Improved PID Control Based on Temperature Compensation for the Incubation Plate of Chemiluminescent Immunoassay Analyzer

Zhaoyang Wang[1][a], Jing Wang[2], Bo Liang[1], Xuesong Ye[1] and Congcong Zhou[2][b]

[1]*Biosensor National Special Laboratory, College of Biomedical Engineering and Instrument Science, Zhejiang University, Hangzhou, Zhejiang, 310027, China*

[2]*Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, National Engineering Research Center for Innovation and Application of Minimally Invasive Devices, East Qingchun Road, Hangzhou, Zhejiang, 310016, China*

Keywords: Temperature Compensation, Improved PID Control, Incubation Plate, Constant Temperature Incubation.

Abstract: This paper proposes an improved PID control based on temperature compensation strategy, which can dynamically adjust the target temperature value of the PID controller according to the ambient temperature and the preset temperature compensation curve, thus basically eliminating the influence of ambient temperature on the reaction liquid temperature, and ultimately achieving stable reaction liquid at the preset temperature under different ambient temperature conditions. Through experiments, it was found that after adding temperature compensation strategy to the PID control, the maximum steady-state temperature difference of the reaction liquid decreased from 0.31℃ to 0.11℃, and the coefficient of variation (CV) of Relative Light Units (RLU) decreased from 4.22% to 1.43%.

1 INTRODUCTION

Chemiluminescence immunoassay (CLIA) is an analytical method based on the principle of immune reaction. It utilizes the specific binding between antigen and antibody to detect the presence and quantity of specific substances in samples, including proteins, hormones, tumor markers, etc(Boolani et al., 2019; Khan et al., 2023; Xiao & Xu, 2020). Constant temperature incubation is an important step in CLIA, aiming to enhance the efficiency of antigen-antibody binding and reduce non-specific reactions, thus improving the sensitivity and accuracy of detection results(Suan Ng, Ling Lee, Bothi Raja, & Doong, 2022). In chemiluminescent immunoassay analyzers, constant temperature incubation is usually performed in an incubation plate, with the incubation temperature typically set at 37℃, similar to human body temperature(Yalcin, oezkan, & Shah, 2022). Studies have shown that different incubation temperatures can affect the rate of antigen-antibody binding and the accuracy and reproducibility of the luminescence signal(Yufeng, Shizhou, Bo, & Jianwen, 2010). Therefore, it is of great significance to control the temperature of the reaction solution in the incubation plate at a stable 37℃ for the accuracy and reliability of detection results.

The current incubation strategy of the instrument is to control the temperature of the incubation plate to remain stable at the preset temperature, and then place the reaction cups containing the reaction liquid into the incubation plate for incubation(Feng-Mei, Da-Qing, Jian-Ning, & Pan-Fei, 2019). Due to the open top of the reaction cup, the reaction liquid is in direct contact with the air, and in fact, the temperature of the reaction liquid is affected by both the temperature of the incubation plate and the ambient temperature.

In temperature sensing technology, studies have shown that monitoring environmental temperature has a significant impact on sensor design and measurement results(Ren, Zhang, Ye, & Zhou, 2023). However, most existing instruments set the incubation temperature on a fixed value using the PID algorithm, without considering the influence of environmental temperature. This leads to differences in the incubation temperature of the reaction liquid at

[a] https://orcid.org/0009-0004-8996-8743
[b] https://orcid.org/0000-0001-8397-1491

Wang, Z., Wang, J., Liang, B., Ye, X. and Zhou, C.
Improved PID Control Based on Temperature Compensation for the Incubation Plate of Chemiluminescent Immunoassay Analyzer.
DOI: 10.5220/0012573300003657

In *Proceedings of the 17th International Joint Conference on Biomedical Engineering Systems and Technologies (BIOSTEC 2024) - Volume 1*, pages 811-816
ISBN: 978-989-758-688-0; ISSN: 2184-4305

different ambient temperatures, resulting in variations in the detection results of the same sample.

This paper proposes an improved PID control based on temperature compensation, which can dynamically adjust the target temperature value of the PID controller based on different environmental temperatures. The ultimate goal is to ensure that the reaction liquid remains stable at the preset temperature under different ambient temperatures. The application of this improved PID control based on temperature compensation for the incubation plate will help improve the accuracy and reliability of chemiluminescent immunoassay detection results, especially in cases where laboratory environmental temperatures fluctuate significantly. Furthermore, this control strategy can also be applied to other experimental scenarios requiring precise temperature control, demonstrating a certain degree of universality and practicality.

2 IMPROVED PID CONTROL BASED ON TEMPERATURE COMPENSATION

2.1 Principle of the Improved PID Control

Conventional PID control is a closed-loop control method based on three components: proportional, integral, and derivative(Borase, Maghade, Sondkar, & Pawar, 2021). It is used to regulate the output of a system to stabilize target variables such as temperature at a set value. The proportional, integral, and derivative components work together to adjust the controller's output to influence the actuator, thereby achieving precise control of the target variable of the controlled object(Kaul, Tiwari, Yadav, & Kumar, 2021; Phu Nguyen, Hung Nguyen, Ahmadian, & Senu, 2020). The schematic diagram of conventional PID control is shown in the Figure 1, where r(t) represents the set value, y(t) represents the measurement value, e(t) is the error value, and u(t) is the output value of the PID controller.

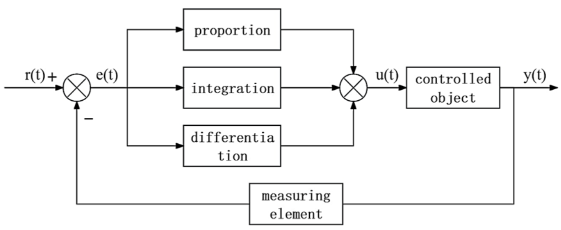

Figure 1: Conventional PID control.

In conventional PID control, the set value r(t) is a fixed value(Joseph, Dada, Abidemi, Oyewola, & Khammas, 2022; Kaul et al., 2021). However, in a constant-temperature incubation module, the temperature of the reaction solution may be affected by the ambient temperature. Therefore, we propose an improved PID control based on temperature compensation, where the set value of the PID controller can be dynamically adjusted according to the ambient temperature. Specifically, at high ambient temperatures, the set value r(t) needs to be appropriately reduced to avoid overheating of the reaction solution, while at low ambient temperatures, the set value r(t) needs to be correspondingly increased to maintain stable temperature of the reaction solution. The schematic diagram of the improved PID control is shown in the Figure 2.

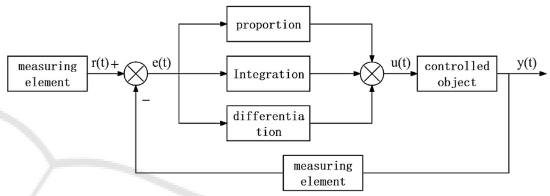

Figure 2: Improved PID control.

The dynamic adjustment of the set value r(t) is mainly achieved through the ambient temperature and a preset temperature compensation curve. The adjustment block diagram of r(t) is shown in the Figure 3. The temperature sensing sensor collects the ambient temperature in the first step. In the second step, the controller calculates the temperature compensation value for the incubation plate based on the acquired ambient temperature and the preset temperature compensation curve. Finally, the target temperature value for the incubation plate r(t) is determined in the third step.

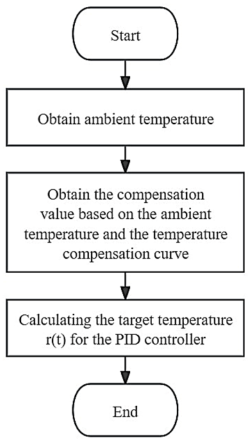

Figure 3: Adjustment block diagram of the set value r(t).

2.2 Acquisition of the Temperature Compensation Curve

The core of improved PID control lies in obtaining the temperature compensation curve. The steps to obtain the temperature compensation curve are as follows:

Step 1: Place the incubation plate in an environment with adjustable temperature and use the ambient temperature as the independent variable x_1 、x_2、 ⋯ 、x_n . Adjust the incubation plate temperature to stabilize the reaction liquid temperature at a preset temperature of 37°C. Record the corresponding incubation plate temperature compensation values y_1、y_2、 ⋯ 、y_n at different ambient temperatures. Obtain a set of data points $p_i(x_i, y_i), i = 1,2, \cdots, n$.

Step 2: Obtain the temperature compensation curve through polynomial fitting. Select the fitting curve based on the principle of minimizing the sum of squared deviations, ensuring that the fitted curve deviates minimally from the actual temperature compensation curve $y = f(x)$.

The process of polynomial least squares fitting is as follows:

1. Assume the k_{th}-order polynomial for the fitting is given by equation (1):

$$y = a_0 + a_1 x + \cdots + a_k x^k \tag{1}$$

2. The sum of squared deviations, which represents the distance between each temperature compensation value point and the fitted curve, is denoted as the sum of squared errors in equation (2).

$$R^2 = \sum_{i=1}^{n} [y_i - (a_0 + a_1 x_i + \cdots + a_k x_i{}^k)]^2 \tag{2}$$

3. In order to minimize the sum of squared errors, a_0 、a_1、 ⋯ 、a_k should satisfy the condition that the partial derivatives of equation (2) with respect to a_{i} are equal to zero.

$$\begin{aligned} -2\sum_{i=1}^{n} [y_i - (a_0 + a_1 x_i + \cdots + a_k x_i{}^k)] = 0 \\ -2\sum_{i=1}^{n} [y_i - (a_0 + a_1 x_i + \cdots + a_k x_i{}^k)]x_i = 0 \\ \cdots \\ -2\sum_{i=1}^{n} [y_i - (a_0 + a_1 x_i + \cdots + a_k x_i{}^k)]x_i{}^k = 0 \end{aligned} \tag{3}$$

4. By simplifying each equation in equation (3) and representing them in matrix form, we obtain the matrix shown in equation (4).

$$\begin{bmatrix} n & \sum_{i=1}^{n} x_i & \cdots & \sum_{i=1}^{n} x_i{}^k \\ \sum_{i=1}^{n} x_i & \sum_{i=1}^{n} x_i{}^2 & \cdots & \sum_{i=1}^{n} x_i{}^{k+1} \\ \vdots & \vdots & \ddots & \vdots \\ \sum_{i=1}^{n} x_i{}^k & \sum_{i=1}^{n} x_i{}^{k+1} & \cdots & \sum_{i=1}^{n} x_i{}^{2k} \end{bmatrix} \begin{bmatrix} a_0 \\ a_1 \\ \vdots \\ a_k \end{bmatrix} = \begin{bmatrix} \sum_{i=1}^{n} y_i \\ \sum_{i=1}^{n} x_i y_i \\ \vdots \\ \sum_{i=1}^{n} x_i{}^k y_i \end{bmatrix} \tag{4}$$

5. Let matrix $\boldsymbol{X}$, $\boldsymbol{A}$, and $\boldsymbol{Y}$ be defined as follows:

$$\boldsymbol{X} = \begin{bmatrix} 1 & 1 & \cdots & 1 \\ x_1 & x_2 & \cdots & x_n \\ \vdots & \vdots & \ddots & \vdots \\ x_1{}^k & x_2{}^k & \cdots & x_n{}^k \end{bmatrix}, \boldsymbol{A} = \begin{bmatrix} a_0 \\ a_1 \\ \vdots \\ a_k \end{bmatrix}, \boldsymbol{Y} = \begin{bmatrix} y_1 \\ y_2 \\ \vdots \\ y_n \end{bmatrix} \tag{5}$$

According to equation (4), we have $\boldsymbol{XX^TA = XY}$. Therefore, the coefficient matrix of the fitting polynomial can be obtained $\boldsymbol{A} = (\boldsymbol{XX^T})^{-1}\boldsymbol{XY}$. This provides us with the coefficients of the fitting polynomial and thus the temperature compensation curve.

With the help of Matlab, the results of third-order polynomial fitting can be visualized. By inputting different ambient temperatures and their corresponding temperature compensation values, the polyfit function can be used to achieve polynomial curve fitting and obtain the temperature compensation curve. The third-order polynomial fitting result is shown in Figure 4.

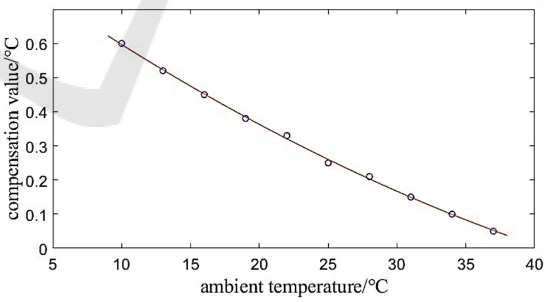

Figure 4: The results of third-order polynomial fitting.

2.3 The Construction of a Constant Temperature Incubation Platform

We constructed a constant temperature incubation platform according to the experimental requirements, as shown in the Figure 5. The constant temperature incubation platform includes an aluminum incubation plate, heating film, temperature sensor, and controller. The aluminum incubation plate is used to hold the reaction vessels, providing a stable incubation environment for the reaction solution. The heating film is pasted around the incubation plate to heat it. The constant temperature incubation platform is equipped with two temperature sensors, one of which is embedded inside the incubation plate to collect the temperature of the incubation plate, while the other temperature sensor is placed in the air to collect the ambient temperature. The core of the controller is an STM32 microcontroller, which changes the duty cycle of the Pulse-Width Modulation (PWM) signal output pin through the PID temperature control algorithm to achieve precise control of the temperature of the incubation plate.

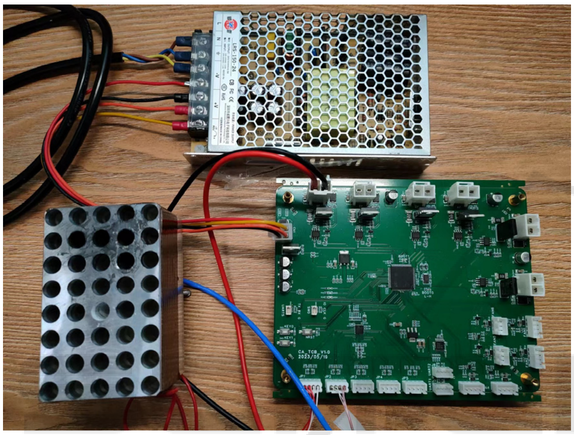

Figure 5: Constant temperature incubation platform.

3 RESULTS AND DISCUSSION

3.1 Effects of Improved PID Control

To compare the effects of temperature compensation strategies versus no temperature compensation strategy on the incubation temperature of the reaction solution, we placed the incubation plate in a temperature-controlled incubator and varied the temperature of the incubator to simulate changes in ambient temperature. We added 300 μL of reaction solution with an initial temperature of 7°C to the reaction vessels and measured the temperature changes of the reaction solution during incubation at different ambient temperatures.

In the first set of experiments, the PID temperature control algorithm did not consider temperature compensation strategies. The incubation plate temperature was fixed at 37°C, and the temperature changes of the reaction solution were observed at ambient temperatures of 15°C, 20°C, 25°C, and 30°C. To clearly observe the steady-state temperature differences of the reaction solution, only the temperature change curves from 100-400 s after placing the reaction solution in the incubation plate are shown in the Figure 6. From the test results, it can be observed that the ambient temperature has a significant impact on the steady-state temperature of the reaction solution. At an ambient temperature of 30°C, the steady-state temperature of the reaction solution is 36.86°C. However, at an ambient temperature of 15°C, the steady-state temperature of the reaction solution is 36.55°C, resulting in a difference of 0.31°C.

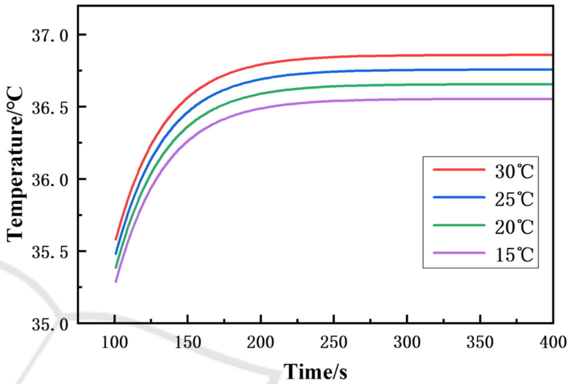

Figure 6: Temperature of reaction liquid under different ambient temperatures (without temperature compensation).

In the second set of experiments, the PID temperature control algorithm considered temperature compensation strategies, and the set temperature of the incubation plate was dynamically adjusted according to the ambient temperature and the preset temperature compensation curve. The temperature changes of the reaction solution during incubation at ambient temperatures of 15°C, 20°C, 25°C, and 30°C were observed. Similarly, the temperature change curves from 100-400 s after placing the reaction solution in the incubation plate are shown in the Figure 7. From the test results, it can be observed that with temperature compensation at different ambient temperatures, the steady-state temperature difference of the reaction solution is very small. The steady-state temperature of the reaction solution is maintained at 37 ± 0.1°C after temperature compensation, with a maximum temperature difference of 0.11°C. Comparing the results of the two experimental groups, it can be observed that improved PID control can significantly reduce the steady-state temperature difference during incubation of the reaction solution at different environmental temperatures.

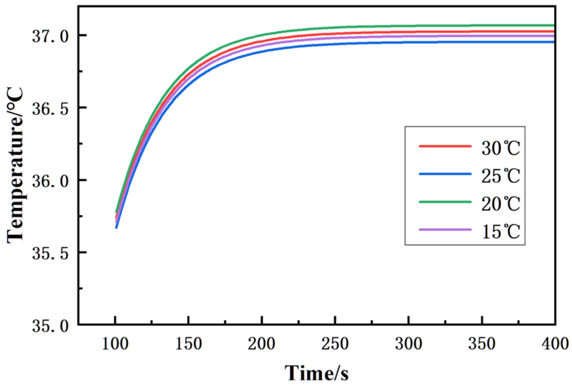

Figure 7: Temperature of reaction liquid under different ambient temperatures (with temperature compensation).

3.2 Impact of Improved PID Control on the RLU

Taking the Interleukin-6 (IL-6) chemiluminescence system as an example, we explored the influence of improved PID control on the results of chemiluminescence immunoassay. In the first set of experiments, the PID temperature control algorithm did not consider temperature compensation strategies. The same samples were incubated at ambient temperatures of 15°C, 20°C, 25°C, and 30°C for 30 minutes. After magnetic separation and washing, the reaction cups were placed in a photomultiplier tube for reading. In the second set of experiments, the PID temperature control algorithm considered temperature compensation strategies, and the subsequent experimental procedures were the same as those of the first set. By analyzing the differences of RLU between the two sets of experiments, the final results are shown in the Table 1.

Table 1: The impact of improved PID control.

Ambient temperature/°C	RLU without temperature compensation	RLU with temperature compensation
15	1921244	2163580
20	2063019	2188961
25	2125171	2143365
30	2143024	2226606
CV	**4.22%**	**1.43%**

From preliminary experimental results, it can be observed that when temperature compensation strategy is not considered, there is a significant difference in the steady-state temperature of the reaction solution at different ambient temperatures, resulting in a high CV in the RLU, reaching 4.22%. However, when temperature compensation strategy is taken into account, the steady-state temperature difference of the reaction solution at different ambient temperatures is reduced, leading to a lower CV in the final RLU, which is only 1.43%.

The above experiments demonstrate that by incorporating temperature compensation strategy into the PID algorithm, the influence of environmental temperature on the steady-state temperature of the reaction solution can be effectively eliminated. This ensures that the reaction solution remains stable at the set temperature under different environmental conditions. This finding is of great significance in reducing the CV in the detection results and improving the accuracy of the detection results.

4 CONCLUSIONS

In this work, we propose an improved PID control algorithm based on temperature compensation. By sensing the environmental temperature and obtaining the temperature compensation value through the preset temperature compensation curve, the influence of environmental temperature on the reaction solution temperature can be effectively eliminated. The temperature compensation curve is fitted using a third-order polynomial. By comparing the steady-state temperatures of the reaction solution before and after considering the temperature compensation strategy, it can be observed that the improved PID control can reduce the maximum steady-state temperature difference of the reaction solution from 0.31°C to 0.11°C. The improved PID control also reduces the CV of the detection results for the same sample at different environmental temperatures. By considering the temperature compensation strategy, the CV of the RLU decreases from 4.22% to 1.43%. This is of significant importance in improving instrument performance and enhancing the accuracy of the detection results.

In future work, we plan to explore alternative fitting methods to further reduce the steady-state temperature difference of the reaction solution under different environmental temperatures. Additionally, we will also explore other chemiluminescence systems to further investigate the impact of improved PID control on the results of chemiluminescence detection.

ACKNOWLEDGEMENTS

This work was supported in part by Zhejiang Provincial Natural Science Foundation of China under Grant No. LY22H180006 and the National Key R&D Program of China under Grant No. 2017YFF0210803.

REFERENCES

Boolani, A., Channaveerappa, D., Dupree, E. J., Jayathirtha, M., Aslebagh, R., Grobe, S., . . . Darie, C. C. (2019). Trends in Analysis of Cortisol and Its Derivatives. In A. G. Woods & C. C. Darie (Eds.), *Advancements of Mass Spectrometry in Biomedical Research, 2nd Edition* (Vol. 1140, pp. 649-664).

Borase, R. P., Maghade, D. K., Sondkar, S. Y., & Pawar, S. N. (2021). A review of PID control, tuning methods and applications. *International Journal of Dynamics and Control, 9*(2), 818-827. doi:10.1007/s40435-020-00665-4

Feng-Mei, F., Da-Qing, L., Jian-Ning, Z., & Pan-Fei, H. (2019). Performance Verification of CA125 in Roche Cobas6000 Automatic Electrochemiluminescence Immunoassay Analyzer. *World Latest Medicine Information*.

Joseph, S. B., Dada, E. G., Abidemi, A., Oyewola, D. O., & Khammas, B. M. (2022). Metaheuristic algorithms for PID controller parameters tuning: review, approaches and open problems. *Heliyon, 8*(5). doi:10.1016/j.heliyon.2022.e09399

Kaul, S., Tiwari, N., Yadav, S., & Kumar, A. (2021). Comparative Analysis and Controller Design for BLDC Motor Using PID and Adaptive PID Controller. *Recent Advances in Electrical & Electronic Engineering, 14*(6), 671-682. doi:10.2174/23520965146662108231 52446

Khan, M., Shah, S. H., Salman, M., Abdullah, M., Hayat, F., & Akbar, S. (2023). Enzyme-Linked Immunosorbent Assay versus Chemiluminescent Immunoassay: A General Overview. *Global Journal of Medical Pharmaceutical and Biomedical Update, 18*(1). doi:10.25259/gjmpbu_77_2022

Phu Nguyen, D., Hung Nguyen, N., Ahmadian, A., & Senu, N. (2020). A New Fuzzy PID Control System Based on Fuzzy PID Controller and Fuzzy Control Process. *International Journal of Fuzzy Systems, 22*(7), 2163-2187. doi:10.1007/s40815-020-00904-y

Ren, X., Zhang, Y., Ye, X., & Zhou, C. (2023). Study of perfusion based theoretical model and experimental evaluation for wearable CBT measurement. *Measurement, 206*. doi:10.1016/j.measurement.2022.112338

Suan Ng, S., Ling Lee, H., Bothi Raja, P., & Doong, R.-a. (2022). Recent Advances in Nanomaterial-based Optical Biosensors as Potential Point-of-Care Testing (PoCT) Probes in Carcinoembryonic Antigen Detection. *Chemistry-an Asian Journal, 17*(14). doi:10.1002/asia.202200287

Xiao, Q., & Xu, C. (2020). Research progress on chemiluminescence immunoassay combined with novel technologies. *Trac-Trends in Analytical Chemistry, 124*. doi:10.1016/j.trac.2019.115780

Yalcin, S., oezkan, S., & Shah, T. (2022). Incubation Temperature and Lighting: Effect on Embryonic Development, Post-Hatch Growth, and Adaptive Response. *Frontiers in Physiology, 13*. doi:10.3389/fphys.2022.899977

Yufeng, Y., Shizhou, L., Bo, H., & Jianwen, Z. (2010). *Automated Chemiluminescence Immunoassay Analyzer*. Paper presented at the 2010 International Conference on Intelligent Computation Technology and Automation.