Generalized Born : Energies, Forces and Hessian

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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)

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

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 $\frac{\partial \tanh(x)}{\partial x} = (1 - \tanh^2(x)))$

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

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

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

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

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

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

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

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

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

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

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

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

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

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,

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

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

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

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

$$\begin{aligned}\frac{\partial f_{ij}^{GB}}{\partial r_{ij}} \quad = \quad & \frac{1}{2f_{ij}^{GB}}\left[2r_{ij} + \frac{\partial R_i}{\partial r_{ij}} R_j \exp\left(-\frac{r_{ij}^2}{4R_i R_j}\right) + R_i \frac{\partial R_j}{\partial r_{ij}} \exp\left(-\frac{r_{ij}^2}{4R_i R_j}\right)\right. \\ & \left. + R_i R_j \exp\left(-\frac{r_{ij}^2}{4R_i R_j}\right)\left(-\frac{r_{ij}}{2R_i R_j} + \frac{1}{4}\frac{r_{ij}^2}{R_i^2 R_j}\frac{\partial R_i}{\partial r_{ij}} + \frac{1}{4}\frac{r_{ij}^2}{R_i R_j^2}\frac{\partial R_j}{\partial r_{ij}}\right)\right].\end{aligned} \tag{19}$$

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

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

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

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

1.1 Force in $\mathbf{r}_i$

To obtain the force we need to find

$$\frac{\mathrm{d}r_{ij}}{\mathrm{d}\mathbf{r}_i} = \frac{\mathrm{d}||\mathbf{r}_j - \mathbf{r}_i||}{\mathrm{d}\mathbf{r}_i} \;=\; -\frac{||\mathbf{r}_j - \mathbf{r}_i||}{r_{ij}} \;=\; -\hat{\mathbf{r}}_{ij}, \tag{22}$$

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

$$\nabla_{ij} E_{GB} \;=\; \frac{\partial E_{GB}}{\partial r_{ij}} \left[-\hat{\mathbf{r}}_{ij} \quad \hat{\mathbf{r}}_{ij} \;\right]. \tag{23}$$

For the force

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

2 Hessians

Second derivative of G_{np} is given by

$$\begin{aligned}\frac{\partial^2 G^{np}}{\partial r_{ij}^2} \;&=\; 24\pi\sigma \left[(\rho_i + \rho_s)^2 \frac{{\rho_i}^6}{R_i^7} \left(\frac{7}{R_i} \left(\frac{\partial R_i}{\partial r_{ij}} \right)^2 - \frac{\partial^2 R_i}{\partial r_{ij}^2} \right) \right. \\ &\left. + (\rho_j + \rho_s)^2 \frac{{\rho_j}^6}{R_j^7} \left(\frac{7}{R_j} \left(\frac{\partial R_j}{\partial r_{ij}} \right)^2 - \frac{\partial^2 R_j}{\partial r_{ij}^2} \right) \right].\end{aligned} \tag{25}$$

Second derivative of E_{GB} is given by

$$\begin{aligned}\frac{\partial^2 E_{GB}}{\partial r_{ij}^2} \;&=\; \left(\frac{1}{\epsilon_S} - \frac{1}{\epsilon_w} \right) \left[\sum_{k \neq i,j} \left(\frac{q_i q_k}{{f_{ik}^{GB}}^2} \frac{\partial^2 f_{ik}^{GB}}{\partial r_{ij}^2} - \frac{2}{{f_{ik}^{GB}}^3} \left(\frac{\partial f_{ik}^{GB}}{\partial r_{ij}} \right)^2 \right) \right. \\ &+ \sum_{l \neq i,j} \left(\frac{q_j q_l}{{f_{jl}^{GB}}^2} \frac{\partial^2 f_{jl}^{GB}}{\partial r_{ij}^2} - \frac{2}{{f_{jl}^{GB}}^3} \left(\frac{\partial f_{jl}^{GB}}{\partial r_{ij}} \right)^2 \right) \\ &\left. + \left(\frac{q_i q_j}{{f_{ij}^{GB}}^2} \frac{\partial^2 f_{ij}^{GB}}{\partial r_{ij}^2} - \frac{2}{{f_{ij}^{GB}}^3} \left(\frac{\partial f_{ij}^{GB}}{\partial r_{ij}} \right)^2 \right) \right].\end{aligned} \tag{26}$$

Second derivative of the Born Radius R_i (see Equation (25)) is given by

$$
\begin{aligned}
\frac{\partial^2 R_i}{\partial r_{ij}^2} &= 2\frac{R_i^3}{\rho^2}\left(\frac{\partial \Psi}{\partial r_{ij}}\right)^2 (1-\tanh^2(\alpha\Psi-\beta\Psi^2+\gamma\Psi^3))^2(\alpha-2\beta\Psi+3\gamma\Psi^2)^2 \\
&\quad -2\frac{R_i^2}{\rho}(1-\tanh^2(\alpha\Psi-\beta\Psi^2+\gamma\Psi^3))\left(\frac{\partial \Psi_i}{\partial r_{ij}}\right)^2 \tanh(\alpha\Psi-\beta\Psi^2+\gamma\Psi^3) \\
&\qquad (\alpha-2\beta\Psi+3\gamma\Psi^2)^2 \\
&\quad +\frac{R_i^2}{\rho_i}(1-\tanh^2(\alpha\Psi-\beta\Psi^2+\gamma\Psi^3))\left(\alpha\frac{\partial^2\Psi_i}{\partial r_{ij}^2} - 2\beta\left(\frac{\partial \Psi_i}{\partial r_{ij}}\right)^2 - 2\beta\Psi_i\frac{\partial^2\Psi_i}{\partial r_{ij}^2}\right. \\
&\qquad \left. + 6\gamma\Psi_i\left(\frac{\partial \Psi_i}{\partial r_{ij}}\right)^2 + 3\gamma\Psi_i^2\frac{\partial^2\Psi_i}{\partial r_{ij}^2}\right). \qquad (27)
\end{aligned}
$$

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

$$
\begin{aligned}
\frac{\partial^2 f_{ij}^{GB}}{\partial r_{ij}^2} &= -\frac{1}{f_{ij}^{GB}}\left(\frac{\partial f_{ij}^{GB}}{\partial r_{ij}}\right)^2 + \frac{1}{f_{ij}^{GB}} \\
&\quad +\frac{1}{2f_{ij}^{GB}}\exp\left(-\frac{r_{ij}^2}{4R_iR_j}\right)\Bigg[\quad \frac{\partial^2 R_i}{\partial r_{ij}^2}R_j + 2\frac{\partial R_i}{\partial r_{ij}}\frac{\partial R_j}{\partial r_{ij}} \\
&\qquad +2\frac{\partial R_i}{\partial r_{ij}}R_j\left(-\frac{r_{ij}}{2R_iR_j} + \frac{r_{ij}^2}{4R_i^2R_j}\frac{\partial R_i}{\partial r_{ij}} + \frac{r_{ij}^2}{4R_iR_j^2}\frac{\partial R_j}{\partial r_{ij}}\right) \\
&\qquad +R_i\frac{\partial^2 R_j}{\partial r_{ij}^2} \\
&\qquad +2R_i\frac{\partial R_j}{\partial r_{ij}}\left(-\frac{r_{ij}}{2R_iR_j} + \frac{r_{ij}^2}{4R_i^2R_j}\frac{\partial R_i}{\partial r_{ij}} + \frac{r_{ij}^2}{4R_iR_j^2}\frac{\partial R_j}{\partial r_{ij}}\right) \\
&\qquad +R_iR_j\left(-\frac{1}{2R_iR_j} + \frac{r_{ij}}{R_i^2R_j}\frac{\partial R_i}{\partial r_{ij}} + \frac{r_{ij}}{R_iR_j^2}\frac{\partial R_j}{\partial r_{ij}} - \frac{r_{ij}^2}{2R_i^2R_j^2}\frac{\partial R_i}{\partial r_{ij}}\frac{\partial R_j}{\partial r_{ij}}\right) \\
&\qquad +R_iR_j\left(\frac{r_{ij}^2}{4R_i^2R_j}\frac{\partial^2 R_i}{\partial r_{ij}^2} + \frac{r_{ij}^2}{4R_iR_j^2}\frac{\partial^2 R_j}{\partial r_{ij}^2} - \frac{r_{ij}^2}{2R_iR_j^3}\left(\frac{\partial R_j}{\partial r_{ij}}\right)^2 - \frac{r_{ij}^2}{2R_i^3R_j}\left(\frac{\partial R_i}{\partial r_{ij}}\right)^2\right) \\
&\qquad + R_iR_j\left(-\frac{r_{ij}}{2R_iR_j} + \frac{r_{ij}^2}{4R_i^2R_j}\frac{\partial R_i}{\partial r_{ij}} + \frac{r_{ij}^2}{4R_iR_j^2}\frac{\partial R_j}{\partial r_{ij}}\right)^2 \quad \Bigg]. \qquad (28)
\end{aligned}
$$

Similarly, we can find,

$$
\begin{aligned}
\frac{\partial^2 f_{ik}^{GB}}{\partial r_{ij}^2} &= -\frac{1}{f_{ik}^{GB}}\left(\frac{\partial f_{ik}^{GB}}{\partial r_{ij}}\right)^2 \\
&\quad +\frac{1}{2f_{ik}^{GB}}\exp\left(-\frac{r_{ik}^2}{4R_iR_k}\right)\left[\frac{\partial^2 R_i}{\partial r_{ij}^2}\left(R_k+\frac{r_{ik}^2}{4R_i}\right)\right. \\
&\qquad \left. +\frac{r_{ik}^4}{16R_i^3R_j}\left(\frac{\partial R_i}{\partial r_{ij}}\right)^2\right].
\end{aligned} \tag{29}
$$

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

Note that

$$
\frac{\partial^2 \Psi_i}{\partial r_{ij}^2} = \frac{\partial^2 I_i}{\partial r_{ij}^2}\tilde{\rho}_i. \tag{30}
$$

where

$$
\begin{aligned}
\frac{\partial^2 I_i}{\partial r_{ij}^2} &= \frac{1}{L_{ij}^3}\left(\frac{\partial L_{ij}}{\partial r_{ij}}\right)^2 - \frac{1}{U_{ij}^3}\left(\frac{\partial U_{ij}}{\partial r_{ij}}\right)^2 + \frac{1}{2L_{ij}^3}\frac{\partial L_{ij}}{\partial r_{ij}} - \frac{1}{2U_{ij}^3}\frac{\partial U_{ij}}{\partial r_{ij}} \\
&\quad +\frac{r_{ij}}{4}\left(\frac{3}{U_{ij}^4}\left(\frac{\partial U_{ij}}{\partial r_{ij}}\right)^2 - \frac{3}{L_{ij}^4}\left(\frac{\partial L_{ij}}{\partial r_{ij}}\right)^2\right) + \frac{1}{2r_{ij}^3}\log\left(\frac{L_{ij}}{U_{ij}}\right) \\
&\quad +\frac{1}{2r_{ij}^2 L_{ij}}\left(\frac{L_{ij}}{U_{ij}}\frac{\partial U_{ij}}{\partial r_{ij}} - \frac{\partial L_{ij}}{\partial r_{ij}}\right) + \frac{1}{2r_{ij}L_{ij}U_{ij}}\left(\frac{L_{ij}}{U_{ij}}\left(\frac{\partial U_{ij}}{\partial r_{ij}}\right)^2 - \frac{\partial U_{ij}}{\partial r_{ij}}\frac{\partial L_{ij}}{\partial r_{ij}}\right) \\
&\quad +\frac{1}{4r_{ij}L_{ij}^2}\frac{\partial L_{ij}}{\partial r_{ij}}\left(\frac{L_{ij}}{U_{ij}}\frac{\partial U_{ij}}{\partial r_{ij}} - \frac{\partial L_{ij}}{\partial r_{ij}}\right) - \frac{1}{4r_{ij}L_{ij}U_{ij}}\frac{\partial U_{ij}}{\partial r_{ij}}\left(\frac{L_{ij}}{U_{ij}}\frac{\partial U_{ij}}{\partial r_{ij}} - \frac{\partial L_{ij}}{\partial r_{ij}}\right) \\
&\quad +\frac{S_j^2\tilde{\rho}_i^2}{4r_{ij}^3}\left(\frac{1}{L_{ij}^2} - \frac{1}{U_{ij}^2}\right) - \frac{S_j^2\tilde{\rho}_i^2}{2r_{ij}^2}\left(\frac{1}{U_{ij}^3}\frac{\partial U_{ij}}{\partial r_{ij}} - \frac{1}{L_{ij}^3}\frac{\partial L_{ij}}{\partial r_{ij}}\right) \\
&\quad +\frac{S_j^2\tilde{\rho}_i^2}{4r_{ij}}\left(\frac{3}{L_{ij}^4}\left(\frac{\partial L_{ij}}{\partial r_{ij}}\right)^2 - \frac{3}{U_{ij}^4}\left(\frac{\partial U_{ij}}{\partial r_{ij}}\right)^2\right).
\end{aligned} \tag{31}
$$

Hessian for $\mathbf{r}_i$.

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

$$
\mathbf{H}_{ij} = \frac{\partial E_{GB}}{\partial r_{ij}}\frac{1}{r_{ij}}\begin{bmatrix} \mathbf{I} & -\mathbf{I} \\ -\mathbf{I} & \mathbf{I}\end{bmatrix} + \left(\frac{\partial^2 E_{GB}}{\partial r_{ij}^2} - \frac{\partial E_{GB}}{\partial r_{ij}}\frac{1}{r_{ij}}\right)\begin{bmatrix} \hat{\mathbf{r}}_{ij}\hat{\mathbf{r}}_{ij}^{\mathrm{T}} & -\hat{\mathbf{r}}_{ij}\hat{\mathbf{r}}_{ij}^{\mathrm{T}} \\ -\hat{\mathbf{r}}_{ij}\hat{\mathbf{r}}_{ij}^{\mathrm{T}} & \hat{\mathbf{r}}_{ij}\hat{\mathbf{r}}_{ij}^{\mathrm{T}}\end{bmatrix}. \tag{32}
$$