

## synQUAD Technology - Theory and Applications

### synQUAD Technical Note 102

#### Introduction

The drive to achieve results faster and with greater reproducibility has led to an increased emphasis on automation and miniaturization of experimental set up leading to automated liquid handlers becoming standard instruments in modern laboratories. These systems offer the researcher the opportunity to increase throughput, filling assay plates faster and with lower costs due to lower reagent usage. The ability to deliver sub-microliter volumes can also facilitate the development of new applications, for example protein arrays.

#### synQUAD Technology

Delivering low volumes accurately and precisely with no contact between tip and destination requires a specially designed system. Unlike typical syringe pump technologies, the synQUAD principal of operation combines the opening and closing of a solenoid valve with the movement of a high resolution syringe pump (figure 1.) to release drops from a ceramic tip. A system fluid fills all the syringe pumps and lines providing a non-compressable environment. A stepper motor drives the syringe plunger and pushes the programmed volume of liquid into the closed solenoid valve. The actuation of the valve releases the pressure that has been created within the system and a drop is accelerated out and onto (or into) the target. The combination of the pressure generated by the syringe and the acceleration of the fluid by the valve allows very small drops to be released cleanly from the tip. Placing the valve as close as possible to the dispense tip produces the best results and the greatest control of the dispensing process.

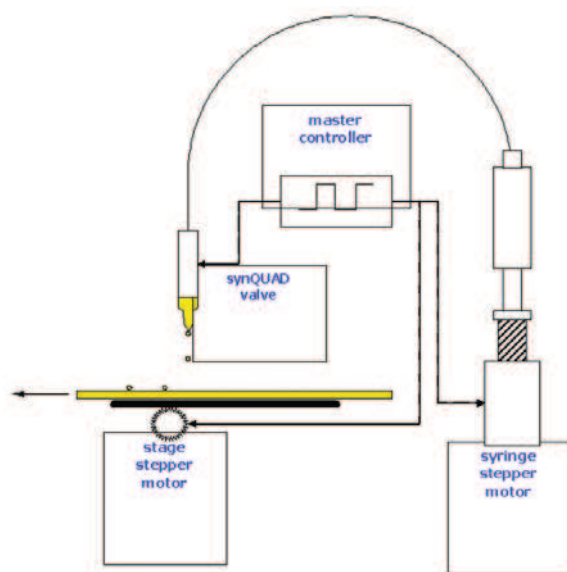


Figure 1. synQUAD - Synchronization of valve, syringe and stage

The speed of the syringe and the opening and closing of the solenoid valve are the critical issues in the control of nanoliter dispensing using syringe pumps. The Digilab synQUAD effectively addresses these problems allowing the scientist to control both parameters.

Not all solutions behave identically when being dispensed using automated pumps. Low viscosity and low boiling liquids such as methanol will behave far differently to high viscosity liquids e.g. 30% polyethylene glycol solutions. These solutions and complex mixtures such as SPA bead suspensions have been successfully dispensed using the Digilab synQUAD pumps.

Liquid can be dispensed in a variety of ways using synQUAD technology, by controlling the various components that make up each channel:

- Discrete drops (20 nL - several microliters). Individual drops are useful for applying small drops on to a solid target substrate or into a well.
- Burst of drops (e.g. 1.0 µl dispensed as 10 x 100 nl drops). This method improves mixing when dispensing into filled wells of a plate and reduces splashing if a large volume is dispensed into filled wells of a plate.
- Fast stream (dispensing of large volumes -up to full syringe volume). This method is ideal for applications where filling a target well with a large volume of sample or diluent is required.
- Line of drops (control of drop size and spacing). Line mode allows for rapid dispensing onto target substrate or into a target plate in a non-contact way.

Several parameters must be controlled in order to dispense fluid through the solenoid valve:

1. The syringe speed for fluid movement
2. The volume required
3. The control of the solenoid valve

In order to achieve good dispensing it is important to achieve steady state pressure (maintaining a constant flow inside the fluid lines so there is no residual pressures from previous syringe movements). To develop this pressure the synQUAD dispenser pre-dispenses a number of drops, typically 5-10% of the total drops, back into the source container. Sample wastage can be limited to just 10% of the amount aspirated by recovering these pre-dispense drops.

### **Bulk Fill or Aspirate/Dispense**

The Digilab synQUAD can be used in two basic dispense modes: Continuous (bulk) Dispense and as Aspirate/Dispense Transfer.

For bulk dispensing the system is filled with the reagent and then programmed to dispense only. Its main application is for filling plates or dispensing, onto or into other devices in high throughput production.

To maximize efficiency and versatility, not all the channels need to be primed with the same reagent or even used at all. This relies on the fact that the speed of synQUAD dispensing in line mode is so high that only one or two channels may be needed to fill a plate, thereby reserving other channels for use with another reagent or diluent. Most of the unused reagents in the lines can be recovered by back-flushing the unused reagent back into the system liquid bottle.

The aspirate and dispense mode simply involves aspirating a sample from a source and then transferring aliquots to a destination area or plate.

## High Speed

The synQUAD dispensers enable the researcher to select the motion of dispense. When high speed is the priority, drops can be dispensed 'on-the-fly' and a single channel can fill a 1536 well plate in less than two minutes. 'On the fly' dispensing is achieved by synchronizing not only the syringe and valve, but also the movement of the platform. As the head or platform moves from target-to-target (well-to-well) the movement of the syringe is synchronized to displace the required drop volume. When the tip is positioned over the target, the solenoid is actuated, ejecting the drop.

Some applications do not require the highest speed but do require good positional accuracy. The 'stop-and-drop' dispense mode is ideal for these applications, placing the dispense tip less than a millimeter (or more) above the destination and positioning the drop with exceptional accuracy. The x, y motor resolution of the synQUAD is 1.5  $\mu\text{m}$  and the positional accuracy is  $\pm 10 \mu\text{m}$  at 95% confidence. This stop-and-drop motion can generate arrays within the well of a 96 well plate (see figure 2).

*Figure 2.* 20 nL protein drops in a 96 well plate



## Applications

The Digilab synQUAD has a proven track record in routine applications such as addition of proteins, buffers and substrates to assays. However, the requirements of many other applications can also be met using this technology, including:

- Whole cell and SPA bead dispensing.
- Protein arrays - at least 400 spots per  $\text{cm}^2$ .
- Sequencing and PCR applications - sub-microliter addition of reagents.
- Protein crystallization screening - accurate and precise addition of even the most viscous solutions at sub-microliter volumes (e.g. 30% 8K PEG at 100 nL)

While the synQUAD dispensers routinely work with targets such as 96/384/1536 well plates, other plate formats including 2800 and 3456 can also be used. However, the synQUAD is not restricted to working with plates as targets and applications requiring dispensing onto surfaces such as gold, slides, membranes and coverslips have all yielded excellent results using this technology.

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Protein Crystallization

Non-Contact Arrays

Integration

## Hardware

Digilab synQUAD dispensing technology is available on four different instruments with options that can be configured to meet the requirements of the application. This choice of system ensures that the throughput requirements of every researcher can be met. In addition to a choice of plate capacity, the user also has the option to configure the system with automated plate handling. In order that the maximum number of applications can be studied, enclosures and humidity control options are available for each system. If required, extended dispense heads of different capacities can be added to isolate the reagents from the solenoid valves. Other options include on deck cooling and choice of wash stations where special cleaning protocols are needed. This flexibility of the Digilab synQUAD dispensers ensures the researcher is able to tailor the system to meet the exact requirements of every project.

## Software

The Digilab synQUAD dispensers use software specifically developed for automated low volume liquid handling applications. Axsys, the powerful Windows-based control software, allows the user maximum flexibility to control the instrument.

## Summary

The Digilab synQUAD dispensers have proven themselves to be able to deliver sub-microliter drops at high speed. Even 'difficult' liquids have been successfully dispensed at these low volumes e.g., highly viscous 30% 8K PEG. Drops are always delivered with no contact between the syringe and the target ensuring higher speeds and low risk of contamination. A variety of hardware options enable the Digilab synQUAD dispensers to deliver flexible solutions to many liquid-handling applications.

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