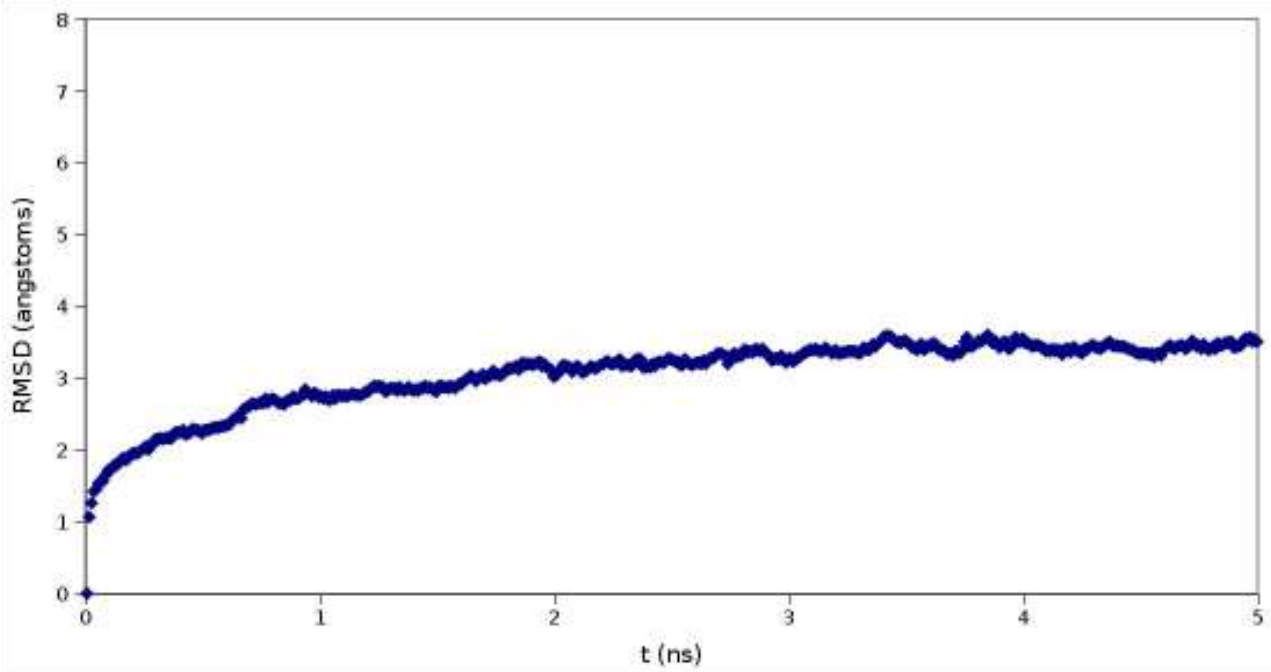
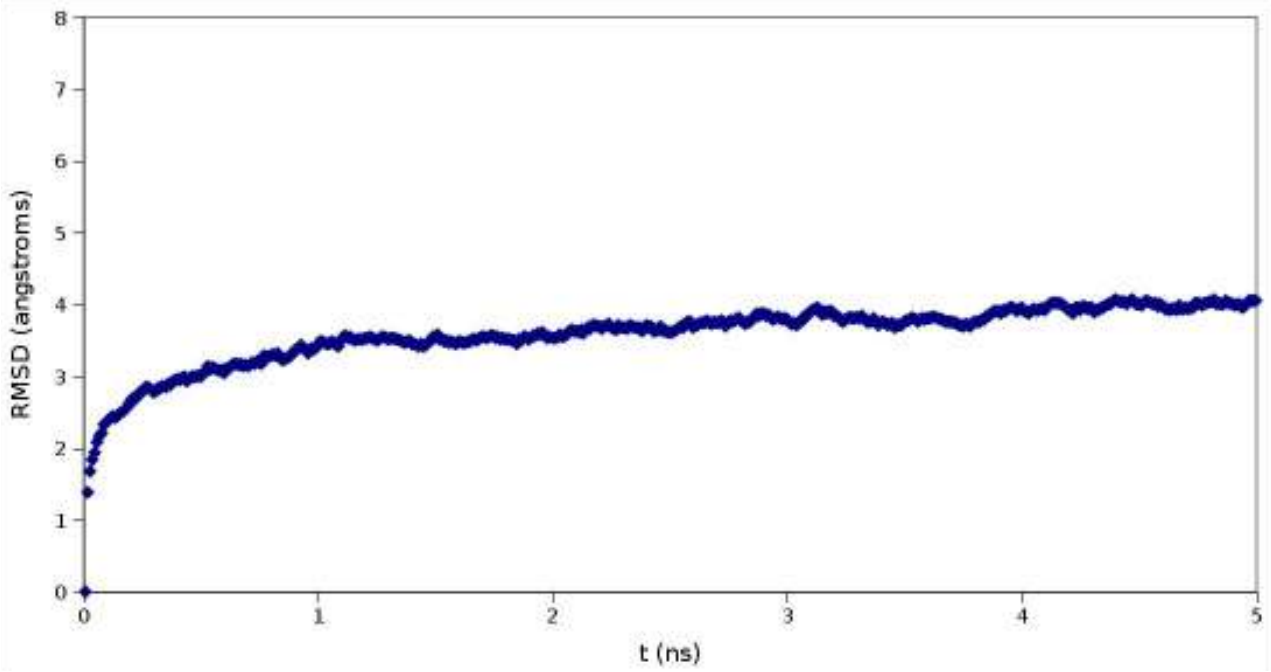
Supplementary Information



Supplementary fig. S1 RMSD calculated on the Cα atoms of the linear tetramer during the 5 ns simulation.



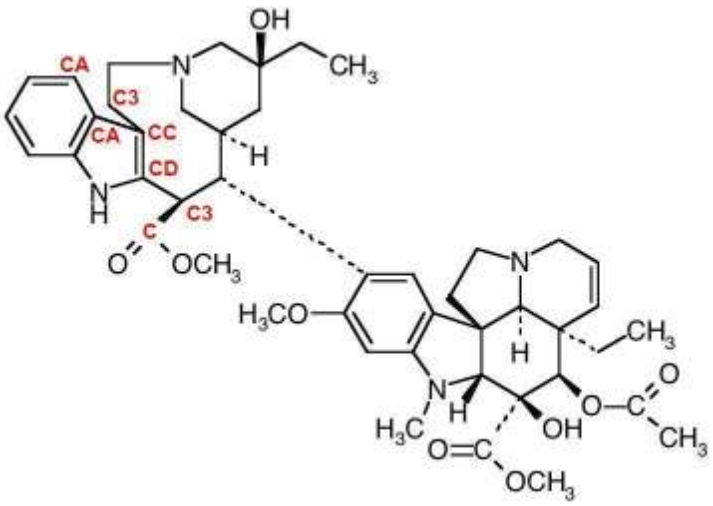
Supplementary fig. S2 RMSD calculated on the Cα atoms of the bent, vinblastine bound, tetramer during the 5 ns simulation.

Residue	ΔΔG straight tetramer ± s.e.m. (kcal mol^{-1})			ΔΔG VLB as part of α subunit ± s.e.m. (kcal mol^{-1})			ΔΔG VLB as part of β subunit ± s.e.m. (kcal mol^{-1})		
Arg 2	10.70	±	0.14	5.09	±	0.15	5.08	±	0.15
Leu 248	3.43	±	0.06	0.33	±	0.01	4.46	±	0.06
Thr 257	1.44	±	0.09	2.34	±	0.06	2.35	±	0.06
Asn 258	11.66	±	0.12	1.56	±	0.08	1.54	±	0.08
Tyr 262	3.62	±	0.05	1.72	±	0.05	1.72	±	0.05
Lys 326	2.86	±	0.08	1.44	±	0.09	2.39	±	0.10
Trp 346	6.92	±	0.08	6.29	±	0.07	6.31	±	0.07
Pro 348	2.48	±	0.05	0.43	±	0.01	0.51	±	0.01
Thr 349	4.60	±	0.09	2.10	±	0.09	3.14	±	0.10
Lys 352	19.90	±	0.17	2.69	±	0.16	2.58	±	0.17
Glu 69’	10.83	±	0.20	2.60	±	0.16	2.64	±	0.16
Gln 94’	3.18	±	0.11	1.68	±	0.10	1.68	±	0.10
Asn 99’	7.32	±	0.08	1.22	±	0.06	1.22	±	0.06
Val 175’	0.86	±	0.05	2.64	±	0.05	0.89	±	0.03
Asp 177’	17.43	±	0.18	3.21	±	0.15	2.72	±	0.15
Thr 178’	5.63	±	0.07	4.60	±	0.11	4.84	±	0.11
Tyr 208’	3.94	±	0.07	3.83	±	0.06	−0.01	±	0.00
Tyr 222’	4.85	±	0.07	3.89	±	0.05	0.60	±	0.02
Met 388’	3.32	±	0.05	1.39	±	0.05	1.38	±	0.05
Arg 391’	5.12	±	0.06	4.55	±	0.21	4.56	±	0.21
Lys 392’	13.10	±	0.17	10.69	±	0.13	10.70	±	0.13
Phe 394’	4.12	±	0.06	3.52	±	0.07	3.51	±	0.07
His 396’	2.14	±	0.06	3.64	±	0.09	3.64	±	0.09
Trp 397’	13.27	±	0.08	8.87	±	0.09	8.87	±	0.09

Supplementary table S1 Residues at the tubulin-tubulin interface that are hot or warm spot either in the linear or in the vinblastine bound tetramer.

c-c3-cd angle	Force constant (kcal mol^{-1} rad^{-2})		Equilibrium angle (degrees)	
	65.54		106.06	
x-ca-cc-x torsion	**IDIVF**	**PK**	**PHASE**	**PN**
	4	20.64	180	2

Supplementary table S2 Missing vinblastine parameters in the force field GAFF.



Supplementary figure S3. Angles and torsions for which parameters missed.

α

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        10          20          30          40          50          60
MRECISIHVG QAGVQIGNAC WELYCLEHGI QPDGQMPSDK TIGGGDDSFN TFFSETGAGK
        70          80          90         100         110         120
HVPRAVFVDL EPTVIDEVRT GTYRQLFHPE QLITGKEDAA NNYARGHYTI GKEIIDLVLD
       130         140         150         160         170         180
RIRKLADQCT GLQGFSVFHS FGGGTGSGFT SLLMERLSVD YGKKSKLEFS IYPAPQVSTA
       190         200         210         220         230         240
VVEPYNSILT THTTLEHSDC AFMVDNEAIY DICRRNLDIE RPTYTNLNRL IGQIVSSITA
       250         260         270         280         290         300
SLRFDGALNV DLTEFQTNLV PYPRAHFPLA TYAPVISAEK AYHEQLSVAE ITNACFEPAN
       310         320         330         340         350         360
QMVKCDPRHG KYMACCLLYR GDVVPKDVNA AIATIKTKRT IQFVDWCPTG FKVGINYEPP
       370         380         390         400         410         420
TVVPGGDLAK VQRAVCMLSN TTAIAEAWAR LDHKFDLMYA KRAFVHWYVG EGMEEGEFSE
       430         440         450
AREDMAALEK DYEEVGVDSV EGEGEEEGEE Y
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β

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        10          20          30          40          50          60
MREIVHIQAG QCGNQIGAKF WEVISDEHGI DPTGSYHGDS DLQLERINVY YNEAAGNKYV
        70          80          90         100         110         120
PRAILVDLEP GTMDSVRSGP FGQIFRPDNF VFGQSGAGNN WAKGHYTEGA ELVDSVLDVV
       130         140         150         160         170         180
RKESESCDCL QGFQLTHSLG GGTGSGMGTL LISKIREEYP DRIMNTFSVV PSPKVSDTVV
       190         200         210         220         230         240
EPYNATLSVH QLVENTDETY CIDNEALYDI CFRTLKLTTP TYGDLNHLVS ATMSGVTTCL
       250         260         270         280         290         300
RFPGQLNADL RKLAVNMVPF PRLHFFMPGF APLTSRGSQQ YRALTVPELT QQMFDAKNMM
       310         320         330         340         350         360
AACDPRHGRY LTVAAVFRGR MSMKEVDEQM LNVQNKNSSY FVEWIPNNVK TAVCDIPPRG
       370         380         390         400         410         420
LKMSATFIGN STAIQELFKR ISEQFTAMFR RKAFLHWYTG EGMDEMEFTE AESNMNDLVS
       430         440
EYQQYQDATA DEQGEFEEEG EEDEA
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Supplementary table S3.

Tubulin sequences of the α and β subunits (sub Alpha: UniProtKB/Swiss-Prot**P02550 ;** sub Beta: UniProtKB/Swiss-Prot **P02554)**.