An Attempt at Implementing the MMFF94 for Linear Alkanes.

CHEM179: Final Project

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Merck Molecular Force Field. I. Basis, Form, Scope, Parameterization, and Performance of MMFF94*

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$$\vec{F} = -\nabla U(\vec{r})$$

Form of the MMFF94

Build lists:
-Neighbors
-Bond lengths
-Bond angles
-Out of plane angles
-Torsion angles
-Interacting atoms

$$E_{MMFF} = \sum EB_{ij} + \sum EA_{ijk} + \sum EBA_{ijk} + \sum EOOP_{ijk;l} + \sum ET_{ijkl} + \sum EvdW_{ij} + \sum EQ_{ij}$$

$$EB_{ij} = 143.9325 \frac{k_{b_{IJ}}}{2} \Delta r_{ij}^2 \left(1 + cs\,\Delta r_{ij} + \frac{7}{12} cs^2 \Delta r_{ij}^2\right)$$

$$EA_{ijk} = 0.043844 k_{a_{IJK}} \Delta\vartheta_{ijk}^2 (1 + cb\,\Delta\vartheta_{ijk})$$

$$EBA_{ijk} = 2.51210(kba_{IJK}\Delta r_{ij} + kba_{KIJ}\Delta r_{kj})\Delta\vartheta_{ijk}$$

$$EOOP_{ijk;l} = 0.043844 \frac{koop_{IJK:L}}{2} \chi_{ijk;l}^2$$

$$ET_{ijkl} = 0.5\left[V_1(1 + \cos\Phi) + V_2(1 - \cos 2\Phi) + V_3(1 + \cos 3\Phi)\right]$$

$$EvdW_{ij} = \varepsilon_{IJ}\left(\frac{1.07R_{IJ}^*}{R_{ij} + 0.07R_{IJ}^*}\right)^7 \left[\frac{1.12(R_{IJ}^*)^7}{R_{ij}^7 + 0.12(R_{IJ}^*)^7} - 2\right]$$

$$EQ_{ij} = 332.0716 \frac{q_i q_j}{D(R_{ij} + \delta)^n}$$

$$q_i = q_i^0 + \sum \omega_{KI}$$

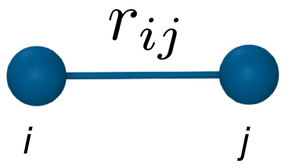
$$\omega_{KI} = \rho_I - \rho_K$$

$$R_{II}^* = A_I \alpha_I^{1/4} \qquad \gamma_{IJ} = \frac{R_{II}^* - R_{JJ}^*}{R_{II}^* + R_{JJ}^*}$$

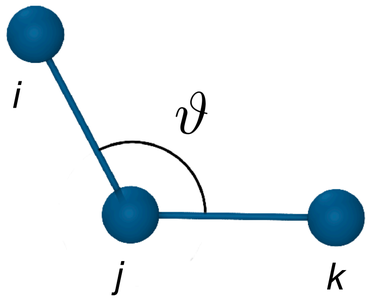
$$R_{IJ}^* = 0.5(R_{II}^* + R_{JJ}^*)\left[1 + 0.2(1 - \exp(-12\gamma_{IJ}^2))\right]$$

$$\varepsilon_{IJ} = 181.16 G_I G_J \alpha_I \alpha_J \left(\frac{1}{(\alpha_I/N_I)^{1/2} + (\alpha_J/N_J)^{1/2}}\right) \frac{1}{(R_{IJ}^*)^6}$$

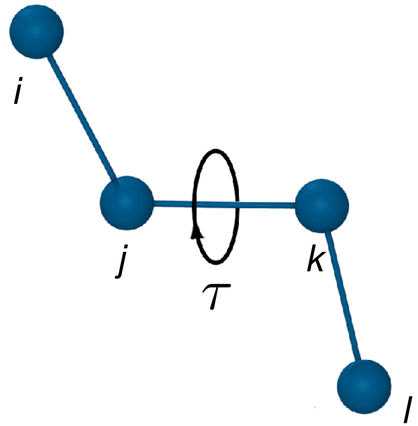
From .xyz to bonds and angles



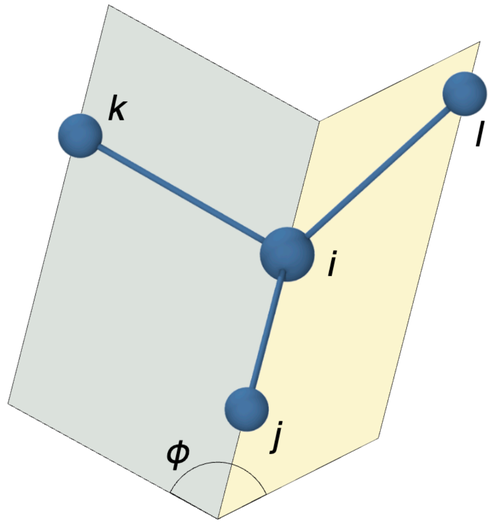
$$r_{ij} = \sqrt{(x_i - x_j)^2 + (y_i - y_j)^2 + (z_i - z_j)^2}$$



$$\cos\vartheta = \mathbf{e}_{ji} \cdot \mathbf{e}_{jk}$$

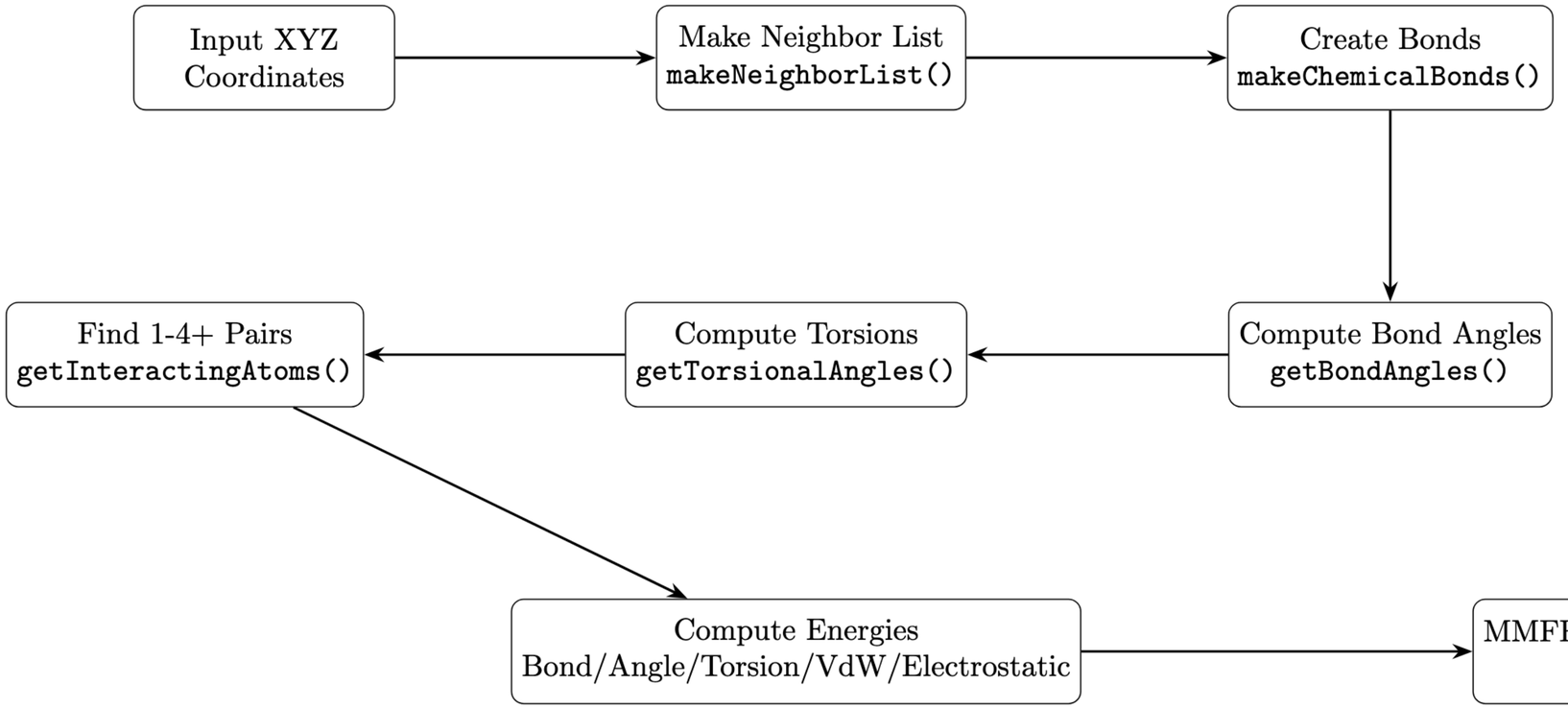


$$\cos\tau = \frac{(\mathbf{e}_{ji} \times \mathbf{e}_{jk}) \cdot (\mathbf{e}_{jk} \times \mathbf{e}_{kl})}{\sin\vartheta_{ijk} \sin\vartheta_{jkl}}$$



$$\sin\phi = \frac{\mathbf{e}_{ij} \times \mathbf{e}_{ik}}{\sin\vartheta_{jik}} \cdot \mathbf{e}_{il}$$

Workflow



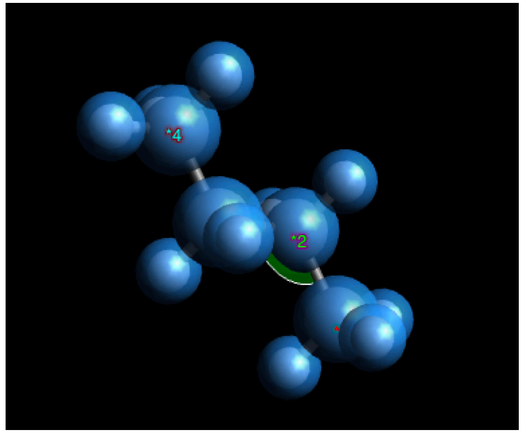

```
/*
STRUCTS AND CLASSES USED TO REPRESENT THE MOLECULAR TOPOLOGY:
*/

struct Bond {
        double distance;
        int atom1;
        int atom2;
};


class Molecule {
public:
        // Attributes
        int nr_atoms;
        arma::vec atom_vec;
        arma::vec enumerated_atom_vec;
        arma::mat xyz_mat;
        std::vector<std::pair<int, arma::vec>> neighbor_vec;
        std::vector<Bond> bond_vec;
        std::vector<std::pair<double, std::array<int, 3>>> bond_angles;
        std::vector<double> improper_angles;
        std::vector<std::pair<double, std::array<int, 4>>> torsional_angles;
        std::vector<std::pair<int, int>> interacting_atoms;
```

A First Challenge

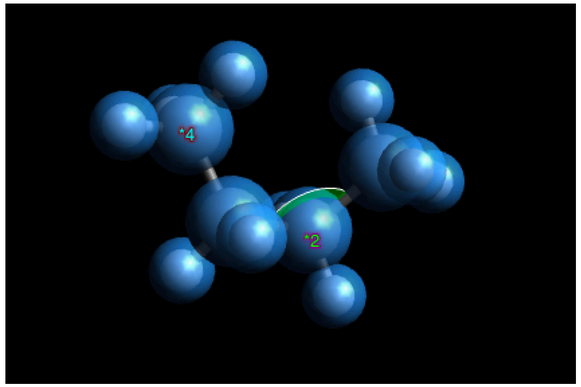
TABLE II.
(continued)

Conformational comparison	Relative energy, enthalpy, or free energy: Exp.	"MP4"[a]	MMFF94	MM2X	MM3
Isopropylamine, lp — N — C — H anti–gauche	0.45[t]	0.50	0.45	0.10	0.22[t]
Cyclohexylamine, ax–eq	1.1–1.8[u]	0.69	0.67	1.17	—
Piperidine, ax–eq	0.4[t]	0.78	0.90	−0.30	0.29[t]
N-methylpiperidine, ax–eq	3.15[v]	3.58	3.28	2.23	—
Ethanol, gauche–anti	0.12,[w] 0.4[x]	−0.06	0.18	0.62	0.40[s]
Isopropanol, H — C — O — H anti–gauche	0.28[y]	0.20	0.17	0.60	—
Cyclohexanol, ax C_1–eq C_1	0.52[s]	0.33	0.32	0.75	0.74[s]
Methyl ethyl ether, gauche–anti	1.5[s]	1.41	1.50	1.75	1.49[s]
Methyl vinyl ether, C=C—O—C skew–cis	1.7[z]	2.27	2.22	—	2.44[z]
Diethyl ether, (C — C — O — C a, C — O — C — C g) –(C — C — O — C a, C — O — C — C a)	1.1[s]	1.48	1.52	1.77	1.51[s]
Methoxycyclohexane, ax C_1–eq C_1	0.45[aa]	−0.01	0.41	0.74	0.77[s]
Butane, gauche–anti	0.75,[bb] 0.97[v]	0.65	0.78	0.36	0.81[bb]
Cyclohexane, twist–boat–chair	5.5[cc]	6.14	5.93	5.52	5.76[bb]
Methylcyclohexane, ax–eq	1.75[dd]	1.69	1.37	1.86	1.77[bb]
2,3-Dimethylbutane, H — C_2 — C_3 — H gauche –H — C_2 — C_3 — H anti	0.05, 0.17[dd]	0.04	−0.23	0.17	0.38[bb]
Cyclooctane, D_{4d}–C_s boat chair	1.9[bb]	2.00	1.44	0.97	1.12[bb]
Cyclononane, [255] C_2–[333] D_3	0.95[ee]	0.98	1.21	0.67	0.84[bb]
1-Butene, cis–skew	0.53[ff]	0.26	0.26	1.10	0.69[ff]
2-Butene, cis–trans	1.0[ff]	1.27	1.35	1.55	—
(rms value), rms deviation vs. exp.	(2.33)	0.37[gg]	0.38[gg]	0.84[gg]	0.37[hh]
rms deviation vs. "MP4SDQ / TZP"	—	—	0.33	0.81	0.49

[a] "MP4SDQ / TZP" calculations (see text).
[b] Average of values cited in: D. M. Schnur, Y. H. Yuh, and D. R. Dalton, *J. Org. Chem.*, **54**, 3779–3785 (1989).
[c] Ref. 32.
[d] Ref. 33.
[e] Ref. 34.
[f] As cited in ref. 35.
[g] B. P. van Eijc and F. B. van Duijneveldt, *J. Mol. Struct.*, **39**, 157–163 (1977).
[h] J. R. Durig, D. A. C. Compton, and A. Q. McArver, *J. Chem. Phys.*, **73**, 719–724 (1980).
[i] As cited in N. L. Allinger, K. Chen, M. Rahman, and A. Pathiaseril, *J. Am. Chem. Soc.*, **113**, 4505–4517 (1991).
[j] Ref. 36.
[k] Average of values cited in K. B. Wiberg, P. R. Rablen, and M. Marquez, *J. Am. Chem. Soc.*, **114**, 8654–8668 (1992).
[l] Ref. 57.
[m] Y. N. Panchenko, V. I. Pupyshev, A. V. Abramenkov, M. Traetteberg, and S. J. Cyvin, *J. Mol. Struct.*, **130**, 355–359 (1985).
[n] N. L. Allinger, S. Rodriguez, and K. Chen, *J. Mol. Struct.*, **260**, 161–178 (1992).
[o] Preferred value cited in ref. 38. Other cited values range from −1.41 to +1.98 kcal / mol.
[p] Average of 13 experimental determinations cited in ref. 39.
[q] Ref. 40.
[r] Ref. 41.
[s] As cited in ref. 43.
[t] As cited in L. R. Schmitz and N. L. Allinger, *J. Am. Chem. Soc.*, **112**, 8307–8315 (1990).
[u] As reported by and cited in ref. 44.
[v] As cited in ref. 30.
[w] Ref. 46.
[x] Ref. 45.
[y] E. Hirota, as cited in W. A. Latham, L. Radom, W. J. Hehre, and J. A. Pople, *J. Am. Chem. Soc.*, **95**, 699 (1973).
[z] As cited in N. L. Allinger and L. Yan, *J. Am. Chem. Soc.*, **115**, 11918–11925 (1993).
[aa] As cited in N. L. Allinger and D. Y. Chung, *J. Am. Chem. Soc.*, **98**, 6798 (1976).
[bb] As cited in ref. 7.
[cc] M. Squillacote, R. S. Sheridan, O. L. Chapman, and F. A. L. Anet, *J. Am. Chem. Soc.*, **97**, 3244–3246 (1975).
[dd] As cited in ref. 29b.
[ee] Ref. 51.
[ff] As cited in N. L. Allinger, F. Li, and L. Yan, *J. Comput. Chem.*, **11**, 848–867 (1990).
[gg] Computed using the experimental result closest to the MP4SDQ / TZP value when more than one experimental value is listed.
[hh] Computed using the experimental result closest to the MM3 value.



Anti



Gauche

My code: 0.807905 kcal/mol

Table 1
Conformational energies and barrier heights of *n*-butane

Method	Energies (kcal/mol): trans	gauche
HF/6-31G*//HF/6-31G*	0.0	0.95
MP2/6-31G*//MP2/6-31G*	0.0	0.68
MP3/6-31G*//MP2/6-31G*	0.0	0.74
MP4(SDTQ)/6-31G*//MP2/6-31G*	0.0	0.69
CCSD(T)/6-31G*//MP2/6-31G*	0.0	0.70
QCISD(T)/6-31G*//MP2/6-31G*	0.0	0.70
BLYP/6-31G*//MP2/6-31G*	0.0	0.68
BLYP/6-31G*//BLYP/6-31G*	0.0	0.85
electron diffraction [c]	0.0	0.75 ± 0.24
IR in solid neon [d]	0.0	< 0.73

[a] Internal rotational barrier height between the trans and the gauche rotamers.
[b] Internal rotational barrier height of the eclipse saddle point.
[c] Ref. [22]. [d] Ref. [23].

A Big Challenge

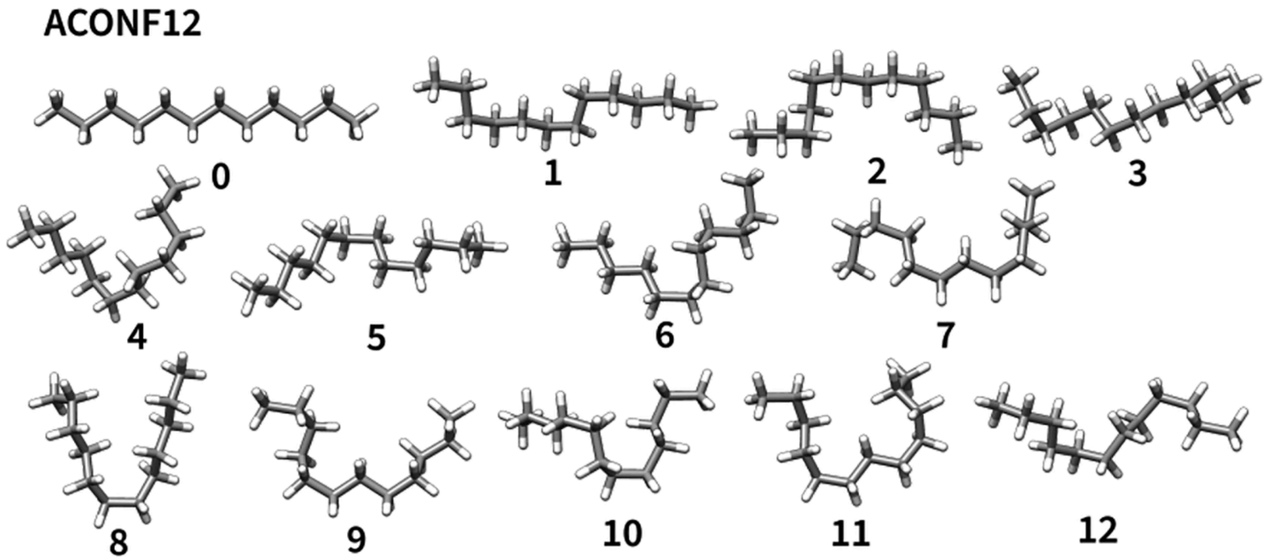


Figure 1. Thirteen *n*-dodecane conformers of the ACONF12 subset. The conformer **0** is the lowest conformer, and the numbering of the conformers does not necessarily correspond to their energetic order.

Problems Encountered

-no koop parameters for H-C-C-H or C-C-C-H

-double counting angles

-how many torsions (unique or all permutations)

-constants defined per bond or per angle?

-checking that the number of angles and 1-4+ interactions are correct (9N-1 for N >= 4, angles)

-«shooting in the dark» at 0.78 kcal/mol

-Ideally a pentane test too (geometric type)

Thank you, questions?