rapidly fill a 96-well plate with 20 µl per well in 5 s and a 384-well plate with 20 µl per well in 14 s with good precision. The plate moves under the 8-channel dispensing head and in the 384-well mode, each plate is filled by two passes under the head. The plate is offset on the second pass to allow alternate rows to be filled. The 96-well version of the Multidrop has been widely used for dispensing cells and has been integrated onto many HTS robotic systems. The Multidrop has a serial RS232C interface for communication with PCs.

BioRobotics (Cambridge, UK) have developed a 96/384-well bulk dispensor called the BioFill. The BioFill has a 16-probe dispense head attached to a cross slide that allows access to four plates on the stage of the instrument. The BioFill can add a single reagent to an entire 384-well plate in 40 s. In 384-well mode, the BioFill has a volume range of 20–90 µl in 10 µl increments. During the filling procedure, the probes can optionally be lowered to the bottom of the well and withdrawn as the well fills thereby, as BioRobotics claims, minimizing bubbles or drops at the end of the probe.

Nanolitre dispensing

Some companies are developing very low volume dispensers but there are significant issues relating to the accuracy of dispensing low volumes in high density formats and speed of dispensing which need to be addressed before these systems can be used for HTS.

Piezoelectric technology. Drs Roeland Papen and Al Kolb from Packard Biosciences (Meriden, CT, USA) reported on the development of their MultiPROBE nl (a nanolitre liquid-handling workstation) and the BIOCHIP processor for liquid handling in miniaturized screening formats. The MultiPROBE has been 'developed with piezo-drop-on-demand technology to a high precision XYZ-robot with integration of aspiration and positive feedback'. This allows for accurate nl dispensing of reagents. Volumes from 250 pl to 25 µl can be dispensed, allowing direct dilution of compounds from stock solutions. It is also possible to set up dilution curves spanning five orders of magnitude directly from stock solutions of compounds. Packard's piezoelectric dispensing system is based on glass capillary tubes with a bonded ceramic collar. Voltage applied to the ceramic collar causes contraction that results in dispensing a 200 pl droplet. A high frequency voltage pulse causes multiple droplet release; a frequency of 1,000 Hz results in the dispensing of one 200 nl droplet per second. In addition, the system has built in ultrasonic cleaning of the capillary tubes. The Packard system will dispense compounds without predilution directly into miniaturized assay volumes. Data from a cell-based luciferase reporter gene assay substantiated these claims. It is envisaged that the MultiPROBE nl will be one of a new generation of nanolitre dispensing systems that will make miniaturization of HTS a realistic short-term goal.

Inkjet technology. A group from Cartesian Engineering (Durham, NC, USA) reported at MipTec on their nanolitre four-channel inkjet dispensing system for microscale HTS assays. Cartesian are developing solenoid-based inkjet dispensing to deliver chemical or biological reagents to high-density formats. Cartesian state that 'the technology couples the precision of a syringe pump with the high speed, nanolitre dispensing capabilities of a solenoid inkjet valve for nanolitre dispensing and aspiration capabilities'. Cartesian claim that their system has a large volume range (4 nl to 4 ml) and accurate dispense capabilities. In addition, Cartesian point out that because the dispense tips do not touch the liquid, no tip wash step is required and rapid dispense times are possible taking seconds per plate.

Mark V. Rogers
Glaxo Wellcome
Stevenage, UK SG1 2NY
fax: +44 1438 764210
e-mail: mvr43718@ggr.co.uk

Emerging molecular targets

Gelatinase A and platelet activation

Gelatinase A, also known as matrix metalloproteinase-2, MMP-2 and type IV collagenase, is important in the remodelling of the extracellular matrix. Now Grzegorz Sawicki and coworkers at the University of Alberta (Alberta, Canada) have presented data that suggest that gelatinase A may also play an important role in platelet aggregation.

The Canadian investigators found that small amounts of gelatinase A are released in a dose-dependent manner when platelets are activated by collagen or thrombin. A specific antibody against gelatinase A, as well as two different inhibitors of the enzyme, phenanthroline (Sigma) and SC44463 (Pfizer), inhibited the aggregation of platelets that normally occurs in response to either collagen or thrombin. Addition of recombinant gelatinase A to stirred platelets did not trigger aggregation, but it did amplify the aggregatory effects of collagen. Most intriguing, the investigators report that phenanthroline inhibited platelet aggregation that is insensitive to inhibition by aspirin and apyrase, which suggests that the mechanism by which gelatinase A inhibits platelet aggregation is independent of the activation pathway of thromboxane A_2 and ADP [*Nature* (1997) 386, 616–618].

The researchers believe that gelatinase A may prove to be an effective new target for the discovery of antiplatelet agents. It is released from the platelet as an inactive proenzyme of 72 kD and then processed into an active 64 kD form. Either gelatinase A itself or its processing enzyme is likely to serve as an effective target for drug discovery.

Robert W. Wallace
Wallace and Associates
532 La Guardia Place
Suite 510
New York
NY 10012, USA
fax: +1 212 254 3322
e-mail: RobWallace@nasw.org