Supplementary Information



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



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

Residue	∆∆G straight tetramer ± s.e.m. (kcal mol ⁻¹)		$\Delta\Delta G VLB as part of \alpha$ 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	Forc (kcal	ee constant mol ⁻¹ rad ⁻²)	Equilibrium angle (degrees)			
		65.54	106.06			
x-ca-cc-x torsion	IDIVF	РК	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					
10	20	30	40	50	60
MRECISIHVG	QAGVQIGNAC	WELYCLEHGI	QPDGQMPSDK	TIGGGDDSFN	TFFSETGAGK
70	80	90	100	110	120
HVPRAVFVDL	EPTVIDEVRT	GTYRQLFHPE	QLITGKEDAA	NNYARGHYTI	GKEIIDLVLD
190	200	210	SLLMERLSVD 220	230	240
VVEPYNSTLT	THTTI FHSDC	AFMVDNFATY	DTCRRNI DTF	RPTYTNI NRI	TGOTVSSTTA
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
I VVPGGDLAK	VQRAVCMLSN	IIALAEAWAR	LDHKFDLMYA	KRAFVHWYVG	EGMEEGEFSE
			v		
AREDMAALEN	DIEEVGVDSV	EGEGEEEGEE	T		
ß					
β	20	30	40	50	60
β 10 MREIVHIOAG	20 OCGNOIGAKF	30 WEVISDEHGI	40 DPTGSYHGDS	50 DLOLERINVY	60 YNEAAGNKYV
$\begin{array}{c} \beta \\ 10 \\ \text{MREIVHIQAG} \\ 70 \end{array}$	20 QCGNQIGAKF 80	30 WEVISDEHGI 90	40 DPTGSYHGDS 100	50 DLQLERINVY 110	60 YNEAAGNKYV 120
β MREIVHIQAG 70 PRAILVDLEP	20 QCGNQIGAKF 80 GTMDSVRSGP	30 WEVISDEHGI 90 FGQIFRPDNF	40 DPTGSYHGDS 100 VFGQSGAGNN	50 DLQLERINVY 110 WAKGHYTEGA	60 YNEAAGNKYV 120 ELVDSVLDVV
$\begin{array}{c} \beta \\ \text{MREIVHIQAG} \\ \text{70} \\ \text{PRAILVDLEP} \\ 130 \end{array}$	20 QCGNQIGAKF 80 GTMDSVRSGP 140	30 WEVISDEHGI 90 FGQIFRPDNF 150	40 DPTGSYHGDS 100 VFGQSGAGNN 160	50 DLQLERINVY 110 WAKGHYTEGA 170	60 YNEAAGNKYV 120 ELVDSVLDVV 180
β MREIVHIQAG 70 PRAILVDLEP 130 RKESESCDCL	20 QCGNQIGAKF 80 GTMDSVRSGP 140 QGFQLTHSLG	30 WEVISDEHGI 90 FGQIFRPDNF 150 GGTGSGMGTL	40 DPTGSYHGDS 100 VFGQSGAGNN 160 LISKIREEYP	50 DLQLERINVY 110 WAKGHYTEGA 170 DRIMNTFSVV	60 YNEAAGNKYV 120 ELVDSVLDVV 180 PSPKVSDTVV
β MREIVHIQAG 70 PRAILVDLEP 130 RKESESCDCL 190	20 QCGNQIGAKF 80 GTMDSVRSGP 140 QGFQLTHSLG 200	30 WEVISDEHGI 90 FGQIFRPDNF 150 GGTGSGMGTL 210	40 DPTGSYHGDS 100 VFGQSGAGNN 160 LISKIREEYP 220	50 DLQLERINVY 110 WAKGHYTEGA 170 DRIMNTFSVV 230	60 YNEAAGNKYV 120 ELVDSVLDVV 180 PSPKVSDTVV 240
β MREIVHIQAG 70 PRAILVDLEP 130 RKESESCDCL 190 EPYNATLSVH	20 QCGNQIGAKF 80 GTMDSVRSGP 140 QGFQLTHSLG 200 QLVENTDETY 260	30 WEVISDEHGI 90 FGQIFRPDNF 150 GGTGSGMGTL 210 CIDNEALYDI 270	40 DPTGSYHGDS 100 VFGQSGAGNN 160 LISKIREEYP 220 CFRTLKLTTP	50 DLQLERINVY 110 WAKGHYTEGA 170 DRIMNTFSVV 230 TYGDLNHLVS	60 YNEAAGNKYV 120 ELVDSVLDVV 180 PSPKVSDTVV 240 ATMSGVTTCL
β MREIVHIQAG 70 PRAILVDLEP 130 RKESESCDCL 190 EPYNATLSVH 250 PEPGOLNADI	20 QCGNQIGAKF 80 GTMDSVRSGP 140 QGFQLTHSLG 200 QLVENTDETY 260 PKI AV/NMVPE	30 WEVISDEHGI 90 FGQIFRPDNF 150 GGTGSGMGTL 210 CIDNEALYDI 270 PPI HEEMPCE	40 DPTGSYHGDS 100 VFGQSGAGNN 160 LISKIREEYP 220 CFRTLKLTTP 280 API TSPGSOO	50 DLQLERINVY 110 WAKGHYTEGA 170 DRIMNTFSVV 230 TYGDLNHLVS 290 VPALTVPELT	60 YNEAAGNKYV 120 ELVDSVLDVV 180 PSPKVSDTVV 240 ATMSGVTTCL 300 OOMEDAKNMM
β 10 MREIVHIQAG 70 PRAILVDLEP 130 RKESESCDCL 190 EPYNATLSVH 250 RFPGQLNADL 310	20 QCGNQIGAKF 80 GTMDSVRSGP 140 QGFQLTHSLG 200 QLVENTDETY 260 RKLAVNMVPF 320	30 WEVISDEHGI 90 FGQIFRPDNF 150 GGTGSGMGTL 210 CIDNEALYDI 270 PRLHFFMPGF 330	40 DPTGSYHGDS 100 VFGQSGAGNN 160 LISKIREEYP 220 CFRTLKLTTP 280 APLTSRGSQQ 340	50 DLQLERINVY 110 WAKGHYTEGA 170 DRIMNTFSVV 230 TYGDLNHLVS 290 YRALTVPELT 350	60 YNEAAGNKYV 120 ELVDSVLDVV 180 PSPKVSDTVV 240 ATMSGVTTCL 300 QQMFDAKNMM 360
β 10 MREIVHIQAG 70 PRAILVDLEP 130 RKESESCDCL 190 EPYNATLSVH 250 RFPGQLNADL 310 AACDPRHGRY	20 QCGNQIGAKF 80 GTMDSVRSGP 140 QGFQLTHSLG 200 QLVENTDETY 260 RKLAVNMVPF 320 LTVAAVERGR	30 WEVISDEHGI 90 FGQIFRPDNF 150 GGTGSGMGTL 210 CIDNEALYDI 270 PRLHFFMPGF 330 MSMKEVDEOM	40 DPTGSYHGDS 100 VFGQSGAGNN 160 LISKIREEYP 220 CFRTLKLTTP 280 APLTSRGSQQ 340 LNVONKNSSY	50 DLQLERINVY 110 WAKGHYTEGA 170 DRIMNTFSVV 230 TYGDLNHLVS 290 YRALTVPELT 350 FVEWIPNNVK	60 YNEAAGNKYV 120 ELVDSVLDVV 180 PSPKVSDTVV 240 ATMSGVTTCL 300 QQMFDAKNMM 360 TAVCDIPPRG
β MREIVHIQAG 70 PRAILVDLEP 130 RKESESCDCL 190 EPYNATLSVH 250 RFPGQLNADL 310 AACDPRHGRY 370	20 QCGNQIGAKF 80 GTMDSVRSGP 140 QGFQLTHSLG 200 QLVENTDETY 260 RKLAVNMVPF 320 LTVAAVFRGR 380	30 WEVISDEHGI 90 FGQIFRPDNF 150 GGTGSGMGTL 210 CIDNEALYDI 270 PRLHFFMPGF 330 MSMKEVDEQM 390	40 DPTGSYHGDS 100 VFGQSGAGNN 160 LISKIREEYP 220 CFRTLKLTTP 280 APLTSRGSQQ 340 LNVQNKNSSY 400	50 DLQLERINVY 110 WAKGHYTEGA 170 DRIMNTFSVV 230 TYGDLNHLVS 290 YRALTVPELT 350 FVEWIPNNVK 410	60 YNEAAGNKYV 120 ELVDSVLDVV 180 PSPKVSDTVV 240 ATMSGVTTCL 300 QQMFDAKNMM 360 TAVCDIPPRG 420
β MREIVHIQAG 70 PRAILVDLEP 130 RKESESCDCL 190 EPYNATLSVH 250 RFPGQLNADL 310 AACDPRHGRY 370 LKMSATFIGN	20 QCGNQIGAKF 80 GTMDSVRSGP 140 QGFQLTHSLG 200 QLVENTDETY 260 RKLAVNMVPF 320 LTVAAVFRGR 380 STAIQELFKR	30 WEVISDEHGI 90 FGQIFRPDNF 150 GGTGSGMGTL 210 CIDNEALYDI 270 PRLHFFMPGF 330 MSMKEVDEQM 390 ISEQFTAMFR	40 DPTGSYHGDS 100 VFGQSGAGNN 160 LISKIREEYP 220 CFRTLKLTTP 280 APLTSRGSQQ 340 LNVQNKNSSY 400 RKAFLHWYTG	50 DLQLERINVY 110 WAKGHYTEGA 170 DRIMNTFSVV 230 TYGDLNHLVS 290 YRALTVPELT 350 FVEWIPNNVK 410 EGMDEMEFTE	60 YNEAAGNKYV 120 ELVDSVLDVV 180 PSPKVSDTVV 240 ATMSGVTTCL 300 QQMFDAKNMM 360 TAVCDIPPRG 420 AESNMNDLVS
β MREIVHIQAG 70 PRAILVDLEP 130 RKESESCDCL 190 EPYNATLSVH 250 RFPGQLNADL 310 AACDPRHGRY 370 LKMSATFIGN 430	20 QCGNQIGAKF 80 GTMDSVRSGP 140 QGFQLTHSLG 200 QLVENTDETY 260 RKLAVNMVPF 320 LTVAAVFRGR 380 STAIQELFKR 440	30 WEVISDEHGI 90 FGQIFRPDNF 150 GGTGSGMGTL 210 CIDNEALYDI 270 PRLHFFMPGF 330 MSMKEVDEQM 390 ISEQFTAMFR	40 DPTGSYHGDS 100 VFGQSGAGNN 160 LISKIREEYP 220 CFRTLKLTTP 280 APLTSRGSQQ 340 LNVQNKNSSY 400 RKAFLHWYTG	50 DLQLERINVY 110 WAKGHYTEGA 170 DRIMNTFSVV 230 TYGDLNHLVS 290 YRALTVPELT 350 FVEWIPNNVK 410 EGMDEMEFTE	60 YNEAAGNKYV 120 ELVDSVLDVV 180 PSPKVSDTVV 240 ATMSGVTTCL 300 QQMFDAKNMM 360 TAVCDIPPRG 420 AESNMNDLVS

Supplementary table S3.

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