SUPPLEMENTARY INFORMATION: NMRlipids III: Lipid-cholesterol interactions in atomistic resolution molecular dynamics simulations

Fernando Favela-Rosales,[†] Peter Heftberger,[‡] Matti Javanainen,[¶] Josef Melcr,[‖] Markus Miettinen,[⊥] O. H. Samuli Ollila,[*,‖] Georg Pabst,[‡] and Thomas Piggot[@]

†*Departamento de Física, Centro de Investigación y de Estudios Avanzados del IPN, Apartado Postal 14-740, 07000 México D.F., México*

‡*University of Graz*

¶*Department of Physics, Tampere University of Technology, Tampere, Finland*

§*University of Helsinki*

‖*Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Prague 6, Czech Republic*

⊥*MPI*

#*Institute of Biotechnology, University of Helsinki*

@*University of Southampton*

E-mail: samuli.ollila@helsinki.fi

S1 CHARMM36 results from different simulation packages

The results from CHARMM36 model for lipid bilayers from different simulation packages have been reported to give different results in the literature.[1,2] The results are mainly dependent on different Lennard-Jones cut-off settings, but all the details are not quite understood. In this work we use the results from Gromacs 5 with settings suggested to be optimal by Gromacs webpage. List these settings here or in SI. We also compared the results from Gromacs 5 with these settings to the results simulated with NAMD, OpenMM and literature values. Based on comparison shown in Fig. S1, we conclude that Gromacs 5 with settings suggested in webpage gives consistent results with the literature and other simulation packages. Thus these results are used in the main body of the paper. However, order parameters are slightly overestimated respected to the experiments also with these settings.

Should be extend this discussion based on discussion at https://github.com/NMRLipids/NmrLipidsCholXray ?

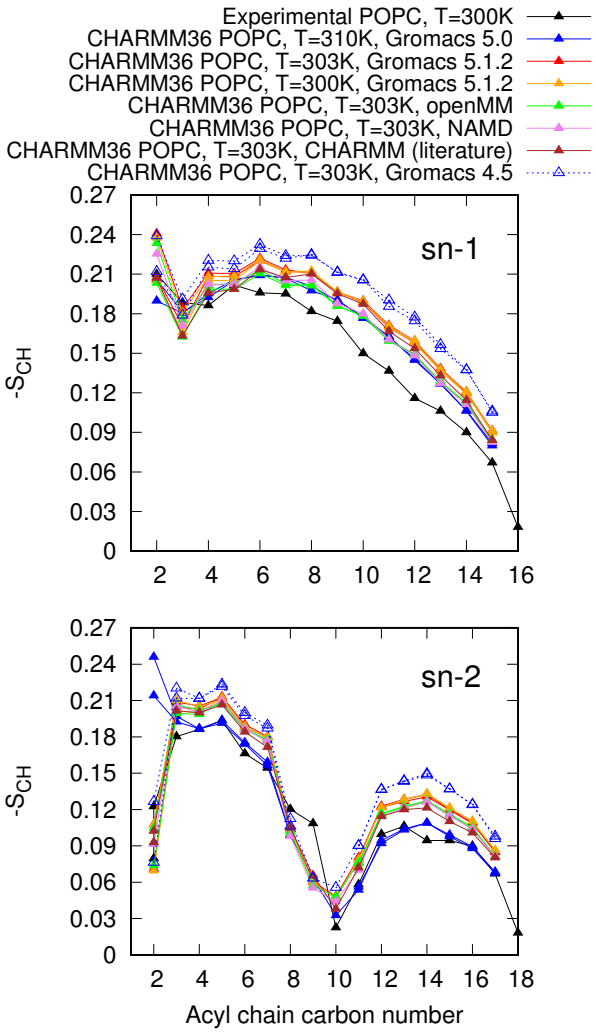

Figure S1: Results for CHARMM36 model[3] from different simulation packages. Discussion going on at *https://github.com/NMRLipids/NmrLipidsCholXray/issues/4*.

S2 Order parameter slopes as a function of cholesterol

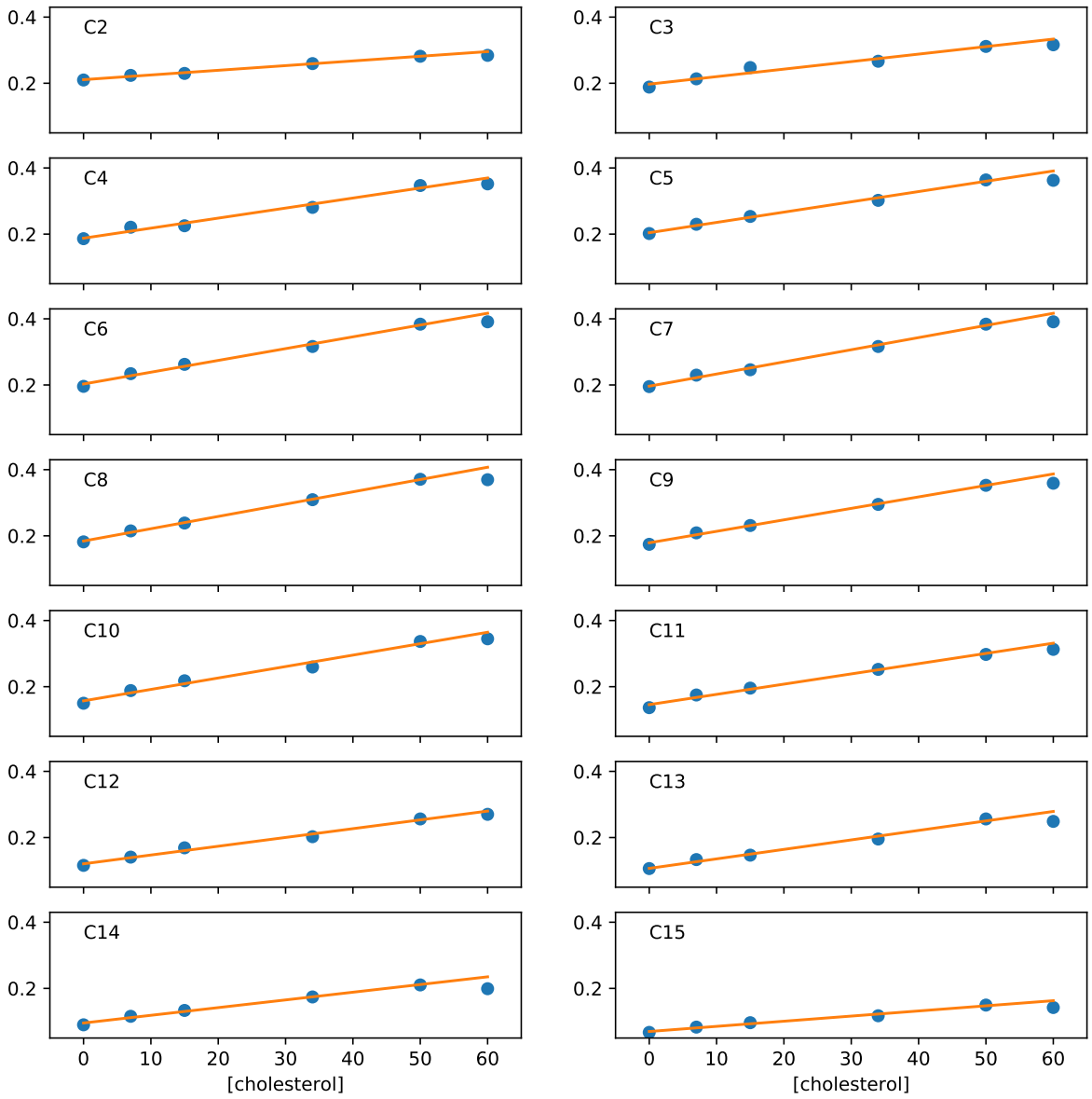

Figure S2: Slopes of order parameters as a function of cholesterol from experiments.[4]

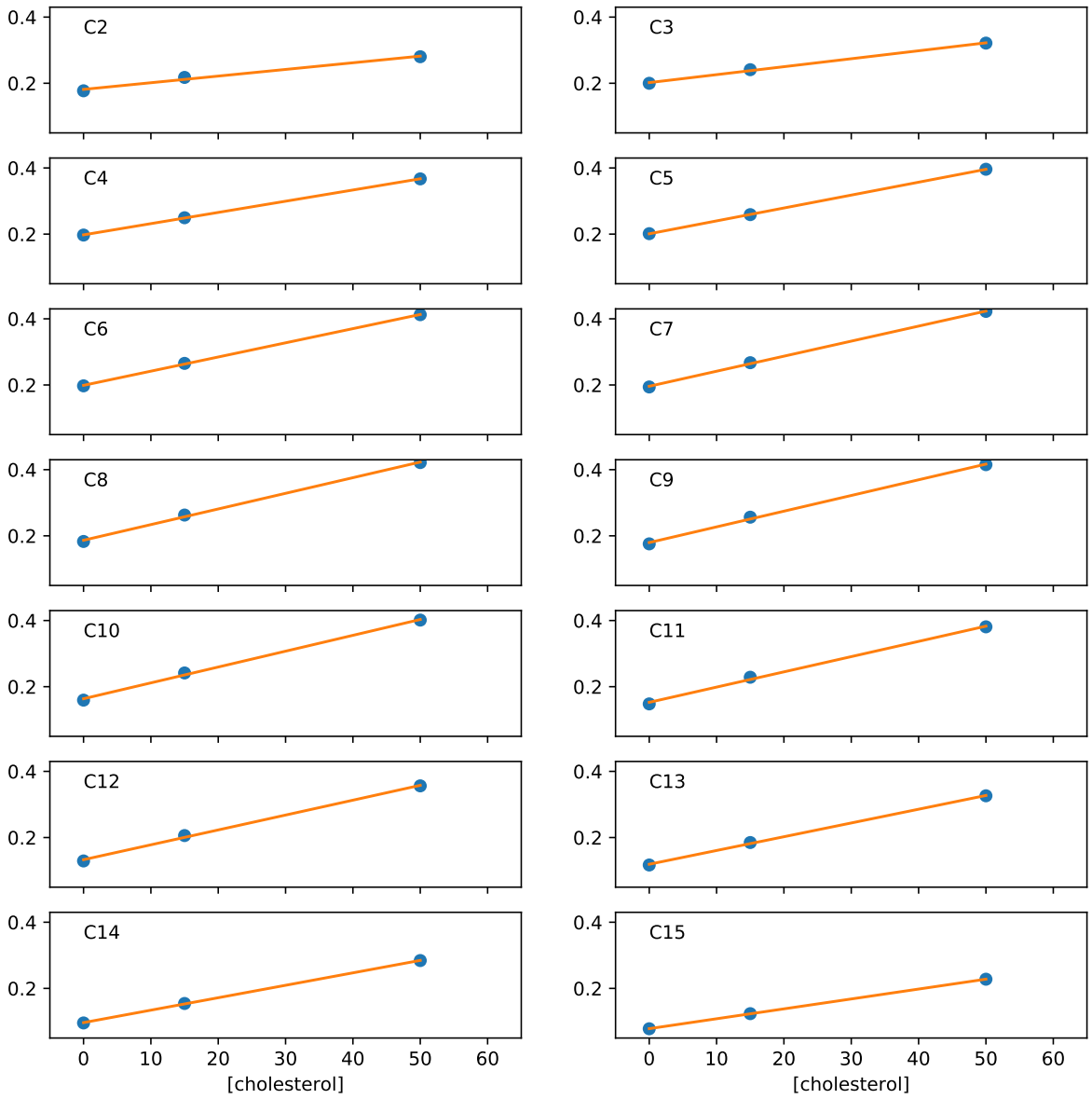

Figure S3: Slopes of order parameters as a function of cholesterol from Berger simulations.

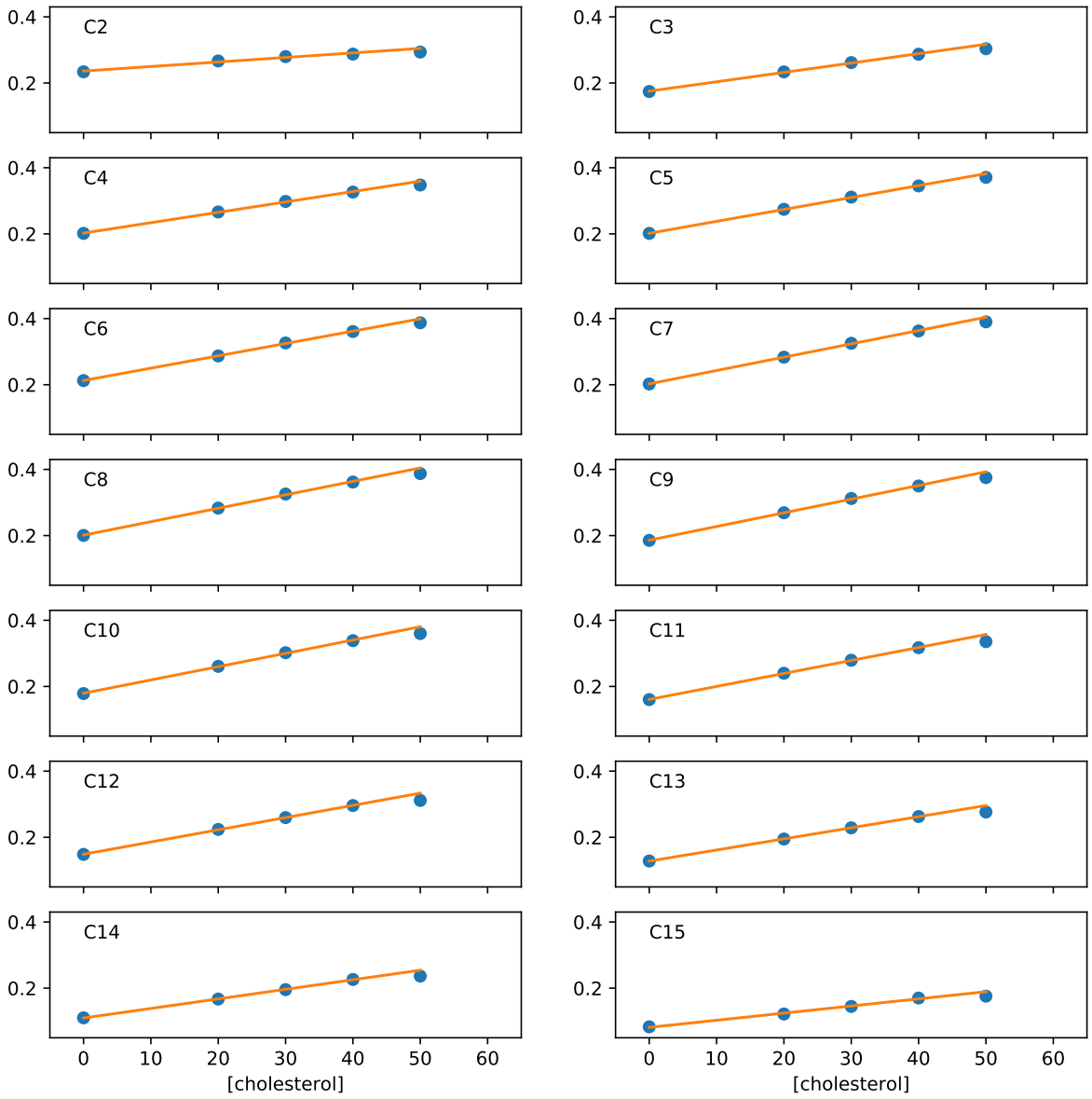

Figure S4: Slopes of order parameters as a function of cholesterol from CHARMM36 simulations.

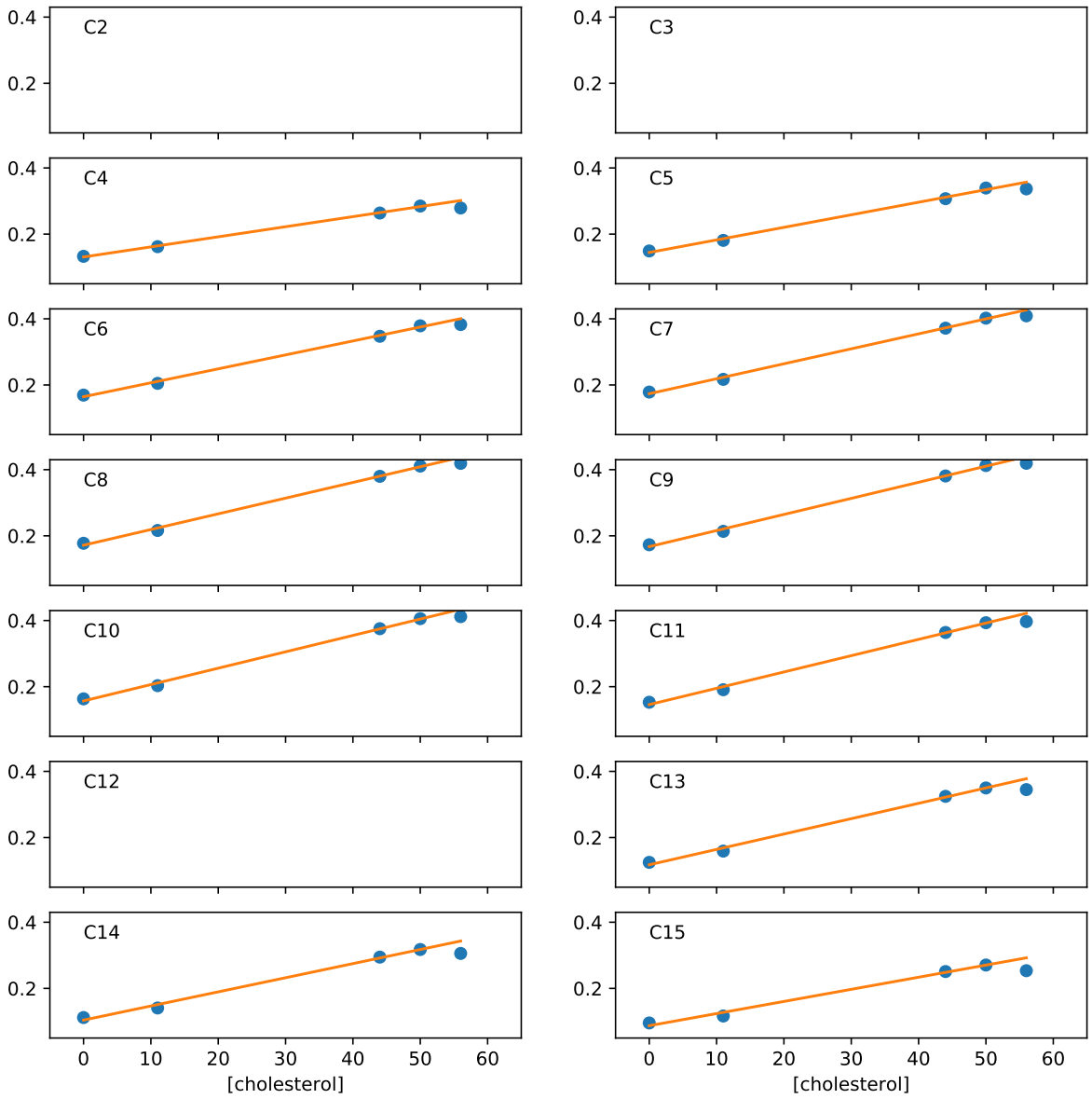

Figure S5: Slopes of order parameters as a function of cholesterol from MacRog simulations.

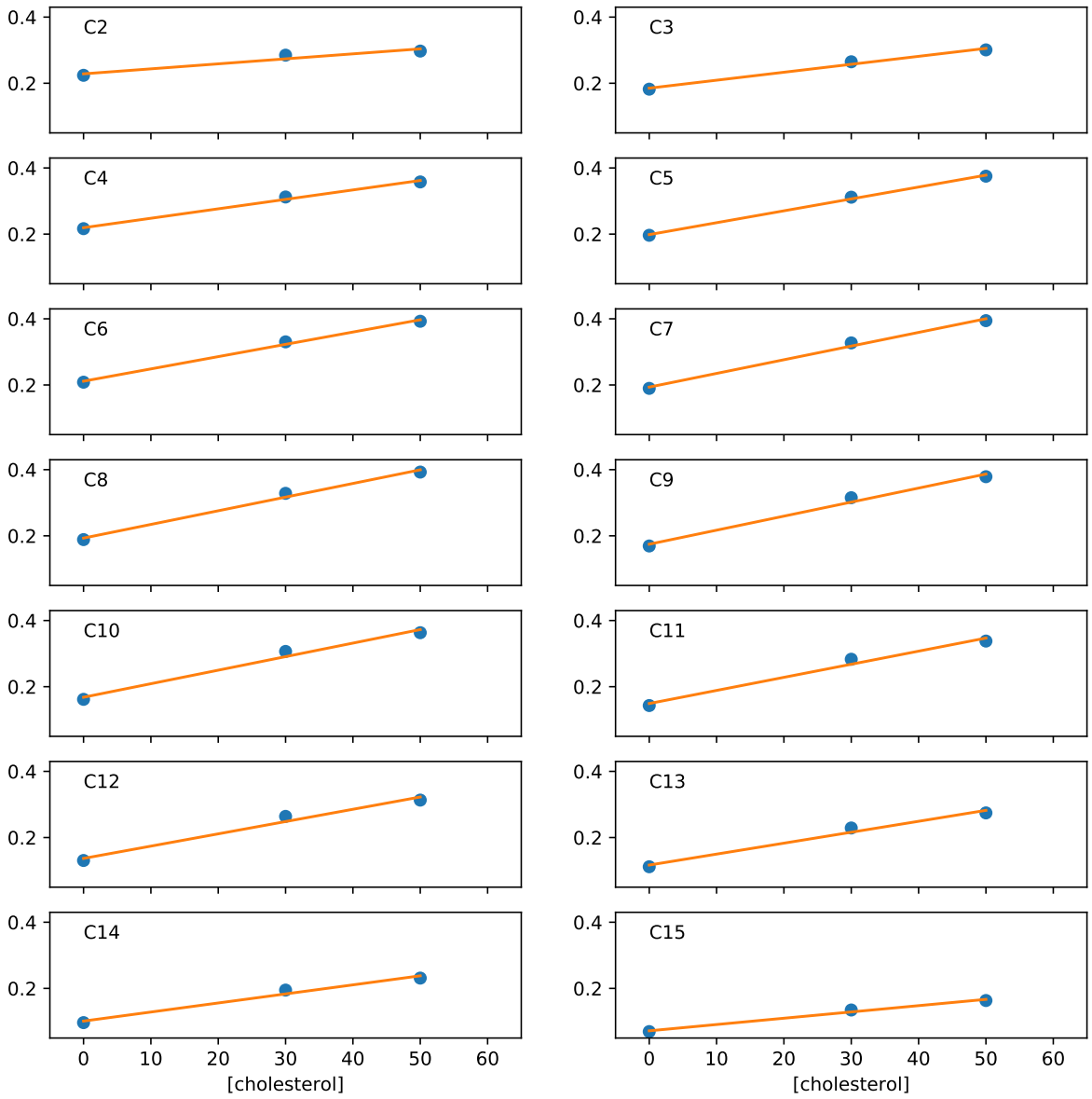

Figure S6: Slopes of order parameters as a function of cholesterol from Slipids simulations.

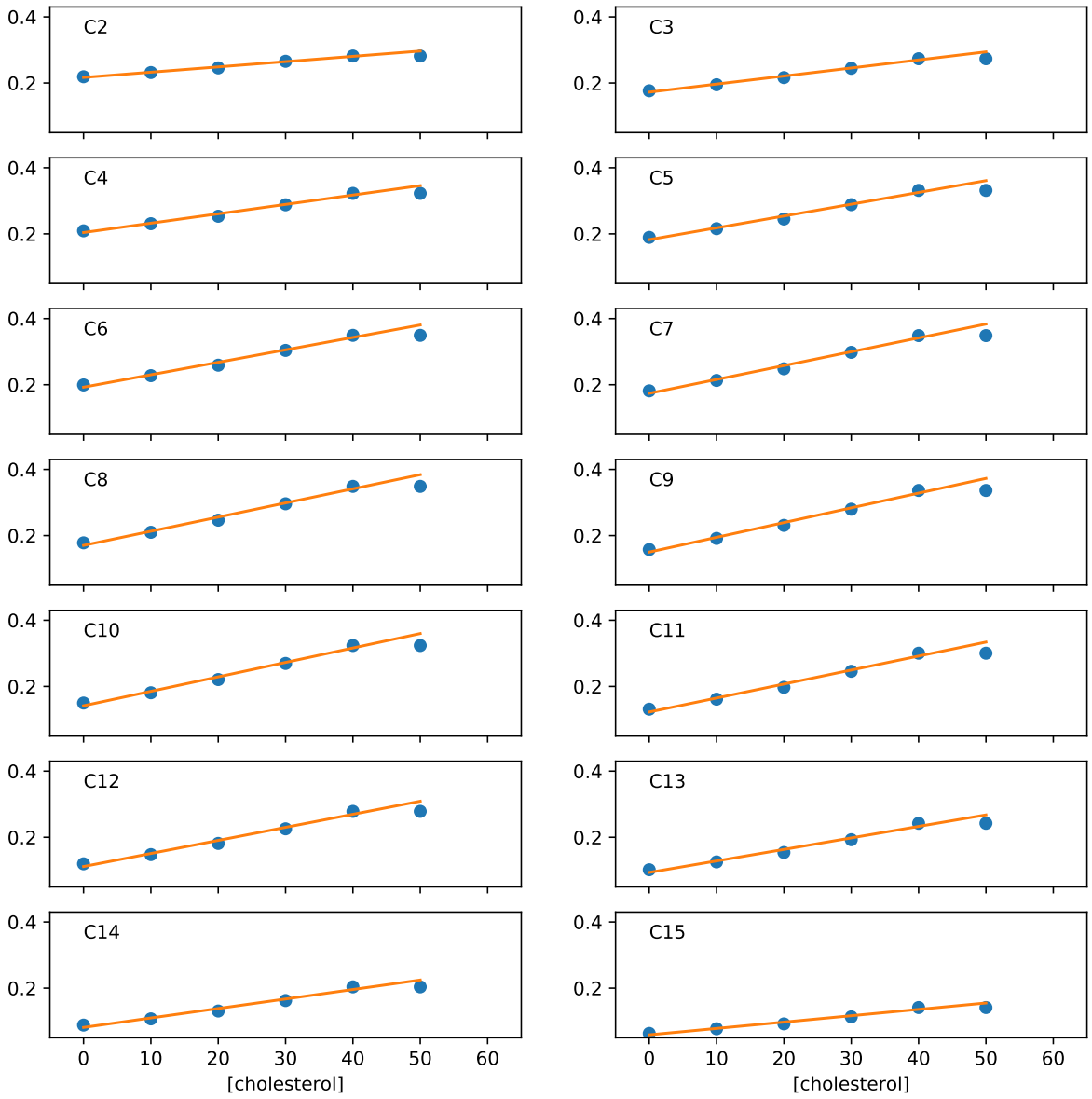

Figure S7: Slopes of order parameters as a function of cholesterol from Slipids simulations at 298 K.

S3 Effect of undulations on order parameters

This should be written based on contributions in this issue: https://github.com/NMRLipids/NmrLipidsCholX

References

(1) Piggot, T. J.; Piñeiro, Á.; Khalid, S. Molecular Dynamics Simulations of Phosphatidylcholine Membranes: A Comparative Force Field Study. *J. Chem. Theory Comput.* **2012**, *8*, 4593–4609.

(2) Lee, J.; Cheng, X.; Swails, J. M.; Yeom, M. S.; Eastman, P. K.; Lemkul, J. A.; Wei, S.; Buckner, J.; Jeong, J. C.; Qi, Y. et al. CHARMM-GUI Input Generator for NAMD, GROMACS, AMBER, OpenMM, and CHARMM/OpenMM Simulations Using the CHARMM36 Additive Force Field. *Journal of Chemical Theory and Computation* **2016**, *12*, 405–413.

(3) Klauda, J. B.; Venable, R. M.; Freites, J. A.; O'Connor, J. W.; Tobias, D. J.; Mondragon-Ramirez, C.; Vorobyov, I.; MacKerell Jr, A. D.; Pastor, R. W. Update of the CHARMM All-Atom Additive Force Field for Lipids: Validation on Six Lipid Types. *J. Phys. Chem. B* **2010**, *114*, 7830–7843.

(4) Ferreira, T. M.; Coreta-Gomes, F.; Ollila, O. H. S.; Moreno, M. J.; Vaz, W. L. C.; Topgaard, D. Cholesterol and POPC segmental order parameters in lipid membranes: solid state ^{1}H-^{13}C NMR and MD simulation studies. *Phys. Chem. Chem. Phys.* **2013**, *15*, 1976–1989.