

Applications of Diffusing Wave Spectroscopy in Pharmaceutical Formulation Technology

Webinar Q&A Transcript

1 How is I^* calculated?

I^* is calculated by measuring the count rates of the transmission and backscattering signals and then using pre-entered calibration data. For more information, please read the following paper:

[Improved diffusing wave spectroscopy based on the automatized determination of the optical transport and absorption mean free path.](#)

2 When comparing DWS microrheology and oscillatory measurements, you mentioned an occasional mismatch between macro- and micro-rheology. Have you found a way to correct for things like shear-thinning that are likely to drive those disagreements?

In the case of simple systems, such as gels or diluted dispersions with just one polymer that determines the rheological properties of the external phase, there is often a good agreement between macro- and microrheology.

However, many products are more complicated, for example, topical pharmaceutical or cosmetic formulations that show a long list of excipients. There is typically more than one component that forms a structure: crystallizing fats may play a role in determining overall bulk properties, on top of surfactants and polymers. In such cases, we see often a mismatch between the results obtained via these two techniques. This is because what is relevant to the microscopic environment of the tracer particles is not necessarily the same as the overall bulk structure that is probed by a mechanical rheometer.

Our approach was very practical in analyzing complex pharmaceutical or personal care products. One has to deconstruct the formulation by preparing simplified

versions of the composition to better understand what determines the micro- and macrorheology.

3 Have you tried relating the DWS data to steady shear data without using Cox-Merz?

The Cox-Merz rule holds primarily for polymeric systems in a limited range of steady-state shear. However, it is a practical approach to estimate relevant shear rates in a given industrial process and to compare it with the corresponding frequency range in the DWS measurement. A first step can be to find qualitative rank correlations between the mechanical properties and the process performance of the formulation. Escalating this to quantitative model predictions is certainly more ambitious but could be the next step.

4 You mentioned that DWS relies on knowing particle size to get viscosity. Are there equations that allow for use with high aspect ratio, or large size distribution particle suspensions?

It is important to note that tracers are never perfectly monodisperse, and broad particle size distributions are not a hindrance to the calculation of the rheological data. For a monomodal size distribution, up to a polydispersity of 30-50%, DWS Microrheology is only weakly affected by polydispersity.

Concerning the high aspect ratio: what is relevant to DWS is the diffusive motion of the particle, which is then converted to a size using the Stokes-Einstein equation. In the case of anisotropic particles, one could measure their hydrodynamic radius through DLS and use this value to determine the viscosity through DWS.

5 What about liquid biological formulations (proteins, mAbs, peptides)?

DWS provides significant advantages in this field. Mechanical rheometry is only safe to use when the sheared sample remains homogenous. However, there are often surface effects observed with analysis of peptides and proteins as they can accumulate at the interface to where mechanical shear is applied. These kind of measurement issues provide a strong rationale to use DWS. Interesting is to follow the storage modulus G' in samples that exhibit some structuring in the course of protein aggregation.

For zero-shear viscosity measurements on such systems, we also recommend watching our [webinar on the topic](#) or to view our recent [poster](#).

6 Can you talk about any attempts to selectively partition tracer probes into one phase of a phase-separated system (i.e. a nucleated gel phase of interest surrounded by a Newtonian solvent phase)?

If this partitioning would prove too difficult, can you comment on strategies to decouple scattering signals from multiple phases in a DWS sample?

In DWS; one measures the local environment of the tracer. In the case of phase separation, the tracer particle may concentrate preferentially in one phase. If this can be tuned so that tracer particles inform about a phase separation then this is indeed a very interesting application of DWS. In other cases of unclear separation of tracer particles, experimental results can become rather difficult to interpret and it would be a nuisance if you think of the system as homogeneous.

To decouple the scattering signal we recommend using the LS Spectrometer. Due to the multiple light scattering principle, the DWS RheoLab does not allow disentangling the MSD data for multi-modal particle size distributions.

7 What would your next projects be?

There have been quite some advancements, and we continue to work towards using DWS for the characterization of emulsions, monitoring of their homogenization process as well as prediction of physical stability. Compared to the field of lipid-based formulations, DWS applied to solid dispersions is less advanced, and much work remains to be done here as well.