MAUI® Hybridization System

User's Guide

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TRADEMARKS

RESTRICTIONS AND LIABILITIES

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SAFETY INSTRUCTIONS

Please read the entire user's guide prior to operating the MAUI® Hybridization System.

- **Safety Precautions:** Appropriate safety precautions should be taken when working with any laboratory equipment. Always wear appropriate protective equipment such as gloves and protective eyewear.
- **Environmental Conditions:** Use the MAUI System on a dry, flat surface away from intense light, and humidity and temperature extremes.
- **CAUTION: [Spills]** Avoid spilling liquids on the MAUI System, particularly on the electronics module. Fluid seepage into internal components creates a potential shock hazard. If a spill should occur, unplug the System and wipe up immediately to prevent electrical shock.
- **CAUTION: [Hot]** The MAUI System operates at high temperatures (42°C - 67°C) for extended periods of time and can cause skin burns. Use caution when handling System components or accessories.

- **CAUTION: [Broken Glass]** Improper use of the gasket brayer during sealing of the MAUI Mixer or improper slide placement within the MAUI System may result in broken glass slides. To avoid injury, use caution when performing these activities. Should breakage occur, immediately clean up any broken glass.

When operated in a safe environment, according to the instructions in this user's guide, there are no known hazards associated with the MAUI Hybridization System.

CARE AND MAINTENANCE

- Always ensure the power is disconnected from the MAUI System prior to any cleaning. The MAUI® Hybridization System is designed to be maintenance free. The MAUI System may be cleaned with a cloth dampened with a mild solution of soapy water. Solvents and aggressive chemicals should not be used to clean the MAUI System.
- When not in use, switch the mixing component of the MAUI off.
- The MAUI System should only be serviced by BioMicro Systems, Inc. authorized personnel.

If the MAUI Hybridization System is in need of service or if you have any questions, please contact:

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INTENDED USE STATEMENT

The MAUI Hybridization System is designed specifically for use in the semi-automated hybridization of standard 1" x 3" glass microarray slides. This System is currently validated to operate at temperatures between 42°C and 67°C.

CHAPTER 1: INTRODUCTION

This chapter introduces the MAUI® Hybridization System, and describes its hardware and software features.

SYSTEM BENEFITS AND ADVANTAGES

The MAUI Hybridization System is an ultra-low volume microarray processing system designed to continuously mix hybridization solutions to enhance the overall performance compared to conventional cover slip methods or other microarray auto processors.

Advantages over the traditional cover slip method include:

- Continuous mixing of the hybridization solution
- Increased sensitivity (signal vs. noise)
- Uniform hybridization solution layer above the microarray
- Reduced evaporation
- More accurate temperature control

Advantages over other microarray-automated processors include:

- Reduced hybridization chamber volume
- Increased sensitivity analysis due to lower volume/higher concentration hybridizations
- Reduced start up costs
- Reduced maintenance

INCREASED SENSITIVITY

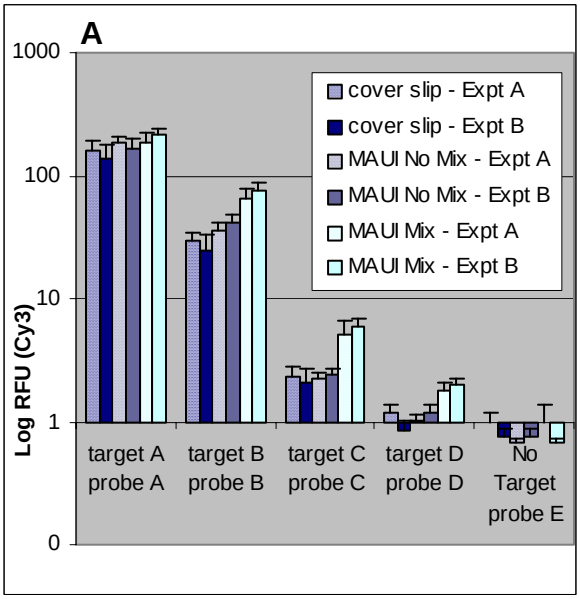


Figure 1: Sensitivity Gains Maximized at Lowest Labeled Target Concentrations

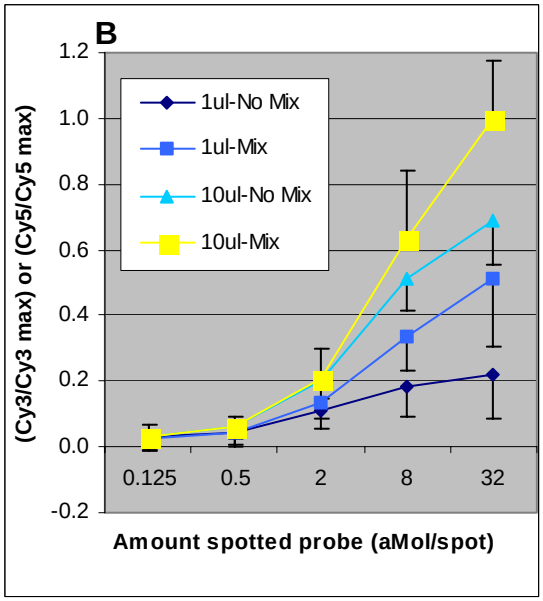


Figure 2: Sensitivity Gains Maximized at Highest Spotted Probe Concentrations

SYSTEM OVERVIEW

The MAUI System is designed to accommodate 1" x 3" glass slide microarrays. The system is comprised of a consumable MAUI Mixer Hybridization Chamber and a reusable base unit, which provides the mixing action and maintains a constant incubation temperature. The MAUI Mixer sticks to the microarray slide via an adhesive gasket forming a uniform, low volume, sealed hybridization chamber. This chamber is clamped into one of the heated slide bays in the base unit, where hybridization takes place. The MAUI Mixer contains two air bladders, driven by an air pump in the base unit, that continually mix the hybridization solution in the chamber with user-selected mixing parameters. The effect of active sample mixing is significant enhancement of sensitivity relative to other hybridization methods.

FILLING OVERVIEW

Two forces introduce hybridization solution into the MAUI Mixer; pressure exerted by a syringe or pipette that pushes the solution in, and capillary action that pulls the solution in. BioMicro Systems recommends using pressurized injection because it is less likely to trap air bubbles in the chamber.

Standard pipettes do not provide adequate force for pressurized injection. We recommend filling the MAUI Mixers with a positive displacement pipette such as the Gilson Microman® M-100 or a syringe with a BioMicro pipette tip.

MAUI HYBRIDIZATION SYSTEM BASE UNIT

System Cover

The hinged cover assists in maintaining system temperature and prevents photo bleaching of the labeled target.

Air Pump System

The air pump system mixes the hybridization solution by alternately pressurizing and evacuating the MAUI Mixer air bladders. The user has the ability to choose between four (4-Bay MAUI) or two (12-Bay MAUI) pre-programmed mix modes.

Heat Block

The MAUI 4-Bay System can be separated from the heat block and a separate instruction manual is provided for that heat block. The MAUI 12-Bay System has an integrated heat block, which may not be separated from the mixing unit.

Slide Bays

The slide bays hold the MAUI Mixer-slide assemblies during hybridization.

Bay Clamps

Bay clamps are located directly above each slide bay. Each clamp allows visualization of the MAUI Mixer during incubation. To open, push in on the tab located to the right of each slide bay and lift up on the clamp. To close, push down on the textured portion of the clamp. The bay clamps ensure a connection between the MAUI Mixer air ports and the air pump system via two small O-rings located on the right of each slide bay.

Warming Holes

Solution warming holes, designed to hold 1.5 ml microcentrifuge tubes containing buffer solution, are located on the interface plate.

Temperature Set Point

The user-adjustable System hybridization temperature set point is located on the heat block front panel.

Thermometer Port

The slide bay thermometer port is located in the center of the base unit (look for the cutout in the lift-up cover). A thermometer can be inserted into the port to confirm the temperature of the slide bays.

Power Supply

A DC power supply is provided for the MAUI 4-Bay System. This power supply may be plugged into a wall power receptacle or into the receptacle provided on the back of the heat block (110 V 60 Hz systems only). DO NOT PLUG ANY OTHER ELECTRICAL APPLIANCE INTO THE HEAT BLOCK POWER RECEPTACLE.

Power Switch

There are two power switches for the MAUI System. One controls the heat block and the other controls the mixing system. Both must be on for heat and mixing.

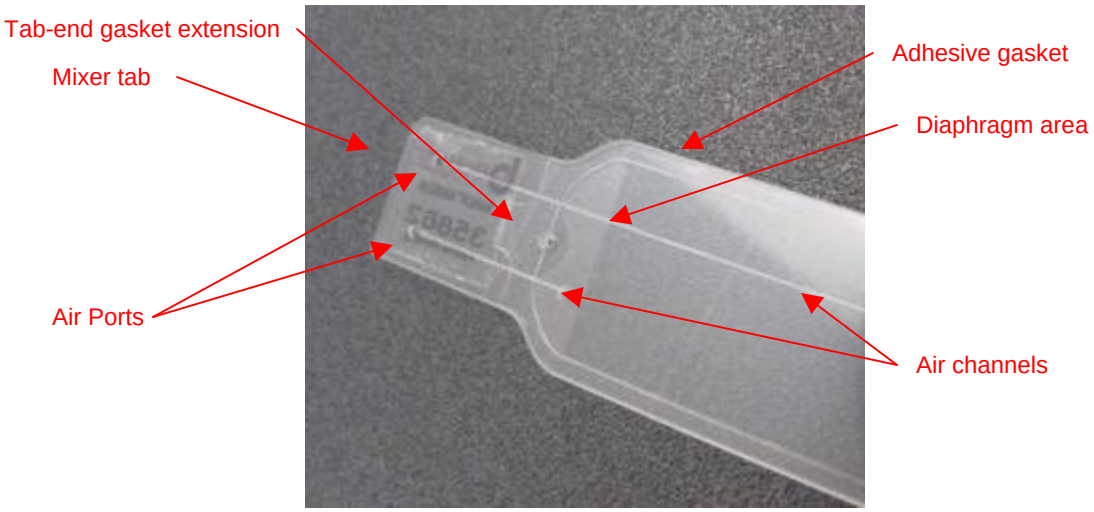


Figure 3: MAUI Mixer Detail

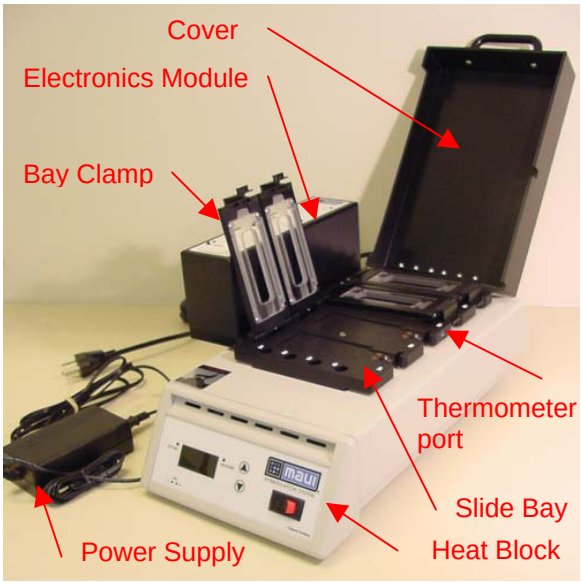


Figure 4: MAUI 4-Bay System

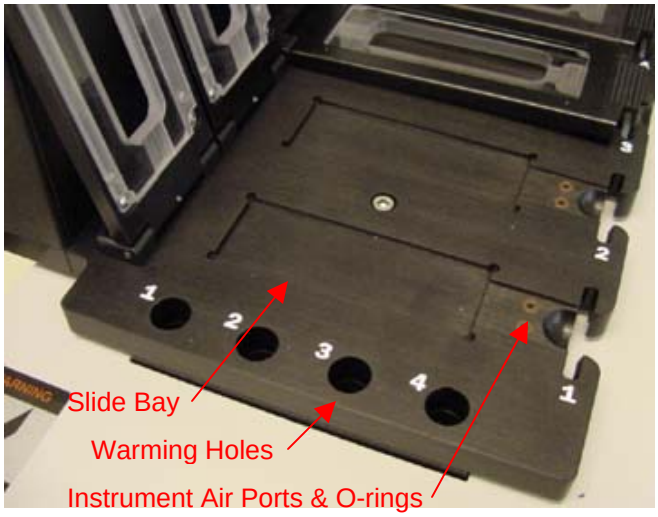


Figure 5: MAUI 4-Bay System Detail

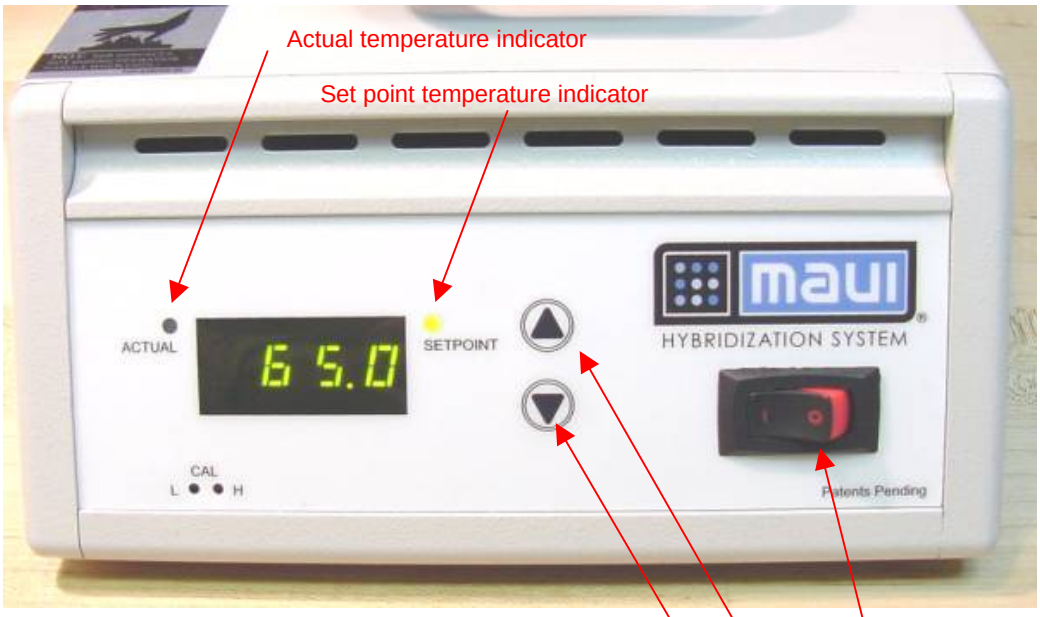


Figure 6: 4-Bay MAUI Heating Panel

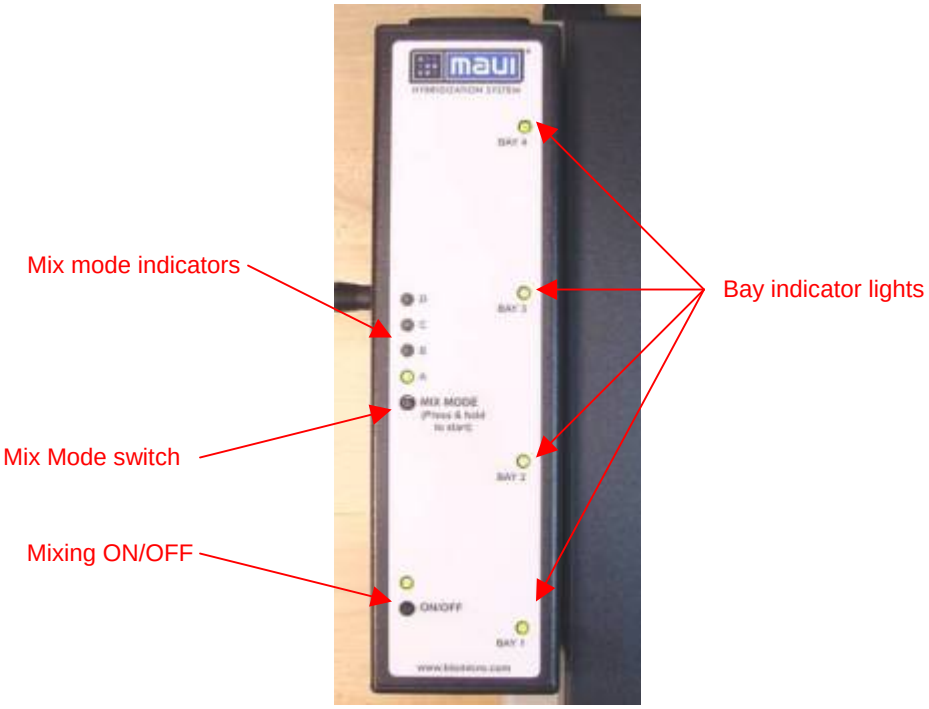


Figure 7: 4-Bay MAUI Mixing Panel

Figure 8: 12-Bay MAUI

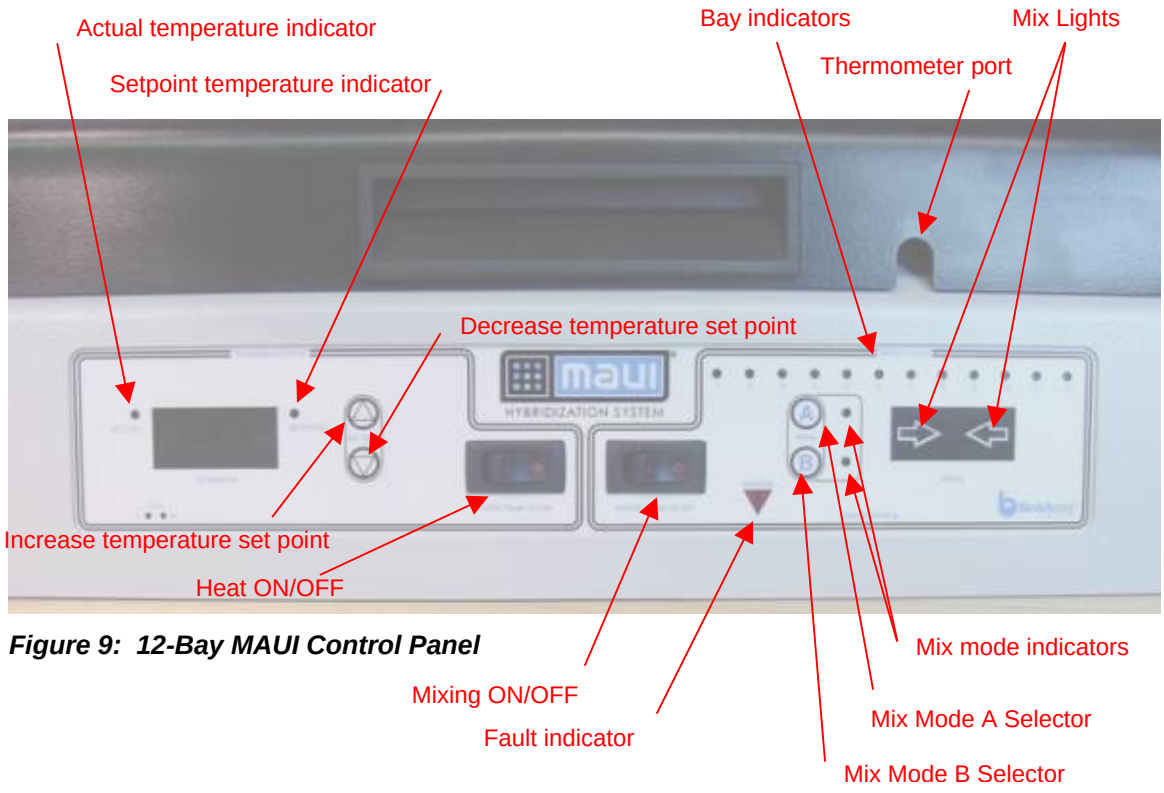


Figure 9: 12-Bay MAUI Control Panel

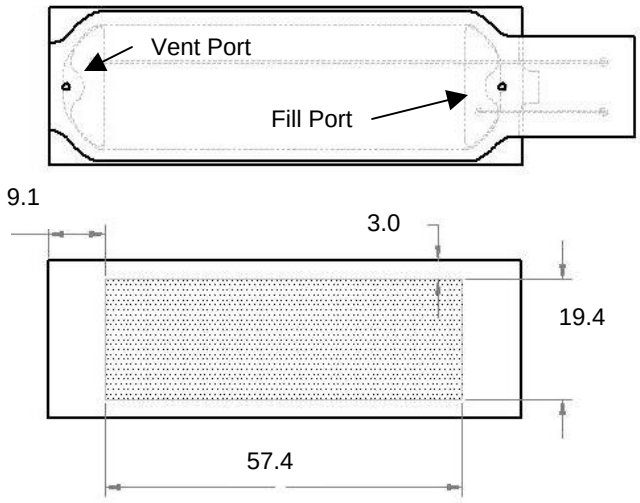
ACCESSORIES

- Assembly/Disassembly (AD) jig
- Gasket brayer
- Forceps
- Practice slides
- Port seals
- MAUI® Mixer Hybridization Chambers
- MAUI® Hybridization System Quick-Start Guide
- Replacement O-rings
- System Verification Assemblies
- Standard laboratory heat block (not provided by BioMicro Systems)
- Empty pipette tip box lid (not provided by BioMicro Systems)
- Styrofoam shipping container (not provided by BioMicro Systems)
- Laboratory thermometer (not provided by BioMicro Systems

PRINTING AND ALIGNMENT CONSIDERATIONS

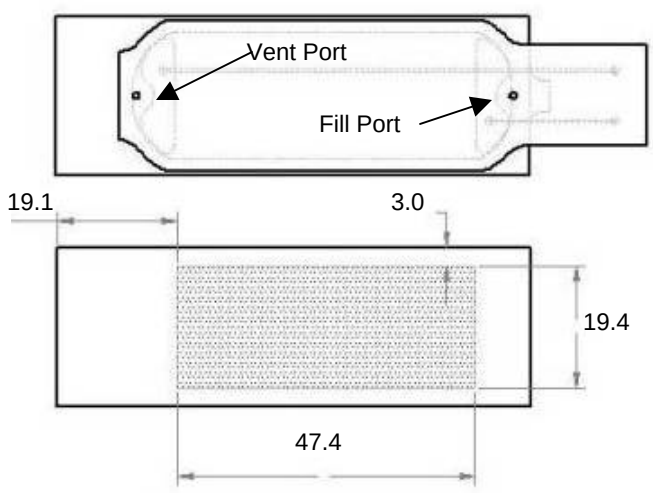
- The different MAUI Mixer configurations and recommended printing areas are shown in Figs. 10 -16. All dimensions are in mm.
- Proper MAUI Mixer/slide alignment is critical to ensure all microarray spots are within the MAUI Mixer and not covered by the adhesive gasket.
- An Assembly/Disassembly jig specific for each type of MAUI Mixer will correctly align the MAUI Mixer to the microarray slide under these printing and alignment conditions.

BioMicro Systems can make custom Mixer configurations to meet your individual microarray needs. Contact us for additional details.



Chamber volume = 40 μl

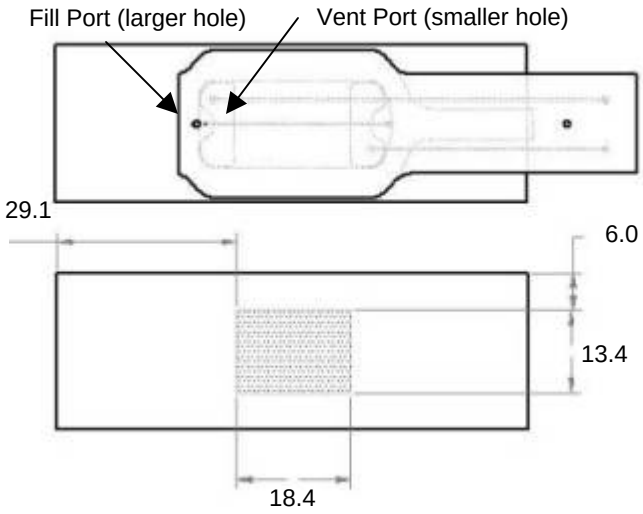
Figure 10: MAUI Mixer FL



Chamber volume = 34 μl

Recommended Array Region

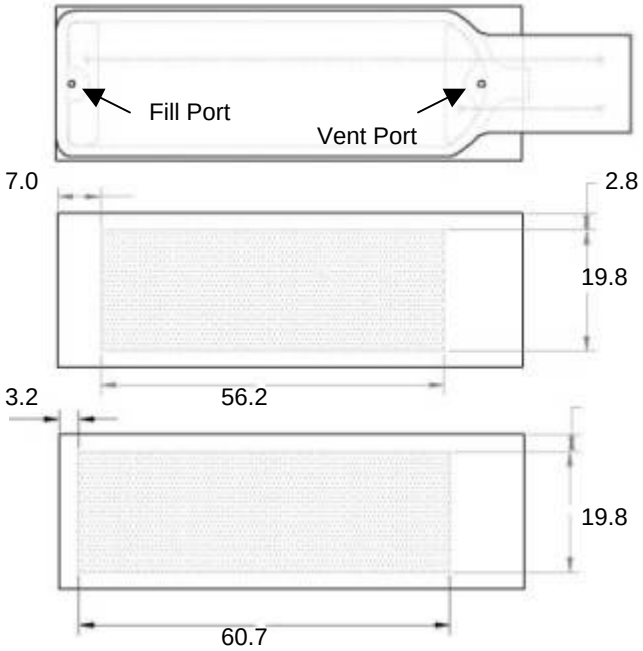
Figure 11: MAUI Mixer SL



Chamber volume = 15 μl
Fill from non-tab port

Recommended Array Region

Figure 12: MAUI Mixer NG



Chamber volume = 36 μl
Fill from the non-tab port

Recommended Array Region

Alternate Array Region

Figure 13: MAUI Mixer AO

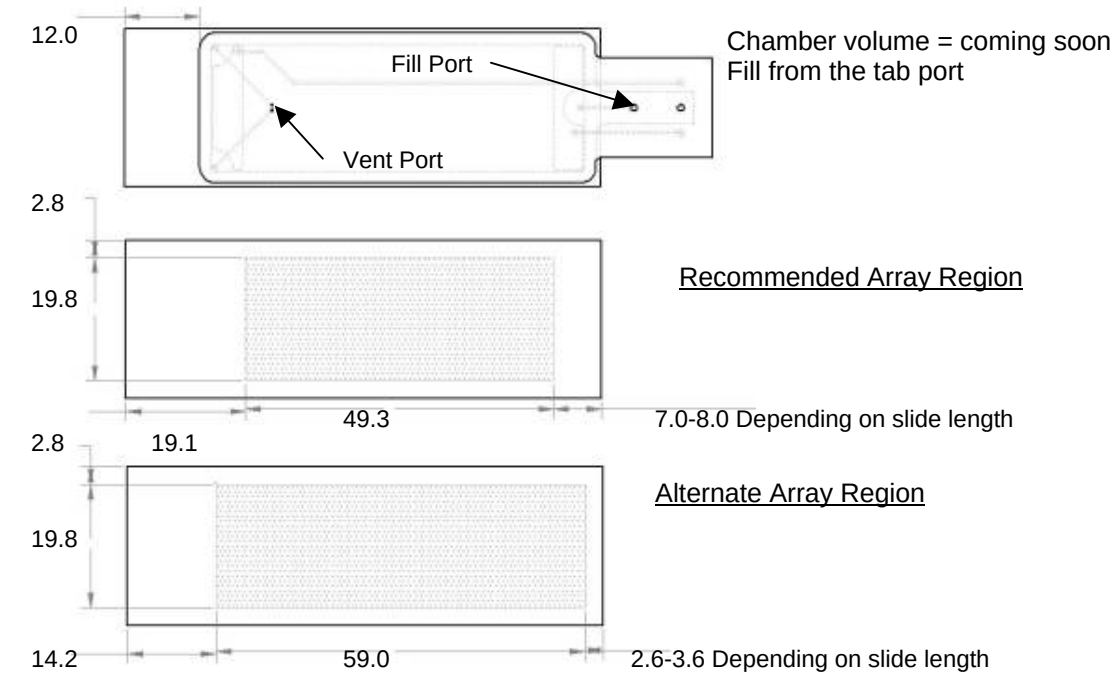


Figure 14: MAUI Mixer AC

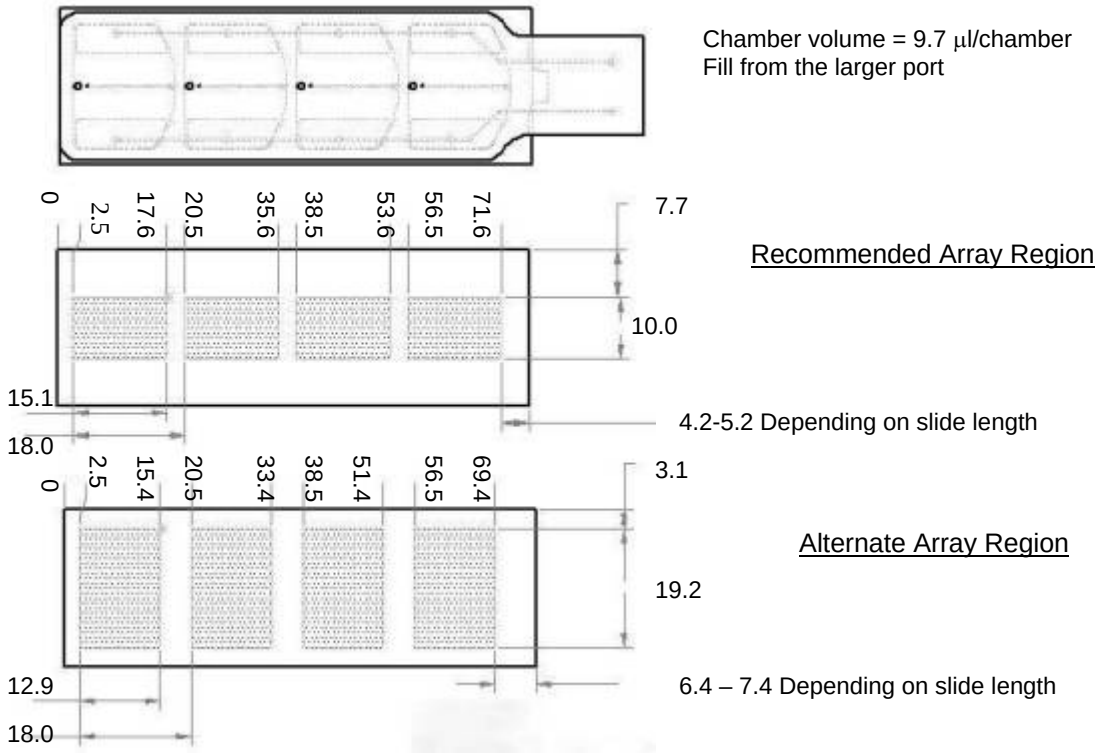


Figure 15: MAUI Mixer M4

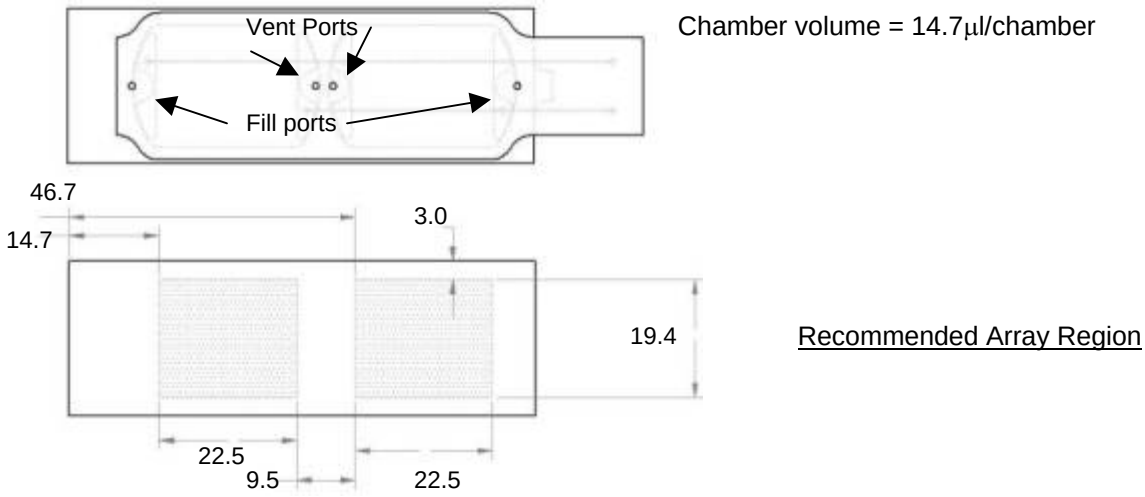


Figure 16: MAUI Mixer DC

SLIDE COMPATIBILITY EVALUATIONS

Not all " 1 inch x 3 inch" glass slides are exactly the same size. It is recommended that you verify your slide compatibility with MAUI System. This can easily be performed as follows:

Dimensional Compatibility Evaluation

Determine whether the microarray slide fits within the A/D jig. A slide should fit easily into the slot in the A/D jig.

The A/D jig will accommodate standard microarray slides with the following dimensions:

- 24.9 – 25.5 mm wide (25.2 to 26.2 mm wide for Matsunami slides)
- 75.4 – 76.6 mm long

If you have difficulty inserting your microarray slide into the A/D jig, please contact BioMicro Systems, Inc.

Surface Compatibility Evaluation

The MAUI System has been used successfully with a large variety of microarray surfaces. These include most commercial coatings such as aminosilane, epoxy, and aldehyde, and most BSA or similar blocking protocols. Most polylysine surfaces and associated blocking protocols are compatible, but care should be taken, as the polylysine coating is fragile. The Agilent slide surface is less adherent than many other slide coatings, but is successfully used in many laboratories. Plain glass is prone to leakage and should not be used without special equipment (contact BioMicro Systems, Inc.). If you suspect surface chemistry incompatibility, see the Troubleshooting section. Mixer to slide adherence can be assessed by performing a mock hybridization experiment.

MAUI MIXER STORAGE AND USAGE RECOMMENDATIONS

- Store sealed foil pouches at room temperature until ready to use.
- Use MAUI Mixer prior to expiration date on the individual foil pouch label.
- MAUI Mixers should be attached to slides, filled, and sealed within 30 minutes of opening the vacuum-sealed package.

BIOCHEMICAL CONSIDERATIONS

BioMicro Systems, Inc. suggests using the following buffer with the MAUI Hybridization System.

1X SSCD Buffer:

5X SSC
0.1% SDS
0.1 μg/μL human Cot-1 DNA
5X Denhardt's
50% Formamide
0.05% Bromophenol Blue (for visualization purposes)

Many other hybridization buffers are compatible with the MAUI system. However, viscous buffers, for example those containing more than 5% dextran sulfate, can be difficult to fill and may mix poorly or not at all. BioMicro recommends avoiding viscous buffers and buffer components whenever possible and warming the buffer solution prior to filling the Mixer.

A second biochemical consideration is the quantity of probe spotted on the slide. Mixing improves signal only when the labeled target is in limiting quantity. BioMicro Systems, Inc. recommends maximizing spotted probe concentrations (see Figure 2).

Table 1: MAUI® Hybridization System Specifications

DIMENSIONS (width x depth x height)	Cover Open	20 x 37 x 39 cm (4-Bay) 29 x 73 x 14 cm (12-Bay)
	Cover Closed	20 x 37 x 17 cm (4-Bay) 29 x 73 x 30 cm (12-Bay)
WEIGHT		7.9 kg (4-Bay) 19.0 kg (12-Bay)
CAPACITY		4 slides (4-Bay) 12 slides (12-Bay)
SLIDE FORMATS		24.9 – 25.5 mm x 75.4 – 76.4 mm
ELECTRICAL REQUIREMENTS	Power	210 W (heating) 12 W (mixing) (4-Bay) 580 W total (12-Bay)
	Voltage	100-110 V 60 Hz (standard) 220-230 V 50 Hz (optional)
TEMPERATURE	Ambient operating temperature	16.5 – 27.5°C (61.7 – 81.5°F)
	Incubation temperature range	Ambient to 67°C
	Temperature control precision	± 0.5°C
MAUI MIXER HYBRIDIZATION CHAMBERS*	Microarray size (single chamber)	See Figs. 10 – 16
	Volume	See Figs. 10 – 16
	Shelf life	12 Months
MIXING PARAMETERS		Four pre-programmed mix modes (4-Bay) Two pre-programmed mix modes (12-Bay)

CHAPTER 2: INSTALLATION

This chapter describes how to install and verify performance of the MAUI Hybridization System.

INSPECTING THE INSTRUMENT

1. Inspect the shipping box, packaging, instrument, and accessories for damage. If the System is damaged, notify the carrier and BioMicro Systems.

2. Save all packaging materials. You will need the original packing materials if it is necessary to send the System back to BioMicro for service or repair.

OPERATING ENVIRONMENT

For optimal operation, install the MAUI System on a solid, level surface away from excessive humidity, intense light, air drafts, and temperature extremes.

INSTALLING THE MAUI HYBRIDIZATION SYSTEM

1. Plug in the base unit power cord.

2. Attach power supply to the air pump system and plug in to a wall power receptacle or into the receptacle provided on the back of the heat block (110V 60Hz 4-Bay MAUI only). DO NOT PLUG ANY OTHER ELECTRICAL APPLIANCE INTO THE HEAT BLOCK RECEPTACLE.

SYSTEM VERIFICATION

1. Turn the MAUI System heat on with the Heat On/Off Switch.

2. Adjust the temperature set point to the desired hybridization temperature. The temperature display alternates between the actual temperature and temperature set point. When the “Actual” light is lit, the actual temperature is being displayed. When the “Set Point” light is lit, the set point temperature is being displayed. Press the ∇ or Δ arrows to select the desired temperature.

3. It will take at least 3 hours for the heat block to stabilize at the target temperature with the cover closed.

4. Place the supplied System Verification assemblies into the slide bays. Make sure each assembly is seated completely within the bay.

   Remove the system verification assemblies from the MAUI System when not in use.
   It is ok to run the MAUI system with some of the bays empty
   Mixing will automatically stop if the mixing power is on and all bays are empty or contain mixers that are not properly seated.

5. Turn the MAUI System on with the Mixing On/Off switch.

5.1 MAUI 4-Bay Hybridization System:

5.1.1 All lights will flash briefly.

5.1.2 You will see a solid green light next to the On/Off switch and a flashing green light next to the last mix mode used.

5.1.3 You can toggle through the mix modes by pressing the Mix Mode switch until the light is flashing next to the desired mode.

5.1.4 Press and hold the Mix Mode switch for approximately 2 seconds to begin mixing.

5.1.5 If a Mix Mode is not selected, the last mode used will be selected and mixing will begin automatically after 10 seconds.

5.2 MAUI 12-Bay Hybridization System:

5.2.1 The two green Mix Mode lights on the front panel will flash for 5 seconds.

5.2.2 Press the A or B Mix Mode switch to select the desired Mix Mode while the lights are flashing. If no mode is selected, the last mode used will automatically be selected.

5.2.3 After 5 seconds, mixing will begin automatically.

4-Bay Mix Mode	12-Bay Mix Mode	½ Cycle Time
A	**A**	3.3 seconds
B		4.3 seconds
C		6.3 seconds
D	**B**	6.7 seconds

Table 2: Factory Defined Mix Mode Parameters

When using low viscosity hybridization solutions, all modes should work equally well. BioMicro Systems normally recommends using Mix Mode A.
Longer Mix Modes, like Mix mode D (or B for the 12-Bay System) is recommended for more viscous hybridization solutions.

6. The mixing system will perform an initial Station Seal Test (SST) before mixing begins. This test checks all slide bays to make sure they are filled properly.

    6.1 MAUI 4-Bay Hybridization System:

        6.1.1 The light beside each slide bay will light as that bay passes the test.

        6.1.2 If a Mixer is properly seated in a bay, the light beside that bay will turn green and stay lit as long as there is a functional Mixer remains in that slide bay.

        6.1.3 If the slide bay is empty or if the Mixer is not seated properly, the light will turn orange and the turn off and remain off until the MAUI System is restarted with a Mixer properly seated. Note that pumping in that bay will not automatically begin if a Mixer is placed in that bay after mixing begins.

    6.2 MAUI 12-Bay Hybridization System:

        6.2.1 Each front panel slide bay indicator will light up green as the corresponding slide bay passes the test.

        6.2.2 If a slide bay is empty or if the slide is not properly seated, the indicator light for that bay will remain off.

7. If an occupied slide bay fails the initial SST, turn the MAUI System off to evaluate the cause of failure.

    7.1 Check the seating of the MAUI Mixer-slide assembly in the slide bay. Make sure the MAUI Mixer removal tab is lying flat against the O-rings. The tab must completely cover the O-rings.

    7.2 Check for the presence of O-rings in that bay. If an O-ring is missing, replace it with an extra O-ring provided by BioMicro Systems.

    7.3 Make sure the clamp is tightly engaged. Push down firmly on the textured portion of the clamp and listen for an audible snap.

8. Repeat steps 5 and 6. If all bays pass inspection, you are ready to continue with the experiment. If the same slide bay fails a second time, call BioMicro Systems for technical support.

9. Normal mixing

    9.1 MAUI 4-Bay Hybridization System: The green light beside each bay will remain on steadily in each populated bay as long as normal mixing continues.

    9.2 MAUI 12-Bay Hybridization System: The green light for each slide bay indicator will remain on steadily for each populated bay as long

as normal mixing continues. In addition, the left and right MIX lights on the front panel will alternately flash.

10. If a slide is removed from a bay while mixing is in progress or if a leak occurs, the MAUI System will detect a fault and perform an SST. If the MAUI System is unable to reestablish mixing within that slide bay, pressure to that bay will shut off and the indicator light will change from green to red and remain red until the MAUI System is restarted.

11. If power to the MAUI System is interrupted and restored, it will perform an SST and then mixing will automatically resume using the last Mix Mode selected.

12. To pause the MAUI System during a hybridization experiment:

    12.1 MAUI 4-Bay Hybridization System:

        12.1.1 Press the Mix Mode switch to pause mixing allowing the user to remove and examine slides.
        12.1.2 The light indicating the current Mix mode will flash green.
        12.1.3 Press the Mix Mode Switch again to resume mixing.

    12.2 MAUI 12-Bay Hybridization System:

        12.1.4 Pressing the active Mix Mode switch (Mode A or Mode B) will pause mixing, allowing the user to remove and examine slides.
        12.1.5 Both Mix Mode lights will flash green while the MAUI is in Pause mode
        12.1.6 Press the previously active Mix Mode switch (Mode A or Mode B) to resume mixing. The MAUI System will resume pumping automatically after approximately 20 minutes if the Mode switch is not pressed.

CHAPTER 3: OPERATION

This chapter describes how to perform a hybridization experiment using the MAUI Hybridization System. Please consult the troubleshooting section if you encounter difficulties.

PREPARATION OVERVIEW

It is not necessary to fill all slide bays. All unpopulated bays will be inactivated prior to hybridization.

Prior to performing your microarray experiment, BioMicro Systems recommends that the user proceed through the entire hybridization protocol using the provided practice slides and a hybridization buffer containing 0.01% Bromophenol Blue.

PREPARATION TIPS

- *Cleanliness is critical for all microarray hybridization.*
- *You can independently confirm the slide bay temperatures with a standard thermometer. Take a slide bay temperature reading by inserting a thermometer into the slide bay thermometer port located in the center of the MAUI base unit.*

  The MAUI System is calibrated to maintain the desired incubation temperature at the surface of the microarray slide. The temperature at the thermometer port will typically read 0.5°C greater than the desired temperature.
- *Ensure that the work surface used to mount the MAUI Mixer onto the Microarray slide and to fill the Mixer is hard, flat, clean, and debris free. Flexible, uneven, or dirty surfaces will often lead to cracked slides upon braying.*
- *Viscous hybridization solutions may be difficult to load into the MAUI Mixer. Viscosity can be reduced by pre-warming the hybridization solution and by using low molecular weight polymers, such as smaller fragments of carrier DNA.*

PREPARATION PROCEDURE

1. Inspect all items (A/D Jig, Gasket Brayer, Forceps, etc.) necessary to perform the hybridization experiment and the work environment. Cleanliness is essential for optimum results. All items should be free from contamination prior to beginning the experiment.

2. Verify that the MAUI System has equilibrated to desired incubation temperature.

3. BioMicro Systems recommends that you pre-warm the microarray slides to approximately 42°C to ease the MAUI Mixer application process and allow the adhesive gasket to form a better seal. A standard laboratory hot block, inverted to provide a flat surface, may be used.

   Using a hot block is not necessary but recommended for applying the MAUI Mixer to the microarray slide. Heat facilitates the gasket braying process. If you do not have a hot block, you can pre-warm your slides in the base unit slide bays.

4. The hybridization buffer may be pre-warmed by placing it in a 1.5 mL microcentrifuge tube and placing it in the warming holes. Close the MAUI System cover to maintain temperature and to avoid photo bleaching of the labeled target.

MAUI MIXER-SLIDE ASSEMBLY

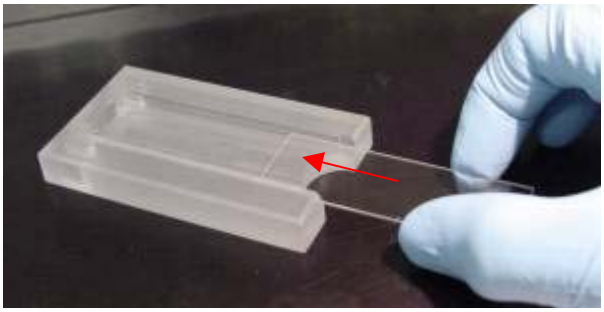
MAUI Mixers must be attached to slides, filled, and sealed within 30 minutes of opening the vacuum-sealed package to prevent absorption of air into the plastic Mixers, which can cause formation of air bubbles in the chamber during hybridization.

ASSEMBLY PROCEDURE

1. Fully insert the microarray slide, labeled end first and array side up, into the Assembly/Disassembly jig. (Fig. 17)

   Ensure the microarray slide is fully and properly inserted into the A/D jig or the gasket may cover some of your microarray spots.

Figure 17: Microarray Slide into A/D jig



2. Remove the Mixer from the protective vacuum-sealed packaging. Inspect the adhesive gasket side of the MAUI Mixer.
   If you see dust on the inside of the chamber, use clean compressed air to remove it prior to removing the adhesive gasket release liner.
   The clear plastic boxes and protective foam sheets may be returned to BioMicro Systems for reuse and reduce packaging waste.

3. Grasp the tab portion of the MAUI Mixer with one hand. With the other hand, remove the adhesive gasket release liner by rolling your finger toward the release liner along a corner near the vent port. Do not touch either the gasket or the inside of the chamber.
   If the liner does not peel off easily, try rolling your finger along a different edge of the mixer.

Figure 18: Release Liner Removal

4. Hold the MAUI Mixer adhesive side down. Align the non-tab end against the inner edge of the A/D jig.
   The non-tab end of the MAUI Mixer should make first contact with the slide.
   Do not touch the adhesive gasket to an undesired point on the slide. Once the MAUI Mixer makes contact with the slide, you may not be able to reposition it.

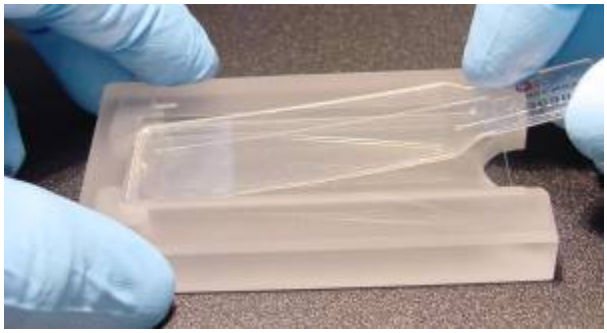


Figure 19: MAUI Mixer Alignment

5. Once aligned correctly, slowly lower the MAUI Mixer down on top of the microarray slide to lightly adhere it to the slide.

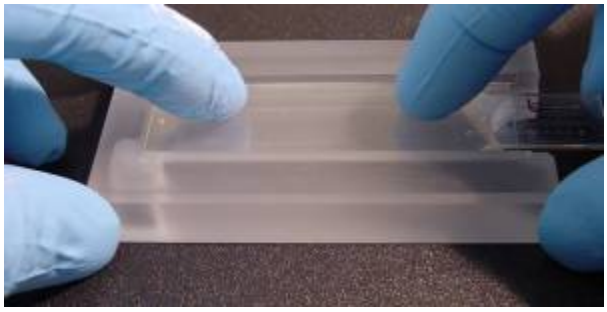


Figure 20: Lowering MAUI Mixer Into Position

6. Remove the MAUI Mixer-slide assembly from the A/D jig and place the assembly, Mixer side up, on the inverted hot block or a slide warmer if available. A hard, flat, clean surface will be sufficient if a warmed surface is not available.

   Mixer to microarray slide alignment may be lost if excessive force is used to remove the assembly from the A/D jig or if the adhesive gasket is not tacked down to the slide before removal from the jig.

7. Using moderate pressure, rub the gasket brayer over the top of the MAUI Mixer to ensure good contact between all portions of the adhesive gasket and the glass slide, paying close attention to the ends of the Mixer. (Fig. 21)

   Concentrate pressure along the adhesive gasket of the Mixer. If a pre-heated slide and braying surface are not used, additional braying may be required.

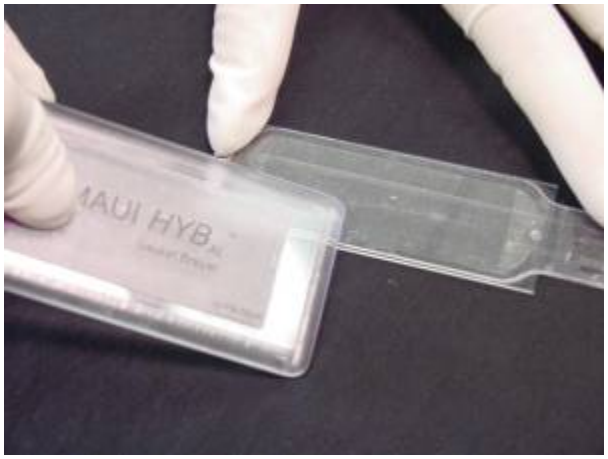


Figure 21: Adhesive Gasket Braying

8. Visually inspect the gasket for voids. Most voids can be eliminated with additional braying.

   A perfect gasket seal will appear completely clear and uniform; an improper seal will contain cloudy non-uniform portions, bubbles between the gasket and slide, or other types of voids. Most voids are easily eliminated by repeated braying over the effected areas while being careful not to damage the edges of the fill port, which may create filling difficulties. Excessive braying is an indication of a damaged or dirty gasket (see troubleshooting section). Small voids that do not transverse the gasket are unlikely to cause a problem, but large voids that create a path for liquid or vapor to escape are. If repeated braying does not remove the voids, heat the slide, remove the MAUI Mixer using the A/D jig, and replace with another MAUI Mixer. Please contact BioMicro Systems with the Mixer serial number and a description of the problem including the location on the adhesive gasket the where problem was noted.

9. Place the MAUI Mixer-slide assembly; slide side down, in one of the slide bays. Make sure the Mixer tab is properly covering the air port o-rings.

   See troubles shooting section for additional details if air ports do not line up properly with the O-rings.

10. Repeat steps 1-9 for other microarrays as necessary.

FILLING AND SEALING PROCEDURE

1. Slowly fill the pipette tip with pre-warmed hybridization buffer. Pipette the sample up and down at least once to wet the inner pipette tip surface and eliminate air bubbles.

   You should use 3-8 µl more hybridization fluid than the chamber volume of the hybridization chamber to ensure complete filling. As you become more familiar with filling, you may find that you need less volume to achieve complete filling. You should experiment with actual filling volume and be aware that filling volume will vary slightly from Mixer to Mixer.

2. Visually inspect the filled tip to ensure that air bubbles do not exist in the column of liquid.

3. Insert the end of the pipette tip into the fill port.
   - *The position of the pipette tip should be perpendicular to the plane of the MAUI Mixer to ensure proper filling.*
   - *The AO Mixer must be filled from the squared off (non-tab) end.*
   - *FL and SL Mixers should be filled from tab end.*
   - *DC Mixers should be filled from outer ends to reduce chance of cross contamination.*
   - *M4 and AC Mixers have a larger diameter fill port and a smaller vent port. Filling must be done through the larger port.*

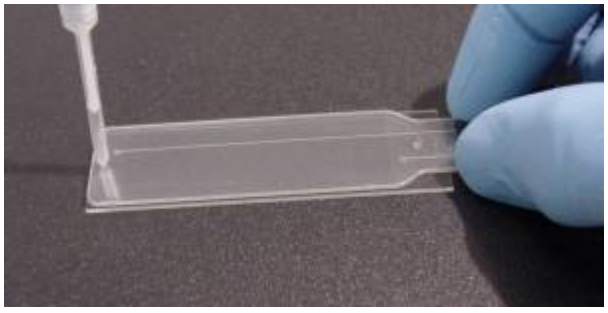


Figure 22: Positioning the Pipette Tip

4. Apply slight downward force (approximately 0.5 Kgf.) to the tip to ensure a tight seal.
   Too little force may cause a poor seal around the fill port, resulting in leaking or pooling of hybridization solution on top of the Mixer. Too much force causes deformation of the tip or collapse of Mixer onto slide surface.

5. With a continuous motion, slowly inject the hybridization solution into the fill port. Leave the pipette tip in place with the pipette plunger depressed until hybridization solution emerges from the vent port.
   If an air bubble is introduced at the end of the injection process, next time be sure to pipette the solution up and down to clear trapped air from pipette tip. Also slow the filling rate, especially at the end of the filling process.

   If hybridization solution pools above the fill port rather then entering to Mixer, see the Trouble shooting section.

6. Keep the pipette actuator depressed (Gilson Microman® Pipette) and remove the tip from the Mixer. The pipette tip can then be used to suck excess hybridization fluid away from the fill and vent ports, making it easier to wipe the surface clean. (Fig. 23)

   Hybridization solution will continue to emerge from the fill and vent ports until equilibrium is reached within the hybridization chamber. Allow the chamber to rest for about 15 seconds or until hybridization solution stops emerging from fill and vent ports.

Figure 23: MAUI Mixer Filled with Dyed Solution

7. Gently use a tissue to completely wipe off any excess liquid that may remain around the fill or vent ports. Avoid excess wiping to prevent wicking from the ports. (Fig. 24)

   Wicking excess liquid out of the hybridization chamber by resting the tissue over the fill or vent ports will allow an air bubble to form when the port seal is applied.
   However, it is critical that the MAUI Mixer is wiped dry around the fill and vent ports or the hybridization solution (which often contains detergents and other blocking reagents) will prevent the port seal from adhering completely. This may result in leakage of the hybridization solution during mixing yielding poor microarray data

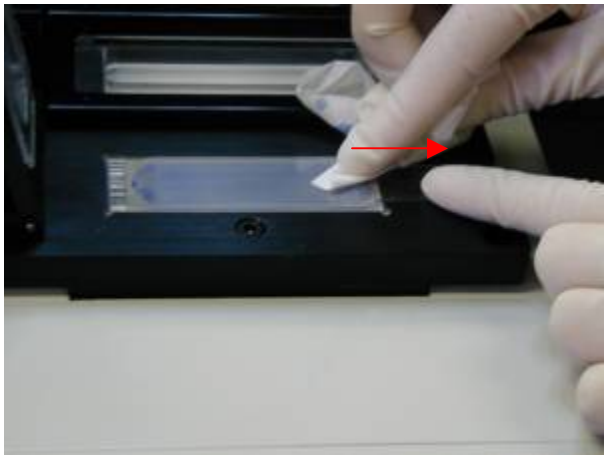


Figure 24: Drying Fill/Vent Ports

8. Using a pair of forceps, lightly place an adhesive port seal directly over the fill and vent ports. The long edges of the port seals should align with the long edges of the MAUI Mixer and the port seal should be approximately centered over the fill and vent holes. Use a finger on each port seal to press each port seal firmly down. (Figs. 25 to 27)

Pressure must be applied uniformly to each port seal <u>at the same time</u> to prevent liquid from being forced out of either port, which would compromise the adhesive seal. If you suspect that liquid may have compromised the seal, remove the port seal with forceps, wipe the Mixer surface dry again, and replace with a new port seal.
It is sometimes helpful to rub down the port seals using a fingernail or the handle end of a pair of forceps to make sure they are securely in place and any excess liquid has been forced our from underneath them. Always start with the portion of the port seal directly over the port.

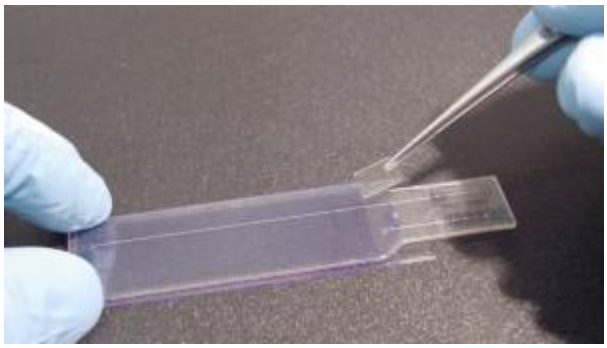


Figure 25: Placing Port Seals

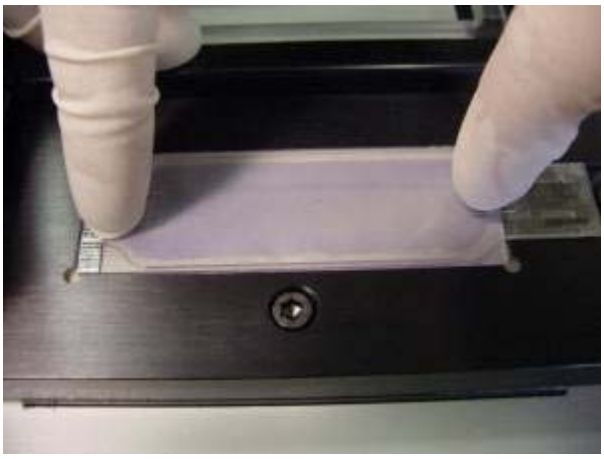


Figure 26: Securing Port Seals

Figure 27: Correct Port Seal Placement

9. Repeat steps 1-11 for other microarrays as necessary.

10. Close the corresponding individual bay clamp by pushing down firmly on the textured portion of the clamp. (Fig. 28)

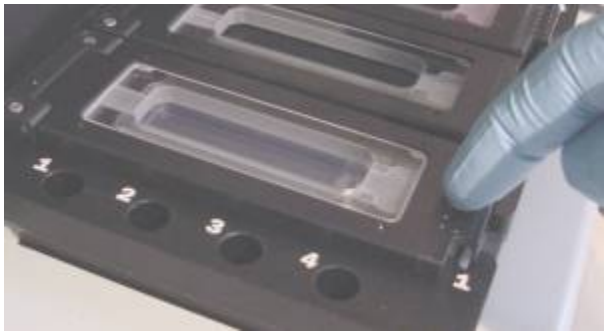


Figure 28: Closing Bay Clamp

MAUI SYSTEM OPERATION

1. Begin mixing as described in the System Verification section.

2. Verify that the air bladders are moving. BioMicro has found that adding 0.01% BPB to the hybridization buffer allows better visualization without interfering with the hybridization results. If you choose not to add BPB, watch closely for a slight deflection of the plastic air bladders during pumping to verify that pumping is occurring in the hybridization chambers.

   To visualize the bladder movement, you may have to look at the Mixer from different angles.

3. Close the MAUI System cover to prevent photo bleaching of the labeled target. Allow hybridization to proceed for desired length of time.

4. The MAUI System detects changes in the System pressure. If a sizeable change in pressure is detected during an experiment, (i.e., a slide is removed), it will perform an additional SST without pausing or stopping your experiment. If it detects an open slide bay, it will inactivate that slide bay, change that bay indicator light to red, and the bay will remain inactive for the duration of the experiment. The remaining bays will continue to be active and hybridization will continue.

REMOVAL OF THE MAUI MIXER FROM THE MICROARRAY SLIDE

As with any hybridization protocol, drying of the slide prior to completion of the wash steps may result in high background. BioMicro Systems recommends the following:

1. Place a clean lid from an empty 1mL pipette tip box (or a similar size container) on a standard lab hot block that has been inverted in its base unit. This lid will serve as a basin in which MAUI Mixer removal will take place. Place the A/D jig inside. Set the hot block temperature to 45-50°C,

(depending on laboratory temperature and airflow to maintain a wash solution temperature of 40-42°C)

2. Add sufficient pre-warmed wash buffer #1 to the pipette lid to cover the top of the jig. The wash buffer will prevent the array from drying and help the adhesive gasket release from the microarray slide.
   If the hybridization is performed at 42°C with formamide, heating the slide above 42°C prior to removal of the formamide can denature the annealed target and result in a loss of signal.

3. If necessary, cover the entire hot block unit with a box to insulate the lid and keep the solution warm without exceeding the hybridization temperature.

4. Turn the mixing off and release the bay clamp.

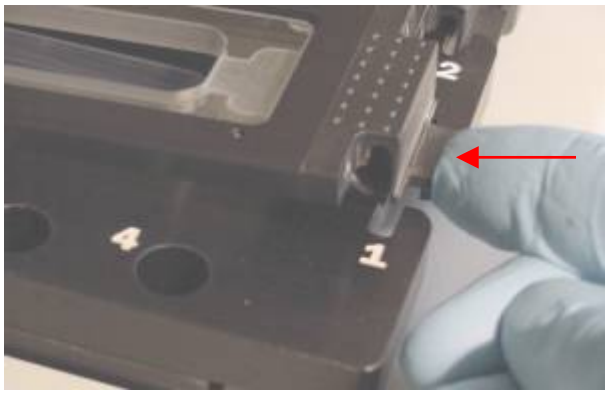


Figure 29: Releasing the Bay Clamp

5. While wearing gloves, remove the MAUI Mixer-slide assembly from the base unit and quickly slide it into the immersed A/D jig to prevent cooling of the slide.

6. Hold the A/D jig firmly in place. With the other hand, grasp the removal tab portion of the MAUI Mixer and **SLOWLY** peel the Mixer from the slide. Discard the MAUI Mixer. (Fig 30).
   Bend and twist the MAUI Mixer slightly as you peel it away from the slide. Rapid peeling can lead to broken slides or adhesive residue left behind on the slide.

Figure 30: MAUI Mixer Removal

7. Remove the slide from the A/D jig and quickly (to prevent drying) place in a new basin containing wash buffer, and continue with standard wash procedures. Cover the hot block to prevent cooling.

   If a piece of the adhesive gasket remains bound to the slide, remove it prior to drying the microarray slide, or immediately after the quick dry. The adhesive is more easily removed while the slide is still wet.

8. Repeat for other microarrays as necessary. Depending on the experiment, it may be advisable to wash the AD jig and lid and replace the wash buffer to prevent carry-over of the labeled target to the next microarray slide.

CHAPTER 4: TROUBLE SHOOTING GUIDE

Bay Indicator Light	Indication	Recommendation
Solid green	Slide bay passed Station Seal Test and test is continuing normally	• Continue with hybridization experiment
Orange (temporarily, then switches off)	Slide bay did not pass SST	Assuming a slide is in the bay: • Stop the test and verify that the clamp is closed and both o-rings are present and intact • Restart the test • Call BioMicro if condition persists
Solid red	Slide bay failed secondary Station Seal Test and is inactivated The slide has been removed from the bay or some other leak in the system has been detected. The experiment will continue on remaining slide bays. It is OK to run the MAUI with some bays empty.	Assuming a slide is in the bay: • Stop the test and verify that the clamp is closed and both o-rings are present and intact • Restart the test • Call BioMicro if condition persists
Flashing red	MAUI System fault	• Call for technical support
No light	Slide bay failed initial Station Seal Test. The experiment will continue on remaining slide bays.	Assuming a slide is in the bay: • Stop the test and verify that the clamp is closed and both o-rings are present and intact • Restart the test • Call BioMicro is condition persists

Table 3: Slide Bay Indicator Light Code (MAUI 4-Bay System)

Mix Mode Indicator Light	Indication	Recommendation
Solid green	Slide bay passed Station Seal Test and test is continuing normally	• Continue with hybridization experiment
Flashing green	System is in Pause Mode	• Press and hold the Mix Mode switch to start experiment
Flashing green (alternating one light, then 3 lights)	A potential system fault has been detected	• Allow the experiment to continue to completion • Contact BioMicro at your earliest convenience
No light	The mixing unit is not receiving power	• Verify that the power switch is on • Verify that the AC adapter cord is plugged in to the MAUI and to a live receptacle • Call BioMicro if condition persists

Table 4: Mix Mode Indicator Light Code (MAUI 4-Bay System)

Bay Indicator Light	Indication	Recommendation
Solid green	Slide bay passed Station Seal Test and test is continuing normally	• Continue with hybridization experiment
Solid red	Slide bay failed secondary Station Seal Test and is inactivated The slide has been removed from the bay or some other leak in the system has been detected. The experiment will continue on remaining slide bays. It is OK to run the MAUI with some bays empty.	Assuming a slide is in the bay: • Stop the test and verify that the clamp is closed and both o-rings are present and intact • Restart the test • Call BioMicro if condition persists
No light	Slide bay failed initial Station Seal Test. The experiment will continue on remaining slide bays.	Assuming a slide is in the bay: • Stop the test and verify that the clamp is closed and both o-rings are present and intact • Restart the test • Call BioMicro is condition persists

Table 5: Slide Bay Indicator Light Code (MAUI 12-Bay System)

Mix Mode Indicator Light	Indication	Recommendation
Solid green (1 light)	The Mix Mode next to that light is active	• Continue with hybridization experiment
Flashing green (both lights)	System is waiting for a Mix Mode to be chosen	• Press the desired Mix Mode switch to start experiment or • Do nothing and mixing will begin automatically in 5 seconds using the last Mix Mode used
No light (both lights)	The mixing unit is not receiving power	• Verify that the power switch is on • Verify that the power cord is plugged in to a live receptacle • Call BioMicro if condition persists

Table 6: Mix Mode Indicator Light Code (MAUI 12-Bay System)

Mix Mode Indicator Light	Indication	Recommendation
Both lights flashing green at the same time	System is in Pause Mode	• Press either Mix Mode switch to resume mixing
Alternately flashing green	Test is continuing normally	• Continue with experiment
No light	The mixing unit is not receiving power	• Verify that the power switch is on • Verify that the power cord is plugged in to a live receptacle • Call BioMicro if condition persists

Table 7: Mixing Lights (MAUI 12-Bay System)

DIFFICULTY ASSEMBLING THE MAUI MIXER-SLIDE ASSEMBLY

Mixer-Slide Alignment

The MAUI Hybridization System was designed to work with standard 1” x 3” (25.4 mm x 76.2 mm) glass slides (see "Slide Compatibility Evaluations" for slide dimensional tolerances). The A/D jig is used to align the slide and Mixer such that all spotted probes are contained within the Mixer chamber and the air ports in the bottom of the tab align with the O-rings in the MAUI base unit. If this is not the case, ensure the appropriate A/D jig is being used. If you have already filled the Mixer with hybridization solution when the misalignment is noted, proceed with the hybridization without mixing, you should be able to recover some usable data.

Removal Of Release Liner

If you have difficulty removing the release liner as described under "MAUI Mixer-slide assembly", it is possible to separate the extension portion of the release liner under the tab (see Figure 3) from the adhesive gasket using a sharp object such as a razor blade, then grasp the extension portion and slowly peal the release liner from the Mixer. If you prefer this method, do not damage in any way the portion of the adhesive gasket that binds to the slide surface, otherwise leaks will result.

Braying

Failure to obtain a clear seal can be caused by particle contamination, damage to the adhesive gasket, non-compatible slide surfaces or coatings, or excessive entrapment of air between the adhesive gasket and slide during the braying process. To avoid air entrapment, bray from one end of the Mixer to the other in one continuous motion followed by additional braying on specific portions of the gasket if necessary. If multiple Mixer failures occur, please contact BioMicro with the Mixer serial numbers and descriptions and locations on the adhesive gasket the failures were noted.

Mixer Does Not Adhere To Slide

First ensure that the slide and Mixer are completely dry and free of fingerprints, oils, and other contamination before assembly. Visually confirm the Mixer is not bent or warped which can cause it to detach from weakly adherent surfaces. (See Slide Compatibility Evaluation in Chapter 1).

DIFFICULT FILLING THE PIPETTE TIPS OR MIXERS

Air Bubbles In The Pipette Tip

Bubbles can result from excessive or rapid aspiration, and the use of viscous, foamy or an insufficient volume of hybridization solution; make necessary adjustments. If air bubbles exist in your target containing solution, dispense back into the microcentrifuge tube, centrifuge the hybridization solution to eliminate bubbles, and repeat the filling process with a new tip.

Like loading gels, successfully filling MAUI Mixers is a matter of practice.

Pooling Of Hybridization Buffer Above the Fill Port

Pooling of hybridization solution on top of the Mixer around the fill port during filling can be caused by too much or too little pressure being applied to the pipette tip, the pipette not being held vertical, or excessively viscous hybridization solution; make necessary adjustments. This problem can also be caused by damage to either the tip or the fill port, particularly during braying. Please report any unresolved difficulties to BioMicro Systems.

Slow Filling Mixers

Upon sample injection, the MAUI Mixer should be completely filled within five seconds. Slow sample injection can be caused by:

- Applying too much pressure to the pipette tip during filling causing the Mixer to distort.
- Excessive air above the fluid layer in the injection device. Air can be minimized using the recommended filling device.
- Excessively viscous hybridization solution. Pre-warming both the assembled MAUI Mixer-slide assembly and the hybridization solution reduces the viscosity and insures complete solubility of the SDS, thus facilitating filling. Using low molecular weight polymers will help reduce viscosity as well.

Carrier DNA is a prime example of a high molecular weight polymer. Run a sample of carrier DNA on a gel to ensure the size is below 1000bp ideally being near or below 500bp.

Air Bubbles Trapped In The Hybridization Chamber

Air bubbles in the hybridization chamber can be a result of:

- Sample injection too slow or too fast. Filling should be done in one continuous motion and should take several seconds.
- Over injection of the hybridization buffer and subsequent injection of air. Pipette the hybridization solution up and down at least once prior to Mixer filling to completely remove air from pipette tip.
- Outgassing of the plastic Mixer during hybridization. MAUI Mixers are vacuum packed to prevent out-gassing during hybridization. It is important that the assembly, filling, and sealing of each MAUI Mixer be completed within 30 minutes of opening the sealed foil package.
- Particle contamination in hybridization chamber; improve work area cleanliness.

DIFFICULTY REMOVING MAUI MIXER FROM SLIDE

Adhesive Remains Bound To The Slide After Disassembly

Adhesive left on the slide usually results from disassembly at temperatures below 40°C or from an excessively adherent slide coating. If adhesive consistently sticks to the slide while removing the Mixer at temperatures above 40°C and the residual adhesive causes difficulties, please contact Biomicro Systems.

FLUID LOSS FROM THE MAUI MIXER

Evaporation And Absorption

It is normal for a small amount of solution to be lost by evaporation from and by absorption into the Mixer. While there are normally no significant consequences during overnight hybridizations, fluid losses can mount during multi-day hybridizations, especially at high temperatures and low ambient humidity. Formamide typically is not lost and thus the effective formamide concentration could increase.

If you plan to perform multi-day hybridizations, it is advisable to occasionally monitor fluid loss as described below. (See Test for Hybridization Buffer Loss)

Adhesive Gasket Leaks

Adhesive gasket leaks can be caused by:

- Debris, fingerprints, or physical damage to the gasket caused during removal of the release liner, handling, or placement and subsequent removal and replacement. Local areas of inadequate gasket bonding are usually visible, appearing cloudy or as an air bubble inclusion.
- Failure to remove air from the bond line between the adhesive gasket and the slide during the braying process. The bond line should appear clear and uniform.
- Bent or warped Mixers, particularly when combined with low adherent slide coatings.
- Non-adherent slide surfaces or incompatible hybridization chemistries. Please contact BioMicro Systems for further information.

Fill/Vent Port Leaks

Port leaks are a result of wet surfaces under the port seals. The detergent in hybridization solution makes it particularly disruptive to sealing properly. Be careful to thoroughly dry the lid surface around the ports and do not apply pressure to the top of the Mixer when placing the port seals. Pressing on the chamber before the port seals are firmly adhered will force the hybridization solution out of the chamber.

Test For Hybridization Buffer Loss

An analytical scale that can accurately distinguish 1 mg differences can be used to quantify fluid loss. The scale must be accurate and calibrated. Accurate weighing is essential and a significant weight change is near the resolution limit of many commonly available laboratory scales. If the scale is suspect, it may be useful to confirm weight measurements by also weighing another object of known, unchanging weight similar to that of the mixer/slide assembly (7-8 g) before and after weighing the mixer. If you do not get consistent weights for an

unchanging object, the scale may not be consistent or accurate enough for the purpose.
Attach MAUI Mixer to the microarray slide and record Mixer serial number. Place 2 port seals on the edge of the Mixer and weigh the mixer, slide, and port seals together. Fill the Mixer and use the attached port seals to seal the Mixer in the usual manner. Weigh the filled Mixer. Perform the hybridization experiment for the appropriate length of time. Weigh the Mixer again after the hybridization. Remove the Mixer from the slide (do not remove port seals from Mixer) and, while washing the slides in the usual manner, rinse and completely dry the detached Mixer with compressed air. As soon as the slide and Mixer are dry, weigh them together. By performing this experiment you can determine the following:

- The weight of hybridization solution injected into the Mixer
- The weight of hybridization buffer lost during the hybridization, and
- The weight of hybridization buffer absorbed by the Mixer.

By weighing the filled mixer/slide assembly before and after hybridization only, you can quantify the amount of fluid lost during the hybridization process.

DIFFICULTY REMOVING MAUI MIXER FROM SLIDE

Adhesive Remains Bound To The Slide After Disassembly

Depending on the slide surface chemistry, adhesive may remain bound to the slide after Mixer disassembly. Try removing Mixer above 40°C or changing slide surface or blocking chemistry. If adhesive consistently sticks to the slide, please contact Biomicro Systems.

DIFFICULTIES WITH HYBRIDIZATION RESULTS

It is important to remember that many sources of compromised microarray data exist, including, but not limited to: slide coating, probe printing, slide blocking, target preparation, hybridization buffer composition, particle contamination, washing, and scanning. In addition to the suggestions below, it is highly recommended that MAUI System users consult more general microarray resources such as "DNA Microarrays" (Edited by David Bowtell and Joseph Sambrook, 2003, Cold Spring Harbor Laboratory Press), which contains an excellent troubleshooting section.

Signal Non-Uniformity And High Background

Fluid Loss

The most likely MAUI related cause of signal non-uniformity and high background is hybridization fluid loss. You may wish to test for Hybridization Buffer Loss (see above).

Signal Reduction Or Smearing Of The Brighter Probe Spots

These problems can be caused by excess target hybridization to the complementary probe spot, which leads to dye auto quenching, or in the case of multistage hybridizations, excessive complex formation. BioMicro does not know of a simple solution that will not affect intensities from lower abundance targets. A more complex solution would be to print fewer probe molecules of the higher abundance targets.

Uniform But Reduced Signal Intensities Relative To Static Hybridizations

Because the MAUI Mixer contains significantly less volume than other types of hybridization chambers and elevated cover slips, the same molar quantity of labeled target, rather than the same concentration of labeled target, should be used for an accurate comparison. If mechanically printed microarrays were used, try repeating the experiment, as considerable variation can exist among arrays printed in the same run.

If the problem persists, consider the following test to determine if an incompatibility exists between the microarray biochemistry and the mixing function. Set up two identical MAUI hybridization experiments except prevent mixing in one Mixers by covering the air ports on the underside of the removal tab with a piece of thin (scotch) tape. If Mixing reduces the signal intensities, consider changing the hybridization buffer, slide surface chemistry, or labeled target.

Another possible cause of reduced signal intensities is that the mixing function may not have been properly activated and functioning on the MAUI System. This is particularly possible with older versions of the MAUI 4-Bay System. If you are certain that the mixing function was properly activated, follow the instructions below to verify that mixing is actually taking place. (See Failure to mix).

Little Signal Gain Relative To Static Hybridizations

Excessively Stringent Hybridization Conditions

If the hybridization conditions are too close to the melting range of the target-probe, it is theoretically possible to reach equilibrium during the hybridization process such that the on and off rates are equal and continued hybridization with or without mixing will have no effect. In this case, BioMicro recommends reducing the temperature or modifying the hybridization buffer chemistry (for example, reduce formamide or increase salt concentrations).

Failure To Mix

Failure to mix during the hybridization can be cause by:

- Excessively viscous buffers
- Misalignment of MAUI Mixer air ports with MAUI System O-rings

- MAUI System air pump failure
- Failure to activate mixing

If you suspect this as an issue, verify that mixing is taking place prior to beginning the incubation period as well as at the end of the incubation period. The movement of the mixing bladders should be visible, although it may be difficult to see.

If uncertainty remains, BioMicro Systems has found that adding bromophenol blue (BPB) to 0.1% in the final buffer allows visualization of the filling and mixing steps without interfering with the hybridization results. The user should verify this for their specific hybridization conditions.

Insufficient Spotted Probe

Mixing provides gains in microarray sensitivity because it prevents localized depletion of labeled target around a particular spotted probe. Therefore, mixing can improve signal only when the spotted probe is in excess and the labeled target is in limiting supply. The greatest gains will be observed when using more than 50 aMols/spot and when labeled targets are near the limits of detection.

APPENDIX

ORDERING INFORMATION

To place an for order additional supplies or consumables call:

Biomicro Systems Inc.
1 (801) 303 -1470 or *Toll Free* 1 (800) 454 -1485

CATALOG NUMBER	PRODUCT
02-A002-02	MAUI 4-Bay Hybridization System (110V)
02-A002-03	MAUI 4-Bay Hybridization System (220V)
02-033-03	SL Assembly/Disassembly Jig
02-033-02	DC Assembly/Disassembly Jig
02-088-00	FL/AO/M4 Assembly/Disassembly Jig
02-088-01	FL/AO/M4 Matsunami Assembly/Disassembly Jig
02-033-05	NG Assembly/Disassembly Jig
02-33-06	AC Assembly/Disassembly Jig
02-S002-02	12-Month Extended MAUI System Warranty
02-041-00	Port Seals
02-054-00	Gasket Brayer
02-044-00	MAUI System User's Guide
02-A008-03	MAUI Mixer SL Shelf Box
02-A008-05	MAUI Mixer DC Shelf Box
02-A008-07	MAUI Mixer FL Shelf Box
02-A008-09	MAUI Mixer AO Shelf Box
02-A008-11	MAUI Mixer M4 Shelf Box
02-A008-13	MAUI Mixer NG Shelf Box
02-A008-15	MAUI Mixer AC Shelf Box
01-014-00	Gilson M-100 Microman Pipet
01-015-00	CP-100 Capillaries/Pistons (Qty. 96/box)

ONE YEAR LIMITED WARRANTY

Warranty and Claims.

1. Goods. BioMicro warrants that its Goods meet BioMicro's specifications at the time of shipment. All warranty claims on Goods must be made within thirty (30) days of installation of the Goods or, if not theretofore installed, then within sixty (60) days following Customer's receipt of the Goods. BioMicro's sole liability and Customer's exclusive remedy for a breach of this warranty is limited to repair, replacement or refund of the BioMicro supplied equipment at the sole option of BioMicro.

2. Equipment. BioMicro's Equipment of its own manufacture is warranted from date of shipment to be free of defects in workmanship or materials under normal usage for a period of one year following the earlier of: date of installation or the sixtieth (60th) day following Customer's receipt of the Equipment. All warranty claims must be asserted as follows: 1) claims as to matters apparent at the time of installation must be asserted within thirty (30) days after installation or if not theretofore installed, then within sixty (60) days after Customer's receipt of the Equipment; 2) claims as to matters not apparent at time of installation must be asserted within sixty (60) days after Customer becomes aware of claim. BioMicro's sole liability and Customer's exclusive remedy for a breach of this warranty is limited to repair, replacement or refund of the BioMicro supplied equipment at the sole option of BioMicro.

3. BioMicro will use reasonable efforts to obtain for Customer any warranty provided by the other manufacturer of any component of the goods sold by BioMicro which is not manufactured by BioMicro. Customer may notify BioMicro of warranty claims under such warranties and BioMicro will use reasonable efforts to communicate them to the proper manufacturer on Customer's behalf. BioMicro does not guarantee or otherwise assure performance of any such other manufacturer's warranty. Any claim on account of any such other manufacturer's warranty may be asserted solely against the other manufacturer and, notwithstanding any such claim, the purchase price will be paid on the terms set forth in BioMicro's proposal and invoice. If there is no warranty provided by any such other manufacturer, then such other manufacturer's components included in the goods are sold "as is."

4. Customer waives and releases BioMicro from any liability for damages, whether direct, incidental, special, or consequential, for breach of warranty other than under the express limited warranties referred to in paragraphs 1, 2 and 3.

5. In no event will BioMicro have any liability for any incidental or consequential damages arising out of or in connection with a breach of the sale or any other duty of BioMicro with respect to the goods, including, but not limited to, incidental or consequential damages for lost profits, lost sales or injury to persons or property.

6. Any production figures quoted are approximate, based on the conditions as understood by BioMicro but actual figures may vary substantially depending on operating conditions. Hence, no such figures are guaranteed.

7. BioMicro's liability on any claim of any kind, including but not limited to warranty, negligence, strict liability, and any other cause of action, for any loss of damage arising out of, in connection with, or resulting from the performance or breach of the terms of sale of any goods, or from the design, manufacture, sale, delivery, resale, installation, technical direction of installation, inspection, repair, operation or use of any goods or services or part of those goods or services will in no case exceed the purchase price allocable to the goods or services or part of those goods or services that gives rise to the claim.

8. Customer assumes all responsibility for use of the goods and for training the persons who will use the goods. Customer will indemnify, defend and hold BioMicro harmless from any claim, demand, loss, liability, damage or expense arising in any way from use of the goods by Customer to its employees, agents, contractors, assigns or successors.

9. Customer agrees to indemnify, defend and hold BioMicro harmless from any and all claims, demand, liability, losses, expenses, attorneys fees, and other obligations incurred by BioMicro which arise out of Customer's acts or omissions with respect to any goods sold by BioMicro to Customer or with respect to any other matter or transaction between the parties or which arise out of Customer's violation of any law.

10. BioMicro is not responsible for any use of the goods. Customer will be responsible for safe use of all goods.

Limit of Liability.

11. BioMicro shall have no liability under the warranties stated above in respect of any defect in the Products arising from specifications or materials supplied by Customer; fair wear and tear; willful damage or negligence of Customer or its employees or agents; abnormal working conditions at Customer's premises; failure to follow BioMicro's instructions (whether oral or in writing); misuse or alteration or repair of the Products without BioMicro's approval; or if the total price for the products has not been paid.

12. BioMicro shall in no event be liable for any indirect or consequential, or punitive damages of any kind from any cause arising out of the sale, installation, use or inability to use any product or service, including without limitation, loss of profits, goodwill or business interruption.

13. This warranty is limited to the original Customer and cannot be assigned or transferred. An authorized representative of BioMicro must perform all warranty inspections. To confirm decontamination from biological, chemical, and radioactive hazards, no products will be accepted without a return authorization from BioMicro.

If you have any questions concerning service of this product, please contact:

BioMicro Systems, Inc.
1290 West 2320 South, Suite D
Salt Lake City, UT 84119-1476
Phone: 801.303.1470; Toll Free: 800.454.1485
www.biomicro.com
Email: support@biomicro.com

Evidence of original purchase is required. It is important to hold onto your sales receipt or packaging slip.

These limited warranty terms are included among BioMicro System's Terms and Conditions of sale governing the customer's purchase and use of the MAUI® Hybridization System. (Refer to your copy of the Terms and Conditions).