Principles of centerband-only detection of exchange in solid-state nuclear magnetic resonance, and extension to four-time centerband-only detection of exchange

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Received 15 December 1999; accepted 24 February 2000

Theoretical principles and experimental details of the centerband-only detection of exchange (CODEX) nuclear magnetic resonance (NMR) experiment for characterizing slow segmental dynamics in solids are described. The experiment, which is performed under magic-angle spinning, employs recoupling of the chemical-shift anisotropy before and after a long mixing time during which molecular reorientations may occur. By an analysis in terms of the difference tensor of the chemical shifts before and after the mixing time, the dependence on the reorientation angle is obtained analytically for uniaxial interactions, and a relation to two-dimensional exchange NMR patterns is established; the same theory can also be applied for analyzing stimulated-echo and pure-exchange NMR data. A favorable linear dependence is derived generally for small rotations, which makes the experiment suitable for detecting small-amplitude motions. Quantification is excellent because the peaks are narrow and intense, unlike the broad powder or sideband spectra that are characteristic of all previous NMR experiments for probing slow segmental rotations. We also introduce and demonstrate a four-time CODEX experiment that yields information previously obtained only in 3D (three-dimensional) and reduced 4D (four-dimensional) exchange NMR experiments, such as the number of orientational sites accessible to the mobile groups. Chemical-shift anisotropies required in the CODEX analysis of motional amplitudes can be estimated using a closely related chemical-shift recoupling experiment. The implementation of total suppression of sidebands before detection is also explained. The experiments are demonstrated on dimethylsulfone, isotactic polypropylene, and poly(methyl methacrylate), PMMA. In isotactic poly(1-butene), the signals of the amorphous and interfacial regions have been observed selectively by using pure-exchange CODEX near the glass transition. The four-time CODEX experiment confirms that in the β-relaxation process of glassy PMMA, fewer than half of the sidegroups perform jumps between two orientations. © 2000 American Institute of Physics.

INTRODUCTION

Solid-state nuclear magnetic resonance (NMR) provides the most powerful techniques for elucidating details of segmental dynamics in solid materials. 1 While fast dynamics can be characterized to some extent by line shape 2–4 or relaxation-time measurements 5 the most specific information is obtained in exchange NMR experiments, where relatively slow segmental reorientations with rates of 0.1/s–10 000/s are observed in terms of changes of orientation-dependent NMR frequencies. 1 Correlation times 6,7 and their distributions, 8 reorientation-angle distributions, 9,10 orientational memory, 11 rate memory, 12,13 the existence of dynamic heterogeneities, 12 and their size 14 can be characterized by 1D, 2D, 3D, and reduced 4D exchange NMR. However, the sensitivity and resolution of these traditional exchange-NMR techniques have been limited, since anisotropy-broadened lineshapes or strong sidebands in magic-angle spinning spectra were required. Only by specific isotopic labeling could these limitations be overcome in part.

Recently, we introduced a new exchange NMR technique, centerband-only detection of exchange (CODEX) that makes it possible to observe and characterize slow (k
=0.1/s–3000/s) segmental reorientations with the highest available NMR sensitivity and site resolution, in sideband-free magic-angle spinning (MAS) spectra.15 From short series of one-dimensional MAS spectra, the correlation function and correlation time can be determined, and it can be established whether the motion is diffusive or whether it involves jumps between discrete sites, whose number can be measured precisely if all segments are mobile. In addition, motional amplitudes can be estimated, with good sensitivity to small-angle motions. This information is obtained for each site with a resolved line in the sideband-free MAS spectrum.

In this paper, we describe the theoretical principles of the CODEX technique. Parts of the theory can also be directly applied to the analysis of stimulated-echo7,16,17 or 1D pure-exchange (PUREX)18 experiments, which are closely related except that their resolution and sensitivity are more than an order of magnitude lower. We also demonstrate extensions of CODEX to a four-time exchange experiment that can yield information previously accessible only in 3D and reduced 4D experiments.12–14 Applications to two semicrystalline polymers and a glassy one are shown, and the use of CODEX as a dynamic filter is demonstrated.

EXPERIMENT

Samples

Dimethyl sulfone, DMS, (CH3)2SO2, was used in powder form as received from Aldrich. Isotactic polypropylene, iPP, [-CH2–CH(CH3)]n of Mw = 250 000 was molded above 463 K into a cylindrical block and annealed at 413 K for 1 h to obtain the pure α-phase.19 Two samples of glassy poly(methyl methacrylate) PMMA, [-CH2–C(CH3)(CO2CH3)]n were studied. One was an industrial material (Plexiglas®); the other sample was purchased from Scientific Polymer Products, Inc. (approximate MW = 35 000) and melt-compressed into a cylinder fitting snugly into the NMR rotor. Isotactic poly(1-buten), iPB, [-CH2–CHR–]n with R = CH3–CH=, of Mn = 570 000, was obtained from Aldrich. The as-received iPB pellets were prepared for the NMR studies by melting at ∼423 K, followed by slow cooling and storage at room temperature for several weeks to ensure complete conversion to crystal form I (iPB-I).20,21

NMR

The NMR experiments were performed at 75 MHz for 13C on a BRUKER DSX-300 spectrometer. Most data were acquired in a 7 mm double-resonance MAS probehead, with a 13C 90° pulse length of 3.9 μs and 1H decoupling at γB1/2π = 70 kHz, at spinning rates ranging from 4.0 to 6.5 kHz. A few measurements were also performed in a 4-mm double-resonance MAS probehead, with 13C and 1H 90° pulse lengths of 3.5 μs, at 5–10 kHz MAS. The recycle delays utilized were 1.5, 2.5, 2.5, and 3.5 s for PMMA, DMS, iPB, and iPP, respectively. The cross-polarization (CP) times were 1.5 ms for PMMA, and 1 ms for DMS, iPB, and iPP. The longest measuring time per pure-exchange CODEX spectrum was 2.0 h, for PMMA. The four-time CODEX experiments on PMMA were performed in 30 h.

FIG. 1. (a) Basic CODEX pulse sequence and its synchronization with the sample rotation. The reference signal S0 is obtained after inverting t_m and t_r. (b) Close-up on the central recoupling and mixing periods. The phases ±Φ_A,n and ±Φ_B,n acquired by the magnetization between 180° pulses are indicated as ±A1, ±B1, ±A2, ±B2 above the sequence. Without exchange during t_m, Φ_A,1 = φ_A,1 and Φ_B,1 = φ_B,1, so that the total acquired phase is zero and no dephasing occurs. (c) Detection scheme for (a) with sideband suppression by TOSS combined with incrementation of the z filter over a full rotation period.

NMR THEORY

In the following, we describe various aspects of the CODEX technique. After a general overview, a treatment in terms of the chemical-shift difference tensor is given and spinning-speed independent master-curves are presented. Then, the four-time CODEX experiment is described and analyzed. Detection after TOSS (total suppression of sidebands sequence)22 and auxiliary measurements of chemical-shift anisotropies (CSAs) are also discussed. Finally, some aspects of the implementation of CODEX are addressed.

Simple description of CODEX

Figure 1 shows the pulse sequence of the CODEX experiment. After cross-polarization (or single-pulse excitation), the magnetization evolves purely under the anisotropic chemical shift, recoupled by a series of 180° pulses spaced by t_r/2 (for more details see below).23 Then, one component of the magnetization is stored for the mixing time t_m, during which motion can occur. The mixing time is a multiple of the rotation period t_r; for mixing times of the order of seconds, this requires rotation-synchronized timing of the read-out pulse. In successive scans, the phases of the 90°-pulses flanking the mixing time are changed together by 90°, so that both components, cos φ_1 and sin φ_1, of the magnetization are retained alternately. If the storage pulse and the read-out pulse always have opposite signs, the sum of two scans yields cos φ_1 + i sin φ_1. Except for a prefactor of 0.5, the signal is effectively the same as if no 90°-pulses and mixing time had been applied. If the storage and the read-out pulse have the same sign, the same result is obtained by inverting the receiver phase.
The total phase $\Phi_1 + \Phi_2$ of the magnetization at the end of the second recoupling period of duration $N/2t_r$ is obtained from

$$\Phi_1 = N/2(-\Phi_{A,1} + \Phi_{B,1}),$$  
$$\Phi_2 = N/2(\Phi_{A,2} - \Phi_{B,2}),$$  

(1a)  

(1b)

where

$$\Phi_{A,n} = \int_0^{t_r/2} \omega_n(t)dt \quad \text{and} \quad \Phi_{B,n} = \int_{t_r/2}^{t_r} \omega_n(t)dt,$$

(2)

with the frequencies $\omega_1(t)$ and $\omega_2(t)$ before and after $t_m$, respectively. Every 180° pulse inverts the sign of the phase, so that $\Phi_{A,n}$ and $\Phi_{B,n}$ have opposite signs. Without a 180° pulse in the place of the 90° pulse after the second recoupling period of duration $N/2$, both phases in the two halves of the recoupling period are opposite, see Eq. (1). If $\omega_1(t) = \omega_2(t)$, i.e., if no exchange occurs, this leads to $\Phi_1 + \Phi_2 = 0$; in other words, the magnetization is refocused along its original direction.

At the end of the second recoupling period, the total magnetization is along the original direction that it had during CP; that this holds even with exchange is proven below. Thus, the magnetization is stored along the z axis during the period $t_z$, and subsequently read out for detection. To suppress spinning sidebands during detection, the total suppression of sidebands (TOSS) sequence$^{22}$ can be used before detection. Since motion-induced dephasing can break the cylindrical symmetry around the rotor axis required for TOSS, the duration of $t_z$ is incremented in $K$ steps over a full rotation period. This ensures that TOSS suppresses all sidebands except for orders $nK$ (for details see below).

In a simple CODEX experiment, the signal intensity $S(t_m, \delta Nt_r)$ is observed; here we have normalized the time $Nt_r$ with the chemical-shift anisotropy parameter $\delta$. To remove effects of $T_1$ relaxation during $t_m$ and of $T_2$ relaxation during $Nt_r$, a reference spectrum $S_0 = S(0, \delta Nt_r)$ is required which has all the same relaxation factors but no motion during $t_m$. This is achieved by simply interchanging the durations of $t_m$ and $t_z$. More generally, the requirement is that in the reference experiment $t_m$ is very short ($t_m < 1$ ms) while the sum $t_m + t_z$ is the same as in the actual CODEX spectrum. The ratio $S(t_m, \delta Nt_r)/S(0, \delta Nt_r)$ can be plotted as a function of $t_m$ and $\delta Nt_r$, to characterize the correlation time and motional geometry, respectively.

**Pure-exchange CODEX**

Often, it is advantageous to subtract the CODEX spectrum $S(t_m, \delta Nt_r)$ from the reference spectrum $S(0, \delta Nt_r)$, to obtain a pure-exchange CODEX spectrum. In this difference spectrum, the signals of nonexchanging components are removed from the spectrum. This can also serve as a useful “filter” for certain signals in a multicomponent system, based on their slow mobility.

Correspondingly, the normalized pure-exchange CODEX intensity is

$$E(t_m, \delta Nt_r) = \frac{\Delta S(t_m, \delta Nt_r)}{S(0, \delta Nt_r)}.$$  

(3)

The nomenclature was chosen in analogy to rotational-echo double resonance (REDOR), where the normalized dephasing provides information on internuclear distances.$^{23}$

**Recoupling of the chemical shift anisotropy**

In order to be able to observe changes in the anisotropic chemical shift during the mixing time $t_m$, the chemical-shift anisotropy, which is averaged to zero by magic-angle spinning, must be reintroduced. This recoupling is achieved by 180° pulses spaced by half a rotation period. The total phase acquired by the magnetization under this pulse sequence after $N/2$ rotation periods before the mixing time is

$$\Phi_1 = \frac{N}{2} \left( \int_0^{t_r/2} \omega_1(t)dt + \int_{t_r/2}^{t_r} \omega_1(t)dt \right).$$  

(4)

The isotropic chemical shift is refocused since the first and second integral cancel. However, for the anisotropic chemical shift, the two integrals add up with equal magnitude. This is shown easily from the fundamental fact that under MAS, the total chemical-shift-anisotropy phase acquired over an undisturbed rotation period vanishes

$$\int_0^{t_r} \omega_n(t)dt = \int_0^{t_r/2} \omega_n(t)dt + \int_{t_r/2}^{t_r} \omega_n(t)dt = 0$$  

(5)

Here, $\omega_n(t)$ is the instantaneous anisotropic chemical shift before ($n=1$) or after ($n=2$) the mixing time. Comparison with Eq. (2) shows that this means that $\Phi_{A,n} = - \Phi_{B,n}$. Inserting Eq. (2) into Eq. (4), we obtain the phase acquired before $t_m$

$$\Phi_1 = - \frac{N}{2} \int_0^{t_r/2} \omega_1(t)dt.$$  

(6)

Correspondingly, from Eqs. (1b), (2), and (5), we find the phase after $t_m$

$$\Phi_2 = \frac{N}{2} \int_0^{t_r/2} \omega_2(t)dt.$$  

(7)

**Analysis using the scaled difference tensor**

The spins evolve for $N/2$ rotor periods with the phase $\Phi_1$ before $t_m$, and for $N/2$ rotor periods with the corresponding phase $\Phi_2$ after $t_m$. The dephasing factor modulating the amplitude of the signal component detected in the CODEX MAS signal is therefore
\[ D(t_m, \delta N_t) = \frac{S(t_m, \delta N_t)}{S(0, \delta N_t)} = \text{Re}(\exp(i(\Phi_1 + \Phi_2))) = \text{Re}(\exp(i||\Phi_2|| - ||\Phi_1||)) = \text{Re}\left( \exp \left( i \int_0^{t/2} (N\omega_2(t) - N\omega_1(t)) dt \right) \right) = \text{Re}(i\Phi^A(\delta N_t, \alpha_R, \beta_R, \gamma_R)). \] (8)

The pointed brackets indicate the powder average. Note that according to Eqs. (3) and (8), the pure-exchange signal is related directly to the dephasing factor, \( E(t_m, \delta N_t) = 1 - D(t_m, \delta N_t) \). In Eq. (8), the phase \( \Phi^A(\delta N_t, \alpha_R, \beta_R, \gamma_R) \) can be considered as the phase acquired within a time of \( t/2 \) under the action of the scaled chemical-shift difference tensor

\[
N\vec{\omega}^A = N(\vec{\omega}_2 - \vec{\omega}_1),
\] (9a)
since

\[
\omega_2 - \omega_1 = \frac{\vec{B}_0^T}{B_0} (\vec{\omega}_2 - \vec{\omega}_1) \frac{\vec{B}_B}{B_0}.
\] (9b)

The “width” (principal-value range) \( N|\omega_{33}^A - \omega_{11}^A| \) of the scaled chemical-shift difference tensor \( N\vec{\omega}^A \) relative to the spinning speed \( \omega_r \) determines whether there is significant dephasing due to the anisotropy, i.e., whether the experiment is sensitive to the principal reorientation. By increasing the number of rotor cycles \( N \), we can enhance the anisotropy to large values \( N|\omega_{33}^A - \omega_{11}^A| \gg \omega_r \).

### Difference tensor for uniaxial interactions

Uniaxial interactions (i.e., with \( \eta = 0 \)) are commonly found, e.g., for dipolar couplings in a spin pair or for the \( ^2\text{H} \) quadrupolar coupling, and are particularly convenient to treat analytically. Therefore, it is instructive to calculate the difference tensor analytically for \( \eta = 0 \). Due to the uniaxiality, the reorientation is fully characterized by a single reorientation (“jump”) angle \( \beta_R \) between the unique principal axis before and after the mixing time. In this specific case of \( \eta = 0 \), the asymmetry parameter of the difference tensor is always \( \eta^A = 1 \) and two of the principal axes make a 45° angle with the bisector between the unique axes before and after the jump, regardless of motional geometry. The third principal axis is perpendicular to the unique axes before and after the jump. The principal values are \( \omega_{33}^A = 0 \) and

\[
\omega_{33}^A - \omega_{11}^A = \frac{9}{2}\delta \left( 3 \cos^2 \left( \frac{\beta_R}{2} \right) + 45° - 1 \right) = \frac{9}{2}\delta \sin \beta_R.
\] (10)

The full-width anisotropy \( |\omega_{33}^A - \omega_{11}^A| \) of the difference tensor, i.e., the range of possible frequency differences, is

\[
|\omega_{33}^A - \omega_{11}^A| = 2\times3/2|\delta| \sin \beta_R = |\omega_{33} - \omega_{11}| 2 \sin \beta_R.
\] (11)

where we have used that \( |\omega_{33} - \omega_{11}| = \frac{3}{2}|\delta| \) for \( \eta = 0 \). This represents a strong linear dependence on the reorientation angle for \( \beta_R < 45° \), which permits relatively easy detection of small-angle motions. It compares favorably with the more common \( (3 \cos^2 \beta_R - 1)/2 \) angle dependence, which is very insensitive to \( \beta_R \) for \( \beta_R < 15° \).

Results equivalent to those presented in this section are contained in the analysis of 2D exchange spectra and time signals by Wefing and Speiss, but their potential for the analysis of stimulated-echo experiments has not been realized. This is partly due to the fact that most \(^2\text{H}\) stimulated-echo experiments have involved impure stimulated echoes of only the sine–sine or cosine–cosine components, where artifacts due to an “anti-echo” obscure the simple behavior found here.

### Nonuniaxial interactions

In the most general case, the reorientation of a principal-axes system must be described in terms of three transformation coordinates. As already indicated above, these are usually chosen as the Euler angles \( \alpha_R, \beta_R, \gamma_R \) between the initial and final principal-axes system (PAS) orientations.

As for \( \eta = 0 \), calculations of the width of the difference tensor \( |\omega_{33}^A - \omega_{11}^A| \) for general values of \( \eta \) show an initial linear dependence on the reorientation angles \( \beta_R \) and \( \varepsilon_R = \alpha_R + \gamma_R \). This can be generally proved by considering the difference tensor for small values of \( \beta_R \) and \( \varepsilon_R \). The reorientations are described by Euler rotation matrices

\[
R(\alpha_R, \beta_R, \gamma_R) = R_z(-\gamma_R) R_x(-\beta_R) R_z(-\alpha_R)
\] for small angles

\[
R_\beta(-\beta_R) = \begin{pmatrix}
\cos \beta_R & 0 & -\sin \beta_R \\
0 & 1 & 0 \\
\sin \beta_R & 0 & \cos \beta_R
\end{pmatrix}
\]

\[
\cong \begin{pmatrix}
1 & 0 & 0 \\
0 & 1 & 0 \\
0 & 0 & 1
\end{pmatrix} + \beta_R \begin{pmatrix}
0 & 0 & -1 \\
0 & 0 & 0 \\
1 & 0 & 0
\end{pmatrix}
\]

\[
= 1 + \beta_R B,
\] (12)

which defines the matrix \( B \) whose only nonvanishing elements are \( B_{13} = B_{31} = -1 \), and similarly

\[
R_\alpha(-\gamma_R) R_\beta(-\alpha_R) \cong 1 + (\alpha_R + \gamma_R) C,
\] (13)

where the only nonvanishing elements of \( C \) are \( C_{12} = -C_{21} = 1 \). Thus, to first order in \( \beta_R \) and \( \varepsilon_R = \alpha_R + \gamma_R \), the difference tensor is

\[
\omega^A = R(\alpha_R, \beta_R, \gamma_R) \omega^{PAS} R(\alpha_R, \beta_R, \gamma_R) - \omega^{PAS}
\]

\[
\cong \beta_R (D \omega^{PAS} + (D \omega^{PAS})^T) + \varepsilon_R (C \omega^{PAS} + (C \omega^{PAS})^T),
\] (14)

where
FIG. 2. Relation between a 2D exchange spectrum and the corresponding 1D difference-tensor spectrum as probed by stimulated-echo, PUREX, and CODEX experiments. The difference spectrum is the projection of the 2D spectrum after \(-45^\circ\) shearing along \(\omega_2\). Equivalently, it is the projection after a rotation of the 2D spectrum by \(45^\circ\) (and an expansion by \(2^{1/2}\)). The close relation between these two procedures is indicated in (a): After the \(-45^\circ\) horizontal shearing, a 26.56°-shearing and a factor of 2 expansion is applied in the vertical direction, both of which do not change the projection onto the horizontal direction. The CODEX NMR, dephasing is the MAS time signal of the difference tensors of all the segments in the sample. (b) Left: 2D exchange pattern for uniaxial interaction \((\eta = 0)\); it is symmetric with respect to the diagonal. The difference-tensor spectrum on the right, which is the projection of the rotated and expanded 2D pattern as shown, has the symmetric lineshape characteristic of \(\eta^2 = 1\). (b) Nonuniaxial interaction (specifically, \(\eta = 0.5\)). Due to the symmetry of the 2D exchange pattern, the difference-tensor spectrum again has \(\eta^2 = 1\). (d) CODEX time signal is asymmetric, \(\eta^2 \neq 1\). Both signal combined, however, produce a symmetric signal. Based on Fourier theorems, this ensures that the CODEX time signal is purely real.

This holds, for instance, if the axis of rotation is perpendicular to a principal axis of the original interaction tensor, as is the case for \(\alpha_R = -\gamma_R\) or \(\pm \alpha_R = 180^\circ \pm \gamma_R\). This includes rotations around a principal axis. Any two-site jump process also fulfills the symmetry condition (Ref. 1, Sec. 7.6).

Figure 2 shows the relation between the 2D exchange pattern \(S_{2D}(\omega_1, \omega_2)\) and the 1D chemical-shift difference spectrum \(S(\omega_1 - \omega_2)\). \(S(\omega_1 - \omega_2)\) is seen to be the (integral) projection of the 2D exchange pattern rotated by \(45^\circ\) and expanded by a factor of \(2\). The matrix describing the transformation from \((\omega_1, \omega_2)\) to \((\omega_1 + \omega_2, \omega_2 - \omega_1)\) is indeed recognized as essentially a \(45^\circ\) rotation

\[
\begin{pmatrix}
1 & 1 \\
-1 & 1
\end{pmatrix}
\begin{pmatrix}
\omega_1 \\
\omega_2
\end{pmatrix} = \begin{pmatrix}
\omega_1 + \omega_2 \\
\omega_2 - \omega_1
\end{pmatrix}
\]

and

\[
\begin{pmatrix}
1 & 1 \\
-1 & 1
\end{pmatrix} = \sqrt{2} \begin{pmatrix}
1 \\
1
\end{pmatrix}
\]


\[
\Delta \omega = \omega_2 - \omega_1
\]

The transformation of one coordinate to the difference frequency \(\omega_1 - \omega_2\) is necessary, while the transformation of the vertical coordinate is somewhat arbitrary; the transformation to \(\omega_1 + \omega_2\) chosen here has the merit of reproducing the 2D exchange pattern undistorted (except for the \(\sqrt{2}\)-expansion). A similar procedure, characterized as a projection onto the anti-diagonal, has been discussed by Wefing and Spiess,\(^7\) who derived it based on the projection—cross-section theorem of two-dimensional Fourier transformation.

As indicated at the top of the figure, the transformation can also be viewed as a series of two shearing procedures and a vertical expansion by a factor of 2. In this way, it is clear that the horizontal dimension undergoes only a shear-

\[
D = R_x(-\gamma_R)BR_x(-\alpha_R) = \begin{pmatrix}
0 & 0 & -\cos \gamma_R \\
0 & 0 & \sin \gamma_R \\
\cos \alpha_R & \sin \alpha_R & 0
\end{pmatrix}
\]

Since \(\beta_R\) and \(\epsilon_R = \alpha_R + \gamma_R\) simply multiply the matrices, they will also multiply the principal values of the matrices, so that the eigenvalues of \(\omega^D\) depend linearly on these reorientation angles. (In contrast, the principal values of the sum tensor \(\omega^R + \omega^A\) depend on \(\beta_R\) and \(\epsilon_R\), due to the nonlinearity of the characteristic polynomial and the fact that \(D\) and \(C\) have vanishing diagonal elements.

**Difference tensor and 2D-exchange spectrum**

The spectrum \(S(\omega_2 - \omega_1)\) of the difference tensor is related to the 2D exchange spectrum \(S_{2D}(\omega_1, \omega_2)\), whose dependence on the reorientation angles has been studied in some detail.\(^1\) With \(\Delta \omega = \omega_2 - \omega_1\), the spectrum of the difference frequency can be expressed as

\[
S(\Delta \omega) = \int_{-\delta}^{\delta} S_{2D}(\omega_1, \Delta \omega + \omega_1)d\omega_1,
\]

This immediately shows that \(S(\Delta \omega)\) is symmetric with \(S(\Delta \omega) = S(-\Delta \omega)\) if \(S_{2D}(\omega_1, \omega_2) = S_{2D}(\omega_2, \omega_1)\). This is valuable since \(S(\Delta \omega) = S(-\Delta \omega)\) can hold only if the asymmetry parameter of the difference tensor \(\eta^A = 1\); generally, \(\eta^A\) can differ significantly from 1 [for instance, see Fig. 2(d)]. So \(\eta^A = 1\) applies in all cases where the corresponding 2D exchange spectrum of the (forward) jump is symmetric.
ing by 45°, which transforms from \( \omega_2 \) to \( \omega_2 - \omega_1 \). The two other transformation steps affect only the vertical dimension.

The dependence of \( \delta^\Delta \) on the reorientation angle can then be determined by investigating the largest frequency distance from the diagonal in the 2D exchange pattern. For instance, for a rotation around the \( \omega_{33} \) axis by an angle \( \beta_R \), the most extended part of the exchange pattern is an ellipse inscribed in the square with corners at \((\omega_{11}, \omega_{11})\) and \((\omega_{22}, \omega_{22})\). The axis of the ellipse perpendicular to the diagonal has a length \( v \Delta \omega_{11} - \omega_{22} \) \( 2 \sin \beta_R \). On this basis, we find that \( \omega_{33}^\Delta = 0 \) and
\[
|\omega_{33}^\Delta - \omega_{11}| = |\omega_{11} - \omega_{22}| 2 \sin \beta_R ,
\]
in complete analogy to Eq. (11). Corresponding results are found for rotations around the other principal axes.

**Purely real modulation factor**

In Eq. (8), we assumed that the modulation factor is purely real. This can be proven as follows: In detailed balance ("dynamic equilibrium"), both forward and return jumps must occur equally often. The frequency \( \omega_1 \) in the forward jump is equal to the frequency \( \omega_2 \) in the return jump, and the frequency \( \omega_2 \) in the forward jump is equal to the frequency \( \omega_1 \) in the return jump. Indicating the forward jump by a superscript \( f \) and the return jump by \( r \), we thus find
\[
\Phi_f = -\frac{N}{2} \int_0^{t_r/2} \omega_f(t) dt = -\frac{N}{2} \int_0^{t_f/2} \omega_f(t) dt = -\Phi_r
\]
and
\[
\Phi_f = -\Phi_r .
\]
(19)
The observed dephasing is, therefore, the average of \( \langle \exp(i(\Phi_f + \Phi_r)) \rangle \) and \( \langle \exp(i(\Phi_f - \Phi_r)) \rangle = \langle \exp(-i(\Phi_f + \Phi_r)) \rangle \)
\[
D(t_m, \delta N t_r) = \frac{1}{2} \langle \exp(i(\Phi_f + \Phi_r)) \rangle

+ \exp(-i(\Phi_f + \Phi_r))

= \langle \cos(\Phi_f + \Phi_r) \rangle + \text{Re} \langle \exp(i(\Phi_f + \Phi_r)) \rangle ,
\]
(20)
as written above in Eq. (8). As a result, the dephasing is a real factor and does not introduce a phase distortion of the MAS centerband, even without a z-filter before detection.

**Speed independence and master curves**

In an alternative view, traditionally taken in REDOR, rather than considering \( N \) as scaling the difference tensor relative to the spinning speed, it is considered that \( N t_r \) is the total time of anisotropic evolution. Then it is found that the dephasing is independent of the spinning speed and only depends on the total time \( N t_r \).
\[
\Phi^\Delta = N \left( \Phi_f \frac{t_r}{2} - \Phi_r \frac{t_r}{2} \right)

= N \frac{\delta}{\omega_r} \left( \chi_1 \frac{t_r}{2} - \chi_2 \frac{t_r}{2} \right) = N t_r \frac{\delta}{2 \pi} \left( \chi_1 \frac{t_r}{2} - \chi_2 \frac{t_r}{2} \right) ,
\]
(21)
where
\[
\chi_n \left( \frac{t_r}{2} \right) = (\bar{S}_1(\alpha_n, \beta_n, \gamma_n) - \frac{1}{2} \bar{S}_2(\alpha_n, \beta_n, \gamma_n))/\delta ,
\]
(22)
with the coefficients \( \bar{S}_1(\alpha_n, \beta_n, \gamma_n) \) and \( \bar{S}_2(\alpha_n, \beta_n, \gamma_n) \) as given in Ref. 1 in terms of the Euler angles \( (\alpha_n, \beta_n, \gamma_n) \) of principal-axes system \( n = 1 \) or 2 with respect to the rotor-fixed system. For instance, for \( \eta = 0 \), one has
\[
\chi_n(t_r/2) = (1/2)^{1/2} \sin 2 \beta_n \sin \gamma_n - 1/4 \sin^2 \beta_n \sin 2 \gamma_n .
\]
(23)
Due to the \( \omega_\perp \)-independence of the phase difference in Eq. (21), the CODEX pulse sequence works up to very high spinning speeds. Only when the pulse-length is more than 10% of the rotation period and the total number of pulses becomes large, a significant deterioration of the performance is expected. Spinning-speed-independent master curves of the dephasing or exchange signals can be plotted as a function of \( \delta N t_r \) for specific reorientation angles or reorientation-angle distributions.

Taking into account the results of the previous section, it is easy to see that the dephasing curves for a uniaxial interaction (\( \eta = 0 \)) can be collapsed onto one master curve \( E(t_m, \phi) \) if plotted as a function of the phase variable
\[
\phi = \delta N t_r, 1.5 \sin \beta_R .
\]
(24)
In other words, two cases that produce the same \( \phi \) value will have the same exchange intensity, even if their individual \( \delta \), \( N t_r \), or \( \beta_R \) differ. Figure 3 shows this master curve. For \( \eta \neq 0 \), the shape of the \( \delta N t_r \)-dependence of the \( E(t_m, \delta N t_r) \) curves will depend on several reorientation angles, and a general master-curve cannot be constructed.

**Reorientation-angle distribution**

In the case of a uniaxial NMR interaction, the information content of an exchange experiment at a given mixing time \( t_m \) can be summarized in terms of the reorientation-angle distribution \( R(\beta_R, t_m) \). The dephasing or pure-exchange intensity curves are simply \( R(\beta_R, t_m) \)-weighted superpositions of the curves for specific \( \beta_R \) values. For instance, for the two-site jump in DMS

**FIG. 3. Master curve for the dependence of the pure-exchange CODEX intensity on the normalized dephasing time \( \delta N t_r \), for \( \eta = 0 \). Experimental data for DMS are also shown, on the scale given on the right. In fact, they are the average of the curves for \( \beta_R = 0^\circ \) and \( \beta_R = 105^\circ \) (see text).**
\[ R(\beta_R|t_m) = 0.5\{1 - \exp(-t_m/\tau_c)\} \delta(\beta_R - 0^\circ) \\
+ 0.5 \exp(-t_m/\tau_c) \delta(\beta_R - 108^\circ), \tag{25} \]

and the pure-exchange CODEX intensity curve is
\[
E(t_m, \delta N t_r) = 0.5\{1 - \exp(-t_m/\tau_c)\} \epsilon(\delta N t_r; 0^\circ) \\
+ 0.5 \exp(-t_m/\tau_c) \epsilon(\delta N t_r; 108^\circ) \\
= 0.5 \exp(-t_m/\tau_c) \epsilon(\delta N t_r; 108^\circ), \tag{26} \]

where \(\epsilon(\delta N t_r; \beta_R)\) is the normalized pure-exchange intensity for the reorientation angle \(\beta_R\), including a powder average. Relation (26) was used in plotting the DMS data onto the master curve in Fig. 3.

More generally, the relation between the exchange intensity and the reorientation angle distribution can be written as \[\text{ref.}\] 
\[
E(t_m, \delta N t_r) = \int_0^{90^\circ} R(\beta_R|t_m) \epsilon(\delta N t_r; \beta_R) d\beta_R. \tag{27} \]

The integration weighting by \[\sin\beta_R\] is contained in \(R(\beta_R|t_m)\). Note that while all \(\epsilon(\delta N t_r; \beta_R)\) have the same shape except for the \(\sin\beta_R\)-scaling of their x axes, their superposition \(E(t_m, \delta N t_r)\) in general has a different shape. (To visualize this, consider that similarly the sum of Gaussian bell curves of different widths, even when they have the same center, is not a Gaussian.)

### Number of accessible orientations, fraction of mobile segments

In complex systems such as amorphous polymers, distributions of correlation times, and motional amplitudes often result in a distribution of exchange behavior. It is often a good approximation to analyze such situations in terms of a fraction \(f_m\) of significantly exchanging segments, and a component \((1 - f_m)\) that does not exchange significantly, so that it can be treated as immobile. The case of a homogeneous system in which all equivalent segments are moving similarly, as is true for most crystals, is obtained by setting \(f_m = 1\).

Information about the fraction \(f_m\) and the number \(M\) of equivalent orientational sites accessible to the mobile segments is obtained from the final exchange intensity \(E_\infty\). Since a fraction \(1/M\) of the mobile species will reside in the originally selected site, we have
\[
E_\infty = E(t_m \gg \tau_c, \delta N t_r \gg 1) = \left(1 - \frac{1}{M}\right) f_m = \frac{M - 1}{M} f_m. \tag{28} \]

For \(f_m = 1\), the minimum \(E_\infty\) is 1/2, obtained for \(M = 2\). For diffusive reorientations of all segments, \(M \gg 1\) and \(E_\infty \approx 1\). However, if the diffusion is restricted, very large phases \(\delta N t_r\) will be required to reach the final state.

If \(E_\infty < 1/2\), the fraction of mobile sites must be smaller than unity. In fact, Eq. (28) directly yields rigorous limits for \(f_m\) in terms of \(E_\infty\)
\[
E_\infty < f_m \leq 2E_\infty. \tag{29} \]

### Four-time CODEX

From \(E_\infty\) alone, \(f_m\) and \(M\) cannot be determined unambiguously. Fortunately, the number of sites \(M\) can be determined in a four-time CODEX experiment. It is produced by concatenating two CODEX pulse sequences. Using the matched pair of pulse sequences shown in Fig. 4, we select the mobile groups in a regular PUREX MAS difference experiment with mixing time \(t_{ma}\), and then characterize their exchange behavior, with a final value of \(1/M\), selectively in another CODEX MAS section by changing the mixing time \(t_{mc}\).

Effects of \(T_1\) relaxation decay can be eliminated by keeping the total z time \(t_{mc} + t_z\) constant. Therefore, no difference is required in the second half of the experiment.

We consider the normalized signal as a function of the mixing times \(t_{ma}\) and \(t_{mc}\)
\[
D_4(t_{ma}, t_{mc}) = \frac{S(t_{ma}, t_{mc})}{S(0,0)}.
\]

Obviously, the signal also depends on the dephasing times \(t_1 + t_2 = N_{12f_2}\) and \(t_3 + t_4 = N_{34f_2}\). However, for the sake of brevity we will not write these arguments explicitly. In fact, it will be seen that the final intensity ratio does not depend on \(t_1 + t_2\). Initially, we will assume that \(\delta N_{34f_2} > 1\).

In the reference experiment with short \(t_{ma}\), i.e., without selection, the signal has the same decay as in a regular CODEX experiment, only scaled down by 0.5. For sake of clarity and since only signal ratios will be considered in the analysis, we will normalize this prefactor away. Thus, the reference signal without selection
\[
D_4(t_{ma} = 0, t_{mc} = 0) = 1, \tag{30} \]

at short \(t_{mc}\) and
\[
D_4(0, \infty) = (1 - f_m) + f_m 1/M, \tag{31} \]

at long \(t_{mc}\). CODEX selection during \(N_{12f_2}\) and around \(t_{ma}\) will reduce the mobile-segment signal by a factor
\[
r(0, \delta N_{12f_2}) = r(t_{ma}; 0) = 1 \tag{32} \]

and
\[
r(t_{ma} \gg \tau_c, \delta N_{12f_2} \gg 1) = 1/M, \tag{33} \]

for complete dephasing. The immobile fraction \((1 - f_m)\) remains unaffected. Thus, the signal at short \(t_{mc}\) is
\[
D_4(t_{ma} = 0) = (1 - f_m) + r(t_{ma}) f_m 1/M. \tag{34} \]
where in $r(t_{ma})$ we have dropped the $\delta N_{3,dt}$-dependence. At long $t_{mc}$ and large dephasing angle $\delta t_3 + \delta t_4 = \delta N_{3,dt}$ around it, the mobile components dephase to a $1/M$ fraction, so the remaining signal is

$$D_4(t_{ma}, \infty) = (1 - f_m) + r(t_{ma})f_m1/M^2.$$  

(35)

The intensity of the segments exchanging during $t_{ma}$ (i.e., the mobile fraction) is

$$ED_4(t_{ma}, \infty) = D_4(0,0) - D_4(t_{ma},0) = f_m(1 - r/M),$$  

(36)

at short $t_{mc}$ and

$$ED_4(t_{ma}, \infty) = D_4(0,0) - D_4(t_{ma}, \infty) = (1/M)f_m(1 - r/M)$$  

(37)

at long $t_{mc}$. The nomenclature of “$ED$” is used to indicate that the signal is a pure-exchange signal ($E$) with respect to $t_{ma}$, but a dephasing signal ($D$) with respect to $t_{mc}$. As predicted from the simpler argument above, the difference signal decays by a factor of

$$ED_4(t_{ma}, \infty)/ED_4(t_{ma},0) = 1/M.$$  

(38)

From the number $M$ of accessible orientations thus obtained, we can also back calculate the fraction $f_m$ of mobile groups, rewriting Eq. (28)

$$f_m = E_4M/(M - 1).$$  

(39)

The result of Eq. (38) is independent of the $t_{ma}$ and $N_{1,2t_f}$. What happens if either of these times is too short? Then, the exchange intensities $ED_4(t_{ma}, \infty)$ and $ED_4(t_{ma},0)$ are both small and much signal averaging is required.

To obtain Eq. (35), it was assumed that the dephasing around $t_{mc}$ is complete. But possibly, the dephasing angle $\delta t_3 + \delta t_4 = \delta N_{3,dt}$ was not large enough, producing incomplete dephasing of the mobile fraction, to $r(t_{mc}, \delta N_{3,dt}) > 1/M$. Then

$$D_4(t_{ma}, \infty) = (1 - f_m) + r(t_{ma})f_m1/M r(t_{mc}, \delta N_{3,dt}).$$  

(40)

The difference intensities are now

$$ED_4(t_{ma},0) = f_m(1 - r(t_{ma}))/M,$$  

(41)

$$ED_4(t_{ma}, \infty) = r(t_{mc}, \delta N_{3,dt})f_m(1 - r(t_{ma}))/M,$$  

(42)

and their ratio is

$$ED_4(t_{ma}, \infty)/ED_4(t_{ma},0) = r(t_{mc}, \delta N_{3,dt}).$$  

(43)

For $\delta N_{3,dt} \gg 1$, based on Eq. (33) the general Eq. (43) reproduces the special case of Eq. (38).

The shape of $r(t_{mc}, \delta N_{t_f})$ can be extracted from regular (two-time) CODEX, whose dephasing behavior is given simply by

$$D(t_{mc}, \delta N_{t_f}) = (1 - f_m) + f_m r(t_{mc}, \delta N_{t_f}).$$  

(44)

One obtains

$$r(t_{mc}, \delta N_{t_f}) = \{D(t_{mc}, \delta N_{t_f}) - (1 - f_m)f_m\}/f_m.$$  

(45)

Thus, even if only one or a few points of $ED_4(t_{ma}, \infty)/ED_4(t_{ma},0)$ have been measured, the full curve can be predicted, by fitting the CODEX dephasing curve $D(t_{mc}, \delta N_{t_f})$, shifted and scaled according to Eq. (41), by simply varying $f_m$. The number $M$ of sites is obtained from the long-time value of $r(t_{mc}, \delta N_{t_f})$, which is $1/M$ according to Eq. (33).

The case of “immobile” and “mobile” segments considered here can be generalized to describe other situations. To a good approximation, sites that do not exchange significantly within $t_{ma}$, given the $N_{1,2t_f}$ dephasing period, can be treated as effectively immobile (if others exchange significantly under these conditions). Such a lack of exchange could be due to a correlation time $\tau_c \gg t_{ma}$, as is the case for the slow-moving segments selected in amorphous materials above $T_g$ by the reduced 4D experiment.12,13 Alternatively, it could also arise from a small angular amplitude that leads to negligible dephasing during $N_{1,2t_f}$. The data for the quaternary carbon of PMMA shown below are consistent with the latter description: Some backbone segments in PMMA move with relatively large ($\pm 10^0$), others with very small ($\pm 4^0$) amplitudes.

### Determination of chemical-shift parameters

For a quantitative or semiquantitative evaluation of the CODEX MAS dephasing curves in terms of the motional amplitude, the chemical-shift anisotropy parameter $\delta$ must be known. It can be characterized using a pulse sequence which resembles the CODEX sequence closely, except that the $90^0 - t_{mc} - 90^0 - (\alpha)$ block is replaced by a $180^0$ pulse, which gives $S_{180^0}$, or by no pulse, to give $S_0$. This yields a relative dephasing signal of

$$S_{180^0}(N_{t_f})/S_0(N_{t_f}) = \left\langle \exp\left\{i2N\int_0^{r/2} \omega(t)dt\right\}\right\rangle = \left\langle \exp\left\{i2N\Phi\left(\frac{r}{2}\right)\right\}\right\rangle = \left\langle \cos(2N\delta\frac{t_f}{2}\cos(\frac{r}{2}))\right\rangle = \left\langle \cos(2N\delta(S_2(\alpha, \beta, \gamma, \delta, \eta))/2\pi)\right\rangle.$$  

(46)

After powder averaging over $\alpha$, $\beta$, and $\gamma$, this decay curve depends only on the chemical-shift anisotropy parameter $\delta$ and the asymmetry parameter $\eta$, which can be determined by least-squares fitting.

Alternatively, the chemical shift anisotropy parameters can also be measured using the original CODEX pulse sequence with the phase cycling slightly modified. Acquiring only the sine—sine component of the magnetization in the CODEX pulse sequence and making the mixing time short enough that no motion occurs, the modulation in the CODEX signal amplitude is
The duration of the \( z \) filter is incremented in \( K \) steps of \( t/K \), \( k = 0, \ldots, K - 1 \), and the signals are added during the experiment. Heuristically, this can be considered as a discrete approximation of the integral over the PAS orientation angle \( \gamma \) that is required for sideband suppression in TOSS for one-dimensional experiments. Without approximation, the resulting side-band intensities are calculated, with \( F_N(\alpha_2, \beta_2) \) defined as in Ref. 1

\[
\bar{I}_N(\alpha_2, \beta_2, \gamma_2) = \frac{d(\alpha_2, \beta_2, \gamma_2)}{N} F_N(\alpha_2, \beta_2)
\]

\[
\times \sum_{k=0}^{K-1} \exp \left( i \frac{N}{K} \frac{2 \pi}{K} \right) \delta_{m,K,N} \ 	ext{with } m \text{ integer.} \tag{51}
\]

The result means that for \( K \) increments, only sidebands of order \( N = mK \) will be observed. In other words, the centerband \((N = 0)\) is always present, while the sidebands out to the \( \pm K \)th sidebands are completely suppressed. Since the sideband intensities decrease rapidly with increasing order, usually \( K = 5 \) increments are sufficient. The incrementation does not reduce the sensitivity in any way. It only increases the minimum number of scans per experiment to \( K^*64 \), with a phase cycle that requires 64 scans.

The simple approach of sideband suppression of TOSS with \( \gamma \)-summation presented here can be used in any two-dimensional MAS experiment to achieve sideband-free detection.

**Implementation of the CODEX pulse sequence**

Due to the simplicity of the CODEX pulse sequence, the implementation of the technique is mostly straightforward. However, since the method relies on measuring signal amplitudes rather than frequency positions, some care should be taken to avoid artifacts.

Rotor synchronization is an important detail in the CODEX implementation. Synchronization errors on the order of 4 \( \mu \)s can produce a significant effect in the CODEX experiment. Consistent triggering should be ensured, for instance by making sure that the trigger mark on the rotor is sharp.

Effects of pulse imperfections and \( T_1 \) relaxation are minimized or eliminated using the phase cycling summarized in Table I. In order to obtain the complete phase cycling, the phase angle \( \phi \) must be incremented in 90° steps, which results in a total of 64 scans per cycle. Elimination of artifacts from \( T_1 \)-relaxation during \( t_m \) is accomplished by inverting the phases of the pulses \( c \) and of the receiver as shown, for instance, in rows 1 and 5 of Table I. Suppression of direct-polarization artifacts is performed by inverting the phase of the \( ^1H \) 90° pulse and the pulse \( f \), as indicated in the first row by the symbol “+.” Implementation of perfect quadrature detection (CYCLOPS) is performed, simultaneously, by
changing the pulses phases $a, c, d, e, f$ and the receiver phase as indicated above. A $\pi/8$ scheme$^{28}$ to avoid imperfections in the $180^\circ$ pulses is also performed as indicated in column $c$. The phase cycling for the CSA measurements using CODEX can be obtained easily by separately considering the rows which lead to $\sin \Phi_1 \sin \Phi_2$ and to $\cos \Phi_1 \cos \Phi_2$ components in Table I.

To eliminate effects of spectrometer drift, measurements are alternated between CODEX and reference signal approximately every five minutes.

The four-time CODEX phase cycling is shown in Table II. The same compensation scheme as in CODEX is performed for the first and second part of the sequence. The symbols $\overline{e}$ and $\overline{f}$ in Fig. 4 mean inverted phases $e$ and $f$ in Table II.

## RESULTS

### Chemical-shift anisotropies

Figure 5 shows the determination or confirmation of the chemical-shift anisotropy parameters for six aliphatic residues, in DMS, iPP, and PMMA. The close spacing of the points along the time axis was achieved by measurements at various spinning speeds, ranging from 3 to 5.5 kHz (up to 10 kHz for the CH$_2$ group of PMMA). The small scatter of the points from measurements at different spinning speeds is an indication of the reliability of the technique. The curves are fits with the anisotropies $\delta$ and asymmetry parameters $\eta$ as given in the figure; the agreement with the literature values,$^{29,30}$ which are given in brackets, is good or satisfactory.

### CODEX as a dynamic filter

The use of the CODEX experiment as a filter for slowly moving segments is shown in Fig. 6. Figure 6(a) presents the relatively trivial example of a mixture of iPB and DMS at 293 K. In the CODEX spectrum with a 20 ms mixing time, as expected only the DMS signal is observed; DMS undergoes two-site jumps with a correlation time of a few milliseconds at this temperature,$^{31}$ while iPB exhibits no motions with correlation times on the millisecond time scale. The suppression of the immobile components is seen to be excellent.

In Fig. 6(b), selection of slow-moving segments in the amorphous domains of iPB near the glass transition temperature is demonstrated. While the reference spectrum (top) is dominated by the sharp signal of the crystallites, the integral intensity in the pure-exchange CODEX spectrum (bottom) is mostly due to broad signals that can be assigned to the conformationally disordered amorphous regions. In the reference spectrum, this signal represent a hardly detectable broad background.

### Remarks

Table II. Phase cycling for four-time CODEX. The symbol $\overline{\cdot}$ indicates that the phase is the same as in the previous line. The phase angles $\phi$ and $\varphi$ are incremented independently in $90^\circ$ and $180^\circ$ steps, resulting in 128 scans per cycle.

<table>
<thead>
<tr>
<th>1H CP</th>
<th>180°</th>
<th>store</th>
<th>read</th>
<th>store</th>
<th>read</th>
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<td>$+y + \phi$</td>
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strated by their intensity ratios: While the central CH peak is nearly three times higher than the methylene signals in the reference spectrum, it is of nearly equal height as the left CH2 peak in the pure-exchange CODEX spectrum. This can be explained by the smaller chemical-shift anisotropy of the CH site, which results in a less efficient signal generation in the CODEX difference spectrum. The sharp peaks can probably be assigned to segments on the crystalline side of the crystalline–amorphous interface. These have a conformation similar as found in the core of the crystallite, but experience some of the dynamics occurring in the amorphous regions. Further investigations of these complex dynamics by PUREX and CODEX are in progress.

**CODEX studies of backbone dynamics in iPP and PMMA**

In Fig. 7(a), the $\delta N t_r$ time dependence of the iPP and PMMA backbone CODEX signals is plotted. The faster the rise of the intensity with $\delta N t_r$, the larger the reorientation amplitude of the chemical shift tensor. The plot immediately reveals that the CH and CH2 segments in the crystallites of iPP are undergoing large-amplitude motions at 365 K. For PMMA, with its slower rises, it strongly suggests that the amplitudes of the slow backbone motions at 293 K are significantly smaller. Both conclusions are confirmed by simulations, plotted as curves through the data. The iPP data can be fit well using the model of helical jumps between three sites, which has been proven by 2D exchange spectra and the CODEX equilibration at $E_\infty \approx 2/3$. The distribution of rotation angles $\psi$ around the chain axis used to produce the fit curve is shown in Fig. 7(c). The widths estimated here are somewhat smaller than those derived from 2D exchange NMR on a 13C-labeled PMMA. The reasons for this discrepancy are currently under investigation.

The motion in PMMA is associated with the $\beta$-relaxation of PMMA, which is the main reason for the reduced brittleness of this glassy polymer at ambient and elevated temperatures. Previously, detailed NMR studies of the $\beta$-relaxation dynamics in PMMA were possible only after expensive, laborious 13C- and 2H-labeling combined with extensive 2D, 3D, and MESSAGE exchange NMR studies. From the CODEX data in Fig. 7, the root-mean-square amplitude of the backbone motion in PMMA is estimated as 10°. The distribution of rotation angles $\psi$ around the chain axis used to produce the fit curve is shown in Fig. 7(c). The widths estimated here are somewhat smaller than those derived from 2D exchange NMR on a 13C-labeled PMMA. The reasons for this discrepancy are currently under investigation.

**Four-time CODEX**

The CODEX data shown in Ref. 15 [see also Fig. 8(b)] confirmed that the sidegroups in PMMA undergo large-amplitude motions. It was found that the final exchange intensity for the side-groups signals of PMMA is only $E_\infty$. The motion in PMMA is associated with the $\beta$-relaxation of PMMA, which is the main reason for the reduced brittleness of this glassy polymer at ambient and elevated temperatures. Previously, detailed NMR studies of the $\beta$-relaxation dynamics in PMMA were possible only after expensive, laborious 13C- and 2H-labeling combined with extensive 2D, 3D, and MESSAGE exchange NMR studies. From the CODEX data in Fig. 7, the root-mean-square amplitude of the backbone motion in PMMA is estimated as 10°. The distribution of rotation angles $\psi$ around the chain axis used to produce the fit curve is shown in Fig. 7(c). The widths estimated here are somewhat smaller than those derived from 2D exchange NMR on a 13C-labeled PMMA. The reasons for this discrepancy are currently under investigation.

**FIG. 5.** Use of the CODEX experiment with short $t_m$ and modified phase cycle for the determination of chemical-shift anisotropy parameters (see text for details). CH2 groups in: (a) DMS, (b) iPP; CH groups in: (c) PMMA. (d) iPP; a quaternary C in (e) PMMA; and a CH group in (f) iPP. The parameters of the fit curves are given in the figure, with the corresponding literature values (Refs. 29 and 30) in brackets.

**FIG. 6.** Pure-exchange CODEX spectra for mixing times as indicated in the figure. Scaled reference spectra are shown at the top. (a) DMS mixed with iPB. Spinning speed: 6 kHz; $N t_r = 667$ μs; $T = 293$ K. (b) iPP at 260 K. The signals of the amorphous regions, otherwise unobservable under the high crystalline peaks, are selectively detected.
groups. To determine \( f_m \) corresponds to a fraction of the crystallites of iPP, measured at 365 K, \( t_m = 1 \) s, \( \nu_r = 4.5 \) kHz. Fit curves: Helical jumps. Open symbols: PMMA at 293 K, \( t_m = 500 \) ms, \( \nu_r = 5.5 \) kHz. CH2 group: squares; quaternary carbon: triangles. (b) Rotation-angle distribution (around the chain axis) used for producing the fit curves for the iPP data, based on helical jumps by 120° angles. The final state, where the intensity at a rotation angle of 120° is twice that at zero, has not yet been reached. The full mixing time dependence, with the expected equilibrium value reached after 20 s, is shown in Ref. 15. (c) Rotation-angle distribution that yielded the fit curve for the PMMA data.

\[ \frac{1}{\tau_c} = \frac{1}{\tau_m} + \frac{1}{\tau_{mb}} + \frac{1}{\tau_{mc}} + \frac{1}{\tau_z} \]

As \( \Delta N = 8 \pi \). According to Eq. (29), this corresponds to a fraction \( f_m \) of between 23% and 46% mobile side groups. To determine \( f_m \) and the number \( M \) of different orientational sites in the side-group motion, we performed a four-time CODEX experiment on unlabeled PMMA. The resulting data are shown in Fig. 8.

In Fig. 8(a), we show a reference spectrum without dephasing but with a total z storage time of 1 s, which is equal to the sum of \( t_{ma} + t_{mb} + t_{mc} + t_z \) in the four-time CODEX experiments. The dephasing and rephasing times in the pulse sequence of Fig. 4 were set to \( t_1 = t_2 = t_3 = t_4 = 545 \) \( \mu \)s, yielding \( \Delta N = \delta(t_1 + t_2) = \delta(t_3 + t_4) = 15 \pi \) for the COO site. This time provides sensitivity to the large-amplitude side group motions that we would like to characterize, while it is short enough that small-amplitude segmental rotations affect the signal only little. Four spectra were measured, with \( t_{ma}, t_{mb} \) of (1 ms, 1 ms); (500 ms, 1 ms); (500 ms, 1 ms); and (500 ms, 500 ms). The difference of the first two yields the spectrum of the mobile segments without exchange during \( t_{mc} \), which is shown in Fig. 8(b). The difference of the third and fourth spectrum, which is shown in Fig. 8(c), represents the \( t_m = 500 \) ms CODEX spectrum of the mobile segments. Compared to the reference with \( t_m = 1 \) ms in Fig. 8(c), the signal intensity is strongly reduced. For the COO signal, the dephased intensity is 0.48±0.17 of the reference. This agrees with the ratio of 0.5 expected for a two-site jump. Two-site jumps were established previously in a reduced 3D spectrum of \(^1^3\)C-labeled PMMA.

To demonstrate that the dephasing for the selected mobile segments is much more pronounced than for the overall sample, Fig. 9 compares the decay data \( D(t_m, \Delta N) \) found in the two-time CODEX experiment with the four-time CODEX data \( E_{D_t}(t_{ma}, t_{mc})/E_{D_0}(t_{ma}, 0) \) with the same \( \Delta N \). At a mixing time of 500 ms, the two-time CODEX data have essentially equilibrated at 0.75; the selected mobile units in the four-time CODEX data, at the same time, have decayed to 0.48.

**DISCUSSION**

**Range of correlation times**

The rates for which dephasing is observed in CODEX NMR range from \( \sim 0.1/s \) to \( \sim 5,000/s \). Very slow motions, which require long mixing times, can be studied better by CODEX than by other NMR techniques. The high sensitivity and good dynamic range of CODEX NMR enables detection of the \( \sim 10\% \) exchange intensity that arises already within \( t_m = 0.1 \tau_c \), and makes it less sensitive to sensitivity reduction by \( \tau_1 \)-relaxation and the increased experiment duration.

**FIG. 7.** Normalized pure-exchange CODEX intensities \( E(t_m, \Delta N) \) plotted as a function of \( \Delta N \). Filled symbols: CH and CH2 signals from the crystallites of iPP, measured at 365 K, \( t_m = 1 \) s, \( \nu_r = 4.5 \) kHz. Fit curves: Helical jumps. Open symbols: PMMA at 293 K, \( t_m = 500 \) ms, \( \nu_r = 5.5 \) kHz. CH2 group: squares; quaternary carbon: triangles. (b) Rotation-angle distribution (around the chain axis) used for producing the fit curves for the iPP data, based on helical jumps by 120° angles. The final state, where the intensity at a rotation angle of 120° is twice that at zero, has not yet been reached. The full mixing time dependence, with the expected equilibrium value reached after 20 s, is shown in Ref. 15. (c) Rotation-angle distribution that yielded the fit curve for the PMMA data.

**FIG. 8.** Four-time CODEX measurement of the number of orientational sites in PMMA, at \( T = 293 \) K, \( \nu_r = 5.5 \) kHz, with \( \delta(t_1 + t_2) = \delta(t_3 + t_4) = 15 \pi \), \( t_{ma} + t_{mb} = 501 \) ms. (a) Reference spectrum; the CH2 signal is suppressed by relaxation during a 1 s z filter. (b) Selective spectrum of mobile segments, without dephasing \( t_{ma} = 1 \) ms. (c) Selective spectrum of mobile segments, after \( t_{ma} = 500 \) ms dephasing. Compared to (b), stronger dephasing of the selected mobile groups is observed.

**FIG. 9.** Mixing-time dependent dephasing intensities \( D(t_m, \Delta N) \) of the COO groups in PMMA obtained by (two-time) CODEX compared with four-time CODEX \( E_{D_t}(t_{ma}, t_{mc})/E_{D_0}(t_{ma}, 0) \) at the same \( \Delta N \). The selected mobile groups exhibit dephasing to the value of 1/2 expected for two-site jumps.
when the mixing time exceeds the recycle delay. Exchange due to dipolar spin diffusion, which competes with motional exchange, is the main limitation for detecting very slow motions. Even in this aspect, CODEX is often superior; in systems that previously required $^{13}$C enrichment for achieving sufficient sensitivity, e.g., benzene undergoing jumps and diffusion in zeolites, the superior sensitivity of CODEX will permit a reduction in the isotopic labeling level, or even measurements on $^{13}$C in natural abundance. This will result in a slow-down of spin diffusion and enable the study of slower motions.

In fact, CODEX at very high spinning speeds may potentially quench $^{13}$C spin diffusion, by averaging away all relevant dipolar couplings. This possibility has not been explored before, since CODEX is the first technique that can measure slow reorientations under fast MAS.

The main limitation of the CODEX experiment may be that very fast motions are not detected. At high rates, a clean exchange experiment requires that no motion occurs during the de- and rephasing periods $N_{tr}$ (i.e., $k<1000/s$). Nevertheless, even with frequency changes during those periods, motional dephasing will happen. Its strong dependence on the dephasing time and near independence from the mixing time will identify its high rate. The ultimate high-rate limit is that for rates exceeding the chemical-shift anisotropy significantly, motionally averaged frequencies are obtained which do not change during the course of the experiment. This will lead to a corresponding reduction in $E_{\tau}$. Therefore, care must be taken not to interpret this portion of the signal incorrectly as immobile.

Fortunately, significant motions with rates exceeding 10 000/s can be detected by other experiments. The most detailed information on such fast dynamics is provided by $^2$H quadrupolar line shapes and $T_2$ relaxation times. If deuteration is not possible, $^{1}$H–$^{13}$C dipolar sideband patterns can be analyzed. Semi quantitative information on fast motions is also provided by shortened $T_{1p}$ relaxation times, increased time constants $T_{CH}$ in cross polarization, broadened MAS line shapes, or narrowed chemical-shift anisotropies. The two-dimensional wideline separation (WISE) experiment or its one-dimensional version, which yields a $T_{2,1p}$-dephased $^{13}$C spectrum, can qualitatively identify segments with high-frequency (>300 kHz), large-amplitude mobility.

## CODEX and 2D exchange spectra

The relation between CODEX and the projection of the corresponding 2D exchange pattern parallel to the diagonal was pointed out above. Overall, CODEX is complementary to detailed 2D exchange NMR studies without sample rotation, often done best in the 2D PUREX fashion so that the dominant diagonal ridge is suppressed. The information on the reorientation angle that is contained in 2D exchange patterns is still unparalleled, in particular for distributions of reorientation angles, and for large reorientation angles. For aliphatic carbons, the amplitude measurement by CODEX will in general be only semi quantitative, while $^2$H quadrupolar or $^{13}$C–$^{13}$C dipolar interactions in exchange experiments without MAS provide the most detailed and reliable information on the motional geometry. The CODEX MAS approach, which is sensitive enough for $^{13}$C and $^{29}$Si in natural abundance, makes it easy to identify groups with interesting dynamics, characterize their correlation times, and estimate the motional amplitude. Given enough interest, these sites can then be isotopically labeled by $^2$H or $^{13}$C to determine the details of the reorientation process by 2D and 3D exchange NMR.

### Four-time CODEX

The four-time CODEX experiment has close analogies to a reduced four-dimensional (4D) exchange NMR experiment, where the orientation-dependent frequency is probed at four different times. The reduced 4D exchange method, and the closely related four-time exchange experiment have been used to identify the origins of the nonexponential loss of correlation above the glass-transition temperature and to estimate the size of dynamic heterogeneities. Here, we have demonstrated the clean selection of the relatively small fraction of mobile side-groups in PMMA by four-time CODEX. This is complementary to the suppression of the mobile-segment signal achieved in the reduced 4D experiment. In fact, the same (partial) suppression of the mobile-segment magnetization is directly accomplished in the part
of the experiment with dephasing in $t_{na}$. The pure mobile-segment signal is obtained by taking the difference with a reference signal.

Instead of the subsequent analysis of the number of accessible sites $M$ demonstrated here for PMMA, the correlation times of the selected segments and their dependence on $t_{mb}$ could be studied, in complete analogy to the stimulated-echo version of the reduced 4D experiment.\textsuperscript{12,13}

**Further developments**

In the description and demonstrations of CODEX given here, the chemical-shift anisotropy was used as the orientational probe. This is convenient and usually sufficient to identify slow-moving segments, measure their correlation function, and estimate the motional amplitude. However, for a quantitative analysis of the motional amplitude, other couplings with well-defined principal-axes orientations may be preferable, in particular for complex dynamic processes. To achieve this, the dephasing can be produced by homo- or heteronuclear dipolar couplings, including C–H couplings. In addition, the above-mentioned possibility of using CODEX at high-spinning speeds to observe slow reorientations without interference from spin diffusion will be explored.

**CONCLUSIONS**

We have given a detailed quantitative description of the centerband-only detection of exchange (CODEX) experiment, which combines chemical-shift recoupling by $180^\circ$-pulses with exchange NMR. The analysis in terms of the chemical-shift difference tensor explains the surprising sensitivity of the experiment to small-amplitude motions, and relates it to two-dimensional exchange NMR patterns. For uniaxial interactions ($\eta=0$), a simple analytical relation between the range of chemical shift differences and the reorientation angle has been derived, and a master-curve for the exchange intensity was obtained. The extension of the technique to a four-time CODEX experiment permits the determination of the number of orientational sites accessible to the mobile segments, and of the fraction of mobile units. It can also provide the information of reduced-4D or four-time exchange NMR with greatly enhanced sensitivity. Pure-exchange CODEX can be used as a dynamic filter. For instance, the signals of the amorphous and interfacial regions in a semicrystalline polymer, which are often almost invisible due to the dominant crystalline peaks, were observed selectively in a CODEX spectrum taken near the glass-transition temperature of the amorphous regions. CODEX with total suppression of spinning sidebands before detection, and a closely related auxiliary experiment for determining the chemical shift anisotropy have also been presented.

**ACKNOWLEDGMENTS**

Financial support by NSF (Grant No. DMR-9703916) is gratefully acknowledged. K.S.R. thanks the Arnold and Mabel Beckman Foundation for a Young Investigator Award that helped to support this work. E.R.d.A. and T.J.B. thank the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP)-Brazil for fellowships. NSF/MRSEC provided partial support of the NMR facility.