









# Work Package 3: Advanced drug delivery systems and in vivo theranostic tools for personalized medicine

**Prof. Casettari** 









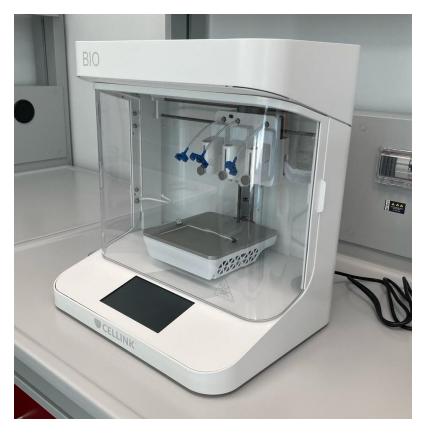












The **BIO X** 3D printer is classified as a bioprinter among additive manufacturing technologies.

It allows the use of different types of materials of biological, semi-synthetic and synthetic origin with the possibility of adding cell cultures into the construct.

#### **General applications**

The fields of application are varied both in the pharmaceutical field with the production of drugs or medical devices and in the biological field with the possibility of building complex in vitro systems containing or not cells.

#### Technological and industrial applications

Materials

Polymers

Pharmaceutical

Biological

Tissue engineering

#### Available techniques

Temperature-controlled printing bed

Clean print chamber technology (UV HEPA filter)

Classic pneumatic syringe print head

Temperature controlled pneumatic syringe print head (4-65°C)

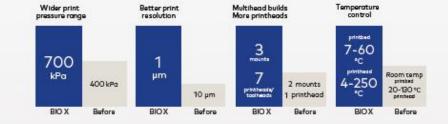
Pneumatic print head for extrusion of thermoplastic materials (up to 250 °C)

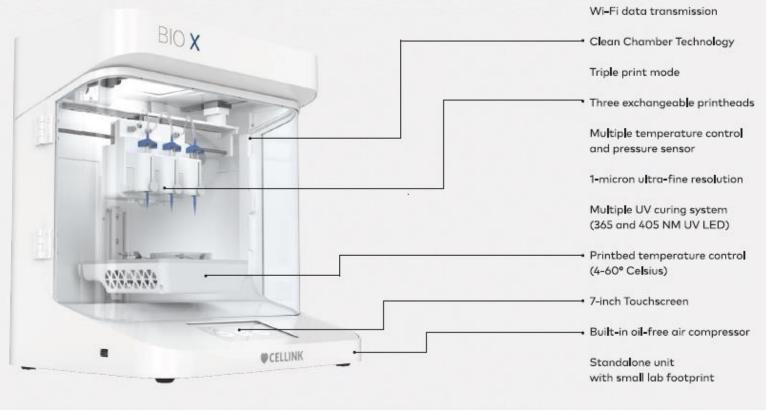
# Meet the BIO X

BIO X is the most user-friendly and flexible bioprinter in the world, providing the user with an unparalleled bioprinting experience. The built-in features along with the new BIO X software managed through the large touchscreen display minimize the learning curve and ensure you will receive the results you want.

Bioprinted tissue can be used in drug discovery where researchers can test new potential treatments and evaluate efficacy in very early stages. New drugs and treatments will potentially reach clinical trials faster with a decreased number of failures and reduced need for animal testing.

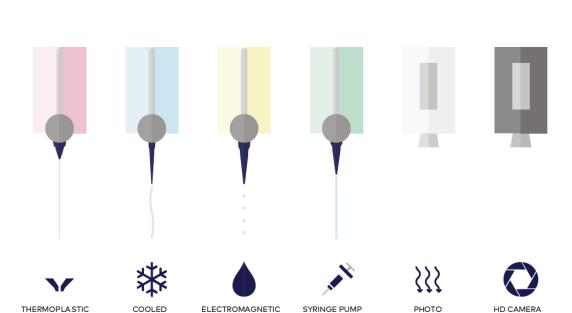
BIO X is the next-generation bioprinter, bringing scientists closer to the future of medicine.







#### LIST OF BIOINKS AND THEIR PRINTING EXTRUSION METHODS



PRINTHEAD

CURING TOOL

HEAD

TOOL HEAD

DROPLET PRINTHEAD

EXTRUDER

PNEUMATIC

HEAD

	Pneumatic-driven Extrusion	Piston-driven Extrusion (syringe)	Inkjet	Thermoplastic Extrusion
Gelatin Methacryloyl	Gelatin Methacryloyl		~	
Collagen methacryloyl (Collagen solution and precipitated)	~	~	~	
Hyaluronan	~	~	~	
Alginate	~	~	~	
Chitosan	~	~	~	
Silk	~	~		
Nanocellulose	~	~	~	
PEG/PEGDA	~	~	~	
Fibrinogen/thrombin	~	~	~	
Decellularized ECM	~	~	~	
Pluronics F127	~	~	~	
PropyleneG lycol	~	~	~	
Polycaprolactone	(heated)	(heated)		~
Polylacatic Acid				~









The **Lumen X** 3D printer uses DLP (Digital Light Processing) technology among additive manufacturing technologies. It allows the use of different types of photopolymerizing materials dedicated to this process with the possibility of adding cell cultures into the construct.

#### **General applications**

The fields of application are varied both in the pharmaceutical field with the production of drugs, medical devices and production/analysis devices and in the biological field with the possibility of building complex in vitro systems containing or not cells (e.g. Organ on chip).

#### Technological and industrial applications

Materials
Polymers
Pharmaceutical
Organic
Medical

#### Available techniques

Material containment tank at controlled temperature (up to 60°C). Autoclavable printing plate XYZ axis accuracy up to 50 µm









• Leverages more than 1 million simultaneous points of light to bioprint microscopic features down to 200 microns.

 Photographically cures entire layers at once to crosslink structures 50 times faster than other printing methods.





 Complements the state-of-the-art capabilities of CELLINK's BIO X system. You can use BIO X to print living cells within a Lumen X-fabricated structure and strengthen your work in applications like organ-on-a-chip and multimaterial research.

#### Our Photoinks

Browse our entire category of photoinks for bioprinting with the LUMEN X series and BIONOVA X. Click on the links to learn more about the bioinks and their individual attributes.

#### Universal Photoinks

#### PEGDA Photoink

- » PEGDA Soft Photoink Kit
- » PEGDA X

#### GelMA Photoink

» GelMA 95% DS - Photoink Kit

#### **BIONOVA X**

#### PEGDA Photoink

» PEGDA-INK

#### Alginate Photoink

» PhotoAlginate-INK

#### GelMA Photoink

- » PhotoGel-INK 95% DOS
- » PhotoGel-INK 50% DOS

#### HAMA Photoink

- » PhotoHA-INK Stiff
- » PhotoHA-INK Soft

#### Related biomaterials

#### Photoinitiators

- » Xcite
- » Irgacure 2959
- » LAP
- » Ruthenium

#### Photoabsorbers

» Xsorb

#### Technology and hardware

Projection stereolithography

>1 million simultaneous points of light

Projected image: 1280 x 800 pixels

Pixel resolution (XY): 50 μm

Z-precision (motor-driven): 5 μm

Max build volume:

64 x 40 x 50 mm (Metal platform)

40 x 25 x 50 mm (Glass platform)

#### Projected light

Biocompatible wavelength: 405 nm

Intensity range: 10 - 30 mW/cm<sup>2</sup>

Distortion: <1%

#### Additional features

Disposable, quick-change sterile vats Heated platform: Up to 37° C









The rotational **Rheometer MCR302e** is an instrument that allows you to determine rheological parameters (viscosity, elastic modulus, plastic modulus, fluidity, smoothness, etc.) of fluid systems (melts, solutions, suspensions, emulsions, pastes, gels and colloidal systems).

#### **General applications**

The technique finds application in various sectors such as the plastics sector (for evaluating the processability of a polymeric material), the cosmetic, pharmaceutical and food sector (for quality control analysis of creams, gels, etc.) and the biological/medical sector (in particular for hemorheology analyses).

#### Technological and industrial applications

Materials science
Polymers
Pharmaceutical & Biopharmaceutical
Food
Medical
Cosmetic

#### Available techniques

Compact modular rotor with thermostatic bath Plate-to-plate and plate-to-cone measuring systems Peltier for temperature analysis (from -10° to 220°C) Oven for temperature analyzes (from -10 to 600°C) Rheocompass software for data reprocessing







#### MCR 302e

IL REOMETRO UNIVERSALE AFFERMATO
PIÙ VENDUTO. PUNTO DI RIFERIMENTO SUL MERCATO
PER TEST QC AVANZATI E RICERCA REOLOGICA. SI
ADATTA A TUTTE LE VOSTRE ESIGENZE ATTUALI E
FUTURE.

- Intervallo di coppia da 0,5 nNm a 230 mNm
- Gestione termica attiva del motore e del cuscinetto per misure a lungo termine anche a coppie elevate
- Regolatori adattivi al campione (TruStrain™, TruRate™) inclusi
- Più spazio per la manipolazione dei campioni e la sostituzione degli, piena compatibilità con il CTD 1000



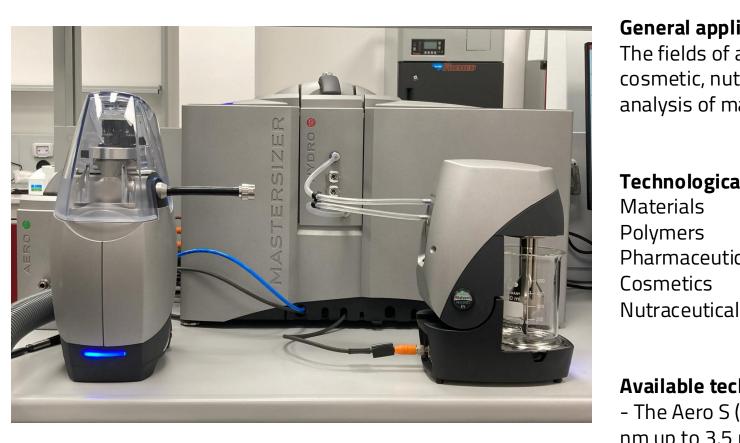
Ollindro concentrico(OC)	Doppio gap (DG)	Piatto-cono (CP)	Piatto parallelo (PP)	Agitatori	Sistemi tribologici	Sistemi a polvere	Afferraggi DMA
~	~	~	~	~	~		
~	~	~	/	~	~		
		~	~				
		~	~	~	~		
		~	~		~		
			~		~		~
			~				
~				~		~	
					~		~
	Clindro concentrico(O)	Cilindro concentrico(Cd Compio gap (DG)	<ul> <li>Cliindro concentrico(Cd</li> <l< td=""><td>Cilindro concentrico(CG              Doppio gap (DG)</td><td>Cilindro concentrico(CG               Doppio gap (DG)</td><td>Cilindro concentrico(CG            Cilindro concentrico(CG</td><td>  Cilindro concentrico(O</td></l<></ul>	Cilindro concentrico(CG              Doppio gap (DG)	Cilindro concentrico(CG               Doppio gap (DG)	Cilindro concentrico(CG            Cilindro concentrico(CG	Cilindro concentrico(O











#### **MASTERSIZER 3000**

The granulometer is based on the principle of laser diffraction. It offers a wide resolution range for dry and wet sample analysis.

### General applications

The fields of application are varied both in the pharmaceutical, cosmetic, nutraceutical, but also food, biomedical fields and in the analysis of materials for different types of industries.

#### Technological and industrial applications

Materials Polymers Pharmaceutical Cosmetics

## Available techniques

- The Aero S (dry) sampler can handle particle sizes ranging from 100 nm up to 3.5 mm.
- The Hydro EV (liquid) sampler uses 250, 600 or 1000 ml beakers to analyze emulsions/suspensions with dimensions from 10 nm to 2 mm.







# Aero M dry powder disperser

#### **Bulk dry powder dispersion**



The Aero M is an entry-level dry powder disperser for the Mastersizer 3000E, enabling particle size distribution measurements to be made for bulk dry powder samples. Its design achieves robust particle size measurements in industrial applications and also ensures it is easy to maintain during routine use.

The use of dry powder dispersion for particle size measurements is advantageous when measuring bulk materials, as a large mass of powder can be measured. This ensures effective sampling is achieved. In addition, dry powder dispersion avoids the need for liquid dispersants, reducing the cost of measurement and increasing sample through-put.

#### **Specifications**

Parameter	Specification
Measurement modes	Manual measurement sequence control
Measurement size range	0.1 - 1000 µm †
Dispersion pressure range	0 - 4 bar
Pressure setting precision	+/- 0.1 bar
Pressure setting accuracy	+/- 0.03 bar
Feed rate range	0 - 58 ms-2 (expressed as 0-100%)
Feed rate precision	+/- 2% FS
Materials in contact with sample ††	316 stainless 410 hardened stainless Borosilicate glass EPDM PTFE Polyurethane Carbon filled acetal Aluminium Neoprene
Maximum particle size	1000 μm †
Minimum time between measurements	less than 60 sec*
Dimensions	260 mm x 180 mm x 380 mm (L x W x H)
Mass	10.5 kg

- $\uparrow$  Sample dependent. Relates to the use of the unit with the Mastersizer 3000E, which also has an upper size limit of 1000  $\mu m$
- †† Ceramic venturi dispersers are available for use with abrasive samples

- Measures dry powder particle size distributions over a 0.1-1000 µm range
- Manual measurement control, with appropriate user prompts provided to help ensure reproducible measurements are made
- Configurable for different applications through the purchase of additional sample trays and powder hoppers
- Abrasive samples can be measured through the use of ceramic venturi dispersers.









# **Hydro EV**

#### Flexible volume wet dispersion



The Hydro EV has a unique dip-in centrifugal pump and stirrer design that achieves full and rapid dispersion in standard laboratory beakers, allowing close matching of the dispersant volume to the application requirements. Following measurement, the dispersion head can be raised out of the beaker, enabling quick cleaning and sample recovery.

- Compatible with 250 mL, 600 mL and 1000mL laboratory beakers
- Patented 40 W in-line sonication probe, for rapid agglomerate dispersion
- Dip-in centrifugal pump and stirrer design
- Sample easily recovered following analysis
- Chemically compatible with a wide choice of organic and inorganic dispersants
- Full software control of pump / stirrer and sonication
- · Integral sample tank light.

#### **Specifications**

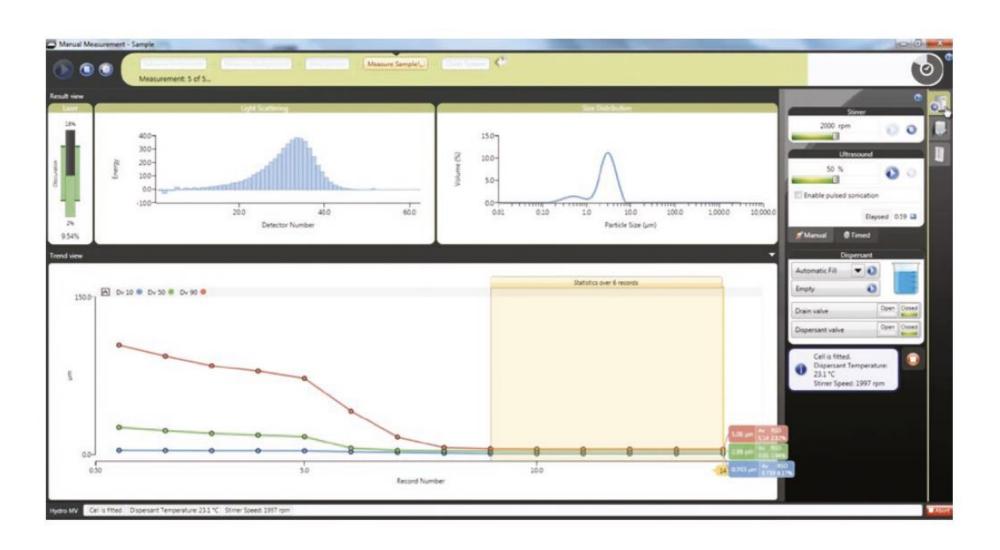
Parameter	Specification			
Pump speed range	0-3500 rpm †			
Pump speed resolution	+/- 10 rpm			
Pump speed accuracy	+/- 50 rpm			
Maximum flow rate	1.7 L/min †			
Sonication power & frequency	40 W max, 40 kHz (nominal) †			
Volume	250 mL / 600 mL / 1000 mL (using lab beaker)			
Materials in contact with sample	316 stainless Borosilicate glass Tygon® FKM (cell seal only - FFKM available) PTFE PEEK Titanium Nitride			
Maximum particle size	2100 µm † †			
Minimum time between measurements	less than 60 sec † †			
Dimensions	220 mm x 150 mm x 300 mm (L x W x H)			
Mass	4 kg			

















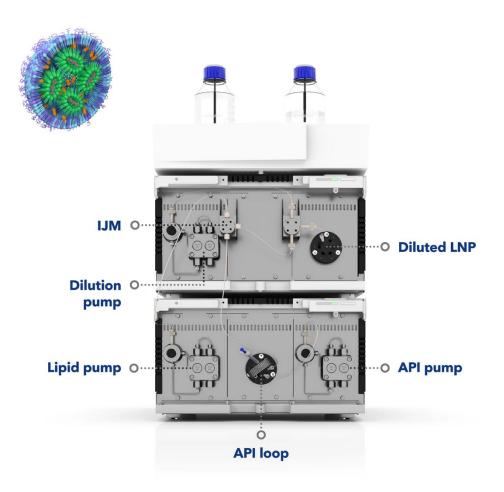
API identity & total concentration, API %

encapsulation, Total API (RNA) purity,

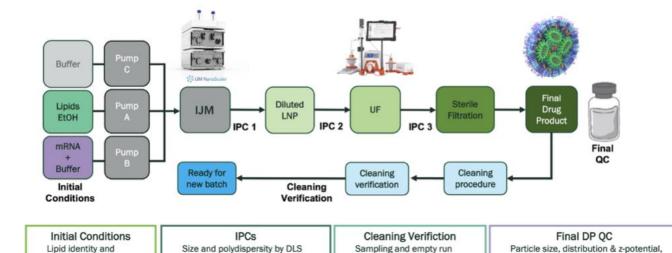
Lipid and polymer excipient identity &

concentration, Impurities, Sterility,

bioburden, SVP



# **Development and optimization of LNP formulations -** using the KNAUER NanoScaler



Lipid concentration (HPLC-

mRNA concentration (UV-Vis.

Buffer concent (IC), TOC

CAD),

LC, CE).

Fig. 1 Process workflow for LNP formulation using NanoScaler.

(Stunner), mRNA encapsulation

(Fluorescence assay), mRNA

content (UV assay) (Stunner),

mRNA integrity (gel or capilary

electrophoresis), pH

concentration (HPLC-

(UV-Vis) and

CAD, MS), mRNA content

identity/integrity (CE, LC),

pH, buffer content (IC)