echeminfo

Community of Practice for
Drug Discovery & Development

Drug Discovery Design Methods & Applications

A Hands-On Practical Approach
Oxford, July 26 - 30, 2010

Interactive pragmatic workshops with leading experts and industry practitioners...

- Protein Target & Ligand Modelling
- Virtual Screening & Docking
- Structure-based Drug Design
- Pharmacophore Models
- Consensus Strategies
- Focused Library Design
- Quantum Chemical Filters
- Pharmacokinetics & Lead Optimisation
- Fragment-based Drug Design

Use leading-edge methods and software applied to drug discovery problems. Discuss practical examples, methods and emerging techniques.

- Class facilitation, discussions and support led by Community Manager Dr. Barry Hardy and an international faculty team of expert drug discovery application practitioners
- Use leading drug discovery software packages from BioSolveIT, CCG, Cyprotex, Inte:Ligand, OpenEye, QuantumBio, and SimBioSys
- Integrating a case study approach and group work throughout the week on methods, datasets, challenging problems and discussion of results obtained
- One year's membership of eCheminfo included

The workshops will take place at the Medical Sciences Teaching Center, Oxford University.

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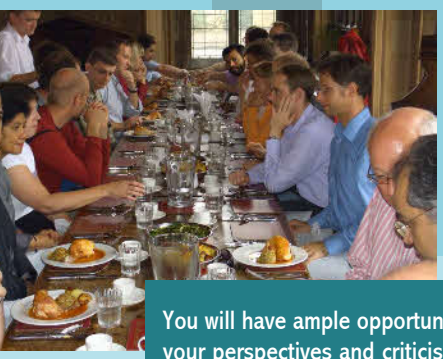
Insights into Kinase Structures and Ligand Design
Jeffrey Wiseman (Pharmatrope) & Barry Hardy (Douglas Connect)

- Analysing the Kinome and Kinase Families
- Biology of Human and Parasitic Kinases
- Target Selection & Validation
- Modelling Target Structures
- Kinase Inhibition Features and Ligand Design Strategies
- Addressing Potency and Selectivity Issues

"I must say I took home a lot of new ideas – things I would like to try out as soon as possible to improve the support of the work of our medicinal chemists"



You will have ample opportunity to discuss your perspectives and criticisms of the methods studied and you'll take-away key nuggets of understanding from these intensive sessions.

Structure-focused Pharmacophores for the Identification of Novel Leads, Gerhard Wolber (Inte:Ligand)

- Derive structure- and ligand-based pharmacophores
- Overlay and interpolate pharmacophores
- Apply fast chemical-feature-based alignment algorithm
- Carry out binding site analysis
- Create shared feature models
- Validate models and assess predictivity

Shape and Electrostatics in Virtual Screening and Lead Hopping
Paul Hawkins (OpenEye)

- Apply ROCS for shape-based virtual screening and lead-hopping
- Apply BROOD for bioisostere identification using shape and electrostatics
- Merge multiple molecules into a single query
- Validate queries in retrospective virtual screens
- Apply robust statistical methods to virtual screening
- Choose the best query for prospective experiments
- Learn how similarity can be applied at the fragment level

"Great week with a very well balanced distribution of talks, hands-on tutorials and social events. All presentations very relevant and enough social activities to get the participants together to engage in discussions."

A fully equipped IT classroom and a variety of software packages will be at your disposal to work through the problems posed by the instructors.

Consensus Strategies for Challenging Dockings
Alessandro Contini (University of Milan)

- Develop docking protocols for protein-protein interaction inhibitors
- Develop method using protein-protein complex structure
- Develop method using crystal structure with co-crystallized inhibitor
- Analyze complexes, finding and fixing all possible sources of error
- Test protocols through docking of compounds with known activity
- Develop consensus protocols across multiple procedures
- Compare hits obtained from different protocols

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Theory to Application: How Quantum Mechanics can be Applied to Structure-Based Drug Discovery, Lance Westerhoff (QuantumBio)

- Analyse interactions with QM-based interaction profiling tools
- Analyse QM simulations of protein kinase B inhibitors
- Apply mixed QM-MM scoring functions
- Analyse Interaction Energy Map of ligand binding residues
- Apply SAR Map to residues for potency evaluation
- Prepare QM simulations using the MOE GUI

"Excellent workshop. Informative and enjoyable from start to finish. Lots of new ideas and best practices to implement asap. It was a great group with lots of different areas of expertise. Scientists from all over the world meant that discussions were interesting and informative."

Return to your lab with new ideas, best practices and software experiences to maximise productivity in your own drug discovery research activities.

User-friendly Ligand-based Filtering and Docking: Results Analysis and Visualization, Katie Simmons (University of Leeds and SimBioSys)

- Combine *de novo* design with virtual high-throughput screening
- Apply eHiTS LASSO as a ligand-based filter
- Create pseudo-pharmacophore for rapid screening of large databases
- Carry out accurate fragment-based docking
- Visualise how ligand hits interact with receptors
- Analyse plasmodium falciparum dihydroorotate dehydrogenase inhibition

Fragment-Based Ligand Design: Teaming up Medicinal and Computational Chemists, Peter Oledzki (BioSolveIT)

- Start design with active small fragment binders
- Develop into a lead structure
- Grow fragment 'needles' into the depths of the pocket
- Merge multiple overlapping binders into a single potent lead
- Link two or more fragments into one compound with optimized potency
- Generate synthetically accessible compounds

"Plenty of diversity in topics. Excellent facilities. I did not realise how many tools were out there. The course structure was good. Social events especially punting facilitated discussion. Good contacts made. Put a lot in context. Hands-on approach a big bonus over lectures."

Pharmacokinetic Modeling and Lead Optimisation Simon Thomas (Cyprotex)

- Apply PBPK modelling to drug design
- Integrate ADME and physicochemical data to predict *in vivo* PK
- Model Human Intestinal Absorption
- Select compounds to have appropriate PK *in vivo*
- Apply sensitivity analysis to direct lead optimisation chemistry
- Apply ADME and PBPK analysis to case study libraries

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Experimental Testing of Predictions
Barry Hardy (Douglas Connect)

- Discuss and select promising predictions for neglected disease targets
- Review the experimental design and planning for the testing of predictions

Group Work & Discussion on Workshop Case Study Problems

At the beginning of the week participants will form themselves into small groups depending on their interests and team diversity. These groups will be given case studies and the associated data and, having agreed on which problem they wish to focus, they will decide on their strategy using the methods and software studied during the workshop. Finally, they will present their results to the rest of the participants for discussion.

Join this international community of leading scientists...

Founded in 2003, eCheminfo is an ongoing Community of Practice (CoP) committed to the core value of outreach with diverse groups in the commercial, government and academic sectors for the sharing of best practices and the development of strategies, resources and methodologies that address specific issues in improved drug discovery and productivity.

The network involves a diversity of subject matter expertise comprised of experienced professionals from the life science and pharmaceutical industry, vendors, research institutes, universities and government.

A strong emphasis on science and innovation in addition to networking and personal contacts and discussion is followed at eCheminfo events. Collaborative research projects furthering drug discovery and safety innovation goals are currently being pursued to advance the creation of a community of research approach to challenging problems and issues.

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Register now for eCheminfo's Workshop Week on
Drug Discovery Design
Methods & Applications

5 ways to register...

- ✓ **Online** at
  http://echem2010-dd.eventsbot.com/
  http://www.echeminfo.com (Ticket Office is only visible after login)
- ✓ **Email** echeminfo at douglasconnect.com
- ✓ **Phone** Nicki Douglas on +41 61 851 04 61
- ✓ **Fax** +44 870 112 38 44 (eFax)
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Payments by bank transfer, cheque or credit card (Amex, MasterCard,

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