iCELLis™

SINGLE-USE FIXED-BED BIOREACTOR SYSTEMS

iCELLis™ fixed-bed bioreactors are a robust, compact adherent cell culture solution delivering scalable performance from 0.5 to 500 m^2 to support clinical and commercial production. These bioreactors can reduce space demands by up to 65% and labor costs by up to 67% when compared to traditional flatware solutions (1). iCELLis bioreactors are fully closed systems, capable of maintaining low shear environments. They come integrated with pH, dissolved oxygen (DO), and biomass sensors, and they are supplied with Code of Federal Regulations (CFR) Title 21, Part 11 compatible software. They deliver consistent high cell density, product titer, and vector quality. This safeguards and accelerates the time to your next milestone and provides intrinsic readiness for proven industrial-scale success.

Fig 1. iCELLis Nano bioreactor with mPath™ control tower.

Performance and scale-up

While flatware is the go-to format during R&D and preclinical process development, it has severe limitations as scales increase, and the need to produce efficiently under good manufacture practice (GMP) conditions becomes a priority. Planning for an intrinsically industrializable manufacturing process early in development reduces delays and risks associated with technology transfer.

The iCELLis bioreactor technology also provides opportunities for process optimization and simplification that can make the difference between commercial viability and costly process inefficiency.

- Large volume production achieving high cell density and high yield in a small footprint
- Closed, automated operation minimizing risk and maximizing ease of use
- Seed cell densities as low as 3000 cells/cm^2 to simplify the seed train demands and streamline the upstream process
- Capable of supporting continuous perfusion processes without modification

Table 1. Available largest surface area in the iCELLis Nano bioreactor and iCELLis 500+ bioreactor in comparison to multitray Nunc Cell Factory systems/roller bottles

	Fixed-bed volume (L)	Equivalent culture surface (m^2)	Equivalent Nunc Cell Factory 10-layer systems (6300 cm^2)	Equivalent roller bottles (850 cm^2)
iCELLis Nano bioreactor (4 m^2)	0.2	4.0	6	47
iCELLis 500+ bioreactor (500 m^2)	25	500	794	5882

Together, the fixed-bed system design, integrated process monitoring, and control features enable higher specific productivity compared to other culture systems.

Table 2 shows published data for some common applications across a range of cell lines and vector types and exceed the published value for 2D flatware.

Table 2. Specific productivities achieved using iCELLis bioreactor systems with several types of vectors produced from different mammalian cell lines. VG = viral genomes, TU = transducing units, VT = viral titer, VP = viral particles

Vector	Cell	Size	Yield/cm²	Unit	Yield extrapolatied to 500 m²	Reference
Adeno-Associated Virus (AAV)	HEK293T	0.53 m^2	2.12×10^{10}	VG	1.08×10^{17}	(2)
	HEK293T/17	0.53 m^2	9.06×10^{10}	VG	4.53×10^{17}	(3)
Lentiviral	HEK293T	2.7 m^2	1.05×10^{6}	TU	5.25×10^{12}	(4)
Retroviral	HEK293-Vec	2.7 m^2	9.38×10^{7} (stable)	TU	4.65×10^{14}	(5)
Adenoviral	HEK293	100 m^2	6.10×10^{9}	VP	3.05×10^{16}	(6)

Scalability

The iCELLis bioreactor is currently available in two formats, each with a range of bed heights to provide a range of surface areas (Table 3):

- The iCELLis Nano bioreactor is optimized for process development but is also suitable for small-scale clinical production (~ 0.5 to 4 m^2). It mirrors the iCELLis 500+ bioreactors characteristics which can be used to predict process performance at larger scales.
- The iCELLis 500+ bioreactor is optimized for the large-scale production (66 to 500 m^2) and delivers a robust automated platform for the production of high-quality viral vectors.

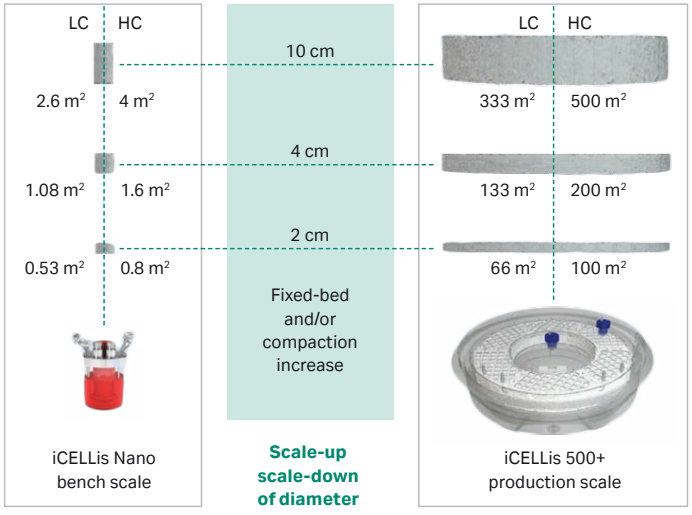


Fig 2. Scale-up options strategy between the iCELLis Nano (bench-scale) bioreactor and iCELLis 500+ bioreactor. LC = low compaction, HC = high compaction.

Table 3. Configuration of iCELLis bioreactors

Bioreactor	Diameter (cm)	Bed height (cm)	Bed volume (L)	Volume (L)	Low compaction surface area (m^2)	High compaction surface area (m^2)
iCELLis Nano bioreactor	11	2	0.04	1	0.53	0.8
iCELLis Nano bioreactor	11	4	0.08	1	1.06	1.6
iCELLis Nano bioreactor	11	10	0.2	1	2.65	4
iCELLis 500+/100 bioreactor	86	2	5	70	66	100
iCELLis 500+/200 bioreactor	86	4	10	70	133	200
iCELLis 500+/500 bioreactor	86	10	25	70	333	500

Platform overview

1) The fixed-bed substrate uses USP class VI polyethylene terephthalate (PET) carriers that are common to all iCELLis bioreactors. Both the iCELLis Nano bioreactor and the iCELLis 500+ bioreactor includes a variety of bed heights and compaction factors to deliver scalability across a range of surface areas (Table 3).
2) Agitation of the culture media and reagents is driven with a magnetically coupled impeller isolated from the carriers to minimize any shear on the cell culture.
3) After passing through the carriers, media overflows the outer wall of the fixed-bed, creating a falling film. This generates high rates of bubble-free oxygen transfer and CO_2 stripping, allowing the iCELLis bioreactor to maintain high cell densities.
4) Integrated DO, pH, and biomass sensors continuously measure critical culture conditions and cell density.
5) Each system permits the extraction of sample carriers to measure cell density directly.

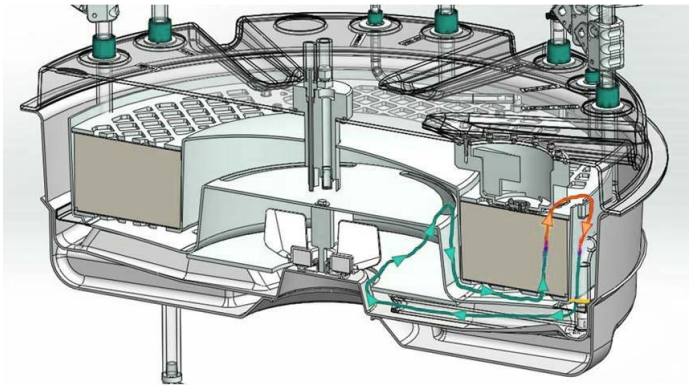


Fig 3. Features illustrated on the iCELLis 500+ bioreactor.

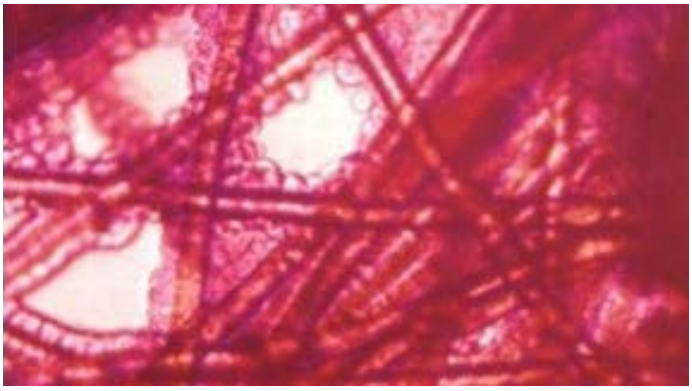
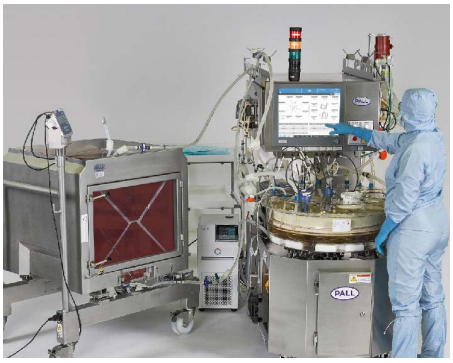


Fig 4. Madin-Darby canine kidney (MDCK) cells attached to iCELLis bioreactor carriers.

System overview



Name	iCELLis Nano bioreactor	iCELLis 500+ bioreactor
Components	Docking station mPath control tower iCELLis Nano bioreactor vessel Tubing manifolds mPath Link server	Integrated skid with docking station and control tower Temperature control unit (TCU) iCELLis 500+ bioreactor vessel Tubing manifolds
Surface area range	~ 0.5 to 4 m^2	66 to 500 m^2
Sensors	pH, DO, temperature, and biomass	pH, DO, temperature, biomass, weight, and pressure
Gas handling	Six thermal mass flow controllers (MFCs) Custom gas blends for precise pH and DO control	Four thermal MFCs Custom gas blends for precise pH and DO control
Enhanced process analytic technology (PAT)	Biomass probe for cell density	Biomass probe for cell density
21 CFR Part 11 compatible software	Suitable for the manufacture of small batches in a GMP environment	Bioreactor can be easily used to manufacture in a GMP environment
Control tower	mPath control tower (see separate data file)	Integrated
Other	iOS and Android™ phone app: users can control their iCELLis Nano bioreactor from anywhere, and can receive email or text message alerts when the bioreactor is in alarm, or another critical event has occurred	

General system specifications

	iCELLis Nano bioreactor system	iCELLis 500+ bioreactor system
Dimensions (W × D × H)		1038 × 1609 × 2122 mm
Controller	230 × 600 × 450 mm	
Docking station	340 × 360 × 290 mm	
Weight		650 kg (without TCU)
Controller	20 kg	
Docking station	6.7 kg	
Gases connections	Quick connectors 6 mm	Male swagelock ¼ in. connector
Control	TMFC	TMFC
O_2	0 to 1000 mL/min	0 to 7000 mL/min
CO_2	0 to 1000 mL/min	0 to 1500 mL/min
N_2	0 to 1000 mL/min	0 to 1500 mL/min
Air	0 to 1000 mL/min	0 to 3000 mL/min
Pumps	3 × (base, perfusion in-out)	5 × (perfusion in-out, base addition, sampling and inoculation), (7 if optional fill and drain pumps are ordered)
Agitation control and range	Magnetic drive impeller (100 to 1500 rpm)	Magnetic drive impeller (0 to 450 rpm)
Temperature control and range	Resistors – Peltier elements 20°C to 40°C	Double jacket – TCU 25°C to 40°C
pH control	Electrochemical, re-use 0 to 14	Single-use, optical 3 to 10
DO control	Electrochemical, re-use 0% to 150% air saturation	Single-use, optical 0% to 300% air saturation
Control architecture	Programmable logic controller (PLC)	PLC
Supervisory control and data acquistion (SCADA) software	mPath Link software – any device connected	Wonderware®

Ordering information

Please contact us to receive a quote for any materials

iCELLis bioreactor system hardware

Material description	Product code
iCELLis Nano bioreactor control system	ICLNANOBRS-FULL
mPath Link server and SCADA software	MPATHLINKV2
iCELLis 500+ bioreactor control system	ICL500CSSSIPS
iCELLis 500+ high speed pumps (optional)	ICL500HFLPUMP
iCELLis 500+ TCU (110 or 230 V)	ICL500LTCU120
iCELLis 500+ TCU (110 or 230 V)	ICL500LTCU230

iCELLis Nano bioreactor single-use vessels

Surface area (m^2)	Fixed-bed height (cm)	Compaction	Product code
0.53	2	Low (1×)	4415-40-LC-BM
0.8	2	High (1.5×)	4415-40-HC-BM
1.06	4	Low (1×)	4415-80-LC-BM
1.6	4	High (1.5×)	4415-80-HC-BM
2.65	10	Low (1×)	4415-200-LC-BM
4.0	10	High (1.5×)	4415-200-HC-BM

iCELLis Nano bioreactor single-use tubing manifolds

Tubing type	Material description	Product code
Platinum-cured silicone with MPC connectors	Lid tubing manifolds	6415-0474V
Platinum-cured silicone with MPC connectors	Base addition manifold	6415-0474M
Platinum-cured silicone with MPC connectors	Sampling and 1 L seeding manifold	6415-0474N
Platinum-cured silicone with MPC connectors	2 L recirculation manifold	6415-0473U
Platinum-cured silicone with MPC connectors	10 L recirculation manifold	6415-0454E
Weldable AdvantaFlex® with MPC connectors	Lid tubing manifolds	6415-1384W
Weldable AdvantaFlex with MPC connectors	Base addition manifold	6415-1384T
Weldable AdvantaFlex with MPC connectors	Sampling and 1 L seeding manifold	6415-1384U
Weldable AdvantaFlex with MPC connectors	2 L recirculation manifold	6415-1384S
Weldable AdvantaFlex with MPC connectors	5 L recirculation manifold	6415-1540F
Weldable AdvantaFlex with MPC connectors	10 L recirculation manifold	6415-1540G

All iCELLis Nano bioreactor manifolds are supplied gamma irradiated.

iCELLis 500+ bioreactor single-use vessels

Surface area (m^2)	Fixed-bed height (cm)	Compaction	Product code
66	2	Low (1×)	4415-R66BM
100	2	High (1.5×)	4415-R100BM
133	4	Low (1×)	4415-R133BM
200	4	High (1.5×)	4415-R200BM
333	10	Low (1×)	4415-R333BM
500	10	High (1.5×)	4415-R500BM

All iCELLis 500+ bioreactor vessels are equipped with weldable tubing, Kleenpak™ Presto sterile connectors, and are supplied gamma irradiated.

iCELLis 500+ bioreactor single-use tubing manifolds

Material description	Flow rate	Comments	Product code
Starter kit	High flow (⅜ in.internal diameter (ID) × ½ in. outer diameter (OD) pump tubing) – for recirculation	Includes feed-in 1/preheater, feed-in 2, harvest/feed-out, inoculum, base, and sampling manifolds	6415-I500MFHA
Starter	Low flow (¼ in. ID × ⅜ in. OD pump tubing) – for perfusion	Includes feed-in 1/preheater, feed-in 2, harvest/feed-out, inoculum, base, and sampling manifolds	6415-I500MFLA
Feed-in 1 – preheater manifold	High flow	N/A	6415-0615R
Feed-in 1 – preheater manifold	Low flow	N/A	6415-0615V
Feed-in 2 manifold	High flow	N/A	6415-0464C
Feed-in 2 manifold	Low flow	N/A	6415-0464F
Harvest/feed-out manifold	High flow	N/A	6415-0458Z
Harvest/feed-out manifold	Low flow	N/A	6415-0464G
Inoculum manifold	N/A	N/A	6415-0615S
Base manifold	N/A	N/A	6415-0615T
Sampling manifold	N/A	N/A	6415-0615U

All iCELLis 500+ bioreactor manifolds are supplied gamma irradiated. The iCELLis bioreactors are available as standard models and both the bioreactor hardware and consumables can be customized. Please contact a representative to find the optimal solution for your application. Our teams are specialized in upstream and downstream processing and will gladly help find the right technology for any part of your manufacturing process.

It is possible to combine products to meet any requirement in the upstream part of the process:

- Media preparation
- Buffer preparation
- Media sterilization and aseptic transfer liquid transfer into the bioreactor (e.g. glucose, anti-foam, base, etc.)
- Seed train solutions
- Cell harvest and separation

Please contact us for a total solution discussion on your process.

References

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