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Design and Validation of New Data Acquisition System for Isolated Muscle Experiments: Application to Pharmacology Teaching and Research

Abdel-Motaal Fouda[1], Mohamed H. Qutb[2], Gamal M. Dahab[3]

1Associate Professor of Clinical Pharmacology, Mansoura University Faculty of Medicine, Mansoura 35516, Egypt.

2Freelance electronics engineer, Mansoura 35111, Egypt.

3Professor of Clinical Pharmacology, Mansoura University Faculty of Medicine, Mansoura 35516, Egypt.

Corresponding author
Abdel-Motaal Fouda
Email: foudaamm@mans.edu.eg
Tel: 0020501113974766

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ABSTRACT

In this paper we describe a new data acquisition (DAQ) system for pharmacology experiments involving isolated muscle contraction. The system is composed of hardware acquisition unit and computer software for analysis of signals representing muscle contractions. As compared to mechanoelectrical DAQ systems of other constructions, the advantages of the new system include a high sensitivity (in the order of 1 μN), a wide range of forces recorded (1 μN to 100 mN), linearity throughout the whole range, easy assembly, low costs, long-term calibration stability, good dynamic characteristics and full control graphical interface. The device can be readily adjusted to actual experimental conditions and a variety of muscle preparations. Experimental validation of our DAQ inside the Clinical Pharmacology Department at Mansoura University Faculty of Medicine showed that it can record contractions of isolated muscle preparations with good precision and accuracy. Accordingly, the DAQ system design presented herein with its dedicated software is largely suitable for isolated muscle experiments in both teaching and research in biomedical fields.

Key words: data acquisition system; isolated muscles; experimental pharmacology DAQ; load cell sensor.

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INTRODUCTION

Experiments utilizing isolated muscles including skeletal, smooth, and cardiac muscles are central component of research involving screening of new drugs, as well as demonstration of drug effects on tissues in the practical classes of undergraduate pharmacology curriculum in medical, pharmaceutical, and science colleges worldwide [1]. In these experiments, the isolated muscle preparation is usually fixed at one end within the organ bath, and the other end is attached to data acquisition system (DAQ) consisting of a isometric/isotonic transducer that converts mechanical force/displacement value into analogous electrical signal which then passes to a processing unit at which the signal is amplified, noise-reduced, and digitized before being displayed on screen by specialized computer software or recorded on a graph paper for remote analysis. Different models of DAQ systems for isolated tissue preparations are available in different technology forms. The PC-based DAQ provide a more powerful and flexible solution in both experimental research and teaching purposes than traditional graph paper systems [2].

A wide variety of simulation software and android applications have recently introduced in the cyberspace to fill the gap in experimental class teaching, however, concerns have arisen against the use of these simulation software in the teaching of laboratory classes as they do not enhance the physical skills of students nor implicit understanding for working experiments in the laboratory [3]. Additionally, these simulation software could not be used for research purpose as they lack interaction with living tissue and display only programmed results stored in the application files for just demonstration.

Unfortunately, the medical instruments are much expensive, and one PC-based DAQ system for isolated muscle experiments may cost thousands of dollars. This may add another challenge to teaching practical pharmacology to undergraduate students as it would be difficult to obtain multiple units to match the increased number of students even in small group teaching. Recognizing this fact, a survey of medical graduates revealed that while a majority considered pharmacology as the most important basic science, they also recognized the pharmacology laboratories as the most boring and least useful practical laboratories [4]. Therefore, the need for efficient, flexible, and economic solutions that help in teaching practical laboratory classes to undergraduate students, as well as in medical research, is strongly required.

In this article we describe and validate a new versatile and low-cost, digital DAQ system for isolated muscle experiments that does not utilize piezoelectric transducers or complex expensive technology. This new DAQ system consists of acquisition unit and dedicated software. The low cost, efficiency, and flexibility of the design presented herein enables it to be used widely in all experiments involving different types of isolated muscles preparations. Finally, we used simple technical terms and avoided complexities of mathematical equations of the acquisition unit components' working principles aiming at encouraging students and teachers to build this simple DAQ system and use it in their practical classes or home experiments.

MATERIALS AND METHODS

Device construction

The circuit represented in Fig 1 utilizes double bending beam load cell sensor which measure tension force of muscular tissue. The load cell sensor is a changeable component to adapt to ranges of muscle force from 0 to 750 g. The sensor is connected to special amplifier and noise filter circuit. The output goes to programmed microcontroller to send the data to dedicated computer software. The load cell, connected to the muscular tissue under test, converts tension forces into microcurrent which will be then amplified and filtered to eliminate potential noise before entering to a microcontroller. The microcontroller sends digitized data via universal serial bus (USB) to computer software with graphical interface mounted on Dell Inspiron n5010 laptop with Intel core i3 processor, 4.0 GB RAM and built-in HD graphics on Windows 7, 64-bit OS (Microsoft Corp, USA). We used Arduino configuration as communication device between computer and hardware using analog input to feed software with signal information (Fig 3).

Calibration and verification

The system was calibrated and verified by performing three verification tests:

Repeatability test: was done to make sure that there is no deviation of the repeatability due to some interactions of the environment with the sensor. The same weight (1, 5, 10, 20, 50, 100, 200 g) was added and removed several times and the changes in the scale rated capacity were recorded [5].

Creep test: was done to detect any tension that will relax due to the application of the weight. The test was performed by adding a weight on the scale and waiting for 5 min. During the waiting time the changes in the scale rated capacity were recorded [6].

Linearity test: weights are added step by step on the scale, then removed. Readings are compared to calibrated value of the weight to detect any deviation of linearity or hysteresis that could be the indicator of an incorrect calibration [5].

Isolated smooth muscle experiments

The new DAQ system was subjected to a number of validation experiments inside the Clinical Pharmacology Department at Mansoura University Faculty of Medicine, to ensure sensitivity and reliability in live tissue experiments. These experiments included isolated rabbit intestine, guinea pig ileum, and rat uterus. Experiments on isolated rabbit intestine were conducted according to the protocol of Jespersen et al. [7]. Experiments on isolated rat uterus were conducted according to the protocol of Darios et al. [8]. All animal works were conducted in accordance with Mansoura University Institutional Research Board and the Guide to the Care and Use of Laboratory Animals (8th edition, 2011, The National Academic Press, Washington, DC, USA).

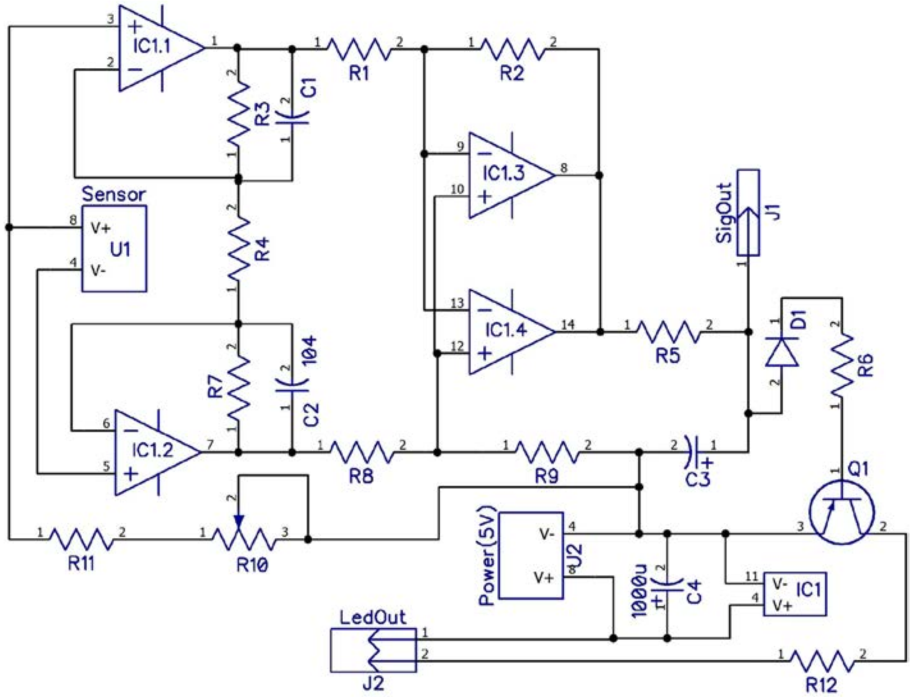

Fig 1. Components of the electronic circuit. The 100 g load sensor in this circuit is connected to the inputs of differential amplifier which detects minimal voltage difference thereby amplifies the minimum load pressure on the sensor. The three operational amplifiers are connected in instrumentation amplifier (INA) configuration so the output of differential amplifier is forwarded to another operational amplifier to amplify the signal (2 parallel opamps are used for more stability). The last stage is the filter circuit formed by R5+C3 which filter internal and external noise and provide smooth signal. D1+R6+Q1+R12 feed external light-emitting diode (LED) which provides visual feedback of sensor pressure. R10 is used for sensor balancing.

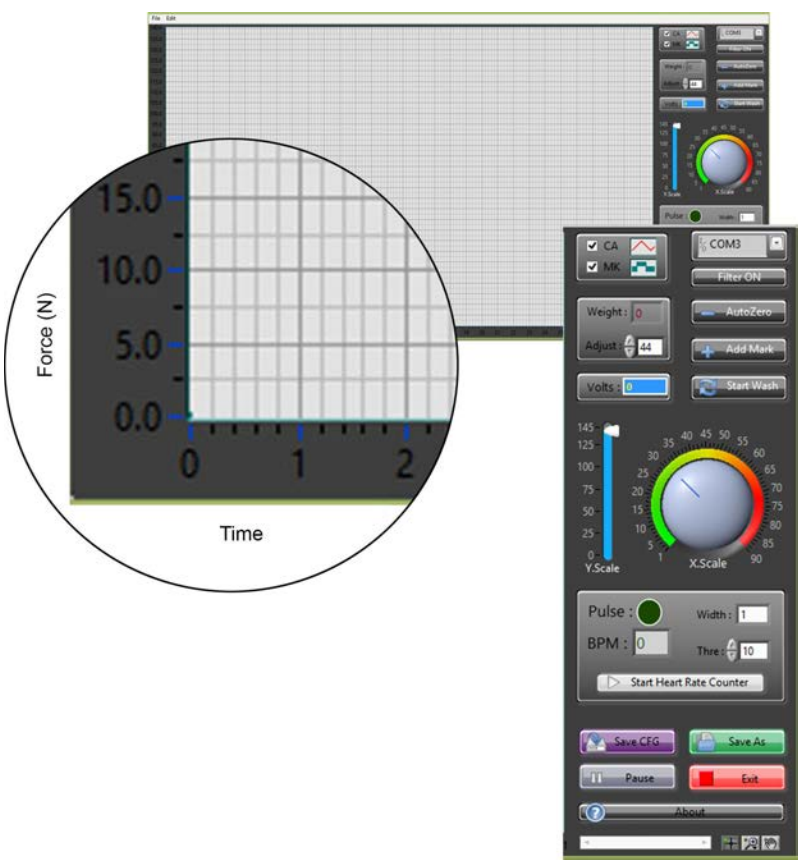

Fig 2. Graphical interface of operating software. The horizontal scale measures time in customizable units while the vertical axis measures muscle force in Newton. The right dashboard contains controls for variable analyzable data such as heart rate, recording speed, force units, wave amplitude and area under the curve (AUC).

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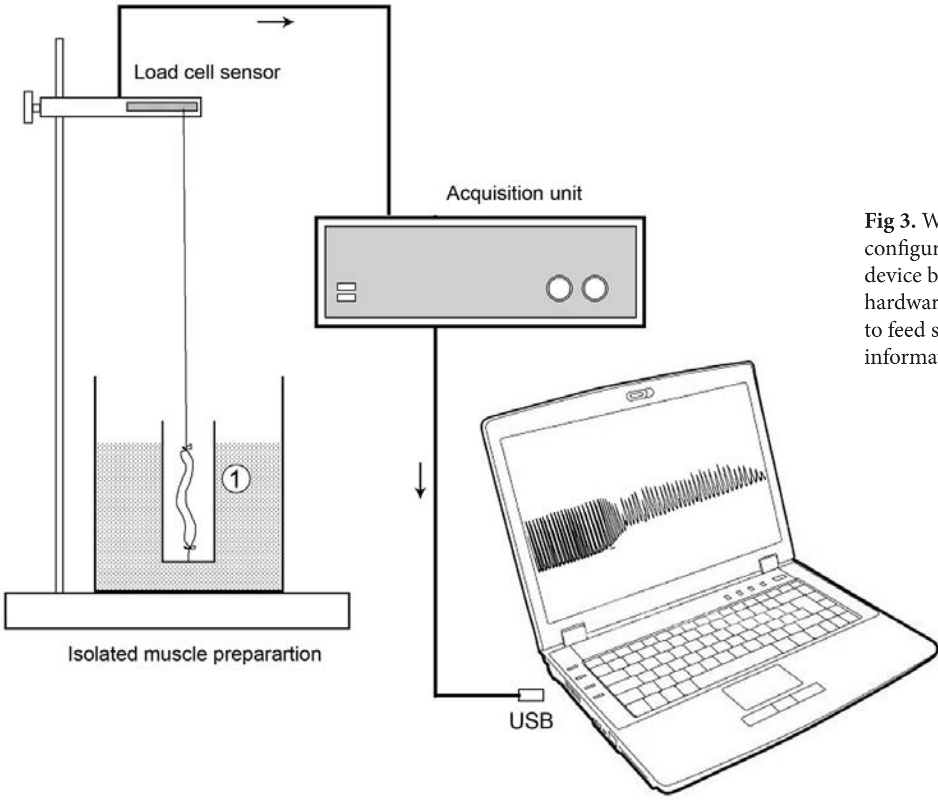

Fig 3. We used Arduino configuration as communication device between computer and hardware using analog input to feed software with signal information

RESULTS

Calibration and verification

The new DAQ system was subjected to three basic tests to ensure precision and accuracy. The device showed high sensitivity in recording tension forces in the order of 1 µN and a wide range of forces recorded (1 µN to 100 mN). Friction test showed no deviation of the repeatability with application and removal of the same weight (1, 5, 10, 20, 50, 100, 200 g) several times. Rresults of the creep testing showed that 60 min creep for the load cell sensor is equivalent to about 0.03 % to 0.05 % of the applied load. Linearity test was done to detect any deviation of linearity or hysteresis that could be the indicator of an incorrect calibration. Experimental testing of linearity showed that the device is capable of recording muscle forces between 1µN and 100 mN with good linearity over the entire range (Fig 4). The reported discrimination ability was about 1 mV which corresponded to a force of 1 µN.

Isolated smooth muscle experiments

Pharmacological experiments with isolated smooth muscles preparations revealed very good sensitivity and discrimination ability. The primary signal was precise and

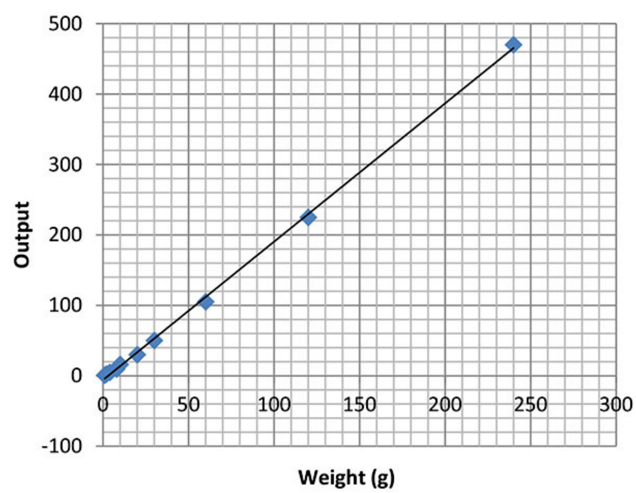

Fig 4. Experimental testing of linearity showed that the device is capable of recording traction weight with good linearity over the whole range.

free of noise. The graphical interface of the software has functions to analyze the waves. Figures 5, and 6, show traces of recorded experiments.

DISCUSSION

Isolated organ bath experiments provide evidence for char-

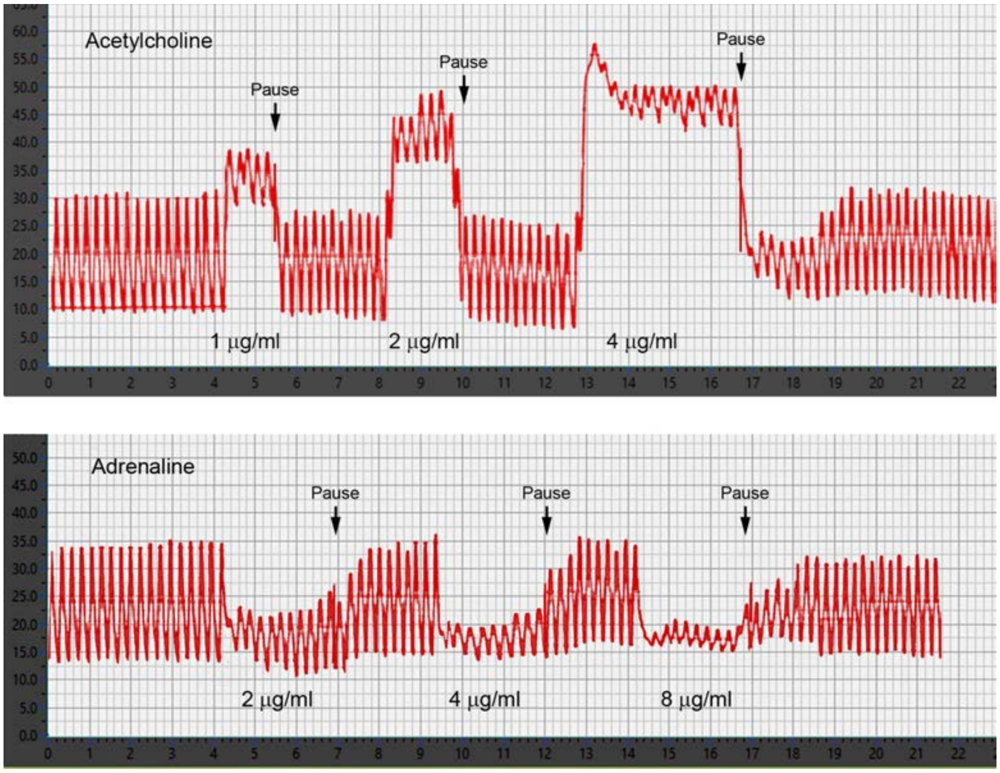

Fig 5. Representative recordings of isolated rabbit intestine showing the effect of different concentrations of acetylcholine (above) and adrenaline (below). Both traces show good discrimination of contraction waves. Both time and amplitude are measured on the X and Y axes respectively.

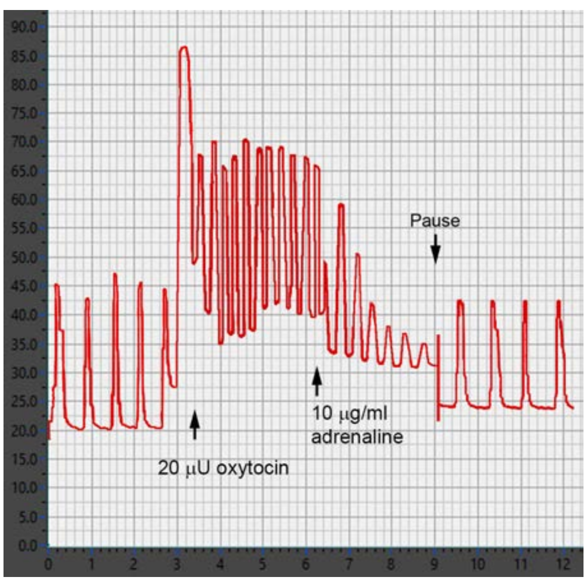

Fig 6. Representative recording of isolated rat uterine strip preparation showing the spontaneous contractions and the effect of both oxytocin and adrenaline. The recording shows good response rate of the sensor with no creep.

acterization of drug effect in biological tissues which can be directly translated to human studies [9]. Both teaching and research within the discipline of pharmacology commonly utilize experiments that require excised isolated organs or tissues to allow for the study of drugs and their interactions within these tissues [1]. Unfortunately, implementation of the practical component in pharmacology teaching to undergraduate students is a tedious task as it is difficult to obtain multiple units to match the increased number of students even in small group teaching and there is need to ensure cost efficiencies.

The DAQ system described herein is widely applicable for various biological experiments involving isolated muscle contraction and may successfully replace devices used so far. The method is highly sensitive and easy to build up. It uses commercial small load cell sensor that can convert muscle tension into analogue signal. The acquired signal then passes to an electronic circuit to amplify, digitize, and reduce noise of the analogue signal. The resulted digital signal can be displayed and analyzed with computer software with graphical interface and wide range of functions. As compared to mechanoelectrical DAQ systems of other constructions, the advantages of our system include a high sensitivity (in the order of 1 µN), a wide range of forces recorded (1 µN to 100 mN), linearity throughout the whole range, easy assembly, low costs, long-term calibration stability, good dynamic characteristics and full control graphical interface. The device can be readily adjusted to actual experimental conditions and a variety of muscle preparations. The range of muscle contractions to be measured and/or dynamic properties of the recording unit can be customized by the selection of the appropriate load cell sensor.

Accuracy of DAQ systems concerned with recording forces such as muscle contractions depends on many factors including precision, repeatability, linearity and hysteresis. The concept of precision refers to the degree of reproducibility (or repeatability) of a measurement. In other words, if exactly the same value (e.g. muscle contraction) was measured a number of times, an ideal sensor would measure exactly the same value every time. Likewise, load cell creep is the difference between initial response when force applied and the response at a later time [10]; accordingly, ideal sensor has minimal creep response. We performed both the friction and creeping test to ensure good precision and repeatability of our system. The readings of the two tests showed that the acquisition load cell sensor has very good precision and stability. Our results of creep testing showed that 60 min creep for the load cell sensor is equivalent to about 0.03 % to 0.05 % of the applied load

Linearity is another characteristic of a measurement system in which output is linearly proportional to the input. So, linearity is graphically represented as a straight line (a relation between input and output). In measuring muscle cell contractions the actual range of contractions will be 1μN – 10mN. This range corresponds to deformations of ±1 x 10–3 with a transmission linearity better than 0.8 % [11]. Experimental validation of our data acquiring sensor showed that it can record muscle forces above this range with good linearity over the entire range. Accordingly, the load cell transducer design presented herein and its electronic circuit is largely suitable for dynamic measurements.

Ideal DAQ systems have good discrimination ability known as the ability to eliminate noise without negative effect on the measured signal. In our design, the noise could be efficiently reduced by filtering the high frequency noise using a low frequency filter at the output of the amplifier circuit, or by limiting the frequency characteristics of amplifiers using suitable capacitors in feedback connection. The reported discrimination ability was about 1 mV which corresponded to a force of 1 μN.

In conclusion, we described in the article the technical and applied aspects of new and cost-effective DAQ system suitable for teaching and biomedical research concerned with isolated muscle contractions. The system is sensitive, precise, has good discrimination, repeatability and linearity. The ease of construction and cost-effective value elect it to replace old kymographs utilizing smoky paper and the recent expensive units, and enable its manufacture on large scale to meet the expanding number of undergraduate students in biomedical fields.

Conflict of interest

The authors declare that they have no conflict of interest.

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