Supplementary Information for The Effect of Non-native Interactions on the Energy Landscapes of Frustrated Model Proteins

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I. EXAMPLE GMIN INPUT FILES

GMIN input file for optimisation of BLN-46 with a genetic algorithm.

```
BLN 231.2 20.0D0

TARGET -53.31379205

TIGHTCONV 0.0000001

SLOPPYCONV 0.01

UPDATES 50

DGUESS 10.0

RADIUS 100.0

SAVE 1

CENTRE

EDIFF 0.001

STEPS 0 1.0

MAXBFGS 0.3

MAXIT 10000 10000

GA 140 126 10000

GAMUTRATE 0.05

GADUPPRED 0.1

GAEPOCH 0.01 0

GASELTOURN 3
```

`GMIN` input file for optimisation of BLN-46 with basin-hopping.

```
BLN 231.2 20.0D0

TARGET -53.31379205

TIGHTCONV 0.0000001

SLOPPYCONV 0.0075

UPDATES 50

DGUESS 10.0

RADIUS 100.0

SAVE 1

CENTRE

EDIFF 0.001

STEPS 10000000 1.0

MAXBFGS 0.3

MAXIT 10000 10000

TEMPERATURE 2.3

NEWRESTART 3500

AVOID 11.5 20 F

STEP 0.65
```

GMIN input file for optimisation of BLN-69 with a genetic algorithm.

```
BLN 231.2 20.0D0

TARGET -105.1596201486

TIGHTCONV 0.0000001

SLOPPYCONV 0.01

UPDATES 50

DGUESS 10.0

RADIUS 100.0

SAVE 1

CENTRE

EDIFF 0.001

STEPS 0 1.0

MAXBFGS 0.3

MAXIT 10000 10000

GA 200 180 10000

GAMUTRATE 0.05

GADUPPRED 0.1

GAEPOCH 0.01 1

GASELTOURN 3
```

`GMIN` input file for optimisation of BLN-69 with a basin-hopping.

```
BLN 231.2 20.0D0

TARGET -105.1596201486

SLOPPYCONV 0.005

TIGHTCONV 0.0000001

UPDATES 50

DGUESS 10.0

RADIUS 100.0

SAVE 1

CENTRE

EDIFF 0.001

STEPS 10000000 1.0

MAXBFGS 0.3

MAXIT 10000 10000

TEMPERATURE 3.4

NEWRESTART 20000

AVOID 12.0 20 F

STEP 0.70
```

II.   MEAN FIRST ENCOUNTER TIMES FOR ALL GLOBAL OPTIMISATIONS

λ	Mean first encounter time			
	Energy evaluations	Minimisations	Generations	Time / s
0.00	$6.4 \times 10^5 (1.5 \times 10^4)$	$2.9 \times 10^3 (1.2 \times 10^2)$	20(0.85)	82(1.9)
0.10	$6.2 \times 10^5 (1.4 \times 10^4)$	$2.7 \times 10^3 (1.1 \times 10^2)$	19(0.76)	78(1.8)
0.20	$6.1 \times 10^5 (1.3 \times 10^4)$	$2.7 \times 10^3 (9.8 \times 10^1)$	18(0.70)	77(1.6)
0.30	$5.8 \times 10^5 (1.1 \times 10^4)$	$2.5 \times 10^3 (7.6 \times 10^1)$	17(0.55)	73(1.4)
0.40	$5.6 \times 10^5 (1.2 \times 10^4)$	$2.4 \times 10^3 (9.1 \times 10^1)$	16(0.65)	71(1.4)
0.50	$5.4 \times 10^5 (1.1 \times 10^4)$	$2.3 \times 10^3 (7.0 \times 10^1)$	16(0.50)	69(1.4)
0.60	$5.4 \times 10^5 (1.1 \times 10^4)$	$2.4 \times 10^3 (7.2 \times 10^1)$	16(0.52)	68(1.3)
0.70	$5.6 \times 10^5 (1.2 \times 10^4)$	$2.5 \times 10^3 (7.6 \times 10^1)$	17(0.54)	70(1.4)
0.80	$5.8 \times 10^5 (1.4 \times 10^4)$	$2.8 \times 10^3 (9.2 \times 10^1)$	19(0.66)	73(1.7)
0.90	$6.7 \times 10^5 (2.0 \times 10^4)$	$3.5 \times 10^3 (1.4 \times 10^2)$	24(1.0)	85(2.5)
0.95	$7.7 \times 10^5 (4.2 \times 10^4)$	$4.3 \times 10^3 (2.8 \times 10^2)$	30(2.0)	97(5.2)
0.99	$1.1 \times 10^6 (1.1 \times 10^5)$	$6.4 \times 10^3 (7.0 \times 10^2)$	45(5.0)	140(13)
1.00	$1.5 \times 10^6 (2.1 \times 10^5)$	$9.1 \times 10^3 (1.4 \times 10^3)$	64(10)	190(26)

TABLE I. Mean first encounter times for 100 genetic algorithm runs of the BLN-46 protein. Initial gemometries were generated by randomly placing the residues inside a sphere of radius $3\,\sigma$. Values in parentheses are the uncertainties calculated at the 95% level. Each search was performed on a single core of dual-core 64-bit 2.6 GHz AMD Opteron processor.

		Mean first encounter time		
λ	Energy evaluations	Minimisations	Generations	Time / s
0.00	$6.4 \times 10^5 (1.8 \times 10^4)$	$3.2 \times 10^3 (1.3 \times 10^2)$	22(0.95)	81(2.2)
0.10	$6.4 \times 10^5 (1.5 \times 10^4)$	$3.1 \times 10^3 (1.1 \times 10^2)$	21(0.81)	80(1.9)
0.20	$6.3 \times 10^5 (1.5 \times 10^4)$	$3.0 \times 10^3 (1.1 \times 10^2)$	21(0.80)	80(1.9)
0.30	$6.2 \times 10^5 (1.4 \times 10^4)$	$3.0 \times 10^3 (1.1 \times 10^2)$	20(0.77)	78(1.8)
0.40	$6.0 \times 10^5 (1.2 \times 10^4)$	$2.8 \times 10^3 (9.1 \times 10^1)$	19(0.66)	76(1.6)
0.50	$5.9 \times 10^5 (1.3 \times 10^4)$	$2.7 \times 10^3 (9.1 \times 10^1)$	18(0.66)	73(1.7)
0.60	$5.9 \times 10^5 (1.2 \times 10^4)$	$2.8 \times 10^3 (8.3 \times 10^1)$	19(0.59)	74(1.5)
0.70	$5.8 \times 10^5 (1.2 \times 10^4)$	$2.7 \times 10^3 (8.4 \times 10^1)$	19(0.60)	73(1.5)
0.80	$6.2 \times 10^5 (1.5 \times 10^4)$	$3.0 \times 10^3 (1.0 \times 10^2)$	21(0.73)	77(1.8)
0.90	$7.0 \times 10^5 (2.6 \times 10^4)$	$3.6 \times 10^3 (1.7 \times 10^2)$	25(1.2)	87(3.2)
0.95	$8.0 \times 10^5 (5.0 \times 10^4)$	$4.3 \times 10^3 (3.3 \times 10^2)$	30(2.3)	100(6.4)
0.99	$1.2 \times 10^6 (1.2 \times 10^5)$	$6.9 \times 10^3 (8.2 \times 10^2)$	48(5.8)	145(15)
1.00	$1.3 \times 10^6 (1.8 \times 10^5)$	$8.0 \times 10^3 (1.2 \times 10^3)$	56(8.2)	166(22)

TABLE II. Mean first encounter times for 100 genetic algorithm runs of the BLN-46 protein. Initial gemometries were generated by random assignment of the backbone torsion angles of the protein. Values in parentheses are the uncertainties calculated at the 95% level. Each search was performed on a single core of dual-core 64-bit 2.6 GHz AMD Opteron processor.

	Mean first encounter time		
λ	Energy evaluations	Minimisations	Time / s
0.00	$4.2 \times 10^5 (3.2 \times 10^5)$	$2.4 \times 10^3 (2.1 \times 10^3)$	52(40)
0.10	$3.5 \times 10^5 (2.6 \times 10^5)$	$2.1 \times 10^3 (1.7 \times 10^3)$	43(32)
0.20	$5.3 \times 10^5 (4.6 \times 10^5)$	$3.3 \times 10^3 (3.1 \times 10^3)$	65(57)
0.30	$5.0 \times 10^5 (3.4 \times 10^5)$	$3.2 \times 10^3 (2.3 \times 10^3)$	62(42)
0.40	$5.5 \times 10^5 (3.6 \times 10^5)$	$3.6 \times 10^3 (2.4 \times 10^3)$	68(45)
0.50	$4.6 \times 10^5 (3.4 \times 10^5)$	$3.0 \times 10^3 (2.3 \times 10^3)$	57(42)
0.60	$5.4 \times 10^5 (3.4 \times 10^5)$	$3.5 \times 10^3 (2.3 \times 10^3)$	66(42)
0.70	$1.5 \times 10^5 (7.3 \times 10^4)$	$9.2 \times 10^2 (4.8 \times 10^2)$	18(9.0)
0.80	$2.3 \times 10^5 (1.1 \times 10^5)$	$1.4 \times 10^3 (7.0 \times 10^2)$	28(13)
0.90	$2.1 \times 10^5 (6.2 \times 10^4)$	$1.3 \times 10^3 (4.1 \times 10^2)$	26(7.7)
0.95	$2.9 \times 10^5 (4.9 \times 10^4)$	$1.8 \times 10^3 (3.2 \times 10^2)$	36(6.1)
0.99	$1.1 \times 10^6 (9.0 \times 10^4)$	$4.1 \times 10^3 (6.0 \times 10^2)$	77(11)
1.00	$1.5 \times 10^6 (1.2 \times 10^5)$	$5.8 \times 10^3 (8.4 \times 10^2)$	110(15)

TABLE III. Mean first encounter times for 100 basin-hopping runs of the BLN-46 protein. Initial gemometries were generated by randomly placing the residues inside a sphere of radius $3\,\sigma$. Values in parentheses are the uncertainties calculated at the 95% level. Each search was performed on a single core of dual-core 64-bit 2.6 GHz AMD Opteron processor.

	Mean first encounter time		
λ	Energy evaluations	Minimisations	Time / s
0.00	$1.2 \times 10^5 (1.8 \times 10^4)$	$4.5 \times 10^2 (7.6 \times 10^1)$	14(2.2)
0.10	$9.7 \times 10^4 (1.5 \times 10^4)$	$3.8 \times 10^2 (6.5 \times 10^1)$	12(2.0)
0.20	$7.7 \times 10^4 (1.1 \times 10^4)$	$3.0 \times 10^2 (4.4 \times 10^1)$	9.7(1.4)
0.30	$1.4 \times 10^5 (9.5 \times 10^4)$	$7.5 \times 10^2 (6.4 \times 10^2)$	18(12)
0.40	$5.2 \times 10^4 (7.9 \times 10^3)$	$2.1 \times 10^2 (3.1 \times 10^1)$	6.6(1.0)
0.50	$4.8 \times 10^4 (6.8 \times 10^3)$	$2.0 \times 10^2 (3.1 \times 10^1)$	6.1(0.85)
0.60	$9.2 \times 10^4 (1.0 \times 10^5)$	$5.3 \times 10^2 (6.9 \times 10^2)$	11(13)
0.70	$8.2 \times 10^4 (4.4 \times 10^4)$	$4.7 \times 10^2 (2.9 \times 10^2)$	10(5.4)
0.80	$8.9 \times 10^4 (5.2 \times 10^4)$	$5.1 \times 10^2 (3.5 \times 10^2)$	11(6.4)
0.90	$1.3 \times 10^5 (3.5 \times 10^4)$	$7.8 \times 10^2 (2.3 \times 10^2)$	16(4.3)
0.95	$2.3 \times 10^5 (3.1 \times 10^4)$	$1.5 \times 10^3 (2.1 \times 10^2)$	28(3.8)
0.99	$6.1 \times 10^5 (9.9 \times 10^4)$	$4.0 \times 10^3 (6.7 \times 10^2)$	74(12)
1.00	$7.5 \times 10^5 (1.1 \times 10^5)$	$5.0 \times 10^3 (7.3 \times 10^2)$	92(13)

TABLE IV. Mean first encounter times for 100 basin-hopping runs of the BLN-46 protein. Initial gemometries were generated by random assignment of the backbone torsion angles of the protein. Values in parentheses are the uncertainties calculated at the 95% level. Each search was performed on a single core of dual-core 64-bit 2.6 GHz AMD Opteron processor.

λ	Energy evaluations	Mean first encounter time Minimisations	Generations	Time / s
0.00	$1.5 \times 10^6 (4.9 \times 10^4)$	$5.8 \times 10^3 (3.2 \times 10^2)$	28(1.6)	360(11)
0.10	$1.4 \times 10^6 (3.2 \times 10^4)$	$5.4 \times 10^3 (2.5 \times 10^2)$	26(1.2)	340(7.6)
0.20	$1.4 \times 10^6 (3.0 \times 10^4)$	$5.1 \times 10^3 (2.3 \times 10^2)$	24(1.1)	330(7.2)
0.30	$1.3 \times 10^6 (2.7 \times 10^4)$	$4.5 \times 10^3 (1.9 \times 10^2)$	22(0.96)	310(6.1)
0.40	$1.3 \times 10^6 (2.3 \times 10^4)$	$4.3 \times 10^3 (1.7 \times 10^2)$	21(0.85)	300(5.3)
0.50	$1.3 \times 10^6 (3.3 \times 10^4)$	$4.5 \times 10^3 (2.4 \times 10^2)$	21(1.2)	300(7.7)
0.60	$1.3 \times 10^6 (2.2 \times 10^4)$	$4.3 \times 10^3 (1.4 \times 10^2)$	21(0.72)	300(5.2)
0.70	$1.3 \times 10^6 (4.4 \times 10^4)$	$4.8 \times 10^3 (3.0 \times 10^2)$	23(1.5)	310(10)
0.80	$1.4 \times 10^6 (4.4 \times 10^4)$	$5.2 \times 10^3 (2.7 \times 10^2)$	25(1.4)	320(10)
0.90	$1.6 \times 10^6 (4.1 \times 10^4)$	$6.8 \times 10^3 (2.6 \times 10^2)$	33(1.3)	380(9.5)
0.95	$2.1 \times 10^6 (1.1 \times 10^5)$	$9.6 \times 10^3 (6.4 \times 10^2)$	47(3.2)	490(25)
0.99	$3.7 \times 10^6 (4.5 \times 10^5)$	$1.9 \times 10^4 (2.5 \times 10^3)$	92(13)	870(110)
1.00	$4.6 \times 10^6 (5.3 \times 10^5)$	$2.4 \times 10^4 (3.0 \times 10^3)$	120(15)	1100(120)

TABLE V. Mean first encounter times for 100 genetic algorithm runs of the BLN-69 protein. Initial gemometries were generated by randomly placing the residues inside a sphere of radius $3\,\sigma$. Values in parentheses are the uncertainties calculated at the 95% level. Each search was performed on a single core of dual-core 64-bit 2.6 GHz AMD Opteron processor.

	Mean first encounter time			
λ	Energy evaluations	Minimisations	Generations	Time / s
0.00	$1.6 \times 10^6 (3.9 \times 10^4)$	$6.7 \times 10^3 (2.9 \times 10^2)$	32(1.6)	360(9.1)
0.10	$1.5 \times 10^6 (4.4 \times 10^4)$	$6.2 \times 10^3 (3.2 \times 10^2)$	30(1.2)	340(10)
0.20	$1.5 \times 10^6 (4.9 \times 10^4)$	$6.0 \times 10^3 (3.2 \times 10^2)$	29(1.1)	330(12)
0.30	$1.4 \times 10^6 (5.6 \times 10^4)$	$5.4 \times 10^3 (3.4 \times 10^2)$	26(0.96)	310(13)
0.40	$1.4 \times 10^6 (2.7 \times 10^4)$	$5.3 \times 10^3 (2.1 \times 10^2)$	26(0.85)	300(6.4)
0.50	$1.4 \times 10^6 (3.4 \times 10^4)$	$5.2 \times 10^3 (2.4 \times 10^2)$	25(1.2)	300(8.0)
0.60	$1.4 \times 10^6 (2.3 \times 10^4)$	$5.1 \times 10^3 (1.8 \times 10^2)$	24(0.72)	300(5.4)
0.70	$1.4 \times 10^6 (2.3 \times 10^4)$	$5.0 \times 10^3 (1.6 \times 10^2)$	24(1.5)	310(5.2)
0.80	$1.5 \times 10^6 (5.2 \times 10^4)$	$5.7 \times 10^3 (3.0 \times 10^2)$	27(1.4)	320(12)
0.90	$1.8 \times 10^6 (4.6 \times 10^4)$	$7.3 \times 10^3 (2.8 \times 10^2)$	36(1.3)	380(11)
0.95	$2.2 \times 10^6 (8.7 \times 10^4)$	$9.8 \times 10^3 (5.3 \times 10^2)$	48(3.2)	490(20)
0.99	$3.7 \times 10^6 (3.4 \times 10^5)$	$1.8 \times 10^4 (1.9 \times 10^3)$	90(13)	870(78)
1.00	$4.8 \times 10^6 (4.9 \times 10^5)$	$2.4 \times 10^4 (2.7 \times 10^3)$	120(15)	1100(110)

TABLE VI. Mean first encounter times for 100 genetic algorithm runs of the BLN-69 protein. Initial gemometries were generated by random assignment of the backbone torsion angles of the protein. Values in parentheses are the uncertainties calculated at the 95% level. Each search was performed on a single core of dual-core 64-bit 2.6 GHz AMD Opteron processor.

	Mean first encounter time		
λ	Energy evaluations	Minimisations	Time / s
0.00	$8.5 \times 10^5 (2.9 \times 10^5)$	$3.2 \times 10^3 (1.1 \times 10^3)$	200(67)
0.10	$7.3 \times 10^5 (2.6 \times 10^5)$	$3.0 \times 10^3 (1.2 \times 10^3)$	170(60)
0.20	$8.3 \times 10^5 (2.5 \times 10^5)$	$3.6 \times 10^3 (1.3 \times 10^3)$	190(58)
0.30	$6.7 \times 10^5 (2.3 \times 10^5)$	$3.0 \times 10^3 (1.1 \times 10^3)$	160(53)
0.40	$8.7 \times 10^5 (2.6 \times 10^5)$	$4.4 \times 10^3 (1.4 \times 10^3)$	200(60)
0.50	$1.1 \times 10^6 (4.9 \times 10^5)$	$5.7 \times 10^3 (2.8 \times 10^3)$	250(110)
0.60	$1.7 \times 10^6 (6.9 \times 10^5)$	$9.7 \times 10^3 (4.1 \times 10^3)$	400(160)
0.70	$2.3 \times 10^6 (8.3 \times 10^5)$	$1.4 \times 10^4 (5.2 \times 10^3)$	520(190)
0.80	$1.7 \times 10^6 (7.0 \times 10^5)$	$1.0 \times 10^4 (4.4 \times 10^3)$	400(160)
0.90	$1.4 \times 10^6 (4.6 \times 10^5)$	$8.0 \times 10^3 (2.8 \times 10^3)$	330(110)
0.95	$1.6 \times 10^6 (3.0 \times 10^5)$	$8.8 \times 10^3 (1.7 \times 10^3)$	380(70)
0.99	$3.7 \times 10^6 (5.4 \times 10^5)$	$2.0 \times 10^4 (3.0 \times 10^3)$	860(120)
1.00	$4.8 \times 10^6 (7.0 \times 10^5)$	$2.6 \times 10^4 (3.9 \times 10^3)$	1100(160)

TABLE VII. Mean first encounter times for 100 basin-hopping runs of the BLN-69 protein. Initial gemometries were generated by randomly placing the residues inside a sphere of radius $3\,\sigma$. Values in parentheses are the uncertainties calculated at the 95% level. Each search was performed on a single core of dual-core 64-bit 2.6 GHz AMD Opteron processor.

	Mean first encounter time		
λ	Energy evaluations	Minimisations	Time / s
0.00	$6.4 \times 10^5 (1.6 \times 10^5)$	$2.4 \times 10^3 (6.9 \times 10^2)$	150(38)
0.10	$5.7 \times 10^5 (1.7 \times 10^5)$	$2.2 \times 10^3 (7.4 \times 10^2)$	130(39)
0.20	$6.9 \times 10^5 (3.3 \times 10^5)$	$3.0 \times 10^3 (1.7 \times 10^3)$	160(75)
0.30	$1.0 \times 10^6 (3.6 \times 10^5)$	$4.5 \times 10^3 (1.7 \times 10^3)$	240(84)
0.40	$1.1 \times 10^6 (4.2 \times 10^5)$	$5.9 \times 10^3 (2.3 \times 10^3)$	260(97)
0.50	$2.3 \times 10^6 (8.5 \times 10^5)$	$1.3 \times 10^4 (4.9 \times 10^3)$	530(190)
0.60	$1.8 \times 10^6 (9.8 \times 10^5)$	$1.0 \times 10^4 (5.8 \times 10^3)$	400(220)
0.70	$2.5 \times 10^6 (1.2 \times 10^6)$	$1.5 \times 10^4 (7.6 \times 10^3)$	570(280)
0.80	$1.3 \times 10^6 (4.5 \times 10^5)$	$7.6 \times 10^3 (2.8 \times 10^3)$	300(100)
0.90	$1.5 \times 10^6 (4.1 \times 10^5)$	$8.6 \times 10^3 (2.4 \times 10^3)$	350(95)
0.95	$1.5 \times 10^6 (2.6 \times 10^5)$	$8.1 \times 10^3 (1.4 \times 10^3)$	350(60)
0.99	$3.4 \times 10^6 (5.0 \times 10^5)$	$1.9 \times 10^4 (2.8 \times 10^3)$	790(120)
1.00	$5.2 \times 10^6 (7.7 \times 10^5)$	$2.8 \times 10^4 (4.2 \times 10^3)$	1200(180)

TABLE VIII. Mean first encounter times for 100 basin-hopping runs of the BLN-69 protein. Initial gemometries were generated by random assignment of the backbone torsion angles of the protein. Values in parentheses are the uncertainties calculated at the 95% level. Each search was performed on a single core of dual-core 64-bit 2.6 GHz AMD Opteron processor.