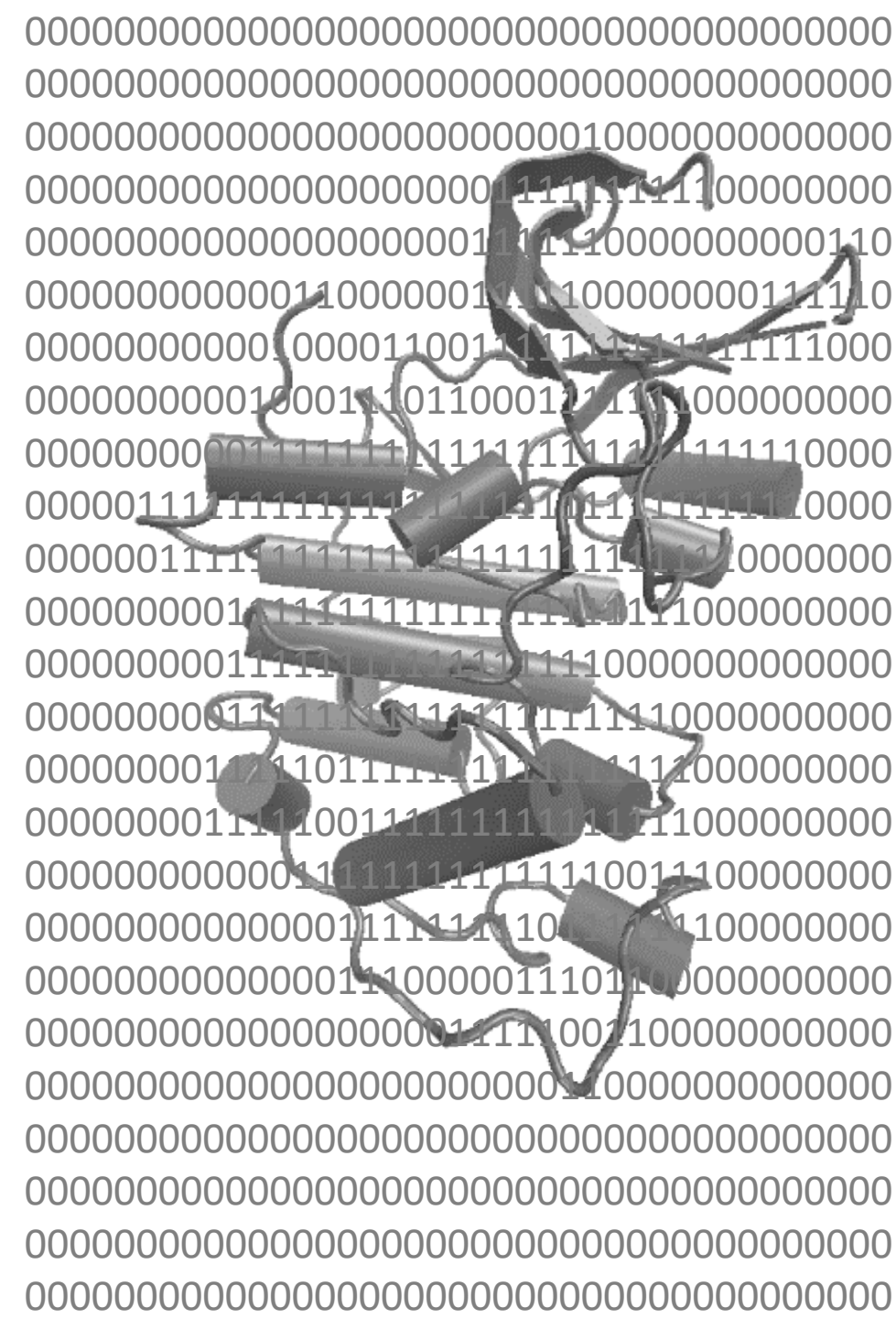


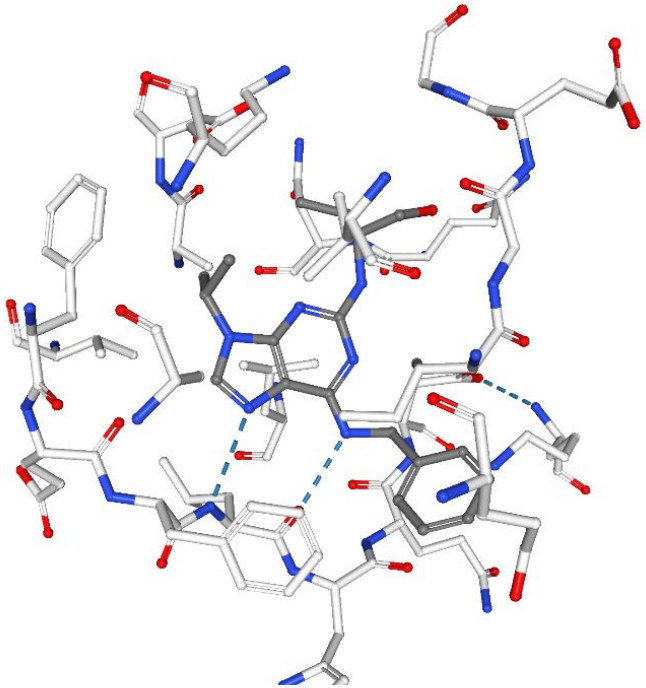
Van der Waals Potential in Protein Complexes

Previously, we saw that the potential energy (V) of a protein-ligand complex can be expressed by the following equation,

$$V = \alpha_1 \sum_{i,j} \left(\frac{A_{ij}}{r_{ij}^{12}} - \frac{B_{ij}}{r_{ij}^{6}} \right) + \alpha_2 \sum_{i,j} E(t) \left(\frac{C_{ij}}{r_{ij}^{12}} - \frac{D_{ij}}{r_{ij}^{10}} \right)$$
$$+ \alpha_3 \sum_{i,j} \frac{q_i q_j}{\varepsilon(r_{ij}) r_{ij}} + \alpha_4 \sum_{i,j} \left(S_i V_j + S_j V_i \right) \mathrm{e}^{-r_{ij}^2/2\sigma^2}$$

where r_{ij} indicates the interatomic distance, q_i and q_j are the electric charges, e is the s permittivity of the material, A, B, C, D, s are constants related to the type of interaction, E is a term to account for directions in hydrogen bonds. We also have the volume of atoms (V_i or V_j) multiplied by a solvation parameter (S_i or S_j) in the above equation. The a's are the relative weight of each energy term.

As previously highlighted, to determine the potential energy of the protein-ligand system, we use the atomic coordinates of the complex.

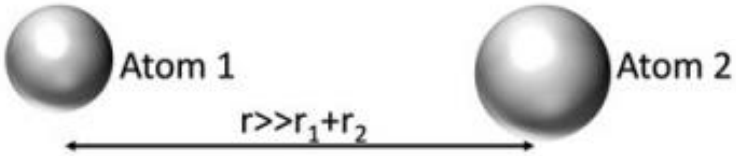


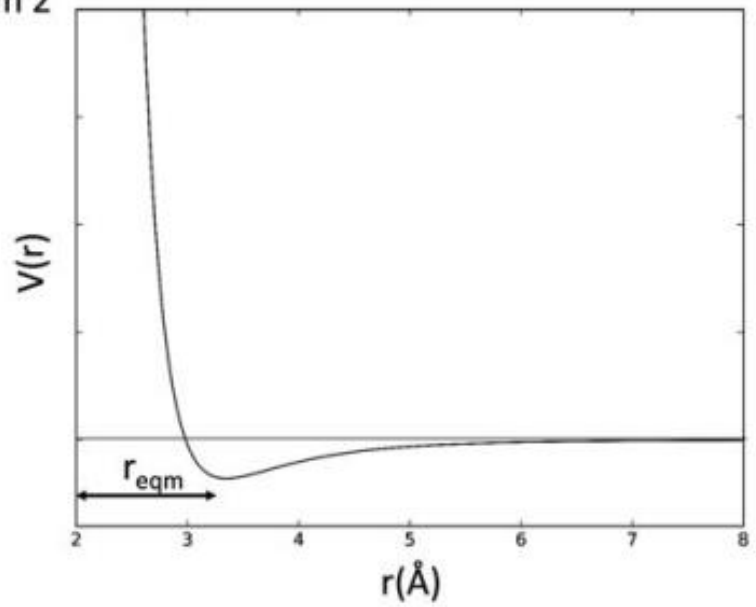
Click on the structure to access 3D-View

$$V = \alpha_1 \sum_{i,j} \left(\frac{A_{ij}}{r_{ij}^{12}} - \frac{B_{ij}}{r_{ij}^{6}} \right) + \alpha_2 \sum_{i,j} E(t) \left(\frac{C_{ij}}{r_{ij}^{12}} - \frac{D_{ij}}{r_{ij}^{10}} \right)$$

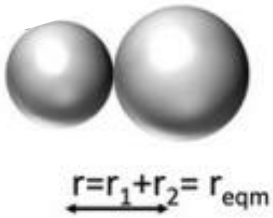
$$+ \alpha_3 \sum_{i,j} \frac{q_i q_j}{\varepsilon(r_{ij}) r_{ij}} + \alpha_4 \sum_{i,j} \left(S_i V_j + S_j V_i \right) e^{-r_{ij}^2/2\sigma^2}$$

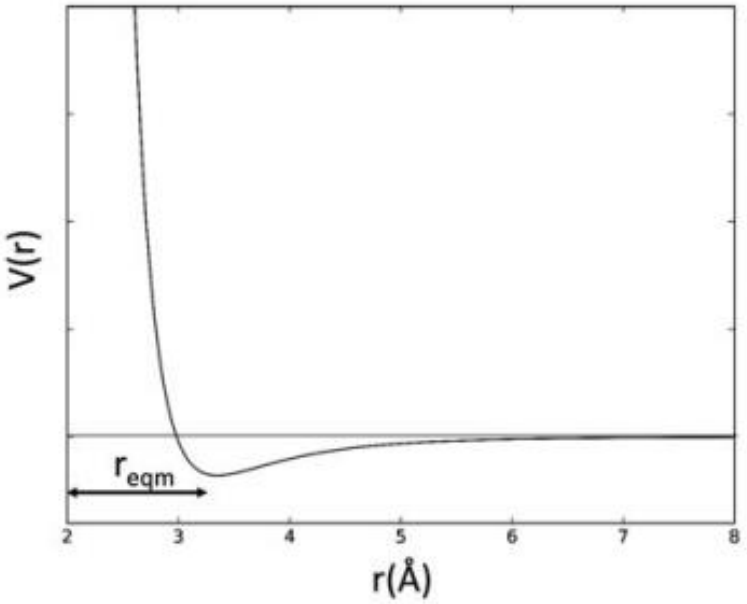
Van der Waals Interactions





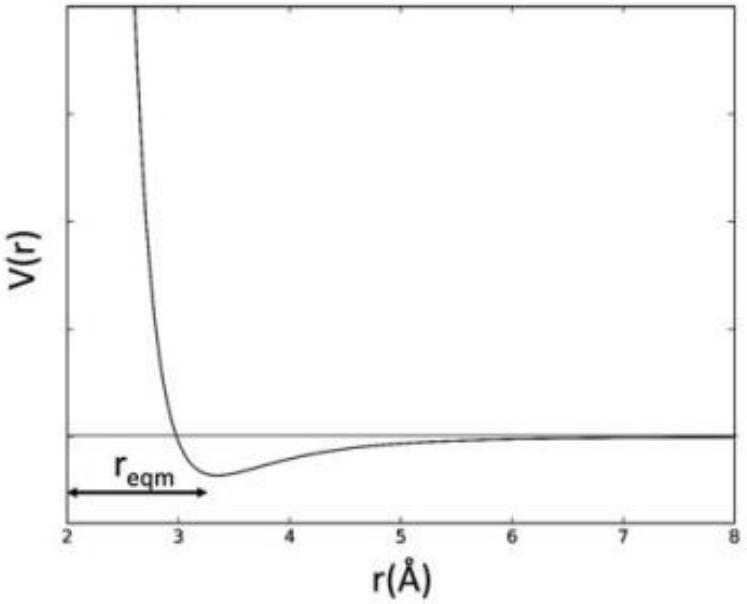
Van der Waals Interactions

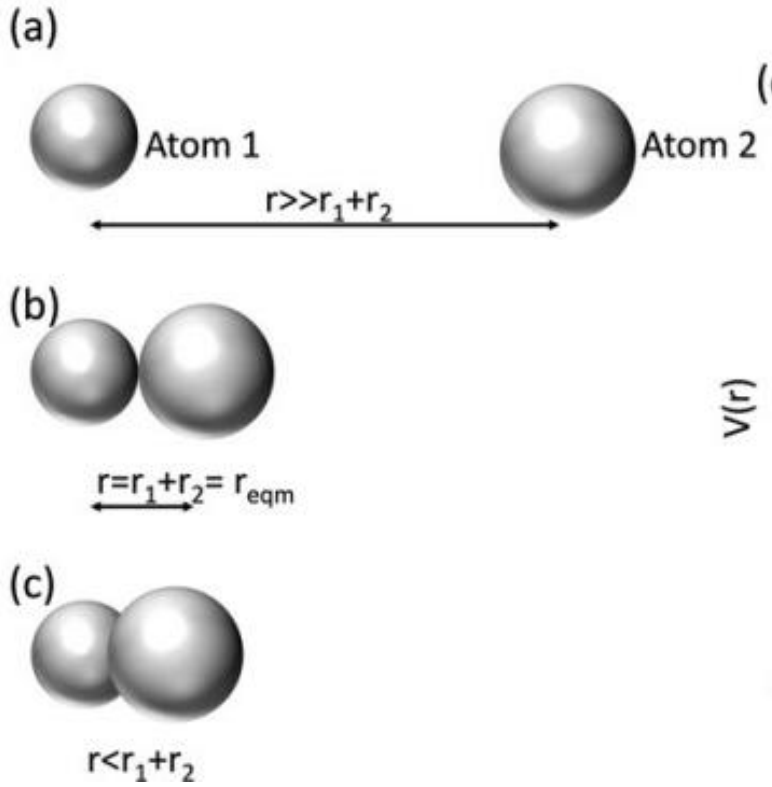


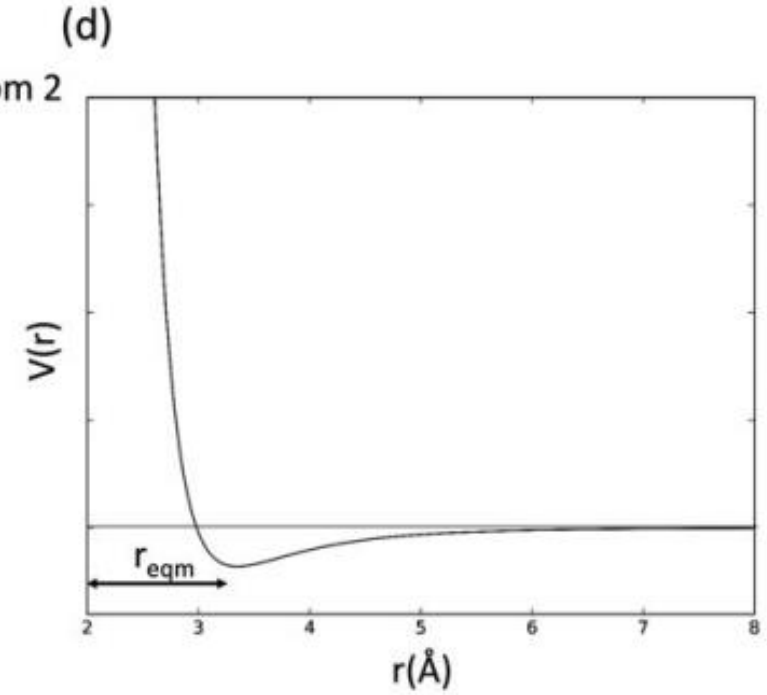


Van der Waals Interactions

$r < r_1 + r_2$



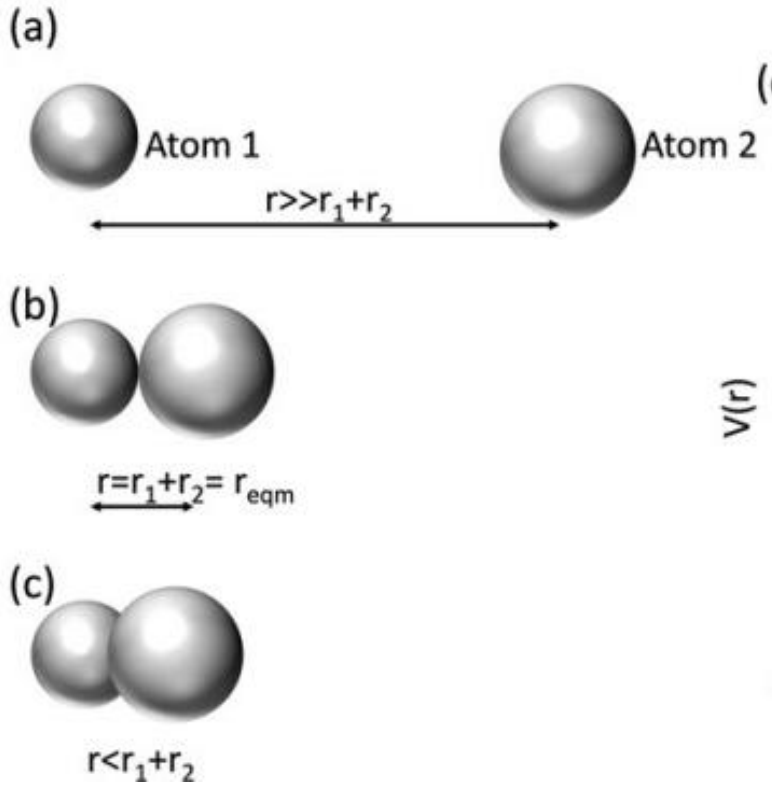


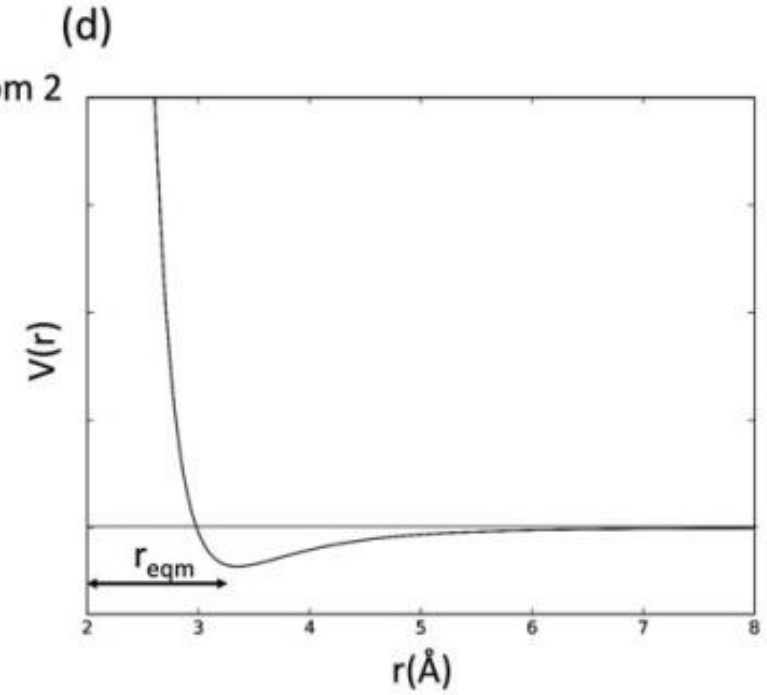


$$V(r) = \frac{Ae^{-br}}{r} - \frac{C_6}{r^6}$$

$$\frac{A}{r}e^{-br} \approx \frac{C_{12}}{r^{12}}$$

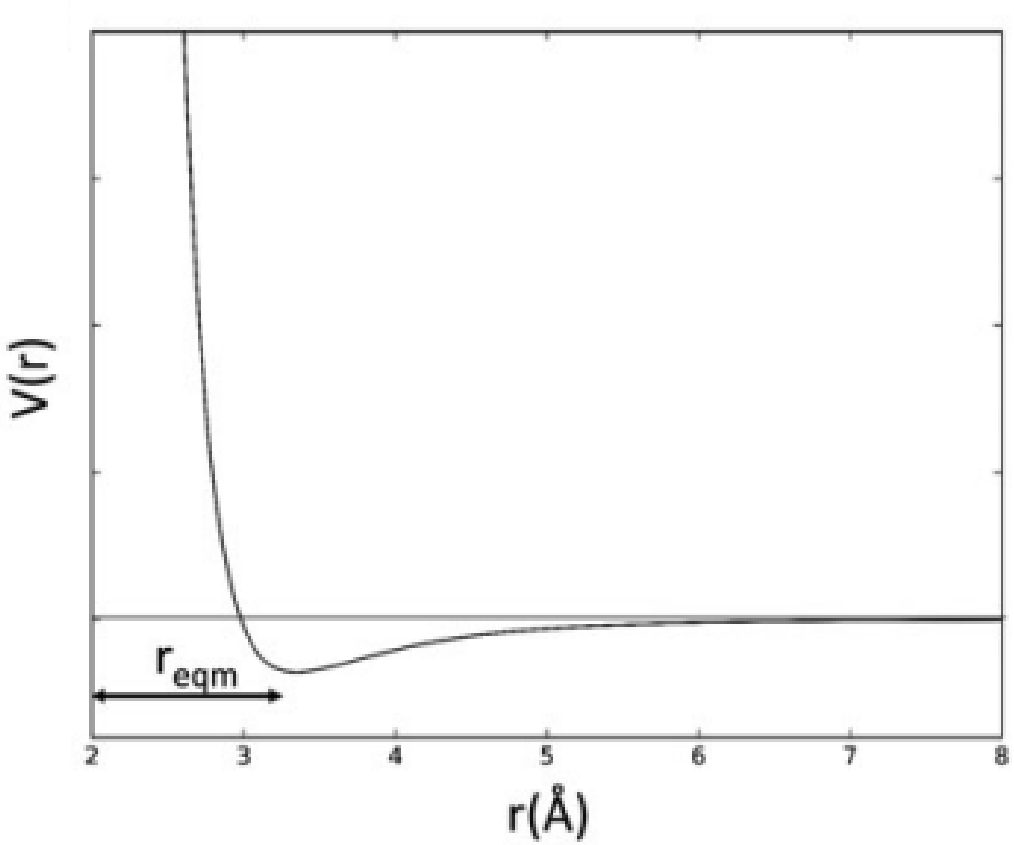
Lennard-Jones Potential





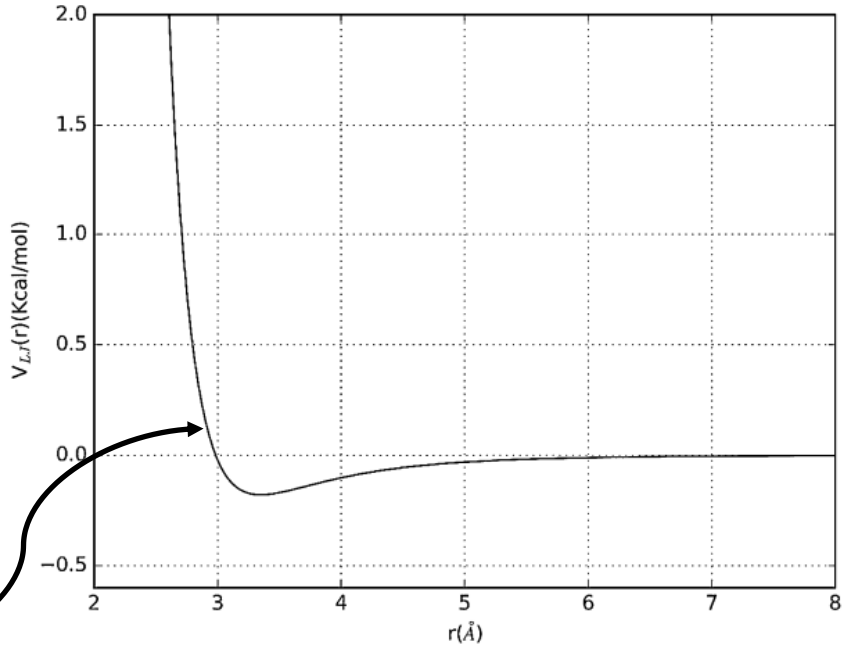
$$V(r) \approx \frac{C_n}{r^n} - \frac{C_m}{r^m} = C_n r^{-n} - C_m r^{-m}$$

Lennard-Jones Potential



$$V_{\mathrm{LJ}}(r) \approx \frac{\frac{m}{n-m}\varepsilon r_{\mathrm{eqm}}^{\,n}}{r^{n}} - \frac{\frac{n}{n-m}\varepsilon r_{\mathrm{eqm}}^{\,m}}{r^{m}}$$

To calculate the potential energy of the protein-ligand system, we use the atomic coordinates of the protein-ligand complex.

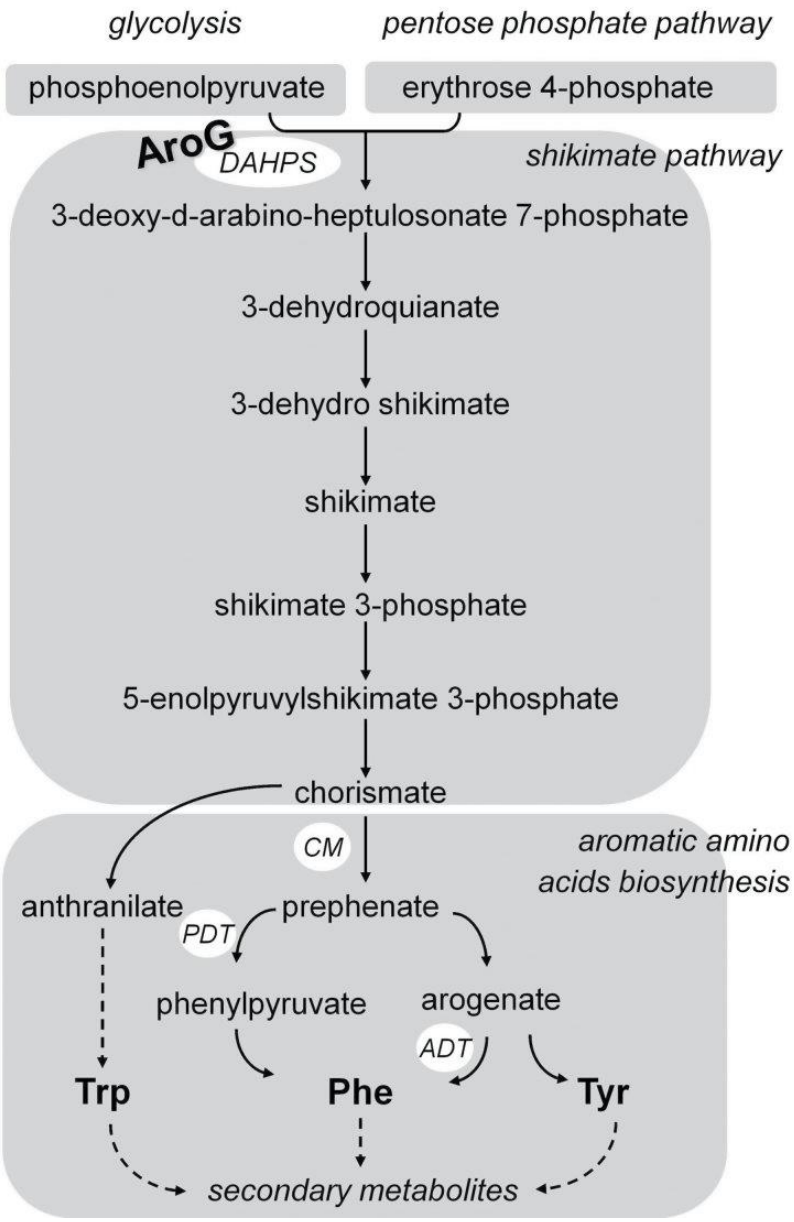


Lennard-Jones 12-6 potential for nitrogen-oxygen

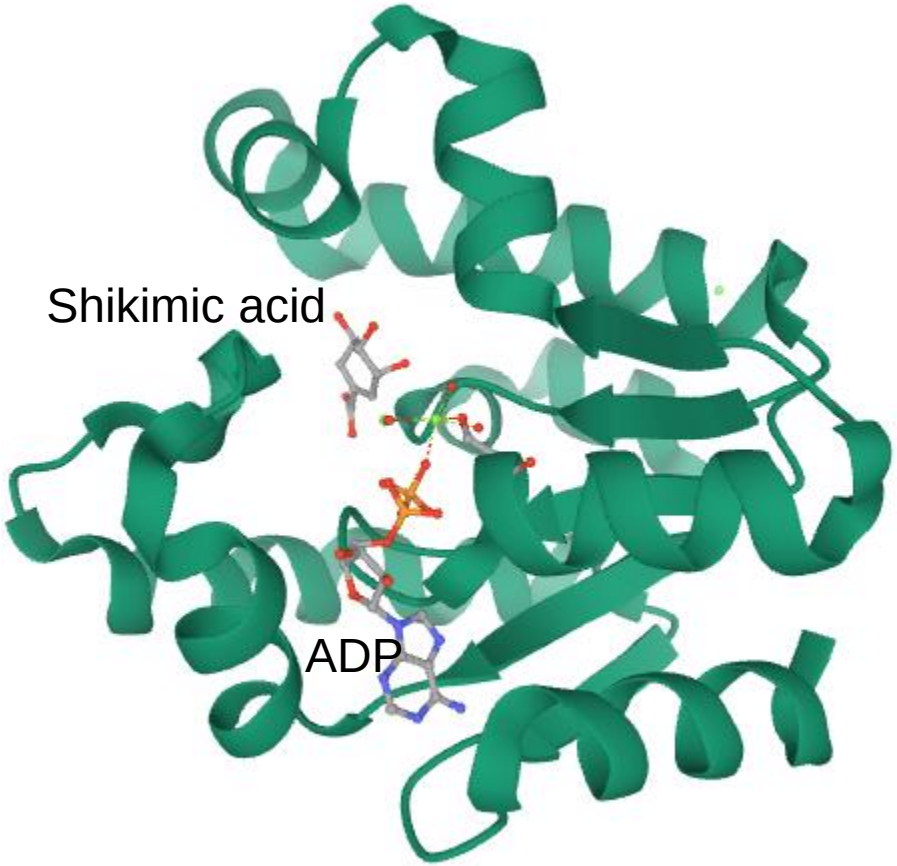
$$V = \alpha_1 \sum_{i,j} \left(\frac{A_{ij}}{r_{ij}^{12}} - \frac{B_{ij}}{r_{ij}^{6}} \right) + \alpha_2 \sum_{i,j} E(t) \left(\frac{C_{ij}}{r_{ij}^{12}} - \frac{D_{ij}}{r_{ij}^{10}} \right)$$

$$+ \alpha_3 \sum_{i,j} \frac{q_i q_j}{\varepsilon(r_{ij}) r_{ij}} + \alpha_4 \sum_{i,j} \left(S_i V_j + S_j V_i \right) \mathrm{e}^{-r_{ij}^2/2\sigma^2}$$

Shikimate Pathway

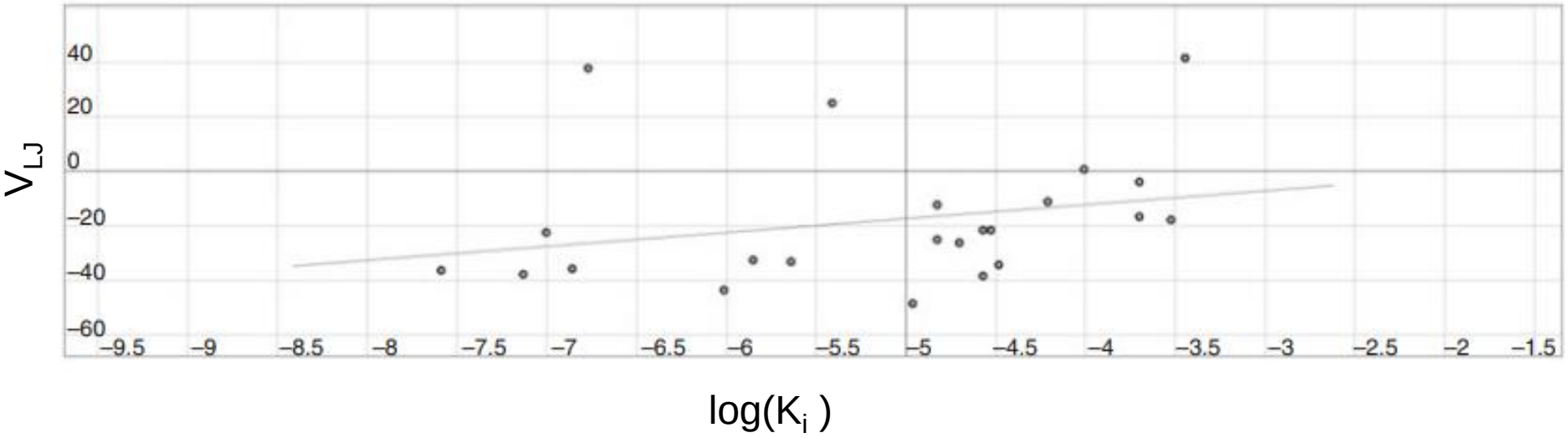


Crystallographic structure of shikimate kinase in complex with ADP and shikimic acid.



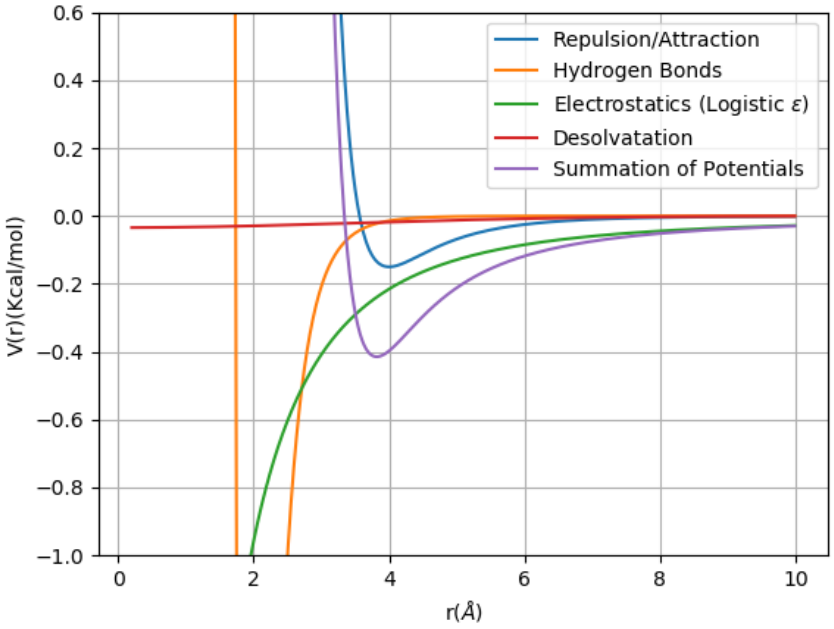
Click on the structure to access 3D-View

Calculated Lennard-Jones Potential Energy



Scatter plot for V_{LJ} against experimental log(K_i). We generated this plot with the program Molegro Data Modeller (MDM). Spearman's rank correlation between experimental log(K_i) and V_{LJ} is 0.51 (p-value = 0.01).

PDB access codes
4UMA, 4UMB, 4UMC, 4BQS, 1H0R, 1GU1, 1V1J, 2BT4, 2C4W, 2XB8, 2XB9, 3N76, 3N7A, 3N86, 3N87, 3N8K, 3N8N, 4B6O, 4B6P, 4B6R, 4B6S, 4CIW, 4CIY



Repulsion/Atraction potential

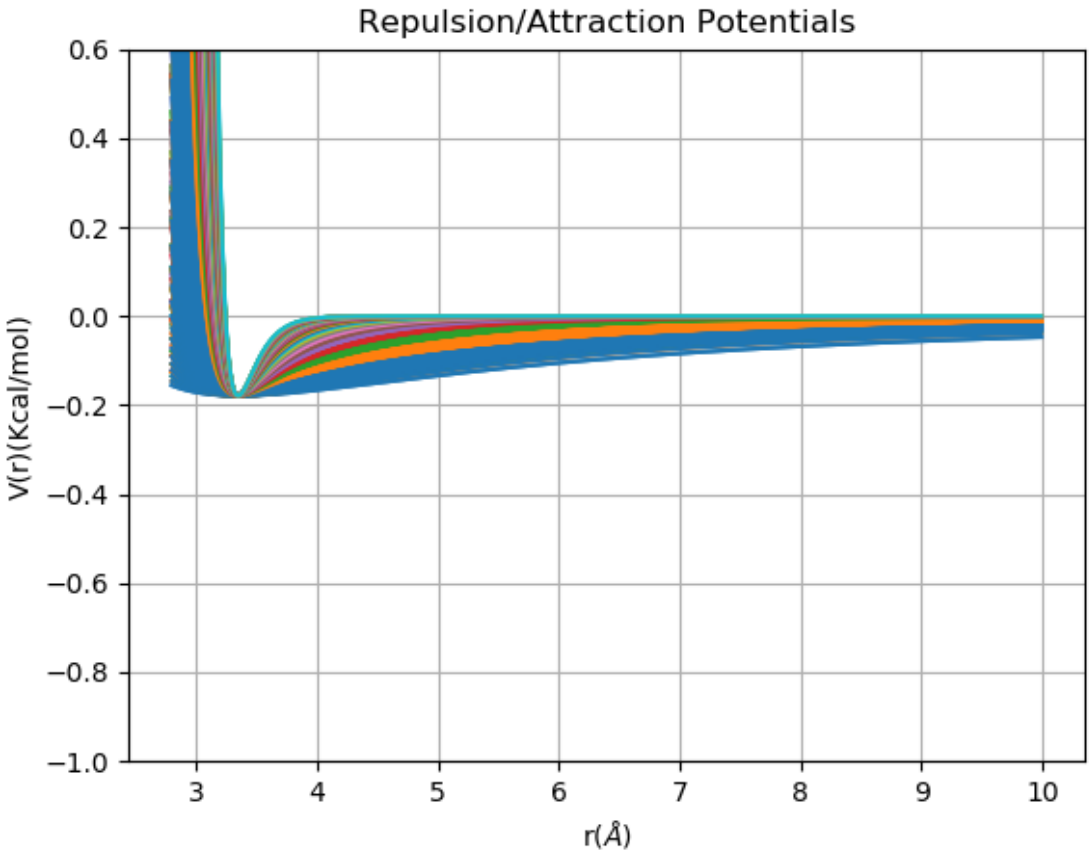
Hydrogen-bond potential

$$V = \alpha_1 \sum_{i,j} \left(\frac{A_{ij}}{r_{ij}^{12}} - \frac{B_{ij}}{r_{ij}^{6}} \right) + \alpha_2 \sum_{i,j} E(t) \left(\frac{C_{ij}}{r_{ij}^{12}} - \frac{D_{ij}}{r_{ij}^{10}} \right)$$

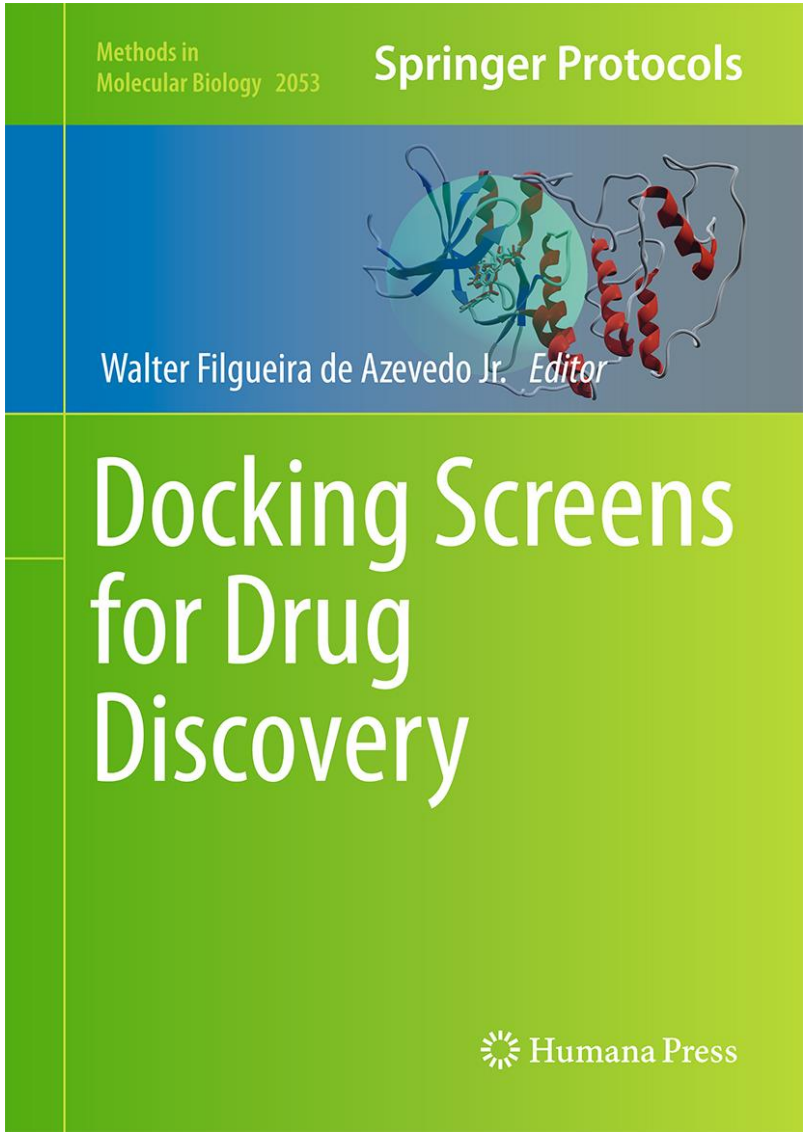
$$+ \alpha_3 \sum_{i,j} \frac{q_i q_j}{\varepsilon(r_{ij}) r_{ij}} + \alpha_4 \sum_{i,j} \left(S_i V_j + S_j V_i \right) e^{-r_{ij}^2 / 2\sigma^2}$$

Electrostatic potential

Desolvation potential



$$V_{LJ} = -\sum_{i,j}\left(\frac{\frac{m}{n-m}\varepsilon_{i,j}r_{eqm,i,j}^{n}}{r_{i,j}^{n}} - \frac{\frac{n}{n-m}\varepsilon_{i,j}r_{eqm,i,j}^{m}}{r_{i,j}^{m}}\right)$$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