

GenePix 4000A

MICROARRAY SCANNER

User's Guide

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QUESTIONS? Phone: +1 (650) 571-9400
 Fax: +1 (650) 571-9500
 E-mail: tech@axon.com
 Web: www.axon.com

Important Safety Information for the GenePix 4000A



Laser Safety

- Do not stick anything into the openings or vents of the GenePix 4000A, other than loading the slide. You may cause an interlock to fail.
- Do not attempt to move any parts below the slideholder. You may cause an interlock to fail.

The Protective Housing

The GenePix 4000A is a Class I laser device. There are higher power lasers embedded inside it, but the user can not access these. Slides can be placed safely in the laser's scanning area because the slide loading door has redundant interlocks which block the beams. There are two

panels on the device which are not interlocked, but these are fastened with screws and require a tool to remove them. They are shown below. Do not remove any screws to open the housing!

- The lasers inside can cause eye damage before you have a chance to blink!
- There are high voltages inside.
- There are no user serviceable parts inside.
- The unit will be damaged if you attempt to open the protective housing.

Interlock Failure Symptoms

If you experience any of the following symptoms, you may have an interlock failure. It is unsafe to continue to use the GenePix 4000A with only one interlock functioning. Please contact Axon Instruments immediately at either of the numbers indicated on the rear panel of the GenePix 4000A.

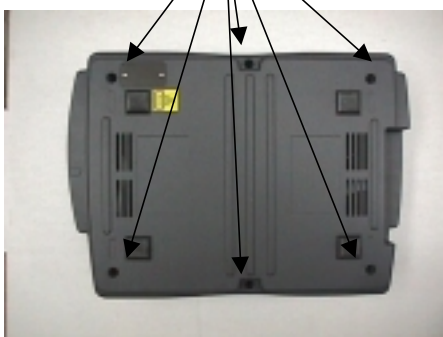
1. Mirror and lens assembly keeps moving below the slide after the door is opened.
2. The blue “Scanning” LED on top of GenePix 4000A doesn’t extinguish when the door is open.
3. The user can’t scan any slides. There are other possible causes too.
4. The user can no longer hear the distinctive metal on metal “clink” that the mechanical interlock makes when it falls into place. This normally happens when the slideloading door has opened about a ¼”.

Non-Interlocked Panels

View of the bottom of the GenePix showing the screws which hold the top part of the protective housing.

DO NOT REMOVE THESE SIX SCREWS!

DANGER
Laser radiation when open
AVOID DIRECT EXPOSURE TO BEAM



View of the bottom of the GenePix showing the access panel near the front end.

DO NOT REMOVE THESE TWO SCREWS!

DANGER
Laser Radiation When Open
AVOID DIRECT EXPOSURE TO BEAM.



Maintenance and Service

No user maintenance is required. No user service is allowed. If there is a problem, please contact Axon Instruments at either of the numbers shown on the label.

List of Controls

This Guide constitutes a list of controls. Caution – use of controls or adjustments or performance of procedures other than those specified herein may result in hazardous radiation exposure.

Embedded Laser Classification and Power

Wavelength	Power	Divergence	Duration	Embedded Laser's Class
532 nm	20 mW	< 1.2 mrad	Continuous	Class IIIb
635 nm	15 mW	0.7 mrad	Continuous	Class IIIb

Electrical Ratings

Input (DC)	Max
+ 15 V	5.5 A
+ 5 V	2.5 A
-15 V	0.5 A

Warning Symbols



Figure 1. Service Contacts and Warnings Label
 Label is affixed at the rear of the GenePix 4000A on the upper half of the protective housing. Actual size.

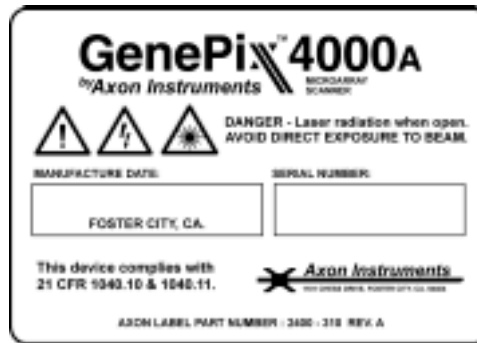







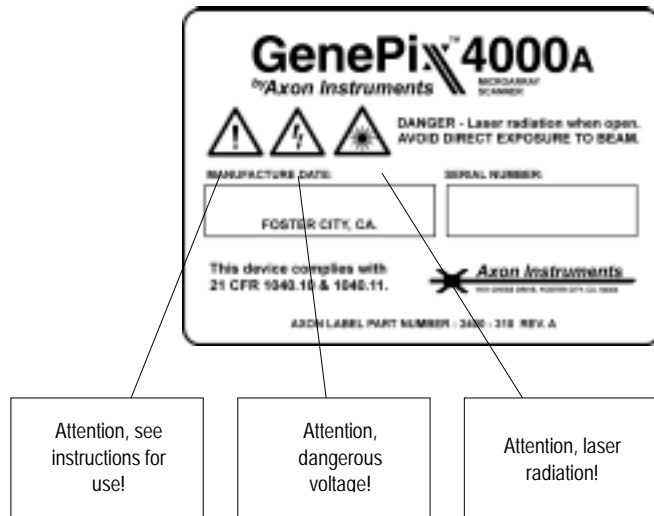
Figure 2. Identification and Certification Label
 Label is affixed at the rear of the GenePix on the lower half of the protective housing. Actual size.



Figure 3. Access Panel Caution Label
 Label is affixed to the bottom of the GenePix alongside the adjustment access panel. Actual size.

Symbol Explanations

	<p>Part of device switched on. This switches on +5 V power only. The ± 15 V power is always present until the power supply is unplugged.</p>
	<p>Part of device switched off. This switches off +5 V power only. The ± 15 V power is always present until the power supply is unplugged.</p>
	<p>Device standby Ready to scan slide. Stage waiting at the start position.</p>
	<p>Scanning.</p>
	<p>Eject. Slideholder ready to be unloaded.</p>



Informations de sécurité importantes sur le GenePix 4000A



Sécurité concernant les Lasers

- Ne rien introduire dans les ouvertures ou aérations du GenePix 4000A, à part une lame de microscope dans le compartiment prévu pour son chargement. Vous pourriez provoquer une défaillance des systèmes de sécurité (systèmes à double verrouillage).
- Ne pas essayer de déplacer une quelconque pièce en-dessous du support de lame. Vous pourriez provoquer une défaillance des systèmes de sécurité.

Boîtier et Sécurité des Personnes

Le GenePix 4000A est un instrument à laser de Classe I. Il incorpore des lasers de puissance, auxquels l'utilisateur ne peut pas accéder.

Les lames peuvent être placées en toute sécurité dans la zone de balayage des lasers : la porte coulissante bloque automatiquement l'émission des rayons lors de son ouverture (double système de sécurité).

Il y a deux accès potentiels sous l'appareil qui ne possèdent pas cette protection : ils sont fermés par des vis et requièrent donc l'usage d'outils pour leur ouverture (voir les figures ci-dessous). N'enlevez aucune vis pour tenter d'ouvrir le boîtier ou pour toute autre raison.

- Les lasers internes peuvent endommager vos yeux avant que vous n'ayez le temps de les fermer !
- Attention ! Présence de haute tension électrique à l'intérieur.
- L'utilisateur ne doit procéder à aucune intervention à l'intérieur du boîtier.
- L'appareil peut être endommagé par une simple tentative d'ouverture du boîtier.

Symptômes Liés aux Problèmes de Verrouillage - Contrôles

L'apparition de l'un des symptômes suivants signe un problème sur la double protection. Il est dangereux de continuer à utiliser le GenePix 4000A si seul l'un des deux verrouillages de sécurité fonctionne. Prière de contacter Axon Instruments immédiatement à l'un des numéros indiqués à l'arrière du GenePix 4000A (voir ci-après).

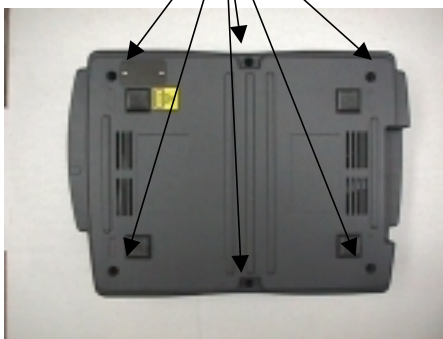
1. L'ensemble miroirs lentilles continue à se déplacer sous de la lame après ouverture de la porte coulissante.
2. La LED "Scanning" (voyant bleu) sur le dessus du GenePix 4000A ne s'éteint pas quand la porte est ouverte.
3. Impossibilité de scanner une lame (d'autres causes peuvent donner ce symptôme).
4. L'utilisateur n'entend plus le bruit métallique caractéristique (clic !) que provoque le verrouillage mécanique lorsqu'il est enclenché. Ce clic s'entend normalement dès que la porte coulissante est ouverte d'un quart de pouce (environ 6 mm).

Accès non verrouillés par la Double Protection

Vue de dessous du GenePix montrant les vis qui maintiennent la partie supérieure du boîtier.

NE PAS RETIRER CES SIX VIS !

DANGER !
Radiation laser lorsque ouvert
EVITER IMPERATIVEMENT
L'EXPOSITION DIRECTE AUX RAYONS



Vue de dessous du GenePix montrant le panneau d'accès - situé vers l'avant.

NE PAS RETIRER CES DEUX VIS !

DANGER !
Radiation Laser lorsque ouvert
EVITER IMPERATIVEMENT
L'EXPOSITION DIRECTE AUX RAYONS



Maintenance et Service

Aucune maintenance de la part de l'utilisateur n'est nécessaire. De plus aucun service de maintenance tierce n'est autorisé. Si un problème apparaît, prière de contacter Axon Instruments à l'un des numéros notés sur l'étiquette (voir ci-dessous).

Liste des Contrôles

Ce guide constitue une liste des contrôles à effectuer régulièrement. Attention ! Tout contrôle, réglage ou tentative de procédures autres que ceux spécifiés ci-dessus peuvent entraîner un risque d'exposition dangereuse à des rayonnements.

Puissance et Classification des Lasers Utilisés

Longueur d'onde	Puissance	Divergence	Durée	Classe des lasers embarqués
532 nm	20 mW	< 1.2 mrad	Continue	Classe IIIb
635 nm	15 mW	0.7 mrad	Continue	Classe IIIb

Consommation Maximale

Entrée (courant continu)	Maximum
+15 V	5.5 A
+5 V	2.5 A
-15 V	0.5 A

Symboles d'alerte (Signalétique)



Figure 1. Adresse et avertissements

Cette étiquette est collée à l'arrière du GenePix 4000A sur la partie supérieure du boîtier (taille réelle).



Figure 2. Identification et étiquette de certification





Cette étiquette est collée à l'arrière du GenePix sur la partie inférieure du boîtier (taille réelle).

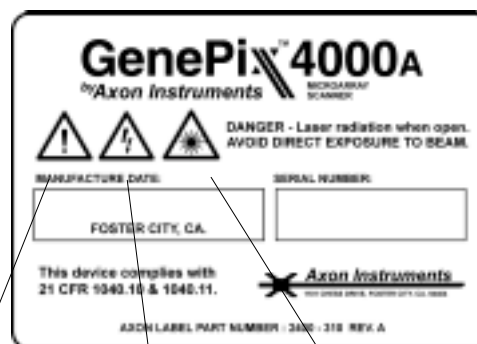


Figure 3. Etiquette de danger d'ouverture

Cette étiquette est fixée sur le bas du GenePix, le long du panneau d'accès aux réglages (taille réelle).

Significations des Symboles

	<p>Sous-ensemble allumé.</p> <p>Ne concerne que le +5 Volts. Le ± 15 Volts est constamment allumé tant que l'alimentation est branchée.</p>
	<p>Sous-ensemble éteint.</p> <p>Ne concerne que le +5 Volts. Le ± 15 Volts est constamment allumé tant que l'alimentation est branchée.</p>
	<p>Appareil en attente.</p> <p>Prêt à scanner une lame. Attend en position de départ.</p>
	<p>Balayage en cours.</p>
	<p>Ejection.</p> <p>Support de lame accessible.</p>



Attention, voir les instructions d'utilisation !

Attention, haute tension !
Danger !

Attention, rayonnement Laser !

Información Importante sobre la Seguridad del GenePix 4000A



Seguridad del Laser

- No inserte ningún objeto en las aperturas o respiraderos del GenePix 4000A diferente de la placa. Puede ocasionar fallas en el circuito de seguridad.
- No intente mover ningún componente debajo de la platina. Usted puede causar fallas en el circuito de seguridad.

La Cubierta Protectora

El GenePix 4000A es un equipo de laser de Clase I. Adentro se localizan láseres de alta potencia fuera del alcance del usuario. Las placas pueden colocarse sin peligro en la región del area de barrido del laser porque la entrada de las placas tiene circuitos de seguridad redundantes que bloquean los rayos de luz. Hay dos paneles en el equipo que no son parte del

circuito de seguridad, pero que están asegurados con tornillos que requieren una herramienta para sacarlos. Estos están indicados mas adelante. No remueva ningún tornillo para abrir la cubierta!

- Los láseres interiores pueden dañar sus ojos antes de que pueda pestañear.
- Interiormente hay altos voltajes.
- En el interior no hay partes que requieran servicio por parte del usuario.
- La unidad se dañará si usted intenta abrir la cubierta protectora.

Síntomas de Daños en el Circuito de Seguridad

Si usted encuentra cualquiera de los siguientes síntomas, el circuito de seguridad podría estar dañado. Es peligroso continuar usando el GenePix 4000A cuando hay sólo un circuito de seguridad funcionando. Comuníquese con Axon Instruments inmediatamente a cualquiera de los números telefónicos indicados en la parte posterior del GenePix 4000A.

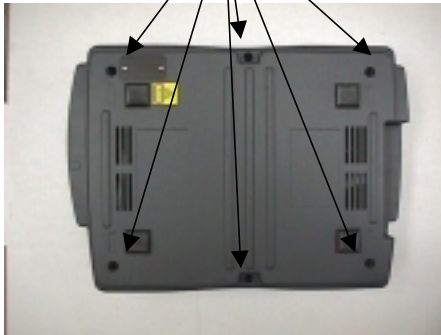
1. El espejo y el montaje de los lentes siguen moviéndose por debajo de la placa después de abrir la puerta.
2. La luz azul emitida por el diodo (“LED”) localizado en la parte superior del GenePix 4000A no se extingue cuando la puerta está abierta.
3. El usuario no puede registrar ninguna placa, aunque hay otras posibles causas.
4. No se puede escuchar el sonido “clinc” característico del contacto entre metales producido por el circuito de seguridad cuando se ajusta en su lugar. Este ocurre normalmente cuando la apertura donde se coloca la placa se abre aproximadamente 6 mm.

Paneles Que No Forman Parte del Circuito de Seguridad

Vista de la base del GenePix mostrando los tornillos que aseguran la parte superior de la cubierta protectora.

NO REMUEVA ESTOS SEIS TORNILLOS!

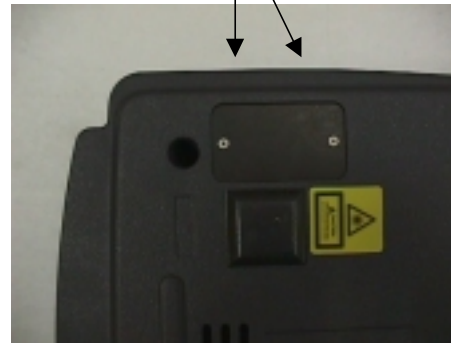
PELIGRO
Radiación con laser si se abre
EVITE EXPOSICIÓN DIRECTA AL RAYO LASER



Vista de la base del GenePix mostrando el panel de acceso cercano al extremo anterior.

NO REMUEVA ESTOS DOS TORNILLOS!

PELIGRO
Radiación con laser si se abre
EVITE EXPOSICIÓN DIRECTA AL RAYO LASER



Mantenimiento y Reparación

No se requiere ningún mantenimiento por parte del usuario. Este no está autorizado para ejecutar ninguna reparación. Si hay algún problema por favor comuníquese con Axon Instruments a cualquiera de los números telefónicos indicados en la etiqueta.

Lista de Controles

Este guía provee una lista de controles. Precaución – el uso de los controles, el ajuste o la ejecución de procedimientos diferentes de los especificados aquí puede resultar en exposición peligrosa a la radiación del laser.

Clasificación y Potencia de los Láseres Incluidos

Longitud de Onda	Potencia	Divergencia	Duración	Tipo de Laser
532 nm	20 mW	<1.2 mrad	Continua	Clase IIIb
635 nm	15 mW	0.7 mrad	Continua	Clase IIIb

Electrical Ratings

Entrada (corriente continua)	Máxima
+15 V	5.5 A
+5 V	2.5 A
-15 V	0.5 A

Símbolos de Advertencia



Figura 1. Etiqueta con Advertencias y Contactos para Reparación

La etiqueta está fijada a la parte posterior del GenePix 4000A en la mitad superior de la cubierta protectora. Tamaño real.

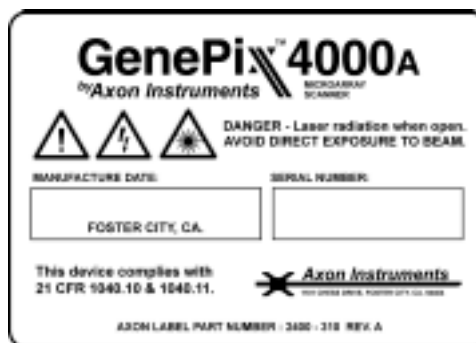


Figura 2. Etiqueta de Identificación y Certificación

La etiqueta está fijada a la parte posterior del GenePix 4000A en la mitad inferior de la cubierta protectora. Tamaño real.

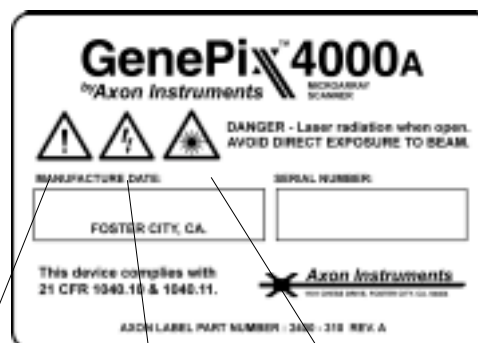


Figura 3. Etiqueta de Precaución del Panel de Acceso

La etiqueta está fijada en la base del GenePix 4000A junto al panel de acceso para ajuste. Tamaño real.

Explicaciones de los Símbolos

	Parte del equipo está encendido. Este interruptor activa solamente el voltaje de +5 V. El voltaje de ± 15 V está siempre presente hasta que se desconecte el suministro de energía.
	Parte del equipo está apagado. Este interruptor apaga solamente el voltaje de +5 V. El voltaje de ± 15 V está siempre presente hasta que se desconecte el suministro de energía.
	El equipo está a la espera ("Standby"). La platina está lista en posición de cargar la diapositiva y empezar.
	Registrando ("Scanning").
	Expulse ("Eject"). La platina está lista para descargar.



Atención, vea instrucciones para su uso!

Atención, voltajes peligrosos!

Atención, radiación del láser!

Wichtige Sicherheitsmassnahmen für "GenePix 4000A"



Lasersicherheit

- Mit Ausnahme des Objektträgers dürfen unter keinen Umständen Gegenstände in die Öffnungen oder Ausgänge des GenePix 4000A gesteckt werden, da sonst ein Versagen der elektrischen Verriegelung verursacht werden könnte.
- Unterhalb des Objektträgers dürfen keine Teile bewegt werden, auch dies könnte ein Versagen der elektrischen Verriegelung verursachen.

Das Schutzgehäuse

Der GenePix 4000A ist ein Laserprodukt der Klasse I. Auf den auf Bereich der im Gerät entstehenden stärkeren Laserstrahlen hat der Benutzer keinen Zugriff. Glasstreifen können sicher in den Laserrasterbereich eingeführt werden. Die sich vor dem Rasterbereich befindende Ladetür enthält eine doppelte elektrische Verriegelung, die den Benutzer des GenePix 4000A vor den Laserstrahlen abschirmt.

Der GenePix4000A enthält zwei Öffnungen, die nicht elektrisch verriegelt, sondern mit Schrauben befestigt sind (siehe nachfolgende Abbildungen). Diese können nur mit der Hilfe

eines Werkzeuges entfernt werden. Entfernen Sie niemals die Schrauben, um das Gehäuse zu öffnen!

- Die im Gerät entstehenden Laserstrahlen können Ihre Augen beschädigen, bevor Sie Gelegenheit haben sich zu schützen!
- Im Gerät entstehen hohe Spannungen.
- Wenn Sie versuchen das Schutzgehäuse zu öffnen, kann dies eine Beschädigung des Gerätes zur Folge haben.
- Es befinden sich im Gerät keine für den Nutzer justierbaren Teile.

Hinweise auf ein Versagen der elektrischen Verriegelung:

Wenn Sie eines der nachfolgend beschriebenen Probleme vorfinden, hat wahrscheinlich eine Verriegelung versagt. Es ist sehr gefährlich den GenePix 4000A zu benutzen, wenn nur eine elektrische Verriegelung funktioniert. Bitte rufen Sie sofort bei Axon Instruments an, sobald eines der unten beschriebenen Symptome auftritt. Die Service-Nummern für Axon befinden sich auf der hinteren Seite des Gerätes.

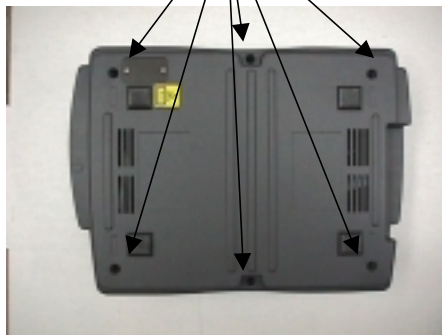
1. Spiegel- und Linsensysteme bewegen sich weiterhin unter den Objektträger nachdem die Tür geöffnet wurde.
2. Die blaue "Scanning" Lichtdiode oben auf dem GenePix 4000A erlischt nicht wenn die Tür geöffnet wird.
3. Das Gerät liest keine Objektträger. (Dies kann auch andere Ursachen haben).
4. Der Benutzer hört nicht mehr das metallene "Klick", welches bei normaler Funktion durch das Einrasten der mechanische Verriegelung ausgelöst wird. Dies passiert normalerweise, wenn die Tür ungefähr 6 mm geöffnet ist.

Geräteöffnungen Ohne Elektrische Verriegelung

Die untere Ansicht des GenePix zeigt die Schrauben welche den oberen Teil des Schutzgehäuses zusammenhalten.

ENTFERNEN SIE DIESE SECHS SCHRAUBEN UNTER KEINEN UMSTÄNDEN!

VORSICHT!!
Laserbestrahlung wenn geöffnet!!
VERMEIDEN SIE DIREKTEN KONTAKT MIT DEM LASERSTRAHL!



Die Ansicht des GenePix zeigt eine Öffnung im vorderen Bereich der Unterseite.

ENTFERNEN SIE DIE ZWEI SCHRAUBEN UNTER KEINEN UMSTÄNDEN!!

VORSICHT!!
Laserbestrahlung wenn geöffnet!
VERMEIDEN SIE DIREKTEN KONTAKT MIT DEM LASERSTRAHL!



Instandhaltung Und Vorsorge

Es ist keine Vorsorge oder Wartung des GenePix 4000A durch den Benutzer nötig. Jede eigenmächtige Reparatur durch den Benutzer ist untersagt und führt zum Erlöschen der Gewährleistung. Falls es ein Problem geben sollte, setzen Sie sich bitte mit Axon Instruments in Verbindung. Benutzen Sie eine der Service-Nummern, die auf dem Etikett auf der Rückseite des Gerätes stehen.

Liste Von Kontrollvorrichtungen

Diese Gebrauchsanweisung enthält eine Liste der Kontrollvorrichtungen. Achtung - Der Gebrauch von Kontrollvorrichtungen oder Einstellungen bzw. die Ausführung von Handlungen außer denen, die in dieser Anweisung beschrieben sind, können zu gefährlichen Strahlungen führen.

Klassifizierung und Intensität der benutzen Laser

Wellenlänge	Stärke	Divergenz	Betriebsart	Klassifizierung
532 nm	20 mW	<1.2 mrad	kontinuierlich	Klasse IIIb
635 nm	15 mW	0.7 mrad	kontinuierlich	Klasse IIIb

Elektrische Grenzdaten

Eingabe (Gleichström)	Maxima
+ 15 V	5.5 A
+ 5 V	2.5 A
-15 V	0.5 A

Abbildungen mit Sicherheitshinweisen



Abbildung 1.: Kundendienst und Warnetiketten
Das Etikett ist auf der Rückseite des GenePix 4000A auf dem oberen Teil des Schutzgehäuses befestigt. (Wirkliche Grösse).

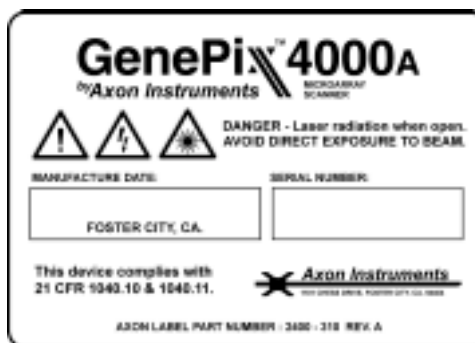







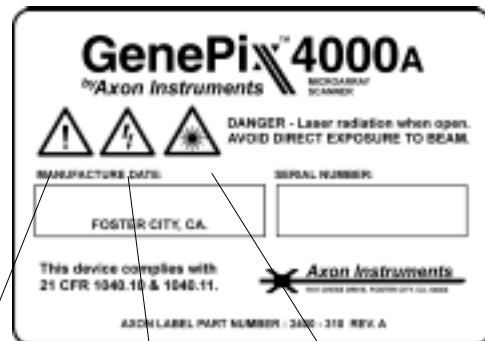
Abbildung 2. Identifikations- und Beglaubigungsetikett
Das Etikett ist auf der Rückseite des GenePix an der unteren Hälfte des Schutzgehäuses befestigt. (Wirkliche Grösse).



Abbildung 3. Zugangsschalttafel Sicherheitsetikett
Das Etikett ist unten am GenePix entlang der Einstellungszugangsöffnung befestigt. (Wirkliche Grösse).

Erklärung Der Symbole

	<p>Gerät aktivieren. (Aktiviert nur den +5 Volt Spannungsbereich. Die ± 15 Volt Spannungsversorgung ist aktiv, solange das Gerät mit dem Netz verbunden ist)</p>
	<p>Gerät deaktivieren. (Deaktiviert nur den +5 Volt Spannungsbereich. Die ± 15 Volt Spannungsversorgung ist aktiv, solange das Gerät mit dem Netz verbunden ist)</p>
	<p>Standby-Modus. (Gerät ist bereit einen Objektträger zu lesen. Führung des Objektträgers in Startposition)</p>
	<p>Scanning.</p>
	<p>Eject. (Gerät ist bereit zur Ausgabe des Objektträgers)</p>



Achtung!!
 Vor Benutzung unbedingt die Gebrauchsanweisung lesen!

Achtung!!
 Gefährlicher Stromkreis!

Achtung!!
 Laserbestrahlung!!

Declaration of Conformity

Axon Instruments, Inc. declares the

GenePix™ 4000A MicroArray Scanner

conforms to the following Directives and is fit for CE marking.

(Signature on file)

Alan Finkel, CEO

(Signature on file)

Richard Goldsmith, Quality Assurance and Regulatory Affairs Manager

Directive	Standard	Title
Low Voltage	EN61010-1	Safety requirements for electrical equipment for measurement, control, and laboratory use. Part 1. General requirements.
EMC	EN50081-2	Generic emissions standard. Part 2. Industrial.
	EN50082-2	Generic immunity standard. Part 2. Industrial.
Laser	EN60825-1	Safety of laser products. Part 1 Equipment classification, requirements, and user's guide.

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VERIFICATION

This instrument is extensively tested and thoroughly calibrated before leaving the factory. Nevertheless, researchers should independently verify the basic accuracy of the instrument using suitable test samples.

CAUTION

Do not open the unit. There are no user-serviceable parts inside.

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Chapter 1

Installing GenePix

Checklist of Parts

The following items are included in your GenePix package:

- GenePix 4000A bench top instrument APN: 2300-343
- PCI-SCSI adapter for host computer APN: 6130-004
- Driver diskette for SCSI card APN: 2700-089
- SCSI data transfer cable APN: 2100-408
- Power supply unit power cord APN: 3420-014
- Power cord for power supply APN: 3010-011, 013, 014 or 015
- Three copies of GenePix Pro 3.0 software for
Windows 95/98 or NT, each of which contains:
 - ◆ GenePix Pro 3.0 Installation CD-ROM APN: 2700-090
 - ◆ GenePix 4000A User's Guide APN: 2500-131
 - ◆ GenePix Pro 3.0 User's Guide APN: 2500-137
 - ◆ Parallel port security dongle APN: 6190-014
- GenePix cover letter APN: 9320-090

- GenePix Test Slides APN: GP-2
- Bundled host computer (optional) APN: 7800-382

Computer Requirements

Minimum System Requirements

- IBM-AT compatible computer with a Pentium 200 MHz or faster processor
- Windows 95 or 98 operating system (dual-boot systems are not recommended)
- 128 MB RAM
- Hard disk with 4 GB free (for image storage)
- CD-ROM drive
- 1024×768 display system with 65K colors
- Parallel port

Recommended System Requirements

- IBM-AT compatible computer with a Pentium III 500 MHz or faster processor
- Windows NT 4.0 operating system (dual-boot systems are not recommended)
- 256 MB RAM or more
- Hard disk with 10 GB free (for image storage)
- Recordable / Rewriteable CD-ROM or Jaz drive
- 1280×1024 display system with 16M colors
- Parallel or USB port

Preparing to Install GenePix

If you have purchased GenePix *without the optional host computer* please follow the instructions below. If you purchased GenePix *with the bundled host computer*, our Applications Scientists have already installed the necessary hardware and software on the host computer. In this case, you can omit the instructions on the **Installation of the SCSI card**, and the **Installation of GenePix Pro 3.0**; go straight to **Connecting the GenePix 4000A to the Computer**.

Quick Overview of GenePix Hardware and Software Installation

For users who require a minimal level of detail, the following outlines the steps necessary to install GenePix hardware and software. If you do not follow the instructions in the order specified below you may damage your instrument.

1. Initially, do not attach the GenePix 4000A to your computer.
2. Install the SCSI card.
3. Start the computer.
4. Install GenePix Pro 3.0.
5. Shutdown the computer.
6. Attach the GenePix 4000A to the computer with the SCSI cable.
7. Attach the power supply to the GenePix 4000A, making sure the power supply is turned off while you are doing this.
8. Turn on the power supply.
9. Turn on the GenePix 4000A.
10. Attach the security dongle to parallel port.
11. Turn on the computer.
12. Windows will automatically find the scanner and install the appropriate driver.
13. Start GenePix Pro 3.0 using the GenePix Pro icon on the desktop.
14. Start scanning!

Installation of the SCSI card

Included with your GenePix 4000A is a SCSI adapter card for your host computer. This card is used to transfer data and instructions between the host computer and the GenePix 4000A hardware.

The SCSI card that is included with GenePix 4000A is a PCI-based Plug'n'Play card that will install easily on most computers. We recommend that you use the included SCSI card. Please follow the instructions included with the adapter for the proper installation of the card.

If you already have a SCSI card installed on your host computer and do not want to replace it with the included SCSI card, you must verify that it is a SCSI-2 device that is Win-ASPI compliant. You must also ensure that you have the proper cabling to connect the SCSI card to the GenePix 4000A. While it is possible that an existing SCSI card may work with the GenePix 4000A, Axon Instruments can provide technical support only for the SCSI card that is bundled with the GenePix 4000A. If you are using the GenePix 4000A on a computer with multiple SCSI devices please ensure that there are no SCSI ID conflicts. At the factory, the GenePix SCSI ID is set to 4, but the ID can be easily changed using the SCSI ID switch found at the back of the GenePix 4000A.

Installation of GenePix Pro 3.0

GenePix Pro 3.0 is on the included CD-ROM. Simply insert the CD-ROM into your computer and the installation program automatically starts. If the installation program does not start automatically, perhaps because you have the auto-start feature of Windows disabled, you can manually start the installation by running the Setup.exe program file on the CD-ROM. This file is found in the GenePix subdirectory on the CD-ROM.

To start the setup program manually, from the *Start* menu select "Run", and type `x:\GenePix\setup.exe` where "x" is the drive letter of your CD-ROM drive.

When the installer has finished, you will be given the choice of restarting or shutting down your computer. Select the "Yes, I want to shut down my computer now and install the hardware" option. Once your computer has shut down, proceed below to "Connecting the GenePix 4000A to the Computer" section.

Connecting the GenePix 4000A to the Computer

Note: failure to follow these instructions in the correct order can lead to damage to your instrument.

Before connecting the GenePix 4000A to your SCSI connector, please ensure that your computer has been turned off, and that the GenePix power supply is turned off. Once the computer has been turned off, connect the 50-pin data cable between the SCSI adapter of your computer and the GenePix hardware. The SCSI connector and power connector are located at the back of the GenePix 4000A.

Once the SCSI connection has been made, check that the power supply is turned off, then connect the power cord to GenePix. Turn on the power supply, then turn on the GenePix 4000A. The power switch can be found on the left-hand side of the scanner, towards the rear of the instrument. After the scanner has been turned on, turn on your computer.

Windows 95 and Windows 98

If the connections have been made correctly, when you restart your computer Windows will show a message that indicates that “New Hardware” has been detected. Windows will automatically install the necessary driver for the GenePix 4000A scanner.

If Windows does not automatically find the driver, you can manually select the driver using the *Add New Hardware Wizard*. This wizard starts any time a new Plug’n’Play device is detected. Working through the wizard, select the option to “Search for the best driver for your device”. Press *Next*. Select the CD-ROM as one of the locations to search for the driver. Press *Next*. Windows will now find the correct driver for the GenePix 4000A.

If you are connecting the GenePix 4000A to a computer that was bundled with the GenePix by an Axon Applications Scientist, the driver was already installed at Axon.

Windows NT

Since Windows NT is not Plug’n’Play, you will be able verify that the GenePix scanner has been successfully installed when you start GenePix Pro 3.0. This is outlined further below.

Connecting the Security Dongle

GenePix Pro 3.0 requires a security dongle to operate. If the dongle is absent you will be able to open images in GenePix Pro, but you will not be able to save your settings files or save your analysis results. In addition, you can analyze only 100 features without a dongle.

Installation of the dongle is straightforward. Simply connect it to the parallel port of your computer. If you have a printer already installed, do not worry. The dongle is a “pass-through” device and you simply connect the dongle to the parallel port, then connect your printer to the dongle. A USB-based dongle is also available. Please contact Axon Technical Support for further details if you require a USB dongle.

Starting GenePix Pro 3.0

After the successful installation of the software, you will find the entry “Axon Laboratory” in your list of Programs in the Start menu, and there will be two new icons your desktop. There are “GenePix Pro 3.0”, and “GenePix Pro 3.0 (demo)” entries in your Axon Laboratory group, and icons for these on your desktop. Both of these shortcuts will start GenePix Pro. *The only difference between the demo version and the non-demo version is that the demo version does not interact with the scanner.* Typically if you are only analyzing data and are not doing any image acquisition, you would select the demo version. For acquisition, select “GenePix Pro 3.0”.

After the software has completed loading and the scanner has successfully initialized, you will see a message in the bottom left corner of the software that indicates “Eject position – the slide may be removed”. This message indicates that the GenePix 4000A had been initialized and you can load your first microarray slide!

Troubleshooting Installation

SCSI Card Installation Problems

If you encounter any problems with the installation of the included SCSI adapter card, please refer to the instructions that came with the card. If you require further assistance on

installation of the included SCSI card, contact Axon Instruments Technical Support. If you are using a SCSI card that was already installed in your computer, Axon Instruments will *not* be able provide any support for such adapters.

Hardware Problems

GenePix Pro 3.0 automatically detects the GenePix 4000A. If this does not occur please verify the following items:

- The data cable between the computer and GenePix 4000A is securely connected.
- The GenePix 4000A is turned on (the green power light on the top of the scanner will be glowing).
- The SCSI card is operational (see above).
- The GenePix SCSI ID 4 does not conflict with any other SCSI devices that you may have already installed on your computer (*e.g.*, a Jaz drive).

Software Problems

If you have purchased your GenePix with the bundled host computer, the software has already been installed at Axon Instruments. If you are using a previously purchased computer, please consider the following:

- GenePix Pro 3.0 requires a minimum of 128 MB of RAM to acquire images. GenePix Pro is capable of analyzing data when less than 128 MB of RAM is present, but the maximum image size is reduced and performance will be non-optimal.
- GenePix Pro 3.0 requires a security dongle to enable saving of results or settings files. If the dongle is not found, the software operates with limited file-saving functionality.

Contacting Axon Instruments

If you need help to resolve a problem, there are several ways to contact Axon Instruments:

World Wide Web

Home: <http://www.axon.com>.

Technical Support: http://www.axon.com/MR_Technical_Support.html.

GenePix Feedback: http://www.axon.com/GenePix_Feedback.htm.

E-mail

Axon Technical Support: tech@axon.com.

Phone

+1 (650) 571-9400

Fax

+1 (650) 571-9500

Mail

Axon Instruments, Inc.
1101 Chess Drive
Foster City, CA
94404-1102
U.S.A.

Chapter 2

Introduction to GenePix 4000A

The GenePix™ 4000A from Axon Instruments, Inc., is the first fully integrated microarray scanning and software system available in the world today. With superb engineering and a simple yet powerful software interface, the GenePix 4000A has been designed to bring the revolution of DNA microarray analysis into life sciences laboratories everywhere.

Axon Instruments has consulted widely among the scientific pioneers of genetic microarray techniques to produce an instrument that fulfills all their image acquisition and primary analysis needs.

GenePix 4000A Features

The GenePix 4000A scanner:

- simultaneously scans microarray slides at two wavelengths using a dual-laser scanning system, which dramatically reduces scan time (5 minutes for full scan), and which eliminates the need for image alignment after acquisition;
- has precisely controlled laser temperature for constant power output;
- uses 16-bit digitization;
- has a dynamic detection range of four orders of magnitude, linear over three orders;
- possesses extra-high signal-to-noise scan mode;
- offers two scanning modes: a Preview Scan at 40 μm resolution and a Data Scan at 10 μm resolution.

Axon's Commitment to Genomics

The GenePix 4000A is the first in a new line of Genomics products that Axon Instruments is committed to developing for the biological sciences and medical research communities. Axon has established expertise in:

- Electrophysiology: high-precision and high-speed data acquisition and analysis, including the world's lowest noise amplifiers.
- Cellular Neuroscience: high quality scientific imaging hardware and software.
- Functional Neurosurgery: intraoperative microelectrode guidance systems.

Our engineers are applying proven designs and technology to the new and exciting field of Genomics. We at Axon believe that dependable and durable scientific instruments cannot be made overnight. The design and construction of the GenePix 4000A, its reliability and ease of use, are all products of our extensive engineering capabilities that have been built up over the past decade and a half. By providing unlimited technical support, and continuing our extensive research and development, we will continue to enhance, refine and add value to our Genomics products for many years to come.

About This User's Guide

This User's Guide focuses on the technical and theoretical aspects of the GenePix 4000A hardware. We recommend that you use this Guide in conjunction with the GenePix Pro 3.0 User's Guide, and the on-line Help within GenePix Pro 3.0 (press "F1"). For information on setting up your GenePix 4000A scanner and software, please refer to Chapter 1. For a guided tutorial on scanning your first microarray slide, see Chapter 3 of the GenePix Pro 3.0 User's Guide.

Acknowledgments

Axon Instruments, Inc., would like to extend its thanks to the numerous academic and corporate scientists who provided critical input during the planning, evaluation and testing of the GenePix 4000A system. In particular, Drs Stephen J. Smith and Michael B. Eisen of the Stanford University School of Medicine and Dr. Joseph L. DeRisi of the University of California at San Francisco were instrumental in the development of the GenePix scanner and software, helping to make the GenePix 4000A an instrument designed for the research community.

Chapter 3

GenePix 4000A Functional Checkout


The following Functional Checkout procedure is to help you confirm that your GenePix 4000A microarray scanner is performing according to the specifications set by Axon Instruments, Inc. A similar, but much more detailed procedure was performed at the factory prior to shipping this unit to you. We recommend that you follow the procedure once upon receiving the instrument and then any time after that if you wish to check the performance of the instrument.

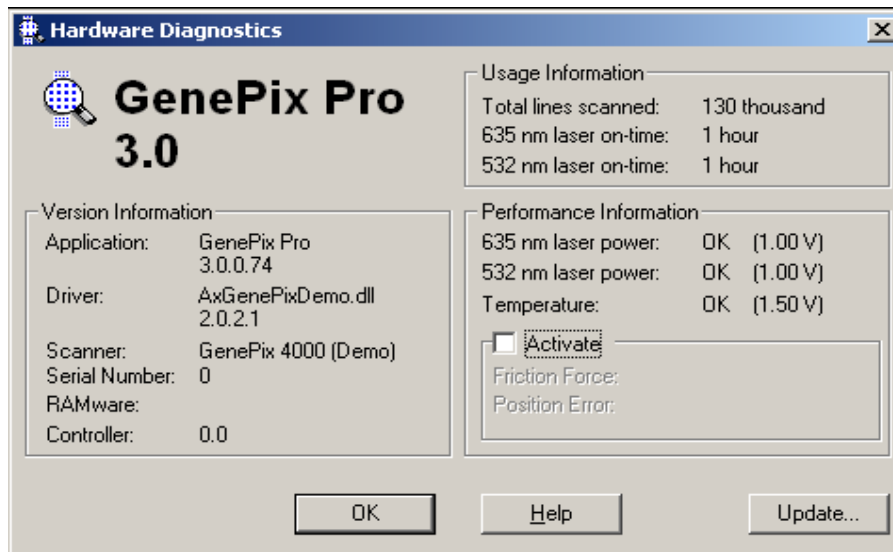
The GenePix 4000A microarray scanner has been designed to provide robust, long-lived microarray scanning for years of normal use. However, if the images you acquire on the GenePix 4000A scanner do not appear correct and if you believe there is a problem with the scanner, it is important to follow these instructions before contacting Axon Instruments. You will be asked the results of the following simple tests once you contact Axon.

The Functional Checkout assumes that you already have a basic working knowledge of how to operate the instrument. If you have not already done so, please go through the GenePix Pro 3.0 Tutorial (chapter 3 of the GenePix Pro 3.0 User's Guide).

Step 1: Basic Laser Power, Temperature and Mechanical Motion Performance

The GenePix 4000A hardware and software are a completely integrated package that allows both the software to control the hardware and the hardware to report critical performance information to the software. This tight integration can be used to evaluate system performance.

Open the *Hardware Diagnostics* dialog box by pressing its button  on the right side of the Image tab. A dialog box similar to the one below will open. Here you will find most of the information necessary to evaluate the basic operation of your GenePix 4000A microarray scanner. The presence of Performance Information within this dialog box also indicates that the SCSI connection between the scanner and computer is operational.

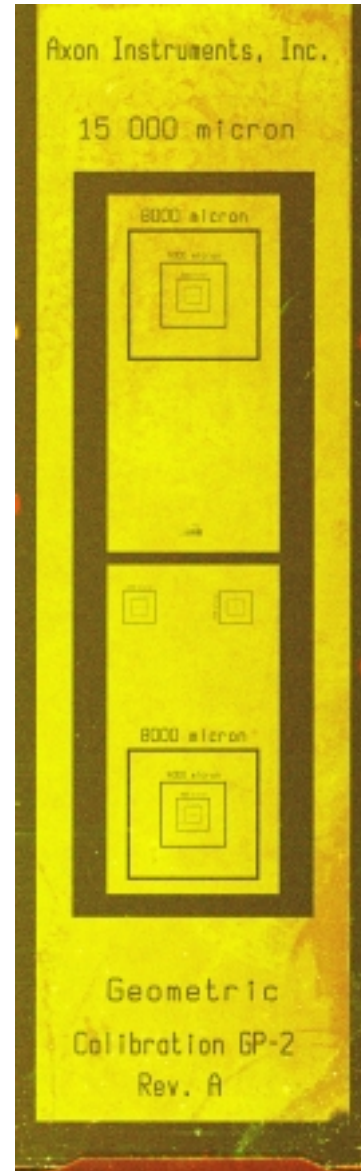


Under Performance Information, please note whether any of the performance measures are reporting anything but 'OK'. For example, if the red laser power were low, '635 nm laser power' would report 'Low' and report a voltage within the parentheses. These voltage values should be noted. The mechanical performance can be evaluated by clicking in the checkbox next to 'Activate'. If there is a problem with the mechanical movement within the scanner, it is reported here. If any of the Performance Information parameters report anything but 'OK', please contact Axon Instruments, Inc.

Step 2: Geometric Mechanical Performance

The purpose of Step 2 in this Functional Checkout is to evaluate the performance of the system as a whole, while focusing on the geometric mechanical performance. To perform Step 2 of this Functional Checkout, it will be necessary to locate the Geometric Calibration slide that was shipped with the unit, Axon Part No. GP-2. To run this test, follow these instructions.

1. Insert the GP-2 slide into the slide holder, secure it in place and close the door.
2. In the *Hardware Settings* dialog box, set both the 532 nm and 635 nm PMT voltages to 1000 V.
3. Scan the entire slide at 10 μm resolution (*i.e.*, do a Data Scan). The resulting image will be quite dim, requiring you to increase both the image brightness and the contrast. The faint image indicates that the system is operating correctly and properly filtering out reflected laser light. The image should appear similar to the image shown right.
4. The image itself confirms that the mechanical motion systems, lasers and computer connections are fully operational.
5. Fit a 'block' of feature indicators onto any one of the squares evident in the image: press the *New Blocks* button (or use the Hot Key Ctrl+N) midway down the left-hand side of the Image tab. By resizing the block, you should be able to fit it *exactly* to the sides of any square on the image. If the block cannot be perfectly fit to a square in the image, please contact Axon Instruments Technical Support.



Chapter 4

Imaging System Hardware

The GenePix 4000A scanner is one of the fastest and most sensitive scanners currently available. This chapter introduces some of the fundamental hardware concepts needed to understand the operation of the GenePix 4000A.

Overall Features

The GenePix 4000A is designed for simultaneous scanning of two wavelengths of excitation laser light. Axon's patent-pending design eliminates the image alignment problems associated with sequential scanning systems while also abolishing channel crosstalk problems associated with multi-wavelength designs, permitting high-precision real-time acquisition and display of ratio images.

Discussion of Hardware Components

When discussing the hardware components of the GenePix 4000A it is convenient to reduce the system to its optical, mechanical and electrical components.

Optics

Fundamentally, the GenePix 4000A uses a laser-excitation-based epifluorescence scanning system. The optical system can be considered in terms of excitation light, mirrors, lenses, filters and photo-detection.

Excitation

In the GenePix 4000A laser excitation is provided by individual 635 nm and 532 nm lasers. These wavelengths correspond to the ideal wavelengths used to excite the fluorophores Cy3 and Cy5 (Amersham Pharmacia Biotech), which are currently the most widely used fluorescent probes for microarray imaging. 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 GenePix 4000A uses an active temperature stabilization design to minimize temperature-based laser fluctuations. Furthermore, each laser has stabilized feedback output to ensure that photon output is constant.

Laser excitation sources are often used in scanning systems instead of conventional wide-band white light sources such as a Xenon or Mercury light source. The reasons for this are quite simple: conventional wide-band light sources do not deliver high enough photon density at the appropriate wavelength to a sample in a scanning system. In addition, it is often difficult to use optical filters to obtain spectrally pure, narrow-band excitation light.

Mirrors, Lenses, and Filters

Excitation laser light is directed onto the microarray after passing through a series of filters and mirrors. While laser light is by definition very narrow band, the GenePix 4000A employs additional optical filters to ensure that no spurious excitation light is directed onto the microarray. If the laser light impinges on an appropriate fluorophore bound on the microarray, emission light of a different wavelength is emitted. These emission photons are directed back through the optical system where they pass through another set of filters before reaching the dual photodetectors.

One of the problems faced by a dual scanning system 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 into the detector for the second fluorophore. Crosstalk is often a concern when one is 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 4000A 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 patent-pending optical design guarantees that spectral overlap is zero.

Photo-Detection

The GenePix 4000A uses a pair of high-sensitivity, low-noise photo-multiplier tubes (PMTs) to detect the emitted fluorescent light. Loosely defined, PMTs are optical components that convert incident photons into electrons via the photoelectric effect. When an incident photon impinges on the active surface of the PMT (the photocathode), an electron is generated. This 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 amount of incident light at the photocathode.

The amount of amplification that a PMT can produce depends on the number of dynodes in the PMT, and the voltage that is applied to the PMT. With PMTs it is possible to achieve a gain of 10^7 . When you increase the PMT voltage setting in the GenePix 4000A software, you are increasing the gain of the PMTs.

Note: It is important to realize that when you increase the gain of the system, you are also increasing the sensitivity to non-specific fluorescence, thus increasing any electronic noise in the system. This increase in noise can often be overcome by line averaging but the cost is decreased acquisition speed. 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. However, there is a very non-linear relationship between the gain of the PMT and the applied PMT voltage. **Therefore, a microarray scanned at a PMT voltage of 800 V will not be twice as bright as the same microarray scanned at 400 V.**

The PMTs in the GenePix 4000A meet two essential criteria for high-quality imaging. First, since different photocathodes have varying sensitivities to specific wavelengths of light (quantum efficiency), the PMTs have been optimized for the typical wavelengths of fluorescence emission light produced by microarrays. Second, the PMTs have been further selected for their reliability and optimal signal-to-noise performance.

Mechanical

The GenePix 4000A is a mechanical device. Its laser-based scanning system uses a patent-pending mechanical design. The GenePix 4000A operates by slowly scanning the microarray in the y -direction, and rapidly scanning in the x -direction. The design of the GenePix 4000A allows a rapid scan of a 25 mm \times 75 mm microarray slide at 10 μ m resolution in about 5 minutes.

When using such a mechanical device, one must be able to monitor the variability in the performance of its mechanical components. The GenePix 4000A has been designed with a number of optimizations to ensure that variability in the mechanical performance is monitored in real time during acquisition, and corrected. The utmost attention has been given to selecting and implementing components to create a highly reliable, high-performance instrument.

Electronic

While the optical components of the GenePix 4000A are indispensable for generating the electrical current from PMTs, the electronic components are just as important. They govern the operation of the PMTs and the conversion of their analog current signals into a digital signal that can be processed by the host computer.

Axon Instruments is the world leader in the design and construction of low-noise amplifiers. Our amplifiers are used around the world by researchers in the neuroscience community. We have worked hard for over a decade to create low-noise amplifiers and high-performance computer hardware to digitize these signals. Our expertise in this area has been applied to the GenePix 4000A. Integrated with the GenePix 4000A is not only our high-performance analog-digital converter, but also the experience and knowledge to create low-noise, high-performance amplifiers. We have employed a unique design to ensure that the PMTs in GenePix are linear over a wide dynamic range, and that the signal-to-noise level exceeds all other currently available microarray scanners.

General Items of Interest

Spatial Resolution

The GenePix 4000A is a scanning instrument. This means that a single point of light is rapidly scanned across the microarray, and a composite image is created from the digitized signals from the PMT. The spatial resolution of the system refers to the size of this single scanning point. In the GenePix 4000A, the spatial resolution is 10 μm for a *Data Scan*, and 40 μm for a *Preview Scan*. During the Preview Scan, the same 10 μm spot is scanned, however the slow y-direction scanning operates four times faster, and only one quarter of the samples in the x-direction are used.

It is possible to change the resolution of Data Scans. Using the software you can specify a resolution that is a multiple of 10. When the slide is scanned the appropriate number of pixels are averaged to create a single pixel representation. For example, if you set the resolution to 20 μm , 4 raw data pixels are averaged to produce each pixel in the final image. This option is often useful if you have large features and you do not need to scan at maximum resolution. As you decrease the resolution, you will decrease the final image size (in MB). However, keep in mind that you need to acquire enough pixels for each feature in order to make accurate measurements. Finally, reducing the scanner resolution in software does not reduce the scan time: it only reduces the final image file size. It also increases signal-to-noise by the square root of the number of pixels averaged.

Dynamic Range and Sensitivity

The dynamic range of an instrument is the signal width that can be resolved above the noise the instrument produces. The dynamic range depends on all the components in a given system. For example, if you use a PMT with a dynamic range of 10^6 but process the signals through a sub-standard 8-bit analog-to-digital converter, you will end up with an instrument with a poor dynamic range. Furthermore, while an instrument may have a large dynamic range, one may not be able to use the whole range reliably if the response is non-linear. Therefore when rating an instrument one must consider the range over which its response remains linear. For the GenePix 4000A, the dynamic range is 10^4 , and it is linear over 3 orders of magnitude.

The dynamic range of an instrument is often considered in conjunction with its sensitivity. The sensitivity is defined as the minimum detectable signal above background noise.

Although you may be able to see features below this level, the minimum signal that can be accurately quantified is the dye concentration for which the signal is three times the background noise. For the GenePix 4000A, the sensitivity is on the order of 0.1 fluorophores / μm^2 for Cy3 and Cy5.

Limitations

GenePix 4000A is an acquisition and first-pass data analysis system for microarray experiments. It has been designed to fulfill all your primary acquisition and analysis needs, extracting data from microarrays and exporting it to advanced data analysis and presentation software.

The data extracted and displayed by GenePix 4000A can only be as good as the arraying and hybridization of features on slides: the better the slides, the better the data that GenePix will return to you.

Summary

The GenePix 4000A is a high-performance instrument that has been designed to maximize the quality of data that it generates. The utmost attention has been given to creating a fast, low-noise, high-sensitivity instrument.

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