Journal of Critical Reviews

ISSN- 2394-5125 Vol 7, Issue 4, 2020

Review Article

OPTIMIZATION AND PROCESS FLOW OF LABORATORY BASED LIQUID HANDLING ROBOT

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Received: 26.12.2019 *Revised: 20.01.2020* *Accepted: 13.02.2020*

Abstract
A machine is a mechanical device or structure which uses power to start the device. The machine converts the electrical energy into the mechanical energy. The mechanical movements will control the actions to be performed. Machines can be driven by so many means, like humans, animals, natural forces like wind, water, thermal, chemical and also electrical. We use sensors and actuators to run the machine. The actuator inputs are taken into account to achieve a particular application of output movements and forces. We also use computer programming and embedded programming for the movements, to monitor the performances and for the movement planning. A Liquid Handling robot is one such machine which takes the electrical energy and convert that into mechanical. It is type of machine which is used for the automation of chemical liquids and biomedical laboratory solutions. It dispenses a particular amount of liquid/reagent in a designated test tube which contains the substrate. The reaction happens after that. A simple machine of liquid handling robot just dispenses an allotted amount into the test tube. But more complicated machine not only just dispense the liquid, it can also change the position of the test tube, can take the test tube and keep in a spectrometer for the analysis and can also include many other laboratory devices. The machine has more than 94% accuracy in the testing for which it is well suited in laboratories.

Keywords: Cartesian Coordinate System, Contact Dispensing, Liquid Handling Robot, Pipette, Robotic Arm, Stations, Throughput.

 DOI: http://dx.doi.org/10.31838/jcr.07.04.55

INTRODUCTION

As the technology is increasing, the creation and exploration of new things happening actively. Those things need to be processed, observed and further have to be analysed under critical conditions. Bioassay is one of the important things now a days. We need to analyse and determine the concentration of a substance based upon the living cells and the tissues inside it. By that we can monitor the environment quality, we can improve the quality of the food product. For the biological testing, they need to be exposed in small units like multi well plates for prolonged incubation period. To analyse and observe, well equipped laboratories are required, which include state of art equipment. When these come into picture, human errors can be minimized. Laboratory based Liquid Handling Robot is the one among the equipment's which will buttress the scientist's exploration.

The biology research laboratories and drug develop centres are the one which have very less contamination of the sample by using the liquid handling robot [1] which are multifunctional work stations and also which have more than one pipette which can add so many reagents at a time. The stations make sure to measure the liquids adding them with reagents and assure the reaction is successful. The automated work station and measuring the liquids is the resilient feature to be considered while purchasing. Other important features which are considered while purchasing the Liquid Handling Robot is the size of the footprint and its use, software interfacing. So, we include these features in our model.

Liquid handling [2] is an application which fills by a volume of product opposed to weight or level. In the chemical field, there will be high, medium and low viscosity liquids. When viscous liquid senses any external touch, their viscosity might get affected. That may affect the result. So, to overcome the problem we need Liquid Handling robot. There are two ways to go with the building of the Liquid Handling Robot. One method is to build based on the robotic hand model. The other is to build it based on the 3D printing technology which includes Cartesian co-ordinate system. The robotic arm mimics the human hand. The arm includes multiple beams which are connected to multiple hinges. They are operated and powered by the actuators. One end of the hand is still and it is connected to a base. The other end will be moved with the help of hinges which are powered by the actuators. At the other end we attach the pipette or syringe to pick and place the desired liquid.

The latter is based on 3D printing technology [19]. We have implemented the robot based on Cartesian co-ordinate system, where the axes won't rotate, but move in a linear way. This is the most effective system and also widely used in industries as they are simple in mechanism and also the construction is not convoluted. One of the most prominent application is 3D printer and CNC (computer numerical control) machine. The simple application is to draw and create a design which is precise. It done by the pen or router with the help of milling. The pen moves through the X and Y direction and at the position it is raised and lowered for the drawing. Machines used for the pick and place are based on the Cartesian coordinate technology. In the z-axis we kept the pipette, which will pick the liquid and place in a test tube which is at a desired position. As per our requirement, there should be three stations in the workspace. They are- Pickup, Mixing, and Cleaning. In the first station, the pipette will absorb the liquid into it. The user will specify test tube in which it has to be disposed. The pipette will move to that particular location with the help of X, Y and Z axes. In the cleaning station the lid will be dropped into the ethanol liquid. The ethanol solution will act as anti-bacterial solution. We can add some modules (add-ons) to the Liquid handling robot for further analysis. They include heat modules, shakers, test tube pickers of some colony pickers, spectrometer etc. some Liquid handling robots use Acoustic model which include usage of the sound instead of using the pipette or syringe.

There are two types of Liquid Handling Robots – 1) Automatic 2) Semi-Automatic

Automatic: This is a type where the robot doesn't need any operator assistance. The liquid that need to be filled in the test tubes are kept in the pickup station. Instead of having a single channel pipette, it will have multiple channels. The liquid is taken and it will fill the no. of test tubes which are mentioned in the program. So, this is totally based on the program, and we need to mention everything i.e. pickup quantity, no. of test tubes to be filled and no. of rounds to be repeated etc.

Semi-Automatic: This is a type where the robot needs an operator assistance. The liquid that need to be filled in the test tubes are kept in the pickup station. It can have single pipette or multiple pipette which is decided by the user. The liquid is taken and it will fill the no. of test tubes which are mentioned by the operator. So, this is not totally based on the program, but only the pipette pickup quantity is mentioned in the program and remaining things will be asked.

We built Semi-Automatic, so it is not fixed and can be used by various users according to the user's requirement. Control software is a very important. It can be either on a connected computer, or can be directly integrate into software. When we directly integrate in the software the amount of liquid to be added and other information is included in it or allow the user to customize. The control software that we use is Arduino IDE interfacing with Raspberry Pi. The user interface software used is Marlin.

METHODOLOGY

Design of the machine

The design of the model is done in a software. But the hardware of the model [4] is built with the required dimensions to satisfy the working function. There are many conditions and parameters to keep in view to fabricate the model and also to design it. There are many processes involved. We designed the model in the software as our reference to fabricate the actual design model. The main aim is build the model involves low cost and small size and easily carriable. As we use the 3D printing technology, the model might partly depict the 3D printer. The dimensions of the model is 80 x 60 x 40 cm. There are 3 dimensional moments which are in X, Y and Z directions [8]. All the moments has to be in synchronization. The core moments are X and Y axis. The Z axis will control the movement of the dispensing. The motors used in this mechanism are three servo motors. Two are for X and Y axis each, for the to and fro movements. And the Z axis need one for up and down movement. A stepper motor is fixed to the lead screws to control pipette movement. The gap in between the test tubes should be 1cm. The accuracy the machine should have is ±1mm distance between the test tubes and ±1ml for sucking the liquid.

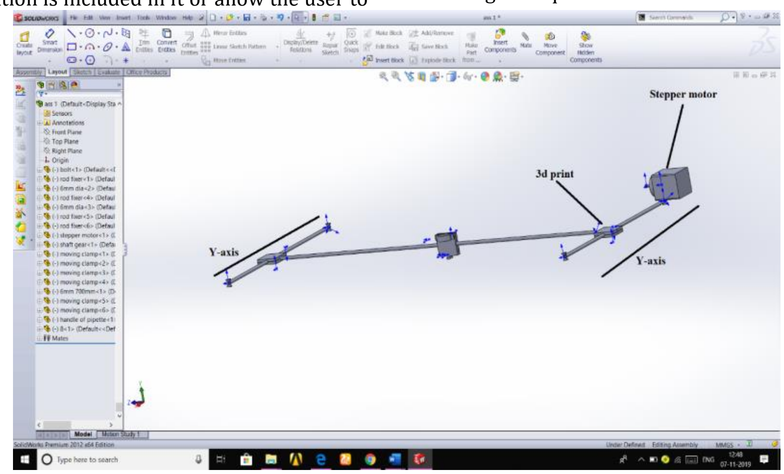

Fig. 1: The basic machine axes of the system which is based on the Cartesian coordinate system with a stepper motor mount

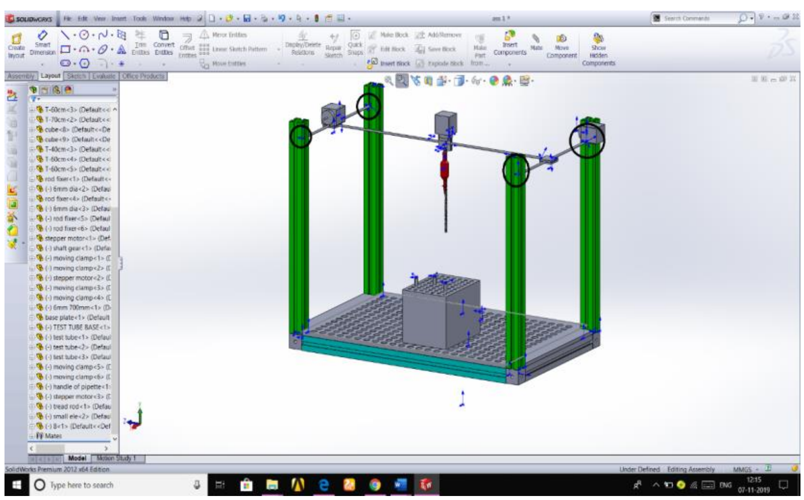

Fig. 2: The highlighted portions indicate the holes on the Aluminium T slot that are made to fix the cylindrical rods for the axes

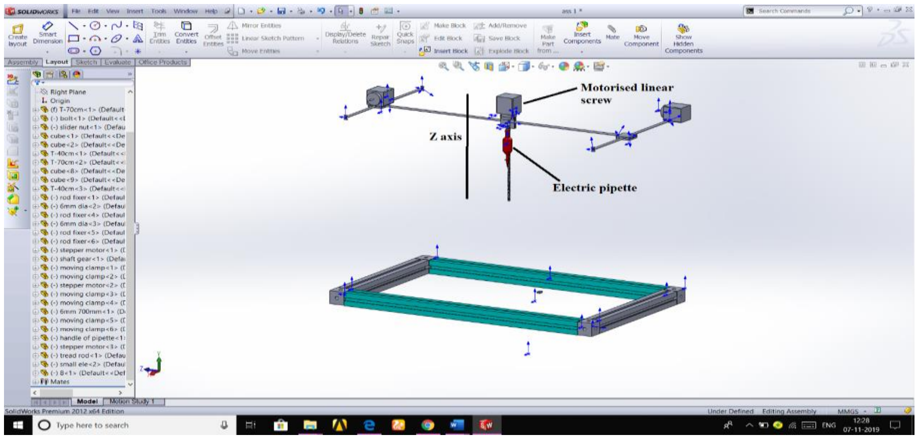

Fig. 3: The below part is the upper part of the frame onto which the axes are to be mounted

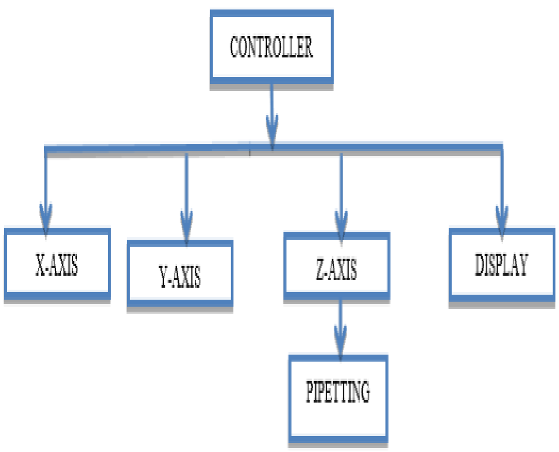

Fig. 4: System flow block diagram describes the process flow of the system controller

Arduino is the controller in this Liquid Handling Robot. The control program is dumped into the Arduino. Accordingly, the instructions are been transferred to the axes and display. X axis and Y axis are the movement controllers. They guide the pipette to the designated location. The location may be given by the user or programmed in the computer. When going to a particular location, there might be multiple paths to reach the position. But we require the best, simple and fast reach path. So, depending on the present location it will check the possibilities and will move towards the designated position. The next comes the workstations. The main components of this robot workstation, which integrates the dispensing heads and actuators, substrates, robots, washing modules. And we keep all the sensors together for high precise of automation. Now coming into to the Z axis. The working of the z axis is very important. All the liquid dispensing [9] is done by the Z axis. So, there shouldn't be any error for the measure of liquid picking and dispensing. There are two types of dispensing technologies 1) Contact dispensing [10] 2) Non-Contact dispensing [11].

Contact Dispensing: Contact dispensing is a one of the important dispensing technique which include the touch of the pipette with the substrate and the liquid will be dispensed. When the liquid touches the substrate, a drag back action will occur, so to avoid the surface tension in between the liquid and the pipetting lid. This contact dispensing is one of the popular dispensing technique because of its simplicity, reliability, and it can be implemented in low cost. It dispenses in a small volume of liquid like from Nano litres to micro litres range. To do this reliable dispensing, a perfect and accurate positioning system is required. We need to take precaution with the pipette lid. It shouldn't have contact with any other material, if not the lid may break. We need to change the tip, after each and every operation to avoid the contamination of the substrate.

Non-contact Dispensing: Non-contact dispensing is not common technique that is used in the industries very frequently. It has some disadvantages when we compare it with the contact dispensing. The liquid will be dispensed from an orifice. There won't be any contact between the substrate and the liquid. There might be the possibility of error happening. The most common non-contact dispensing method used in the industries is Inkjet printing technology. We used Contact Dispensing. Contact Dispensing is very easy to be processed. It is more precise dispensing method especially at the bead dispensing. It can't be dispensed without contact. The contact can act as an acknowledgement for the robot, after that the liquid is dispensed. There is no stress for the user as it dispenses smoothly. The process is very slow. This can be advantage and also a drawback depending on the application. For the display we have used Marlin software interface. The Marlin firmware runs on the control boards of the machine with which we interface it. The firmware will manage all the activities of the machine and maintain the synchronization between the stepper motors, drivers, sensors, actuators, buttons, displays etc.

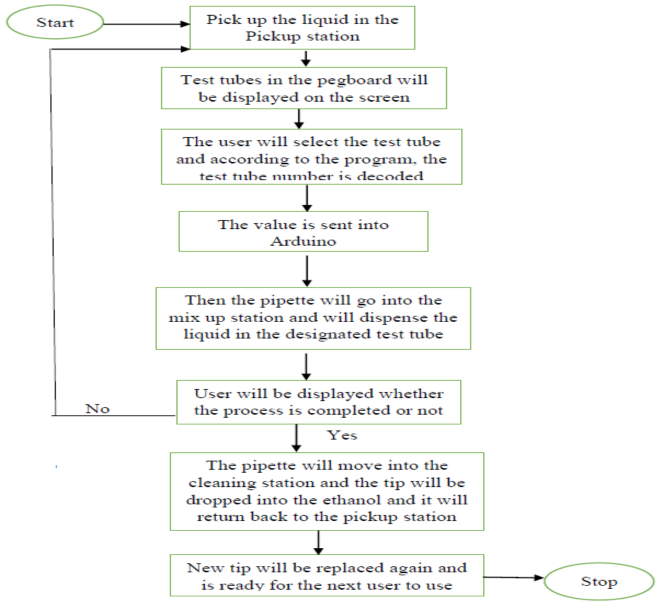

Fig. 5: The flowchart describes the entire processes and methodology of the machine.

When the power is switched on, the controller will be activated and it will power all the motors through motor shield. We have fixed DC motors for the X, Y axes, and Stepper motor for the Z axis. All the motors are further connected to the motor shield. Raspberry Pi is also powered on which is interfaced with Arduino. The Raspberry Pi display is also powered on. X, Y axes doesn't require any positioning operations. So we used DC motor. But for the Z axis position is very important. So we used Stepper Motor. Depending upon the application the type of stepper motor is decided. After that all the axes will move to the initial position. Delimiter switches are used to detect the end of the axes. Each delimiter is placed at one end and accordingly is programmed in the code. Z axis delimiter switch is connected to the stepper motor. The pipette will move up which is its initial position. After that a condition will be checked for force stop. After each and every operation, this condition is checked. It is the time for the user to give the input. The inputs include the position of the test tube into which the reagent should be added, no. of times the process has to repeat, amount of the reagent to add each time. Each and every input given will be executed in the form of a queue. Incubation time is calculated. Then the pipette will move to the pickup station. Pickup station is the one where the solution or reagent will be present. X, Y axes take the pipette to the designated location. Then, an acknowledgement will be passed as the position is reached. Then the stepper motor attached to the Z axis start and slowly the pipette goes down. After the pipette is in contact with the test tube, an acknowledgement is passed to the system. Immediately the pipette start to suck the liquid satisfying the user's input. After that, the pipette again moves up to its initial position. Then the system will check the position that the user has given. The dropping location will be in mixing station which is the second station. The dc motors start moving towards the position. After reaching the position, system will get an acknowledgement. Then again the same process will be repeated as mentioned above. Then the system will check the next process in the queue. Again the axes will be set to initial positions. The same process mentioned above will be repeated. After the execution of each and every entry in the queue, the system will get an acknowledgement saying the mixing process has been completed. Then the system will take the pipette into the cleaning station by moving the axes. Ethanol is present in the cleaning station. The position where the pipette has to stop in the cleaning station is programmed in the system. It will stop at that particular position. Then the pipette will release the lid and the lid will fall into the ethanol. Now we again fix the lid to the pipette. All the axes will be moved to their respective initial positions. The system is again ready to take new inputs from the user.

RESULTS AND DISCUSSION

We have prepared to models, one is simulated and the other is simulated and constructed. The first model is built, as it is not fulfilling our requirements, we have gone for the second design. It worked well and fulfilled our requirements.

First Model

The first designed model is in MATLAB. The model is Liquid Handling Robotic Arm [5] [12] [15]. The toolbox used to implement the design is 'Open Manipulator'. This toolbox is very useful because, there are some files in it which gives the robot pre visualization for us to re-correct it. We can use these libraries in MATLAB.

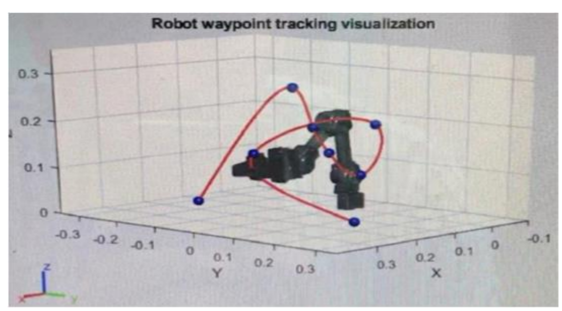

Fig. 6: This is the first model of our Liquid handling robot which is done with the help of open manipulator

Reasons to go for Alternative

Though the design is highly recommended, it takes a lot of effort and money to maintain it. The design which we desire to develop has to be within 2-3 lakhs. But the design can't get completed within the given budget. The accuracy we need is less than 2mm. But if we compromise on the budget, we might miss the required accuracy. The motors that to be used need to be very smooth. We need to have 360 degrees servo motors for the smoothness. Multi micro pipetting can't be possible with the robotic arm. The base might be an objection to the test tube plates and can affect the end result. The design also to be equipped with a spectrometer to analyse the result, i.e. whether the mixture that the robot had mixed reaches the requirement or not. When we go with this design the building might be complex.

Second Model

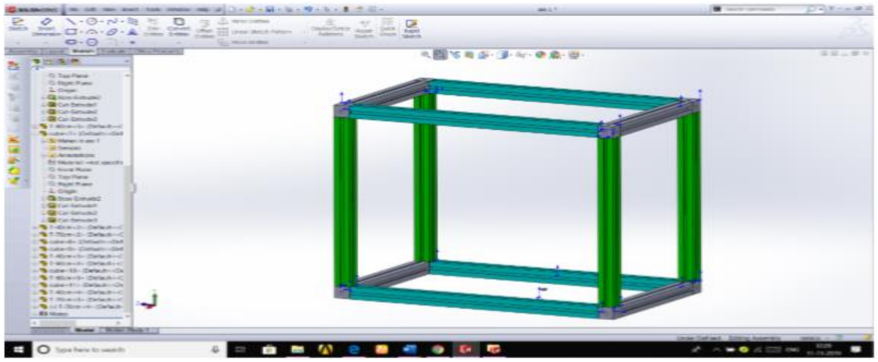

Fig. 7: The end result of our machine system designed in solid works

This is the basic frame of the Liquid Handling Robot. This is the simulation model done in Solid works and analysis is done Ansys [13]. The frame dimensions are 80 x 60 x 40 cm. The frame is built by Aluminium T slot 2020 which is used in all the manufacturing of CNC [16] Laser Engraving Machine, 3D printer, Camera Sliders, Robotics. We constructed the frame in cuboid shape. To join the frames, we used M5 T sliding nuts and L-Shape Interior inside Corner Connect.

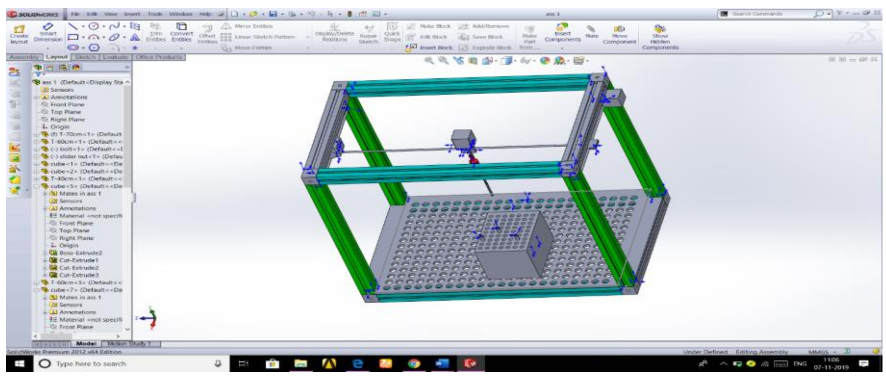

Fig. 8: This is the top view of the frame. This include pegboard and test tube holder in it

In this X axis the Z axis mount is placed on it. The motion which comes by the motor in Y axis is converted to a linear motion. The linear motion has to go onto the timing pulley belt. It goes by the help of flange bearings. The pipette tip is the main part of the machine for functioning. The leading screws are provided for its movement in the horizontal direction. We can connect the pipette to one side of the cylindrical rod. But that may result in the imbalance and machine failure. To avoid that we have connected it for two rods for the balance. Now the pipette rod is fixed. The rod to which the pipette is connected to is slided into the holes of Y axis which moves in vertical direction. The timing belt is mounted on to the pulley. It is driven by the motor which is on one side and the other side is mounted with other pulley.

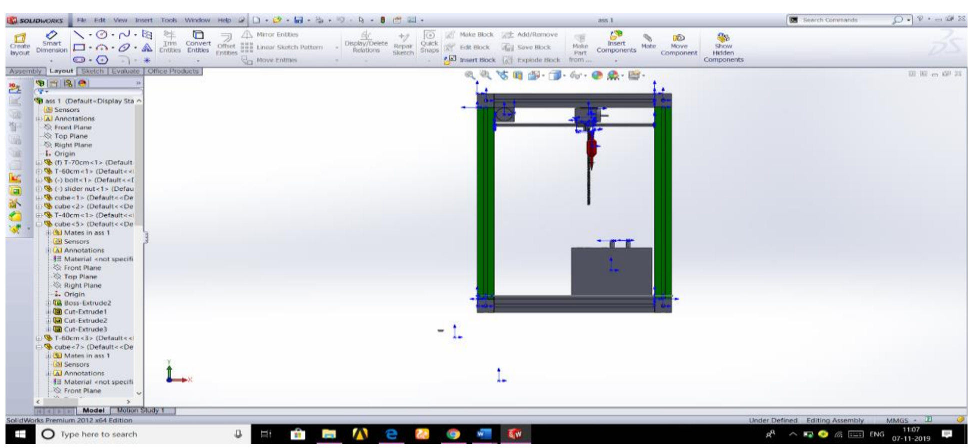

Fig. 9: This is the side view of the machine in which we can clearly see the pipette and the motor mounts

The rotatory motion of the motor is the one which helps in the linear motion of the axes. The rods to which the X axis is connected to are fixed to the Aluminium slots to the side of the machine. With the help of the linear bearings the movement and sliding in the X direction is done smoothly [20]. The rods are fixed rigidly. For the movement in the X direction also we will take a timing belt pulley to transfer the linear movement. Here also the timing belt pulley is driven by the motor which is on one side and the other side is mounted with another pulley. The X axis mount is fixed to the lower side of the belt. So, when the motor moves, the belt which is connected to it will also move accordingly. The timer belt will move accordingly with the orientation of the motion. If we fix one direction of the rotation to move the belt front and back, when we reverse the direction the direction of the belt also be reversed. The motors should be in a great synchronization for perfect functioning of the machine. For keeping the motor mounts, we have designed carriages. For the mechanism of the X and Y axis we keep the carriages. The carriages which we keep in the machine are symmetric. So, there is no worry for the imbalance of the machine. The carriage dimensions are decided according to the dimensions of the motor mount, pulleys and the holes which hold the cylindrical rods.

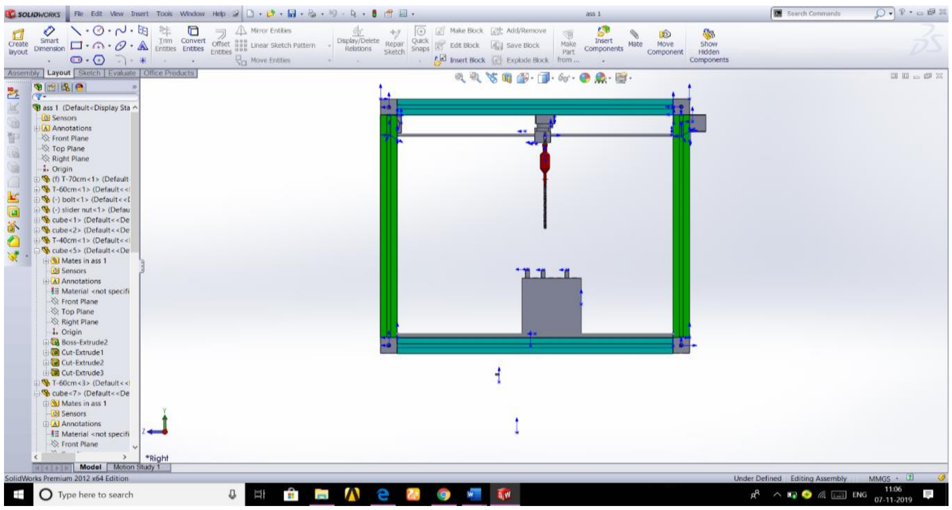

Fig. 10: This is the front view of the machine. We can clearly see the Z axis motor mount which is fixed on the Z axis, test tubes in the test tube Holder

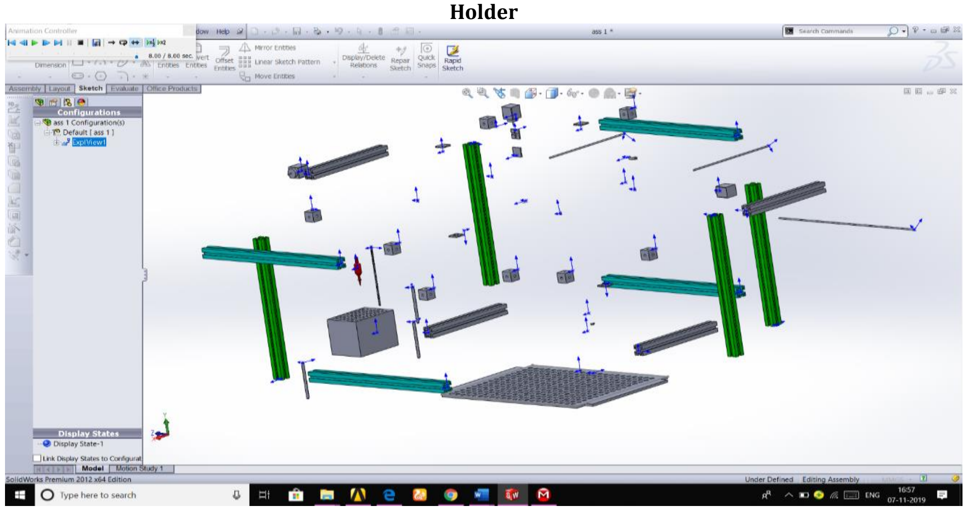

Fig. 11: This is the blast view of the system in which we can see each and every component that we used for the designing of the machine

The rotary motion of the motor is converted into linear motion by stepper motor lead screw. The Z axis rod is fixed to the mount of the X axis which is placed at the centre of the frame and this z mount contains the electric pipette which picks the solution and places it in to the given test tube by giving instruction through Arduino Program. The blast view includes all part which are constrained in making this frame. This shows the components of the machine separately and also separated by certain distance in the three-dimensional space. It can also be called as the exploded view.

Futere Developments

Spectrometer is a very essential scientific instrument which analyse the continuous variation in the physical phenomena of the liquid and also can separate the spectral components of the liquid. As the spectral components are mixed variedly, the reaction happens differently. But sometimes the reaction can't happen completely. So as we keep the reaction into the spectrometer, it checks the acidic/basic reaction and will display the result. We will check the result with our requirement and accordingly take the decision.

CONCLUSION

The Application Based Robot is a very useful machine which could decrease the human effort and increase the accuracy and success rate of the chemical and bio medical experimentation. A robust liquid handling machine is done which could dispense the liquid into a test tube with at most accuracy and precision. According to the observation, a highly viscous liquid dispensing has to be very particularly careful as there can be a lot of result change for a minute mistake. Based upon the theoretical analysis that is made, the dispensing height from which the liquid is being dispensed is very important. The height is designated in the program and accordingly the limiter switch is set. The machine has more than 94% accuracy in the testing. The testing is done for mixing a reagent into ten given test tubes. The main component used to construct the frame is Aluminium T- slot. We can go for Aluminium V- slot also. But when we compare the both, constructing with the T- slot makes the construction simple for the model. The advantages and disadvantages are compared between the robotic arm and 3D printing technology. There are less complications in the 3D printing technology, so based on that technology the machine is build. One of the arising laboratory instruments where the work can be done with high end degree precision.

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