Characterization of peptide binding to the SARS-CoV-2 host factor neuropilin

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SUPPLEMENTARY INFORMATION

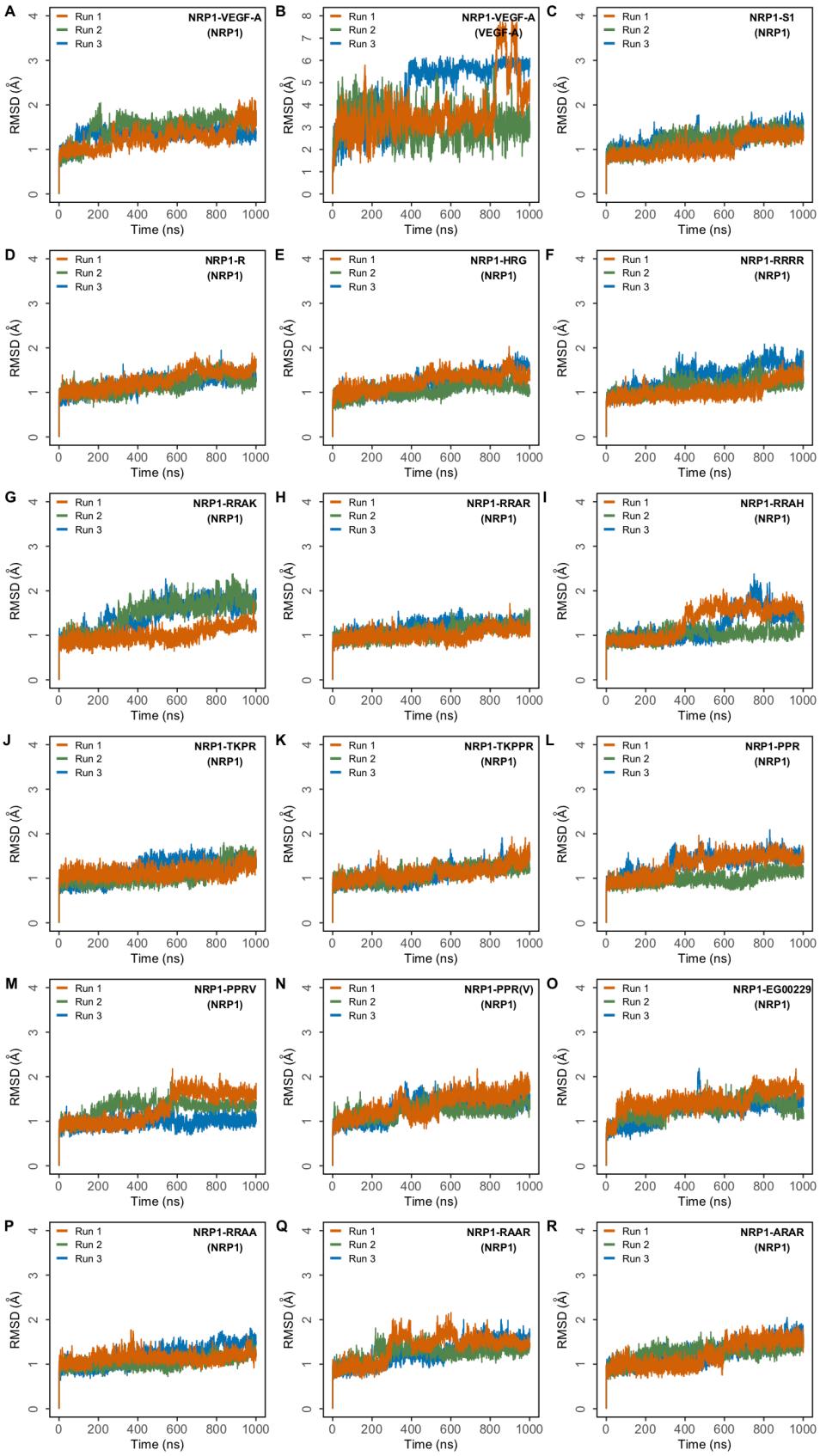

Figure S1. Root mean square deviation (RMSD) of protein Cα atoms with respect to the initial structure obtained from three independent runs of the different peptides bound to NRP1. (**A**) NRP1 in the NRP1–VEGF-A complex; (**B**) VEGF-A in the NRP1–VEGF-A complex; (**C**) NRP1 in the NRP1–S1 complex; (**D**) NRP1 in the NRP1–R complex; (**E**) NRP1 in the NRP1–HRG complex; (**F**) NRP1 in the NRP1–RRRR complex; (**G**) NRP1 in the NRP1–RRAK complex; (**H**) NRP1 in the NRP1–RRAR complex; (**I**) NRP1 in the NRP1–RRAH complex; (**J**) NRP1 in the NRP1–TKPR complex; (**K**) NRP1 in the NRP1–TKPPR complex; (**L**) NRP1 in the NRP1–PPR complex; (**M**) NRP1 in the NRP1–PPRV complex; (**N**) NRP1 in the NRP1–PPR(V) complex; **(O)** NRP1 in the NRP1–EG00229 complex; (**P**) NRP1 in the NRP1–RRAA complex; (**Q**) NRP1 in the NRP1–RAAR complex; (**R**) NRP1 in the NRP1–ARAR complex.

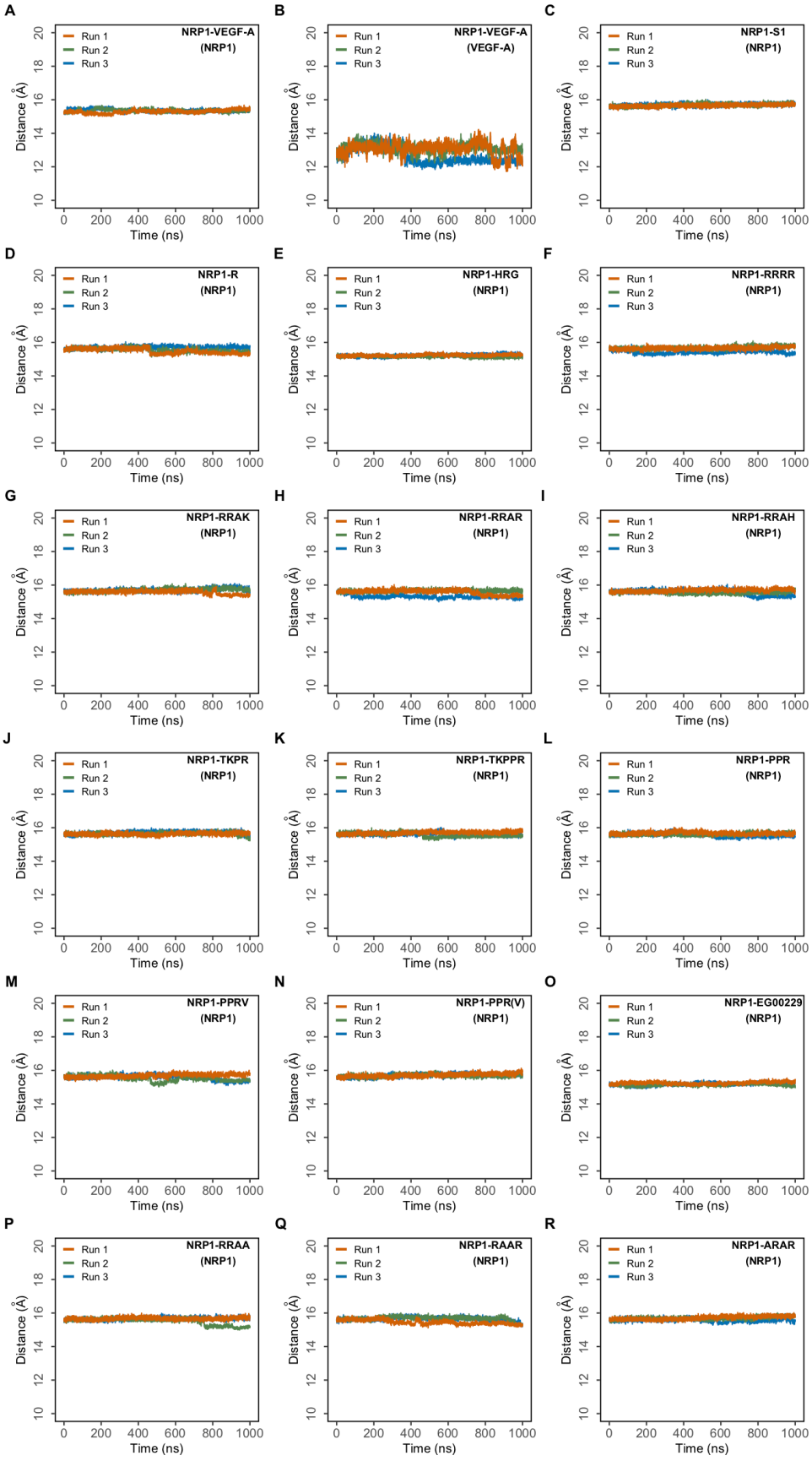

Figure S2. Radius of gyration (Rg) of NRP1 or bound protein. Three 1 μs simulations of each NRP1-peptide complex were performed. (**A**) Rg of NRP1 in NRP1–VEGF-A complex; (**B**) Rg of VEGF-A in NRP1–VEGF-A complex; (**C**) Rg of NRP1 in NRP1–S1 complex; (**D**) Rg of NRP1 in NRP1–R complex; (**E**) Rg of NRP1 in NRP1–HRG complex; (**F**) Rg of NRP1 in NRP1–RRRR complex; (**G**) Rg of NRP1 in NRP1–RRAK complex; (**H**) Rg of NRP1 in NRP1–RRAR complex; (**I**) Rg of NRP1 in NRP1–RRAH complex; (**J**) Rg of NRP1 in NRP1–TKPR complex; (**K**) Rg of NRP1 in NRP1–TKPPR complex; (**L**) Rg of NRP1 in NRP1–PPR complex; (**M**) Rg of NRP1 in NRP1–PPRV complex; (**N**) Rg of NRP1 in NRP1–PPR(V) complex; **(O)** Rg of NRP1 in the NRP1–EG00229 complex; (**P**) Rg of NRP1 in the NRP1–RRAA complex; (**Q**) Rg of NRP1 in the NRP1–RAAR complex; (**R**) Rg of NRP1 in the NRP1–ARAR complex.

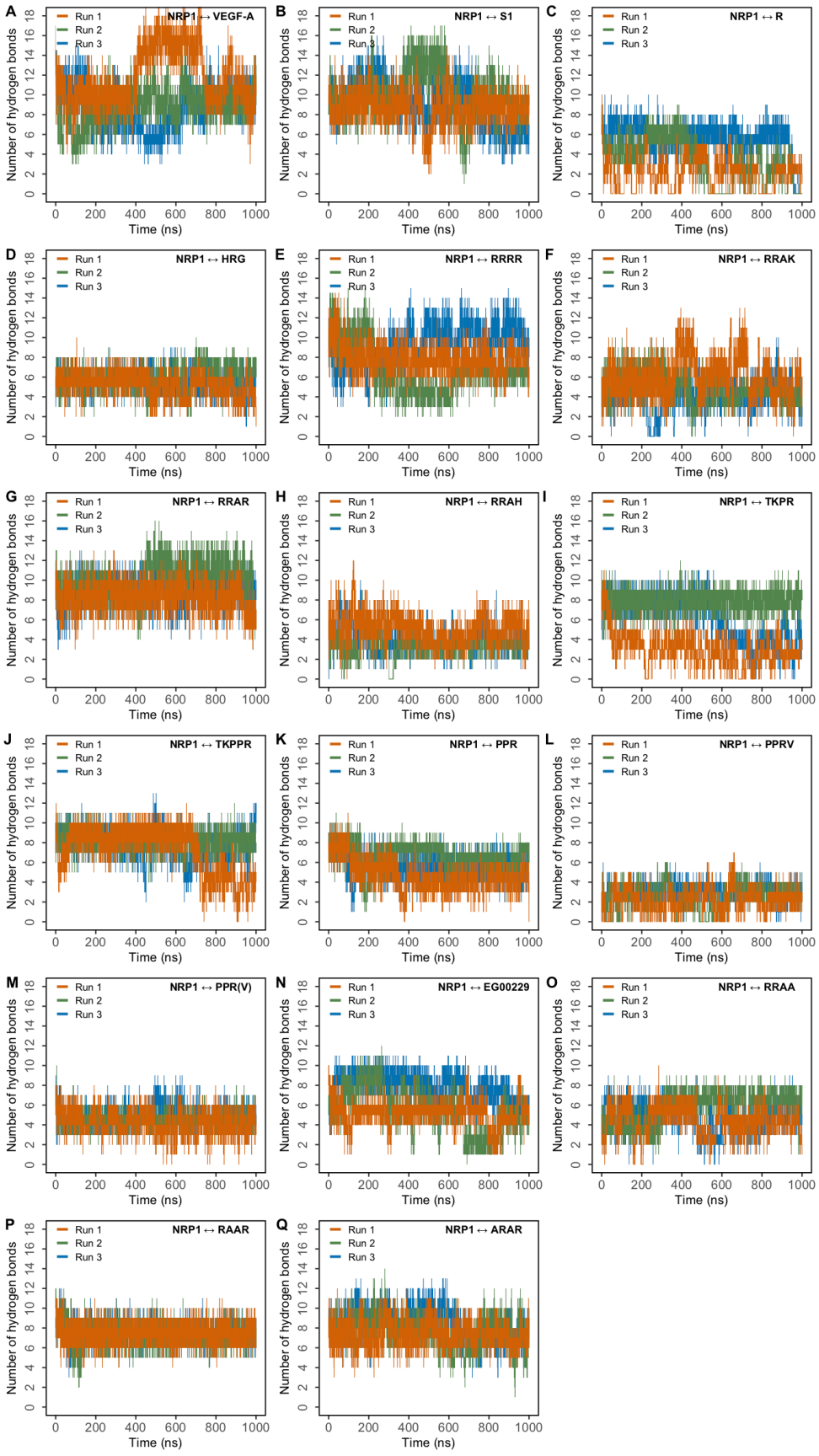

Figure S3. Number of intermolecular hydrogen bonds formed between NRP1 and the bound peptide from three independent 1 μs simulations. (**A**) Between NRP1 and VEGF-A; (**B**) between NRP1 and S1; (**C**) between NRP1 and R; (**D**) between NRP1 and HRG; (**E**) between NRP1 and RRRR; (**F**) between NRP1 and RRAK; (**G**) between NRP1 and RRAR; (**H**) between NRP1 and RRAH; (**I**) between NRP1 and TKPR; (**J**) between NRP1 and TKPPR; (**K**) between NRP1 and PPR; (**L**) between NRP1 and PPRV; (**M**) between NRP1 and PPR(V); (**N**) between NRP1 and EG00229; (**O**) between NRP1 and RRAA; (**P**) between NRP1 and RAAR; (**Q**) between NRP1 and ARAR.

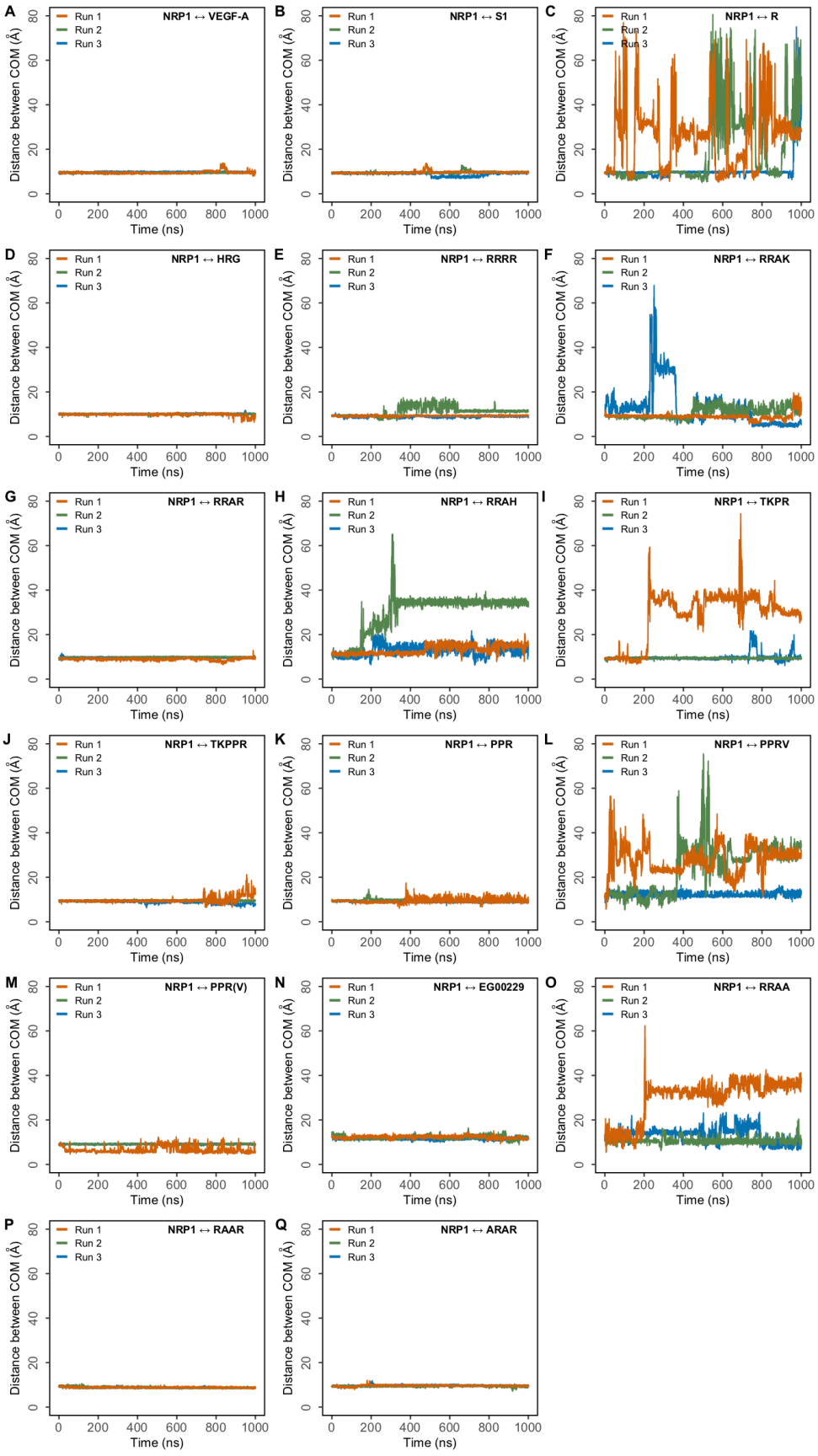

Figure S4: Distance between the center of mass (COM) of Cα atom of NRP1:Asp320 and Cα atom of the peptide residue equivalent to the terminal arginine (position 685). (**A**) between NRP1 and VEGF-A; (**B**) between NRP1 and S1; (**C**) between NRP1 and R; (**D**) between NRP1 and HRG; (**E**) between NRP1 and RRRR; (**F**) between NRP1 and RRAK; (**G**) between NRP1 and RRAR; (**H**) between NRP1 and RRAH; (**I**) between NRP1 and TKPR; (**J**) between NRP1 and TKPPR; (**K**) between NRP1 and PPR; (**L**) between NRP1 and PPRV; (**M**) between NRP1 and PPR(V); (**N**) between NRP1 and EG00229; (**O**) between NRP1 and RRAA; (**P**) between NRP1 and RAAR; (**Q**) between NRP1 and ARAR.

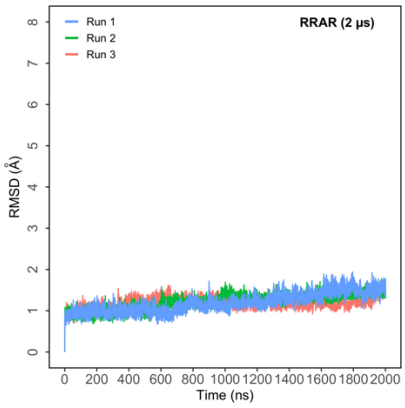

Figure S5: Root mean square deviation (RMSD) of protein Cα atoms with respect to the initial structure obtained from three independent 2 µs runs of the peptide RRAR bound to NRP1.

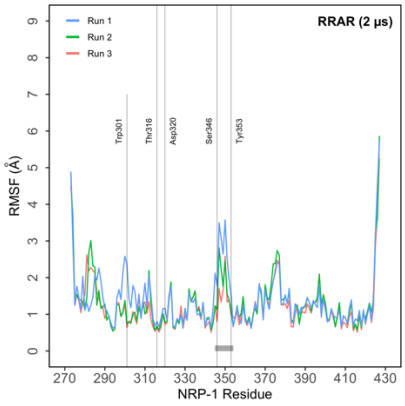

Figure S6: Root mean square fluctuation (RMSF) of protein Cα atoms obtained from three independent 2 µs runs of the peptide RRAR bound to NRP.

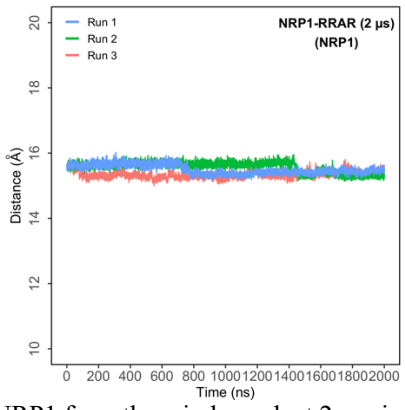

Figure S7. Radius of gyration (Rg) of NRP1 from three independent 2 µs simulations of RRAR bound to NRP1.

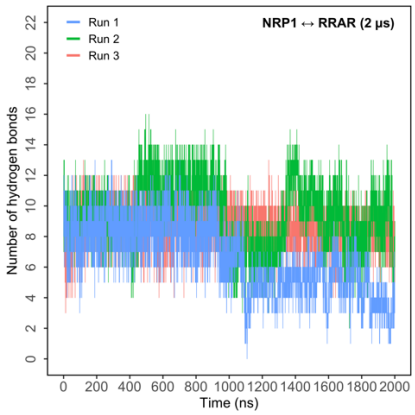

Figure S8. Number of intermolecular hydrogen bonds formed between NRP1 and the bound RRAR peptide from three independent 2 µs simulations.

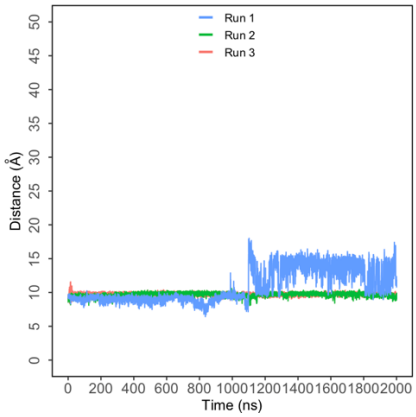

Figure S9: Distance between the center of mass of Cα atom of NRP1:Asp320 and Cα atom of C-terminal arginine of RRAR from three independent 2 µs simulations.

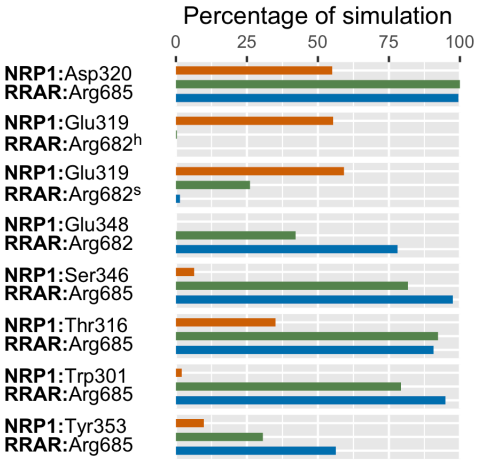

Figure S10: The percentage of simulation time during which intermolecular polar contacts were retained between NRP1 and the peptide RRAR in three independent 2 μs runs.

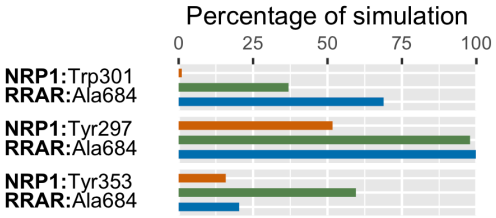

Figure S11: The percentage of simulation time during which intermolecular hydrophobic contacts were retained between NRP1 and the peptide RRAR in three independent 2 μs runs.

Table S1. Free energy of binding (ΔG_{bind}) of peptides in the simulated systems computed using the MM-GBSA method. Rows in red text represent simulations in which the peptide dissociates from NRP1.

Peptide	Run	ΔG_{bind} (kcal/mol)		Peptide	Run	ΔG_{bind} (kcal/mol)
VEGF A	run1	-85.81 ± 18.66		RRRR	run1	-79.22 ± 6.48
	run2	-67.34 ± 11.27			run2	-53.71 ± 17.68
	run3	-82.07 ± 18.59			run3	-80.54 ± 12.06
HRG	run1	-54.44 ± 5.63		RRAH	run1	-58.28 ± 12.83
	run2	-57.00 ± 4.91			run2	-43.40 ± 22.11
	run3	-57.53 ± 4.29			run3	-41.66 ± 12.47
S1	run1	-73.14 ± 11.75		RRAK	run1	-58.86 ± 11.55
	run2	-90.93 ± 16.09			run2	-48.88 ± 10.65
	run3	-86.31 ± 14.15			run3	-47.68 ± 19.12
R	run1	-15.68 ± 10.18		TKPPR	run1	-57.68 ± 14.23
	run2	-26.31 ± 17.57			run2	-63.05 ± 5.14
	run3	-43.65 ± 10.86			run3	-74.50 ± 12.19
PPR	run1	-44.62 ± 10.76		TKPR	run1	-23.67 ± 11.80
	run2	-61.39 ± 6.14			run2	-67.33 ± 5.31
	run3	-56.56 ± 5.11			run3	-51.48 ± 19.13
PPRV	run1	-36.60 ± 10.45		ARAR	run1	-72.63 ± 7.79
	run2	-37.90 ± 13.62			run2	-66.50 ± 7.86
	run3	-40.26 ± 4.85			run3	-74.16 ± 6.97
PPR(V)	run1	-57.49 ± 7.16		RRAA	run1	-45.00 ± 9.49
	run2	-64.12 ± 5.11			run2	-54.63 ± 6.46
	run3	-68.26 ± 6.97			run3	-50.23 ± 10.64
RRAR	run1	-72.97 ± 7.26		RAAR	run1	-70.05 ± 5.27
	run2	-84.60 ± 10.84			run2	-68.95 ± 4.78
	run3	-80.68 ± 7.38			run3	-71.53 ± 6.08
RRAR (2μs)	run1	-59.37 ± 15.56		EG00229	run1	-78.92 ± 5.70
	run2	-82.30 ± 10.52			run2	-76.74 ± 10.52
	run3	-80.81 ± 7.67			run3	-93.05 ± 7.67