Supporting Information

Binding Affinity of Inorganic Mercury and Cadmium to Biomimetic Erythrocyte Membranes

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Calculation of the [LUV]

1) Under our experimental conditions, only the outer leaflet of LUVs is available for metal binding. Due to the curvature of a membrane, more lipids (~55%) are found on the outer layer to reduce headgroup crowding on the inner layer [1]. Multiplying the total concentration of phospholipids in solution by 0.55 yielded the available number of phospholipids ($[L]_{available}$) for metal binding.
2) The surface area of each LUV was calculated by assuming a spherical shape and using the radius of the LUV as determined by DLS.
3) Assuming that each phospholipid occupies a surface area of ~ 68 $Å^2$ [2] the number of phospholipids in the outer leaflet ($N_{lipids\ OL}$) of each LUV was estimated by dividing the surface area determined in step 2 by the surface area of each phospholipid headgroup.
4) The concentration of LUVs was calculated as:

$$[LUV] = \frac{[L]_{available}}{N_{lipids\ OL}} \quad (1)$$

Table S1. Lipid systems used in isothermal titration calorimetry experiments and their respective average sizes as measured using dynamic light scattering. [LUVs] was determined as explained in section 2.6.

Lipid System	LUV Radius (nm)	[LUVs] at 1.65 mM lipid (nM)
PC	51.6 ± 3.0	37.4 ± 4.0
PC : PE	52.5 ± 0.9	33.9 ± 0.6
PC : PS	48.9 ± 1.6	38.0 ± 2.4

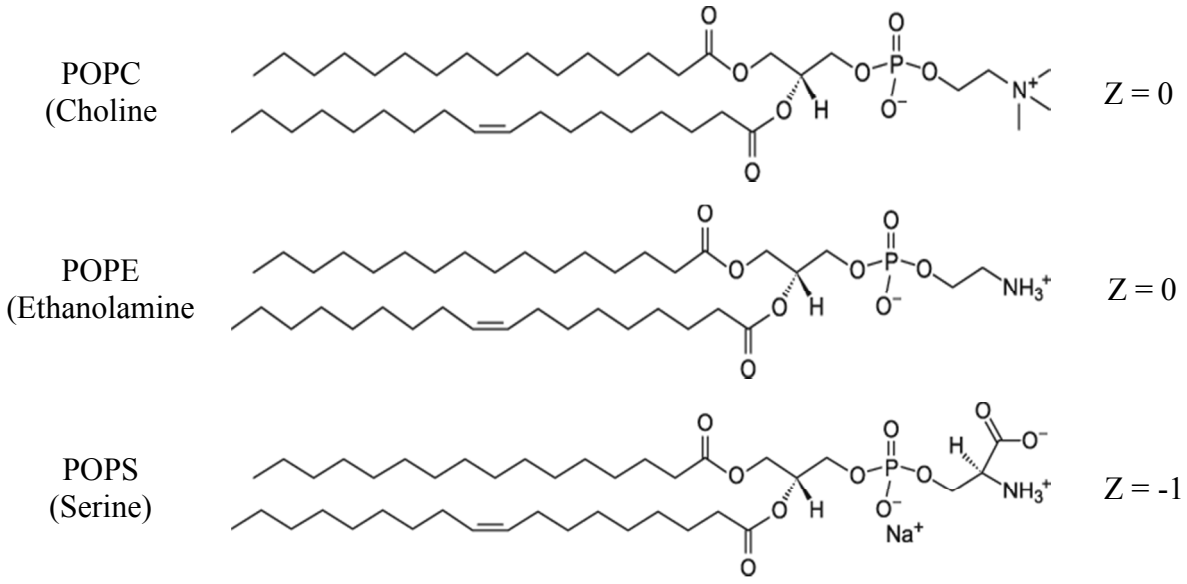

Figure S1. Structure of lipids used in this study. Z represents the overall charge of each lipid. POP- = Palmitoyl (16:0) oleoyl (18:1) phospho-.

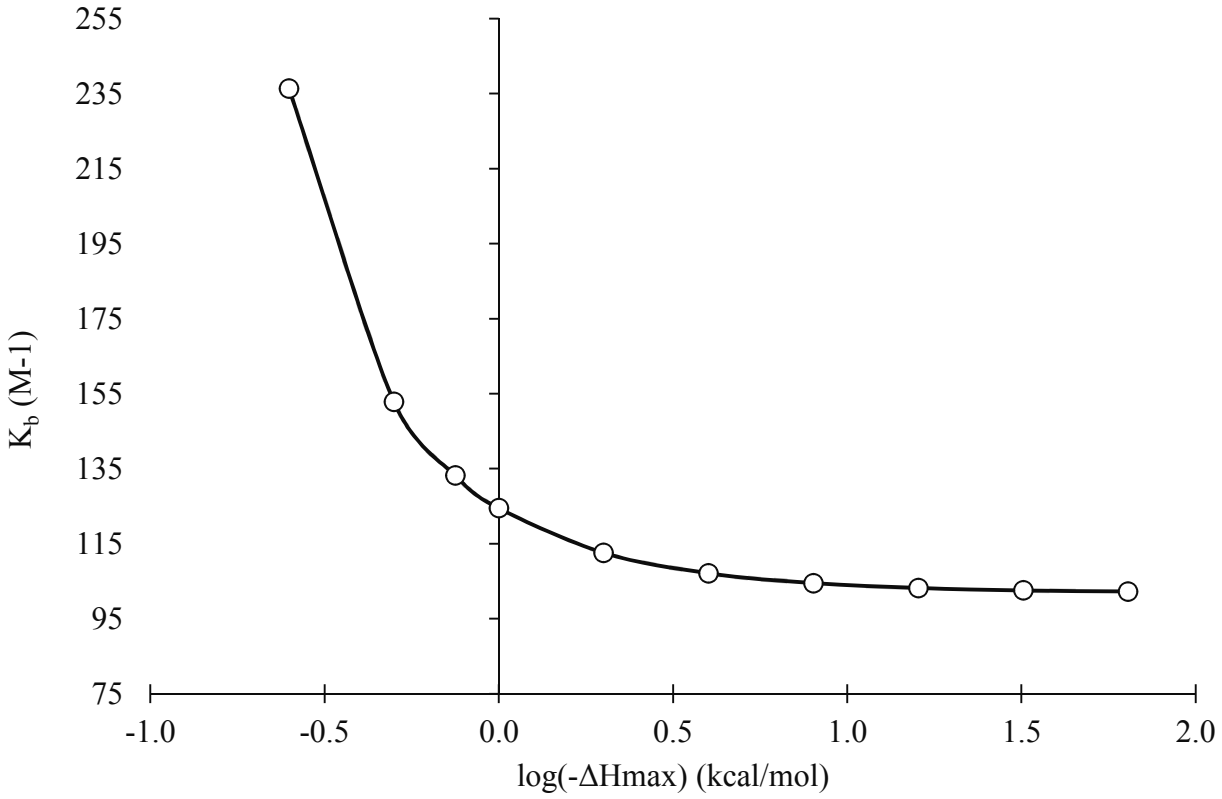

Figure S2. Calculation of K_b of Hg binding to 85/15 POPC/POPS.

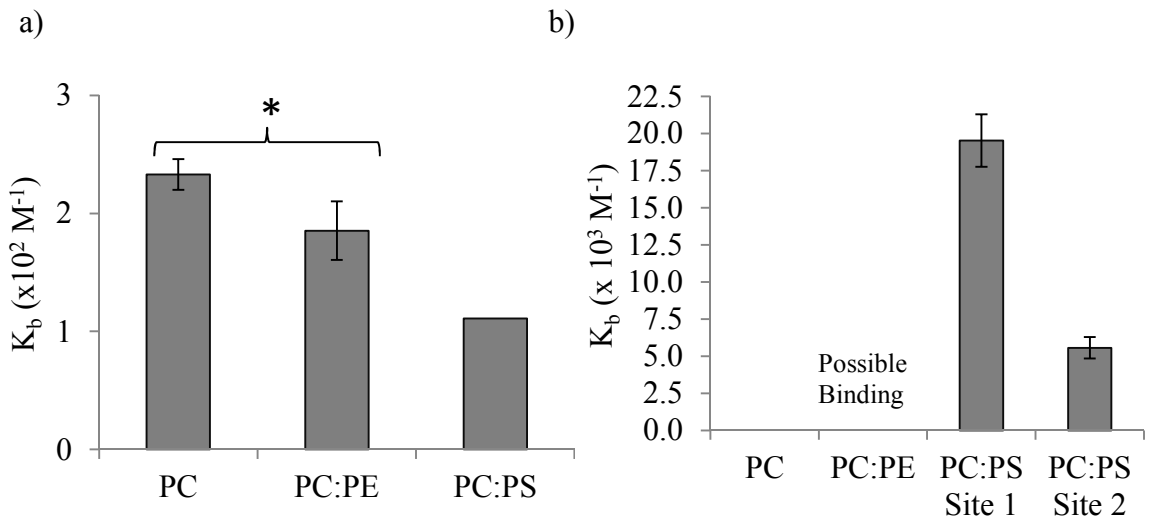

Figure S3. Summary of binding constants of a) Hg and b) Cd interactions with various model membranes. * = $p < 0.05$

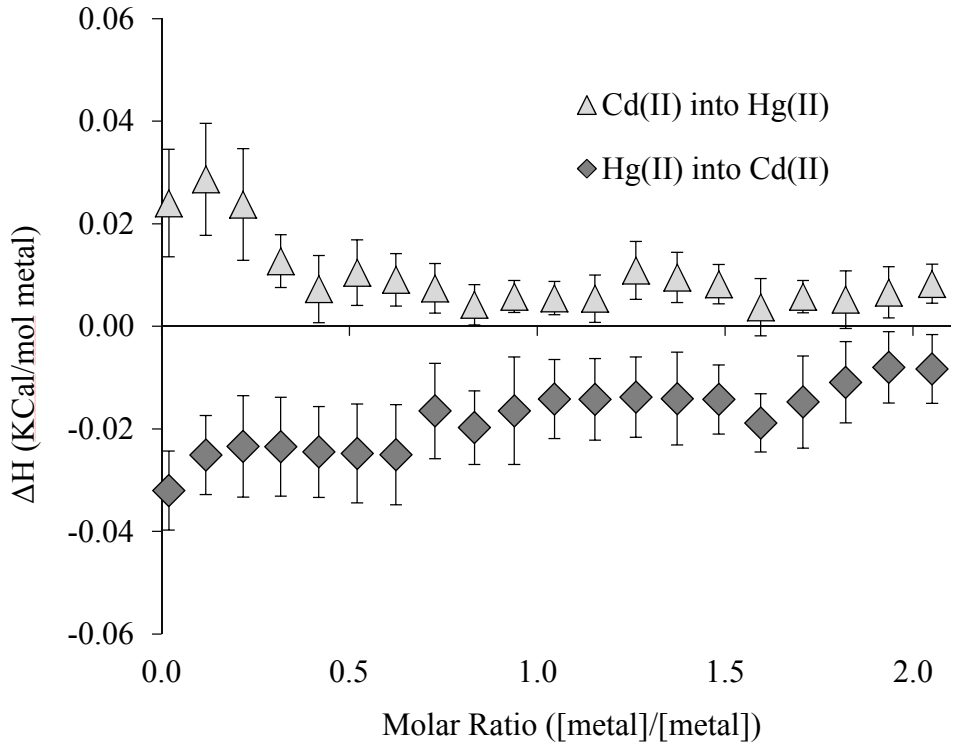

Figure S4. Isothermal titration calorimetry experiments of 10 mM Cd injections into 1 mM Hg and vice versa. All trials conducted in 100 mM NaCl adjusted to pH 7.4 at 37 °C.

References

(1) Marquardt, D.; Geier, B.; Pabst, G. Asymmetric Lipid Membranes: Towards More Realistic Model Systems. *Membranes* **2015**, *5* (2), 180–196.

(2) Kučerka, N.; Tristram-Nagle, S.; Nagle, J. F. Structure of Fully Hydrated Fluid Phase Lipid Bilayers with Monounsaturated Chains. *Journal of Membrane Biology* **2006**, *208* (3), 193–202.