academicJournals

Vol. 6(6), pp. 36-40, September 2015
DOI: 10.5897/JMLD2015.0110
Article Number: 10A5CDC55333
ISSN 2141-2618 ©2015

http://www.academicjournals.org/JMLD

Journal of Medical Laboratory and Diagnosis

Full Length Research Paper

A novel method for reducing human pipetting errors

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Received 26 June, 2015; Accepted 27 August, 2015

Human errors in clinical and research laboratories constitute a substantial source of lost productivity. Here we present a novel method for reducing human errors in pipetting by providing real time feedback to the laboratory worker. The system uses light emitting diodes to indicate wells that have been accessed for pipetting using a system that is based on Faraday's principle of electromagnetic induction.This system has the potential to substantially reduce the number of errors made in the course of performing laboratory experiments.

Key words: Human error, pipette, magnet.

INTRODUCTION

In clinical and industrial laboratories, there has been a push for increased automation of tasks in order to increase efficiency while reducing cost and error (Elliott et al., 2007; Seaberg et al., 2000). Despite this push towards automation, the capital investment required makes this approach untenable for small research and forensic laboratories (Blow, 2008; Cechetto et al., 2004). In these situations, namely small-scale reactions and in the development of novel techniques, the chance for human error in performing laboratory tasks increases. For example, in a typical academic molecular biology laboratory using a standard 96 well plate to perform a polymerase chain reaction (PCR); it is common for a user to pipette into the plate over 500 distinct times. Because the wells are identical and closely placed, it is not uncommon for a user to inadvertently skip a well or pipette duplicate material into a single well. Unexpected results in an experiment requiring multiple pipetting steps often raise the question as to whether pipetting errors are to blame (Ewen et al., 2000)

Without a means to document pipetting steps, many experiments in which there is a suspicion of error are repeated (Procop et al., 2014) causing unnecessary loss of technician time and wasting of expensive reagents. As such, there is a need for an easy and reliable method for a laboratory worker to determine which specific receptacles they have already pipetted reagents into. This need becomes even more acute in medical and forensic laboratories, where human errors in pipetting have legal and clinical ramifications (Plebani, 2006; Bonini et al., 2002). We have developed a system for laboratory workers to determine which wells or reaction tubes they have already pipetted into; therefore providing a method of reducing human error. In this report, we describe our method for providing real time feedback to a laboratory worker performing an experiment, thus improving the system the technician operates in and reducing the likelihood of error (Reason, 2000).

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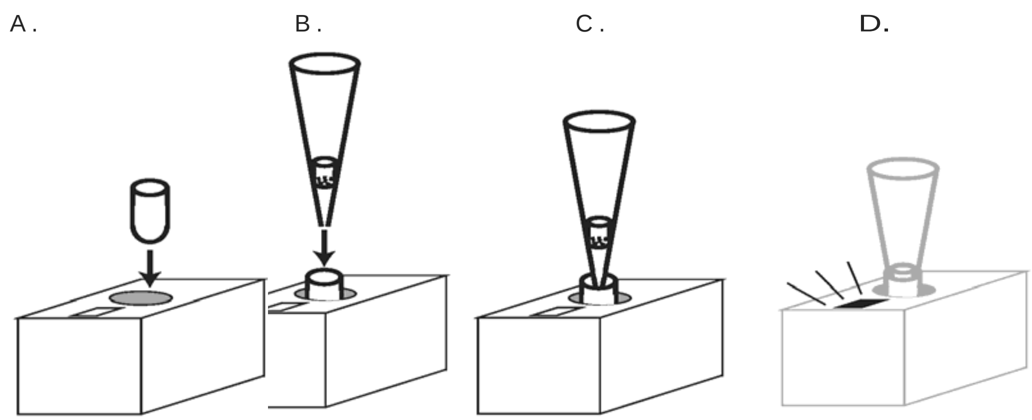

Figure 1. Basic operation of the system. (A): Consumable plasticware is placed into the signal well; (B, C): Signal tip is used to add liquid to the consumable plasticware; (D): As the signal tip passes into the consumable, the magnet located in the signal tip induces an EMF in the signal well. This EMF elicits the illumination of a LED by the microprocessor.

MATERIALS AND METHODS

Custom made Teflon coated cylindrical N50 Neodymium magnets with outside diameter 2 mm, inside diameter 1 mm and height 1 mm were purchased from AZ Industries (Ash Flat, AZ, USA). Pipette tips were purchased from Denville Scientific (South Plainfield, NJ, USA). Size 42 American Wire Gauge (AWG) wire was used for lining the walls of the prototype plates. 96 well PCR plates were purchased from VWR International (Batavia, IL, USA). Arduino Uno Microprocessor Starter Kit was purchased from Arduino (Ivrea, Italy). Magnets were applied over the tip of standard pipette tips and remained in place by friction. Each well of the 96 well plates was manually wrapped with wire.

RESULTS AND DISCUSSION

The method is based on Faraday's law of induction, whereby a magnet passing through a series of coiled wires produces an electromotive force (EMF) (Galili et al., 2006). In the operation of our system, the magnet is incorporated into a pipette tip and is passed into a plastic consumable that is housed within a series of coiled wires in a board (Figure 1). As the pipette tip enters the consumable, an EMF is generated in the coiled wires. This EMF is detected by a microprocessor connected to the coiled wire. In response to this signal, a light emitting diode (LED) located below the well that was pipetted into is illuminated. By sequentially repeating this task, the user illuminates the board as they progress through their experiment (Figure 2). The system consists of two components:

(1) A signal tip - these are standard disposable pipette tips of any volume and functionality (filtered, RNAse free, autoclavable, etc) that have been modified to function with a signal well.
(2) A signal well - an adaptor/detector component that is capable of holding sample tubes and detecting the signal tip.

The basic operation of the system is displayed in Figure 1. First, the laboratory consumable; an Eppendorf tube, 96 well plate, etc., is placed into the signal well (Figure 1A). Then the signal tip is used to load the well (Figure 1B, C), and once the magnetic component of the tip crosses into the signal well, a light emitting diode (LED) is illuminated (Figure 1D). The signal wells can be combined and scaled to any size and incorporated into multi-well arrays we call a "signaling block".

Operation of the system consists of the laboratory worker placing their consumable plasticware into the signaling block. The laboratory worker then turns on the power supply to the signaling block, and (using the signal tip pipettes described below) begins adding reagents to each well of the consumable. Once the user puts the signal tip into a single well of the consumable (and thus into the lumen of a signal well within the signaling block), a position-specific LED incorporated into the signaling block illuminates, which is then visible through the consumable (Figure 2). In this fashion, as the user pipettes across the block, the LEDs corresponding to each well are illuminated so that the user can easily see which wells have already had reagent added to them. After completing the first reagent, the user depresses the reset button to turn all of the LEDs off, allowing the user to again record their progress pipetting samples into the consumable plasticware wells.

The single feature of our single tips necessary to function in our system is the incorporation of a magnet at the delivery end of the plastic pipette. The magnet can be added externally over the tip of the pipette (Figure 3B) internally (Figure 3C) or manufactured within the wall of the plastic pipette tip (Figure 3D). Note that placing a magnet in the pipette tip creates the risk that liquids being handled by the pipette tip may inadvertently come into

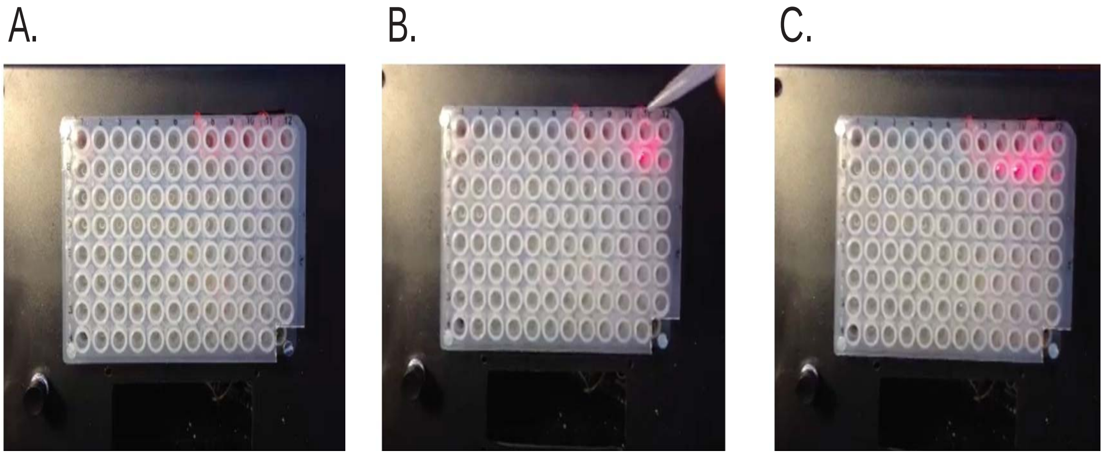

Figure 2. Images from prototype. (A): Prior to use, all LEDs in the signaling block are off; (B): A pipette is used to add liquid to one well of the signaling block, causing one LED to be illuminated; (C): As pipetting continues, additional wells are illuminated.

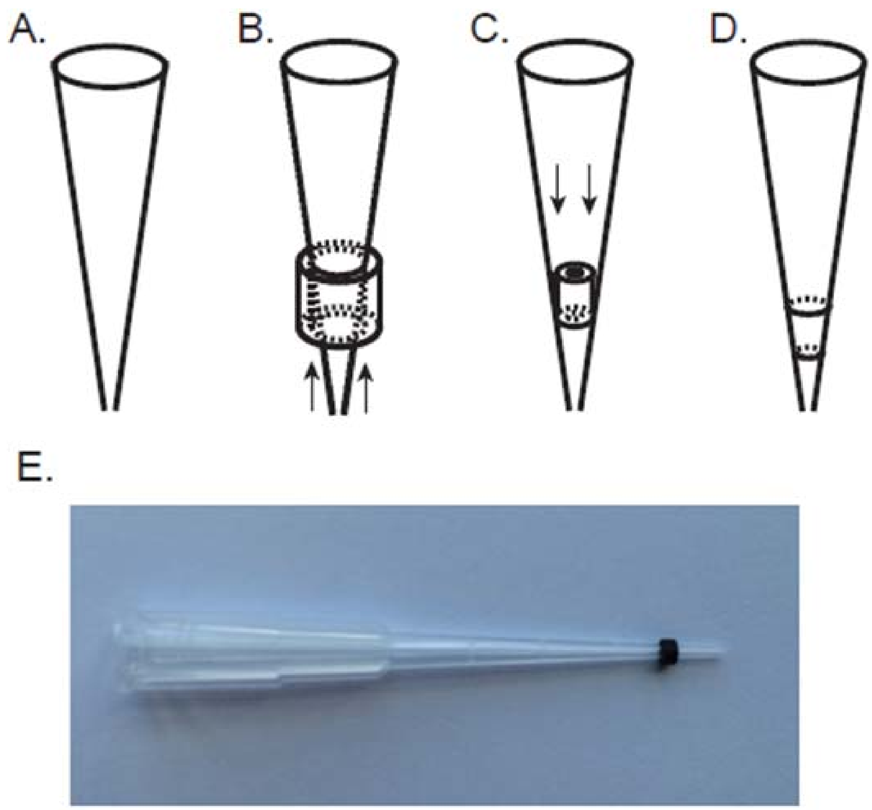

Figure 3. Diagram of signal tip configurations. (A): Pipette tip; (B): Signaling tip with magnet placed over the outside of the pipette. This configuration is ideal for small diameter pipette tips; (C): Signaling tip with magnet placed inside of the pipette tip, a configuration appropriate for larger pipette tips; (D): Unrealized magnet configuration, with magnet housed within the plastic wall of the pipette tip; (E): Pipette tip with magnet configuration shown in "B" used to develop the prototype.

contact with the magnet, generating unforeseen chemical consequences (Giakisikli and Anthemidis, 2013). To circumvent these issues, we have employed Teflon coated cylindrical magnets that pass over the tip of the

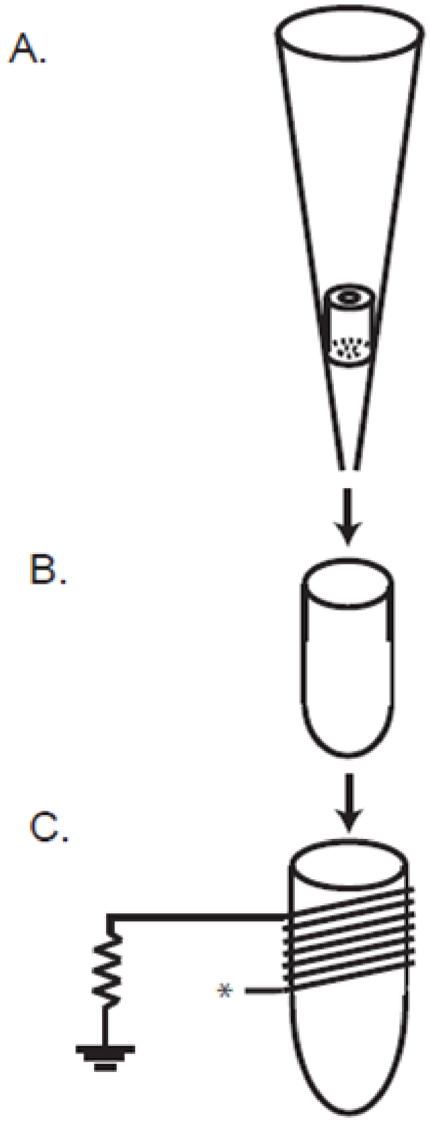

Figure 4. Operation of the system. (A): Signal tip with magnet deposits liquid into the plastic consumable; (B): Housed within the signaling block; (C): The signaling well located in the signaling block has a wire wrapping around its diameter. As the signaling tip passes into the consumable, an EMF is generated in the wire and detected by a microcontroller (denoted here by an asterisk).

pipette in the prototype shown here (Figure 3E) (Grover et al., 2008). Teflon is routinely employed to coat magnets used in the laboratory setting (such as stir-bars) to prevent issues associated with placing a magnet in a solution. Next we describe the "signal well"; the basic unit of a signaling block that achieve two functions:

(1) Signal wells are lined by a conical plastic adaptor that holds the laboratory consumable containing the reagents being pipetted (adaptor function).
(2) Signal wells are also comprised of coils of wire that are wrapped around the liner/adaptor, which are necessary to induce an electromagnetic force (EMF) when the Signal tip enters the well (detector function).

In Figure 4C, the configuration for a single signal well is shown. Besides accommodating the consumable, the signal well has a wire that wraps around the adaptor. In our prototype, we used 42AWG wire (0.064 mm diameter), although any wire diameter small enough to fit will suffice. Additionally, we used 500 turns of wire to wrap each signaling block. Afterward, one end of the wire is connected to a 20,000 Ohm resistor which itself is connected to ground. The other end of the wire (marked with an asterisk in Figure 4C) connects to a microcontroller. When the magnet in the pipette (Figure 4A) passes into the consumable (Figure 4B) which is housed in the signaling well (Figure 4C), an EMF is induced in the wire wrapping the adaptor. This EMF is then detected in the microcontroller. In response to a sufficiently large EMF, the microcontroller subsequently illuminates the LED corresponding to the signal well.

The electromotive force induced

The operation of the system is based on Faraday's law of induction (Galili et al., 2006). This fundamental physical principle states that when a changing magnetic field passes through a coil of wire, an electromotive force (EMF) is induced in the wire. The relationship is described by the following equation:

$$\varepsilon = \frac{-n\Delta\Phi}{\Delta t}$$

Where ε is the EMF induced in n turns of wire, $\Delta\Phi/\Delta t$ is the change in magnetic field strength with respect to time.

In our signaling well, the EMF is induced in the specific signal well adaptor and is transmitted to the microcontroller. In developing the board, we have used n = 500 turns of wire with a small magnet to induce an EMF of approximately 15 millivolts. This signal is well above the noise level and 'False-positive' detections virtually never occur. It should be noted that in preliminary testing (with n = 50 to 100 turns of wire), we did note a greater number of false positives.

Conclusion

Here we have presented a method to provide real time feedback about experimenter progress to help minimize error. Future work may integrate this system with a computer interface to track when and where a user has pipetted in order to document experiments and track samples. In industrial and research settings, tracking pipetting would help curtail costly repetition of experiments as well as provide a way to track laboratory worker efficiency and use of reagents. We envision use of the system combined with location and time of event tracking in forensic laboratories could provide documentation of sample processing important for legal proceedings. This advance could thus reduce the potential for fraud in result reporting that, among other issues, can contribute to improper determination of guilt and innocence in criminal cases.

Conflicts of interest

Authors have none to declare.

Abbreviations

EMF, Electromotive force; **MM,** Millimeter; **PCR,** polymerase chain reaction.

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