MULTIMODALITY INVESTIGATION OF MICROSTRUCTURES BY THE COMBINATION OF DIFFUSION NMR AND DIFFUSE OPTICAL SPECTROSCOPY

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Target audience Biophysical modelling and microstructure imaging researchers.

Overview This work presents a proof of principle that a model informed by Diffuse Optical Spectroscopy (DOS) and Diffusion NMR (dNMR) may increase the accuracy in estimation of microstructural parameters compared to biophysical model of tissue microstructure informed by either modality alone.

Purposes Investigation of tissue microstructure with non-invasive histology is a key challenge for medical imaging. dNMR can investigate the dimension of compartments (such as cells or axons) restricting and hindering the diffusion of water molecules. DOS measures the Temporal Point Spread Function (TPSF) of the photons emerging from a sample, and is sensitive to size and density of scatterers in the tissue (e.g. nucleii and organelles). The two techniques may complement each other, yet no demonstration of a combined model exists in literature. Here, we provide a proof of concept that combining information from dNMR and DOS, via a joint signal model, improves estimation of microstructural features.

Methods To demonstrate the idea, we used an oil-in-water emulsion sample (Sainsbury's commercial light mayonnaise) containing oil droplets in water and emulsifiers. The microstructure in the sample is modeled as a set of spherical elements with average radius r, log-normally distributed with spread parameter σ, and volume fraction ψ. The diffusion of oil molecules is constrained inside the droplets while the interface between oil and water causes optical scattering.

dNMR measurements were performed with a Stimulated Echo sequence applied with a 9.4T Varian experimental system (Δ=100-700ms, δ=3ms G=0-0.95 T/m, TR=4s, with minimum echo time). We acquired 4 repetitions along each direction of three orthogonal gradient directions for all the 30 combinations of parameters. The signal model assumes restricted diffusion in spherical compartments. The parameters are diffusivity coefficient D, r and σ[1].

Figure 1: The combined model

DOS measurements were performed with a time-domain system transilluminating a sample in a container of 17x48x52mm³ across the smaller dimension with a 780nm wavelength pulse laser, and a detector measures the TPSF. The model assumes a Diffusion Approximation [2], and uses Mie theory [3] to relate a single scatterer size parameter, r, and volume fraction, ψ, to the TPSF. Additional parameters are the apparent scattering and absorption coefficients μ_s' and μ_a introduced respectively.

The combined model and estimation procedure are presented in figure 1. Signals are also fitted for each modality individually by minimizing the sum of squared differences of the model and measured signal. DOS alone provides r and ψ, dNMR alone provides r and σ. Combined model fitting minimizes a weighted sum of the fitting errors from the two signals to obtain, r, σ, and ψ, at the same time.

Confocal Laser Scanning Microscopy (CLSM) provides ground truth r, σ, and ψ for the sample. For further validation, synthetic datasets were independently generated with different SNR at realistic values of parameters by introducing a Rician noise in dNMR signals and a Gaussian noise in DOS.

model	1 μm	2 μm	3 μm
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)
Com	1.02(0.31)	1.98(0.21)	3.14(0.38)

Table 1: Estimation of r (and its standard deviation in brackets) from 150 synthetic datasets generated with SNR=16 and r=1,2,3μm, σ=1.5μm, and ψ=0.2.

Results Table 1 shows recovered values of r from the synthetic data from dNMR alone, DOS alone, and the combined model (Com). The combined model provides more accurate and precise parameter estimates especially for larger values of r. In dNMR, a low diffusivity coefficient (10^{-11}μm²/s) and a consequently long Δ may introduce a bias for the estimation of larger r. DOS has a better performance with smaller values of r, accordingly to the reduction of accuracy observed when Mie theory is adopted for the sizing of scatterers with a dimension much larger then the laser wavelength.

Figure 2 shows the estimates of r and ψ obtained from experimental signals. The combined model shows much more accurate and precise estimates of r compared to dNMR alone and slight improvements over dNMR alone. The error bars represent the standard deviation of the chain of estimates obtained with a

Figure 2: Estimation of r and ψ obtained from the experimental signals and theiraccuracy obtained with MCMC.

MCMC algorithm. The standard deviation in combined model is 1/4 of dNMR ones. Finally, combining dNMR with DOS improves the estimation of ψ reducing the error to less then 2% even though dNMR is not directly sensitive to ψ; the improvement comes about by improving the estimate of r, which is linked to ψ via DOS model.

Discussion and conclusions A common model informed by both DOS and dNMR signals refines the estimation of parameters detectable with both of them since it fuses complementary information. Moreover, the fitting of the non-common parameters is facilitated, leading to a better performance. The two modalities exploit different physical phenomena thus providing complementary information. In conclusion, a model informed by the two modalities leads to a natural enhancement of the parameters estimation, since the model exploits the strength of DOS and dNMR. A natural application of this modality is the study of cellular structure in cancer, where Diffuse Optical Imaging and diffusion MRI can be combined.

References [1] G. Zaccanti et al., Appied Optics, 36(19):4587-4599, 1997. [2] W. J. Wiscombe, Applied Optics, 19(9):1505-1509, 1980 . [3] R.M. Cotts et al., The Journ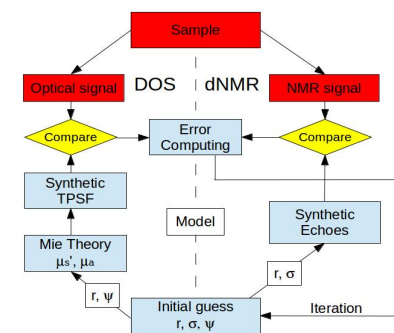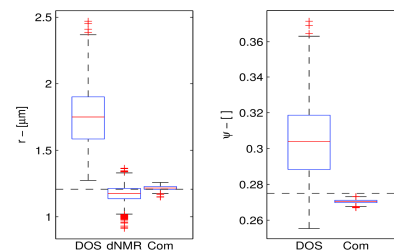al of Chemical Physics, 48(11):4938-4945, 1968