

Supporting Information

Towards the Quantum Chemical Calculation of NMR Chemical Shifts of Proteins 2: Level of Theory, Basis Set, and Solvents Model Dependence

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Table S1: Mean error (ME) and standard deviation of errors (STE) of ^1H NMR chemical shifts of the HA2 domain including and excluding H^{N} calculated with different density functionals and basis sets as well the empirical SHIFTX+ methods ^{1,2}. Calculations with implicit solvents and/or charges to describe additional surroundings are marked with a “+” in the corresponding column.

	Method	Basis set	Implicit Solvent	Charges	All hydrogens (ppm)		Without H^{N} (ppm)	
					ME	STE	ME	STE
a	B3LYP	6-31g(d)	–	–	0.96	1.35	0.42	0.81
b		6-311g(d)	–	–	0.80	1.35	0.27	0.83
c			+	+	0.55	1.13	0.16	0.75
d	mPW1PW91	6-31g(d)	–	–	1.42	1.34	0.91	0.82
e		6-311g(d)	–	–	0.72	1.36	0.18	0.84
f			+	+	0.56	1.19	0.10	0.75
g	SHIFTX+				0.47	0.63	0.50	0.66

Table S2: Mean error (ME) and standard deviation of errors (STE) of ^{13}C NMR chemical shifts of the HA2 domain calculated with different density functionals and basis sets as well two empirical methods: Additionally to the results for all carbons, for which experimental values are available, results for the SPARTA+ subset (backbone and some C^β) are given. Calculations with implicit solvents and/or charges to describe additional surroundings are marked with a “+” in the corresponding column.

	Method	Basis set	Implicit Solvent	Charges	All Carbons (ppm)		Subset of SPARTA+ (ppm)	
					ME	STE	ME	STE
a	B3LYP	6-31g	–	–	5.65	6.03	6.64	6.29
b		6-31g(d)	–	–	7.34	7.05	8.59	7.31
c			+	–	6.90	6.06	7.94	6.31
d		6-31g(d)/3-21g(d)	–	–	7.20	7.29	8.60	7.40
e		6-311g	–	–	-0.87	3.01	-0.89	3.14
f			+	–	-1.35	2.29	-1.59	2.20
g			–	+	-1.04	3.68	-1.07	3.92
h			+	+	-1.34	2.31	-1.57	2.22
i		6-311g(d)	–	–	-0.24	2.87	-0.27	2.97
kj			+	–	-0.80	2.27	-1.10	2.15
l			–	+	-0.46	3.54	-0.52	3.77
m			+	+	-0.82	2.32	-1.12	2.21
n		6-311g(d)/6-31g(d)	–	–	-0.21	2.86	-0.24	2.96
o	mPW1PW91	6-31g(d)	–	–	9.91	5.16	10.76	5.34
p		6-311g(d)	–	–	0.56	2.58	0.59	2.67
q			+	+	0.13	1.92	-0.07	1.84
r	HCTH	6-311g(d)	–	–	9.92	7.20	10.94	7.62
s			+	+	-2.39	2.33	-2.69	2.23
t	VSXC	6-31g(d)	–	–	5.36	13.61	7.69	14.18
u		6-311g(d)	+	+	-2.63	8.87	-1.66	9.35
v	SHIFTX+ ^(a)				0.45	1.91	0.35	1.21
w	SPARTA+						0.24	0.77

Table S3: Mean error (ME) and standard deviation of errors (STE) of ^{13}C NMR chemical shifts for the subset of fragments of the HA2 domain, which could be calculated up to the MP2 level of theory. Calculations with implicit solvents and/or charges to describe additional surroundings are marked with a “+” in the corresponding column.

	Method	Basis set	Implicit Solvent	Charges	Subset of MP2 (ppm)	
					ME	STE
a	B3LYP	6-31g(d)	–	–	6.54	6.80
b		6-311g(d)	–	–	-0.74	3.13
c			+	+	-1.11	2.57
d	mPW1PW91	6-311g(d)	+	+	-0.02	2.11
e	MP2	6-31g(d)	–	–	5.91	8.36
f		6-311g(d)/3-21g	–	–	1.54	4.75
g	SHIFTX+				0.58	1.96

Table S4: Mean error (ME) and standard deviation of errors (STE) of ^{13}C NMR chemical shifts of p63 and the complex of Tfb1 with a p53 fragment calculated with different density functionals and basis sets as well the empirical SHIFTX+ methods ^{1,2}. Calculations with implicit solvents and/or charges to describe additional surroundings are marked with a “+” in the corresponding column.

	Method	Basis set	Implicit Solvent	Charges	p63 (ppm)		Tfb1/p53 (ppm)	
					ME	STE	ME	STE
a	B3LYP	6-31g(d)/3-21g(d)	–	–	6.50	9.82	6.48	7.81
b		6-311g(d)	–	–	4.75	5.27	4.52	4.69
c			+	+	-0.83	4.42	4.29	3.48
d	mPW1PW91	6-311g(d)	+	+	-0.03	4.10	-0.17	3.32
e	SHIFTX+				0.37	2.14	0.81	2.33

^(a) Results are taken from Frank et al. ¹⁷.

Table S5: Mean error (ME) and standard deviation of errors (STE) of ^{15}N NMR chemical shifts of the HA2 domain calculated with different density functionals and basis sets as well the empirical SHIFTX+ methods^{1,2}. Calculations with implicit solvents and/or charges to describe additional surroundings are marked with a “+” in the corresponding column.

	Method	Basis set	Implicit Solvent	Charges	All Nitrogens (ppm)	
					ME	STE
a	B3LYP	6-31g(d)	–	–	-5.95	6.40
b		6-311g(d)	–	–	-42.14	7.46
c			+	+	-44.60	5.62
d	mPW1PW91	6-31g(d)	–	–	-7.45	6.64
e		6-311g(d)	–	–	-37.60	7.03
f			+	+	-40.58	5.42
g	MP2	6-31g(d)	–	–	7.85 ^(a)	7.23 ^(a)
h		6-311g(d)/3-21g	–	–	-19.14 ^(a)	8.04 ^(a)
i	SHIFTX+				-1.10	4.47

^(a) MAE was calculated for the subset of 23 out of 36 fragments, which could be calculated with MP2, only.