NANOLITRE DISPENSING – *on the point of delivery*

Precise low-volume liquid handling methodologies are still sought after by those interested in enabling miniaturised HTS. This article reviews the need for nanolitre dispensing and provides a current perspective on those emerging technologies that have the potential to deliver in the short term. It is clear that the future lies in non-contact methods of droplet ejection.

By Dr John Comley

The drive to deliver low nanolitre volumes has intensified recently as interest in enabling more cost-effective miniaturised screening assays (≤5µL) has assumed greater importance. Fast compound reformatting remains a significant HTS bottleneck in need of a breakthrough in low-volume liquid handling. The recent Pre-Conference Symposium at IBC's ScreenTech 2002 in San Diego on March 4, 2002, provided a timely forum for discussions of today's leading edge nanolitre dispensing technologies. The reality is that there are now several (not one) emerging technologies with nanolitre dispensing or delivery capability nearing commercialisation. These include: 1) contact printing methodologies; 2) non-contact highly parallel drop ejection; 3) true contactless serial dispensers; 4) on-chip micro pumps and valves and 5) nanofluidic microchannel arrays. It is clear that current strategies for uHTS miniaturisation will need to be reassessed once these new low-volume dispensing and delivery tools are fully enabled.

What is compound reformatting?

Compound reformatting is the process by which aliquots of samples in a liquid compound library are transferred from the stock into the microplate in which the assay will be performed. Typically stocks are dissolved in 100% DMSO and stored in deepwell blocks or plated arrays of microtubes, these are often referred to as mother plates. The assay plate is sometimes called a daughter plate, depending on whether there is an intermediate dilution plate. Reformatting can take place between plates of the same density (eg both mother and daughter are 96 or 384-well plates) or between plates of different densities (eg four 96-well plates are transferred to one 384-well plate, or four 384 plates are transferred to one 1536-well plate, or even sixteen 96-well plates transferred to one 1536-well plate). For most HTS campaigns compound reformatting takes place immediately prior to running the screen. Since the reformatting process can take many days depending on the number of plates prepared, it is usual to store reformatted plates prior to running the HTS. However, there is little agreement between Pharma companies as to optimal storage conditions of assay ready plates. As the desirability of using plates of higher density (384 and 1536) became evident and the final assay volume decreased, the need to reformat nanolitre volumes has become more critical.

Why is nanolitre dispensing needed in compound reformatting?

- Driven by assay miniaturisation to higher density plate formats.
- Want to use less compound per assay data point generated.
- Need to transfer samples from neat DMSO stock to assays in ≤5µL.
- Desire to keep the DMSO concentration as low as possible (≤1%).
- Desire to maintain sample concentration as high as possible.
- Uncertainty over compound stability if prediluted in aqueous.
- Preference to prepare assay plates by direct dilution – saving on compounds, dilution steps, money and time.

Therefore need to dispense 50nL or less.

Owing to the previous lack of fast, robust and reliable nanolitre dispensing, most Pharma that have enabled HTS today in low volumes (≤5µl) or in higher densities (1536 and above) have tended to opt for a pragmatic approach in which stock samples are either: 1) diluted with aqueous and dispensed in a more easily managed volume (>500nL); or 2) diluted and/or evaporated from a larger volume (>1µL) of a volatile solvent (eg ethanol). There being general consensus in the industry that the practical lower volume limit on most disposable tip liquid handlers using air-displacement technology is of the region of 500nL.

Driven by the desire to meet customer demands in miniaturised HTS or in search of an application to apply their new liquid handling technology, companies with nanolitre dispensing capability have recently begun to focus their resources in this area. Many of these companies presented details of their technological developments, some for the first time, at IBC's ScreenTech 2002 Pre-conference Symposium entitled 'Liquid Handling Challenges and Solutions in an HTS Environment'. The following are some of the highlights of this rapidly evolving race to dispense smaller volumes, faster and smarter, with less waste and greater precision.

Different approaches used to dispense nanolitre drops:

- Contact dispensing
  – requires surface tension (touch off on destination substrate) to remove drop from dispensing element.
- Non-contact dispensing
  – relies on force to eject aspirated drop from dispensing element, does not involve contact with destination substrate.
- True contactless dispensing
  – involves liquid drop ejection from source without entry of dispensing element into source or contact with destination substrate.

Contact dispensing

Up until very recently nearly all methods of dispensing low (nanolitre) volumes involved contact (tip touch) between the substrate (usually a polystyrene plate) and the dispensing tip, needle, nozzle, pin or probe. Herein lies the biggest weakness of this approach, in that depends on the tolerance (flatness) of the microplate substrate, the quality of the individual probes (length, straightness, material qualities, surface coating etc) in the dispensing head and the uniformity of the withdrawal process from the contacted surface. Despite these limitations several companies (eg Robbins Scientific – Tango and Zymark Corp – SciClone ALH) have recently introduced low volume dispense heads on their liquid handlers, with sub 200nL capability. The Tango system uses glass syringe-pumps attached to DuraFlex^{TM} needles, which are made of a flexible titanium alloy tubing that snaps back to its original shape, even after severe bending. This enables firm contact with the base of the microplate without risk of damage to the needles. In contrast, the Sciclone ALH dispense head has rigid fixed cannulas and uses a reduced-sized piston driven by high resolution motors. Zymark claims its system has an operating range of 100nL to 5µL – delivering CVs of better than 5%. Another contact technology making something of a comeback recently is pin tools. BeckmanCoulter Inc was one of the first companies to offer a 384 pin tool on its Biomek workstation in the mid-1990s, now most liquid handling companies offer this option (eg PerkinElmer Life Sciences supplies a series of pin tools for use on the PlateTrak).

Basically, most pin tools are suspended arrays of solid nails in which the volume dispensed can be directly related to the surface area of the base of the pin. The main advantages of pin tools is they are inexpensive, can be arrayed at high density (eg 1536), can be made to float independently within the array (so uniformity in the substrate is less important) and can easily be attached to existing dispensing systems which have control over dispense head movement. Contact printing with pin tools has emerged as the main method used in the production (arraying) of biochips and a wide variety of pin types (eg split pins, slots, quills, tweezers, pin-in-ring) are now available (see Telechem International Inc and Point Technologies Inc). The uptake of pintools by HTS user has however been rather limited. This may reflect the difficulty in matching large arrays of pins to minimise the inter-pin variation. In addition, the volume requirements for HTS are currently significantly larger than for biochips and where precision of pin tool dispensing in a production environment typically is between 10-25%CV, although some pin manufacturers claim a lot better results (V&P Scientific Inc).

When you consider all the other variables in the screening process, particularly the compound concentration in the library stock solution which is rarely known with great accuracy, the variation associated with pin tools should be acceptable for most HTS. However, most screeners seem to demand that new dispensing systems have a precision of less that 10%CV. Needless to say pin tools can be successfully applied to HTS as Tim Walton from Arena Pharmaceuticals Inc illustrated at the

Figure 1

A continuous reel of TTP LabTech's Mosquito precision pipettes (left). Pipettes consist of stainless steel piston in a close fitting polyethylene barrel, ultrasonically welded to carrier tape to provide a continuous feed system (right)

Symposium with his elegant paper on the use of a 1536 pin tool for GPCR screening using melanophores in a lawn format.

Another new development in contact dispensing presented at the Symposium was Mosquito technology from TTP LabTech Ltd described by Tom Edwards. This technology utilises a continuous reel of miniature precision pipettes mounted on a bandolier to combine the performance of fixed head dispensers with the convenience of disposable tips (**Figure 1**). Each pipette is a positive displacement device capable of dispensing between 50 and 500nl of a wide range of fluids precisely and reliably. Although originally developed to dispense into a continuous tape of depressed mini-wells, which formed part of the Acumen uHTS system, Mosquito technology is now available as a compact, bench-top instrument (Probosys) designed for 384 and 1536 plates. A possible limitation of this technology is that processing is currently limited to 16 pipettes at the time, so reformat cycles for an entire plate, even without washing tend to be slower 384 head devices.

Non-contact dispensing

The key benefit of non-contact dispensing is that it is independent of tip touch, you therefore do not need to enter the wells of microplate to dispense and potential collision and contamination issues are avoided. Owing to the fact that dispensing can occur from the top of the well, plate processing times can be significantly faster when drops are dispensed serially on the fly. For several years dispensers with reliable non-contact nanolitre capability have been available from Cartesian Technologies utilising its high speed synQUAD^{TM} dispensing technology based on a microsolenoid valve coupled with a syringe pump, synchronised with an XY translation stage. Other systems based on similar syringe-solenoid technology have emerged in the past year (eg Gilson Inc's. Constellation 1200). Piezoelectric dispensers are also available from Gesim mbH with drop on demand capability down to 100pL. However when it comes to reformatting high density plates all these systems, which usually have between 4, 8 or 12 channels, are fundamentally slow, owing to the larger number of repeat aspirate-dispense-wash cycles in this process. The value of a highly parallel non-contact dispense system has therefore been recognised for some time, but few have been commercialised until this year. Earlier efforts by Packard and Aurora BioSciences in the late 1990s to develop 96-channel piezo dispense heads and more recently by Cartesian Technologies to promote 96-channel synQUAD heads were not widely taken up owing to their high cost, large dead volume, mixing with the system liquid and mechanical (service) complexity.

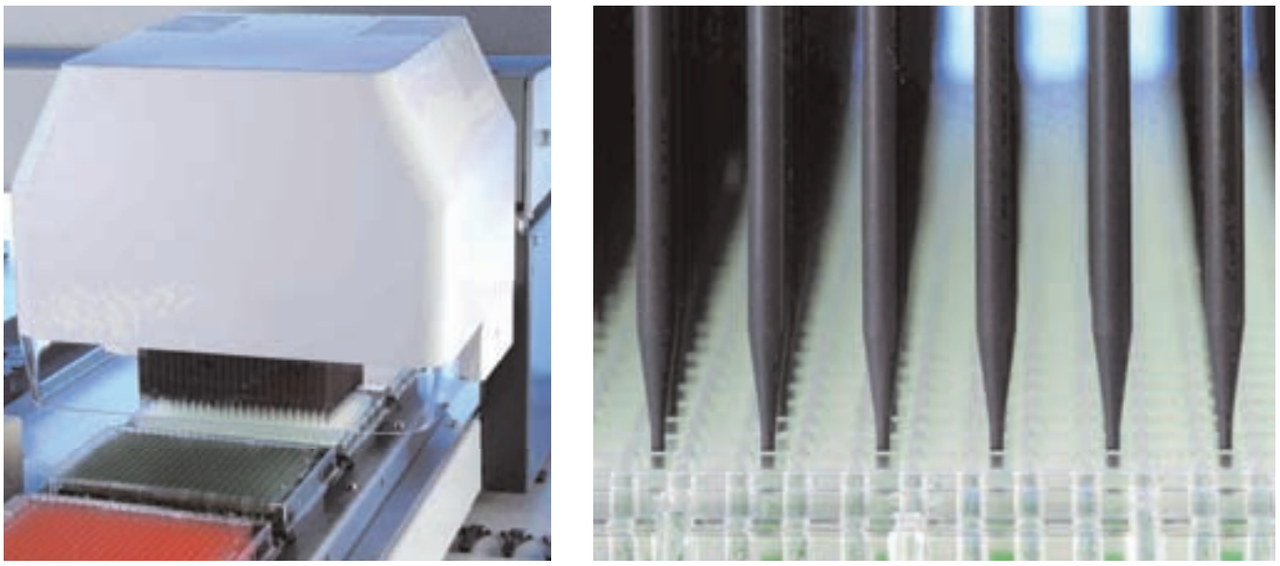

Figure 2
Tecan's 384-channel Impulse™ pipetting head on a Genesis® workstation (left). Close-up of the fixed tips on the Impulse™ head, entering a 1536 plate

Impulse™ is new non-contact pipetting technology recently launched by Tecan at LabAutomation 2002 (Palm Springs, January 27-30, 2002). Impulse™ technology is based on a piezo-actuated 384 piston integrated fluid-filled system with fixed tips. It is available with Tecan's new 384-channel pipetting heads for the Genesis® workstation, TeMO™ multipipetting option (**Figure 2**). The 384 Impulse head is capable of non-contact dispensing over a broad dynamic range (50nL to 50µL). Impulse™ sounds very impressive, but it is too early to comment on the reliability of its piezo-actuated fluidic mechanism or if the tip washing will be as efficient as Tecan claim.

Equally exciting is the newly released Hummingbird™ technology described by Don Rose of Cartesian Technologies Inc at the Symposium. This non-contact technology transfers sample by dipping an array of narrow-bore glass capillaries (currently limited to a 96 or 384 head) into a source plate, filling the capillaries by capillary action and dispensing into the destination plate by applying pressure to the back side of the capillaries. The transfer volume is determined by the volume of the capillary and the technology has been proven down to 20nL. The appeal of this technology is its simplicity; there are no moving parts like syringe pumps involved and there is no dilution or sample loss during transfer. As the outer diameter of a 50nL capillary is <400µm it is possible to make a 1536 head and as the capillaries are inexpensive a disposable head is a likely next development. Cartesian currently offers the Hummingbird™ dispense head as part of a compact benchtop workstation with two plate positions (with active positioning) and a wash station (**Figure 3**). The system comes with pre-programmed reformatting methods and is capable of local and remote control.

The Dispensing Well Plate (DWP) concept[1] discussed by Peter Koltay of IMTEK has some similarities to the Hummingbird™ in that both offer highly parallel non-contact nanolitre dispensing with capillary filling and pneumatic actuation. Where the DWP differs is that it consists of an array of 1536 nozzles (the geometric dimensions of which precisely determines the dispense volume) each connected by a capillary to a separate reservoir, laid out like a conventional 1536 plate (**Figure 4**). The reservoir is designed to be filled by conventional disposable tip 384 dispensers with several µLs of sample. The nozzles then fill from the reservoirs automatically by capillary action. Application of a pressure pulse across the top of the entire DWP held within an actuation unit leads to the simultaneous ejection of a fixed volume (eg 50nL) to all wells of a destination 1536-well plate positioned beneath the DWP. The DWP is capable of making multiple dispenses at 10ms intervals within the limits of the volume contained within the reservoir, with minimal dead volume. So far extraordinary dispensing performance of 50nl

(<1%CV) has been demonstrated with water or DMSO using a prototype silicon-glass DWP. The DWP, unlike Hummingbird, is an extremely robust technology in that the dispensed volume is independent of the pressure pulse length and duration, so the same volume is always dispensed irrespective of the viscosity and varying atmospheric (laboratory) conditions. Efforts are now under way to make a 1536 disposable DWP using plastic production technologies. IMTEK are currently in discussion with a plastics partner (Greiner Bio-One GmbH) and several liquid handling/automation companies. The target date for the launch of a disposable DWP is September 2003. If multiple copies of the library stored within the DWP are not needed right away the possibility exists that the DWP could be used as a short term library storage device. Apart from reformatting applications the DWP has other potential in uHTS eg simultaneous compound addition to a time-dependent assay (dispense and image) or bulk reagent addition of volumes of 1µL or less to all wells at once with extremely high precision. There is no reason why the DWP plate format has to be 1536, lower formats (eg 384) are possible. In addition, a DWP has been designed where the same reagent is dispensed from all 1536 or 384 nozzles.

The idea of combining the shipping, storing and dispensing within the same device is taken further by the SmartPlate™ concept from Boston Innovation Inc. The SmartPlate™ assigns a 100% DMSO dissolved compound to a sealed tap (maximum volume about 15µL), formatted in a 384 array. The samples are never exposed to air, moisture or light. The tap is the storage, metering and dispensing element, capable of delivering volumes from 5-100nl in a non-contact manner by utilising direct dilution with a larger volume (1-6µL) of diluent (eg buffer or DMSO). Reformatting, disposable tips and wash cycles are all eliminated in the process. In addition to parallel dispensing for HTS, all SmartPlate™ channels are individually addressable enabling hit picking for confirmation and secondary screening. The SmartPlate™ is currently at an early stage of evaluation with selected Pharma partners.

Figure 3
Cartesian Technologies Hummingbird™ benchtop workstation (left). Close up of a 50nL Hummingbird™ capillary cassette, showing 384 capillaries which are about 5mm in length (right)

True contactless liquid handling

Picoliter Inc recently featured in DDT[2] as one of the top 10 start-up companies in 2001. Rich Ellson from Picoliter Inc gave the first public presentation of its Drop Ejection Technology based on acoustic transduction at the Symposium. This unique technology enables single liquid drops in the volume range of 0.1pL to more than 1 µL to be ejected from starting volumes as low as 1nL. The advantages of the contactless drop ejection mechanism is no plugging, no cleaning, no cross-contamination and no waste, together with compatibility over a broad viscosity and liquid vapour pressure range. The ejection has low shear and as such is ideally suited to maintaining bioactivity of proteins and viability of cells. The technology is compatible with a wide range of source and target plate formats, from 384, 1536, 3456 and microscope slides. The process involves coupling the transducer to the bottom of the source plate with water and in the case of a destination microplate (or microscope slide) mounting it inverted on an X-Y stage, directly above the source plate. Surface tension forces dominate over gravitational forces for liquids in these small wells, and the liquid is held in place even though the plate is inverted. Non-contact and rapid serial processing leads to quick plate reformatting, eg about three minutes for 1536 well plate to well transfer with no waste and clean-up hassles. Part of the ejection process involves the ultrasonic interrogation of the well surface, a capability that has potential application in HTS, both in determining well volume, fluid characterisation and for internal standardisation of high density assays. It will be interesting to see if the potential of this technology is commercially realised over the next 12 months.

Alternative HTS strategies utilising nanoscale liquid handling

BioTrove Inc gave a technology seminar at ScreenTech describing its Living Chip™, a nanofluidic platform made up of a uniform and addressable array of precisely machined through-holes. Each through-hole is capable of holding 50nL of solution in isolation. Capillary action draws fluid into the through-holes and surface tension holds them in place. Stacking of two or more precision aligned arrays (nanoplates) results in massively parallel mixing and initiation of reactions (currently around 10,000/chip) between fluids of co-registered through-holes. Inter-channel cross-talk is prevented through application of exterior hydrophobic coating. Automated fluidic handling using an array of micro-syringes inserted into the through-holes of a stack of nanoplates into the wells of a microplate located beneath the stack has enabled fluidic interfacing of the Living Chip™ with 96 and 384 well plates. Using this approach it has been possible to simultaneously load multiple arrays from a single aspirate. In addition, dispensing from the nanoplates can be achieved by applying a focused gas jet to the liquid retained in a through-hole with the liquid collected into a microwell positioned beneath. Relative to other microfluidic platforms, the Living Chip™ enables conservation of scarce samples by decreasing storage and assay volumes by around 100 fold and combines it with ultra high throughput analysis (possibly up to 106 data points/day). Integration of

library storage with screening in the Living Chip™ potentially eliminates the materials bottleneck associated with storage in conventional microplates. Interestingly the Living Chip™ has many similarities to the GigaMatrix™ plates that Diversa Corp recently described at LabAutomation 2002. These 100,000-well plates hold 250nL per microchannel and are being used at Diversa for the uHTS of large gene libraries[3].

Ian Manger presented Fluidigm Corp's alternative approach to microfluidics at the Symposium. Its on-chip pumps and valves enable precise mechanical pumping and switching of minute (nL) quantities of fluid. Fluidigm uses a technique called multi-layered soft lithography to fabricate at the microscale its four basic microfluidic tools (a pump, valve, mixer and multiplexer). The beauty of this technique is that is possible to rapidly iterate between one chip design and another, which is of value in rapid device prototyping for assay development. By combination of Fluidigm's toolbox it can create and control basic or complex fluidic networks in an integrated chip (**Figure 5**), allowing the user to perform specific bioassay applications. Fluidigm's on-chip technology even allows for high-density multiplexing and parallelisation of processes, with arrays containing up to 5,000 elements possible.

Impact of new nanolitre technologies on HTS

The suitability of the emerging nanolitre dispensing technologies for HTS compound reformatting is compared in **Table 1**. Of the new technologies presented at the Symposium, Cartesian's Hummingbird™ looks most likely to make an immediate impact as it is relatively easy to see how it could be incorporated as a dispensing module or upgrade in existing library reformatting systems. Developments like IMTEK's DWP potentially offer a lot more in that the DWP is ideally suited to support 'just-in-time' dispensing, where compound is stored in a ready to screen format and dispensed immediately prior to assay assembly to either an empty plate; into buffer or even into the assay itself (the latter being the preferred mode of dispensing for most cell-based assays and absolutely required for ion channel assays). The major driver for a 'just-in-time' strategy, however, is that it takes the uncertainty out of compound storage (unknown degradation in dry films) and redissolution back into aqueous. However, one shouldn't overlook the fact that implementation of a 'just-in-time' strategy would necessitate significant change to existing compound management practices, which would not happen overnight and could impact on the rate of introduction and potential customer acceptance of the DWP.

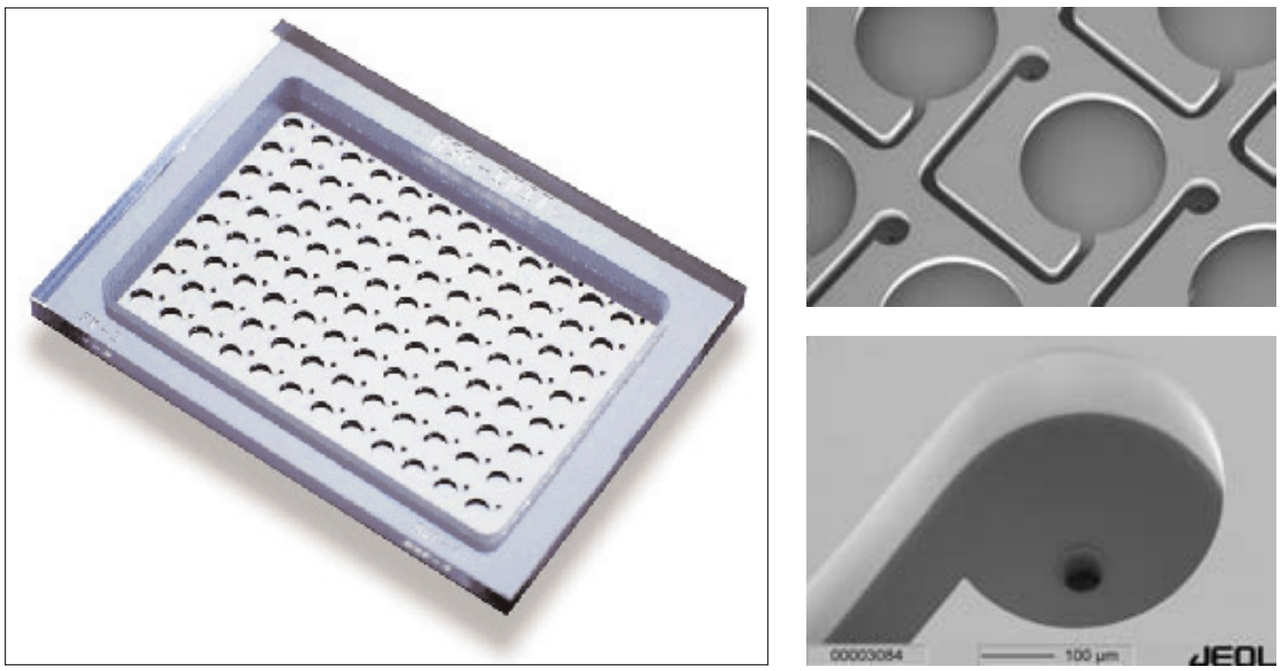

Figure 4

IMTEK's 96-channel silicon/pyrex prototype Dispensing Well Plate (DWP) with reservoirs at 2.25mm pitch (left). SEM image of DWP reservoirs connected via a long microchannel to the dispense nozzle (top right). SEM image of dispense nozzle showing orifice in centre (bottom right)

References

1 Koltay, P, Birkenmeier, B, Steger, R, Sandmaier, H and Zengerle, R (2002). Massive Parallel Liquid Dispensing in the Nanolitre Range by Pneumatic Actuation. Actuator 2002, Bremen, Germany, 10 June 2002.

2 Ellson, R (2002). Picoliter: enabling precise transfer of nanolitre and picoliter volumes. DDT. 7, No.5 (Suppl.), S32-S34.

3 Lafferty, WM (2002). GigaMatrix™: 100,000-well screening platform. Abstract HT2. LabAutomation2002, Palm Springs, USA, January 27-30, 2002.

Websites or e-mails of companies cited in this article

Allegro Technologies Ltd
www.allegro-technologies.com
Arena Pharmaceuticals Inc
www.arenapharm.com
Biotrove Inc
www.biotrove.com
BeckmanCoulter Inc
www.beckman.com
Boston Innovation Inc
www.bostoninnovation.com
Cartesian Technologies Inc
www.cartesiantech.com
Fluidigm Corp
www.fluidigm.com
FLS (Fluilogic Systems Oy)
www.fluilogic.fi
Gesim mbH
www.gesim.de
Gilson Inc.
www.gilson.com
IMTEK
www.imtek.uni-freiburg.de/anwendungen/DWP.htm
LabAutomation 2002
www.labautomation.org/LA/LA02/index.htm
Nanolitre
www.nanolitre.com
Nanolytics Inc
www.nanolytics.com
PerkinElmer Life Sciences
www.perkinelmer.com
PicoLiter Inc
www.picoliterinc.com
Point Technologies Inc
www.pointtech.com
Robbins Scientific
www.robsci.com

Continued on page 44

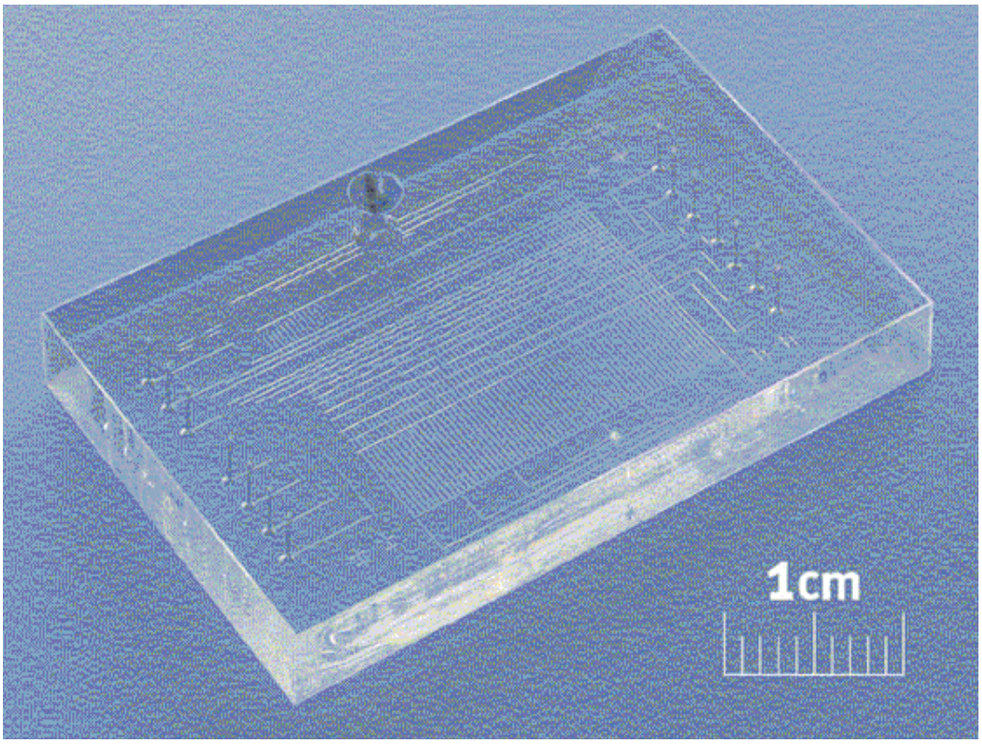

Figure 5
An example of one of Fluidigm's integrated bioassay chips made by soft lithography. The microfluidic network on this chip is capable of multiplexing

The DWP and Picoliter's Drop Ejection technology also have potential to rewrite existing paradigms in HTS in that they also have the capability to support high density library storage (eg the DWP in 1536, and Picoliter in 3456 plates). This makes the average compound library more manageable and more amenable to distribution outside the centralised store. It is possible to envisage the distribution of aliquots of as little as a few µLs of compound to multiple end-user laboratories. This amount serving multiple assays, rather than just one or two as is the case at present. Reformatting to the assay plate then becomes part of the assay process rather than a task for compound management. This effective miniaturisation of reformatting would also be more attractive to Biotechs, who have less infrastructurally hurdles to overcome when implementing radical change compared to big Pharma. If you couple this with the other attributes of Picoliter's true contactless dispensing, eg full random access cherry picking and serial dilution on the fly by direct volumetric dispensing over seven orders of magnitude, it is possible to envisage the next generation of retest robots.

Although many of the new nanolitre dispensing technologies discussed at the Symposium have real potential to impact on miniaturised assays by improving the efficiency of uHTS, assays in conventional microplates are still limited by volume (to around 1µL) and the logistics of enabling the screening process. Developments like Biotrove's Living Chip™ are therefore very exciting as they appear to offer a way round these difficulties by combining the advantages of the nanolitre processing volumes of lab-on-a-chip devices with the isolated reaction containers of a microplate. One might also predict that Fluidigm's microfluidic pumping systems are destined to become core components of a new breed of instruments which will facilitate reduced sample volumes and high levels of process automation capable of accelerating HTS and drug discovery.

Emerging nanolitre technologies

There are an increasing number of companies now developing low-volume liquid handling technology. These include Nanolitre which is promoting its induction-based fluidics approach to liquid transport in which liquids in gaussian surfaces (eg a tube) are energised by electric fields. Allegro

Technologies Ltd is a new start-up which announced at ScreenTech that it is developing the AccuDrop pipetting station for delivery of liquid volumes down to 30nL per single drop. It is based on magnetic boss moving inside a plastic tip, effectively a disposable microvalve. The boss is actuated by means of external coil. Of critical importance is the control of the valve, since the opening times required to dispense submicrolitre volumes are very short (mS or even a fraction of mS). Allegro's technology allows accurate timing of the opening and closing events by means of smart electronics. FLS (Fluilogic Systems Oy) is another company developing nanolitre volume dispensers, with an eye on drug discovery applications. FLS utilises bellows dispensing technology, which is slide friction free and has no wearing parts. Therefore FLS technology offers constant high performance, excellent precision, high resolution and is capable of nanolitre stepping. Nanolytics, is using electrowetting technology to develop a general-purpose liquid handling system for forming and positionally manipulating nanolitre- and subnanolitre-sized droplets in an enclosed environment of a biochip.

Table 1

Suitability of emerging nanolitre dispensing technologies for HTS compound reformatting

	COMPANY						
	Cartesian Technologies Inc Hummingbird™	**IMTEK** Dispensing Well Plate (DWP)	**Picoliter Inc** Acoustic Transducer	**PerkinElmer Life Sciences** PlateTrak PinTools	**Boston Innovation Inc** SmartPlate™	**TTP LabTech Ltd** Mosquito -Proboscys	**Tecan** Te-Mo™, Impulse Technology
PARAMETER							
Non-Contact Dispensing	✓	✓	✓		✓		✓
True Contact-Less Dispensing			✓				
Highly Parallel Dispensing	✓	✓		✓	✓		✓
Variable Dispense Volumes			✓		✓	✓	✓
Lowest Dispense Volume	20nL	10nL	0.1pL	5nL	5nL	50nL	50nL
Multiple Dispense Capability		✓	✓		✓	✓	✓
Liquid Storage Capability		✓			✓		
Disposable Dispense Head	✓	✓				✓	
384 Reformat Time (sec)	<30	<10	60	30	60	150	15
1536 Dispense Head Option	✓	✓		✓			
Rate Limiting Step	Washing head	Loading DWP with liquid	Moving between wells	Washing pins	Dilution in SmartPlate, moving plates	Moving between wells	Washing head, moving plates
Commercially Available	✓			✓		✓	✓

Continued from page 42

ScreenTech 2002
www.lifescienceinfo.com/screentech
Tecan
www.tecan.com
Telechem International Inc
www.arrayit.com
TTP LabTech Ltd
www.ttplatech.com
V&P Scientific Inc
www.vp-scientific.com
Zymark Corp
www.zymark.com

Issues related to nanolitre dispensing

The Symposium was followed by a lively panel discussion. The following are a few of the issues that raised interesting debate:

1) Are we seeing a pull back on 1536 adoption rates? Is low volume 384 the current plateau in the evolution of uHTS? And if so, where does that leave microfluidic chip systems for doing HTS?

2) How can we avoid clogging in nanolitre delivery systems as most new technologies involve movement of liquids through very narrow microchannels or orifices?

3) Potential for cross-contamination using pin tools (and fixed tips) in liquid handling? Are current washing methods adequate?

4) Is a further volume reduction to assay volumes down to and below 1uL really needed? Assuming the value of conducting reactions in low nanolitre volumes, how can these be put together?

5. Advantages of high speed serial versus parallel dispensing for low-CV, contactless applications? Do we get better information out of a screen if the reactions in all wells start simultaneously (parallel versus serial liquid handling)? DDW

Dr John Comley *has more than 20 years' experience in Drug Discovery. He received his PhD at Imperial College, London University in 1978. After post-doctoral work at the University of Liverpool and the University of Vermont he joined the Wellcome Research Laboratories, Beckenham, UK in 1982. Following the merger of GlaxoWellcome in 1995 he worked in the Lead Discovery Unit at Stevenage. At GlaxoWellcome he pioneered investigations into uHTS (implementation of 1536 well technology). He joined PerkinElmer Life Sciences at Wallac Oy, Turku, Finland in 1999 as Manager HTS Technologies. He was responsible for the development of the Fillwell Liquid Handling Workstation and for the assessment of novel enabling HTS technologies. Dr Comley left PerkinElmer in February 2002 and is now an independent HTS consultant.*