Supporting Information for

A General Protocol for Constructing Molecular Models of Nanodiscs

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Constructing a Cα-trace using geometrical equations.

It's possible to describe the α-helix using a geometric equation such as Eq. 1:

$$\begin{bmatrix} x_i \\ y_i \\ z_i \end{bmatrix} = \begin{bmatrix} x_0 \\ y_0 \\ z_0 \end{bmatrix} + \begin{bmatrix} r \cdot \sin(t \cdot i) \\ r \cdot \cos(t \cdot i) \\ p \cdot i \end{bmatrix} \quad (1)$$

Where $[x_i, y_i, z_i]$ is the vector identifying the position of the i-th C_α atom of the helix, $[x_0, y_0, z_0]$ indicates the origin for the helix system and the helical axis $\hat{\mathbf{n}}$ is parallel with the z-axis. The three parameters, radius (r), translation or pitch (p) and turn angle (t) are chosen to be 2.314 Å, 100.1, 1.516 Å, respectively.

Since we are interested in building a circular α-helix in the xy-plane, we need to first rotate the helical axis to be parallel with the y-axis instead. Change the helical axis from being parallel with $\hat{\boldsymbol{n}}$ to be parallel with $\hat{\boldsymbol{j}}$. In order to achieve this we need to apply a transformation such that ($\hat{\boldsymbol{n}} = \hat{\mathbf{j}}$) ; this is a rotation around the x axis of -90 degrees.

The general expression for the three dimensional rotation matrix around an axis parallel to $\vec{\boldsymbol{u}}$ with an angle θ can be written as:

$$\boldsymbol{R}(\vec{\boldsymbol{u}}|\theta) = \begin{bmatrix} cos\theta + u_x^2 \cdot (1 - cos\theta) & u_x u_y \cdot (1 - cos\theta) - u_z \cdot sin\theta & u_x u_z \cdot (1 - cos\theta) + u_y \cdot sin\theta \\ u_x u_y \cdot (1 - cos\theta) + u_z \cdot sin\theta & cos\theta + u_y^2 \cdot (1 - cos\theta) & u_y u_z \cdot (1 - cos\theta) - u_x \cdot sin\theta \\ u_x u_z \cdot (1 - cos\theta) - u_y \cdot sin\theta & u_y u_z \cdot (1 - cos\theta) + u_x \cdot sin\theta & cos\theta + u_z^2 \cdot (1 - cos\theta) \end{bmatrix} \quad (2)$$

We can apply $\vec{\boldsymbol{u}}$ = (1,0,0) and θ=90° into the general form for the rotation matrix resulting in R':

$$\boldsymbol{R}' = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 0 & 1 \\ 0 & -1 & 0 \end{bmatrix} \quad (3)$$

The positions of the Cα atoms of an α-helix along the y-axis will then be given by:

$$\begin{bmatrix} x_i \\ y_i \\ z_i \end{bmatrix} = \begin{bmatrix} x_0 \\ y_0 \\ z_0 \end{bmatrix} + \mathbf{R}' \begin{bmatrix} r \cdot \sin(t \cdot i) \\ r \cdot \cos(t \cdot i) \\ p \cdot i \end{bmatrix} = \begin{bmatrix} x_0 \\ y_0 \\ z_0 \end{bmatrix} + \quad (4)$$

The helical axis is now parallel with the y-axis. We then need to formulate the general form for building an α-helix in a circle of radius R_0 in the xy-plane. The helical axis ($\hat{\boldsymbol{n}}$) is constantly updated (every turn, 4 consecutive Cα atoms) with a corresponding origin for each selected point on the circle. This means the origin can be described as:

$$Origin = \begin{bmatrix} R_0 \cdot \cos\alpha \\ R_0 \cdot \sin\alpha \\ 0 \end{bmatrix} \quad (5)$$

Where the angle of rotation $\theta = \alpha$ and $\vec{\boldsymbol{u}}$ = (0,0,1), in the general rotation matrix from in Eq.2, which results in the matrix describing the rotation in the xy-plane, around the z-axis with the form:

$$R'' = \begin{bmatrix} cos\alpha & -sin\alpha & 0 \\ sin\alpha & cos\alpha & 0 \\ 0 & 0 & 1 \end{bmatrix} \quad (6)$$

The angle α is described as

$$\alpha = 2 \cdot \frac{\pi}{number\ of\ turns} \quad (7)$$

Where the number of turns is calculated from the input sequence by:

$$number\ of\ turns = \frac{number\ of\ residues\ in\ the\ sequence}{4} + 1 \quad (8)$$

The Cα positions of a circular α-helix in the xy-axis with radius R_0, can then be obtained with the following Eq. 9:

$$\begin{bmatrix} x_i \\ y_i \\ z_i \end{bmatrix} = \begin{bmatrix} x_0 \\ y_0 \\ z_0 \end{bmatrix} + \mathbf{R}'' \begin{bmatrix} r \cdot \sin(t \cdot i) \\ p \cdot i \\ -r \cdot \cos(t \cdot i) \end{bmatrix} = \begin{bmatrix} R_0 \cos\alpha \\ R_0 \sin\alpha \\ 0 \end{bmatrix} + \begin{bmatrix} r \cdot \sin(t \cdot i) \cdot \cos\alpha - p \cdot i \cdot \sin\alpha \\ r \cdot \sin(t \cdot i) \cdot \sin\alpha + p \cdot i \cdot \cos\alpha \\ -r \cdot \cos(t \cdot i) \end{bmatrix} \quad (9)$$

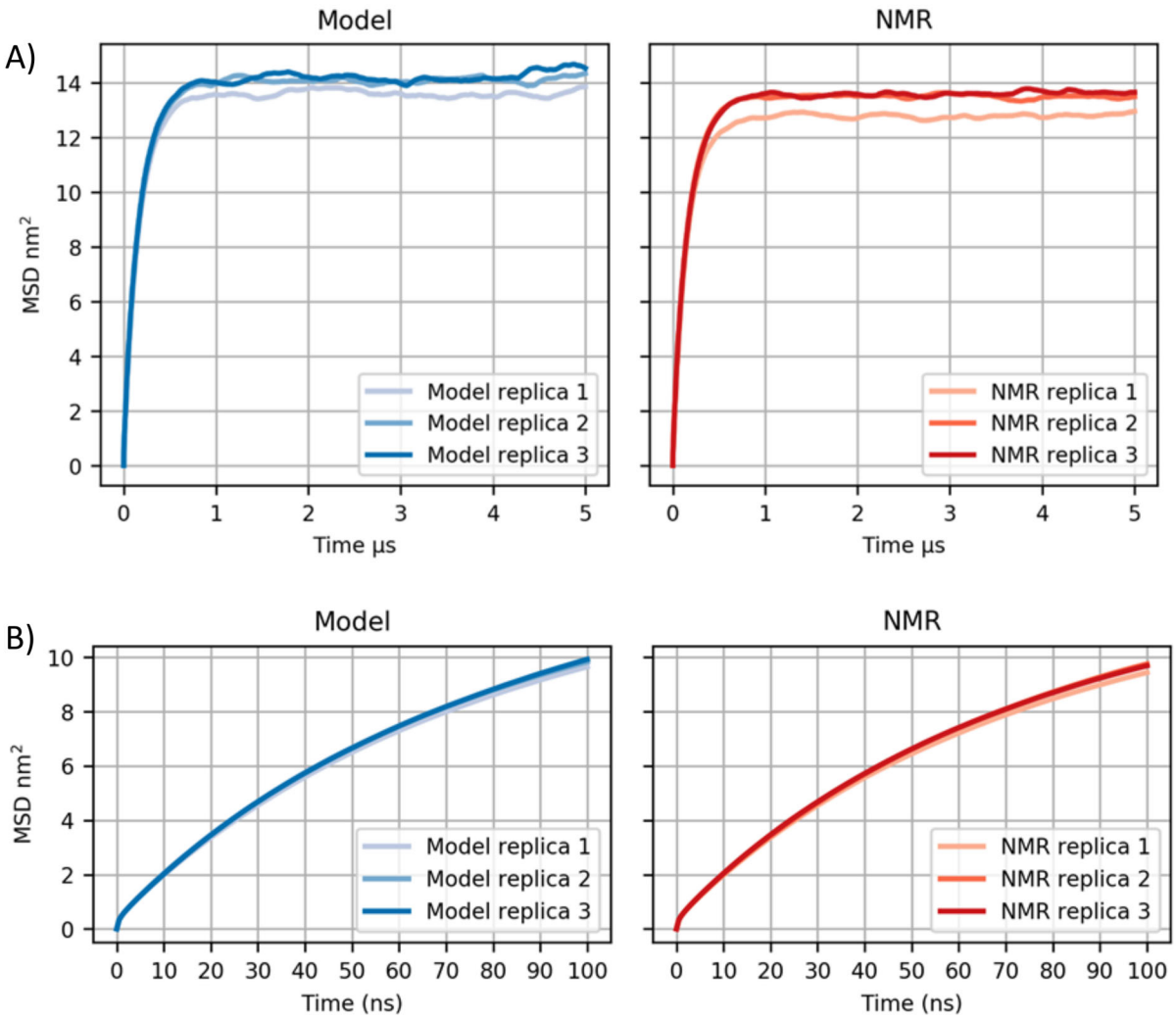

Figure S1: MSD of the Model and NMR systems for 5 µs and the first 100 ns in respectively A and B.

Regression of secondary structure chemical shift data

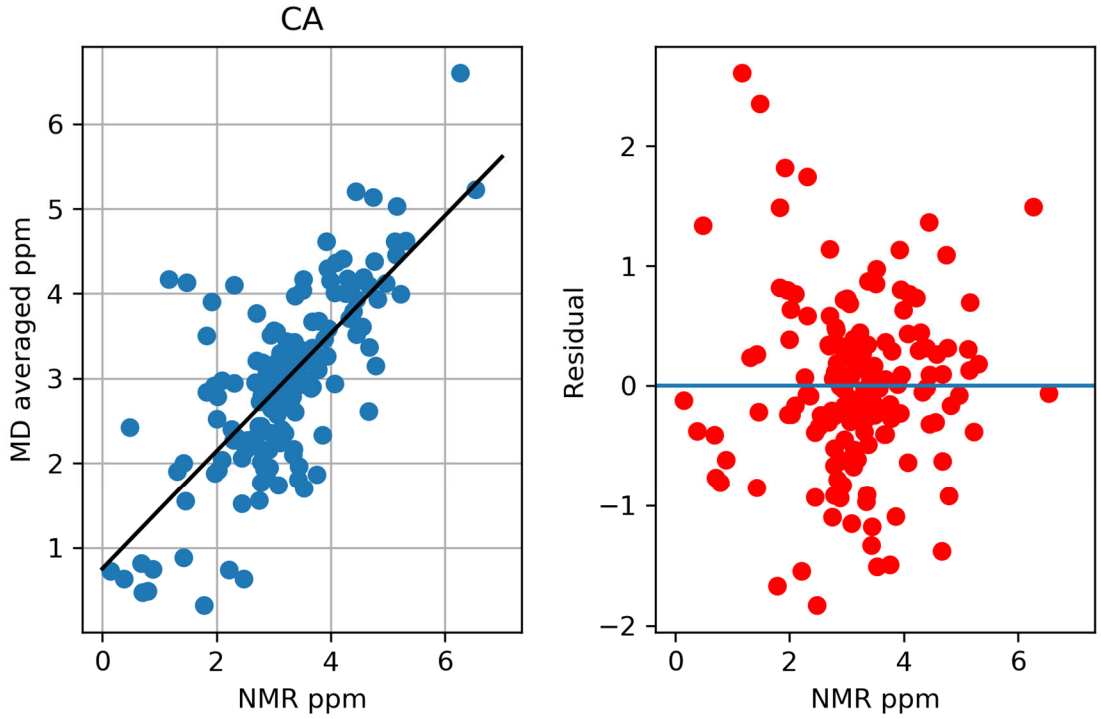

Figure S2: On the left, the Cα chemical shifts from the MD ensemble are plotted vs the chemical shifts from the NMR ensemble, with the black line representing the linear regression, without any weights. On the right, the residual is plotted.

Difference between the predicted Cα chemical shifts from the MD ensemble and the measured chemical shifts from the NMR ensemble

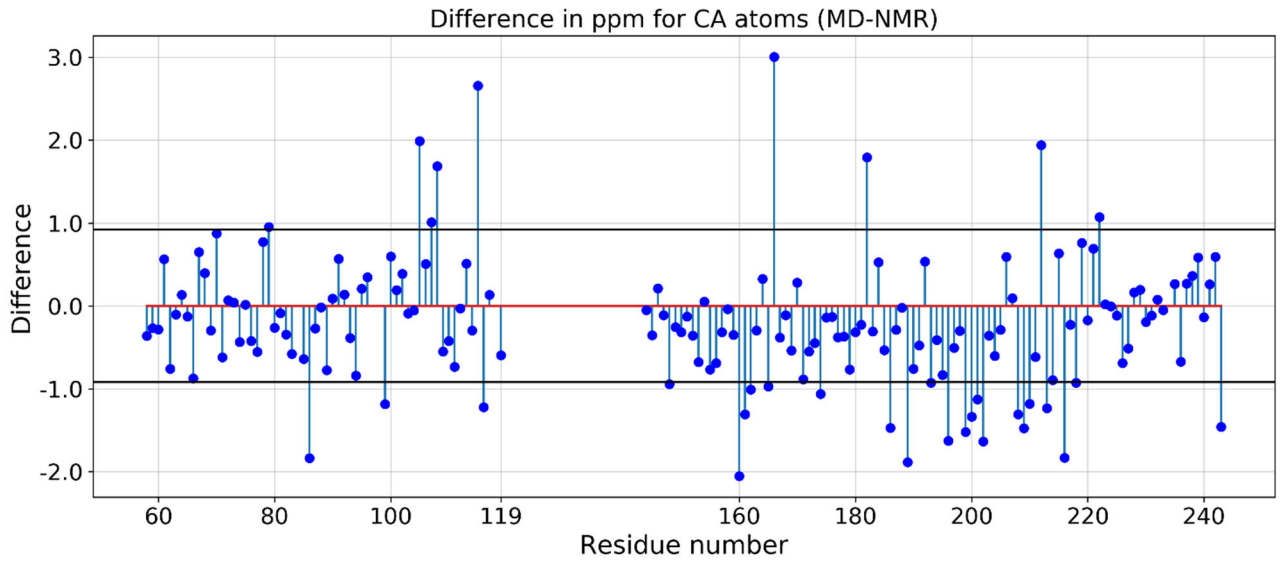

Figure S3: The difference in chemical shift for Cα atoms for the MD and NMR ensemble. The standard error for the software SPARTA+ is 0.92 ppm for Cα atoms, and shows here as a black horizontal line.

The uncertainty for using the SPARTA+ software for predicting the chemical shifts in the MD ensemble is 0.92 ppm for Cα-atoms. The uncertainty for the measured chemical shifts from NMR depends on several factors, but typically are around 1-2 ppm for Cα-atoms. When comparing the chemical shifts from the MD and NMR ensemble, the uncertainty from the SPARTA+ software and from the experiment needs to be added.

Weighted least squared of the secondary structure chemical shift (CS)

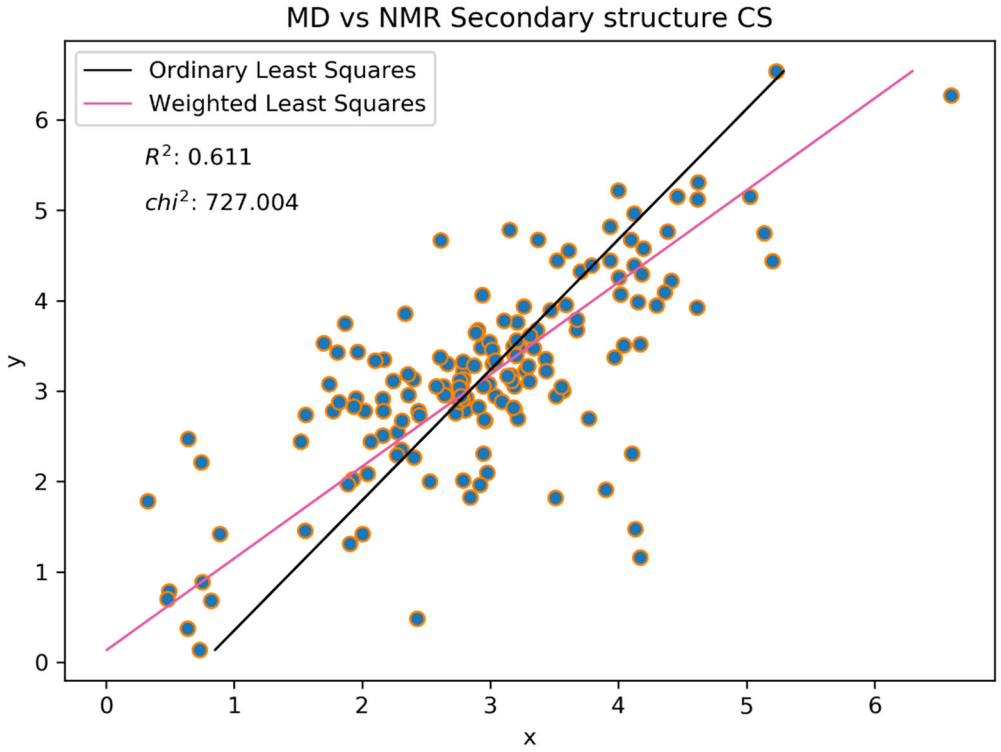

Figure S4: The secondary structure chemical shift (CS) from the MD ensemble on the x-axis vs the secondary structure chemical shift from the NMR ensemble on the y-axis. The weights used are the variance between the three MD replicas.

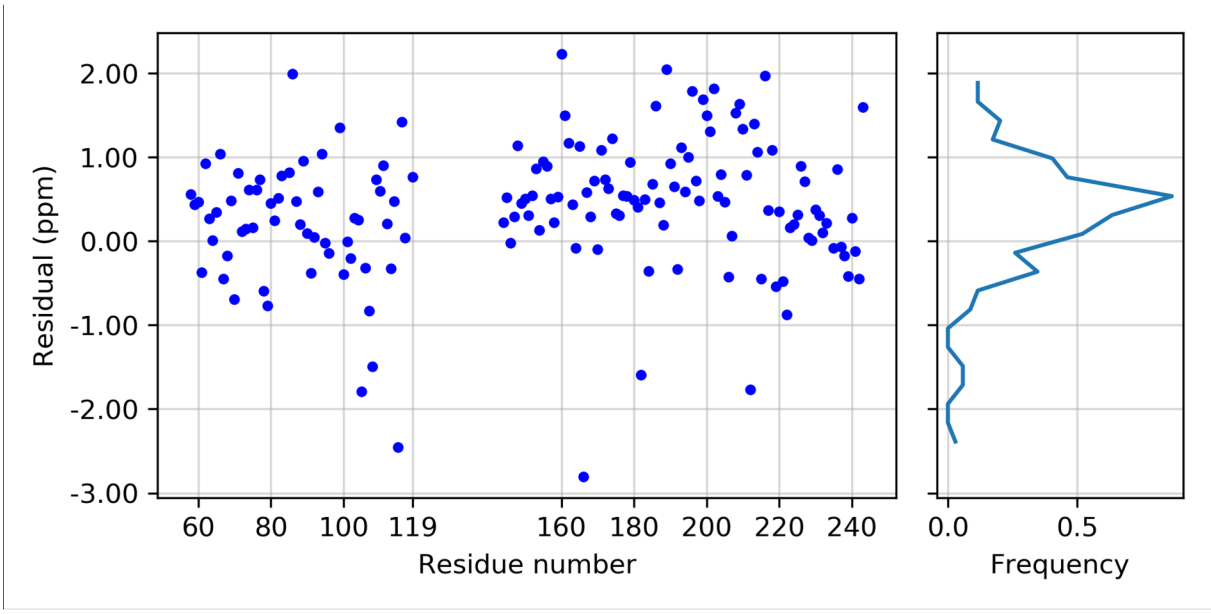

Figure S5: Residuals of the secondary structure chemical shift from the MD ensemble vs the secondary structure chemical shift from the NMR ensemble. From the weighted least squared regression using weights, the variance between the three MD replicas.

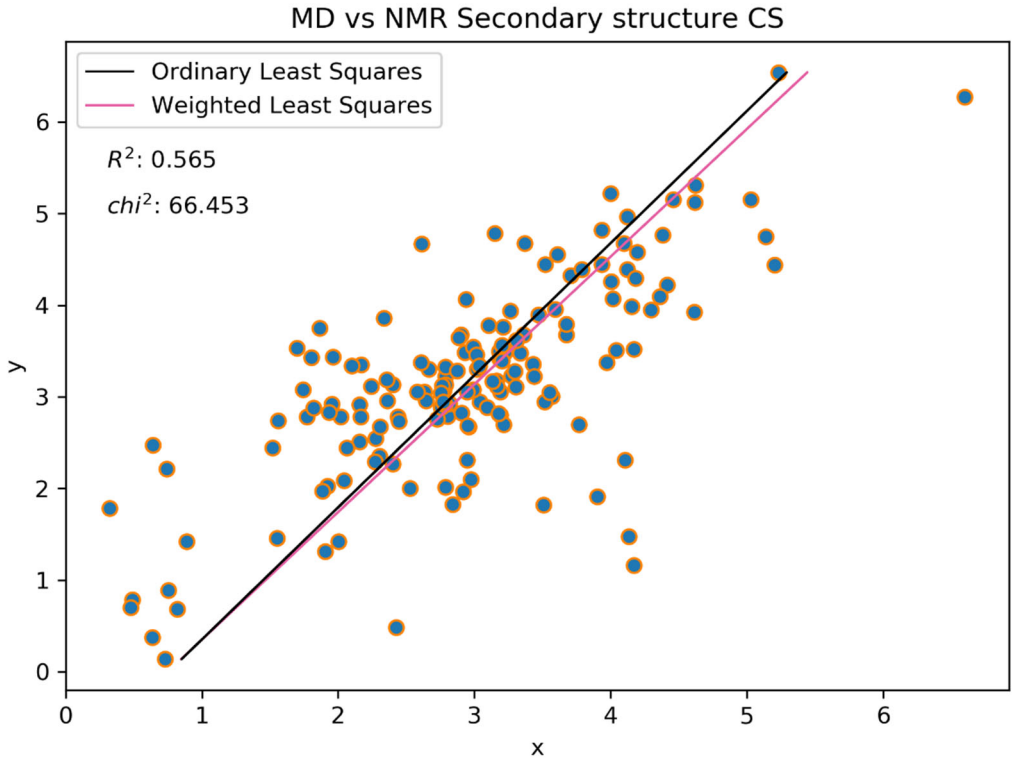

Figure S6: The Secondary structure chemical shift (CS) from the MD ensemble on the x-axis vs the secondary structure chemical shift from the NMR ensemble on the y-axis. The weights used are the variance between the three MD replicas plus the uncertainty from the predictor SPARTA+ (0.92 ppm).

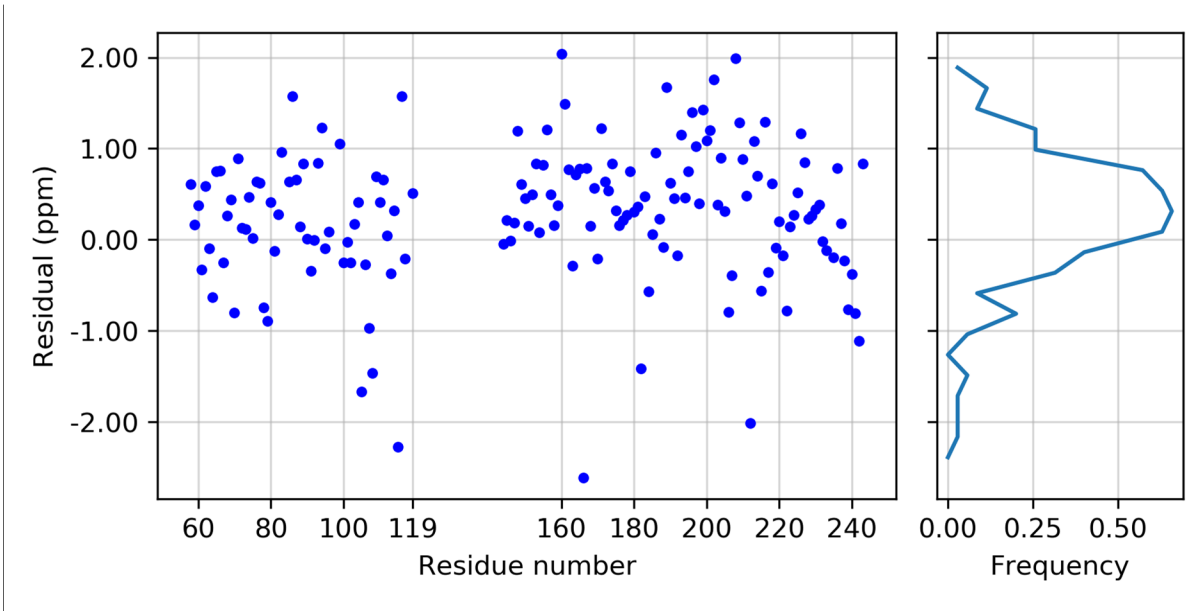

Figure S7: Residuals of the secondary structure chemical shift from the MD ensemble vs the secondary structure chemical shift from the NMR ensemble. From the weighted least squared regression using weights, the variance between the three MD replicas plus the uncertainty from the predictor SPARTA+ (0.92 ppm).

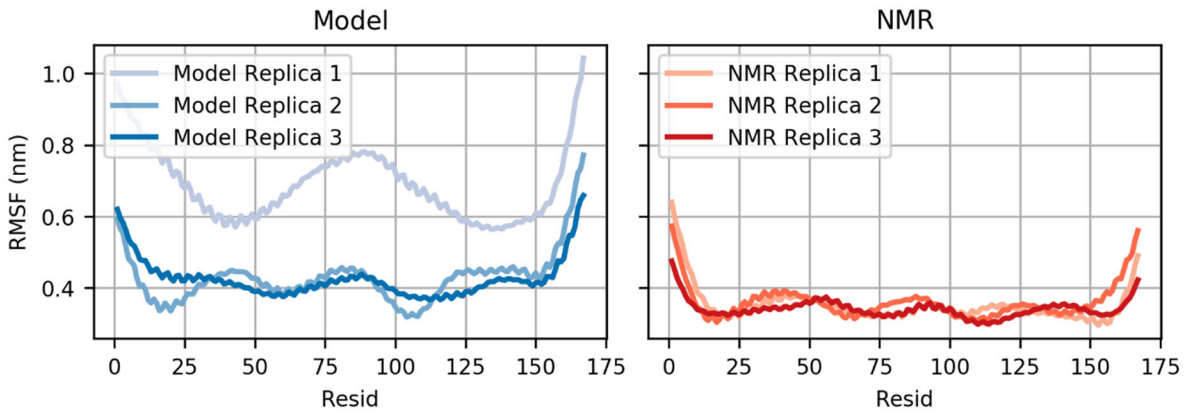

Figure S8: RMSF of backbone beads of the MSPs for the Model and NMR systems, using the first frame as reference structure. The RMSF is averaged across the two MSP chains and calculated between 2.5 to 4 µs.

Table S1: P-values from a one-sided Mann Whitney test of the shape factors calculated for the systems 1D1, 1E3D1, 2N2, NW9, NW11, and NW13.

	1D1	1E3D1	2N2	NW9	NW11	NW13
1D1	0.5	0	0	0,3	3,6E-267	3,6E-258
1E3D1		0.5	6,6E-81	7,1E-237	1,7E-17	3,8E-70
2N2			0.5	4,2E-302	3,7E-33	0,1
NW9				0.5	1,4E-233	3,3e.251
NW11					0.5	6,2E-28
NW13						0.5