Flexible solutions for your virology research

BMG LABTECH

The Microplate Reader Company

Dedicated solutions from immunoassays to anti-viral screenings

A flexible platform

Viruses pose growing risks to our health, society and economy. BMG LABTECH single- and multi-mode plate readers provide a versatile platform that can cover a multitude of assays used in modern virology, from basic research to drug screening.

Functional virus assays

The analysis of host-virus interactions clarifies the cellular and molecular mechanisms behind infection. Infection, replication and neutralization assays can be monitored by fluorescent or luminescent reporter proteins in live cells. Viability, cytopathic effect (CPE) and TCID50 of infected cells can also be efficiently measured on plate readers with atmospheric and temperature control, enabling real-time kinetic data acquisition.
Labelled substrates allow plate reader-based detection of enzymatic assays such as neuraminidase or RNA-dependent RNA polymerase activity and inhibition.

Screening for anti-virals

Once druggable targets are identified, assays need to be scaled up to screen for anti-viral molecules. Technologies such as FRET, BRET, TR-FRET, fluorescence polarization and AlphaScreen® are extremely useful to analyse virus-host protein interactions and of utmost importance for anti-viral drug screening.
BMG LABTECH microplate readers provide the highest sensitivity and speed for interaction assays, delivering robust and reproducible results. For higher throughput, all readers are robot compatible and can be easily integrated into all automated systems.

Diagnostic assays

Fast, quantitative detection methods rely mainly on the detection of the viral genome in patient samples (PCR, LAMP) or on serological tests (ELISA). PCR and LAMP products can be easily detected on a plate reader either by absorbance or fluorescence. In addition, LAMP assays can be directly run and measured in real-time on plate readers with 65°C heating.
ELISAs for the quantification of antibodies and viral antigens or cytokines in serological samples rely on a colorimetric, fluorescent, or luminescent output, all of which can be easily detected on a microplate reader.

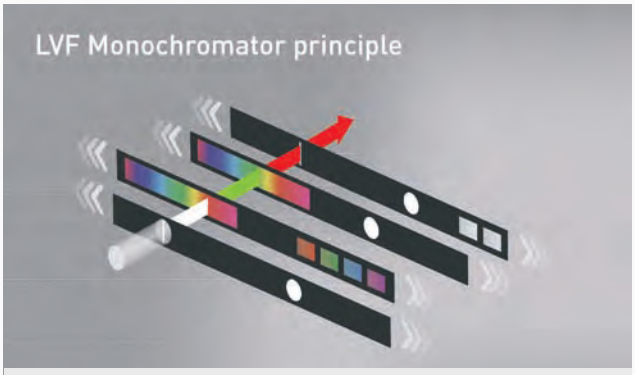
Key features of a microplate reader for virology research

All detection modes and plate formats

All BMG LABTECH multi-mode readers can be equipped with all the leading non-isotopic detection technologies. From basic research to screening, we offer plate readers compatible with formats from 6 up to 3456 wells.

Wavelength flexibility

Wavelength selection in fluorescence and luminescence can be accomplished either with filters or with our patented LVF Monochromators™. For fluorescence polarization, time-resolved fluorescence, TR-FRET and AlphaScreen®, our readers use specialised filters that guarantee exceptional performance. A UV/vis spectrometer enables full absorbance spectral acquisition (220 - 1000 nm) in less than 1 second/well.



Simplified schematic of the LVF Monochromator technology.

Simplified assay setup

Thanks to the Enhanced Dynamic Range (EDR) technology, every sample is automatically measured with the ideal settings. EDR grants a dynamic range of 8 concentration decades in a single measurement, ensuring reliable detection of highly divergent signals or kinetic assays, with no manual intervention. EDR significantly simplifies measurement setup and provides an easier solution for assay development.

Fast interaction assays

Interaction assays often require the detection of two emission wavelengths. Simultaneous Dual Emission (SDE) detection enables the concomitant acquisition of two separate emission signals in one single measurement. In FRET, TR-FRET, BRET, FP and AlphaPlex™, SDE halves read times, reduces data variability and eliminates the drawbacks of sequential detection.

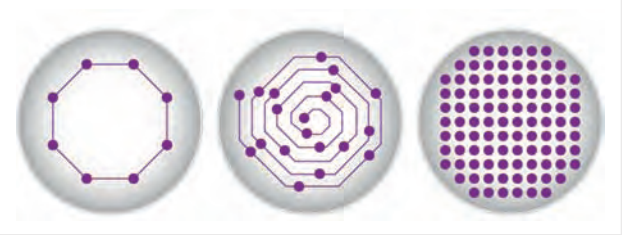
Optimal conditions for live cell-based assays

To understand virus-host mechanisms many assays rely on the infection of live cells. The Atmospheric Control Unit regulates O_2 and CO_2 inside the plate reader. Together with temperature incubation up to 45°C, ideal conditions can be established for all live cell-based assays. Kinetic assays can be run at stable gas and temperature conditions, and data can be acquired in real-time, providing a true "walk-away" solution.

The Atmospheric Control Unit perfectly regulates both O_2 and CO_2.

Best data for cell-based assays

Adherent cell layers are most often non-homogenous. Data usually benefit from signal detection from the bottom of the well over its whole surface. On our readers, bottom reading can be implemented by one mouse click, no displacements needed. Spiral/orbital averaging, or a matrix scan with up to 900 points/well ensure the best data quality for cell-based assays.



Orbital, spiral averaging, and matrix scan.

Multiplexing

For multiple parameter analysis, fluorescent detection of up to 5 different dyes can be combined with absorbance and luminescence in the same run. This allows for the parallel characterisation of different parameters in infection or the normalisation of reporter assays.

Comprehensive data analysis

The multi-user MARS data analysis software provides an extensive range of data processing tools and is fully compliant with FDA regulation 21 CFR Part 11.

Studying viral infection and replication in host cells in real time

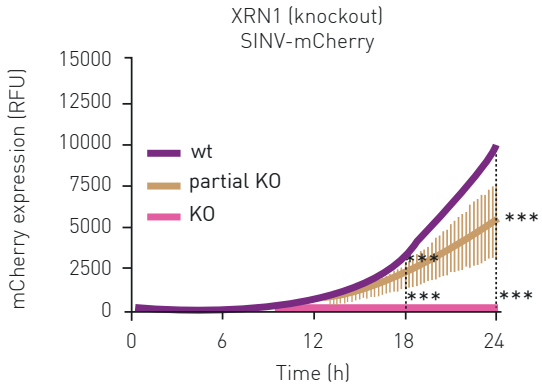
A fluorescent-based approach to study the molecular mechanisms of viral infection

Understanding host-virus interactions is crucial to uncover the molecular mechanisms of infection and to develop new treatments. To test the importance of cellular proteins in virus infection, robust and high-throughput methods are required to measure viral fitness.

Reporter gene methods to monitor viral gene expression in host cells can be easily run on a CLARIOstar *Plus* with Atmospheric Control Unit.

As a proof of principle, a Sindbis virus expressing fluorescent mCherry was used to monitor viral infection and gene expression in real time in host cells.

This assay can be used to test if a given condition inhibits or enhances viral infection, enabling drug library screenings or gene knock-out/knock-down approaches. Insights into kinetic effects can be gained up to 72 hours post infection.



Detection of mCherry fluorescence signal in HEK293 cells as a proxy for viral replication. The high sensitivity of the assay allows for the profiling of intermediate phenotypes in a very reproducible manner, e.g., when XRN1 is partially depleted, infection is delayed.

For more information please refer to BMG LABTECH application note 353.

Screening for anti-viral drugs with a protein-protein interaction assay

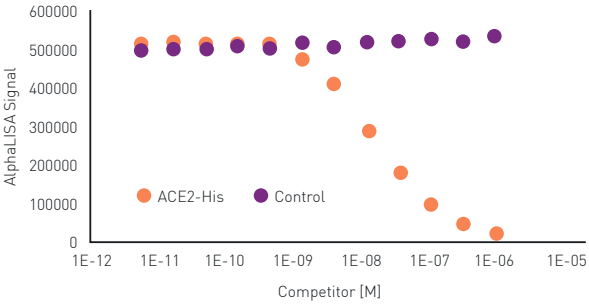
Development of an AlphaLISA® interaction assay to screen for repurposed drugs

Repurposing of approved or highly tested drugs is an option to quickly respond to emerging diseases.

AlphaLISA® assays provide a flexible platform to investigate protein-protein interactions linked to infection. This approach is intended to be used to search for existing drugs disrupting the interaction between the cellular angiotensin-converting enzyme 2 (ACE2) and the SARS-CoV-2 Spike protein. Further, a counterscreen was used to eliminate false-positives and compounds that interfere with the assay.

To analyse the disruption of the protein interaction, as a proof of principle, unlabelled versions of the interacting proteins (ACE2-His and His-S1) were employed in competition binding assays. As expected, AlphaLISA signals decreased with increasing concentrations of ACE2-His.

This provides an example of how improved assay and microplate reader technologies can be leveraged to develop new screens to improve our ability to respond to emerging diseases.



Untagged ACE2-His lowers AlphaLISA signal in an ACE2-Spike competitive binding assay. As proof of performance, addition of increasing ACE2-His exhibits a dose-dependent decrease in AlphaLISA signal.

For more information please refer to BMG LABTECH application note 357.

Enzymatic characterisation of viral RNA-dependent RNA polymerase

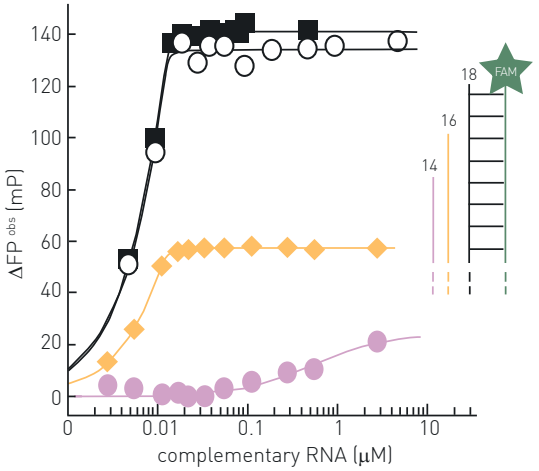
A fluorescence polarization-based analysis of viral RNA synthesis

Viral RNA-dependent RNA polymerase (RdRp) is essential to the propagation of RNA viruses, as it amplifies the viral genome and transcribes for viral proteins. Consequently, it is considered an attractive target for anti-viral drug treatment.

Fluorescence polarization can be used to directly analyse RdRp dependent RNA synthesis and is compatible with high-throughput screening.

The *in vitro* enzymatic characterisation of the influenza virus RdRp was performed analysing the changes in fluorescence polarization originated by double-strand RNA synthesis of an 18 nucleotide 5'-end FAM-labelled single-stranded RNA "model template".

The assay is suited for mechanism of action-studies and can easily be performed in 384-well microplates. It reliably reports on compounds inhibiting RNA synthesis, providing an attractive choice for drug discovery campaigns.



Fluorescence polarization values are related to the complementation of a 18 nt FAM-labelled single-stranded template RNA. Complementary 18 nt and 16 nt, and non-perfectly complementary 14 nt RNAs show different values.

For more information please refer to BMG LABTECH application note 326.

Colorimetric LAMP assay for viral genome detection

Real-time detection of colorimetric changes as a measure of viral RNA amplification

The reverse transcription loop-mediated isothermal amplification (RT-LAMP) assay recognizes the target RNA by several distinct sequences and amplifies it with high selectivity, showing comparable sensitivity and specificity to PCR-based methods.

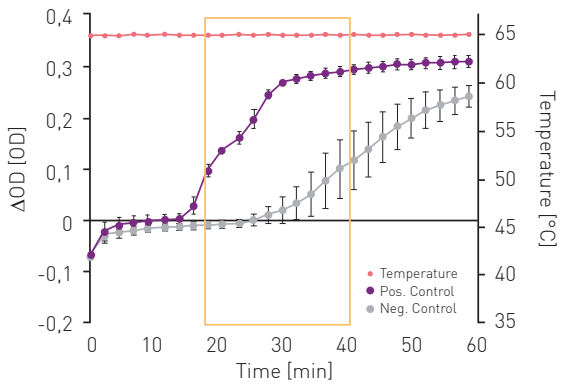
In contrast to PCR, LAMP works at 65°C and can be performed under isothermal conditions in about 30 min on a plate reader.

The 65°C heating capability of the BMG LABTECH plate reader enables the simultaneous incubation and analysis of LAMP assays in real time for the identification of the ideal cut-off points when establishing new assays.

In this assay, the amplification of SARS-CoV-2 RNA is detected as an increase in absorbance at 415 nm and a decrease at 560 nm.

In virus-positive samples, a substantial shift was noticed just after 18 minutes from the start.

Spectrometer-based absorbance detection enables simultaneous measurements at 415 nm and 560 nm and allows for a cycle time of only 2 mins and 13 s per 384-well plate.



Kinetic measurement of the SARS-CoV-2 LAMP assay over 60 min. Data is displayed as ΔOD (415 nm-560 nm). The optional measurement window is marked in orange.

For more information please refer to BMG LABTECH application note 356.

PHERAstar® *FSX*	CLARIOstar® *Plus*	VANTAstar®	Omega series	SPECTROstar® *Nano*	
✓	✓	✓	✓		Multi-mode detection
✓	✓			✓	Up to 1536-well plates
✓	✓	✓	✓	✓	Spectrometer (ABS)
	✓	✓			LVF Monochromator (FI and Lum)
✓	✓	✓	✓		Filters
✓	✓				Top sensitivity in its class
	✓	✓	✓		Suitable for live cell assays
✓	✓	✓	✓	✓	Well scan modes
✓			✓		Simultaneous Dual Emission
	✓	✓			Enhanced Dynamic Range (FI and Lum)
✓					High-throughput screening
	✓		✓		Suitable for LAMP (65°C)
✓	✓	✓	✓	✓	Multi-user software
✓	✓	✓	✓	✓	Automation friendly
The gold-standard plate reader for high-throughput screening. It is ideally suited for all assays requiring high sensitivity and fast detection, and for all ratiometric assays.	The most sensitive mono-chromator-based microplate reader. Its sensitivity and flexibility make it a great choice for assay development and validation.	A compact multi-mode plate reader conceived for ease-of-use and flexibility. Every plate is automatically read with the best possible settings.	A cost-efficient, filter-based, single- to multi-mode modular reader platform. It supports absorbance, fluorescence and luminescence detection.	Absorbance reader that acquires a whole spectrum in less than 1 s/well. This is the perfect device for all colorimetric assays in microplates or cuvettes.	What else should you know

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