Next generation accuracy for microfluidic control

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Accurate microfluidic dosing is essential for life science and genomics research, as well as the administration of medical care. For OEMs developing microfluidic dosing machines, accurate valve control ensures precise results. However, to specify the optimum valve system, consideration over criteria from material compatibility to manifold integration is vital to ensure repeatable accuracy.

Troy Stehr, Industry Account Manager for Lab & MedTech applications at fluid control specialist Bürkert, discusses requirements for accurate microfluidic control.

Reagents are integral to research in life sciences, and the result of how they chemically react with other substances, by measuring, detecting, or examining an outcome, is vital for the development of medical treatments. Essential to this process is accurate, repeatable control of reagent dosing, in microfluidic volumes down to 1µl and below. These same requirements apply to genomics, such as conducting a polymerase chain reaction (PCR) technique to amplify select DNA segments. Accurate and reliable microfluidic dosing can also be life dependent for many medical applications.

Today, machines can replace manual handling of pipettes with more accurate and consistent dosing. Automation not only saves the time of skilled humans, but fast

dosing of multiple channels improves productivity too. To achieve these results, there's high reliance on a dosing machine's valve control system.

Open or closed loop?

Understanding the required dosing accuracy is typically the starting point in valve system specification. Patients are treated or diagnosed based on lab results, so the accuracy requirement of the intended assessment determines the dosing precision the machine has to provide. Optimising volume use is also important to control costs, both in the use and the disposal of some very expensive reagents and involved substances.

Sufficient for many microfluidic applications, time-pressure dosing provides precision of <1% with repeatable volumetric accuracy between 2-5%. With this technique, media flow is controlled by valve opening or closing for a defined time for each switching cycle. Using air or an inert gas to pressurise the fluid reservoir, combined with a dosing valve, this technique enables controlled dosing down to single digit µl (microlitre) volumes.

Bürkert's microvalves for time pressure dosing are capable of ~10µs (microsecond) control signal steps for high accuracy valve control lower than 1%. If even greater accuracy is required, Bürkert also provides closed loop valve control. These systems incorporate a sensor, providing feedback on actual valve status that enables constant adjustment to valve opening/closing rates. Alternatively, an open loop system, like time-pressure dosing, operates purely on the valve's input command, irrespective of changes that could impact its switching time, and as a result, the actual dosing volume.

µl and nl dosing accuracy

Closed loop systems often operate on the Coriolis principle, where vibrations of a liquid-carrying tube are measured with a resulting flow-proportional output. With this technology, Bürkert's mass flow controller/meter can achieve dosing accuracy at levels below 1ml. However, a new innovation is set to become the first device available on the market with µl (microlitre) measurement and closed loop control accuracy, with a differential pressure sensor integrated in a device together with a valve. Bürkert's new dosing system measures and controls drops down to 50nl (nanolitres), with closer than 1% accuracy measured over millions of cycles completed in trials so far.

Crucial to control over time is compatibility between the media and the material fluid block and seals, especially when multiple reagents and substances are involved. Depending on the media properties, different seal materials might be required and their selection requires careful consideration. Compatibility challenges can result in swollen seals, through to rupture over time, and when dealing with microfluidics, resulting control problems are amplified. Within Bürkert's system, PEEK, used for valve bodies, and the sealing material FFKM or EPDM are the only wetted materials.

Precision-engineered manifolds

To separate and control media flow, the valve system requires a manifold array with the number of inlets and outlets to suit the variety of required substances. Incorporating bespoke manifold design and manufacture with the selected valve is advantageous, particularly for microfluidic applications, to ensure optimised pressure management and heat exchange properties. As per valve design, the manifold is also subject to materials compatibility, so relying on the same vendor

gives greater security in an efficient outcome. Bürkert precision engineers bespoke, plastic injection moulded manifolds specific for microfluidic control applications.

To optimise productivity, 10 or even more channels might be required, with high-speed dispensing. Combined with repeatable accuracy, to achieve system reliability over millions of valve cycles, a remote diagnostics capability, enabled by Industry 4.0 Ethernet communications, confirms actual valve operation data. Not only does this capability remove the time required for a physical human check, it provides a certainty, unattainable by a manual inspection alone, that the well plates are filled with the right volume and proportion of reagents.

Image captions:

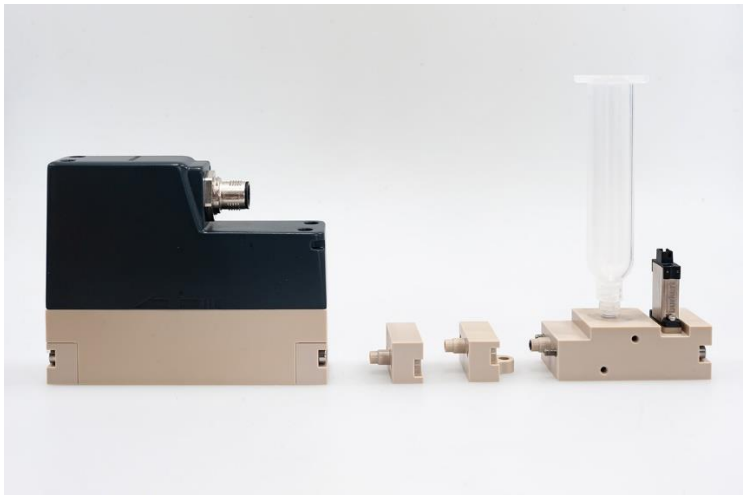

Image 1: Bürkert's new dosing system measures and controls drops down to 50nl (nanolitres), with closer than 1% accuracy measured over millions of cycles completed in trials so far.

Image 2: Bürkert's mass flow controller/meter can achieve dosing accuracy at levels below 1ml.

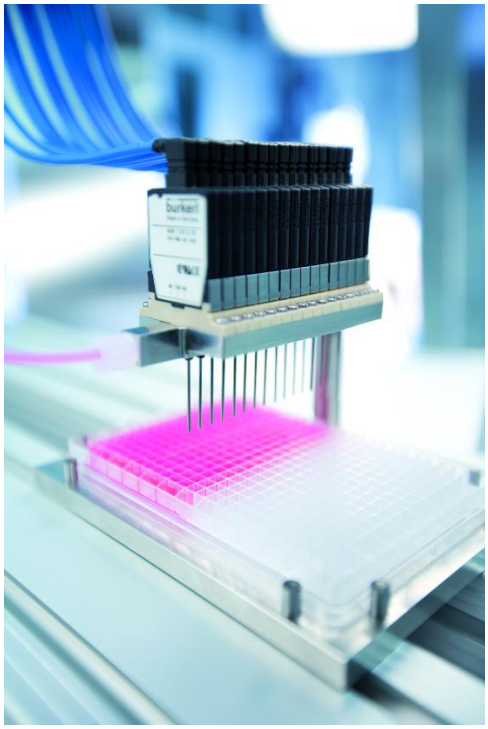

Image 3: Accurate microfluidic dosing is essential for life science and genomics research, as well as the administration of medical care.

About Bürkert

Bürkert Fluid Control Systems is one of the leading manufacturers of control and measuring systems for fluids and gases. The products have a wide variety of applications and are used by breweries and laboratories as well as in medical engineering and space technology. The company employs over 2,200 people and has a comprehensive network of branches in 35 countries world-wide.

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