

NEXT GENERATION  
BIOANALYTICAL TECHNOLOGY



BLINK<sup>+</sup>DX

# NEXT GENERATION BIOANALYTICAL TECHNOLOGY

# BLINK DX

## OUR TECHNOLOGY MAKES QUANTITATIVE MULTIPLEXING A REALITY.

As the needs of the bioanalysis and diagnostics sectors become increasingly advanced, they require reagents and instrumentation to keep pace. BLINK's next-generation digital assay design offers a simplified, robust, and rapid sample-to-answer workflow with dramatically improved sample utilization, multiplexing and quantification.

Our technology enables microfluidics-free dPCR, eliminating the need for expensive disposable microfluidic devices. It facilitates cross-reactivity free multiplexing and full digital and real time target quantification for each individual assay parameter.

BLINK's technology offering is based on a novel reagent, BLINK Beads. These nanoreactor beads are a nucleic acid purification tool, an amplification and detection compartment, and a fluorescence-encoded carrier for target specific reagents. Every assay is developed on BLINK Beads and can be run in a laboratory format or on a point-of-care platform.

We have developed a laboratory instrument, the BLINK X and disposable chambers for processing Bead-based assays, enabling opportunities for Bead exploration. We have also developed an integrated cartridge for Bead assays and cartridge-processing instrument, the BLINK One.

These tools are now available for collaborators to explore and identify areas of interest and to define specifications for dedicated products.



# BLINK BEADS

BLINK BEADS ARE THE FOUNDATION FOR NEXT GENERATION MOLECULAR ASSAY DESIGN, OFFERING A SIMPLIFIED, ROBUST, RAPID AND UNDISRUPTED SAMPLE-TO-ANSWER WORKFLOW WITH DRAMATICALLY IMPROVED SAMPLE UTILIZATION AND ASSAY PERFORMANCE.

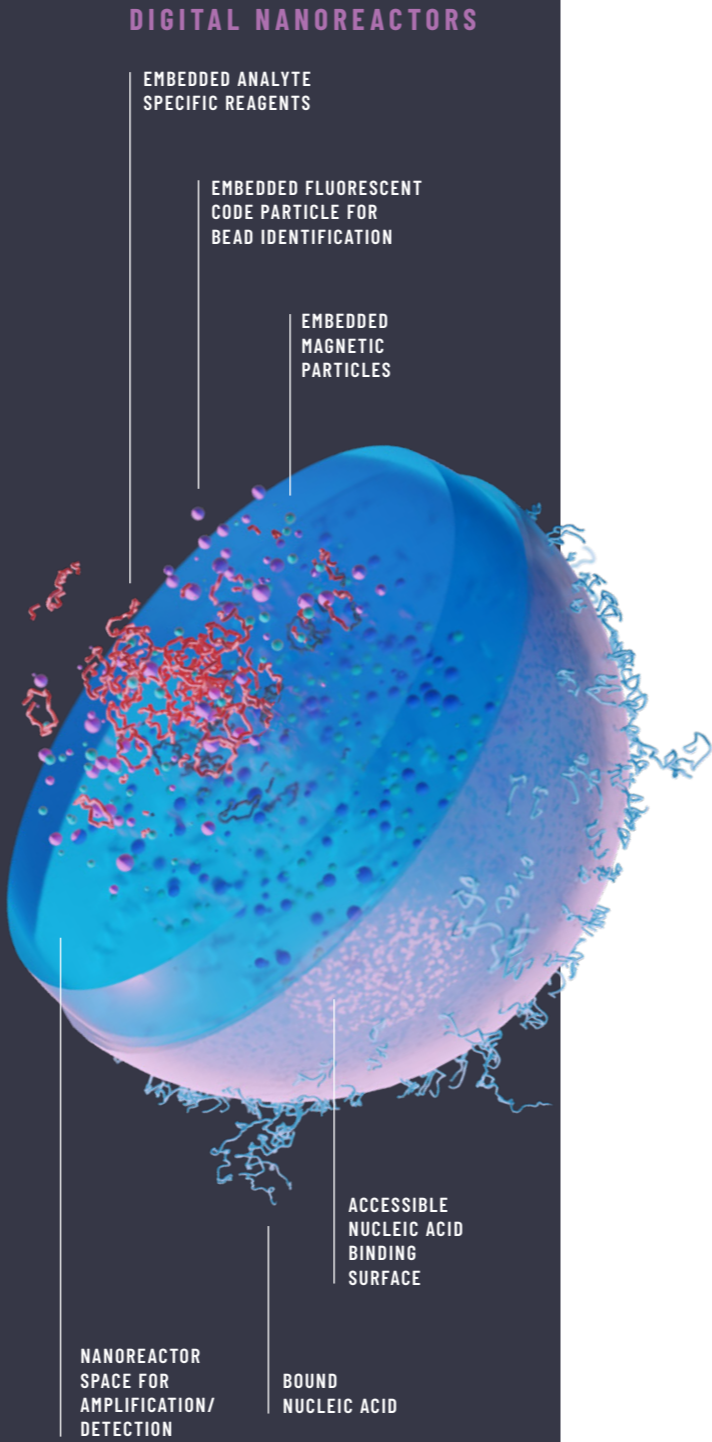
The Beads are magnetic fluorescence encoded nanoreactors equipped with target specific reagents that facilitate digital multiplex assays. They are comprised of a porous matrix that provides a surface for random distribution and binding of targets and the compartment for the amplification and detection reaction.

Beads enable complex analysis that traditionally require multiple separate workflows and assays to be performed with a single test. PCR reactions can be performed within 10 minutes on a simple laboratory instrument, the BLINK X, while the multiplexing capabilities enable more than 50 assays to be performed

in parallel on one sample. Importantly, BLINK Beads are still compatible with existent assays and device platforms.

Compartmentalisation is an integral component of any BLINK Bead workflow, so each assay can be performed in a digital format. With BLINK Beads, digital PCR becomes a tool that is as accessible and easy-to-use as qPCR.

Bead-based dPCR assays are microfluidics-free. Sample compartmentalization is provided by pre-made hydrogel beads and does not require microfluidic droplet generators or expensive nano-well plates with precise amplification volumes.



BLINK BEADS CAN BE EASILY LOADED WITH ANALYTE/TARGET SPECIFIC REAGENTS. THESE DIFFERENT PRE-MADE BEAD ASSAYS CAN BE COMBINED FREELY INTO COMPLEX DIGITAL TEST PANELS.

## BASIC ASSAY FORMATS



### SIMPLE dPCR

Sensitivity & exquisite target quantification.

BLINK Beads encoded with a dye for automatic Bead recognition can be used with any primers/probes to design and perform a digital assay with exquisite quantification. When used on the BLINK X platform, digital PCR can be performed in under 15 minutes.



### ULTRAPLEX

Quantitative, ultra-sensitive target multiplexing.

Ultrplexing is highly flexible, extensive detection and quantification of multiple targets from a sample with single molecule sensitivity. This process allows each panel member to be quantitated without cross-interference. Beads with different fluorescence codes are equipped with analyte specific reagents and used in parallel.



### SAMPLE MULTIPLEXING

Multiple sample parallel processing.

Sample Multiplexing involves selective encoding of individual samples with encoded beads, allowing for parallel processing of multiple samples in one test assay. Once the targets are bound to the Beads the detection reaction is carried out simultaneously on all samples in the respective reaction compartments provided by the Beads.

# BLINK BEAD ANALYSES



## dPCR

Analytes in a known volume of sample are randomly distributed across a known number of Bead nanoreactors, which are used as individual amplification and detection compartments for dPCR. Beads are then washed and loaded with generic PCR reagents and encapsulated in oil, preventing liquid exchange between Beads. They are then arranged in a plate for exquisite temperature control and fluorescence detection, after which a simple algorithm is applied to quantitate positive reactions. Applying Poisson statistics, which models the random distribution of the target into the partitions, this results in absolute target concentration.

Unlike in other digital PCR concepts random distribution of targets across the Beads is achieved by binding the nucleic acid to the Beads. Compartmentalisation is achieved without the need for sophisticated disposable plastics or microfluidics.

For Bead assays only the number of Beads interrogated with a known volume of sample is relevant. Since targets are bound to the Beads, different sample volumes can be used for digital analysis.



## qRT-PCR

During PCR, amplification can be monitored by real time fluorescence detection for each Bead, thus each Bead becomes an individual qPCR assay. This provides for quantification by Ct analysis when the digital measurement range is exceeded due to high target concentration or the level of multiplexing is very high.

By combining digital and real-time analysis, an unprecedented measurement of >8 logs range is facilitated, while sample can be quantitated without any diluting steps. Ct analysis also provides for trouble shooting during assay development as the Ct value is a great indicator for sample purity.



## THE MONOLAYER

For detection and optimal temperature control, our product features self-arrangement of nanoreactors in a monolayer. This process is fast, robust and provides for quick thermocycling, allowing PCR reactions within 10 minutes. The monolayer arrangement simplifies imaging and even enables advanced features such as real-time imaging (qPCR) and melt curve analysis.



## MELT CURVE ANALYSIS

Real-time monitoring of Bead-specific fluorescence also provides for melt curve analysis. A  $T_m$  value can be assigned to every individual amplification product formed on the Beads and used for specificity analysis. This provides a straightforward technical approach for massively parallel, rapid mutation analysis and assuring specificity for rare or even single amplification events.



## NO CROSS-INTERFERENCE

Primers and probes are reversibly bound to the encoded Beads so that different Beads can be used together for sample prep. Once accommodated in oil, the primers and probes are released for amplification and detection. Since each reaction is carried out in an individual compartment, Beads, and as such assays, with different target specificities can be safely combined in a single workflow without cross interference.



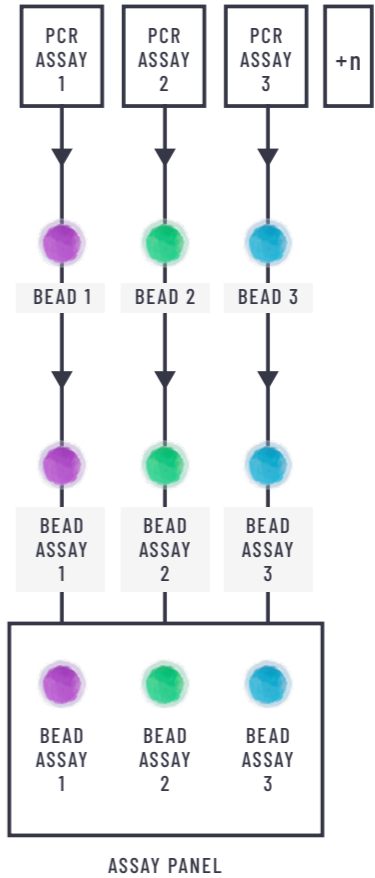
## SCALABLE

Integration of BLINK Beads on automated laboratory tools or transfer to point-of-care platforms is straightforward.



## CUSTOMIZABLE

BLINK Beads can be customized for specific applications with different primers and probes.



# MASSIVE MULTIPLEXING

Fluorescence-encoded Beads equipped with different primers and probes can be combined to form complex digital multiplex panels. Compartmentalisation facilitated by the Bead design results in multiplex assays that are free from any cross-interference.



## LOWER COST & COMPLEXITY

Using Beads for dPCR lowers both the cost and the complexity of the process. Additional sample preparation kits are not needed for "sample-to-answer" assays.



## REDUCED HANDS-ON TIME

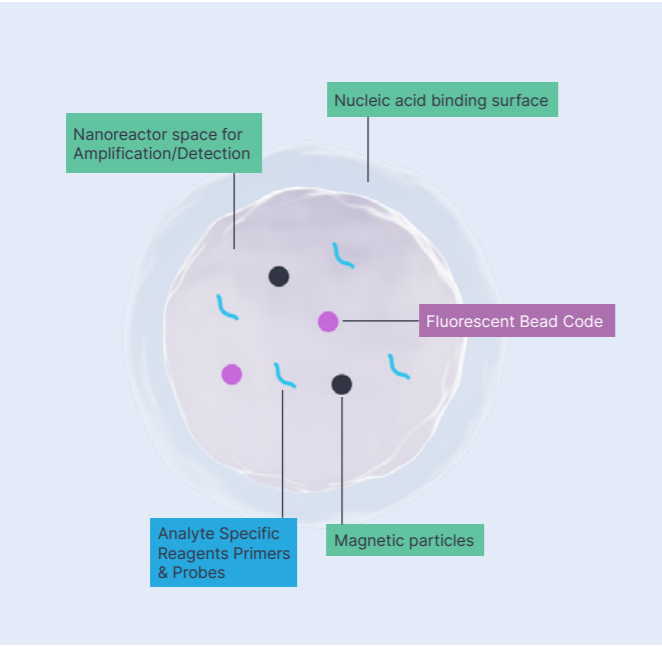
Beads can be equipped with assay specific reagents so that only generic reagents need to be added.



## INCREASED SENSITIVITY & PRECISION

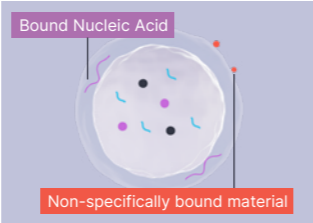
The entire sample volume can be used for analysis, increasing both the sensitivity & precision of the assay.

# BLINK BEAD WORKFLOW



## BEAD ARCHITECTURE

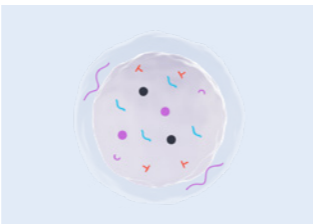
BLINK Beads comprise a hydrogel matrix that defines the actual space for amplification and detection. Each Bead is encoded with a fluorescent code and carries magnetic particles for ease of handling. Moreover, the matrix is derivatized with streptavidin providing a simple means for reversibly attaching primer and probe oligonucleotides to the matrix. The hydrogel matrix is coated with a crosslinked polymer for efficient binding of nucleic acids.



1. In a suitable binding buffer nucleic acids contained in a lysed sample bind to the Bead surface.



2. A wash step removes un-specifically bound materials leaving purified nucleic acid bound to the Bead.



3. The generic PCR mix containing enzymes, dNTPs and buffer diffuses into Beads.



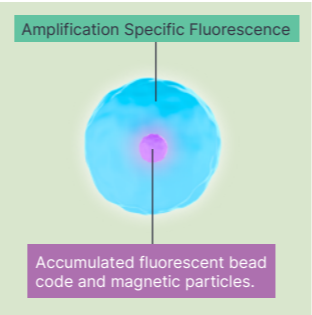
4. Beads are suspended in oil, resulting in individual reaction volumes.



5. Hydrogel core liquifies at elevated temperature and forms a droplet. Primers & probes are released. Enzymes are activated. PCR begins. All code and magnetic particles are confined within a space formed by the contracting binding layer, thus clearing up the nanoreactor space for amplification and fluorescence detection.



6. Target specific amplification is performed within the nanoreactor space formed by the Bead.



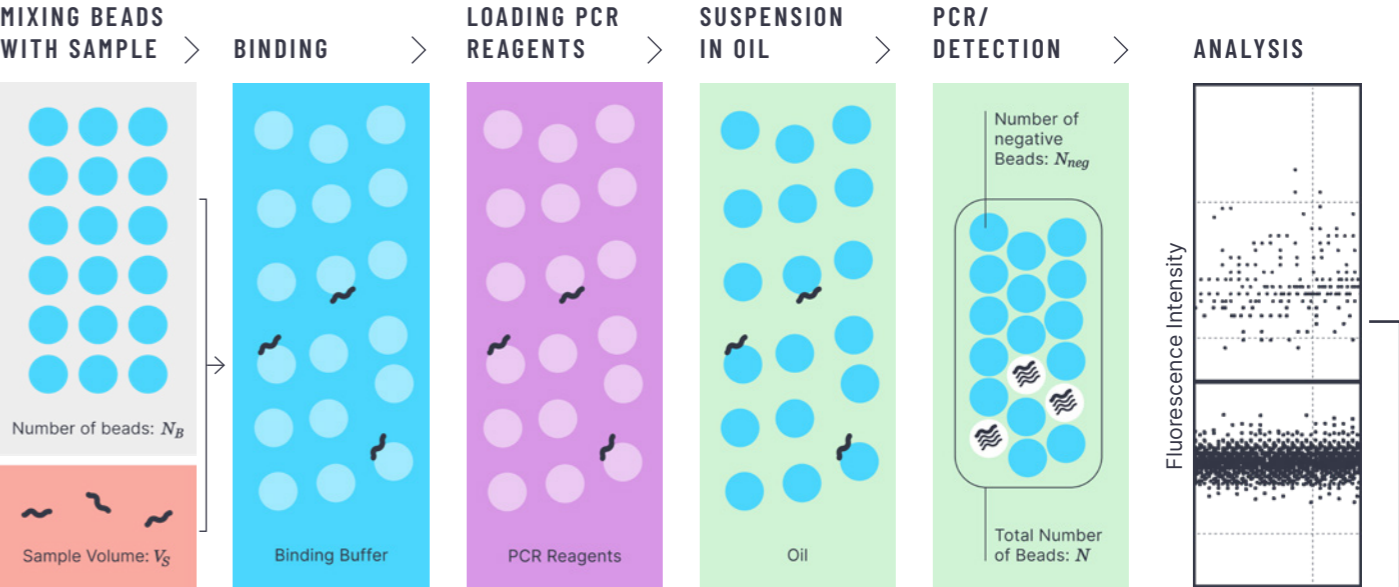
7. Due to spatial separation fluorescence signal formed by the amplification reaction can be read simultaneously with the fluorescent Bead code by fluorescence imaging.

# ABSOLUTE QUANTITATION

Conventional dPCR provides for absolute quantitation based on the compartmentalized sample volume.

The BLINK approach allows for enrichment of targets from different sample volumes and provides for target quantification without relying on a precise measure for the volume of the amplification compartments. To calculate the number of amplified targets, this approach, unlike conventional dPCR, does not require a precise determination of the volume of the compartments used, but only their number.

With BLINK Beads, random distribution of nucleic acids contained in a sample is achieved by binding the NA molecules to the Beads present in the sample. The mean number of targets per Bead is calculated using the same Poisson statistics as for conventional dPCR. However, no information on the bead volume needs to be taken into consideration for calculating the target concentration in the sample. Instead, the total number of beads applied to the sample  $N_B$  is simply divided by the volume of the sample containing the targets  $V_S$ .



READ PUBLICATION  
Heinrich, T., *et al* (2023)

TARGET CONCENTRATION:  $C_S = \frac{N_B}{V_S} \cdot -\ln\left(\frac{N_{neg}}{N}\right)$

# BLINK



BLINK X IS THE PATHWAY TO  
BLINK BEAD EXPLORATION,  
OPENING A WORLD OF  
POSSIBILITIES TO CREATE  
MICROFLUIDICS-FREE  
MULTIPLEX DIGITAL-PCR  
ASSAYS WITH UNPRECEDENTED  
PERFORMANCE.

The BLINK X is an integrated bioanalytical product platform designed to provide you extensive flexibility for BLINK Bead assay development and exploration.

With the BLINK X you can explore the unique and potent performance characteristics of the BLINK Beads and develop novel test assays, whether for your research, laboratory assays or with an eye to future product development.

The BLINK X is designed to provide a smooth transfer of developed laboratory assays onto fully automated platforms such as the BLINK One, for point-of-care use, or other high-throughput platforms.

DEVELOP NOVEL BLINK BEAD TEST ASSAYS  
XPLORE THE DIGITAL DIMENSION.

XTEND THE DIGITAL DIMENSION WITH REAL-TIME PCR AND MELT CURVE ANALYSIS.

## BLINK X INSTRUMENT

A four-channel fluorescence imager with integrated thermocycling module for BLINK X Mini-plate

*Fluorescence imager*

*Thermocycling module*

## BLINK X SHAKER

A small vertical shaker for efficient transfer of BLINK Beads from aqueous solutions to an oil phase, providing for a stable Bead suspension and cross-talk free target amplification

## BLINK X PROCESSING RACK

A magnetic rack for manual processing of BLINK Beads in microwell strips or tubes for nucleic acid extraction and purification

## BLINK X LOADING RACK & MINI PLATE

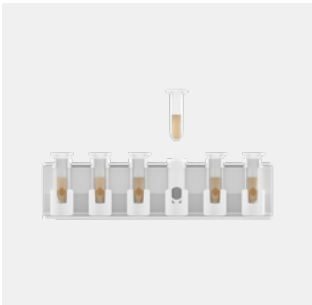
A magnetic rack that accommodates the BLINK X Mini-plate. It facilitates simple loading of processed Bead samples onto the Mini-plate and alignment of the Beads in a self-assembled monolayer for detection.



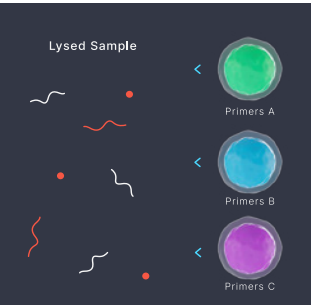
# BLINK X WORKFLOW



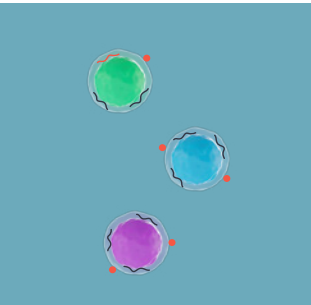
**1. SAMPLE**  
Different samples can be processed with BLINK Beads.



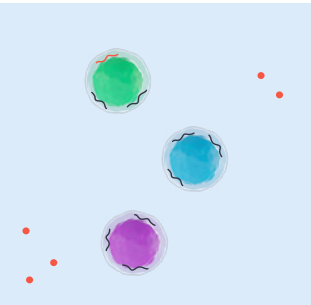
**2. BLINK X PROCESSING RACK**  
Nucleic acid extraction steps and loading of amplification reagents are performed on the Processing Rack.



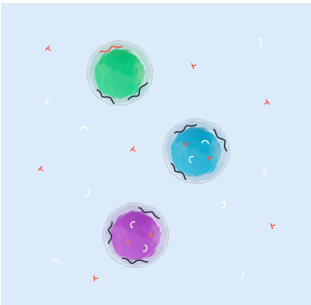
**3. LYSIS AND BINDING**  
The sample material is lysed and contacted with Beads.



**4. BINDING**  
An optimized binding buffer is added to the solution. Nucleic acids bind to Beads.



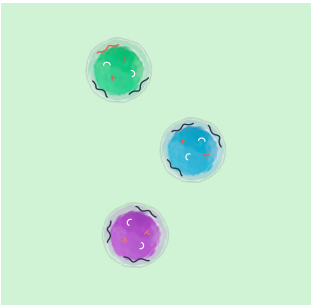
**5. WASHING**  
A wash step removes un-specifically bound materials leaving purified nucleic acid bound to the Bead.



**6. BEAD LOADING**  
Amplification reagents (RT/PCR enzymes, dNTPs) are added to the Beads.



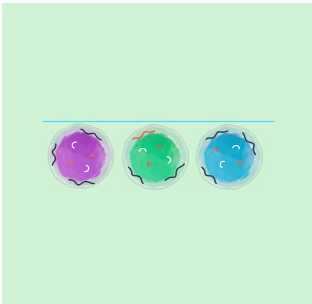
**7. BLINK X SHAKER**  
A suspension of Beads in oil is generated with the Shaker.



**8. BEAD SUSPENSION IN OIL**  
Beads are separated by oil and contain defined volume of amplification solution.



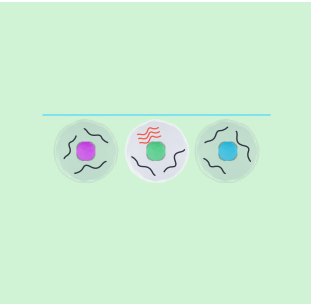
**9. BLINK X LOADING RACK**  
Loading of Beads on Mini-Plate is facilitated with the Loading Rack.



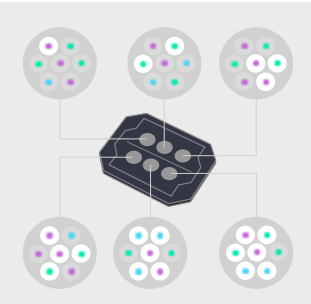
**10. BEAD MONOLAYER FORMATION**  
Beads are placed in wells and self-assemble in a monolayer for thermocycling and fluorescence imaging.



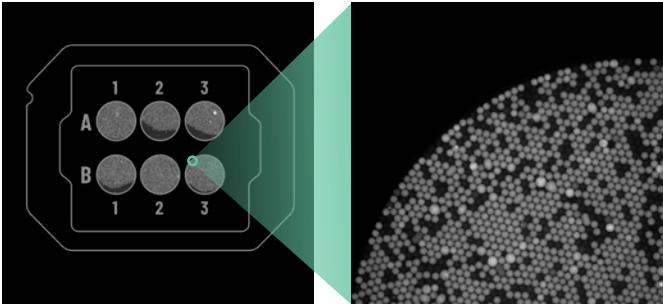
**11. BLINK X INSTRUMENT**  
Thermocycling and fluorescence imaging are performed on the Instrument.



**12. THERMOCYCLING AND FLUORESCENCE DETECTION**  
Endpoint PCR (digital PCR), qPCR and Melting Curve Analysis are possible.



**13. DECODING AND ANALYSIS**  
Image analysis provides for Bead decoding and PCR analysis. The quantity of each amplified target is determined for the according group of Beads coding for a certain sample or target.



# BLINK ONE

## CARTRIDGE-BASED RAPID ULTRAPLEX DIGITAL TEST ASSAYS

The BLINK One is a cartridge-based platform that integrates BLINK Bead assays into a fully automated sample-to-answer system without the need for laboratory infrastructure. The system enables highly multiplexed molecular assays in 15 minutes.

The BLINK One is a fully integrated instrument for processing BLINK Bead-based assays on the BLINK One Cartridge. The One platform comprises a cartridge and instrument.

The system allows for direct transfer of BLINK Bead assays developed on the BLINK X system into a closed, self-contained test format that features multiplex digital PCR and integrated nucleic acid extraction. The One Cartridge is a fully functional pre-assembled unit that is filled with the assay specific BLINK Beads and generic reagents necessary to run a test.

### THE BLINK ONE INSTRUMENT

The BLINK One Instrument is designed to process a variety of Bead assays on the BLINK One Cartridge. The Instrument is equipped with a Peltier-based incubation module for rapid PCR featuring heating and cooling ramps of >30K / sec.

Its integrated fluorescence micro-imager has four LED/Filter combinations available for Bead decoding and PCR signal detection.

The Instrument is also equipped with a valve and pump actuator, a magnetic actuator for Bead handling and an additional temperature control for the heat lysis module.

### THE BLINK ONE CARTRIDGE

The One Cartridge is closed system designed to accommodate a broad range of sample types and sample volumes. It is equipped with a pump and rotary valve to provide for flexible liquid handling workflows. It features storage chambers for liquid (lysis and binding buffer, re-suspension of buffer PCR pellet) and solid reagents (PCR pellet, lyophilised Beads). The Cartridge design allows for heat lysis by heating a sample to 95°C and for mechanical lysis with an integrated bead mill. It is equipped with a module to facilitate seamless suspension of BLINK Beads in an oil matrix for dPCR and detection.

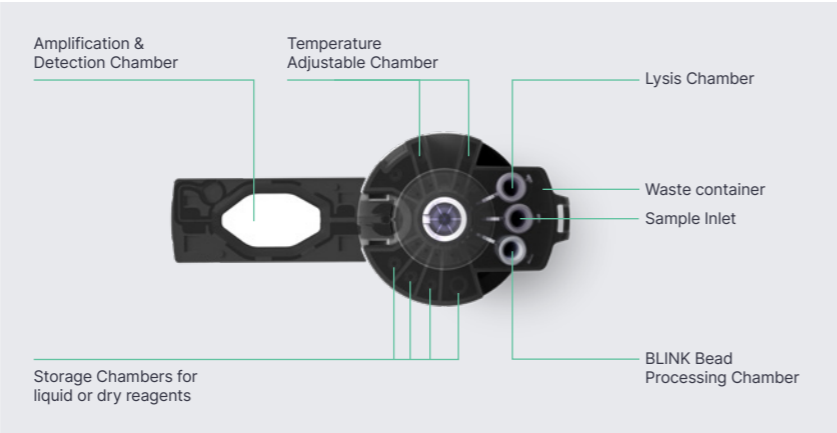


# BLINK ONE WORKFLOW

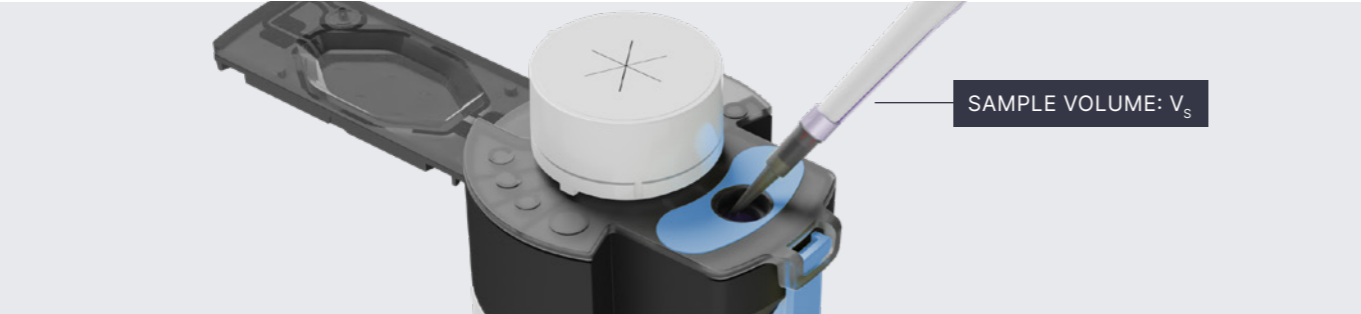


## 1. CARTRIDGE

The Cartridge features a central body with an integrated pump and rotary valve, allowing for liquid handling between the different Chambers.

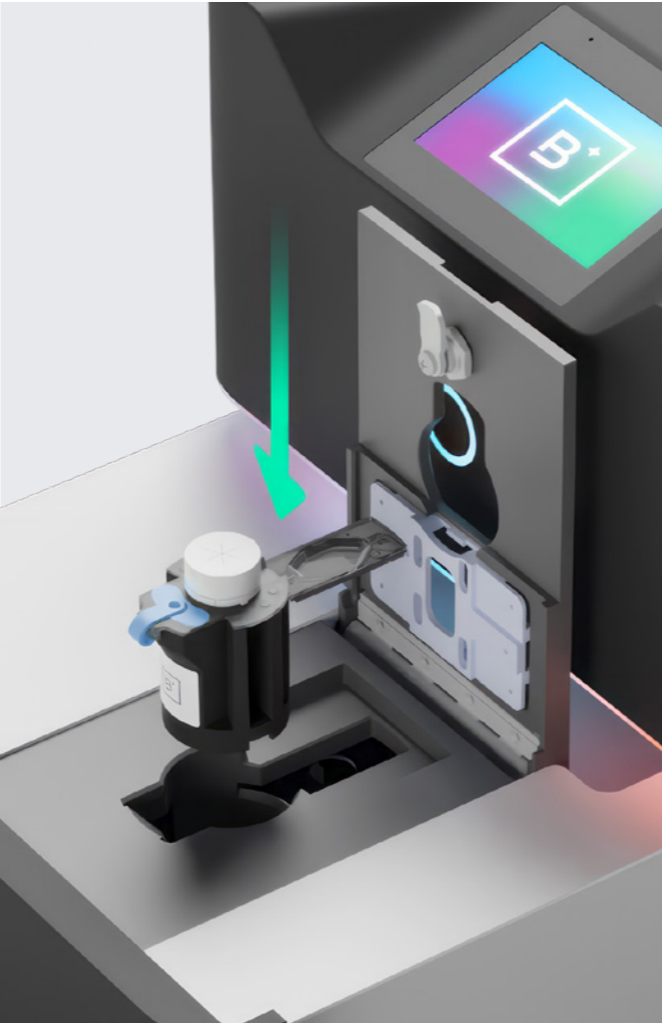


It contains specialised chambers for sample input, sample lysis (chemical, mechanical, heat), nanoreactor Bead processing including phase transfer and for thermocycling and fluorescence imaging of the Beads.



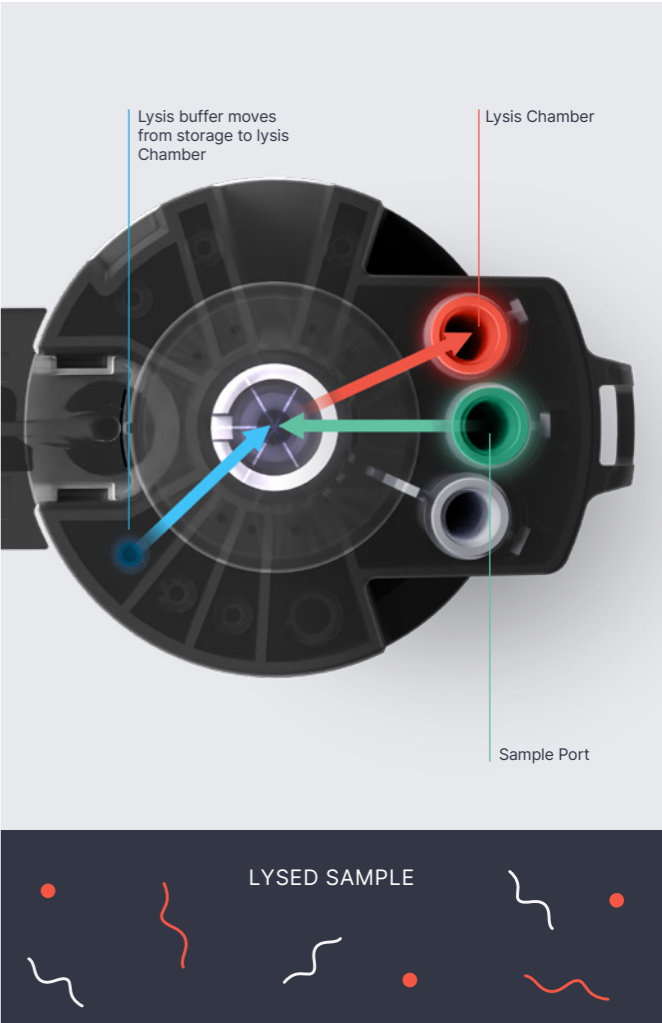
## 2. SAMPLE

Different samples (e.g. cultured cells, swabs, plasma, etc.) can be applied to and processed with BLINK Beads on the ONE cartridge.



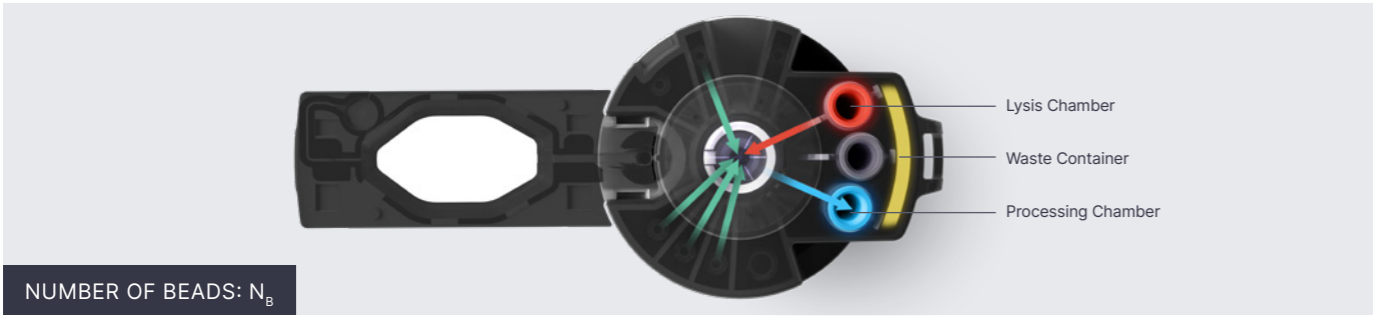
## 3. BLINK ONE INSTRUMENT

The filled Cartridge is loaded in the Instrument and the test run is initiated. The instrument features actuators for rotary valve and pump operation, a magnetic actuator for Bead handling on the cartridge and for integrated Bead milling, as well as a thermocycling module and fluorescence imaging module for PCR detection and Bead encoding.



## 4. LYSIS & BINDING

The sample is transferred from the **Sample Port** to the **Lysis Chamber** and lysed with lysis reagents and/or mechanically by Bead milling.



5.  
PROCESSING

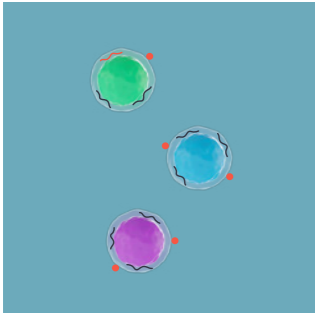
**Lysate** is moved to the **Processing Chamber** containing the Beads in binding buffer, which has been moved onto the Beads before from the respective storage Chamber.

Beads are agitated by applying external magnetic force for incubation.

Beads are held in position, **supernatant moved to waste**. Wash buffer is added to Chamber from respective storage.

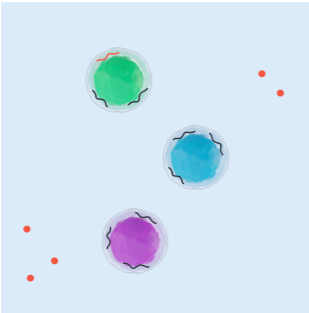
Wash buffer is replaced (**goes to waste**) by generic PCR buffer. Beads are agitated. Thereafter oil is added and an oil suspension formed by magnetic mixing.

The figures below illustrate the process at the Bead-level.



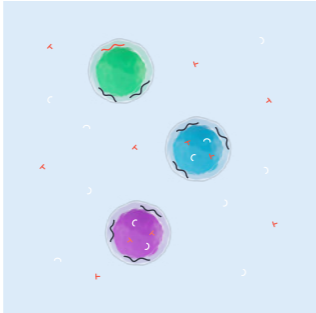
**BINDING**

An optimized binding buffer is added to the solution. Nucleic acids bind to Beads.



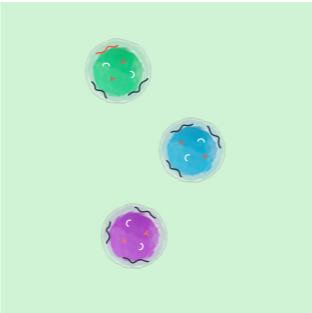
**WASHING**

A wash step removes un-specifically bound materials leaving purified nucleic acid bound to the Bead.



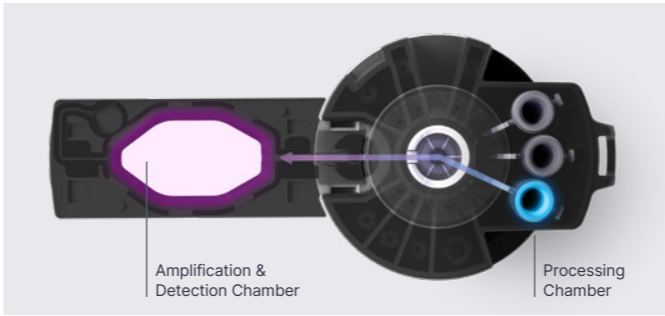
**BEAD LOADING**

Amplification reagents (RT/PCR enzymes, dNTPs) are added to the Beads.



**BEAD SUSPENSION IN OIL**

Beads are separated by oil and contain defined volume of amplification solution.

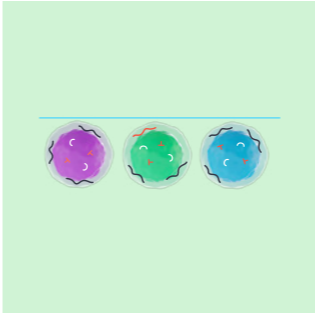


6.  
DETECTION & IMAGING

Beads-in-Oil Suspension is pumped from the **Processing Chamber** into the **Amplification & Detection Chamber**, where a Bead monolayer forms.

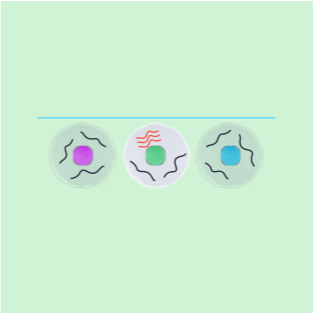
Thermocycling and fluorescence detection of Bead codes and PCR signal are performed.

The figures below illustrate the process at the Bead-level.



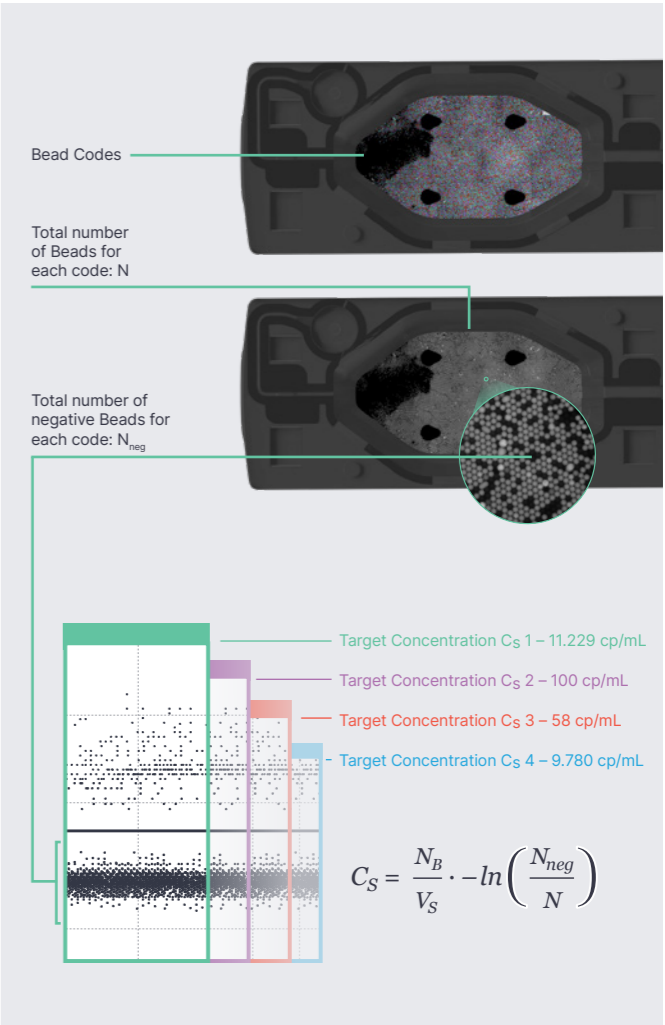
**BEAD MONOLAYER FORMATION**

Beads self-align in monolayer formation for thermocycling and fluorescence imaging.



**THERMOCYCLING & FLUORESCENCE DETECTION**

PCR amplification and fluorescence detection are performed on the Beads with the BLINK One Instrument.



7.  
DECODING AND ANALYSIS

Fluorescence imaging reveals Bead codes and PCR-positive and negative Beads. Subsequently each detected target is quantified by data analysis. Beads are counted for each Code present in the assay. The Quantification formula is applied to calculate the concentration of each individual target in the sample.

# GETTING STARTED IS SIMPLE

**THE BLINK PLATFORMS ARE DESIGNED TO DEMONSTRATE THE EXTENSIVE FUNCTIONALITY AND PERFORMANCE OFFERED BY THE BEAD TECHNOLOGY IN DIFFERENT SETTINGS.**

Both the BLINK X and the BLINK One come equipped with the BLINK Toolbox assay design and development software package.

It is connected to the BLINK Hub, a cloud-based development portal managed by BLINK. The BLINK team is there to support you all the way, providing training and support throughout your development journey.

- Extensive data analysis tools
- Assay programming interface
- Fluorescence imager with integrated thermocycler
- Open-access software package with pre-made assay templates

With the ability to provide a complete analysis workflow on a single reagent carrier, single molecule sensitivity, exquisite quantification and results in less than 30 minutes, the BLINK Beads applied on a BLINK platform is a pathway to endless possibilities.



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