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Diffusion Measurements Using the Nonlinear Stimulated Echo

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The nonlinear stimulated echo that is generated by a sequence of three radiofrequency pulses, 90°–τ_1–90°–τ_2–45°, in high magnetic fields (or at low temperatures) in the presence of pulsed or steady field gradients can be applied for measurements of the diffusion coefficient. Corresponding test experiments are reported. Steady gradients can be used without knowledge of the relaxation times. Remarkably the attenuation of the nonlinear stimulated echo by diffusion is substantially stronger than in the case of the ordinary stimulated echo. © 2000 Academic Press

Key Words: **NMR; diffusion; demagnetizing field; stimulated echo; field gradient.**

1. INTRODUCTION

NMR self-diffusion measurements in liquids are often carried out with the aid of stimulated echoes (*1*) produced under the action of gradients of the magnetic flux density $\mathbf{B}_0$. The field gradients can be applied either in pulsed form between the radiofrequency (RF) pulses (*2, 3*) or as steady gradients. For the latter variant, the stationary fringe field gradients of superconducting magnets turned out to be particularly favorable (*4*). The use of gradients of the RF field amplitude instead of $\mathbf{B}_0$ gradients has also been suggested (*5, 6*).

All of these methods are based on conventional schemes of coherence evolution in the laboratory or rotating frames. More recently, exploitation of multiple echoes (*7, 8*) for diffusion measurements was proposed (*9*). These echoes arise as a consequence of coherence evolution in the presence of the demagnetizing field which is produced by the longitudinal magnetization in the sample. The prerequisite for strong multiple echo signals therefore is a high magnetization. That is, in particular, the flux density of the external magnetic field must be high enough and/or the temperature should be moderate.

The demagnetizing field in liquids has its origin in long-range dipolar interactions which are not averaged out by translational diffusion. On the time scale of NMR experiments, diffusion in liquids affects dipolar interaction only over distances of up to a few micrometers. Because the *long-range* dipolar coupling involves many particles by nature, it can be considered globally in the continuum limit in the form of a mean field usually called the *demagnetizing field.* This field depends on the spatial distribution of the magnetization $\mathbf{M}(\mathbf{r})$, which, in turn, is a function of the coherence evolution during the pulse sequence in the presence of field gradients. To a minor degree, the sample shape also plays a role (*10, 11*). If the magnetization is modulated along a direction with unit vector $\mathbf{u}_s$, the spatial distribution of the resulting dipolar demagnetizing field is given by (*7–9*)

$$\mathbf{B}_d(\mathbf{r}) = \mu_0\Delta\left[M_z(s)\mathbf{u}_z - \frac{1}{3}\mathbf{M}(s)\right], \qquad [1]$$

where

$$\Delta = \frac{3(\mathbf{u}_s \cdot \mathbf{u}_z)^2 - 1}{2}, \qquad [2]$$

and μ_0 is the magnetic field constant. Here the coordinate along the $\mathbf{u}_s$ direction is $s = \mathbf{r} \cdot \mathbf{u}_s$ and the unit vector $\mathbf{u}_z$ is directed along the magnetic field relevant for coherence evolution ($\mathbf{B}_0$ in the following).

It has been shown in Refs. (*12, 13*) that a pulse sequence like that shown in Fig. 1 produces a train of *multiple nonlinear stimulated echoes* (NOSE) in the presence of the demagnetizing field and also modifies the ordinary *stimulated echo* (STE) (*1*). The ordinary stimulated echo appears at a time τ_1 after the third pulse, whereas the multiple nonlinear stimulated echoes are refocused at times $2\tau_1, 3\tau_1, \ldots$, with varying amplitude. In the absence of intramolecular spin couplings the appearance of such echoes can be described on the basis of the Bloch equations modified with the demagnetizing field (*12*). Alternately and if intramolecular spin–spin coupling is to be included, a spin operator formalism (*13–15*) can be used as well. In this case, the effects of different spin species can readily be accounted for.

Note that the demagnetizing field is only appropriate for the treatment of the evolution of spin systems whose operator representation is restricted to the motional-averaging regime of dipolar couplings. That is, only intramolecular spin couplings can explicitly be taken into account on this basis. In the literature, treating long-range dipolar couplings exceeding the

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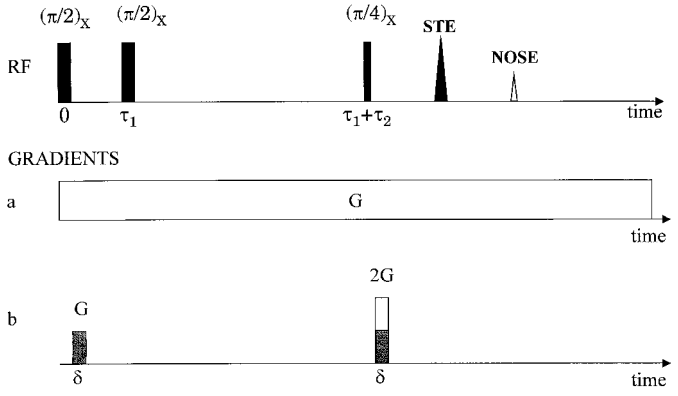

FIG. 1. Pulse sequences producing a stimulated echo (STE) at τ_1 and nonlinear stimulated echoes (NOSE) at positions $2\tau_1$, $3\tau_1$, and so on. The gradient, oriented along the z-direction, can be applied either in steady (a) or in pulsed (b) form. The strength of the second gradient pulse must be $2G$ in the case of the first NOSE.

motional-averaging regime explicitly by considering the full set of spin operator terms the density operator consists of has been suggested (*16–19*). In this case, *short-* as well as *long-range* dipolar interactions may be regarded at one time. In the present study, we restrict ourselves to intramolecularly uncoupled spins and to the linear density operator term so that a treatment based on the Bloch equations becomes feasible. Under such circumstances, diffusion effects can be implemented very easily into the formalism. Furthermore we will refer to isotropic diffusion in a uniform sample, for simplicity, although restricted diffusion may be treated in principle on the basis of the same formalism.

2. THEORY

Figure 1 shows the pulse sequences to be considered. The formalism refers to a steady gradient as represented by Fig. 1a. On this basis a generalization to pulsed gradients, Fig. 1b, is readily feasible. Provided that τ_1 is short enough, displacements by diffusion in the second pulse interval, τ_2, will dominate. The RF pulses are assumed to be "hard," i.e., they excite all spins within the sample in the same way. The gradient $\mathbf{G}$ is assumed to be spatially constant and oriented along the z-direction so that $\Delta = 1$ in Eq. [1].

Just before the first $(\pi/2)_x$ RF pulse, the equilibrium magnetization $\mathbf{M}_0$ is aligned along the z-direction. The evolution of the magnetization during the pulse sequence is described on the basis of the modified Bloch equations (*7*),

$$\frac{M_z(z,\,t)}{dt} = -\frac{M_z(z,\,t) - M_0}{T_1} + D\nabla^2 M_z(z,\,t), \qquad [3]$$

for the longitudinal, and

$$\frac{M_+(z,\,t)}{dt} = -i\gamma[Gz + B_d(z)]M_+(z,\,t) - \frac{M_+(z,\,t)}{T_2} + D\nabla^2 M_+(z,\,t) \qquad [4]$$

for the transverse component. Here γ represents the magnetogyric ratio and D the self-diffusion coefficient. T_1 and T_2 denote the longitudinal and transverse relaxation times, respectively. The complex transverse magnetization is defined as $M_+(z,\,t) = M_x(z,\,t) + iM_y(z,\,t)$. In the current case, the Laplace operator is reduced to $\nabla^2 = d^2/dz^2$ because only displacement components along the z-axis are relevant with this choice of the gradient direction. The demagnetizing field $B_d(z)$ in the above equation is given by Eq. [1], from which it becomes obvious that the component pertinent for the evolution of the transverse magnetization is parallel to the z-axis (*7, 8*). Provided that longitudinal relaxation is negligible during the first evolution interval, i.e., $T_1 \gg \tau_1$, ideally no longitudinal magnetization component exists in this interval. In a sample with spherical symmetry, therefore no demagnetizing-field effects need to be considered so far (*7, 8, 12, 13, 18*). The magnetization after the second RF pulse is then given by

$$M_x(z,\,\tau_1^+) = M_0 e^{-\tau_1/T_2}\sin(\gamma G z \tau_1), \qquad [5]$$

$$M_y(z,\,\tau_1^+) = 0, \qquad [6]$$

$$M_z(z,\,\tau_1^+) = -M_0 e^{-\tau_1/T_2}\cos(\gamma G z \tau_1). \qquad [7]$$

The longitudinal magnetization component is now cosine modulated along the z-direction. That is, the spherical symmetry is broken, and a finite demagnetizing field arises. As a consequence, the evolution of the transverse magnetization is influenced by this field according to Eq. [4].

We now assume complete cancellation of the transverse magnetization component in the τ_2 interval as a result of field inhomogeneities and T_2 relaxation effects, so that only the longitudinal component after the second pulse will be retained at the end of this interval, that is, Eq. [3] has merely to be solved in order to find the evolution of this component under relaxation and diffusion effects. In case some residual transverse magnetization survives the second pulse interval, additional echo phenomena will occur as shown in Ref. (*13*). That is, the degree of spoiling of the coherences during τ_2 can readily be checked in an experiment.

In this context it may be worth mentioning that even intermolecular zero-quantum coherences arising from higher order expansion terms of the density operator (*18*) tend to be spoiled by the gradient because the coupling partners are separated farther than the motional averaging distance, i.e., the root mean squared displacement to be probed in a diffusion experiment

per definitionem. Zero-quantum coupling partners with internuclear vectors perpendicular to the gradient direction do not contribute to any refocusing process anyway.

The prevailing effect of diffusion in the τ_2 interval is that the cosine modulation of the z-magnetization is attenuated, that is, the minute change of the magnetization by diffusion does not perceptibly affect spin–lattice relaxation. Diffusion and relaxation therefore may be regarded to occur independently of each other. Under this assumption, the solution of Eq. [3] is

$$M_z(z,\ \tau_1 + \tau_2^-) = M_0(1 - e^{-\tau_2/T_1}) - M_0 e^{-\tau_1/T_2} e^{-\tau_2/T_1} e^{-D(\gamma G)^2 \tau_1^2 \tau_2} \cos(\gamma G z \tau_1), \quad [8]$$

where a time $t = \tau_1 + \tau_2^-$ just before the third RF pulse is considered.

The third RF pulse, $(\pi/4)_x$, transfers the longitudinal magnetization into

$$M_x(z,\ \tau_1 + \tau_2^+) = 0, \quad [9]$$

$$M_y(z,\ \tau_1 + \tau_2^+) = \frac{1}{\sqrt{2}} M_0(1 - e^{-\tau_2/T_1}) - \frac{1}{\sqrt{2}} M_0 e^{-\tau_1/T_2} \times e^{-\tau_2/T_1} e^{-D(\gamma G)^2 \tau_1^2 \tau_2} \cos(\gamma G z \tau_1), \quad [10]$$

$$M_z(z,\ \tau_1 + \tau_2^+) = \frac{1}{\sqrt{2}} M_0(1 - e^{-\tau_2/T_1}) - \frac{1}{\sqrt{2}} M_0 e^{-\tau_1/T_2} \times e^{-\tau_2/T_1} e^{-D(\gamma G)^2 \tau_1^2 \tau_2} \cos(\gamma G z \tau_1). \quad [11]$$

By virtue of the $\pi/4$ tip angle (instead of $\pi/2$ in a conventional stimulated-echo experiment) the longitudinal magnetization given by Eq. [8] is split into two components. The transverse component evolves in the presence of the demagnetizing field created by the longitudinal component. Here one should keep in mind that it is the demagnetizing field originating from this modulated longitudinal component which is responsible for the generation of multiple echoes (*7, 8*). Otherwise no multiple echoes would arise. A flip angle of $\pi/4$ ensures maximum signal intensity of the nonlinear stimulated echo (*12*).

Since the longitudinal component is not changed by free evolution and because it will not contribute to the signal, we focus our attention only on the evolution of the transverse component. The demagnetizing field created by the modulated longitudinal component is given by

$$B_d(z) = \mu_0 M_z(z) = -\mu_0 \frac{1}{\sqrt{2}} M_0 e^{-\tau_1/T_2} e^{-\tau_2/T_1} e^{-D(\gamma G)^2 \tau_1^2 \tau_2} \cos(\gamma G z \tau_1). \quad [12]$$

As has been shown in Refs. (*12, 13*), the echoes of interest appear at τ_1 (STE) and $2\tau_1$ (NOSE) so that self-diffusion and longitudinal relaxation effects can be neglected again. Inserting the expression for the demagnetizing field, $B_d(z)$, given in Eq. [12], into Eq. [4] gives

$$M_+(z,\ \tau_1 + \tau_2 + t) = M_+(z,\ \tau_1 + \tau_2^+) e^{-t/T_2} e^{i\xi(t)\cos(\gamma G z \tau_1)}, \quad [13]$$

where

$$\xi(t) = \frac{1}{\sqrt{2}} \gamma \mu_0 M_0 t e^{-\tau_1/T_2} e^{-\tau_2/T_1} e^{-D(\gamma G)^2 \tau_1^2 \tau_2}. \quad [14]$$

The transverse component can be written in a more convenient form using the Bessel function expansion (*7, 20*),

$$e^{i\xi\cos\alpha'} = \sum_{n=-\infty}^{+\infty} i^n J_n(\xi) e^{in\alpha'}, \quad [15]$$

and the properties of Bessel functions, $J_n(\xi)$, of integer order,

$$J_{n-1}(\xi) - J_{n+1}(\xi) = 2 \frac{d}{d\xi} J_n(\xi), \quad [16]$$

$$J_{-n}(\xi) = (-1)^n J_n(\xi). \quad [17]$$

With the above expansion, Eq. [13] can be rewritten as

$$M_+(z,\ \tau_1 + \tau_2 + t) = \frac{1}{\sqrt{2}} M_0(1 - e^{-\tau_2/T_1}) e^{-t/T_2} \sum_{n=-\infty}^{+\infty} i^{n+1} J_n(\xi) e^{i\gamma G z (n\tau_1 - t)} - \frac{1}{\sqrt{2}} M_0 e^{-(\tau_1 + t)/T_2} e^{-\tau_2/T_1} e^{-D(\gamma G)^2 \tau_1^2 \tau_2} \times \sum_{n=-\infty}^{+\infty} i^n \frac{d}{d\xi} J_n(\xi) e^{i\gamma G z (n\tau_1 - t)}. \quad [18]$$

The NMR signal finally to be detected is an average over all z-positions in the sample. This average vanishes at times other than $t = n\tau_1$ for which the echoes appear. The amplitude of these echoes can be simply computed by employing the approximation for Bessel functions (*20*),

$$J_n(\xi) \cong \frac{1}{n!} \left(\frac{\xi}{2}\right)^n, \quad [19]$$

valid for time intervals, τ_1, for which the condition $\gamma \mu_0 M_0 \tau_1 \ll 1$ is satisfied (*7, 8*). With this approximation the amplitude

of the stimulated echo appearing at a time $t = \tau_1$ after the third pulse is given by

$$A_{\mathrm{STE}}(\tau_1,\ \tau_2) = -\frac{i}{2\sqrt{2}} M_0 e^{-2\tau_1/T_2} e^{-\tau_2/T_1} e^{-D(\gamma G)^2 \tau_1^2 \tau_2}. \quad [20]$$

Here we have neglected the demagnetizing-field effect on the amplitude of the stimulated echo that would result from the first term in Eq. [18] if the condition $\gamma\mu_0 M_0 \tau_1 \ll 1$ is violated.

The amplitude of the nonlinear stimulated echo at $t = 2\tau_1$ can be calculated in a similar way as

$$A_{\mathrm{NOSE}}(\tau_1,\ \tau_2) = \frac{1}{4} \gamma\mu_0 M_0^2 \tau_1 e^{-4\tau_1/T_2} e^{-2\tau_2/T_1} e^{-2D(\gamma G)^2 \tau_1^2 \tau_2}, \quad [21]$$

where higher order contributions have been neglected again.

Analogously the pulsed gradient variant shown in Fig. 1b produces a nonlinear stimulated echo with the amplitude

$$A_{\mathrm{NOSE}}(\tau_1,\ \tau_2) = \frac{1}{4} \gamma\mu_0 M_0^2 \tau_1 e^{-4\tau_1/T_2} e^{-2\tau_2/T_1} e^{-2D(\gamma G)^2 \delta^2 \tau_2}. \quad [22]$$

Here G represents the gradient pulse strength of duration δ oriented again along the z-direction. Note that the second gradient pulse must be of double "area" in order to produce a nonlinear stimulated echo. Equations [21, 22] remarkably suggest a stronger dependence of the amplitude of the nonlinear stimulated echo on the self-diffusion coefficient compared with the conventional stimulated echo.

The new method for the determination of the diffusion coefficient we propose here is based on the comparison of two experiments where one is performed with double pulse intervals. Forming the quotient of the amplitudes of the stimulated echo, $A_{\mathrm{STE}}(2\tau_1, 2\tau_2)$, acquired with double pulse intervals and of the nonlinear stimulated echo, $A_{\mathrm{NOSE}}(\tau_1, \tau_2)$, recorded with single intervals,

$$\frac{A_{\mathrm{STE}}(2\tau_1,\ 2\tau_2)}{A_{\mathrm{NOSE}}(\tau_1,\ \tau_2)} = -i \frac{\sqrt{2}}{M_0 \gamma\mu_0 \tau_1} e^{-4D(\gamma G)^2 \tau_1^2 \tau_2} \quad [23]$$

obviously leads to an expression independent of the relaxation times. Only diffusion effects matter. Varying the evolution interval τ_2, a simple evaluation of the self-diffusion coefficient becomes possible without knowledge of the relaxation times.

3. EXPERIMENTAL

Diffusion measurements were carried out cyclohexane and water at 298 K using a Bruker DSX400 NMR spectrometer. The equilibrium magnetization at $B_0 \approx 9.4$ T is high enough to allow for a good detection sensitivity of nonlinear echoes (*7*, *8*, *12*, *13*). The RF pulse width for a flip angle of $\pi/2$ was 12 μs. A steady magnetic field gradient was produced by shifting the probe in the fringe field of the magnet. Calibration of the gradient was performed with the aid of the known value for the acetone diffusion coefficient. The result is $G = 4.1$ mT/m. Small sample heights (≈6 mm) in a 5-mm-diameter tube were used in order to avoid any nonuniformity of the gradient across the sample. The pulse intervals were adjusted to $\tau_1 = 25$ ms and $\tau_2 = 350 \ldots 650$ ms.

The gradient pulses had a width of $\delta = 1$ ms in the first evolution interval and δ (STE) or 2δ (NOSE) in the second one. They were applied immediately after the first and the third RF pulses. The gradient strength was varied in the range 0.027 to 0.1 T/m. The background gradient was estimated to be 0.1 mT/m. In the pulsed gradient experiment, the pulse intervals were $\tau_1 = 20$ ms and $\tau_2 = 900$ ms, respectively.

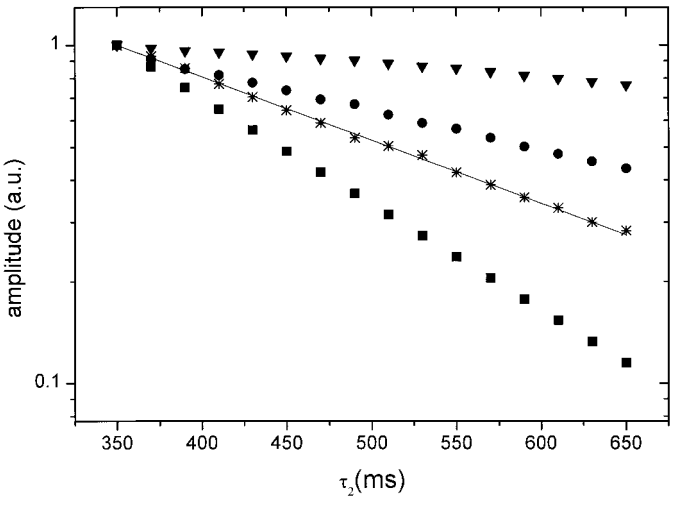

FIG. 2. Echo attenuation by diffusion in cyclohexane at T = 298 K. The data refer to the steady gradient variant shown in Fig. 1a. The plot relates the normalized amplitudes of the stimulated echo, $A_{\mathrm{STE}}(\tau_1,\ \tau_2)$ (upside-down triangles), nonlinear stimulated echo, $A_{\mathrm{NOSE}}(\tau_1, \tau_2)$ (circles), stimulated echo at double time interval, $A_{\mathrm{STE}}(2\tau_1,\ 2\tau_2)$ (squares), and the ratio $R = A_{\mathrm{STE}}(2\tau_1, 2\tau_2)/A_{\mathrm{NOSE}}(\tau_1,\ \tau_2)$ (stars) with τ_2. The solid line represents the best fit of Eq. [23]. The first interpulse duration was fixed at $\tau_1 = 25$ ms. A total number of 16 transients with a repetition time 15 s were accumulated.

4. RESULTS

In a first experiment we have tested the steady gradient variant (Fig. 1a). Figure 2 shows a plot of $A_{\mathrm{STE}}(\tau_1, \tau_2)$ (upside-down triangles), $A_{\mathrm{NOSE}}(\tau_1, \tau_2)$ (circles), $A_{\mathrm{STE}}(2\tau_1, 2\tau_2)$ (squares), and the ratio $A_{\mathrm{STE}}(2\tau_1, 2\tau_2)/A_{\mathrm{NOSE}}(\tau_1, \tau_2)$ (stars) as a function of τ_2. From a fit of Eq. [23] to these data (solid line), the self-diffusion coefficient was evaluated as $D = (1.44 \pm 0.03) \times 10^{-9}$ m^2/s. This result is in good agreement with data previously reported (*21*).

The results obtained with water at 298 K using the pulsed-

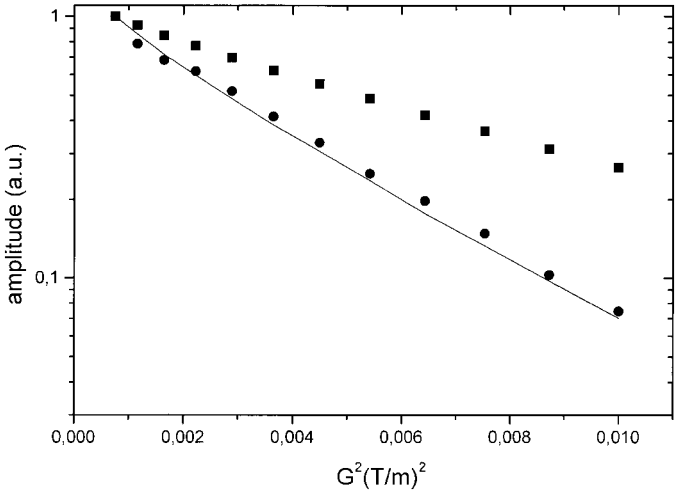

FIG. 3. Echo attenuation by diffusion in water at T = 298 K. The data refer to the pulsed-gradient version shown in Fig. 1b. The normalized amplitudes of the stimulated echo (squares) and nonlinear stimulated echoes (circle) are plotted as a function of the square of the gradient strength. The continuum line represents the square of the stimulated-echo amplitude. A total number of 16 transients with a repetition time 20 s were accumulated.

gradient experiment (Fig. 1b) are shown in Fig. 3. The normalized amplitudes of the stimulated echo (squares) and nonlinear stimulated echo (circles) are plotted as a function of the squared gradient strength. The data for the NOSE amplitude depend more strongly on the gradient strength than those for the STE amplitude. The self-diffusion coefficient was determined as $D = (2.3 \pm 0.04) \times 10^{-9}$ m^2/s. The solid line was calculated as the square of the stimulated echo amplitude. That is, the theoretical prediction is verified.

5. CONCLUSIONS

We have shown that the nonlinear stimulated echo can be used successfully as a tool for diffusion measurements. The method proposed here, a combination between stimulated echo and nonlinear stimulated echo, does not require the knowledge of relaxation times. Steady as well as pulsed field gradients can be employed. The only prerequisite is that the magnetic field is higher than $\approx$7 T in order to ensure detectable nonlinear stimulated echoes. This method is of particular interest for diffusion measurements in highly viscous materials provided that T_2 is long enough. It is also applicable in the strong gradients provided by the fringe field of superconducting magnets. It is noteworthy that the nonlinear stimulated echo shows a stronger attenuation by diffusion than the ordinary stimulated echo.

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