

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

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

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

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

and S_j are given constants.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

1.1 Force in \mathbf{r}_i

To obtain the force we need to find

$$\frac{dr_{ij}}{d\mathbf{r}_i} = \frac{d\|\mathbf{r}_j - \mathbf{r}_i\|}{d\mathbf{r}_i} = -\frac{\|\mathbf{r}_j - \mathbf{r}_i\|}{r_{ij}} = -\hat{\mathbf{r}}_{ij}, \quad (22)$$

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

$$\nabla_{ij} E_{GB} = \frac{\partial E_{GB}}{\partial r_{ij}} [-\hat{\mathbf{r}}_{ij} \quad \hat{\mathbf{r}}_{ij}]. \quad (23)$$

For the force

$$\mathbf{F}_{ij} = -\nabla_{ij} E_{GB} = \frac{\partial E_{GB}}{\partial r_{ij}} [\hat{\mathbf{r}}_{ij} \quad -\hat{\mathbf{r}}_{ij}]. \quad (24)$$

2 Hessians

Second derivative of G_{np} is given by

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

Second derivative of E_{GB} is given by

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

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

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

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

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

Similarly, we can find,

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

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

Note that

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

where

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

Hessian for \mathbf{r}_i .

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

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