Supporting Information

Effect of Cholesterol on the Interaction of Cytochrome P450 substrate Drug Chlorzoxazone with the Phosphatidylcholine Bilayers

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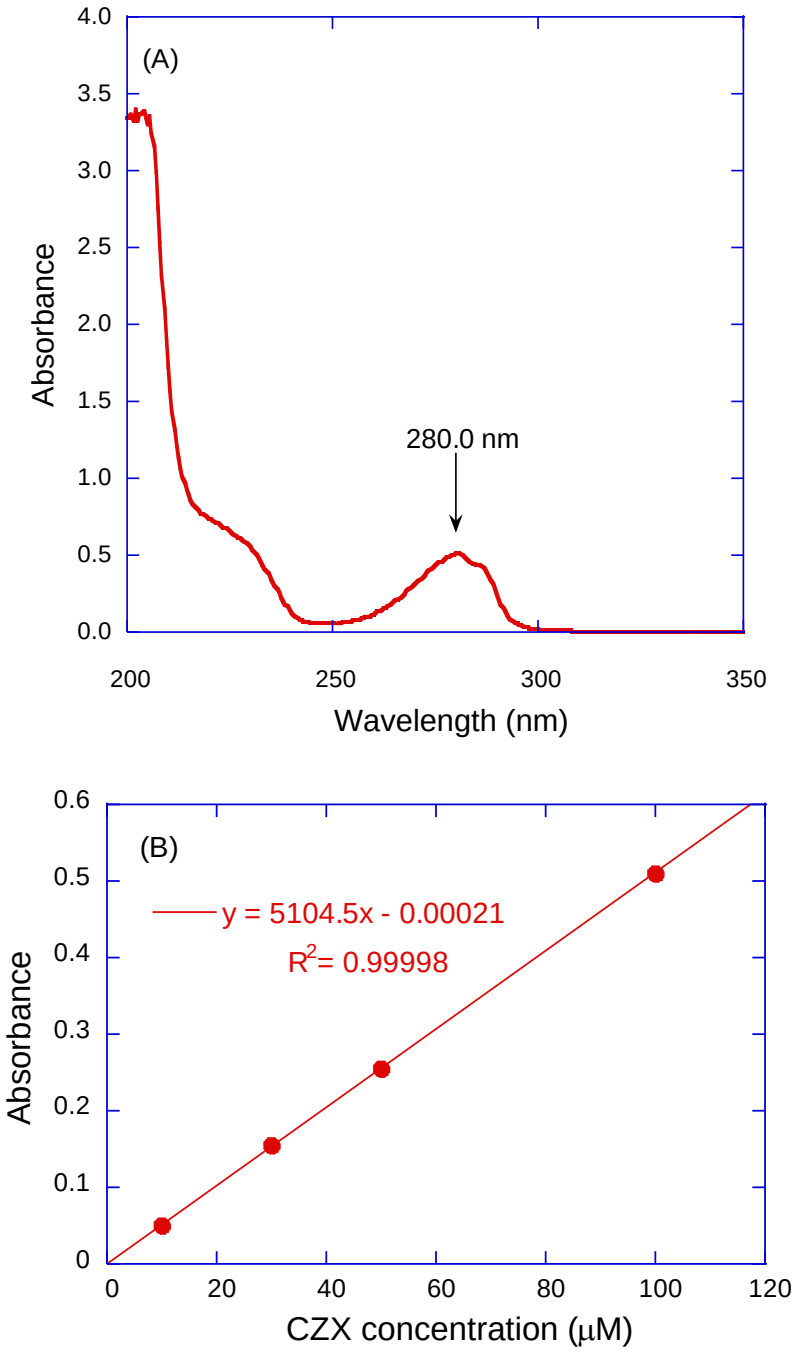

Figure S1. (A) Absorption UV-visible spectrum of CZX solution (0.1 mM). (B) Absorbance versus concentration graph. The line was determined by least squares linear fitting. In the equation of the graph, *x* and *y* correspond to CZX concentration and the absorbance, respectively.

Additional Description for Reconstruction of Electron Density Profiles

In order to calculate the integrated intensities ($I_{\mathrm{obs}}(h)$), the fitting of X-ray lamellar diffraction peaks was performed by using non-linear fitting module of KaleidaGraph 4.5 software (Japanese version). The fitting software is based on the Levenberg-Marquardt algorithm (see. http://www.synergy.com/Tools/curvefitting.pdf.).

After normalization of the observed structure factors ($|F_{\mathrm{obs}}(h)|=\sqrt{\alpha h^2 I_{\mathrm{obs}}(h)}$), we plotted these values ($|F_{\mathrm{obs}}(h)|$) against Q. Considering both the tendencies of the scattering of data in the plots and already known phase angles of pure POPC bilayers, we first roughly decided the phase angle for the each data, i.e., + or – and then, we drew the curves by using Shannon sampling theorem ($F(Q)=\sum F_{\mathrm{obs}}(h)\,\mathrm{sinc}\left(\frac{dQ}{2}-h\pi\right)$). When there were some data points that did not lay on the curves, we changed the sign of several data. This process is not logical, and trial and error is needed. We decided the final phase angle set in order that all data points should come as close as possible to the curve (Figure S2).

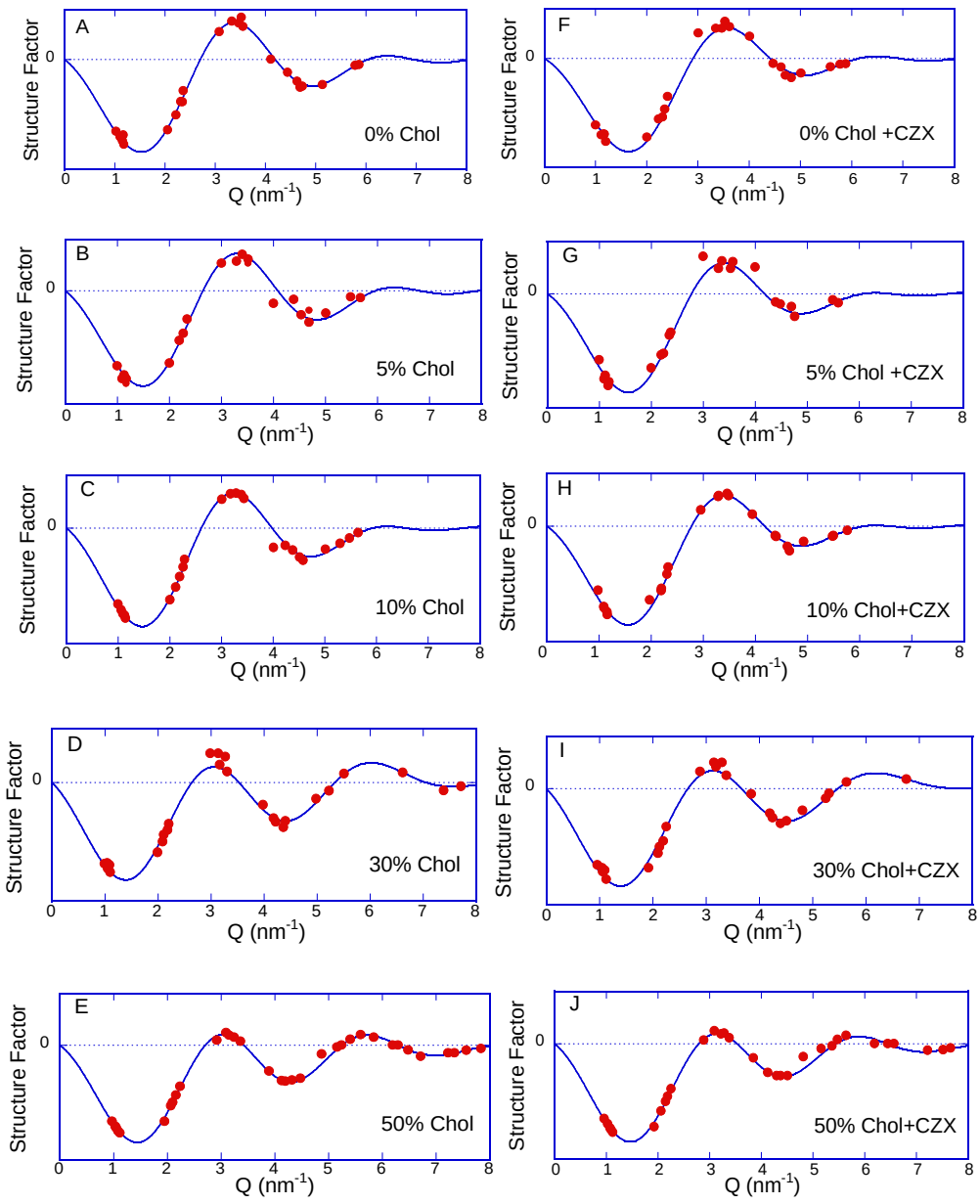

Figure S2. Phase assignment by the swelling method. Normalized structure factors ($F_{\mathrm{obs}}(h)$) calculated from the observed lamellar diffraction intensity data are plotted against the scattering vector magnitude (Q). The solid curves are the continuous Fourier transform calculated using Shannon's sampling theorem with the data obtained in the presence of PVP 30% except for the samples containing 30mol% cholesterol. For the samples, the data of PVP 50% were used. (A-E) Samples without CZX, and (F-J) samples with CZX. The molar concentrations of cholesterol are shown in the figures.

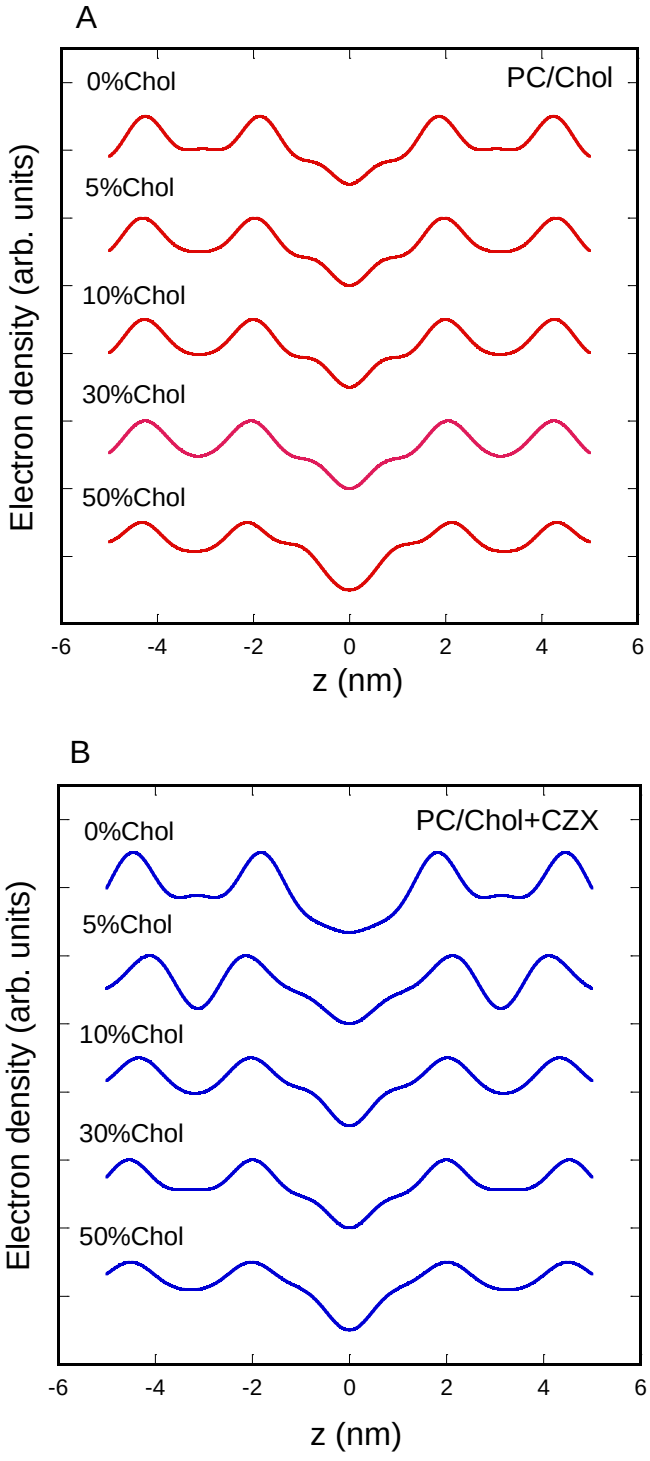

Figure S3. Electron density profiles for POPC/cholesterol bilayer samples (A) without CZX and (B) with CZX. The molar concentrations of cholesterol are shown in the figures. The values of the vertical axis of each profile are arbitrary units and cannot be compared.

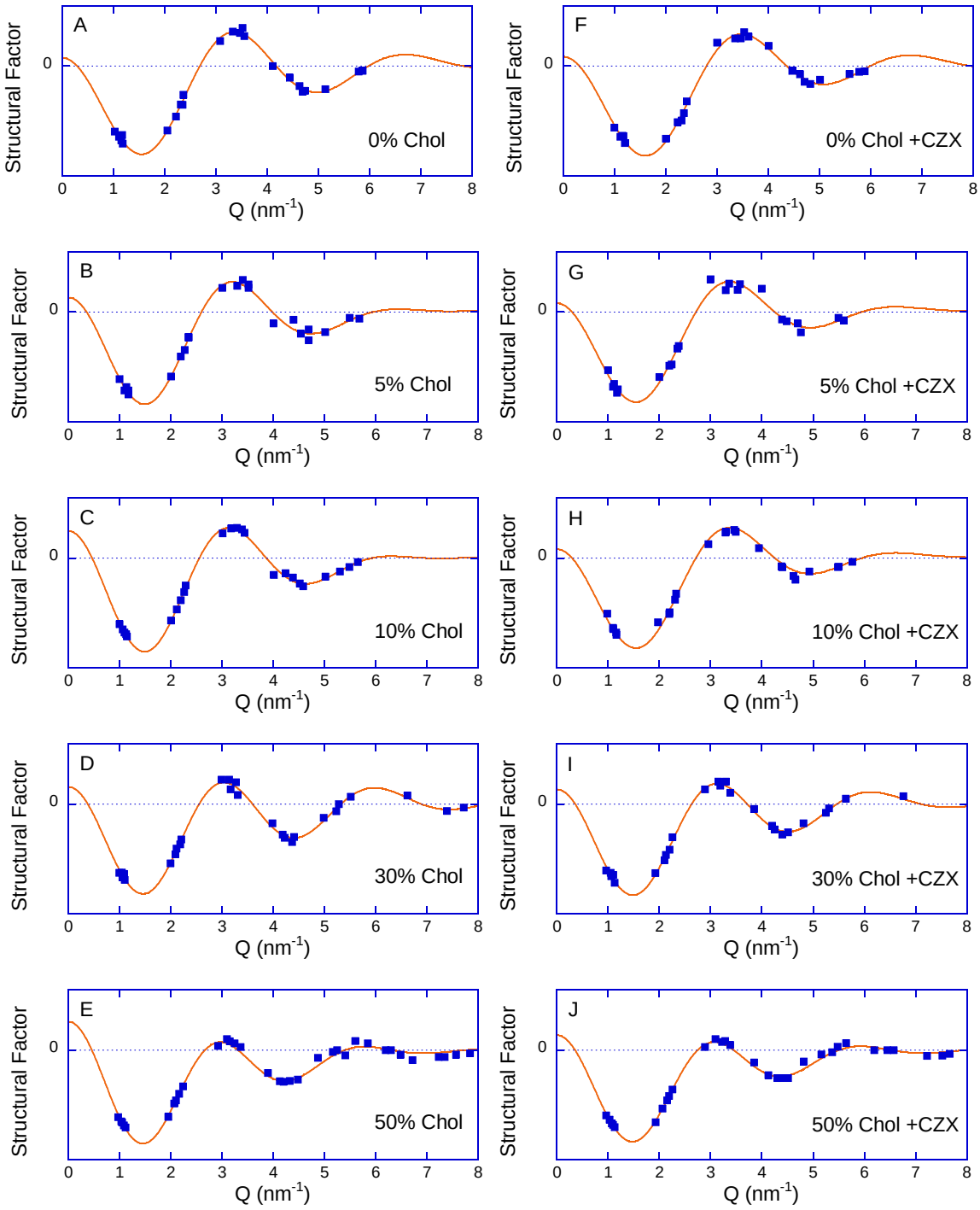

Figure S4. Comparison between normalized experimental structure factors ($F_{\mathrm{obs}}(h)$) and the theoretical structure factor ($F_{\mathrm{cal}}(Q)$) curves calculated from the model electron density profiles with best fit parameters (see text). (A-E) Samples without CZX, and (F-J) samples with CZX. The molar concentrations of cholesterol are shown in the figures.