

Tessellations

News And Technical Updates From Tessella

Edition 64, Summer 2008

Boosting DNA – to help solve crimes

Recent advances in DNA sequencing technology have allowed forensic science to play an increasingly important part in providing evidence in criminal cases, including several recent high-profile murders. However, interpreting DNA test results is far from straightforward. DNA samples retrieved from crime scenes can be unsatisfactory for a number of reasons, including:

- Samples may contain genetic information from several contributors (e.g. if taken from the rim of a coffee cup or from a cigarette butt)
- On certain occasions only minuscule quantities of material can be retrieved (in the nanogram range), which means it may not be possible to determine a full profile using standard DNA sample tests. Consider, for example, the small amount of DNA which might be found on the trigger of a gun used in a murder, but also how critical it may be to the investigation
- The integrity of DNA samples can degrade over time, so there may be a limited window of opportunity to analyze them

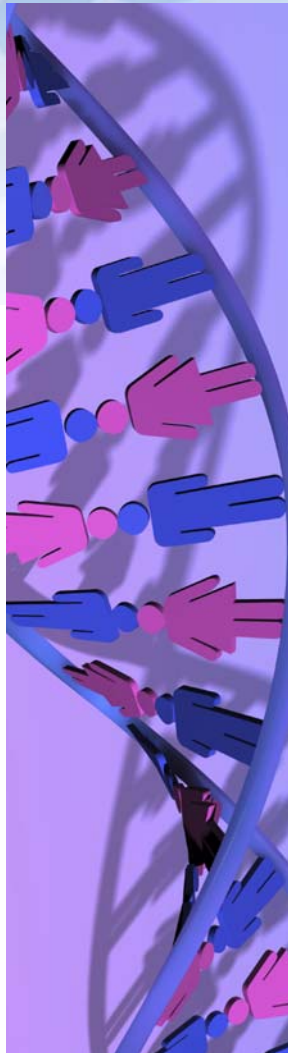
Any of these factors may mean that a sample cannot be interpreted by traditional DNA profiling techniques – and therefore that a serious crime could go unsolved.

Working with incomplete profiles

The UK's Forensic Science Service® (FSS) is the market leader in the supply of forensic science services to police forces in England and Wales, as well as being a source of training, consultancy and scientific support. The FSS has an unrivalled reputation for the integrity, impartiality and accuracy of its findings.

DNABOOST is a set of technologies developed by the FSS which overcomes many of the limitations of poor sample quality by separating mixtures into their component profiles and allowing for loss of information and partial profiles. Rather than searching for an exact match in a database of DNA profiles, the system compares the candidate profile extracted from the sample, however incomplete, against every profile in the database and then ranks them according to how closely they match. An incomplete profile can still provide useful suggestions which investigators can follow up, even though it may not be enough by itself to contribute to the body of prosecuting evidence. The technology, therefore, helps investigators to form a more accurate picture of who might have been at a particular crime scene.

Tessella and the FSS have been working together for several years to deliver the software components of innovative products, such as the FSS-i³ DNA expert system suite, which is made available to law enforcement agencies throughout the world.



Tessella's contribution to the DNABOOST project was in efficiently implementing the FSS's profile search algorithms in software, and providing a web-based user interface to enable operators to run comparisons quickly against a large database of stored DNA profiles.

DNABOOST and real-world crime scene data

DNABOOST was recently piloted with four police forces in the north of England, with very encouraging results – 55% of the samples which were examined using DNABOOST resulted in a new intelligence lead, and a number of prosecutions have been brought as a result of investigations in which DNABOOST played a part. DNABOOST was also shown to increase success rates by as much as 30% in sample types that most commonly yield mixtures (typically, cigarette butts and saliva samples).

In combination with the FSS's portfolio of techniques and technologies, such as Low Copy Number (LCN) which enables profile matches to be determined from very small quantities of genetic material, the potential applications of DNABOOST are further extended. The FSS also conceived, developed and now run the UK's 'National DNA Database', which contains information about both individuals and crime scenes, under a UK Home Office contract. DNABOOST can help to ensure that the data contained in the database works as hard as possible by, for example, allowing previously unsolved cases to be revisited.

Interestingly, the technology may theoretically be applicable to other fields, such as metagenomics, the study and classification of the genetic material found in environmental samples. Such samples often contain information from previously undiscovered microorganisms, which can be exploited in new drug treatments. Academics in this field have begun to

speculate that the ideas at the heart of DNABOOST may help them sort the confusion of DNA found in soil and ocean samples.

The future

DNABOOST has already demonstrated its ability to generate new intelligence leads from crime scene samples which until recently would have been considered useless.

At a time when even many developed countries have only rudimentary DNA databases, and interest in more sophisticated technology is rising quickly, this consolidates both the FSS's international reputation for innovation and their position as a world leader in the provision of forensic services. DNABOOST is also becoming a key tool to help protect the public and to ensure that the victims of crime see justice done.

FOR FURTHER INFORMATION:

- On the Forensic Science Service please visit: www.forensic.gov.uk
- On Tessella please visit www.tessella.com or email info@tessella.com



Scientific software solutions

Less risky business



Image copyright BP p.l.c.

As one of the world's largest energy companies, BP has massive global investments in oil and natural gas exploration and production.

To maintain and run these facilities requires large numbers of people – people whom BP is committed to keep safe. BP constantly strives to eliminate or minimize the risks associated with producing and transporting oil and gas, for the benefit of its own staff, the public and the environment alike.

BP's Major Accident Risk (MAR) team specializes in assessing and modelling the major accident hazards associated with BP's operations. Major accidents, in this context, are those resulting in severe safety or environmental consequences. Led by BP experts **Mike Considine** and **Dave Fargie**, the MAR team had developed specialist tools for modelling onshore and offshore facilities, but recognized that their offshore model suffered from a number of drawbacks.

As Dave puts it, "Although the offshore tool understood the concepts of regions, populations and hazards for a platform, it did not contain any real spatial information. Essentially, the tool relied on the user's individual expertise to assess the likely impact of an event such as an explosion or fire, requiring judgements about what the consequences of an event may be. For instance, will a fire at a given point generate smoke that makes an evacuation route impassable? This reliance on individual expertise meant that, whilst the tool was undoubtedly valuable for risk management, its use was limited to specialists, and since the package relied on individual judgement, this could result in varying results."

In early 2007, Tessella and BP began working on a radically re-thought implementation of the offshore modelling tool. Instead of relying on complex spreadsheets to model offshore facilities, Tessella prototyped a package that allowed the user to graphically construct a model in three dimensions.

The new modelling tool will help to keep people safe on BP's offshore facilities

Tessella's project manager for the work, **Andrew Bowen**, takes up the story: "The aim was to let the modeller see the facility on the screen, matched to the original two dimensional facility plans, but with the ability to zoom and fly through the model in 3d. We wanted to give the user a much better feel for the 3d nature of offshore facilities, and how the elements in an offshore facility hang together." BP was impressed by the prototype system's user interface, and even more impressed by Tessella's record in major accident risk models for other oil and gas clients.

In the summer of 2007, Tessella began work on the first implementation of a full, 3d modelling tool. Not only did this need a sophisticated user interface, but the backend risk models had to be robustly implemented and carefully validated. Andrew's developers at Tessella distilled more complex models of fire and explosion propagation into a single package.

Mike explains, "Each event that we model, say a release of hydrocarbon gas, can have multiple outcomes. In the case of a gas release, it might ignite immediately, resulting in a fire, or it might ignite after a delay, so then there's the risk of an explosion. Or it may not ignite at all, but then we still need to look at the environmental impact. We have to look at the immediate consequences of a modelled event, and all the knock-on effects that can happen afterwards – for example how people move to areas of safety if escape routes are impaired. For a structure as complicated as an oil rig, the number of possibilities can be truly enormous."

Despite the complexity of the software, Tessella delivered a working modelling tool to BP at the start of 2008. The new offshore modelling package, christened OMAR, will add another tool to BP's fight to minimize risks and keep its staff, the public and the environment safe.

"OMAR will give us a better tool to help prevent the occurrence of a serious accident on our facilities," says Mike.

"This is a tool that will make a real contribution to keeping people safe on our offshore facilities," adds Dave. "Modelling offshore facilities in OMAR will help us to target our investment towards the biggest safety gains, and to identify the most effective remedial actions." To find out more about

Tessella's experience and capabilities in the energy sector please email info@tessella.com



*Andrew Bowen
Project Manager
Tessella*



*Warrick Cooke
System Architect
Tessella*

If you would like further information, or back issues of Tessellations, please email info@tessella.com

Clinical trials – the patent clock is ticking

Developing new pharmaceutical products is an expensive and risky proposition. Estimates for the cost of developing a new drug vary from a low of \$800 million to nearly \$1.2 billion per drug. Each successful compound developed typically leaves five to ten thousand failures in its wake, and only for three out of ten marketed drugs does the eventual revenue exceed its development costs, leaving most efforts operating at a loss.

Clinical trials test the efficacy and safety of new pharmaceuticals in humans. Back in 2003, a study of the costs of drug development showed a strong trend towards the clinical trials phase contributing a larger and larger portion of the cost.

By the time a drug reaches clinical trial, pharmaceutical companies have typically invested three to six years in discovery and pre-clinical development at a cost of \$400-600 million, have six or seven years of clinical trials ahead of them, and the patent clock is ticking. At the end of the 20-year patent life, competitors and generic drugs manufacturers are free to share in the revenue, impinging on the developer's ability to recoup its investment. This makes the efficient management of clinical trials a major focus for drug development companies.

The challenges of managing clinical trials extend from selecting a statistically significant study design, through recruiting study *subjects* (healthy patients or those afflicted with the target disease or condition), to screening to ascertain critical health statistics, and finally to administering treatment and tracking a patient's response to the treatment. Tessella's clients report that their studies may extend over dozens of countries and hundreds of clinical sites or centres where patients are treated. Phase III trials, the final phase before approval, involve thousands of subjects.

Once the statistical design for a clinical trial is complete, sites are selected, and processes to collect data from the clinical centres are put in place (often an interactive voice response system).

At each centre, subjects are *recruited* onto the trial according to specific criteria. After an optional initial screening, subjects are randomly placed in one of the *treatment groups*; this process is called *randomization*. Each treatment group receives a different treatment – possibly one of several different doses of the drug being tested, or a competitive product, or a placebo.

To ensure adequate supply at hundreds of sites, drug supply managers require a crystal ball. They must cope with different customs regulations, shipping companies and delivery times, and provide instructions in multiple languages. In addition, they must predict the number of subjects that will be recruited onto the trial (and predict the treatment groups to which they will be assigned), predict the number of subjects in each treatment group that will drop out of the study, and predict delivery delays, loss of supply due to damage in transit, and more.

By far the most costly issues result when the statistical validity of the trial is questioned and (either during the trial or at the end of the trial) it is determined that the study did not provide adequate data to either prove or disprove the efficacy and safety claims of the drug. When a subject is randomized to a treatment arm, if the appropriate treatment is not available, the subject may be switched to a different treatment group; this is called *forced randomization*.

The problem with forced randomization is that it may cause the subjects to be unevenly distributed among the treatment groups, jeopardizing the statistical validity of the trial. Another possibility when the appropriate treatment is not available is that the subject's participation in the trial may be terminated resulting in *lost subjects*. This can also jeopardize the validity of the trial by leaving the trial with too few patients.



Image copyright Stockphoto.com/Paul Klime

This leads many planning efforts to simply predict the worse case scenario and make and distribute enough drug for this case. However, drug supply is often costly and the amount of waste at the end of the trial causes concern.

These conditions have given rise to a new breed of tools for drug supply management: modelling tools that can predict the behaviour of different events during a clinical trial.

At Tessella, we have applied our extensive experience solving complex problems, and our advanced statistical modelling expertise to addressing these needs, and have launched the **Tessella Supply Forecasting Tool** (SFT) to provide drug supply managers with that illusive crystal ball.

SFT provides an intuitive easy-to-use interface, and the capability to import data, lists of centres, standard shipping times, etc, to allow the rapid development of drug supply plans. The tool's advanced modelling of events, and simulation of the clinical supply chain, predicts how well a particular drug supply plan is likely to perform.

Adopting SFT across an organization facilitates the sharing of expertise and encourages standardized techniques providing for more consistent drug supply management. The future of drug supply management will not become less complex, but tools that model the supply chain and trial events and perform hundreds of simulations can make the task more manageable.

To find out how SFT can help with your potential requirements in the area of drug supply modelling and forecasting, or to discuss how Tessella's clinical trials experience might be applied to your unique business problem, please email info@tessella.com

Tessella Supply Forecasting Tool:

- Easy-to-use intuitive interface
- Rapid development of drug supply plan
- Easily integrates with other clinical systems through its import capabilities
- Models and simulates clinical trial events for more accurate forecasting
- Facilitates sharing expertise
- Encourages standardized techniques for more consistent drug supply management



Kathy Reinold
Clinical Technologies
Product Manager
Tessella

Swiss Federal Archive takes SDB

Tessella is delighted to announce a 1.3M CHF contract award to deliver a Digital Archive solution enabling the long-term preservation and management of the digital records of the Schweizerisches Bundesarchiv (Swiss Federal Archive).

The solution will be based on the tried and tested **Safety Deposit Box (SDB)**, developed by Tessella in partnership with The National Archives of the UK (TNA), to help memory institutions (including libraries and archives) face the problems posed by preserving material stored in digital formats.

The core software has already been in use at TNA for four years, as the basis of their award-winning 'Digital Archive' system, and is currently being significantly enhanced as part of TNA's Seamless Flow programme. Other users of SDB include the British Library and the National Archives of the Netherlands and Malaysia.

Jean-Marc Comment, responsible for delivering the project for the Bundesarchiv, said "Tessella's reputation as technology leaders in Digital Archiving and the growing acceptance that **SDB is the solution of choice to the archiving community** convinced us to select them for this demanding project".

Dr Robert Sharpe, Tessella's Head of Digital Archiving Solutions, explained: "We are delighted that the Bundesarchiv have joined the growing SDB community to use our advanced archiving solution. We are especially excited about using the Active Preservation technology to add true policy-driven long term preservation capabilities".



The challenges of Digital Preservation are considerable and best faced by leading institutions working together.

This contract will allow Tessella to continue to build its technology so that the whole SDB user community can benefit.

In combination with our work on the US National Archives and Records Administration (through Lockheed Martin), and the PLANETS European Commission funded research programme, we will be able to continue to offer innovative solutions to these complex problems. We are delighted to be supporting the Swiss Federal Archive.

Face-to-Face

Tessella's technical and industry experts regularly present or exhibit at conferences:

- In April 2008, Tessella's Kathy Reinold presented at the Clinical Supply Forecasting Summit, in Philadelphia, US



- Tom Parke (pictured above), Tessella's Head of Clinical Trials Solutions, regularly presents at conferences in Europe and the US. He will be delivering a half-day seminar on Implementing Adaptive Phase II Dose Ranging Studies, in London on 2nd July, plus presenting on Adaptive Clinical Trials at the Trial Design Conference, in Washington, DC, 14-15 July 2008
- Dr Robert Sharpe (pictured to the left) will be delivering a workshop on "The Problems of Digital Preservation in Archives" at the International Congress of Archives, which is being held in Kuala Lumpur, Malaysia, 21-27 July 2008

To find out more about the conferences that Tessella will be attending in the coming year please email info@tessella.com

Supporting HTE

High-Throughput Experimentation (HTE) is finding increasing use across a range of industries as a means of accelerating the R&D process, developing innovative technology, and bringing products to market faster. HTE has a broad range of applications in the development of formulations, coatings, chemical synthesis, polymers and catalysts, as well as applications in the study of biological systems. To request a copy of Tessella's new capability statement on HTE please email info@tessella.com

Burton office expands

The number of Tessella clients served from our office in Burton upon Trent, UK, is on the increase, and consequently the team has moved into larger offices. Although still within the same building on the Bretby Business Park, there will be more working space for Tessella staff and visitors alike.

Tessella – Providing innovative solutions to scientific, technical and engineering problems

Tessella uses its unique blend of scientific, engineering and IT skills to solve the most complex of technical and business problems in a highly cost-effective way. We have a proven 28-year history of excellence, adding value to demanding public sector and commercial R&D based customers.

Tessella comprises Tessella Support Services plc and Tessella Inc. Our space and defence business, previously trading as Analyticon, is now fully integrated into Tessella.

The group's services include software design and development, mathematical modelling and simulation, algorithm development, infrastructure support, project management and consultancy.

Our enviable reputation for providing high-quality, low-risk, value for money services is backed up by many successful, high-profile projects, plus a high level of repeat business.

For each client problem we develop a fundamental understanding within the 'big picture' context – so our solutions fit. We focus on the details (however intricate) so our solutions work. Our ultimate aim is that the systems we deliver are used by our clients with great enthusiasm.

www.tessella.com

info@tessella.com

Abingdon, UK (Head Office)

Tel: +44 (0)1235 555511

Burton upon Trent, UK

Tel: +44 (0)1283 559150 (new)

Cambridge, UK

Tel: +44 (0)1223 897770

Stevenage, UK

Tel: +44 (0)1438 749886

Warrington, UK

Tel: +44 (0)1925 286800

Winchester, UK

Tel: +44 (0)1962 850055

Den Haag, the Netherlands

Tel: +31 70 354 2296

Boston, USA

Tel: +1 617 454 1220

Washington DC, USA

Tel: +1 240 235 6052

Tessellations is published by Tessella Support Services plc. Our aim is to provide you with interesting information on topical technology issues and to outline key projects which we hope you will find of use. We depend on the feedback from our readers to help us develop Tessellations and to maximize its usefulness. Your input is always appreciated; please send to The Editor (Alison Smith) at info@tessella.com