



Full wwPDB X-ray Structure Validation Report ⓘ

Aug 28, 2017 – 06:16 PM EDT

PDB ID : 5K7K
Title : Design and Optimization of Biaryl Ether Aryl Sulfonamides as Selective Inhibitors of NaV1.7: Discovery of Clinical Candidate PF-05089771
Authors : Swain, N.; Chrencik, J.
Deposited on : unknown
Resolution : 2.30 Å(reported)

This is a Full wwPDB X-ray Structure Validation Report for a publicly released PDB entry.

We welcome your comments at validation@mail.wwpdb.org

A user guide is available at

<http://wwpdb.org/validation/2016/XrayValidationReportHelp>

with specific help available everywhere you see the ⓘ symbol.

The following versions of software and data (see [references ⓘ](#)) were used in the production of this report:

MolProbity : 4.02b-467
Mogul : 1.7.2 (RC1), CSD as538be (2017)
Xtriage (Phenix) : 1.9-1692
EDS : rb-20029824
Percentile statistics : 20161228.v01 (using entries in the PDB archive December 28th 2016)
Refmac : 5.8.0135
CCP4 : 6.5.0
Ideal geometry (proteins) : Engh & Huber (2001)
Ideal geometry (DNA, RNA) : Parkinson et al. (1996)
Validation Pipeline (wwPDB-VP) : rb-20029824

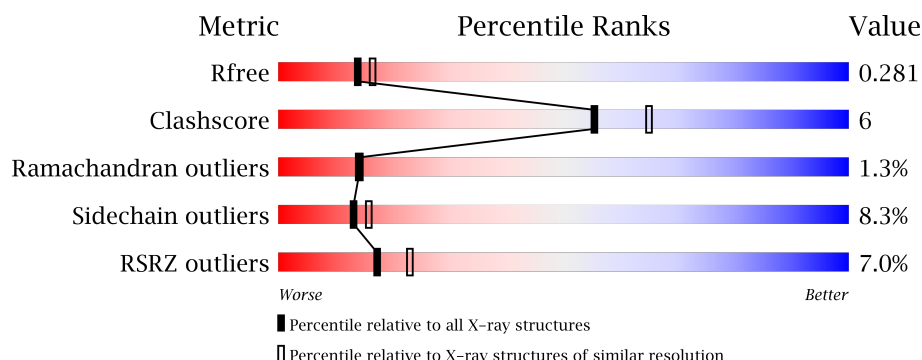
1 Overall quality at a glance

The following experimental techniques were used to determine the structure:

X-RAY DIFFRACTION

The reported resolution of this entry is 2.30 Å.

Percentile scores (ranging between 0-100) for global validation metrics of the entry are shown in the following graphic. The table shows the number of entries on which the scores are based.



Metric	Whole archive (#Entries)	Similar resolution (#Entries, resolution range(Å))
R_{free}	100719	4130 (2.30-2.30)
Clashscore	112137	4751 (2.30-2.30)
Ramachandran outliers	110173	4705 (2.30-2.30)
Sidechain outliers	110143	4704 (2.30-2.30)
RSRZ outliers	101464	4156 (2.30-2.30)

The table below summarises the geometric issues observed across the polymeric chains and their fit to the electron density. The red, orange, yellow and green segments on the lower bar indicate the fraction of residues that contain outliers for ≥ 3 , 2, 1 and 0 types of geometric quality criteria. A grey segment represents the fraction of residues that are not modelled. The numeric value for each fraction is indicated below the corresponding segment, with a dot representing fractions $\leq 5\%$. The upper red bar (where present) indicates the fraction of residues that have poor fit to the electron density. The numeric value is given above the bar.

Mol	Chain	Length	Quality of chain
1	A	477	

2 Entry composition

There are 4 unique types of molecules in this entry. The entry contains 3756 atoms, of which 0 are hydrogens and 0 are deuteriums.

In the tables below, the ZeroOcc column contains the number of atoms modelled with zero occupancy, the AltConf column contains the number of residues with at least one atom in alternate conformation and the Trace column contains the number of residues modelled with at most 2 atoms.

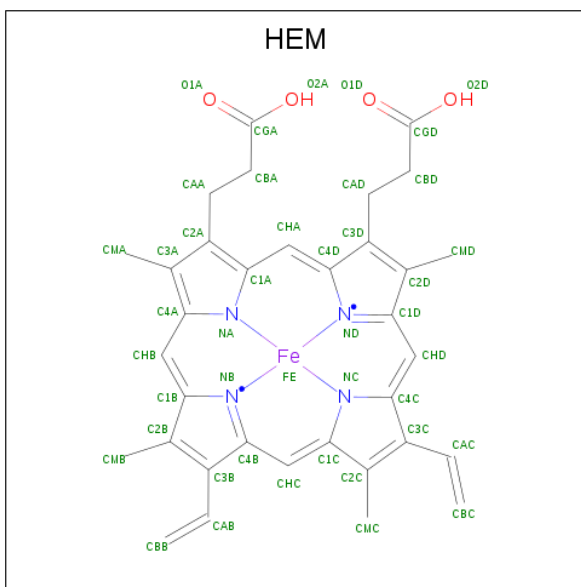
- Molecule 1 is a protein called Cytochrome P450 2C9.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
1	A	455	Total	C	N	O	S	0	0	0
			3646	2353	614	656	23			

There are 10 discrepancies between the modelled and reference sequences:

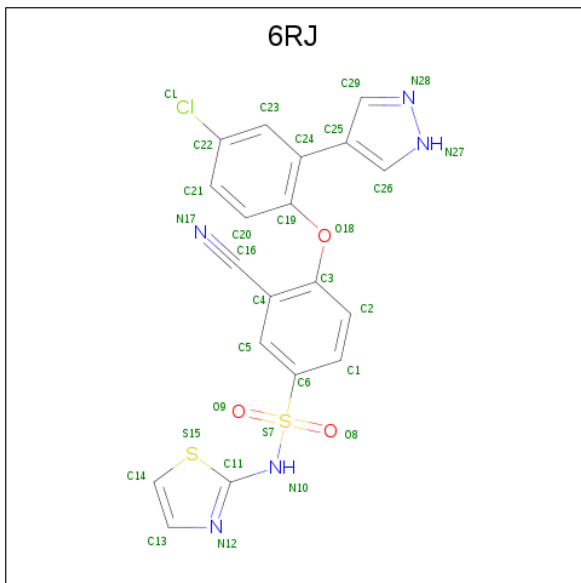
Chain	Residue	Modelled	Actual	Comment	Reference
A	18	MET	-	expression tag	UNP P11712
A	19	ALA	-	expression tag	UNP P11712
A	20	LYS	-	expression tag	UNP P11712
A	21	LYS	-	expression tag	UNP P11712
A	22	THR	-	expression tag	UNP P11712
A	490	ILE	-	expression tag	UNP P11712
A	491	HIS	-	expression tag	UNP P11712
A	492	HIS	-	expression tag	UNP P11712
A	493	HIS	-	expression tag	UNP P11712
A	494	HIS	-	expression tag	UNP P11712

- Molecule 2 is PROTOPORPHYRIN IX CONTAINING FE (three-letter code: HEM) (formula: $C_{34}H_{32}FeN_4O_4$).



Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
2	A	1	Total 43	C 34	Fe 1	N 4	O 4	0	0

- Molecule 3 is 4-[4-chloranyl-2-(1 {H}-pyrazol-4-yl)phenoxy]-3-cyano- {N}-(1,3-thiazol-2-yl) benzenesulfonamide (three-letter code: 6RJ) (formula: C₁₉H₁₂ClN₅O₃S₂).



Mol	Chain	Residues	Atoms						ZeroOcc	AltConf
3	A	1	Total	C	Cl	N	O	S	0	0
			30	19	1	5	3	2		

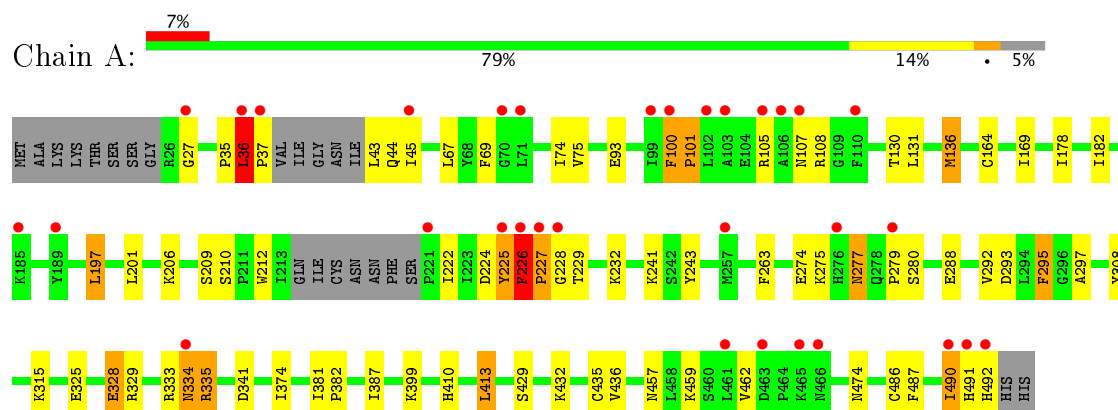
- Molecule 4 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
4	A	37	Total 37	O 37	0	0

3 Residue-property plots [i](#)

These plots are drawn for all protein, RNA and DNA chains in the entry. The first graphic for a chain summarises the proportions of the various outlier classes displayed in the second graphic. The second graphic shows the sequence view annotated by issues in geometry and electron density. Residues are color-coded according to the number of geometric quality criteria for which they contain at least one outlier: green = 0, yellow = 1, orange = 2 and red = 3 or more. A red dot above a residue indicates a poor fit to the electron density ($RSRZ > 2$). Stretches of 2 or more consecutive residues without any outlier are shown as a green connector. Residues present in the sample, but not in the model, are shown in grey.

• Molecule 1: Cytochrome P450 2C9



4 Data and refinement statistics

Property	Value	Source
Space group	H 3	Depositor
Cell constants a, b, c, α , β , γ	91.69Å 91.69Å 169.88Å 90.00° 90.00° 120.00°	Depositor
Resolution (Å)	17.33 – 2.30 17.33 – 2.30	Depositor EDS
% Data completeness (in resolution range)	98.6 (17.33-2.30) 98.8 (17.33-2.30)	Depositor EDS
R_{merge}	(Not available)	Depositor
R_{sym}	(Not available)	Depositor
$\langle I/\sigma(I) \rangle$ ¹	4.05 (at 2.30Å)	Xtriage
Refinement program	REFMAC 5.8.0073	Depositor
R, R_{free}	0.224 , 0.272 0.225 , 0.281	Depositor DCC
R_{free} test set	1191 reflections (5.38%)	DCC
Wilson B-factor (Å ²)	46.6	Xtriage
Anisotropy	0.021	Xtriage
Bulk solvent k_{sol} (e/Å ³), B_{sol} (Å ²)	0.34 , 47.8	EDS
L-test for twinning ²	$\langle L \rangle = 0.50$, $\langle L^2 \rangle = 0.33$	Xtriage
Estimated twinning fraction	0.032 for h,-h-k,-l	Xtriage
F_o, F_c correlation	0.94	EDS
Total number of atoms	3756	wwPDB-VP
Average B, all atoms (Å ²)	59.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 4.80% of the height of the origin peak. No significant pseudotranslation is detected.*

¹Intensities estimated from amplitudes.

²Theoretical values of $\langle |L| \rangle$, $\langle L^2 \rangle$ for acentric reflections are 0.5, 0.333 respectively for untwinned datasets, and 0.375, 0.2 for perfectly twinned datasets.

5 Model quality ⓘ

5.1 Standard geometry ⓘ

Bond lengths and bond angles in the following residue types are not validated in this section: 6RJ, HEM

The Z score for a bond length (or angle) is the number of standard deviations the observed value is removed from the expected value. A bond length (or angle) with $|Z| > 5$ is considered an outlier worth inspection. RMSZ is the root-mean-square of all Z scores of the bond lengths (or angles).

Mol	Chain	Bond lengths		Bond angles	
		RMSZ	$\# Z > 5$	RMSZ	$\# Z > 5$
1	A	0.58	1/3735 (0.0%)	0.75	8/5047 (0.2%)

All (1) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
1	A	279	PRO	N-CD	5.75	1.55	1.47

All (8) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
1	A	225	TYR	N-CA-C	11.63	142.40	111.00
1	A	225	TYR	CB-CA-C	-8.82	92.76	110.40
1	A	227	PRO	CB-CA-C	-7.44	93.39	112.00
1	A	227	PRO	N-CA-C	-6.44	95.35	112.10
1	A	228	GLY	N-CA-C	5.95	127.97	113.10
1	A	226	PHE	N-CA-CB	-5.60	100.52	110.60
1	A	67	LEU	N-CA-C	-5.18	97.02	111.00
1	A	67	LEU	CB-CA-C	5.12	119.93	110.20

There are no chirality outliers.

There are no planarity outliers.

5.2 Too-close contacts ⓘ

In the following table, the Non-H and H(model) columns list the number of non-hydrogen atoms and hydrogen atoms in the chain respectively. The H(added) column lists the number of hydrogen atoms added and optimized by MolProbity. The Clashes column lists the number of clashes within the asymmetric unit, whereas Symm-Clashes lists symmetry related clashes.

Mol	Chain	Non-H	H(model)	H(added)	Clashes	Symm-Clashes
1	A	3646	0	3678	40	1
2	A	43	0	30	6	0
3	A	30	0	0	6	0
4	A	37	0	0	2	0
All	All	3756	0	3708	44	1

The all-atom clashscore is defined as the number of clashes found per 1000 atoms (including hydrogen atoms). The all-atom clashscore for this structure is 6.

All (44) close contacts within the same asymmetric unit are listed below, sorted by their clash magnitude.

Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
1:A:277:ASN:O	1:A:277:ASN:ND2	1.92	1.02
1:A:108:ARG:NH2	1:A:293:ASP:OD1	1.92	1.02
1:A:225:TYR:O	1:A:229:THR:OG1	1.89	0.88
1:A:241:LYS:HG2	1:A:288:GLU:HG2	1.56	0.87
1:A:241:LYS:HG2	1:A:288:GLU:CG	2.06	0.86
2:A:501:HEM:HMB2	2:A:501:HEM:HBB2	1.68	0.75
1:A:334:ASN:N	1:A:334:ASN:HD22	1.91	0.68
1:A:100:PHE:HB3	1:A:101:PRO:HD3	1.76	0.68
1:A:169:ILE:HG13	4:A:609:HOH:O	2.01	0.60
1:A:435:CYS:HB2	2:A:501:HEM:NA	2.17	0.60
1:A:410:HIS:HA	1:A:413:LEU:HB2	1.84	0.59
2:A:501:HEM:CMB	2:A:501:HEM:HBB2	2.35	0.56
1:A:328:GLU:OE1	1:A:328:GLU:HA	2.05	0.56
3:A:502:6RJ:C20	3:A:502:6RJ:C4	2.78	0.55
1:A:178:ILE:HG21	1:A:295:PHE:HA	1.87	0.54
1:A:459:LYS:HB3	1:A:486:CYS:HB2	1.89	0.54
1:A:35:PRO:O	1:A:36:LEU:HB2	2.09	0.52
1:A:487:PHE:O	4:A:601:HOH:O	2.19	0.51
1:A:292:VAL:HG12	3:A:502:6RJ:N12	2.26	0.50
1:A:334:ASN:N	1:A:334:ASN:ND2	2.60	0.49
1:A:100:PHE:CB	1:A:101:PRO:HD3	2.43	0.49
1:A:275:LYS:C	1:A:277:ASN:H	2.16	0.49
1:A:241:LYS:HG2	1:A:288:GLU:HG3	1.92	0.48
1:A:197:LEU:HD11	1:A:243:TYR:CE2	2.49	0.48
1:A:36:LEU:N	1:A:37:PRO:HD3	2.30	0.47
1:A:27:GLY:HA3	1:A:382:PRO:HG3	1.96	0.47
1:A:436:VAL:CG1	2:A:501:HEM:HMD2	2.45	0.47
3:A:502:6RJ:C16	3:A:502:6RJ:C19	2.92	0.47
1:A:297:ALA:HA	3:A:502:6RJ:C26	2.44	0.47
1:A:209:SER:HB2	1:A:474:ASN:ND2	2.30	0.47

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Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
1:A:292:VAL:HG12	3:A:502:6RJ:C13	2.44	0.47
1:A:130:THR:HG23	1:A:136:MET:HG3	1.97	0.45
1:A:69:PHE:CE2	1:A:74:ILE:HD12	2.52	0.45
1:A:335:ARG:HH22	1:A:341:ASP:CG	2.20	0.45
1:A:182:ILE:HA	1:A:263:PHE:HB3	1.99	0.44
1:A:292:VAL:CG1	3:A:502:6RJ:C13	2.95	0.44
1:A:241:LYS:CG	1:A:288:GLU:HG2	2.39	0.43
1:A:93:GLU:HG2	1:A:374:ILE:HD13	2.01	0.42
1:A:335:ARG:NH2	1:A:341:ASP:OD2	2.51	0.42
1:A:75:VAL:HB	1:A:387:ILE:HD13	2.01	0.41
1:A:436:VAL:HG12	2:A:501:HEM:HMD2	2.03	0.41
1:A:435:CYS:HB2	2:A:501:HEM:C4A	2.55	0.41
1:A:45:ILE:HG23	1:A:212:TRP:HB2	2.03	0.41
1:A:457:ASN:OD1	1:A:490:ILE:HD12	2.21	0.40

All (1) symmetry-related close contacts are listed below. The label for Atom-2 includes the symmetry operator and encoded unit-cell translations to be applied.

Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
1:A:44:GLN:NE2	1:A:226:PHE:O[2_545]	2.17	0.03

5.3 Torsion angles [i](#)

5.3.1 Protein backbone [i](#)

In the following table, the Percentiles column shows the percent Ramachandran outliers of the chain as a percentile score with respect to all X-ray entries followed by that with respect to entries of similar resolution.

The Analysed column shows the number of residues for which the backbone conformation was analysed, and the total number of residues.

Mol	Chain	Analysed	Favoured	Allowed	Outliers	Percentiles
1	A	449/477 (94%)	421 (94%)	22 (5%)	6 (1%)	14 14

All (6) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	A	36	LEU
1	A	101	PRO

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Mol	Chain	Res	Type
1	A	100	PHE
1	A	227	PRO
1	A	429	SER
1	A	226	PHE

5.3.2 Protein sidechains ⓘ

In the following table, the Percentiles column shows the percent sidechain outliers of the chain as a percentile score with respect to all X-ray entries followed by that with respect to entries of similar resolution.

The Analysed column shows the number of residues for which the sidechain conformation was analysed, and the total number of residues.

Mol	Chain	Analysed	Rotameric	Outliers	Percentiles	
1	A	410/430 (95%)	376 (92%)	34 (8%)	13	16

All (34) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	36	LEU
1	A	43	LEU
1	A	105	ARG
1	A	107	ASN
1	A	131	LEU
1	A	136	MET
1	A	164	CYS
1	A	197	LEU
1	A	201	LEU
1	A	206	LYS
1	A	210	SER
1	A	222	ILE
1	A	224	ASP
1	A	232	LYS
1	A	274	GLU
1	A	277	ASN
1	A	280	SER
1	A	295	PHE
1	A	308	TYR
1	A	315	LYS
1	A	325	GLU
1	A	328	GLU

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Mol	Chain	Res	Type
1	A	329	ARG
1	A	333	ARG
1	A	334	ASN
1	A	335	ARG
1	A	381	ILE
1	A	399	LYS
1	A	413	LEU
1	A	432	LYS
1	A	462	VAL
1	A	490	ILE
1	A	491	HIS
1	A	492	HIS

Some sidechains can be flipped to improve hydrogen bonding and reduce clashes. All (3) such sidechains are listed below:

Mol	Chain	Res	Type
1	A	334	ASN
1	A	466	ASN
1	A	484	GLN

5.3.3 RNA [i](#)

There are no RNA molecules in this entry.

5.4 Non-standard residues in protein, DNA, RNA chains [i](#)

There are no non-standard protein/DNA/RNA residues in this entry.

5.5 Carbohydrates [i](#)

There are no carbohydrates in this entry.

5.6 Ligand geometry [i](#)

2 ligands are modelled in this entry.

In the following table, the Counts columns list the number of bonds (or angles) for which Mogul statistics could be retrieved, the number of bonds (or angles) that are observed in the model and the number of bonds (or angles) that are defined in the chemical component dictionary. The Link

column lists molecule types, if any, to which the group is linked. The Z score for a bond length (or angle) is the number of standard deviations the observed value is removed from the expected value. A bond length (or angle) with $|Z| > 2$ is considered an outlier worth inspection. RMSZ is the root-mean-square of all Z scores of the bond lengths (or angles).

Mol	Type	Chain	Res	Link	Bond lengths			Bond angles		
					Counts	RMSZ	$\# Z > 2$	Counts	RMSZ	$\# Z > 2$
2	HEM	A	501	1,3	28,50,50	4.10	16 (57%)	17,82,82	2.53	10 (58%)
3	6RJ	A	502	2	29,33,33	0.72	1 (3%)	34,47,47	0.98	2 (5%)

In the following table, the Chirals column lists the number of chiral outliers, the number of chiral centers analysed, the number of these observed in the model and the number defined in the chemical component dictionary. Similar counts are reported in the Torsion and Rings columns. '-' means no outliers of that kind were identified.

Mol	Type	Chain	Res	Link	Chirals	Torsions	Rings
2	HEM	A	501	1,3	-	0/6/54/54	0/0/8/8
3	6RJ	A	502	2	-	0/17/21/21	0/4/4/4

All (17) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
3	A	502	6RJ	C11-N10	-2.56	1.35	1.40
2	A	501	HEM	C1C-NC	-2.52	1.33	1.36
2	A	501	HEM	C3B-C2B	-2.44	1.37	1.40
2	A	501	HEM	C3D-C2D	2.14	1.44	1.37
2	A	501	HEM	CMD-C2D	2.26	1.56	1.51
2	A	501	HEM	CMA-C3A	2.73	1.57	1.51
2	A	501	HEM	CAA-C2A	2.95	1.57	1.52
2	A	501	HEM	C4B-NB	3.19	1.43	1.36
2	A	501	HEM	CAD-C3D	3.64	1.59	1.52
2	A	501	HEM	C4A-NA	4.41	1.45	1.36
2	A	501	HEM	C3C-CAC	4.51	1.56	1.47
2	A	501	HEM	C1D-ND	4.79	1.46	1.36
2	A	501	HEM	C3B-CAB	4.80	1.57	1.47
2	A	501	HEM	C4C-NC	5.50	1.43	1.36
2	A	501	HEM	CMB-C2B	7.11	1.66	1.51
2	A	501	HEM	C4D-ND	7.71	1.45	1.36
2	A	501	HEM	C1B-NB	13.07	1.52	1.36

All (12) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
3	A	502	6RJ	C11-N10-S7	-4.50	116.89	124.33

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Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
2	A	501	HEM	CMA-C3A-C4A	-3.84	122.56	128.46
2	A	501	HEM	CMD-C2D-C3D	-3.28	118.76	124.94
2	A	501	HEM	CAA-CBA-CGA	-3.07	107.42	112.66
2	A	501	HEM	CBD-CAD-C3D	-2.74	107.25	112.47
3	A	502	6RJ	C6-S7-N10	-2.69	103.38	106.83
2	A	501	HEM	CAD-C3D-C2D	-2.55	121.73	129.00
2	A	501	HEM	CAD-CBD-CGD	-2.49	108.41	112.66
2	A	501	HEM	C4A-C3A-C2A	2.79	108.94	107.00
2	A	501	HEM	CMB-C2B-C3B	2.92	130.32	124.89
2	A	501	HEM	CMD-C2D-C1D	3.04	133.14	128.46
2	A	501	HEM	CMC-C2C-C3C	4.09	132.47	124.89

There are no chirality outliers.

There are no torsion outliers.

There are no ring outliers.

2 monomers are involved in 12 short contacts:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
2	A	501	HEM	6	0
3	A	502	6RJ	6	0

5.7 Other polymers [i](#)

There are no such residues in this entry.

5.8 Polymer linkage issues [i](#)

There are no chain breaks in this entry.

6 Fit of model and data ⓘ

6.1 Protein, DNA and RNA chains ⓘ

In the following table, the column labelled ‘#RSRZ> 2’ contains the number (and percentage) of RSRZ outliers, followed by percent RSRZ outliers for the chain as percentile scores relative to all X-ray entries and entries of similar resolution. The OWAB column contains the minimum, median, 95th percentile and maximum values of the occupancy-weighted average B-factor per residue. The column labelled ‘Q< 0.9’ lists the number of (and percentage) of residues with an average occupancy less than 0.9.

Mol	Chain	Analysed	<RSRZ>	#RSRZ>2	OWAB(Å ²)	Q<0.9
1	A	455/477 (95%)	0.33	32 (7%) 17 23	27, 55, 100, 156	0

All (32) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	A	225	TYR	8.2
1	A	276	HIS	8.0
1	A	106	ALA	7.6
1	A	71	LEU	5.7
1	A	103	ALA	5.6
1	A	221	PRO	5.5
1	A	105	ARG	5.4
1	A	107	ASN	4.9
1	A	37	PRO	4.6
1	A	102	LEU	4.6
1	A	279	PRO	4.4
1	A	492	HIS	4.3
1	A	226	PHE	3.8
1	A	36	LEU	3.6
1	A	99	ILE	3.6
1	A	45	ILE	3.6
1	A	257	MET	3.6
1	A	70	GLY	3.6
1	A	466	ASN	3.2
1	A	227	PRO	3.2
1	A	110	PHE	3.1
1	A	228	GLY	3.1
1	A	490	ILE	3.0
1	A	334	ASN	2.8
1	A	463	ASP	2.8
1	A	465	LYS	2.8
1	A	491	HIS	2.4

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Mol	Chain	Res	Type	RSRZ
1	A	185	LYS	2.3
1	A	100	PHE	2.3
1	A	461	LEU	2.1
1	A	189	TYR	2.0
1	A	27	GLY	2.0

6.2 Non-standard residues in protein, DNA, RNA chains [i](#)

There are no non-standard protein/DNA/RNA residues in this entry.

6.3 Carbohydrates [i](#)

There are no carbohydrates in this entry.

6.4 Ligands [i](#)

In the following table, the Atoms column lists the number of modelled atoms in the group and the number defined in the chemical component dictionary. LLDF column lists the quality of electron density of the group with respect to its neighbouring residues in protein, DNA or RNA chains. The B-factors column lists the minimum, median, 95th percentile and maximum values of B factors of atoms in the group. The column labelled 'Q < 0.9' lists the number of atoms with occupancy less than 0.9.

Mol	Type	Chain	Res	Atoms	RSCC	RSR	LLDF	B-factors(Å ²)	Q<0.9
3	6RJ	A	502	30/30	0.88	0.16	0.39	55,79,92,93	0
2	HEM	A	501	43/43	0.97	0.14	0.21	26,31,40,42	0

6.5 Other polymers [i](#)

There are no such residues in this entry.