DESIGN OF INNOVATIVE PERFUSION SYSTEM FOR IN-VITRO DRUG TESTING

Suvam Pokharel[1], Karan Venaik[1]
Hassan El-Kishky[1], Nael Barakat[1], and Ayman K. Hamouda[2]
[1]College of Engineering, University of Texas at Tyler, Tyler, Texas, USA
[2]Fisch College of Pharmacy, University of Texas at Tyler, Tyler, Texas, USA

ABSTRACT

A perfusion system is used by researchers to test the effects of chemical libraries in a potential biological target. This project is aimed at developing a medium throughput perfusion and drug exchange system for drugs testing under conditions that simulate normal biological conditions. The proposed system is governed by a computer-based control system that will allow for remote operation and control via secured access. Moreover, the proposed perfusion system will allow testing of a wide spectrum of the circulatory fluid compositions, through controlled addition of drugs, and accurate monitoring of its effect on living cells. Furthermore, the proposed system is expected to improve the throughput of current research in pharmaceutical drug screening to find a therapy for drug addiction, while enhancing the infrastructure of collaborative research at UT Tyler. Initial design data and test results are presented here, while the complete design and characterization results will be disseminated upon completion of the project.

BACKGROUND AND INTRODUCTION

Perfusion is the passage of fluids, such as blood in the case of humans, over cells in a living body, allowing exchange of components in a circulatory arrangement.[McGraw-Hill Concise Dictionary of Modern Medicine. (2002)] A perfusion system simulator is a critical device in the laboratory for simulating and testing cell reactions to any type of surrounding, particularly pharmaceutical products.

Figure 1: Current Setup used as perfusion system at College of Pharmacy

- Accurate testing of pharmaceutical products as they interact with biological cells and living organisms, as well as the ability to monitor real time response of cells, is critical to carry out effective research work that produces reliable outcomes.
- This type of testing requires perfusion system to simulate real life conditions and capture cell reactions as they happen. The system currently in use has numerous parts and occupies more space.
- A new, space-efficient, cost-effective, enclosed, remotely controlled perfusion system is designed, prototyped, and tested in this project to replace the existing perfusion system.

PROJECT GOALS

The objective of the project is to develop a cost-effective, space-efficient, medium throughput drug perfusion system using advanced engineering designing programs, additive manufacturing techniques, and medical application certified materials to simulate in-vitro cell reactions. The system will allow user remote control of an optimal number of components to be mixed and added to living cells, as well as simultaneously monitoring process parameters while reporting back to the user.

PARTS DESIGN AND ASSEMBLY

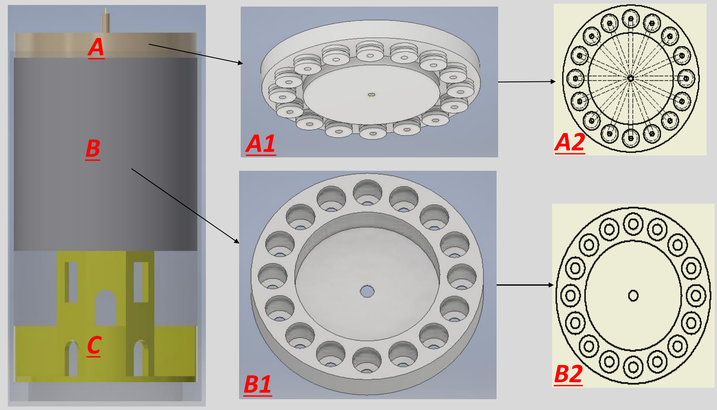

Figure 2: Assembled system containing three parts and a transparent shell covering the entire system.

Part A is the Pressure Cap whose angled view [A1] and Top Orthographic view [A2] is shown. Pressure cap is 20 mm thick and has 16 circular lids of external diameter 20 mm and a central lid of diameter 100 mm. An internal tube 5 mm in diameter runs from the top to the 17 lids to transmit equal air pressure. Part B is the perfusion chamber whose angled view [B1] and Top Orthographic view [B2] is shown. It is 155 mm tall containing 16 chambers 20 mm in diameter each and a central chamber 100 mm in diameter. Part C is the base upon which the perfusion chamber rests. The entire system is covered by a shell which is semi-transparent in the figure.

ELECTRICAL PARTS AND FUNCTIONS

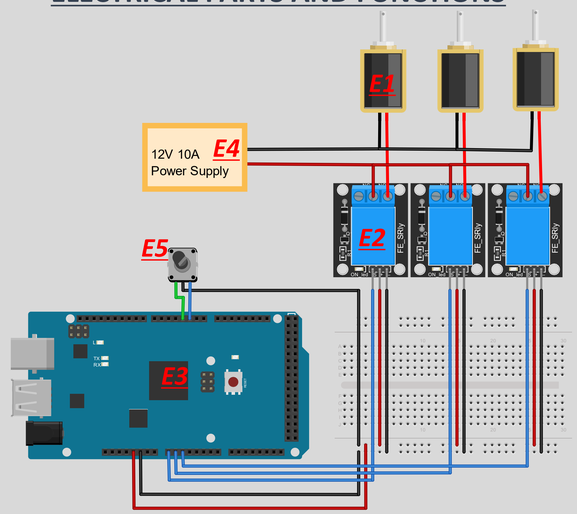

Figure 3: Truncated Assembled electrical subsystem showing five major components

Part E1 is the 12V actuated solenoid pinch valve used to control the drug flow - on applying 12V the fluid is released. Part E2 is the relay used to switch the pinch valves. Part E3 is an Arduino Mega MCU that switches the relays E2 using digital logic. The voltage required to activate the pinch valves is provided by E4. The whole system can be interacted by using the rotary encoder E5 and an Arduino shield display (not pictured).

TEST RESULTS

The CAD designs were printed, and a prototype of the perfusion chamber and the pressure cap was tested for structural integrity and leakage. The first and second set of the prototype were printed using PLA and ABS plastic, respectively. PLA could not hold the atmospheric pressure while the ABS started leaking after 0.5 psi applied pressure. Nylon 12 met our requirement of 4 psi pressure as the material was able to hold the applied pressure as much as 20 psi.

Table 1: Different materials and the maximum applied pressure held

Material Type	Leakage (Y/N)	Maximum applied pressure held
PLA	Yes	0 psi
ABS	Yes	0.5 psi
Nylon 12	No	20 psi

BROADER IMPACT

Through this project, an advanced and reliable perfusion and drug exchange system will be developed and deployed for utilization in ongoing pharmaceutical science research. It will lead to a successful development of a proven and reproducible methodology for design and manufacture of cost-effective and accurate drug delivery systems for medium throughput drug screening. The project will have a significant positive impact on academic drug discovery and will pave a way for academic institutions like UT Tyler to apply a cost effective and highly efficient drug screening method in future researches.

FUTURE DESIGNS

1. After successfully testing the prototype, an enclosure for the entire perfusion system along with electrical parts.
2. The enclosure/housing will need to accommodate Arduino, shield display, rotary encoder, power inlet, and the existing mechanical parts of the perfusion system.
3. WiFi/Bluetooth capability will be added to the system to upload perfusion schema to the system wirelessly as well remotely.