GenePix® 4000B Microarray Scanner

User Guide

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Molecular Devices

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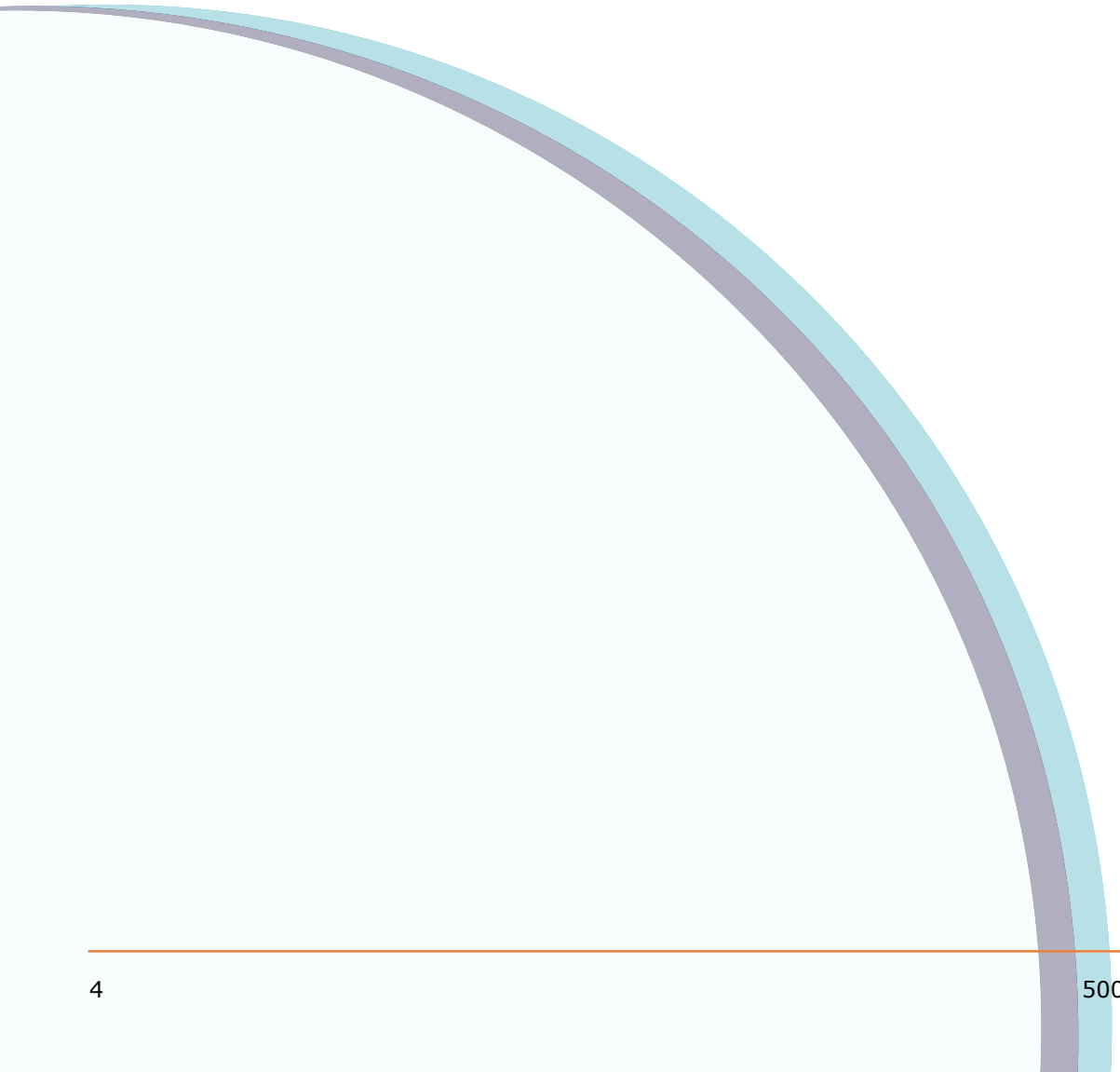


Contents

Foreword

The foreword describes the intended audience for the manual. It defines the typographical conventions used in the manual and lists the related documentation.

Who This Manual Is For

This manual is written for the GenePix® 4000B Microarray Scanner user. The manual contains the information required to install the scanner, turn it on, and perform maintenance procedures.

Conventions

Within the scope of this manual, the following typographical conventions are used:

WARNING! A warning indicates an operation that can cause personal injury if precautions are not followed.

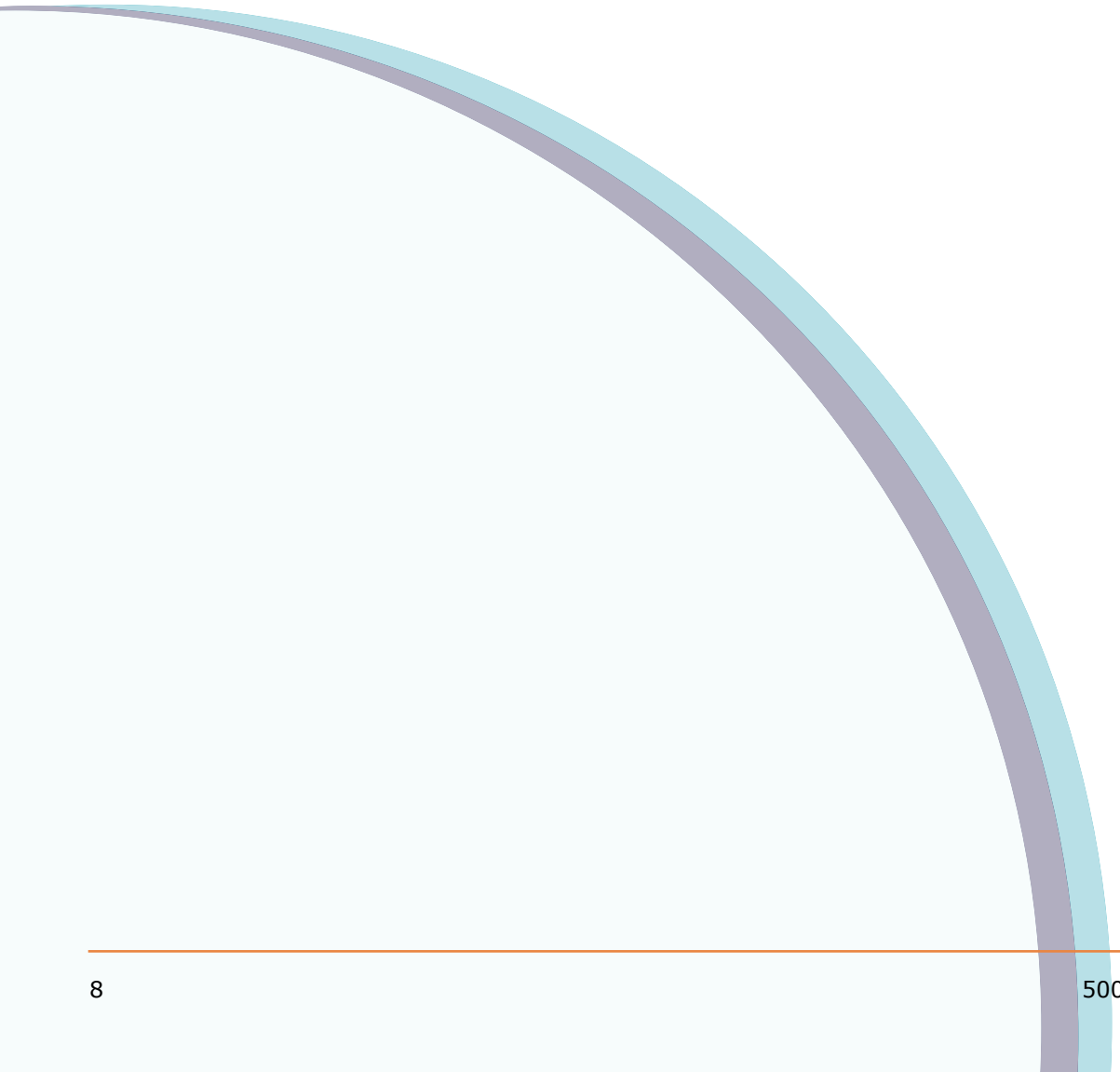
CAUTION! Indicates an operation that can cause damage to the instrument, device, or data, if precautions are not followed.

Tip! Provides useful information that helps apply the techniques and procedures in the text to your specific needs, and provides shortcuts, but is not essential to the completion of a procedure.

Note: Provides essential information for the completion of a procedure.

Related Documentation

The customer documentation for the GenePix 4000B Microarray Scanner includes the *GenePix® Pro Software Reference Guide, Safety Practices* manual, and the *GenePix® Pro online Help*.



1 Principles of Operation

The GenePix® 4000B Microarray Scanner uses a laser-excitation based fluorescence scanning and imaging system. The laser-based scanning system operates by slowly moving the slide in the Y–direction, while the slide is rapidly scanned in the X–direction. The design of the scanner allows you to scan a 25 mm by 75 mm slide at up to two wavelengths:

- 10 µm resolution in approximately 6.5 minutes
- 5 µm resolution in approximately 13 minutes

Scanner Features

- Two internally installed laser-excitation sources
- A user-attenuated lasers allowing 10%, 33%, and 100% transmission
- Simultaneous scanning of two wavelengths
- User-adjustable focus
- Precisely controlled automatic laser power monitoring with pixel-by-pixel correction
- Data Scan pixel resolution from 5 µm to 100 µm
- Fast Preview Scan pixel resolution at 40 µm
- 16-bit ultra-low-noise digitization
- Dynamic range of 10^4
- Two filters (670DF40 and 575DF35)
- Capacity for one standard 1 inch by 3 inch (25 mm by 75 mm, or 26 mm by 76 mm) microscope slide-based microarray
- Full integration with GenePix Pro Software and Acuity® Microarray Informatics Software

Scanner Components

The main components of the GenePix 4000B Microarray Scanner are:

- Protective enclosure
- Optics
- Lasers
- Optical path
- Emission filters
- PMTs (photo-multiplier tubes)
- Status lights
- External power supply

Figure 1-1 GenePix® 4000B Microarray Scanner

For detailed information about each component, see Instrument Components on page 25.

Scanner Specifications

Table 1-1 Specifications

Sample type	Standard microscope slides (1 inch by 3 inches, 25 mm by 75 mm or 26 mm by 76 mm; 0.9 to 1.2 mm thick)
Maximum scan area	22 mm by 72 mm
Maximum resolution	5 µm
Scan mode and order	Simultaneous scanning of two wavelengths
Detector	Dual PMTs
Signal digital output	16-bit
Image format	Single or multi-image TIFF
Computer interface	USB 2.0
Scan time	6.5 minutes at 10 µm resolution
Dynamic range	Four orders of magnitude
Uniformity	Plus or minus 10%
Dimensions	13 inches wide by 8.7 inches high by 17.4 inches long (36 cm by 22 cm by 44 cm).
Weight	35.8 lb (16.2 kg)
Power supply	Line voltage: 85 to 264 VAC (110 to 340 VDC) universal voltage input
Line frequency	50 to 60 Hz
Power	85 W, Fuse: 2.0 A slow. 5 to 20 mm

Site Requirements

Table 1-2 Site Requirements

Temperature	50 to 86ºF (15 to 30ºC)
Humidity	5 to 95% non-condensing
Power	Universal input 50 to 60 Hz, 100 to 240 VAC, 2A max
Space	25.6 inches deep by 16.9 inches wide by 13.4 inches high (65 cm by 43 cm by 34 cm). An additional 6 inches (15.2 cm) for clearance.
Bench support	Sufficient to support 40 lbs (18 kg) with minimal vibration
Uninterruptible power supply (UPS)	We recommend the use of a 325 VA UPS

Installation and Operation

2

The GenePix® 4000B Microarray Scanner should be unpacked and in position on a flat level surface before performing any of the installation procedures. Perform the procedures in the following order.

- Unpack the scanner and position it on the bench
- Install the software
- Turn on the scanner
- Insert a slide

Unpacking the scanner and positioning it on the bench

The GenePix 4000B Microarray Scanner is packed in a specially designed crate. Retain the crate and the packing materials. If the scanner requires repair, you must return it in the original packaging. If the crate has been damaged in transit, you must retain it for inspection by the carrier.

WARNING! Shock Hazard. In an emergency, users must be able to safely disconnect the main power cable without moving the scanner. Locate the scanner so that either the power outlet or the scanner's appliance connector is accessible.

WARNING! The scanner weighs 35.8 pounds (16.2 kg). To avoid potential injury, a minimum of two people are needed to lift the scanner.

WARNING! Biohazardous Material. Do not operate the scanner in an environment where potentially damaging liquids or gases are present, or in a room with a temperature below 15°C.

To unpack the scanner and position it on the bench

1. Open the crate and remove any foam blocks used to protect the scanner from excessive shock and vibration during shipping.

CAUTION! Do not touch or loosen any screws or parts other than those specifically described in the instructions. Doing so can cause misalignment and voids the scanner warranty.

Note: Do not tilt or slide the scanner when transferring it from the crate to its final position on a bench or desk.

2. Lift and then place the scanner on a flat level surface, away from direct sunlight, dust, drafts, vibration, and moisture. Carefully move the scanner to its final position.

Tip! For proper ventilation and cooling, leave at least six inches of space between the back of the scanner and the nearest object or surface.

3. Plug the USB cable into the USB type B port on the back of the scanner, and the USB type A port on the control computer.

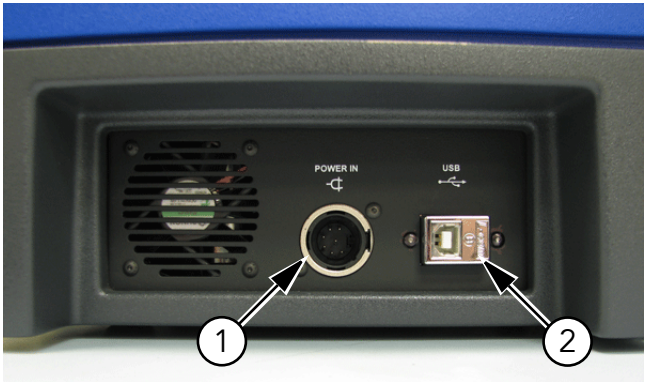


Figure 2-1 Connections on back of the scanner

Item	Name
1	Round port for main power supply cable
2	USB type B port

4. Plug the round connector of the cable leading from the external power supply into the matching power port on the back of the scanner. Plug the main power supply cable into the external power supply, and the lab's power outlet.

   We recommend you use a surge protector between the main power cable and the power outlet.

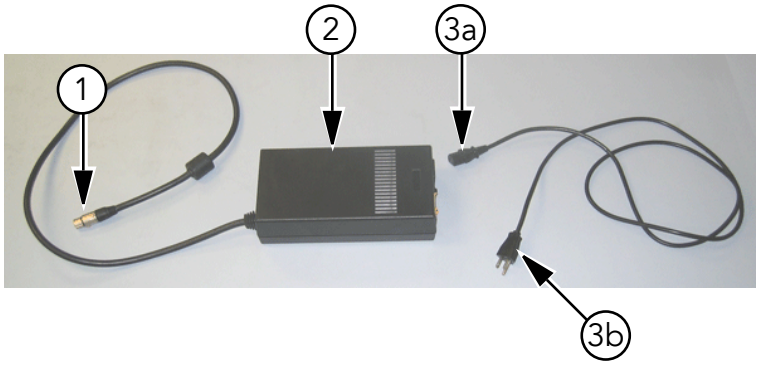


Figure 2-2 Main power supply cable components

Item	Name	Description
1	Round connector	Plug into the matching power port on instrument's back panel
2	External power supply	
3	Main power cable	Plug end 3a into the external power supply. Plug end 3b into the lab's power outlet.

Installing the Software

Before operating the scanner, you must install the GenePix Pro Software on a Windows-based control computer.

To install the software

1. Locate the GenePix Pro Software CD.

Note: You must be fully aware of the information contained in the *GenePix® Pro Software Reference Guide* to ensure a successful software installation. The installation instructions are provided in hard copy, and soft copy on the GenePix Pro Software CD.

2. Read the supplied software installation instructions.
3. Insert the GenePix Pro Software CD into the computer. Follow the InstallShield Wizard instructions to install the GenePix Pro Software.

CAUTION! Do not to insert the security key into the control computer until after the GenePix Pro Software has been installed.

4. Install the security key. For more information, see the *GenePix® Pro Software Reference Guide* included with the GenePix Pro Software.

Turning on the Scanner

Proper startup of the GenePix 4000B Microarray Scanner includes a functional checkout procedure to confirm that the scanner is performing according to the specifications established during commissioning before the scanner left the factory.

To turn on the scanner

1. Make sure the slide door is closed.
2. Turn on the scanner power switch.

Tip! The GenePix 4000B Microarray Scanner power switch is located on the instrument's external power supply module.

3. Turn on the control computer.
4. Click **Start > Programs > Molecular Devices > GenePix Pro,** and then click the **Report** tab.
5. Click **Functional Checkout** in the Hardware Diagnostics Reports area, and follow the steps in the Wizard.

   The GenePix Pro Software automatically logs hardware performance events into the Hardware Diagnostics Report every two hours during operation.

Note: For optimum performance, allow the GenePix 4000B Microarray Scanner to warm up for 15 minutes before scanning slides with the GenePix Pro Software.

Inserting a Slide

The slide holder is a precision component designed to ensure proper focusing and field uniformity. Improper handling can damage the slide holder and affect imaging performance.

CAUTION! Never touch the slide holder while it is moving. Never force the slide holder closed, or apply significant pressure to it.

To insert a slide

1. Move the slide door to the left.

   The slide holder moves forward into the load position.
2. Raise the top of the slider holder.

3. With the slide held between your thumb and finger, carefully place the slide, feature-side down into the slide holder.

Note: Make sure the barcode on the slide is facing the front of the scanner.

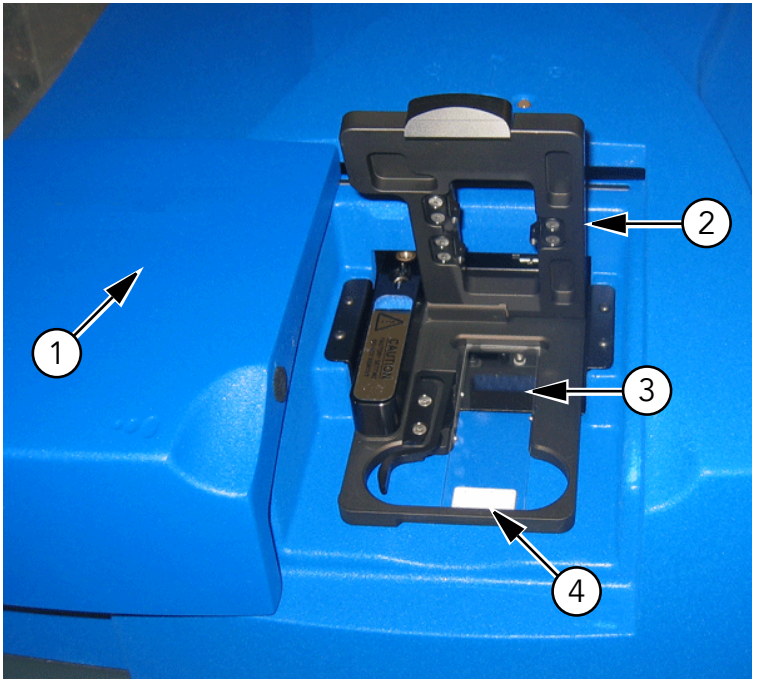


Figure 2-3 Slider holder

Item	Name	Description
1	Slide door	In open position
2	Slide holder	In load position
3	Slide	Place feature-side down
4	Barcode	Barcode is facing the front of the scanner

4. Lower the top of the slide holder.

CAUTION! Make sure the top of the slide holder is lowered before closing the slide door.

5. Move the slide door to the right.
   The slide holder moves into the scan position.

Shutting Down the Scanner

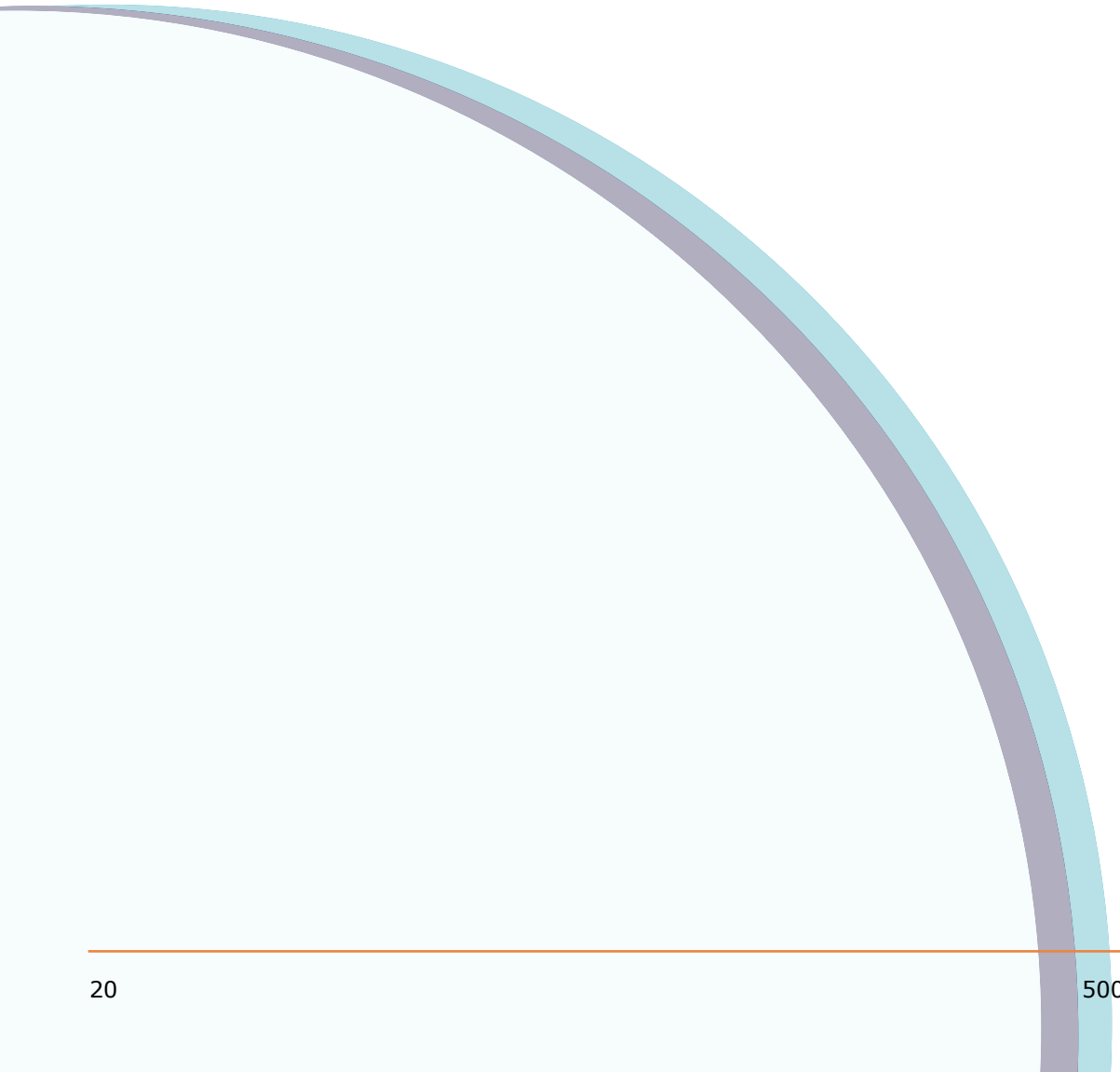
Proper shutdown of the GenePix 4000B Microarray Scanner ensures the scanner or software are not damaged.

To shut down the scanner

1. Close the GenePix Pro Software.
2. Turn off the scanner power switch.

Tip! The GenePix 4000B Microarray Scanner power switch is located on the instrument's external power supply module.

3. Turn off the control computer.



Maintenance & Troubleshooting

3

The GenePix® 4000B Microarray Scanner requires very little maintenance.

WARNING! Biohazardous Material. It is your responsibility to decontaminate the scanner, as well as any accessories, before requesting service, or before returning the scanner or any components.

WARNING! Biohazardous Material. Never perform any maintenance procedures on the scanner in an environment where potentially damaging gases or liquids are present.

WARNING! Shock Hazard. Do not remove the protective enclosure or any covers marked with the high-voltage warning symbol.

WARNING! Shock Hazard. Always turn the power switch off and disconnect the main power cable before performing any maintenance procedures.

WARNING! The scanner weighs 35.8 pounds (16.2 kg). To avoid potential injury, a minimum of two people are needed to lift the scanner.

CAUTION! Do not touch or loosen any screws or parts other than those specifically described in the maintenance procedures. Doing so can cause misalignment, and voids the scanner warranty.

Moving the Scanner

If the GenePix 4000B Microarray Scanner must be moved within the lab, or returned to the factory for service, the scanner must be prepared for transport.

If you do not have the original shipping crate, contact us and a new crate can be provided for an additional charge.

To move the scanner

CAUTION! Always use the Park Scanner utility prior to moving the scanner. Failure to park the scanner can result in misalignment or damage of the optical system.

1. Remove any slide from the slide holder.
2. Close the GenePix Pro Software.
3. Click **Start > Programs > Molecular Devices > GenePix Pro > GenePix Utilities.**

   The GenePix Utilities window appears
4. Click **Park Scanner for Shipping.**

   A message box appears informing you that the scanner has been successfully parked.

   CAUTION! Always turn off power to the scanner using the power switch. Do not turn off the power by unplugging the main power cable from the power outlet.
5. Turn off the scanner power switch.

Tip! The GenePix 4000B Microarray Scanner power switch is located on the instrument's external power supply module.

Tip! Do not turn on the power switch after parking the scanner.

6. Unplug the main power cable (including the external power supply) from the back of the scanner and the lab's power outlet.

   CAUTION! Never unplug the USB cable unless the scanner has been turned off and the main power cable has been disconnected.

7. Unplug the USB cable from the back of the scanner and the control computer.

CAUTION! Do not tilt or stand the scanner on its end when moving it within the lab, or transferring it from the bench to the shipping crate.

8. If the scanner is to returned for service, pack the scanner in its original shipping crate. Otherwise, have two people lift the scanner or place it on a rolling cart to transport it to the new location.
9. For information on installing the scanner in a new location, see Unpacking the scanner and positioning it on the bench on page 13.

Note: When the scanner is turned on, the scanner is automatically removed from park state.

Interlock Failure Symptoms

WARNING! Laser Hazard. Never operate the scanner if you suspect an interlock has failed. Doing so exposes the user to laser radiation.

If an interlock fails, do not operate the 4000B Microarray Scanner. Shut down the scanner and contact Technical Support immediately.

The following are typical symptoms of an interlock failure.

- The mirror and lens assembly keep moving below the slide after the door is opened.
- The blue Scanning LED on the front of the scanner does not extinguish when the slide door is open.
- The GenePix Pro Software does not recognize the scanner or the slide.
- You can no longer hear the distinctive metal-on-metal sound that the mechanical interlock makes when it falls into place. This occurs when the slide loading door has opened about one quarter inch.

Fuses

If the GenePix 4000B Microarray Scanner does not start up, a fuse might no longer be functioning. If you suspect a fuse has stopped functioning, contact Technical Support.

Instrument Components

A

The main components of the GenePix® 4000B Microarray Scanner are described below.

Protective enclosure

The protective enclosure protects the user from exposure to laser radiation, high voltage, and moving parts.

WARNING! Laser Hazard! Do not remove the protective enclosure. Operating the scanner with the protective enclosure removed exposes the user to laser radiation.

Optics

The GenePix 4000B Microarray Scanner uses a laser-excitation based fluorescence scanning and imaging system. The optical system consists of excitation light, mirrors, lenses, filters, and photo-detection.

Lasers

In the GenePix 4000B Microarray Scanner, laser excitation is provided by individual 532 nm and 635 nm lasers. These wavelengths correspond to the ideal wavelengths used to excite the fluorophores Cy3 and Cy5 (GE Healthcare), or other fluorophores with similar fluorescent characteristics. The individual lasers have been selected because of their superior optical performance and reliability. Since the performance of such lasers is often sensitive to external temperature fluctuations, the scanner uses an active temperature stabilization design to minimize temperature-based laser fluctuations. The GenePix 4000B Microarray Scanner automatically corrects fluorescent intensity for normal variations on a pixel-by-pixel basis.

With the GenePix 4000B Microarray Scanner, laser power can be set to 100%, 33%, or 10% of the total laser output. This feature can be used when the fluorescence of the sample is too bright, or when photobleaching is a problem.

Optical Path

Excitation laser light is directed onto the slide after passing through a series of filters and mirrors. While laser light is by definition very narrow band, the GenePix 4000B Microarray Scanner employs additional optical filters to make sure that no spurious excitation light is directed onto the slide. If the laser light impinges on an appropriate fluorophore bound on the slide, emission light of a longer wavelength is emitted. These emission photons are directed back through the optical system where they pass through another bandpass filter before reaching the photodetector.

One problem faced by dual scanning systems is crosstalk, where the two different wavelengths of light are not sufficiently separated in the scanning system. For example, emission light from one fluorophore can be recorded by the detector for the second fluorophore, or spurious excitation light for the first fluorophore can bleed back in into the detector for the second fluorophore. Crosstalk is often a concern when using a pair of fluorophores that have similar spectral properties. The result can be an erroneous contribution of fluorescence from one optical channel to the other.

The GenePix 4000B Microarray Scanner employs two approaches to reduce crosstalk to negligible levels. First, the filter sets and excitation lasers have been carefully chosen to ensure that crosstalk between the two fluorophores is minimized. Second, and more importantly, the patented optical design guarantees that the light paths of the two channels are spatially separated.

The GenePix 4000B Microarray Scanner includes a user-controlled focusing feature. The focal plane at the zero position is at the surface of the glass slide, with a total depth of focus of 64 µm, equally distributed on both sides of the focal plane (depth of focus is defined as the range over which the signal is within 50% of the maximum signal). The GenePix Pro Software allows you to set the focal plane from –50 µm to +200 µm relative to the zero position. Positive positions refer to focal planes above the microarray surface while negative positions are within the slide.

Emission Filters

The GenePix 4000B Microarray Scanner is equipped with two lasers. Each laser (red and green) includes a matching pre-installed emission filter.

- Standard red (660 nm to 690 nm; 670DF40)
- Standard green (558 nm to 593 nm; 575DF35575)

Each emission filter is optimized for the emission spectrum of the respective dye, designed to reject laser light at OD 8 (optical density) for each respective laser excitation, and reject broad-spectrum light at OD 5.

PMT

The GenePix 4000B Microarray Scanner uses two high-sensitivity, low-noise PMTs to detect the emitted fluorescent light. A PMT converts incident photons into electrons through the photoelectric effect. When an incident photon impinges on the active surface of the PMT (the photocathode), an electron is generated. The electron flows through a series of electron multipliers (dynodes) to the anode. The amount of current that flows from the anode is directly proportional to the number of photons at the photocathode.

The amount of amplification a PMT can produce depends on the number of dynodes in the PMT, and the voltage that is applied to the PMT. It is possible to achieve a signal amplification of 10^7. Increasing the PMT voltage setting in the GenePix Pro Software, increases the signal amplification of the PMT.

Note: When the PMT gain is increased, the sensitivity to non-specific fluorescence is also increased, as is the electronic noise in the system. The increase in noise can often be overcome by line averaging; however, the result is decreased acquisition speed and increased photobleaching. In general, the signal-to-noise ratio is not improved by increasing the PMT voltage.

The output of a PMT is typically linear over a wide range of incident light intensities. However, there is a very non-linear relationship between the voltage of the PMT and the PMT output. Therefore, a slide scanned at a PMT voltage of 800 V will not be twice as bright as the same slide scanned at 400 V.

Signal amplification by the PMT is controlled by adjusting the PMT gain in the GenePix Pro Software. The PMT gain is related to the PMT voltage by a calibration constant such that:

PMT gain = PMT voltage / calibration constant

The calibration constant is derived by performing the system calibration in Hardware Diagnostics and will ensure that the scanner performance is self-consistent over time. For an uncalibrated scanner the constant is 1.000.

Status Lights

Three lights on the front of the GenePix 4000B Microarray Scanner indicate status.

- Device standby
- Scanning
- Eject

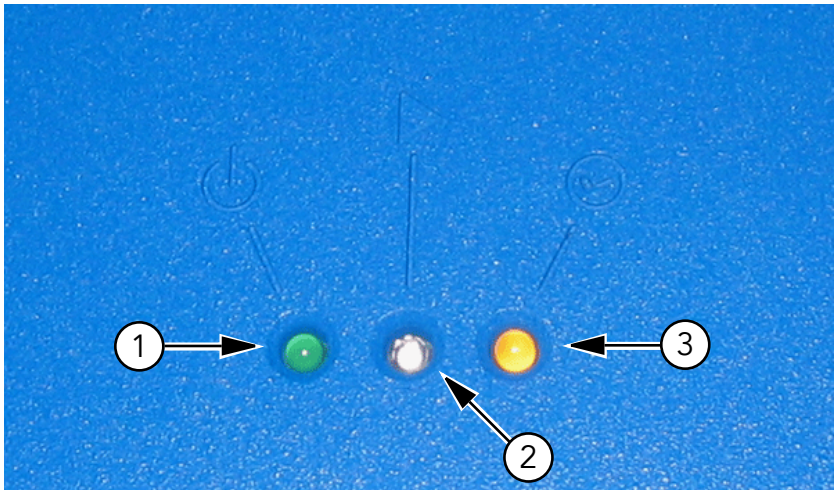


Figure A-1 Status lights – GenePix® 4000B Microarray Scanner

Item	Color	Name	Description
1	Green	Device standby	The scanner is powered up and ready to scan a slide
2	Blue	Scanning	The slide is in the load position and is being scanned
3	Orange	Eject	The slideholder is ready to be unloaded

Instrument Performance Factors

B

Spatial resolution, and dynamic range and detection limits are two key principles of the GenePix® 4000B Microarray Scanner operation.

Spatial Resolution

In the GenePix 4000B Microarray Scanner, a single beam of light is rapidly scanned across the microarray, and a composite pixelated image is created from the digitized signals from the PMT. The spatial resolution of the system refers to the size of the pixel. It determines the minimum distance that can be distinguished between two points of light. In the GenePix 4000B Microarray Scanner, the smallest spatial resolution is 5 µm.

It is possible to change the resolution of data scans by changing the pixel size setting in the GenePix Pro Software. It is important to note that this does not change the size of the scanning beam. The GenePix 4000B Microarray Scanner implements changes in resolution by increasing the Y-direction step size and averaging the X-direction samples over multiples of 5 µm spots. For example, to change the pixel size from 5 µm to 10 µm, the instrument only scans every second X-direction line (by increasing each Y-direction step from 5 µm to 10 µm). Consequently a 10 µm scan is twice as fast as a scan at 5 µm, and outputs the average of each adjacent pair of 5 µm spots in the X-direction as the value of a single 10 µm pixel. Similarly, a scan at 20 µm pixel size is implemented by scanning every fourth X-direction line (and so is four times faster than at 5 µm) and using the average of four contiguous 5 µm spots on each X-direction line as the value of a 20 µm pixel.

Data scan pixel size can be increased beyond 20 µm in increments of 20 µm, but the scanning pattern (and therefore scan duration) remains the same. Every fourth X-direction line is scanned, and the spots within the larger pixel size are averaged. For example, a 60 µm data scan will average the values of thirty-six 5 µm spots (three X-direction lines contribute twelve 5 µm spots each) to calculate the value for each 60 µm pixel. See Figure B-1 Data scans on page 30.

Changing the resolution of a data scan can often be useful if you have large features and you do not need to scan at maximum resolution. As the resolution is decreased, so is the final image size (in megabytes). However, keep in mind that you need to acquire enough pixels for each feature in order to make accurate measurements.

For a preview scan, the same 5 µm spots are scanned. However the Y-direction step size is increased to 40 µm, and each 40 µm preview scan pixel is an average of eight contiguous 5 µm spots in the X-direction. This speeds image acquisition for balancing the PMT gains while minimizing photobleaching.

Figure B-1 Data scans.is a representation of how the GenePix 4000B Microarray Scanner samples 5 µm spots and averages them to calculate the values of the image pixels for the various scan modes and pixel sizes. On the left side of each image pair is the raw data scan from the scanner. Each square represents a 5 µm by 5 µm spot as scanned by the 5 µm laser beam. On the right are the resultant image pixels at various resolutions. The shading indicates the spots that are scanned as well as the corresponding pixels in the final image.

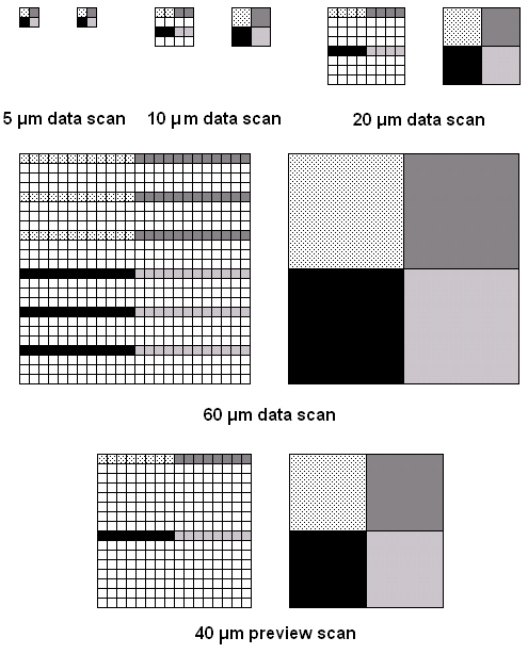


Figure B-1 Data scans

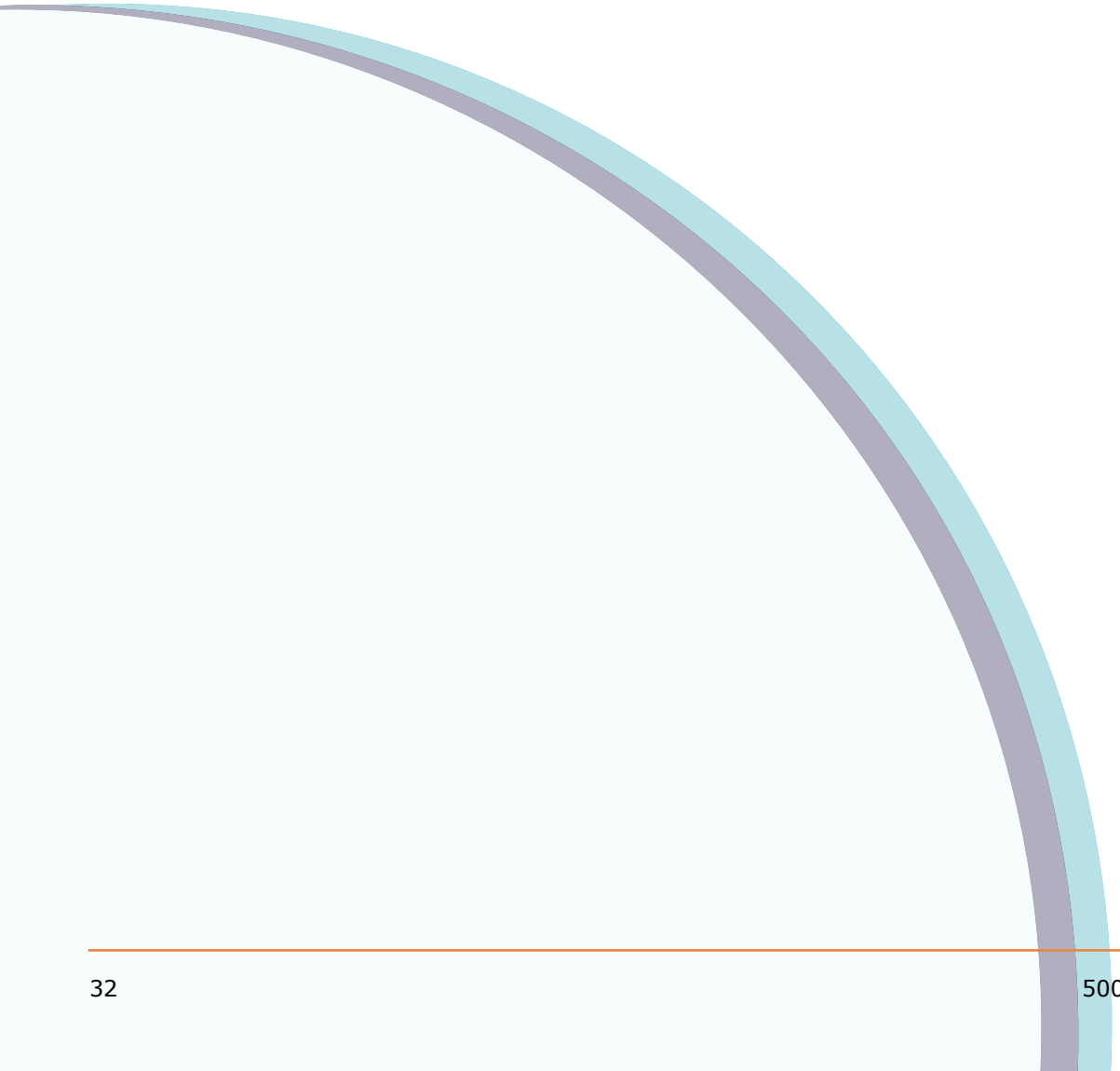
Dynamic Range and Detection Limit

The dynamic range of an instrument is the range of signal values over which the instrument can accurately measure change. The GenePix 4000B Microarray Scanner has a dynamic range of 10^4. Dynamic range is determined primarily by the design of the PMT. In the 4000B Microarray Scanner, the voltage (gain) applied to the PMT can be adjusted to change the amplification of the signal as electrons pass through the PMT. The optimum working range is 400 V to 1000 V. If the gain is set below this range, the probability that each impinging photon will be converted to an electron is diminished, and the dynamic range will be limited on the low end. Above this range, noise begins to interfere with accurate signal measurement. Both of these cases will limit the dynamic range.

The dynamic range of an instrument is often considered in conjunction with its detection limit. The detection limit is defined as the dye concentration for which the signal-to-noise ratio = 3. Signal-to-noise ratio is calculated as:

(Signal – Background) / Standard Deviation of Background

Although you might be able to see features below this level, the quantitative accuracy diminishes significantly.



Warranty and Service

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Molecular Devices is committed to ensuring the highest quality of our products and customer service.

If you have any problems with your GenePix® 4000B Microarray Scanner, contact our Technical Support group. In the US, contact us at 1-800-635-5577. For locations outside the United States, please contact your local sales representative.

Standard Warranty

Molecular Devices warrants its non-consumable hardware products to be free from defects in materials and workmanship for 12 months from date of invoice or date of purchased installation visit, whichever is later. The warranty covers the cost of parts and labor to repair the product.

Please keep the shipping container for future use. If you require an additional container, one can be provided for an additional charge. Products returned to Molecular Devices for repair should be properly packaged with transportation charges prepaid. Molecular Devices will pay for the return shipping of the product to the customer. If the shipment is to a location outside the United States, the customer is responsible for all duties, taxes and freight clearance charges.

The warranty is valid when the product is used for its intended purpose and does not cover products which have been modified without approval from Molecular Devices, or which have been damaged by abuse, accident or connection to incompatible equipment.

This warranty is in lieu of all other warranties, expressed or implied.

Out-of-Warranty Repair Service

Out-of-warranty repair service is available. Contact Molecular Devices Technical Support for more information.

Optional Service Agreement

Purchasing an optional Service Agreement extends the coverage of the Standard Warranty. Contact the supplier for current rates.

Technical Support

In order to receive the best possible technical support, we encourage you to register on our website www.moleculardevices.com, especially if your sales transaction was conducted by a purchasing agent. Your name in our database ensures that we can contact you directly with important information about product upgrades and special promotional opportunities. Once you register your name, you can then register your instrument.

If you require advice on the use of your GenePix 4000B Microarray Scanner, do not hesitate to contact Molecular Devices Technical Support. Visit the website http://support.moleculardevices.com and complete the Technical Support Request form. You can also phone Molecular Devices Technical Support.at 800-635-5577. Follow the prompts for "GenePix Technical Support".

At Molecular Devices, staying in touch with all our customers is a valuable part of our ongoing development process, ensuring the excellence of every product we offer.