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Research Article

Implementation of Scheduling Algorithm with Robotic Arm and Analytical Plate for Clinical Chemistry Analyzer

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Abstract: Complete automation is the ultimate goal in health care industry and this is of utmost importance in clinical laboratories. Processor based bio robots are involved in all these automation procedures. In this study, the indigenous robotic platform, used in clinical chemistry analyzers, which is highly flexible and user friendly for small or medium sized hospitals, is designed. A microcontroller based robotic arm is put forth as the robotic platform and this is capable of handling blood samples, reagents, etc. The basic design is of a compact, three circular analytical plates, placed one inside the other. The samples and reagents are loaded onto the analytical plate; the arm then transfers the blood samples and reagents successively to the reaction cell and if required, next to an incubating unit. Two different arms perform all the different tasks based on the controlling algorithm. The circuit manipulating the path of the robot arm, along with other controlling circuitry of the arm is embedded within the arm itself. By automating this unit, the flexibility and throughput of the tests will be increased. Controlled and precise use of reagents and high accuracy of results are additional advantages. Data handling is also simplified. The robotic arm and analytical plate has been designed, a prototype model has been made and synchronization between the two has been achieved. The clear description of arm and analytical plate movement along with the synchronization algorithms are presented in this study.

Keywords: Analytical plate, automation, clinical chemistry analyzer, robotic arm, sampling system

INTRODUCTION

One of the different parameters of automation is the high cost associated with the fabrication of analytical instruments. In this study, the fabrication of a low cost automated servomotor controlled robotic arm is put forth to handle the samples and reagents from the analytical plate to the testing unit. By increasing the level of automation, accurate use of reagents and samples is feasible leading to valid results. The use of manpower is also minimized in clinical laboratories. The automatic blood sampling unit is incorporated and it is used only for measuring the blood glucose level. RIT (Reduced Idle Time) algorithm and it carries the job without job delay time. Even this requires the further future improvements in interfacing, optimization of the hardware components, and schedulers. Transfer of samples and reagents in the micro plates and other communicating devices are communicated to each other and all the patient information can be recognized by the Radio Frequency Identification (RFID) system. The feasibility of the system is validated through its preliminary experiments (Choi *et al*., 2011a, b). The robotic arm controlled by a microcontroller and driven by the stepper motor has 4 degrees of freedom. Choi *et al*. (2006) have suggested the robotic platform for the clinical tests in the hospitals which satisfied 70 analytical methods for clinical test and also reduced the amount of reagents consumed. Nakamachi (2010) has been presented with Self Monitoring Blood Glucose device (SMBG) which comprises of automatic blood sampling unit with blood glucose measurement. Infrared imaging is employed in this methodology. The major drawback of this method is that it is a prototype best suited only for measuring the blood glucose and not for carrying out other analytical clinical tests. Choi *et al.* (2008) proposed the technique for retrieving the patient information can be easily recognized through the RFID and by making all the components easily replaceable, the operation process and maintenance of the system is improved. The pneumatic pipette tip which is presented exclusively in each sample tube is to avoid the cross contamination between the samples. The proposed system design is capable of handling the samples in fully automated storage and sample retrieval, including entering and dispatching of stored sample (Saitoh and Yoshimori, 2008). A compatible system which is developed is capable of handling any reagent kit which is available in the market can be used for the testing purpose and this system is working based on the principle of absorbance transmittance photometry (Taneja *et al*., 2005). Bhatia *et al.* (1998)

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have been designed an expert system which can perform the different iterative modifications to the model until all the requirements are been satisfied. Er (2001) proposed a Hybrid Adaptive Fuzzy Controller (HAFC) for selectively compliance assembly robot arm for the applications which are best suited with industries. The major advantage of this technique is that it does not require mathematical model. HPFC prototype was successfully simulated and implemented in real time which resulted with reduced development time as well as the reduction in cost.

MATERIALS AND METHODS

The analyzer system comprises of four units, viz.:

- Analytical Plate
- Sampling System
- Controlling unit
- Measuring unit

The Analytical plate contains three circular plates, with the innermost one containing the samples and the middle plate holding the reagents. The outermost one comprises of the reaction cells. Each of the 3 rotatable plates is driven independently by servo motors with all of them being controlled by a micro controller. The sampling system has two arms. They are perfectly synchronized with the analytical plate so as to pick up the samples and reagents from inner and middle plate. Rotation of analytical plate and moving of the arm is programmed and controlled through the microcontroller. All the reagent containers and sample tubes have their own respective pipette tips. The pipettor in the arm positions the pipette tip in first reagent container and transfers it to the required number of reaction cells. This is based on the number of samples loaded in the sampling system. For N number of samples and M number of reagents, the arm needs to take up reagents totally M×N times. Each time when the reagent and samples are loaded in the reaction cell, the temperature will be maintained at 37°C. This is achieved by incorporating the Peltier system around the reaction cells. The stirring arm stirs each reaction cell contents and transfers the content to micro flow cell and goes for wash cycle. Once readings are recorded, the micro flow cell is washed, next reaction mixture loaded and similarly processed. In this study unique analytical plate is designed and it consists of three circular plates kept one inside the other. The rotation of each plate is individually controlled by three independent servo motors and programmed through microcontroller. The design of sample and reagent containers tray are having an exclusive pneumatic pipette tips mainly to avoid the cross contamination between the samples and to eliminate the wash cycle process. The number of reagent containers corresponds to the number of tests, which could be performed for each patient. Three different robotic arms are incorporated. These arms are intended to handle the sample, reagent, stirring the reaction cells and transferring the contents to the micro flow cell. The results will be read out from the micro flow cell and stored in the memory. Arm and analytical plate rotations are controlled by the ATMega2561 processor.

Analytical plate: Here an analytical plate containing 3 circular plates is proposed. The inner plate holds containers for 24 samples along with six standards and 2 controls each with a capacity of 0.8 mL. The middle plate is a reagent tray with 36 reagent containers each with a capacity of 25 mL. This reagent tray is designed to easily detachable and can be refrigerated. The outer most circular plate has 128 reaction cells each with a capacity of 1.2 mL. This reaction cell array is maintained at 37°C. With these 128 reaction cells, at least 4 different tests for each patient can be performed. After performing four different tests for each patient the reaction cell array goes into the wash cycle mode and all the reaction cells are cleaned. Then the arm starts the process again for the fifth test. Each sample tube contains the blood samples and a pipette tip inside. The tip can be easily locked with the pneumatic pipette tip which is attached to the arm. The same arrangement is made for the reagent containers also. The reagent arm picks up one particular reagent and puts it in the reaction cell. The number of times this action needs to be performed can be decided by the number of samples loaded in the sampler.

Likewise the sampler arm needs to take the samples from each sampler tube and put it in the reaction cells. By accessing each sample tube by the sampler arm, all the sample tubes are loaded by the pipette. Figure 1 shows the analytical plate with three different circular rotations. To complete 36 tests for each patient, this whole cycle is repeated 9 times. It means that the machine hence performs 1152 tests for one complete batch. Every time a new parameter needs to be estimated with reagent, it runs 6 standards and 2 controls before proceeding to the patient samples. By testing the standards and comparing the results we are calibrating the system every time each type of test proceeds.

Sampling system: Sampling system consists of two robotic arms and a stirrer arm. One of the robotic arms handles the samples loaded in the sample tray and the other arm handles the reagents loaded in the reagent tray. The stirrer arm serves to stir the contents of the reaction cell and also caters to washing and transporting the reaction cell contents to micro flow cell for

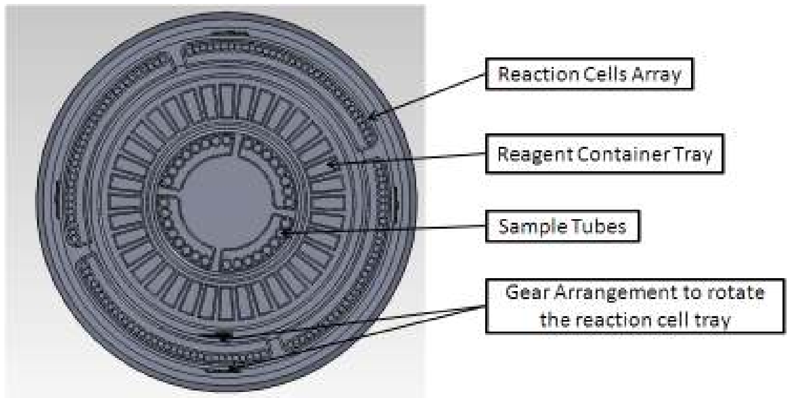

Fig. 1: CAD drawing of analytical plate top view

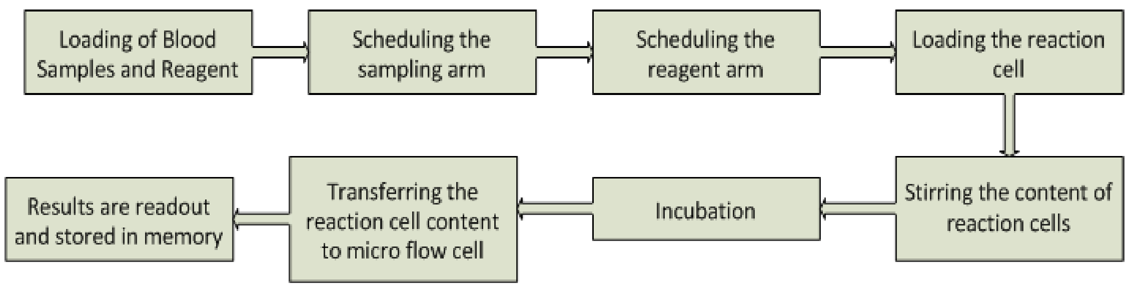

Fig. 2: Block diagram of robotic arm

measurement purposes. Figure 2 depicts the block diagram of arm function. Two different arms for samples and reagents are provided to avoid cross contamination between them. The sampling system manages the loading, identification of each sample, path manipulation of arm and transportation of blood samples. The path of arms handling the reagents and samples are manipulated in the flow diagram as shown in Fig. 3 and 4. Both the arms are positioned in the origin. Number of samples to be loaded is given as count value of N, the number of reagent containers loaded is given as count value of M.

When the process starts, the pneumatic pipettor locks the pipette tip which is placed in the first reagent container. It sucks 4 μL of reagent and transport to the first reaction cell. The arm repeats the process with the same reagent N times. For transfer of samples, the pneumatic pipettor locks the pipette tip which is placed in the first sample tube. It sucks 0.5 μL of sample and transport to the first reaction cell. Then arm replaces the pipette tip in the same sample tube and comes to the origin position. Now the count value (N) = count (N) - 1. The sample tray and reaction cell tray rotates one step clock wise for the purpose of loading the next sample in the next reaction cell. Next process of cycle starts for the second sample and continues N number of samples. All the time the reagent tray remains in the fixed position as the reagent arm has accessed only one particular reagent container. For one complete cycle, the Reagent count (M) = Count (M) - 1. The sample count is reloaded again as N for the next type of test. The process then repeats for the second parameter with all the samples i.e., N times.

The stirrer arm each time takes care of mixing, incubating and transferring the incubated contents to micro flow cell. All these arm and plate movements are controlled by the micro controller and driven by the servo motor. The value of counts loaded is done by microcontroller programming. In 128 reaction cells 4 different types of tests for each patient can be performed. The cleaning of whole reaction tray subsequently needs to be done before the next 4 tests are performed. For the 36 set of tests for each patient, the whole process has to be repeated 12 times if the numbers of samples loaded are 24. Based on the number of samples, the testing cycle can be reduced through the programming. The Robot Arm which is

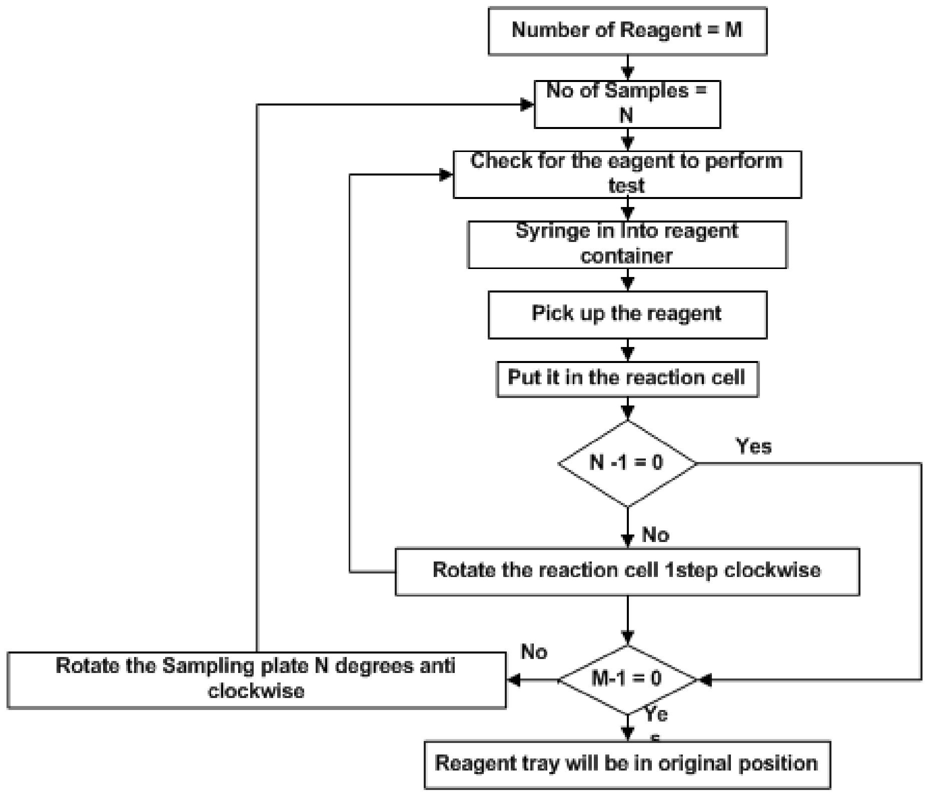

Fig. 3: Transferring of reagent to reaction cells

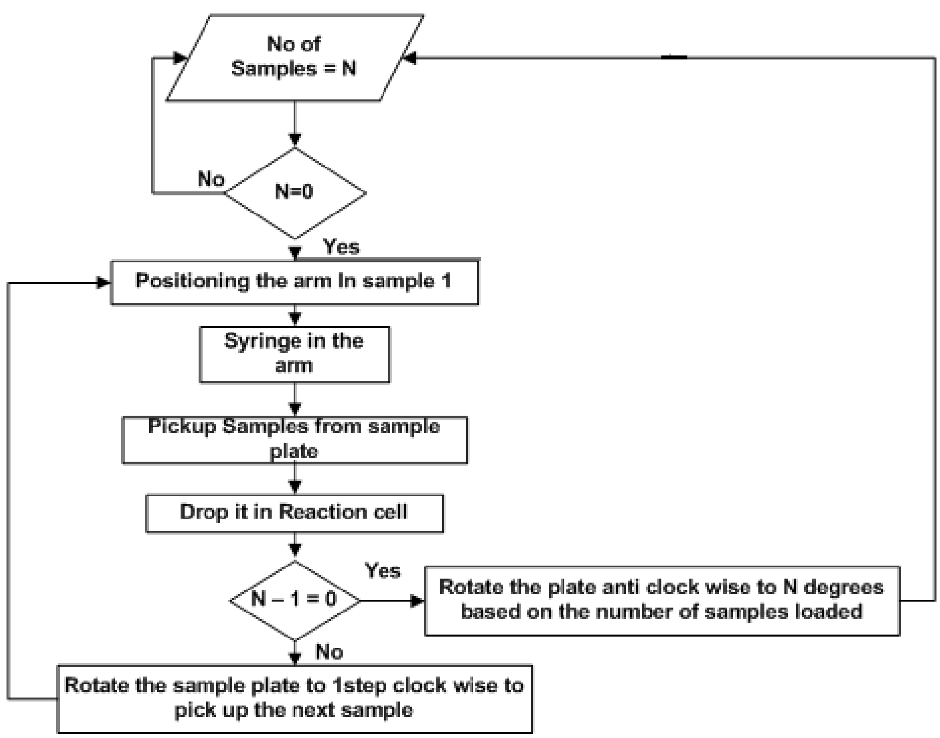

Fig. 4: Transferring of samples to reaction cell

Fig. 5: Front view of sample/reagent arm

Fig. 6: Side view of sample/reagent arm

Table 1: Specification for analytical plate and arm function

Total number of tests	1152 tests/batch
Number of testing cycles	9 cycles/batch
Number of tests/cycle	128 tests
Sample tray capacity	0.8 mL tube, 32 samples
Micropipette for dispensing sample	0.1 mL resolution
Reagent tray capacity	25 mL tube, 36 reagents
Micropipette for dispensing reagent	1 and 0.2 ML resolution
Reaction cell tray capacity	1.2 mL, 128 cells
Temperature of reaction cell array	37°C, ±1°C resolution

handling the samples and reagents has a 4 Degrees of Freedom (DOF) and the 3rd Arm is used to stir the reaction cell content and move the contents to the micro flow cell for the processing.

Each arm has separate pneumatic pipettor. The task of handling each arm contains the movement of in and out. It encompasses x-y-z or z-θ sample, reagent arm movement and the conveyance of samples arm to the reaction cells. Figure 5 and 6 shows CAD drawing of Robotic arm in front and side view. Both the sampling and Reagent arm looks the same. At the end of the arm, the liquid handler, i.e., pneumatic pipettor is attached. Table 1 shows the specification of analytical plate and arm dimensions. This system can able to perform 36 tests per patient. So totally it runs up to 1152 tests per batch. Controlling Unit consists of the micro controller and all its associated circuitries. This unit controls the entire system. For controlling the arm we are proposing the scheduling algorithm.

Controlling unit: We are using a control module type controller with an ATMega 2561 MCU installed on it. The operating voltage range is +7 to +35 V with an overall maximum current ratings 10 A. There are temperature and voltage sensors added to the circuit for the data about the working atmosphere. It has a working temperature range of -5 to +70°C. It uses TTL/RS485 communication protocol for communicating with Dynamixel servo motors.

The motors we have used are Dynamixel Servo motors supplied by Robots (Cm 700 manual.com. 2012).They provide no load speed of 54 rpm and holding torque of 24 kgf.cm at a 12 Volts DC supply. They have an in-built STM32 series MCU that has the ARM Cortex M3 architecture. These motors have almost had a 0° to 360° full sweep. It also has a 12 bit position sensor to depict the shaft position, providing a feedback path for errors. It works on PID control algorithm to enhance the precision. PID control actually helps in considering the current error (P), integrate the previous errors (I) and derive the value for future errors (D).

Other than position feedback, it also gives temperature and load values to prevent from overheating and overloading. It has an analog resolution of 4096 for 360° giving us a 0.08789° angle resolution. It has a standby current of 100 mA and operating current around 1.5 a, this reduces the power consumption during no operation. Then the communication between the STM32 (present in the Dynamixel) and ATMega 2561 (present on CM700), it's a Half-Duplex Asynchronous serial communication. All the motors are connected in a Daisy chain physical link with the help of a daisy chain type connector. Then each motor is assigned a specific ID to be identified in the chain. This ID number can vary from 0×00 to 0×FD giving us total 254 options. This ID can be saved in the EEPROM of the motor MCU. Along with this data the 0 position, maximum temperature limit and other necessary data about the motor are saved in the EEPROM of STM32. Now whenever a specific angle is to be obtained, ATMega 2561 board is programmed to send the analog value along with the ID of motor where shaft movement has to take place as a digital data packet to STM32 MCU. The target motor controller interprets the data packet and instructs DC motor to move, with the help of the position sensor installed inside the motor the high precision movement of DC motor can be achieved and hence completing the motion of the arm. Figure 7 shows the job scheduling algorithm which describes the total functions of Analytical Plate and Robotic Arm movement. Based on this algorithm the Arm movement is manipulated through the following equations:

$$\sum_{P=1}^{N} \mathrm{Re}_N = R_1 + \sum_{N=1}^{N} S_N \qquad (1)$$

where,

Re : Reaction cell
R : Reagent container
S : Sample tubes, for the first type of test of all the patients

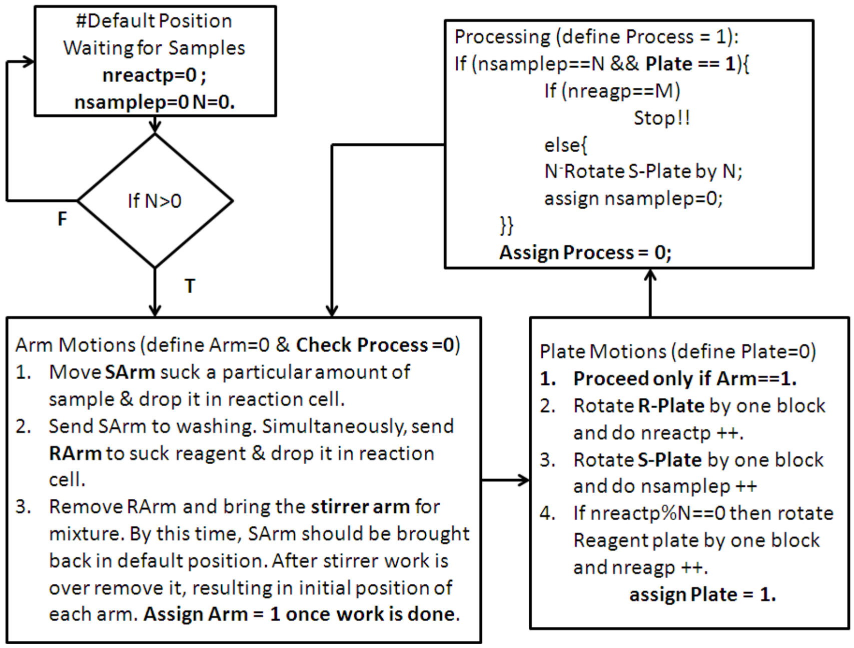

Fig. 7: Algorithm for sampler, reagent arm function and analytical plate rotation

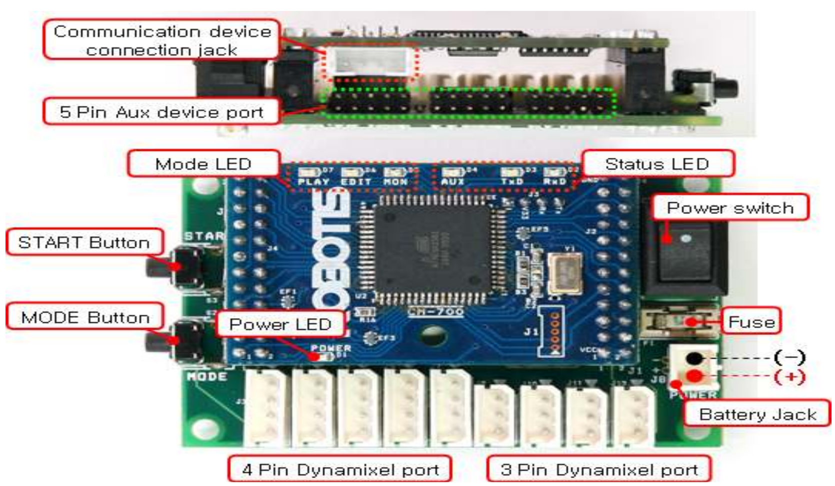

Fig. 8: CM 700 development board with at Mega 2561 (cm 700 manual.com. 2012)

Likewise the following equations describes for the complete test sequence:

$$\sum_{P=N+1}^{2N} \mathrm{Re}_{2N} = R_2 + \sum_{N=1}^{N} S_N \tag{2}$$

$$\sum_{P=2N+1}^{3N} \mathrm{Re}_{3N} = R_2 + \sum_{N=1}^{N} S_N \tag{3}$$

From the above 3 Eq. (1), (2) and (3) we can summarize the movement of plate and arm, in a generalized equation:

$$\sum_{P=MN+1}^{(M+1)N} \mathrm{Re}_{(M+1)N} = \sum_{M=0}^{M+1} R_{M+1} + \sum_{N=1}^{N} S_N \tag{4}$$

Eq. (4) denotes,

M : The total number of reagents used for one batch process
N : The number of samples loaded
P : The number of reaction cells

ATMegha 2561 microcontroller unit has the RXD1 bit 2 and TXD1 bit 3 pins are connected with the daisy chain link. MX 28 servo motor has ARM cortex M3

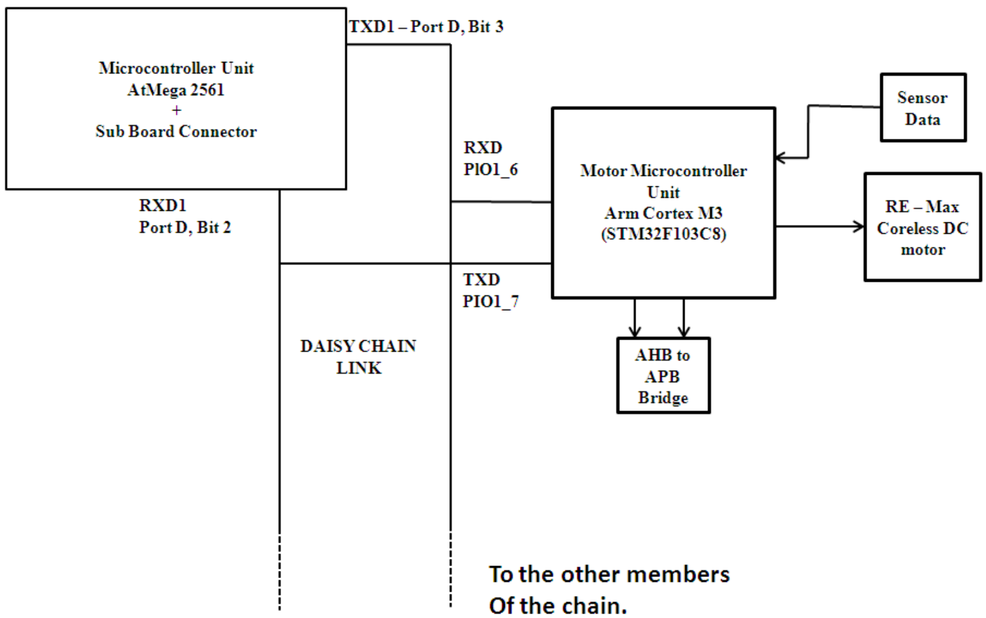

Fig. 9: Interfacing servomotors with microcontrollers in daisy chain link

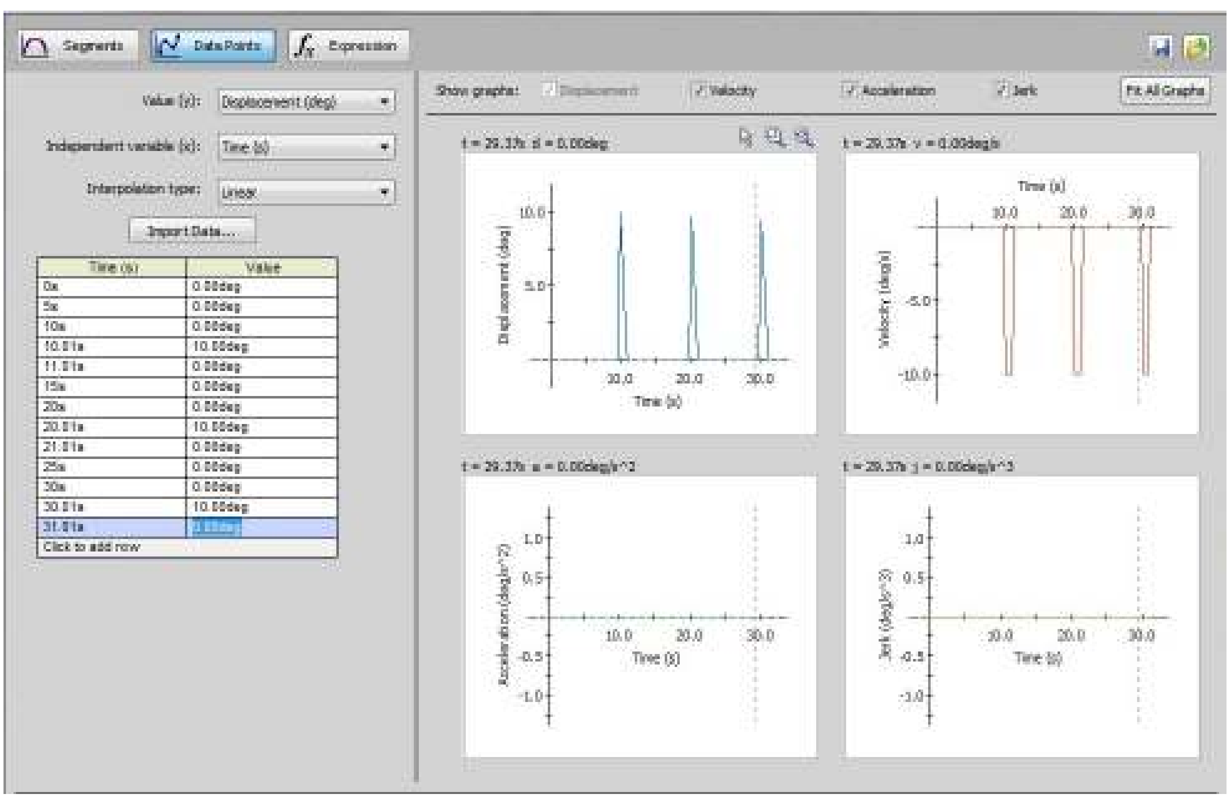

Fig. 10: Time response of sample and reagent tray

processor, each processor receives data and sends to the next motor because of daisy chain link is activated. The motor has inbuilt sensory circuits that will detect the temperature and sends data to the motor Fig. 8 shows

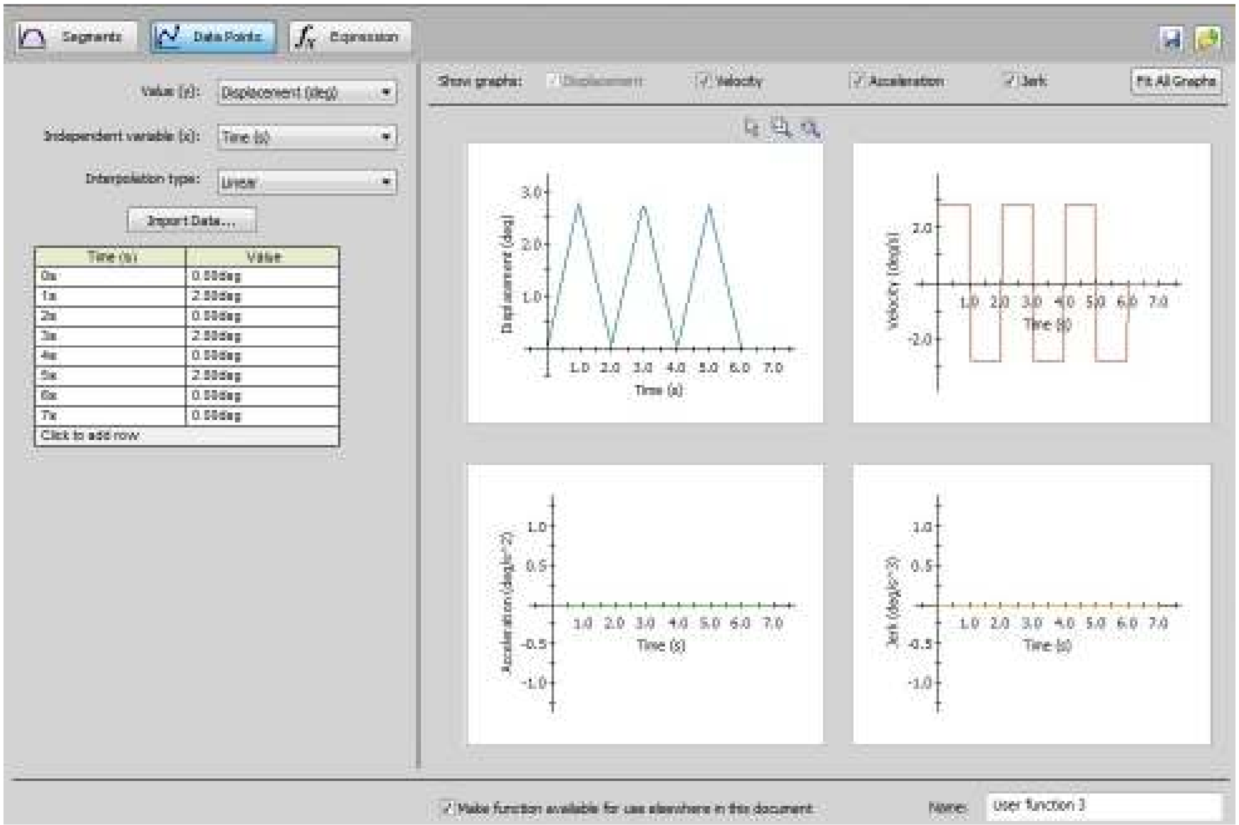

Fig. 11: Time response of reagent cells tray

the development board (CM 700) which has the control module type controller and having a ATMegha 2561 processor.

RESULTS AND DISCUSSION

In this study the preliminary results of integration between Arm and Analytical Plate has been presented. The Robotic arm and Analytical Plate configurations are user friendly and the reagent tray, which is presented here, is easily removable. Three circular plates have the different rotations and can be controlled and programmed easily. Each time the number of sample loaded can be varied up to 24. Based on the sample size the operation can be adjusted automatically. Figure 9 shows the Interfacing of servo motors with microcontrollers. This board has the connection of daisy chain link. With the daisy chain link we can able to connect multiple servo motors one by one or in a ring pattern. Each connecting motor acts as a master to the next motor. It receives the data packets and sends the information to the next. This system can able to run up to 1152 tests/batch with 36 different kinds of tests. The servo motor which is used here has an inbuilt ARM cortex M3 processor. So it automatically corrects its previous position and locates exactly where the cells are presented. Figure 10 shows the result of time response for sample and reagent tray rotations. This is the result taken by running the sample tray and reagent tray with simulated in 3D CAD Design Software Solid works. Figure 11 shows the time response of reagent cells tray this is also taken by simulating the reagent tray in 3D CAD Design Software Solid works.

CONCLUSION

This study gives the overview and test results of the Robotic Arm and Analytical Plate, which is simulated, and the preliminary test results of the Robotic Arm and Analytical Plate which is used in the Clinical Chemistry Analyzer. These results are taken from the 3D CAD Design Software Solid works. This type of Arm and Plate can be used in the Complete Automatic Analyzer that is used for small, medium sized hospitals and the primary health centers. The ultimate aim of this automated system is to bring out the changes in human resource and precise use of reagent by providing the automatic pipette tip. The future work is carried out with the mathematical model of the Robotic Arm, validating the synchronization between the Robotic Arm Movement and Analytical Plate and providing the menu driven software, which is user friendly. The integrated system has to be implemented in hospitals and validate system in real time.

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