STM32 microcontroller-based automated control system for high-throughput cell sphere culture chips

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Abstract. 3D cell culture technology has gradually become a hotspot in biomedical research in recent years, traditional cell culture methods are complex, inefficient and unable to simulate the three-dimensional structure of cells in vivo and extracellular plasmic interactions, high-throughput screening (HTS) technology and automation technology is a necessary technology for modern biomedical research, and the automated cultivation devices on the market are generally larger and more expensive, which are not suitable for the promotion of laboratory. In this paper, a microfluidic chip automation control system based on STM32F103C8T6 microcontroller is proposed, which integrates lifting, oscillating and suctioning devices, realises the full automation of the cell culture process, and significantly improves the culture efficiency, and is compact and lightweight, suitable for laboratory promotion, which greatly saves the financial and material resources of researchers. This study provides important technical support for the automation and high-throughput development of cell culture technology.

Keywords: high-throughput cell sphere culture chip, 3D cell culture, automation technology, STM32 microcontroller.

1. Introduction

3D cell sphere culture technology, an in vitro method that mimics the in vivo microenvironment, is widely used in cancer research, drug screening, and stem cell studies due to its ability to replicate in vivo cell structures and functions [1]. Studies show that 3D culture improves cell proliferation, differentiation, and drug response accuracy [2]. However, traditional manual methods suffer from low efficiency, poor reproducibility, and operator dependence, leading to inconsistent results [3]. To address these issues, automated systems have been developed, using robotic platforms with sensors and control algorithms to partially automate the culture process [4]. Despite progress, challenges in nutrient replenishment and waste removal remain [5]. This paper presents a compact, low-cost automated control system that automates sample loading, nutrient replenishment, and waste removal, enhancing experimental reliability and efficiency. The system includes a lifting device controlled by an STM32 system and a spiral stepper motor for precise movement, a suction device using STM32 and DS1302 for timed operation, and an oscillation device optimized for stability and reduced splashing. This system promotes laboratory automation, reduces research costs, and advances cell culture technology. The schematic diagram of the device structure is shown in Figure 1

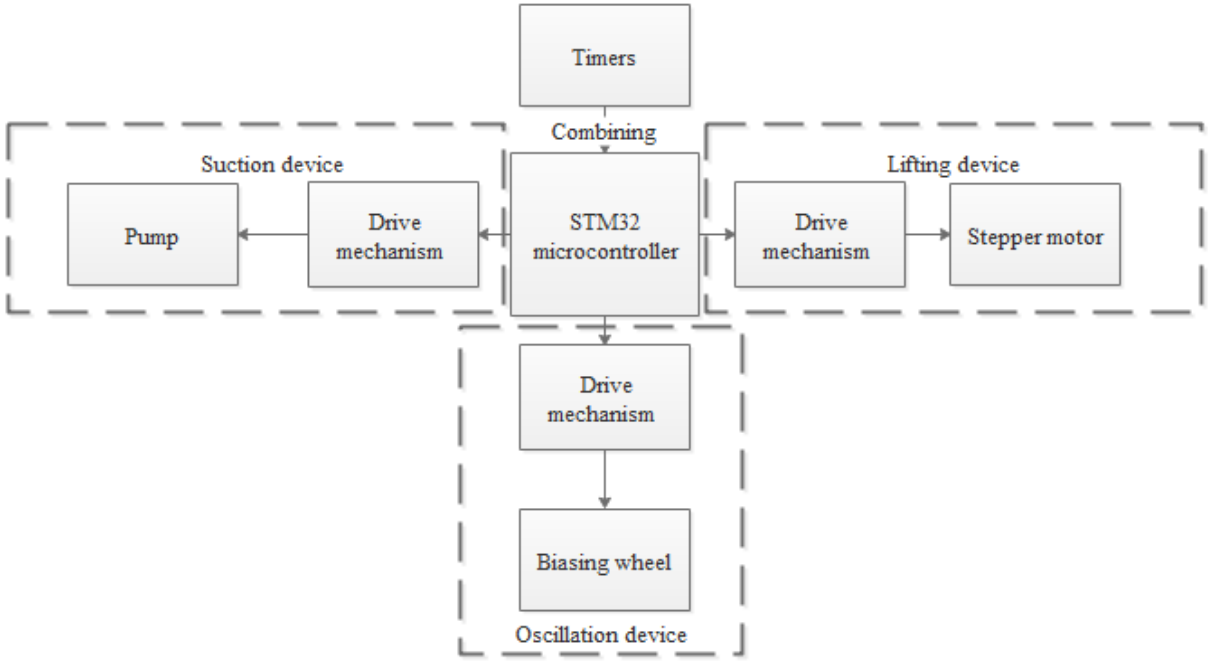


Fig. 1 Schematic diagram of the device structure

2. Structure and working principle of the equipment

The general assembly of the automatic control device is shown in Fig. 2. The device consists of three parts, which are lifting structure, oscillation structure and suction structure, as shown in Fig. 3. This device is capable of automated control of a variety of culture chips. In this paper, high throughput cell sphere culture is studied as an example, and its chip structure is shown in Figure 4.

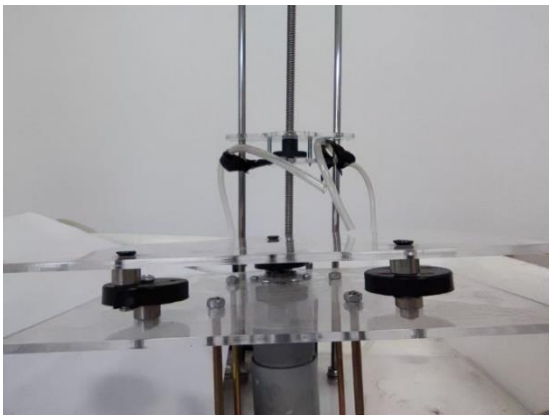


Fig. 2 General assembly of the automatic control device

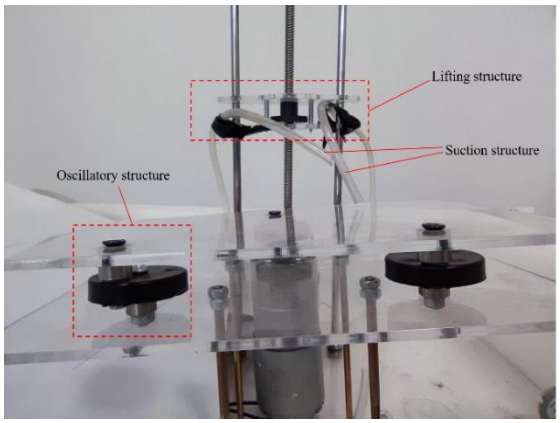


Fig. 3 Schematic diagram of each structure of the automatic control device

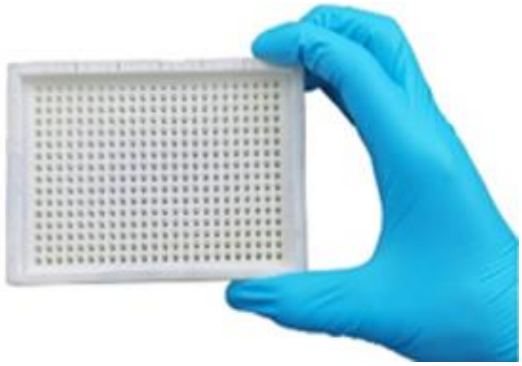


Fig. 4 High-throughput cell sphere culture microarray diagram

2.1. Lifting and lowering structure

The basic lifting device uses a spiral single-axis stepper motor, which is of the pulse motor type. The STM32 microcontroller controls the operation of the stepper motor by generating pulse signals to achieve precise displacement control and timing operation [6]. This configuration ensures high accuracy and stability of the lifting device in different application scenarios. The 3D model of the spiral single-axis stepper motor is shown in Fig. 5, and Fig. 6 illustrates its physical drawing.

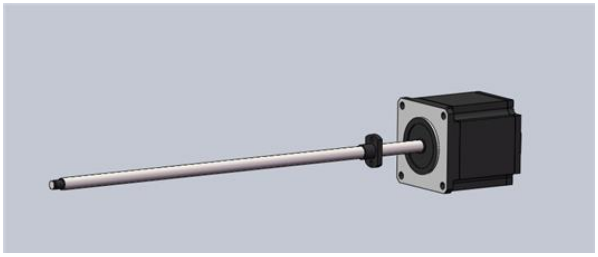


Fig. 5 3D model of helical single-axis stepper motor



Fig. 6 Physical drawing of helical single-axis stepper motor

The core component of this system is the STM32 microcontroller, which is responsible for receiving input signals and controlling the motor, which drives the lifting mechanism. In addition, the system includes the following key components:

1. Control unit: this unit is centred on the STM32 microcontroller and is responsible for executing the control logic of the system. Its main functions include receiving user inputs, processing sensor data, and generating control signals for driving the motor.

2. Driving unit: it consists of the electric motor and its driving module. The motor provides the necessary power, while the drive module adjusts the speed and direction of the motor according to the control signals from the MCU to achieve precise control.

3. Lifting unit: It includes guide rail, lifting platform and transmission system connecting with motor. The guide rail ensures the stability and accuracy of the vertical movement of the platform, while the transmission system is responsible for converting the rotary movement of the motor into the linear movement of the platform.

2.2. Suction Structure

In order to realise the automation of the cell ball culture chip, the timed control of the suction device is the key link. In this paper, the precise timing control of the suction device is realised by STM32 microcontroller, and the timing device is developed independently. The device integrates STM32 microcontroller and DS1302 clock chip, and combines with LCD1602 liquid crystal display for displaying relevant data. Figure 7 shows the structure of the timing device.

In addition, a compact and efficient frame model was designed and constructed in this paper to optimise the addition of sample liquid and extraction of waste liquid during the incubation process. In order to improve the efficiency of the pumping device, a small water pump with unidirectional pumping is used in this paper. By using two pumps in opposite directions, precise addition of sample liquid and efficient extraction of waste liquid were successfully achieved [7]. Figure 8 shows the structure of the small water pump.



Fig. 7 Timing device diagram



Fig. 8 Small pump diagram

The small water pump has a rated voltage of 12 V and a rated power of 5 W. However, the experimental results show that when the pump is working at its rated power, the extraction rate of the sample liquid is too fast to meet the titration requirements. To solve this problem, this paper reduces the power of the pump by lowering its input voltage. Experimental results show that when the input voltage is reduced to 3V, the pump's extraction rate can meet the titration requirements.

2.3. Oscillation structure

A simple oscillation device was developed using the STM32 microcontroller, aiming to achieve uniform oscillation of the liquid. However, in practice, the device was exposed to problems such as uneven oscillation of the liquid, splashing of the liquid due to too fast an oscillation rate, and unstable support points. The STM32 oscillating device is shown in Fig. 9, and Fig. 10 demonstrates a schematic of the oscillator section.



Fig. 9 STM32 oscillator device

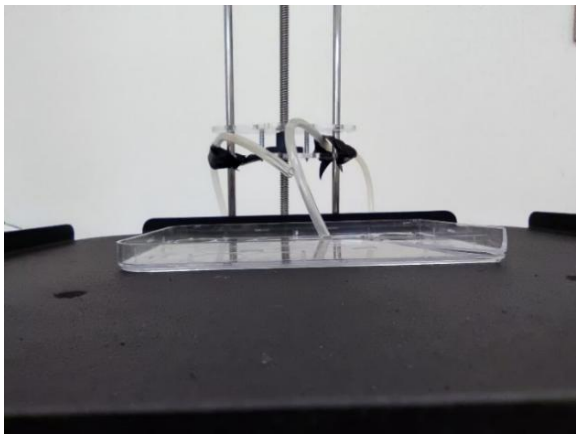


Fig. 10 Schematic of oscillator section (with parts not shown)

The basic structure of an oscillator consists of a switch, a timer, an electric motor, an eccentric wheel and a tray. To solve the problem of uneven liquid oscillation, this paper designs a structure that combines the electric motor and the eccentric wheel, so that the device can achieve circular motion and improve the uniform oscillation effect of the liquid. To address the problem of liquid splashing due to excessive oscillation speed, this paper introduces a speed control plate to achieve constant low-speed operation of the motor to maintain stable low-speed oscillation and reduce liquid splashing[8].

In addition, in order to improve the stability of the device, this paper adopts the structure of three eccentric wheels fixing the tray to form a triangular stable support point, in which one of the eccentric wheels drives the rotation of the other two slave eccentric wheels by connecting to the electric motor,

which effectively solves the problem of unstable support point. Figure 11 shows a diagram of the eccentric wheel, Figure 12 shows the internal structure of the eccentric wheel, Figure 13 shows the speed regulating device, and Figure 14 shows the triangular structure of the three eccentric wheels.

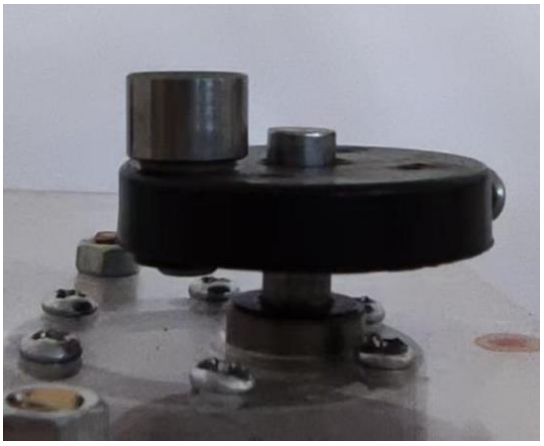


Fig. 11 Diagram of eccentric wheel



Fig. 12 Internal structure of eccentric wheel

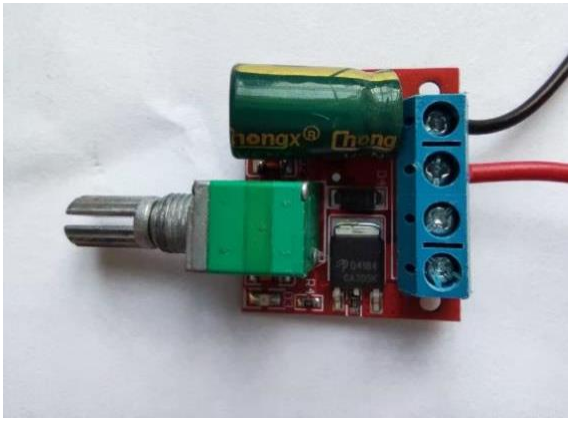


Fig. 13 Partial view of the speed regulator



Fig. 14 Three eccentric wheels in a triangular Configuration

In the study of timers, this paper focuses on two main parts:

2.4. Visualisation structure

LCD1602 is a widely used character-based liquid crystal display module with the advantages of low power consumption, small size, low radiation, etc.[9].LCD1602 liquid crystal display is mainly composed of a character-based liquid crystal display (LCD), a control driver main circuit HD44780 and its extended driver circuit HD44100, as well as a small number of resistive and capacitive components and structural parts, etc., which are assembled on a PCB board. The display can display 2 lines of 16 characters and has 16 pins, including the 8-bit data bus D0-D7, as well as RS, R/W, EN three control ports. It operates at 5V and is equipped with a character contrast adjustment port V0 and a backlight AK. Figure 15 shows the soldered pinout of the LCD.



Fig. 15 LCD Liquid Crystal Display Soldering Pinouts

In this paper, the DB0-DB7 interfaces of LCD1602 are connected to the PA7-PA0 interfaces of STM32F103C8T6 in order to realise data input and output. The timing of LCD1602 is simulated through the GPIO port of the microcontroller to achieve the display control of LCD1602.

In the design, this paper mainly implements the operations of LCD1602 such as read state, read data, write command and write data. After experimental verification, this paper successfully implements the control of LCD1602 LCD display by STM32F103C8T6 microcontroller. By simulating the timing of LCD1602 through the GPIO port, it is able to achieve the read and write operations of LCD1602 and display the desired characters and graphics on the LCD. Experimental results show that the design scheme is feasible and has stable and reliable performance.

2.5. DS1302 clock chip

DS1302 is a real-time clock chip from DALLAS, with a variety of functions and features for precise timing and date recording. Figure 16 shows the DS1302 clock chip.



Fig. 16 DS1302 clock chip diagram

The DS1302 features low power consumption and can be recharged by a small current, making it ideal for long operation scenarios. It accurately records time parameters, including year, month, day, week, hour, minute, and second, and integrates 31 bytes of internal RAM for storing real-time clock data [7]. The DS1302 communicates with the microprocessor via a simple serial interface, storing clock data in the RAM[10].

In this paper, the DS1302 is controlled by the STM32F103C8T6 microcontroller, with RST connected to PB15, I/O to PB14, and SCLK to PB13. The design achieves second-level timing accuracy, with experimental results confirming the feasibility, stability, and reliability of the system.

3. Timing device production

For the timing device, the microcontroller is mainly used in this paper is STM32F103C8T6. Figure 17 shows the timing device diagram.

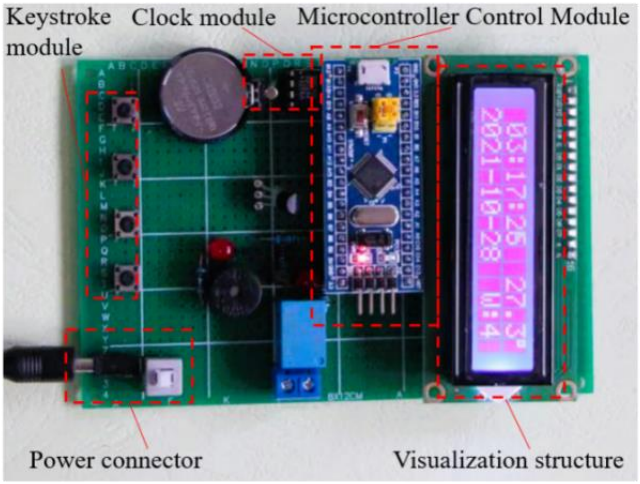


Fig. 17 STM32 timing device diagram

In the STM32F103C8T6 based timing device design, the GPIO interface is used to process the digital signals from the keys and LEDs. The keys are connected to PA0 and PC13, and the pins are configured in input mode and external interrupt (EXTI) is enabled to ensure that the system responds and starts the timing function in time; the LEDs indicate the timing status through the PA5 and PA6 pins. The timer generates precise time intervals through TIM2 and TIM3, and the PWM signal is output through PA0 of TIM2 to control the buzzer tone or stepper motor speed. For data communication, PA9 and PA10 of USART1 are connected to the serial display to show the timing results, and PA2 and PA3 of USART2 are used for Bluetooth communication; I2C is connected to the OLED display to show the system status through PB6 and PB7, and SPI is connected to the flash memory or TFT display through PA5, PA6, and PA7, and PB0 is used for the chip-select signal control. ADC is connected to the sensor through PA0 connects to the sensor to convert the analogue signal to digital signal to achieve intelligent timing control. After adding the timing device, the overall operation flowchart is shown in Figure 18.

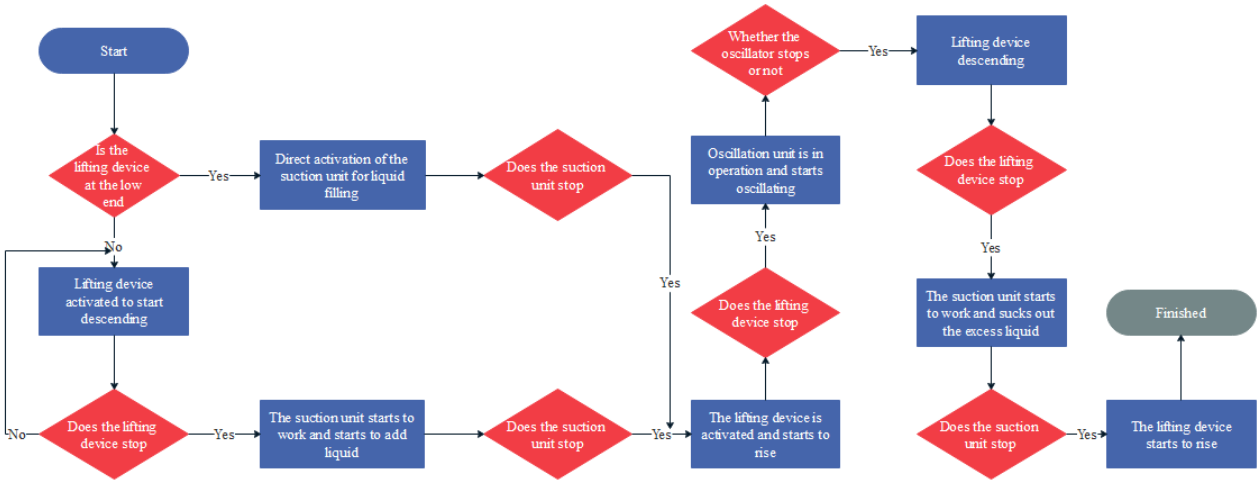


Fig. 18 Flow chart of unit operation

4. Conclusions

Through our research, we have successfully developed an automated control system for 3D cell culture within a high-throughput spheroid culture chip, achieving precise timed lifting, suction, and oscillation. The coordinated interaction of these functions enables automated operations, including liquid filling, waste extraction, and oscillation, all without interference. This system integrates 3D cell culture, microfluidic technology, and automation control.

Despite initial success, further improvements are necessary. The current motor control of the lifting structure is imprecise, leading to position deviations and slow response times. We plan to optimize the pulse width modulation (PWM) control strategy and motor algorithm to improve response speed and accuracy. Additionally, modifications to the lifting platform and suction pipe will enhance stability. For the oscillation system, optimization of the eccentric wheel position and tray size is required. We propose using CAD simulations to achieve the best configuration and integrating an intelligent control system for automated oscillation adjustments. The suction system needs better timing precision and environmental adaptability. We plan to integrate advanced timer chips and sensors for real-time adjustments, while redesigning the connection ports and suction tube ends for improved precision and efficiency.

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