Monte Carlo Simulation of Magnetic Nanoparticle Clustering

O. Zurkiya[1], X. Hu[1]
[1]Biomedical Engineering, Georgia Tech/Emory University, Atlanta, GA, United States

Introduction:

An important feature of targeted contrast agents for MRI is a controllable switching mechanism. Monocrystalline iron oxide nanoparticles (MION) have been explored as switchable magnetic "nanosensors" [1] where clustering of particles can have a significant effect on R2. There is interest in designing controllable systems in which a limited number of particles come together. While such clustering has been experimentally demonstrated to alter relaxivity, its effect has not been systematically examined numerically. Here we present Monte Carlo simulations on the effect of clustering of magnetic nanoparticles. We explore issues such as number of particles involved in clustering, effects of binding efficiency, and binding distance between particles.

Methods:

Monte Carlo simulations were performed as previously described [2,3]. In this case, however, rather than increasing particle size, particles were allowed to come together in groups of 2, 3 and 4. For the three particle case, an equilateral triangle was formed. For the four particle case, a triangular pyramid was formed. This allowed each particle in a cluster to be equidistant and this distance was a parameter in the simulations. Clusters were randomly distributed in space. Protons take random walks through the particle fields. At each time step, the sum of B_z due to the particle dipolar fields is computed and the proton accumulates a phase according to $\Phi=\gamma B_z \Delta t$ (where γ is the gyromagnetic ratio and Δt, time step, 200 μs). Simulations were performed using 5000 protons, and magnetic parameters used were representative of MION 46-L particles (2064 Fe atoms per particle, 65emu/g Fe, average diameter 4.6 nm). Phase changes were accumulated in 1ms intervals and R2 and R2* were calculated as previously described [2].

We define a parameter, binding efficiency, (b.e.) which represents the percentage of successful clustering. For instance, for 1000 particles in the case of two particle clustering, a b.e. of 1.0 corresponds to 500 pairs. A b.e. of 0.5 corresponds to 250 pairs and 500 free particles. For the four particle case, a b.e. of 1.0 corresponds to 250 clusters whereas a b.e. of 0.5 corresponds to 125 clusters and 500 free particles. Simulations were performed varying binding efficiency, binding distance and number of particles involved in clustering.

Results:

In all cases, values for R2 and R2* are the same. This is expected for the motion averaging regime for superparamagnetic particles of small radius. Figure 1 shows an approximately linear effect of binding efficiency on R2 for the two particle clusters. A binding efficiency as low as 25% can be distinguished from the case of no binding. Figure 2 shows the increase in R2 with particle number involved in clustering. Figure 3 shows the effect of binding distance on R2. The results show that although R2 begins to decrease after 100nm, binding distances as large as 1μm still produce significant effects.

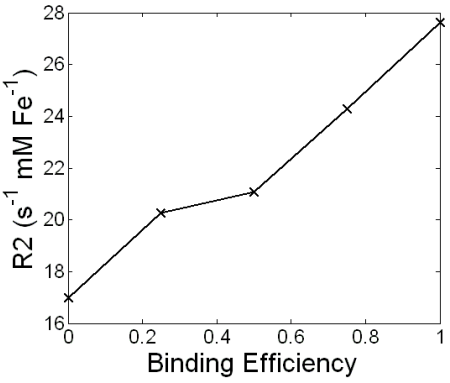

Fig. 1: Effect of Binding Efficiency of R2. Data plotted for two particle clusters.

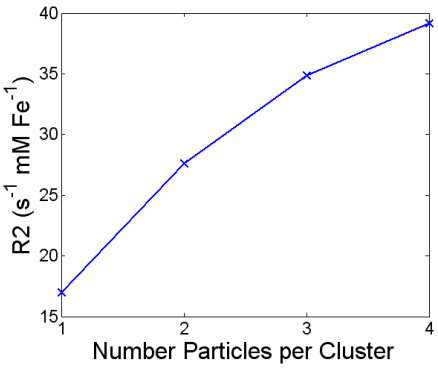

Fig. 2: Number of particles involved in clustering vs. R2. Data plotted for constant binding efficiency of 1.00.

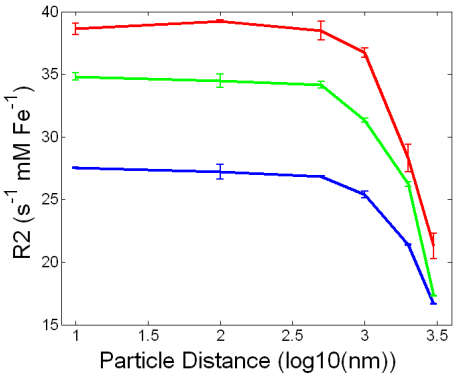

Fig. 3: Effect of Particle Binding Distance on R2. Data plotted for two (bottom), three (middle) and four (top) particle clusters.

Discussion:

Our results indicate that significant changes in R2 can be achieved in cases of limited clustering. Low binding efficiencies can be expected in in-vivo applications of molecular imaging thus requiring the identification of positive binding in a background of unbound particles. Our results also indicate that clusters involving small numbers of particles can be distinguished as may be desired in "molecular beacon" type applications. Additionally, large binding distances allow for the assembly of complex structures of particles with various sensing and targeting molecules. These results are useful for designing switchable magnetic nanosensors and applications where a limited number of particles may be involved in clustering.

References:

1. Josephson, L., Perez, J.M., Weissleder, *Angew. Chem. Int. Ed.*, 40, No.17, 3204-3206 (2001).
2. Weisskoff, R.M., Zuo, C.S., Boxerman, J.L., Rosen, B.R., *MRM,*31, 601-610, (1994).
3. Gillis, P., Moiny, F., Brooks, R.A., *MRM*, 47, 257–263, (2002).
4. Shen, T., Weissleder, R., Papisov, M., Bogdanov, A., Brady, T.J., *MRM*, 29, 599-604 (1993).

Acknowledgements: This work was supported by DARPA Grant #: F49620-03-1-0320.