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)

$$I_i = \frac{1}{2}\sum_j \left(\left[\frac{1}{L_{ij}} - \frac{1}{U_{ij}} + \frac{r_{ij}}{4}\left(\frac{1}{U_{ij}^2} - \frac{1}{L_{ij}^2}\right) + \frac{1}{2r_{ij}} \log\frac{L_{ij}}{U_{ij}} + \frac{S_j^2 {\tilde{\rho}_j}^2}{4r_{ij}}\left(\frac{1}{L_{ij}^2} - \frac{1}{U_{ij}^2}\right)\right] + C_{ij} \right), \tag{5}$$

where

$$L_{ij} = \left\{ \begin{array}{rl} 1 & , \tilde{\rho}_i \geq r_{ij} + S_j\tilde{\rho}_j \\ \tilde{\rho}_i & , r_{ij} + S_j\tilde{\rho}_j \geq \tilde{\rho}_i \geq r_{ij} - S_j\tilde{\rho}_j \\ r_{ij} - S_j\tilde{\rho}_j & , r_{ij} - S_j\tilde{\rho}_j \geq \tilde{\rho}_i \end{array} \right\}, \tag{6}$$

$$U_{ij} = \left\{ \begin{array}{rl} 1 & , \tilde{\rho}_i \geq r_{ij} + S_j\tilde{\rho}_j \\ r_{ij} + S_j\tilde{\rho}_j & , \tilde{\rho}_i < r_{ij} + S_j\tilde{\rho}_j \end{array} \right\} \tag{7}$$

and

$$C_i = \left\{ \begin{array}{rl} 2(\frac{1}{\tilde{\rho}_i} - \frac{1}{L_{ij}}) & , \tilde{\rho}_i < (\tilde{\rho}_j S_j - r_{ij}) \\ 0 & \text{otherwise} \end{array} \right\} \tag{8}$$

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

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

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

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

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

$$\frac{\partial L_{ij}}{\partial r_{ij}} = \left\{\begin{array}{ll} 1 & , r_{ij} - S_{ij}\tilde{\rho}_j \geq \tilde{\rho}_i \\ 0 & , \text{otherwise} \end{array}\right\} \tag{11}$$

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

$$\frac{\partial U_{ij}}{\partial r_{ij}} = \left\{\begin{array}{ll} 1 & , \tilde{\rho}_i < r_{ij} + S_{ij}\tilde{\rho}_j \\ 0 & , \text{otherwise} \end{array}\right\}. \tag{12}$$

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

$$\frac{\partial C_{ij}}{\partial r_{ij}} = \left\{\begin{array}{cl} 2\frac{1}{L_{ij}^2}\frac{\partial L_{ij}}{\partial r_{ij}} & , \tilde{\rho}_i < (\tilde{\rho}_j S_{ij}) - r_{ij} \\ 0 & , \text{otherwise} \end{array}\right\} \tag{13}$$

ACE Solvation term The nonpolar ACE solvation energy is given by

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

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

$$\frac{\partial G^{np}}{\partial r_{ij}} = -24\pi\sigma\left((\rho_i + \rho_s)^2\frac{\rho_i^6}{R_i^6}\frac{1}{R_i}\frac{\partial R_i}{\partial r_{ij}} + (\rho_j + \rho_s)^2\frac{\rho_j^6}{R_j^6}\frac{1}{R_j}\frac{\partial R_j}{\partial r_{ij}}\right). \tag{15}$$

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

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

In Equation (16), ϵ_S is the solute dielectric, R_i and R_j are effective Born radii of atoms i and j respectively. The function f_{ij}^{GB} is given by,

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

Note that in Equation (16), the self terms are given by

$$f_{ii}^{GB} = \sqrt{r_{ii}^2 + R_i R_i \exp^{-\frac{r_{ii}^2}{4R_i R_i}}} = R_i. \tag{18}$$

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

$$\frac{\partial E_{GB}}{\partial r_{ij}} = -\left[\frac{\partial}{\partial r_{ij}}\left(\frac{q_i q_j}{f_{ij}^{GB}}\right) + \sum_k \sum_l q_k q_l \frac{\partial}{\partial r_{ij}}\left(\frac{1}{f_{kl}^{GB}}\right)\right], \tag{19}$$

where $k = i, j$ and $l \neq j$ if $k = i$ and $l \neq i$ if $k = j$. Derivative of f_{ij}^{GB} (Equation (17)) w. r. t. r_{ij} can be written as

$$\begin{aligned}\frac{\partial f_{ij}^{GB}}{\partial r_{ij}} &= \frac{1}{2}\frac{1}{\sqrt{r_{ij}^2 + R_i R_j \exp(-\frac{r_{ij}^2}{4R_i R_j})}}(2r_{ij} + \frac{\partial R_i}{\partial r_{ij}} R_j \exp(-\frac{r_{ij}^2}{4R_i R_j}) \\ &+R_i \frac{\partial R_j}{\partial r_{ij}} \exp(-\frac{r_{ij}^2}{4R_i R_j}) + R_i R_j \exp(-\frac{r_{ij}^2}{4R_i R_j})\left(-\frac{r_{ij}}{2R_i R_j} + \frac{1}{4}\frac{r_{ij}^2}{R_i^2 R_j}\frac{\partial R_i}{\partial r_{ij}} + \frac{1}{4}\frac{r_{ij}^2}{R_i R_j^2}\frac{\partial R_j}{\partial r_{ij}}\right)).\end{aligned} \tag{20}$$

The off-diagonal terms in the force equation are given by

$$\frac{\partial}{\partial r_{ij}}\left(\frac{1}{f_{ij}^{GB}}\right) = -\frac{1}{{f_{ij}^{GB}}^2}\frac{\partial f_{ij}^{GB}}{\partial r_{ij}}. \tag{21}$$

$$\frac{\partial}{\partial r_{ij}}\left(\frac{1}{f_{kl}^{GB}}\right) = -\frac{1}{{f_{kl}^{GB}}^2}\frac{\partial f_{kl}^{GB}}{\partial r_{ij}}. \tag{22}$$

Derivative $\frac{\partial f_{ij}^{GB}}{\partial r_{ij}}$ in Equation (22) can be obtained from Equation (20). $\frac{\partial f_{kl}^{GB}}{\partial r_{ij}}$ for $k = i$ is given by

$$\frac{\partial f_{il}^{GB}}{\partial r_{ij}} = \frac{1}{f_{il}^{GB}}\left[\frac{\partial R_i}{\partial r_{ij}} R_l \exp^{-\frac{r_{il}^2}{4R_i R_l}} - R_i R_l \exp^{-\frac{r_{il}^2}{4R_i R_l}}(-\frac{r_{il}^2}{4R_i^2 R_l}\frac{\partial R_i}{\partial r_{ij}})\right], \tag{23}$$

which can be simplified to

$$\frac{\partial f_{il}^{GB}}{\partial r_{ij}} = \frac{1}{f_{il}^{GB}}\left[R_l + \frac{r_{il}^2}{4R_i}\right]\exp^{-\frac{r_{il}^2}{4R_i R_l}}\frac{\partial R_i}{\partial r_{ij}}. \tag{24}$$

Similarly, for $k = j$, we can write

$$\frac{\partial f_{jl}^{GB}}{\partial r_{ij}} = \frac{1}{f_{jl}^{GB}}\left[R_l + \frac{r_{jl}^2}{4R_j}\right]\exp^{-\frac{r_{jl}^2}{4R_j R_l}}\frac{\partial R_j}{\partial r_{ij}}. \tag{25}$$

Derivative of the self terms (from Equation (fGBself)) are given by

$$\frac{\partial f_{ii}^{GB}}{\partial r_{ij}} = -q_i^2 \frac{1}{R_i^2}\frac{\partial R_i}{\partial r_{ij}} \tag{26}$$

2 Hessian

Second derivative of G_{np} is given by

$$\frac{\partial^2 G^{np}}{\partial r_{ij}^2} = 4\pi\sigma \left[6(\rho_i+\rho_s)^2 {\rho_i}^6 \left(7(\frac{\partial R_i}{\partial r_{ij}})^2 \frac{1}{R_i^8} - \frac{\partial^2 R_i}{\partial r_{ij}^2} \right) + 6(\rho_j+\rho_s)^2 {\rho_j}^6 \left(\frac{7}{R_j^8} (\frac{\partial R_j}{\partial r_{ij}})^2 - \frac{1}{R_j^7} \frac{\partial^2 R_j}{\partial r_{ij}^2} \right) \right]. \tag{27}$$

Second derivative of E_{GB} is given by

$$\frac{\partial^2 E_{GB}}{\partial r_{ij}^2} = \left[q_i q_j \left(\frac{1}{{f_{ij}^{GB}}^2} \frac{\partial^2 f_{ij}^{GB}}{\partial r_{ij}^2} - \frac{2}{{f_{ij}^{GB}}^3} \left(\frac{\partial f_{ij}^{GB}}{\partial r_{ij}} \right)^2 \right) + \sum_k \sum_l q_k q_l \left(\frac{1}{{f_{kl}^{GB}}^2} \frac{\partial^2 f_{kl}^{GB}}{\partial r_{ij}^2} - \frac{2}{{f_{kl}^{GB}}^3} \left(\frac{\partial f_{kl}^{GB}}{\partial r_{ij}} \right)^2 \right) \right]. \tag{28}$$

Second derivative of the Born Radius R_i (see Equation (27)) is given by

$$\begin{aligned}
\frac{\partial^2 R_i}{\partial r_{ij}^2} \quad = \quad & 2(1-\tanh(\alpha\Psi - \beta\Psi^2 + \gamma\Psi^3))^2 (\frac{\partial \Psi}{\partial r_{ij}})^2 (\alpha - 2\beta\Psi + 3\gamma\Psi^2)^2 \frac{R_i^3}{\rho^2} \qquad (29) \\
& -2R_i^2 \tanh(\alpha\Psi - \beta\Psi^2 + \gamma\Psi^3)(1-\tanh(\alpha\Psi - \beta\Psi^2 + \gamma\Psi^3)^2) \\
& \left(\frac{\partial \Psi_i}{\partial r_{ij}} \right)^2 (\alpha - 2\beta\Psi + 3\gamma\Psi^2)^2 \frac{1}{\rho} \\
& R_i^2 (1-\tanh(\alpha\Psi - \beta\Psi^2 + \gamma\Psi^3)^2)(\alpha \frac{\partial^2 \Psi_i}{\partial r_{ij}^2} - 2\beta(\frac{\partial \Psi_i}{\partial r_{ij}})^2 - 2\beta\Psi_i \frac{\partial^2 \Psi_i}{\partial r_{ij}^2}) \frac{1}{\rho_i} \\
& +R_i^2 (1-\tanh(\alpha\Psi - \beta\Psi^2 + \gamma\Psi^3)^2)(6\gamma\Psi_i (\frac{\partial \Psi_i}{\partial r_{ij}})^2 + 3\gamma\Psi_i^2 \frac{\partial^2 \Psi_i}{\partial r_{ij}^2}) \frac{1}{\rho_i}.
\end{aligned}$$

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

$$
\begin{aligned}
\frac{\partial^2 f_{ij}^{GB}}{\partial r_{ij}^2} &= -\frac{1}{4}\frac{1}{f_{ij}^{GB}} 4\left(f_{ij}^{GB}\right)^2 \left(\frac{\partial f_{ij}^{GB}}{\partial r_{ij}}\right)^2 \qquad (30)\\
&+\frac{1}{2f_{ij}^{GB}}\left[2+\frac{\partial^2 R_i}{\partial r_{ij}^2}R_j \exp(-\frac{r_{ij}^2}{4R_iR_j}) + 2\frac{\partial R_i}{\partial r_{ij}}\frac{\partial R_j}{\partial r_{ij}}\exp(-\frac{r_{ij}^2}{4R_iR_j})\right]\\
&+\frac{1}{2f_{ij}^{GB}}\left[2\frac{\partial R_i}{\partial r_{ij}}R_j\left(-\frac{r_{ij}}{R_iR_j}+\frac{r_{ij}^2}{4R_i^2R_j}\frac{\partial R_i}{\partial r_{ij}}+\frac{r_{ij}^2}{4R_iR_j^2}\frac{\partial R_j}{\partial r_{ij}}\right)\exp(-\frac{r_{ij}^2}{4R_iR_j})\right]\\
&+\frac{1}{2f_{ij}^{GB}}\left[R_i\frac{\partial^2 R_j}{\partial r_{ij}^2}\exp(-\frac{r_{ij}^2}{4R_iR_j})\right]\\
&+\frac{1}{2f_{ij}^{GB}}\left[2R_j\frac{\partial R_i}{\partial r_{ij}}\left(-\frac{r_{ij}}{2R_iR_j}+\frac{r_{ij}^2}{4R_i^2R_j}\frac{\partial R_i}{\partial r_{ij}}+\frac{r_{ij}^2}{4R_iR_j^2}\frac{\partial R_j}{\partial r_{ij}}\right)\exp(-\frac{r_{ij}^2}{4R_iR_j})\right]\\
&+\frac{1}{2f_{ij}^{GB}}\left[R_iR_j\left(-\frac{1}{2R_iR_j}+\frac{r_{ij}}{4R_i^2R_j}\frac{\partial R_i}{\partial r_{ij}}+\frac{r_{ij}}{4R_iR_j^2}\frac{\partial R_j}{\partial r_{ij}}-\frac{r_{ij}^2}{2R_i^2R_j^2}\frac{\partial R_i}{\partial r_{ij}}\frac{\partial R_j}{\partial r_{ij}}\right)\exp(-\frac{r_{ij}^2}{4R_iR_j})\right]\\
&+\frac{1}{2f_{ij}^{GB}}\left[R_iR_j\left(\frac{r_{ij}^2}{4R_i^2R_j}\frac{\partial^2 R_i}{\partial r_{ij}^2}+\frac{r_{ij}^2}{4R_iR_j^2}\frac{\partial^2 R_j}{\partial r_{ij}^2}-\frac{r_{ij}^2}{2R_iR_j^3}(\frac{\partial R_j}{\partial r_{ij}})^2\right)\exp(-\frac{r_{ij}^2}{4R_iR_j})\right]\\
&+\frac{1}{2f_{ij}^{GB}}\left[R_iR_j\left(-\frac{r_{ij}}{2R_iR_j}+\frac{r_{ij}^2}{4R_i^2R_j}\frac{\partial R_i}{\partial r_{ij}}+\frac{r_{ij}^2}{4R_iR_j^2}\frac{\partial R_j}{\partial r_{ij}}\right)\exp(-\frac{r_{ij}^2}{4R_iR_j})\right].
\end{aligned}
$$

Similarly, we can find,

$$
\begin{aligned}
\frac{\partial^2 f_{il}^{GB}}{\partial r_{ij}^2} &= \frac{1}{f_{il}^{GB}}\exp(-\frac{r_{il}^2}{4R_iR_l})(R_l+\frac{r_{il}^2}{4R_i})\left[\frac{\partial^2 R_i}{\partial r_{ij}}-\frac{\partial R_i}{\partial r_{ij}}\left(\frac{1}{f_{il}^{GB}}\right)\frac{\partial f_{il}^{GB}}{\partial r_{ij}}\right] \qquad (31)\\
&+\frac{1}{f_{il}^{GB}}\exp(-\frac{r_{il}^2}{4R_iR_j})\left(\frac{\partial R_i}{\partial r_{ij}}\right)^2\left[(R_l+\left(-\frac{r_{il}^2}{4R_i}\right))\frac{-r_{il}^2}{4R_i^2R_l}-\frac{r_{il}^2}{4R_i}\right]
\end{aligned}
$$

and

$$
\begin{aligned}
\frac{\partial^2 f_{jl}^{GB}}{\partial r_{ij}^2} &= \frac{1}{f_{jl}^{GB}}\exp(-\frac{r_{jl}^2}{4R_jR_l})(R_l+\frac{r_{jl}^2}{4R_j})\left[\frac{\partial^2 R_j}{\partial r_{ij}}-\frac{\partial R_j}{\partial r_{ij}}\left(\frac{1}{f_{jl}^{GB}}\right)\frac{\partial f_{jl}^{GB}}{\partial r_{ij}}\right] \qquad (32)\\
&+\frac{1}{f_{jl}^{GB}}\exp(-\frac{r_{jl}^2}{4R_jR_j})\left(\frac{\partial R_j}{\partial r_{ij}}\right)^2\left[(R_l+\left(-\frac{r_{jl}^2}{4R_j}\right))\frac{-r_{jl}^2}{4R_j^2R_l}-\frac{r_{jl}^2}{4R_j}\right]
\end{aligned}
$$

Note that

$$\frac{\partial^2 \Psi_i}{\partial r_{ij}^2} = \frac{\partial^2 I_i}{\partial r_{ij}^2}\tilde{\rho}_i. \qquad (33)$$

where

$$
\begin{aligned}
\frac{\partial^2 I_i}{\partial r_{ij}^2} \quad = \quad & \left[\frac{1}{L_{ij}^3}\left(\frac{\partial L_{ij}}{\partial r_{ij}}\right)^2 - \frac{1}{U_{ij}^3}\left(\frac{\partial U_{ij}}{\partial r_{ij}}\right)^2 + \left(\frac{1}{4L_{ij}^3}\frac{\partial L_{ij}}{\partial r_{ij}} - \frac{1}{4U_{ij}^3}\frac{\partial U_{ij}}{\partial r_{ij}}\right)\right] \qquad (34) \\
& + \left[\frac{1}{8}\left(\frac{2}{L_{ij}^3}\frac{\partial L_{ij}}{\partial r_{ij}} - \frac{2}{U_{ij}^3}\frac{\partial U_{ij}}{\partial r_{ij}}\right) - \frac{r_{ij}}{4}\left(\frac{3}{U_{ij}^4}\left(\frac{\partial U_{ij}}{\partial r_{ij}}\right)^2 - \frac{3}{L_{ij}^4}\left(\frac{\partial L_{ij}}{\partial r_{ij}}\right)^2\right)\right] \\
& + \left[\frac{1}{2r_{ij}^3}\log(\frac{L_{ij}}{U_{ij}}) - \frac{1}{2}\frac{U_{ij}}{r_{ij}^2 L_{ij}}\left(\frac{1}{U_{ij}}\frac{\partial L_{ij}}{\partial r_{ij}} - \frac{L_{ij}}{U_{ij}^2}\frac{\partial U_{ij}}{\partial r_{ij}}\right) + \frac{1}{4}\frac{U_{ij}}{r_{ij}L_{ij}}\left(\frac{2L_{ij}}{U_{ij}^3}\left(\frac{\partial U_{ij}}{\partial r_{ij}}\right)^2 - 2\frac{\frac{\partial L_{ij}}{\partial r_{ij}}\frac{\partial U_{ij}}{\partial r_{ij}}}{U_{ij}^2}\right)\right] \\
& - \left[\frac{1}{4}\frac{U_{ij}}{r_{ij}L_{ij}^2}\frac{\partial L_{ij}}{\partial r_{ij}}\left(\frac{1}{U_{ij}}\frac{\partial L_{ij}}{\partial r_{ij}} - \frac{L_{ij}}{U_{ij}^2}\frac{\partial U_{ij}}{\partial r_{ij}}\right) + \frac{1}{4}\frac{1}{r_{ij}L_{ij}}\frac{\partial U_{ij}}{\partial r_{ij}}\left(\frac{1}{U_{ij}}\frac{\partial L_{ij}}{\partial r_{ij}} - \frac{L_{ij}}{U_{ij}^2}\frac{\partial U_{ij}}{\partial r_{ij}}\right)\right] \\
& + \frac{S_j^2\tilde{\rho}_i^2}{4r_{ij}}\left[\frac{1}{r_{ij}^2}\left(\frac{1}{L_{ij}^2} - \frac{1}{U_{ij}^2}\right) - \frac{2}{r_{ij}^2 U_{ij}^3}\frac{\partial U_{ij}}{\partial r_{ij}} - \frac{3}{U_{ij}^4}\left(\frac{\partial U_{ij}}{\partial r_{ij}}\right)^2\right]
\end{aligned}
$$