

核磁共振中多量子相干扩散行为 的理论表述和计算机模拟*

林巧玲^a, 蔡淑惠^{a**}, 陈忠^{a,b**}, 蔡聪波^a

(a. 厦门大学物理系, 固体表面物理化学国家重点实验室, 厦门 361005 ;

b. 中国科学院武汉物理与数学研究所, 波谱与原子分子物理国家重点实验室, 武汉 430071)

摘要: 改进了 Warren 所提出的 CRAZED 脉冲序列以研究分子间多量子相干的扩散过程, 讨论了利用核磁共振测量分子内和分子间多量子相干表观自扩散系数的理论表述. 采用粒子的随机行走模型模拟其扩散行为. 在短脉冲近似和长脉冲梯度场两种实验条件下, 分别获得了因扩散引起的不同相干阶数的相对信号衰减强度随梯度场脉冲间隔时间的变化曲线, 由此得到分子内多量子相干和分子间多量子相干的表观扩散率与溶液分子扩散系数的关系. 还将计算机模拟结果与理论预测进行分析和比较, 发现二者能很好地吻合. 研究结果表明, 分子间多量子相干的表观扩散率与常规的分子内多量子相干的表观扩散率明显不同, 因此, 分子间多量子相干的表观扩散率可能提供一种新的核磁共振成像的对比度机理.

关键词: NMR; 扩散; 分子间多量子相干; 分子内多量子相干

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Theoretical Expression and Computer Simulation of Diffusion Behaviors in Multiple-Quantum Coherence NMR*

Lin Qiaoling^a, Cai Shuhui^{a**}, Chen Zhong^{a,b**}, Cai Congbo^a

(a. Department of Physics, State Key Laboratory for Physical Chemistry of Solid Surface, Xiamen University, Xiamen 361005 ;

b. State Key Laboratory of Magnetic Resonance and Atomic Molecular Physics, Wuhan Institute of Physics and Mathematics, The Chinese Academy of Sciences, Wuhan 430071)

Abstract Self-diffusion is one of the most fundamental motions of particles in liquid. Nuclear magnetic resonance (NMR) provides a convenient and noninvasive means for accurately measuring the self-diffusion coefficient of molecules in solution. The theoretical expressions of apparent diffusion rates of MQCs are given and computer simulation based on the method to measure the self-diffusion coefficient by NMR was discussed and the random walk model of particles is used to simulate the apparent diffusion behaviors of intra-molecular and inter-molecular multiple-quantum coherences (MQCs). The results of computer simulation agree well with theoretical predictions.

Keywords NMR, Diffusion, Multiple-quantum coherences

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** Corresponding authors, Tel : +86-592-2183046, Fax : +86-592-2188054, E-mail : shcai@jingxian.xmu.edu.cn ; chenz@jingxian.xmu.edu.cn Received 22 April 2003.

1 Introduction

Pulsed field gradient NMR has long been recognized as a useful means for detecting migration of nuclear spins. When a two-pulse NMR sequence separated by a time interval is applied to a highly polarized system, multiple spin echoes (MSEs) can be observed in the presence of magnetic field gradients, as seen in solid He, liquid He, and water^[1]. Warren and co-workers designed a simple pulse sequence called CRAZED (Fig. 1) to detect inter-molecular multiple-quantum coherences (MQCs) and explained the obser-

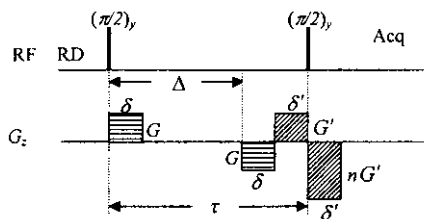


Fig. 1 CRAZED pulse sequence

n is coherence order, δ and δ' are the durations of gradient pulses, G and G' are the magnitudes of gradient pulses, τ is the evolution period, and Δ is the interval time of the first two gradient pulses.

vation theoretically^[2,3]. However, as intra-molecular and inter-molecular MQCs represent different physical processes, their diffusion rates may be different. Recently Chen and co-workers has found, that the apparent diffusion rate of inter-molecular MQCs does not coincide with the relationship $D_n^{app} = n^2 D_T$ ($n \neq 0$) which is satisfied by the apparent diffusion rate of intra-molecular MQCs^[4,5], where D_n^{app} is the n -quantum coherence apparent diffusion rate, D_T is the translational molecular diffusion rate of the single quantum coherences (SQC), and n represents coherence order. To understand the two processes more clearly, in this paper, the theoretical expressions of apparent diffusion rates of MQCs were given and computer simulation of intra-molecular and inter-molecular MQCs was performed.

2 Theoretical description

The concept of inter-molecular MQCs was originally proposed by Warren and co-workers^[2]. The first

$\pi/2$ pulse in the CRAZED sequence is applied to a thermal equilibrium system to generate inter-molecular MQCs during the evolution period τ . The inter-molecular MQCs are then transferred into observable SQC signals by the second $\pi/2$ pulse during detection the period^[2,6].

The signal in CRAZED experiments is sensitive to molecular diffusion^[5,7], dipolar correlation distance^[8,9], radiation damping^[10], inhomogeneous broadening^[11], and nuclear spin relaxation^[12-14]. These factors may directly impose effects on the precision and accuracy of the diffusion measurement. When transverse relaxation, diffusion, and inhomogeneous broadening are taken into account during τ and the detection period t_2 , we have^[5]

$$M_n^+(\tau, t_2) = i^{n-1} n M_0 e^{-in\Omega\tau} e^{i\Omega t_2} \left(\frac{\tau_d}{t_2 \Delta_s}\right) J_n\left(\frac{t_2 \Delta_s}{\tau_d}\right) \times e^{-\tau/T_{2n}^{app}} e^{-t_2/T_2} e^{-(t_2 - n\tau)^2 / (4a)^2} \times e^{-b_1 D_n^{app} \mathcal{F}(\delta', G', n)} \quad (1)$$

where $M_n^+(\tau, t_2)$ is the transverse magnetization for the apparent n -quantum CRAZED signal; M_0 is the equilibrium magnetization per unit volume; Ω is the resonance offset in the rotating frame; τ and t_2 are the time intervals of the CRAZED sequence during the evolution and detection periods respectively; T_2 is the SQC transverse relaxation time; b_1 is the diffusion weighting factor caused by the first two gradients; a is a coefficient of the Gaussian function; $\tau_d = (\gamma \mu_0 M_0)^{-1}$ is the dipolar demagnetizing time, where μ_0 is the magnetic permeability constant; T_{2n}^{app} is the apparent transverse relaxation time of the apparent coherence order n ; D_n^{app} is the apparent diffusion rate of inter-molecular n -quantum coherences; $\Delta_s \equiv [3(\hat{s} \cdot \hat{z})^2 - 1]/2$, where \hat{s} is the direction of coherence-selection gradients, and \hat{z} is the direction of the static magnetic field. J_n is the n -order Bessel function representing dipolar interactions; $e^{-b_1 D_n^{app}}$ represents the attenuation of the apparent MQCs caused by the first two gradients during the evolution period; $e^{-\tau/T_{2n}^{app}}$ represents the attenuation of the apparent MQCs due to relaxation; $e^{-(t_2 - n\tau)^2 / (4a)^2}$ represents the attenuation due to inhomogeneous broadening; the complex function, $\mathcal{F}(\delta', G', n)$, represents the diffusion attenuation caused by the coherence-se-

lection gradient pair located immediately before and after the second RF pulse. The attenuation due to dipolar correlation distance, relaxation, and inhomogeneous broadening is independent of Δ or G , so one can eliminate them from relative attenuation factor E_n , leaving only the attenuation due to diffusion:

$$E_n = e^{-b_1 D_n^{app}} \quad (2)$$

The diffusion weighting factor b_1 for CRAZED sequence is deduced to be:

$$b_1 = \gamma^2 G^2 \delta^2 (\Delta - \delta/3) \quad (3)$$

Equations (2) and (3) show that E_n depends on D_n^{app} only if γ, G, δ , and Δ are given. Therefore, D_n^{app} can be calculated if E_n is known.

NMR is concerned with an ensemble of nuclei. The relative signal attenuation of spin i due to diffusion is given by^[15]:

$$E_i(\Delta) = \int_{-\infty}^{\infty} P_i(\Phi_i, \Delta) \cos \Phi_i d\Phi_i \quad (4)$$

where Φ_i is the phase shift, the spin i experiences due to diffusion in the period Δ , $P_i(\Phi_i, \Delta)$ is the phase-distribution function of spin i . In the case of free diffusion, $P_i(\Phi_i, \Delta)$ satisfies the Gaussian phase distribution (GPD) approximation. Therefore, $E_i(\Delta)$ can be simplified to^[15]:

$$\begin{aligned} E_i(\Delta) &= \int_{-\infty}^{\infty} P_i(\Phi_i, \Delta) \cos \Phi_i d\Phi_i \\ &= \exp(-\Phi_i^2 / 2) \\ &= \exp(-bD_T) \end{aligned} \quad (5)$$

It is known that the intra-molecular MQCs are properties of the spins in each individual molecule and different kinds of nuclear spins in each individual molecule not only have the same D_T but also a fixed phase relation. Since Pines and co-workers have pointed out that the phase shift of an intra-molecular n -quantum coherences is n times sensitive to field gradients^[16,17], the attenuation of the intra-molecular n -quantum coherences due to diffusion can be given:

$$\begin{aligned} E_n(\Delta) &= \exp(-n^2 \Phi_i^2 / 2) \\ &= \exp(-bn^2 D_T) \\ &(n = 0, \pm 1, \pm 2, \dots) \end{aligned} \quad (6)$$

Equation (6) shows that the apparent diffusion rates for the intra-molecular MQCs can be described as:

$$D_n^{app} = n^2 D_T \quad (n = 0, \pm 1, \pm 2, \dots) \quad (7)$$

As inter-molecular MQCs describe an aspect of the collective behavior of all spins in the sample^[2,18], the phase relation of each individual spin is random. The signal attenuation of inter-molecular n -quantum coherences due to diffusion is given by:

$$\begin{aligned} E_n(\Delta) &= \int_{-\infty}^{\infty} \dots \int_{-\infty}^{\infty} \left[\prod_i P_i(\Phi_i, \Delta) \right] \times \\ &\quad \cos\left(\sum_i \Phi_i\right) d\Phi_1 \dots d\Phi_n \\ &= \prod_{i=1}^n \left[\int_{-\infty}^{\infty} P_i(\Phi_i, \Delta) \cos \Phi_i d\Phi_i \right] \end{aligned} \quad (8)$$

Therefore, the apparent diffusion rates for the inter-molecular n -quantum coherences are^[19]:

$$\begin{cases} D_n^{app} = |n| D_T \quad (n = \pm 1, \pm 2, \pm 3, \dots) \\ D_0^{app} = 2D_T \quad (n = 0) \end{cases} \quad (9)$$

The theoretical predictions of Eq.(9) are in excellent agreement with the experimental measurements we reported for $n=0$ ^[12], $n = \pm 1$ ^[14], and other orders^[13].

3 Computer simulation and discussions

A common way to simulate self-diffusion is to represent the diffusion as a random walk of particles. Because the magnetic gradient is applied along z direction, only the displacement of the particle along the z direction needs to be considered. This displacement can be represented as a sequence of small random walks

$$\mathbf{x}(t + \Delta t) = \mathbf{x}(t) + \Delta z \quad (10)$$

The random walk displacement, Δz , is given by

$$\Delta z = \sqrt{2D\Delta t} \xi \quad (11)$$

where ξ is a random number. The random numbers are uncorrelated and distributed according to the Gaussian distribution with standard deviation $\sigma = 1$ ^[20]:

$$P(\xi) = \frac{1}{\sqrt{2\pi}} e^{-\xi^2/2} \quad (12)$$

Therefore, ξ can be represented as:

$$\xi = \frac{1}{k} \sum_{i=1}^k r_i - \frac{1}{2} \sqrt{\frac{1}{12k}} \quad (13)$$

where r_i is the random number between 0 and 1 produced by computers, k is the number of r_i . In this paper, $k = 12$ was used, so Eq.(13) can be simplified

to :

$$\xi = \sum_{i=1}^{12} r_i - 6 \quad (14)$$

The intra-molecular MQCs and the inter-molecular MQCs signal attenuation factors are simulated by free diffusion under short gradient pulse (SGP) approximation and under long gradient pulse (LGP) respectively. In the following simulation, we only simulate the signal attenuation factors for $n \geq 0$, because the cases of $n \leq 0$ are just the same as those of $n \geq 0$. In the case of free diffusion, both the spin phase-distributions under these two conditions satisfy the GPD approximation. Therefore, the simulation results can be compared to the theoretical prediction.

3.1 Intra-molecular MQC signal attenuation factor under SGP approximation

CRAZED sequence (Fig. 1) is employed in simulation. The parameters used in simulation are: particles number $N = 6 \times 10^4$, step = 1000, $t = 0 \sim 80$ ms, $\Delta = t$, $\delta = 0.2$ ms, $\gamma = 2.675 \times 10^8$ rad/T s, $D = 2 \times 10^{-9}$ m²/s, and $G = 0.5$ T/m. Generally, the more the particle number is, the better the simulation result is. However, increasing the particle number implies the increase of computational time. To avoid the huge amount of computational effect, 6×10^4 particles are used in our simulation, which is shown to yield results with enough accuracy for our problem. The diffusion during the gradient pulse is neglected because the pulse duration δ is much shorter than the diffusion interval Δ between the two gradient pulses. The simulated spin phase shift for a single spin i is given by:

$$\theta_i = \gamma g \alpha (z_i(\Delta) - z_i(0)) \quad (16)$$

Fig. 2(a) shows that the natural logarithm of the relative signal intensity is inversely proportional to Δ . The simulated and theoretical results for $\Delta = 40$ ms and $\delta = 0.2$ ms are listed in Table 1, together with the ratios of simulated D_n^{app}/D_T . All the simulations suggest that an approximate $n^2:1$ relationship exists between the apparent diffusion rates of intra-molecular n -quantum coherences and those of SQC, in agreement with Eq.(7).

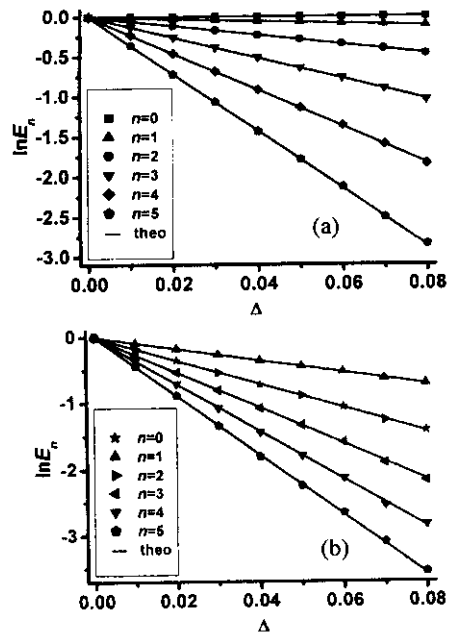


Fig. 2 Simulated and theoretical results of signal attenuation versus Δ under SGP approximation
a. Intra-molecular MQCs; b. Inter-molecular MQCs.
Symbols indicate the simulated results and lines represent theoretical ones.

Table 1 Simulated diffusion attenuation ($\ln E_{sim}$) and theoretical diffusion attenuation ($\ln E_{theo}$) of intra-molecular MQCs when $\Delta = 40$ ms and $\delta = 0.2$ ms

n	0	1	2	3	4	5
$\ln E_{sim}$	0	-0.057	-0.229	-0.515	-0.915	-1.430
$\ln E_{theo}$	0	-0.057	-0.229	-0.515	-0.916	-1.431
D_n^{app}/D_T	0.00	1.00	4.02	9.04	16.05	25.09

3.2 Inter-molecular MQC signal attenuation factor under SGP approximation

The parameters applied in the computer simulation of inter-molecular MQCs are the same as those used in the intra-molecular MQC simulation except that $\Delta = 0 \sim 80$ ms, $\delta = 0.5$ ms. The simulated results are shown in Fig. 2(b). The results of zero-quantum coherences overlap with those of the two-quantum coherences. Table 2 lists the natural logarithms of the relative signal intensities of inter-molecular MQCs versus n when $\Delta = 60$ ms and $\delta = 0.2$ ms. The simulated relationship between D_n^{app} and D_T satisfies Eq.(9), i. e., $n:1$ between the apparent diffusion rates of inter-molecular n -quantum coherences and those of SQC.

Table 2 Simulated diffusion attenuation ($\ln E_{\text{sim}}$) and theoretical diffusion attenuation ($\ln E_{\text{theo}}$) of inter-molecular MQCs when $\Delta = 60$ ms and $\delta = 0.2$ ms

n	0	1	2	3	4	5
$\ln E_{\text{sim}}$	-0.171	-0.086	-0.171	-0.257	-0.342	-0.428
$\ln E_{\text{theo}}$	-0.172	-0.086	-0.172	-0.258	-0.344	-0.429
D_n^{app}/D_T	1.99	1.00	1.99	2.99	3.98	4.98

3.3 Intra-molecular MQC signal attenuation factor under LGP

The parameters applied in the computer simulation of intra-molecular MQCs under LGP are the same as those under SGP approximation except that $\Delta = 0 \sim 6$ ms and $\delta = \Delta/10$. In such case the diffusion during the gradient pulse cannot be neglected because δ does not satisfy the condition $\delta \ll \Delta$. The spin phase shift for a single spin i is then given by

$$\theta_i = \gamma g \Delta t \left[\sum_{t=t_0}^{t \leq \delta} z_i(t) - \sum_{t=t_0+\Delta}^{t \leq t_0+\Delta+\delta} z_i(t) \right] \quad (17)$$

The simulated results are in good accord with the theoretical values (Fig. 3(a)). The natural logarithms of the relative signal intensities of intra-molecular MQCs versus n when $\Delta = 5$ ms and $\delta = \Delta/10$ are listed in Table 3. Obviously, the simulated D_n^{app}/D_T satisfies Eq.(7), that is, the same $n^2:1$ ratio exists between the apparent diffusion rates of intra-molecular n -quantum coherences and those of SQC under LGP as under SGP approximation. The $2^2:1$ relationship is also verified by intra-molecular double-quantum coherence ^{19}F NMR experiments of 1,1,3-trichloro-2,2,3-trifluorocyclobutane dissolved in ethylene glycol although the different diffusion weighting factors are realized by varying field gradient G instead of Δ in experiments^[20].

Table 3 Simulated diffusion attenuation ($\ln E_{\text{sim}}$) and theoretical diffusion attenuation ($\ln E_{\text{theo}}$) of inter-molecular MQCs when $\Delta = 5$ ms and $\delta = 0.5$ ms

n	0	1	2	3	4	5
$\ln E_{\text{sim}}$	0	-0.043	-0.173	-0.388	-0.690	-1.077
$\ln E_{\text{theo}}$	0	-0.043	-0.173	-0.389	-0.692	-1.081
D_n^{app}/D_T	0.00	1.00	4.02	9.02	16.05	25.05

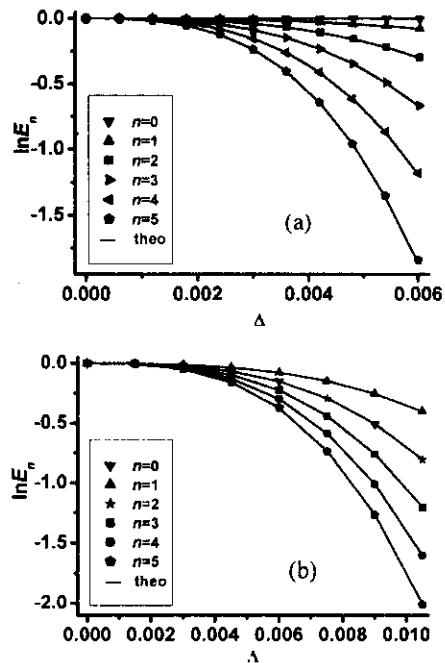


Fig. 3 Simulated and theoretical results of signal attenuation versus Δ under LGP

- (a) Intra-molecular MQCs ;
(b) Inter-molecular MQCs.

Symbols indicate the simulated results and lines represent theoretical ones.

3.4 Inter-molecular MQCs signal attenuation factor under LGP

The parameters applied in the computer simulation of inter-molecular MQCs under LGP are the same as those adopted in the intra-molecular MQCs except that $\Delta = 0 \sim 10.5$ ms. The simulation results are shown in Fig. 3(b). The results of zero-quantum coherences coincide with those of the two-quantum coherences.

Table 4 Simulated diffusion attenuation ($\ln E_{\text{sim}}$) and theoretical diffusion attenuation ($\ln E_{\text{theo}}$) of inter-molecular MQCs when $\Delta = 9$ ms and $\delta = 0.9$ ms

n	0	1	2	3	4	5
$\ln E_{\text{sim}}$	-0.503	-0.252	-0.503	-0.757	-1.010	-1.257
$\ln E_{\text{theo}}$	-0.504	-0.252	-0.504	-0.756	-1.009	-1.261
D_n^{app}/D_T	2.00	1.00	2.00	3.00	4.01	4.99

Table 4 gives the natural logarithms of the relative signal intensities of inter-molecular MQCs versus n when $\Delta = 9$ ms and $\delta = \Delta/10$. The simulated D_n^{app}/D_T

values also satisfy Eq. (9). This relationship is also verified by ^1H NMR experiments of 20% D_2O in $\text{H}_2\text{O}^{[17]}$ although in experiments different diffusion weighting factors are achieved by varying field gradient G instead of Δ (Fig. 1).

4 Conclusions

In this paper, the theoretical expression of apparent diffusion rates of intra-molecular and inter-molecular MQCs is given and the random walk model of particles is employed to simulate the apparent diffusion behaviors of intra-molecular and inter-molecular multiple-quantum coherences. Both the theoretical predictions and computer simulations demonstrate that: ① the apparent diffusion rates for the intra-molecular MQCs can be described as $D_n^{app} = n^2 D_T$ for $n = 0, \pm 1, \pm 2, \dots$; ② the apparent diffusion rates for the inter-molecular MQCs can be described as $D_0^{app} = 2D_T$ for $n = 0$ and $D_n^{app} = |n| D_T$ for $n = \pm 1, \pm 2, \dots$. The higher sensitivity of the inter-molecular MQC diffusion compared to SQC may provide a valuable way in diffusion weighted MRI^[21]. The results show that the computer simulations presented herein can validate the correctness of theoretical predictions and can also be used to predict experimental results. In this paper, the theoretical curves are well coincident with the simulation results under the free self-diffusion. It proves that the mathematical model of the computer simulation presented herein is reasonable, and it has enough precision. Because, it is hard to get the analytical expression for many complex cases, for example, the self-diffusion under restricted diffusion or non-linear gradient magnetic field, the inter-molecular multiple-quantum coherences between two separated parts of a sample such as co-axis tubes, the present method may be extended to simulate more complex cases with appropriate correction of mathematical models. Further research will be reported in another paper.

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