Supporting Information

Predicting Diamagnetic Susceptibility and Diamagnetic Anisotropy of Membrane Proteins from Structural Subunits

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Supporting Information file includes: SI Section 1: Calculating the Magnetic Properties of Amino Acid Subunits; SI Section 2: Comparison Between RealTime Predictor™ and Experimental Values for Estimating the Diamagnetic Anisotropy of Amino Acids; SI Section 3: Determining the Molar Volume of Membrane Proteins; SI Section 4: Magnetic Properties of Membrane Proteins; SI Section 5: Membrane Proteins Used for Extracting the Spatial Coordinates of the Secondary Structures.

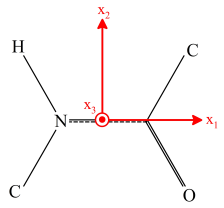
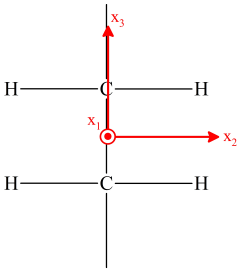
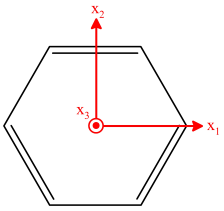
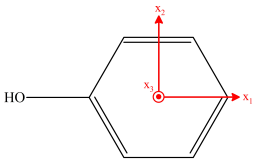
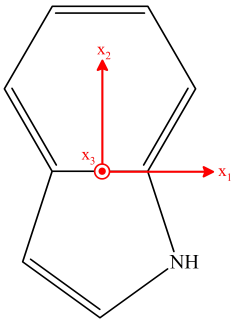
SI Section 1: Calculating the Magnetic Properties of Amino Acid Subunits

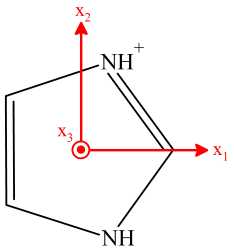
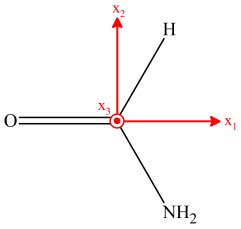
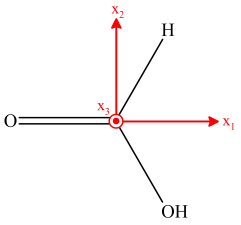
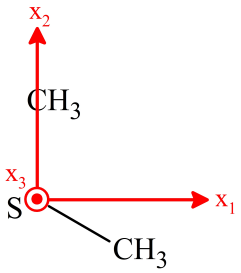
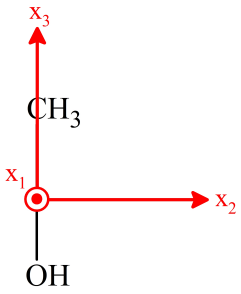
To obtain the coordinates of individual amino acids, we imported all atom coordinates of a PDB file. Calculations were based on coordinates taken from 2omf.pdb and 2i7u.pdb, and MATLAB commands were used to obtain coordinate data within the .pdb file. The coordinates for all atoms in the membrane protein (MP) were stored and indexed by the type of amino acid that they belonged to.

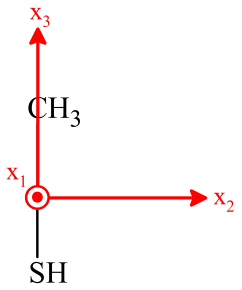
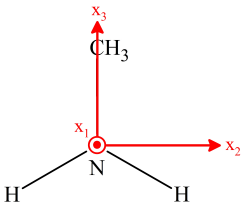
An amino acid is selected, and the first atom (nitrogen) of each occurrence of the selected amino acid is stored. One specific amino acid is selected, and the names of all atoms of that amino acid are obtained. The coordinates of each of those atoms are then obtained. The calculations were performed for several amino acids within a protein, and across amino acids in different proteins.

With knowledge of the type of amino acid and the coordinates of all atoms within the amino acid, the magnetic properties can be calculated. Each amino acid was broken down into groups based on the structure. When possible, data from previous literature was used for bonds groups such as alkane bonds or peptide bonds. However, most side groups cannot be accurately represented with a series of bonds due to resonance or to unique atoms such as nitrogen, oxygen, or sulfur. The properties of several small molecules were used to approximate principle magnetic susceptibility of these side groups. To account for the difference between a free molecule and a group bonded to an amino acid, the mean magnetic susceptibility of a c-h bond was subtracted, and the mean magnetic susceptibility of a c-c bond was added to the available value of the mean magnetic susceptibility of the free molecule. These values used in these approximations are shown Table S1. A function for each of the various functional groups was used to calculate the local coordinates from the coordinates found in the PDB file.

Table S1: Tabulated summary of moieties used to approximate the magnetic properties of amino acids. For each we report, the group name, structure, name of amino acid containing this moiety, and literature values of experimentally determined or calculated molar diamagnetic anisotropy or molar diamagnetic susceptibility. Citations to each reference are provided at the end of the supplementary information file.

Group Name	Structure	Used In	$\Delta\chi$ $(\times 10^{-6}\ \mathrm{cm}^3/\mathrm{mol})$	χ_m $(\times 10^{-6}\ \mathrm{cm}^3/\mathrm{mol})$
Peptide Bond		All Amino Acids	-5.36[1]	-40.30[2]
Alkane Bond		ALA, VAL, LEU, ILE, PHE, TYR, TRP, HIS, LYS, PRO, ARG, THR, MET, ASP, GLU, ASN, GLN	-1.63[3]	-11.64[4,5]
Benzene		PHE	-63.40[6]	-55.30[7]
Phenol		TYR	-63.40[8]	-60.90[2]
Indole		TRP	-86.08[8]	-85.00[2]

Imidazole		HIS	-24.41	-43.05[2]
Formamide		ASN, GLN	-9.00	-22.97
Formic Acid		ASP, GLU	-9.43	-19.20
Dimethyl Sulfide		MET	-3.5[9]	-44.9[2]
Methanol		SER, THR	-1.00[10]	-21.37[2]

Methanethiol		CYS	-1.00[10]	-35.26[2]
Methylamine		PRO, LYS, ARG	-1.63[3]	-11.64[4]
Carbon Hydrogen Bond	C——H	PHE, TYR, TRP, HIS, ASN, GLN, ASP, GLU, MET, SER, THR, CYS	-3.00[10]	-4.25[2]
Carbon Carbon Bond	C——C	PHE, TYR, TRP, HIS, ASN, GLN, ASP, GLU, MET, SER, THR, CYS	-1.00[10]	-2.92[2]

SI Section 2: Comparison Between RealTime Predictor™ and Experimental Values for Estimating the Diamagnetic Anisotropy of Amino Acids

Experimentally measured mean magnetic susceptibility is not available for six of the twenty amino acids. For the unreported amino acids, THR, CYS, PRO, CLN, PHE, and ARG, we use estimates derived using RealTime Predictor™.[11] The values from this predictor do not match the experimental values in all cases. Mean magnetic susceptibility from both methods and the deviation between them are presented in Table S2. The deviation is less than 3% for all the amino acids with smaller experimental mean susceptibility compared to RealTime values. However, when the RealTime Predictor underestimates the magnetic susceptibility, the deviation increases to more than 24%.

Table S2: Experimental and RealTime Predictor™ estimates of the mean magnetic susceptibility of amino acids.

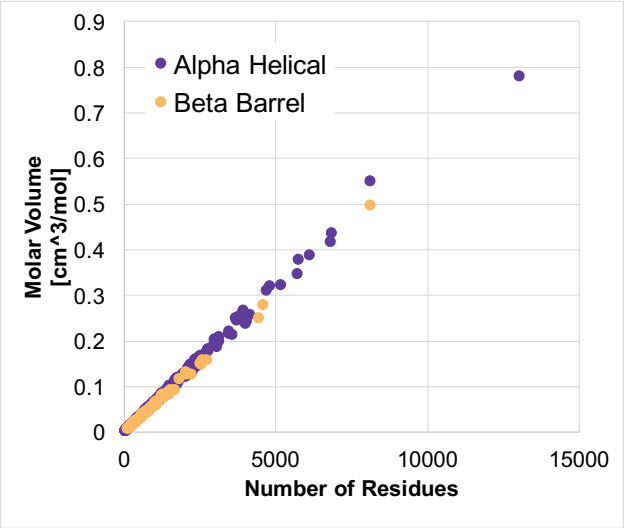
Amino Acid	Experimental Mean Magnetic Susceptibility $(\times 10^{-6}\ cm^3/mol)$	RealTime Predictor™ Mean Magnetic Susceptibility $(\times 10^{-6}\ cm^3/mol)$	Calculated Mean Magnetic Susceptibility $(\times 10^{-6}\ cm^3/mol)$	Deviation Between Experimental and RealTime Prediction (%)	Deviation Between Calculated and Available Data (%)
GLY	-40.30	-40.90	-40.00	1.50	-0.74
ALA	-50.50	-51.79	-51.82	2.56	0.06
SER	-56.30	-57.11	-59.92	1.43	4.92
ASP	-64.60	-59.96	-69.67	-7.18	7.85
THR	-	-68.78	-71.84	-	4.44
ASN	-69.50	-67.90	-72.93	-2.30	4.94
CYS	-	-69.70	-73.91	-	6.05
PRO	-	-69.33	-75.46	-	8.84
VAL	-74.30	-74.56	-75.46	0.36	1.21
GLU	-78.00	-71.34	-81.49	-8.54	4.47
GLN	-	-79.14	-85.26	-	7.73
LEU	-84.90	-85.77	-87.28	1.03	1.76
ILE	-84.90	-93.06	-87.28	9.61	2.80
MET	-91.00	-91.37	-95.37	0.41	4.38

HIS	-85.60	-87.33	-96.22	2.03	10.18
LYS	-104.80	-93.06	-99.60	-11.20	-4.96
PHE	-	-94.82	-108.47	-	14.39
TYR	-105.30	-79.95	-114.07	-24.07	8.33
ARG	-	-105.28	-122.74	-	16.59
TRP	-132.00	-115.97	-138.17	-12.14	4.67

SI Section 3: Determining the Molar Volume of Membrane Proteins

We used the rolling probe method implemented in 3V server to determine the volume of a protein molecule.[12] As an input for assessing the volume, the website takes the PDB file for the MP, the probe radius, and the grid resolution. We define the probe size to be 5A° and the grid resolution to be high.

Figure S1: Relationship between the Number of Amino Acid Residues in a Membrane Protein and the Molar Volume of that Membrane Protein.



SI Section 4: Magnetic Properties of Membrane Proteins

Table S3: Tabulated summary of Figure 3A and 3B for each membrane protein, including the PDB code, name of structure, family and subfamily of the structure, number of residues in the structure, calculated molar diamagnetic anisotropy using 4 different methods, molar volume, and calculated volumetric diamagnetic anisotropy using 4 different methods. Membrane proteins are grouped based on their tertiary structures as beta-barrel, alpha helical, or monotopic. A list of MPs with unavailable structures is presented at the end. Each group is then sorted based on the number of residues in their structures.

SI Section 5: Membrane Proteins Used for Extracting the Spatial Coordinates of the Secondary Structures

The PDB file represents the tertiary structure of a MP, which is a combination of different secondary structures. To investigate the magnetic properties of secondary structures, we extracted the spatial coordinates of those structures from the PDB files by selecting MPs with a large number of secondary structures. The list of MPs from which the alpha helical and beta strands are chosen is presented in Table S4.

Table S4: List of MPs from which the secondary structures, helices and strands are extracted.

Type of Membrane Protein	PDB	Number of Helices	Number of Strands
Alpha Helical	1C3W	8	0
	1H2S	10	0
	1Q16	57	40
	2B2H	23	0
	2H88	19	22
	2I5N	21	0
	2J8C	8	0
	3LDC	3	0
	3S8G	31	0
	3WG7	26	0
	4Y9H	9	0
Beta Barrel	1FI1	0	35
	1I78	0	12
	1QFF	0	35
	2VDF	0	11
	2W6T	0	41
	2X9K	0	14
	3DWO	0	19

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