

Using Technology to Measure Adherence of Complicated Medication Regimens

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ABSTRACT

Seventy-five percent of all patients do not take their medications according to their doctors' prescriptions. Dr. Timothy Juergens, a geriatric psychiatrist and sleep specialist at the University of Wisconsin - Madison Hospital and Veterans Affairs Hospital requested a method of determining causes of non-adherence. To fulfill these needs, the Electronic Medication Adherence Device (EMAD) was designed. The EMAD consists of a standard 7 x 4 compartment pillbox and a complex circuit with a PIC18F4550 microcontroller that is capable of monitoring when each compartment is opened. Additionally, the date and time of these opening are stored and can be accessed by the physician with a computer using Microsoft Excel®. To remind patients to take their medications, a piezoelectric buzzer acts as an alarm. Tests were conducted to verify the functionality of the EMAD's ability to record a single button, transmit patient data and log time and date accurately. Test results indicate that the EMAD is able to complete these tasks successfully. However, the switch matrix connections have an unknown fault, which will require troubleshooting. A completed EMAD will enable Dr. Juergens to identify reasons for medication non-compliance as well as promote adherence.

INTRODUCTION

An important problem in today's medical world is the significant failure to follow prescribed medication regimens. This is specifically true for the elderly. Often, these users take medications multiple times throughout the day. Most patients do not comply with their medication regimen. Reasons for this may include forgetting to take the medication or refusal to take a prescribed dosage. Regardless of the reasons, only 1 in 4 patients take his or her medications correctly (Osterberg & Blaschke, 2005). Our client, Dr. Timothy Juergens, is interested in determining the cause of this non-adherence by recording pill access times. Furthermore, he has presented this case to promote adherence among geriatric patients.

This severe failure to follow doctor-prescribed medications is a significant cause of illness in these individuals. Clearly, a medication is unable to work unless it is taken correctly by the patient. This inability to adhere to medications causes numerous deaths each year (Osterberg & Blaschke, 2005). According to an article in *The New England Journal of Medicine*, non-adherence adds almost \$100 billion to current hospital admissions.

To avoid being seen as a bad patient by their physician, people often lie to their doctor about their medication compliance. This has an adverse affect on both the patient and physician.

In order to better understand the long-term results of non-compliance, a pillbox was constructed to record removal of prescribed pills. By recording such information, it is hopeful that

physicians will be able to target the root causes of non-compliance. The appliance, Electronic Medication Adherence Device (EMAD), is safe for home use and provides physicians with vital information regarding when medications are taken by patients.

METHODS

Pillbox

The pillbox layout suggested to us by our VA contact requires the use of a 7x4 design. This design allows the user to separate 4 medication regimens per day for morning, noon, evening and bedtime. The switches that were installed were single pole, double throw, Submini Roller Lever Switch (275-017A). The installation is designed to create a reliable activation of the switch each time the lid is opened for more than one second. In each compartment, a small Plexiglas plate is used to separate the medications from the switches to avoid contamination.

To improve the aesthetic quality of EMAD, a wooden box was created to enclose all circuitry. Open circuitry can cause intimidation and possibly lead to failure of the prescribed regimen. The hidden circuitry still allows access to the computer's USB port. In order to provide circuit maintenance, the circuit board can be accessed by removal of the pillbox (see figure 1).



Figure 1. Electronic Medication Adherence Device (EMAD): a pillbox with a circuit to monitor the opening of the compartments. The circuit is held within the wooden box to ensure the patient is not apprehensive about using the box.

Circuit

In order to accurately record the time and date of each compartment opening, a switch matrix is required to process all voltage differences caused by switch activations. The circuit consists of a few key components including the microprocessor, watch chip, and the Universal Serial Bus (USB) converter. The circuit acts as a communication link between the pillbox and the software made entirely from Visual Basic. Each component serves a specific purpose to relay information to the user.

Ribbon cables are used to attach the independent switches from each compartment to the circuit board. The circuit board is designed to direct the current to its appropriate position on the switch matrix. Each cell on the matrix consists of a switch and diode (1N4148) to ensure current flows away from the switch towards the microprocessor inputs. This can be seen in Figures 2a and 2b.

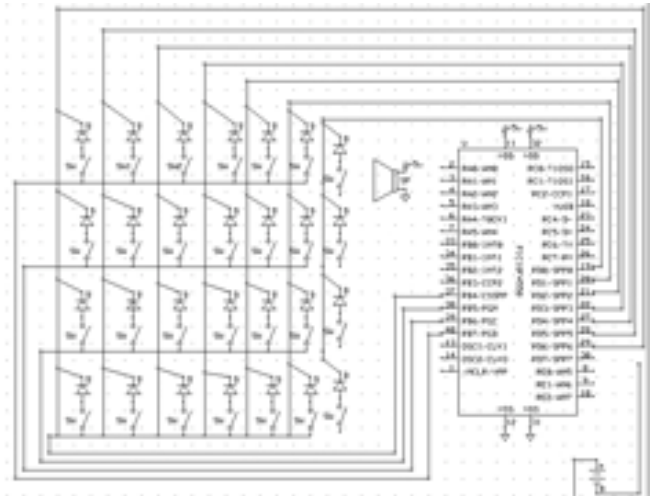


Figure 2a. A schematic representation of the switch matrix connected to the microcontroller.

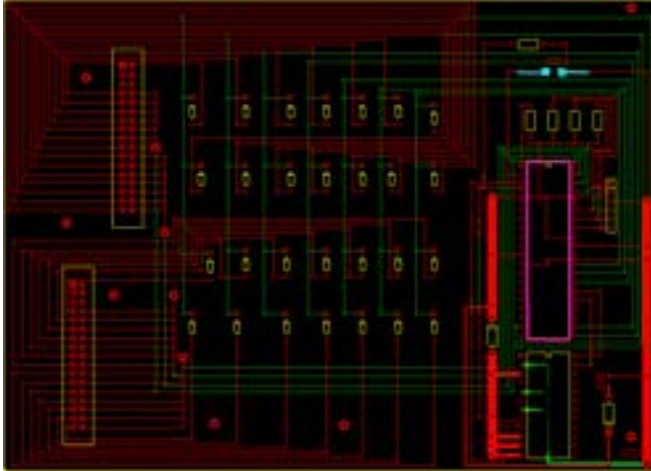


Figure 2b. The completed PC board design with all circuit components.

The switch matrix consists of 7 columns and 4 rows. However, one can also recognize this setup as 4 inputs and 7 outputs. Each input would normally require a pull-up resistor to separate voltage values. Fortunately, the Microchip PIC18F4550 has this functionality built-in and must be activated by the BASIC code. This helps minimize the weight of the circuit and reduce cost.

The microprocessor, shown with a pink outline in Figure 2b, connects all of the circuit elements together. It communicates with the watch chip, the USB converter, the entire switch matrix, and the alarm. Every resistor seen on the circuit is 10K Ω and the larger Schottky diodes, not included in the switch matrix, are to prevent current from returning to the battery or the USB component. The software sends information to store on the microprocessor and receives the data when the doctor requires it. Two regular AA batteries would be used to power the microprocessor and the entire circuit. However, the microprocessor has the capability to determine where its power source originates. Thus, when the USB is connected, the batteries are at rest and the computer powers the circuit. This will increase battery life, which is very important to Dr. Juergens and his patients.

Directly beneath the microprocessor lies the Transistor-Transistor Logic (TTL) Serial to USB converter; this was ordered from DLP Design under part number DLP-USB232M. This piece

was a crucial element in the setup because it converted the electronic serial data into usable USB information. Thus, clinicians can plug the pillbox into any computer with a USB port. The converter is connected directly to the microprocessor in addition to the 5 volts and ground ports. Normally, an LPT port would have to be utilized without this converter making accessibility very difficult.

A piezoelectric buzzer is placed, as an alarm, right above the microprocessor on the PC board and is shown in light blue on Figure 2b. This alarm is designed to sound when the watch chip sends a signal to the microprocessor at a specific date and time. Loudness is a factor that was tested to make sure it would get the attention of the geriatric patient. The piezoelectric alarm receives only 3 volts from the microprocessor to activate and the actual noise is dampened because it is surrounded by the wood used to create the prototype. Many individuals that heard the alarm agreed with initial thoughts that it would be loud enough to attract patient attention, but not loud enough that the patient would ask their doctor to disable the alarm upon refilling the pillbox.

Keeping accurate time is done by the watch chip from Spark Fun electronics (DS-1307), which can be found to the right of the microprocessor. This real-time clock connects to the microprocessor in order to send the time and date when it is requested.

Microcontroller Algorithm

A bootloader (TinyBLD) is installed on the PIC 18F4550 microcontroller to facilitate the installation of new programs. The microcontroller was programmed in MikroBasic using the BASIC programming language. It features the ability to detect button activations and store button activation times efficiently. In addition, it allows storage for 500 compartment openings, the ability to respond to serial commands sent from a computer, and store pertinent patient details.

The time-storage algorithm is made efficient because it does not store the entire time and date

information (month, day, year, hour and minute) for each switch activation. Instead, the microcontroller stores the start time and date information, and increments a counter every 15 minutes. When a switch is activated, the microcontroller records how many 15 minute increments have occurred. Using this mechanism, a patient can keep the pillbox up to 1.8 years after their pills are empty (Yamdagni, et. al). Considering the fact that a patient is only to open each compartment once, proper use would dictate that only 28 time slots are used. However, to counteract extreme patient error, the microcontroller may store 500 time slots, giving the microcontroller the ability to withstand each compartment being opened 17 times (Yamdagni, et. al.).

Graphical User Interface

The Graphical User Interface (GUI) was developed using Microsoft Visual Basic Express (see figure 3).

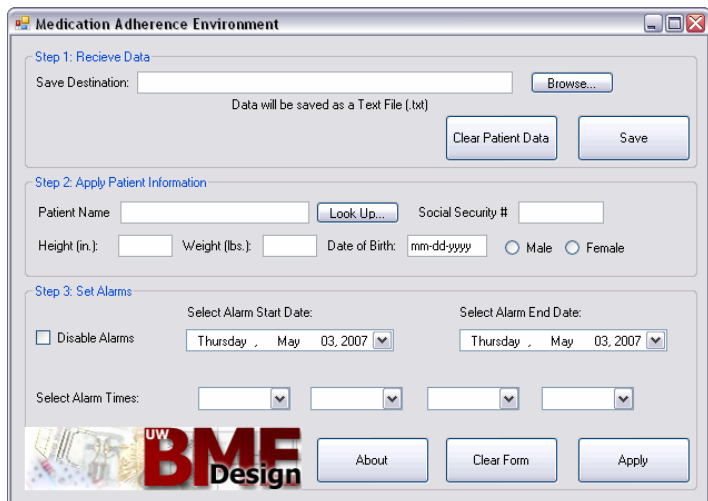


Figure 3. Graphical User Interface used by physician to enter patient data and set alarm times.

Prior to giving EMAD to a patient, the physician is given the ability to enter patient information and set up to four alarms. Patient data includes the patient's name, social security number, date of birth, height, weight and gender. In addition to the four alarms, the physician has the ability to disable them completely. This would be a useful tool if the doctor would like to test the effects of the alarm on a patient's behavior.

After the patient returns EMAD to the physician, the GUI allows the physician to choose the location to save the patient adherence data on the computer (Yamdagni, et. al).

Single Button Testing

By utilizing a single switch for testing, the code was able to be verified quickly. Connecting a switch directly to the microprocessor inputs and outputs allowed the date and time to be received for that single switch. Hopefully, this miniature model would depict the behavior of a switch matrix system with multiple switches and diodes. The BASIC code was written to recognize when the switch is pressed. Next, it would communicate with the real-time clock and request the time and date of the voltage drop seen. The button was pressed fifty times sequentially, and the number of successful activations was recorded.

Accuracy of Time & Date Logging

PIC microcontrollers have a built-in oscillator, which can potentially keep track of time. However, they are known to have an error of approximately 1%. Over time, this causes significant inaccuracies in the recorded date and time. To prevent this error, a watch chip was used. Several tests were conducted to verify the accuracy of the time kept by the watch chip. After setting the time initially, the time was recorded after 10 minutes, 30 minutes, 1 hour, 24 hours and 48 hours. The power to the microcontroller, and thus the watch chip, was interrupted several times during these trials.

Patient Data Transmission

A physician or pharmacy technician will use the stored patient data to verify that the recorded adherence data is correct. It is imperative that the patient data, entered by a physician or pharmacy technician prior to issuing the pillbox to the patient, is accurately recovered once the patient requires an EMAD refill. To test for this, fictitious patient details were entered into the pillbox and were subsequently recovered. The data entries and the recovered data were compared for accuracy. Additionally, the device

was tested for the scenario in which the physician or the pharmacy technician leaves a data field empty. The GUI was programmed to have a limit of 20 characters for the patient name, 11 characters for the social security number, eight characters for date of birth, three characters for height and three characters for weight. This is vital in efforts to reduce data corruption and run-time errors. To test these safeguards, extremely long strings were entered, and the results were analyzed and recorded.

RESULTS

Single button recording

After performing the specified test, the microcontroller was able to record every switch activation. The data received was accurate and corresponded correctly to the expected output for both the date and time. Additionally, the microcontroller did not record any false positive switch activations, nor did it fail to record any intentional activation. Therefore, a correctly constructed switch matrix with the same code would ideally produce the same results.

Accuracy of Time & Date Logging

Several days of testing revealed that the watch chip retained accurate time and date. Additionally, the watch chip was able to send the date and time through USB to a comma separated text file. The clinician would be able to open this comma separated file in Microsoft Excel®. The time received from the microcontroller is in 24hr format (see figure 4).

The screenshot shows a Microsoft Excel spreadsheet with the following data:

	A	B	C	D	E	F	G	H	
1	Name:	John Doe							
2	SS#:	123-90-7414							
3	DOB:	12/26/85							
4	Height:	72							
5	Weight:	200							
6	Gender:	Male							
7	Start Date:	03/22/07							
8	End Date:	03/29/07							
9									
10	MONDAY	MONDAY	MONDAY	MONDAY	TUESDAY	TUESDAY	TUESDAY	TUESDAY	
11	AM	Noon	PM	Night	AM	Noon	PM	Night	
12		8:15	11:45	15:45	18:45	8:15	11:30	15:30	19:00
13			11:45						
14			12:00						

Figure 4. A screen shot displaying the Microsoft Excel® file with the patient data, the recorded date and time of switch activation.

Patient Data Transmission

The GUI, as seen in figure 3, and the microcontroller were tested with a variety of different fictitious patient data as specified previously. The EMAD did not corrupt the data or have any run-time errors, regardless of the length of the entered data.

DISCUSSION

Following application testing on our medication adherence instrument, it was noted that the switch matrix does not function properly. However, during the development of the prototype, data gathered from a single compartment was accurately recorded. It is necessary that this function is corrected by troubleshooting the switch matrix. Further application testing is necessary to maximize instrument reliability. Patient apprehension towards the EMAD can be reduced with a reduction in size of the circuitry, thereby decreasing the weight of the EMAD. In order to ensure durability, the device must be tested in a manner similar to an average patient's usage. The results of these tests will allow further information regarding material choices for the EMAD. Material properties of various polymers will be reconsidered in the event of frequent physical failures. Nonetheless, the final material will provide the highest durability, so it can undergo the same clinical rigors as current medication boxes. A circuitry enclosure

provides protection for the circuit against physical damage from foreign objects.

If the EMAD is commercially produced, the enclosure would need to be water resistant, and inconspicuous to the user. Such an enclosure would allow washing the EMAD without damage to its circuitry, and eliminate patient anxiety toward the box. With professional construction, the switch in each compartment will be incorporated into the walls of each compartment in the EMAD, thereby increasing the volume of each compartment. To improve the aesthetics and usability of data visualization in Microsoft Excel®, colors and formatting techniques should be integrated.

Industry standards are crucial for the medical field and any future work done on the project must test to ensure that these requirements are met. Two specific standards were identified dealing with the biological evaluation of medical devices. ISO/NP 10993-3 (Tests for genotoxicity, carcinogenicity and reproductive toxicity) and ISO/DIS 10993-9 (Framework for identification and quantification of potential degradation products) pertain to this project and must be satisfied. Prior to clinical testing, these standards should be validated and verified to ensure the safety of the product during normal operation.

By using the EMAD, clinicians will be able to conduct experiments to determine causes of patient prescription non-adherence. Two clinical studies can be conducted. One study will test the effects of a patient's awareness of the electronic monitoring system in his/her pill box. A second study will determine the effectiveness of an alarm on patient medication adherence. In addition, switches that remains anonymous to can ensure that promising results. Statistically significant improvements in patient adherence due to the EMAD will aid in the possibility of mass production.

ACKNOWLEDGEMENTS

David Markovitch, Medical School Research Support Programs, University of Wisconsin - Madison

Professor William Murphy, Department of Biomedical Engineering, University of Wisconsin - Madison

Dr. Timothy Juergens, geriatric psychiatrist/sleep specialist, University of Wisconsin Hospital and Veterans Affairs Hospital

Ben Yaroch, VIASYS Healthcare Inc.

L. Burke O'Neal, Department of Biomedical Engineering, University of Wisconsin - Madison

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