FRACTION FINDER *ULTRA*

In-Line Chromatography Process Monitoring Using Fluorescence Spectroscopy

AROMETRIX

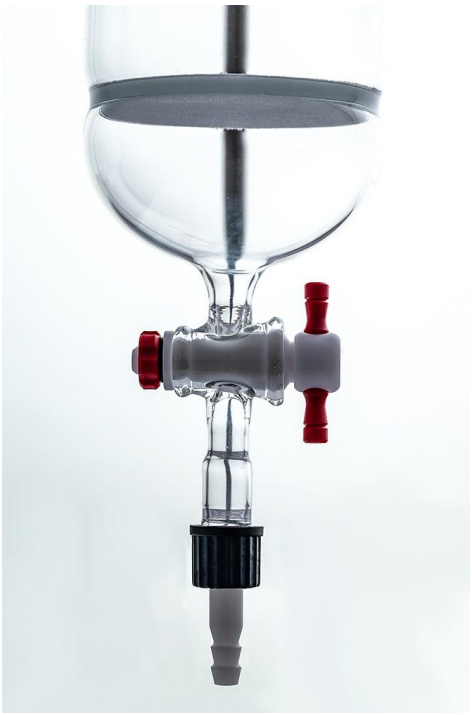
Introduction

Chromatography is a common purification technique utilized in the life sciences industry to isolate, or separate a desired compound from a mixture. In Hemp and Marijuana processing applications, it is commonly used to obtain specific cannabis compounds (e.g. THC, CBD). There are many different types of chromatography processes; generally, it involves a vertical glass column that is packed with a highly potent distillate mixture, solvent, and silica. After passing through the column, individual fractions elute (or travel down through the column) at different times. Chromatography often requires a great deal of experimentation and optimization in order to achieve desirable results. During the process, it can be challenging to time fraction changes for precise, consistent separations. To assist, it is recommended that chromatography operators pair their columns with on-site analytics in order to confirm collected fractions; however, this equipment can be incredibly expensive and complicated. Arometrix's solution, the FRACTION FINDER *ULTRA*, is a UV fluorescence spectroscopic monitoring system that can be used during chromatography processes to track real-time levels of key molecules. This is a more affordable, straightforward alternative that allows operators to easily monitor fraction peaks in real-time to ***know when to stop eluting, switch fractions, or switch columns***. Having this information helps increase precision and consistency of fraction separations during chromatography.

OVERVIEW OF CHROMATOGRAPHY

Introduction: Typically, distillation is the final step for a botanical processing facility; however, due to increasing interest in specific cannabis compounds, chromatography is growing exceptionally popular. Chromatography is a process that isolates small quantities of specific compounds from a high-potency mixture. This process allows for the separation of compounds that are not easily separable by boiling point during the distillation process (e.g. THC, CBD). Traditionally, after fractions are collected in different containers, they are then analyzed to see which contain the desirable or undesirable contents, kept separate, then the desired fractions are combined. The resulting product is then typically used in various medical applications.

Specifics: Specifically, chromatography is a process in which a chemical mixture carried by a liquid or gas is separated into components, as a result of differential distribution of the solutes as they flow over a stationary liquid or solid phase. Silica gel (e.g. CL-18 silica) is packed and compressed into the column, solvents are added, and a high potency compound is added for isolation. A great deal of care is placed in preparation and packing each layer in a horizontal line, so that the fractions are layered in bands and elute one at a time.



Types: There are many types of chromatography processes. This paper will focus on normal phase, reverse phase, and color remediation. **Normal-phase chromatography** is a rapid technique that uses pressurized gas to drive the mobile phase through the column. In this process for the Hemp/Marijuana application, the THC fraction will elute before the CBD fraction. **Reverse-phase chromatography** uses a special silica that reverses the elution order; so, instead the CBD fraction will elute before the THC fraction. This technique is growing increasingly popular as it is great for removing THC from CBD, in order to create CBD products with less than 0.3% THC, so as to meet regulatory and federal requirements. **Color remediation chromatography** is a chromatography technique that targets dark pigments in the mixture, improving purity, color, and taste.

PAIN POINTS DURING CHROMATOGRAPHY

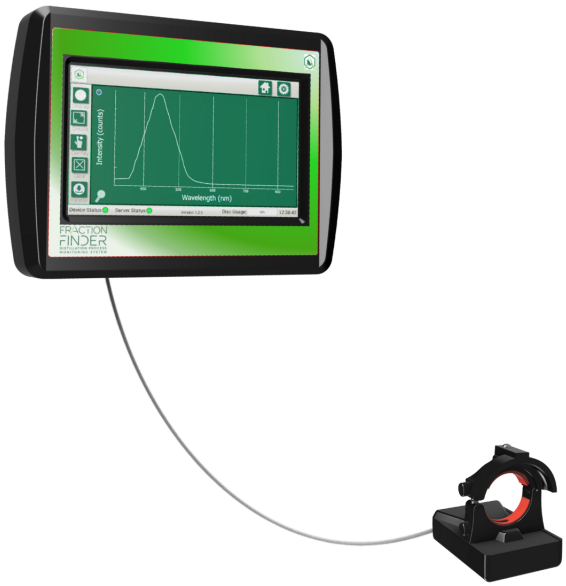
Regardless of technique, chromatography can be a very complex process. The goal is to efficiently produce clean fraction cuts. In order to achieve this, operators typically learn by trial and error in timing when to stop eluting, switch fractions, or switch columns.

Without analytics, accurately timing elution is very challenging: A common question from chromatography operators is “When is my compound going to elute?” It can be challenging to time when a fraction is truly over for precise separation, let alone do it consistently. Knowing and timing exactly when each fraction starts is a major driver of precise, consistent separation of fractions.

Chromatography analytics are expensive and complicated: It is commonly recommended that chromatography operators pair their columns with on-site analytics, such as an HPLC (high-performance liquid chromatography) in order to confirm collected fractions. However, this can be incredibly expensive, as most HPLCs on the market start at $50,000. This price tag is often out-of-budget for small to mid-sized processing companies. Additionally, this type of analytical equipment requires trained, specialized operators, further increasing costs. Another issue is that most chromatography processes don't use UV detection as a gross source of flow data; rather; they extend the process with a long, thin tube where multiple sensors provide UV data readings. The equipment is often hardware-hungry and data interpretation can be difficult. In summary, there is a lack of reasonably affordable and straightforward analytics during chromatography.

SOLUTION: FRACTION FINDER *ULTRA*

Arometrix saw an opportunity to offer a new solution: the FRACTION FINDER *ULTRA*.



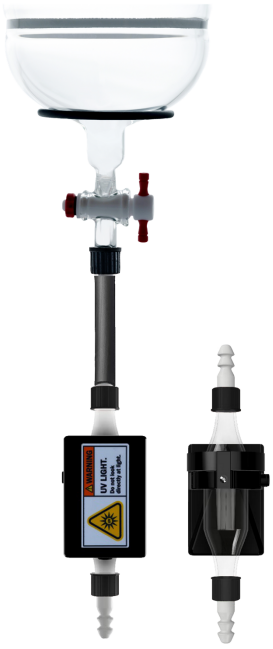
Time fractions during elution: The FRACTION FINDER ULTRA is a miniature monitoring system that will let you easily monitor fraction peaks in real-time to know when to stop eluting, switch fractions, or switch columns.

Affordable and straightforward analytics: The system starts at ~$4,800; additionally, the included sensor installs easily and directly in-line on the process prior to collection point.

The product: The FRACTION FINDER ULTRA features a brand new, ultra-sensitive sensor, designed with chromatography in mind. The sensor is easily installed directly in-line, wrapping around the column's glassware; alternatively, it can be installed using one of our sight glass or adapters, such as our GL18 Chroma Adapter.

The touch-screen display connects and interprets the wavelength information from the sensor, then displays real-time molecular information about the contents of your fractions throughout the process. The touch-screen interface is feature-rich; capabilities include allowing users to select from a menu of key molecules, track intensity values, and log run data for traceability purposes.

EXAMPLES OF FRACTION FINDER *ULTRA* APPLICATIONS



The FRACTION FINDER ULTRA system can be used for a variety of chromatography processes. Chromatography processes that Arometrix is aware of customers using this system for include:

- Normal-phase chromatography
- Reverse-phase chromatography
- Color remediation chromatography
- Lipid removal chromatography

The FRACTION FINDER ULTRA can also be easily disconnected. It can then be used for the same processes that the original FRACTION FINDER can be used for, including:

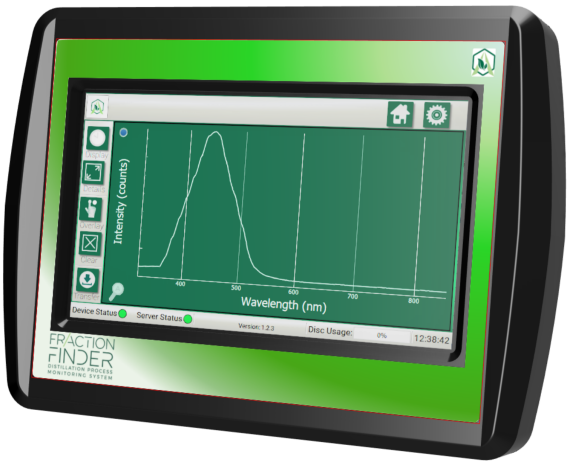
- Short path distillation
- Wiped film evaporation
- Thin film distillation

Additionally, the system has also been used on industrial stainless steel **conversion reactors** to monitor synthesis; although, data for this application is currently very limited. Note: The system is NOT intended for pesticide or terpene detection.

OVERVIEW OF TECHNOLOGY

Fluorescence spectroscopy: Arometrix's patent-pending technology utilizes autofluorescence resulting from the excitation of molecules present during the processing of cannabinoids and botanical oils. Many large organic molecules (such as aromatic-containing oils) and their derivatives will create a fluorescence response when exposed to electromagnetic radiation, while smaller molecules, mostly aliphatic, chemical compounds generally do not exhibit such behaviour. Measuring the fluorescence response of complex chemical solutions provides contrast between these compounds, allowing for the detection of only the fluorescing constituents without complicated data interpretation and complex analytical chemistry methods.

Technical components: The system uses a LED light source and a full wavelength spectrometer along with signal conditioning circuitry in the optical transducer (sensor). This information is digitally transmitted to the compute module (display), where the spectra is cataloged, analyzed, graphed and displayed as a function of time. The software does additional math on this multi-wavelength spectral temporal data and creates a visualization for the user where both flow and relative potency are deduced.



Detection and signal information: Arometrix's platform is a fluorescence monitoring system that includes a full broad-spectrum detector. The system's wavelength of excitation is 365nm; many organic compounds fluoresce when excited at this wavelength. Any signal other than the 365nm signal is a relevant process signal. Our system's wavelength detection range is 300 - 1000 nm. The system's limit of detection (also known as lower detection limit) is *less than 0.1 mg/mL at a volume of 1 cubic centimeter of oil*. Borosilicate glass does not affect sensor signal, as its optical properties are lower in the UV than our excitation peak.

Resolution: Spectral resolution is 15 nm max. Spectral resolution represents the resolving power of the detector, or in other words, the sensor's ability to distinguish between two peaks (or signals). For example, assume there are two peaks/signals on the Fraction Finder. If they are greater than 15 nm apart, you will see two unique peaks. If they are less than 15 nm apart, they will merge together and you will only see one peak.

HOW FRACTION FINDER ULTRA IS DIFFERENT

The FRACTION FINDER *ULTRA* is a modified version of Arometrix's initial system (FRACTION FINDER), which was designed specifically for fractional distillation. The ULTRA differs from the original system in that it features a new, ultra-sensitive sensor. The ULTRA sensor includes a new filter that improves detection capabilities and cuts down background signal noise, allowing it to be significantly more sensitive, in fact, **over 10 times more sensitive than the standard Fraction Finder sensor**. This modification expands our technology's applicability to chromatography processes, which generally use high amounts of solvent. The more solvent used, the greater the detection capabilities need to be, hence, the ULTRA was created. While the sensor is different, the FRACTION FINDER ULTRA features the same, high-quality display and feature-rich software, as our initial FRACTION FINDER solution. However, molecular signals will appear much stronger.

FRACTION FINDER

- Standard sensor
- Used for distillations (short path, wiped film, thin film)

VS

NEW FRACTION FINDER *ULTRA*

- Ultra-sensitive sensor
- Used for chromatography + distillations + conversions

FRACTION FINDER ULTRA vs. HPLCS

While both technologies use spectroscopic analysis for high sensitivity and detection of specific molecules, there are three key differences.

1. **Different types of spectroscopy detection methods.** FRACTION FINDER ULTRA utilizes induced fluorescence spectroscopy. HPLC utilizes absorption spectroscopy.
2. **Different UV regimes.** FRACTION FINDER ULTRA operates in the near UV. Most HPLCs operate in the deep UV.
3. **Different use cases.** FRACTION FINDER ULTRA is used for in-line monitoring during the process. HPLCs are used for quantitative sample analysis after, or at the end of, the process.

SUMMARY

Chromatography is an increasingly popular process used to target and separate specific compounds for purification purposes. Analytics are essential in optimizing this process; however, current analytical equipment is highly expensive and complicated. The FRACTION FINDER ULTRA is a molecular monitoring system that aims to solve these pain points. The system is composed of an in-line ultra-sensitive sensor, connected to a digital display that provides real-time data to a feature-rich interface. Using this system enables affordable, straightforward fraction awareness.

ABOUT AROMETRIX

AROMETRIX

Mission: To develop and manufacture optical measurement technology for botanical extraction facilities to improve their process and output quality.

Vision: To be the standard for quality monitoring, compliance, and purity of life-transforming plant oils.

Looking to learn more about FRACTION FINDER *ULTRA*? Please reach out with any questions:

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