

**Modelling the Adsorption of Phospholipid Vesicles to a Silicon Dioxide Surface using
Langmuir Kinetics**

Supporting Information

Iad Alhallak,^a Peter J. N. Kett^a

^a Department of Chemistry, Hendrix College, 1600 Washington Avenue, Conway, Arkansas
72032.

Error Analysis

Calculating the Error in Δf_{max}

The error in Δf_{max} , $e_{\Delta f_{max}}$, is given by,

$$e_{\Delta f_{max}} = \frac{1}{b^2} e_b \quad \#(S1)$$

where b and e_b are the y-intercept, and the error in the y-intercept of the graph of Δf_{eq}^{-1} against $[DOPC]^{-1}$ (Figure 3).

Calculating the Error in K

The error in the equilibrium constant, e_K , is given by,

$$e_K = \left| \frac{1}{m \Delta f_{max}} \right| \sqrt{\left(\frac{e_m}{m} \right)^2 + \left(\frac{e_{\Delta f_{max}}}{\Delta f_{max}} \right)^2} \quad \#(S2)$$

where m and e_m are the slope, and the error in the slope of the graph of Δf_{eq}^{-1} against $[DOPC]^{-1}$ (Figure 3).

Calculating the Error in k_d

The error in the rate constant for desorption, e_{k_d} , is given by,

$$e_{k_d} = \frac{1}{K} \sqrt{\left(\frac{k_a}{K} e_K \right)^2 + e_{k_a}^2} \quad \#(S3)$$

where e_{k_a} is the error in the rate constant for adsorption k_a .

Equation Derivation

Relationship Between Surface Coverage and Frequency Change

The frequency change at any time, Δf_t , is linearly related to the adsorbed mass, $m_{adsorbed}$,

$$\Delta f_t = -R m_{adsorbed} \quad \#(S4)$$

where R is the linear response factor. The adsorbed mass depends on the number of vesicles on the surface, $n_{vesicles}$, and the mass per vesicle including any trapped buffer, $m_{vesicle}$,

$$\Delta f_t = -Rm_{adsorbed} = -R(n_{vesicles} \times m_{vesicle}) = -Rn_{vesicles}m_{vesicle} \#(S5)$$

The surface coverage at time t , θ_t , is the ratio of the number of adsorbed vesicles at time t to the maximum number of vesicles that can adsorb to the surface, n_{max} , and thus,

$$\Delta f_t = -R(\theta_t \times n_{max})m_{vesicle} = -R\theta_t n_{max}m_{vesicle} \quad \text{as } \theta_t = \frac{n_{vesicles}}{n_{max}} \#(S6)$$

The maximum frequency change, Δf_{max} , occurs when $n_{vesicles} = n_{max}$ and $\theta_t = 1$ such that,

$$\Delta f_{max} = -Rn_{max}m_{vesicle} \#(S7)$$

Substituting equation S7 into equation S6 gives a relationship between surface coverage and frequency change,

$$\Delta f_t = (-Rn_{max}m_{vesicle})\theta_t = \Delta f_{max}\theta_t \quad \text{or} \quad \theta_t = \frac{\Delta f_t}{\Delta f_{max}} \#(S8)$$

To derive this equation we have assumed that the mass change that occurs on the addition of each new vesicle to the surface is the same. Bingen et al. and Tellechea et al. have shown that when a heterogeneous film is adsorbed to a surface the amount of water coupled to the adsorbate is coverage dependent and that as θ increases the amount of water coupled to the film decreases, so that the mass of each vesicle cannot be considered to be fully independent of surface coverage.^{1,2} To fully account for the effect of the changes in hydration on the mass of the adsorbed film it is therefore necessary to use a complementary technique, such as DPI³ that can discriminate between the “wet” and “dry” mass adsorbed on the surface which is something that cannot be done with a QCM alone, and is thus beyond the scope of this work. As such, assuming that the mass change that occurs on the adsorption of each vesicle is independent of the surface coverage will introduce a small error to our calculated values.⁴⁻⁶

Relationships Between Frequency Change and Time, and Frequency Change at Equilibrium and Lipid Concentration

The relationship between surface coverage, lipid concentration, and time is given by Equation 7. Substituting in the expression which relates surface coverage to frequency change (Equation S8) gives,

$$\frac{\Delta f_t}{\Delta f_{max}} = \theta_{eq} \left(1 - e^{-k_a \left([S] + \frac{1}{K} \right) t} \right)$$

$$\Delta f_t = \Delta f_{max} \theta_{eq} \left(1 - e^{-k_a \left([S] + \frac{1}{K} \right) t} \right) = -R n_{max} m_{vesicle} \times \frac{n_{eq}}{n_{max}} \left(1 - e^{-k_a \left([S] + \frac{1}{K} \right) t} \right)$$

$$\Delta f_t = -R m_{vesicle} n_{eq} \left(1 - e^{-k_a \left([S] + \frac{1}{K} \right) t} \right) = \Delta f_{eq} \left(1 - e^{-k_a \left([L] + \frac{1}{K} \right) t} \right) \#(S9)$$

where Δf_{eq} is the frequency change at equilibrium. Likewise, an equation relating the frequency change at equilibrium to the lipid concentration, $[L]$, can be achieved by substituting Equation S8 into Equation 6,

$$\frac{1}{\left(\frac{\Delta f_{eq}}{\Delta f_{max}} \right)} = \frac{1}{K[L]} + 1$$

$$\frac{\Delta f_{max}}{\Delta f_{eq}} = \frac{1}{K[S]} + 1 = \frac{1 + K[S]}{K[S]}$$

$$\frac{\Delta f_{eq}}{\Delta f_{max}} = \frac{K[S]}{1 + K[S]}$$

$$\Delta f_{eq} = \Delta f_{max} \frac{K[S]}{1 + K[S]} \#(S10)$$

as $\Delta f_{eq} = \Delta f_{max} \theta_{eq}$ (Equation S9).

Solution of the “Mixing Tank” Differential Equation

In the “mixing tank” differential equation the rate of change of mass of lipid in the flow-cell, m_{lipid} , is the difference between the rate at which the lipids enter and exit the flow-cell:

$$\frac{dm_{lipid}}{dt} = F[L] - \frac{F}{V}L = \frac{F}{V}([L]V - m_{lipid}) \#(S11)$$

where F is the flow rate, $[L]$ is the steady-state concentration of the solute, and V is the volume of the flow cell. Rearranging Equation S11 and integrating with the boundary condition that the lipid concentration is zero at $t = 0$ one obtains:

$$[L]_t = [L](1 - e^{-tF/V}) = [L](1 - e^{-\alpha t}) \quad \alpha = \frac{F}{V} \#(S12)$$

where $[L]_t$ is the concentration of lipid in the flow-cell at time t , and is given by m_{lipid}/V .

Differential Equation Relating Frequency Change to Time when the Flow Cell does not Reach Steady-State Concentration Instantaneously

Equation 14 describes the rate of change of the surface coverage with respect to time when it is assumed that the steady-state concentration of the lipid vesicles in the flow-cell is not achieved instantaneously. Substituting equation S8 into Equation 14 gives,

$$\frac{d}{dt}\left(\frac{\Delta f}{\Delta f_{max}}\right) = k_a[L](1 - e^{-\alpha t})\left(1 - \frac{\Delta f}{\Delta f_{max}}\right) - k_d\frac{\Delta f}{\Delta f_{max}}$$

$$\frac{1}{\Delta f_{max}} \frac{d\Delta f}{dt} = \frac{1}{\Delta f_{max}} \{k_a[L](1 - e^{-\alpha t})(\Delta f_{max} - \Delta f) - k_d\Delta f\}$$

$$\frac{d\Delta f}{dt} = k_a[L](1 - e^{-\alpha t})(\Delta f_{max} - \Delta f) - k_d\Delta f \quad \#(S13)$$

As the equilibrium constant, K , is the ratio of the rate constants for adsorption and desorption, equation S13 can be simplified to,

$$\frac{d\Delta f}{dt} = k_a \left\{ [L](1 - e^{-\alpha t})(\Delta f_{max} - \Delta f) - \frac{1}{K}\Delta f \right\} \quad \#(S14)$$

Using the values for Δf_{max} and K obtained in this study, equation S14 can be rewritten as,

$$\frac{d\Delta f}{dt} = k_a \left\{ [L](1 - e^{-\alpha t})(-350 - \Delta f) - \frac{1}{18}\Delta f \right\} \quad \#(S15)$$

Equations Relating Surface Coverage and Frequency Change to Time when $k_d = 0$ and Flow Cell does not Reach Steady-State Concentration Instantaneously

The differential equation describing the rate of change of the surface coverage with respect to time when there is a finite time required to reach the steady state concentration of lipid in the flow-cell is given by Equation 15. When there is no desorption of lipids from the surface such that $k_d = 0$, equation 15 simplifies down to,

$$\frac{d\theta}{dt} = k_a[L](1 - e^{-\alpha t})(1 - \theta) \quad \#(S16)$$

Rearranging this equation and setting the boundary condition that the surface coverage is zero at $t = 0$ leads to:

$$\int_0^\theta \frac{1}{1 - \theta} d\theta = k_a[L] \int_0^t (1 - e^{-\alpha t'}) dt' \quad \#(S17)$$

where t' is a dummy variable. The solution to this equation is given by,

$$\theta_t = 1 - e^{-k_a[L]\left\{t + \frac{1}{\alpha}(e^{-\alpha t} - 1)\right\}} \quad \#(S18)$$

As the change in frequency is linearly related to the surface coverage (Equation S8), the change in frequency is given by,

$$\begin{aligned} \Delta f_t &= -Rn_{max}m_{vesicle}\theta_t = -Rn_{max}m_{vesicle}\left(1 - e^{-k_a[L]\left\{t + \frac{1}{\alpha}(e^{-\alpha t} - 1)\right\}}\right) \\ &= \Delta f_{max}\left(1 - e^{-k_a[V]\left\{t + \frac{1}{\alpha}(e^{-\alpha t} - 1)\right\}}\right) \quad \#(S19) \end{aligned}$$

Using the equation for the maximum frequency change given above (Equation S8).

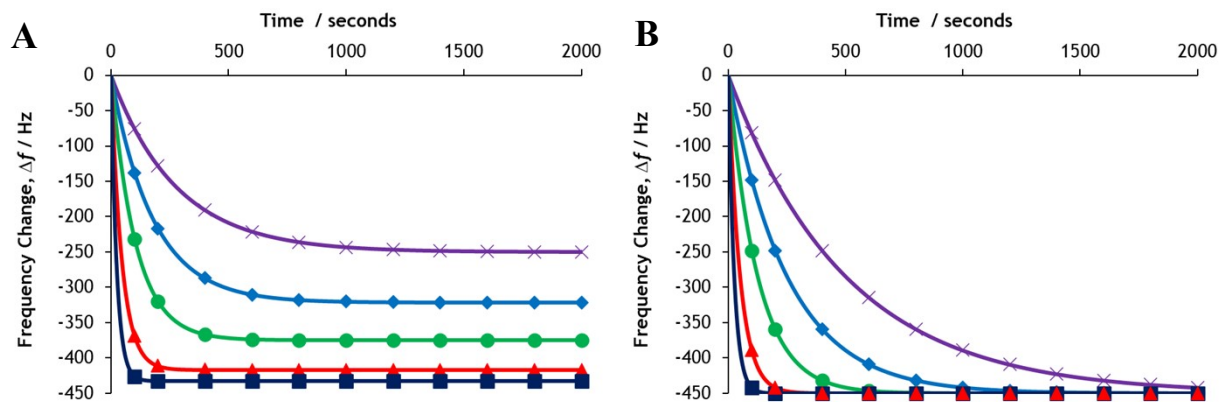


Figure S1. Changes in the frequency for the adsorption of vesicles to a surface if (A) there is desorption from the surface, or (B) there is no desorption from the surface, with $k_a = 0.04 \text{ mL mg}^{-1} \text{ s}^{-1}$, $k_d = 1.6 \times 10^{-3} \text{ s}^{-1}$ (and $K = 25$), $\Delta f_{\text{max}} = -450 \text{ Hz}$, and $[L] = 0.05 \text{ mg mL}^{-1}$ (purple line, X), 0.1 mg mL^{-1} (blue line, ◆), 0.2 mg mL^{-1} (green line, ●), 0.5 mg mL^{-1} (red line, ▲), or 1.0 mg mL^{-1} (black line, ■). The data presented were generated using (A) Equation 8a, and (B) Equation 9.

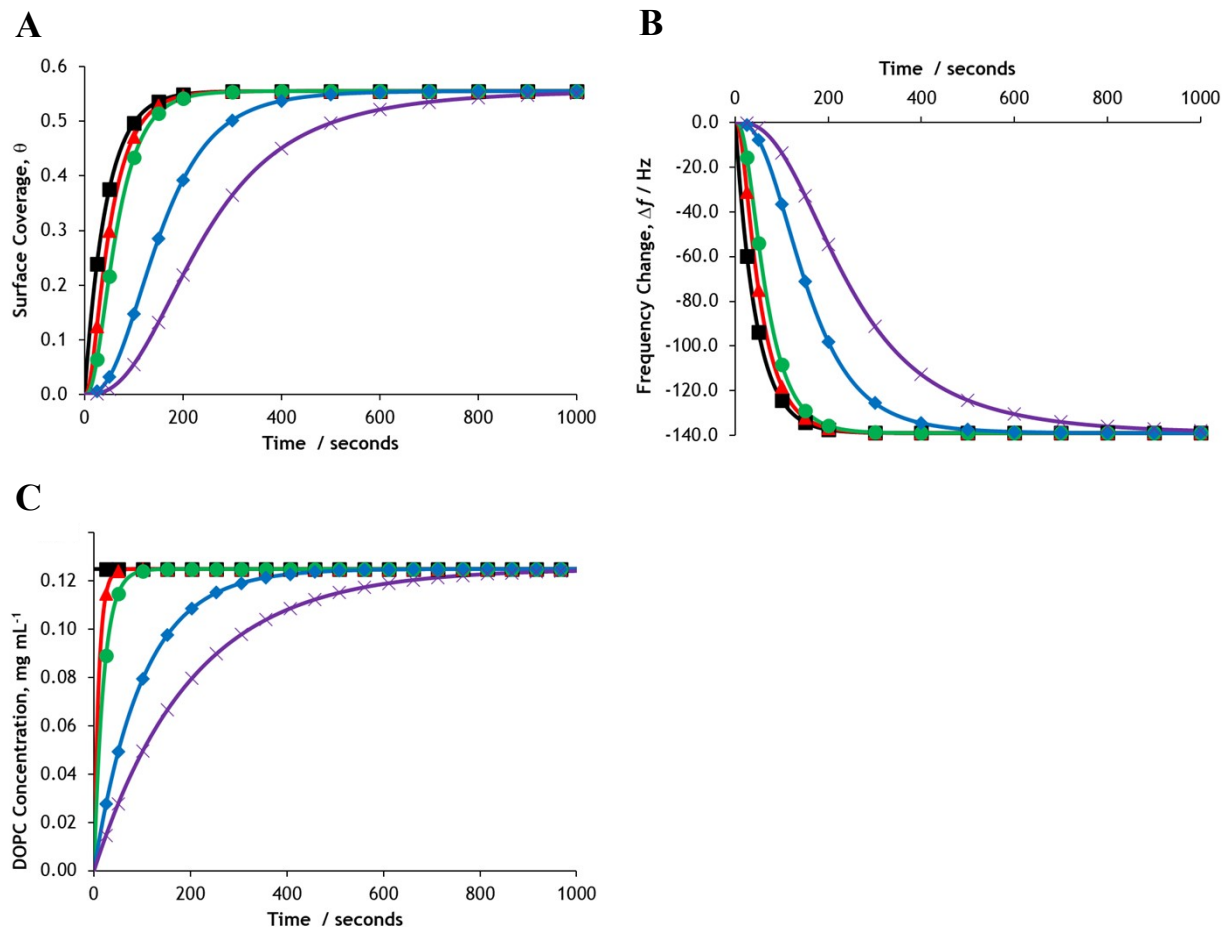


Figure S2. Changes in the (A) surface coverage, (B) frequency change, and (C) DOPC concentration, for the adsorption of vesicles to a surface with $\Delta f_{max} = -250 \text{ Hz}$, $[L] = 0.13 \text{ mg mL}^{-1}$, $k_a = 0.1 \text{ mL mg}^{-1} \text{ s}^{-1}$, and $k_d = 0.01 \text{ s}^{-1}$, with $\alpha = 0.005 \text{ s}^{-1}$ (red line, ▲), 0.01 s^{-1} (green line, ●), 0.05 s^{-1} (blue line, ◆) and 0.1 s^{-1} (purple line, X). For a flow cell with a volume of 0.15 mL this corresponds to flow rates of 2.7 mL hr^{-1} , 5.4 mL hr^{-1} , 27 mL hr^{-1} , and 54 mL hr^{-1} , respectively. The black line (■) represents the surface coverage, frequency change, and lipid concentration that would occur if the steady state concentration of the lipid were reached instantaneously upon introducing the lipid solution into the flow cell.

References

1. P. Bingen, G. Wang, N. F. Steinmetz, M. Rodahl, R. P. Richter, *Anal. Chem.*, 2008, **80**, 8880-8890.
2. E. Tellechea, D. Johannsmann, N. F. Steinmetz, R. P. Richter, I. Reviakine, *Langmuir*, 2009, **25**, 5177-5184.
3. T. J. Zwang, W. R. Fletcher, T. J. Lane, M. S. Johal, *Langmuir*, 2010, **26**, 4598-4601.
4. K. Kastl, M. Ross, V. Gerke, C. Steinem, *Biochemistry*, 2002, **41**, 10087-10094.
5. B. Wu, K. Wu, P. Wang, D.-M. Zhu, *J. Phys. Chem. C*, 2007, **111**, 1131-1135.
6. Y. Hussaina, J. Krim, C. Granta, *Colloids Surf., A*, 2005, **262**, 81-86.