KOOP'

AUTUMN '06

Opening Ceremony at HKU, from left to right, Prof Hannah (Dept of Biochemistry, HKUST), Dr Lionel Binns (Worldwide Life Sciences Manager, HP), Prof Ronald Chin (Vice President, HKUST), and Mr Lim Teck Sin (CEO, KP)

Hong Kong University of Science and Technology chooses Hewlett Packard and KOOPrime as key technology partners to accelerate Genomics and Chinese medicine research and discoveries.

Hong Kong, September 4, 2006 – The Hong Kong University of Science & Technology (HKUST) announced today the setting-up of a Bio-informatics facility using HP's Proliant DL580 server with the Linux operating system and KOOPrime's integrated bio-software solutions. This shared facility will focus mainly on genomics and Chinese medicine research and discoveries.

Through this collaboration HKUST, HP and KOOPrime are coming together to address the requirements of important life science issues in Hong Kong and beyond.

With the declaration of the first draft sequence of the human genome in 2000, the three organizations have been pioneering development that are critical to the growth of the life sciences industry.

HKUST is strong in research dedicated to eliciting new knowledge on human diseases via ge-

Contents

Editor's Blog

In this issue of KOOP', I am happy to announce the joint venture of HKU, HP and KOOPrime in a Genomics and TCM R&D facility in Hong Kong. From conceptualization to planning to the establishment, it has taken more than a year of efforts for the facility to materialize. I hereby with to congratulate all the collaborators for the important milestone achieved. Also in this issue, we focus on the healthcare sector, showcasing two IT systems, the PCL CS4 and the Clinical Research Platform. Via close collaborations with the scientists and clinicians, the systems are designed to aid medical practitioners towards a more effective and personalized system for healthcare treatment. Happy reading.

- Sean Koh

nomics and bio-molecular development. Commercially, both HP and KOOPrime have been providing technological infrastructures that help accelerate applied research.

By forming a strong alliance, a comprehensive platform is established to develop core competencies and to tap on resources and expertise within Hong Kong and beyond to meet its objectives. The facility aims to be the leading bioinformatics hub to accelerate scientific advancement in the application of genomics to Chinese medicine and various life science initiatives.

The HKH Bioinformatics Center serves the fundamental HKUST mission: "To advance learning and knowledge through teaching and research, and to assist in the economic and social development of Hong Kong."

HKUST through their understanding of critical biomedical research issues will utilize the bio-informatics platform to enhance their research and extend their collaboration with mainland Chinese and international research institutions and enterprises.

HP will provide scalable high-performance computing hardware initially with the HP Proliant DL580 compute server, and KOOPrime of Singapore will provide their integrated bio-software systems to HKUST for their applied research and development in TCM and genomics.

Besides the opportunity to enhance the competitiveness of the life sciences industry, another significant objective of this collaboration will be to train and develop a talent pool that can help nurture creativeness and collaboration amongst the research institutions and industries in Hong Kong and beyond.

"KOOPrime provides informatics services and products that accelerate biomedical R&D for bioresearch, clinical and pharmaceutical organizations. Given our roots in natural products screening at Singapore, we have interest to leverage on HKH to further our competence in Chinese medicine. Together with HKUST and HP, KOOPrime aims to make Hong Kong a leading knowledge-based Chinese medicine hub across the region" said TeckSin Lim, CEO for KOOPrime.

Advancement in predictive medicine

Singapore, July, 2006 - When treating diseases, the ability to distinguish the subtypes of a disease is important in the application of suitable clinical therapies. Unfortunately, it is not always feasible for clinicians to differentiate the subtypes via visual inspection, despite the use of microscopes to scrutinize the morphology at cellular level. Instead, batteries of tests have to be performed, although they are time consuming, imprecise and expensive.

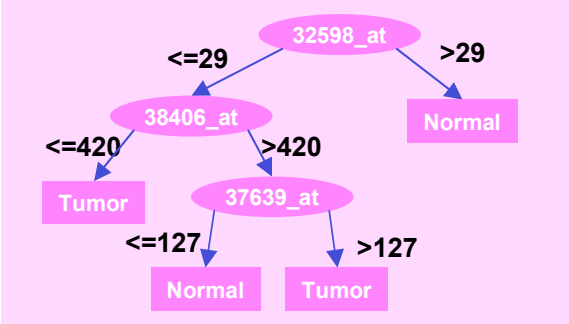
Given the recent advancement in the Genomics, it is now feasible to apply gene chips to tackle such issues for diseases which are hereditary in nature. Embedded within each of these chips are tens to thousands of diagnostic genetic fragments. By analyzing the molecular differences encoded in the genes, it is now feasible to profile the subtypes accurately and quickly.

Such an approach was adopted between St. Jude Children's Research Hospital, National University Hospital and Institute of Infocomm Research Singapore to combat lymphoblastic leukaemia, a disease that afflicts young patients. The hope is to develop a simple and cheap mean of differentiating the types of patients, for example, between those who have high and low risk of relapse, so that clinicians can rapidly 'personalize' the treatment, thus cutting down side effects.

The team, led by Dr Jin Yan, won the Gold Award in the Far Eastern Economic Review's Asian Innovation Awards as a result of this collaboration. The deliverables of the team include a couple of data mining algorithms, namely CS4 and PCL which can sieve out important profiles/ patterns by scanning the huge amount of information that are generated as a result of the gene chips application. A*STAR/ I2R have licensed these technologies for applications within and beyond clinical environment, i.e. for agriculture and bio-energy purposes. Described below is one of

Dr Jin Yan, team leader for CS4 PCL

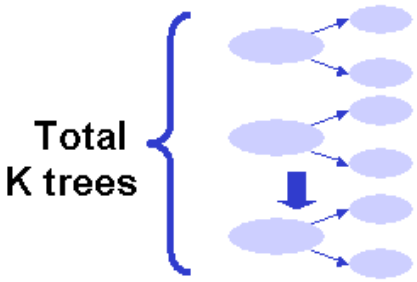
the algorithms, CS4. (refer to seankoh@kooprime.com for more information)



IF activity_gene32598_at <= 29 and activity_gene38406_at <= 420, THEN this sample is Tumor

A challenge for gene chips analysis is the huge and high-dimensional data generated. Powerful computational tools are required to discover significant rules so as to facilitate the translation from complex raw data to clinically relevant and useful diagnostic / prognostic knowledge. CS4 is one such tool that is able to discover rules as decision trees, able to generate and combine multiple decision trees, resulting in the capability to discover multiple diversified and significant rules.

The accuracy of CS4 has also been found to be comparable then SVM and better than neural

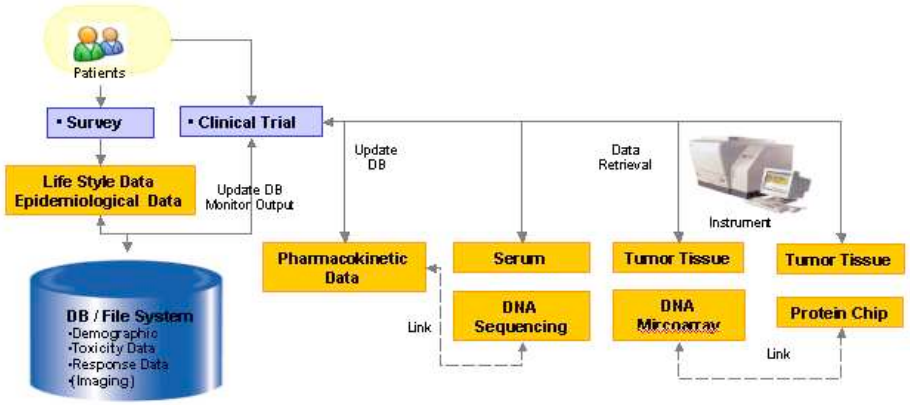


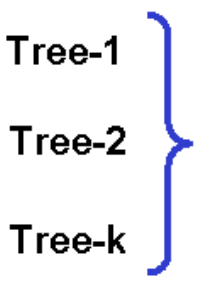
networks and other decision tree generating algorithms.

Deployment of Clinical Research Platform (CRP) for holistic integration of clinical, life style and bio-molecular data

Singapore, August, 2006 - To satisfy the converging needs of clinicians for personalized medicine, drug studies, epidemiological studies, laboratory results collection, etc., there is a requirement for an integrative research platform that can span across both bio-research and medical-research space. Integrating Artificial Intelligence with web technologies and bio-medical repositories, CRP is a platform that manages subjects, protocols, clinical results, genomic tests, etc. for holistic research on diseases and populations. The objective is to execute the research consistently over years of studies and to produce clear, consistent results for clinicians to analyze, ultimately facilitating new discovery and pushing the frontier in healthcare. The benefits for adopting CRP include

- An integrated platform to collect both bio-research and clinical-research data
- Web based interfaces to access system from any computer any where
- An end-to-end system to manage processes for questionnaire surveys, subject recruitment, appointment booking, registration, bio-medical screening, protocol management and laboratory results sharing





The Heart of CRP, Clinical Decision Support System (CDSS)

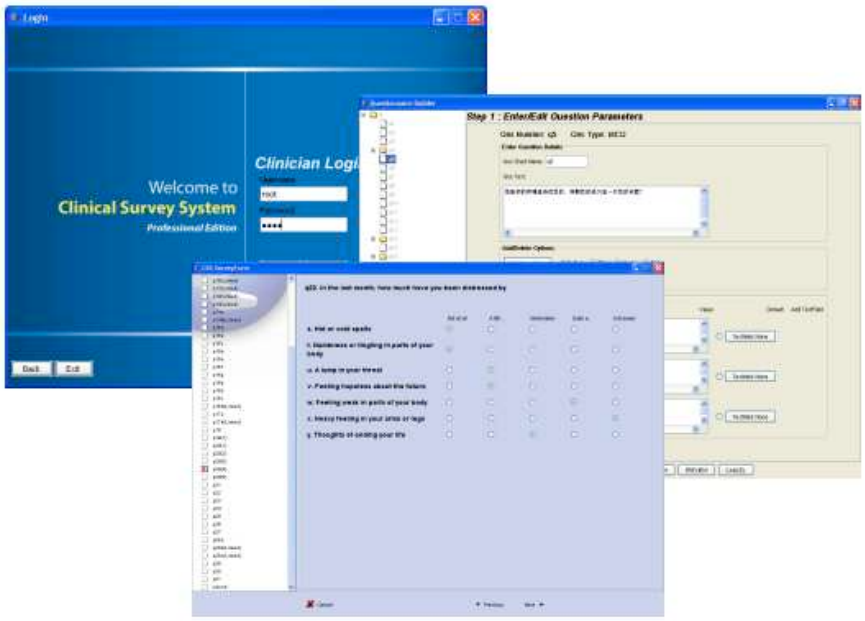
Singapore, August, 2006 - CDSS has been deployed successfully to assist the diagnosis of diseases (e.g. for Temporal Mandibular Disease described in KOOP' Spring issue). It is also feasible to adopt CDSS for CRP implementation, e.g. to verify collection of epidemiological and life style data of subjects who are undergoing trials, to intelligently execute clinical protocols for subjects, etc.

An important challenge will be the selection of suitable AI tools that facilitate the building and maintaining of rules. Probably the most popular expert system available is CLIPS. This is a system that was originally developed at the NASA' Johnson Space Centre for space shuttle diagnostics. The strength of CLIPS lies in its flexibility to be embedded within larger systems, its performance and its ease of maintaining the rules as IF-THEN-ELSE statements, e.g.

(defrule <rule name> "comment"
<condition1> <condition2>…<conditionM>
=>
<action1> <action2> … <actionN>)

CLIPS is a forward chaining engine in that if a given set of data is able to satisfy the conditions of a rule, actions will be executed and this may satisfy the conditions of another rule, and so-on, thus triggering an 'intelligent' chain firing of rules.

Hereby, what is important is knowledge engineering expertise to sniff out the important rules from the domain. Once this is achieved, the rules can then be readily encoded onto systems like CLIPS for intelligent automation of various decision making efforts.



Snapshots of a Clinical Decision Support System that is embedded with CLIPS and developed for biomedical deployment purposes

Automating the Drug Discovery Laboratory – a simple look at implementing a GLP system

Singapore, August, 2006 - "Before 2000, drugs entering the first stage of testing on humans, known as phase I trials, had a 14% chance of reaching the market; today that figure is a mere 7%." – Nature

This narrowing of the funnel for the commercialization of new drugs has resulted in a call of for better operating and documentation practices - a need for greater transparency and credible data in research and development of new drugs. GLP focus on best safety, operating, and documentation practices of research laboratories

Implementation of GLP in the research laboratory can result in increased bureaucracy and paperwork. A recent article by Micheal H. Eillott, President of Atrium Research, stated that discovery chemists spend approximately 20% of their time on non-productive activity like transcription, collation of data for analysis, report writing and notebook entries. In his article, Eillott stated that "In essence, the scientist has become the "data integrator," performing tasks that take time from designing and performing

experiments."

Information Technology hereby holds the key to taking away the hassle of paperwork. The solution is to automate the laboratory. Examples of such solutions include ELN – or Electronic Laboratory Notebook; Chromatography Data Systems, and Laboratory Information Management System, or simply put, paperless laboratory systems.

The first step is to conduct a Risk Assessment which identifies the activities that are to be managed and map out the "To-Be" work flow. Based on operating procedures, User Requirement Specification is put together, which will be used as the basis for vendor selection.

Several ELN, LIMS and CDS packages are available on the market, each having different strengths and weaknesses. A key challenge is to pick the one that will most suit the users needs. Key areas to look at, in no particular order are:

- level of service support
- scale up of the system
- user friendliness
- infrastructure required
- licensing
- web-based
- 21CFR Part 11 – use of Audit Trails and E-signatures
- Matching the Design Specifications to the User Requirements, ensure most of requirements are met.

Concurrent to selecting the right vendor, guidelines and procedures for implementation have to be planned out. Ideally for large scale research centers with multiple laboratories, the system should be done on a pilot scale in a selected laboratory and there after deployed across other labs.

Validation is a highly disciplined process of providing a high degree of assurance that the system performs as required. The Validation Plan sets the standard for conducting the project, and details the various activities required to install a GLP compliant system.

Generally, Validation will consist of 3 phases. The list below states non-exclusively the considerations required to validate an ELN:

1. Installation Qualification – Installation Verification

- Verification of hardware configuration
- Verification of software application files
- Software configuration
- Security settings
- Data back-up and restore
- SOP verification

2. Operational Qualification – Functional Verification

- system start-up / shutdown
- application security setting
- system settings
- data entry boundary test
- functional testing – e.g. sample login, results processing tests
- reports verification

3. Performance Qualification – User Acceptance Testing

- Performance testing – sample life cycle
- Multiple users
- Systems stress test

Validation does not always have to be a lengthy and tedious process. A key to successful validation exercise is pragmatic, clear and testable specifications and requirements with sensible and achievable acceptance criteria and integrity to uncover anomalies and gaps.

Studies have shown more than 80% of laboratories are still practicing a paper laboratory notebook system. This is fast changing with the maturing of paperless laboratory information systems, scientists can focus on drug discovery and not worry about where information is stored. He/she can easily access and obtain information in real time where necessary.

Nansha Science and Technology Forum

China, August, 2006 - The Nansha Science & Technology Forum on "Bioinformatics and Future Medicine" was held at Nanshan during 25 - 26 Aug. Key speakers from Celera Diagnostics, KOOPrime, HKUST, China MOH, Novartis, etc. discussed about their bioinformatics experience in the area of biomedical sciences. Latest issues in personalized medicine, advancement in chinese medicine and bioinformatics computing development were shared with more than 400 participants.

The organizers look forward to having such conferences in the near future so as too encourage further exchange between scientists in China, Hong Kong and beyond.

About KOOPrime

Since 1996, a group of scholars, researchers and IT professionals have been working with one of the largest pharmaceutical giants in the world to develop a system to enhance overall productivity in pharmaceutical laboratories. KOOPrime Pte Ltd was established in 2000 as a result of this endeavor. KOOPrime is the leading provider of IT products and solutions for the biomedical industry. This is made feasible via its workflow-agent platform (KOOPlatform) that integrates components dealing with Data Collection, Data Warehousing, Data Mining and Data Visualization. Systems delivered are Cross-Platform, Cross-Language and Cross-Domain. KOOPrime has operations in the US and also an established presence in Asia, in particular Singapore, Japan, Malaysia, Thailand, China and India. Find out more at www.kooprime.com.

KOOPRIME PTE LTD

21 SCIENCE PARK ROAD
#03-28 THE AQUARIUS
SINGAPORE SCIENCE PARK II
SINGAPORE 117628

TEL: +65 6775 4220
FAX: +65 6775 4206