Multimodality investigation of microstructure: the combination of diffusion NMR and diffuse optical spectroscopy

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Abstract

We propose that multimodality imaging may be enhanced by combining datasets with a model of the underlying physics prior to image reconstruction, as opposed to the traditional approach of combining the reconstructed image. Here, we demonstrate this approach by merging near infrared diffuse optical spectroscopy with diffusion NMR to inform a model describing the microstructure of a sample. A computational validation of the results, produced with synthetic datasets, shows the enhanced accuracy of the estimation, while an application of the model on experimental measurements confirms the validity of the models.

1 Introduction

Traditional multimodality imaging relies on combining reconstructed images to produce information which is not available when using one modality alone. Here, we propose a new approach which is to use data acquired prior to reconstruction to inform a model of the underlying physics of the phenomenon under examination.

This work provides a proof of principle of the idea that the fusion of two modalities increases the accuracy compared to using a single modality. A multimodality investigation of microstructure has been designed by combining near infrared diffuse optical spectroscopy (DOS) and diffusion NMR (dNMR). Ultimately, we intend that this approach will lead to a new method for imaging tumour microstructure.

The modalities inform a common model able to estimate the microstructure parameters of interest. The two modalities measure different aspects of the physics. DOS is sensitive

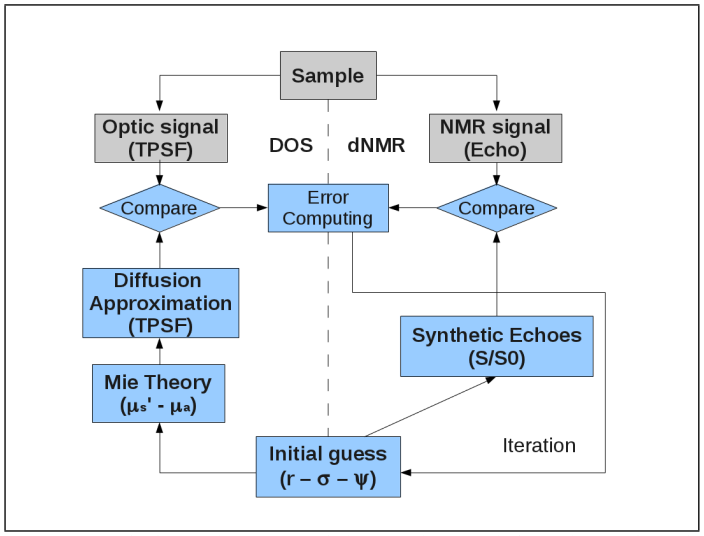


Figure 1: A scheme explaining the algorithm adopted for the mixed model approach.

to the absorption, and to the number and the size of scatterers in the sample, while dNMR observes the effect of molecular diffusion constrained by microstructural compartments.

2 Methods

We derive the distribution of size and the volume fraction of oil particles suspended in a water-based compound. The sample was commercial light mayonnaise (J Sainsbury plc, Basic Mayonnaise). It is a homogeneous and isotropic material with a stable microstructure composed of microspheres in a dispersion medium sensitive to DOS and to dNMR. The optical signal is affected by the change of refractive index between oil globules and dispersion medium, while the dNMR depends on the constrained diffusion of oil particles. The dispersion medium is predominantly water with some other components (proteins, carbohydrates) and within it are oil droplets. The microstructural parameters of interest are the distribution of radii of the microspheres, modeled as log-Normal, with mean r, standard deviation , and volume fraction .

2.1 NIR diffuse optical spectroscopy

Time-domain DOS consists of the observation of Temporal Point Spread Functions (TPSF) recorded in transmission through a homogeneous slab when the number of scattering events is large enough for the light transport to be assumed to be diffusive.

We used time-domain DOS to build up a histogram of the time taken for individual photons to diffuse through a homogeneous slab of mayonnaise. The measurements were obtained using a time-domain optical tomography system known as MONSTIR [4]. The sample was contained in a 17 48 $52mm^3$ transparent plastic box and the source was a laser that emitted 5ps pulses of light at 780nm. On the opposite face, a 5 $5mm$ diameter detector recorded the TPSF. The measurements were averaged for a duration of $10s$ and the final result was calibrated by deconvolving it with a reference measurement acquired without the sample.

The TPSF is fitted with a Diffusion Approximation (DA) model [1], using a Levenberg-Marquardt algorithm. The apparent scattering $_s$ and absorption $_a$ coefficients are esti-

mated. From the optical parameters, a linear interpolation of the dispersion medium and oil absorption coefficients are able to provide the volume fraction and the refractive index as

$$\begin{matrix} n_s & n_i & 1 & n_o \\ {}_{a\,s} & {}_{a\,i} & 1 & {}_{a\,o} \end{matrix} \tag{1}$$

where n is the refractive index (the subscripts o indicates the dispersion medium compartment, i the microspheres, and s the sample as a whole). The scattering coefficient is provided by the Mie theory [6], depending on the ratio $n_r \quad n_i \; n_o$ and the shape factor $k \quad r$, where is the wavelength of the incident beam. Mie theory provides the scattering coefficient ${}_{s\,Mie}$ and anisotropy factor g_{Mie} relative to a single scattering event, and the scaling on the number of particles per unit of volume provide the sample apparent scattering coefficient as follows:

$$N_V \quad \frac{3}{4 \quad r^3}, \qquad {}_{s\,s} \quad N_V \quad {}_{s\,Mie}. \tag{2}$$

The use of the optical modality alone is not able to define the distribution of radii but only the mean value r. However, optics can determine the volume fraction .

2.2 Diffusion NMR

For Diffusion NMR modality, we applied a Stimulated Echo sequence to a 20 20 $20mm^3$ sample using a 9.4T Varian preclinical scanner. The signal attenuations for the different parameters were calculated by normalizing the peak amplitudes in the diffusion weighted spectra with the corresponding peaks the unweighted spectra. These attenuations represent the effect of constrained diffusion of oil and water molecules. A set of measurements with a combination of diffusion times 50 100 150 200 250 400 $700ms$ and gradients G 0 0 1 0 2 0 4 0 6 0 8 0 $95T \;\; m$, with TR $4s$ and $5ms$ was obtained.

The signal attenuations were fitted with the analytical model representing the diffusion in spherical compartments as presented in literature [3]. Since the size of microspheres contained in the sample may be described by a log-Normal distribution of probability, the signals produced by all the possible radii have been integrated to obtain the global contribution [2]. The fitting of the the experimental data with the model discussed has been implemented with a Levenberg-Marquardt algorithm, and the diffusivity coefficient D has also been estimated. The dNMR modality can provide r and but not .

2.3 Mixed model

The multimodality approach fits the microstructural parameters by optimizing the difference between the experimental and the analytical signals in the two modalities as shown in figure 1. The difference between the experimental signal and the simulated value in each modality are combined as

$$E_{MIX} \quad w \;\; TPSF_{EXP} \quad TPSF \;\; r \quad t_0 \qquad 1 \quad w \quad S_{EXP} \quad S \;\; r \quad D \tag{3}$$

where w is the weighting factor, set to 0.5. In this formula, the subscription EXP refers to data measured during the experiments while the others are generated by the analytical model. $TPSF$ describes the signal in the DOS modality, while S the echoes attenuation. E_{MIX} is minimized and an optimal solution is retrieved. Since the optical modality is unable to estimate the distribution of radii, but only their mean value, a representation of radii

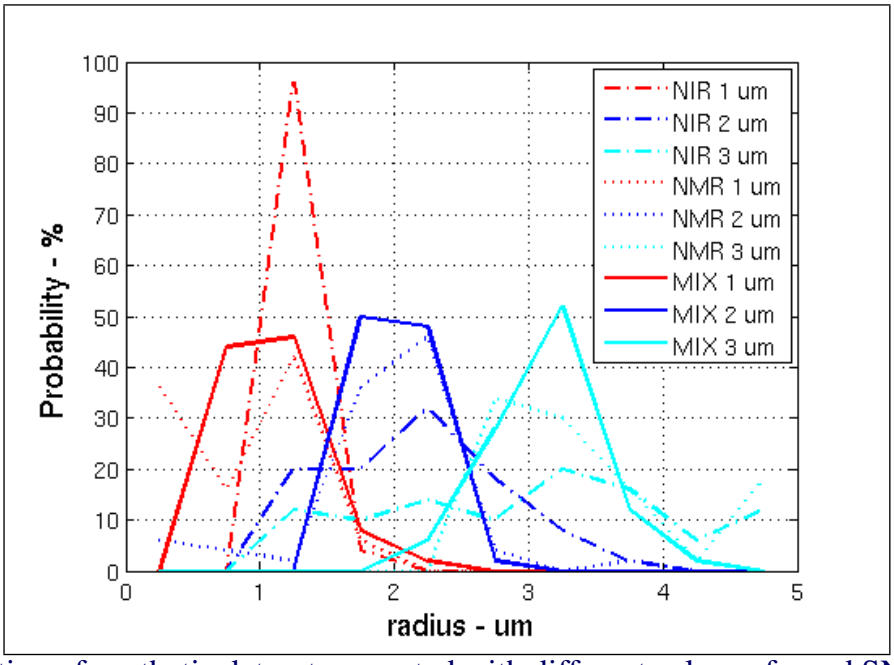


Figure 2: Fitting of synthetic dataset generated with different values of r and SNR = 16. The dataset are fitted with the two modalities independently and with the combined approach, and the estimated values of r are shown in this graph.

distribution has been adopted to match the information contained in dNMR data to make them compatible with DOS modality. The optical properties are generated by considering a poly-disperse distribution of microsphere sizes [5].

3 Results

In order to validate the model, 50 synthetic datasets were generated for every set of microstructural parameters. Noise was added such that the SNR was 16, and the parameters considered were r 1 2 3 m, 1 2 3 m and 0 1 0 2 0 3. Here, on every single dataset, the three models have been applied and the estimated values of average radius are shown in figure 2. Table 1 shows the mean and the associated error of the fitted values of r averaged over the 50 dataset. The combined model produces more accurate results in terms of average r fitted and associated error, and the improvement against the single modalities increases with the size considered. DOS tends to provide better estimations than dNMR in terms of fitted values and error of estimation, but figure 2 shows some bad estimations for lower values of r which are not highlighted by the data in table 1. Further, an increased number of repetitions in the NMR scans may improve the performances of the method with a resulting increase of acquisition time.

The estimation of the parameters and follow the same trend, but the results are not explicitly shown. The quantification of , which directly depends only on dNMR, is improved indirectly by the estimation of r using DOS in this combined approach. In the same way, drastically increases its accuracy in the mixed model especially for the of interest (around 30%).

The fitting of experimental data is shown in figure 3. DOS is able to fit the TPSF when the sample is sufficiently thick as shown in figure 3(a). The number of scattering events is

model	1 m	2 m	3 m
DOS	1.09±0.16	2.13±0.67	3.06±1.34
dNMR	0.82±0.57	1.93±0.63	3.75±1.49
MIX	1.02±0.31	1.98±0.21	3.14±0.38

Table 1: Average estimated value of r and error of the data shown in figure 2.

sufficiently high to ensure the applicability of the diffusion approximation. The good fitting is not related to the application of Mie theory but only on an analytical description of the signal. dNMR signal presents a good fitting shown in 3(b). The fitted value of diffusivity coefficient is D 0 0098 m^2 ms which is in agreement with the expected values found in literature [2].

4 Discussion

The use of a single modality provides a partial solution of the problem. DOS estimates r and , while dNMR provides r and but not . Only their combination may obtain the whole set of parameters at the same time.

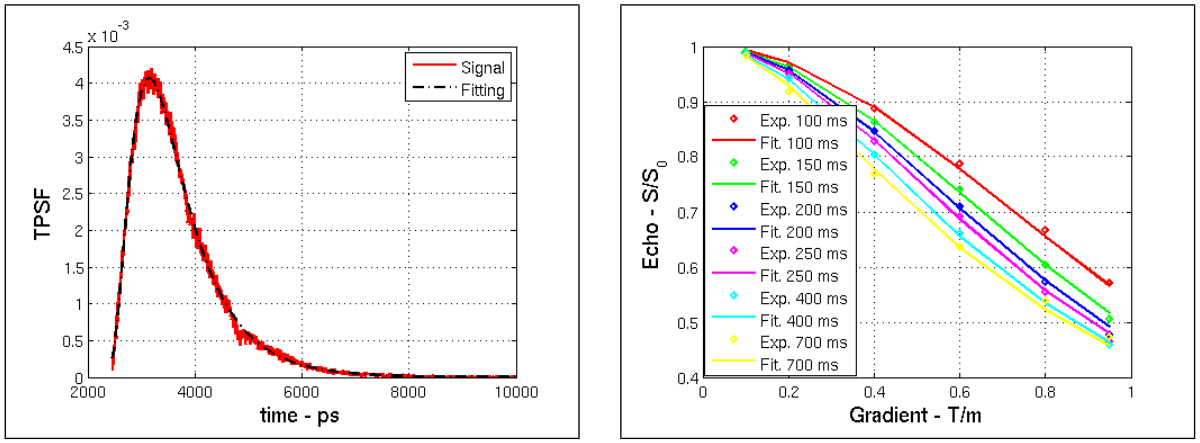
The DOS model requires knowledge of the absorption coefficient and refractive index of the two compartments, which have been retrieved from the literature. The parameters of the inner compartment are well known while the absorption of the dispersion medium has been deduced from its chemical composition. Further experiments are required to obtain the absorption coefficients and refractive indexes more accurately. A second point is the consideration that Mie theory identifies similar pairs ($_s$, $_a$) for different microstructural parameters; therefore, a precise choice of the initial guess is required in order to converge to an accurate solution. This dependency on initial guess is the main disadvantage of this modality. A further disadvantage is the lack of sensitivity to the distribution of sizes.

The dNMR model is instead able to fit the echoes very well. No input parameters are required, and the obtained value of the diffusivity coefficient is a confirmation of the accuracy of the model, which appears close to the expected value from literature. The model is very sensitive to the inner microstructure and the fitting depends only slightly on the initial guess. The time required for the fitting is short and the model is well tested. This modality is limited by the fact that it does not provide information about the volume fraction, but the model fits the real data accurately.

The combined model provides an enhanced accuracy with respect to the single modalities. It is insensitive to the initial guess since it exploits the dNMR properties, but the fitting of distribution width is improved thanks to the contribution of optical modality which cross-informs the model about r. Finally, the estimation of concentration is also improved due to the contemporary fitting of the size with a robust model such that of dNMR.

5 Conclusion

The use of combined models increases the accuracy of the fitting because of the cross-talking between the single techniques. The approach is general and may be extended to other modalities without any complex additional work. The necessity of a more advanced validation, such as a microscopy investigation, is strong. Finally a calibration of the input parameters and of the weight w is required.



(a) (b)

Figure 3: Fitting of experimental data obtained from mayonnaise in DOS modality (a), and in the dNMR modality (b).

The extension of the microstructural model to anisotropic cases will provide practical applications to biological tissues, and the ultimate result will be the solution of an imaging problem with the multimodality information of a microstructural model in a three dimensional space.

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