A straightforward derivation of the Michaelis-Mention Equation for Enzyme Kinetics

We start with a very simple expression for formation of the enzyme-substrate complex, *ES*, from free enzyme, *E*, and free substrate, *S*. The rate constants for formation and breakdown back to reactants are k_{+1} and k_{-1} , respectively. The rate constant for formation of the product is k_{+2} , and to further simplify our treatment, we wil work within the approximation that we can neglect the back-reaction, k_{-2} . We can therefore write a simple kinetic scheme as follows:

$$[E] + [S] \xleftarrow{k+1/k-1} [ES] \xrightarrow{k+2} [E] + [P]$$

We will work within an approximation called the steady-state approximation, in which the rate of formation of the enzyme-substrate complex is equal to its rate of decay, and is therefore zero, *i.e.*,

$$\frac{d[ES]}{dt} = -\frac{d[ES]}{dt} = 0$$

It is also useful to write down two other definitions and assumptions before we continue:

1. The first thing we need to realize is that the total concentration of enzyme in all of its forms should be equal to the original free enzyme concentration:

$$[E]_{tatal} = [E]_{0} = [E] + [ES]$$

2. The second point is that the rate of the reaction should be equal to formation of products, so the initial velocity, vo, and maximum possible velocity, or Vmax, obtained when all the enzyme is substrate-bound, can be written as

$$V_0 \equiv k_{\pm 2}[ES]_{and} V_{max} \equiv k_{\pm 2}[E]_{total} = k_{\pm 2}[E]_0$$

Now, before making the steady-state approximation, we can look at the kinetic scheme above and deduce that the rate of change in the concentration of the enzyme-substrate complex should be equal to the rate of formation of the complex minus the rate of decay of the complex. The rate of formation is dependent upon the rate constant k+2 and the enzyme and substrate complexes. The rate of decay involves two possible pathways. One is to form products, and the other is to reform the reactants. Therefore the rate of decay of the enzyme-substrate complex will be the sum of two rate constants, k+2 and k-1. Therefore we can write

$$\frac{d[ES]}{dt} = k \cdot [E][S] - (k \cdot 2 + k - 1)[ES]$$

and from the steady-state approximation, this has to equal zero. Before making this approximation, that equation is insoluble. Now, however, you can solve it fairly simply (despite what I did in class). First, if the steady-state approximation holds, then you can rearrange the equation to look like this:

$$k + [E][S] = (k + 2 + k - 1)[ES]$$

Now group all of the rate constants together

$$[E][S] = \left(\frac{(k_{+2} + k_{-1})}{k_{+1}}\right)[ES]$$

We can define this collection of rate constants as something called the Michaelis Constant, or Km. Note that this is *not* an equilibrium constant.

$$K_m = \left(\frac{(k_{+2}+k_{-1})}{k_{+1}}\right)$$

Now we have an even simpler expression:

$[E][S] = K_m[ES]$

We are almost done. However, we want an expression in terms of constants and measurable quantities such as the substrate concentration, [S], and the initial velocity, *vo*. To get the equation into that form, we need two things from above. The first is our statement that the total enzyme concentration is equal to the concentration of enzyme in all of its forms, which in turn is the same as the starting concentration of enzyme, *i.e.*,

[E] = [E] = [E] + [ES], or more conveniently, [E] = [E] - [ES]. Then we can substitute that into our previously simplified equation to obtain

$([E]_{\circ}-[ES])[S]=K_{m}[ES]$

Now solve this for [ES]:

$$[E]_{0}[S] = [ES][S] + K_{m}[ES] = (K_{m} + [S])[ES]$$

or

$$[ES] = \frac{[E] \circ [S]}{K_m + [S]}$$

Now multiply both sides by k_{+2} :

$$k_{+2}[ES] = \frac{k_{+2}[E]_{0}[S]}{K_{m} + [S]}$$

Using the definitions of initial and maxiumum velocity, *i.e.*,

$$\mathbf{V}_{\bullet} \equiv \mathbf{k} \cdot \mathbf{J}[ES]_{\text{and}} \mathbf{V}_{\text{max}} \equiv \mathbf{k} \cdot \mathbf{J}[E]_{\text{max}} = \mathbf{k} \cdot \mathbf{J}[E]_{\bullet}$$

we finish the derivation by substituting in these values directly:

$$\mathbf{v}_{0} = \frac{V \max[S]}{K_{m} + [S]}$$