



Dr. Oligo® -96 / 192 DNA / RNA High throughput Synthesizer



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Dr. Oligo® High Throughput Oligo Synthesizer

The Dr. Oligo® High Throughput Oligo Synthesizer is available in a one plate version (Dr. Oligo® 96) and a two plate version (Dr. Oligo® 192). Dr. Oligo® is designed to automate the synthesis of DNA or RNA Oligos using the phosphoramidite chemistry. This is the chemistry used in all modern DNA – RNA synthesizers. The Dr. Oligo® instruments can synthesize high quality, long, short and mixed length oligos faster than any other commercially available synthesizer at lower cost.

Key Features

When it comes to high throughput instruments each user has their own ideas of what they would like to see as key features. We believe that most users are looking for things like ease of operation, low maintenance, and high quality production. We have designed our hardware and software with a focus on these key features.

| | |
|------------------------------------|---|
| Ease to operate the Hardware | Easy access to reagent reservoirs, plates and controls. Plates do not need to be screwed in place, just place them in the instrument and go. |
| Easy to operate Software | Software designed to be intuitive and easy to use. Each screen has a help button that brings up a screen that explains all features on that screen. |
| High Quality Production | Hardware and software designed to produce very high quality oligos. We have designed our hardware and software to address the unique issues related to synthesizing variable length oligos in a parallel system. |
| Low Maintenance | We have minimized the need for user maintenance. Changing bottle O-rings and filters is about all that the user needs to do. Valves are very reliable but if one does need changing, it is very easy for the operator to change. |
| Flexibility | Hardware and Software designed to allow for use of all available synthesis media systems which include fritted plates with loose CPG, 3900 style columns and CPG Frits. And, Azco provides many synthesis options for you to choose from. |
| Easy to trouble shoot and maintain | Trouble shooting is taught at the install and is documented for easy recall. If a problem does arise, determining the cause of the problem and resolving the issue is very easy by following the included documentation. Technical Support and on site service is available for any issues that can not be easily rectified by the operator on their own. |
| Upgradeable | Start with a basic unit with 6 amidites and add additional amidites as your needs change. We design upgrades to be field installable. |
| Throughput | On the Dr. Oligo® instruments you can synthesize up to 96 or 192 oligos in parallel. The cycle time depends on the number of oligos being synthesized but it can be as short as 4 minutes or as long as 6.5 minutes. This means that we can synthesize 192 oligos that are 20 bases long in only 2.5 hours |
| Synthesis Scales | We can synthesize one or two scales in the same run. Scales can vary from 20nm to 1um. The software automatically adjusts reagent delivery according to the scale of the synthesis. |
| Low Gas Consumption | Gas consumption is minimized by utilizing a very small chamber above the reaction plates. |
| Mixed Site Synthesis | Using the standard IUB codes, automatically synthesize mixed sites. |
| Trityl Monitoring | Collect trityls and analyze them in a plate reader off line. |
| Control | A PC is used for control. The PC can be running Win 2k, or Win XP. |

Introduction

To introduce you to our high throughput oligo synthesizer we will start by showing you the different parts of the instrument and pointing out the features we think are important in each shot. We are showing the Dr. Oligo®-192 in this document however all the features (except throughput) apply to both the 96 and the 192.

Front View of the instrument.

The Dr. Oligo® instrument comes complete with a cart so you do not have to search for bench space. The cart contains the waste, Wash and Deblock on the left hand side and is accessible via sliding doors on the front. The computer and other electronics are contained in an isolated space on the right hand side of the cart and are also accessible via a sliding door on the front.

The top of the cart has a liner to capture any drips or spilled reagents.

The cart has four each four inch swivel and lockable wheels making access to the rear very easy.



Main Control Panel:

Pressures can be set individual for 3 groups of reagents to allow for finer tuning of flow rates. Reagents can be individually vented or pressurized.

Large indicators warn the operator if they have forgotten to pressurize reagents or the Purge / Drain system. In addition the software warns if pressure is too low. The operator can select from one of three actions (pause now, pause on cycle or ignore) if the pressure drops during a synthesis

Three drain levels are available allowing flexibility to use any synthesis media. The drain pressure on the top of the plate is displayed to allow for easy adjustment to accommodate different synthesis media.



Expansion of Amidite Positions is Optional

We can add up to four additional amidite reservoir and delivery systems to our basic six amidite system to give a total of ten amidite positions. If more than 10 amidites are required, we can add more but it will take some minor frame changes.



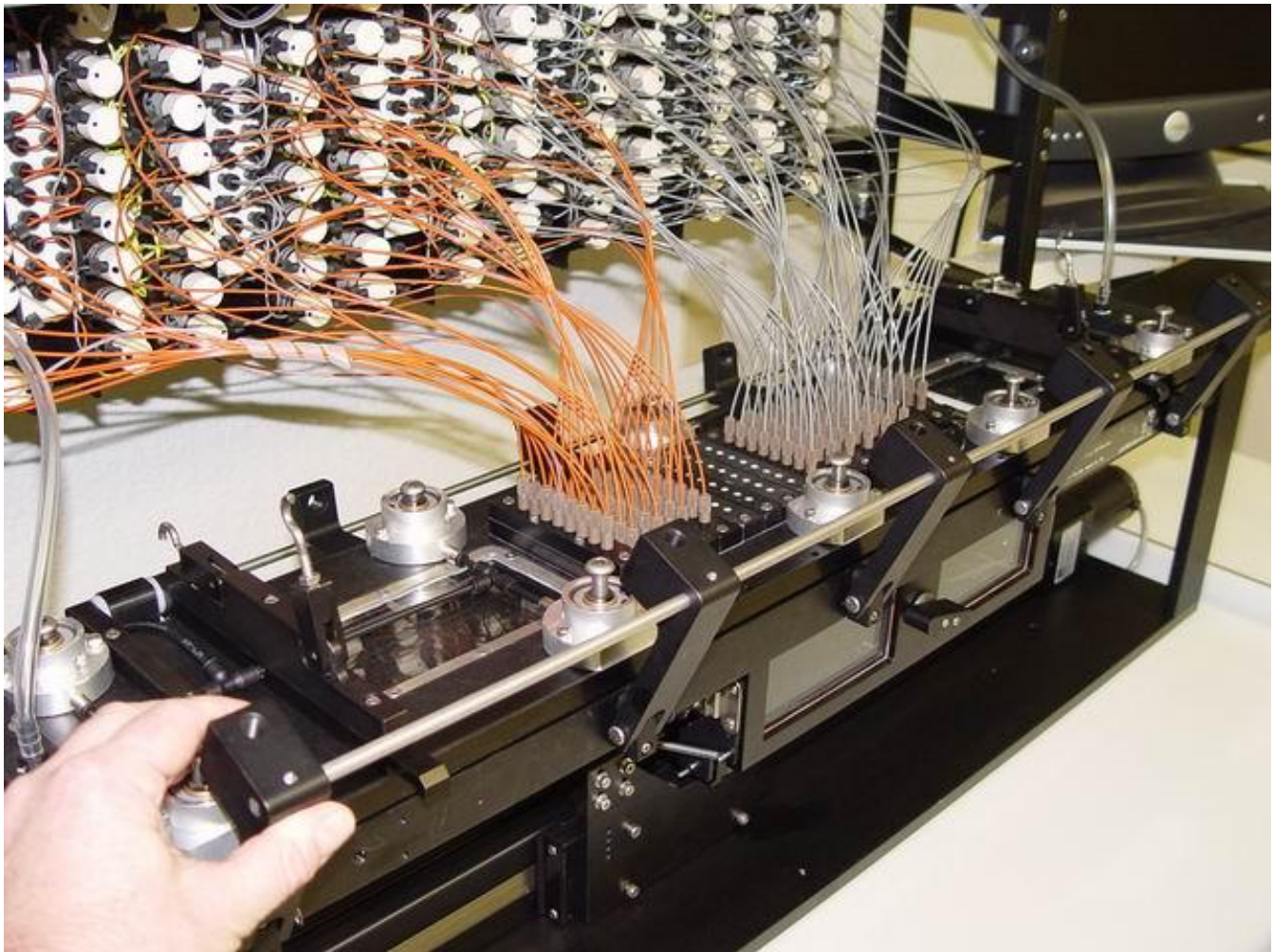
Unique Design Reaction Chamber and sealing system

Minimizes gas consumption and automatically seals plates without the need for screws.



Easy Access to Plates and Nozzles

Installing synthesis Plates / Racks is very easy. Simply flip down the front and rear clamp bars and lift the nozzle plate which is assisted with gas springs.



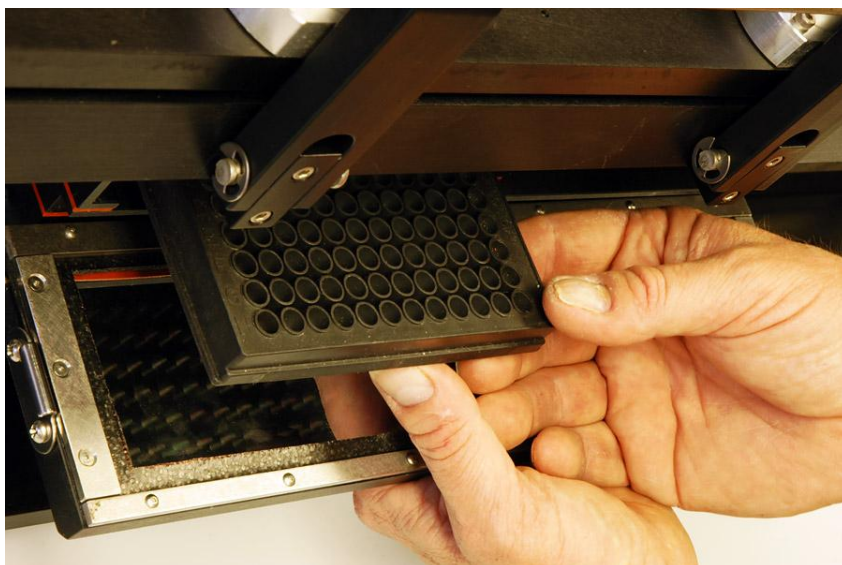
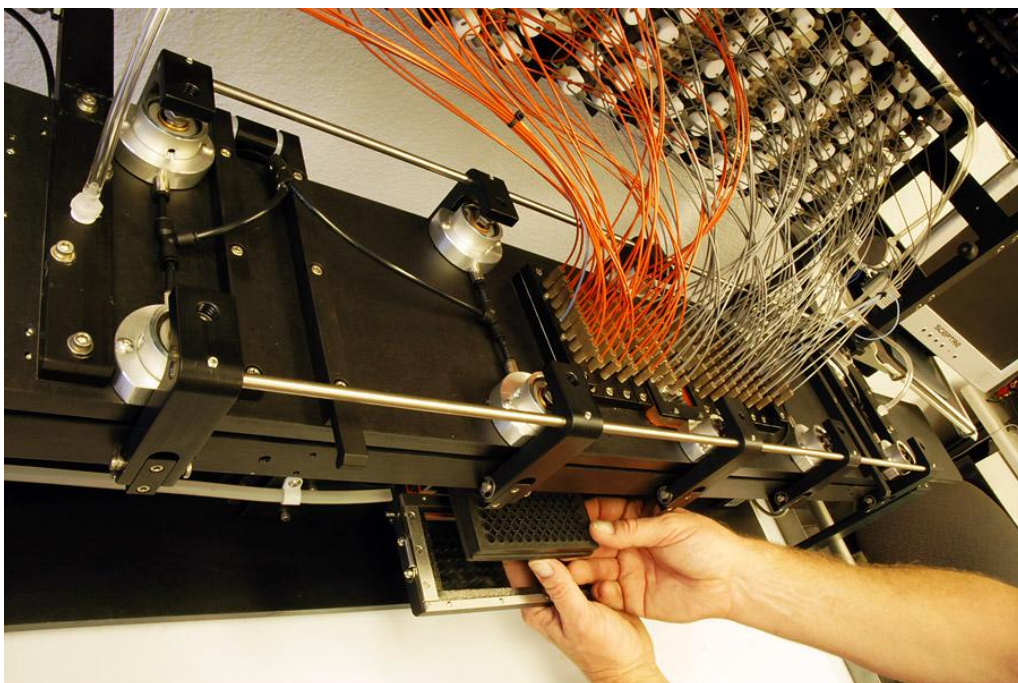
Loading Synthesis Plates / Racks

Either Fritted Plates, 3900 column racks (the one on the right in the picture) or CT Gen Frits (the one on the left in the picture) can be used in the Dr. Oligo®-192. Plates are just set into the instrument, **no need to screw them down**. Our unique reaction chamber sealing system maintains the inert atmosphere integrity of the reaction chamber as well as maintaining the plate seal for draining.



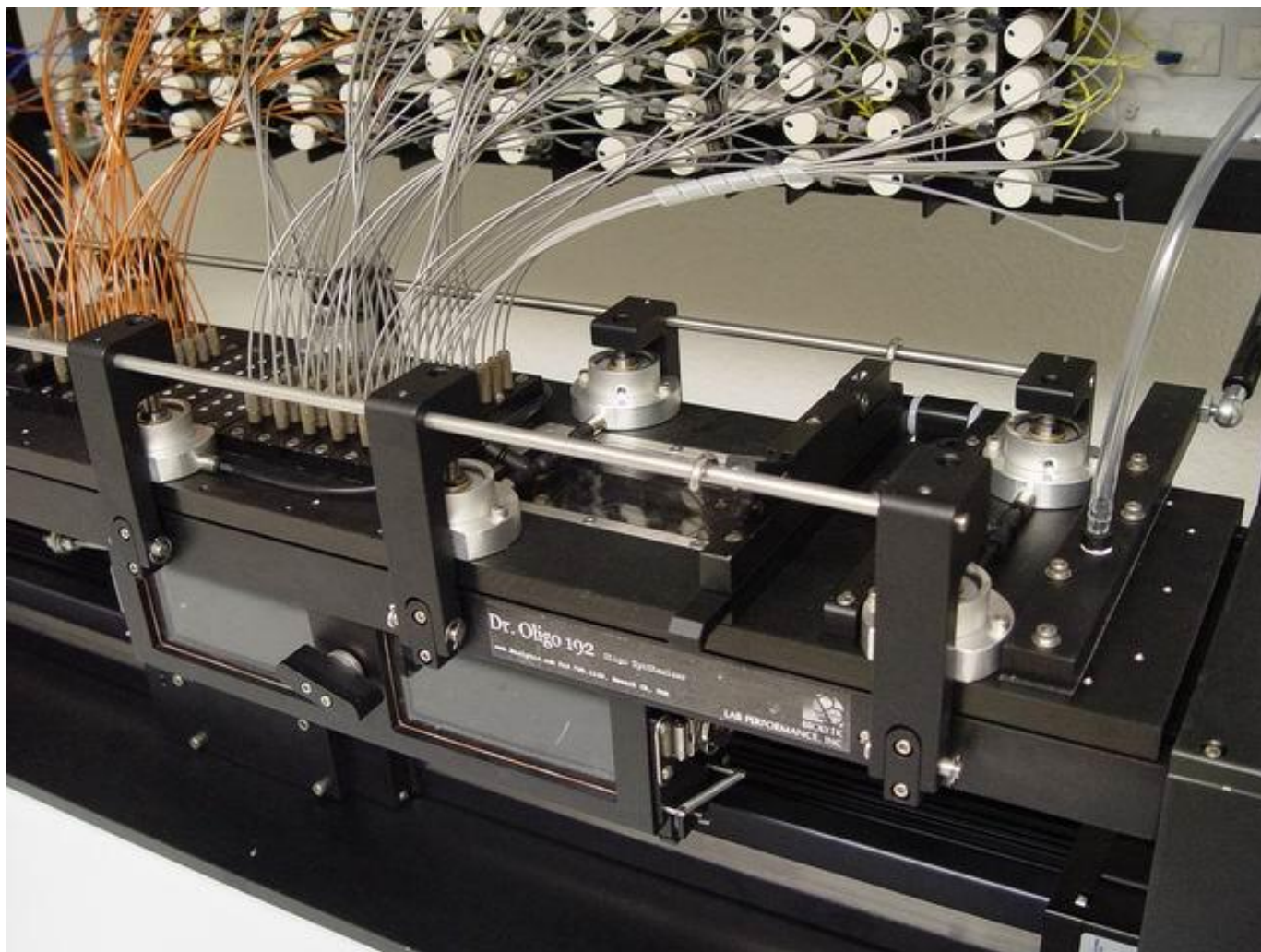
Trityl Collection

For collecting trityls (it is not required that you collect trityls) a collection plate is placed in the chamber below the synthesis plate. When Deblock is complete the collection plate is removed and either read by eye or placed into a plate reader.



Purge and Drain System

A unique system is used to provide a constant purge of the reaction area with pure dry gas (Argon) to maintain an inert atmosphere at the reaction site while allowing the plates to move for alignment with delivery nozzles. Positive inert gas pressure is used for draining the reagents out of the wells in the plate(s). A pneumatic clamp system is used to maintain a positive seal when the pressure on the top of the plate rises during drains.



Low Volume Delivery System for special amidite is optional

We have designed a delivery system that uses very small valves in a manifold positioned directly over the synthesis plate. This reduces the system volume (volume needed to fill one delivery position with reagent) from 2.5 ml for a standard amidite to less than 200 μ l. This is especially useful when synthesis calls for the use of expensive special amidites, dyes, linkers etc.

The low volume delivery system can be put on as many amidite positions as you like.



Dr. Oligo® Options & Features:

The following is a list of hardware options that are available when purchasing a Dr. Oligo® synthesizer. The Dr. Oligo® instrument is now available in either 1 plate (Dr. Oligo®-96) or 2 plates (Dr. Oligo®-192).

Hardware Options & Upgrades:

| Option | Description | Benefits |
|--|---|---|
| Add up to a total of 8 special amidite Standard Delivery Systems | The standard instrument comes with 2 specials and 4 standard (ACGT). This option allows you to have a total of 12 amidite positions which would be the 4 main amidites (ACGT) plus 8 for special amidites | Synthesize mixed DNA / RNA and add dyes or other special monomers. |
| Convert any amidites to low system volume. Can convert the 2 spares on a standard system to low volume. | The standard amidite system volume is 1.5 ml. The low volume system is 300ul. The low volume system comes with a reservoir that can hold a maximum of 100 ml. | Minimize waste of expensive special amidites / dyes. Need only 300ul to fill the system. |
| Add a low volume amidite system (maximum is 8). | The standard amidite system volume is 1.5 ml. The low volume system is 300ul. The low volume system comes with a reservoir that can hold a maximum of 100 ml. | Minimize waste of expensive special amidites / dyes. Need only 300ul to fill the system. |
| Convert any amidites to Dual Volume systems Can convert the 2 spares on a standard system to dual volume. | The standard amidite system volume is 1.5 ml. The low volume system is 300ul. The dual volume system comes with a reservoir that can hold a maximum of 100 ml in the low volume side and a standard size reservoir. This allows one to switch between the smaller reservoir and the standard size reservoir. | Minimize waste of expensive special amidites / dyes. Need only 300ul to fill the system. And still use specials for adding larger quantities of specials if needed. |
| Add a dual volume amidite system (maximum is 8). | The standard amidite system volume is 1.5 ml. The low volume system is 300ul. The dual volume system comes with a reservoir that can hold a maximum of 100 ml in the low volume side and a standard size reservoir. This allows one to switch between the smaller reservoir and the standard size reservoir.. | Minimize waste of expensive special amidites / dyes. Need only 300ul to fill the system. And still use specials for adding larger quantities of specials if needed. |
| Add extra Oxidizer | Add an additional Oxidizer. . | Perform 2 different oxidation chemistries in the same synthesis run. |

Hardware Options (continued)

| Option | Description | Benefits |
|--|--|---|
| Combine Caps to Pre Mix | Pre Mix the Cap-A & Cap-B reagents just prior to use. Keep them separate for storage on the instrument so they do not deteriorate. | Achieve better and more efficient capping by mixing the Cap-A & Cap-B reagents just prior to delivery. |
| Add Additional Wash Bottles | The standard instrument has provision for 2 ea 4 liter bottles for Wash Reagent. This allows you to add more Wash capacity. | Do not have to add Wash Reagent as frequently |
| Add Additional Deblock Bottles | The standard instrument has provision for 1 ea 4 liter bottle of Deblock Reagent., This allows you to add more Deblock capacity. | Do not have to add Deblock Reagent as frequently |
| Use 2 gases, one for Bottle Blanketing and a different one for Purge / Drain | We can connect the gas system so that the customer can use high quality Argon to the reagent bottles and less costly Nitrogen for purge and drain. | Saves money on gas by using less costly Nitrogen for the higher consumed gas for purge & drain while using Argon for the lower consumption function of reagent bottle pressure. |
| Specify Reservoir Cap Sizes | The standard instrument comes with 28 mm screw caps for Amidites, 45 mm screw caps for the Act, Caps & Ox, 38 mm caps for Wash & Deblock. You can request different size bottle caps for the reagent reservoirs. | You can request reservoir caps that fit the bottles you purchase your reagents in so that you can put the reagents directly on the instrument without pouring. |

One can use Stainless Steel Drums for reagents to feed the system if you desire. These drums are usually available from reagent suppliers such as Azco, AIC and EMD Chemicals.

Dr. Oligo®-192 USA List Price

USA List Price \$135,000 which includes 6 standard amidites, one oxidizer, Cap-A & B as separate delivery systems, 2 ea 4 liter Wash Reagent Bottle Positions and 1 ea Deblock Reagent Bottle Position.

Dr. Oligo®-96 USA List Price

USA List Price \$99,950 which includes 5 standard amidites, one oxidizer, Cap-A & B as separate delivery systems, 1 ea 4 liter Wash Reagent Bottle Positions and 1 ea Deblock Reagent Bottle Position.

Software Features

The Dr. Oligo® instruments have a unique set of software features designed to make the hardware work more efficiently with the chemistry. With over 20 years oligo experience we have designed the system with years of user input. During this time we have gained a lot of experience and understanding of the unique challenges that parallel high throughput synthesis presents. We have used our expertise in delivery systems and oligo synthesis chemistry to put together a parallel high throughput oligo synthesis system that is designed to optimally synthesize short and / or long (130 mers) using the same hardware and protocol. Our system offers a unique ability to automatically adjust reagent deliveries, drain times, reaction times based on the scale of synthesis, the cycle that is being synthesized and the base that is being added.

| Feature | Description | Benefits |
|--|--|--|
| Map Amidites | You can map any base code (A,C,G,T) or special to any reservoir | If a problem occurs with an amidite delivery system and you want to switch to a different delivery system but do not want to have to go through all your sequences and change the base code you can remap. |
| Intelligent auto purge of amidite nozzles | Set a purge interval and volume. The software will only purge a nozzle if it has not been used for the number of cycles set as the purge interval and only if that nozzle is going to be used on the current cycle. | Minimizes waste of amidites due to purging while insuring fresh amidite is always available for use. |
| Separate Auto Purge control for each special amidite | Set the Purge criteria as described above separately for each special amidite | Minimize waste of special expensive amidites. |
| Variable Amidite Reaction Time based on the amidite used | Vary amidite reaction time based on the amidites delivered in each cycle. Reaction times are assigned to each amidite position on the instrument. The longest reaction time is used from all amidites that are delivered in a given cycle. | Allows you to attach specials amidites at any point in the synthesis automatically and extend the reaction time only for the specials that need it and only for the cycle where the special is attached. |

Software Features (continued)

| Feature | Description | Benefits |
|--|---|---|
| Variable Amidite Reaction Time based on the cycle. | You can use multipliers to adjust the reaction time of the amidites based on the cycle number. | As sequences get longer, more time may be needed for the coupling reaction to complete. This allows you to optimize the cycle time by extending the reaction time only for longer sequences. |
| Variable Oxidizer Reaction Time based on the Oxidizer Used | Vary Oxidizer reaction time based on the Oxidizer delivered in each cycle. Reaction times are assigned to each Oxidizer position on the instrument. The longest reaction time is used from the Oxidizers that are delivered in a given cycle. | Allows you to do different Oxidation chemistry at any point in the synthesis automatically and extend the reaction time only for the Oxidation chemistries that need it. |
| Variable Oxidizer Reaction Time based on the cycle | You can use multipliers to adjust the reaction time of the Oxidizers based on the cycle number. | As sequences get longer, more time may be needed for the Oxidation reaction to complete. This allows you to optimize the cycle time by extending the reaction time only for longer sequences. |
| Variable Hold (reaction) Time | You can use multipliers to adjust the reaction time of any reagent based on the cycle number. | As sequences get longer, more time may be needed for reactions to complete. This allows you to optimize the cycle time by extending the reaction time only for longer sequences. |
| Variable Drains based on the % of done oligos | You can use multipliers to adjust the drain times based on the % of oligos that are finished | Use shorter drain times when many oligos are running, As shorter oligos finish, more drain time is needed because of a pressure drop due to gas escaping through the done oligos. Saves time and gas. |

Software Features (continued)

| Feature | Description | Benefits |
|---|--|---|
| Vary the protocol based on Cycle | You can have completely different chemistry protocols based on the cycle that is running. | Allows one to optimize the chemistry based on the cycle. As oligos get longer, the stoichiometry changes and so does the dynamics of the chemistry. This feature allows one to deal with these changes to optimize the chemistry. |
| View Synthesis Information at any time during the synthesis | Show all parameters that were set to perform the current synthesis | Easily check if one set all the parameters as they intended for the current synthesis. |
| Flexible Loading of Oligos onto the plate(s) | Allows one to load oligos starting at any location and from different types of files | More flexibility is using the instrument to synthesize oligos from different customers on the same plate and keep them separate. |
| Manual Mode Auto Clean of Nozzles | One button to set an automated manual run to clean all nozzles. | Reduces time needed to clean the instrument after synthesis. (only done if a new synthesis is not going to be started within 6 to 8 hours). |
| Standard & Universal Support i | You can select to use Standard Support or Universal Support. The software knows to add the 3' base or not. | No need to add an extra dummy base character to the 3' end if you are using Universal Support |
| Easier Protocol Construction | The Protocol now uses macros or subroutines that can be built and called by the main protocol any time. | Easier to construct and maintain protocols. |
| Cap-A & Cap-B Per Mix | If you have the hardware option, you can tell the system to premix Cap-A & Cap-B so that they activate prior to delivery | Improves the performance of Capping while allowing for long term storage of the reagents on the instrument without degradation. |
| Pause Ahead | Allows one to select a step and cycle to pause after completing | Adds flexibility to deal with the need to pause in the future. |

Software Features (continued)

| Feature | Description | Benefits |
|--|--|--|
| Programmed Pause | This is a new protocol step that allows us to pre-program in pauses that will automatically occur during the synthesis. | Adds flexibility to allow for pausing the synthesis at predetermined point to allow the operator to perform some task (refill bottles, add a special that you do not want sitting on the instrument etc.). |
| 5' Special Amidite added all at the end of synthesis | If you have variable length Oligos and some or all need a special amidite added at the 5' end, you can choose to add the 5' specials as the oligos finish or wait and add the 5' specials all at the same time after all oligos finish. | Better efficiency in adding expensive specials to the 5' end of the oligos. |
| DMT OFF / ON is per oligo | You can specify for each individual oligo in a synthesis run if the 5' DMT is to be taken off or left on. | Adds flexibility. |
| Stall Detect | We use a state of the art motor drive that can detect a stall and tell the software about the stall so the software can pause the synthesis. | If the motor can not go to the correct location due to some obstruction, the run can be salvaged. |
| Integrate with customer's Lab Management System | We can provide customization to allow for easy import of sequences from the customer's Lab Management System. As this is a custom service we can not say what it will look like but we can say that we are open and willing to do this based on the customer's need. | Easy to integrate into production. |

What is Included with the Synthesizer

The Synthesizer includes all

- Reagent bottles for 192
 - 2 each 4 liter for Acetonitrile Wash Solvent (with standard 38 mm caps).
 - 2 each 4 liter for Deblock (with standard 38 mm caps)
 - 2 each 1 liter for Activator (with standard 45 mm caps)
 - 2 each 1 liter for Cap-A (with standard 45 mm caps)
 - 2 each 1 liter for Cap-B (with standard 45 mm caps)
 - 2 each 1 liter for Oxidizer (with standard 45 mm caps)
 - Amidites, can be specified by the customer, choose from 20 mm, 24 mm, 28 mm or clip caps.
- Reagent bottles for 96
 - 1 each 4 liter for Acetonitrile Wash Solvent (with standard 38 mm caps).
 - 1 each 4 liter for Deblock (with standard 38 mm caps)
 - 1 each 1 liter for Activator (with standard 45 mm caps)
 - 1 each 1 liter for Cap-A (with standard 45 mm caps)
 - 1 each 1 liter for Cap-B (with standard 45 mm caps)
 - 1 each 1 liter for Oxidizer (with standard 45 mm caps)
 - Amidites, can be specified by the customer, choose from 20 mm, 24 mm, 28 mm or clip caps.
- Waste Carboy, 20 liter with cap assembly.
- Plumbing lines
- Fittings
- Connections
- 96 column holders for synthesizing using columns (2 ea for the 192 & 1 ea for the 96)
- Software
- Hardware
- Firmware
- And any other items needed to make a fully functional unit except as excluded below.

What the end user will supply

- Synthesis reagents
- Synthesis media (columns, plates, CPG etc)
- High purity compressed inert gas regulated at a pressure of 100 psi. The inert gas is used for reagent blanketing, reagent delivery and to operate the pneumatic cylinders.
- Power, 120 VAC (+/- 15%) at 60 Hz, 10 amps

Performance Specifications

Number of Oligos that can be loaded for unattended synthesis 1 to 192

High Quality Oligos that can be synthesized in 24 hours (30 bases in length). 1152

This represents 6 runs of 2 plates per run and allows 30 min between runs for setup

Method for synthesis Parallel

Parallel means that all loaded oligos are synthesized simultaneously

High Quality Long Oligos can be synthesized using one of the following:

Super columns from BiosearchTechnologies Inc.

ABI 3900 Polystyrene columns

Universal Frits from CTGen Inc.

Scalable: Our software uses the scale of synthesis for automatically delivering the desired volume of all reagents except Wash & Deblock which are delivered by volume.

Synthesis Scales: We supply and have tested protocols for synthesis scales of 50 nm, 100 nm, 200 nm and 1 μ m using commercially available synthesis media as specified in this document.

Resources Requirements: The synthesis software generates a report for each synthesis that tells the operator how much volume of each reagent is required to complete the synthesis run. In addition, the synthesis screen on the computer updates the volume of each reagent required to complete the synthesis once for each synthesis cycle so the operator can see at a glance how much reagent is required to complete the synthesis from its current cycle.

Reagent Delivery System: All reagents are maintained under an inert gas pressure which is also used to deliver the reagent to the reaction site via tubing and solenoid valves.

Column Loading: For Standard Support Synthesis (the 3' base is already attached to the support) a loading map is viewable on the computer screen and may be printed that indicates which wells need to be loaded with which 3' support columns. If Universal Support is used, the instrument attaches the 3' base to the support and so no such loading map is needed.

Reagent Gas System: The inert gas that is supplied to the reagent bottles is regulated by 3 different regulators in the instrument for more independent reagent delivery flow rates. Each regulator has a pressure gauge to indicate the pressure to that reagent. Each reagent also has a vent pressure valve that allows each to be vented or pressurized. Each system also contains an over pressure valve that is set to relieve bottle pressure if it exceeds 15 psi. This is a safety precaution to keep high pressure from going to the bottles. Finally, each reagent has a pressure sensor that is set to alert the user if the pressure to that reagent has dropped too low. These pressure sensors are tied into the software and will pause the synthesis if a low pressure is detected. This feature can be overridden in the software.

Reagent Auto Priming: An auto Prime function automatically primes all nozzles that will be used in a given synthesis.

Reagent Priming from Manual Mode: An automatic prime function can be executed from the manual mode screen that primes all reagent nozzles.

Amidite & Activator Nozzle Auto Purge: The Activator & Amidite nozzles are able to be Purged of old reagent just prior to use automatically during the synthesis run based on user settings that are set prior to the execution of the synthesis run.

Amidite & Activator First Use Delivery Control: The Activator & Amidites can be told to automatically deliver an additional percentage of reagent the first time they are used in each cycle.

Amidite Ports (Reservoirs): The synthesizer comes with 6 amidite ports and can be expanded to 10 total amidite ports.

Mixed Bases: The Synthesizer can synthesize Mixed (degenerate) base oligos in one of 2 ways. Either one can have the synthesizer mix the bases on the fly (as they are needed from the reservoirs on the instrument) or one can pre mix them and put the pre mixed bases in the spare amidite reservoirs. The standard IUB codes are pre programmed into the software to use for on the fly mixing. All amidite reservoirs on the instrument are available for creating on the fly mixed bases.

Any Mixed bases that is required in a given cycle is delivered in its own separate movement to minimize the time between putting each amidite into the wells.

Protocol Editor: Our software includes an extremely flexible protocol editor which allows the operator to modify the included protocols and save them under a new name or write protocols from scratch. Protocols are included for different synthesis media as well as different synthesis scales and sequence lengths. Included protocols are designed for use with the industry standard Cyanoethyl phosphoramidite chemistry. We have the additional flexibility that allows one to write protocols that can run a completely different chemistry depending on the synthesis cycle. Therefore one could perform a chemistry on the first cycle and then perform a different chemistry on the second cycle.

Synthesizer Control: The Synthesizer is controlled via an industry standard PC. We use a PC from Dell that is on average a medium power computer. The minimum specifications of the PC we use are as follows:

- Pentium 4, 2.4 GHz
- 256 MB RAM
- 15" SVGA LCD Monitor with at least a resolution of 1024 x 768
- CDRW Drive
- Hard Drive of 40 GB
- Operable on voltage from 90 to 240 VAC, 50 / 60 Hz
- RJ-45 Network Port
- Mouse
- Keyboard
- Windows 2000 or XP

Software: The Computer that is supplied to control the synthesizer is equipped with all software that is necessary to operate the synthesizer. All software is also supplied with installable versions on CD and with legal licenses. The software that is supplied is:

- Windows Operation System
- Drivers of the Valve Control System
- Instrument control software
- Oligo Calculator, used to import sequences from a csv file.

Synthesis File: The instrument constructs a text file capturing all the input the user provided to set up the synthesis run. This file is stored in a location chosen by the user and may be printed at any time. This file includes all aspects of the synthesis such as:

- Oligo Sequences, names and which well they are assigned to.
- What type of Support is used
- All Synthesis Run Parameters that the user can change
- The Protocol that is being run

- The Resource Requirements for the run (how much of each reagent is needed)
- Pauses that the user executes during the synthesis.

Power Failure: The instrument is supplied with a UPS (uninterruptible power supply) which is capable of operating the instrument for up to 45 minutes. During this time the operator will need to determine if the power will return or not before the UPS battery dies. If the power will not return, the user should use the “Pause On Cycle” function in the synthesizer control software to pause the synthesizer at a safe point in the synthesis. Then the user will need to put the computer into a Hibernation mode so if the power goes away it remembers where it was and what it was doing. When the power returns, the computer can be brought out of hibernation mode and the synthesis can be continued. If the run will be paused for a long time (3 to 4 hours) we recommend taking the plate(s) out of the synthesizer and storing them in a freezer until the power returns.

Gas Failure: If gas pressure drops too low, the synthesis will be automatically paused. The user can replenish the gas and continue the run.

Valve Failure: If a valve fails, the instrument control software has no way of knowing that. If a valve fails the only way to know it is if one is monitoring the Trityl one should see a drop in Trityl Color. In our instrument one can monitor the trityl output if one wants to. In many instruments monitoring of Trityl is not possible so one has no way of knowing if the synthesis is proceeding correctly or not.

Documentation: The instrument includes an operators manual which covers the hardware, maintenance, control software, operation and parts. In addition all documentation that comes with the PC, the operating system, the drive system and the valve control system is supplied. There is also a context sensitive help system built into the software that gives help for the screen that one is on.

Installation & Training: The instrument comes with a three day onsite installation and training which consists of the following:

Training

- **Duration:** 4 to 6 hours depending on questions presented by students.
- **Covers:** Instrument Hardware functionality and maintenance. The subsystems of the instrument hardware are:
 - Reagent Flow System
 - Purge and Drain Systems
 - The Plate Drive System.

In addition we cover the control software which consists of the following operational areas:

- System Settings
- Base Code Settings
- Manual Mode
- Protocol Editing
- Automatic Operation

Finally we cover operation of the Oligo Calculator which is a software package that we provide with the instrument for the purpose of importing sequences from .CSV files into the format the synthesizer can use.

Patent Information:

This Instrument is manufactured and licensed under the USA Patents 5,368,823 and 5,541,314 European Patent 0683790 & Japan Patent 6-518236.

Warranty: The instrument comes with a 12 month Parts Labor & Travel Warranty.

Additional Warranty: The original warranty may be extended at the time of purchase or any time during the 12 month warranty period with no additional cost for waiting. If the original warranty is allowed to expire for more than 30 days, a pre inspection will be required to before we will accept the instrument on a service plan.

Cleavage & Deprotection

Cleavage & deprotection protocols will depend on several things. These are as follows:

- The Synthesis Media
 - CPG Plate with Standard Support
 - Super Columns with Standard Support
 - CTGen Frits (Universal Support)
- The protecting groups on the amidites used to synthesize the oligos
 - C - Acetiel
 - G – DMF
 - G - IBU
- The protecting groups on the 3' base if using Standard Support
 - C - Acetiel
 - G – DMF
 - G - IBU
- The reagent used for Cleavage & Deprotection
 - Concentrated Ammonium Hydroxide in DI Water
 - Ammonium Hydroxide & Methyl Amine, 1:1

Cleavage

The first part of this reaction is Cleavage of the Oligo from the solid support. This reaction may be combined with the Deprotection reaction or they may be performed separately. The Cleavage reaction is usually relatively fast (typically 30 minutes at room temperature).

Deprotection

The Deprotection reaction will take longer than the cleavage reaction. It is important to completely remove all protecting groups from the bases on the oligo. The fastest way to remove the protecting groups is to raise the temperature. While one can go to 85° C, sometimes the plastics used to contain the solution can soften therefore we recommend keeping the temperature lower to 75° C.

Distributors & Sales

Instruments sold outside the USA pricing may vary due to shipping and import duties.

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Reagent Consumption

The following table gives reagent consumptions per cycle (per base addition) per oligo synthesized for different synthesis media used on our Dr. Oligo®-192 high throughput oligo synthesizer. Reagent consumption is given in molar excess and in ul. The first number is the molar excess and the second number is the volumes in ul (molar excess / volume ul). Acetonitrile and Deblock are given in volume only as the term molar excess does not apply.

| Reagent | Concentration mM | Reagent | Concentration mM |
|-----------------|------------------|---------|-------------------|
| Activator (ETT) | 250 | Amidite | 50 (20 ml / gram) |
| Oxidizer | 20 | Cap-A | 1000 |
| Cap-B | 1000 | Deblock | 3% TCA in DCM |

| Ln | Media Type Scale | Activator Excess / ul | Amidite Excess / ul | Cap-A Excess / ul | Cap-B Excess / ul | Oxidizer Excess / ul | Acetonitrile ul | Deblock ul |
|----|---------------------------|-----------------------|---------------------|-------------------|-------------------|----------------------|-----------------|------------|
| 1 | ABI Polystyrene | | | | | | | |
| 2 | 200 nm | 75 / 60 | 12.5 / 50 | 62 / 50 | 62 / 50 | 10 / 100 | 560 | 300 |
| 3 | 40 nm | 312 / 50 | 50 / 40 | 250 / 40 | 250 / 40 | 30 / 60 | 400 | 200 |
| 4 | Biosearch Technologies | | | | | | | |
| 5 | 200 nm CPG | 100 / 80 | 15 / 60 | 62 / 50 | 62 / 50 | 10 / 100 | 560 | 300 |
| 6 | 50 nm CPG | 250 / 50 | 40 / 40 | 250 / 50 | 250 / 50 | 24 / 60 | 400 | 200 |
| 7 | CTGen Universal CPG Frits | | | | | | | |
| 8 | 200 nm | 65 / 52 | 12 / 48 | 100 / 80 | 100 / 80 | 9 / 90 | 600 | 300 |
| 9 | 100 nm | 100 / 40 | 18 / 36 | 125 / 50 | 125 / 50 | 14 / 70 | 500 | 250 |
| 10 | 50 nm | 150 / 30 | 25 / 25 | 200 / 40 | 200 / 40 | 24 / 60 | 400 | 200 |
| 11 | 25 nm | 200 / 20 | 30 / 15 | 300 / 30 | 300 / 30 | 40 / 50 | 400 | 200 |
| 12 | CPG Plates from Orachem | | | | | | | |
| 13 | 200 nm CPG | 150 / 120 | 25 / 100 | 125 / 100 | 125 / 100 | 5 / 50 | 800 | 300 |
| 14 | 50 nm CPG | 450 / 90 | 75 / 75 | 375 / 75 | 375 / 75 | 18 / 40 | 600 | 250 |
| 15 | 20 nm CPG | 750 / 60 | 125 / 50 | 625 / 50 | 625 / 50 | 30 / 30 | 600 | 200 |

Note: The Dr. Oligo®-192 has the ability to vary the reagent deliveries based on the cycle. This table assumes a consistent reagent delivery throughout the entire synthesis. For oligos longer than 60 mers we recommend a slight increase in Deblock and Wash.