Indian Journal of Biochemistry & Biophysics
Vol. 63, February 2026, pp. 190-199
DOI: 10.56042/ijbb.v63i2.19623

Computational analysis of non-competitive enzyme inhibition in microbial and biomedical applications

Patel K, and Kumawat J*

Department of Mathematics, Veer Narmad South Gujarat University, Surat-395 007, Gujarat, India

Received 11 May 2025; *revised 28 May 2025*

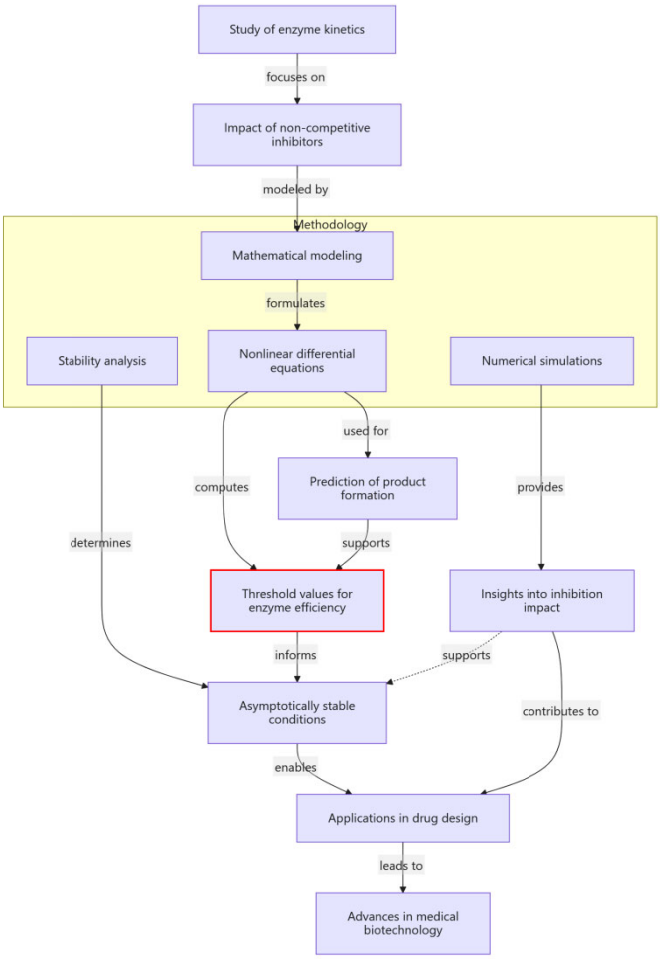
Understanding physiological responses within the human body requires a detailed investigation of enzyme kinetics, a fundamental aspect of biochemical processes. This study employs mathematical modeling to analyze enzyme behavior in living organisms, focusing on the impact of non-competitive inhibitors on catalytic activity. Enzyme inhibitors are known to modify enzyme-substrate interactions, either slowing down or completely halting catalytic reactions. Unlike competitive inhibitors, non-competitive inhibitors bind to enzymes in a way that prevents direct competition with the substrate, altering the reaction dynamics. This work formulates a system of nonlinear differential equations to predict product formation in enzyme-substrate-inhibitor interactions. By computing threshold values, the study examines enzyme efficiency, substrate conversion rates, and complexity in biochemical reactions. Stability analysis is conducted to determine asymptotically stable conditions for optimal enzyme-substrate reactions. Numerical simulations provide insights into the impact of inhibition on biochemical pathways, offering applications in drug design, enzyme regulation, and metabolic engineering. The findings contribute to medical biotechnology and bio-informatics by enhancing our understanding of enzymatic control mechanisms and their relevance in therapeutic interventions.

Keywords: Asymptotic behaviour, Kinetics, Mathematical modelling, Sensitive analysis, Stability analysis, Thermodynamics

Biological reactions in anthropology, follows varied study. Large amounts of similar physiological reactions are analyzed through Enzyme kinetics using Mathematical modelling, which help to predict enzyme behavior in living organisms. For a reaction to take place, a quantity of energy, called the activation energy, is needed irrespective of whether the reaction consumes or releases energy. All enzymes being protein in nature increase the rate of this chemical reactions or chemical process in mortal body. These biocatalysts act upon molecules called Substrates to accelerate product conformation by reducing the needed activation energy, deprived of being absorbed during the procedure. Enzyme-catalyzed reactions take place at more faster rates than reactions without enzyme. Enzymes are precise by their kinetic performance of binding with the substrate for product conformation, which is much further alluring in scientific and technological advances which grease the study of enzymes and their operations. countless operations of enzymes have been extensively explored and advanced in biotechnology, industrial applications, and pharmaceutical research. Some common operations of enzymes are in Medicines, food processing, biofuels, and so on. Before an operation for an enzyme can be developed, its medium of action must first be understood. Besides complex natural experimental studies, to Completely understand similar intricate reactions, one must explore beyond the confines of chemical and natural tools and look towards fine modelling and model reduction ways to give a vast array of analysis tools for similar models.

Substances that reduce the effort of an enzyme-catalyzed response are known as impediments. Principally, impediments are low molecular weight composites that form an enzyme- asset complex which bind with the enzyme, thereby reducing or fully inhibiting the catalytic exertion of the enzyme and hence reducing the rate of response. Even though catalysts are significant ever, high enzyme exertion can also give rise to some abnormal conditions and may lead to certain conditions. Hence, hyperactive enzymes are seductive targets for outgrowth of asset molecules (specific compunds designed to regulate enzyme activity and decrease disease conditions) to relieve complaint conditions. Manipulation of enzyme catalysis with impediments is critical for forestallment of contagious conditions, treatment of hypertension,

*Correspondence:
E-mail: jyotikmwt13@gmail.com



Graphical abstract

control of seditious response and further. Besides impediments that are acting as remedial agents, these also play pivotal places in natural and clinical exploration. The entry of substrate to the active point of enzyme can be choked by binding of an asset patch to that point. Alternately, occasionally impediments not only bind to the active point of enzyme but can also bind to a point other than the active point and develop a conformational change that stops the entry of substrate to the active point. Impediments take measures directly or laterally affecting the catalytic parcels of the active point. They're involved with catalytic and enzymatic reactions. Enzyme impediments are classified into different categories, one of which is reversible inhibition. Reversible inhibition can be further divided into three types as competitive, Non-Competitive and Un- competitive inhibition[1]. Enzymatic inhibition processes are veritably common mechanisms in cellular metabolism. We can cure number of pathological conditions by using enzyme impediments. occasionally receptor blocking is not getting net effect what we want, at that stage we can inhibit target enzyme which give proper and perfect result[2]. In the Non-Competitive inhibition process, the enzyme patch has two binding spots, one for the substrate (active point) and another for the asset (non-competitive point)[3]. The list of an asset patch to an enzyme patch deactivates the active point of the enzyme patch. In non-competitive product inhibition of an enzyme, the product acts as an inhibitor. It binds to the enzyme at a site other than the active site, either to the free enzyme substrate (ES) complex[4].

As per till date inquiries, fine models have been established to analyze enzymatic reactions of cellular metabolism that have a special interest with biotechnology[7]. Fang, X. established a fine model of enzymatic inhibition that's used to pretend two separate inhibition mechanisms for the growth of Tuberculosis cells in an *in vitro* terrain[5]. The kinetic dynamics in miscellaneous enzymatic hydrolysis of Cellulose were

studied[6] and kinetic equations for reversible enzyme reactions with some logical approximate results were also established[8,9]. The formulation of algebraic model for the kinetics of covalent enzyme inhibition under less substrate involvement has also been generated in this continued study[10]. Model reduction is a strategy for dwindling the computational intricacy of fine models. Working the complex enzymatic reactions is a clumsy task and hence some well-known styles have been applied to describe their dynamics. Quasi-equilibrium approximation (QEA) and quasi steady- state approximation (QSSA) are the two standard styles whose approaches can be applied in natural systems, to reduce variables and parameters for similar systems[11,12]. Several fine workshops have explored models of biochemistry using differential equation systems[13-16]. Biochemical response networks, similar as model reductions in chemical dynamics, slow steady manifolds, thermodynamic estimates, response graph analysis by smearing fine modelling ways have been applied to enzyme impediments with slow and fast subsystems[18] also, a fine model has been established which gives an approximate logical result using Homotopy anxiety system and develop logical results to the fine model[19].

In this analysis, we aim to study fine forms for developing enzyme- substrates reactions for product conformation predicated on time under the influence of Non-competitive Impediments. Formulate the model as a system of nonlinear differential equations that predicts the product conformation predicated on Enzyme- substrate- asset response parameters. Reckon the threshold value for studying the enzyme effectiveness, complexity, and other parameters for the substrate product. Study the stability analysis for the ideal product conformation and hence decide asymptotically stable results for the Enzyme-Substrate model with numerical simulation.

Materials and Methods

The mathematical expression of the enzyme kinematics problem with Non-competitive impediments in biochemical systems has been modeled using ordinary differential equations. The impediments reduce the activity of enzymes and bind equally well to the enzyme whether it has already bound the substrate and forms two different complexes namely Enzyme impediment complex and Enzyme-substrate-impediment complex which hinders the product formation. whereas It's to be noted that enzyme may bind with substrate at its active site equally well and form Enzyme-substrate complex which releases a product and free enzyme. The free enzyme is then available for another reaction to produce a new reaction. Here the system is written as:

The fundamental enzymatic reaction for Non-competitive inhibitors:

$$e+s \underset{(rr)_2}{\overset{(rr)_1}{\rightleftharpoons}} es \xrightarrow[h_3]{} e+p\,, e+i \underset{(rr)_5}{\overset{(rr)_4}{\rightleftharpoons}} ei, \qquad es+i \underset{h_7}{\overset{(rr)_6}{\rightleftharpoons}} esi \quad \ldots (1)$$

Where i is the inhibitor, $es, ei,$ and esi are complex intermediate components. The model has seven parameters $(rr)_1\,(rr), (rr)_3, (rr)_4, (rr)_5, (rr)_6$ and $(rr)_7$. Model variables are $s = [s], e = [e], c_1 = [es]$, $c_2 = [ei], c_3 = [esi]$ and $p = [p]$ in their normalized concentrations to be 1 mg.

This mechanism illustrates the binding of substrate s and the release of product p in the presence of a Non-competitive inhibitor "i". "e" is the free enzyme, "c_1" is the enzyme-substrate complex "c_2" is the enzyme impediment and "c_3" is the enzyme-substrate-impediment complex. Also $(rr)_1, (rr)_2$, $(rr)_3, (rr)_4, (rr)_5, (rr)_6\ and\ (rr)_7$ denote the measure of the rate of reaction of all processes. Note that substrate binding, first complex binding and inhibitor binding are reversible, but product release is not. This chemical reaction, can be converted to a mathematical model using the law of mass action and favorable analysis, the system of following non-linear reaction equations as follows[17,20]:

$$\frac{ds}{dt} = -(rr)_1 es + (rr)_2 c_1 \quad \ldots (2a)$$

$$\frac{de}{dt} = -(rr)_1 es + (rr)_2 c_1 + (rr)_3 c_1 - (rr)_4 ei + (rr)_5 c_2 \quad \ldots (2b)$$

$$\frac{di}{dt} = (rr)_5 c_2 - (rr)_4 ei - (rr)_6 c_1 i + (rr)_7 c_3 \ldots (2c)$$

$$\frac{dc_1}{dt} = (rr)_1 es - (rr)_2 c_1 - (rr)_3 c_1 - (rr)_6 c_1 i + (rr)_7 c_3 \quad \ldots (2d)$$

$$\frac{dp}{dt} = (rr)_3 c_1 \quad \ldots (2e)$$

$$\frac{dc_2}{dt} = (rr)_4 ei - (rr)_5 c_2 \quad \ldots (2f)$$

$$\frac{dc_3}{dt} = (rr)_6 c_1 i - (rr)_7 c_3 \quad \ldots (2g)$$

Where $(rr)_1$ is the measure of the forward rate of complex formation c_1, $(rr)_2$ is the measure of the

backward rate constant, $(rr)_3$ is the rate of product formation and enzyme release, $(rr)_4$is the measure of the forward rate of complex formationc_2, $(rr)_5$ is the measure of the backward rate constant,$(rr)_6$is the measure of the forward rate of complex formation c_3, $(rr)_7$ is the measure of the backward rate constantand c_1, c_2 and c_3 are the complex intermediate components

Consider the normalized initial conditions for substrate s, enzyme e, complex c, and product p as follows:

$$s(0) = s_0, e(0) = e_0,\ i(0) = i_0,\ c_1(0) = c_2(0) = c_3(0) = p(0) = 0. \quad \dots (3)$$

Where, equation (2e) is directly integrable and system equation along with the initial conditions in equation (3) states that,

$$e(t) + c_1(t) + c_2(t) + c_3(t) = e_0, \quad \dots (4a)$$

$$c_2(t) + c_3(t) + i(t) = i_0 \text{and} \quad \dots (4b)$$

$$c_1(t) + s(t) + p(t) + c_3(t) = s_0 \quad \dots (4c)$$

Thus the revised differential equations of the model reduces to,s, i and $c_1$as:

$$\frac{ds}{dt} = -(rr)_1 s(e_0 - i_0 + i - c_1) + (rr)_2 c_1 \quad \dots (5a)$$

$$\frac{di}{dt} = -(rr)_4 i(e_0 - i_0 + i - c_1) + (rr)_5(s + pc_1 + i_0 - s_0 - i) - (rr)_6 ic_1 + (rr)_7(s_0 - s - c_1 - p) \quad \dots (5b)$$

$$\frac{dc_1}{dt} = (rr)_1 s(e_0 - i_0 + i - c_1) - ((rr)_2 + (rr)_3 + (rr)_6 i)c_1 + (rr)_7(s_0 - s - c_1 - p) \quad \dots (5c)$$

Where each one of them has normalized initial conditions

The stability of this system

Theorem: *A system of a differential equation is asymptotically stable if and only if its basic reproduction number* (R_0) *is less than 1.*

To determine basic reproduction number using Next Generation Matrix. FV^{-1} is next generation matrix, where F and V both are Jacobian of Σ and Λ evaluated for Enzyme, Substrate, Non-competitive inhibitor, product and both Complexes at an equilibrium point[21,22].

So, $\Sigma(X) = \begin{bmatrix} (rr)_1 s(i_0 + c_1) \\ (rr)_4 i(i_0 - c_1) \\ 0 \end{bmatrix}$ and

$$\Lambda(X) = \begin{bmatrix} -\left((rr)_1 s(e_0 + i)\right) + (rr)_2 c_1 \\ -(rr)_4 i(e_0 + i) + (rr)_5(s + pc_1 + i_0 - s_0 - i) - \\ (rr)_6 ic_1 + (rr)_7(s_0 - s - c_1 - p) \\ (rr)_1 s(e_0 - i_0 + i - c_1) - \left((rr)_2 + (rr)_3 + (rr)_6 i\right) \\ c_1 + (rr)_7(s_0 - s - c_1 - p) \end{bmatrix}$$

Where, $X = (s, c)^t, \Sigma(X)$ denotes the entrance to the compartment and $\Lambda(X)$ denotes transferring to another compartment or leaving the system. Then the Jacobian at the equilibrium point is given by

$F = \left[\frac{\partial \Sigma}{\partial X_i}\right]$ and $V = \left[\frac{\partial \Lambda}{\partial X_i}\right]$, *where* $i = 1,2,3.$

As a result,

$$F = \begin{bmatrix} (rr)_1(i_0 + c_1) & 0 & (rr)_1 s \\ 0 & (rr)_4(i_0 - c_1) & -(rr)_4 i \\ 0 & 0 & 0 \end{bmatrix} \text{and}$$

$$V = \begin{bmatrix} -(rr)_1(e_0 + i) & -(rr)_1 s & (rr)_2 \\ (rr)_5 - (rr)_7 & -2(rr)_4 i - (rr)_5 - (rr)_6 c_1 & p(rr)_5 - (rr)_6 i - (rr)_7 \\ (rr)_1(e_0 - i_0 + i - c_1) - (rr)_7 & (rr)_1 s - (rr)_2(rr)_6 c_1 & -((rr)_1 s + (rr)_6(rr)_2 i + (rr)_7) \end{bmatrix}$$

Theorem: *If the determinant of a matrix is non-zero then its inverse does exist.*

Accordingly for our model we have, $|V| =$

$$\begin{aligned} &(rr)_1^2(rr)_7 s^2 - (rr)_1^2(rr)_5 s^2 - (rr)_2(rr)_5(rr)_7 - c_1(rr)_1(rr)_2(rr)_5 - c_1(rr)_2(rr)_6(rr)_7 \\ &+ e_0(rr)_1(rr)_2(rr)_5 - e_0(rr)_1(rr)_5(rr)_7 + i(rr)_1(rr)_2(rr)_5 \\ &- i_0(rr)_1(rr)_2(rr)_5 - i(rr)_1(rr)_5(rr)_7 - 2i(rr)_2(rr)_4(rr)_7 \\ &+ (rr)_1(rr)_2(rr)_5 s - (rr)_1(rr)_2(rr)_7 s - (rr)_1(rr)_5(rr)_7 s \\ &- c_1^2(rr)_1(rr)_2(rr)_6 - c_1(rr)_2^2(rr)_5(rr)_6 + c_1(rr)_2^2(rr)_6(rr)_7 \\ &+ 2i^2(rr)_1(rr)_2(rr)_4 - c_1(rr)_1^2(rr)_7 s - 2i^2(rr)_1(rr)_4(rr)_7 - e_0(rr)_1^2(rr)_5 s \\ &- i(rr)_1^2(rr)_5 s - i_0(rr)_1{}^2(rr)_7 s - 2i^2(rr)_1{}^2(rr)_4 s + c_1 e_0(rr)_1(rr)_2(rr)_6 \\ &- c_1 e_0(rr)_1(rr)_6(rr)_7 - 2c_1 i(rr)_1(rr)_2(rr)_4 + c_1 i(rr)_1(rr)_2(rr)_6 \\ &- c_1 i_0(rr)_1(rr)_2(rr)_6 - c_1 i(rr)_1(rr)_6(rr)_7 + 2e_0 i(rr)_1(rr)_2(rr)_4 \\ &- 2e_0 i(rr)_1(rr)_4(rr)_7 - 2ii_0(rr)_1(rr)_2(rr)_4 - i(rr)_1(rr)_6(rr)_7 s \\ &+ (rr)_1(rr)_5(rr)_7 ps - c_1 e_0(rr)_1{}^2(rr)_6 s - 2c_1 i(rr)_1{}^2(rr)_6 s \\ &- 2e_0 i(rr)_1^2(rr)_4 s - i^2(rr)_1(rr)_2(rr)_5(rr)_6 - 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 \\ &- ii_0(rr)_1^2(rr)_5 s + c_1(rr)_1^2(rr)_5 ps + i_0(rr)_1^2(rr)_5 ps \\ &- 2e_0 i^2(rr)_1(rr)_2(rr)_4(rr)_6 + c_1 e_0(rr)_1(rr)_2(rr)_6(rr)_7 \\ &+ c_1 i(rr)_1(rr)_2(rr)_6(rr)_7 - e_0 i(rr)_1(rr)_2(rr)_5(rr)_6 - i(rr)_1(rr)_2(rr)_5(rr)_6 s \\ &+ i(rr)_1(rr)_2(rr)_6(rr)_7 s - c_1 e_0(rr)_1(rr)_2(rr)_5(rr)_6 p \\ &- c_1 i(rr)_1(rr)_2(rr)_5(rr)_6 p \neq 0 \end{aligned}$$

Since determinant of V is non-zero: $V^{-1} = \begin{bmatrix} V_{11} & V_{12} & V_{13} \\ V_{21} & V_{22} & V_{23} \\ V_{31} & V_{32} & V_{33} \end{bmatrix}$

Where;

$$\begin{aligned} V_{11} = \ &-((rr)_5(rr)_7 + c_1(rr)_6(rr)_7 + 2i(rr)_4(rr)_7 + (rr)_1(rr)_5 s + (rr)_1(rr)_7 s \\ &- c_1(rr)_2(rr)_6(rr)_7 + c_1(rr)_1(rr)_5 s + i(rr)_2(rr)_5(rr)_6 + 2i(rr)_1(rr)_4 s \\ &+ i(rr)_1(rr)_6 s - (rr)_1(rr)_5 ps + 2i^2(rr)_2(rr)_4(rr)_6 \\ &+ c_1(rr)_2(rr)_5(rr)_6 p)/((rr)_1^2(rr)_5 s^2 - (rr)_1^2(rr)_7 s^2 + (rr)_2(rr)_5(rr)_7 \\ &+ c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 \\ &+ e_0(rr)_1(rr)_5(rr)_7 - i(rr)_1(rr)_2(rr)_5 + i_0(rr)_1(rr)_2(rr)_5 \\ &+ i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 - (rr)_1(rr)_2(rr)_5 s \\ &+ (rr)_1(rr)_2(rr)_7 s + (rr)_1(rr)_5(rr)_7 s + c_1^2(rr)_1(rr)_2(rr)_6 \\ &+ c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 \\ &+ c_1(rr)_1^2(rr)_7 s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2(rr)_5 s + i(rr)_1^2(rr)_5 s \\ &+ i_0(rr)_1^2(rr)_7 s + 2i^2(rr)_1^2(rr)_4 s - c_1 e_0(rr)_1(rr)_2(rr)_6 \\ &+ c_1 e_0(rr)_1(rr)_6(rr)_7 + 2c_1 i(rr)_1(rr)_2(rr)_4 - c_1 i(rr)_1(rr)_2(rr)_6 \\ &+ c_1 i_0(rr)_1(rr)_2(rr)_6 + c_1 i(rr)_1(rr)_6(rr)_7 - 2e_0 i(rr)_1(rr)_2(rr)_4 \\ &+ 2e_0 i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7 s \\ &- (rr)_1(rr)_5(rr)_7 ps + c_1 e_0(rr)_1^2(rr)_6 s + 2c_1 i(rr)_1^2(rr)_6 s + 2e_0 i(rr)_1^2(rr)_4 s \\ &+ i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6 s \\ &- c_1(rr)_1^2(rr)_5 ps - i_0(rr)1^2(rr)_5 ps + 2e_0 i^2(rr)_1(rr)_2(rr)_4(rr)_6 \\ &- c_1 e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1 i(rr)_1(rr)_2(rr)_6(rr)_7 \\ &+ e_0 i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6 s - i(rr)_1(rr)_2(rr)_6(rr)_7 s \\ &+ c_1 e_0(rr)_1(rr)_2(rr)_5(rr)_6 p + c_1 i(rr)_1(rr)_2(rr)_5(rr)_6 p \end{aligned}$$

$$V_{12} = ((rr)_1^2 s^2 - (rr)_1(rr)_2 s + (rr)_1(rr)_7 s + c_1(rr)_2^2(rr)_6 + i(rr)_1(rr)_2(rr)_6 s)/((rr)_1^2(rr)_5 s^2 - (rr)_1^2(rr)_7 s^2 + (rr)_2(rr)_5(rr)_7 + c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7 - i(rr)_1(rr)_2(rr)_5 s + i_0(rr)_1(rr)_2(rr)_5 + i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 - (rr)_1(rr)_2(rr)_5 s + (rr)_1(rr)_2(rr)_7 s + (rr)_1(rr)_5(rr)_7 s + c_1^2(rr)_1(rr)_2(rr)_6 + c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 + c_1(rr)_1^2(rr)_7 s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2 s + i(rr)_1^2(rr)_5 s + i_0(rr)_1^2(rr)_7 s + 2i^2(rr)_1^2(rr)_4 s - c_1 e_0(rr)_1(rr)_2(rr)_6 + c_1 e_0(rr)_1(rr)_6(rr)_7 + 2c_1 i(rr)_1(rr)_2(rr)_4 - c_1 i(rr)_1(rr)_2(rr)_6 + c_1 i_0(rr)_1(rr)_2(rr)_6 + c_1 i(rr)_1(rr)_6(rr)_7 - 2e_0 i(rr)_1(rr)_2(rr)_4 + 2e_0 i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7 s - (rr)_1(rr)_5(rr)_7 ps + c_1 e_0(rr)_1^2(rr)_6 s + 2c_1 i(rr)_1^2(rr)_6 s + 2e_0 i(rr)_1^2(rr)_4 s + i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6 s - c_1(rr)_1^2(rr)_5 ps - i_0(rr)_1^2(rr)_5 ps + 2e_0 i^2(rr)_1(rr)_2(rr)_4(rr)_6 - c_1 e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1 i(rr)_1(rr)_2(rr)_6(rr)_7 + e_0 i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6 s - i(rr)_1(rr)_2(rr)_6(rr)_7 s + c_1 e_0(rr)_1(rr)_2(rr)_5(rr)_6 p + c_1 i(rr)_1(rr)_2(rr)_5(rr)_6 p)$$

$$V_{13} = -((rr)_2(rr)_5 + c_1(rr)_2(rr)_6 + 2i(rr)_2(rr)_4 + (rr)_1(rr)_7 s + i(rr)_1(rr)_5 s - (rr)_1(rr)_5 ps)/((rr)_1^2(rr)_5 s^2 - (rr)_1^2(rr)_7 s^2 + (rr)_2(rr)_5(rr)_7 + c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7 - i(rr)_1(rr)_2(rr)_5 + i_0(rr)_1(rr)_2(rr)_5 + i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 - (rr)_1(rr)_2(rr)_5 s + (rr)_1(rr)_2(rr)_7 s + (rr)_1(rr)_5(rr)_7 s + c_1^2(rr)_1(rr)_2(rr)_6 + c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 + c_1(rr)_1^2(rr)_7 s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2(rr)_5 s + i(rr)_1^2(rr)_5 s + i_0(rr)_1^2(rr)_7 s + 2i^2(rr)_1^2(rr)_4 s - c_1 e_0(rr)_1(rr)_2(rr)_6 + c_1 e_0(rr)_1(rr)_6(rr)_7 + 2c_1 i(rr)_1(rr)_2(rr)_4 - c_1 i(rr)_1(rr)_2(rr)_6 + c_1 i_0(rr)_1(rr)_2(rr)_6 + c_1 i(rr)_1(rr)_6(rr)_7 - 2e_0 i(rr)_1(rr)_2(rr)_4 + 2e_0 i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7 s - (rr)_1(rr)_5(rr)_7 ps + c_1 e_0(rr)_1^2(rr)_6 s + 2c_1 i(rr)_1^2(rr)_6 s + 2e_0 i(rr)_1^2(rr)_4 s + i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6 s - c_1(rr)_1^2(rr)_5 ps - i_0(rr)_1^2(rr)_5 ps + 2e_0 i^2(rr)_1(rr)_2(rr)_4(rr)_6 - c_1 e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1 i(rr)_1(rr)_2(rr)_6(rr)_7 + e_0 i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6 s - i(rr)_1(rr)_2(rr)_6(rr)_7 s + c_1 e_0(rr)_1(rr)_2(rr)_5(rr)_6 p + c_1 i(rr)_1(rr)_2(rr)_5(rr)_6 p)$$

$$V_{21} = -((rr)_5(rr)_7 - i^2(rr)_1(rr)_6 + c_1(rr)_1(rr)_7 - e_0(rr)_1(rr)_7 - i(rr)_1(rr)_7 + i_0(rr)_1(rr)_7 + i(rr)_6(rr)_7 - (rr)_5(rr)_7 p + (rr)_1(rr)_5 s - (rr)_1(rr)_7 s + c_1 i(rr)_1(rr)_6 - e_0 i(rr)_1(rr)_6 + ii_0(rr)_1(rr)_6 - c_1(rr)_1(rr)_5 p + e_0(rr)_1(rr)_5 p + i(rr)_2(rr)_5(rr)_6 - i(rr)_2(rr)_6(rr)_7 + i(rr)_1(rr)_5 p - i_0(rr)_1(rr)_5 p)/((rr)_1^2(rr)_5 s^2 - (rr)_1^2(rr)_7 s^2 + (rr)_2(rr)_5(rr)_7 + c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7 - i(rr)_1(rr)_2(rr)_5 + i_0(rr)_1(rr)_2(rr)_5 + i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 - (rr)_1(rr)_2(rr)_5 s + (rr)_1(rr)_2(rr)_7 s + (rr)_1(rr)_5(rr)_7 s + c_1^2(rr)_1(rr)_2(rr)_6 + c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 + c_1(rr)_1^2(rr)_7 s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2(rr)_5 s + i(rr)_1^2(rr)_5 s + i_0(rr)_1^2(rr)_7 s + 2i^2(rr)_1^2(rr)_4 s - c_1 e_0(rr)_1(rr)_2(rr)_6 + c_1 e_0(rr)_1(rr)_6(rr)_7 + 2c_1 i(rr)_1(rr)_2(rr)_4 - c_1 i(rr)_1(rr)_2(rr)_6 + c_1 i_0(rr)_1(rr)_2(rr)_6 + c_1 i(rr)_1(rr)_6(rr)_7 - 2e_0 i(rr)_1(rr)_2(rr)_4 + 2e_0 i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7 s - (rr)_1(rr)_5(rr)_7 ps + c_1 e_0(rr)_1^2(rr)_6 s + 2c_1 i(rr)_1^2(rr)_6 s + 2e_0 i(rr)_1^2(rr)_4 s + i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6 s - c_1(rr)_1^2(rr)_5 ps - i_0(rr)_1^2(rr)_5 ps + 2e_0 i^2(rr)_1(rr)_2(rr)_4(rr)_6 - c_1 e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1 i(rr)_1(rr)_2(rr)_6(rr)_7 + e_0 i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6 s - i(rr)_1(rr)_2(rr)_6(rr)_7 s + c_1 e_0(rr)_1(rr)_2(rr)_5(rr)_6 p + c_1 i(rr)_1(rr)_2(rr)_5(rr)_6 p)$$

$$V_{22} = -((rr)_2(rr)_7 + e_0(rr)_1^2 s + i(rr)_1^2 s + c_1(rr)_1(rr)_2 - e_0(rr)_1(rr)_2 + e_0(rr)_1(rr)_7 - i(rr)_1(rr)_2 + i_0(rr)_1(rr)_2 + i(rr)_1(rr)_7 + i^2(rr)_1(rr)_2(rr)_6 + e_0 i(rr)_1(rr)_2(rr)_6)/((rr)_1^2(rr)_5 s^2 - (rr)_1^2(rr)_7 s^2 + (rr)_2(rr)_5(rr)_7 + c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7 - i(rr)_1(rr)_2(rr)_5 + i_0(rr)_1(rr)_2(rr)_5 + i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 - (rr)_1(rr)_2(rr)_5 s + (rr)_1(rr)_2(rr)_7 s + (rr)_1(rr)_5(rr)_7 s + c_1^2(rr)_1(rr)_2(rr)_6 + c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 + c_1(rr)_1^2(rr)_7 s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2(rr)_5 s + i(rr)_1^2(rr)_5 s + i_0(rr)_1^2(rr)_7 s + 2i^2(rr)_1^2(rr)_4 s - c_1 e_0(rr)_1(rr)_2(rr)_6 + c_1 e_0(rr)_1(rr)_6(rr)_7 + 2c_1 i(rr)_1(rr)_2(rr)_4 - c_1 i(rr)_1(rr)_2(rr)_6 + c_1 i_0(rr)_1(rr)_2(rr)_6 + c_1 i(rr)_1(rr)_6(rr)_7 - 2e_0 i(rr)_1(rr)_2(rr)_4 + 2e_0 i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7 s - (rr)_1(rr)_5(rr)_7 ps + c_1 e_0(rr)_1^2(rr)_6 s + 2c_1 i(rr)_1^2(rr)_6 s + 2e_0 i(rr)_1^2(rr)_4 s + i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6 s - c_1(rr)_1^2(rr)_5 ps - i_0(rr)_1^2(rr)_5 ps + 2e_0 i^2(rr)_1(rr)_2(rr)_4(rr)_6 - c_1 e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1 i(rr)_1(rr)_2(rr)_6(rr)_7 + e_0 i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6 s - i(rr)_1(rr)_2(rr)_6(rr)_7 s + c_1 e_0(rr)_1(rr)_2(rr)_5(rr)_6 p + c_1 i(rr)_1(rr)_2(rr)_5(rr)_6 p)$$

$$V_{23} = ((rr)_2(rr)_7 - (rr)_2(rr)_5 + i^2(rr)_1(rr)_6 + e_0(rr)_1(rr)_7 + i(rr)_1(rr)_7 + e_0 i(rr)_1(rr)_6 - e_0(rr)_1(rr)_5 p - i(rr)_1(rr)_5 p)/((rr)_1^2(rr)_5 s^2 - (rr)_1^2(rr)_7 s^2 + (rr)_2(rr)_5(rr)_7 + c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7 - i(rr)_1(rr)_2(rr)_5 + i_0(rr)_1(rr)_2(rr)_5 + i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 - (rr)_1(rr)_2(rr)_5 s + (rr)_1(rr)_2(rr)_7 s + (rr)_1(rr)_5(rr)_7 s + c_1^2(rr)_1(rr)_2(rr)_6 + c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 + c_1(rr)_1^2(rr)_7 s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2(rr)_5 s + i(rr)_1^2(rr)_5 s + i_0(rr)_1^2(rr)_7 s + 2i^2(rr)_1^2(rr)_4 s - c_1 e_0(rr)_1(rr)_2(rr)_6 + c_1 e_0(rr)_1(rr)_6(rr)_7 + 2c_1 i(rr)_1(rr)_2(rr)_4 - c_1 i(rr)_1(rr)_2(rr)_6 + c_1 i_0(rr)_1(rr)_2(rr)_6 + c_1 i(rr)_1(rr)_6(rr)_7 - 2e_0 i(rr)_1(rr)_2(rr)_4 + 2e_0 i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7 s - (rr)_1(rr)_5(rr)_7 ps + c_1 e_0(rr)_1^2(rr)_6 s + 2c_1 i(rr)_1^2(rr)_6 s + 2e_0 i(rr)_1^2(rr)_4 s + i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6 s - c_1(rr)_1^2(rr)_5 ps - i_0(rr)_1^2(rr)_5 ps + 2e_0 i^2(rr)_1(rr)_2(rr)_4(rr)_6 - c_1 e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1 i(rr)_1(rr)_2(rr)_6(rr)_7 + e_0 i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6 s - i(rr)_1(rr)_2(rr)_6(rr)_7 s + c_1 e_0(rr)_1(rr)_2(rr)_5(rr)_6 p + c_1 i(rr)_1(rr)_2(rr)_5(rr)_6 p)$$

$$V_{31} = ((rr)_5(rr)_7 - 2i^2(rr)_1(rr)_4 + c_1(rr)_1(rr)_5 + c_1(rr)_6(rr)_7 - e_0(rr)_1(rr)_5 - i(rr)_1(rr)_5 + i_0(rr)_1(rr)_5 + 2i(rr)_4(rr)_7 - (rr)_1(rr)_5 s + (rr)_1(rr)_7 s + c_1^2(rr)_1(rr)_6 - c_1 e_0(rr)_1(rr)_6 + 2c_1 i(rr)_1(rr)_4 - c_1 i(rr)_1(rr)_6 + c_1 i_0(rr)_1(rr)_6 - 2e_0 i(rr)_1(rr)_4 + c_1(rr)_2(rr)_5(rr)_6 - c_1(rr)_2(rr)_6(rr)_7 + 2ii_0(rr)_1(rr)_4)/((rr)_1^2(rr)_5 s^2 - (rr)_1^2(rr)_7 s^2 + (rr)_2(rr)_5(rr)_7 + c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7 - i(rr)_1(rr)_2(rr)_5 + i_0(rr)_1(rr)_2(rr)_5 + i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 - (rr)_1(rr)_2(rr)_5 s + (rr)_1(rr)_2(rr)_7 s + (rr)_1(rr)_5(rr)_7 s + c_1^2(rr)_1(rr)_2(rr)_6 + c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 + c_1(rr)_1^2(rr)_7 s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2(rr)_5 s + i(rr)_1^2(rr)_5 s + i_0(rr)_1^2(rr)_7 s + 2i^2(rr)_1^2(rr)_4 s - c_1 e_0(rr)_1(rr)_2(rr)_6 + c_1 e_0(rr)_1(rr)_6(rr)_7 + 2c_1 i(rr)_1(rr)_2(rr)_4 - c_1 i(rr)_1(rr)_2(rr)_6 + c_1 i(rr)_1(rr)_6(rr)_7 + c_1 i_0(rr)_1(rr)_2(rr)_6 - 2e_0 i(rr)_1(rr)_2(rr)_4 + 2e_0 i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7 s - (rr)_1(rr)_5(rr)_7 ps + c_1 e_0(rr)_1^2(rr)_6 s + 2c_1 i(rr)_1^2(rr)_6 s + 2e_0 i(rr)_1^2(rr)_4 s + i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6 s - c_1(rr)_1^2(rr)_5 ps - i_0(rr)_1^2(rr)_5 ps + 2e_0 i^2(rr)_1(rr)_2(rr)_4(rr)_6 - c_1 e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1 i(rr)_1(rr)_2(rr)_6(rr)_7 + e_0 i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6 s - i(rr)_1(rr)_2(rr)_6(rr)_7 s + c_1 e_0(rr)_1(rr)_2(rr)_5(rr)_6 p + c_1 i(rr)_1(rr)_2(rr)_5(rr)_6 p)$$

$$V_{32} = -(c_1(rr)_1^2 s + i_0(rr)_1^2 s + (rr)_1(rr)_7 s - c_1 e_0(rr)_1(rr)_2(rr)_6 - c_1 i(rr)_1(rr)_2(rr)_6)/((rr)_1^2(rr)_5 s^2 - (rr)_1^2(rr)_7 s^2 + (rr)_2(rr)_5(rr)_7 + c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7 - i(rr)_1(rr)_2(rr)_5 + i_0(rr)_1(rr)_2(rr)_5 + i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 + i_0(rr)_1(rr)_2(rr)_5 - (rr)_1(rr)_2(rr)_5 s + (rr)_1(rr)_2(rr)_7 s + (rr)_1(rr)_5(rr)_7 s + c_1^2(rr)_1(rr)_2(rr)_6 + c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 + c_1(rr)_1^2(rr)_7 s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2(rr)_5 s + i(rr)_1^2(rr)_5 s + i_0(rr)_1^2(rr)_7 s + 2i^2(rr)_1^2(rr)_4 s - c_1 e_0(rr)_1(rr)_2(rr)_6 + c_1 e_0(rr)_1(rr)_6(rr)_7 + 2c_1 i(rr)_1(rr)_2(rr)_4 - c_1 i(rr)_1(rr)_2(rr)_6 + c_1 i_0(rr)_1(rr)_2(rr)_6 + c_1 i(rr)_1(rr)_6(rr)_7 + c_1 i_0(rr)_1(rr)_2(rr)_6 - 2e_0 i(rr)_1(rr)_2(rr)_4 + 2e_0 i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7 s - (rr)_1(rr)_5(rr)_7 ps + c_1 e_0(rr)_1^2(rr)_6 s + 2c_1 i(rr)_1^2(rr)_6 s + 2e_0 i(rr)_1^2(rr)_4 s + i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6 s - c_1(rr)_1^2(rr)_5 ps - i_0(rr)_1^2(rr)_5 ps + 2e_0 i^2(rr)_1(rr)_2(rr)_4(rr)_6 - c_1 e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1 i(rr)_1(rr)_2(rr)_6(rr)_7 + e_0 i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6 s - i(rr)_1(rr)_2(rr)_6(rr)_7 s + c_1 e_0(rr)_1(rr)_2(rr)_5(rr)_6 p + c_1 i(rr)_1(rr)_2(rr)_5(rr)_6 p)$$

$$V_{33} = -(2i^2(rr)_1(rr)_4 + e_0(rr)_1(rr)_5 + i(rr)_1(rr)_5 + (rr)_1(rr)_5 s - (rr)_1(rr)_7 s + c_1 e_0(rr)_1(rr)_6 + c_1 i(rr)_1(rr)_6 + 2e_0 i(rr)_1(rr)_4)/((rr)_1^2(rr)_5 s^2 - (rr)_1^2(rr)_7 s^2 + (rr)_2(rr)_5(rr)_7 + c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7 - i(rr)_1(rr)_2(rr)_5 + i_0(rr)_1(rr)_2(rr)_5 + i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 + i_0(rr)_1(rr)_2(rr)_5 - (rr)_1(rr)_2(rr)_5 s + (rr)_1(rr)_2(rr)_7 s + (rr)_1(rr)_5(rr)_7 s + c_1^2(rr)_1(rr)_2(rr)_6 + c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 + c_1(rr)_1^2(rr)_7 s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2(rr)_5 s + i(rr)_1^2(rr)_5 s + i_0(rr)_1^2(rr)_7 s + 2i^2(rr)_1^2(rr)_4 s - c_1 e_0(rr)_1(rr)_2(rr)_6 + c_1 e_0(rr)_1(rr)_6(rr)_7 + 2c_1 i(rr)_1(rr)_2(rr)_4 - c_1 i(rr)_1(rr)_2(rr)_6 + c_1 i_0(rr)_1(rr)_2(rr)_6 + c_1 i(rr)_1(rr)_6(rr)_7 - 2e_0 i(rr)_1(rr)_2(rr)_4 + 2e_0 i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7 s - (rr)_1(rr)_5(rr)_7 ps + c_1 e_0(rr)_1^2(rr)_6 s + 2c_1 i(rr)_1^2(rr)_6 s + 2e_0 i(rr)_1^2(rr)_4 s + i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6 s - c_1(rr)_1^2(rr)_5 ps - i_0(rr)_1^2(rr)_5 ps + 2e_0 i^2(rr)_1(rr)_2(rr)_4(rr)_6 - c_1 e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1 i(rr)_1(rr)_2(rr)_6(rr)_7 + e_0 i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6 s - i(rr)_1(rr)_2(rr)_6(rr)_7 s + c_1 e_0(rr)_1(rr)_2(rr)_5(rr)_6 p + c_1 i(rr)_1(rr)_2(rr)_5(rr)_6 p)$$

As a result, $K = FV^{-1} = \begin{bmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ 0 & 0 & 0 \end{bmatrix}$

Where;

$$a_{11} = -(rr)_1 s(((rr)_5(rr)_7 - 2i^2(rr)_1(rr)_4 + c_1(rr)_1(rr)_5 + c_1(rr)_6(rr)_7 - e_0(rr)_1(rr)_5 - i(rr)_1(rr)_5 + 2i(rr)_4(rr)_7 + i_0(rr)_1(rr)_5 - (rr)_1(rr)_5 s + (rr)_1(rr)_7 s + c_1^2(rr)_1(rr)_6 - c_1 e_0(rr)_1(rr)_6 + 2c_1 i(rr)_1(rr)_4 - c_1 i(rr)_1(rr)_6 + c_1 i_0(rr)_1(rr)_6 - 2e_0 i(rr)_1(rr)_4 + c_1(rr)_2(rr)_5(rr)_6 - c_1(rr)_2(rr)_6(rr)_7 + 2ii_0(rr)_1(rr)_4) - (c_1(rr)_1 + i_0(rr)_1)((rr)_5(rr)_7 + c_1(rr)_6(rr)_7 + 2i(rr)_4(rr)_7 + (rr)_1(rr)_5 s + (rr)_1(rr)_7 s - c_1(rr)_2(rr)_6(rr)_7 + c_1(rr)_1(rr)_6 s + i(rr)_2(rr)_5(rr)_6 + 2i(rr)_1(rr)_4 s + i(rr)_1(rr)_6 s - (rr)_1(rr)_5 ps + 2i^2(rr)_2(rr)_4(rr)_6 + c_1(rr)_2(rr)_5(rr)_6 p)/((rr)_1^2(rr)_5 s^2 - (rr)_1^2(rr)_7 s^2 + (rr)_2(rr)_5(rr)_7 + c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7 - i(rr)_1(rr)_2(rr)_5 + i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 + i_0(rr)_1(rr)_2(rr)_5 - (rr)_1(rr)_2(rr)_5 s + (rr)_1(rr)_2(rr)_7 s + (rr)_1(rr)_5(rr)_7 s + c_1^2(rr)_1(rr)_2(rr)_6 + c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 + c_1(rr)_1^2(rr)_7 s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2(rr)_5 s + i(rr)_1^2(rr)_5 s + i_0(rr)_1^2(rr)_7 s + 2i^2(rr)_1^2(rr)_4 s - c_1 e_0(rr)_1(rr)_2(rr)_6 + c_1 e_0(rr)_1(rr)_6(rr)_7 + 2c_1 i(rr)_1(rr)_2(rr)_4 - c_1 i(rr)_1(rr)_2(rr)_6 + c_1 i(rr)_1(rr)_6(rr)_7 + c_1 i_0(rr)_1(rr)_2(rr)_6 - 2e_0 i(rr)_1(rr)_2(rr)_4 + 2e_0 i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7 s - (rr)_1(rr)_5(rr)_7 ps + c_1 e_0(rr)_1^2(rr)_6 s + 2c_1 i(rr)_1^2(rr)_6 s + 2e_0 i(rr)_1^2(rr)_4 s + i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6 s - c_1(rr)_1^2(rr)_5 ps - i_0(rr)_1^2(rr)_5 ps + 2e_0 i^2(rr)_1(rr)_2(rr)_4(rr)_6 - c_1 e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1 i(rr)_1(rr)_2(rr)_6(rr)_7 + e_0 i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6 s - i(rr)_1(rr)_2(rr)_6(rr)_7 s + c_1 e_0(rr)_1(rr)_2(rr)_5(rr)_6 p + c_1 i(rr)_1(rr)_2(rr)_5(rr)_6 p)$$

$$a_{12} = ((rr)_1(c_1^2(rr)_2^2(rr)_6 - (rr)_1(rr)_7s^2 - c_1(rr)_1(rr)_2s + c_1(rr)_1(rr)_7s - i_0(rr)_1(rr)_2s + i_0(rr)_1(rr)_7s + c_1i_0(rr)_2^2(rr)_6 + c_1e_0(rr)_1(rr)_2(rr)_6s + 2c_1i(rr)_1(rr)_2(rr)_6s + ii_0(rr)_1(rr)_2(rr)_6s))/((rr)_1^2(rr)_5s^2 - (rr)_1^2(rr)_7s^2 + (rr)_2(rr)_5(rr)_7 + c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7 - i(rr)_1(rr)_2(rr)_5 + i_0(rr)_1(rr)_2(rr)_5 + i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 - (rr)_1(rr)_2(rr)_5s + (rr)_1(rr)_2(rr)_7s + (rr)_1(rr)_5(rr)_7s + c_1^2(rr)_1(rr)_2(rr)_6 + c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 + c_1(rr)_1^2(rr)_7s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2(rr)_5s + i(rr)_1^2(rr)_5s + i_0(rr)_1^2(rr)_7s + 2i^2(rr)_1^2(rr)_4s - c_1e_0(rr)_1(rr)_2(rr)_6 + c_1e_0(rr)_1(rr)_6(rr)_7 + 2c_1i(rr)_1(rr)_2(rr)_4 - c_1i(rr)_1(rr)_2(rr)_6 + c_1i_0(rr)_1(rr)_2(rr)_6 + c_1i(rr)_1(rr)_6(rr)_7 - 2e_0i(rr)_1(rr)_2(rr)_4 + 2e_3i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7s - (rr)_1(rr)_5(rr)_7ps + c_1e_0(rr)_1^2(rr)_6s + 2c_1i(rr)_1^2(rr)_6s + 2e_0i(rr)_1^2(rr)_4s + i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6s - c_1(rr)_1^2(rr)_5ps - i_0(rr)_1^2(rr)_5ps + 2e_0i^2(rr)_1(rr)_2(rr)_4(rr)_6 - c_1e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1i(rr)_1(rr)_2(rr)_6(rr)_7 + e_0i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6s - i(rr)_1(rr)_2(rr)_6(rr)_7s - c_1e_0(rr)_1(rr)_2(rr)_5(rr)_6p + c_1i(rr)_1(rr)_2(rr)_5(rr)_6p)$$

$$a_{13} = (-(c_1(rr)_1 - i_0(rr)_1)((rr)_2(rr)_5 + c_1(rr)_2(rr)_6 + 2i(rr)_2(rr)_4 + (rr)_1(rr)_7s + i(rr)_1(rr)_6s - (rr)_1(rr)_5ps) - (rr)_1s(2i^2(rr)_1(rr)_4 + e_0(rr)_1(rr)_5 + i(rr)_1(rr)_5 + (rr)_1(rr)_5s + 2e_6i(rr)_1(rr)_4) / ((rr)_1^2(rr)_5s^2 - (rr)_1^2(rr)_7s^2 + (rr)_2(rr)_5(rr)_7 + c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7 - i(rr)_1(rr)_2(rr)_5 + i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 + i_0(rr)_1(rr)_2(rr)_5 - (rr)_1(rr)_2(rr)_5s + (rr)_1(rr)_2(rr)_7s + (rr)_1(rr)_5(rr)_7s + c_1^2(rr)_1(rr)_2(rr)_6 + c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 + c_1(rr)_1^2(rr)_7s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2(rr)_5s + i(rr)_1^2(rr)_5s + i_0(rr)_1^2(rr)_7s + 2i^2(rr)_1^2(rr)_4s - c_1e_0(rr)_1(rr)_2(rr)_6 + c_1e_0(rr)_1(rr)_6(rr)_7 + 2c_1i(rr)_1(rr)_2(rr)_4 - c_1i(rr)_1(rr)_2(rr)_6 + c_1i_0(rr)_1(rr)_2(rr)_6 + c_1i(rr)_1(rr)_6(rr)_7 - 2e_0i(rr)_1(rr)_2(rr)_4 + 2e_3i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7s - (rr)_1(rr)_5(rr)_7ps + c_1e_0(rr)_1^2(rr)_6s + 2c_1i(rr)_1^2(rr)_6s + 2e_0i(rr)_1^2(rr)_4s + i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6s - c_1(rr)_1^2(rr)_5ps - i_0(rr)_1^2(rr)_5ps + 2e_0i^2(rr)_1(rr)_2(rr)_4(rr)_6 - c_1e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1i(rr)_1(rr)_2(rr)_6(rr)_7 + e_0i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6s - i(rr)_1(rr)_2(rr)_6(rr)_7s - c_1e_0(rr)_1(rr)_2(rr)_5(rr)_6p + c_1i(rr)_1(rr)_2(rr)_5(rr)_6p)$$

$$a_{21} = -((rr)_4(i_0^2(rr)_1(rr)_7 - 2i^3(rr)_1(rr)_4 - i^2(rr)_1(rr)_5 + 2i^2(rr)_4(rr)_7 - c_1(rr)_5(rr)_7 + i(rr)_5(rr)_7 + i_0(rr)_5(rr)_7 - c_1^2(rr)_1(rr)_7 + c_1e_0(rr)_1(rr)_7 + c_1i(rr)_1(rr)_5 + c_1i(rr)_1(rr)_7 - e_0i(rr)_1(rr)_5 - e_0i_0(rr)_1(rr)_7 + ii_0(rr)_1(rr)_5 - ii_0(rr)_1(rr)_7 + ii_0(rr)_6(rr)_7 + c_1(rr)_5(rr)_7p - c_1(rr)_1(rr)_5s + c_1(rr)_1(rr)_7s - i_0(rr)_5(rr)_7p - i(rr)_1(rr)_5s + i_0(rr)_1(rr)_5s + i(rr)_1(rr)_7s - i_0(rr)_1(rr)_7s + 2c_1i^2(rr)_1(rr)_4 - 2e_8i^2(rr)_1(rr)_4 + 2i^2i_0(rr)_1(rr)_4 + ii_0^2(rr)_1(rr)_6 - i^2i_0(rr)_1(rr)_6 + c_1^2(rr)_1(rr)_5p - i_0^2(rr)_1(rr)_5p + c_1ii_0(rr)_1(rr)_6 - e_0ii_0(rr)_1(rr)_6 - c_1e_0(rr)_1(rr)_5p - c_1i(rr)_1(rr)_5p + e_0i_0(rr)_1(rr)_5p + ii_0(rr)_2(rr)_5(rr)_6 - ii_0(rr)_2(rr)_6(rr)_7 + ii_0(rr)_1(rr)_5p))/((rr)_1^2(rr)_5s^2 - (rr)_1^2(rr)_7s^2 + (rr)_2(rr)_5(rr)_7 + c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7 - i(rr)_1(rr)_2(rr)_5 + i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 + i_0(rr)_1(rr)_2(rr)_5 - (rr)_1(rr)_2(rr)_5s + (rr)_1(rr)_2(rr)_7s + (rr)_1(rr)_5(rr)_7s + c_1^2(rr)_1(rr)_2(rr)_6 + c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 + c_1(rr)_1^2(rr)_7s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2(rr)_5s + i(rr)_1^2(rr)_5s + i_0(rr)_1^2(rr)_7s + 2i^2(rr)_1^2(rr)_4s - c_1e_0(rr)_1(rr)_2(rr)_6 + c_1e_0(rr)_1(rr)_6(rr)_7 + 2c_1i(rr)_1(rr)_2(rr)_4 - c_1i(rr)_1(rr)_2(rr)_6 + c_1i_5(rr)_1(rr)_2(rr)_6 + c_1i(rr)_1(rr)_6(rr)_7 - 2e_0i(rr)_1(rr)_2(rr)_4 + 2e_8i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7s - (rr)_1(rr)_5(rr)_7ps + c_1e_0(rr)_1^2(rr)_6s + 2c_1i(rr)_1^2(rr)_6s + 2e_0i(rr)_1^2(rr)_4s + i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6s - c_1(rr)_1^2(rr)_5ps - i_0(rr)_1^2(rr)_5ps + 2e_0i^2(rr)_1(rr)_2(rr)_4(rr)_6 - c_1e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1i(rr)_1(rr)_2(rr)_6(rr)_7 + e_0i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6s - i(rr)_1(rr)_2(rr)_6(rr)_7s + c_1e_0(rr)_1(rr)_2(rr)_5(rr)_6p + c_1i(rr)_1(rr)_2(rr)_5(rr)_6p)$$

$$a_{22} = (i(rr)_4(c_1(rr)_1^2s + i_0(rr)_1^2s + (rr)_1(rr)_7s - c_1e_0(rr)_1(rr)_2(rr)_6 - c_1i(rr)_1(rr)_2(rr)_6) + (rr)_4(c_1 - i_0)((rr)_2(rr)_7 + e_0(rr)_1^2s + i(rr)_1^2s + c_1(rr)_1(rr)_2 - e_0(rr)_1(rr)_2 + e_0(rr)_1(rr)_7 - i(rr)_1(rr)_2 + i(rr)_1(rr)_7 + i_0(rr)_1(rr)_2 + i^2(rr)_1(rr)_2(rr)_6 + e_0i(rr)_1(rr)_2(rr)_6)) / ((rr)_1^2(rr)_5s^2 - (rr)_1^2(rr)_7s^2 + (rr)_2(rr)_5(rr)_7 + c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7 - i(rr)_1(rr)_2(rr)_5 + i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 + i_0(rr)_1(rr)_2(rr)_5 - (rr)_1(rr)_2(rr)_5s + (rr)_1(rr)_2(rr)_7s + (rr)_1(rr)_5(rr)_7s + c_1^2(rr)_1(rr)_2(rr)_6 + c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 + c_1(rr)_1^2(rr)_7s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2(rr)_5s + i(rr)_1^2(rr)_5s + i_0(rr)_1^2(rr)_7s + 2i^2(rr)_1^2(rr)_4s - c_1e_0(rr)_1(rr)_2(rr)_6 + c_1e_0(rr)_1(rr)_6(rr)_7 + 2c_1i(rr)_1(rr)_2(rr)_4 - c_1i(rr)_1(rr)_2(rr)_6 + c_1i_0(rr)_1(rr)_2(rr)_6 + c_1i(rr)_1(rr)_6(rr)_7 - 2e_0i(rr)_1(rr)_2(rr)_4 + 2e_3i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7s - (rr)_1(rr)_5(rr)_7ps + c_1e_0(rr)_1^2(rr)_6s + 2c_1i(rr)_1^2(rr)_6s + 2e_0i(rr)_1^2(rr)_4s + i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6s - c_1(rr)_1^2(rr)_5ps - i_0(rr)_1^2(rr)_5ps + 2e_0i^2(rr)_1(rr)_2(rr)_4(rr)_6 - c_1e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1i(rr)_1(rr)_2(rr)_6(rr)_7 + e_0i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6s - i(rr)_1(rr)_2(rr)_6(rr)_7s + c_1e_0(rr)_1(rr)_2(rr)_5(rr)_6p + c_1i(rr)_1(rr)_2(rr)_5(rr)_6p)$$

$$a_{23} = (i(rr)_4(2i^2(rr)_1(rr)_4 + e_0(rr)_1(rr)_5 + i(rr)_1(rr)_5 + (rr)_1(rr)_5s - (rr)_1(rr)_7s + c_1e_0(rr)_1(rr)_6 + c_1i(rr)_1(rr)_6 + 2e_0i(rr)_1(rr)_4) - (rr)_4(c_1 - i_0)((rr)_2(rr)_7 - (rr)_2(rr)_5 + i^2(rr)_1(rr)_6 + e_0(rr)_1(rr)_7 + i(rr)_1(rr)_7 + e_0i(rr)_1(rr)_6 - e_0(rr)_1(rr)_5p - i(rr)_1(rr)_5p) / ((rr)_1^2(rr)_5s^2 - (rr)_1^2(rr)_7s^2 + (rr)_2(rr)_5(rr)_7 + c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7 + i(rr)_1(rr)_2(rr)_5 + c_1(rr)_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7i(rr)_1(rr)_2(rr)_5 + i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 + i_0(rr)_1(rr)_2(rr)_5 - (rr)_1(rr)_2(rr)_5s + (rr)_1(rr)_2(rr)_7s + (rr)_1(rr)_5(rr)_7s + c_1^2(rr)_1(rr)_2(rr)_6 + c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 + c_1(rr)_1^2(rr)_7s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2(rr)_5s + i(rr)_1^2(rr)_5s + i_0(rr)_1^2(rr)_7s + 2i^2(rr)_1^2(rr)_4s - c_1e_0(rr)_1(rr)_2(rr)_6 + c_1e_0(rr)_1(rr)_6(rr)_7 + 2c_1i(rr)_1(rr)_2(rr)_4 - c_1i(rr)_1(rr)_2(rr)_6 + c_1i_0(rr)_1(rr)_2(rr)_6 + c_1i(rr)_1(rr)_6(rr)_7 - 2e_0i(rr)_1(rr)_2(rr)_4 + 2e_3i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7s - (rr)_1(rr)_5(rr)_7ps + c_1e_0(rr)_1^2(rr)_6s + 2c_1i(rr)_1^2(rr)_6s + 2e_0i(rr)_1^2(rr)_4s + i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6s - c_1(rr)_1^2(rr)_5ps - i_0(rr)_1^2(rr)_5ps + 2e_0i^2(rr)_1(rr)_2(rr)_4(rr)_6 - c_1e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1i(rr)_1(rr)_2(rr)_6(rr)_7 + e_0i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6s - i(rr)_1(rr)_2(rr)_6(rr)_7s + c_1e_0(rr)_1(rr)_2(rr)_5(rr)_6p + c_1i(rr)_1(rr)_2(rr)_5(rr)_6p)$$

The basic reproduction number is defined to be the spectral radius which is the magnitude of the largest eigenvalue of the matrix K.

So, $Spectral\ Radius\ \lambda =$

$$|(-(c_1(rr)_1 + i_0(rr)_1)((rr)_2(rr)_5 + c_1(rr)_2(rr)_6 + 2i(rr)_2(rr)_4 + (rr)_1(rr)_7s + i(rr)_1(rr)_6s - (rr)_1) - (rr)_1s(2i^2(rr)_1(rr)_4 + e_0(rr)_1(rr)_5 + i(rr)_1(rr)_5 + (rr)_1(rr)_5s - (rr)_1(rr)_7s + c_1e_0(rr)_1(rr)_6 + c_1i(rr)_1(rr)_6 + 2e_0i(rr)_1(rr)_4))/((rr)_1^2(rr)_5s^2 - (rr)_1^2(rr)_7s^2 + (rr)_2(rr)_5(rr)_7 + c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7 - i(rr)_1(rr)_2(rr)_5 + i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 + i_0(rr)_1(rr)_2(rr)_5 - (rr)_1(rr)_2(rr)_5s + (rr)_1(rr)_2(rr)_7s + (rr)_1(rr)_5(rr)_7s + c_1^2(rr)_1(rr)_2(rr)_6 + c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 + c_1(rr)_1^2(rr)_7s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2(rr)_5s + i(rr)_1^2(rr)_5s + i_0(rr)_1^2(rr)_7s + 2i^2(rr)_1^2(rr)_4s - c_1e_0(rr)_1(rr)_2(rr)_6 + c_1e_0(rr)_1(rr)_6(rr)_7 + 2c_1i(rr)_1(rr)_2(rr)_4 - c_1i(rr)_1(rr)_2(rr)_6 + c_1i_0(rr)_1(rr)_2(rr)_6 + c_1i(rr)_1(rr)_6(rr)_7 - 2e_0i(rr)_1(rr)_2(rr)_4 + 2e_0i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7s - (rr)_1(rr)_5(rr)_7ps + c_1e_0(rr)_1^2(rr)_6s + 2c_1i(rr)_1^2(rr)_6s + 2e_0i(rr)_1^2(rr)_4s + i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6s - c_1(rr)_1^2(rr)_5ps - i_0(rr)_1^2(rr)_5ps + 2e_0i^2(rr)_1(rr)_2(rr)_4(rr)_6 - c_1e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1i(rr)_1(rr)_2(rr)_6(rr)_7 + e_0i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6s - i(rr)_1(rr)_2(rr)_6(rr)_7s + c_1e_0(rr)_1(rr)_2(rr)_5(rr)_6p + c_1i(rr)_1(rr)_2(rr)_5(rr)_6p)|$$

Therefore, $R_0 =$

$$|(-(c_1(rr)_1 + i_0(rr)_1)((rr)_2(rr)_5 + c_1(rr)_2(rr)_6 + 2i(rr)_2(rr)_4 + (rr)_1(rr)_7s + i(rr)_1(rr)_6s - (rr)_1) - (rr)_1s(2i^2(rr)_1(rr)_4 + e_0(rr)_1(rr)_5 + i(rr)_1(rr)_5 + (rr)_1(rr)_5s - (rr)_1(rr)_7s + c_1e_0(rr)_1(rr)_6 + c_1i(rr)_1(rr)_6 + 2e_0i(rr)_1(rr)_4))/((rr)_1^2(rr)_5s^2 - (rr)_1^2(rr)_7s^2 + (rr)_2(rr)_5(rr)_7 + c_1(rr)_1(rr)_2(rr)_5 + c_1(rr)_2(rr)_6(rr)_7 - e_0(rr)_1(rr)_2(rr)_5 + e_0(rr)_1(rr)_5(rr)_7 - i(rr)_1(rr)_2(rr)_5 + i(rr)_1(rr)_5(rr)_7 + 2i(rr)_2(rr)_4(rr)_7 + i_0(rr)_1(rr)_2(rr)_5 - (rr)_1(rr)_2(rr)_5s + (rr)_1(rr)_2(rr)_7s + (rr)_1(rr)_5(rr)_7s + c_1^2(rr)_1(rr)_2(rr)_6 + c_1(rr)_2^2(rr)_5(rr)_6 - c_1(rr)_2^2(rr)_6(rr)_7 - 2i^2(rr)_1(rr)_2(rr)_4 + c_1(rr)_1^2(rr)_7s + 2i^2(rr)_1(rr)_4(rr)_7 + e_0(rr)_1^2(rr)_5s + i(rr)_1^2(rr)_5s + i_0(rr)_1^2(rr)_7s + 2i^2(rr)_1^2(rr)_4s - c_1e_0(rr)_1(rr)_2(rr)_6 + c_1e_0(rr)_1(rr)_6(rr)_7 + 2c_1i(rr)_1(rr)_2(rr)_4 - c_1i(rr)_1(rr)_2(rr)_6 + c_1i_0(rr)_1(rr)_2(rr)_6 + c_1i(rr)_1(rr)_6(rr)_7 - 2e_0i(rr)_1(rr)_2(rr)_4 + 2e_0i(rr)_1(rr)_4(rr)_7 + 2ii_0(rr)_1(rr)_2(rr)_4 + i(rr)_1(rr)_6(rr)_7s - (rr)_1(rr)_5(rr)_7ps + c_1e_0(rr)_1^2(rr)_6s + 2c_1i(rr)_1^2(rr)_6s + 2e_0i(rr)_1^2(rr)_4s + i^2(rr)_1(rr)_2(rr)_5(rr)_6 + 2i^3(rr)_1(rr)_2(rr)_4(rr)_6 + ii_0(rr)_1^2(rr)_6s - c_1(rr)_1^2(rr)_5ps - i_0(rr)_1^2(rr)_5ps + 2e_0i^2(rr)_1(rr)_2(rr)_4(rr)_6 - c_1e_0(rr)_1(rr)_2(rr)_6(rr)_7 - c_1i(rr)_1(rr)_2(rr)_6(rr)_7 + e_0i(rr)_1(rr)_2(rr)_5(rr)_6 + i(rr)_1(rr)_2(rr)_5(rr)_6s - i(rr)_1(rr)_2(rr)_6(rr)_7s + c_1e_0(rr)_1(rr)_2(rr)_5(rr)_6p + c_1i(rr)_1(rr)_2(rr)_5(rr)_6p)|$$

Consequently, for all possible positive parametric values, the basic Reproduction number (R_0) of our system of differential equation is less than 1. Hence the system is asymptotically Stable.

Boundedness / Existence of solution

Theorem: *Let* $D \subseteq \mathbb{R} \times \mathbb{R}^n$ *e a closed rectangle with* $(t_0, y_0) \in D$. *Let* $f: D \rightarrow \mathbb{R}^n$ *be a function that is continuous in t and Lipchitz Continuous in y. Then, there exists some* $\varepsilon > 0$ *such that the initial value problem* $y'(t) = f(t, y(t)), y(t_0) = y_0. =$ *has a unique solution* $y(t)$ *on the interval* $[t_0 - \varepsilon, t_0 + \varepsilon]$.

The mathematical model of our system is well-posed. Picard's theorem states that its unique solution exist and is constantly dependent on the initial data. Because we are dealing with the human population, we must guarantee that our solutions are positive and bound[23].

Equilibrium Point and their existence:

Solving the algebraic equations(6a) (6b) and (6c),

$$\frac{ds}{dt} = -(rr)_1 s(e_0 - i_0 + i - c_1) + (rr)_2 c_1 \quad \text{... (6a)}$$

$$\frac{di}{dt} = -(rr)_4 i(e_0 - i_0 + i - c_1) + (rr)_5(s + pc_1 + i_0 - s_0 - i) - (rr)_6 ic_1 + (rr)_7(s_0 - s - c_1 - p) \quad \text{... (6b)}$$

$$\frac{dc_1}{dt} = (rr)_1 s(e_0 - i_0 + i - c_1) - ((rr)_2 + (rr)_3 + (rr)_6 i)c_1 + (rr)_7(s_0 - s - c_1 - p) \quad \text{... (6c)}$$

The equilibrium points of System are defined to be: There are four equilibrium points $E_i(s, i, c_1)$ as:

1. $E_1\left(\frac{(rr)_2 c_1}{(rr)_1(e_0 - i_0 + i - c_1)}, \frac{7(rr)_2(p - s_0) + s(7 + 5(rr)_1 - (rr)_2)}{-6s(rr)_1}, \frac{7(rr)_1(p - s_0)}{(rr)_2 - 7 - 12(rr)_1 - 6i(rr)_1}\right)$.

2. $E_2\left(0, \frac{-((rr)_5 - (rr)_4(i_0 - e_0)) \pm \sqrt{((rr)_5 - (rr)_4(i_0 - e_0))^2 - 4(rr)_4((rr)_5(i_0 - p))}}{(rr)_4 c_1 + (rr)_5}, 0\right)$ exists under the condition, $s_0 = p$.

3. $E_3\left(\begin{array}{c} \left(\frac{(rr)_2 (rr)_7 (s_0 - s - p)}{(rr)_1 (e_0 - i_0 + i)\left((rr)_2 + (rr)_3 + (rr)_6 i + (rr)_7\right)}\right), \\ \frac{(rr)_5 (s + pc_1 + i_0 - s_0) + (rr)_7 (s_0 - s - c_1 - p)}{(rr)_4 (e_0 - i_0 + i - c_1) + c_1 (rr)_6 + (rr)_5}, \\ \frac{(rr)_1 s (e_0 - i_0 + i) + (rr)_7 (s_0 - s - p)}{(rr)_1 s + (rr)_2 + (rr)_3 + (rr)_6 i + (rr)_7} \end{array}\right)$

4. $E_4(s^*, i^*, c^*)$where,

$$s^* = (-2(rr)m_4 r_2 c_1)/(-2(rr)_4 (i_0 - e_0 + c_1) - [(rr)_4 (e_0 - i_0 - c_1) + (rr)_6 c_1 + (rr)_5 \pm \sqrt{(((rr)_4(e_0 - i_0 - c_1) + (rr)_6 c_1 + (rr)_5)^2 + 4(rr)_4 ((rr)_5 (s + pc_1 + i_0 - s_0)) + (rr)_7 (s_0 - s - c_1 - p))})$$

$$i^* = ((rr)_4 (e_0 - i_0 - c_1) + (rr)_6 c_1 + (rr)_5 \pm \sqrt{(((rr)_4(e_0 - i_0 - c_1) + (rr)_6 c_1 + (rr)_5)^2 + 4(rr)_4 ((rr)_5 (s + pc_1 + i_0 - s_0)) + (rr)_7 (s_0 - s - c_1 - p))})/(-2(rr)_4)$$

$$c^* = \frac{7(p - s_0)}{(rr)_2 - (12 + 6i) - \left[\frac{7(rr)_2}{(rr)_1(e_0 - i_0 + i - c_1)}\right]}$$

Stability analysis

The local/global stability behaviour of equilibrium points is determined by eigenvalues of corresponding Jacobian Matrix[24-27].

Theorem: *The equilibrium point is asymptotically stable if all the Eigenvalues of a* $n \times n$ *matrix must be negative, provided they are real.*

Theorem: *The equilibrium point is asymptotically stable if the real part of each complex Eigenvalues of a* $n \times n$ *matrix is negative.*

The general Jacobian Matrix M for our model (7a) (7b) and (7c) is given as:

$$M = \begin{bmatrix} -(rr)_1(e_0 - i_0 + i - c_1) & -(rr)_1 s & (rr)_1 s + (rr)_2 \\ (rr)_5 - (rr)_7 & -2(rr)_4 i - (rr)_5 - (rr)_6 c_1 & ((rr)_4 - (rr)_6)i + (rr)_5 p - (rr)_7 \\ (rr)_1(e_0 - i_0 + i - c_1) - (rr)_7 & (rr)_1 s - (rr)_6 c_1 & -((rr)_1 s + (rr)_2 + (rr)_3 + (rr)_6 i + (rr)_7) \end{bmatrix}$$

Let M_i, Where $i = 1,2,3$ & 4 be the matrix evaluated at the equilibrium point $E_i$where $i = 1,2,3$ & 4.

Then the matrix M_1 evaluated at the equilibrium E_1 is represented as follows:

$$M_1 = \begin{bmatrix} -(rr)_1(e_0 - i_0 + i - c_1) & -(rr)_1 s & (rr)_1 s + (rr)_2 \\ (rr)_5 - (rr)_7 & -2(rr)_4 i - (rr)_5 - (rr)_6 c_1 & ((rr)_4 - (rr)_6)i + (rr)_5 p - (rr)_7 \\ (rr)_1(e_0 - i_0 + i - c_1) - (rr)_7 & (rr)_1 s - (rr)_6 c_1 & -((rr)_1 s + (rr)_2 + (rr)_3 + (rr)_6 i + (rr)_7) \end{bmatrix}$$

Where;

$$s = \left(\frac{(rr)_2 c_1}{(rr)_1(e_0 - i_0 + i - c_1)}\right), i = \frac{7(rr)_2(p - s_0) + s(7 + 5(rr)_1 - (rr)_2)}{-6s(rr)_1}, and$$

$$c_1 = \frac{7(rr)_1(p - s_0)}{(rr)_2 - 7 - 12(rr)_1 - 6i(rr)_1}$$

Since, the matrix M_1 has negative eigen values hence, $E_1$is a stable equilibrium point.

Now, M_2 be the matrix evaluated at the equilibrium E_2 is symbolized as follows:

$$M_2 = \begin{bmatrix} -(rr)_1(e_0 - i_0 + i) & -(rr)_1 & (rr)_1 + (rr)_2 \\ (rr)_5 - (rr)_7 & -2(rr)_4 i - (rr)_5 - (rr)_6 & ((rr)_4 - (rr)_6)i + (rr)_5 p - (rr)_7 \\ (rr)_1(e_0 - i_0 + i) - (rr)_7 & (rr)_1 - (rr)_6 & -((rr)_1 s + (rr)_2 + (rr)_3 + (rr)_6 i + (rr)_7) \end{bmatrix}$$

Where;

$$i = \frac{-((rr)_5 - (rr)_4(i_0 - e_0)) \pm \sqrt{((rr)_5 - (rr)_4(i_0 - e_0))^2 - 4(rr)_4\left((rr)_5(i_0 - p)\right)}}{(rr)_4 c_1 + (rr)_5},$$

As the matrix M_2 contributes the negative eigen values under the condition: $s_0 = p$, E_2 is a stable equilibrium point.

Again, the matrix M_3 calculated at the equilibrium E_3 is characterized as follows:

$$M_3=\begin{bmatrix} -(rr)_1(e_0-i_0+i-c_1) & -(rr)_1 s & (rr)_1 s+(rr)_2 \\ (rr)_5-(rr)_7 & -2(rr)_4 i-(rr)_5-(rr)_6 c_1 & ((rr)_4-(rr)_6)i+(rr)_5 p-(rr)_7 \\ (rr)_1(e_0-i_0+i-c_1)-(rr)_7 & (rr)_1 s-(rr)_6 c_1 & -((rr)_1 s+(rr)_2+(rr)_3+(rr)_6 i+(rr)_7) \end{bmatrix}$$

Where;

$$s=\frac{(rr)_2(rr)_7(s_0-s-p)}{(rr)_1(e_0-i_0+i)((rr)_2+(rr)_3+(rr)_6 i+(rr)_7)}$$

$$i=\frac{(rr)_5(s+pc_1+i_0-s_0)+(rr)_7(s_0-s-c_1-p)}{(rr)_4(e_0-i_0+i-c_1)+c_1(rr)_6+(rr)_5} \text{ and}$$

$$c_1=\left(\frac{(rr)_1 s(e_0-i_0+i)+(rr)_7(s_0-s-p)}{(rr)_1 s+(rr)_2+(rr)_3+(rr)_6 i+(rr)_7}\right)$$

]

Since, the matrix M_3 contributes negative Eigen values, E_3 is a stable equilibrium point.

Similarly, the matrix M_4 calculated at the equilibrium E_4 is characterized as follows:

$$M_4=\begin{bmatrix} -(rr)_1(e_0-i_0+i-c_1) & -(rr)_1 s & (rr)_1 s+(rr)_2 \\ (rr)_5-(rr)_7 & -2(rr)_4 i-(rr)_5-(rr)_6 c_1 & ((rr)_4-(rr)_6)i+(rr)_5 p-(rr)_7 \\ (rr)_1(e_0-i_0+i-c_1)-(rr)_7 & (rr)_1 s-(rr)_6 c_1 & -((rr)_1 s+(rr)_2+(rr)_3+(rr)_6 i+(rr)_7) \end{bmatrix}-$$

$$s^*=(-2(rr)_4 r_2 c_1)/(-2(rr)_4(i_0-e_0+c_1)-[(rr)_4(e_0-i_0-c_1)+(rr)_6 c_1+(rr)_5 \pm\sqrt{(((rr)_4(e_0-i_0-c_1)+(rr)_6 c_1+(rr)_5)^2+4(rr)_4((rr)_5(s+pc_1+i_0-s_0))+(rr)_7(s_0-s-c_1-p))})$$

$$i^*=((rr)_4(e_0-i_0-c_1)+(rr)_6 c_1+(rr)_5 \pm\sqrt{(((rr)_4(e_0-i_0-c_1)+(rr)_6 c_1+(rr)_5)^2+4(rr)_4((rr)_5(s+pc_1+i_0-s_0))+(rr)_7(s_0-s-c_1-p))})/(-2(rr)_4)$$

$$c^*=\frac{7(p-s_0)}{(rr)_2-(12+6i)-\left[\frac{7(rr)_2}{(rr)_1(e_0-i_0+i-c_1)}\right]}$$

Since, the matrix M_4 contributes negative Eigen values, E_4 is a stable equilibrium point.

Sensitive analysis

On considering the initial conditions to be equal for all quantities. (as $e(0)=s(0)=i(0)=1\,mg.$) The corresponding parametric values can be measured one by one keeping any one of them fixed. As we keep particular parameter fixed, total 720 different possibilities of other parameters could be analyzed as per their time consumption which is possible for all seven parameters and hence total five thousand and forty cases do exist. These cases can be analyzed to understand the mechanism of variables and conclude the pattern or ranges of the parameters for optimal results. Analysis of the parameters in our study states that value of parameter $(rr)_3$ shall be maximized, this can be proved from the equation of product which is directly integrable. It is also analyzed that the value of parameters $(rr)_4, (rr)_2$ and $(rr)_6$ shall be keep smaller as compared to the others. It is to be noted that values of parameters $(rr)_4 to\ (rr)_7$ must be optimized for ideal product formation. we conclude that under the assumption $(rr)_2<(rr)_5<(rr)_6<(rr)_4<(rr)_3<(rr)_1<(rr)_7$ time consumption is minimum whereas it is maximum in $(rr)_1<(rr)_7<(rr)_3<(rr)_4<(rr)_5<(rr)_4<(rr)_2$. It is important to look that taking any parametric values to be non – positive, it results to the failure. Hence system is stable for positive values only.

Results and Discussion

As the minimum time consumption for product formation is under the assumption $(rr)_2<(rr)_5<(rr)_6<(rr)_4<(rr)_3<(rr)_1<(rr)_7$, keeping the parameters to be fixed at $(rr)_1=0.8,(rr)_2=0.3,(rr)_3=0.7,(rr)_4=0.6,(rr)_5=0.4,(rr)_6=0.5,(rr)_7=0.9$. The rate of change of reaction for enzyme-substrate in presence of Un-Competitive inhibitor for this hypothesis is studied as follows:

Case-I: The initial concentration of enzyme is less than inhibitor is less than that of substrate $(e(0)=0.8\,mg, i(0)=1\,mg and s(0)=1.2mg)$(Fig. 1a).

Case-II: The initial concentration of enzyme is less than substrate is less than that of inhibitor $(e(0)=0.8\,mg, s(0)=1\,mg\ and\ i(0)=1.2\,mg)$(Fig. 1b).

Case-III: The initial concentration of substrate is less than inhibitor is less than that of enzyme $(s(0)=0.8\,mg, i(0)=1\,mg\ and\ e(0)=1.2\,mg)$(Fig. 1c).

Case-IV: The initial concentration of inhibitor is less than substrate is less than that of enzyme $(i(0)=0.8\,mg, s(0)=1\,mg\ and\ e(0)=1.2\,mg)$(Fig. 1d)

Case-V: The initial concentration of inhibitor is less than enzyme is less than that of substrate $(i(0)=0.8\,mg, e(0)=1\,mg\ and\ s(0)=1.2\,mg)$ (Fig. 1e)

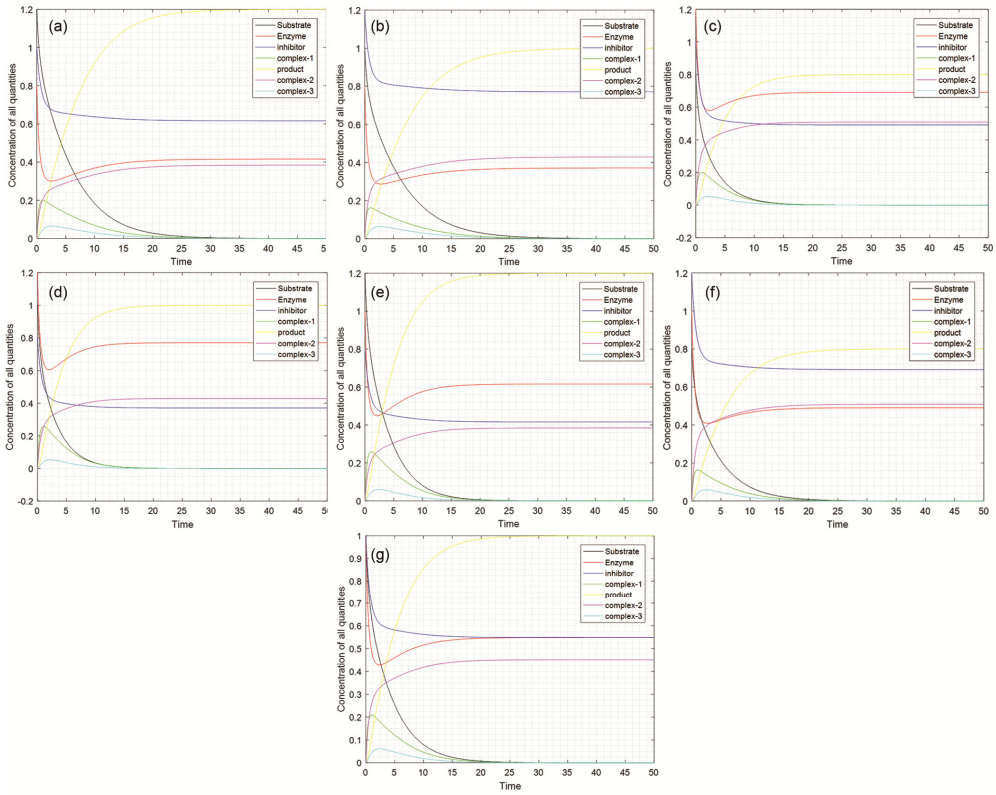


Fig. 1 — Time – Concentration relation for (a) $e(0) < i(0) < s(0)$; (b) $e(0) < s(0) < i(0)$; (c) $s(0) < i(0) < e(0)$; (d) $i(0) < s(0) < e(0)$; (e) $i(0) < e(0) < s(0)$; (f) $s(0) < e(0) < i(0)$; and (g) $e(0) = i(0) = s(0)$

Case-VI: The initial concentration of substrate is less than enzyme is less than that of inhibitor $(s(0) = 0.8\,mg, e(0) = 1\,mg\ and\ i(0) = 1.2\,mg)$(Fig. 1f)

Case-VII: The initial concentration of all enzyme, Inhibitor and substrate is taken to be equal $(e(0) = s(0) = i(0) = 1\,mg)$(Fig. 1g)

It is noted that, while compelling all the possible ratios of concentration of substrate, enzyme and inhibitor with fixed parametric values respectively, the timing of product formation does vary. Which states that even after keeping the parametric values constant, a slight variation in concentration of any of the three variables leads to dynamic change in ideal product formation.

Conclusion

This study reveals that experimentally observed enzyme-substrate relationships under the influence of uncompetitive inhibitors align with theoretical calculations. The computed reproduction numberof -0.4 serves as a threshold value for optimal product formation, reinforcing the predictive accuracy of mathematical modeling in biochemical processes. Stability analysis confirms that variations in rate constants significantly affect the time required for product formation, demonstrating the sensitivity of enzymatic reactions to environmental fluctuations.

The findings emphasize that enzyme concentration must be lower than substrate and inhibitor levels for ideal product formation, while substrate and inhibitor concentrations may be equal or slightly elevated. Conversely, excess enzyme concentration prolongs the reaction time, which has direct implications for drug design and metabolic regulation. These insights contribute to medical biotechnology, particularly in optimizing enzyme-based therapeutic formulations and pharmacokinetics.

From a bioinformatics perspective, the derived model and parametric evaluations provide a foundation for computational simulations of enzyme-inhibitor interactions**,** assisting in predictive analytics for drug efficacy and biochemical stability**.** The restrictions outlined for initial conditions could be integrated into machine-learning models for designing enzyme-targeted pharmaceuticals with enhanced efficiency. This analytical framework advances enzyme-based drug development, ensuring precision in therapeutic interventions and biotechnological innovations.

Acknowledgement

The authors are thankful to anonymous referees for their valuable suggestions and comments to improve this manuscript.

Conflict of interest

Both the authors declare no conflict of interest.

References

1 Alsanosi SMM, Skiffington C & Padmanabhan S, Pharmacokinetic pharmacogenomics. *Handb Pharmacogenomics Stratified Med*, 2014, 365.

2 Mazzei L, Ciurli S & Zambelli B, Isothermal titration calorimetry to characterize enzymatic reactions. *Methods Enzymol*, 567 (2016) 215.

3 Alam F, Shafique Z, Amjad ST & Hassan Bin Asad MH, Enzyme inhibitors from natural sources with antidiabetic activity. *Phytother Res*, 33 (2019) 41.

4 Cornish-Bowden A, Enzyme kinetics from a metabolic perspective. *Biochem Soc Trans*, 27 (1999) 281.

5 Fang X, Anders W & Jaques R, A systems biology framework for modeling metabolic enzyme inhibition of *Mycobacterium tuberculosis*. *BMC Syst Biol*, 3 (2009) 92.

6 Gan Q, Allen SJ & Taylor G, Kinetic dynamics in heterogeneous enzymatic hydrolysis of cellulose: An overview, an experimental study and mathematical modeling. *Process Biochem*, 38 (2003) 1003.

7 Gombert AK & Nielsen J, Mathematical modeling of metabolism. *Curr Opin Biotechnol*, 11 (2000) 180.

8 Hamden K, Mnafgui K, Amri Z, Aloulou A & Elfeki A, Inhibition of key digestive enzymes related to diabetes and hyperlipidemia and protection of liver-kidney functions by trigonelline in diabetic rats. *Sci Pharm*, 81 (2013) 233.

9 Khoshnaw SHA, Iterative approximate solutions of kinetic equations for reversible enzyme reactions. *Nat Sci*, 5 (2013) 740.

10 Kuzmic P, Soloweij J & Murray BW, An algebraic model for the kinetics of covalent enzyme inhibition at low substrate concentrations. *Anal Biochem*, 484 (2015) 82.

11 Schnell S & Maini PK, Enzyme kinetics far from the standard quasi-steady-state and equilibrium approximations. *Math Comput Model*, 35 (2002) 137.

12 Segel LA & Slemrod M, The quasi-steady-state assumption: A case study in perturbation. *SIAM Rev*, 31 (1989) 446.

13 Sharmila MC, Parveen T & Rajendran L, Mathematical modeling and analysis of nonlinear enzyme catalyzed reaction processes. *J Theor Chem*, 2013 (2013) 1.

14 Meena A, Eswari L & Rajendran L, Mathematical modeling of enzyme kinetics reaction mechanisms and analytical solutions of non-linear equations. *J Math Chem*, 48 (2010) 179.

15 Khoshnaw SHA, Model reduction in biochemical reaction networks. *PhD Thesis Univ Leicester* (2015) 1.

16 Eilertsen J & Santiago S, The quasi-steady-state approximations revisited: Timescales, small parameters, singularities, and normal forms in enzyme kinetics. *Math Biosci*, 325 (2020) 108.

17 Bhat R & Khanday MA, An algebraic mathematical model for non-competitive enzyme inhibitors with slow and fast subsystems. *Appl Math E-Notes*, 22 (2022) 362.

18 Hamad HJ, Khoshnaw SHA & Shahazad M, Slow and fast subsystems for complex uncompetitive inhibitor mechanisms. *Malays J Sci*, 42 (2023) 22.

19 Chitra Devi M, Pirabaharan P & Rajendran L, Amperometric biosensors in an uncompetitive inhibition process: A complete theoretical and numerical analysis. *React Kinet Mech Cat*, 133 (2021) 655.

20 Akgul A, Khoshnaw SHA & Abdalrahman AS, Mathematical modelling for enzyme inhibitors with slow and fast subsystems. *Arab J Basic Appl Sci*, 27 (2020) 442.

21 Ismail I, Oluleye G, Oluwafemi IJ, Omafurna OI & Olufemi AS,Mathematical modelling of an enzyme-based biosensor. *Int J Biosens Bioelectron*, 3 (2017) 265.

22 Fantaye AK, Goshu MD, Zeleke BB, Gessesse AA, Endalew MF & Birhanu ZK, Mathematical model and stability analysis on the transmission dynamics of skin sores. *Epidemiol Infect*, 150 (2022) e207.

23 Huo HF & Feng LX, Global stability of an epidemic model with incomplete treatment and vaccination. *J Appl Math*, 2012 (2012) 530267.

24 Daniel EE, Daniel OE, Ibrahim IA & Adamu MU, Stability analysis on SIR and SIS compartmental epidemiological models. *FTST J*, 6 (2021) 289.

25 James AA & Babatunde SO, Boundedness and stability properties of solutions of mathematical model of measles. *Tamkang J Math*, 52 (2021) 91.

26 Joko H & Titik S, Local stability analysis of an SVIR epidemic model. *J Matematika Murni Apl*, 5 (2017) 20.

27 Kumawat J & Patel K, Study the dynamic behavior of the enzyme-substrate reaction using mathematical modeling. *Biosci Biotechnol Res Asia*, 20 (2023) 1.