Internet. Web sites such as YouTube, and Facebook, in addition to various blogs and wikis attract hundreds of millions of people. Yet this Web 2.0 transformation of science and chemical visualization in particular is just in process. How close we are to so called “Science 2.0”? Since its inception, the Internet has changed the ways scientists work, communicate, collaborate, and educate. Successful scientific collaboratories among researchers, engineering innovations through open-source software, and community-based participation in projects are all indicators of the transformative nature of collaboration. However, what is the influence on chemical visualization? What are the novel ways to display graphical information in the web? What are the possible workflows? With this presentation, I would like to overview some of the latest trends and rich internet applications that aim to bring us a step closer to the Science 2.0.

CINF 93

CAS and ACS publications: Together, providing new pathways to chemical research

J. Morgan[1], j_morgan@acs.org, and **M. Dennis**[2], mdennis@acs.org. [1]Publications Division, American Chemical Society, Washington, DC, United States, [2]Chemical Abstracts Service (CAS) Division, American Chemical Society, Columbus, OH, United States

ACS Publications’ newest delivery platform and CAS’ latest *SciFinder*® enhancements continue to help scientists locate quality chemical information with efficiency, while promoting electronic collaboration. This talk demonstrates these two technologies, and how when used in concert, aid in the process of scientific research and discovery. The presentation concludes with a discussion to garner feedback regarding concepts for future collaborative enhancements and its potential usefulness to scholarly communication and chemical research.

CINF 94

Adding structure to publishing chemistry

J. N. Wilde, j.wilde@nature.com. Nature Publishing Group, London, United Kingdom

The way chemical research is published is moving at an ever-increasing speed. From new systems of indexing chemical structures to new methods of searching for chemical information, development in this field is fast and furious. The challenge for both publishers and authors is to ensure that the research being published is understandable not only to chemists but also to computers. Machine readable research means that content can be linked into related articles, databases, protocols and products, as well as ensuring that the content can be internally (by journal, publisher, Institutional Archive etc...) indexed and searchable. Nature Publishing Group, over the past few years, have been developing new tools and systems to reduce the requirement for authors to submit ever increasing amounts of additional information, whilst also developing automated workflows to take author files (text and chemical structures) and link them into the information world beyond the paper.

CINF 95

Under the hood: A technical view on publishing chemistry in the future

R. Kidd, kiddr@rsc.org. Informatics Department, Royal Society of Chemistry, Cambridge, United Kingdom

The Royal Society of Chemistry’s developments and experiences in semantic publishing will be summarised, along with the platforms for delivering our published content with additional functionality. The development and application of open standards for linking publications and data with the end user offers new opportunities in the ecosystem of the chemical sciences, and several projects with relevance to scholarly communication will be discussed with their implications.

CINF 96

Interactive publishing of crystal structure data

B. McMahon, bm@iucr.org, and P. R. Strickland. International Union of Crystallography, Chester, United Kingdom

Crystal structure determinations published in IUCr journals include structural (geometry, atomic displacements) and experimental data (structure factors). Nowadays these are in the Crystallographic Information Framework (CIF) standard. CIF has become the vehicle for submission of short structure reports, allowing the development of software that improves consistency and integrity of the publication, and permits semi-automated assessment of data quality during peer review. New authoring tools increase the coupling between data and article. For macromolecules, an article can be built from a Protein Data Bank deposition, incorporating deposited data, prompting for additional data items, and providing wizards to retrieve and insert data from other online resources. Another toolkit allows authors with no prior experience to create interactive three-dimensional visualizations using Jmol. Expert Jmol scripts are also supported. The resultant figure is an integral part of the publication, allowing readers to manipulate the structural model independently or according to the author's preferred views.

CINF 97

Science video journal to increase efficiency and standardization in experimental research

M. Pritsker, moshe.pritsker@jove.com. JoVE, Somerville, MA, United States

Biological and medical sciences chronically suffer from the low reproducibility of experiments, as they are typically described in the Materials and Methods sections of scientific articles. This is due to the fact that the traditional text format cannot adequately describe complex experimental procedures, creating a critical problem for academic research and drug discovery. Journal of Visualized Experiments (JoVE) applies video online to create visualized publication of experimental studies. Visualization greatly enables unambiguous presentation of experimental techniques and methods, and therefore increases the overall efficiency and standardization of biological research. During three years of its operations, JoVE has published 33 monthly issues including over 450 video-articles on experimental approaches in neuroscience, immunology, developmental biology, bioengineering and other fields. To facilitate integration of video into scientific publishing, JoVE has developed an organizational and technological structure to conduct production of scientific videos in research labs in the USA, Europe and Japan. This video-based approach to scientific publishing can be expanded to increase efficiency in other areas of experimental research including chemistry and engineering.

CINF 98

Nano-Publication

J. J. J. M. Velterop, velterop@conceptweballiance.org. Concept Web Alliance, Nijmegen, The Netherlands

What if we could freely get to all the essential knowledge contained in scientific articles, without those articles themselves necessarily being open access? And what if such free access to the essential knowledge is actually in the interest of publishers as well? For that, we need to split the roles of papers as 'scientific record keeping' (the 'interface with officialdom') on the one hand, and 'knowledge dissemination' on the other. This is made possible by what we call "nano-

publication”. The essence of scientifically meaningful content, especially in the natural sciences, can to a very large degree – often completely – be expressed in statements such as ‘DMD interacts with SNT1’, which are virtually always ‘triples’ of the form subject > predicate > object. Such triples can be extracted from the literature, and, particularly when semantically disambiguated, lend themselves optimally for machine reading on a large scale and for efficiently conveying knowledge and facilitating analyses, even for quasi-mathematical ‘reasoning’. Triples can be seen – and published – as ‘nano-publications’. And they would naturally be open access. Whilst in principle nano-publications extracted from classical papers would be subject to copyright, this could in practice only be used to ensure proper acknowledgement (science is an ‘acknowledge economy’ after all). Nano-publications that are rich semantic triples are in essence references, and wide and open availability of references to the content they publish is what most publishers crave. Nano-publications are therefore necessarily open access. And this open access is actually beneficial not just to scientists, but to publishers as well, be they open access publishers or traditional ones. In addition, one can imagine business models that financially support open access nano-publications. A concrete example will be presented.

CINF 99

Speeding up chemical database searches

R. J. Nasr, rnasr@ics.uci.edu, and P. Baldi, pfbaldi@ics.uci.edu. Department of Computer Science, University of California, Irvine, Irvine, CA, United States

In many large chemoinformatics database systems, molecules are represented by long binary fingerprint vectors whose components record the presence or absence of particular functional groups or combinatorial features. To speedup database searches, we develop and validate two new approaches. In the first approach, we compute for each fingerprint a corresponding small count vector containing the sums of hashed subsets of components. From these count vectors, we derive tight bounds on fingerprint similarity measures, such as the Tanimoto measure. During a database search, every time these bounds are unfavorable, the corresponding molecule can be discarded with no need for further inspection. The second approach adapts techniques from text search based on inverted indices to chemical fingerprints. For both approaches we construct probabilistic models that allow us to estimate the level of pruning under different conditions. These theoretical results are corroborated by experimental results obtained on a large set of molecules.

CINF 100

Comparison of backfiles offered by major publishers of chemical journals

A. D. Bolek, bolek@uakron.edu. Science-Technology Library, The University of Akron, Akron, OH, United States

Most of the major publishers of chemical journals offer their backfiles in packages of several titles, including the American Chemical Society, the Royal Society of Chemistry, Elsevier, Springer, and Taylor & Francis. At the beginning of 2009, Wiley permitted organizations to purchase titles individually, or in the previously offered packages. Some publishers allow you to pay a one-time fee for the backfile with permanent access, while others require an additional access fee each year. Some allow you to lease the backfile each year, while others include the backfile with a current subscription. Most publishers allow you to purchase an article on a pay-per-view basis, with the major exceptions being JSTOR and Portico. A few publishers make their backfiles free, as does J-STAGE's Journal@rchive, the Japan Science and Technology Information Aggregator, Electronic. This poster will compare what is offered by the major publishers of chemical journals at the beginning of 2010.

CINF 101

Marketing chemical research with custom web databases

B. Brandys, brandysb@mail.nih.gov. Department of Library Services, National Institutes of Health, Bethesda, Maryland, United States

This poster is a flow chart of the development of web-accessible databases of research compounds synthesized by NIH laboratories. Two databases containing Image Probes and Nitric Oxide generating compounds are used as examples. These databases enable public access to the laboratories' research, and provide an easily accessible medium for marketing and collaboration for further development.

CINF 102

Advanced materials/processes for information technology: Microfluidic synthesis, nanofabrication, and soft lithography

K. Choi, choikm@uci.edu. Chemistry, University of California, Irvine, CA, United States

Nanotechnology has been widely investigated due to specific advantages arise from their small scale in sizes. Chemists/materials scientists have shown intensive challenges on the development of new materials/processes to improve performances of information technologies. For chemist, the overall object of nanotechnology is to carry out the entire operations normally performed in a chemical laboratory including synthesis, processing, mixing, purification and analysis efficiently using small amounts of reagents. For example, microfluidic synthesis has taken a great attention due to advantages, which can't be achieved by conventional wet chemistry. Patterns fabricated using functional polymers is also promising for applications in information technology to integrate high performance optoelectronic devices. We demonstrate nanofabrication generated using functional polymers. For example, functional polymers can be produced by “molecular imprinting technique”, which is a general protocol for “synthetic receptor sites” with specific molecular recognitions. To seek for advanced process, we also develop a new class of PDMS stamps for nano-resolution soft lithography to overcome the limitations and thus to extend current soft lithography to advanced level.

CINF 103

New Knovel interface

S. Gurke, sgurke@knovel.com. Knovel Corp., New York, New York, United States

In the past year Knovel interface has undergone several facelifts and some more serious changes. This paper discusses user centric approach to design and implementation of new GUI. New features, including Knovel Lab, GET Search, autocomplete, spell checker, browse interface and Knovel Math are discussed. Current work and plans for the future enhancements, including expansion of content coverage, are discussed as well.

CINF 104

Expanding and understanding metabolite space

J. E. Peironcely[1,2], peironcely@chem.leidenuniv.nl, A. Bender[3], M. Rojas-Chertó[2,4], T. Reijmers[2,4], L. Coulier[1], and T. Hankemeier[2,4]. [1]Quality of Life, TNO, Zeist, The Netherlands, [2]Department of Netherlands Metabolomics Centre, Leiden University, Leiden, The Netherlands, [3]Department of Medicinal Chemistry, Leiden University, Leiden, The Netherlands, [4]Department of Analytical Biosciences, Leiden University, Leiden, Zuid Holland, The Netherlands

The ‘Metabolite Space’ is the total chemical universe of metabolites present in all compartments and in all states from any organism. We build models based on discriminative features that predict ‘metabolite likeness’. Here, we focus on the human metabolite space, including both endogenous and exogenous metabolites. Metabolites are compared with other molecules representative from different areas of the whole chemical space. We also explore the regions that lay outside the known metabolite space. In order to expand ‘Metabolite Space’ we employ RECAP to generate new molecules that possess features similar to those present in metabolites. We study how discernible these new molecules are from real metabolites. The new chemistry present in the expanded metabolite space is analyzed by looking at Murcko assemblies, ring systems, and other chemical properties. By combining all the above analyses we expect to characterize better the metabolite space, and to predict the metabolite-likeness of a molecule.

CINF 105

Metabolite identification based on MS fragmentation

M. Rojas-Chertó[1,2], m.rojas@lacdr.leidenuniv.nl, P. T. Kasper[1,2], J. E. Peironcely[1,3], T. Reijmers[1,2], R. J. Vreeken[1,2], and T. Hankemeier[1,2]. [1]Department of Netherlands Metabolomics Centre, Leiden University, Leiden, ZH, The Netherlands, [2]Department of Analytical Biosciences, Leiden University, Leiden, ZH, The Netherlands, [3]Department of Quality of Life, TNO, Zeist, Utrecht, The Netherlands

Identification of metabolites in studies of biological samples can be in principle achieved using high resolution multistage mass spectrometry (MS^n) because it provides a feature rich fingerprint of the precursor structure. However, neither general methodology for the identification nor extensive databases of metabolites with multistage mass spectrometric data are available at the moment. High resolution multi stage MS experiments were performed on LTQ-Orbitrap (Thermo) equipped with Triversa nanoMate (Advion) nanoelectrospray ion source. A defined protocol was established for the reliable and reproducible acquisition of mass spectral trees. An in-house developed software, the Multi-stage Elemental Formula (MEF) tool, integrating among others: Chemistry Development Kit (CDK) and XCMS libraries, was used for spectral data processing. MEF uses a method to resolve the elemental composition of the compound and fragment ions derived from MS^n data using a cyclic constraining process. Resulting fragmentation trees were stored in a database. Our results provide firm basis for developing a generic, multi stage mass spectrometry based platform for efficient identification of metabolites. We also present a powerful tool to discriminate metabolite isomers with the same elemental composition and an only slightly different structure.

CINF 106

Fragment database analysis using molecular shape fingerprints

J. D. MacCuish[1], john.maccuish@mesaac.com, N. E. MacCuish[1], M. Hawrylycz[2], and M. Chapman[1]. [1]Mesa Analytics & Computing, Inc., Santa Fe, New Mexico, United States, [2]Allen Institute for Brain Science, Seattle, Washington, United States

Shape clustering of fragment databases using both 3D shape fingerprints (generated via Quasi-Monte Carlo integration) and 2D structure fingerprints will be described. Individual clusters are then analyzed with 3D shape fingerprints incorporating substructure information, akin to substructure commonality programs with 2D fingerprints, such as Stigmata and ChemTattoo.

CINF 107

Qsearch: Pharmacophore-based search in fragment spaces

T. Lippert, lippert@zbh.uni-hamburg.de, and M. Rarey. Zentrum für Bioinformatik, Universität Hamburg, Hamburg, Germany

Fragment spaces have proven to be a valuable source of molecules that are biologically active and synthetically feasible. A fragment space consists of a set of molecular fragments with defined linking positions and a set of rules to combine fragments to new molecules. We have developed an expert system for medicinal chemists to allow to search fragment spaces for molecules that can fulfill a chosen three dimensional pharmacophore. The fragment space is searched with an evolutionary approach, where partial solutions evolve to fit the posed query by adding, deleting of replacing fragments. The fitness of a partial solution is calculated by its ability to obey to the constraints of the pharmacophore. We tested the program by searching several focused fragment spaces with pharmacophores for common drug targets. The resulting molecules obey to the input pharmacophore and look chemically sound.

CINF 108

Fragment-based lead discovery through chemotype evolution

D. Erlanson, derlanson@carmot.us. Carmot Therapeutics, Inc., San Francisco, CA, United States

Fragment-based ligand discovery has established itself as a powerful method to identify drug leads. The two primary practical challenges in applying fragment-based methods have been finding fragments and linking (or growing) them. The first challenge has recently become much easier. Advancing fragments to leads, however, remains a significant hurdle. We have developed a technology, Chemotype Evolution, which uses rapid in-situ chemistry to expand a fragment into a diverse range of hits. Chemotype Evolution is amenable to elaborating fragments found using any method: a starting fragment can be a privileged pharmacophore derived from a known inhibitor, substrate, or cofactor, or a fragment identified through a previous screen. Through iterative application of Chemotype Evolution, the starting fragment can be transformed into novel, varied chemotypes, while desired properties can be enhanced by incorporating counter screens. Chemotype Evolution provides a general solution to the question of how to turn promising fragments into promising leads.

CINF 109

Leading fragments to lead structures: Fragment evolution, merging and core replacement, and…docking

C. Detering, detering@biosolveit.de, M. Gastreich, and C. Lemmen. BioSolveIT, Sankt Augustin, Germany

Lead discovery often starts from small fragment binders for which experimental evidence has been found in an active site. Development into a lead structure can involve three possible scenarios: a) to grow from these ‘needles’ into the depth of the pocket; b) linkage of two or more fragments into one compound with optimized potency; or c) merging two or more fragments in regions of mutual overlap. These tasks can now be accomplished with a novel software tool***,*** which comprises the interactive fragment based software ***ReCore*** and the well established docking engine ***FlexX***. With ***ReCore***, synthetically accessible compounds can be generated in seconds by using an indexed 3D fragment library on fragments or compounds that should be altered. The results can then be validated by docking without leaving the software environment. We will elucidate the basic principles and give examples which map onto experimental data and evolve into novel lead ideas.

CINF 110

Fragment-based drug design using PASS approach

O. A. Filz, fioland@yandex.ru, A. A. Lagunin, alexey.lagunin@ibmc.msk.ru, D. A. Filimonov, dmitry.filimonov@ibmc.msk.ru, and **V. V. Poroikov**, vladimir.poroikov@ibmc.msk.ru. Department for Bioinformatics, Institute of Biomedical Chemistry of Rus. Acad. Med. Sci., Moscow, Russian Federation

Fragments are considered as important entities in medicinal chemistry, because they are (1) the determinants of presence/absence of certain biological activity, (2) key elements of structural modifications for obtaining new molecules with the required properties. The role of structural fragments in chemical series is analyzed by experimental methods (X-ray crystallography, NMR, surface plasmon resonance) and by molecular modelling or (Q)SAR. We have developed computer program PASS that predicts more than 3000 biological activities on the basis of structural formula of chemical compounds (http://www.ibmc.msk.ru/PASS; Filimonov and Poroikov, in: Chemoinformatics Approaches to Virtual Screening. A. Varnek and A. Tropsha, Eds. RSC Publishing, 2008, 182-216). Prediction is based on SAR analysis of the training set containing over 200000 biologically active compounds collected from different sources. PASS calculates the impact of each of atoms in a molecule into a certain activity using MNA descriptors for particular atom and its immediate neighbours. These estimations could be used for identification of fragments responsible for binding chemical compounds with a specific target, and for further computer-aided design or generation of new “candidates” with the required biological activity. The proposed approach: (1) does not require information about 3D structure of the target, (2) could be applied for finding multitargeted ligands, and (3) provides medicinal chemist to make a design *in silico* of synthesizable molecules. Examples of fragment-based design for endothelin receptor antagonists, cyclin-dependent kinase inhibitors, ligands of 5HT and D2 receptors will be discussed.

CINF 111

Use of virtual fragment screening for lead modification

Y. Xu, yongjin.xu@novartis.com, H. Jansen, and E. Martin. Global Discovery Chemistry/Oncology & Exploratory Chemistry, Novartis Institutes for Biomedical Research, Emeryville, CA, United States

In many drug discovery programs, lead structures often need to be modified while maintaining biological activity. With binding site information, modifications can be proposed using two conceptually different approaches, named “cut and fit” and “fit and cut”. The “cut and fit” approach, which is under development, starts by fragmenting a compound database and then replacing a portion of the lead molecule with the fragments. The “fit and cut” approach starts with whole molecules from a compound database, evaluates whether any part of these molecules provides a good fit for the region under consideration. Selected fragments are separated and merged with relevant parts of the lead molecule. Finally, the fitting of the new modifications are confirmed with docking method. This method has produced interesting ideas in multiple kinase projects. As a validation of the method, a case study with the P38 ATP pocket and the MDDR database will be described.

CINF 112

IUPAC InChI project: A status report

S. R. Heller, steve@hellers.com, and A. McNaught, mcnaught@ntlworld.com. CBRD, MS-8320, NIST, Gaithersburg, MD, United States

The current status of the IUPAC InChI project will be described. The relationship with and the activities of the related InChI Trust will be presented and show how the InChI and InChIKey are being used in scientific publications and scientific databases to enhance the linking and connecting of chemical information and data from a variety of sources and resources. The cooperation between IUPAC, the major organizations in the scientific publishing community, and chemical software companies will be presented to show how this widely diverse group of national and international organizations are collaborating.

CINF 113

Tools for the scholarly communication lifecycle

A. D. Wade, alex.wade@microsoft.com, and L. Dirks. Microsoft Research, Redmond, WA, United States

Microsoft External Research strongly supports the process of research and its role in the innovation ecosystem. We are dedicated to supporting research efforts and to developing new tools to enhance the broadest goals of the scholarly communication lifecycle. Through collaborations with universities, national libraries, publishers, and governmental organizations, we seek to develop

software and services that will advance the process of scholarly information capture and dissemination. Such collaborations demonstrate our ongoing work towards producing next-generation documents that increase productivity and empower authors to increase the discoverability and appropriate re-use of their work. Throughout the research process, software can and should assist us in the process of information capture, organization, analysis, collaboration, authoring, dissemination and long-term information preservation. This session will highlight several freely available and open source efforts from Microsoft External Research, and will demonstrate how these can help to enhance and evolve the process of scholarly communication.

CINF 114

Integrated language for chemical publication

P. Murray-Rust, pm286@cam.ac.uk, J. A. Townsend, and L. Hawizy. Department of Chemistry, University of Cambridge, Cambridge, Greater East Anglia within England, United Kingdom

Chemical communication involves many languages: text, speech, graphics, numerical information, chemical structures and computations. Many concepts are confined to one sublanguage (“lower alkyls” is linguistic , “dotted bond” is graphical and “1.3kcal” is computational). Normal publications reduce these to a single medium such as PDF, computer logs, or audio but this introduces loss and semantic ambiguity. We describe the systematisation and integration of chemical sublanguages through markup, ontologies and knowledgebases. The combination of information (graphical, linguistic) can resolve ambiguity and leads to an adaptive machine-learning process. We have developed tools to support authoring of semantic documents (datuments) and to read current chemical documents (text, graphics, computation) into this infrastructure. Humans and machines can now communicate in a natural manner (speech, text, gestures) leading to a simple level of articficial intelligence.We have a complete Open toolchain and propose this approach for formal scholarly communication.

CINF 115

Chem4Word

J. A. Townsend[1], jat45@cam.ac.uk, P. Muray-Rust[1], J. Downing[1], T. Haughton[2], A. Wade[3], and L. Dirks[3]. [1]Department of Chemistry, Univeristy of Cambridge, Cambridge, CAMBS, United Kingdom, [2]Microsoft Research, Cambridge, CAMBS, United Kingdom, [3]Microsoft Research, Redmond, Washington, United States

Chem4Word is an Open Source Add-in for Word2007 developed in a collaborative project (Cambridge/Microsoft) for enhancing scholarly communication in chemistry. Version 1 supports a complete datument (text, formulae, chemical structures, navigation and indexing) and is adaptive, learning

from the author's previous actions and updates through the web. All components are semantic so that chemical structures or other graphics cannot be misinterpreted by machines or humans. Multi-interface tools (speech, gestures, PDAs, etc.) are supported. The system captures the complete semantic history of chemistry in the document and Chemical Styles allow consistent look-and-feel to be applied to the entire document. Version 2 is being developed to support scholarly communication to and from undergraduates and introduces peaklists, spectral data and reactions. C4W manages many of the components in a mainstream chemical publication and our Open governance model and deliberately extensible add-in architecture invites those interested to develop community components for Open re-use.

CINF 116

Capturing and publishing chemistry from the bench to paper: Does Google Wave offer a solution?

C. Neylon, cameron.neylon@stfc.ac.uk. ISIS, Science and Technology Facilities Council, Didcot, OXON, United Kingdom

Google Wave is a new communication and document management platform that takes advantage of advances in web technology to provide a wide range of functionality to the user in an integrated fashion. Documents or "waves" can be shared in real time between multiple participants, which can include automated web-based agents ("Robots") that can read, parse, and modify the wave. Rich visualisation and control functionality can be added javascript "gadgets" that might include three dimensional chemical models, instrument control, or data visualisation. The combinaton of these features offers an enormous potential to deliver a rich chemical authoring experience including automated and user-guided markup of a chemical record as well as publishing that record in different forms to the web. This talk will discuss progress on developing tools within the Wave framework for chemical authoring and publishing and the prospects for using Wave as an integrating technology for chemistry on the web.

CINF 117

CAS REGISTRY: Maintaining quality standards as scientific discovery accelerates

M. J. Toussant, mtoussant@cas.org. Chemical Abstracts Service (CAS) Division, American Chemical Society, Columbus, OH, United States

CAS REGISTRY is the world's most comprehensive and fastest growing compendium of publicly disclosed chemical substance information, comprising more than 50 million organic and inorganic substances (as of 9/09) and 61 million sequences. In recent years, the pace of discovery of new substances has accelerated dramatically and further growth is anticipated. This talk will focus on the strategies, policies, technology and organizational approaches employed by

CAS to meet its mission (to organize and make available for research publicly disclosed chemical information) in light of this growth, and in particular to ensure the quality of the substance information in REGISTRY.

CINF 118

Chempedia: A social medium for chemical information

R. L. Apodaca, rapodaca@metamolecular.com. Metamolecular, LLC, La Jolla, CA, United States

Chempedia (http://chempedia.com) is a free service designed to solve the problem of uniquely identifying and naming chemical substances. With the Web's ever-increasing role in chemistry comes the need for a free substance registry as a platform on which to build the chemical information systems of the future. Chempedia addresses this need by offering a peer-reviewed, real-time platform that can be read from, written to, and republished by the global chemistry community free of charge. Created with the recognition that chemistry is an inherently social activity, Chempedia adapts many of the best practices and technologies used in modern social media. This talk will discuss the importance of a free substance registry to the future of chemical comminication, the principles and technologies applied to Chempedia, and the ways Chempedia is now being used.

CINF 119

Enhancing discoverability across Royal Society of Chemistry content by integrating to ChemSpider, an online database of chemical structures

A. J. Williams, antony.williams@chemspider.com, V. Tkachenko, S. Shevelev, and R. Kidd. Royal Society of Chemistry, Wake Forest, NC, United States

The ability to query across a chemistry publishers content using chemical structure searching can dramatically enhance discoverability. RSC has been applying a number of procedures to integrate RSC's ChemSpider community resource with our published content and databases. These include: 1) entity extraction procedures 2) chemical name conversion procedures using software algorithms and curated dictionaries 3) semantic markup and 4) a crowdsourced curation processes. This presentation will provide an overview of the processes we have utilized in order to provide structure-based integration to RSC content. We will discuss our ongoing efforts to extend the approaches to the mining of data from the rich supplementary information sections of many RSC publications. Our intention is to provide access to synthesis procedures and analytical data and further enrich the ChemSpider database for the benefit of the chemistry community.

CINF 120

Fragment-based screening of stabilized G protein-coupled receptors

M. Congreve, miles.congreve@heptares.com. Chemistry, Heptares Therapeutics Ltd, Welwyn Garden City, Hertfordshire, United Kingdom

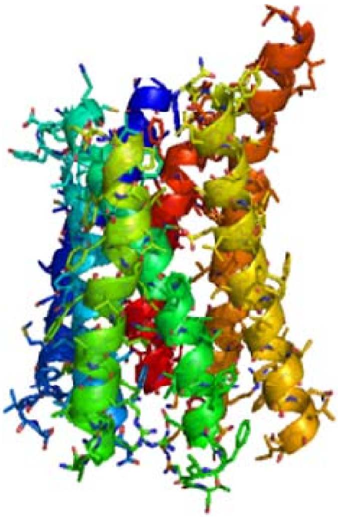
GPCRs as a target class are notoriously difficult proteins to work with because conformational flexibility, heterogeneity and instability outside of the cell membrane makes them particularly hard to crystallize and limits their use in screening applications. Heptares is developing a technology that expedites the study of GPCRs by dramatically stabilizing these important receptors outside of the cell membrane. The new stabilized receptors (StaRs) are much more robust than the corresponding wild type proteins making them amenable to crystallography and to biophysical screening techniques. Screening results from both TINS-NMR and Surface Plasmon Resonance (SPR) binding studies for representative StaR proteins using libraries of fragments will be outlined. Computational approaches to interpret the screening results will be discussed, and the potential for in-silco design using fragments as start points for lead identification presented.

CINF 121

Novel histamine GPCR family antagonists by fragment screening and molecular modeling

R. J. Law[1], richard.law@evotec.com, T. Hesterkamp[2], A. Kahrs[2], M. Whittaker[3], S. Pal[1], and A. Heifetz[1]. [1]Computational Chemistry, Evotec, Abingdon, Oxfordshire, United Kingdom, [2]Evotec AG, Hamburg, Germany, [3]Evotec UK, Abingdon, United Kingdom

We have applied a small fragment collection to the screening of three histamine receptors with the goal to identify subtype specific antagonists. The rationale for doing this is to cover as much chemical diversity as possible in a small screening effort and to meet the chemical space of the natural ligand, histamine. We have followed up on the resulting fragment hits by building H3 and H4 receptor models based on similarity to known GPCR crystal structures andoptimized using a series of molecular dynamics procedures. These models were used for a docking procedure to reveal the bioactive conformation of the bound ligands, with a view to structure-guided fragment-to-lead expansion. A subsequent shape-based analogue search provided a short list of hits from which we have been able to obtain novel submicromolar and lead-like H3 and H4 antagonists.



CINF 122

Mitotic kinesin Eg5 inhibitors generation by computational MED-portion based drug design at PDB scale

K. Oguievetskaia[1], L. Martin-Chanas[1], lmartin@medit.fr, A. Vorotyntsev[1], O. Doppelt-Azeroual[1], X. Brotel[1], S. Adcock[1], A. de Brevern[2], **F. Delfaud**[1], fdelfaud@medit.fr, and **F. Moriaud**[1], fmoriaud@medit.fr. [1]MEDIT SA, Palaiseau, Idf, France, [2]Equipe DSIMB, Dynamique des Structures et Interactions des Macromolécules Biologiques, INSERM UMR-S 665, Paris, Idf, France

Eg5, a mitotic kinesin exclusively involved in the formation and function of the mitotic spindle has attracted interest as an anticancer drug target. Eg5 is co-crystallized with several inhibitors bound to its allosteric binding pocket. Each of these occupies a pocket formed by loop5/helix α2. Recently designed inhibitors additionally occupy a hydrophobic pocket of this site. The goal of the present study was to identify new fragments which fill this hydrophobic pocket and might be interesting chemical moieties to design new inhibitors.

CINF 123

Starting small and staying small: Fragment-based lead discovery in CNS disease

V. L. Nienaber, vicki@zenobiatherapeutics.com. Drug Discovery, Zenobia Therapeutics, La Jolla, CA, United States

Diseases of the central nervous system (CNS) are among the most devastating to patients and their families. Despite this, treatments have lagged behind other therapeutic areas in part because of the challenge for compounds that cross the blood brain barrier. Recent analyses of successful drugs have shown that their chemical properties have not changed substantially over the past 40 years while

the properties of compounds entering the clinic have become inflated. This property inflation has only exacerbated the challenges of CNS drug discovery as the requirements for delivery to the brain are even more stringent than those for other tissues. In this presentation, we will discuss the merits of fragment based lead discovery and how we have adapted our approach to address the chemical property challenges of CNS drug discovery. We include results from our internal programs targeting protein kinases and other enzyme classes in neurodegenerative diseases.

CINF 124

Finding druggable sites in protein-protein interfaces by computational fragment mapping

D. Kozakov, midas@bu.edu, and S. Vajda. Department of Biomedical Engineering, Boston University, Boston, MA, United States

Development of small-molecule inhibitors that disrupt protein–protein interfaces has received considerable attention in recent years. We describe a method based on computational fragment mapping to identify “hot spot” regions in protein-protein interfaces that are most likely capable of binding small molecules. The method places molecular probes – small molecules or functional groups – on the protein surface, and finds and clusters the energetically favorable sites for a variety of probes. Application of mapping to a number of PPI targets has shown that the method always finds at least some part of the appropriate sites. To account for protein plasticity we then use an algorithm combining statistical analysis and energy minimization to identify the nearby “moveable” side chains, and generate and then map the alternative protein structures. Results are presented for a number of protein-protein interaction targets, including interleukin-2, Bcl-xL, MDM2, HPV-11 E2, ZipA, TNF-alpha, and NEMO.

CINF 125

Peer review is not perfect but are the alternatives worse?

W. A. Warr, wendy@warr.com. Wendy Warr & Associates, Holmes Chapel, Cheshire, United Kingdom

Scientists are generally agreed that publication of learned articles should not be a free-for-all, and that some form of quality control is necessary. On the other hand anyone who has studied peer review even cursorily has to admit that the traditional system is far from perfect. It succeeds as a compromise for the quality journals because of the way it is administered by journal editors. Some of the alternatives that have been proposed, such as double blind peer review or open peer review are simply modifications of the traditional process. Other options (usually in addition to the traditional method) are post-publication review and services such as Faculty of 1000. More progressive are concepts such as

computer-assisted peer review; reputation; moderated peer review and systems such as Roy Rustum's "super peer review"; volunteer review, voting and systematic aggregation of reviews; and use of crowdsourcing and the blogosphere. This author (a journal editor) is skeptical about some of the alternatives, but nevertheless, the presentation will concentrate more on revolution than on evolution.

CINF 126

Interactive open access publishing and public peer review: Perspectives and effectiveness of transparency and self-regulation in scientific communication and quality assurance

U. Pöschl, poeschl@mpch-mainzh.mpg.de. Biogeochemistry Department, Max Planck Institute for Chemistry, Mainz, Germany

The traditional forms of scientific publishing and peer review do not live up to the demands of efficient communication and quality assurance in today's highly diverse and rapidly evolving world of science. They need to be advanced and complemented by interactive and transparent forms of review, publication, and discussion that are open to the scientific community and to the public. The advantages of open access, public peer review and interactive discussion can be efficiently and flexibly combined with the strengths of traditional publishing and peer review. Since 2001 the benefits and viability of this approach are clearly demonstrated by the highly successful interactive open access journal Atmospheric Chemistry and Physics (ACP, www.atmos-chem-phys.net) and a growing number of sister journals launched by the publisher Copernicus (www.copernicus.org) and the European Geosciences Union (EGU, www.egu.eu). These journals are practicing a two-stage process of publication and peer review combined with interactive public discussion, which effectively resolves the dilemma between rapid scientific exchange and thorough quality assurance. The same or similar concepts have recently also been adopted in other disciplines, including the life sciences and economics. Note, however, that alternative approaches where interactive commenting and public discussion are not fully integrated with formal peer review by designated referees tend to be less successful. The principles, key aspects and achievements of interactive open access publishing (top quality & impact, efficient self-regulation & low rejection rates, little waste & low cost) will be presented and discussed. Moreover, perspectives for future developments in scientific communication and and quality assurance will be oulined. For more information see: www.atmospheric-chemistry-and-physics.net/general_information/public_relations.html

CINF 127

Impact factors, post-publication peer review and other metrics

R. P. Grant, richard.grant@f1000.com. Faculty of 1000, London, United Kingdom

The ISI Impact Factor (IF) is the de facto standard for assessing ‘quality’ and importance of published research. It suffers many problems: it is slow, at least two years out of date; it depends on accurate and relevant citation; it is unduly skewed by review articles; it cannot reliably predict quality; it is irrelevant to non-citable research or non-citing communities; and important research does get published in low IF journals. Alternative indicators include usage data, network analysis and comment aggregation. We have developed a metric that harnesses expert review and the power of the social web, and that can furthermore predict citation rates. We have used this to rank journals and institutions according to research quality rather than IF. We also propose that it is a more relevant measure of an individual scientist’s output than one based on citation rates.

CINF 128

Eigenfactor: Ranking and mapping the scholarly literature

J. D. West, jevinw@u.washington.edu. Department of Biology, University of Washington, Seattle, WA, United States

Each year, tens of thousands of scholarly journals publish hundreds of thousands of scholarly papers, collectively containing tens of millions of citations. As De Solla Price recognized in 1965, these citations form a vast network linking up the collective research output of the scholarly community. In our lab, we have developed a set of tools to mine the wealth of information contained within the full structure of these citation networks. In this talk, I will give an overview of the Eigenfactor project and how we are using centrality approaches to better evaluate and navigate the ever-expanding, scholarly literature.

CINF 129

Applying domain expertise assessment to compound annotation for enhanced collaborations between chemists and biologists

Y. Pouliot, ypouliot@researchscorecard.com. ResearchScorecard Inc., Belmont, California, United States

Medicinal chemistry and other fields require close collaboration between chemists and biologists. Because of their cross-disciplinary nature, the success of these collaborations is particularly dependent on making an optimal choice of collaborators. Unfortunately, finding and selecting potential collaborators remains a haphazard process. ResearchScorecard addresses this issue by applying data mining algorithms to comprehensive descriptors of academic researchers. By facilitating the assessment of the quality and volume of research data conveyed by databases, we believe that the combination of such “expertise data” with compound properties can enhance researchers’ understanding of these compounds. This is enabled by ResearchScorecard’s use of data gathered automatically from public sources, followed by heavy cleansing and semantic integration. Such an objective approach enables the approximate ranking of

researchers based on their degree of domain expertise and their overall prominence. Some of the applications of automated domain expertise assessment to compound annotation will be discussed.

CINF 130

Exploring molecular networks for polypharmacology analysis

S. Zhang, shuzhang@mdanderson.org. Department of Experimental Therapeutics, MD Anderson Cancer Center, Houston, TX, United States

In silico prediction of molecular polypharmacology is of great importance as it helps to design safer drugs with higher efficacy. We recently have embarked on the construction of chemical and biological databases with annotation of molecular biological functions and 2D/3D structures. The information was then employed to analyze the relationships among drugs and targets based on drug chemical similarity search and their interactions with multiple targets. The derived molecular networks were visualized in 2D graphs, and the prediction of potential drug off-target properties and toxicities was conducted. Based on known biological and pharmacological functions, about 3933 out of 5059 drugs were found interacting with multiple targets. On the other hand, chemical similarity search demonstrated that 2528 drugs share >85% structure similarities with some other drugs, indicating these drugs might have similar bioactivities. With this implementation, we provided an efficient way to evaluate the polypharmacology of chemical compounds.

CINF 131

Picking novel actives from large databases using a combined ranking method

D. Marcus, david.marcus1@mail.huji.ac.il, D. Barasch, A. Rayan, and A. Goldblum. Institute of Drug Research, The Hebrew University of Jerusalem, Jerusalem, Israel

Early stages of modern drug discovery often involve screening of small molecular libraries to find “hits”. In order to construct highly enriched libraries, we developed a ranking method that combines predictions from several models to supply an index for each compound and swiftly rank large compound databases. The method is based on our Iterative Stochastic Elimination algorithm that can locate the best model sets out of a huge number of possible solutions. Models are assigned to distinguish between multiple activity classes (inactive, modestly active, highly active) and taken together with different weights for each model and class, a combined ranking index is produced. We found that this index has a higher reliability and correlativity to experimental values than the common approach based solely on classification of two activities. This method was applied successfully in a few test cases (Estrogen receptor, Acetylcholine Esterase) and is able to pick highly enriched libraries.

CINF 132

Human proteome in the context of pathways, diseases, drugs, and tool compounds

F. Nigsch, florian.nigsch@novartis.com, and J. Jenkins. Center for Proteomic Chemistry, Lead Discovery Informatics, Novartis Institutes for Biomedical Research, Cambridge, Massachusetts, United States

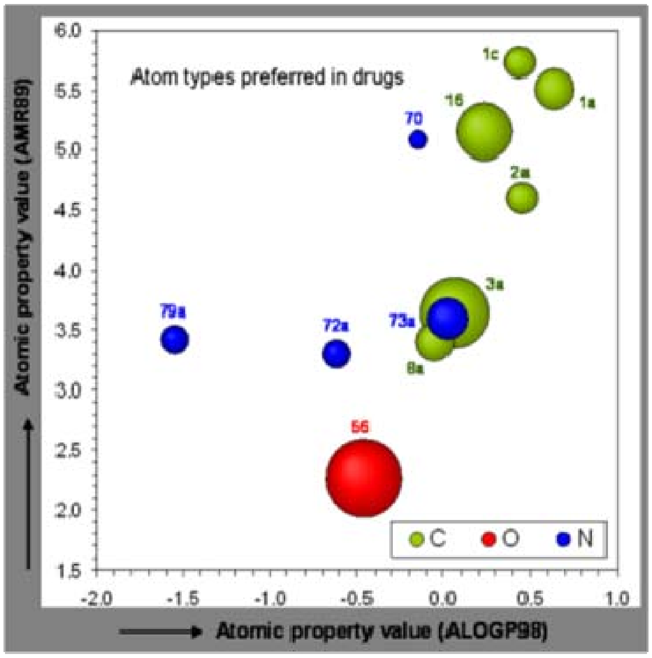
To get an overview of chemical matter currently known to be biologically active, we accumulated several sources of compound-target activity information into a repository comprising 20 million activity records of 3 million distinct compounds. Extensive target normalization and the use of a commercial database of curated pathways, regulatory network, disease and other relevant information for drug discovery (GeneGo Metabase) was used to place compound-target associations into a rich biological context. Analysis of this wealth of data reveals pharmacological hotspots and also provides information on the global coverage of the human proteome. Apart from the amount of data, however, a prime focus was put on target annotation in an effort to be able to relate the effects of compounds to the biological networks they act upon. The workflows that are made possible in this way span methods from both bioinformatics and cheminformatics and provide novel methodology to enable drug discovery research.

CINF 133

Atom type preferences, constitutional diversity, and property profiles of known drugs: A knowledge-intensive, comparative assessment of drugability

V. N. Viswanadhan, vellarkad_viswanadhan@jubilantbiosys.com, H. Rajesh, and V. N. Balaji. Department of Computational Chemistry, Jubilant Biosys Ltd, Bangalore, Karnataka, India

A novel characterization of known drugs and an improved drugability score are presented based on an analysis of physicochemical and topological properties at different levels: atom types, functional groups, and the whole molecule. A new united atom classification, UALOGP, is proposed and validated, extending the earlier ALOGP method. UALOGP was used to analyze atom type distributions and identify atom types preferred in drugs, relative to a non-drug database, with a similar MW distribution. Using a new quantification of atom type diversity, it is shown that drug molecules are intrinsically more *diverse*. A critical re-examination of well-known characterizations of drugability, such as the Ro5 and GVW criteria, is accomplished based on an analysis of physicochemical property distributions. A comparative analysis of the present and older drug property ranges leads to an improved drugability filter and scores, correctly identifying the chemical space occupied by orally bioavailable drugs.



CINF 134

Improving the consistency of data fusion in virtual screening

I. Mott[1], P. Gedeck[2], and **V. J. Gillet**[1], v.gillet@sheffield.ac.uk. [1]Department of Information Studies, University of Sheffield, Sheffield, United Kingdom, [2]Novartis Institutes for BioMedical Research, CH-4002 Basel, Switzerland

It is well known that different virtual screening methods capture different aspects of structure-activity relationships and this has led to the use of data fusion or consensus scoring methods to combine the output from different methods. For example, it has been shown that enrichments in docking can be improved by combining the results obtained with different scoring functions. Data fusion involves combining the ranks produced by the individual methods typically using either the minimum rank (the MIN rule) or the average rank (the SUM rule). The relative abilities of these two rules to improve virtual screening results depend on the distributions of pairwise similarity values in the dataset which is difficult to predict upfront. Here we investigate the use of Pareto ranking for data fusion and show that greater consistency can be achieved over different datasets compared to the use of either the MIN or the SUM rule.

CINF 135

Extending interaction fingerprints: A novel approach to characterizing protein binding sites

C. Higgs[1], chris.higgs@schrodinger.com, W. Sherman[1], and J. Blaney[2]. [1]Department of Application Science, Schrodinger, New York, NY, United States,

[2]Department of Discovery Chemistry, Genentech, South San Francisco, California, United States

The characterization of the protein binding sites based on protein-ligand interactions can be valuable in structure-based drug design and successful applications using interaction fingerprints have been published. However, most methods are limited to characterizing binding sites of the same or related proteins due to the fingerprints being dependent on a consistent numbering of the atoms in the binding site. Here we present a new type of interaction fingerprint based on geometric profiling that is independent of the atom/residue numbering and can be compared between any targets. In addition to using this fingerprint method as a tool to post-process docking results, the fingerprints can be used to find other complexes with similar protein-ligand interaction motifs, cluster complexes based on interaction profiles, and perform substructure searches to find regions of the binding site that may be similar to unrelated proteins.

CINF 136

Molecular signatures of promiscuous enzyme-substrate interactions

J.-L. Faulon, jfaulon@gmail.com, and P. Carbonell, pcarbonell@epigenomique.genopole.fr. Department of Biology, University of Evry, Evry, France

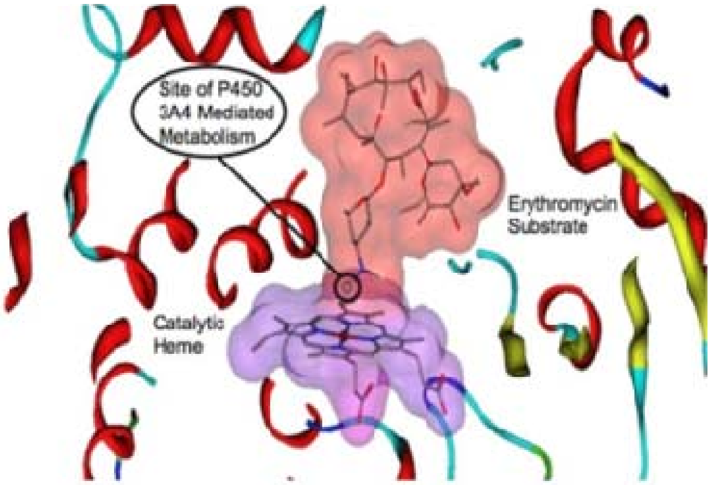
Catalytic promiscuity, the ability of enzymes to catalyze more than one reaction, has been used to engineer enzymes with altered activities. However, the plasticity mechanism that makes a promiscuous catalytic active site able to accommodate different substrates is at present not fully understood. In this work, we use a graph-based representation known as molecular signatures to characterize both sides of the promiscuous enzyme-substrate binding process. In particular, we dissect the structural determinants of promiscuity at catalytic sites, and how chemical similarity is involved in substrate recognition. Performing this study for the entire KEGG database allows us to get insights about evolutionary relationships between different metabolic pathways, and how new catalytic functions are acquired. We show here an enzyme engineering application of this method to the directed evolution of natural occurring protein scaffolds with latent catalytic activities.

CINF 137

Metabolic regioselectivity models for nine CYP P450 isozymes

J. M. Zaretzki[1], zaretj@gmail.com, T.-W. Huang[1], C. M. Breneman[1], C. Bergeron[2], and K. P. Bennett[2]. [1]Department of Chemistry, Rensselaer Polytechnic Institute, Troy, NY, United States, [2]Department of Mathematics, Rensselaer Polytechnic Institute, Troy, NY, United States

Computational models for rapidly predicting the susceptibility of sites on small drug-like molecules to oxidative metabolism have been extended to include cytochrome isozymes 1A2, 2A6, 2B6, 2C19, 2C8, 2C9, 2D6, 2E1, as well as 3A4. Within this methodology, topologically distinct regions of each ligand are quantified using 540 2D and QM-based electronic descriptors, and ranked according to their susceptibility as metabolic sites. A quick and accurate tool for making these predictions on substrate databases is now available online.



CINF 138

Novel topological molecular key for cheminformatics

P. Liu, pliu24@its.jnj.com, and D. Agrafiotis. Johnson & Johnson PRD, Exton, PA, United States

Representing molecules in the form of numerical or symbolic keys is increasingly employed to capture the structural characteristics and chemical properties in chemoinformatics research. Here we present a novel topological molecular key to encode the connecting atoms and bonds into two separate components, which allows the convenient comparison of each individual component. We have applied this new key for the screening stage of substructure search on a relational database for a dataset of about 1 million compounds. The screening efficiency with this new key is greater than 99.9%. More importantly, this set of new keys can uniquely determine the correct hits for certain generic queries in a fraction of seconds, which is usually a challenging task for other substructure search methods. It also has potential in similarity search and clustering.

CINF 139

Classification of enzyme function based on similarities in reaction mechanisms and common substrate substructures

D. E. Almonacid, daniel.almonacid@ucsf.edu, and P. C. Babbitt. Departments of Bioengineering and Therapeutic Sciences, and Pharmaceutical Chemistry, and California Institute for Quantitative Biosciences, University of California San Francisco, San Francisco, California, United States

Historically proteins have been studied and classified in terms of their sequence and structure, and then often independently associated with function. Sophisticated mathematical methods have been developed to measure similarities between protein sequences and structures, generating robust classification schemes. In contrast, for protein function, most, if not all, classification systems are based on qualitative conceptual frameworks rather than on quantitative measures. Here, we classify enzyme molecular functions based on two quantitative measures: (1) similarity of enzyme reaction mechanisms and (2) common substrate substructures between reactions. We apply this new classification to families of evolutionarily related enzymes in our Structure-Function Linkage Database. The results indicate that similarities in reaction mechanisms and substrate substructures are orthogonal and thus complementary to classifications based on sequence and structure. We discuss the value of quantification of function similarity for functional prediction, annotation and engineering of enzyme functions.

CINF 140

Chem_BLAST: A rule-based method to develop advanced structural ontologies for chemical bioinformatics and the PDB, the PubChem

T. N. Bhat, bhat@nist.gov. CSTL, NIST, Gaithersburg, MD, United States

Today’s Chemical Bioinformatics community must interact with a variety of information standalone applications and ontologies. This limitation promotes the need to define and develop rule-based stringent ontologies for information processing and sharing. Chemical Block Layered Alignment of Substructure Technique (Chem-BLAST) first recursively dissects chemical structures into blocks of substructures using rules that operate on atomic connectivity and then aligns them one against another to develop first Chemical Resource Description Framework (RDF) and then chemical ontologies in the form of a ‘tree’ made up of ‘hub-and-spoke’. The technique was applied for (a) both 2-D and 3-D structural data for AIDS (http://bioinfo.nist.gov/SemanticWeb_pr2d/chemblast.do); (b) to ~;60000 structures from the PDB which is now available from the RCSB/PDB Web site (http://www.rcsb.org/pdb/explore/externalReferences.do?structureId=3GGT) and advanced features at http://xpdb.nist.gov/chemblast/pdb.html . Full description of the Chem_BLAST along with recent results and illustrations including those for approximately a million compounds from the PDB and PubChem will be presented.

http://www.rcsb.org/pdb/explore/externalReferences.do?structureId=3GGT

CINF 141

Chemical entity extraction and interpretation

D. M. Lowe[1], dl387@cam.ac.uk, P. T. Corbett[2], P. Murray-Rust[1], and R. C. Glen[1]. [1]Chemistry, University of Cambridge, Cambridge, Cambridgeshire, United Kingdom, [2]Linguamatics, Cambridge, Cambridgeshire, United Kingdom

OSCAR is an extensible Open-source system for chemical entity recognition in text which has recently been re-factored through UK eScience (OMII). Using pattern based and machine learning techniques (with interchangeable tools) OSCAR recognises chemical compounds, reactions, enzyme names and other chemical terms. To create structure searchable corpora and to enhance viewing of documents chemical names can be resolved to structures. This is achieved either through lookup (ChEBI, Pubchem) or complete parsing of systematic names using the OPSIN module. Using a regular grammar, several chemical dialects, and a largely complete list of IUPAC name components OPSIN employs finite-state parsing to recognise IUPAC morphemes and disambiguate their meaning. A connection table, including atom numbering, is then built and output as CML (Chemical Markup Language) and hence other formats such as SMILES. Additions to OPSIN's vocabulary can be made without code modification. Metrics showing OPSIN's current performance on chemical names will be presented.

CINF 142

PolyGWT: A Google Web Toolkit application to assist polymer research

E. O. Cannon, eoc21@cam.ac.uk, and P. Murray-Rust. Department of Chemistry, University of Cambridge, Cambridge, Cambridgeshire, United Kingdom

As we move into the 21st century, demand for open source software for polymer scientists has never been greater. We introduce PolyGWT, an open source state of the art three-tier architecture semantic web application for polymer science, based on the Google Web Toolkit (GWT) software framework, Restlet and an Apache Derby relational database. The application addresses a number of issues: building and displaying polymers, searching for repeat units by substructure and by property using ontology browsing. It also allows repeat unit property calculation on the fly and a suite of machine learning tools for classification and clustering of new repeat units. We expect this application to be of primary use to polymer chemists wishing to develop a strategy for a laboratory synthesis. It will also be of interest to software engineers to develop or extend, as an application programming interface is provided.

CINF 143

OpenTox: An open source predictive toxicology software framework

B. Hardy[1], barry.hardy@douglasconnect.com, **D. A. Gallagher**[2], gallagher.da@gmail.com, and S. Chawla[3], sunil@seascapelearning.com. [1]Douglas Connect, Switzerland, [2]CAChe Research LLC, United States, [3]Seascape Learning, India

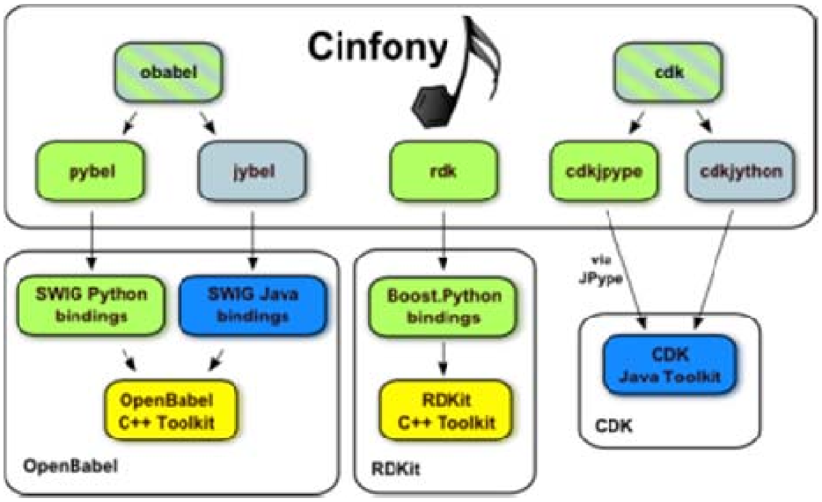
Recent (Q)SAR developments allow a much more accurate prediction of complex toxicological endpoints than a few years ago. This progress has been caused by (i) the development of improved (Q)SAR algorithms and (ii) by the availability of larger and better curated public databases. The routine application of these new generation models is however still rare, because of incomplete, incompatible toxicity databases and QSAR models. The European Commission has hence seed funded OpenTox (www.opentox.org) under the FP7 R&D Framework that provides a unified access to toxicity data, (Q)SAR models; and procedures supporting validation and reporting requirements of REACH. Now, at the halfway stage of the initial three-year project, the technical developments including architecture design, interfaces, ontologies, and approach to web services will be presented and discussed. The experiences with developing initial software prototypes based on the OpenTox approach will be reviewed.

CINF 144

Combining disparate cheminformatics resources into a single toolkit: The Cinfony library

N. M. O’Boyle[1], n.oboyle@ucc.ie, and G. R. Hutchison[2]. [1]School of Pharmacy, University College Cork, Cork, Co. Cork, Ireland, [2]Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania, United States

Open Source cheminformatics toolkits such as OpenBabel, the CDK and the RDKit share the same core functionality but complement each other in their support for different file formats and forcefields, and molecular fingerprints and descriptors. However using these toolkits in the same program is difficult as they are implemented in different languages (C++ versus Java), have different underlying chemical models and have different application programming interfaces (APIs). We describe Cinfony, a Python module that presents a common interface to all three of these toolkits, allowing the user to easily combine methods and results from any of the toolkits.



CINF 145

Role of Rh(III) as negative catalyst in N-chlorosuccinimide oxidation of glycine in alkaline medium: A kinetic and mechanistic study

A. K. Singh, ashokeks@rediffmail.com, M. Singh, dr.manjulasngh@rediffmail.com, R. Srivastava, rashmisri11@rediffmail.com, J. Srivastava, sri_jayasri@rediffmail.com, and S. Rahmani, shahlaau@rediffmail.com. Chemistry, University of Allahabad, Allahabad, Uttar Pradesh, India

Kinetics and mechanism of N-chlorosuccinimide (NCS) oxidation of glycine in aqueous alkaline medium using Rh(III) as negative catalyst have been studied at 35^{0}C. The observed kinetic data suggest that order with respect to [NCS] is unity throughout its ten-fold variation. Making basis to pseudo-first-order rate constant (k_1) values for varying concentration of glycine and OH$^-$ ions, it is concluded that the first -order kinetics observed at low concentration of each reactant changes to zero-order at its higher concentrations. The significant feature of the reaction under investigation is that there is inverse proportionality between pseudo-first-

order rate constant (k_1) and [Rh(III)]. Inverse fractional order in [NHS] and nil effect in [$Cl^–$] were observed throughout their variations. The reaction rates remain unaffected by the change in ionic strength (m) and dielectric constant (D) of the medium. The reaction has been studied at four different temperatures and with the help of observed k_1 values, various activation parameters including the entropy of activation ($\Delta S^{\#}$) were calculated. Spectral studies for the verification of the formation of complex species during the course of reaction have been made by the help of Varian Cary 300 Bio UV-Vis spectrophotometer. Suitable mechanism, consistent with the observed kinetic data together with reactive species of NCS, Rh(III) and glycine in alkaline medium and spectrophotometric evidence for the formation of complex species, has been proposed for oxidation of glycine by NCS in presence of Rh(III) as negative catalyst.

CINF 146

Psychological barriers to good decision-making: How addressing cognitive biases could improve drug discovery

M. D. Segall[1], matt.segall@optibrium.com, and A. Chadwick[2]. [1]Optibrium, Cambridge, Cambridgeshire, United Kingdom, [2]Tessella, Burton upon Trent, Staffordshire, United Kingdom

Better individual and team decision-making could enhance R&D performance. Reproducible biases effecting human decision making, known as cognitive biases, have been understood by psychologists for at least half a century. These threaten objectivity and balance and so are credible causes for continuing unpleasant surprises in late development and high operating costs of compound discovery. For four of the most common and insidious cognitive biases we will consider the risks to R&D decision-making. We will suggest approaches for overcoming these, such as strategies adapted from evidence-based medicine and computational tools that seek to guide the decision making process, encouraging objective consideration of all of the available information and explicit consideration of the impact of uncertainty in drug discovery.

CINF 147

NCI/CADD: Open-access chemical structure web platform

M. Sitzmann[1], sitzmann@helix.nih.gov, W.-D. Ihlenfeldt[2], and M. C. Nicklaus[1]. [1]Chemical Biology Laboratory, Center for Cancer Research, National Cancer Institute, National Institutes of Health, DHHS, Frederick, MD, United States, [2]Xemistry GmbH, Lahntal, Germany

We present an update on the Chemical Structure Lookup Service, the Chemical Identifier Resolver and further services available at the web server (http://cactus.nci.nih.gov) of the NCI/CADD Group. They all have been implemented on the basis our new open-access chemical structure web platform.

We will give an overview on how this resources can be integrated and linked in into one's own web applications. The chemical structure web platform also includes open access to the underlying chemical structure database which currently indexes approx. 103 million chemical structure records representing about approx. 70 million unique chemical structures.

CINF 148

OrbDB: A database of molecular orbital interactions

M. A. Kayala, mkayala@ics.uci.edu, C. A. Azencott, J. H. Chen, and P. F. Baldi. Department of Computer Science, University of California - Irvine, Irvine, CA, United States

The ability to anticipate the course of a reaction is essential to the practice of chemistry. This aptitude relies on the understanding of elementary mechanistic steps, which can be described as the interaction of filled and unfilled molecular orbitals. Here, we create a database of mechanistic steps from previous work on a rule-based expert system (ReactionExplorer). We derive 21,000 priority ordered favorable elementary steps for 7800 distinct reactants or intermediates. All other filled to unfilled molecular orbital interactions yield 106 million unfavorable elementary steps. To predict the course of reactions, one must recover the relative priority of these elementary steps. Initial cross-validated results for a neural network on several stratified samples indicate we are able to retrieve this ordering with a precision of 98.9%. The quality of our database makes it an invaluable resource for the prediction of elementary reactions, and therefore of full chemical processes.

CINF 149

Application of crowdsourcing for metadata curation of digitized texts

A. J. Williams, antony.williams@chemspider.com, R. Kidd, V. Tkachenko, and S. Shevelev. ChemSpider, Royal Society of Chemistry, Wake Forest, NC, United States

The Royal Society of Chemistry has tens of thousands of digitized texts in their archive representing over a hundred years of chemistry research. ChemSpider is the RSC's internet based community resource of structure-based chemistry, serving resources including chemical compounds, synthesis procedures and associated meta-data. We have initiated a project to facilitate structure searching of the RSC archive by integrating the chemical structures associated with the RSC publications into the ChemSpider database. This has involved chemical name extraction and conversion from the publication and manual validation of the resulting data. The resulting data collection demands a crowdsourced approach for data curation. This presentation will discuss the progress of our project, will provide an overview of the associated workflows and provide an overview of how

to utilize crowdsourcing for the purpose of curating the metadata associated with digitized texts.

CINF 150

Five years of collaborative drug discovery in the cloud

B. A. Bunin, bbunin@collaborativedrug.com, S. Ekins, sekins@collaborativedrug.com, M. Hohman, moses@collaborativedrug.com, S. Ernst, sylvia@collaborativedrug.com, and K. Gregory, kgregory@collaborativedrug.com. Collaborative Drug Discovery (CDD), Burlingame, CA, United States

Collaborative Drug Discovery hosts a widely used drug discovery data cloud platform. The CDD Vault is a secure, private industrial-strength database combining traditional drug discovery informatics (registration and SAR) with social networking capabilities. CDD Collaborate enables real-time collaboration by securely exchanging selected confidential data. Traditional drug discovery capabilities include the ability to import/export to Excel™ and sdfiles, Boolean queries for potency, selectively, and therapeutic windows for small molecule enzyme, cell, and animal data, substructure and Tanimoto similarity search, physical chemical property search, as well as IC50 calculation/curve generation, heat-maps, and Z/Z' statistics for archived data (protocols, molecules, plates, hyperlinked files). CDD Public has unique, constantly growing drug discovery SAR content. The CDD Vault, Collaborate, and Public together allow, for example, literature Tuberculosis, gene-family-wide, and private SAR data to be simultaneously queried with commercial compounds for screening (~;3M). Case studies from neglected infectious disease (Malaria, TB, African Sleeping Sickness, etc) and secure traditional commercial drug discovery with global teams of researchers in virtual pharmaceutical companies and between companies (i.e. PI3 Kinase inhibitors for NSCLC) will be presented.

CINF 151

CWM Global Search: An Internet search engine for the chemist

A. J. Kos, software@akosgmbh.de, and H.-J. Himmler. AKos GmbH, Steinen, Baden-Württemberg, Germany

The Internet is a rich source of data and information for chemist. There are numerous multidisciplinary databases available for free on the Internet. Some examples of such data repositories are: PubChem, ChemSpider, eMolecules, Drugbank, KEGG, NIST, ChemSynthesis, PharmGKB, Free patents online ... It should be obvious that an end user is a) not aware of all the resources, and b) has not the time to learn every user interface and is unable to search over all of them. We provide CWM Global Search as an application that enables to search by structure, CAS Registry Number and free text over all these sources.

Presently CWM Global Search performs searches in 30 databases and search engines accessing more than 100 million pages that associate data with structures.

CINF 152

www.emolecules.com: The comprehensive source of commercially available, in stock chemicals

K. Gubernator, klaus@emolecules.com. eMolecules, Inc., Del Mar, CA, United States

Samples of research chemicals are at the core of life science and chemical research organizations. Synthetic chemists use them as building blocks in their synthesis, and biological screening experts use them in their high throughput assays. In order to make the selection and procurement of these chemicals a deterministic process, the catalog data used in the selection process must be reflective of actual in stock availability. eMolecules uses electronic data uploads from most of the top suppliers to achieve 96% reliability of it’s catalog data. The www.emolecules.com web site offers sophisticated data import, exact and substructure searches, and methods for refining searches on an easy-to-use website. Compounds selected can be purchased online on the eCommerce system. As a result, procurement of research chemicals becomes a seamless and predictable process.

CINF 153

Petascale lattice-Boltzmann simulations of dynamical processes in ternary amphiphilic liquid crystalline systems

R. S. Saksena, r.saksena@ucl.ac.uk, and **P. V. Coveney**, p.v.coveney@ucl.ac.uk. Department of Chemistry, University College London, London, United Kingdom

We present large-scale kinetic lattice-Boltzmann simulations of the spontaneous self-assembly of periodic lamellar, hexagonal and cubic (gyroid, diamond and primitive) amphiphilic mesophases in a mixture of oil, water and amphiphiles.. Different types of periodic mesophases are formed as pressure and relative concentration of the component species is varied, in agreement with experiments. We use state-of-the-art grid middleware to explore the mesophase diagram. The Application Hosting Environment facilitates construction of complex workflows involving deployment of simulations on geographically distributed supercomputers and access to terascale computational storage and visualization resources. Our lattice-Boltzmann code LB3D exhibits excellent parallel scaling performance on petascale supercomputers, allowing us to efficiently run large-scale simulations free of finite-size effects. This computational infrastructure has allowed analysis of multi-scale dynamical processes in these nanomaterials at high temporal resolution which was not feasible previously in a production sense.

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Novel, accurate high-throughput 3D pharmacophore screening algorithm

G. Wolber[1,2], wolber@inteligand.com, T. Seidel[1], F. Bendix[1], and P. Markt[2]. [1]Science & Technology, Inte:Ligand GmbH, Vienna, Austria, [2]Centre for Molecular Biosciences Innsbruck, Institute of pharmacy, Dptmt. pharm chemistry, University of Innsbruck, Innsbruck, Austria

Virtual screening using three-dimensional arrangements of chemical features (3D pharmacophores) has become an important method in computer-aided drug design. Although frequently used, considerable differences exist in the interpretation of these chemical features and their corresponding 3D overlay algorithms. We have recently developed an efficient and accurate 3D alignment algorithm based on a pattern recognition technique [1]. In the presented work, we extend this algorithm to be used for high-performance virtual database screening and investigate, whether applying this geometrically more accurate 3D alignment algorithm improves virtual screening results over conventional incremental n-point distance matching approaches.

[1] G. Wolber, A. Dornhofer, and T. Langer. Efficient overlay of small molecules using 3-D pharmacophores. J. Comput.-Aided Mol. Design, 20(12): 773-788 (2006)

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Structure – toxicity relationship study for organophosphorus compounds: QSAR analysis

Y. Paukku[1], yuliya@ccmsi.us, D. Magers[2], and G. Hill[1]. [1]Department of Chemistry, Jackson State University, Jackson, MS, United States, [2]Department of Chemistry and Biochemistry, Mississippi College, Clinton, MS, United States

A QSAR study is performed on a set of organophosphorus compounds in order to reveal structural and quantum-chemical features responsible for toxic effect. The development of QSAR equations which will accurately predict toxicity for organophosphorus compounds is in high demand. Current study is devoted to the investigation of a relationship between structure and acute toxicity of organophosphates by application of quantum-chemical techniques and QSAR approach followed by subsequent validation of the results. Obtained QSAR models are beneficial for virtual screening of toxicity for new compounds of interest. All experimental data have been collected from literature sources. Toxicity of organophosphorus compounds is dependent on conformational properties. Therefore, in order to find the lowest-energy structures, conformational search has been performed prior to optimization of geometries. Quantum-chemical calculations are carried out at DFT/B3LYP level of theory with

6-311++G(d,p) basis set for global minima optimization with further evaluation of electronic properties of target molecules.

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EEM-Hückel model for partial atomic charges

M. Waldman, marv@simulations-plus.com, R. Fraczkiewicz, and W. S. Woltosz. Simulations Plus, Inc., Lancaster, CA, United States

Partial atomic charges are employed in a variety of molecular modeling and cheminformatics applications including force fields and as descriptors in modeling numerous biopharmaceutical properties such as pKa, log P, activity, toxicity, and metabolism. We present a new model for partial atomic charges covering an extremely broad range of chemistries. The model was parameterized using an *ab initio* dataset of almost 1000 molecules and over 19,000 atoms. The partial charges were separated into sigma and pi components using Natural Atomic Orbitals (NAO) and Natural Bond Orbitals (NBO) analysis. The sigma charges were modeled using an Electronegativity Equalization Method (EEM) and pi charges using a Huckel model approach. Performance of the model on both training and external test sets achieved root mean squared errors (RMSE) below 0.05 a.u. Performance on various complex molecules will be discussed along with an analysis of parameter coverage on several large databases.

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PropOrb: A frontier molecular orbital interaction proposer

C.-A. Azencott, cazencot@ics.uci.edu, M. A. Kayala, mkayala@ics.uci.edu, and P. Baldi, pfbaldi@ics.uci.edu. Department of Information and Computer Science, UC Irvine, Irvine, CA, United States

Chemoinformatics methods to assist chemists in the essential problem of reaction prediction are highly desirable. Brute force examination of all potentially interacting molecular orbitals (MOs) is computationally intractable. For example, concurrent work to develop a database of MO interactions yields more than 100 million interactions for a few thousand systems. Inspired by human chemists, we leverage the principles of frontier orbital theory to propose a tool that rapidly identifies the most reactive molecular orbitals in a given system. Due to the simplicity of our approach, we aim to identify only a few top candidates. Further resource intensive refinement, such as quantum mechanical or statistical approaches, might then be necessary to differentiate between the proposer’s suggestions. However, our approach significantly reduces the number of possibilities for downstream analysis. The speed, simplicity, and efficacy of our MO interaction proposer make it an essential component of a reaction prediction system.

CINF 158

Fast and accurate prediction of the 3D structure of small molecules

A. Andronico, aandroni@uci.edu, A. Randall, and P. Baldi. Institute for Genomics and Bioinformatics, University of California Irvine, Irvine, CA, Afghanistan

A large variety of chemical and biological properties of a molecule are related to the spatial arrangement if its atoms (its 3D structure). The positioning of atoms in space can be accurately predicted via quantum mechanics, but, when dealing with large numbers of molecules, it is necessary to resort to less time-consuming methods. In this paper, we present a fast method for generating the 3D structure of small molecules. The prediction is obtained by fragmenting the molecule into rigid segments of known 3D structure: these fragments, stored in a database, are then joined back together using torsions information also obtained from experimental data. Whenever a fragment is not found in the database, different steps are taken, depending on the complexity of its structure. By comparison with other conformation predicting programs, we show that our method produces high-quality 3D structures of organic and organometallic molecules with sub-second prediction time.