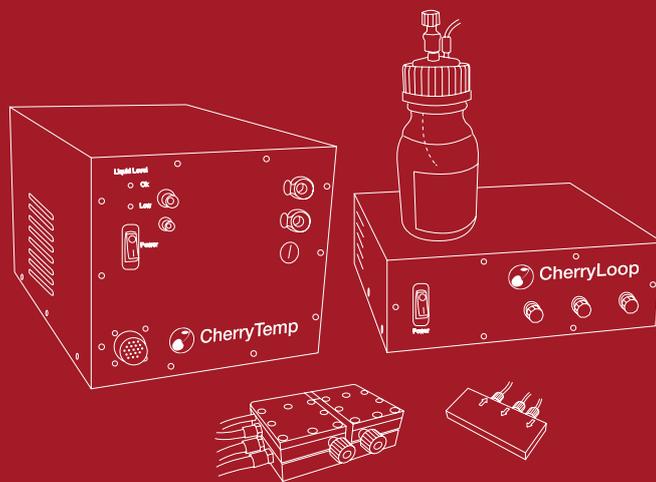


CherryTemp™ User Guide



The chips are fixed with a glass coverslip for optimal heat transfer. Inappropriate handling can result in micro breaks of the coverslips, eventually leading to failure of the microsystem. This can result in leaks etc. Cherry Biotech is not liable for failure coming from improper manipulation of the chips.

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CherryTemp Installation

For an easy and rapid CherryTemp installation, please refer to the «Installation Guide» provided with the system.

If you have any enquiry while installing the set-up on your microscope, feel free to contact us.

Make sure you follow the start up check list on page 17 of this user guide before starting the system

Golden list: 7 rules to get full efficiency

1. Use only the sample mounting standards of CherryTemp

 - ✓ We designed a simple Cherry mounting system, flexible with a wide range of applications. Just put your sample on the slide, add the liquid medium and cover with our chip
 - ✗ Do not add cover slips/pads/oil...or anything in between our chip and your sample except if validated by our expert team.
2. Keep the provided tubing

 - ✓ Our system is calibrated to bring you unprecedented temperature control. Our fluidic actuation loop is designed to optimize this control.
 - ✗ Do not change the length and type of the chip inlets or outlets. Only use the provided tubing and their connectors.
3. Secure the exchanger holder

 - ✓ We provide customized exchanger holders for a perfect integration with your microscope. Always attach the holder plate with provided screws to securely fix the exchangers on its holder.
 - ✗ Do not add extra-weight on the exchanger holder (other than the exchangers, for instance handling pressure).
4. Check the overall platform before starting

 - ✓ Thanks to the so-called «Final check» last page of the «CherryTemp Installation Guide», you have an overview of the full CherryTemp platform, once installed on your setup. Before starting the CherrySoft and your experiments, check that the platform is correctly installed.
 - ✗ Do not start the system without first checking all the connections (especially fluidic tubing connections). Attach particular attention not to wedge/pinch tubing. Wedged/pinched tubing might damage the system and be source of unexpected heating.
5. Follow the software initialization sequence

 - ✓ Before an experiment, respect the initialization sequence of the software. This is a short sequence to ensure proper filling of the fluidic system.
 - ✗ Do not skip the initialization step otherwise thermalization efficiency will not be warranted.

6. Choose your temperature calibration and correctly place the sensor
 - ✓ Carefully choose your temperature calibration in the software corresponding to your observation conditions (no calibration, air objective lens, immersion objective lens). For immersion mode, place the sensor around the objective lens. For other modes, place it either on the objective or in contact with the microscope plate.
 - ✗ Accuracy of CherryTemp is highly dependent on these criteria. Inappropriate calibration will cause temperature inaccuracy.
7. Respect the cleaning sequence and storage conditions
 - ✓ Change the thermalization solution every two months.
 - ✓ Do a cleaning sequence every six months.
 - ✓ If you do not use the system during a period of time exceeding 5 days, strictly follow the cleaning steps.
 - ✗ Thermalization solution is not suitable for long-term storage (more than 5 days).

Cleaning procedure

1. Close the software
2. Replace the thermalization tank bottle with cleaning solution
3. Close the bottle with cap (storage, up to 2 months)
4. Start again the software
5. Run the initialization step
6. Switch all the system off.

Your CherryTemp is clean and secured!



The Cherry Biotech team wishes you unprecedented experiments!

User guidelines

Notes

The information contained herein is offered in good faith and is believed to be accurate.

Diagrams

- Security related note
- Cherry Biotech system utilization important notes
(Pictures and drawings are non-contractual.)

General description

CherryTemp is a microfluidic device. This system dynamically heats and cools down samples. The system has been originally developed to dynamically control biological samples during live-cell imaging experiments. Therefore, ergonomic elements are dedicated to microscopy but the core system listed below might be used for other applications upon validation by our expert team (e.g. live-observation of polymer properties, analysis of samples without microscopes...).

Core system:

- CherryTemp (temperature controller)
- CherryLoop (temperature-optimized fluidic actuation system)
- Heat Exchangers (heating and cooling elements composed of two independent channels)
- Tank reservoir
- Thermalization chip pack (4 chips)
- 4 cables (3 to use, + 1 free)
- Click and seal closures (3 clics, as with the heat exchangers connectors)

Coverslips not provided (for inverted microscopes, coverslips size can be 24x60 or 24x40 mm)

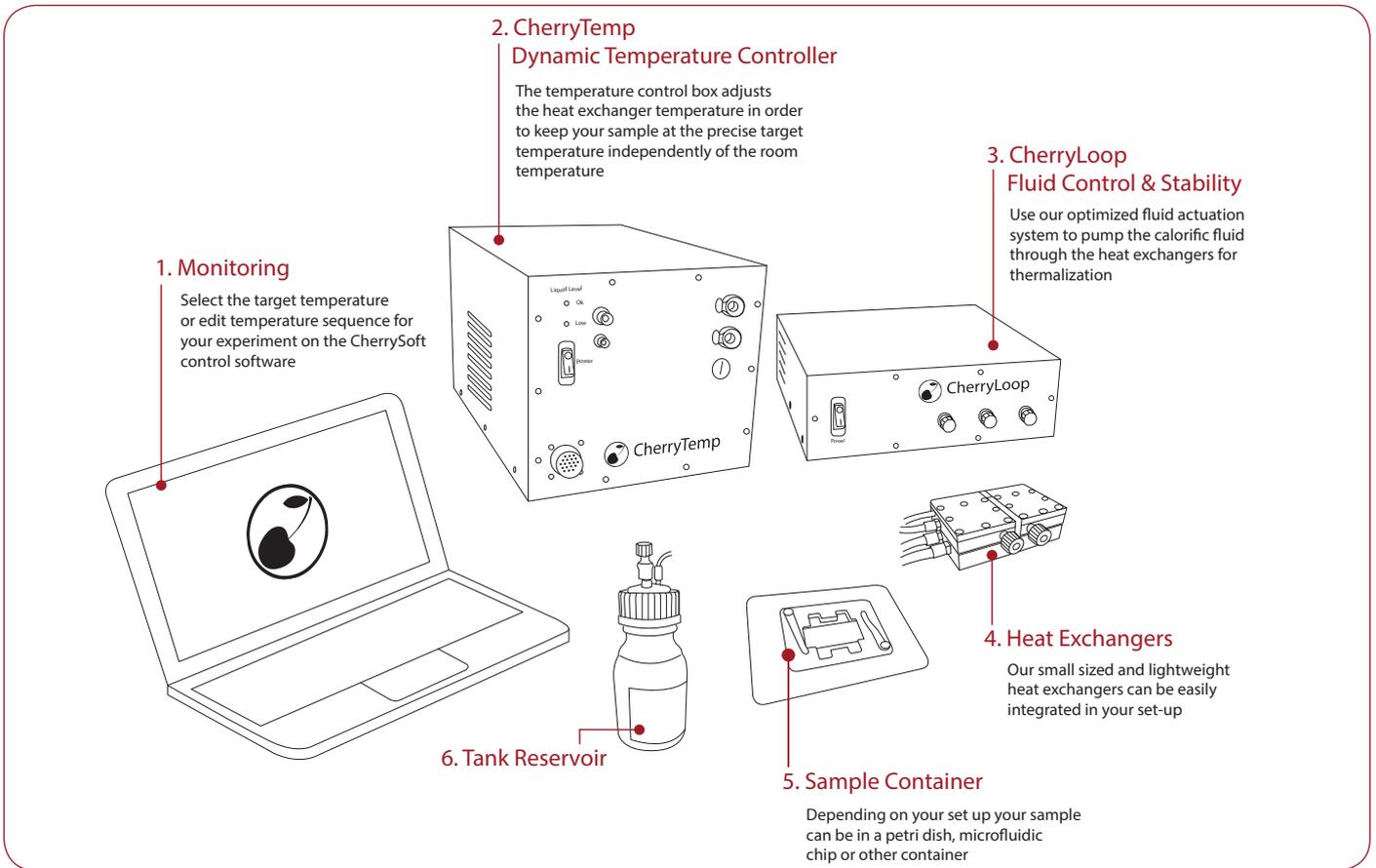


Figure 1: The core CherryTemp system is composed of the CherryTemp (2), the CherryLoop (3), heat exchangers (4), the tank reservoir (6) and is controlled by a dedicated software (1)

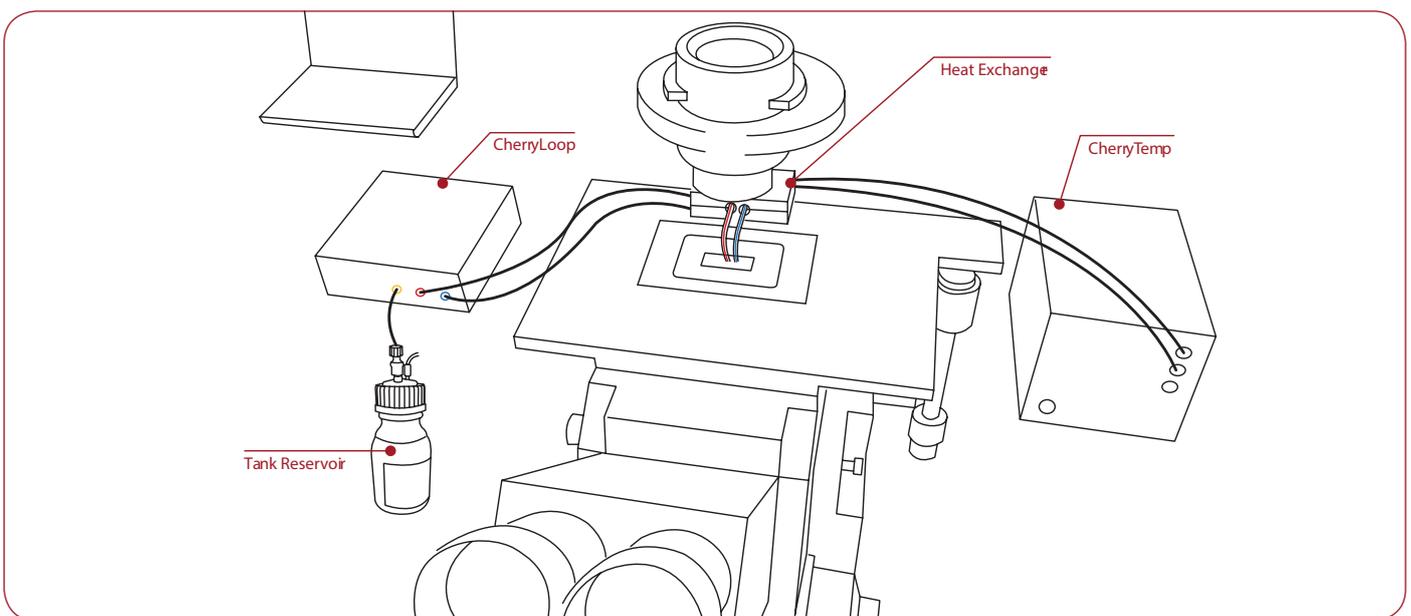


Figure 2: Schematic CherryTemp integration on a standard inverted microscope

Description of the CherryTemp platform

The CherryTemp system is composed of several elements. Together, these elements define the overall CherryTemp platform. Although each element has a distinct role and some may be functional out of the CherryTemp context, we disclaim any responsibility of usage out of the complete and exclusive platform context as described below in these user guidelines.

Each element is hereby described: the CherryTemp dual channel temperature controller, the CherryLoop fluid controller, the heat exchangers, the microfluidic chips, the tank reservoir and the thermalization liquid, the fluidic tubing, the micro-tubing, the ergonomic elements.

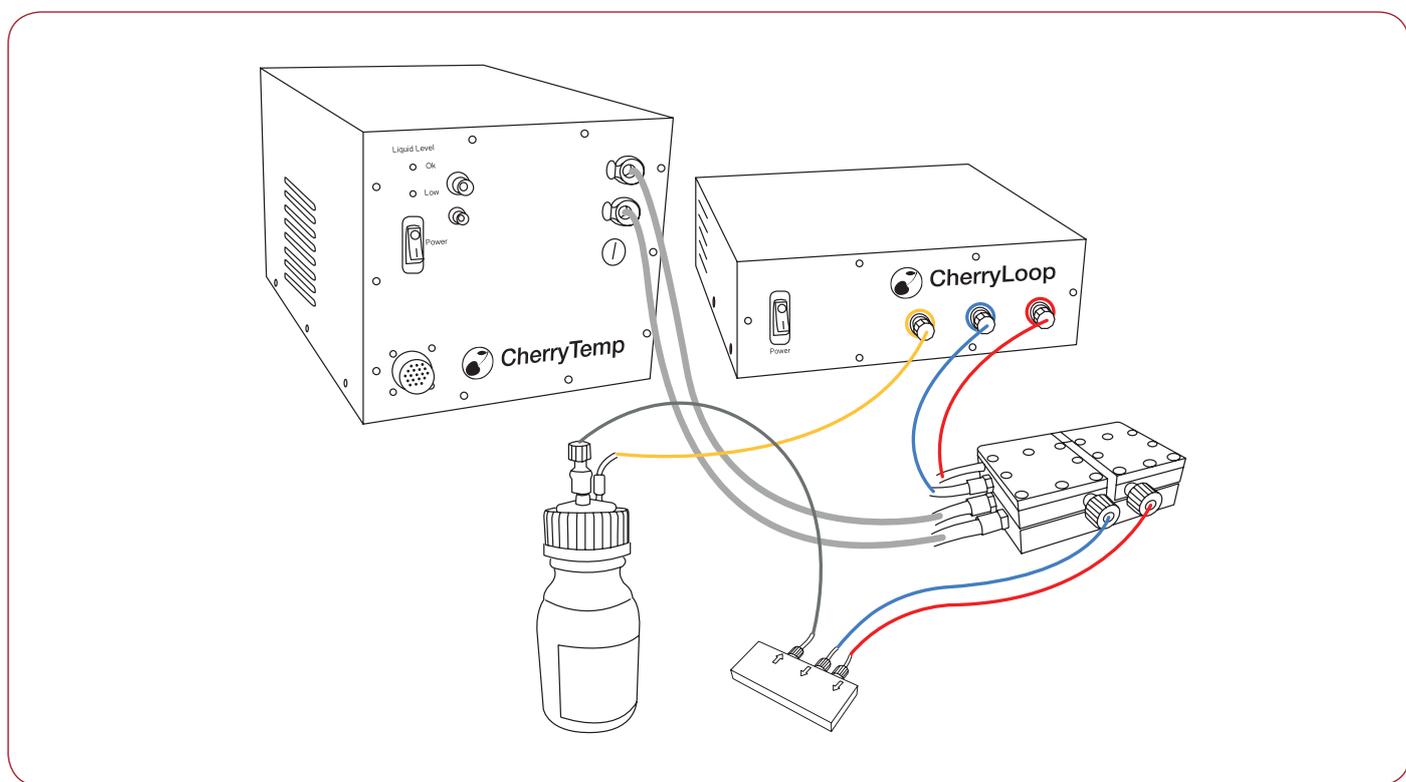


Figure 3: General connections between each element of the CherryTemp platform

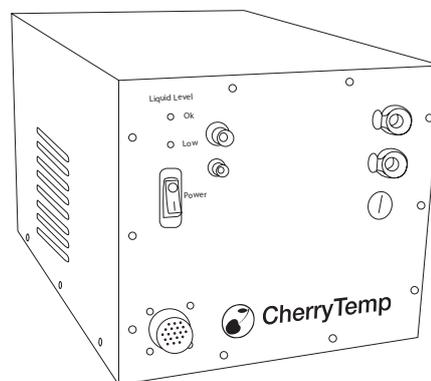
CherryTemp description

Although this element is manufactured according to UE directives 2006/42/EC (Machinery Directive), and 2006/95/EC (Low-Voltage Directive), we strongly advise to read the following description for a secured use of the system.



CAUTION - The CherryTemp must never be switched on if electrically connected to the heat exchangers without a properly connected chilling circuit.

The CherryTemp box allows dual channel temperature control of the Heat Exchangers. To this extent both elements (CherryTemp and Heat Exchangers) are connected to each other by an electric cable (see Fig. 4, Legend #2; Fig.11, Legend #7; Fig.12, Legend #7) and fluidic tubings (see Fig. 5, Legend #5 and #6; Fig.11, Legend #3 and #4; Fig.12, Legend #3 and #4).



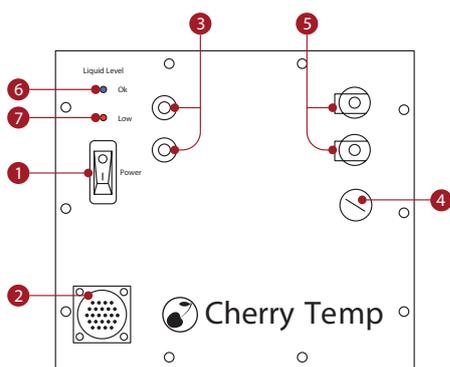
Dimensions (LxWxH; mm): 270x190x170

Weight: 4.5kg

Power supply:120V-60Hz / 230V-50Hz (US/EU)

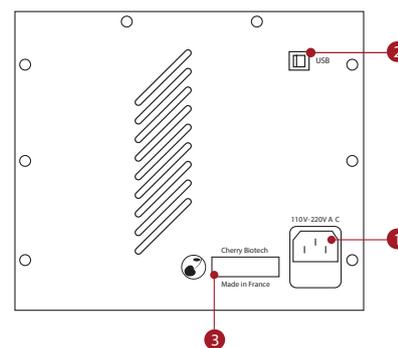
Input voltage: 12-24V nominal

Figure 4: CherryTemp dimensions and general features



1. on/off power switch button
2. exchangers' electronic connector
3. temperature sensor connector
4. chilling reservoir aperture
5. Heat Exchangers chilling connectors
6. blue light for chilling reservoir level «Ok»
7. red light for chilling reservoir «low» level

Figure 5: CherryTemp front face



1. power supply
2. USB connection
3. serial number

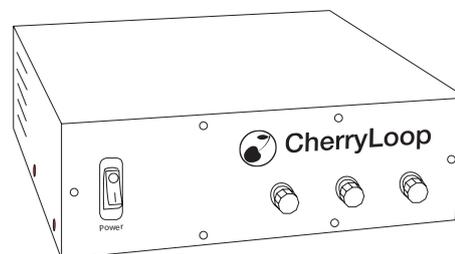
Figure 6: CherryTemp rear side

CherryLoop description



CAUTION - The CherryLoop must never be switched on if electrically supplied without a properly connected actuation circuit (tank reservoir inlet and exchangers inlets).

Although this element is manufactured according to UE directives 2006/42/EC (Machinery Directive), we strongly advice to read the following description for a secured use of the system. The CherryLoop is the fluidic actuation controller. It allows flowing of the thermalization liquid from the tank reservoir to the exchangers (top part) and the chip. It is a closed circuit which allows very long-term use of the system without refilling. To this extent, the CherryLoop is connected to the tank reservoir (Fig. 8, Legend #2; Fig 13, Legend #5) and to the exchangers Fig. 11, Legend #5 and #6; Fig. 12, Legend #5 and #6).



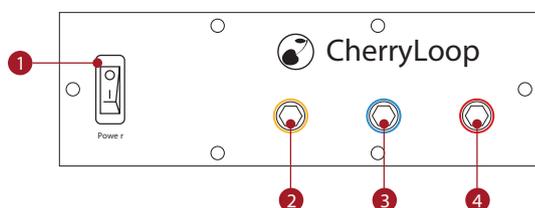
Dimensions (LxWxH; mm): 210x210x70

Weight: 1.4kg

Power supply: 120V-60Hz / 230V-50Hz (US/EU)

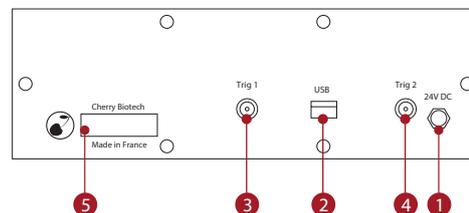
Input voltage: 12-24V nominal

Figure 7: CherryLoop dimensions and general features



1. on/off power switch button
2. In = Inlet for reservoir tubing
3. Out1 = inlet for exchangers' channel 1 (blue)
4. Out2 = inlet for exchangers' channel 2 (red)

Figure 8: CherryLoop front face



1. power supply
2. USB connection
3. TTL signal Trigger 1
4. TTL signal Trigger 2
5. serial number

Figure 9: CherryLoop rear side

Temperature exchangers description

The temperature exchangers are electronically controlled by the CherryTemp box and thermalization fluid is actuated by the CherryLoop. As a consequence, the thermalization liquid is actuated from the tank reservoir toward the heat exchangers and is thermalized to a target temperature (two independent settings, set by the user through the software interface) inside the exchangers. It is composed of two independent channels each separately connected to the CherryTemp (Fig. 5, Legend #2; Fig. 12, Legend #7) and to the CherryLoop (Fig. 8, Legend #3 and #4; Fig. 11, Legend #5 and #6; Fig. 12, Legend #5 and #6).

Heat exchangers important notes



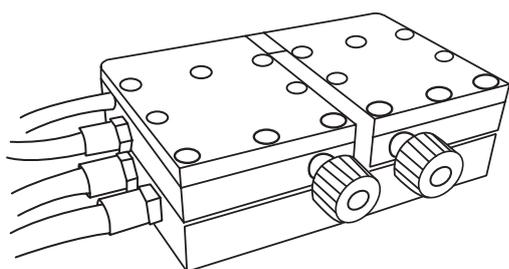
CAUTION: CHECK CONNEXION -

The CherryTemp platform must never be switched on (both the CherryTemp box and the CherryLoop box) if the heat exchangers are not properly connected (1) to the CherryTemp box through the electronic cables and the chilling circuit (two transparent tubings) and (2) to the CherryLoop box through the two blue and red connectors (Out1 and Out2).



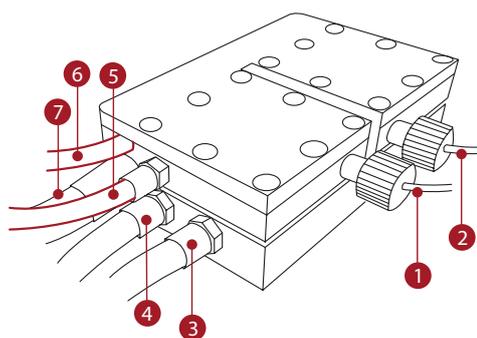
CAUTION: CONDENSATION -

When thermalizing one or both channel(s) below room temperature, condensation is likely to appear on the heat exchangers as well as on the microtubings. Give a special attention to protect your microscope set-up for both medium term (minutes) and long-term cooling experimentations.



Dimensions (LxWxH; mm): 54x86x22mm
Weight (kg): 400g

Figure 10: Exchangers dimensions and general features



1. exchangers outlet channel #1
2. exchangers outlet channel #2
3. cooling circuit connected to CherryTemp
4. cooling circuit connected to CherryTemp
5. thermalization channel #1 connected to CherryLoop
6. thermalization channel #2 connected to CherryLoop
7. electronic temperature control connected to CherryTemp

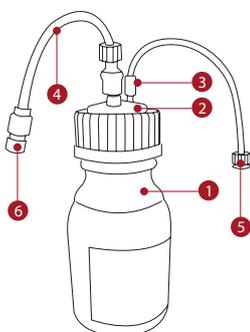
Figure 11: Exchangers global picture

Tank reservoir (thermalizing solution) description



CAUTION-The provided pieces and tubing must not be changed. Each tubing parameters (diameters, compliance, length) and parts are determined by Cherry Biotech's engineers and related specifications ensure proper functioning of the CherryTemp platform.

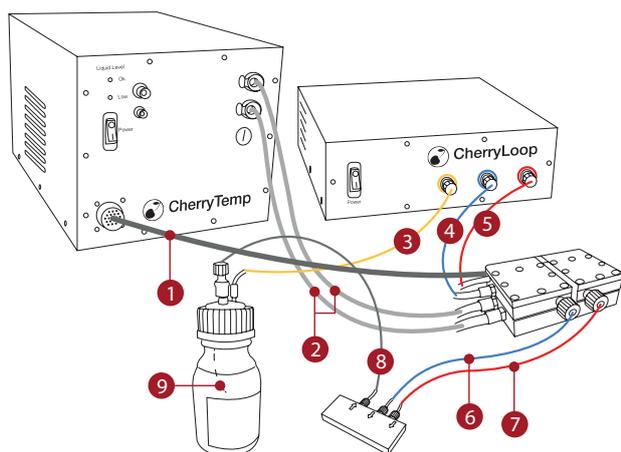
The tank reservoir is a standard laboratory bottle of 250ml. A specific cap is provided and ensures proper and secured actuation of the fluidic thermalization circuit.



1. tank reservoir
2. cap with holes
3. tank-Loop «In» tubing (connected to CherryLoop)
4. tank-chip tubing (connected to the chip)
5. Loop «In» connector (connected to CherryLoop, yellow)
6. Chip outlet return connector (connected to the chip, black) composed of a one-way valve, an adaptor and a connector.

Figure 12: Tank reservoir and tubing picture

Fluidic tubing description



1. exchangers electronic control, 2m
 2. exchangers cooling fluidic circuit(*)
 3. «in» fluidic tubing (yellow), 0.5m
 4. thermalization channel #1 (blue), 2m
 5. thermalization channel #2 (red), 2m
 6. chip inlet micro-tube channel #1
 7. chip inlet micro-tube channel #2
 8. chip outlet return (tank tubing, black)
 9. inner-tank tubing
- (*) no polarity for plugging
 length is given in meters

Figure 13: CherryTemp tubing description



CAUTION-Tubing must not be wedged/pinched. Cherry Biotech disclaims any liability for unsecured installation and consequent leakage which may damage surrounding technical elements (microscope, lasers, stages... -partial list -) or cause hazards such as injury, burning, electrocution. Strictly refer to the installation guide.

Microfluidic chips description



CAUTION - Thermalization must be achieved through Cherry Biotech's thermalization chips. We disclaim liability for inaccurate temperature control using other devices.

CherryTemp is a microfluidic device allowing rapid temperature shift in a spatially controlled environment. The heart of this system is based on microfluidics. Cherry Biotech provides its own microfluidic chips for efficient, accurate and dynamic temperature control. Several versions can be provided and the following diagram (Fig. 15) displays general features of these chips. All material used for the production of these chips are either compliant with the REACH products list (PMMA = Poly(methyl methacrylate) = methyl methacrylate polymer = EC #201-297-1; CAS #80-62-6) or approved by internal expertise (PDMS = Polydimethylsiloxane = security and expertise supported by the supplier (document available on demand); not suitable for medicine or pharmaceutical uses).

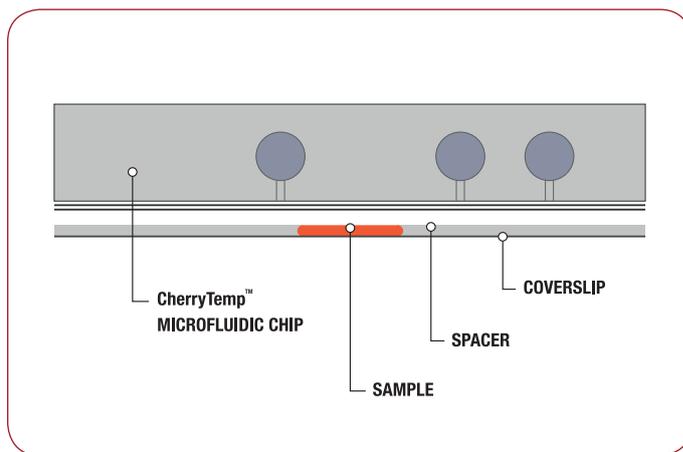


Figure 14: Front view of the chip mounting



CAUTION - A cover slip is binded to the bottom part of the thermalization chips. As a consequence, chips must be handled carefully



CAUTION - Thermalization must be achieved according to Cherry Biotech's mounting standards.. We disclaim liability for inaccurate temperature control using other devices

CherryTemp standards are measured with a liquid continuum from the chip thermalization area until the cover slip were biological samples are located.

Ergonomic elements description

Cherry Biotech provides ergonomic elements in order to fit any inverted microscope environment.



CAUTION - Ergonomic elements are important for proper utilization of the system. We disclaim liability for non-use of the ergonomic elements and possible damage consequences on surrounding equipments.

Heat exchanger holder

These elements are designed by Cherry Biotech's expert team and fit most inverted microscopes. They are designed to support the Heat Exchangers (described above) and integrate them in the confined microscope environment without interfering with the observation area (e.g. Piezo systems, motorized condensers...). The following figures 15 and 16 give an example of an exchangers' holder fitting a standard inverted microscope.

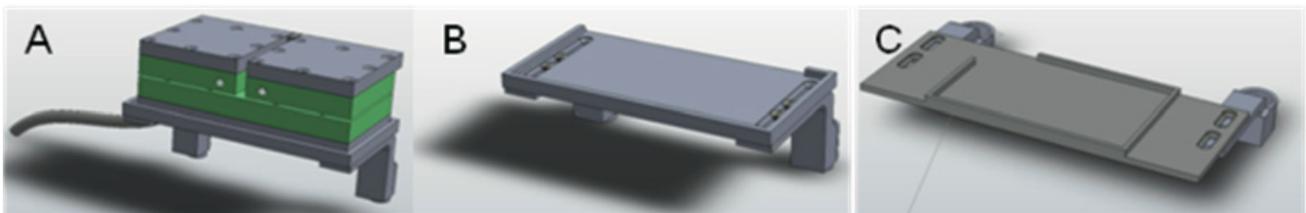


Figure 15: Example of heat exchanger's holders fitting widely commercialized inverted microscopes from Zeiss, Nikon, Olympus and Leica. A is a CAD drawing of an exchangers' holder with the heat exchangers elements on it, B and C are two different models.

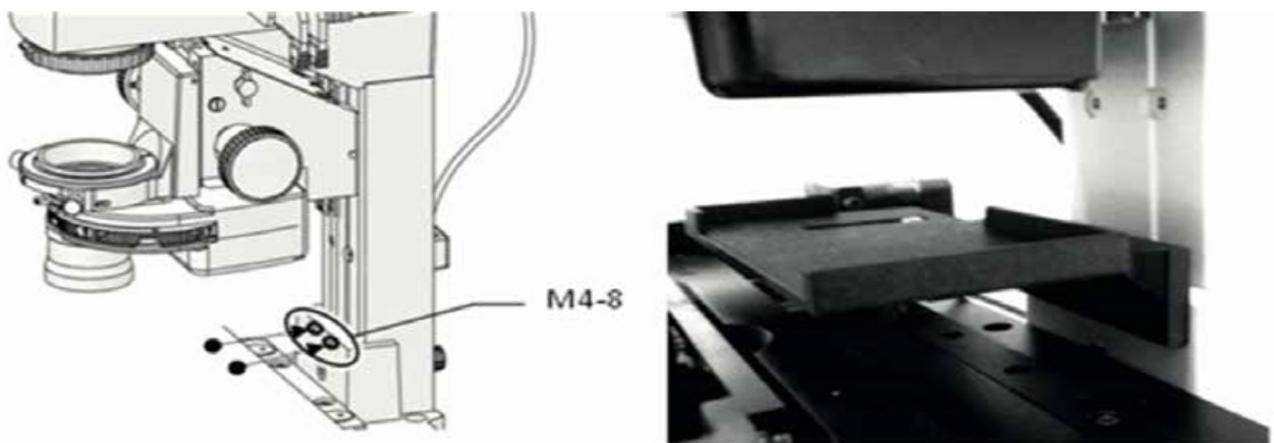


Figure 16: Cherry Biotech designed exchangers' holder fitting standard inverted microscopes. This drawing and picture shows a customized Nikon Ti Eclipse exchangers' holder.

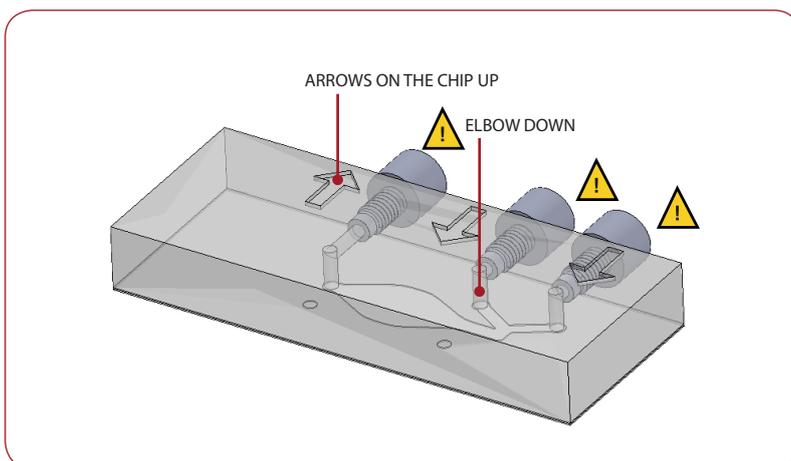
Sample mounting system

We design a sample mounting system, flexible with all range of microscopes. You simply place a standard cover slip into our Cherry insert, add a provided spacer and cover on top of our microfluidic chip



CAUTION - Please give a special attention to the objective lens and surrounding elements when installing the inserts. We disclaim liability for shocks that may cause breaking, scratches or other types of damage to these elements.

CherryTemp microfluidic chip



- ✓ Standard mounting of samples
- ✓ Absence of cell shear stress
- ✓ No direct contact between thermalization fluid and your sample
- ✓ Totally transparent materials
- ✓ Close and independant fluidic circuit
- ✓ 2 inlets for ultra-fast temperature shifts

Figure 17: On an inverted microscope, the chip has to be with the arrows up.



CAUTION - Check that your chip is in the proper side: your sample should be in contact with the chipface opposite of the side with the arrows



CAUTION - Don't tighten too much the connectors: when you tighten the connectors to the chip, make sure you tighten only until you touch the black o-ring (until the black o-ring expands).

Figure 18: 3D detailed view of the multiple layers of the CherryTemp microfluidic chip

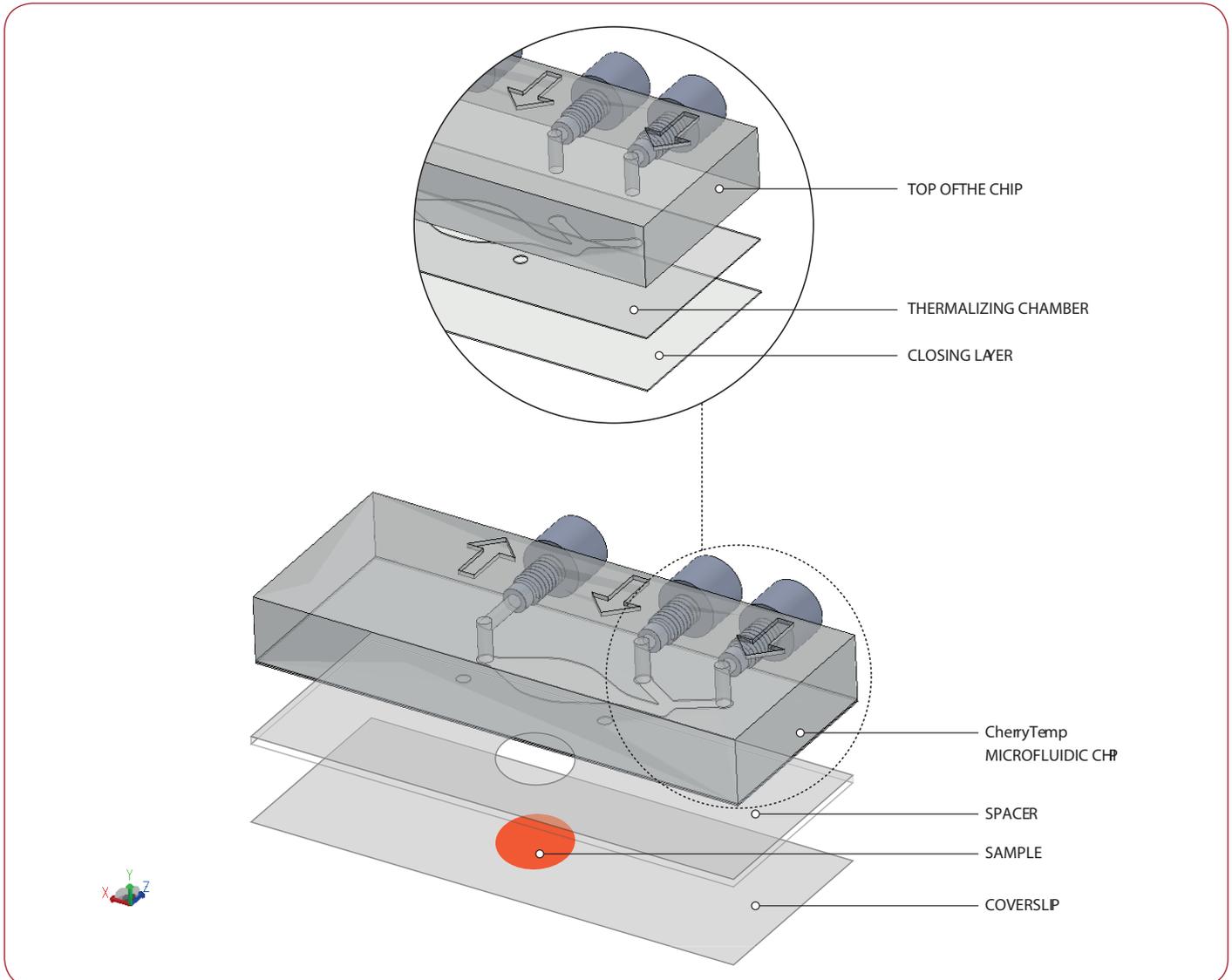
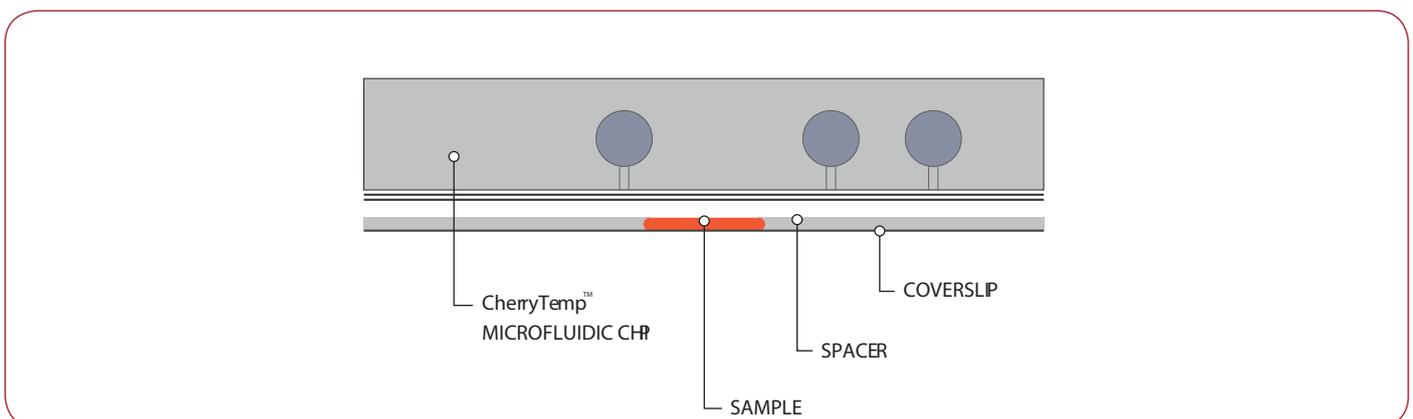


Figure 19: 3D sandwich view of the mounting

Figure 20: Front view of the mounting (inverted microscope)



CherryTemp initialization and software interface



CAUTION - (1) We highly recommend to follow the «check-up list» pointed out below before starting using the system. (2) Please, refer to the «Security, handling and assistance» section for safety purposes.

Start-up check list

Before starting to use the system (i.e. switching on both CherryTemp and CherryLoop and starting the CherrySoft), we highly recommend to strictly follow this check-up list (also present at the end of the «Installation guide»):

- ✓ CherryTemp & CherryLoop both power supplied and USB-connected to your computer
- ✓ «In» (yellow) tubing of tank plugged to CherryLoop
- ✓ Channel 1 (blue) & Channel 2 (red) connected from Heat Exchangers to CherryLoop
- ✓ Cooling circuit connected from Heat Exchangers to CherryTemp (no polarity).
- ✓ Ambient temperature sensor connected to CherryTemp and attached to your microscope body (dry conditions) OR microscope objective lens (immersion conditions).
- ✓ Thermalization bottle filled up with a minimum of 75ml of thermalization liquid.
- ✓ Chip inlets (no polarity) and outlet securely connected.

Reminder: CherryTemp is a microfluidic system carrying fluids through tubing. It is important for leakage prevention and potential consequent injury/electrocution/material damage (CherryTemp and surrounding material), to perform a systematic control of the platform before starting.

Software interface: Cherry Soft

CherryTemp's software is an intuitive interface which allows a simple and straightforward temperature control with a real-time feedback of the temperature experienced by the sample.

Figure 21 shows the starting sequence. The next paragraphs describe the different steps as well as the main control window.

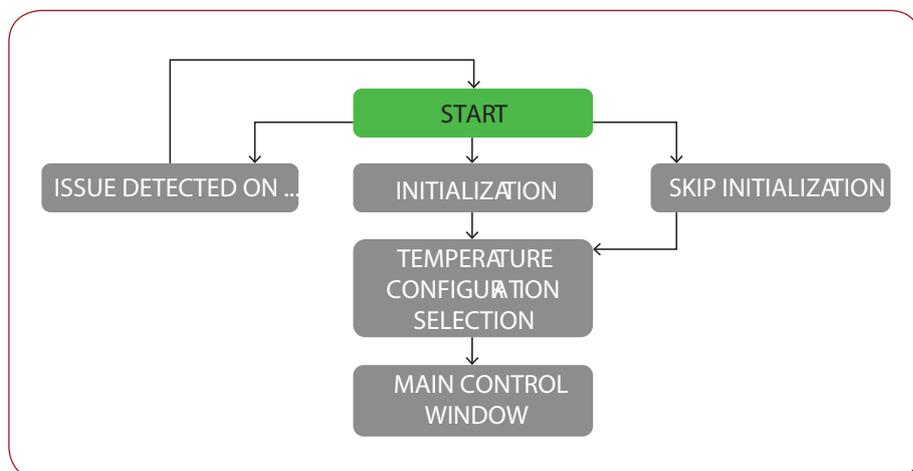


Figure 21: Software first steps

Initialization sequence



CAUTION - Initialization process corresponds to a complete filling of the fluidic system with the thermalization liquid. Please check that all tubing are securely connected and not wedged/pinched.

When launching the software, a first pop-up invites you to perform an initialization step. This step aims at filling the entire fluidic actuation system. Consequently, make sure that you properly followed the «check-up list» of the previous paragraph.

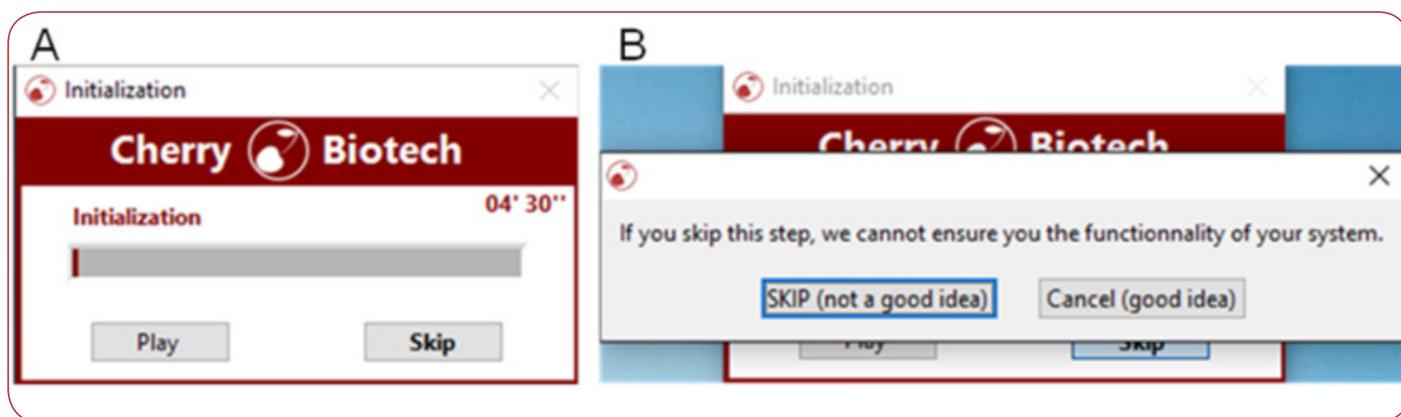


Figure 22: Initialization step. (A) Initialization sequence window; (B) Pop-up window when the sequence is skipped.

The initialization step is a short automatic sequence over which both channels of the platform are being filled with the thermalization liquid contained by the tank reservoir in a closed-loop circuit. It is crucial to remove air from the circuit in order to ensure proper thermalization of the samples thereafter.

A «Skip» button is available at this step (Figure 22, B). Only experienced users should decide to skip this starting sequence as air bubbles might alter thermalization efficiency. We recommend to perform this step to ensure proper filling of the fluidic system.

Temperature configuration selection

Once the initialization step has finished, a selection window invites you to select the type of temperature calibration you will apply to the system. Select the ad-hoc calibration in the scrolling menu.

You can always access to the calibration selection through Menu > Edit > Select Temperature Conversion Mode.



CAUTION - «Temperature configuration» is crucial as CherryTemp temperature accuracy relies on it.

Main control window

This main control window allows easy temperature shifts from one temperature setting to any other in the range limits of CherryTemp. You access to this mode after the initialization sequence.

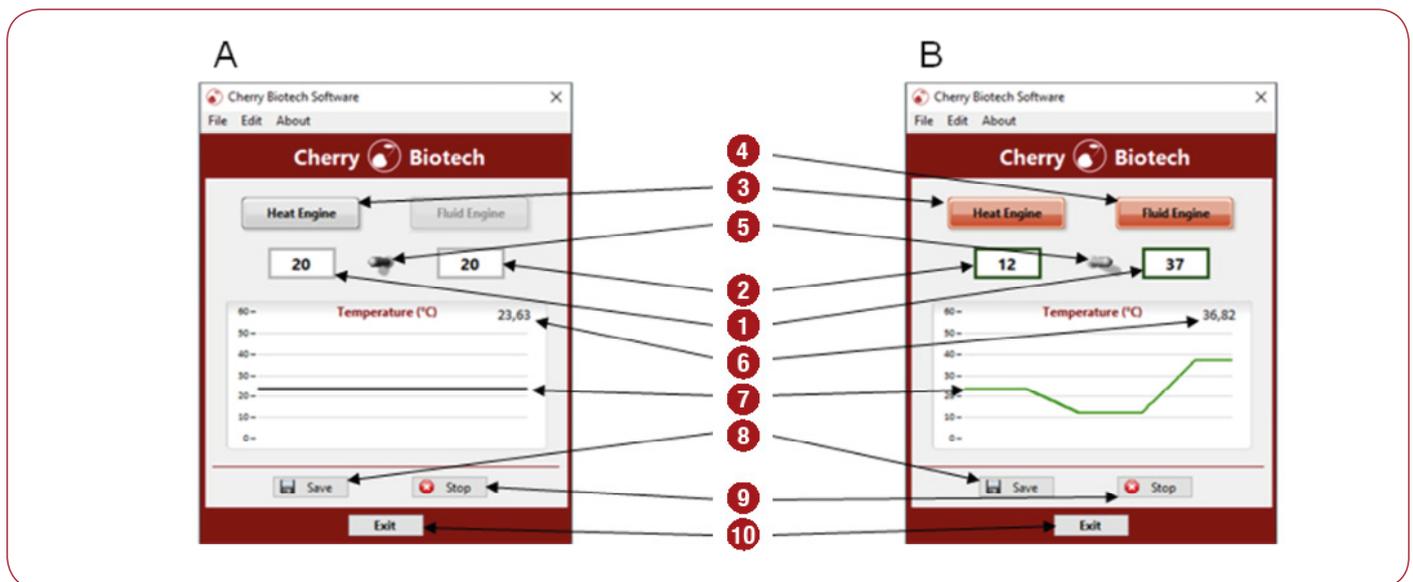


Figure 23: Software main control window. (A) Inactive thermalization; (B) Activated thermalization.

1. temperature setting channel 1 (box turns green when temperature is stabilized)
2. temperature setting channel 2 (box turns green when temperature is stabilized)
3. activation of Heat Exchangers' thermalization
4. activation of flow = sample thermalization (inactive if Heat Exchangers' thermalisation is switched off)
5. temperature shift button from one channel to the other
6. sample's real time temperature (numerical)
7. sample's real time temperature (graph, turns green when temperature is stabilized)
8. save button (exports data in CSV file)
9. stop button (turns off the entire system)
10. exit button

If an error occurs during the platform utilization, a pop-up opens and invites the user to check some points. If further assistance is needed, our FAQ is available at www.cherrybiotech.com/FAQ. In any case, do not hesitate to contact our support team [support@cherrybiotech.com] will answer you within 24h (working days).

Automatic metrology

Cherry Biotech systems are submitted to several tests (mechanical, physical, electrical and IT tests). CherryTemp platforms follow a metrology process during their all lifespan. It consists of auto-calibration points, an approximate 20 minutes long sequence.

Automatic metrology sequences are performed as so:

- Production test (Start point)
- First installation on a microscope
- Once per month

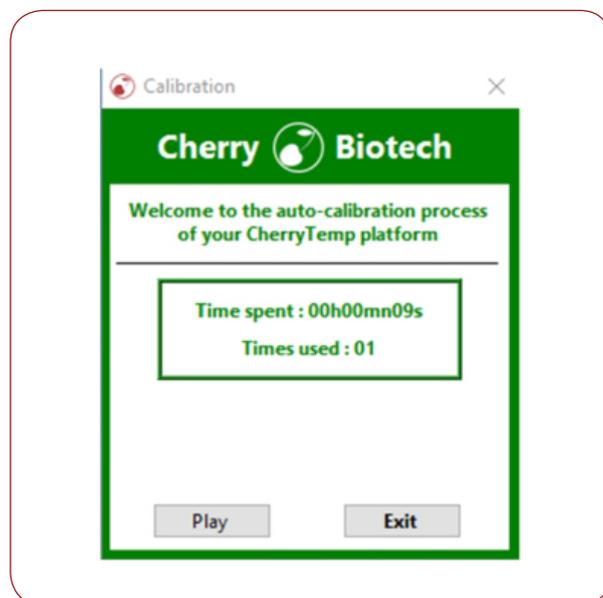


Figure 24: Auto-calibration window

End of experiment - long-term storage

Cleaning sequence



CAUTION - The cleaning process prevents the fluidic systems from microbial development. Perform this quick step for long-term storage (more than 5 days) and every six months.

CherryTemp systems thermalize your samples through fluidic actuation. The tubing circuit has to be carefully cleaned after each experimentation.

Follow this steps at the end of each experimentation:

Cleaning procedure

1. Close the software
2. Replace the thermalization tank bottle with cleaning solution
3. Close the bottle with cap (storage, up to 2 months)
4. Start again the software
5. Run the initialization step
6. Switch all the system off.

Your CherryTemp is clean and secured!

Refilling the CherryTemp box

The CherryTemp box has an integrated chilling reservoir, used for the chiller circuit. This circuit is closed and allows long-term use without regular refilling.

However, if CherryTemp requires additional fluid, the red light “Liquid level Low” warns when the chiller reservoir should be filled. This security is sensitive and turns the light on early to ensure that the tank remains always filled.

If the light turns red, please follow these steps to ensure the filling of the CherryTemp reservoir:

1. Switch off CherryTemp box
2. Unplug the supply cable of the CherryTemp box
3. Unplug all the connectors (fluidic and electric) of the CherryTemp box
4. Put your CherryTemp box vertically
5. Put on gloves and safety glasses
6. Unscrew the metallic cap on the front panel of your CherryTemp using a coin.
7. Place a funnel in the tank hole
8. Fill the tank with 60 mL of the «cleaning solution» from the refill bottle.
9. Replace the cap
10. Wipe the eventual drops that have fallen on the machine or on the workbench, using cleaning paper
11. Replace your machine normally and replug it.

Security, handling and assistance

Important notifications regarding handling

Cleaning of the fluidic actuation :

We advice renewing the thermalization liquid every 2 months. If you do not use the system during a period of time exceeding 5 days, strictly follow the cleaning steps.

When re-using the system after this period, follow the «cleaning procedure» plus the normal «initialization procedure».



CAUTION - The following security advices aim at preventing from injury, burning, electrocution, fire risks, water leakage risks and chemical risks. Carefully consider these information before using the system.

Cleaning procedure:

1. Close the software.
2. Replace the tank bottle containing the thermalization solution by the one containing the cleaning solution.
3. Start again the software
4. Run the initialization step.
5. Switch all the system off.



CAUTION - Do not actuate other liquids inside the system as it might damage the fluidic circuit and/or the pumps/valves or other elements of the system.

Your CherryTemp is secured!

Use of electric and fluidic connectors and buttons/switches

Never force or apply an inappropriate force when pushing/pulling on buttons/switches or wires. If connectors and plugs cannot be easily connected, they might probably not be compatible; please refer to the installation guide.

Warranty & support

Cherry Biotech warranty for the intended and proper use of the equipment includes:

- 24h maximum delay for email answering
- remote assistance
- solution (see above paragraphs).

Cherry Biotech hardware products are warranted against defects in material and work-manship for a period from 1 year to 2 years depending on the country starting from date of delivery.

Cherry Biotech accessories are warranted 60 days from date of delivery

Cherry Biotech software and firmware products, that are designated by Cherry Biotech for use with a hardware product and when properly installed on that product, warranted not to fail to execute their programming instructions due to defects in material and workmanship for a period of 90 days from date of delivery.

During the warranty period, Cherry Biotech will either repair or replace products that prove to be defective. Cherry Biotech does not warrant that the operation for the software, firmware or hardware shall be uninterrupted or error free. For warranty service, this product must be returned to a service facility designated by Cherry Biotech. Customer shall prepay shipping charges (and shall pay all duty and taxes) for products returned to Cherry Biotech for warranty service. Except for products returned to a Customer from another country, Cherry Biotech shall pay for return of products to the Customer. If Cherry Biotech is unable, within a reasonable time to repair or replace any product to condition as warranted, the Customer shall be entitled to a refund of the purchase price upon return of the product to Cherry Biotech. This warranty does not apply to any equipment which has not been installed and used within the specifications recommended by Cherry Biotech for the intended and proper use of the equipment

Process:

Please contact our support team at «support@cherrybiotech.com».

Cherry Biotech systems are submitted to several tests (mechanical, physical, electrical and IT tests). CherryTemp platforms follow a metrology process during their all lifespan. It consists of auto-calibration points, an approximate 10 minutes long sequence.

Support service at Cherry Biotech is defined as so:

1. Support service contacted by the user (support@cherrybiotech.com)
2. Support team comes back to the user to diagnose the system
3. A solution is given to the user depending on the issue's features (hardware vs software):
 - remote problem solving
 - return of the system (parts or entire system) following a dedicated procedure

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Cherry  Biotech

Dynamic Temperature Control