micromeritics®
Effective Solutions for Material Characterization

QBD SOLID FRACTION ANALYSIS IN ROLLER COMPACTION OPERATIONS

ACCUPYC II 1345 GAS PYCNOMETER GEOPYC 1365 ENVELOPE & T.A.P. DENSITY ANALYZER

THE IMPORTANCE OF SOLID FRACTION DATA IN ROLLER COMPACTION OPERATIONS

Roller compaction is a continuous dry granulation process to increase the bulk density and uniformity of powders into free flowing granules used in downstream manufacturing operations. It is a complex procedure due to the diversity of available powder blends and the control and adjustment parameters involved in the process. The character and homogeneity of the produced ribbon is controlled by a number of factors, such as the properties of the individual powders themselves, roll speed, roll gap/nip angle, and feeding speed; all of which subsequently determine the character of the produced granules (size distribution, density and flow behavior).

It is critical to produce uniform and specified ribbon densities throughout the process, as well as throughout the ribbon itself. This is important in order to achieve analogous tensile strengths and desired particle size distributions of the milled materials. Specified ribbon densities can be achieved by maintaining equivalent compaction pressure applied by the rolls on the ribbon for a specified gap distance and speed. In pharmaceutical operations, the roller compaction process has significant effect on particle size distribution, porosity, flowability in downstream operations, homogeneity, compactability and compressibility of the Active Pharmaceutical Ingredient (API), additives/excipients. These factors influence dissolution profiles, disintegration time, and hardness of the produced solid dosage form.

Regulatory agencies worldwide are now emphasizing the employment of a Quality by Design (QbD) approach. Companies are being required to show a greater understanding of the way in which variability in raw materials, process design and operating conditions affect final product quality and use this knowledge to implement effective quality control strategies. To date, roller compaction operations have utilized mostly mathematical modeling and operator experience as the identified process controls.

SOLID FRACTION

Solid Fraction, determined through data driven instrumental methods, is an excellent path to achieve roller compaction operations that incorporate a QbD policy. Solid Fraction can be used as an important Critical Process Parameter (CPP) and is determined using the following formula:

$$SF = \frac{P_e}{P_o}$$

SF= Solid Fraction (relative density)
P_e = envelope density of the ribbon
P_o = true density of the granules

While skeletal and envelope volume measurements are significant in their importance as individual quantities, their combination permits the pharmaceutical scientist to also accurately calculate percent porosity. With this data a process engineer or quality assurance scientist can have greater knowledge of their process for improvement in both quality of product and optimization of the manufacturing process.

Combining the Micromeritics AccuPyc pycnometer and the Micromeritics GeoPyc envelope density analyzer can achieve data driven, instrumental analysis to employ Solid Fraction as a CCP in pharmaceutical densification operations.

GEOPYC 1365

ENVELOPE DENSITY ANALYZER

- Highly accurate and reproducible results
- Fast operation in a small bench-top instrument
- Fully automated data acquisition and reporting
- Nondestructive analysis maintains sample integrity
- Intelligent touch panel for ease of operation and reporting

The Micromeritics GeoPyc envelope density analyzer employs a unique displacement measurement technique that uses DryFlo, a quasi-fluid composed of small, rigid spheres having a high degree of flow-ability. The sample is placed in a bed of DryFlo which is agitated and gently consolidated about the sample. The GeoPyc collects the displacement data, performs the calculations, and displays or prints the results.

The unit also reports percentage porosity and specific pore volume when absolute density information (density excluding pore and small cavity volume obtained from a Micromeritics AccuPyc II pycnometer) is entered.

T.A.P. DENSITY OPTION

The GeoPyc Transverse Axial Pressure (T.A.P.) density option obtains precise results comparable to conventional tap density analyzers, only it does it faster, quieter, and with a higher degree of reproducibility.

When equipped with the T.A.P. density option, the GeoPyc measures the packing volume and calculates the bulk density of granular and powdered samples, including pharmaceutical and electrochemical materials, under a wide range of compaction conditions.

To determine T.A.P. density, the sample chamber is rotated and agitated while a precise specified force is applied to the sample. A force transducer measures the consolidation force in newtons and the distance over which the consolidation piston and plunger travel is measured in steps. The user specifies the force applied and the number of consolidations per analysis. The GeoPyc averages the measurements from each consolidation and automatically calculates volume and density, and reports the results in cm^3 and g/cm^3.

TECHNIQUE

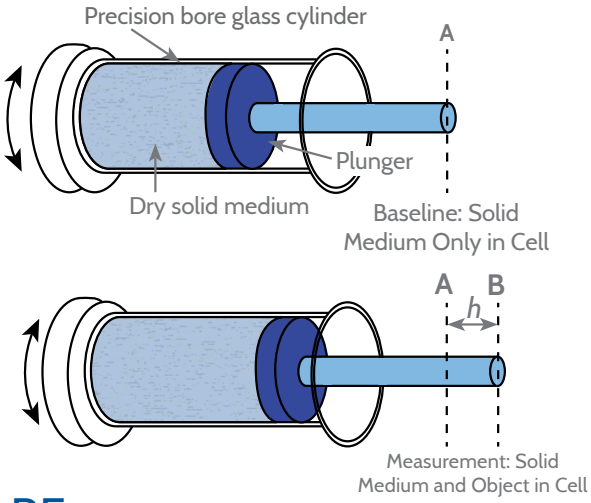
The GeoPyc analyzer automatically determines the volume and density of a solid object by displacement of DryFlo, a solid medium. The medium is a narrow distribution of small, rigid spheres that have a high degree of flow ability and achieve close packing around the object under investigation. The particles are sufficiently small that during consolidation they conform closely to the surface of the object, yet do not invade pore space.

Repeatability and reproducibility are achieved by a controlled method of compaction. The sample cell in which the dry medium is placed is a precision cylinder. A plunger compresses the powder as the cell vibrates; the force of compression is selectable and, therefore repeatable from test to test. A preliminary compaction with only the displacement medium in the cell establishes a zero-volume baseline.

The sample is then placed in the cylinder with the dry medium and the compaction process is repeated. The difference in the distance h_t the piston penetrates the cylinder during the test and the distance h_0 it penetrates during the baseline procedure ($h=h_0-h_t$) is used to calculate the volume of the displaced medium. The relationship between h and volume may be determined by calibration with an object of known volume, or from the geometric volume of a cylinder.

The GeoPyc envelope density analyzer is operated from an intelligent touch screen. Data acquisition and reporting are fully automated for convenient incorporation in LIMS or other data concentrating systems.

A variety of sample chambers is available to accommodate a wide range of sample sizes. After the analysis, a light shaking or dusting removes virtually all of the DryFlo so the samples can be reused or retested. During analysis, indications of progress and preliminary results make it possible to track what is occurring.

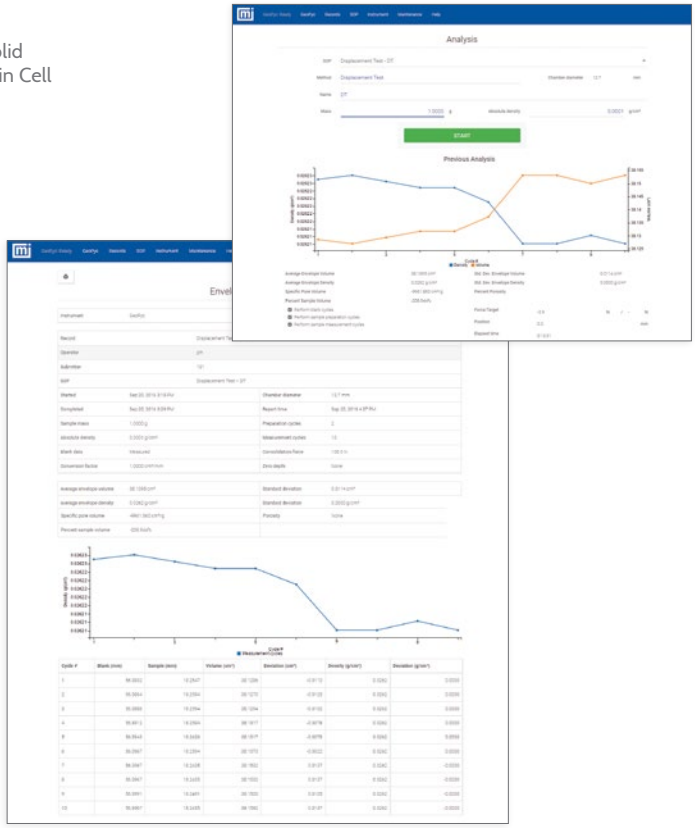


SOFTWARE

The GeoPyc has multiple operational modes that are accessed through the instruments smart touch screen. Operating modes including full blank, computed blank, and reference solid calibration with variance, which allows you to optimize speed and accuracy for your specific application.

During analysis, indications of progress and preliminary results make it possible to track what is occurring. Sample-specific information can be entered into the analysis reports.

Available Reports: Envelope Density, Volume Calibration, Blank Report, Force Calibration, Instrument Log



ACCUPYC II

GAS DISPLACEMENT PYCNOMETRY SYSTEM

Gas pycnometry is recognized as one of the most reliable techniques for obtaining true, absolute, skeletal, and apparent volume and density. This technique is non-destructive as it uses the gas displacement method to measure volume. Inert gases, such as helium or nitrogen, are used as the displacement medium. Density calculations using the gas displacement method are much more accurate and reproducible than the traditional Archimedes water displacement method.

The Micromeritics AccuPyc II 1345 series pycnometers are fast, fully automatic pycnometers that provide high-speed, high-precision volume measurements and true density calculations on a wide variety of powders, solids, and slurries. After analyses are started with a few keystrokes – using either the integrated keyboard and microcomputer or via our PC control software – data are collected, calculations are performed, and results displayed. A minimal amount of operator attention is required.

BENEFITS

Maintain product integrity with this non-destructive test

Eliminate error with programmable automatic repeat and data acquisition set to your tolerances to comply with your SOPs

Use a variety of gases

Adapt instrument configuration to meet your sample size needs

Minimize cost and space requirements; low maintenance and small footprint

Increase efficiency and compliance with barcoding compatibility

Maximize your results with superior speed of analysis, accuracy, repeatability, and reproducibility

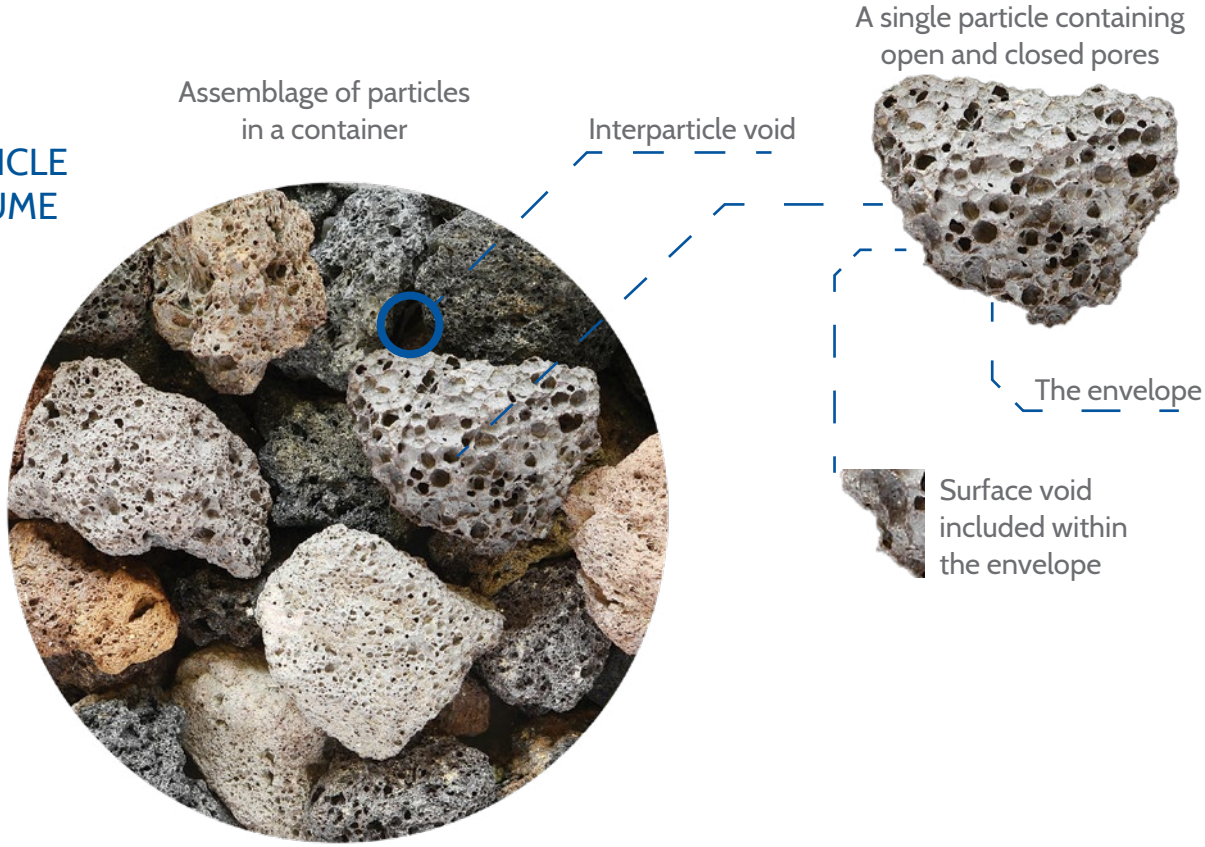
Operate with either a keypad or Windows® software

Eliminate procedural steps with direct input from an analytical balance

DENSITY MEASUREMENT

On an elementary level, the volume of a solid material can be calculated by measuring its length, width, and thickness. However, many materials have within their structure surface irregularities, small fractures, fissures, and pores. Some of these voids or pores are open to the surface or closed within the structure of the solid material. Therefore, differences in the material volume depend on the measurement technique, measurement method, and the conditions under which the measurements were performed.

PARTICLE VOLUME

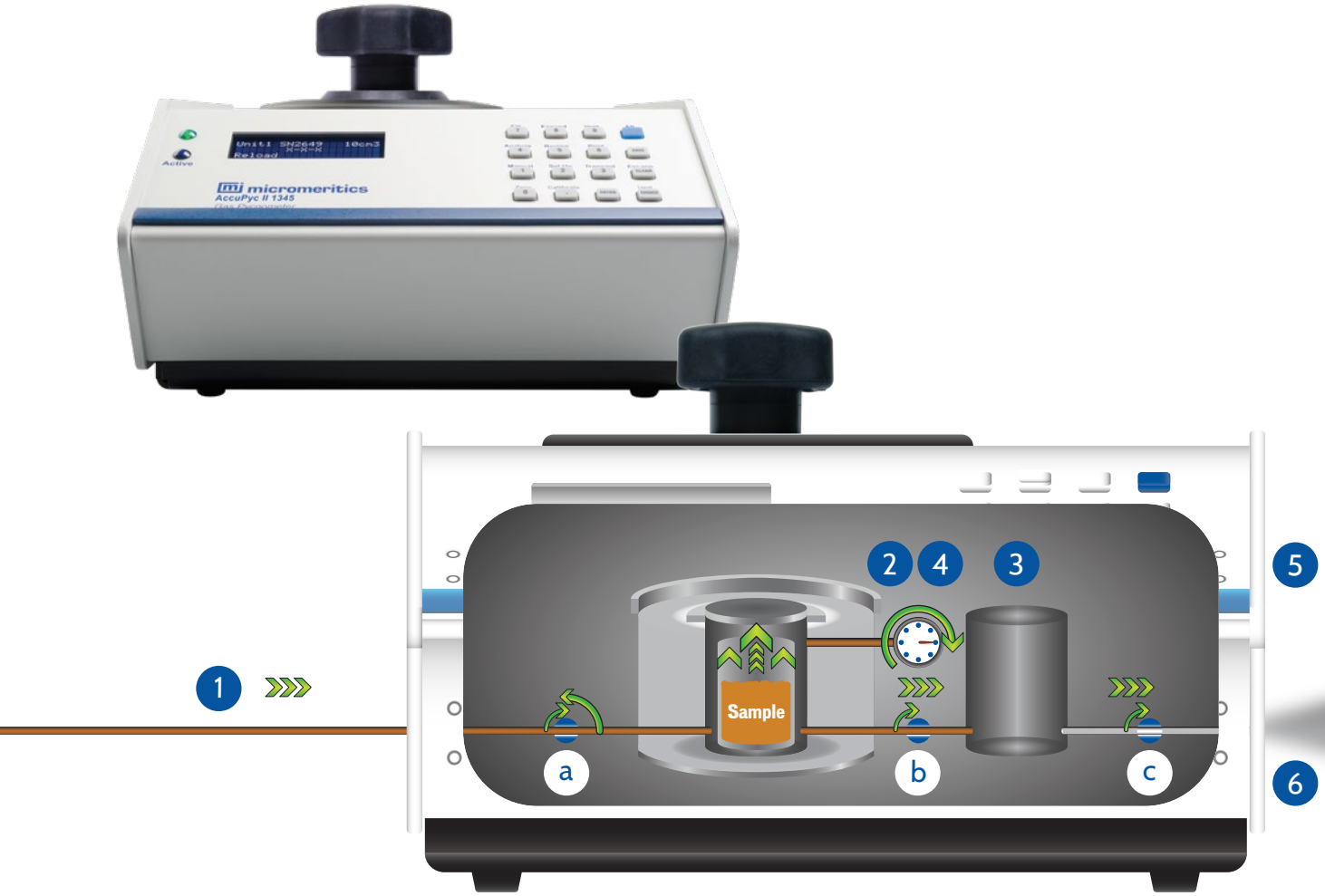


Density Type	Definition	Material Volume	Open-Pore Volume	Closed-Pore Volume	Inter particle Volume	External Void Volume	Addressed by
True (Absolute)	The mass of a substance divided by its volume, excluding open and closed (or blind) pores	◎					AccuPyc II
Skeletal (Apparent)	The ratio of the mass of the solid material to the sum of the volume including closed (or blind) pores	◎		◎			AccuPyc II
Envelope	The ratio of the mass of a substance to the envelope volume (imaginary boundary surrounding the particle)	◎	◎	◎		◎	GeoPyc
Bulk	Mass of the material divided by the volume occupied that includes interstitial space	◎	◎	◎	◎		GeoPyc
T.A.P.	Apparent powder density obtained under stated conditions of tapping	◎	◎	◎	◎		GeoPyc with T.A.P. function

GAS DISPLACEMENT PYCNOMETRY

Principle of Operation

This technique uses the gas displacement method to measure volume accurately. Inert gases, such as helium or nitrogen, are used as the displacement medium. The sample is sealed in the instrument compartment of known volume, the appropriate inert gas is admitted, and then expanded into another precision internal volume. The pressures observed upon filling the sample chamber and then discharging it into a second empty chamber allow computation of the sample solid phase volume. Helium molecules rapidly fill pores as small as one angstrom in diameter; only the solid phase of the sample displaces the gas. Dividing this volume into the sample weight gives the gas displacement density.



1. Inert gas flows Into sample chamber. Valve "a" opens, then closes.
2. Equilibrium is reached.
3. Gas flows into second chamber for volume measurement. Valve "b" opens.
4. Equilibrium is reached again.
5. Volume divided into sample weight determines density.
6. Pressure vented off to atmosphere. Valve "c" opens.

MODEL SELECTION

Sample Cup Capacity	Sample Cup Dimensions	Available MultiVolume Insert Kits	Temp Control Type	Catalog Number
AccuPyc II 1345 Instruments				
1 cm^3	1.14 cm ID x 1.1 cm D	0.1 cm^3	N/A	134/50001/00
10 cm^3	1.85 cm ID x 3.95 cm D	1.0 and 3.5 cm^3		134/50000/00
100 cm^3	4.62 cm ID x 6.18 cm D	10 and 35 cm^3		134/50002/00
AccuPyc II 1345 Remote Analysis Instruments **Bundle includes control module and 2-ft cable connected to analysis modules.**				
1 cm^3	1.14 cm ID x 1.1 cm D	0.1 cm^3	N/A	134/50031/00
10 cm^3	1.85 cm ID x 3.95 cm D	1.0 and 3.5 cm^3		134/50030/00
100 cm^3	4.62 cm ID x 6.18 cm D	10 and 35 cm^3		134/50032/00
350 cm^3	5.84 cm ID x 13.94 cm D	N/A		134/50033/00
2000 cm^3	9.52 cm ID x 26.00 cm D	650 and 1300 cm^3		134/50034/00
Remote analysis modules only. Remote analysis units require connection to a control module or AccuPyc II 1345.				
1 cm^3	1.14 cm ID x 1.1 cm D	0.1 cm^3	N/A	134/50041/00
10 cm^3	1.85 cm ID x 3.95 cm D	1.0 and 3.5 cm^3		134/50040/00
100 cm^3	4.62 cm ID x 6.18 cm D	10 and 35 cm^3		134/50042/00
350 cm^3	5.84 cm ID x 13.94 cm D	N/A		134/50043/00
2000 cm^3	9.52 cm ID x 26.00 cm D	650 and 1300 cm^3		134/50046/00
Control module only. Up to 6 analysis modules can be connected to a single control module.				
N/A	N/A	N/A	N/A	134/50005/00
AccuPyc II 1345 High Pressure (500 psi) Remote Analysis Instruments **Bundle includes control module and 2-ft cable connected to analysis module.**				
100 cm^3	4.62 cm ID x 6.18 cm D	10 and 35 cm^3	N/A	134/50037/00
Remote analysis module only. Remote analysis unit requires connection to a control module or AccuPyc II 1345.				
100 cm^3	4.62 cm ID x 6.18 cm D	10 and 35 cm^3	N/A	134/50049/00
AccuPyc II 1345 Temperature-Controlled Instruments				
10 cm^3	1.85 cm ID x 3.95 cm D	1.0 and 3.5 cm^3	Use with External Recirculating Bath 15-50 °C	134/50010/00
100 cm^3	4.62 cm ID x 6.18 cm D	10 and 35 cm^3		134/50020/00
10 cm^3	1.85 cm ID x 3.95 cm D	1.0 and 3.5 cm^3	Integral Thermoelectric Cooling 15-36 °C ±0.1 °C	134/50050/00
100 cm^3	4.62 cm ID x 6.18 cm D	10 and 35 cm^3		134/50051/00
AccuPyc II 1345 Temperature-Controlled Remote Analysis Instruments **Bundle includes control module and 2-ft cable connected to temperature-controlled analysis modules.**				
10 cm^3	1.85 cm ID x 3.95 cm D	1.0 and 3.5 cm^3	Integral Thermoelectric Cooling 15-36 °C ±0.1 °C	134/50035/00
100 cm^3	4.62 cm ID x 6.18 cm D	10 and 35 cm^3		134/50036/00
Remote analysis modules only. Remote analysis units require connection to a control module or AccuPyc II 1345.				
10 cm^3	1.85 cm ID x 3.95 cm D	1.0 and 3.5 cm^3	Use with External Recirculating Bath 15-50 °C	134/50044/00
100 cm^3	4.62 cm ID x 6.18 cm D	10 and 35 cm^3		134/50045/00
10 cm^3	1.85 cm ID x 3.95 cm D	1.0 and 3.5 cm^3	Integral Thermoelectric Cooling 15-36 °C ±0.1 °C	134/50047/00
100 cm^3	4.62 cm ID x 6.18 cm D	10 and 35 cm^3		134/50048/00

Research grade helium or nitrogen is strongly recommended. High purity carbon dioxide, dry air, or argon may be used. A multigas option for up to four gases on one analysis unit is available.

** Subject to environmental operating conditions*

HIGHLY ADAPTIVE SYSTEM

The AccuPyc II pycnometer consists of an integrated control and analysis module. For those who require high throughput, analysis modules are also available in a single configuration, allowing you to attach up to five additional analysis modules to a single controlling unit. Each module has its own gas connection. A variety of sample chamber sizes can be selected to provide the best fit with your samples. The run precision mode allows you to achieve high repeatability. The instrument purges water and volatiles from the sample and then repeats the analysis until successive measurements converge upon a consistent result.

UNIQUE RUN PRECISION

Increases the precision of analysis results by reporting data from five consecutive measurements that are within a user-specified tolerance. This feature allows early termination of analysis, thereby decreasing the number of cycles needed for accurate results.

MULTILINGUAL

The AccuPyc may be operated in five languages: English, French, German, Italian, or Spanish.

INTEGRATED CONTROL AND ANALYSIS MODULE

Can control up to five additional external analysis modules.

ETHERNET PORT

An Ethernet port on the rear panel of the control module enables you to email reports, send data to a web browser for archiving, or interface with the AccuPyc Windows application.

USB PORTS

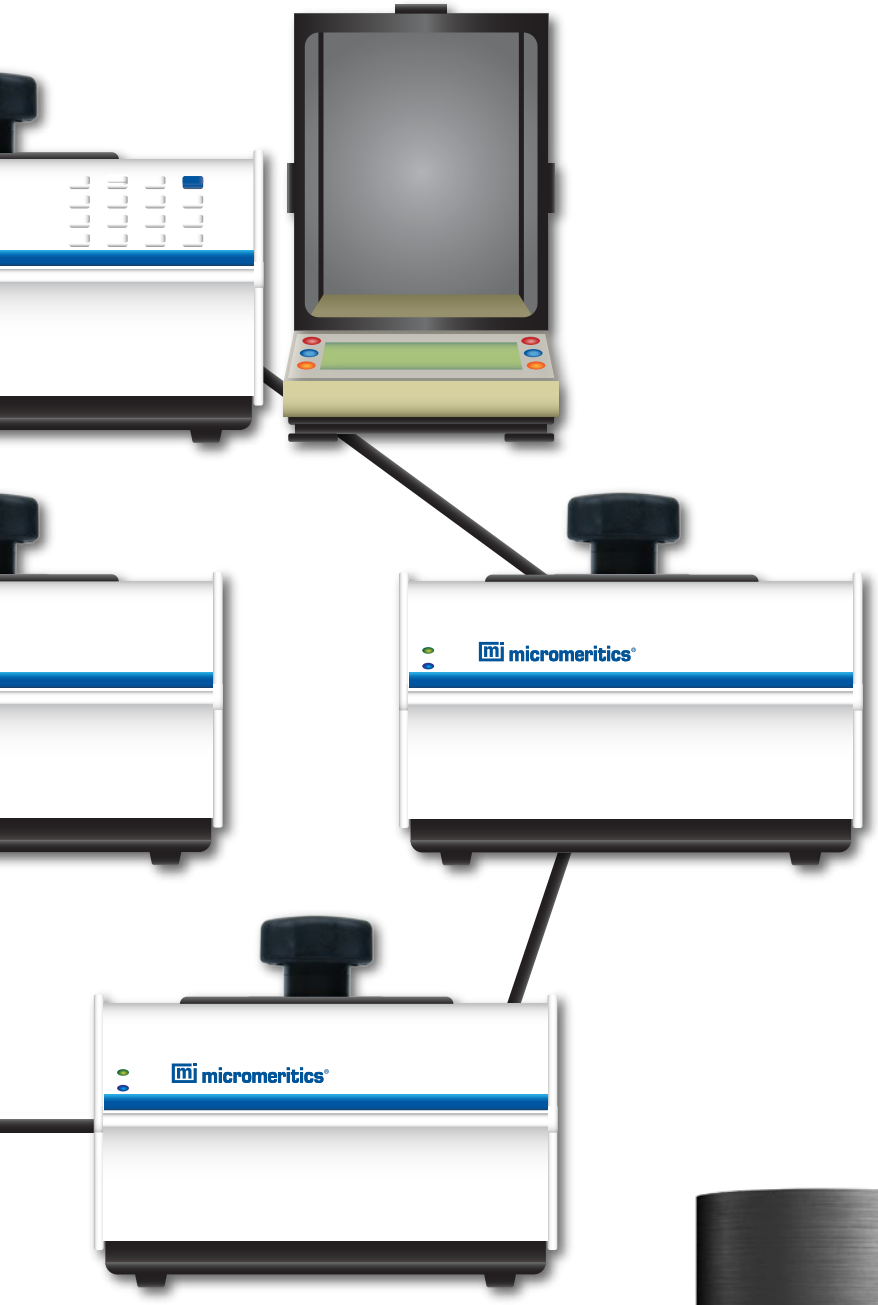
USB ports on the rear panel of the control module allow for connection to a printer (output of analysis and calibration results in either ASCII or Excel formats) and keyboard (alphanumeric character input). The USB port is also used for installing software upgrades.

SIMPLE CALIBRATION PROCESS

Allows you to easily determine the volume of the instrument sample cell and expansion chambers using a traceable standard volume. After calibration, the cell and expansion chamber volumes are stored automatically.

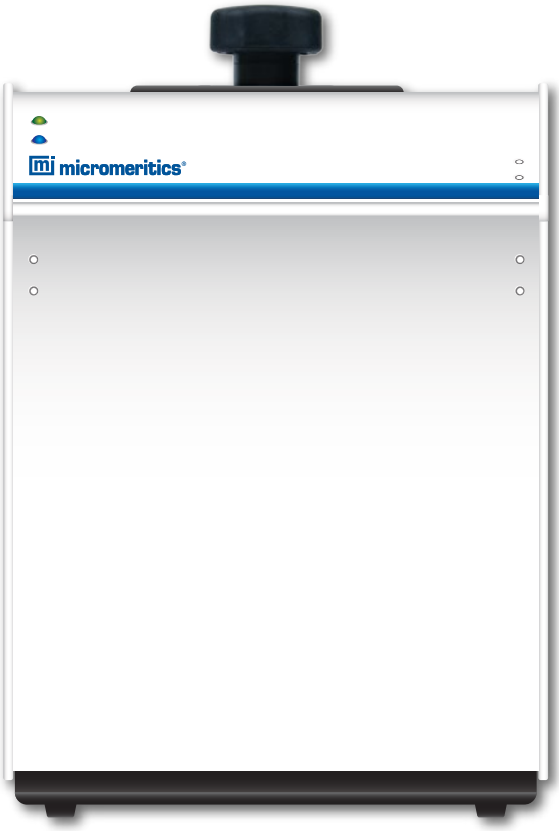
DIRECT SAMPLE MASS INPUT

Sample mass may be directly input from an analytical balance.



COREPYC

Specialized unit with 2000 cm^3 sample chamber size.



BAYONET CAP FITTING

Provides superior repeatable seal compared to screw-type fitting.

FIVE STANDARD SAMPLE CHAMBER SIZES

1 cm^3, 10 cm^3, 100 cm^3, 350 cm^3, and 2000 cm^3.

2000 cm^3

350 cm^3 *100 cm^3* *10 cm^3* *1 cm^3*

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HARDWARE VERSATILITY

MULTIVOLUME KITS

A MultiVolume option allowing you to analyze smaller-sized samples with your current AccuPyc model is available for configurations listed below.

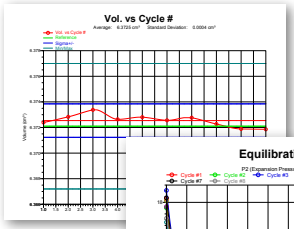
Each kit includes appropriate insert(s), reference standard(s), and sample cup(s).

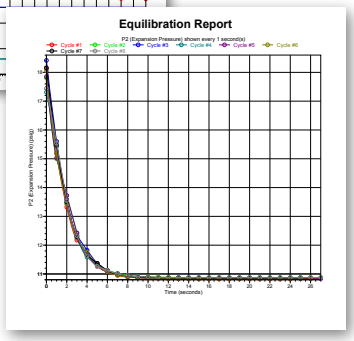
2000-cm³ nominal cell volume
650- and 1300-cm³ cups

100-cm³ nominal cell volume
10- and 35-cm³ cups

10-cm³ nominal cell volume
1- and 3.5-cm³ cups

1-cm³ nominal cell volume
0.1-cm³ cup





SOFTWARE VERSATILITY

DATA PRESENTATION

The AccuPyc II can be operated with a full keyboard or an optional Windows® interface that provides exceptional reporting and archiving capability. Both versions include direct sample mass input from a balance and cycle-based displacement volume reporting. With the Windows interface, features such as time-based pressure equilibration reporting and additional calculations such as percent solids content and total pore volume are included. Operational status can also be continually monitored in a status window on the monitor screen.

- Combined Report
- Summary Report
- User-Defined Tabular Reports
- Volume vs. Cycle #
- Density vs. Time
- Total Pore Volume vs. Temperature
- Density vs. Cycle #
- Density at 60 °F
- Volume at 60 °F
- Options Report
- Equilibration Report
- Sample Log
- Specific Gravity

Micromeritics Instrument Corp.
4356 Communications Drive
Norcross, GA 30093 • USA
Tel.: +1 770 662-3636

info@micromeritics.com
micromeritics.com

BELGIUM
micromeritics.benelux@micromeritics.com

CHINA
micromeritics.china@micromeritics.com

FRANCE
micromeritics.fr@micromeritics.com

GERMANY
micromeritics.de@micromeritics.com

THE NETHERLANDS
micromeritics.benelux@micromeritics.com

UK
micromeritics.uk@micromeritics.com

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