

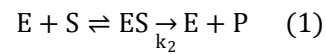
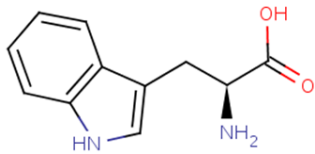
# MODEL 1 IDO Catalyzed Reactions

## 1 Modeling of the Reactions

For the reaction,

REACTION 1: L-tryptophan + O<sub>2</sub> = N-formyl-L-kynurenine

L-Tryptophan

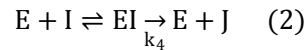
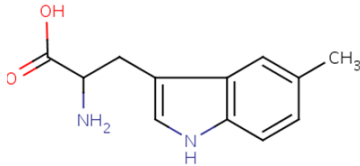


Here, E stands for IDO, S for L-tryptophan, P for N-formyl-L-kynurenine.

REACTION 2:

5-methyl-tryptophan + O<sub>2</sub> = 4-(2-amino-5-methylphenyl)-2-(formylamino)-4-oxobutanoic acid? ?

5-methyl-DL-tryptophan



E stands for IDO, I for 5-methyl-tryptophan, J for the product.

## 2 Calculation

For reaction(1), we have  $\frac{d[ES]}{dt} = k_1([E]_0 - [ES] - [EI])[S] - (k_{-1} + k_2)[ES]$

At pseudo steady state,  $\frac{d[ES]}{dt} = k_1([E]_0 - [ES] - [EI])[S] - (k_{-1} + k_2)[ES] = 0$

We define that  $k_{m1} = (k_{-1} + k_2)/k_1$ , thus:

$$([E]_0 - [ES] - [EI])[S] = k_{m1}[ES]$$

Similarly,  $([E]_0 - [ES] - [EI])[I] = k_{m2}[EI]$

$$\therefore \frac{[ES]}{[EI]} = \frac{k_{m2}[S]}{k_{m1}[I]}$$

$$\therefore [ES] = \frac{[E]_0[S]}{\left\{ [S] + \frac{k_{m1}}{k_{m2}} [I] + k_{m1} \right\}}$$

$$\frac{d[S]}{dt} = k_{-1}[ES] - k_1([E]_0 - [ES] - [EI])[S]$$

$$= k_{-1}[ES] - \frac{d[ES]}{dt} - (k_{-1} + k_2)[ES] = -\frac{d[ES]}{dt} - k_2[ES] = -k_2[ES]$$

Similarly, we have:  $\frac{d[I]}{dt} = -k_4[EI]$

$$v_1 = k_2[ES], v_2 = k_4[EI]$$

Here,  $v_1$  is defined as the the production rate of P,  $v_2$  production rate of J.

Thus, the standard equation set is like:

$$\left\{ \begin{array}{l} \frac{d[S]}{dt} = -\frac{k_2[E]_0[S]}{\left\{ [S] + \frac{k_{m1}}{k_{m2}} [I] + k_{m1} \right\}} \\ \frac{d[I]}{dt} = -\frac{k_4[E]_0[I]}{\left\{ [I] + \frac{k_{m2}}{k_{m1}} [S] + k_{m2} \right\}} \\ \frac{d[P]}{dt} = \frac{k_2[E]_0[S]}{\left\{ [S] + \frac{k_{m1}}{k_{m2}} [I] + k_{m1} \right\}} \\ \frac{d[J]}{dt} = \frac{k_4[E]_0[I]}{\left\{ [I] + \frac{k_{m2}}{k_{m1}} [S] + k_{m2} \right\}} \end{array} \right.$$

Apparently, these equations are symmetrical. If we use symmetrical initial values and constants, the figure of concentration variation is as follows:

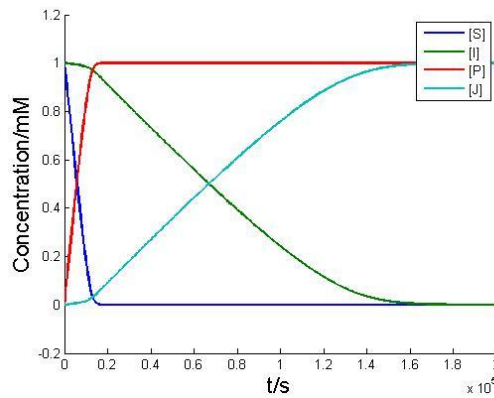


Fig. 1

Experimental concentration levels (from Internet):

Constant name	Approximate value (Experimental Condition)	Approximate value (In Vitro)
$k_{m1}$	0.009mM	0.009mM
$k_{m2}$	0.1mM	0.1mM
$[E]_0$	0.01mM	3e-3mM
$[S]_0$	10mM	0.05mM

$[I]_0$	0.5mM	2.28e-6mM
$k_2$	$1.4s^{-1}$	$1.4s^{-1}$
$k_4$	$3.78s^{-1}$	$3.78s^{-1}$

Km:

0.113	-	5-methoxy-DL-tryptophan	<a href="#">Homo sapiens</a>	50 mM potassium phosphate, pH 6.5, 10 mM ascorbic acid, 0.01 mM methylene blue, 0.1 mg catalase, 37°C, 10 min
0.088	-	5-methyl-DL-tryptophan	<a href="#">Homo sapiens</a>	50 mM potassium phosphate, pH 6.5, 10 mM ascorbic acid, 0.01 mM methylene blue, 0.1 mg catalase, 37°C, 10 min
0.0089	-	L-Tryptophan	<a href="#">Homo sapiens</a>	V109A mutant, 50 mM potassium phosphate buffer (pH 6.5), 20 mM ascorbic acid, 0.3 mg/ml catalase, 0.01 mM methylene blue, 0.4 mM tryptophan, 37°C, 10-60 min
0.009	-	L-Tryptophan	<a href="#">Cryptosporidium parvum</a>	pH 7.5

With these data, we came to the following figures:

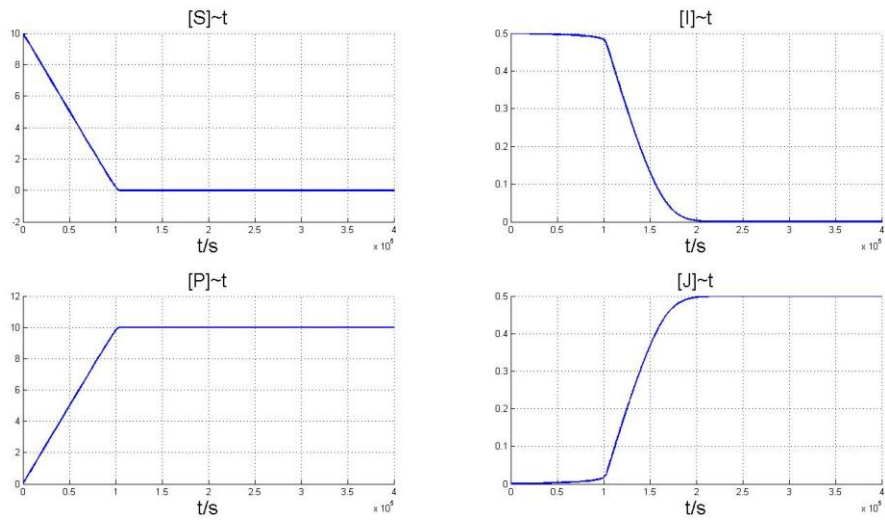


Fig. 2 Experimental Level

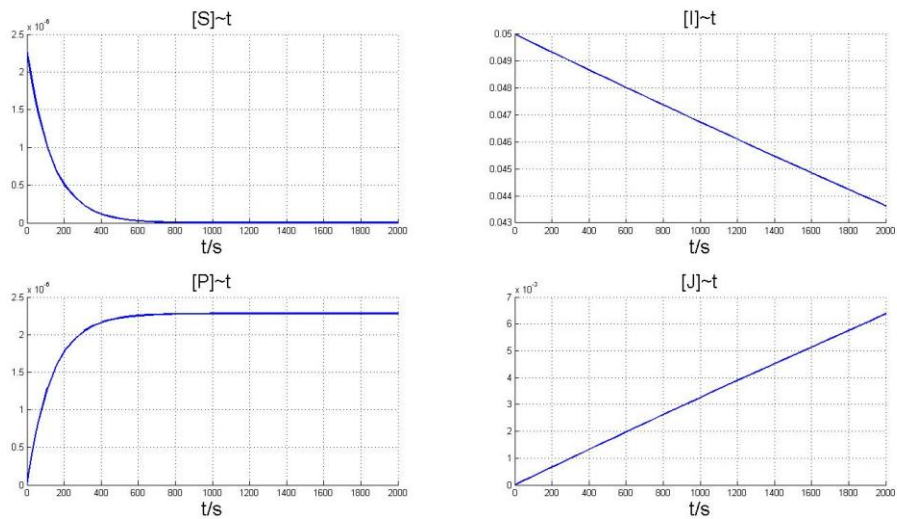


Fig. 3 In Vitro(Long time span)

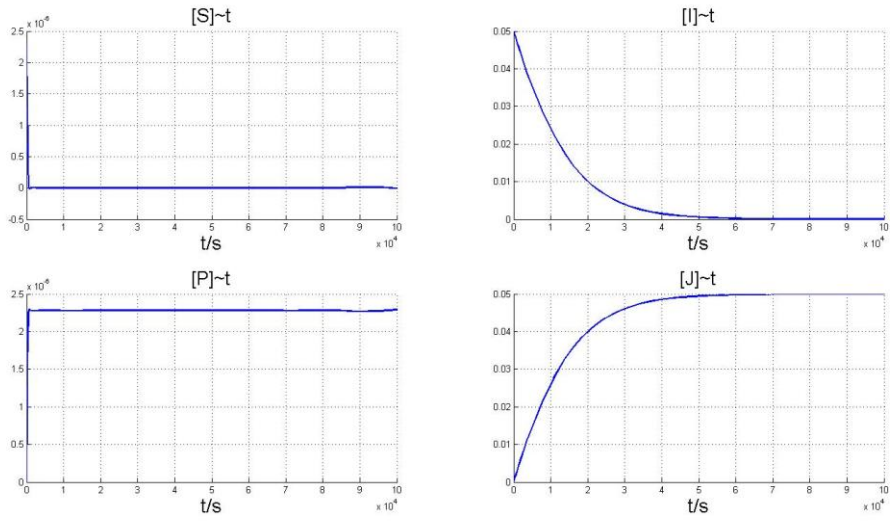


Fig. 4 In vitro data (short time span)

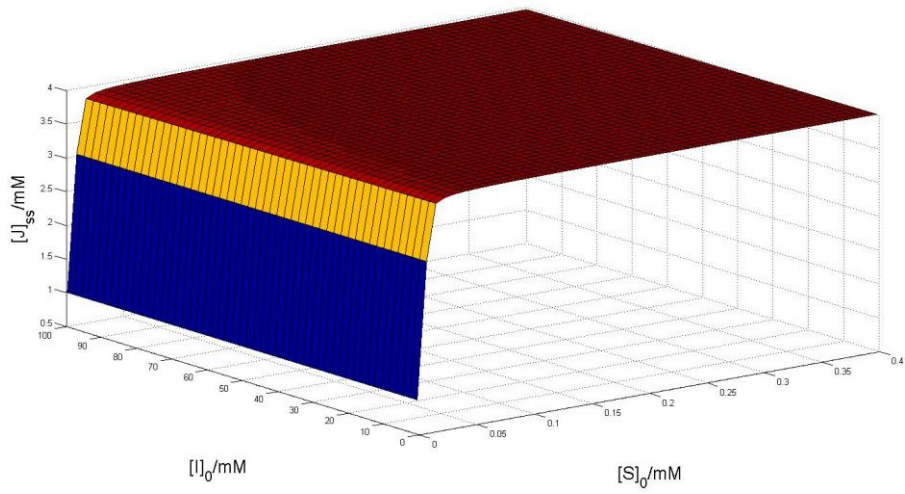


Fig. 5

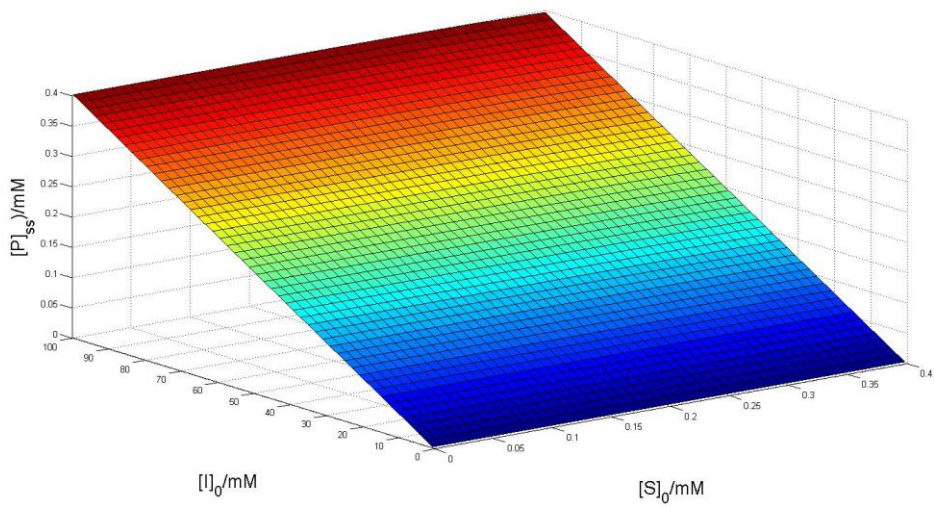


Fig. 6