USER GUIDE

nirrin

Atlas™

User Guide Rev. 2.1
Software Version 2.0
November 2024

illuminating insights

Company Statements

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Preface

Nirrin Technologies provides next generation sensors and analytics that enable real-time process monitoring for process development applications in the biopharma and life science industries. Nirrin is focused on enabling tools and analytics for complex biologics and advanced therapies where there is a need to develop, optimize, control, or operate a bioproduction process. Nirrin specializes in proprietary high precision tunable laser spectroscopy (HPTLS™) which is at the core of Atlas enabled by built-in patented wavelength and amplitude technology to deliver long-term stability and transferability of analysis methods. The platform also features integrated patented optical designs and intelligent analytics to offer an out-of-the-box solution.

Atlas operates in the near infrared (NIR) region and offers quantitation of critical components in formulations across a range of applications in downstream bioprocessing. Atlas provides protein titer and excipient concentrations for a single sample over a wide dynamic range with high accuracy and precision without the need for dilution in minutes. Atlas allows for simple, fast, and accurate results to improve confidence in formulation components throughout key process steps enabling reduced time and cost for drug development.

This manual is intended to serve as an introduction to our technology, a training aid, and a source of reference information. It is advised that the user keep a copy of this manual in a convenient location to refer to as needed. If at any time, questions arise, please contact the Nirrin team at help@nirrin.tech or at (781)285-5450.

Contents

Section 1 - Getting Started with Atlas

1.1 About Atlas

The Nirrin Atlas is a groundbreaking at-line analyzer that measures excipients and monoclonal antibodies in real-time throughout downstream process development. It requires no dilution, sample preparation, or assay development. A single 14-microliter sample provides quick results for wide-ranging drug substance concentrations and relevant excipients. In under a minute, this simple workflow delivers accurate results for the dynamic conditions of bioprocessing.

1.2 Safety Information

Before operating an Atlas instrument, please read the safety information and follow its recommendations for the system.

	Please follow the following guidelines below and read the manual fully to completely understand the safe operation of this system.

Operating Atlas without any side panels exposes the user to safety hazard with the sharp edges of the panels and the exposed electrical components. We require our users not to disassemble the unit in any way without the knowledge and assistance of a Nirrin expert.

Atlas is specifically designed for indoor use under the following conditions:

- Operational Temperature Range: 20-25°C
- Operational Humidity Limit: 65% relative non-condensing
-

Atlas is equipped with a 115V power supply. Use only the power supply provided with the instrument by Nirrin to avoid any electrical issues. This cord must be plugged into a properly grounded outlet.

	To Avoid Electrical Shock

- Do not remove the enclosed sides or panels of the device.
- Completely disconnect the device from its main power supply before performing any maintenance work.
- Turn off device while not in use.
- The inside of the device is a high voltage area and is very dangerous.
- Repairs to the system may only be performed by our trained and certified Nirrin approved technicians.
- The device must be connected to a power outlet that has a protective ground connection.
- If the device is used in a manner that is not specified by Nirrin, the protection provided by the instrument may be hindered.
- During scheduled maintenance, conduct an inspection of all electrical components to identify any potential electrical issues.
- Avoid storing liquids near the device to prevent any spills that could cause an electrical shock.
- Ensure that your hands are dry as you are handling the electrical components.
- Inspect power cable and other exposed wiring to ensure that the wires do not have any faults that can cause electrical shock.

	To Avoid Damage to the Instrument

- Do not allow any liquid to enter the device.
- Do not operate the system in a hazardous environment.
- Use compatible accessories recommended by Nirrin to avoid any compatibility issues that could cause damage.
- To avoid risk of injury, use proper lifting techniques when lifting or moving the instrument.
- If there are any abnormalities or any malfunctions, the user is instructed to stop using the device immediately and contact Nirrin customer support at help@nirrin.tech.

⚠	Hazardous Materials

- Prevent personal injury. Keep combustible materials and solvents away from the instrument. Ensure that there is adequate ventilation in the workspace.
- This device is prohibited from being used with BSL3 or higher pathogens.

⚠	Laser

- Class 1 Laser Radiation
- This device complies with Part 15 of the FCC Rules. Operation is subject to the following conditions: (1) this device may not cause harmful interference, and (2) this device must accept any interference received, including interferences that may cause undesired operation.

Figure 1. Atlas Certification Label

1.3 Compliance Labelling

Note: the Atlas product label resides on the back panel of the system as shown in the example below. The label includes model and serial number, power requirements, compliance markings, and the customer support line at (781)531-9371.

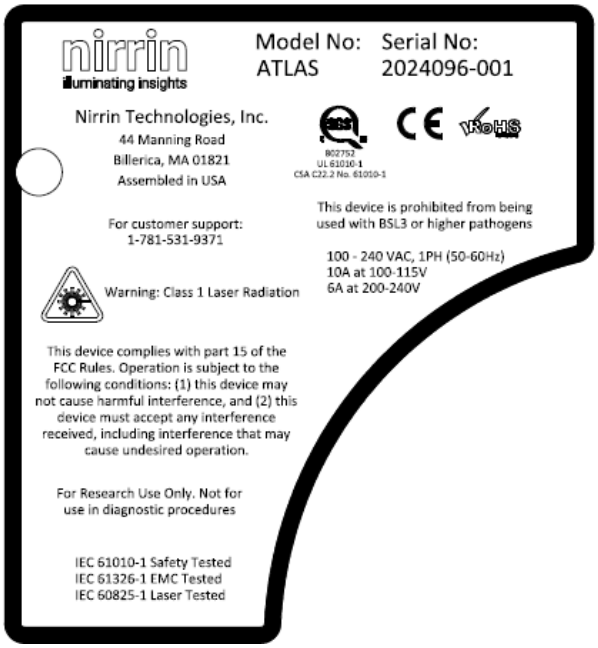

Figure 2. Atlas Unit Compliance Label located on the backside of the system (example).

This model of Atlas is for Research Use Only, not for use in diagnostic procedures and prohibited from use with pathogens in BSL3 or higher.

1.4 Operational Requirements

In addition to the safety information as detailed in Section 1.2, to ensure proper operational excellence, all operational requirements as detailed here must be followed.

Along with all information presented in Section 3.2, the following Operational Requirements must be followed to ensure operational excellence of Atlas.

1.4.1 General Requirements

1. Do not put the unit into, on, or near any large amount of liquid, as to not cause any electrical or corrosion issues.
2. Do not store any chemicals on top of the unit.

3. Volatile chemicals in the same environment can contaminate the sample if not properly stored away from the unit.
4. Ensure the power supply is stable and there are no fluctuations in supply from the outlet that could damage the instrument.
5. Keep the unit away from any high vibration areas that can affect laser alignment.
6. Do not unplug the unit without switching the power button off.
7. Place the unit in an area away from exhaust fans, HVAC vents, or other instruments with large amounts of air output.
8. Place the unit away from direct sunlight or radiative heat sources.
9. Do not open the device cover while scanning a sample. Although the device is equipped with a laser interlock for safety, opening during scanning will cause the laser to stop and may cause erroneous results.
10. Do not scan samples without allowing them to equilibrate to room temperature to ensure no erroneous data.
11. Do not use any accessories not supplied or recommended by Nirrin.
12. Do not use Atlas if it is not working properly, or if it has suffered any damage, for example:
    a. Damage to the power cord or plug
    b. Damage caused by dropping the instrument
    c. Damage caused by liquid splashing on the instrument

1.4.2 Environmental Requirements

Parameter	Requirement
Allowed Location	Indoor use only, out of direct sunlight
Ambient Temperature, operation	20°C - 25°C
Ambient Temperature, storage	-35°C - 75°C
Relative Humidity Limit, operation	65%
Relative Humidity, storage	65%

1.4.3 Instrument Placement Requirements

Atlas must be placed on a clean, flat, and stable lab bench that is able to support the weight of Atlas. Atlas must be placed away from direct sunlight.

Atlas is configured to accept only a US standard 120-volt electrical supply – do not use any other power inputs as to avoid harm to the system.

Atlas cools the internal computer with a fan, which can be seen at the back of the unit. This draws in air from under the instrument and out the back. Do not block the underside air intake vent or the rear output vent! In addition, ensure that spills of volatile liquid that

reach underneath the system are cleaned promptly, to avoid corrosion of the internal components from chemical contact.

Atlas is a temperature-controlled device. Do not operate the instrument below required temperature range, such as in a cold room/workspace or on a lab bench in direct sunlight. In addition, do not operate Atlas above the required temperature range (20-25°C ambient), as the temperature control setpoint is 27°C.

If moving Atlas from a storage location outside the operational range, allow the unit to sit for 1 hour at operational temperature range before powering the system on.

1.4.4 Operator Requirements

Users must wear protective PPE such as nitrile gloves and safety glasses to reduce any contamination in samples and to protect users from common hazardous in laboratory environment.

Section 2 - Atlas Overview

2.1 Anatomy

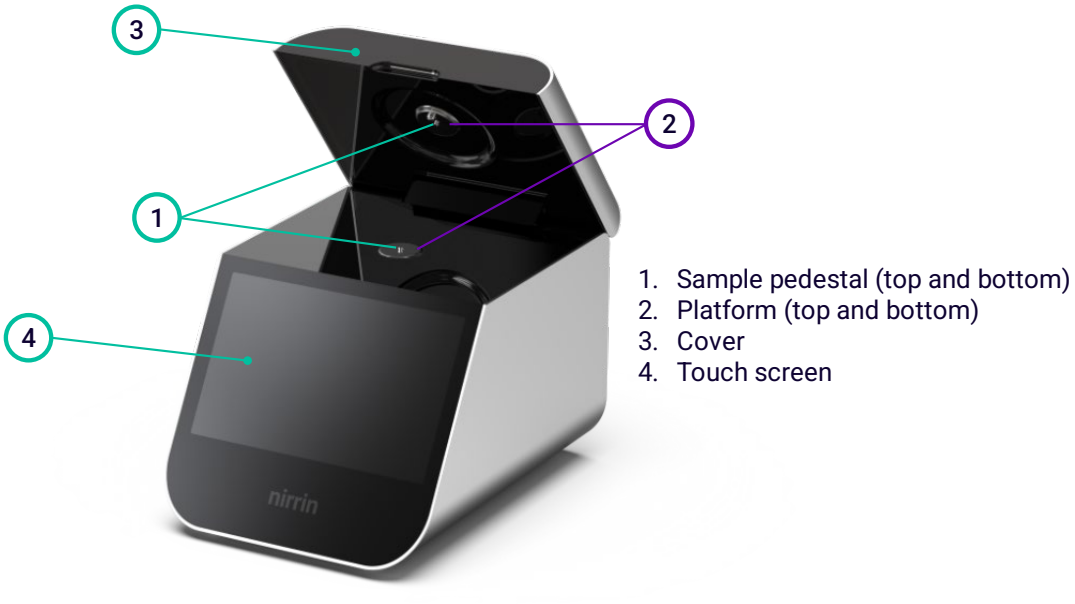

Figure 3. Atlas features a 10.1" interactive touchscreen, a soft close cover, and sapphire pedestals with platform heaters on the cover (top) and base (bottom) panels.

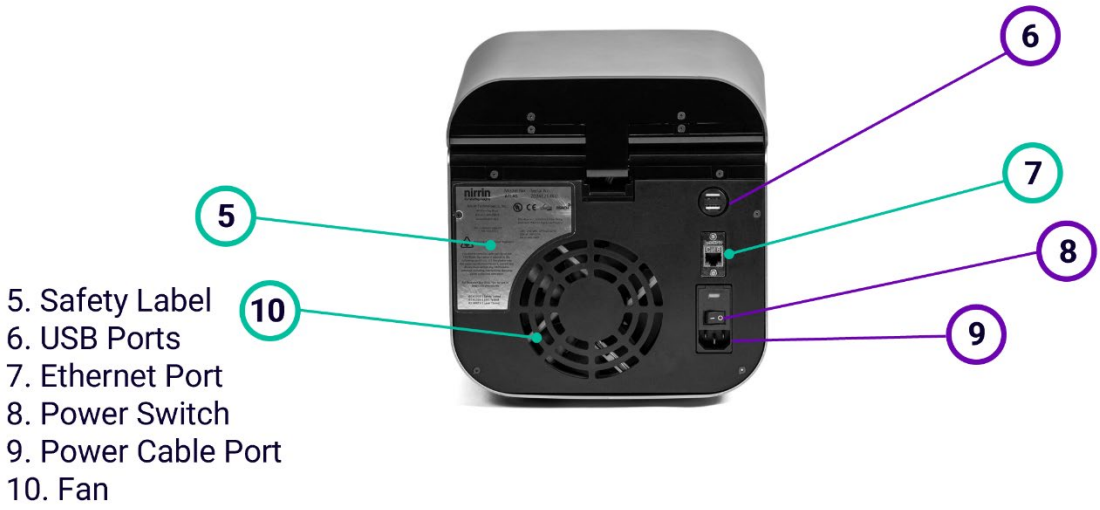

Figure 4. Atlas features 1x Ethernet port, 2x USB ports for data transfer, 1x power switch, 240V power input (cord included).

2.2 Physical Dimensions

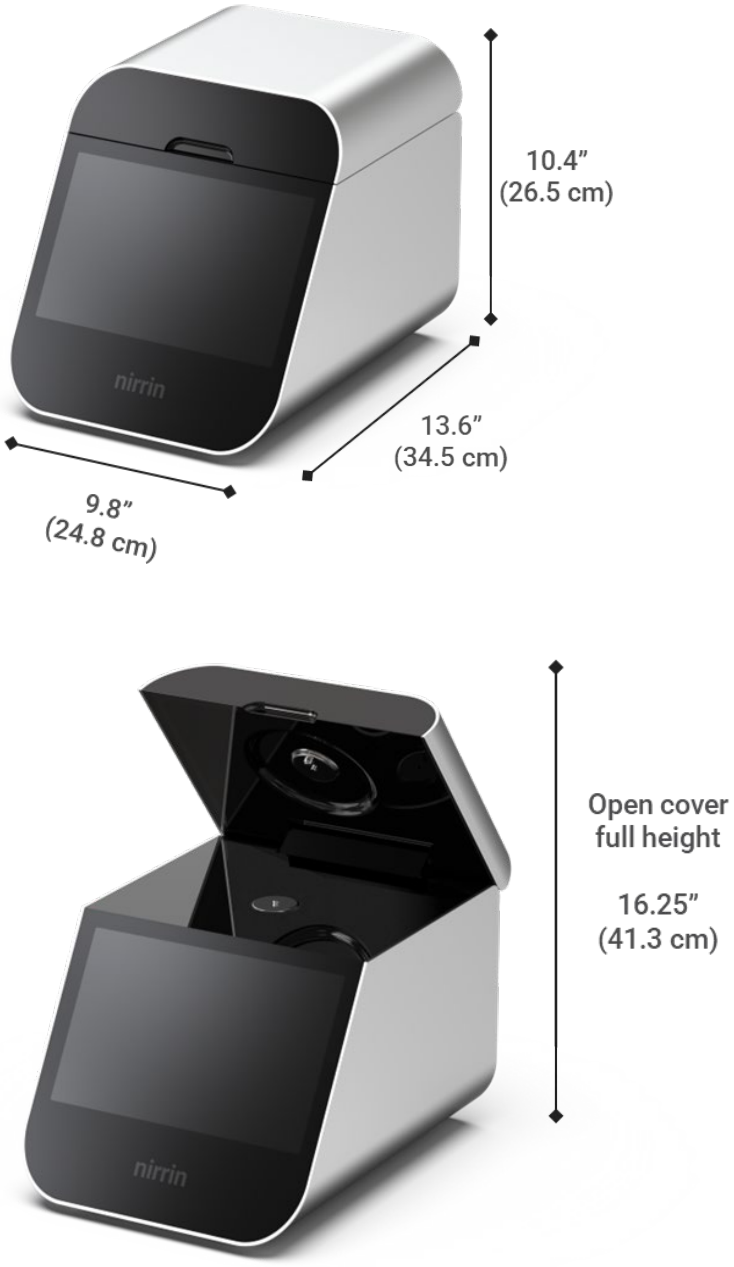

Figure 5. Atlas exterior dimensions are 13.6"L x 9.8"W x 10.4"H (34.5 cm L x 24.8 cm W x 26.5 cm H) with a full open cover height of 16.25" (41.3 cm).

2.3 Instrument Specifications

Technology	High precision tunable laser spectroscopy (HPTLS)
Instrument Control	Embedded 10.1" touchscreen (1280x800)
Dimensions (l x w x h)	13.6"L × 9.8"W × 10.4"H (34.5 cm L × 24.8 cm W × 26.5 cm H)
Weight	23 lbs (10.4 kg)
Power Requirements	100–240VAC, 50-60 Hz (Current 10A @ 100-115VAC and 6A @ 200-240VAC)
Mains Supply Fluctuations	+/-10%
Overvoltage	Category II
System Warmup	60 minutes from cold start for full operation
Regulatory Compliance	Meets IEC/UL/CSA-61010-1, CE, RoHS Standards
Near Infrared Laser Classification	Class 1 (eye-safe), 200 nm tunable range, 0.1 nm repeatability
Measurement Mode	At-line with manual pipetting and cleaning protocol
Sample Volume	14 µL
Measurement Time	<3 min time-to-result
Analyte Coverage	• Pre-loaded library includes ~30 excipients featuring validated analytes (buffer components, tonicity agents, antioxidants, stabilizers & surfactants) • Custom analytes and mAb added by user (non-validated)
Accuracy	+/- 5% of known concentration, analyte and mixture-dependent (*validated excipients in single component solutions)
Precision	+/- 1% error measurement-to-measurement
Operational Temperature Range	20°C - 25°C ambient
Operational Humidity Limit	65% relative non-condensing
Altitude	<2000m

Note: Specifications may be subject to change at any time. For integration in 21 CFR Part 11 or GMP process, please contact Nirrin for more info.

Section 3 - Basic Installation

3.1 Packaging Contents

All Atlas instruments come with the following components in the quantities indicated.

Component	Quantity Provided
Atlas Unit	1PC
Atlas Power Cable	1PC
User Manual	1PC or digital

Additional required parts (not supplied) are as follows.

Component	Quantity Needed
Ethernet Cable	1PC

In addition, consumables are required for cleaning the sample pedestals and sample introduction to Atlas. These are typical lab supplies which are not included with the instrument. This includes lint-free wipes, deionized water wipes, foam-tip swabs, and any calibrant solutions. Consumables will need to be purchased separately.

Nirrin recommends the following consumables (or equivalent) for use with Atlas.

Laboratory Supplies	Example Supplier (Catalog Number) or equivalent
Premoistened Clean Wipes, 100% DI Water, Lint-free	Fisherbrand (Cat No 06-665-23) or Cole-Palmer (Cat No 33675-05) or equivalent
P20 Single Channel, Calibrated 2-20 µL	Eppendorf Research Plus P20 (Cat No 3123000039) or equivalent
P20 Pipette Tips	Eppendorf epT.I.P.S. Racks (Cat No 0030075226) or equivalent
Kimtech Kimwipes	Fisher Scientific (Cat No S47299) or equivalent

3.2 Unpacking

Open the packaged unit, and carefully note that all packaging contents are present in the package. If any items are missing or damaged, contact the Nirrin service provider to ensure all items are received properly. Refer to the step-wise guide “Unboxing Atlas” for more information.

3.3 Installation

1. Atlas must be placed on a clean, flat, and stable lab bench that is able to support the weight of Atlas.
2. Prior to plugging in the power cable on Atlas, ensure that the power switch is toggled to the OFF position.
3. Connect the power cable to the back port of Atlas and then plug into the outlet. The outlet should be standard US 120 volts.
4. Power on Atlas by toggling the power switch ON from the back of the unit.
5. Once Atlas is powered on, the UI should illuminate and the fan on the back of the unit will turn on.
6. Atlas can be setup in an online mode or offline mode for user preferences:
    a. For online mode, an ethernet cable is plugged into the ethernet port in the back of the unit and the other end into a wall ethernet port.
    b. For offline use, data can be exported manually via USB drive on the back of the unit.
7. Now that Atlas is powered on and ready for connection, installation is complete.

3.4 Setup and System Preparation

1. Once your Atlas system is properly installed on your lab bench, the system is turned on by flipping the power switch to the ON position. The power switch is located on the back of the unit by the power cable.
    - If the instrument is coming from a storage location that is far outside of the operational temperature range, allow the unit to sit at room temperature for 1 hour prior to switching it on for the first time.
2. After switching on the unit, the user must wait for the system to warm up.
    - The unit needs 60 minutes to equilibrate to 27°C.
3. Once equilibrated, the unit is ready for sample testing and analysis.

Section 4 - Understanding your Atlas

4.1 System Concept

The Atlas system is a laser-based spectroscopy device, designed for bioprocessing applications. This instrument is comprised of many optical, electrical, and machined parts to create a simple user workflow. Understanding your Atlas is the first step to success and ease of use.

4.2 Laser and Optics Platform

The Atlas utilizes a patented laser platform, that is designed for HPTLS, or High-Precision Tunable Laser Spectroscopy, with the press of a button.

The Atlas laser platform is primarily in the Near-Infrared (NIR) spectral region, which allows for access to specific and unique chemical information that is not seen in regions like Ultraviolet or FTIR. The Atlas laser platform is also unique, in that through laser innovation technology it can operate with higher power and precision when compared to any other NIR laser system.

This laser platform is highly stable, repeatable, and with micro-absorbance unit noise. What this means for a user is that unlike other laser systems, constant realignment is not required to maintain accuracy. Instead, we recommend official maintenance only once per year, just to ensure continued successful operation.

Beyond the laser platform is an optics arrangement to get maximum signal out of your sample. The sample placement area is comprised of two optic rods, one on the bottom and one on the top of the inner lid. It is through these rods that the laser is focused, passing through your sample, and reaches the detector.

Since the Atlas laser platform is highly precise, keeping the pathway from laser to sample clean is very important. Sapphire is specifically chosen for the sample pedestal rods to allow for high amounts of scrubbing and wiping, so that users can clean their samples effectively and fully without fear of damage. Chipping of the rods is possible, so keeping metal tools and items away from the pedestal is important.

Following the Nirrin cleaning procedure (Section 5.4) ensures a clear optics pathway. In addition, the Atlas laser platform is powerful enough to detect changes in water that are otherwise impossible to measure. For users, this means background scans should be close to actual sample runs, to reduce noise resulting from water variability between days (or even hours).

4.3 Atlas Cover

As detailed above, Atlas relies on two optic rods, that bridge the gap between laser, sample, and detector. The alignment of these rods is carefully done when a system is built, to ensure the laser can reach the detector at maximum power. In addition, the space between the top and bottom rod is calibrated and measured at time of build.

With proper use, the distance and alignment of the optical rods will not drift over the Atlas instrument's lifetime. Within Atlas, there is a specially-designed soft-close mechanism that controls the rate of cover closing. Allowing this mechanism to close the cover on its own is vital. Allowing the mechanism to close the cover ensures no drift over 16,000 samples, or approximately 3 years of data. Atlas systems that reach 3 years of use will be evaluated for re-calibration and in-depth maintenance by Nirrin.

4.3.1 Opening and Closing Atlas Cover

Opening

- When opening the Atlas cover, grab the front finger grip with one hand and lift the cover until it is upright and in place.
- Do not open the device cover while scanning a sample. Although the device is equipped with a laser interlock for safety, opening during scanning will cause the laser to stop and may cause erroneous results.

Closing

- To close the cover, use one or two hands to slowly begin to lower the cover.
- The unit is equipped with a built-in damper to allow soft closing of the cover, but additional assistance with closing the cover is acceptable.

4.3.2 Atlas Inner High Gloss Panels

Atlas has two high gloss black panels, on the top and bottom, that surround the sample areas. These panels are rated for accidental liquid exposure, but keeping the area clean is important to instrument success.

Keeping the inner panels clean reduces incidental sample contamination. Dust and debris on these panels can migrate to the sample area with small drafts or air flow. Cleaning the inner panels gently with a lint-free microfiber cloth or wipe can ensure no incidental sample contamination.

4.4 Platform Heaters

The Atlas system has the distinct advantage of high sensitivity, which also means that careful environmental control is needed to ensure the best data quality. All components used in solutions have some response to temperature, which can impact equilibration and dynamics.

To account for temperature effects, heaters have been integrated into both the top and bottom platforms of Atlas. These are set to heat and maintain the platforms at a temperature of 27.0°C, so that all measurements taken will be under the same temperature conditions. This means even though your room temperature might vary, the results will remain the same.

To reach running temperature, all Atlas units require 1 hour of warming (from an initial ambient temperature of 20-25°C). This one-hour heating time allows the optic rods and the surrounding platforms to equilibrate fully to the final set temperature. Atlas can be used during this warm-up period, but any resulting data will not be within the accuracy specifications of the system.

Section 5 - General Operating Instructions

5.1 Ensuring success with the Atlas

1. User PPE:
   - Users must wear protective PPE such as nitrile gloves and safety glasses to reduce any contamination in your sample and to protect yourself.
2. User Supplied Tools:
   - Users should employ a calibrated pipette for sampling to ensure accurate sampling volumes.
3. Water Purity Requirements:
   - Users should use Type 1 or Type 2 grade water for backgrounding and diluting for sample analysis.
4. Pipette Tip Usage:
   - Users should use separate pipette tips for DI Water and each protein and/or excipient sample to prevent carry over.
5. Sample Deposit Verification:
   - User should visually verify that the sample is correctly deposited on static optic rod.
6. Sample Homogeneity:
   - User shall sufficiently mix protein/excipient sample to ensure homogeneity prior to drawing up with pipette and dispensing on the device.

7. Visual Check:
    - User should visually check that no air bubbles exist in deposited sample.
8. Sample Temperature:
    - User shall let samples come to room temperature prior to dispensing into system for measurement.
9. Evaporation:
    - Do not allow sample to rest on pedestal for an extended period to avoid evaporation that can affect concentration readings in your data.
    - Evaporation of the sample during a normal sample analysis is minimal and will not affect concentration reading, but repeated measurements of the same sample aliquot can result in an increasing sample concentration measurement.
10. Sample Volume:
    - Sample volume is 14 µL based on pathlength of the Atlas system.
    - Higher or lower sample volumes greatly reduce the accuracy of your analysis.

5.2 Sample Application and Pipetting Technique

To ensure that no bubbles get into any sample that can affect the user's data, Nirrin recommends using a **reverse pipetting** technique for all samples.

By using air displacement to distribute a measured amount of liquid, reverse pipetting lowers the possibility of froth, bubbles, or splashing. When it comes to dispensing small amounts of liquids containing biological solutions and proteins, reverse pipetting is more accurate than forward pipetting.

5.3 Sample Application Protocol – Reverse Pipetting Method

1. Place the correct size pipette tip onto a calibrated 20µL pipette to accurately accommodate dispensing a **14 µL droplet** of water or sample.
2. Press the plunger on the pipette to the second stop and dip the tip into the solution at an appropriate depth and slowly release the plunger.
3. Once the button is fully released, withdraw the tip from the liquid, touching it against the edge of the reservoir to remove any microdroplets that may remain on the outside of the pipette tip.
4. Dispense the liquid onto the sample pedestal, by gently pressing the button down to the first stop while keeping it steadily in contact with the rod surface.
5. Gently remove the pipette tip away from the pedestal to not disturb the droplet and close the cover to begin scanning.
6. To reuse pipette tips within a single sample (recommended for water scans), aspirate the remaining liquid in the pipette tip against the side of the sample container, making sure to press all the way down to the second stop. Do this

before placing the tip back into sample, to avoid creating an air bubble at the tip of the pipette.

7. We do not recommend reusing pipette tips when analyzing multiple samples to reduce any cross contamination.

5.4 Sample Cleaning Procedure

To ensure no crossover contamination between samples, Nirrin has developed and recommends the following cleaning procedure. Failure to clean the instrument properly in between samples can result in erroneous readings.

Materials:

- Kimwipes
- DI Wipes
- DI Water
- Wash bottle with DI water
- 70% IPA

Procedure:

1. Fold a Kimwipe in half four times over until it is a small square with roughly 1-inch sides.
2. Wet Kimwipe with deionized water for initial cleaning, until thoroughly damp but not dripping wet.
    a. If using protein, surfactant, or sugar samples, instead wet the entire Kimwipe with 70% IPA until it is damp and use this for the initial cleaning step.
    b. DO NOT dispense any liquid directly onto the pedestal or surrounding panel areas.
3. Gently use the corner or edge of the damp Kimwipe to soak up sample on **both** top and bottom pedestal.
4. Once most of the sample is removed, gently wipe down the top and bottom pedestal with the wetted Kimwipe, making sure to only apply light pressure as to not rip or tear the Kimwipe.
5. Take a deionized water wipe and fold it four times over until you get a small square with roughly 2-inch sides.
6. Gently wipe down both the top and bottom pedestal and ensure all sample liquid is removed.

    Recommended technique: Press down, and use a twisting or circular motion, or wipe in small circular motions with adequate pressure.

7. Once the sample is completely removed and the pedestal is polished, there should be very little (if any) liquid left on the surface of the rod.
8. If streaks, particles, or other debris are seen on the pedestal, use the deionized wipe to lightly wipe away any liquid or particles on the pedestal.
9. Visually inspect the pedestal to ensure no liquid or contaminants are on or near the pedestal, as to ensure following scans are free from sample-crossover.

Suggested disinfection agents for Atlas: 70% IPA, 70% Ethanol. Never spray any cleaning agents directly into electronic ports or instrument ventilation holes.

5.5 System Hygiene Recommendations

It is suggested to clean your instrument at the following intervals to ensure quality data.

Between Measurements

In between scanning samples, follow the normal cleaning procedure as described above.

Between Users

- Users should do a cleaning prior to running any scans and do one final cleaning after the last scan is complete.
- Leaving samples uncleaned or dried on the pedestal will cause difficulty in cleaning and restoring the pedestal to its original condition.

Additional Cleaning

- Additional cleaning with a 70% IPA-wetted Kimwipe should be done when dealing with certain proteins and surfactants that adhere more to the sapphire rod.
- Always follow IPA cleaning with a water cleaning, to avoid IPA contamination of subsequent samples.

Over Time

- Initial cleaning should be made prior to the first scan of each day to ensure no dust or contaminants are on the pedestal after sitting for long periods of time.

In addition, it is recommended that users run water background scans at regular intervals during use, especially prior to scanning low concentration or high priority samples. Additional water scans will help to remove any remaining contaminants that may not be removed with regular cleaning (ex. high concentration surfactants).

5.5.1 Pedestal Recovery Cleaning

If a sample is allowed to dry on the pedestal, the following technique should be used to return the pedestal to its original condition.

1. Using a deionized wipe, gently scrub away any visible residue from both the upper and lower pedestals.
2. Pipette on WFI/deionized water and close the cover. Allow the system to sit undisturbed for 3-5 minutes.
3. Open the lid and complete a full clean, with the addition of an IPA step (as described in Section 5.4 “Cleaning Procedure”)
4. Run scans of 3 water samples, making sure to do a regular cleaning protocol after each sample.
5. In most cases, this will fully recover the pedestal to its original condition.
    a. If still uncertain, water samples can be analyzed for components of the dried sample to confirm if cleaning is complete.
    b. If contamination remains, continue to scan water until no contamination is seen, or contact your Nirrin representative for assistance with pedestal recovery.

Section 6 - Using your Atlas

To get the best quality data from an Atlas system, it is suggested that all users follow the guidelines below. Each technique has been tested and confirmed against alternative procedures, and has been optimized for repeatability, ease of use, and data quality.

From a high level, a user will follow the basic workflow shown in Figure 6.

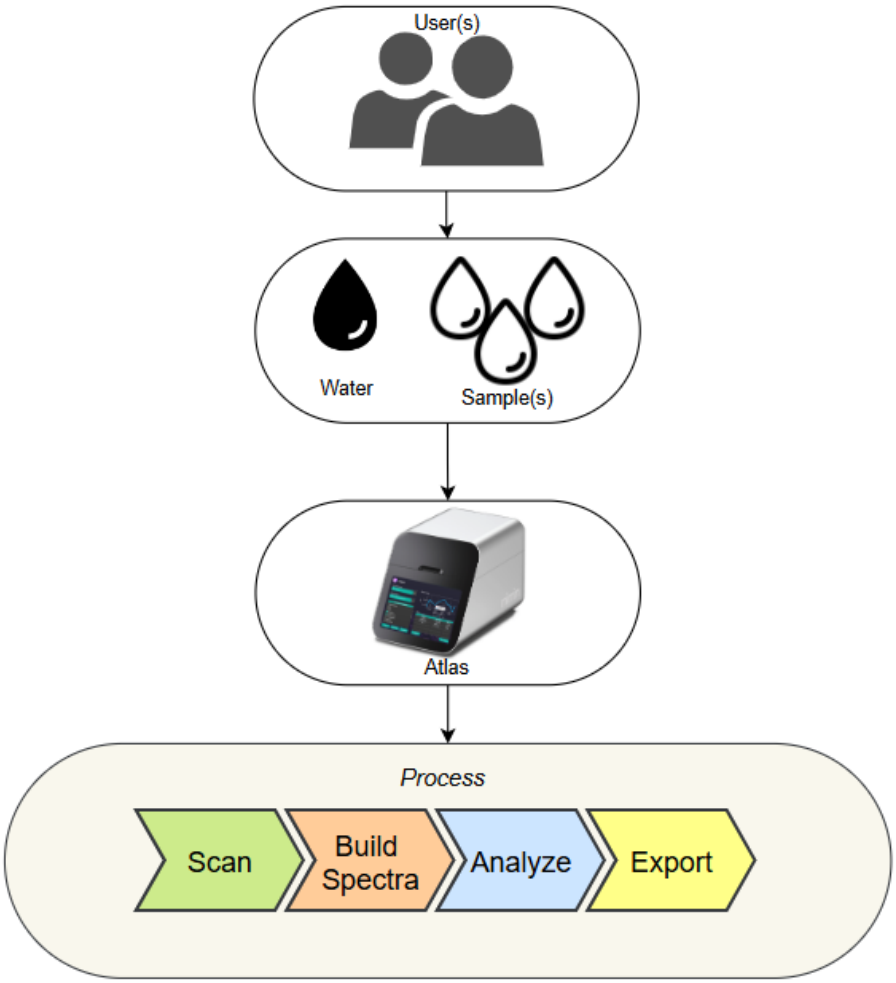

Figure 6. Overview of the user workflow for sample analysis with Atlas.

For easy navigation, both the Dashboard and the Navigation Bar (left, ☰) host quick links to the primary steps for sample analysis (Scan, Build Spectra, Analyze, and Export) as well as Libraries and Settings as shown in Figure 7.

Figure 7. Atlas navigation dashboard for easy access to modes and functions.

6.1 Recommended Sample Preparation

Before measurement on the Atlas system, ensure that all samples have been equilibrated to room temperature (where possible).

- Take care to ensure that samples are well-mixed.
- **Avoid use of vortexes prior to sampling**, as this will create microbubbles in samples that can interfere with measurement.
    - Vortexes can be used, only if this is followed by light centrifugation. Vortexed samples can also be used once given an appropriate amount of time to settle, but this is not recommended as microbubbles can sometimes take hours to dissipate.
- It is recommended to mix all samples via aspiration, or up-and-down pipetting, as this will not form microbubbles.
- For high viscosity samples, such as those containing high amounts of sugars or proteins, samples should be mixed soon before measurement on Atlas.

- If there is concern over sample homogeneity, it is suggested to run duplicates of those samples. Duplicate measurements can help confirm mixing effectiveness and robustness of data.
- **Triplicates** are officially recommended for all critical data.

6.2 Background

Before running a single sample or small batch for analysis, a background needs to be scanned**. It is important to run a background scan after system start-up/power cycle and as a best practice, within an hour of the sample intended for analysis.**

The Nirrin analysis software utilizes a background reference method as part of analysis to reduce noise in samples that originate from environmental interference or water quality.

In most cases, PCR Certified water is recommended for backgrounding to ensure successful sample analysis.

It is possible to use complex backgrounds, such as buffers or protein samples. In this case, ensure that the background sample is properly similar to that of the target sample. For example, if spiking a surfactant into a protein sample, aliquot the pre-spike protein sample as a background before spiking (instead of using a separate representative lot). Atlas is sensitive to all excipients in solution, so lot-to-lot variation will impact analysis results.

6.3 Scan

1. On the Dashboard or navigation bar, select “Scan” to begin (Fig. 8).
2. On the Scan menu, in Tag Data, select the relevant tag(s) to designate as either a sample or a background, or both. Further, select whether the scan is for either a library addition or sample analysis, or both (Fig. 9).

   NOTE: A background scan should be run first prior to running any samples.
3. Press ‘Name’ to enter a custom name for the background or sample to be scanned. By default, the filename will include a date/timestamp for easy tracking. If no

Figure 8. Atlas dashboard – SCAN mode

custom name provided, the sample will be auto-named. Click 'next'. Tags may be modified at any time before scanning the sample.

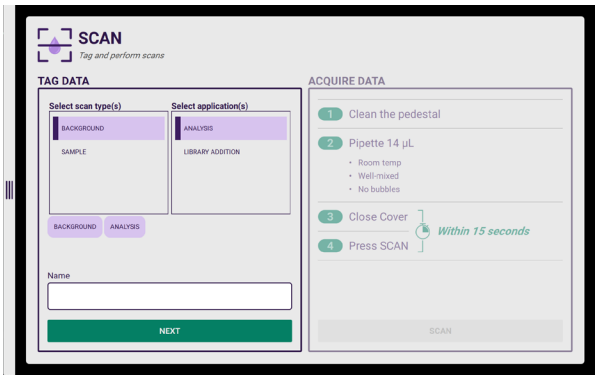

Figure 9. Tag data by scan type [background, sample] and intended purpose [analysis, library addition] before scanning.

4. **Carefully follow Steps 1-4 on-screen (Fig. 10).** Clean the pedestal and pipette 14 µL sample (room temp, well-mixed, no bubbles) onto the pedestal. Perform a visual check to ensure the droplet is well-positioned on the pedestal and that no bubbles are present in the sample is necessary before scanning. If bubbles or spilling are noticed, clean and reload the droplet.
5. **Within 15 seconds of pipetting the sample**, close the cover, and hit SCAN.
6. Scanning will take roughly 30 seconds to finish and present a confirmation when successful. A green circle with a check mark indicates the scan passes internal QC criteria (Fig. 11).
    - **To proceed WITHOUT saving**, hit "New Scan" to try again or to exit.
    - **To successfully SAVE,** hit "Save Scan".
7. A reminder will appear to follow the cleaning method for the pedestal.
8. After fully cleaning, if another sample or background is planned, continue again through the Scan page.

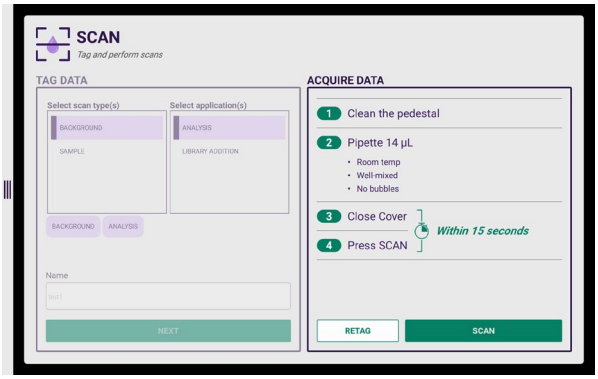

Figure 10. For optimal results, follow steps 1-4 to acquire scan data.

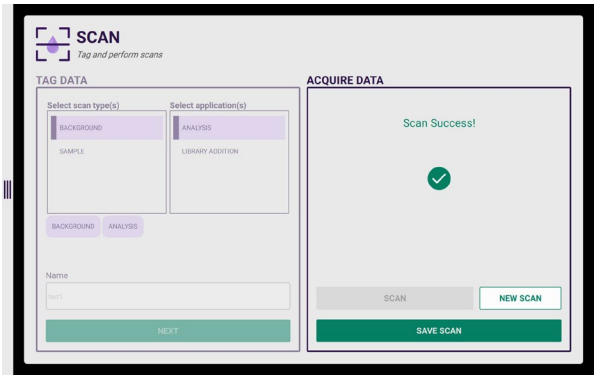

Figure 11. Confirmation that scan is successful and ready to save.

6.4 Build Spectra

1. On the Dashboard or navigation bar, select “Build Spectra” to begin (Fig. 12).
2. The Build Spectra screen is for either a library addition or sample analysis, or both (Fig. 13).
3. Press ‘spectrum name’ to enter a custom name for the background or sample. By default, the filename will include a date/timestamp for easy tracking. If no custom name provided, the sample will be auto-named. Click ‘BUILD.
4. A preview of the resulting spectrum is shown at right. Click “SAVE” to save spectrum shown and move on to quantitative analysis.

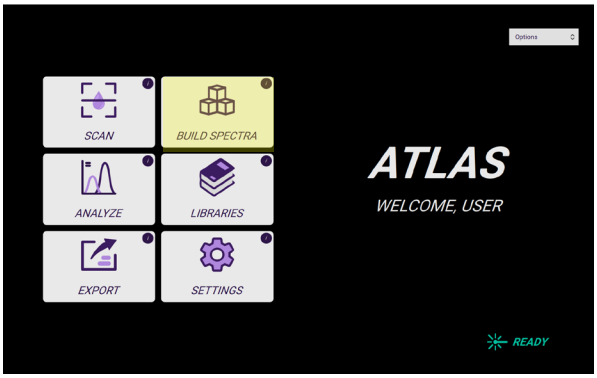

Figure 12. Build spectra from the dashboard

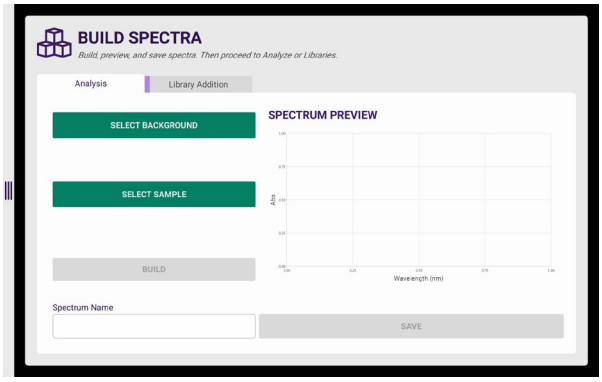

Figure 13. Tag data by scan type [background, sample] and intended purpose [analysis, library addition] before scanning.

6.5 Analyze Results

1. From the Dashboard or the navigation bar at left, select “Analyze”.

2. All scans can be sorted by Date/Time and Name (Fig. 14). Next to the headers, press the up/down sort icon to reorder files as needed.

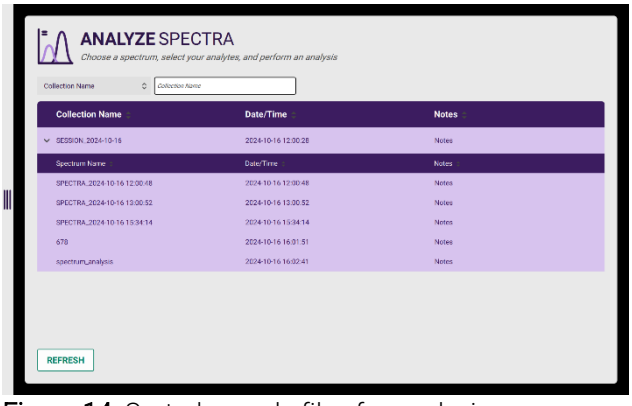

Figure 14. Sorted sample files for analysis

3. Each sample can be analyzed by selecting that file and selecting all the analytes in your sample for quantitative analysis (Fig. 15). Click “Analyze”. Concentration units can be changed once the file is analyzed. e.g. mg/mL, %, or mM, as applicable.

4. Add or remove analytes from the analysis and re-analyze as needed. If the selected analytes change, the file must be saved again.

5. The hit score is a quality index corresponding to multiple attributes of spectral matching from sample spectra to the library, which relate to signal-to-noise, goodness of fit and analyte-specific extinction coefficient.
   - **Hit score > 0.7 = high confidence**
   - **Hit score 0.4 – 0.7 = lower quality fit, possible low SNR**
   - **Hit score below 0.4 = low confidence**

   If low hit score, consider the following actions:

   1. Repeating background and sample scans ensuring samples are homogeneous, well-mixed 14 µL droplets on a clean pedestal. Droplets can roll off, or micro dust particles may be on the pedestal.
   2. Ensuring all components in your sample are selected.
   3. Confirming sample integrity including correct labeling and appropriate storage conditions.

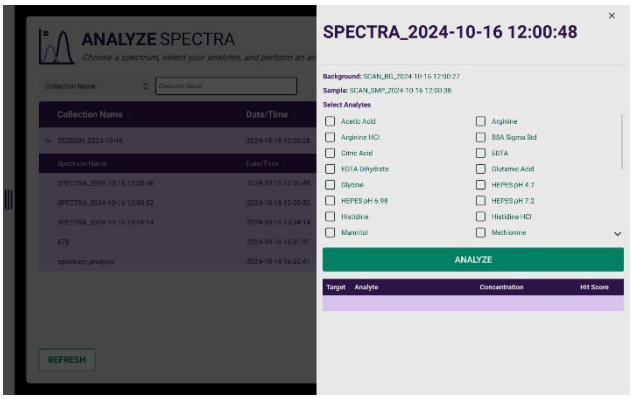

Figure 15. Select all Analytes in the sample for analysis and hit ‘Analyze’ to review quantitative results.

6.6 Library Addition

1. When scanning a sample or a background for library addition, ensure that you tag both the background and sample as a library addition (Fig. 16).

2. Select the library addition tab (Fig. 17) and follow the steps from Section 6.4 to link the relevant background and sample scan to build the candidate Spectrum for your new custom analyte.

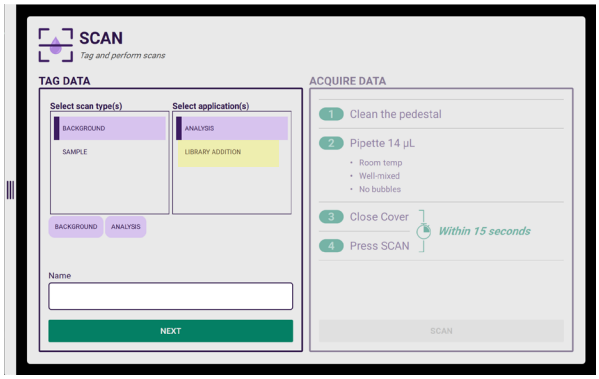

Figure 16. Tag background and sample scans with 'Library Addition' (yellow)

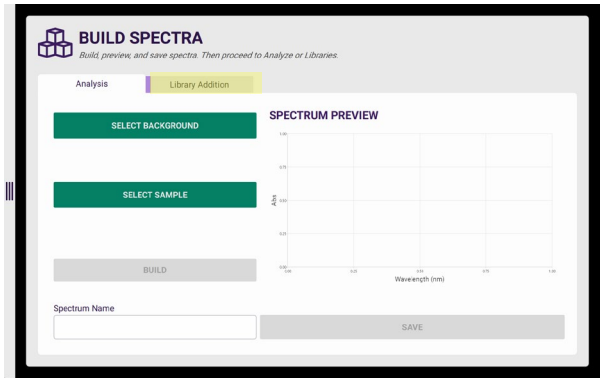

Figure 17. Library addition tab (yellow) selected for building spectra for new library components.

3. From the Dashboard or the navigation bar on the left, select "Libraries".

4. Once in the Libraries Tab, click on the file name that was saved previously in the "Build Spectra" page (Fig. 18).

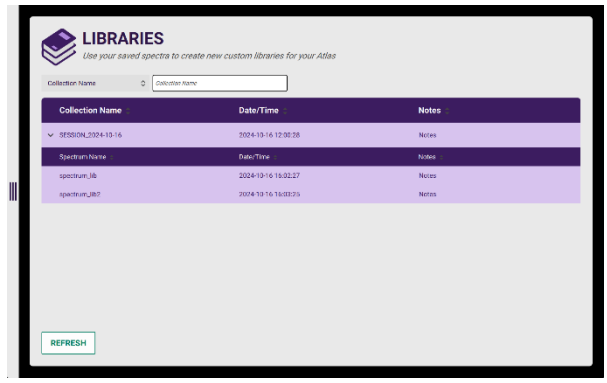

Figure 18. Select a spectrum to create a new custom analyte for the library

5. The user will then name the new file for their library addition and indicate if the new addition is a mAb (Fig. 19).

6. Note: If the new addition is a mAb then the molar mass, concentration, and unit fields are not needed.

7. If the new addition is a buffer component or excipient as the analyte, NOT a mAb, then molar mass, concentration, and units need to be filled in accurately for quantitation.

8. Once all information is filled in correctly, click “Add to Library”.

9. To confirm the user will go to the “Settings” tab in the dashboard and click on the “Libraries” tab (Fig. 20). Scroll down and find the new analyte in the library and ensure it is selected, so the new analyte is visible as an option in Analyze mode.

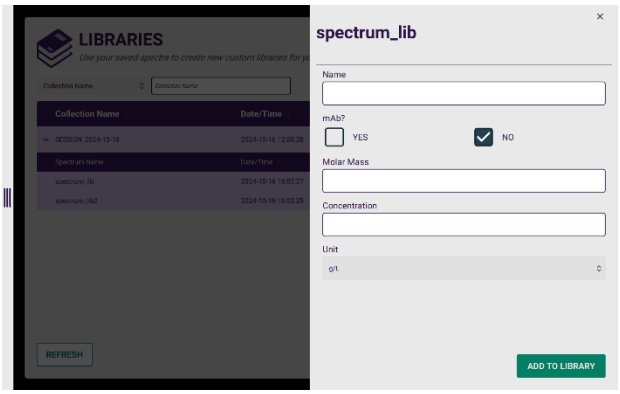

Figure 19. Required information for new Library Additions that are non-mAb analytes: molar mass, concentration and units

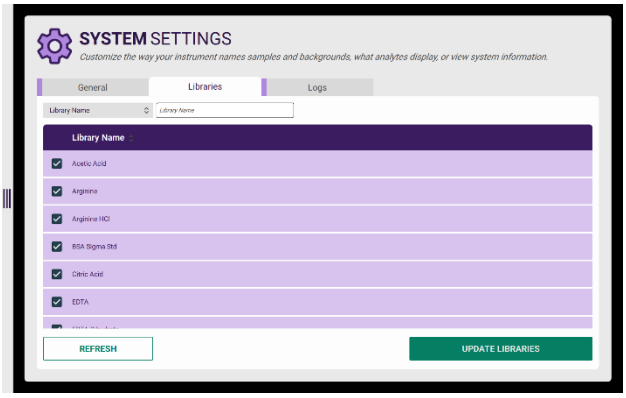

Figure 20. In System Settings, under the Libraries tab, confirm the newly added analyte is selected to be active during analysis

6.7 Export Results

10. From the Dashboard or the navigation bar at left, select “Export”.

11. All saved scans and collections are displayed.

12. Files are organized by collection name, sample name, and date/time. The files can also be filtered or sorted by name or date/time as well to easily locate any files (Fig. 21).

13. Select a specific file and preview the analyte concentration, as well as the file and collection name.

14. To export files, sample collections or individual sample files must be toggled by checking the empty box on the left side of the file name.

15. Once selected, the Atlas recognizes the presence of USB or ethernet connection and provides the option to select directory for export (Fig. 22).

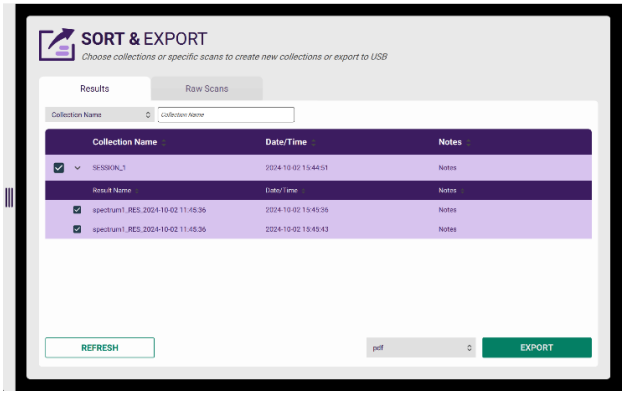

Figure 21. Chronological logs of all collection files for the system that are ready for export.

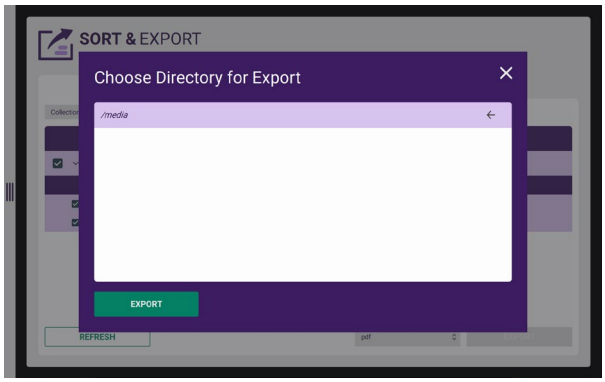

Figure 22. Select the directory for export.

6.8 System Settings

16. From the Dashboard or the navigation bar at left, select “Settings”.

17. Under the “General” tab, the user will find necessary information about the system such as (Fig. 23):

    - Device Hostname
    - Pathlength
    - Atlas Software Version
    - Analysis Software Version
    - Spectrometer serial number
    - Spectrometer Connection Status
    - Platform Heater Status and Temperatures

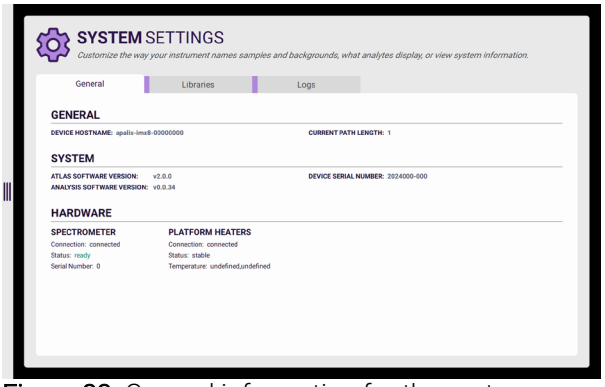

Figure 23. General information for the system

18. Under the “Logs” tab in System Settings, the User will be able to export (Fig. 24):
    - System Log
    - Exception Log
    - Settings Log
    - Temperature Log
    - Diagnostic Log

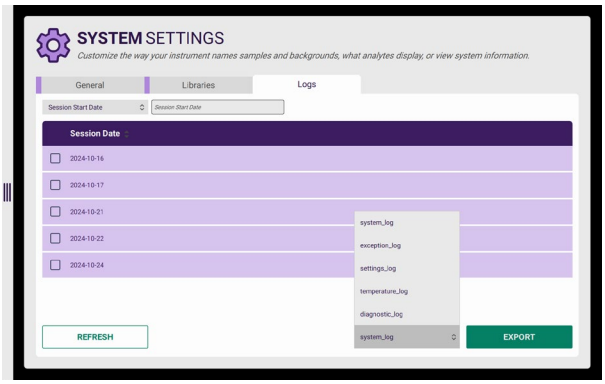

Figure 24. Logs available for export

19. The user can export this manually with a USB drive or a network using an ethernet cable.

20. Under the “Libraries” tab, select which analytes are actively visible in the Library available in Analyze mode (Fig. 25). To filter by analyte, type in the “Library Name” field (this refers to the analyte name).

21. To select or unselect, click on the box on the left side of the excipient to add or remove and hit “Update Libraries” to successfully update the library. Once updated, the analytes available in Analyze mode.

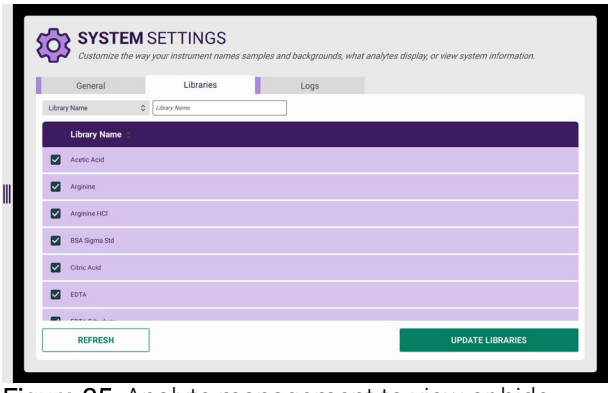

Figure 25. Analyte management to view or hide analytes available in Analyze mode

Section 7 - Atlas Maintenance and Troubleshooting

7.1 Cleaning the Exterior

The primary requirement for maintenance of Atlas is keeping both optic rods as well as the exterior of the system.

CAUTION: Disconnect Power. Power should always be disconnected before cleaning the unit externally.

The following materials are needed for cleaning:

- Microfiber cloth
- 20% IPA (Optional)

Instructions:

1. Turn off the instrument and disconnect the power cord from the wall plug.
2. Wipe off any dust or residue on the instrument using the microfiber cloth.
3. If residue is present on external surfaces (not including the sample application areas), lightly dampen the microfiber cloth with 20% IPA to wipe affected areas.
4. Never spray your instrument directly for cleaning. In all cases, avoid wiping electrical components.
5. Let the instrument fully dry before plugging in the instrument and turning it on.

7.2 Cleaning the Touchscreen Display

To clean the screen on Atlas, we recommend gently wiping the screen with a soft, lint-free microfiber cloth. If necessary, spray a small amount of IPA onto a a microfiber cloth and wipe the screen. Do not spray the IPA directly onto the instrument. Avoid saturating the cleaning cloth with IPA, as to reduce the possibility of getting liquid in the system.

DO NOT:

- Apply excessive pressure
- Spray liquid directly onto the screen
- Clean with an abrasive material (such as a paper towel)

7.3 Rebooting Instrument

When rebooting Atlas, do not unplug the unit while it is still powered. On the UI, turn off the screen by pressing “Power” then “Shut Off”. This allows the software to properly close its processes and to power down the laser.

Once shut down, flip the power switch on the back of the unit to the “OFF” (O) position, before unplugging the unit. If transporting the unit, hold the unit in an upright position by the bottom edges, so to not damage any hardware within the unit and to ensure the lid does not open in transport.

7.4 Maintenance Schedule

Regular maintenance of Atlas ensures that your unit is still working properly within the specified parameters that Nirrin sets for the performance of Atlas. Users can extend the life of their Atlas and preserve dependable analytical data for their applications by following a thorough annual maintenance routine.

7.4.1 Daily Maintenance

- Clean pedestal with lint free deionized water optic wipes
- Clean top and bottom panels around pedestal

7.4.2 Weekly Maintenance

- Clean touchscreen with a microfiber cloth
- Power down and turn off instrument when anticipating no usage (ex. weekends)

7.4.3 Yearly Maintenance

- Contact your Nirrin service member for detailed information or refer to the service plan received at time of purchase.

Over long periods of use, Atlas accuracy will be confirmed by calibration checks. The hardware and software of the device are also routinely inspected to spot such problems early on and fix them. Please contact Nirrin to learn more.

7.5 Troubleshooting

Issue	Action
Pedestal Not Warming Up	• Confirm the system is switched on. If not, switch the unit on with the power switch on the back of the unit. • Check to make sure power cable is secure into the power port on back of system.
Touch Screen Not Working	• Ensure there is not liquid on the screen that could be making false inputs on the UI.
Inconsistent Measurement Reading	• Ensure that the pedestal is thoroughly cleaned prior to pipetting any sample or background onto the pedestal. • Follow the reverse pipetting protocol that Nirrin recommends to prevent bubbles in your sample. • Check background or sample solution for particles or debris in the solution that could affect absorbance and in turn affect data consistency. • Ensure water purity for backgrounding is Type 1 or Type 2 grade water. • Rerun background and sample
High Error Value	• Ensure that all analytes in your solution are selected during your analysis. • Check background or sample solution for particles or debris in the solution that could affect absorbance and in turn affect data consistency. • Check system settings to confirm that the pedestal heaters are stable at the recommended temp of 27°C, +/- 0.1°C. • Confirm the lid is completely shut prior to scanning your background or sample.
Files Not Exporting	• Offline - Ensure the USB stick is properly inserted into the USB port on the back of the system. • Online – Ensure the ethernet cable is properly inserted in the ethernet port on the back of the unit as well as in the wall ethernet port.

If you are experiencing any further problems with your Atlas system, refer to the troubleshooting information. If the problem continues, please contact us.

7.6 Returning the Instrument for Service

If your Atlas needs to be returned to the manufacturer for service, the unit should be packaged identically to how it was received to avoid any damage in transit. Get in touch with your Nirrin contact if for troubleshooting and technical support before shipment.

7.7 Updating Software

Atlas software can be updated either via USB with an update file provided by Nirrin or remotely by the Nirrin software team (if the system is connected via ethernet to cloud-based services). Nirrin will notify the main contact of the user's company to ensure that the user knows of an upcoming software update and its availability upon release. The software version is documented in the diagnostic log file for reference and tracking. The current version is also available under System Settings

7.8 Connectivity Options

Atlas can be connected to a wireless network for easy exporting onto a web base. To connect Atlas wirelessly, an ethernet cable is connected to the back port on the device and the other end is connected to the wall ethernet port. This will then connect your Atlas to the local network and allow for easier data transfer. Atlas can also be used standalone offline, and data can be exported manually using a USB stick.

Frequently Asked Questions (FAQs)

Q1: Is simply wiping the pedestal surface enough to prevent any carryover?

A1: Certain proteins and surfactants can slightly adhere to the sapphire rod so simply wiping the pedestal is not enough to confidently say that there will be no carryover. The proper cleaning protocol should be followed accurately after every scan to ensure there is no sample carryover.

Q2: Can Atlas differentiate between different excipients in a mixture?

A2: Yes, our device can differentiate between different excipients in a mixture by using spectroscopy coupled with a multivariant analysis to distinguish the different spectra in complex mixtures with high accuracy and precision.

Q3: What type of sample preparation is needed before analysis on Atlas?

A3: No sample preparation is needed prior to scanning on Atlas. The use of a water background scan prior to sample scanning allows for no sample prep because instead of isolating the excipient we simply calculate out the water absorbance.

Q4: What is the accuracy of excipient quantitation on Atlas?

A4: The accuracy of excipient scans on Atlas is +/- 5%

Q5: What is the precision of excipient quantitation on Atlas?

A5: The precision of excipient scans on Atlas is +/- 1%

Q6: Can I add a custom excipient into the library that isn't in Nirrin current qualified library?

A6: Yes, Atlas can allow users to add a custom excipient or custom protein into the systems library by following the Nirrin protocol of adding a custom excipient or custom protein. Please contact the Nirrin team.

Q7: What is the best naming convention when the user prefers to rename their sample?

A7: YYYYMMDD_Experiment_SampleSpecifics_RepeatNumber

- i.e. 20240717_SurfactantStudy_200mMPS80_r1

Glossary

It's helpful to be aware of and comprehend the many naming standards, meanings, and words related to your Atlas. As a quick reference, this section of the manual offers an outline of these terms.

Background Scan: A background measurement is the sampling conditions of the instrument in the absence of any sample. The final sample spectrum is produced by dividing the sample data by the background measurement after the background and sample have been measured.

Beer-Lambert Law: The law of physics that describes the proportional relationship between absorbance, pathlength, and concentration.

Collection: Multiple individual scans stored together on the Atlas as a group based on an experiment or related scans. (note: this feature coming in future software release)

Detector: A device used to detect signal being transmitted through the sample.

Pathlength: The distance the measured light moves through the sample, when making absorbance spectroscopy measurements based on the Beer-Lambert Law. This distance, which is commonly measured in millimeters in the variable pathlength system, is determined by the actual gap between the sapphire pedestal's top and bottom.

Reverse Pipetting: By using air displacement to distribute a measured amount of liquid, reverse pipetting lowers the possibility of froth, bubbles, or splashing. When it comes to dispensing small amounts of liquids containing biological solutions and proteins, reverse pipetting is more accurate than forward pipetting.

Scatter Correction: The adjustment of absorbance values that takes away absorbance contributions related to particle dispersion or molecular interactions with incident light.

Spectrum/Spectra: *XY* data set(s) consisting of absorbance data at a fixed pathlength as a function of wavelength in absorbance spectroscopy.

Type 1 Water: Critical laboratory applications such as the preparation of HPLC mobile phases, blanks and sample dilution in GC, HPLC, AA, ICP-MS, and other advanced analytical techniques; the creation of reagents for molecular biology applications (DNA sequencing, PCR); and the preparation of solutions for electrophoresis and blotting all require type 1 laboratory grade water.

Type 2 Water: For general laboratory purposes, such as buffers, pH solutions, and the preparation of microbiological culture media, type 2 laboratory grade water is utilized. It can also be fed into Type 1 water systems, clinical analyzers, cell culture incubators, weathering test chambers, and be used to prepare reagents for chemical analysis or synthesis.

Contact Technical Support

For U.S./Canada Technical Support, please contact:

Nirrin Technologies

44 Manning Road

Billerica, MA 01821, USA

E-mail: help@nirrin.tech

Website: https://www.nirrin.tech/

Phone Number: (781)-285-5450

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Safety information

Your Atlas system should be operated according to the instructions in this user manual. It is important to use this equipment as specified in this manual; using this equipment in a different manner may impair the safety precautions of the Atlas System. Never open the system, even when the power switch has been switched off. Hazardous voltage is present with a hazard of electrical arc flash. Will cause death or serious injury. It is not sufficient to stop all power to system, the plug must be physically removed from its power source. Installation and maintenance should only be done by a qualified person. Appropriate personal protective equipment (PPE) must be worn, and safe work practices must be followed. Document Reference: Atlas User Manual Revision: V1.4


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illuminating insights