|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Fe | O | Por | SMe |
| MR | 0.55 (0.03) | -0.41 (0.05) | -0.05 (0.06) | -0.09 (0.03) |
| MA | 0.54 (0.04) | -0.45 (0.06) | -0.02 (0.07) | -0.07 (0.07) |
| SR | 0.53 (0.03) | -0.41 (0.01) | -0.04 (0.05) | -0.08 (0.04) |
| SA | 0.55 (0.03) | -0.45 (0.04) | 0.00 (0.06) | -0.10 (0.06) |

Table S3. Average values of the Mulliken atomic charges computed for the membrane-bound and solubilized CYP3A4 with R-warfarin bound (MR and SR, respectively) and without warfarin bound (MA and SA, respectively) optimized at the B3LYP-D:6-31G/CHARMM27 level of theory (average values are displayed in Figure 6A). Calculated for 15 structures optimized at 5ns intervals over the last 20 ns of three 50 ns atomistic MD simulations. Standard deviations are given in parentheses.