Supporting Information for "Molecular Dynamics Modeling of Methylene Blue-DOPC Lipid Bilayer Interactions"

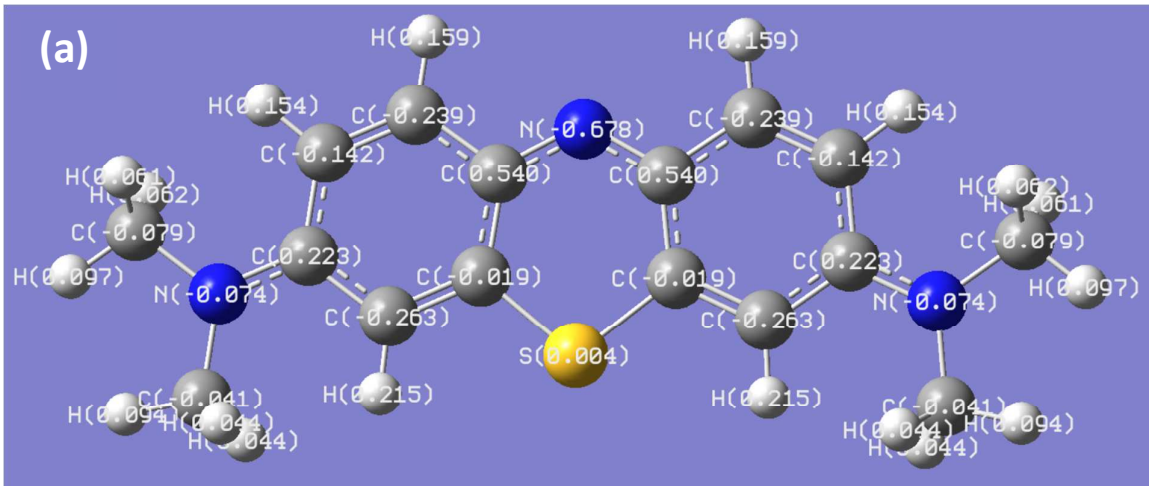
Nazar Ileri Ercan[1,2,3], Pieter Stroeve[1], Joseph W. Tringe[2] and Roland Faller[1*]

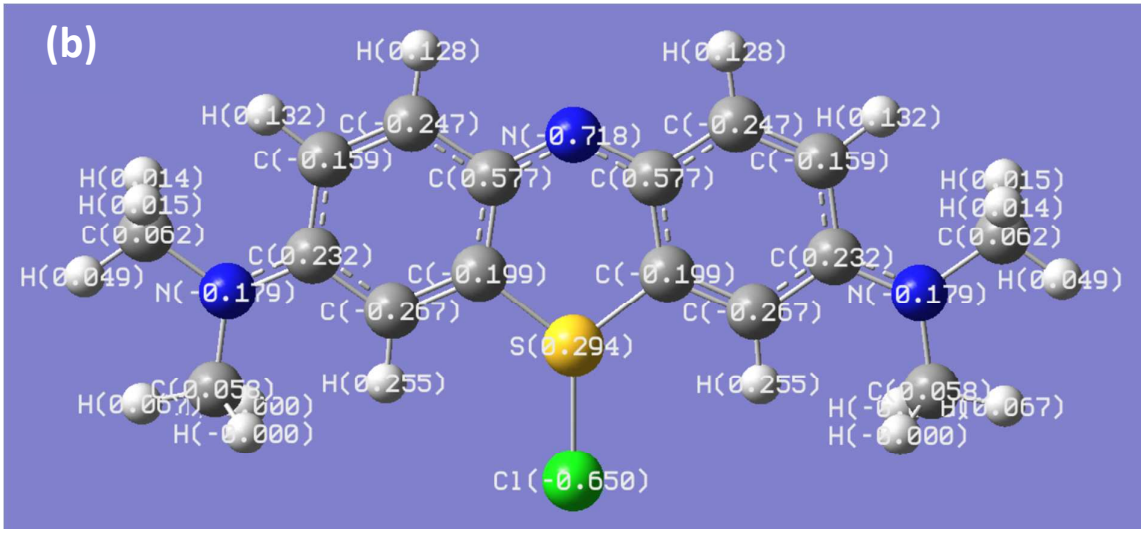
[1] Department of Chemical Engineering, University of California Davis, One Shields Avenue, Davis, CA 95616, USA

[2] Lawrence Livermore National Laboratory, 7000 East Avenue, Livermore, CA 94551, USA

[3] Chemical Engineering Department, Bogazici University, Bebek 34342, Istanbul, Turkey

* rfaller@ucdavis.edu


(a)
H(0.159)
H(0.159)
H(0.154)
C(-0.239)
N(-0.678)
C(-0.239)
H(0.154)
C(-0.142)
C(0.540)
C(0.540)
C(-0.142)
H(0.061)
H(0.062)
H(0.062)
H(0.061)
C(-0.079)
C(-0.079)
H(0.097)
C(0.223)
C(-0.019)
C(-0.019)
C(0.223)
H(0.097)
N(-0.074)
N(-0.074)
C(-0.263)
C(-0.263)
S(0.004)
H(0.215)
H(0.215)
C(-0.041)
C(-0.041)
H(0.094)
H(0.044)
H(0.044)
H(0.094)
H(0.044)
H(0.044)


(b)
H(0.128)
H(0.128)
H(0.132)
C(-0.247)
N(-0.718)
C(-0.247)
H(0.132)
C(-0.159)
C(0.577)
C(0.577)
C(-0.159)
H(0.014)
H(0.015)
H(0.015)
H(0.014)
C(0.062)
C(0.062)
C(0.232)
C(0.232)
H(0.049)
C(-0.199)
C(-0.199)
H(0.049)
N(-0.179)
N(-0.179)
C(-0.267)
C(-0.267)
S(0.294)
C(0.058)
C(0.058)
H(0.255)
H(0.255)
H(0.067)
H(0.067)
H(-0.000)
H(-0.000)
Cl(-0.650)

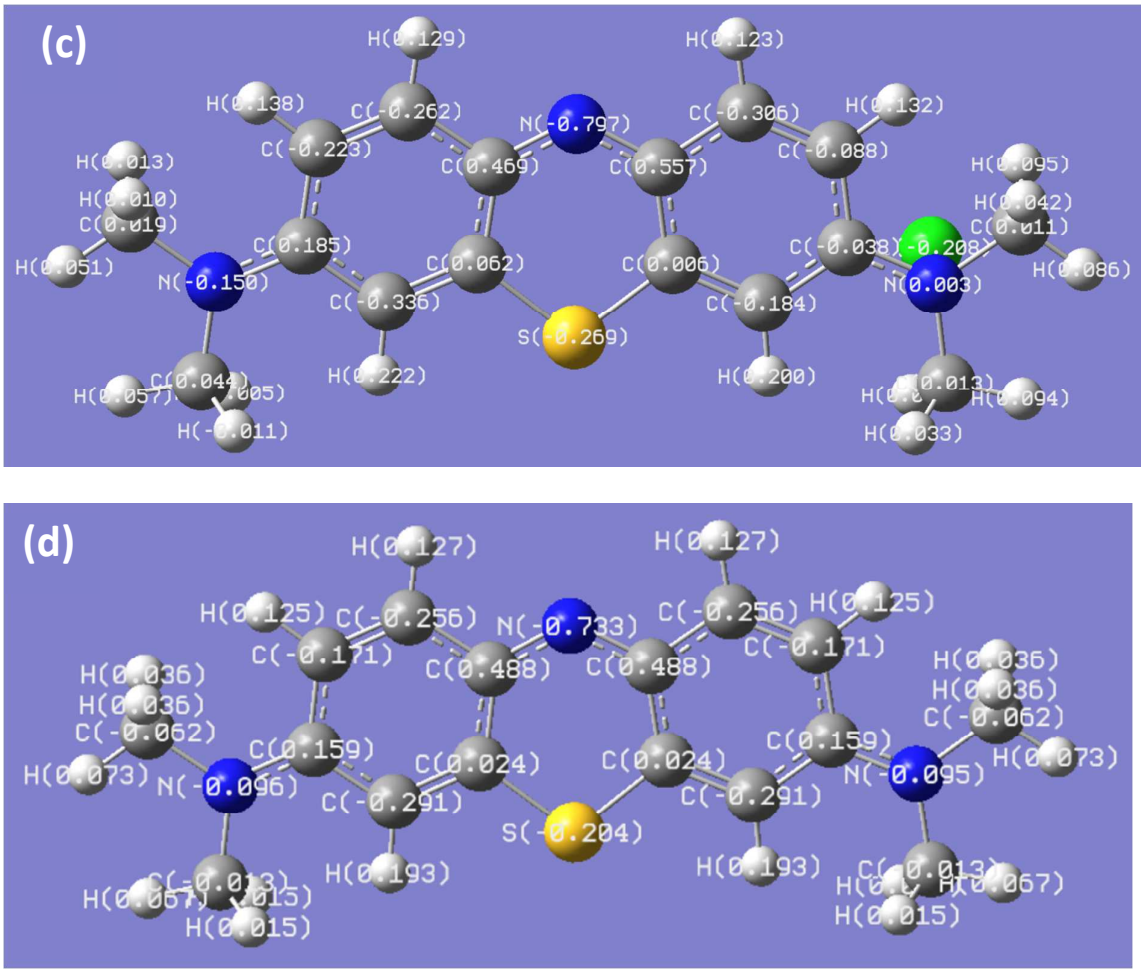
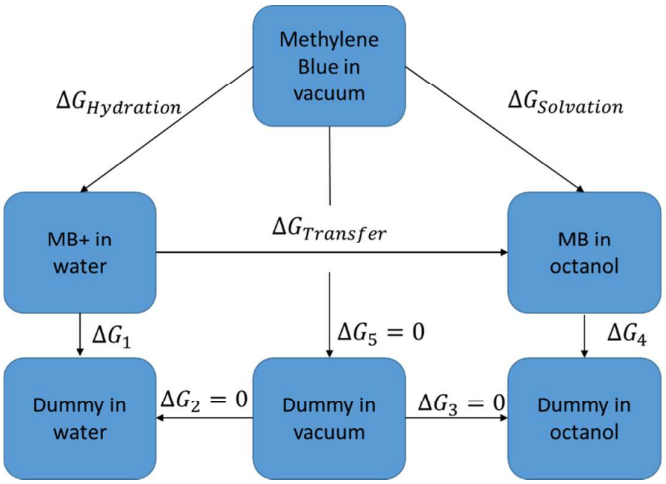


Figure S1. Distribution of partial charges for MB obtained from DFT calculations. (a) Cationic form is solvated in water. Undissociated form, where Cl is connected to (b) S or (c) one of side N, was solvated in heptane. Rreduced form of MB (d) was solvated in heptane.



$$\Delta G_{Hydration} = \Delta G_5 + \Delta G_2 - \Delta G_1$$

$$\Delta G_{Solvation} = \Delta G_5 + \Delta G_3 - \Delta G_4$$

$$\Delta G_{Transfer} = \Delta G_{Solvation} - \Delta G_{Hydration}$$

$$\Delta G_{Transfer} = \Delta G_1 - \Delta G_4$$

and

$$logP = \frac{-\Delta G_{Transfer}}{RTln(10)}$$

Figure S2. Thermodynamic cycle and related equations used in this study. ΔG_5 is the energy required to remove all internal nonbonded interactions of the compound in vacuum. Since the internal non-bonded interactions were excluded due to small molecule size, this term is set to zero. Moreover, by definition dummy does not interact with the rest of the system. Therefore ΔG_2 and ΔG_3 terms are zero.

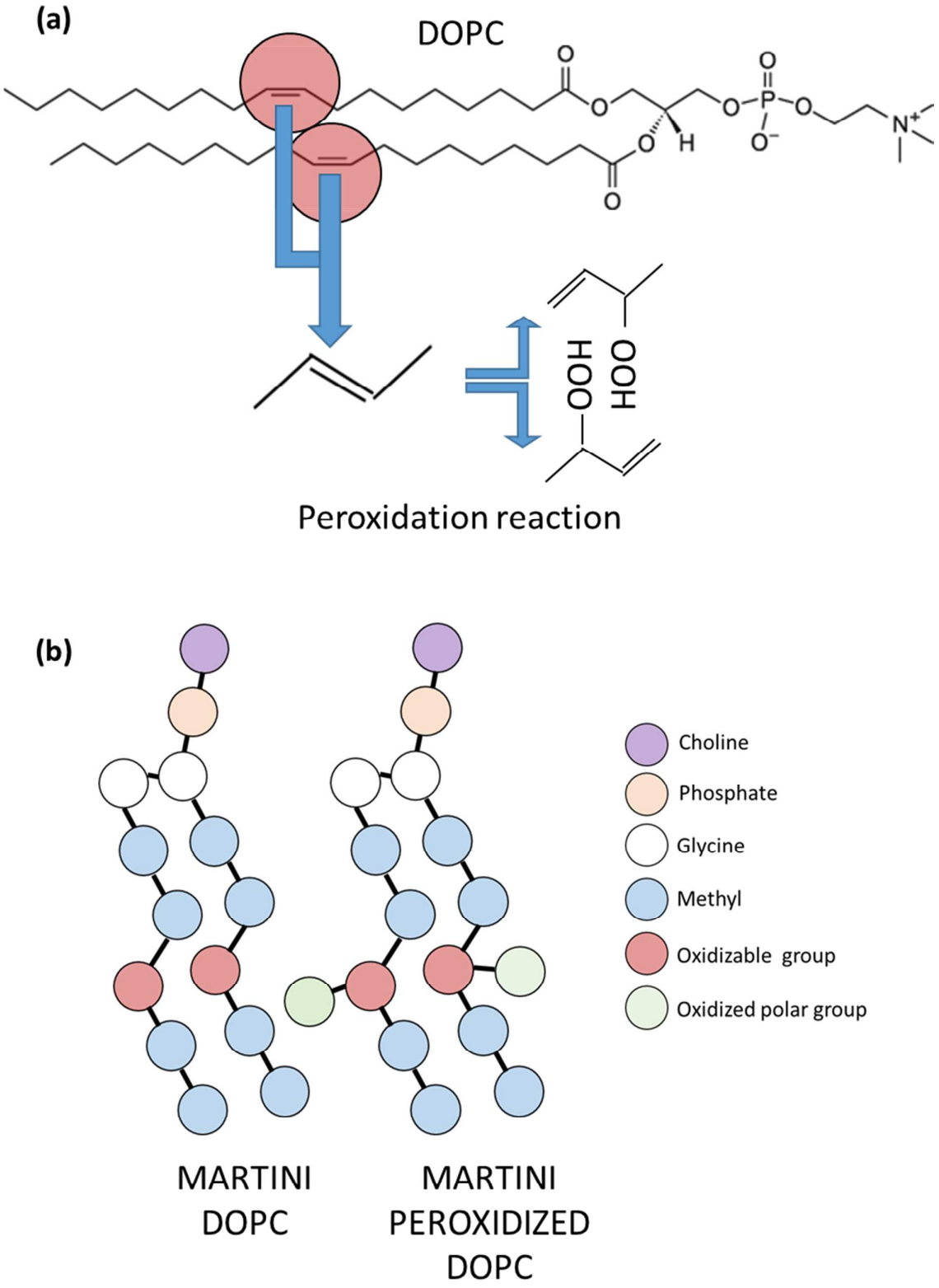


Figure S3. (a) Peroxidation reaction upon addition of singlet oxygen (b) Regular and oxidized DOPC based on MARTINI model. "*" next to P2 indicates the separation distance being 0.33 nm instead of the standard lipid bonding distance 0.47nm.

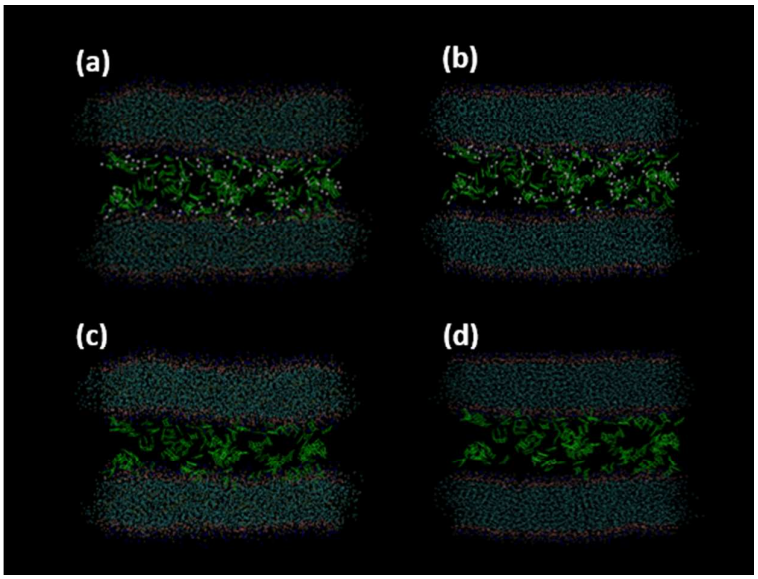


Figure S4. Initial configurations of MB distributions with respect to lipid bilayers systems: (a) MB^{+}-peroxidized DOPC, (b) MB^{+}- regular DOPC, (c) MB salt or neutral MB - peroxidized DOPC, (d) MB salt or neutral MB– regular DOPC.

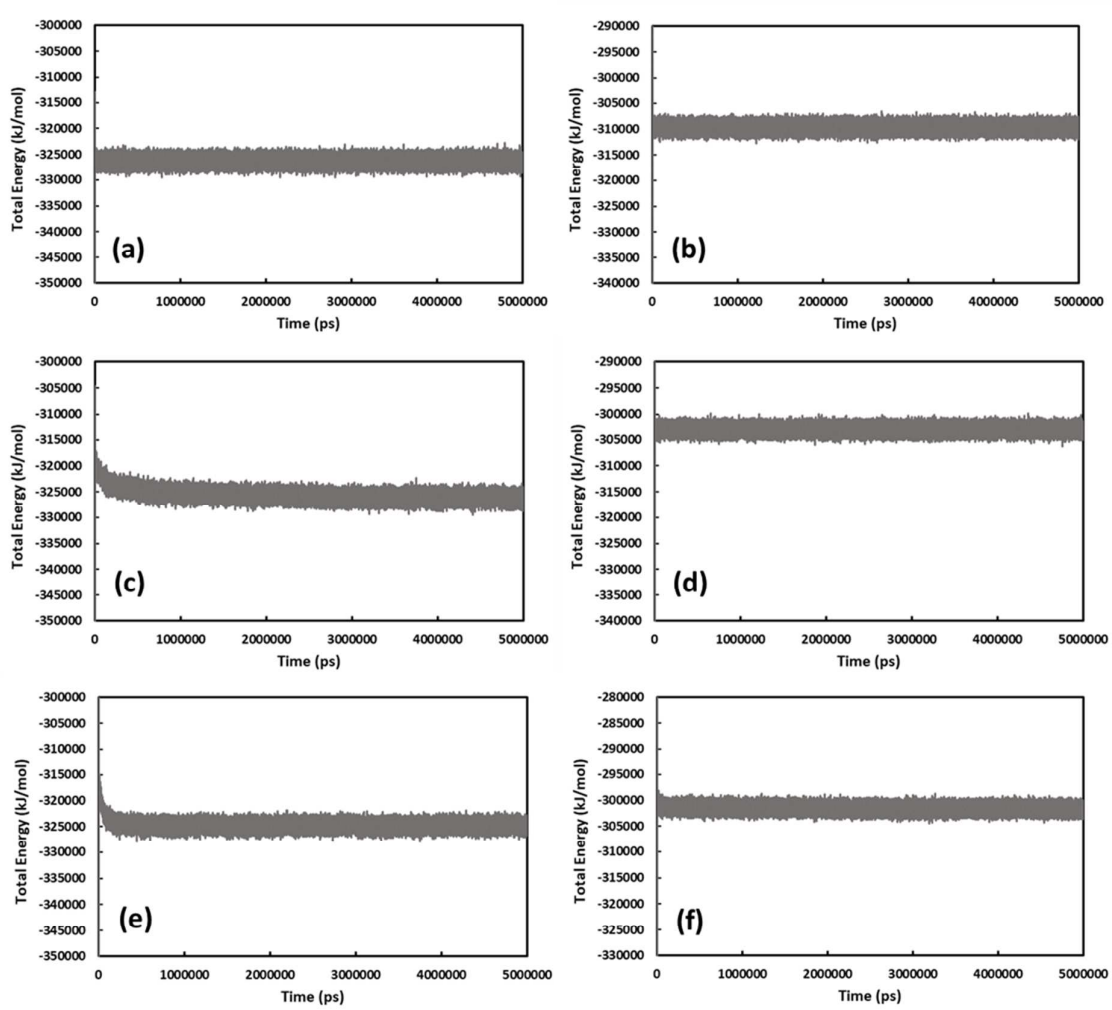


Figure S5. Total energy profiles throughout the simulations for: (a) MB^{+}- peroxidized DOPC, (b) MB^{+}- regular DOPC, (c) MB salt - peroxidized DOPC, (d) MB salt – regular DOPC, c) Neutral MB - peroxidized DOPC, (d) Neutral MB – regular DOPC.

Table S1. Partial charge values obtained from DFT calculations for MB+ in water as well as MB salt and neutral MB in heptane.

	Charge Value			
	MB^+ in water	MB in heptane		
		Cl^- bonded to S	Cl^- bonded to side N	Neutral MB
C1	-0.142	-0.159	-0.088	-0.171
C2	-0.239	-0.247	-0.306	-0.256
C3	0.540	0.577	0.557	0.488
C4	-0.019	-0.199	0.006	0.024
C5	-0.263	-0.267	-0.184	-0.291
C6	0.223	0.232	-0.038	0.159
C7	-0.019	-0.199	0.062	0.024
C8	0.540	0.577	0.469	0.488
C9	-0.239	-0.247	-0.262	-0.256
H1	0.159	0.128	0.129	0.127
C10	-0.142	-0.159	-0.223	-0.171
C11	0.223	0.232	0.185	0.159
C12	-0.263	-0.267	-0.336	-0.291
H2	0.154	0.132	0.132	0.125
H3	0.159	0.128	0.123	0.127
H4	0.215	0.255	0.200	0.193
H5	0.154	0.132	0.138	0.125
H6	0.215	0.255	0.222	0.193
S	0.004	0.294	-0.269	-0.204
N1	-0.678	-0.718	-0.797	-0.734
C13	-0.041	0.058	0.044	-0.013
C14	-0.079	0.062	0.019	-0.062
H7	0.044	0.000	-0.011	0.015
H8	0.094	0.067	0.057	0.067
H9	0.044	0.000	-0.005	0.015
H10	0.062	0.014	0.010	0.036
H11	0.062	0.014	0.012	0.036
H12	0.097	0.049	0.051	0.073
C15	-0.079	0.062	0.011	-0.062
C16	-0.041	0.058	0.013	-0.013
H13	0.062	0.014	0.042	0.036
H14	0.097	0.049	0.086	0.073
H15	0.062	0.014	0.095	0.036
H16	0.044	0.000	0.033	0.015
H17	0.044	0.000	0.084	0.015
H18	0.094	0.067	0.094	0.067
N2	-0.074	-0.179	0.003	-0.096
N3	-0.074	-0.179	-0.150	-0.096
Cl	-	-0.650	-0.208	-

Table S2. Hydration and solvation free energies obtained from the MARTINI model.

		ΔG_{ow} (kJ/mol)
Experimental[60-65]		-4.54 – +10.83
All-atom simulations	MB^+ in water	82.373
	Cl bonded to S in 1-octanol	76.863
	Cl bonded to side N in 1-octanol	72.491
	Neutral MB in 1-octanol	61.766
	Between MB^+ in water and 1-octanol	149.49
Coarse-grained simulations	MB^+ in water	167.666
	Undissociated MB salt in 1-octanol	159.89
	Neutral MB in 1-octanol	145.287