

Centerband-Only Detection of Exchange: Efficient Analysis of Dynamics in Solids by NMR

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Molecular dynamics have important effects on mechanical and conduction properties of polymers,^{1,2} activity of proteins,³ stability of pharmaceuticals,⁴ transport properties in zeolites,⁵ and behavior of amorphous materials near the glass transition.⁶ Solid-state NMR provides powerful techniques for characterizing such dynamics in detail, in particular through multidimensional exchange experiments.⁷ So far, however, the sensitivity and resolution of most of these NMR techniques has been limited, since anisotropy-broadened line shapes or strong sidebands in magic-angle spinning spectra (MAS) were required. In this paper, we describe a new NMR pulse sequence for observing and characterizing slow ($k = 0.2/s$ to $2000/s$) segmental reorientations with the highest available NMR sensitivity and site resolution, in sideband-free ^{13}C , ^{29}Si , ^{31}P , or ^{15}N MAS spectra. It is termed centerband-only detection of exchange, CODEX. From two short series of one-dimensional MAS spectra, the correlation function, correlation time, and motional amplitude can be determined for each site with a resolved line in the MAS spectrum.

The pulse sequence for the CODEX experiment is shown in Figure 1. For $N/2$ rotation periods, the spins evolve under the anisotropic chemical shift, which is recoupled⁸ by two 180° pulses per rotation period t_r in a spinning-speed independent fashion.⁹ Then, the magnetization is stored along the z -direction, so that it does not precess or dephase during the long mixing time t_m , which is an integer multiple of t_r . If no motions occurred during t_m , the chemical-shift evolution, after a read-out pulse and another $N/2$ rotation period under the recoupled chemical-shift anisotropy, is refocused at the start of detection. If segmental reorientation did occur during t_m , the orientation-dependent frequency has changed and the chemical-shift anisotropy is not completely refocused. The dephasing is observed with high sensitivity as a decrease in the detected line intensity. High spinning rates ν_r can be used to obtain virtually sideband-free spectra, since the dephasing is only a function of the total time Nt_r .

The often dominant signal of immobile sites can be removed by subtracting the CODEX spectrum from a reference spectrum, without an adjustable scaling factor. This reference spectrum is obtained simply by interchanging t_m and Δ in the pulse sequence

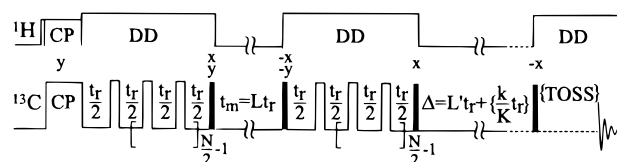


Figure 1. Pulse sequence for CODEX NMR: 90° pulses are filled black, 180° pulses white. CP: Cross polarization, DD: dipolar decoupling. The basic phase cycle of the 90° pulses is indicated, to be complemented by phase cycles to remove artifacts from T_1 relaxation during t_m and Δ . TOSS (total suppression of spinning sidebands) can be applied before detection with incremented rotor phase kt_r/K . Pure-exchange CODEX spectra are obtained by measuring a reference spectrum with t_m and Δ interchanged and subtracting the CODEX spectrum from it. Measurements are alternated between CODEX and reference spectrum every 5 min to eliminate the effects of spectrometer drift.

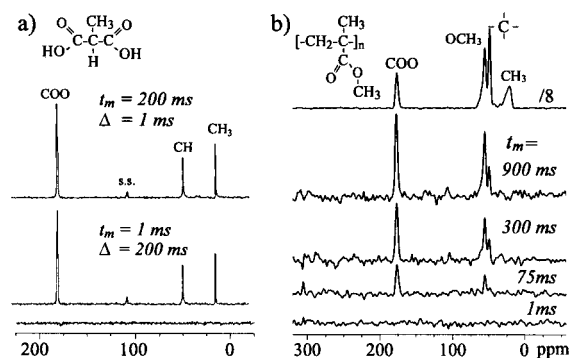


Figure 2. (a) CODEX of unlabeled methylmalonic acid at $\nu_r = 5.5$ kHz. Middle: CODEX spectrum with $t_m = 200$ ms and $\Delta = 1$ ms. Top: Reference spectrum with $\Delta = 200$ ms and $t_m = 1$ ms. Bottom: The difference between the top and middle (the pure-exchange CODEX spectrum). For the COO carbon, $\delta Nt_r = 7.6\pi$. "s.s.": spinning sideband. (b) Series of pure-exchange CODEX spectra of unlabeled PMMA at 300 K, $\nu_r = 6.5$ kHz, and $Nt_r = 615$ μs , as a function of t_m as indicated. For the COO carbon, $\delta = 2\pi(91 \text{ ppm}) = 2\pi(6.9 \text{ kHz})$ so that $\delta Nt_r = 8\pi$; for the OCH₃ group, $\delta Nt_r = 3.8\pi$. Large-amplitude side group and smaller-amplitude backbone motions are observed. Top: Full reference spectrum, scaled down 8 times. Experiments were performed at 75 MHz for ^{13}C in a 7-mm MAS probehead on a BRUKER DSX-300 spectrometer. ^{13}C 90° pulse length, 3.9 μs ; ^1H decoupling at $\gamma B_1/2\pi = 70$ kHz; recycle delay, 1.5 s; CP time, 1.5 ms.; measuring time per PMMA spectrum, 2.5 h.

of Figure 1. Since the resulting difference spectrum is exclusively due to the exchanging sites, we term this pure-exchange CODEX NMR.

The smaller the motional amplitude, the longer the time Nt_r must be to produce significant dephasing. Taking into account the size δ of the chemical-shift anisotropy,⁷ the reorientation angle can be estimated from the dependence of the intensity on δNt_r (see Figure 4 below). In another series of experiments, the correlation time τ_c is obtained as the time constant of the t_m -dependent intensity change. The information content of the normalized exchange intensity $E(t_m, \delta Nt_r)$, obtained as the ratio of the pure-exchange CODEX to the reference intensity, is similar to that of 1D PUREX¹⁰ and stimulated-echo^{11,12} data, which, however, are measured without sample spinning and thus have much inferior sensitivity and resolution. Information about the number M of equivalent orientational sites accessible in the motional process and the fraction f_m of mobile segments is obtained from the final exchange intensity $E_\infty = E(t_m \gg \tau_c, \delta Nt_r \gg 1)$

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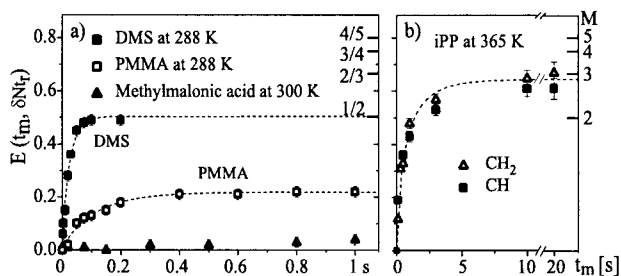


Figure 3. Normalized pure-exchange CODEX intensities $E(t_m, \delta N_{tr})$ as a function of t_m for (a) COO groups in methylmalonic acid ($T = 300$ K, $\delta N_{tr} = 7.6\pi$), COO in PMMA ($T = 288$ K, $\delta N_{tr} = 8\pi$), and CH₃ groups in DMS ($T = 288$ K, $\delta N_{tr} = 12.4\pi$) and (b) CH and CH₂ groups in iPP ($T = 365$ K; $\delta N_{tr} = 3.6\pi$ and 8.5π , respectively, with $\delta = 2\pi(11$ ppm) for the CH groups). The fit curve for PMMA is a stretched exponential $\exp(-(t_m/\tau_0)^\beta)$ with $\beta = 0.92$ and $\tau_0 = 110$ ms; iPP is fit with $\beta = 0.69$ and $\tau_0 = 690$ ms.

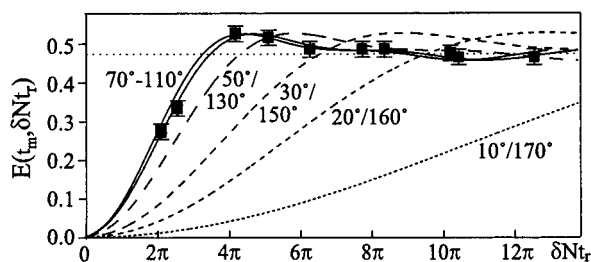


Figure 4. Normalized pure-exchange CODEX intensities $E(t_m, \delta N_{tr})$ as a function of δN_{tr} for DMS at 288 K, $t_m = 75$ ms, and $\nu_r = 5.5$ kHz. Also shown are simulations for reorientations of the S-CH₃ axes by 10° or 170°, 20° or 160°, 30° or 150°, 50° or 130°, and 70° to 110° (curves in this large-amplitude range are virtually indistinguishable).

$= f_m(M-1)/M$. For $f_m = 1$, the minimum E_∞ is $1/2$, obtained for $M = 2$. Generally, $E_\infty < f_m \leq 2E_\infty$.

A reference virtually without exchange is provided by unlabeled methylmalonic acid. Figure 2a displays its CODEX spectrum for $t_m = 200$ ms and $\Delta = 1$ ms, the reference spectrum with Δ and t_m interchanged, and their difference, the pure-exchange CODEX spectrum. The absence of intensity in the latter shows that no slow motions occur.

In contrast, large-amplitude motions of COOCH₃ sidegroups on a ~ 50 -ms time scale at 300 K are easily observed by CODEX in amorphous poly(methyl methacrylate), PMMA (Plexiglas), $[-CH_2-C(CH_3)(CO-O-CH_3)-]_n$, see Figure 2b. This motion is associated with the β -relaxation of PMMA,¹³ which imparts reduced brittleness to this glassy polymer at ambient and elevated temperatures. Previously, detailed NMR studies of the β -relaxation

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dynamics in PMMA^{14,15} required expensive ¹³C and ²H labeling combined with extensive multidimensional exchange NMR studies. It was concluded that $\sim 50\%$ of the sidegroups undergo 180° flips coupled to $\sim \pm 25^\circ$ rotations around the local chain axis. Using CODEX, this process can now be characterized in unlabeled industrial PMMA. Not only the sidegroup but also the backbone motions are detected directly in the pure-exchange CODEX spectra of Figure 2b.

In Figure 3, the t_m dependence of the CODEX exchange intensity is plotted for four samples. For the carboxyl line of methylmalonic acid, only a few percent of exchange intensity is observed on a 1-s time scale, most likely due to ¹³C spin diffusion. In dimethyl sulfone (DMS), (CH₃)₂SO₂, the CH₃ axes reorient by 108° due to a 2-site jump process.¹⁶ The CODEX data of Figure 3a show that the jumps of DMS indeed occur with $M = 2$ ($E_\infty = 0.50 \pm 0.04$) and $\tau_c = 25$ ms. Isotactic polypropylene (iPP), $[-CH_2-CH(CH_3)-]_n$, is a semicrystalline polymer that can undergo jumps around the 3₁-helix axis in the crystalline regions.^{17,18} The equilibration at $E_\infty = 0.64$ (CH) and 0.67 (CH₂) in Figure 3b confirms that the chains perform jumps between $M = 3$ NMR-distinguishable orientational sites. For PMMA at 288 K, E_∞ of only 0.23 ± 0.02 in the exchange-intensity curve of Figure 3a shows that less than 46% of all sidegroups undergo large-amplitude motions. This estimate of the fraction f_m of flipping sidegroups from CODEX data is more precise than that obtained from static spectra in ref 14.

Estimates of the motional amplitudes can be obtained from the δN_{tr} -dependence, as shown for DMS in Figure 4. The simulations for different reorientation angles plotted for comparison exhibit a strong sensitivity to small-amplitude motions.

The efficiency of CODEX facilitates systematic studies of molecular dynamics as a function of temperature, processing, chemical modifications, etc. Various further developments of the CODEX technique are in progress.⁹ With spin diffusion during t_m , CODEX will also be useful for conformational analysis in ¹³C-labeled materials. It is anticipated that the sensitive and relatively simple CODEX experiment will be applied routinely in solid-state NMR investigations of organic materials.

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