Cadence™

INLINE DIAFILTRATION MODULES

The Cadence™ inline diafiltration (ILDF) module (Fig 1) enables continuous processing of the final ultrafiltration/diafiltration (UF/DF) of drug substances and offers benefits in shear-sensitive batch processes.

This method has many benefits, including:

- Fully continuous diafiltration in the downstream processing (DSP) steps
- Potential reduction of product damage or aggregation due to reduced residence time and shear exposure
- Significantly reduced system hold-up volume
- User-friendly, holder-less design
- Scalable formats using standard TFF cassette building blocks

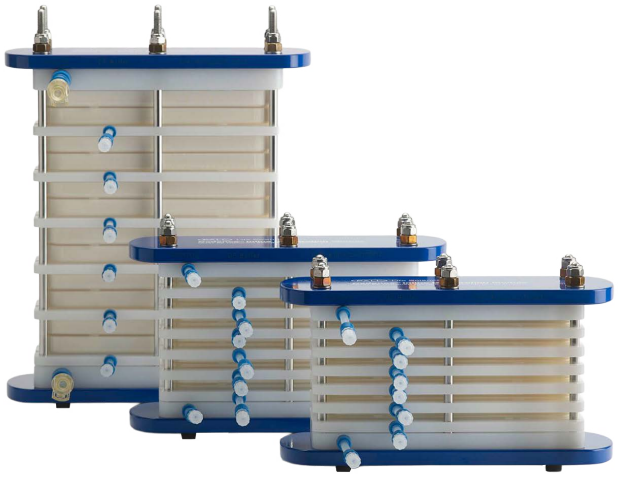

Fig 1. Cadence inline diafiltration modules.

Overview

Cadence inline diafiltration modules are preassembled and do not require a holder. Each module includes a pre-configured flow kit that is connected to a feed pump and a diafiltration buffer pump. Torque the module to the recommended setting and it is ready to operate.

The Cadence ILDF technology allows for removal factors of ≥ 3-log of impurities for robust product quality profile. Using conventional TFF cassette building blocks ensures accurate scalability and proven selectivity, and low protein-binding attributes, in either Delta regenerated cellulose or Omega™ polyethersulfone membrane.

Applications and operational benefits

The Cadence inline diafiltration module is designed for continuous processing, in-process buffer exchange, or contaminant removal in various processes, throughout a wide range of applications in the biopharmaceutical industry.

Enable continuous processing

Single-pass diafiltration enables continuous processing via staging that provides repeated dilution and concentration cycles without a recirculation loop.

Stable processing with high removal factors

The Cadence ILDF technology allows for removal factors of ≥ 3-log. The number of diavolumes required for your process, determined in optimization studies, is easily achieved using the modules by adjusting the flow rate on the buffer addition pump (Fig 2). Both process performance and product stability are maintained over extended processing times (Fig 3 and 4).

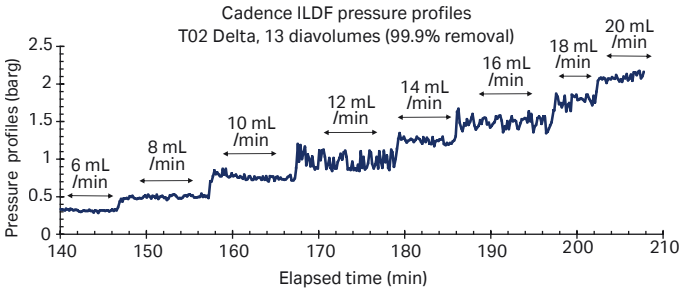

Fig 2. Ability to adjust % removal with instantaneous adjustment of applied diafiltration volumes through pumping adjustment. Removal % adjustment at a constant feed flow rate using 60g/L IgG.

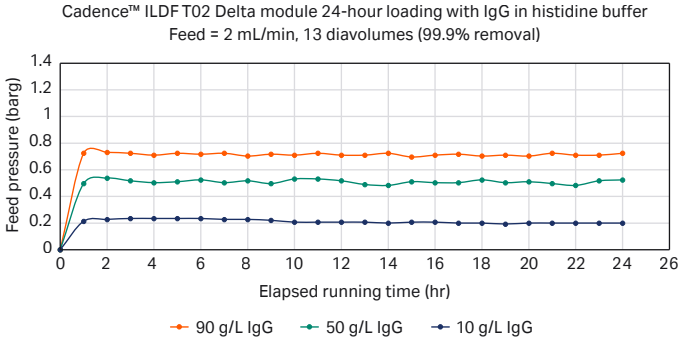

Fig 3. Stable performance when operating over extended time. T02 modules tested with varying concentrations of IgG.

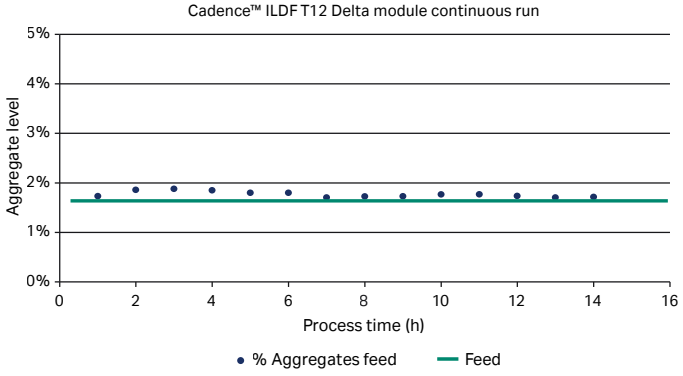

Fig 4. Stable aggregate profile over extended continuous processing performance when operating over extended time. T12 module tested with our in-house mAb.

Optimize processing of highly shear-sensitive products

Processing occurs in a single pass through the pump and module, therefore reducing shear exposure compared to conventional TFF. Further benefits are achieved by eliminating any mixing or foaming issues associated with the feed tank.

No holder required

Cadence ILDF modules come assembled, and the cassettes and flow kits are configured between two end plates with no extra holder needed. A pre-configured flow kit is also provided. To operate, torque the module to the recommended setting and attach the flow kit to a feed pump and diafiltration buffer pump.

Product platform

Similar to other Cadence SPTFF modules, the Cadence inline diafiltration module uses our standard T-Series cassettes as the building blocks for the module. These modules are offered with either Delta regenerated cellulose or Omega polyethersulfone membranes providing the high-flux, high selectivity and low-protein-binding characteristics that are associated with these membranes. They are available in a range of size formats to accommodate various processing volumes. A standard flow kit is provided with each module.

Scalability

The modules are available in three different sizes, ranging from 0.1 to 1.2 m^2 and have been shown to have scalable feed pressure over a wide range of operational feed flux (Fig 5).

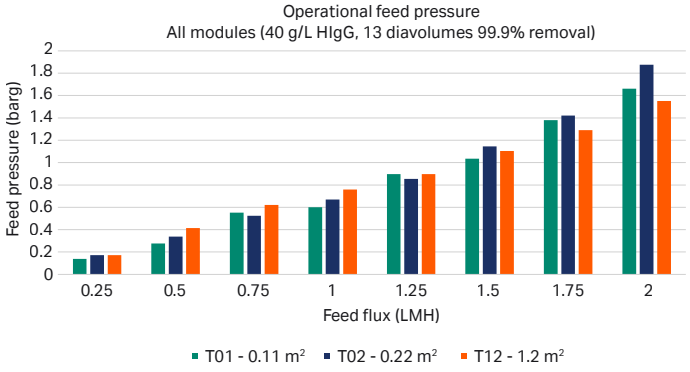

Fig 5. Scaled operational performance across different sizes of the Cadence inline diafiltration modules. All modules tested with 40g/L HIgG and 13 diafiltration volumes.

Auxiliary equipment

The Cadence ILDF module requires two standard peristaltic pumps for operation: a two-headed pump to control the feed and retentate, and a six-headed pump to control the buffer injection. The feed and retentate lines on the supplied flow kit include PendoTECH pressure transducers and conductivity sensors. A PendoTECH PMAT pressure monitoring module is required to monitor the feed and retentate pressure, and a PendoTECH CMONT module is required to measure conductivity. Use a torque wrench to tighten the module to the recommended level.

Specifications

Establish the operating characteristics for any SPTFF process by performing trials and analyzing the results. Our team of technical specialists is available to assist with conducting trials to develop operating conditions necessary to achieve the desired process objectives.

Materials of construction

Cassettes	Delta regenerated cellulose or Omega polyethersulfone 30 kDa membranes with polypropylene screen, white polyurethane encapsulant with white pigment (TiO_2), and medical-grade silicone for the permeate seals
Gaskets	Medical-grade, platinum-cured silicone
Flow kit plates	Ultra-high-molecular-weight polyethylene
Connections	T01/T02 – female luer connection and cap: polypropylene T12 – female MPC quick-disconnect connector and plug: polysulfone
Flow paths	Polypropylene, polysulfone, and platinum-cured silicone
Pump head tubing	Platinum-cured silicone
	Flow path connections on flow kits are open to the feed container/vessel
Operating limits	Maximum pressure: 4.1 barg (60 psig)
	Processing temperature range: 15°C to 25°C for extended use (freezing may damage the module). Up to 40°C for four-hour cleaning
pH range	2 to 13

Typical feed flow rates

Module	Area (m^2)	10 g/L feed flow range (mL/min)	55 g/L feed flow range (mL/min)
T01	0.1	0.5 to 10	0.5 to 4
T02	0.2	1.0 to 18	1.0 to 10
T12	1.2	5.0 to 90*	5.0 to 55

* Scaled calculation due to pump selection

Module integrity test

Delta	4.1 barg (60 psig)
Omega	2.1 barg (30 psig)
Acceptable	Delta: < 538 sccm/m^2 (< 50 sccm/ft^2)
Forward flow rate	Omega: < 1600 sccm/m^2 (< 150 sccm/ft^2)

Each Cadence module has a unique serial number for full traceability

Shelf life

The shelf life of the Cadence ILDF modules, packaged in preservative, is three years from the date of manufacture when the modules are stored unopened in the original packaging at a temperature up to 25°C and protected from direct light.

Biological safety

Materials of construction for the Cadence ILDF modules have been tested and meet the requirements for the biological reactivity tests listed in the United States Pharmacopeia (USP) <88> for Class VI – 70°C plastics.

Documentation

Comprehensive documentation is available to ensure the Cadence ILDF module is operated successfully.

- Certificate of quality
- Installation guide
- Material and safety data sheet (MSDS) for the module preservative solution
- Care and use manual
- Validation guide
- Validation service for your specific tests such as compatibility testing with your product fluid

Training and technical support is available to help optimize your process using Cadence inline diafiltration modules.

Ordering information

Identify and order Cadence inline diafiltration modules using the table below.

Guide to the Cadence inline diafiltration module product codes

Description	Product code
Inline diafiltration device module	**DF**
Delta regenerated cellulose or Omega polyethersulfone membrane	**DC/OS**
Nominal molecular weight cut-off (MWCO)	**030**
Cassette format	**T02**
Number of stages in series	**06**
Number of cassettes per module	**12**

For example, a T02 module with 30 kDa Delta regenerated cellulose membrane area of 0.22 m^2 is product code DFDC030T020612.

Cadence inline diafiltration module product codes and membrane area (m^2)

Membrane	Cassette format	Membrane area (m^2)	MWCO (kDa)	Product code
Delta	T01	0.1	30	DFDC030T010612
Delta	T02	0.2	30	DFDC030T020612
Delta	T12	1.2	30	DFDC030T120612
Omega	T01	0.1	30	DFOS030T010612
Omega	T02	0.2	30	DFOS030T020612
Omega	T12	1.2	30	DFOS030T120612

Additional recommended equipment for operation (not provided by us)†

Description	Vendor	Quantity	Product code
Masterflex L/S pump	Avantor	2	07522-20
Masterflex Easy Load II pump head	Avantor	2	77201-60
Masterflex L/S cartridge pump head (six channel, six roller)	Avantor	1	07519-15
Masterflex L/S pump head cartridges, large	Avantor	6	07519-75
PendoTECH PMAT 4 pressure monitor	PendoTECH	1	PMAT4A
PendoTECH CMONT conductivity monitor	PendoTECH	1	CMONT
PendoTECH software licenses, one per PC	PendoTECH	1	PMATP-GUI
Masterflex mounting hardware (for two pumps heads)	Avantor	1	77200-02
Torque driver	McMaster-Carr	1	5716A21
9/16 in. deep socket	McMaster-Carr	1	5544A45

† This is the equipment that is recommended by us and has been demonstrated to perform as required. It is possible that other similarly functioning equipment could be used.

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For local office contact information, visit cytiva.com/contact

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