Supplementary Information for:

Binding of Congo red to amyloid protofibrils of the Alzheimer $A\beta_{9-40}$ *peptide probed by molecular dynamics simulations by Chun Wu, Justin Scott and Joan-Emma sheal*

Table S1 This table list the initial contact residues and the final binding mode between the protofibril and the two CRs (one binds to the N-terminal (Nt) sheet-layer and the other binds to the C-terminal (Ct) sheet-layer) in the first seven trajectories. Only cases in which no CR dimers are formed are considered here (Figure S4).

	Binding to	Nt- sheet-layer	Binding to	Ct-sheet-layer
Traj. ID	Initial Contact residues	Final binding mode	Initial Contact residues	Final binding mode
1	K16	Groove F20_V18_K16	I31	Parallel to β-stand
2	K16	Groove K16_H14_V12	A30,I31,M35	Parallel to β-stand
3	K16, F20	Groove F20_V18_K16	M35	Groove I31__M35
4	K16	Groove H14_V12	G37	Groove G20_I31
5	K16	Parallel to β-stand	V40	Sheet edges
6	K16	Groove F20_V18_K16	G38	Parallel to β-stand
7	K16, H14	Groove K16_H14_V12	V39	Sheet edges

Figure S1 the constructed starting structure for the binding simulations.

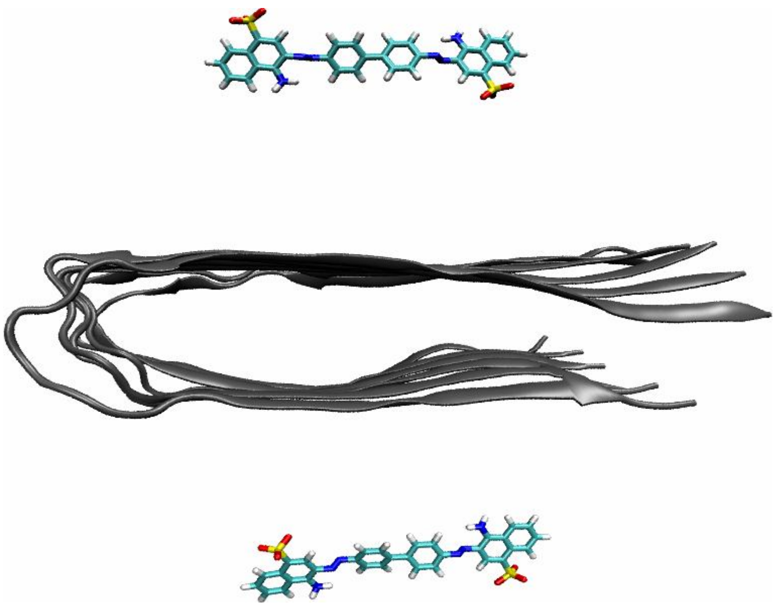


Figure S2 Cα RMSD of the A$\beta_{9\text{-}40}$ protofibril in all 8 trajectories.

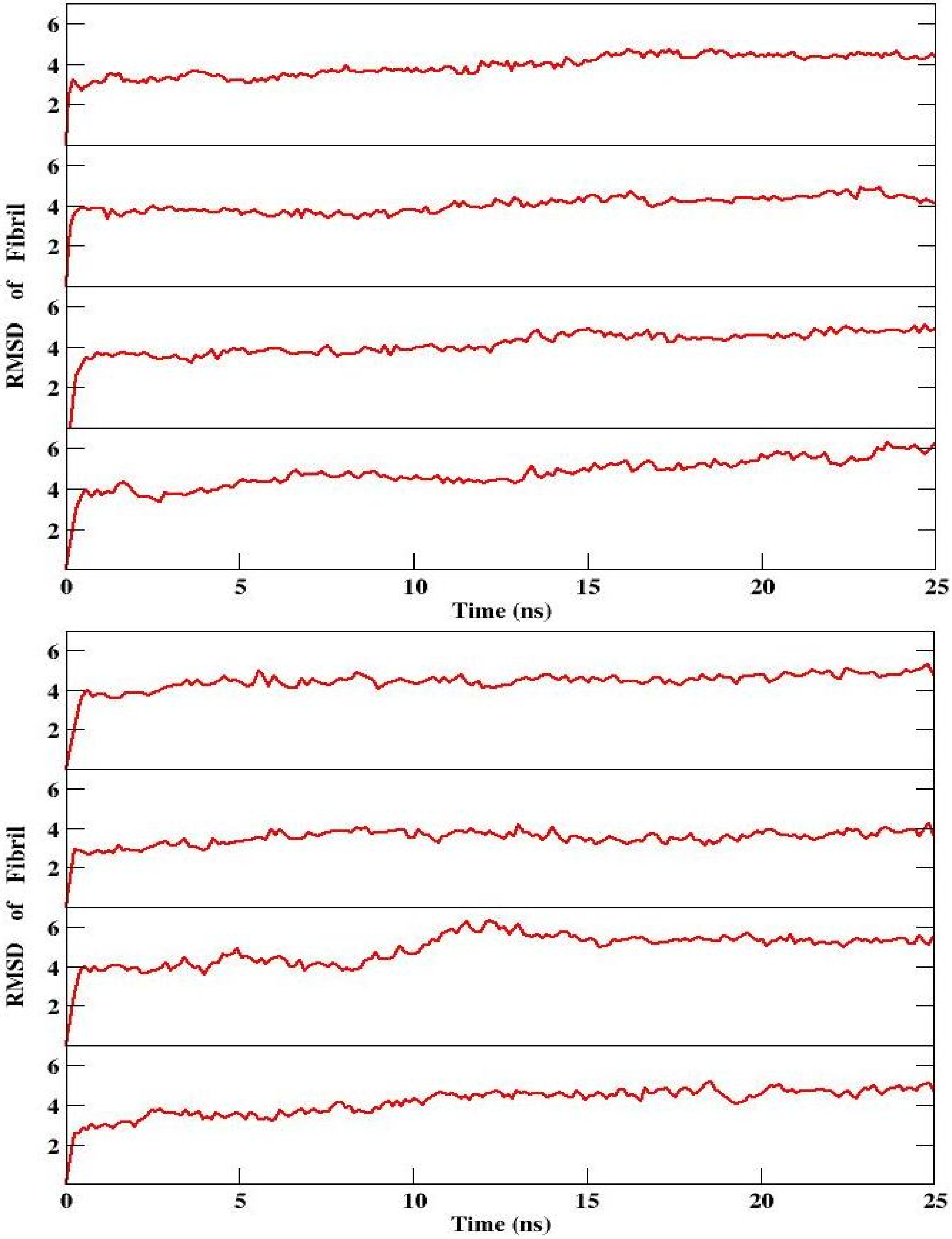
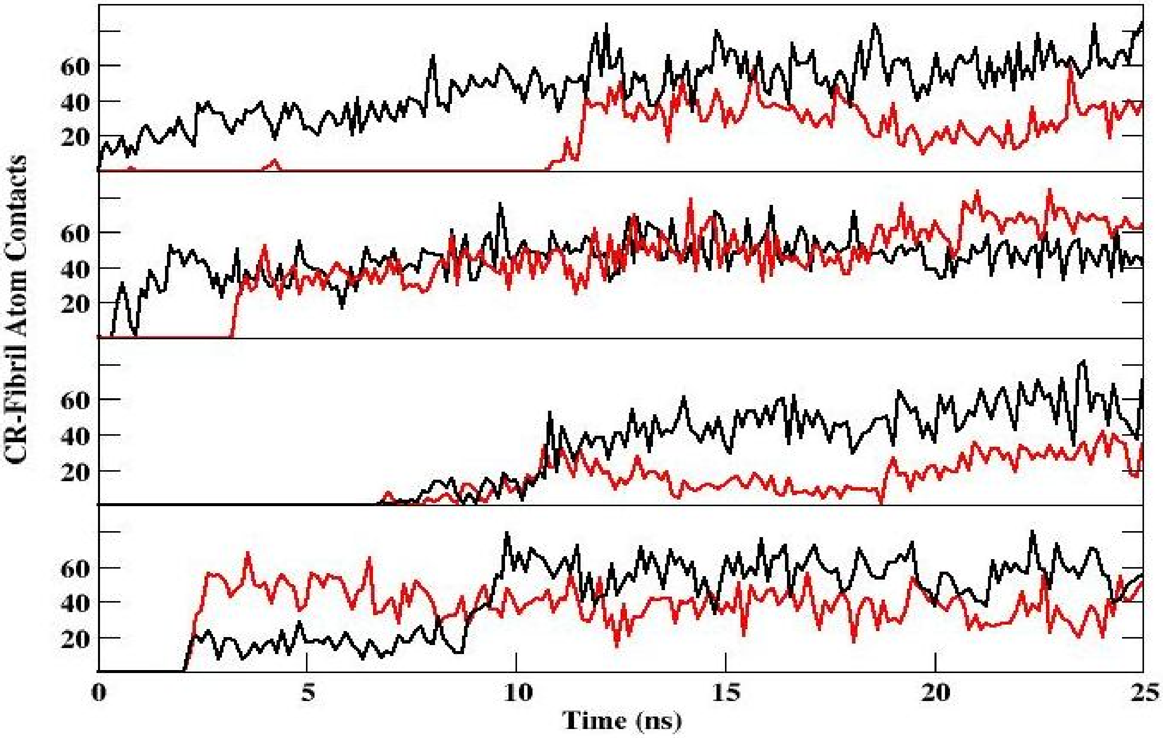


Figure S3 Binding of two CR molecules (red and black line) to the Aβ_{9-40} protofibril in for 8 trajectories. The distance cutoff for atom contacts between dye and the cross-β-subunit is set to be 3 Å. If the number of atom contacts is bigger than 20, then the system is designated as being in the bound state, otherwise it belongs the unbound state.



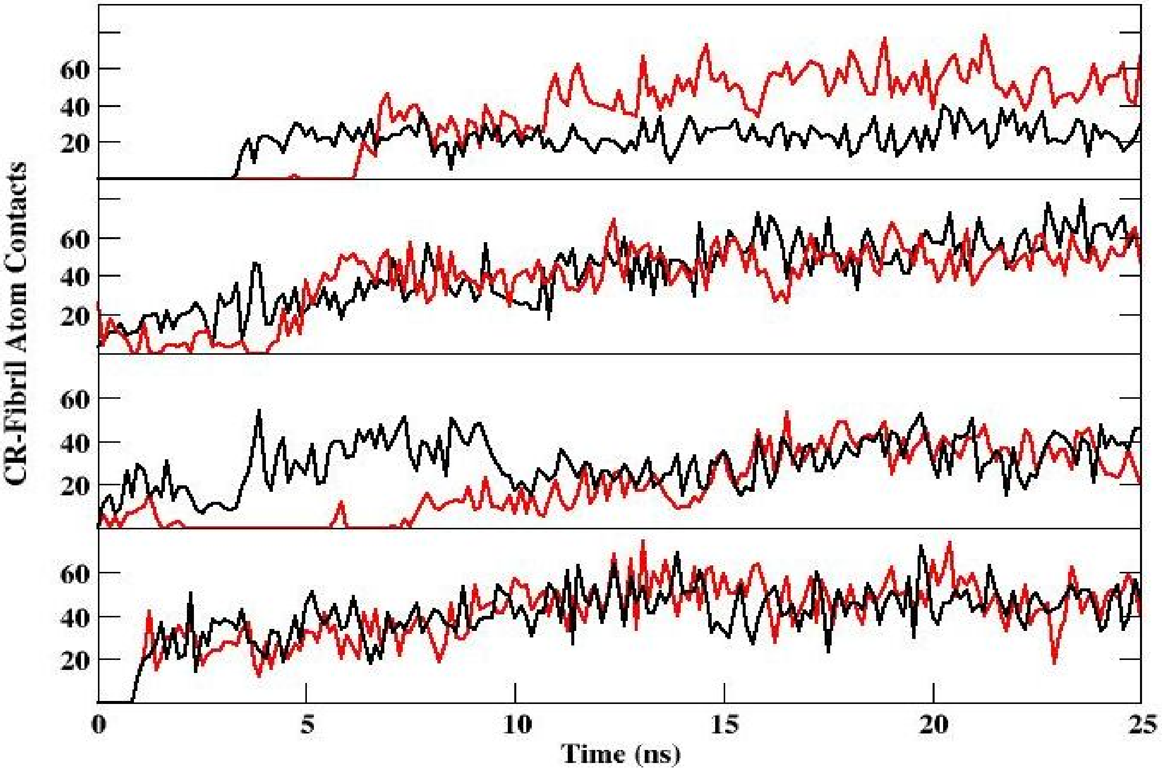
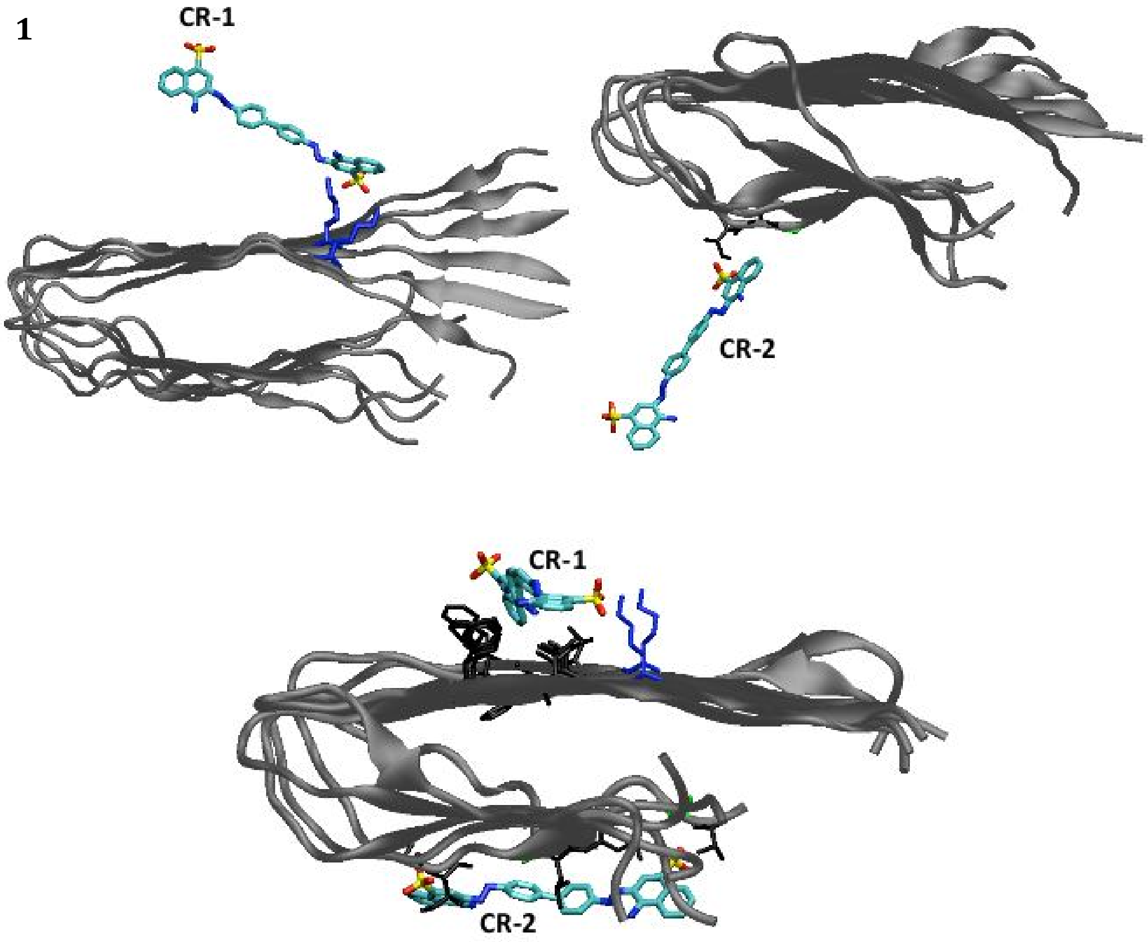


Figure S4 The initial and final contacts between the protofibril and two CRs in the eight trajectories.



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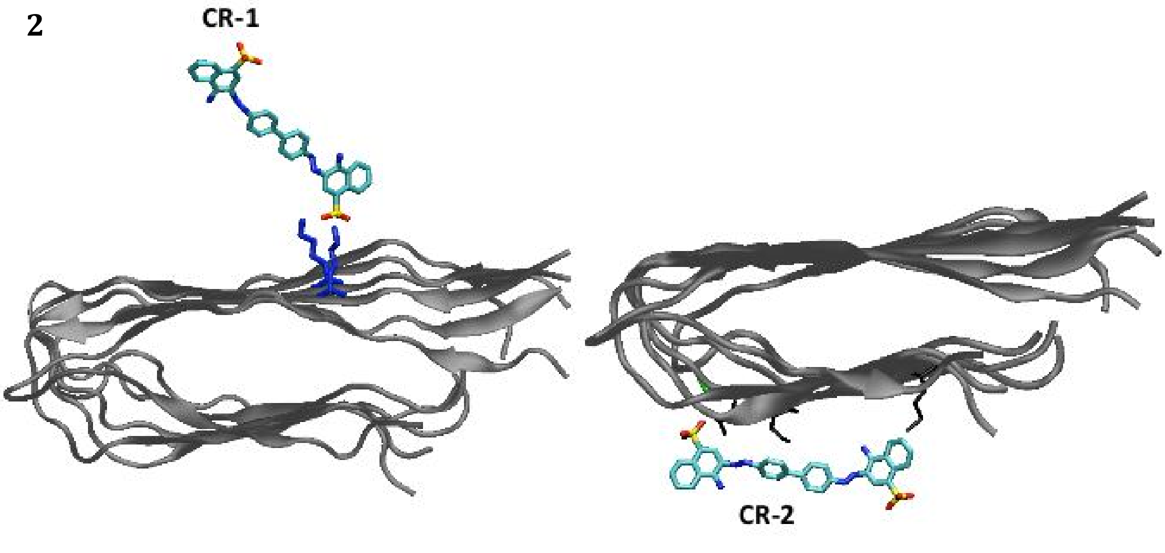

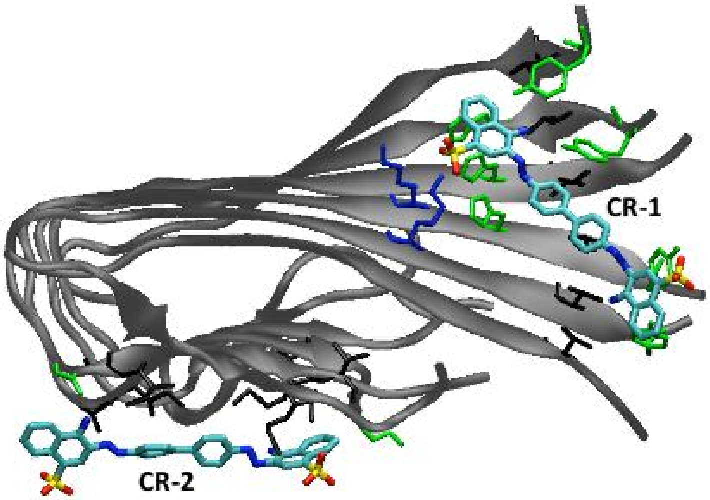

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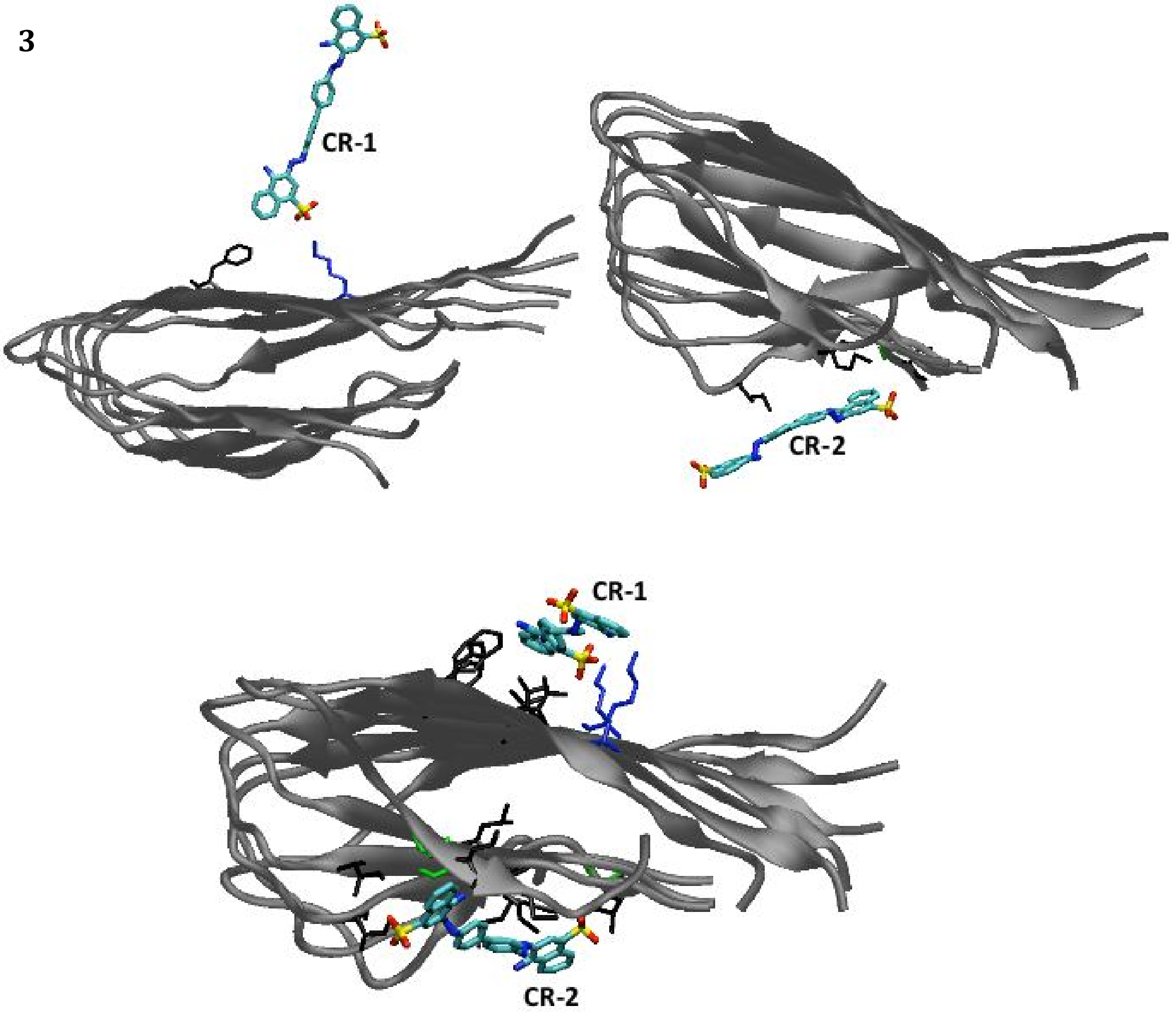

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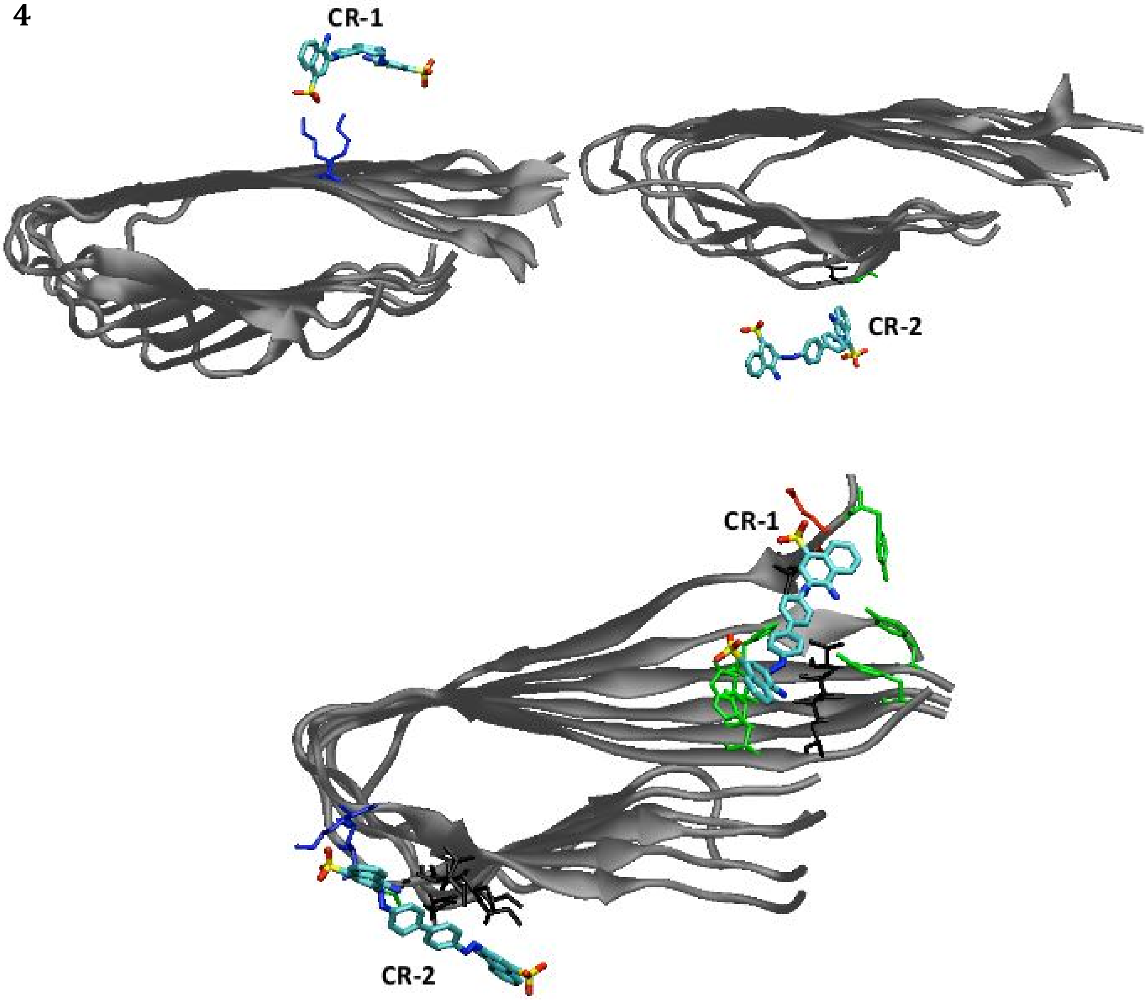

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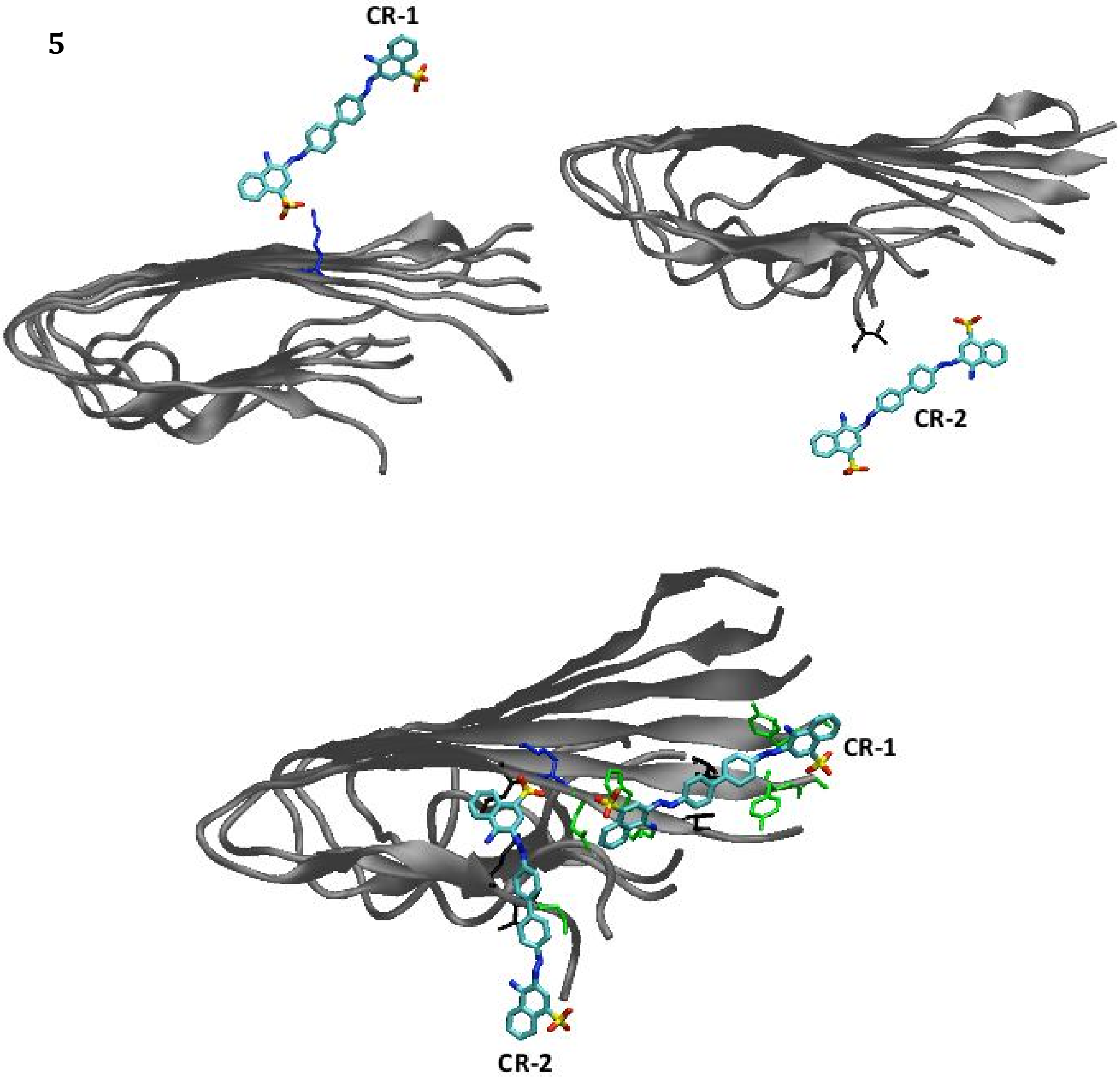

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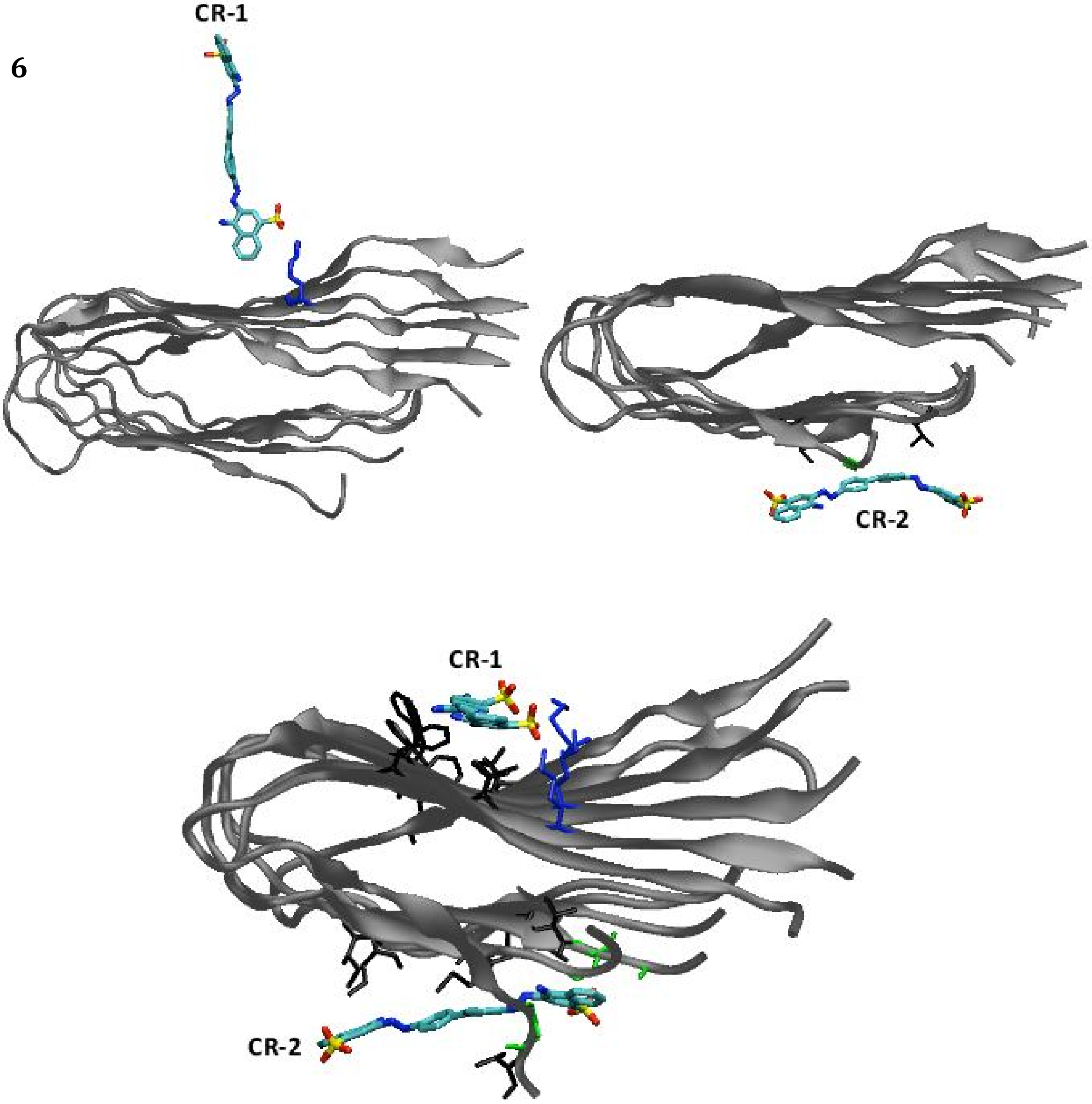

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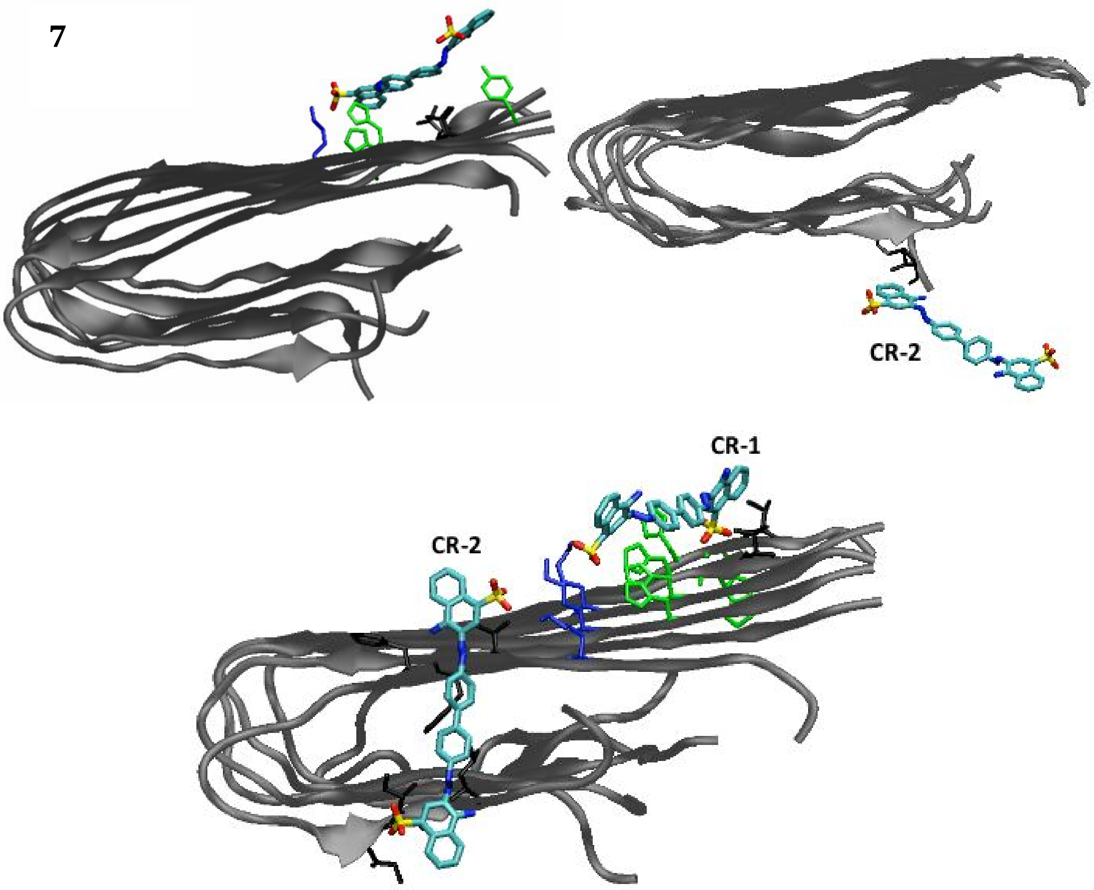

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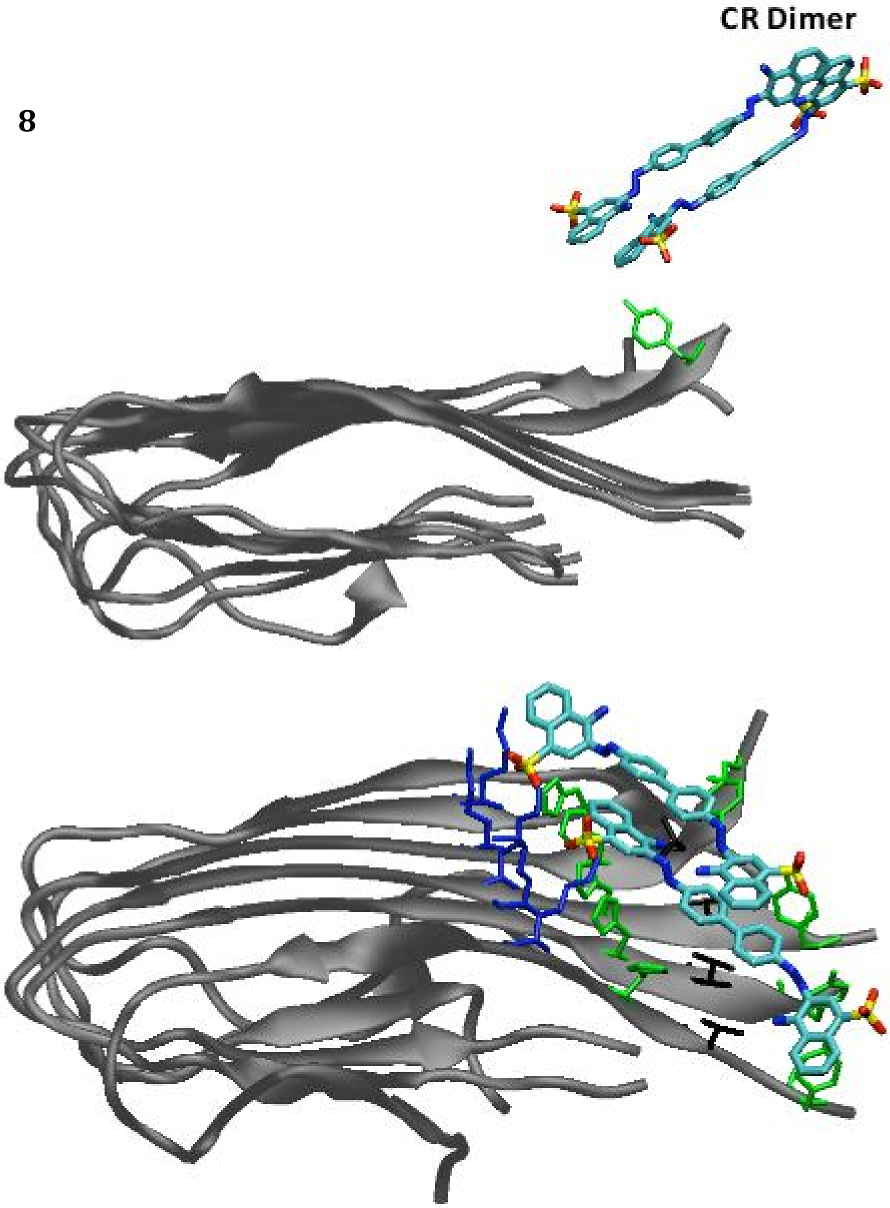
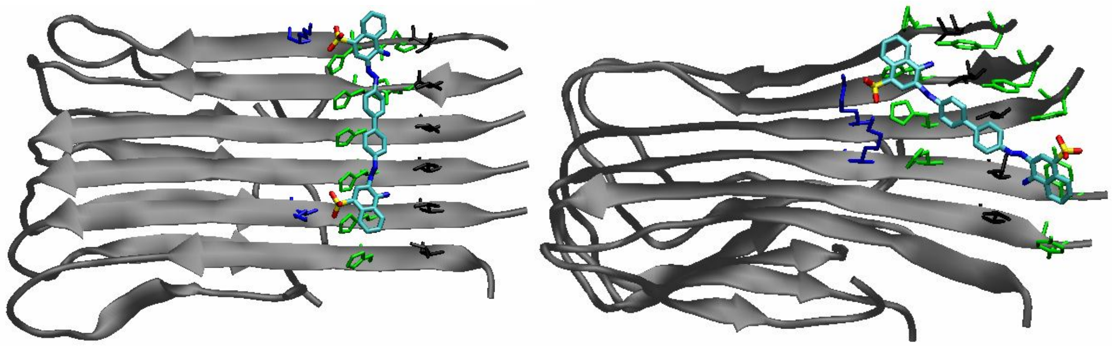
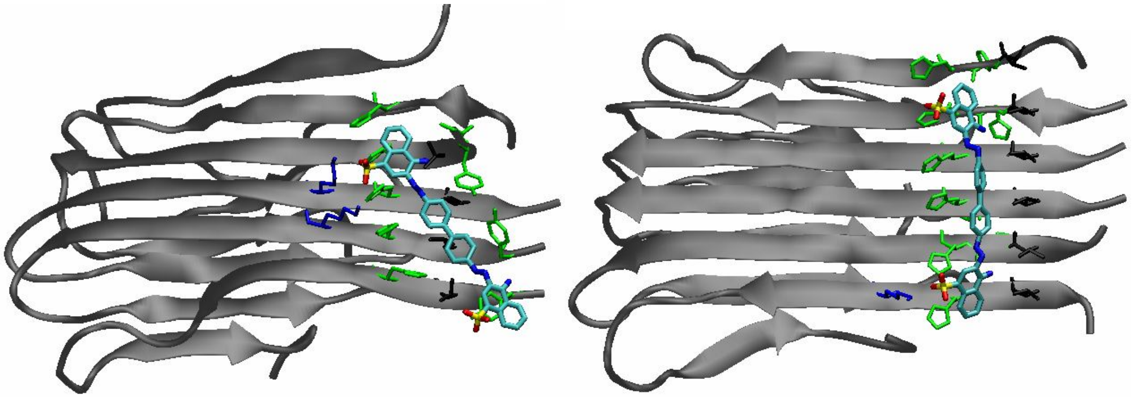


Figure S5 The centroid structures from the clustering. The centroids are further merged into different binding types (Type I-VII) based on binding sites.



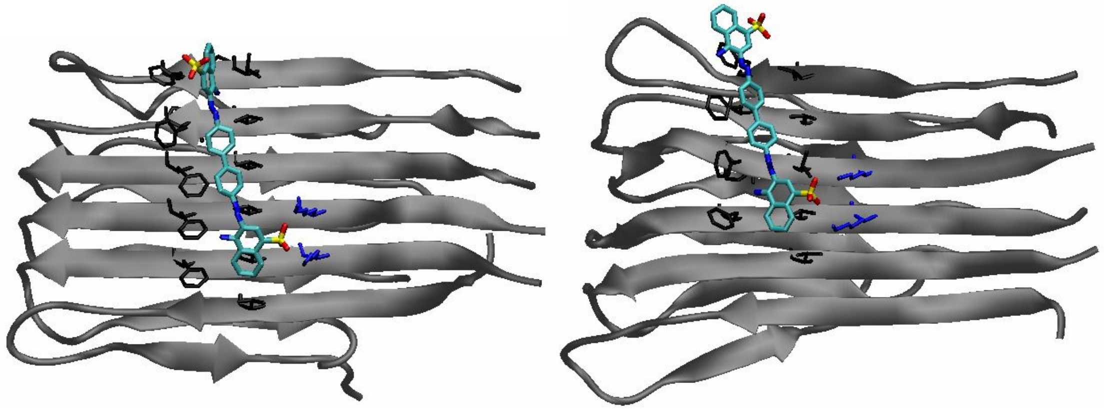
Type I 13.98%

Type I 5.98%



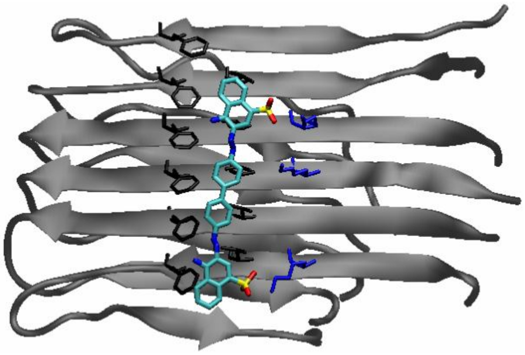
Type I 4.81%

Type I 1.93%

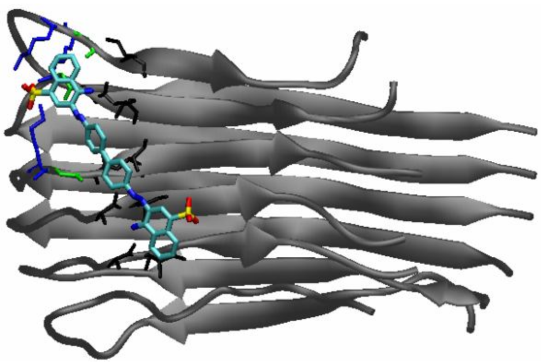


Type II 14.3%

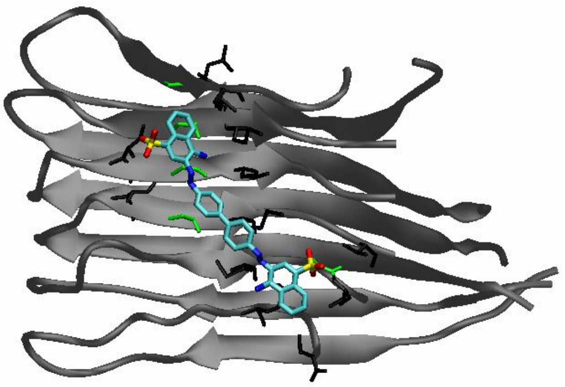
Type II 7.15%



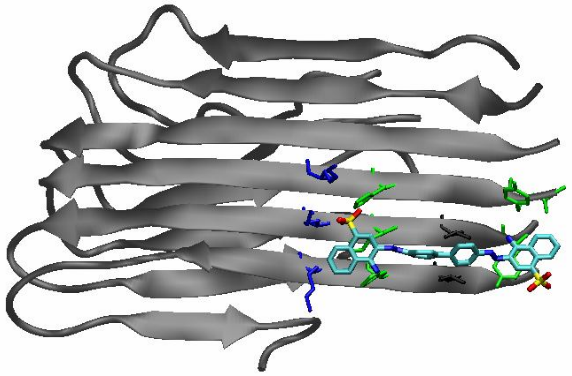
Type II 2.74%



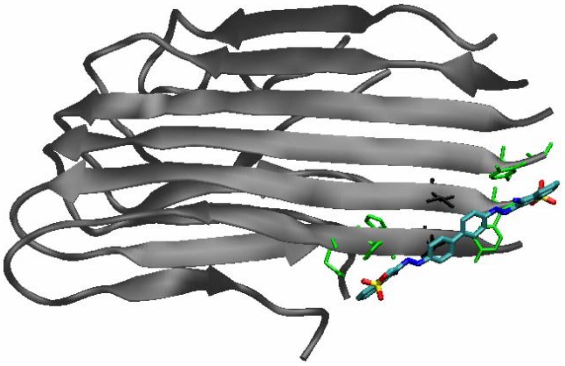
Type III 5.76%



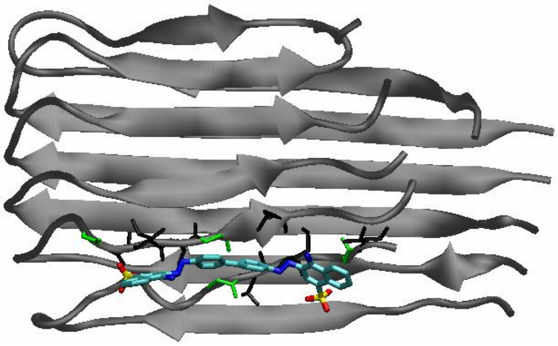
Type IV 4.79%



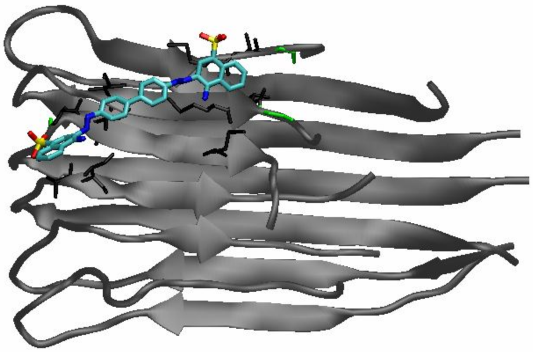
Type V 3.10%



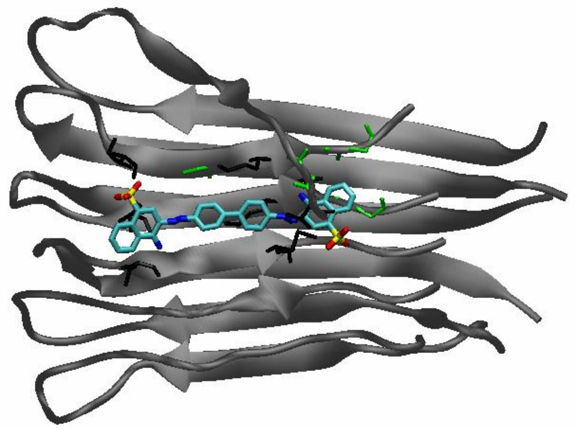
Type V 1.51 %



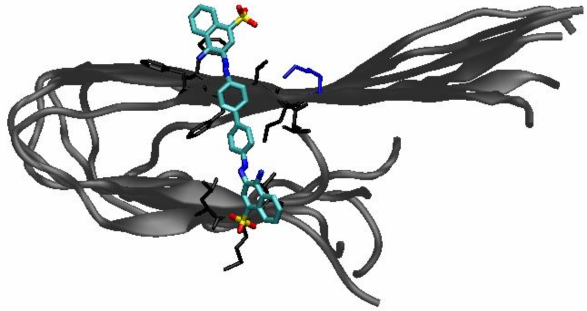
Type VI 8.09%



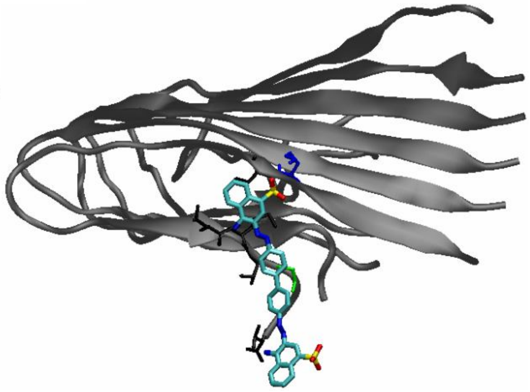
Type VI 6.29%



Type VI 1.93%

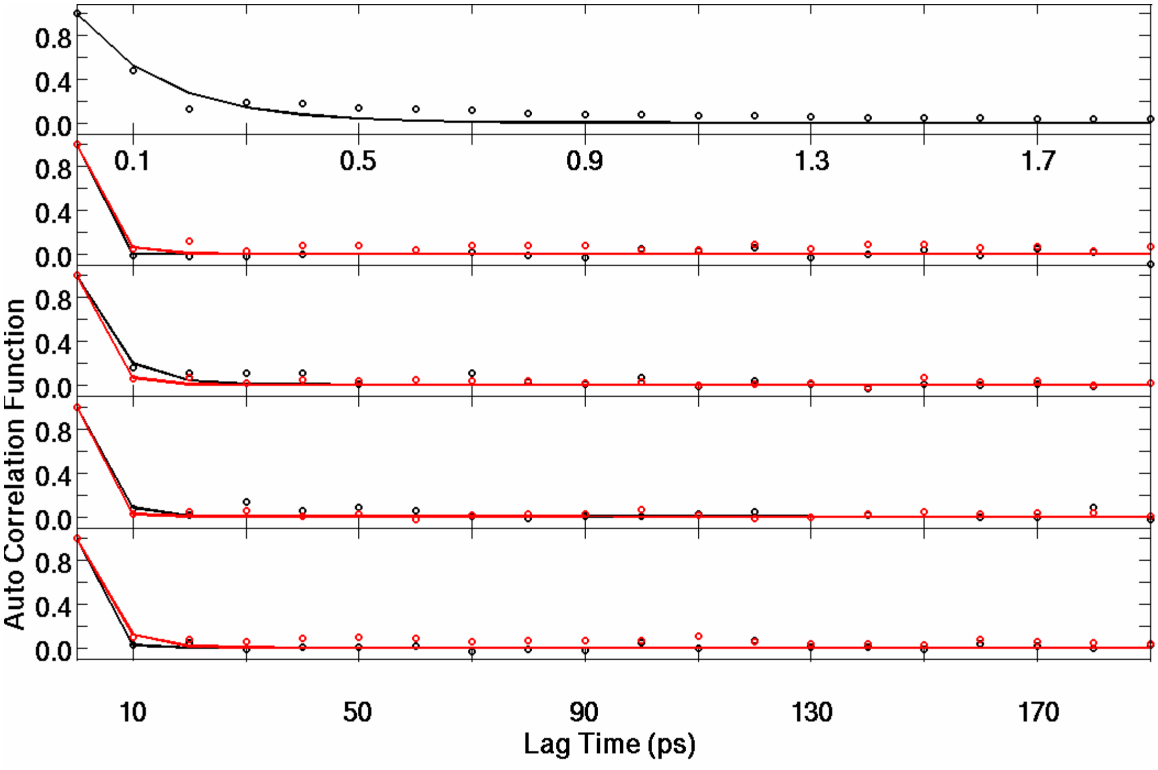


Type VII 10.16%



Type VII 2.47%

Figure S6 Auto-correlation function of the Central torsion angle of CR. Top 1: One free CR Top 2-4: Two CR molecules (red and black) bound to the Aβ_{9-40} protofibril. The fitted lines to exponential decay are in solid, the data points are in cycles.



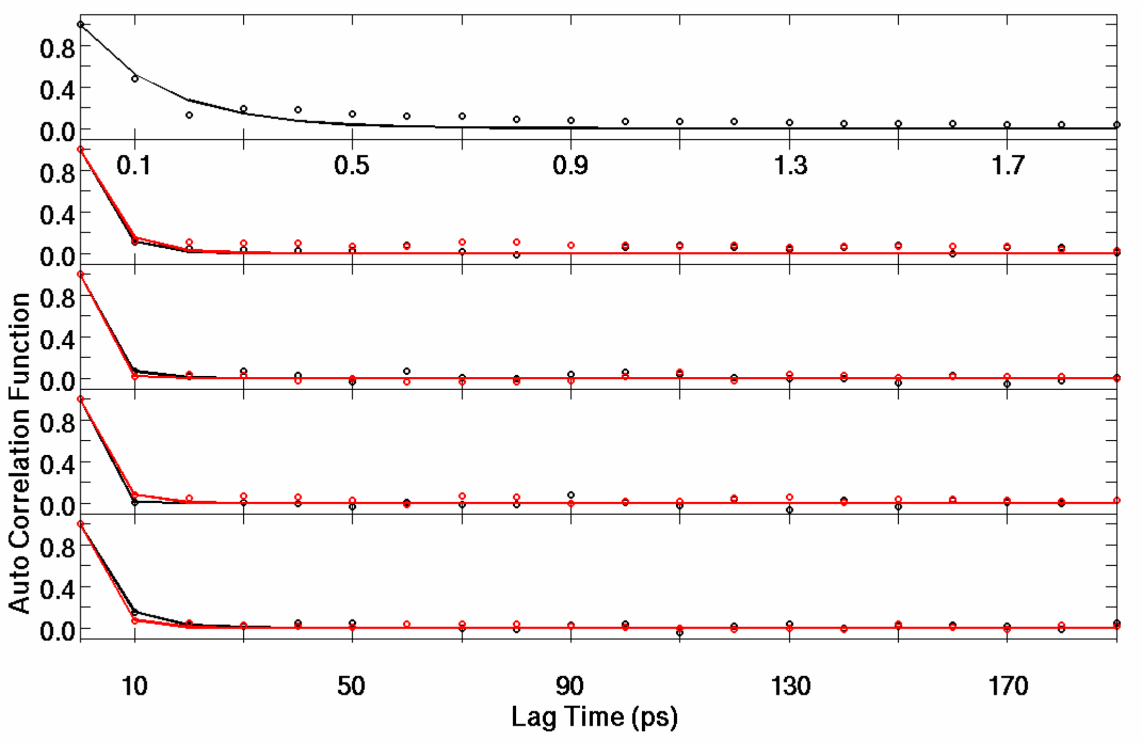
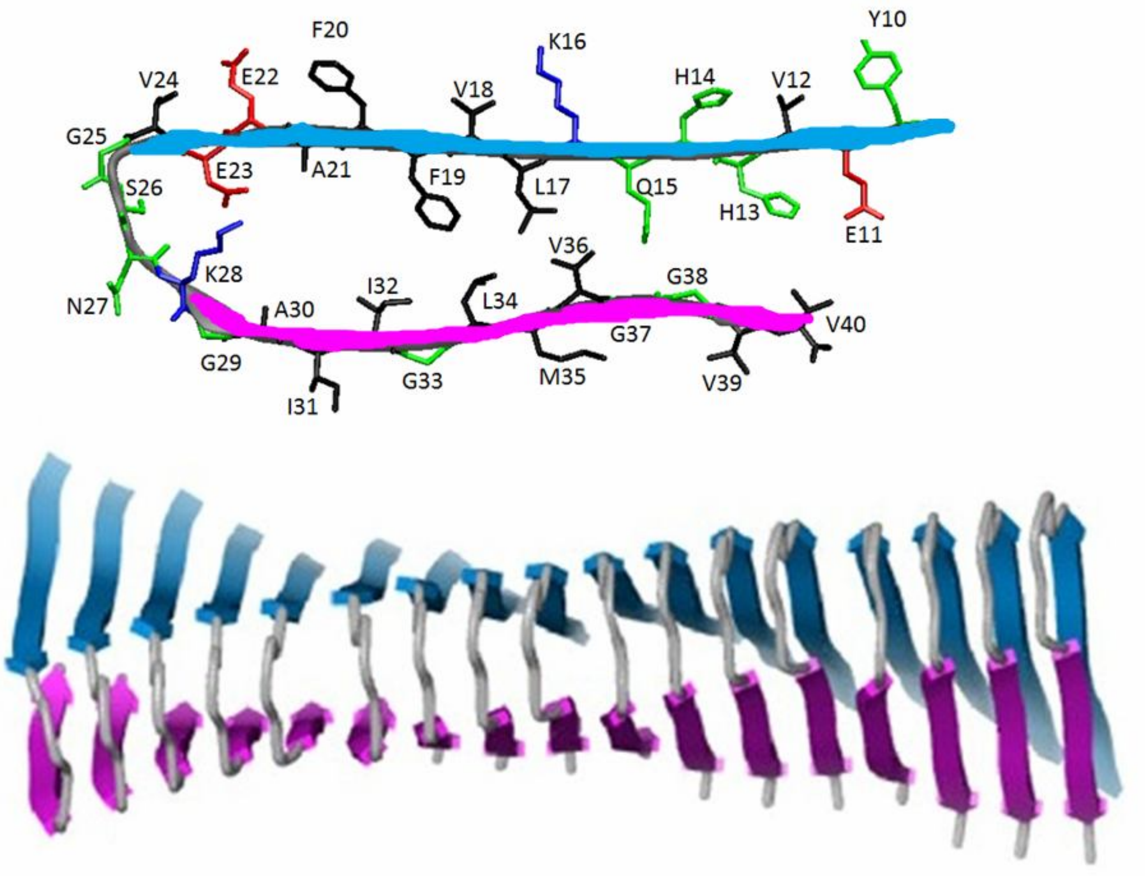

0.8
0.4
0.0
0.1
0.5
0.9
1.3
1.7
Auto Correlation Function
10
50
90
130
170
Lag Time (ps)

Figure S7 Long range twisting of $A\beta_{9\text{-}40}$ fibril.



The fibril structure is adapted from reference 1

Reference

1. Kajava, A. V., U. Baxa, and A. C. Steven. 2010. β–arcades: recurring motifs in naturally occurring and disease-related amyloid fibrils. Faseb Journal 24:1311-1319.

Appendix A the force field of acidic Congo red molcule in MOL2 format

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CRA
  68   73    1    0    1
SMALL
USER_CHARGES
@<TRIPOS>ATOM
  1 C9     3.536914    1.422858   -0.000002 ca    1 CRA    -0.0885 ****
  2 C10     4.956279    1.392528    0.061005 ca    1 CRA     0.0362 ****
  3 C1     5.732216    2.522086    0.500030 ca    1 CRA    -0.1512 ****
  4 S1     4.948198    4.068812    0.990089 sy    1 CRA     1.1310 ****
  5 O1     6.050543    4.933870    1.355071 o     1 CRA    -0.6604 ****
  6 O2     4.220306    4.491489   -0.193051 o     1 CRA    -0.6604 ****
  7 O3     4.082160    3.703296    2.096742 o     1 CRA    -0.6604 ****
  8 C2     7.076907    2.424663    0.546015 ca    1 CRA    -0.0825 ****
  9 H1     7.652192    3.263577    0.877937 ha    1 CRA     0.0944 ****
 10 H5     3.030305    2.323749    0.272951 ha    1 CRA     0.1423 ****
 11 C8     2.830146    0.327778   -0.391921 ca    1 CRA    -0.1353 ****
 12 H4     1.754774    0.374754   -0.427927 ha    1 CRA     0.1231 ****
 13 C7     3.488250   -0.869679   -0.735836 ca    1 CRA    -0.2128 ****
 14 H3     2.917042   -1.736536   -1.018780 ha    1 CRA     0.1337 ****
 15 C6     4.846301   -0.929113   -0.693838 ca    1 CRA    -0.1513 ****
 16 H2     5.344154   -1.852353   -0.919892 ha    1 CRA     0.1282 ****
 17 C5     5.613347    0.202582   -0.313748 ca    1 CRA     0.0508 ****
 18 C4     7.047269    0.148283   -0.301753 ca    1 CRA     0.1944 ****
 19 N3     7.684422   -1.032419   -0.701728 nh    1 CRA    -0.8470 ****
 20 H21     7.338134   -1.383010   -1.569584 hn    1 CRA     0.3410 ****
 21 H22     8.673659   -0.909502   -0.749753 hn    1 CRA     0.3410 ****
 22 C3     7.751272    1.239686    0.134274 ca    1 CRA     0.0598 ****
 23 N1     9.154672    1.116319    0.111270 ne    1 CRA    -0.1008 ****
 24 N2     9.802728    2.060286    0.538160 nf    1 CRA    -0.0748 ****
 25 C11    11.210626    1.906979    0.491164 ca    1 CRA     0.1248 ****
 26 C16    11.950411    3.026196    0.839110 ca    1 CRA    -0.1583 ****
 27 C15    13.334853    2.990780    0.822102 ca    1 CRA    -0.1306 ****
 28 H8    13.888410    3.866109    1.110198 ha    1 CRA     0.1311 ****
 29 H9    11.425493    3.919624    1.125244 ha    1 CRA     0.1191 ****
 30 C12    11.879813    0.738241    0.139162 ca    1 CRA    -0.1583 ****
 31 H6    11.318324   -0.135027   -0.127891 ha    1 CRA     0.1191 ****
 32 C13    13.258403    0.706832    0.127160 ca    1 CRA    -0.1306 ****
 33 H7    13.759994   -0.197069   -0.167786 ha    1 CRA     0.1311 ****
 34 C14    14.015577    1.832643    0.464268 cp    1 CRA     0.0019 ****
 35 C17    15.503704    1.789414    0.437264 cp    1 CRA     0.0019 ****
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 36 C19    16.203782    0.698677    0.942302 ca    1 CRA    -0.1306 ****
 37 C21    17.587700    0.660263    0.903311 ca    1 CRA    -0.1583 ****
 38 H13    18.127495   -0.183080    1.294488 ha    1 CRA     0.1191 ****
 39 H11    15.667503   -0.121027    1.385152 ha    1 CRA     0.1311 ****
 40 C18    16.240667    2.843698   -0.107694 ca    1 CRA    -0.1306 ****
 41 H10    15.722954    3.684959   -0.531815 ha    1 CRA     0.1311 ****
 42 C20    17.619910    2.814284   -0.142709 ca    1 CRA    -0.1583 ****
 43 H12    18.166428    3.626374   -0.579756 ha    1 CRA     0.1191 ****
 44 C22    18.308172    1.717269    0.370420 ca    1 CRA     0.1248 ****
 45 N4     19.718677    1.571885    0.378406 ne    1 CRA    -0.0748 ****
 46 N5     20.352544    2.572670    0.078530 nf    1 CRA    -0.1008 ****
 47 C23    21.756362    2.464335    0.073513 ca    1 CRA     0.0598 ****
 48 C25    22.441076    3.595375   -0.285395 ca    1 CRA     0.1944 ****
 49 N6     21.781714    4.771413   -0.662458 nh    1 CRA    -0.8470 ****
 50 H19    22.149161    5.583020   -0.210486 hn    1 CRA     0.3410 ****
 51 H20    20.800293    4.703598   -0.500524 hn    1 CRA     0.3410 ****
 52 C24    22.451446    1.276891    0.440407 ca    1 CRA    -0.0825 ****
 53 H14    21.891063    0.408797    0.718405 ha    1 CRA     0.0944 ****
 54 C26    23.800355    1.230425    0.468394 ca    1 CRA    -0.1512 ****
 55 S2     24.614042   -0.293756    0.980244 sy    1 CRA     1.1310 ****
 56 O4     23.525743   -1.203803    1.275235 o     1 CRA    -0.6604 ****
 57 O5     25.402130    0.092585    2.136947 o     1 CRA    -0.6604 ****
 58 O6     25.421481   -0.676097   -0.164379 o     1 CRA    -0.6604 ****
 59 C28    24.555062    2.393675    0.087461 ca    1 CRA     0.0362 ****
 60 C27    23.874738    3.563645   -0.311601 ca    1 CRA     0.0508 ****
 61 C29    24.620597    4.692021   -0.740579 ca    1 CRA    -0.1513 ****
 62 H15    24.101806    5.560321   -1.101670 ha    1 CRA     0.1282 ****
 63 C31    25.980469    4.673581   -0.737585 ca    1 CRA    -0.2128 ****
 64 H17    26.533926    5.533746   -1.071616 ha    1 CRA     0.1337 ****
 65 C32    26.662420    3.517221   -0.309736 ca    1 CRA    -0.1353 ****
 66 H18    27.738342    3.505231   -0.304730 ha    1 CRA     0.1231 ****
 67 C30    25.975651    2.410187    0.084150 ca    1 CRA    -0.0885 ****
 68 H16    26.500259    1.532213    0.395129 ha    1 CRA     0.1423 ****
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   6    3    4 1
   7    3    8 1
   8    4    5 1
   9    4    6 1
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  71   65   66 1
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  73   67   68 1
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