

10.5 Stochastic single-molecule enzyme kinetics

Let us revisit the Michaelis-Menten (MM) enzyme kinetics, which has produced the celebrated double reciprocal relation between the rate of an enzymatic reaction, $\frac{1}{v}$, and the concentration of the substrate $\frac{1}{[S]}$. For a single enzyme, the MM kinetic scheme given in Eq. 9 can be expressed as



Note all three quantities, $k_{+1}[S]$, k_{-1} , and k_2 have the physical dimension of $[\text{time}]^{-1}$, as the rates of exponentially distributed waiting time for stochastic elementary reactions.

Let $\langle T \rangle$ be the mean time for the completion of a kinetic cycle, e.g., from the E on the left to the E on the right of (176). We add the mean time for each and every step. First, the transition from $E \rightarrow SE$ has a mean time of $(k_{+1}[S])^{-1}$, this is followed by a waiting time in the state SE , $(k_{-1} + k_2)^{-1}$. After that, there are two possibilities: the $SE \rightarrow S + E$ with a probability $\frac{k_{-1}}{k_{-1} + k_2}$ and the $SE \rightarrow P + E$ with a probability $\frac{k_2}{k_{-1} + k_2}$. Therefore, the mean time to produce a P , from state SE , is $\frac{k_{-1}\langle T \rangle + k_2 \cdot 0}{k_{-1} + k_2}$. Putting all these together, we have

$$\langle T \rangle = \frac{1}{k_{+1}[S]} + \frac{1}{k_{-1} + k_2} + \frac{k_{-1}\langle T \rangle}{k_{-1} + k_2}, \quad (177)$$

from this one can solve $\langle T \rangle$. Noting the the rate of the enzyme reaction is the reciprocal of the mean time per product formation, we have

$$\frac{1}{v} = \langle T \rangle = \frac{k_{-1} + k_2}{k_{+1}k_2[S]} + \frac{1}{k_2}, \quad (178)$$

or,

$$v = \frac{k_{+1}k_2[S]}{k_{-1} + k_2 + k_{+1}[S]} = \frac{V_{max}[S]}{K_M + [S]}, \quad (179)$$

in which Michaelis constant $K_M = \frac{k_{-1} + k_2}{k_{+1}}$, and $V_{max} = k_2$. In the standard theory of MM enzyme kinetics, the $V_{max} = k_2 \times \text{enzyme concentration}$. This is precisely expected from many enzymes working together with each individual molecule having the rate given in (179).

This stochastic formulation is the ultimate scenario of $[E] \ll [S]$.