

either large samples or automatic batch scanning of a column of smaller samples. The system obtains multiple X-ray "shadow" transmission images of the object from different angular views, as the object rotates on a high-precision stage. From these shadow images, cross-section images of the object are reconstructed by a modified Feldkamp cone-beam algorithm, creating a complete 3D representation of internal microstructure and density over a selected range of heights in the transmission images. The best micro-CT scan images are obtained from objects in which microstructure coincides with contrast in X-ray absorption of the sample's constituent materials.

LVIII. COLOR

The color of a powder sample is used to indicate presence of solvents, distribution of particle size, and other possible differences in different lots of a new lead compound. In some instances, degradation of drug can be correlated with color changes to such degree that accurate color measurements can be used as a tool to provide product specification. The compendia often describe color of substances but mostly in subjective terms. Historically, the color evaluation has been a subjective measurement; however, newer quantitative measurement systems make this a more objective process. There are two basic methods for measuring the colors of surfaces.

- The first is to imitate the analysis made by the eye in terms of responses to three stimuli. This technique, known as "tristimulus colorimetry," sets out to measure X, Y, and Z directly.
- The second method is to determine reflectance (R) for each wavelength band across the range of the spectrum to which the eye is sensitive, and then to calculate the visual responses by summing products of R and the standard values for distribution of the sensitivity of the three-color responses.

The tristimulus method has theoretical advantages where the materials to be measured are fluorescent, but there are serious practical problems in assuming that a tristimulus colorimeter exactly matches human vision, that is, in eliminating color blindness from the instrument.

Two commonly used types of color measurement equipment are a colorimeter and a spectrophotometer. A tristimulus colorimeter has three main components

- a source of illumination (usually a lamp functioning at a constant voltage);
- a combination of filters used to modify the energy distribution of the incident/reflected light; and
- a photoelectric detector that converts the reflected light into an electrical output.

Each color has a fingerprint reflectance pattern in the spectrum. The colorimeter measures color through three wide-band filters corresponding to the spectral sensitivity curves. Measurements made on a tristimulus colorimeter are normally comparative, the instrument being standardized on glass or ceramic standards. To achieve the most accurate measurements, it is necessary to use calibrated standards of similar colors to the materials to be measured. This "hitching post" technique enables reasonably accurate tristimulus values to be obtained even when the colorimeter is demonstrably colorblind. Tristimulus colorimeters are most useful

for quick comparison of near-matching colors. They are not very accurate. Large differences are evident between the various instrument manufacturers. However, colorimeters are less expensive than spectrophotometers.

To get a precise measurement of color, it is advisable to use a spectrophotometer. A spectrophotometer measures the reflectance for each wavelength, and allows to calculate tristimulus values. The advantage over tristimulus colorimetry is that adequate information is obtained to calculate color values for any illuminant and that metamerism is automatically detected. Metamerism is a psychophysical phenomenon commonly defined incompletely as "two samples which match when illuminated by a particular light source and then do not match when illuminated by a different light source." In actuality, there are several types of metamerism, of which the sample and illuminant metamerism are most common. In sample metamerism, two color samples appear to match under a particular light source, and then do not match under a different light source. Illuminant metamerism appears when different light sources illuminate same sample and differences are revealed. The observer metamerism refers to where each individual perceives color slightly differently. The geometric metamerism arises when identical colors appear different when viewed at different angles, distances, light positions, etc.

In a spectrophotometer, the light is usually split into a spectrum by a prism or a diffraction grating before each wavelength band is selected for measurement. Instruments have also been developed in which narrow bands are selected by interference filters. The spectral resolution of the instrument depends on the narrowness of the bands utilized for each successive measurement. In theory, a spectrophotometer could be set up to compare reflected light directly with incident light, but it is more usual to calibrate against an opal glass standard that has been calibrated by an internationally recognized laboratory. Checks must also be made on the optical zero, for example, by measurements with a black light trap, because dust or other problems can give rise to stray light in an instrument (which would give false readings). Spectrophotometers contain monochromators and photodiodes that measure the reflectance curve of color every 10 nm or less. The analysis generates typically 30 or more data points, with which a precise color composition can be calculated.

A large number of suppliers provided colorimeters including such large array of equipment from Hunter Lab's Labscan XE with special adapter for small quantity of powders offers an excellent choice in preformulation work. The instrument has a 3-mm port and requires 0.4-cm³ powder to perform the testing. (<http://www.hunterlab.com/>)

LIX. ELECTROSTATICITY

When subjected to attrition, powders can acquire an electrostatic charge, the intensity of which is often proportional to physical force applied as static electrification of two dissimilar materials occurs by the making and breaking of surface contacts (tribo-electrification or friction electrification). Electrostatic charges are often used to induce adhesive character to bind drugs to carrier systems, for example, glass beads coated with HPMC containing drugs. The net charge on a powder may be either electropositive or electronegative depending on the direction of electron transfer. The mass charge density can vary from 10–5 to 100 $\mu\text{C}/\text{kg}$ depending on the