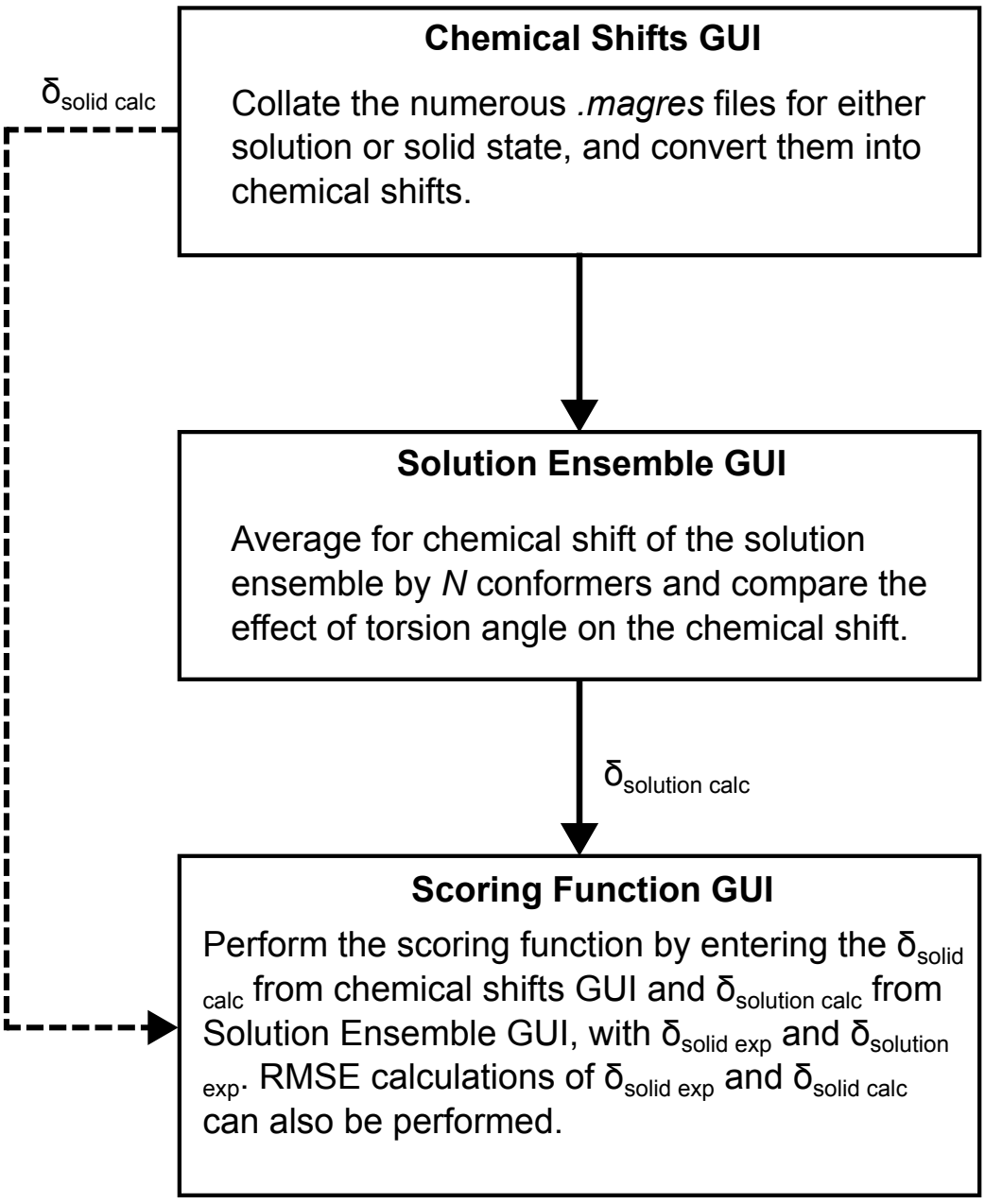
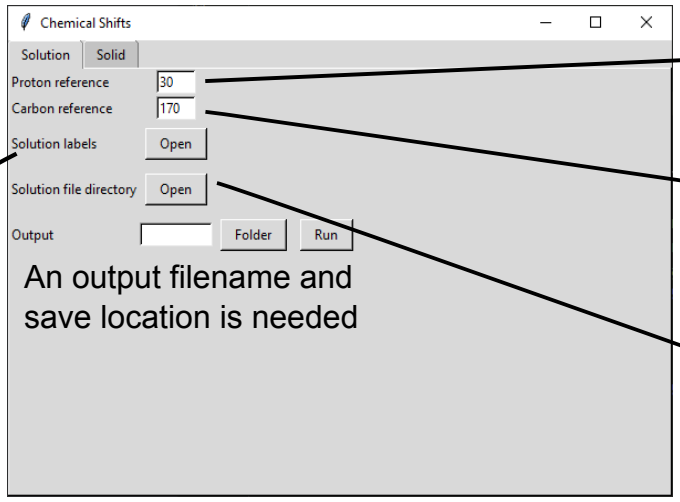
Workflow


Chemical Shifts GUI
Collate the numerous .magres files for either solution or solid state, and convert them into chemical shifts.
δsolid calc
Solution Ensemble GUI
Average for chemical shift of the solution ensemble by N conformers and compare the effect of torsion angle on the chemical shift.
δsolution calc
Scoring Function GUI
Perform the scoring function by entering the δsolid calc from chemical shifts GUI and δsolution calc from Solution Ensemble GUI, with δsolid exp and δsolution exp. RMSE calculations of δsolid exp and δsolid calc can also be performed.

Chemical shifts GUI

G1a Extracting solution chemical shifts into a single .csv file

(Note: solution ensembles must be seperated by an '_' followed by their number e.g. 'name_1'), this can be done by Babel.



Enter ^{1}H reference value (30 by default).

Enter ^{13}C reference value (170 by default).

A directory to solution *.magres* files to be converted into chemical shifts is selected.

User Generated

My label	Solution Magres
H1	H1
H2	H2
H3	H3
H4	H4
H5	H5
H6	H6
H7	H7
H8	H8
H9	H9
H10	H10
C1	C1
C2	C2
C3	C3
C4	C4
C5	C5
C6	C6
C7	C7
C8	C8
C9	C9
C10	C10
C11	C11
C12	C12

Solution labels refer to a *.csv* file containing users custom labels e.g. *'My label'*, which correpond to the labels in the *.magres* file.

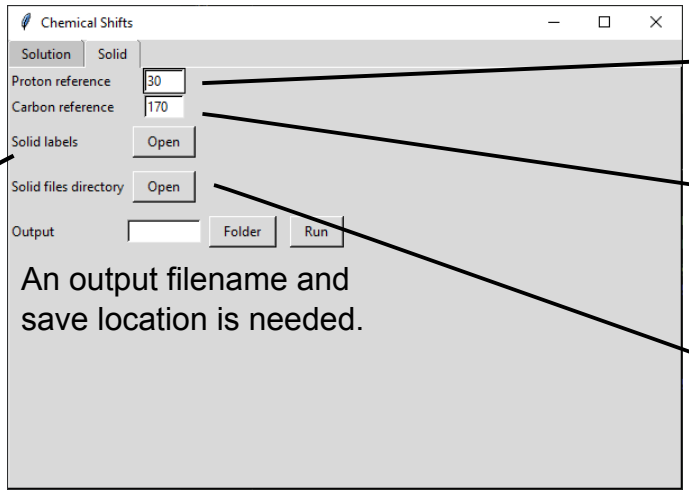
Output 1

(*)

My label	Fur_773.magres	Fur_1987.magres	Fur_295.magres
H1	7.0667	7.1157	7.0398
H2	5.9772	6.0097	5.9411
H3	5.7788	5.9946	5.7671
H4	4.7926	3.6364	3.4522
H5	3.5593	3.9559	4.2104
H6	8.6042	9.1213	8.0828
H7	6.4482	6.1864	6.504
H8	7.9956	8.0217	7.8727
H9	3.1656	4.538	3.133
H10	4.6675	3.1557	4.5375
H11	4.8188	4.8634	4.9052
C1	142.9409	143.1234	142.4584
C2	108.344	107.9127	108.1467
C3	105.9354	109.8521	105.914
C4	152.3404	151.768	154.5729
C5	35.5835	37.2505	35.265
C6	150.2973	149.8395	149.801
C7	110.6024	111.903	112.7887
C8	143.3685	142.1504	142.8847
C9	131.1223	131.3453	130.963
C10	133.7064	133.6889	132.7405
C11	103.2962	103.8551	104.5404
C12	169.1447	169.0953	169.7027

A *.csv* file containing the chemical shift for each *.magres* file is produced.

G1b Extracting the calculated solid chemical shifts into a single file



Enter ^{1}H reference value (30 by default).

Enter ^{13}C reference value (170 by default.)

A directory to solid *.magres* files to be converted into chemical shifts is selected.

User Generated

Column header must match filenname without extension

label	FURSEM13_NMR_molA	FURSEM13_NMR_molB	FURSEM14_NMR
H1	H27	H7	H17
H2	H23	H25	H21
H3	H21	H11	H25
H4	H13	H17	H9
H5	H15	H19	H13
H6	H31	H29	H29
H7	H5	H9	H5
H8	H1	H3	H1
H9	H37	H43	H37
H10	H41	H39	H41
H11	H35	H33	H33
C1	C47	C25	C37
C2	C41	C43	C41
C3	C39	C33	C45
C4	C45	C29	C17
C5	C35	C37	C33
C6	C19	C17	C21
C7	C21	C31	C5
C8	C5	C15	C13
C9	C3	C27	C29
C10	C1	C7	C1
C11	C13	C23	C25
C12	C11	C9	C9

Solid labels are different for each file, and each filename is needed without the *.magres* extenstion. If there are more than one molecule per .magres file, use *'_mol'* as a seperator. Please do not have any further underscores in the filename.

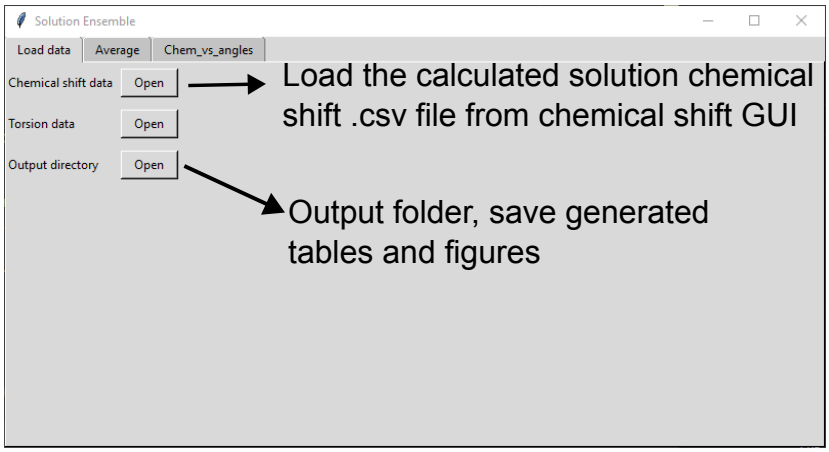
Output 2

label	FURSEM01_NMR_molA	FURSEM01_NMR_molB	FURSEM15_form1_NMR
H1	6.3972	7.7533	7.8685
H2	6.4241	5.9938	7.4615
H3	5.1043	5.9031	5.769
H4	4.6212	4.5214	3.6164
H5	3.8654	3.4992	3.4836
H6	7.9961	8.4557	8.0947
H7	7.198	5.0139	4.8844
H8	8.1216	7.9903	7.3252
H9	5.7912	6.8906	7.2933
H10	7.0155	7.2458	6.1508
H11	14.1813	14.3412	13.2779
C1	142.5233	145.7456	146.6416
C2	112.3228	110.2586	114.9906
C3	109.5858	112.2776	111.779
C4	155.3735	152.2619	147.0341
C5	36.6175	36.459	38.9586
C6	151.7128	150.7127	148.699
C7	116.3592	116.6053	111.2057
C8	141.9728	141.5158	145.9296
C9	126.0016	127.9526	130.1407
C10	136.0487	134.3644	134.2614
C11	104.9061	107.0035	105.7995
C12	173.5453	173.6375	175.0075

A *.csv* file containing the chemical shift for each *.magres* file is produced.

Solution Ensemble GUI

G2a Analysing dependence of the chemical shift, on each atom and specific torsion agnle

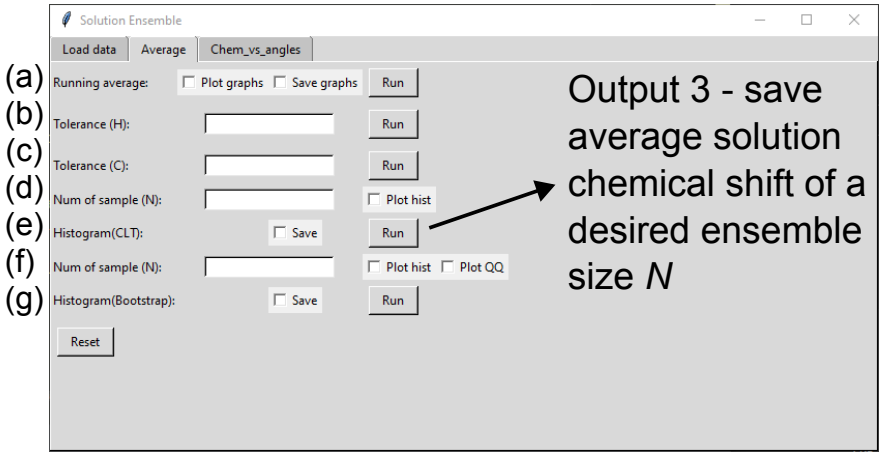


Requires Output 1 (see page 1)

```
** Measure set 1: neutral_ensemble.sdf **
Torsion: mean = 181.96 sd = 113.27 range = [12.89,342.67] {O:8,C:7,C:9,N:12;}
1_ensemble4D_1 72.49
2_ensemble4D_2 36.56
3_ensemble4D_3 53.87
4_ensemble4D_4 285.99
5_ensemble4D_5 169.13
6_ensemble4D_6 298.27
7_ensemble4D_7 293.48
8_ensemble4D_8 180.35
9_ensemble4D_9 62.58
10_ensemble4D_10 58.72
11_ensemble4D_11 189.45
12_ensemble4D_12 88.48
13_ensemble4D_13 284.46
14_ensemble4D_14 36.20
15_ensemble4D_15 303.29
16_ensemble4D_16 80.74
17_ensemble4D_17 81.09
18_ensemble4D_18 52.85
19_ensemble4D_19 308.83
```

Torsion angles are passed as a '*.txt*' file and each number corresponds to the number of the '*.magres*' file. Torsion angles are weighted according to their gaussian distribution in solution.

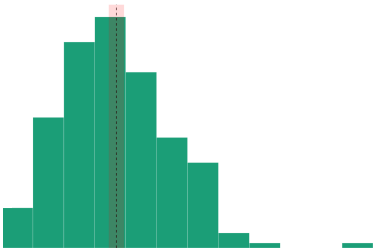
G2b Determining $\delta_{solution\ calc}$



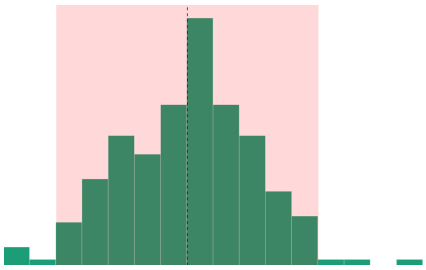
(a) A running average and running standard deviation can be viewed/saved for each of the '*.magres*' files.

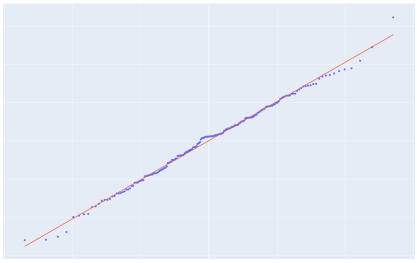
(b) & (c) The number of samples are calculated to achieve a set tolerance e.g. a standard deviation of 0.1 ppm, which is different for each isotope.

(d) & (e) The number of samples to be averaged and used as the calculated solution chemical shift ($\delta_{solution\ calc}$) are specified here. Further a histogram can be plotted to see the spread for each atomic shift.



(f) & (g) In most cases, the spread does not appear to be normally distributed, therefore a select sample e.g. 1000 conformers are resampled (M = 1000 by default). This creates a bootstrap mean which can be used inplace of the sample means (from d & e). A new histogram of the bootsrap means can be plotted, in addition to a Q-Q plot, which tests for normality.

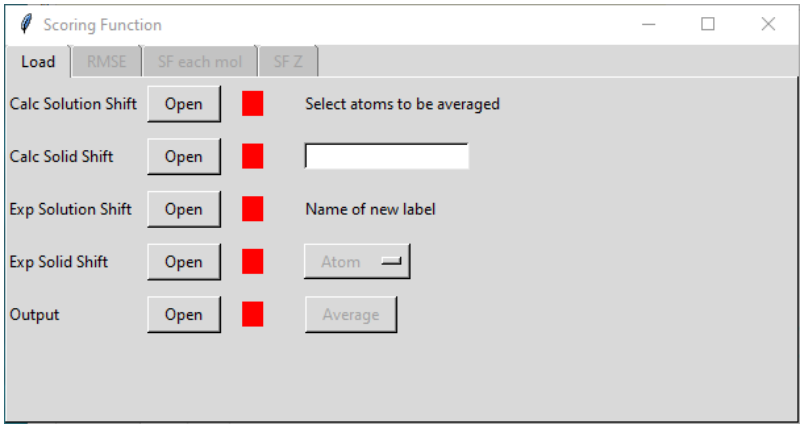




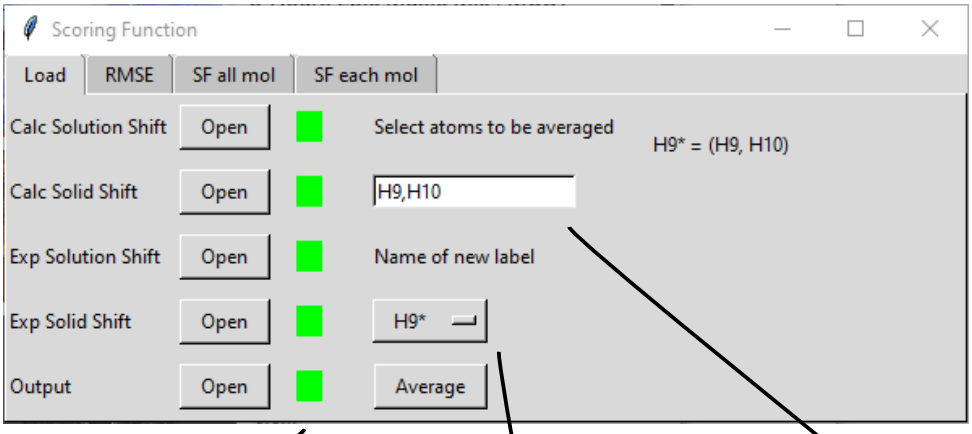
The red box in the histogram plot corresponds to the 95% confidence interval. Note the substantial increase for the bootstrap means, which corresponds to a reduced standard error for the chemical shift.

Scoring Function GUI

G3a Scoring Functions inputs



The scoring function procedure, which uses both calculated and experimental solution- and solid- state chemical shifts is performed here. The input .csv files containing calculated chemical shifts can be obtained from G1a and G1b. See attached example files of the calculated and experimental solution- and solid- state input files.



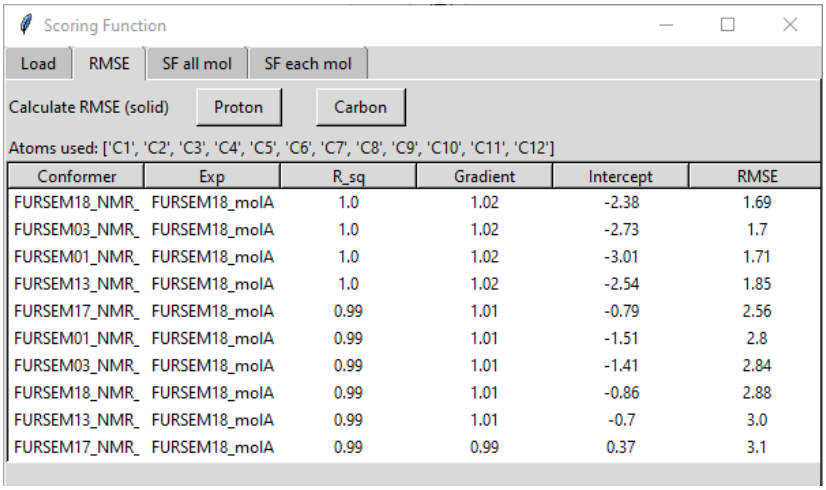
Once the files have been loaded and a folder to save the outputs, such as the scoring funciton tables, has been specified the boxes go green.

Select the experimental atom label, which is assigned to the average of the calculated chemical shifts.

Atom labels from the calculated chemical shifts that are to be averaged are written here.

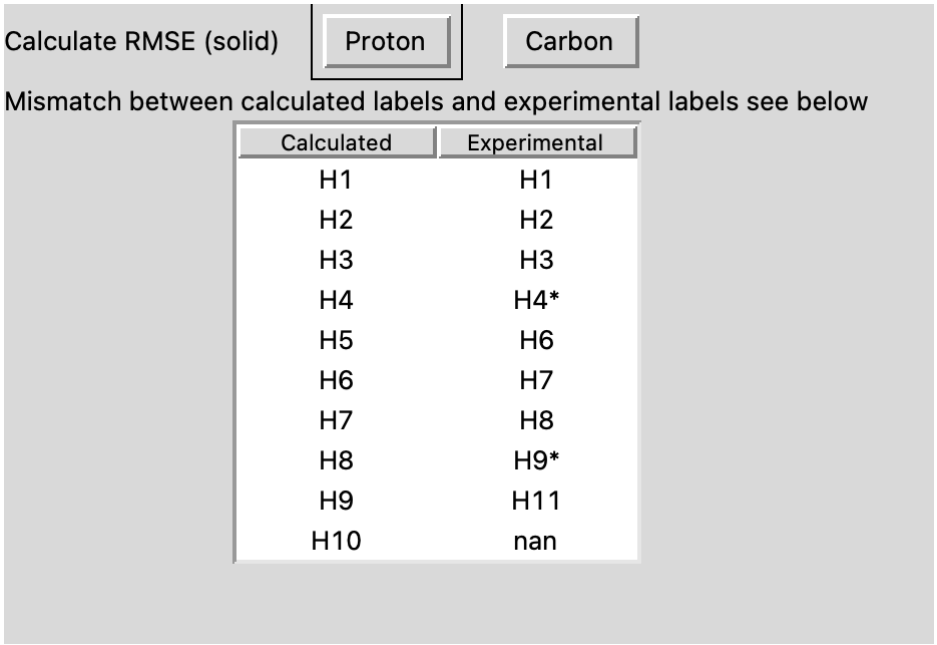
G3b Calculate RMSE

See Table ...



Conformer	Exp	R_sq	Gradient	Intercept	RMSE
FURSEM18_NMR_	FURSEM18_molA	1.0	1.02	-2.38	1.69
FURSEM03_NMR_	FURSEM18_molA	1.0	1.02	-2.73	1.7
FURSEM01_NMR_	FURSEM18_molA	1.0	1.02	-3.01	1.71
FURSEM13_NMR_	FURSEM18_molA	1.0	1.02	-2.54	1.85
FURSEM17_NMR_	FURSEM18_molA	0.99	1.01	-0.79	2.56
FURSEM01_NMR_	FURSEM18_molA	0.99	1.01	-1.51	2.8
FURSEM03_NMR_	FURSEM18_molA	0.99	1.01	-1.41	2.84
FURSEM18_NMR_	FURSEM18_molA	0.99	1.01	-0.86	2.88
FURSEM13_NMR_	FURSEM18_molA	0.99	1.01	-0.7	3.0
FURSEM17_NMR_	FURSEM18_molA	0.99	0.99	0.37	3.1

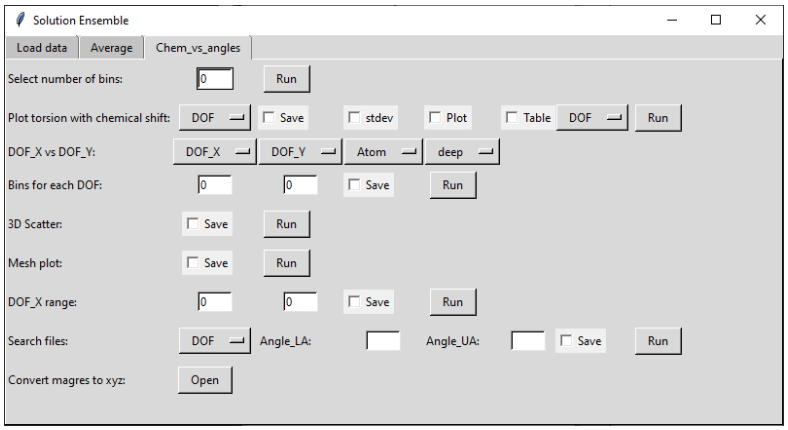
RMSE calculations using experimental and calculated solid-state chemical shifts. By default they are saved in the specified output directory. If there is a mismatch between labels i.e. a proton chemical shift is not averaged, an error will be shown.



Calculated	Experimental
H1	H1
H2	H2
H3	H3
H4	H4*
H5	H6
H6	H7
H7	H8
H8	H9*
H9	H11
H10	nan

Error displaying mismtach between calculated and experimental labels. Non existant labels are ignored, however, experimnetal chemical shift labels that are not found in the calculated form raise an error.

G2c Chemical shift against torsion angle



(h) Torsion angles can be grouped together by setting the number of bins, or plotted individually by setting the number of bins to zero.

(i) The rotatable bond would need to be selected, which can either be plotted or tabulated. By default the bins use the range but this can be changed to the st. dev. Further the plot and or table can be saved if there is an output.

(j) Comparison between two rotatable bonds can be made here for each atom. A colour sheme is needed.

(k) Each rotatable bond can be grouped together in specified bins below each DOF in (j), which produces a contour plot.

(l) & (m) A 3D scatter and mesh plot can be viewed respectively. The mesh plot uses the bins defined in (j).

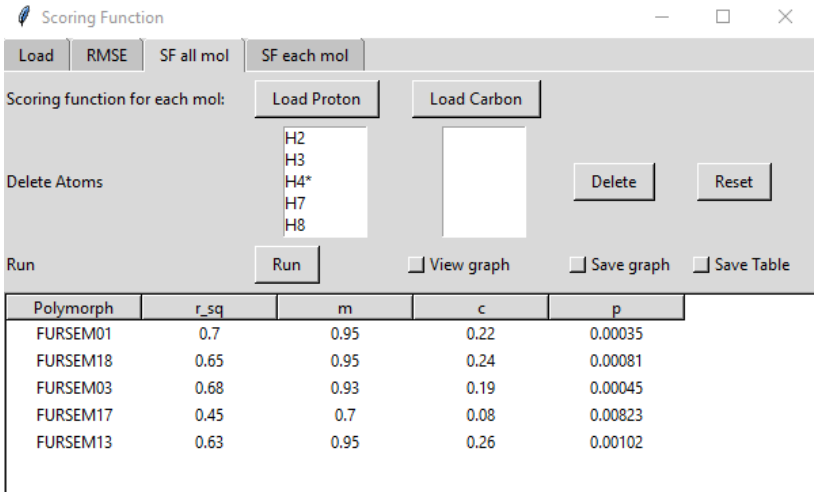
(n) Search for a range of files where one DOF is within the angles of another DOF. In this case all files of DOF_Y that are within the angles defined for DOF_X can be searched.

(o) Search for files that are within the angles defined for each DOF (LA - lower angle, UA - upper angle)

(p) Convert a *.magres* file into a *.xyz* file, to view the 3D conformation in other plotting programmes.

G3c Scoring Function for all moleculese in unit cell

See Table ...



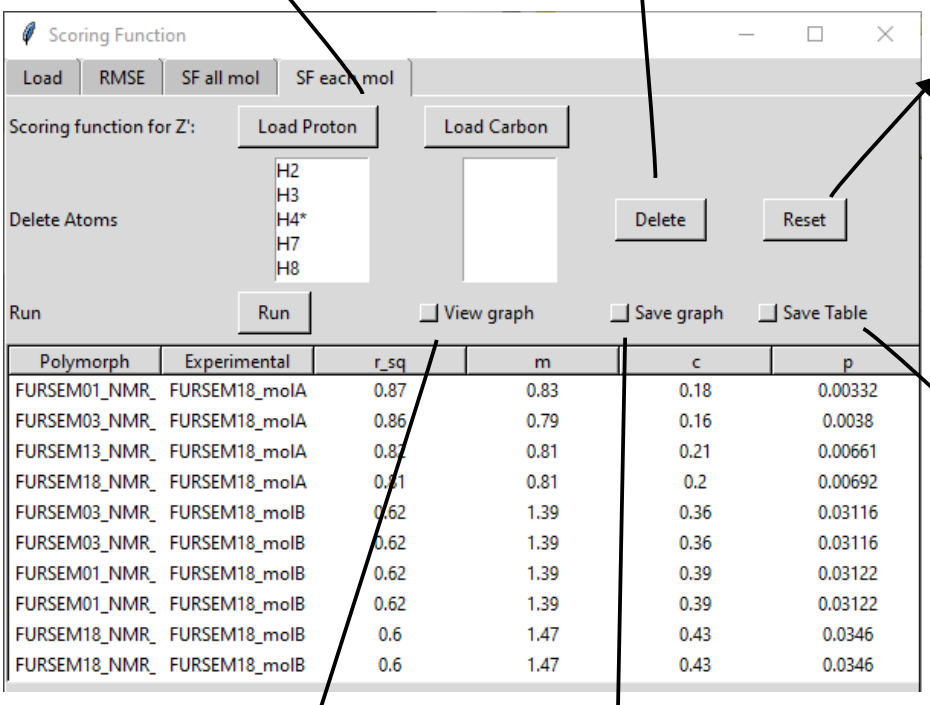
Polymorph	r_sq	m	c	p
FURSEM01	0.7	0.95	0.22	0.00035
FURSEM18	0.65	0.95	0.24	0.00081
FURSEM03	0.68	0.93	0.19	0.00045
FURSEM17	0.45	0.7	0.08	0.00823
FURSEM13	0.63	0.95	0.26	0.00102

The scoring function procedure can be performed by combining multiple molecules in the asymmetric unit cell together. This should account for any miss assignement or lack of chemical shift from either molecule. See next page for a guide to the functions.

G3d Scoring function performed for each molecule in the asymetric unit cell

Select the nuclei.

Atoms in exchange or with unreliable chemical shifts can be removed here.



Polymorph	Experimental	r_sq	m	c	p
FURSEM01_NMR_	FURSEM18_molA	0.87	0.83	0.18	0.00332
FURSEM03_NMR_	FURSEM18_molA	0.86	0.79	0.16	0.0038
FURSEM13_NMR_	FURSEM18_molA	0.8	0.81	0.21	0.00661
FURSEM18_NMR_	FURSEM18_molA	0.81	0.81	0.2	0.00692
FURSEM03_NMR_	FURSEM18_molB	0.62	1.39	0.36	0.03116
FURSEM03_NMR_	FURSEM18_molB	0.62	1.39	0.36	0.03116
FURSEM01_NMR_	FURSEM18_molB	0.62	1.39	0.39	0.03122
FURSEM01_NMR_	FURSEM18_molB	0.62	1.39	0.39	0.03122
FURSEM18_NMR_	FURSEM18_molB	0.6	1.47	0.43	0.0346
FURSEM18_NMR_	FURSEM18_molB	0.6	1.47	0.43	0.0346

Reset will return all the atoms that were at the start of the calculation.

Save the table displayed in the image.

View the linear graphical plots of $\Delta\delta_{\text{solution calc}}$ vs $\Delta\delta_{\text{solid calc}}$.

Save graphical plots of $\Delta\delta_{\text{solution calc}}$ vs $\Delta_{\delta\text{solid calc}}$.