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Existence of solution of Hypothalamo- Pituitary - Adrenocortical Mathematical Model

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Abstract: Homotopy analysis method is attempted to evaluate the hypothalamo- pituitary - adrenocortical mathematical model. The effects of hypothalamo- pituitary adrenocortical,corticotrophin releasing hormone, denocorticotropin, are discussed in this work.
AMS Subject Classiftcation: 65L11, 65L99, 92C50

Key Words and Phrases: hypothalamo- pituitary - adrenocortical, corticotrophin, adenocorticotropin.

I. INTRODUCTION

HPA axis is the most significant biological system in mammal stress response. Its main goal is to alarm the creature and rapidly regu- lates energy to the muscles and brain in stress. Naturally HPA axis react immediately in stress and come back soon. Glucocorticoids the end product of HPA axis is a key physiological regulator that plays vital role between the master peace maker and peripheral oscillators. If this could be disturbed then the synchronization of body system would be disturbed which could even leads to lethal. So the study of HPA axis dynamics is so important..

$$\frac{dx}{dt} = k_1\left(1 - \frac{\eta z}{k_d + z}\right) - k_2 x$$

(1)

$$\frac{dy}{dt} = k_2 x - k_3 y$$

(2)

$$\frac{dz}{dt} = k_3 y - k_4 z$$

(3)

Where *x, y, z* are the concentrations of CRH,ACTH, CORT hormones, the reaction rate constants k_1, k_2, k_3, and k_4. k_d is the desolation constants of CRH. $\frac{\eta z}{k_4 + z}$ represents regulation function. In this work we attempted to find the analytic approximation for the above dynamical model.

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II. MATHEMATICAL MODELING

Hypothalamus and pituitary-adrenal cortex are the two major struc- tures of HPA axis. Hypothalamus furtive Corticotrophin releasing hormones (CRH) which stimulates the pituitary to produce adreno- corticotropin (ACTH) production. ACTH stimulates adrenal cor- tex to produce glucocorticoids known particularly for its anti- in- flammatory and immune suppressive actions. This suppress the production of both CRH and ACTH. Though many factors influ- ence the HPA axis (1-2), these three are major hormones. Gonzalez and Lenbury (3-4) describes the cortisol dynamics. Some statisti- cal and dynamical models (7-9) attempted to fit with clinical data. Many of these models use trigonometric functions, do not explain the origin of observed behaviors. Londergan (5) describes chaos based model. Lenbury (4) study the stability of the mathematical model. Danku savic. et. al (6)formed and analysis stability of a dynamical model

III. HOMOTOPY ANALYSIS METHOD

Choose the auxiliary linear operators t
$L_x[\varphi(t;p)] = \frac{d\varphi(t;p)}{dt}$, $L_y[\phi(t;p)] = \frac{d\phi(t;p)}{dt}$,

$L_z[\xi(t;p)] = \frac{d\xi(t;p)}{dt}$ with the property $L_x[C_1] = 0$, $L_y[C_2] = 0$, $L_z[C_3] = 0$ where C_1, C_2 and C_3 are constant coefficients, φ, ϕ, ξ are real functions. We define the operators

$$N_x\left[\varphi(t;p), \xi(t,p))\right] = \frac{d\varphi(t;p)}{dt} + k_1\left(\frac{\eta\xi(t,p)}{k_d + \xi(t;p)} - 1\right) + k_2\varphi(t;p),$$

$$Ny\left[\varphi(t,p), \phi(t,p)\right] = \frac{d\phi(t;p)}{dt} - k_2\varphi(t;p) + k_3\phi(t;p)$$

$$Nz\left[\phi(t,p), \xi(t,p)\right] = \frac{d\xi(t,p)}{dt} - k_3\phi(t,p) + k_4\xi(t;p)$$

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where $p\epsilon[0,1]$ is the embedding parameter, $\varphi(t;p)$, $\varphi(t;p)$, $\xi(t;p)$are real functions of t, p. Let h_x, h_y, h_z be the nonzero auxiliary operators, H_x, H_y, H_z are the non zero auxiliary functions respectively. construct the nonzero deformation equations as follows,

$$(1-p)L_x[[\varphi(t;p)-x_0t] = ph_xH_x(t)N_x[\varphi(t;p),\xi(t;p)] \quad (4)$$

$$(1-p)L_y[[\phi(t;p)-y_0t] = ph_yH_y(t)N_y[\varphi(t;p),\phi(t;p)]$$

$$(1-p)L_z[[\xi(t;p)-z_0t] = ph_zH_z(t)N_z[\phi(t;p),\xi(t;p)]$$

When $p = 0$ provides that

$$\varphi(t;0)=x_0(t),\ \phi(t;0)=y_0(t),\ \xi(t;0)=z_0(t)$$

When $p = 1$ it is obvious that

$$\varphi(t;1)=x(t),\ \phi(t;1)=y(t),\ \xi(t;1)=z(t)$$

where p varies from 0 *to* 1, $\varphi(t;p)$, $\phi(t;p)$, $\xi(t;p)$ from the initial guesses $x_0(t)$, $y_0(t)$, $z_0(t)$ to the exact solution $x(t)$, $y(t)$, $z(t)$. The zero-order deformation (4)- (6), contains three auxiliary parameters h_x, h_y, h_z and three auxiliary functions H_x, H_y, H_z. Assume all the parameters chosen so that the terms

$$x_n(t)=\left[\frac{1}{n!}\frac{d^n\varphi(t;p)}{dt^n}\right]_{p=0}$$

$$y_n(t)=\left[\frac{1}{n!}\frac{d^n\phi(t;p)}{dt^n}\right]_{p=0}$$

$$z_n(t)=\left[\frac{1}{n!}\frac{d^n\xi(t;p)}{dt^n}\right]_{p=0}$$

Exists for $n\geq 1$. Then using Taylors theorem and (7) we have

$$\varphi(t,p)=x_0(t)+\sum_{n=1}^{\infty}x_n(t)p^n \quad (9)$$

$$\phi(t,p)=y_0(t)+\sum_{n=1}^{\infty}y_n(t)p^n \quad (10)$$

$$\xi(t,p)=z_0(t)+\sum_{n=1}^{\infty}z_n(t)p^n \quad (11)$$

As h_x, h_y, h_z, $H_x(t)$, $H_y(t)$, $H_z(t)$ are properly chosen so that the series (9)-(11) are convergent at $p = 1$ so using (8) we procure

$$\varphi(t,p)=x_0(t)+\sum_{n=1}^{\infty}x_n(t) \quad (9)$$

$$\phi(t,p)=y_0(t)+\sum_{n=1}^{\infty}y_n(t) \quad (10)$$

$$\xi(t,p)=z_0(t)+\sum_{n=1}^{\infty}z_n(t) \quad (11)$$

Differentiating (4)-(6 n times with respect to p and dividing by $n!$, and finally put $p = 0$,we have the deformation equations

$$L_x\left[x_n(t)-\varsigma_n x_{n-1}(t)\right]=h_xH_x(t)R_n^x(x_{n-1},z_{n-1}) \quad (6)$$

$$L_y\left[y_n(t)-\varsigma_n y_{n-1}(t)\right]=h_yH_y(t)R_n^y(x_{n-1},z_{n-1}) \quad (7)$$

$$L_z\left[z_n(t)-\varsigma_n z_{n-1}(t)\right]=h_zH_z(t)R_n^z(z_{n-1},z_{n-1}) \quad (8)$$

where ζ_n is defined as

$\zeta_n = o,\ n\leq 1$

$1, n > 1.$

$$R_n^x(x_{n-1},z_{n-1})=\left[\frac{1}{(n-1)!}\frac{d^{(n-1)}N_x\left[\varphi(t;p),\xi(t,p)\right]}{dp^{(n-1)}}\right]_{p=0}$$

$$R_n^y(x_{n-1},y_{n-1})=\left[\frac{1}{(n-1)!}\frac{d^{(n-1)}N_y\left[\varphi(t;p),\phi(t,p)\right]}{dp^{(n-1)}}\right]_{p=0}$$

$$R_n^z(y_{n-1},z_{n-1})=\left[\frac{1}{(n-1)!}\frac{d^{(n-1)}N_z\left[\phi(t;p),\xi(t,p)\right]}{dp^{(n-1)}}\right]_{p=0}$$

For simplicity, $H_x = H_y = H_z = 1$, $h_x = h_y = h_z = h$. So, the approximations of $x(t), y(t), z(t)$ are only dependent on h. As we select $x_0(t) = x(0) = I_1$, $y_0(t) = y(0) = I_2$, $z_0(t) = z(0) = I_3$, the other components of $x_k(t)$, $y_k(t)$ and $z_k(t)$ are obtained.

$$\frac{dx_1}{dt}=h\left[\frac{dx_0}{dt}-k_1\left(1-\frac{\eta z_0}{k_d+z_0}\right)-k_2x_0\right]$$

$$\frac{dy_1}{dt}=h\left[\frac{dy_0}{dt}-k_2x_0+k_3y_0\right]$$

$$\frac{dz_1}{dt}=h\left[\frac{dz_0}{dt}-k_3y_0+k_4z_0\right]$$

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$$\frac{dx_2}{dt} = h\left[\frac{dx_1}{dt} + \left(\frac{k_1 \eta z_1 k_d}{(k_d + z_0)^2}\right) + k_2 x_1\right] + \frac{dx_1}{dt}$$

$$\frac{dy_2}{dt} = h\left[\frac{dy_1}{dt} - k_2 x_1 + k_3 y_2\right] + \frac{dy_1}{dt}$$

$$\frac{dz_2}{dt} = h\left[\frac{dz_1}{dt} - k_3 y_1 + k_4 z_1\right] + \frac{dz_1}{dt}$$

$$\frac{dx_3}{dt} = h\left[\frac{dx_2}{dt} + \left(\frac{k_1 \eta z_2 k_d}{(k_d + z_0)^3}\right)\left(k_d + z_0 - z_1^2\right) + k_2 x_2\right] + \frac{dx_2}{dt}$$

$$\frac{dy_3}{dt} = h\left[\frac{dy_2}{dt} - k_2 x_2 + k_3 y_2\right] + \frac{dy_2}{dt}$$

$$\frac{dz_3}{dt} = h\left[\frac{dz_2}{dt} - k_3 y_2 + k_4 z_2\right] + \frac{dz_2}{dt}$$

$$\frac{dx_4}{dt} = h\left[\frac{dx_3}{dt} + \left(\frac{k_1 \eta k_d}{(k_d + z_0)^3}\right)\left(k_d z_3 + z_0 z_3 - \frac{4}{3} z_1 z_2\right) + k_2 x_3\right] + \frac{dx_3}{dt}$$

$$\frac{dy_4}{dt} = h\left[\frac{dy_3}{dt} - k_2 x_3 + k_3 y_3\right] + \frac{dy_3}{dt}$$

$$\frac{dz_4}{dt} = h\left[\frac{dz_3}{dt} - k_3 y_3 + k_4 z_3\right] + \frac{dz_3}{dt}$$

$$x_1 = A_1 t + I_1$$

$$y_1 = A_2 t + I_2$$

$$z_1 = A_3 t + I_3$$

$$x_2 = A_4 t^2 + A_5 t + I_1$$

$$y_2 = A_6 t^2 + A_7 t + I_2$$

$$z_2 = A_8 t^2 + A_9 t + I_3$$

$$x_3 = A_{10} t^5 + A_{11} t^4 + A_{12} t^3 + A_{13} t^2 + A_{14} t + I_1$$

$$y_3 = A_{15} t^3 + A_{16} t^2 + A_{17} t + I_2$$

$$z_3 = A_{18} t^3 + A_{19} t^2 + A_{20} t + I_3$$

$$x_4 = \frac{k_2 h A_{10}}{6} t^6 + A_{21} t^5 + A_{22} t^4 + A_{23} t^3 + A_{24} t^2 + A_{25} t + I_1$$

$$y_4 = -\frac{k_2 h A_{10}}{6} t^6 - \frac{h}{5} k_2 A_{11} t^5 + A_{26} t^4 + A_{27} t^3 + A_{28} t^2 + A_{29} t + I_2$$

$$z_4 = A_{30} t^4 + A_{31} t^3 + A_{32} t^2 + A_{33} t + I_3$$

First we plot the h-curve and investigate the influence of h. The h-curve are depicted in Fig.(1-3). These curves contains horizontal line segments. These horizontal line segments reveals the region of convergence of h. It is perceived that the valid region for h is $1 < h < 0.3$. Thus we take h as-0.1 Fig.4 shows the parametric plot of x and y. As x increasing y increases for a particular pe- riod then return back. Fig.5 shows the parametric plot of x and z. As x increasing z increases suddenly then come down. Fig.6 shows the parametric plot of z and y. As y increasing z increases for aparticular period then return back.

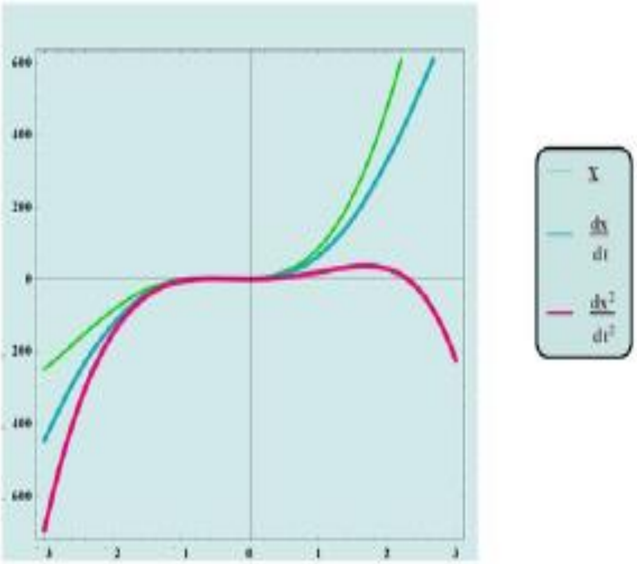

Figure 1: The h-curve of x and its derivatives for fourth order approximation

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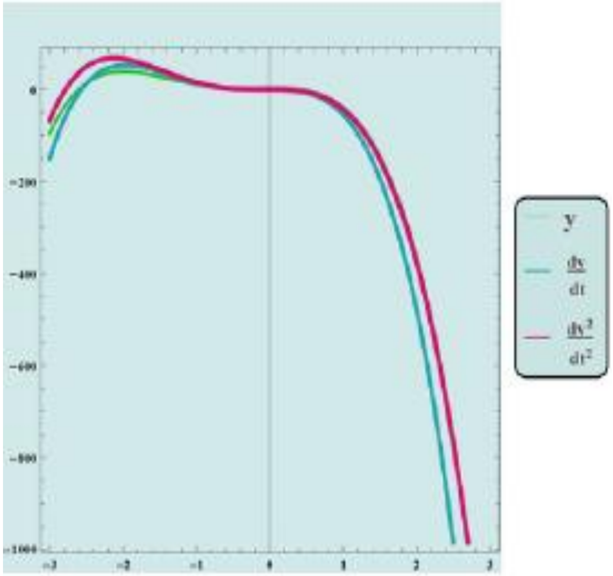

Figure 2: The *h*-curve of *y* and its derivatives for fourth order

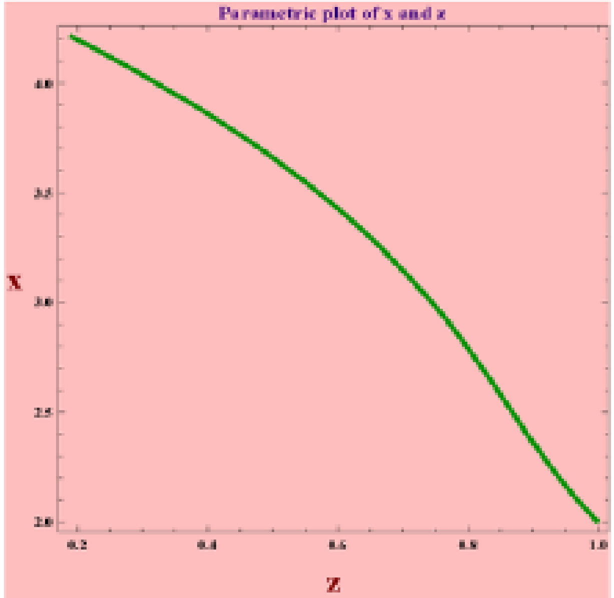

Figure 5: Parametric plot between x and z.

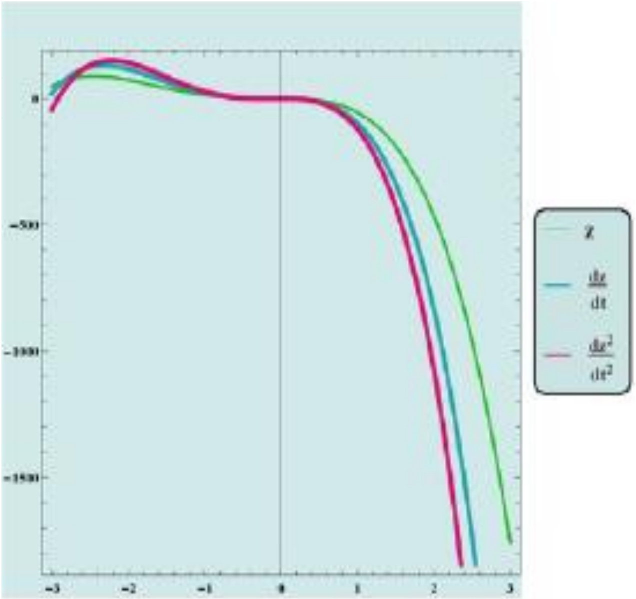

Figure 3: The *h*-curve of *z* and its derivatives for fourth order approximation

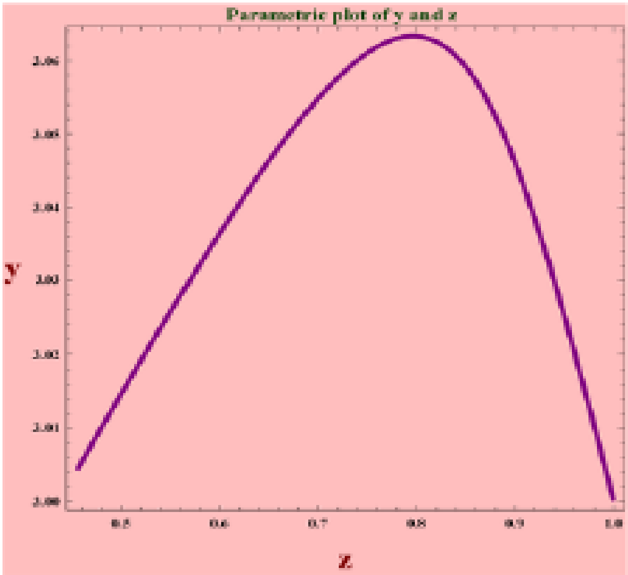

Figure 6: Parametric plot between *z* and *y*.

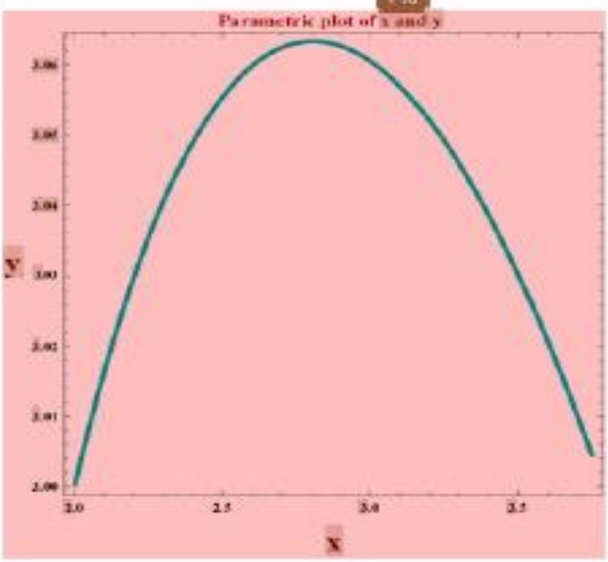

Figure 4: Parametric plot between *x* and *y*

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