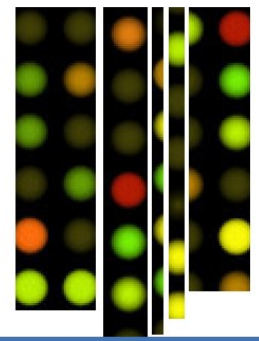




**Caduceus
Biotechnology Inc.**

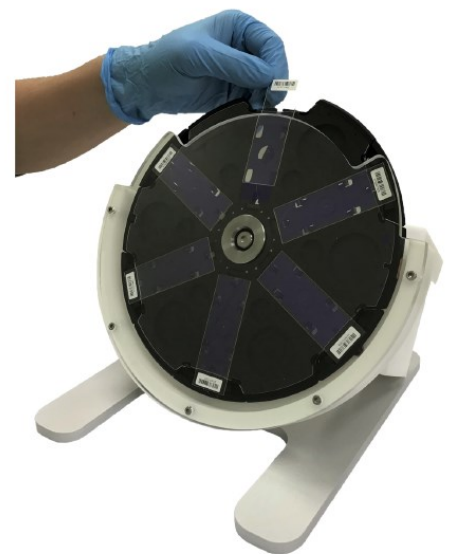


**HC-BS01 Dual Wavelength
HC-BS02 Single Wavelength**

“Caduceus” SpinScan Microarray Scanner

User Manual

Version 4.1



IVD

WWW.CADUCEUS.COM.TW



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<http://www.caduceus.com>



Caduceus Biotechnology Inc.

9F-5, No. 66, Shengyi 5th Rd., Zhubei City, Hsinchu
County, 302041, Taiwan (R.O.C.)
TEL: +886-3-5790188
<http://www.caduceus.com.tw>



MedNet EC-REP GmbH,
Borkstrasse 10, 48163 Münster, Germany,

Preface

Welcome to the microarray scanner system user manual. User should read this manual carefully, follow the manual instructions and understand every item of the precaution notes. Please read the original manual before use. The scanners included in this manual contain models, HC-BS01 (dual-wavelength excitation laser source) and HC-BS02 (single-wavelength excitation laser source).

Content

Section	Overview
1. Important safety information	In order to safely use the microarray scanner system, users should read carefully “The Important Safety Information of User Guide” before installing or using the scanner system.
2. System overview	Describe the system features, working principle, expected application and the technical specifications.
3. Hardware installation	Describe the system hardware specifications, installation steps and requirements.
4. Software Installation	Describe the system software specifications, installation steps and requirements.
5. BioScan Control user guide and instruction	Explain the system and BioScan Control software operational process flow and the precaution notes.
6. BioImage Analysis user guide and instruction	Explain the system and BioImage Analysis software operational process flow and the precaution notes.
7. System maintenance and failure inspection	Describes system maintenance precaution notes, common problem and the solutions.


Technical support and contact information

If you have any question or need help when installing or using the microarray scanner, please contact Caduceus Biotechnology Inc. for technical support in time. The contact method is as follows.

- Address : 9F-5, No. 66, Shengyi 5th Road 1, Biomedical Park, Zhubei City, Hsinchu County, 302041, Taiwan.
- Website: www.caduceus.com.tw
- Tel (technical support / products consultation): +886 3 5790188
- Fax: +886 3 5790298
- E-mail (technical support / products consultation): info@caduceus.com.tw

In order to quickly and correctly provide technical support or product advice service, please prepare the following information.

- Serial number of the microarray scanner (on the back side of the instrument).
- BioScan Control software version.
- Description of the problem when installing or using the scanner system.
- Your phone number, fax number and e-mail address for contact.

	<p>Note: Dual-wavelength microarray scanner (HC-BS01) is available for 532nm and 635nm models and the single-wavelength microarray scanner (HC-BS02) is available in 532nm or 635nm models (HC-BS02(G)/ HC-BS02(R)).</p> <p>All models use the same version of control software, and the operation is basically the same. This manual mainly uses the HC-BS01 model as an example to carry out relevant operation instructions. HC-BS02 model does not support all operations related to dual lasers, and no further explanation in this manual.</p>
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Important safety information

Warning:







When users use or maintain the system, if not in accordance with the contents of this user manual, it may result in product damage, data loss, data anomalies or may suffer from laser radiation hazards, dangerous voltage hazards and collision danger of the mechanical parts.

Microarray scanner is a professional equipment. Users should accept and take the user training course offered by Caduceus Biotechnology Inc. before using the microarray scanner.



1. Mark symbol and meaning

mark symbol	mark symbol meaning
	Laser radiation hazard label: Caution the laser hazard.
	Voltage hazard label: Beware of electric shock hazard.

	Warning label: Precautions.
	In-Vitro-Diagnostic device
	Catalogue number
	Serial number
	Date of manufacture
	Consult instructions for use



2. Laser radiation

Microarray scanner is equipped with two laser sources for exciting fluorescences, the wavelengths were 532nm and (or) 635nm, and set the maximum laser output power of 13mW. To avoid the risk of being exposed to laser radiation when using the scanner, user must close the cover of microarray scanner before using the scanner for scanning and analyzing the fluorescent images. If user opens the scanner cover during the scanning of fluorescent images or doing the system test functions, system will turn off the laser source and the moving mechanical parts. User should not try to change this setting in any way, otherwise the risk of being exposed to laser radiation when using the scanner.

3. Scanner cover


To avoid the risk of being exposed to laser radiation and collision risk of mechanical parts when using the scanner, user must close the cover of

microarray scanner during the fluorescent detection and scanning. If user opens the scanner cover during the scanning of fluorescent image or doing system verification process, system will turn off laser source and stop moving mechanical parts. Users should not try to change this setting in any way, otherwise, risk of laser radiation being exposed when using the scanner that may cause hazard or damage. It may also result in missing data or abnormal data. Therefore, users should avoid opening scanner cover during functions such as fluorescence detecting/scanning and the system verification process.

	Warning: Do not allow the user to remove scanner cover or attempt to change the scanner cover safety setting in any way. Otherwise, it will cause failure or violation of the product warranty agreement.
	Warning: User is not allowed to remove the scanner housing or touch, disassemble the internal parts of the product (exception if noted in the manual). Otherwise, it will cause failure or violation of the product warranty agreement.

4. Power supply

Microarray scanner uses 100 ~ 240 Volts AC, 50 ~ 60 Hz power supply. Please ensure that it matches the power supply or the same. Otherwise, it may cause risk of electric shock, or even damage the scanner and cause fire hazard.

	Warning: Please make sure that power supply matches the scanner.
---	--

5. Wire and grounding

This system is shipped to users with the power cord specifications of 300V-3×0.824mm² (18AWG) -1.8m. Users are not advised to change power cord specifications to avoid the risk of electric shock, even damaging the scanner and creating a fire hazard.

The system through a power cord to ground, please use the original power cord or the same specification, and with a good grounding outlet.



Please ensure to use matched or the same spec. of power supply. Otherwise, it may cause risk of electric shock, even damaging the scanner and creating a fire hazard.

6. Fuse

There is a fuse in the microarray scanner with spec. of U/C-GFE-3A /250V. Users can change fuses according to specifications. The fuse holder is located on the back side of scanner (above power cord connector). Improper replacement may result in the risk of electric shock, even damaging scanner and creating a fire hazard.




Warning: Please use the same size of fuse, or it may cause risk of electric shock, or even damage the scanner and create a fire hazard.

7. Fan


The scanner has two cooling fans and two air inlets. It is forbidden for users to block two fan outlets and two air inlets. Otherwise, the internal components of the scanner will rise in temperature and damage the scanner

and may even result in risk of electric shock and fire.

	<p>Warning: The scanner has two cooling fans and two air inlets. It is forbidden for users to block two fan outlets and two air inlets. Otherwise, the internal components of the scanner will rise in temperature and damage the scanner and may even result in risk of electric shock and fire.</p>
---	---


8. Moving parts

Microarray scanner features the use of a rotary scan for fluorescence scanning of microarray slides. Thus, before performing the fluorescence image scanning, user needs to load the slide into the slide holder according to the instruction manual and the slide holder is loaded onto central axis of rotation as specified in the user manual and the slide holder rotates rapidly during fluorescent scanning. User must close cover of microarray scanner before using the scanner for scanning and analyzing the fluorescent images. If user opens the scanner cover during the scanning of fluorescent images or doing the system test functions. System will turn off the laser source and the moving mechanical parts. User should not try to change this setting in any way, otherwise the risk of being exposed to laser radiation when using the scanner.

	<p>Warning: Users are not allowed to remove the scanner cover or try to change cover safety setting in any way. Otherwise, user may be exposed to the risk of collision with mechanical parts when using the scanner.</p>
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9. Maintenance

Only authorized service engineers may work on microarray scanner repairs. Maintenance related information, please consult the service of Caduceus Biotechnology Inc. For more information, please see the preface section "Technical Support and Contact Information".

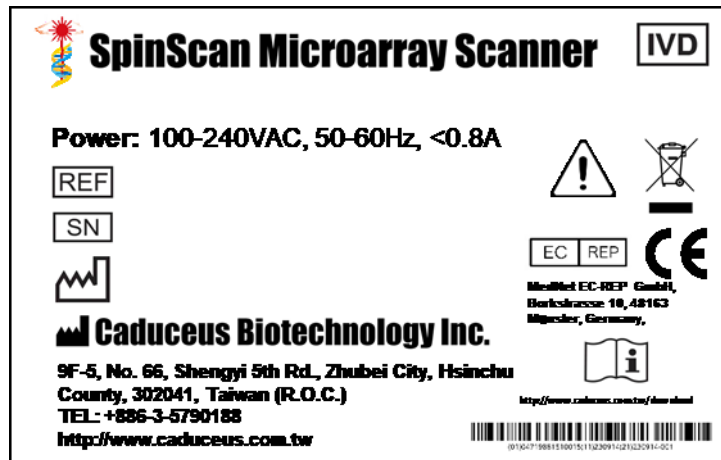
	<p>Warning:</p> <p>Users are not allowed to dismantle the scanner shell or touch or disassemble internal parts of the product (except those specified in the manual), otherwise, the product warranty agreement will be invalidated.</p>
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10. Transport, packaging and storage

Microarray scanner is a high-precision optical inspection instrument. If long-distance transport is required, the original carton and cushioning protective material should be used to re-package the instrument to ensure that transport process will not cause any damage to the scanner. If moving for a short distance, you can move it with human power or a solid handling tool that prevents microarray scanner from being hit or dropped during handling.

This product should be stored at a temperature of $-10^{\circ}\text{C}\sim+45^{\circ}\text{C}$ after packaging, ventilated interior and with top of the machine facing up and horizontally.

11. Product labeling and standards



Microarray scanner manufacturing, inspection after the product label affixed to the rear of the scanner, the product label as shown above.

- Model No.: HC-BS01/ HC-BS02(G)/ HC-BS02(R)
- Serial No.: HC-BSxx-yymmdd-ooo
 - 1 ~ 6 code: product code (HC-BS01/ HC-BS02)
 - 7 ~ 12 code: two codes for years and each two codes for month and date.
 - 13 ~ 15 code: serial production with 3 code numbers.

The SpinScan microarray scanner is designed to comply with the following EC Council Directives and product safety standards:

Application of Council Directives:


- Conformity with the essential requirements and provisions of **Regulation (EU) 2017/746 of European Parliament and of the council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU.**

Application of Harmonized Standards:

- **IEC 61010-1:2010/AMD1:2016 & EN61010-1:2010+A1:2019**
- IEC 61010-2-101:2018
- **IEC 61326-1 : 2012 & EN 61326-1 : 2013**
- **IEC 61326-2-6 : 2012 & EN 61326-2-6 : 2013**

- IEC 61000-3-2 : 2014
- IEC 61000-3-3 : 2013
- IEC 61000-4-2 : 2008
- IEC 61000-4-3 : 2006+A1:2007+A2:2010
- IEC 61000-4-4 : 2012
- IEC 61000-4-5 : 2014
- IEC 61000-4-6 : 2013
- IEC 61000-4-8 : 2009
- IEC 61000-4-11 : 2004
- IEC 60601-1-6: 2010+A1:2013
- IEC 62304:2006
- IEC 62366-1:2015/COR:2016
- IEC 60825-1:2014
- EN 13612:2002
- ISO 15223-1:2016

12. Disposal

	<p>This symbol on the product or package states that this product must not be disposed of with your other household waste, and you are responsible for delivering this product to waste electrical and electronic equipment recovery collection points for disposal of the obsolete equipment.</p> <p>Separation of waste equipment by collecting or recycling helps to conserve natural resources and ensures that recovery is done in a manner that protects human health and the environment. Disposal of discarded equipment of your product for recycling, please contact your local government agency or distributor.</p>
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13. Education Training

Microarray scanner is a high-precision optical inspection instrument. User must receive training for at least two hours, which provided by the original authorized engineers. Through relevant teaching materials and the practical operational training, user will be familiarized with the machine operations and certification passed. In addition, user must be a professional inspector, such as the medical examiner, engineer or researcher.

The re-training would be executed when Microarray scanner is renewed or updated.

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Ch01 System Introduction

1.1 Product features, working principle and intended use

1.1.1 Product features

Microarray scanners are biochip signal detection and analysis systems. Through the scanner, it can obtain sample reaction of fluorescence signal for microarray slide. By analyzing sample point of the target design and its fluorescent signal strength, it can quickly and accurately provide biological information about the microarray i.e. a key instrument and important support platform of biochip applications. It plays a key role on the development and validation of biochip and applications.

Unlike conventional microarray scanners, microarray scanners use a high-precision, fast-spin mechanism for fluorescent image scanning simultaneously up to maximum of six slides. Microarray scanner, combined with a real-time autofocus system, allows the laser to be correctly focused on the surface of slides so that it delivers user bio-fluorescence signals more precisely. Microarray scanner compatible biochip slide with the specifications such as length of $76 \pm 0.5\text{mm}$, width of $25.1 \pm 0.2\text{mm}$, and the thickness of $1.0 \pm 0.1\text{mm}$ (borderless slide), and the compatible fluorescent dyes that can be excited by lasers at wavelengths of 532 nm and (or) 635 nm.

1.1.2 Working principle

The fluorescence signal detection principle of microarray scanner is as follows.

(1). Before carrying out the fluorescence image scanning, user needs to

load 6 slides into the slide holder and load the slide holder on the central rotary shaft according to the user instruction manual.

- (2). When performing a fluorescence image scan, slide holder rotates rapidly. Microarray scanner's real-time autofocus optical system focuses the laser correctly on the surface of slide and excites the fluorescent molecules to fluorescence. After collected by the autofocus optical system immediately after formation of parallel fluorescent light beam, and the emission of light filters by the receiving objective lens to re-gather and form a fluorescent spot coupled to the optical fiber, and finally into the photomultiplier tube (PMT). The light intensity received by PMT is proportional to the analog signal. This signal is converted to a 16-bit digital signal by a digital-to-analog converter circuit and transmitted to the computer. After that, computer program will convert fluorescent signal at R- θ position into a signal pattern at X-Y position of the six slides to build the scanned fluorescence image.

1.1.3 Intended use

Microarray scanner can be used to obtain response of fluorescent signals emitted from slides. By analyzing the strength of fluorescent signal that comes from designing of microarray samples, it can provide fast and accurate bio-information. For professional in vitro diagnostic use only.

1.2 Product specifications

Model	HC-BS01 (Dual wavelength (532&635 nm) microarray scanner) HC-BS02(G) (Single wavelength (532 nm) microarray scanner) HC-BS02(R) (Single wavelength (635 nm) microarray scanner)
Scan resolution	2, 5, 10, 40 $\mu\text{m}/\text{pixel}$
Excitation wavelength	532 nm / 635 nm

Emission wavelength	572±17nm / 670±15nm
Size of slide (W x H x T)	25.1±0.2 mm × 76.0±0.5 mm × 1.0±0.1 mm
No. of slides per scan	6 slides/run
Focus mode	Real time dynamic auto-focus
PMT sensors	Two PMT (HC-BS01) Single PMT (HC-BS02)
PMT gain	Adjustable range 5~100%
Laser power	13±10% mW
Max scan area	66 mm × 22 mm
Max scan speed	21 min/run @ 10 μm/pixel
Barcode read	Yes
Dynamic range	≥ 10 ⁴
Sensitivity	≤ 0.2 fluor/μm ²
Image format	16 bits TIFF
Uniformity	CV < 5%
Repeatability	≥ 95%
Scan precision for image pixel location	≤ 1 pixel (10 μm)
Size (W x D x H)	550(L) mm×335(W) mm×220(H) mm
Weight	< 22 kg

Ch02 Install of Hardware

2.1 Overview

Microarray scanner can only be installed by original authorized engineer or user. Before install the hardware and software, user should carefully read in detail and understand the installation requirement and steps noted in the user manual. Users should also follow the manual installation steps exactly to avoid damage to the scanner.

2.2 Requirement of installation

2.2.1 Computer workstation specifications

Computer workstation specifications for the microarray scanner system are as follows.

Operation system

- Windows 10 64-bit professional operating system

Hardware specifications

- CPU: Intel Core i5-6500 of equivalent or higher
- Memory: 16 GB DDR4 RAM or more.

(If there is a requirement for 2 μm high-resolution fluorescent image scanning, 32 GB RAM is required)

- Hard disk capacity: 1.0 TB
- USB interface: USB3.0
- Display: 17-inch or larger color display, 1920×1080 pixel resolution
- Mouse: optical mouse, USB interface
- Keyboard: USB interface

2.2.2 Power supply

Microarray scanner consumes less than 70W and has a maximum input current of 0.8A (with 100 ~ 240 Volts AC, 50 ~ 60 Hz of power supply). To avoid the risk of electric shock, please use power cord provided by qualified manufacturer or the same specification to connect to a well-grounded electrical outlet.

2.2.3 Environmental needs

Microarray scanners should be installed in a place that meets the following environmental conditions.

- Operating temperature requirements: 15~30°C
- Relative humidity: 30~85% RH at 30°C
- Installation location: indoor
- Because the scanner is a precision optical instrument, please try your best to keep the environment clean (The most recommended installation and installation location: a clean room with well controlled of temperature and humidity).
- Mains supply voltage fluctuations less than $\pm 10\%$.
- Pollution Degree: 2 (Normally only nonconductive pollution occurs).

2.2.4 Space

The size of the microarray scanner is about 550mm×335mm×220mm. When placing the scanner, please ensure that there is enough space between the backplate and the wall and make the power cable, USB3.0 signal line and backplane power connector, USB3.0 interface are easy to connect. The sides of the scanner should be well ventilated and user is prohibited from

blocking the two fan outlets and the two air inlets. Otherwise, internal components of the scanner will rise in temperature and damage the scanner, which may even result in the risk of electric shock and fire hazard. To keep a clear head space above the scanner to prevent scanner cover from opening completely or debris falling onto the scanner. The workbench that carries the scanner must be solid and flat, with a weight stand of at least 40 Kg.

2.2.5 Other issues of consideration

Scanner installation should be away from high electromagnetic radiation facilities or strong magnetic field, such as a welding equipment.

- The scanner should be installed away from high power or high vibration equipment such as centrifuges.
- The scanner should be used in a dry environment.
- Do not share the scanner with many devices on the same power source.
- If it is considered that data is lost or damaged during scanning process due to the momentary power failure, users are advised to install an uninterruptible power system.
- In order to maintain the stability of scanner system, in addition to the software/hardware that provided and approved by Caduceus Biotechnology Inc., please do not install any additional software/hardware on the computer used by scanner system and it may violate the product warranty agreement.

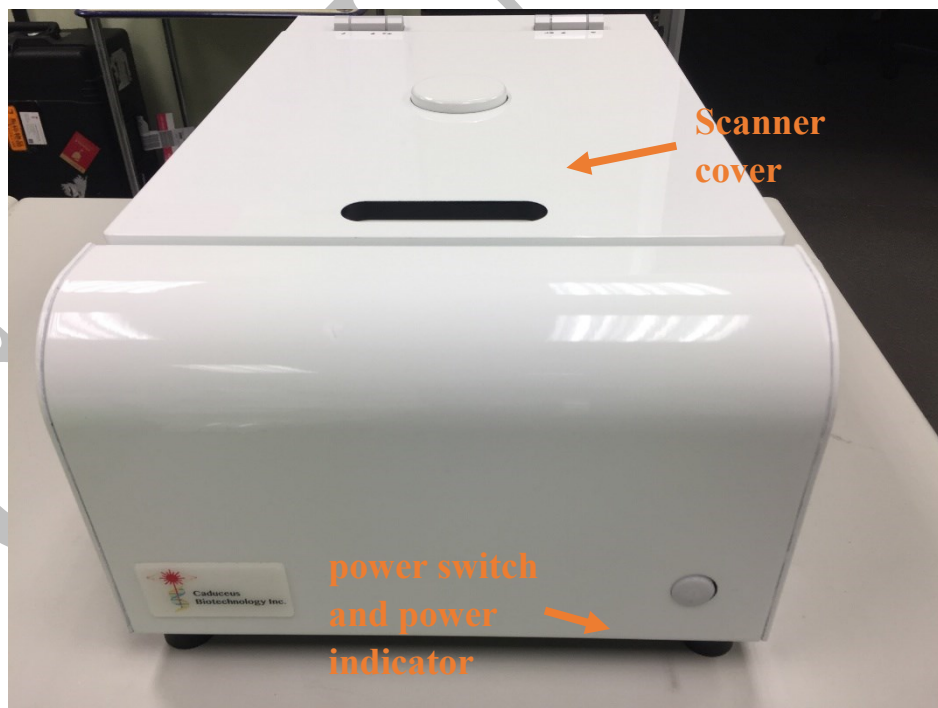
2.3 Receive Check


After opening the package, please check content of the package according to the list in the packing box, and check whether the scanner has any damage. If you find any scanner damage or content items are not complete, please indicate the damage on the receipt of the document or incomplete items, and contact your agent or Caduceus Biotechnology Inc., immediately.

Please keep all packaging materials. If you need a long-distance transport, the original carton and cushioning protection materials should be used to re-package the instrument, to ensure that the transport process will not cause damage to the instrument.

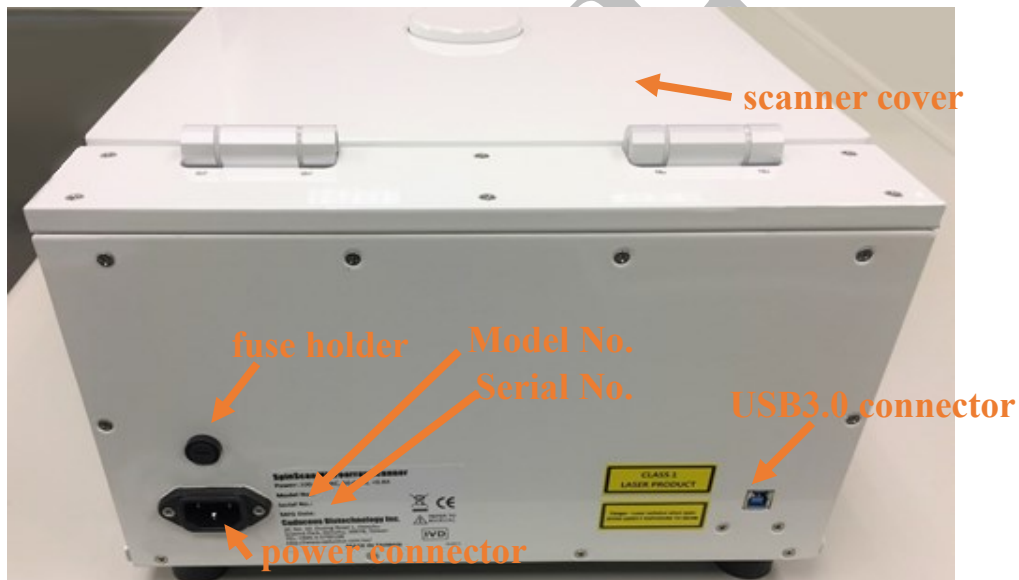
2.4 Hardware system introduction

2.4.1 Front panel




	<p>Warning:</p> <p>Please confirm that the scanner is connected to the power supply and then press the power switch to turn on the scanner and confirm that the power indicator LED is a "ON" status. If you cannot open the scanner power, please contact your agent or Caduceus Biotechnology Inc.</p> <p>To avoid damaging the scanner, please confirm that scanner is turned off before removing the power cord (power indicator LED is on a "OFF" status).</p>
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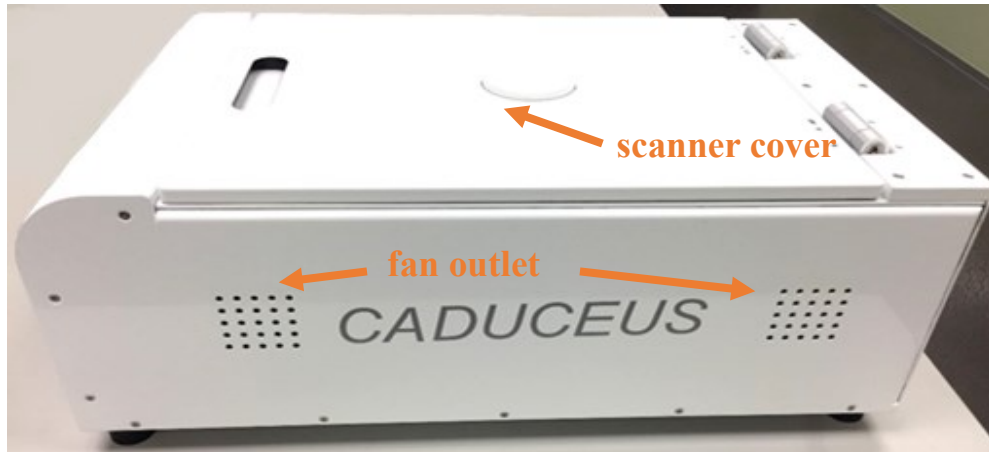
2.4.2 Backplane



Please confirm the receipt of the document on the scanner to identify the scanner model and serial number on the back of the scanner. If inconsistent, please contact your agent or Caduceus Biotechnology Inc.

	<p>Warning:</p> <p>To ensure the stability of USB3.0 signal transmission, please install or use the USB3.0 fixing kit for engineer or user to connect the USB3.0 signal cable to the back of the scanner.</p>
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2.4.3 Side panel

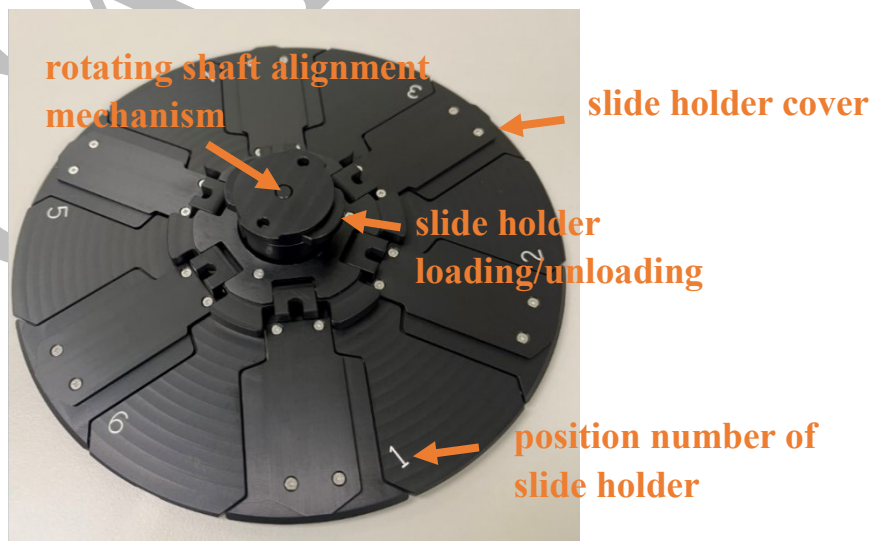


Warning:

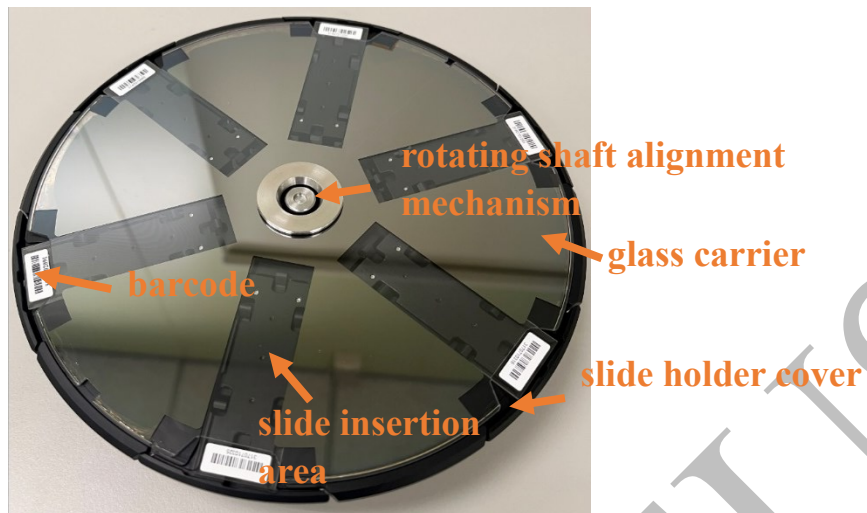
It is forbidden for user to block the air outlet of the two fans and the two air inlets. Otherwise, internal parts of the scanner will rise in temperature and damage the scanner, which may even result in the risk of electric shock and fire hazard.

2.4.4 Slide holder

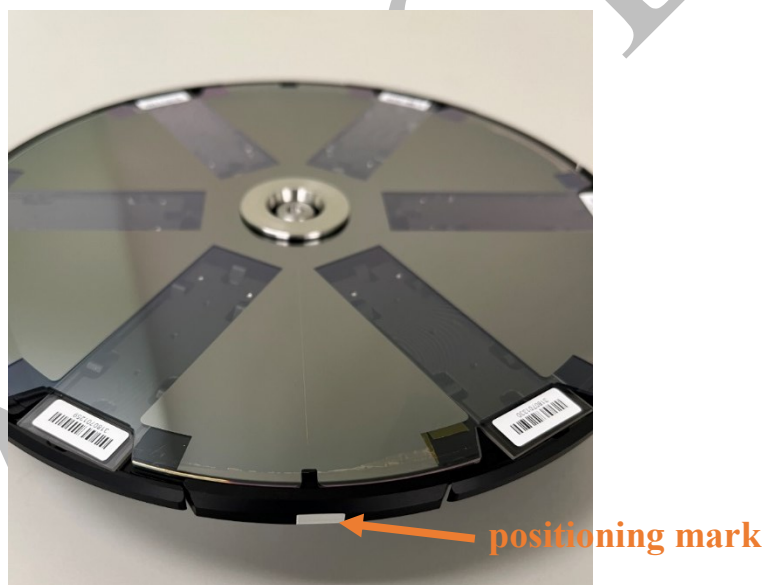
Top view



Under view



Side View



Notes:

- The bottom of the slide holder is made of glass material. Users should avoid collision and fall when using, otherwise it may damage the slide holder.
- The bottom of the slide holder is made of glass material. Users should keep it clean when it is used. Otherwise, the quality of the fluorescent

image scanning will be affected. Users should wear clean gloves when using the slide holder.

- Clean slide holder and wipe it by using cotton-free material without fluorescent and anhydrous alcohol.
- Do not use any liquid or organic solvent other than anhydrous alcohol.
- Users should regularly clean the slide holder or consult the original factory for cleaning according to the frequency of use to ensure the quality of fluorescent image scanning.
- Users do not arbitrarily disassemble any component on the slide holder, otherwise it may cause damage to the slide holder.
- When a user load or unload the slide from the slide holder, it should be confirmed that the slide is completely inserted in or completely removed before closing the slide holder cover, otherwise the slide holder may be damaged.
- Users do not load liquid or contaminated slides into the slide holder. Use dry nitrogen to remove contaminants from the slides or blow dry the wet slides.

2.4.6 Power cable and USB 3.0 signal line



Precaution Notes:

- Users please use the original power cord or the same specifications.

2.4.7 Software installation USB flash drive and hardware protection lock

The microarray scanner system contains two softwares:

- (1) BioScan Control
- (2) BioImage Analyzer

The microarray scanner system is accompanied with a software-installed USB flash drive and a hardware dongle (for related installation steps, please refer to Appendix-A). User must insert the dongle into the USB port of the computer workstation in advance, otherwise the BioImage Analyzer fluorescence image analysis software will not be able to be executed. (See Chapter 3 of this manual for details.)

Before installing and using it for the first time, users must first install the hardware driver (only need to install once) and set up 2 sets of COM communication ports. Please refer to Appendix B for related installation steps.

2.5 Hardware installation



Step 1:

Place the microarray scanner horizontally on a stable workbench and make sure there is enough space on the back of the scanner and the wall.

Keep both sides of the scanner well-ventilated. It is forbidden for users to block two fan outlets and two air inlets. Scanner and control computer workstation should be maintained at an appropriate distance, and confirm both the power switch is not turned on.

Step 2:

Make sure the connection of power cable to the power connector on the back side of microarray scanner.

Step 3:

Uses USB3.0 fixing kit to attach the USB3.0 signal cable to the USB3.0 interface on the back side of the scanner.

Step 4:

Make sure that the other end of USB3.0 signal line is connected to the USB3.0 interface on the back of the computer workstation.

2.6 Start the scanner system

Step 1:

Power on the computer workstation.

Step 2:

Turn on the microarray scanner, check if the power indicator LED is on and the scanner fan is operating normally.

Step 3:

If the microarray scanner control software, BioScan Control, is installed on a computer workstation, you can execute it to confirm that the scanner is properly connected to the computer workstation.

2.7 Turn off the scanner system

Step 1:

The process execution of the scanner is controlled by the BoScan Control software. When the measurement process is completed, click the "EXIT" button to turn off BioScan Control software. If the execution is not completed yet and you want to interrupt, you can click "STOP" button of BioScan Control software to stop the execution.

Step 2:

Turn off the microarray scanner, check if the power LED is off and the scanner fan is off.

Step 3:

Turn off the computer workstation.

Ch03 System Software Installation

3.1 Overview

The microarray scanner system contains two softwares: (1) BioScan Control for scanning control and (2) BioImage Analyzer for image analysis.

The fluorescent image scanning & reconstruction of microarray scanner is controlled by BioScan Control. The real-time data scanning and transmission between the scanner and control computer is using USB3.0 for data transmission, digital image processing, and real-time preview of the fluorescence images reconstruction.

Since the microarray scanner provides fast and accurate fluorescent image scanning and reconstruction of slides, users can use BioImage Analyzer as a fluorescence image analysis software or other compatible software for fluorescence image numerical analysis.

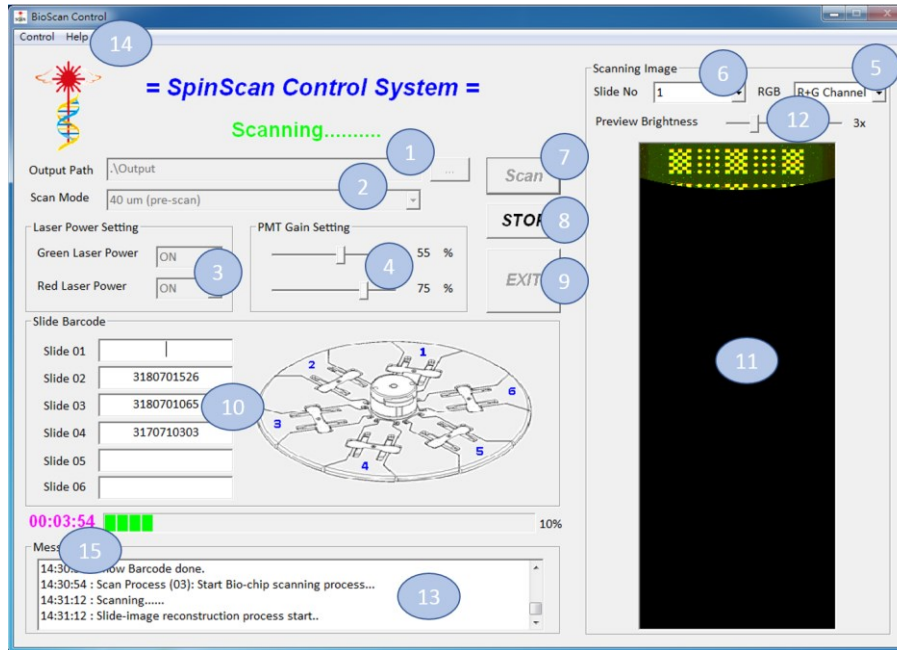
BioImage Analyzer fluorescence image analysis software provides the following features:

- Friendly GUI interface for reading and displaying 16 bit TIFF image files.
- GenePix Array List File or MSK file.
- Optical image multi-block circular array of fluorescent spots.
- Tiff image generated by the automatic selection of slide bits on the fluorescence spots.
- Adjustable image brightness and contrast.
- Display the bar chart distribution of the fluorescent reaction of wavelengths 532nm and (or) 635nm.
- Display scatter plot and M-A plot.

After the analysis is completed, the data can be stored separately to provide users with follow-up analysis and diagnosis

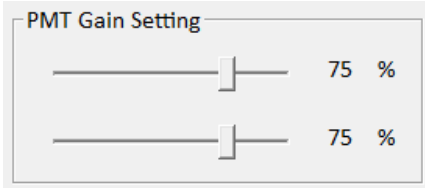
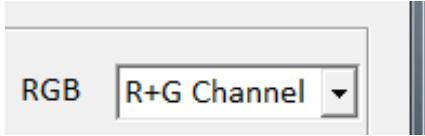
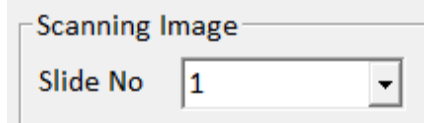



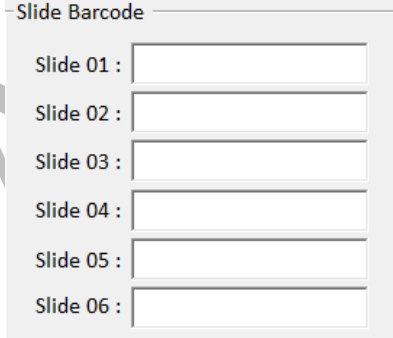
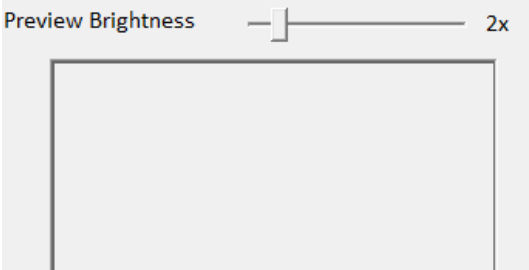
3.1.1 BioScan Control operation interface


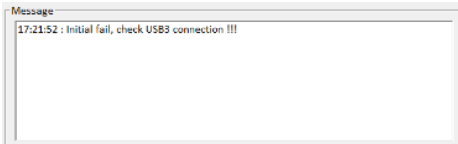
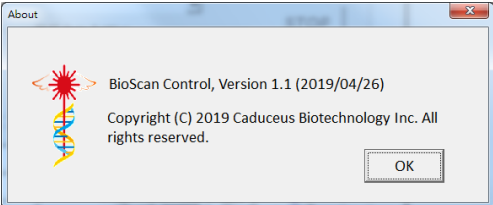
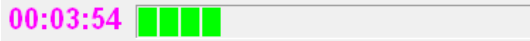
BioScan Control software has easy-to-use and related fool-proofing features to avoid false operation, and the main window operation interface is shown below.



BioScan Control main window operation interface

Item	Icon	Description
1		Image output and save directory and path
2		Scan mode setting
3		Select laser power of both green and red channels

4		Set the gain value of photomultiplier tube (PMT)
5		Selection of image preview and channels of image include "red" and/or "green" channel.
6		Select slide (from 1 to 6) for image preview
7		Start scan button
8		Stop scan button
9		Exit button
10		Display barcode number
11		Show the area of preview image

12		Show the histogram of the scanned image area
13		Show the current status and related information
14		Version of the BioScan Control software
15		Display countdown timer (scanning estimated remaining time)

Note:

The actual location of the marked items please refer to the above figure.

3.2 Hardware install requirements and protection lock

The specifications of computer workstation used by the microarray scanner system are shown as follows:

Operation system

- Windows 10 64-bit Professional operating system

Hardware specification

- CPU: Intel Core i5-6500 of equivalent or higher
- Memory: 16 GB DDR4 RAM or more.

(If there is a requirement for 2 μm high-resolution fluorescent image scanning, 32 GB RAM is required)

- Hard disk capacity: 1.0 TB
- USB interface: USB 3.0
- Display: 17-inch or larger color display, 1920×1080 pixel resolution
- Mouse: optical mouse, USB interface
- Keyboard: USB interface

BioImage Analyzer fluorescent image analysis software requires a dongle for installation and use. A dongle is shipped with the microarray scanner, which must be inserted into the computer workstation's USB port, otherwise, the BioImage Analyzer software cannot work. In that case, a dialog of "hardware protection lock" will pop-up on the box message prompts.

3.3 Software Installation

When microarray scanner system is shipped from the factory, relevant software has already been installed on computer. If you install or re-install it by yourself, please confirm the computer's regional language settings correctly correspond to the local regional language, to ensure that BioScan Control interface can display fonts correctly and BioImage Analyzer can open Tiff image correctly (for example, when the name of path or file containing Chinese).

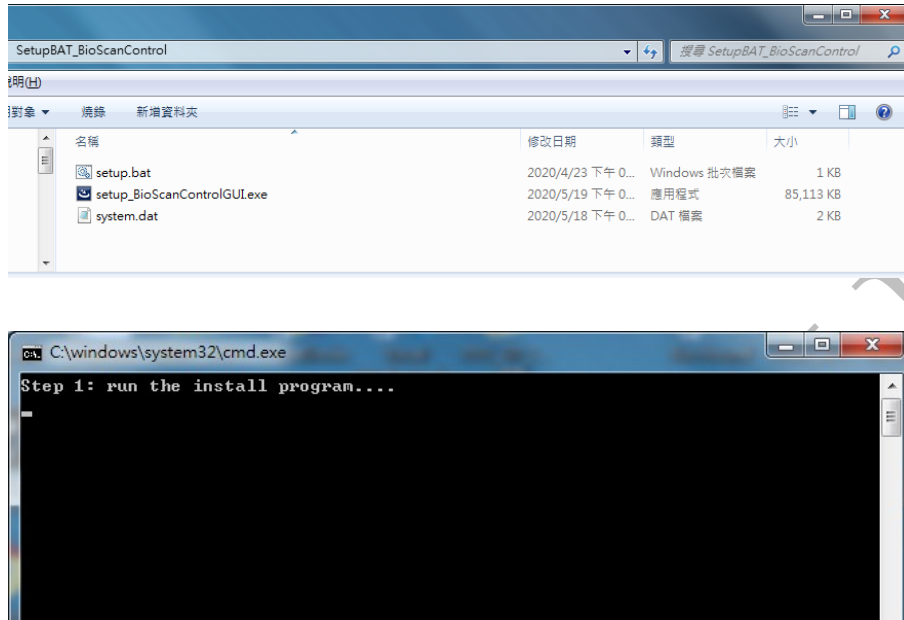
3.3.1 BioScan Control software installation

Step 1 Turn on the computer workstation.

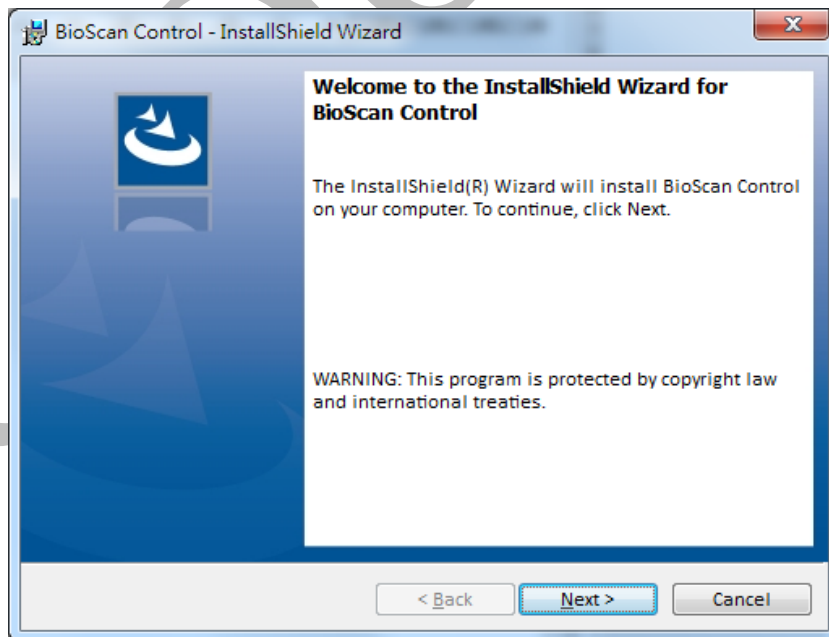
Step 2 Insert the USB flash drive with software installation program into computer workstation.

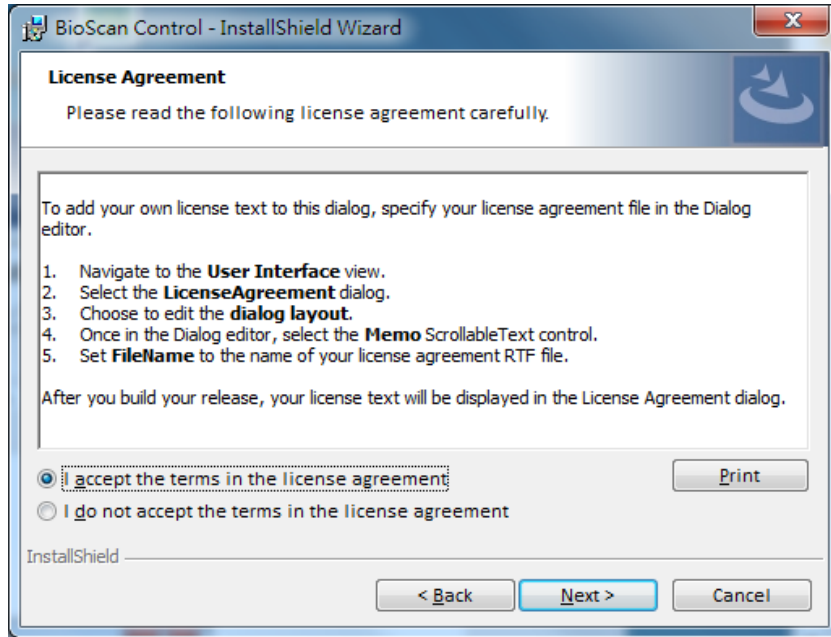
Step 3 Browse the USB flash drive directory and find the directory (:\SetupBAT_BioScanControl), then execute the "setup.bat" in the

directory to install the batch file. Double-click the file to enter the installation guide (for related installation steps, please refer to: Appendix-A).

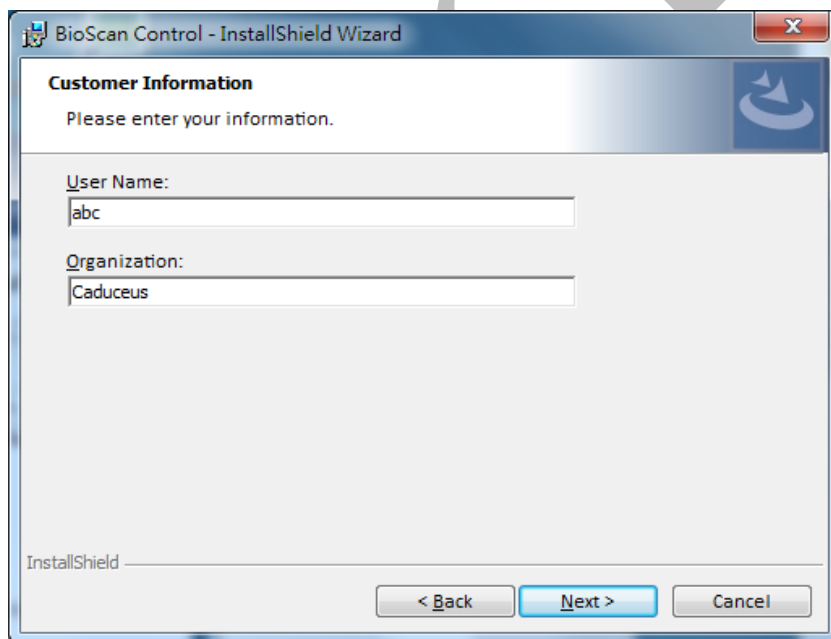


Step 4 Welcome to the Installation Interface of BioScan Control, then press “Next” button.



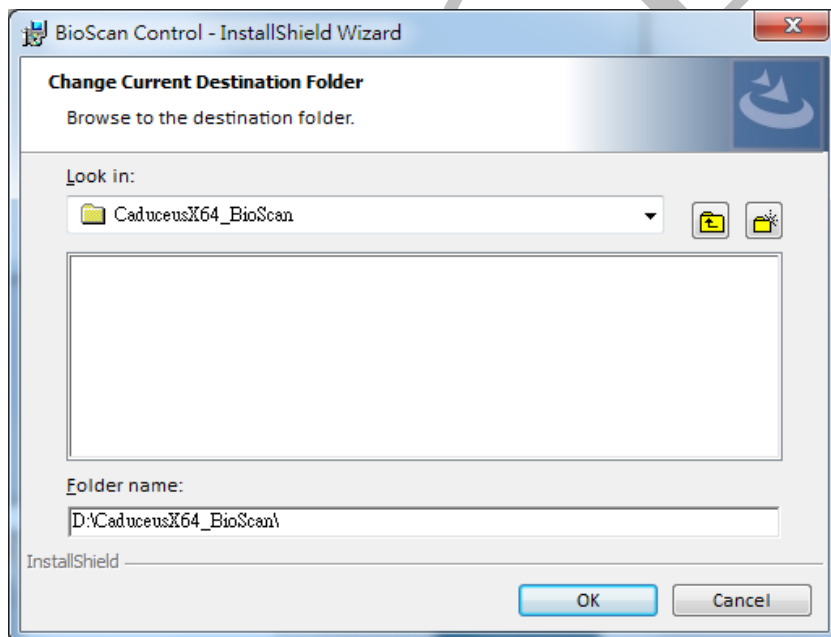
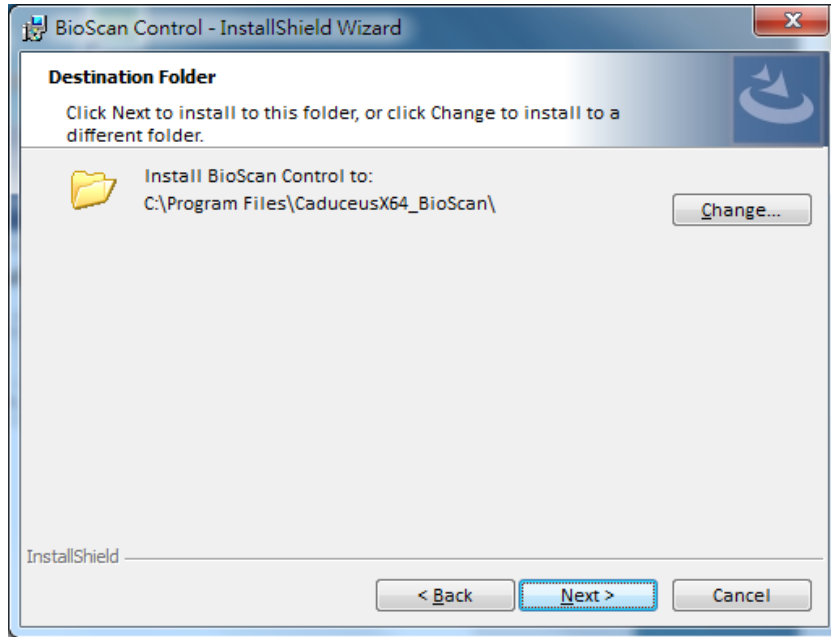


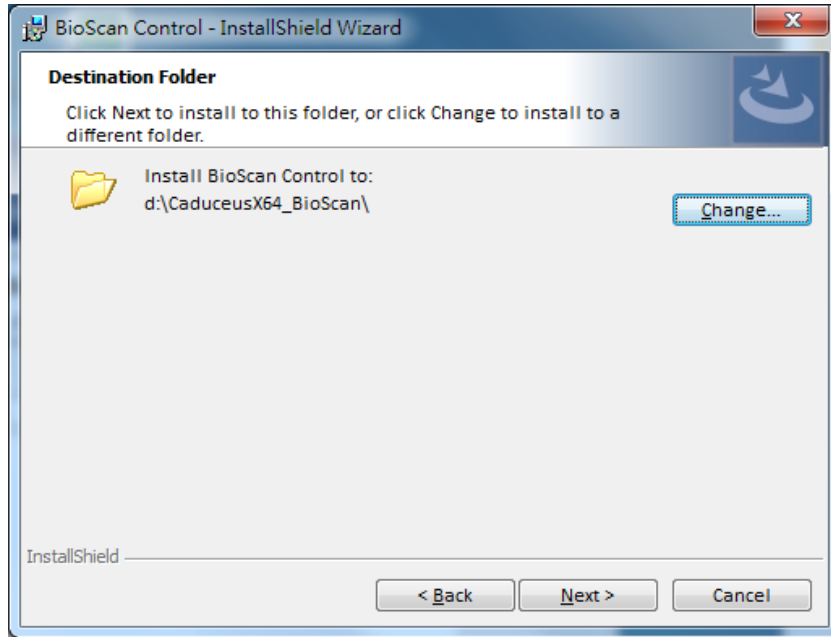
Step 5 Enter the user name and unit information, then press “Next” button.



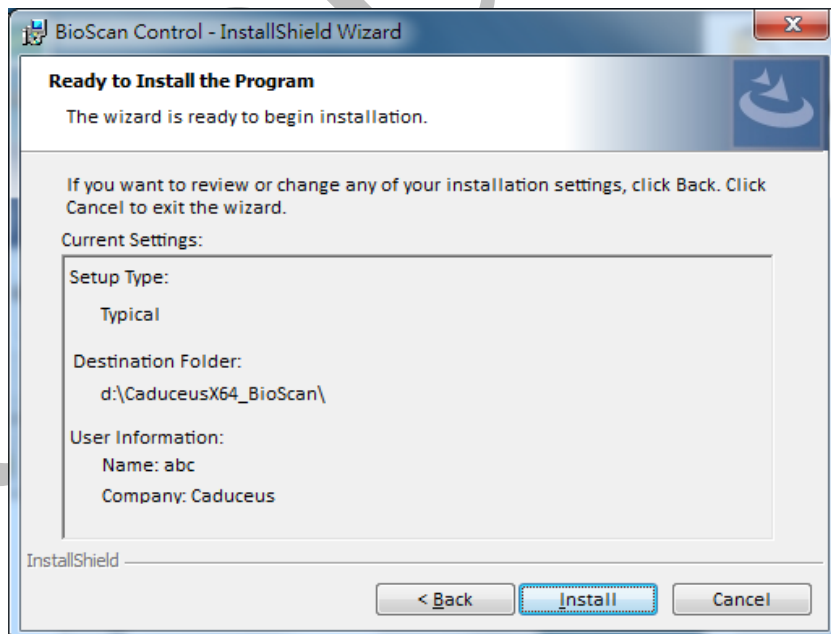
Step 6 Click the “Next” button to install BioScan Control to the destination folder named as “D:\CaduceusX64_BioScan\” , or click the “Change” button to update the folder name.

Then click "OK" button, return to the destination folder window, and click "Next" button.

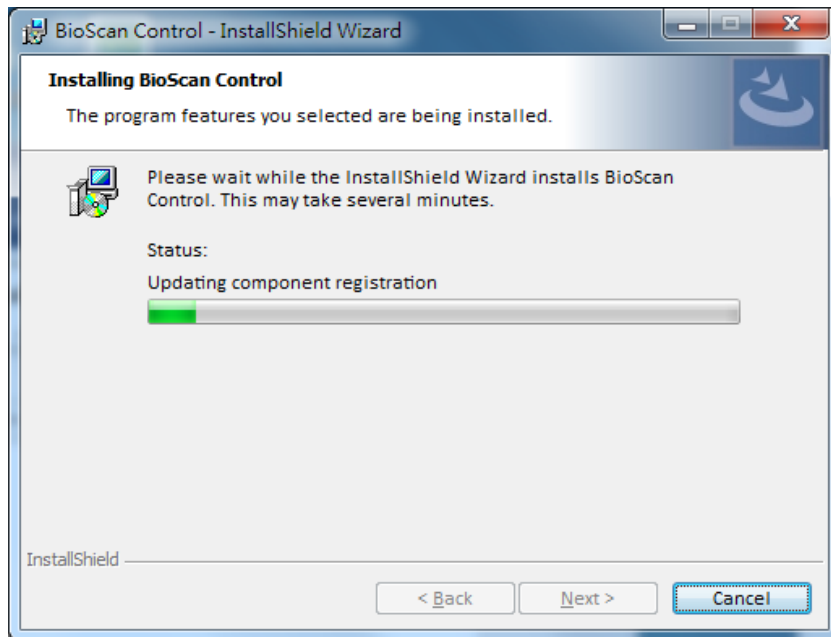




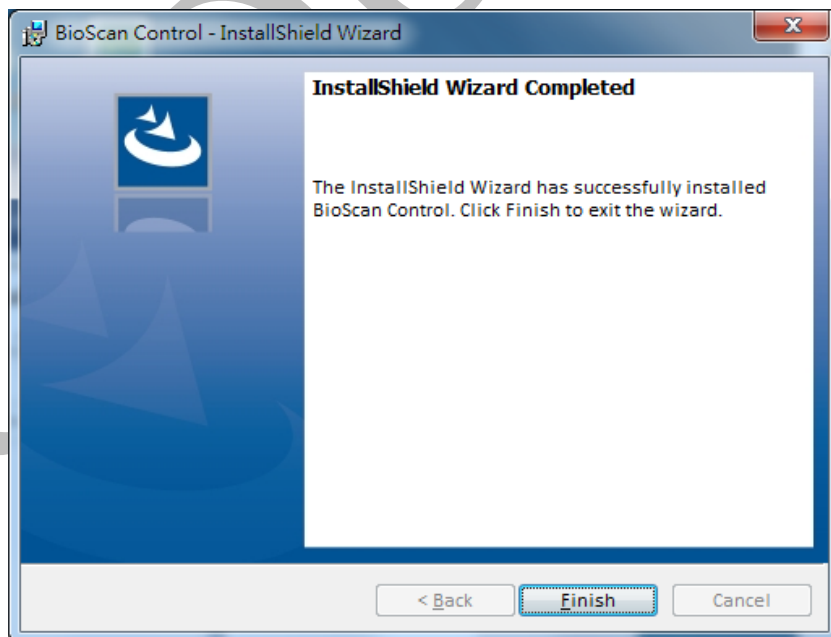
Step 7 Press the “Install” button to confirm and begin the installation process.

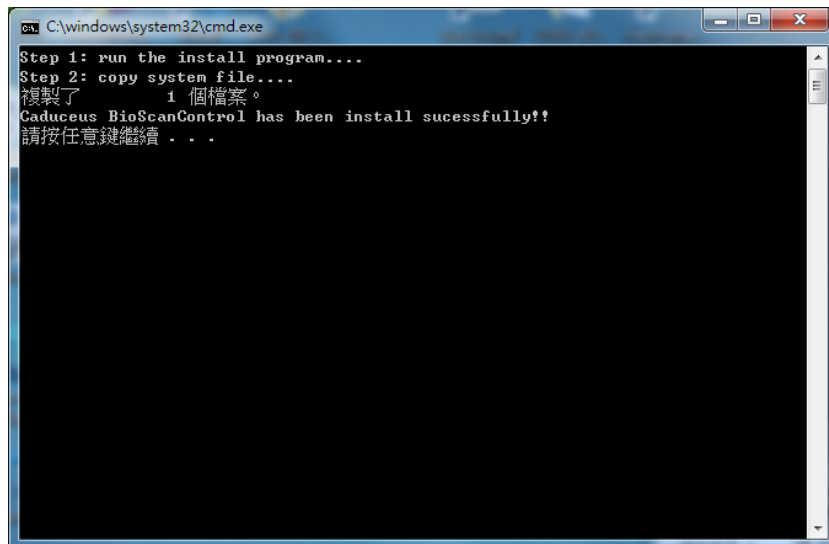


Step 8 Dynamic indication of installation process.



Step 9 When installation is completed, press "Finish" button and exit the Installation guide. Windows operation system will reboot and update settings. You can also choose to restart later.





```
C:\windows\system32\cmd.exe
Step 1: run the install program...
Step 2: copy system file...
複製了 1 個檔案。
Caduceus BioScanControl has been install sucessfully!!
請按任意鍵繼續 . . .
```

3.3.2 BioScan Control software uninstall

As with typical Microsoft Windows® applications, you can uninstall the BioScan Control software from the PC console, please find and launch "Add or Remove Programs" from the console. And you can find "BioScan Control" in the list of installed programs, select "Delete" and select "Yes" when the confirmation prompt appears, the program will be uninstalled.

3.3.3 BioImage Analyzer software installation

Step 1:

Power on the computer workstation.

Step 2:

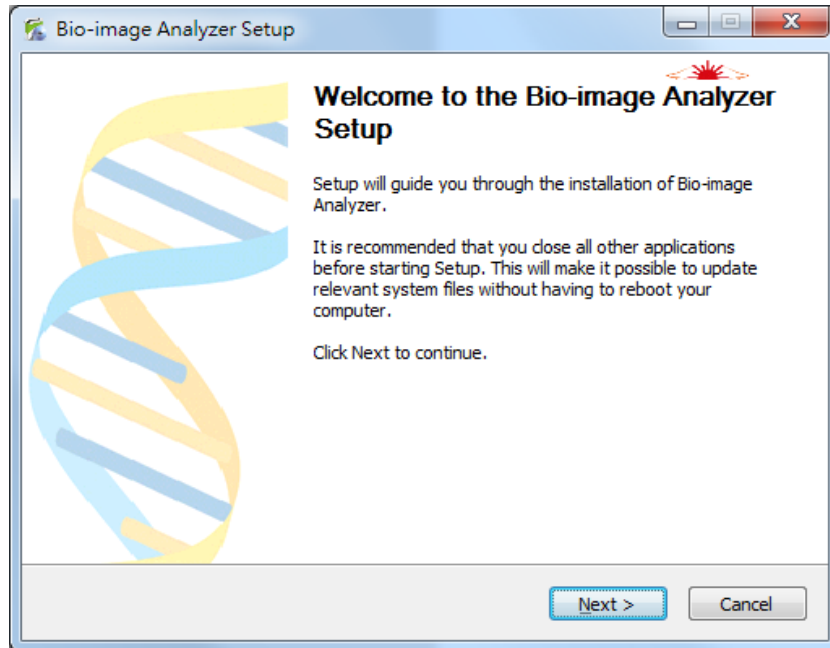
Insert the software installation USB flash drive into USB port of the computer workstation.

Step 3:

Browse USB flash drive directory and find "Setup.exe" installation file. Press the file twice to enter the installation guide.

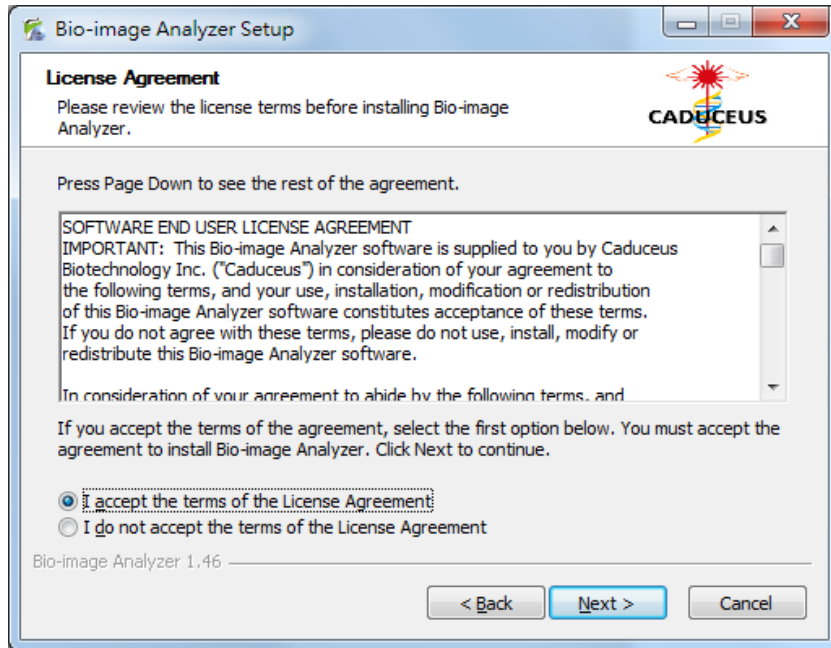
Step 4:

Welcome to use BioImage Analyzer installation interface, then click the "Next" button.



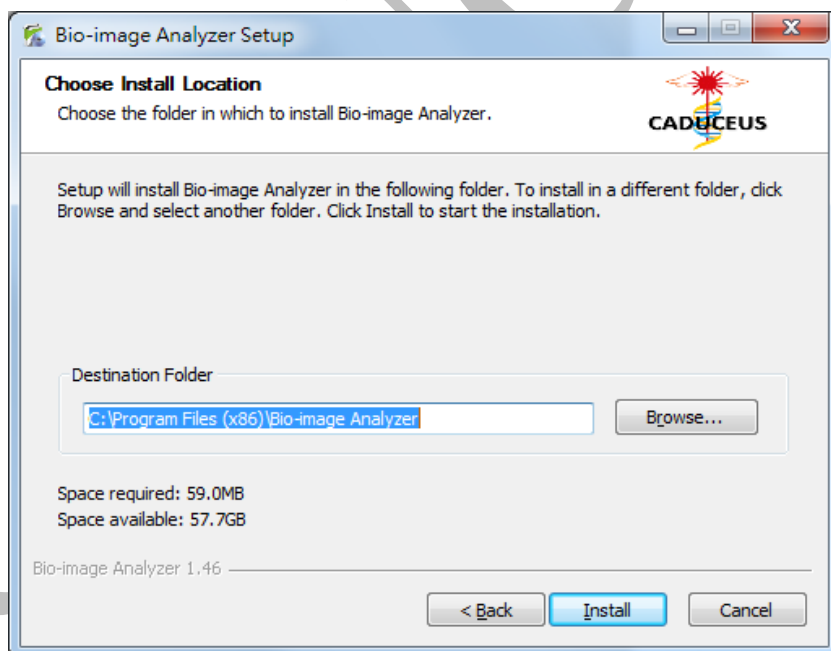
Step 5:

Click the "Accept the license agreement" terms, and click the "Next" button.



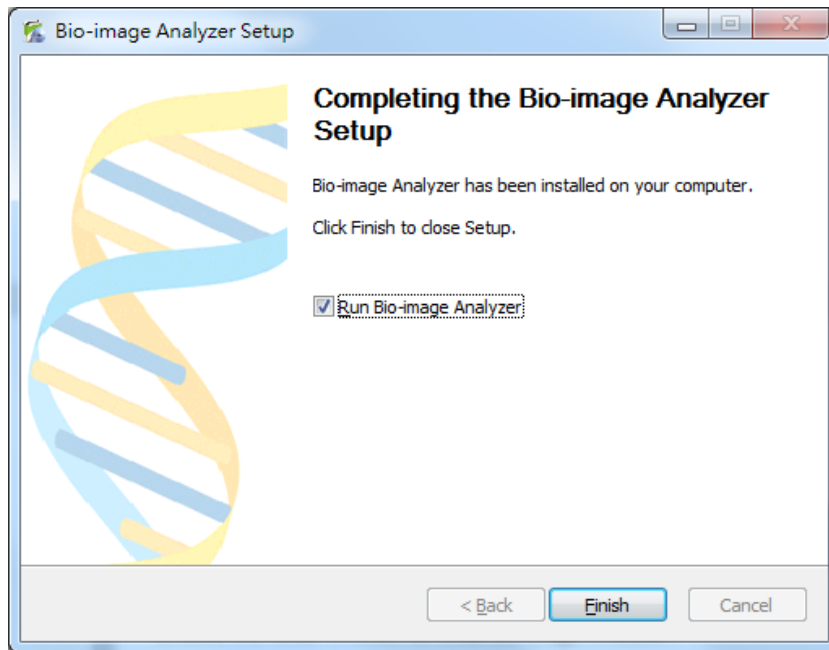
Step 6:

Select the destination folder to install, and click the "Next" button



Step 7:

When the installation is completed, click the "Finish" button to exit the installation guide. The operating system will reboot to update the settings, or you can choose to reboot later.



3.3.4 BioImage Analyzer image analysis software uninstallation

You can uninstall the BioImage Analyzer image analysis software from the PC console, please find and launch "Add" or "Remove" programs from the console. And you can find "BioImage Analyzer" in the list of installed programs, select "Delete" and select "Yes" when the confirmation prompt appears, the program will be uninstalled.

Ch04 BioScan Control Software

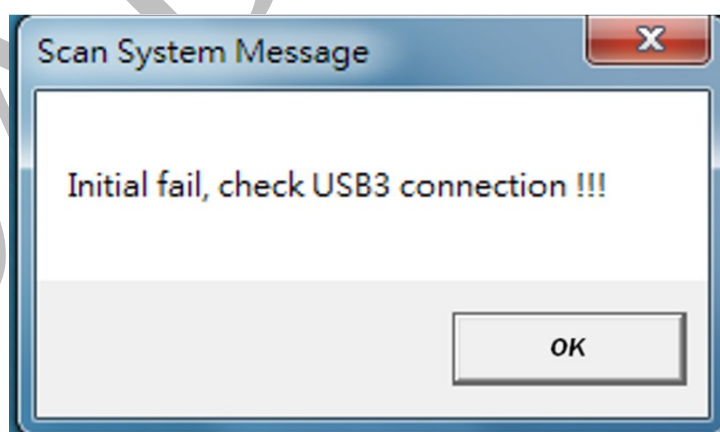
4.1 Overview

In this chapter, this instruction manual will teach you how to achieve microarray biochip fluorescence image scanning through hardware and software operations.

4.2 Step of scan process

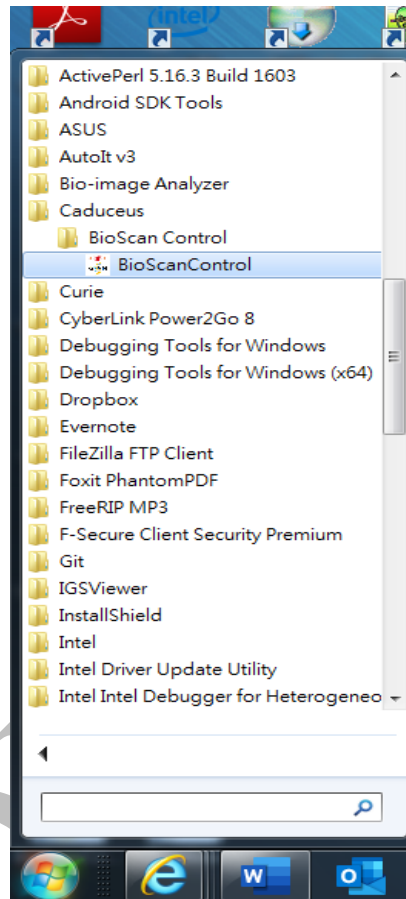
Step 1 : Start the system

1. Turn on the microarray scanner and start the scanner.
2. Open the computer workstation.
3. Connect the scanner and computer with a USB cable (connector section, with reinforced connection holder, so the connector does not disconnect easily). A USB device icon appears in the Microsoft Windows® desktop working menu. If the USB cable cannot be connected properly, the following message window will appear.



After checking and confirming that USB cable is properly connected, the system will return to the initial state as ready for scan.

4. Start Menu from Microsoft Windows® Select "All Programs"> Caduceus> BioScan Control to launch the BioScan Control application. The program begins to search for scanner and system status self-diagnostic process.



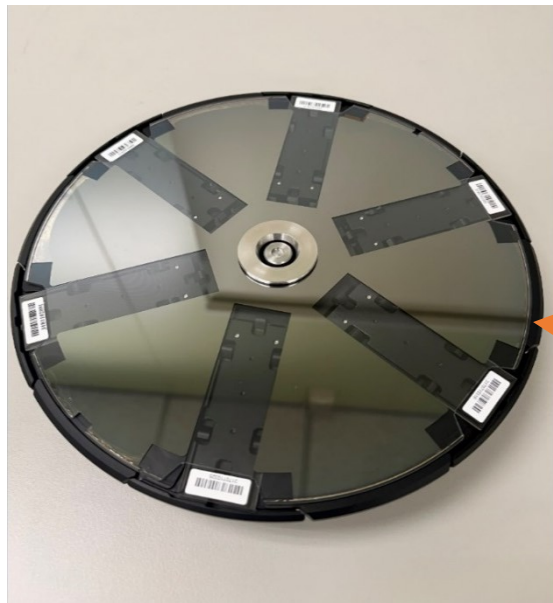
Start Menu's BioScan Control application and icon

Step 2 : Microarray slide loading

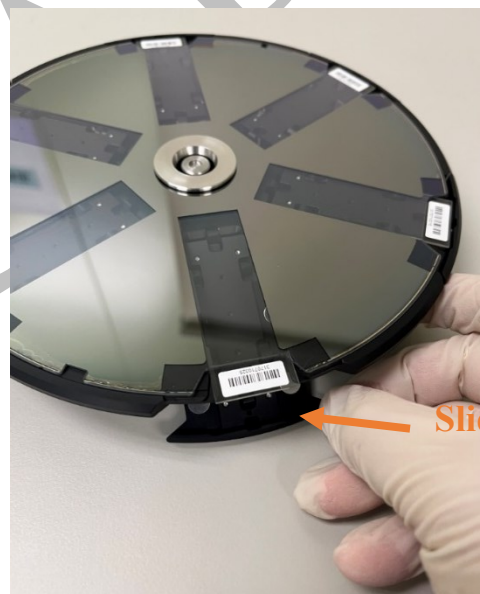
1. After scanner is started, the slides to be scanned can be prepared, and fluorescence images of up to 6 slides can be simultaneously scanned. It

should be noted that before loading the slide into the slide holder, ensure that the slide is dry and clean, and confirm that the slide size specifications are compatible with the slide holder specifications. Microarray slide loading process is as follows.

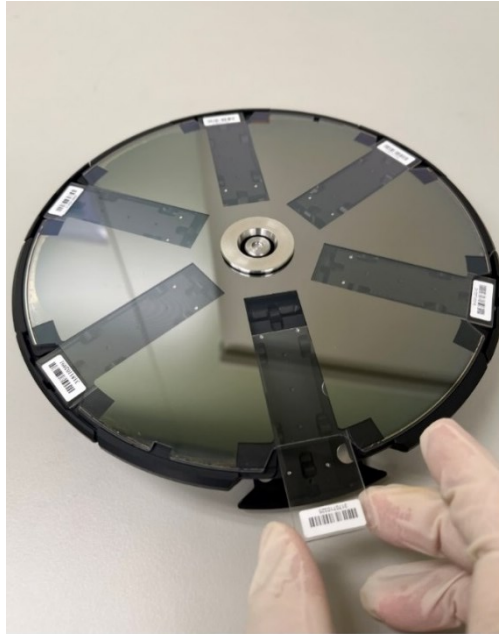
2. Place the slide holder on a stable and clean table.



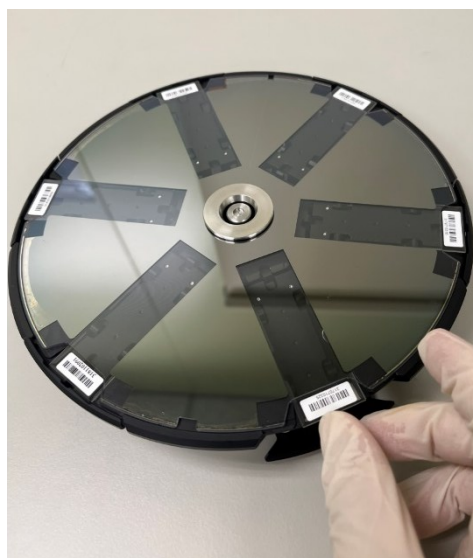
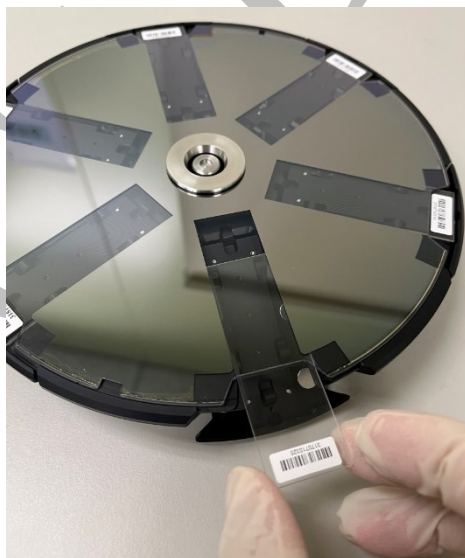
3. Open the slide holder cover.



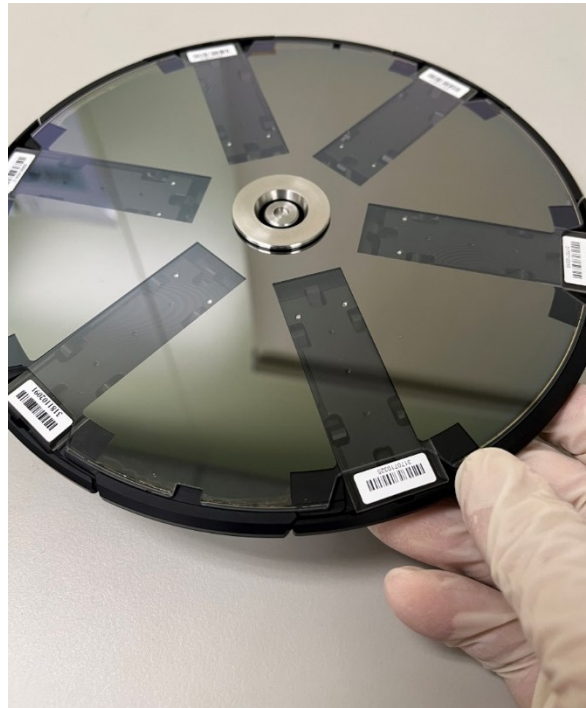
4. Remove the blank slide or slide from the slide holder along the black metal guide slot horizontally. Blank slide or slide should avoid to rub inner surface of the glass carrier.



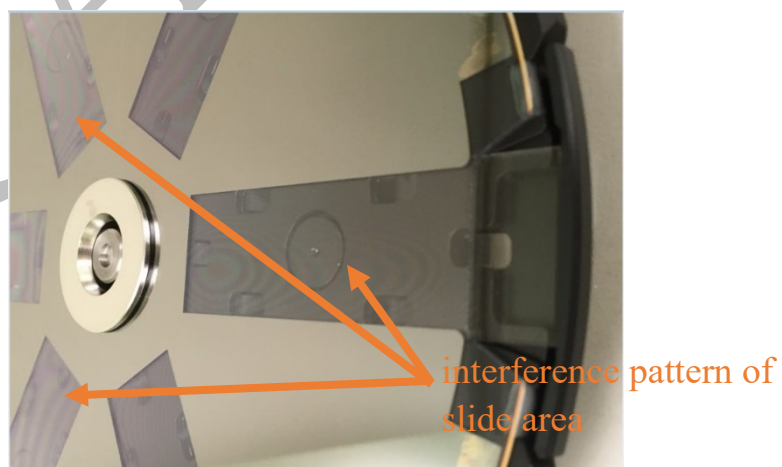
5. Inserted the slide into the slide holder (scan side up) along the black metal guide slot horizontally. The slide should avoid to rub inner surface of the glass carrier. Confirm the slide is inserted into the slide holder completely.



6. Close the slide holder cover.



7. Repeat steps 3 through 6 and load the other slides to the slide holder.
8. Check interference pattern of slide area to confirm that all the slides in the slide holder are in close contact with the glass surface of the slide holder.



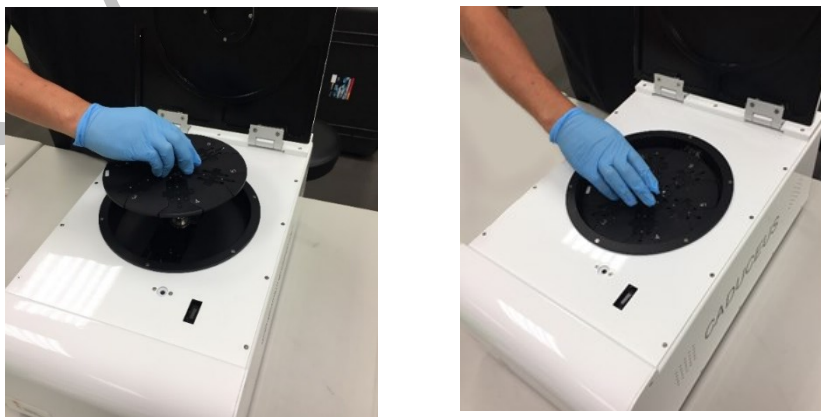
Precaution notes:

If biochip slide itself is warped or the surface is significantly contaminated or uneven, it may not fit snugly against the glass surface of slide holder and may result in an incorrect scanned image.

9. Open the upper cover of microarray scanner, hold the loading/unloading mechanism of the slide holder, and load the slide holder onto the rotation axis of the scanner carefully.



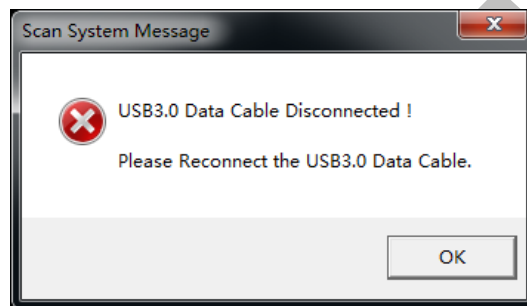
10. Release the loading/unloading mechanism of slide holder and verify that the slide holder is loaded properly by rotation the slide holder manually.



11. Close the scanner cover.
12. Start the implementation of the BioScan Control fluorescent image scanning software, which is installed in the computer workstation.

Step 3 : BioScan Control connection test with the scanner system

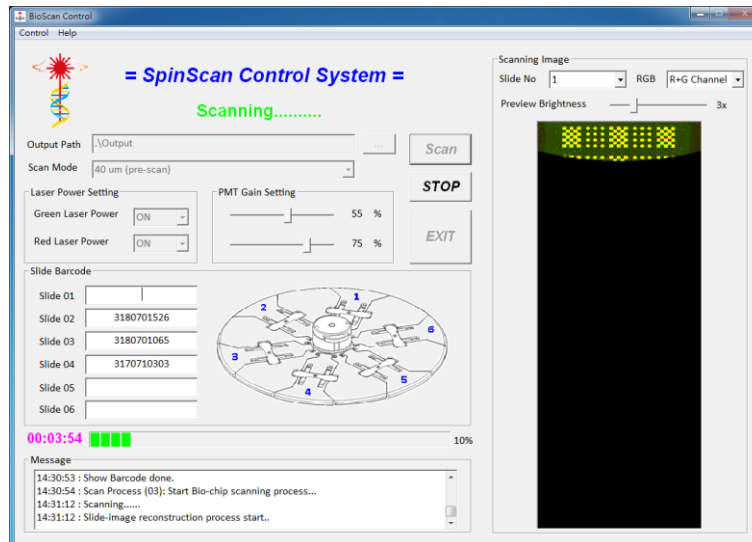
1. After starting the main window of BioScan Control, it will automatically test connection with scanner system. After the connection test is completed, user can perform the operation option of operation step-4. At the same time, during the scan, if it cannot be connected properly, the following message window will appear.



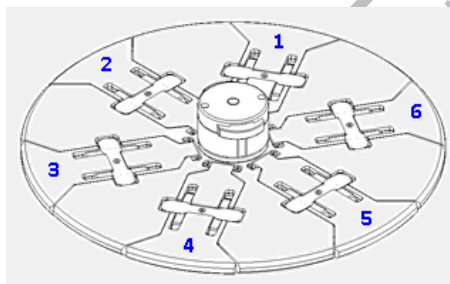
After checking and confirming that USB cable is properly connected, the system will return to the initial state as ready for scan.

Step 4 : Scan mode and parameter setting

1. Click on the fluorescent image output directory marked item (1) in the main window, scanned fluorescence image will be automatically saved as multi-page 16 bit TIFF format for subsequent image analysis. The file name will automatically be displayed in the order of slides from 01 to 06 and the barcode number attached to each slide as the image file name.

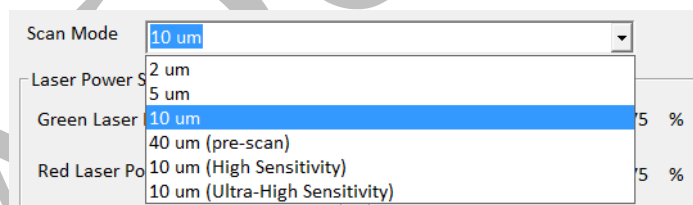


BioScan Control software main window operation interface



Slides with number 1 ~ 6 schematic

2. Click on the main window marked item (2). Select the scan mode



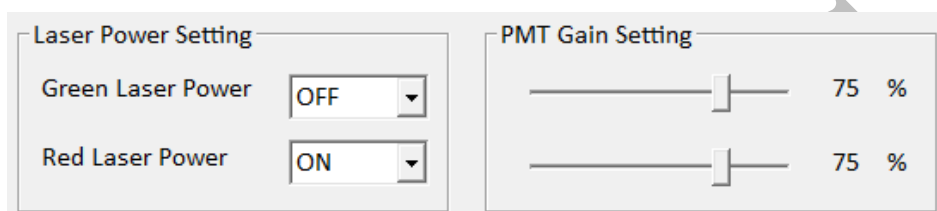
settings and the output of fluorescence image resolution. Scan mode settings include: 2 μm , 5 μm , 10 μm (normal, high sensitivity, and ultrahigh sensitivity), and 40 μm (pre-scan).

Select scan mode setting

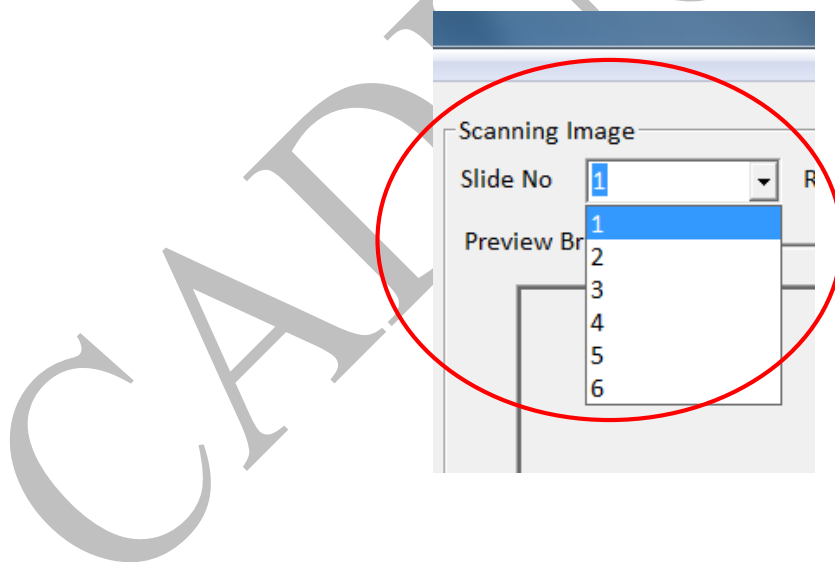
3. Click on the main window marked item (3). Laser powers of wavelengths 532 nm and (or) 635 nm can be set as ON or OFF. The higher the laser power, the stronger the fluorescent signal is obtained. The signal value of scanned fluorescence image increases with

increasing laser power. Users are advised to be familiar with the scanner application and use the optimal settings to get the proper data.

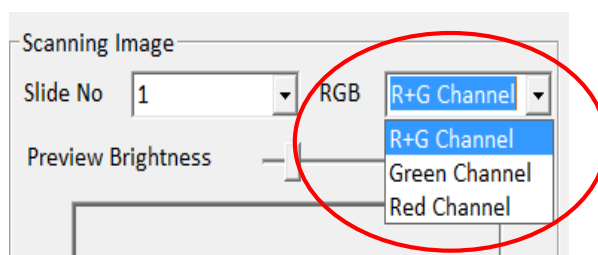
4. Click on the main window marked item (4). Select the PMT signal gain scaling factor, you can choose to set 20 different levels of signal gain scaling factors, each level increases of 5%.



5. Click the mark item in the main window (5) to select whether to preview scanned image, and to select the preview image of biochip slides numbered from 1 to 6 and image channel of "Red channel" and/or "Green channel".



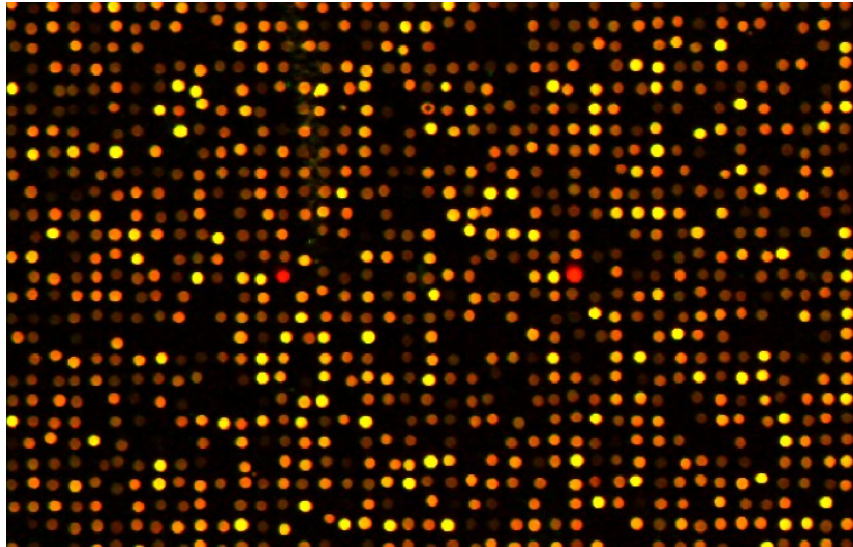
Select Preview to scan 1 ~ 6 slide images



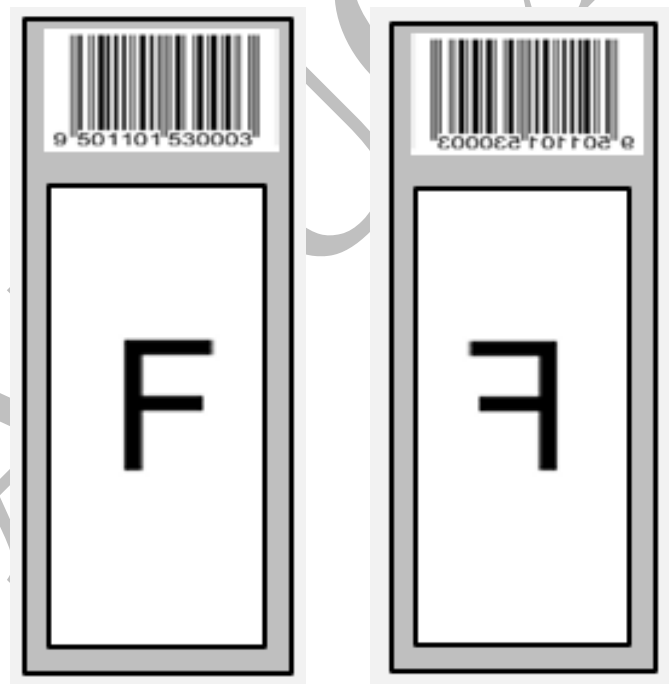
Select the preview image channel, including "red channel" and / or "green channel"

Step 5 : Start scanning and stop scanning

1. Click on the "**Scan**" button, marked item (7), to start scanning. Before scanning, scan and read the barcode will be performed first. After reading the barcode, the scanning and reading of the fluorescence data will be started and the image will be reconstructed. Process status will be displayed on marked item (11) in the main window. When the scanning area (100%) is completed, system will prompt to complete the scanning message and user can remove the scanned slide and reload a new batch of 6 slides and click the "**Scan**" button for another fluorescent image scanning. In order to avoid the misoperation of BioScan Control software, the relevant operation button has a fool-proof design that only the proper executing button can work.
2. Click the "**Stop**" button, marked item (8), to stop the current scanning process if you want to interrupt the scanning process.
3. After the completion of scanning process, click on the "**Exit**" button, marked item (9), to exit the application.
4. Based on the scanned fluorescence data, the fluorescence intensity of each spot is reconstructed and displayed.



Based on the scanned fluorescence data, reconstructed fluorescence image is performed. Schematic diagram of the relative relationship between microarray slide (active microarray surface view) and Tiff image orientation is shown as follows.

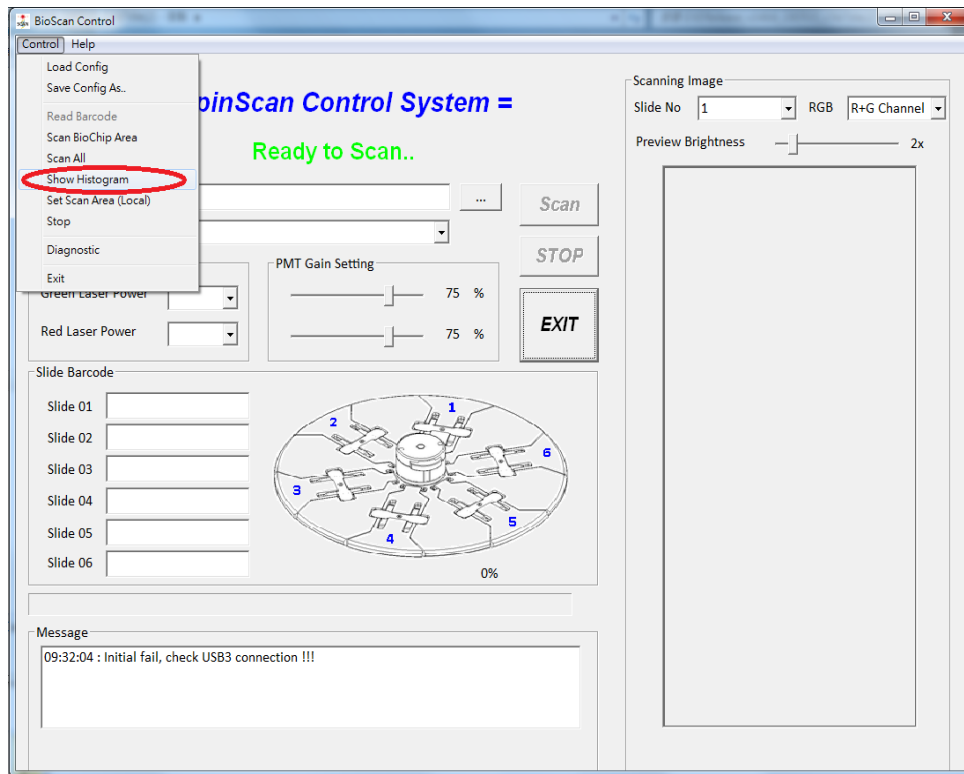


Microarray slide

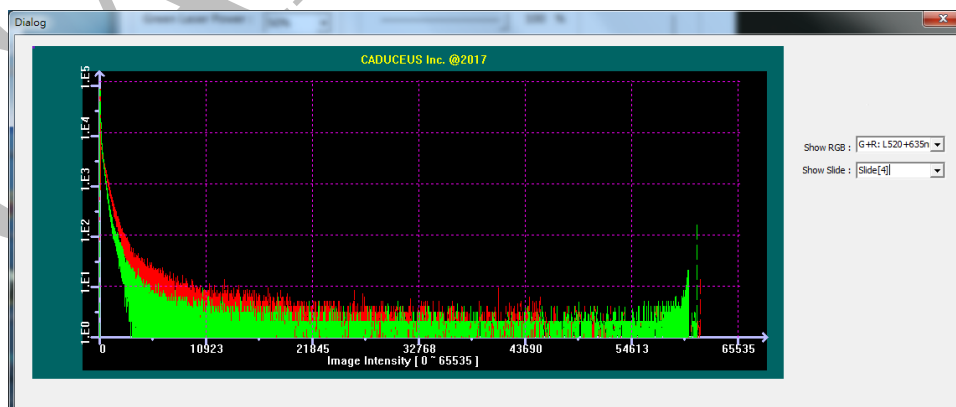
Tiff image

Step 6 : Display image histogram

1. After scanning, user can click "**Show Histogram**" button to display the histogram distribution of the fluorescent image, and provide as a reference for adjusting the related parameter settings.



Switching setting and buttons for image histogram display



Dialog for display of image histogram

Ch05 BioImage Analysis Software

5.1 Overview

In this chapter, this instruction manual will teach users how to use the BioImage Analyzer software to perform microarray fluorescence image analysis of biological chips and produce analysis charts and analysis numerical files to provide users with follow-up analysis and diagnosis.

5.2 BioImage Analyzer GUI interface

BioImage Analyzer main window operation interface is shown in below.



BioImage Analyzer software main window operation interface

BioImage Analyzer main window operation interface and classification is shown as follows.



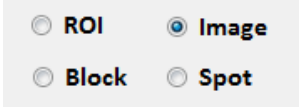




Main window operating interface






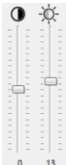
Main window operating interface and classification

Item	Interface classification	Description
1	Commands and menu lists	Provide command and control instructions.
2	Tab menu bar	Image and data analysis and results display including histogram distribution, scatter plot and M-A Plot.
3	Tool bar	Zoom out / zoom in / image moving, move/stretch 4 corners of GAL and MSK image, "Align" and "Analyze" buttons.
4	Fluorescent spot data display area	Image analysis of local area and fluorescence spot related information.

Item	Interface classification	Description
5	Result display area	Image and data analysis results, including histogram distribution, scatter plot and M-A plot.

Toolbar function description:

Toolbar button	Description
	<ul style="list-style-type: none"> ● Check the region of interest (ROI) to enlarge/reduce image in local area. ● Check image to zoom in/out or move image by mouse handling. ● Check item “Block” to use the mouse to move the GAL and MSK file multi-array images as a whole, use the mouse with Shift-key to move a single array within multi-array image of the GAL and MSK files. It can also use the mouse to stretch the array image of the GAL and MSK file. ● Check item “Spot” can be clicked after "Align" button clicked, use the mouse to individually align fluorescent dots after automatically alignment, and then manually move the fluorescent dots that are still deviated for further alignment adjustment. Move the mouse up and down with Shift-key to adjust the size of the alignment circle.
	Zoom out
	Show all to fit window
	Zoom in
	Anti-clockwise rotation

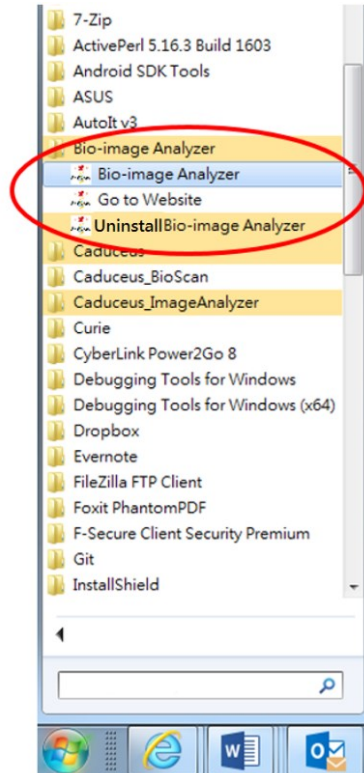
Toolbar button	Description
	clockwise rotation
	Image vertical flip
	Fluorescent spot alignment
	Data analysis
	Fluorescent spot alignment parameter setting
	Image brightness and contrast adjustment

5.3 Step of analysis

Step 1 Power on the computer workstation.

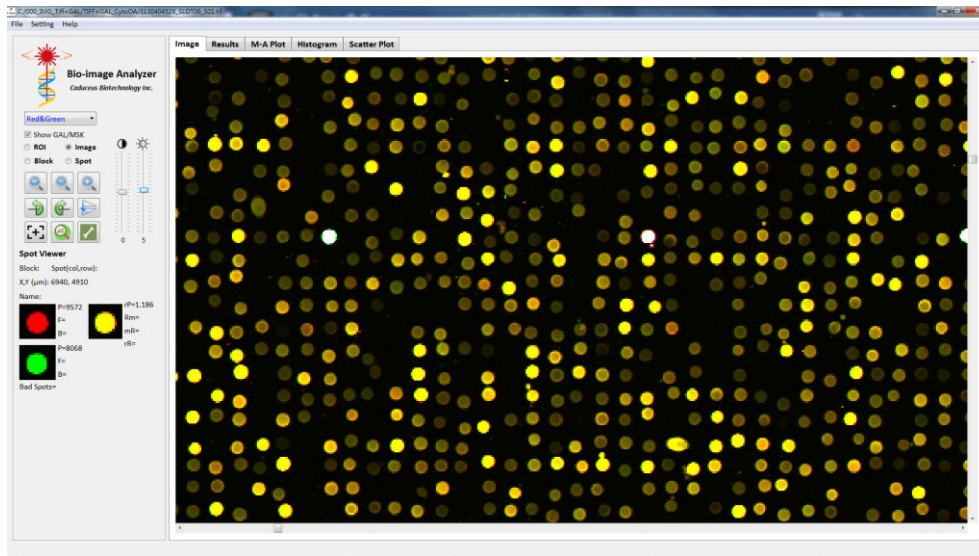
Step 2 Make sure that the dongle has been inserted into USB port of the computer workstation.

Step 3 Select "All Programs"> Caduceus> BioImage Analyzer to start BioImage Analyzer application from Start menu of Microsoft Windows® desktop.



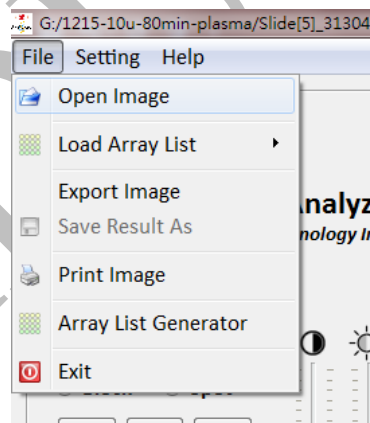
Start menu of BioImage Analyzer applications and icons

Step 4 Open BioImage Analyzer interface. BioImage Analyzer image analysis software has a user-friendly GUI interface to read and display 16 bit Tiff image files of 635nm (red channel) and 532 nm (green channel) image channels. Set related parameters will be able to generate multi-block GAL/MSK file.

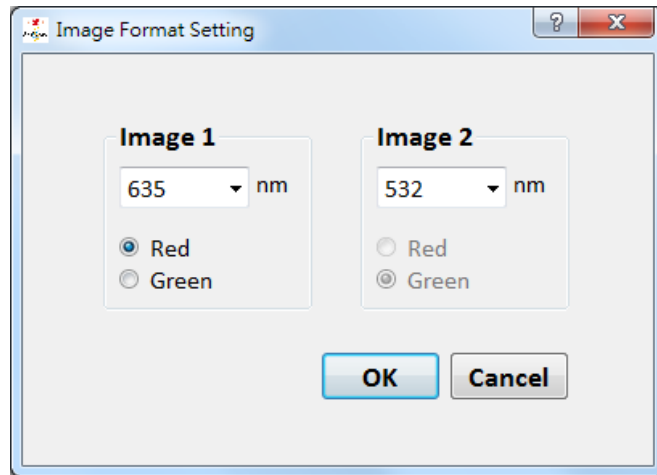


BioImage Analyzer image analysis software interface

Step 5 Click the "File" option on the menu, then click "Open Image" to load the image. The 16 bit Tiff format image file scanned and generated by BioScan Control is opened and displayed. The first page Image (Image 1) is preset to 635 nm (red channel) and the second page Image (Image 2) is 532 nm (green channel)

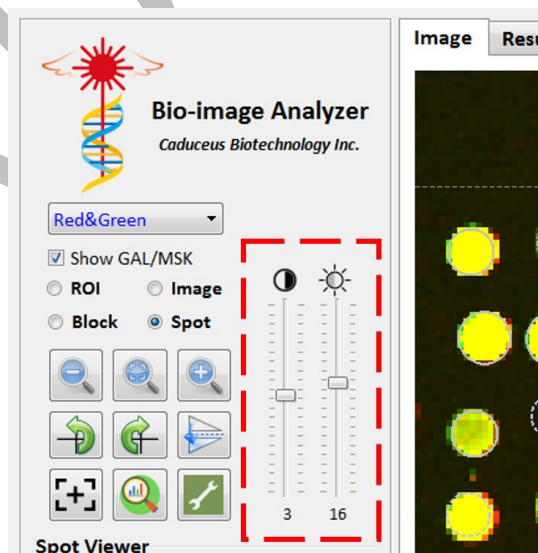


"File" option of the menu



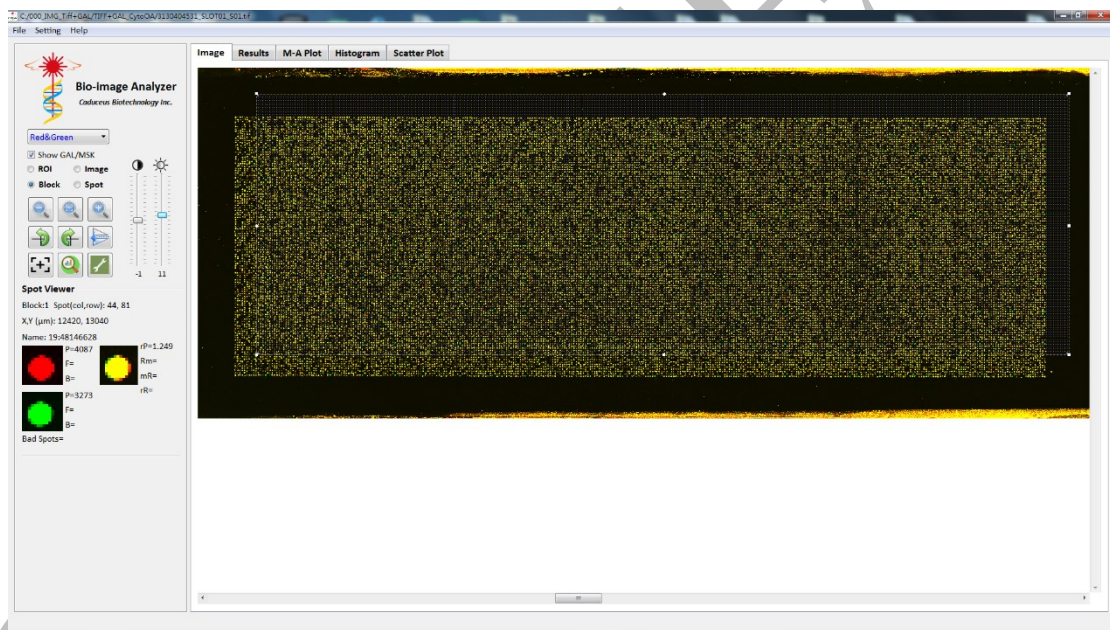
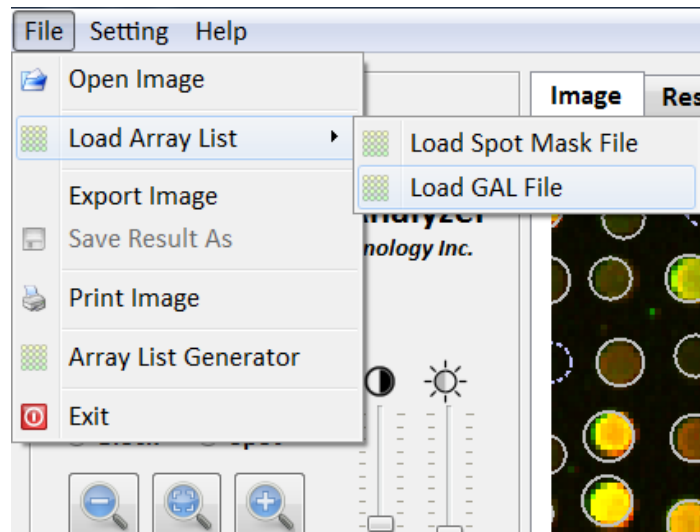
Load Tiff image settings

Step 6 After loading a 16-bit Tiff-format fluorescent image file, you can adjust brightness and contrast of the image window by dragging vertical slide control. Each pixel in each channel of the scanned image is a 16-bit grayscale signal. The BioImage Analyzer software provides a rich method of displaying scanned images in an image window for an easy way of analysis. Most of these operations are performed on the Toolbar. No matter how the image's display method and state changes, it will not affect or modify the original image data of scanned image.

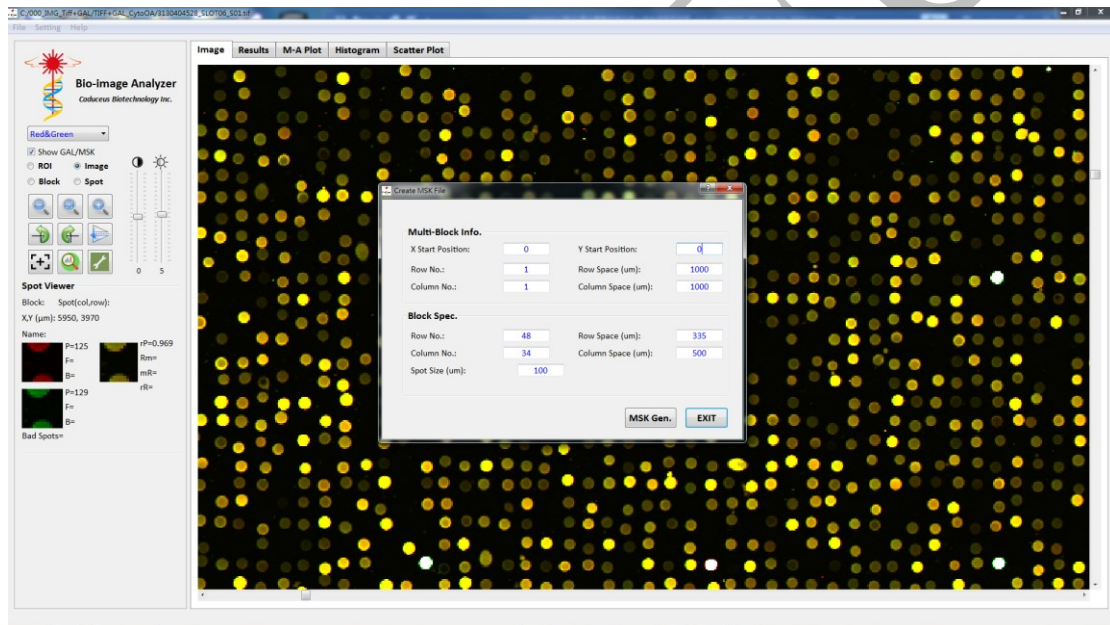
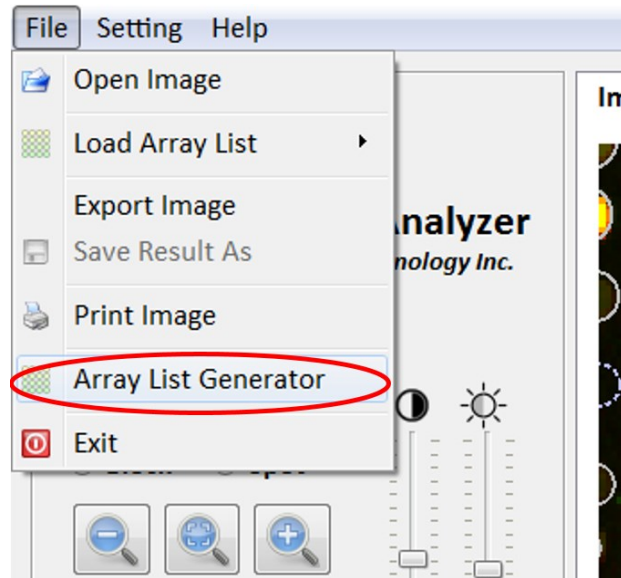


Adjust the image brightness and contrast

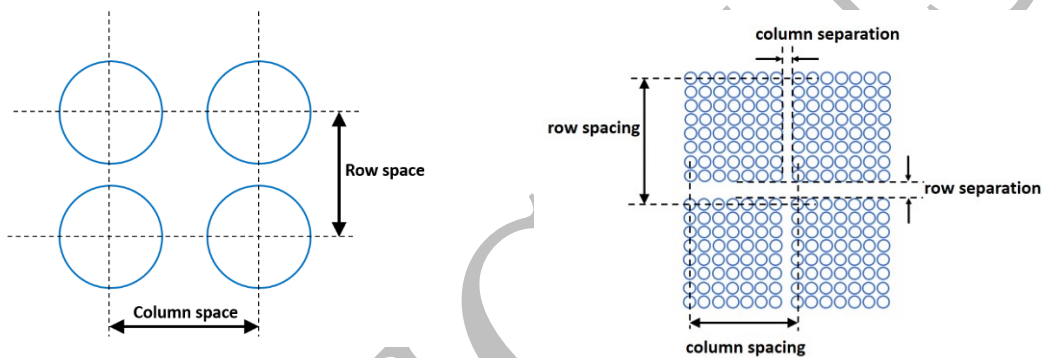
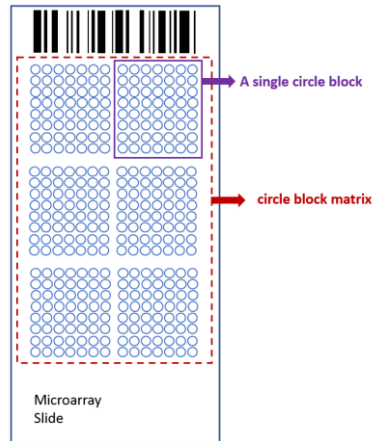
Step 7 Click the menu option "Load Array List" to load the GAL/MSK array for further selection to read the GAL/MSK array.



Alternatively, you can click on the "Array List Generator" to generate the array list file menu option to set the relevant parameters (column spacing, row spacing, number of blocks, number of rows, columns, etc.) that correspond to the circle array.

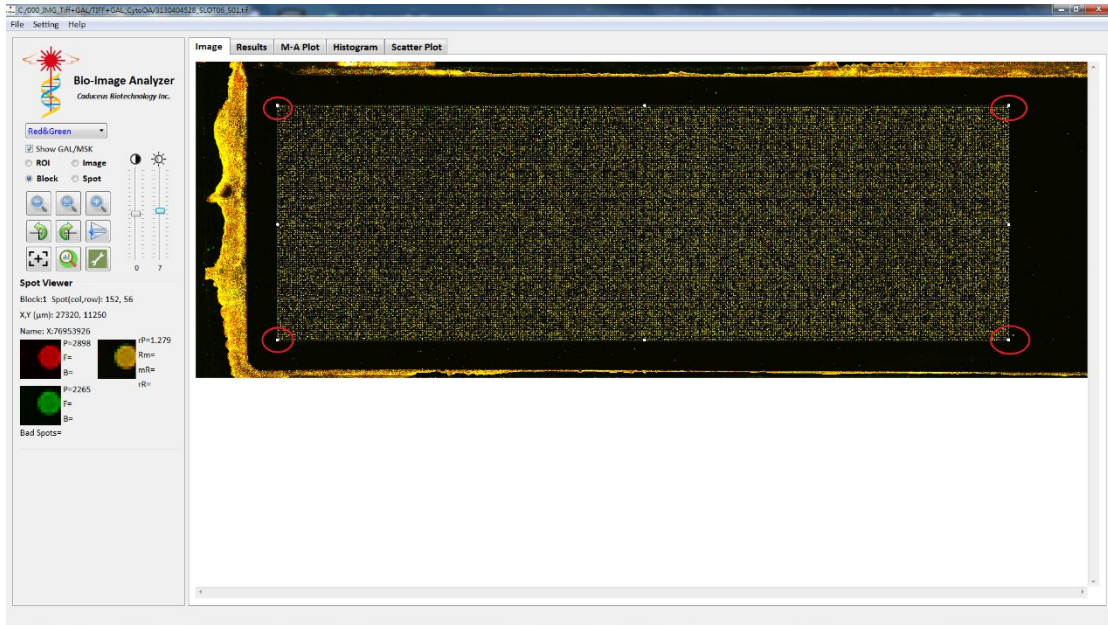


Multi-block array list (MSK) parameter setting interface

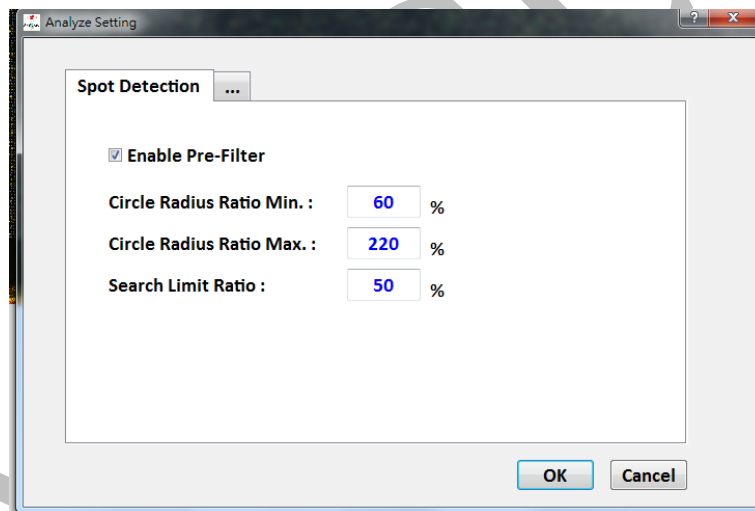


MSK file related parameter definitions

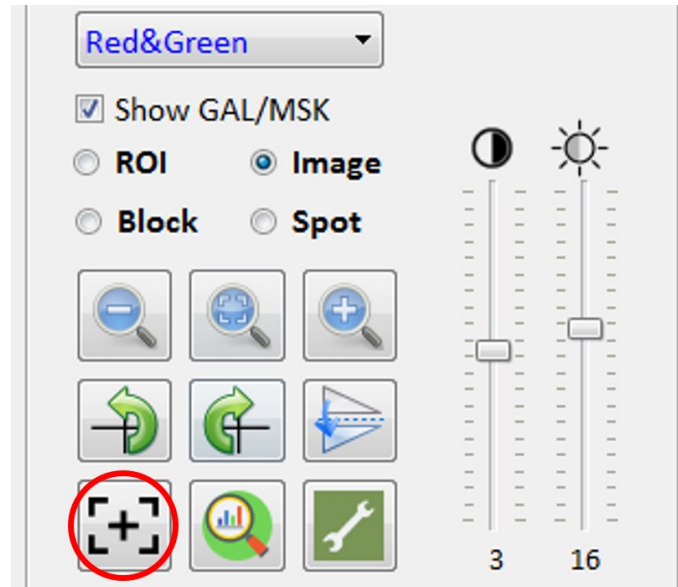
Step 8 Dynamically move four corner points of the stretched GAL/MSK image, adjust the relative positions of GAL/MSK and spot to perform a preliminary large-scale rough alignment. After finishing the above step, you can press "Spot Detection" button to set parameters such as the maximum radius, minimum radius and search range. Next, press the "Feature Detection" button to align the spots. Press the "Feature Detection" alignment button to perform fluorescent spot alignment, and then use the menu option "Load Array List" to store the GAL/MSK array for the next alignment analysis.




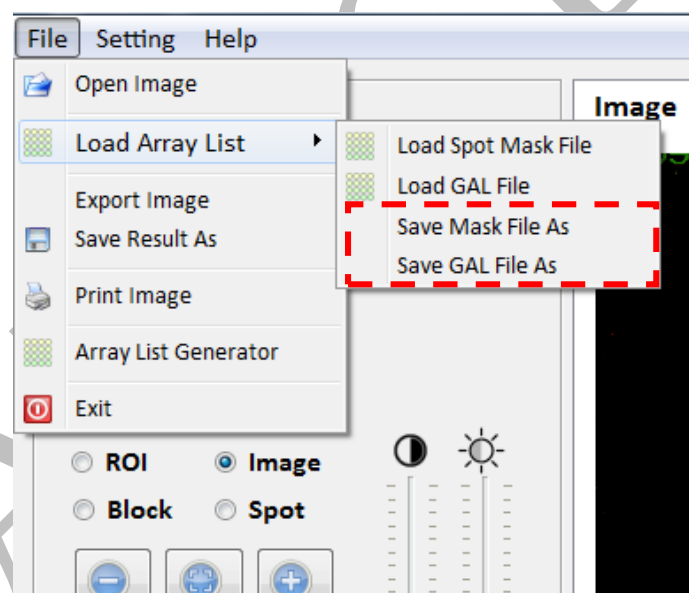
Dynamically drag the 4 corners of the GAL/MSK image



Fluorescent spot alignment parameters set



Press the  "Feature Detection" registration button to align the fluorescence point




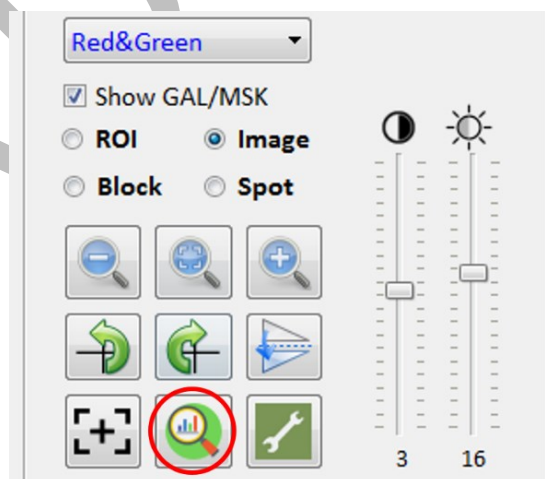
Use the menu option "Load Array List" to store the GAL/MSK array, which can be used for the next alignment analysis

Step 9 Put GAL/MSK circle array image in the window can immediately show intensity, red/green light intensity ratio and other information after mouse points to that position.

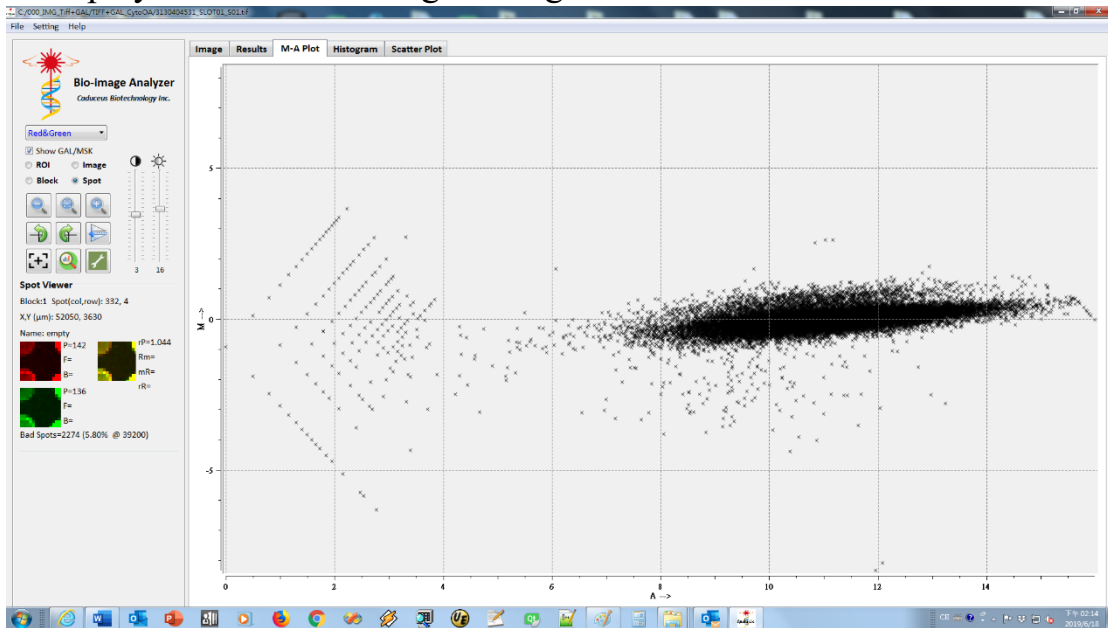


Real time displays information such as intensity of fluorescent spot pointed by mouse

Step 10 If few spots were not successful aligned after completing the automatic alignment of the fluorescent spots, users can click the "Spot" by using mouse cursor and the mouse cursor + shift to manually adjust the position and size of the circle selected points, and press the  "Analyze Image" operation analysis button to generate the "Result" tab data and output.

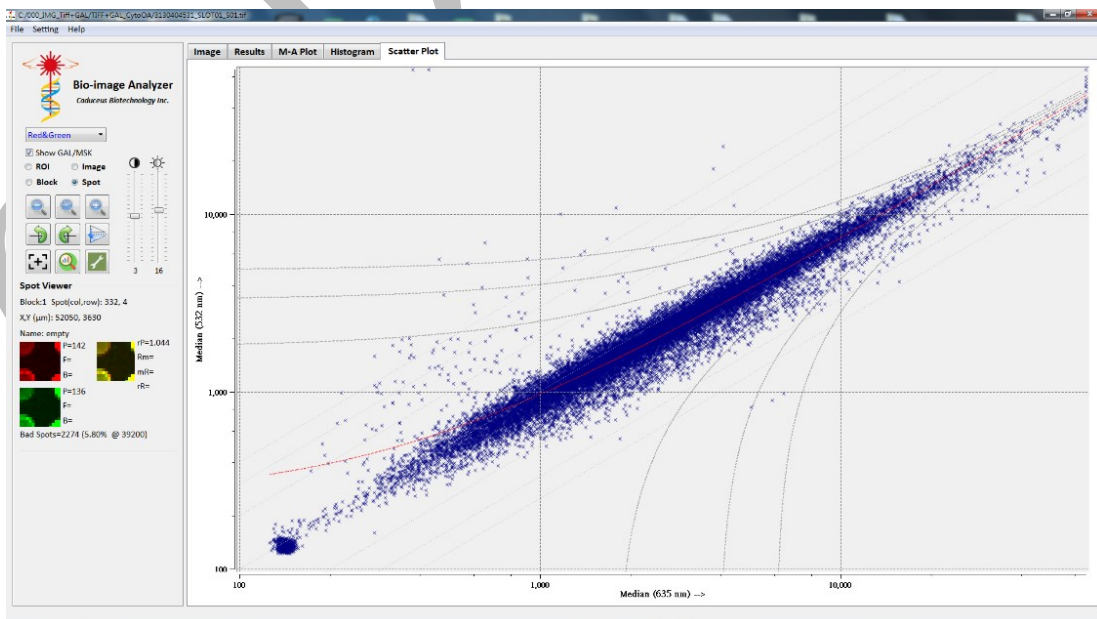


Step 12 After generating the "Result" tab data output, click "M-A Plot" tab to display the M-A Plot image through the data statistics method.




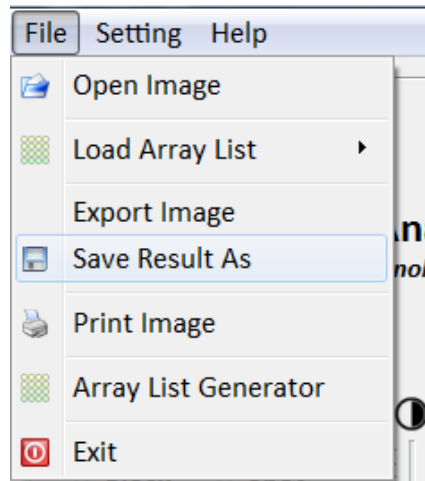
M-A Plot

Step 13 After generating the "Result" tab data output, click "Scatter Plot" tab to open the scatter plot chart window.

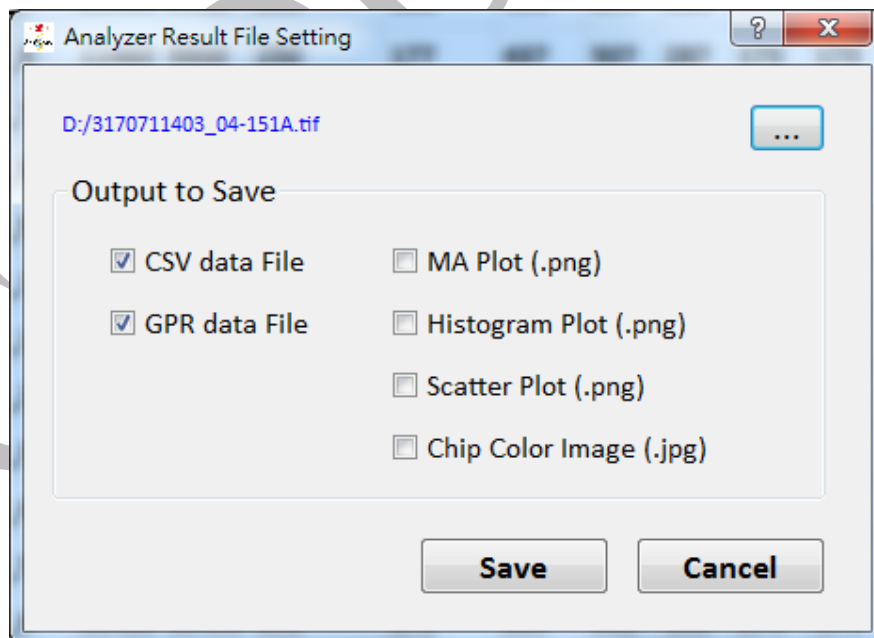


Scatter plot chart

Step 14 Click the  "Analysis" button. After the analysis is complete, you can click the menu "File" option and select the "Save Result As" option to save data, you can choose to save the analyzed numerical data or image as CSV (*.csv), GPR(*.gpr), MA Plot(*.png), Histogram Plot(*.png), Scatter Plot(*.png), Chip Color Image(.jpg) files. It can also print images and export various image data files.



Click "Save Data" option to save data file



Option to save analysis data or image to files

5.4 Definition of data column

Column Name	Definition
No.	The index number of a <i>circle</i> on the <i>grid</i> .
Block	The index number of a <i>block</i> .
Row	The row number of a <i>circle</i> .
Column	The column number of a <i>circle</i> .
ID	The accession number of the substance associated with a <i>circle</i> derived from an <i>Array List</i> (GAL/MSK) file.
Name	The substance name associated with a <i>circle</i> derived from an <i>Array List</i> (GAL/MSK) file.
Flag	Flag for alignment, positive value means successful alignment and negative value means failed alignment.
Diameter	The diameter of a <i>circle</i> (μm).
X	The X-coordinate (unit: μm) of the center of the <i>circle</i> associated with the <i>spot</i> , where (0,0) is the top left corner of the image of channel (\$1/\$2).
Y	The Y-coordinate (unit: μm) of the center of the <i>circle</i> associated with the <i>spot</i> , where (0,0) is the top left corner of the image of channel (\$1/\$2).
(FS1/FS2)_Median	The median of the values of all the pixels in a <i>spot</i> region of channel (\$1/\$2) image.
(FS1/FS2)_Mean	The mean of the values of all the pixels in a <i>spot</i> region of channel (\$1/\$2) image.

Column Name	Definition
(F\$1/F\$2)_SD	The Standard Deviation of the all pixel values in a <i>spot</i> region of channel (\$1/\$2) image.
(B\$1/B\$2)_Median	The median of the values of all the local <i>background</i> pixels of channel (\$1/\$2) image.
(B\$1/B\$2)_Mean	The mean of the values of all the local <i>background</i> pixels of channel (\$1/\$2) image.
(B\$1/B\$2)_SD	The Standard Deviation of the values of all the local <i>background</i> pixels of channel (\$1/\$2) image.
(B\$1/B\$2)_CV	The Coefficient of Variance of the values of the local <i>background</i> pixels of channel (\$1/\$2) image.
(F\$1/F\$2)_CV	The Coefficient of Variance of the values of all the pixels in the <i>spot</i> region of channel (\$1/\$2) image.
SNR_\$1	signal to noise ratio of image channel (\$1).
SNR_\$2	signal to noise ratio of image channel (\$ 2).
\$1_Total Intensity	image of channel (\$1) corresponds to sum of the intensity values of all pixels within the phosphor spot.
\$2_Total Intensity	image of channel (\$ 2) corresponds to sum of the intensity values of all pixels within the phosphor spot
F_pixels	image pixels corresponds to sum of all the intensity values within the fluorescence spot.
B_pixels	image pixels corresponds to the sum of all the entities in the background of the luminescent spot

Column Name	Definition
Ratio of Mean(\$1/\$2)	The ratio of the background-subtracted mean intensities of channel \$1 to the background-subtracted mean intensities of channel \$2.
Ratio of Median(\$1/\$2)	The ratio of the background-subtracted median intensities of channel \$1 to the background-subtracted median intensities of channel \$2.
Ratios SD(\$1/\$2)	Ratio of the SD value of image channel (\$1) to the SD value of image channel (\$2)
Rgn R2 (\$1/\$2)	Linear regression coefficients for image channel (\$1) and image channel (\$2)
Sum of Medians(\$1/\$2)	Sum of the background median intensities of channel \$1 correspond to the background median intensities of channel \$2.
Sum of Means(\$1/\$2)	Sum of the background mean intensities of channel \$1 correspond to the background mean intensities of channel \$2.
(F \$1)% Sat.	Image of channel (\$1) corresponds to the ratio of the proportion of supersaturation of all pixels in the fluorescence spot.
(F \$2)% Sat.	Image of channel (\$2) corresponds to the ratio of the proportion of supersaturation of all the elements in the fluorescence spot

Note:

Image channel(\$1/\$2) :

\$1: 635nm, Red channel.

\$2: 532nm, Green channel.

F (Foreground): inside the spot of fluorescence.

B (Background): correspond to the background area of fluorescence spot.

5.5 Algorithm and formula

- **signal value**

The *spot Signal* is defined as the signal intensities of the pixels within the associated *circle*, and is expressed in terms of *Mean of Intensities*, *Median of Intensities* and *Standard Deviation of Intensities*. A *circle* may be larger or smaller than its associated *spot*, thus the actual number of the pixels of the *spot* can be less or more than the pixels within the *circle*.

- **mean of signal value**

The arithmetic mean of intensities of all the pixels within the *circle* is defined as

$$Mean = \frac{\sum D(m,n)}{S_{FG}}$$

Where $D(m, n)$ denotes the intensity D of the pixel at row m and column n ; S_{FG} denotes the total number of the pixels within the *circle*

- **median of signal values**

After the intensities of all the pixels within the *circle* are sorted, the pixel value at the middle of the sorted pixels is taken as the *Median of the Signal Intensities*.

- **STD_{FG} , Standard deviation of signal values**

The *Standard Deviation* (STD_{FG}) of all the pixel values within the *circle* is defined as

$$STD_{FG} = \sqrt{\frac{\sum (D(m,n) - Mean)^2}{S_{FG}}}$$

Where $D(m,n)$ denotes the intensity D of the pixel at row m and column n ; S_{FG} denotes the total number of the pixels within the *circle*, $Mean$ is the *Mean of Signal Intensities*.

- **background values**

The *Background* is defined as the pixel intensities outside the associated *circle*. The background pixel intensity can be contributed by auto-fluorescence from slide, fluorescent residues from the hybridization materials and by airborne dusts. The software performs a background extraction to subtract the background noise from the signal.

- **mean of background values**

The arithmetic mean of intensities of all the pixels within the *Background* is

$$Mean = \frac{\sum D(m,n)}{S_{BG}}$$

Where $D(m,n)$ denotes the intensity D of the pixel at row m and column n ; S_{BG} denotes the total number of the pixels within *Background*.

- **median of background values**

After the intensities of all the pixels within the *Background* are sorted, the pixel value at the middle of the sorted pixels is taken as the *Median of Background Intensities*.

- **standard deviation of background values, STD_{BG}**

The *Standard Deviation* of all the pixel values within the *Background* is defined as

$$STD_{BG} = \sqrt{\frac{\sum (D(m,n) - Mean)^2}{S_{BG}}}$$

Where $D(m, n)$ denotes the intensity D of the pixel at row m and column n ; S_{BG} denotes the total number of the pixels within the *Background*; $Mean$ is the *Mean of Background Intensities*.

Ch06 Maintenance and Troubleshooting

6.1 Overview


Microarray scanner is a precision optical and precision mechanical composition of instruments, need regular maintenance and calibration to ensure its operational quality. In addition, microarray scanner users may encounter some problems, this manual provides user reference suggestions and basic solutions. If these methods do not solve your problem, please contact our technical support department. For more information, please refer to the "Technical Support and Contact Information".

6.2 System maintain notice

- Install and use the scanner according to the operating procedures provided in this manual.
- The workbench that carries the scanner must be flat and smooth.
- Please install the scanner in a room with good temperature and humidity control.
- The sides of the scanner should be well-ventilated, do not block the fan air outlet and air inlet.
- Do not share the scanner with many devices on the same power source.
- Do not switch the scanner on and off, at least 20 seconds after the shutdown and then boot.
- Do not load slides with liquids or contaminants into the slide holder.
- Please prevent the slide holder from being polluted, bumping or falling.
- If you need to move the scanner, prevent the scanner from being hit or fallen during the process.

6.3 Machine cleaning

Microarray scanner is a highly precision optical detection instrument, user can only clean the machine when cleaning the machine shell, cover and center of the upper surface of the rotating shaft. Before cleaning the machine, please make sure the machine is off and unplug the power supply. Use a clean, soft cloth or tissue-free paper to clean the machine, but do not use liquid detergent or organic solvent on the upper surface of the top cover and the center axis of rotating shaft.

	<p>Warning:</p> <p>Users are not allowed to dismantle the scanner shell or touch or disassemble internal parts of the product (except those specified in the manual), otherwise, the product warranty agreement will be invalidated.</p>
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6.4 Slide holder disk usage precautions and cleaning

6.4.1 Slide holder disk usage precautions

- The bottom of the slide holder disk is made of glass. Users should avoid collision and slump when using it, otherwise it may be damaged.
- When the user loads slide into slide holder or removes from the slide holder, it should be confirmed that the slide holder is closed after the slide is completely inserted or completely removed, otherwise it may be damaged.
- Users should not load liquid or contaminated slide into the holder. Use dry nitrogen gas to remove contaminants from the slide or to dry the liquid.
- If the slide itself is too warped or the surface is significantly contaminated, the unevenness will result in the slide not being able to fit snugly against the glass surface of the slide holder. If the slide cannot cling to the glass surface of the slide holder disk, which may

result in an incorrect scanned image.

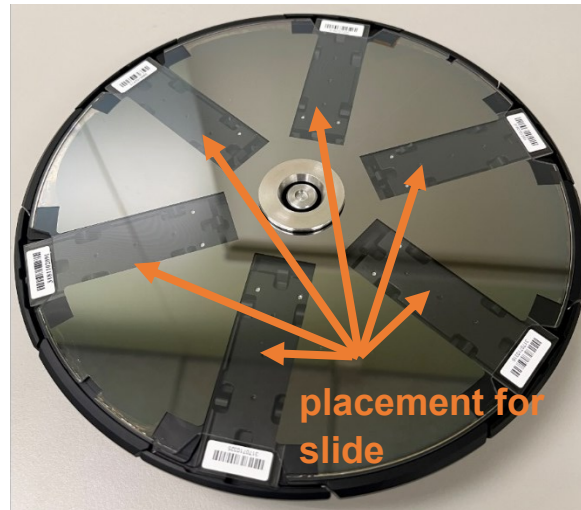
- If the slide has frame on its surface, please do not load slide into slide holder.
- The bottom of the slide holder disk is made of glass, it should be kept clean when used by user. Otherwise, the quality of the fluorescent image scanning will be affected. Users should wear clean gloves when using the slide holder disk.
- The cleaning slide holder disk can be wiped with absolute alcohol and the non-fluorescent, non-absorbent or non-woven cloth.
- Do not use any liquid or organic solvents other than absolute alcohol.
- Users should periodically clean the slide holder or contact the factory to clean according to the frequency of use to ensure the quality of fluorescent image scanning.
- Users should not arbitrarily disassemble all the components on the slide holder disk, otherwise it may be damaged.

6.4.2 Slide holder glass outer surface cleaning

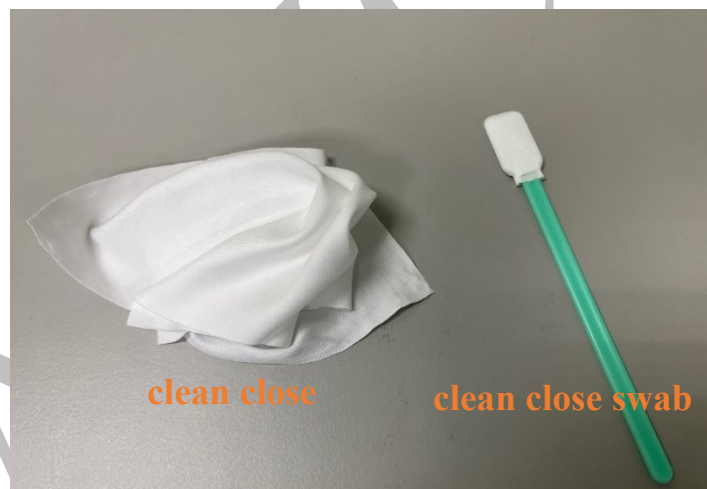
- When should the outer surface of slide holder disk be cleaned: if the outer surface of slide holder disk is contaminated.
- When cleaning the outer surface of slide holder glass, please use a non-fluorescent and non-cotton cloth and wipe it with a proper amount of absolute alcohol and wear clean gloves when handling.

6.4.3 Slide holder glass inner surface cleaning

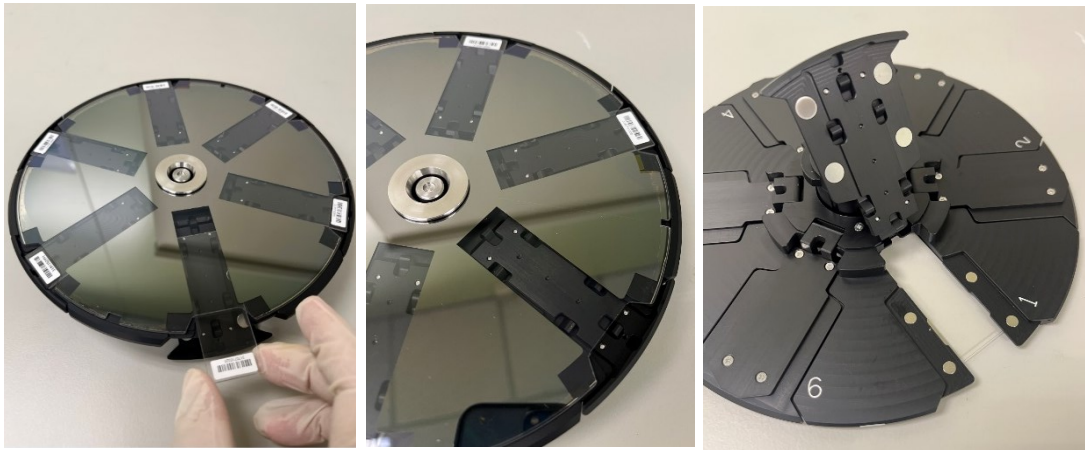
- Timing of cleaning inner surface of slide holder disk: (1) contamination of the inner surface after loading contaminated slide into the holder disk. (2) loading the slide into slide holder after repeated and frequent operations.
- When the user cleans the inner surface of slide holder glass, it only needs to clean the slide insertion area, as shown below.



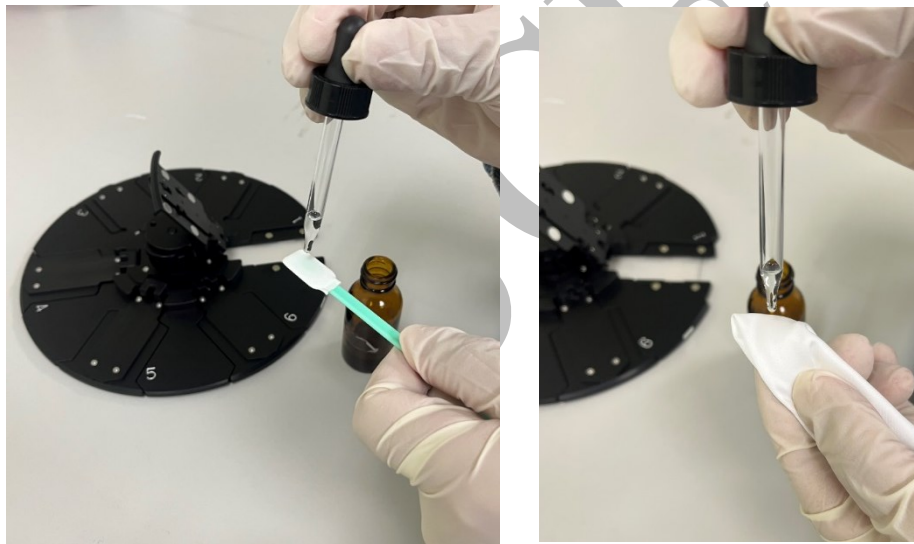
- In order to ensure the cleaning effect of inner surface of slide holder glass, user needs to use cleaning tool when cleaning inner surface of slide holder glass. As shown in the figure below, clean gloves should be worn during operation.



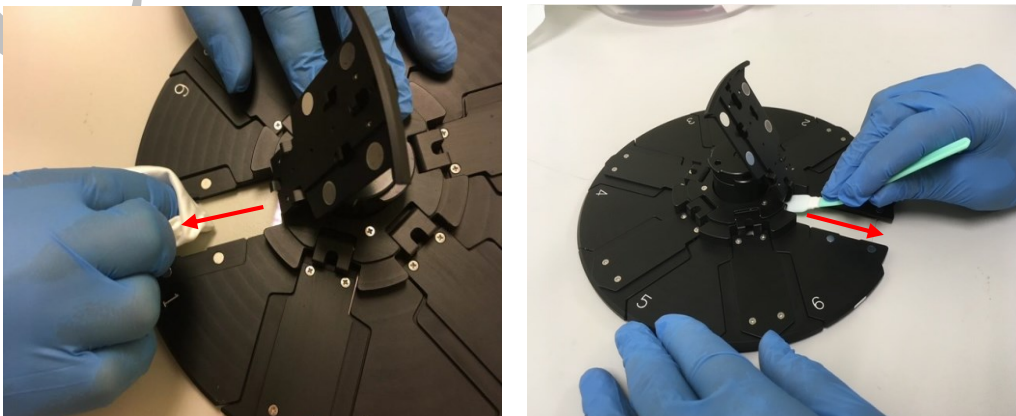
- Slide holder glass inner surface cleaning steps:
 - (1) Please wear clean gloves when handling.
 - (2) Place the slide holder on a stable and clean table (bottom side up). Open the slide holder cover and remove the slide from the slide holder. Close the slide holder cover. Place the slide holder on a stable and clean table (top side up) and open the slide holder cover.



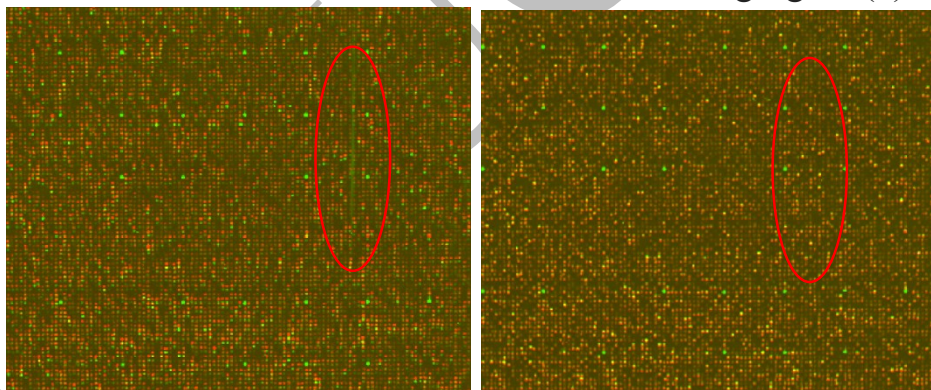
(3) Use a dropper to drop 2~3 drops of absolute alcohol on the clean cloth or clean close swab



(4) Slowly scrape out the clean cloth or clean close swab with 2~3 drops of absolute alcohol. Please don't reuse the clean cloth or clean close swab.



- (5) Repeat steps 3~4 (for two to three times) then load the clean slide into the slide holder.
- (6) Repeat steps 2 ~ 5 to clean the slide insertion area in sequence.
- (7) Insert the clean slide into the slide holder and place the slide holder into HC-BS01 or HC-BS02 microarray scanner for pre-scan (Laser Power=100%, PMT Gain=50%, Scan Mode: 40 μ m) and use BioImage Analyzer to check if each slide's fluorescent image has a partial background fluorescence residue.
- (8) If there is partial background fluorescence residual, as shown in the following figure (1), repeat steps 2~5 for the wafer insertion area and perform step-7 to confirm that the local background fluorescence residual condition has been removed, as shown in the following figure (2).



(1)

(2)

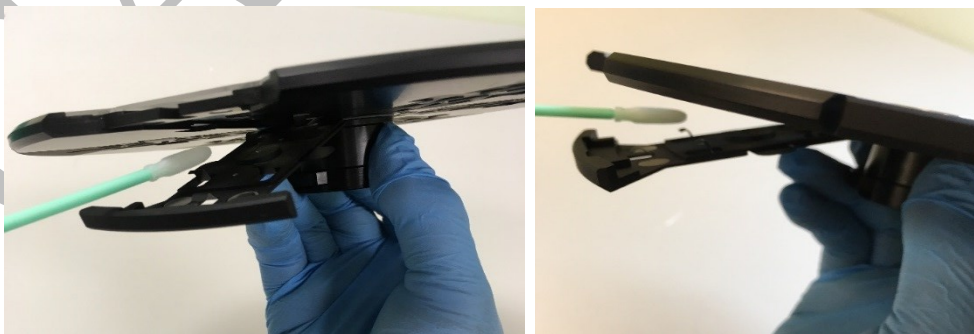
6.4.4 Slide holder disk shrapnel cleaning

- When should the slide holder disk shrapnel be cleaned: (1) The contaminated slide is loaded into slide holder and cause contamination of slide holder shrapnel. (2) After loading the slide into slide holder for a long time and frequently.

- In order to ensure the cleaning effect of the slide holder disk, user needs to use a dust-free cleaning bar when cleaning the slide holder disk. As shown in the figure below, and also the clean gloves should be worn during operation.



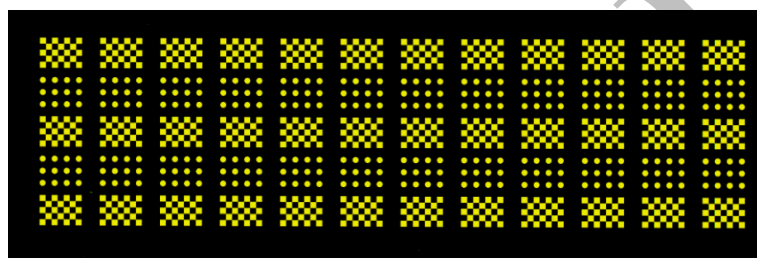
- Slide holder disk shrapnel cleaning step:
 1. Use a dropper to drop 1~2 drops of absolute alcohol on the front end of clean cleaning rod.
 2. Open up each top-cover of slide holder and remove slide from slide holder.
 3. Wipe the slide holder disk spring (with the slide contact surface) by using a dust-free cleaning rod that has been dripped with absolute alcohol, as shown below.



4. Load the clean slide into slide holder.
5. Repeat steps 1~4 to clean the slide holder disk shrapnel in sequence.

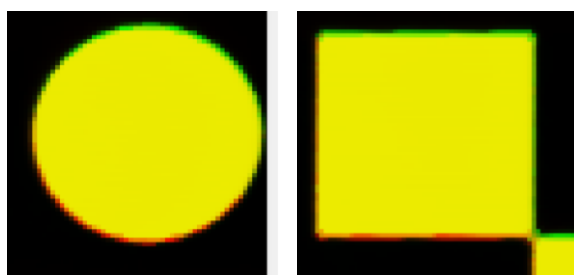
6.5 Regular inspection and calibration

Only authorized service engineers may periodically calibrate the system using Caduceus Calibration Slide-01. The calibration items include two-color phosphor dot alignment and fluorescence signal strength verification. Caduceus Calibration Slide-01 contains 36 square arrays of fluorescent spots and 24 groups of circular fluorescent spots, the square fluorescent spot length of 500 μ m; circular fluorescent spot diameter of 500 μ m (as shown in below Figure). The fluorescent spot also contains a fixed concentration of green and red fluorescent substance.



Caduceus Calibration Slide-01

Only authorized service engineers can load the Caduceus Calibration Slide-01 into the slide holder (Caduceus Calibration Slide-01) and use the original factory recommended scanning parameters for scanning. Fluorescence signal strength after scanning compared with the original factory value, can be a verification for the fluorescent signal repeatability, consistency and fluorescence intensity calibration. In addition, the fluorescence image after scanning with Caduceus Calibration Slide-01 can also check the entire piece of two-color fluorescent alignment error, if the error is greater than 10 μ m and affect the user's subsequent numerical analysis, please contact our technical support department.



Check two-color fluorescence alignment error

6.6 Problems and solutions

Problems	Solutions
Batch file (setup.bat) installation failed	<ul style="list-style-type: none"> ● Directly execute the installation file (setup_BioScanControlGUI.exe) ● Copy the parameter file (system.dat) to the installation directory (the default directory is D:\CaduceusX64_BioScan)
Scanner cannot not start	<ul style="list-style-type: none"> ● Check the power system, including: power socket, power cord, and power outlet. ● After turning power off, check the fuses on the scanner backplane. ● Check the power specifications are correct.
Scanner cannot be linked correctly	<ul style="list-style-type: none"> ● Make sure the scanner power is on. ● Confirm USB3.0 signal cable is connected to the scanner and computer workstation. ● Check if the computer's workstation COM port is correct.
Scanner cannot respond to the software operation	<ul style="list-style-type: none"> ● Make sure the scanner power is on. ● Confirm USB3.0 signal cable is connected to the scanner and computer workstation. ● Make sure the scanner cover is closed.
Barcode cannot read	<ul style="list-style-type: none"> ● Check barcode on the slide. ● Check barcode on the slide face down (with the same test surface).

Problems	Solutions
Scanned image cannot be produced after scanning	<ul style="list-style-type: none"> ● Check if there are 6 slides loaded in the slide holder. ● Check if laser is function normal. ● Check the interference pattern in slide area to confirm that all slides in the slide holder are in close contact with the glass surface of the slide holder. ● Check the slide size is correct.
Two-color fluorescent alignment is not good	<ul style="list-style-type: none"> ● Check the slide size is correct.
Scanner cannot stop normally or cannot stop using the software stop button	<ul style="list-style-type: none"> ● Confirm USB3.0 signal cable is connected to the scanner and computer workstation. ● Click the "STOP" button in the BioScan Control Software control UI. ● Make sure scanning is not working and then turn off the scanner.

Note: If these methods do not solve your problem, please contact our technical support department. For more information, please refer to the "Technical Support and Contact Information" in this manual.

Appendix-A : Software Quick Installation Steps

Software quick installation steps are briefly explained as:

1. Insert the software installation CD into the CD-ROM drive, or insert a USB flash drive into the computer's USB flash drive slot.
2. First, follow the [:\document\user_manual\Caduceus_Microarray_Biochip_Scanner_System_UserManual.pdf](#) manual description, to execute the following BioScan Control and BioImage Analyzer software installation program files. (After the installation of BioScan Control is completed, please do not execute it, and then execute it after Step-3 is finished.)

CD-ROM:\software\
C

- a). .\SetupBAT_BioScanControl\setup.bat
- b). Bio-image Analyzer_x.x.x.exe

3. Next please follow the [:\document\user_manual\Caduceus_Microarray_Biochip_Scanner_System_UserManual.pdf](#) file in Appendix-B : "Hardware Driver Installation Instructions", and execute the following program files.

CD-ROM:\software\
C

- a). CypressDrivers_1_2_3_20.zip
(USB3.0 driver)
- b). PL2303_Prolific_DriverInstaller_v1_12_0.zip
(COM port driver)

4. Finally, please follow the [:\document\chip_loading\Caduceus_microarray_chip_loading_steps.pdf](#) file in Appendix-C : "Microarray chip loading steps description" to load the microarray chip.

Appendix-B : Hardware Driver Installation Instructions

Chapter 1 Overview

Caduceus microarray scanner communicates with PC via USB3.0, also two fixed COM ports are necessary. Before you run the program, you need to install the hardware device driver first. This document guides you how to install the USB driver and setup the fixed COM port numbers step by step.

1.1 Hardware driver

Two hardware device driver we need to install, they are listing below. The first one is for USB3.0 communication, PC can recognize our microarray scanner as USB3.0 device, the other one is the COM port driver, we use COM port communication to control the hardware process. You can find these two zip files in our software package.

- USB3.0 driver: CypressDrivers_1_2_3_20.zip
- COM port driver: PL2303_Prolific_DriverInstaller_v1_12_0.zip

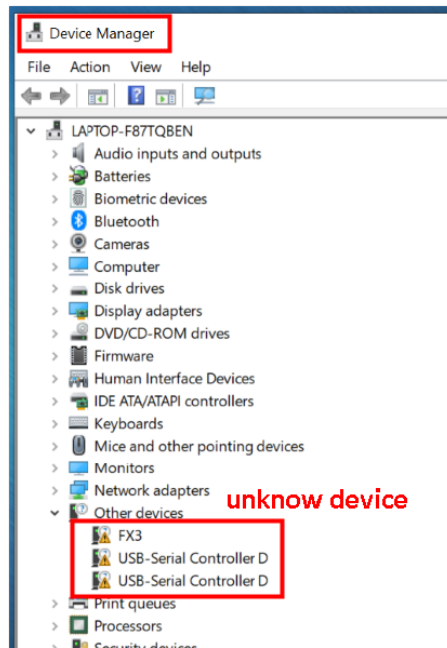
1.2 Install the usb3.0 driver

Step 1: unzip the driver file and remember where the unzip folder is.

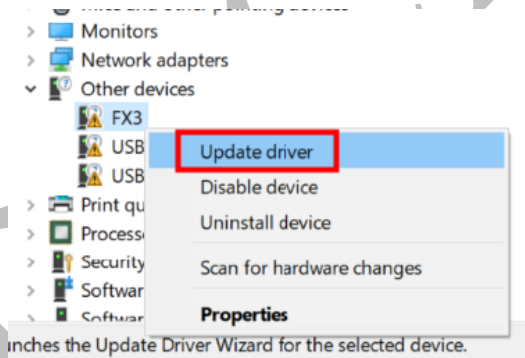
Step 2: connect the microarray scanner to PC via USB3.0 cable.

Step 3: turn the microarray scanner power ON.

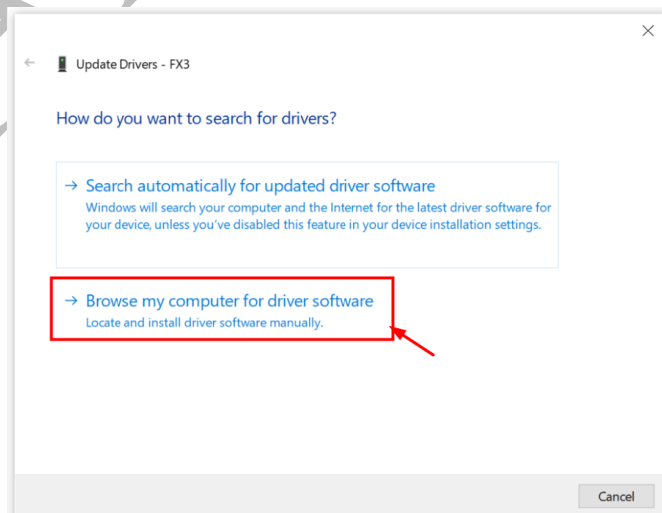
Step 4: open Windows Device Manager, you will see three unknown USB device.



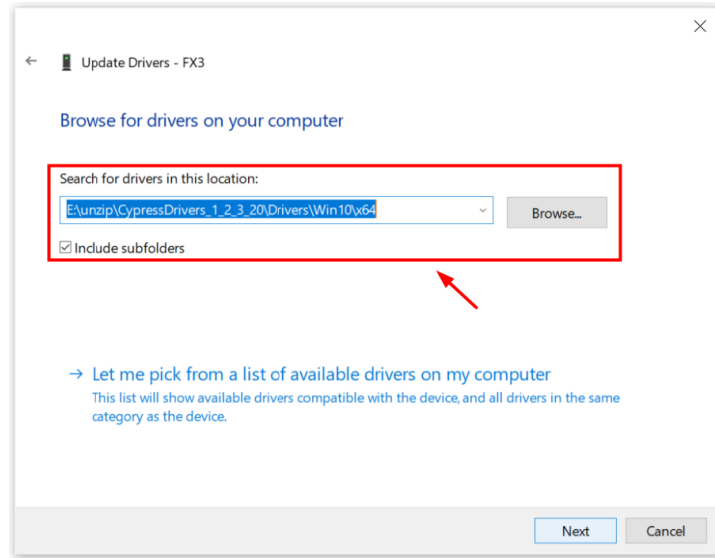
Step 5: update the unknow USB device driver, select the “FX3” and right-click on the mouse button then select the “update driver”. Set the path of the driver, and then install step by step as the figure show below.



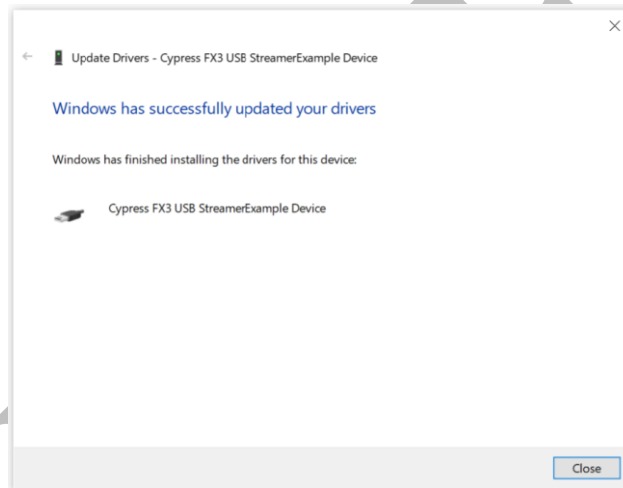
a. select update driver



b. select locate and install driver software manually

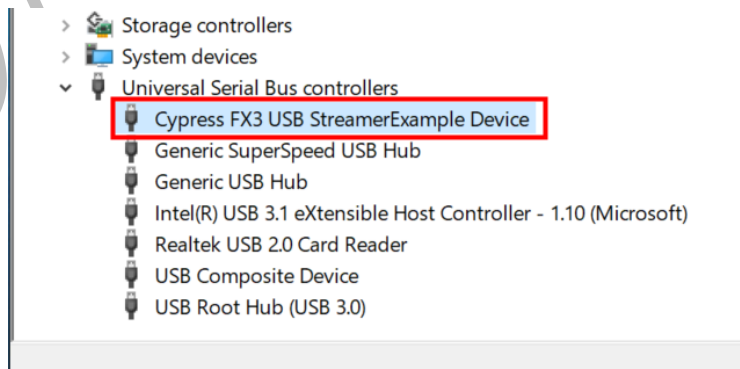


c. set the path of the driver and go to NEXT



d. done the FX3 driver install

Step 6: Check the device name.

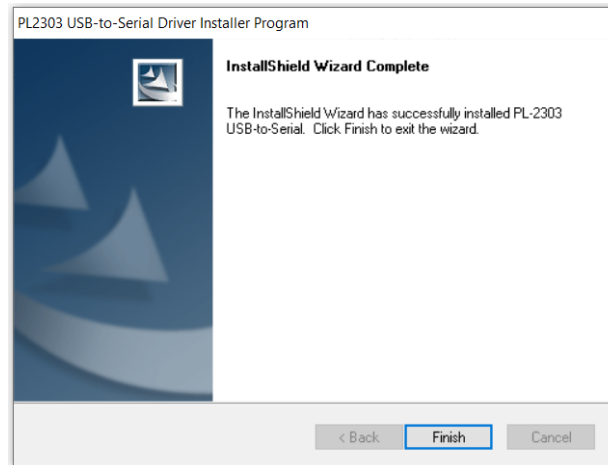


e. Device has been recognized

1.3 Install the COM port driver

Step 1: unzip the driver file.

Step 2: run the file PL2303_Prolific_DriverInstaller_v1.12.0.exe, and then restart the computer.

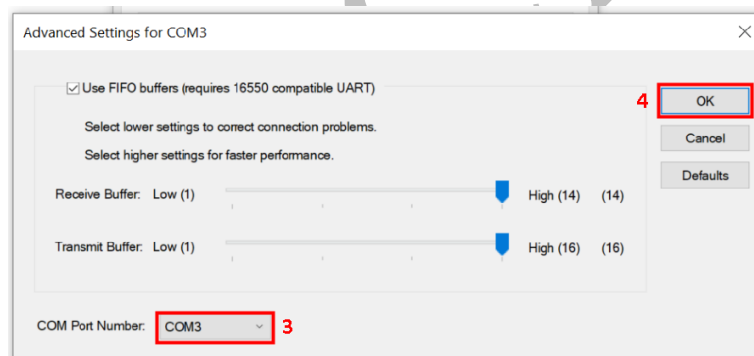
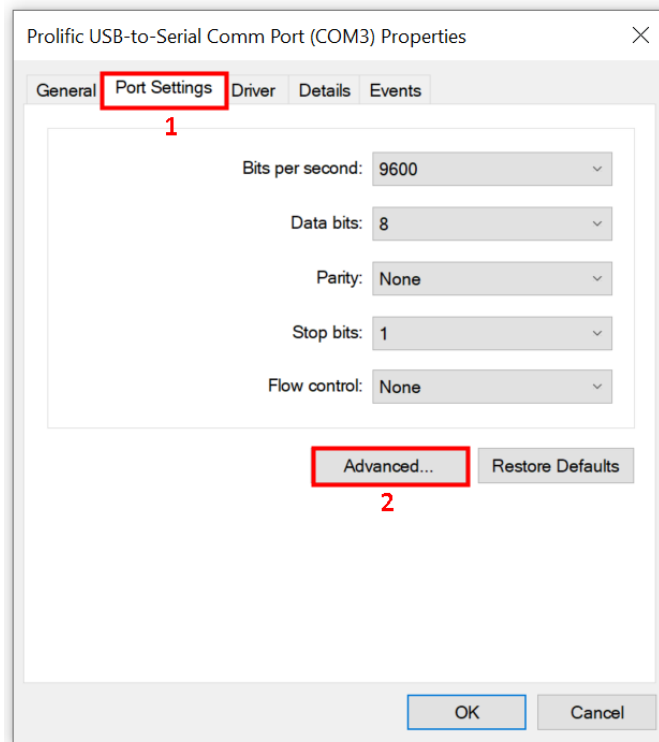


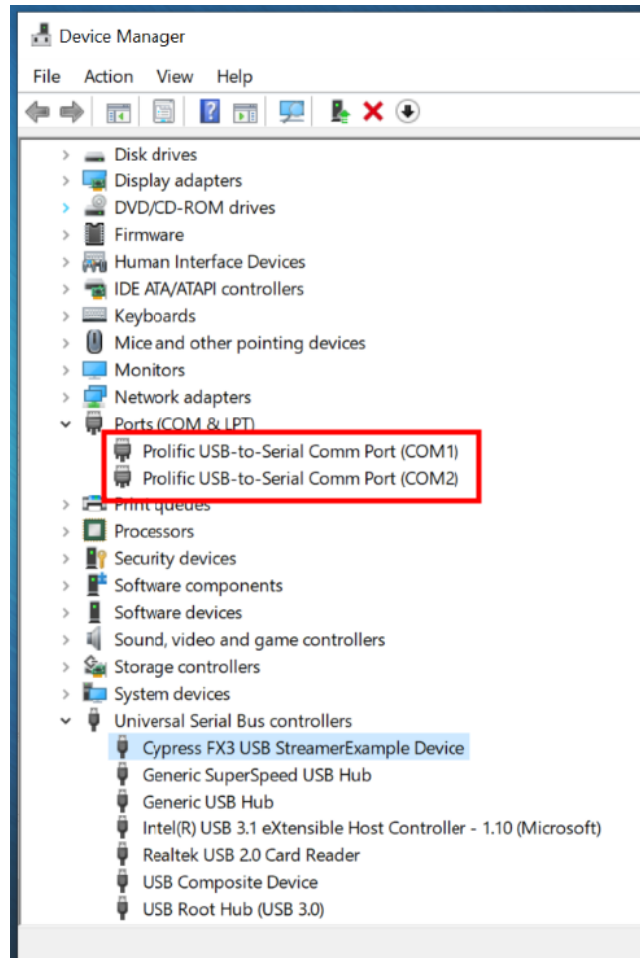
Step 3: connect the microarray scanner to PC via USB3.0 cable.

Step 4: open Windows Device Manager, you can see the two COM ports has been recognized. But, the COM port number was not meet our request.



Step 5: Two COM ports named “Prolific USB-to-Serial xxx” set to COM 1 and COM 2. Select the first “Prolific USB-to-Serial xxx” device and set it to COM 1. Then, select the second one and set it to COM 2. Latter we will check the device if they are correct or need to switch with each other.





Note: (1) For HC-BS02 Green (532nm Laser), please set to COM 2 directly.

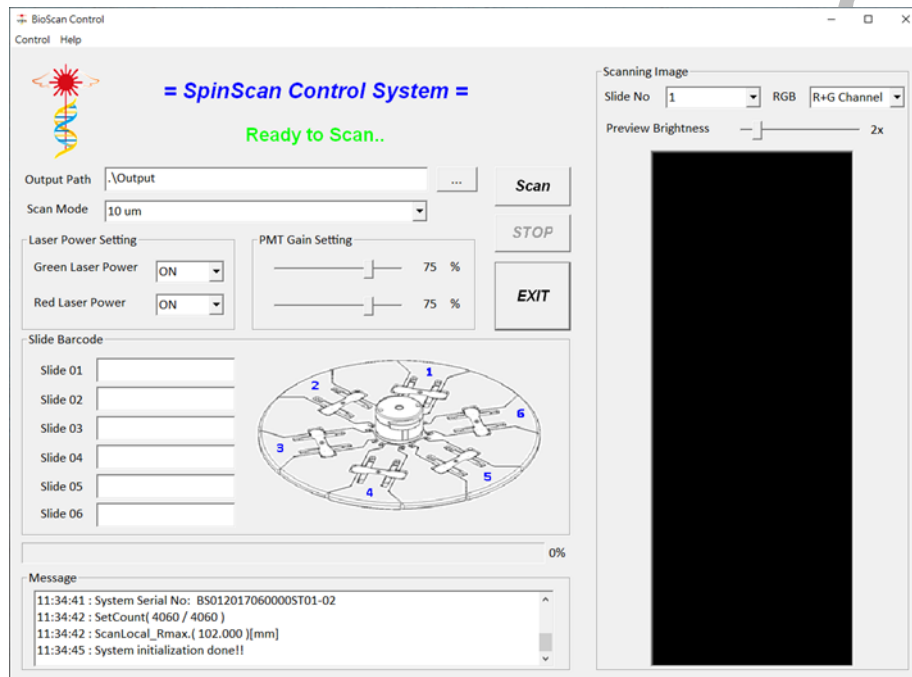
(2) For HC-BS02 Red (635nm Laser), please set to COM 1 directly.

Step 6: Restart the computer to enable the new COM port setting.

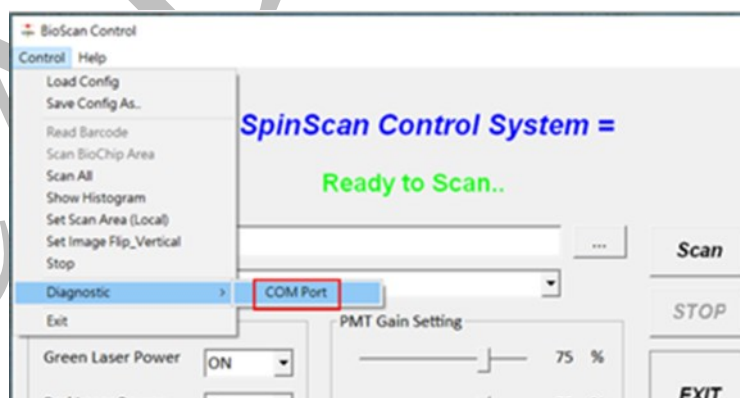
1.4 Verified the COM port setting

Step 1: Make sure the slide holder is in microarray scanner.

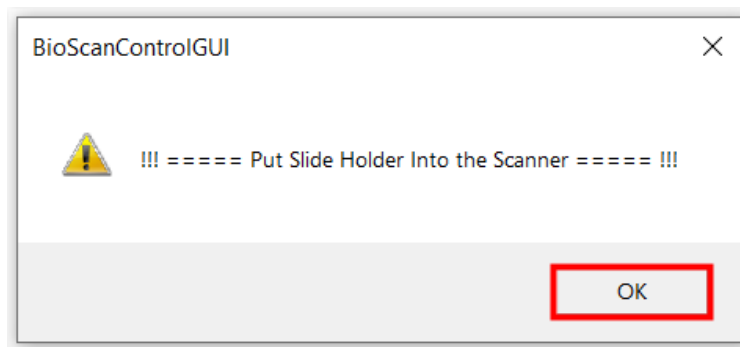
Step 2: run the program BioScan Control GUI. (Before running the BioScan Control, user must install it first, which should follow the install procedures as described in the user manual of Caduceus SpinScan Microarray Scanner.)



Step 3: Select "Control" >> "Diagnostic" >> "COM Port"

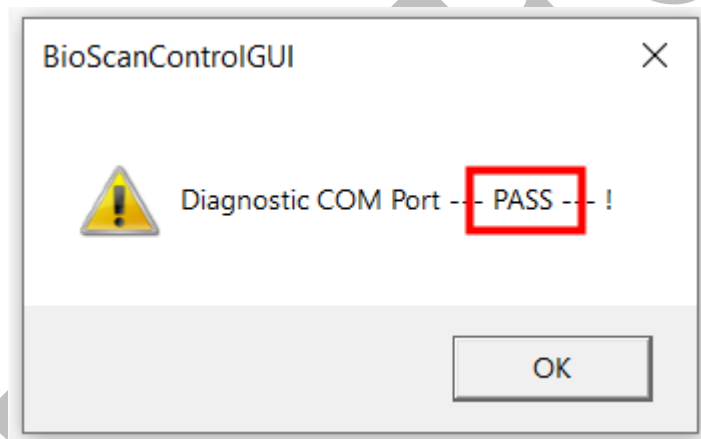


Step 4: Confirm the slide holder already in the Scanner and click “OK”



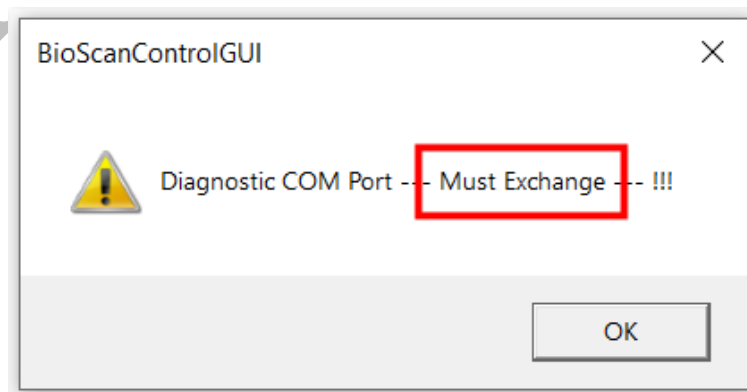
Step 5: Wait for the checking, and will feedback to you by WINDOW Message BOX.

Case 1: PASS message, COM Port Setting meet the request.



In this case the COM Port setting is correct, please click “OK” Button and then exit the program.

Case 2: Wrong message, COM Port must Exchange



In this case the COM Port setting is wrong. User must exchange COM1 and COM2. Please follow 1.3 Step4 ~ Step6 to do the COM port setting.

The exchange sequence as follow:

- a. COM1 set to COM3
- b. COM2 set to COM1
- c. COM3 set to COM2
- d. Restart the computer to enable the new COM port setting.

Step 6: Run Step 2 to Step 5 again. Make sure you got the PASS message.

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Appendix-C : Slide holder disk usage precautions

- The bottom of the slide holder disk is made of glass. Users should avoid collision and slump when using it, otherwise it may be damaged.
- When the user loads slide into slide holder or removes from the slide holder, it should be confirmed that the slide holder is closed after the slide is completely inserted or completely removed, otherwise it may be damaged.
- Users should not load liquid or contaminated slide into the holder. Use dry nitrogen gas to remove contaminants from the slide or to dry the liquid.
- If the slide itself is too warped or the surface is significantly contaminated, the unevenness will result in the slide not being able to fit snugly against the glass surface of the slide holder. If the slide cannot cling to the glass surface of the slide holder disk, which may result in an incorrect scanned image.
- If the slide has frame on its surface, please do not loads slide into slide holder.
- The bottom of the slide holder disk is made of glass, it should be kept clean when used by user. Otherwise, the quality of the fluorescent image scanning will be affected. Users should wear clean gloves when using the slide holder disk.
- The cleaning slide holder disk can be wiped with absolute alcohol and the non-fluorescent, non-absorbent or non-woven cloth.
- Do not use any liquid or organic solvents other than absolute alcohol.
- Users should periodically clean the slide holder or contact the factory to clean according to the frequency of use to ensure the quality of fluorescent image scanning.
- Users should not arbitrarily disassemble all the components on the slide holder disk, otherwise it may be damaged.

