

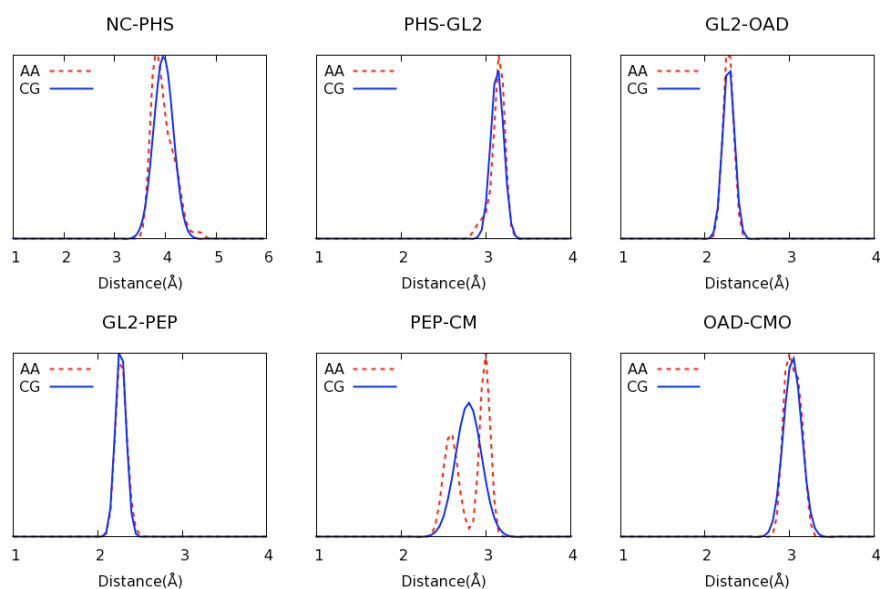
## Supporting Information

# SPICA Force Field for Lipid Membranes: Domain Formation Induced by Cholesterol

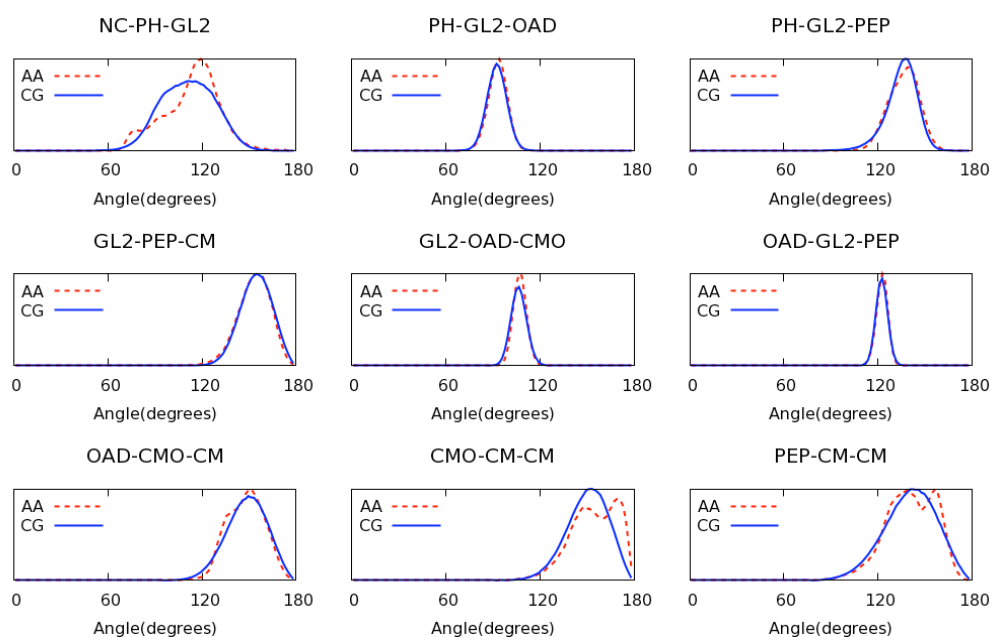
*Sangjae Seo<sup>1</sup> and Wataru Shinoda<sup>1\*</sup>*

<sup>1</sup>Department of Materials Chemistry, Nagoya University, Furo-cho, Chikusa-ku, Nagoya,  
464-8603, Japan

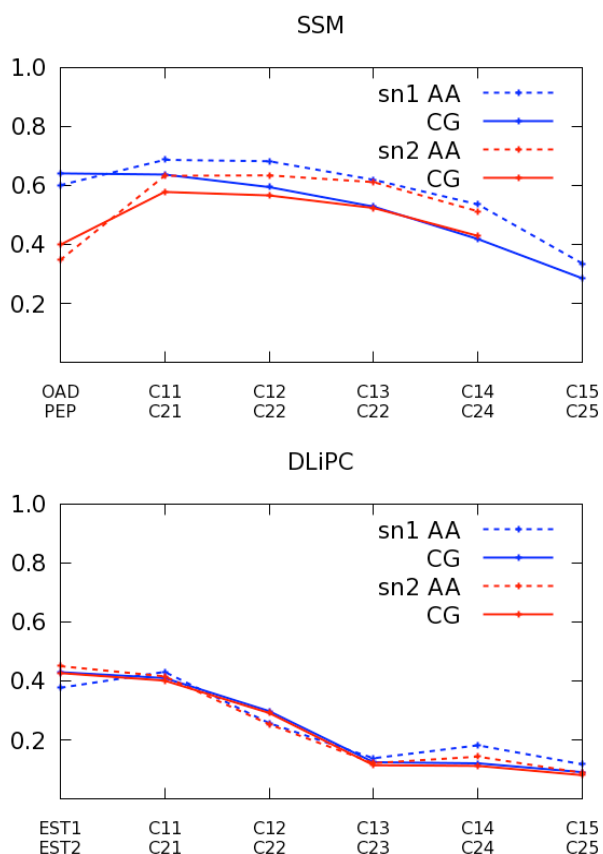
\* w.shinoda@chembio.nagoya-u.ac.jp



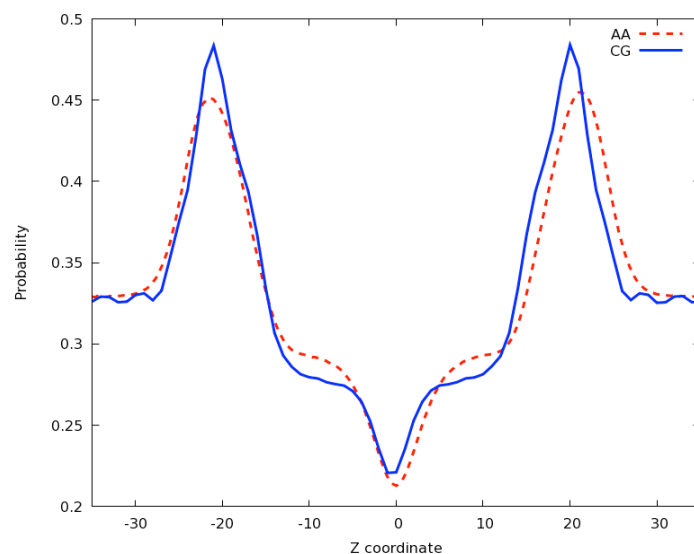
**Figure S1.** Bond distribution of SM from both AA and CG-MD simulations.



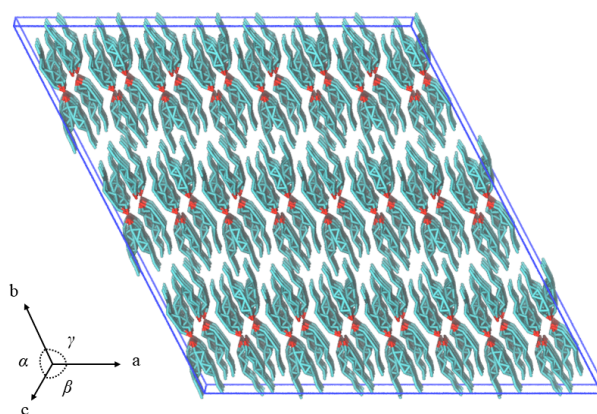
**Figure S2.** Angular distribution of SM from both AA and CG-MD simulations.



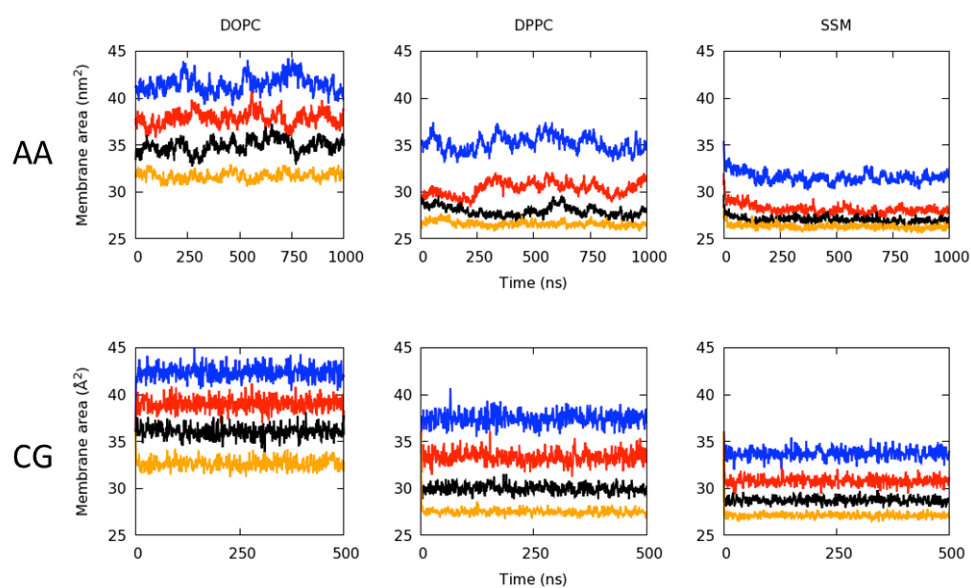
**Figure S3.** CG order parameters of SSM and DLiPC. First line and second line in x-label corresponds to the *sn*-1 and *sn*-2 segments, respectively.



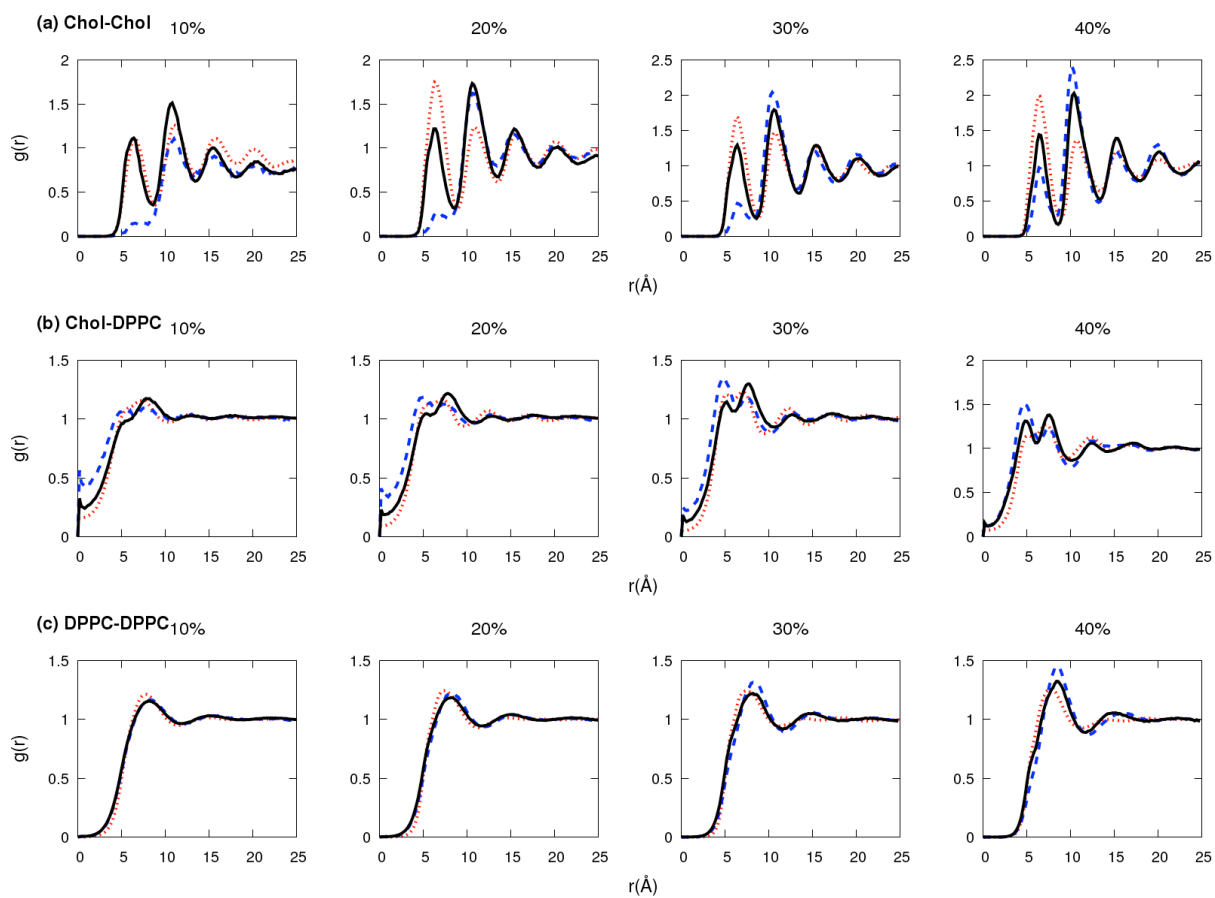
**Figure S4.** Electron density profile of SSM along the bilayer normal. The bilayer center was taken at  $Z = 0$ .



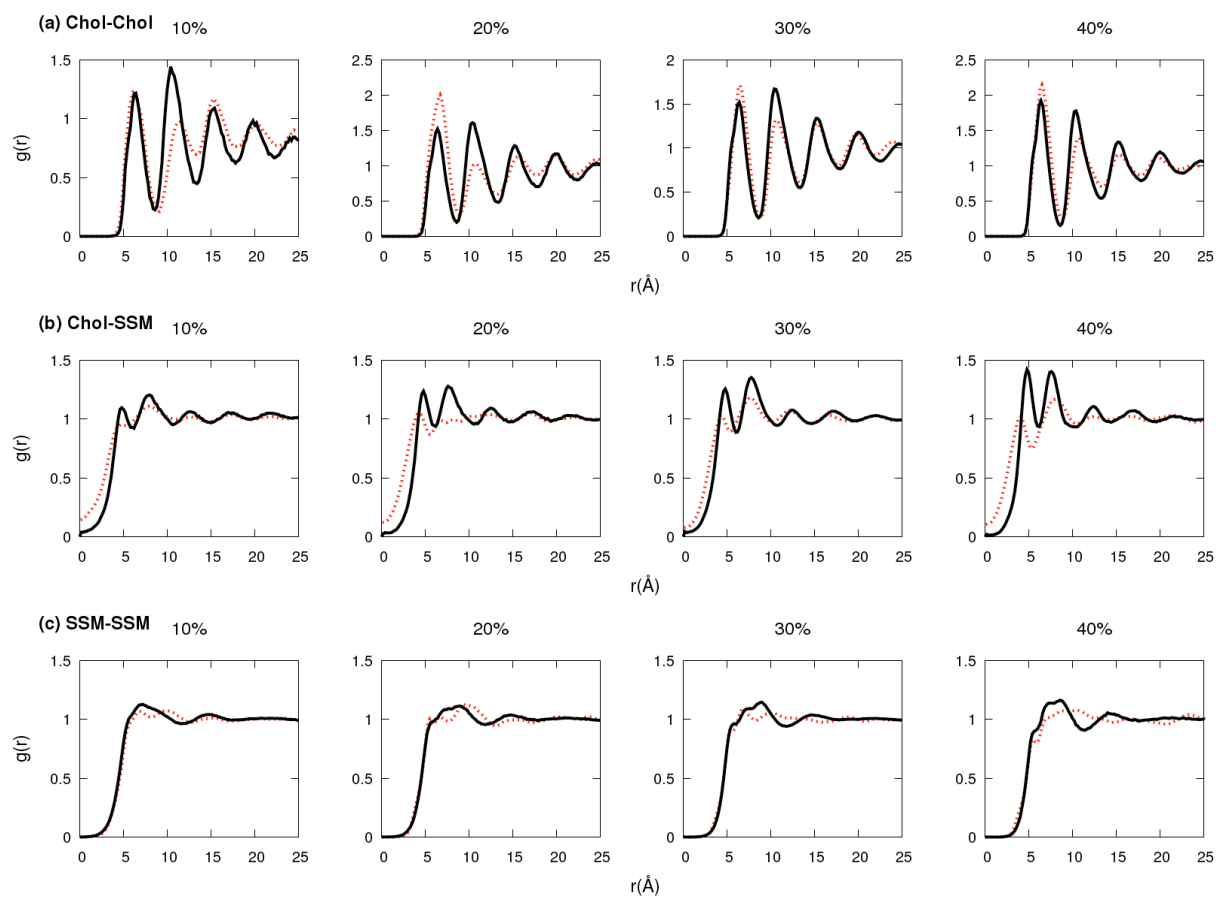
**Figure S5.** The configuration of crystal structure of CHOL. The initial coordinate of the crystal structure was downloaded from The Cambridge Crystallographic Data Centre (<https://www.ccdc.cam.ac.uk/>).



**Figure S6.** Time evolution of membrane area fluctuation. Color code is as follows; Blue-10% Chol, Red-20% Chol, Black-30% Chol, Orange-40% Chol.



**Figure S7.** 2D RDF of DPPC-CHOL membrane. Red dotted and blue dashed lines are the results obtained from AA-MD and CG-MD with previous SDK force field, respectively. Black solid lines represent the results from CG-MD with the current SPICA force field.



**Figure S8.** 2D RDF of SSM-CHOL membrane. Red dotted lines are the RDF obtained from AA-MD simulation and black solid lines are the results obtained from CG-MD with the SPICA force field.

**Table S1.** Summary of the simulated bilayer systems.

| System                       | Lipid composition | Chol. contents | # of water <sup>a</sup> | # of lipid | Temp. <sup>b</sup> | Simulation time     |
|------------------------------|-------------------|----------------|-------------------------|------------|--------------------|---------------------|
| Pure                         | SSM               | -              | 4304                    | 128        | 323 K              | 500 ns <sup>c</sup> |
|                              | PSM               | -              | 4678                    |            |                    |                     |
|                              | DLiPC             | -              | 5696                    |            |                    |                     |
| Binary mixture               | DOPC/Chol         | 10%            | 4200                    | 128        | 323 K              | 500 ns <sup>c</sup> |
|                              |                   | 20%            | 4200                    |            |                    |                     |
|                              |                   | 30%            | 4200                    |            |                    |                     |
|                              |                   | 40%            | 4200                    |            |                    |                     |
|                              | DPPC/Chol         | 10%            | 4017                    |            |                    |                     |
|                              |                   | 20%            | 4017                    |            |                    |                     |
|                              |                   | 30%            | 4017                    |            |                    |                     |
|                              |                   | 40%            | 4017                    |            |                    |                     |
|                              | SSM/Chol          | 10%            | 4445                    |            |                    |                     |
|                              |                   | 20%            | 4620                    |            |                    |                     |
|                              |                   | 30%            | 4758                    |            |                    |                     |
|                              |                   | 40%            | 4954                    |            |                    |                     |
|                              | DLiPC/Chol        | 10%            | 5506                    |            |                    |                     |
|                              |                   | 20%            | 5220                    |            |                    |                     |
| Ternary mixture <sup>d</sup> | DPPC/DOPC/Chol    | 33%            | 88767                   | 2700       | 298 K              | 4 $\mu$ s           |
|                              | DPPC/DLiPC/Chol   |                | 100350                  |            |                    |                     |
|                              | SSM/DOPC/Chol     |                | 81243                   |            |                    |                     |
|                              | SSM/POPC/Chol     |                | 92376                   |            |                    |                     |

<sup>a</sup> The number of CG water beads can be calculated by dividing three.

<sup>b</sup> The temperature of one component and binary mixture system was set to 323 K, which is above phase transition temperature of DPPC (314 K) and SSM (318 K). For ternary mixture, the temperature selected to follow the experiment condition.

<sup>c</sup> AA simulation for reference data was conducted for 1  $\mu$ s. Refer to the text.

<sup>d</sup> Ternary mixtures consist of [saturated lipid]:[unsaturated lipid]:Chol=1:1:1.