Supplementary Material for The binding process of a non-specific sequence enzyme with DNA

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Computational details

The desolvation energy of the protein (DNA), due to the presence of DNA (protein), may be approximated (1) as

$$\Delta G_{ds,BD} = \alpha \frac{\varepsilon_{out} - \varepsilon_{in}}{\varepsilon_{out}(2\varepsilon_{out} + \varepsilon_{in})} \sum_{ij} (1 + \kappa r_{ij})^2 e^{-2\kappa r_{ij}} \frac{q_i^{\,2} a_j^{\,3}}{r_{ij}^{\,4}}, \qquad (1)$$

where α is the scaling factor and is set to 1.67 from Wade (2), κ is the Debye-Hückel screening parameter, q_i is the effective charge on the ith atom of the protein (DNA), a_j is the radius of the jth atom of the DNA (protein), and r_{ij} is the distance between the two atoms. The summation is carried out over all possible pairs of effective charges on the protein (DNA) with atoms on the DNA (protein).

Translational and rotational diffusion constant of the protein, $D_{T,pro}$ and $D_{R,pro}$ are estimated to be 0.0132 Å^2/ps and 3.572 × 10^{-5} radian^2/ps, respectively, by using the Stokes-Einstein relation and assuming a spherical shape: $D_{T,pro} = \frac{k_B T}{6\pi\eta R}$, $D_{R,pro} = \frac{k_B T}{8\pi\eta R^3}$,

where η is the viscosity of the solvent at T = 300 K, and R is the effective hydrodynamic radius of the protein. The translational and rotational diffusion constant of the DNA, $D_{T,DNA}$ and $D_{R,DNA}$, are estimated to be 0.01376 Å^2/ps and 2.8445 × 10^{-5} radian^2/ps, respectively, by modeling the short fragment of DNA as a rod (3),

$$D_{T,DNA} = \frac{k_B T}{3\pi\eta L}\left(\ln\frac{L}{d} + \nu\right), \text{ with } \nu = 0.312 + 0.565\left(\frac{L}{d}\right)^{-1} - 0.100\left(\frac{L}{d}\right)^{-2}, \qquad (2)$$

$$D_{R,DNA} = \frac{3k_B T}{\pi\eta L^3}\left(\ln\frac{L}{d} + \delta\right), \text{ with } \delta = -0.662 + 0.917\left(\frac{L}{d}\right)^{-1} - 0.050\left(\frac{L}{d}\right)^{-2}, \qquad (3)$$

where L = 40.8 Å and d = 20.0 Å are the length and diameter of the rod, respectively. Here $\left(\ln\frac{L}{d} + \nu\right)$ and $\left(\ln\frac{L}{d} + \delta\right)$ are the traditional end effect corrections.

References

1. Elcock, A.H., R.R. Gabdoulline, R.C. Wade, and J.A. McCammon. 1999. Computer simulation of protein-protein association kinetics: acetylcholinesterase-fasciculin. J. Mol. Biol. 291:149-162.
2. Gabdoulline, R.R., and R.C. Wade. 2001. Protein-protein association: Investigation of factors influencing association rates by Brownian Dynamics simulations. J. Mol. Biol., 306:1139-1155.
3. Tirado, M.M., C.L. Mainez, and J.G. de la Torre. 1984. Comparison of theories for the translational and rotational diffusion coefficients of rod-like macromolecules. Application to short DNA fragments. J. Chem. Phys. 4:2047-2052.

Supplementary Table

Model II

	d_{min} (Å)	r (Å)	z (Å)	φ (º)	r_p (Å)	θ_P (º)	φ_P (º)
initial	13.5	36.5	0.0	0.0	10.6	152.3	0.0
approach (~350 ps)	4.4	26.0	-8.7	-18.0	11.1	143.1	-35.3
encounter (~3 ns)	2.6	20.2	0.17	-3.7	10.9	125.2	1.9
association (50~100ns)	2.6	22.5	-0.3	0.1	11.0	111.2	-7.4
	(0.1)	(0.8)	(1.2)	(5.2)	(0.3)	(7.5)	(5.4)

Model III

	d_{min} (Å)	r (Å)	z (Å)	φ (º)	r_p (Å)	θ_P (º)	φ_P (º)
initial	12.3	36.5	0.0	50.0	10.6	152.3	50.0
approach (~580 ps)	2.7	25.6	-5.7	12.0	11.7	136.8	8.0
encounter (~29 ns)	2.7	22.7	-14.4	-43.3	11.4	86.0	-61.9
association (30~100ns)	2.7	22.6	-12.7	-36.3	11.4	89.7	-52.5
	(0.1)	(0.7)	(2.1)	(5.3)	(0.3)	(7.5)	(6.7)

Model VI

	d_{min} (Å)	r (Å)	z (Å)	φ (º)	r_p (Å)	θ_P (º)	φ_P (º)
initial	12.9	36.5	0.0	110.0	10.6	152.3	110.0
approach (~420 ps)	3.06	28.3	-0.6	153.8	11.3	163.0	106.7
encounter (~49 ns)	2.5	19.6	-6.3	151.3	11.0	118.8	141.1

association (50~110 ns)	2.6	19.0	-6.2	151.2	10.8	124.2	139.8
	(0.1)	(0.4)	(1.0)	(3.0)	(0.3)	(6.1)	(4.6)
			Model V				
	d_{min} (Å)	r (Å)	z (Å)	φ (º)	r_p (Å)	θ_P (º)	φ_P (º)
initial	7.1	36.5	0.0	0.0	10.6	152.3	90.0
approach (~250 ps)	4.41	32.1	4.4	42.1	11.4	128.6	123.9
encounter (~ 59 ns)	2.6	24.2	2.1	-32.2	10.7	132.5	36.4
association (60~100ns)	2.6	24.1	1.5	-32.4	10.8	131.1	33.6
	(0.1)	(0.4)	(0.8)	(3.6)	(0.3)	(5.8)	(4.7)
			Model VI				
	d_{min} (Å)	r (Å)	z (Å)	φ (º)	r_p (Å)	θ_P (º)	φ_P (º)
initial	9.6	36.5	0.0	0.0	10.6	152.3	-90.0
approach (~ 650 ps)	2.8	35.1	1.87	-30.0	12.5	144.7	-122.7
encounter (~40 ns)	2.6	26.7	-9.2	47.1	12.5	137.4	-28.7
association (50~100 ns)	2.7	27.0	-11.2	45.4	12.9	144.5	-32.6
	(0.1)	(0.6)	(1.3)	(3.4)	(1.1)	(6.0)	(19.6)

Table S1. The position and orientation of the protein respect to the DNA at the starting point and at the end of each binding stage. For the associating stage, the average and the standard deviation in parenthesis are shown.

Supplementary Figure legends

Figure S1. The total electrostatic binding free energy $\Delta G_{ele,MD}$ in variation with r and φ.
Figure S2. Time development of the binding free energy of the complex. Here the entropy term is not shown in the calculation of the total binding free energy.
Figure S3. Time development of the position and orientation of the protein with respect to the DNA for Model I.
Figure S4. Time development of the position and orientation of the protein with respect to the DNA for Model II.
Figure S5. Time development of the position and orientation of the protein with respect to the DNA for Model III.
Figure S6. Time development of the position and orientation of the protein with respect to the DNA for Model IV.
Figure S7. Time development of the position and orientation of the protein with respect to the DNA for Model V.
Figure S8. Time development of the position and orientation of the protein with respect to the DNA for Model VI.

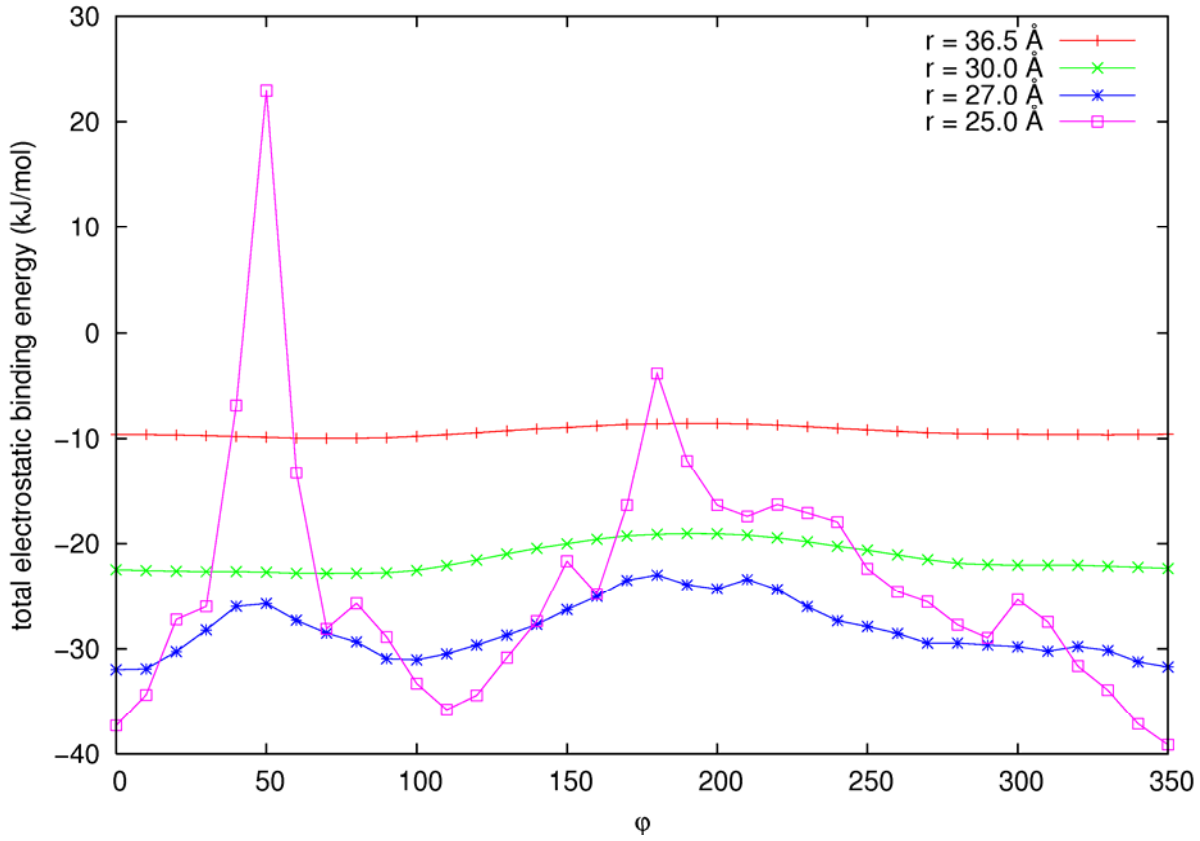
r = 36.5 Å
r = 30.0 Å
r = 27.0 Å
r = 25.0 Å
total electrostatic binding energy (kJ/mol)
φ
30
20
10
0
−10
−20
−30
−40
0
50
100
150
200
250
300
350

Figure S1

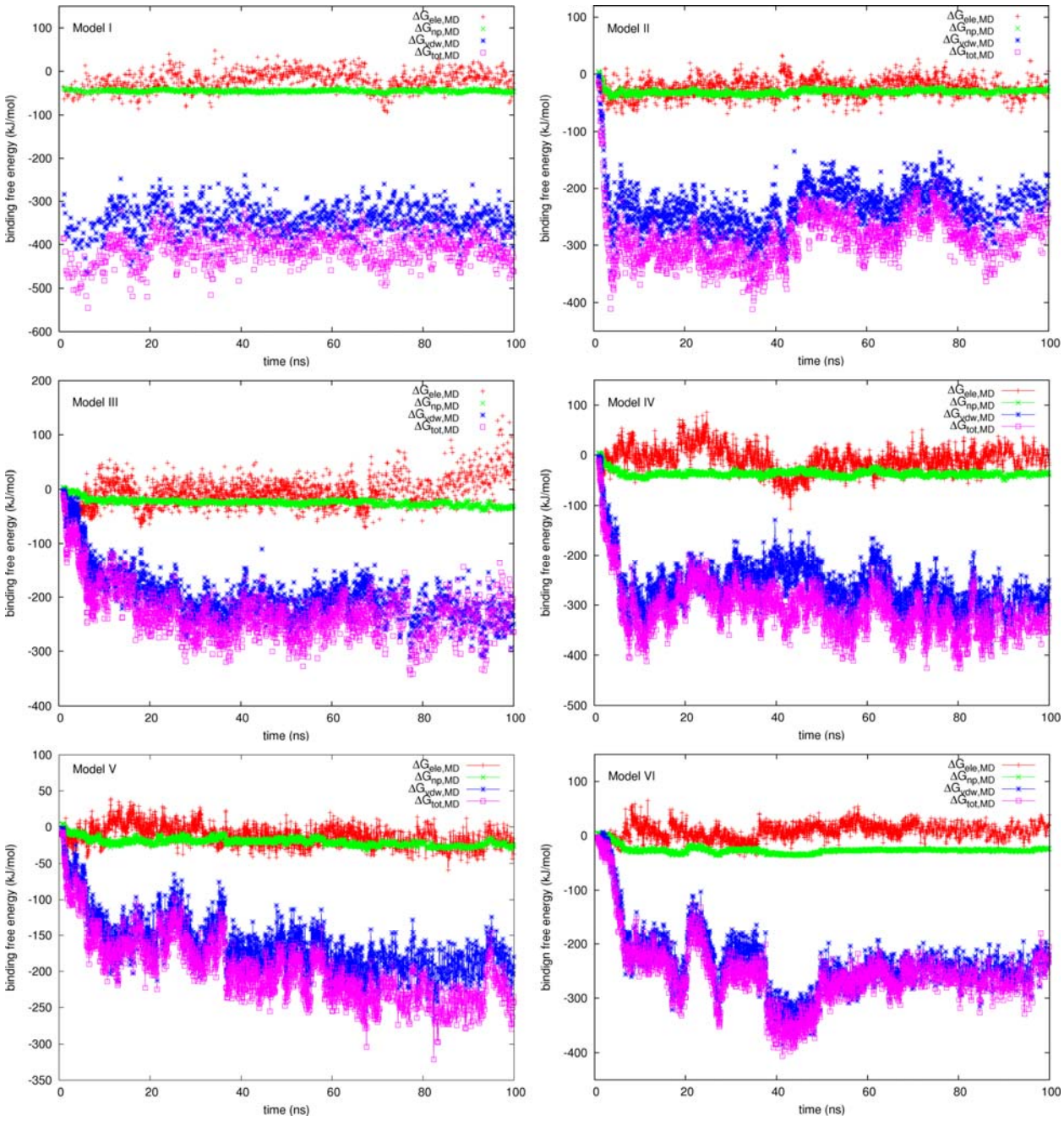
Model I
Model II
Model III
Model IV
Model V
Model VI
ΔG_ele,MD
ΔG_np,MD
ΔG_vdw,MD
ΔG_tot,MD
binding free energy (kJ/mol)
bindign free energy (kJ/mol)
time (ns)

Figure S2

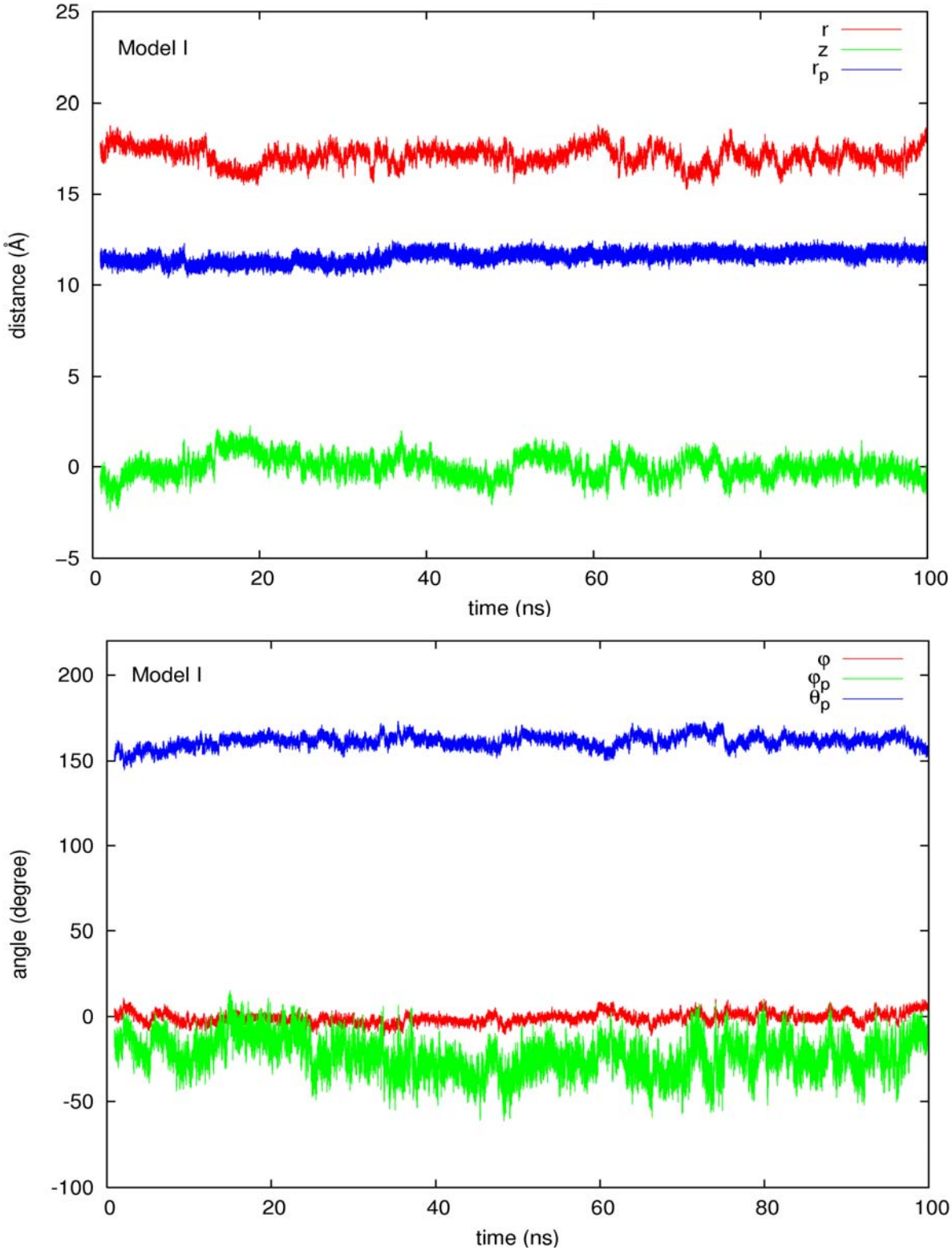
Model I
r
z
r_p
distance (Å)
time (ns)
Model I
φ
φ_p
θ_p
angle (degree)
time (ns)

Figure S3

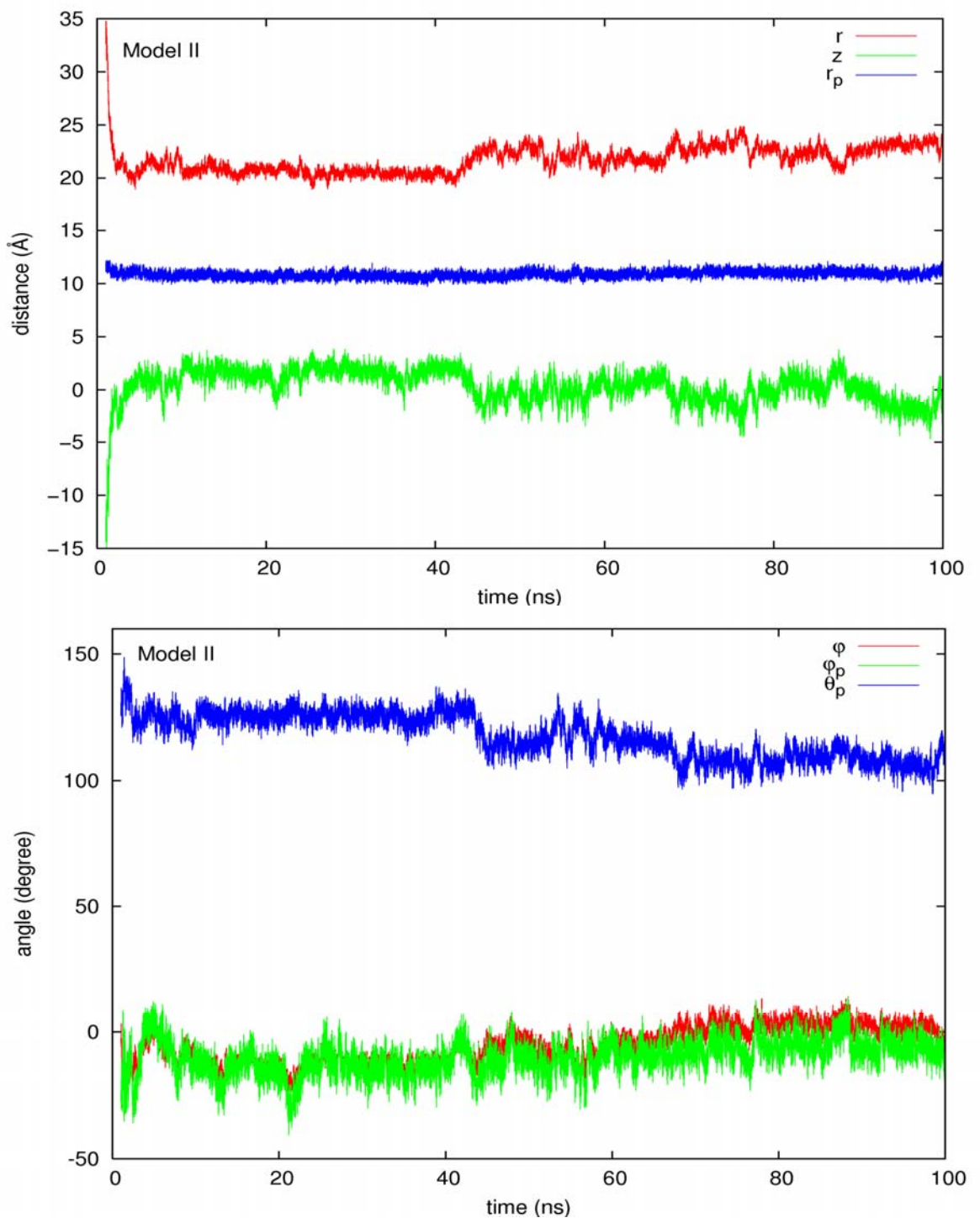
Model II
r
z
r_p
distance (Å)
time (ns)
Model II
φ
φ_p
θ_p
angle (degree)
time (ns)

Figure S4

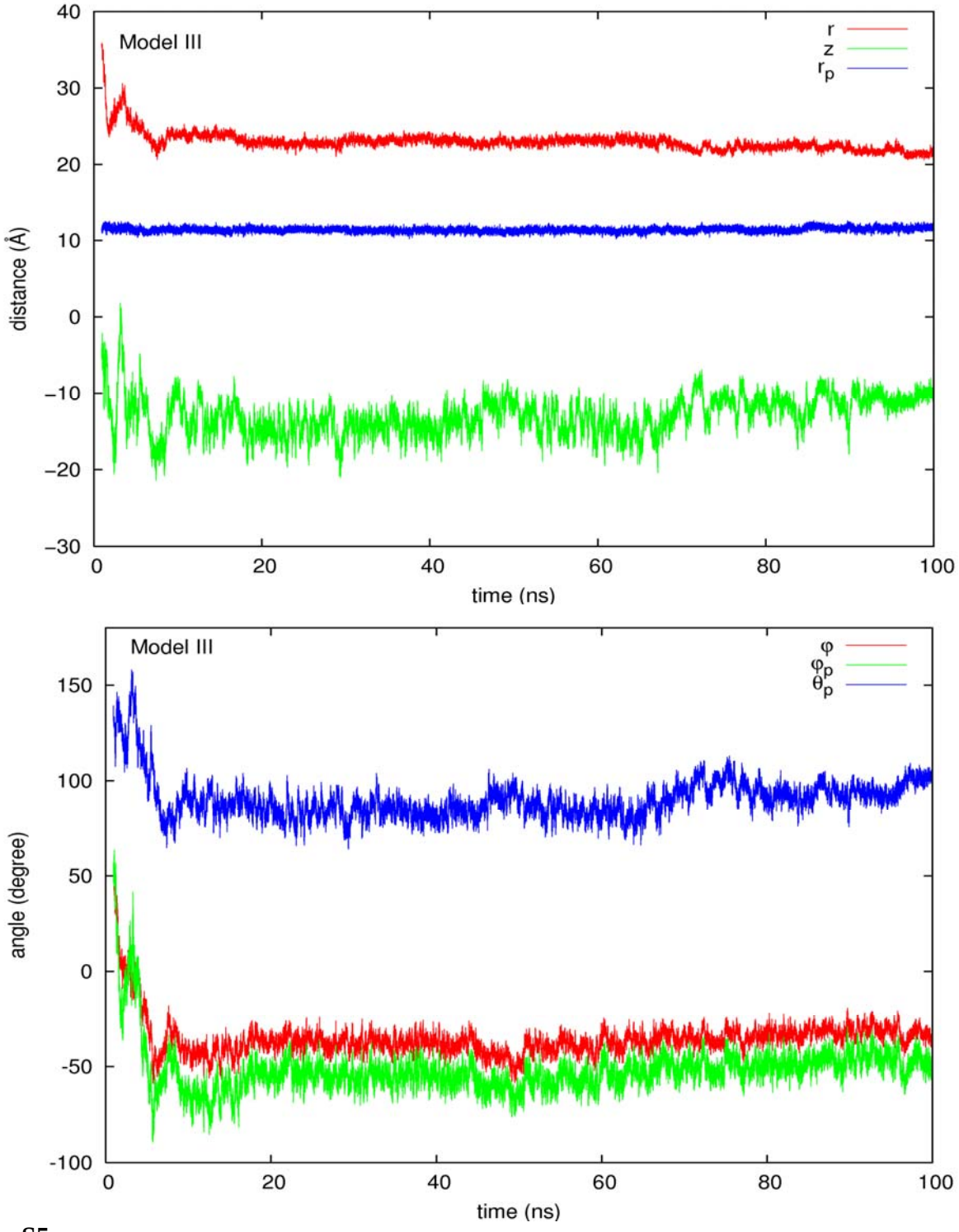
Model III
r
z
r_p
distance (Å)
time (ns)
Model III
φ
φ_p
θ_p
angle (degree)
time (ns)

Figure S5

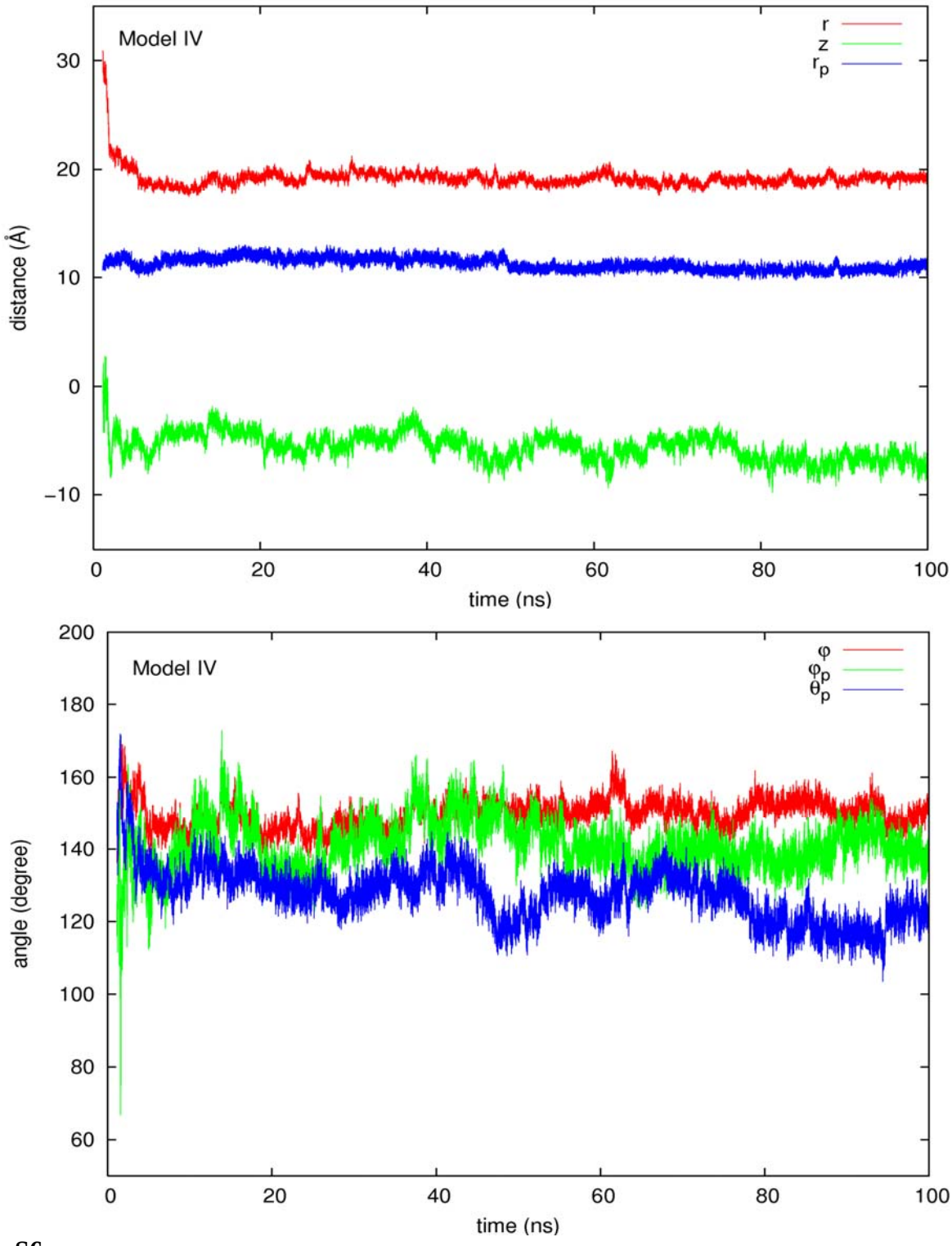
Model IV
r
z
r_p
distance (Å)
30
20
10
0
−10
0
20
40
60
80
100
time (ns)
Model IV
φ
φ_p
θ_p
angle (degree)
200
180
160
140
120
100
80
60
0
20
40
60
80
100
time (ns)

Figure S6

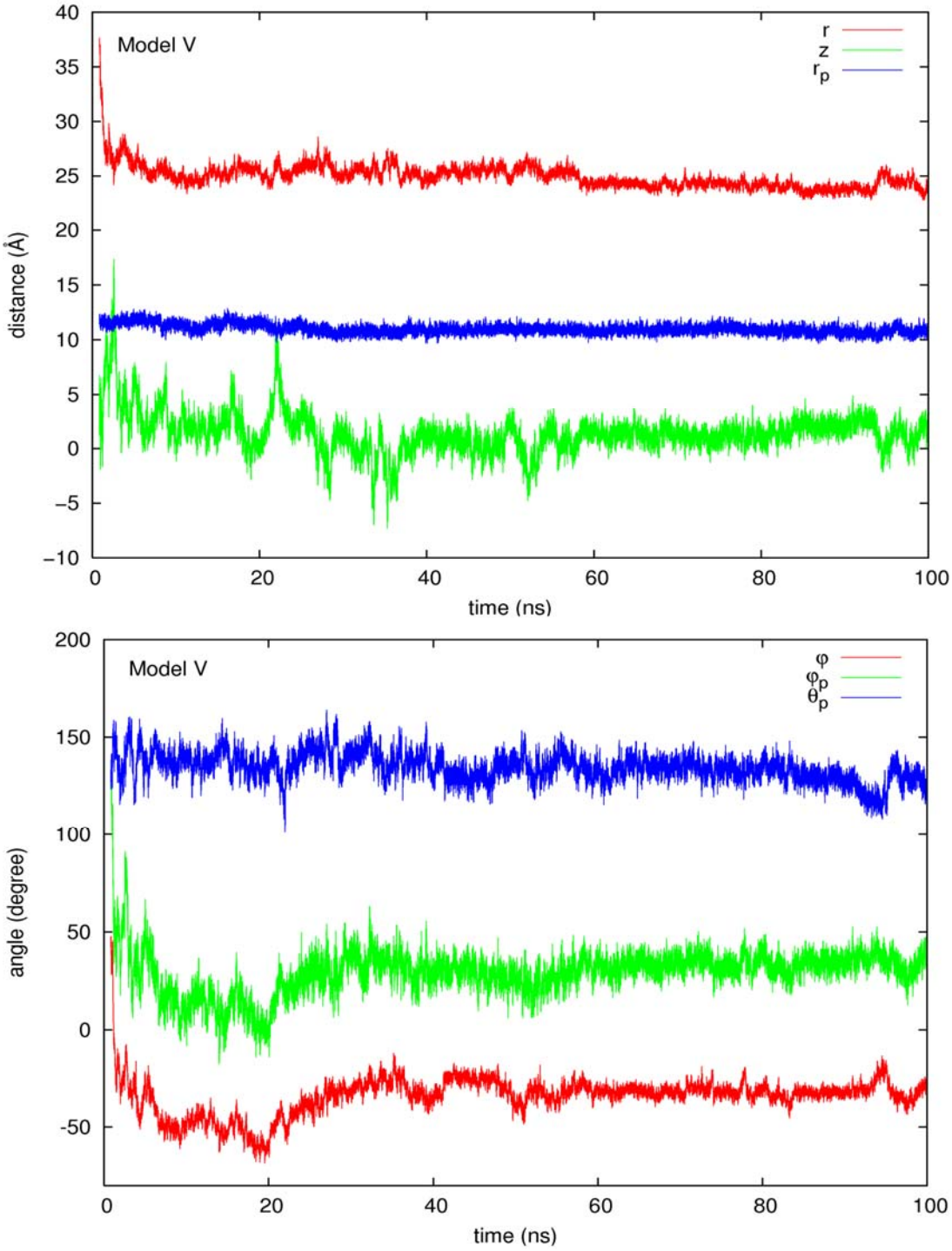
Model V
r
z
r_p
distance (Å)
time (ns)
Model V
φ
φ_p
θ_p
angle (degree)
time (ns)

Figure S7

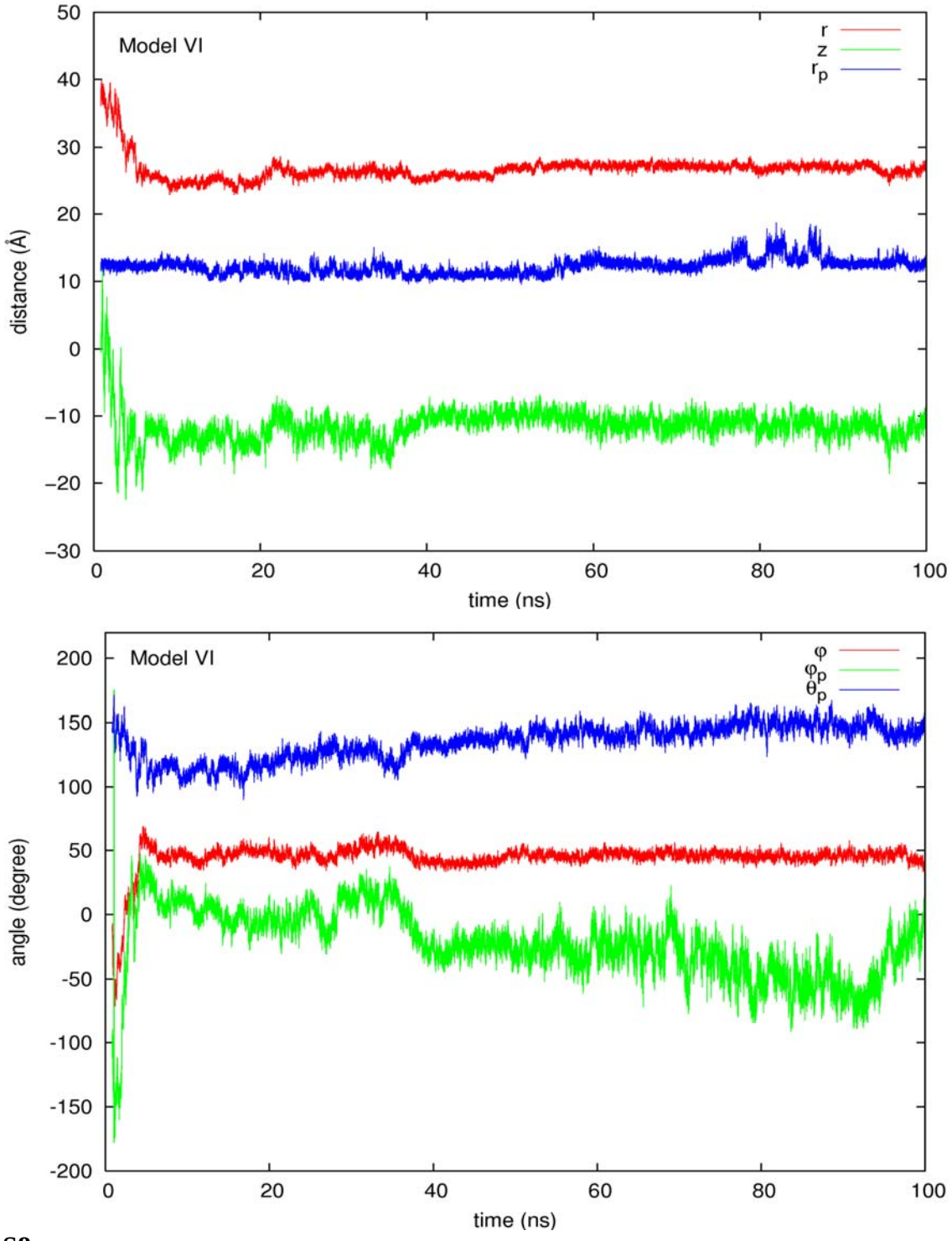
Model VI
r
z
r_p
distance (Å)
time (ns)
Model VI
φ
φ_p
θ_p
angle (degree)
time (ns)

Figure S8