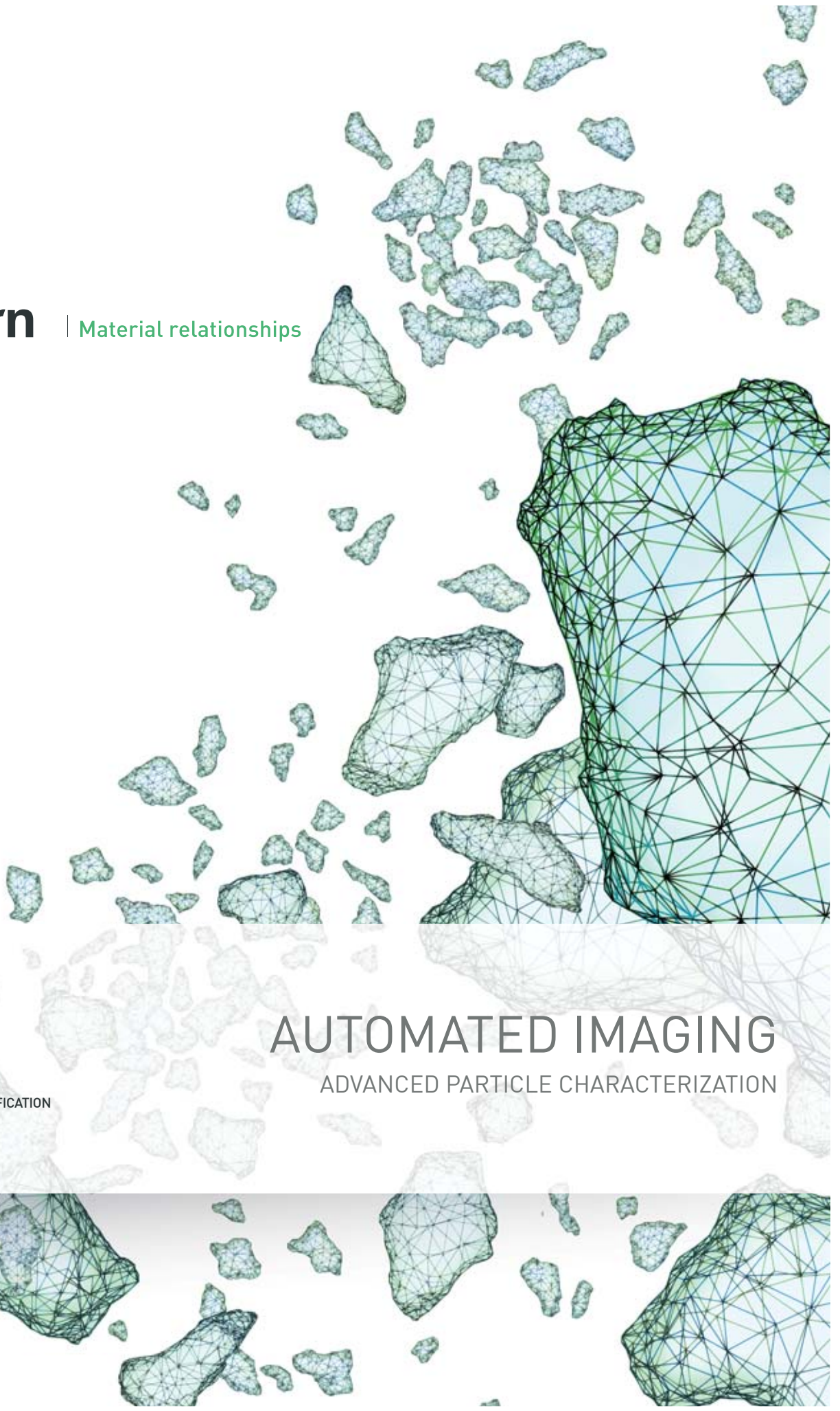# Malvern

Material relationships

PARTICLE SIZE

PARTICLE SHAPE

CHEMICAL IDENTIFICATION

AUTOMATED IMAGING

ADVANCED PARTICLE CHARACTERIZATION

INTRODUCTION

Automated imaging provides high resolution direct measurement of the size, shape and other properties of particles from below one micron up to several millimeters in size. It is often used in conjunction with other particle characterization techniques, to gain a deeper understanding of the sample or to cross-validate particle sizing methods.

Malvern Instruments has a range of automated imaging instrumentation which can be used to solve particle characterization problems such as:

- Measurement of shape differences where particle size alone does not allow differentiation

- Detection and enumeration of agglomerates, oversized particles and contaminant particles

- Size measurement of non-spherical particles such as needle shaped crystals

- Automation of manual methods such as microscopy

- Physical characterization of individual components within a mixture

- Cross-validation of particle size measurements such as laser diffraction.

Why consider automated imaging?

Better understanding of particle properties

Automated imaging can provide data on particle size, shape, transparency and chemical identity in one measurement. In contrast to ensemble-based techniques such as laser diffraction, each individual particle in the sample is measured one-by-one, providing high resolution detailed information. This is often used to complement data from other particle sizing techniques.

More robust than manual methods

Automated imaging instruments typically measure tens to hundreds of thousands of particles in the same amount of time needed to measure a very small number by manual microscopy. This makes the measurement much more statistically robust. In addition, all the particle images are automatically and objectively captured, measured, analysed and classified for inclusion/exclusion, vastly reducing any operator subjectivity.

A picture paints a thousand particles

Individual images of every particle are stored for each measurement and are easily displayed together with the size and shape data for the sample. This provides a powerful visual verification of results, such as confirming the presence of agglomerates in the sample dispersion, or the presence of unwanted particles.

WHAT IS AUTOMATED IMAGING?

Automated imaging techniques use a digital camera to capture 2D images of a dispersed particulate sample. Individual particle images are identified using digital thresholding techniques, and then analyzed to determine their particle size, particle shape and other physical properties such as transparency.

Statistically representative distributions can be constructed by automatically analysing tens to hundreds of thousands of particles per measurement providing valuable information on the sample as whole. The measurement process is automated through electronic standard operating procedures (SOPs)

which control and record all the important measurement parameters. These allow reproducible measurements to be made from operator to operator and from instrument to instrument.
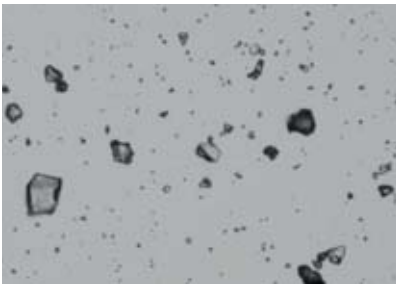
Sample presentation
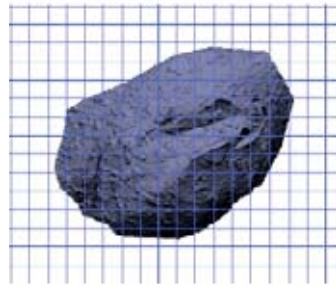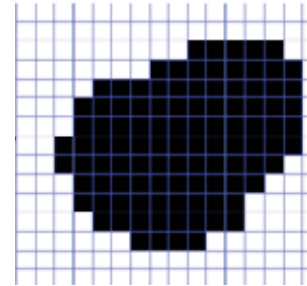

Image Capture

Image analysis

Static imaging or dynamic imaging?

Automated imaging instrumentation divides into static imaging systems, which require a stationary dispersed sample, and dynamic imaging systems where the sample flows past the image capture optics. Static imaging systems are more flexible in terms of sample presentation and having the ability to reanalyze exactly the same particles, whereas dynamic imaging systems offer advantages in speed of measurement and ease of sample preparation.

Measuring the appropriate particle size parameters

Automated imaging measures many different size and shape parameters from a single particle image. The relevance of each parameter will depend upon the type of sample and the kind of information required. Traditionally, particle size is most often represented by a single value such as the diameter of a sphere with an equivalent volume to the particle (laser diffraction). This may be appropriate for many samples and

automated imaging allows us to measure related parameters such as the diameter of a circle with the equivalent area (circle equivalent or CE diameter). However, for non-spherical and irregular particles automated imaging allows us to more appropriately describe their size in terms of other parameters such as particle length and width.
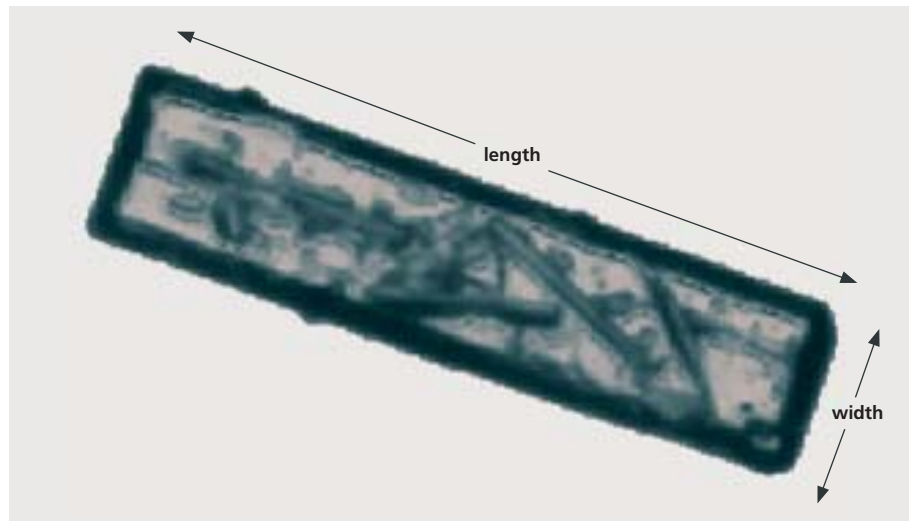
PARTICLE SHAPE, WHEN SIZE ALONE ISN'T ENOUGH

For many applications, a particle size distribution provides adequate information about the sample. However, for some applications particle shape can provide more appropriate or complementary information. There are three main categories where this is relevant.

Single particles or agglomerates?

Many particle sizing methods require complete dispersion of any agglomerates in the sample in order to make an appropriate measurement. Being able to view individual images in the dispersion and analyze them in terms of their outline shape allows the user to determine whether or not agglomerates are present and the extent of agglomeration in the sample.

Regular or elongated?

Size reduction by milling can change the shape as well as the size of particles. This may have desirable or undesirable consequences for the processing behaviour and final properties of the material. By measuring shape parameters such as elongation or circularity, the overall sample form can be monitored and changes made to the process if required.

Rough or smooth?

The effectiveness of abrasive powders and powder flow can both be influenced by how rough or smooth the surfaces of the particles are. For example shape parameters that give information on the overall form as well as the outline of particles are useful in assessing if an abrasive powder has become worn, or if a powder is more or less likely to stick in a hopper.

| Single particle | Agglomerate | Regular | Elongated | Rough | Smooth |

Beyond size and shape

Although automated imaging is a 2D technique, information about other physical properties of a particle such as particle thickness, or even particle heterogeneity can be determined from the amount of light passing through or being reflected from the surface of the particle. Here it is important to capture greyscale rather than binary 'shadow' images of the particle in order to access this information.

Particles in a mixture

Sometimes a material may be composed of different types of particles and it may be necessary to understand the composition in terms of the individual components. In some cases this may be possible by classing the different types of particle according to their shape. In other instances a combination of automated imaging and chemical identification technique such as Raman spectroscopy may be required.

| Dark | Light |

| Component 'A' | Component 'B' |
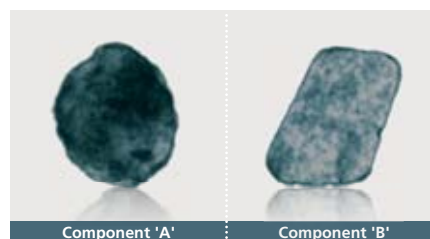
AUTOMATED IMAGING PRODUCT RANGE OVERVIEW

SYSMEX **FPIA-3000**

Rapid particle size and shape analysis of suspensions

PARTICLE SIZE

PARTICLE SHAPE

The Sysmex FPIA-3000 is a fully automated dynamic flow particle imaging instrument for the rapid and reliable measurement of the shape and size of particles in suspension.

- Particle size and shape from 0.8μm to 300μm
- Sonication probe option to aid sample dispersion
- Simple automated SOP operation
- Rapid measurements ideal for QA/QC.

MORPHOLOGI **G3**

Advanced particle characterization made easy

PARTICLE SIZE

PARTICLE SHAPE

The Morphologi G3 provides an advanced yet easy to use particle characterization tool for measuring the particle size and shape of dry powders, particulates on membrane filters and suspensions.

- Particle size and shape from 0.5μm to 1000μm
- Integrated dry powder disperser option
- Powerful automated SOP operation
- Flexible instrument suitable for both R&D and QA/QC.

MORPHOLOGI **G3-ID**

Automated measurement of particle size, shape and chemical identity

PARTICLE SIZE

PARTICLE SHAPE

CHEMICAL IDENTIFICATION

The Morphologi G3-ID brings a significant additional capability to the Morphologi range of instruments – the ability to provide chemical identification of individual particles using Raman spectroscopy.

- Integrates particle size, shape and chemical identity in one platform
- Fully automated Raman chemical classification of thousands of particles
- Automated SOP operation
- Powerful additional capability, ideal for R&D.

CHOOSING THE RIGHT AUTOMATED IMAGING SOLUTION

When choosing the most appropriate automated imaging solution for your needs, there are a number of questions to consider:

What types of material do I need to measure?

Will I only measure samples as a wet dispersion or do I need the flexibility to measure dry powders as well?

Do I need to measure samples collected on a specific substrate such as a filter membrane?

Over what particle size range do I need to measure?

Where will the instrument be used?

Will it be used in central R&D as a shared resource where there are many users and different types of samples might be measured?

Will it be used in a QC environment where simple method setup and rapid measurement times are more important?

Will my needs change in the future?

Will different types of sample be measured in the future, such as dry powders or suspensions in solvents?

Will options such as chemical identification be a valuable enhancement of capability?

QUICK REFERENCE GUIDE

To help you choose the most appropriate instrument from the Malvern automated imaging product range, we have put together this quick reference guide below:

Instrument	Sysmex FPIA-3000	Morphologi G3	Morphologi G3-ID
Technology	Dynamic imaging	Static imaging	Static imaging + Raman spectroscopy
Particle properties	Size, shape, transparency, count per frame	Size, shape, transparency, count, location	Size, shape, transparency, count, location, chemical indentity
Particle size range	0.8 – 300µm	0.5 – 1000µm	Sample and sample substrate dependent
Sample illumination	Diascopic, brightfield	Diascopic, episcopic, brightfield, darkfield	Diascopic, episcopic, brightfield, darkfield
Wet dispersion	Sheath flow cell	Microscope slide/wet cell	Microscope slide
Sonication option	■	-	-
Solvent option	■	-	-
Dry dispersion option	-	■	■
Membrane filter option	-	■	■
SOP operation	■	■	■
Typical measurement time	<3 minutes	10 - 30 minutes	30 mins – 12 hours
Manual analysis	-	Return to selected particle	Return to selected particle
Z-stack	-	■	■
Timed frame capture	-	■	■
CFR21 part 11 option	■	■	■
Upgrades	-	Morphologi G3-ID	-

■ Yes   - No

SYSMEX **FPIA-3000**

Rapid particle size and shape analysis of suspensions

Designed with the needs of a busy QC lab in mind, the Sysmex FPIA-3000 makes size and shape analysis of particles in suspension a straightforward and routine task.

All of the sample preparation, measurement and cleaning can be taken care of by the instrument itself. Equally the unparalleled image quality and flexible software makes it a highly effective R&D tool.

- Particle size and shape of wet suspensions from 0.8μm to 300μm
- Fully automated analysis and self-cleaning in less than 3 minutes
- Unique sheath flow technology keeps even the smallest particles in sharp focus
- Simple easy-to-use SOP operation, ideal for routine QA/QC analysis
- In-built sonication option for difficult to disperse samples
- Solvent compatible version available
- 21 CFR part 11 option.

Unrivalled dynamic imaging performance

The Sysmex FPIA-3000 employs a unique sheath flow mechanism for particle size and shape measurements of wet suspensions, ensuring that good image focus, a prerequisite for high quality measurements, is maintained even for small particles. This is essential where particle shape below 10 microns is important such as analysis of abrasives and toner particles.

Simple to use and maintain

The Sysmex FPIA-3000 is extremely straightforward to use, requiring minimal operator sample preparation and providing full automation of the measurement and cleaning operations. The sheath flow mechanism prevents the fouling of optical windows that is sometimes seen on other dynamic imaging systems. made to the process if required.

Rapid and robust results

The Sysmex FPIA-3000 is ideal for routine analyses in a QC environment. Sample introduction, measurement and cleaning takes less than 3 minutes per measurement. Automated SOP control of all the measurement parameters provides robust and repeatable measurement methods.
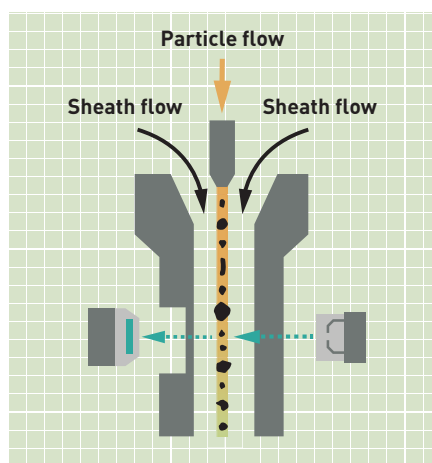
HOW THE SYSMEX FPIA-3000 WORKS

Introduce sample

Capture particle images
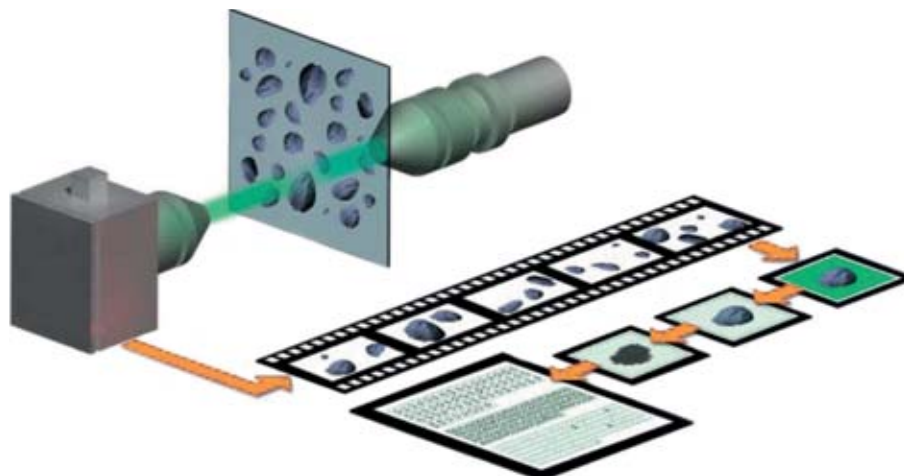
Measure size and shape

Keeping particles in focus

The Sysmex FPIA-3000's unique sheath flow mechanism keeps all the particles flowing through the measurement cell in a very precisely defined flow path. This ensures that even the smallest particles in the sample stay at the focal plane of the measuring optics, delivering unrivalled image quality for particles below 10μm in size. An added benefit of the sheath flow is that it prevents particles from the sample touching the optical windows, substantially reducing particle wear and window fouling.

Why choose the Sysmex FPIA-3000?

Straightforward routine operation

Automated SOP operation means that the Sysmex FPIA-3000 can automatically takes care of all stages of the measurement process from sample preparation, measurement and cleaning through to results analysis. This means less time spent on supervising and maintaining the instrument and more time available for other tasks.

Traceable and validatable performance

The Sysmex FPIA-3000 is calibrated and validated in the factory using a range of traceable latex particle size standards. Daily verification of performance takes just minutes and ensures measurement validity for QC analysis.

Options to suit your needs

For water soluble materials such as many pharmaceutical actives, a solvent compatible version of the Sysmex FPIA-3000 is available. There is also an in-built sonication option for samples that are difficult to disperse in aqueous media. High magnification (20x) and low magnification (5x) lens options can be added with the standard 10x measurement lens.

SYSMEX FPIA-3000 APPLICATIONS

The Sysmex FPIA-3000 is used in many applications where particle size and shape of powders, slurries and suspensions are important. Some key applications include:

- Monitoring of abrasive slurries e.g SiC wiresaw for silicon wafer production

- Detection of agglomerates in pharmaceutical suspensions such as eye formulations

- Quality control of particle size and shape in toners

- Identification of oversize particles in parenterals and injectables such as vaccines
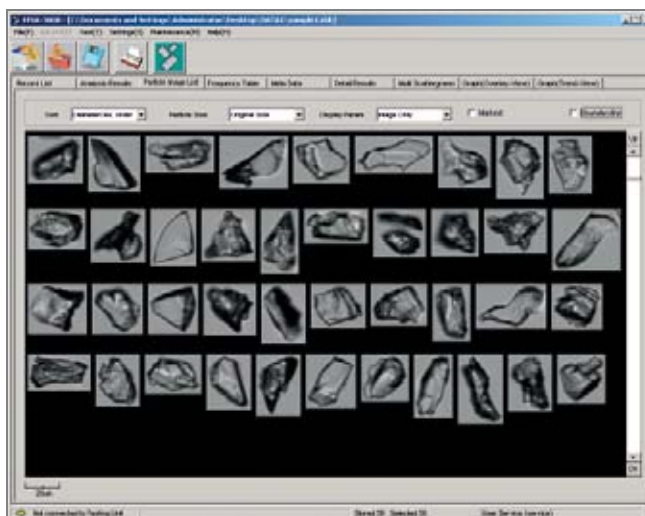
SYSMEX FPIA-3000 SPECIFICATIONS

Technology	Dynamic flow particle imaging	
Particle Size Range	0.8µm – 300µm*	
Particle properties measured	Size, shape, transparency	
Sample dispersion	Stirred with ultrasound option	
Particle flow	Hydrodynamic focused sheath flow	
Sheath liquid (standard)	Aqueous 'Particle Sheath Reagent', methanol, ethanol, isopropyl alcohol, ethylene glycol solution (25%)	
Sheath liquid (solvent option)	Compatible with most commonly used solvent dispersants such as: Toluene, acetone, heptane and hexane	
Typical measurement time	<3 minutes including self-cleaning cycle	
Illumination	White light, brightfield, 60Hz strobe	
Detector	CCD array	
Lens size ranges	High power (x2)	Low power (x0.5)
10x (standard)	1.5µm – 40µm	8µm – 160µm
20x (option)	0.8µm – 20µm	4µm – 80µm
5x (option)	3.0µm – 80µm	16µm – 300µm
Dimensions	900mm (W) x 475mm (D) x 455mm (H)	
Weight	59.5kg	
Power requirements	100/240V ac 50/60Hz	
Notes	*Sample dependent	

MORPHOLOGI **G3** OVERVIEW
Advanced particle characterization made easy

The Morphologi G3 measures the particle size and shape of dry powders, wet suspensions and particulates on filter membranes using the technique of automated static image analysis. The instrument is designed with the diverse needs of a multidisciplinary R&D lab in mind, while automation of analysis using SOPs makes it the ideal replacement for costly and time-consuming manual microscopy measurements.

KEY FEATURES INCLUDE:

- Particle size range from 0.5µm to 1000µm

- Integrated dry powder dispersion option

- Automated SOP control from sample dispersion to results analysis

- Rapid automated particle counting on membrane filters

- Wet cell accessory for suspensions (>10µm)

- Excellent quality microscope images ensuring accurate characterization

- Advanced manual microscope control mode

- Powerful and intuitive software interface

- 21 CFR part 11 software feature key.

One solution for many applications

The Morphologi G3 is designed to be flexible, measuring particle size and shape of dry powders, wet suspensions, and particulates on filter membranes all on the same instrument. The incorporation of an advanced manual microscope interface in the software and contrast enhancement options such as polarizers and DIC allows you to get the best value out of a shared laboratory resource.

Results you can rely upon

Robust, repeatable measurement methods are achieved via simple SOP driven operation, including a unique dry powder sample dispersion option. All critical factors affecting the results are carefully controlled and audited, from dispersion conditions, sample focus and illumination through to data analysis and reporting.

Save time and free up resource

Compared to manual methods, substantial time savings can be achieved for routine analyses, where not only is the measurement time less, but the need for lengthy specialist training is also greatly reduced. An additional benefit of automated unattended SOP operation is that it allows users to get on with other tasks while the instrument is measuring.

WHY CHOOSE THE MORPHOLOGI G3?

Easy, reproducible sample dispersion

Appropriate dispersion of the individual particles and agglomerates within a sample is critical to achieving meaningful results. Good spatial separation and representative sampling of the particles is required. An integrated dry powder disperser option makes preparing dry powder samples simple and reproducible. A precise amount of sample is dispersed automatically using a unique compressed air dispersion mechanism controlled from within the software for reproducible dispersions every time. A range of accessories also supports manual preparation of samples on microscope slides, in wet suspensions or on membrane filters.

High quality measurements

After sample dispersion, the next most important factor affecting your results is the quality of the particle images captured. The Morphologi G3 uses infinity corrected microscope optics and high signal to noise CCD camera to provide grayscale image quality unrivalled in a particle characterization instrument. In addition every measurement has calibration checks for the camera pixel size and sample illumination intensity, providing particle measurement methods that are both robust and repeatable.

Powerful yet intuitive software

From setting up and running fully automated SOP methods to in-depth reviewing of results and producing custom reports, the Morphologi G3 software provides a flexible yet intuitive interface that allows you to get the most out of your investment. A key feature of the software is the particle view tab, which allows the user to view individual particle images against a scattergram plot of any two size and shape variables. This provides a way to gain an in-depth understanding of your sample as well as providing a quick and easy way to create classifications based upon the size and shape of the particles. A comprehensive range of pre-formatted reports can be customised to show your final data in the way that you want, including statistical distributions, trend plots, particle images and custom parameters.
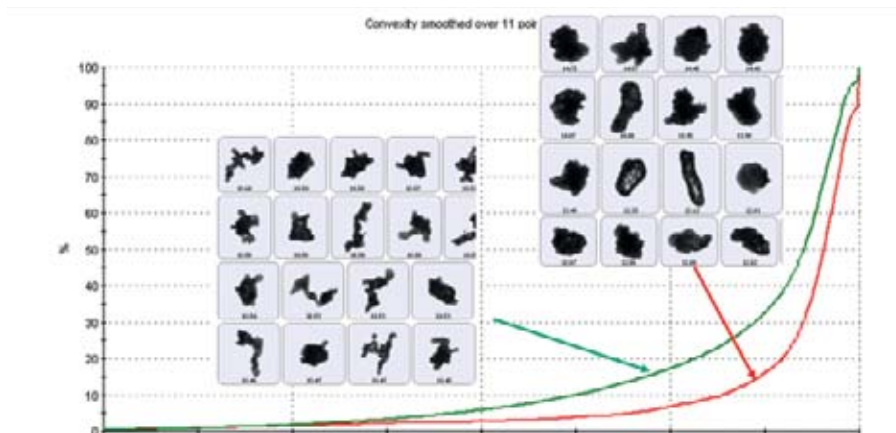
Taking a closer look

A powerful manual microscope interface allows the instrument to return to the selected particle for more in-depth analysis at higher or lower magnifications. The ability to change sample illumination, use contrast enhancement accessories and colour mode can all be used to study materials that have specific optical properties such as birefringent crystals.
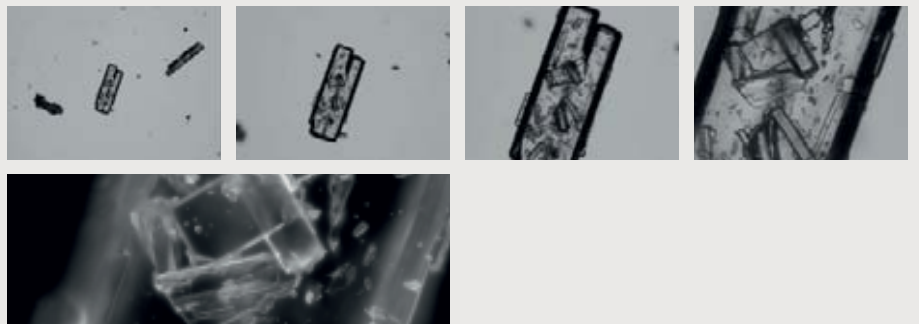
MORPHOLOGI G3 APPLICATIONS

- Discovery/R&D screening tool ie. only milligrams of sample needed
- Crystallization engineering
- Formulation development and optimization
- Process scale-up and optimization
- Troubleshooting and root cause analysis in manufacturing
- Automation of microscopy methods e.g. detection and enumeration of foreign particulates
- Validation of QC particle sizing methods e.g. laser diffraction.

MORPHOLOGI G3 SPECIFICATIONS

Technology	Static automated imaging
Particle Size Range	0.5µm – 1000µm*(upper limit may be extended up to 10mm for some applications*)
Particle properties measured	Size, shape, transparency, count, location
Particle size parameters	Circle equivalent (CE) diameter, length, width, perimeter, area, max distance, sphere equivalent (SE) volume
Particle shape parameters	Aspect ratio, circularity, convexity, elongation, high sensitivity (HS) circularity, solidity
Particle transparency parameters	Intensity mean, intensity standard deviation (STD)
Integrated sample dispersion unit option (Morphologi® G3S only)	For fully automated dispersion and measurement of dry powders. Manual or SOP control of dispersion pressure, injection time and settling time.
Sample presentation options	4 slide holder for standard microscope slides
	2 slide holder for large microscope slides
	Large glass plate for integrated dry powder dispersion option
	Wet cell for large particles in suspension
	25mm and 47mm dia. holders for membrane filters
Illumination	White light, brightfield diascopic and episcopic, darkfield episcopic
	Polarizer/analyser and DIC contrast enhancement options
Detector	5M pixel 2592 x 1944 colour CCD array, pixel size 2.78µm x 2.78µm
Optical system	Nikon CFI 60 brightfield/darkfield system
Lens Particle size range in µm (nominal)	2.5x 5x 10x 20x 50x 13-1000 6.5-420 3.5-210 1.75-100 0.5-40
Dimensions	440mm (W) x 760mm (D) x 700mm
Weight	80kg approx.
Power requirements	100-240V ac 50/60Hz 5.0A
Notes	*Sample and sample substrate dependent

MORPHOLOGI **G3-ID**

Automated measurement of particle size, shape and chemical identity

The Morphologi G3-ID provides a unique capability, combining automated static imaging features of the Morphologi G3 with chemical identification of individual particles using Raman spectroscopy. This fully automated instrument is designed to allow both particle characterization scientists with limited spectroscopy experience and more experienced spectroscopists to get an in-depth understanding of their particulate samples.

KEY FEATURES

- Measures particle size, shape and chemical identity in one platform

- Automates Morphologi G3 with Kaiser Optical Systems inc. RamanRxn1 spectrometer.

- Integrated dry powder dispersion option

- Simple SOP operation from sample dispersion through to size, shape and chemical analysis

- Automatic selection, targeting and chemical classification of 1000's of individual particles

- Export function for third party forensic library investigations

- Single point manual targeting

- Powerful and intuitive software interface

- 21 CFR part 11 software feature key.

Unique solution

The Morphologi G3-ID integrates the measurement of particle size, shape and chemical identity in one instrument providing a powerful analytical tool complementary to existing particle characterization techniques. This allows the chemical identity of individual particles to be used to measure the particle size and shape of specific chemical components in a mixture.

Simple automated operation

The instrument has been specifically designed to be used by non-experts in spectroscopy. Automated SOP operation, allows control of sample dispersion, size, shape and chemical analysis in one simple method. This provides a route to robust, operator independent results.

Save time and free up resource

Compared to manual Raman spectroscopic methods, the chemical analysis of a large number of particles with the Morphologi G3-ID delivers substantial time savings. An additional benefit of automated unattended SOP operation is that it allows users to get on with other tasks while the instrument is measuring during experiments that might take several hours.

HOW THE MORPHOLOGI G3-ID WORKS

The Morphologi G3-ID workflow is divided into three distinct steps: sample preparation, measurement of particle size and shape and finally chemical identification of individual particles. Each of the steps can be carried out individually and then combined later into a single SOP to provide complete automation of your final method.

Sample Preparation

Particle size and shape

Chemical identification

Dry powders, suspensions and filters

The Morphologi G3-ID can accept most of the same sample types measurable on the Morphologi G3. Sample substrates that are suitable for Raman chemical analysis are provided for material prepared on microscope slides, including suspensions, and for the automated dry powder dispersion option. Particulate samples collected on filter membranes can also be measured provided that the filter material is appropriate for Raman analysis.

Why choose the Morphologi G3-ID?

Particle size and shape with no compromise

The instrument automatically measures the size and shape of particles in a dispersed sample in exactly the same manner as the Morphologi G3. This ensures there is no compromise on the reliability of the particle size and shape data, which is not the case with many chemical mapping and imaging techniques.

Objective and efficient targeting of particles for chemical ID

One of the main advantages of the Morphologi G3-ID is having the ability to select the particles for automated chemical identification based upon their size and/or shape. This removes any operator subjectivity ensuring representative sampling as well as allowing more efficient use of instrument time by only spending time collecting Raman spectra from particles of interest.

Automated chemical identification and classification

The instrument will automatically find the selected particles and collect a Raman spectrum from the center of each one. Chemical identification of individual particles based upon established spectroscopic algorithms is incorporated in the Morphologi G3-ID software. This allows enumeration of defined classes of particles as well as the measurement of component specific characteristics in a blend, such as the particle size distribution of an active ingredient.

MORPHOLOGI G3-ID APPLICATIONS

The MorphologiG3-ID is ideally suited to solving complex particle characterization problems where particle size and shape do not provide sufficient information. Typical examples include:

Particle size of a specific ingredient

Measuring the size and or shape of particulates of a specific chemical species in a mixture such as a powder blend or suspension. e.g. nasal sprays and asthma inhalers

Contaminant identification

Providing chemical identification capability of contaminant or suspicious particles in a blend, suspension or collected on a filter membrane. e.g. parenteral and injectable medicines.

MORPHOLOGI G3-ID SPECIFICATIONS

Technology	Static automated imaging combined with Raman spectroscopy		
Morphological analysis	**Static automated imaging**		
Particle Size Range	0.5µm – 1000µm* (upper limit may be extended up to 10mm for some applications*)		
Particle properties measured	Size, shape, transparency, count, location		
Particle size parameters	Circle equivalent (CE) diameter, length, width, perimeter, area, max distance, sphere equivalent (SE) volume		
Particle shape parameters	Aspect ratio, circularity, convexity, elongation, high sensitivity (HS) circularity, solidity		
Particle transparency parameters	Intensity mean, intensity standard deviation (STD)		
Integrated sample dispersion unit option (Morphologi® G3S-ID only)	For fully automated dispersion and measurement of dry powders. Manual or SOP control of dispersion pressure, injection time and settling time.		
Sample presentation options	4 slide holder for standard microscope slides 2 slide holder for large microscope slides Large glass plate for integrated dry powder dispersion option Wet cell for large particles in suspension** 25mm and 47mm dia. holders for membrane filters		
Illumination	White light, brightfield diascopic and episcopic, darkfield episcopic Polarizer/analyser and DIC contrast enhancement options**		
Detector	5M pixel 2592 x 1944 colour CCD array, pixel size 2.78µm x 2.78µm		
Optical system	Nikon CFI 60 brightfield/darkfield system		
Lens	2.5x 5x 10x 20x 50x		
Particle size range in µm (nominal)	13-1000 6.5-420 3.5-210 1.75-100 0.5-40		
Chemical analysis	**Raman spectroscopy**		
Size range for chemical ID	Measurement lens, sample and sample substrate dependent		
Raman spectometer	Kaiser Optical Systems Inc. RamanRxn1		
Spectral performance	150cm^{-1} to 1850cm^{-1}, 4cm^{-1} resolution in mid-range		
Laser specifications	Wavelength 785nm, power output from spectrometer <500mW, power output at sample >10mW, laser spot size 3µm at 50x magnification		
Laser safety	INVISIBLE LASER RADIATION AVOID EXPOSURE TO BEAM CLASS 3B LASER PRODUCT		
Chemical identification method	Spectral correlation		
System	**Main instrument**	**Spectrometer**	
Dimensions	440mm (W) x 760mm (D) x 750mm (H)	584mm (W) x 448mm (D) x 203mm (H)	
Weight	80kg approx.	27.7kg	
Power requirements	100-240V ac 50/60Hz 6.0A		
Notes	*Sample and sample substrate dependent **Morphological analysis only		

Malvern

MRK1900-01

Malvern Solutions: Advanced technology made simple – distributor details