Using Mageleka *MagnoMeter* XRS™ *RelaxoMeter* Measurements to Study and Fingerprint Microemulsion Systems

Introduction

Isotropic mixtures of oil, water, and surfactant are called microemulsions. Owing in part to their ease of formation and stability, the effective use of microemulsions has increased dramatically as major industrial applications have expanded in a variety of fields. Two important examples are enhanced oil recovery and drug carrier systems for oral, topical, and parenteral administration. In the former application, microemulsions are the key to efficient extraction of crude oil by dramatically reducing the interfacial tension ("chemical flooding"). In the latter, they offer the advantage of ease of manufacturing and scale-up, and improved drug solubilization and bioavailability.

In practice, microemulsions usually contain a co-surfactant (and/or co-solvent), and the oil itself is often a mixture of different hydrocarbons and olefins. In contrast to ordinary emulsions, which are thermodynamically unstable and will phase separate, microemulsions are thermodynamically stable and, importantly, do not require high inputs of energy or shear conditions for their formation – a commercial economic benefit. The significance and potential that researchers attach to microemulsions are, in no small part, because of their unique properties: low interfacial tension, high thermodynamic stability, high interfacial area, and the ability to solubilize immiscible liquids.

Thorough characterization of any microemulsion system is essential but is problematic because microemulsion domains exist at fairly specific concentrations of the three basic components and so dilution is not generally an option. Hence, studying these systems *in situ* is not straightforward and there are few tools available with which to directly measure microemulsion characteristics. Since microemulsion systems are clear, conventional light scattering is difficult (if not impossible). X-ray and neutron scattering, and dielectric measurements, have been used to provide insight to the structure and dynamics of the particular microemulsion, but they are not routine and not suited to standard laboratory analysis.

In contrast, the nuclear magnetic resonance (NMR) relaxation technology employed by the Mageleka *M*agno*M*eter XRS™ *R*elaxo*M*eter, is easy to use, produces rapid results, and requires limited input data. Importantly, and as we will explore in this Application Note, it is an ideal technique for fingerprinting microemulsion systems. Here, we present data obtained on a model microemulsion system to illustrate both the utility and simplicity of the *R*elaxo*M*eter as a routine aid in formulation by fingerprinting not only the initial and final compositions of both the oil and water phases, but also the subsequent microemulsion system created.

About NMR Relaxation

NMR spectroscopy is one of the most powerful analytical tools used to probe details of molecular structure and dynamics. Traditional devices employing NMR technology require

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high magnetic fields and, hence, large magnets and related instrumentation. However, the advent of small powerful magnets has allowed instruments such as the *R*elaxo*M*eter to be designed that have small footprints and are suited to normal, routine laboratory analysis.

The *R*elaxo*M*eter has harnessed the power of NMR spectroscopy to measure liquid relaxation. Importantly, the relaxation time is a fundamental intrinsic property of liquids, and its measurement provides direct information about the extent and nature of any liquid-liquid interface (i.e., emulsions).

What the *R*elaxo*M*eter measures is the extent of molecular motion as protons interact when perturbed by local magnetic fields, and the resulting relaxation time obtained for a bulk liquid is an average value that is dependent upon the exact composition of the liquid, whether it is pure, mixed, or contains dissolved moieties. It can be bi/multi-modal if there are distinct phases.

What does the *R*elaxo*M*eter do?

Regular emulsions are two-phase systems and so there will be two major intrinsic relaxations – a short time and a long time – characteristic for the total oil phase and for the total water phase, respectively. Critically, the *R*elaxo*M*eter's measurement technique is noninvasive and nondestructive, and it can work with any type of emulsion – whether oil in water or water in oil – and, importantly, irrespective of the internal phase concentration. Indeed, in principle it can determine which phase is the internal one. Of practical utility, the *R*elaxo*M*eter eliminates the dilution issues inherent in making measurements using, for example, traditional light scattering techniques. The simple measurement technique takes only minutes. Samples can be stored under thermally controlled conditions (e.g., ICH guidelines) and reanalyzed to understand thermodynamic stability. Also, emulsion microstructure can be investigated with exquisite clarity via NMR relaxation. Thus, the *R*elaxo*M*eter provides complementary information to traditional particle characterization devices. But it also provides additional interfacial insight not possible with those devices.

Using the *R*elaxo*M*eter to fingerprint microemulsions

Below, we illustrate the use of the *R*elaxo*M*eter to study a series of three simple model microemulsions. The water phase was the same for each formulation and comprised 4% of a surfactant, 5% of a co-solvent, plus 2% NaCl. The component composition is shown in Table 1.

Table 1. Formulation composition to create model microemulsions.

Formula	Initial Composition Oil: Water Ratio (%)
1	47:53
2	62:38
3	77:23

The photograph (Fig. 1) shows an example of the three phases created in each of the three formulations. A small amount of a dye (Sudan Red) had been added to the base oil (n-decane) to more clearly distinguish the three phases.

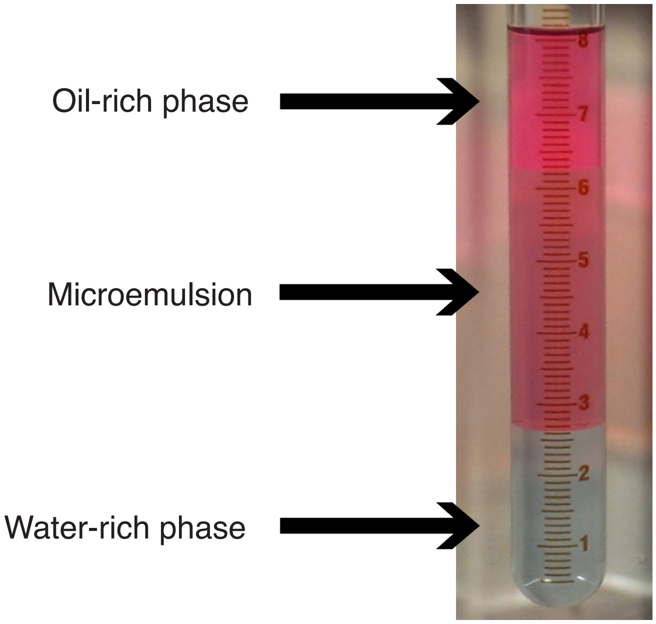

Figure 1. Photograph of Formulation #2.

As might be expected, the volume of each of the phases formed differed for each formulation (Table 2).

Table 2. Approximate volume of the phases (mL) of three model formulations.

Formula	Top phase	Middle phase (microemulsion)	Bottom phase
1	1.3	3.7	3.1
2	1.9	3.6	2.6
3	2.4	3.5	2.1

The top phase is primarily oil but could also likely contain a very small amount of emulsified water, as well as any fraction of the surfactant and co-solvent not used to create the microemulsion phase that can partition into the base oil. Conversely, the bottom phase is primarily water but also could contain a very small amount of emulsified oil and any residue of surfactant and co-solvent.

The middle (microemulsion) phases were extracted, and the relaxation time measured directly using the *R*elaxo*M*eter. As with regular emulsions, two major intrinsic relaxations (a short time and a long time) characteristic for the total oil phase and for the total water phase, respectively, were found. The results are summarized in Table 3.

Table 3. Average relaxation times for the microemulsion phase of three formulations.

Formula	**Average Relaxation time (ms)**		
	Short	Long	Ratio
1	714	1982	0.360
2	508	1400	0.363
3	393	1091	0.360

The results show that the short relaxation times track directly with the amount of base oil used to prepare the microemulsions (Figure 2). This would be expected because the relaxation time measured separately for the n-decane alone is much shorter (*ca.* 1250ms) than that for water alone (*ca.* 2350ms). For both, only a single exponential fit was found.

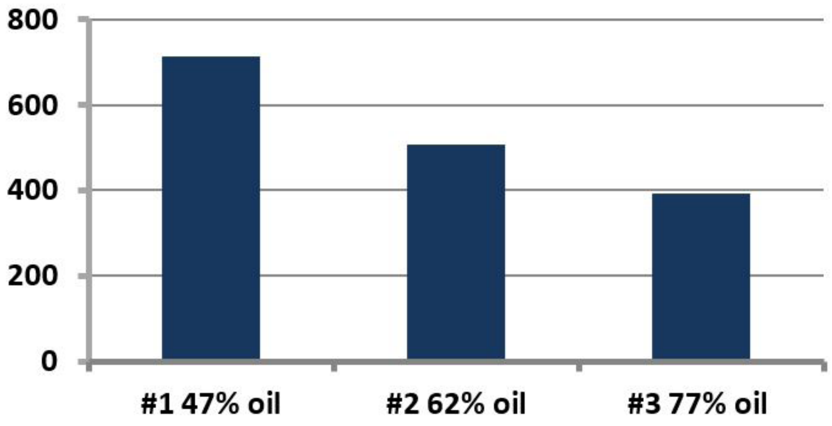

Figure 2. Average short relaxation time (ms) as a function of base oil amount of three formulations using data from Table 2.

The data in Table 2 and Figure 2 provide two insights. First, while the relaxation time decreases markedly from formulations 1 to 3 with increasing amount of oil, the volume of the middle phase decreases only slightly. This suggests an increase in the total number of oil droplets and/or a decrease in oil droplet size in the microemulsion. Second, the ratio of the short-to-long relaxation times is fairly constant, suggesting that the nature of the interfacial bound layer between the two liquids in the microemulsion is similar.

In Table 4, the relaxation time of the water phases – both before and after emulsification – are compared (shown graphically in Figure 3) for Formula 2. Here, as expected, only a single exponential fit was found.

Table 4. Average relaxation times for water samples from Formula 2.

Water Sample	Average Relaxation time (ms)
1: Original aqueous phase used to prepare Formula 2	1480
2: Aqueous phase extracted from 3-phase system of Formula 2	2307
3: 2% NaCl	2348
4: Distilled water	2350

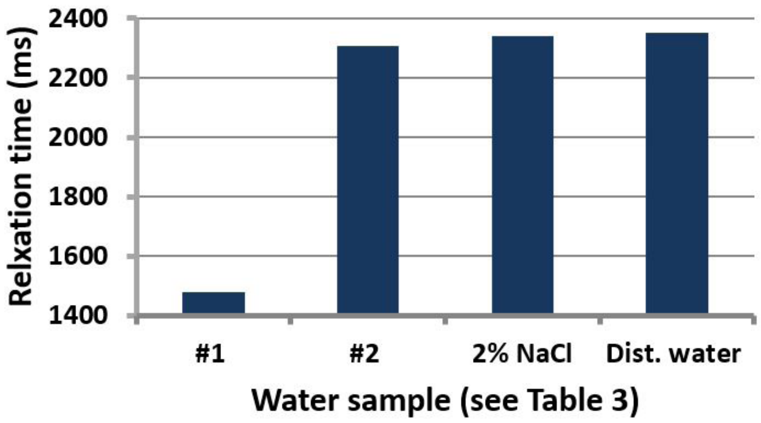

Figure 3. Comparison of the average relaxation times (ms) of various water samples using data from Table 4.

The data in Table 4 and Figure 3 provide two insights. First, it can be seen that the presence of 2% NaCl has no effect on the relaxation time of distilled water. Second, virtually all the surfactant and co-solvent in the original water phase has been used to create the microemulsion.

In summary, the findings above are just a few examples of information that can be obtained directly from an NMR relaxation time analysis of microemulsions using the *R*elaxo*M*eter. Such analysis is not possible with traditional laboratory instrumentation. It is worth mentioning that each of the relaxation time measurements presented took approximately 10 seconds using the *R*elaxo*M*eter. Thus, *R*elaxo*M*eter measurements can be used to quickly, routinely, and noninvasively fingerprint not only the initial and final compositions of both the oil and water phases but also the subsequent microemulsion system created.

Additional important information regarding the behavioral characteristics of liquids – whether pure, mixed, or containing dissolved moieties – can be obtained by measuring their self-diffusion coefficients using a Mageleka *D*iffusio*M*eter. This information complements relaxation data and is particularly useful for studies of emulsions.

For more information, to send samples, to arrange a demonstration of the MagnoMeter at your facility, or to talk to one of Mageleka's technical applications specialists, please email roger@mageleka.com