Review of: "The Fundamental Problem With Enzyme Inhibition Theory"

Françoise Couenne[1]

1 Université Claude Bernard (Lyon I)

Potential competing interests: No potential competing interests to declare.

The target is to emphasize some alternative representation of the inhibition term that clearly distinguishes between the chemical equilibrium and the effect inhibitor binding in the reaction rate

Some aspects of the the paper deserve to be clarified:

The author develops various inhibition and catalytic reaction schemes. The author states that the one represented by equation 66 provides a unified equation for the modeling of inhibitory and activator effects on enzymatic activity. Nevertheless it corresponds to some assumptions even of the catalytic reaction. Please could you clarify.

Finally It is not clear why it is important to have these two terms in Eq 66.

Could the author explain what delta Km or delta V physically correspond to in the reaction scheme or equilibria?

I will propose an introduction in order to present the development of the paper and the interest of each section.

In the text, I will propose to write the reactional equation associated to each section.

In each section, it would be interesting to have a reference that uses the inhibition presented.

My comments by section :

Chemical equilibriums in biological studies

I propose to authors to write “the use of equilibrium binding relations” instead “the use of binding curves”.

Remove Eq 8- write Eq 9 directly.

In order to prepare the next sections give the %unbinding (link with eq 21or 24 after) At least we obtain the denominator of Eq24.

Michaelis Menten equation

In my opinion, giving the chemical equations would support the author's point. In fact, the balanced reaction gives chemical equilibrium, and an unbalanced reaction gives the information about products.

To prepare for the rest of the article, a discussion of Vmax and Km and their possible changes could be useful.

Traditional inhibition term

What is traditional inhibition in terms of mechanism? Explain or give a reference

Give a reference for eq 19.

The author write:" In this term, you can clearly see the inhibitor's chemical equilibrium constant"

How to be sure it is an equilibrium constant?

The sentence "Traditional inhibition equations use the inhibition term (equation 19) to define inhibition" is not clear. The authors must indicate where and how appear the inhibition term in the binding equation.

It would be interesting to explain how this term is obtained. Can it be represented by a reaction scheme?

"The subtraction of the binding curve from one indicates that this term also

Defines the fraction of the enzyme population that is not bound by the inhibitor."

Is it possible to develop this point?

Noncompetitive inhibition equation

For Eq. 25, give a reference.

Could you explain the introduction of a deltaV in Eq. 32? Two kinds of sites?

Competitive inhibition equation

Give a reference.