



Full wwPDB X-ray Structure Validation Report ⓘ

May 10, 2016 – 04:57 PM EDT

PDB ID : 4ZOP
Title : Co-crystal Structure of Lipid Kinase PI3K alpha with a selective phosphatidylinositol-3 kinase alpha inhibitor
Authors : Knapp, M.S.; Elling, R.A.
Deposited on : 2015-05-06
Resolution : 2.62 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 : 1.7.1 (RC1), CSD as537be (2016)
Xtriage (Phenix) : 1.9-1692
EDS : rb-20027457
Percentile statistics : 20151230.v01 (using entries in the PDB archive December 30th 2015)
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-20027457

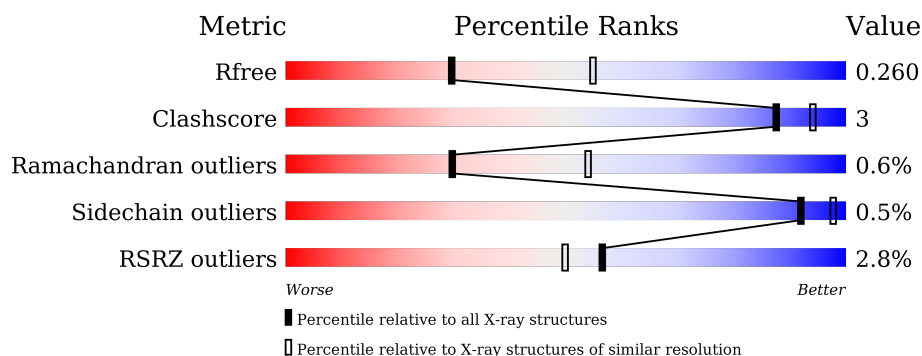
1 Overall quality at a glance

The following experimental techniques were used to determine the structure:

X-RAY DIFFRACTION

The reported resolution of this entry is 2.62 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}	91344	2700 (2.64-2.60)
Clashscore	102246	3065 (2.64-2.60)
Ramachandran outliers	100387	3015 (2.64-2.60)
Sidechain outliers	100360	3015 (2.64-2.60)
RSRZ outliers	91569	2706 (2.64-2.60)

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	1074	<div> <div>2%</div> <div> <div></div> <div>88%</div> <div>5%</div> <div>7%</div> </div> </div>
2	B	290	<div> <div>4%</div> <div> <div></div> <div>78%</div> <div>• •</div> <div>17%</div> </div> </div>

2 Entry composition

There are 4 unique types of molecules in this entry. The entry contains 10227 atoms, of which 26 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 Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha isoform.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
1	A	1000	Total	C	N	O	S	0	1	0
			8080	5169	1378	1468	65			

There are 8 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	232	LYS	MET	engineered mutation	UNP P42336
A	233	LYS	LEU	engineered mutation	UNP P42336
A	1069	HIS	-	expression tag	UNP P42336
A	1070	HIS	-	expression tag	UNP P42336
A	1071	HIS	-	expression tag	UNP P42336
A	1072	HIS	-	expression tag	UNP P42336
A	1073	HIS	-	expression tag	UNP P42336
A	1074	HIS	-	expression tag	UNP P42336

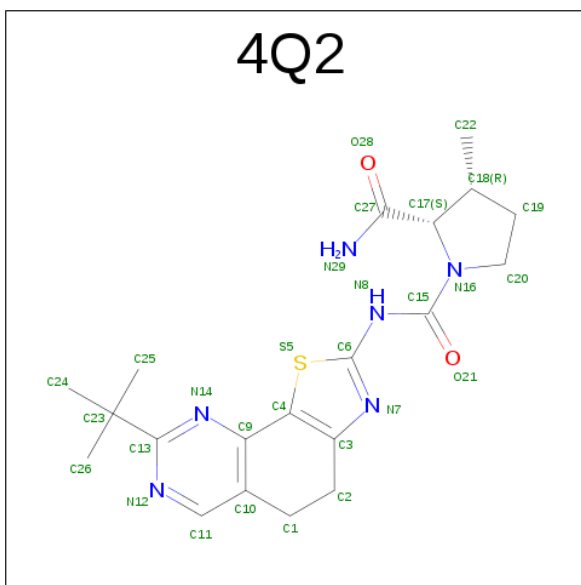
- Molecule 2 is a protein called Phosphatidylinositol 3-kinase regulatory subunit alpha.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
2	B	240	Total	C	N	O	S	0	0	0
			1965	1231	349	381	4			

There is a discrepancy between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
B	306	TYR	THR	conflict	UNP P27986

- Molecule 3 is (2S,3R)-N 1 -(8-tert-butyl-4,5-dihydro[1,3]thiazolo[4,5-h]quinazolin-2-yl)-3-methylpyrrolidine-1,2-dicarboxamide (three-letter code: 4Q2) (formula: C₂₀H₂₆N₆O₂S).



Mol	Chain	Residues	Atoms						ZeroOcc	AltConf
3	A	1	Total	C	H	N	O	S	0	0
			55	20	26	6	2	1		

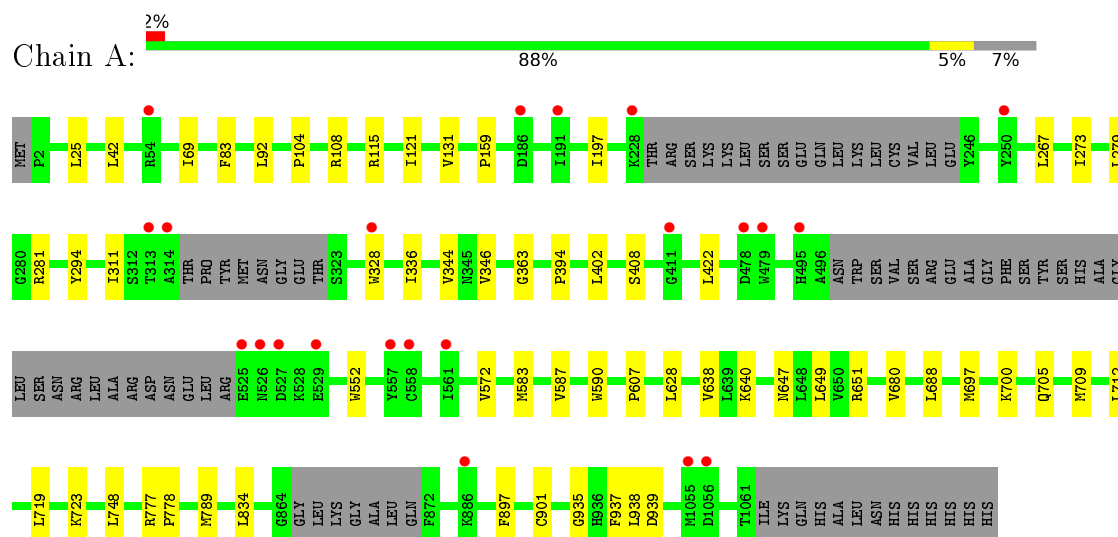
- Molecule 4 is water.

Mol	Chain	Residues	Atoms	ZeroOcc	AltConf
4	A	111	Total O 111 111	0	0
4	B	16	Total O 16 16	0	0

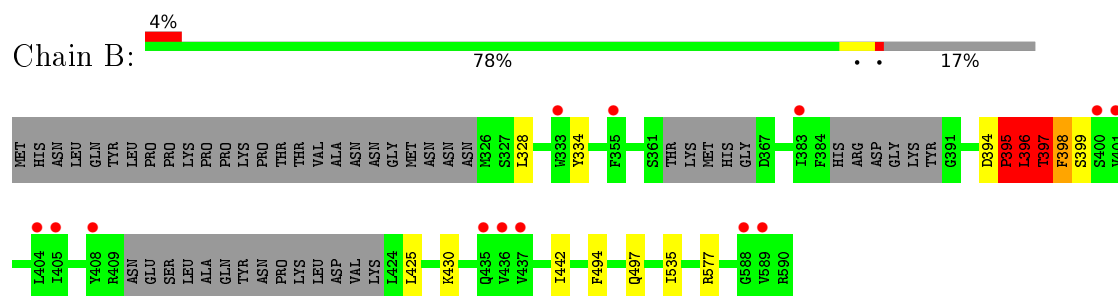
3 Residue-property plots [i](#)

These plots are drawn for all protein, RNA and DNA chains in the entry. The first graphic for a chain summarises the proportions of errors 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 ($\text{RSRZ} > 2$). 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: Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha isoform



- Molecule 2: Phosphatidylinositol 3-kinase regulatory subunit alpha



4 Data and refinement statistics

Property	Value	Source
Space group	P 21 21 21	Depositor
Cell constants a, b, c, α , β , γ	104.81Å 106.56Å 134.79Å 90.00° 90.00° 90.00°	Depositor
Resolution (Å)	47.49 – 2.62 47.49 – 2.62	Depositor EDS
% Data completeness (in resolution range)	100.0 (47.49-2.62) 100.0 (47.49-2.62)	Depositor EDS
R_{merge}	0.07	Depositor
R_{sym}	(Not available)	Depositor
$\langle I/\sigma(I) \rangle$ ¹	2.31 (at 2.61Å)	Xtriage
Refinement program	BUSTER-TNT	Depositor
R, R_{free}	0.193 , 0.258 0.195 , 0.260	Depositor DCC
R_{free} test set	2200 reflections (5.00%)	DCC
Wilson B-factor (Å ²)	59.5	Xtriage
Anisotropy	0.073	Xtriage
Bulk solvent k_{sol} (e/Å ³), B_{sol} (Å ²)	0.29 , 42.9	EDS
L-test for twinning ²	$\langle L \rangle = 0.49$, $\langle L^2 \rangle = 0.33$	Xtriage
Estimated twinning fraction	0.016 for k,h,-l	Xtriage
F_o, F_c correlation	0.95	EDS
Total number of atoms	10227	wwPDB-VP
Average B, all atoms (Å ²)	68.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 3.31% 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, 0.375 respectively for untwinned datasets, and 0.333, 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: 4Q2

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	0.52	0/8264	0.69	0/11188
2	B	0.54	1/1994 (0.1%)	0.73	3/2678 (0.1%)
All	All	0.52	1/10258 (0.0%)	0.70	3/13866 (0.0%)

Chiral center outliers are detected by calculating the chiral volume of a chiral center and verifying if the center is modelled as a planar moiety or with the opposite hand. A planarity outlier is detected by checking planarity of atoms in a peptide group, atoms in a mainchain group or atoms of a sidechain that are expected to be planar.

Mol	Chain	#Chirality outliers	#Planarity outliers
2	B	0	1

All (1) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	B	395	PRO	N-CD	7.49	1.58	1.47

All (3) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
2	B	396	LEU	C-N-CA	8.68	143.39	121.70
2	B	397	THR	N-CA-CB	5.96	121.62	110.30
2	B	396	LEU	CB-CA-C	-5.47	99.81	110.20

There are no chirality outliers.

All (1) planarity outliers are listed below:

Mol	Chain	Res	Type	Group
2	B	398	PHE	Mainchain

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	8080	0	7981	32	0
2	B	1965	0	1870	20	0
3	A	29	26	0	1	0
4	A	111	0	0	0	0
4	B	16	0	0	0	0
All	All	10201	26	9851	51	0

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 3.

All (51) 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)
2:B:396:LEU:HD22	2:B:398:PHE:CE2	1.52	1.43
2:B:396:LEU:CD2	2:B:398:PHE:HE2	1.70	1.04
2:B:396:LEU:CD2	2:B:398:PHE:CE2	2.48	0.90
1:A:897:PHE:O	1:A:901:CYS:HB2	1.83	0.78
2:B:396:LEU:HD12	2:B:397:THR:N	2.01	0.76
1:A:121:ILE:HG12	1:A:688:LEU:HB3	1.71	0.71
2:B:494:PHE:HB3	2:B:535:ILE:HG12	1.73	0.70
2:B:394:ASP:HB2	2:B:395:PRO:HA	1.77	0.65
2:B:396:LEU:C	2:B:396:LEU:HD12	2.18	0.63
2:B:396:LEU:CD1	2:B:397:THR:N	2.63	0.62
1:A:712:LEU:HD21	1:A:748:LEU:HD21	1.83	0.61
1:A:697:MET:SD	1:A:700:LYS:HD2	2.42	0.59
2:B:334:TYR:O	2:B:430:LYS:HE2	2.04	0.56
1:A:640:LYS:HG2	1:A:680:VAL:HG11	1.87	0.55
2:B:577:ARG:HH11	2:B:577:ARG:HG2	1.72	0.55
1:A:25:LEU:HD13	2:B:497:GLN:HG3	1.90	0.54
1:A:937:PHE:HD1	1:A:938:LEU:HG	1.74	0.53
1:A:42:LEU:HD21	1:A:92:LEU:HD11	1.92	0.52
2:B:396:LEU:HD12	2:B:397:THR:CA	2.40	0.51
1:A:279:LEU:HB2	1:A:281:ARG:HG2	1.92	0.51
1:A:572:VAL:HG21	1:A:583:MET:HG2	1.92	0.51
2:B:396:LEU:HD22	2:B:398:PHE:CD2	2.32	0.51

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Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
2:B:396:LEU:HB2	2:B:398:PHE:HD2	1.76	0.50
2:B:396:LEU:HD12	2:B:397:THR:HA	1.92	0.50
1:A:328:TRP:HA	1:A:394:PRO:HB3	1.94	0.50
1:A:25:LEU:HD13	2:B:497:GLN:CG	2.41	0.50
1:A:279:LEU:CB	1:A:281:ARG:HG2	2.41	0.49
2:B:396:LEU:HD22	2:B:398:PHE:HE2	0.83	0.49
2:B:396:LEU:HB2	2:B:398:PHE:CD2	2.48	0.48
1:A:363:GLY:N	1:A:607:PRO:HG3	2.28	0.48
1:A:311:ILE:H	1:A:311:ILE:HD12	1.80	0.47
1:A:267:LEU:HG	1:A:273:ILE:HG13	1.95	0.47
1:A:336:ILE:HD13	1:A:402:LEU:HD22	1.95	0.47
3:A:1101:4Q2:S5	3:A:1101:4Q2:O21	2.73	0.47
1:A:197:ILE:HD11	1:A:789:MET:HE2	1.96	0.46
1:A:83:PHE:CE1	1:A:108:ARG:HG3	2.52	0.45
1:A:937:PHE:CD1	1:A:938:LEU:HG	2.52	0.43
1:A:344:VAL:HG23	1:A:346:VAL:HG22	2.00	0.43
1:A:552:TRP:HZ3	1:A:583:MET:HE2	1.84	0.43
1:A:705:GLN:O	1:A:709:MET:HG2	2.18	0.43
1:A:69:ILE:HG23	1:A:104:PRO:HG3	2.01	0.42
2:B:396:LEU:C	2:B:396:LEU:CD1	2.84	0.42
1:A:408:SER:HB3	1:A:422:LEU:HD21	2.02	0.42
1:A:719:LEU:HA	1:A:723:LYS:HB2	2.02	0.42
2:B:396:LEU:CD1	2:B:397:THR:HA	2.50	0.41
1:A:712:LEU:CD2	1:A:748:LEU:HD21	2.50	0.41
1:A:587:VAL:HA	1:A:590:TRP:HB2	2.02	0.41
1:A:647:ASN:O	1:A:651:ARG:HG3	2.21	0.41
1:A:777:ARG:N	1:A:778:PRO:HD3	2.36	0.40
1:A:638:VAL:HG23	1:A:649:LEU:HD21	2.03	0.40
1:A:159:PRO:HG2	1:A:294:TYR:CD2	2.57	0.40

There are no symmetry-related clashes.

5.3 Torsion angles ⓘ

5.3.1 Protein backbone ⓘ

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	991/1074 (92%)	945 (95%)	44 (4%)	2 (0%)	52 76
2	B	232/290 (80%)	220 (95%)	7 (3%)	5 (2%)	8 14
All	All	1223/1364 (90%)	1165 (95%)	51 (4%)	7 (1%)	30 54

All (7) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
2	B	396	LEU
2	B	397	THR
2	B	399	SER
1	A	131	VAL
2	B	425	LEU
2	B	395	PRO
1	A	935	GLY

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	890/980 (91%)	886 (100%)	4 (0%)	93 98
2	B	203/269 (76%)	201 (99%)	2 (1%)	82 93
All	All	1093/1249 (88%)	1087 (100%)	6 (0%)	92 98

All (6) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	115	ARG
1	A	628	LEU
1	A	834	LEU
1	A	939	ASP
2	B	328	LEU
2	B	442	ILE

Some sidechains can be flipped to improve hydrogen bonding and reduce clashes. There are no such sidechains identified.

5.3.3 RNA ⓘ

There are no RNA molecules in this entry.

5.4 Non-standard residues in protein, DNA, RNA chains ⓘ

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

5.5 Carbohydrates ⓘ

There are no carbohydrates in this entry.

5.6 Ligand geometry ⓘ

1 ligand is 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$
3	4Q2	A	1101	-	28,32,32	0.74	2 (7%)	29,49,49	1.48	3 (10%)

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
3	4Q2	A	1101	-	-	0/16/40/40	0/4/4/4

All (2) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
3	A	1101	4Q2	C9-C4	-2.59	1.42	1.47
3	A	1101	4Q2	C15-N8	2.62	1.40	1.36

All (3) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed($^{\circ}$)	Ideal($^{\circ}$)
3	A	1101	4Q2	C6-N8-C15	-4.81	123.54	130.00
3	A	1101	4Q2	C2-C1-C10	2.02	115.89	110.69
3	A	1101	4Q2	C1-C2-C3	4.73	113.37	109.84

There are no chirality outliers.

There are no torsion outliers.

There are no ring outliers.

1 monomer is involved in 1 short contact:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
3	A	1101	4Q2	1	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	1000/1074 (93%)	-0.18	22 (2%) 65 59	36, 63, 99, 150	0
2	B	240/290 (82%)	0.05	13 (5%) 29 22	48, 77, 127, 143	0
All	All	1240/1364 (90%)	-0.13	35 (2%) 56 50	36, 66, 108, 150	0

All (35) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	A	1055	MET	5.4
1	A	557	TYR	4.5
2	B	404	LEU	4.4
2	B	405	ILE	4.0
2	B	589	VAL	3.9
2	B	437	VAL	3.9
2	B	588	GLY	3.8
1	A	529	GLU	3.6
1	A	495	HIS	3.5
2	B	401	VAL	3.3
2	B	436	VAL	3.3
1	A	313	THR	3.2
2	B	408	TYR	3.1
1	A	411	GLY	3.1
1	A	527	ASP	3.0
1	A	478	ASP	3.0
1	A	314	ALA	2.9
1	A	186	ASP	2.9
2	B	400	SER	2.8
2	B	383	ILE	2.8
1	A	561	ILE	2.7
1	A	250	TYR	2.7
1	A	558	CYS	2.6
1	A	525	GLU	2.6

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Mol	Chain	Res	Type	RSRZ
2	B	435	GLN	2.6
1	A	191	ILE	2.6
1	A	54	ARG	2.4
2	B	333	TRP	2.4
1	A	526	ASN	2.4
1	A	886	LYS	2.2
1	A	1056	ASP	2.2
1	A	479	TRP	2.2
1	A	328	TRP	2.1
1	A	228	LYS	2.0
2	B	355	PHE	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(\AA^2)	Q<0.9
3	4Q2	A	1101	29/29	0.98	0.15	-0.27	35,41,54,56	0

6.5 Other polymers [i](#)

There are no such residues in this entry.