

UNDERSTANDING THE CHI SQUARE AND R PARAMETER CALCULATIONS

The LA-960 software provides two different calculations to quantify both the quality of the raw data and the calculation of the reported particle size distribution. The equations for Chi square and residual R parameter are shown below:

$$\chi^2 = \sum \left\{ \frac{1}{\sigma_i^2} [y_i - y(x_i)]^2 \right\}$$

$$R = \frac{1}{N} \sum_{i=1}^N \left\{ \frac{1}{y(x_i)} |y_i - y(x_i)| \right\}$$

- y_i The measured scattered light at each channel (i) of the detector.
- $y(x_i)$ The calculated scattered light at each channel (i) of the detector based on the chosen refractive index kernel and reported particle size distribution.
- σ_i The standard deviation of the scattered light intensity at each channel (i) of the detector. A larger σ_i indicates lower reliability of the signal on a given detector.
- N The number of detectors used for the calculation.

Both of these calculations can be used to validate the choice of the refractive index (RI) kernel. Choosing the refractive index for an unknown sample can be facilitated by measuring the sample once, changing refractive index kernel, and checking if the Chi square or R parameter values decrease or increase. These calculations compare the measured raw data in each channel (i.e. detector) to the amount of light scattering predicted for the reported particle size distribution. *This is the $y_i - y(x_i)$ part of the calculation.* A lower value for either Chi square or R parameter indicates a better fit of the raw data to the calculated particle size distribution.

The Chi square calculation also checks the stability of the raw data on each channel. *This is the σ_i part of the calculation.* The conversion from scattered light to particle size distribution is based on the average light intensity on each detector, but it is useful to measure how stable the raw data is. Instability in scattered light on any channel will

cause a change in both the σ_i and Chi square value. A high Chi square value indicates a certain amount of instability during the measurement which, in turn, could indicate that the sample is undergoing dissolution, agglomeration, sedimentation, swelling, or some other chemical reaction.

Which calculation to use depends on how the numbers are being used. If the only goal is to verify choice of refractive index kernel, then the residual R value may be better. If the goal is to quantify the quality of an experiment, the Chi square value provides more information.

In order to view the intensity graph of the raw and theoretical data, select the “Advanced Function” menu and then “Intensity Graph.” The Chi square and R parameter values may be viewed here in addition to the light scattering signal used in the particle size distribution calculation. Chi square and R parameter values may also be displayed in the Result Data View panes and any print template for generating a report. An example of the Intensity Graph is shown in Figure 1 below.

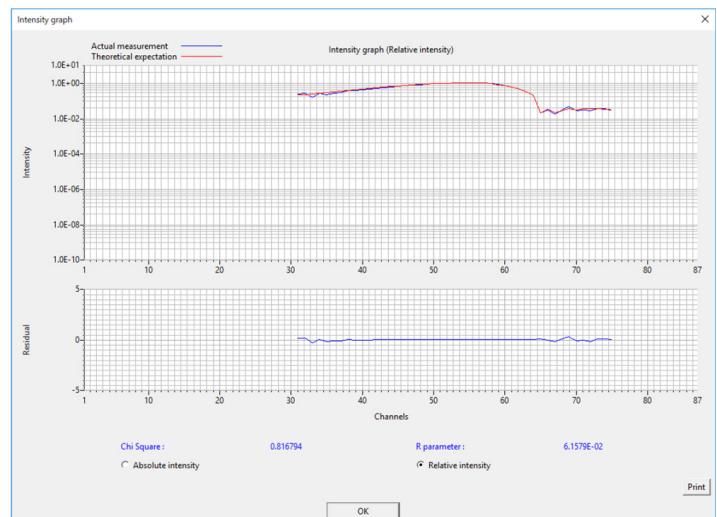


Figure 1. Intensity graph

The blue line shows the actual scattered light signal collected during the measurement. The red line shows the theoretical light scattering that should be observed for the particle size distribution reported as the result. In the ideal case, these lines should overlap as closely as possible. Note that only those detectors used for the result calculation are shown.

Example 1

Using Chi Square to Determine Optimum T%

An emulsion sample was measured on the LA-960V2 at varying concentrations (T%). Results of the median particle size (D50) vary from 0.57 to 0.41 depending on the concentration. Figure 2 below shows T% on the x-axis, Chi square on the left y-axis, and D50 on the right y-axis. As you can see, the Chi square values are significantly higher when the T% is above 95%. Chi square values above around 15 indicate instability in the raw data. Both the Chi square and D50 values stabilize once the T% is below 95%. In this case, it appears that the raw data is unstable at the lower concentrations due to a low signal to noise ratio. This study indicates that this sample should be measured with a T% around 93-94%.

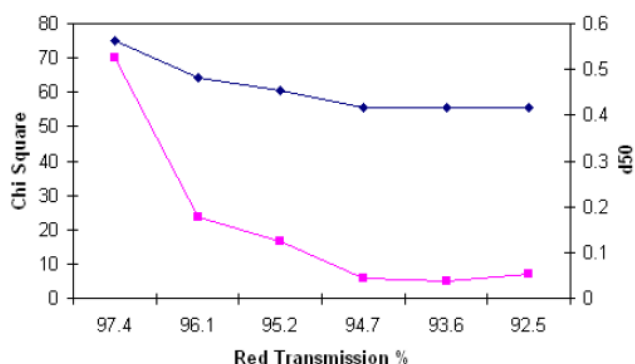


Figure 2

Chi square is used in this example to effectively show when a sufficient quantity of particles are available to generate sufficiently stable scattered light to all detectors.

Example 2

Determining the Imaginary Refractive Index Component

The real refractive index component of a pharmaceutical white powder sample was determined to be 1.57 using the Becke line procedure. The sample was measured on the LA-960V2 in water and then used to investigate the best choice for the imaginary component. Figure 3 below shows the results calculated by keeping the real component fixed and varying the imaginary component value to 0, 0.1, and 1.0.

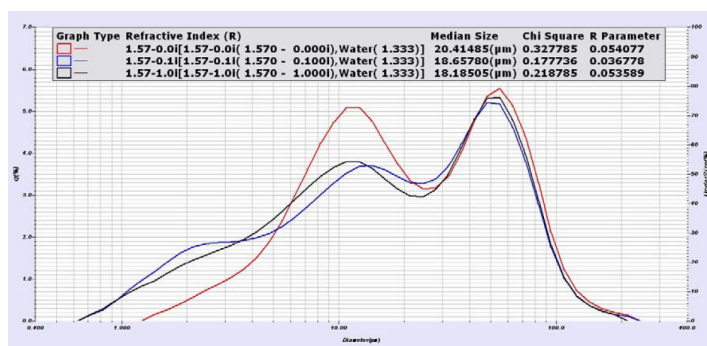


Figure 3

Both the Chi square and the R parameter values are lowest when the imaginary component is 0.1. This also makes intuitive sense because an imaginary component of 0 implies a transparent material (used for glass beads and latex standards) and a value of 1.0 and above implies a very opaque material. A word of caution is given that not all experiments are this easy to conclude and common sense must always be part of the decision making process. Comparison to results by image analysis is suggested when possible but may not be feasible when looking for particles below 1 µm using white light microscopy.