

Calculating electrostatic component of binding energy

Here we demonstrate how to calculate the electrostatic binding energy for the barnase-barstar complex. For this purpose, we calculate the sum of Coulombic and solvation (rxn) energies of the complex and that of the separated barnase and barstar molecules. The difference of these two terms returns the electrostatic component of the binding energy. This example will illustrate how to calculate the electrostatic component of the binding energy at zero salt and how to do the same if salt concentration is not zero. In case of modeling the electrostatic component of binding energy at NON zero salt, two different protocols are demonstrated (Method 1 and Method 2). Method 1 utilizes grid energy difference while Method 2 uses energy partitioning. Details are as follows:

Open the bash script `./binding.sh` in a text editor. In line 3, locate `"DELPHI_COMMAND"` and replace its value `"_DELPHI_COMMAND_"` with the appropriate command to run delphi.

E.g. To run delphi's sequential version, replace `"_DELPHI_COMMAND_"` with `"<absolute/path/of/Delphi/executable>"`

Run the script called `"binding.sh"`. To run this script, you must make sure that the file has executable permission. To assign executable permission, run the command:

```
$ chmod a+x binding.sh
```

Then type

```
$ ./binding.sh
```

It will run DelPhi six times on six different parameter files.

The first run will be on the complex, second on the barnase and the third on the barstar molecules. One should keep the molecules at the same positions in all runs (this is required for Method 1 calculations, since it uses grid energy differences and artificial grid energy terms must be canceled out). Linear Poisson-Boltzmann equation will be solved at ionic salt concentration (salt=0.1). For Method 1, we perform runs at zero and then at particular salt concentrations. For Method 2, we need only a run at a particular ionic strength. Note that if one wants to model the electrostatic component of binding energy at zero ionic strength, the protocol becomes much simpler, the calculation only needs to be run at zero salt concentration (salt=0), and also, there is no requirement to keep the molecules at the same position.

Type:

```
$ grep -i 'total grid' *_nosalt.log
```

The results for salt=0.0 are shown below:

```
(1) complex_nosalt.log: Energy> Total grid energy
: 132916.40 kT
(2) barnase_nosalt.log: Energy> Total grid energy
: 73515.46 kT
(3) barstar_nosalt.log: Energy> Total grid energy
: 59388.52 kT
```

In addition to these numbers, one needs to know the Coulombic interactions and reaction field energies at zero salt.

Type:

```
$ grep -i 'coulombic energy' *_nosalt.log
(1) complex_nosalt.log: Energy> Coulombic energy
: -44990.50 kT
(2) barnase_nosalt.log: Energy> Coulombic energy
: -25009.84 kT
(3) barstar_nosalt.log: Energy> Coulombic energy
: -19433.73 kT

$ grep -i 'corrected reaction field' *_nosalt.log
(4) complex_nosalt.log: Energy> Corrected reaction field energy
: -1737.29 kT
(5) barnase_nosalt.log: Energy> Corrected reaction field energy
: -1020.39 kT
(6) barstar_nosalt.log: Energy> Corrected reaction field energy
: -1265.72 kT

$ grep -i 'all required energy' *_nosalt.log
(7) complex_nosalt.log: Energy> All required energy terms but grid energy
: -46727.79 kT
(8) barnase_nosalt.log: Energy> All required energy terms but grid energy
: -26030.24 kT
(9) barstar_nosalt.log: Energy> All required energy terms but grid energy
: -20699.45 kT
```

Note: „All required energy terms but grid energy,“ is the sum of Coulombic energy, Corrected reaction field energy and ion energy (ion energy is 0 when there is no salt).

The results for salt=0.1 are shown below:

```
$ grep -i 'total grid' `ls *.log` | grep -v '_'`
(10) complex.log: Energy> Total grid energy
132912.93 kT
(11) barnase.log: Energy> Total grid energy
73513.71 kT
(12) barstar.log: Energy> Total grid energy
59382.30 kT

$ grep -i 'all required energy' `ls *.log` | grep -v '_'`
(13) complex.log: Energy> All required energy terms but grid energy
-46730.75 kT
(14) barnase.log: Energy> All required energy terms but grid energy
-26031.94 kT
(15) barstar.log: Energy> All required energy terms but grid energy
-20704.96 kT
```

Calculation of electrostatic component of binding energy at zero salt:

Note that molecules do not have to be kept at the same position (a center is not needed but it is not wrong if you use it). Calculation of the binding energy for non-zero salt:

Method 1:

```
delG(binding) = G(grid, complex)-G(grid, barnase)-G(grid, barstar)
delG(binding) = 132916.40 - 73515.46 - 59388.52 = 12.42 (kT)
```

Method 2 (Energy partitioning)

```
delG(binding)=G(coulombic)+G(reaction field)+G(ions)
=G(complex, all required energy terms) ,À G(barnase, all required energy terms)
- G(barstar, all required energy terms)
= -46727.79 - (-26030.24) - (-20699.45) = 1.9 kT
```

Thus, delG(binding)= +1.9kT

Note that the calculated electrostatic component of binding energy via Method 1 and Method 2 is different. This is due to the fact that Method 1 does not fully cancel so termed ,Àartificial grid energy,À arising from real charges partitioning onto the grid. This we recommend using Method 2, the energy partitioning method in case of energy calculations with zero salt.

Calculation of electrostatic component of binding energy at salt = 0.1:

Method 1:

```
delG(binding) = G(grid, complex)-G(grid, barnase)-G(grid, barstar)
delG(binding) = 132912.93 - 73513.71 - 59382.30 = 16.92 kT
```

Method 2 (Energy partitioning)

```
delG(binding)=G(coulombic)+G(reaction field)+G(ions)
=G(complex, all required energy terms) ,À G(barnase, all required energy terms)
- G(barstar, all required energy terms)
= -46730.75 - (-26031.94) - (-20704.96) = 6.15 kT
```

Thus, delG(binding)= +1.9kT

Note that there is a difference between the results from Method 1 and Method 2. This is because of the above mentioned ,Àartificial grid energy,À effect and because of the relatively large filling of the computational box (the molecule occupies most of the space of the computational box) and this results in non-zero potential at the box sides/surfaces (molecule charged atoms are too close to the box sides/surfaces). Because of that Method 2 omits ion contributions from ions being outside the computational box. If one decreases the filling, the results obtained with Method 1 and 2 will be closer to each other, but this will dramatically increase the computational time. Thus, we recommend using Method 1 in case of having significant contribution of ions to the calculated energies. However, if the ion contribution is low, we recommend using Method 2.