Chapter 1

Electronegativity equalization method

Electronegativity equalization method (EEM) [1, 2, 3, 4, 5] is a fast empirical method for atomic charge calculation. Its main advantage in comparison with QM methods is the time complexity $\mathcal{O}(n^3)$ where n denotes the number of atoms in the molecule [6].

According to [1], the electronegativity of an atom can be expressed as:

$$\overline{\chi} = \chi_i = A_i + B_i q_i + \kappa \sum_{i \neq j} \frac{q_j}{r_{i,j}} \tag{1.1}$$

where χ_i denotes the electronegativity of atom i (which is the same as $\overline{\chi}$ due to the Sanderson's equalization principle, A_i, B_i, κ are empirical parameters, q_i and q_j are the charges of atoms i and j respectively, and finally $r_{i,j}$ is the distance between atoms i and j.

Translating equation (1.1) into the system of linear equations describing one particular molecule gives us final EEM system of $n + 1$ equations with $n + 1$ unknowns $(q_1, \ldots, q_n, \overline{\chi})$ used for calculating atomic charges:

$$\begin{pmatrix} B_1 & \frac{\kappa}{r_{1,2}} & \cdots & \frac{\kappa}{r_{1,n}} & -1 \\ \frac{\kappa}{r_{1,2}} & B_2 & \cdots & \frac{\kappa}{r_{2,n}} & -1 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \frac{\kappa}{r_{1,n}} & \frac{\kappa}{r_{2,n}} & \cdots & B_n & -1 \\ 1 & 1 & \cdots & 1 & 0 \end{pmatrix} \cdot \begin{pmatrix} q_1 \\ q_2 \\ \vdots \\ q_n \\ \overline{\chi} \end{pmatrix} = \begin{pmatrix} -A_1 \\ -A_2 \\ \vdots \\ -A_n \\ Q \end{pmatrix} \tag{1.2}$$

where Q denotes the sum of all charges in the molecule, that is

$$Q = \sum_{i=1}^{n} q_i \tag{1.3}$$

Chapter 2

Parameterization of EEM

The most challenging phase of using EEM is its parameterization, that is obtaining parameters κ, A_i, B_i. To be able to do this, we must be provided with the training set of molecules with previously computed QM charges.

Introducing following substitutions

$$x_i = q_i \tag{2.1}$$

$$y_i = \chi_i - \kappa \sum_{i \neq j} \frac{q_j}{r_{i,j}} \tag{2.2}$$

we can rewrite equation (1.1) as

$$y_i = A_t + B_t x_i \tag{2.3}$$

where A_t and B_t are the parameters for a particular atom type t.

These parameters can then be calculated from the following equations obtained by the application of the least squares method (see [**?**] for the full derivation):

$$B_t = \frac{n \sum_{i=1}^{n} x_i y_i - \sum_{i=1}^{n} x_i \sum_{i=1}^{n} y_i}{n \sum_{i=1}^{n} x_i^2 - \left(\sum_{i=1}^{n} x_i\right)^2} \tag{2.4}$$

$$A_t = \frac{\sum_{i=1}^{n} y_i - B_t \sum_{i=1}^{n} x_i}{n} \tag{2.5}$$

2.1 Basic parameterization process

The basic process of the parameterization and thus the main topic of our work can be expressed by the means of the following algorithm [7]:

Input: Structural molecular data with reference QM charges

Output: Set of EEM parameters

1. For every admissible κ value:
   a) Compute pair of parameters (A_t, B_t) using equations (2.4), (2.5) for every atom type
   b) Solve EEM system (1.2) to get EEM charges
   c) Calculate correlation between EEM and QM charges
2. Return κ (and associated parameters) with the largest correlation coefficient

2.2 Optimization of the parameterization process

Although algorithmically rather simple, the parameterization process contains two challenges which must be resolved:

1. Finding the best κ value within the specified interval in a reasonable number of steps.

2. The next issue is therefore to determine the optimal subset of molecules for parameters calculation. Note that although the molecules are excluded from this calculation, the correlation coefficient is then computed for the full set of molecules.

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