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Development of PCR Control Software for Smartphone Using both Wired and Wireless Communications

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Abstract

The polymerase chain reaction (PCR) is a detection method used in almost all the experimental processes that involve manipulation of the current genetic materials to amplify the specific target genetic material to be preferably detected. The recent PCR thermal cycler has adopted a general-purpose computing platform in which specific operation systems run in a computing device to support the GUI. In this paper, Smartphone PCR control software, including the GUI, which can be run on not only Bluetooth, but also USB Communications, is proposed. The GUI is implemented in Android platform, and the connection to the PCR device uses a standard interface USB and Bluetooth to minimize the dependence on the platform. The proposed system has been verified to run in the commercial system using Smartphone.

Keywords: *PCR thermal cycler, USB Communication, Bluetooth Communication*

1. Introduction

Polymerase Chain Reaction (PCR) is a common method to amplify DNA in molecular biology [1]. PCR thermocycler is a device controlling the temperature required for PCR by controlling the temperature of the chamber. PCR thermocycler should not only have the biochemical control function that controls the temperature of the chamber which in turn controls the temperature of the sample prepared for PCR [2], but also should have other system management functions such as data analysis and user interface [3-8]. Recently, even the simplest electronic devices require graphical user interface (GUI) and data accessibility through the internet, there is a high advantage when managing the system using a computer [9-10].

Other than these, the essential functions of the PCR control software include PCR protocol creation, editing, storing, and transmission to the PCR device. Further, it should include a function for updating the firmware of the PCR device via the web. Therefore, even if the PCR thermal cycler is standalone type, internally, for the user interface, the use of a general-purpose computing platform has many benefits.

In this study, we developed PCR control software, which significantly reduces the expenses related to software development and maintenance and supports Smartphone applications; further, we verified its operation. We have developed a PCR control software

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using the USB communication in reliable wired environment as well as using Bluetooth communication in convenient wireless environment. The Smartphone connected to the PCR device by the USB and Bluetooth; this minimized the dependence on the platform.

In most thermal cycler, the all-in-one device has the GUI. Since the computing device performing GUI takes the possession of the cost, it makes the PCR device be expensive. We had developed low-cost PCR device in which a PC that is the general computing platform performs GUI and the PCR device only concentrate the basic function of PCR as controlling temperature [11]. The proposed PCR control software was applied to this PCR device. The PCR control software was designed to run on all Smartphones by supporting the Bluetooth [12] and USB communication.

And we made the update function of the firmware of the PCR device through web. This means that if the PCR device meets an unrecoverable systematic problem, then it can be automatically updated without bothering the user. Through this function, the maintenance cost will be dramatically reduced.

This paper introduces the protocol of PCR and communication protocol in Section 2, presents detail implementation method and actual application in Section 3, and the conclusion is made in Section 4.

2. PCR Protocol and Communication Protocol

The PCR device uses a heater and a fan for heating and cooling; further, other than basic functions such as temperature measurement, it should have a protocol processing function by which the PCR protocol, consisting of a permutation of a temperature and time pair, is interpreted, thereby maintaining the required temperature for a given period of time.

Table 1 is the example of the protocol used in PCR thermal cycling. The No. 1 item in the table implies that a temperature of 95°C was maintained for 30 seconds for warming up the chamber. No. 2, 3, and 4 pertain to the processes of PCR degeneration, restoration, and extension, respectively, and convey that the amplification process occurred once up to this point. The GOTO label is for the flow control, indicating the cycle to return to the No. 2 for 34 times. The example consists of 35 cycles in total. In general, the PCR is completed by inserting the last extension process such as No. 5.

Table 1. Protocol Example

Label	Temperature (℃)	Duration(sec)
1	95	30
2	95	30
3	55	30
4	72	30
GOTO	2	34
5	72	180

This protocol can be stored, modified, and deleted by the PCR control software to be run later. The PCR control software sends data via the Bluetooth interface or USB interface to control the devices or transmit the PCR protocol to the PCR devices. To transmit data, messages in Table 2 are used.

Table 2. Function of each Message

Message	Function
STATUS	Get status of PCR
TASK_WRITE	Write TASK to PCR machine
TASK_END	Notify user that TASK is successfully written
GO	Start PCR protocol
STOP	Stop PCR protocol

Table 2 shows the messages shown in the GUI of the Smartphone and its functions. 'STATUS' message receives the status of the PCR thermocycler every 0.1 seconds after it is connected to the Smartphone. The reply of this message includes the current temperature and TASK of the PCR machine, and the remaining time. If there is a malfunction in the PCR thermocycler, or if the TASK value that increases the temperature is too high, the PCR protocol stops and the error value is transmitted to the Smartphone. 'TASK_WRITE' message and 'TASK_END' message determine the duration and temperature for each steps of the PCR protocol. 'GO' message orders the PCR thermocycler to start with the given TASK values. 'STOP' message can end the PCR protocol manually. The interaction diagram between the PCR controller and smartphone is shown in Figure 1.

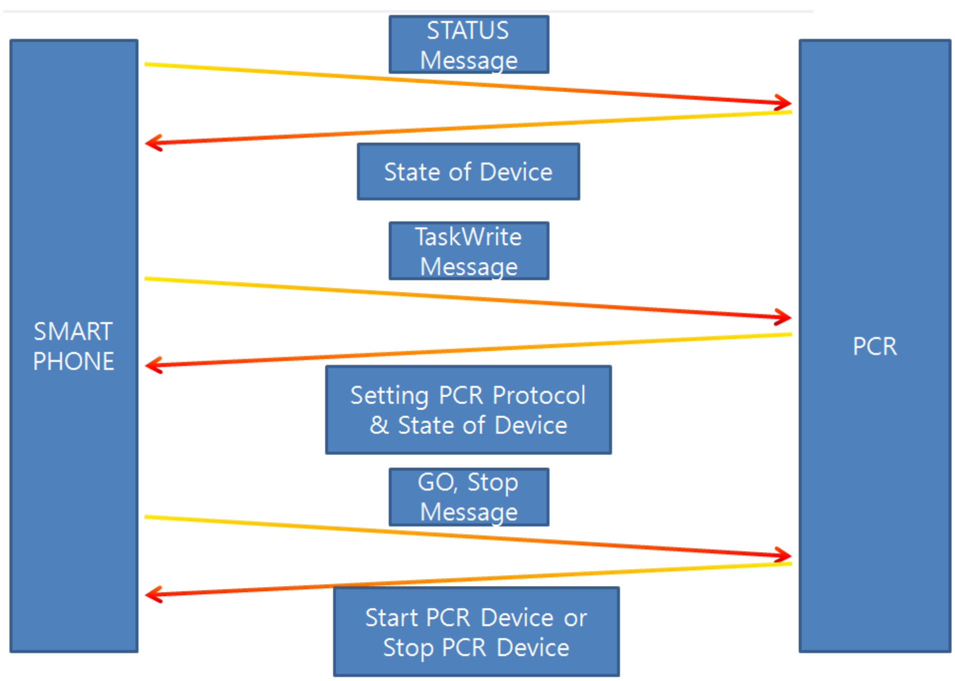

Figure 1. Interaction between PCR Controller and Smartphone

3. Realization

The PCR device used for the experiment was MyPCR from Labasis Inc. shown in Figure 2 [11]. A Smartphone controlled the operation through the Bluetooth or USB. Once a RUN command was given from the controller to PCR, the PCR device was run normally even if the connection was disconnected because it can operate as an independent device. Using this device, the proposed software which could be run in Smartphone environment was implemented.

Figure 2. Labasis My PCR Device

The following four parts were implemented in Smartphone software: the Bluetooth communication system, the USB communication system, the GUI configuration, and the web interface. The Android platform includes support for the Bluetooth network stack, which allows a device to wirelessly exchange data with other Bluetooth devices. The application framework provides access to the Bluetooth functionality through the Android Bluetooth APIs, These APIs let applications wirelessly connect to other Bluetooth devices, enabling point-to-point communication. In case the Bluetooth communication, when you click the software "Start" button to search for Bluetooth devices around, trying to connect with the PCR device. If the connection is completed, it is possible to write data in communication.

The USB communication also support in Android platform. This function is acts as the USB host, powers the bus, and enumerates connected USB devices. After installing the software, connecting the PCR device, software is automatically executed. When the software is executed, attempts to communicate the USB device, if the connection is successful, getting the serial number of the current device and it is possible to run the PCR device by transmitting the PCR protocol by "Start" button. If the connection is failed, ends the program.

From the GUI, the serial number of the current device or chamber temperature and the LID temperature were checked through the received data, as well as the remaining time of the protocol currently running, and the label location of the running protocol. “Protocol” button is possible to creation, modification, deletion of the protocols. After the protocol was show the Main UI, display the current temperature and remaining time. Once a connection was made with the PCR device, the version of the firmware, which was installed from the device, was checked first. Then, the up-to-date firmware version was checked via the web server, and if the version was not up-to-date, the most recent version was downloaded from the web server and stored. Then, once the PCR device was modified to be run in the boot loader mode, the updated firmware was loaded. Once updating was completed, the PCR device would rerun automatically. If the PCR control software showed the serial number correctly, the update was completed. Smartphone is always connected to the network, it can easily update. When the device was not connected to the Internet or the web server was down, the PCR device was controlled via the loaded firmware.

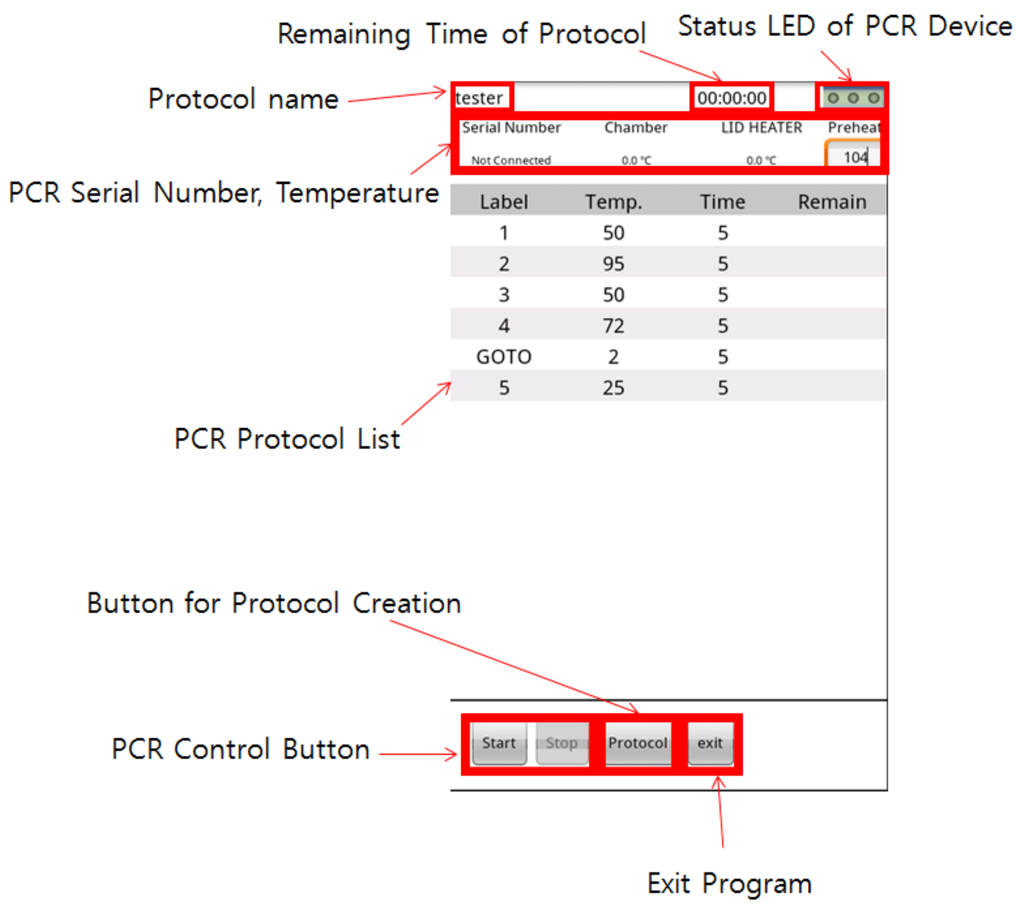

Figure 3. Android Smartphone Main UI

Figure 3 illustrates the Smartphone main UI of the PCR control application. Main UI will show you what the status of the LED device of PCR and the remaining time of the protocol name and protocol, which has been read with the Protocol button. Also, it displays in real time the temperature of the Chamber and the PCR connected serial number, the temperature of the LID heater. The user can create their own TASK and save them in a list by pressing the 'Protocol' button, and also choose which TASK to send from the list. When a protocol(TASK) is selected, the 'Start' button activates. If the application is Bluetooth, the Bluetooth devices are detected by pressing the 'Start' button, and the protocol(TASK) is only transmitted when MyPCR is selected from the list of devices. If the application is USB version, the protocol(TASK) is transmitted and received the PCR status information.

Figure 4. Android Smartphone Protocol Generation UI

Figure 4 is a UI to create a protocol for communicating with MyPCR. You can set the operation temperature for seconds. GOTO Label is a means to move only the value of the Time to Label which is set to Temp. You can enter a value for the temperature in the range that can be controlled by MyPCR, and setting a value of 0 Time, an infinite amount of time to work.

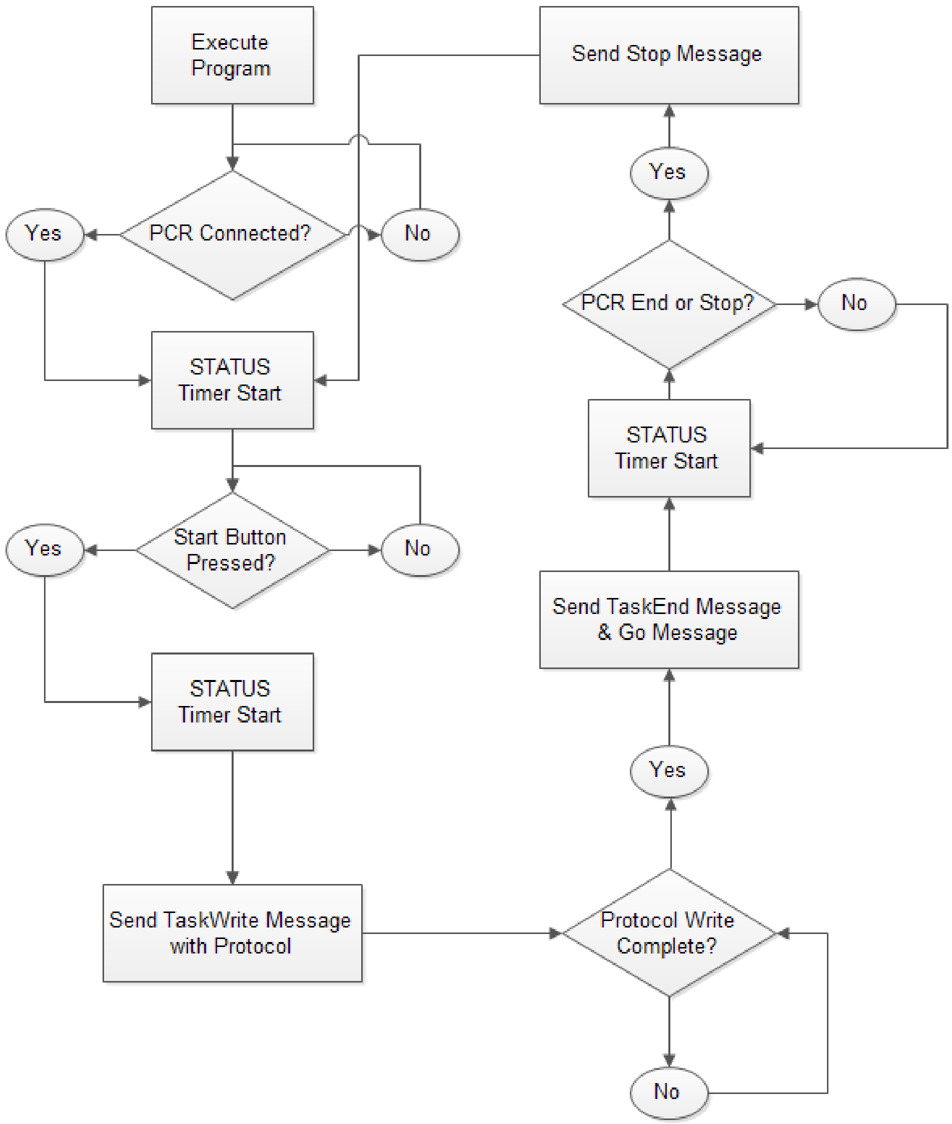

Figure 5. Flow chart of the PCR control program

Figure 5 shows the flow chart of the PCR control program. Once a connection was done with the PCR device, a timer was run to transmit the STATUS message in every 0.1 seconds, thereby receiving the status of the device. When the PCR is connected, if the Start button is pressed, then the software sends the protocol information to be read to the PCR device. In this time, the software stops the STATUS timer and transmits the value of the protocol with TASK_WRITE message. If the transmission of the whole contents of the protocol is done, the software sends TASK_END message along with GO message which can make the PCR device run with the received protocol. Just after sending the GO message, the software runs the STATUS timer to receive the recent status of the PCR device. When the PCR device was running, if the control program was started, the protocol list and the device information running in the current device were fetched and displayed.

4. Conclusion

This paper, by using the Bluetooth and USB communication with Smartphone to develop a PCR control software, because to reduce the installation costs by reducing the need for host PC. By increasing the stability of the communication support USB communication as compared to PCR control software that was only support Bluetooth communication, it is possible to be able to support the PCR control software on all the type of Smartphones. Through these developments, not only was the cost of the PCR device reduced, but the inconvenience of PCR use in a small laboratory environment was also minimized. If the developed PCR control software that supported multi-communications use has a function that monitors multiple PCR devices at the same time, one Smartphone can run multiple PCRs with minimal effort at the same time, and hence, the costs related to the PCR purchase and installation can be reduced significantly.

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