

CANTY

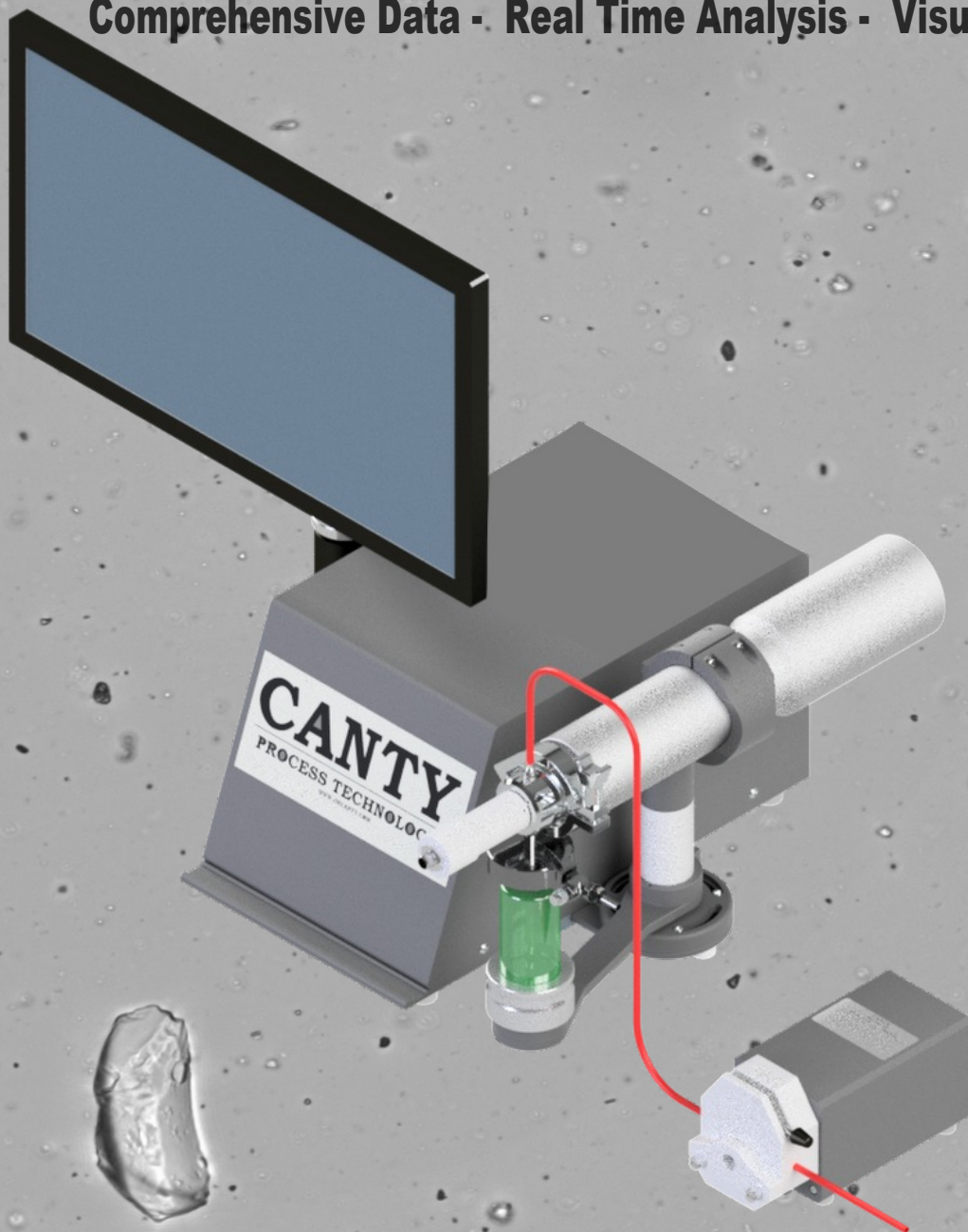
PROCESS TECHNOLOGY

Lab & PAT Imaging PSSA

PSSA - Particle Size & Shape Distributions and Concentration

Imaging Based Technology - Lab, At-Line, and In-Line Options

Comprehensive Data - Real Time Analysis - Visual Verification



PARTICLE CONCENTRATION - PARTICLE SIZE - PARTICLE SHAPE

Canty mini Inflow analyzers utilize the latest in visible-spectrum microscopic imaging technology. Canty's Gigabit Ethernet cameras, microscopic lenses, trademark fused glass, LED cool lighting systems, and proprietary CANTYVISION Intelligent Analysis software combine to provide the very best in real time analysis of particle concentration & size and shape distributions

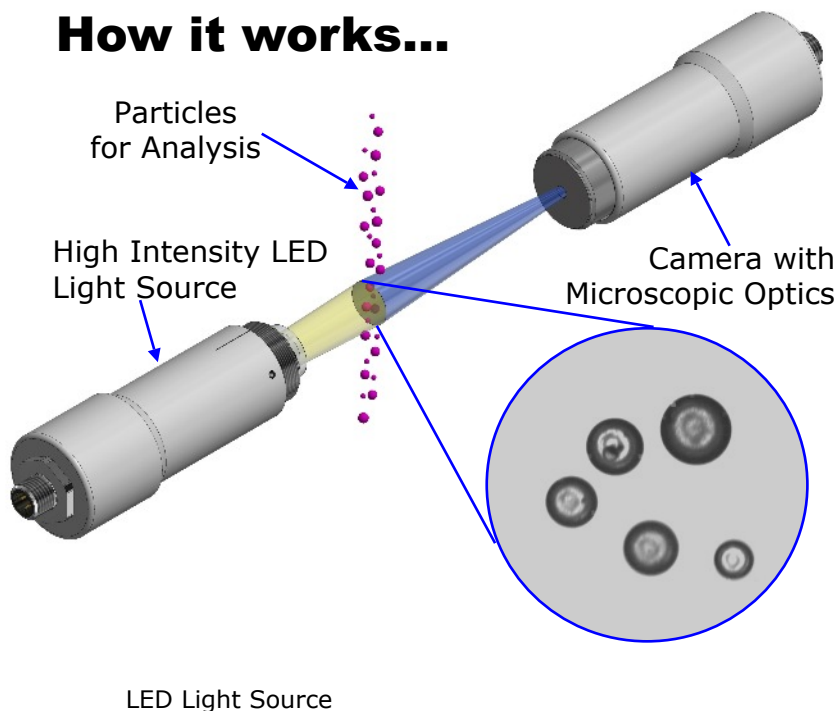
Canty's Mini Inflow product line can be set up in a variety of configurations to be used anywhere within a pharmaceutical process in order to ensure that processes are running at their maximum efficiency and to bring awareness to process upset conditions in real-time.

A variety of processes within the pharmaceutical industry require a specific particle size, shape, and concentration in order to run effectively and create the high quality products the industry is known for. This includes processes such as crystallization, separation, wastewater, etc. An accurate, repeatable, and real-time measurement of these parameters allows for more responsive control and can be the difference between scrapping or keeping a batch.



SEPARATION OPTIMIZATION - CRYSTALLIZATION CONTROL ENVIRONMENTAL REPORTING

How it works...



Simply put, Canty's particle size analyzers functionally emulate an inverted microscope. Material passes between a high resolution camera with microscopic optics and a cool LED visible light source. As the material flows by, the camera takes video images of the process. These images are passed from the analyzer to Canty's Vector Control Module for analysis within the CANTYVISION Intelligent Analysis (CVIA) software.

Every image taken is combed over by our algorithms which determine what particles are in focus. These particles can range from solids to droplets to gas bubbles. Each "particle" then has over 40 shape and size parameters measured which allows the software to both classify the type of material it analyzed and calculate concentrations and size and shape distributions for each class of "particle".

Key Technologies

CANTY’s **FLOW CELL** is specially designed to run with precise gaps along with perfectly flat glass that acts as windows to the process for our camera and lighting technologies. This design allows for the best possible image and most representative flow while mitigating the ability for particles to stick in the cell. The design also allows for CIP and SIP procedures

CANTY’s belief is that there are 3 keys to a high quality image:

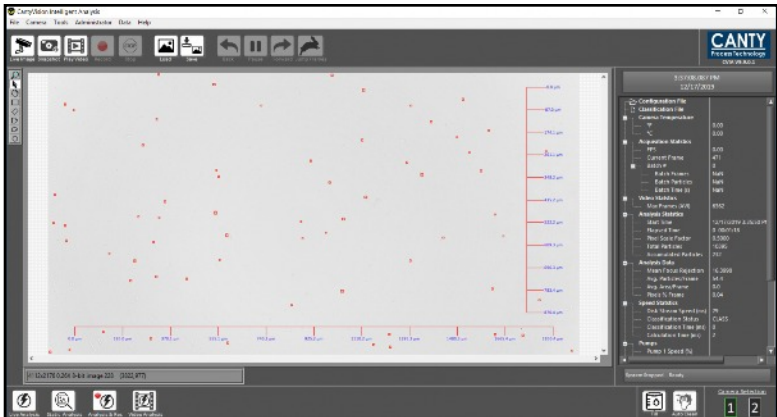
LIGHTING, LIGHTING, and LIGHTING

With our roots in process lighting dating back to the 1970’s, we understand the importance of the brightness, angles, and mechanical design to create the best image possible. Image quality directly relates to the ability to accurately analyse an image, which is directly impacted by our industry-leading process lighting. This, of course, combines with a guarantee of reliability. Each Cauty LED light source is rated for 50,000 hours of continuous use.



CANTY goes to great lengths to provide the best available **CAMERA OPTICS** on the market while maintaining an affordable cost. New cameras and lenses are constantly being researched and rigorously tested to balance the latest and greatest innovations with the confidence that any given optic will be reliable across the wide range of process conditions we design for. Different processes sometimes call for different ranges of analysis, and CANTY has high resolution cameras and lenses to cover all of our customers’ applications.

CantyVision Software analyses each particle for 40+ visual shape and size parameters, allowing the system to differentiate between solids, droplets, and gas. It even allows for further classification within each of those categories if there is a morphological difference between the components. The high speed processor ensures all of this is done in real time. The intuitive CVIA interface allows the user to visually verify what the system is analysing, and view real time graphical trends for any parameters they may be interested in, while the user friendly functionality means adjusting any analysis parameters is a simple task.



A picture is worth a thousand instruments...

Why Use Dynamic Imaging Technology?

To put it simply, Dynamic Imaging based analysis is the most comprehensive and representative type of technology for measuring particle shape, size, and concentration. With a single device, all of these measurements can be made simultaneously.

Unlike other technologies in use in the industry, Dynamic Imaging is a direct measurement technique. It is completely unaffected by changes in the chemical composition or salinity of the process stream, or the types of materials being measured within those streams. It essentially provides eyes in your process, with software constantly evaluating what those eyes are seeing. This, of course, provides the added benefit of you being able to see what the system is measuring, and visually verifying that the measurement parameters are correctly configured. Nervous that the data was not accurate for that process upset? Play back the video and prove it to yourself.

RELIABLE, REPEATABLE & DIRECT MULTI PARAMETER MEASUREMENT, WITH VISUAL VERIFICATION

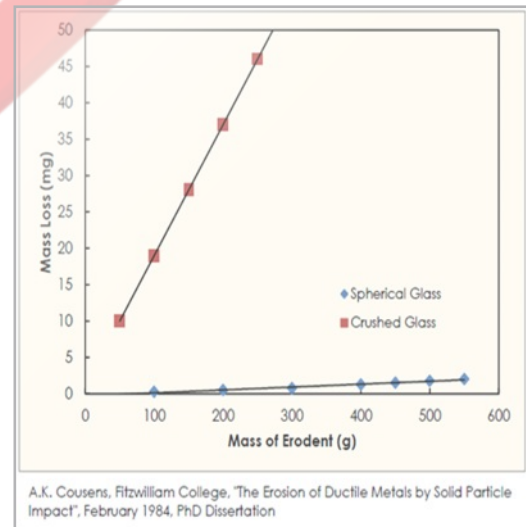
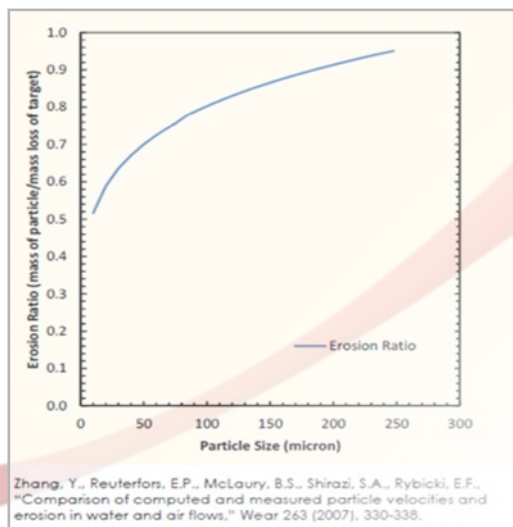
Importance of Particle Size AND Shape

Measuring particle concentration is very important, but in reality it only gives part of the picture.

Many common processes either require a specific particle size or can be optimized by knowing the particle size. Sometimes it is critical to the specification of an end product. Other times your chemical dosing or physical properties can be adjusted to optimize the process based on the sizing data.

Over the past several decades, there has been a growing understanding of the importance of particle shape to the ways in which particles interact physically and/or chemically with what they are in contact with. Sometimes, certain shapes are a goal for a product. Other times, particle shape can provide insight as to how particles form and/or where they come from. Measuring in 2 dimensions also means that particle size is measured in more than 1 direction which is critical, depending on the particle shape.

Process Performance



Process Understanding

Typical Mini Inflow Applications

Powder Analysis



CANTY provides particle size and shape analysis for powders. Unlike other technologies, dynamic imaging allows the 2D shape of every particle seen to be measured, providing greater analytical capability. Not every particle will be spherical, and the shape of these particles will greatly impact the performance of the powder. The Mini Inflow allows a suspension of these solids in any desired fluid ranging from water to oil to mother liquors and can be made with Hastelloy and Kalrez wetted material if needed. Typical configurations used include funnel feed, recirculation, and auto-dilution which are covered on the upcoming pages.

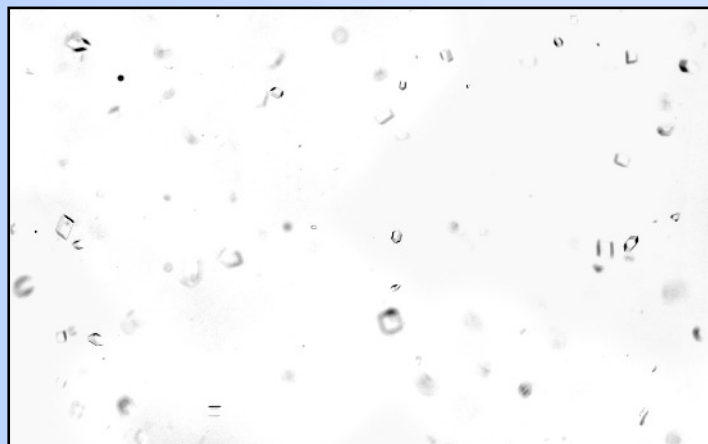
Crystallization

There are several areas within crystallization that CANTY can help with analysis:

While developing your process, it will be critical to know size AND shape of your crystals. CANTY's Mini Inflow measures over 40 shape and size parameter on every particle seen. If your concentration is too high, run the auto-dilution configuration and don't worry about human error impacting your results! During production, the main control point is seeding. CANTY can provide the size distribution and concentration of crystals during seeding, allowing you to make changes to your batch while there is still time. For large crystals, CANTY can provide accurate shape and size information. This may require dilution depending on concentrations. Oiling out can also be identified and studied.

Dissolution

Dissolution is used across many applications. It is often the beginning step in crystallization where the primary components are added as a solid and dissolved prior to the seeding step. The order and rate of addition of these solids has a significant impact on dissolution. The Mini Inflow allows a researcher the ability to study the order and rate of additions in order to optimise the dissolution of components and avoid false crystallization.



USP 1788/788

Regulations require many pharmaceuticals and associated manufacturing processes to undergo testing to quantify particulate matter via USP1788. This includes water for injection (WFI), tube spallation detection, single use bag particle count cleanliness, single use component particle count cleanliness, and single use assembled system testing for particle count. CANTY's Mini Inflow is perfect for performing this analysis either in samples brought to your lab or directly online.

Typical Configurations: **Jar/Bottle Feed**

For situations where samples are required to be pulled, CANTY's Mini Inflow can be configured to run samples from jars or vials either at-line or in the lab. After analysis, sample can run to another container or to waste.



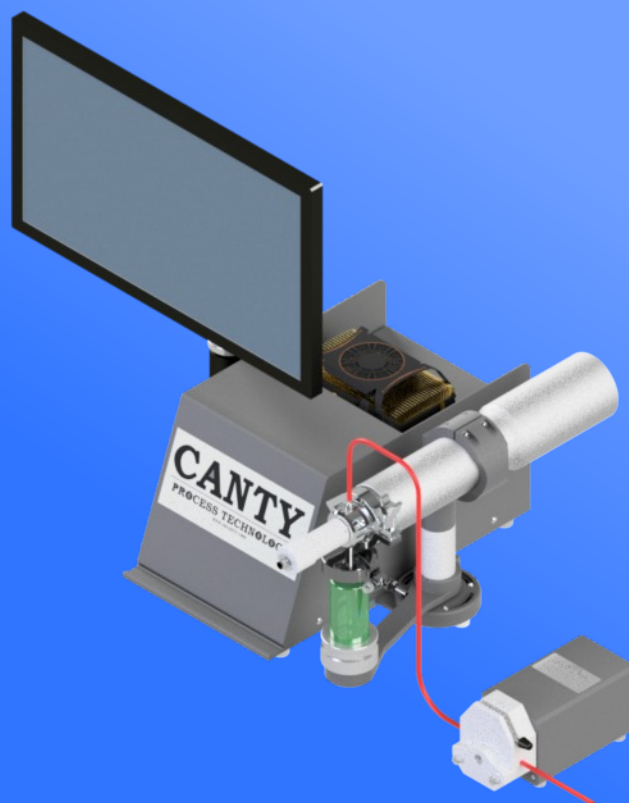
CANTY recognizes that every company uses vials or jars that may be unique in size and geometry. To accommodate, CANTY provides a wide range of sample tube lengths and spring cups, a wide gasket for sealing, and an adjustable arm height.

While a vision system can distinguish between a gas bubble and other particles, if a sample is too highly concentrated with gas, they can block the view of other particles. This may happen on samples in a highly viscous fluid. CANTY provides a vacuum pump that can automatically run before analysis to prevent too many bubbles.

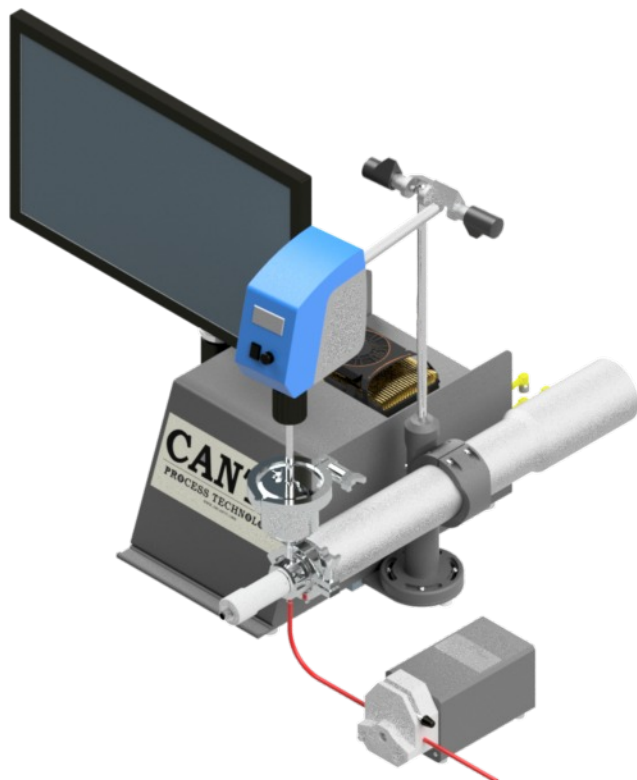
Labs tend to get very busy and require a lot of time from their skilled technicians. CANTY offers automated systems that can agitate, load, and run a cue of samples without operator intervention. Contact the factory for details.

Key Features:

- At-Line or Lab
- Adjustments to accommodate varying sample jar sizes and geometries
- Automated system available
- Can pull vacuum before running samples



Typical Configurations: **Funnel Feed**



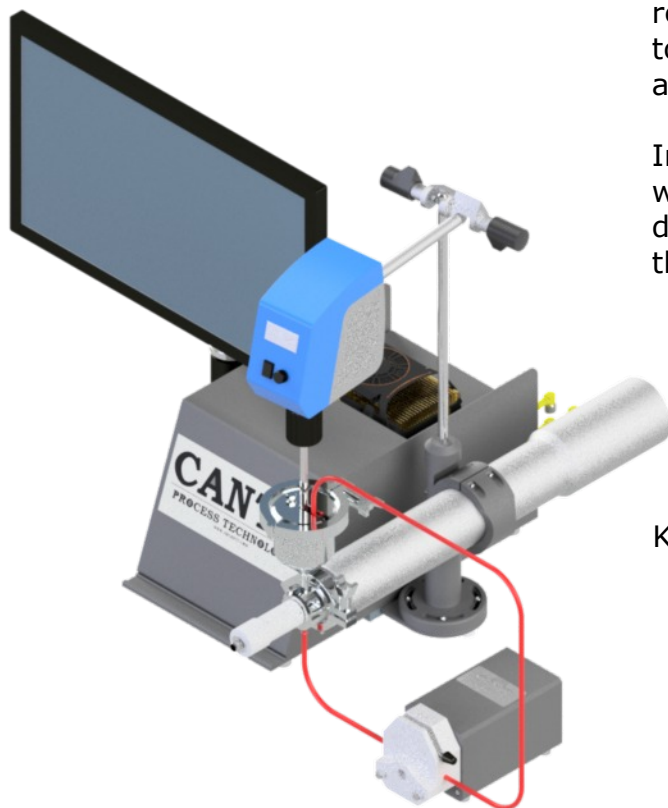
When a sample needs to be run of a solid or slurry, but dilution is not desired or needed, a sample can be run via the funnel feed configuration.

In this configuration, a sample is added to the vessel above the analyzer. The mixer keeps the sample well mixed and suspended. When analysis begins, the pump pulls the sample through the analyzer and to waste or another container.

Key Features:

- Simple to run
- Initial sample can be dry or a slurry
- Material runs through the analyzer before running into the pump

Typical Configurations: **Recirculation**



Similar to the funnel feed configuration, a recirculation setup allows you to add a sample to the vessel above the analyzer without additional dilution.

In this configuration, the sample is also kept well mixed and suspended by the mixer. The difference here is that the sample is returned to the vessel after passing through the analyzer.

Key Features:

- Material recirculates, allowing the user to measure changes over time
- Initial sample can be dry or a slurry
- Easily allows for dissolution studies

Typical Configurations: **Auto-Dilution System**

When is Dilution Needed?

When a process is too highly concentrated, particles begin to overlap. This overlap can make it impossible to distinguish where individual particles begin and end, reducing the accuracy of particle size analysis. To combat this, CANTY has developed a patented Auto-Dilution System.

Image of Undiluted Sample

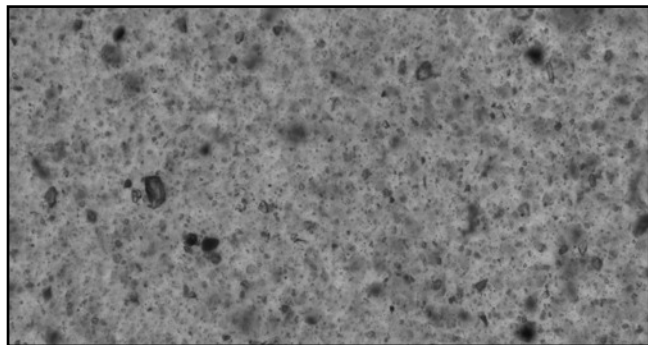
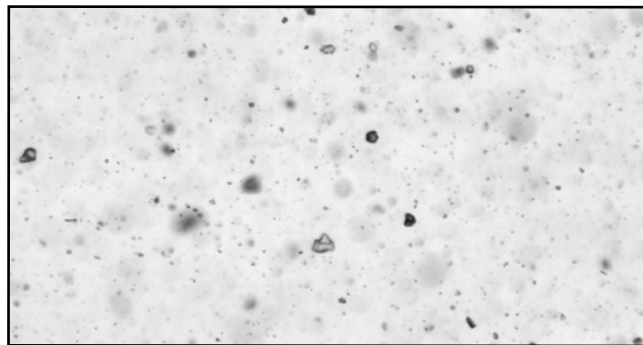
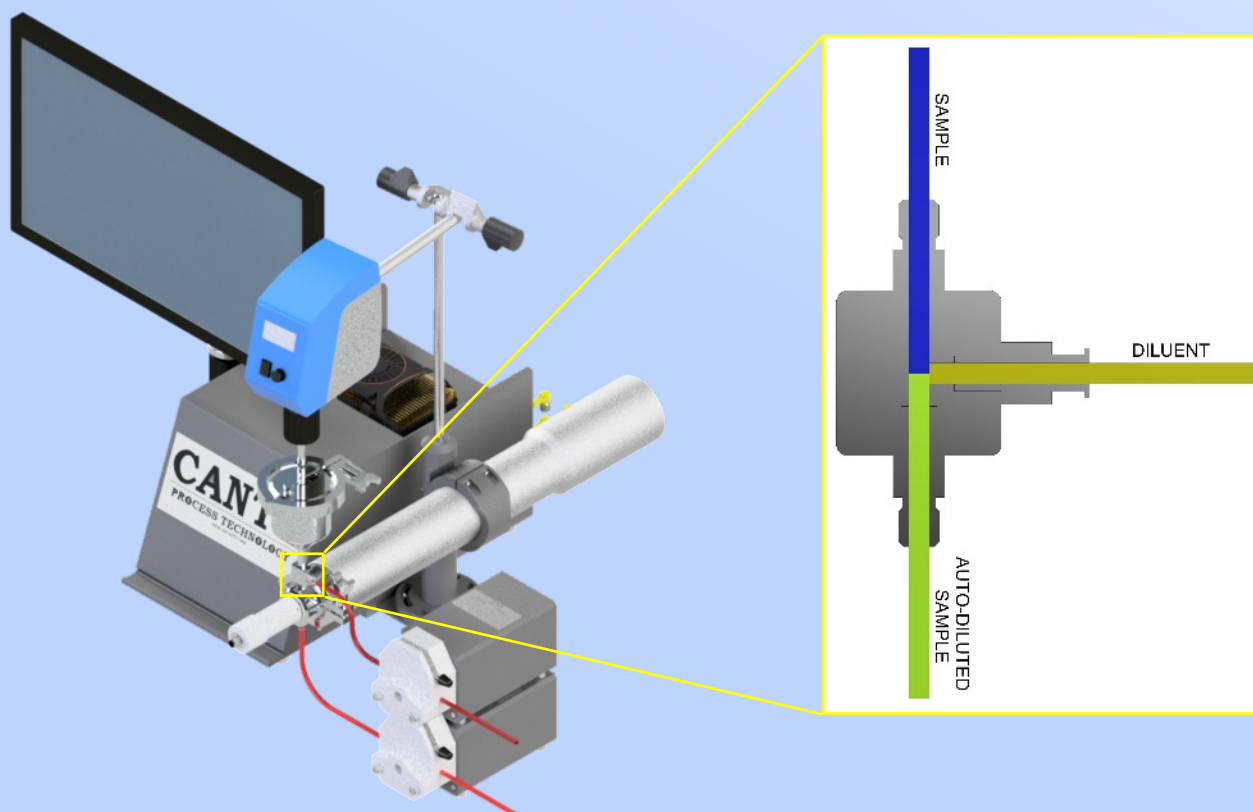


Image of Auto-Diluted Sample

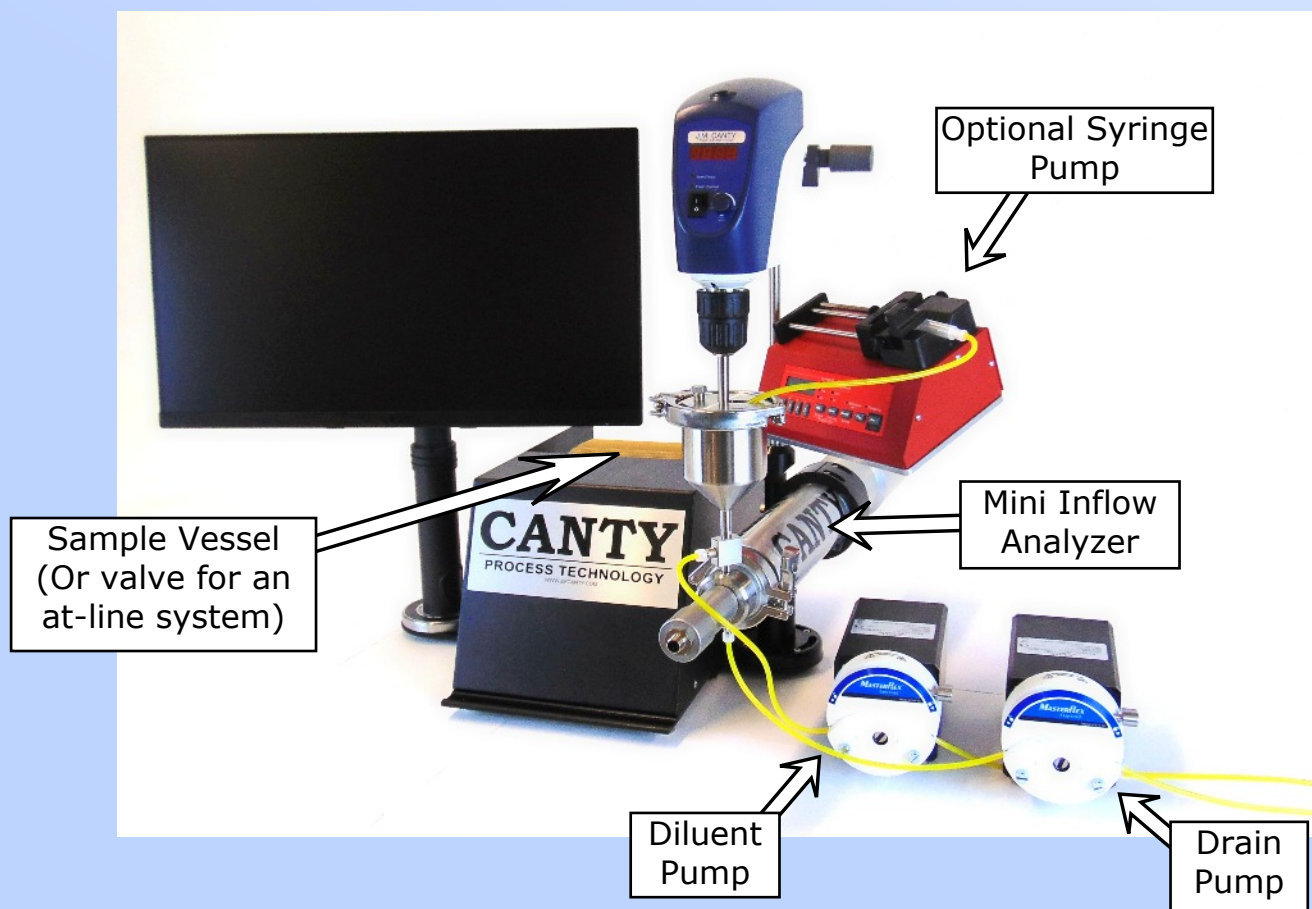


How does CANTY's Auto-Dilution Work?

CANTY's Auto-Dilution System meters in known quantities of diluent based on the images acquired by the camera system. When there is extra space between particles, the software will lower the diluent flowrate. Conversely, if the image becomes too crowded, the software increases the diluent flowrate.



Typical Configurations: **Auto-Dilution System** (Continued)



Sample Addition Options:

- Open
 - ☐ Samples can be directly added into the sample vessel before beginning analysis
- Syringe Pump*
 - ☐ Slurries can be metered out of a syringe and into the sample vessel over time throughout analysis
- Vibratory Feeder*
 - ☐ Dry samples are fed into the sample vessel over time throughout analysis

Key Features:

- On-line and at-line solutions
- Minimizes amount of diluent needed for a dynamic imaging analysis
- No human control required for dilution
- Can utilize any process-compatible diluents
- Can be used for any concentration

*Methods involving adding sample over time are useful for high density materials or for materials that do not mix well in the sample vessel.

Typical Configurations: **Online Auto-Sampling**

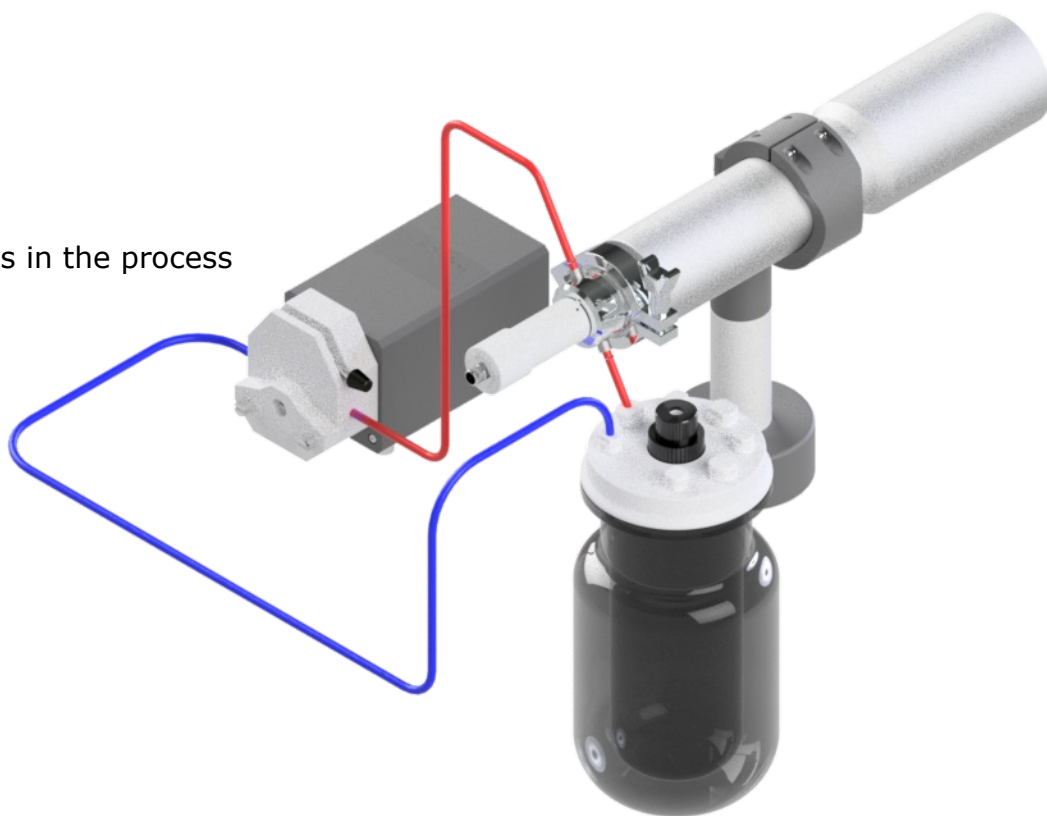


In an online auto-sampling configuration, the analyzer is mounted onto a nozzle that has a line that dips into the process. At regular intervals, a pump pulls a vacuum that causes process fluid to pull through the analyzer and either into additional tubing, or re-circulates back into the vessel.

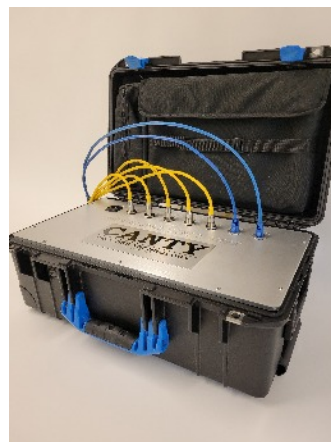
For many types of particles, running process fluid through a pump can damage those particles, resulting in an inaccurate analysis or causing harm to the particles after analysis. With the non-recirculation method, material never passes through a pump head.

Key Features:

- On-line
- Non-destructive
- CIP/SIP
- All material stays in the process



All configurations can be made available with a mobile PAT power supply or a Lab Core Unit



Comparison to Other Technologies

	CANTY Imaging	Laser Diffraction	Light Obscuration	Manual Sieving
Direct / Relative Measurement	DIRECT	RELATIVE	RELATIVE	DIRECT
Multi Dimension Size Measurement	YES	NO - 1D	NO - 1D	NO - 1D
Shape Characterization	YES	NO	NO	NO
Differentiation of Particle Types	YES	NO	NO	NO
Visual Verification	YES	NO	NO	LIMITED

Related CANTY Products

CANTY SolidSizer



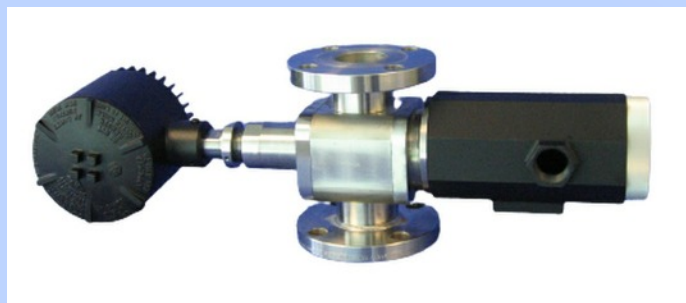
Refer to TA11500-1003

CANTY Crystalscope



Refer to TA10493-100

CANTY Inflow



Refer to TA10601-1

**CANTY'S GOAL IS TO PROVIDE EQUIPMENT TO ENHANCE PROCESS
UNDERSTANDING AND CONTROL. WE ACCOMPLISH THIS BY DESIGNING,
MANUFACTURING AND SERVICING THE FINEST EQUIPMENT IN THE WORLD**

CANTY

PROCESS TECHNOLOGY

SOME OF THE COMPANIES WE HAVE WORKED WITH

ABBOTT LABORATORIES

CELGENE

MERCK & CO.

ABBVIE

COVIDIEN

NOVARTIS

ALLERGAN

ELI LILLY & CO.

NOVO NORDISK

AMGEN

GILEAD SCIENCES

PFIZER

ASTRAZENECA

GLAXOSMITHKLINE

REGENERON PHARMACEUTICALS

BAXTER INTERNATIONAL

HUMAN GENOME

ROCHE

BAYER

JOHNSON & JOHNSON

SANOFI

BIOGEN

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SHIRE PHARMACEUTICALS

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