Supporting Information

for

Structural Evolution of Environmentally Responsive Cationic Liposome–DNA Complexes with a Reducible Lipid Linker

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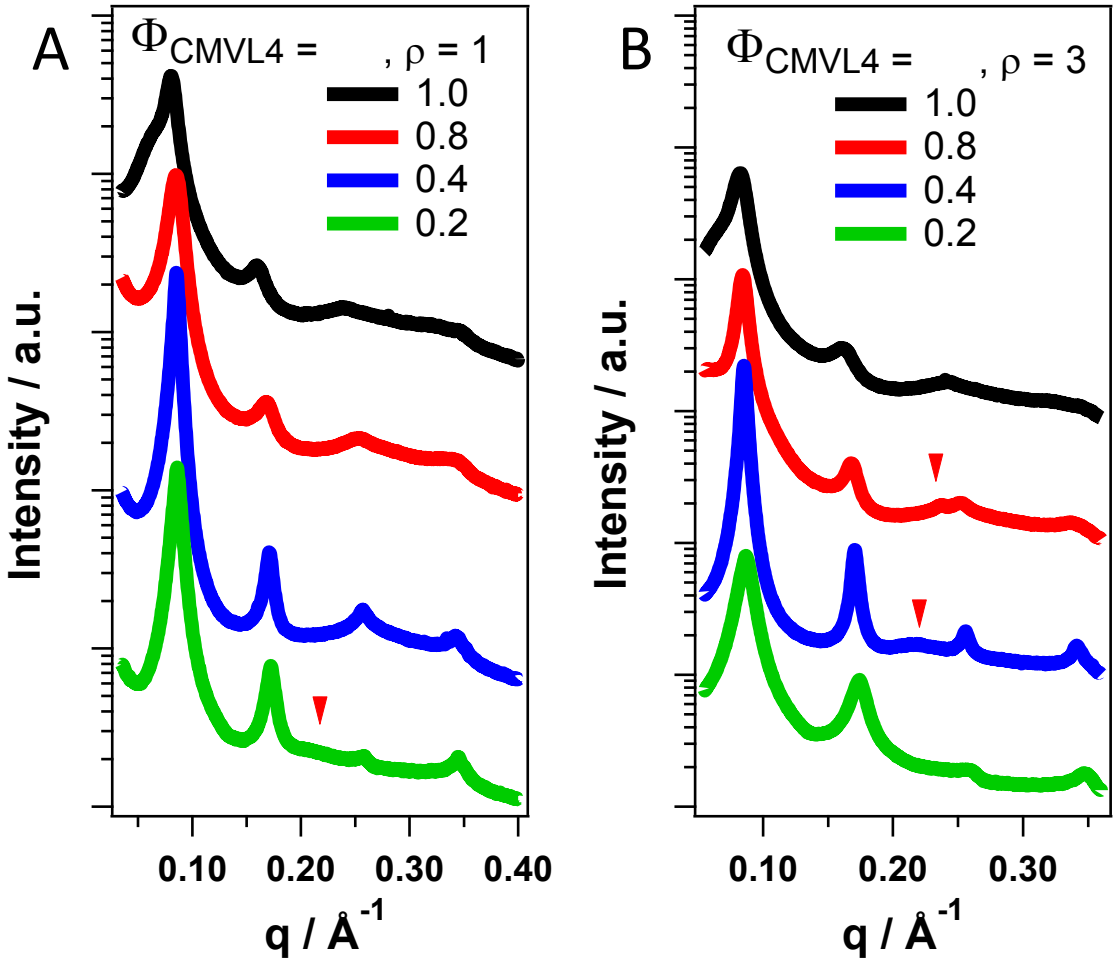

Figure S1. SAXS patterns of CMVL4/DOPC–DNA complexes at Φ_{CMVL4} = 0.2, 0.4, 0.8, and 1 at room temperature in nonreducing media for ρ = 1 (A) and ρ = 3 (B). The patterns are characteristic for lamellar complexes. Red arrowheads point to q_{DNA}.

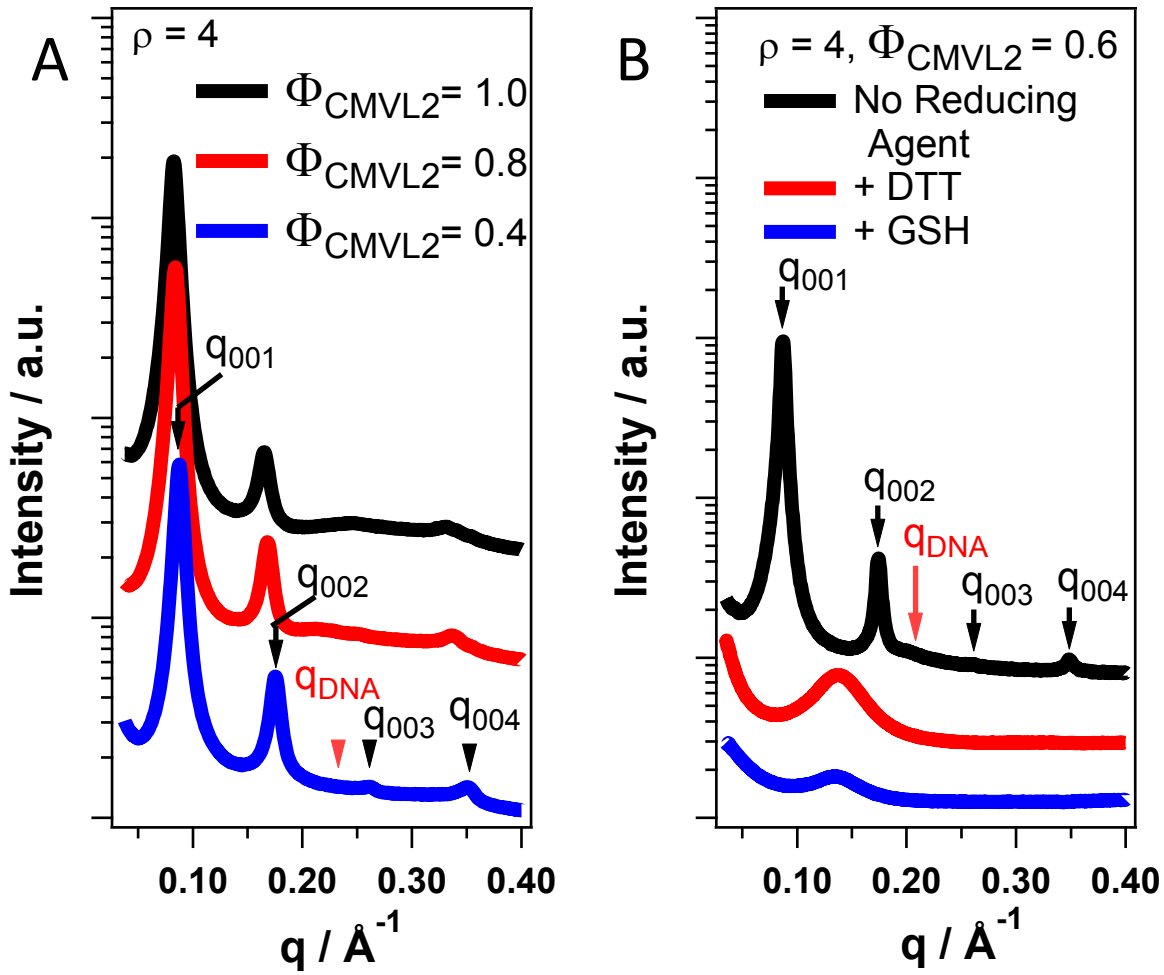

Figure S2. SAXS patterns of positively charged (ρ = 4) CMVL2/DOPC–DNA complexes at room temperature in reducing and nonreducing media. (A) SAXS data for complexes of varied Φ_{CMVL2} (0.4, 0.8, and 1.0) in nonreducing media. The complexes are lamellar, as indicated by the characteristic peaks of the lamellar phase at q_{00n} (black arrows) and DNA–DNA correlation q_{DNA} (red arrow). (B) The scattering pattern of complexes at $\Phi_{CMVL2} = 0.6$ in nonreducing media (black curve, top) also shows the characteristic peaks of the lamellar phase at q_{00n} (black arrows) and q_{DNA} (red arrow). Upon addition of the reducing agent DTT (red curve, middle) or GSH (blue curve, bottom) the lamellar peaks are replaced by a broad peak at $q \approx 0.14$ Å^{-1}.

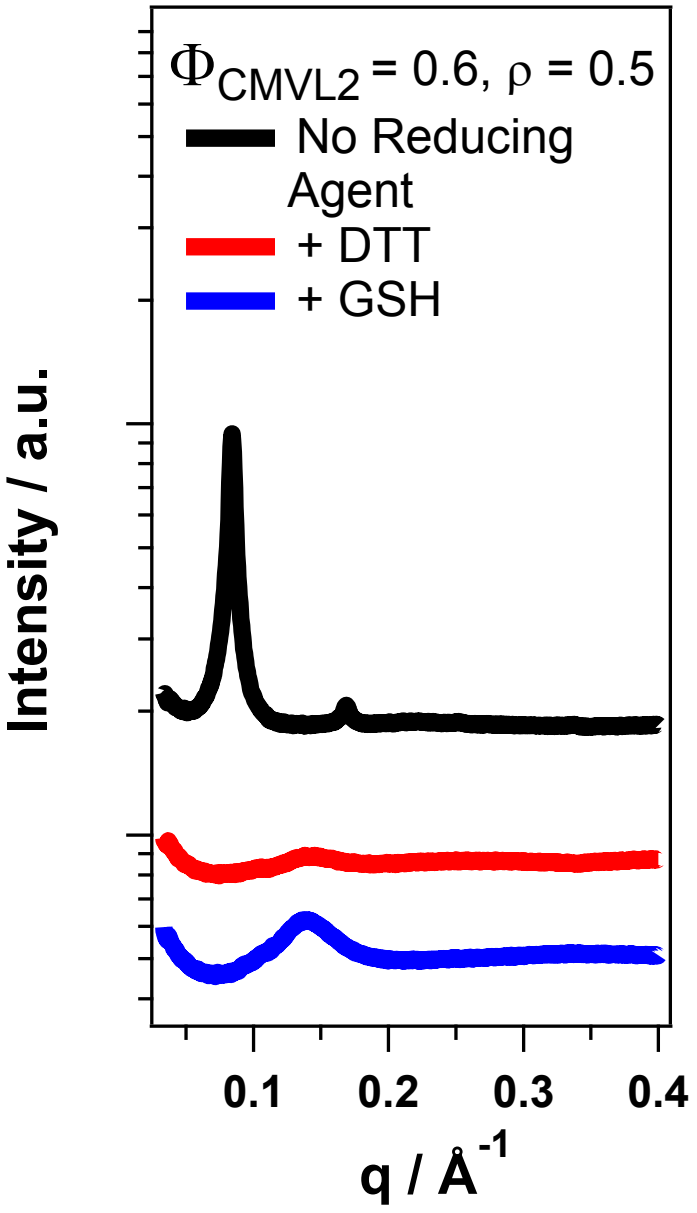

Figure S3. SAXS patterns demonstrating the effect of reducing agent on the structure of anionic and isoelectric (ρ = 0.5 and 1, respectively) CMVL2/DOPC–DNA complexes (Φ_{CMVL2} = 0.6). Anionic CMVL2/DOPC–DNA complexes (ρ = 0.5) in nonreducing media (black curve, top) display a scattering pattern characteristic for lamellar complexes. After addition of the reducing agents DTT (red curve, middle) or GSH (blue curve, bottom) at room temperature, the lamellar peaks are replaced by a broad peak at $q \approx 0.14$ Å^{-1}.

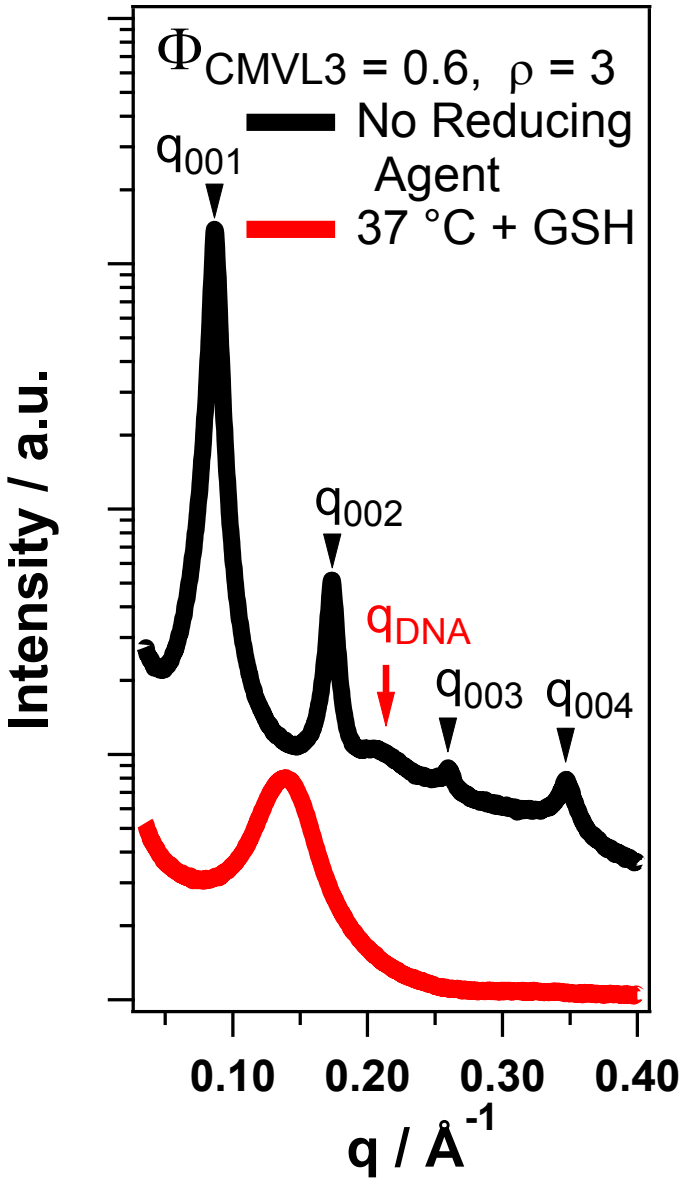

Figure S4. SAXS patterns demonstrating the effect of reducing agent on the structure of CMVL3/DOPC–DNA complexes at $\rho = 3$ and $\Phi_{CMVL3} = 0.6$. The CMVL3/DOPC–DNA complexes in nonreducing media (black curve, top) display a scattering pattern characteristic for lamellar complexes. Upon incubation with the reducing agent GSH at 37 °C, the lamellar peaks are replaced by a broad peak at $q \approx 0.14$ Å^{-1}.

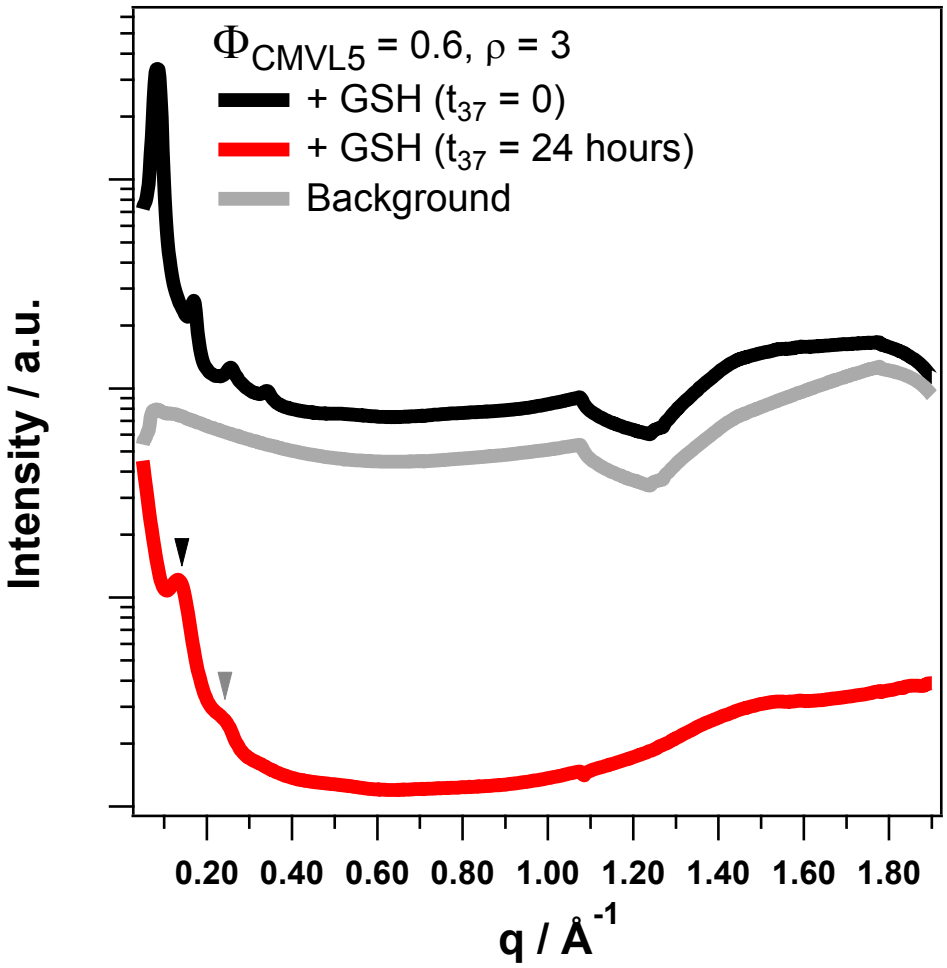

Figure S5. Time evolution of the synchrotron X-ray scattering profiles (small and wide angle) of CMVL5/DOPC–DNA complexes at $\rho = 3$ and $\Phi_{CMVL5} = 0.6$ on incubation with the reducing agent GSH at 37 °C. Immediately after addition of GSH (t = 0; red curve, top), the sample still displays a scattering pattern characteristic for lamellar complexes (q_{001} = 0.0825 Å^{-1}). Note that the comparison of this pattern with the corresponding scattering background shows that the dip in scattering intensity between q = 1 and 1.4 Å^{-1} is an artifact. The absence of sharp peaks at large q indicates that the lipid tails are in the chain-melted phase. After 24 hours of incubation at 37 °C (green curve, bottom), the sharp peaks of the lamellar phase have been replaced by broad peaks at q = 0.134 Å^{-1} and q = 0.235 (arrowheads). The absence of sharp wide-angle peaks demonstrates that the lipid tails remain in the chain-melted phase, in contrast to what we observed with the reducing agent DTT (cf. manuscript).

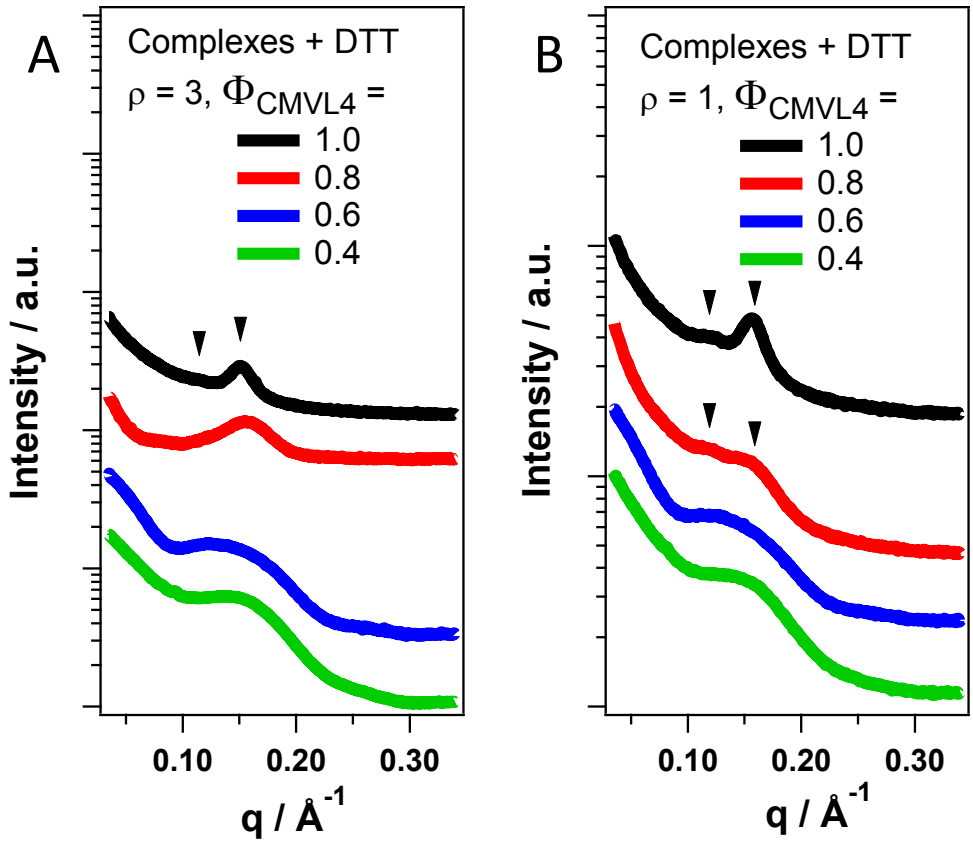

Figure S6. Synchrotron SAXS profiles of positively charged (A) and isoelectric (B) CMVL4/DOPC–DNA complexes (ρ = 3 and ρ = 1, respectively) at varied Φ_{CMVL4} after treatment with the reducing agent DTT at room temperature. At low Φ_{CMVL4} of 0.4 (green curves) and 0.6 (blue curves), i. e., high DOPC content, the SAXS profiles appear to show one very broad peak at $q \approx 0.15$ Å^{-1}. At higher Φ_{CMVL4}, this peaks resolves into two broad peaks, at $q = 0.12$ Å^{-1} and $q = 0.156$ Å^{-1}. The data is consistent with our hypothesis that the broad peak at $q = 0.156$ Å^{-1} is the DNA–DNA correlation peak resulting from the "loosely organized" DNA–CMVL headgroup phase, while the peak at $q = 0.12$ Å^{-1} stems from a disordered (defect-rich) lamellar phase of bilayers containing DOPC and the cleaved CMVL tails. The amount of DNA (and thus CMVL at a given ρ) per sample is constant, which means that the amount of DOPC and therefore the membrane volume increases with decreasing Φ_{CMVL4}. Thus, for low Φ_{CMVL4}, the broad peak stemming from the disordered lamellar phase at $q = 0.12$ Å^{-1} increases in intensity, merging with the peak at $q = 0.156$ Å^{-1} (whose intensity does not change with Φ_{CMVL4}) and covering it.

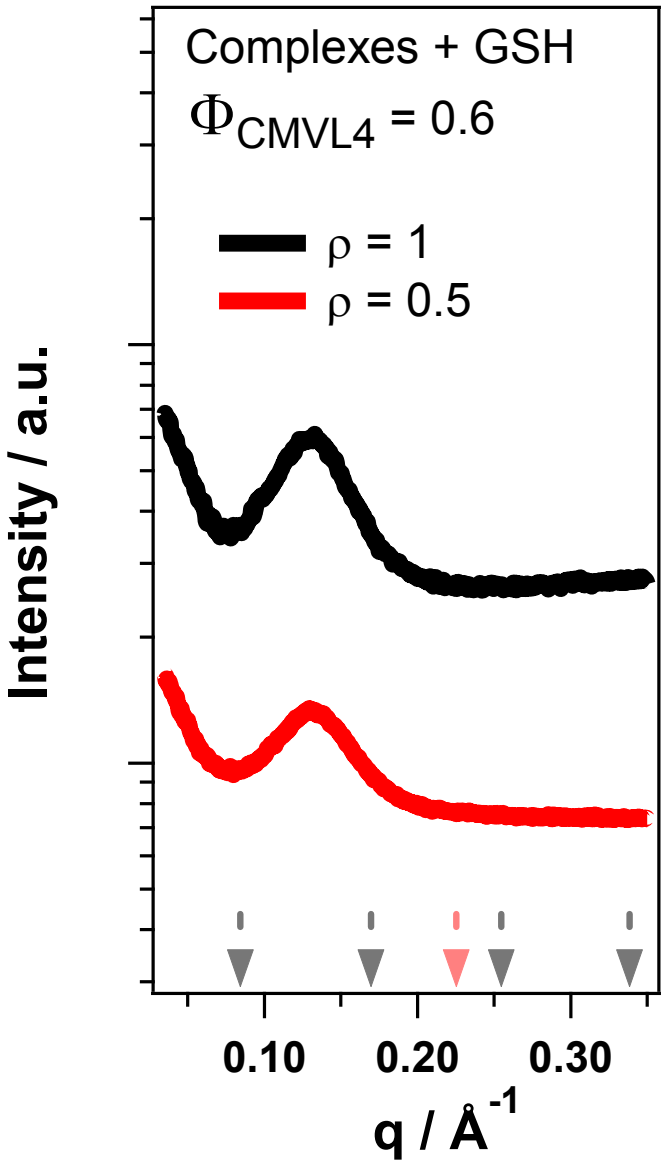

Figure S7. Synchrotron SAXS profiles of negatively charged (bottom) and isoelectric (top) CMVL4/DOPC–DNA complexes (ρ = 0.5 and ρ = 1, respectively) at Φ_{CMVL4} = 0.6 after treatment with the reducing agent GSH at 37 °C for hours. The scattering patterns exhibit a broad peak at $q \approx 0.13$ Å^{-1} and no reflections stemming from a lamellar phase.