

ÄKTA oligosynt™ oligonucleotide synthesizer

OLIGONUCLEOTIDE SYNTHESIS

The ÄKTA oligosynt™ oligonucleotide synthesizer is a compact, fully automated oligonucleotide synthesizer built for research and process development laboratories (Fig 1). The system supports a robust and easily scalable oligonucleotide synthesis process and transfer to larger oligonucleotide synthesizers with high yield and quality.

The ÄKTA oligosynt™ system's flow-through technology, high pump accuracy, wide scale and the low hold-up volume make it suitable for different scales and types of oligonucleotides. Process development and optimization are supported by flexible and easy method creation and transfer that support scale up, while the system's advanced data processing capabilities and analytical tools allow efficient monitoring and control of the synthesis. An interactive process picture (Fig 4), placement of all modules on system front, and transparent method overview make the system easy to use.

System benefits

- The broad synthesis scale and optimized hold-up volume combined with a small system footprint enable a broad and flexible use for research and development requirements.
- Flexible and easy method editing, and the interactive user interface offer ease of use and support scale-up requirements.
- Robust process control is supported by sensors measuring pressure, air, temperature, UV, and conductivity. Input from external modules is also possible.

System overview

The ÄKTA oligosynt™ oligo synthesizer is a compact system designed for research and process development covering a large scale range, up to 12 mmol. The system is based on flow-through reactor technology, the common standard for the oligonucleotide industry, used in process development and when scaling up to hundreds of kilos, or even metric tons, of oligonucleotides every year.



Fig 1. The ÄKTA oligosynt™ oligonucleotide synthesizer is a compact, fully automated system for small-scale synthesis and process development.

The ÄKTA oligosynt™ oligonucleotide synthesizer has 16 amidite inlets, which means that many different types of amidites can be used. Amidite bottles can be positioned using the bottle holders located on the left-hand side of the system. Other reagents and solvents can be placed on the bench or in a suitable storage area nearby.

The system's open front ensures easy access to all modules and full ventilation. The flow path (Fig 2) is optimized for achieving a low hold-up volume, limiting the dilution of expensive amidites and excessive use of reagents and solvents.

Some coupling reactions require a lot of time to move to completion. A recirculation loop in the flow path allows for the coupling liquid to pass through the synthesis reactor several times, giving enough time for coupling reaction and thereby maximizing utilization of the coupling mixture. This is particularly important when using small volumes of high-value monomers.

The inert gas control box on the right-hand side of the system controls the delivery of inert gas to all liquid bottles to keep the moisture away by ensuring a small overpressure. The system is equipped with a tray to collect spillage and adjustable feet to level the instrument.

The instrument control panel shows the system state using four LED lights. The **Pause** and **Continue** buttons can be used to control an ongoing method run.

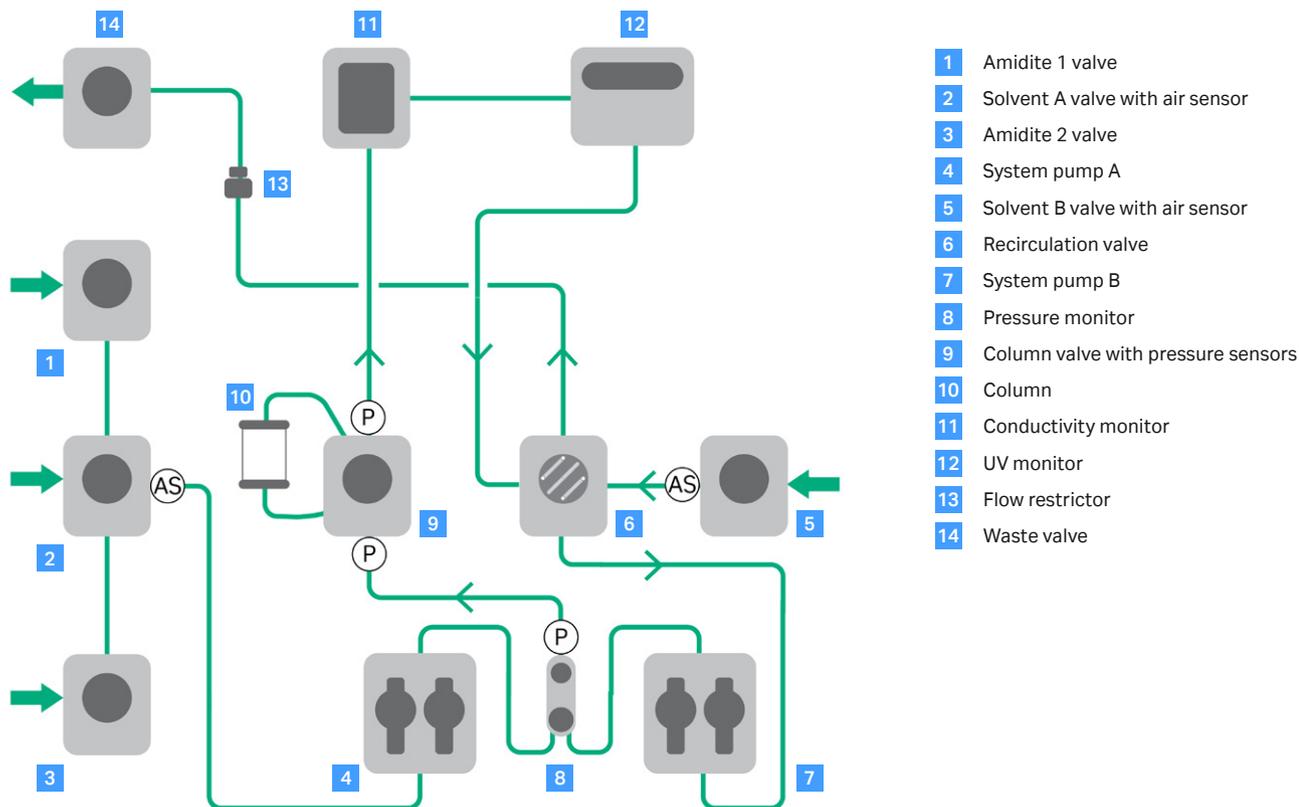


Fig 2. The ÄKTA oligosynt™ flow path is optimized for oligonucleotide synthesis.



Fig 3. System modules for ÄKTA oligosynt™ synthesizer.

System modules

The ÄKTA oligosynt™ synthesizer comes with two high-precision pumps, a pressure monitor, two solvent valves, two amidite valves, a recirculation valve, a column valve, a waste valve, an I/O-box, a UV monitor, and a conductivity monitor (Fig 3).

The solvent inlet valves have built-in air sensors, and the column valve has two built-in pressure sensors, one before and one after the column. Up to five columns can be connected to the column valve. The system's UV monitor measures the UV/Vis absorbance at three wavelengths in the range of 190 to 700 nm, and the conductivity monitor has a built-in temperature sensor.

The pump design uses the same robust and reliable titanium pump heads that are used in well-established chromatography products such as ÄKTA™ avant and ÄKTA pure™ chromatography systems. The system's pump rinsing system protects the pump seals from damage caused by precipitated chemicals in the system. The seal prevents leakage between the pump chamber and the drive mechanism of the pump.

The ÄKTA oligosynt™ oligonucleotide synthesizer can be connected to optional external modules. Using an optional loop valve, multiple heat exchangers can be positioned in line with the flow path. In addition to the conductivity monitor with built-in post-column temperature sensor, an optional pre-column conductivity monitor with built-in temperature sensor is also available. External flow meters and external sensors can be connected through the I/O-box.

Software

The ÄKTA oligosynt™ oligonucleotide synthesizer is controlled by UNICORN™ software, which provides real-time control of the system. Basic methods for the desired target sequence can be created in minutes using pre-defined methods and the sequence editor. UNICORN™ software also supports evaluation of results. The method overview is transparent with limited use of macros.

The real-time unit enables the ÄKTA oligosynt™ system to run methods and collect data independently of IT security solutions, operating system updates, and potential interruptions in network communication.

UNICORN™ software has advanced data processing capabilities and can collect up to 180 000 data points, which allows maintained resolution during longer runs. The database storage supports easy data handling and cross-result data analysis between runs.

UNICORN™ software consists of four modules: **Administration**, **Method editor** (Fig 5 and 6), **System control** (including process picture, Fig 4), and **Evaluation**. The modules work together for increased operational security, efficiency, and productivity.

The **Method editor** module allows you to create a method based on a target sequence and adjust methods to suit your application needs (Fig 5). A method is created by drag and drop of modules called phases (Fig 6). Each phase represents a step in the run — such as initial preparation of the system and column before synthesis, synthesizing the target sequence or finalizing the synthesis and preparing for cleavage from the support — and a synthesis run (method) is normally represented by several phases.

The most vital parameters can be changed in a user-friendly interface, and, for maximum flexibility, you can edit instructions directly in the **Text instructions** tab. Synthesis parameters such as equivalents, recirculation time, and amidite concentration can be modified for all bases simultaneously, per base or even for individual bases.

The **System control** module starts, monitors, and controls a run. The module consists of five panes — **Chromatogram**, **Process picture** (Fig 4), **Synthesis data**, **Run data**, and **Run log** — that provide an overview of the status of the run.

The **Synthesis data** pane shows the oligonucleotide sequence defined in the running method and the values calculated from integrating the detritylation peaks during the run, providing a quick overview of the coupling efficiency in the synthesis.

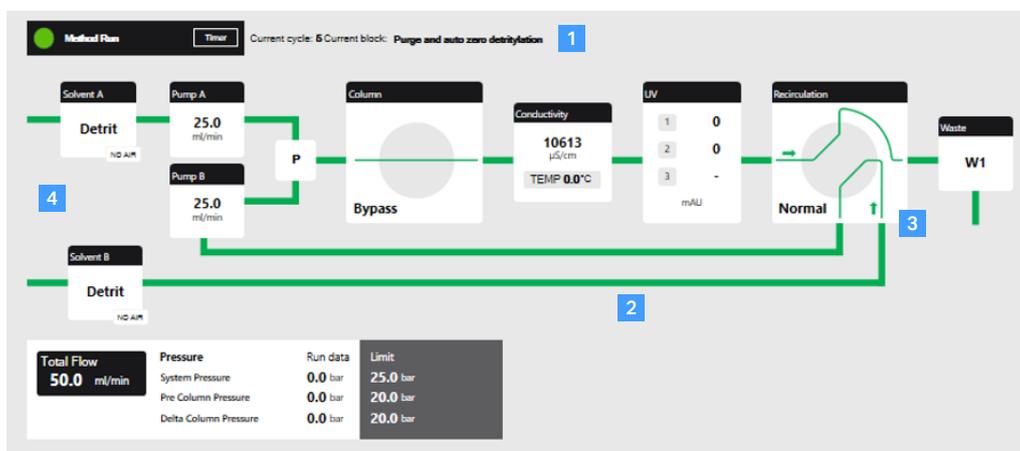
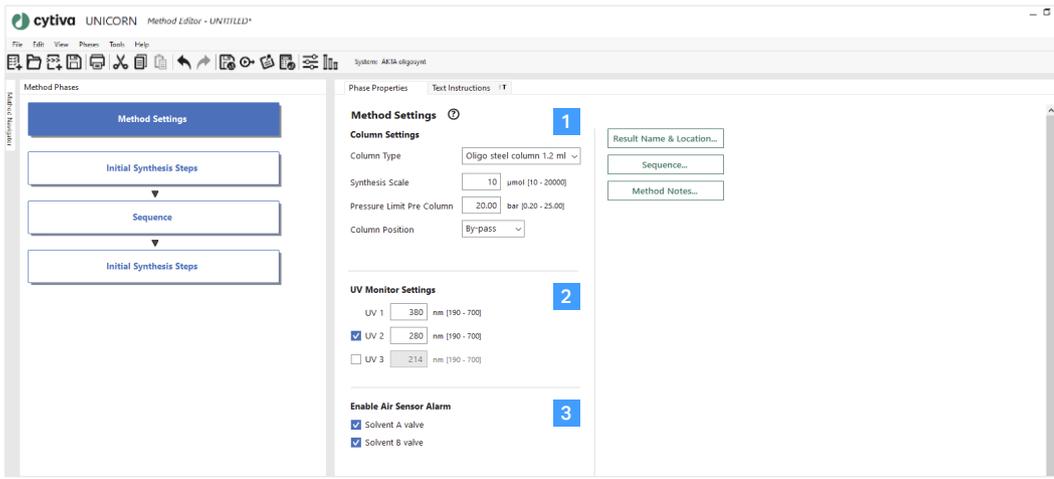
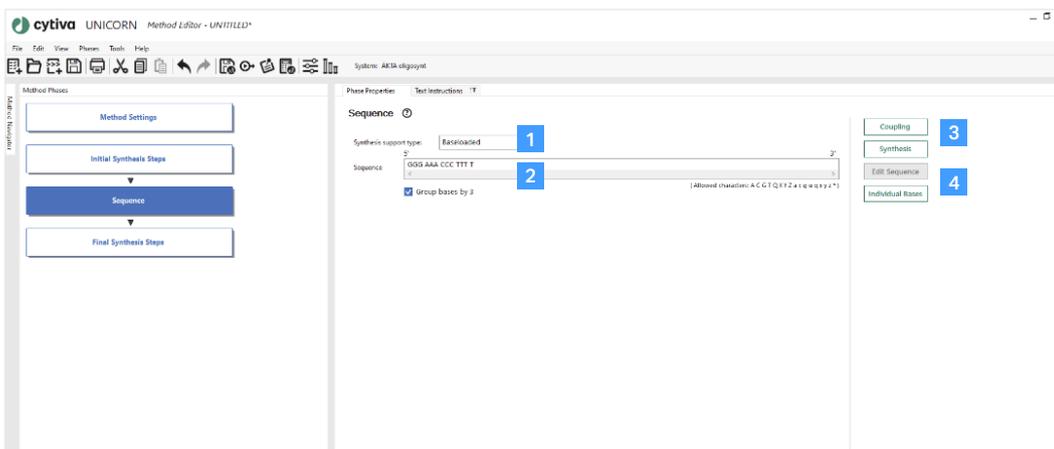


Fig 4. ÄKTA oligosynt™ process picture. Easily view the most common manual interactions by clicking on the process picture to interact with the system.



- 1 Select column settings and synthesis scale
- 2 Select UV wavelengths to monitor
- 3 Edit air sensor alarm settings

Fig 5. ÄKTA oligosynt™ method settings phase. Define settings for the entire synthesis.



- 1 Select synthesis support type
- 2 Enter target sequence
- 3 Set synthesis conditions
- 4 Optimize parameters for single cycles

Fig 6. ÄKTA oligosynt™ sequence phase. Generate a method from a target sequence easily and edit synthesis parameters.

The interactive process picture allows easy monitoring of the run, clearly displaying the most relevant run data and the system state. It also includes easy access to the essential manual instructions for preparing the system including the timer function which provides the possibility of focusing on other tasks instead of monitoring the system. In summary, the process picture gives you intuitive access to the most essential information and functionality.

With UNICORN™ 7 software, the evaluation module enables you to open results and evaluate runs. It also offers easy comparison of results.

Part of a scalable oligonucleotide synthesis platform

The ÄKTA oligosynt™ system is designed to work with UNICORN™ software and Cytiva columns using Primer Support™ 5G to form a solution for small-scale oligonucleotide synthesis. Using the system together with an ÄKTA pure™ chromatography system, AxiChrom™ chromatography columns or FineLINE™ chromatography columns with Capto™ Q ImpRes, Source™ 15Q or Source™ 30Q ion exchange resins and an ÄKTA flux™ tangential flow filtration system, you will have a complete solution for oligonucleotide synthesis.

With the OligoPilot™ oligonucleotide synthesizer for early- to mid-phase clinical trials and the OligoProcess™ oligonucleotide synthesizer for large-scale manufacturing, the ÄKTA oligosynt™ system helps cover a broad nominal synthesis scale, from process development to full-scale manufacturing. All three systems are controlled by the same UNICORN™ software, which efficiently supports scale-up and transfer requirements.

Columns

Cytiva offers a range of columns for oligonucleotide synthesis (Table 1).

Primer Support™ 5G solid support

The ÄKTA oligosynt™ synthesizer and compatible Cytiva columns are designed for use with Primer Support™ 5G polystyrene solid support. This high-loaded solid support for DNA or RNA oligonucleotide synthesis is available using standard DNA and RNA bases as well as with UnyLinker™ solid support as a starting point, making the solid support more flexible for DNA synthesis. Benefits of Primer Support™ 5G solid support include:

- **High loading capacity.** For synthesis of DNA and RNA oligonucleotides of up to 25 bases, a nucleoside loading of 350 µmol/g for DNA and 300 µmol/g for RNA can be used without compromising yield or purity.
- **Cost efficient synthesis.** With higher nucleoside loading, Primer Support™ 5G solid supports deliver major cost savings.
- **Scalability.** Primer Support™ 5G solid supports offer excellent scalability from research to process scale.

The standard products for DNA synthesis (<25-mers) are loaded at 350 µmol/g. The corresponding products for RNA synthesis (<25-mers) are loaded at 300 µmol/g.

Downstream processing

For downstream processing and process development of your oligonucleotides, visit us online or contact a representative to learn more about our ÄKTA pure™ chromatography system, ÄKTA pilot™ 600 chromatography system, AxiChrom™ chromatography columns, and filtration systems.

Table 1. Columns available for oligonucleotide synthesis

		ÄKTA oligosynt™ synthesizer	OligoPilot™ synthesizer	OligoProcess™ synthesizer	Product code
	Scale at 350 µmol/g				
Small stainless steel column 1.2 mL*†	10–50 µmol	■			18110110
Small stainless steel column 6.3 mL*	0.2 mmol	■			18110113
Small stainless steel column 12 mL*	0.5 mmol	■			18110116
Small stainless steel column 24 mL*	0.9 mmol	■			18110119
Small stainless steel column 48 mL*	1.9 mmol	■			18110122
FineLINE™ 35 oligo column	1.1–3.0 mmol	■			28946841
AxiTide™ 50 column	2.3–6.1 mmol	■			29358075
FineLINE™ 70‡ column	4.5–12 mmol	■	■		18115298
FineLINE™ 100‡ column	9.1–25 mmol		■	■	11002798
AxiTide™ 140 column	18–50 mmol		■	■	29358080
FineLINE™ 200‡ column	37–100 mmol		■	■	11003114
FineLINE™ 350 column	112–300 mmol			■	18112793
OligoProcess™ columns, 400 mm up	>300 mmol			■	Request quote

FineLINE™, AxiTide™ and OligoProcess™ columns have a flexibility in bed heights. Bed heights between 3 and 8 cm have been used for this table.

* used with column holder 18113845

† 10 µmol scale using lower loaded support

‡ Used with PFR O-rings and 10 µm filters ordered separately

Specifications

Footprint (W × H × D)	535 × 630 × 470 mm The space required for amidites, and reagents is not included in the footprint. 700 × 630 × 540 mm Fully equipped system
Weight	64 kg Fully equipped
Number of column positions	5
Number of monomer inlets	16 (8 amidite bottle holders included in the standard system)
Number of reagent and solvent inlets	14
Number of waste outlets	11
Piping material	FEP, PEEK, ETFE
Recirculation	Yes
Sensors	<ul style="list-style-type: none"> Conductivity UV Pressure Air Temperature Pre-column sensor for temperature and conductivity available as option.
Heat exchanger	Optional using loop valve and pre-column temperature measurement
Flow meter	Connected through I/O-box
Number of pumps	2
Nominal synthesis scale	10 µmol to 12 mmol
Maximum flow rate	300 mL/min
Maximum operating pressure	25 bar g
Humidity protection	Inert, dry gas
Inert gas supply pressure	5–10 bar g
Inert gas supply requirements	10–50 NL
Power supply	110–230 VAC, 50–60 Hz
Software	UNICORN™ 7.8 or later version

Ordering information

Main system and software	Product code
ÅKTA oligosynt™ synthesizer (supplied with 8 amidite bottle holders, 1 × 6.3 mL column reactor and 1 column holder, 8 bottle caps and an accessory assortment box)	29628148
UNICORN™ 7 workstation license	29702890
UNICORN™ 7 Remote	29702882
UNICORN™ 7 Dry	29702884
UNICORN™ 7 Standalone Evaluation	29702886
UNICORN™ 7 Evaluation Classic	29702888

Amidite bottle holders and bottle caps

Threaded amidite bottle holder incl. connectors	29711497
Bottle cap complete, black PEEK, 4 × 5/16 connections	29711676
Bottle cap sealing PFR94	28948609
Screw lid GL45 opener	28407902

Columns and column holders

Fixed volume columns	
1.2 mL column reactor	18110110
6.3 mL column reactor	18110113
12 mL column reactor	18110116
24 mL column reactor	18110119
48 mL column reactor	18110122
Column holder for 1.2, 6.3, 12, 24, 48 mL columns	18113845
Adjustable volume columns	
FineLINE™ 35 oligo	28946841
AxiTide™ 50	29358075
FineLINE™ 70	18115298
10 µm adaptor/top frit	18115367
10 µm bottom frit	18115368
RPC O-ring kit	18115543
Ball valve 12 mm	18110537

Accessories

Pump purge kit: tube, luer union and syringe	18112453
Conductivity monitor C9	28956495
I/O-box E9	29011361
Loop valve kit	29090689

A range of service agreements and validation support offerings are available.

cytiva.com/aktaoligosynt

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

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