The anomalous diffusion parameter α provides the most relevant information of structural complexity in heterogeneous media

Marco Palombo[1,2], Andrea Gabrielli[3], Giancarlo Ruocco[1,2], and Silvia Capuani[1,2]

[1]Physics Department, Sapienza University, Rome, Rome, Italy, [2]CNR IPCF UOS Roma, Sapienza University, Rome, Rome, Italy, [3]ISC-CNR, Rome, Rome, Italy

Target audience. This study is addressed to researchers involved in the development of advanced diffusion NMR technique to probe microstructures in tissue.

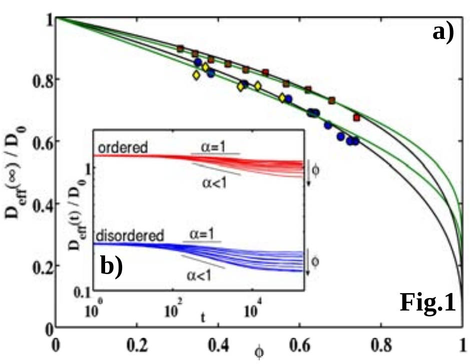
Purpose. α anomalous diffusion parameter, which quantifies sub-diffusion processes[1], is easily measurable by using diffusion-time varying NMR techniques[1,2]. Our aim was to show that α provides microstructural information related to the disorder degree of complex systems. Toward this goal we performed numerical simulations to investigate diffusion as a function of time, $D(t)$, and α behavior as a function of the sphere-density ϕ in micro-beads mono-dispersed in water. Then, by employing a diffusion-time varying pulse field gradient (PFG) technique[1] we obtained experimental results and compared them with results from numerical simulations.

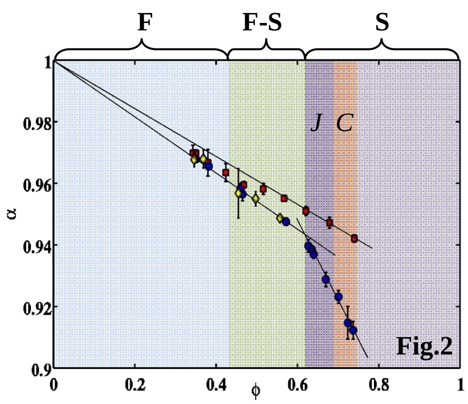
Methods. *Theory*: The PFG signal attenuation, $S(q,\Delta)$, which depends on both the diffusion gradient strength, g (through the wave vector $\boldsymbol{q} = 1/(2\pi)\gamma \boldsymbol{g}\delta$ with γ the gyromagnetic ratio and δ the pulse gradient duration) and the diffusion time Δ, is the Fourier Transform (FT) of the motion propagator (MP). When the MP is Gaussian, $S(q,\Delta)$ as a function of $b=q^2\Delta$ follows a mono-exponential decay. On the other hand, when the MP is not Gaussian, $S(q,\Delta)$ deviates from the mono-exponential decay. It is well known that $D(t)$ in heterogeneous systems shows three different behaviours: it is constant and equal to bulk diffusivity D_0 (when the MP is Gaussian) for very short diffusion times, t; it is not constant: $D(t) \propto t^{(\alpha-1)}$ with $\alpha<1$ (when the MP is non-Gaussian and water diffusion is sub-diffusive) for short t; and it is constant again but equal to $D(\infty)<D_0$ for long t.

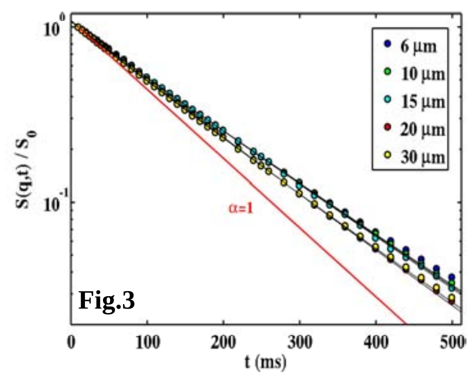
Simulations: three dimensional (3D) molecular dynamics simulations with periodic boundary conditions were performed to mimic systems comprised of mono-sized hard spheres ordered on an fcc lattice (ordered system) and randomly displaced at different ϕ values, ranging from 0.33 to 0.74 (disordered system at different degree). Water diffusion in these 3D obstructed media was modeled as a 3D random flight process by employing a Monte Carlo algorithm. To estimate the ratio $D_{eff}(t)/D_0$, where $D_{eff}(t)=\langle \boldsymbol{r}^2(t)\rangle/(6t)$, with $\langle . \rangle$ the ensemble average and $\boldsymbol{r}(t)$ the particle space displacement, $5 \cdot 10^4$ trajectories were collected.

Experiments: five 10mm NMR tubes were filled with polystyrene beads of diameters: 30.0±1.0, 20.0±1.0, 15.0±1.0, 10.00±0.50 and 6.00±0.50 μm mono-dispersed in a solution of Tween 20 at 10^{-6}M and deionized water, and investigated 4 months after their preparation at fixed temperature of 293K.

The fractional exponent α was measured by collecting $S(q,\Delta)$ as a function of Δ and by using the asymptotic expression of the FT of the MP for the sub-diffusive regime derived in [1]: $S(q,\Delta) \propto \exp(-Kq^2\Delta^{\alpha})$ [1], which hold when $q^2 \ll 1/(K\Delta^{\alpha})$ is kept constant, with K a generalized diffusion constant. A spectroscopic PFG Stimulated Echo (PFG-STE) sequence with δ=2.2ms, g=0.10T/m (i.e. $q \approx 11240\text{m}^{-1}$) along x, y and z directions, TR=2.5s, NS=32 and 48 values of Δ in the range (10–500)ms was used to extract the $\alpha_{i=x,y,z}$ values. Then the mean value, α, was computed by averaging over the three directions. A second spectroscopic PFG-STE with Δ/δ=400/2.2ms, TR=2.5s, NS=16 and 48 gradient amplitude steps from 0.026 to 1.02T/m along x, y and z directions were used to measure the effective diffusion coefficient at long time







$D_{eff}(\infty)$, from the slope of $\ln(S(q,\Delta)/S_0)$ at low q values along each direction and then averaging over the three directions. A Spin Echo imaging sequence with TR=2.5s, 48 values of TE in the range (3–130)ms, NS=16, STH=1mm, field of view FOV=8x8mm and an in plane resolution of 62.5μm were used to estimate ϕ in each sample, as described in [3].

Results. $D_{eff}(\infty)/D_0$ *vs* ϕ from both simulations and experiments is shown in **Fig.1a)**. Red, blue and yellow data points represent the fcc ordered simulated samples, the disordered simulated samples and the experimental values, respectively. The lines represent the theoretical relations by Lerman[4] (green) and Boudreau[5] (black) derived from local geometrical properties of media. **Fig.1b)** shows the simulated time behavior of $D_{eff}(t)/D_0$ *vs* t (in simulation units, arbitrarily shifted to improve readability) with the behaviors when α=1 and α<1 displayed. α values *vs* ϕ obtained from simulation and experimental data is shown in **Fig.2** where red, blue and yellow data points represent the fcc ordered simulated samples, the disordered simulated samples and the experimental values, respectively. The graph in **Fig.3** shows $S(q,t)/S_0$ *vs* $t=\Delta-\delta/3$. The red line represents the $S(q,t)/S_0$ *vs* t behavior when α=1, while the black lines represent the relation [1] with α<1 fitted to the experimental data for all the investigated samples (see the inserted panel in **Fig.3**).

Discussion. The simulated ordered (red points) and disordered (blue points) systems mimic very well the samples investigated (see **Fig.1a)**). Moreover, both measured (in yellow) and simulated (in blue and in red) values of $D_{eff}(\infty)/D_0$ perfectly lie on the theoretical curves predicted in [4,5]. From **Fig.3** it is evident that the theoretical relation [1] well fit to the data and in **Fig.1b)** it is possible to clearly distinguish the three diffusion regimes typically observed in heterogeneous media. The main results of this work are summarized in **Fig.2**. By analyzing the behavior of α as a function of ϕ it is possible to assert that α value quantifies global structural complexity and enables a classification of different kinds of disorder. Indeed, α values in **Fig.2** obtained in micro-beads samples allow to observe the jamming transition occurring at $\phi \sim 0.6$, the full jamming state region J, and allow to classify all the microscopic states of the systems: from random fluid state, **F** (α>0.96) to mixed fluid-solid state, **F-S** (0.94<α<0.96) up to crystal, C, and solid state in general, **S** (α<0.94). On the other hand, $D_{eff}(\infty)/D_0$ is only affected by local properties, as suggested by results in **Fig.1a).** As a consequence $D_{eff}(\infty)/D_0$ does not provide the most relevant information of structural complexity. Moreover, it is possible to measure α in a faster way compared to $D_{eff}(t)/D_0$ *vs* t measurement, by performing a Δ-varying PFG experiment[1]. Last but not least, the spectroscopic protocol to measure α is easily convertible in an imaging protocol[2].

Conclusion. In this work we demonstrated that unlike conventional tortuosity investigations based on long diffusion time behavior of $D(t)/D_0$, α quantifies the global structural complexity (disorder) of heterogeneous systems. Moreover, we show here that α can be measured by using Δ-varying PFG experiment[1] which is faster than the diffusion time behavior of $D(t)/D_0$ study. As a consequence we speculate that our approach could be used as a new tool to probe changes in microstructural properties in healthy and pathological tissues.

References. [1]Palombo M, Gabrielli A, De Santis S et al. Spatio-temporal anomalous diffusion in heterogeneous media by NMR. J. Chem. Phys. 2011;135:034504-034511. [2]Capuani S, Palombo M, Gabrielli A, et al. Spatio-temporal anomalous diffusion imaging: results in controlled phantoms and in excised human meningiomas. Magn. Reson. Imag. 2012, in press, doi: http://dx.doi.org/10.1016/j.mri.2012.08.012.[3]Turney MA, Cheung MK, McCarthy MJ et al. Magnetic resonance imaging study of sedimenting suspensions of noncolloidal spheres. Phys. Fluids 1995;7(5):904-911. [4]Lerman A. Geochemical processes: water and sediment environments, 1979, Weiley, New York. [5]Boudreau PB. The diffusive tortuosity of fine-grained unlithified sediments. Geochim. Cosmochim. Acta 1996;60:3139-3142.