Electronic Supplementary Material (ESI) for Nanoscale.

Supporting information for "Impact of drug aggregation on the structural and dynamic properties of Triton X-100 micelles"

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Starting Configurations of the Systems

Packmol input file used to generate the starting configurations is shown below. The same code, with different files for ibuprofen and indomethacin, was used for both systems:

```
tolerance 2.0
output tx100_ibup_pre.pdb
filetype pdb

structure ibup_ini.pdb
   number 100
   inside box -60.5 -60.5 -60.5 60.5 60.5 60.5
   outside sphere 0. 0. 0. 45.
end structure

structure triton_x100_n_10.pdb
  number 100
  atoms 70
    inside sphere 0. 0. 0. 10.
  end atoms
  atoms 46
    outside sphere 0. 0. 0. 25.
  end atoms
end structure
```

Further analysis

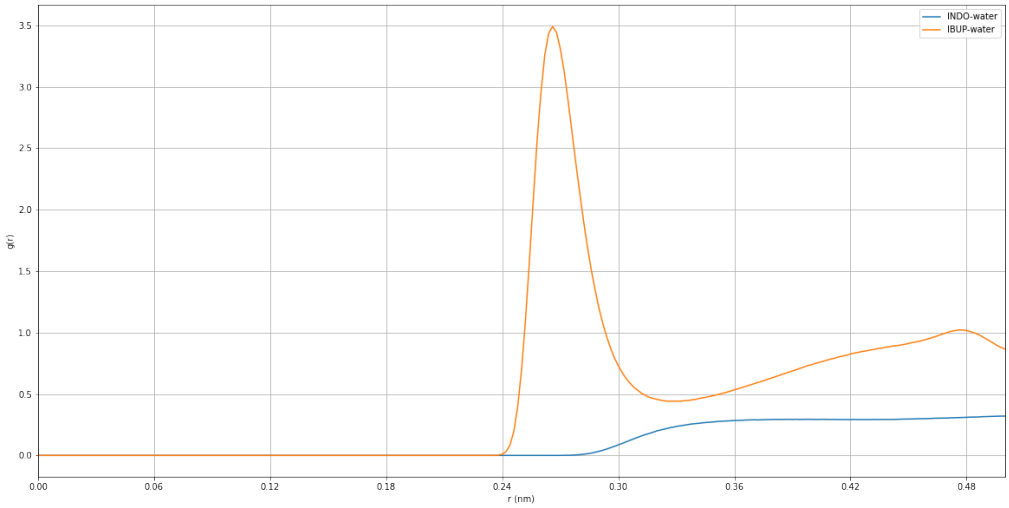
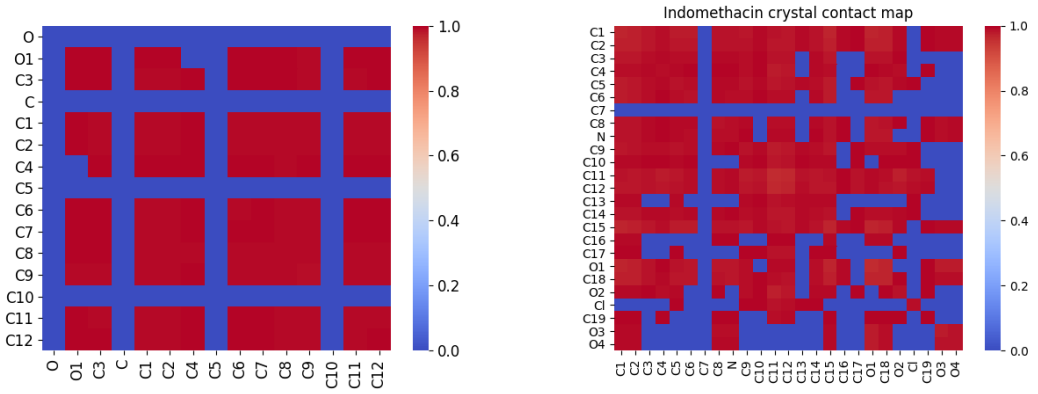


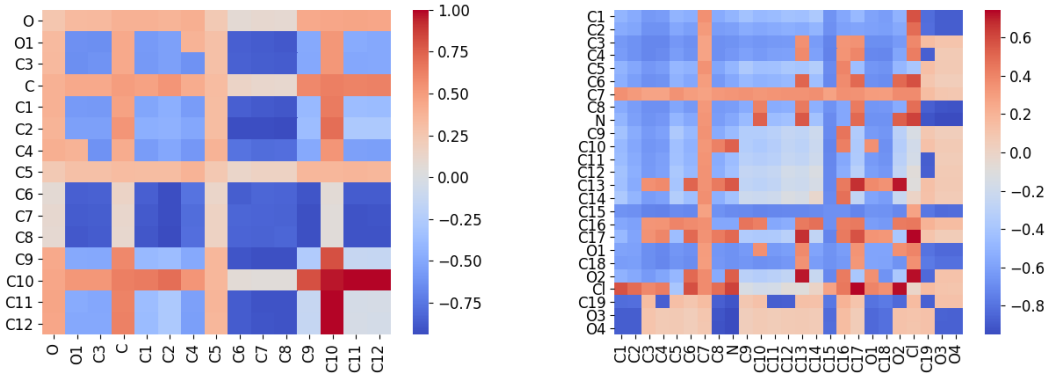
Figure S1: RDF's of oxygen in water with O and O2 in ibuprofen and Cl and N in indomethacin as reference atoms.

Contact Maps of Drugs in a Crystalline Structure



(a) (b)

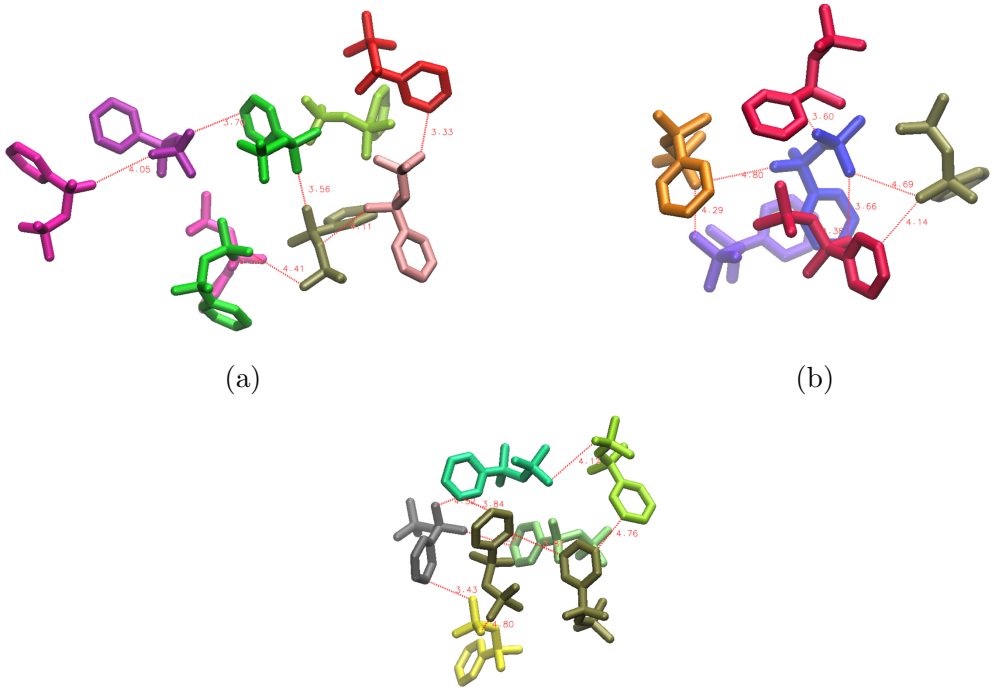
Figure S2: Contact heat maps of the drug - drug interactions for (a) ibuprofen and (b) indomethacin in their crystalline structure.



(a) (b)

Figure S3: Difference in the contact maps of drug-drug interactions within the micelle and in their crystalline structure for (a) ibuprofen and (b) indomethacin. Positive values represent contacts which are more common in the structure taken by the drugs in the core of the micelle, while negative values represent contacts which are more common in the crystalline structure of the drug.

Interaction between Triton X-100 hydrophobic tails

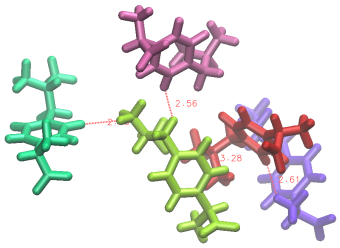


(a) (b)

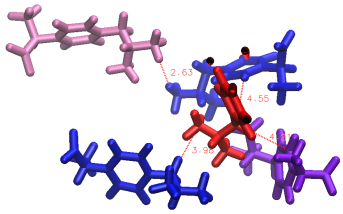
(c)

Figure S4: Snapshots showing the representative interactions between the hydrophobic tails of the Triton X-100 surfactants within the micelles. Generally the surfactant molecules interact via a mixture of hydrophobic contacts between the benzene ring and the methyl groups in their hydrophobic tails. The different colors in (a) - (c) represent different molecules.

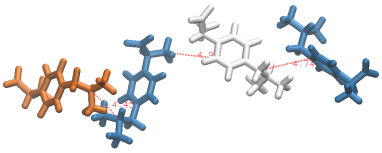
Interaction between encapsulated ibuprofen molecules



(a)



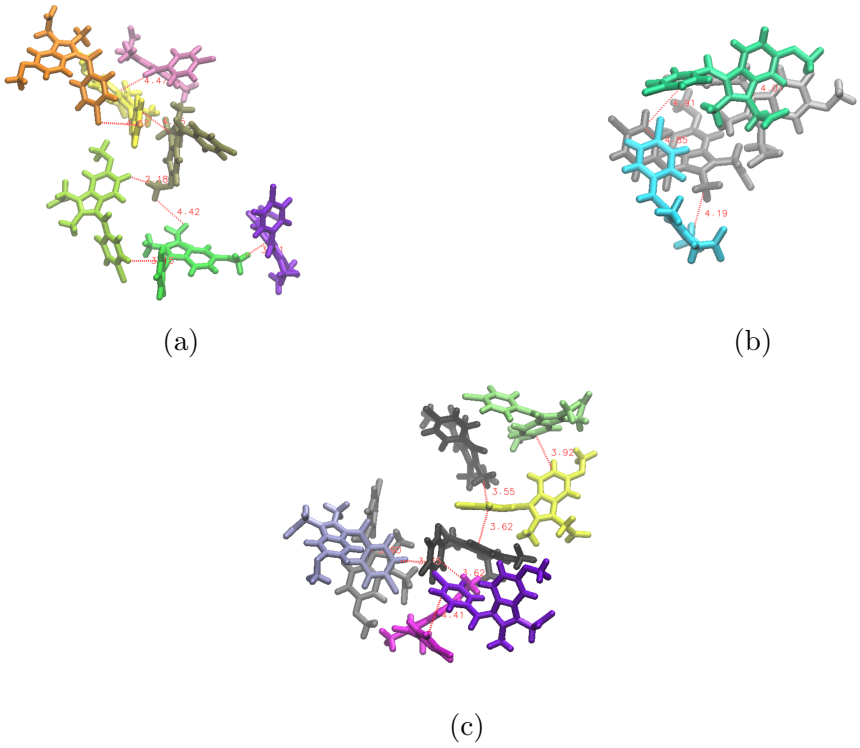
(b)



(c)

Figure S5: Snapshots showing the representative interactions between neighbouring ibuprofen molecules within the core of a Triton X-100 micelle. The different colors in (a) - (c) represent different molecules.

Interaction between encapsulated indomethacin molecules



(a) (b)

(c)

Figure S6: Snapshots showing the representative interactions between neighbouring indomethacin molecules within the core of a Triton X-100 micelle. The different colors in (a) - (c) represent different molecules.

Penetration of water into the core of the micelles

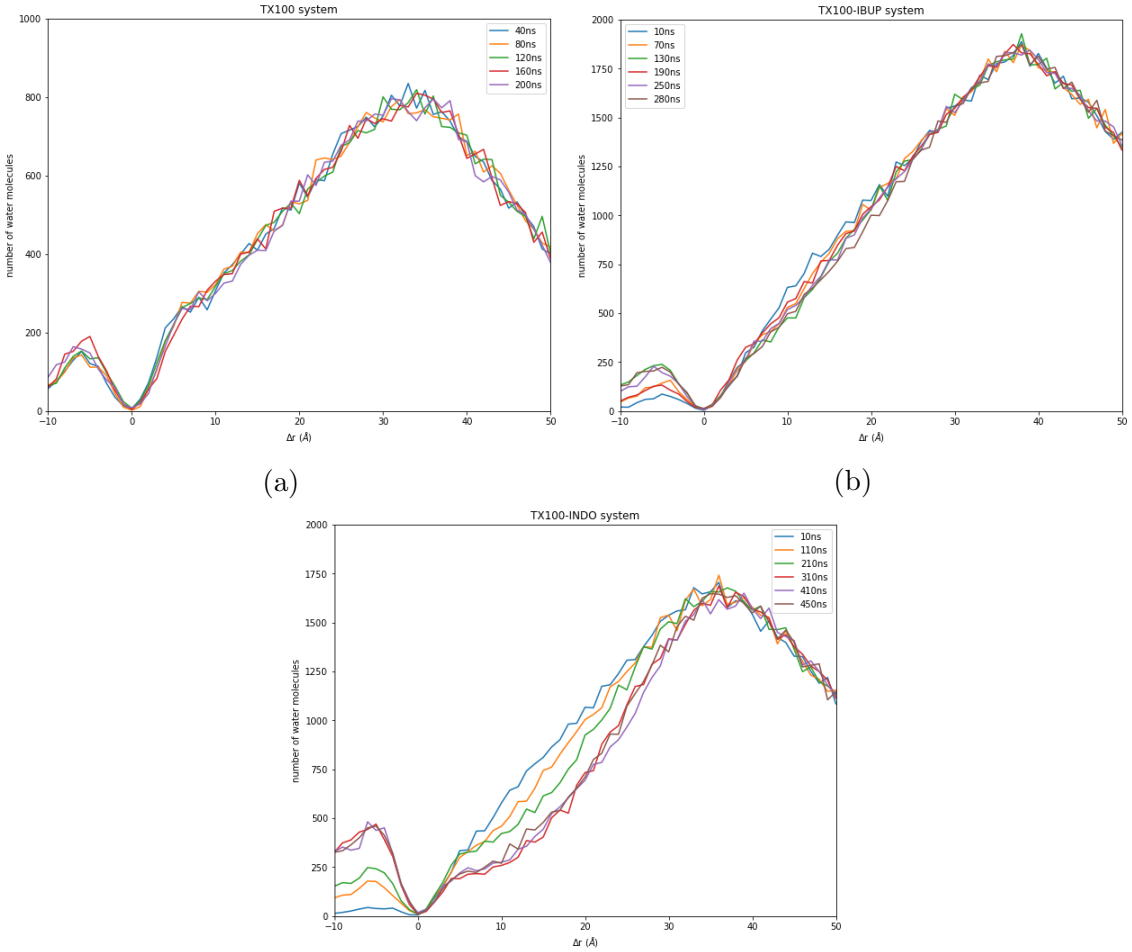


Figure S7: Plots of the amount of water as a function of Δr at various times during the production simulations of the (a) Triton X-100 micelle, (b) the ibuprofen-loaded Triton X-100 micelle and (c) the indomethacin-loaded Triton X-100 micelle.