Autonomous Microbioreactor-Inator

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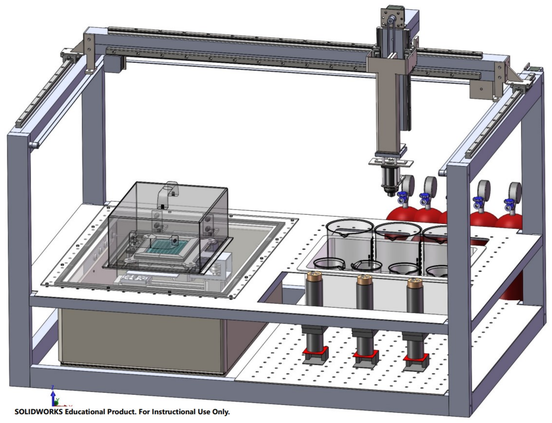
Abstract & Functionality

The autonomous bioreactor we have designed has several stages. The first stage requires human interaction. A person will place cells, stressors, and cleaning fluid into the beakers, and a well tray into the machine. The machine will fill the tray with cells and varying amounts of stressor. Once that is complete, a person will close the well tray chamber. In the experimental stage, the well tray is consistently shaken in linear, orbital and double orbital patterns and enclosed in a chamber which can be set at a temperature between 4°- 70° Celsius. For the third stage, a person opens the lid to the well tray chamber and an ODFI sensor observes the effect of the stressor on the cells. The living cells in each well are identified and moved to the cell proliferation stage. This consists of Turbidostats, small enclosures where the surviving cells have the necessary environment to grow. Once new cells have grown, they will be distributed back into the well plate for another round of experimentation with a higher concentration of stressor.

Most microbioreactors require a person to distribute cells into the wells of the well tray. This is a delicate process because if cells are not placed gently into the wells, they will die on impact. The Microbioreactor-Inator completes this process automatically. Therefore, the Hedgehog Concept for this machine is that this design requires the least amount of technical knowledge of any on the market.

Final Design



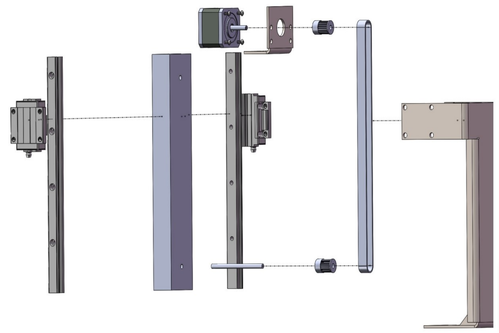
Subsystems

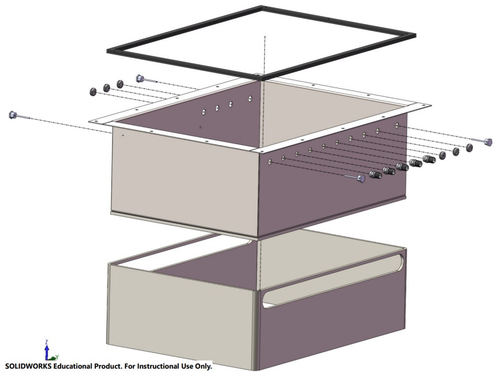
- Liquid Handling – Distributes necessary fluid to each conical tube
- Liquid Control – Accurate and precise movement of liquid between beakers, Turbidostats and well tray
- Chamber Enclosure— An enclosed, gas-regulated space where well tray sits
- Chamber Control – Temperature control for the chamber enclosure
- System Interface – Interface which allows for easy machine and user communication. This subsystem is not shown; however, it consists of an iPad and an iPad stand, and contains controls for the rest of the system.
- Well Tray Movement – A shaker which gives necessary motion to the well tray to promote the oxygenation of cell cultures
- Optical Density and Fluorescent Intensity – A sensor used to identify living and dead cell cultures with optical and light identification

Other components are off-the-shelf parts which include beakers, gas canisters, Turbidostats.

Key Features

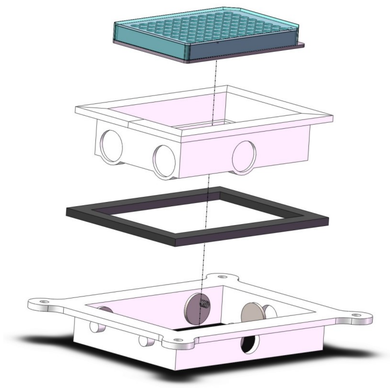
The belt and linear bearings shown control the movement for the liquid control subsystem. The depicted system shows the movement along the z-axis by means of a belt and pulley.



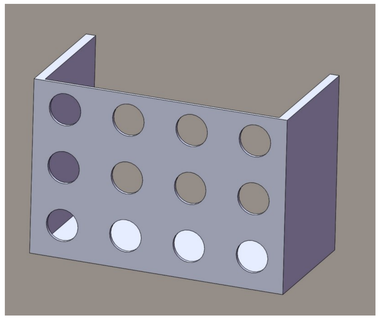


This is the chamber enclosure in which the incubation chamber will lie. This design was chosen to encompass the size specifications of the microbioreactor processes. Rubber padding is used to create a seal to dampen unnecessary vibration.

This is the platform in which the well tray sits while it is shaken. Two linear actuators will be simultaneously pushing, along the x and y axis, against the platform to create motion. Two springs rest against the sides of the tray opposite to the actuators to return the tray to its initial position. This movement allows for linear, orbital, and double orbital shaking patterns.



Unique Features



The most unique feature of this microbioreactor is the application of phase changing wax as a control for temperature within the chamber. During the experimental stage of function, a constant temperature must be able to be maintained within the chamber. Phase changing wax comes in many different compounds; each compound will reach the point where it changes phases at a different temperature. Thermodynamic laws prove that when a substance is changing phases, it maintains a constant temperature. This application will require the user to choose a wax, heat that wax to its phase changing point, then place it in the pocket above (located inside the chamber) to maintain the chamber at a consistent temperature.

Cost Overview

Cost Category	$	Description
OTS Parts	5096.90	OTS part cost
Modified OTS	431.50	Modified OTS part cost
Raw Material	1170.10	Total sheet metal and Al Extrusion cost
Manufacturing & Labor	700.00	10 hours at an average machine shop cost of $70 per hour.
Energy Consumption	N/A	Energy required to manufacturing included in machine shop cost
Assembly Labor	130.00	10 hours for a Research assistant salary of $13 per hour
Total	7528.50	Total Cost

Customer Requirements	Metrics	Functions	Subsystems
C1: Fit inside a research facility on a benchtop	M1: Minimize area (mm^2)	F1 (C1): CE can fit inside a research facility on a benchtop.	Chamber Enclosure
C2: Runs power from standard wall outlet	M2: Requires system wattage to be less than 1800 (W)	F2 (C2): System requires 918.21 W to operate.	
C3: Easily accessible	M3: Must minimize the height of the system (ft)	F3 (C3): CE is accessible to users of average height.	
C4: Assembled/disassembled with minimal know-how	M4: Minimize the number of parts in the system (#)	F4 (C4): All subsystems designed to limit parts required.	
C5: At least 1.15 factor of safety	M5: Requires a minimum factor of safety of at 1.15 (#)	F5 (C5): All mechanical components have at least 1.15 FoS.	
C6: Include fail-safe system with alerts	M6: Maximize number of ways the user was alerted (#)	F6 (C6): iPad can display system alerts on screen.	
C7: Include emergency shut-off system by user	M7: Maximize number of emergency shut-off switches (#)	F7 (C7): iPad interface includes emergency shut-off button.	
C8: Include automatic force-based safety limit switch	M8: Have six or fewer limit switches (#)	F8 (C8): LC & WT subsystems include limit switches.	
C9: Visual indicator off on/off switch and alerts	M9: Maximize the number of visual indicators (#)	F9 (C9): iPad screen serves as visual indicator.	System interface
C10: Minimal operational lifetime of 10 years	M10: Maximize operational lifetime > 10 years	F10 (C10): All components have minimal lifecycle of 10 years.	
C11: Can not exceed $10,000	M11: Minimize cost < $10,000	F11 (C11): Total system cost falls below $10,000.	
C12: No installation of permanent supports or fixtures	M12: No installation of permanent supports or fixtures	F12 (C12): CE subsystem requires no external fixtures.	
C13: Programmable	M13: Use lowest difficulty rating of program	F13 (C13): iPad uses Swift programming language.	Liquid Control
C14: Have an intuitive user interface	M14: Maximize amount of data that can be stored (GB)	F14 (C14): iPad has a 64GB storage capacity.	
C15: Materials can not react to cell cultures/lab chemicals	M15: No reactive materials touch cell cultures (#)	F15 (C15): LH material is nonporous and nonreactive.	
C16: Meet the requirements to work in a BSL-2 lab space	M16: No BSL-2 lab space violations (#)	F16 (C16): Meets all BSL-2 lab setting requirements.	
C17: Exterior surfaces do not exceed 55°C	M17: Minimize exterior surface temperature (°C)	F17 (C17): CE exterior surface does not exceed 55°C	Well Tray Movement
C18: Capable of one hour to two-week incubation period	M18: Maximize incubation period (hours)	F18 (C18): System can be powered constantly through outlet	
C19: Can perform culture condition closed loop control	M19: Maximize closed loop-controlled processes (#)	F19 (C19): Swift language permits closed-loop control.	
C20: Can culture at a temperature range from 40°C to 70°C	M20: Maximize temperature range (°C)	F20 (C20): CC system can operate between 3°C & 93°C.	Chamber Control
C21: Fully enclosed and interchangeable vessels	M21: Minimize number of non-enclosed components (#)	F21 (C21): Incubation chamber is fully enclosed.	
C22: Accommodate 6, 24, 48, 96, deep 96, 384 culture plates	M22: Maximize culture plate size (mm)	F22 (C22): WT subsystem accommodates for all size plates.	
C23: Accommodate 15mL & 50mL conical tubes	M23: Maximize conical tube depth (mm)	F23 (C23): WT subsystem can accommodate conical tubes.	
C24: Uniformly heats wells/tubes to prevent condensation	M24: Minimize height of heating mechanism (mm)	F24 (C24): CC subsystem uniformly heats wells/tubes.	Optical Density and Fluorescent Intensity
C25: Capable of automated liquid handling	M25: Maximize degrees of freedom for LH movement (#)	F25 (C25): LC system moves autonomously on grid.	
C26: Must capture effluent gases	M26: Maximize number of gas exits and entries (#)	F26 (C26): CC system can capture affluent gasses.	
C27: Gas controller regulates N, O, CO2, Methane, and H	M27: Have 5 supply lines and 5 sensors (#)	F27 (C27:) CC has one sensor and controller for each gas.	
C28: Can measure OD and FI in all individual wells	M28: Maximize degrees of freedom sensor can move (#)	F28 (C28:) LC is able to move in the x-, y-, and z-axis	Liquid Handling
C29: Trade-offs in using monochromators vs. filter cubes	M29: Have angular orientation of 90 degrees (°)	F29 (C29): Has an angular orientation of 90°	
C30: Achieve lasting light intensity of 1 kW/cm2 at 640 nm	M30: Maximize light intensity > 1kW/cm^2 at 640 nm	F30 (C300: Wattage substitution clears req'd light intensity	
C31: Linear, Orbital, and Double Orbital shaking patterns	M31: Maximize number of degrees of freedom (#)	F31 (C31): Meets all shaking patterns	
C32: Shaking patterns and atm conditions independent	M32: Maximize number of compatible well tray sizes (#)	F32 (C32): CE sealed environment for well tray	
C33: Dispense rate of 225-300 uL/s for well plates	M33: Maximize dispense rate (uL/s) > 300 uL/s	F33 (C33): Peristaltic pump exceeds the required flow rate	
C34: Deposit volume of fluid in the range of 5–20,000 µL	M34: Maximize volume of fluid deposited (mL) > 20 mL	F34 (C34): Can far exceed amount of volume required	
C35: Dispose and neutralize waste	M35: Minimize volume of cleaning fluid required (mL)	F35 (C35): Can sanitize tubing with cleaning fluid	