Probing Boundary Roughness of Structural Materials by NMR 2D q-Space Imaging

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Cell shape and surface roughness are known to play a significant role in cell-cell interaction and cell-substrate adhesion. Conventional methods to address this problem have largely been confined to electron microscopy. These approaches require substantial sample preparation and are usually destructive. Here we show by simulation in synthetic apertures of varying roughness that 2D NMR **q**-space imaging may be suited for obtaining quantitative information on shape and asperity of such structures. The feasibility of such an approach is demonstrated experimentally with arrays of capillaries.

INTRODUCTION

The morphology of biological tissues and cells are significantly determined by their function and interplay with the local environment. It has been shown that bulk cell deformation and surface asperity play an important role in cell-cell interaction and cell-substrate adhesion (1). Further, changes in morphological complexity have been found to be correlated with the various stages of cell differentiation (2). Previous attempts to quantitatively characterize cell shapes and boundary roughness mostly relied on electron microscopy, and an analysis of the resulting images was based on geometric models. These approaches are destructive and often demand complex analytical procedures. NMR **q**-space imaging (3) has proven useful for obtaining information on heterogeneous systems that exhibit structural regularity on the scale of the diffusion distance (0.1-10μm). Experimental results from studies on porous materials, emulsions (3) and biological tissues (4) have demonstrated the method's potential for obtaining size and size distribution of structures based on the diffraction-like echo attenuation plots.

The objective of this work was to assess the feasibility of characterizing cell boundary roughness by examining the diffraction pattern obtained from the 2D **q**-space echo attenuation. Toward this goal, finite difference simulations of restricted diffusion inside serrated apertures were performed. Further, experimental data of 2D **q**-space echo attenuation were obtained for restricted diffusion inside arrays of capillaries of circular and square cross-section.

MATERALS and METHODS

Computer Simulations

To model cells with different levels of boundary roughness, images of circular, sinusoidally and fractally-serrated aperture arrays were generated. For the former, the radius of the aperture, R, possesses a sinusoidal dependency on azimuthal angle, θ,

$$R(\theta) = a + \eta\cos(n\theta) \qquad [1]$$

where a is the mean radius, η is the a perturbational amplitude (η<<a), and n is an integer that determines the period of this sinusoidal variation, while the band-limited Weierstrass function (5) was exploited to create the radius function of fractally-serrated apertures,

$$R(\theta) = a + \frac{\{2\sigma^2[1-b^{(2D-4)}]\}^{1/2}}{\left[b^{(2D-4)N_1} - b^{(2D-4)(N_2+1)}\right]^{1/2}} \times \sum_{n=N_1}^{N_2} b^{(D-2)n}\cos(b^n\theta + \xi_n) \qquad [2]$$

In Eq. 2 σ^2,b, and D are the variance, a constant greater than unity, and fractal dimension, respectively. There exist (N_2-N_1+1) Fourier components in Eq.[2], and their phase relations are determined by the random variable ξ_n To simulate the NMR signal, a previously described finite-difference PGSE diffusion model was applied (6). Imaging parameters were: TR/TE=1000/65 ms, δ /Δ=3/60 ms, diffusivity of the water inside the apertures=2.5 μm^2/ms (assuming no water outside the apertures and non-permeable boundary).

2D **q**-space sampling was simulated by stepping diffusion gradients in 16 increments from 0 to 75 G/cm, with a 5 G/cm linear increment for each *x* and *y* direction, thus resulting in 256 **q**-values. It is noted that for symmetry reasons it suffices to sample a quadrant of 2D **q**-space only. For the fractally-serrated apertures of Fig. 1C having two-fold symmetry, two adjacent quadrants of **q**-space have to be sampled. The magnetization was calculated and updated for each time step (0.04 msec) of the PGSE sequence, up to the echo time.

NMR Experiments

2D **q**-space imaging experiments were performed on a Bruker Avance DMX 400 MHz micro-imaging system using a pulsed-gradient stimulated echo sequence with diffusion-sensitizing gradients stepped along both directions perpendicular to the long axis of the capillaries. Two types of hollow capillaries were used: square and circular cross-sectional, with 50 μm in I.D., 25 μm wall thickness, and 10 cm in length (VitroCom, Mountain Lakes, NJ, USA). Capillaries were filled with water and sealed both ends. Also, to minimize the susceptibility artifacts, the space between capillaries and the NMR tube was filled with D_2O. Imaging parameters were: TR/TE=2000/9.7 ms, δ/Δ= 2.5/625 ms, and NA=8. The diffusion-sensitizing gradients were incremented linearly from 0 to 50 G/cm with 32 steps for both directions.

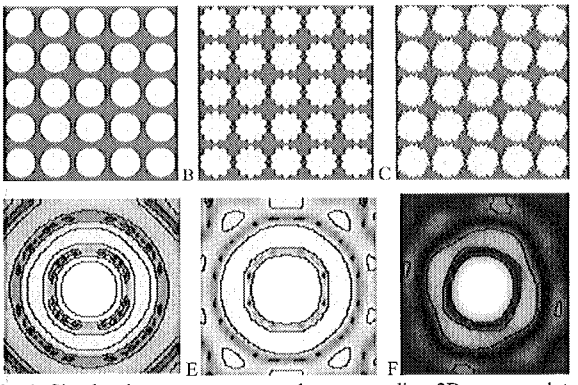

Fig. 1 Simulated aperture arrays and corresponding 2D **q**-space plots: circular (A), sinusoidally-serrated (B; η/n=1.48/10), and fractally-serrated (C; σ/b/D/N_2/N_1 = 1.6/2/1.99/20/1, and ξ has a uniform distribution within [0,1]). D, E, F: corresponding 2D **q**-space diffraction patterns with contour plots superimposed.

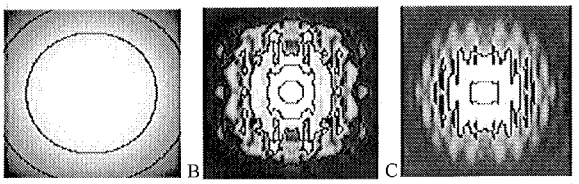

Fig. 2 Experimental data of 2D **q**-space plots: free diffusion water inside the 10mm NMR tube (A), restricted water inside 50μm (ID) capillaries with circular (B) and square (C) cross-section, respectively.

RESULTS and DISCUSSION

Figure 1 shows 200×200 aperture array images (Figs. 1A-C) with a pixel width of 0.93 μm, covering an array of 5×5 apertures (mean radius =29.76 μm) with various boundary roughness, along with simulated 2D **q**-space plots, interpolated to 128×128 (Figs. 1D-F). The rings (diffraction minima) of 2D **q**-space plots reflect the gross shape of the aperture, while the superimposed contour indicates the fine structure embedded at high **q** values. This finding is consistent with the optical experiment by Kim *et al* (5), who found that the angular dependency of diffraction patterns diminishes with increased boundary roughness (Fig. 1F). Experimental data of 2D **q**-space plots for free water and restricted diffusion inside capillaries of circular and square cross-section are shown in Figs. 2A - C, respectively. The diffraction patterns and contour plots clearly distinguish the two basic capillary shapes, whose differentiation by **k**-space imaging would require a pixel size on the order of 10-20 μm. The fine structure seen in the experimental **q**-space plots is likely a consequence of imperfections in surface asperity. In summary, this early work suggests that 2D **q**-space imaging might allow non-destructive probing of boundary roughness of structured materials at cellular resolution.

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ACKNOWLEDGMENTS

Dr. D. L. Jaggard, Dept. of Electrical Engineering, NIH RO1 NS41380-01.