Sunitinib – from charge density studies to interaction with proteins

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Suporting Information

S1. Structural information.

Table S1. Selected geometric parameters for sunitinib malate (Å, º).

F(1)—C(17)	1.3623 (4)	C(8)—H(8A)	1.0920 (4)
O(1)—C(1)	1.2254 (4)	C(8)—H(8B)	1.0920 (7)
O(2)—C(4)	1.2609 (4)	C(9)—C(10)	1.4770 (4)
O(3)—C(4)	1.2545 (5)	C(10)—C(11)	1.4176 (4)
O(4)—C(1)	1.3111 (7)	C(10)—C(22)	1.4033 (4)
O(4)—H(4O)	0.9800 (7)	C(11)—C(12)	1.4037 (4)
O(6)—C(21)	1.2411 (4)	C(11)—C(23)	1.4926 (4)
O(5)—C(3)	1.4067 (4)	C(12)—C(13)	1.4183 (3)
O(5)—H(5O)	0.970 (2)	C(13)—C(14)	1.3682 (3)
O(7)—C(9)	1.2382 (4)	C(13)—H(13)	1.0830 (8)
N(1)—H(1N)	1.0100 (3)	C(14)—C(15)	1.4588 (4)
N(2)—C(8)	1.4598 (4)	C(14)—C(21)	1.4877 (4)
N(2)—C(9)	1.3552 (3)	C(15)—C(16)	1.3932 (4)
N(2)—H(2N)	1.0100 (14)	C(15)—C(20)	1.4068 (4)
N(3)—C(20)	1.3997 (4)	C(16)—C(17)	1.3883 (4)
N(3)—C(21)	1.3670 (4)	C(16)—H(16)	1.0830 (12)
N(3)—H(3N)	1.0100 (10)	C(17)—C(18)	1.3869 (5)
N(4)—C(12)	1.3845 (4)	C(18)—C(19)	1.3989 (5)
N(4)—C(22)	1.3521 (4)	C(18)—H(18)	1.083 (2)
N(4)—H(4N)	1.0100 (13)	C(19)—C(20)	1.3861 (4)
C(1)—C(2)	1.5091 (4)	C(19)—H(19)	1.0830 (12)
C(2)—C(3)	1.5287 (4)	C(22)—C(26)	1.4896 (4)
C(2)—H(2A)	1.0920 (9)	C(23)—H(23A)	1.0990 (11)
C(2)—H(2B)	1.0920 (19)	C(23)—H(23B)	1.0990 (13)
C(3)—C(4)	1.5342 (4)	C(23)—H(23C)	1.099 (3)
C(3)—H(3)	1.0990 (11)	C(24)—C(25)	1.5235 (5)
C(5)—C(6)	1.5162 (5)	C(24)—H(24A)	1.0920 (5)
C(5)—H(5A)	1.0990 (12)	C(24)—H(24B)	1.0920 (11)
C(5)—H(5B)	1.0990 (14)	C(25)—H(25A)	1.0990 (8)
C(5)—H(5C)	1.099 (3)	C(25)—H(25B)	1.099 (3)
C(6)—H(6A)	1.092 (3)	C(25)—H(25C)	1.0990 (9)
C(6)—H(6B)	1.0920 (14)	C(26)—H(26A)	1.0990 (8)
C(7)—C(8)	1.5267 (4)	C(26)—H(26B)	1.099 (3)
C(7)—H(7A)	1.0920 (4)	C(26)—H(26C)	1.0990 (4)
C(7)—H(7B)	1.0920 (11)		
C(1)—O(4)—H(4O)	113.68 (8)	C(12)—C(11)—C(23)	126.28 (2)
C(3)—O(5)—H(5O)	107.78 (7)	N(4)—C(12)—C(11)	107.45 (2)
C(8)—N(2)—C(9)	119.20 (2)	N(4)—C(12)—C(13)	125.25 (2)
C(8)—N(2)—H(2N)	118.38 (7)	C(11)—C(12)—C(13)	127.30 (2)

C(9)—N(2)—H(2N)	118.34 (10)	C(12)—C(13)—C(14)	131.29 (3)
C(20)—N(3)—C(21)	111.26 (3)	C(12)—C(13)—H(13)	115.94 (13)
C(20)—N(3)—H(3N)	120.10 (14)	C(14)—C(13)—H(13)	112.77 (13)
C(21)—N(3)—H(3N)	128.44 (13)	C(13)—C(14)—C(15)	125.06 (2)
C(12)—N(4)—C(22)	110.55 (3)	C(13)—C(14)—C(21)	129.23 (2)
C(12)—N(4)—H(4N)	122.14 (12)	C(15)—C(14)—C(21)	105.72 (2)
C(22)—N(4)—H(4N)	127.30 (12)	C(14)—C(15)—C(16)	132.69 (3)
O(1)—C(1)—O(4)	123.93 (4)	C(14)—C(15)—C(20)	107.38 (2)
O(1)—C(1)—C(2)	122.54 (3)	C(16)—C(15)—C(20)	119.94 (3)
O(4)—C(1)—C(2)	113.53 (3)	C(15)—C(16)—C(17)	116.63 (3)
C(1)—C(2)—C(3)	111.39 (2)	C(15)—C(16)—H(16)	123.44 (11)
C(1)—C(2)—H(2A)	106.23 (2)	C(17)—C(16)—H(16)	119.76 (12)
C(1)—C(2)—H(2B)	108.55 (2)	F(1)—C(17)—C(16)	117.97 (3)
C(3)—C(2)—H(2A)	109.60 (11)	F(1)—C(17)—C(18)	117.88 (3)
C(3)—C(2)—H(2B)	109.76 (9)	C(16)—C(17)—C(18)	124.14 (3)
H(2A)—C(2)—H(2B)	111.3 (2)	C(17)—C(18)—C(19)	119.07 (3)
O(5)—C(3)—C(2)	107.28 (2)	C(17)—C(18)—H(18)	118.40 (3)
O(5)—C(3)—C(4)	114.40 (2)	C(19)—C(18)—H(18)	122.52 (3)
O(5)—C(3)—H(3)	109.58 (12)	C(18)—C(19)—C(20)	117.72 (3)
C(2)—C(3)—C(4)	108.34 (2)	C(18)—C(19)—H(19)	122.88 (12)
C(2)—C(3)—H(3)	111.24 (11)	C(20)—C(19)—H(19)	119.39 (12)
C(4)—C(3)—H(3)	106.06 (3)	N(3)—C(20)—C(15)	108.77 (2)
O(2)—C(4)—O(3)	125.51 (3)	N(3)—C(20)—C(19)	128.74 (3)
O(2)—C(4)—C(3)	116.67 (3)	C(15)—C(20)—C(19)	122.49 (3)
O(3)—C(4)—C(3)	117.81 (3)	O(6)—C(21)—N(3)	123.62 (3)
C(6)—C(5)—H(5A)	116.96 (5)	O(6)—C(21)—C(14)	129.51 (3)
C(6)—C(5)—H(5B)	106.72 (4)	N(3)—C(21)—C(14)	106.86 (2)
C(6)—C(5)—H(5C)	111.16 (5)	N(4)—C(22)—C(10)	107.53 (2)
H(5A)—C(5)—H(5B)	103.61 (17)	N(4)—C(22)—C(26)	120.99 (2)
H(5A)—C(5)—H(5C)	108.02 (11)	C(10)—C(22)—C(26)	131.43 (2)
H(5B)—C(5)—H(5C)	110.00 (10)	C(11)—C(23)—H(23A)	111.42 (5)
C(5)—C(6)—H(6A)	111.56 (5)	C(11)—C(23)—H(23B)	108.47 (5)
C(5)—C(6)—H(6B)	107.79 (5)	C(11)—C(23)—H(23C)	113.10 (5)
H(6A)—C(6)—H(6B)	112.41 (10)	H(23A)—C(23)—H(23B)	109.33 (17)
C(8)—C(7)—H(7A)	110.48 (14)	H(23A)—C(23)—H(23C)	103.26 (10)
C(8)—C(7)—H(7B)	106.10 (13)	H(23B)—C(23)—H(23C)	111.17 (11)
H(7A)—C(7)—H(7B)	112.23 (11)	C(25)—C(24)—H(24A)	109.43 (8)
N(2)—C(8)—C(7)	114.74 (2)	C(25)—C(24)—H(24B)	113.19 (9)
N(2)—C(8)—H(8A)	108.98 (10)	H(24A)—C(24)—H(24B)	105.56 (11)
N(2)—C(8)—H(8B)	108.85 (10)	C(24)—C(25)—H(25A)	112.93 (9)
C(7)—C(8)—H(8A)	108.56 (14)	C(24)—C(25)—H(25B)	107.11 (4)
C(7)—C(8)—H(8B)	105.57 (14)	C(24)—C(25)—H(25C)	112.07 (9)

H(8A)—C(8)—H(8B)	110.06 (8)	H(25A)—C(25)—H(25B)	112.21 (16)
O(7)—C(9)—N(2)	121.43 (3)	H(25A)—C(25)—H(25C)	103.05 (11)
O(7)—C(9)—C(10)	121.05 (3)	H(25B)—C(25)—H(25C)	109.51 (14)
N(2)—C(9)—C(10)	117.37 (2)	C(22)—C(26)—H(26A)	111.33 (10)
C(9)—C(10)—C(11)	122.69 (2)	C(22)—C(26)—H(26B)	106.92 (5)
C(9)—C(10)—C(22)	129.25 (2)	C(22)—C(26)—H(26C)	108.46 (9)
C(11)—C(10)—C(22)	107.93 (2)	H(26A)—C(26)—H(26B)	113.52 (14)
C(10)—C(11)—C(12)	106.53 (2)	H(26A)—C(26)—H(26C)	107.94 (8)
C(10)—C(11)—C(23)	127.19 (2)	H(26B)—C(26)—H(26C)	108.56 (17)
H(4O)—O(4)—C(1)—O(1)	1.40 (16)	C(9)—C(10)—C(11)—C(23)	4.07 (15)
H(4O)—O(4)—C(1)—C(2)	-178.1 (2)	C(9)—C(10)—C(22)—N(4)	175.2 (2)
H(5O)—O(5)—C(3)—C(2)	-178.49 (18)	C(9)—C(10)—C(22)—C(26)	-7.72 (16)
H(5O)—O(5)—C(3)—C(4)	-58.30 (15)	C(11)—C(10)—C(22)—N(4)	-0.79 (14)
H(5O)—O(5)—C(3)—H(3)	60.63 (15)	C(22)—C(10)—C(11)—C(12)	1.32 (14)
C(8)—N(2)—C(9)—O(7)	11.15 (16)	C(22)—C(10)—C(11)—C(23)	-179.6 (2)
C(9)—N(2)—C(8)—C(7)	-87.23 (18)	C(11)—C(10)—C(22)—C(26)	176.3 (2)
C(8)—N(2)—C(9)—C(10)	-164.5 (2)	C(10)—C(11)—C(12)—N(4)	-1.35 (14)
C(9)—N(2)—C(8)—H(8A)	150.8 (2)	C(10)—C(11)—C(12)—C(13)	178.0 (2)
C(9)—N(2)—C(8)—H(8B)	30.78 (15)	C(10)—C(11)—C(23)—H(23A)	87.84 (19)
H(2N)—N(2)—C(8)—C(7)	115.8 (2)	C(10)—C(11)—C(23)—H(23B)	-32.55 (15)
H(2N)—N(2)—C(8)—H(8A)	-6.12 (14)	C(10)—C(11)—C(23)—H(23C)	-156.4 (2)
H(2N)—N(2)—C(8)—H(8B)	-126.2 (2)	C(23)—C(11)—C(12)—N(4)	179.6 (2)
H(2N)—N(2)—C(9)—O(7)	168.1 (3)	C(23)—C(11)—C(12)—C(13)	-1.09 (16)
H(2N)—N(2)—C(9)—C(10)	-7.55 (14)	C(12)—C(11)—C(23)—H(23A)	-93.3 (2)
C(20)—N(3)—C(21)—O(6)	177.9 (2)	C(12)—C(11)—C(23)—H(23B)	146.3 (2)
C(20)—N(3)—C(21)—C(14)	-1.18 (13)	C(12)—C(11)—C(23)—H(23C)	22.54 (15)
C(21)—N(3)—C(20)—C(15)	0.73 (14)	N(4)—C(12)—C(13)—C(14)	1.22 (17)
C(21)—N(3)—C(20)—C(19)	-179.6 (2)	N(4)—C(12)—C(13)—H(13)	-179.0 (2)
H(3N)—N(3)—C(20)—C(15)	176.0 (2)	C(11)—C(12)—C(13)—C(14)	-178.0 (3)
H(3N)—N(3)—C(20)—C(19)	-4.39 (16)	C(11)—C(12)—C(13)—H(13)	1.79 (15)
H(3N)—N(3)—C(21)—O(6)	3.15 (17)	C(12)—C(13)—C(14)—C(15)	-179.9 (3)
H(3N)—N(3)—C(21)—C(14)	-175.9 (2)	C(12)—C(13)—C(14)—C(21)	-0.12 (16)
C(12)—N(4)—C(22)—C(10)	-0.06 (14)	H(13)—C(13)—C(14)—C(15)	0.28 (14)
C(22)—N(4)—C(12)—C(11)	0.90 (14)	H(13)—C(13)—C(14)—C(21)	-179.9 (2)
C(22)—N(4)—C(12)—C(13)	-178.5 (2)	C(13)—C(14)—C(15)—C(16)	-0.64 (17)
C(12)—N(4)—C(22)—C(26)	-177.5 (2)	C(13)—C(14)—C(15)—C(20)	179.1 (2)
H(4N)—N(4)—C(12)—C(11)	179.3 (2)	C(13)—C(14)—C(21)—O(6)	2.32 (18)
H(4N)—N(4)—C(12)—C(13)	-0.02 (15)	C(13)—C(14)—C(21)—N(3)	-178.7 (2)
H(4N)—N(4)—C(22)—C(10)	-178.4 (2)	C(15)—C(14)—C(21)—O(6)	-177.9 (2)
H(4N)—N(4)—C(22)—C(26)	4.15 (16)	C(15)—C(14)—C(21)—N(3)	1.16 (13)
O(1)—C(1)—C(2)—C(3)	125.7 (2)	C(21)—C(14)—C(15)—C(16)	179.5 (2)

O(1)—C(1)—C(2)—H(2A)	6.41 (16)	C(21)—C(14)—C(15)—C(20)	-0.73 (13)
O(1)—C(1)—C(2)—H(2B)	-113.3 (2)	C(14)—C(15)—C(16)—C(17)	-180.0 (3)
O(4)—C(1)—C(2)—C(3)	-54.84 (16)	C(14)—C(15)—C(16)—H(16)	-4.81 (16)
O(4)—C(1)—C(2)—H(2A)	-174.13 (19)	C(14)—C(15)—C(20)—N(3)	0.05 (13)
O(4)—C(1)—C(2)—H(2B)	66.12 (16)	C(14)—C(15)—C(20)—C(19)	-179.6 (2)
C(1)—C(2)—C(3)—O(5)	-62.80 (15)	C(16)—C(15)—C(20)—N(3)	179.8 (2)
C(1)—C(2)—C(3)—C(4)	173.22 (18)	C(20)—C(15)—C(16)—C(17)	0.30 (15)
C(1)—C(2)—C(3)—H(3)	57.02 (14)	C(16)—C(15)—C(20)—C(19)	0.17 (15)
H(2A)—C(2)—C(3)—O(5)	54.46 (14)	C(20)—C(15)—C(16)—H(16)	175.5 (3)
H(2A)—C(2)—C(3)—C(4)	-69.52 (14)	C(15)—C(16)—C(17)—F(1)	179.3 (2)
H(2A)—C(2)—C(3)—H(3)	174.28 (19)	C(15)—C(16)—C(17)—C(18)	-0.21 (15)
H(2B)—C(2)—C(3)—O(5)	176.95 (18)	H(16)—C(16)—C(17)—F(1)	3.96 (15)
H(2B)—C(2)—C(3)—C(4)	52.98 (14)	H(16)—C(16)—C(17)—C(18)	-175.6 (3)
H(2B)—C(2)—C(3)—H(3)	-63.22 (15)	F(1)—C(17)—C(18)—C(19)	-179.9 (2)
O(5)—C(3)—C(4)—O(2)	169.7 (2)	F(1)—C(17)—C(18)—H(18)	0.56 (14)
O(5)—C(3)—C(4)—O(3)	-10.97 (16)	C(16)—C(17)—C(18)—C(19)	-0.36 (15)
C(2)—C(3)—C(4)—O(2)	-70.69 (17)	C(16)—C(17)—C(18)—H(18)	-179.9 (3)
C(2)—C(3)—C(4)—O(3)	108.64 (19)	C(17)—C(18)—C(19)—C(20)	0.81 (15)
H(3)—C(3)—C(4)—O(2)	48.82 (16)	C(17)—C(18)—C(19)—H(19)	-177.7 (2)
H(3)—C(3)—C(4)—O(3)	-131.9 (2)	H(18)—C(18)—C(19)—C(20)	-179.7 (2)
H(5A)—C(5)—C(6)—H(6A)	60.78 (15)	H(18)—C(18)—C(19)—H(19)	1.78 (14)
H(5A)—C(5)—C(6)—H(6B)	-175.3 (2)	C(18)—C(19)—C(20)—N(3)	179.7 (3)
H(5B)—C(5)—C(6)—H(6A)	-54.58 (14)	C(18)—C(19)—C(20)—C(15)	-0.74 (15)
H(5B)—C(5)—C(6)—H(6B)	69.29 (14)	H(19)—C(19)—C(20)—N(3)	-1.71 (15)
H(5C)—C(5)—C(6)—H(6A)	-174.53 (19)	H(19)—C(19)—C(20)—C(15)	177.9 (2)
H(5C)—C(5)—C(6)—H(6B)	-50.66 (14)	N(4)—C(22)—C(26)—H(26A)	-80.46 (18)
H(7A)—C(7)—C(8)—N(2)	26.10 (13)	N(4)—C(22)—C(26)—H(26B)	155.0 (2)
H(7A)—C(7)—C(8)—H(8A)	148.27 (18)	N(4)—C(22)—C(26)—H(26C)	38.15 (15)
H(7A)—C(7)—C(8)—H(8B)	-93.75 (16)	C(10)—C(22)—C(26)—H(26A)	102.8 (2)
H(7B)—C(7)—C(8)—N(2)	147.98 (18)	C(10)—C(22)—C(26)—H(26B)	-21.72 (16)
H(7B)—C(7)—C(8)—H(8A)	-89.85 (15)	C(10)—C(22)—C(26)—H(26C)	-138.6 (2)
H(7B)—C(7)—C(8)—H(8B)	28.13 (13)	H(24A)—C(24)—C(25)—H(25A)	49.36 (14)
O(7)—C(9)—C(10)—C(11)	-40.09 (17)	H(24A)—C(24)—C(25)—H(25B)	-74.67 (15)
O(7)—C(9)—C(10)—C(22)	144.4 (3)	H(24A)—C(24)—C(25)—H(25C)	165.21 (19)
N(2)—C(9)—C(10)—C(11)	135.6 (2)	H(24B)—C(24)—C(25)—H(25A)	166.8 (2)
N(2)—C(9)—C(10)—C(22)	-39.87 (18)	H(24B)—C(24)—C(25)—H(25B)	42.75 (14)
C(9)—C(10)—C(11)—C(12)	-175.0 (2)	H(24B)—C(24)—C(25)—H(25C)	-77.37 (16)

Table S2. Geometrical parameters for selected interactions in the SUM crystal structure.

	Hydrogen bond	H...A	D...A	<(DHA)
1	O4-H4O...O3#1	1.5195(7)	2.4930(9)	171.46(8)
2	N1-H1N...O2#2	1.7488(4)	2.7577(5)	176.68(7)
3	O5-H5O...O2#2	1.805(2)	2.763(3)	168.70(7)
4	N3-H3N...O7#3	1.814(1)	2.808(2)	167.33(7)
5	N2-H2N...O1#4	1.949(1)	2.945(2)	168.22 (7)
6	N4-H4N...O6	1.765(2)	2.682(3)	149.13(7)
	C-H...F			
7	C23-H23A...F1#5	2.514(1)	3.438(2)	140.92(6)
8	C13-H13...F1#6	2.4645(4)	3.4976(7)	159.09(6)
9	C16-H16...F1#6	2.433(2)	3.398(2)	147.61(6)
10	C23-H23C...F1#6	2.667(1)	3.483(3)	130.60(6)
	O... H-C			
11	O3...H8A-C8	2.2472(9)	3.319(1)	166.65(6)

S2. Hansen-Coppens formalism.

In the Hansen-Coppens formalism(Hansen & Coppens, 1978), the total atomic electron density (of the *k*-th atom) is the sum of three components:

$$\rho_k(\mathbf{r}) = P_{kc}\rho_{kc}(r) + P_{kv}\kappa_k^3\rho_{kv}(\kappa r) + \sum_{l=0}^{l_{max}}\sum_{m=-l}^{l} P_{klm}\kappa'^3_{kl} R_{kl}(\kappa'_{kl}\, r) d_{klm}(\theta,\varphi)$$

where ρ_{kc} and ρ_{kv} are spherical core and valence densities, respectively. The third term contains the sum of the angular functions (d_{klm}) which model aspherical deformations. The angular functions d_{klm} consist real spherical harmonic functions normalized to the electron density. The coefficients P_{kv} and P_{klm} stand for multipole populations of the valence and deformation density multipoles, respectively. Radial function (R_{kl}) is defined as:

$$R_{kl}(r) = \frac{\zeta_{kl}^{n_{kl}+3}}{(n_{kl}+2)!}\exp(-\zeta_{kl} r)$$

where ζ_{kl} and n_{kl} are parameters assigned to each element type separately. κ and κ' are scaling parameters, which control the expansion and contraction of the valence spherical and deformation densities, respectively. Within this formalism, P_{kv}, P_{klm}, κ and κ' are refineable parameters together with the atomic coordinates and thermal motion coefficients. Here, the P_{k00} parameter was not refined as it is highly correlated with P_{kv}.

Table S3. The definition of local coordination system for all atoms in SUM. Restrictions for κ and κ' parameters applied in the multipole refinement. KAPPA is a sequential number showing which atoms have the same values of the κ and κ' parameters. SITESYM -local symmetry used during the multipole refinement.

	Local coordination system							
ATOM	**ATOM0**	**AX1**	**ATOM1**	**ATOM2**	**AX2**	**R/L**	**KAPPA**	**SITESYM**
F(1)	C(17)	X	F(1)	C(18)	Y	R	1	m
O(1)	C(1)	X	O(1)	O(4)	Y	R	2	m
O(2)	C(4)	X	O(2)	O(3)	Y	R	3	m
O(3)	C(4)	X	O(3)	O(2)	Y	R	3	m
O(4)	C(1)	X	O(4)	H(4O)	Y	R	4	m
O(6)	C(21)	X	O(6)	N(3)	Y	R	5	m
O(5)	C(3)	X	O(5)	H(5O)	Y	R	6	m
O(7)	C(9)	X	O(7)	N(2)	Y	R	7	m
N(1)	H(1N)	Z	N(1)	C(7)	X	R	8	3m
N(2)	C(9)	X	N(2)	C(8)	Y	R	9	m
N(3)	DUM1	X	N(3)	C(21)	Y	R	10	m

N(4)	DUM2	X	N(4)	C(22)	Y	R	10	m
C(1)	O(1)	X	C(1)	O(4)	Y	R	11	m
C(2)	C(1)	X	C(2)	C(3)	Y	R	12	m
C(3)	O(6)	X	C(3)	C(4)	Y	R	13	NO
C(4)	C(3)	Z	C(4)	O(3)	X	R	14	mm2
C(5)	C(6)	Z	C(5)	H(5C)	X	R	15	3m
C(6)	N(1)	X	C(6)	C(5)	Y	R	16	m
C(7)	N(1)	X	C(7)	C(8)	Y	R	16	m
C(8)	N(2)	X	C(8)	C(7)	Y	R	17	m
C(9)	O(7)	X	C(9)	N(2)	Y	R	18	m
C(10)	DUM2	X	C(10)	C(22)	Y	R	19	m
C(11)	DUM2	X	C(11)	C(12)	Y	R	19	m
C(12)	DUM2	X	C(12)	N(4)	Y	R	20	m
C(13)	DUM3	Z	C(13)	C(14)	X	R	21	mm2
C(14)	DUM1	X	C(14)	C(15)	Y	R	19	m
C(15)	C(20)	X	C(15)	C(16)	Y	R	22	m
C(16)	DUM4	X	C(16)	C(17)	Y	R	23	m
C(17)	DUM4	X	C(17)	C(18)	Y	R	24	m
C(18)	DUM4	X	C(18)	C(17)	Y	R	23	m
C(19)	DUM4	X	C(19)	C(20)	Y	R	23	m
C(20)	C(15)	X	C(20)	C(19)	Y	R	25	m
C(21)	DUM1	X	C(21)	N(3)	Y	R	26	m
C(22)	DUM2	X	C(22)	N(4)	Y	R	20	m
C(23)	C(11)	Z	C(23)	H(23C)	X	R	15	3m
C(24)	N(1)	X	C(24)	C(25)	Y	R	16	m
C(25)	C(24)	Z	C(25)	H(25C)	X	R	15	3m
C(26)	C(22)	Z	C(26)	H(26B)	X	R	15	3m
H(2A)	C(2)	Z	H(2A)	C(1)	Y	R	27	NO
H(2B)	C(2)	Z	H(2B)	C(1)	Y	R	27	NO
H(3)	C(3)	Z	H(3)	O(5)	Y	R	27	NO
H(5A)	C(5)	Z	H(5A)	C(6)	Y	R	27	NO
H(5B)	C(5)	Z	H(5B)	C(6)	Y	R	27	NO
H(5C)	C(5)	Z	H(5C)	C(6)	Y	R	27	NO
H(6A)	C(6)	Z	H(6A)	N(1)	Y	R	27	NO
H(6B)	C(6)	Z	H(6B)	N(1)	Y	R	27	NO
H(7A)	C(7)	Z	H(7A)	N(1)	Y	R	27	NO
H(7B)	C(7)	Z	H(7B)	N(1)	Y	R	27	NO
H(8A)	C(8)	Z	H(8A)	N(2)	Y	R	27	NO
H(8B)	C(8)	Z	H(8B)	N(2)	Y	R	27	NO
H(13)	C(13)	Z	H(13)	C(14)	Y	R	27	NO
H(16)	C(16)	Z	H(16)	C(17)	Y	R	27	NO
H(18)	C(18)	Z	H(18)	C(17)	Y	R	27	NO
H(19)	C(19)	Z	H(19)	C(20)	Y	R	27	NO
H(23A)	C(23)	Z	H(23A)	C(11)	Y	R	27	NO
H(23B)	C(23)	Z	H(23B)	C(11)	Y	R	27	NO
H(23C)	C(23)	Z	H(23C)	C(11)	Y	R	27	NO

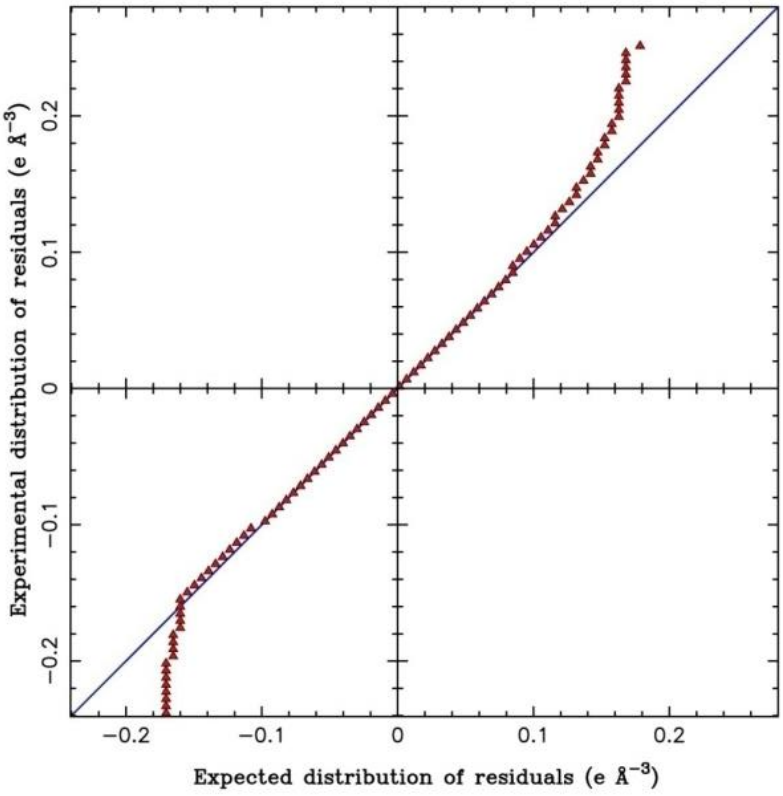
H(24A)	C(24)	Z	H(24A)	N(1)	Y	R	27	NO
H(24B)	C(24)	Z	H(24B)	N(1)	Y	R	27	NO
H(25A)	C(25)	Z	H(25A)	C(24)	Y	R	27	NO
H(25B)	C(25)	Z	H(25B)	C(24)	Y	R	27	NO
H(25C)	C(25)	Z	H(25C)	C(24)	Y	R	27	NO
H(26A)	C(26)	Z	H(26A)	C(22)	Y	R	27	NO
H(26B)	C(26)	Z	H(26B)	C(22)	Y	R	27	NO
H(26C)	C(26)	Z	H(26C)	C(22)	Y	R	27	NO
H(1N)	N(1)	Z	H(1N)	C(7)	Y	R	27	NO
H(2N)	N(2)	Z	H(2N)	C(9)	Y	R	27	NO
H(3N)	N(3)	Z	H(3N)	C(21)	Y	R	27	NO
H(4N)	N(4)	Z	H(4N)	C(22)	Y	R	27	NO
H(4O)	O(4)	Z	H(4O)	C(1)	Y	R	27	NO
H(5O)	O(5)	Z	H(5O)	C(3)	Y	R	27	NO

Table S4. Final refined values of κ and κ' parameters.

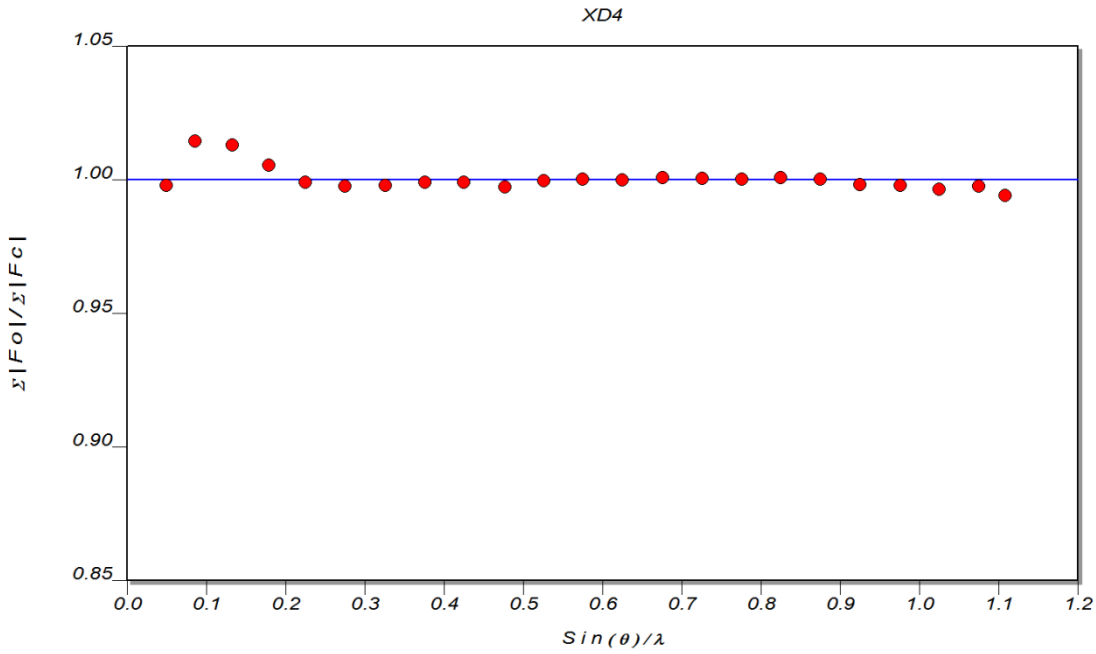
1	0.990359	0.857568
2	0.988221	1.015367
3	0.980929	1.082788
4	0.986795	1.482199
5	0.992144	0.984399
6	0.984880	0.950732
7	0.985241	0.933458
8	0.985293	0.800563
9	0.986661	0.928518
10	0.993124	0.941485
11	1.013525	0.851833
12	1.012126	0.930172
13	1.008723	0.912860
14	1.013639	0.840140
15	0.998561	0.876138
16	1.017581	0.943373
17	1.012332	0.924074
18	1.014469	0.847218
19	1.009225	0.886212
20	1.011762	0.877731
21	1.004289	0.886027
22	1.013056	0.875932
23	1.019582	0.907131
24	1.017222	0.890812
25	1.015334	0.889894
26	1.014068	0.835580
27	1.130000	1.290000

Table S5. Fractional coordinates of the used dummy atoms.

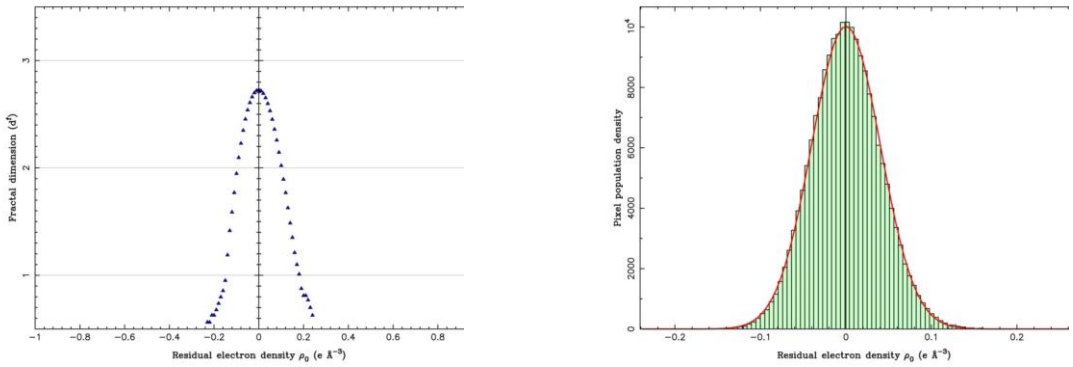
DUM1	-0.0235	-0.4699	0.884
DUM2	0.188	0.0311	0.8192
DUM3	0.1449	-0.2295	0.8629
DUM4	0.106	-0.6693	0.9402



(a) Normal probability plots for the final model



(b) Scale plot for the final multipole model



(c) Fractal dimension plot

Figure S1. Supplementary plots and figures regarding the SUM charge density model.

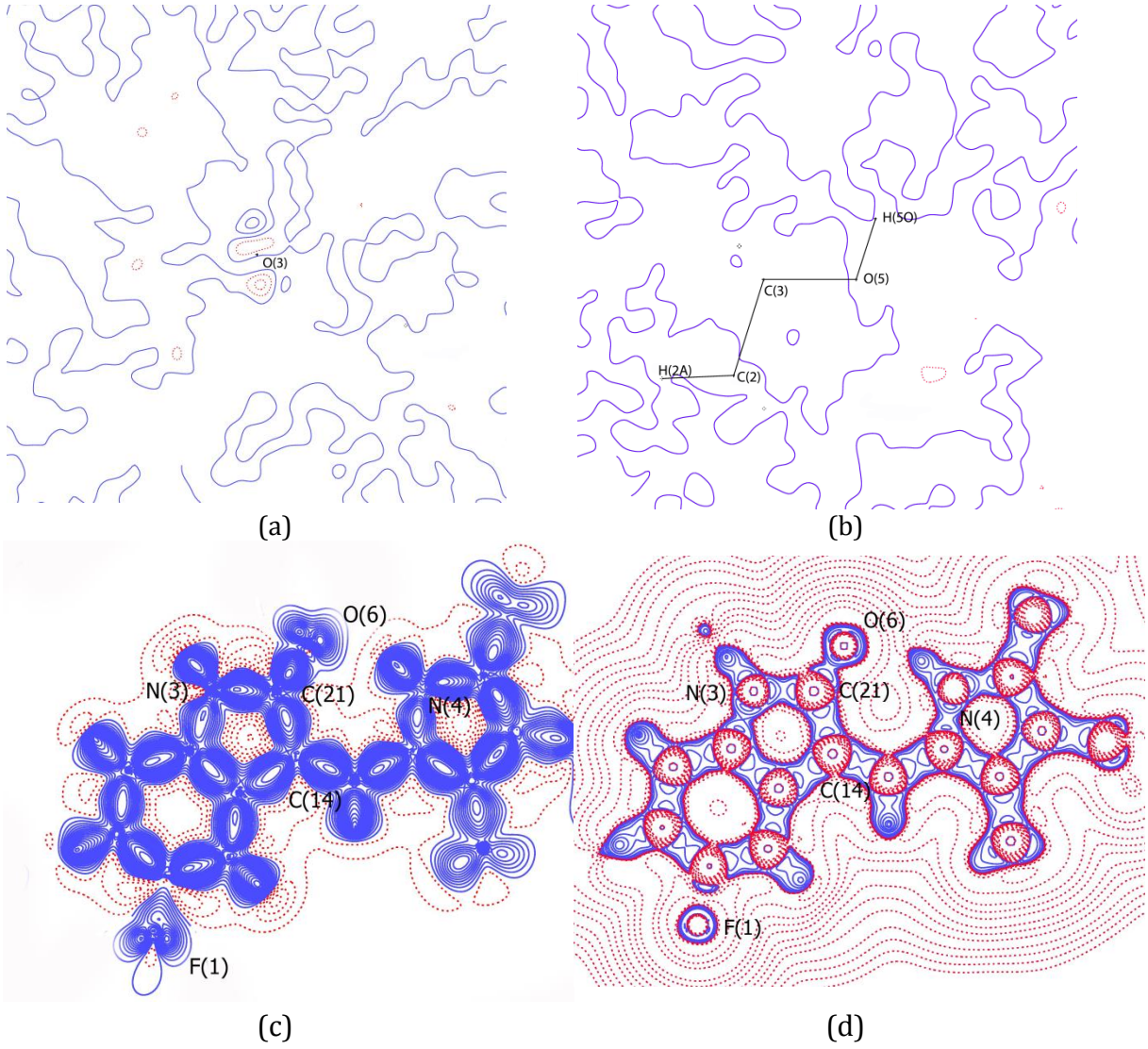


Figure S2. Residual electron density maps for the malate anion: (*a*) in the plane perpendicular to O(3)C(3)C(4) ; (*b*) in the C(3)O(5)H(5O) plane. Blue solid line – positive values, red dashed lines – negative ones. Contours at ± n·0.1e·Å^{-3} (n = 1, 2, ...), (c) Static deformation density map (contours are drawn at 0.05 eA^{-3}) (d) Laplacian map (contours are drawn at logarithmic intervals of $\nabla^2\rho(r)$ eÅ^{-5}) for the N(3) C(21) C(14) plane of SU. Blue lines indicate positive contours and red dotted lines indicate negative contours.

Table S6. Minima and maxima of residual density for SUM

peak		x	y	z	height
PK(1)	is 0.49 A from O(3)	0.4182	0.2853	0.547	0.28
PK(2)	is 0.20 A from C(6)	0.1707	0.6335	0.631	0.2
PK(3)	is 0.09 A from O(4)	1.0763	0.2901	0.5077	0.19
PK(4)	.....	0.9687	0.3132	0.7299	0.19
PK(5)	is 0.65 A from N(2)	0.3704	0.2927	0.7505	0.19
PK(6)	.....	0.0767	0.1793	0.3443	0.18
PK(7)	is 0.07 A from C(7)	0.4457	0.6268	0.7129	0.17
PK(8)	is 0.05 A from C(22)	0.0811	0.1102	0.7877	0.16

PK(9)	.....	0.7995	0.3085	0.295	0.16
PK(10)	is 0.12 A from O(1)	1.1048	0.1784	0.6195	0.16
HL(1)	is 0.52 A from O(3)	0.3947	0.3971	0.5292	-0.24
HL(2)	.....	0.9464	0.4646	0.852	-0.19
HL(3)	.....	0.247	0.021	0.7502	-0.17
HL(4)	.....	0.2482	-0.0023	0.2782	-0.15
HL(5)	.....	0.4488	0.022	0.5483	-0.15
HL(6)	.....	0.6961	0.4513	0.915	-0.15
HL(7)	.....	0.2025	0.2894	0.4884	-0.15
HL(8)	.....	0.1971	0.4431	0.7785	-0.15
HL(9)	.....	0.6704	0.1689	0.9922	-0.14
HL(10)	is 0.54 A from C(26)	-0.13	0.2034	0.7399	-0.14

S3. Topological analysis of the SUM crystal charge density.

The **SUM** single-crystal X-ray diffraction data was collected up to 0.44 Å resolution at 90K. A physically reasonable model of the **SUM** electron density distribution was achieved, and subsequently, $\rho(\boldsymbol{r})$, and its Laplacian, $\nabla^2\rho(\boldsymbol{r})$ were obtained and analysed by means of the Quantum Theory of Atoms in Molecules (Table 7S and Table 8S).

The values of $\rho(\boldsymbol{r})$ and $\nabla^2\rho(\boldsymbol{r})$ at BCP for the C(17)-F(1) bond are equal to 1.85(3) eÅ^{-3} and -16.3(1) eA^{-5}, respectively. The negative value of Laplacian indicates a strong covalent character of this bond. The values of $\rho(\boldsymbol{r})$ and $\nabla^2\rho(\boldsymbol{r})$ at BCP for the O(6)-C(21) carbonyl bond in the oxindole group amount to 2.84(2) eÅ^{-3}and -33.0(1) eÅ^{-5}. The acquired BCP for oxindole ring are in agreement with the previously reported for adenine molecule. Co-planarity of fluorinated oxindole ring and pyrrole are enforced by methylene bridge and the intramolecular hydrogen bond, H(4N)...O(6).

Formation of the hydrogen bonds between two malic acid molecules, H(4O)...O(3)#1(for symmetry card definitions see the footnote [1], D1 in Figure 5) and H(5O)...O(2)#2 (D3 in Figure 5), leads to a layer motif of the malate anions. The detected BCPs matching these interactions are characterised by the charge density value of 0.44(8)eÅ^{-3}, 0.23(5)eÅ^{-3}, and Laplacian equal to 4.2(3)eÅ^{-5}and 0.2(1)eÅ^{-5}, respectively. This indicates their very strong bonding character, but with no covalent contribution. Each malate anion interacts with a SU cation via two N-H···O interactions forming two tiers. The nitrogen atom from the amide bond and the quaternary nitrogen atom form hydrogen bonds with the O(1) and O(2) oxygen atoms from the carboxylic group. The electron densities at BCPs for the H(1N)···O(2)#2 (D2 in Figure 5) and H(2N)···O(1)#4 contacts (D5 in Figure 5) are equal to 0.28(5), 0.18(1) eÅ^{-3} with corresponding Laplacian values 2.2(1) and 1.0(1)eÅ^{-5}, respectively. The former one represents a strong hydrogen bond. The parallel tape motifs of cations connected by the H(3N)···O(7)#3 (D4 in Figure 4) hydrogen bonds are linked together by the network of weak C-H···π and C-H···F interactions. The BCPs of the C-H···F interactions, occurring between the SU layers, are characterised by an average value of charge density equal to 0.04eÅ^{-3}and Laplacian to 0.6 eÅ^{-5}. There are also plenty of other weak interactions, such as C-H···O and C-H···π -for example H(8A)...O(3) and H(5A)...C(14)#5, which are described by BCPs with $\rho(\boldsymbol{r})$ and $\nabla^2\rho(\boldsymbol{r})$ equal to 0.10(3) eÅ^{-3},

[1]Symmetry operators: #1, *x+1,y,z*; #2, *-x+1,y+1/2,-z+1*; #3, *x-1,y-1,z,* #4, *x-1,y,z;* #5 *x,y+1,z*; #6, *-x+1,y-1/2,-z+2; #7, -x+1, y+1/2, -z+2*

1.2(1) eÅ^{-5}and 0.04(1) eÅ^{-3} and 0.2(1) eÅ^{-5}, respectively. These numbers are naturally of significantly lower magnitude than the ones describing strong interatomic contacts.

Table S7. Selected topological parameters $\rho(r_{BCP})$ and $L(\rho(r_{BCP}))$ for SUM, where ρ is electron density, L stands for the negative Laplacian, Gr stands for kinetic energy density at BCP, Vr stands for potential energy density at BCP, Hr stands for total energy density at BCP.

	Atom1-Atom2	RHO	LAPL	Gr	Vr	Hr	E
covalent bonds	F(1)-C(17)	1.85(3)	-16.3(1)	0.220	-0.609	-0.389	-191.3
	O(1)-C(1)	2.98(2)	-28.7(1)	0.537	-1.372	-0.834	-430.9
	O(2)-C(4)	2.42(2)	-14.9(8)	0.416	-0.987	-0.571	-310.0
	O(3)-C(4)	2.55(2)	-2.36(9)	0.549	-1.123	-0.574	-352.7
	O(4)-C(1)	2.40(3)	-25.9(1)	0.332	-0.933	-0.601	-293.0
	O(4)-H(4)	2.20(9)	-52.2(8)	0.084	-0.709	-0.626	-222.7
	O(6)-C(21)	2.84(2)	-33.0(1)	0.451	-1.246	-0.794	-391.3
	O(5)-C(3)	2.03(3)	-17.4(1)	0.268	-0.717	-0.449	-225.2
	O(5)-H(5O)	2.6(1)	-80.7(9)	0.042	-0.921	-0.879	-289.2
	O(7)-C(9)	2.75(2)	-25.9(1)	0.464	-1.197	-0.733	-375.9
	N(1)-C(6)	1.60(3)	-8.2(1)	0.205	-0.495	-0.290	-155.5
	N(1)-C(7)	1.69(3)	-13.3(1)	0.196	-0.530	-0.334	-166.4
	N(1)-C(24)	1.57(3)	-8.2(1)	0.197	-0.479	-0.282	-150.4
	N(1)-H(1N)	2.3(1)	-43.4(8)	0.181	-0.812	-0.631	-255.0
	N(2)-C(8)	1.77(3)	-12.5(1)	0.222	-0.575	-0.353	-180.6
	N(2)-C(9)	2.23(2)	-25.9(1)	0.275	-0.818	-0.544	-256.9
	N(2)-H(2N)	2.3(1)	-40.1(6)	0.201	-0.818	-0.617	-256.9
	N(3)-C(20)	1.96(3)	-9.9(1)	0.297	-0.697	-0.400	-218.9
	N(3)-C(21)	2.25(2)	-23.78(9)	0.298	-0.843	-0.545	-264.7
	N(3)-H(3N)	2.1(1)	-46.1(8)	0.091	-0.659	-0.569	-207.0
	N(4)-C(12)	1.96(3)	-15.1(1)	0.264	-0.685	-0.421	-215.1
	N(4)-C(22)	2.28(3)	-24.9(1)	0.297	-0.854	-0.556	-268.2
	N(4)-H(4N)	2.2(1)	-36.7(8)	0.189	-0.759	-0.570	-238.4
	C(1)-C(2)	1.78(3)	-14.29(7)	0.214	-0.577	-0.362	-181.2
	C(2)-C(3)	1.77(3)	-14.03(7)	0.211	-0.568	-0.357	-178.4
	C(2)-H(2A)	1.89(8)	-19.5(4)	0.209	-0.620	-0.412	-194.7
	C(2)-H(2B)	1.84(9)	-21.0(4)	0.185	-0.589	-0.404	-185.0
	C(3)-C(4)	1.72(2)	-16.9(6)	0.178	-0.533	-0.354	-167.4
	C(3)-H(3)	2.01(9)	-29.8(4)	0.175	-0.659	-0.484	-207.0
	C(5)-C(6)	1.69(3)	-12.57(7)	0.200	-0.530	-0.330	-166.4
	C(5)-H(5A)	1.91(9)	-21.4(3)	0.203	-0.627	-0.425	-196.9
	C(5)-H(5B)	1.8(1)	-16.0(3)	0.215	-0.595	-0.381	-186.9
	C(5)-H(5C)	1.7(1)	-20.5(4)	0.171	-0.554	-0.384	-174.0
	C(6)-H(6A)	2.00(9)	-24.0(4)	0.212	-0.673	-0.461	-211.4
	C(6)-H(6B)	1.9(9)	-22.7(4)	0.201	-0.636	-0.436	-199.7
	C(7)-C(8)	1.76(3)	-11.94(8)	0.222	-0.568	-0.346	-178.4
	C(7)-H(7A)	1.95(9)	-21.4(3)	0.215	-0.653	-0.437	-205.1
	C(7)-H(7B)	1.8(1)	-20.544(4)	0.192	-0.598	-0.405	-187.8

C(8)-H(8A)	1.89(9)	-21.0(3)	0.198	-0.614	-0.417	-192.8
C(8)-H(8B)	1.91(9)	-21.7(4)	0.201	-0.627	-0.426	-196.9
C(9)-C(10)	1.89(2)	-14.75(6)	0.242	-0.636	-0.395	-199.7
C(10)-C(11)	2.15(2)	-21.83(7)	0.278	-0.783	-0.505	-245.9
C(10)-C(22)	2.11(2)	-18.77(8)	0.285	-0.764	-0.479	-239.9
C(11)-C(12)	2.26(2)	-22.41(7)	0.308	-0.848	-0.540	-266.3
C(11)-C(23)	1.74(3)	-12.77(7)	0.212	-0.557	-0.345	-174.9
C(12)-C(13)	2.14(2)	-20.15(7)	0.283	-0.775	-0.492	-243.4
C(13)-C(14)	2.30(2)	-20.86(7)	0.335	-0.886	-0.551	-278.3
C(13)-H(13)	1.96(9)	-22.19(4)	0.211	-0.652	-0.441	-204.8
C(14)-C(15)	1.94(2)	-1630(7)	0.247	-0.663	-0.416	-208.2
C(14)-C(21)	1.84(2)	-16.03(6)	0.219	-0.604	-0.385	-189.7
C(15)-C(16)	2.12(3)	-18.07(8)	0.292	-0.771	-0.479	-242.1
C(15)-C(20)	2.16(2)	-20.22(7)	0.292	-0.793	-0.501	-249.0
C(16)-C(17)	2.30(3)	-20.20(9)	0.337	-0.883	-0.546	-277.3
C(16)-H(16)	2.0(1)	-25.19(3)	0.208	-0.678	-0.470	-212.9
C(17)-C(18)	2.19(3)	-22.63(9)	0.283	-0.801	-0.518	-251.6
C(18)-C(19)	2.05(3)	-19.60(9)	0.260	-0.723	-0.463	-227.1
C(18)-H(18)	2.0(1)	-25.25(4)	0.201	-0.664	-0.463	-208.5
C(19)-C(20)	2.21(3)	-20.39(9)	0.309	-0.829	-0.520	-260.4
C(19)-H(19)	2.0(1)	-26.50(4)	0.193	-0.660	-0.467	-207.3
C(22)-C(26)	1.78(2)	-10.64(7)	0.239	-0.588	-0.349	-184.7
C(23)-H(23A)	1.82(9)	-20.2(4)	0.185	-0.579	-0.394	-181.8
C(23)-H(23B)	1.7(1)	-19.8(4)	0.166	-0.537	-0.371	-168.6
C(23)-H(23C)	1.9(1)	-23.3(4)	0.171	-0.584	-0.413	-183.4
C(24)-C(25)	1.76(3)	-13.86(8)	0.210	-0.565	-0.354	-177.4
C(24)-H(24A)	1.93(9)	-22.1(3)	0.204	-0.638	-0.433	-200.4
C(24)-H(24B)	2.0(1)	-26.6(4)	0.190	-0.656	-0.466	-206.0
C(25)-H(25A)	1.72(1)	-16.6(4)	0.180	-0.533	-0.352	-167.4
C(25)-H(25B)	1.9(1)	-26.1(4)	0.170	-0.612	-0.441	-192.2
C(25)-H(25C)	1.99(9)	-24.4(3)	0.207	-0.667	-0.460	-209.5
C(26)-H(26A)	1.87(9)	-23.7(4)	0.175	-0.597	-0.421	-187.5
C(26)-H(26B)	1.68(1)	-17.4(5)	0.162	-0.505	-0.343	-158.6
C(26)-H(26C)	1.8(1)	-21.0(4)	0.186	-0.590	-0.405	-185.3

Table S8. Selected topological parameters $\rho(r_{BCP})$ and $L(\rho(r_{BCP}))$ for SUM interactions, where ρ is electron density, L stands for the negative Laplacian, Gr stands for kinetic energy density at BCP, Vr stands for potential energy density at BCP and E(HB) stands for the energy of hydrogen bonds (Espinosa approximation(Espinosa et al., 1998))

	Atom1-Atom2	RHO	LAPL	Gr	Vr	Hr	E
hydrogen bonds	H(5O)-O(2)_2.656	0.23(6)	0.2(1)	0.011	-0.021	-0.010	-6.6
	H(4O)-O(3)_1.655	0.44(8)	4.2(3)	0.059	-0.076	-0.016	-23.9
	H(1N)-O(2)_2.656	0.28(5)	2.2(1)	0.030	-0.037	-0.007	-11.6
	H(2N)-O(1)_1.445	0.182(4)	0.99(6)	0.014	-0.017	-0.004	-5.3
	H(4N)-O(6)	0.25(4)	3.29(7)	0.034	-0.035	0.000	-11.0
	H(3N)-O(7)_1.445	0.21(5)	1.49(1)	0.019	-0.022	-0.003	-6.9

C-H…F	H(23A)-F(1)_1.545	0.035(5)	0.580(3)	0.004	-0.003	0.002	-0.9
	H(16)-F(1)_2.657	0.04(2)	0.54(1)	0.004	-0.003	0.001	-0.9
	H(13)-F(1)_2.657	0.05(1)	0.648(7)	0.005	-0.004	0.001	-1.3
	H(23C)-F(1)_2.657	0.032(4)	0.450(2)	0.003	-0.002	0.001	-0.6
C-H…O	O(3)-H(8A)	0.10(3)	1.221(3)	0.011	-0.009	0.002	-2.8
	O(1)-H(24B)_1.665	0.08(1)	0.664(9)	0.006	-0.005	0.001	-1.6
	O(4)-H(6B)_2.646	0.082(6)	0.773(3)	0.007	-0.006	0.001	-1.9
	O(6)-H(7B)_1.445	0.049(9)	0.647(6)	0.005	-0.004	0.001	-1.3
	O(1)-H(26A)_1.655	0.037(8)	0.538(5)	0.004	-0.003	0.001	-0.9
	O(2)-H(25C)_2.646	0.047(5)	0.446(3)	0.004	-0.003	0.001	-0.9
	O(5)-H(5B)_1_655	0.041(9)	0.743(5)	0.006	-0.004	0.002	-1.3
	O(6)-H(23C)_1_455	0.032(5)	0.442(3)	0.003	-0.002	0.001	-0.6
C-H…π	H(5A) -C(14)_1.565	0.04(1)	0.24(3)	0.002	-0.002	0.000	-0.6

S4. Espinosa approach

In order to compare relative strengths of hydrogen bond interactions on the basis of charge density topological parameters, we used a simple empirical formula proposed by Espinosa *et al.*(Espinosa et al., 1998). Within this approach, the interaction energy E of a given hydrogen bond is determined by applying the following equation:

$$E=1/2V_{\mathrm{BCP}}$$

where V_{BCP} is the potential energy density at the BCP of the corresponding bond path. The V_{BCP} value can be estimated using the Abramov's approximation(Abramov, 1997).

Table S9. Integrated atomic charges (*Q*) for SUM. *L* stands for the integrated Laplacian

	atom	Q	L
1	F(1)	-0.717	2.48E-04
2	O(1)	-1.283	2.41E-04
3	O(2)	-1.329	1.28E-04
4	O(3)	-1.222	-4.04E-05
5	O(4)	-1.167	3.09E-04
7	O(5)	-1.174	5.83E-04
6	O(6)	-1.101	2.81E-04
8	O(7)	-1.216	2.44E-04
9	N(1)	-1.100	6.04E-04
10	N(2)	-1.125	7.60E-04
11	N(3)	-1.146	4.25E-04
12	N(4)	-1.097	3.75E-05
13	C(1)	1.471	5.83E-04
14	C(2)	-0.159	6.75E-04
15	C(3)	0.334	1.24E-04
16	C(4)	1.644	5.16E-04
17	C(5)	-0.078	9.43E-04

18	C(6)	0.170	-1.28E-04
19	C(7)	0.300	2.91E-03
20	C(8)	0.060	1.07E-03
21	C(9)	1.255	4.97E-04
22	C(10)	0.006	2.78E-04
23	C(11)	0.117	1.04E-04
24	C(12)	0.317	-2.04E-04
25	C(13)	-0.144	4.80E-04
26	C(14)	0.064	3.01E-04
27	C(15)	0.068	3.00E-04
28	C(16)	0.057	6.02E-04
29	C(17)	0.371	1.69E-04
30	C(18)	0.114	9.12E-04
31	C(19)	0.013	6.44E-04
32	C(20)	0.233	5.41E-05
33	C(21)	1.152	2.21E-04
34	C(22)	0.246	7.80E-04
35	C(23)	-0.240	9.46E-04
36	C(24)	0.357	1.26E-03
37	C(25)	-0.394	-1.35E-04
38	C(26)	-0.455	1.39E-03
39	H(1N)	0.459	-3.62E-04
40	H(2N)	0.537	1.48E-04
41	H(3N)	0.575	1.03E-04
42	H(4N)	0.469	-1.91E-04
43	H(4O)	0.678	1.06E-03
44	H(5O)	0.710	-1.18E-04
45	H(2A)	0.113	7.86E-05
46	H(2B)	0.087	3.84E-04
47	H(3)	0.093	-2.83E-05
48	H(5A)	0.084	1.21E-04
49	H(5B)	0.026	2.42E-05
50	H(5C)	0.178	2.87E-05
51	H(6A)	0.059	-1.47E-04
52	H(6B)	0.050	7.09E-05
53	H(7A)	0.035	2.07E-04
54	H(7B)	0.086	1.41E-03
55	H(8A)	0.114	3.07E-04
56	H(8B)	0.062	-8.01E-05
57	H(13)	0.078	7.64E-05
58	H(16)	0.123	-3.97E-04
59	H(18)	0.075	3.67E-05
60	H(19)	0.135	-1.18E-04
61	H(23A)	0.097	1.25E-04
62	H(23B)	0.150	7.49E-05
63	H(23C)	0.237	5.69E-04

64	H(24A)	0.011	1.71E-04
65	H(24B)	0.153	2.10E-04
66	H(25A)	0.141	9.46E-04
67	H(25B)	0.249	-8.34E-04
68	H(25C)	0.186	-5.23E-05
69	H(26A)	0.277	2.68E-04
70	H(26B)	0.296	-1.79E-04
71	H(26C)	0.175	9.32E-04
	SU	**1.205**	
	ACID	**-1.206**	
	Σ	**-0.001**	

S5. Total interaction energy obtained for selected dimers extracted from the SUM crystal structure.

Table S10. Interaction energy of molecular pairs evaluated with three different density functionals using charged crystal-like and hypothetical neutral components.

		Dimer1	**dimer 2**	**dimer 3**	**dimer 4**	**dimer 5**	**dimer 6**	**dimer7**	**Dimer8**
B97D	6-311++G(2d,2p)	29	-96	47	15	-64	-75	17	16
M06	6-311++G(2d,2p)	28	-96	47	17	-	-	22	18

Table S11. Energy describing different optimised isolated conformers of sunitinib (B97D/6-311G).**

C(11)C(10)C(9)O(7) torsion angle [°]	Energy [kJ mol^{-1}]
-12.91	-3475008
-166.66	-3475014

S6. Hirshfeld surface analysis.

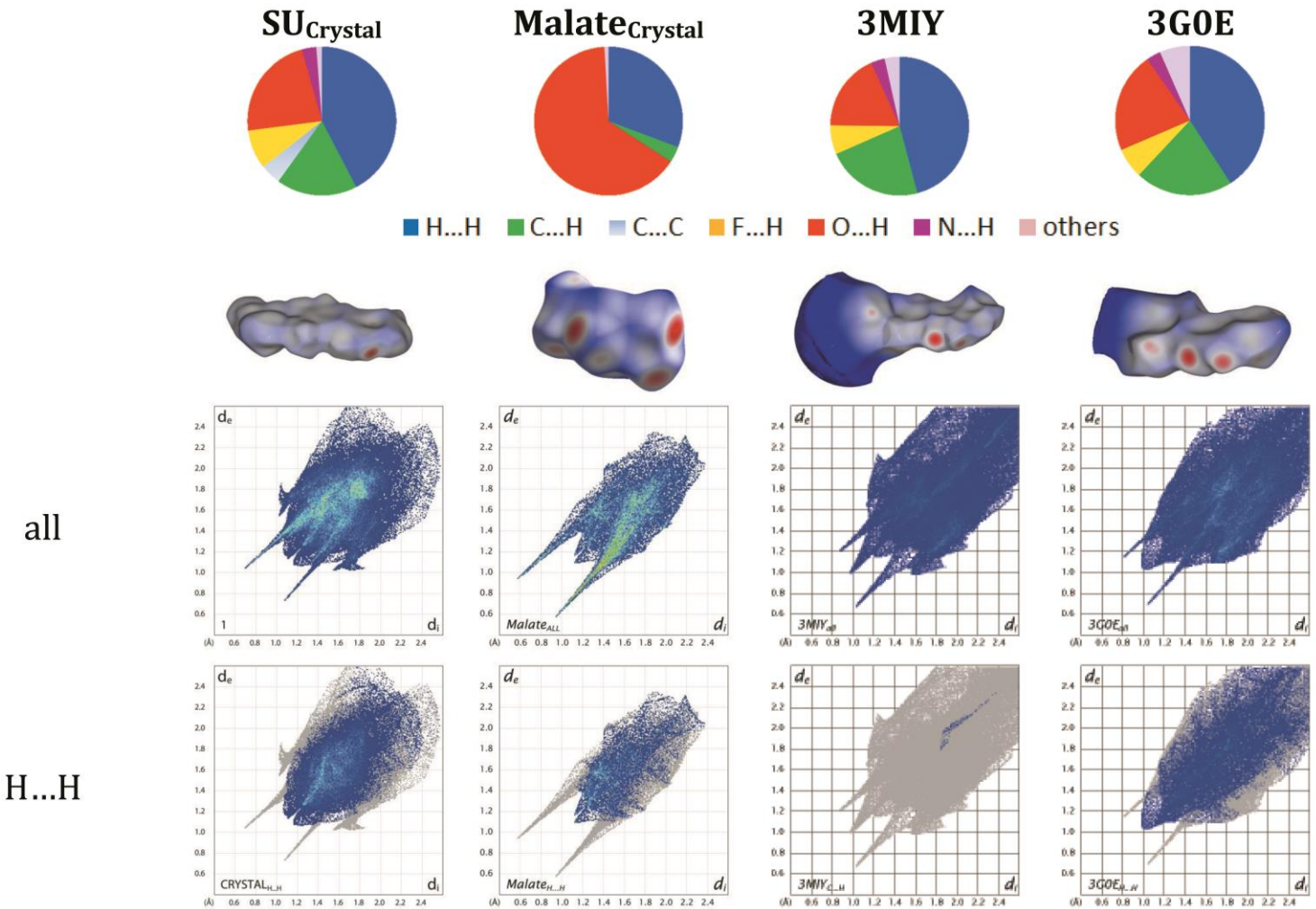
To compare intermolecular interactions in the investigated structures we used fingerprint plots generated from the so-called Hirshfeld surfaces(Spackman & Jayatilaka, 2009). A following weighing function was applied to define Hirshfeld surface:

$$w_M(\mathbf{r}) = \frac{\sum_{k \in M} \rho_k(\mathbf{r} - \mathbf{r}_k)}{\sum_{k \in C} \rho_k(\mathbf{r} - \mathbf{r}_k)}$$

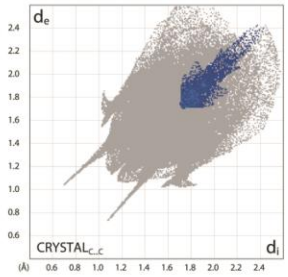
where M is the molecule, C stands for the whole crystal, ρ_i is the spherically averaged atomic electron density of the i-th atom in the molecule (centred at point $\mathbf{r}_k$) and ρ_k the electron density of k-th atom surrounding a particular molecule in the crystal. This weighing function defines the Hirshfeld surface for molecule M while $w_M(\mathbf{r}) = 0.5$ for every $\mathbf{r}$ point located at the surface. Within the model, the promolecule electron density dominates over the procrystal electron density. Consequently, it is possible to map different properties on such derived surfaces: these describing the shape of the surface (*e.g.* curvedness) and also those related to distances: d_e– external distance from the Hirshfeld surface to an atom belonging to the closest molecule outside the surface, d_i– internal distance from the surface to an atom inside the surface and $d_{norm,}$ which combines both d_e and d_i, each normalised by the van der Waals (vdW) radius for particular atoms involved in the close proximity to the surface. When d_e and d_i are calculated for each point of the Hirshfeld surface, a 2D fingerprint plot (d_e*vs.*d_i) can be created. As on Hirshfeld surfaces the closest contacts between a surface point and a particular atom, both inside and outside the surface, can be illustrated, one can easily compute relative contributions to the Hirshfeld surface area from the various close intermolecular interactions. All of interactions sum up to 100%, so the percentage contribution of each particular interaction type can be estimated. The presented figures of Hirshfeld surface and fingerprint plots (Figure 3S) were prepared in *CRYSTALEXPLORER* program(Spackman & Jayatilaka, 2009).

All fingerprint plots show a pair of long sharp spikes characteristic for hydrogen bonds (Figure 3S). Shorter and wider spikes are present in the fingerprint plot generated for the protein complexes, which indicates a less directional character of these contacts and is probably a consequence of the lower quality of the associated atomic position determination.

The percentage contributions to the Hirshfeld surface from all types of interactions for the ADP molecule is 97%. The hydrogen bond contacts (N…H and O…H) after summation cover half of the Hirshfeld surface. Additionally, the volume of Hirshfeld surface for atoms of SU surrounded by proteins (taking into account fragments 1-3 plus the amide bond atoms belonging to fragment 4) and for atoms of the ADP molecule bound to the KIT protein amount to 441 $Å^3$ and 435 $Å^3$, respectively. The equivalent surface volume obtained for the SUM crystal is equal to *c.a*. 327 $Å^3$, which indicates a more efficient crystal packing in this case when compared to the protein crystals.


SU Crystal
Malate Crystal
3MIY
3G0E
H...H
C...H
C...C
F...H
O...H
N...H
others
all
H...H

C…C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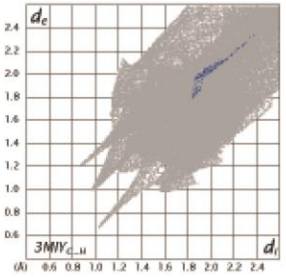
d_i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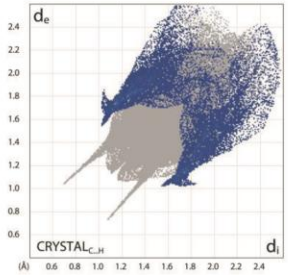
d_i

-

C…H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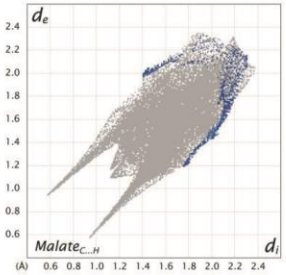
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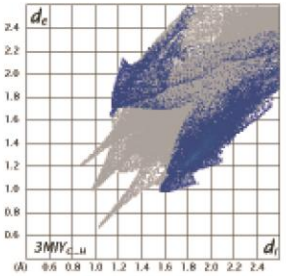
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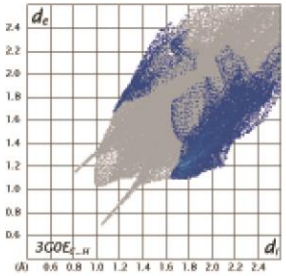
d_i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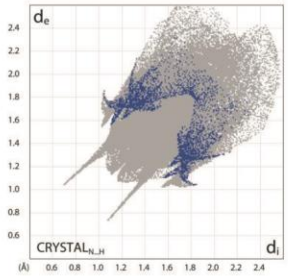
d_i

N…H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d_i

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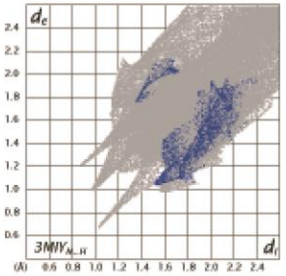
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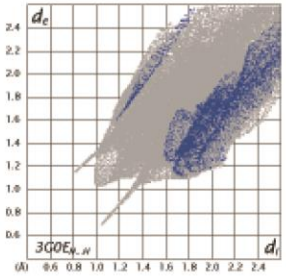
d_i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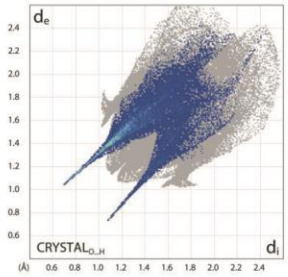
d_i

O…H


d_e
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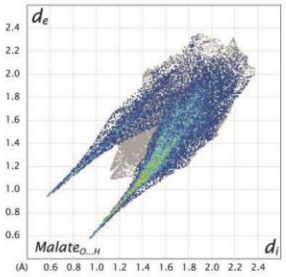
d_i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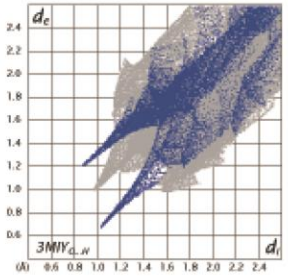
d_i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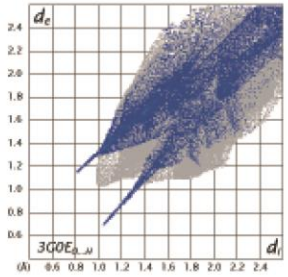
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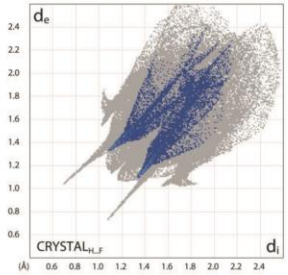
d_i

F…H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d_i

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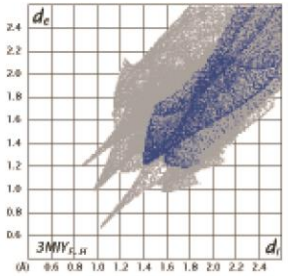
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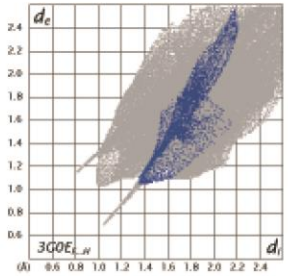
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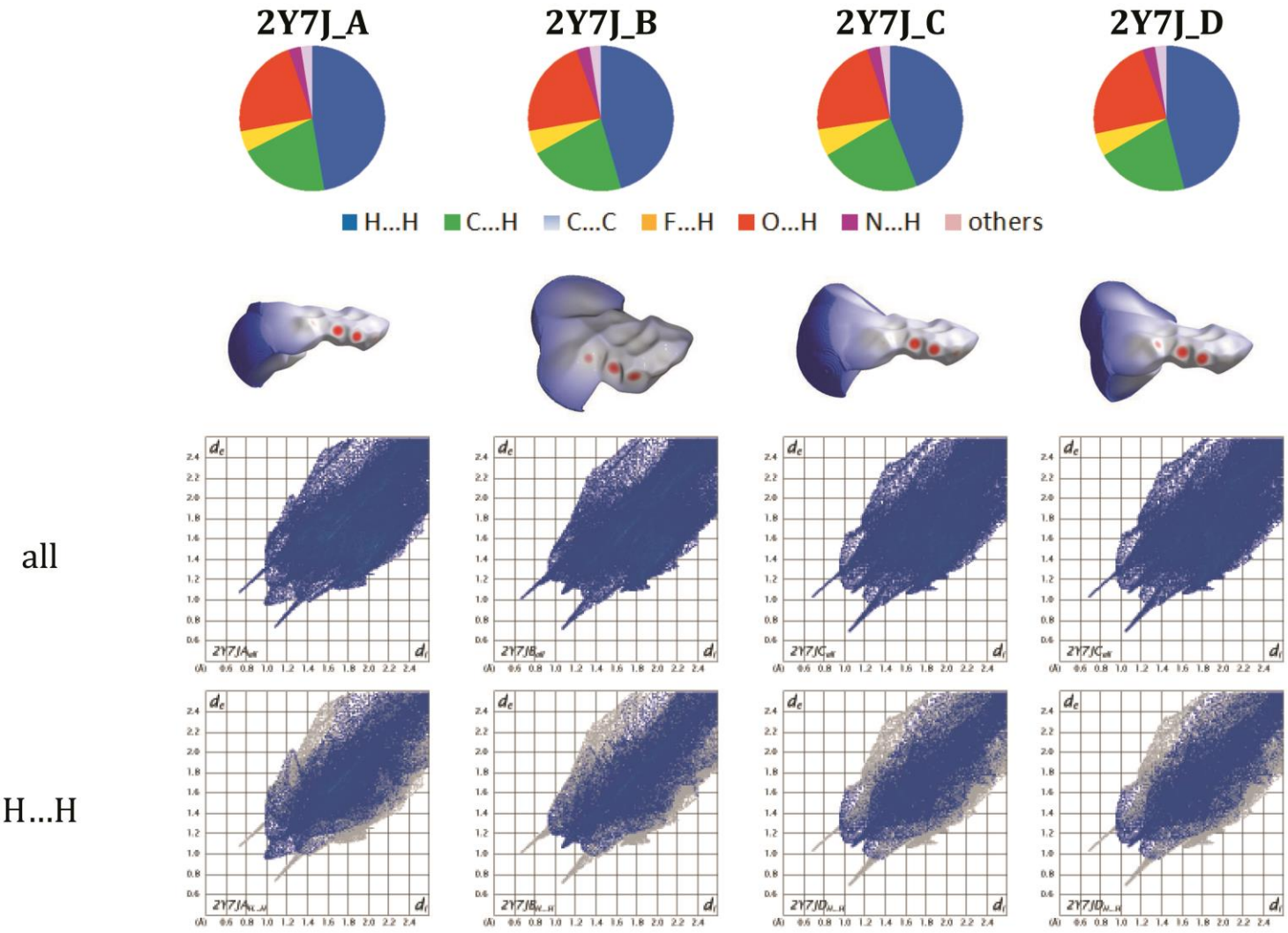
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2Y7J_C
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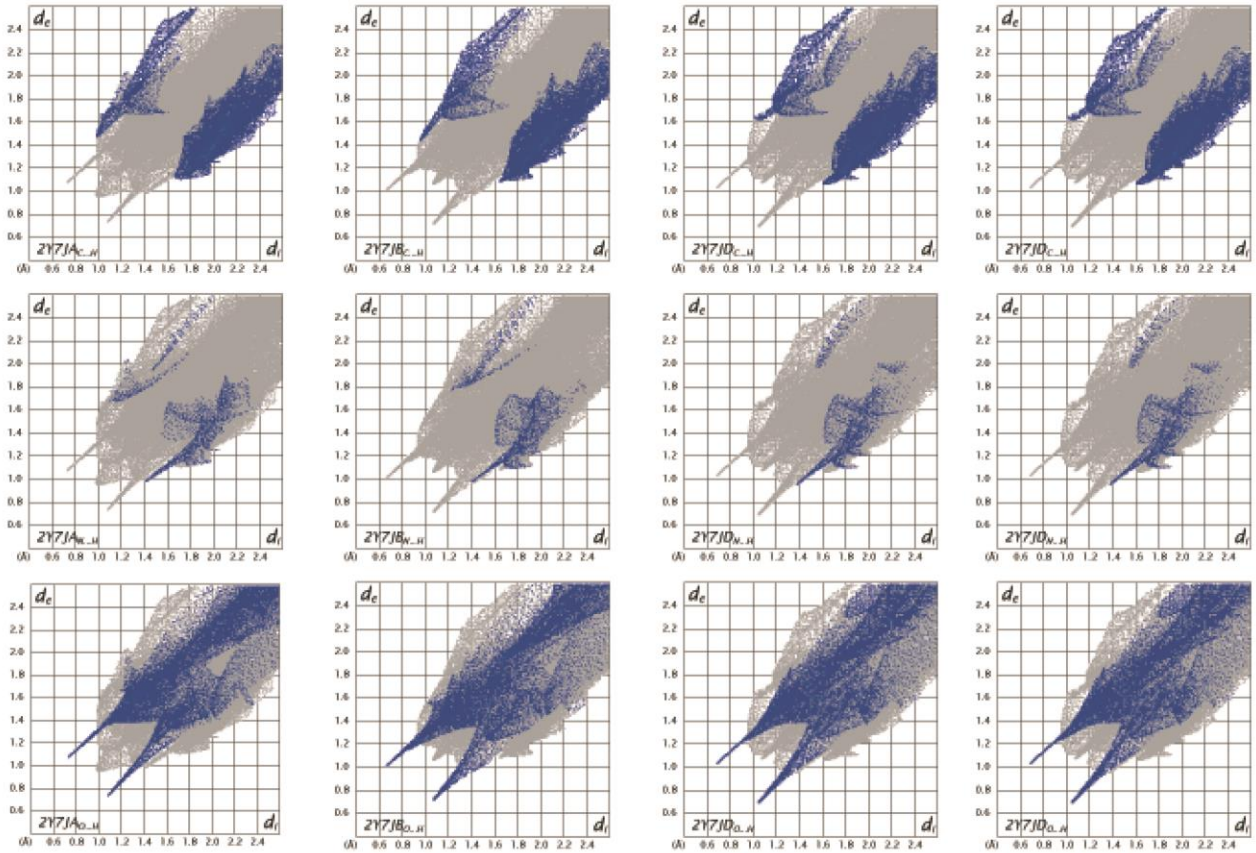
others
all
H...H

C…C

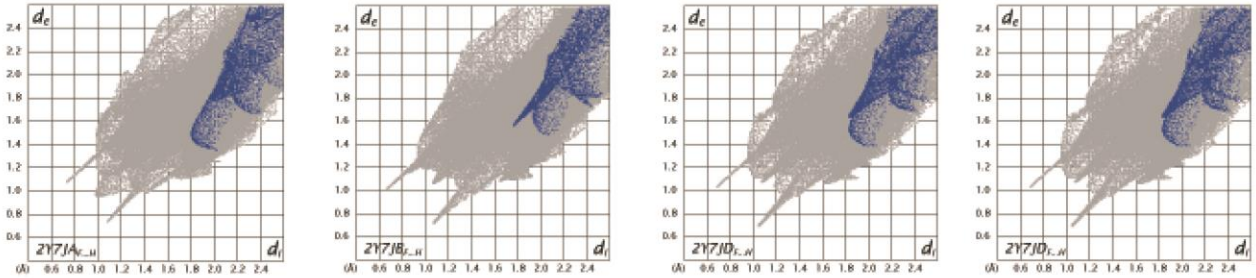
C…H

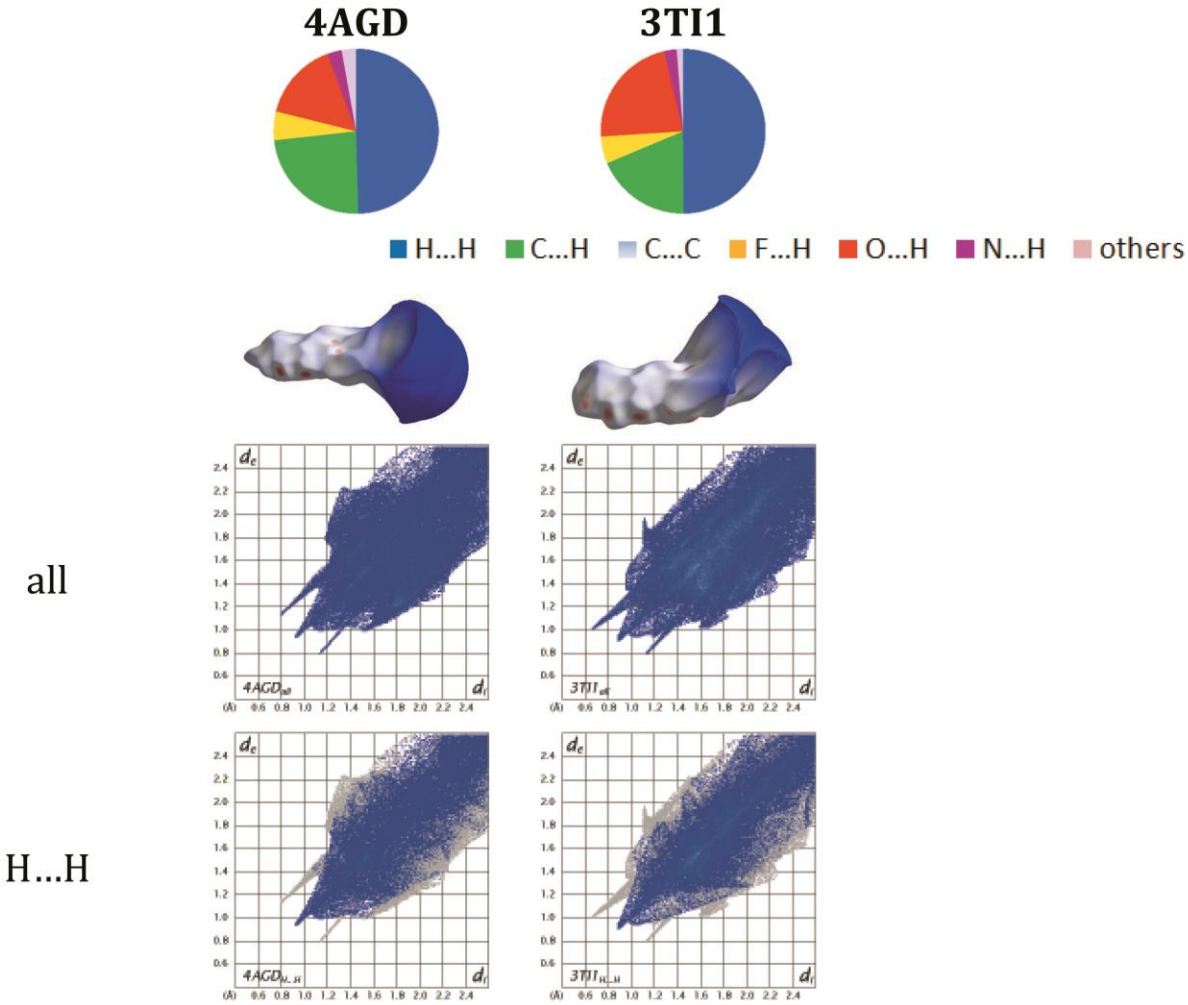
N…H

O…H



F...H

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C...C
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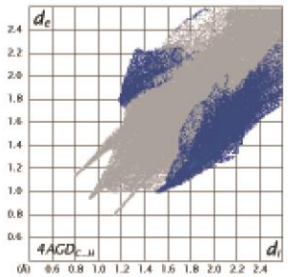
N...H
others
all
H...H
C...C

C…H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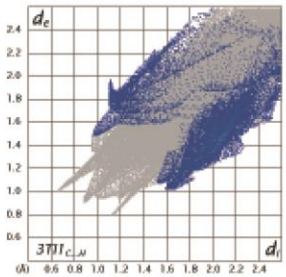
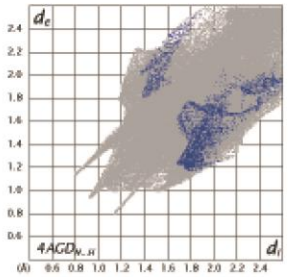
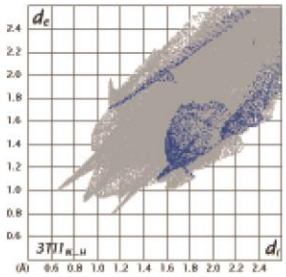
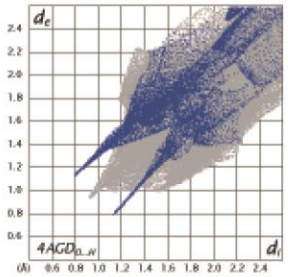

d_e
$3TIT_{C\_H}$
d_i

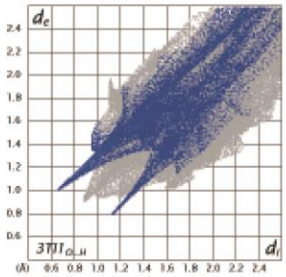
N…H


d_e
$4AGD_{N\_H}$
d_i


d_e
$3TIT_{N\_H}$
d_i

O…H


d_e
$4AGD_{O\_H}$
d_i


d_e
$3TIT_{O\_H}$
d_i

F…H

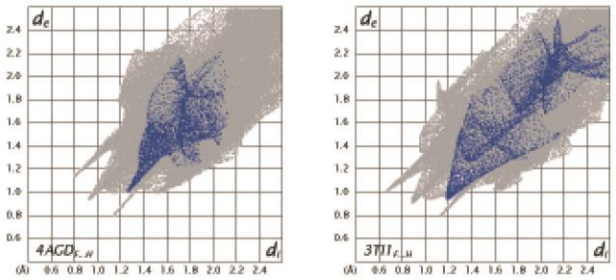


Figure S3. In the first row proportional pie diagram with percentage contributions of the H…H (blue), C…H (green), C…C (light blue), F…H (yellow), O…H (red), N…H (purple) contacts and other (pink) interaction contributions to the Hirshfeld surface. In the following rows d_{norm} mapped on Hirsfeld surfaces is shown and in the following rows fingerprint plots with marked main interactions found in the studied structures.

S7. Topological analysis of sunitinib-protein complexes.

Table S12. The list of amino acids and atom names for which the bond paths have been found between the sunitinib molecules and the VEGFR2 protein. E stands for the interaction energy calculated using the empirical formula proposed by Espinosa et al(Espinosa et al., 1998).

		VEGFR2 4AGD				
Res		E_{HB}				
LYS	838	0				
LEU	840	-4	**O**	HB3	HD22	**HD13**
VAL	848	-1	CG2			
ALA	866	0				
LYS	868	-2				
VAL	899	-2				
VAL	916	-1				
GLU	917	-6	**O**			
PHE	918	-1	CZ	CE1		
CYS	919	-8	**O**	**H**		
LYS	920	-1	**O**			
GLY	922	-1	**HA2**	N		
LEU	1035	-2	**HD13**	HD12		
CYS	1045	-1				
ASP	1046	-1				
PHE	1047	-6				
	∑	-37				

Table S13. The list of amino acids and atom names for which the bond paths have been found between the sunitinib molecules and the CDK2 protein. E stands for the interaction energy calculated using the empirical formula proposed by Espinosa et al**(Espinosa et al., 1998)**

		CDK2 3TI1				
Res		E_{HB}				
ILE	10	-10	HG13	**HD12**	HB	**O**
GLY	11	-1				
VAL	79	-15				
PHE	80	-4	HB3			
GLU	81	-5	**O**			
PHE	82	-3	CZ			
LEU	83	-10	**O**	**H**		
HIS	84	-3	**O**			
GLN	85	-1				
ASP	86	-22				
LYS	89	-1				
GLN	131	-1				

LEU	134	-6	**HD13**	HD11	HA	HB3
ALA	144	-1				
ASP	145	-5				
	∑	-87				

Table S14. The list of amino acids and atom names for which the bond paths have been found between the sunitinib molecules and the ITK protein. E stands for the interaction energy calculated using the empirical formula proposed by Espinosa et al**(Espinosa et al., 1998)**

ITK 3MIY_A			ITK 3MIY_B					
AA		E_{HB}	AA		E_{HB}			
LYS	391	-1	LYS	391	-3	**O**	**HD12**	HB
ILE	369	-3	ILE	369	-3			
VAL	377	0						
ALA	389	-1						
MET	438	-16	MET	438	-16	**O**	**H**	HG2
VAL	419	-1	VAL	419	-1			
GLY	441	-1	GLY	441	-2	HA2		
PHE	437	-1	PHE	437	-1	CZ		
GLU	436	-4	GLU	436	-3	**O**		
PHE	435	-3	PHE	435	-2	HB3		
HIS	440	-2						
LEU	489	-2	LEU	489	-2	**HD22**	HD13	
GLU	439	-1	GLU	439	-3	**O**		
CYS	442	-1	CYS	442	-1			
SER	499	0						
	∑	-37			-35			

Table S15. The list of amino acids and atom names for which the bond paths have been found between the sunitinib molecules and the G2K protein. E stands for the interaction energy calculated using the empirical formula proposed by Espinosa et al**(Espinosa et al., 1998)**

G2K_A			G2K_B			G2K_C			G2K_D		
Res		E_{HB}	Res		E_{HB}	Res		E_{HB}	Res		E_{HB}
			VAL	29	0						
ILE	30	-9	ILE	30	-15	ILE	30	-7	ILE	30	-10
			GLY	31	0				GLY	31	-1
ARG	32	-2									
			VAL	38	-1	VAL	38	-1	VAL	38	-1
ALA	51	-1	ALA	51	-1	ALA	51	-1	ALA	51	-1
ILE	91	-1	ILE	91	-1	ILE	91	-1	ILE	91	-1
PHE	107	-2	PHE	107	-3	PHE	107	-3	PHE	107	-3
ASP	108	-9	ASP	108	-14	ASP	108	-12	ASP	108	-15
LEU	109	-1	LEU	109	-1	LEU	109	-1	LEU	109	-1
MET	110	-12	MET	110	-14	MET	110	-15	MET	110	-15
ARG	111	-1	ARG	111	-2	ARG	111	-2	ARG	111	-2

GLY	113	-1	GLY	113	-2				GLY	113	-2
GLU	114	-1	GLU	114	-1	GLU	114	-1	GLU	114	0
						ASP	117	-2	ASP	117	0
LEU	160	-1	LEU	160	-1	LEU	160	-1	LEU	160	-2
ASP	171	0									
	∑	-41			-55			-46			-53
ILE	30	**HD12**	**O**	HB							
PHE	107	CB									
ASP	108	**O**									
LEU	109	HD12									
MET	110	**H**	**O**								
ARG	111	HA	**O**								
GLY	113	**HA2**	N								
LEU	60	**HD22**									

Table S16. The list of amino acids and atom names for which the bond paths have been found between the sunitinib molecules and the KIT protein. E stands for the interaction energy calculated using the empirical formula proposed by Espinosa et al**(Espinosa et al., 1998)**

	KIT 3G0E				
Res		E_{HB}			
LEU	595	-4	HB3	**O**	**HD22**
VAL	603	-2			
ALA	621	-1			
LYS	623	0			
VAL	654	-1			
THR	670	-2	OG1		
GLU	671	-5	**O**		
TYR	672	-1	OH	HA	
CYS	673	-15	**O**	**H**	
CYS	674	-1	**O**		
GLY	676	-2	**HA2**	N	HA3
LEU	799	-1	**HD11**		
CYS	809	-1			
ASP	810	-1			
PHE	811	-3			
	∑	-41			

Table S17. The list of amino acids and atom names for which the bond paths have been found between the sunitinib molecules and the KIT protein. E stands for the interaction energy calculated using the empirical formula proposed by Espinosa et al**(Espinosa et al., 1998)**

Mutant KIT_A 3G0F			Mutant KIT_B 3G0F						
Res		E	Res		E				
LEU	595	-3	LEU	595	-3	HB3	HD13	**O**	**HD22**

VAL	603	-2	VAL	603	-3			
ALA	621	-1	ALA	621	-1			
			LYS	623	0			
VAL	654	-1	VAL	654	-1			
THR	670	-2	THR	670	-2	OG1		
GLU	671	-5	GLU	671	-5	**O**		
			TYR	672	-1			
CYS	673	-19	CYS	673	-9	**O**	**H**	
CYS	674	-1	CYS	674	0	**O**		
GLY	676	-2	GLY	676	-2	N	**HA2**	HA3
LEU	799	-1	LEU	799	-2			
CYS	809	-1	CYS	809	-1			
			ASP	810	-1			
PHE	811	-1	PHE	811	-3			
	∑	-39			-34			

Table S18. Energy [kcal·mol^{-1}] obtained from Espinosa et. al approach(Espinosa et al., 1998) between sunitinib fragments (sum for fragment 1-3 and 1-4) and amino acids. In the case of proteins with more than one molecule in the asymmetric unit the results were averaged.

Res	SU	4AGD	3TI1	3MIY	2Y7JA	3G0E	3G0FA
	Frag	VEGFR2	CDK2	ITK	G2K	KIT	KITmutant
All	1-4	-37	-87	-36	-46	-41	-37
All	1-3	-37	-52	-33	-40	-41	-37
Conserved	1-3	-32	-26	-29	-33	-35	-30
Alignment	1-3	-31	-37	-33	-39	-38	-34

S8. Electrostatic energy of interactions in the protein binding pockets

The conserved aspartate (Res22), lysine (Res8) and valine/isoleucina (Res9) residues are located in the vicinity of the fluorine atom. Since the advent of 5-fluorouracil, fluorine substitution has become a common strategy in drug design procedures, which was applied for example to obtain torvastatin and lansoprazole(O'Hagan & S. Rzepa, 1997). Fluorination influences the acidic character of the active molecule, changes the charge distribution, and usually enhances hydrophobic interactions between the drug and binding sites of receptors or enzymes. Res8, 9 and 22 residues form interaction with the SU moiety which are different in nature. The electrostatic interaction energy for aspartate is attractive because of the long-distance electrostatic interactions with Fragment 3 (and even stronger with Fragment 4, on average -21 kcal·mol^{-1}). However, the considered interaction with Fragment 1 is repulsive due to the negatively-charged carboxylic group of the aspartate. Lysine interacts inversely when compared to aspartate. Thanks to its positive charge, the electrostatic contact with the fluorinated oxindole ring of SU is beneficial, although the overall lysine-SU interaction exhibits repulsive character (on

average 7 kcal·mol^{-1}). Finally, hydrophobic and neutral valine/isolucine is rather electrostatically insensitive but may participate in some vdW-type interactions with SU. In the case of the SUM crystal, it is also difficult to uniquely asses the nature and strength of the C-H…F contact itself due to the strong repulsive electrostatic forces resulting from the positive charge of the interacting SU moieties. Consequently, the total interaction energy of the related D3 dimer amounts to 16 kcal·mol^{-1}, while the electrostatic component is equal to 19 kcal·mol^{-1}. This shows that some of the other total interaction energy contributions are slightly stabilizing.

Table S19. The C(11)C(10)C(9)O(7) (protein C(13)C(19)C(22)O(22)) torsion angle in the analysed proteins.

CDK2	G2K	ITK	VEGFR2	CRYSTAL
-140.8	-168.3	-27.3	0.0	-39.94
	-166.3			
	-157.4			
	-148.0			

Table S20. Alignment with detailed numerical labelling of particular residues building the pocket for, i.e. VEGFR2-4AGD, CDK2-3TI1, ITK-3MIY, G2K-2Y7J, KIT-3G0E. Phe* (23) may occupy different positions depending on the protein crystal.

	VEGFR2		CDK2		ITK		G2K		KIT	
1	LYS	838	GLU	8	GLN	367	ASP	28	LYS	593
2	PRO	839	LYS	9	GLU	368	VAL	29	THR	594
3	LEU	840	ILE	10	ILE	369	ILE	30	LEU	595
4	GLY	841	GLY	11	GLY	370	GLY	31	GLY	596
5	ARG	842	GLU	12	SER	371	ARG	32	ALA	597
6	VAL	848	VAL	18	VAL	377	VAL	38	VAL	603
7	ALA	866	ALA	31	ALA	389	ALA	51	ALA	621
8	LYS	868	LYS	33	LYS	391	LYS	53	LYS	623
9	VAL	899	VAL	64	VAL	419	ILE	91	VAL	654
10	VAL	916	PHE	80	PHE	435	PHE	107	THR	670
11	GLU	917	GLU	81	GLU	436	ASP	108	GLU	671
12	PHE	918	PHE	82	PHE	437	LEU	109	TYR	672
13	CYS	919	LEU	83	MET	438	MET	110	CYS	673
14	LYS	920	HIS	84	GLU	439	ARG	111	CYS	674
15	PHE	921	GLN	85	HIS	440	LYS	112	TYR	675
16	GLY	922			GLY	441	GLY	113	GLY	676
17	ASN	923	ASP	86	CYS	442	GLU	114	ASP	677
18	SER	925	LEU	87	SER	444	PHE	116	LEU	679
19	THR	926	LYS	88	ASP	445	ASP	117	ASN	680
20	LEU	1035	LEU	134	LEU	489	LEU	160	LEU	799
21	CYS	1045	ALA	144	SER	499	SER	170	CYS	809
22	ASP	1046	ASP	145	ASP	500	ASP	171	ASP	810
23	PHE	1047	PHE	146	PHE	501	PHE	172	PHE	811
24	GLY	1048	GLY	147	GLY	502	GLY	173	GLY	812

Table S21. Electrostatic interaction energy values [kcal·mol^{-1}] for chosen interactions of sunitinib fragments (sum for fragment 1-3) with the selected amino acids.

	VEGFR2	CDK2	ITK_A	ITK_B	G2K_A	G2K_B	G2K_C	G2K_D
1	9	-10	0	-1	-10	-10	-10	-10
2	-1	8	-8	-8	-1	-1	-1	-1
3	-6	-3	-4	-4	-6	-5	-6	-7
4	1	1	1	1	1	1	1	1
5	7	-8	0	0	8	7	7	8
6	-1	0	0	0	-1	0	-1	-1
7	0	0	-1	0	0	0	0	0
8	5	7	5	4	7	6	6	6
9	1	0	1	1	1	1	1	1
10	0	-4	-2	-2	-2	-2	-2	-2
11	-24	-23	-21	-20	-27	-31	-29	-32
12	0	0	0	0	0	0	0	0
13	-12	-11	-16	-16	-15	-16	-17	-17
14	8	-3	-11	-11	9	10	10	9
15	-1	0	-1	-1	7	7	7	7
16	1	0	0	0	0	0	0	0
17	2	-13	-1	-1	-13	-13	-13	-13
18	0	0	0	0	0	1	0	0
19	1	7	-11	-11	-10	-10	-10	-10
20	-1	-2	-1	-1	0	-1	-1	-1
21	0	0	0	1	0	1	0	0
22	-5	-9	-5	-6	-6	-6	-7	-6
23	-2	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0

	KIT	KIT mutantA	KIT mutantB
1	11	11	11
2	-1	-1	-1
3	-6	-4	-5
4	1	1	1
5	0	-1	-1
6	-3	-2	-3
7	1	1	1
8	10	7	8
9	1	1	1
10	-2	-1	-2
11	-22	-23	-22
12	-1	-1	-1
13	-16	-20	-12
14	0	0	0
15	-1	-1	-1
16	0	1	0
17	-11	-12	-11

18	-2	-2	-3
19	1	1	1
20	0	0	0
21	-2	-2	-3
22	-6	-6	-6
23	0	1	-1
24	0	0	0

Table S22. Electrostatic interaction energy values [kcal·mol^{-1}] for chosen interactions of sunitinib fragments (sum for fragment 1-4) with the selected amino acids. In the case of proteins with more than one molecule in the asymmetric unit the corresponding results were averaged.

	VEGFR2	CDK2	ITK	G2K
1	50	-33	-1	-35
2	-3	35	-27	-6
3	-5	-21	-2	-18
4	1	5	2	3
5	23	-32	0	36
6	-1	1	0	-2
7	1	1	0	1
8	17	24	17	22
9	1	1	2	2
10	0	-4	-2	-2
11	-36	-36	-36	-42
12	0	0	1	0
13	-13	-12	-19	-16
14	29	-3	-44	23
15	-2	-2	-4	21
16	2	0	2	0
17	2	-92	-2	-39
18	-1	-2	-1	0
19	0	43	-31	-46
20	-1	-1	-1	0
21	0	0	1	0
22	-15	-29	-17	-22
23	-1	0	0	1
24	0	0	0	1
∑	**49**	**-156**	**-162**	**-117**

Table S23. Electrostatic energy [kcal·mol^{-1}] for chosen interactions of sunitinib fragments (sum for fragment 1-4) with selected amino acids.

	VEGFR2	CDK2	ITK_A	ITK_B	G2K_A	G2K_B	G2K_C	G2K_D
1	50	-33	0	-1	-39	-36	-33	-31
2	-3	35	-27	-27	-7	-7	-4	-4
3	-5	-21	-2	-2	-17	-23	-16	-18

4	1	5	2	2	4	4	3	4
5	23	-32	0	0	47	35	27	34
6	-1	1	0	0	-2	-2	-1	-1
7	1	1	0	0	1	1	1	1
8	17	24	17	16	23	22	21	22
9	1	1	2	2	2	2	2	2
10	0	-4	-2	-2	-2	-2	-2	-2
11	-36	-36	-36	-35	-39	-43	-41	-44
12	0	0	1	1	0	0	0	0
13	-13	-12	-19	-18	-14	-15	-17	-17
14	29	-3	-44	-44	23	23	23	22
15	-2	-2	-5	-4	20	20	23	20
16	2		2	2	0	0	1	1
17	2	-92	-2	-2	-39	-38	-40	-41
18	-1	-2	-1	-1	0	0	0	0
19	0	43	-31	-31	-39	-42	-50	-54
20	-1	-1	-1	-1	1	0	0	0
21	0	0	0	2	0	0	0	0
22	-15	-29	-17	-17	-22	-21	-21	-22
23	-1	0		1	1	1	1	1
24	0	0	0	0	1	1	1	1

Table S24. Electrostatic energy [kcal·mol^{-1}] for chosen interactions of sunitinib fragments (1-4) with selected amino acids (VEGFR2).

			1	**2**	**3**	**4**	**∑(1-4)**
1	LYS	838	-4	1	13	40	50
2	PRO	839	0	0	-1	-2	-3
3	LEU	840	-1	0	-5	2	-5
4	GLY	841	0	0	1	0	1
5	ARG	842	-3	2	9	16	23
6	VAL	848	-1	0	0	-1	-1
7	ALA	866	-1	0	1	1	1
8	LYS	868	-9	3	11	12	17
9	VAL	899	0	0	1	1	1
10	VAL	916	0	0	0	0	0
11	GLU	917	-11	-1	-12	-12	-36
12	PHE	918	0	0	0	1	0
13	CYS	919	-10	0	-2	-1	-13
14	LYS	920	-4	1	11	21	29
15	PHE	921	0	0	-1	-1	-2
16	GLY	922	-2	0	3	1	2
17	ASN	923	-1	1	3	-1	2
18	SER	925	0	0	0	-1	-1
19	THR	926	0	0	1	0	0
20	LEU	1035	-2	0	1	0	-1

21	CYS	1045	0	0	0	0	0
22	ASP	1046	6	-2	-8	-10	-15
23	PHE	1047	-3	0	0	0	-1
24	Gly	1048	0	0	0	0	0
			-46	**5**	**25**	**65**	**49**

Table S25. Electrostatic energy [kcal·mol[1]] for chosen interactions of sunitinib fragments (1-4) with selected amino acids (CDK2).

			1	**2**	**3**	**4**	**∑(1-4)**
1	GLU	8	5	-2	-13	-23	-33
2	LYS	9	-4	2	10	27	35
3	ILE	10	-1	0	-2	-19	-21
4	GLY	11	0	0	1	4	5
5	GLU	12	4	-2	-9	-24	-32
6	VAL	18	-1	1	0	0	1
7	ALA	31	-1	0	2	1	1
8	LYS	33	-6	3	10	17	24
9	VAL	64	-1	0	1	1	1
10	PHE	80	-4	0	0	0	-4
11	GLU	81	-9	-1	-13	-13	-36
12	PHE	82	0	0	0	0	0
13	LEU	83	-4	0	-8	0	-12
14	HIS	84	0	0	-3	0	-3
15	GLN	85	0	0	0	-2	-2
16							
17	ASP	86	5	-2	-16	-79	-92
18	LEU	87	0	0	0	-2	-2
19	LYS	88	-3	2	9	36	43
20	LEU	134	-3	0	1	1	-1
21	ALA	144	0	0	1	0	0
22	ASP	145	5	-3	-10	-20	-29
23	PHE	146	0	0	0	0	0
24	GLY	147	0	0	0	0	0
		∑	**-16**	**-3**	**-41**	**-96**	**-156**

Table S26. Electrostatic energy [kcal·mol^{-1}] for chosen interactions of sunitinib fragments (1-4) with selected amino acids (ITK, A chain).

			1	**2**	**3**	**4**	**∑(1-4)**
1	GLN	367	0	0	-1	1	0
2	GLU	368	4	-2	-10	-19	-27
3	ILE	369	0	0	-4	2	-2
4	GLY	370	0	0	1	0	2
5	SER	371	0	0	0	0	0
6	VAL	377	0	1	0	-1	0
7	ALA	389	-2	0	1	1	0

8	LYS	391	-8	3	10	12	17
9	VAL	419	0	0	1	1	2
10	PHE	435	-1	0	0	0	-2
11	GLU	436	-8	-1	-12	-15	-36
12	PHE	437	0	0	-1	2	1
13	MET	438	-13	0	-3	-3	-19
14	GLU	439	5	-1	-15	-33	-44
15	HIS	440	0	0	-1	-4	-5
16	GLY	441	-2	0	2	2	2
17	CYS	442	0	0	0	-1	-2
18	SER	444	0	0	0	-1	-1
19	ASP	445	4	-2	-13	-20	-31
20	LEU	489	-2	0	1	0	-1
21	SER	499	-1	0	1	1	0
22	ASP	500	6	-2	-9	-11	-17
		∑	-19	-5	-52	-86	-161

Table S27. Electrostatic energy [kcal·mol^{-1}] for chosen interactions of sunitinib fragments (1-4) with selected amino acids (ITK, B chain).

		1	**2**	**3**	**4**	**∑(1-4)**
GLN	367	0	0	-1	-1	-1
GLU	368	4	-2	-10	-19	-27
ILE	369	-1	0	-4	2	-2
GLY	370	0	0	1	0	2
SER	371	0	0	0	0	0
VAL	377	0	1	0	-1	0
ALA	389	-2	0	1	1	0
LYS	391	-10	3	11	12	16
VAL	419	0	0	1	1	2
PHE	435	-2	0	0	0	-2
GLU	436	-7	-1	-12	-15	-35
PHE	437	1	0	-1	2	1
MET	438	-12	0	-3	-2	-18
GLU	439	5	-1	-15	-34	-44
HIS	440	0	0	-1	-3	-4
GLY	441	-2	0	2	2	2
CYS	442	0	0	0	-1	-2
SER	444	0	0	0	-1	-1
ASP	445	4	-2	-13	-21	-31
LEU	489	-2	0	1	0	-1
SER	499	1	0	0	0	2
ASP	500	6	-2	-9	-11	-17
PHE	501	0	0	0	0	1
GLY	502	0	0	0	0	0
	∑	-16	-5	-53	-88	-162

Table S28. Electrostatic energy [kcal·mol[1]] for chosen interactions of sunitinib fragments (1-4) with selected amino acids (G2K, A chain).

		1	2	3	4	∑(1-4)
ASP	28	5	-1	-14	-29	-39
VAL	29	0	0	-1	-7	-7
ILE	30	-1	-1	-4	-11	-17
GLY	31	0	0	1	3	4
ARG	32	-4	2	10	39	47
VAL	38	-1	0	0	-2	-2
ALA	51	-1	0	1	1	1
LYS	53	-5	3	10	16	23
ILE	91	0	0	1	1	2
PHE	107	-2	0	0	0	-2
ASP	108	-13	-1	-12	-12	-39
LEU	109	0	0	0	0	0
MET	110	-10	0	-4	0	-14
ARG	111	-5	1	14	14	23
LYS	112	-4	1	10	13	20
GLY	113	-1	0	2	0	0
GLU	114	5	-4	-15	-25	-39
SER	170	0	0	0	0	0
ASP	117	4	-2	-12	-30	-39
LEU	160	-2	0	1	1	1
SER	170	0	0	0	0	0
ASP	171	7	-3	-10	-16	-22
PHE	172	0	0	0	0	1
GLY	173	0	0	0	1	1
		-28	**-4**	**-22**	**-42**	**-97**

Table S29. Electrostatic energy [kcal·mol^{-1}] for chosen interactions of sunitinib fragments (1-4) with selected amino acids (G2K, B chain).

	G2K_B	1	2	3	4	∑(1-4)
ASP	28	5	-1	-14	-26	-36
VAL	29	0	0	-1	-6	-7
ILE	30	-1	0	-4	-17	-23
GLY	31	0	0	1	2	4
ARG	32	-3	2	9	28	35
VAL	38	-1	1	0	-1	-2
ALA	51	-1	0	1	1	1
LYS	53	-6	3	10	16	22
ILE	91	0	0	1	1	2
PHE	107	-2	0	0	0	-2
ASP	108	-18	-1	-12	-12	-43
LEU	109	0	0	0	0	0
MET	110	-10	0	-5	0	-15

ARG	111	-5	1	14	13	23
LYS	112	-3	1	10	12	20
GLY	113	-1	0	1	0	0
GLU	114	5	-4	-15	-25	-38
SER	170	1	0	0	0	0
ASP	117	4	-2	-12	-32	-42
LEU	160	-2	0	1	1	0
SER	170	1	0	0	0	0
ASP	171	6	-3	-10	-15	-21
PHE	172	0	0	0	0	1
GLY	173	0	0	0	1	0
	∑	**-33**	**-4**	**-24**	**-59**	**-120**

Table S30. Electrostatic energy [kcal·mol^{-1}] for chosen interactions of sunitinib fragments (1-4) with selected amino acids (G2K, C chain).

	2Y7JC	**1**	**2**	**3**	**4**	**∑(1-4)**
ASP	28	5	-1	-14	-23	-33
VAL	29	0	0	-1	-3	-4
ILE	30	-1	-1	-5	-10	-16
GLY	31	0	0	1	2	3
ARG	32	-3	2	9	20	27
VAL	38	-1	0	0	-1	-1
ALA	51	-1	0	1	1	1
LYS	53	-6	3	10	14	21
ILE	91	0	0	1	1	2
PHE	107	-2	0	0	0	-2
ASP	108	-16	-1	-12	-12	-41
LEU	109	0	0	0	0	0
MET	110	-12	0	-5	0	-17
ARG	111	-5	1	14	14	23
LYS	112	-3	1	10	15	23
GLY	113	-1	0	2	0	1
GLU	114	5	-3	-15	-27	-40
SER	170	0	0	0	0	0
ASP	117	4	-2	-12	-40	-50
LEU	160	-2	0	1	1	0
SER	170	0	0	0	0	0
ASP	171	6	-3	-10	-15	-21
PHE	172	0	0	0	0	1
GLY	173	0	0	0	1	1
	∑	**-33**	**-4**	**-24**	**-61**	**-123**

Table S31. Electrostatic energy [kcal·mol^{-1}] for chosen interactions of sunitinib fragments (1-4) with selected amino acids (G2K, D chain).

	2Y7JD	**1**	**2**	**3**	**4**	**∑(1-4)**

ASP	28	5	-1	-14	-20	-31
VAL	29	0	0	-1	-3	-4
ILE	30	-1	0	-6	-12	-18
GLY	31	0	0	1	2	4
ARG	32	-3	2	9	26	34
VAL	38	-1	1	0	-1	-1
ALA	51	-1	0	1	0	1
LYS	53	-6	3	10	16	22
ILE	91	0	0	1	1	2
PHE	107	-2	0	0	0	-2
ASP	108	-18	-1	-12	-12	-44
LEU	109	-1	0	0	0	0
MET	110	-12	0	-6	0	-17
ARG	111	-5	1	14	12	22
LYS	112	-3	1	10	13	20
GLY	113	-1	0	2	1	1
GLU	114	5	-4	-14	-28	-41
SER	170	0	0	0	0	0
ASP	117	4	-2	-13	-43	-54
LEU	160	-2	0	1	1	0
SER	170	0	0	0	0	0
ASP	171	7	-3	-10	-16	-22
PHE	172	0	0	0	0	1
GLY	173	0	0	0	1	1
		-36	-4	-25	-62	-126

Table S32. Electrostatic energy [kcal·mol^{-1}] for chosen interactions of sunitinib fragments (1-3) with selected amino acids (KIT).

		1	**2**	**3**	**∑(1-3)**
LYS	593	-5	1	15	11
THR	594	0	0	-1	-1
LEU	595	-1	-1	-4	-6
GLY	596	0	0	1	1
ALA	597	0	0	0	0
VAL	603	-3	0	0	-3
ALA	621	-1	0	1	1
LYS	623	-2	2	10	10
VAL	654	0	0	1	1
THR	670	-1	0	-1	-2
GLU	671	-10	-1	-12	-22
TYR	672	1	0	-2	-1
CYS	673	-14	0	-2	-16
CYS	674	-1	0	0	0
TYR	675	0	0	-1	-1
GLY	676	-1	0	1	0
ASP	677	5	-2	-13	-11

CYS	809	-2	0	0	-2
ASN	680	-1	0	1	1
LEU	799	-2	0	1	0
CYS	809	-2	0	0	-2
ASP	810	5	-2	-8	-6
PHE	811	-1	0	1	0
GLY	812	0	0	0	0
	∑	-35	-1	-11	-48

Table S33. Electrostatic energy [kcal·mol^{-1}] for chosen interactions of sunitinib fragments (1-3) with selected amino acids (KIT mutant, A chain).

			1	**2**	**3**	**∑(1-3)**
1	LYS	593	-5	1	15	11
2	THR	594	0	0	-1	-1
3	LEU	595	-1	-1	-2	-4
4	GLY	596	0	0	1	1
5	ALA	597	1	0	-1	-1
6	VAL	603	-2	0	0	-2
7	ALA	621	0	0	1	1
8	LYS	623	-5	2	9	7
9	VAL	654	0	0	1	1
10	THR	670	0	0	-1	-1
11	GLU	671	-10	-1	-12	-23
12	TYR	672	1	0	-2	-1
13	CYS	673	-19	0	-2	-20
14	CYS	674	-1	0	0	0
15	TYR	675	0	0	-1	-1
16	GLY	676	-1	0	2	1
17	ASP	677	5	-2	-15	-12
18	CYS	809	-3	0	0	-2
19	ASN	680	0	0	1	1
20	LEU	799	-2	0	1	0
21	CYS	809	-3	0	0	-2
22	ASP	810	4	-2	-8	-6
23	PHE	811	-1	1	1	1
24	GLY	812	0	0	0	0
		∑	-43	-1	-10	-54

Table S34. Electrostatic energy [kcal·mol^{-1}] for chosen interactions of sunitinib fragments (1-3) with selected amino acids (KIT mutant, B chain).

		1	**2**	**3**	**∑(1-3)**
LYS	593	-5	2	15	11
THR	594	0	0	-1	-1
LEU	595	-1	-1	-3	-5
GLY	596	0	0	1	1

ALA	597	0	0	-1	-1
VAL	603	-4	0	0	-3
ALA	621	0	0	1	1
LYS	623	-4	2	9	8
VAL	654	0	0	1	1
THR	670	-1	0	-1	-2
GLU	671	-9	-1	-12	-22
TYR	672	0	0	-1	-1
CYS	673	-11	0	-1	-12
CYS	674	-1	0	1	0
TYR	675	0	0	-1	-1
GLY	676	-1	0	2	0
ASP	677	5	-2	-13	-11
CYS	809	-3	0	0	-3
ASN	680	0	0	1	1
LEU	799	-2	0	1	0
CYS	809	-3	0	0	-3
ASP	810	5	-2	-8	-6
PHE	811	-2	0	1	-1
GLY	812	0	0	0	0
	∑	-38	-1	-9	-48

Table S35. Electrostatic energy [kcal·mol^{-1}] chosen interactions of sunitinib fragments (sum for fragment 1-4 and 1-3) with the selected amino acids for the VEGFR2:SU complexes. Sunitinib molecules with neutral charge.

	Res		1-4	1-3
1	LYS	838	5	-1
2	PRO	839	1	0
3	LEU	840	-4	-7
4	GLY	841	0	0
5	ARG	842	-2	-1
6	VAL	848	-1	-1
7	ALA	866	-1	-1
8	LYS	868	-11	-10
9	VAL	899	-1	-1
10	VAL	916	0	0
11	GLU	917	-11	-11
12	PHE	918	-1	-1
13	CYS	919	-11	-11
14	LYS	920	2	-1
15	PHE	921	1	0
16	GLY	922	-2	-1
17	ASN	923	-2	0
18	SER	925	0	0
19	THR	926	-1	0
20	LEU	1035	-3	-3

21	CYS	1045	-1	-1
22	ASP	1046	6	5
23	PHE	1047	-3	-3
24	GLY	1048	0	0
		∑	-42	-48

Table S36. Electrostatic energy [kcal·mol^{-1}] for chosen interactions of ADP adenine ring and ADP+Mg^{2+} with selected amino acids (KIT kinase, 1PKG).

ADP+Mg					Res No.	Adenine	Frag1/SU
LEU	595	-1	LEU	595	Res3	-1	-1
GLY	596	1	GLY	596	Res4	-1	0
ALA	597	3	ALA	597	Res5	0	0
GLY	598	-29	VAL	603	Res6	-4	-3
ALA	599	3	ALA	621	Res7	-2	-1
PHE	600	-13	LYS	623	Res8	-12	-2
GLY	601	-17	VAL	654	Res9	-1	0
LYS	602	-35	THR	670	Res10	-4	-1
VAL	603	-11	GLU	671	Res11	2	-10
GLU	605	26	TYR	672	Res12	0	1
VAL	620	2	CYS	673	Res13	-10	-14
ALA	621	-2	GLY	676	Res16	-2	-1
LYS	623	-159	ASP	677	Res17	14	5
LYS	626	-47	LEU	799	Res20	-7	-2
GLU	640	63	CYS	809	Res21	-1	-2
VAL	654	-2	ASP	810	Res22	8	5
ASN	655	1		∑		-22	-26
THR	670	-7					
GLU	671	19					
TYR	672	-2					
CYS	673	-11					
CYS	674	-1					
TYR	675	1					
GLY	676	-3					
ASP	677	13					
LEU	678	0					
LEU	679	1					
ASN	680	2					
ARG	684	-19					
ASP	792	16					
ALA	795	-1					
ARG	796	-5					
ASN	797	-30					
ILE	798	1					
LEU	799	-10					
LEU	800	1					

CYS	809	0
ASP	810	55
PHE	811	0
GLY	812	-7
	∑	-202

(a)

(b)

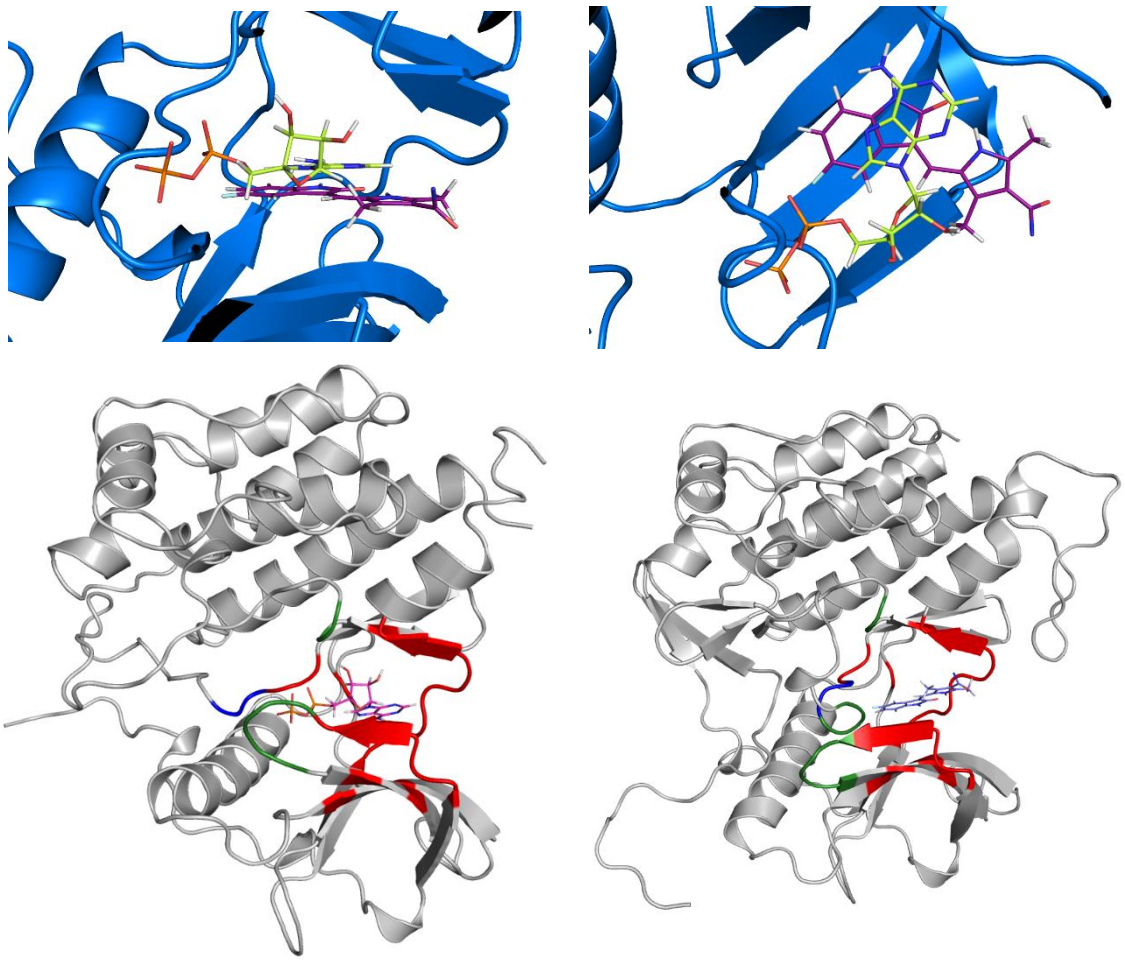


Figure S4. (a) Overlay of the protein binding pocket with sunitinib (purple) and ADP (lemon) molecules with the KIT proteins (cartoon representation). Only KIT (PDBID:1PKG) is shown for clarity. (b) ADP and SU binding pocket with residues forming binding pocket of KIT protein. Red colour indicate common residues, green residues connect to ADP only and blue residues connect to SU only. Picture representative only for KIT case.

S9. Electrostatic potential

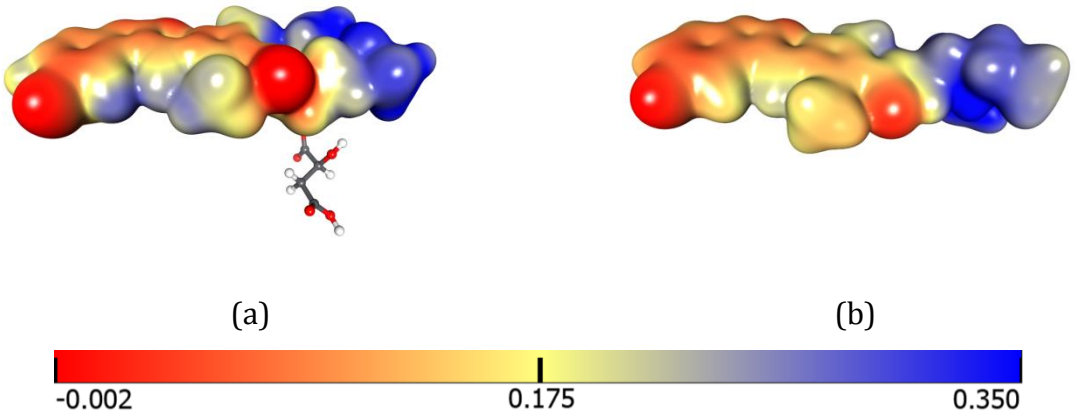
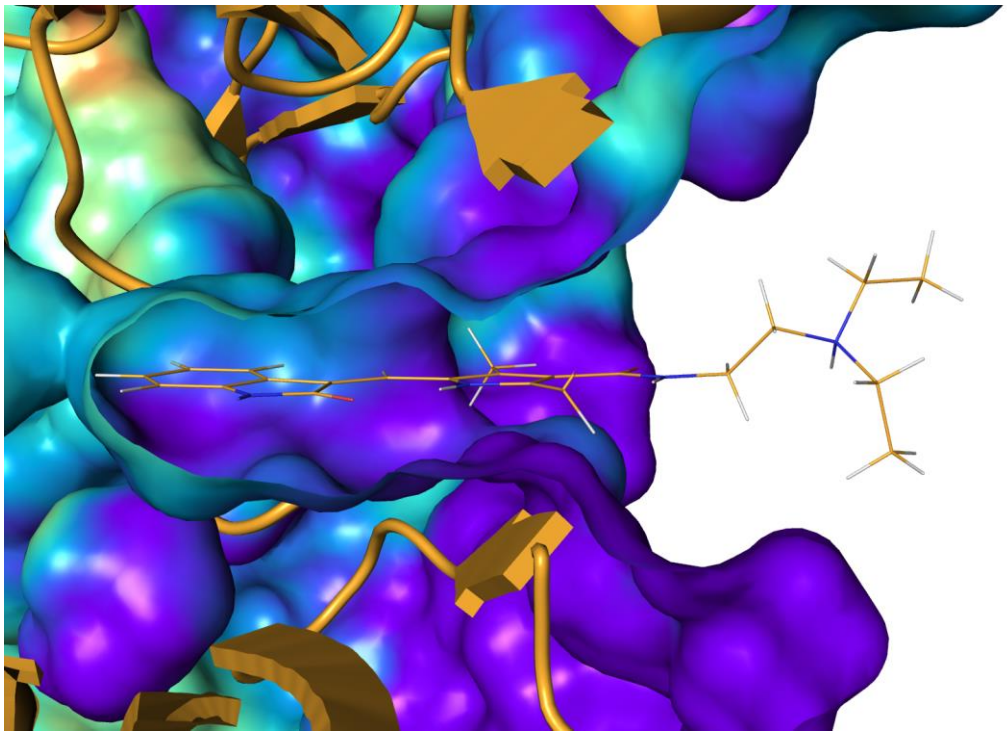
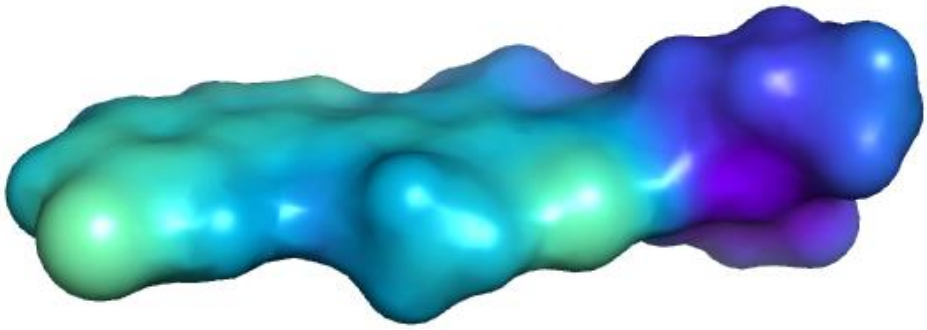


Figure S5. Electrostatic Potential Isosurfaces at isodensity contour level 0.0135 e·A^{-3} for (a) sunitinib in crystal, (b) in the active site of VEGFR2. Electropositive, electronegative and neutral isosurface regions are indicated by blue, red and yellow colours, respectively.

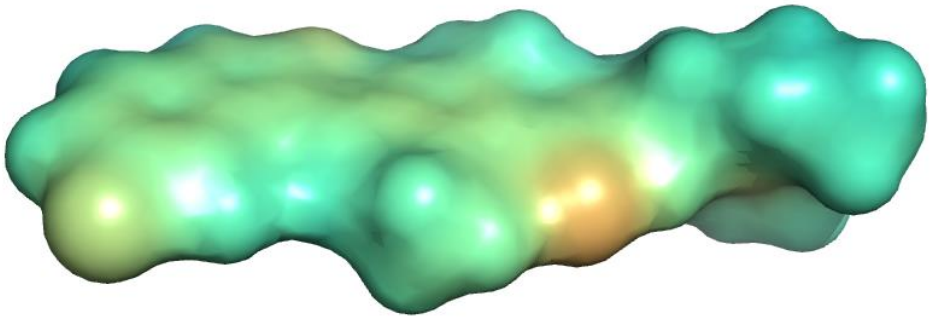
(a)



(b)



(c)



(d)

Figure S6. Electrostatic Potential mapped on van der Waals surface for VEGRF binding pocket (a) protonated sunitinib ligand (charge +1) (b) unprotonated sunitinib ligand (charge 0). (d) ESP scale for all figures.

S10. Cartesian coordinates used for calculations in the Gaussian09 package(Frisch et al.)

Table S37. Cartesian coordinates of dimers used in the supermolecular calculation

DIMER 1

F(Fragment=1)	0.02600000	-6.79200000	20.22600000
O(Fragment=1)	-3.90900000	-2.18200000	16.40500000
O(Fragment=1)	1.30000000	2.81700000	16.62400000
N(Fragment=1)	0.59200000	5.91100000	13.19200000
N(Fragment=1)	0.40300000	2.82100000	14.54700000
N(Fragment=1)	-3.92000000	-4.22900000	17.45300000
N(Fragment=1)	-2.06400000	-0.23800000	16.30400000
C(Fragment=1)	-1.82900000	5.48200000	13.83700000
C(Fragment=1)	-0.74400000	5.34000000	12.78600000
C(Fragment=1)	1.25200000	5.17800000	14.32200000
C(Fragment=1)	1.46100000	3.69200000	14.04200000
C(Fragment=1)	0.47700000	2.36100000	15.81900000
C(Fragment=1)	-0.39600000	1.22600000	16.18200000
C(Fragment=1)	0.06400000	0.11600000	16.93500000
C(Fragment=1)	-0.99700000	-0.80100000	16.98300000
C(Fragment=1)	-0.99800000	-2.08200000	17.59200000
C(Fragment=1)	-1.96300000	-3.05000000	17.65700000
C(Fragment=1)	-1.81700000	-4.33500000	18.33100000
C(Fragment=1)	-0.76400000	-4.92000000	19.03100000
C(Fragment=1)	-0.99000000	-6.18900000	19.54900000
C(Fragment=1)	-2.18200000	-6.88400000	19.41200000
C(Fragment=1)	-3.24100000	-6.28900000	18.71900000
C(Fragment=1)	-3.03300000	-5.02700000	18.18500000
C(Fragment=1)	-3.34000000	-3.04500000	17.09200000
C(Fragment=1)	-1.72700000	0.97700000	15.81500000
C(Fragment=1)	1.41500000	-0.06300000	17.54400000
C(Fragment=1)	0.50000000	7.38200000	13.48800000
C(Fragment=1)	1.86900000	8.03700000	13.61500000
C(Fragment=1)	-2.72300000	1.81500000	15.09100000
H(Fragment=1)	-1.63000000	5.03400000	14.82000000
H(Fragment=1)	-2.69800000	4.92000000	13.47000000
H(Fragment=1)	-2.09800000	6.53700000	13.98900000
H(Fragment=1)	-0.54000000	4.29100000	12.56000000
H(Fragment=1)	-1.05900000	5.90100000	11.90300000
H(Fragment=1)	0.63100000	5.31400000	15.21000000
H(Fragment=1)	2.25100000	5.60400000	14.44600000
H(Fragment=1)	1.55200000	3.54900000	12.96400000
H(Fragment=1)	2.39900000	3.42700000	14.53500000
H(Fragment=1)	-0.08500000	-2.36900000	18.09900000
H(Fragment=1)	0.21800000	-4.47300000	19.11800000
H(Fragment=1)	-2.25600000	-7.87000000	19.85500000
H(Fragment=1)	-4.20800000	-6.76300000	18.60600000
H(Fragment=1)	1.46200000	0.36800000	18.55400000
H(Fragment=1)	2.15600000	0.43100000	16.90000000
H(Fragment=1)	1.67600000	-1.11700000	17.71000000
H(Fragment=1)	-0.06500000	7.53500000	14.41000000
H(Fragment=1)	-0.11200000	7.81200000	12.69200000
H(Fragment=1)	2.38800000	7.76500000	14.54600000
H(Fragment=1)	1.71800000	9.12100000	13.52200000
H(Fragment=1)	2.56400000	7.69300000	12.83600000
H(Fragment=1)	-2.83200000	1.48900000	14.04700000
H(Fragment=1)	-2.39800000	2.85900000	15.19500000
H(Fragment=1)	-3.69800000	1.69900000	15.58400000
H(Fragment=1)	-0.14900000	2.30000000	13.88100000
H(Fragment=1)	-4.82800000	-4.58900000	17.19500000
H(Fragment=1)	-2.94400000	-0.72100000	16.19500000
O(Fragment=2)	6.50762924	1.55087818	12.32865909
O(Fragment=2)	2.26162924	1.81287818	9.03165909
O(Fragment=2)	1.43962924	2.85187818	10.83265909
O(Fragment=2)	6.62162924	2.35987818	10.24365909
O(Fragment=2)	3.88362924	3.77687818	11.57065909
C(Fragment=2)	5.98162924	1.82987818	11.25765909
C(Fragment=2)	4.51962924	1.57687818	10.98165909
C(Fragment=2)	3.81162924	2.84887818	10.51665909
C(Fragment=2)	2.38262924	2.47987818	10.09465909
H(Fragment=2)	4.08462924	1.23787818	11.92365909
H(Fragment=2)	4.43962924	0.80587818	10.21165909

H(Fragment=2)	4.29362924	3.26687818	9.62165909
H(Fragment=2)	7.57762924	2.49587818	10.41065909
H(Fragment=2)	3.41462924	4.57887818	11.29065909
H(Fragment=2)	1.31331799	1.62791043	8.86826782

DIMER 2

O(Fragment=1)	6.49800000	1.54900000	12.32700000
O(Fragment=1)	2.25200000	1.81100000	9.03000000
O(Fragment=1)	1.43000000	2.85000000	10.83100000
O(Fragment=1)	6.61200000	2.35800000	10.24200000
O(Fragment=1)	3.87400000	3.77500000	11.56900000
C(Fragment=1)	5.97200000	1.82800000	11.25600000
C(Fragment=1)	4.51000000	1.57500000	10.98000000
C(Fragment=1)	3.80200000	2.84700000	10.51500000
C(Fragment=1)	2.37300000	2.47800000	10.09300000
H(Fragment=1)	4.07500000	1.23600000	11.92200000
H(Fragment=1)	4.43000000	0.80400000	10.21000000
H(Fragment=1)	4.28400000	3.26500000	9.62000000
H(Fragment=1)	7.56800000	2.49400000	10.40900000
H(Fragment=1)	3.40500000	4.57700000	11.28900000
O(Fragment=2)	-1.05500000	1.54900000	12.32700000
O(Fragment=2)	-5.30100000	1.81100000	9.03000000
O(Fragment=2)	-6.12300000	2.85000000	10.83100000
O(Fragment=2)	-0.94100000	2.35800000	10.24200000
O(Fragment=2)	-3.67900000	3.77500000	11.56900000
C(Fragment=2)	-1.58100000	1.82800000	11.25600000
C(Fragment=2)	-3.04300000	1.57500000	10.98000000
C(Fragment=2)	-3.75100000	2.84700000	10.51500000
C(Fragment=2)	-5.18000000	2.47800000	10.09300000
H(Fragment=2)	-3.47800000	1.23600000	11.92200000
H(Fragment=2)	-3.12300000	0.80400000	10.21000000
H(Fragment=2)	-3.26900000	3.26500000	9.62000000
H(Fragment=2)	0.01500000	2.49400000	10.40900000
H(Fragment=2)	-4.14800000	4.57700000	11.28900000
H(Fragment=1)	3.12220678	1.59553488	8.68661255
H(Fragment=2)	-4.43079322	1.59553488	8.68661255

DIMER 3

F(Fragment=1)	0.02600000	-6.79200000	20.22600000
O(Fragment=1)	-3.90900000	-2.18200000	16.40500000
O(Fragment=1)	1.30000000	2.81700000	16.62400000
N(Fragment=1)	0.59200000	5.91100000	13.19200000
N(Fragment=1)	0.40300000	2.82100000	14.54700000
N(Fragment=1)	-3.92000000	-4.22900000	17.45300000
N(Fragment=1)	-2.06400000	-0.23800000	16.30400000
C(Fragment=1)	-1.82900000	5.48200000	13.83700000
C(Fragment=1)	-0.74400000	5.34000000	12.78600000
C(Fragment=1)	1.25200000	5.17800000	14.32200000
C(Fragment=1)	1.46100000	3.69200000	14.04200000
C(Fragment=1)	0.47700000	2.36100000	15.81900000
C(Fragment=1)	-0.39600000	1.22600000	16.18200000
C(Fragment=1)	0.06400000	0.11600000	16.93500000
C(Fragment=1)	-0.99700000	-0.80100000	16.98300000
C(Fragment=1)	-0.99800000	-2.08200000	17.59200000
C(Fragment=1)	-1.96300000	-3.05000000	17.65700000
C(Fragment=1)	-1.81700000	-4.33500000	18.33100000
C(Fragment=1)	-0.76400000	-4.92000000	19.03100000
C(Fragment=1)	-0.99000000	-6.18900000	19.54900000
C(Fragment=1)	-2.18200000	-6.88400000	19.41200000
C(Fragment=1)	-3.24100000	-6.28900000	18.71900000
C(Fragment=1)	-3.03300000	-5.02700000	18.18500000
C(Fragment=1)	-3.34000000	-3.04500000	17.09200000
C(Fragment=1)	-1.72700000	0.97700000	15.81500000
C(Fragment=1)	1.41500000	-0.06300000	17.54400000
C(Fragment=1)	0.50000000	7.38200000	13.48800000
C(Fragment=1)	1.86900000	8.03700000	13.61500000
C(Fragment=1)	-2.72300000	1.81500000	15.09100000
H(Fragment=1)	-1.63000000	5.03400000	14.82000000
H(Fragment=1)	-2.69800000	4.92000000	13.47000000
H(Fragment=1)	-2.09800000	6.53700000	13.98900000
H(Fragment=1)	-0.54000000	4.29100000	12.56000000
H(Fragment=1)	-1.05900000	5.90100000	11.90300000
H(Fragment=1)	0.63100000	5.31400000	15.21000000
H(Fragment=1)	2.25100000	5.60400000	14.44600000

H(Fragment=1)	1.55200000	3.54900000	12.96400000
H(Fragment=1)	2.39900000	3.42700000	14.53500000
H(Fragment=1)	-0.08500000	-2.36900000	18.09900000
H(Fragment=1)	0.21800000	-4.47300000	19.11800000
H(Fragment=1)	-2.25600000	-7.87000000	19.85500000
H(Fragment=1)	-4.20800000	-6.76300000	18.60600000
H(Fragment=1)	1.46200000	0.36800000	18.55400000
H(Fragment=1)	2.15600000	0.43100000	16.90000000
H(Fragment=1)	1.67600000	-1.11700000	17.71000000
H(Fragment=1)	-0.06500000	7.53500000	14.41000000
H(Fragment=1)	-0.11200000	7.81200000	12.69200000
H(Fragment=1)	2.38800000	7.76500000	14.54600000
H(Fragment=1)	1.71800000	9.12100000	13.52200000
H(Fragment=1)	2.56400000	7.69300000	12.83600000
H(Fragment=1)	-2.83200000	1.48900000	14.04700000
H(Fragment=1)	-2.39800000	2.85900000	15.19500000
H(Fragment=1)	-3.69800000	1.69900000	15.58400000
H(Fragment=1)	-0.14900000	2.30000000	13.88100000
H(Fragment=1)	-4.82800000	-4.58900000	17.19500000
H(Fragment=1)	-2.94400000	-0.72100000	16.19500000
F(Fragment=2)	1.56000000	-2.60700000	19.91900000
O(Fragment=2)	5.49500000	2.00300000	23.74000000
O(Fragment=2)	0.28600000	7.00200000	23.52100000
N(Fragment=2)	0.99400000	10.09600000	26.95200000
N(Fragment=2)	1.18300000	7.00700000	25.59800000
N(Fragment=2)	5.50700000	-0.04400000	22.69200000
N(Fragment=2)	3.65000000	3.94800000	23.84000000
C(Fragment=2)	3.41500000	9.66800000	26.30800000
C(Fragment=2)	2.33100000	9.52500000	27.35900000
C(Fragment=2)	0.33400000	9.36400000	25.82200000
C(Fragment=2)	0.12500000	7.87800000	26.10200000
C(Fragment=2)	1.11000000	6.54700000	24.32600000
C(Fragment=2)	1.98300000	5.41200000	23.96200000
C(Fragment=2)	1.52200000	4.30200000	23.21000000
C(Fragment=2)	2.58300000	3.38400000	23.16200000
C(Fragment=2)	2.58400000	2.10400000	22.55300000
C(Fragment=2)	3.55000000	1.13600000	22.48800000
C(Fragment=2)	3.40400000	-0.15000000	21.81400000
C(Fragment=2)	2.35100000	-0.73500000	21.11400000
C(Fragment=2)	2.57700000	-2.00300000	20.59600000
C(Fragment=2)	3.76800000	-2.69900000	20.73300000
C(Fragment=2)	4.82800000	-2.10400000	21.42600000
C(Fragment=2)	4.62000000	-0.84100000	21.96000000
C(Fragment=2)	4.92600000	1.14000000	23.05300000
C(Fragment=2)	3.31400000	5.16200000	24.33000000
C(Fragment=2)	0.17100000	4.12300000	22.60100000
C(Fragment=2)	1.08700000	11.56700000	26.65700000
C(Fragment=2)	-0.28300000	12.22200000	26.53000000
C(Fragment=2)	4.30900000	6.00000000	25.05400000
H(Fragment=2)	3.21600000	9.21900000	25.32500000
H(Fragment=2)	4.28500000	9.10500000	26.67500000
H(Fragment=2)	3.68400000	10.72200000	26.15500000
H(Fragment=2)	2.12700000	8.47700000	27.58500000
H(Fragment=2)	2.64500000	10.08600000	28.24100000
H(Fragment=2)	0.95500000	9.50000000	24.93500000
H(Fragment=2)	-0.66400000	9.78900000	25.69900000
H(Fragment=2)	0.03500000	7.73400000	27.18100000
H(Fragment=2)	-0.81300000	7.61300000	25.61000000
H(Fragment=2)	1.67100000	1.81600000	22.04600000
H(Fragment=2)	1.36800000	-0.28800000	21.02700000
H(Fragment=2)	3.84300000	-3.68500000	20.29000000
H(Fragment=2)	5.79500000	-2.57800000	21.53800000
H(Fragment=2)	0.12400000	4.55400000	21.59100000
H(Fragment=2)	-0.57000000	4.61700000	23.24500000
H(Fragment=2)	-0.09000000	3.06800000	22.43500000
H(Fragment=2)	1.65100000	11.72000000	25.73500000
H(Fragment=2)	1.69800000	11.99800000	27.45300000
H(Fragment=2)	-0.80100000	11.95100000	25.59900000
H(Fragment=2)	-0.13200000	13.30700000	26.62300000
H(Fragment=2)	-0.97800000	11.87800000	27.30800000
H(Fragment=2)	4.41900000	5.67500000	26.09800000
H(Fragment=2)	3.98400000	7.04500000	24.95000000
H(Fragment=2)	5.28500000	5.88400000	24.56100000
H(Fragment=2)	1.73600000	6.48600000	26.26400000

H(Fragment=2)	6.41500000	-0.40400000	22.94900000
H(Fragment=2)	4.53100000	3.46500000	23.95000000

DIMER 4

F(Fragment=1)	1.56000000	-2.60700000	19.91900000
O(Fragment=1)	5.49500000	2.00300000	23.74000000
O(Fragment=1)	0.28600000	7.00200000	23.52100000
N(Fragment=1)	0.99400000	10.09600000	26.95200000
N(Fragment=1)	1.18300000	7.00700000	25.59800000
N(Fragment=1)	5.50700000	-0.04400000	22.69200000
N(Fragment=1)	3.65000000	3.94800000	23.84000000
C(Fragment=1)	3.41500000	9.66800000	26.30800000
C(Fragment=1)	2.33100000	9.52500000	27.35900000
C(Fragment=1)	0.33400000	9.36400000	25.82200000
C(Fragment=1)	0.12500000	7.87800000	26.10200000
C(Fragment=1)	1.11000000	6.54700000	24.32600000
C(Fragment=1)	1.98300000	5.41200000	23.96200000
C(Fragment=1)	1.52200000	4.30200000	23.21000000
C(Fragment=1)	2.58300000	3.38400000	23.16200000
C(Fragment=1)	2.58400000	2.10400000	22.55300000
C(Fragment=1)	3.55000000	1.13600000	22.48800000
C(Fragment=1)	3.40400000	-0.15000000	21.81400000
C(Fragment=1)	2.35100000	-0.73500000	21.11400000
C(Fragment=1)	2.57700000	-2.00300000	20.59600000
C(Fragment=1)	3.76800000	-2.69900000	20.73300000
C(Fragment=1)	4.82800000	-2.10400000	21.42600000
C(Fragment=1)	4.62000000	-0.84100000	21.96000000
C(Fragment=1)	4.92600000	1.14000000	23.05300000
C(Fragment=1)	3.31400000	5.16200000	24.33000000
C(Fragment=1)	0.17100000	4.12300000	22.60100000
C(Fragment=1)	1.08700000	11.56700000	26.65700000
C(Fragment=1)	-0.28300000	12.22200000	26.53000000
C(Fragment=1)	4.30900000	6.00000000	25.05400000
H(Fragment=1)	3.21600000	9.21900000	25.32500000
H(Fragment=1)	4.28500000	9.10500000	26.67500000
H(Fragment=1)	3.68400000	10.72200000	26.15500000
H(Fragment=1)	2.12700000	8.47700000	27.58500000
H(Fragment=1)	2.64500000	10.08600000	28.24100000
H(Fragment=1)	0.95500000	9.50000000	24.93500000
H(Fragment=1)	-0.66400000	9.78900000	25.69900000
H(Fragment=1)	0.03500000	7.73400000	27.18100000
H(Fragment=1)	-0.81300000	7.61300000	25.61000000
H(Fragment=1)	1.67100000	1.81600000	22.04600000
H(Fragment=1)	1.36800000	-0.28800000	21.02700000
H(Fragment=1)	3.84300000	-3.68500000	20.29000000
H(Fragment=1)	5.79500000	-2.57800000	21.53800000
H(Fragment=1)	0.12400000	4.55400000	21.59100000
H(Fragment=1)	-0.57000000	4.61700000	23.24500000
H(Fragment=1)	-0.09000000	3.06800000	22.43500000
H(Fragment=1)	1.65100000	11.72000000	25.73500000
H(Fragment=1)	1.69800000	11.99800000	27.45300000
H(Fragment=1)	-0.80100000	11.95100000	25.59900000
H(Fragment=1)	-0.13200000	13.30700000	26.62300000
H(Fragment=1)	-0.97800000	11.87800000	27.30800000
H(Fragment=1)	4.41900000	5.67500000	26.09800000
H(Fragment=1)	3.98400000	7.04500000	24.95000000
H(Fragment=1)	5.28500000	5.88400000	24.56100000
H(Fragment=1)	1.73600000	6.48600000	26.26400000
H(Fragment=1)	6.41500000	-0.40400000	22.94900000
H(Fragment=1)	4.53100000	3.46500000	23.95000000
F(Fragment=2)	-5.99300000	5.76400000	19.91900000
O(Fragment=2)	-2.05800000	10.37400000	23.74000000
O(Fragment=2)	-7.26700000	15.37300000	23.52100000
N(Fragment=2)	-6.55900000	18.46700000	26.95200000
N(Fragment=2)	-6.37000000	15.37800000	25.59800000
N(Fragment=2)	-2.04700000	8.32700000	22.69200000
N(Fragment=2)	-3.90300000	12.31900000	23.84000000
C(Fragment=2)	-4.13800000	18.03900000	26.30800000
C(Fragment=2)	-5.22200000	17.89600000	27.35900000
C(Fragment=2)	-7.21900000	17.73500000	25.82200000
C(Fragment=2)	-7.42800000	16.24900000	26.10200000
C(Fragment=2)	-6.44400000	14.91800000	24.32600000
C(Fragment=2)	-5.57100000	13.78300000	23.96200000
C(Fragment=2)	-6.03100000	12.67300000	23.21000000

C(Fragment=2)	-4.97000000	11.75500000	23.16200000
C(Fragment=2)	-4.96900000	10.47500000	22.55300000
C(Fragment=2)	-4.00300000	9.50700000	22.48800000
C(Fragment=2)	-4.15000000	8.22100000	21.81400000
C(Fragment=2)	-5.20200000	7.63600000	21.11400000
C(Fragment=2)	-4.97700000	6.36800000	20.59600000
C(Fragment=2)	-3.78500000	5.67200000	20.73300000
C(Fragment=2)	-2.72500000	6.26700000	21.42600000
C(Fragment=2)	-2.93300000	7.53000000	21.96000000
C(Fragment=2)	-2.62700000	9.51100000	23.05300000
C(Fragment=2)	-4.23900000	13.53300000	24.33000000
C(Fragment=2)	-7.38200000	12.49400000	22.60100000
C(Fragment=2)	-6.46600000	19.93800000	26.65700000
C(Fragment=2)	-7.83600000	20.59300000	26.53000000
C(Fragment=2)	-3.24400000	14.37100000	25.05400000
H(Fragment=2)	-4.33700000	17.59000000	25.32500000
H(Fragment=2)	-3.26800000	17.47600000	26.67500000
H(Fragment=2)	-3.86900000	19.09300000	26.15500000
H(Fragment=2)	-5.42600000	16.84800000	27.58500000
H(Fragment=2)	-4.90800000	18.45700000	28.24100000
H(Fragment=2)	-6.59800000	17.87100000	24.93500000
H(Fragment=2)	-8.21700000	18.16000000	25.69900000
H(Fragment=2)	-7.51900000	16.10500000	27.18100000
H(Fragment=2)	-8.36600000	15.98400000	25.61000000
H(Fragment=2)	-5.88200000	10.18700000	22.04600000
H(Fragment=2)	-6.18500000	8.08300000	21.02700000
H(Fragment=2)	-3.71000000	4.68600000	20.29000000
H(Fragment=2)	-1.75900000	5.79300000	21.53800000
H(Fragment=2)	-7.42900000	12.92500000	21.59100000
H(Fragment=2)	-8.12300000	12.98800000	23.24500000
H(Fragment=2)	-7.64300000	11.43900000	22.43500000
H(Fragment=2)	-5.90200000	20.09100000	25.73500000
H(Fragment=2)	-5.85500000	20.36900000	27.45300000
H(Fragment=2)	-8.35400000	20.32200000	25.59900000
H(Fragment=2)	-7.68500000	21.67800000	26.62300000
H(Fragment=2)	-8.53100000	20.24900000	27.30800000
H(Fragment=2)	-3.13400000	14.04600000	26.09800000
H(Fragment=2)	-3.56900000	15.41600000	24.95000000
H(Fragment=2)	-2.26800000	14.25500000	24.56100000
H(Fragment=2)	-5.81700000	14.85700000	26.26400000
H(Fragment=2)	-1.13900000	7.96700000	22.94900000
H(Fragment=2)	-3.02300000	11.83600000	23.95000000

DIMER 5

F(Fragment=1)	0.02600000	-6.79200000	20.22600000
O(Fragment=1)	-3.90900000	-2.18200000	16.40500000
O(Fragment=1)	1.30000000	2.81700000	16.62400000
N(Fragment=1)	0.59200000	5.91100000	13.19200000
N(Fragment=1)	0.40300000	2.82100000	14.54700000
N(Fragment=1)	-3.92000000	-4.22900000	17.45300000
N(Fragment=1)	-2.06400000	-0.23800000	16.30400000
C(Fragment=1)	-1.82900000	5.48200000	13.83700000
C(Fragment=1)	-0.74400000	5.34000000	12.78600000
C(Fragment=1)	1.25200000	5.17800000	14.32200000
C(Fragment=1)	1.46100000	3.69200000	14.04200000
C(Fragment=1)	0.47700000	2.36100000	15.81900000
C(Fragment=1)	-0.39600000	1.22600000	16.18200000
C(Fragment=1)	0.06400000	0.11600000	16.93500000
C(Fragment=1)	-0.99700000	-0.80100000	16.98300000
C(Fragment=1)	-0.99800000	-2.08200000	17.59200000
C(Fragment=1)	-1.96300000	-3.05000000	17.65700000
C(Fragment=1)	-1.81700000	-4.33500000	18.33100000
C(Fragment=1)	-0.76400000	-4.92000000	19.03100000
C(Fragment=1)	-0.99000000	-6.18900000	19.54900000
C(Fragment=1)	-2.18200000	-6.88400000	19.41200000
C(Fragment=1)	-3.24100000	-6.28900000	18.71900000
C(Fragment=1)	-3.03300000	-5.02700000	18.18500000
C(Fragment=1)	-3.34000000	-3.04500000	17.09200000
C(Fragment=1)	-1.72700000	0.97700000	15.81500000
C(Fragment=1)	1.41500000	-0.06300000	17.54400000
C(Fragment=1)	0.50000000	7.38200000	13.48800000
C(Fragment=1)	1.86900000	8.03700000	13.61500000
C(Fragment=1)	-2.72300000	1.81500000	15.09100000
H(Fragment=1)	-1.63000000	5.03400000	14.82000000

H(Fragment=1)	-2.69800000	4.92000000	13.47000000
H(Fragment=1)	-2.09800000	6.53700000	13.98900000
H(Fragment=1)	-0.54000000	4.29100000	12.56000000
H(Fragment=1)	-1.05900000	5.90100000	11.90300000
H(Fragment=1)	0.63100000	5.31400000	15.21000000
H(Fragment=1)	2.25100000	5.60400000	14.44600000
H(Fragment=1)	1.55200000	3.54900000	12.96400000
H(Fragment=1)	2.39900000	3.42700000	14.53500000
H(Fragment=1)	-0.08500000	-2.36900000	18.09900000
H(Fragment=1)	0.21800000	-4.47300000	19.11800000
H(Fragment=1)	-2.25600000	-7.87000000	19.85500000
H(Fragment=1)	-4.20800000	-6.76300000	18.60600000
H(Fragment=1)	1.46200000	0.36800000	18.55400000
H(Fragment=1)	2.15600000	0.43100000	16.90000000
H(Fragment=1)	1.67600000	-1.11700000	17.71000000
H(Fragment=1)	-0.06500000	7.53500000	14.41000000
H(Fragment=1)	-0.11200000	7.81200000	12.69200000
H(Fragment=1)	2.38800000	7.76500000	14.54600000
H(Fragment=1)	1.71800000	9.12100000	13.52200000
H(Fragment=1)	2.56400000	7.69300000	12.83600000
H(Fragment=1)	-2.83200000	1.48900000	14.04700000
H(Fragment=1)	-2.39800000	2.85900000	15.19500000
H(Fragment=1)	-3.69800000	1.69900000	15.58400000
H(Fragment=1)	-0.14900000	2.30000000	13.88100000
H(Fragment=1)	-4.82800000	-4.58900000	17.19500000
H(Fragment=1)	-2.94400000	-0.72100000	16.19500000
O(Fragment=2)	-1.04532237	1.55088762	12.32866743
O(Fragment=2)	-5.29132237	1.81288762	9.03166743
O(Fragment=2)	-6.11332237	2.85188762	10.83266743
O(Fragment=2)	-0.93132237	2.35988762	10.24366743
O(Fragment=2)	-3.66932237	3.77688762	11.57066743
C(Fragment=2)	-1.57132237	1.82988762	11.25766743
C(Fragment=2)	-3.03332237	1.57688762	10.98166743
C(Fragment=2)	-3.74132237	2.84888762	10.51666743
C(Fragment=2)	-5.17032237	2.47988762	10.09466743
H(Fragment=2)	-3.46832237	1.23788762	11.92366743
H(Fragment=2)	-3.11332237	0.80588762	10.21166743
H(Fragment=2)	-3.25932237	3.26688762	9.62166743
H(Fragment=2)	0.02467763	2.49588762	10.41066743
H(Fragment=2)	-4.13832237	4.57888762	11.29066743
H(Fragment=2)	-6.23973040	1.62790099	8.86825948

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C(Fragment=1)	-1.82800000	5.48200000	13.83700000
C(Fragment=1)	-0.74300000	5.34000000	12.78600000
C(Fragment=1)	1.25300000	5.17800000	14.32200000
C(Fragment=1)	1.46200000	3.69200000	14.04200000
C(Fragment=1)	0.47800000	2.36100000	15.81900000
C(Fragment=1)	-0.39500000	1.22600000	16.18200000
C(Fragment=1)	0.06500000	0.11600000	16.93500000
C(Fragment=1)	-0.99600000	-0.80100000	16.98300000
C(Fragment=1)	-0.99700000	-2.08200000	17.59200000
C(Fragment=1)	-1.96200000	-3.05000000	17.65700000
C(Fragment=1)	-1.81600000	-4.33500000	18.33100000
C(Fragment=1)	-0.76300000	-4.92000000	19.03100000
C(Fragment=1)	-0.98900000	-6.18900000	19.54900000
C(Fragment=1)	-2.18100000	-6.88400000	19.41200000
C(Fragment=1)	-3.24000000	-6.28900000	18.71900000
C(Fragment=1)	-3.03200000	-5.02700000	18.18500000
C(Fragment=1)	-3.33900000	-3.04500000	17.09200000
C(Fragment=1)	-1.72600000	0.97700000	15.81500000
C(Fragment=1)	1.41600000	-0.06300000	17.54400000
C(Fragment=1)	0.50100000	7.38200000	13.48800000
C(Fragment=1)	1.87000000	8.03700000	13.61500000
C(Fragment=1)	-2.72200000	1.81500000	15.09100000
F(Fragment=1)	0.02700000	-6.79200000	20.22600000
O(Fragment=1)	-3.90800000	-2.18200000	16.40500000
O(Fragment=1)	1.30100000	2.81700000	16.62400000
N(Fragment=1)	0.59300000	5.91100000	13.19200000
N(Fragment=1)	0.40400000	2.82100000	14.54700000
N(Fragment=1)	-3.91900000	-4.22900000	17.45300000
N(Fragment=1)	-2.06300000	-0.23800000	16.30400000
H(Fragment=1)	-1.62900000	5.03400000	14.82000000
H(Fragment=1)	-2.69700000	4.92000000	13.47000000

H(Fragment=1)	-2.09700000	6.53700000	13.98900000
H(Fragment=1)	-0.53900000	4.29100000	12.56000000
H(Fragment=1)	-1.05800000	5.90100000	11.90300000
H(Fragment=1)	0.63200000	5.31400000	15.21000000
H(Fragment=1)	2.25200000	5.60400000	14.44600000
H(Fragment=1)	1.55300000	3.54900000	12.96400000
H(Fragment=1)	2.40000000	3.42700000	14.53500000
H(Fragment=1)	-0.08400000	-2.36900000	18.09900000
H(Fragment=1)	0.21900000	-4.47300000	19.11800000
H(Fragment=1)	-2.25500000	-7.87000000	19.85500000
H(Fragment=1)	-4.20700000	-6.76300000	18.60600000
H(Fragment=1)	1.46300000	0.36800000	18.55400000
H(Fragment=1)	2.15700000	0.43100000	16.90000000
H(Fragment=1)	1.67700000	-1.11700000	17.71000000
H(Fragment=1)	-0.06400000	7.53500000	14.41000000
H(Fragment=1)	-0.11100000	7.81200000	12.69200000
H(Fragment=1)	2.38900000	7.76500000	14.54600000
H(Fragment=1)	1.71900000	9.12100000	13.52200000
H(Fragment=1)	2.56500000	7.69300000	12.83600000
H(Fragment=1)	-2.83100000	1.48900000	14.04700000
H(Fragment=1)	-2.39700000	2.85900000	15.19500000
H(Fragment=1)	-3.69700000	1.69900000	15.58400000
H(Fragment=1)	-0.14800000	2.30000000	13.88100000
H(Fragment=1)	-4.82700000	-4.58900000	17.19500000
H(Fragment=1)	-2.94300000	-0.72100000	16.19500000
C(Fragment=2)	-1.40200000	6.01300000	8.81600000
C(Fragment=2)	0.06000000	5.76000000	9.09200000
C(Fragment=2)	0.76800000	7.03200000	9.55700000
C(Fragment=2)	2.19700000	6.66300000	9.97900000
O(Fragment=2)	-1.92800000	5.73400000	7.74500000
O(Fragment=2)	2.31800000	5.99600000	11.04200000
O(Fragment=2)	3.14000000	7.03500000	9.24100000
O(Fragment=2)	-2.04200000	6.54300000	9.83000000
O(Fragment=2)	0.69600000	7.96000000	8.50300000
H(Fragment=2)	1.70700000	5.91300000	11.80300000
H(Fragment=2)	0.49500000	5.42100000	8.15000000
H(Fragment=2)	0.14000000	4.98900000	9.86200000
H(Fragment=2)	0.28600000	7.45000000	10.45200000
H(Fragment=2)	-2.99800000	6.67900000	9.66300000
H(Fragment=2)	1.16500000	8.76200000	8.78300000

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F(Fragment=1)	1.56000000	-2.60700000	19.91900000
O(Fragment=1)	5.49500000	2.00300000	23.74000000
O(Fragment=1)	0.28600000	7.00200000	23.52100000
N(Fragment=1)	0.99400000	10.09600000	26.95200000
N(Fragment=1)	1.18300000	7.00700000	25.59800000
N(Fragment=1)	5.50700000	-0.04400000	22.69200000
N(Fragment=1)	3.65000000	3.94800000	23.84000000
C(Fragment=1)	3.41500000	9.66800000	26.30800000
C(Fragment=1)	2.33100000	9.52500000	27.35900000
C(Fragment=1)	0.33400000	9.36400000	25.82200000
C(Fragment=1)	0.12500000	7.87800000	26.10200000
C(Fragment=1)	1.11000000	6.54700000	24.32600000
C(Fragment=1)	1.98300000	5.41200000	23.96200000
C(Fragment=1)	1.52200000	4.30200000	23.21000000
C(Fragment=1)	2.58300000	3.38400000	23.16200000
C(Fragment=1)	2.58400000	2.10400000	22.55300000
C(Fragment=1)	3.55000000	1.13600000	22.48800000
C(Fragment=1)	3.40400000	-0.15000000	21.81400000
C(Fragment=1)	2.35100000	-0.73500000	21.11400000
C(Fragment=1)	2.57700000	-2.00300000	20.59600000
C(Fragment=1)	3.76800000	-2.69900000	20.73300000
C(Fragment=1)	4.82800000	-2.10400000	21.42600000
C(Fragment=1)	4.62000000	-0.84100000	21.96000000
C(Fragment=1)	4.92600000	1.14000000	23.05300000
C(Fragment=1)	3.31400000	5.16200000	24.33000000
C(Fragment=1)	0.17100000	4.12300000	22.60100000
C(Fragment=1)	1.08700000	11.56700000	26.65700000
C(Fragment=1)	-0.28300000	12.22200000	26.53000000
C(Fragment=1)	4.30900000	6.00000000	25.05400000
H(Fragment=1)	3.21600000	9.21900000	25.32500000
H(Fragment=1)	4.28500000	9.10500000	26.67500000
H(Fragment=1)	3.68400000	10.72200000	26.15500000

H(Fragment=1)	2.12700000	8.47700000	27.58500000
H(Fragment=1)	2.64500000	10.08600000	28.24100000
H(Fragment=1)	0.95500000	9.50000000	24.93500000
H(Fragment=1)	-0.66400000	9.78900000	25.69900000
H(Fragment=1)	0.03500000	7.73400000	27.18100000
H(Fragment=1)	-0.81300000	7.61300000	25.61000000
H(Fragment=1)	1.67100000	1.81600000	22.04600000
H(Fragment=1)	1.36800000	-0.28800000	21.02700000
H(Fragment=1)	3.84300000	-3.68500000	20.29000000
H(Fragment=1)	5.79500000	-2.57800000	21.53800000
H(Fragment=1)	0.12400000	4.55400000	21.59100000
H(Fragment=1)	-0.57000000	4.61700000	23.24500000
H(Fragment=1)	-0.09000000	3.06800000	22.43500000
H(Fragment=1)	1.65100000	11.72000000	25.73500000
H(Fragment=1)	1.69800000	11.99800000	27.45300000
H(Fragment=1)	-0.80100000	11.95100000	25.59900000
H(Fragment=1)	-0.13200000	13.30700000	26.62300000
H(Fragment=1)	-0.97800000	11.87800000	27.30800000
H(Fragment=1)	4.41900000	5.67500000	26.09800000
H(Fragment=1)	3.98400000	7.04500000	24.95000000
H(Fragment=1)	5.28500000	5.88400000	24.56100000
H(Fragment=1)	1.73600000	6.48600000	26.26400000
H(Fragment=1)	6.41500000	-0.40400000	22.94900000
H(Fragment=1)	4.53100000	3.46500000	23.95000000
F(Fragment=2)	1.56000000	-10.97800000	19.91900000
O(Fragment=2)	5.49500000	-6.36800000	23.74000000
O(Fragment=2)	0.28600000	-1.36900000	23.52100000
N(Fragment=2)	0.99400000	1.72500000	26.95200000
N(Fragment=2)	1.18300000	-1.36400000	25.59800000
N(Fragment=2)	5.50700000	-8.41500000	22.69200000
N(Fragment=2)	3.65000000	-4.42300000	23.84000000
C(Fragment=2)	3.41500000	1.29700000	26.30800000
C(Fragment=2)	2.33100000	1.15400000	27.35900000
C(Fragment=2)	0.33400000	0.99300000	25.82200000
C(Fragment=2)	0.12500000	-0.49300000	26.10200000
C(Fragment=2)	1.11000000	-1.82400000	24.32600000
C(Fragment=2)	1.98300000	-2.95900000	23.96200000
C(Fragment=2)	1.52200000	-4.06900000	23.21000000
C(Fragment=2)	2.58300000	-4.98700000	23.16200000
C(Fragment=2)	2.58400000	-6.26700000	22.55300000
C(Fragment=2)	3.55000000	-7.23500000	22.48800000
C(Fragment=2)	3.40400000	-8.52100000	21.81400000
C(Fragment=2)	2.35100000	-9.10600000	21.11400000
C(Fragment=2)	2.57700000	-10.37400000	20.59600000
C(Fragment=2)	3.76800000	-11.07000000	20.73300000
C(Fragment=2)	4.82800000	-10.47500000	21.42600000
C(Fragment=2)	4.62000000	-9.21200000	21.96000000
C(Fragment=2)	4.92600000	-7.23100000	23.05300000
C(Fragment=2)	3.31400000	-3.20900000	24.33000000
C(Fragment=2)	0.17100000	-4.24800000	22.60100000
C(Fragment=2)	1.08700000	3.19600000	26.65700000
C(Fragment=2)	-0.28300000	3.85100000	26.53000000
C(Fragment=2)	4.30900000	-2.37100000	25.05400000
H(Fragment=2)	3.21600000	0.84800000	25.32500000
H(Fragment=2)	4.28500000	0.73400000	26.67500000
H(Fragment=2)	3.68400000	2.35100000	26.15500000
H(Fragment=2)	2.12700000	0.10600000	27.58500000
H(Fragment=2)	2.64500000	1.71500000	28.24100000
H(Fragment=2)	0.95500000	1.12900000	24.93500000
H(Fragment=2)	-0.66400000	1.41800000	25.69900000
H(Fragment=2)	0.03500000	-0.63700000	27.18100000
H(Fragment=2)	-0.81300000	-0.75800000	25.61000000
H(Fragment=2)	1.67100000	-6.55500000	22.04600000
H(Fragment=2)	1.36800000	-8.65900000	21.02700000
H(Fragment=2)	3.84300000	-12.05600000	20.29000000
H(Fragment=2)	5.79500000	-10.94900000	21.53800000
H(Fragment=2)	0.12400000	-3.81700000	21.59100000
H(Fragment=2)	-0.57000000	-3.75400000	23.24500000
H(Fragment=2)	-0.09000000	-5.30300000	22.43500000
H(Fragment=2)	1.65100000	3.34900000	25.73500000
H(Fragment=2)	1.69800000	3.62700000	27.45300000
H(Fragment=2)	-0.80100000	3.58000000	25.59900000
H(Fragment=2)	-0.13200000	4.93600000	26.62300000
H(Fragment=2)	-0.97800000	3.50700000	27.30800000

H(Fragment=2)	4.41900000	-2.69600000	26.09800000
H(Fragment=2)	3.98400000	-1.32600000	24.95000000
H(Fragment=2)	5.28500000	-2.48700000	24.56100000
H(Fragment=2)	1.73600000	-1.88500000	26.26400000
H(Fragment=2)	6.41500000	-8.77500000	22.94900000
H(Fragment=2)	4.53100000	-4.90600000	23.95000000

DIMER 8

O(Fragment=1)	6.49714637	1.54690980	12.32285330
O(Fragment=1)	2.25114637	1.80890980	9.02585330
O(Fragment=1)	1.42914637	2.84790980	10.82685330
O(Fragment=1)	6.61114637	2.35590980	10.23785330
O(Fragment=1)	3.87314637	3.77290980	11.56485330
C(Fragment=1)	5.97114637	1.82590980	11.25185330
C(Fragment=1)	4.50914637	1.57290980	10.97585330
C(Fragment=1)	3.80114637	2.84490980	10.51085330
C(Fragment=1)	2.37214637	2.47590980	10.08885330
H(Fragment=1)	4.07414637	1.23390980	11.91785330
H(Fragment=1)	4.42914637	0.80190980	10.20585330
H(Fragment=1)	4.28314637	3.26290980	9.61585330
H(Fragment=1)	7.56714637	2.49190980	10.40485330
H(Fragment=1)	3.40414637	4.57490980	11.28485330
O(Fragment=2)	-1.93285319	-2.63636075	7.74398123
O(Fragment=2)	2.31414681	-2.37436075	11.04098123
O(Fragment=2)	3.13514681	-1.33536075	9.23998123
O(Fragment=2)	-2.04685319	-1.82736075	9.82898123
O(Fragment=2)	0.69114681	-0.41036075	8.50198123
C(Fragment=2)	-1.40685319	-2.35736075	8.81498123
C(Fragment=2)	0.05514681	-2.61036075	9.09098123
C(Fragment=2)	0.76314681	-1.33836075	9.55598123
C(Fragment=2)	2.19214681	-1.70736075	9.97798123
H(Fragment=2)	0.49014681	-2.94936075	8.14898123
H(Fragment=2)	0.13514681	-3.38136075	9.86098123
H(Fragment=2)	0.28114681	-0.92036075	10.45098123
H(Fragment=2)	-3.00285319	-1.69136075	9.66198123
H(Fragment=2)	1.16014681	0.39163925	8.78198123
H(Fragment=2)	3.25566616	-2.49837438	11.23862214
H(Fragment=1)	1.78875129	3.25340946	11.63131232

Table S38. Cartesian coordinates of the sunitinib cation after optimization in Gaussian09 – B97D with 6-311G basis set, with the C(11)C(10)C(9)O(7) torsion angle equal to -12.91°.**

F	-1.25234600	-5.63510700	21.17610300
O	-3.65370300	-2.41994800	15.27362700
O	1.48456000	2.60145600	15.68187700
N	0.30146800	5.90336600	13.70691900
N	0.53170700	2.70264900	13.64099000
N	-4.02266500	-4.14097600	16.73798800
N	-1.76825000	-0.55105200	15.18120900
C	-1.29206900	4.99107900	15.45036700
C	-1.06215500	5.30834500	13.99358500
C	1.46601700	4.99402500	14.01343400
C	1.50462600	3.69423200	13.22983100
C	0.68145600	2.11508500	14.89643400
C	-0.16967400	0.98055100	15.21246500
C	0.01094600	0.14575000	16.35353000
C	-1.00120000	-0.80982700	16.30290700
C	-1.24781300	-1.88034000	17.20452700
C	-2.20952600	-2.84097000	17.22652800
C	-2.32856000	-3.89425000	18.22694000
C	-1.57205400	-4.21478200	19.34510300
C	-1.96959400	-5.30943400	20.09503900
C	-3.07497300	-6.08097200	19.77485900
C	-3.83642300	-5.76118100	18.65169800
C	-3.44787200	-4.67229400	17.89796900
C	-3.33647700	-3.05085500	16.27973300
C	-1.29444600	0.50557300	14.51222600
C	1.07624400	0.26119500	17.38287400
C	0.47278900	7.24857700	14.37129500
C	1.52987600	8.09454500	13.70292300
C	-1.97809100	0.97151700	13.27591600

H	-0.56536300	4.27640600	15.84820700
H	-2.27943700	4.53036000	15.54398900
H	-1.29512000	5.88527700	16.08007100
H	-1.13173900	4.40899400	13.37873200
H	-1.78208600	6.04443600	13.62102200
H	1.45963600	4.79586600	15.08644300
H	2.36362200	5.56966700	13.77437700
H	1.36600000	3.88762800	12.15841400
H	2.52770400	3.31295400	13.35492900
H	-0.52698900	-1.93016900	18.02051000
H	-0.69478900	-3.65178100	19.64835300
H	-3.32903400	-6.92515500	20.40583200
H	-4.70417500	-6.35611100	18.38665300
H	1.00485900	1.21098300	17.92107300
H	2.07069900	0.24536000	16.92637400
H	1.02379400	-0.55162000	18.11122300
H	0.70444200	7.04880800	15.42115500
H	-0.50546500	7.73675900	14.32595700
H	2.53744200	7.68595700	13.81179800
H	1.53419400	9.08344600	14.16738000
H	1.31855800	8.24056700	12.63769200
H	-1.39447800	0.75431200	12.37146300
H	-2.17641100	2.04869900	13.30277900
H	-2.93723900	0.46079200	13.15849500
H	0.32101400	6.07799100	12.69869300
H	0.16160600	2.11775700	12.90616600
H	-4.83837500	-4.49305600	16.26150700
H	-2.59114500	-1.13775500	14.96112600

Table S39. Cartesian coordinates of the sunitinib cation after optimization in Gaussian09 – B97D with 6-311g basis set, with the C(11)C(10)C(9)O(7) torsion angle equal to 166.66°.**

F	-1.52637100	-6.31095500	21.14211100
O	-3.17031400	-2.49442100	15.34025600
O	0.34356300	3.24301800	15.37999300
N	3.94791300	4.21640000	17.08775900
N	0.97345900	3.07760700	17.53790700
N	-3.55594300	-4.46528900	16.44285400
N	-1.62400400	-0.39996900	15.92553600
C	3.85206800	1.87447400	16.13259700
C	4.03291200	2.72932900	17.36129200
C	2.61161200	4.68790500	16.56814800
C	1.43874800	4.44786100	17.50302500
C	0.31796500	2.58450300	16.41264200
C	-0.32300800	1.28644600	16.52700800
C	-0.23804000	0.29103300	17.54403800
C	-1.06167700	-0.75753100	17.13869500
C	-1.31024300	-1.98764900	17.80451400
C	-2.09730500	-3.04915300	17.48625500
C	-2.24824500	-4.25752100	18.28580100
C	-1.68956800	-4.66279000	19.48995100
C	-2.05624600	-5.90431900	19.98190600
C	-2.94482700	-6.74187800	19.32766600
C	-3.50741700	-6.33757100	18.11770800
C	-3.14761100	-5.10186500	17.61871100
C	-2.96922600	-3.23747700	16.29512500
C	-1.19662200	0.80445500	15.53427100
C	0.57976300	0.31312000	18.79006800
C	5.07426900	4.69113400	16.20052700
C	5.37329500	6.15916900	16.38874300
C	-1.64864800	1.41561200	14.26308900
H	2.87642600	2.01729100	15.65934800
H	3.90953800	0.82637800	16.43856300
H	4.63663900	2.03470900	15.38771100
H	3.26464500	2.51454800	18.10714100
H	5.01545200	2.57618000	17.81971500
H	2.44372800	4.20780000	15.60165300
H	2.71948400	5.76264600	16.40268500
H	1.69359200	4.75405700	18.52581300
H	0.64386900	5.12252900	17.15746400
H	-0.76807800	-2.08864500	18.74480200

H	-0.98848000	-4.05378600	20.05211900
H	-3.18797300	-7.70133800	19.76991700
H	-4.20480000	-6.98138400	17.59212500
H	0.19244800	1.02342500	19.53408800
H	1.62408700	0.57881500	18.58314900
H	0.59300700	-0.66235300	19.28189300
H	4.78277700	4.45599600	15.17318200
H	5.94436600	4.07878900	16.45558700
H	4.55522000	6.80844900	16.06708200
H	6.24566400	6.42235200	15.78596800
H	5.62111300	6.39031400	17.43086900
H	-0.82650700	1.47308500	13.54326800
H	-1.99078400	2.44178300	14.41969700
H	-2.45892100	0.82837000	13.82364100
H	4.08814400	4.67203500	17.99355900
H	0.66659800	2.72856400	18.43399400
H	-4.19916700	-4.83166600	15.75857300
H	-2.28527500	-1.02938800	15.44235900

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