

## Supplementary Material - File S1

### S1. NVT Equilibration Convergence Profiles

This annex provides the potential energy convergence profiles and dynamic summary statistics obtained during the NVT molecular dynamics equilibration of the protein systems (COX-1, COX-2, and CFP) evaluated with the DREIDING and COMPASS II force fields. For each system, the energy profile as a function of simulation time (Figures S1-S6) and the corresponding thermodynamic summary (Tables S1-S6) are reported. The profiles show an initial relaxation of the potential energy during the early portion of the NVT trajectory, followed by a comparatively stable energy region maintained throughout the remainder of the 100 ps simulation. These profiles provide direct evidence that the potential energy had stabilized within the time scale evaluated before the energetic descriptors used in the subsequent analyses were obtained.

#### S1.1 Cyclooxygenase-1 (COX-1)

##### S1.1.1 Force field: DREIDING

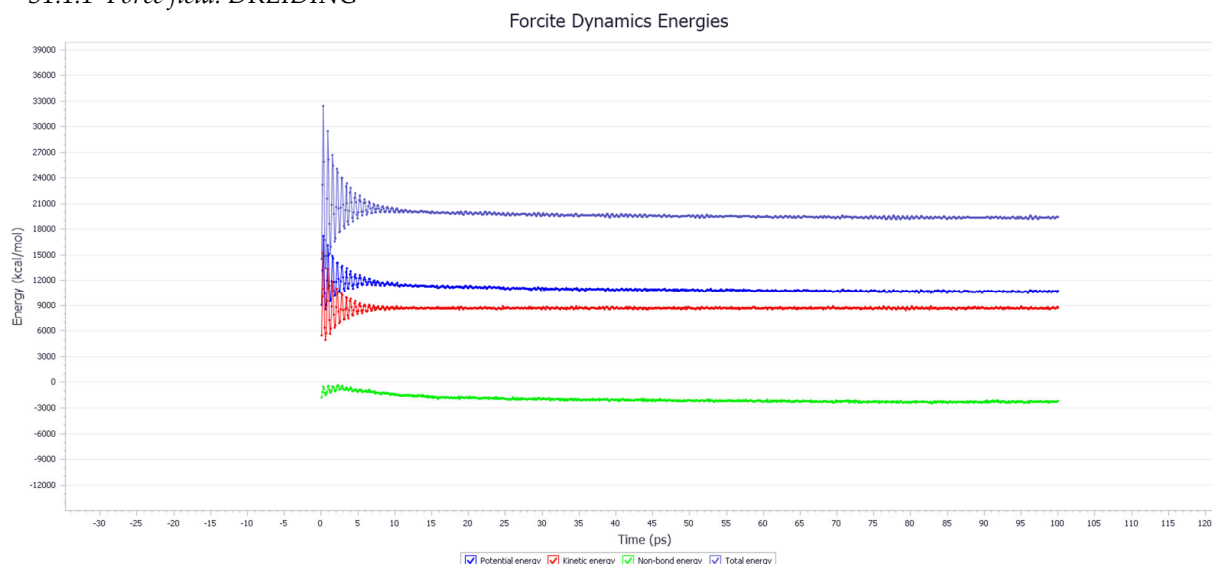


**Figure S1.** Potential energy convergence profile during NVT equilibration of COX-1 using DREIDING force field.

Total CPU time used by Forcite: 15:36:42 hours.

**Table S1.** Dynamic Summary of NVT equilibration for COX-1 with DREIDING force field.

|                  | Initial     | Final       | Average     | Standard deviation |
|------------------|-------------|-------------|-------------|--------------------|
| Total energy     | 12,171.534  | 19,427.433  | 19,685.965  | 943.123            |
| Potential energy | 3,484.022   | 10,739.599  | 10,998.417  | 564.079            |
| Kinetic Energy   | 8,687.512   | 8,687.512   | 8,687.547   | 452.747            |
| Total Enthalpy   | 18,019.082  | 18,279.156  | 18,824.734  | 1,476.022          |
| Temperature      | 303.150     | 303.161     | 303.151     | 15.799             |
| Pressure         | 0.081       | -0.016      | -0.012      | 0.014              |
| Volume           | 499,255.186 | 499,255.186 | 499,255.186 | 0.000              |
| Density          | 0.228       | 0.228       | 0.228       | 0.000              |

All energies are in kcal/mol, temperature in K, the pressure in GPa, volume in Å<sup>3</sup> and density in g/cm<sup>3</sup>.

### S1.1.2 Force field: COMPASS II

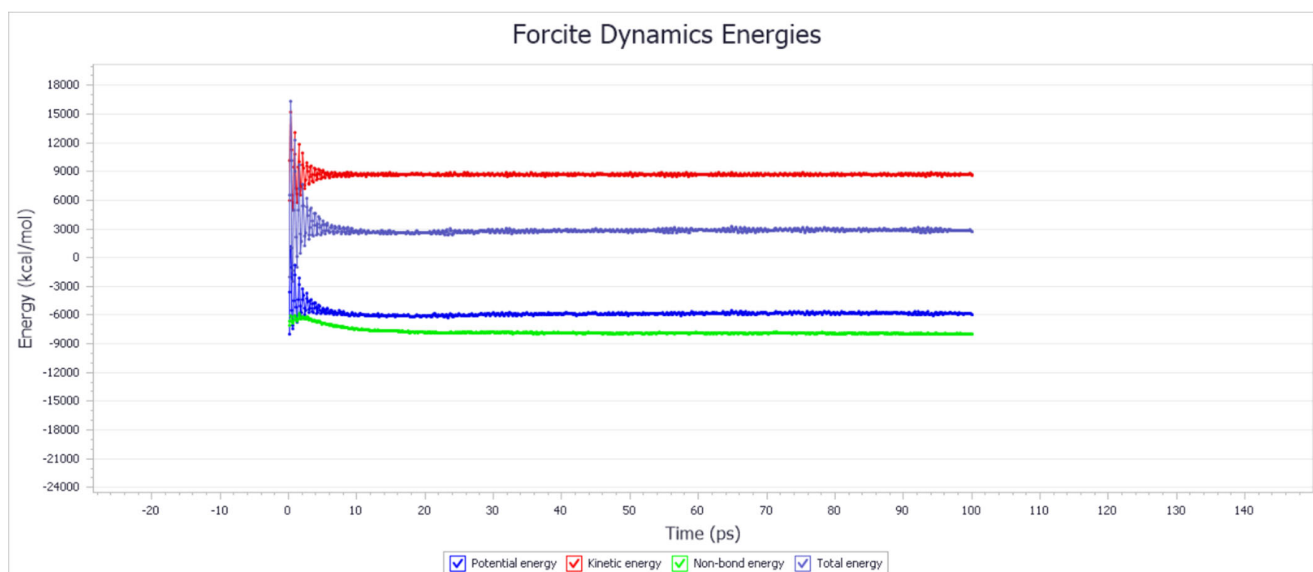


**Figure S2.** Potential energy convergence profile during NVT equilibration of COX-1 using COMPASS II force field.

Total CPU time used by Forcite: 26:56:50 hours.

**Table S2.** Dynamic Summary of NVT equilibration for COX-1 with COMPASS II force field.

|                  | Initial       | Final         | Average       | Standard deviation |
|------------------|---------------|---------------|---------------|--------------------|
| Total energy     | -4,279.704    | 2,703.622     | 2,873.417     | 832.021            |
| Potential energy | -12,967.216   | -5,974.989    | -5,814.106    | 462.153            |
| Kinetic Energy   | 8,687.512     | 8,678.611     | 8,687.523     | 422.597            |
| Total Enthalpy   | 1,553.087     | 3,483.840     | 2,943.363     | 1,326.922          |
| Temperature      | 303.150       | 302.839       | 303.150       | 14.746             |
| Pressure         | 0.019         | 0.003         | 0.000         | 0.003              |
| Volume           | 2,164,598.555 | 2,164,598.555 | 2,164,598.555 | 0.000              |
| Density          | 0.053         | 0.053         | 0.053         | 0.000              |

All energies are in kcal/mol, temperature in K, the pressure in GPa, volume in  $\text{\AA}^3$  and density in  $\text{g/cm}^3$ .

S1.2 Cyclooxygenase-2 (COX-2)  
S1.2.1 Force field: DREIDING

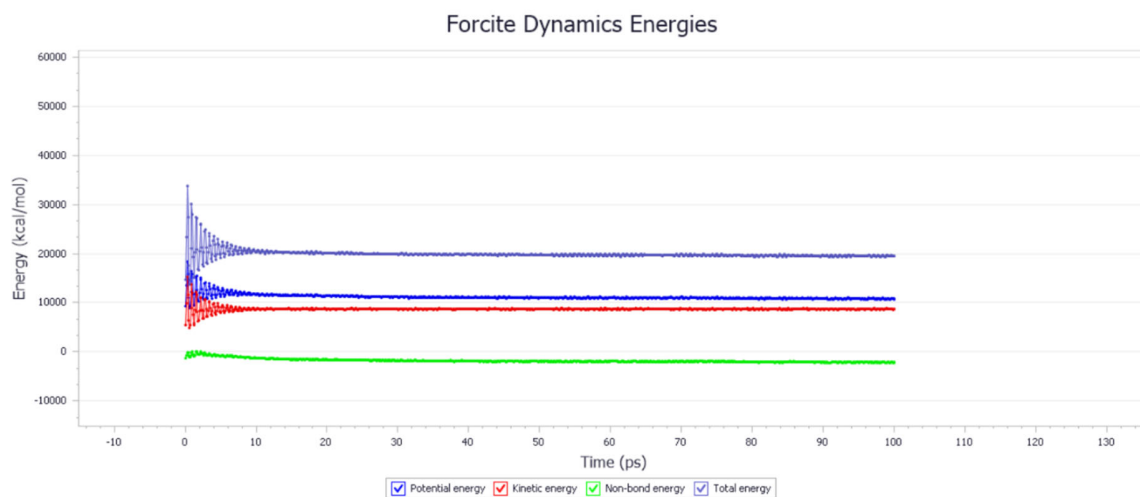


**Figure S3.** Potential energy convergence profile during NVT equilibration of COX-2 using DREIDING force field.

Total CPU time used by Forcite: 28:11:36 hours.

**Table S3.** Dynamic Summary of NVT equilibration for COX-2 with DREIDING force field.

|                  | Initial       | Final         | Average       | Standard deviation |
|------------------|---------------|---------------|---------------|--------------------|
| Total energy     | 12,356.333    | 19,453.026    | 19,906.616    | 1,040.643          |
| Potential energy | 3,638.097     | 10,736.710    | 11,188.402    | 616.162            |
| Kinetic Energy   | 8,718.236     | 8,716.317     | 8,718.214     | 498.190            |
| Total Enthalpy   | 18,165.641    | 18,550.854    | 19,143.449    | 1,564.531          |
| Temperature      | 303.150       | 303.083       | 303.149       | 17.323             |
| Pressure         | 0.018         | -0.003        | -0.002        | 0.003              |
| Volume           | 2,210,782.776 | 2,210,782.776 | 2,210,782.776 | 0.000              |
| Density          | 0.052         | 0.052         | 0.052         | 0.000              |

All energies are in kcal/mol, temperature in K, the pressure in GPa, volume in  $\text{\AA}^3$  and density in  $\text{g/cm}^3$ .

### S1.2.2 Force field: COMPASS II

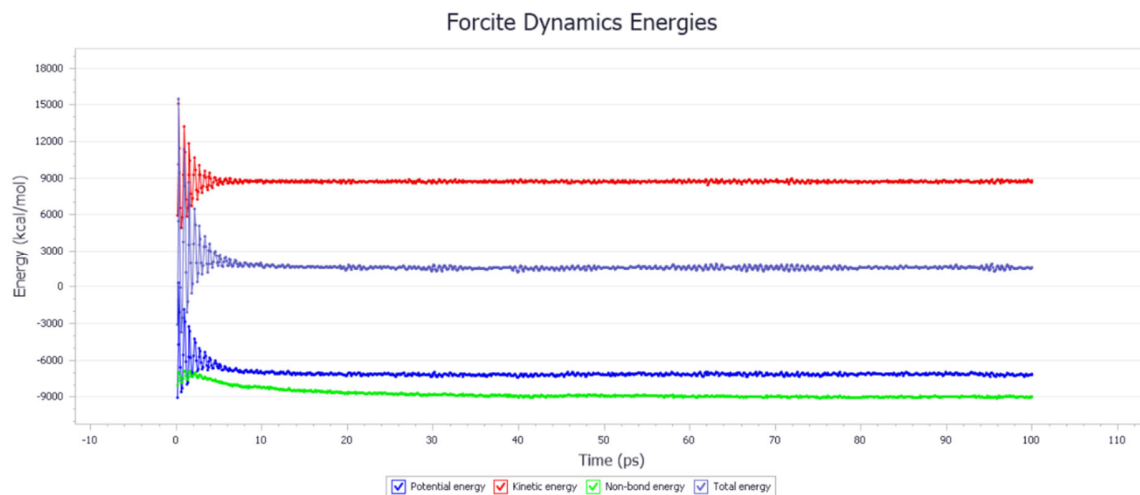


**Figure S4.** Potential energy convergence profile during NVT equilibration of COX-2 using COMPASS II force field.

Total CPU time used by Forcite: 30:10:38 hours.

**Table S4.** Dynamic Summary of NVT equilibration for COX-2 with COMPASS II force field.

|                  | Initial       | Final         | Average       | Standard deviation |
|------------------|---------------|---------------|---------------|--------------------|
| Total energy     | -5,384.967    | 1,593.995     | 1,663.513     | 853.265            |
| Potential energy | -14,103.203   | -7,087.745    | -7,054.693    | 493.682            |
| Kinetic Energy   | 8,718.236     | 8,681.740     | 8,718.206     | 421.053            |
| Total Enthalpy   | 425.066       | 2,364.334     | 1,762.553     | 1,359.131          |
| Temperature      | 303.150       | 301.881       | 303.149       | 14.641             |
| Pressure         | 0.016         | 0.002         | 0.000         | 0.003              |
| Volume           | 2,550,883.538 | 2,550,883.538 | 2,550,883.538 | 0.000              |
| Density          | 0.045         | 0.045         | 0.045         | 0.000              |

All energies are in kcal/mol, temperature in K, the pressure in GPa, volume in  $\text{\AA}^3$  and density in  $\text{g/cm}^3$ .

### S1.3 Cottonseed Flour Protein (CFP)

#### S1.3.1 Force field: DREIDING

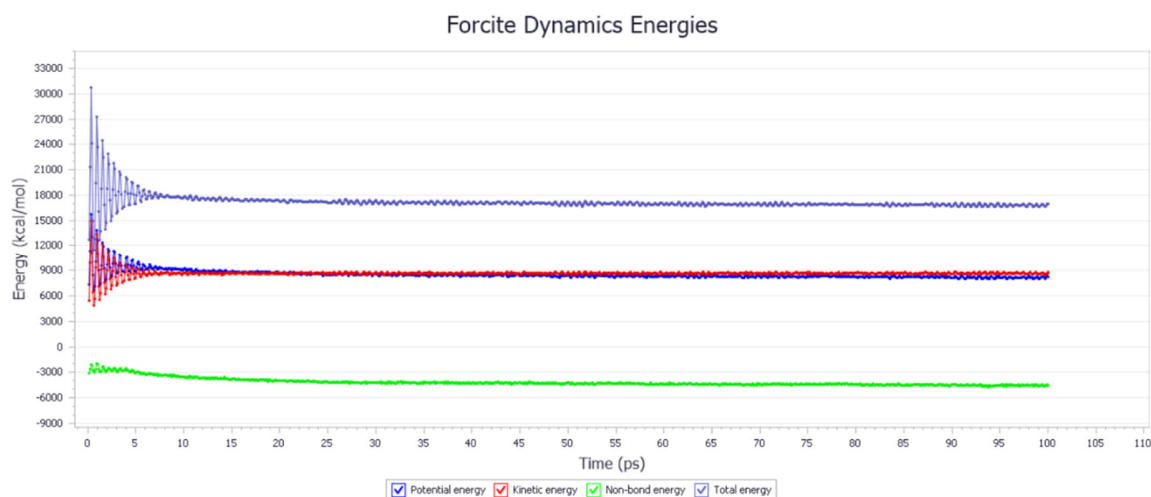


**Figure S5.** Potential energy convergence profile during NVT equilibration of CFP using DREIDING force field.

Total CPU time used by Forcite: 12:19:58 hours.

**Table S5.** Dynamic Summary of NVT equilibration for CFP with DREIDING force field.

|                  | Initial     | Final       | Average     | Standard deviation |
|------------------|-------------|-------------|-------------|--------------------|
| Total energy     | 10,368.948  | 16,977.644  | 17,164.041  | 949.864            |
| Potential energy | 1,721.196   | 8,217.355   | 8,516.262   | 576.773            |
| Kinetic Energy   | 8,647.753   | 8,760.289   | 8,647.779   | 455.309            |
| Total Enthalpy   | 16,137.080  | 17,530.109  | 15,388.866  | 1,469.342          |
| Temperature      | 303.150     | 307.095     | 303.151     | 15.961             |
| Pressure         | 0.094       | 0.009       | -0.029      | 0.016              |
| Volume           | 426,320.857 | 426,320.857 | 426,320.857 | 0.000              |
| Density          | 0.272       | 0.272       | 0.272       | 0.000              |

All energies are in kcal/mol, temperature in K, the pressure in GPa, volume in Å<sup>3</sup> and density in g/cm<sup>3</sup>.

### S1.3.2 Force field: COMPASS II

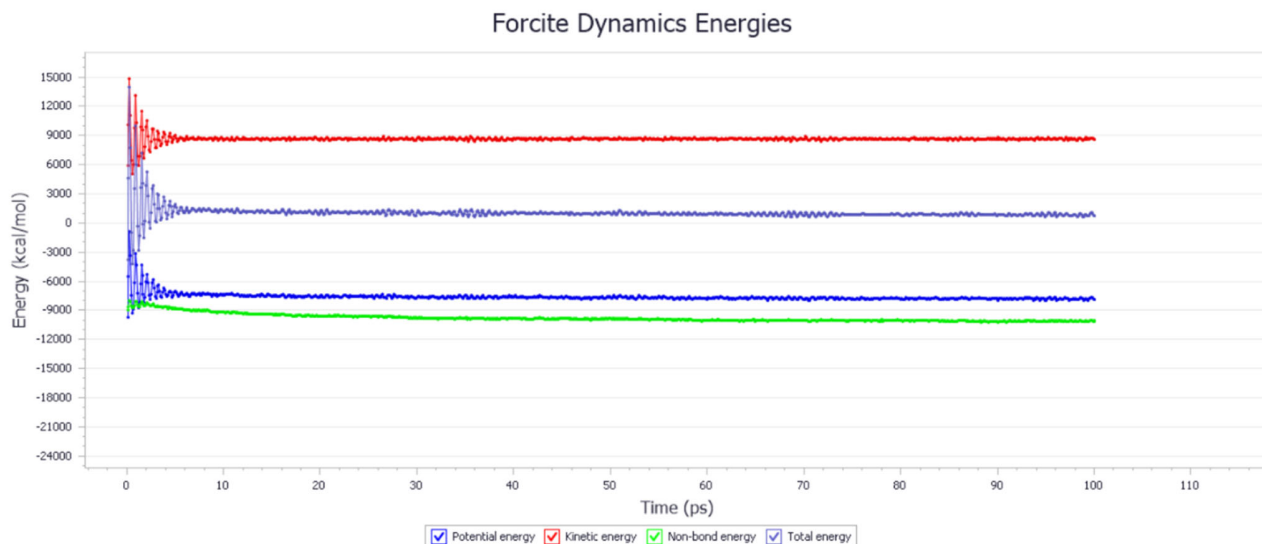


**Figure S6.** Potential energy convergence profile during NVT equilibration of CFP using COMPASS II force field.

Total CPU time used by Forcite: 17:54:13 hours.

**Table S6.** Dynamic Summary of NVT equilibration for CFP with COMPASS II force field.

|                  | Initial       | Final         | Average       | Standard deviation |
|------------------|---------------|---------------|---------------|--------------------|
| Total energy     | -6073.543     | 717.520       | 1,026.175     | 786.237            |
| Potential energy | -14,721.295   | -7835.154     | -7621.617     | 428.275            |
| Kinetic Energy   | 8,647.753     | 8,552.673     | 8,647.791     | 407.663            |
| Total Enthalpy   | -334.564      | 465.745       | 936.125       | 1,264.416          |
| Temperature      | 303.150       | 299.817       | 303.151       | 14.291             |
| Pressure         | 0.022         | -0.001        | 0.000         | 0.004              |
| Volume           | 1,779,365.115 | 1,779,365.115 | 1,779,365.115 | 0.000              |
| Density          | 0.065         | 0.065         | 0.065         | 0.000              |

All energies are in kcal/mol, temperature in K, the pressure in GPa, volume in Å<sup>3</sup> and density in g/cm<sup>3</sup>.

NOTE: Structural RMSD profiles could not be generated because the trajectory files required for this analysis were not retained for the protein NVT simulations. Therefore, structural convergence could not be independently assessed by RMSD. The potential-energy profiles presented in Figures 1–6 nevertheless show an initial relaxation followed by a comparatively stable energy region over the remainder of the 100 ps NVT simulations. Accordingly, these profiles support energetic stabilization within the simulated time scale, while the absence of RMSD analysis and the limited 100 ps trajectory length are acknowledged as limitations of the present exploratory computational study.