Electronic Supplementary Information

Rational Design of Nanosystems for Simultaneous Drug Delivery and Photodynamic Therapy by Quantum Mechanical Modeling

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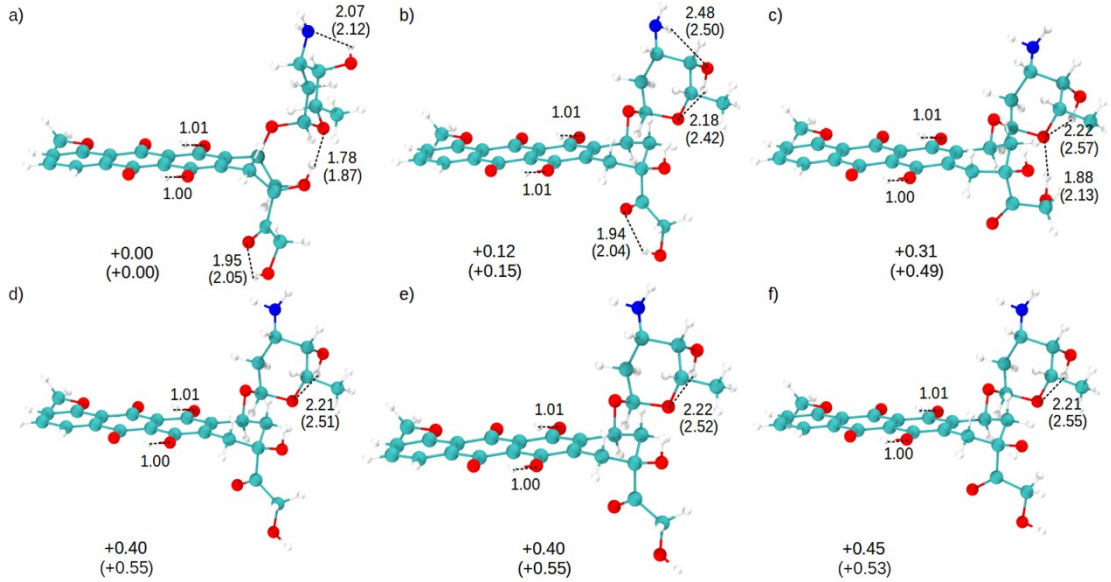

Figure S1. a-e) Optimized structures of DOX after performing MD using DFTB(DFT) package with molecular formula, $C_{27}H_{29}NO_{11}$. **f)** Optimized structure of DOX before performing MD. C atoms are in cyan, H atoms are in white, the N atom is in blue and O atoms are in red. Relevant distances are reported in Å in proximity of the dashed lines. The relative energies with respect to **a** configuration are reported in eV.

Table S1. Spectroscopic Parameters of DOX in its ground state geometry (S_0) and with one proton transferred from the OH to the C=O group ($S_0^{'}$) in different solvents calculated by Gaussian 16. The numbers in the parenthesis are from the experimental data and square brackets are from the theoretical calculations.

	S_0		$S_0^{'}$	
Solvent	Absorbance (λ_{max} (nm))	Fluorescence λ_f(nm)	Absorbance (λ_{max} (nm))	Fluorescence λ_f(nm)
Vacuum	483.68	567.58	525.96	584.83
H_2O	490.39 (479)[a]	605.43 (594)[a]	542.59	661.34
methanol (MeOH)	490.32 (476)[a]	603.82 (578)[a]	542.40	658.40
dimethylformamide (DMF)	492.52 (480)[a]	604.13 (582)[a]	546.02	659.02
acetonitrile (ACN)	490.31 (475)[a] [492][b]	604.03 (580)[a] [600][b]	542.98	658.83[663][b]

(a) Rana, D. K.; Dhar, S.; Sarkar, A.; Bhattacharya, S. C. *J. Phys. Chem. A* **2011**, *115*, 9169–9179.
(b) Jia, M.; Song, X.; Zhang, Q.; Yang, D. A. *J. Clus. Sci.* **2018**, *29*, 673–678.

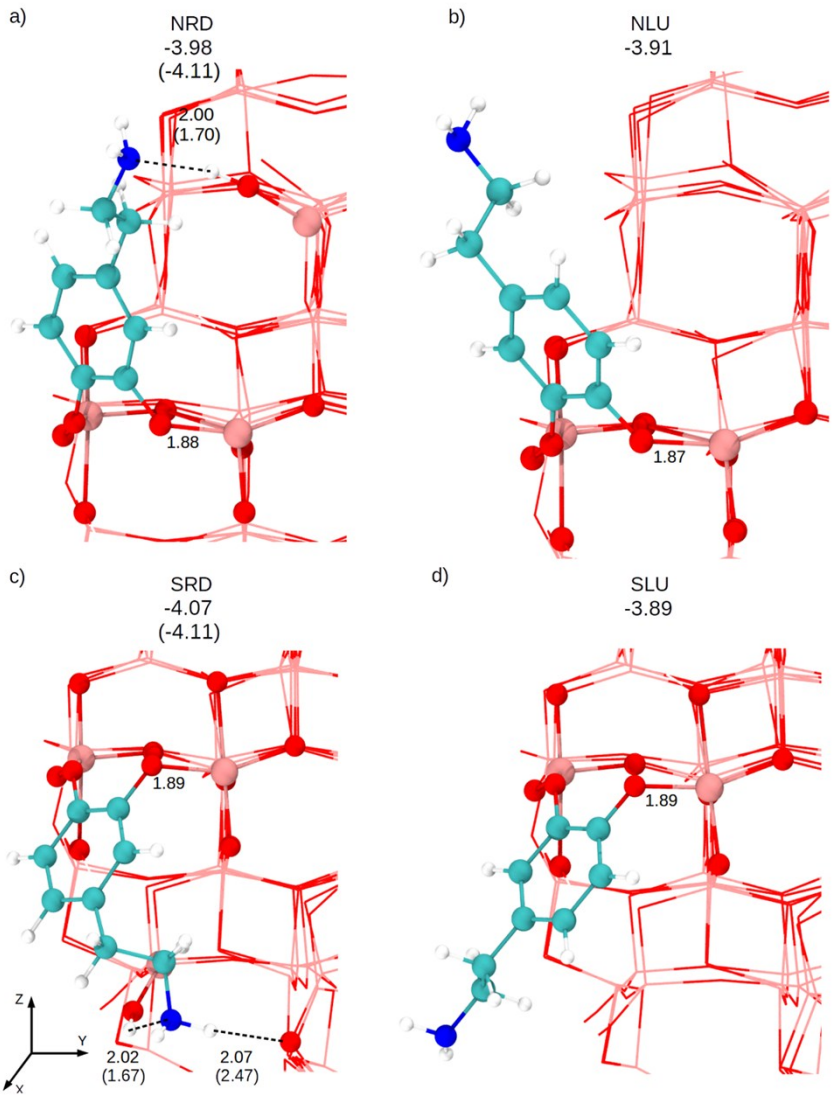

Figure S2. Adsorption configurations (side views) and energies per molecule in eV (E^{DOPA}_{ads}) for one dopamine molecule on the surface of the spherical NP, as obtained by DFTB(DFT) calculations. **a)** dopamine molecule is directed to the north and bent towards the surface of the NP making a H-bond with the hydrogen of the hydroxyl group of the surface. The ethyl-amino functional group is on the right hand side (NRD); **b)** the dopamine molecule is directed to the north and stand up towards the vacuum, the ethyl-amino functional group is on the left (NLU); **c)** the dopamine molecule is directed to the south and bent towards the surface making a H-bond, the ethyl-amino functional group is on the right hand side (SRD); **d)** the dopamine molecule is directed to the south and stand up toward the vacuum, the ethyl-amino functional group is on the left (SLU) hand side. H atoms are white, C atoms are green, O atoms are red, N atom is blue and Ti atoms are shown in pink colors. Relevant distances are reported in Å in proximity of the dashed lines. Adsorption energies are in eV.

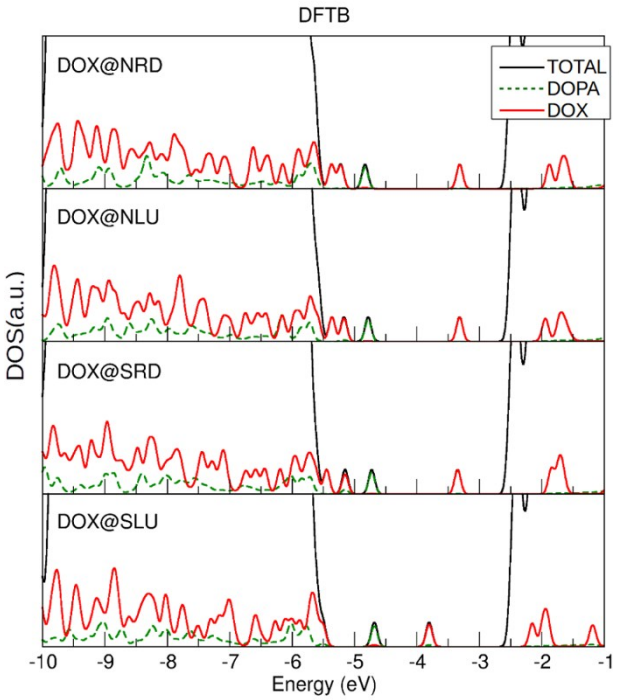

Figure S3. Total (DOS) and projected (PDOS) density of states calculated by DFTB for the structures shown in **Figure. 2** of the main text.

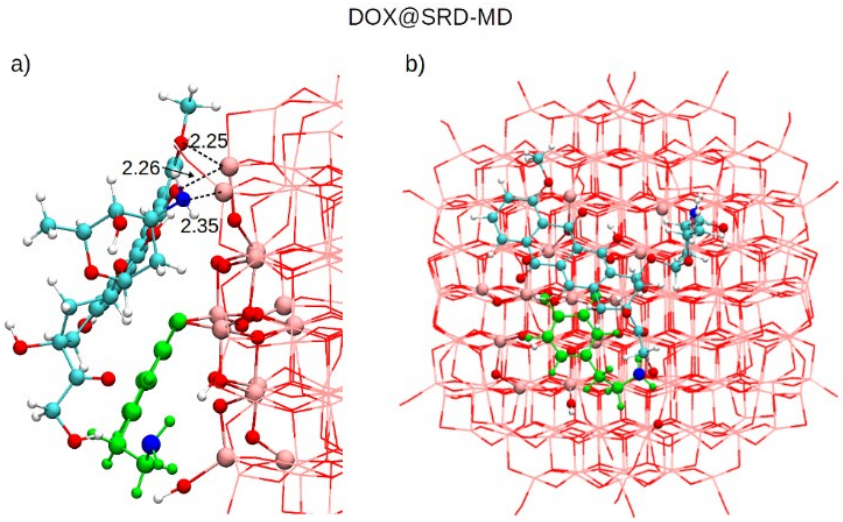

Figure S4. Optimized structures after performing MD on the corresponding configuration shown in **Figure 2c** (**DOX@SRD**), as obtained by DFTB calculations. For more clarity, the atoms of the dopamine are colored in light green except the N atom that is in blue. DOX C atoms are in cyan, H atoms are in white and the N atom is in blue. O atoms are in red and Ti atoms of the NP are in pink. Relevant distances are reported in Å in proximity of the dashed lines.

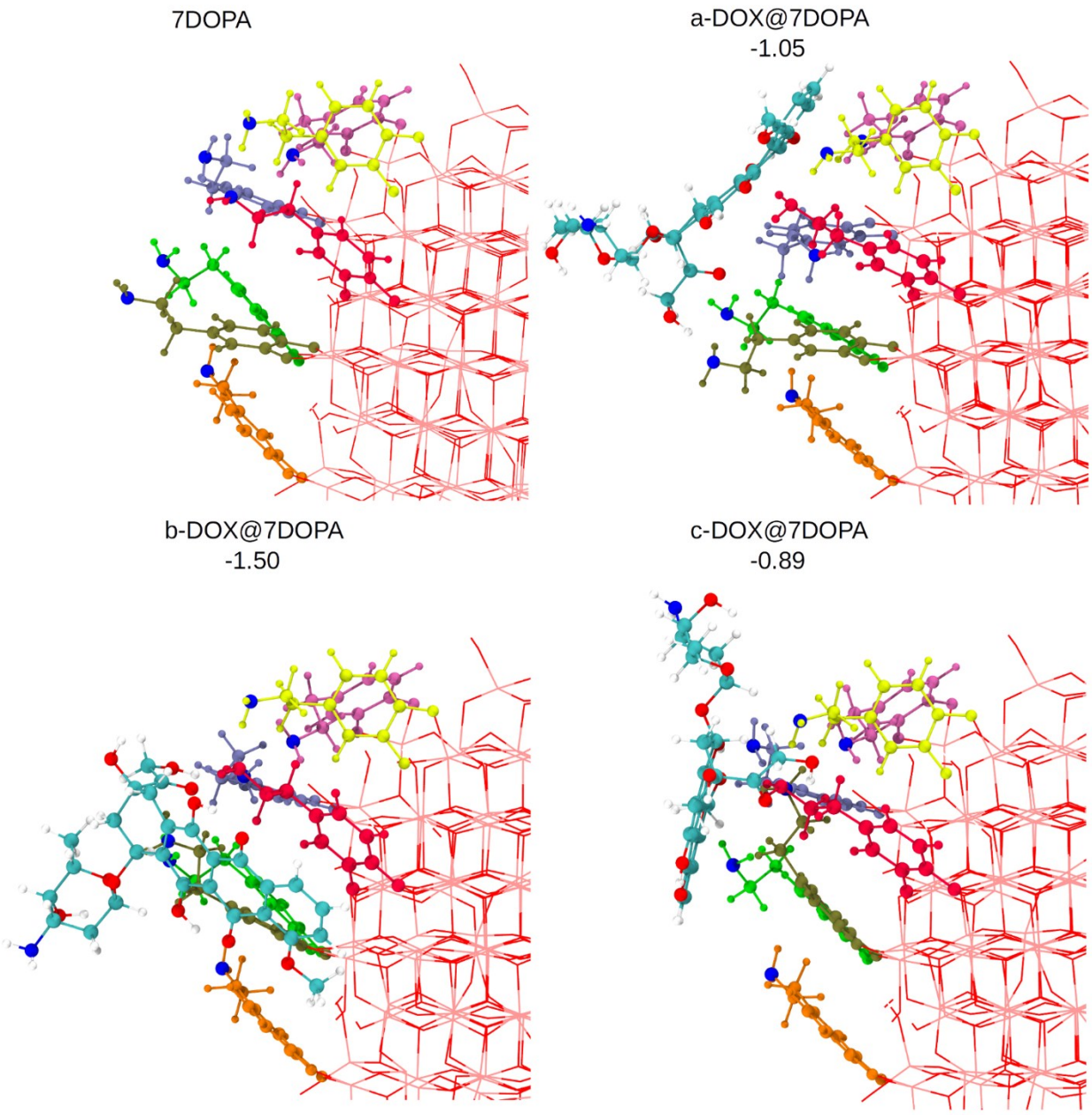

Figure S5. a) Top view of the optimized structure with 7 dopamine on the surface of the NP as obtained by DFTB calculations. **b-d)** The optimized structures of the 7 dopamine with one DOX (DOX@7DOPA) combination. For the sake of simplicity, we color coded the dopamine molecules as explained in the main text. In addition, all the N atoms of the -NH_2 groups from the dopamine molecules and the DOX molecule are in blue. DOX C atoms are in cyan, H atoms are in white and the N atom is in blue. O atoms are in red and Ti atoms of the NP are in pink. Adsorption energies are in eV. The interactions between DOX and dopamine, dopamine/dopamine molecules and dopamine molecules with the surface of the NP are listed in **Table S2.** The corresponding electronic structures are shown in **Figure S6**.

Table S2: Interactions between DOX and dopamine (DOX/Dopamine), dopamine molecules (Dopamine/Dopamine) and dopamine molecules with the surface of the NP (Dopamone/NP). All the distances are in Å.

Configuration	DOX/Dopamine	Dopamine/NP	Dopamine/Dopamine
a-DOX@7DOPA	OH- - -NH_{tan} 2.00 O- - -HNH_{green} 2.06 O- - -HNH_{red} 1.97	$HNH_{ice–blue}$ - - -OHTi 2.29	$H2N_{geen}$ - - -HNH_{tan} 2.02 $H2N_{red}$ - - -HNH_{yellow} 2.02
b-DOX@7DOPA	OH- - -$NH_{ice–blue}$ 2.01 OH- - -N_{tan} 1.99 OH- - -N_{red} 2.01 O- - -H_2N_{red} 2.17 O- - -H_2N_{tan} 2.07	—	H_2N_{green} - - -HNH_{tan} 2.04 H_2N_{pink} - - -HNH_{ice}–blue 2.02 H_2N_{yellow} - - -HNH_{red} 2.06
c-DOX@7DOPA	O- - -HNH_{yellow} 2.21 O- - -HNH_{tan} 2.03 O- - -HNH_{red} 2.22	—	H_2N_{yellow} - - -HNH_{red} 2.02 H_2N_{tan} - - -$HNH_{ice–blue}$ 2.01 HNH_{tan}- - -NH_{2pink} 2.03

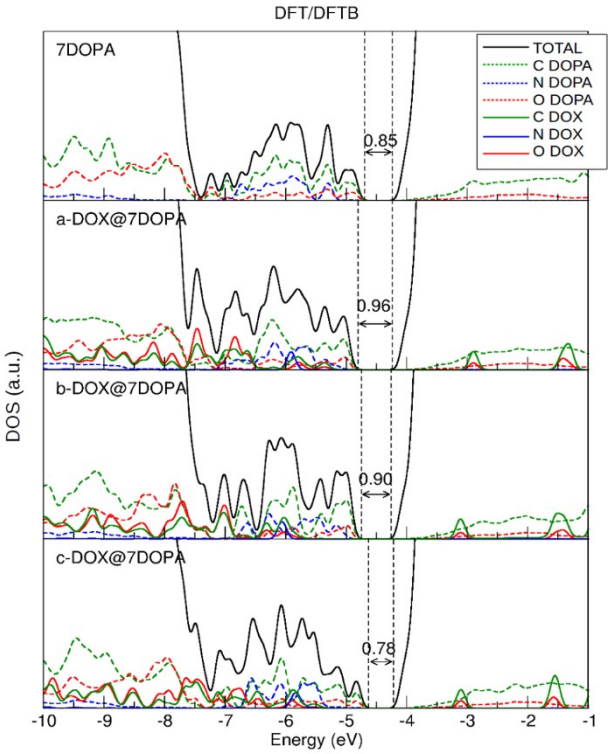

Figure S6: Total (DOS) and projected (PDOS) density of states using DFT/DFTB calculations for the a) 7DOPA and **b-d)** for the **a-**, **b-** and **c-DOX@7DOPA** structures. See the geometry optimized structures in **Figure S5**.

Table S3: Interactions between DOX and dopamine (DOX/Dopamine), between the dopamine molecules (Dopamine/Dopamine) and between the dopamine molecules and NP (Dopamine/NP) after performing MD. All the distances are in Å.

Configuration	DOX/Dopamine	Dopamine/NP	Dopamine/Dopamine
b-DOX@7DOPA	HO- - -$HNH_{ice\text{-}blue}$ 2.32 OH- - - N_{pink} 2.00 O- - -H_2N_{tan} 2.03 O- - -H_2N_{red} 1.94 HO- - -HNH_{red} 2.17	—	$H2N_{tan}$- - - $HNH_{ice-blue}$ 2.01
a-DOX@7DOPA	OH- - -NH_{tan} 2.01 HO- - -HNH_{green} 1.94 O- - -HNH_{red} 2.15	$H_2N_{ice-blue}$- - -HOTI 2.04	—
c-DOX@7DOPA	HO- - -HNH_{red} 2.16	—	H_2N_{pink} - - - HNH_{tan} 2.02

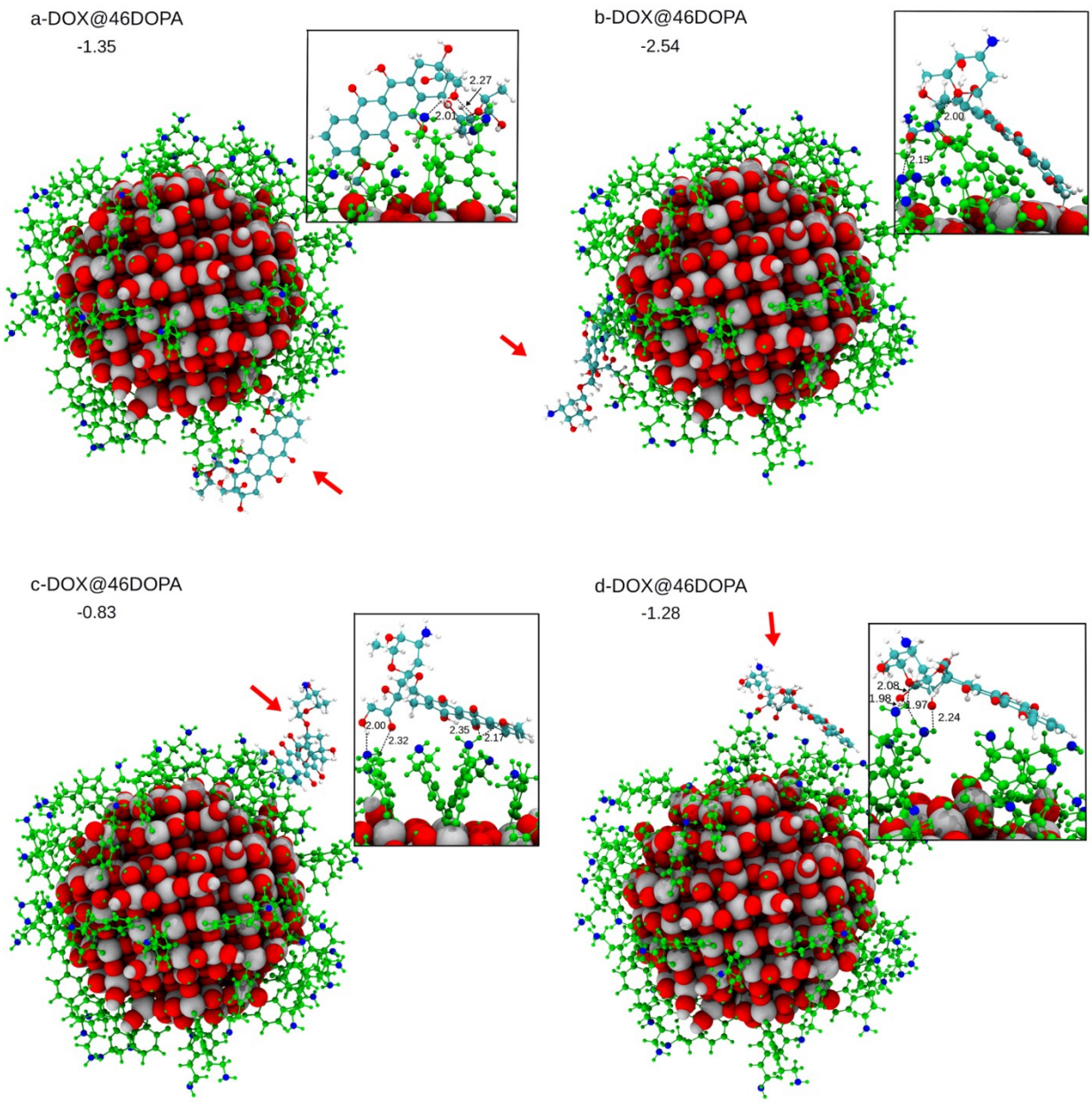

Figure S7: The optimized structures of the DOX@46DOPA using DFTB package. For clearance all the 46 dopamine molecules on the surface of the NP are colored in green except for the N atoms that are in blue. For the sake of clarity, all of the 46 dopamine molecules on the surface of the NP are colored in green except for the N atoms that are in blue. DOX C atoms are in cyan, H atoms are in white and the N atom is in blue. O atoms are in red and Ti atoms of the NP are in pink. Relevant distances are reported in Å in proximity of the dashed lines. Adsorption energies are in eV. See **Figure S9** for DOS of structure c.

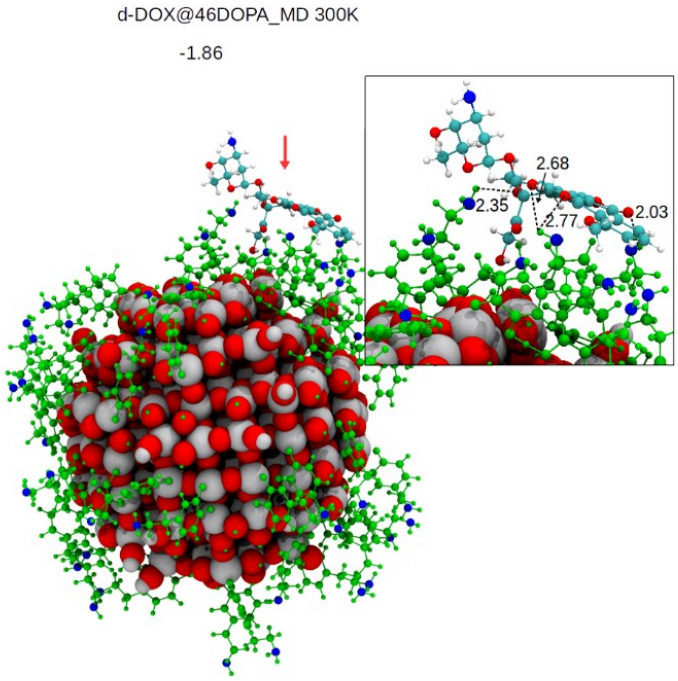

Figure S8: Optimized DFTB model structure of d-DOX@46DOPA-MD, after performing MD at 300 K. In the inset the DOX fragment is magnified. Red arrow indicates the position of the DOX on the dopamine-functionalized TiO_2 NP. For the sake of clarity, all of the 46 dopamine molecules on the surface of the NP are colored in green except for the N atoms that are in blue. DOX C atoms are in cyan, H atoms are in white and the N atom is in blue. O atoms are in red and Ti atoms of the NP are in pink. Relevant distances are reported in Å in proximity of the dashed lines. Adsorption energies are in eV.

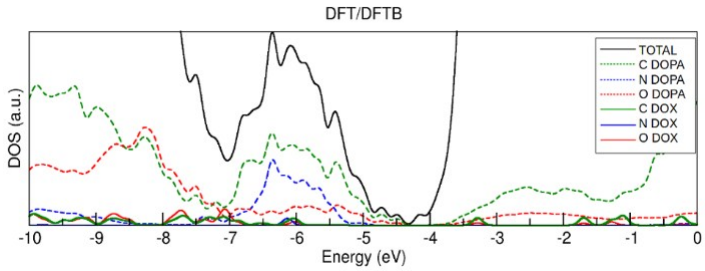

Figure S9: Total (DOS) and projected (PDOS) density of states for configuration **c-DOX@46DOPA** shown in **Figure S7**.

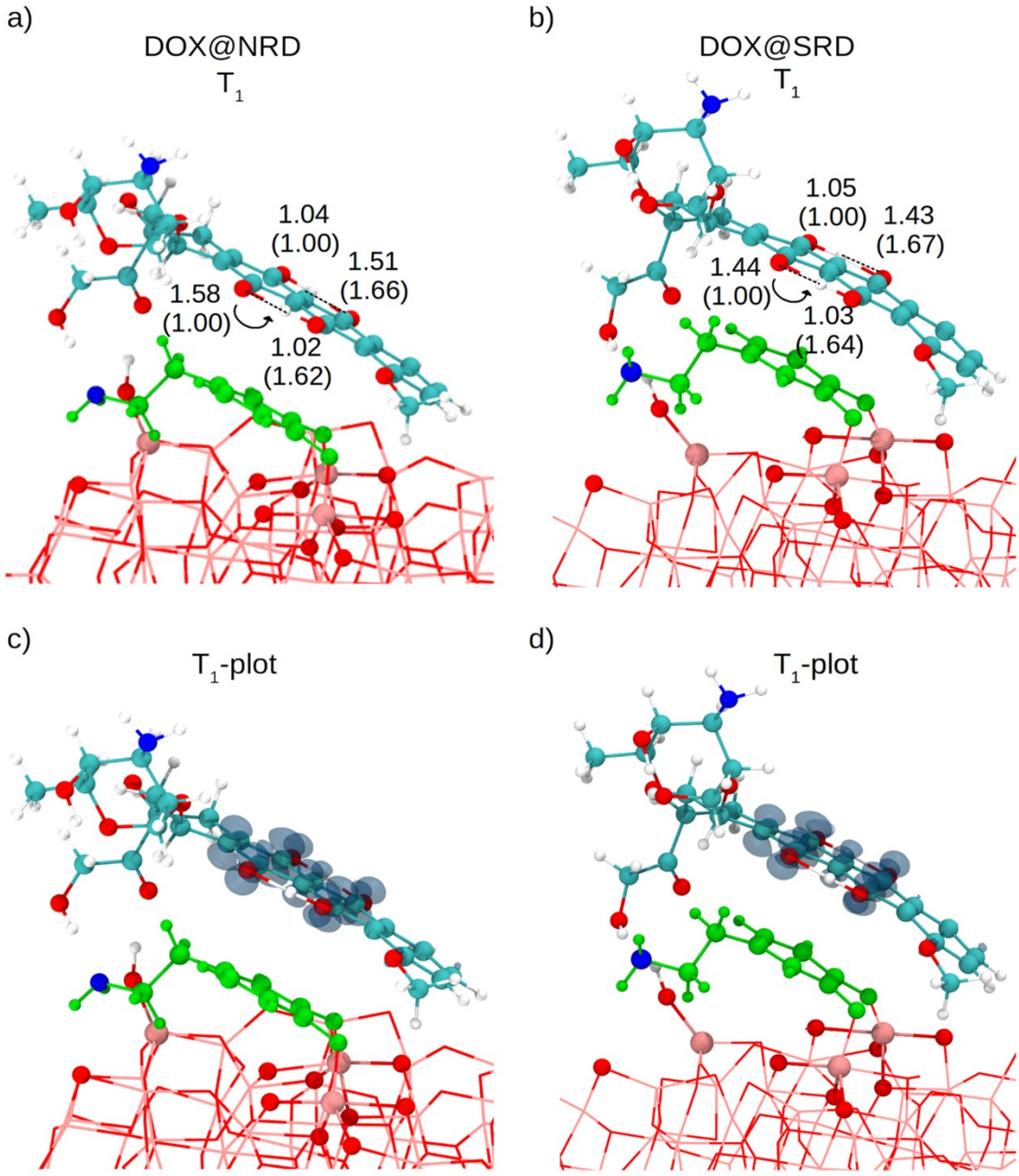

Figure S10. DFT optimized structures triplet exciton a(b) and spin density plots c(d) for DOX@NRD in the left panel and DOX@SRD in the right panel along with their spin density plot. The numbers in parenthesis are refer to the ground state distances. For more clarity, the atoms of the dopamine are colored in light green except the N atom that is in blue. DOX C atoms are in cyan, H atoms are in white and the N atom is in blue. O atoms are in red and Ti atoms of the NP are in pink. Relevant distances are reported in Å in proximity of the dashed lines. Corresponding DOS of the structures are shown in **Figure S11**.

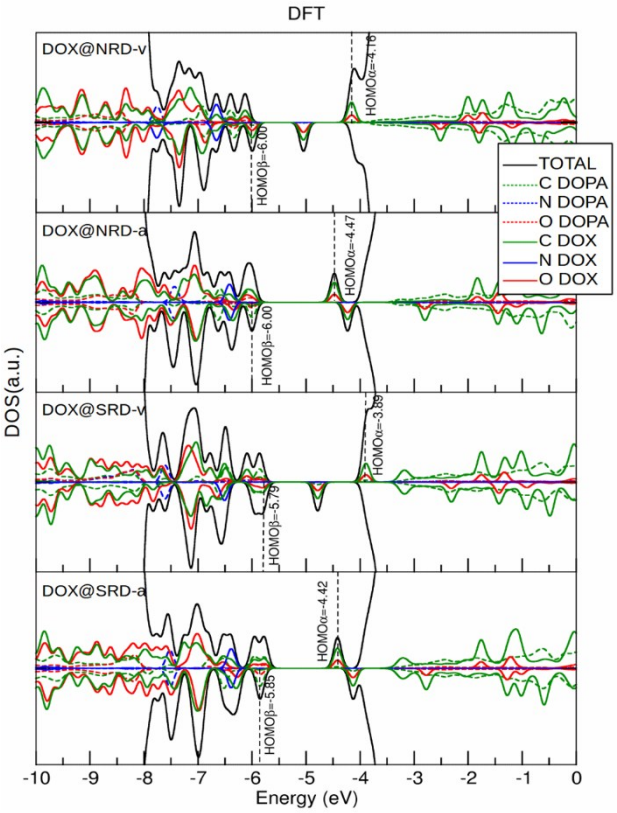

Figure S11. Total (DOS) and projected (PDOS) for the vertical (v) and adiabatic (a) calculations of the DOX@NRD and DOX@SRD configurations as obtained by DFT calculations. Structures are shown in **Figure S10**.

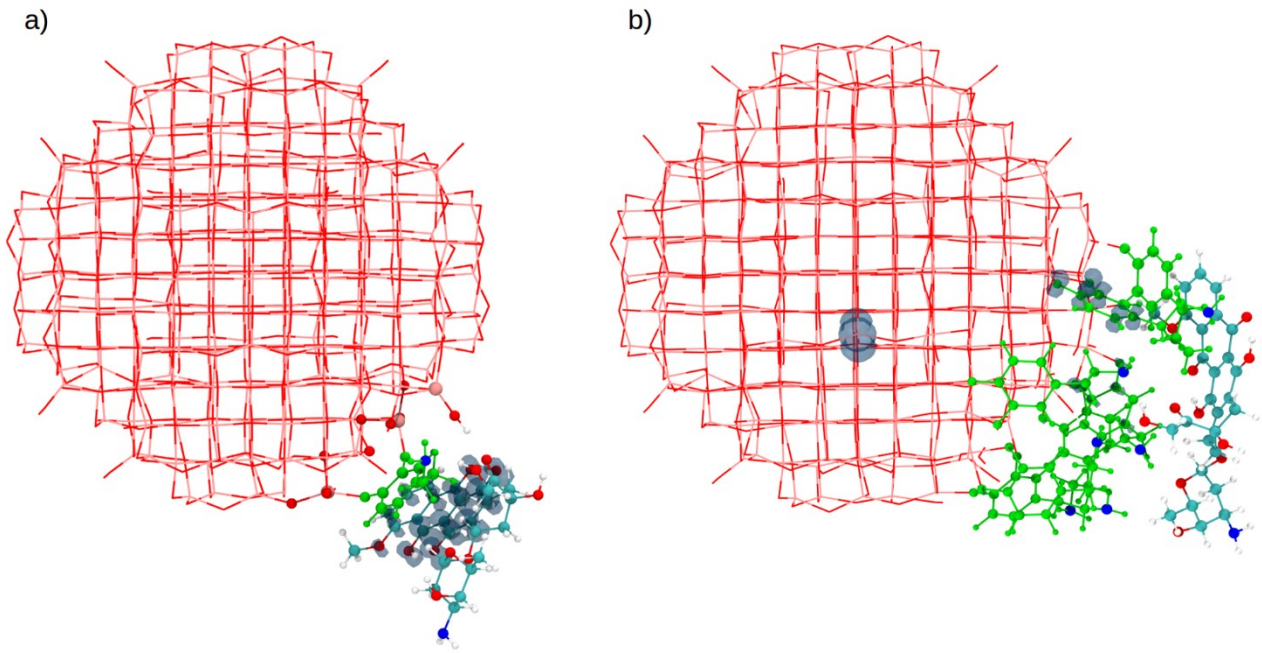

Figure S12. Top views of the spin density plots using DFTB+U for **a)** DOX@NRD with e^- and h^+ localized on the DOX molecule and **b)** for **b-DOX@7DOPA-MD** structure shown in **Figure 6** of the paper. Here the h^+ is localized on the dopamine molecules and the e^- on the surface Ti atom. For more clarity, the atoms of the dopamine are colored in light green except the N atom that is in blue. DOX C atoms are in cyan, H atoms are in white and the N atom is in blue. O atoms are in red and Ti atoms of the NP are in pink.