Detection and Identification of Infectious Disease

Scoping Workshop Summary

Summary

Future user requirements

- Transparent international surveillance systems
- Integrated and linked computer systems that can manage data and respond to queries within hours
- Real-time surveillance
- The ability to identify unusual patterns of disease in large volumes of noisy data
- Homogenisation of heterogeneous data
- Cheap, non-invasive, non-specific, mass produced, generic tests useable by the public
- Self-testing, diagnosis and treatment, particularly non-invasive procedures
- Improved monitoring of population movements in the developing world
- Use of general health surveillance to monitor infectious diseases
- Non-medical surrogate markers for infectious disease
- Identifying sick people who are not displaying symptoms
- Improved contact tracing and backtracking to identify a diseases origin
- Understanding biological noise, and using that information to improve our ability to filter biological information from 'noise'
- Monitoring of wild animals and plants
- Consideration of confidentiality, appropriateness, data protection, storage and freedom of information issues
- Access to and storage of large volumes of data
- Information from data analysis/mining that leads to knowledge about infectious diseases
- Cheap, large-scale sampling for infectious disease identification
- Biological signal amplification and transduction
- Integrating detection/identification/monitoring systems with other technologies – e.g.: mobile phones
- Low technology solutions that are applicable in poor countries

Suggestions for science reviews

- Remote sensing - e.g.: Autonomous intelligent sensor networks, Earth observation (satellites to spot the progression of plant diseases)
- Non-invasive screening and sampling
- Distributed computing
- Nanotechnology, nanochemistry; miniaturisaton of gas chromatography, mass spectrometry etc.
- Smart sensors – e.g.: sensors that can be ingested or implanted in the body
- GM plants
- Integrating detection/monitoring systems with other pervasive technologies – e.g.: mobile phones, intelligent buildings, pervasive communications, GPS etc.
- Data collection, fusion, warehousing, management and analysis, including data mining
- Data filtration to meet user needs
- Pattern recognition software to look at surveillance/monitoring data
- DataGrids, specifically Grid/Web services for homogenous access to heterogenous data and data analysis
- Metadata

- Semantics, including the Semantic Web and semantic and content based search, retrieval and analysis
- Biological sensors: signal amplification and transduction; the detection of small quantities of pathogens in large samples; coated fibre-optic sensors
- Imaging
- Genomics – rapid determination of the genomes of viruses and other pathogens; taxonomy of genomes
- Interrogating natural signals from disease hosts to detect diseases
- Ethical and social issues, including data protection, privacy and IT security
- Lab on a chip
- Smart biomaterials
- Surface interfacial chemistry to detect antigens etc.
- Full use of the electromagnetic spectrum
- Military developments
- Integration of antigen detection to electronic signals, and automatic communication and collection of data

Introduction
On 18 November 2004 the Academy of Medical Sciences and Department of Trade and Industry (DTI) held a scoping workshop to inform the development of part of the Office of Science and Technology's Foresight project on the Detection and Identification of Infectious Diseases (DIID) in humans, animals and plants.

Its objectives were to: explore the cross-fertilisation of ideas from diverse areas of science and technology; identify future user challenges/requirements for DIID as well as explore the technical challenges posed by them; and suggest themes for the Project's state-of-the-art science reviews. The workshop sought to look 10-25 years into the future and encourage expansive and radical thinking.

Key future challenges for DIID and promising areas for science reviews identified at this workshop, in parallel with those from previous workshops, will help the DTI commission reviews of 10-15 areas of science from leading experts in the relevant fields.

SESSION 1: Identifying future user requirements for DIID and exploring the associated technological challenges

Different users have different requirements for the DIID. International agencies have needs that are distinct from those of general practitioners that in turn differ from those of patients or farmers. The needs and boundaries of these stakeholders groups will change over time. Future DIID will therefore be driven by the diverse requirements of many communities that are in constant flux.

Surveillance, screening and health monitoring
In the future international surveillance systems will be required. These will be driven by the developed world in the context of risk-assessed priorities. Such systems will need to be open, transparent and subject to constant review and improvement.

The SARS crisis demonstrated the need for a single international integrated real-time information net that could be filtered for different data. Computer architecture issues will have to be considered when the IT systems belonging to primary care, national and international organisations are integrated and linked. Another important challenge will be ensuring homogenous access to heterogeneous information that allows users to view and compare disparate datasets.

At an individual level people generally want to know whether they are unwell, what they can do about it and whether they need to see a medical specialist. To monitor disease at the level of the individual tests will need to be cheap so they can be produced en masse. Cheap tests are likely to be generic, testing for symptoms rather than specific diseases. Such frequent routine testing of the ‘worried well’ is unlikely to be acceptable if it is more invasive than a saliva swab.

Surveillance and screening solutions need not be over-engineered or high tech. In the developed and even developing world, where population movements are more difficult to track, mobile phones provide a convenient interface for this type of monitoring. Mobile phone companies are already looking at adding features such as glucose tests for diabetics and continuous monitoring of user’s heart rate.

As self-diagnosis becomes more common GP’s might be bypassed in favour of unconstrained walk-in and gated systems to access the national and international agencies. However, unspecific tests carried out by non-specialists might produce large numbers of false positive and negative results. Even very low error rates can have a dramatic effect when applied population wide. Self-testing might lead to self-treatment that could be harmful if the initial diagnostic information was incorrect. Thus information needs to be used responsibly as false cases consume medical resources. To avoid mass confusion/panic access to such tests would have to managed, especially in crisis situations.

Large-scale detection of infectious disease could be achieved through general health surveillance. Rather than looking for specific infections individual’s symptoms could be monitored. Pattern recognition software similar to that used by financial institutions monitoring money laundering could be used to look for anything unusual. Non-specific individual information could then be integrated to provide a population view. This would be particularly effective when dealing with novel pathogens or those with an asymptomatic infectious stage such as influenza or HIV. Non-molecular markers such as measuring the height of crops using radar or people’s spending patterns might also be used as indicators. Once unusual patterns are found contact tracing will be required to identify cases.

One important challenge for such large-scale unspecific monitoring would be distinguishing ‘normal’ and ‘abnormal’ patterns. Diagnostic data would need filtering from biological noise. Initiatives like Biobank could help inform such monitoring. One issue to consider is ensuring that users’ are in control of data as opposed to providing them exclusively with automated results .

Currently plants are routinely screened at national borders for infectious disease. Such measures are also effective for humans, especially when performed at airports. However, outside times of crisis the public might not find mass screening acceptable. Consideration should also be given to the fate of those who test positive.

National borders that contain people and domestic animals/plants prove less of a barrier to wild species. Rather than trying to look at whole wild animals populations it might be easier to use sampling techniques similar to those developed by ecologists.

Increasing surveillance and monitoring raises issues of confidentiality, appropriateness, data protection, storage and freedom of information. These issues are less of a concern when dealing with infectious disease in animals and plants.

Data Management
Augmented detection and identification will produce large quantities of data that will need to be stored and managed. These data will have to then be analysed and/or mined to produce useful information that then requires interpretation to be converted into knowledge. To achieve this goal issues of data filtration, storage and quality will have to be considered. These and other functions will need to be coordinated, processed and managed through international organisations such as the European Centre for Disease Prevention and Control.

Sampling frequency
Real-time monitoring will be affected by the frequency at which different databases are up-dated. Front-end applications might be up-dated hourly while central data warehouses might be up-dated daily or even less frequently. Similar challenges have already been encountered in supermarket supply chains. Further, individuals might monitor their own health on a daily

basis but visit their GP less frequently. Real-time monitoring will also require cheap large-scale rapid sampling that cannot be delivered by PCR. A technological step change is required to achieve this goal.

In contrast to humans or animals plant diagnostics tend to be cheaper and can accommodate larger samples, although factors such as pests, spread of resistance and wild plants need consideration.

Identification
Tests for infectious disease can be divided into specific, non-specific and those that recognise patterns in other data. First-pass tests need to be non-specific, non-invasive, cheap and quick. Second or third pass tests need to be more specific and warrant more invasive, slower and more expensive approaches. Of course different criteria apply to animals and plants where more robust approaches are more acceptable in most contexts.

Another important user requirement is amplification of biological signal. Currently samples may be too small or contain too little material to provide useful data. Signal transduction from the chemical to electrical interface could address this challenge. Parallel simultaneous sample analysis might offer another area for exploration.

SESSION 2: Overarching themes for science review

Defence
Exploring developments in the Defence industry/MoD which might have cross-over into DIID - either as a separate theme or as a consideration in those highlighted

Remote sensing
Scientists in the defence industry are already researching ‘smart dust’, tiny wireless networked autonomous units that are spread from the air, to provide monitoring and surveillance. These intelligent units might take the form of small aircraft or vehicles that use distributed computing to intelligently react and respond to their environment all the while transmitting data. On a smaller scale ‘nanosensors’ based on similar principles could be used for *in vitro* monitoring. These could replace invasive procedures such as biopsy, although potential safety issues would need to be considered and overcome. Chip implants already used in domestic animals might also be extended to humans.

CCTV cameras have the potential to provide images of the infrared and terahertz regions of the electromagnetic spectrum as well as visible light. For example, thermal imaging has been used to screen for SARS by picking out those that may have had a fever at airports. In addition many infectious diseases are carried via airborne particles that could be picked up using sampling devices in air conditioning systems. Plants could also be genetically modified to have ‘built-in’ diagnostics and soil microbes used for monitoring purposes.

Intelligent buildings
Intelligent buildings equipped with remote sensing devices could help monitor infectious disease. Both medical and non-medical data such as people’s movement between rooms might provide surrogate markers of infectious disease when considered by pattern recognition software. Fibre optics could be used as a basis for chemical alert systems in structural/environmental monitoring.

IT and data
As has been discussed the data produced by detection and identification will need to be converted into knowledge. Pattern recognition software is used as part of data mining and ‘artificial intelligence’ might be useful when reasoning over mined data. Heterogeneous data will have to be fused to produce a homogenous output. Today metadata (data about data) is labouriously produced by humans, in the future it might be automatically generated by computers.

Increasing use of GRID computing, including Data Grids; seamless global networking of IP addresses; access to heterogeneous information through interconnected but disparate sets of data; increasing computer power ; metadata; semantic data, including the semantic web; semantic and content-based searching; retrieval and analysis all paly a part in DIID.

Signal amplification and transduction
There is a need to amplify signals from organic samples, especially when the sample is small or the chemical under consideration sparse. Methods of transducing organic into inorganic signals are also required. Signal amplification and transduction requires organic/inorganic interfaces that bind and recognise appropriate molecules. Research into material, surface and solid-state chemistry is likely to be required to achieve this goal. Issues of sensitivity, specificity, labelling, signal vs. noise and transience will also have to be addressed.

Miniaturisation
Bulky equipment/techniques such as gas chromatography could be reduced in size increasingly their applicability.

Imaging
Non-invasive screening is key to monitoring infectious disease. Imaging provides a method of achieving this goal. Materials produced using nanotechnology might help provide smart contrast agents to aid imaging modalities. Some imaging techniques such as X-rays carry risk so may be less appropriate for mass screening.

Interrogating natural signals
All organisms emit natural biosignals. For example, chemicals in the breath, sweat or wound sites. These could be exploited for detection and identification purposes using existing technologies such as gene arrays, MRI etc.

Miscellaneous:

- Genetic interrogation using techniques such as gene arrays or microwave radiation.
- Retinal monitoring as another form of non-invasive surveillance.
- Bioinformatics to distinguish useful biological information from 'noise'

Ethics and social:
Genetic Modification of plants have been controversial in the UK and Europe despite enthusiastic up-take elsewhere. Lessons about communication and perception of risk from the GM experience might be applied to the new technologies required for DIID.

Data protection issues are important in relation to detection and identification of infectious disease. In particular the technical issues are likely to increase with the increasing volume and access to data. All aspects of access including authorisation, authentication and auditing are key. Increased monitoring and surveillance increases potential for abuse of data. These all link to a related panoply of IT security issues.

An important step to allay public concerns about new DIID technology would be to show how it benefits individuals. For example, mobile phones were rapidly adopted despite some fears about microwave radiation as they produced immediate individual benefit.

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