Generalized Born : Energies, Forces and Hessian

Santanu Chatterjee

1 Energy and Force Equations

Effective Born radii for atom i is given by

$$R_i^{-1} = \tilde{\rho}_i^{-1} - \rho_i^{-1} \tanh(\alpha\Psi_i - \beta\Psi_i^2 + \gamma\Psi_i^3). \tag{1}$$

or

$$R_i = \frac{\tilde{\rho}_i\rho_i}{\rho_i - \tilde{\rho}_i \tanh(\alpha\Psi_i - \beta\Psi_i^2 + \gamma\Psi_i^3)}. \tag{2}$$

where

$$\Psi_i = I_i\tilde{\rho}_i. \tag{3}$$

Note that,

$$\tilde{\rho}_i = \rho_i - p. \tag{4}$$

where p is dielectric offset and $p = 0.09\,\mathring{A}$ and ρ_i is the radius of atom i. I_i for atom i is given by (according to HCT paper)

$$
\begin{aligned}
I_i \;=\; & \frac{1}{2}\sum_{j\neq i}\left(\left[\frac{1}{L_{ij}} - \frac{1}{U_{ij}} + \frac{r_{ij}}{4}\left(\frac{1}{U_{ij}^2} - \frac{1}{L_{ij}^2}\right)\right.\right.\\
& \left.\left.+\frac{1}{2r_{ij}}\log\frac{L_{ij}}{U_{ij}} + \frac{S_j^2\tilde{\rho}_j^{\,2}}{4r_{ij}}\left(\frac{1}{L_{ij}^2} - \frac{1}{U_{ij}^2}\right)\right] + C_{ij}\right),
\end{aligned}
\tag{5}
$$

where

$$
L_{ij} \;=\; \begin{cases} 1 & , \tilde{\rho}_i \geq r_{ij} + S_j\tilde{\rho}_j \\ \tilde{\rho}_i & , r_{ij} + S_j\tilde{\rho}_j \geq \tilde{\rho}_i \geq r_{ij} - S_j\tilde{\rho}_j \\ r_{ij} - S_j\tilde{\rho}_j & , r_{ij} - S_j\tilde{\rho}_j \geq \tilde{\rho}_i \end{cases} , \tag{6}
$$

$$
U_{ij} \;=\; \begin{cases} 1 & , \tilde{\rho}_i \geq r_{ij} + S_j\tilde{\rho}_j \\ r_{ij} + S_j\tilde{\rho}_j & , \tilde{\rho}_i < r_{ij} + S_j\tilde{\rho}_j \end{cases} , \tag{7}
$$

$$
C_{ij} \;=\; \begin{cases} 2(\frac{1}{\tilde{\rho}_i} - \frac{1}{L_{ij}}) & , \tilde{\rho}_i < (\tilde{\rho}_j S_j - r_{ij}) \\ 0 & \text{otherwise} \end{cases} , \tag{8}
$$

and S_j are given constants.

Derivative of Born Radius R_i w.r.t. r_{ij} is given by (note that $\frac{\partial \tanh(x)}{\partial x} = (1 - \tanh^2(x))$)

$$\frac{\partial R_i}{\partial r_{ij}} = \frac{R_i^2}{\rho_i} \left(1 - \tanh^2\left(\alpha\Psi_i - \beta{\Psi_i}^2 + \gamma{\Psi_i}^3\right)\right) \left(\alpha - 2\beta\Psi_i + 3\gamma{\Psi_i}^2\right) \tilde{\rho}_i \frac{\partial I_i}{\partial r_{ij}}. \qquad (9)$$

Derivative of the burial term in Equation (5) is given by

$$\begin{aligned}
\frac{\partial I_i}{\partial r_{ij}} &= -\frac{1}{2}\frac{\partial L_{ij}}{\partial r_{ij}}\frac{1}{L_{ij}^2} + \frac{1}{2}\frac{\partial U_{ij}}{\partial r_{ij}}\frac{1}{U_{ij}^2} + \left(\frac{1}{8U_{ij}^2} - \frac{1}{8L_{ij}^2}\right) \\
&\quad + \frac{1}{4}r_{ij}\left(-\frac{1}{U_{ij}^3}\frac{\partial U_{ij}}{\partial r_{ij}} + \frac{1}{L_{ij}^3}\frac{\partial L_{ij}}{\partial r_{ij}}\right) - \frac{1}{4r_{ij}^2}\log\left(\frac{L_{ij}}{U_{ij}}\right) + \frac{1}{4r_{ij}L_{ij}}\left(\frac{\partial L_{ij}}{\partial r_{ij}} - \frac{L_{ij}}{U_{ij}}\frac{\partial U_{ij}}{\partial r_{ij}}\right) \\
&\quad - \frac{S_j^2\tilde{\rho}_j^2}{8r_{ij}^2}\left(\frac{1}{L_{ij}^2} - \frac{1}{U_{ij}^2}\right) + \frac{S_j^2\tilde{\rho}_j^2}{4r_{ij}U_{ij}^3}\frac{\partial U_{ij}}{\partial r_{ij}} - \frac{S_j^2\tilde{\rho}_j^2}{4r_{ij}L_{ij}^3}\frac{\partial L_{ij}}{\partial r_{ij}} + \frac{\partial C_{ij}}{\partial r_{ij}} \qquad (10)
\end{aligned}$$

Derivative of L_{ij} (Equation (6)) w. r. t. r_{ij} is given by

$$\frac{\partial L_{ij}}{\partial r_{ij}} = \begin{cases} 1 & , r_{ij} - S_j\tilde{\rho}_j \geq \tilde{\rho}_i \\ 0 & , \text{otherwise} \end{cases}. \qquad (11)$$

Derivative of U_{ij} (Equation (7)) w. r. t. r_{ij} is given by

$$\frac{\partial U_{ij}}{\partial r_{ij}} = \begin{cases} 1 & , \tilde{\rho}_i < r_{ij} + S_j\tilde{\rho}_j \\ 0 & , \text{otherwise} \end{cases}. \qquad (12)$$

Derivative of C_{ij} (Equation (8)) w. r. t. r_{ij} is given by

$$\frac{\partial C_{ij}}{\partial r_{ij}} = \begin{cases} 2\frac{1}{L_{ij}^2}\frac{\partial L_{ij}}{\partial r_{ij}} & , \tilde{\rho}_i < (\tilde{\rho}_j S_j) - r_{ij} \\ 0 & , \text{otherwise} \end{cases}. \qquad (13)$$

We assume that $r_{ij} - S_j\tilde{\rho}_j \geq 0$ and so $\partial C_{ij}/\partial r_{ij} = 0$ here.

ACE Solvation term   The nonpolar ACE solvation energy is given by

$$G^{np} = \sum_i G_i^{np} = 4\pi\sigma\sum_i(\rho_i + \rho_s)^2\left(\frac{\rho_i}{R_i}\right)^6, \qquad (14)$$

where ρ_s is the radius of water probe sphere. Derivative of G^{np} is given by

$$\frac{\partial G^{np}}{\partial r_{ij}} = -24\pi\sigma\left((\rho_i + \rho_s)^2\frac{\rho_i^6}{R_i^7}\frac{\partial R_i}{\partial r_{ij}} + (\rho_j + \rho_s)^2\frac{\rho_j^6}{R_j^7}\frac{\partial R_j}{\partial r_{ij}}\right). \qquad (15)$$

Generalized Born potential The Generalized-Born potential energy function in OpenMM is given by

$$E_{GB} = -\frac{1}{2} \left(\frac{1}{\epsilon_S} - \frac{1}{\epsilon_w} \right) \sum_i \sum_j \frac{q_i q_j}{f_{ij}^{GB}(r_{ij}, R_i, R_j)}. \tag{16}$$

In Equation (16), ϵ_S is the solute dielectric, R_i and R_j are effective Born radii of atoms i and j respectively. Note we have now calculated the 'self' term as OpenMM assumes the derivative of the 'self' term is non-zero, i.e. includes the $j = 1$ term. The function f_{ij}^{GB} is given by,

$$f_{ij}^{GB} = \left(r_{ij}^2 + R_i R_j \exp \left(-\frac{r_{ij}^2}{4 R_i R_j} \right) \right)^{\frac{1}{2}}. \tag{17}$$

The pairwise force term can be obtained by taking the negative of the derivative of E_{GB} w. r. t. r_{ij}.

$$\frac{\partial E_{GB}}{\partial r_{ij}} = \left(\frac{1}{\epsilon_S} - \frac{1}{\epsilon_w} \right) \left(\sum_{k \neq i,j} \frac{q_i q_k}{(f_{ik}^{GB})^2} \frac{\partial f_{ik}^{GB}}{\partial r_{ij}} + \sum_{l \neq i,j} \frac{q_j q_l}{(f_{jl}^{GB})^2} \frac{\partial f_{jl}^{GB}}{\partial r_{ij}} + \right.$$
$$\left. \frac{q_i q_j}{(f_{ij}^{GB})^2} \frac{\partial f_{ij}^{GB}}{\partial r_{ij}} + \frac{1}{2} \frac{q_i^2}{R_i^2} \frac{\partial R_i}{\partial r_{ij}} + \frac{1}{2} \frac{q_j^2}{R_j^2} \frac{\partial R_j}{\partial r_{ij}} \right). \tag{18}$$

Note that this equation removes the factor of one half in Eqn.(16), for the first three terms in the second brackets, by observing that $f_{ik}^{GB} = f_{ki}^{GB}$, from Eqn.(17), and only summing terms in f_{i*}^{GB} and f_{j*}^{GB}. Also note that the 'self terms' (the last two terms in Eqn.(18)) were not used in the first implementation of the code, and

$$\frac{q_i q_i}{(f_{ii}^{GB})^2} \frac{\partial f_{ii}^{GB}}{\partial r_{ij}} = \frac{q_i^2}{R_i^2} \frac{\partial R_i}{\partial r_{ij}}, \tag{19}$$

etc.

Derivative of f_{ij}^{GB} (Equation (17)) w. r. t. r_{ij} can be written as

$$\frac{\partial f_{ij}^{GB}}{\partial r_{ij}} = \frac{1}{2 f_{ij}^{GB}} \left[2 r_{ij} + \frac{\partial R_i}{\partial r_{ij}} R_j \exp \left(-\frac{r_{ij}^2}{4 R_i R_j} \right) + R_i \frac{\partial R_j}{\partial r_{ij}} \exp \left(-\frac{r_{ij}^2}{4 R_i R_j} \right) \right.$$
$$\left. + R_i R_j \exp \left(-\frac{r_{ij}^2}{4 R_i R_j} \right) \left(-\frac{r_{ij}}{2 R_i R_j} + \frac{1}{4} \frac{r_{ij}^2}{R_i^2 R_j} \frac{\partial R_i}{\partial r_{ij}} + \frac{1}{4} \frac{r_{ij}^2}{R_i R_j^2} \frac{\partial R_j}{\partial r_{ij}} \right) \right]. \tag{20}$$

Derivative of f_{ik}^{GB} w. r. t. r_{ij} is then

$$\frac{\partial f_{ik}^{GB}}{\partial r_{ij}} = \frac{1}{2 f_{ik}^{GB}} \left(R_k + \frac{r_{ik}^2}{4 R_i} \right) \exp \left(-\frac{r_{ik}^2}{4 R_i R_k} \right) \frac{\partial R_i}{\partial r_{ij}}. \tag{21}$$

Similarly, the derivative of f_{jl}^{GB} w. r. t. r_{ij} is

$$\frac{\partial f_{jl}^{GB}}{\partial r_{ij}} = \frac{1}{2 f_{jl}^{GB}} \left(R_l + \frac{r_{jl}^2}{4 R_j} \right) \exp \left(-\frac{r_{jl}^2}{4 R_j R_l} \right) \frac{\partial R_j}{\partial r_{ij}}. \tag{22}$$

3

1.1 Force in $\mathbf{r}_i$

To obtain the force we need to find

$$\frac{\mathrm{d}r_{ij}}{\mathrm{d}\mathbf{r}_i} = \frac{\mathrm{d}||\mathbf{r}_j - \mathbf{r}_i||}{\mathrm{d}\mathbf{r}_i} = -\frac{||\mathbf{r}_j - \mathbf{r}_i||}{r_{ij}} = -\hat{\mathbf{r}}_{ij}, \tag{23}$$

and similarly for $\mathbf{r}_j$, then apply the chain rule to get

$$\nabla_{ij}E_{GB} = \frac{\partial E_{GB}}{\partial r_{ij}} \left[-\hat{\mathbf{r}}_{ij} \ \ \hat{\mathbf{r}}_{ij} \right]. \tag{24}$$

For the force

$$\mathbf{F}_{ij} = -\nabla_{ij}E_{GB} = \frac{\partial E_{GB}}{\partial r_{ij}} \left[\ \hat{\mathbf{r}}_{ij} \ -\hat{\mathbf{r}}_{ij} \ \right]. \tag{25}$$

2 Hessians

Second derivative of G_{np} is given by

$$\frac{\partial^2 G^{np}}{\partial r_{ij}^2} = 24\pi\sigma \left[(\rho_i + \rho_s)^2 \frac{\rho_i^6}{R_i^7} \left(\frac{7}{R_i} \left(\frac{\partial R_i}{\partial r_{ij}} \right)^2 - \frac{\partial^2 R_i}{\partial r_{ij}^2} \right) \right.$$
$$\left. + (\rho_j + \rho_s)^2 \frac{\rho_j^6}{R_j^7} \left(\frac{7}{R_j} \left(\frac{\partial R_j}{\partial r_{ij}} \right)^2 - \frac{\partial^2 R_j}{\partial r_{ij}^2} \right) \right]. \tag{26}$$

Second derivative of E_{GB} is given by

$$\frac{\partial^2 E_{GB}}{\partial r_{ij}^2} = \left(\frac{1}{\epsilon_S} - \frac{1}{\epsilon_w} \right) \left[\sum_{k \neq i,j} \left(\frac{q_i q_k}{f_{ik}^{GB2}} \frac{\partial^2 f_{ik}^{GB}}{\partial r_{ij}^2} - \frac{2}{f_{ik}^{GB3}} \left(\frac{\partial f_{ik}^{GB}}{\partial r_{ij}} \right)^2 \right) \right.$$
$$+ \sum_{l \neq i,j} \left(\frac{q_j q_l}{f_{jl}^{GB2}} \frac{\partial^2 f_{jl}^{GB}}{\partial r_{ij}^2} - \frac{2}{f_{jl}^{GB3}} \left(\frac{\partial f_{jl}^{GB}}{\partial r_{ij}} \right)^2 \right)$$
$$\left. + \left(\frac{q_i q_j}{f_{ij}^{GB2}} \frac{\partial^2 f_{ij}^{GB}}{\partial r_{ij}^2} - \frac{2}{f_{ij}^{GB3}} \left(\frac{\partial f_{ij}^{GB}}{\partial r_{ij}} \right)^2 \right) \right]. \tag{27}$$

Second derivative of the Born Radius R_i (see Equation (26)) is given by

$$
\begin{aligned}
\frac{\partial^2 R_i}{\partial r_{ij}^2} &= 2\frac{R_i^3}{\rho^2}\left(\frac{\partial \Psi}{\partial r_{ij}}\right)^2 (1 - \tanh^2(\alpha\Psi - \beta\Psi^2 + \gamma\Psi^3))^2(\alpha - 2\beta\Psi + 3\gamma\Psi^2)^2 \\
&\quad -2\frac{R_i^2}{\rho}(1 - \tanh^2(\alpha\Psi - \beta\Psi^2 + \gamma\Psi^3))\left(\frac{\partial \Psi_i}{\partial r_{ij}}\right)^2 \tanh(\alpha\Psi - \beta\Psi^2 + \gamma\Psi^3) \\
&\quad (\alpha - 2\beta\Psi + 3\gamma\Psi^2)^2 \\
&\quad +\frac{R_i^2}{\rho_i}(1 - \tanh^2(\alpha\Psi - \beta\Psi^2 + \gamma\Psi^3))\left(\alpha\frac{\partial^2 \Psi_i}{\partial r_{ij}^2} - 2\beta\left(\frac{\partial \Psi_i}{\partial r_{ij}}\right)^2 - 2\beta\Psi_i\frac{\partial^2 \Psi_i}{\partial r_{ij}^2}\right. \\
&\quad \left. + 6\gamma\Psi_i\left(\frac{\partial \Psi_i}{\partial r_{ij}}\right)^2 + 3\gamma\Psi_i^2\frac{\partial^2 \Psi_i}{\partial r_{ij}^2}\right). \qquad (28)
\end{aligned}
$$

Second derivative of f_{ij}^{GB} is given by

$$
\begin{aligned}
\frac{\partial^2 f_{ij}^{GB}}{\partial r_{ij}^2} &= -\frac{1}{f_{ij}^{GB}}\left(\frac{\partial f_{ij}^{GB}}{\partial r_{ij}}\right)^2 + \frac{1}{f_{ij}^{GB}} \\
&\quad +\frac{1}{2f_{ij}^{GB}}\exp\left(-\frac{r_{ij}^2}{4R_iR_j}\right)\left[\quad \frac{\partial^2 R_i}{\partial r_{ij}^2}R_j + 2\frac{\partial R_i}{\partial r_{ij}}\frac{\partial R_j}{\partial r_{ij}}\right. \\
&\quad +2\frac{\partial R_i}{\partial r_{ij}}R_j\left(-\frac{r_{ij}}{2R_iR_j} + \frac{r_{ij}^2}{4R_i^2R_j}\frac{\partial R_i}{\partial r_{ij}} + \frac{r_{ij}^2}{4R_iR_j^2}\frac{\partial R_j}{\partial r_{ij}}\right) \\
&\quad +R_i\frac{\partial^2 R_j}{\partial r_{ij}^2} \\
&\quad +2R_i\frac{\partial R_j}{\partial r_{ij}}\left(-\frac{r_{ij}}{2R_iR_j} + \frac{r_{ij}^2}{4R_i^2R_j}\frac{\partial R_i}{\partial r_{ij}} + \frac{r_{ij}^2}{4R_iR_j^2}\frac{\partial R_j}{\partial r_{ij}}\right) \\
&\quad +R_iR_j\left(-\frac{1}{2R_iR_j} + \frac{r_{ij}}{R_i^2R_j}\frac{\partial R_i}{\partial r_{ij}} + \frac{r_{ij}}{R_iR_j^2}\frac{\partial R_j}{\partial r_{ij}} - \frac{r_{ij}^2}{2R_i^2R_j^2}\frac{\partial R_i}{\partial r_{ij}}\frac{\partial R_j}{\partial r_{ij}}\right) \\
&\quad +R_iR_j\left(\frac{r_{ij}^2}{4R_i^2R_j}\frac{\partial^2 R_i}{\partial r_{ij}^2} + \frac{r_{ij}^2}{4R_iR_j^2}\frac{\partial^2 R_j}{\partial r_{ij}^2} - \frac{r_{ij}^2}{2R_iR_j^3}\left(\frac{\partial R_j}{\partial r_{ij}}\right)^2 - \frac{r_{ij}^2}{2R_i^3R_j}\left(\frac{\partial R_i}{\partial r_{ij}}\right)^2\right) \\
&\quad \left. + R_iR_j\left(-\frac{r_{ij}}{2R_iR_j} + \frac{r_{ij}^2}{4R_i^2R_j}\frac{\partial R_i}{\partial r_{ij}} + \frac{r_{ij}^2}{4R_iR_j^2}\frac{\partial R_j}{\partial r_{ij}}\right)^2 \quad\right]. \qquad (29)
\end{aligned}
$$

Similarly, we can find,

$$
\frac{\partial^2 f_{ik}^{GB}}{\partial r_{ij}^2} = -\frac{1}{f_{ik}^{GB}} \left(\frac{\partial f_{ik}^{GB}}{\partial r_{ij}} \right)^2
$$
$$
+ \frac{1}{2 f_{ik}^{GB}} \exp\left(-\frac{r_{ik}^2}{4 R_i R_k} \right) \left[\frac{\partial^2 R_i}{\partial r_{ij}^2} \left(R_k + \frac{r_{ik}^2}{4 R_i} \right) \right.
$$
$$
\left. + \frac{r_{ik}^4}{16 R_i^3 R_j} \left(\frac{\partial R_i}{\partial r_{ij}} \right)^2 \right]. \tag{30}
$$

The $\partial^2 f_{jk}^{GB} / \partial r_{ij}^2$ term can be written similarly.

Note that
$$
\frac{\partial^2 \Psi_i}{\partial r_{ij}^2} = \frac{\partial^2 I_i}{\partial r_{ij}^2} \tilde{\rho}_i. \tag{31}
$$

where

$$
\frac{\partial^2 I_i}{\partial r_{ij}^2} = \frac{1}{L_{ij}^3} \left(\frac{\partial L_{ij}}{\partial r_{ij}} \right)^2 - \frac{1}{U_{ij}^3} \left(\frac{\partial U_{ij}}{\partial r_{ij}} \right)^2 + \frac{1}{2 L_{ij}^3} \frac{\partial L_{ij}}{\partial r_{ij}} - \frac{1}{2 U_{ij}^3} \frac{\partial U_{ij}}{\partial r_{ij}}
$$
$$
+ \frac{r_{ij}}{4} \left(\frac{3}{U_{ij}^4} \left(\frac{\partial U_{ij}}{\partial r_{ij}} \right)^2 - \frac{3}{L_{ij}^4} \left(\frac{\partial L_{ij}}{\partial r_{ij}} \right)^2 \right) + \frac{1}{2 r_{ij}^3} \log\left(\frac{L_{ij}}{U_{ij}} \right)
$$
$$
+ \frac{1}{2 r_{ij}^2 L_{ij}} \left(\frac{L_{ij}}{U_{ij}} \frac{\partial U_{ij}}{\partial r_{ij}} - \frac{\partial L_{ij}}{\partial r_{ij}} \right) + \frac{1}{2 r_{ij} L_{ij} U_{ij}} \left(\frac{L_{ij}}{U_{ij}} \left(\frac{\partial U_{ij}}{\partial r_{ij}} \right)^2 - \frac{\partial U_{ij}}{\partial r_{ij}} \frac{\partial L_{ij}}{\partial r_{ij}} \right)
$$
$$
+ \frac{1}{4 r_{ij} L_{ij}^2} \frac{\partial L_{ij}}{\partial r_{ij}} \left(\frac{L_{ij}}{U_{ij}} \frac{\partial U_{ij}}{\partial r_{ij}} - \frac{\partial L_{ij}}{\partial r_{ij}} \right) - \frac{1}{4 r_{ij} L_{ij} U_{ij}} \frac{\partial U_{ij}}{\partial r_{ij}} \left(\frac{L_{ij}}{U_{ij}} \frac{\partial U_{ij}}{\partial r_{ij}} - \frac{\partial L_{ij}}{\partial r_{ij}} \right)
$$
$$
+ \frac{S_j^2 \tilde{\rho}_i^2}{4 r_{ij}^3} \left(\frac{1}{L_{ij}^2} - \frac{1}{U_{ij}^2} \right) - \frac{S_j^2 \tilde{\rho}_i^2}{2 r_{ij}^2} \left(\frac{1}{U_{ij}^3} \frac{\partial U_{ij}}{\partial r_{ij}} - \frac{1}{L_{ij}^3} \frac{\partial L_{ij}}{\partial r_{ij}} \right)
$$
$$
+ \frac{S_j^2 \tilde{\rho}_i^2}{4 r_{ij}} \left(\frac{3}{L_{ij}^4} \left(\frac{\partial L_{ij}}{\partial r_{ij}} \right)^2 - \frac{3}{U_{ij}^4} \left(\frac{\partial U_{ij}}{\partial r_{ij}} \right)^2 \right). \tag{32}
$$

Hessian for $\mathbf{r}_i$.

We can now differentiate w.r.t. $\mathbf{r}_{ij}$ to get the Hessian for atoms i and j.

$$
\mathbf{H}_{ij} = \frac{\partial E_{GB}}{\partial r_{ij}} \frac{1}{r_{ij}} \begin{bmatrix} \mathbf{I} & -\mathbf{I} \\ -\mathbf{I} & \mathbf{I} \end{bmatrix} + \left(\frac{\partial^2 E_{GB}}{\partial r_{ij}^2} - \frac{\partial E_{GB}}{\partial r_{ij}} \frac{1}{r_{ij}} \right) \begin{bmatrix} \hat{\mathbf{r}}_{ij} \hat{\mathbf{r}}_{ij}^{\mathrm{T}} & -\hat{\mathbf{r}}_{ij} \hat{\mathbf{r}}_{ij}^{\mathrm{T}} \\ -\hat{\mathbf{r}}_{ij} \hat{\mathbf{r}}_{ij}^{\mathrm{T}} & \hat{\mathbf{r}}_{ij} \hat{\mathbf{r}}_{ij}^{\mathrm{T}} \end{bmatrix}. \tag{33}
$$