Supplementary Information (SI) for Physical Chemistry Chemical Physics.


# Influence of terahertz waves on the binding of choline to choline acetyltransferase: insights from molecular dynamics simulations

Hui Ning, Kaicheng Wang, Qin Zhang, Lianghao Guo, Shaomeng Wang , Lixia Yang*, and Yubin Gong*

**Table S1 GROMACS parameters (including atom types, electric charges and mass) for choline. We used RESP2 for the calculation of charge.**

| No. | Type | Atom | Charge | Mass |
|---|---|---|---|---|
| 1 | Oh | O | -0.646070965 | 15.999405 |
| 2 | N4 | N | 0.155798932 | 14.006703 |
| 3 | C3 | C | -0.420941554 | 12.010736 |
| 4 | C3 | C | -0.440659971 | 12.010736 |
| 5 | C3 | C | -0.245637696 | 12.010736 |
| 6 | C3 | C | 0.356035158 | 12.010736 |
| 7 | C3 | C | -0.198375958 | 12.010736 |
| 8 | Ho | H | 0.431640718 | 1.007941 |
| 9 | Hx | H | 0.195700039 | 1.007941 |
| 10 | Hx | H | 0.195700039 | 1.007941 |
| 11 | Hx | H | 0.195700039 | 1.007941 |
| 12 | Hx | H | 0.209203437 | 1.007941 |
| 13 | Hx | H | 0.209203437 | 1.007941 |
| 14 | Hx | H | 0.209203437 | 1.007941 |
| 15 | Hx | H | 0.16150935 | 1.007941 |
| 16 | Hx | H | 0.16150935 | 1.007941 |
| 17 | Hx | H | 0.16150935 | 1.007941 |
| 18 | H1 | H | 0.016704068 | 1.007941 |
| 19 | H1 | H | 0.016704068 | 1.007941 |
| 20 | Hx | H | 0.137782362 | 1.007941 |
| 21 | hx | H | 0.137782362 | 1.007941 |

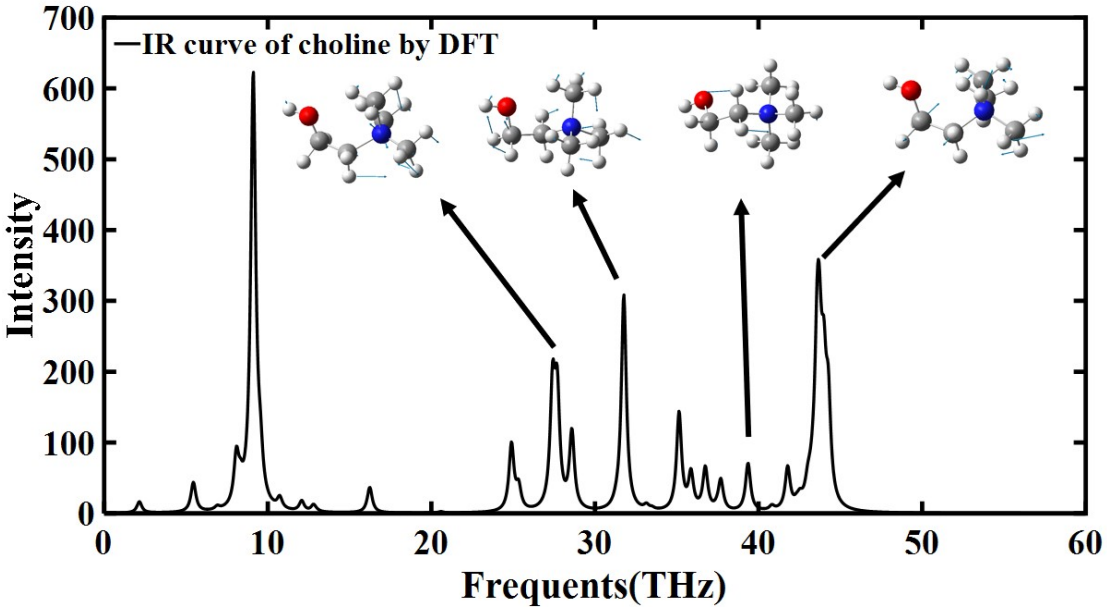



**Figure S1 The vibration spectrum of choline calculated based on DFT, using the functional B3LYP, the basis set def2-TZVP, and the auxiliary basis set def2/J and D3BJ dispersion correction. We consider the stronger absorption peaks (45.3 THz).**

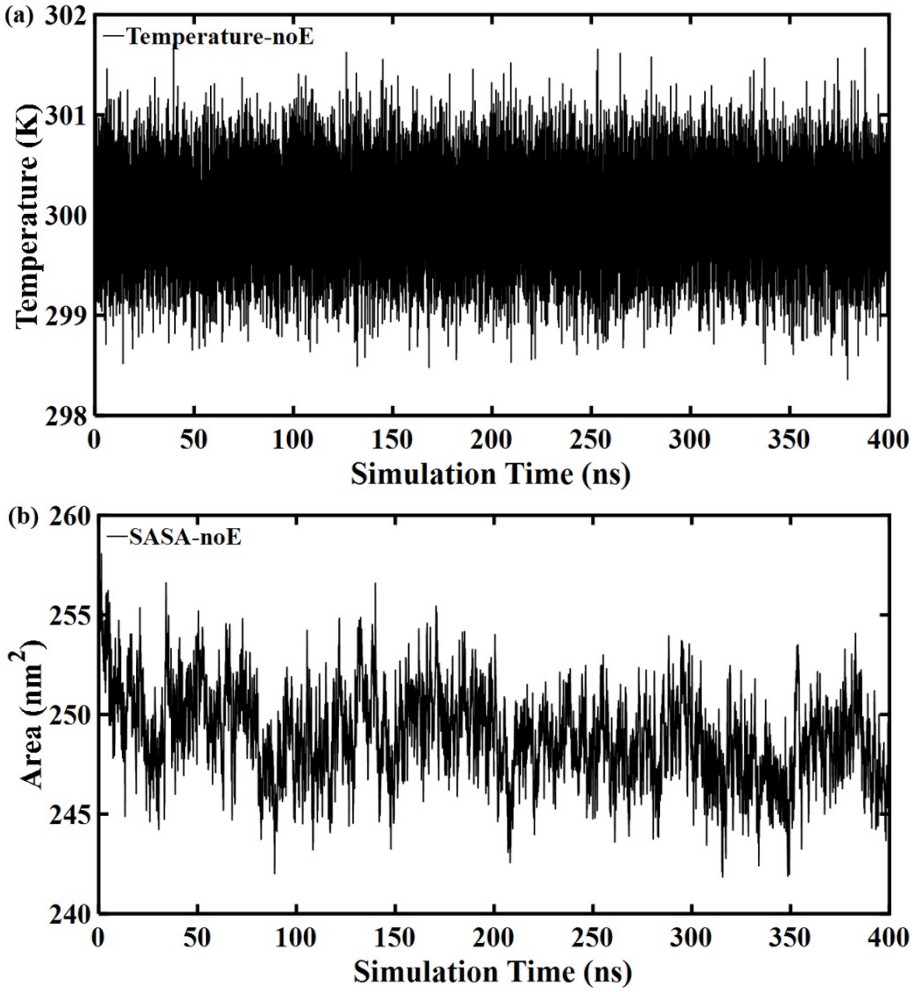



**Figure S2 The change curves of system temperature (a) and SASA (b) with simulation time during the 400 ns MD simulation process. Each curve was plotted from the average of 3 sets. The average temperature of the system is 300.0442 K.**

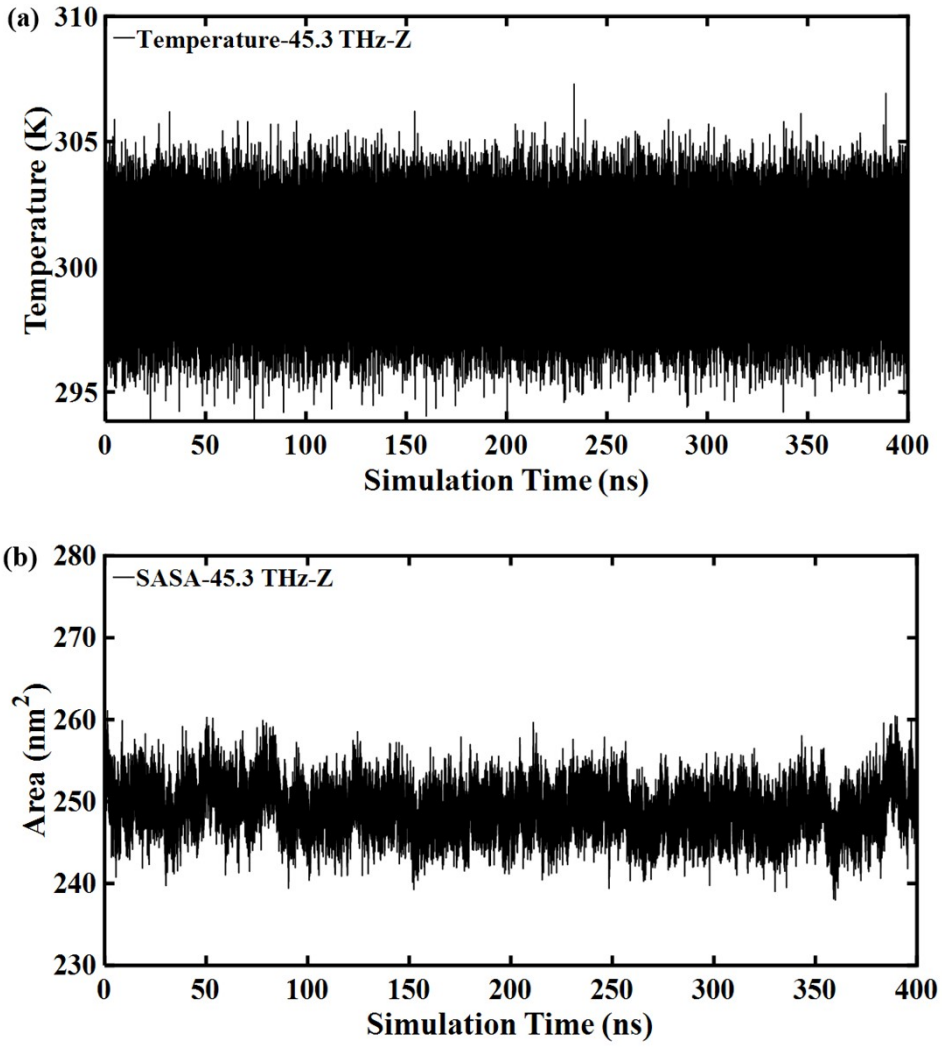
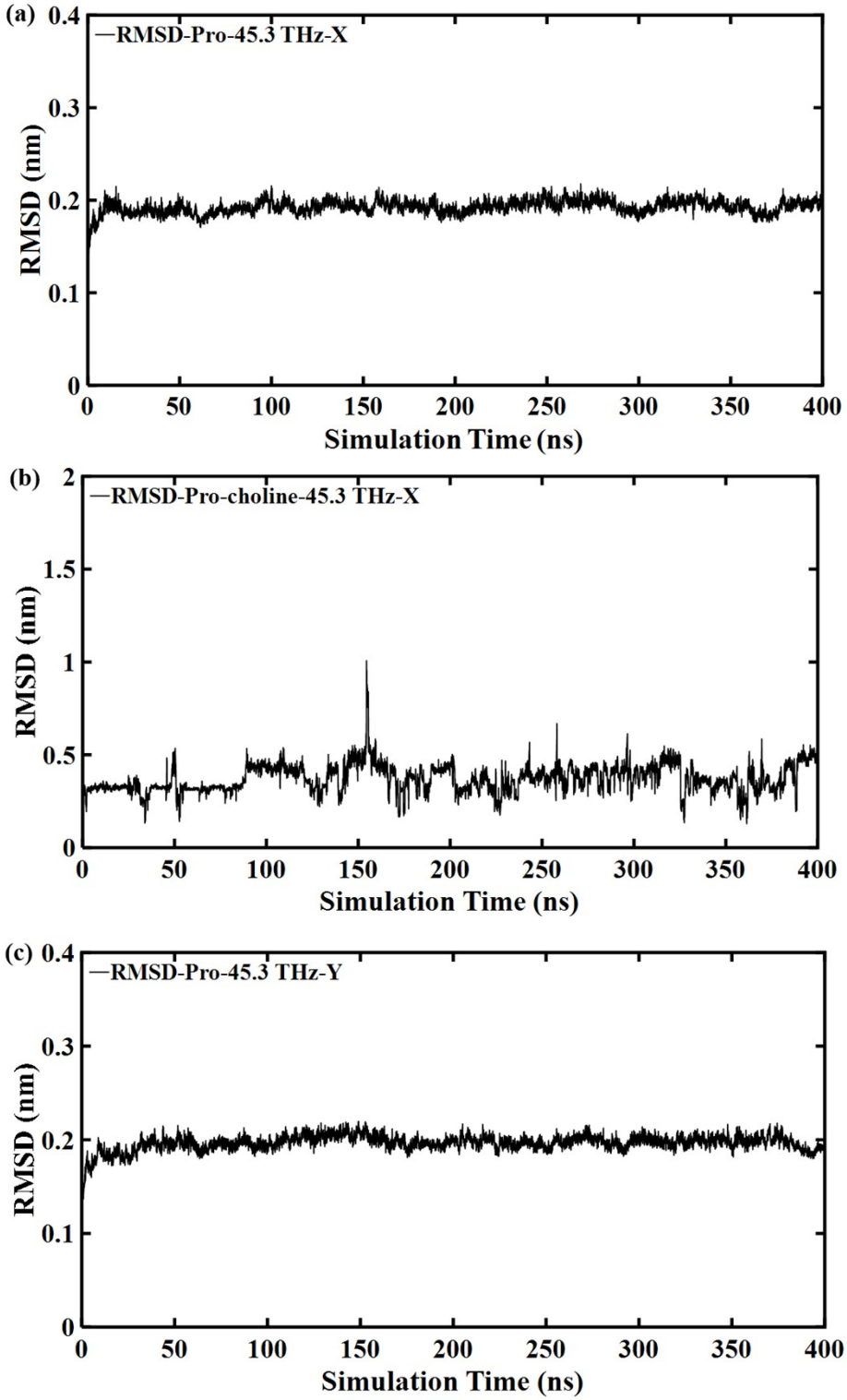



**Figure S3 The change curves of system temperature (a) and SASA (b) with simulation time during the 400 ns MD simulation process under the external THz wave in the Z direction. Each curve was plotted from the average of 3 sets. During the simulation 45.3 THz, the average temperature of the system is 300.0951 K.**


(a)
—RMSD-Pro-45.3 THz-X
RMSD (nm)
Simulation Time (ns)
(b)
—RMSD-Pro-choline-45.3 THz-X
RMSD (nm)
Simulation Time (ns)
(c)
—RMSD-Pro-45.3 THz-Y
RMSD (nm)
Simulation Time (ns)

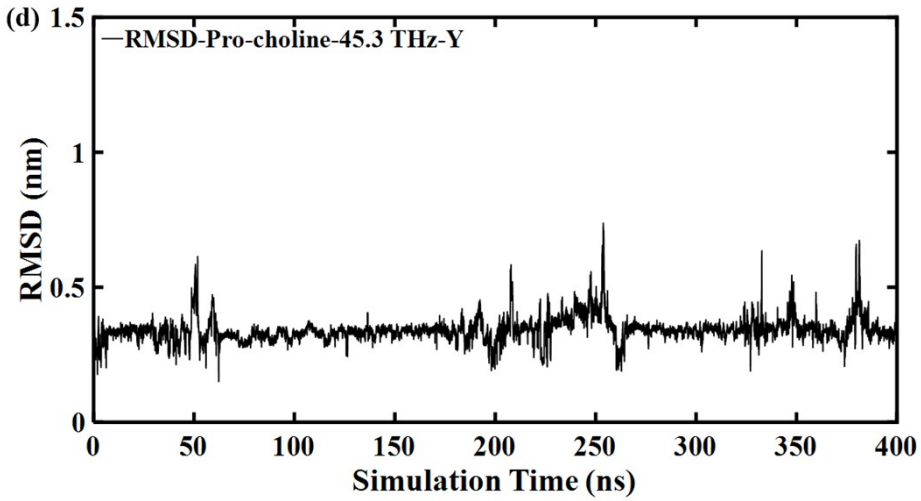



**Figure S4 The stability of the whole simulation process during 400 ns simulation under 45.3 THz wave. (a) and (b) are under X direction, (c) and (d) are under Y direction. The (a) and (c) are the RMSD of ChAT skeleton Cα relative to initial crystal structure, the (b) and (d) are the RMSD of choline relative to the ChAT skeleton Cα.**

**Table S2 Binding free energy of choline-ChAT active site calculated based on the MMPBSA method, data collection started from the 350 ns full equilibrium time point.**

| Frequency (THz) | Electrostattic energy (kJ/mol) | Polar solvation energy (kJ/mol) | SASA energy (kJ/mol) | van der Waals energy (kJ/mol) | Binding energy (kJ/mol) |
|---|---|---|---|---|---|
| noE | -18.774 +/- 0.865 | 13.740 +/- 3.708 | -6.044 +/- 0.062 | -21.923 +/- 0.437 | -32.830 +/- 3.473 |
| 45.3-X | -19.823 +/- 0.957 | 28.930 +/- 4.318 | -6.911 +/- 0.057 | -30.603 +/- 0.388 | -28.310 +/- 3.922 |
| 45.3-Y | -33.743 +/- 0.985 | 35.068 +/- 12.982 | -7.455 +/- 0.052 | -34.250 +/- 0.517 | -40.847 +/- 13.461 |
| 45.3-Z | -20.505 +/- 0.560 | -29.604 +/- 32.339 | -7.141 +/- 0.053 | -32.227 +/- 0.429 | -88.895 +/- 32.825 |

**Table S3 Binding free energy of choline-ChAT calculated based on the MMPBSA method, data collection started from the 350 ns full equilibrium time point. The unit of frequency is THz, and the unit of energy is KJ/mol.**

| | noE | 45.3-X | 45.3-Y | 45.3-Z |
|---|---|---|---|---|
| **Tyr85** | **0.3241** | **-0.2173** | **-0.2180** | **-0.7784** |
| **His324** | **0.5929** | **-0.6596** | **-1.6629** | **-1.5113** |
| **Ser438** | **0.1445** | **-0.3355** | **1.3544** | **0.3769** |
| **Ser538** | **1.8636** | **0.8654** | **1.6434** | **2.5595** |
| **Thr539** | **-0.5819** | **0.3464** | **-1.0104** | **-1.0598** |
| **Tyr552** | **-0.5258** | **-2.3865** | **-1.6016** | **0.4531** |
| **Val555** | **-0.6734** | **-2.3738** | **-1.6720** | **-3.6663** |
| **acetyl-CoA** | **-0.7197** | **-0.2473** | **-1.1440** | **-0.8778** |

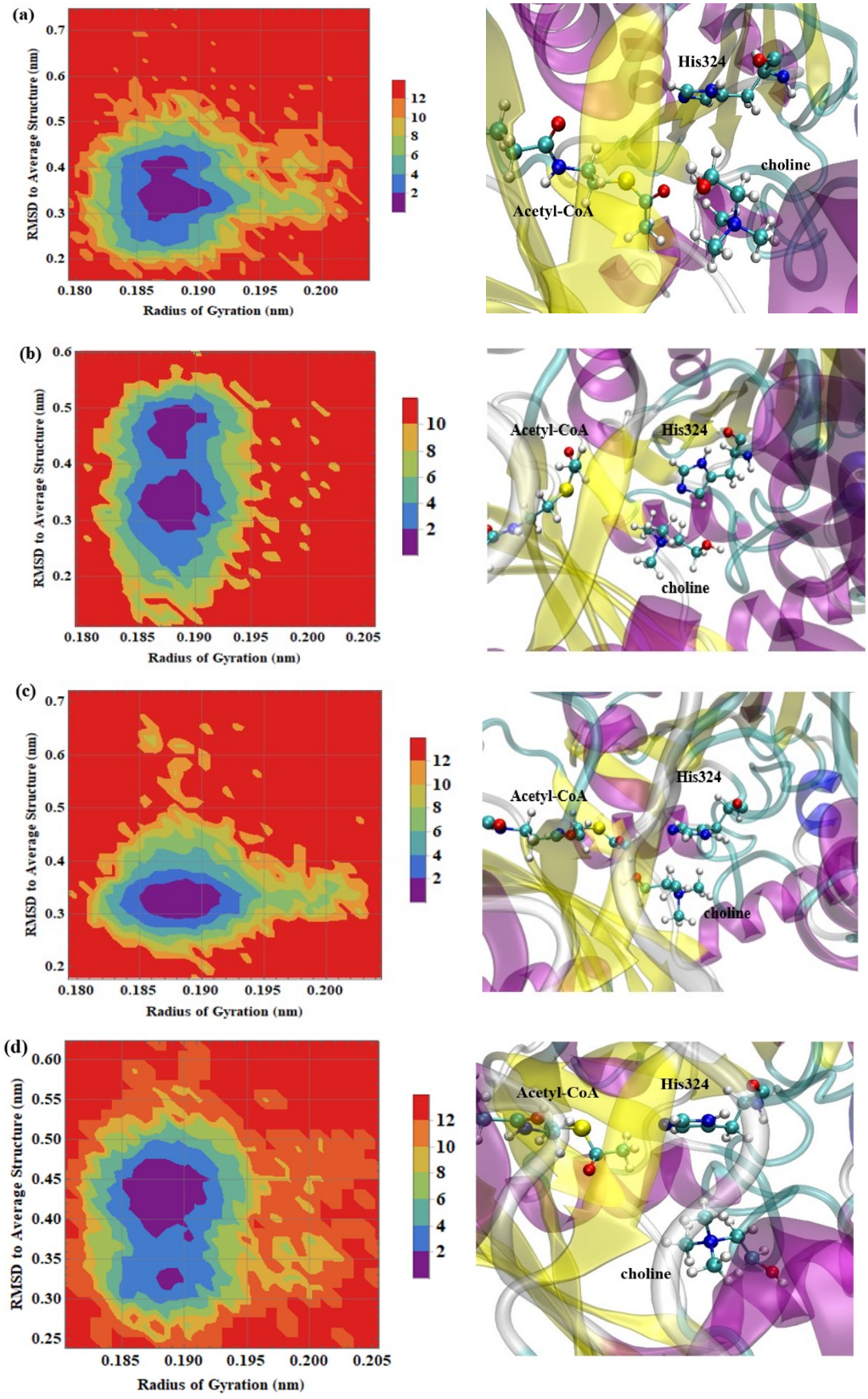



**Figure S5 The 2D free energy landscape diagrams as a function of RMSD and Rg as the two coordinates that depict the choline. The free energy is displayed in terms of kJ/mol in the indicated**

**colour bar where the purple colour represents lowest energy and red the highest energy. The (a) is noE, (b)-(d) are 45.3 THz wave in X-Z direction, The right side of the free energy surface diagram shows representative conformations in the lower free energy region.**