

NEPHELOstar[®] Plus

Laser-based Microplate Nephelometer
for light scattering detection




BMG LABTECH

The Microplate Reader Company



NEPHELOstar® Plus

"We have four BMG LABTECH plate readers and they are all used heavily. They are **smart, reliable** and help my company to achieve its strategic goals. More than this, the **support team and servicing engineers are brilliant!**

Thank you BMG!"

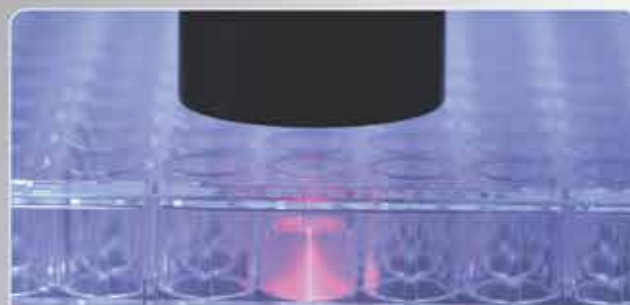
*Hayley Jones
Scientist, MRC Technology, London, UK*

Flexibility

The NEPHELOstar^{Plus} is a microplate nephelometer that detects insoluble particles in liquid samples by measuring forward scattered light.

Light scattered by insoluble samples is detected at incident angles up to 80 degrees, making the reader approximately thirty times more sensitive than traditional transmission readers that measure the reduction in direct light passing through a sample well.

The key feature of the NEPHELOstar^{Plus} is its robust optical system employing a self-monitoring laser diode that offers adjustable intensity and beam diameter. These features allow to reduce the influence of meniscus effects, to optimize sensitivity, and to perform measurements in up to 384-well plate formats.



Insoluble particles in solution in a microplate well scatter laser light

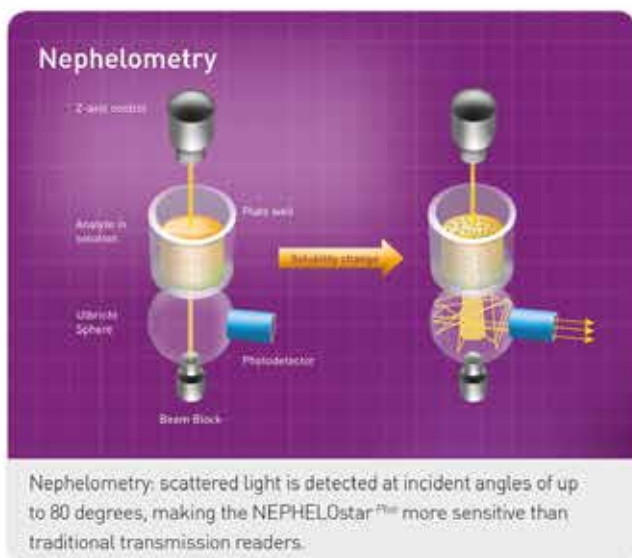
Up to two on-board reagent injectors, precise temperature control, multi-mode shaking capabilities, Stacker plate handler, and compatibility with robotic systems further enhance instrument flexibility.

Optical design

The high-intensity light source of the NEPHELOstar^{Plus} is a laser diode (at 635 nm) with a highly collimated beam. The laser beam passes through the sample well into a scattered light detector (Ulbricht sphere). If the light is not deflected by particles, it passes straight through the sphere and no signal is generated. If particles are present in the sample, the light is scattered and reflected around the interior of the sphere and ultimately detected by a photodiode.

In liquid solutions, the relationship between the concentration of scattering particles and scattered light

intensity is linear over a wide range of concentrations. An exclusive feature of the NEPHELOstar^{Plus} is the ability to adjust the laser intensity and the beam width for best performance. With a narrow beam width, liquid surface effects such as a strong meniscus are reduced.



Liquid handling

Two precise on-board injectors allow simultaneous reagent injection and detection. Concurrent reading and injection ensures that even the initial part of fast kinetic reactions can be monitored. Kinetic data can be collected as fast as 50 reading points per second or as slow as one measurement every 2.5 h. The injectors are readily accessible and are housed within the instrument to safeguard any light sensitive reagents.



The exceptionally small dead volume and back flushing ensure that precious reagents are conserved. Users can tune all parameters, such as plate shaking, injection speed, timing, and the number of injections per well to automatically produce dilution schemes and concentration gradients across the microplate.

Assays

The flexibility and performance of the NEPHELOstar^{Plus} allows more applications to be adapted to microplate-based laser nephelometry than ever before.

Flocculation assays, drug solubility determination, bacterial and fungal growth kinetics, and determination of precipitation of particles in solution are amongst a variety of possible studies. Four examples are outlined below:

Automated drug solubility screening

Determining aqueous compound solubility has become an essential early measurement in the drug discovery process to avoid time-consuming and costly ADME screens of low solubility compounds. Developed to meet high-throughput demands, the NEPHELOstar^{Plus} offers HTS/drug screening laboratories a fast and simple method for checking compound solubility, which can be fully automated. The nephelometric method has been shown to produce results equivalent to those produced by an HPLC method and to be largely unaffected by colored solutions.

Microbial growth kinetics

Continuous nephelometric monitoring of changes in the turbidity can be used to test antimicrobial drugs and their effects on microbial growth kinetics. Among various parameters of the growth curves, the duration of the lag phase is strongly affected by the presence of antimicrobial drugs. Using the NEPHELOstar^{Plus} instead of a traditional photometer, this early part of the growth curve can be monitored more exactly. Featuring additional precise temperature control, multi-mode shaking capabilities, and a gas vent, the instrument is a perfect tool to study microbial growth.

□ Quantification of proteins

In clinical chemistry, immunonephelometric assays are used to determine the concentration of serum immunoglobulin (IgA, IgG, IgM), complement components (C3, C4), acute phase reactant proteins (CRP, transferrin), albumin, and α -1-antitrypsin.

Protein precipitation of globular proteins refers to the formation of protein aggregates by adding e.g. salt or organic solvent. In contrast, immunoprecipitation allows a given protein to be precipitated selectively via an antibody-antigen reaction.

□ Monitoring of polymerization

In organic chemistry, nephelometry is used to quantify macromolecules, e.g. by monitoring of a polymerization reaction.

The NEPHELOstar^{Plus} unique combination of features is ideal for all four application areas.

Stacker and robot compatibility

For medium level throughput, BMG LABTECH offers a Stacker that can be used with the NEPHELOstar^{Plus}. The Stacker is an ideal solution for mid-throughput labs that wish to have the small footprint of an automated plate feeder along with the simplicity and reliability the Stacker offers. It provides loading, unloading, restacking and a continuous load feature of up to 50 microplates.

The script mode of the Stacker software gives the user unlimited flexibility to run diverse assays.

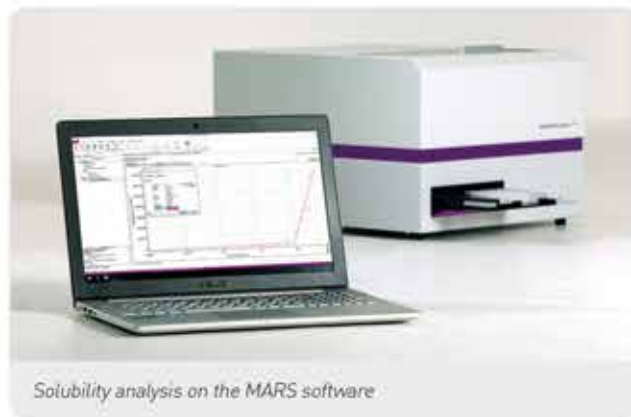
This function can be used to choose different test definitions for different plates in one batch run, or to perform more than one measurement on one plate.



Automated microplate handling with Stacker.

Control and MARS data analysis software

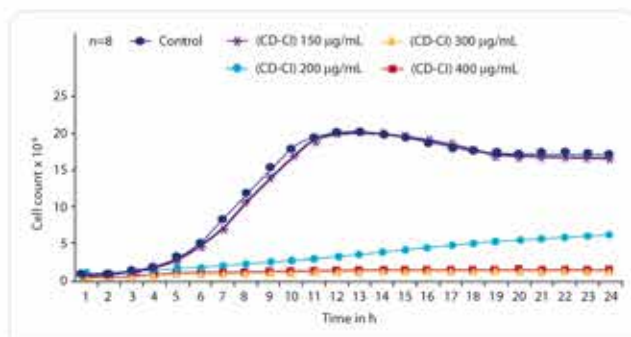
The NEPHELOstar^{Plus} software package provides an extensive range of possibilities for both test protocol definitions and data analysis. The Reader Control part of the software allows users to define instrument parameters and test protocols, and MARS offers various tools to easily determine compound solubility or microbial growth kinetics.



Solubility analysis on the MARS software

Well organized, versatile, easy to use and powerful are just a few of the ways the MARS data analysis software package is described by users. MARS provides several options to display data in a clear and concise format.

Data can be processed with powerful predefined templates or by using an extensive range of data calculation features. For example the automatic determination of compound solubility by a segmental regression fit can be done, or a standard curve can be generated based on different curve fitting algorithms to calculate EC_{50} , IC_{50} , and r^2 values.



The MARS data analysis software provides sophisticated tools for automated data reduction.

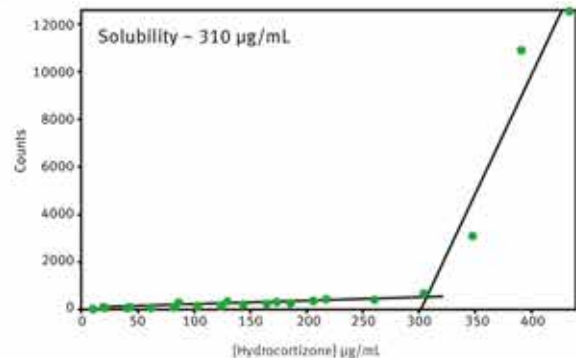
Applications center

The NEPHELOstar^{Plus} has been cited in numerous publications such as peer-reviewed papers, application notes and scientific posters, exemplifying its versatility. The following main categories are amongst a wide range of possible applications:

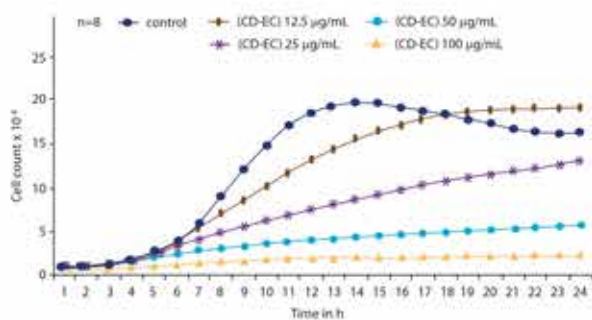
- Automated drug solubility screening
- Microbial growth kinetics
- Quantification of proteins

The NEPHELOstar^{Plus} versatility and flexibility are illustrated by the following examples for:

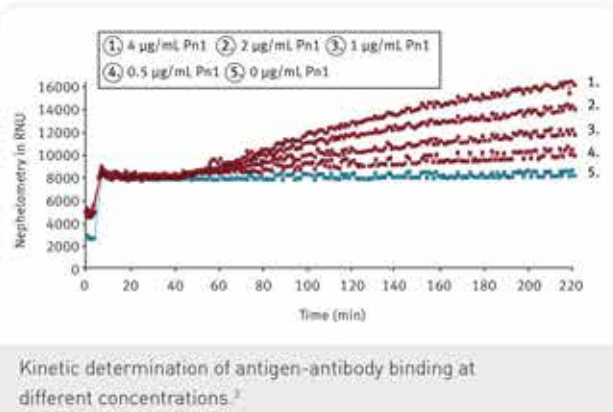
- Solubility screen of the corticosteroid hydrocortizone
- Monitoring of antifungal agents
- Antigen-antibody binding



Solubility screen of hydrocortizone. The intersection at 310 µg/L indicates the point of precipitation.¹



The antifungal econazole nitrate complex (CD-EC) inhibits growth of *Candida albicans*.²



Kinetic determination of antigen-antibody binding at different concentrations.³

BMG LABTECH continuously works with all major reagent companies to develop protocols and to optimize instrument settings for their existing assays and their newest kits.

Visit BMG LABTECH's applications center online to download all the leading applications, listed as:

- Application notes
- Peer-reviewed papers

BMG LABTECH's comprehensive searchable applications database reflects more than 25 years of expertise and innovations in microplate reading technology. Over 4.000 references exemplify the flexibility and versatility of our readers, as well as their use in the chemical and biological sciences.

Support and training

BMG LABTECH operates globally through an extensive network of subsidiaries and well trained distributors. Customers can rely on PhD level support and assistance with regard to software, assay development, or general enquiries related to the NEPHELOstar^{Plus} and all other BMG LABTECH microplate reading solutions.

^{1,2,3} The graphs were taken from BMG LABTECH's Application Notes AN 117, AN 174 and we kindly thank Dr. Nelius Swart for the antigen-antibody binding figure.

Due to the modularity of BMG LABTECH's instruments, all, or combinations of the features below can be installed at purchase or upgraded at any time. Please contact your local representative for more details or a quote.

Detection modes	Nephelometry (light scattering)
Measurement modes	Endpoint and kinetic
Microplate formats	Up to 384-well plates
Microplate Carrier	Robot compatible
Light sources	Self-monitoring laser diode Wavelength 635±10 nm Stability <0.2% deviation Lifetime 20,000 hours Output: 1 mW Selectable beam width: 1.5 to 3.5 mm Selectable intensity 0-100% Scattering angle: detects up to 80° full cone angle
Detectors	Side window photodiode detector
Wavelength Selection	Photodiode Wavelength 635±10 nm
Sensitivity	Depends on particle size and liquid properties Silica detection (particle size 0.5 to 10 µm) 800 nM Dynamic Range: 5 decades Maximum count rate (2,000,000 Relative Nephelometry Units (RNUs) per second)
Read times	Depend on assay conditions and liquid surface stability Shortest times possible: 16 s (96), 47 s (384)
Reagent injection	Up to 2 built-in reagent injectors Injection at measurement position (6 to 384-well) Individual injection volumes for each well (3 to 500 µL) Variable injection speed up to 420 µL / s Up to four injection events per well Reagent back flushing
Shaking	Linear, orbital, and double-orbital with user-definable time and speed
Purge Gas Vent	System to inject an atmosphere or to pull a vacuum into the reader
Incubation	+4°C above ambient up to 45 °C or 60 °C The upper heating plate of the incubation chamber operates at 0.5 °C more than the lower plate. This prevents condensation build-up on the lid or sealer.
Software	Multi-user Reader Control and MARS Data Analysis Software included FDA 21 CFR Part 11 compliant
Dimensions	Width: 44 cm, depth: 48 cm, height: 32 cm; weight: 25 kg
	Optional 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%
Upgrades	Please contact your local representative for upgrades including options such as detection modes, reagent injectors, etc.

*Limit of detection (sensitivity) was calculated according to the IUPAC standard: $3 \times (SD_{blank}) / \text{slope}$
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Headquarters Germany
BMG LABTECH GmbH
Allmendgrün 8
77799 Ortenberg
Tel. +49 781 96968 -0
germany@bmglabtech.com

Australia
BMG LABTECH Pty. Ltd.
2/24 Carbine Way
Mornington, Victoria, 3931
Tel. +61 3 5973 4744
australia@bmglabtech.com

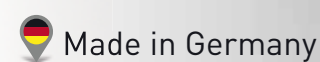
France
BMG LABTECH SARL
7, Rue Roland Martin
94500 Champigny s/Marne
Tel. +33 1 48 86 20 20
france@bmglabtech.com

Japan
BMG LABTECH JAPAN Ltd.
1-6-2, Shimo-cho
Omiya-ku
330-0844 Saitama City
Tel. +81 48 647 7217
japan@bmglabtech.com

UK
BMG LABTECH Ltd.
8 Bell Business Park
Smeaton Close
Aylesbury
Bucks
HP19 8JR
Tel. +44 1296 336650
uksales@bmglabtech.com

USA
BMG LABTECH Inc.
13000 Weston Parkway
Suite 109
Cary, NC 27513
Tel. +1 877 264 5227
usa@bmglabtech.com

www.bmglabtech.com



Your local distributor:



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WWW.ISOGEN-LIFESCIENCE.COM

Benelux

Isogen Life Science B.V.
Veldzigt 2a
3454 PW De Meern
The Netherlands
tel. +31 30 688 0771

Spain and Portugal

Isogen Life Science B.V.
Veldzigt 2a
3454 PW De Meern
The Netherlands
tel. +34 936 365 178

For service questions, please contact
service@isogen-lifescience.com

For all other questions, please contact
support@isogen-lifescience.com