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The Core Mathematical Error in the Protein-Ligand Binding Expression rotein-Ligand Binding Expression Receiving date: 2024, July 22 Accepting date: 2024, Aug 15 publishing date: 2024, Aug 27 **The Core Mathematical Error**

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Protein in solution in solution in solution can exist in the protein in the protein in solution can exist in the protein in the pro Manjunath. R, Department of Mathematics, India. **Communation:** $\mathbf{C} = \mathbf{C} \mathbf{C} \mathbf{C}$ Error in the Protein-Ligand Binding affinity for the ligand, a portion of the protein may bind to the protein may bind to the rest rest rest remains

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Abstract *reaction PL* ⇌ *P + L, with the equilibrium relationship defined by the dissociation constant and <i>represent* the initial total total

The dissociation of a **protein-ligand complex** (PL) can be represented by the equilibrium reaction $PL \rightleftharpoons P + L$, with the The aissociation of a **protein-ligand complex** (PL) can be represented by the equilibrium reaction $PL \cong P + L$, with the
equilibrium relationship defined by the dissociation constant K such that $K = \frac{[P][L]}{[PL]}$. In this eq [L] = [L]_T – [PL], where [P]_T and [L]_T represent the initial total concentrations of the protein and ligand, respectively. \mathfrak{r} \mathfrak{m}

Case1 becomes K = [] – []) [] – []

Case1
If we substitute [P]_T – [PL] for [P] and [L]_T – [PL] for [L], then equilibrium relationship becomes $K = \frac{([P]_T - [PL]) ([L]_T - [PL])}{[PL]}$. *From this, it follows that* $[PL] = \frac{[P][L]_T}{K+[P]}.$ initial total concentrations of the protein and ligand, respectively. The **dissociation constant** in equilibrium relationship becomes $K = \frac{(P(TT - [FL])}{[PL]}$.

Case2

Case2
If we substitute [L]_r – [PL] for [L], [P]_r – [PL] for [P], and [P]_r – [P] for [PL], the equilibrium relationship becomes $K = \frac{([P]_T - [PL]) (L]_T - [PL])}{[L]_T - [PL]}$ *From this it follows that* $K - [L] = K F_{FP} - F_{BP} [L]$ (which is an incorrect result). $K = \frac{(|P|_T - |PL|)(|L|_T - |PL|)}{[P|_T - |P|]}$ From this it follows that $K - |L| = K F_{FP} - F_{BP} |L|$ (which is an incorrect result). protein needed to achieve a significant level of interaction with the ligand. Specifically, when \mathcal{L} $K\dot{F}_{\text{FP}} - F_{\text{RP}}$ [L] (which is an incorrect result).

$$

To avoid obtaining incorrect results, substitutions for ' [PL] ' should not be used in conjunction with substitutions for ' [L] ' and ' [P] '. equilibrium relationship becomes K iii FBB is unitations for $[FLJ]$ *should not be used in confunction with substitutions f* and *f* [*P*] *l*. $A \rightarrow B$ is the canonical canonical can exist in two forms: bound and unbound and p chould not be used in conjunction with substitutions for $^{\prime}$ [H]. should not be used in conjunction with substitutions for ' [L] $\,$

Keywords: Protein-Ligand Binding, Protein-Ligand Complex, Equilibrium Reaction, Dissociation Constant *To avoid obtaining incorrect results, substitutions for ' [PL] ' should not be used in To avoid obtaining incorrect results, substitutions for ' [PL] ' should not be used in The Wards: Protein-Ligand Binding Protein-Ligand Complex Foullibrium Reaction Dissociation Constant* uilibrium Reaction, Dissociation Cons

conjunction with substitutions for ' [L] ' and ' [P] '. **1. Introduction 1. Introduction**

Depending on the protein's affinity for the ligand, a portion of the indicate stronger binding af A protein in solution can exist in two forms: bound and unbound. Should have a K value of $1 \times$ protein may bind to the ligand while the rest remains unbound. If the binding between the protein and ligand is reversible, a chemical equilibrium is established between the bound and 2 . Case 1 unbound states, represented by the reaction:

 $P(\text{protein}) + L(\text{ligand}) \rightleftharpoons PL(\text{protein-ligand complex})$ The dissociation constant for this equilibrium is: The dissociation constant for this equilibrium is:

$$
K=\frac{\left[P\right] \left[L\right] }{\left[PL\right] }
$$

In this equation, $[P] = [P]_T - [PL]$ and $[L] = [L]_T - [PL]$, where $[P]_T$ and $[L]_T$ represent the initial total concentrations of the Dividing throughout by [PL] g protein and ligand, respectively. The **dissociation constant** K is a key measure of a protein's affinity for its ligand. It indicates the $K = \frac{115 \text{ TeV}}{\text{pH}} - [P]_T - [L]_T$ concentration of the protein needed to achieve a significant level of interaction with the ligand. Specifically, when the protein concentration equals K, 50% of the ligand will be bound in the $[P]_T = [PL] + [P]$ protein-ligand complex, and the remaining 50% will be free And, therefore: "[L]". This is true when the protein is present in excess relative

to the ligand. Generally, for effective ligand binding, proteins to the figure. Generally, for effective figure binding, proteins
should have a K value of 1×10^{-6} M or lower. Smaller K values indicate stronger binding affinity, while higher K values suggest
weaken hinding weaker binding. **2. 2. Case 12. Ca**

$\sum_{k=1}^{\infty}$ Protein-Ligand Binding, Protein-Ligand Complex, Equilibrium Reaction, Equi **2. Case 1** U sing the equilibrium relationship K = \mathbb{R} \mathbb{R}

Using the equilibrium relationship $K = \frac{P \mid L}{[PL]}$ and substituting,
 $[PI] - [PI]$ for $[PI]$ $[P]_T - [PL]$ for $[P]$ $[L]_T$ – [PL] for [L] Gives: \mathcal{L} and substituting, we have the substituting of \mathcal{L} Using the equilibrius $[PP]$ $\frac{2.4881}{2.5}$

$$
K = \frac{([P]_T - [PL]) ([L]_T - [PL])}{[PL]}
$$

K $[PL] = [P]_{T} [L]_{T} - [P]_{T} [PL] - [PL] [L]_{T} + [PL]^{2}$ Dividing throughout by [PL] gives: Dividing throughout by [PL] gives: $K = \frac{1}{2}$ is a protein its ligand. It is indicated that it is ligand. It is indicates the concentration of the con

$$
K = \frac{[P]_T [L]_T}{[PL]} - [P]_T - [L]_T + [PL]
$$

But But $[{\rm P}]_{\rm T}^{} = [{\rm PL}] + [{\rm P}]$ And, therefore: $\begin{bmatrix} 1 & 0 \\ 1 & 0 \end{bmatrix}$ + $\begin{bmatrix} 1 & 0 \\ 0 & 0 \end{bmatrix}$ + $\begin{bmatrix} 1 & 0 \\ 0 & 0 \end{bmatrix}$

And, therefore:

$$
K = \frac{[P]_T [L]_T}{[PL]} - [P] - [L]_T
$$

$$
K = \frac{[P]_T [L]_T}{[PL]} - [L]_T - [P]
$$

$$
K = [L]_T (\frac{[P]_T}{[PL]} - 1) - [P]
$$

From this it follows that:

From this it follows that:

$$
K + [P] = \frac{[P] [L]_T}{[PL]}
$$

And, therefore:

Rearranging: g :

 $[PL] = \frac{[P] [L]_T}{K + [P]} \dots [1]$ S^{c} S^{c} and $[P][L]$ and $[1]$ $K + [P]$ = $\frac{1}{2}$ **Discussion** This describes a rectangular hyperbola with key properties:

Discussion

This describes a rectangular hyperbola with key properties: **Discussion Saturation:** When $[P] \gg K$, $[PL]$ approaches $[L]_T$ **Discussion** both $F_{FP} = F_{BP} = I$.
This describes a rectangular hyperbola with key properties: Since $F_{TP} = F_{DP} \neq 0$.

• **Half-saturation:** When $[P] = K$, $[PL] = \frac{[H]T}{2}$. This means the dissociation constant equals the free protein concentration needed for 50% of the ligand to be bound. • Half-saturation: When $[P] = K$, $[PL] = \frac{[L]_T}{2}$. This means Ine dissociation constant equals the free protein concentrulation constant equals the line bound **A** Half saturation: When $[PI] = K$ $[PI] = \frac{[L]_T}{K}$ This means **Saturation:** When the dissociation: constant equals the free protein concent **Saturation:** When $[P] \gg K$, $[PL]$ approaches $[L]_T$
 Half-saturation: When $[P] = K$, $[PL] = \frac{[L]_T}{2}$. This means **4. Conclusion**

In Case 1, the substitutions the dissociation constant equals the free protein concentration In Case t_{reced} needed for **the free protein is the free proton** $\overline{[b]}$ of \overline{b} is the means. 4. Conclusion the dissociation constant equals the free protein concentration $\frac{111 \text{ Case 1}}{11}$, the substitut needed for 50% of the ligand to be bound

Contained Linearity: When $[P] \ll K$, $[PL]$ is roughly proportional to $[P]$ $[PL]$ $[PL]$ $[KL]$ $[$ with a slope of $\frac{|L| \cdot T}{K}$. $\frac{K}{T}$

3. Case 2

Using the equilibrium relationship $K = \frac{[P][L]}{[PL]}$ and substituting, $[PL]$ along with substitution
 $[PL]$ = $[PL]$ = $[PL]$ and substituting, $[PL]$ along with substitution $[P]_T$ – $[PL]$ for $[P]$ $\left[L\right] _{\text{T}}-\left[PL\right]$ for $\left[L\right]$ $[P]_T - [P]$ for $[PL]$ Gives: **3. Case 2 3. Case 2** $\begin{bmatrix} -[PL] & \text{for } [P] \\ \text{In } R \end{bmatrix}$ Using the equilibrium relationship $K = \frac{|P| [L]}{[PL]}$ and substituting, \mathbf{L} \mathbf{L} \mathbf{L} \mathbf{L} \mathbf{L} \mathbf{L} \mathbf{L}

 $\mathbb{E} \left(\left[P \right]_T - \left[P \right] \right)$ $K = \frac{([P]_T - [PL]) ([L]_T - [PL])}{([P]_T - [P])}$ \int [D] [DL] \int \int [L] $\sqrt{[P]_T - [P]}$ $K = \frac{(P_{\text{H}} - (P_{\text{H}}))}{(P_{\text{H}} - (P_{\text{H}}))}$

K ([P] $_T - [P]$) = ([P] $_T - [PL]$) ([L] $_T - [PL]$) K $[P]_T$ – K $[P] = [P]_T [L]_T - [P]_T [PL] - [PL] [L]_T + [PL]^2$ $\overline{}$ 2. $K[\overline{P}]_{T} - K[\overline{P}] = [\overline{P}]_{T}$ $\overline{}$ 2. $K([P]_T - [P]) = ([P]_T - [PL]) ([L]_T - [PL])$
 $K[P] - K[P] = [P] [L] - [P] [P] [P] - [P] [L] [L]$ $\frac{1}{2}$ \mathbf{K} [P]_T – **K** [P] – [P]_T [P] _T – [P]_T [PL] – [PL] [P]_T + [PE] K ([P] $_{\rm T}$ – [P]) = ([P] $_{\rm T}$ – [P
K [P] $_{\rm T}$ – K [P] = [P] $_{\rm T}$ [L] $_{\rm T}$

Rearranging: \mathbf{P}

 $K[P]_{T} - [P]_{T} [L]_{T} + [P]_{T} [PL] = - [PL] [L]_{T} + [PL]^{2} + K [P]$ $[P]_T (K - [L]_T + [PL]) = [PL] (- [L]_T + [PL]) + K [P]$ ζ [P]_T – [P]_T [L]_T + [P]_T [PL] $\mathbb{R} \rightarrow \mathbb{R}$, $\mathbb{R} \rightarrow \mathbb{R}$, $\mathbb{R} \rightarrow \mathbb{R}$ $[\mathbf{P}]_{\text{T}} - [\mathbf{P}]_{\text{T}} [\mathbf{L}]_{\text{T}} + [\mathbf{P}]_{\text{T}} [\mathbf{P} \mathbf{L}]$ \mathbf{r} – \mathbf{r} – \mathbf{r} – \mathbf{r} – \mathbf{r} – \mathbf{r} K [P] $-$ [P] H .] $+$ [P] $[$ [PI] F $[P]_T (K - [L]_T + [PL]) = [P]$ Rearranging:

K [P]_T – [P]_T [L]_T + [P]_T [PL] = – [PL] [L]_T + [PL]² + K [P]

Further, if we substitute: $[L]_T = [PL] + [L]$ Then we get: 6 First we get. Γ hen we get. Further, if we substitute:
 $\begin{bmatrix} \overline{y} & \overline{y} & \overline{y} \\ \overline{y} & \overline{y} & \overline{y} \\ \overline{y} & \overline{y} & \overline{y} \end{bmatrix}$

 $[P]_T (K - [PL] - [L] + [PL]) = [PL] (-[PL] - [L] + [PL]) + K [P]$ $\begin{bmatrix} \text{F1} & \text{F2} & \text{F3} & \text{F4} & \text{F5} \end{bmatrix}$ $\begin{bmatrix} \text{F1} & \text{F2} & \text{F3} & \text{F4} \end{bmatrix}$ $\begin{bmatrix} \text{F1} & \text{F2} & \text{F3} & \text{F5} \end{bmatrix}$ $\mathcal{L}=\mathcal{$

$$
[P]_T (K - [L]) = - [PL] [L] + K [P]
$$

Which is the same as: $[P]_T (K - [L]) = K [P] - [PL] [L]$ W – \mathbb{R} is the same set \mathbb{R} \mathcal{L} , $[P]_T (K - [L]) = K [P] - [PL] [L]$

$$
K - [L] = K \, \frac{[P]}{[P]_T} - \frac{[PL]}{[P]_T} \, [L]
$$

Labeling $\frac{P}{[P]_T}$ as F_{FP} (fraction of free protein) and $\frac{[PL]}{[P]_T}$ as F_{BP} (fraction of bound protein), the above expression can be rewritten as: protein) and $\frac{[PL]}{[PL]}$ \mathbf{F}_{BP} (fraction c protein) and $\frac{[PL]}{[PL]}$ \mathbf{r}_{BP} (fraction c $nrotein)$ and $[PL]$ F_{BP} (fraction) Labeling $\frac{[P]}{[P]}$ as F_{FD} (fraction of free protein) and $\frac{[PL]}{[D]}$ as r_{BP} (fraction of bound protein), the a μ Labeling $\frac{[P]}{[P]_T}$ as F_{FP} (\hat{P} = P (fraction of bound protein), the above expression rewritten as: free protein) and $\frac{[PL]}{[P]_T}$ as above expre

$$
K - [L] = K F_{FP} - F_{BP} [L] \dots [2]
$$

J Math Techniques Comput Math, 2024 https://opastpublishers.com Volume 3 | Issue 9 | 2

Discussion \mathbf{D} is expected.

• If $F_{FP} = F_{BP} = 1$, then the left-hand side (LHS) equals the righthand side (RHS), making Equation (2) true.

• If $F_{FP} = F_{BP} \neq 1$, then the left-hand side (LHS) does not equal the right-hand side (RHS), rendering Equation (2) invalid.

• Let's verify the condition " $F_{F_P} = F_{BP} = 1$."

According to the protein conservation law:

 $[P]_n = [PL] + [P]$ From this, we get: If we assume FBP = FFP =1, we get: $1 = F_{BP} + F_{FP}$ If we assume $F_{BP} = F_{FP} = 1$, we get: $1 = 2$ $1 = F_{1}$ This shows that the condition $\frac{1}{8}$ $\frac{1}{8}$ $\frac{1}{8}$ is not give.

This shows that the condition $F_{FP} = F_{BP} = 1$ is impossible, since 1 is not equal to 2.

In fact, the only way it can happen that $K - [L] = K - [L]$ is if both $F_{FP} = F_{BP} = 1$.

sy properties: Since $\overrightarrow{F}_{FP} = \overrightarrow{F}_{BP} \neq 1$, Equation (2) is not valid.

4. Conclusion

In Case 1, the substitutions correctly lead to: In Case 1, the substitutions correctly lead to:

 $[PL] = \frac{[P][L]_T}{K + [P]}$

ortional to $[P]$ $\begin{bmatrix} R + [P] \\ \text{In Case 2, the substitutions produce an incorrect result:} \end{bmatrix}$ In Case 2, the substitutions produce an incorrect result.
 $V = [I] - V E = E - [I]$

$$
K - [L] = K F_{pp} - F_{pp} [L]
$$

ase 2 **the free protein concentration** \mathbf{R} $[\mathbf{L}]$ $[\mathbf{R}]$ $[\mathbf{r}_F]$ $[PL]$ along with substitutions for $[L]$ and $[P]$ should be avoided to prevent incorrect results [PL] along with substitution:
to prevent incorrect results.

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