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A numerical modelling of an amperometric-enzymatic based uric acid biosensor for GOUT arthritis diseases

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ABSTRACT

A numerical model of an amperometric-enzymatic uric acid biosensor for a non-relentless condition has been developed. This model depends on the arrangement of nonlinear reaction diffusion equations for Michaelis-Menten formalism that depicts the concentrations of substrate and product. The new rough scientific articulations for the concentration of substrate (uricase enzyme) and product and the corresponding current response have been derived for all estimations of parameters utilizing the new perturbation technique. The non-dimensional numerical model of the amperometric biosensor can be effectively used to examine the responses. Moreover, the relative impact of these parameters is chosen by the Damkohler number and the impact of current density on this number likewise contemplated. All the analytical results are compared with simulation results using MATLAB program and the numerical outcomes concur with fitting hypotheses. Notwithstanding, strikingly the model likewise proposed that the choice of substrate and product for uric acid biosensor for the application of kidney disease and GOUT arthritis diseases.

1. Introduction

A biosensor is a logical gadget which utilizes a living being or natural particles, particularly proteins or antibodies, to recognize the presence of chemicals. Enzymes are the most widely recognized bio-recognition parts of biosensors. Numerous impediments still lie in the method for the boundless commercialization of biosensor framework. Endeavours have been made to get around the issue with enzyme-based framework [1]. An amperometric biosensor is a kind of bio-sensor that might be utilized to discover the concentration of some components of the analyte. These sensors measure the electrical capability of an electrode when no voltage is present. These kinds of biosensors have been generally utilized as a part of natural, restorative, modern, environmental, medical and industrial applications [2]. For a long time, significant exertion has been given to the innovative work of biosensors for the utilization of GOUT joint pain and kidney diseases. Alongside the preparation and the acknowledgment of the real sensor, the advancement and investigation of a scientific model that guides in the comprehension of the conduct of the sensor is additionally critical [3–7].

As of late, amperometric electrochemical biosensors are exceedingly utilized for quick and precise identification [8]. The operations of electrochemical sensors are extremely straightforward and never influence the host material [9,10]. These biosensors, produces the output current in view of the detecting materials on the working electrode go about as an impetus and catalyse the redox response. Amid estimation, the electrode potential is kept constant while the current is observed. Improvement of biosensor is a tedious procedure, for which scientific and mathematical demonstration is utilized to decrease the streamlining time, cost and upgrade the logical qualities of a genuine biosensor [11].

The theoretical demonstration of biosensors includes unravelling the arrangement of linear/non-linear reaction-diffusion equations for substrate and product with a term containing a rate of bio-catalytical change of substrate. The intricacies of modelling emerge because of settling the partially differential equations with non-linear reaction term and with complex starting and boundary conditions. The modelling of biosensor is broken down by numerical [12] and analytical methods of partial differential equation with various boundary conditions. As of late, a hypothetical model of a pH-based potentiometric biosensor was derived [13]. A few scientists exhibited the arrangement of relentless state substrate concentration in the action of biosensor response with blended enzyme kinetics under a Michalis-Menten conspire [14] and the scientific answers for the unfaltering state current at a micro disk chemical sensor [15]. As of late, the concentration profile of the product of the enzyme reaction and the electrode current for all estimations of Michalis-Menten

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constant using the Homotopy perturbation method was determined [16].

Numerical simulations were produced for modelling the reaction and diffusion processes that emerge in the functional enzyme membranes of such systems. These simulations represent some sort of virtual examinations and they enabled it to get understanding into the concentration profiles and fluxes of substrate and product species and attributes to the final response characteristics of enzyme-based sensors and reactors [17–21]. In this paper, we set forward the rough analytical expressions for the amperometric biosensor prepared by RF sputtering technique on a Pt electrode adjusted with NiO film with urease as an immobilized enzyme which is taken as a product and substrate [22].

Dissimilar to past numerical models, this work meant to mathematically demonstrate the influence of uric acid on the performance of an uricase enzyme-based amperometric bio-biosensor. As far as anyone is concerned, no general and broad articulations/expressions for the concentration of substrate, product and dimensionless current for the diffusion parameters have been accounted for. The motivation behind this article is to derive a systematic/analytical expression for substrate, product concentrations and current using non-linear equations and analysis of substrate concentration with current was done by utilizing kinetics of enzymatic reactions which is more influenced by Damkohler number. This kind of model is much reasonable for the determination of substrate and other parameters for the advancement of enzyme based uric acid biosensor for the application of GOUT arthritis (joint inflammation) and kidney diseases.

2. Mathematical formation of the problem

In this present work, we contemplate indicative structure in perspective of an enzyme-containing mass film of thickness T that contains a uniform aggregate concentration of the enzyme TC_e which is touched on one side with an aqueous solution of the substrate $??_a$.

During electrochemical transformation, the product is produced at the electrode. The rate of the product formation at the electrode is corresponding to the rate of conversion of the substrate. At the point, when the substrate is well-stirred outside the membrane, then at that point thickness of the diffusion layer stays steady [23].

The substrate molecules diffuse into the film stage where they react according to the Michaelis-Menten write catalyst catalyzed response to yield an electro dynamic product ?? By considering non-linear time dependent reaction diffusion equation for menten's constant, the equation is derived as follows [24],

$$TC_e + S_a \underset{K1,K2}{\Leftrightarrow} TC_e S_a \rightarrow_{K3} P_r \omega e_p \tag{1}$$

$$K_m = \frac{K_2 + K_3}{K_1} \tag{2}$$

where TC_eS_a is the interposed enzyme-substrate complex, ω is the number of product species obtained per substrate molecule, ??1, ??2, and??3 are the rate constants of the individual partial reactions, and ??m is the Michaelis constant characterized in (equation (2)). The impact on reaction and diffusion processes for the species S_a and e_p in the enzyme membrane are accompanied by the following nonlinear governing equation,

$$\frac{\partial [S_a]_{e_m}}{\partial t} = M_s \frac{\partial^2 [S_a]_{e_m}}{\partial x^2} - K_3 [TC_e] \times \frac{[S_a]_{e_m}}{[S_a]_{e_m} + K_m} \tag{3}$$

$$\frac{\partial [e_p]_{e_m}}{\partial t} = M_p \frac{\partial^2 [e_p]_{e_m}}{\partial x^2} + \omega K_3 [TC_e] \times \frac{[S_a]_{e_m}}{[S_a]_{e_m} + K_m} \tag{4}$$

where $[S_a]_{e_m}$ and $[e_p]_{e_m}$ are the concentration of the species in the enzyme layer, M_s and M_p are the corresponding diffusion coefficients, ω is the number of product species obtained per substrate molecule, and K_3 is the rate constant for the irreversible step of product formation [18,19].

Presently, (3) are solved by assuming the zero fluxes at ?? = 0 and of equilibrium distribution at x = q and the underlying state is given by the zero concentration (in the reference19, 20)

$$\left.\begin{array}{c} \frac{\partial [S_a]_{e_m}}{\partial t} = 0, \frac{\partial [e_p]_{e_m}}{\partial t} = 0 where x = 0 \\ [S_a]_{e_m} = R_s [S_a]_{a_q}, [e_p]_{e_m} = R_p [e_p]_{a_q} where x = q \\ [S_a]_{e_m} = 0, [S_a]_{e_m} = 0 when t = 0 \end{array}\right\} \tag{5}$$

The flux of the product species at $x = q$ is described by the following equation,

$$F_p = -M_p \frac{\partial [e_p]_{e_m}}{\partial x} \tag{6}$$

Again by considering the condition equation (1) by joining the enzyme-catalyzed reaction in the enzyme layer with the one-dimensional-in-space diffusion (by Fick's law), the equation is derived as follows,

$$\frac{\partial TC_e}{\partial x} = M_s \frac{\partial^2 TC_e}{\partial x^2} + \frac{V_{max} e_p}{K_m + e_p}, o < x < d \tag{7}$$

$$\frac{\partial e_p}{\partial x} = M_p \frac{\partial^2 e_p}{\partial x^2} + \frac{V_{max} e_p}{K_m + e_p}, o < x < d \tag{8}$$

Where x and d represents space and the thickness of the enzyme layer respectively, M_s and M_p are the diffusion coefficients of the substrate and product respectively. Electrode surface is represented by x = 0 plane and x = d represents the bulk solution (mass arrangement)/membrane interface.

$$TC_e(x,0) = 0, TC_e(d,0) = TC_{e0}, 0 \le x < d \tag{9}$$

$$e_p(x,0) = 0, 0 \le x \le d \tag{10}$$

Where TC_{e0} is the concentration of substrate in the bulk solution.

Therefore, the concentration of substrate as well as the product over the enzyme surface (bulk solution/membrane interface) stays steady while the biosensor interacts with the solution of substrate. This is utilized as part of boundary conditions $o < t < T$ given by:

$$M_p = \frac{\partial e_p}{\partial x_{x=0}} = -M_s \frac{\partial TC_e}{\partial x_{x=0}} \tag{11}$$

The current is estimated as a response of the biosensor and the density I (T) can be acquired unequivocally from Faraday's law and Fick's law utilizing the flux of the concentration S at the surface of the electrode:

$$I(T) = n_e F M_s \frac{\partial TC_e}{\partial x_{x=0}} \tag{12}$$

2.1. Non-dimensional form for the equation (6)

The Non dimensional Form of the Problem (for equation (6)) can be formulated by utilizing and formulate the partial differential equations (equation (3)) in dimensionless form by defining the following parameters:

$$u = \frac{[TC_e]_{em}}{K_s [TC_e]_{aq}}, v = \frac{[e_p]_{em}}{K_s [TC_e]_{aq}}, X = \frac{x}{d}, \propto = \frac{K_s [TC_e]_{aq}}{K_m}, \beta = \frac{K_p [e_p]_{aq}}{K_m}, \gamma = \sqrt{\frac{Kd^2}{M_s}} \tag{13}$$

Where ?? and V represents the dimensionless concentration of

substrate and product, ?? and ?? are saturation parameters, and ?? is the reaction diffusion parameter (like in Thiele modulus). Presently, the boundary conditions (limit conditions) might be displayed as takes after (from Ref. [19])

$$\frac{\partial u}{\partial X} = 0, \frac{\partial v}{\partial X} = 0 when X = 0 \tag{14}$$

$$u = 1, v = \frac{\beta}{\propto} when X = 1 \tag{15}$$

From the above equation (condition), the standardized flux becomes

$$\varphi = \frac{F_p d}{DK_s [TC_e]_{aq}} \tag{16}$$

Analytical Expressions for substrate and product Concentrations and Current for all Values of Parameters are formulated by utilizing Laplace transform technique and new Homotopy perturbation method (See Appendix A in the reference [20]),

$$u(x,\tau) = \frac{cosh\sqrt{ax}}{cosh\sqrt{a}} - \sum_{m=0}^{\infty} \frac{\boldsymbol{\pi}(-1)^m (2m+1)}{f_m} e^{-(f_m \tau)} \cos\frac{(2m+1)\pi X}{2} \tag{17}$$

$$v(x,\tau) = \left(\frac{\beta}{\alpha} + \gamma\right)\left(1 - \frac{4}{\pi}\sum_{m=0}^{\infty}\left[\left(\frac{-1^m}{2m+1}\right) e^{-\left(\pi^2 \frac{(2m+1)^2}{4}\right)\tau} \times cos\frac{(2m+1)\pi X}{2}\right]\right) \tag{18}$$

The expression for the dimensionless current (flux) is given by

$$\varphi = \left(\frac{\beta}{\alpha} + v\right)\left[\sum_{m=0}^{\infty} 2(-1)^m e^{\frac{\left(-\pi^2(2m-1)^2\right)\tau}{4}}\right] - \gamma\left[\sqrt{a}\tanh\sqrt{a} + \sum_{m=0}^{\infty}\frac{2\pi^2(2m+1)^2 e^{(-f_m)\tau}}{\pi^2(2m+1)^2 + 4a}\right] \tag{19}$$

2.2. Non-dimensional form for the equation (12)

The accompanying parameters are utilized to convert the above Equations (7) and (8) into normalized (standardized) form.

$$TC_e = \frac{TC_e}{K_m}, e_p = \frac{e_p}{K_m}, x = \frac{x}{d}, t = \frac{M_s t}{d^2}, R = \frac{M_p}{M_s} \tag{20}$$

Using the above normalizing parameters, the equation for depletion rate of substrate can be composed as:

$$\frac{dTC_e}{dt} = \frac{d^2 TC_e}{dx^2} + \varepsilon^2\left(\frac{e_p}{1+e_p}\right) \tag{21}$$

$$\varepsilon^2 = \frac{v_{max} d^2}{M_s K_m} \tag{22}$$

Whereε^2 is the Damkohler number.

Damkohler number is additionally named as diffusion modulus which is utilized to compare the rate of enzyme reaction $\left(\frac{v_{max}}{K_m}\right)$with the rate of diffusion through the enzymatic layer$\left(\frac{M_s}{d^2}\right)$. In this entire strategy, if Damkohler number is under 1 then the enzyme kinetics controls the biosensor response. Furthermore, if the Damkohler number is more noteworthy than 1 then the diffusion rate controls the biosensor response.

The dimensionless form of Equation (12) is standardized $I_0 = Fv_{max}d$to give:

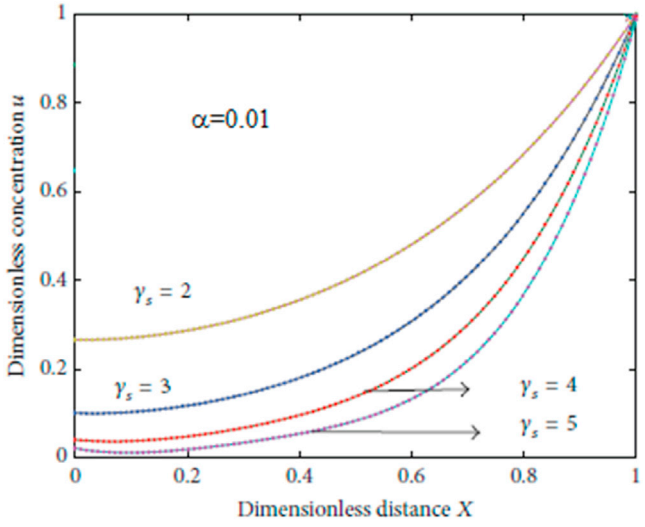

Fig. 1. Plot between dimensionless concentration (u) and distance for α = 0.01.

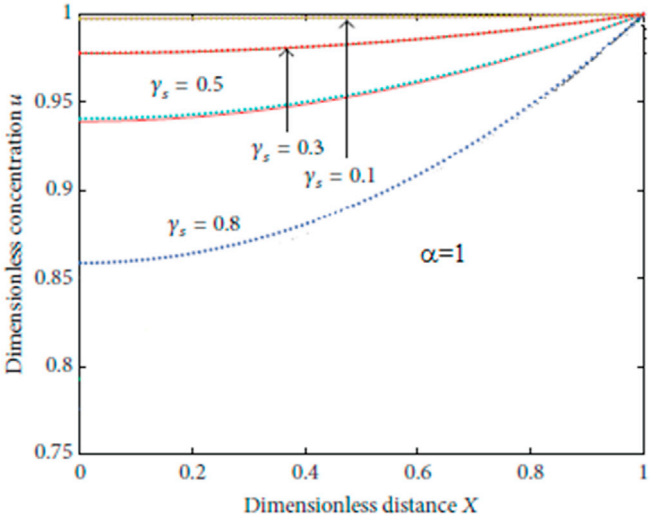

Fig. 2. Plot between dimensionless concentration (u) and distance for α = 1.

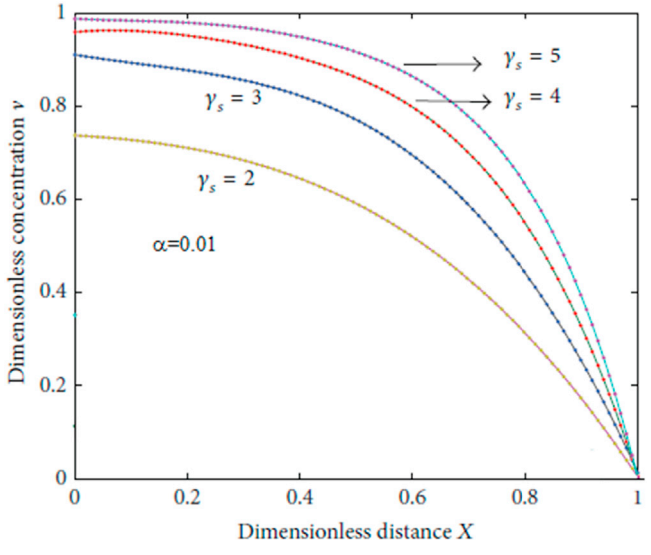

Fig. 3. Plot between dimensionless concentration (*v*) and distance for α = 0.01.

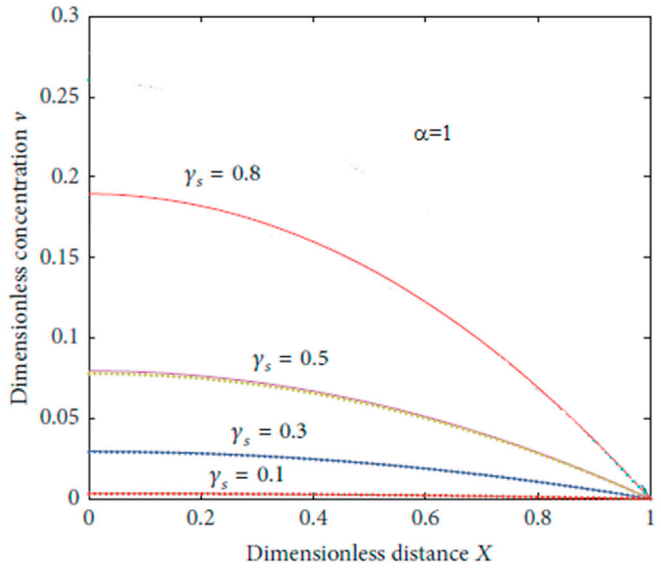

Fig. 4. Plot between dimensionless concentration (v) and distance for $\alpha = 1$.

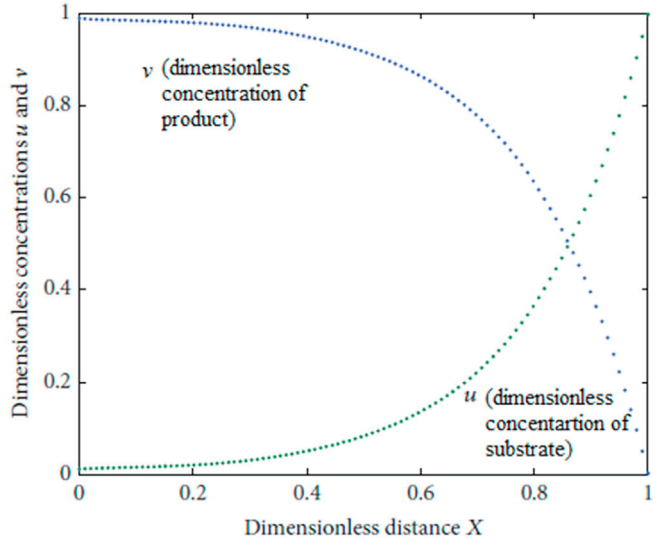

Fig. 5. Plot between dimensionless concentrations (u and v) and distance (X).

$$I^*(T^*) = \frac{I(T)}{I_0} = \frac{n_e M_s K_m}{v_{max} d^2} \times \frac{\partial T C_e^*}{\partial x^*_{x^*=0}} \tag{23}$$

3. Results and discussion

Equations (17) and (18) represents the analytical equation for the concentrations of all parameters and equation (19) represents the dimensionless current expression.

Fig. 1 and Fig. 2 demonstrates the plot between the substrate concentration u and dimensionless distance in the amperometric bio-sensor for the different estimation of parameters like α and γ. The diffusion reaction parameter γ is the marker between the reaction and diffusion. At the point when ?? is small, the kinetics dominates and the uptake of the substrate is kinetically controlled. Form the Fig. 1, we notice that, when we expand the diffusion parameter γ it commonly increments the substrate concentration values u, similarly when there is increment in γ, the concentration of the substrate u decreases despite the fact that the value of α in increases. Now from the Figs. 3 and 4, concentration of the product decreases, when there is a decrease in the γ value for the constant

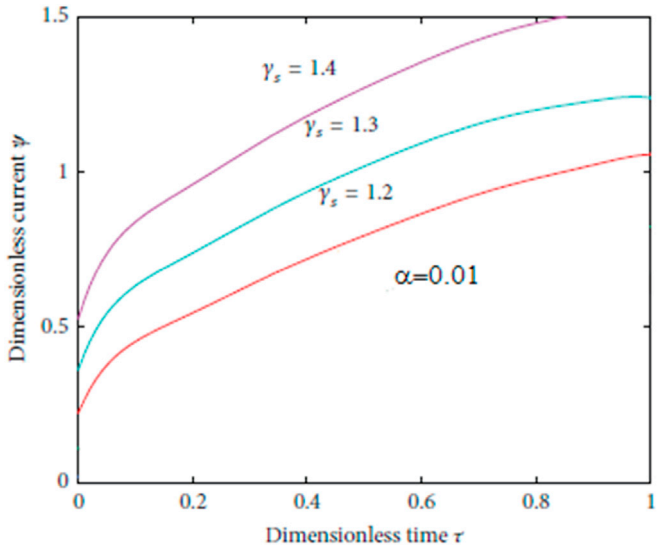

Fig. 6. Plot between dimensionless concentration current (¥) and dimensionless time for the various values of γ and fixed value of α ($\alpha = 0.01$).

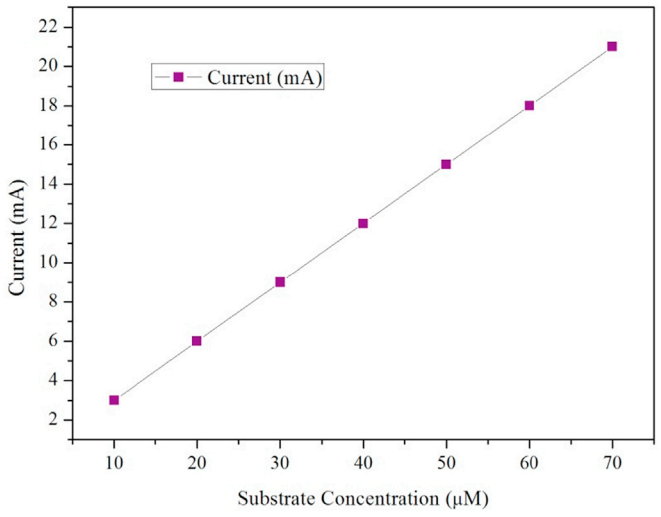

Fig. 7. Plot between substrate concentration (μm) and current (mA).

$\alpha = 0.01$. Despite in fact that there is an increase in α value from 0.01 to 1, the concentration v decreases for the all values of γ. This reveals that the parameters γ and α has high influence on diffusion.

Fig. 5 demonstrates the plot between the dimensionless concentration of the substrate and product for the approximate values of the parameters (α and γ) and dimensionless distance. From which we can comprehend that, at time ?? = 0, the film surface at X has come in contact with a substrate sample and the substrate molecules at that point begin to diffuse into the enzyme layer.

Fig. 6 demonstrates the diagram between the dimensionless current and dimensionless time for various values of the diffusion-reaction parameters ?? (γ = 1.2, 1.3, 1.4) and for some ?? (α = 0.01) and the figure reveals that the value of the current increments as ?? increments. For the similar examination of substrate and product concentration we used the Michaelis-Menten constant and non-linear diffusion equations (equations (20) and (21)). The positive impact of these parameters is based on the non-dimensional number called Damkohler number, which is the proportion of diffusion and enzymatic rate and it's furthermore noticed that in the Fig. 7, current density increases with decrease in Damkohler number and the other way around.

4. Conclusion

The dimensionless numerical examination of an amperometric biosensor and its current concentration behaviour depending on the Damkohler number was studied. The nonlinear diffusion-reaction equations have been unraveled numerically. Also we have procured the analytical expressions for the substrate, product concentrations and current. The analytical results will be utilized for deciding the kinetic characteristics of the biosensor. The hypothetical model displayed here can be used for the plan improvement of the biosensor. Moreover, in light of the result of this work, there is a possibility of stretching out the method to locate the inexact measure of substrate concentration, product concentrations and current for the diffusion process. It has been discovered that the current density increments with the decline in Damkohler number and the other way around.

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