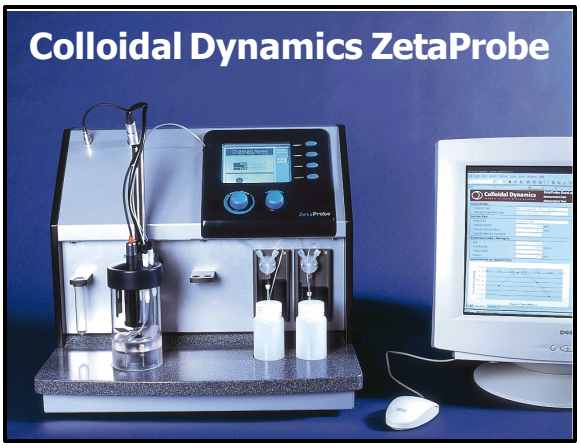
Colloidal Dynamics
leaders in colloid measurement

MEASURING PARTICLE SIZE AND STABLIITY OF EMULSIONS: The Colloidal Dynamics ZetaProbe and AcoustoSizer II

The ZetaProbe and the AcoustoSizer II allow the direct measurement of particle size and zeta potential in concentrated emulsions. Other devices need to dilute the sample to make these measurements. The dilution takes time, and it often alters the very things you are trying to measure.

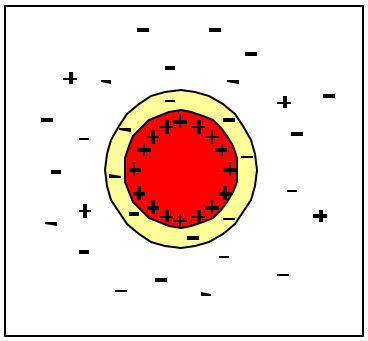
Our products
The ZetaProbe and AcoustoSizer-II are powerful tools for the measurement of droplet size and zeta potential in emulsion systems. The great advantage of these devices over the competing technologies is that they can measure size and zeta *without dilution*.



Other products require sample dilution
The traditional devices for measuring size and zeta use optical techniques such as light scattering. The samples need to be quite transparent to use these products, and this usually means they must be diluted down to concentrations of approximately 10 mg per litre. Even the more recent developments in optical devices that claim to be able to measure zeta potential in 'concentrated' suspensions can only do so at concentrations of 0.5 % w/v under favourable conditions of low opacity. This is still one to two orders of magnitude more dilute than most emulsion formulations.

What's so bad about dilution?
This dilution is time consuming, but worse, it can lead to large errors in the zeta potential due to a change in the concentration of the background electrolyte.

Background: What is the Zeta Potential?
Emulsion droplets are usually electrically charged. They are surrounded, in the emulsion by a cloud of ions which carry an equal and opposite charge.



Distribution of ions around a charged colloidal particle

The zeta potential is the voltage difference between the droplet surface and the liquid beyond the charge cloud. In emulsions which are electrostatically stabilized, zeta provides a measure of the electrical repulsive force between the particles. For other systems where the stability comes from steric components, the zeta potential can be used as a measure of the state of the surface. It can be used to monitor optimum levels of dispersant or other agents to be added to the droplets.

Thus zeta potential can be used for monitoring and controlling emulsion stability and as an indicator of surface chemistry.

The suspension has to be diluted with an electrolyte that is exactly the same as the electrolyte beyond the double layers. But even when the diluent is carefully matched to the inter-particle solution, the electrolyte

concentration can be altered by the release of ions which are soluble in both phases.

Furthermore, the diluted sample has such a small total droplet surface area that the zeta can be altered by trace amounts of surface-active impurities in the sample.

Why our products are able to measure without dilution

The AcoustoSizer-II and the ZetaProbe are able to measure without *any* dilution. The reason for this is that they measure sound, rather than light, so it is not necessary to see through the emulsion to make the measurements. In the ZetaProbe, the droplet zeta potential is determined by an *electroacoustic* technique. This involves applying a high frequency electric field across the emulsion and measuring an ultrasound signal generated by the motion of the charged particles in the alternating field. In the AcoustoSizer-II we combine the Electroacoustic technique with the measurement of ultrasound attenuation to determine both zeta potential *and* droplet size distribution.

The AcoustoSizer II

Applications

Emulsion applications studied include:

* Pharmaceutical emulsions e.g. stability of parenteral nutrition and anaesthetic emulsions
* Food emulsions e.g. fat droplets in dairy cream
* Industrial emulsions e.g lubricating oils
* Water-in-oil emulsions
* Fluorocarbon emulsions
* Cosmetic emulsions
* Microemulsions
* Bitumen emulsions
* Surfactant-free emulsions

Below we show two simple case studies that illustrate the power of these techniques. One study uses the combined simultaneous measurement of droplet size and zeta potential to show the dramatic destabilisation of a propofol/triglyceride anaesthetic emulsion when a local anaesthetic, lignocaine, is added.

Application 1. The stability of an anaesthetic emulsion[1]

Intravenous emulsions are used to provide nutrition for patients who cannot be fed orally and as drug delivery vehicles. This study is concerned with a commercial anasthetic emulsion, Diprivan (ICI Pharmaceuticals, England), which is a 10 volume percent oil in water emulsion. The soyabean oil droplets contain propofol anaesthetic. While Diprivan is a safe and reliable means of administering propofol, it is

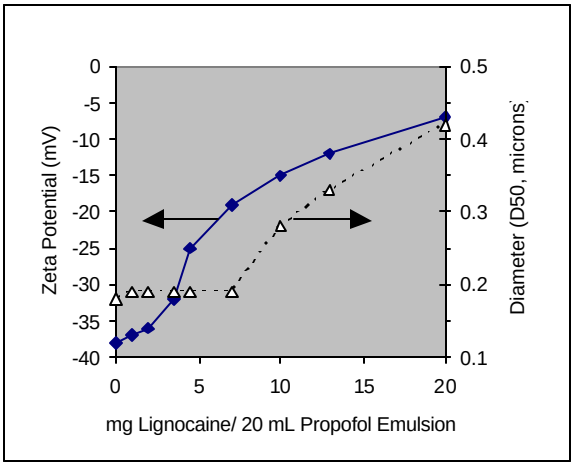


Figure 1 *Instability induced in anaesthetic emulsion by addition of lignocaine*

often mixed with other drugs such as muscle relaxants and narcotics. It is important that the droplet size is not increased by the extra components, since that can render the emulsion unsuitable for infusion.

The aim of this study was to measure the stability of Diprivan in the presence of additional drugs. Several drugs were used in this study, but we will focus here on the effect of lignocaine hydrochloride, a local anaesthetic used to reduce the pain on injection of Diprivan.

In figure 1 we show the AcoustoSizer measurements of the droplet size and zeta potential of the Diprivan at different levels of lignocaine addition. Clearly the lignocaine decreases the magnitude of the zeta potential, and thus the e lectrostatic repulsive forces between the droplets is reduced. This does not affect the droplet size until the lignocaine level reaches about 10 mg/mL of emulsion. At this point the zeta is too small to provide stability for the suspension, and the droplets grow. The droplet size continued to grow on standing and the suspension creamed overnight. Clearly the simultaneous measurement of zeta and size, which is provide by the AcoustoSizer, is able to provide a clear explanation, and a way of preventing the on set of instability.

Application 2. The monitoring of emulsion production by high-pressure homogenisation[2]

Emulsions can be made by pumping the oil/water mixture through a series of small orifices.

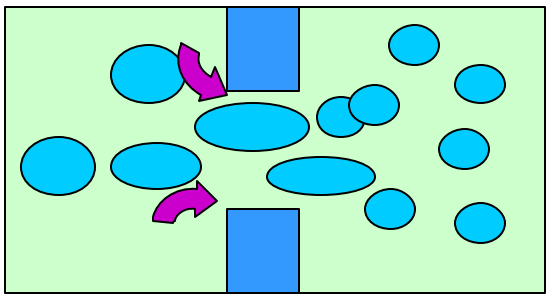


Figure 2 *Droplets break up as they are pumped through the small openings in a homogeniser*

The extensional stressed placed on the drops as they squeeze through the orifice cause the larger droplets to rupture. The stresses increase with droplet concentration, and the ability of the droplet to withstand these stresses depends on the type and concentration of sufactant. Thus the resulting size distrib ution depends on these factors, and on the number of times the emulsion is passed through the homogeniser.

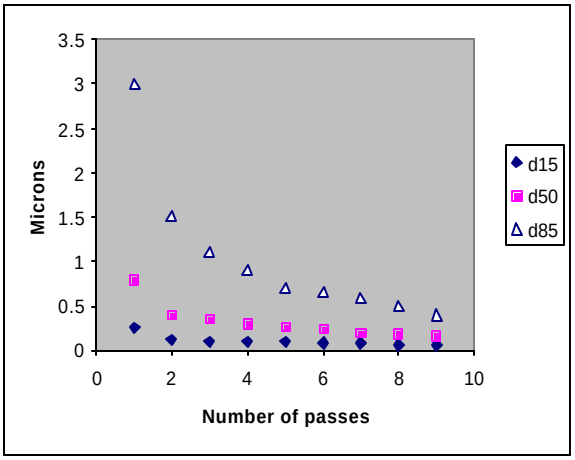


Figure 3 The decrease in particle size with the number of homogeniser passes

In figure 3 we show the change in size and zeta with the number of passes through the instrument.

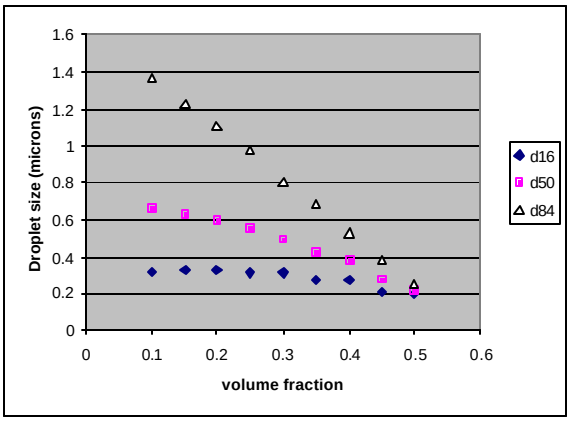


Figure 4 *The decrease in particle size with increase in volume fraction of oil phase*

In figure 4 we show the effect of droplet concentration on the resulting size

distribution after 15 passes through the homogeniser.

Since the AcoustoSizer and ZetaProbe both come with flow through cells, it is a simple matter to incorporated them into the flow loop and monitor the droplet size reduction in real time, without the need for dilution. Thus processes can be tailored in the R&D lab to optimise the final product, and they can be monitored online, in the production process to keep the emulsion within specification. This ability to ma ke rapid and precise measurements on these concentrated emulsions is one of the great advantages of this technology.

References:

1. Lilley E.M. Isert P.R. Carasso M.L. and Kennedy R.A. *Does the addition of Lignocaine to Propofol destabilise Propofol emulsions?* Anaesthesia 52 [3]: 288.

2. L. Kong, J.K.Beattie and R.J.Hunter *Electroacoustic determination of size and charge of sunflower oil-in –water emulsions made by high -pressure homogenising.* Chem. Eng. Processs. 40(2001) 421-429.