

Generalized Born : Energies, Forces and Hessian

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1 Energy and Force Equations

Effective Born radii for atom i is given by

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

or

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

where

$$\Psi_i = I_i \tilde{\rho}_i. \quad (3)$$

Note that,

$$\tilde{\rho}_i = \rho_i - p. \quad (4)$$

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

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

where

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

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

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

and S_j are given constants.

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

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

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

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

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

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

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

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

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

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

Question: Does $\partial C_{ij} / \partial r_{ij} = 0$?

ACE Solvation term The nonpolar ACE solvation energy is given by

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

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

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

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

$$E_{GB} = -\frac{1}{2} \left(\frac{1}{\epsilon_s} - \frac{1}{\epsilon_w} \right) \sum_i \sum_{j \neq i} \frac{q_i q_j}{f_{ij}^{GB}(r_{ij}, R_i, R_j)}. \quad (16)$$

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 not calculated the ‘self’ term as OpenMM assumes the derivative of the ‘self’ term is zero. The function f_{ij}^{GB} is given by,

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

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

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

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

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

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

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

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

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

2 Hessian

Second derivative of G_{np} is given by

$$\frac{\partial^2 G_{np}}{\partial r_{ij}^2} = 4\pi\sigma \left[6(\rho_i + \rho_s)^2 \rho_i^6 \left(7 \left(\frac{\partial R_i}{\partial r_{ij}} \right)^2 \frac{1}{R_i^8} - \frac{\partial^2 R_i}{\partial r_{ij}^2} \right) + 6(\rho_j + \rho_s)^2 \rho_j^6 \left(\frac{7}{R_j^8} \left(\frac{\partial R_j}{\partial r_{ij}} \right)^2 - \frac{1}{R_j^7} \frac{\partial^2 R_j}{\partial r_{ij}^2} \right) \right]. \quad (22)$$

Second derivative of E_{GB} is given by

$$\frac{\partial^2 E_{GB}}{\partial r_{ij}^2} = \left[q_i q_j \left(\frac{1}{f_{ij}^{GB^2}} \frac{\partial^2 f_{ij}^{GB}}{\partial r_{ij}^2} - \frac{2}{f_{ij}^{GB^3}} \left(\frac{\partial f_{ij}^{GB}}{\partial r_{ij}} \right)^2 \right) + \sum_k \sum_l q_k q_l \left(\frac{1}{f_{kl}^{GB^2}} \frac{\partial^2 f_{kl}^{GB}}{\partial r_{ij}^2} - \frac{2}{f_{kl}^{GB^3}} \left(\frac{\partial f_{kl}^{GB}}{\partial r_{ij}} \right)^2 \right) \right]. \quad (23)$$

Second derivative of the Born Radius R_i (see Equation (22)) is given by

$$\begin{aligned}
\frac{\partial^2 R_i}{\partial r_{ij}^2} = & 2(1 - \tanh(\alpha\Psi - \beta\Psi^2 + \gamma\Psi^3))^2 \left(\frac{\partial\Psi}{\partial r_{ij}} \right)^2 (\alpha - 2\beta\Psi + 3\gamma\Psi^2)^2 \frac{R_i^3}{\rho^2} \\
& - 2R_i^2 \tanh(\alpha\Psi - \beta\Psi^2 + \gamma\Psi^3) (1 - \tanh(\alpha\Psi - \beta\Psi^2 + \gamma\Psi^3))^2 \\
& \left(\frac{\partial\Psi_i}{\partial r_{ij}} \right)^2 (\alpha - 2\beta\Psi + 3\gamma\Psi^2)^2 \frac{1}{\rho} \\
& R_i^2 (1 - \tanh(\alpha\Psi - \beta\Psi^2 + \gamma\Psi^3)^2) \left(\alpha \frac{\partial^2 \Psi_i}{\partial r_{ij}^2} - 2\beta \left(\frac{\partial\Psi_i}{\partial r_{ij}} \right)^2 - 2\beta\Psi_i \frac{\partial^2 \Psi_i}{\partial r_{ij}^2} \right) \frac{1}{\rho_i} \\
& + R_i^2 (1 - \tanh(\alpha\Psi - \beta\Psi^2 + \gamma\Psi^3)^2) \left(6\gamma\Psi_i \left(\frac{\partial\Psi_i}{\partial r_{ij}} \right)^2 + 3\gamma\Psi_i^2 \frac{\partial^2 \Psi_i}{\partial r_{ij}^2} \right) \frac{1}{\rho_i}.
\end{aligned} \tag{24}$$

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 (f_{ij}^{GB})^2 \left(\frac{\partial f_{ij}^{GB}}{\partial r_{ij}} \right)^2 \\
& + \frac{1}{2f_{ij}^{GB}} \left[2 + \frac{\partial^2 R_i}{\partial r_{ij}^2} R_j \exp\left(-\frac{r_{ij}^2}{4R_i R_j}\right) + 2 \frac{\partial R_i}{\partial r_{ij}} \frac{\partial R_j}{\partial r_{ij}} \exp\left(-\frac{r_{ij}^2}{4R_i R_j}\right) \right] \\
& + \frac{1}{2f_{ij}^{GB}} \left[2 \frac{\partial R_i}{\partial r_{ij}} R_j \left(-\frac{r_{ij}}{R_i R_j} + \frac{r_{ij}^2}{4R_i^2 R_j} \frac{\partial R_i}{\partial r_{ij}} + \frac{r_{ij}^2}{4R_i R_j^2} \frac{\partial R_j}{\partial r_{ij}} \right) \exp\left(-\frac{r_{ij}^2}{4R_i R_j}\right) \right] \\
& + \frac{1}{2f_{ij}^{GB}} \left[R_i \frac{\partial^2 R_j}{\partial r_{ij}^2} \exp\left(-\frac{r_{ij}^2}{4R_i R_j}\right) \right] \\
& + \frac{1}{2f_{ij}^{GB}} \left[2R_j \frac{\partial R_i}{\partial r_{ij}} \left(-\frac{r_{ij}}{2R_i R_j} + \frac{r_{ij}^2}{4R_i^2 R_j} \frac{\partial R_i}{\partial r_{ij}} + \frac{r_{ij}^2}{4R_i R_j^2} \frac{\partial R_j}{\partial r_{ij}} \right) \exp\left(-\frac{r_{ij}^2}{4R_i R_j}\right) \right] \\
& + \frac{1}{2f_{ij}^{GB}} \left[R_i R_j \left(-\frac{1}{2R_i R_j} + \frac{r_{ij}}{4R_i^2 R_j} \frac{\partial R_i}{\partial r_{ij}} + \frac{r_{ij}}{4R_i R_j^2} \frac{\partial R_j}{\partial r_{ij}} - \frac{r_{ij}^2}{2R_i^2 R_j^2} \frac{\partial R_i}{\partial r_{ij}} \frac{\partial R_j}{\partial r_{ij}} \right) \exp\left(-\frac{r_{ij}^2}{4R_i R_j}\right) \right] \\
& + \frac{1}{2f_{ij}^{GB}} \left[R_i R_j \left(\frac{r_{ij}^2}{4R_i^2 R_j} \frac{\partial^2 R_i}{\partial r_{ij}^2} + \frac{r_{ij}^2}{4R_i R_j^2} \frac{\partial^2 R_j}{\partial r_{ij}^2} - \frac{r_{ij}^2}{2R_i R_j^3} \left(\frac{\partial R_j}{\partial r_{ij}} \right)^2 \right) \exp\left(-\frac{r_{ij}^2}{4R_i R_j}\right) \right] \\
& + \frac{1}{2f_{ij}^{GB}} \left[R_i R_j \left(-\frac{r_{ij}}{2R_i R_j} + \frac{r_{ij}^2}{4R_i^2 R_j} \frac{\partial R_i}{\partial r_{ij}} + \frac{r_{ij}^2}{4R_i R_j^2} \frac{\partial R_j}{\partial r_{ij}} \right) \exp\left(-\frac{r_{ij}^2}{4R_i R_j}\right) \right].
\end{aligned} \tag{25}$$

Similarly, we can find,

$$\begin{aligned}
\frac{\partial^2 f_{il}^{GB}}{\partial r_{ij}^2} = & \frac{1}{f_{il}^{GB}} \exp\left(-\frac{r_{il}^2}{4R_i R_l}\right) \left(R_l + \frac{r_{il}^2}{4R_i} \right) \left[\frac{\partial^2 R_i}{\partial r_{ij}^2} - \frac{\partial R_i}{\partial r_{ij}} \left(\frac{1}{f_{il}^{GB}} \right) \frac{\partial f_{il}^{GB}}{\partial r_{ij}} \right] \\
& + \frac{1}{f_{il}^{GB}} \exp\left(-\frac{r_{il}^2}{4R_i R_j}\right) \left(\frac{\partial R_i}{\partial r_{ij}} \right)^2 \left[\left(R_l + \left(-\frac{r_{il}^2}{4R_i} \right) \right) \frac{-r_{il}^2}{4R_i^2 R_l} - \frac{r_{il}^2}{4R_i} \right]
\end{aligned} \tag{26}$$

and

$$\begin{aligned} \frac{\partial^2 f_{jl}^{GB}}{\partial r_{ij}^2} &= \frac{1}{f_{jl}^{GB}} \exp\left(-\frac{r_{jl}^2}{4R_j R_l}\right) \left(R_l + \frac{r_{jl}^2}{4R_j}\right) \left[\frac{\partial^2 R_j}{\partial r_{ij}} - \frac{\partial R_j}{\partial r_{ij}} \left(\frac{1}{f_{jl}^{GB}}\right) \frac{\partial f_{jl}^{GB}}{\partial r_{ij}}\right] \\ &+ \frac{1}{f_{jl}^{GB}} \exp\left(-\frac{r_{jl}^2}{4R_j R_j}\right) \left(\frac{\partial R_j}{\partial r_{ij}}\right)^2 \left[\left(R_l + \left(-\frac{r_{jl}^2}{4R_j}\right)\right) \frac{-r_{jl}^2}{4R_j^2 R_l} - \frac{r_{jl}^2}{4R_j}\right] \end{aligned} \quad (27)$$

Note that

$$\frac{\partial^2 \Psi_i}{\partial r_{ij}^2} = \frac{\partial^2 I_i}{\partial r_{ij}^2} \tilde{\rho}_i. \quad (28)$$

where

$$\begin{aligned} \frac{\partial^2 I_i}{\partial r_{ij}^2} &= \left[\frac{1}{L_{ij}^3} \left(\frac{\partial L_{ij}}{\partial r_{ij}}\right)^2 - \frac{1}{U_{ij}^3} \left(\frac{\partial U_{ij}}{\partial r_{ij}}\right)^2 + \left(\frac{1}{4L_{ij}^3} \frac{\partial L_{ij}}{\partial r_{ij}} - \frac{1}{4U_{ij}^3} \frac{\partial U_{ij}}{\partial r_{ij}}\right) \right] \\ &+ \left[\frac{1}{8} \left(\frac{2}{L_{ij}^3} \frac{\partial L_{ij}}{\partial r_{ij}} - \frac{2}{U_{ij}^3} \frac{\partial U_{ij}}{\partial r_{ij}}\right) - \frac{r_{ij}}{4} \left(\frac{3}{U_{ij}^4} \left(\frac{\partial U_{ij}}{\partial r_{ij}}\right)^2 - \frac{3}{L_{ij}^4} \left(\frac{\partial L_{ij}}{\partial r_{ij}}\right)^2\right) \right] \\ &+ \left[\frac{1}{2r_{ij}^3} \log\left(\frac{L_{ij}}{U_{ij}}\right) - \frac{1}{2r_{ij}^2 L_{ij}} \left(\frac{1}{U_{ij}} \frac{\partial L_{ij}}{\partial r_{ij}} - \frac{L_{ij}}{U_{ij}^2} \frac{\partial U_{ij}}{\partial r_{ij}}\right) + \frac{1}{4r_{ij} L_{ij}} \left(\frac{2L_{ij}}{U_{ij}^3} \left(\frac{\partial U_{ij}}{\partial r_{ij}}\right)^2 - 2\frac{\frac{\partial L_{ij}}{\partial r_{ij}} \frac{\partial U_{ij}}{\partial r_{ij}}}{U_{ij}^2}\right) \right] \\ &- \left[\frac{1}{4r_{ij} L_{ij}^2} \frac{\partial L_{ij}}{\partial r_{ij}} \left(\frac{1}{U_{ij}} \frac{\partial L_{ij}}{\partial r_{ij}} - \frac{L_{ij}}{U_{ij}^2} \frac{\partial U_{ij}}{\partial r_{ij}}\right) + \frac{1}{4r_{ij} L_{ij}} \frac{\partial U_{ij}}{\partial r_{ij}} \left(\frac{1}{U_{ij}} \frac{\partial L_{ij}}{\partial r_{ij}} - \frac{L_{ij}}{U_{ij}^2} \frac{\partial U_{ij}}{\partial r_{ij}}\right) \right] \\ &+ \frac{S_j^2 \tilde{\rho}_i^2}{4r_{ij}} \left[\frac{1}{r_{ij}^2} \left(\frac{1}{L_{ij}^2} - \frac{1}{U_{ij}^2}\right) - \frac{2}{r_{ij}^2 U_{ij}^3} \frac{\partial U_{ij}}{\partial r_{ij}} - \frac{3}{U_{ij}^4} \left(\frac{\partial U_{ij}}{\partial r_{ij}}\right)^2 \right] \end{aligned} \quad (29)$$