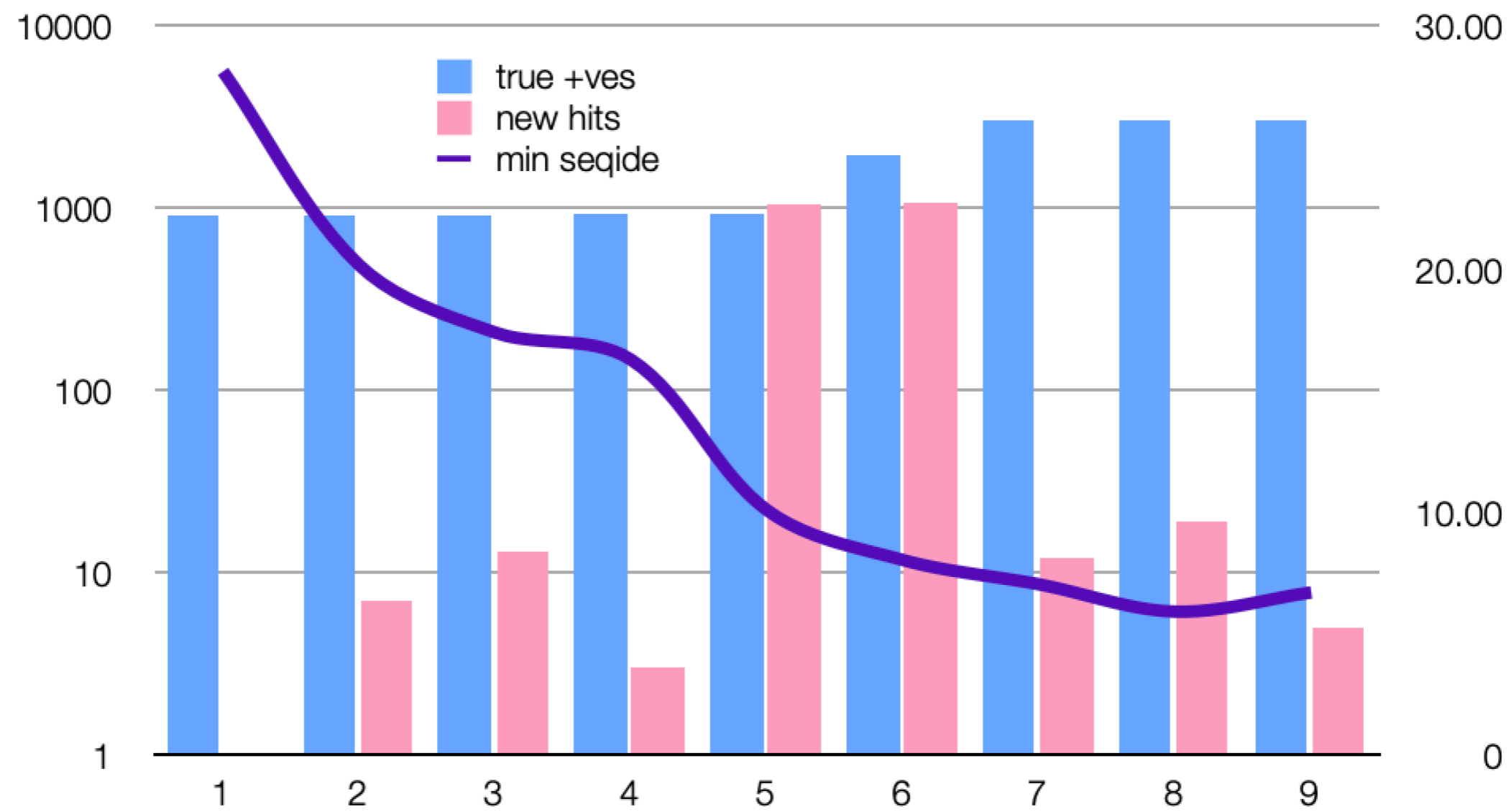


Figure S1





# Figure S3

(a)

```
SLPFGLIIVGVALLAVFQASAKIITLKKRWQLALSKGVHFC-----VAA 45
SLPFGLIIVGVALLAVFQASAKIITLKKRWQLALSKGVHFCNLLLEFVTVYSHLLVA 99
GLEAPFLYLYALVYFLOSINEV---R---KCRSKNPLLYDANYFLCWETNICYDYCIE 96
GLEAPFLYLYALVYFLOSINEVRIIMRLNCKRKRKPLLYDANYFLCWETNICYDYCIE 159
YNSV-----ITSGDGTTSPISEHDIYQGGYTERWESGVKDCVVLRSYFTSDYYQLYSTOL 151
YNSVTS-----ITSGDGTTSPISEHDIYQGGYTERWESGVKDCVVLRSYFTSDYYQLYSTOL 219
STDGVEHVTFFIYNKIVD 170
STDGVEHVTFFIYNKIVD 238
```

(b)

```
AGDI CLTIFLLVYIISWFLRADSI PAVIL--RFALTITGTF-----IA 42
SLPFGLIIVGVALLAVFQASAKIITLKKRWQLALSKGVHFCNLLLEFVTVYSHLLVA 99
VAVTIVAY-----VG---C---RCVSWLPLMADDDCFVVCYQSGGYNYCFPE 81
GLEAPFLYLYALVYFLOSINEVRIIMRLNCKRKRKPLLYDANYFLCWETNICYDYCIE 159
YDP-----NGPYVTLTVHNNGVTCGSHTIYGSVSVADRIQVVTIRNKNSYIQLONTF 132
YNSVTS-----ITSGDGTTSPISEHDIYQGGYTERWESGVKDCVVLRSYFTSDYYQLYSTOL 219
--DTGICIIAFYIADIAV- 148
STDGVEHVTFFIYNKIVD 238
```

(c)

```
TADIMLCIFLVIYLCYFLRSDSFIADVFKYLAGLLTGGFLC-----ATI 45
SLPFGLIIVGVALLAVFQASAKIITLKKRWQLALSKGVHFCNLLLEFVTVYSHLLVA 99
GVV-----LFMFSLGI---C---RCKSLVPLCADDCCFVNYVAGGKPYCMP 86
GLEAPFLYLYALVYFLOSINEVRIIMRLNCKRKRKPLLYDANYFLCWETNICYDYCIE 159
FDP-----NEPYLTLVHQNGITCGSYKLYGDVSIADRIYLYTLTKSVPYSLONTF 137
YNSVTS-----ITSGDGTTSPISEHDIYQGGYTERWESGVKDCVVLRSYFTSDYYQLYSTOL 219
--DAELCTIAFYIADIAVI 154
STDGVEHVTFFIYNKIVD 238
```

(d)

```
AYANRRFLYIIKLIFLWLLWPVTLACFVLAAYRINWITGG-----IA 43
SLPFGLIIVGVALLAVFQASAKIITLKKRWQLALSKGVHFCNLLLEFVTVYSHLLVA 98
IAMACLVRMLWLSYFIASFRLF---A---RTRSMWSEFNPELNILNVPVHGTILTRP 94
GLEAPFLYLYALVYFLOSINEVRIIMRLNCKRKRKPLLYDANYFLCWETNICYDYCIE 158
LLEG-----AVILRGHLRIAGHHLGRCDIK-----DLPKEITVATSRTLSYYKLGASO 142
YNSVTS-----ITSGDGTTSPISEHDIYQGGYTERWESGVKDCVVLRSYFTSDYYQLYSTOL 218
--RVAGDSGFAAYSRYRIGN- 160
STDGVEHVTFFIYNKIVD 238
```

(e)

```
AYANRRFLYIIKLIFLWLLWPVTLACFVLAAYRINWITGG-----IA 43
SLPFGLIIVGVALLAVFQASAKIITLKKRWQLALSKGVHFCNLLLEFVTVYSHLLVA 99
IAMACLVRMLWLSYFIASFRLF---A---RTRSMWSEFNPELNILNVPVHGTILTRP 94
GLEAPFLYLYALVYFLOSINEVRIIMRLNCKRKRKPLLYDANYFLCWETNICYDYCIE 159
LLEG-----AVILRGHLRIAGHHLGRCDIK-----DLPKEITVATSRTLSYYKLGASO 141
YNSVTS-----ITSGDGTTSPISEHDIYQGGYTERWESGVKDCVVLRSYFTSDYYQLYSTOL 219
--RVAGDSGFAAYSRYRIGN 159
STDGVEHVTFFIYNKIVD 238
```

(f)

```
AYANRRFLYIIKLIFLWLLWPVTLACFVLAAYRINWITGG-----IA 43
SLPFGLIIVGVALLAVFQASAKIITLKKRWQLALSKGVHFCNLLLEFVTVYSHLLVA 99
IAMTCLVRMLWLSYFIASFRLF---A---RTRSMWSEFNPELNILNVPVHGTILTRP 94
GLEAPFLYLYALVYFLOSINEVRIIMRLNCKRKRKPLLYDANYFLCWETNICYDYCIE 159
LLEG-----AVILRGHLRIAGHHLGRCDIK-----DLPKEITVATSRTLSYYKLGASO 142
YNSVTS-----ITSGDGTTSPISEHDIYQGGYTERWESGVKDCVVLRSYFTSDYYQLYSTOL 219
--RVAGDSGFAAYSRYRIGN 160
STDGVEHVTFFIYNKIVD 238
```

(g)

```
AYSNRRFLYIIKLIFLWLLWPVTLACFVLAAYRINWITGG-----IA 43
SLPFGLIIVGVALLAVFQASAKIITLKKRWQLALSKGVHFCNLLLEFVTVYSHLLVA 99
IAMACIVRMLWLSYFVASFRLF---A---RTRSMWSEFNPELNILNVPVHGTILTRP 94
GLEAPFLYLYALVYFLOSINEVRIIMRLNCKRKRKPLLYDANYFLCWETNICYDYCIE 159
LLEG-----AVILRGHLRMAGHSLGRCDIK-----DLPKEITVATSRTLSYYKLGASO 142
YNSVTS-----ITSGDGTTSPISEHDIYQGGYTERWESGVKDCVVLRSYFTSDYYQLYSTOL 219
--RVADSGFAVYHRYRIGN 160
STDGVEHVTFFIYNKIVD 238
```

(h)

```
AYATRSLLYIILKLVLLWLLWPVTLACFVLAAYRINWITGG-----IA 43
SLPFGLIIVGVALLAVFQASAKIITLKKRWQLALSKGVHFCNLLLEFVTVYSHLLVA 99
ITFAIIVRMLWLSYFVASFRLF---R---RTGSAWSEFNPELNILNVPVHGTILTRP 94
GLEAPFLYLYALVYFLOSINEVRIIMRLNCKRKRKPLLYDANYFLCWETNICYDYCIE 159
LQEV-----ATVARGVAVFAGHKLGRADL-----ESLPNEITVATSRTLSYFKMSRKY 142
YNSVTS-----ITSGDGTTSPISEHDIYQGGYTERWESGVKDCVVLRSYFTSDYYQLYSTOL 219
--NIGVSGVATYLRKIVGN 160
STDGVEHVTFFIYNKIVD 238
```

(i)

```
AYATRNLLYIILKLVLLWLLWPVTLACFVLAAYRINWITGG-----IA 43
SLPFGLIIVGVALLAVFQASAKIITLKKRWQLALSKGVHFCNLLLEFVTVYSHLLVA 99
VFFASAIRMLWLSYFVASFRLF---R---RTGSAWSEFNPELNILNVPVHGTILTRP 94
GLEAPFLYLYALVYFLOSINEVRIIMRLNCKRKRKPLLYDANYFLCWETNICYDYCIE 159
VPEV-----ATVYRSHLIVAGHKLGRADLSSISTE-----VTVATARTLSYKLSWRKE 143
YNSVTS-----ITSGDGTTSPISEHDIYQGGYTERWESGVKDCVVLRSYFTSDYYQLYSTOL 219
AGACN--GVVYLRKIVGN 160
STDGVEHVTFFIYNKIVD 238
```

**Figure S4**

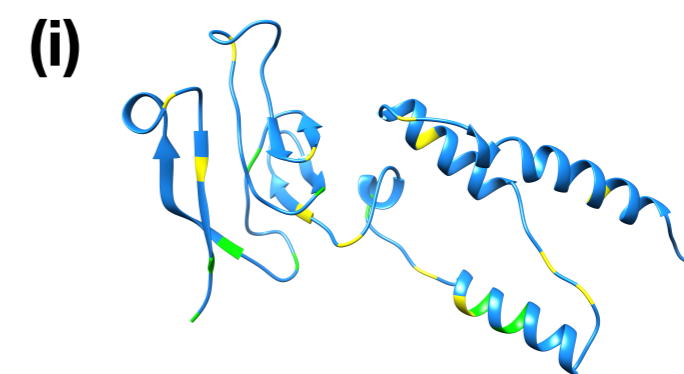
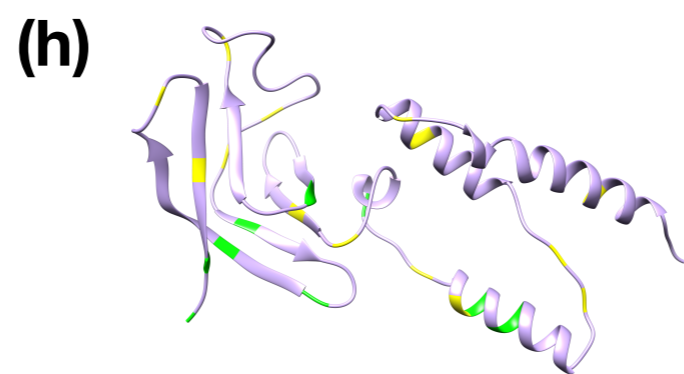
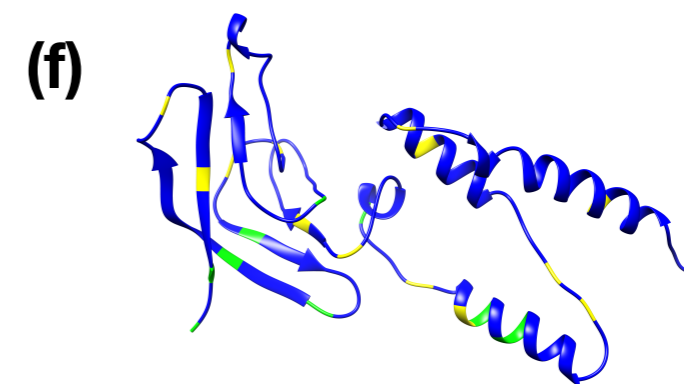
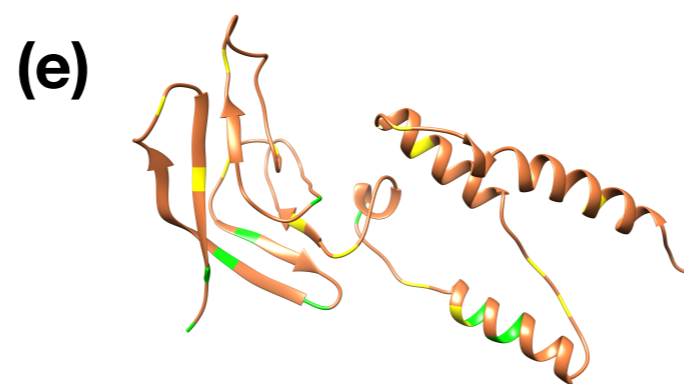
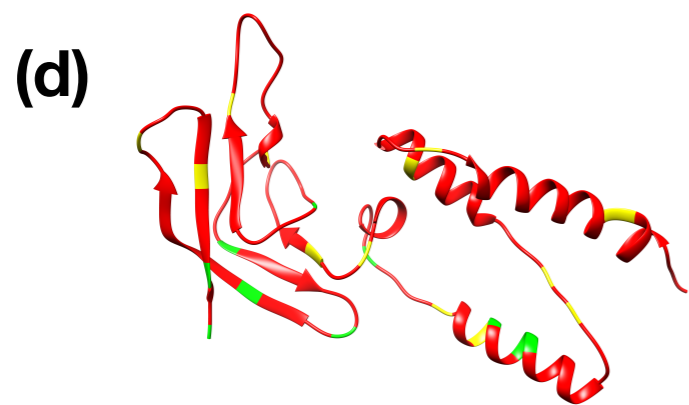
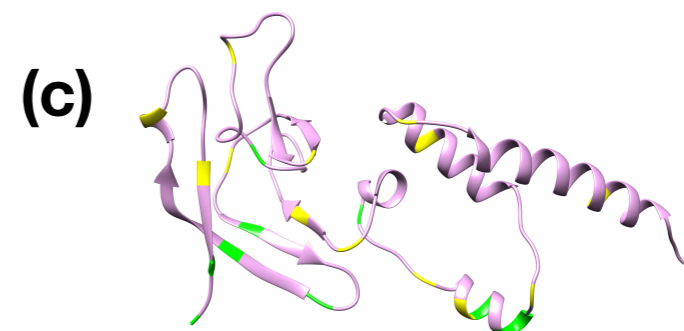
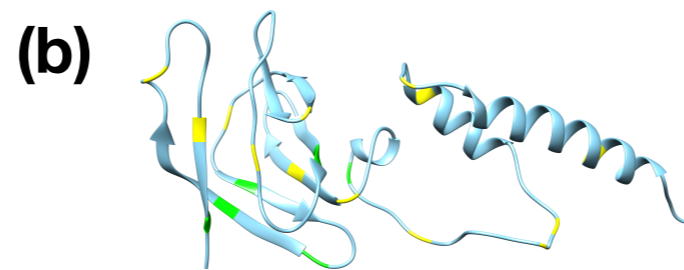
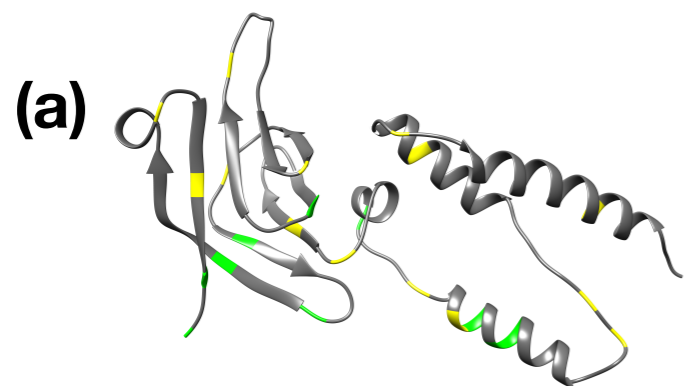


Figure S5

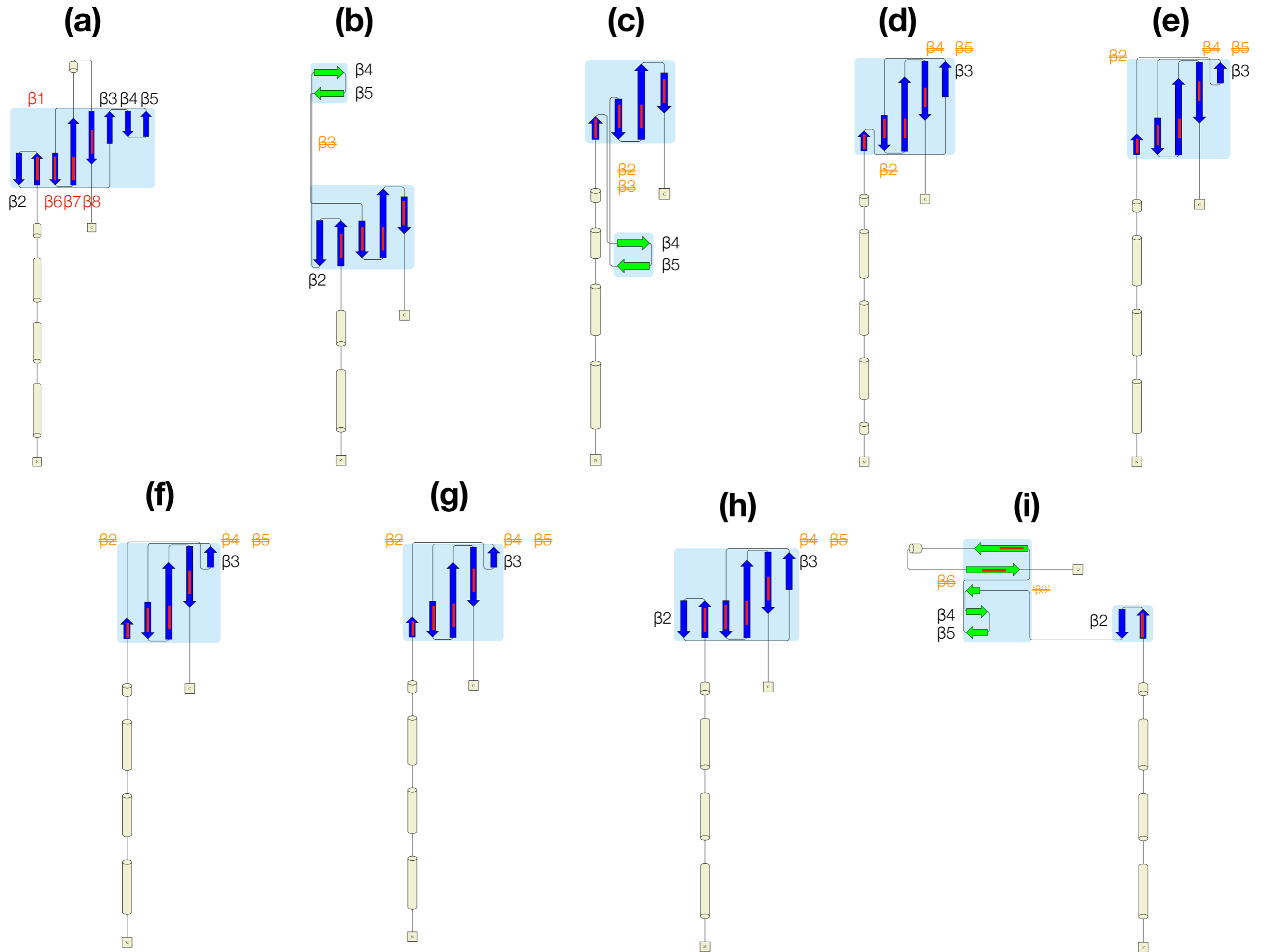
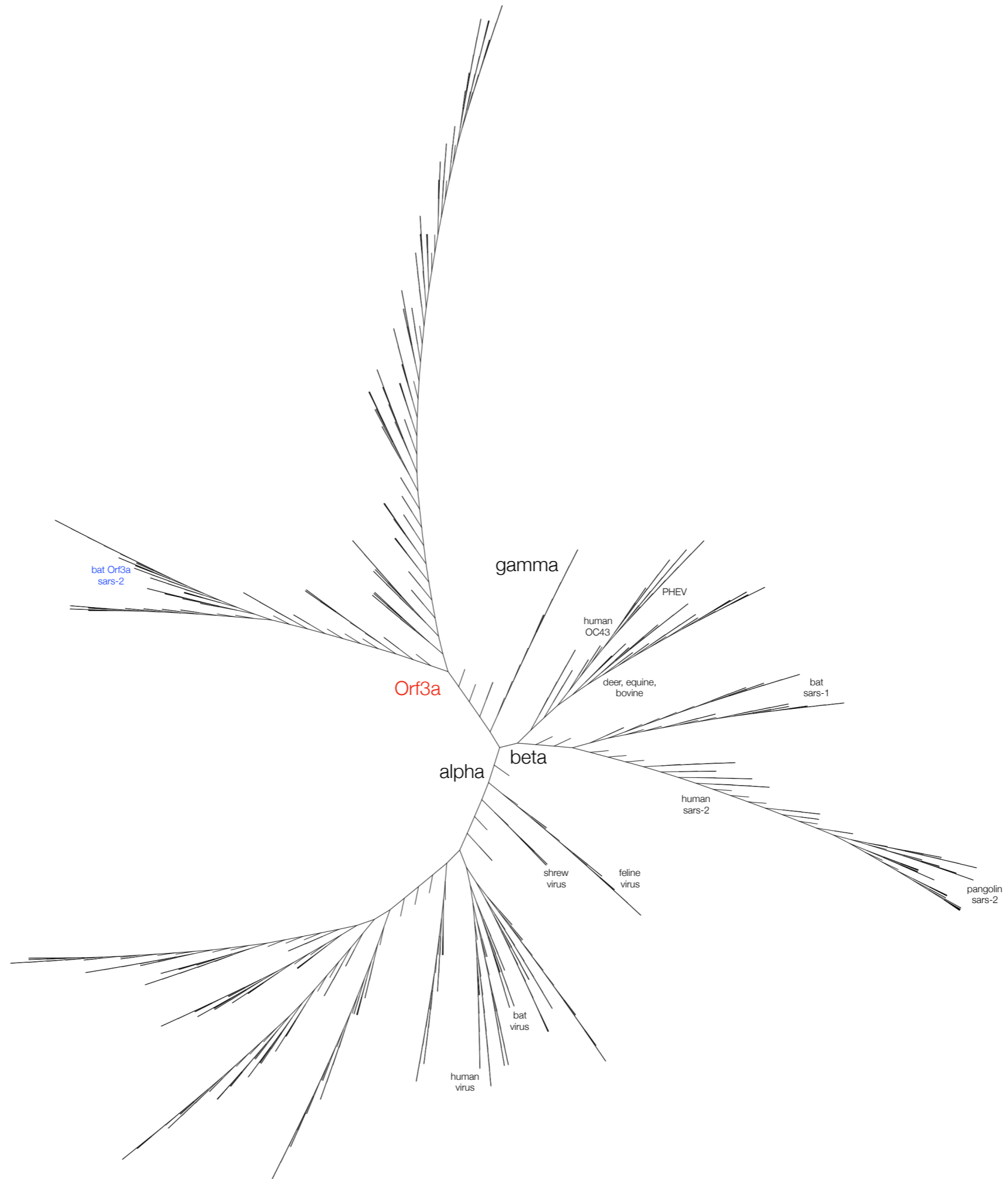


Figure S6



Figure S7



# Figure S8

Query: PF11289.8; AP3A\_CVHSA/1-273; Coronavirus accessory protein 3a  
Template: PF01635.18; VME1\_FIPV/40-260; Coronavirus M matrix/glycoprotein

```
143 ANYFVCWHTHNYDYCI PYN SVTD TIVVTEGDGISTPKLKEDYQIGGYSEDRHSGVKDYVVVHGYFTEVYYQLESTQITTD TGIENATF 230  
114 TNAILCVNALGRSYVLP LDGTPTGVTLTLLSGN---LYAEGFKMAGGLTIEH--LPKYVMIATPSRTIVYTLVGKQLKATTATGWAYY 196
```



[http://ffas.godziklab.org/ffas-cgi/cgi/get\\_mu.pl?ses=&rv=PfamA32U\\*PfamA32U\\*re\\*PF11289&lv=](http://ffas.godziklab.org/ffas-cgi/cgi/get_mu.pl?ses=&rv=PfamA32U*PfamA32U*re*PF11289&lv=)

#	Score	Template	Links and tools	%id
1	-160.000	<a href="#">PF11289.8</a> ; AP3A_CVHSA/1-273; Coronavirus accessory protein 3a	<a href="#">ali</a>	100
2	-11.600	<a href="#">PF01635.18</a> ; VME1_FIPV/40-260; Coronavirus M matrix/glycoprotein	<a href="#">ali</a> <a href="#">follow..</a>	17



# Table S1

Run #	true +ves	new hits	all hits	excluded	final hits	PDB ids	min seqide	precision	comment	pfam	save archive
1	898	0	898	0	898	6xdc	28.10	100.00	orf3a homologs	PF11289	KGB7F59A014
2	898	7	905	0	905	na	20.14	100.00	hypothetical bat orf3a's	na	KGBF0TZE014
3	905	13	918	0	918	na	17.36	100.00	orf3a homologs only	na	KGC2RBC0014
4	918	3	921	0	921	na	16.24	100.00	first 'feline' M proteins	PF01635	KGCB6UR6014
5	921	1034	1955	0	1955	na	10.05	100.00	almost 1000 M proteins	na	KGCTVD93014
6	1955	1069	3024	0	3024	na	8.00	100.00	another 1000 M proteins	na	KGD3TX9B016
7	3024	12	3036	25	3011	na	7.00	100.00	partial sequences (excluded)	na	KGER1U38014
8	3011	19	3030	0	3025	na	5.88	100.00	more partial sequences	na	KGFXSXGP016
9	3025	5*	3025	0	3025	na	6.67	100.00	no hits, convergence	na	KGGMKT62014

**Table S2**

sequence id	description	model	length	seq identity	QMEAN	C-beta	all-atom	solvation	torsion
<b>a-6xdcA</b>	SARS-CoV-2 Orf3a	3fnkwV	170	100.00	-4.53	-3.99	-1.14	-3.06	-2.64
<b>b-ADY17912.1</b>	Zaria bat CoV ZBCoV Orf3	Krxq5Y	148	20.95	-5.61	-3.51	-3.02	-6.10	-2.79
<b>c-YP_009072441.1</b>	Bat Hp Beta CoV Zhejiang2013	4cdPqa	154	20.78	-7.41	-4.43	-2.18	-6.94	-4.36
<b>d-QIG55988.1</b>	SARS-CoV-2 M	JBtQPZ	160	5.66	-6.13	-3.95	-1.98	-5.01	-3.67
<b>e-QMJ19959.1</b>	SARS-CoV-2 M	3dyh3c	159	12.58	-7.00	-3.92	-2.50	-4.98	-4.53
<b>f-QIQ54051.1</b>	Pangolin CoV M	KrDHuh	160	13.13	-6.11	-3.42	-2.29	-5.05	-3.73
<b>g-YP_003858587.1</b>	Bat CoV BM48-31/BGR2008 M	2kGQSz	160	13.13	-6.61	-4.30	-2.41	-4.72	-4.17
<b>h-YP_009072443.1</b>	Bat Hp Beta CoV Zhejiang2013 M	TJjzr2	160	13.75	-5.65	-4.44	-1.61	-5.09	-3.05
<b>i-ADY69165.1</b>	Zaria bat CoV ZBCoV M	F2S4AZ	160	16.25	-7.31	-3.95	-2.55	-5.42	-4.72
<b>average of a-i</b>			159	24.03	-6.26	-3.99	-2.19	-5.15	-3.74
<b>native 6xdc</b>	monomer of 6xdc	na	238	100.00	-3.22	-3.46	0.72	-1.30	-2.05
<b>native 6xdc</b>	dimeric form (as in PDB)	na	238	100.00	-2.97	-3.63	0.67	-0.90	-2.23