### 7.2.2 Particle Size Distribution

Particle size reduction particularly mandates the study of particle size distribution by using techniques such as sieving, optical microscopy in conjunction with image analysis, electron microscopy, the Coulter counter, and laser diffractometers, depending on the anticipated size of the particles. Although the size characterization is simple for spherical particles, the study of irregular particles requires specialized methods. The Malvern Mastersizer series (3) is an example of an instrument that measures particle size by laser diffraction. The use of this technique is based on light scattered through various angles, which is directly related to the diameter of the particle. Thus, by measuring the angles and intensity of scattered light from the particles, a particle size distribution can be deduced. It should be noted that the particle diameters reported are the same as those produced by spherical particles under similar conditions. In the former, each particle is treated as spherical and essentially opaque to the impinging laser light. Figure 7.4 shows different methods of detection and the size of the particles.

Two different light scattering (DLS) methodologies can be used to characterize particles. The classical, also known as "static" or "Rayleigh" scattering or multiple-angle laser light scattering, provides a direct measure of mass.

The DLS, which is also known as "photon correlation spectroscopy" (PCS) or "quasi-elastic light scattering" (QELS), uses the scattered light to measure the rate of diffusion of the particles. This motion data is conventionally processed to derive a size distribution for the sample, where the size is given by the "Stokes radius" or "hydrodynamic radius" of the protein particle. This hydrodynamic size depends on

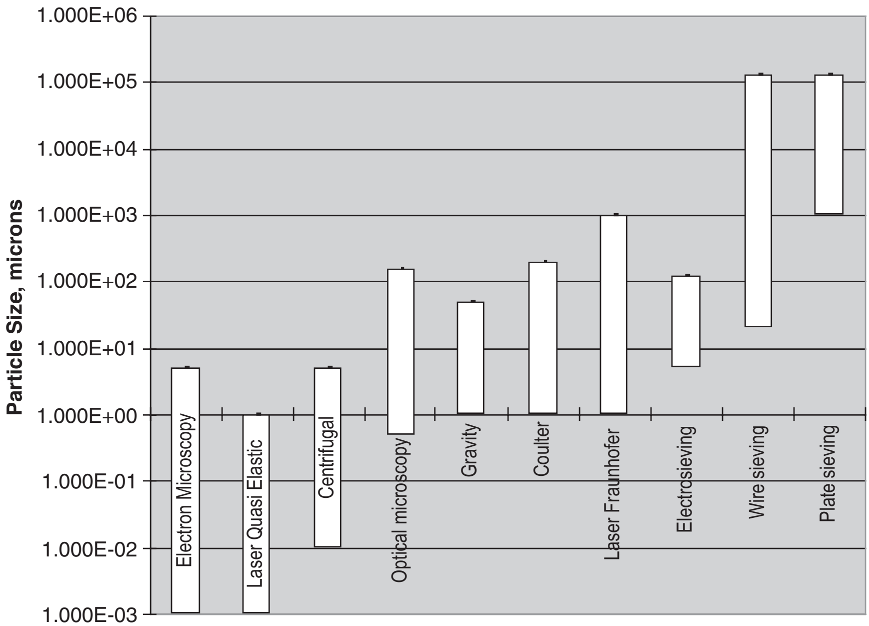


**FIGURE 7.4** Techniques of particle size detection and their limits.