

Chat on a chip

Dr Ian Lawston, Chief Scientist of DSTL Porton Down's Detection Department, talks to Gwyn Winfield about how he sees "lab on a chip" and other biological detectors developing

GW: There is a lot of talk about "lab on a chip" devices and the wonders they can perform, but developers often miss the fact, while miniaturisation makes a great deal of sense in the lab, the finished products often lack the necessary robustness for working with soldiers. Is the future with lab on a chip or does it lie with more deployable PCR or Elisa etc?

IL: One of the problems with miniaturisation is that you have to consider the sensor element in the context of the whole system. You are always going to have to collect large volumes of air and process that air in order to present what you have collected to the sensor, so the sensor is only one part of a larger system. We are interested in "lab on a chip" devices, but they tend to need a scientist or a technician to process the sample, before using "lab on a chip" technology to analyse it. That doesn't sit well in a military environment, where you want a single system that will collect, process and deliver a result automatically. Our view at the moment is that the ancillary parts offer the most scope for miniaturisation, but we are keeping an open mind and there are some interesting developments where some of the laboratory equipment that we use has shrunk from filing cabinet size down to a handheld device.

In terms of detect-to-treat and detect-to-warn, one of the issues is the speed with which you can generate an alarm. If you want detect-to-warn you

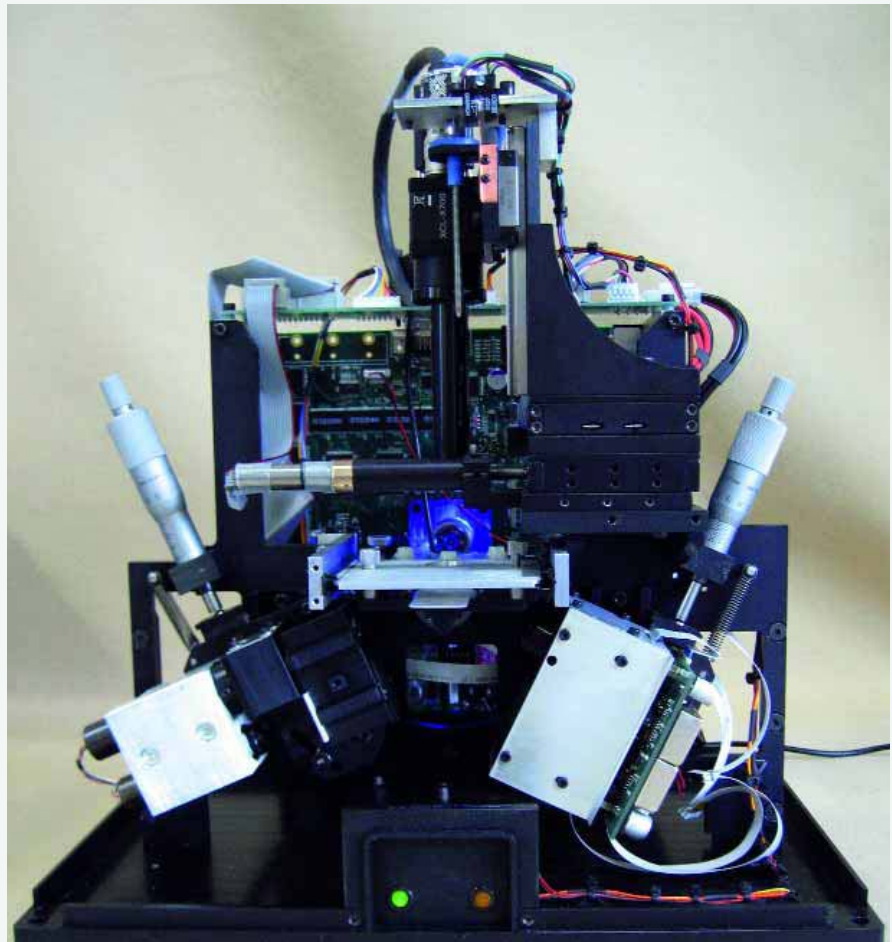
eventually come to the conclusion that you need to provide detection over an area. If we could detect material as it comes into an area and then we might be able to give a warning whereas at present we have to rely on placing detectors upwind.

GW: Yet where is upwind nowadays? During the Cold War it was easy because we knew where "they" were and could site our detectors appropriately. If you are doing detect-to-warn, whether size and shape or fluorescence, then you need the background readings – otherwise you can get false alarms. There would seem to be a technology stumbling block:

that we need environmental background readings to work, meaning that you can't deploy detect-to-warn systems without it. Is there anything that will cut that knot?

IL: One technology that is showing promise at the moment is UV Lidar. The technology has been developed at Porton over the past ten years and we are now in a position where we can interrogate a cloud, decide if it is likely to be biological and work out where it is going – so that could be an element of detect-to-warn. The problem is that we need to work with the user to help develop concepts to make best use of this type of system.

Another approach to area coverage is

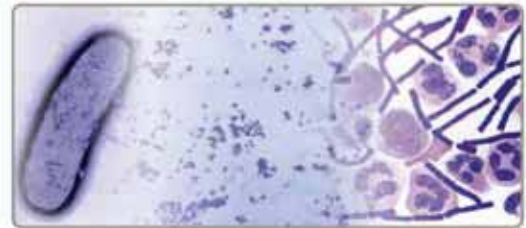


Light Scattering SPR has been suggested as one of the best ways forward in bio detection ©Crown Copyright

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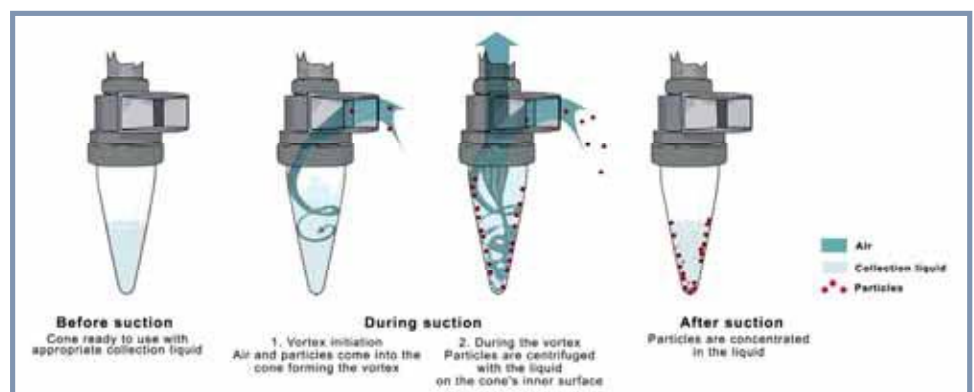
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to have much simpler sensors, but network their output – through a system such as ISMS [Integrated Sensor Management System]. ISMS is the carrier backbone and currently includes a specific instrument, but there is no reason why you couldn't change that instrument for one with different capabilities. Our problem is knowing what information the system needs to improve its performance and then developing the technology to provide that information. My opinion is that, in future, ISMS is likely to be a complex network with fairly simple physical detectors, like fluorescence, that we know work. One of the other possibilities is to measure the static charge that aerosols take on when they are released into the environment.

The problem with the network approach is that we have to think about the threat; most of our defensive posture is based on the Cold War where large areas might be contaminated, whereas now we are probably looking at smaller local issues. One of the issues for ISMS is how the system will identify a local release. You could argue that one of the things that we need is smaller, more capable, point detectors where we have a high degree of confidence that, if the system alarms, a release has occurred.

GW: Doesn't that mean we end up with a Biowatch-type system, where we have simple aerosol capture devices but then use lab on a chip detectors to improve the turn-around?

IL: Personally I think Biowatch-type systems are limited by the logistic issues. It is easy enough to collect the samples and analyse them, and you can get some good high-throughput systems to help you, but the difficulty is the logistic burden associated with having to go out and physically collect samples. You need a large number of people to go out and get the samples, label them correctly, bring them back and process them through the analytical system. All that has to happen in a limited space of time and I am not sure whether it is logistically feasible. I know the US have used Biowatch-type systems in some specific city locations but it is very resource-intensive to run that kind of system.

I favour the development of much smaller point detectors so we can have more of them and distribute them as we need to. Previously our detectors have been stand-alone. They provide an alert but basically the operator of the system has to input information into the network manually. We are getting to the stage where we should think of an integrated system that reaches back automatically to the commanders' battlefield management system.

GW: Down to what level should you proliferate them though? At the Battlegroup, the vehicle, the soldier? As soon as you move down to the lower levels you hit the power requirement and the sustainment that comes with it, and for the dismounted soldier the ability to pass the information on in a timely fashion.

IL: This is where we have the technology issues. With the technology that we have at the moment we have the possibility of shrinking the IBDS concept down from a four-ton truck to a suitcase-sized detector with all the communications and processing within that system. Such systems would be more deployable and less resource-intensive as they don't require specialist operators. The next stage is to go down to something smaller, possibly the size of an MCAD.

GW: But if you wanted a detection capability that small you could go out and buy a COTS General Dynamics



Preparation and sampling is slowly catching up with detection
©CBRN World

4Warn suitcase version [Sentry 3000] tomorrow, but that doesn't have the IBDS capability...

IL: And that is the challenge. With the Portable Integrated Biological Battlefield Detection System (PIBBDS) we are trying to get a capability similar to IBDS into a suitcase-sized format. That means we have to be aware of power issues and look for technology that is less power-hungry than, say, a Cyclone but which can process similar volumes of air. We have been looking at electro-static precipitation as a collection technology – to get a much-reduced power requirement for that part of the system – microfluidics for handling and processing the material collected and a highly capable identification sub-system at the end. Currently, we are looking at light scattering surface plasmon resonance (LS-SPR), which I think is a mature enough technology to enter the procurement chain. 4Warn is a good instrument but it doesn't identify, so we are looking for something in a slightly larger format than 4Warn but which will have greater capability.

GW: IBDS increased the automation, making it easier than PBDS, but if you are going to proliferate the battlefield you cannot rely on skilled people to operate it. Also, if you are looking at some form of sample collection, then you are back into air intake, power and space problems. Power and training might be two of the softer issues but they are going to be as hard to solve as the technical solutions.

IL: I agree. We have been aiming at a power budget that would enable us to move away from a generator and power PIBBD with batteries, preferably small ones, but there is quite a large jump between the power output of the largest battery and the smallest generator. Once you go over the limit for a battery you are committed to a generator, which is a sizeable piece of equipment. We hope to get PIBBDS into development with industry in the next year or so and want a complete system that will collect biological agent from the air, automatically separate and concentrate the agent, and present it to the sensor in the correct format to give relatively quick identification. Looking at aerosol

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detection, the major problem is getting the sample into the collector and the time it takes to go through fluidics and reach the sensor. We believe that we can demonstrate that capability within a ten-minute cycle. The challenge for industry will be to develop an integrated system with improved performance

GW: One of the findings from Impact [See CBRNe World Winter 2006] was the problem of sampling time. If you have spaces between sampling then small releases are completely missed, but if sampling time goes up you're into larger power requirement and then a generator – and once that happens you lose that mobility so what does it matter how small the detector is! This would seem to militate towards a revolution in air sampling or batteries as being the biggest step.

IL: I'd agree with that. The area that I see the least research being done outside MoD, and where there is the biggest potential gain, is in collection and processing technology – it is a very unfashionable area. We have switched from Cyclones, which are relatively power-hungry, to electrostatic precipitation because we can get comparable performance for lower power expenditure. Electrostatic precipitation can give a similar concentration effect as a Cyclone (one cubic metre of air is concentrated into one millilitre of liquid sample) but at a much lower power consumption. At the same time, we are investigating reducing the size and power consumption of the Cyclone while maintaining the efficiency of collection. The problem with that approach is that there is limit to the extent you can reduce the size of the Cyclone and retain its performance.

GW: Part of the problem is that the user always wants a CBR detector in the size of a dosimeter. Yet, as you saw with the Thomsen Bioscience PCR detector, the air intake is smaller than that of the man operating it – meaning that the man remains a far more efficient collector of pathogens than the machine could ever be. It is difficult to deal with the user requirement saying “We want to be really small”, as this translates to the amount that it can detect needing to

be very large – perhaps more than Med CM can deal with.

IL: With personal detection that will always be the case; the speed of response means you are detecting to treat and you will need to take Med Cm if you are wearing it – that will always be a limitation. The user wants a device that is as small as possible and the technology has to get as close to that aspiration as we can. The problem in biological detection is the maturity of the technology in most areas. For example, we can make good PCR systems but PCR suffers from a number of problems that mitigate against its use such as inhibition by environmental contaminants, which means that you need to purify the sample – once you've done that it's excellent and you can have high confidence in it. The trade-off is that you need a bulky system. While the user would really like something small, the ability of technology to provide solutions is not great.

GW: Something that you've not mentioned is flame spectrophotometry, like Proengin's MAB. Does that have legs? It would seem to tick a lot of the boxes – detect to treat, low power, small, accurate...

IL: Flame photometry looks at the chemical elements that are present, and the problem with that is if you are looking for biological material you have a lot of biological background. The air we breathe has millions of particles per cubic metre that are very similar in terms of their constituent elements to biological agents, and the issue is whether flame photometry can give you that level of discrimination...

GW: Yet neither can UV lidar! It has the same lack of discrimination but far higher power requirements. It will tell you whether it has NADH or tryptophan, but not whether it is alive or dead, or pollen...

IL: That is one of its limitations, but we are talking about using it in a remote, stand-off application...

GW: But only during the hours of low light, darkness, dusk or dawn...

IL: One of our recent breakthroughs was being able to work at moderate daylight levels (such as a bright but cloudy day). It would certainly work in the light levels that we have today [a bleak February morning]



*Welcome to the future: an electro-static aerosol sampler
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GW: But is that at an eye-safe level though?

IL: That is one of the issues we need help from other people to solve. It could be a showstopper, but there is knowledge outside DSTL about whether that problem can be overcome or not. We've also looked at firing vertically at a cloud and having an array of detectors looking up about 10 metres, which would reduce the power requirement of the laser. The difference between that concept and UV Lidar is that it can only detect at a point, whereas UV Lidar systems should be able to detect remotely out to a few kilometres. The real issue is what's the best mix of detectors to have – an ISMS system with a variety of point detectors and a stand-off one to help out as well? That is a concept that requires a lot of work.

GW: Will we see PIBBDS married to a single detector or plug-and-play?

IL: One of the aims of the programme is

to come up with a system where you could swap technologies as more capable ones become available. The demands of the microfluidic handling and sample processing systems mean that is not as easy as you might think – you can't plug and play. But if you can configure a candidate technology to work within the specifications of the core system, then you should be able to make it modular. For future systems we are interested in reducing the size of PIBBDS from a suitcase to something smaller (such as shoebox size). To achieve this we are looking at technologies like the Metal-Clad-Leaky-Waveguide (MCLW). This is an optical biosensor that utilises an evanescent wave to directly detect the capture of bacteria, viruses and toxins at the surface of an antibody coated waveguide. Although its mode of operation is similar to that of the Light Scattering Surface Plasmon Resonance instrument already under investigation at Dstl, it has greater potential for

miniaturisation and should be capable of operating with low cost, disposable plastic sensor chips. This is many years in the future – it will be three or four years before we could recommend the development of it; clearly in that time other candidates will come along. Smart holograms are another promising technology, where contact with an agent of interest causes a change in image, colour or brightness of the hologram.

Part of Dstl's job is to work with academia, SMEs and industrial partners to spot emerging technologies like these and exploit them for MoD's benefit. For example, we have a project with academic partners on Whispering Gallery Mode biosensors, investigating the exploitation of light trapped within antibody coated microspheres for the detection and identification of biological and chemical agents. You can get exquisitely sensitive detection but this technology is still a long way from being ready to exploit.

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