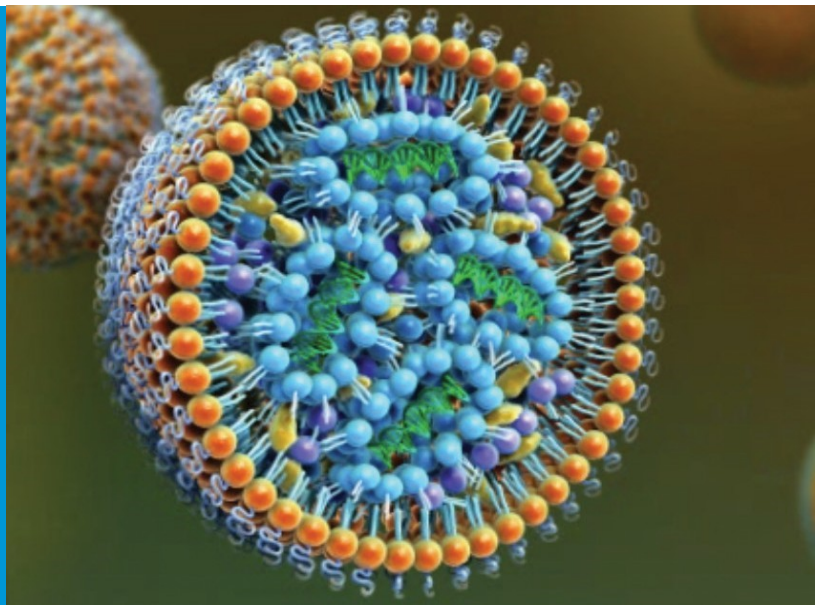
LATEST TECHNOLOGIES: ACCELERATE BIOTHERAPEUTIC DEVELOPMENT AND MANUFACTURE

ATA SCIENTIFIC instruments

www.atascientific.com.au

DEVELOP REPEATABLE, SCALEABLE FORMULATIONS



Nanomedicines currently being developed, are at the heart of next-generation genetic medicines that will allow otherwise untreatable diseases to be addressed.

Commonly formulated to deliver pharmaceutical drugs packaged into nano-sized carriers made of excipients, like lipids and polymers, these nanomedicines are traditionally made by extrusion or sonication which can be costly, labour-intensive, prone to batch-to-batch variations and difficult to scale.

The NanoAssemblr platform from Precision NanoSystems (PNI) is uniquely positioned with NxGen technology to help lower existing barriers to accelerate the discovery and development of novel nanomedicines. Meeting the need for robust and reproducible low volume production of nanoparticles containing genetic payloads, the NanoAssemblr also allows formulations to be scaled in volume across several orders of magnitude to suit various stages of development, from formulation to full GMP through one single mixing element.

Using microfluidic mixing under laminar flow conditions, NanoAssemblr enables the rapid self-assembly of nanoparticles with defined size (20nm to 200nm), payload (e.g. nucleic acids, hydrophobic drugs) and excipient characteristics (e.g. charge and pH tuning). Precise control of particle size is maintained by optimising parameters such as mixing ratios and flow rate. Highly reproducible lipid nanoparticles (LNPs) and liposomes can be formulated in one single step to rapidly encapsulate a payload such as an mRNA with high efficacy and potency within seconds. The system is ready in 3 simple steps with no priming or cleaning required - simply insert the cartridge, load syringes and start formulating!

Personalised, rapid, cost-effective development of non-viral based vaccines, cell therapies and gene therapies in the prevention and treatment of infectious disease, rare disease and cancer.

NanoAssemblr Ignite:

- **Controlled assembly** - Tune particle size with precise control over fluid flow rates
- **Fast & Precise** – Non-turbulent particle formulation in less than a minute ensures the most reproducible results for a wide range of nanoparticle types.
- **Versatile** - Formulate small molecules, peptides, and nucleic acids into lipid, polymer or hybrid nanoparticles, and more.
- **Scalable** – More than 25X single mixer throughput simplifies scaling up while maintaining particle quality and batch-to-batch reproducibility. Optimised formulations can be scaled to advanced preclinical and clinical scale with Blaze™ and GMP Systems.

PREDICT STABLE FORMULATIONS

The ability to predict product stability early in the development pipeline, with the use of low concentration formulations, can streamline early formulation development. By optimising particle size and zeta potential, production of effective therapeutics can be delivered safely while also reducing development time and costs.

Zeta potential (ZP) is a measure of intermolecular electrostatic interactions. Higher zeta potential increases repulsion amongst molecules, thereby minimising the formation of native aggregates. While native aggregates are often reversible, their presence is a significant risk factor for the formation of denatured aggregates which are generally non-reversible. The more positive B22 and KD values (second virial coefficient and DLS interaction parameter) are indicative of more stable formulations, so both of these parameters are effective predictors of stability. B22, KD and ZP can all be obtained using a Zetasizer Ultra, with its best-in-class concentration range and broadest buffer composition capability.

The Zetasizer Ultra uses Non-Invasive Back Scatter (NIBS) and, Multi-Angle Dynamic Light Scattering (MADLS) technology for the measurement of particle and molecular size. NIBS provides the versatility and sensitivity to measure over a wide concentration range, while MADLS permits a higher resolution view into nanoparticle size distribution and particle concentration. The measurement of particle concentration is suitable for a wide range of materials, requires no or little dilution, and is quick to use – all of which make it ideal as a screening technique. This is a unique capability of the Zetasizer Ultra which can even be applied to samples such as viruses and virus-like particles (VLPs), which were previously very challenging to measure.

The Zetasizer determines a protein's hydrodynamic size as well as detecting the presence of larger aggregated species.

Zetasizer Ultra:

- Rapid, **Multi-Angle Dynamic Light Scattering** (MADLS) measurements for absolute confidence in particle and molecular size distribution analysis.
- **Dynamic Light Scattering** (DLS) measures particle and molecule size, from below 1 nm to 10 µm.
- **Adaptive Correlation** for faster, more reproducible sizing measurements with less sample preparation.
- **Disposable capillary sizing cell** provides the ultimate in non-destructive, low volume (down to 3 µL) analysis.
- **Industry-leading technology**, with exceptional sensitivity and compatibility with broad range of sample attributes and protein concentrations.
- **Intuitive software**, simplified data analysis, built-in procedures and calculators specifically for proteins.
- **21CFR compliant** capability.

DETECT AND CHARACTERISE AGGREGATES AND SUBVISIBLE NANOPARTICLES

Protein aggregation and subvisible particles in biopharmaceuticals is of particular concern, reducing product efficacy and stability and increasing immunogenic risk. Malvern's highly sensitive protein aggregation characterisation tools allow complete evaluation of therapeutic proteins and early identification of potential stability concerns.

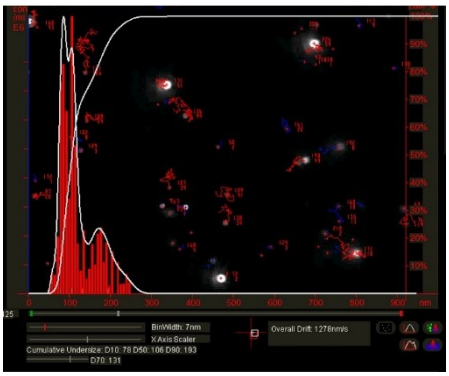
Malvern NanoSight uses nanoparticle tracking analysis (NTA) to characterise nanoparticles from in solution. Based around a high-resolution camera and specially designed software, NTA measures Brownian motion of each individual particle to determine hydrodynamic size. The result is high-resolution particle size distributions, within a known sample volume, allowing the concentration of particles to be determined.

The particle-by-particle approach used by NanoSight is particularly appropriate for polydisperse samples. Labelled or naturally fluorescent particles can also be detected with a choice of laser wavelengths and a motorised fluorescence disc. The size range and particle information provided by NTA offers data complementary to other sizing tools such as the Malvern Zetasizer.

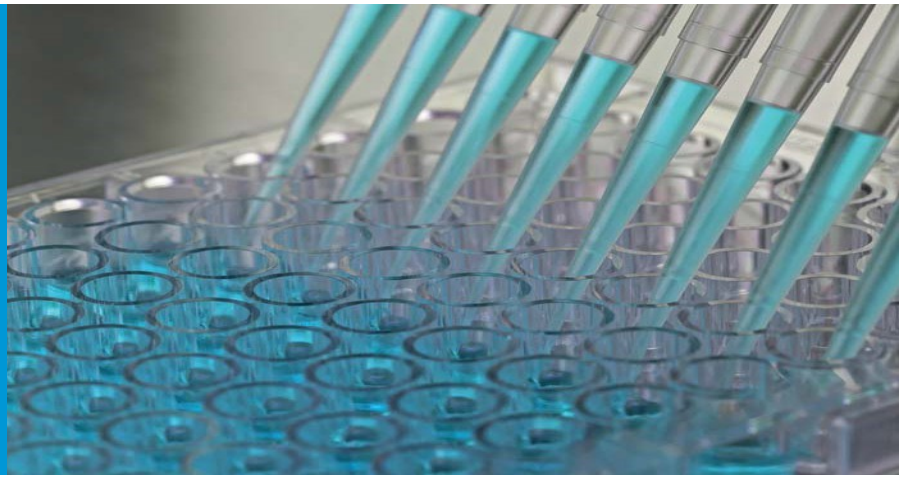
NTA is ideally suited to study the size of nanoparticle drugs from early-stage research through to candidate screening, formulation development and clinical batch monitoring whilst the concentration measurement allows for dose determination of the final product as well as for use in in vitro and in vivo assays.

NanoSight range:

- Number-weighted **concentration and high resolution size** distributions in the size range 10 nm – 2000 nm
- Visual validation of results gives extra confidence
- Minimal sample preparation
- Fluorescence capability, allowing differentiation of sub-populations



CHARACTERISE STRUCTURAL STABILITY



Thermal stability is a widely used parameter for measuring protein stability, enabling screening of different formulations and comparisons of different candidates.

MicroCal differential scanning microcalorimeters (DSC) provide fast and accurate determination of melting transition midpoint (T_M) and changes in enthalpy (ΔH), as indicators of thermal stability. These changes occur as the protein unfolds, allowing DSC to detect denaturing events. Any increase in T_M seen when comparing native and modified forms during formulation screening, can be associated with an increase in stability.

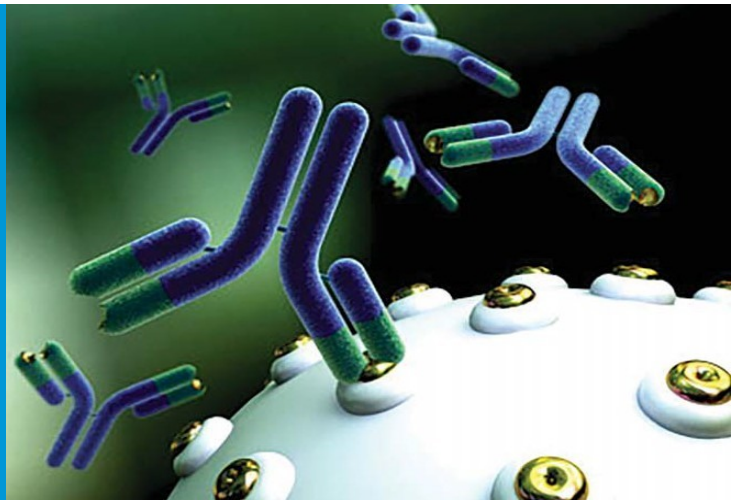
The aggregation temperature (Tagg), can be measured using the Zetasizer series by performing thermal ramps up to 90°C and collecting data at predetermined temperatures. Low volume cuvettes minimise sample volume requirements. The inherent sensitivity of dynamic light scattering (DLS) to the presence of aggregates allows very small changes to be detected and subtle differences between formulations and candidates to be reported. These differences may arise from the formation of aggregates in response to thermal stress and are a direct indication of protein stability.

DSC and DLS are complementary technologies which combine perfectly to evaluate the stability of biotherapeutics. While DSC detects unfolding of the protein structure and the resultant change in heat capacity, DLS detects changes in protein size as a result of aggregate formation. The combination of these two techniques provides insights into changes induced by protein instability resulting from thermal stress. Together, DLS and DSC can provide a highly robust determination of formulation and candidate stability, critically supporting the development process.

MicroCal DSC range:

- Compatible with a variety of sample types, including high concentration, colored and turbid, as well as a broad range of solvents and buffers
- Rapid identification of formulation conditions, utilising label-free, universal stability assay
- Simple assay development
- Full automation using standard 96-well plate format ensures high capacity and easy loading, with thermostatically- controlled storage of up to 6 plates.

ASSESS AND OPTIMISE DRUG BIOACTIVITY

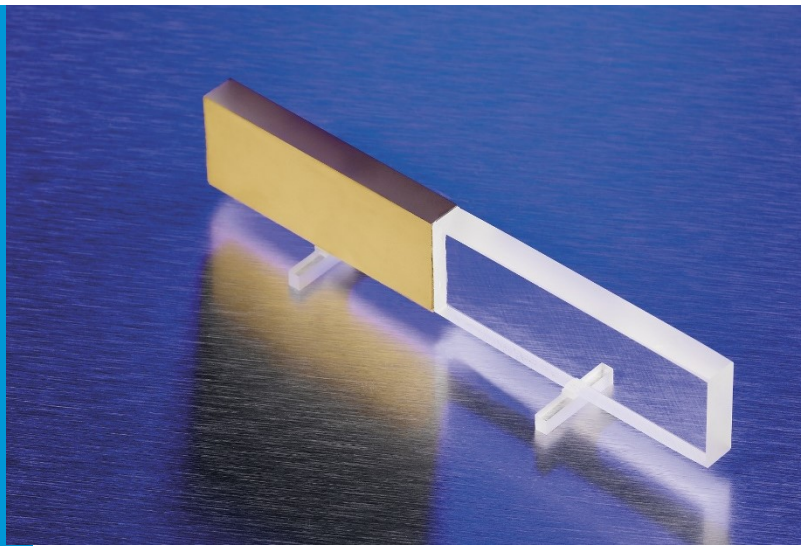


Candidate optimisation is often driven by studying the affinity of interactions between candidate and target molecules. However, thermodynamic variables underlying these interactions, such as ΔH and ΔS, are also fundamental to this process and provide deeper insights into the drivers for such interactions. MicroCal PEAQ ITC calorimeters have the sensitivity and throughput for efficient determination of all the binding parameters that may guide candidate optimisation and formulation development activities. MicroCal isothermal titration calorimeters (ITC) all allow direct, label-free, in-solution measurement of binding affinity and thermodynamics in a single experiment, enabling the accurate determination of binding constants (K_D), reaction stoichiometry (n), enthalpy (ΔH) and entropy (ΔS). These provide a complete thermodynamic profile of the molecular interaction, enabling the user to go beyond binding affinities and elucidating the mechanisms which underlie molecular interactions. Hydrogen bonding, measured by ΔH, is often a more effective predictor of efficacy than hydrophobic interactions, measured by ΔS, and so more effective therapeutics usually focus on optimising ΔH. ITC permits a multi-dimensional approach, where the contribution of enthalpy and entropy to affinity is used to screen for the most effective biological candidates, support engineering to design better biotherapeutics or ensure biological activity is maintained during formulation screening.

MicroCal PEAQ ITC:

- **All binding parameters** (affinity, stoichiometry, enthalpy and entropy) in a single experiment
- **High signal-to-noise** increases confidence in data quality and relevance of generated affinity and thermodynamic parameters
- Identification of stabilising excipients
- **Automated washing** (with detergent) of the sample cell and titration syringe assists in producing high quality reproducible data
- **Fully automated** with capacity to run 4× 96-well plates unattended

EXPLORE THE STRUCTURE AND STABILITY OF BIOMOLECULES



Circular dichroism (CD) spectroscopy is routinely used in the biopharmaceutical industry to study protein conformation and stability and the effects of manufacturing, formulation, and storage conditions on drug performance. Notably, the technique can be used to determine the stereochemistry of chiral drugs and proteins, and for monitoring and characterising molecular interactions in solution. Although both DSC and CD spectroscopy can measure thermal denaturation of proteins, CD uses lower concentrations of proteins than DSC and can also be measured at various pHs and in a wider range of solvent conditions.

The JASCO's new J-1500 CD spectrometer allows users to carry out measurements with high S/N ratio in the vacuum UV region down to 163nm, by incorporating several advances such as high-throughput optics and a highly effective nitrogen gas purging system based on computational fluid simulation. The dual polarizing prism optical design results in very low stray light enabling the instruments to obtain high-quality CD data even under conditions with high absorbance. High sensitivity and fast scan speed allows the system to measure samples quickly minimising time exposure of biological samples to the high-energy UV light which reduces the risk of sample degradation.

The J-1500 allows for the maximum flexibility to upgrade your CD system with different measurement techniques as requirements evolve. While the standard measurement modes are CD, linear dichroism (LD) and absorbance, up to four simultaneous modes can be measured when combined with a wide range of sampling accessories including fluorescence, fluorescence-detected CD/LD and fluorescence anisotropy.

JASCO CD J-1000 series:

- **Wide spectral range** from vacuum UV to Near-IR (J-1700, 163nm up to 2500nm)
- **Standard built-in mercury lamp** and optional NIST traceable standard sample for system validation
- **High-efficiency purge** capability enabling to enhanced vacuum UV measurement
- **Extremely low stray light and high S/N** ratio providing wide dynamic range
- **Simultaneous Multi-probe measurements (SMP**) with acquisition of up to four data channels
- **Flexible** design allowing field upgrades for different measurement modes and accessories as applications evolve
- **Cross platform Spectra Manager II** or Spectra Manager CFR (For regulated labs.

Versatile for a wide range of applications:

- Study Protein folding/conformation
- DNA/RNA interactions
- Enzyme kinetics/ Temperature ramping
- Purity testing of optically active substances
- Quantitative analysis of pharmaceuticals
- Rapid scanning (time resolved) experiments

NON-INVASIVE TRACKING FOR INDIVIDUAL CELLS

Within heterogeneous culture systems, important cellular events are often missed that, if detected, could give a whole new level of biological insight. For example, cell growth is more complex than just cells simply multiplying. They can increase in size without dividing, they can divide asymmetrically, they can grow to a certain size then stop. All these aspects of cell growth are lost with most live cell assays, particularly when using manual tracking and analysis methods.

Phasefocus™, Livecyte eliminates these constraints providing a more accurate and realistic account of treatment driven changes in cell behaviour. Using ptychographic quantitative phase imaging (QPI), Livecyte enables quantitative, label free, live cell imaging and analysis of single and multiple cell types in heterogeneous cell populations. Requiring only low-level illumination, Livecyte provides a non-invasive, gentle experimental environment, minimising interference and phototoxicity, making it suitable for more clinically and physiologically relevant primary, neural and stem cell populations, alongside traditional cell assays.

Livecyte easily produces high resolution, high contrast images from which individual cells can be readily defined and tracked for prolonged periods. The nature of the technique allows the areas of investigation larger than the field of view of the objective lens without the need for any image stitching, while also making it possible to automatically focus your sample post acquisition. This ensures that the microscope is not sensitive to focal drifts during a long-term time lapse, or differing focus positions across an entire well plate. Correlate changes in proliferation, motility and morphology, from every experiment.

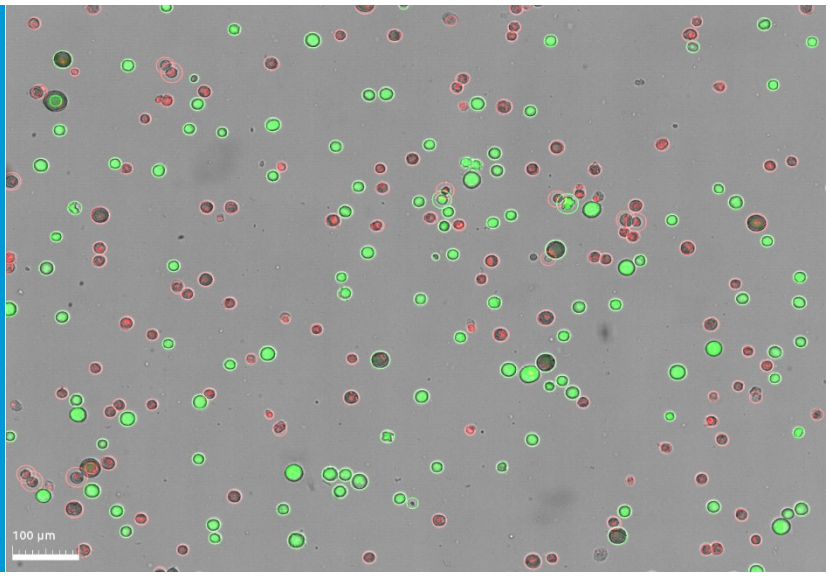
Phasefocus Livecyte:

- **High contrast time-lapse videos** using patented Ptychographic quantitative phase imaging (QPI) technology for label-free assays with or without up to **seven channels of complementary fluorescence.**
- **Automated single-cell tracking** of even the most sensitive cells quickly reveals subtle phenotypic differences in unperturbed cell populations.
- **Easy-to-use Dashboards** present coherent and concise results from up to 96 wells at a time whilst retaining the ability to investigate individual cell behaviour and outlying characteristics.

Livecyte answers questions that no other system can.

Phasefocus was awarded a Microscope Today Innovation Award in 2013 for the technology, and won a second award in 2017 for Livecyte itself. In 2018, researchers from Cornell University set the Guinness World Record for the highest resolution microscope using Ptychography on an Electron Microscope.

ACCURATELY MONITOR CELL CONCENTRATION AND VIABILITY



The biomanufacturing industry is experiencing rapid growth due to improvements in cell therapies, such as CAR-T cell therapy, and increasing bioactive production, which is expected to grow further over the next decade. In response to these demands, biomanufacturers have been expanding the production capacity while maintaining quality and regulatory compliance. The ability to monitor cell growth and health accurately while managing multiple cell batches is critical to ensure a more efficient workflow.

LUNA-FX7™ Automated Cell Counter provides the highest cell counting accuracy and suitable for a variety of cell types. Users can analyse up to eight samples simultaneously by using the 8-channel slide, with a maximum counting volume of 5 µL in the single-channel slide (10 times that of conventional cell counters). Using brightfield and dual fluorescent detection, precision autofocus, advanced optics and a clever declustering algorithm, the LUNA-FX7 delivers reliable results for almost every cell type. Its broad cell detection range eliminates the need to dilute or concentrate samples, making the system ideal for diverse cell counting applications including single-cell sequencing and CAR-T cell therapy.

The Bioprocess option in the LUNA-FX7™ reduces unnecessary effort by automating the recording and analysing status indicators such as cell growth and viability, simultaneously for multiple cell culture batches using 3 different counting modes.

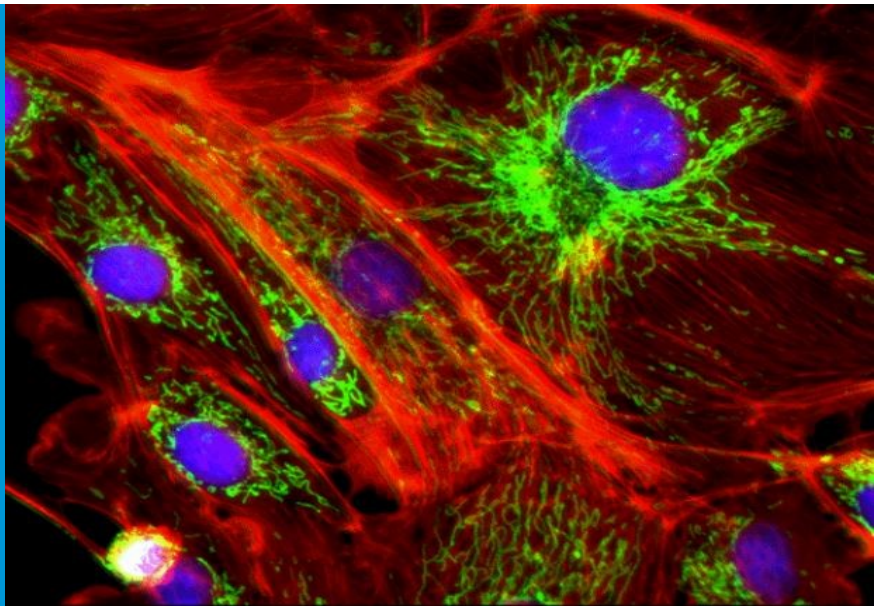
Automated calculations of doubling times, growth curves, and viability status provide information to monitor and forecast bioprocess production timelines reliably and accurately. When combined with the CountWire™ software package, the Bioprocess feature allows team members to monitor multiple culture batches in real-time across multiple facilities.

The LUNA family of automated counters has been awarded a **Platinum seal of quality from SelectScience** in recognition of outstanding feedback received from scientists globally – one of just 6 winners since the awards were launched in 2017!

LUNA FX-7:

- East-to-use, Accurate, High-speed cell counting
- Advanced optics and intelligent declustering algorithm
- High speed precision autofocus
- Multiple slide options (8-, 3-, 2-, 1-chamber formats)
- Data transfer via Wi-Fi, USB device, or Ethernet
- COUNTWIRE software compliant with 21CRF PART11/GMP requirements

HIGH CONTENT IMAGING AND ANALYSIS



Cytotoxicity assays are a crucial step in screening for and developing therapeutic drugs. Most assays designed to measure cytotoxicity in vitro evaluate cell membrane integrity or metabolic activity after exposure, but are typically based on studying a single time point and require disturbing the growth of cells in culture.

Cell confluency is the proportion of a surface covered by adherent cells and is an indication of cell growth and density. The traditional way to measure cell confluency is to estimate cell confluency by the human eye and using a light microscope. This carries several problems, as total cell count estimates are entirely subjective and can vary greatly for the same cell culture at the same (objective) confluency depending on external factors.

The CELENA X High Content Imaging System combines automated, digital brightfield imaging with high content analysis to provide quantitative readouts for assessing and comparing confluency changes over time. This automated, non-destructive method uses brightfield imaging, which avoids the use of fluorescent stains that can have toxic effects in and of themselves over long incubation times. The onstage incubator allows users to quickly and easily set up high-content imaging experiments to measure phenotypes of interest objectively, quantitatively and reproducibly within a precisely controlled environment.
With four-channel fluorescence, brightfield, colour brightfield, and phase contrast imaging modes, together with laser autofocusing and motorised positioning of the XYZ stage, the CELENA X ensures rapid, reproducible and clear images every time. The intuitive user interface makes creating imaging protocols accessible to all users from experienced to novice.

CELENA-X:

- Fully automated plate and slide imaging
- Laser autofocus
- Fluorescence imaging in four channels, bridhtfield, color brightfield, and phase contrast imaging
- Powerful, easy-to-use user interface and data analysis software
- Customisable high content analysis

The CELENA X is as flexible as it is powerful, with interchangeable objectives and filter cubes to accommodate a wide range of fixed and live cell imaging applications.

RAPID AND EFFICIENT WHOLE TISSUE CLEARING

Tissue clearing techniques have allowed biologists to acquire high-resolution volumetric images without the need to reduce samples to thin serial sections. One major limitation to some techniques is preserving the signal from endogenous fluorescent proteins (FPs). Although recent solvent-based techniques have attempted to address this issue, these methods still can only maintain FP emission for a few days, can require a significant time investment and are limited to small tissue samples.

The X-CLARITY system and reagents for tissue clearing are based on the CLARITY principle and have been developed to standardise, simplify, and accelerate each step of the tissue clearing process. The electrophoretic tissue clearing (ETC) chamber with platinum-plated electrodes and built-in cooling system ensures efficient tissue clearing for subsequent volumetric imaging of large samples at single-cell resolution. X-CLARITY allows a whole mouse brain to clear in just 6 hours while also preserving endogenous FP signals. Applications for the X-Clarity method extend beyond brains, virtually any organ can be cleared, even organoids.

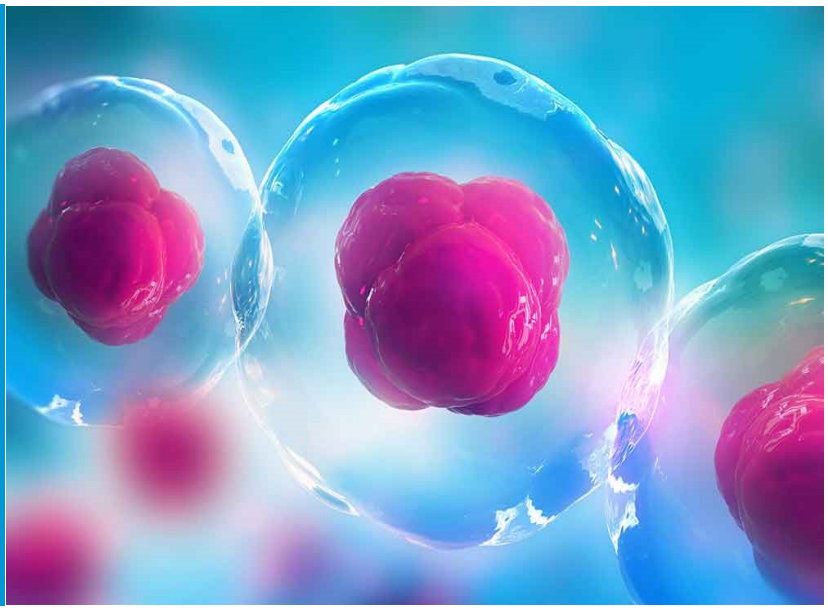
Transparent samples can be labelled using the DeepLabel Antibody Staining Kit, which enhances antibody penetration deep into clarified tissues. A refractive index matching solution (RIMS), reduces light scatter, which in turn increases optical transparency and consequently increases image quality and imaging depth.

X-CLARITY Tissue Clearing System components:

- **Polymeriser,** Sets the infused hydrogel – bolstering the tissue structural components.
- **Electrophoretic Tissue Clearing (ETC) chamber,** Lipids are extracted actively through electrophoresis or passively, leaving behind a stable and transparent tissue-hydrogel hybrid that is chemically accessible for molecular phenotyping.
- **Control Tower** with built-in cooling system for efficient tissue clearing.

www.atascientific.com.au

SAFE AND RELIABLE LIVE CELL TRANSPORT



Transporting living complex cells while retaining their full viability and functionality can be challenging. Traditionally, cells and other biological material have been stored and transported at low to cryogenic temperatures. During this process, cells often suffer from exposure to sub-optimal life-sustaining conditions (e.g. temperature, pH, etc) as well as damage due to shear stress. Not only does cell viability need to be considered, but inadequate cryopreservation may introduce variations between different batches or could even cause genetic and epigenetic modifications.

Cellbox is the first portable CO2 incubator that enables safe shipping of intact cell/tissue constructs from one facility to another that overcomes these obstacles. Ideal for air and ground transport, Cellbox provides a regulated CO2 environment and can maintain temperatures between 28 and 37° C while also monitoring the health of cells via the Cellbox App.

Specially developed for the transport of sensitive cells and cell cultures, the Cellbox is ideal for:

- iPSC's and iPSC-derived cells, such as sensory neurons, microglia and cardiomyocytes.

Cells can be transported under laboratory conditions, in the Cellbox while avoiding unwanted changes in metabolism, gene expression and protein profiles.

- Long-term cell storage and biobanks can benefit from receiving fresh material and performing the cryopreservation in-house. Recipients can benefit from the Cellbox by receiving thawed and recovered cells from a biobank, ready-to-use.
- Lab-on-a-Chip or Tissue-on-a-Chip products can be seeded with living cells before shipping under laboratory conditions in the Cellbox.

CELLBOX Live cell shipper

- **Portable CO2 Incubator** for convenient transport of cells by car, train, ship or as air cargo
- **Maintains temperature** between 28-38°C
- Provides **regulated CO2 environment**
- **Rechargeable, Li-ION battery** with external 100 – 230V power supply
- **Versatile,** suitable for multi-well plates, T-Flasks, Tubes and other CO2 permeable cell culture vessels
- Data logging and export via **Cellbox App**

Your Complete Technology Toolbox:
Accelerate development and manufacture of new drugs

Development Stages	Key steps and processes	Latest Technologies	Measurements
Drug Design and Discovery Develop nanomedicines like vaccines, gene therapy, cell therapy	Bioefficacy Label Free samples Structure/Activity	Malvern PEAQ ITC Malvern Zetasizer Ultra Jasco J-1500 CD	• Advanced binding affinity • Particle size screening • Molecular structure
Drug Formulation Create small molecules, peptides and, nucleic acids into lipid, polymer or hybrid nanoparticles	Scalability Bioequivalence Excipients	NanoAssemblr Ignite Malvern Zetasizer Ultra	• Repeatable and rapid formulation • Particle size and concentration
Drug Bioactivity Live cell analysis, and whole tissue clearing	Cell counting Live cell imaging Live cell transport Tissue clearing	LUNA FX7 X-CLARITY CELENA X LIVECYTE CELLBOX	• Accurate cell counting • Tissue clearing and RI matching • High content Imaging and Fluorescence • Long term individual cell tracking and analysis • Safe transport of live cells with temperature control and CO2 incubation
Drug Optimisation Advanced understanding of complex therapeutics	Stability Solubility Aggregate detection	Malvern Zetasizer Ultra Malvern PEAQ DSC Malvern NanoSight	• Particle size and concentration • Structural/ Temperature stability • Size and concentration of protein aggregates
Drug Manufacture Deliver therapies rapidly and safely when needed.	QA/QC Validation Final testing Drug Manufacture	NanoAssemblr Blaze Malvern Zetasizer Ultra	• Large scale formulation • Particle size and concentration

For more information contact us
ATA Scientific Pty Ltd
E: enquiries@atascientific.com.au
P: +612 9541 3500