ANALYSIS AND OPTIMIZATION ON POLY-CHAMBERS MODELS OF ENDOCRINE DISRUPTOR BENZENE MOVING IN HUMAN BODY COMPLEXITY SYSTEM

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Abstract. Due to the complexity of interaction among constituents inside the whole system, it is difficult to establish accurate mathematics models to exactly describe and analyze the complex systems. There is little attempt concerning on the moving process of endocrine disruptor within human body, which has been the polluted material worldwide related to the reproduction, existence and development of human being. Focusing on such two challenging issues, a Poly-chambers Model of endocrine disruptor Benzene moving in the human body complex system is established in this paper. Furthermore, stability analysis and its associated optimization are performed. The research results reflect the real physiological process of Benzene moving in the human body, which will offer the important theory basis for the quantitative study of complex systems and the application of cybernetics methods on complex systems.

Key Words. Complexity system, Complexity science, Endocrine disruptor, Poly-chambers, Optimization

1. Introduction

Complexity system refers to a integrated and complex whole that is constituted by some simple components with complex interaction\cite{1}. The complex system covers various fields of practical systems, such as economic system, social system, engineer system and biological system\cite{2}. The ecosystem is generally characterized with large quantity and various species. Therefore, the biocomplexity system is called complex large system\cite{3}, which is the most complex one in the complex systems.

Complex science focuses on the investigation of complex system, which is a newly developed subject and highly prized as 'The 21st Science' by academician Ruwei Dai\cite{4}. In the viewpoint of methodology, the conversional decomposing-reduction method, which is normally utilized in the 20th century, is not suitable for the recent investigation. Consequently, the innovation of methodology is badly in need, which concentrates on the integral investigation of system. It should be noted that it is difficult to qualitatively investigate the complex system, especially biological system, due to the complexity of interaction among constituents inside the whole system. Furthermore, it is still challenging to establish exact mathematical model and make deduction, theoretical analysis and quantitatively computation, etc.
Environmental Hormone (Endocrine disruptors) totally refers to the chemicals that influence and disrupt the discrete system in biological system, whose impact may involve the procreation function, neural system and immunity in different kinds of biological species including human. Hence, it may lead to worldwide pollution issue that affects the sustainable development of human\(^6\). The body complex system consists of blood cycle, assimilation, procreation, egest and some more subsystems. Various function is arisen within the interaction of these mentioned subsystems. The circle process of environmental hormone within human body interprets the interactions of these subsystems. There are some work concerning on the environmental hormone. However, it only qualitatively refines to disadvantageous effect on animal, especially, the model investigation for circle process of environmental hormone in the human body is seldom\(^7\)\(^-\)\(^13\). Benzene is one of important environmental hormones, which is rampantly left in the atmosphere due to its extensively industrial use, especially in the decorated room. By breathing the benzene, people may feel comatose, headache, exhausted and insomnia, even get aplastic anemia. Consequently, the model for the investigation of benzene in the human body is not only of inspiration for people to study the inherent of moving of benzene in human body, but also provides the theoretical basis for the quantitatively investigation of other biological complex systems.

2. Model Formulation

According to environmental disruptor benzene moving in the physical process of human body, the poly-chamber model is established as follows,

Some notes about Figure 1 is made as follows,

i: The arrows \(\Rightarrow\) in Figure 1 represent the single-direction moving of benzene, and the arrows \(\leftrightarrow\) in Figure 2 represent the double-direction moving of benzene.

ii: The arabian number and letter in Figure 1 represent the system functioned by hydroxybenzene and associated organs, respectively. 1B1: cycle system, blood; 2Fa: fat tissue; 3Lu: respiration system, lung; In: input.

iii: Blood represents the central cavity that provides the carrier for moving of benzene around the organs. The main input of benzene is made by respiration system.

iv: About 50 percent of benzene is discharged by respiration \((y_1)\); 40 percent of benzene is left in the body by oxidation, and then results in hydroxybenzene, dihydroxyphenzene, pyrocatechol, etc.; by conjugating with vitriol and glucuronic acid, these metabolic material discharge by means of urine \((y_2)\);
Some benzene still left in body distribute in bone marrow, brain, neural system and other tissues with much fat tissue.

Let $x_1, x_2, x_3$ represent the environmental disruptor; $k_{ij}$ represent the moving velocity constant from the $i$ room to $j$ room ($i, j = 1, 2, 3$); $In$ represents the input. The moving process is expressed by the first class of dynamics\(^\text{[14]}\). Based on the relationship in the defined model shown in Figure 1, the following differential-algebraic model can be expressed as follows,

The state equation of model system is as follows,

$$
\dot{x}(t) = Ax(t) + Bu(t),
$$

(3)

where

$$
A = \begin{bmatrix}
-k_{12} - k_{10} & k_{21} & k_{31} \\
-k_{12} & -k_{21} & 0 \\
0 & 0 & -k_{31} - k_{30}
\end{bmatrix},
B = \begin{bmatrix}
0 \\
0 \\
1
\end{bmatrix},
C = \begin{bmatrix}
0 & 0 & k_{30} \\
k_{10} & 0 & 0
\end{bmatrix},
D = 0.
$$

It follows from the moving rule of benzene in human body, the $k_{ij}$ can be valued as follows, $k_{10} = 0.35, k_{12} = 0.41, k_{21} = 0.01, k_{30} = 4.62, k_{31} = 1.51$.

Supposing the density of benzene is $30 \text{mg/m}^2$, the average wet air is $400 \text{ml/time}$, the average time of breath is $18 \text{time/min}$.

According to the input rule of benzene into the body,

$$
\begin{align*}
\dot{x}(t) &= (k_{30} x_3) + 3.6 \times 10^{-3} t. \\
\end{align*}
$$

The above mentioned poly-chambers models can exactly reflect the main moving process of benzene within the human body from an extensive viewpoint, which is beneficial to qualitatively studying the complex systems. It may also provide theoretical basis for the quantitative investigation for the main physical process of bio-complex system by using control theory and method.

3. System Analysis for Model System

3.1. Controllability analysis. The sufficient and necessary conditions of controllability for model system (3) is $P_c$ is full-rank.

By virtue of values of $k_{ij}$, it can be obtained by simple computation,

$$
P_c = \begin{bmatrix}
0 & 1.51 & -10.4 \\
0 & 0 & 0.62 \\
1 & -6.13 & 37.58
\end{bmatrix},
$$
It is easy to show that rank($P_c$) = 3, hence model system (3) is completely controllable.

The definition of normal form of controllable system is $^{[15]}$

For the input system $\{A, b\}$, if the state matrix and input matrix take the following standard form,

$A = \begin{bmatrix}
0 & 1 & 0 & \cdots & 0 & 0 \\
0 & 0 & 1 & \cdots & 0 & 0 \\
\vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\
0 & 0 & 0 & \cdots & 1 & 0 \\
0 & 0 & 0 & \cdots & 0 & 1 \\
-a_0 & -a_{n-1} & -a_{n-2} & \cdots & -a_2 & -a_1
\end{bmatrix}$, $b = \begin{bmatrix}
0 \\
0 \\
\vdots \\
0 \\
0 \\
1
\end{bmatrix}$,

then this system can be called controllable normal system. The matrix pair $\{A_k, b\}$ is the normal controllable form. The sufficient and necessary condition of model system $\{A_k, b\}$ is:

Given a linear transformation $T$, $\{TA_kT^{-1}, Tb\}$ is a controllable normal system and $T$ is unique.

By simple computing, it is easy to show that the model system (3) is controllable normal form, the corresponding transformation and controllable normal form are given as follows,

$T = \begin{bmatrix}
-0.812 & 0.201 & -0.201 \\
0.699 & -0.01 & 0.01 \\
-0.535 & 0.007 & 0.993
\end{bmatrix}$, $A_k = \begin{bmatrix}
0 & 1 & 0 \\
0 & 0 & 1 \\
-0.022 & -4.724 & -6.9
\end{bmatrix}$, $b = \begin{bmatrix}
0 \\
0 \\
1
\end{bmatrix}$.

For two arbitrary outputs $y_0$ and $y_1$, if its state can be controlled from $y(t_0) = y_0$ to $y(t_f) = y_1$, then the model system is output controllable$^{[15]}$.

The sufficient and necessary condition of the model system (3) is output controllable is the output controllable matrix $P_k$ is full row-rank,

$P_k = [CB, CAB, CA^2B, \cdots, CA^{n-1}B, D]$.

By virtue of values of $k_{ij}$, it is easy to show that the model system (3) is output controllable.

$P_k = \begin{bmatrix}
4.62 & -28.32 & 173.6 \\
0 & 0.53 & -3.64
\end{bmatrix}$, and rank($P_k$) = 2. Consequently, the model system (3) is output controllable.

3.2. The observability analysis. The sufficient and necessary condition of the model system (3) is observable is the observable matrix $P_o$ is full rank.

$P_o = \begin{bmatrix}
C \\
CA \\
CA^2 \\
\vdots \\
CA^{n-1}
\end{bmatrix}$.

By virtue of values of $k_{ij}$, it is easy to show that the controllable matrix of model system (3) is,
and rank\( (P_0) = 0 \). Therefore, the model system (3) is observable.

**Remark 1.** The biological interpretations of the above analysis (controllability and observability of model system (3)) are also obvious, which are introduced in the following two aspects.

- In the practical industry and social life, we may minimize the damage of benzene to human body regulate the input of amount of benzene in the atmosphere;
- With the development of biological technology and gene engineering, the above mentioned regulation can be achieved by means of molecular motion. By control the metabolize in human body, the benzene is broke down to some advantageous materials or some materials that can be drainaged timely, as is in line with the motivation that minimize the damage to human body.

### 3.3. Stability Analysis of Model System.

Based on Lyapunov theory\(^{[16]}\), set the positive real symmetric matrix \( Q = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} \), it follows from the values of \( k_{ij} \) that the matrix equation of model system (3) is as follows,

\[
A^T P + PA = -Q
\]

has an only positive definite symmetric solution \( P \):

\[
P = \begin{bmatrix} 31.8553 & 57.8293 & 7.8284 \\ 57.8293 & 107.8293 & 14.2346 \\ 7.8284 & 14.2346 & 2.0099 \end{bmatrix}
\]

Select a Lyapunov function \( V(x) = x^T P x = 31.86 x_1^2 + 107.83 x_2^2 + 2.01 x_3^2 + 115.66 x_1 x_2 + 15.66 x_1 x_2 + 28.47 x_2 x_3 \), it is easy to show the positivity of \( V(x) \), where \( x \) is subjected to model system (3). Further computations reveals that,

\[
\dot{x} = x^T (-Q) x = -(x_1^2 + x_2^2 + x_3^2) < 0.
\]

Hence, model system (3) is asymptotically stable around equilibrium \((0.7, 28.81, 0.16)\). According to the interpretations of state variables in model system (3), the biggest amount of benzene stored in the organ of human body is as follows, blood 0.7mg, fat 28.81mg and lung 0.16mg. The dynamical responses of model system (3) can be shown in Figure 2.

**Remark 2.** The above theoretical findings are in accordance with the physical characteristic and general rules of human body complex system. The biological unit
is of open structure. Such system obtain energy and material from the surrounding environment, and then release entropy vice versa, so that the self-stabilization can be maintained by self organization\textsuperscript{[18]}. In the case of stabilization, the biggest amount of benzene stored in the organ of human body comply with the physical rules of benzene moving in the human complex system, which reveals that the absorptive rate of benzene comes to its summit during the first few minutes. The benzene absorbed into the human body will mainly distributed in the tissues and organs with more fat.

4. Optimization Simulation

It follows from the Pontryagin’s maximum principle\textsuperscript{[17]}, an optimization problem associated with model system (3) can be established,

\[
J = \int_{t_0}^{t_f} F(x, u, t) dt = \int_{0}^{1200} (u - y_1 - y_2) dt = \int_{0}^{1200} (u - k_{30} x_3 - k_{10} x_1) dt = \int_{0}^{1200} (1/2u - k_{10} x_1) dt,
\]

the Hamilton function is as follows,

\[
H = 1/2u - k_{10} x_1 + \lambda_1[-(k_{12} + k_{10}) x_1 + k_{21} x_2 + k_{31} x_3] + \lambda_2(k_{12} x_1 - k_{21} x_2) + \lambda_3[-(k_{30} + k_{31}) x_3] + u_i,
\]

where \(\lambda_i, i = 1, 2, 3\) are adjoint variables, \(u\) is the control variable. For adjoint variables, we have

\[
\dot{\lambda}_1(t) = -k_{12} \lambda_2 + 2k_{10} + k_{12},
\]

\[
\dot{\lambda}_2(t) = -k_{21} \lambda_1 + k_{10} \lambda_2,
\]

\[
\dot{\lambda}_3 = -k_{31} \lambda_1 + (k_{30} + k_{31}) \lambda_3.
\]

The condition for a singular control to be optimal can be obtained that \(\frac{\partial H}{\partial u} = 1/2 + \lambda_3\), and then the optimal control can be computed as follows,
Further computations show the optimal trajectory is as follows and shown in Figure 3.

\[
\begin{align*}
    u^* &= \begin{cases} 
    0 & \lambda_3 > 1/2, \\
    1 & \lambda_3 < -1/2. 
    \end{cases}
\end{align*}
\]

\[
\begin{align*}
    x_1 &= \frac{3020}{4291}[1 - \exp(-6.13t)], \\
    x_2 &= \frac{123820}{4291}[1 - \exp(-6.13t)], \\
    x_3 &= \frac{100}{613}[1 - \exp(-6.13t)].
\end{align*}
\]

**Remark 3.** As reflected from the Figure 2 and Figure 3, the biggest amount of benzene stored remains constant. However, as far as the time to achieve stable state is concerned, it is shorten compared with the case without the optimal control. The biological interpretations are also obvious, the more absorption rate of benzene into human body, the less damage done to human body.

5. Conclusion

The poly-chambers differential model is established to model the moving process of environmental disruptor in the human body. By using control theory, the stability analysis and optimal control are performed in this paper. The research reveals that some physical process in human body complex system can be quantitatively expressed. Some results associated with the controllability, observability and asymptotical stability of model system are in accordance with the some biological rules of human complex system. They are of biological significance that may provide important theoretical basis for future investigation on biological control of benzene. With the simulation analysis on the optimal control on biological complex system, the application of control theory is extended, especially some methods concerning on human complex systems are made that may be theoretical inspiration of quantitative investigation of economic system, social system and biological system.
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References


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