Generating Effective Charge (ECM) sites for small molecules

Effective Charges for Macromolecules in solvent (ECM) are fitted charges in a uniform dielectric that can reproduce the electrostatic potential of the molecule computed with the use of all atomic charges in a heterogeneous dielectric. The accurate evaluation of electrostatic forces and interaction free energies for protein-ligand association is computationally not feasible for realistic systems with thousands of atomic charges in an environment with a non-uniform dielectric permittivity and a solvent of non-zero ionic strength. Therefore, a small number of effective charges are calculated for each molecule that will reproduce the intermolecular electrostatic interactions with high accuracy in a uniform dielectric.

Name of the Script: `ECM_ligand.py`

Description:

This Python script generate test charge file (**.tcha file**) with ECM sites that is required by the SDA software to calculate Effective Charges for Macromolecules (ECM) for small molecules (ligands).

Input parameters:

It takes total 2 parameters as input where 2nd parameter is optional (number of ECM sites):

1) PQR file of the ligand (with .pqr extension).
2) Number of ECM sites to be generated (OPTIONAL parameter).

By default, the particular number of these ECM sites are calculated depending upon the size of the ligand and the distribution of charge across the structure of molecule, e.g. a positively charged ligand will get a higher number of positive ECM sites to maintain the total overall charge.
Default number of ECM sites is given as:

$$n_{sites} = (Total\ number\ of\ atoms)/4 + 2 \times (total\ charge\ on\ ligand).$$

*** In case the charge fitting after effective charge calculation with default number of ECM sites is not satisfactory, it is recommended to recalculate effective charges by changing the number of ECM sites by ± 2 that can be specified using 2nd input parameter. ***

Usage:

```
python  ECM_ligand.py  ligand_pqr  number_sites
```

`ligand_pqr` - Name of PQR file for the ligand with .pqr extension

`number_sites` - Number of ECM sites (optional parameter)

Example:

We have used PQR file of Rivaroxaban (**RIV.pqr**), a direct Human Coagulation Factor Xa inhibitor for generation of ECM sites to be used in association rate calculations of Rivaroxaban and Factor Xa binding.

The Script was run as:

```
ganotrgv@arete:~/sda/auxi/Kon-rates-SmallMolecule/Generate-ECMSites-SmallMol$ python ECM_Ligand.py RIV.pqr
```

*** Output file is generated in the same directory with name : **RIV.tcha**

```
ganotrgv@arete:~/sda/auxi/Kon-rates-SmallMolecule/Generate-ECMSites-SmallMol$ cat RIV.tcha
ATOM      4   C4 RIV     1       7.671   2.122  16.881        0.500
ATOM     13  O13 RIV     1       6.583   2.613  16.630       -0.500
ATOM     15  C15 RIV     1       5.040   5.543  22.995        0.500
ATOM     19  O19 RIV     1       4.634   4.419  23.228       -0.500
ATOM     22  C22 RIV     1       8.402   8.558  24.672        0.500
ATOM     28  O28 RIV     1       8.611   9.379  23.797       -0.500
```

RUN with specified number of ECM sites (number_sites=10)

```
ganotrgv@arete:~/sda/auxi/Kon-rates-SmallMolecule/Generate-ECMSites-SmallMol$ python ECM_Ligand.py RIV.pqr 10
```

```
ganotrgv@arete:~/sda/auxi/Kon-rates-SmallMolecule/Generate-ECMSites-SmallMol$ cat RIV.tcha

ATOM      3   C3 RIV     1      10.053   0.667  17.441        0.500
ATOM      4   C4 RIV     1       7.671   2.122  16.881        0.500
ATOM      5   O5 RIV     1       9.768   1.124  16.111       -0.500
ATOM     13  O13 RIV     1       6.583   2.613  16.630       -0.500
ATOM     15  C15 RIV     1       5.040   5.543  22.995        0.500
ATOM     17  O17 RIV     1       4.690   6.614  23.757       -0.500
ATOM     19  O19 RIV     1       4.634   4.419  23.228       -0.500
ATOM     20  C20 RIV     1       5.924   8.721  24.155        0.500
ATOM     22  C22 RIV     1       8.402   8.558  24.672        0.500
ATOM     28  O28 RIV     1       8.611   9.379  23.797       -0.500
```