A New Approach for the Characterization of the Joint Particle Property Distribution of Micron and Sub-micron Particulate Systems: Biological and Synthetic Particles.

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ABSTRACT

Micron and sub-micron particles are characterized by a joint particle property distribution (size, shape, chemical composition, surface charge, and internal structure). Two measurement regimes are of interest, dilute (approximately 10^{-3} to 10^{-5} g/cc), and concentrated particle suspensions (40% by volume). To date, major industrial and academic efforts have been primarily focused on the measurement of the size distribution and on the development of on-line particle sizing instrumentation. If the problem of particle characterization is posed in terms of the joint particle property distribution, and if the issues related to dilute and concentrated dispersions are considered in the context of a sampling problem, it is then possible to formulate a strategy to address both problems with a unified technology. Light scattering and other spectroscopy methods are ideally suited for this purpose. Furthermore, by basing the strategy on recent developments in fiber optics based spectroscopy, the concept of bringing measurements to the process, and the concept of multi-sensor platforms can be readily implemented. This paper discusses a unified strategy for the continuing development of particle characterization technology. Examples of the progress made using the proposed strategy are also presented and discussed. Among these are the characterization and identification of microorganisms in drinking water, the spectroscopy characterization of blood, and the analysis of aggregation in colloidal systems. Practical applications include on-line measurements of the evolution of the particle size distribution in emulsion polymerization reactors and the detection of oxygen saturation level in the blood stream.

Introduction

Fiber optic based detection systems coupled with miniaturized spectrometers have added degrees of freedom for the development of specialized instrumentation for research, laboratory and on-line process monitoring. For the purpose of describing the technology, the detection system is divided into the following elements: the sensor, the detector (spectrometer), and the interpretation software. The sensors are generally positioned at the process end of the fiber optics and typically consist of membranes with immobilized chromophores (colorimetric reagents or indicators). The spectrometer measures the changes induced by the process in the sensor, and the software interprets the response of the detector on the basis of fundamental physico-chemical models and /or multivariate calibrations. The size and flexibility of the fiber optics enables the concept of a multi-sensor approach where specialized fibers can be used to monitor one, or several, properties of the process. The position of the fibers can also be adapted in different geometrical arrangements to extract the information as function of depth and/or to average the property being measured as a function of the vessel geometry. In other words, the fiber optics technology enables the sensors to be configured for specific analytes and to obtain measurements as function of time and space. The miniaturized spectrometer technology enables similar concepts to be applied to the detection element. The spectrometers can be arranged in a variety of configurations to maximize the information obtained from the process, to maximize sampling rates, and to increase the redundancy of information to improve on the statistics of the measurements. The advances made in the memory and speed computers have enabled efficient acquisition of large amounts of data and the utilization in real time of sophisticated theoretical and empirical modeling techniques for the interpretation of the data. The net result of these technological advances is that measurements can now be taken to the process and tailored to maximize the amount and relevance of the information extracted. This paper presents several examples of sensor and detector configurations for specific applications. The characterization of micron and submicron particles, and support technologies for on-line process monitoring are emphasized throughout.

Case I: Detector Configuration:

Commercially available techniques have focused on the estimation of a single particle property, generally the particle size distribution, although it is well known that particle size, shape, chemical composition and orientation are reflected in the measurements. These difficulties and the need to better characterize and control processes involving particle suspensions make the understanding of the measurements used for particle characterization, an issue of industrial importance. Traditional particle characterization methods are based on single scattering approximation (10^{-3} to 10^{-5} g/cc), whereas most industrial process streams operate at relatively high particle concentrations (40-60% by volume). Clearly, if optical techniques are to be the basis of the measurements, the forward scattering and transmission measurements will be effective for dilute suspensions, whereas the backscattering and reflectance measurements will be effective at high concentration or for measurements involving optically dense media. Recently [1], it has been shown that complementary information on the joint particle property distribution is available from angular measurements of combined absorption and scattering spectra. On the basis of this concept miniaturized spectrometers have been geometrically configured and a new Multiangle-Multiwavelength optical bench (MAMW) has been developed [1]. Figure 1 shows the concept behind this development. The multiangle-multiwavelength spectrophotometer was designed and constructed utilizing Ocean Optics Inc. miniature fiber optic spectrophotometers. These miniaturized spectrophotometers measure a specified range of wavelengths simultaneously, for this case 200 to 750 nm. Four spectrophotometer cards, allowing simultaneous measurements at four angles, were placed in a Pentium computer for data acquisition and analysis. UV/vis transparent fibers are connected from the spectrophotometer cards to collimating lenses, which are attached to the optical board (see Figure 2). Dilute and concentrated particle suspensions have been characterized using this device. Figures 3-4 shows the two-dimensional (scattering intensity versus observation angle and wavelength) for polystyrene latex standards in concentrated suspensions, and for red blood cells in the dilute regime. This technology has been particularly effective in providing guidelines and sensitivity information for the development of measurement and interpretation techniques in specific applications where the complete MAMW spectra are not required. Continuing research with the MAMW concept includes the use of polarization elements, and the coupling of flow, magnetic, and electric fields to enhance the resolution and to orient the particles relative to the incident light. The development of interpretation models based on imaging techniques is being pursued in parallel.

Case II: Fiber Optic Sensor Configuration:

Multi-wavelength reflectance and transmittance spectroscopy measurements contain information on several particle properties of interest such as particle size, particle counts, and chemical composition. These measurements are particularly appealing for industrial and bioengineering applications because they can be setup in a noninvasive manner. The use of miniaturized fiber-optic based spectrometer technology enables a large variety of probe configurations to enhance the detection and estimation of particle properties in optically dense media and at high concentration [2]. The definition of depth of sampling and the definition of the scattering volume to obtain particle counts can be achieved through manipulation of the source fiber-collection fiber configuration. Several commercial probe configurations have been tested to address issues related to the understanding of the optical sampling and the interpretation and quantification of the resulting spectra. Figure 5 shows some of the source-collection configurations tested. Figure 6 shows the spectral response during an emulsion polymerization reaction. Figure 7 shows the response as function of the particle size. It is evident that multi-wavelength reflection probes provide adequate discrimination for the estimation of the particle size, chemical composition, and particle concentration. Figure 8 demonstrates the importance of the fiber source-collection configuration in being able to extract the ratio of the venous to arterial flows in a real-time continuous monitoring during a blood oximetry experiment. Work in progress includes applications in other types of dense scattering media such as human tissue and blood cells. By taking advantage of the flexibility in the configuration of the probes, these simple spectroscopy measurements have already resulted in substantial improvements of non-invasive diagnosis tools for tissue and blood-gas analysis.

Case III: Fiber Optic Multi-Sensor Configuration:

The technology for the implementation of selective indicators or chemical sensors at the process end of the fiber optic is well established. Sol-gel and polymer membranes are extensively used for this purpose [3, 4]. The miniaturized spectrometers add an element of flexibility to these detection systems. However, one of the most exciting characteristics of the fiber optics chemical sensors is that the small size of the fibers enables multi-detector configurations through the use of fiber bundles, where each of the fibers responds to a particular analyte or series of analytes, depending upon their spectral response. In this manner, pH and conductivity (ionic strength) detectors have been constructed using pH indicator dyes with varying pKa values [3]. The combined used of pH sensors and bare fibers for particle characterization are being developed for the continuous monitoring of chemical mechanical processes in the microelectronics and photonics industries.

Case IV: Support Technology: Dilution-Transmission Measurements.

The development of new detection systems addresses only one part of the measurement and characterization problem of particle dispersions. Sampling and the analysis of the fluid structure (particle-particle interactions) are also key elements in the development of any on-line characterization strategy. In fact, the type of sampling strategy determines, to a large extent, the type of detection system to be used. For example, by optically interrogating the process through a window or through a fiber optic, concentrated particle dispersions can be analyzed undiluted, directly within the process vessel or from a sample stream. As discussed in the previous sections, under these conditions the angular position of the source and the detector(s) will determine the sampling volume from which the concentration can be established. The signal from the detector(s) will contain information on the particle size, the particle shape, and the fluid structure arising from the flow field and the colloidal forces particular to the system being analyzed. The combined problem of sampling and measurement from concentrated dispersions is clearly a formidable one for which a general solution is still forthcoming. An intermediate step in this development is the use of appropriate sampling and dilution strategies [5,7]. Simultaneous monitoring of conversion and particle growth in emulsion polymerization reactors has been reported using a novel automatic sampling and dilution system [6] coupled with a miniaturized spectrophotometer Figure 9. The advantage of using spectrometers as part of the detection systems can be appreciated in Figure 10-11, where the evolution of the particle size and the residual monomer analysis from a commercial latex reactor are shown. The enormous potential for analysis of these systems can be appreciated in Figure 12 where the spectrum of cryptosporidium a water born pathogen, is reported. Notice the deconvolution in terms of size, internal structure and chemical composition. This information provides quantitative elements of classification to assign in real-time measurements the presence of water born pathogens or infectious diseases from measurements taken from body fluids [8-9].

Summary

Fiber optics based sensor technology coupled miniaturized detector technology with clearly offers additional degrees of freedom for the design and implementation of sensors for the chemical and biomedical industries. In particular, a unified strategy for the continuing development of particle characterization technology seems feasible. Examples of the progress made using the proposed strategy have been presented and discussed. Among these are the characterization and identification of microorganisms in drinking water, the spectroscopy characterization of blood, and the analysis of aggregation in colloidal systems. Practical implementation of the proposed technology is in progress for applications including on-line measurements of the evolution of the particle size distribution in emulsion polymerization reactors and the detection of oxygen saturation level in the blood stream.

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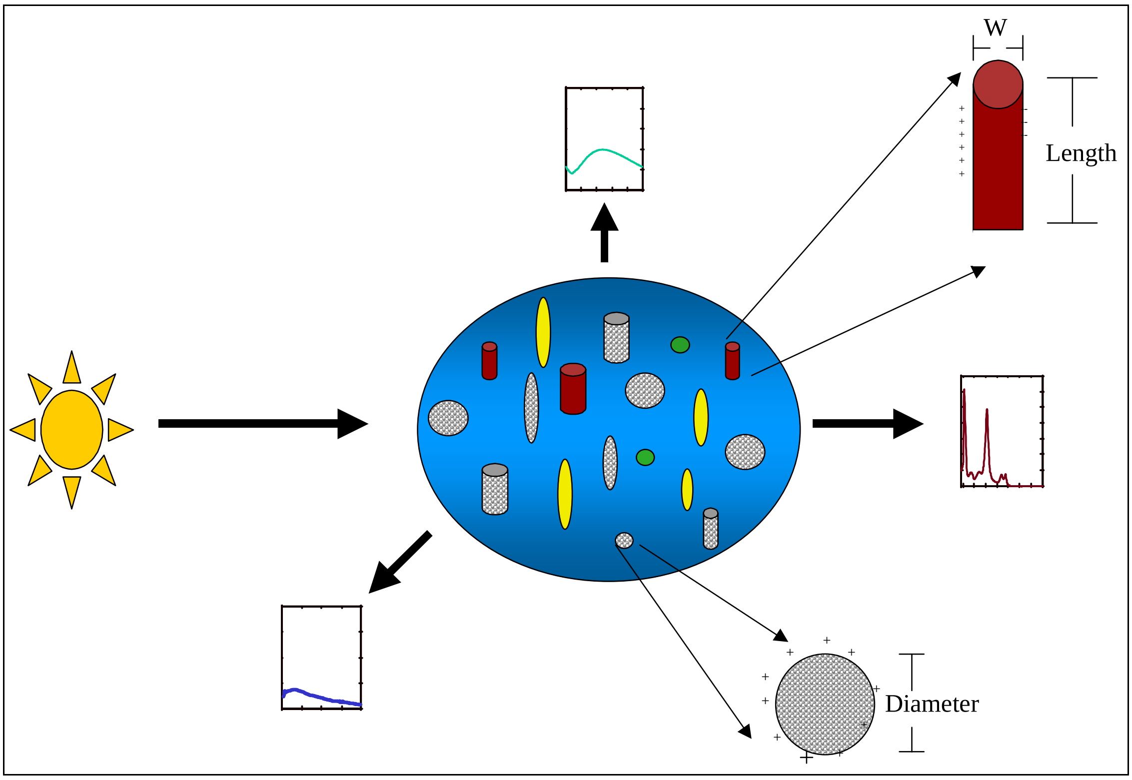


Figure 1: Multiangle Multiwavelength Concept.

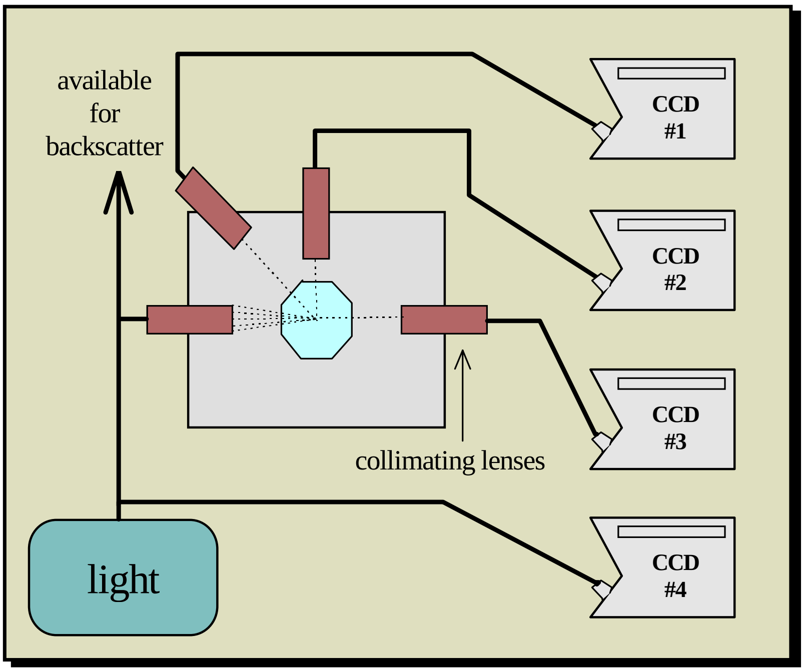


Figure 2: Prototype Optical Bench.

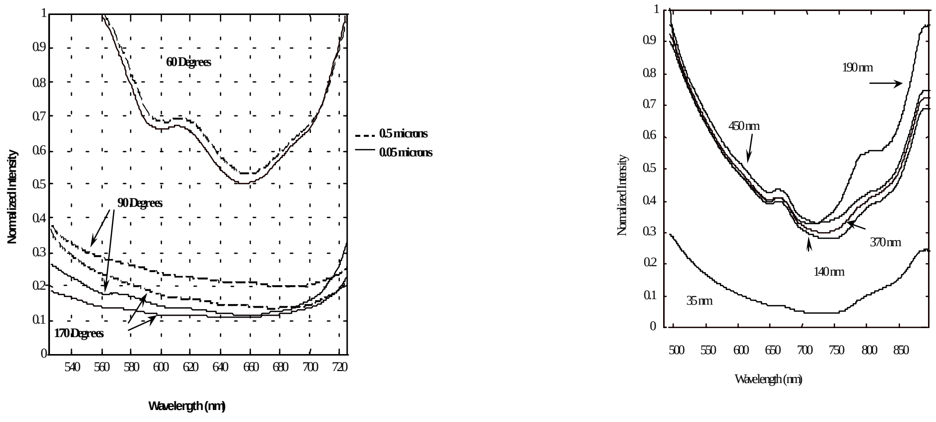


Figure 3: MAMW Response Surfaces for Polystyrene Latex Standards.

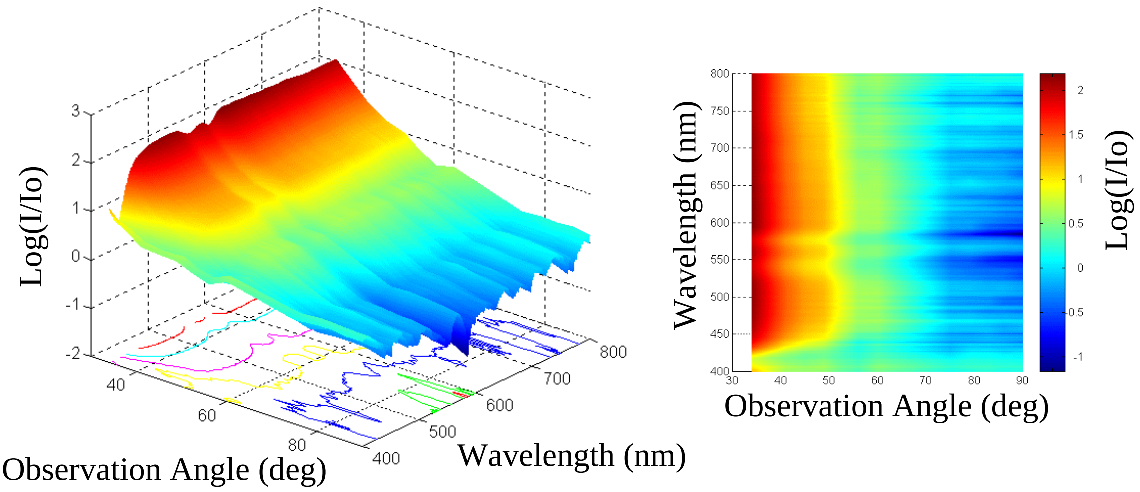


Figure 4: MAMW Response Surface for Red Blood Cells.

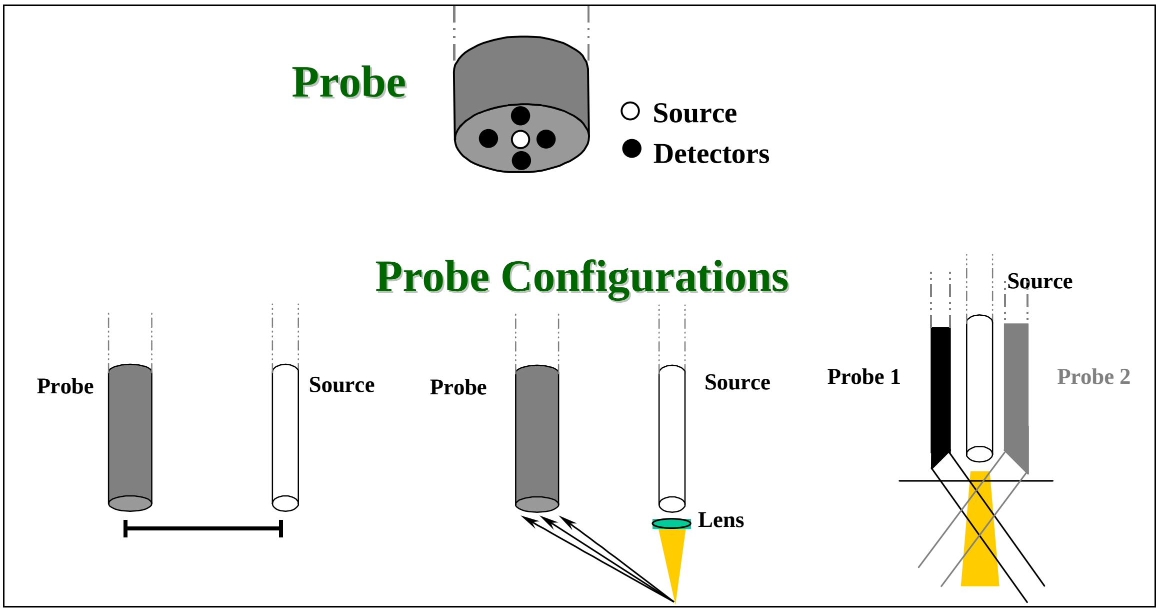
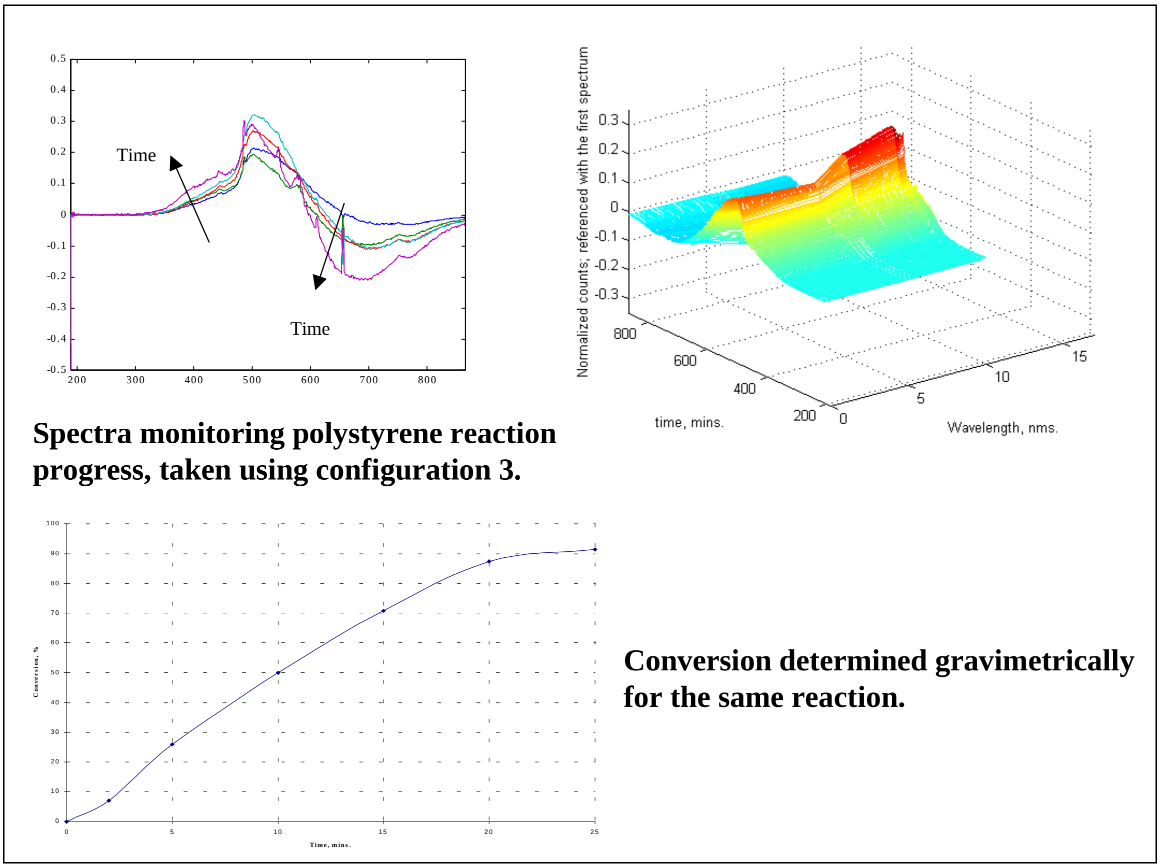


Figure 5: Probe Configurations for Reflectance/Scattering Measurements.



Spectra monitoring polystyrene reaction progress, taken using configuration 3.

Conversion determined gravimetrically for the same reaction.

Figure 6: Detector Response during Polymerization Reaction.

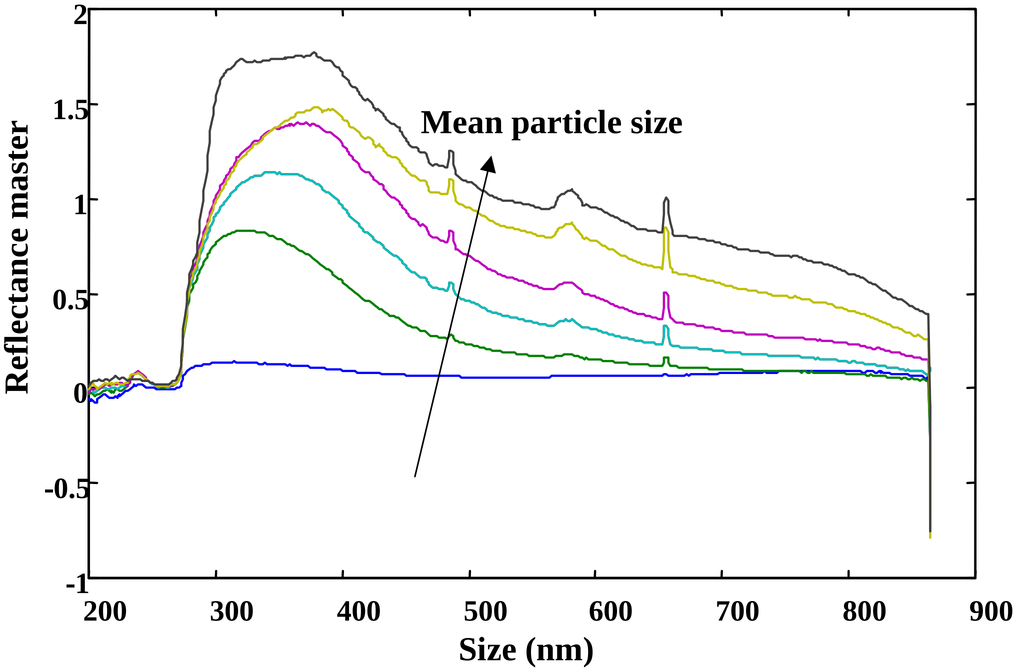


Figure 7: Reflectance measurements for probe configuration 2. Fiber closest to delivering fiber. Particle size effect on the reflection spectra.

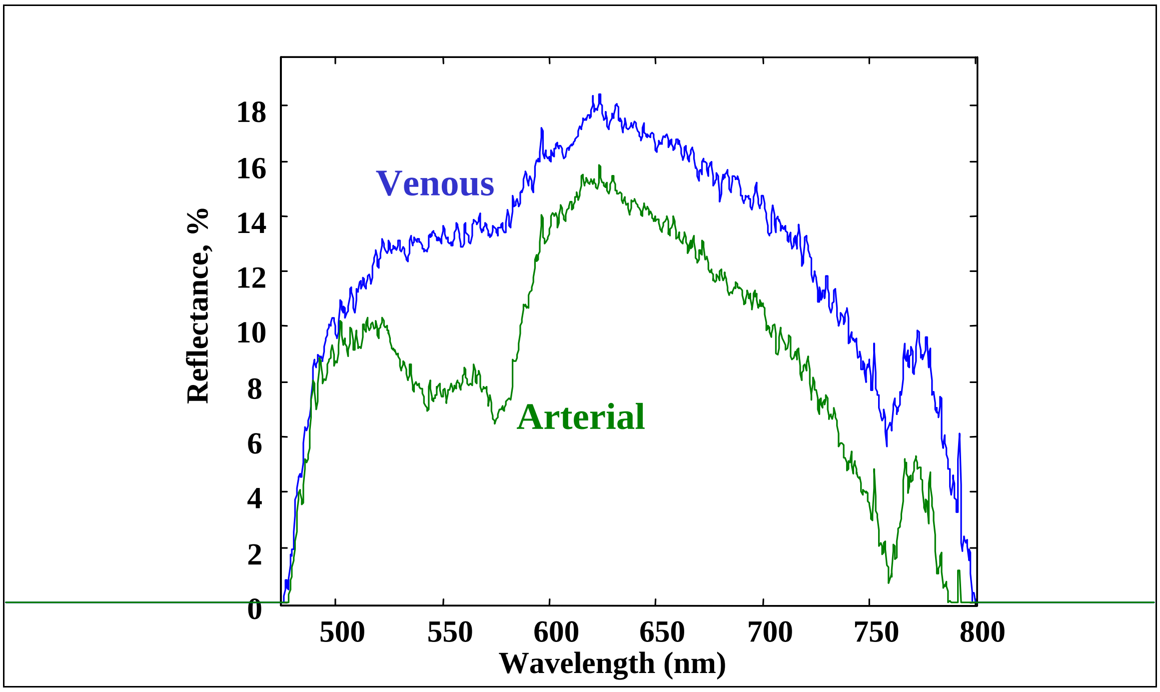


Figure 8: Non-Invasive Spectra for Arterial and Venuos Blood

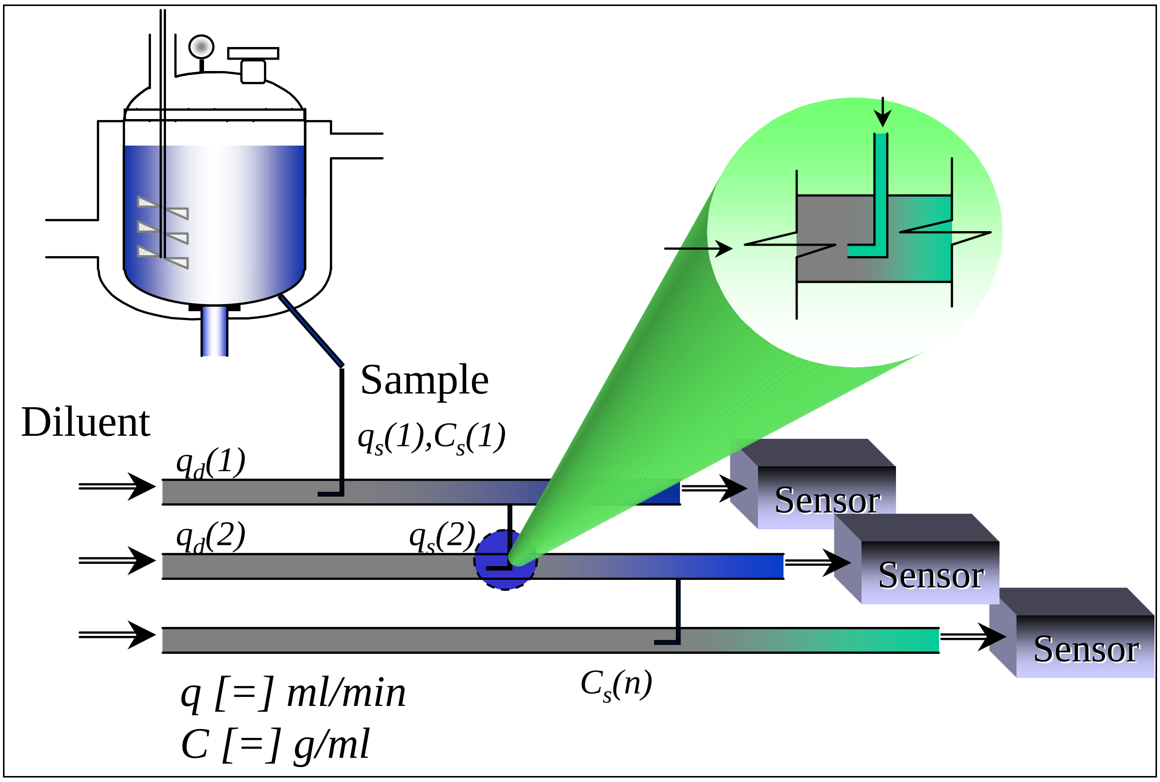


Figure 9: Automatic Dilution/Dissolution System. Parallel Dilution Schematic

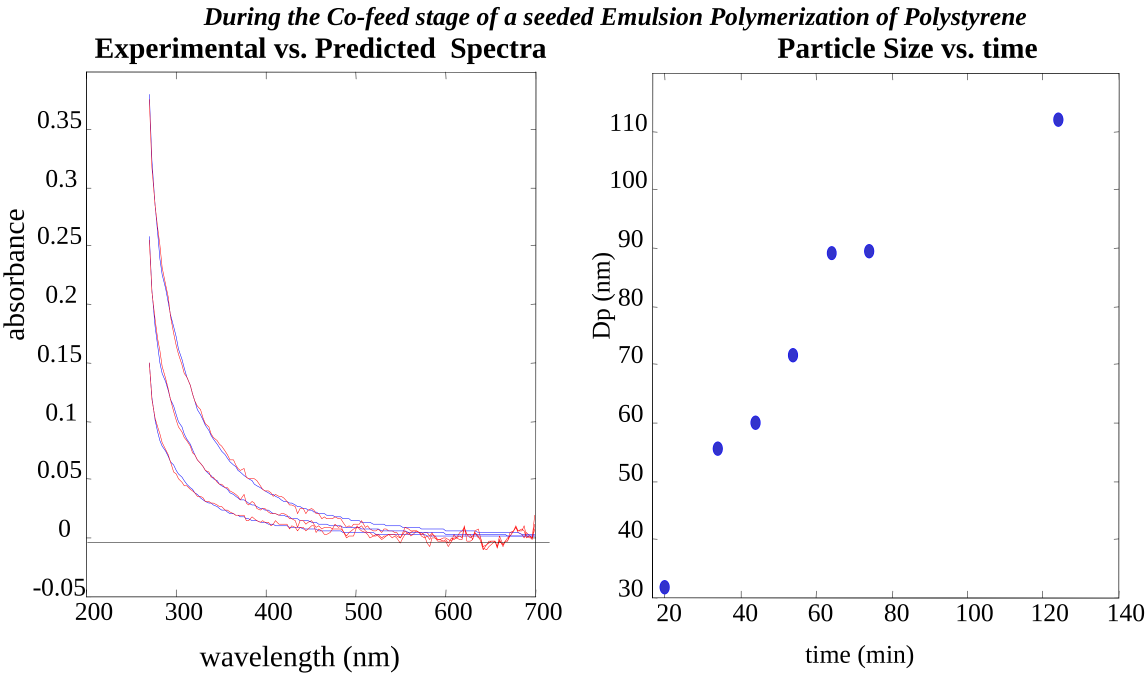


Figure 10: Experimental mean diameter estimates employing the automatic dilution system coupled with a fiber optic UV-Vis spectrometer.

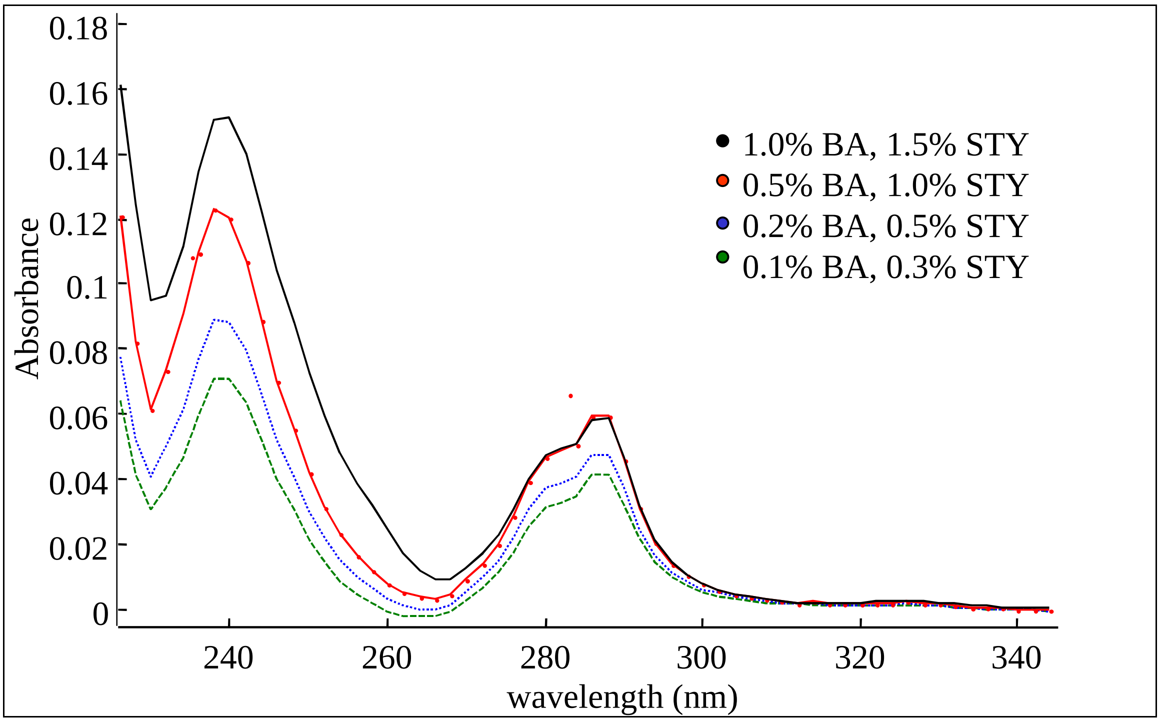


Figure 11: Absorption Component of four sample of Epoxy Acrylic Latex

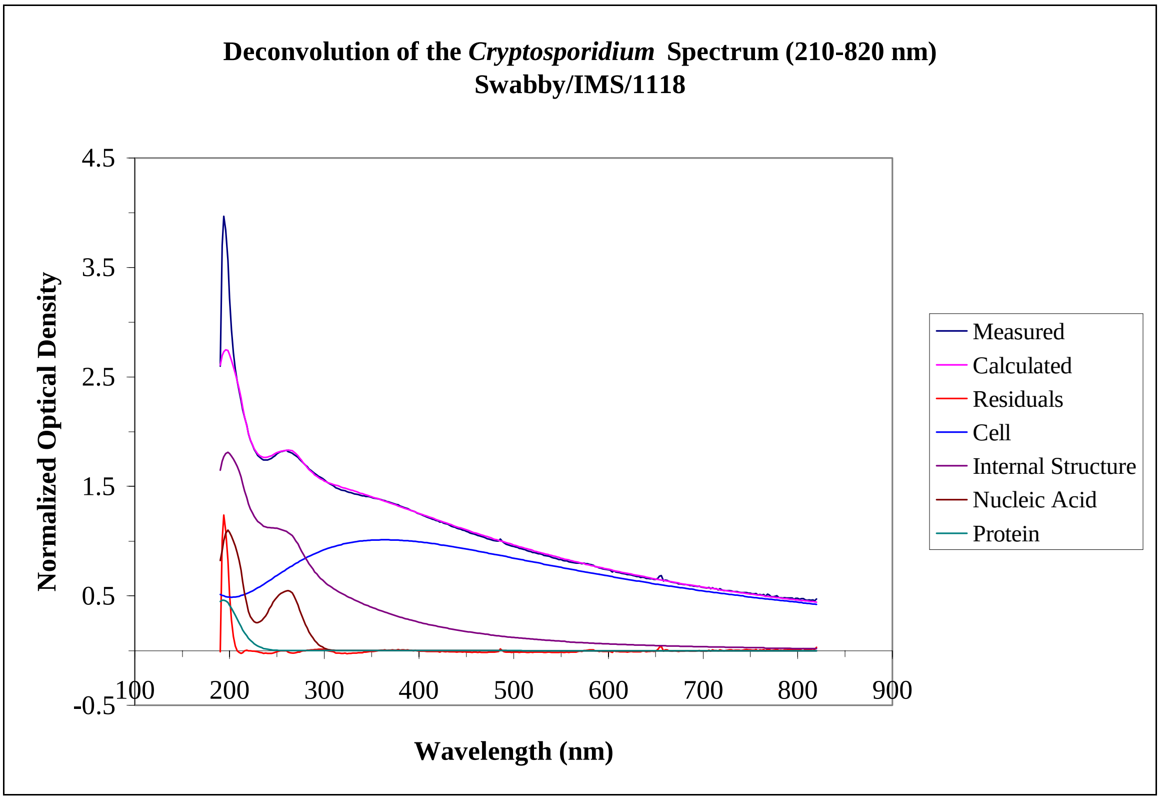


Figure 12: Deconvolution of Cryptosporidium Transmission Spectra