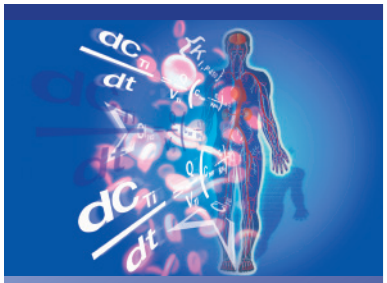
cyprotex AN EVOTEC COMPANY

In Silico **Prediction**

The Cyprotex Discovery Bus

Background Information



Collaboration Opportunities

Let us talk to you about how the Discovery Bus can help your business. We are keen to collaborate with external partners to trial and develop the Discovery Bus further.

Cyprotex's Drug Discovery Bus is an integrated IT solution for the drug discovery industry which automates decision making and information processing. It enables the steps carried out by a human expert to be modelled as a workflow and the decomposition of a more complex task into series of linked steps, each step of which can be implemented by specialist programs known as agents. Intelligent workflow techniques identify when an agent should be called and which tasks are appropriate for an agent to solve. A collection of specialist agents work together in a highly organised and efficient manner with other agents providing management and control.

The applications of the Discovery Bus are numerous and extend to a number of different industries. However some examples of the main applications which are relevant to the Drug Discovery industry include auto-QSAR and laboratory workflow processes which streamline the flow of compounds into assays and, subsequently, the capture and interpretation of instrument data.

How can the Discovery Bus revolutionise your drug discovery business?

Dramatically reduces operating costs by enhancing productivity of resource intensive processes

Enables knowledge to be captured from individuals and shared

Enables more efficient use of internal resources

Less dependency on internal resources therefore provides a higher degree of security and stability in timelines

Reduces bias and subjective human intervention ensuring more consistent analysis

Explores all potential combinations of components resulting in an exhaustive exploration of possible solutions

Automates human decision making processes traditionally performed by resource intensive human experts

Learns from its experiences and continually updates

Reactive to change:
Structural (new methods, new strategies)
Dynamic (new structures, new data)

To find out more contact **enquiries@cyprotex.com**

The Discovery Bus is a novel and powerful software platform designed to enhance efficiency in Drug Discovery by automating human processes using intelligent workflow.

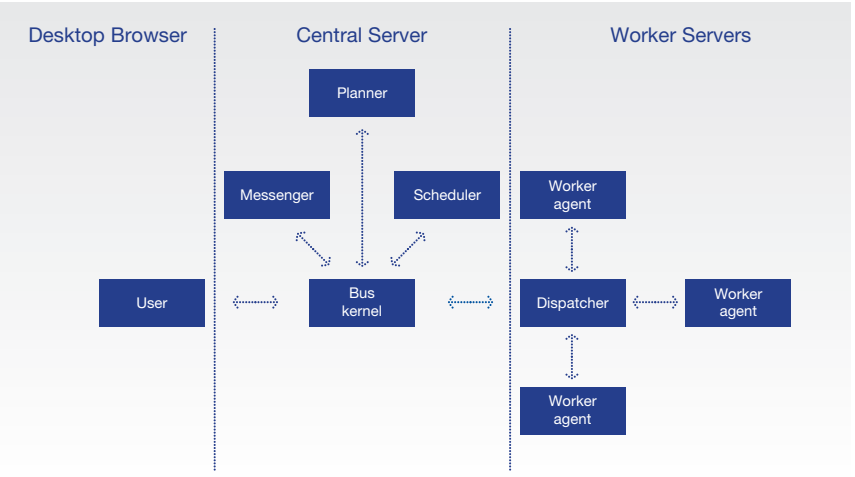
What has Cyprotex to offer?

- Cyprotex has over 14 years experience working in the Drug Discovery Industry and has gained experience from working with a large number of different clients.
- It has a team of software and systems engineers who are continually working on improving processes and efficiency both in the laboratory and in predictive technology.
- Cyprotex recognise that there is an overall drive in the Pharmaceutical Industry to improve efficiency and reduce operating costs, and we are focused on enabling this and a wealth of other benefits through rigorous support for automation of key processes.

What is unique about the Discovery Bus?

- Cyprotex's Drug Discovery Bus comprises of multiple independent software agents distributed across a grid of servers. It implements an innovative software architecture termed competitive workflow.
- The competitive workflow concept has been designed and developed by Cyprotex. It automates human workflow (processes) using a competitive multi-agent software system. Implementing multiple pathways (agents) is significantly more efficient than a standard workflow approach. Where multiple strategies, algorithms or datasets exist, the Discovery Bus explores all potential combinations of components resulting in an exhaustive exploration of possible solutions. The agents compete with each other to achieve the optimal outcome available.
- It is a constantly evolving system. New components or strategies can be introduced and the system is continuously updating in response to newly acquired knowledge such as new screening data. As additional methods are deployed and as wider searches of the solution space are undertaken, solutions to problems improve over time. The Discovery Bus architecture supports extreme late binding: as new agents are deployed they are applied competitively to pre-existing problems.
- The system as a whole learns from experience: pathways which lead to the most successful outcomes are memorised and are given increased priority for CPU resource in subsequent problem solving.

Figure 1
The Discovery Bus Architecture.



The user interacts with the Discovery Bus via a desktop browser. All communication is mediated by the Bus Kernel which controls interaction between user, messenger, planner, scheduler and dispatcher.

The Planner Agent has the task of decomposing (complex) requests and implementing them by coordination of the work of simpler agents. The Messenger Agent enables communication between different workflows. One example of this is that it enables communication of successful approaches between workflows instantiated to solve different but related problems. The Scheduler uses the priorities which have been set to decide what work should be done next. It interacts with the Dispatchers which communicate requests from the Scheduler to the Worker Agents. The Worker Agents perform the individual tasks. The overall process is constantly being monitored by separate agents (meta-agents) involved in controlling and learning from the history of operation maintained by the Bus Kernel.

Application of the Discovery Bus

The Discovery Bus can be applied to numerous different scenarios and industries to improve efficiency. Within the Pharmaceutical Industry, a dramatic change is required to reduce the escalating cost associated with R&D. Two specific areas where the Discovery Bus can have significant impact include applications for *in silico* predictive modelling and laboratory workflow processes.

i. QSPR Modelling

In silico predictive technologies are growing in popularity as the awareness to reduce costs in drug discovery increases This is typically performed by human experts making key decisions about which type of modelling techniques are employed, which molecular descriptors to use and which is the most appropriate set of descriptors to ensure an uncorrelated feature set is selected. Figure 2 illustrates the typical workflow for QSPR model building used.

QSPR model development can be subjective and labour intensive. Rework of the model is required every time new data is available and capacity is limited by human resource. The Discovery Bus is closely integrated with the generation of experimental data. It is programmed to search exhaustively for the optimal QSPR model and continuously update when new data become available. Although the Discovery Bus has a number of well known and reliable model building techniques in-built within the system, in-house favoured techniques can be easily introduced. The performance of the Discovery Bus has been evaluated using previously published datasets. The results shown in figure 3 demonstrate that the automated QSPR modelling process implemented on the Discovery Bus can reproduce previously published QSPR models generated by human experts for two ADME properties, aqueous solubility and human serum albumin binding. This success occurs with full automation and no human decisions about model building techniques, descriptor selection or filtering methods thus reducing the prejudice and drastically increasing speed.

The Discovery Bus has machine learning capabilities which enable the most successful modelling techniques in previous assessments to have increased priority for future evaluations. It frees the time of the human expert to allow them to concentrate on the design and implementation of novel algorithms rather than the repetitive processing of information.

ii. Automation of Laboratory Workflow

Sophisticated instruments are now widely available for liquid handling and analysis which enable rapid screening and data generation for large numbers of compounds. As a consequence, the bottleneck has now shifted to the stage of data and information handling which traditionally is highly resource intensive. Intelligent workflow plays a major role in meeting this challenge.

Expert knowledge is typically based on experience and often not shared within organisations. Building workflow plan specifications requires a compilation of knowledge with best practices implemented. Utilising human resource is expensive, time consuming and subject to prejudice. Automating workflow processes addresses these issues by ensuring improved data consistency with rapid and reliable timelines and ultimately provides a cost effective solution. An example of a laboratory workflow is illustrated in figure 4. The Discovery Bus can capture and automate all aspects of this workflow.

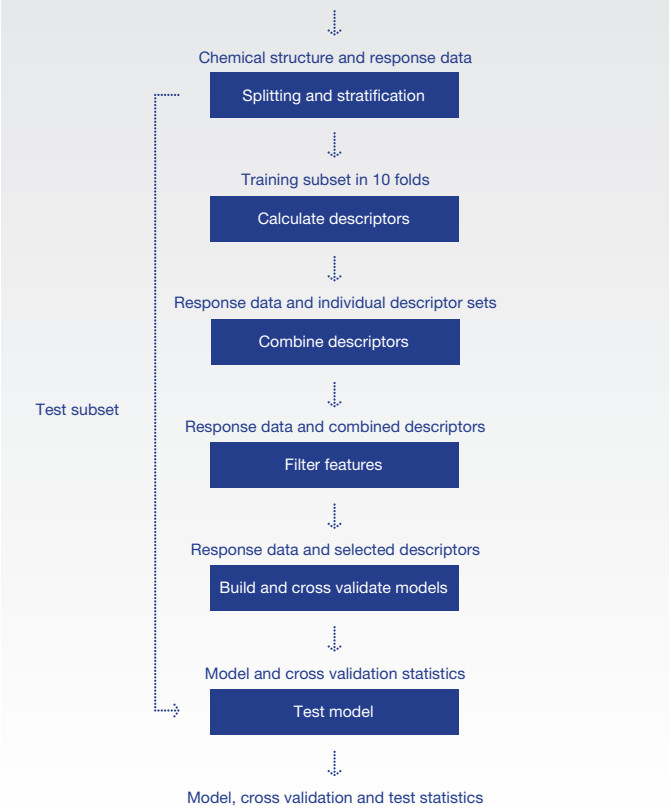
About the team

Cyprotex's team of software and systems engineers work closely with the Cyprotex scientific team. This has been a key component in enabling the current Cyprotex operation to deliver thousands of ADME screening results per month to our customers worldwide. The team was recruited from a number of software consultancies and ISPs and have a wealth of experience in software development and operation across a wide variety of industries.

The team at Cyprotex is led by Dr John Cartmell. Prior to joining Cyprotex, John has worked in a number of different roles. During his time in the theoretical computer science group at the University of Edinburgh, he published several papers on theoretical foundations including algebraic aspects of logic, algebraic descriptions of databases and of programming languages. For many years he specialised in development of computer aided software engineering (CASE) tools and meta-CASE tools based on an algebraically enriched database. The CASE technology was used on projects as diverse as the software and systems design phase of the European Fighter Aircraft and a year 2K systems rewrite conducted by an international bank. As chief designer John worked with and joint architected systems for numerous banks, insurance companies, wholesalers and other organisations. He has at one time worked as a consultant for the CCTA and he was also a member of a core design team for a UK-US collaborative effort to standardise environments for whole process support of software engineering projects. His latest project has been the development of the Cyprotex Discovery Bus and its further evolution into an integrated auto-QSAR system.

Figure 2

Typical QSPR Workflow.



This schematic illustrates the step by step processes undertaken when performing QSPR model building.

Figure 3

Correlation of predicted values generated by the Discovery Bus with actual values for (a) aqueous solubility and [b] human serum albumin binding.

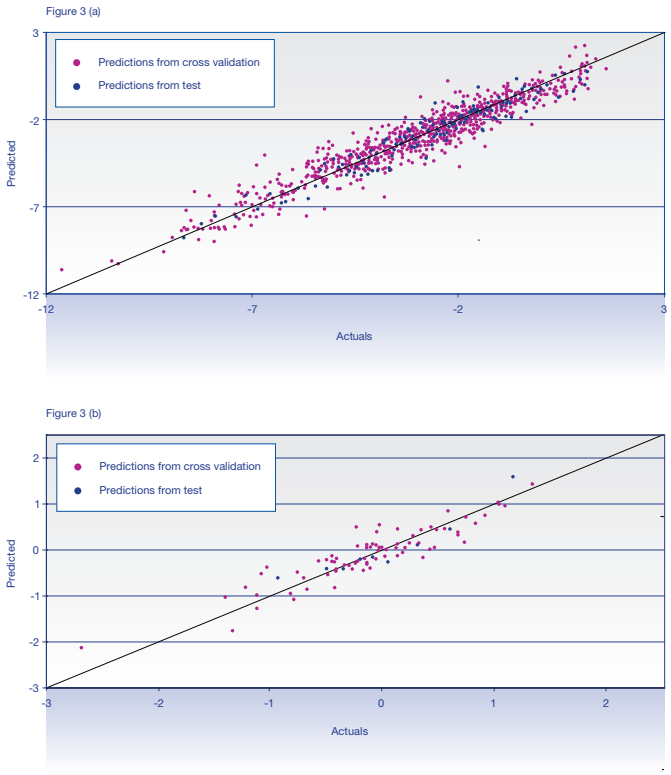
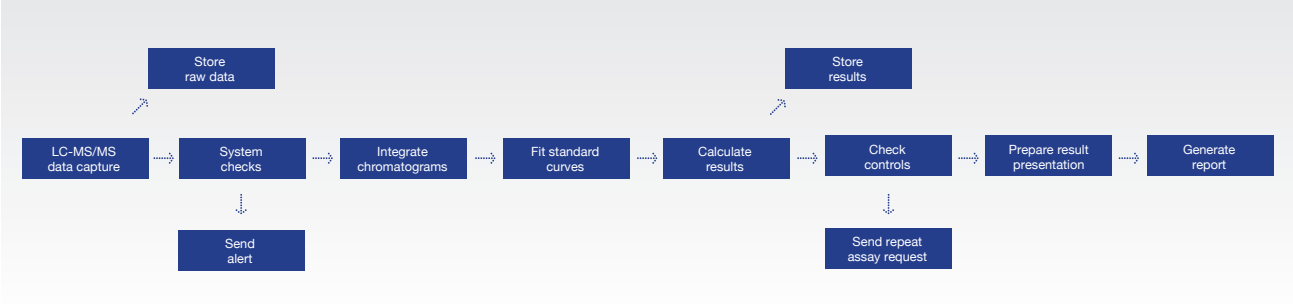


Figure 4

Example of a laboratory workflow process for data capture.



All aspects of the illustrated workflow can be automated enabling tasks to be implemented with limited or no human intervention enhancing both speed and consistency of information handling. This concept can be implemented for other areas of laboratory workflow including assay design and set-up.

References

[1] Cartmell J *et al*, (2005) *J Comput Aided Mol Des* **19**; 821-33

[2] Cartmell J *et al*, (2007) *Curr Opin Drug Discov Devel* **10**; 347-52