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Autonomous Human Body Control, Part VI: Low Density Cholesterol Control using PD-I, PD-PI Controllers and I-first Order Compensator Compared with a PI Controller

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Abstract:
This paper investigates the tuning of PI, PD-I and PD-PI controllers from the second generation of PID controllers and an I-first order compensator from the second generation of control compensators when used to control the low dynasty cholesterol of an autonomous human body. The proposed controllers are tuned using a hybrid approach based on zero/pole cancellation and MATLAB optimization toolbox minimizing an ITAE performance index. The tuning results are presented and applied to generate the step time response for reference input tracking of a specific level. Transfer function of low density cholesterol as a process is identified using experimental work from previous work. The characteristics of the step time responses are compared with those of a conventional PI controller. The best controller/compensator for the control of the human low density cholesterol is assigned.

Keywords **— Autonomous human body control, low density cholestrol control, PI controller, PD-I controller, PD-PI controller, I-first order compensator, controller/compensator tuning.**

I. INTRODUCTION

This is the sixth paper of a series of research papers oriented towards the study of autonomous human body control to help reducing the human suffering due to the deficiencies in his operating physical elements such as heart, liver, kidney, lung, prostate, etc. and the bad diets he is practicing everyday The paper deals with the control of the serum low density lipoprotein cholesterol (LDLC) or LDC in the human blood where if it is too much (> 100 mg/dL) can raise the risk of heart disease and stroke [1]. This is why controlling the human serum LDC is important to save both heart and brain. Here are some of the research efforts regarding the modeling and control of the LDC since 2000:

Ratushny et al. (2000) stated that an adequate mathematical model of the complex nonlinear gene network regulating cholesterol synthesis in the cell is necessary for determining the optimal strategies of its corrections. They described the dynamic model in terms of elementary processes and biochemical reactions and obtained the optimal parameters of the model with numerical simulation of patterns of the system behavior [2]. August, Parker and Barahona (2006) presented a dynamic model of lipoprotein metabolism and indicated through sensitivity analysis that the intracellular concentration of cholesterol is robust to parametric variations while the plasma cholesterol can vary widely. They presented the time response of the LDC (in g/L) against time (in years) for an input [in g/(Lh)] over a time up to 15 years [3]. Demerezen and Barlas (2009) constructed a simulation model for blood cholesterol generating long-term dynamics of cholesterol metabolism in healthy and hypercholesterolemic persons with respect to body weight, diet and exercise. They showed that exercise was more effective than diet and showed also how the patient can reach healthier cholesterol levels. They presented time responses for LDLC, IDLC, HDLC and total cholesterol for reduced dietary, reduced weight and increased exercise [4]. Naik (2012) stated that elevated levels of cholesterol would be a risk factor for cardiovascular diseases. He developed a mathematical dynamic model for the cholesterol biosynthesis network and used a cascade control with hierarchical arrangement to control the cholesterol levels using a PI control algorithm [5].

Bhattachary et al. (2014) formulated a deterministic nonlinear ordinary differential equation model of the Sterol Regularity Element Binding Protein 2 (SREBP-2) cholesterol genetic regulatory pathway. They used a negative feedback formulation for cholesterol synthesis and discussed the advantages of their model formulation with respect to other models of genetic regulation [6].

Morgan et al. (2016) explored how to use mathematical modeling to show how the cholesterol metabolism is affected by the ageing process. They used acute cholesterol feeding to explore the effectiveness of the regularity mechanism. They presented graphical cholesterol profile over 15 days' time span for VLDL, IDLC LDLC and HDLC [7]. Kuzmenko, Gornov and Anikin (2018) compared the accuracy of various mathematical models to calculate the concentration of LDL cholesterol. They concluded that the use of mathematical models based on Shepard's method made it possible to obtain minimum errors and their tested errors allowed to reduce the errors of the calculation method [8]. Kubica and Balbus (2020) presented a simplified mathematical model of cholesterolhomostasis consisting of two differential equations. They applied the Runge-Kutta method to solve the differential equations. Their model allowed to investigate the effectiveness of therapy with drugs [9].

Zhang, Macshane, Searcy and Huang (2022) examined existing models in the literature and discussed the findings presented in these models for possible combination to form a comprehensive model of cholesterol within the entire body [10]. Davies, Morgan and Auley (2023) described how a model of cholesterol metabolism was combined with a model of atherosclerotic plaque formation. They demonstrated how the new model can be utilized to lower LDL-C and abrogate plaque formation [11]. Carstensen et al. (2024) a whole body mathematical model for cholesterol metabolism and transport which can simulate the effects of lipid-lowering drugs like statins and anti-PCSK9. They validated heir model against literature data and presented LDL-C profiles for statin treatment and combined statin and anti-PCSK9 dosing for dosing in the range of 101 to 731 mg/day [12]. Su et al. (2025) explored the relationship between NHHR and mortality among hypertension patients using multivariate Cox regression and restricted cubic splines. The segmental Cox model they used evaluated the threshold effects while the sensitivity analysis confirmed results robustness. They used machine learning algorithms to establish a prediction model [13].

II. THE CONTROLLED LOW DENSITY CHOLESTEROL AS A PROCESS

In the work of Demirezen and Barlas (2009), they presented graphical profile of the variation of the serum low density cholesterol (LDC) over a time period of 100 days for a statin dose of 20 g [4]. They didn't give any mathematical models for these cholesterol changes. The profile had a clear time delay with approximately first-order dynamics. I have used MATLAB to fit a model for the LDC process using a code written by the author as one of a set of codes used as an '*identification toolbox*' with Pade approximation for the time delay term of first-order, second-order and third-order [14]. The time response profile for the statin input dose with the three Pade approximations is shown in Fig.1 as generated by the step command of MATLAB [15] for the LDC change.

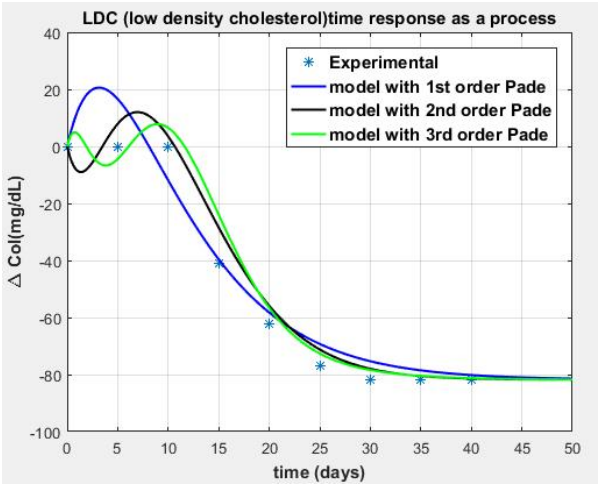

Fig.1 Step time response of the LDC as a process.

The fitted first-order transfer function model with a Pade first-order approximation as a process [$G_{LDC}(s)$] with 0.9798 correlation coefficient is given by:

$$G_{LDC}(s) = [K_p/(1+T_ps)]\ [(2-T_ds)/(2+T_ds)] \qquad (1)$$

Where:

K_p = process gain = -4.0909 (mg/dL)/g

T_p = LDC process time constant = 5.285 days

T_d = time delay of the LDC process = 13.45 days

COMMENTS:

- The LDC is a stable process.

- Steady state time response change: -80 mg/(dL) for the 20 g statin dose input.
- Maximum overshoot: zero
- Maximum undershoot: 20 mg/(dL)
- Settling time: 35.0 days

III. LDC CONTROL USING A PI CONTROLLER

- As a reference for control system characteristic comparison, a conventional PI controller from the first-generation of PID controllers is proposed to control the LDC. The PI controller transfer function has the transfer function, $G_{PI}(s)$ given by:

$$G_{PI}(s) = K_{pc1}+(K_{i1}/s) = (K_{i1}/s)[(K_{pc1}/K_{i1})s+1) \quad (2)$$

- The two elements: $G_{PI}(s)$ and $G_{LDC}(s)$ in a single-loop control system are cascaded in series.
- Multiplying $G_{PI}(s)$ by $G_{LDC}(s)$ gives the open-loop transfer function of the control system. Applying the zero/pole cancellation technique [16] gives the following relationships between the PI controller parameters:

$$K_{pc1} = T_p K_{i1} \quad (3)$$

- Now, the closed-loop transfer function of the control system, $G_{PI}(s)G_{LDC}(s)/[1+ G_{PI}(s)G_{LDC}(s)]$ can be derived using Eqs.1, 2 and 3.
- The closed-loop transfer function of the control system will be function in one unknown which is the integral gain K_{i1} of the PI controller.
- The ITAE performance index [17] as function of the error signal of the control system is used to tune the PI controller using the MATLAB optimization toolbox [18]. The result of this process with the help of Eq.3 gives the PI controller parameters as:

$$K_{pc1} = -0.06940, K_{i1} = -0.0131315 \quad (4)$$

- The step time response of the low density cholesterol for a 80 mg/(dL) desired LDC [-80 mg/(dL) LDC change from 160 mg/(dL) initial level] when using a PI controller is shown in Fig.2.

COMMENTS:

- Maximum overshoot: 17.24 %
- Maximum undershoot: 8.798 mg/(dL)
- Settling time: 92.80 days
- Steady-state error: zero

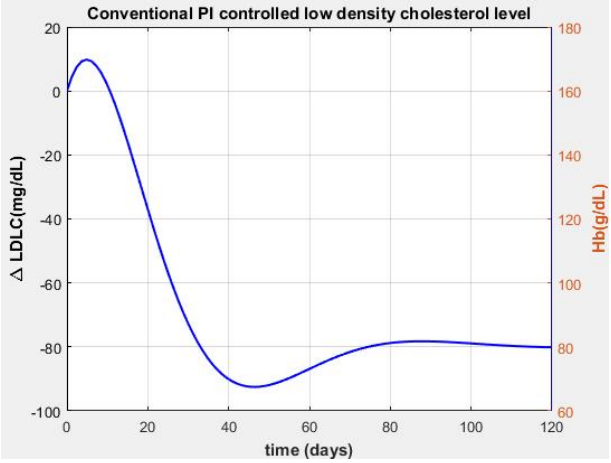

Fig.4 Low density cholesterol control using a PI controller.

IV. LDC CONTROL USING A PD-I CONTROLLER

- The PD-I controller is one of the second generation of PID controllers. It was introduced by the author in 2018 to control underdamped second-order-like processes [19]. It has the transfer function, $G_{PDI}(s)$ given by [19]:

$$G_{PDI}(s) = (K_{pc2}+K_{d2}s)(K_{i2}/s) = K_{pc2}K_{i2}[1+(K_{d2}/K_{pc2})s]/s \quad (5)$$

Where K_{pc2}, K_{d2} an K_{i2} are the proportional, derivative and integral gains of the PD-I controller.

- Multiplying $G_{PDI}(s)$ by $G_{LDC}(s)$ and applying the zero/pole cancellation technique [16] gives the following relationships between the PD controller element parameters K_{pc2} and K_{d2} as:

$$K_{d2} = T_p K_{pc2} \quad (6)$$

- Now, the open loop transfer function $G_{PDI}(s)G_{LDC}(s)$ becomes:

$$G_{PDI}(s)G_{LDC}(s) = (-K_{21}T_ds+2K_{21}/(T_ds^2+2s) \quad (7)$$

Where $K_{21} = K_{pc2}K_{i2}K_p$

- Now, the closed-loop transfer function of the control system is derived as function only of one parameter K_{21}.
- An ITAE performance index [17] is minimized using the MATLAB optimization toolbox [18] in terms of K_{21}. With K_{21} identified, assuming $K_{pc2} = 1$ and using Eq.6 give the PD-I controller parameters as:

  $K_{pc2} = 1$, $K_{d2} = 13.45$, $K_{i2} = -0.013056$ (8)
- The step time response of the low density cholesterol for a 80 mg/(dL) desired LDC [-80 mg/(dL) LDC change from 160 mg/(dL) initial level] when using a PD-I controller is shown in Fig.3.

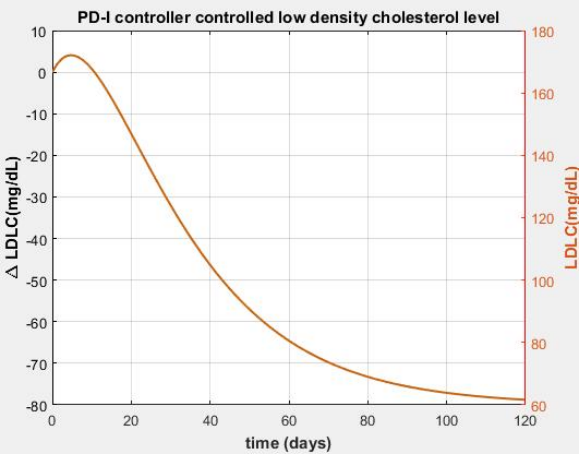

Fig.3 LDC control using a PD-I controller.

COMMENTS:

- Maximum overshoot: 15.517 % (compared with 17.24 % for PI controller).
- Maximum undershoot: 9.333 mg/(dL) (compared with 8.798 mg/(dL) for PI controller).
- Settling time: 92.06 days (compared with 92.80 days for PI controller).
- Steady-state error: zero

V. LDC CONTROL USING A PD-PI CONTROLLER

- The PD-PI controller was introduced by the author in April 2014 to control first-order delayed processes as one of the second generation of PID controllers introduced by the author since 2014. [20]. The PD-PI controller is consisted of two cascaded control modes: PD and PI set in the single-loop block diagram of a linear control system just after the error detector. It has a transfer function $G_{PDPI}(s)$ given by:

  $G_{PDPI}(s) = (K_{pc4}+K_{d4}s)[K_{pc5}+(K_{i5}/s)]$

  $= K_{pc4}K_{pc5}[1+(K_{d4}/K_{pc4})s][1+(K_{pc5}/K_{i5})s]/s$ (9)

Where K_{pc4}, K_{d4}, K_{pc5} and K_{i5} are the gain parameters of the PD-PI controller.

- Multiplying $G_{PDPI}(s)$ by $G_{LDC}(s)$ and applying the zero/pole cancellation technique [16] gives the following relationship between the PD control elements parameters K_{pc3} , K_{d3} as:

  $K_{d3} = T_p K_{pc3}$ (10)
- The closed-loop transfer function of the control system incorporating the PD-PI controller is derived as $G_{PDPI}(s)G_{LDC}(s)/[1+G_{PDPI}(s)G_{LDC}(s)]$.
- Now, the closed-loop transfer function of the control system in Fig.2 will be function of the controller gain parameters: K_{pc3}, K_{pc4} and K_{i4}.
- Using the ITAE performance index [17] and the MATLAB optimization toolbox [18] tunes the three PD-PI controller parameters for minimum ITAE providing with Eq.10:

  $K_{pc3} = -0.268075$, $K_{d3} = -1.416778$

  $K_{pc4} = 0.214748$, $K_{i4} = 0.055258$ (11)
- The step time response of the low density cholesterol for a 80 mg/(dL) desired LDC [-80 mg/(dL) LDC change from 160 mg/(dL) initial level] when using a PD-PI controller is shown in Fig.4.

COMMENTS:

- Maximum overshoot: 4.166 % (compared with 17.24 % for PI controller).
- Maximum undershoot: 20.8 mg/(dL) (compared with 8.798 mg/(dL) for PI controller).

- Settling time: 55.7 days (compared with 92.80 days for PI controller).
- Steady-state error: zero

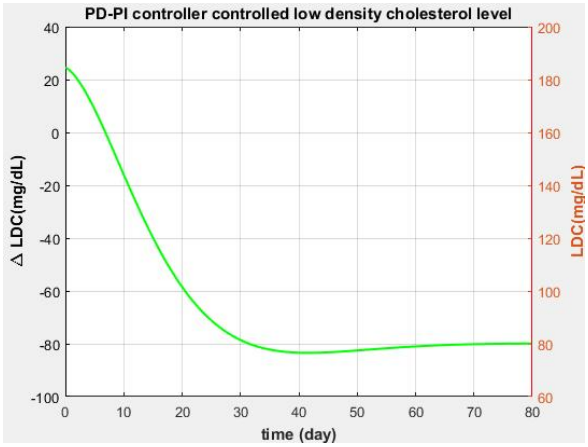

Fig.4 LDC control using a PD-PI controller.

VI. LDC CONTROL USING AN I-FIRST ORDER COMPENSATOR

The author presented the I-first order compensator as one of the compensators of the second generation of control compensators he introduced since 2014. He proposed the use of an I-first order compensator in September 2024 to control the longitudinal velocity of an autonomous car [21]. The I-first order compensator is composed of feedforward two cascade elements located in a single-loop block diagram of the control system used to control the low density cholesterol just after the error detector (integrator and first-order compensator elements).

An I-first order compensator has the transfer function $G_{I1st}(s)$ given by:

$$G_{I1st}(s) = K_{i5}(1+T_{zc}s)/[s(1+T_{pc}s)] \quad (12)$$

It has three parameters: integrator gain K_{i5}, first-order compensator zero time constant T_{zc} and first-order compensator pole time constant T_{pc}. The three compensator parameters are tuned as follows:

- The zero/pole cancellation technique [16] is used to cancel the simple zero of the I-first order compensator (Eq.12) with the process simple pole (Eq.1) in the open-loop transfer function. This step gives the time constant of the compensator zero as:
  $T_{zc} = T_p \quad (13)$
- Using the ITAE performance index [17] and the MATLAB optimization toolbox [18] tunes the two I-first order compensator parameters for minimum ITAE providing with Eq.13:
  $K_{i5} = -0.00596$, $T_{zc} = 5.285$
  $T_{pc} = 0.000000453 \quad (14)$
- The step time response of the low density cholesterol for a 80 mg/(dL) desired LDC [-80 mg/(dL) LDC change from 160 mg/(dL) initial level] when using an I-first order compensator is shown in Fig.5.

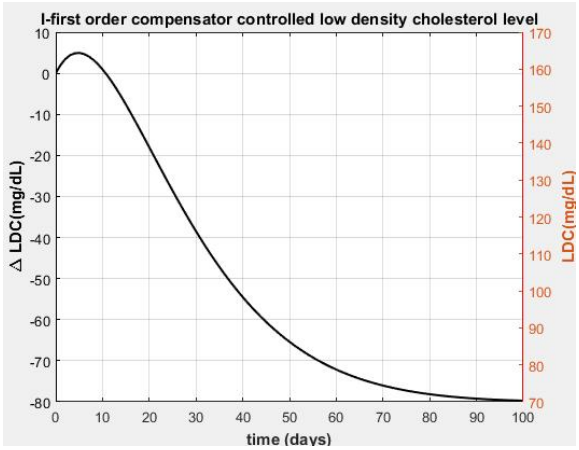

Fig.5 LDC control using an I-first order compensator.

COMMENTS:

- Maximum overshoot: zero % (compared with 17.24 % for PI controller).
- Maximum undershoot: 4.5 mg/(dL) (compared with 8.798 mg/(dL) for PI controller).
- Settling time: 80 days (compared with 92.80 days for PI controller).
- Steady-state error: zero

VII. COMPARISON OF TIME BASED CHARACTERISTICS

Graphical Comparison:

- The time-based characteristics of the control systems incorporating the proposed controllers/compensator proposed to control the low density cholesterol are compared graphically through the step time response as depicted in Fig.6 for a desired cholesterol level of 80 mg/dL (-80 mg/dL change).

Numerical Comparison:

- Numerical comparison for the time-based characteristics of the step time response for reference input tracking of the control system with the proposed controllers/compensator is presented in Table 1 with comparison with the application of a conventional PI controller used to control the same process.

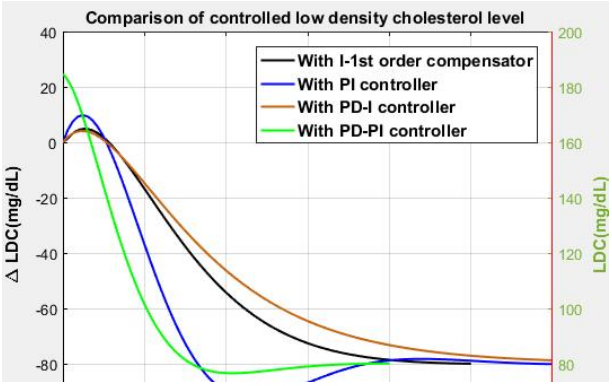

TABLE 1
TIME-BASED CHARACTERISTICS FOR REFERENCE INPUT TRACKING OF LOW DENSITY CHOLESTEROL

Controller/ Compensator	PI controller	PD-I controller	PD-PI controller	I-1st order compensator
Generation	first	second	second	second
OS_{max} (%)	17.24	0	4.166	0
US_{max} (mg/dL)	8.798	4.00	20.80	4.50
T_s (days)	92.80	110	55.70	80.00
e_{ss} (mg/dL)	0	0	0	0

OS_{max}: Maximum overshoot.
US_{max}: Maximum undershoot.
T_s: Settling time to ± 2 % tolerance.
e_{ss}: Steady-state error.

VIII. CONCLUSIONS

- The research work presented in this research paper handled the tuning of three controllers and one compensator proposed to control an autonomous serum low density cholesterol.
- The paper presented one controllers from the first generation of PID controllers (PI controller), two controllers from the second generation of PID controllers (PD-I and PD-PI controllers) and one compensator from the second generation of control compensators.
- The controlled process (low density cholesterol) was identified as a delayed-first-order one having 13.45 days' time delay, 5.285 days' time constant and -4.0909 (mg/dL)/g process gain when excited by a 20 g statin dose as an input
- Three Pade approximation orders (first, second and third) were investigated to replace the time delay element in the process transfer function. The first-order approximation was selected with correlation coefficient of 0.9798.
- The proposed controllers/compensator were tuned using hybrid approach based on applying the zero/pole cancellation technique and the MATLAB optimization toolbox minimizing an ITAE performance index.
- All the proposed controllers/compensator succeeded to eliminate completely the steady-state error of the control system.
- The proposed PD-I controller and I-first order compensator succeeded to eliminate completely the maximum percentage overshoot of the control system compared with 17.24 % for the PI controller.
- All the proposed controllers succeeded to eliminate completely the steady-state error of the control system.
- The PD-PI controller succeeded to reduce the settling time of the control system to 55.7 days compared with 92.8 days for the PI controller.
- If the criteria for selecting the best controller/compensator is the maximum overshoot, then the I-first order compensator is the best since it had a settling time less than that of the PD-I controller.
- If the criteria for selecting the best controller/compensator are the settling time, then the PD-PI controller is the best since it had the minimum settling time within the proposed group.

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DEDICATION

ABDUL-RAHMAN GALAL HASSAAN

- I dedicate this research work to my son Abdul-Rahman Galal, Why?

- He is a highly qualified mechanical engineer practiced industrial engineering in Egypt, Saudi Arabia and UK. Some of his qualifications:
- BSc in Mechanical Design and Production Engineering, Cairo University, July 2003.
- British Bachelor Standard, National Academic Recognition Information Centre (NARIC) for the United Kingdom, November 2003.
- Certified in Production and Inventory Management (CPIM), APICS the association for supply chain and operations management, March 2011.
- Master of Business Administration (MBA), Edinburgh Business School, Heriot-Watt University, UK, June 2020
- **PROFESSIONAL OVERVIEW:** Dynamics 365 Solutions Architect and Senior Manufacturing Consultant with proven track record of working with clients to implement Business Applications with focus on Manufacturing and Supply Chain Management.
- Good luck, highly qualified Mechanical Engineer Abdul-Rahman.

BIOGRAPHY

Galal Ali Hassaan

- Emeritus Professor of System Dynamics and Automatic Control.
- Has got his B.Sc. and M.Sc. from Cairo University in 1970 and 1974.
- Has got his Ph.D. in 1979 from Bradford University, UK under the supervision of Late Prof. John Parnaby.
- Now with the Faculty of Engineering, Cairo University, EGYPT.
- Research on Automatic Control, Mechanical Vibrations, Mechanism Synthesis and History of Mechanical Engineering.
- Published more than 350 research papers in international journals and conferences.
- Author of books on Experimental Systems Control, Experimental Vibrations and Evolution of Mechanical Engineering.
- Chief Justice of the International Journal of Computer Techniques.
- Member of the Editorial Board of IJET.
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