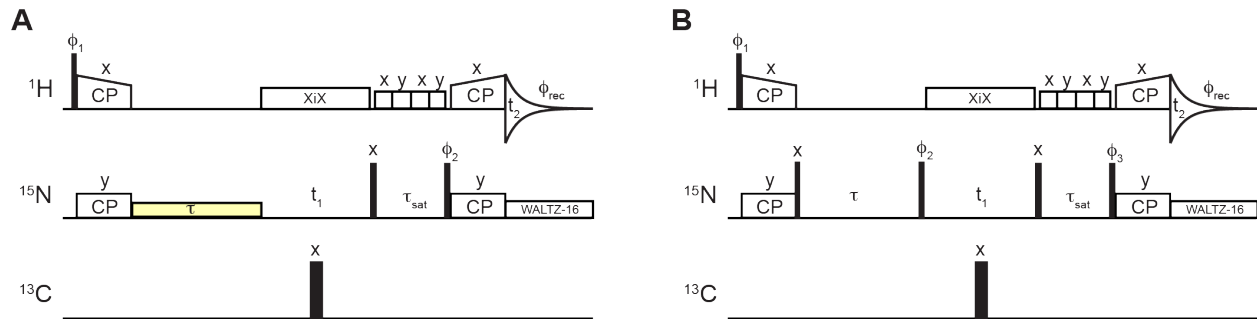
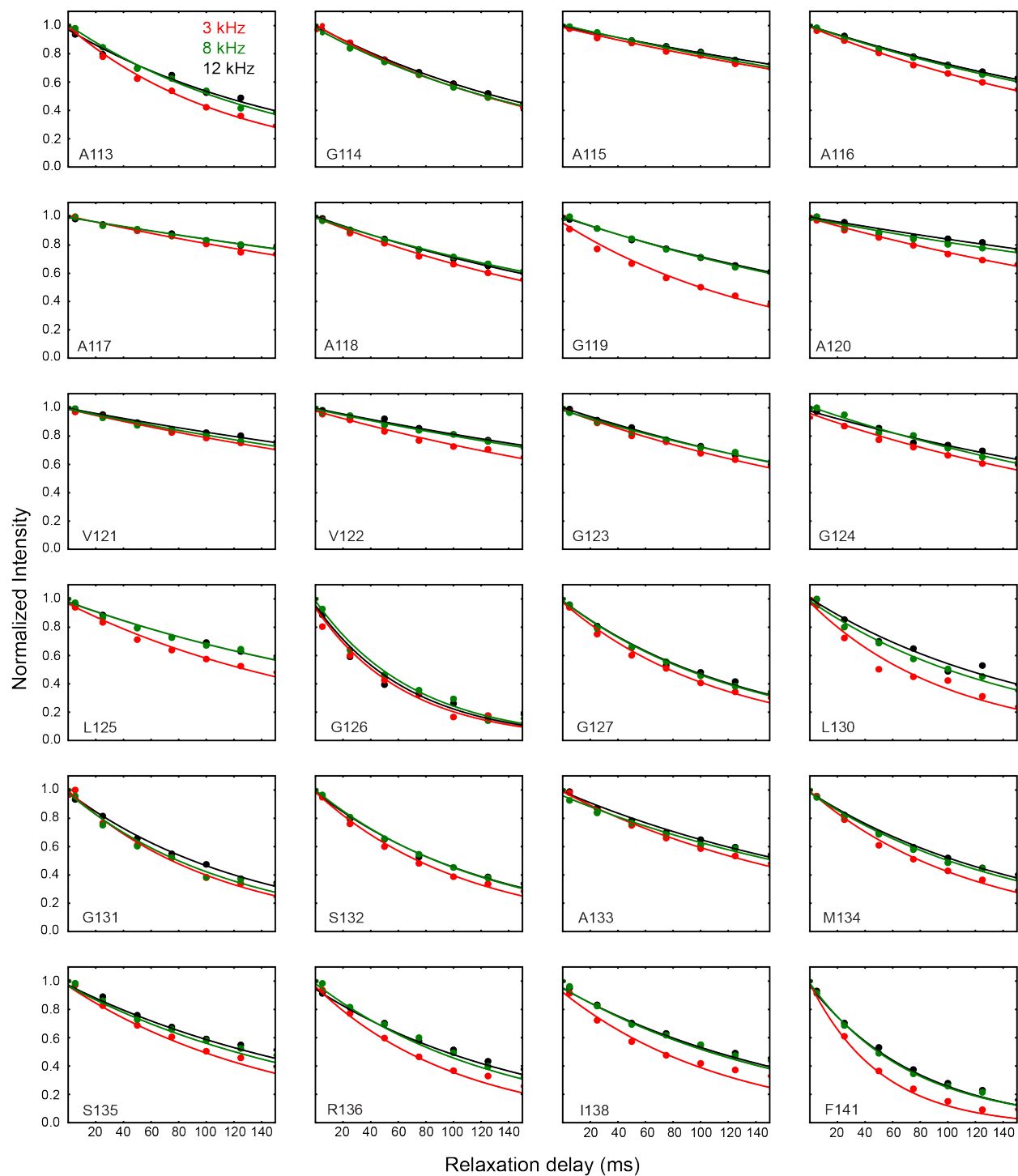


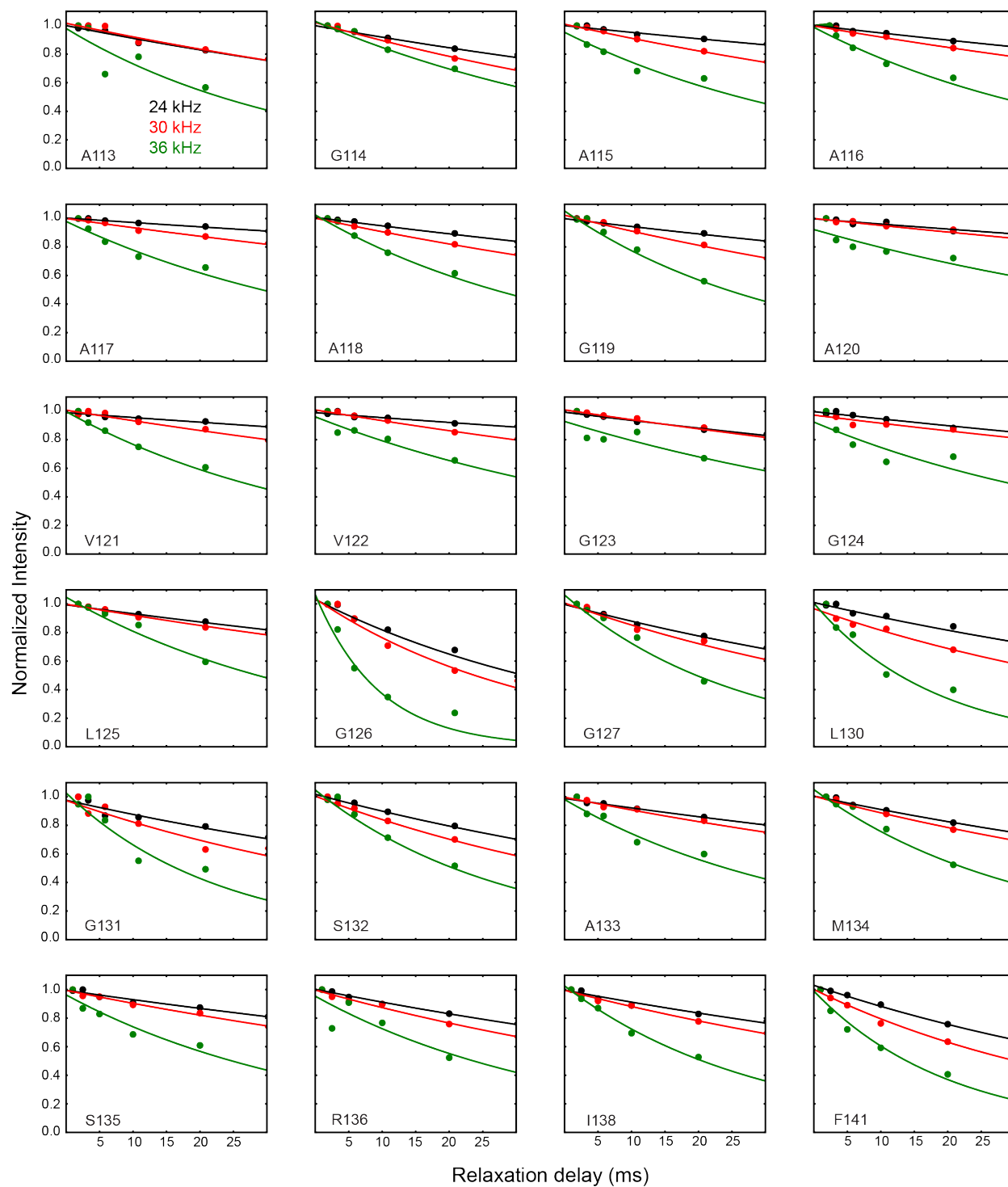
**Figure S1.** (A) 2D NCA projection from a 3D hCANH experiment for amyloid fibrils generated from  $^2\text{H}$ ,  $^{13}\text{C}$ ,  $^{15}\text{N}$ -labeled huPrP23-144 back-exchanged in a 1:1 mixture of  $\text{H}_2\text{O}$  and  $\text{D}_2\text{O}$ , recorded as described in the Experimental Section of the main text with a total measurement time of 10 h. (B) 2D NCO projection from a 3D hCONH experiment on the same fibril sample, recorded with a 6.5 h measurement time. (C,D) Representative strips for selected residues in huPrP23-144 fibrils taken from the (C) 3D hCANH and (D) 3D hCONH spectra.



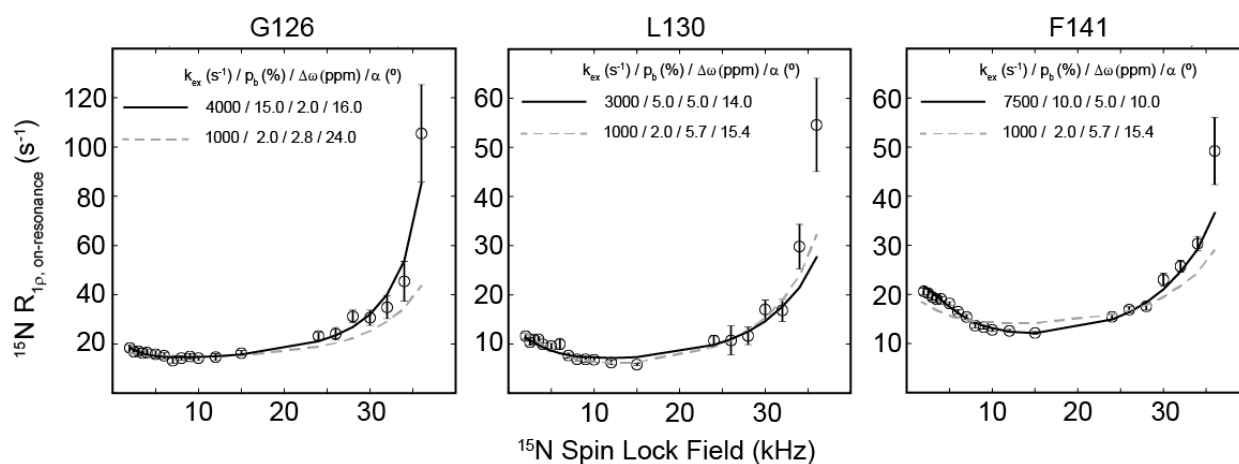
**Figure S2.** (A) Pulse sequence used to measure the residue-specific  $^{15}\text{N}$   $R_{1\rho}$  rate constants in a pseudo 3D fashion by varying the relaxation delay,  $\tau$ , for a specified amplitude of the  $^{15}\text{N}$  spin-lock field. The phase cycle was as follows:  $\phi_1 = y, -y$ ;  $\phi_2 = x, x, -x, -x$ ;  $\phi_{\text{rec}} = x, -x, -x, x$ . (B) Pulse sequence used to measure the residue-specific  $^{15}\text{N}$   $R_1$  rate constants in a pseudo 3D fashion by varying the relaxation delay,  $\tau$ . The phase cycle was as follows:  $\phi_1 = y, -y$ ;  $\phi_2 = x, x, -x, -x$ ;  $\phi_3 = x, x, x, x, -x, -x, -x, -x$ ;  $\phi_{\text{rec}} = x, -x, -x, x, -x, x, x, -x$ .



**Figure S3.** Residue-specific relaxation trajectories for huPrP23-144 fibrils recorded using the pulse sequence in Figure S2A with representative  $^{15}\text{N}$  spin-lock fields of 3, 8, and 12 kHz as indicated in the inset. Experimental trajectories are shown as circles and best fits to decaying single exponentials are shown as lines of the corresponding color.



**Figure S4.** Residue-specific relaxation trajectories for huPrP23-144 fibrils recorded using the pulse sequence in Figure S2A with representative  $^{15}\text{N}$  spin-lock fields of 24, 30, and 36 kHz as indicated in the inset. Experimental trajectories are shown as circles and best fits to decaying single exponentials are shown as lines of the corresponding color.



**Figure S5.**  $^{15}\text{N}$   $R_{1\rho}$  relaxation dispersion profiles for residues G126, L130 and F141 in huPrP23-144 amyloid fibrils, for which fitting the experimental RD data using independent values of the exchange rate ( $k_{\text{ex}}$ ) and minor conformer population ( $p_{\text{B}}$ ) yielded a statistically significant improvement in fit quality (i.e.,  $\chi^2$ ) according to an F-test, compared to the global fit with  $k_{\text{ex}} = 1,000 \text{ s}^{-1}$  and  $p_{\text{B}} = 2\%$  (see main text for additional details). The individual and global fits of the RD data are shown in solid and dashed lines, respectively, and the corresponding fit parameters are listed in the insets.