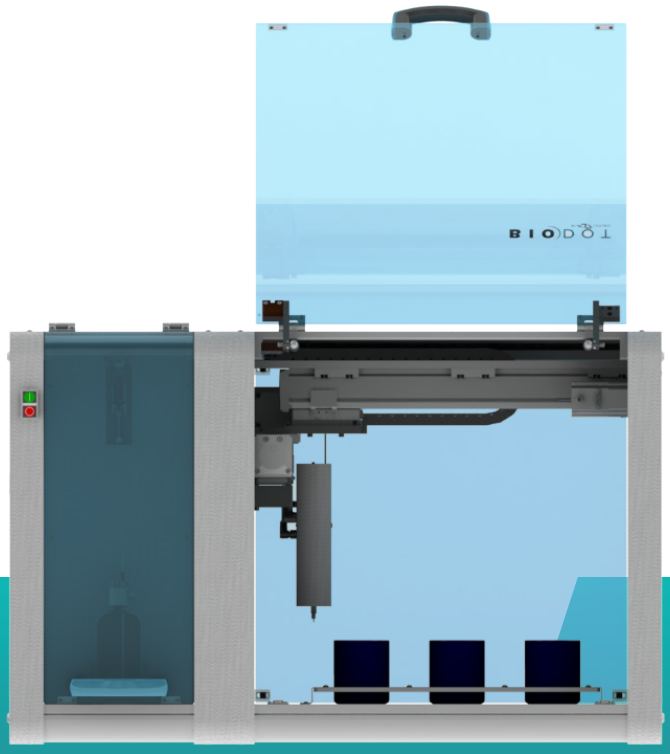
Introducing the

Sphera™ Discovery



Precision Lyobead Dispensing at Your Fingertips

Compact. Efficient. Easy to Use.

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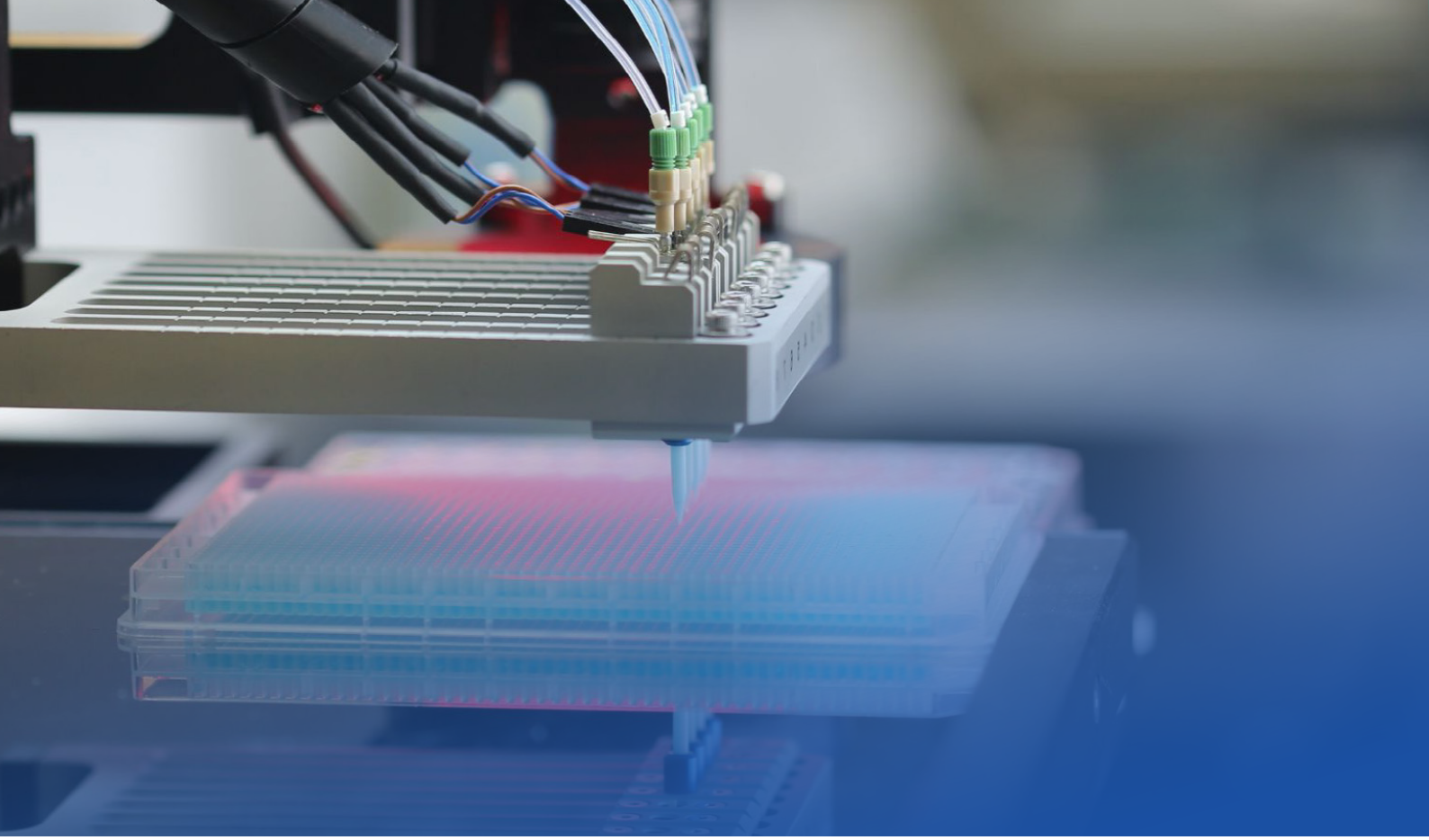

"We are **creating a world** where every **scientist's vision** is met with the **precision** it deserves."

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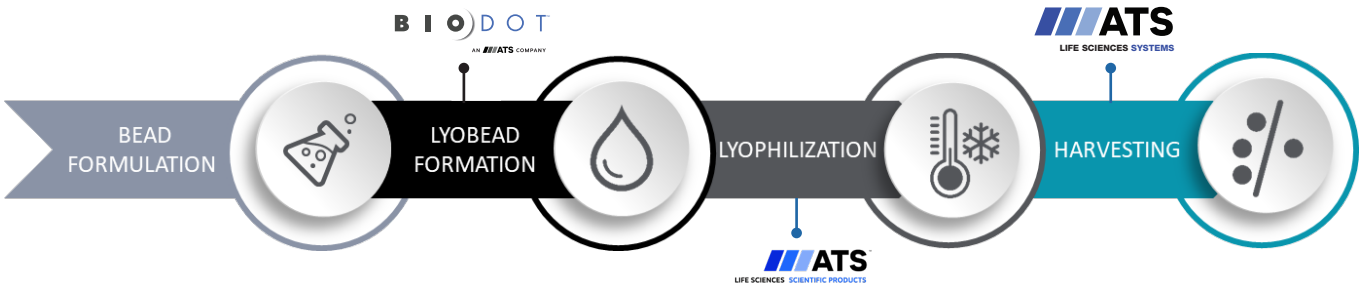
What Are Lyophilized Beads?

Understanding Lyophilized Beads:
The Future of Stability and Precision

Lyophilized beads are small, dry spheres created through the process of freeze-drying. These beads maintain the stability and integrity of sensitive biological materials, making them ideal for various applications, including diagnostics, pharmaceuticals, and research. Their uniformity and long shelf life ensure consistent results and easy handling. Freeze-drying is used in lyophilized bead technology to dehydrate the reagent while preserving the protein and enzyme activity systems.

End-to-End Process Design and Implementation



1 Lyobead Formation

Starting with precise Bead Formulation, BioDot ensures that each bead is carefully crafted to maintain the integrity and quality of the biological materials. The Lyobead Formation step leverages BioDot's advanced technologies **Sphera™** and **Sphera Discovery** to form uniform droplets, ensuring consistency in size and composition.

2 Harvesting

The final stage, Harvesting, guarantees the careful collection of perfectly formed lyophilized beads ready for use in diagnostics, pharmaceuticals, or research. **ATS Life Sciences Group** offers variety of solutions as support for this step.

3 Lyophilization

This is followed by Lyophilization, where the beads undergo a freeze-drying process to preserve their active components, ensuring long-term stability without compromising performance. This step is supported by **ATS Life Sciences Scientific Products** solutions.

Through this workflow, BioDot adds exceptional value through precision engineering, ensuring reliability, reproducibility, and quality in every bead. Our process supports a wide range of applications, empowering labs and industries to achieve their goals with confidence.

Need support on any step of the workflow?
Contact us now **www.biodot.com/contact-us**

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Things to Consider When Forming Lyobeads

The Scientific Art of Lyobead Formation: **Quality Matters**

Creating high-quality lyophilized beads requires precision and attention to detail. Factors such as bead size, composition, and freeze-drying parameters significantly impact the final product's quality. BioDot's Lyobead solutions are engineered to optimize these variables, ensuring that every bead meets the highest standards for research and development.

Key Considerations:

- Bead Size Uniformity
- Composition Control
- Freeze-Drying Parameters

The Sphera™ Discovery system is highlighted as the superior choice for lyobead production due to its precision, efficiency, compact/standardized design, reduced reagent waste, scalability, and cost-effectiveness, making it an ideal solution for labs of all sizes.

Criteria	Sphera™ Discovery	Sphera™	Manual Lyobead Formation Solution	In-House Engineering System
Consistency in Bead Size & Quality	Precise and Uniform – Ensures consistent size and composition, reducing variability	Reliable – Engineered for consistent size and quality across production runs, reducing variability and improving reproducibility	Inconsistent – Variable sizes, shapes, and compositions, impacting stability and performance	Potential variability in bead size and composition, affecting performance
Production Efficiency	Efficient – Automated process increases speed, boosting throughput with less labor	High Efficiency – Automation streamlines processes, increasing output with minimal manual intervention	Labor-Intensive – Time-consuming manual processes limit scalability	Potentially Labor-Intensive – High manual intervention, increasing labor costs and error potential
Design & User Accessibility	Compact & User-Friendly – Small footprint, easy-to-use, accessible to all labs	Intuitive Design – Minimal training required; adaptable to different lab workflows	Can be user specific - Whereby the SOP is not readily executed by all technicians equally	Engineering-Dependent – Requires extensive internal engineering for setup, maintenance, and trouble-shooting
Reagent Usage & Waste	Low Waste – Automated precision minimizes reagent loss	Optimized Usage – Accurate dispensing lowers reagent waste and cost	High Waste – Manual inefficiencies lead to significant reagent waste	Possible High Waste – Variability in manual processes increases reagent loss and costs
Scalability for Growing Needs	Scalable – BioDot offers Sphera Platform to support scale-up when needed.	Easily Scalable – Modular and flexible system design can be expanded as demand grows	Limited Scalability – Manual process limitations create bottlenecks	Scalability Issues – Struggles to scale as production needs increase requiring precious in-house engineering resources to support growth
Operational Cost	Cost-Effective – Efficient automation reduces labor and waste costs	Cost-Effective – Efficient automation, Reduced need for manual labor and minimizes waste	High Cost – Increased labor and material waste drive up costs	High Cost – Labor, engineering dependence, and reagent waste raise operational expenses
Standardized Product	Core Competency of BioDot - currently two platforms available to address the application; the product will evolve based on lyobead user feedback	Standardized and Modular – Proven track record across multiple labs; evolves with customer input	Myopic Perspective - Looking at the lyobead needs within a single organization and not on the evolving need of the lyobead formation application	Unique Solution - As a result, it lacks reliable components and is prone to obsolescence when it comes to supporting and developing automation
Throughput	Designed for development, can scale to 6 beads/ min ; higher throughputs available with Sphera when development of reagents is complete	High Throughput – Engineered for efficient lyobead formation at scale. Up to 1000 beads/ hour	Limited Throughput - Limited by throughput of operators, so need to add FTEs or but additional low throughput equipment	Limited Throughput - Often need to copycat Low throughput options require more engineering time to deploy a low throughput option

Meet the Sphera™ Discovery

Your Gateway to Advanced Lyobead Formation

The Sphera Discovery brings the power of our cutting-edge Sphera lyobead formation system to your laboratory in a compact, research level platform. Designed for researchers, small-scale production facilities, and innovative startups, the Sphera Discovery delivers precise, reliable lyobead formation without compromising on quality or performance.

Why Choose the Sphera Discovery
Unleash the Power of Precision in a Compact Format

Precision Redefined
Achieve volume precision of < 3% CV, rivaling larger systems.

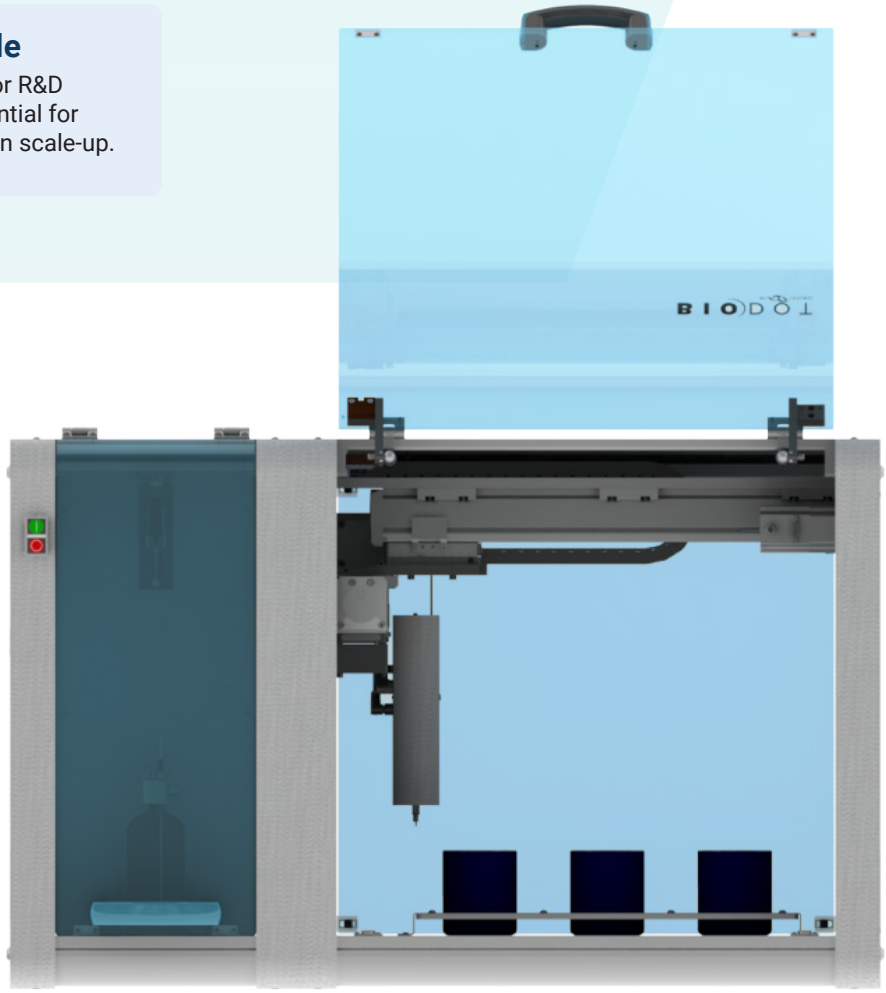
Space-Efficient
Compact design fits seamlessly into any lab environment.(System measurements are 41” Width x 28” Height x 20” Depth).

Cost-Effective
Entry-level pricing without compromising on quality.

Versatile Applications
From diagnostic reagents to bacterial vaccines.

User-Friendly
Intuitive interface for easy operation and quick setup.

Scalable
Perfect for R&D with potential for production scale-up.



Need more details?
Contact your Sales Rep directly or contact BioDot
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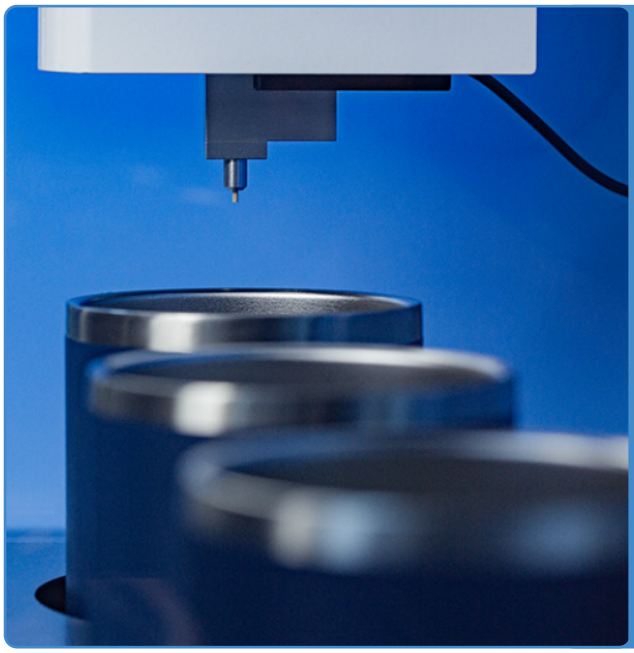
Sphera™ Discovery, Powered by the BioJet™

The Sphera Discovery utilizes our proprietary Discrete Droplet Dispensing™ BioJet technology to create uniform, precise lyobeads.



Bio-Jet: High-speed, non contact dispensing

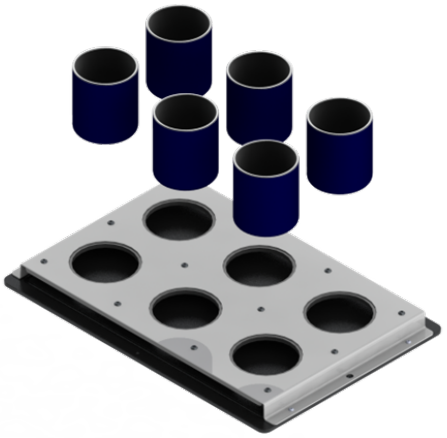
This proprietary, quantitative, non-contact technology couples the BioJet "Drop-on-Demand" valve with a high-resolution syringe pump.

The BioJet meters precise amounts of reagent, incorporating the benefits of non-contact dispensing and the ability to program exact drop volumes.

BioJet allows you to tune bead size quickly, speeding development time.

Benefits and Features of Sphera Discovery:

- Volumes: 2 µL- 30 µL as a single drop
- Volume precision of < 3% CV
- High-speed, non-contact dispensing
- Dispense 6 to 8 beads per minute
- Scalable from R&D to production environments
- Step-and-repeat printing mode
- On-board containers reduce liquid nitrogen usage and minimize cold-chain logistics and costs
- Lyobeads are thermally stable with a long shelf life
- Lyobeads have lower risk of contamination
- Lyobeads can have better reconstitution properties than traditional lyocakes
- Lyobeads are easily transported using on-board Dewars



Need more details on specifications: **www.biodot.com/news-resources/sphera-tm-discovery-datasheet**

From R&D to Full-Scale Production

Bigger Batches: Choose the Sphera™

As your production needs grow, BioDot's Sphera is here to support your transition from small-scale R&D to full-scale commercial production. While the Sphera Discovery is perfect for R&D-level applications and small batches, the Sphera provides the capacity and power to meet higher throughput requirements, ensuring scalability without compromising on quality.

Why Choose the Sphera for Larger Batches?

Horizontal Camera For Advanced In-Process Testing

The Sphera is equipped with a horizontal camera for real-time, in-process testing, ensuring each batch meets the highest quality standards without slowing down production.

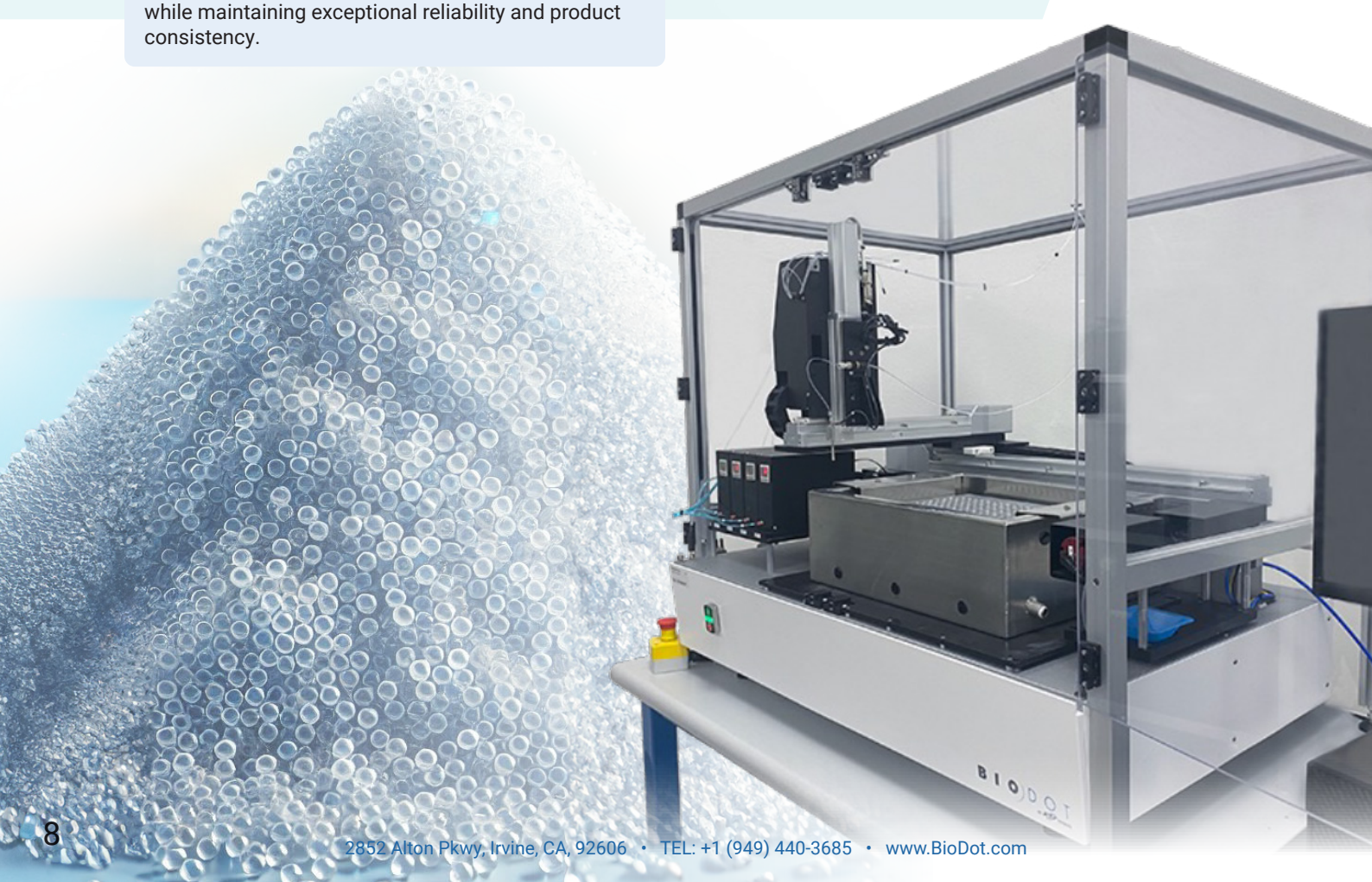
High-Throughput Performance

Delivers faster processing and higher throughput, with the ability to create 10-40K beads per hour, making it ideal for high-demand production environments.

* Reagent dependent

Robust Performance and High Efficiency

Offers advanced control over lyophilization settings, allowing you to tailor bead production to your specific needs. In addition, the Sphera is designed for continuous, high-demand production environments while maintaining exceptional reliability and product consistency.



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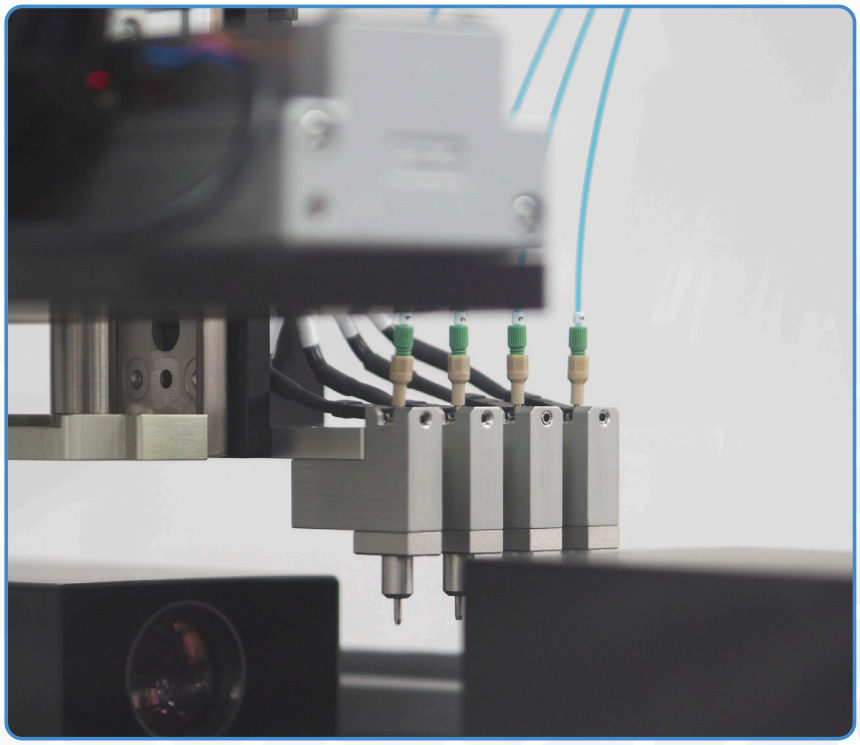
Sphera Features & Benefits

BioDot Sphera For Lyobead Formation

The lyobead formation system dispenses precise and accurate droplet (spheres) into an onboard liquid nitrogen bath. Our unique precision, accuracy, and throughput specifications are achieved by coupling a high-resolution adaptive pneumatic pump with our high-speed BioJet™ valve. A single tip can produce up to 10,000 beads per hour, while four tips can produce up to 40,000 beads per hour.

- Volumes: 2 µL- 30 µL as a single drop
- Volume precision of < 3% CV
- High speed, non-contact dispensing
- Continuous (bulk) dispense
- Scalable from R&D to production environments
- Step-and-repeat and On-the-fly printing modes
- Minimization of cold-chain logistics and costs
- Lyobeads are thermally stable with a long shelf life
- Lyobeads have lower risk of contamination
- Lyobeads can have better reconstitution properties than traditional lyocakes



BioJet Pneumatic Pump

Lyobead Applications

Versatility Across Industries

Lyophilized beads (Lyobeads) are a revolutionary solution for stabilizing and preserving sensitive biological materials. Their compact, dry form makes them easy to handle, transport, and store while maintaining their biological activity over long periods. These versatile beads have applications in a wide range of industries:

Diagnostics

Lyobeads are used in diagnostic kits to ensure consistent, reliable results, enabling accurate disease detection and monitoring.

Pharmaceuticals

Ideal for drug formulation, Lyobeads help maintain the stability and potency of active ingredients, extending shelf life and facilitating dosage accuracy.

Research and Development

Lyobeads provide researchers with stable and consistent samples for experiments, reducing variability and improving experimental outcomes.

Biotechnology

These beads are used in enzyme storage, vaccine formulation, and other biotech applications, ensuring materials are stable and effective even under challenging conditions.

With BioDot's advanced Lyobead maker(s), labs and companies across these industries can efficiently produce high-quality lyophilized beads, ensuring precision, reliability, and reproducibility in every application.

Additional applications:

- Enzymes
- Buffers
- Chromophores
- Probiotics
- Vaccines
- Calibrators
- PCR assays
- Antibodies
- Diagnostic reagents
- Magnetic/ Fluorescent Particles

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Lyophilized Beads: Efficient, Scalable Production

Challenge

Production of lyophilized beads at the microliter scale results can be difficult to achieve with conventional dispensing technologies. Production environments are often forced to manage inconsistent drop volumes, poor and inconsistent bead morphologies, and low throughput. These inconsistencies lead to poor yield and ultimately increase the cost of manufacturing when valuable reagents and personnel time are lost.

Additionally, significant yield loss occurs in common production settings due to a lack of in-process QC control. In most production facilities, waiting to measure bead accuracy until after lyophilization means that entire batches can be lost along with days of production time. This study evaluates the use of a horizontal droplet camera to accurately and effectively measure drop volumes as an in-process, proactive QC tool.

Brian Kirk, VP Engineering
Brian Kirk has been with BioDot since 2001 and has spent that time designing, developing, and marketing high throughput manufacturing systems for many of the world's leading diagnostic and life science companies. As a member of the original team who developed the patented FISHArray™ technology and CellWriter™ workstation for cytogenetics, Brian now leads the Business Development team within BioDot where he leverages BioDot's expertise in high throughput nanoliter and picoliter printing technologies to commercialize important tools for emerging life science markets.

Method

Three standard volumes (2µL, 10µL, and 30µL) of qPCR mastermix solution were dispensed into isolated wells chilled with liquid nitrogen (LN2). The total number of dispenses were recorded, including a standard set of calibration dispenses (50).

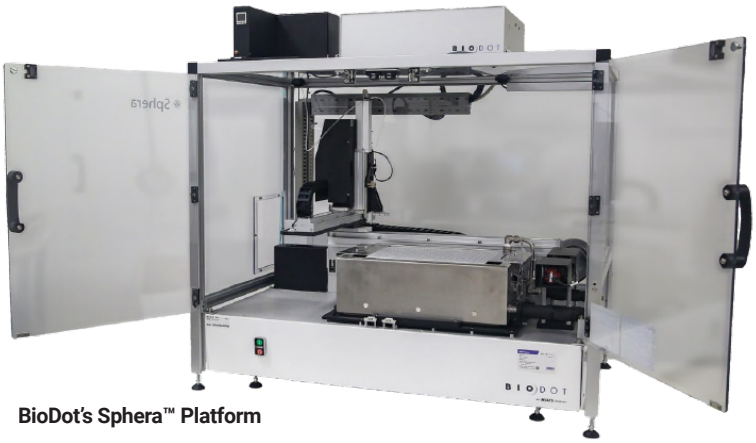
- For 2µL, 845 dispenses (723.75µL total solution) were performed, resulting in 795 lyobeads (50 used in calibration).
- For 10µL, 289 dispenses (1237.50µL total solution) were performed, resulting in 239 lyobeads (50 spent in calibration).
- For 30µL, 139 dispenses (1788.75µL total solution) were performed, resulting in 89 lyobeads (50 used in calibration).

Dispense values including pressures and open times were optimized and recorded. Coefficient of variation and average drop volume were recorded via the on-board horizontal drop camera. Fresh lyobeads were then measured after formation and once more after to lyophilization to understand total end product diameter. Broken, merged (doublet/triplet), and other damaged beads were recorded so that true product yield could be assessed, and shrinkage after drying was also measured.

Solution

Using BioDot's patented Sphera dispensing technology, lyophilized beads were created with minimal loss. BioDot's Sphera instrument produced consistent lyobeads at 2µL,10µL, and 30µL, and exhibited a yield of 96%, 96.6%, and 96.6%, respectively.

Faulty beads were minimized with individual partition holes, allowing the beads to form without defects. The dispense process only took 1 hour (20 minutes per dispense volume size) and an additional 75 hours for full lyophilization. By reducing defects and automating the dispense process, BioDot's Sphera saved time and labor in lyobead production.



BioDot's Sphera™ Platform

Results

- The coefficient of variation (CV) for all dispenses was approximately 1%.
- Of the 795 2µL droplets, a total of 22 beads were broken (2.8%) and 10 were doublets (1.3%), for a total yield of 96.0%
- Of the 239 10µL droplets, a total of 6 beads were broken (2.5%) and 2 were doublets (0.8%), for a total yield of 96.6%
- Of the 89 30µL droplets, a total of 2 were broken, (2.2%) and one was a double (1.1%), for a total yield of 96.6%
- Out of 1123 total beads (excluding calibration dispenses), 43 were lost due to breakage or doubling (96.2% yield).

As expected, (due to water expansion during the freezing process), we found an increase in volume/diameter when we compared the data from our horizontal drop camera to the measured frozen bead diameters. The average volume increase was 4.5% (2µL), 4.9% (10µL) and 4.4% (30µL). While water expands by an average of 9% when it freezes, it is unclear what the expected increase is for qPCR mastermix.

When comparing volumes from the horizontal camera to the measured volumes after lyophilization, a strong correlation was observed. The horizontal camera had accuracies of 98.8% (2µL), 98.2% (10µL) and 100.1% (30µL) with respect to target volume. Post lyophilization diameters had accuracies of 100.64% (2µL), 100.00% (10µL) and 100.78% (30µL) with respect to target volume.

Volume	# of Beads	Yield	Horizontal Drop Camera (CV%)	Frozen Beads (CV%)	Lyophilized Beads (CV%)
2 µl	795	96.0%	0.9%	2.3%	3.9%
10 µl	239	96.0%	1.2%	3.6%	4.2%
30 µl	89	96.0%	0.9%	4.1%	3.6%

Comparing the Horizontal Camera Data to Measured Diameters

Horizontal Drop Camera			Frozen Beads		Lyophilized Beads	
Volume	Average Drop Camera Volume (µL)	Diameter Accuracy	AVG Frozen Beads Measurement Diameter (mm)	Diameter Accuracy	AVG Lyophilized Beads Measurement Diameter (mm)	Diameter Accuracy
2 µl	1.98	98.8%	1.63	104.5%	1.57	100.6%
10 µl	9.82	98.2%	2.81	104.9%	2.68	100.0%
30 µl	30.04	100.1%	4.03	104.4%	3.89	100.8%

Lyobeads in liquid nitrogen after dispensing

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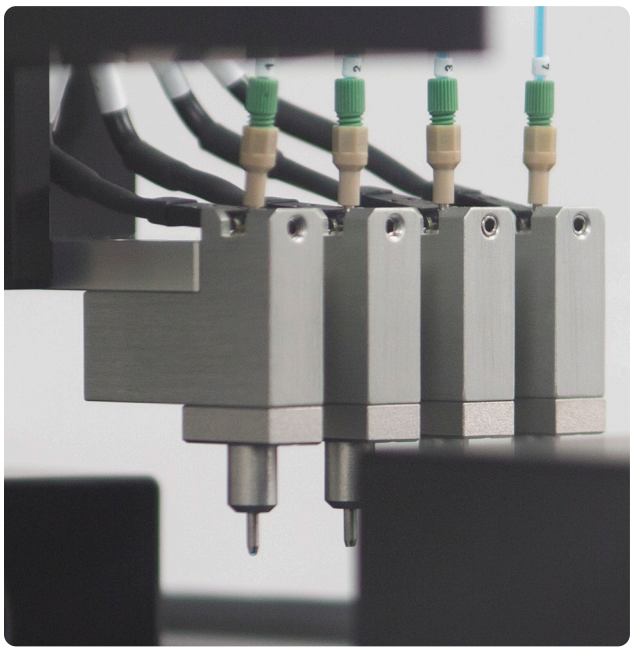
About the Sphera™

The BioDot Sphera allows for scalability and versatility. The system can be configured to dispense a range in drop sizes from 2µL-30µL. The system can scale to address changing throughputs by adding dispense channels, in the field. Multiple channels can be installed on a single dispense arm allowing simultaneous on-the-fly dispensing into isolated wells. Multiple passes are repeated with synchronization of freeze cycles and drop times to generate an optimized number of Lyobeads in liquid nitrogen after dispensing of beads per pass.

Lyobead formation relies on uniformity of bead size to the desired drop volume. An integrated camera is used to measure the volume of the bead in-flight to ensure process performance.

Volume, drop rates, speed, placement in and above the isolated wells, and imaging of the dispense are controllable parameters of the lyobead application on a BioDot Sphera™ platform. The Sphera platform can be configured with multiple dispense channels to address various bead throughputs from 10,000 beads per hour per dispense channel.



In-flight capture of 10µL drops

Conclusions

BioDot's Sphera is extremely efficient at dispensing and creating lyobeads. The beads are high quality with minimal loss of beads to breakage, falling apart or adhering to other beads.

Some companies will dedicate in-house engineering resources to develop a custom solution to create lyobeads. This can take months of learning about the nuances of the science. A homemade solution requires continual support and is best assigned to experts in the application. Unleash the power of BioDot's Discrete Droplet Dispensing™, our platform design expertise and global support are available in an established product for lyobead formation.

1000 drops of 4.2µL in volume captured in-flight showing 0.52% CV

BIODOT

AN ATS COMPANY

Headquarters

BioDot – UNITED STATES

2852 Alton Pkwy
Irvine, CA 92602
TEL: +1 (949) 440-3685

Offices

Europe, Middle East, Africa, Russia)

1, West Barn Old Dairy Lane,
Westergate, Chichester PO20 3AF
United Kingdom

BioDot Shanghai - China

BioDot Shanghai - China
3rd Floor, Building A5, Lane 99,
Jiajie Road, Qingpu District,
Shanghai, China

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