Two heteronuclear dipolar results at the price of one: Quantifying Na/P contacts in phosphosilicate glasses and biomimetic hydroxy-apatite

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The analysis of S[I] recoupling experiments applied to amorphous solids yields a heteronuclear second moment $M_2(S—I)$ that represents the effective through-space dipolar interaction between the detected S spins and the neighboring I-spin species. We show that both $M_2(S—I)$ and $M_2(I—S)$ values are readily accessible from a sole S[I] or I[S] experiment, which may involve either S or I detection, and is naturally selected as the most favorable option under the given experimental conditions. For the common case where I has half-integer spin, an I[S] REDOR implementation is preferred to the S[I] REAPDOR counterpart. We verify the procedure by $^{23}$Na--$^{31}$P REDOR and $^{31}$P--$^{23}$Na REAPDOR NMR applied to Na$_2$O–CaO–SiO$_2$–P$_2$O$_5$ glasses and biomimetic hydroxyapatite, where the $M_2(I—S)$ values directly determined by REAPDOR agree very well with those derived from the corresponding $M_2(S—I)$ results measured by REDOR. Moreover, we show that dipolar second moments are readily extracted from the REAPDOR NMR protocol by a straightforward numerical fitting of the initial dephasing data, in direct analogy with the well-established procedure to determine $M_2(S—I)$ values from REDOR NMR experiments applied to amorphous materials; this avoids the problems with time-consuming numerically exact simulations whose accuracy is limited for describing the dynamics of a priori unknown multi-spin systems in disordered structures.

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1. Introduction

Heteronuclear dipolar recoupling for determining internuclear distances in spin-1/2 pairs undergoing magic-angle-spinning (MAS) is a well-developed area [1–3]. Notably, the rotational echo double resonance (REDOR) [4] protocol is one of the most widely applied techniques in solid state NMR. S[I] REDOR reintroduces the S–I through-space dipolar interactions by application of two $\pi$-pulses per rotational period ($\tau_r = \nu_m^{-1}$, where $\nu_m$ is the MAS frequency in Hz) to either the detected S-spin species, or to its coupled I-spin partner(s). Transverse S-spin magnetization thereby evolves for a controlled recoupling period $\tau_{rec} = 2\pi N_r$ ($n = 1, 2, 3, \ldots$), leading to an attenuated (“dipolar dephased”) NMR signal $S(\tau_{rec})$ relative to a reference counterpart $S_0(\tau_{rec})$, obtained by a spin-echo [4]. Fitting of the $\Delta S/S_0 \equiv [S_0(\tau_{rec})]—S(\tau_{rec})]/S_0(\tau_{rec})$ “dephasing curve” to numerical simulations or an analytical solution [5], allows extraction of the S–I dipolar coupling constant $b_{S—I} = b_{I—S} = -\mu_0 \nu_m^2 \tau_r^2/(8\pi^2 \gamma_s^2 r^2)$). Alternatively, for large $S$,$D$, multi-spin systems where determinations of individual S–I distances are often intractable, fitting of the initial dephasing data $\Delta S/S_0 \lesssim 0.2$ to a parabolic relationship $\sim M_2(S—I)\gamma_s^2$ [1,6–8], yields an estimation of the van Vleck dipolar second moment [9],

$$M_2(S—I) = \frac{4}{15} I(I+1)N_s^{-1} \sum_k \sum_j \left( b_{S—I}^k \right)^2,$$

$$M_2(I—S) = \frac{4}{15} S(S+1)N_I^{-1} \sum_k \sum_j \left( b_{I—S}^k \right)^2,$$

where $N_l$ and $N_s$ represent the respective numbers of I and S sites in the structure, while $I$ and $S$ denote the spin quantum numbers. Note the very similar expressions for $M_2(S—I)$ and $M_2(I—S)$, as well as that $b_{S—I}^k \equiv b_{I—S}^k$.

Dipolar recoupling involving an $s = 1/2$ and a quadrupolar $I > 1/2$ nucleus is significantly more challenging due to the problems of simultaneously arranging efficient dephasing of all I-spin single-quantum transitions [10,11]. Several options are proposed [1,10–18]. The most commonly utilized protocol, rotational echo adiabatic passage double resonance (REAPDOR; [10,11]), extends an existing REDOR implementation in that all $\pi$-pulses are applied to the spin-1/2 (S) species but the central $\pi$-pulse of the I-spin channel is replaced by a strong “adiabatic passage” (AP) pulse.

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lasting for ~ \tau_s/3 \; \cite{10,11}. To achieve efficient dipolar recoupling without a pronounced dependence on the quadrupolar tensor parameters, the experimental conditions should for \( I = 3/2 \) obey the “adiabaticity requirement” \( \pi \equiv 2\nu_1^2/(v_0 C_0) \geq 0.5 \; \cite{11} \), where \( \nu_1 \) is the rf nutation frequency and \( C_0 = e^2 q Q/h \) the quadrupolar coupling constant.

Two main hurdles complicate SI[ ] REAPDOR applications for estimating \( b_{S-I} \) or \( M_2(S-I) \) data: (i) To obey the adiabaticity condition for large quadrupolar couplings, very strong rf powers are generally required (that may be intractable) and/or the MAS rate must be limited, which inflicts a coarser sampling of the recoupling dynamics because \( \Delta \tau_{rec} = 2\tau_c \). These problems may be mitigated by modified experimental protocols where the AP rf pulse is replaced by a longer but less rf power-demanding pulse \cite{14,16–18}. (ii) As opposed to the REDOR dephasing that is analytically solvable \cite{5}, the extraction of internuclear-distance related information from the more complex REAPDOR dynamics has traditionally involved numerically exact simulations. If the AP pulse is truly adiabatic, it has been demonstrated for S–I spin-pairs that the REAPDOR NMR data may be fitted to an empirically deduced “universal curve” \cite{11,19,20}. However, its application for extracting internuclear distances or \( M_2(S-I) \) values from multi-spin systems remains to our knowledge unexplored, particularly for disordered network structures where even numerically exact calculations may lack accuracy because the NMR parameters exhibit a priori unknown distributions, while the simulated spin-system size must naturally be restricted to avoid prohibitive computation times. Herein, we demonstrate that \( M_2(S-I) \) values are directly accessible by fitting experimental SI[ ] REAPDOR NMR data either to the “universal curve” \cite{20}, or to a truncated Taylor expansion (TE) of an analytical S–I two-spin solution \cite{5} in the limit \( M_2(S-I) \Delta \tau_{rec} \ll 1 \); the latter approach prevails REDOR analyses in amorphous materials \cite{1,6–8}.

However, given the complications associated with \( M_2(S-I) \) estimates from REAPDOR experimentation on Si systems in disordered structures—and heteronuclear dipolar recoupling involving non-negligible rf application to quadrupolar nuclei vide infra—we here propose a pragmatic solution: whenever feasible, avoid the S[I] \( (S = 1/2; \; I > 1/2) \) experiment altogether and instead derive the \( M_2(S-I) \) value from its counterpart \( M_2(I-S) \) determined from an I[S] protocol such as REDOR. Provided that the I-spin MAS NMR spectrum is readily detected and its signals are not severely broadened by second-order quadrupolar interactions such that the central-transition (CT) magnetization may be accurately inverted by a CT-selective \( \pi \)-pulse, all dipolar recoupling pulses are applied to the (now non-observed) \( S = 1/2 \) species. The dipolar dephasing is analyzed by a straightforward data fitting \cite{1,6,8}. Next, for known molar fractions \( x_I \) and \( x_S \) of the I and S species in the sample, respectively, the \( M_2(S-I) \) value may be derived from the simple relationship

\[
M_2(S-I) = \frac{f_I x_I (I + 1)}{f_S x_S (S + 1)} M_2(I-S), \tag{2}
\]

where \( f_I \) and \( f_S \) represent the corresponding isotope abundances. Eq. (2) follows directly by combining Eqs. (1a) and (1b), where each product \( f_I x_I \) and \( f_S x_S \) corresponds to \( N_I \) and \( N_S \), respectively.

Consequently, both \( M_2(S-I) \) and \( M_2(I-S) \) values are accessible from one single S[I] or I[S] recoupling experiment, naturally selected as the most favorable option and usually constituting that of I[S]. In the contexts of Na\(_2\)O–CaO–SiO\(_2\)–P\(_2\)O\(_5\) glasses and biometric hydroxyapatite grown in vitro at the surface of a mesoporous bioactive glass, we exploit the high sensitivity and fast \( T_1 \) relaxation of \( \text{\textsuperscript{23}Na} \) to estimate \( M_2(P-Na) \) values by feeding the corresponding \( \text{\textsuperscript{23}Na} \text{\textsuperscript{31}P} \) REDOR-derived \( M_2(Na-P) \) results through Eq. (2).

\section{2. Results and discussion}

\subsection{2.1. Phosphosilicate glasses}

The set of melt-prepared phosphosilicate glasses used herein comprises SiO\(_2\) (40–60 mol%), P\(_2\)O\(_5\) (2–6 mol%), Na\(_2\)O (17–24 mol%) and CaO (22–32 mol%); see Table S1. The glass preparation schemes and experimental/computational procedures are described in the Supplementary Information (SI). Each glass constitutes a network of interconnected SiO\(_2\) tetrahedra, whereas P exists predominantly as orthophosphate (PO\(_4^{3-}\)) groups occupying interstitial positions around the silicate network \cite{21,22}. The \( \text{\textsuperscript{31}P} \text{\textsuperscript{23}Na} \) MAS NMR spectra and the underlying silicate and phosphate speciations were recently discussed \cite{21,22}.

Thanks to the high sensitivity and 100% natural abundance of both \( \text{\textsuperscript{23}Na} \) and \( \text{\textsuperscript{31}P} \), \( \text{\textsuperscript{31}P} \text{\textsuperscript{23}Na} \) REDOR as well as \( \text{\textsuperscript{31}P} \text{\textsuperscript{23}Na} \) REAPDOR data were readily acquired from the glass series, although due to a slow \( \text{\textsuperscript{31}P} \) \( T_1 \) relaxation and low amount of P in the present glasses, the REDOR NMR data collection is significantly faster than that of REAPDOR. The corresponding \( M_2(P-Na) \) and \( M_2(Na-P) \) values were extracted by fitting the initial dephasing regime \( (\Delta S/\Delta t < 0.1) \) to a TE truncated at the second term, whereas the REAPDOR data-sets were also fitted to the “universal curve” of \cite{20}. The SI provides detailed information about the analysis, together with plots of the experimental and best-fit dephasing curves.

Fig. 1a plots the REDOR-stemming best-fit \( M_2(Na-P) \) data (open circles) against the number density of P atoms (\( \rho_p \) in the glass. The observed linear increase of \( M_2(Na-P) \) for growing \( \rho_p \) implies a continuously expanding number of Na–PO\(_4^{3-}\) contacts in the structure, thereby suggesting the absence of any pronounced preference for Na to partition around silicate and phosphate species (or weak trend thereof). The consequences of the observed composition-dependent trends of the Na/P contacts will be discussed in detail elsewhere; herein, we focus solely on demonstrating the \( M_2(S-I) \)–\( M_2(I-S) \) interconversion \cite{Eq. (2)}.

To assess the data accuracy, dephasing curves were recorded from powders of Na\(_2\)PO\(_4\) and NaH\(_2\)PO\(_4\) under identical experimental conditions as for the glasses. This provided best-fits amounting to 69.7% and 68.3% of the respective theoretical \( M_2(Na-P) \) value of the known crystal structures. Our experimentation involved full rotors, which unfortunately emphasizes rf-inhomogeneity effects that are known to diminish the REDOR dephasing \cite{7,23}. Similar tendencies were noted to affect analogous estimates of effective \( 31P \rightarrow 31P \) internuclear contacts by double-quantum \( 31P \) MAS NMR experimentation on these phosphosilicate glass structures \cite{22}. However, the rf (in)homogeneity is independent on the glass sample and its other NMR-parameters, and furthermore appears to be the primary source of systematic experimental errors. Consequently, the best-fit second moment from each glass was scaled by the net factor \((0.697+0.683)/2)^{-1} = 1.449\). Fig. 1a evidences an excellent accordance between the corrected experimental \( M_2(Na-P) \) values (solid circles) and those calculated from the atomic coordinates of glass models generated from atomistic molecular dynamics (MD) simulations (open boxes). See Refs. \cite{21,22} and the SI for further details on the MD simulations.

Fig. 1(b)–(d) presents the \( M_2(P-Na) \) data extracted from the glasses, obtained either from MD simulations or \( \text{\textsuperscript{31}P} \text{\textsuperscript{23}Na} \) REAPDOR NMR experiments. The corresponding REDOR-derived results from Eq. (2) are also displayed, as obtained (b) before and (d) after correction of the experimental data. Note that the \( M_2(P-Na) \) values increase linearly with \( \rho_p \). The REDOR dephasing fits to the universal curve were corrected by utilizing results from Na\(_2\)PO\(_4\) and the same “calibration” procedure as for the REDOR NMR experiment; this provided the scaling factor 0.739\(^{-1}\) = 1.354. Its close value to that obtained from REDOR gives...
further support for our simplistic corrections. Figs. 1b and 1c show the respective (b) uncorrected and (c) corrected $M_2(P-Na)$ values obtained directly by numerical fitting of the initial regime of $^{23}$Na-$^{31}$P REDOR dephasing curves (“uncorr”), and after applying data correction (“corr”), as described in the text. (b)-(d) $M_2(P-Na)$ results obtained either by (b, c) fitting of $^{31}$P($^{23}$Na) REAPDOR dephasing curves, or by converting the REDOR-derived data in (a) via Eq. (2), where (b) and (d) display the $M_2(P-Na)$ estimates before and after correction, respectively. The labels “TE” and “uni” indicate that the experimental $^{31}$P-$^{23}$Na REAPDOR data was fitted to a Taylor expansion [Eq. (S1)] and the universal curve [Eq. (S2)], respectively. All REDOR data fitting involved the Taylor expansion. Error bars below the symbol sizes are not shown. All NMR results were recorded at 9.4 T and 14.0 kHz MAS rate by using full 4 mm zirconia rotors.

It is particularly gratifying that the $M_2(P-Na)$ values obtained indirectly by $^{23}$Na-$^{31}$P REDOR NMR manifest an overall very good agreement with their directly determined REAPDOR counterparts, regardless of whether the “uncorrected” or “corrected” pairs of data sets are compared. Fig. S2 plots the various independent $M_2(P-Na)$ estimates against each other, revealing that the REDOR-derived values are generally $\approx 10\%$ higher than their directly determined counterparts from REAPDOR (see the SI). Moreover, the REDOR data in conjunction with Eq. (2) evidences an even better agreement with the MD-generated $M_2(P-Na)$ values (Fig. 1d) relative to those estimated directly from REAPDOR. Altogether, Fig. 1 provides a mutual validation of the NMR/MD results (where we have previously observed an overall very good accordance between other structural parameters [21,22]), as well as experimentally successful $M_2(S-I) \rightarrow M_2(I-S)$ interconversions.

2.2. Na substitution in biomimetic apatite

Most of the Na$_2$O–CaO–SiO$_2$–P$_2$O$_5$ glasses examined above are bioactive [21,24]: when exposed to (simulated) body fluids, they form a surface layer of hydroxy-carbonate apatite (HCA) [24]. Natural bone mineral and HCA generated in vitro in a simulated body fluid (SBF) feature similar compositions and both comprise small amounts of Na$^+$ cations substituted in the carbonate-bearing hydroxyapatite [Ca$_5$(PO$_4$)$_3$OH] parent lattice. $^{23}$Na NMR parameters are reported for bone [25] and synthetic Na-bearing HCA [26], as well as for biomimetic HCA formed in vitro by immersing mesoporous bioactive glasses (MBGs) in SBF [27].

Fig. 2a shows the $^{23}$Na-$^{31}$P REDOR dephasing curve recorded from an “S90” MBG of nominal composition 10CaO–90SiO$_2$ after its exposure to SBF for 15 days; this specimen is denoted “S90sbf”. It comprises a main Ca-depleted mesoporous silica part ($\approx 90\%$) and a heterogeneous calcium phosphate layer that mainly constitutes HCA. The observation of a rapid $^{23}$Na NMR signal dephasing (only slightly slower than that of Na$_3$PO$_4$) unambiguously establishes the incorporation of Na$^+$ in the HCA structure.
However, its Na content is very low; from elemental analysis it was estimated as one Na⁺ species per ≈30 Ca²⁺ cations (xNa/xCa ≈ 0.03). The high abundance of PO₄³⁻ groups around each Na site in the HCA component of S90bf is reflected in the best-fit value M₂(29Si–P) = (1.00 ± 0.03) · 10⁻⁴ s⁻¹ obtained after using the previously described data correction procedure.

Fig. 2b presents the corresponding ³¹P⁻²⁷Al REAPDOR NMR results. The minute number of Na⁺ ions nearby the PO₄³⁻ groups manifests in a very slow ³¹P dephasing dynamics. The long-term dipolar dephasing (inset of Fig. 2b) deviates markedly from its expected form, mainly attributed to rf inhomogeneity and a severe sensitivity to even minute MAS-rate fluctuations of the REAPDOR experiment [11,13]. The REDOR NMR curves recorded from the phosphosilicate glasses reveal a similar trend (see Fig. S3 of the SI), although the effects are less prominent relative to those of the present ³¹P⁻²⁷Al REAPDOR results. Nevertheless, by restricting the data to ΔS/ΔS₀ < 0.07 in the fit to the “universal curve” [20], we obtained the (corrected) dipolar second moment M₂(P–Na) = (2.2 ± 0.3) · 10⁻⁴ s⁻¹, which may be contrasted with the REDOR-derived counterpart M₂(P–Na) = (2.6 ± 0.1) · 10⁻⁴ s⁻¹ obtained via Eq. (2). Both independent estimates accord within 15%, which is a remarkably good agreement in view of the potentially large number of experimental uncertainties involved (including the sample composition).

3. Conclusions

We have demonstrated a straightforward M₂(S–I) ↔ M₁(I–S) interconversion [Eq. (2)] to simultaneously determine both heteronuclear contacts from a sole recoupling experiment applied to structurally disordered/heterogeneous materials. The procedure was successfully implemented for the {S = Na–P–Al–O} pair of nuclei in bioactive phosphosilicate glasses. Moreover, we provided (i) the first demonstration that REAPDOR NMR data may be analyzed by a straightforward numerical fitting of the initial dephasing regime (without invoking numerical spin-dynamics simulations), analogously to the well-established procedure to derive M₂(S–I) values from REDOR experiments applied to amorphous materials [11]; and (ii) the first quantitative assessment of Na ↔ P contacts in Na-bearing biomimetic HCA formed at the surface of a bioactive glass.

Our proposed second-moment conversion strategy is general and independent of both the spin numbers (S, I) involved and the particular heteronuclear recoupling technique employed. It is applicable to a multitude of other S–I pairs, such as ²⁷Al⁻²³Na, ²³Na–²³Na, ³¹P⁻³¹P{¹¹B–²⁹Si (²⁷Al)}, for subsequently deriving the sample composition.

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Appendix A. Supplementary material

Supplementary text and figures associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jmr.2014.12.002.

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