Molecular exchange in breast cells studied with a new DW-MRI method

D. Topgaard[1], I. Åslund[2], C. Malmborg[3], A. Stenstam[3], K. Bryskhe[3], and S. Oredsson[2]
[1]Physical Chemistry, Lund University, Lund, --, Sweden, [2]Lund University, [3]Colloidal Resource

Introduction

Molecular exchange across cell membranes or between tissue compartments is a potentially useful mechanism for contrast in MRI. An extension of diffusion weighted (DW) MRI, with two DW periods and an intermediate mixing time, has previously been successfully applied to determine intracellular lifetimes and plasma membrane permeability in suspensions of isolated cells [1]. By applying the method to healthy and cancerous breast cells, we take one more step towards the final goal of developing a novel mode of contrast for detecting pathological tissue. A polymer solution and yeast cells are used as phantoms with well-defined exchange behavior.

Methods

MCF-7, MCF-10A, and SK-BR-3 cell lines were purchased from American Type Culture Collection, Manassas, VA, USA, and cultured according to standard procedures. Diffusion MRI experiments were performed at 37 ºC on an aqueous poly(ethylene glycol) solution and centrifuged cell pellets using a Bruker AVII-500 spectrometer and the pulse sequence schematically shown in **Figure 1**. Data was acquired using $\delta_1 = \delta_2 =$ 14.2 ms, $\Delta_1 = \Delta_2 =$16.0 ms, and G_2 incremented in a logarithmic sequence from to 22.2 to 1200 mT/m in 14 steps yielding b_2 from $1.51 \cdot 10^7$ to $4.41 \cdot 10^{10}$ sm^{-2}. The variation of t_{mix} and b_1 is explained in **Figure 2**. With two signal averages per data point and 1 s repetition time, experiments on each sample were completed in less than 2 min.

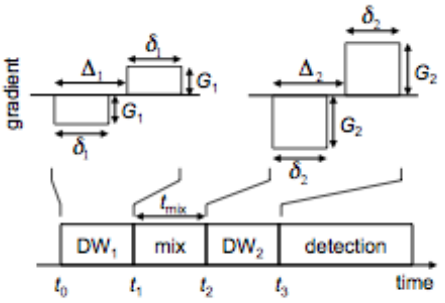

Figure 1. Schematic of the pulse sequence for exchange-sensitive diffusion MRI. A first DW block (DW$_1$) and an adjustable delay for mixing (mix) precede a standard DWI sequence (DW$_2$-detection). Each DW block contains a pair of diffusion sensitizing gradient pulses of length δ and amplitude G. The time between the onset of the pulses in the pulse pair is denoted Δ. For each block a b-value is defined according to $b_{1/2} = (\gamma G_{1/2} \delta_{1/2})^2 (\Delta_{1/2} - \delta_{1/2}/3)$, where γ is the magnetogyric ratio. The parameters of the DW$_1$ block are chosen to remove signal from quickly moving molecules while retaining signal from slower moving ones. Molecular exchange between the populations occurs during the variable delay t_{mix}.

Results

Experimental results are shown in **Figure 2**. The decay of the MR signal is clearly two-component for both the polymer solution and the yeast cells. In the former case there is no reappearance of the fast component with increasing t_{mix} after being removed by the DW$_1$ block. For the yeast cells, the fast component returns exponentially with a rate $R = 4.4$ s^{-1} being independent of b_2. Such behavior can be reproduced with a model having two exchanging sites corresponding to intra- and extracellular water. The trends for the pellets of breast cells are more complex as expected for systems with several exchanging water populations having different diffusion properties. The profiles of R vs b_2 are markedly different for the various cell types.

Conclusions

A novel MRI sequence being sensitive to molecular exchange between components having different diffusion characteristics has been shown to yield significant differences between healthy and cancerous breast cells.

References

[1] Åslund, Nowacka, Nilsson, Topgaard (2008) *in preparation*.

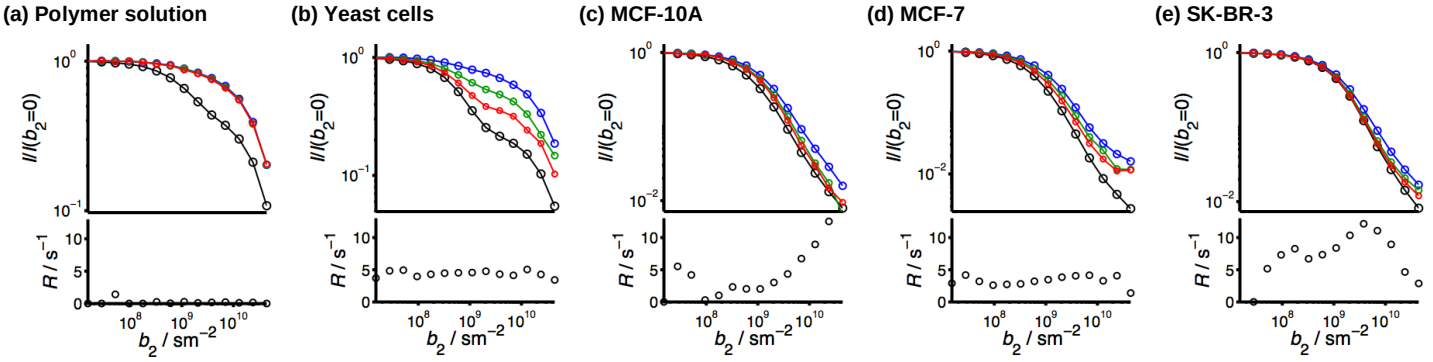

Figure 2. Diffusion exchange experiment in **Figure 1** applied to a polymer solution and cell pellets. The figures show normalized MR signal intensity $I/I(b_2=0)$ and apparent exchange rate R vs. the diffusion sensitizing variable b_2. The signal intensities are color coded as follows: black (b_1 = 0, t_{mix} = 29.0 ms), blue ($b_1 = 2.76 \cdot 10^9$ sm^{-2} , t_{mix} = 29.0 ms), green ($b_1 = 2.76 \cdot 10^9$ sm^{-2} , t_{mix} = 128.0 ms), and red ($b_1 = 2.76 \cdot 10^9$ sm^{-2} , t_{mix} = 328.0 ms). R is evaluated for each value of b_2 assuming exponential decay towards the equilibrium values (black) with increasing t_{mix}. **(a)** Aqueous poly(ethylene glycol) solution. **(b)** Yeast cells. **(c)** MCF-10A healthy breast cells. **(d)** MCF-7 cancerous breast cells with oestrogen receptors. **(e)** SK-BR-3 cancerous breast cells without oestrogen receptors.