SUPPLEMENTARY MATERIAL

Ultrafast molecular dynamics of biofuel extraction for microalgae and bacteria milking: Blocking membrane folding pathways to damaged lipid-bilayer conformations with nano micelles

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A. HEAT CAPACITY PEAKS

In the Methods, we develop a semi-analytical model to compute S from the heat capacity C_v . The complete free energy $G = E - TS$ is computed in this framework that can be generalized to other biomolecular systems. C_v is indeed an important transient descriptor of the conformational changes appearing in biomolecules as proteins and nucleic acids but also phospholipids. The initial C_v value for the time interval from $t = 5$ to $\Delta t = 375$ ps (for the mixture with n-hexane) is set to the Debye-Einstein limit otherwise it would be computed from a microset of states that might be poorly equilibrated. In Fig. S1, the heat capacity is divided by the number of atoms in the MD periodic box and perfect gas constant R to obtain the non-dimensional heat capacity c_v per atom. For the mixture with n-hexane, the computed c_v data are plotted vs. t using circle marks located at the middle of the successive time-averaging intervals of width Δt . Then, these points are linearly interpolated (Fig. S1).

In semi-classical physics of the condensed phase, the maximum value of the static heat capacity should be of $c_v^{stat} = 3$ from the Debye and Einstein solid models at room to high temperature. The $c_v^{stat} = 3$ maximum was obtained for bulk materials showing only minor harmonic fluctuations of the atomic degrees of freedom, treated as phonons thereof. However,

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the long phospholipid and hydrocarbon molecules encounter a number of major conformational changes over time. Therefore, the dynamic heat capacity $c_v^{dyn}(t) = c_v^{stat} + \Delta c_v(t)$ presents peak values above $c_v^{stat} = 3$ (i.e. the Debye-Einstein limit) at each important configuration change where the heat capacity fluctuation Δc_v is of significant positive amplitude. The reduce heat capacity of water $c_v^{wat} = 3.02$ consists of a bulk value of 3 (from the Dulong and Petit law) in addition to a minor quantum correction of 0.02. Hence, the Debye-Einstein limit $c_v^{stat} = 3$ is lower than $c_v^{wat} = 3.02$ by less than 1 % and almost coincides with the water heat capacity. However, water is one of the three constituents of our molecular system (Fig. 2). Due to the high $\log P$ values of the phospholipids and hydrocarbons resulting in their non-mixing with water and formation of a water heat reservoir with a local $c_v \approx 3$, the reduced dynamic heat capacity rarely decreases below $c_v^{stat} = 3$ by more than one unity per atom, as shown in Fig. S1.

Fig. S1. c_v vs. t evolution for the mixture with n-hexane

The green horizontal line is a reference to the Debye-Einstein limit. The seven (t, c_v) points listed as <0>, <1>, <2>, ... and <6> in Fig. S1 give the seven heat capacity values of the

seven conformations indexed as ‘0’, ‘1’, ‘2’, ... and ‘6’ in Figs. 4 and 5 for the n-hexane solvent. The notation $\langle i \rangle$ instead of ‘ i ’ (where i is an integer) is used in Fig. S1. Indeed, the c_v value for $\langle i \rangle$ is the same for all the states (forming a microset) contained in one of the successive time-averaging intervals used to compute c_v . Differently, ‘ i ’ is one of the individual conformers composing this microset. Hence, the time abscissae of the points indicated by $\langle 0 \rangle$, $\langle 1 \rangle$, $\langle 2 \rangle$, ... and $\langle 6 \rangle$ in Fig. S1 may present light shifts with those of the points listed as ‘0’, ‘1’, ‘2’, ... and ‘6’ in Fig. 5. The five c_v peaks $\langle 1 \rangle$, $\langle 2 \rangle$, ... and $\langle 5^* \rangle$ in Fig. S1 have to be matched with the five free-energy local minima ‘1’, ‘2’, ... and ‘5*’ in Fig. 5. Indeed, a c_v peak signals an important conformational change to an intermediate state related to a G local minimum. The peak amplitude (Δc_v) also tends to be larger for the most significant conformation changes. For instance, the second highest c_v peak denoted as $\langle 5^* \rangle$ in Fig. S1 indicates the occurrence of the main intermediate state listed as ‘5*’ in Figs. 4 and 5 between the kinetic microstates {1} (membrane) and {2} (vesicle).

B. DEMONSTRATION OF EQ. (7)

The general Einstein diffusion law (Eq. (6)) is

$$2tD = (n_{\text{dim}})^{-1} \langle |\mathbf{r}_i(t) - \mathbf{r}_i(t_0)|^2 \rangle, \quad (\text{S1})$$

By definition, $\mathbf{r}_i(t)$ and $\mathbf{r}_i(t_0)$ are the coordinates of the solvent carbons in the MD periodic box for the times t and $t_0 \leq t$, respectively. Therefore, $\langle |\mathbf{r}_i(t) - \mathbf{r}_i(t_0)|^2 \rangle = \text{MSD}(t)$ corresponds to the equilibrated Mean Square Deviation of the solvent carbon coordinates vs. t and Eq. (S1) can be rewritten as

$$tD = (2n_{\text{dim}})^{-1} \text{MSD}(t) \quad (\text{S2})$$

for the actual time t . However, t is a discrete variable in MD. Therefore, Eq. (S2) for the next time step $t + \Delta t$ gives

$$(t + \Delta t)D = (2n_{\text{dim}})^{-1} \text{MSD}(t + \Delta t). \quad (\text{S3})$$

After subtraction of Eq. (S3) by Eq. (S2), we obtain

$$D = (2n_{\text{dim}})^{-1} \frac{\text{MSD}(t + \Delta t) - \text{MSD}(t)}{\Delta t}. \quad (\text{S4})$$

However, Δt is a very short time step in MD. The limit for $\Delta t \rightarrow 0$ can be taken in the right-hand side of Eq. (S4) that transforms to

$$D = (2n_{\text{dim}})^{-1} \frac{d[\text{MSD}(t)]}{dt}. \quad (\text{S5})$$

We find back Eq. (7).