wwPDB EM Validation Summary Report

Oct 26, 2026 – 05:09 PM JST

PDB ID	:	26IV / pdb_000026iv
EMDB ID	:	EMD-80690
Title	:	Structure of recombinant RyR2 in complex with Ryanozole in the open conformation (Ca2+ dataset, Local refinement of Core domain)
Authors	:	Otori, Y.; Takeuchi, S.; Ogawa, H.
Deposited on	:	2026-05-01
Resolution	:	2.64 Å(reported)

This is a wwPDB EM Validation Summary Report for a publicly released PDB entry.

We welcome your comments at *validation@mail.wwpdb.org*
A user guide is available at
https://www.wwpdb.org/validation/2017/EMValidationReportHelp
with specific help available everywhere you see the ⓘ symbol.

The types of validation reports are described at
http://www.wwpdb.org/validation/2017/FAQs#types.

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

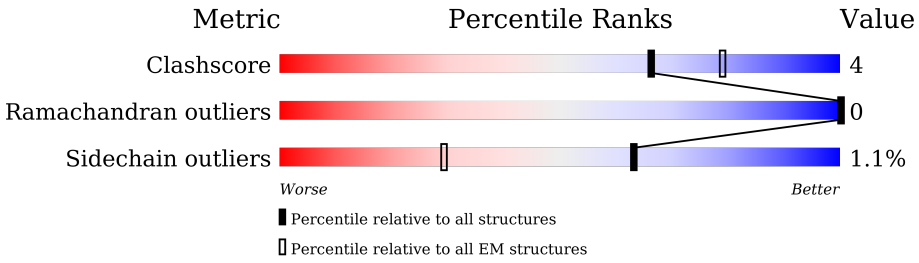
EMDB validation analysis	:	0.0.1.dev133
Mogul	:	1.8.5 (274361), CSD as541be (2020)
MolProbity	:	4-5-2 with Phenix2.2
Buster-report	:	wwPDB partial adaption of 1.1.7 (2018)
Percentile statistics	:	20250101.v01 (using entries in the PDB archive January 1st 2025)
EM percentile statistics	:	202505.v01 (Using data in the EMDB archive up until May 2025)
MapQ	:	1.9.13
Ideal geometry (proteins)	:	Engh & Huber (2001)
Ideal geometry (DNA, RNA)	:	Parkinson et al. (1996)
Validation Pipeline (wwPDB-VP)	:	2.51

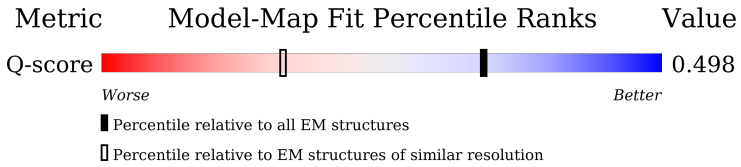
1 Overall quality at a glance (i)

The following experimental techniques were used to determine the structure:
ELECTRON MICROSCOPY

The reported resolution of this entry is 2.64 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)	EM structures (#Entries)	Similar EM resolution (#Entries, resolution range(Å))
Clashscore	229148	23984	-
Ramachandran outliers	224038	23583	-
Sidechain outliers	223484	23102	-
Q-score	-	25397	8968 (2.14 - 3.14)

The table below summarises the geometric issues observed across the polymeric chains and their fit to the map. The red, orange, yellow and green segments of the bar indicate the fraction of residues that contain outliers for >=3, 2, 1 and 0 types of geometric quality criteria respectively. 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 <=5% The upper red bar (where present) indicates the fraction of residues that have poor fit to the EM map (all-atom inclusion < 40%). The numeric value is given above the bar.

Mol	Chain	Length	Quality of chain
1	A	4966	9% 19% 79%
1	B	4966	9% 19% 79%
1	C	4966	9% 19% 79%
1	D	4966	9% 19% 79%

2 Entry composition (i)

There are 4 unique types of molecules in this entry. The entry contains 67360 atoms, of which 33244 are hydrogens and 0 are deuteriums.

In the tables below, 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 Ryanodine receptor 2.

Mol	Chain	Residues	Atoms						AltConf	Trace
1	A	1041	Total	C	H	N	O	S	0	0
			16801	5472	8299	1370	1604	56		
1	B	1041	Total	C	H	N	O	S	0	0
			16801	5472	8299	1370	1604	56		
1	C	1041	Total	C	H	N	O	S	0	0
			16801	5472	8299	1370	1604	56		
1	D	1041	Total	C	H	N	O	S	0	0
			16801	5472	8299	1370	1604	56		

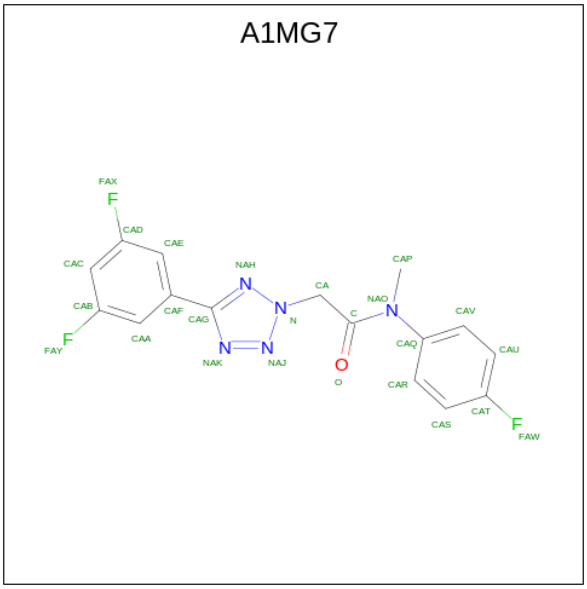
- Molecule 2 is ZINC ION (CCD ID: ZN) (formula: Zn) (labeled as "Ligand of Interest" by depositor).

Mol	Chain	Residues	Atoms		AltConf
2	A	1	Total	Zn	0
			1	1	
2	B	1	Total	Zn	0
			1	1	
2	C	1	Total	Zn	0
			1	1	
2	D	1	Total	Zn	0
			1	1	

- Molecule 3 is CALCIUM ION (CCD ID: CA) (formula: Ca) (labeled as "Ligand of Interest" by depositor).

Mol	Chain	Residues	Atoms		AltConf
3	A	1	Total	Ca	0
			1	1	
3	B	1	Total	Ca	0
			1	1	
3	C	1	Total	Ca	0
			1	1	
3	D	1	Total	Ca	0
			1	1	

- Molecule 4 is Ryanozole (CCD ID: A1MG7) (formula: $C_{16}H_{12}F_3N_5O$) (labeled as "Ligand of Interest" by depositor).



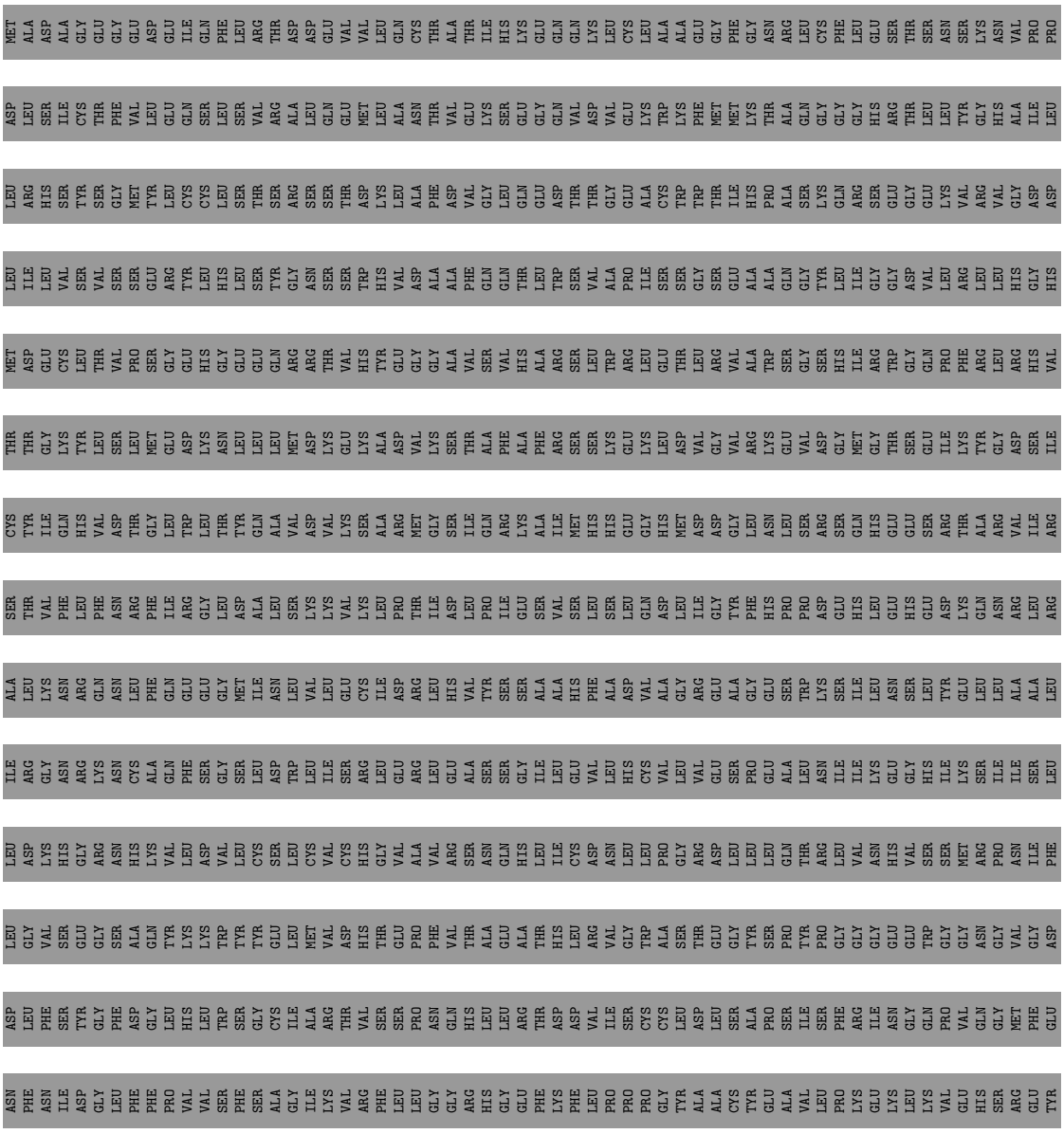
Mol	Chain	Residues	Atoms						AltConf
4	A	1	Total	C	F	H	N	O	0
			37	16	3	12	5	1	
4	B	1	Total	C	F	H	N	O	0
			37	16	3	12	5	1	
4	C	1	Total	C	F	H	N	O	0
			37	16	3	12	5	1	
4	D	1	Total	C	F	H	N	O	0
			37	16	3	12	5	1	

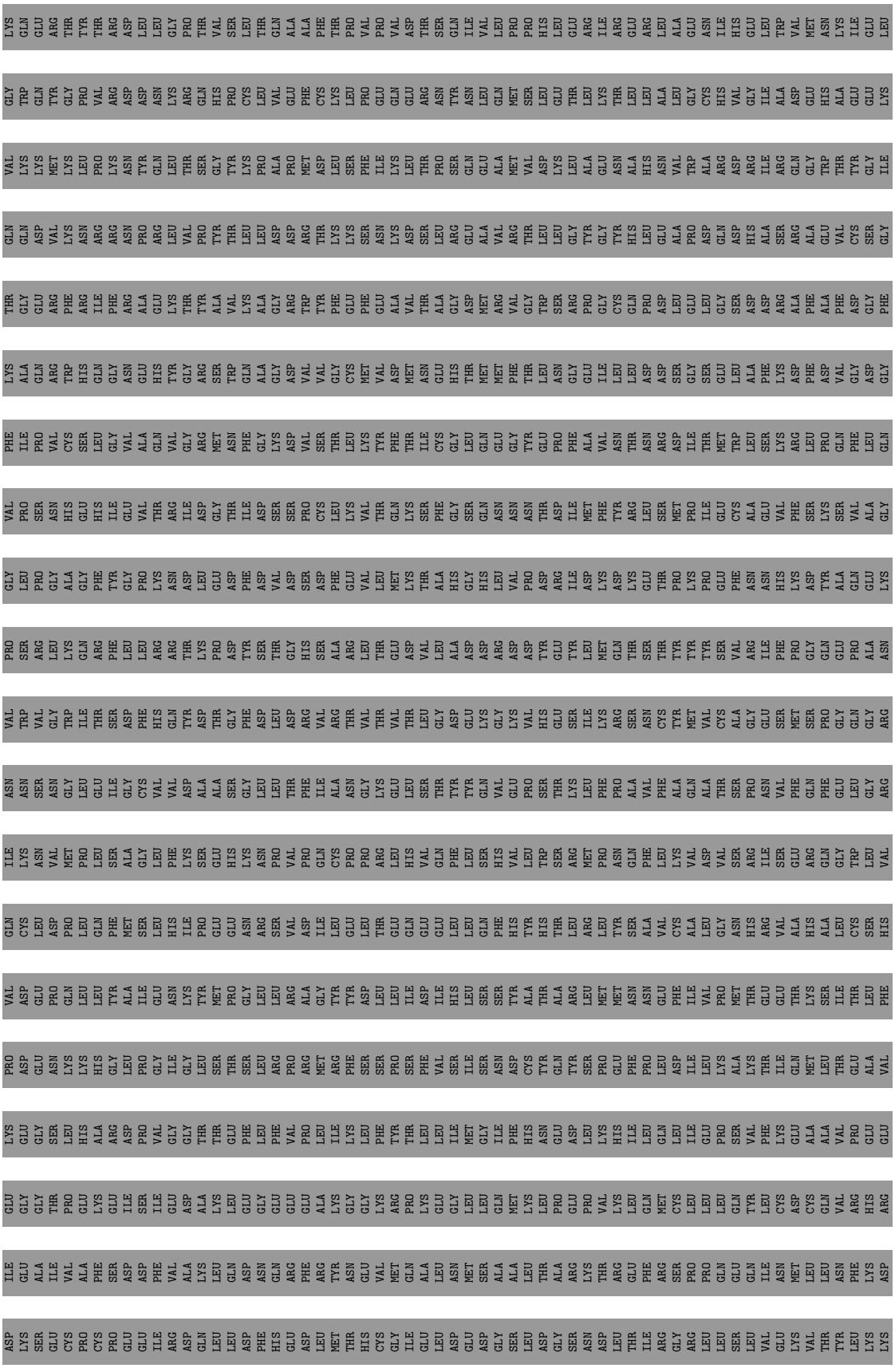
3 Residue-property plots (i)

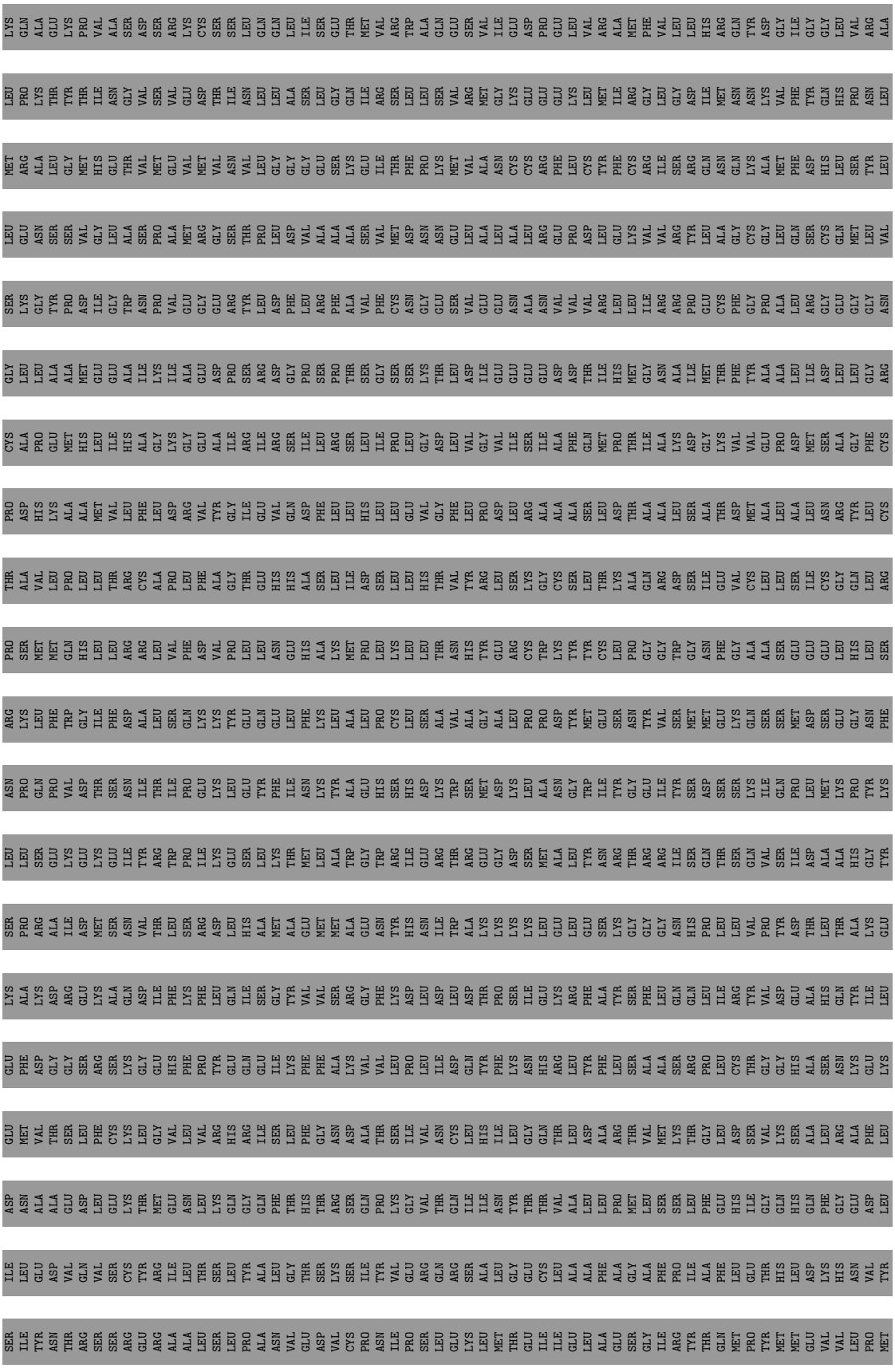
These plots are drawn for all protein, RNA, DNA and oligosaccharide chains in the entry. The first graphic for a chain summarises the proportions of the various outlier classes displayed in the second graphic. The second graphic shows the sequence view annotated by issues in geometry and atom inclusion in map 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 diamond above a residue indicates a poor fit to the EM map for this residue (all-atom inclusion < 40%). 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.

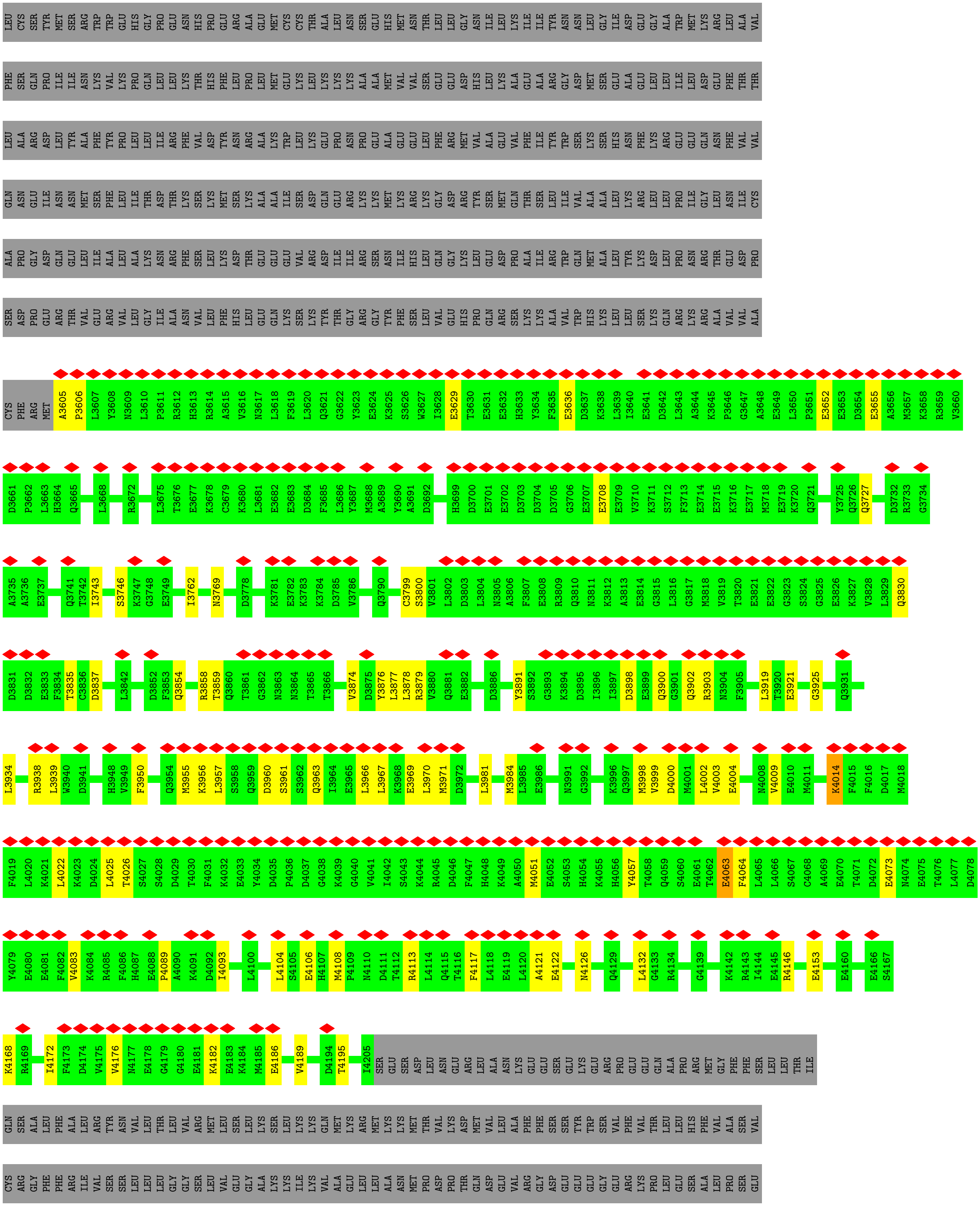
- Molecule 1: Ryanodine receptor 2

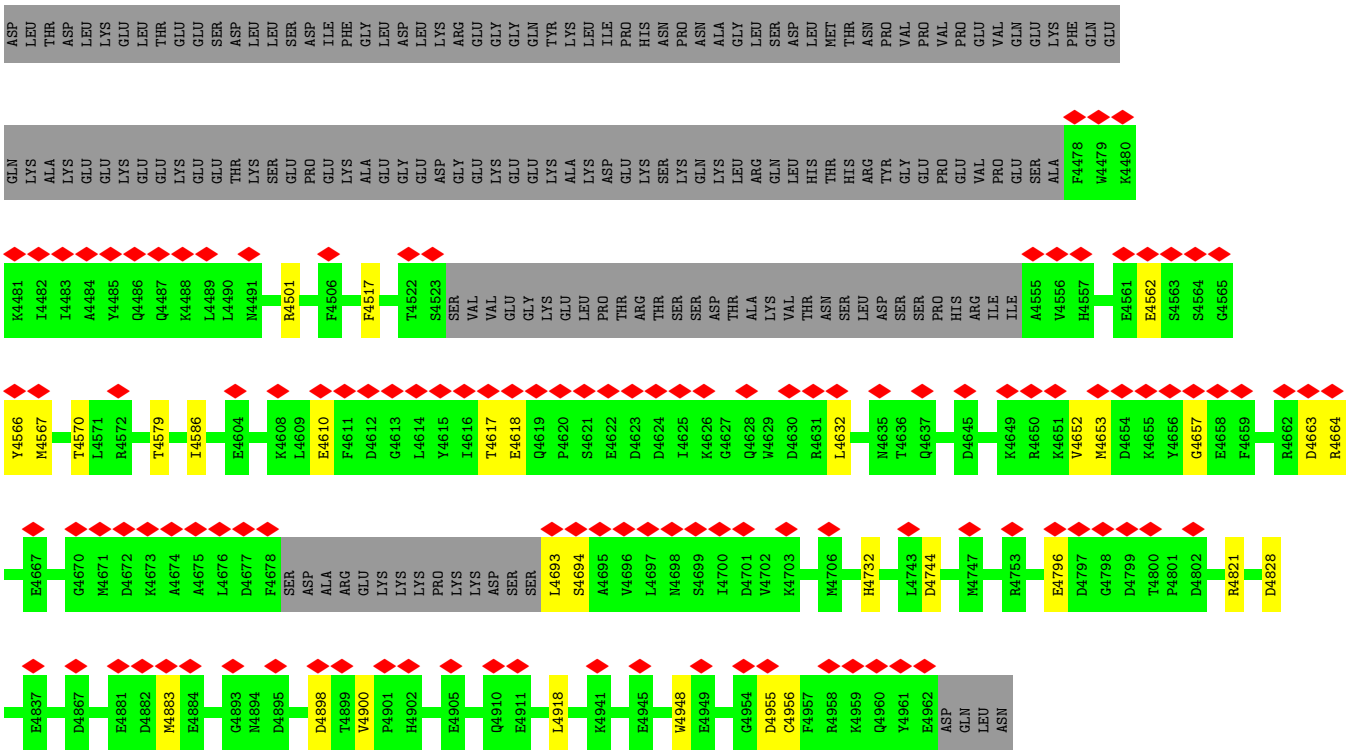





LYS GLN GLU ARG THR TYR THR ARG ASP LEU LEU GLY PRO THR VAL SER LEU THR GLN ALA ALA PHE THR PRO VAL PRO VAL ASP THR SER GLN ILE VAL LEU PRO PRO HIS LEU GLU ARG ILE ARG GLU ARG LEU ALA GLU ASN ILE HIS GLU LEU TRP VAL MET ASN LYS ILE GLU LEU
GLY TRP GLN TYR GLY PRO VAL ARG ASP ASP ASN LYS ARG GLN HIS PRO CYS LEU VAL GLU PHE CYS LYS LEU PRO GLU GLN GLU ARG ASN TYR ASN LEU GLN MET SER LEU GLU THR LEU LYS THR LEU ALA GLU GLY CYS HIS VAL GLY ILE ALA ASP GLU HIS ALA GLU GLU LYS
VAL LYS LYS MET LYS LEU PRO LYS ASN TYR GLN LEU THR SER GLY TYR LYS PRO ALA PRO MET ASP LEU SER PHE ILE LYS LEU THR PRO SER GLN GLU ALA MET VAL ASP LYS LEU ALA GLU ASN ALA HIS ASN VAL TRP ALA ARG ASP ARG ILE ARG SER ARG GLN GLY TRP THR TYR GLY ILE
GLN GLN ASP VAL LYS ASN ARG ASN PRO ARG LEU VAL PRO TYR THR LEU LEU ASP ARG THR LYS LYS SER ASN LYS ASP SER LEU ARG GLU ALA VAL THR ALA GLY ASP ASP ARG GLN LEU GLU VAL LEU GLY TYR GLY TYR HIS LEU GLU ALA PRO ASP GLN ASP HIS ALA SER ARG ALA GLU GLY SER
THR GLY GLU ARG PHE ILE PHE ARG GLU LYS THR TYR ALA VAL LYS ALA GLY ARG TRP TYR PHE GLU PHE GLU LYS PHE GLU GLY ALA VAL THR ALA GLY ASP MET ARG VAL GLY TRP SER ARG PRO GLY CYS GLN PRO ASP LEU GLU GLU LEU GLY SER ASP ASP ARG ALA PHE ALA PHE ASP GLY PHE
LYS ALA GLN ARG TRP HIS GLN GLY ASN GLU HIS TYR GLY ARG ASP VAL VAL GLY CYS MET VAL ASP MET MET ASN GLU HIS THR MET MET PHE THR LEU ASN GLY GLU ILE LEU LEU LEU ASP ASP SER GLY SER GLU LEU LEU ALA PHE LYS ASP PHE ASP VAL GLY ASP
PHE ILE PRO VAL CYS SER LEU GLY VAL ALA GLN VAL GLY ARG MET ASN PHE GLY LYS ASP VAL SER THR LEU LYS TYR PHE THR ILE CYS GLY LEU GLN LEU GLU ILE ALA VAL ASN THR ASN ASN ARG ASP ILE THR MET TRP LEU GLU ILE GLU LEU PHE
VAL PRO SER ASN HIS GLU HIS ILE GLU VAL THR ARG ILE ASP GLY THR ILE ASP SER SER PRO CYS LEU LYS VAL THR GLN LYS SER PHE GLY SER GLN ASN GLU ASN ASN THR ASP ILE MET PHE TYR ARG LEU SER MET PRO ILE GLU CYS ALA GLU VAL PHE SER LYS SER VAL ALA GLY
GLY LEU PRO GLY ALA GLY PHE TYR GLY PRO LYS ASN ASP LEU GLU ASP PHE ASP VAL ASP SER ASP PHE GLU VAL LEU MET LYS THR ALA HIS GLY HIS LEU VAL PRO ASP ARG ILE ASP LYS GLU THR PRO LYS PRO GLU PHE ASN ASN HIS LYS ASP TYR ALA GLN GLU LYS
PRO SER ARG LEU LYS GLN ARG PHE LEU LEU ARG ARG THR LYS PRO ASP TYR SER THR GLY HIS SER ALA ARG LEU THR GLU ASP VAL LEU ALA ASP ASP ARG ASP ASP TYR GLU TYR LEU MET GLN THR SER THR TYR TYR TYR SER VAL ARG ILE PHE PRO GLY GLN GLU PRO ALA ASN
VAL TRP VAL GLY TRP ILE THR SER ASP PHE HIS GLN TYR ASP THR GLY PHE ASP LEU ASP ARG VAL ARG THR VAL THR VAL THR LEU LEU GLY ASP GLU LYS ASP LEU GLU ILE LYS ARG SER ASN CYS TYR MET VAL CYS ALA GLY GLU SER MET SER PRO GLY GLN GLY ARG
ASN ASN SER ASN GLY LEU GLU ILE GLY CYS VAL VAL ASP ALA ALA SER GLY LEU LEU THR PHE ILE ALA ASN GLY LYS GLU LEU SER THR SER HIS VAL GLN PHE LEU SER SER THR TYR TYR GLN TYR VAL GLU PRO SER THR LYS LEU PHE PRO ALA VAL PHE ALA GLN ALA THR SER PRO ASN VAL PHE GLN PHE GLU LEU LEU GLY ARG
ILE LYS ASN VAL MET PRO LEU GLN CYS PRO PRO ARG LEU HIS VAL GLN PHE LEU SER SER HIS VAL LEU TRP SER ARG MET PRO ASN GLN PHE LEU LYS VAL ASP VAL SER ARG GLU GLY TRP LEU VAL
GLN CYS LEU ASP PRO LEU GLN PHE MET SER LEU HIS ILE PRO GLU GLU ASN ARG SER VAL ASP ILE LEU GLU GLU LEU GLU LEU THR GLU GLN GLU GLU LEU LEU GLN PHE HIS TYR HIS THR LEU ARG LEU TYR SER ALA VAL CYS ALA LEU GLY ASN HIS ARG VAL ALA HIS ALA LEU CYS SER HIS
VAL ASP GLU PRO GLN LEU LEU ILE GLU ASN LYS TYR MET PRO GLY LEU LEU ARG ALA ALA GLY TYR TYR ASP LEU LEU LEU ILE ASP ILE HIS LEU SER SER HIS TYR ALA THR ALA ARG LEU MET MET ASN ASN GLU PHE ILE VAL PRO MET THR GLU GLU THR LYS SER ILE THR LEU PHE
PRO ASP GLU ASN LYS HIS GLY PRO GLY LEU SER THR ARG PRO ARG MET ARG PHE SER SER PRO SER PHE VAL SER ILE SER ASN ASP CYS TYR GLN TYR SER PRO GLU PHE PRO LEU ASP ILE LEU LEU LYS ALA LYS THR LEU ILE GLN ILE ASP ALA VAL
LYS GLU GLY SER LEU HIS ALA ARG PRO VAL GLY GLY THR THR GLU LYS PHE LEU PHE VAL PRO LEU LEU LEU ILE MET GLY ILE PHE HIS ASN GLU ASP LEU LYS HIS ILE LEU GLN LEU ILE GLU PRO SER VAL PHE LYS GLU ALA ALA VAL PRO GLU GLU
GLU GLY GLY THR PRO GLU ILE GLU ASP ALA LYS LEU GLU GLY LYS ARG PRO LYS GLU GLY LEU GLN LEU GLU LEU LEU LEU GLN GLN TYR LEU CYS ASP CYS GLN VAL HIS ARG
ILE GLU ALA ILE VAL PHE SER ASP PHE VAL ALA LYS LEU ASN MET GLN ALA LEU ASN MET SER ALA LEU THR ARG GLU PHE ARG SER ASP PRO PRO GLN GLU GLN LEU ILE GLN ASN LEU
ASP LYS SER GLU CYS PRO ILE GLU ASP ILE LEU ASP ARG GLU LEU ASP ASP PHE HIS GLU ASP GLY ASP LEU THR ILE ARG GLY LEU LEU SER LEU VAL VAL GLU LYS VAL THR TYR LEU LYS LYS


LYS GLN ALA GLU LYS PRO VAL ALA SER ASP SER ARG LYS CYS SER SER LEU GLN GLN LEU ILE SER GLU THR MET VAL ARG TRP ALA GLN GLU SER VAL ILE GLU ASP PRO GLU LEU VAL ARG ALA MET PHE VAL LEU LEU HIS ARG GLN TYR ASP GLY ILE GLY LEU VAL ARG
LEU PRO LYS THR TYR THR ILE ASN GLY VAL SER VAL GLU ASP THR ILE ASN LEU LEU ALA SER LEU GLY GLN ILE ARG SER LEU LEU SER VAL ARG MET GLY LYS GLU GLU LYS LEU MET ILE ARG GLY LEU GLY ASP ILE MET ASN GLN LYS VAL PHE TYR GLN HIS PRO ASN LEU
MET ARG ALA LEU GLY MET HIS GLU THR VAL MET GLU VAL MET VAL ASN VAL LEU GLY ARG CYS CYS ARG PHE LEU CYS TYR PHE CYS ARG ILE SER ARG GLN ASN GLN LYS ALA MET PHE ASP HIS LEU SER LEU
LEU GLU ASN SER SER VAL GLY LEU ALA SER PRO ALA MET ARG GLY SER THR PRO LEU ASP VAL ALA ALA ALA SER VAL VAL MET ASP ASN ASN GLU LEU LEU ALA LEU ALA LEU GLN SER CYS GLN MET LEU VAL
SER LYS GLY TYR PRO ASP ILE GLY LEU GLU ALA VAL PHE CYS ASN GLY GLU SER VAL GLU GLU ASN ALA ASN VAL VAL ARG LEU LEU ILE ARG ARG PRO GLU CYS PHE GLY PRO ALA LEU ARG GLY GLY ASN
GLY LEU LEU ALA ALA MET GLU GLU ALA ILE LYS ILE ALA GLU ASP PRO SER PRO THR SER GLY SER SER LYS THR LEU ASP ILE GLU GLU GLU GLU ASP ASP THR ILE HIS MET GLY ASN ALA ALA ILE MET THR PHE TYR ALA ALA LEU ILE ASP LEU LEU GLY ARG
CYS ALA PRO GLU MET HIS LEU ILE HIS ALA GLY LYS GLY GLU ALA ILE ARG SER ILE LEU ARG SER LEU ILE PRO LEU GLU GLY ASP LEU VAL GLY VAL ILE SER ILE ALA ALA PHE GLN MET PRO THR ILE ALA LYS ASP GLY LYS VAL VAL GLU PRO ASP MET SER ALA GLY PHE CYS
PRO ASP HIS LYS ALA ALA MET VAL LEU PHE LEU ASP ARG VAL TYR GLY ILE GLU VAL GLN ASP PHE LEU LEU HIS LEU LEU LEU GLU VAL GLY PHE LEU PRO ASP LEU ARG ALA ALA ALA SER LEU LEU ASP THR ALA ALA SER SER ALA THR ASP MET ALA LEU ALA LEU LEU ASN ARG TYR LEU CYS
THR ALA VAL LEU PRO LEU LEU THR ARG CYS ALA PRO LEU PHE LEU GLU THR ALA GLY THR GLU HIS HIS ALA SER LEU LEU HIS THR VAL TYR ARG LEU SER LYS GLY CYS SER LEU THR LYS ALA GLN ARG ASP SER ILE GLU VAL CYS LEU LEU SER ILE CYS GLY GLN LEU LEU ARG
PRO SER MET MET GLN HIS LEU LEU LEU ARG ARG LEU VAL PHE ASP VAL PRO LEU LEU LEU ASN GLU HIS LEU ALA LYS MET PRO LEU LYS LEU LEU THR ASN HIS TYR GLU ARG CYS TRP LYS TYR TYR CYS LEU PRO GLY GLY TRP GLY ASN PHE GLY ALA ALA SER GLU GLU GLU LEU HIS LEU SER
ARG LYS LEU PHE TRP GLY ILE PHE ASP ALA LEU SER GLN LYS LYS TYR GLU GLN GLU LEU PHE LYS LEU ALA LEU PRO CYS LEU SER ALA VAL ALA GLY ALA LEU LEU SER GLU MET MET GLU LYS GLN LYS LEU SER GLU GLY ASN PHE
ASN PRO GLN PRO VAL ASP THR SER ASN ILE THR LEU PRO GLU LYS LEU GLU GLY TYR PHE ILE ASN LYS TYR ALA GLU HIS SER HIS ASP LYS TRP SER MET ASP LYS LEU ALA ASN GLY TRP ILE TYR SER ASP SER SER LYS LEU GLU ILE TYR SER GLU ILE TYR SER GLN THR SER GLN VAL SER ILE ASP ALA ALA THR ALA LYS GLU
LEU LEU SER GLU LYS GLU ILE TYR ARG TRP PRO ILE LYS GLU SER LEU LYS THR MET LEU ALA TRP GLY TRP ARG ILE GLU ARG THR ARG GLU GLY ASP SER MET ALA ALA LEU TYR ASN ARG THR ARG ARG ILE SER SER GLN THR SER GLN VAL SER ILE ASP THR LEU ASP SER GLU
SER PRO ARG ALA ILE ASP MET SER ASN VAL THR LEU SER ARG ASP LEU HIS ALA MET ALA ALA GLU MET MET ALA GLU ASN TYR HIS ASN ILE TRP ALA LYS LYS LYS LEU GLU LEU GLU SER LYS GLY GLY ASN HIS PRO LEU LEU LEU VAL PRO TYR ASP THR LEU LEU THR GLU
LYS ALA LYS ASP ARG GLU LYS ASP ILE PHE LYS ASP LEU ASP LEU ASP THR PRO SER ILE GLU LYS ARG PHE ALA TYR SER PHE LEU GLN GLN LEU ILE ARG TYR VAL ASP GLU ALA HIS GLN TYR ILE LEU
GLU PHE ASP GLY GLY SER ARG GLY PHE LYS ASP LEU ASP THR PRO SER ILE GLU LYS ARG LEU TYR PHE LEU SER ALA ALA SER ARG PRO LEU CYS THR GLY GLY HIS ALA SER ASN LYS SER GLU
GLU MET VAL THR SER LEU PHE CYS LYS LEU GLY VAL ILE ASP CYS LEU HIS ILE LEU ASN GLY GLN ILE ARG THR VAL MET LYS THR GLY LEU ASP SER VAL LYS SER ALA LEU ARG ALA PHE LEU
ASP ASN ALA ALA GLU ASP LEU GLU LYS THR MET GLU ASN LEU LYS GLN GLY GLN PHE THR HIS THR ARG SER GLN PRO LYS GLY VAL THR GLN ILE ILE ASN TYR THR THR VAL ALA LEU LEU PRO MET LEU SER SER LEU PHE GLU HIS ILE GLY GLN HIS GLN GLN PHE GLY PHE LEU
ILE LEU GLU ASP VAL SER CYS TYR ARG ILE LEU ARG SER ALA LEU GLY CYS LEU ALA ALA PHE ALA GLY ALA PHE PRO ILE ALA PHE LEU GLU THR HIS LEU ASP LYS HIS ASN VAL TYR
SER ILE TYR ASN THR ARG GLU ARG ALA LEU SER LEU PRO ASN ILE PRO SER LEU GLU LYS LEU MET THR GLU ILE ILE GLU LEU ALA GLU SER GLY ILE ARG TYR THR GLN MET PRO TYR MET MET GLU VAL VAL PRO MET

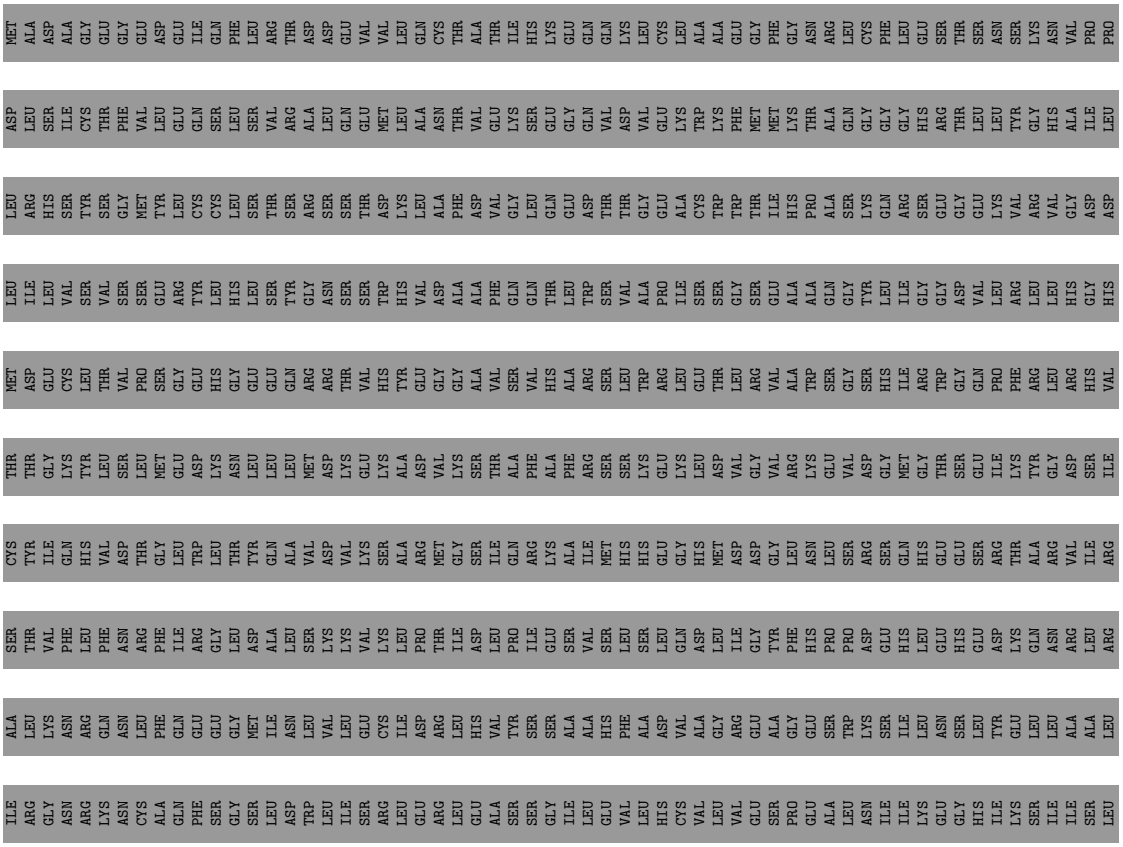

LEU CYS SER TYR MET SER ARG TRP TRP GLU HIS GLY PRO GLU ASN HIS PRO GLU ARG ALA GLU MET CYS CYS THR ALA LEU ASN SER GLU HIS MET ASN THR LEU LEU GLY ASN ILE LEU LYS ILE ILE TYR ASN ASN LEU GLY ILE ASP GLU GLY ALA TRP MET LYS ARG LEU ALA VAL
PHE SER GLN PRO ILE ILE ASN LYS VAL LYS PRO GLN LEU LEU LYS THR HIS PHE LEU PRO LEU MET GLU LYS LEU LYS LYS ALA ALA MET VAL VAL SER GLU GLU ASP HIS LEU LYS ALA GLU ALA ARG GLY ASP MET SER GLU ALA GLU LEU LEU ILE LEU ASP GLU PHE THR THR
LEU ALA ARG ASP LEU TYR ALA PHE TYR PRO LEU LEU ILE ARG PHE VAL ASP TYR ASN ARG ALA LYS TRP LEU LYS GLU PRO ASN PRO GLU ALA GLU GLU LEU PHE ARG MET VAL ALA GLU VAL PHE ILE TYR TRP SER LYS SER HIS ASN PHE LYS ARG GLU GLU GLN ASN PHE VAL VAL
GLN ASN GLU ILE ASN ASN MET SER PHE LEU ILE THR ASP THR LYS SER LYS MET SER LYS ALA ALA ILE SER ASP GLN GLU ARG LYS LYS MET LYS ARG LYS GLY ASP ARG TYR SER MET GLN THR SER LEU ILE VAL ALA ALA LEU LYS ARG LEU LEU PRO ILE GLY LEU ASN ILE CYS
ALA PRO GLY ASP GLN GLU LEU ILE ALA LEU ALA LYS ASN ARG PHE SER LEU LYS ASP THR GLU GLU GLU VAL ARG ASP ILE ILE ARG SER ASN ILE HIS LEU GLN GLY LYS LEU GLU ASP PRO ALA ILE ARG TRP GLN MET ALA LEU TYR LYS ASP LEU PRO ASN ARG THR GLU ASP PRO
SER ASP PRO GLU ARG THR VAL GLU ARG VAL LEU GLY ILE ALA ASN VAL LEU PHE HIS LEU GLU GLN LYS SER LYS TYR THR GLY ARG GLY TYR PHE SER LEU VAL GLU HIS PRO GLN ARG SER LYS LYS ALA VAL TRP HIS LYS LEU LEU SER LYS GLN ARG LYS ARG ALA ALA VAL VAL ALA
CYS PHE ARG MET A3605 P3606 L3607 Y3608 N3609 L3610 P3611 R3612 H3613 R3614 A3615 V3616 N3617 L3618 F3619 L3620 Q3621 G3622 Y3623 E3624 K3625 S3626 W3627 I3628 E3629 T3630 E3631 E3632 H3633 Y3634 F3635 E3636 D3637 K3638 L3639 I3640 E3641 D3642 L3643 A3644 K3645 P3646 G3647 A3648 E3649 L3650 P3651 E3652 E3653 D3654 E3655 A3656 M3657 K3658 R3659 V3660
D3661 P3662 L3663 H3664 Q3665 L3668 R3672 L3675 T3676 E3677 K3678 C3679 K3680 L3681 E3682 E3683 D3684 F3685 L3686 Y3687 M3688 A3689 Y3690 A3691 D3692 H3699 D3700 E3701 E3702 D3703 D3704 D3705 G3706 E3707 E3708 E3709 V3710 K3711 S3712 F3713 E3714 E3715 K3716 E3717 M3718 E3719 K3720 Q3721 Y3725 Q3726 Q3727 D3732 R3733 G3734
A3735 A3736 E3737 Q3741 T3742 I3743 S3746 K3747 G3748 E3749 I3762 N3769 D3778 K3781 E3782 K3783 K3784 D3785 V3786 Q3790 C3799 S3800 V3801 L3802 D3803 L3804 N3805 A3806 F3807 E3808 R3809 Q3810 N3811 K3812 A3813 E3814 G3815 L3816 G3817 M3818 V3819 T3820 E3821 E3822 G3823 S3824 G3825 E3826 K3827 V3828 L3829 Q3830
D3831 D3832 E3833 F3834 T3835 C3836 D3837 L3842 D3852 F3853 Q3854 R3858 T3859 Q3860 T3861 G3862 N3863 N3864 T3865 T3866 V3874 D3875 Y3876 L3877 L3878 R3879 V3880 Q3881 E3882 D3886 Y3891 S3892 G3893 K3894 D3895 I3896 I3897 D3898 E3899 Q3900 G3901 Q3902 R3903 N3904 F3905 L3919 T3920 E3921 G3925 Q3931
L3934 R3938 L3939 W3940 D3941 H3948 V3949 F3950 Q3954 M3955 K3956 L3957 S3958 Q3959 D3960 S3961 S3962 Q3963 I3964 E3965 L3966 L3967 K3968 E3969 L3970 M3971 D3972 L3981 M3984 L3985 E3986 N3991 G3992 K3996 Q3997 M3998 V3999 D4000 M4001 L4002 V4003 E4004 N4008 V4009 E4010 M4011 K4014 F4015 F4016 D4017 M4018
F4019 L4020 K4021 L4022 K4023 D4024 L4025 T4026 S4027 S4028 D4029 T4030 F4031 K4032 E4033 Y4034 D4035 P4036 D4037 G4038 K4039 G4040 V4041 I4042 S4043 K4044 R4045 D4046 F4047 H4048 K4049 A4050 M4051 E4052 S4053 H4054 K4055 H4056 Y4057 T4058 Q4059 S4060 E4061 T4062 E4063 F4064 L4065 L4066 S4067 C4068 A4069 E4070 T4071 D4072 E4073 N4074 E4075 T4076 L4077 D4078
Y4079 E4080 E4081 F4082 V4083 K4084 R4085 F4086 H4087 E4088 P4089 A4090 K4091 D4092 I4093 L4100 L4104 S4105 E4106 H4107 M4108 P4109 N4110 D4111 T4112 R4113 L4114 Q4115 T4116 F4117 L4118 E4119 L4120 A4121 E4122 N4126 Q4129 L4132 G4133 R4134 G4139 K4142 R4143 I4144 E4145 R4146 E4153 E4160 E4166 S4167
K4168 R4169 I4172 F4173 D4174 V4175 V4176 N4177 E4178 G4179 G4180 E4181 K4182 E4183 K4184 M4185 E4186 V4189 D4194 T4195 I4205 SER GLU SER ASP LEU ASN GLU ARG LEU ALA ASN LYS GLU GLU SER GLU LYS GLU ARG PRO GLU GLU GLN ALA PRO ARG MET GLY PHE PHE SER LEU LEU THR ILE
GLN SER ALA LEU PHE ALA LEU ARG TYR ASN VAL LEU THR LEU VAL ARG MET LEU SER LEU LYS SER LEU LYS LYS GLN MET LYS ARG MET LYS LYS MET THR VAL LYS ASP MET VAL LEU ALA PHE SER SER TYR TRP SER VAL PHE VAL THR LEU LEU HIS PHE VAL ALA ALA SER VAL
CYS ARG GLY PHE PHE ARG ILE VAL SER SER LEU LEU LEU GLY GLY SER LEU VAL GLU GLY ALA LYS LYS ILE LYS VAL ALA GLU LEU LEU ALA ASN MET PRO ASP PRO THR GLN ASP GLU VAL ARG GLY ASP GLU GLU GLU GLY GLU ARG LYS PRO LEU GLU SER ALA LEU PRO SER GLU

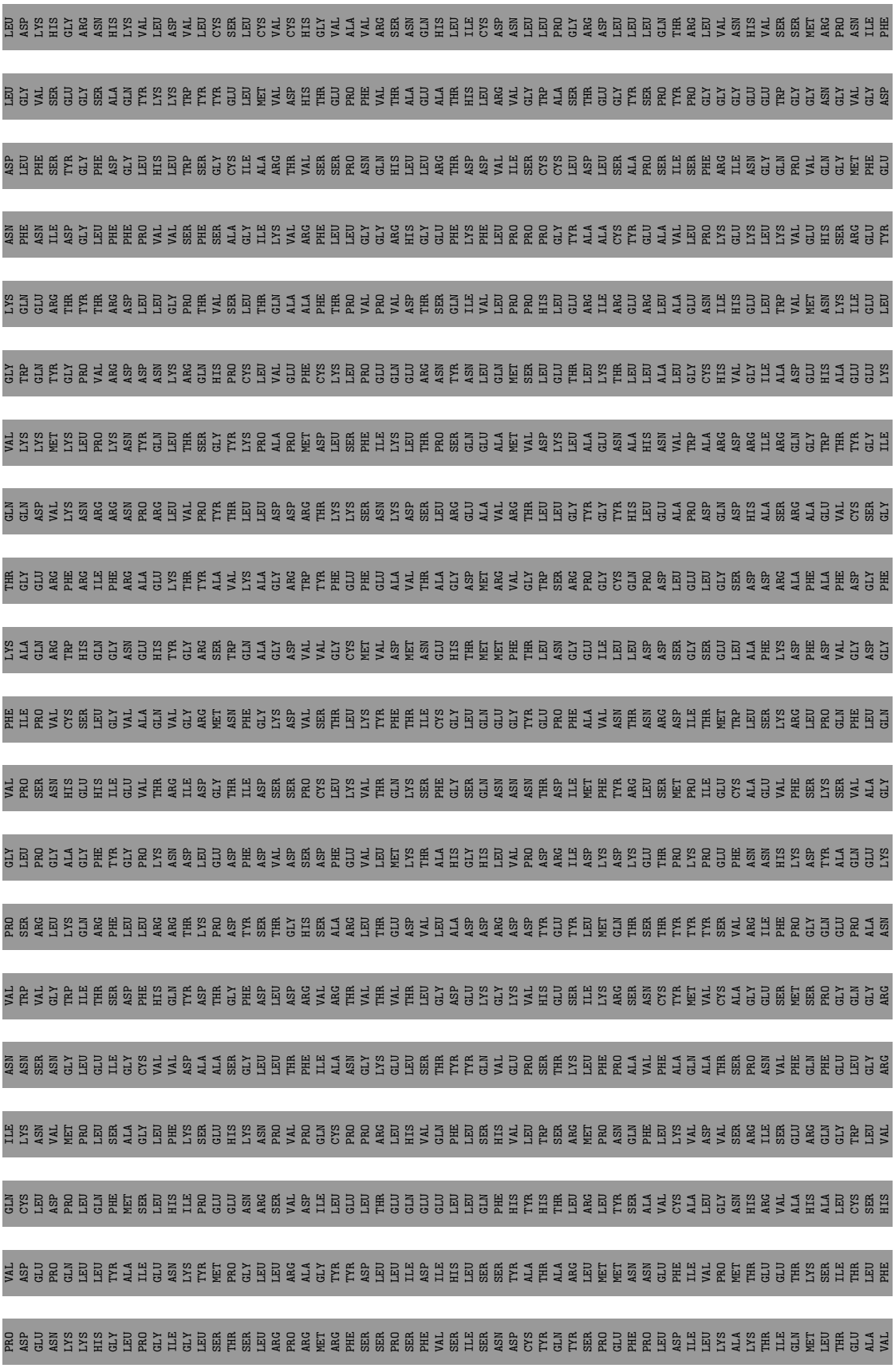


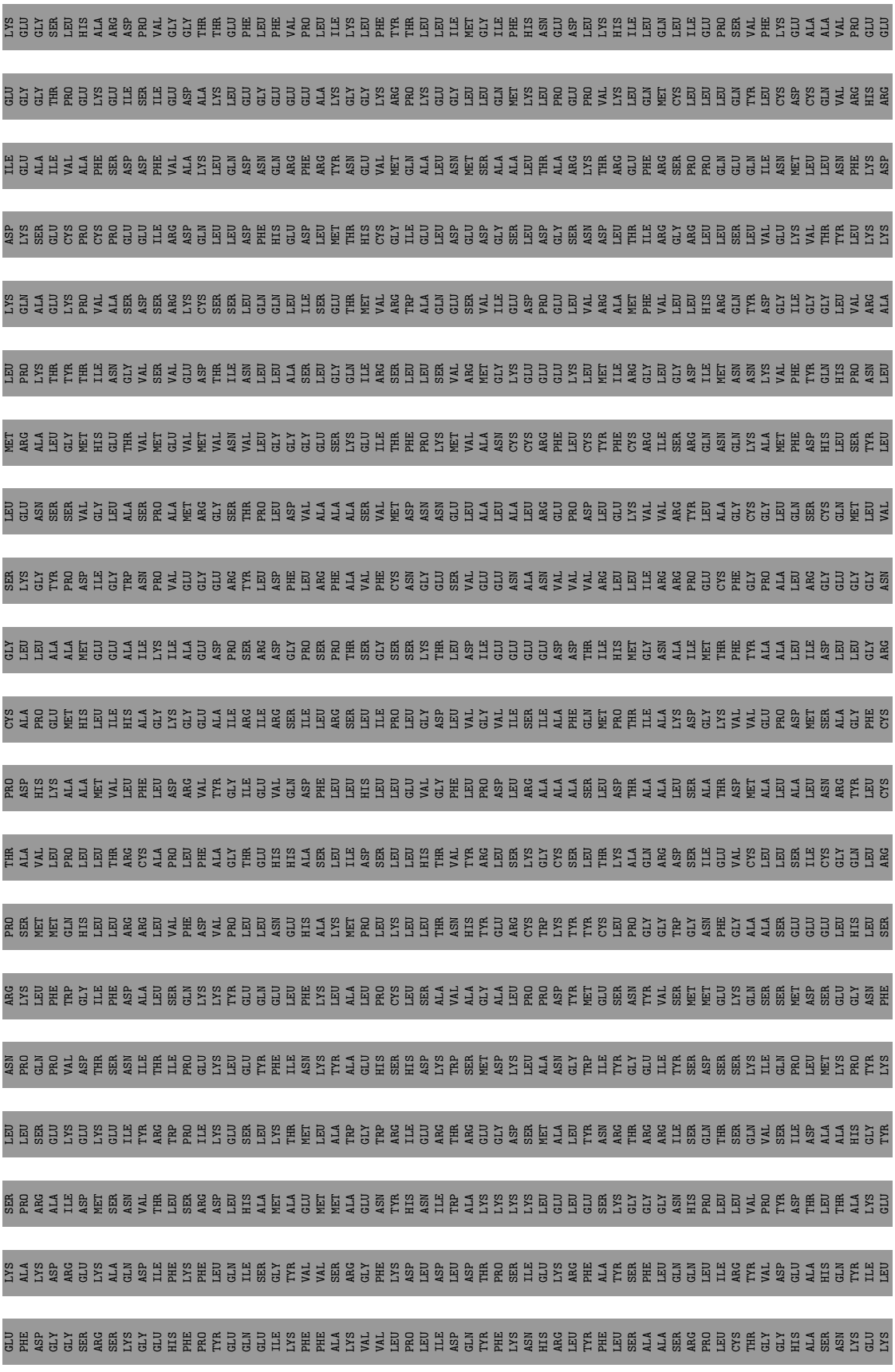
• Molecule 1: Ryanodine receptor 2

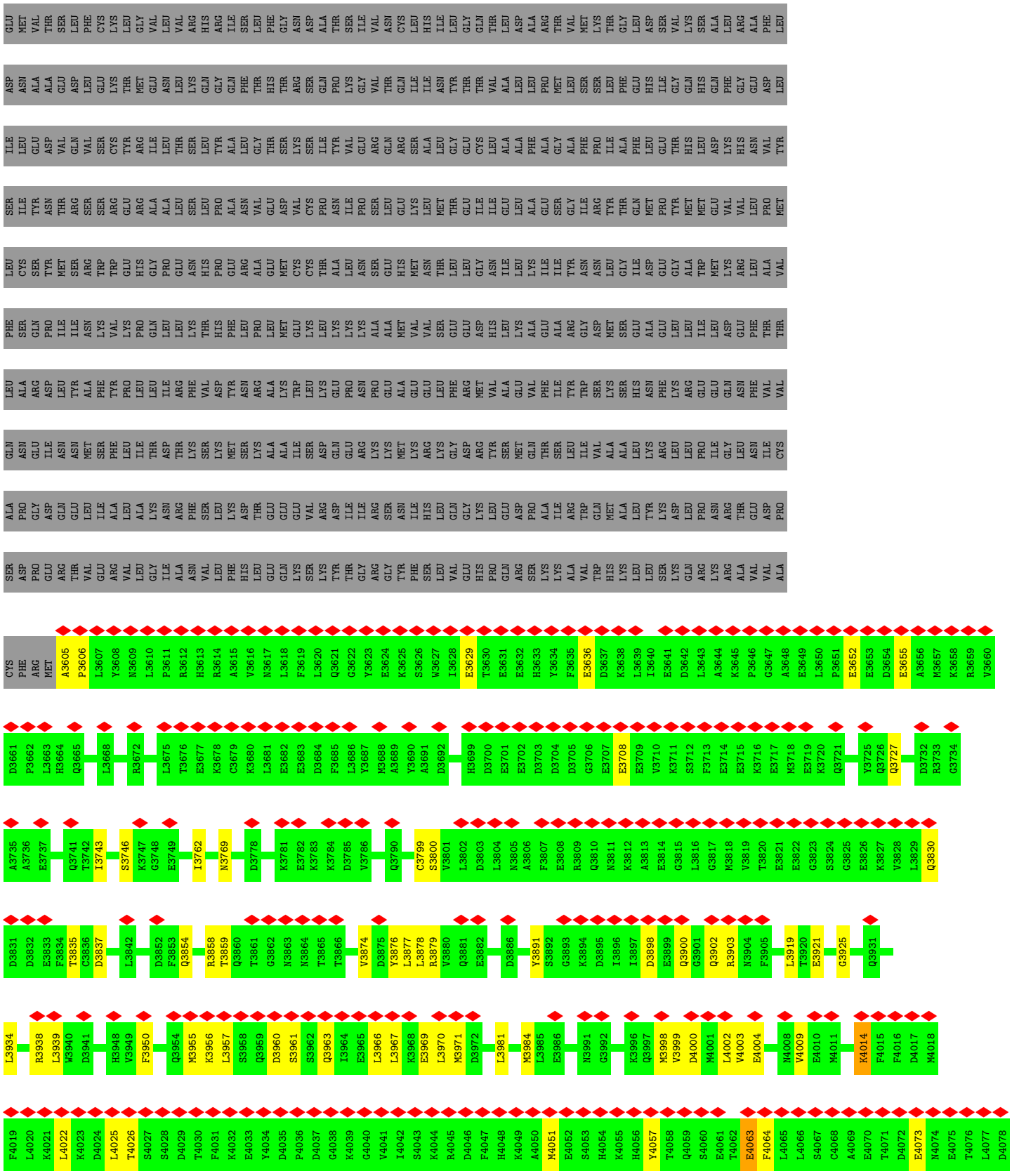
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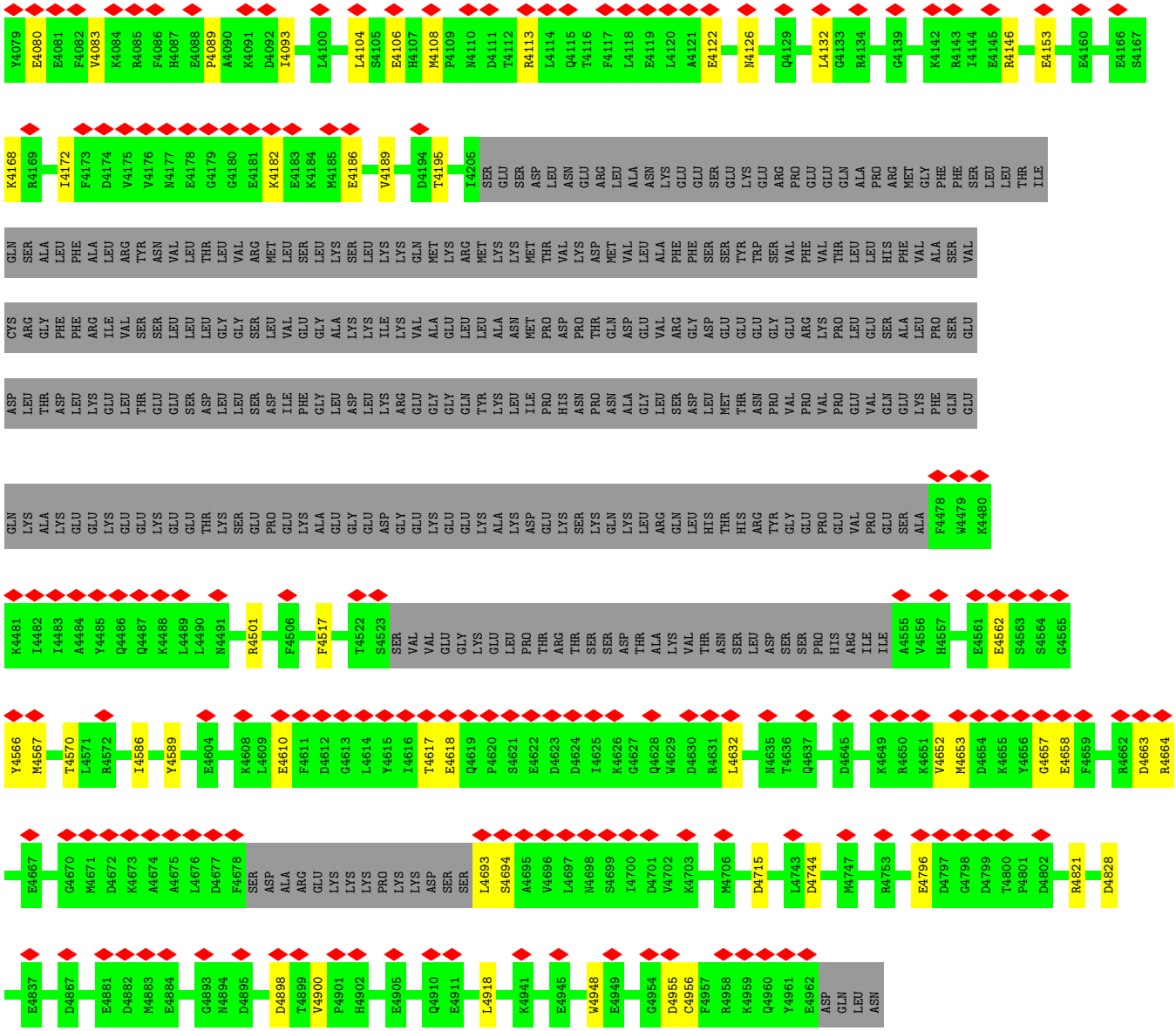





LEU ASP LYS HIS GLY ARG ASN HIS LYS VAL LEU ASP VAL LEU CYS SER LEU CYS VAL CYS HIS GLY VAL ALA VAL ARG SER ASN GLN HIS LEU ILE CYS ASP ASN LEU LEU PRO GLY ARG ASP LEU LEU LEU GLN THR ARG LEU VAL ASN HIS VAL SER SER MET ARG PRO ASN ILE PHE
LEU GLY VAL SER GLU GLY SER ALA GLN TYR LYS LYS TRP TYR TYR GLU LEU MET VAL ASP HIS THR GLU PRO PHE VAL THR ALA GLU ALA THR HIS LEU ARG VAL GLY TRP ALA SER THR GLU GLY TYR SER PRO TYR PRO GLY GLY GLY GLU GLU TRP GLY GLY GLY ASP
ASP LEU PHE SER TYR GLY PHE ASP GLY LEU HIS LEU TRP SER GLY CYS ILE ALA ARG THR VAL SER SER PRO ASN GLN HIS LEU LEU ARG THR ASP ASP VAL ILE SER CYS LEU ASP LEU SER ALA PRO SER PHE ASP ASN GLY GLN PRO VAL GLN GLY MET PHE GLU
ASN PHE ASN ILE ASP GLY LEU PHE PHE PRO VAL VAL SER PHE SER ALA ARG THR VAL SER SER PRO LEU LEU GLY GLY ARG HIS GLY GLU PHE LYS PHE LEU PRO PRO PRO GLY TYR ALA ALA CYS TYR GLU ALA VAL LEU PRO LYS GLU LYS LEU LYS VAL GLU HIS SER ARG GLU TYR
LYS GLN GLU ARG THR TYR THR ARG ASP LEU LEU GLY PRO THR VAL SER LEU THR GLN HIS PRO VAL PRO VAL ASP THR SER GLN ILE VAL LEU PRO PRO HIS LEU GLU GLU ARG ILE ARG GLU GLU ASN LEU LEU TRP VAL MET ASN LYS ILE GLU GLU
GLY TRP GLN TYR GLY PRO VAL ARG ASP ASP ASP LEU LEU ARG GLN ILE ARG ASN TYR ASN LEU GLN MET SER LEU GLU THR LEU LYS THR LEU LEU ALA LEU GLU GLY CYS HIS VAL GLY ILE ALA ASP GLU LYS CYS GLU GLU
VAL LYS LYS MET LYS LEU PRO LYS ASN TYR GLN LEU THR SER GLY TYR LYS PRO ALA PRO MET ASP LEU SER PHE ILE LYS LEU THR PRO SER GLN GLU ALA MET VAL ASP LYS LEU ALA GLU ASN ALA HIS ASN VAL TRP ALA ARG ASP ARG ILE ARG GLN GLY TRP THR TYR GLY ILE
GLN GLN ASP VAL LYS ASN ARG ARG ASN PRO ARG LEU VAL PRO TYR THR LEU LEU ASP ASP ARG THR LYS LYS SER ASN LYS ASP SER LEU ARG GLU ALA VAL THR PRO SER GLN GLU GLU ALA ALA VAL THR ASP SER GLY TYR GLY TYR HIS LEU GLU ALA PRO ASP GLN ASP HIS ALA SER ARG GLN GLY CYS SER GLY
THR GLY GLU ARG PHE ARG ILE PHE ARG ALA GLU LYS THR TYR ALA VAL LYS ALA GLY ARG TRP TYR PHE GLU PHE GLU ALA VAL THR ALA ALA GLY ASP MET ARG VAL ARG THR LEU LEU GLY TYR GLY CYS GLN PRO ASP LEU GLU LEU GLY SER ASP ARG PRO GLY GLY PHE
LYS ALA GLN ARG TRP HIS GLN GLY ASN GLU HIS TYR GLY ARG SER TRP GLN ALA GLY ASP VAL VAL GLY CYS MET VAL ASP MET ASN GLU HIS THR MET MET PHE THR LEU ASN GLY GLU ILE LEU LEU ASP ASP SER GLY SER GLU LEU LEU ASP ASP GLY GLY ASP GLY
PHE ILE PRO VAL CYS SER LEU GLY VAL ALA GLN VAL GLY ARG MET ASN PHE GLY LYS ASP VAL SER THR LEU LYS TYR PHE THR ILE CYS GLY LEU GLN GLU GLY TYR PRO PHE ALA VAL ASN THR ASN ARG ASP ILE THR MET PRO ILE GLU GLN PHE LEU LEU GLN
VAL PRO SER ASN HIS GLU ILE GLU VAL THR THR ARG ILE ASP GLY THR ILE ASP SER SER PRO CYS LEU LYS VAL THR GLN LYS SER PHE GLY SER GLN ASN ASN ASN THR ASP ILE MET PHE TYR ARG LEU SER MET PRO ILE GLU CYS ALA GLU VAL PHE SER LYS SER VAL ALA GLY
GLY LEU PRO GLY ALA GLY PHE TYR GLY PRO LYS ASN ASP LEU GLU ASP PHE GLU VAL LEU MET LYS THR ALA HIS GLY HIS LEU VAL PRO ASP ARG ILE ASP LYS GLU THR PRO LYS PRO GLU GLY PHE ASN ASN HIS LYS ASP TYR ARG GLN GLU LYS
PRO SER ARG LEU LYS GLN ARG PHE LEU LEU ARG ARG THR LYS PRO ASP ASP THR LYS ASP ASP ARG ASP ASP TYR GLU TYR LEU MET GLN THR SER THR TYR TYR TYR SER VAL ARG ILE PHE PRO GLY GLN GLU GLU PRO ALA ASN
VAL TRP VAL GLY TRP ILE THR SER ASP PHE HIS GLN TYR ASP THR GLY PHE ASP LEU ASP ARG VAL THR VAL THR LEU GLY ASP GLU LYS GLY LYS VAL HIS GLU TYR SER ASN CYS TYR MET VAL CYS ALA GLY GLU SER MET SER PRO GLY GLN GLU HIS LYS ASP TYR GLN ALA GLY
ASN ASN SER ASN GLY LEU GLU VAL VAL ASP ALA SER GLY LEU LEU THR PHE ILE ALA ALA ASN GLY LYS GLU LEU SER THR TYR GLN VAL GLU PRO SER THR LYS LEU PHE PRO ALA VAL PHE ALA GLN THR ALA VAL PHE GLN PHE GLU LEU GLY ARG
ILE LYS ASN VAL MET PRO LEU HIS LYS ASN PRO VAL PRO ARG LEU HIS VAL GLN PHE LEU SER HIS VAL LEU TRP SER ARG MET PRO ASN GLN PHE LEU LYS VAL ASP VAL SER ARG ILE SER VAL GLU PRO GLN PHE GLU LEU VAL
GLN CYS LEU ASP PRO LEU GLN PHE MET SER LEU HIS ILE PRO GLU GLU ASN ARG SER VAL ASP ILE LEU ARG LEU GLU THR LEU GLN GLN GLU GLU LEU LEU GLN PHE HIS TYR HIS THR LEU ARG LEU TYR SER ALA VAL CYS ALA LEU GLY ASN HIS ARG VAL ALA HIS ALA LEU CYS SER HIS
VAL ASP GLU PRO GLN LEU TYR ALA ILE GLU GLU ASN LYS TYR MET PRO GLY LEU LEU ARG ALA GLY TYR TYR ASP LEU LEU ILE ASP ILE HIS LEU SER SER TYR ALA THR ALA ARG LEU MET MET ASN ASN GLU PHE ILE VAL PRO MET THR GLU GLU THR LEU LEU PHE
PRO ASP GLU ASN LYS LYS HIS GLY LEU PRO ARG PHE SER SER PRO SER PHE VAL SER ILE SER ASN ASP CYS TYR GLN SER ARG PHE PRO LEU ASP ILE LEU LYS ALA LYS THR ILE GLN THR MET LEU SER GLY


LYS GLU GLY SER LEU HIS ALA ARG ASP PRO VAL GLY GLY THR THR GLU PHE LEU PHE VAL PRO LEU ILE LYS LEU PHE HIS ASN GLU ASP LEU LYS HIS ILE LEU GLN LEU ILE GLU PRO SER VAL PHE LYS GLU ALA ALA VAL PRO GLU GLU
GLU GLY GLY THR PRO GLU LYS GLU ILE SER ILE GLU ASP ALA LYS LEU GLU GLY GLU ALA LYS GLY GLY LYS ARG PRO LYS GLU GLY ILE LYS GLU LEU LEU LEU ILE MET GLY ILE PHE HIS ASN GLU PRO GLU VAL CYS ASP CYS GLN VAL ARG HIS ARG
ILE GLU GLY ILE VAL ALA PHE SER ASP ASP PHE VAL ALA ASP ASN GLN ARG PHE ARG TYR ASN GLU VAL MET GLN ALA LEU ASN MET SER ALA LEU MET GLN MET LYS LEU PRO GLU PRO VAL LYS LEU GLN MET CYS LEU LEU LEU GLN GLN TYR LEU CYS ASP CYS GLN VAL ARG ASP
ASP LYS SER GLU CYS PRO CYS PRO GLU GLU ILE ARG ASP GLN LEU LEU ASP PHE HIS GLU ASP LEU MET THR HIS CYS GLY ILE GLU LEU ASP GLU SER LEU ASP GLU GLN LEU LEU LEU GLU SER LEU VAL LYS VAL THR TYR LEU LYS LYS
LYS GLN ALA GLU LYS PRO VAL ALA SER ARG LYS CYS SER SER LEU GLU THR MET HIS VAL ARG TRP ALA GLN GLU SER VAL ILE GLU ASP PRO GLU LEU VAL ARG ALA MET ILE ARG GLY LEU HIS ARG GLN TYR ASP GLY ILE GLY LYS LEU VAL ARG ALA
LEU PRO LYS THR TYR THR ILE ASN GLY VAL SER GLU ASP THR ILE ASN LEU LEU ALA ALA SER LEU LEU SER VAL ARG TRP GLY GLN ILE ARG SER LEU LEU SER VAL ARG MET PHE GLY LYS GLU GLU LYS LEU VAL ARG GLU PRO ASP LEU GLU ILE MET ILE ARG GLY LEU GLY ASP ILE MET ASN ASN LYS VAL PHE TYR GLN HIS PRO ASN LEU
MET ARG ALA LEU GLY MET HIS GLU THR VAL MET GLU VAL MET VAL ASN VAL LEU GLY GLY GLU SER LYS GLU ILE THR PHE PRO LYS MET VAL ASN CYS CYS ARG PHE LEU CYS TYR PHE CYS ARG ILE SER ARG GLN ASN GLN LYS ALA MET PHE ASP HIS LEU SER TYR LEU
LEU GLU ASN SER SER VAL GLY LEU ALA SER PRO ALA MET ARG GLY SER THR PRO LEU ASP VAL ALA ALA ALA SER VAL LEU ASP ASN ASN GLU LEU ALA LEU ARG GLU PRO ASP LEU GLU GLU ILE ARG GLY LEU GLN SER VAL LYS VAL LEU GLU ARG TYR LEU ALA GLY CYS GLY LEU GLN SER CYS GLN MET LEU VAL
SER LYS GLY TYR PRO ASP ILE GLY TRP ASN PRO VAL GLU GLY GLU ARG TYR LEU ASP PHE LEU ARG PHE ALA VAL PHE CYS ASN GLY GLU SER VAL GLU GLU ASN ALA ASN VAL VAL VAL ARG LEU LEU ILE ARG ARG PRO GLU CYS PHE GLY PRO ALA LEU GLN SER CYS GLN LEU GLY GLU GLY GLY ASN
GLY LEU LEU ALA ILE LYS ILE ALA GLU ASP PRO SER ARG ASP GLY PRO SER PRO THR SER GLY SER SER LYS THR LEU ASP ILE GLU GLU GLU GLU GLU ASP ASP THR ILE HIS MET GLY ASN ALA ILE MET THR PHE TYR ALA ALA LEU ILE ASP LEU LEU GLY ARG
CYS ALA PRO GLU MET HIS LEU ILE HIS ALA GLY LYS GLY GLU ALA ILE ARG ILE ARG SER LEU ILE PRO LEU GLY ASP LEU VAL GLY VAL ILE SER ILE ALA PHE GLN MET PRO THR ILE ALA LYS ASP GLY LYS VAL VAL MET GLU PRO ASP MET SER ALA GLY PHE CYS
PRO ASP HIS LYS ALA ALA MET VAL LEU PHE LEU GLU VAL GLN ASP PHE LEU LEU HIS LEU LEU GLU VAL GLY PHE LEU PRO LEU ASP LEU ARG ALA ALA ALA SER LEU ASP THR ALA ALA LEU SER ALA THR ASP MET ALA LEU ASN ARG TYR TYR LEU PRO
THR ALA VAL LEU PRO LEU LEU THR ARG CYS ALA PRO LEU PHE ASP ALA GLY THR GLU HIS HIS ALA SER LEU ILE ASP SER LEU LEU HIS THR VAL TYR ARG LEU SER LEU THR LYS ALA GLN ARG ASP SER ILE GLU VAL CYS LEU GLU LEU LEU SER GLU ILE GLY LEU
PRO SER MET MET GLN HIS LEU LEU ARG ARG LEU VAL PHE ASP VAL PRO LEU LEU ASN GLU HIS ALA LYS MET PRO LEU LYS LEU HIS THR ASN HIS TYR GLU ARG CYS TRP LYS TYR TYR CYS LEU PRO GLY GLY TRP GLY ASN PHE GLY ALA ALA SER GLU GLU GLU LEU HIS LEU SER
ARG LYS LEU PHE TRP ASP ALA LEU SER ALA VAL ALA GLY ALA LEU PRO PRO ASP TYR MET GLU SER ASN TYR VAL SER MET MET GLU LYS GLN SER SER MET ASP SER GLU LEU GLY ASN PHE
ASN PRO GLN PRO VAL ASP THR SER ASN ILE THR ILE PRO GLU LYS LEU GLU TYR PHE ILE ASN LYS TYR ALA GLU HIS SER HIS ASP LYS TRP SER MET ASP LYS LEU PRO ALA ASN GLY TRP ILE TYR GLY GLU ILE TYR SER ASP SER GLN THR SER SER LYS ILE GLN PRO LEU MET LYS ALA HIS GLY TYR
LEU LEU SER GLU LYS GLU LYS GLU ARG THR ARG GLU GLY ASP SER MET ALA LEU TYR ASN ARG THR ARG ARG ILE SER GLN THR SER GLN VAL SER ILE ASP ALA ALA HIS GLY TYR
SER PRO ARG ALA ILE ASP MET SER ASN VAL THR HIS ASN ILE TRP ALA LYS LYS LYS LEU GLU LEU GLU SER LYS GLY GLY GLY ASN HIS PRO LEU LEU VAL PRO TYR ASP THR LEU ALA LYS GLU
LYS ALA LYS ASP ILE PHE LYS ASP LEU ASP LEU ASP THR PRO SER ILE GLU LYS ARG PHE ALA TYR SER PHE LEU GLN GLN LEU ILE ARG TYR VAL ASP GLU ALA HIS GLN TYR ILE LEU
GLU PHE ASP GLY GLY SER ARG LYS VAL LYS ASN HIS ARG LEU TYR PHE LEU SER ALA ALA SER ARG PRO LEU CYS THR GLY GLY HIS ALA SER ASN LYS GLU LYS


GLU MET VAL THR SER LEU PHE CYS LYS LEU GLY VAL LEU VAL ARG HIS ARG ILE SER LEU PHE GLY ASN ASP ALA ARG THR SER ILE VAL ASN CYS LEU HIS ILE LEU GLY GLN THR LEU ASP ALA ARG THR VAL MET LYS THR GLY LEU ASP SER VAL LYS SER LEU PHE GLU HIS ILE GLY GLN HIS LEU ASP LYS HIS ASN VAL TYR
ASP ASN ALA ALA GLU ASP LEU GLU LYS THR MET GLU ASN LEU LYS GLN GLY GLN PHE THR HIS THR ARG SER GLN PRO LYS GLY VAL THR GLN ILE ILE ASN TYR THR THR VAL ALA LEU LEU PRO MET LEU SER SER LEU PHE GLU HIS ILE GLY GLN HIS GLN PHE GLY GLU ASP LEU
ILE LEU GLU ASP VAL GLN VAL SER CYS TYR ARG ILE LEU THR SER LEU TYR ALA LEU GLY THR GLY VAL GLU ARG GLN ARG SER ALA LEU GLY GLU CYS LEU ALA ALA PHE PRO ILE ALA PHE LEU GLU THR HIS LEU ASP LYS HIS ASN VAL TYR
SER ILE TYR ASN THR ARG SER SER ARG GLU ARG ALA ALA LEU SER LEU PRO ALA ASN VAL GLU ASP VAL CYS PRO ASN ILE PRO SER LEU GLU LYS LEU MET THR GLU ILE ILE GLU LEU ALA GLU SER GLY ILE ARG TYR THR GLN MET PRO TYR MET MET GLU VAL VAL LEU PRO MET
LEU CYS SER TYR MET SER ARG TRP TRP GLU HIS GLY PRO GLU ASN HIS PRO GLU ARG ALA ALA GLU MET CYS CYS THR ALA LEU ASN SER GLU HIS MET ASN THR LEU LEU GLY ASN ILE LEU LYS ILE ILE TYR ASN ASN LEU GLY ILE ASP GLU GLY GLY ALA TRP MET LYS ARG LEU ALA VAL
PHE SER GLN PRO ILE ILE ASN LYS VAL LYS PRO GLN LEU LEU LYS THR HIS PHE LEU PRO ALA GLU LYS LEU LYS LYS LYS ALA MET GLU VAL ALA LEU LYS ALA GLU ALA ALA MET VAL SER GLU GLU ASP HIS LEU LYS ALA GLU VAL ALA PHE ILE TYR ALA ARG GLY ASP MET SER GLU ALA GLU LEU LEU ILE LEU ASP GLU PHE THR THR
LEU ALA ARG ASP LEU TYR PRO LEU LEU LEU ILE ARG PHE VAL ASP TYR ASN ARG ALA ALA LYS TRP LEU LYS GLU GLU PRO GLN ASN PRO GLU ALA ALA MET VAL VAL SER GLU GLU GLU ASP HIS LEU LYS ALA GLU VAL ALA PHE ILE TYR TRP SER LYS SER HIS LEU ASN PHE LYS ARG GLU GLU GLN ASN PHE VAL VAL
GLN ASN GLU ILE ASN ASN MET SER PHE LEU ILE THR ASP THR LYS SER LYS MET SER LYS ALA ALA ILE SER ASP GLN GLU ARG LYS LYS MET LYS ARG LYS GLY ASP ARG TYR SER MET GLN THR SER LEU ILE VAL ALA GLU VAL ALA ALA LEU LYS ARG LEU LEU PRO LEU ILE GLY LEU ASN ILE CYS
ALA PRO GLY ASP GLN GLU LEU ILE ALA LEU ALA LYS ASN ARG PHE SER LEU LYS ASP THR GLU GLU GLU VAL ARG ASP ILE ILE ILE ARG ARG SER ASN ILE HIS LEU GLN GLY LYS LEU GLU ASP PRO ALA ILE ARG TRP GLN MET ALA ALA LEU TYR LYS ASP LEU PRO LEU ILE ASN ARG THR GLU ASP PRO
SER ASP PRO GLU ARG THR VAL GLU ARG VAL LEU LEU GLY ILE ALA ASN VAL LEU PHE HIS LEU GLU GLN LYS SER LYS TYR THR GLY ARG GLY TYR PHE SER LEU VAL GLU HIS PRO GLN ARG SER LYS LYS ALA VAL TRP HIS LYS LEU LEU SER LYS GLN ARG LYS ARG ALA VAL VAL ALA
CYS PHE ARG MET A3605 P3606 L3607 Y3608 N3609 L3610 P3611 R3612 H3613 R3614 A3615 V3616 N3617 L3618 F3619 L3620 Q3621 G3622 Y3623 E3624 K3625 S3626 W3627 I3628 E3629 T3630 E3631 E3632 H3633 Y3634 F3635 E3636 D3637 K3638 L3639 I3640 E3641 D3642 L3643 A3644 K3645 P3646 G3647 A3648 E3649 L3650 P3651 E3652 E3653 D3654 E3655 A3656 M3657 K3658 R3659 V3660
D3661 P3662 L3663 H3664 Q3665 L3668 R3672 L3675 T3676 E3677 K3678 C3679 K3680 L3681 E3682 E3683 D3684 F3685 L3686 Y3687 M3688 A3689 Y3690 A3691 D3692 H3699 D3700 E3701 E3702 D3703 D3704 D3705 G3706 E3707 E3708 E3709 V3710 K3711 S3712 F3713 E3714 E3715 K3716 E3717 M3718 E3719 K3720 Q3721 Y3725 Q3726 Q3727 D3732 R3733 G3734
A3735 A3736 E3737 Q3741 T3742 I3743 S3746 K3747 G3748 E3749 I3762 N3769 D3778 K3781 E3782 K3783 K3784 D3785 V3786 Q3790 C3799 S3800 V3801 L3802 D3803 L3804 N3805 A3806 F3807 E3808 R3809 Q3810 N3811 K3812 A3813 E3814 G3815 L3816 G3817 M3818 V3819 T3820 E3821 E3822 G3823 S3824 G3825 E3826 K3827 V3828 L3829 Q3830
D3831 D3832 E3833 F3834 T3835 C3836 D3837 L3842 D3852 F3853 Q3854 R3858 T3859 Q3860 T3861 G3862 N3863 N3864 T3865 T3866 V3874 D3875 Y3876 L3877 L3878 R3879 V3880 Q3881 E3882 D3886 Y3891 S3892 G3893 K3894 D3895 I3896 I3897 D3898 E3899 Q3900 G3901 Q3902 R3903 N3904 F3905 L3919 T3920 E3921 G3925 Q3931
L3934 R3938 L3939 W3940 D3941 H3948 V3949 F3950 Q3954 M3955 K3956 L3957 S3958 Q3959 D3960 S3961 S3962 Q3963 I3964 E3965 L3966 L3967 K3968 E3969 L3970 M3971 D3972 L3981 M3984 L3985 E3986 N3991 G3992 K3996 Q3997 M3998 V3999 D4000 M4001 L4002 V4003 E4004 N4008 V4009 E4010 M4011 K4014 F4015 F4016 D4017 M4018
F4019 L4020 K4021 L4022 K4023 D4024 L4025 T4026 S4027 S4028 D4029 T4030 F4031 K4032 E4033 Y4034 D4035 P4036 D4037 G4038 K4039 G4040 V4041 I4042 S4043 K4044 R4045 D4046 F4047 H4048 K4049 A4050 M4051 E4052 S4053 H4054 K4055 H4056 Y4057 T4058 Q4059 S4060 E4061 T4062 E4063 F4064 L4065 L4066 S4067 C4068 A4069 E4070 T4071 D4072 E4073 N4074 E4075 T4076 L4077 D4078

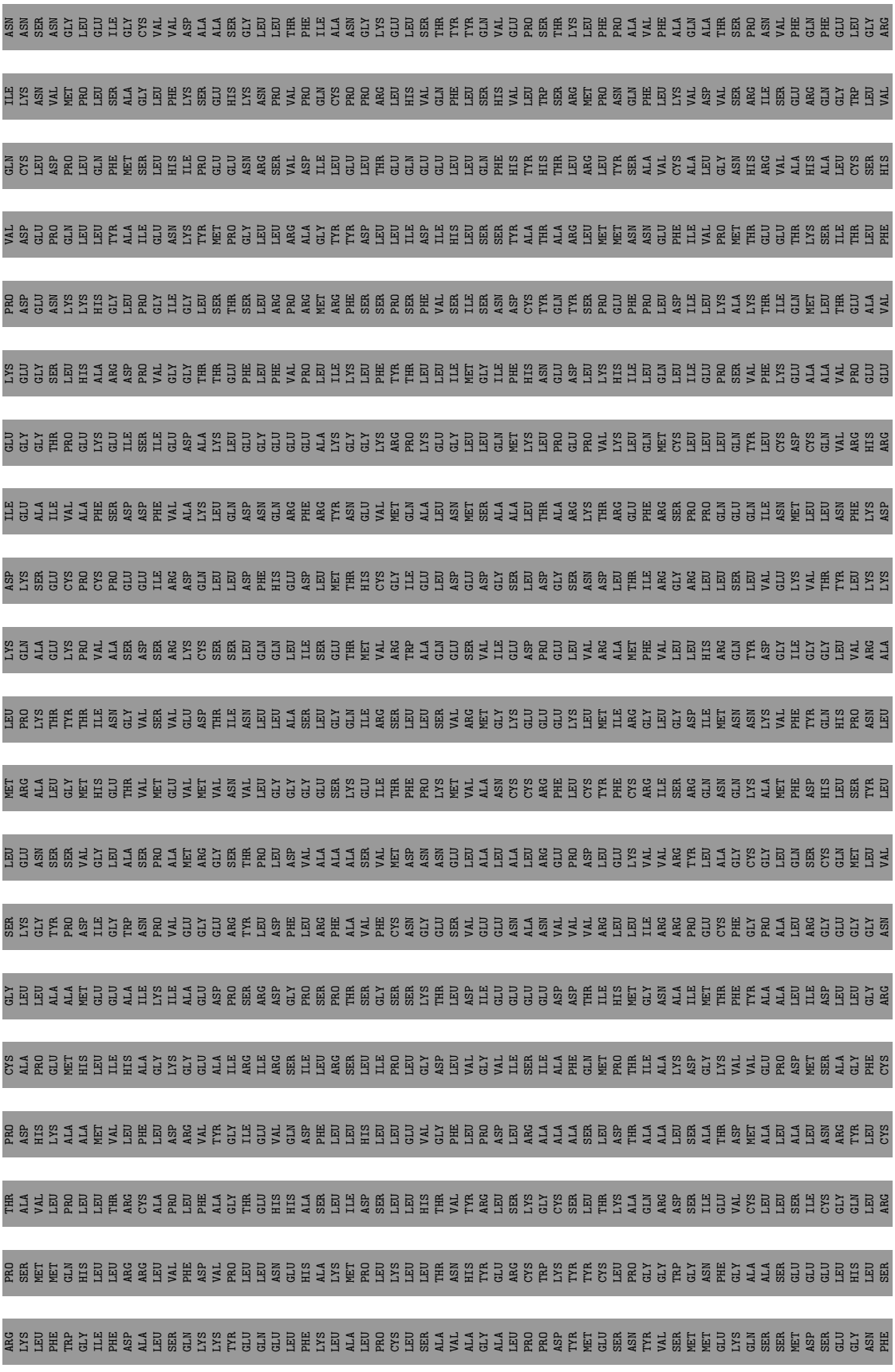


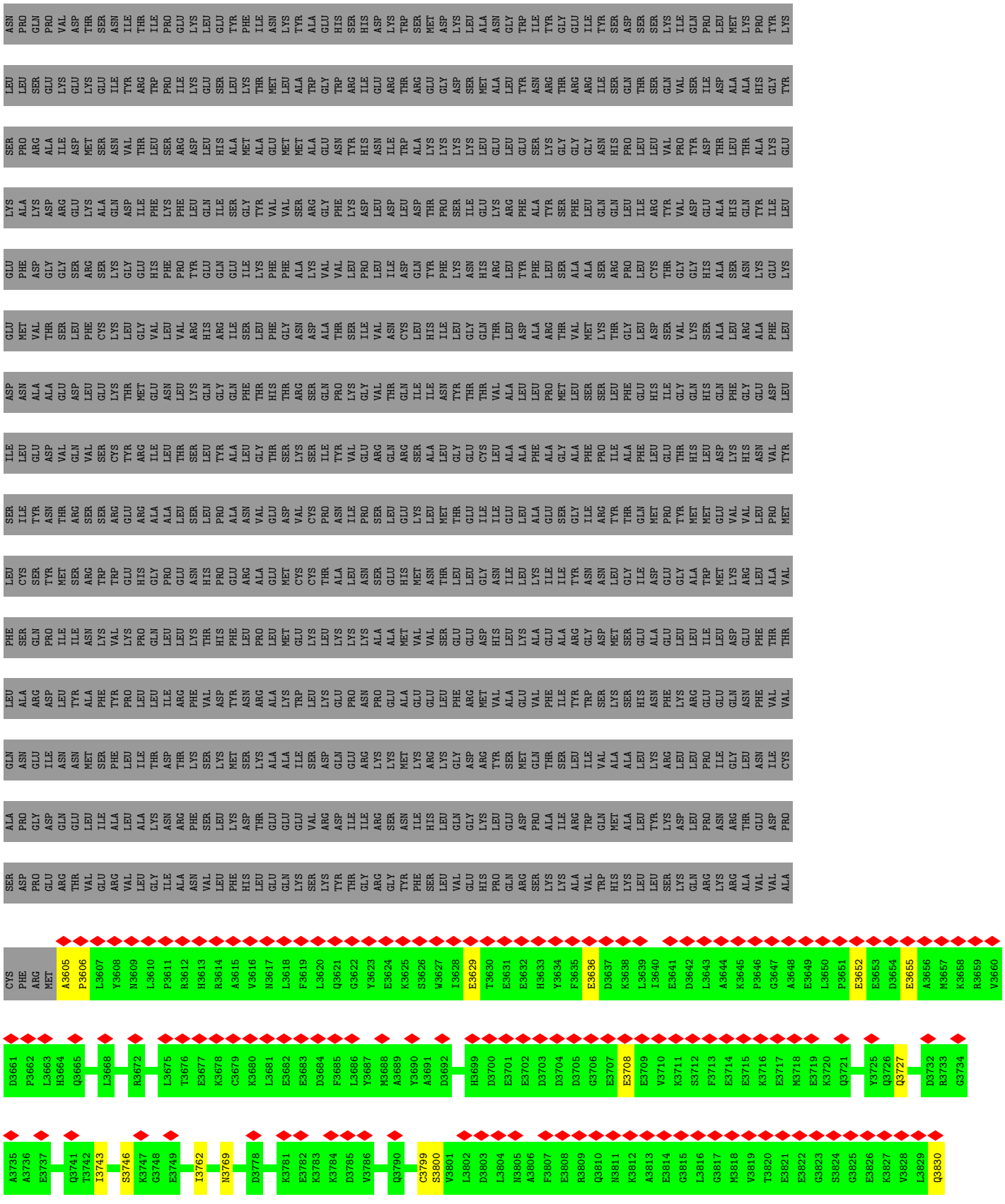
• Molecule 1: Ryanodine receptor 2

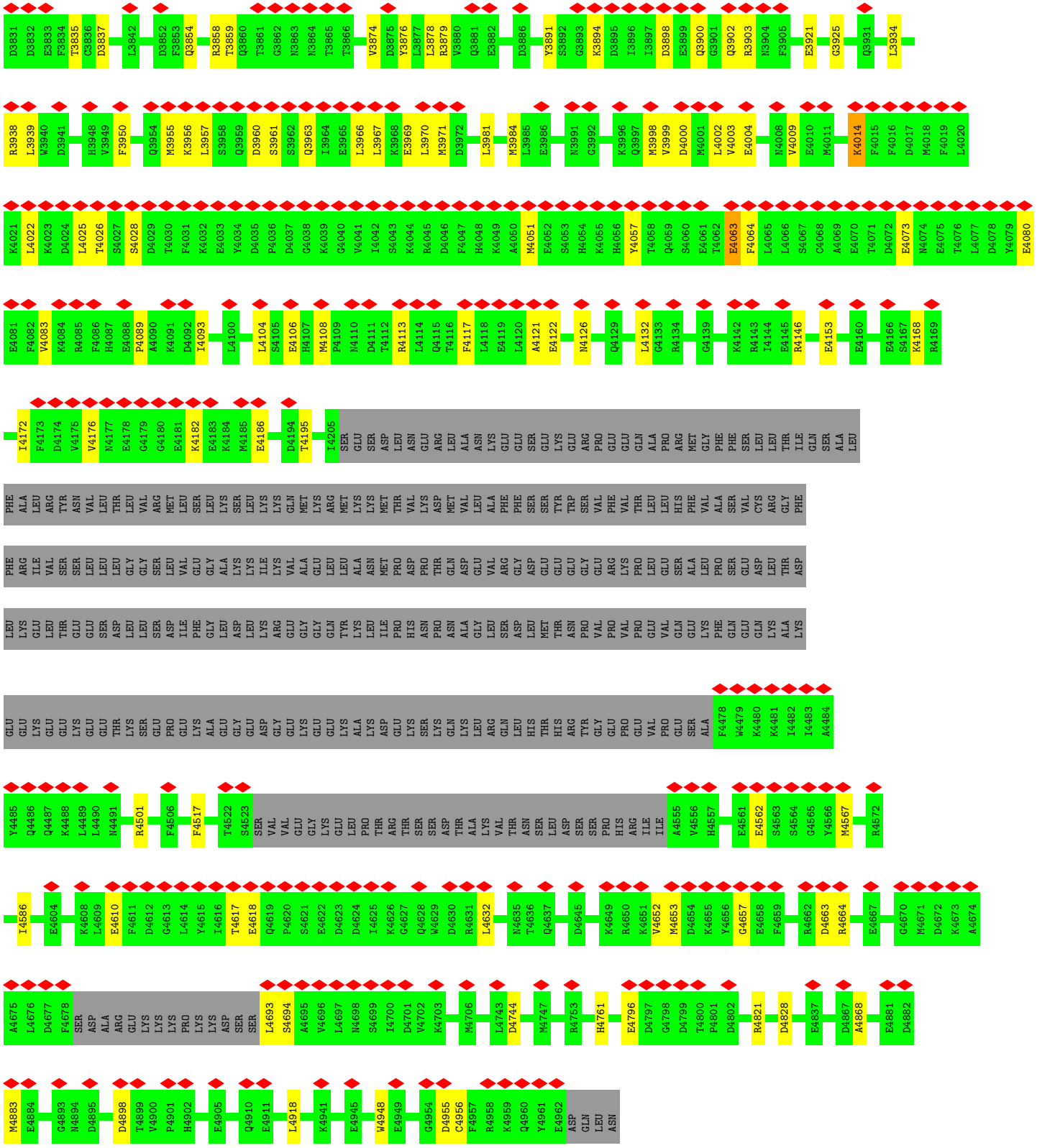
Chain C:






ASN ASN SER ASN GLY LEU GLU ILE GLY CYS VAL VAL ASP ALA ALA SER GLY LEU LEU THR PHE ILE ALA ASN GLY LYS GLU LEU SER THR TYR TYR GLN VAL GLU PRO SER THR LYS LEU PHE PRO ALA VAL PHE ALA GLN ALA THR SER PRO ASN VAL PHE GLN PHE GLU ARG
ILE LYS ASN VAL MET PRO LEU SER ALA GLY LEU PHE LYS SER GLU HIS LYS ASN PRO VAL PRO GLN CYS PRO PRO ARG LEU HIS VAL GLN PHE LEU SER HIS VAL LEU TRP SER ARG MET PRO ASN GLN PHE LEU LYS VAL ASP VAL SER ARG ILE SER GLU ARG GLN GLY TRP LEU VAL
GLN CYS LEU ASP PRO LEU GLN PHE MET SER LEU HIS ILE PRO GLU GLU ASN ARG SER VAL ASP ILE LEU GLU LEU GLU GLU LEU GLN PHE HIS TYR HIS THR LEU THR GLU GLN GLU LEU LEU GLN PHE HIS VAL ALA HIS ALA LEU GLY ASN HIS ARG VAL ALA HIS ALA LEU CYS SER HIS
VAL ASP GLU PRO GLN LEU LEU TYR ALA ILE GLU ASN LYS TYR MET PRO GLY LEU LEU ARG ALA GLY TYR TYR ASP LEU LEU ASP ILE ILE GLU ILE HIS LEU SER SER ASN ASP CYS TYR GLN TYR SER LEU ARG MET MET MET ASN ASN GLU PHE ILE VAL PRO MET THR GLU GLU THR LYS ALA THR ALA ARG LEU MET PRO GLU PHE
PRO ASP GLU ASN LYS LYS HIS GLY LEU PRO GLY ILE GLY LEU SER THR SER LEU ARG PRO GLU MET ARG PHE SER SER PRO SER PHE VAL SER ILE ASN GLN MET GLU PHE PRO LEU ASP ILE LEU LYS ALA LYS ASP PRO LEU GLU
LYS GLU GLY SER LEU HIS ALA ARG ASP PRO VAL GLY GLY THR THR GLU PHE LEU PHE VAL PRO LEU ILE LYS LEU PHE TYR THR LEU LEU ILE MET GLY ILE PHE HIS ASN GLU ASP LEU LYS HIS ILE LEU GLN LEU ILE GLU PRO GLN GLU GLY GLU
GLU GLY GLY THR PRO GLU LYS GLU ILE SER ASP ALA LYS LEU GLU GLY GLU GLU ALA LYS GLY GLY LYS ARG PRO LYS GLU GLY GLU ILE GLN MET LYS LEU PRO GLU PRO VAL LYS LEU GLN MET CYS LEU LEU LEU GLN TYR LEU GLN GLU GLN ILE ASN MET SER ALA LEU ASN MET THR HIS CYS GLY ILE GLU LEU GLU GLY LEU ASP GLU ASP GLY SER LEU ASP GLY SER ASN ASP LEU THR ILE ARG GLY ARG LEU LEU SER LEU VAL GLU LYS VAL THR TYR LEU LYS LYS
ILE GLU ALA ILE VAL ALA PHE SER ASP ASP PHE VAL ALA LYS LEU GLN ASP ASN GLN ARG PHE ARG TYR ASN GLU VAL MET GLN ALA LEU ASN MET SER ALA ALA LEU ASP SER LEU MET THR HIS CYS GLY ILE GLU LEU GLU GLU ASP GLU GLY SER LEU ASP GLY ASP THR ILE GLU ARG GLU PHE ARG SER PRO PRO GLN GLU GLU ILE ASN MET LEU LEU ILE GLN ASP ALA ARG LYS THR ARG GLU PHE ARG SER PRO LEU ASP ILE LYS ASP
ASP LYS SER GLU CYS PRO CYS PRO GLU GLU ILE ARG ASP GLN LEU LEU ASP PHE HIS GLU ASP GLY SER LEU ASP GLY SER ASN ASP LEU THR ILE ARG GLY ARG LEU LEU SER LEU VAL GLU LYS VAL THR TYR LEU LYS LYS
LYS GLN ALA GLU LYS PRO VAL ALA SER ASP SER ARG LYS CYS SER SER LEU GLN GLN LEU ILE SER GLU THR MET VAL ARG TRP ALA GLN GLU SER VAL ILE GLU GLU ASP PRO GLU LEU VAL ARG ALA MET PHE VAL LEU LEU HIS ARG GLN TYR ASP GLY ILE GLY LEU VAL ARG ALA
LEU PRO LYS THR TYR THR ILE ASN GLY VAL SER VAL GLU ASP THR ILE ASN LEU LEU ALA SER LEU GLY GLN ILE ARG SER LEU LEU LEU SER VAL ARG GLU MET GLY LYS GLU GLU LYS LEU MET ILE ARG GLY LEU GLY ASP ILE MET ASN ASN LYS VAL PHE TYR GLN HIS PRO ASN LEU
MET ARG ALA LEU GLY MET HIS GLU GLU THR VAL MET GLU VAL MET MET VAL ASN VAL LEU GLY GLY GLU SER LYS GLU ILE THR PHE PHE PRO LYS MET VAL ALA ASN CYS CYS ARG PHE LEU CYS TYR PHE CYS ARG ILE SER ARG GLN ASN GLN LYS ALA MET PHE ASP HIS LEU SER TYR LEU
LEU GLU ASN SER SER VAL GLY LEU ALA SER ALA ALA ALA SER VAL MET ASP ASN ASN GLU LEU GLY ARG PRO THR SER GLY SER SER LYS THR LEU ASP ILE GLU GLU GLU GLU ASP ILE GLU ALA LEU ARG GLU ASP GLY GLY PRO ASP LEU GLU LEU GLN SER CYS GLN MET LEU VAL
SER LYS GLY TYR PRO ASP ILE GLY TRP ASN PRO VAL GLU GLY GLU ARG TYR LEU ASP PHE LEU ARG PHE ALA VAL PHE CYS ASN GLY GLU SER VAL GLU GLU ASN ALA ASN VAL VAL VAL ARG LEU LEU ILE ARG ARG PRO GLU CYS PHE GLY PRO ALA LEU ARG GLY GLU GLY GLY ASN
GLY LEU LEU ALA ALA MET GLU GLU ALA ILE LYS ILE ALA GLU GLY ASP PRO SER PRO THR SER GLY SER SER LYS THR LEU ASP ILE GLU GLU GLU GLU ASP ASP THR ILE HIS MET GLY ASN ALA ILE MET THR PHE TYR ALA ALA LEU ILE ASP LEU GLU LEU GLY ARG
CYS ALA PRO GLU MET HIS LEU ILE HIS ALA GLY LYS ILE ARG SER ILE LEU ARG SER LEU ILE PRO LEU GLY GLY ASP LEU VAL ILE SER ILE ALA PHE GLN MET PRO THR ILE ALA LYS ASP GLY LYS VAL PRO THR ILE ALA LEU SER ASP ILE GLU PHE CYS
PRO ASP HIS LYS ALA MET VAL LEU PHE LEU VAL GLY PHE LEU LEU PRO ASP LEU ARG SER LEU ASP THR ILE ALA ALA GLN ARG ASP SER ALA THR ASP MET ALA LEU SER LEU ASP ALA LEU ASN ARG TYR LEU CYS
THR ALA VAL LEU PRO LEU THR ARG CYS ALA PRO SER LEU LEU ILE ASP SER LEU LEU HIS THR VAL TYR ARG LEU SER LYS GLY CYS SER LEU THR LYS ALA GLN ARG ASP SER ILE GLU VAL CYS LEU LEU SER LEU ILE CYS GLY GLY GLN LEU ARG
PRO SER MET MET GLN HIS LEU LEU ARG ASN HIS TYR ARG CYS TRP LYS TYR TYR CYS LEU PRO GLY GLY TRP GLY ASN PHE GLY ALA ALA SER GLU GLU GLU LEU HIS LEU LEU
ARG LYS LEU PHE TRP GLY ILE PHE ASP ALA LEU SER LYS LEU ALA LEU PRO CYS LEU SER ALA VAL ALA GLY ALA LEU PRO ASP TYR MET GLU SER ASN TYR VAL SER MET MET GLU LYS GLN SER ASP SER GLU GLY ASN PHE

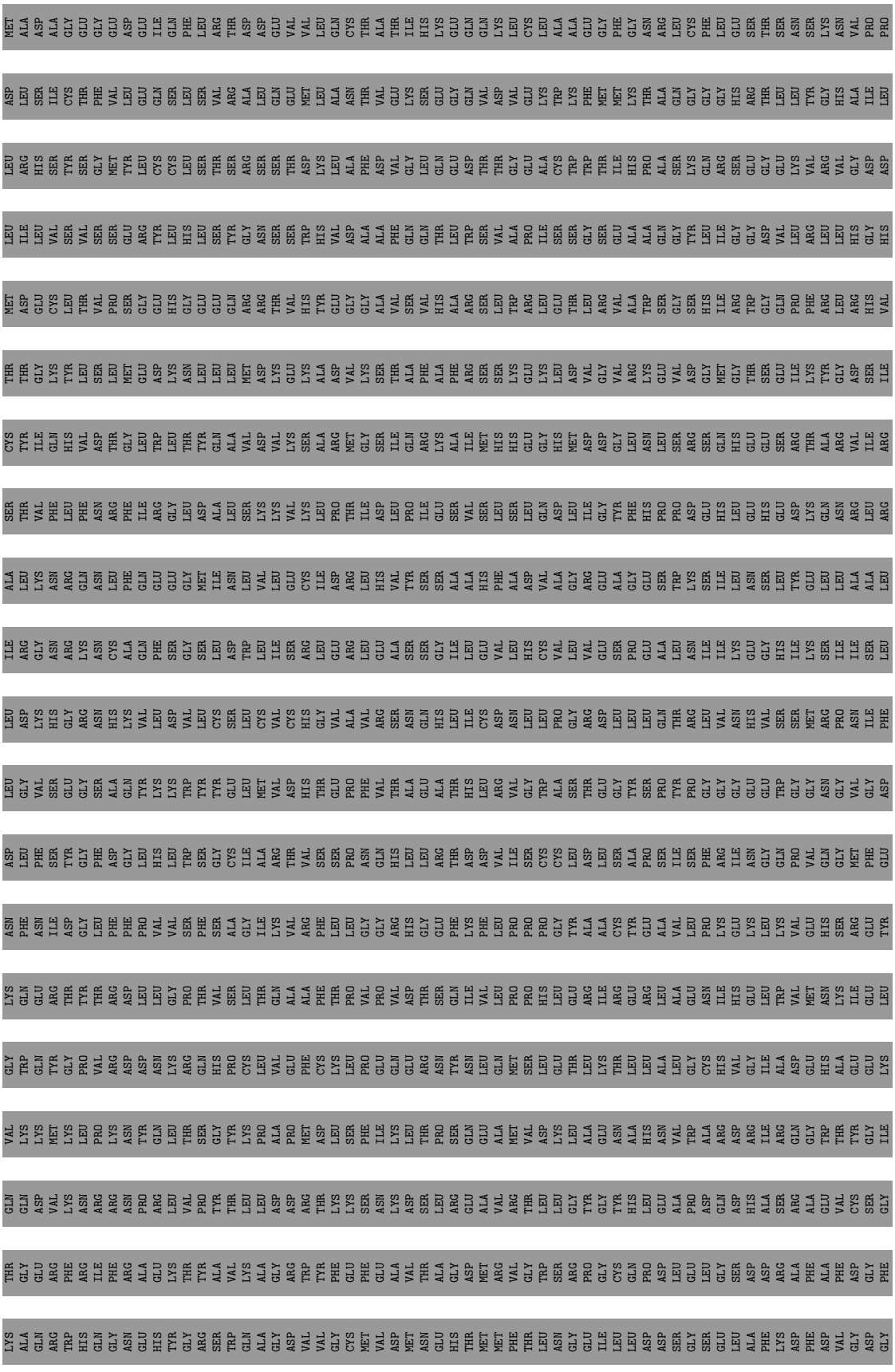

ASN PRO GLN PRO VAL ASP THR SER ASN ILE THR ILE PRO GLU LYS LEU GLU TYR PHE ILE ASN LYS TYR ALA GLU HIS SER HIS ASP LYS TRP SER MET ASP LYS LEU ALA ASN GLY TRP ILE TYR GLY GLU ILE TYR SER ASP SER SER LYS ILE GLN PRO LEU MET LYS PRO TYR LYS
LEU LEU SER GLU LYS GLU LYS GLU ILE TYR ARG TRP PRO ILE LYS GLU SER LEU LYS THR MET LEU ALA TRP GLY TRP ARG ARG ILE GLU ARG THR ARG GLU GLY ASP LYS SER MET ALA ALA LEU TYR ASN ARG THR ARG ARG ILE SER GLN THR SER GLN VAL SER ILE ASP ALA ALA HIS GLY TYR
SER PRO ARG ALA ILE ASP MET SER ASN VAL THR LEU SER ARG ASP LEU HIS ALA MET ALA GLU MET MET MET ALA GLU ASN TYR HIS ASN ILE TRP ALA LYS LYS LYS LYS LEU GLU GLU LEU GLU SER LYS GLY GLY GLY ASN HIS PRO LEU LEU LEU VAL PRO TYR ASP THR LEU THR ALA LYS GLU
LYS ALA LYS ASP ARG GLU LYS ALA GLN ASP ILE PHE LYS PHE LEU GLN ILE SER GLY TYR VAL VAL SER ARG GLY PHE LYS ASP LEU ASP LEU ASP THR PRO SER ILE GLU LYS ARG PHE ALA TYR SER PHE LEU GLN LEU ILE ARG TYR VAL ASP GLU ALA HIS GLN ILE LEU
GLU PHE ASP GLY GLY SER ARG SER LYS GLY GLU HIS PHE PRO TYR GLU GLN GLU ILE LYS PHE PHE ALA LYS VAL VAL LEU LEU PRO LEU ILE ASP GLN TYR PHE LYS ASN HIS ARG LEU TYR PHE LEU SER ALA ALA SER ARG PRO LEU CYS THR GLY GLY GLY HIS ALA SER ASN LYS GLU GLU
GLU MET VAL THR SER LEU PHE CYS LYS LEU GLY VAL LEU ARG HIS THR ARG ILE SER LEU PHE GLY ASN ASP ALA THR SER ILE LEU VAL ASN CYS LEU HIS ILE LEU ASP GLN TYR THR THR VAL LEU ASP ALA ARG THR VAL MET LYS THR GLY LEU ASP SER VAL LYS SER ALA LEU ARG ALA PHE LEU
ASP ASN ALA ALA GLU ASP LEU GLU LYS THR MET GLU ASN LEU LYS GLN GLY GLN PHE THR HIS THR ARG SER GLN PRO LYS GLY VAL THR GLN ILE ILE ASN TYR THR GLN ILE ILE ASN TYR THR GLN ILE ALA LEU LEU PRO MET LEU SER SER LEU PHE GLU HIS ILE GLY GLN HIS GLN PHE GLY GLU ASP ASP
ILE LEU GLU ASP VAL SER CYS TYR ARG ILE LEU THR SER LEU TYR ALA LEU GLY THR SER LYS SER ILE TYR VAL GLU ARG GLN ARG SER ALA LEU GLY GLU CYS LEU ALA ALA ALA PHE PHE ALA GLY ALA PHE PRO ILE ALA PHE LEU GLU HIS ILE GLY GLN HIS GLN PHE GLY GLU ASP LEU
SER ILE TYR ASN THR ARG SER SER ARG GLU ARG ARG ALA ALA LEU SER LEU PRO ALA ASN VAL GLU ASP VAL CYS PRO ASN ILE PRO SER LEU GLU LYS LEU MET THR GLU ILE ILE GLU LEU ALA GLU SER GLY ILE ARG TYR THR GLN MET PRO TYR MET MET GLU VAL VAL LEU PRO MET
LEU CYS SER TYR MET SER ARG TRP TRP GLU HIS GLY PRO GLU ASN HIS PRO GLU ARG ALA GLU MET CYS CYS THR ALA LEU ASN SER GLU HIS MET ASN THR LEU LEU GLY ASN ILE LEU LYS ILE ILE TYR ASN ASN LEU GLY ILE ASP GLU GLY ALA ALA TRP MET LYS ARG LEU ALA VAL
PHE SER GLN PRO ILE ILE ASN LYS VAL LYS PRO GLN LEU LEU LYS THR HIS PHE LEU PRO LEU MET GLU GLU LYS LEU LYS LYS LYS ALA ALA MET VAL VAL SER GLU GLU GLU ASP HIS LEU LYS ALA GLU ILE LEU ASP GLU PHE THR THR
LEU ALA ARG ASP LEU TYR LEU ILE ALA PHE TYR PRO LEU LEU LEU ILE ARG PHE VAL ASP TYR ASN ARG ALA LYS TRP LEU LYS GLU LYS GLU PRO ASN PRO GLU ALA GLU GLU LEU GLU PHE ARG MET VAL ALA GLU VAL PHE ILE TYR TRP SER LYS SER HIS ASN PHE LYS ARG GLU GLU ASN PHE VAL VAL
GLN ASN GLU ILE ASN ASN MET SER PHE LEU ILE THR ASP THR LYS SER LYS MET SER LYS ALA ALA ILE SER ASP GLN GLU ARG LYS LYS MET LYS ARG LYS GLY ASP ARG TYR SER MET GLN THR SER LEU ILE VAL CYS ASN GLU ASP ALA ALA LEU LEU LYS MET SER GLU ALA GLU GLU GLN LEU ASN ILE CYS
ALA PRO GLY ASP GLN GLU LEU ILE ALA LEU ALA LYS ARG SER ASP THR GLU GLU GLU VAL ARG ASP ILE ARG ARG SER ASN ILE HIS LEU GLN GLY LYS LEU GLU ASP PRO ALA ILE ARG TRP GLN MET ALA LEU TYR LYS ASP LEU PRO GLN ASN ARG GLU THR GLU ASP ASP
SER ASP PRO GLU ARG THR GLY ARG GLY TYR PHE SER LEU VAL GLU HIS PRO GLN ARG SER LYS LYS ALA VAL TRP HIS LYS LEU LEU VAL SER LYS SER ARG LEU ARG ARG ALA VAL ILE CYS
CYS PHE ARG MET A3605 P3606 L3607 Y3608 N3609 L3610 P3611 R3612 H3613 R3614 A3615 V3616 N3617 L3618 F3619 L3620 Q3621 G3622 Y3623 E3624 K3625 S3626 W3627 I3628 E3629 T3630 E3631 E3632 H3633 Y3634 F3635 E3636 D3637 K3638 L3639 I3640 E3641 D3642 L3643 A3644 K3645 P3646 G3647 A3648 E3649 L3650 P3651 E3652 E3653 D3654 E3655 A3656 M3657 K3658 R3659 V3660
D3661 P3662 L3663 H3664 Q3665 L3668 R3672 L3675 T3676 E3677 K3678 C3679 K3680 L3681 E3682 E3683 D3684 F3685 L3686 Y3687 M3688 A3689 Y3690 A3691 D3692 H3699 D3700 E3701 E3702 D3703 D3704 D3705 G3706 E3707 E3708 E3709 V3710 K3711 S3712 F3713 E3714 E3715 K3716 E3717 M3718 E3719 K3720 Q3721 Y3725 Q3726 Q3727 D3732 R3733 G3734
A3735 A3736 E3737 Q3741 T3742 I3743 S3746 K3747 G3748 E3749 I3762 N3769 D3778 K3781 E3782 K3783 K3784 D3785 V3786 Q3790 C3799 S3800 V3801 L3802 D3803 L3804 N3805 A3806 F3807 E3808 R3809 Q3810 N3811 K3812 A3813 E3814 G3815 L3816 G3817 M3818 V3819 T3820 E3821 E3822 G3823 S3824 G3825 E3826 K3827 V3828 L3829 Q3830

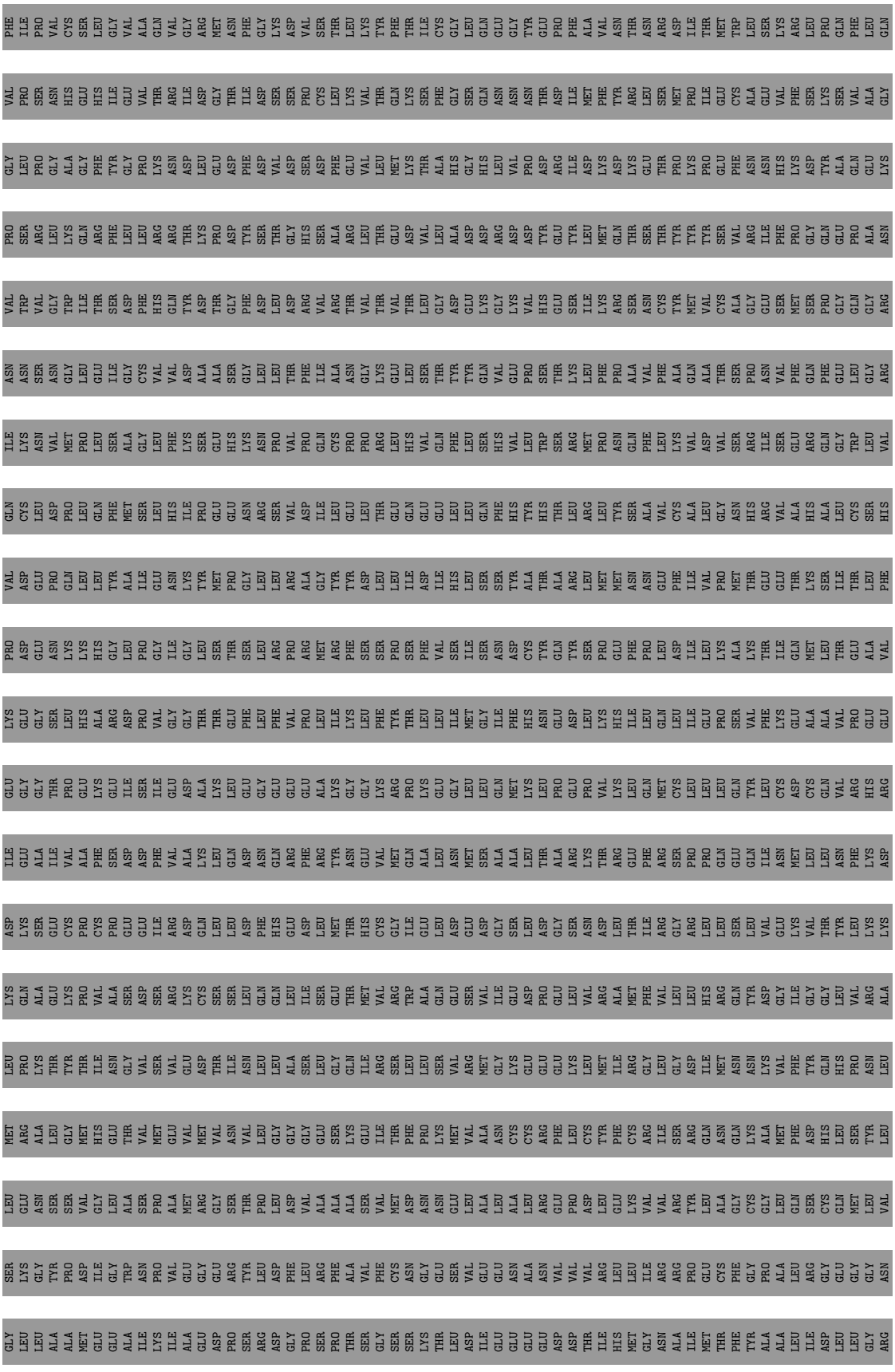


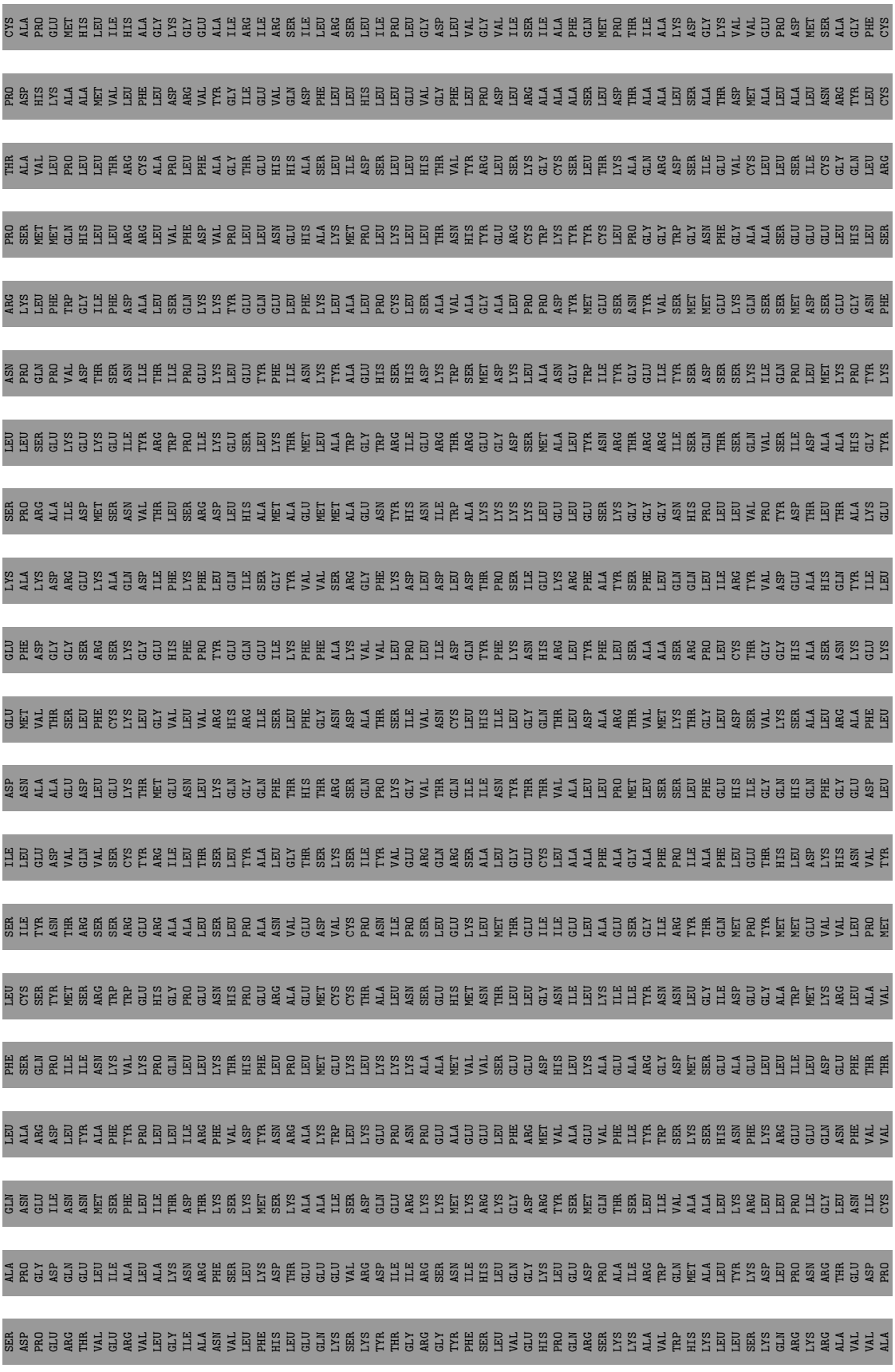
• Molecule 1: Ryanodine receptor 2

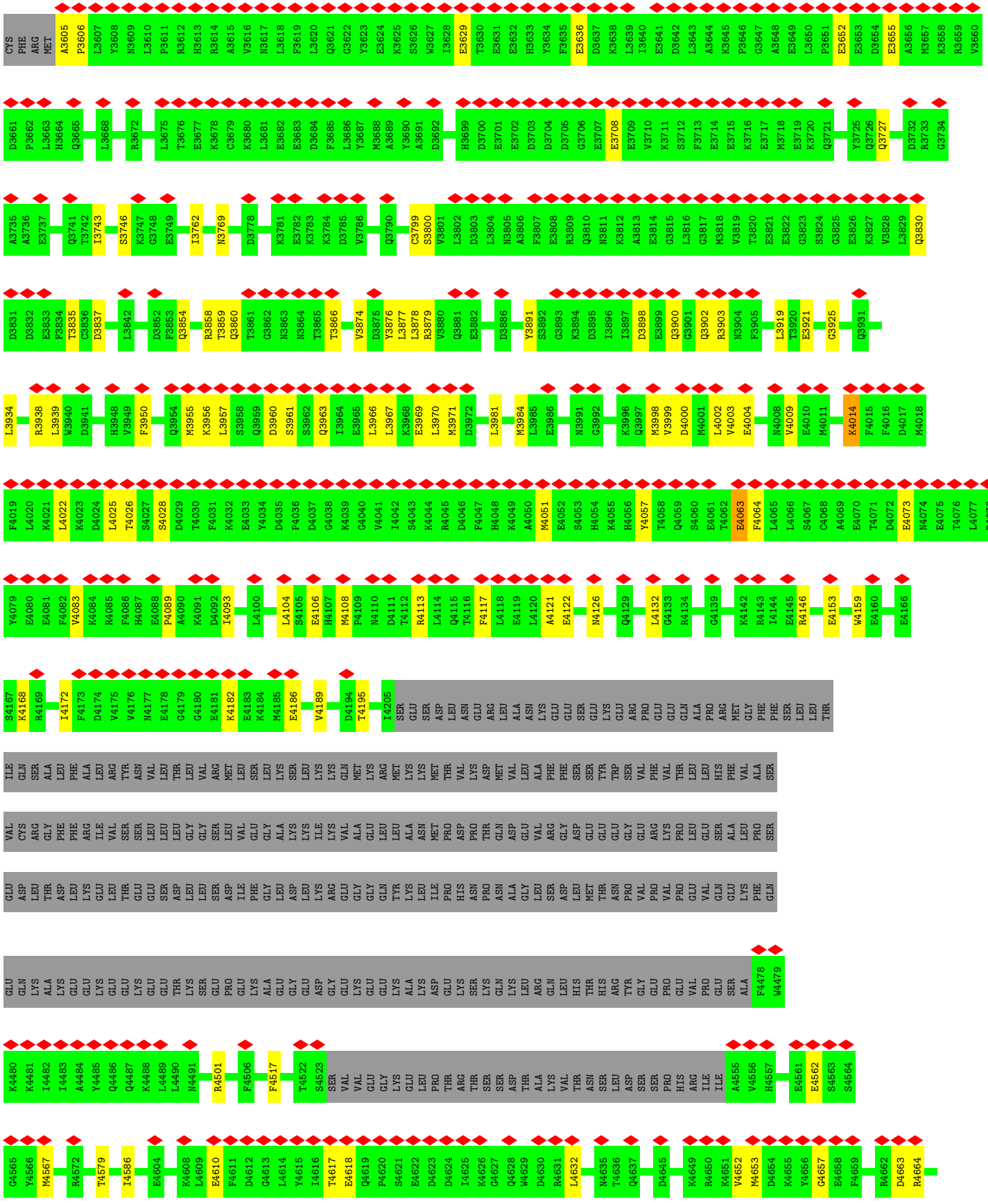
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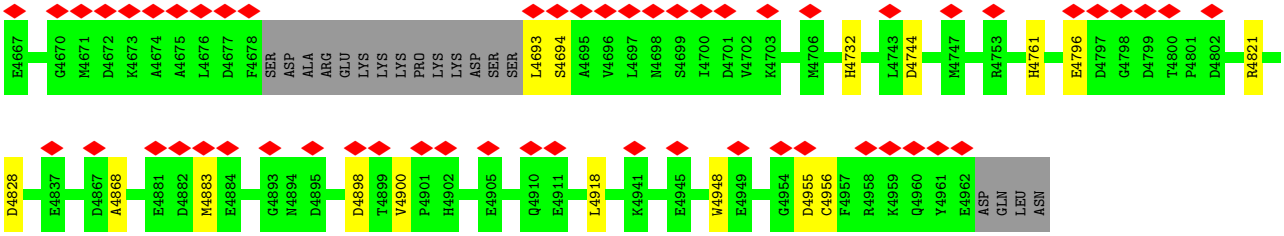



MET ALA ASP ALA GLY GLU GLY GLU ASP GLU ILE GLN PHE LEU ARG THR ASP ASP GLU VAL VAL LEU GLN CYS THR ALA THR ILE HIS LYS GLU GLN GLN LYS LEU CYS LEU ALA ALA GLU GLY PHE GLY ASN ARG LEU CYS PHE LEU GLU SER THR SER ASN SER LYS ASN VAL PRO PRO
ASP LEU SER ILE CYS THR PHE VAL LEU GLU GLN SER LEU SER VAL ARG ALA LEU GLN GLU ALA ASN THR VAL GLU LYS SER GLU GLY GLN VAL ASP VAL GLU LYS TRP LYS PHE MET MET LYS THR ALA GLN GLY GLY GLY HIS ARG THR LEU LEU TYR GLY HIS ALA ILE LEU
LEU ARG HIS SER TYR SER GLY MET TYR LEU CYS CYS LEU SER THR SER ARG ARG ALA SER SER THR ASP LYS LEU ALA PHE ASP VAL GLN GLN THR LEU TRP SER VAL ALA PRO ILE SER SER GLY SER GLU ALA ALA GLN GLY TYR LEU ILE GLY GLY ASP VAL LEU ARG LEU LEU HIS GLY ASP
LEU ILE LEU VAL SER VAL SER GLU ARG TYR LEU HIS LEU SER TYR GLY ASN SER SER TRP HIS VAL ASP ALA ALA PHE GLN GLN THR LEU TRP SER VAL ALA PRO ILE SER SER GLY SER GLU ALA ALA GLN GLY TYR LEU ILE GLY GLY ASP VAL LEU ARG LEU LEU HIS GLY GLY
MET ASP GLU CYS LEU THR VAL PRO SER GLY GLU HIS GLY GLU GLU GLN ARG ARG THR VAL HIS TYR GLU GLY GLY ALA ALA VAL SER GLY VAL HIS ALA ARG SER LEU TRP ARG LEU GLU THR LEU ARG VAL ALA TRP SER GLY TYR SER HIS ILE ARG TRP GLY GLN PRO PHE ARG LEU ARG HIS VAL
THR THR GLY LYS TYR LEU SER LEU MET GLU ASP LYS ASN LEU LEU LEU LEU MET ASP LYS GLU LYS ALA ASP VAL LYS SER THR ALA PHE ALA ARG SER SER LYS GLU LYS LEU ASP VAL GLY VAL ARG LYS GLU VAL ASP GLY MET GLY THR SER GLU ILE LYS TYR GLY ASP SER ILE
CYS TYR ILE GLN HIS VAL ASP THR GLY LEU TRP LEU THR TYR GLN ALA ALA VAL ASP VAL LYS SER ALA ARG MET GLY SER ILE GLN ARG LYS ALA ILE MET HIS HIS GLU GLY HIS MET ASP ASP GLY LEU ASN LEU SER ALA ARG SER GLN HIS GLU GLU SER ARG THR ALA ARG VAL ILE ARG
SER THR VAL PHE LEU PHE ILE ARG GLY LEU ASP ALA LEU SER LYS LYS VAL LYS LEU PRO THR ILE ASP LEU ASP ILE GLU SER VAL SER LEU SER LEU GLN GLN ILE GLU ASP LYS GLN LEU ARG LEU ARG
ALA LEU LYS ASN ARG GLN ASN LEU PHE GLN GLU GLU GLY MET ILE ASN LEU VAL LEU GLU CYS ILE ASP ARG LEU HIS VAL TYR SER SER ALA ALA HIS PHE ALA ASP VAL ALA GLY ARG GLU ALA GLY GLU SER PRO GLU ALA LEU ASN ILE ILE LYS GLU GLY HIS LEU LEU LEU ALA ALA LEU
ILE ARG GLY ASN ARG ARG LYS ASN CYS ALA GLN PHE SER GLY SER LEU ASP TRP LEU ILE SER ARG LEU GLU ARG LEU GLU ALA SER SER GLY ILE LEU GLU GLY SER LEU GLU VAL LEU HIS CYS VAL LEU GLU PRO GLY ARG GLU ASP SER PRO GLU ALA LEU ASN ILE ILE LYS GLU GLY HIS ILE LYS SER ILE ILE SER LEU
LEU ASP LYS HIS GLY ARG ASN HIS LYS VAL LEU ASP VAL LEU CYS SER LEU CYS VAL CYS HIS GLY VAL ALA VAL ARG SER ASN GLN HIS LEU ILE CYS ASP ASN LEU LEU PRO GLY ARG ASP LEU LEU LEU GLN THR ARG LEU VAL ASN HIS VAL SER SER MET ARG PRO ASN ILE PHE
LEU GLY VAL SER GLU GLY GLN TYR LYS LYS TRP TYR TYR GLU LEU MET VAL ASP HIS THR GLU PRO PHE VAL THR HIS LEU ARG VAL GLY TRP ALA SER THR GLU GLY TYR SER PRO TYR PRO GLY GLY GLY GLU GLU TRP GLY GLY ASN GLY VAL GLY ASP
ASP LEU PHE SER TYR GLY PHE ASP GLY LEU HIS LEU TRP SER GLY CYS ILE ALA ARG THR VAL SER SER PRO ASN GLN HIS LEU LEU ARG THR ASP ASP VAL ILE SER CYS CYS LEU ASP LEU SER ALA PRO SER ILE SER PHE ARG ILE ASN GLY GLN PRO VAL GLN GLY MET PHE GLU
ASN PHE ASN ILE ASP GLY LEU PHE PHE PRO VAL VAL SER PHE SER ALA GLY ILE LYS VAL ARG PHE LEU LEU GLY GLY ARG HIS GLY GLU PHE LYS PHE LEU PRO PRO PRO GLY TYR ALA ALA CYS TYR GLU GLU ALA VAL LEU PRO LYS GLU LYS LEU LYS VAL GLU HIS SER ARG GLU TYR
LYS GLN GLU ARG THR TYR THR ARG ASP LEU LEU GLY PRO THR VAL SER LEU THR GLN ALA ALA PHE THR PRO VAL PRO VAL ASP THR SER GLN ILE VAL LEU PRO PRO PRO HIS LEU GLU ARG ILE ARG GLU ARG LEU ALA GLU ASN ILE HIS GLU LEU TRP VAL MET ASN LYS ILE GLU GLU
GLY TRP GLN TYR GLY PRO ASP ASN LYS ARG GLN HIS PRO CYS LYS LEU PRO GLU GLN GLU ARG ASN TYR ASN LEU GLN MET SER LEU GLU THR LEU LYS THR LEU LEU ALA LEU GLY CYS HIS VAL GLY GLU ILE ALA ASP GLU HIS ALA GLU GLU
VAL LYS LYS MET LYS LEU PRO LYS ASN TYR GLN LEU THR SER GLY TYR LYS PRO ALA PRO MET ASP LEU SER PHE ILE LYS LEU THR PRO SER GLN LEU GLU ALA MET SER LEU GLU LYS ASP LYS LEU VAL ALA ASP ARG GLN GLY TRP THR TYR GLY ILE
GLN GLN ASP VAL LYS ASN PRO ARG ARG ASN LEU VAL PRO TYR THR LEU LEU ASP ARG THR LYS LYS SER ASN LYS ASP SER LEU ARG GLU ALA VAL ARG THR LEU LEU GLY TYR GLY TYR HIS LEU GLU ALA HIS ASN VAL TRP ALA ARG ASP ARG ILE ARG GLN GLY ALA GLU VAL CYS SER
THR GLY GLU ARG PHE ARG ILE ALA LYS ALA LYS PHE ARG GLU PHE GLU ALA VAL THR ALA GLY ASP MET THR ARG VAL GLY TRP SER ARG PRO GLY CYS GLN PRO ASP LEU GLU LEU GLY SER ASP ARG ALA PHE ALA ALA GLY ASP ARG TRP TYR PHE GLU PHE GLU ALA VAL THR ALA GLY ASP MET ARG THR LEU LEU ASN GLU ILE LEU LEU ASP SER GLY GLU LEU GLU PHE ASP
LYS ALA GLN ARG TRP HIS GLN GLY ASN GLU HIS THR MET MET PHE THR LEU ASN GLY GLU ILE LEU LEU ASP ASP SER GLY SER GLU LEU ALA PHE LYS ASP PHE ASP VAL GLY ASP GLY


PHE ILE PRO VAL CYS SER LEU GLY VAL ALA GLN VAL GLY ARG MET ASN PHE GLY LYS ASP VAL SER THR LEU LYS TYR PHE THR ILE CYS GLY LEU GLN GLU GLY TYR GLU PRO PHE ALA VAL ASN THR ASN ARG ASP ILE THR MET TRP LEU SER LYS ARG LEU PRO GLN PHE LEU GLN
VAL PRO SER ASN HIS GLU HIS ILE GLU VAL THR ARG ILE ASP GLY THR ILE ASP SER SER PRO CYS LEU LYS VAL THR GLN LYS SER PHE GLY SER GLN ASN ASN THR ASP ILE MET PHE TYR ARG LEU SER MET PRO ILE GLU CYS ALA GLU VAL PHE SER LYS ARG LEU PRO GLN GLU LYS
GLY LEU PRO GLY ALA GLY PHE TYR GLY PRO LYS ASN ASP LEU GLU ASP PHE ASP VAL ASP SER ASP PHE GLU VAL LEU MET LYS THR ALA HIS GLY HIS LEU VAL PRO ASP ASP ILE ASP LYS ASP LYS GLU LYS ASP TYR ALA GLN GLU LYS
PRO SER ARG LEU LYS GLN ARG PHE LEU LEU ARG ARG THR LYS PRO ASP TYR SER THR GLY HIS SER ALA ARG LEU THR GLU ASP VAL LEU ALA ASP ASP ARG ASP ASP TYR GLU TYR LEU MET GLN THR SER THR TYR TYR TYR SER VAL ARG ILE PHE PRO GLY GLN GLU PRO ALA ASN
VAL TRP VAL GLY TRP ILE THR SER ASP PHE HIS GLN TYR ASP THR GLY PHE ASP LEU ASP ARG VAL ARG THR VAL THR VAL THR LEU GLY ASP GLU LYS GLY LYS VAL HIS GLU SER ILE LYS ARG SER ASN CYS TYR MET VAL CYS ALA GLY GLU SER MET SER GLN GLY GLN GLY ARG
ASN ASN SER ASN GLY LEU GLU ILE GLY CYS VAL VAL ASP ALA ALA SER GLY LEU LEU THR PHE ILE ALA ALA ASN GLY LYS GLU LEU GLU THR TYR GLN VAL GLU PRO SER THR LYS LEU PHE PRO ALA VAL PHE ALA GLN GLY ALA THR SER ARG PHE GLU PHE GLU LEU GLY ARG
ILE LYS ASN VAL MET PRO LEU SER ALA GLY LEU HIS LYS SER GLU HIS LYS ASN PRO VAL PRO GLN CYS PRO PRO ARG LEU HIS VAL GLN PHE LEU SER THR GLU GLN GLU GLU LEU LEU GLN PHE HIS TYR HIS THR LEU ARG LEU TYR SER ALA VAL CYS ALA LEU GLY ASN HIS ARG VAL ALA HIS LEU CYS SER HIS
GLN CYS LEU ASP PRO LEU GLN PHE MET SER LEU HIS ILE PRO GLU GLU ASN ARG SER VAL ASP ILE LEU GLU LEU GLU LEU LEU GLN PHE HIS TYR HIS THR LEU ARG LEU TYR SER ALA VAL CYS ALA LEU GLY ASN HIS ARG VAL ALA HIS ALA LEU CYS SER HIS
VAL ASP GLU PRO GLN LEU LEU TYR ALA ILE GLU ASN LYS TYR MET PRO GLY LEU LEU ARG ALA GLY TYR TYR ASP LEU LEU ILE ASP ILE HIS LEU GLN SER SER TYR ALA THR ALA ARG LEU MET MET ASN ASN GLU PHE ILE VAL PRO MET THR GLU GLU THR LYS SER ILE THR LEU PHE
PRO ASP GLU ASN LYS LYS HIS GLY LEU PRO GLY ILE GLY LEU SER THR SER LEU ARG PRO ARG MET ARG PHE SER SER PRO SER PHE VAL SER ILE SER ASN ASP CYS TYR GLN TYR SER PRO GLU PHE PRO LEU ASP ILE LEU LYS ALA LYS THR ILE GLN MET LEU THR GLU ALA VAL
LYS GLU GLY SER LEU HIS ALA ARG ASP PRO GLY THR THR GLU PHE LEU PHE VAL PRO LEU ILE LEU LYS LEU PHE PHE TYR THR LEU LEU LEU ILE MET GLY ILE PHE HIS ASN GLU ASP LEU LYS HIS ILE LEU GLN LEU ILE GLU PRO GLN GLU GLU GLY
GLU GLY GLY THR PRO GLU ILE SER ASP ASP PHE SER ALA GLU GLU GLY GLY LYS ARG PRO LYS LEU GLU GLY LEU LEU LEU LEU ASN MET SER ALA LEU THR ALA ARG LYS THR ARG GLU PHE ARG SER PRO LEU LEU GLN MET CYS LEU LEU LEU GLN GLN TYR LEU CYS ASP CYS GLN VAL ARG HIS ARG
ILE GLU ALA ILE VAL ALA PHE SER ASP ASP PHE VAL ALA LYS LEU GLN ASP ASN GLN ARG PHE ARG TYR ASN GLU VAL MET GLN ALA LEU ASN MET SER ALA ALA LEU ASN ASP LEU THR ILE ARG GLU PHE ARG SER PRO PRO GLN GLU GLN GLN ILE ASN MET ASP THR ILE ARG GLY ARG LEU LEU GLU ASP ASP LYS
ASP LYS SER GLU CYS PRO CYS PRO GLU GLU ILE ARG ASP GLN LEU LEU ASP PHE HIS GLU ASP CYS GLY ILE GLU GLU LEU ASP GLU ASP GLY SER LEU ASP GLY SER ASN ASP LEU THR ILE ARG GLY ARG LEU LEU SER LEU VAL GLU LYS VAL THR TYR LEU LYS LYS
LYS GLN ALA GLU LYS PRO VAL ALA SER ASP SER ARG LYS CYS SER SER LEU GLN LEU ILE SER GLU SER VAL ILE GLU GLU ASP PRO GLU LEU VAL ARG ALA MET PHE VAL LEU LEU HIS ARG GLN TYR ASP GLY ILE GLY LEU VAL ARG ALA
LEU PRO LYS THR TYR THR ILE ASN GLN LEU LEU ALA SER LEU GLY GLN ILE ARG SER LEU LEU LEU SER VAL ARG MET GLY LYS GLU GLU ASP PRO LYS LEU MET ILE ARG GLY PHE TYR GLN ILE ASP ILE MET ASN ASN LYS VAL PHE SER LEU
MET ARG ALA LEU GLY MET HIS GLU THR VAL MET MET GLU VAL MET VAL ASN VAL LEU GLY GLY GLU SER LYS GLU ILE THR PHE PRO LYS GLU VAL ILE THR PHE PHE CYS ARG ILE SER ARG GLN ASN GLN LYS ALA MET PHE ASP HIS LEU SER TYR LEU
LEU GLU ASN SER SER VAL GLY LEU ALA SER PRO ALA MET ARG GLY SER THR PRO LEU ASP VAL ALA ALA ALA SER VAL MET ASP ASN ASN GLU LEU ALA LEU ALA ARG GLU PRO ASP LEU GLU LYS VAL VAL ARG TYR LEU ALA GLY CYS GLY LEU GLN LEU
SER LYS GLY TYR PRO ASN PRO VAL GLU GLY TRP ALA PHE VAL PHE CYS ASN GLY GLU SER VAL GLU GLU ASN ALA ASN VAL VAL ARG LEU LEU ILE ARG ARG PRO GLU CYS PHE GLY PRO ALA LEU ARG GLY GLU GLY GLY ASN
GLY LEU LEU ALA ILE LYS ILE ALA GLU ASP PRO SER PRO THR SER GLY SER SER LYS THR LEU ASP ILE GLU GLU GLU GLU ASP ASP THR ILE HIS MET GLY ASN ALA ILE MET THR PHE TYR ALA ALA LEU ILE ASP LEU LEU GLY ARG


CYS ALA PRO GLU MET HIS LEU ILE HIS ALA GLY LYS GLY GLU ALA ILE ARG ILE ARG SER ILE LEU ARG SER LEU ILE PRO LEU GLY ASP LEU VAL GLY VAL ILE SER ILE ALA PHE GLN MET PRO THR ILE ALA LYS ASP GLY LYS VAL VAL GLU PRO ASP MET SER ALA GLY PRO ASP HIS LYS ALA ALA MET VAL LEU PHE LEU ASP ARG VAL TYR GLY ILE GLU VAL GLN ASP PHE LEU LEU HIS LEU ILE ASP SER LEU LEU HIS THR VAL TYR ARG LEU GLU VAL GLY PHE LEU PRO ASP LEU ARG ALA ALA ALA SER LEU ASP THR ALA ALA LEU SER SER ALA THR ASP MET ALA LEU LEU ALA LEU ASN ARG TYR LEU CYS
THR ALA VAL LEU PRO LEU LEU THR ARG CYS ALA PRO LEU PHE ALA GLY THR GLU HIS HIS ALA SER LEU ILE ASP SER LEU LEU HIS THR VAL TYR ARG LEU GLU PHE ASP VAL PRO LEU GLU ILE PHE ASP ALA LEU LYS MET PRO LEU LYS ILE ARG GLU GLN LEU ASN GLU HIS ALA LYS MET PRO LEU LEU ARG CYS TRP LYS TYR TYR CYS LEU PRO GLY GLY TRP GLY ASN PHE GLY ALA ALA SER SER GLU GLU GLU LEU HIS LEU SER
ARG LYS LEU PHE TRP GLY ILE PHE ASP ALA LEU SER GLN LYS LYS TYR GLU GLN GLU LEU LEU PHE LYS LEU ALA LEU PRO CYS LEU SER ALA VAL HIS THR ASN ALA GLY ALA LEU PRO ASP TYR MET GLU SER ASN TYR VAL SER MET MET GLU LYS GLN SER SER LYS ILE GLN PRO LEU MET LYS PRO TYR TYR
ASN PRO GLN PRO VAL ASP THR SER ASN ILE THR ILE PRO GLU LYS LEU GLU GLN TYR PHE ILE ASN LYS TYR ALA GLU HIS SER HIS ASP LYS TRP SER MET ASP LYS LEU ALA ASN GLY TRP ILE TYR GLY GLU ILE TYR SER ASP SER GLN THR SER LYS ILE GLN PRO LEU MET LYS PRO TYR LYS
LEU LEU SER GLU ILE TYR ARG TRP PRO ILE LYS GLU SER LEU LYS THR MET LEU ALA TRP GLY TRP ARG ILE GLU ARG THR ARG GLY ASP SER MET ALA LEU TYR ASN ARG THR ARG ARG ILE SER GLN THR SER SER GLN VAL SER ILE ASP ALA ALA HIS GLY TYR
SER PRO ARG ALA ILE ASP MET SER ASN VAL THR LEU SER ARG ASP LEU HIS ASN ILE TRP ALA LYS LYS LYS LYS LEU GLU ASN TYR HIS ASN ILE GLU ASP LYS TRP SER HIS SER ASP SER SER LYS GLY GLY GLY ASN HIS PRO LEU LEU VAL PRO TYR ASP THR LEU GLU ALA LYS
LYS ALA LYS ASP ARG GLU LYS ALA GLN ASP ILE PHE LYS PHE LEU GLN ILE SER GLY TYR VAL VAL SER ARG GLY PHE LYS ASP LEU ASP THR PRO SER ILE GLU LYS ARG PHE ALA TYR SER PHE LEU GLN GLN LEU ILE ARG TYR VAL ASP GLU ALA HIS GLN TYR ILE LEU
GLU PHE ASP GLY GLY SER ARG SER LYS GLY GLU HIS PHE PRO TYR GLU GLN GLU ILE LYS PHE PHE ALA LYS VAL VAL LEU PRO LEU ILE ASP GLN TYR PHE LYS ASN HIS ARG LEU TYR PHE LEU SER ALA ALA SER ARG PRO LEU CYS THR GLY GLY HIS ALA SER ASN LYS GLU LYS
GLU MET VAL THR SER LEU PHE CYS LYS LEU GLY VAL LEU VAL ARG HIS ARG ILE SER LEU PHE GLY ASN ASP ALA THR SER ILE VAL ASN CYS LEU HIS ILE LEU GLY GLN THR LEU ASP ALA ARG THR VAL MET LYS THR GLY LEU ASP SER VAL LYS SER ALA LEU ARG ALA PHE LEU
ASP ASN ALA ALA GLU ASP LEU GLU LYS THR GLN LYS GLY GLN PHE THR HIS THR ARG SER GLN PRO LYS GLY VAL THR GLN ILE ILE ASN TYR THR THR VAL ALA LEU LEU SER SER LEU PHE GLU HIS ILE GLY GLN HIS HIS PHE GLY GLU ASP ARG LEU
ILE LEU GLU ASP VAL GLN VAL SER CYS TYR ARG ILE LEU THR SER LEU TYR ALA LEU GLY THR SER LYS SER ILE TYR VAL GLU ARG GLN ARG ARG SER LEU PRO ILE ALA PHE ALA GLY ALA PHE PRO ILE ALA PHE LEU GLU ASP VAL TYR
SER ILE TYR ASN THR ARG SER SER ARG GLU ARG ALA ALA LEU SER LEU PRO ALA ASN VAL GLU ASP VAL CYS PRO ASN ILE PRO SER LEU GLU LYS LEU MET THR GLU ILE ILE GLU LEU ALA GLU SER GLY ILE ARG TYR THR GLN MET PRO TYR MET MET GLU VAL VAL LEU LEU PRO
LEU CYS SER TYR MET SER ARG TRP TRP GLU HIS GLY PRO GLU ARG ALA LEU ASN SER GLU HIS MET ASN THR LEU LEU LEU GLY ASN ILE LEU LYS ILE ILE TYR ASN ASN LEU GLY ILE ASP GLU GLY ALA TRP MET LYS ARG LEU ALA VAL
PHE SER GLN PRO ILE ILE ASN LYS PRO GLN LEU LEU LYS THR HIS PHE LEU PRO LEU MET GLU LYS LYS LYS ALA ALA MET VAL VAL SER GLU GLU GLU ASP HIS LEU LYS ALA GLU ALA LEU LEU ILE LEU ASP GLU PHE THR THR
LEU ALA ARG LEU TYR ALA ASP PHE TYR ASN ARG ALA LYS TRP LEU LYS GLU PRO ASN PRO GLU ALA ALA MET VAL ALA GLU VAL PHE ILE TYR TRP SER LYS SER HIS ASN PHE LYS ARG GLU GLU GLN ASN PHE VAL VAL
GLN ASN GLU ILE ASN ASN MET SER PHE LEU ILE THR ASP THR LYS SER LYS MET SER LYS ALA ALA ILE SER ASP GLN GLU ARG LYS LYS MET LYS ARG LYS GLY ASP ARG TYR SER MET GLN THR SER LEU ILE VAL ALA ALA LEU LYS ARG LEU LEU PRO ILE GLY LEU ASN ILE CYS
ALA PRO GLY ASP GLN GLU LEU ALA LYS ASP SER LEU GLU GLN GLY LYS LEU GLU ASP PRO ALA ILE ARG TRP GLN MET ALA LEU TYR LYS ASP GLU LEU ASP ARG ASP ILE ILE ARG SER ASN ILE HIS LEU GLN GLY LYS LEU GLU ASP PRO ALA ILE ARG TRP GLN MET ALA LEU TYR LYS ASP LEU ARG ASN ARG THR GLU ASP PRO
SER ASP PRO GLU ARG THR VAL GLU ARG GLY TYR PHE SER LEU VAL GLU HIS PRO GLN ARG SER LYS LYS ALA VAL TRP HIS LYS LEU LEU SER LYS GLN ARG LYS ARG ALA VAL VAL ALA


CYS PHE ARG MET A3605 P3606 L3607 Y3608 N3609 L3610 P3611 R3612 H3613 R3614 A3615 V3616 N3617 L3618 F3619 L3620 Q3621 G3622 Y3623 E3624 K3625 S3626 W3627 I3628 E3629 T3630 E3631 E3632 H3633 Y3634 F3635 E3636 D3637 K3638 L3639 I3640 E3641 D3642 L3643 A3644 K3645 P3646 G3647 A3648 E3649 L3650 P3651 E3652 E3653 D3654 E3655 A3656 M3657 K3658 R3659 V3660
D3661 P3662 L3663 H3664 Q3665 L3668 R3672 L3675 T3676 E3677 K3678 C3679 K3680 L3681 E3682 E3683 D3684 F3685 L3686 Y3687 M3688 A3689 Y3690 A3691 D3692 H3699 D3700 E3701 E3702 D3703 D3704 D3705 G3706 E3707 E3708 E3709 V3710 K3711 S3712 F3713 E3714 E3715 K3716 E3717 M3718 E3719 K3720 Q3721 Y3725 Q3726 Q3727 D3732 R3733 G3734
A3735 A3736 E3737 Q3741 T3742 I3743 S3746 K3747 G3748 E3749 I3762 N3769 D3778 K3781 E3782 K3783 K3784 D3785 V3786 Q3790 C3799 S3800 V3801 L3802 D3803 L3804 N3805 A3806 F3807 E3808 R3809 Q3810 N3811 K3812 A3813 E3814 G3815 L3816 G3817 M3818 V3819 T3820 E3821 E3822 G3823 S3824 G3825 E3826 K3827 V3828 L3829 Q3830
D3831 D3832 E3833 F3834 T3835 C3836 D3837 L3842 D3852 F3853 Q3854 R3858 T3859 Q3860 T3861 G3862 N3863 N3864 T3865 T3866 V3874 D3875 Y3876 L3877 L3878 R3879 V3880 Q3881 E3882 D3886 Y3891 S3892 G3893 K3894 D3895 I3896 I3897 D3898 E3899 Q3900 G3901 Q3902 R3903 N3904 F3905 L3919 T3920 E3921 G3925 Q3931
L3934 R3938 L3939 W3940 D3941 H3948 V3949 F3950 Q3954 M3955 K3956 L3957 S3958 Q3959 D3960 S3961 S3962 Q3963 I3964 E3965 L3966 L3967 K3968 E3969 L3970 M3971 D3972 L3981 M3984 L3985 E3986 N3991 G3992 K3996 Q3997 M3998 V3999 D4000 M4001 L4002 V4003 E4004 N4008 V4009 E4010 M4011 K4014 F4015 F4016 D4017 M4018
F4019 L4020 K4021 L4022 K4023 D4024 L4025 T4026 S4027 S4028 D4029 T4030 F4031 K4032 E4033 Y4034 D4035 P4036 D4037 G4038 K4039 G4040 V4041 I4042 S4043 K4044 R4045 D4046 F4047 H4048 K4049 A4050 M4051 E4052 S4053 H4054 K4055 H4056 Y4057 T4058 Q4059 S4060 E4061 T4062 E4063 F4064 L4065 L4066 S4067 C4068 A4069 E4070 T4071 D4072 E4073 N4074 E4075 T4076 L4077 D4078
Y4079 E4080 E4081 F4082 V4083 K4084 R4085 F4086 H4087 E4088 P4089 A4090 K4091 D4092 I4093 L4100 L4104 S4105 E4106 H4107 M4108 P4109 N4110 D4111 T4112 R4113 L4114 Q4115 T4116 F4117 L4118 E4119 L4120 A4121 E4122 N4126 Q4129 L4132 G4133 R4134 G4139 K4142 R4143 I4144 E4145 R4146 E4153 W4159 E4160 E4166
S4167 K4168 R4169 T4172 F4173 D4174 V4175 V4176 N4177 E4178 G4179 G4180 E4181 K4182 E4183 K4184 M4185 E4186 V4189 D4194 T4195 T4205 SER GLU SER ASP LEU ASN GLU ARG LEU ALA ASN LYS GLU GLU SER GLU LYS LYS GLU ARG PRO GLU GLU GLN ALA PRO ARG MET GLY PHE PHE SER LEU LEU THR
ILE GLN SER ALA LEU PHE ALA LEU ARG TYR ASN VAL LEU THR LEU VAL ARG MET LEU SER LEU LYS SER LEU LYS LYS GLN MET LYS ARG MET LYS LYS MET THR VAL LYS ASP MET VAL LEU ALA PHE PHE SER SER TYR TRP SER VAL PHE VAL THR LEU LEU HIS PHE VAL ALA SER
VAL CYS ARG GLY PHE PHE ARG ILE VAL SER SER LEU LEU LEU GLY GLY SER LEU VAL GLU GLY GLY ALA LYS LYS ILE LYS LYS VAL ALA GLU GLU LEU ASN MET PRO ASP PRO PRO THR GLN ASP GLU VAL ARG GLY ASP GLU GLU GLY GLU ARG LYS PRO LEU GLU SER ALA LEU PRO SER
GLU ASP LEU THR ASP LEU LYS GLU LEU THR GLU GLU SER ASP LEU LEU SER ASP ILE PHE GLY LEU ASP LYS LEU LYS ARG GLU GLY GLN TYR LYS LEU ILE PRO HIS ASN PRO ASN ALA GLY LEU SER ASP LEU MET THR ASN PRO VAL PRO GLU VAL GLN GLU LYS PHE GLN
GLU GLN LYS ALA LYS GLU GLU LYS GLU GLU PRO GLU LYS ALA GLU GLY GLU ASP GLY GLU LYS GLU GLU LYS ALA LYS ASP GLU LYS SER LYS GLN LYS LEU ARG GLN LEU VAL THR HIS THR HIS ARG TYR GLY GLU PRO GLU VAL PRO GLU GLU SER ALA F4478 W4479
K4480 K4481 I4482 I4483 A4484 Y4485 Q4486 Q4487 K4488 L4489 L4490 N4491 R4501 F4506 F4517 T4522 S4523 SER VAL VAL GLU GLY LYS GLU LEU PRO THR ARG THR SER SER ASP THR ALA LYS VAL THR ASN SER LEU ASP SER SER PRO HIS ARG ILE ILE A4555 V4556 H4557 E4561 E4562 S4563 S4564
G4565 Y4566 M4567 R4572 T4579 I4586 E4604 K4608 L4609 E4610 F4611 D4612 G4613 L4614 Y4615 A4616 T4617 E4618 Q4619 P4620 S4621 E4622 D4623 D4624 I4625 K4626 G4627 Q4628 W4629 D4630 R4631 L4632 M4635 T4636 Q4637 D4645 K4649 R4650 K4651 V4652 M4653 D4654 K4655 Y4656 C4657 E4658 F4659 R4662 D4663 R4664


E4667
G4670 M4671 D4672 K4673 A4674 A4675 L4676 D4677 F4678
SER ASP ALA ARG GLU LYS LYS LYS PRO LYS LYS ASP SER SER
L4693 S4694 A4695 V4696 L4697 N4698 S4699 I4700 D4701 V4702 K4703 M4706 H4732 L4743 D4744 M4747 R4753 H4761 E4796 D4797 G4798 D4799 T4800 P4801 D4802 R4821
D4828 E4837 D4867 A4868 E4881 D4882 M4883 E4884 G4893 N4894 D4895 D4898 T4899 V4900 P4901 H4902 E4905 Q4910 E4911 L4918 K4941 E4945 W4948 E4949 G4954 D4955 C4956 F4957 R4958 K4959 Q4960 Y4961 E4962
ASP GLN LEU ASN

4 Experimental information (i)

Property	Value	Source
EM reconstruction method	SINGLE PARTICLE	Depositor
Imposed symmetry	POINT, C4	Depositor
Number of particles used	366532	Depositor
Resolution determination method	FSC 0.143 CUT-OFF	Depositor
CTF correction method	PHASE FLIPPING AND AMPLITUDE CORRECTION	Depositor
Microscope	TFS KRIOS	Depositor
Voltage (kV)	300	Depositor
Electron dose ($e^-/Å^2$)	50	Depositor
Minimum defocus (nm)	5000	Depositor
Maximum defocus (nm)	20000	Depositor
Magnification	Not provided	
Image detector	TFS FALCON 4i (4k x 4k)	Depositor
Maximum map value	0.221	Depositor
Minimum map value	-0.089	Depositor
Average map value	0.000	Depositor
Map value standard deviation	0.006	Depositor
Recommended contour level	0.07	Depositor
Map size (Å)	471.04, 471.04, 471.04	wwPDB
Map dimensions	512, 512, 512	wwPDB
Map angles (°)	90.0, 90.0, 90.0	wwPDB
Pixel spacing (Å)	0.92, 0.92, 0.92	Depositor

5 Model quality

5.1 Standard geometry

Bond lengths and bond angles in the following residue types are not validated in this section: ZN, CA, A1MG7

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	0.15	0/8686	0.30	0/11709
1	B	0.15	0/8686	0.30	0/11709
1	C	0.15	0/8686	0.30	0/11709
1	D	0.15	0/8686	0.30	0/11709
All	All	0.15	0/34744	0.30	0/46836

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
1	A	0	1
1	B	0	1
1	C	0	1
1	D	0	1
All	All	0	4

There are no bond length outliers.

There are no bond angle outliers.

There are no chirality outliers.

All (4) planarity outliers are listed below:

Mol	Chain	Res	Type	Group
1	A	3925	GLY	Peptide
1	B	3925	GLY	Peptide
1	C	3925	GLY	Peptide
1	D	3925	GLY	Peptide

5.2 Too-close contacts (i)

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	8502	8299	8299	68	0
1	B	8502	8299	8299	67	0
1	C	8502	8299	8299	68	0
1	D	8502	8299	8299	71	0
2	A	1	0	0	0	0
2	B	1	0	0	0	0
2	C	1	0	0	0	0
2	D	1	0	0	0	0
3	A	1	0	0	0	0
3	B	1	0	0	0	0
3	C	1	0	0	0	0
3	D	1	0	0	0	0
4	A	25	12	0	0	0
4	B	25	12	0	0	0
4	C	25	12	0	0	0
4	D	25	12	0	0	0
All	All	34116	33244	33196	263	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 4.

The worst 5 of 263 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:D:3934:LEU:HD12	1:D:3939:LEU:HD22	1.52	0.92
1:C:3934:LEU:HD12	1:C:3939:LEU:HD22	1.52	0.92
1:B:3934:LEU:HD12	1:B:3939:LEU:HD22	1.52	0.90
1:A:3934:LEU:HD12	1:A:3939:LEU:HD22	1.52	0.89
1:D:3891:TYR:O	1:D:3956:LYS:NZ	2.24	0.71

There are no symmetry-related clashes.

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 PDB entries followed by that with respect to all EM entries.

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	1033/4966 (21%)	1008 (98%)	25 (2%)	0	100	100
1	B	1033/4966 (21%)	1008 (98%)	25 (2%)	0	100	100
1	C	1033/4966 (21%)	1008 (98%)	25 (2%)	0	100	100
1	D	1033/4966 (21%)	1008 (98%)	25 (2%)	0	100	100
All	All	4132/19864 (21%)	4032 (98%)	100 (2%)	0	100	100

There are no Ramachandran outliers to report.

5.3.2 Protein sidechains (i)

In the following table, the Percentiles column shows the percent sidechain outliers of the chain as a percentile score with respect to all PDB entries followed by that with respect to all EM entries.

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	928/4355 (21%)	918 (99%)	10 (1%)	65	79
1	B	928/4355 (21%)	918 (99%)	10 (1%)	65	79
1	C	928/4355 (21%)	918 (99%)	10 (1%)	65	79
1	D	928/4355 (21%)	918 (99%)	10 (1%)	65	79
All	All	3712/17420 (21%)	3672 (99%)	40 (1%)	63	79

5 of 40 residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	C	4586	ILE
1	D	4014	LYS
1	C	4632	LEU

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Continued from previous page...

Mol	Chain	Res	Type
1	D	3969	GLU
1	D	4132	LEU

Sometimes sidechains can be flipped to improve hydrogen bonding and reduce clashes. 5 of 27 such sidechains are listed below:

Mol	Chain	Res	Type
1	C	4096	ASN
1	C	4761	HIS
1	D	4765	GLN
1	C	4637	GLN
1	C	4765	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 oligosaccharides in this entry.

5.6 Ligand geometry (i)

Of 12 ligands modelled in this entry, 8 are monoatomic - leaving 4 for Mogul analysis.

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	$\#\|Z\| > 2$
4	A1MG7	A	5003	-	27,27,27	1.69	5 (18%)	36,38,38	2.57	10 (27%)

Mol	Type	Chain	Res	Link	Bond lengths			Bond angles		
					Counts	RMSZ	$\#\|Z\|>2$	Counts	RMSZ	$\#\|Z\|>2$
4	A1MG7	C	5003	-	27,27,27	1.68	5 (18%)	36,38,38	2.57	10 (27%)
4	A1MG7	B	5003	-	27,27,27	1.68	5 (18%)	36,38,38	2.57	10 (27%)
4	A1MG7	D	5003	-	27,27,27	1.68	5 (18%)	36,38,38	2.56	10 (27%)

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
4	A1MG7	A	5003	-	-	0/16/16/16	0/3/3/3
4	A1MG7	C	5003	-	-	0/16/16/16	0/3/3/3
4	A1MG7	B	5003	-	-	0/16/16/16	0/3/3/3
4	A1MG7	D	5003	-	-	0/16/16/16	0/3/3/3

The worst 5 of 20 bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
4	A	5003	A1MG7	C-NAO	5.00	1.45	1.35
4	D	5003	A1MG7	C-NAO	5.00	1.45	1.35
4	B	5003	A1MG7	C-NAO	4.99	1.45	1.35
4	C	5003	A1MG7	C-NAO	4.99	1.45	1.35
4	A	5003	A1MG7	N-NAH	3.43	1.37	1.33

The worst 5 of 40 bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
4	A	5003	A1MG7	CAG-NAH-N	8.29	108.26	101.70
4	B	5003	A1MG7	CAG-NAH-N	8.29	108.26	101.70
4	C	5003	A1MG7	CAG-NAH-N	8.29	108.26	101.70
4	D	5003	A1MG7	CAG-NAH-N	8.29	108.26	101.70
4	C	5003	A1MG7	NAH-N-NAJ	-7.48	107.69	114.03

There are no chirality outliers.

There are no torsion outliers.

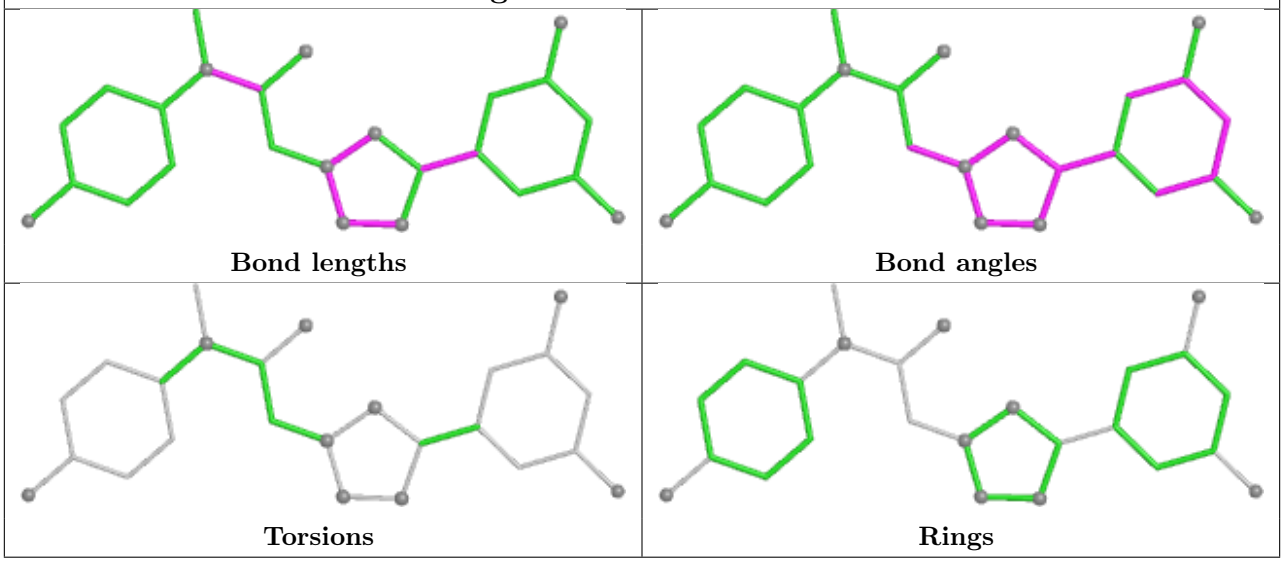
There are no ring outliers.

No monomer is involved in short contacts.

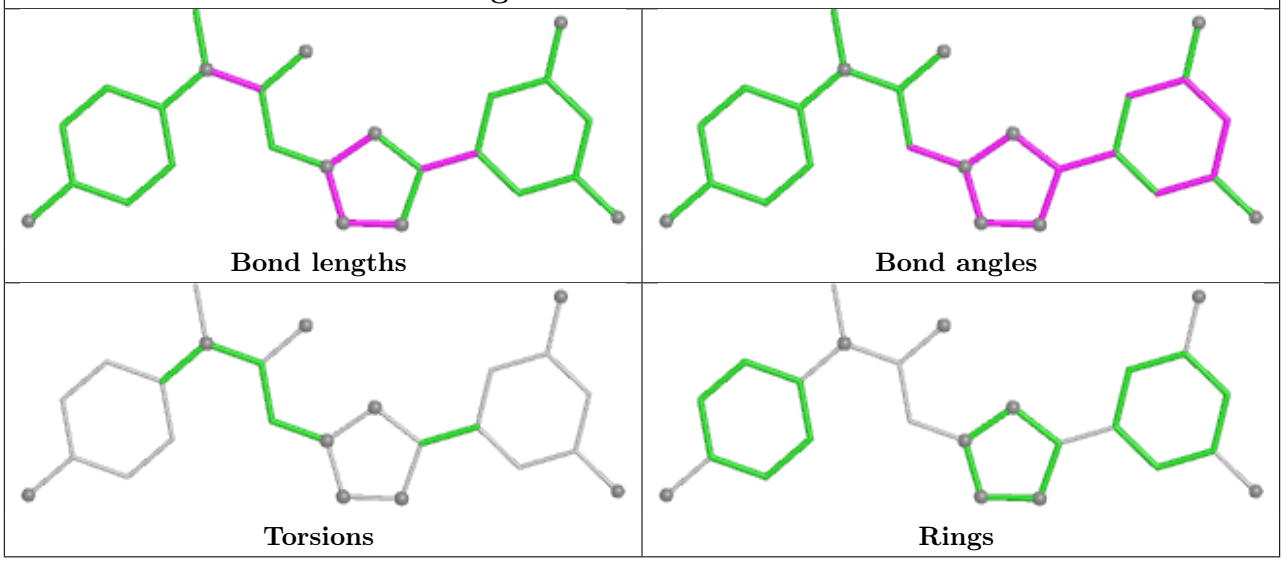
The following is a two-dimensional graphical depiction of Mogul quality analysis of bond lengths, bond angles, torsion angles, and ring geometry for all instances of the Ligand of Interest. In addition, ligands with molecular weight > 250 and outliers as shown on the validation Tables will

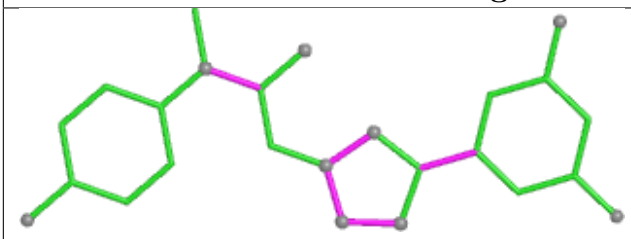
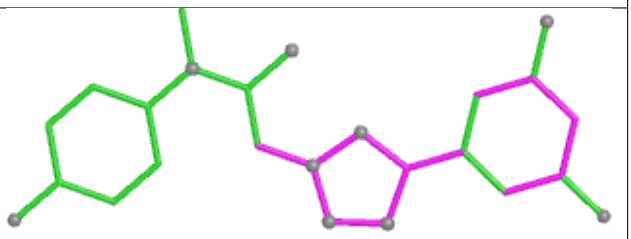
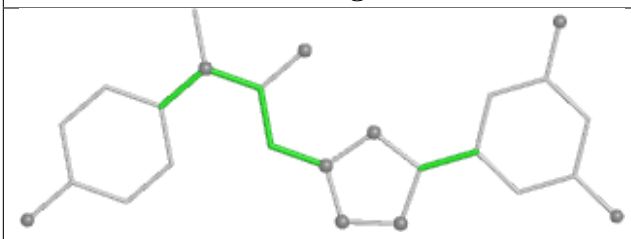
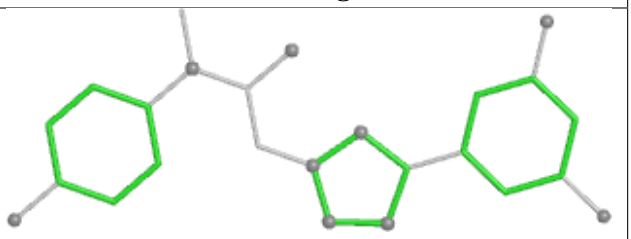
also be included. For torsion angles, if less then 5% of the Mogul distribution of torsion angles is within 10 degrees of the torsion angle in question, then that torsion angle is considered an outlier. Any bond that is central to one or more torsion angles identified as an outlier by Mogul will be highlighted in the graph. For rings, the root-mean-square deviation (RMSD) between the ring in question and similar rings identified by Mogul is calculated over all ring torsion angles. If the average RMSD is greater than 60 degrees and the minimal RMSD between the ring in question and any Mogul-identified rings is also greater than 60 degrees, then that ring is considered an outlier. The outliers are highlighted in purple. The color gray indicates Mogul did not find sufficient equivalents in the CSD to analyse the geometry.

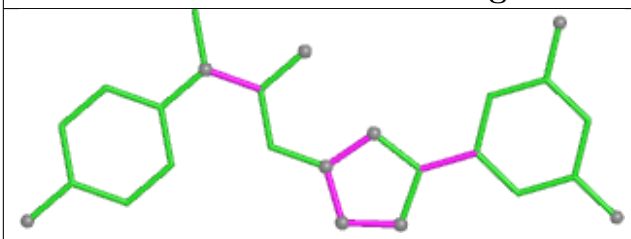
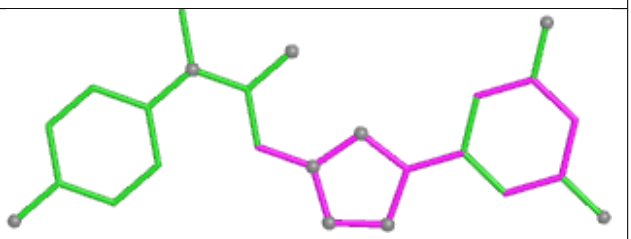
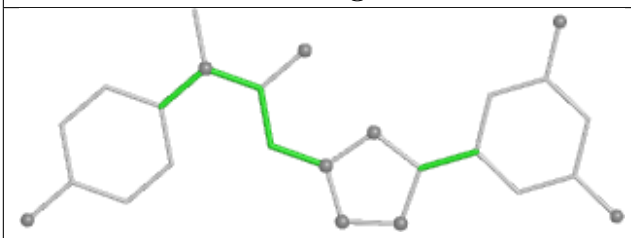
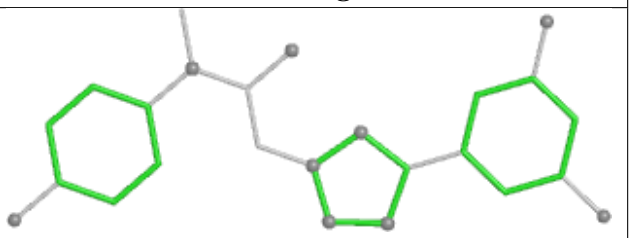
Ligand A1MG7 A 5003



Ligand A1MG7 C 5003



Ligand A1MG7 B 5003	
 Bond lengths	 Bond angles
 Torsions	 Rings

Ligand A1MG7 D 5003	
 Bond lengths	 Bond angles
 Torsions	 Rings

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.

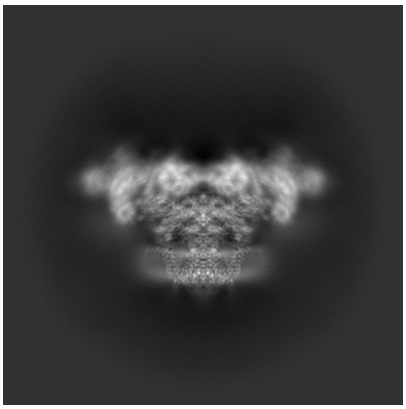
6 Map visualisation

This section contains visualisations of the EMDB entry EMD-80690. These allow visual inspection of the internal detail of the map and identification of artifacts.

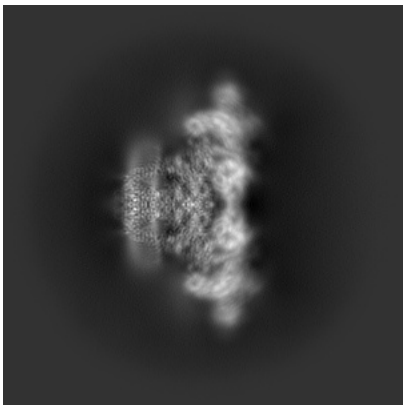
Images derived from a raw map, generated by summing the deposited half-maps, are presented below the corresponding image components of the primary map to allow further visual inspection and comparison with those of the primary map.

6.1 Orthogonal projections

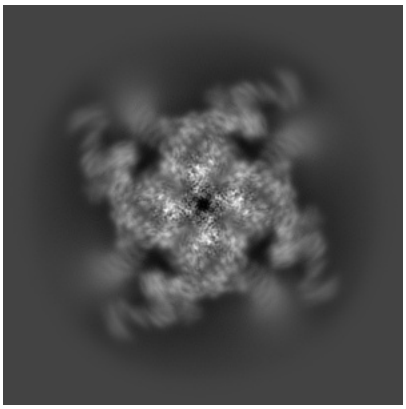
6.1.1 Primary map



X

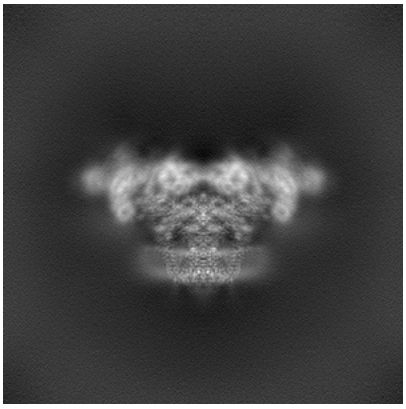


Y

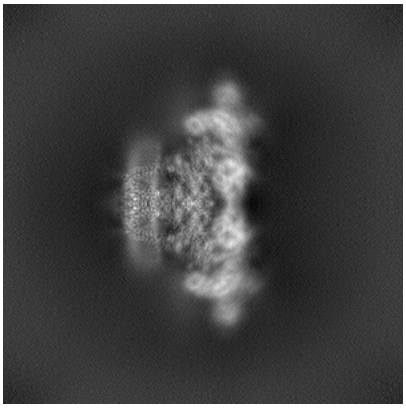


Z

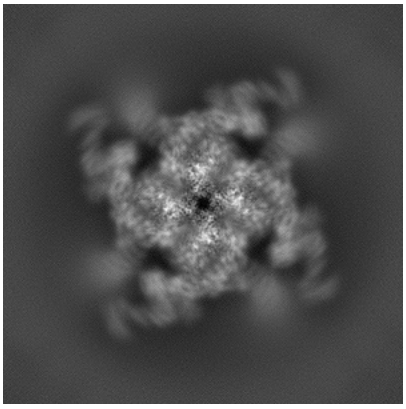
6.1.2 Raw map



X



Y

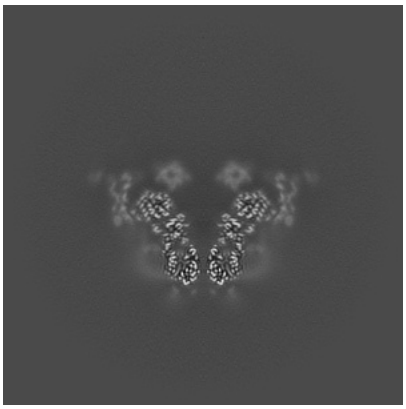


Z

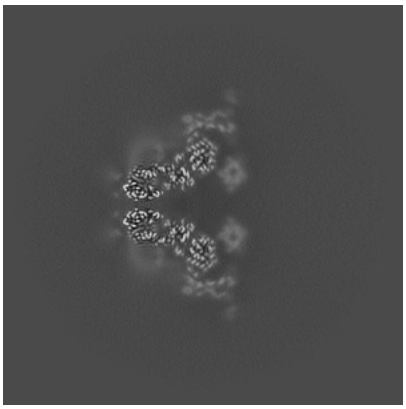
The images above show the map projected in three orthogonal directions.

6.2 Central slices (i)

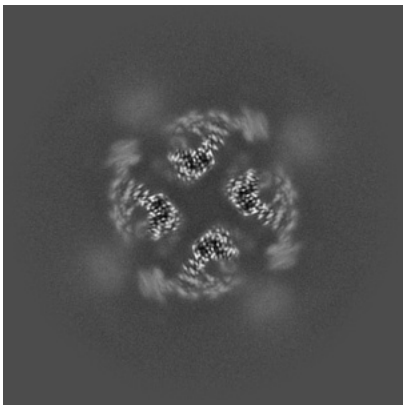
6.2.1 Primary map



X Index: 256

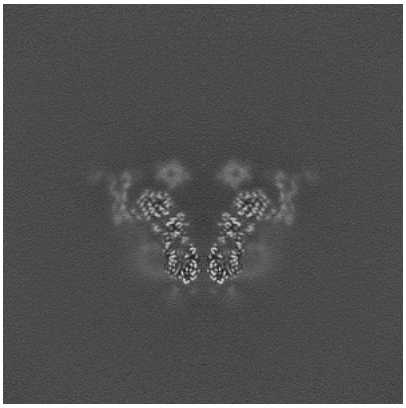


Y Index: 256

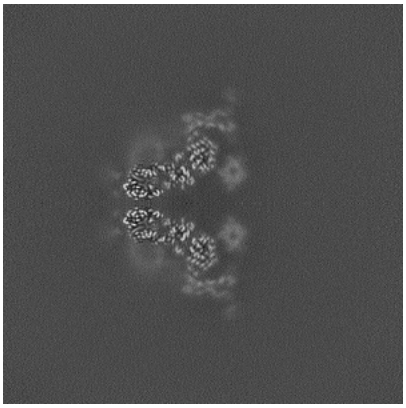


Z Index: 256

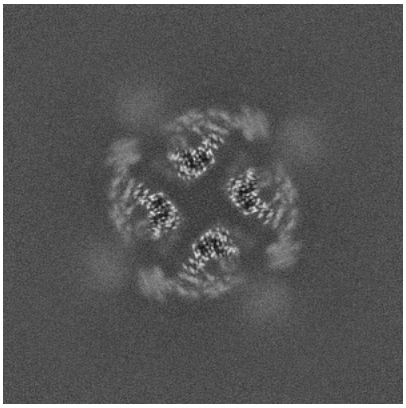
6.2.2 Raw map



X Index: 256



Y Index: 256

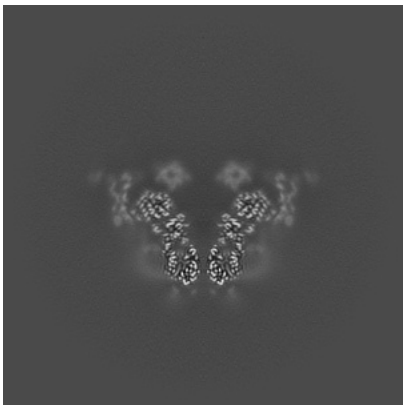


Z Index: 256

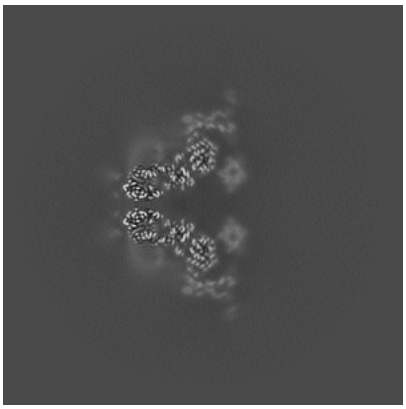
The images above show central slices of the map in three orthogonal directions.

6.3 Largest variance slices (i)

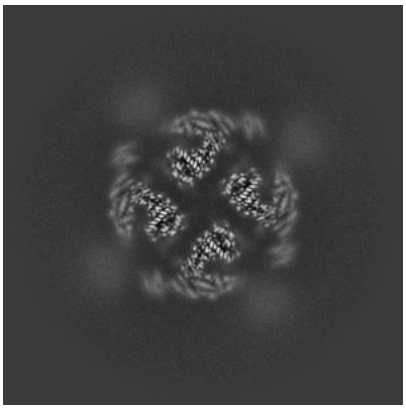
6.3.1 Primary map



X Index: 256

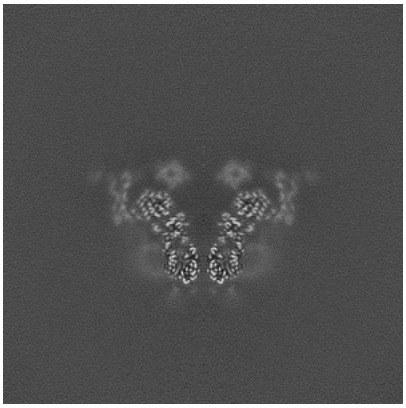


Y Index: 256

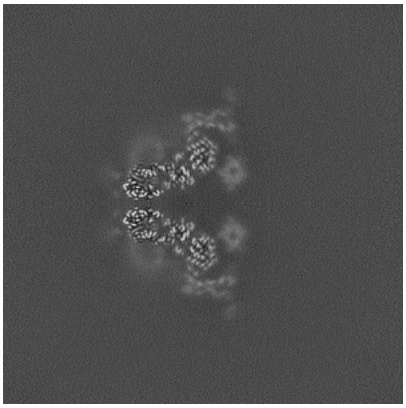


Z Index: 251

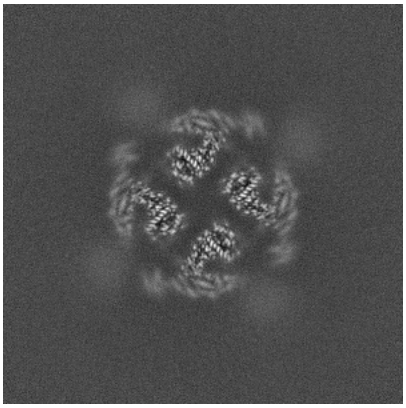
6.3.2 Raw map



X Index: 256



Y Index: 256

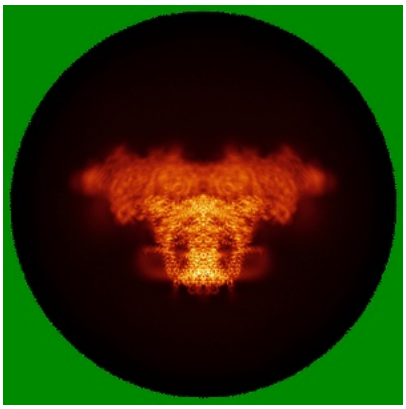


Z Index: 251

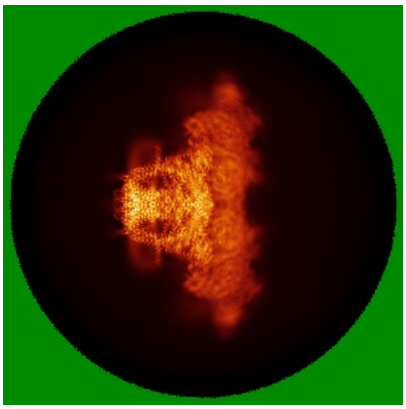
The images above show the largest variance slices of the map in three orthogonal directions.

6.4 Orthogonal standard-deviation projections (False-color) (i)

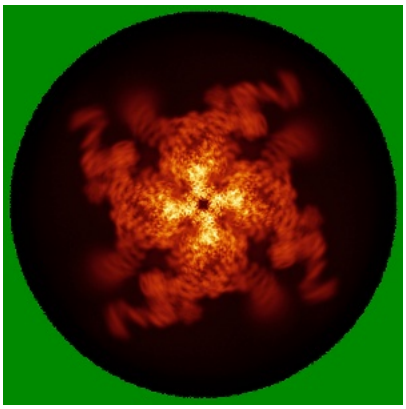
6.4.1 Primary map



X

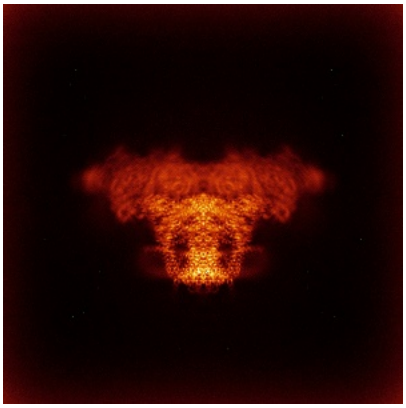


Y

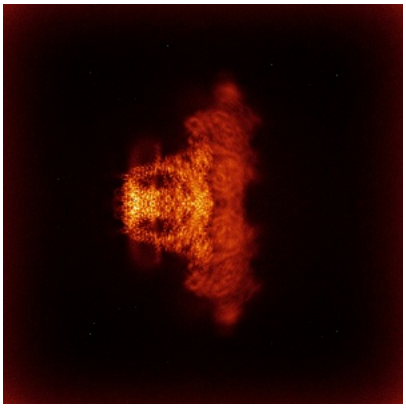


Z

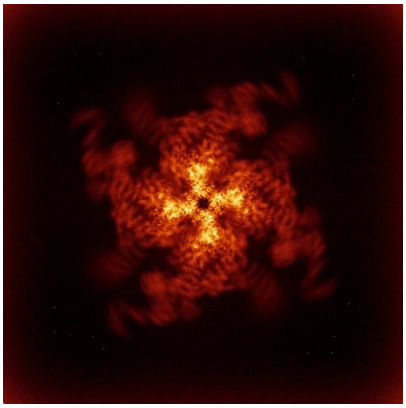
6.4.2 Raw map



X



Y



Z

The images above show the map standard deviation projections with false color in three orthogonal directions. Minimum values are shown in green, max in blue, and dark to light orange shades represent small to large values respectively.

6.5 Orthogonal surface views (i)

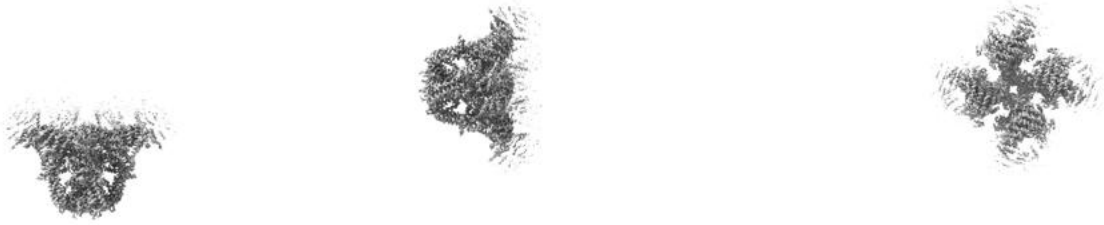
6.5.1 Primary map



X Y Z

The images above show the 3D surface view of the map at the recommended contour level 0.07. These images, in conjunction with the slice images, may facilitate assessment of whether an appropriate contour level has been provided.

6.5.2 Raw map



X Y Z

These images show the 3D surface of the raw map. The raw map's contour level was selected so that its surface encloses the same volume as the primary map does at its recommended contour level.

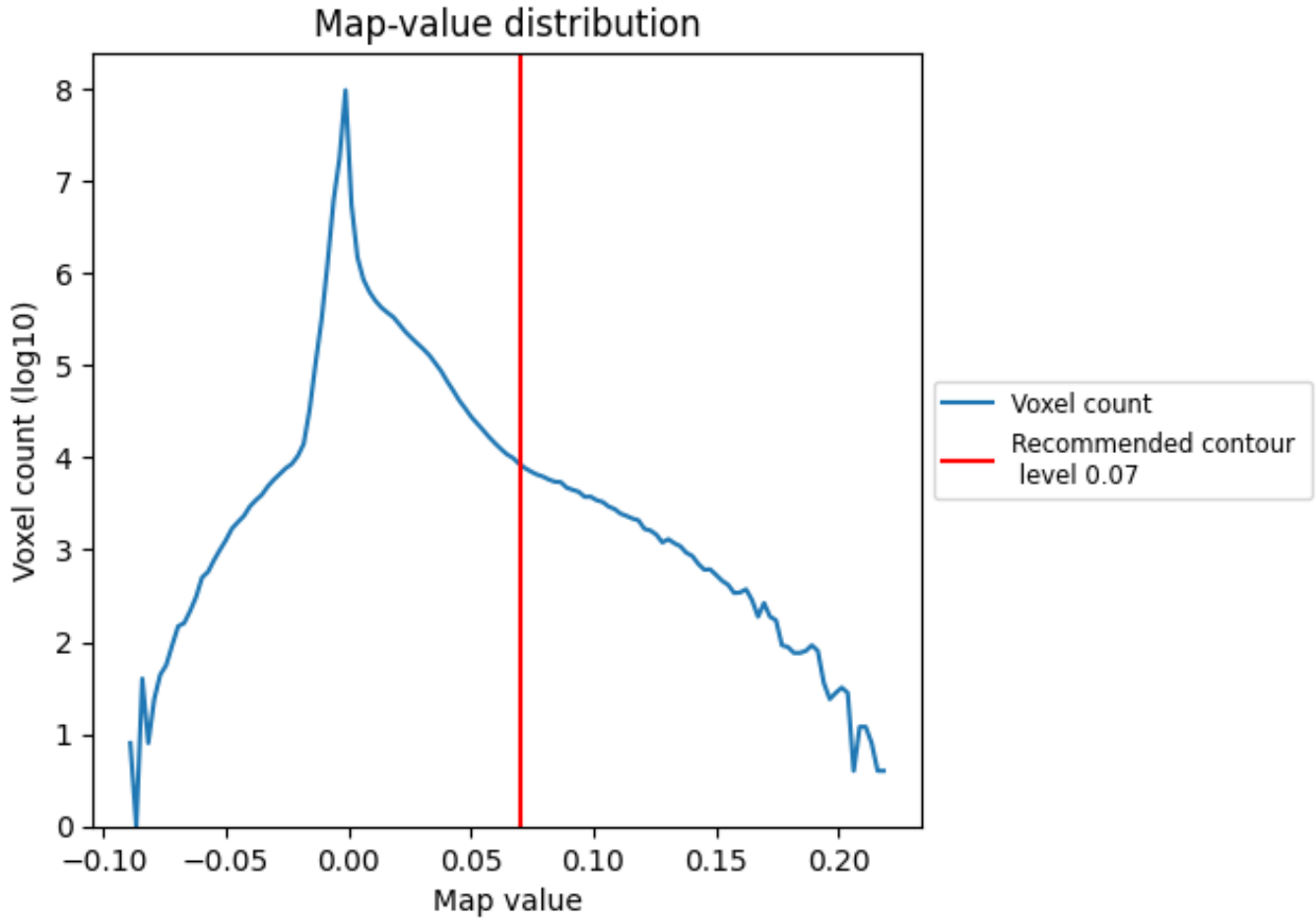
6.6 Mask visualisation (i)

This section was not generated. No masks/segmentation were deposited.

7 Map analysis

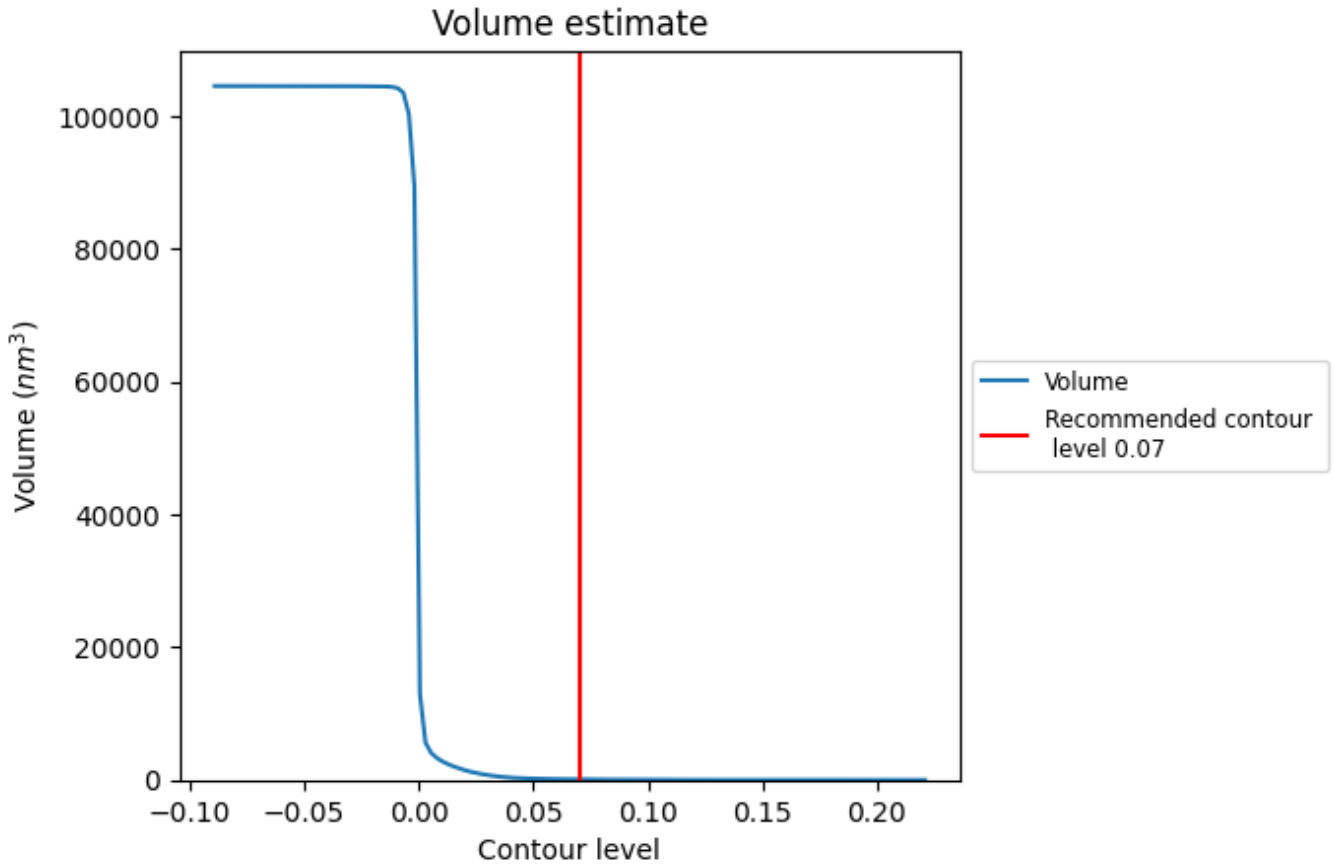
This section contains the results of statistical analysis of the map.

7.1 Map-value distribution



The map-value distribution is plotted in 128 intervals along the x-axis. The y-axis is logarithmic. A spike in this graph at zero usually indicates that the volume has been masked.

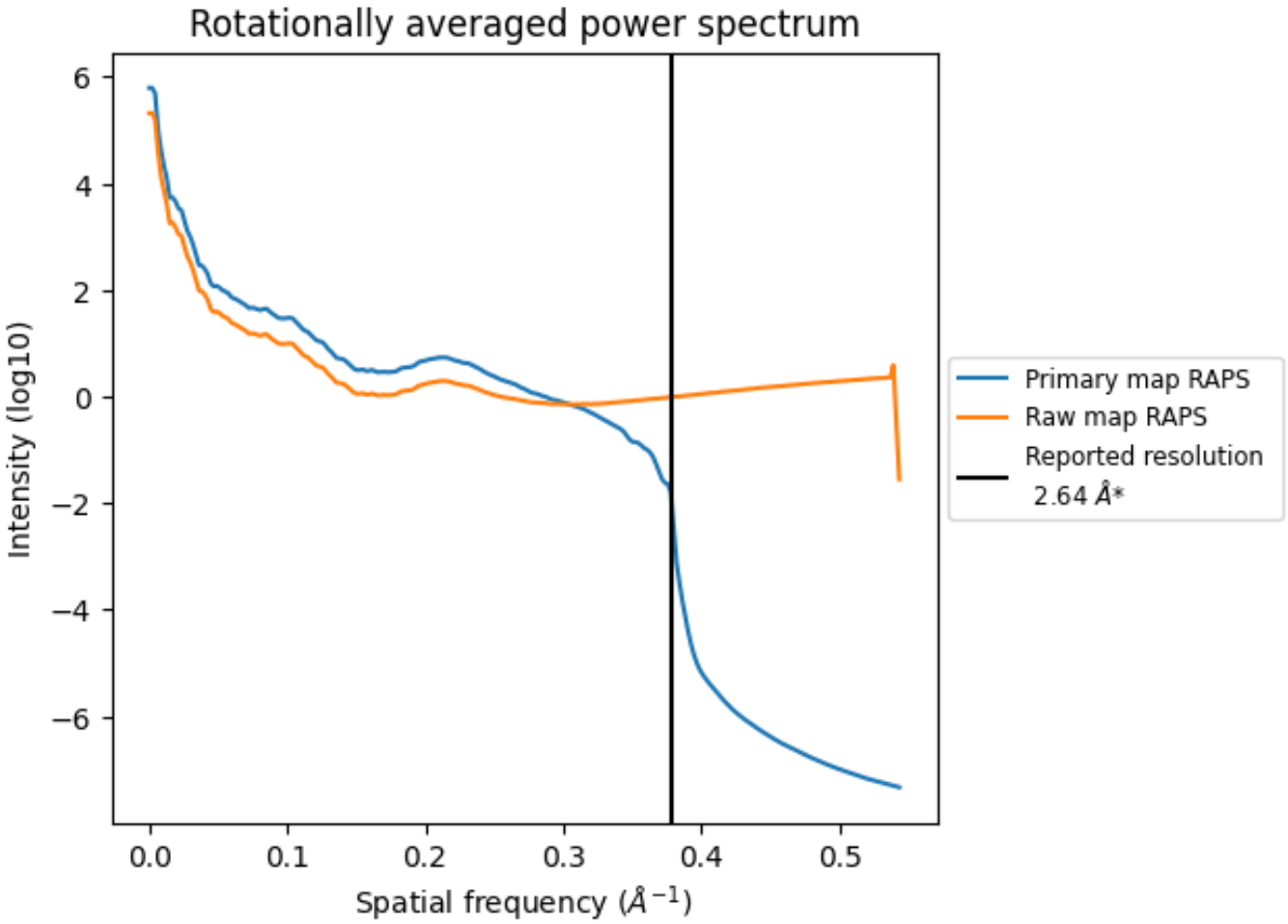
7.2 Volume estimate (i)



The volume at the recommended contour level is 87 nm^3; this corresponds to an approximate mass of 78 kDa.

The volume estimate graph shows how the enclosed volume varies with the contour level. The recommended contour level is shown as a vertical line and the intersection between the line and the curve gives the volume of the enclosed surface at the given level.

7.3 Rotationally averaged power spectrum (i)

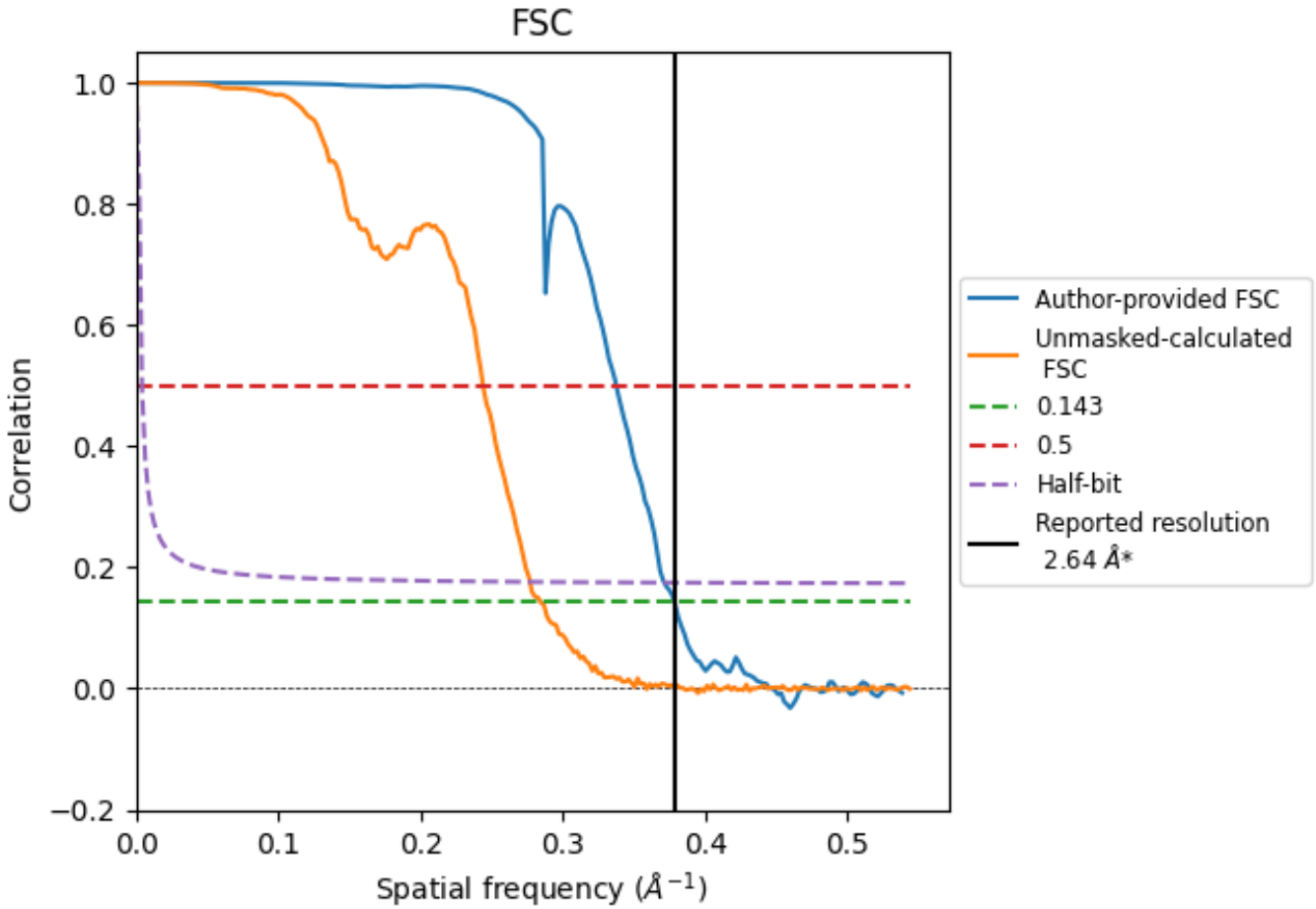


*Reported resolution corresponds to spatial frequency of 0.379 Å^{-1}

8 Fourier-Shell correlation

Fourier-Shell Correlation (FSC) is the most commonly used method to estimate the resolution of single-particle and subtomogram-averaged maps. The shape of the curve depends on the imposed symmetry, mask and whether or not the two 3D reconstructions used were processed from a common reference. The reported resolution is shown as a black line. A curve is displayed for the half-bit criterion in addition to lines showing the 0.143 gold standard cut-off and 0.5 cut-off.

8.1 FSC



*Reported resolution corresponds to spatial frequency of 0.379 Å^{-1}

8.2 Resolution estimates (i)

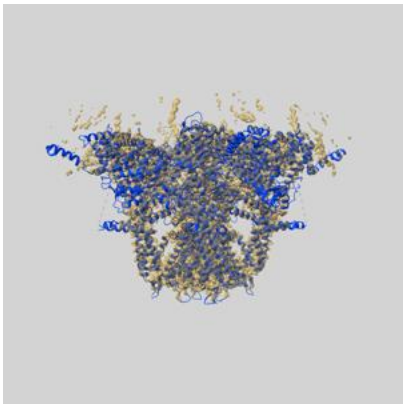
Resolution estimate (Å)	Estimation criterion (FSC cut-off)		
	0.143	0.5	Half-bit
Reported by author	2.64	-	-
Author-provided FSC curve	2.64	2.96	2.69
Unmasked-calculated*	3.52	4.10	3.61

*Resolution estimate based on FSC curve calculated by comparison of deposited half-maps. The value from deposited half-maps intersecting FSC 0.143 CUT-OFF 3.52 differs from the reported value 2.64 by more than 10 %

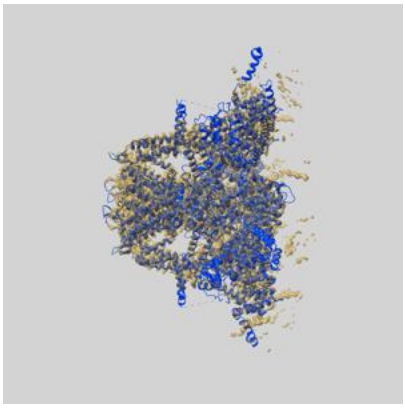
9 Map-model fit

This section contains information regarding the fit between EMDB map EMD-80690 and PDB model 26IV. Per-residue inclusion information can be found in section 3 on page 5.

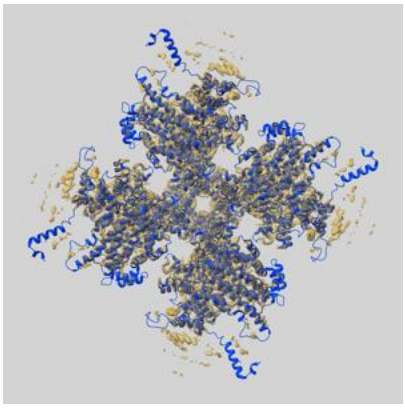
9.1 Map-model overlay



X



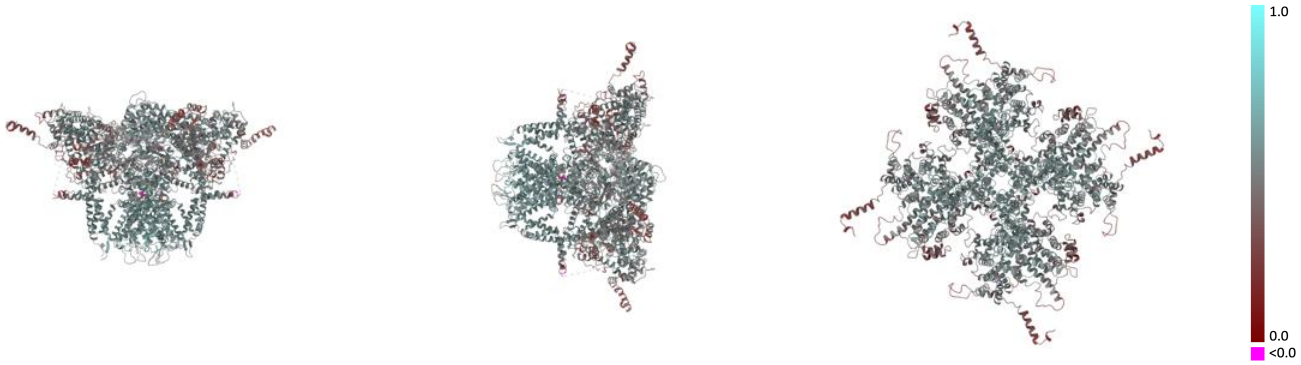
Y



Z

The images above show the 3D surface view of the map at the recommended contour level 0.07 at 50% transparency in yellow overlaid with a ribbon representation of the model coloured in blue. These images allow for the visual assessment of the quality of fit between the atomic model and the map.

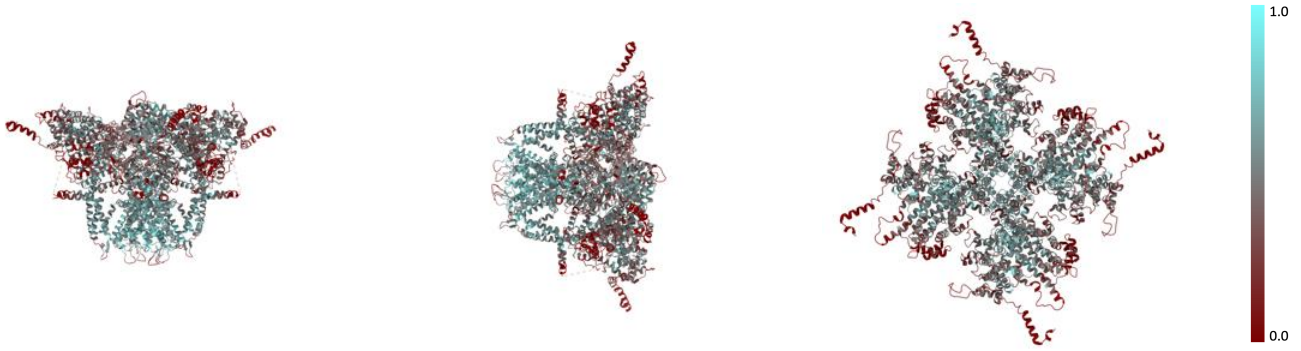
9.2 Q-score mapped to coordinate model (i)



X Y Z

The images above show the model with each residue coloured according its Q-score. This shows their resolvability in the map with higher Q-score values reflecting better resolvability. Please note: Q-score is calculating the resolvability of atoms, and thus high values are only expected at resolutions at which atoms can be resolved. Low Q-score values may therefore be expected for many entries.

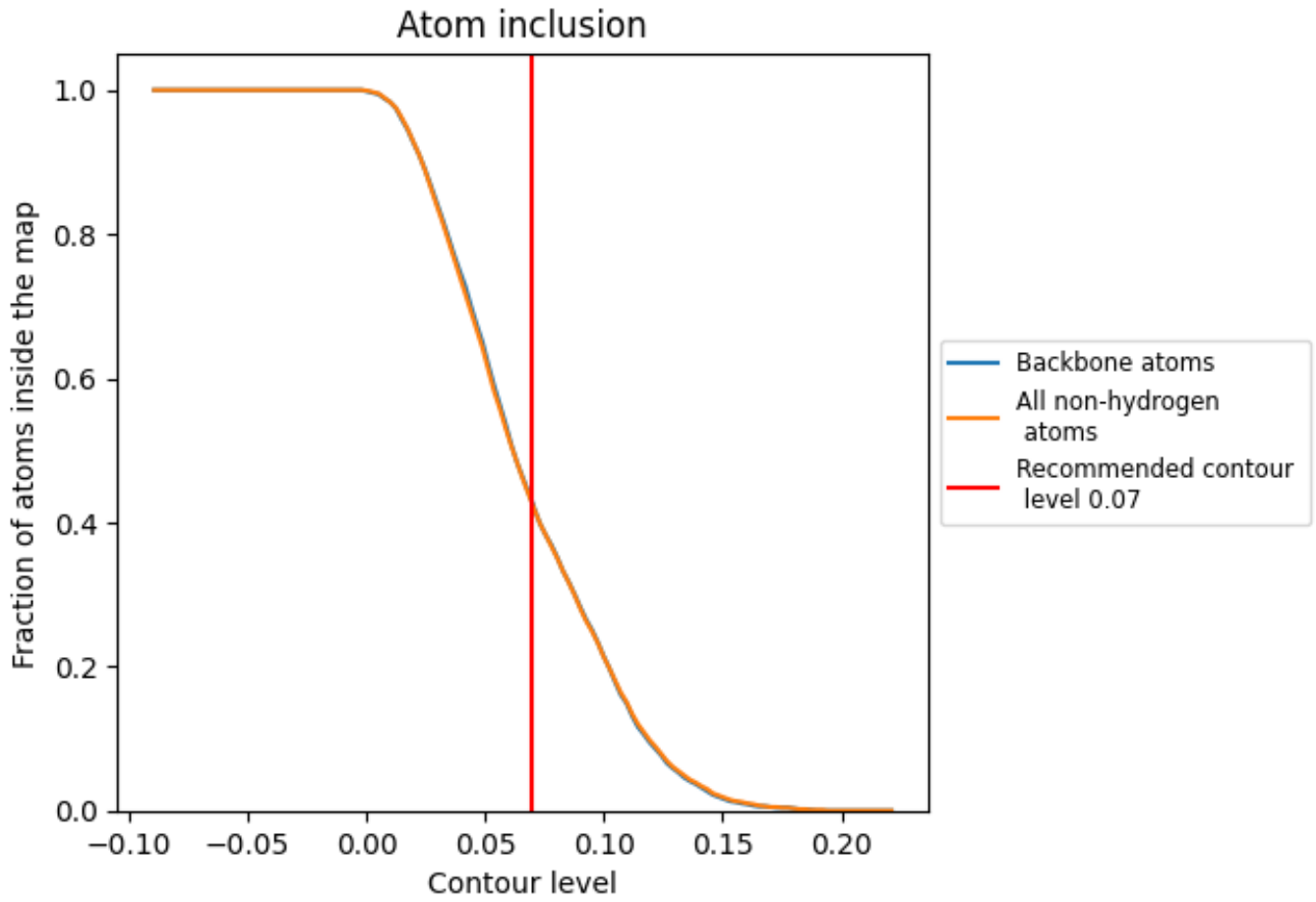
9.3 Atom inclusion mapped to coordinate model (i)



X Y Z

The images above show the model with each residue coloured according to its atom inclusion. This shows to what extent they are inside the map at the recommended contour level (0.07).

9.4 Atom inclusion (i)



At the recommended contour level, 43% of all backbone atoms, 42% of all non-hydrogen atoms, are inside the map.

9.5 Map-model fit summary

The table lists the average atom inclusion at the recommended contour level (0.07) and Q-score for the entire model and for each chain.



Chain	Atom inclusion	Q-score
All	0.4240	0.4980
A	0.4310	0.4990
B	0.4320	0.4980
C	0.4310	0.4980
D	0.4310	0.4980