
**Particle size analysis — Particle
tracking analysis (PTA) method**

*Analyse granulométrique — Méthode d'analyse de suivi de
particule (PTA)*

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Foreword

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For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: www.iso.org/iso/foreword.html

The committee responsible for this document is Technical Committee ISO/TC 24, *Particle characterization including sieving*, Subcommittee SC 4, *Particle characterization*.

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Introduction

Regulatory, scientific and commercial requirements for nanomaterial characterization or characterization of particulate suspensions where particle sizing and counting is required provide a strong case for further development of techniques such as Particle Tracking Analysis (PTA), also known as Nanoparticle Tracking Analysis (NTA) [14]. Due to the fact that the term PTA covers a larger size range and is more generic¹⁾, the term PTA is used throughout this document to refer to NTA and PTA. For all aims and purposes, the term PTA also means NTA in this document.

PTA is based on measuring the diffusion movement of particles in a suspension by means of laser illumination, imaging of scattered light, particle identification and localization, and individual particle tracking²⁾. In this case, suspension is an even dispersion of particles, gas bubbles or other liquid droplets. The hydrodynamic diameter of the individual particles, droplets or bubbles is related to Brownian motion parameters via the Stokes–Einstein equation.

In recent years the academic community working in fields such as liposomes and other drug delivery vehicles, nanotoxicology, viruses, exosomes, protein aggregation, inkjet inks, pigment particles, cosmetics, foodstuffs, fuel additives and fine bubbles began using the PTA technology for characterization. An ASTM standard guide (E2834–12) [10] was developed to give guidance to the measurement of particle size distribution by means of Nanoparticle Tracking Analysis. The present document aims to broaden the scope of the specification and to introduce system tests for PTA operation.

This document outlines the theory and basic principles of the particle tracking analysis method along with its limitations and advantages. It also describes commonly used instrument configurations and measurement procedures as well as system qualifications and data reporting. One of the key aspects is the meaning of the data and its interpretation. It should be noted that the key measurand obtained from PTA measurement is the number-based particle size distribution where the size is taken to mean the hydrodynamic diameter (3.11) of the particles in the sample. This size can be different from other sizes obtained with different techniques such as dynamic light scattering [6] or electron microscopy [4].

1) NTA is the most recognised abbreviation for the technique described in this document. However the Particle Tracking Analysis (PTA) includes NTA in its size range of measurements.

2) For the purpose of this document “tracking” will mean “following in terms of particle x and y position” and the “track” will mean “the path of that particle defined by such x and y coordinates of each step”

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Particle size analysis — Particle tracking analysis (PTA) method

1 Scope

This document describes the evaluation of the number-based particle size distribution in liquid dispersions (solid, liquid or gaseous particles suspended in liquids) using the particle tracking analysis method for diffusion velocity measurements.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

- ISO Online browsing platform: available at <http://www.iso.org/obp>
- IEC Electropedia: available at <http://www.electropedia.org/>

3.1

nanoscale

length range approximately from 1 nm to 100 nm

Note 1 to entry: Properties that are not extrapolations from larger sizes are predominantly exhibited in this length range.

[SOURCE: ISO/TS 80004-1:2015, 2.1]

3.2

nano-object

material with one, two or three external dimensions in the *nanoscale* (3.1)

Note 1 to entry: The second and third external dimensions are orthogonal to the first dimension and to each other.

[SOURCE: ISO/TS 80004-1:2015, 2.5]

3.3

nanoparticle

nano-object (3.2) with all three external dimensions in the *nanoscale* (3.1)

Note 1 to entry: If the lengths of the longest to the shortest axes of the nano-object differ significantly (typically by more than three times), the terms *nanofibre* or *nanoplate* are intended to be used instead of the term nanoparticle.

[SOURCE: ISO/TS 80004-4:2011, 2.4]

3.4

particle

minute piece of matter with defined physical boundaries

Note 1 to entry: A physical boundary can also be described as an interface.

Note 2 to entry: A particle can move as a unit.

Note 3 to entry: This general particle definition applies to *nano-objects* (3.2).

[SOURCE: ISO/TS 80004-6:2013, 2.9]

3.5

agglomerate

collection of weakly bound particles or *aggregates* or mixtures of the two where the resulting external surface area is similar to the sum of the surface areas of the individual components

Note 1 to entry: The forces holding an agglomerate together are weak forces, for example van der Waals forces, or simple physical entanglement.

Note 2 to entry: Agglomerates are also termed secondary particles and the original source particles are termed primary particles.

[SOURCE: ISO/TS 80004-4:2011, 2.8]

3.6

aggregate

particle comprising strongly bonded or fused particles where the resulting external surface area may be significantly smaller than the sum of calculated surface areas of the individual components

Note 1 to entry: The forces holding an aggregate together are strong forces, for example covalent bonds, or those resulting from sintering or complex physical entanglement.

Note 2 to entry: Aggregates are also termed secondary particles and the original source particles are termed primary particles.

[SOURCE: ISO/TS 80004-4:2011, 2.7]

3.7

particle size

linear dimension of a *particle* (3.4) determined by a specified measurement method and under specified measurement conditions

Note 1 to entry: Different methods of analysis are based on the measurement of different physical properties. Independent of the particle property actually measured, the particle size can be reported as a linear dimension, e.g. as an equivalent spherical diameter.

[SOURCE: ISO/TS 80004-6:2013, 3.1.1]

3.8

particle size distribution

distribution of *particles* (3.4) as a function of *particle size* (3.7)

Note 1 to entry: Particle size distribution may be expressed as cumulative distribution or a distribution density (distribution of the fraction of material in a size class, divided by the width of that class).

[SOURCE: ISO/TS 80004-6:2013, 3.1.2]

3.9

equivalent diameter

diameter of a sphere that produces a response by a given particle-sizing method, that is equivalent to the response produced by the particle being measured

Note 1 to entry: The physical property to which the equivalent diameter refers is indicated using a suitable subscript [ISO 9276-1:1998].

Note 2 to entry: For discrete-particle-counting, light-scattering instruments, an equivalent optical diameter is used.

Note 3 to entry: Other material constants like density of the particle are used for the calculation of the equivalent diameter like Stokes diameter or sedimentation equivalent diameter. The material constants, used for the calculation, should be reported additionally.

Note 4 to entry: For inertial instruments, the aerodynamic diameter is used. Aerodynamic diameter is the diameter of a sphere of density $1\,000\text{ kg m}^{-3}$ that has the same settling velocity as the irregular particle.

[SOURCE: ISO/TS 80004-6:2013, 3.1.5]

3.10

light scattering

change in propagation of light at the interface of two media having different optical properties

[SOURCE: ISO 13320:2009, 3.1.17]

3.11

hydrodynamic diameter

equivalent spherical diameter of a particle in a liquid having the same diffusion coefficient as the real particle in that liquid

[SOURCE: ISO/TS 80004-6:2013, 3.2.6]

3.12

particle tracking analysis

PTA

method where particles undergoing Brownian motion in a liquid suspension are illuminated by a laser and the change in position of individual particles is used to determine particle size

Note 1 to entry: Analysis of the time-dependent particle position yields translational diffusion coefficient and hence the particle size as hydrodynamic diameter using the Stokes-Einstein relationship.

Note 2 to entry: Nanoparticle Tracking Analysis (NTA) is often used to describe PTA. NTA is a subset of PTA since PTA covers larger range of particle sizes than *nanoscale* (3.1).

[SOURCE: ISO/TS 80004-6:2013, 3.2.8, modified — Nanoparticle tracking analysis has been removed from the term, and Notes 1 and 2 have been modified.]

3.13

nanomaterial

material with any external dimension in the *nanoscale* (3.1) or having internal structure or surface structure in the nanoscale

[SOURCE: ISO/TS 80004-1:2015, 2.4]

3.14

diluent

non-volatile homogeneous liquid which is used to decrease the number concentration of *particles* (3.4) in a suspension without any deleterious effects such as changing particle total number, state of aggregation, *particle size* (3.7) or surface chemistry

3.15

viscosity

measure of the resistance to flow or deformation of a liquid

[SOURCE: ISO 3104:1994]

3.16

percentile

value of a variable below which a certain percentage of observations fall

[SOURCE: ISO 11064-4:2013, 3.7]