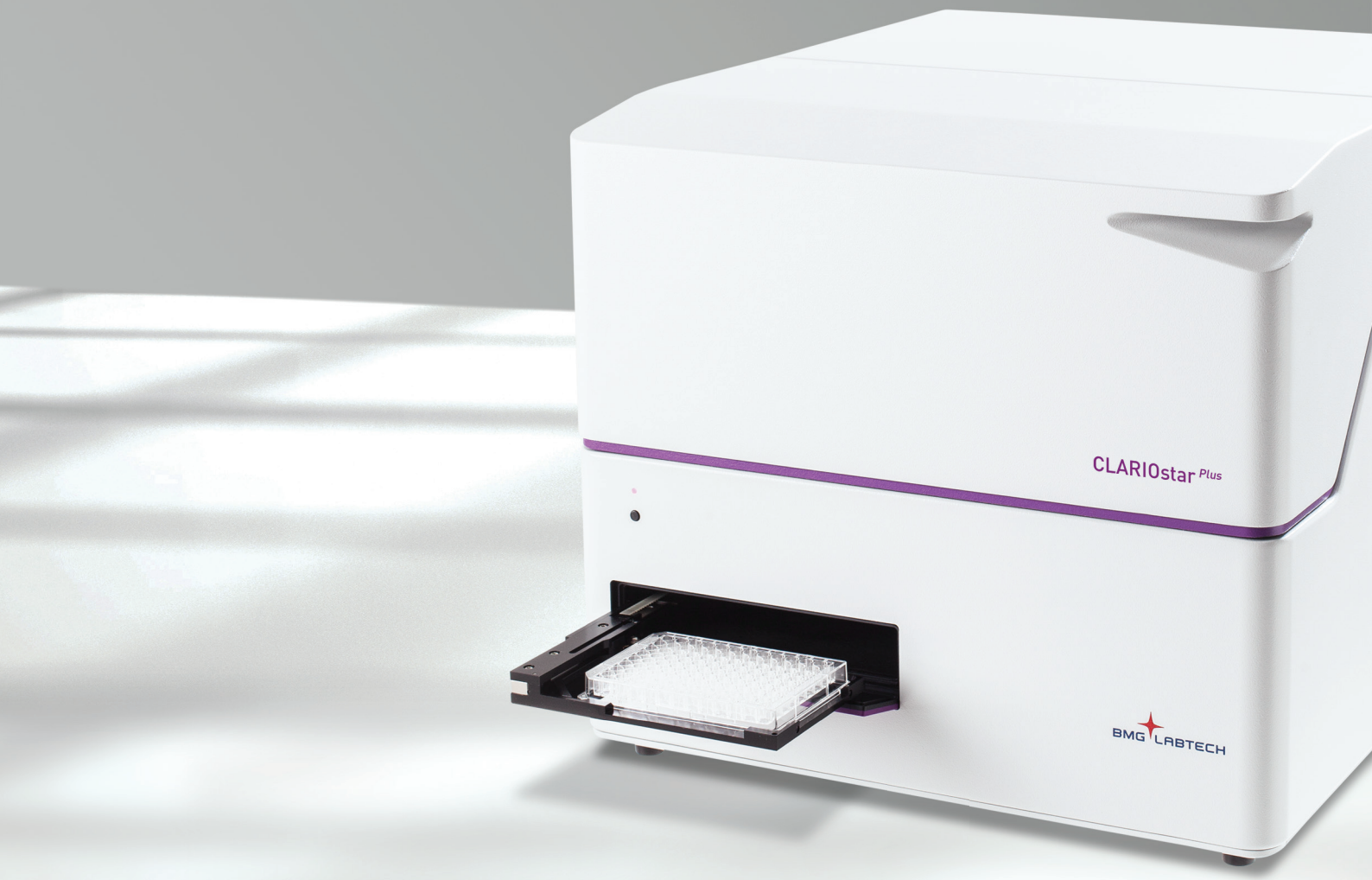
# CLARIOstar® *Plus*

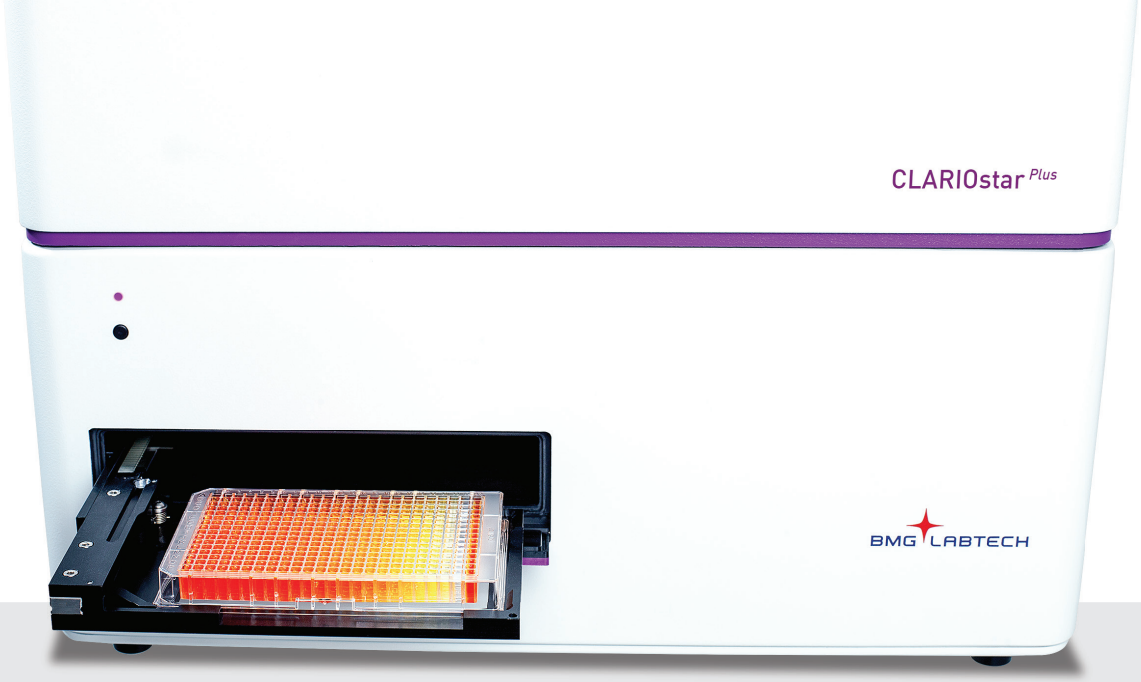
Flexible high-performance microplate reader for all assay needs




BMG LABTECH

*The Microplate Reader Company*

www.bmglabtech.com




## Your benefits at a glance:

- Combines best-in-class sensitivity with flexibility
- No gain or focus adjustment required
- Dedicated detectors for fluorescence and luminescence
- Luminescence and AlphaScreen® cross-talk reduction
- Best sensitivity in fluorescence polarization
- Simultaneous inject & read for fast kinetics
- Atmospheric control with gas ramping function
- Made-in-Germany dependability

## Monochromator. Perfected.

The CLARIOstar® *Plus* is a high-performance microplate reader that fits the current and future needs of your laboratory, whether in academia, a core facility, biotech or pharma.
This multi-mode reader combines the flexibility of monochromators with best-in-class sensitivity and includes features like the **Enhanced Dynamic Range (EDR)** technology that will help simplify your workflow in the lab.
The instrument is upgradable and can be equipped with all the leading non-isotopic detection technologies:

- UV/vis absorbance
- Fluorescence intensity, including FRET
- Luminescence (flash and glow), including BRET
- Fluorescence polarization/anisotropy
- Time-resolved fluorescence, including TR-FRET
- AlphaScreen® / AlphaLISA® / AlphaPlex™

Equipped with our patented LVF Monochromators™, it combines at no compromise the sensitivity of filters with wavelength flexibility and scanning capability.
The following detection technologies guarantee the best performance in any assay:

- **Dual LVF Monochromator system** for the best flexibility and sensitivity in fluorescence intensity (incl. FRET), and flash/glow luminescence (incl. BRET)
- **Filters** for the greatest sensitivity in all fluorescence and luminescence-based detection modes
- **Spectrometer** for the fastest absorbance spectra.

## Sensitivity and flexibility

Our monochromators are based on Linear Variable Filters (LVF), special filters that vary spectral properties over their length, transmitting or blocking specific wavelengths at different positions. LVFs eliminate the need for concave gratings employed in conventional monochromators to separate and mechanically select coloured light. An LVF Monochromator consists of two aligned LVF slides that separate light into distinct wavelengths and bandwidths.
The CLARIOstar *Plus* is equipped with two LVF Monochromators, one for excitation and one for emission. LVF Monochromators ensure filter-like performance combined with wavelength flexibility, so why use filters if you can get comparable sensitivity and additional flexibility from a monochromator?

Benefits of LVF Monochromators include:

- **Filter-like performance:** Linear Variable Filters have light transmitting properties comparable to optical filters. They provide LVF Monochromators with a higher sensitivity over conventional grating-based systems.
- **Linear Variable Dichroic Mirror:** this unique feature is automatically tuned to provide the best characteristics to efficiently separate the excitation from the emission light, significantly reducing background noise.
- **Less noise:** the innovative LVF Monochromator design avoids stray light as it occurs with conventional mono-chromators, decreasing background noise and increasing performance.
- **Adjustable bandwidths from 8 to 100 nm** ensure better performance. Larger bandwidths yield more light for excitation and emission, increasing sensitivity.
- **Combine filters and monochromators** in one measure-ment, exciting with a filter and scanning the emission spectrum, or vice versa.

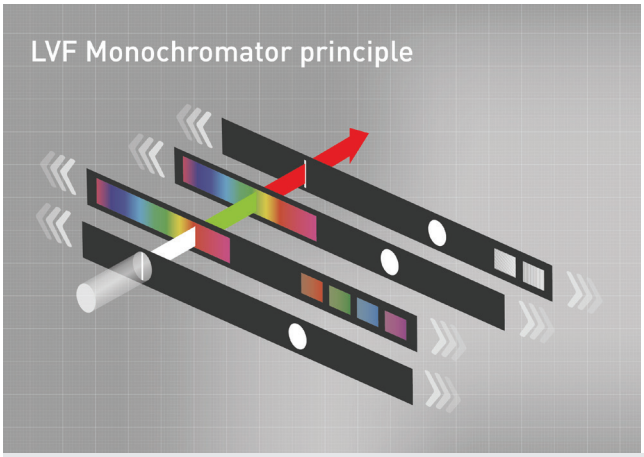
## Simplify your assay setup

Thanks to the Enhanced Dynamic Range (EDR) technology and rapid, full-plate auto-focus, every plate is automatically read with settings that provide the best sensitivity and signal-to-blank ratios – no manual intervention required.

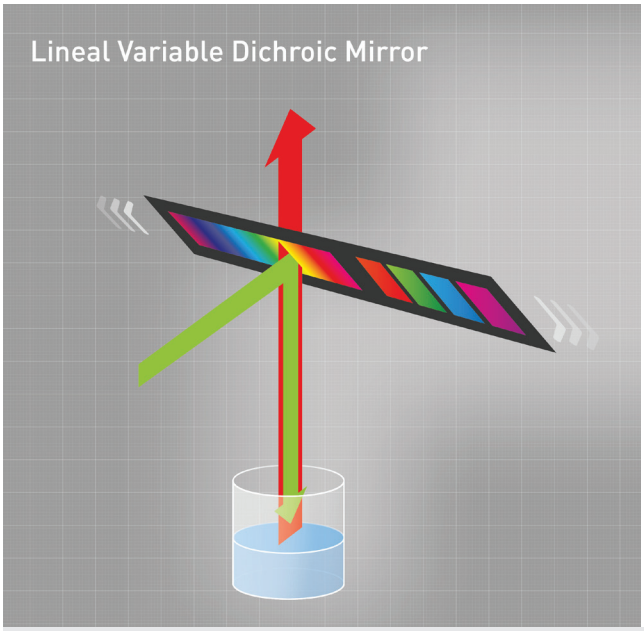
EDR significantly simplifies measurement setup and provides an easier solution for assay development. It grants a dynamic range spanning over 8 concentration decades in a single measurement, ensuring reliable detection of samples at a large range of signal intensities with no manual intervention. In enzymatic or cell-based kinetics with signal intensities increasing over time, EDR avoids detector saturation. In addition, data acquired at different times are comparable as count scales are uniform from day to day and plate to plate.

Focussing excitation light directly onto the sample significantly improves sensitivity and dynamic range. The incorporated auto-focus, rapidly adjusts the focus height for the whole plate, giving excellent sensitivity for both top and bottom reading in all plate formats up to 1536 wells. EDR and auto-focus can be applied in top or bottom fluorescence intensity and luminescence detection, both with filters and LVF Monochromators.

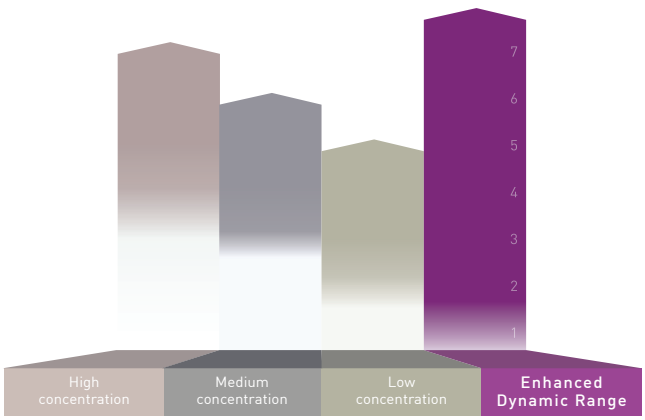
With EDR and auto-focus new users will be able to easily get started, while experienced users will get better data, more quickly.



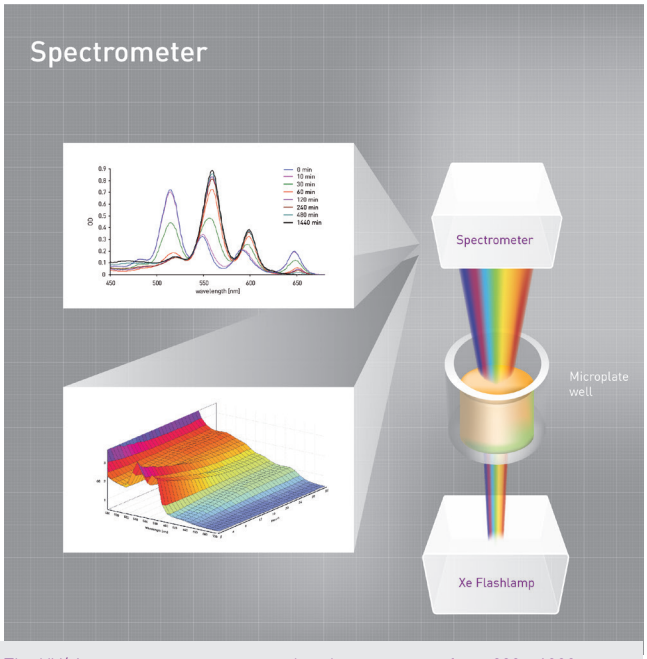

LVF Monochromator schematic: by sliding against each other the LVF slides separate light into distinct wavelengths and bandwidths.



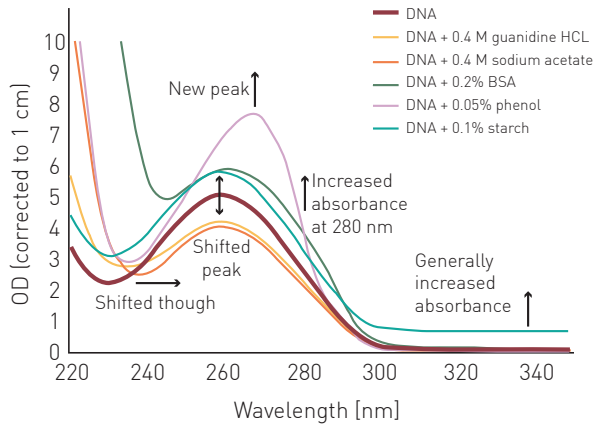

The adjustable Linear Variable Dichroic Mirror positioned between excitation and emission monochromators blocks or transmits different wavelengths.



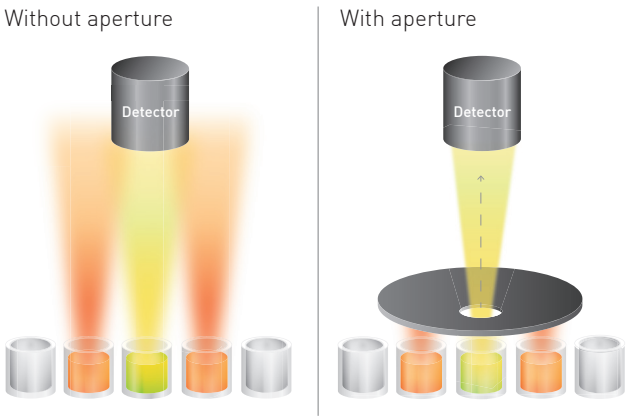

Enhanced Dynamic Range enables detection of signal intensities spanning over 8 concentration decades (orders of magnitude).




The UV/vis spectrometer captures absorbance spectra from 220 - 1000 nm in less than 1 second/well, significantly faster than any monochromator.




Full-spectrum detection improves many absorbance assays: influence of different contaminants on DNA quantification at 260 nm.




The cross-talk reduction package reduces unspecific light signals that are cause of higher background noise and variability.

## Flexibility in detection

The reader comes equipped with a standard low-noise PMT detector for fluorescence and luminescence modes. Users who need the very best performance in far-red fluorescent detection can benefit from a red-sensitive PMT. The use of a dedicated detector for luminescence and AlphaScreen provides the option to measure with the most sensitive PMT for your detection mode without compromise

## Ultra-fast UV/vis absorbance spectra

Why would you measure only a single wavelength if you could acquire a full spectrum in the same time? Full-spectrum detection improves many absorbance assays as it can highlight shifting peaks or the presence of contaminants. Our spectrometer can capture a full 220 to 1000 nm absorbance spectrum at 1 to 10 nm selectable resolutions in less than 1 second per well.
Alternatively, up to 8 discrete wavelengths can be acquired instantaneously and simultaneously. For DNA quantitation, for example, 260-, 280- and 340-nm measurements are all captured with a single flash.

## Dynamic luminescence detection

Flash, glow, Dual Luciferase® Reporter and BRET are some of the most commonly measured luminescence assays. On the CLARIOstar *Plus*, both LVF Monochromators and filters can be used for luminescence detection. LVF Monochromators can acquire spectral scans of luminophores, and with adjustable bandwidths up to 100 nm, are sensitive enough to read dual colour luminescence including BRET, without the need of filters.

## Cross-talk reduction

AlphaScreen/AlphaLISA and glow luminescence assays in 384 and 1536-well plates in particular are often negatively affected by stray light and cross-talk. Unwanted light may diffuse from adjacent wells to the detector, as well as through the plastic walls of the wells. If cross-talk is not reduced, low-signal wells might see more counts from nearby bright wells than from their actual signal. BMG LABTECH's cross-talk reduction package automatically applies an aperture to physically reduce non-specific signal diffusing from nearby wells, and mathematically corrects for light transmitted through the walls of a well.

## Advanced detection modes

For fluorescence polarization, time-resolved fluorescence (TRF and TR-FRET), and AlphaScreen®/AlphaLISA®/ AlphaPlex™ assays, the reader uses dedicated components that guarantee exceptional performance without compromise.

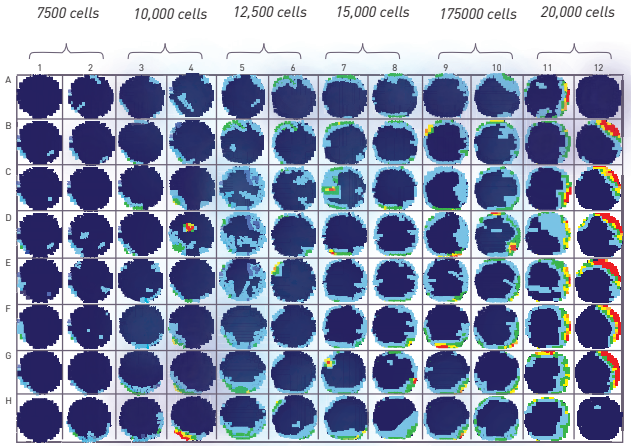
- **Fluorescence polarization:** the CLARIOstar *Plus* is the best fluorescence polarization plate reader on the market. Its unique optical design and instant polarizer switching provide the smallest mP standard deviation in any assay.
- **High-end TR-FRET performance:** certified to measure HTRF® assays in both black or white plates, the reader guarantees no compromises in any TR-FRET assay. The ability to measure HTRF in black plates is only prerogative of the most sensitive readers.
- **AlphaScreen®/AlphaLISA®/AlphaPlex™:** a dedicated excitation laser and speific detection optics ensure the best assay window, speed, and sensitivity.


The Atmospheric Control Unit (ACU) perfectly regulates both $O_2$ and $CO_2$ for all cell-based assays.

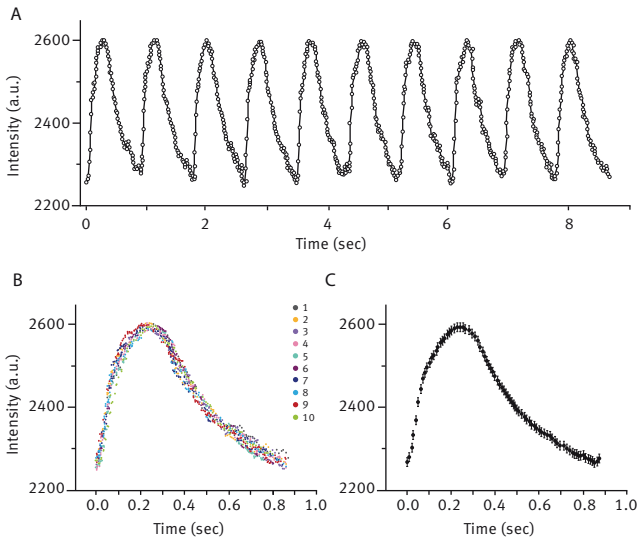
## Cell-based assays

Cell-based assays are increasing in popularity because they better reflect the complexity of biological systems. When running either end-point or real-time kinetic assays with living cells, several factors can beneficially affect the quality of your results:

- **Gas regulation and incubation** are required when running live cell-based experiments and kinetics. The Atmospheric Control Unit (ACU) independently regulates the $O_2$ and $CO_2$ concentration in the reader, while the incubators provide the ideal temperature.
- **Gas ramps** are used in hypoxic and ischemia/reperfusion assays, as well as for metabolic and redox experiments. This unique feature of the CLARIOstar *Plus* allows $O_2$ to be rapidly reduced from ambient to hypoxic and return to ambient whilst maintaining a constant $CO_2$ concentration.
- High-performance **bottom reading** significantly improves data quality of adherent cell samples. On this plate reader you can easily switch from top to bottom detection with a simple mouse click and no hardware displacements.
- **Well surface scan** is the perfect tool to get robust data from non-homogeneously distributed adherent cell samples. Matrix scan takes up to 900 data points/well and creates a map for each sample. Alternatively, orbital or spiral averaging calculate an average of multiple data

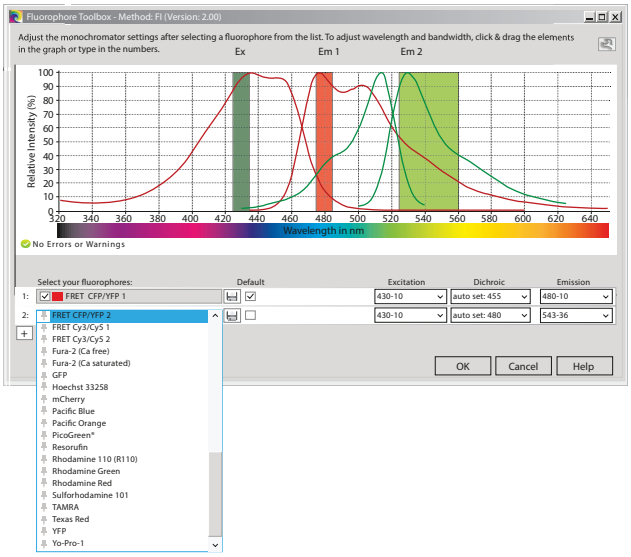



Matrix scanning (15x15) and heat map of a titration of Hoechst-stained HeLa cells across a 96-well plate. Corners contain no cells.




Detection of $Ca^{2+}$ transient measurements using heart tissue and Fluo-4 (A). Overlap (B) and average profile (C) of $Ca^{2+}$ transients of each cardiac twitch.

Easy integration into all leading robotic platforms.




A spectral library with popular fluorophores and luminophores is integrated into the fluorophore toolbox to simplify assay setup by "drag & drop".

points measured on a specific orbit.

- **Reagent injection** can be used to add a stimulus or inhibitor, and to initiate kinetic and enzymatic reactions while detecting in real time the sample's reaction. On our built-in injectors, delivery volumes are adjustable for each well, allowing users to automatically produce dilution schemes and gradients across the microplate. An extremely low dead volume and back flush capability ensure precious reagents are used sparingly and can be recovered.
- **High frequency sampling** acquires with ease extremely fast changing signals and kinetics like calcium flux or fast biological reactions. Thanks to a sampling rate of 100 measurements/second or 1 data point every 0.01 second, no data point will be lost.

## Automation friendly

The CLARIOstar$^{Plus}$ offers excellent robotic integration capabilities, multi-user control, digital signature and FDA 21 CFR part 11 compliance. Its robotic software interface make it easy to integrate into all leading robotic platforms. The instrument comes with two integrated microplate barcode readers and can be equipped with a Stacker.

## Data analysis made easy

The software package includes the SMART Control and MARS data analysis interfaces. This multi-user software can be installed on as many computers as you require, without the need to purchase additional licenses.
The SMART Control software allows to define measurement protocols and acquire data. It is an extremely versatile interface for the straightforward execution of routine tasks, as well as the optimisation of complex operations.
MARS is designed to make data analysis simple and effective, and offers multiple data reduction possibilities such as:

- Standard Curve Wizard for a step-by-step standard curve calculation
- Automatic DNA/RNA concentration determination
- Data display as bar charts, box plots, violin plots etc.
- UV/vis spectral view and analysis
- Background and baseline correction
- Signal interpolation: linear or cubic spline
- Various curve fit models including linear, 4- / 5-parameter, polynomial and user-defined fit models
- Enzyme kinetic analysis using various models
- $EC_{50}$ calculation with confidence intervals

- Binding rates and constants determination
- ANOVA, Student's t-test or multiple comparisons
- Performance evaluation: signal-to-blank, signal-to-noise, %CV, Z-prime, etc.
- Automatic data processing using predefined templates

The software package comes with flexible data export (Excel, ASCII) and integration capabilities, and is compliant with FDA regulation 21 CFR Part 11.

## Applications hub

A perfectly engineered instrument is only part of the solution, it needs to effectively perform all of the leading applications. We continuously work with all major reagent companies to develop protocols and improve instrument settings for their existing assays and their newest kits. The CLARIOstar *Plus* is a user-friendly and flexible instrument that supports all your existing and future applications, including:

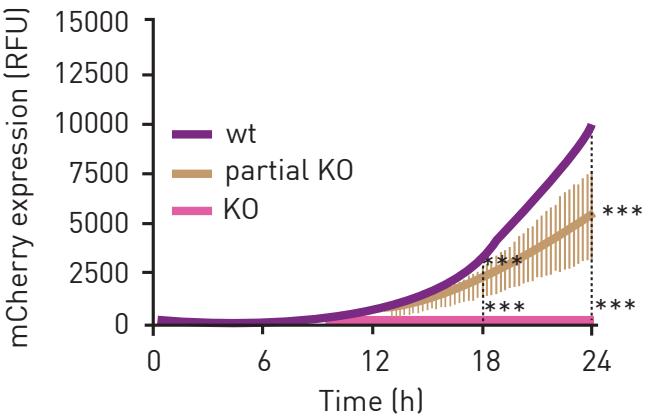
- DNA, RNA, and protein quantification
- Fluorescent and luminescent assay development
- Cell-based and real-time cell-based assays
- Protein - protein interactions
- Molecular binding assays
- Enzymatic activity
- Reporter gene assays

Our comprehensive online application database reflects more than 30 years of expertise and innovations. Over 8,000 published entries of peer-reviewed articles and application notes demonstrate the flexibility and versatility of our readers, and their use in chemical and biological sciences.

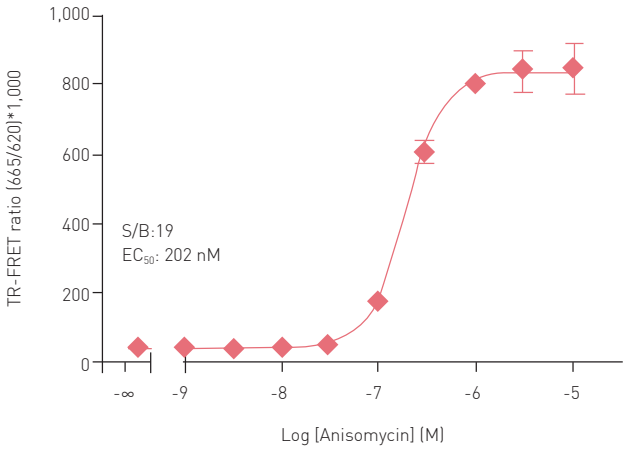
## Support and training

BMG LABTECH operates globally through an extensive network of subsidiaries and trained distributors. Customers can rely on qualified support and assistance with regard to software, assay development, or general enquiries related to the CLARIOstar *Plus* and all our other microplate readers.

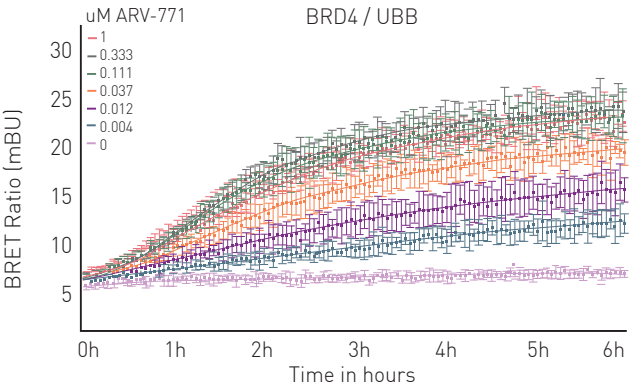
HTRF is a registered trademark of Cisbio Bioassays.
LanthaScreen is a registered trademarks of Thermo Fisher Scientific.
Transcreener is a registered trademark of Bellbrook Labs.
Dual Luciferase Reporter and NanoBRET are trademarks of Promega Corp.
Mycoalert is a trademark of Lonza.
THUNDER is a trademark of Bioauxilium.




Wild type (wt) and XRN1 partial/complete knockout cells infected with SINV-mCherry. Red fluorescence was monitored as a proxy for viral infection.




Phosphorylation of p38αβγ T180/Y182 in HeLa cells stimulated with Anisomycin assessed by TR-FRET.




Real-time assessment of targeted protein degradation by PROTACs with a NanoBRET™ BRD4 ubiquitination assay.

The CLARIOstar Plus can include all or any combination of features/options/accessories listed below at purchase. Upgrading with additional features/options/accessories may be possible after purchase. Contact your local representative for more details or a quote.

| | | |
|---|---|---|
| Detection modes | UV/vis absorbance<br>Fluorescence intensity (incl. FRET)<br>Luminescence (flash and glow) - incl. BRET<br>Fluorescence polarization<br>Time-resolved fluorescence<br>TR-FRET<br>AlphaScreen®/AlphaLISA®/AlphaPlex™ | |
| Measurement modes | Top and bottom reading<br>Endpoint and kinetic<br>Sequential multi-excitation<br>Sequential multi-emission<br>Spectral scanning (fluorescence, luminescence, absorbance)<br>Ratiometric measurements<br>Well scanning | |
| Microplate formats | 6- to 1536-well plates, user-definable<br>LVis Plate with 16 low volume microspots (2 µL) | |
| Microplate carrier | Robot compatible | |
| Light sources | High energy xenon flash lamp<br>Dedicated laser for AlphaScreen®/AlphaLISA®/AlphaPlex™ | |
| Detectors | Low-noise photomultiplier tube<br>Red-sensitive photomultiplier tube<br>CCD spectrometer | |
| Wavelength selection | Dual Linear Variable Filter (LVF) Monochromators™<br>Linear Variable Dichroic Mirror: separates excitation and emission LVF Monochromators<br>Optical filters: excitation and emission slides hold up to 4 filters each<br>LVF Monochromators + optical filters: use one for excitation and the other for emission<br>UV/vis absorbance spectrometer: full spectra or 8 discrete wavelengths in < 1 sec/well | |
| Optical filters | Excitation and emission slides for up to 4 filters each | |
| Optical path | Top and bottom: free-air optical light path guided by motor-driven mirrors and dichroics | |
| Z-adjustment | Automatic focal height adjustment (0.1 mm resolution) | |
| Spectral range | **Filters** | FI, FP, TRF: 240 - 740 nm or 240 - 900 nm (red-shifted PMT)<br>LUM: 240 - 740 nm |
| | **LVF Monochromators™** | FI: 320 - 740 nm or 320 - 840 nm (red-shifted PMT)<br>LUM: 320 - 740 nm |
| | **Linear Variable Dichroic** | 340 - 740 nm or 340 - 760 nm (red-shifted PMT) |
| | **Spectrometer** | ABS: 220 - 1000 nm; wavelength precision: ⩽ 0.5 nm |
| Sensitivity | **FI filters** (top) | < 0.15 pM (< 3 amol/well FITC, 384sv, 20 µL) |
| | **FI filters** (bottom) | < 1.0 pM (< 50 amol/well FITC, 384g, 50 µL) |
| | **FI monochromator** (top) | < 0.35 pM (< 7 amol/well FITC, 384sv, 20 µL) |
| | **FI monochromator** (bottom) | < 3.0 pM (< 150 amol/well FITC, 384g, 50 µL) |
| | **FI dynamic range** | 8 decades in a single measurement |
| | **FP** | < 0.5 mP SD at 1 nM FITC (384sv, 20 µL) |
| | **HTRF®**<br>(black and white microplates) | Reader Control Kit (Eu) after 18h (384sv, 20 µL)<br>Delta F > 880 % (High Calibrator)<br>Delta F > 30 % (Low Calibrator) |
| | **TRF** | < 20 fM europium, 384, 80 µL |
| | **LUM** | < 0.4 pM (< 8 amol/well ATP, 384sv, 20 µL) |
| | **LUM dynamic range** | 8 decades in a single measurement |
| | **AlphaScreen®** with laser | < 5 pM (< 100 amol/well P-Tyr-100, 384sv, 20 µL) |
| | **ABS**<br>with spectrometer | Selectable spectral resolution: 1, 2, 5, and 10 nm<br>OD range: 0 to 4 OD; photometric resolution: 0.001 OD<br>Accuracy: < 1% at 2 OD<br>Precision: < 0.5% at 1 OD and < 0.8% at 2 OD<br>Linearity: ⩽ 0.8% at 2.0 OD |
| Read times | **Flying mode** (1 flash) | 8 sec (96), 15 sec (384), 28 sec (1536) |
| | **10 flashes** | 19 sec (96), 57 sec (384), 3 min 4 sec (1536) |
| Reagent injection | Up to 2 built-in reagent injectors<br>Individual injection volumes for each well: 3 to 500 µL (optionally up to 2 mL)<br>Variable injection speed up to 420 µL/sec<br>Reagent back flushing | |
| Shaking | Linear, orbital, and double-orbital with user-definable time and speed | |
| Integrated barcode reader | Up to two integrated barcode readers | |
| Incubation | +3°C above ambient up to 45°C or 65°C<br>The upper heating plate of the incubation chamber operates at 0.5°C more than the lower plate.<br>This prevents condensation build-up on the lid or sealer. | |
| Software | Multi-user SMART Control and MARS data analysis software included<br>FDA 21 CFR Part 11 compliant<br>Integrated fluorophore library | |
| Dimensions | Width: 45 cm, depth: 51 cm, height: 40 cm; weight: 32 kg | |
| | Accessories | |
| Stacker | Plate handler for up to 50 microplates - continuous loading feature | |
| THERMOstar | Microplate incubator and shaker | |
| Atmospheric Control Unit (ACU) | Actively regulates $O_2$ and $CO_2$ - 0.1-20%<br>Gas ramping function | |
| LVis Plate | Microplate designed to measure 16 low volume (2 µL) samples and standard cuvettes.<br>Incorporating NIST-traceable filters and holmium oxide standards for instrument performance test.<br>Sensitivity: < 2 ng/µL dsDNA | |
| Filters | Optimised for dyes, fluorophores and specific assays<br>Filters for all applications from UV to NIR<br>Customised filters available upon request | |
| Upgrades | Upgrades to include options such as additional detection modes,<br>reagent injectors, extended temperature control, etc. are available.<br>Please contact your local representative for more information. | |

US Patent Number 9,733,124.
Limit of detection (sensitivity) was calculated according to the IUPAC standard: 3x(SDblank) / slope
Specifications are subject to change without notice.
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