Operation Manual

MultiBlock PCR System (MBS)

HBMBSMAN Rev. 5 8 January 2004

MultiBlock System
Authorized Thermal Cycler

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Applied Biosystems does not guarantee the performance of this instrument.

FS31999

MultiBlock System
End-User License Agreement for MBS Software

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5. Product support. Product support for the SOFTWARE is provided by THERMO ELECTRON or its distributors. Should you have any questions concerning this EULA, or if you wish to contact THERMO ELECTRON for any other reason, please refer to the address provided in the user manual.

Warranty

Thermo Electron guarantees that the MultiBlock System you have received has been thoroughly tested and meets its published specification.

This warranty is valid for 12 months* only if the product and functions have been used according to the user instruction manual.

This warranty period can be extended to a total of 24 months (free of charge) by completing the warranty registration card supplied with the instrument, also available online at www.thermo.com/warrantylog.

No liability is accepted for loss or damage arising from the incorrect use of the MultiBlock System. Thermo Electron's liability is limited to the repair or replacement of the block(s) or refund of the purchase price at Thermo Electron's option. Thermo Electron is not liable for any consequential damages.

Thermo reserves the right to alter the specification of the MultiBlock System without prior notice. This will enable us to implement developments as soon as they arise.

The MBSR block is transported with a package piece inserted behind the door of the block. This packaging must be retained and used during all transportation. Failure to pack the block correctly may result in damage. The warranty on all MBS units will be void if not packaged correctly while the unit is being transported. Thermo Electron cannot accept responsibility for any damage incurred if the block is incorrectly packed and transported after the initial shipment.

The MBS is for research use only.

Please read the User Instruction Manual carefully before using the MBS to ensure that you obtain the best possible results from the machine.

NOTE: The MBS should only be used by suitably qualified and trained people. If the MBS is not used as specified in this Manual, the protection provided by the warranty may be impaired.

* Excludes tube thermistor accessory (MBS only), which carries a warranty for 90 days only.

* Excludes computer, keyboard and monitor.

Important Safety Information

General Safety Precautions

- The MBS should only be used by suitably qualified and trained personnel. The MBS should only be used for its intended purpose in accordance with the instructions and safety warnings contained within this manual.
- Before first use, verify that the blocks have been set to the appropriate supply voltage.
- The MBS is a Class 1 appliance. To minimize the risk of electric shock, the block must be connected to a protective earth via the supplied power cord.

⚠WARNING

SHOCK HAZARD!

THIS APPLIANCE MUST BE GROUNDED.

- Replacement fuses must be of the correct rated current, voltage and type (5 x 20 mm 6.3 A (T) 250 V).
- Do not operate the block in an explosive environment.
- Do not operate the block if it appears to be damaged or if a liquid or foreign object has entered the enclosure. Disconnect from the power supply and contact an authorized service centre.
- Do not attempt to dismantle the block. To avoid the risk of personal injury and to ensure that the safety features of this block are maintained, servicing should only be carried out by authorized service personnel.
- The tops of the reaction vessels and the surfaces of the Heated Lid assembly (in particular the inner surfaces) can become very hot during normal operation. Touching the surfaces can cause burns. Do not touch the heated plate without safety gloves.
- This product is fitted with RFI suppression circuitry. Testing of the electrical insulation should only be carried out using a DC voltage. For more information please contact Thermo Electron .
- When stacking MBSR blocks, the four locating pins must be used.

⚠WARNING

Keep your fingers away from the block mechanism when retracting it back into the MBSR machine.

⚠WARNING

The MBSR weighs 20.6 kg - to avoid injury care must be taken when lifting and positioning the unit

Symbols and Conventions

The MultiBlock system has been designed for safe operation. The following symbols appear on the unit and their meanings should be noted.

I — Indicates the ON position of the main power switch.

O — Indicates the OFF position of the main power switch.

WARNING: Indicates a heating hazard. Proceed with caution to avoid burn injury.
ATTENTION: *Surface chaude.*

SAFETY NOTE: **This** symbol indicates high voltage. Risk of electric shock.
AVERTISSEMENT: *Risque de choc électrique.*

GENERAL WARNING: Consult the manual for further information.
ATTENTION: Lire attentivement le manuel pour plus d'information.

In addition, the following conventions are used to indicate a safety hazard

SAFETY NOTE: indicates a potentially hazardous situation, which could result in death or serious injury.

WARNING: indicates a potentially hazardous situation, which could result in minor or moderate injury to the user or damage to the instrument.

Contents

MultiBlock PCR System (MBS)

1. Introduction

1.1 Overview

The MBS is based on the concept of a central computer that executes programs and monitors the performance of a number of satellite blocks. The MBS software will ensure that your system runs smoothly. The MBS system includes both MBS blocks and the newly launched robot compatible MBS (MBSR).

1.2 The MultiBlock System (MBS)

The MBS comprises a central computer with up to thirty individual satellite blocks networked to it. This enables multiple PCR protocols to be performed simultaneously. The total flexibility of the network allows the customer to specify the exact number and type of each block. The PCR blocks are available in 0.2ml, 0.5ml (excluding MBSR) and 384 well formats making this a very flexible system with a design that will maximize customer bench space. The block temperature range is 4°C-99°C, suitable for most molecular biology applications. Gradient blocks are available in both the 0.2ml and 0.5ml (excluding MBSR) formats, which reduce the time required to optimize PCR protocols.

The MBS software features a large graphical display and user-friendly programming. Personal directories and file protection will benefit laboratories with a number of different users. The ability to store extra programs on disk will be advantageous to many users. Adjustable ramping, time/temperature increment and decrement functions are easily programmable for the most complex PCR protocols. Software upgrades will be available, ensuring that your MBS is easily updated.

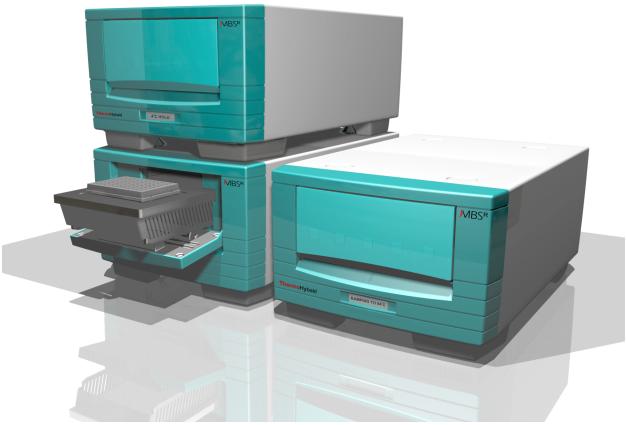
The built-in diagnostics and calibration check facility ensures the continued reliability of the MBS and ease of service. It is possible to print out relevant experimental data after each run in order to adhere to quality standards and for good laboratory practice requirements. All of the MBS components (except the computer) are covered by a 2-year warranty.

1.3 Robot Compatible MBS (MBSR)

To further the robotic nature of the MBS, Thermo Electron has developed the MBSR, the fully robotic MBS. The MBSR follows the principles of flexibility and networkability of the MBS, but unlike the original MBS, the MBSR has an ejectable block with automated heated lid suited for robotic oil free applications.

The MBSR has moved the MBS into a new realm of accessible high throughput PCR due to its innovative block action. The whole block is ejected through the front of the unit, therefore making it fully stackable. This means that more blocks can be placed in reach of the robotic arm thus reducing the total cost and space while increasing PCR throughput. The ejection mechanism also enables the sample block to come within reach of hooded programmable pipette stations. While ejected, the temperature of the block is maintained allowing for temperature controlled sample manipulation during a run.

The MBSR PCR blocks are available in 0.2ml gradient and 384 well formats and uses the intuitive MBS software. The large graphical display provides clear real-time information on block, sample and gradient temperatures. For GLP tracking, a log of all previously run programs is stored, which summarizes both graphical and tabular information on the program, date and time of the run.



NOTE: Throughout this manual 'MBS' refers to both MBS and MBSR, unless otherwise stated.

1.4 Block Compatibility

1.4.1 The 0.2 ml Standard Block (excluding MBSR) & 0.2 ml Gradient Block

This block can hold any of the following:

- 1 x OmniFast 96 skirted polypropylene microplate (HBTC8002N)
- 96 x 0.2 ml OmniStrip tubes (HBTC2662N)
- 96 x 0.2 ml individual OmniTubes (HBTC6202/3372N)

1.4.2 The 0.5 ml Standard Block & 0.5 ml Gradient Block (excluding MBSR)

This block can hold any of the following:

- 1 x Racked OmniTube Plate (96 x 0.3 ml polypropylene tubes) (HBTC4073N)
- 96 x 0.3 ml OmniStrip tubes (HBTC4043N)
- 48 x 0.5 ml individual OmniTubes (HBTC3505/4895N)

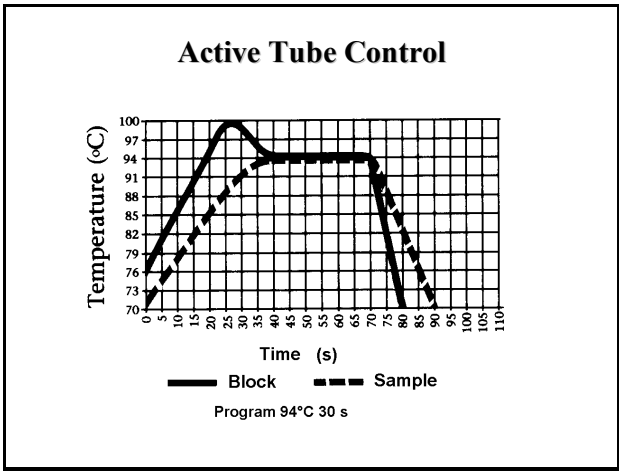
1.4.3 2.4.3 The 384 Well Block

This block accommodates 1 x OmniFast 384 skirted polypropylene plate (HBTC3840N)

1.5 Temperature Control Methods

Crucial to the accurate operation of a thermal cycler is an understanding of the temperature control methodology. The temperature cycling blocks for the system are of a specially coated precision-machined aluminium, ensuring the best possible fit of reaction tubes in the block. This ensures excellent contact between the tubes and the block, enabling rapid and accurate heat transfer from the block to the samples. The coating also helps to protect the block against radioactive contamination.

1.5.1 Active Tube Control (excluding MBSR)



Accurate sample temperature control in 0.2 ml and 0.5 ml block types is achieved by Thermo's Active Tube Control software. This type of control uses the remote thermistor probe mounted in an appropriate tube (the tube should be identical to that used for the samples). The tube thermistor probe monitors the temperature within the dummy sample tube and this information is fed back to precisely control the block temperature to achieve the optimum cycling profile. It is recommended for all reactions above 20ml volume in 0.5 ml and 0.2 ml tubes. A volume of mineral oil equivalent to the total volume in the reaction tubes (including any oil overlay) must be present in the control tube.

The thermistor acts as a simple mimic, monitoring the sample temperatures as it changes during cycling, feeding back this information to the MBS processor. This feedback allows the block to respond to the sample temperature, ensuring that the samples achieve the exact temperatures and times programmed. To bring the sample rapidly to the set temperature, the block is heated/cooled beyond the set temperature for the sample. When designing/transferring to a tube control program it is essential to understand the difference between tube control and block control on a conventional temperature cycling machine. With tube control, the actual samples are held at the programmed temperature for the programmed time. With block control, either on the MBS or a thermal cycler without tube control, there will be a lag between the block reaching target temperature and the sample reaching target temperature. Thus when transferring protocols from a block control machine the incubation times may be reduced by up to 50%, and in some cases the temperatures adjusted slightly.

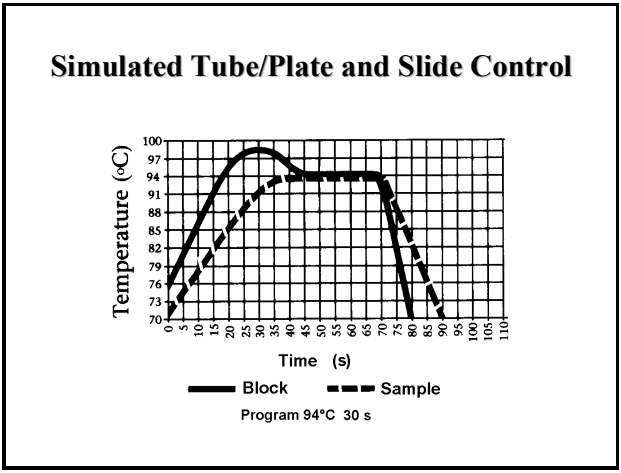
For Tube Control reactions, check that the tube thermistor is connected and located in the block (the tube thermistor should be placed in position G1).

When you receive your MBS, the thermistors are mounted in a HBTC3372 thin walled tube for 0.2ml blocks or a HBTC3505 thin walled tube for 0.5 ml blocks.

NOTE: Do not disconnect a tube thermistor when a program using tube control is in progress. If this does occur, the program will be abandoned and an error message will be displayed.

Protocols from machines that cannot use Active Tube Control can be transferred to the MBS using an extension lead for the thermistor (HBPXETTM). See Section 2.6 for further details.

1.5.2 Simulated Tube/Plate Control (all units)



Simulated Tube Control or Simulated Plate Control may be used for reactions when it is not appropriate to use the tube thermistor probe; for example when very small reaction volumes (<20ml) or 96 well or 384 well microplates are used. A temperature control algorithm is used in a similar way to active tube control, but it is based on calculated values for the sample temperature rather than values fed back by the tube thermistor.

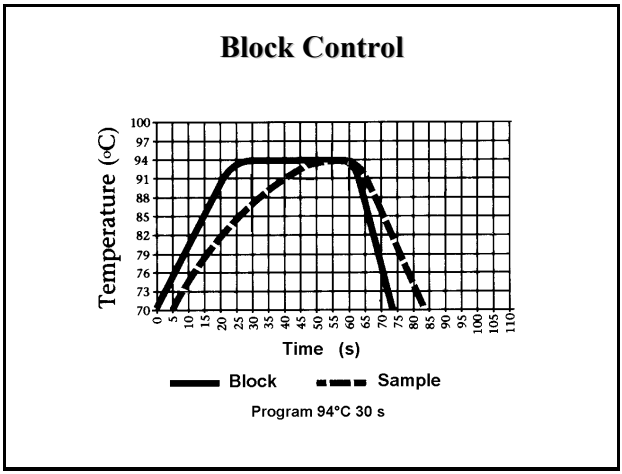
Similar considerations apply when transferring protocols from a block control machine, as discussed above, and the extension lead can again be used.

Reactions using Simulated Tube Control do not require the tube thermistor to be connected, but sample volume details must be entered in the 'Edit a Program' window. For all tube reactions in a 0.2ml or a 0.5ml thin walled tube, the volume to be entered is the total reaction volume in ml in one well, including any oil overlay.

Block Type	Maximum sample volume (ml)
384 well	30
0.2	100
0.5	250

1.5.3 Block Control (all units)

Block Control is used to control the block temperature as on a conventional dry block machine. We do not recommend this means of control for thermal cycling due to the variability in thermal profile obtained with different sample volumes and consumable types.



1.5.4 Heating and Cooling

The MBS units are built to proven designs, providing an accurate and reliable thermal cycling system.

The sub-ambient aluminium block is heated and cooled by the latest in Peltier technology. With proven durability, the blocks excel in performing applications such as RAPD (Random Amplification of Polymorphic DNA) and Differential Display, which require cycling temperatures close to ambient. The blocks will control the temperature of the samples from 20° C to 99° C for cycling reactions in all reaction formats. In addition, static incubation steps may be performed as low as 4° C.

1.6 Transfer of Protocols from a Block Control Machine to Tube Control using the Thermistor Lead Extension (excluding MBSR)

The different modes of control should be considered before transferring protocols directly. For example, a temperature cycling protocol consisting of 1 min. at 95° C followed by 1 min. at 65° C, repeated 30 times. Using block control, the actual sample temperature is at 95° C for just 30 sec at each step, a total of 15 min overall. In contrast, tube control will result in precise one-minute incubations at each step, a total of 30 min at the target denaturation temperature. Even though tube control gives a more accurate representation of the program, transferring such a protocol directly could result in lower yields because the enzyme is exposed to the high temperature for significantly longer, thus reducing its activity in later cycles.

The most accurate way to transfer protocols is to use the control tube of the MBS as a temperature probe in the block control machine as follows:

1. Set an MBS block to run a single program at a set temperature for an extended time. (e.g. 37° C for 4 hrs), ensuring that the heated lid is switched off and the machine is set to block control. This enables the tube thermistor to be used remotely.
2. Connect the thermistor lead extension (HBPXETTM) to the thermistor control tube and plug it into the corresponding thermistor probe socket of the MBS block. Then locate the tube in a well of the block control machine previously used to run the required protocol.
3. Open the 'View Active Block' window. After a short equilibration interval, the display will indicate the sample tube temperature, which should be noted at regular time intervals (e.g. 10 sec. for a number of cycles). The actual length of time spent at the denaturation, annealing and extension stages should be recorded, as well as any temperature overshoot values where the maximum/minimum temperature exceeds the target temperature or undershoots where the target temperature is not actually reached.
4. The temperature profile that the samples in the block control machine actually achieve, rather than simply the block temperature, should be used to program your MBS.

1.7 PC Hardware Specifications

The minimum recommended requirements to run the MBS Software are:

Pentium® class processor running Windows® 95, 98 or NT

330 MHz or faster

32 Mb RAM

Hard disk drive with 100 Mb free

1.44 Mb 3.5 floppy disc drive

SVGA monitor, resolution 800*600 high color 16 bit

RS485 port with no optical isolation operating at half duplex

Parallel printer port

Keyboard and mouse

CD Rom drive

Pentium and Windows are trademarks of Microsoft Corporation.

1.8 Support Services

The MBS has been designed for reliability and for ease of maintenance. Thermo Electron Corporation offers full service and technical support for all its products. International Sales, Services and Technical Support contact your local Thermo Electron Corporation subsidiary or authorized distributor.

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Sample Preparation
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Email: services.sampleprep@thermo.com
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2. Unpacking and Installation

2.1 Unpacking

Before unpacking components of the MBS, please make sure that the outer packaging is undamaged.

After unpacking, ensure all packaging and fixtures are retained, as the MBS should always be transported in the original packing to avoid damage. The MBSR units have a piece of packaging inserted behind the door, this should be removed before use and retained. This packaging should be used during all future transportation. Failure to pack the block correctly may result in damage. The warranty on the MBS units will be void if not packaged correctly while the unit is being transported. Thermo Electron cannot accept responsibility for any damage incurred if the block is incorrectly packed and transported after the initial shipment.

> **NOTE**: If the unit is transported or stored in conditions of high humidity it must be allowed to stabilize at normal ambient temperature before powering up the unit.

⚠WARNING

Keep fingers away from the block mechanism when retracting it back into the MBSR machine.

⚠WARNING

**The MBSR weighs 20.6 kg - to avoid injury care must be taken when lifting and positioning the unit **

2.2 Packing List

- MultiBlock Unit
- Power Cord
- Communications Lead
- Control Thermistor Probe (excluding MBSR)
- Consumable Pack
- Silicone Foam Compression Pad (excluding MBSR)
- Four Locating Pins (MBSR only)
- Warranty
- Installation Instructions

If any item is missing or damaged, contact Thermo Electron or an authorized distributor.

Ensure any padding between the heated lid and the block is removed before using the machine.

2.3 Installation

2.3.1 Computer Installation

The computer supplied by Thermo Electron should be set up according to the manufacturer's instructions. This computer is configured ready for use with the MBS.

NOTE: If the computer is purchased from a supplier other than Thermo Electron, it will require an RS485 port to be fitted. Instructions to fit this port can be found on the supplied CD.

2.3.2 Software Installation

Installing Software for the First Time

The MBS software can be installed using the following procedure (for Windows 95/98/NT):

1. Insert the CD.
2. Open My Computer and double click the Control Panel icon.
3. Open Add/Remove Programs and in the dialogue box select Install. The computer will automatically locate the Setup file on the CD.
4. Follow the prompts on the screen.
5. Following installation, the MBS software can be accessed in the Thermo Electron sub-directory using the Programs directory on the Start menu.

   NOTE: The software is supplied with a Dongle, which needs to be connected to the Printer Port of the MBS computer. This is a security device to prevent software piracy. The software will only run on a computer fitted with this Dongle.

Upgrading Software

1. Identify the port currently being used by your MBS software:
   - Through Windows Explorer enter the Electron directory, click on System, and open the Serial Config text file. Make a note of the first number of the first line.
   - Backup PCR files.
2. Remove the old version of the software
   - In My Computer open the Control Panel.
   - Double click on Add/Remove Programs and select Thermo Electron MultiBlock System.
   - Press the Add/Remove button and follow the on-screen instructions to remove the old version of the software.
3. Install new software
   - Place the CD in the CD driver.
   - In Control Panel click on the Add/Remove Programs and click the Install button.
   - Follow the on-screen instructions.

4. Reconfigure the program
   - In the Electron directory, on the C drive, double click on System, and open the Serial Config text file.
   - Check that the first number of the first line is the same as that noted earlier. If it requires changing, alter it and save the file.
   - Reintroduce PCR program files.

Further information on identifying COM port numbers and how to configure your computer are available on the software CD as word documents.

2.3.3 Block Installation

The first block to be attached to the network can be plugged directly into the RS485 port at the back of the computer using the main communications lead supplied with the computer. Subsequent blocks can be added by connecting them to the previously added block using their individual communications leads. Every time a block is attached to the MBS by a lead it must be added to the network using the software (see Section 3.2.2).

If the MBSR blocks are to be stacked on top of each other, the 4 locating pins (HBMBSRLP) must be used. To do this, remove the four blanking plugs from each corner of the top of the block and screw a locating pin into each hole. Each block also has four holes on the underside that line up with the locating pins. The block to be stacked should be placed on top of the lower block, locating the pins in the holes in the underside of the block.

2.3.4 Thermistor Positioning (excluding MBSR)

The control thermistor probe (when required) should be inserted into socket G1 of the block. Ensure that the tube contains the same volume of mineral oil as the total sample reaction volume, and that the probe is immersed in the oil.

2.3.5 Choosing a Location

1. Where possible, avoid connecting the block to a power supply subject to voltage fluctuations, e.g. a socket shared by an ultracentrifuge or refrigerator.
2. In the MBS, excess heat is removed from the System by a fan. Units may be placed side by side, but there should be at least 15 cm of clearance at the front and back of each block. The air intake is located on the base and air is expelled out of the top and front of each block. Care should be taken not to obstruct the vents with, for example, loose Benchcote® or sheets of paper. The block must not be covered during operation.
3. All MBS equipment should be placed on a stable and level surface, out of direct sunlight. The heated lid should always be closed during temperature cycling, even if the lid is not switched on.
4. The MBS is intended for indoor use at an ambient temperature of 4-34° C in conditions of up to 80% humidity. These specifications have been calculated for operations at between 0 and 2000 m altitude.

2.3.6 Use in Cold Rooms

The MBS may be used in a cold room (down to 4° C). However, when removed to room temperature the machine should be allowed to equilibrate for at least 2 hrs before being switched on.

⚠WARNING

If equilibration is not carried out, condensation may form within the block and cause a short circuit

Please note that if the MBS/MBSR is not used as specified in this manual, the safety protection provided by the equipment may be impaired.

3. Operating Instructions

3.1 Initial Start Up

1. Switch on the PC at the power switch.
2. Open the MBS software program.

   NOTE: Ensure that the security Dongle is fitted; see section 2.3.

3.2 General Programming and Operation

3.2.1 Introduction

Cycling programs are simple to perform, using the user-friendly software. During programmed operation, the screen provides comprehensive information about the blocks including sample temperature, number of cycles completed and estimated time for completion.

The MBS can be programmed to perform all types of temperature-controlled reactions, from simple one step incubations, to complex multi-step temperature cycling protocols and temperature gradient experiments, when gradient blocks are used.

After successful start up, the first screen to be displayed is the 'Main Window' (Figure 3.1). It is possible to return to this menu at any time by choosing the 'Change Window' menu followed by 'Thermo Electron MultiBlock System – Main Menu'. All aspects of the programming are accessed through the Main Window. Clicking on a button or choosing a menu item will access a secondary window, from which programs can be run.

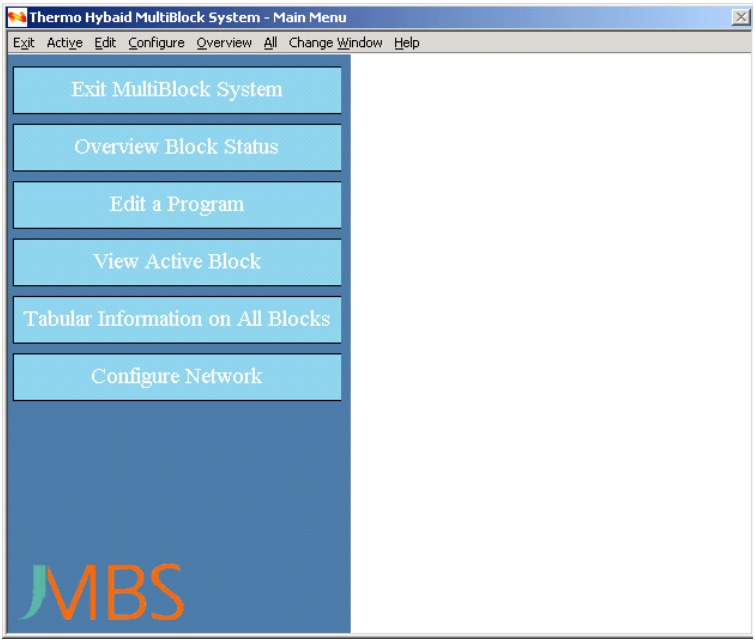


Figure 3.1: Main Window

3.2.2 Adding/Removing Blocks

The first requirement in setting up the MultiBlock System is to add blocks to the network. Blocks can be added to or removed from the network from the 'Configure Network' Window (Figure 3.2).

1. The block must first be plugged into a power source and switched on using the switch at the back. The block is then connected by a lead to the computer.
2. Choose the 'Add/Delete' menu item followed by 'Add a block to the Network' or click the green '+' button. This will bring up a dialog box prompting you to add the block. If the block to be added is an MBS block, click OK and press the arrow button on the front of the MBS block until the block appears on the screen (this must be pressed within 10 seconds of pressing OK). When this has been done and the block has been added, the block can be named for identification purposes. If adding an MBSR, all units except the one to be added must be switched off. Add the MBSR units in turn, switching one off once it has been added and switching on the next one to be added. If MBSR units are present along with MBS units, all MBS units MUST be switched off when adding MBSR units. Blocks will be added to the network in the order that they are assigned. If a block is deleted and a new one added this will appear in place of the first deleted block
3. To delete a block from the network select the block to be deleted and choose 'Delete Block from Network' or click the red '-' button.
4. A block ID can be changed at any time once it has been recognized on the network.

   NOTE: It is recommended that all open programs be closed before trying to add blocks to the network.

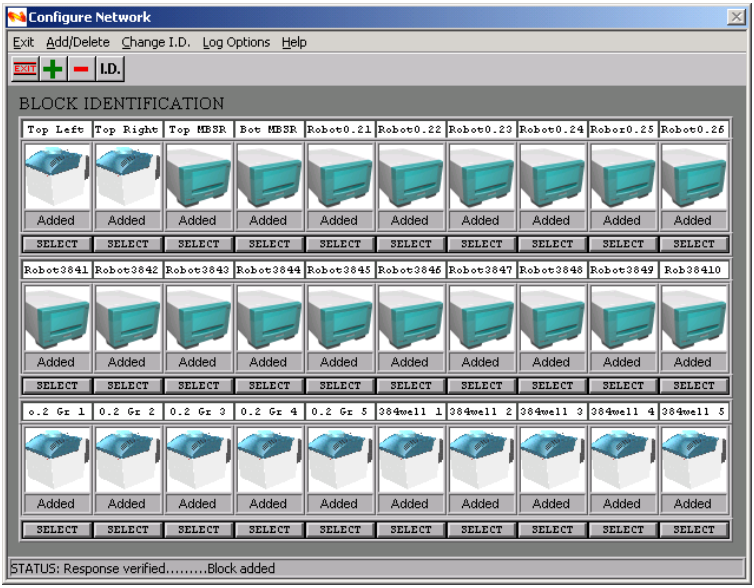


Figure 3.2: Configure Network Window

3.2.3 Program Logging

It is possible to log a trace of all PCR runs from all blocks to produce an historical record of the performance of a block.

1. To set the number of files you wish to be logged per block (between 1 and 50) open the 'Configure Network' window. From within this window, select a block and then open the 'Log Options' menu and select the 'Change number of files logged' option. Select the number of logs you would like to be stored; this can be repeated for all the blocks. If zero is entered then no logging will occur on the chosen block. Once a block has logged the number of files chosen, it will automatically overwrite the oldest file in the log directory.
2. If logged files are to be stored indefinitely they can be copied or moved from the log directory to another directory using Windows Explorer.

   NOTE: If the number of files logged is set to one, every new run will cause the old file log to be overwritten, without prompting.

   For information on how to access logged files, see Section 3.6.

3.2.4 Writing New Programs/Editing Existing Programs

New programs can be written and existing programs can be changed from the 'Edit a Program Window' (Figure 3.3).

From within this window all the program parameters can be set. This includes the advanced cycling functions such as temperature ramping, time/ temperature increment and decrements and even the setting of a temperature gradient across the block.

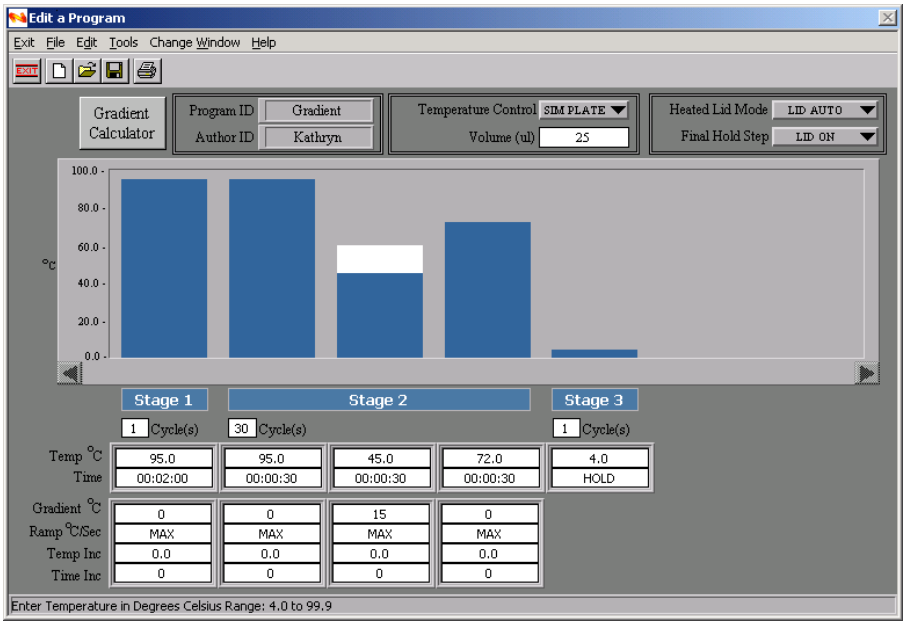


Figure 3.3: Edit a Program Window

Temperature Ramping

The temperature ramping (Ramp Rate) enables the rate of change of sample temperature (°C/s) to be artificially slowed down.

Under normal circumstances the temperature cycling times are very rapid, which minimizes non-specific reactions. The rate of sample temperature change during temperature cycling is controlled so that it is as fast as possible (3° C/s heating; 2° C/s cooling) without affecting the block uniformity and accuracy. In some instances, it may be advantageous to limit the rate of change of temperature, e.g. to allow limited extension of short or degenerate primers between primer annealing and DNA synthesis steps to stabilize the primer/template duplex.

Time/Temperature Increment

These features enable the time interval and/or the temperature of a specified programmed step to be increased or decreased with successive temperature cycles. It may be advantageous to increment the extension time interval to compensate for deterioration of enzyme activity in later cycles. Alternatively, temperature decrements can be used, e.g. in touchdown cycling reactions where the annealing temperature is decreased with successive cycles.

Temperature Gradients

PCR optimization is dependent on a number of factors, including the concentrations of salt and Mg ions as well as primer and DNA templates present in the reaction mixture. The annealing temperature of the primer to the template is affected by these factors and so requires constant optimization each time a modification is made. By using the gradient capabilities of the MultiBlock the correct annealing temperature can be identified in one reaction.

3.2.5 Entering Programs

There are two methods for entering new programs. The first is to enter new stages and steps directly under a new file name; the second is to open an existing file, edit the program and save under a new file name.

1. To write a new program, choose the 'File' menu item followed by 'New' or click the 'New File' tool bar button.
2. To open an existing program, choose the 'File' menu item followed by 'Open' or click the 'Open File' tool bar button.

   NOTE: If a program is Write Protected it can be opened by first turning this feature off in the 'Edit a Program' Window. Select the 'File' menu followed by 'Open' or click the 'Open File' button on the toolbar. Right mouse click on the program you wish to unprotect and select 'Properties'. Tick or deselect the 'Read Only' box in the dialogue box to revoke write protection.

3. To save a program, choose the 'File' menu item followed by 'Save' or click the 'Save File' tool bar button. This will bring up a dialog box where it is possible to choose the file name and directory for saving. In order to Write Protect the program see Note above.

   When overwriting files ensure the file to be overwritten is not a default file.

4. To print out a program choose the 'File' menu item followed by 'Print'. This will print out exactly what is shown on the window at that time.
5. The options at the top of the screen above the graph should be filled in at the start of a program. A program ID and author ID are required for verification purposes. The temperature control method (see 1.5) and heated lid mode (see 3.2.6) can be altered for each program. If using simulated tube or simulated plate control, a volume is requested for accurate cycling calculations (see 1.5.2).
6. Cycling parameters are entered in the table below the graph. If working from an existing program it is possible to alter these values. Complex protocols, such as temperature ramping, thermal gradients or time/ temperature increments (e.g. touchdown) can be programmed by entering the details in the table. The range limits are as follows:
   - Cycles - Enter 1 to 99.
   - Set Temperature - Enter 4.0 to 99.9° C.
   - Set Time - Enter 1 s to 18 hrs (a 'Hold' step can be programmed by entering '0').
   - Gradient - Enter 1 to 15°C (Set Temperature must be between 30 - 70° C). This facility can only be used with Gradient Blocks.
   - Ramp - Enter 0.01 to 3.00° C s-1 (3.00° C s-1 is the maximum ramp rate).
   - Temperature Increment - Enter -20.0° C to +20.0° C (this can be used for touchdown and touchup protocols).

     NOTE: The temperature increment setting multiplied by the number of cycles must be within the specification of the block (see 6.2). For example +2° C each cycle for 15 cycles results in a 30° C temperature rise. Therefore the start temperature must be below 69° C.

   - Time Increment - Enter -9:59 to +9:59 (this can be used to increase the extension time for each cycle, for example).
   - A hold step can only appear at the end of a stage.
   - Touchdown and touchup cannot be used on a single cycle stage.
   - If values out of range are entered, a dialog box will appear to help correct the error. This box can also be used if the user is unsure of how to enter the data correctly.

7. To add a stage to the program, choose the 'Edit' menu item followed by 'Insert a Stage'. This will allow the user to add a stage after any existing stages. The user will be prompted to add the required parameters.
8. To add a step to a stage, choose the 'Edit' menu item followed by 'Insert a Step'. This will allow the user to add a step. The user will be prompted to add the required parameters.
9. To delete a step, choose the 'Edit' menu item followed by 'Delete a Step'. It is then possible to decide which step to remove.
10. If a program is larger than can be displayed on one page, it is possible to click the right arrow below the graph. This will move the user onto the next screen.

3.2.6 Heated Lid Settings

Heated Lid - Automatic Start

This should be selected for robust cycling reactions, where the reactants can withstand being incubated for the duration of the preheating step (about 2 minutes) without the generation of spurious products. In this mode, samples should be loaded and the lid closed before starting the preheating step. The block cools to 4° C while the lid preheats.

Heated Lid - Manual Start (excluding MBSR)

In this mode, the lid heats and then holds the program, whilst the block cools to 4° C. Samples may now be added to the block, the lid closed and the program resumed by pressing the start button on the block.

No Heated Lid

If the heated lid is switched off (for example to perform experiments with oil overlay present), no lid pre-heating will be required; therefore the temperature cycling will commence as soon as the program is run.

3.2.7 Running a Program

Running a pre-stored program is easy on the MBS. Blocks can be run from the 'View Active Block' window, the 'Tabular Information on All Blocks' window or the 'Overview Block Status' window.

1. From the 'View Active Block' Window (Figure 3.4), select the block you want to use by choosing the 'Change Block' menu followed by 'Change Block Displayed', then selecting the required block from the drop down list.
2. Choose the 'File' menu followed by 'Download program', or click the 'Open file' button. The downloaded program will be displayed in the table below the graph.
3. To run the program, choose the 'Control' menu item followed by 'Run' or click on the green arrow button.

   When a program is downloaded to an MBSR unit the drawer will open automatically, the drawer will then close when the run button has been pressed.

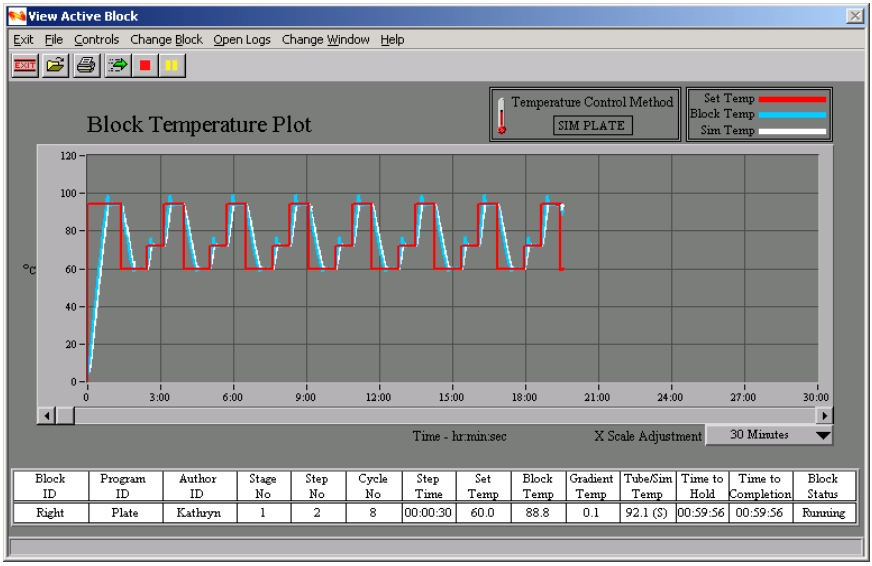
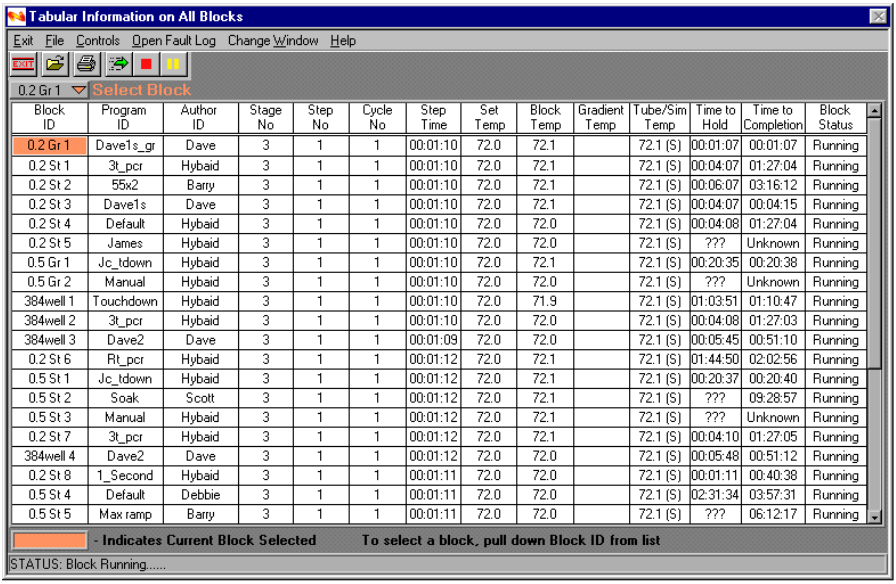


Figure 3.4: View Active Block Window

4. From the 'Tabular Information on All Blocks' Window (Figure 3.5), select a block by clicking on the block ID. This will highlight the selected block. Choose the 'File' menu followed by 'Download program' or click the 'Open file' button. The downloaded program will be displayed in the 'Program ID' column. To run the program, choose the 'Control' menu item followed by 'Run' or click on the green arrow button.



Block ID	Program ID	Author ID	Stage No	Step No	Cycle No	Step Time	Set Temp	Block Temp	Gradient Temp	Tube/Sim Temp	Time to Hold	Time to Completion	Block Status
0.2 Gr 1	Dave1s_gr	Dave	3	1	1	00:01:10	72.0	72.1		72.1 (S)	00:01:07	00:01:07	Running
0.2 St 1	3t_pcr	Hybaid	3	1	1	00:01:10	72.0	72.1		72.1 (S)	00:04:07	01:27:04	Running
0.2 St 2	55x2	Barry	3	1	1	00:01:10	72.0	72.1		72.1 (S)	00:06:07	03:16:12	Running
0.2 St 3	Dave1s	Dave	3	1	1	00:01:10	72.0	72.1		72.1 (S)	00:04:07	00:04:15	Running
0.2 St 4	Default	Hybaid	3	1	1	00:01:10	72.0	72.0		72.1 (S)	00:04:08	01:27:04	Running
0.2 St 5	James	Hybaid	3	1	1	00:01:10	72.0	72.0		72.1 (S)	???	Unknown	Running
0.5 Gr 1	Jc_tdown	Hybaid	3	1	1	00:01:10	72.0	72.1		72.1 (S)	00:20:35	00:20:38	Running
0.5 Gr 2	Manual	Hybaid	3	1	1	00:01:10	72.0	72.0		72.1 (S)	???	Unknown	Running
384well 1	Touchdown	Hybaid	3	1	1	00:01:10	72.0	71.9		72.1 (S)	01:03:51	01:10:47	Running
384well 2	3t_pcr	Hybaid	3	1	1	00:01:10	72.0	72.0		72.1 (S)	00:04:08	01:27:03	Running
384well 3	Dave2	Dave	3	1	1	00:01:09	72.0	72.0		72.1 (S)	00:05:45	00:51:10	Running
0.2 St 6	Rt_pcr	Hybaid	3	1	1	00:01:12	72.0	72.1		72.1 (S)	01:44:50	02:02:56	Running
0.5 St 1	Jc_tdown	Hybaid	3	1	1	00:01:12	72.0	72.1		72.1 (S)	00:20:37	00:20:40	Running
0.5 St 2	Soak	Scott	3	1	1	00:01:12	72.0	72.1		72.1 (S)	???	09:28:57	Running
0.5 St 3	Manual	Hybaid	3	1	1	00:01:12	72.0	72.1		72.1 (S)	???	Unknown	Running
0.2 St 7	3t_pcr	Hybaid	3	1	1	00:01:12	72.0	72.1		72.1 (S)	00:04:10	01:27:05	Running
384well 4	Dave2	Dave	3	1	1	00:01:12	72.0	72.0		72.1 (S)	00:05:48	00:51:12	Running
0.2 St 8	1_Second	Hybaid	3	1	1	00:01:11	72.0	72.0		72.1 (S)	00:01:11	00:40:38	Running
0.5 St 4	Default	Debbie	3	1	1	00:01:11	72.0	72.0		72.1 (S)	02:31:34	03:57:31	Running
0.5 St 5	Max ramp	Barry	3	1	1	00:01:11	72.0	72.0		72.1 (S)	???	06:12:17	Running

Figure 3.5 Tabular Information on all Blocks Window

5. From the 'Overview Block Status' Window (Figure 3.6), select a block by clicking on the 'Select' button. Choose the 'File' menu followed by 'Download program' or click the ‘Open file’ button. The downloaded program will be displayed above the block icon. To run the program, choose the 'Control' menu item followed by 'Run' or click on the green arrow button.

   The block remains selected until it is deselected or until the run is started.

The global control function allows the control of multiple blocks as one. This includes the ability to select between 1 and 30 blocks, download a program to the selected blocks, run the blocks, pause and/or stop all the selected blocks.

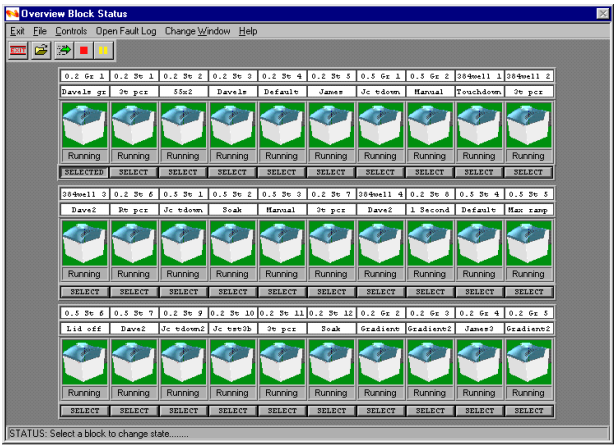


Figure 3.6: Overview Block Status Window

6. Select the 'Overview Block Status' window in order to display a graphical overview of all the blocks. Select individual blocks by clicking on the select button under each block. Multiple blocks can be selected at the same time in this manner. If all or nearly all of the blocks are to be selected then select the 'Global Control' option on the menu bar. It is then possible to select all blocks, or alternatively, deselect all blocks. Once all blocks are selected individual blocks can be deselected in the usual fashion. Once selected a block now remains selected until deselected or run.
7. From any of these windows, programs can be stopped (causing the block to go into an idle state), paused or continued after a pause or hold step by choosing the 'Control' menu item followed by the relevant command. Programs can also be stopped by clicking on the red square button or paused by clicking on the yellow bars button.
8. A block can also be started or paused by pressing the arrow button on the front on the actual block (excluding MBSR).

NOTES:

- Once a program has been downloaded to a block and started, the block will continue to run unless commanded not to, even if the computer is turned off or crashes.
- The block is set to auto-restart following a power failure even if the computer will not restart.
- The door of the MBSR will not open whilst in a paused state.

3.2.8 Loading Samples and Heated Lid Operation

Loading Samples

The following guidelines maximize the uniformity and thermal transfer characteristics of the block:

- Load samples uniformly across the block rather than in clusters. Spreading the thermal load in this way maintains uniformity.
- If small numbers of samples are to be run, use dummy tubes to ensure that there is at least one tube in each quadrant of the block. This facilitates even-heated lid pressure for good thermal transfer to the tubes.
- Care should be taken when matching block, consumable, control mode and sample number (see Section 2.5).
- Ensure tube caps are properly closed before loading the block.

Heated Lid Operation

The adjustable Heated Lid enables the running of temperature cycling protocols without the need for paraffin or mineral oil overlays. Such vapor barriers are normally required to prevent evaporation before thermal cycling is complete. This system is designed to be compatible with most reaction sample formats, i.e. 0.5 ml, 0.3 ml, 0.2 ml tubes and 96/384 well plates. In most cases, the experimental protocol is largely unchanged when switching to an oil free format.

The Heated Lid operates by positioning a heated plate in contact with the top of the reaction tubes or wells. This heated plate then heats the air temperature at the top of each reaction mixture to a temperature that is permanently higher than the sample temperature. This elevated air temperature, relative to the sample temperature, minimizes evaporation so that condensation of the reaction mixture is reduced as it is repeatedly heated and cooled.

Opening the Lid

The MBS (excluding MBSR) lid is opened by turning the knob so that the arrow is aligned with the 'open lid' icon (see Figure 3.7). This releases the catches at the front of the block to raise the lid and expose the block recess.

To open an MBSR block, click on the ‘block eject’ button. The block ejects from the front of the unit. The MBSR block will also open when a file is downloaded to it. It will then close when the ‘run’ button is pressed.

Closing the Lid

To close (excluding MBSR), gently lower the lid. At this point a ‘click’ should be heard as the catches are engaged. This action automatically positions the heated lid to the default upper setting, which should be used in conjunction with tubes and plates of standard profile.

If using low profile plates, the height of the lid can be adjusted to the lower setting by rotating the knob clockwise so that the relevant icon is aligned with the front of the unit. (see Figure 3.7).

Please note that the tube thermistor must be removed before selecting the lower setting.

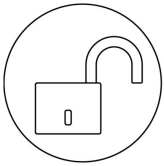
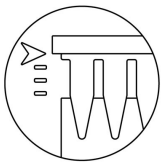
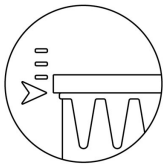




Figure 3.7: Open Lid Icon Upper Setting Icon Lower Setting Icon

To close an MBSR block, click on the 'close block' button  .

The temperature of the heating plate is set at 115° C (max. surface temperature) with power control affected by the control chassis.

The heated plate inside the lid is switched on and off from within the program. The lid operates once a program is activated, with a heating time of typically 2 minutes before cycling commences. The block can be operated with or without the lid being switched on.

⚠WARNING

Both the tops of reaction vessels and the surfaces of the Heated Lid assembly (in particular the inner surfaces) can become very hot during normal operation. Touching the surfaces can cause burns. Do not touch the heated plate without safety gloves.

⚠WARNING

Closing the MBSR door automatically retracts the block into the MBSR unit. Please keep neck ties, long hair and other extremities (fingers etc.) clear of the block whilst it is in motion. Getting these caught in the block during operation may cause injury.

3.3 Block Monitoring and Control

The MultiBlock system offers a variety of ways to monitor and control blocks. Once a block has been selected from within the windows 'View Active Block', 'Tabular Information on All Blocks' or 'Overview Block Status', it is possible to Run, Stop, Pause or Continue that block from the toolbar Controls menu, or from the button bar. A program can be downloaded to a block in any of these windows using the File toolbar menu, or the open file button.

3.3.1 Viewing an Active Block

The 'View Active Block' Window (Figure 3.4) allows you to view detailed information on the block. It also gives a graphical representation of the incoming temperatures. This can be used to see how a program is performing on a single block.

1. To select the block you want to view choose the 'Change Block' menu followed by 'Change Block Displayed', select the required block from the drop down list.
2. The chosen block can be commanded from here using the Run, Stop, Continue and Download Program Commands (a program can only be downloaded when the block is idle).
3. The graph shows the last 10 minutes of temperature data and will continue to update as new data arrive. The data collected are updated once every second. The data displayed will always start from the time that the window is opened.
4. It is possible to change the scale of the data viewed by clicking on the box adjacent to the x-axis time scale.

Within the 'View Active Block' window, the expected time of program completion is detailed. The software has an advanced time to completion function in which the PC constantly monitors the state of the block so it can update the initial finish time estimations.

In addition to this function, when the block finishes a run, reaches a hold step, or is paused, the time to completion will change color to orange and start to count up. If the block is restarted, the time to completion will reappear.

3.3.2 Tabular Information on All Blocks

The 'Tabular Information on All Blocks' window (Figure 3.5) provides information on all of the blocks. From this window, it is possible to monitor the state of the blocks in detail, including Block ID, the current program loaded or being run on any block, as well as temperature and cycle information.

1. Once a block has been selected via the 'select block button' it is possible to Run, Stop, Pause, Continue and Download Program Commands. A program can only be downloaded when the block is idle.
2. From within the File toolbar is the option to print the current display.

3.3.3 Overview Block Status Window

Through the use of color coding, the 'Overview Block Status' window (Figure 3.6) shows at a glance the status of each block. All 30 blocks can be displayed at the same time and each block is identifiable with both block ID and program name (if downloaded).

The key to the background color is as follows:

- Blue – idle
- White/Green flashing – paused
- Yellow – preheating
- Red – faulty
- Green – running
- White – block turned off

The 'Overview Block Status' window also includes the option to select more than one block at a time, either via their individual 'Select' buttons or via the 'Global Control Feature' (for more details see Section 3.2.7).

3.4 Gradient Calculator

The gradient calculator is used to demonstrate the temperature of each row across the block. It is accessed through the 'Edit a Program' window via Tool drop down menu or the Gradient Calculator button.

The type of block, 0.5 ml or 0.2 ml, can be selected and the starting (lower) temperature entered. Once the gradient temperature has been entered, the graphical display changes and the temperature of each row is calculated and displayed.

The gradient calculator may be accessed and used at any time and is unrelated to any program that is running or being edited.

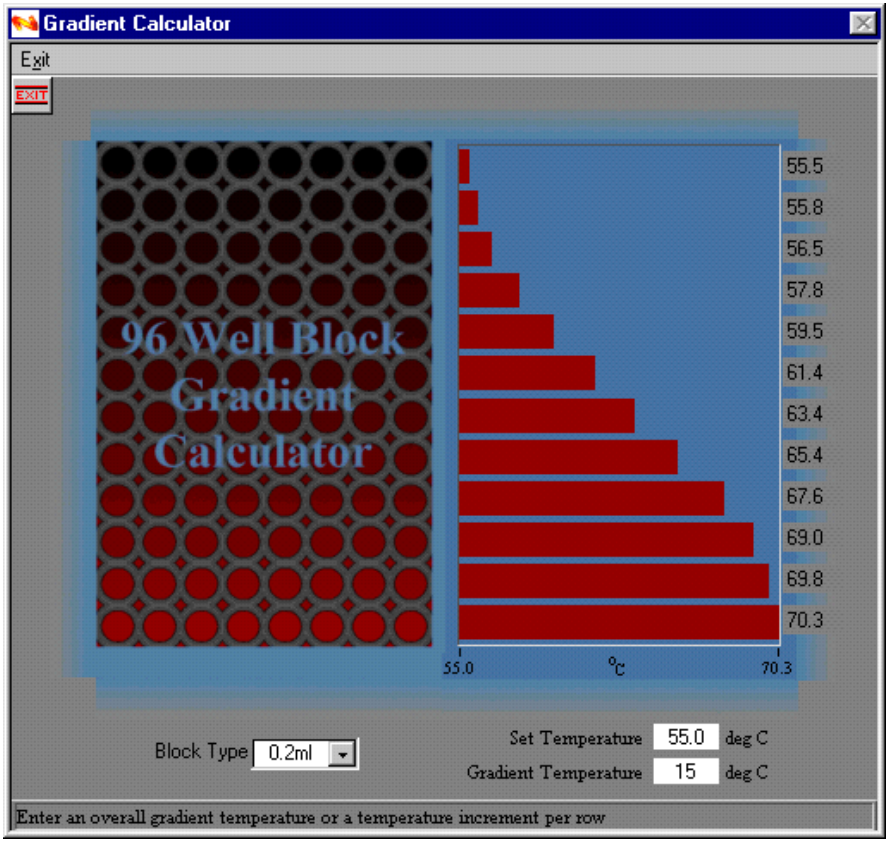


Figure 3.8: Gradient Calculator

3.5 Fault Log

Should a fault occur, the block light will turn red, the block graphic will appear red on the screen and a fault message will appear in the fault log. The fault log can be accessed from pull-down menus in the 'View Active Block' window, 'Tabular Information on all Blocks' window or the 'Overview Block Status' window (Figures 3.4, 3.5 and 3.6, respectively). The block ID is shown on the top line above each block. The current program being run by the block is displayed on the second line below the block ID.

If a fault occurs, the block status will display 'Fault' and a fault message will appear in the fault log. To clear the fault log, select the 'Clear Fault Log' menu to clear all blocks, or to clear the log from a particular block, select the block using the pull down menu at the bottom of the window.

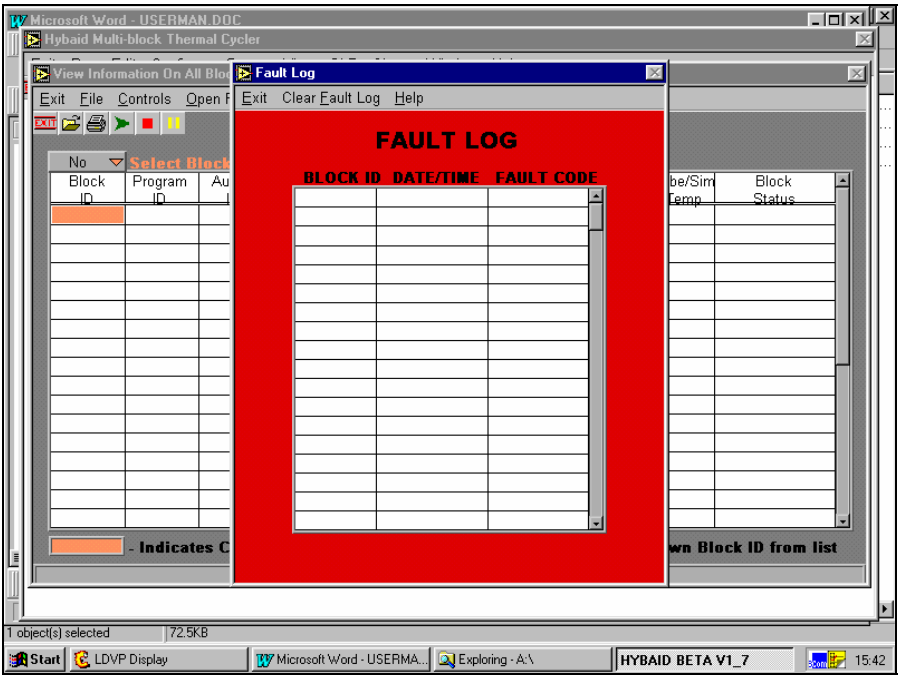


Figure 3.9: Fault Log Window

3.6 Viewing Logged Data

In order to log a trace of all PCR runs from all blocks, a maximum of 50 runs per block can be stored (See Section 3.2.3). To access the block logs open the 'View Active Block' window. Select the 'Open Logs' option and open 'View Logged Data'. An open file window will be displayed, showing the default location of the logged files. If you have moved the file logs to a different location then select the folder you have moved them to. Files are logged automatically by block name, date and time. Select the file you wish to view and open it.

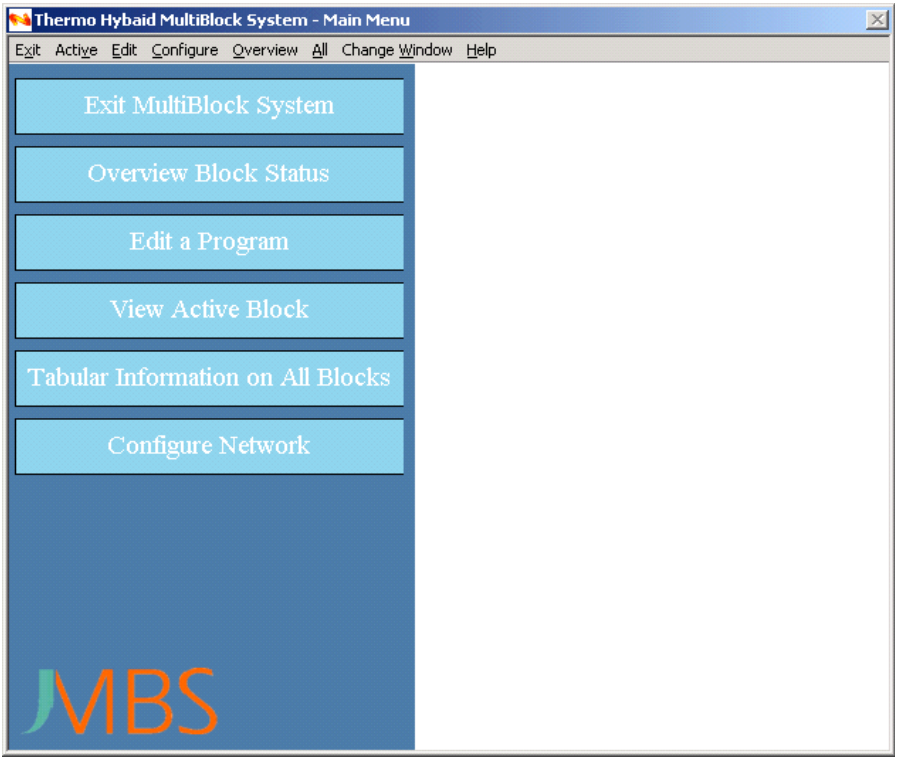
The logged information on that block will now be displayed. This includes a full trace of the whole PCR run on a scalable graph. To scale the graph select the X scale adjustment window and select a scale from 10 minutes to 24 hours. Below the graph is a table containing all the information about the run around the t = 0 time point. By scrolling the graph using the arrow buttons, the information in the table alters to reflect the time, cycle number, temperature, etc., of the PCR run around original t = 0 bar.

To see a summary of the whole run, select 'File' from the menu bar, and open 'View Run Summary'. Information contained within the summary screen includes, block name, program name, program author, start time and date, finish time and date, length of run and maximum and minimum temperatures. The summary also reports on the status of the block during that run. This includes reporting on power failures.

To view another logged file, select 'File' from the menu bar followed by 'Open Log', or alternatively, click on the open file icon on the tool bar.

3.7 Summary of Windows

3.7.1 Main Window



How do I access the Main Window?

- It is displayed on starting the MBS software
- Via the Change Window drop down menu
- By closing all other Windows

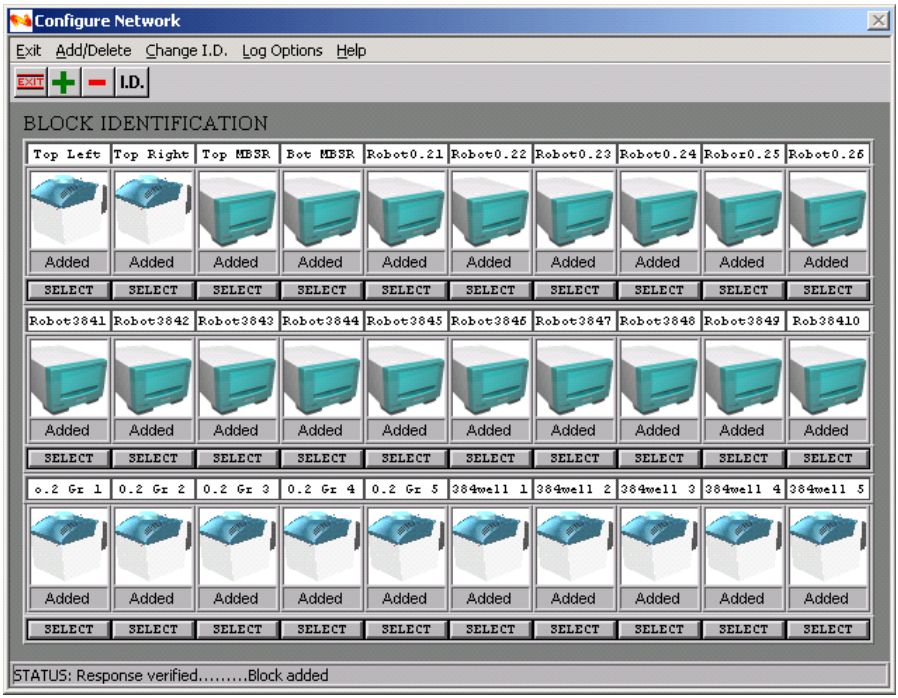
Why access the Main Window?

- To navigate to all other Windows
- To shut down the MBS program

What can I access from the Main Window?

- All other Windows and hence all functions, via the button menu or the drop down menus
- Main exit button

3.7.2 Configure Network Window



How do I access the Configure Network Window?

- Via the buttons in the Main Window
- Via the Configure drop down menu in the Main Window
- If already open, via the Change Window drop down menu from any Window

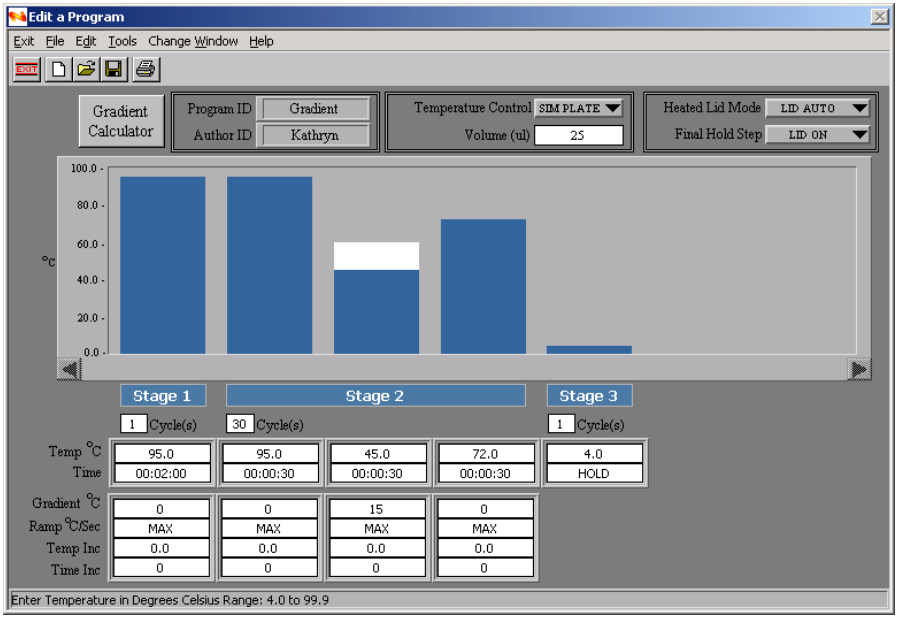
Why access the Configure Network Window?

- To install new blocks to a network
- To delete blocks from a network
- To rename existing blocks with a new "Block ID"
- To set the number of PCR run from each block stored in a log via the 'Log Options' menu

What can I access from the Configure Network Window?

- The previous Window by pressing Exit
- The 'Log Options' menu

3.7.3 Edit a Program Window



How do I access the Edit a Program Window?

- Via the buttons in the Main Window
- Via the Edit drop down menu on the Main Window
- If already open, via the Change Window drop down menu from any Window

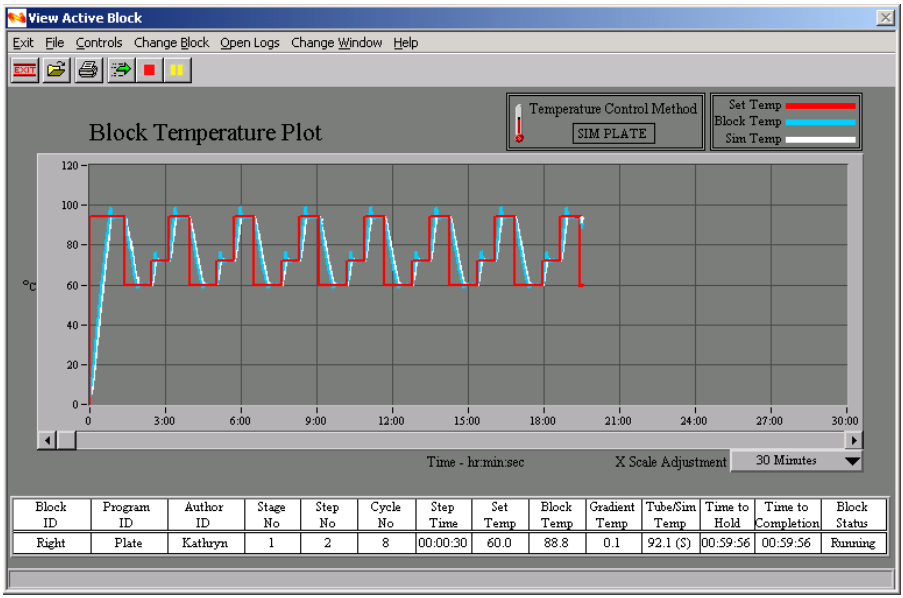
Why access the Edit a Program Window?

- To view existing programs
- To edit existing programs
- To create new programs
- To choose temperature control modes
- To control heated lid operation

What can I access from the Edit a Program Window?

- All other open windows via the Change Window drop down menu
- The Main Window via the Change Window drop down menu
- The previous window by pressing Exit
- The Gradient Calculator via the Gradient Calculator button or the Tools drop down menu
- The Write Protection dialogue box via Open in the File menu. Right mouse click on the program and select Properties.

3.7.4 View Active Block Window



How do I access the View Active Block Window?

- By pressing the button in the Main Window
- Via the Active drop down menu on the Main Window
- If already open, via the Change Window drop down menu from any Window

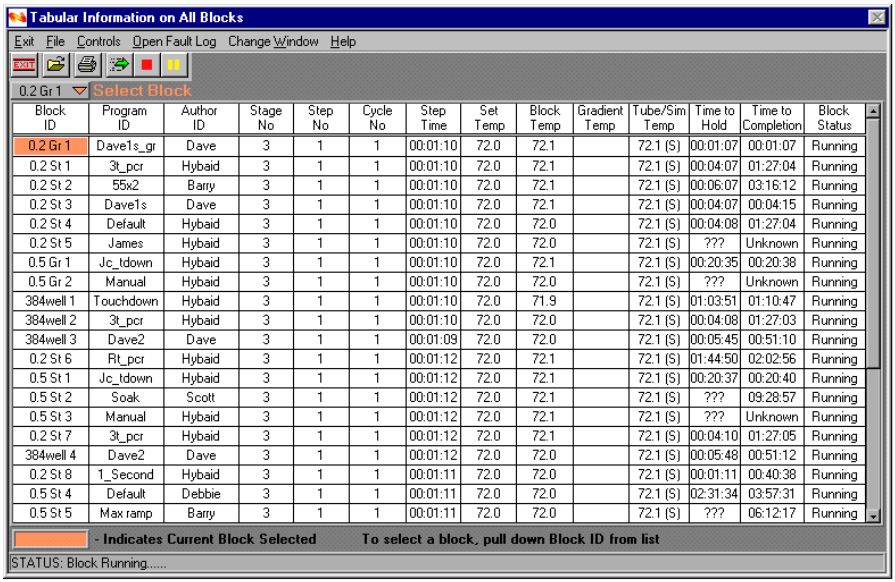
Why access the View Active Block Window?

- To view any block in detail
- To view block, tube and set temperature in both graphical and tabular formats
- To see cycle information, including end of run time for a specific block
- To download a stored program to a selected block
- To run, stop or pause a program on a selected block
- To eject/close the block on the MBSR

What can I access from the View Active Block Window?

- All other open Windows via the Change Window drop down menu
- The Main Window via the Change Window drop down menu
- The previous Window by pressing Exit
- The Fault log from the Open Logs drop down menu
- The Logged Data from the Open Logs drop down menu
- The logged block data from the Open Logs option, then View Logged Data

3.7.5 Tabular Information on All Blocks Window



Block ID	Program ID	Author ID	Stage No	Step No	Cycle No	Step Time	Set Temp	Block Temp	Gradient Temp	Tube/Sim Temp	Time to Hold	Time to Completion	Block Status
0.2 Gr 1	Dave1s_gr	Dave	3	1	1	00:01:10	72.0	72.1		72.1 (S)	00:01:07	00:01:07	Running
0.2 St 1	3t_pcr	Hybaid	3	1	1	00:01:10	72.0	72.1		72.1 (S)	00:04:07	01:27:04	Running
0.2 St 2	55x2	Barry	3	1	1	00:01:10	72.0	72.1		72.1 (S)	00:06:07	03:16:12	Running
0.2 St 3	Dave1s	Dave	3	1	1	00:01:10	72.0	72.1		72.1 (S)	00:04:07	00:04:15	Running
0.2 St 4	Default	Hybaid	3	1	1	00:01:10	72.0	72.0		72.1 (S)	00:04:08	01:27:04	Running
0.2 St 5	James	Hybaid	3	1	1	00:01:10	72.0	72.0		72.1 (S)	???	Unknown	Running
0.5 Gr 1	Jc_tdown	Hybaid	3	1	1	00:01:10	72.0	72.1		72.1 (S)	00:20:35	00:20:38	Running
0.5 Gr 2	Manual	Hybaid	3	1	1	00:01:10	72.0	72.0		72.1 (S)	???	Unknown	Running
384well 1	Touchdown	Hybaid	3	1	1	00:01:10	72.0	71.9		72.1 (S)	01:03:51	01:10:47	Running
384well 2	3t_pcr	Hybaid	3	1	1	00:01:10	72.0	72.0		72.1 (S)	00:04:08	01:27:03	Running
384well 3	Dave2	Dave	3	1	1	00:01:09	72.0	72.0		72.1 (S)	00:05:45	00:51:10	Running
0.2 St 6	Rt_pcr	Hybaid	3	1	1	00:01:12	72.0	72.1		72.1 (S)	01:44:50	02:02:56	Running
0.5 St 1	Jc_tdown	Hybaid	3	1	1	00:01:12	72.0	72.1		72.1 (S)	00:20:37	00:20:40	Running
0.5 St 2	Soak	Scott	3	1	1	00:01:12	72.0	72.1		72.1 (S)	???	09:28:57	Running
0.5 St 3	Manual	Hybaid	3	1	1	00:01:12	72.0	72.1		72.1 (S)	???	Unknown	Running
0.2 St 7	3t_pcr	Hybaid	3	1	1	00:01:12	72.0	72.1		72.1 (S)	00:04:10	01:27:05	Running
384well 4	Dave2	Dave	3	1	1	00:01:12	72.0	72.0		72.1 (S)	00:05:48	00:51:12	Running
0.2 St 8	1_Second	Hybaid	3	1	1	00:01:11	72.0	72.0		72.1 (S)	00:01:11	00:40:38	Running
0.5 St 4	Default	Debbie	3	1	1	00:01:11	72.0	72.0		72.1 (S)	02:31:34	03:57:31	Running
0.5 St 5	Max ramp	Barry	3	1	1	00:01:11	72.0	72.0		72.1 (S)	???	06:12:17	Running

How do I access the Tabular Information on All Blocks Window?

- By pressing the button in the Main Window
- Via the All drop down menu on the Main Window
- If already open, via the Change Window drop down menu from any Window

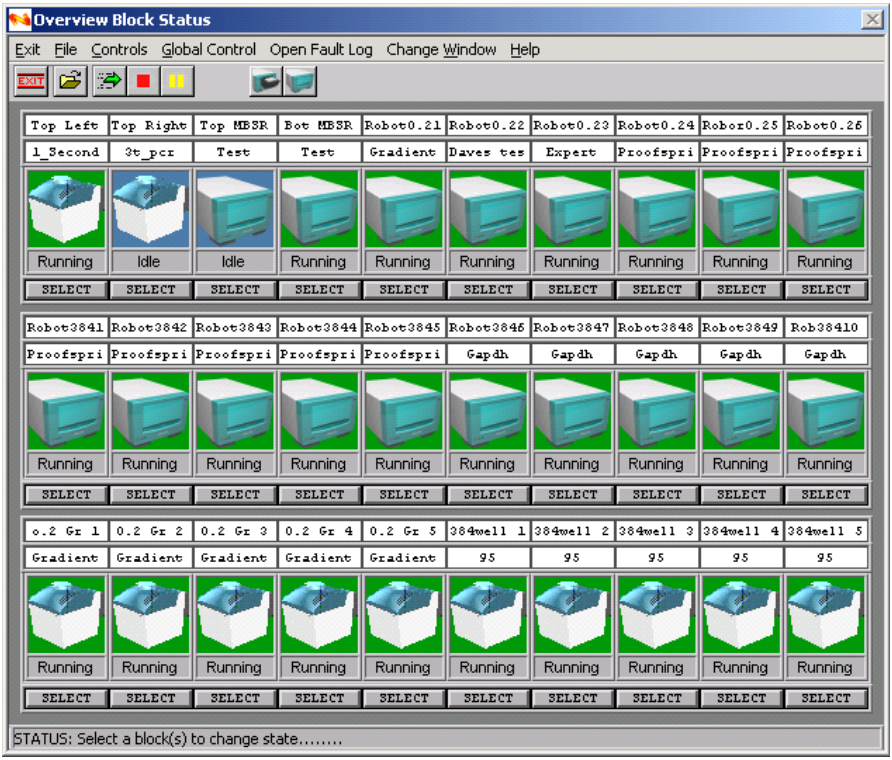
Why access the Tabular Information on All Blocks Window?

- To see in a tabular form, the details of every block at once including:
  - The current program being run on each block (program name and author)
  - Temperature and cycle information
  - Time left until a hold step
- To download a program to a block
- To run, stop or pause a program on a selected block
- To eject/close the block on the MBSR

What can I access from the Tabular Information on All Blocks Window?

- All other open Windows via the Change Window drop down menu
- The Main Window via the Change Window drop down menu
- The previous Window by pressing Exit
- The Fault log from the Open Fault Log drop down menu

3.7.6 Overview Block Status Window



How do I access the Overview Block Status Window?

- Via the buttons in the Main Window
- Via the Overview drop down menu on the Main Window
- If already open, via the Change Window drop down menu from any Window

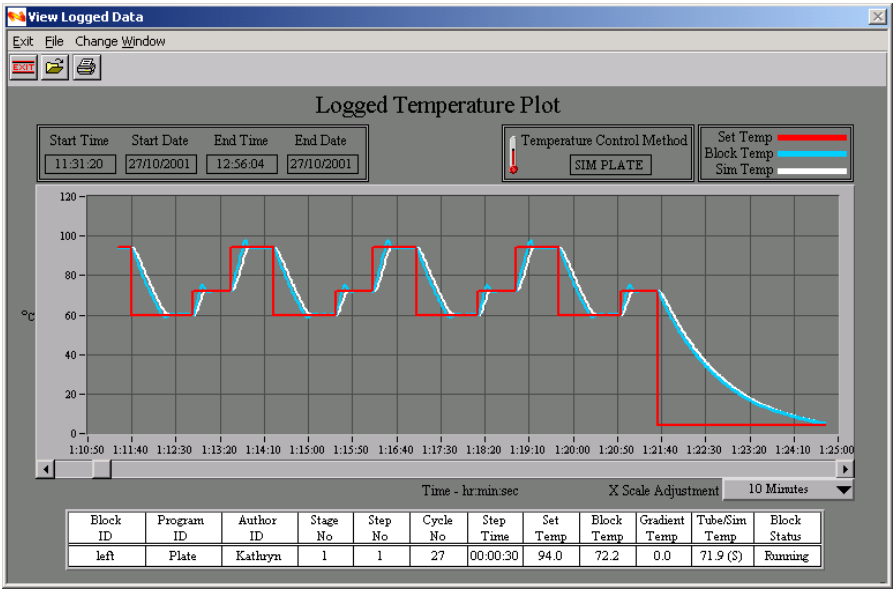
Why access the Overview Status Window?

- To view the status of all blocks via word and color coding
  - Blue – idle
  - White/Green flashing – paused
  - Yellow – preheating
  - Red – faulty
  - Green – running
  - White – block turned off

What can I access from the Overview Block Status Window?

- All other open Windows via the Change Window drop down menu
- The Main Window via the Change Window drop down menu
- The previous Window by pressing Exit
- The Fault log from the drop down menu
- The Global Control Function from the 'Global Control' option on the menu bar

4.7.7 View Logged Data Window



How do I access the View Logged Data Window?

- Via the Open Logs drop down menu in the View Active Block Window
- If already open, via the Change Window drop down menu from any Window

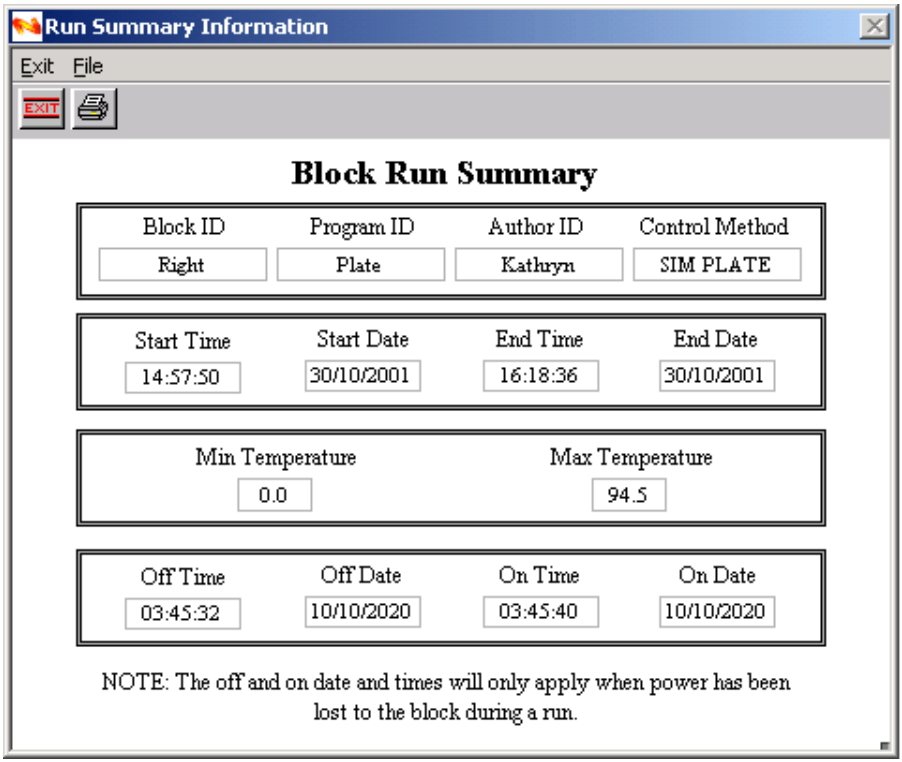
Why access the View Logged Data Window?

- To view the logged data of all previous PCR runs from all blocks including:
- The full trace of the whole PCR run on a scalable graph
- The start time and date and the end time and date
- Block tube and set temperature
- Cycle information

What can I access from the View Logged Data Window?

- The Run Summary Table via the File menu
- All other open Windows via the Change Window drop down menu
- The Main Window via the Change Window drop down menu
- The previous Window by pressing Exit

3.7.7 Block Run Summary Window



How do I access the Block Run Summary Window?

- Via the File menu in the View Logged Data Window
- If already open, via the Change Window drop down menu from any Window

Why access the Block Run Summary Window?

- To view a summary of logged data of a previous PCR runs including:
  - The length of a run and maximum and minimum temperatures
  - The start time and date and the finish time and date
  - The block name, program name and program author
  - Status of the block during the run, including the reporting on block power failures (Power Off and Power On times and dates)

What can I access from the Block Run Summary Window?

- All other open Windows via the Change Window drop down menu
- The Main Window via the Change Window drop down menu
- The previous Window by pressing Exit

4. Troubleshooting

4.1 Error Messages

Fault	Description	Action
Comms Error	No response received from block	Check communications to the block and the block is switched on when carrying out commands
Response Error	A response was received from the block, but it was not expected	No user action required.
Block Thermistor	The block thermistor is faulty or damaged	Contact Thermo Electron.
Heat Sink Thermistor	The heat sink thermistor is faulty or damaged	
Tube Thermistor	The tube thermistor is faulty or damaged	
Lid Thermistor	The lid thermistor is faulty or damaged	
Gradient Thermistor	The gradient thermistor is faulty or damaged	
Program Invalid	The program downloaded is incorrect or corrupt	Check the program and block type and download program again
Block Drive Error	The drive circuitry is faulty or damaged	Contact Thermo Electron.
Block ID Error	The block was not correctly identified	Try reinstalling the block.
Manual Start Time Out	The block has not been started within 90 minutes	The block will automatically return to idle
Hotlid Drive Error	The drive circuitry for the heated lid is faulty or damaged	Contact Thermo Electron.
Heat Sink Over Temperature	The heat sink has overheated	

4.2 Check the Volume in the Tube Thermistor

Check the volume of mineral oil in the control tube (a vial of suitable mineral oil is provided or alternatively Sigma molecular biology grade mineral oil, M5904 or equivalent, can be used). Do not use aqueous solutions in the control tube. Too much oil in the control tube will result in overshoots in the sample tube temperatures, whilst too little oil will result in a time lag in the samples achieving temperature. The volume of oil in the control tube should match that in the reaction tubes (including any oil overlay). Repeated overshoots at the denaturation temperature during temperature cycling will reduce the activity of the thermostable enzyme resulting in poor yields of product. The correct position for the control tube is position G1.

4.3 Check Location of Thermistor within the Control Tube

Always ensure the thermistor probe is located centrally in the control tube and immersed in the liquid. If pushed against the side it will be measuring the temperature of the microcentrifuge tube and not the sample temperature.

4.4 Check the Fit of the Tube in the Block

The MBS blocks accommodate most types of reaction tubes. The tube thermistor supplied with the MBS is mounted in an OmniTube, which should be changed periodically depending on usage, as the fit of the tube will deteriorate with time. Reaction tubes should be distributed evenly in the block. If you are using a reaction tube that has not been recommended, check its fit in the MBS block before use. You should also remount the thermistor probe in this tube to ensure that your samples and the control tube are matched.

4.5 Check through the Program

Before running a program, access the 'Edit a Program' function to check that the correct cycling parameters have been entered.

4.6 Optimization of Protocols

The capability of the MBS programming enables protocol optimizations to be performed very rapidly. Typically, temperature cycling protocols may consist of three distinct steps:

1. Denaturation at an elevated temperature (usually 90-95° C).
2. Annealing at a temperature dictated by the melting temperature (Tm) of the oligonucleotides.
3. Extension from the primer at a temperature dictated by the optimum temperature of the thermostable enzyme being used.

These three steps are typically repeated for twenty to thirty cycles depending on the amount of starting template.

4.7 Denaturation

The denaturation step at each cycle must be sufficient to denature the target DNA completely, including G-C rich regions. However, the effect on the enzyme activity of repeated high temperature incubations should also be considered. An extended initial denaturation step, (3 minutes at 95° C, before enzyme addition) will denature complex high molecular weight DNA template, but for later cycles this should be reduced to a maximum of 30 s at 92-95° C. Optimization of the denaturation step is the most critical factor when transferring a protocol from a block control machine to tube control.

4.8 Annealing

The annealing temperature depends on the size and nucleotide composition of the oligonucleotides used. In general it varies between 50° C and 70° C and as a rough guide should be 5°C below the Tm. This may be calculated approximately using the following formula:

$$Tm = 2 \times (A + T) + 4 \times (G + C)$$

A difference in the annealing temperature of as little as 1°C can affect the specificity of a reaction. It is therefore recommended that a range of temperatures be tested to optimize the annealing temperature for each primer and template combination. This is best achieved using a gradient block.

4.9 Extension

The extension temperature is largely dependent upon the optimum temperature of the enzyme chosen and is usually in the range 70-75° C (see data sheet from manufacturer). The time required depends on the length of product being synthesized.

4.10 Runs using Simulated Control Methods

4.10.1 Simulated Tube

Enter the total reaction volume per tube including any oil overlay.

If using the polypropylene OmniTube 96 use the simulated tube option and enter the correct reaction volume including any oil overlay.

4.10.2 Simulated Plate

0.2 ml Blocks

For the OmniUltra 96 well microplate on a 0.2 ml block, the volume factor entered is +50. For other 96 well microplates the volume factor entered is the individual sample volume. (NB: Polypropylene OmniTube 96 should be run under Sim Tube Control).

0.5 ml Blocks

For 96 well plates on a 0.5 ml block, for example the Costar ThermowellH, the volume factor will not accommodate the non-optimal fit. Increasing dwell times may rectify the discrepancy, but will need to be individually determined.

384 well Blocks

For 384 well blocks the individual well volume should be used for the volume factor.

5. Maintenance

5.1 General Cleaning

Before using any cleaning or decontamination method except those recommended, please contact your local Thermo Electron office or authorized dealer to check that the proposed method will not damage the equipment.

- All surfaces of the MBS and Heated Lid should be cleaned regularly with a soft cloth, hot water and mild detergent.
- It is important to thoroughly dry all surfaces after cleaning.
- The MBS is not intended for use with aggressive chemicals and on no account should organic solvents be used to clean this machine.
- Dampened cotton buds can be used to remove dirt and debris from individual wells. The wells should be kept clean to maintain optimum heat transfer performance.

5.2 Decontamination

When 35S labelled nucleotides are thermally cycled they break down into lower molecular weight forms which are highly volatile and can permeate through the walls of tubes and microtiter plates, thus contaminating the block and possibly the heater plate of the heated lid.

We therefore do not recommend the use of 35S labels, as replacing a dangerously contaminated block is expensive.

If 35S labels are used, we recommend the following to minimize contamination.

1. Use a mineral oil overlay in all reactions, even when the Heated Lid is used.
2. If using tubes, use only the thick walled variety.
3. Use the MBS in a fume hood, to minimize air contamination.
4. If using microtiter plates, coat the plate's under surface with a thin layer of mineral oil.
5. If radioactivity must be used, the thermal cycling block and Heated Lid surfaces can be decontaminated using a 10% v/v solution of Neutracon (Decon Lab Ltd, Conway Street Hove, East Sussex BN3 3LY Tel: +44(0)1273-739241, Fax: +44(0)1273-722088) or PCC-54 (Pierce Eurochemie B.V Holland). Complete decontamination is unlikely, but low level counts can be achieved by repeated application of a fresh solution of 10% v/v Neutracon to the "Hot" area.

All Control Chassis, Block Unit, and Heated Lid components coming into contact with radioactivity should be decontaminated before re-use or transportation. In the event of returning a contaminated item please contact Thermo's Service Department so that the appropriate handling arrangements can be made.

Thermo Electron recommends that if radioisotopes are to be used equipment must be located in a designated Radiation Area. Local Radiation Safety procedures must be followed at all times.

The use of 35S labelled nucleotides is not covered under our warranty agreement and requires special service arrangements.

5.3 Protection of the User

The MBS has been designed with operation safety in mind. In the rare event of an equipment failure, three levels of protection are built in to ensure the block "fails safe". First, the software sets normal operating ranges for the block and lid. Should this fail, electrical circuitry is in place to ensure that safe temperatures are not exceeded. In the unlikely event of this failing, thermal fuses are fitted to shut off the power supply to damaged components.

5.4 Protection of the Equipment

5.4.1 Fuses

The MBS block power inlet is fitted with two T6.3A fuses (20 mm x 5 mm). If necessary these may be replaced by a qualified person.

5.5 Tube Thermistor Care (excluding MBSR)

The tube thermistor assembly ensures that the programmed temperature profile is accurately and reproducibly achieved within all sample tubes. As a 'sample mimic', it is important that the thermistor is as close a representation as possible to the biological samples. To maintain accuracy and longevity of the tube thermistor Thermo Electron recommends the following:

1. Do change the tube thermistor annually. It may be necessary to change the thermistor more often under heavy usage (e.g. frequent removal of the thermistor from the tube).
2. Do check that the mineral oil volume is the same as the reaction volume including any oil overlay.
3. Do check and replace the control tube if it is showing signs of thermal degradation.
4. Do use the same type of tube for the thermistor tube as for the biological samples.
5. Do make sure the sensor part of the thermistor probe is centrally located at the base of the tube and is fully covered by mineral oil.
6. Use only mineral oil in the thermistor tube.
7. Do not remove the control tube from the cap assembly by pulling the wire; gently lever the tube from the cap.
8. Do not kink the thermistor wire or crush the sensor part of the thermistor probe end.
9. Do not remove the thermistor assembly from the block by pulling on the wire, pull from the plug.

6. Technical Specifications & Ordering Information

6.1 Blocks

6.1.1 MBS Standard Blocks (excluding MBSR)

Description	0.5 ml MultiBlock	0.2 ml MultiBlock	384 Well MultiBlock
Block Capacity	48 x 0.5 ml tubes 96 x 0.3 ml tubes 1 x 96 well plate	96 x 0.2 ml tubes 1 OmniUltra	1 OmniFast 384
Temperature Control Available	Tube control Simulated tube control Simulated plate control Block control		Block control Simulated plate control
Block Temperature Range	4° C - 99° C		
Block Heating Rate	Up to 3° C/Sec		
Block Cooling Rate	Up to 2° C/Sec		
Precision Control	1° C		
Block Uniformity	± 0.4° C within 15 secs		
Heated Lid Temperature Range	95° C - 120° C		
Display Resolution	0.1°C		
Standard Accessories	Tube Thermistor 0.5 ml (HBPXTTM05)	Tube Thermistor 0.2 ml (HBPXTTM02)	None
Ingress Protection Rating	20	20	20

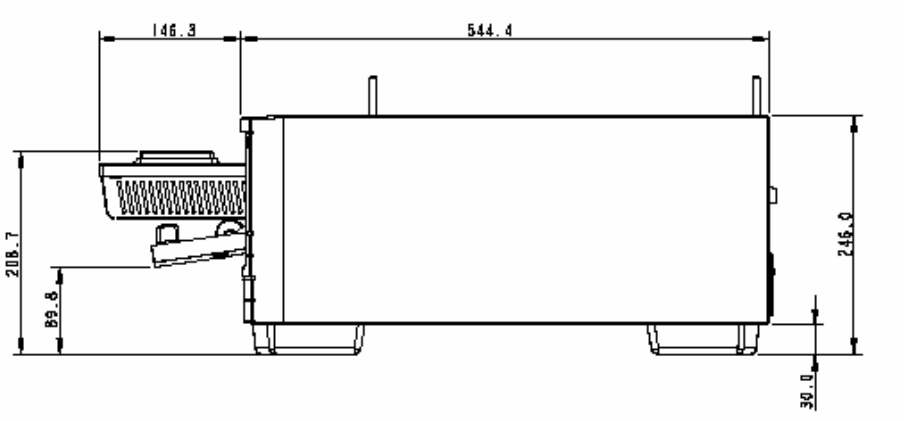
6.1.2 MBS Gradient Blocks (excluding MBSR)

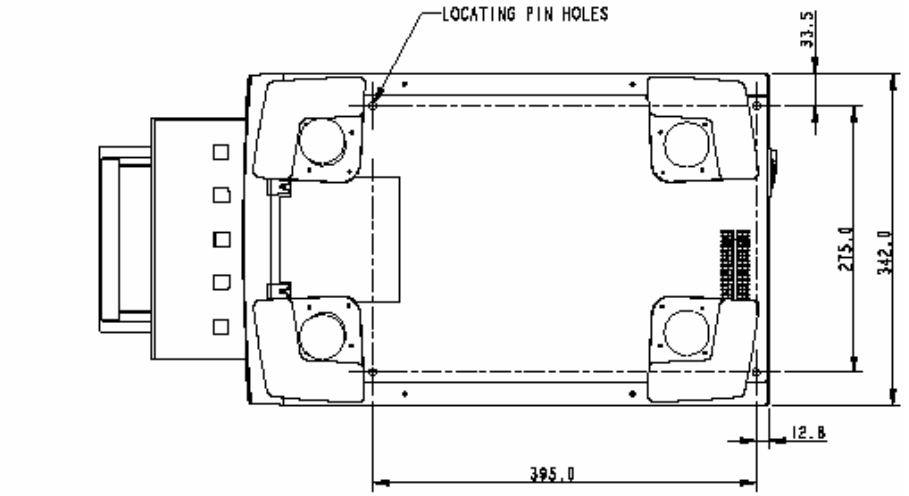
Description	0.5 ml Gradient MultiBlock	0.2 ml Gradient MultiBlock
Block Capacity	96 x 0.5 ml tubes 96 x 0.3 ml tubes 1 x 96 well plate	96 x 0.2 ml tubes 1 OmniUltra 1 OmniTube 96 1 OmniFast 96
Temperature Control Available	Tube control Simulated tube control Simulated plate control Block control	
Block Temperature Range	4° C - 99° C	
Block Heating Rate	Up to 3° C/Sec	
Block Cooling Rate	Up to 2° C/Sec	
Precision Control	1° C	
Block Uniformity	± 0.4° C within 15 secs	
Heated Lid Temperature Range	95° C - 120° C	
Standard Accessories	Tube Thermistor 0.5 ml (HBPXTTM05)	Tube Thermistor 0.2 ml (HBPXTTM02)
Ingress Protection Rating	20	

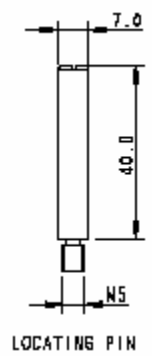
6.1.3 MBSR Blocks

Description	0.2 ml Gradient Block	384 Well Block
Block Capacity	0.2ml x 96 well plate	384 well plate
Temperature Control Available	Simulated plate control	
Block Temperature Range	4° C-99° C	
Block Heating Rate	Up to 3° C/Sec	
Block Cooling Rate	Up to 2° C/Sec	
Precision Control	0.1° C	
Block Uniformity	±4° C within 15s	
Heated Lid Temperature	105° C	
Heated Lid Operation	Auto operation	Auto operation
Gradient Facility	Yes	No
Gradient Temperature Range	Up to 15° C	N/A
Robot Compatible	Yes	
Standard Accessories	1 x 4 Locating pins (HBMBSRLP)	1 x 4 Locating pins (HBMBSRLP)
Ingress Protection Rating	21	

6.1.4 MBSR Dimensions and Footprint







6.2 Programming

Number of programs	N/A
Maximum number of program stages	35
Maximum number of steps per stage	44
Maximum programmed dwell time	18 hrs
Time increment/decrement	Yes
Temp increment/decrement	Yes
Temperature ramping	Yes
Pause facility	Yes
Autostart facility	Yes
Run “end time” calculations	Yes
File protection	Yes
Gradient software	Yes
Non-MBSR Power	550W
Dimensions (WxDxH)	200x300x290 mm
Weight	8.4 kg
MBSR Power	550W
Dimensions (WxDxH)	342x545x246 mm
Weight	20.6 kg

6.3 Working Conditions

Ambient temperatures of 4° C to 34° C
Power requirements: 550W at 115/230V a.c. ±10% and 50/60Hz.
Satisfies the requirements of BS EN 61010-1:1993.

NOTE: When an MBS block is removed from a cold room, it should be left to equilibrate for 2-3 hrs to avoid condensation.

6.4 Consumables

Consumables	Pack Size	Description	Catalogue Number
Sealing Systems			
TDX Tape	100	Sealing tape for polypropylene plates	HBTDTAPE100
Compression Pad	1	Foam pressure pad for use with tape sealing system	HBTDSFOAM
OmniSeal TD Mat	5	Reusable 96 well sealing mat	HBTDMTSRS5

Plasticware

Consumables	Pack Size	Description	Catalogue Number
Plates			
OmniFast 96	25	Polypropylene skirted 96 well plate	HBTC8002N
OmniFast 384	50	Polypropylene skirted 384 well plate	HBTC3840N
OmniTube 96	25	Single piece polypropylene plate	HBTC6002N
Tubes (excluding MBS^{R})			
OmniTube 0.2 ml	1000	0.2 ml individual tubes with integral domed caps	HBTC3372N
OmniTube 0.2 ml	1000	0.2 ml individual tubes with integral flat caps	HBTC6202N
OmniTube 0.5 ml	1000	0.5 ml individual tubes with integral domed caps	HBTC4895N
OmniTube 0.5 ml	1000	0.5 ml individual tubes with integral flat caps	HBTC3505N
OmniStrip 0.2 ml	2000	0.2 ml strips of 8 tubes & caps	HBTC2662N
OmniStrip 0.3 ml	2000	0.3 ml strips of 8 tubes & caps	HBTC4043N
Racked OmniTubes	25	For 0.3 ml 96 well plates (caps not included)	HBTC4073N
OmniTube Caps	2400	For all 0.2 ml and 0.3 ml OmniTube products	HBTC6022N

We recommend that domed cap tubes be used when the temperature control is set to Active Tube and flat cap tubes are used under Simulated Tube Control (excluding MBSR).

7. Sealing Systems

7.1 The OmniSeal TD Mat & TDX Tape:

7.1.1 Overview

Thermo offers two sealing systems to suit individual preferences. The TDX Tape single use adhesive tape suitable for use with 96 well and 384 well systems, and the OmniSeal TD Mat, a reusable silicone rubber mat designed for 96 well systems only.

7.1.2 How to use TDX Tape

TDX Tape

Clear in color and designed for use with polypropylene plates such as OmniTube 96, OmniFast 96 or OmniFast 384.

TDX tape cannot be used on polycarbonate plates as it will bind irreversibly to the polycarbonate.

To secure contact with the heated lid of the MBS and TDX Tape must be used in combination with the reusable TD Compression Pad (HBTDSFOAM) – not applicable to the MBSR.

7.1.3 Sealing a 96/384 Well Plate

1. The tape can be applied to 96/384 well plates by positioning over one of the short edges and peeling back the lining material, allowing the adhesive layer to fall on to the plate. This should be possible without introducing creases. However, before heating, the adhesive is soft enough to be repositioned without adverse effects.
2. The tape should be firmly anchored by pressing over each well. This can be done using a soft roller or by finger pressure.
3. Once in the machine (not MBSR), the Compression Pad must be placed on top of the sealed plate. The Compression Pad performs a dual function: It ensures that the tops of the sealed wells reach the correct temperature and under compression it ensures the sealing between wells is intact. Close the lid and select the “Plates” setting.

7.1.4 Removing the TDX Tape

Prior to removing the TDX Tape from a plate, ensure there is no condensation of the solution inside the wells or on the plugs of the tape by either:

1. Removing the 96 well plate from the block and cooling to 4° C.
2. Cooling down the PCR block to 4° C (if possible).
3. Heating the sample to 35° C for 30 minutes.

This will minimize the risk of well to well contamination when removing the tape from the 96 well plate.

The TDX Tape is most easily removed while the 96 well plate is in a rack or still on the machine. The sheet should be peeled back from one corner diagonally across the plate using a single smooth action. The tape is easily removed and therefore is especially suitable for applications which require additions of reagents part way through the reaction, for example when performing reverse transcription and amplification in two stages.

7.1.5 Resealing Using TDX Tape

TDX Tape is designed for single use. Once heated and compressed, the backing conforms to the plate and cannot be easily repositioned. Reuse is therefore not advised.

7.2 OmniSeal TD Mat

7.2.1 Cleaning & Sterilization Procedures

The OmniSeal TD Mat (Catalog No.: HBTDMTSRS5) is used to seal 96 well plates when using the Heated Lid. Mats can be cleaned and sterilized using the procedures described below.

Soak for 1 min. in either 10% hypochlorite solution, or 0.1M hydrochloric acid solution, then rinse with distilled water. Dry inside an oven at up to 80°C if required. Sterilize in an autoclave at 121° C for 15 minutes.

7.2.2 Sealing a 96 Well Plate

OmniSeal TD Mats have 96 plugs in the underside. They are spaced so that they fit into the wells of a 96 well plate.

The plugs are shaped to expand sideways in order to seal all 96 wells of a 96 well plate, when sufficient pressure is exerted to the upper surface of the mat by the Heated Lid.

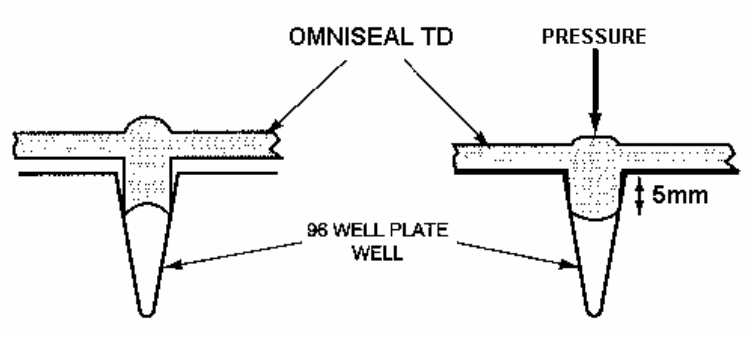


Figure 7.1: Showing how the OmniSeal TD Mat seals the wells of a 96 well plate.

7.2.3 Removing the OmniSeal TD Mat

To minimize the risk of well to well contamination, remove the OmniSeal TD Mat from the 96 well plate whilst the plate is in a rack or on the machine.

7.2.4 Reusability of the OmniSeal TD Mats

The OmniSeal TD Mat can be re-used at least 5 times. Repeated washing and autoclaving of the Mats causes them to crack around the edges. When this starts to happen, they should be discarded.

NOTE: The number of times an OmniSeal TD Mat can be reused is reduced considerably if it is cleaned with alcohol or detergents, or if exposed to UV irradiation.

7.3 Limitation of Microtiter Plate Operations

Some users have reported loss of volume when using microtiter plates for thermal cycling. Recent experiments performed at Thermo have demonstrated that volume loss is independent of sample volume and occurs through the sides of the polycarbonate microtiter plate (all manufacturer plates tested) and is not due to poor sealing. Typically, volume loss of 3μl per well in a 30-cycle reaction can be expected.

If you are working with small sample volumes it may be advisable to switch to polypropylene consumables instead of polycarbonate. These losses, however, are not seen with the OmniUltra Plate.

8. Glossary of Terms

Active Tube Control	This type of control is dependent upon the external thermistor probe located in the microfuge tube. This allows very accurate monitoring and control of sample tube temperature. This feedback control loop allows the transition to target temperature to be accelerated by creating a temperature gradient between the block temperature and the tube temperature.
Block Control	The temperature of the cycling block is monitored and controlled by the thermistor mounted on the block. Because of the time lag between the block and sample reaching temperature we recommend that tube control be used.
Heated Lid	A standard fitting which allows oil free cycling in 0.2, 0.3, 0.5 ml tubes and 96/384 well plates. The auto-height adjusting heated plate in contact with the top of the reaction vessels maintains the temperature above 100ºC, preventing evaporation of the sample.
Hold	A HOLD step may be specified at the end of a stage. Samples are held at this temperature until the green arrow button is pressed to resume the program. This function can be used to hold samples at a fixed temperature while a reagent is added before temperature cycling starts.
Peltier Device	A thermoelectric device incorporating a bismuth telluride semi-conductor crystal array. On passing a current through the crystal, one surface of the crystal is heated, the other cooled. Reversing the current reverses the heat flow.
Ramp Rate (Temperature Ramping)	Ramping precisely controls the rate of change of sample temperature (ºC/sec). This is useful for limiting the rate of change of temperature, to allow partial extension of short or degenerate primers.
Sample Volume	When using simulated tube control methods, the sample volume is entered to ensure precise block heating and cooling.
Simulated Plate Control	Simulated Plate Control incorporates an algorithm to reduce time to reach target temperature, using precise overshoots in block temperature for each set point. Refer to Section 4.5 for instructions on how to use this control option.
Simulated Tube Control	Simulated Tube Control incorporates an algorithm to reduce the time to reach target temperature, using precise overshoots in block temperature for each set point. The calculated sample temperature inside sample tubes and block temperature are displayed during the run.
Stage	One stage of a program consists of one or more steps up to a maximum of 44. A stage may be repeated for temperature cycling. Up to ten stages may be used in one program, and stage to stage linking is automatic.
Step	A step consists of a programmed temperature and time interval. Time increment and ramp rate may also be specified if required.
Sub-ambient Block	The aluminium block used in the MBS. This uses Peltier devices for heating and cooling. Operating range: 4° C to 99° C.
Temperature Increment/Decrement	May be used to increase/decrease a temperature set point at successive cycles. E.g. a decrement of 0.1° C will give 60, 59.9, 59.8, 59.7.... °C. This is useful for touchdown PCR reactions where stringency at the annealing step is decreased as the reaction proceeds.
Thermistor	A thermistor is a resistor, the resistance of which changes with temperature. It can therefore be used as a very accurate temperature probe with small liquid volumes.

Time Increment/ Decrement	May be used to change a time interval to each repeat cycle of a specific step. E.g. an increment of 10 s on a 60 s step will give time intervals of 60, 70, 80, 90, 100…. seconds. This is useful when increasing an incubation step to allow for the depletion of an enzyme.
Touchdown PCR	A gene amplification procedure where the annealing temperature is initially high (e.g. 65° C) to achieve high specificity at the start of the reaction. The temperature (and therefore the stringency) can then be reduced with successive cycles (by e.g. 0.5° C/Cycle). Once the concentration of the desired product has been increased it will be preferentially amplified over less specifically primed products.

9. Pre-Set Programs on the MultiBlock

The MBS is provided with a list of default programs consisting of commonly used cycling protocols. They are as follows:

DEFAULT
94°C for 1 min
94°C for 30 s
55°C for 30 s } 30 cycles
72°C for 30 s
72°C for 5 min
4°C hold

RT_PCR
48°C for 20 min
94°C for 2 min
94°C for 30 s
55°C for 30 s } 30 cycles
72°C for 1 min
72°C for 5 min
4°C hold

TOUCHDOWN
94°C for 1 min
94°C for 1 min
65°C for 30 s } 4 cycles
72°C for 30 s
94°C for 30 s
65°C for 30 s (-1°C per cycle) } 16 cycles
72°C for 30 s
94°C for 30 s
50°C for 30 s } 5 cycles
72°C for 30 s
72°C for 5 min
4°C hold

GRADIENT (to be used with gradient block)

94°C for 1 min

94°C for 30 s
45-60°C for 30 s } 30 cycles
72°C for 30 s

72°C for 5 min

4°C hold

MANUAL

37°C hold step

1_SECOND_3T_PCR (One Second Dwell Time Protocol)

This protocol can be used with Thermo AGSGold DNA Polymerase.

94°C for 2 min.

94°C for 1 s
55°C for 1 s } 30 cycles
72°C for 1 s

72°C for 2 min.

4°C hold

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