Electronic Supplementary Information (ESI)

# Optimisation of <sup>1</sup>H PMLG homonuclear decoupling at 60 kHz MAS to enable <sup>15</sup>N-<sup>1</sup>H through-bond heteronuclear correlation solid-state NMR spectroscopy

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### S1. Product operator formalism - INEPT

We review here a product operator analysis of the refocused INEPT pulse sequence element. At the beginning of the refocused INEPT element, the in-phase magnetization  $\hat{S}_x$  is along the transverse plane for <sup>15</sup>N. During the first echo period ( $\tau_1$ ), the in-phase magnetization is converted into anti-phase  $\hat{S}_x \hat{I}_z$ :

$$\hat{S}_x \xrightarrow{\tau_1 - \pi - \tau_1} \cos\left(2\pi J_{IS}\tau_1\right)\hat{S}_x + \sin\left(2\pi J_{IS}\tau_1\right)\hat{S}_y\hat{I}_z, \qquad (1)$$

where  $\hat{I}$  represents the <sup>1</sup>H spins. The anti-phase coherence is transferred from *S* to *I* with the 90° pulses applied on both channels, which separates the two spin-echo evolution periods:

$$\sin\left(2\pi J_{IS}\tau_{1}\right)\hat{S}_{y}\hat{I}_{z} \xrightarrow{(\pi/2)\hat{I}_{x}} \xrightarrow{(\pi/2)\hat{S}_{x}} \sin\left(2\pi J_{IS}\tau_{1}\right)\hat{S}_{z}\hat{I}_{y}.$$
(2)

Following  $\tau_1$ , in the second echo period ( $\tau_2$ ), the antiphase <sup>1</sup>H coherence is converted into in-phase  $I_x$  that is then detected during acquisition ( $t_2$ ):

$$\sin\left(2\pi J_{IS}\tau_{1}\right)\hat{S}_{z}\hat{I}_{y} \xrightarrow{\tau_{2}-\pi-\tau_{2}} \sin\left(2\pi J_{IS}\tau_{2}\right)\sin\left(2\pi J_{IS}\tau_{1}\right)\hat{I}_{x}.$$
(3)

S2. Optimisation of PMLG <sup>1</sup>H homonuclear decoupling on <sup>15</sup>N-glycine



**Figure S1.** A stacked representation of a two-variable optimization (see **Fig. 3a**) of both  $\tau_{LG_expt}$  (in steps of 0.25 µs) and  $\nu_1$  in a 1D <sup>1</sup>H-CRAMPS ( $\nu_0 = 500$  MHz) MAS ( $\nu_r = 60$  kHz) NMR experiment of <sup>15</sup>N-glycine, in which windowed  $PMLG5_{mm}^{\overline{xt}}$  was applied with  $\tau_{tilt} = 0.54$  µs and a <sup>1</sup>H transmitter offset of -0.6 kHz, corresponding to the data shown in Figure 3a of the main text. 8 co-added transients were collected for each optimization point. On the right, slices from the optimization are shown with the associated  $\tau_{LG_expt}$  and  $\nu_1$ . The relative intensity of the NH<sub>3</sub><sup>+</sup> peak with respect to the best <sup>1</sup>H homonuclear decoupling performance at 2  $\tau_{LG_expt} = 6.25$  µs and  $\nu_1 = 110$  kHz is stated.



**Figure S2**. Zoom of the region between  $\tau_{LG\_expt} = 5.5 \ \mu s - 7.5 \ \mu s$  for the two-variable optimization of  $\tau_{LG\_expt}$  (in steps of 0.25  $\mu s$ ) and  $\nu_1$  in a 1D <sup>1</sup>H-CRAMPS ( $\nu_0 = 500 \text{ MHz}$ ) MAS ( $\nu_r = 60 \text{ kHz}$ ) NMR spectrum of the <sup>15</sup>N-glycine a) CH<sub>2</sub> and b) NH<sub>3</sub><sup>+</sup> peak intensity, corresponding to the data shown in Figure 3a of the main text. Windowed  $PMLG5_{mm}^{\overline{xx}}$  was applied with  $\tau_w = 7.20 \ \mu s$ ,  $\tau_{tilt} = 0.54 \ \mu s$  and a <sup>1</sup>H transmitter offset of -0.6 kHz. 8 co-added transients were collected for each optimization point for a recycle delay of 3 s.

# S3. Optimisation of tilt pulses via the NH<sub>3</sub><sup>+</sup> signal intensity in a 1D CRAMPS experiment of <sup>15</sup>N-glycine

The duration of the tilt pulses,  $\tau_{\text{tilt}}$ , was optimised in a two-variable optimization with  $\tau_{\text{LG}_{expt}}$ , for the intensity of the NH<sub>3</sub><sup>+</sup> resonance in a 1D CRAMPS spectrum of <sup>15</sup>N-glycine at 60 kHz MAS as presented in **Fig. S3a** with windowed  $PMLG5_{mm}^{\text{Tx}}$ . It is evident from **Fig. S3** that the optimum values for the two parameters,  $\tau_{\text{LG}_{expt}}$  and  $\tau_{\text{tilt}}$ , are linked, i.e., when one becomes longer the other shortens, maintaining the same combined length of ~7.1 µs (considering two sandwich pulses per  $PMLGn_R^{\phi}$  block – see **Fig. 2b**) to maintain the same cycle time,  $\tau_c$  (see eq. 11), and hence ensure a constant optimum  $\psi$  (see eq. 12). The couples with best NH<sub>3</sub><sup>+</sup> signal intensity were 6.75 & 0.15 µs, 6.5 & 0.30 µs and 6.25 & 0.45 µs for 2  $\tau_{\text{LG}_{expt}}$  and  $\tau_{\text{tilt}}$ , respectively, with a preference for a longer  $\tau_{\text{LG}_{expt}}$  and shorter  $\tau_{\text{tilt}}$  (see **Fig. S3b**). A fine optimisation with 16 co-added transients was employed to identify the optimum parameters as used in **Fig. 3c** (and repeated in **Fig. S3c**, left-hand spectrum).



**Figure S3.** a) Two-variable optimization of 2  $\pi_{LG_expt}$  (0.25  $\mu$ s step) and  $\tau_{tilt}$  (0.05  $\mu$ s step) for the NH<sub>3</sub><sup>+</sup> peak intensity in a 1D <sup>1</sup>H-CRAMPS ( $\nu_0 = 500$  MHz) MAS ( $\nu_r = 60$  kHz) spectrum of <sup>15</sup>N-labelled glycine. Windowed  $PMLG5_{mm}^{\bar{x}x}$  was applied with  $\nu_1 = 106$  kHz and a <sup>1</sup>H transmitter offset of -0.6 kHz. 4 co-added transients were collected for each optimization point. b) Slices extracted from the contour plot show the best spectrum intensities obtained with the indicated 2  $\pi_{LG_expt}$  and  $\pi_{tilt}$ . c) 1D <sup>1</sup>H CRAMPS <sup>15</sup>N-labelled glycine spectra acquired with windowed  $PMLG5_{mm}^{\bar{x}x}$  using 2  $\pi_{LG_expt} = 6.20$   $\mu$ s and  $\pi_{tilt} = 0.54$   $\mu$ s (left) and windowed  $PMLG5_{mm}^{\bar{x}x}$  without  $\pi_{tilt}$  (right). 32 co-added transients were added. For all experiments with windowed <sup>1</sup>H homonuclear decoupling,  $\tau_w = 7.20$   $\mu$ s.

The <sup>1</sup>H CRAMPS spectrum on the right in **Figure S3c** was acquired with the same nutation frequency and offset, but with no tilt pulses and  $2 \tau_{LG_{expt}}$  was chosen to be 7 µs such that the cycle time and hence  $\psi$  are the same. The intensity of the NH<sub>3</sub><sup>+</sup> peak obtained with windowed  $PMLG5_{nmn}^{\overline{xx}}$  at  $\tau_{LG_{expt}} =$ 6.20 µs and  $\tau_{tilt} = 0.54$  µs is within 5% of that obtained without tilt pulses. Note, however, that the peak widths for  $PMLG5_{mmn}^{\overline{xx}}$  without tilt pulses are 235 Hz for the NH<sub>3</sub><sup>+</sup> peak, and 224 Hz and 231 Hz for the CH<sub>2</sub> peaks. After scaling ( $\lambda_{CS} = 0.80$ ), the FWHM become 294 Hz, 280 Hz and 289 Hz, respectively, which is ~15 Hz larger than those stated in **Table 3** for windowed  $PMLG5_{mmn}^{\overline{xx}}$  with  $\tau_{LG_{expt}} = 6.20$  µs and  $\tau_{tilt} = 0.54$  µs.

## S4. 2D <sup>1</sup>H-<sup>1</sup>H correlation and optimisation of the <sup>15</sup>N-glycine NH<sub>3</sub><sup>+</sup> signal intensity in a 1D-filtered CPrefocused INEPT NMR spectrum for PMLG <sup>1</sup>H decoupling

Each <sup>1</sup>H-detected FID was acquired for 30 ms with a spectral width of 57 ppm. The <sup>1</sup>H indirect dimension was acquired with 96  $t_1$  FIDs with a dwell time of 29.16 µs (57 ppm spectral width - no <sup>1</sup>H homonuclear decoupling), 12.40 µs (134 ppm spectral width - windowless  $PMLG5_{mm}^{\bar{x}t}$ ) and 11.68 µs (143 ppm – windowless  $PMLG9_{mm}^{\bar{x}t}$ ). The maximum  $t_1$  were 1.40 ms, 0.59 ms and 0.56 ms using no <sup>1</sup>H homonuclear decoupling, windowless  $PMLG5_{mm}^{\bar{x}t}$  and windowless  $PMLG9_{mm}^{\bar{x}t}$ , respectively. The States-TPPI method was employed to achieve sign discrimination in the indirect dimension.



**Figure S4**. 2D <sup>1</sup>H-<sup>1</sup>H ( $\nu_0 = 600$  MHz) correlation spectra of <sup>15</sup>N-Glycine acquired at  $\nu_r = 60$  kHz MAS with a) no <sup>1</sup>H homonuclear decoupling, b) windowless  $PMLG5_{mm}^{\bar{x}x}$  ( $\tau_{LG} = 3.10 \,\mu$ s,  $\nu_1 = 104 \,\text{kHz}$ ,  $\Omega = 1 \,\text{kHz}$ ) and c) b) windowless  $PMLG9_{mm}^{\bar{x}x}$  ( $\tau_{LG} = 2.92 \,\mu$ s,  $\nu_1 = 104 \,\text{kHz}$ ,  $\Omega = -0.8 \,\text{kHz}$ ). In all the experiments, 4 transients were coadded for 96  $t_1$  FIDs for a recycle delay of 3 s. The zero-offset is set with the carrier being on resonance with the NH<sub>3</sub><sup>+</sup> peak in the indirect dimension.



**Figure S5.** <sup>1</sup>H RF carrier optimization for a 1D-filtered ( $t_1 = 0$ ) <sup>15</sup>N-<sup>1</sup>H ( $v_0 = 500$  MHz) CP (contact time = 2 ms)-Refocused INEPT MAS ( $v_1 = 60$  kHz) NMR experiment for <sup>15</sup>N-labelled glycine, whereby a) windowed  $PMLG5_{nnn}^{\overline{xx}}$  <sup>1</sup>H homonuclear decoupling (See **Fig. 5**) was applied with  $\pi_{LG\_expt} = 3.1 \ \mu s$ ,  $\pi_{tilt} = 0.54 \ \mu s$  and a <sup>1</sup>H nutation frequency,  $v_1$ , of 106 kHz during  $\tau_1$  (1.999 ms, 69  $\tau_c$ ) and 104 kHz during  $\tau_2$  (1.391 ms ,48  $\pi_c$ ), b) windowless  $PMLG5_{nnn}^{\overline{xx}}$  <sup>1</sup>H homonuclear decoupling was applied with  $\pi_{LG\_expt} = 3.1 \ \mu s$  and a <sup>1</sup>H nutation frequency,  $v_1$ , of 104 kHz during  $\tau_1$  (2.096 ms, 169  $\tau_c$ ) and 102 kHz during  $\tau_2$  (0.496 ms, 40  $\tau_c$ ), c) windowed  $PMLG9_{nnn}^{\overline{xx}}$  <sup>1</sup>H homonuclear decoupling was applied with  $\pi_{LG\_expt} = 3.1 \ \mu s$  and a <sup>1</sup>H nutation frequency,  $v_1$ , of 104 kHz during  $\tau_1$  (2.096 ms, 169  $\tau_c$ ) and 102 kHz during  $\tau_2$  (0.496 ms, 40  $\tau_c$ ), c) windowed  $PMLG9_{nnn}^{\overline{xx}}$  <sup>1</sup>H homonuclear decoupling was applied with  $\pi_{LG\_expt} = 2.92 \ \mu s$ ,  $\pi_{tilt} = 0.82 \ \mu s$  and a <sup>1</sup>H nutation frequency,  $v_1$ , of 104 kHz during  $\tau_1$  (2.085 ms, 71  $\tau_c$ ) and 106 kHz during  $\tau_2$  (1.498 ms, 51  $\tau_c$ ) and d) windowless  $PMLG9_{nnn}^{\overline{xx}}$  <sup>1</sup>H homonuclear decoupling was applied with  $\pi_{LG\_expt} = 2.92 \ \mu s$  and a <sup>1</sup>H nutation frequency,  $v_1$ , of 104 kHz during  $\tau_1$  (2.091 ms, 179  $\tau_c$ ) and 102 kHz during  $\tau_2$  (1.192 ms, 102  $\tau_c$ ). 16 transients were coadded. For all experiments with windowed decoupling,  $\tau_w$  was substituted with a delay of 7.20  $\mu s$ . The zero-offset is set with the carrier being on resonance with the NH<sub>3</sub><sup>+</sup> peak.

#### **S5.** Cimetidine

Here, the normalized intensity is related to the respective maximum intensity for each peak , i.e. the maximum intensity is equal to 1 for all the resonances. However, note that the NH15 proton signal intensity is  $\sim$ 30 % of that of NH3.



**Figure S6**. Dephasing of cimetidine NH proton ( $\nu_0 = 600 \text{ MHz}$ ) resonances as a function of the spin-echo duration,  $\tau$ , with windowed  $PMLG5_{mm}^{\overline{x}x}$  ( $\tau_{LG\_expt} = 3.10 \text{ }\mu\text{s}$ ,  $\tau_{tilt} = 0.54 \text{ }\mu\text{s}$  and  $\tau_w = 7.20 \text{ }\mu\text{s}$ ) for a nutation frequency of 106 kHz. Fits to an exponential decay function are shown, with the spin-echo dephasing times,  $T_2'$ , as listed in **Table S1**. 8 transients were co-added for a recycle delay of 5 s.

**Table S1**. Cimetidine <sup>1</sup>H dephasing time,  $T_2'$ , for the three NH resonances and  $T_2'$  scaled by the experimental  $\lambda_{CS}$ ,  $\lambda_{CS} T_2'$ , acquired on a <sup>1</sup>H spin-echo<sup>a</sup> experiment using windowed  $PMLG5_{mm}^{\overline{xx} \ b}$ 

	δ (ppm)	<i>v</i> 1 (kHz)	$\lambda_{cs}$	<i>T</i> <sub>2</sub> ′ (ms)	λ <sub>cs</sub> <i>T</i> ₂' (ms)
NH3	11.6			1.34	1.10
NH15	9.7	106	0.82	0.58	0.48
NH10	8.2			1.23	1.01

<sup>a</sup>Implemented at  $v_0 = 600$  MHz and  $v_r = 60$  kHz (see Fig. S6). Windowed  $PMLG5_{mm}^{\overline{v}v}$  was implemented with  $\tau_{LG} = 3.10 \ \mu s$ ,  $\tau_{tilt} = 0.54 \ \mu s$  and  $\tau_w = 7.20 \ \mu s$ 

 $^{b}\Omega_{rf}$  = -0.8 kHz, where the zero-offset is set with the carrier being on resonance with the NH<sub>3</sub><sup>+</sup> peak of  $^{15}$ N-glycine

### S6. Simulations of eqs 1 and 2



**Figure S7.** Simulation of dependence of the <sup>15</sup>N-<sup>1</sup>H CP-Refocused INEPT intensity on the spin-echo period,  $\tau_1$ , according to eq. 1 and 2 (from the main text) for a NH (red) or NH<sub>3</sub> (blue) group, for a  $J_{NH}$  equal to: a) 90 Hz, b) 75 Hz and c) 60 Hz ignoring dephasing, and d) 90 Hz, e) 75 Hz and f) 60 Hz with exponential dephasing with a nominal nitrogen  $T_2$ <sup>•</sup> of 35 ms.