Supporting Information

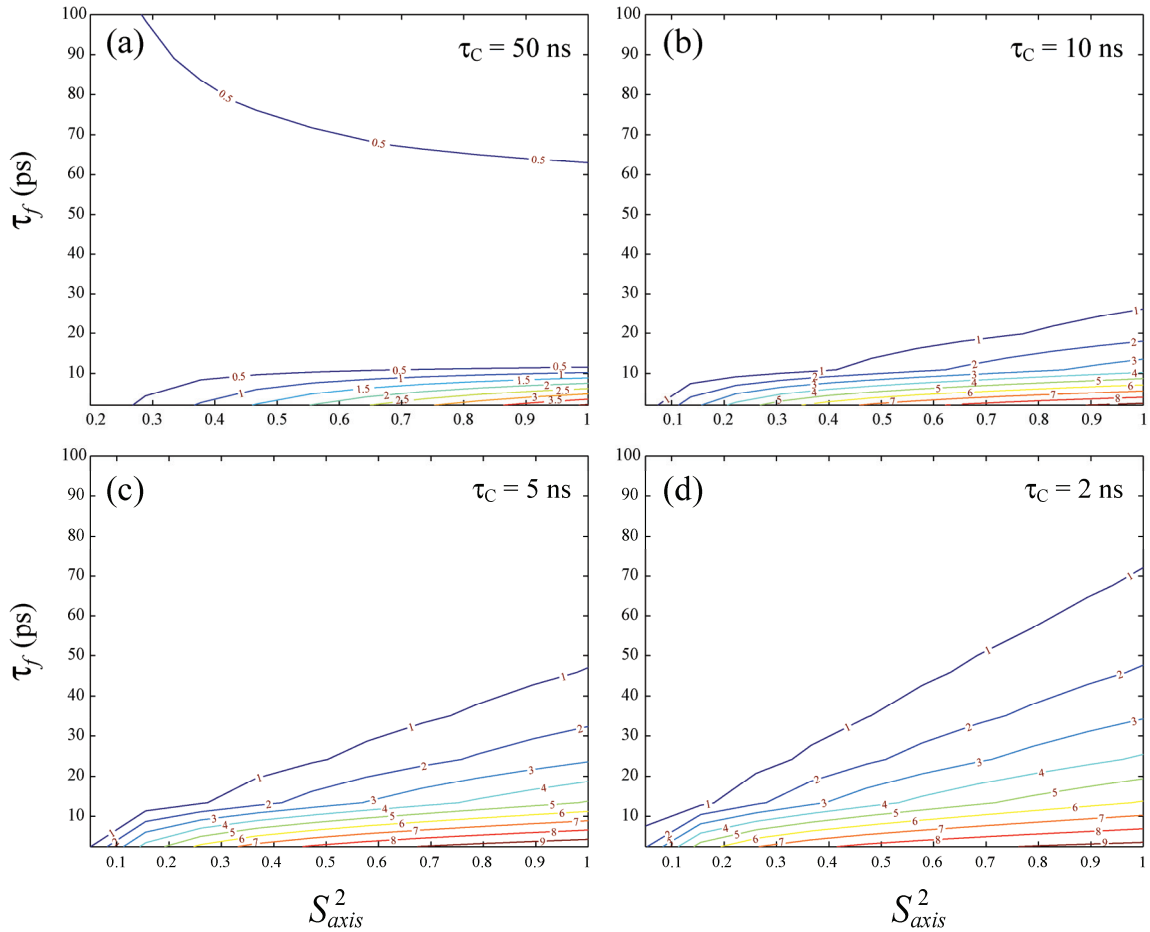

***Figure* S1. (a-d)** Color-coded contour plots of simulated errors in $R_1(M_L)$ as a function of (S^2_{axis}, τ_f) for different values of τ_C. The error values (in %) are indicated on top of each contour and are defined as $100*[R_1(M_L)-R_{1,\text{fitted}}(M_L)]/R_1(M_L)$ where $R_{1,\text{fitted}}(M_L)$ is the rate extracted from fitting the decay curves generated with eq. 11 to a single exponential decay function. The values chosen for τ_C correspond approximately to global rotational correlation times of MSG at 37 °C (a), protein L at 5 °C (b), protein L at 25 °C (c) and protein L at 45 °C (d). Values of $R_1(M_L)$ are strongly dependent only on τ_f in large molecules (MSG) and show some dependence on (S^2_{axis}, τ_f) in low-molecular-weight proteins (protein L).

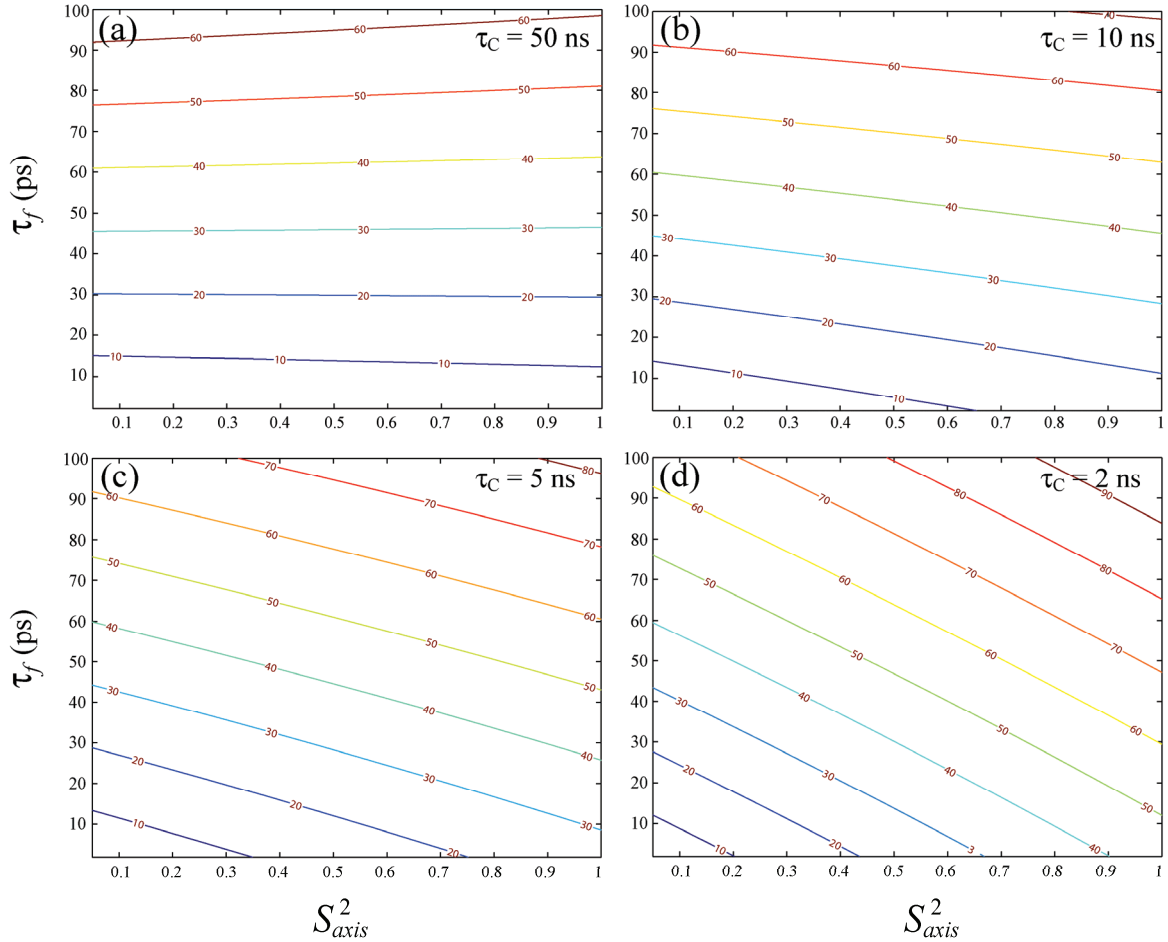

***Figure* S2. (a-d)** Color-coded contour plots of $R_1(M_L)$ (in s^{-1}) as a function of (S^2_{axis}, τ_f) for different values of τ_C.

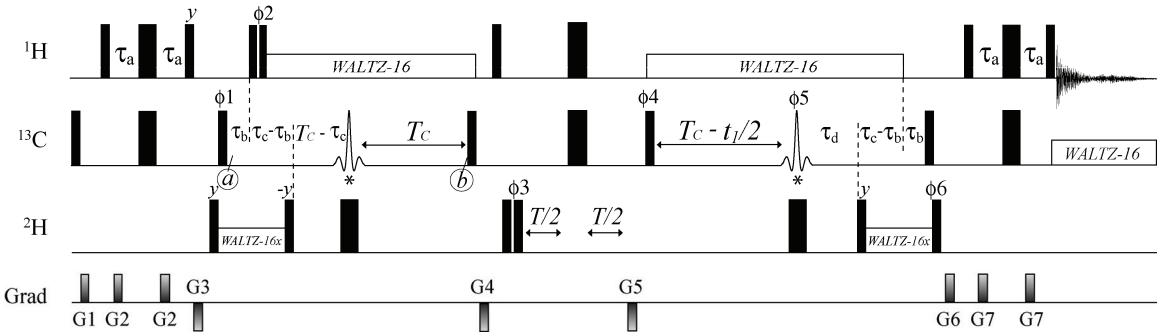

***Figure* S3.** Pulse-scheme for applications involving partially deuterated proteins dissolved in H_2O that actively selects for methyl isotopomers of the $^{13}CHD_2$ variety. All narrow(wide) rectangular pulses are applied with flip angles of 90(180)° along the *x*-axis unless indicated otherwise. All ^1H and ^{13}C pulses are applied with the highest possible power, while a 2 kHz field is used for ^2H pulses. ^{13}C, ^1H and ^2H WALTZ-16 decoupling[1] use 2.2, 5.3 and 0.7 kHz fields, respectively. The ^{13}C and ^2H carriers are placed at 20 and 1 ppm, respectively, while the ^1H carrier is placed initially at the water frequency (~4.7 ppm), shifted to the center of the methyl region (1 ppm) after the ^1H pulse with phase *y*, and shifted back to the water frequency after gradient G6. The pulses marked with asterisks are 400µs (500 MHz) RE-BURP[2] 180° pulses centered in the middle of the ^{13}C aliphatic region (42 ppm). Delays are: τ_a = 1.7 ms; τ_b = 3.85 ms; τ_c = 11.6 ms; $\tau_d = T_C + t_1/2 - \tau_c$; T_C = 14.5 ms; *T* is a variable relaxation delay. Evolution due to J_{CD} coupling between time-points *a* and *b* occurs for a time $2T_C - \tau_c = 1/(3J_{CD})$. The phase cycle is: $\phi1=x,-x$; $\phi2=8(x)$, $8(-x)$; $\phi3=2(x),2(-x)$; $\phi4=x$; $\phi5=4(x),4(y),4(-x),4(-y)$; $\phi6=2(y),2(-y)$; rec=$x,-x,-x,x,-x,x,x,-x$. The durations and strengths of the *z*-gradients in units of (ms;G/cm) are: G1=(0.5;5); G2=(0.3;3); G3=(1.5;-20); G4=(0.3;-25); G5=(0.4;-10); G6=(1;15); G7=(0.3;2). Quadrature detection in t_1 is achieved via States-TPPI[3] of $\phi4$.

References

(1) Shaka, A. J.; Keeler, J.; Frenkiel, T.; Freeman, R. *J. Magn.Reson.* **1983,** *52*, 335-338.

(2) Geen, H.; Freeman, R. *J. Magn. Reson.* **1991,** *93*, 93-141.

(3) Marion, D.; Ikura, M.; Tschudin, R.; Bax, A. *J. Magn. Reson.* **1989,** *85*, 393-399.