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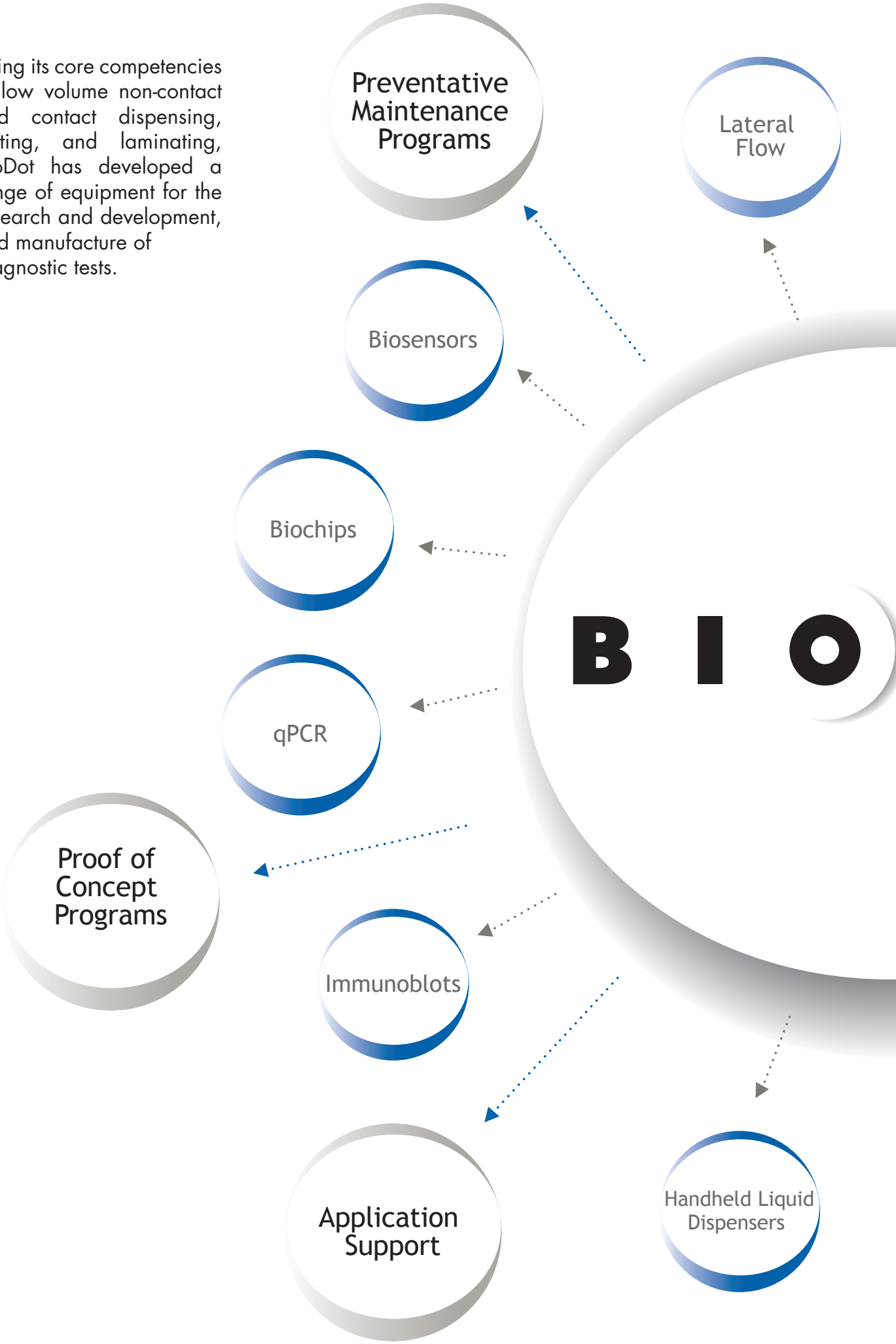
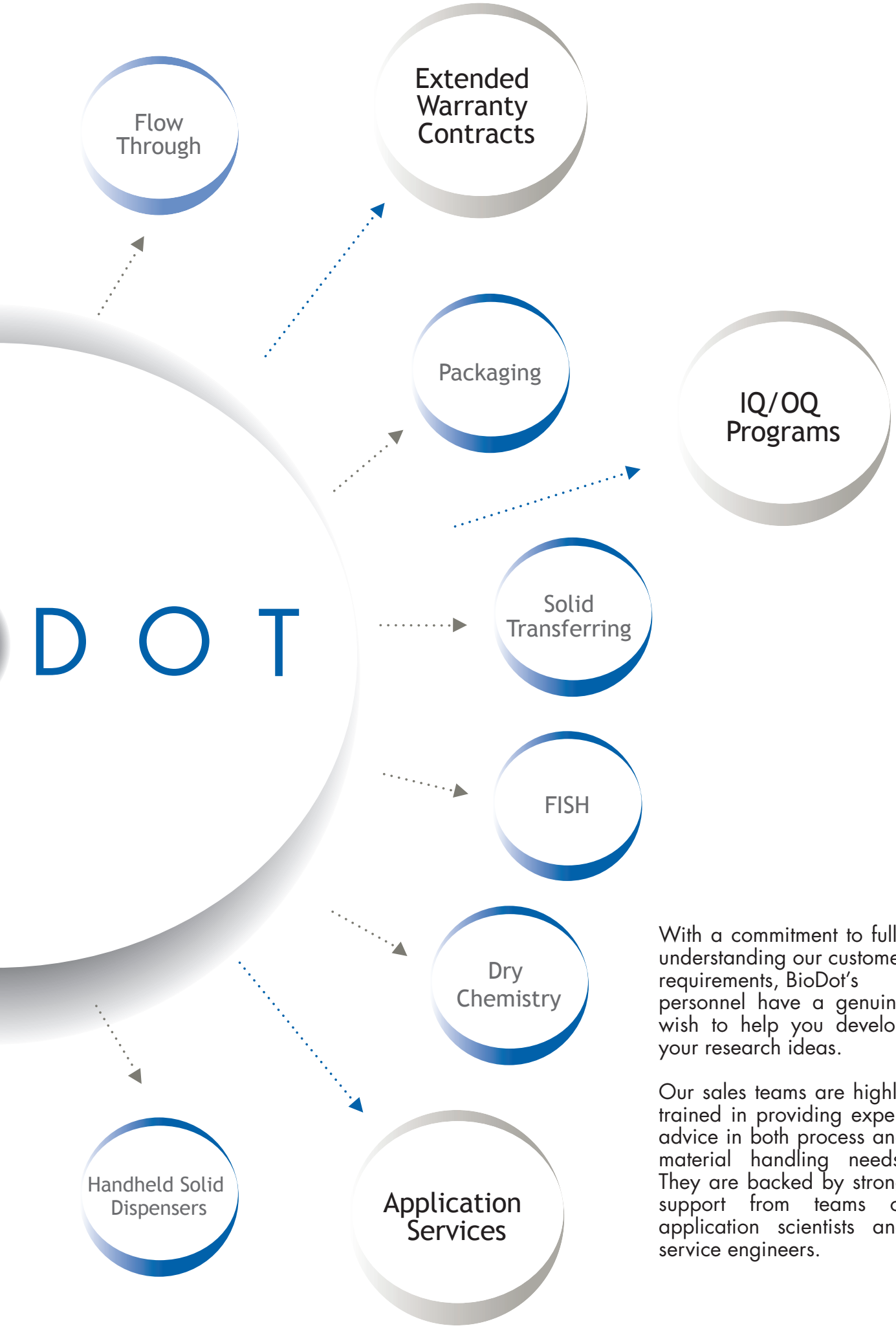
Using its core competencies in low volume non-contact and contact dispensing, cutting, and laminating, BioDot has developed a range of equipment for the research and development, and manufacture of diagnostic tests.





With a commitment to fully understanding our customer requirements, BioDot's personnel have a genuine wish to help you develop your research ideas.

Our sales teams are highly trained in providing expert advice in both process and material handling needs. They are backed by strong support from teams of application scientists and service engineers.

Lateral Flow

Lateral Flow Immunoassays are used by point-of-care markets for immunological testing. Examples of utilization of immunoassays include cholesterol, cardiac arrest, diabetes testing. Recently, and due to some constraining patent issues, many manufacturers of lateral flow assays have invested into R&D to develop multiplexing assays on complex platforms for very specific applications, and to improve the design of current lateral flow substrate to increase reproducibility in the final product.

The lateral flow immunoassay format was developed in the seventies and within 10 years became a standard platform for a variety of Point of Care (POC) tests. The benefits of this format were:

- Ease of use
- Requires relatively small amount of sample
- Adequate level of sensitivity
- Ease of manufacture in large scale
- Stability of the final product at room temperature (shelf life)
- Ease of implementation with a reader technology
- Ease of approval by regulatory instances (format well know by the market)
- Relatively inexpensive to manufacture

For many tests, this format was very attractive. However, recent market needs have evolved into higher demands, requiring LFIA tests to produce more than the traditional "yes/no" result. The progression of lateral flow tests to true quantitative formats is an active area of current research and development.

Traditionally, a lateral flow immunoassay device is assembled with a variety of materials and reagents (Figure 1). Typical components are a backing card, membrane, sample pad, absorbent pad, conjugate pad, and possible a wick. The tests are assembled during a "Batch Process" or an "In Line Process", the first one being far more common until recent years.

The batch process starts with a roll of each material; i.e. membrane, sample pad, conjugate pad, sample pad, wick material, and individual backing cards. Each material goes through its own process independently and then once complete the final test is assembled.

The other alternative to the Batch process is the In-Line method. An In Line process starts with all materials in roll format, and is typically achieved with three types of modules. The first is the reagent dispensing and drying module, the second is the slitting module, where processed webs are cut down to narrower widths for lamination, and the third module is the actual lamination of the LFIA.

Typically In-Line approaches are designed to meet the specific needs of an application. The In Line approach allows multi-tasking between both dispensing and impregnation applications, and has capacity for in-line drying and quality control monitoring.

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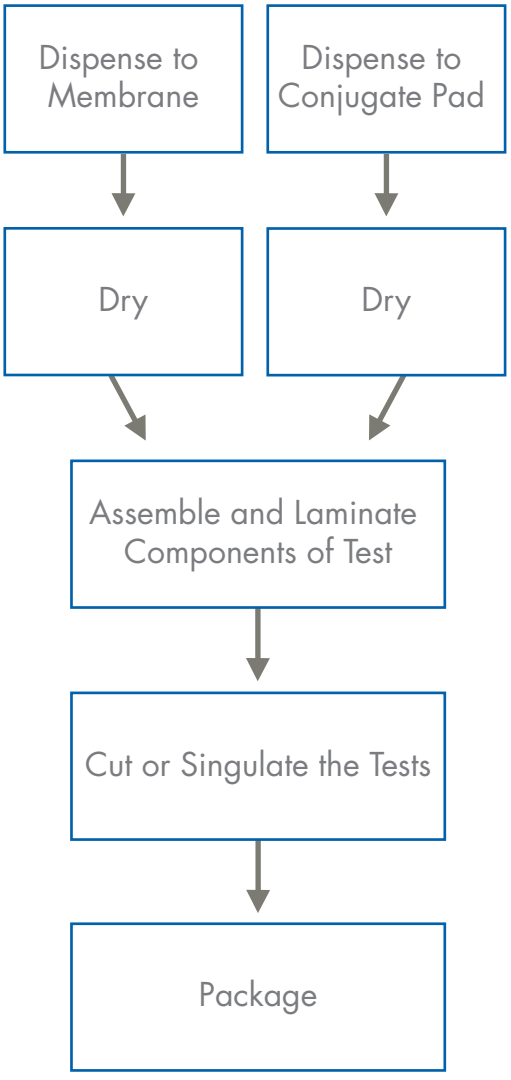
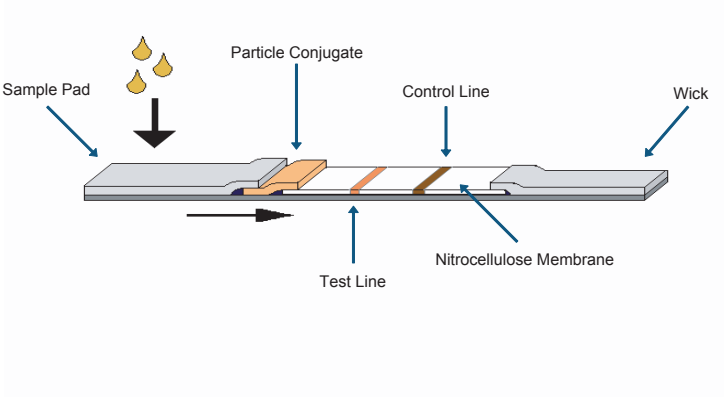
Application Flow Diagram



Typical Lateral-Flow Assay Format

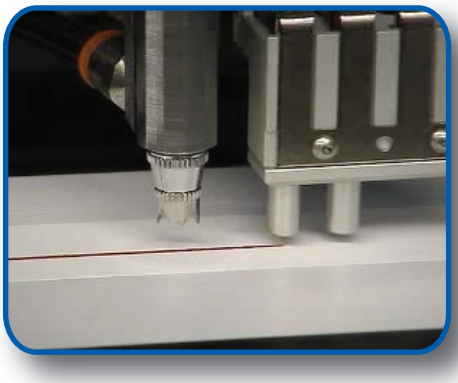


Fact Plus® Pregnancy Test Stick

Dispense to Membrane

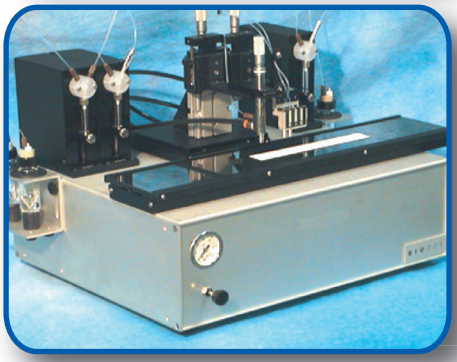
Using either non contact BioJet™ or contact Front Line Dispensing, allows for quantitative dispensing of either discreet droplets or lines. If the application starts with "card stock" material, the dispensers are mounted on our XYZ or ZX platforms. If the application starts with "roll stock" material, the dispensers are configured with our Reel to Reel systems for continuous dispensing.

See In Line Photos under the Dry Chemistry Section



Treatment of Membrane, Conjugate, or Wicking Material

Using either non contact AirJet™ or a submergence technique, the reagents can be applied to the different materials. Quantitative AirJet dispensing sprays a region on the pad and the line width can be modified to cover a specific region. AirJet can be used in "card stock" or in "roll stock" configurations. Additionally with "roll stock" material, a submergence technique can be applied with a Dip Tank. The Dip Tank, configured on a Reel to Reel system, supports a controlled process utilizing fluid level sensors and metering control sensors to assure consistent and complete blocking of the material.



Drying

The drying step is an area that is often overlooked and can have a great deal of variances. If using "card stock", temperature controlled ovens with IR sensors support even distribution of air flow for consistent drying across all cards. If using "roll stock", the Reel to Reel system can be configured with convection based Dry Towers. These 6 zoned temperature controlled towers have consistent clean air passing through which supports a very controlled and consistent drying of the web material. Additionally the Dry Towers can be arranged vertically to save space, or horizontally, if the materials are delicate.

Assemble and Laminate Components of Test

This the step where the "assembly" of the "dispensed materials" are assembled with any other materials needed for the test. Typically, the test would need some sort of plastic, adhesive backing card for support, the pre-dispensed membrane with the test and control lines, the pre-dispensed conjugate pad, a sample pad, wick, and possibly a cover tape. Like the dispensing steps, there are two approaches if your application is using "card stock" or "roll stock".

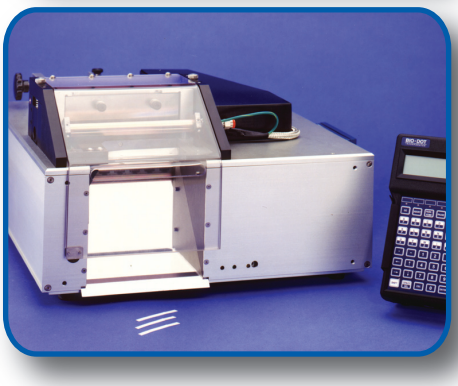
With cardstock, there are several options, with the simplest being a "clamshell laminator". Here is where manually place your materials into an "insert" which aligns the materials. Using both vacuum, mechanical alignment fixtures, and the weight of the device, the individual materials are assembled into one "complete card"

A less manual approach with either card stock or rollstock are the automated laminator systems. Here either "card stock" or "rollstock" can be introduced to the system and there are multiple configurations so it can be configured best for your application. The automated systems can also be configured with a guillotine cutter so that after assembly the "complete card" can be cut into individuals tests.

Cut or Singulate the Tests

Using either a Guillotine cutter or a Rotary Card Cutter, the "complete card" can be singulated to individual tests. With the Guillotine cutter, the strips are "singulated" one at a time with a "scissoring action". The cut widths are flexible and operators can easily adjust cut widths to range from 4 mm and higher. The Rotary Card Cutter has a blade set with multiple blades spaced from 4 mm and higher. Using this configuration, the card is presented and cut at one time. Optional features like target sensors, anti static and collection chutes can be configured to either system.

BioDot also offers optional upgrades to the systems which could include vision systems, bad part marking, humidity or dry enclosures. Additionally, BioDot offers vacuum pumps, and air compressor with noise reduction enclosures, and In Line Degassing.

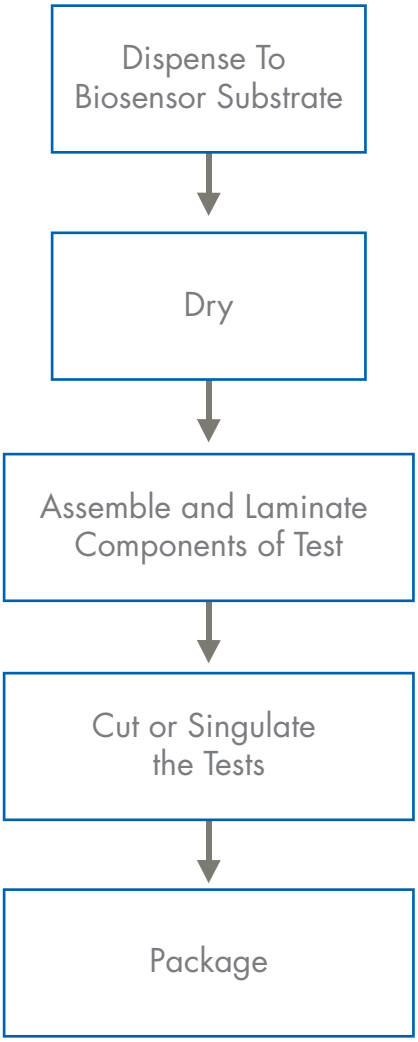


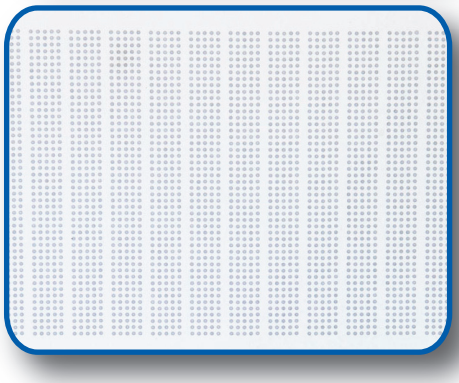
Biosensors

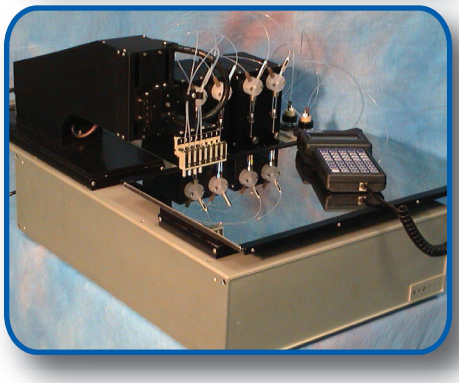
Following advances in microelectronics, biosensor designs are becoming increasingly complex, and focused on miniaturization. The demand for simultaneous measurement of multiple analytes has stimulated development of high density arrays. As a result of this demand, and the advancing capabilities of patterning technologies, research and development programs aimed at sensor arrays containing multiple biomarkers in devices on the order of a square centimeter are underway. Fabrication of these devices typically requires reagent-dispensing approaches capable of delivering volumes ranging from the low microliters to picoliters. Reductions in volume reduce cost of expensive reagents, increase surface dependant reaction rates, and promote adoption of multiplexed diagnostic devices. Dispensing systems used must be compatible with a wide range of reagent classes, including organic solvents, biological fluids, polymeric solutions, as well as the traditional combination of buffer and enzymes. Systems must be robust enough to produce hundreds of thousands to millions of dispenses with a high level of precision and accuracy. Lastly these systems must function in a production environment using less skilled labor and also subject to rigorous regulatory requirements.

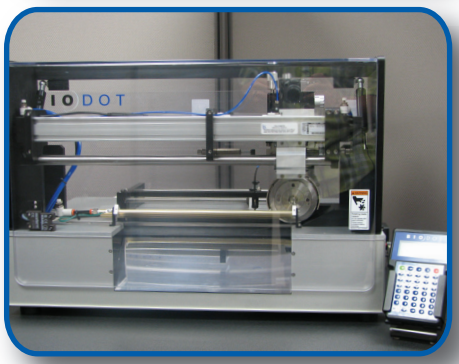
The Glucose biosensor is probably the most common of biosensors where the typical format is a "sheet" and the reagent is dispensed to a pre-printed electrode pattern. In many biosensor applications, multiple layers of different samples are dispensed in different steps requiring great flexibility as well as high positional accuracy. The sample is allowed to dry down and then is cut, and packaged.

Application Flow Diagram







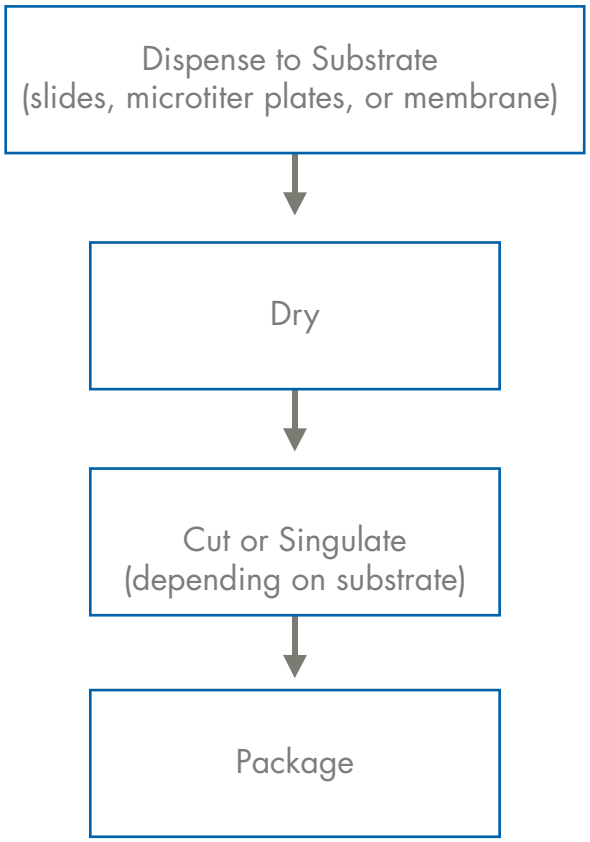


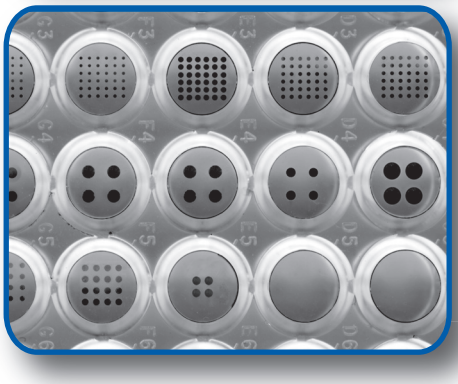
Biochips

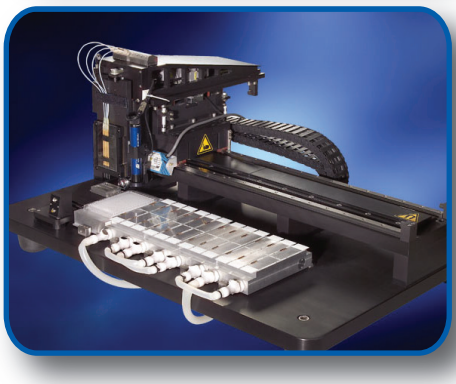
The development of manufactured protein arrays is currently getting a lot of visibility due to the existence of an immense field of applications, including biosensors, diagnostics applications such as serum-based diagnostics, and pharmaceutical target design. The latter typically involves the study of protein targets through protein-protein interactions, enzyme-substrate reactions, receptor-ligand interactions, and drug-target binding. Protein microarrays can also be used to miniaturize and multiplex immunoassays and have performed better than enzyme-linked immunosorbent assays in both sensitivity and quantitative range for use in immunoassays.

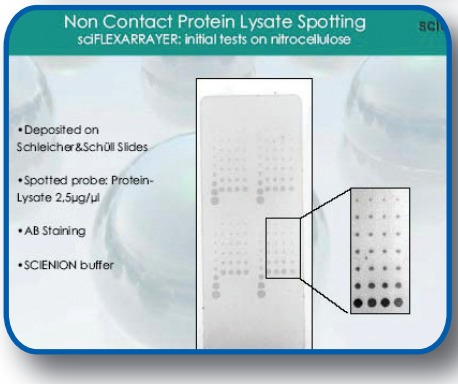
A common operation in multiplexing is gridding proteins onto a substrate in an ordered array. Once arrayed, the substrate is probed with a fluorescent probe of interest, and is then analyzed to detect the locations where the probe bound to the substrate. An alternative to pin gridding, the most common means of achieving high-density arrays, is to use either BioJet Plus or Scienion for a non-contact dispense. Patented BioJet Plus technology involves the coupling of a microsolenoid valve to a high resolution syringe. The system is then synchronized with the XYZ motion allowing for very fast dispense with high accuracy and precision. Scienion dispensing is based on piezo technology that is also very fast. The Scienion technology dispenses from the picoliter range to the low nanoliter range, while as the BioJet Plus technology dispenses from the low nanoliter range to the low microliter.

Application Flow Diagram







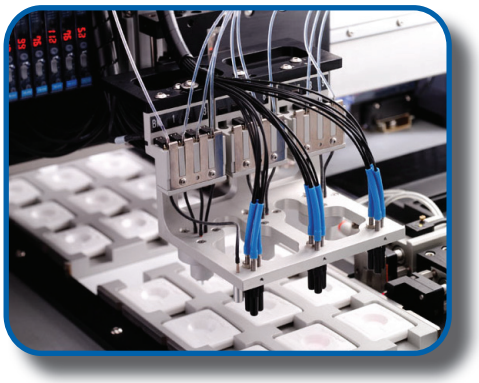


Flow Through

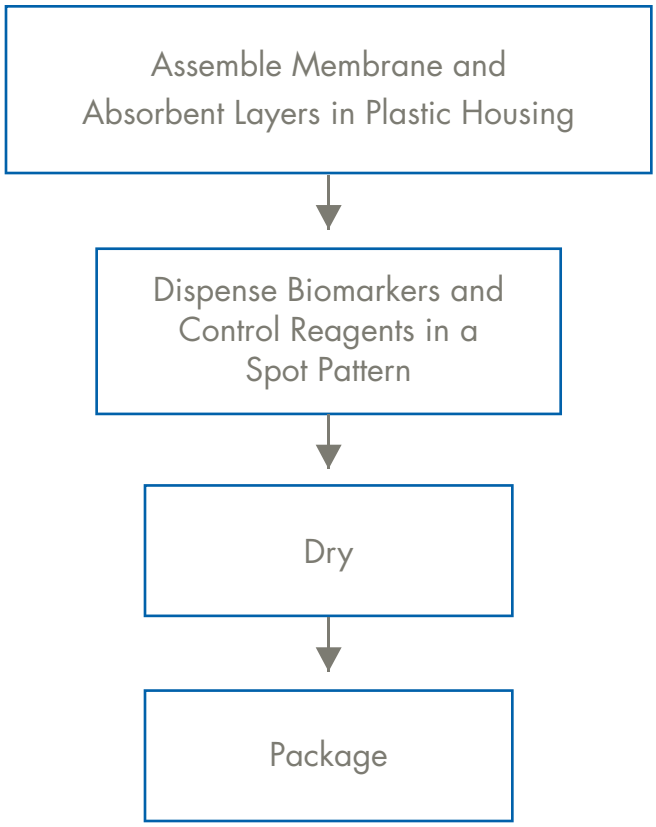
Flow Through and Lateral Flow diagnostic devices both use membranes as the active media on which the relative biomarkers are printed and the assay is executed. In the Flowthrough device the reagents and sample flow normal to the membrane while in the Lateral Flow device they flow parallel and within the membrane. Both employ an absorbing pad where in Flow through it sits under the membrane and for Lateral Flow it sits at the end of the membrane flow path. Hence the assembly and development methods are somewhat different.

In the Flow Through device the conjugate is added in a liquid format after being mixed with the sample and buffers. The original concept for Lateral Flow was to incorporate the conjugate in a dry format on a separate pad along the membrane flow path. More recently this has changed with the use of Lateral Flow devices in that in new test strip designs the conjugate is added in a liquid format mixed with the sample. This is done for several reasons, one being improved performance. The Flow Through device use a dot format for the test and control reagents while a Lateral Flow device uses line formats. The normal flow and spot formats used in the Flow Through device have historically lead to much lower Coefficient of Variable (CVs) that for Lateral Flow and hence the Flow Through technology is considered a quantitative device when used with a reader.

There is growing interest in the Flow Through format as a platform for multiplexed biomarkers using both colorimetric and fluorescent tags due to the ability to achieve quantization and the low cost of producing this type of a format relative to other array formats which require special functional surfaces. The Flow Through format is also more open to multiplexing of biomarkers than Lateral Flow due to the constraints associated to the linear flow limitation associated with the Lateral Flow design. Another trend with the Flow Through is the reduction is size to lower the volume of sample and reagents for development of the test.



Application Flow Diagram



Dry Chemistry

Dry Chemistry (also known as Dip Stick) refers to a diagnostic format where a test pad is bonded to a support structure such as a plastic strip for ease of handling the test pad for exposure to the test sample and read out. The test pad is impregnated with an analyte which when exposed to a test sample will change color or some other physical property which can easily be seen or measured with a reader. One of the most well known applications of Dry Chemistry technology is that of urine testing.

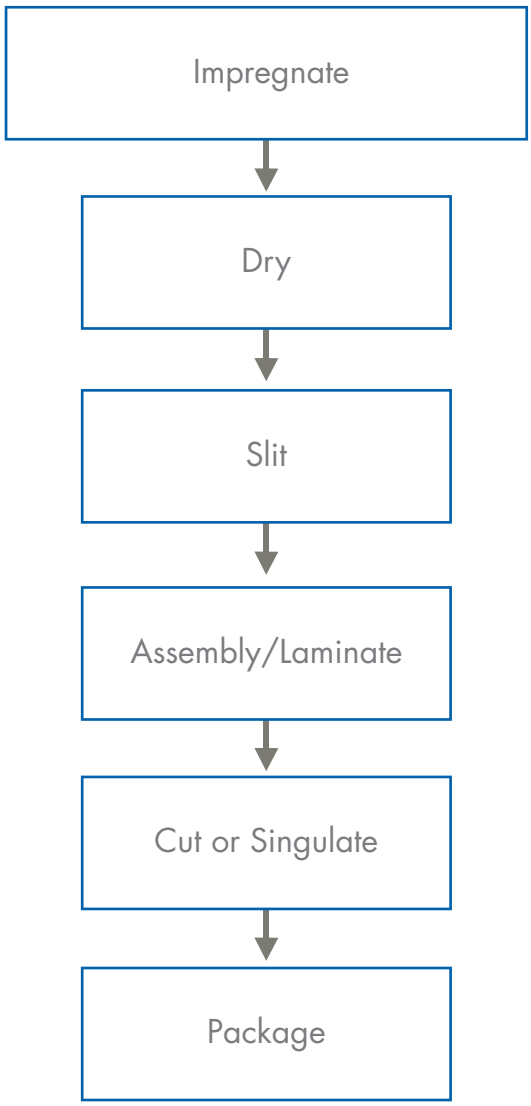
Dry Chemistry tests take on other formats such as simple pads with impregnated chemistry such as for spore testing or multi layered devices. Lateral flow would be an example of a multi layered device where several overlapping impregnated layers are used. Typical applications for Dry Chemistry are for medical, agriculture, veterinary, and water testing. Water testing can include: waste water, boiler/cooling water, pool/spa water and drinking water. Typical measurements would be related to chlorine, bromine, pH, hardness, etc. associated with the use and treatment of water.

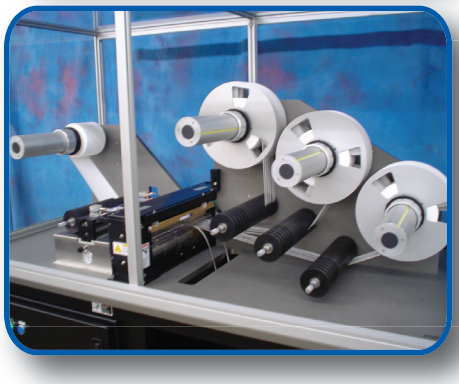
The challenge in the Dry Chemistry marketing is that there are many different formats used for a wide range of applications. The process most likely will include:

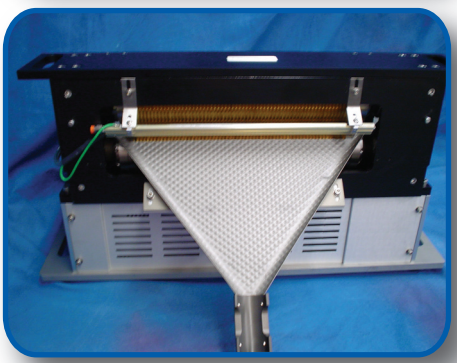
- Dispensing
- Lamination
- Slitting
- Re-Lamination
- Cutting to individual strips
- Placing the strips into Bottles

By combining the BioJet technology either using independent XYZ systems or a Reel to Reel, Autolaminators, and Cutting/Slitting Systems, BioDot can automate the Dry Chemistry Process

Application Flow Diagram







Immunoblots

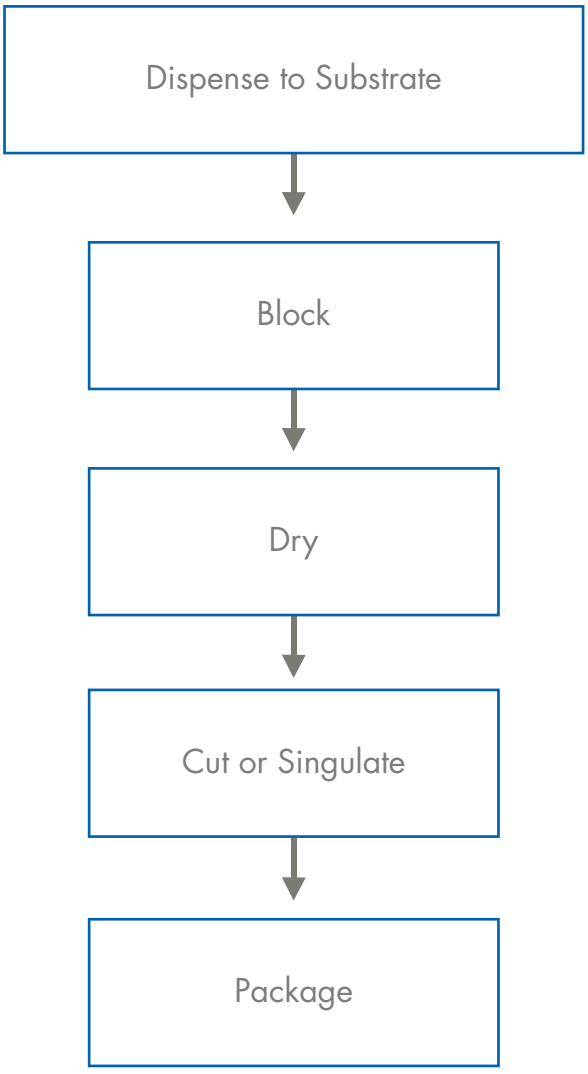
Immunoblotting (alternatively, Western blot, line-ELISA, dot-blot or cold-blot) is an analytical technique used to detect specific proteins in a patients' sample. The proteins to be analyzed are dispensed onto a membrane (typically nitrocellulose, nylon or PVDF), where they are probed by the antibodies of the patient. A simple secondary antibody conjugated to a reporter dye forms the basis of the color reaction which can be read by eye (qualitative) or instrument (qualitative and quantitative).
In the field of diagnostics their use is widespread as a screening tool where a patient can be profiled against multiple markers simultaneously.
Common Immunoblot screening applications include:

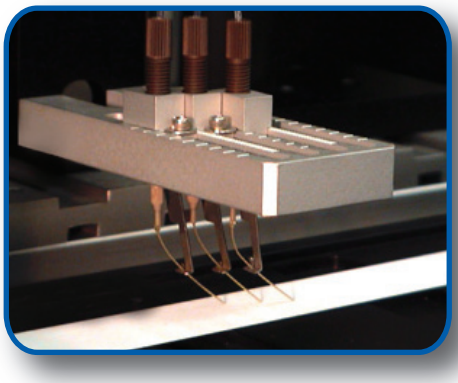
- Allergies
- Cancer Biomarkers
- Autoimmune diseases
- Food intolerance
- Sexually Transmitted Diseases (STDs)

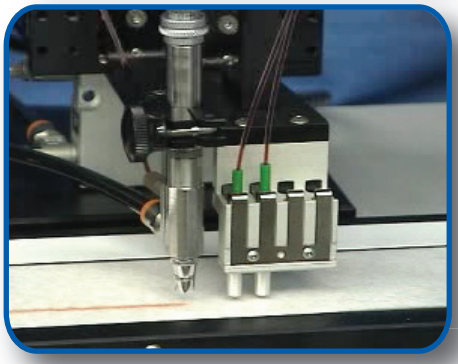
BioDot are at the forefront of the production of Immunoblot diagnostic tests. From a small batch R&D platforms up to large multi-dispenser (32 channels) batch platforms or Reel to Reel systems for full scale production.
Typically proteins (and sometimes DNA) are deposited by a contact or non-contact BioJet Plus dispenser. Once dispensed the 'blots' are blocked then dried. The product is then cut into small strips for their assembly into cassettes.

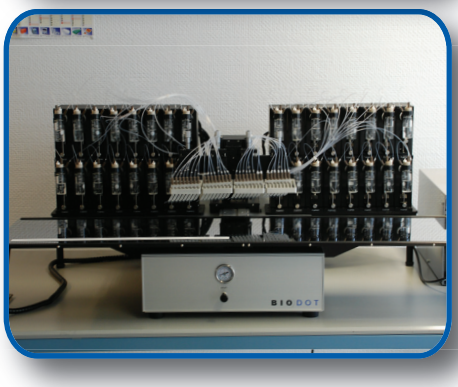
- Front Line or BioJet technology for dispensing the lines
- AirJet equipped dispensing platforms for blocking
- Forced air ovens (with IR sensors) for drying
- Guillotine, rotary cutters and sheet slitters for singulation of tests.

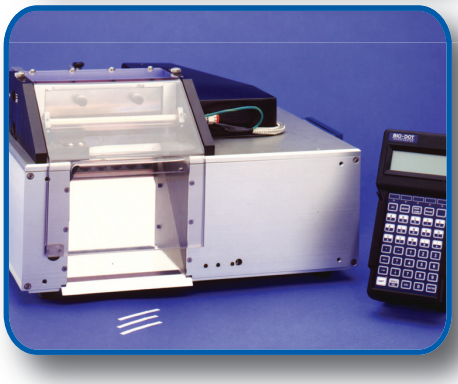
Application Flow Diagram









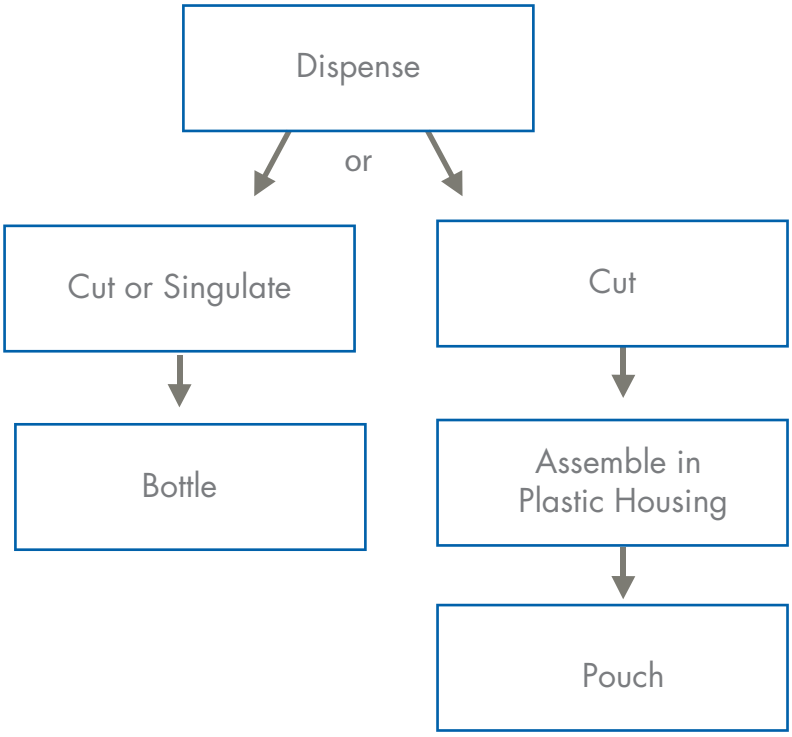


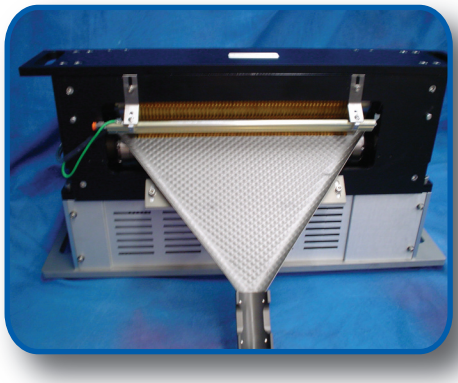
Packaging

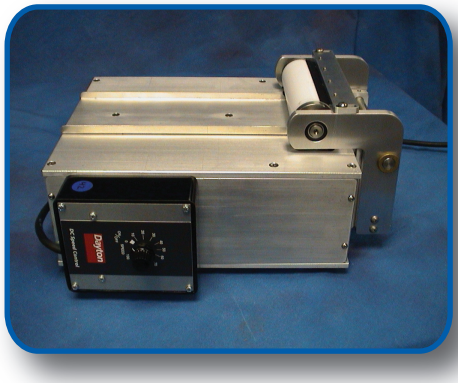
Automated Packaging systems are gaining more acceptances in today's diagnostic marketplace. As the drive to reduce labor costs and injuries, as well as produce consistent quality products, the solution is an Automated Packaging system.

BioDot approaches this by combining our core technology of cutting and slitting with conveyors and pick and place mechanisms to offer complete automated systems or options for a semi automated process.

Application Flow Diagrams







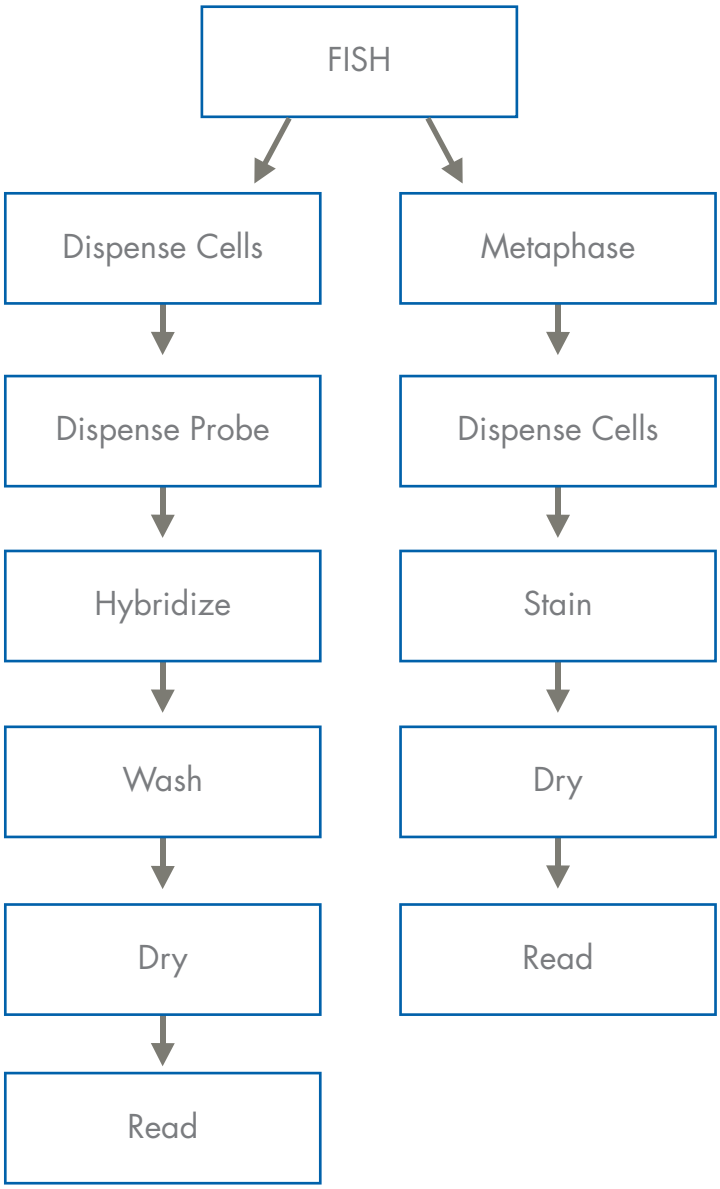
FISH

Use of cells for rapid analysis of chromosomal analysis and genomic diagnostics continues to expand and increase in clinical and research applications. Both direct interphase analysis using FISH and analysis of chromosomes through karyotyping have proven to be successful in providing relevant chromosomal information. With the expansion of these analytical techniques increased throughput and decreased cost of sample preparation and processing have become critical and important factors.

The BioDot automation and dispensing technology have been demonstrated to enable sample and probe multiplexing along with miniaturizing sample volumes, thereby reducing costs, increasing sample throughput, and improving test accuracy.

The BioDot technology can be used for both spotting of cells or metaphase chromosome preparations in nanoliter volumes for FISH and microscopic analysis. After spotting of cell or chromosome preparations, the BioDot technology can also be used to spot probe preparations onto samples in reduced volumes, saving on reagent usage and enabling multiplexing of samples and probes.

Application Flow Diagram



BioDot's Biojet Plus™ Dispensing Technology can be configured on an R&D platform through to production systems, enabling complete scale up solutions with the same technology

AD1500

AD3400

AD6000

qPCR

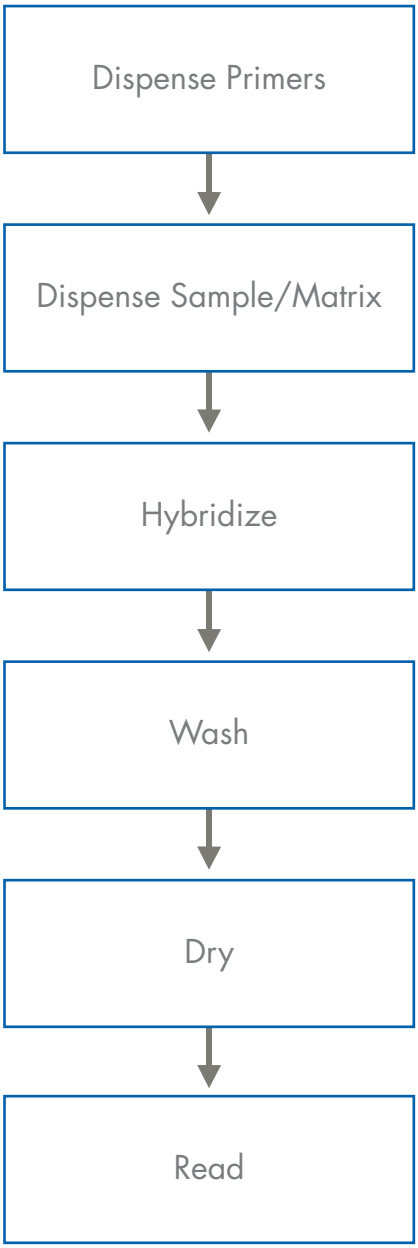
RT-qPCR analysis of genomic and genetic samples has become a standard in genetic research and diagnostics. With the increased usage and acceptance of this analytical approach has come the need to increase sample analysis and throughput along with improved performance.

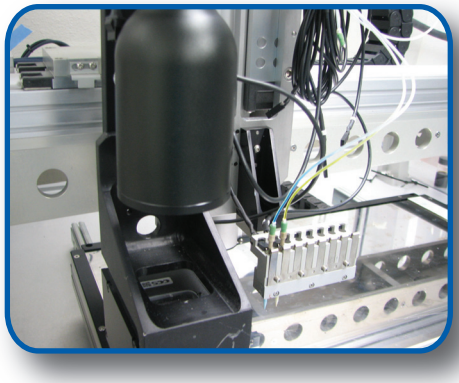
Different areas of qPCR workflow which can be addressed with the BioDot technology include: qPCR reaction make-up, sample distribution, and reaction miniaturization.

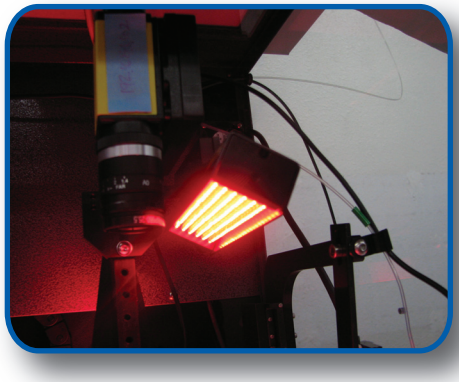
Use of the BioDot technologies and approaches enable increased sample throughput through increased parallelization of sample and reactions, and reduced test costs through miniaturization of reaction test volumes.

With the BioDot dispensing systems, improved accuracy and test performance is achieved through greater control and precision of the qPCR workflow.

Application Flow Diagram







In addition to having the system that allows scale ability, BioDot also offers a complete turn key configuration with vision systems and analysis as well as IQ/OQ support programs.

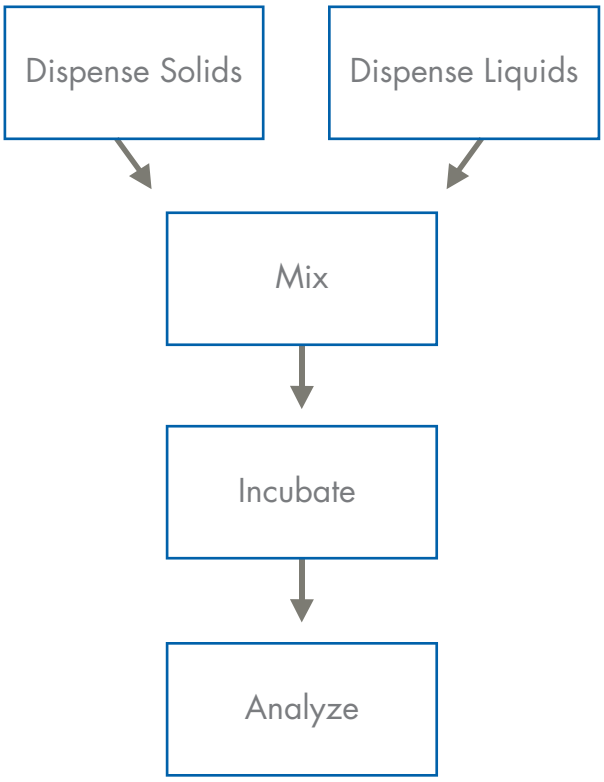
Solid Transferring

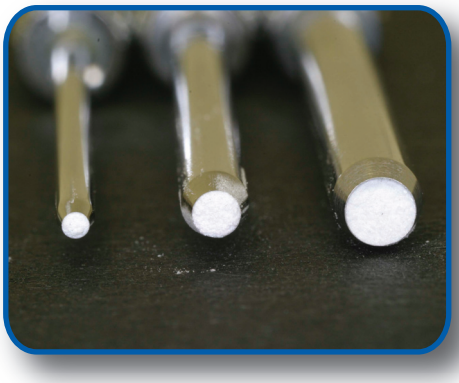
Transferring materials in the solid state has been a challenge for automation for years. Transfer of solid samples with a wide range of properties has proven even more difficult. To further complicate matters, many experiments require sample mass in the microgram range. BioDot's Dispo solid transfer technology provides the ideal solution to these challenges.
By coupling a pneumatically actuated z-axis with a cylindrical probe containing a motorized plunger, which is adjusted according to the desired mass, precise amounts of an array of powder types can be aliquoted. The pneumatic action sends the probe down into the source powder, compacting it into the cavity of the probe. With air pressure as the probe's driving force, the amount transferred will remain equivalent even as the source progressively decreases to minimal levels. To dispense, the plunger is lowered down the shaft, thus displacing the powder into a target vial or tray. Air pressure, probe size, and transfer mechanism may be optimized accordingly based on a compound's specific properties.

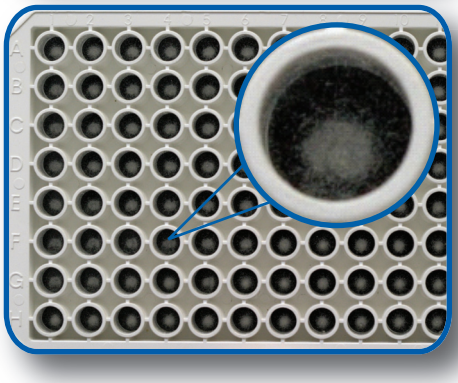
Key Benefits:

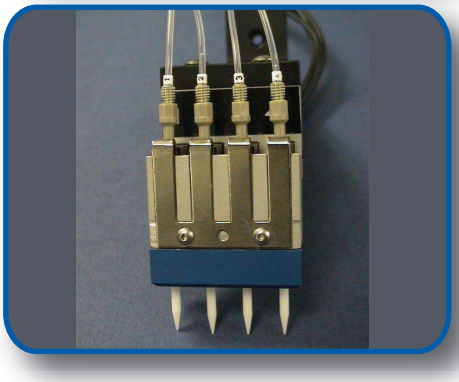
- Works with as little as 50 mg of starting material
- Mass dispense range of 100 ug to 100 mg.
- Non-vibratory operation prevents segregation effects.

Application Flow Diagram









Handheld Solid and Liquid Dispensers

Solid Dispensers

BioDot offers a unique solid transfer approach with it DisPo series of platforms. To both aid in application development with the automated DisPo platforms as well as for general laboratory solid transfer applications, BioDot has developed the DisPo Handheld series of solid dispensers. These handheld solid dispensers operate much like a conventional liquid pipetter with the noted exception that they deliver solid material. Any application where repetitive or frequent manual weighing of solid material occurs is an ideal candidate for the DisPo Handheld dispensers.

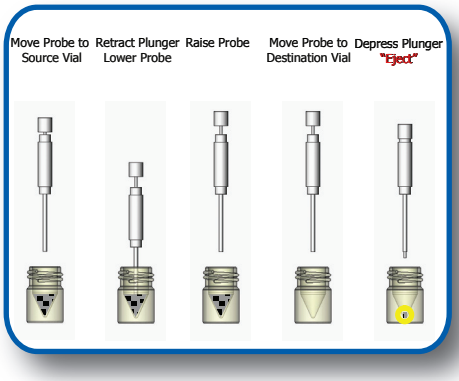
The M series of dispensers come in a range of fixed mass dispensers covering the 100 ug to 100 mg range in 8 individual handheld dispensers. The MA series allows fine adjustment around a fixed mass for applications that require optimization or delivery of a mass that is different than the fixed mass of the M series dispensers. The MR series of dispensers provides a removable dispensing probe option to the fixed mass offerings of the M series and is ideal for applications where cross contamination is a concern. Lastly, the MAR series provides the fine mass adjustment of the MA series with the removable probe option of the MR series for the ultimate in flexibility and dispensing performance.

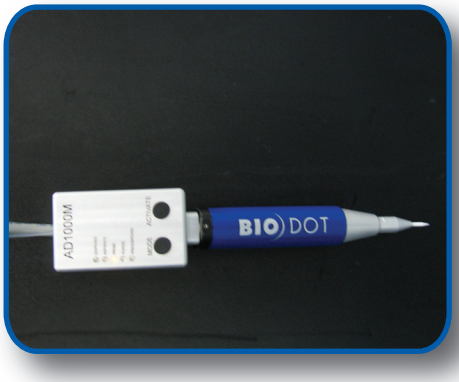
Liquid Dispensers:

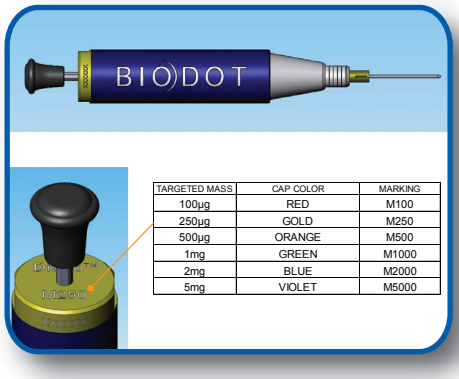
The laboratory manual pipetting market is currently dominated by air displacement handheld mechanical pipettors. However, air displacement pipettes are relatively poor at both accurately and precisely displacing sub-microliter volumes as well as poor at delivering these volumes to their targets. For most applications of sub-microliter dispensing with an air displacement pipettor, "touch-off" contact dispensing is the only means of delivery.

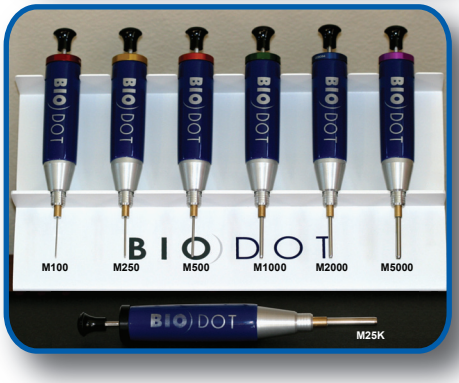
The BioDotter™ liquid dispenser brings the patented BioJetTM non-contact dispensing technology to handheld laboratory pipetting applications. The BioDotter™ is a handheld, simple to use, version of the dispensers found in BioDot's series of automated platforms. This handheld dispenser is ideal for any laboratory application where dispense volumes in the low microliter range or less are required. Compared to air displacement handheld pipettors the BioDotter offers:

- Significantly better precision and accuracy at low volumes
- Extremely effective drop ejection for high speed dispensing
- Wide dynamic range of dispense volumes in a single dispenser
- Unrivaled low-end volume capability; down to 50 nL









BioDot enables, inspires, and educates scientists to commercialize their ideas from R&D through to manufactured product.

www.biodot.com