Dynamic Hi-Resolution Horizontal Microscope for Monitoring and Manipulating Real-Time Tissue Assembly

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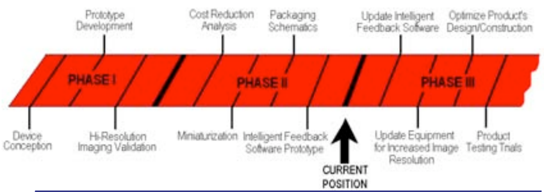
BIOMEDICAL NEED

Problem: Regenerative Medicine and Tissue Engineering lack a non-invasive technique for monitoring and manipulating tissue assembly from specific cell sources

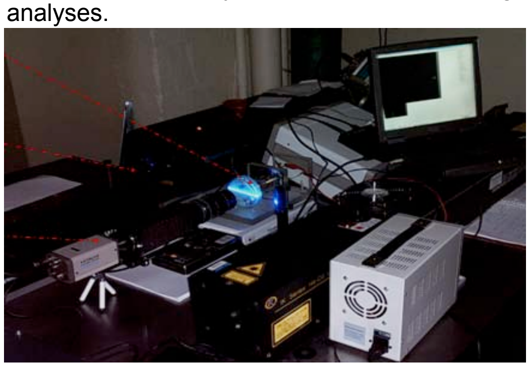
Resolution: Create an intelligent system to automatically diagnose, monitor, and control tissue growth in real-time

Approach: A versatile hi-resolution horizontal microscope that assess tissue growth parameters within a bioreactor and intelligently controls their development *in vitro*



PHASE I: PROTOTYPE SYNTHESIS

- The prototype incorporates a blue laser which fluoresces an RWV containing either calibration beads or PC12 cells.
- A hi-resolution CCD Camera captures the emission at and relays it to a computer for image analyses.



HI RESOLUTION IMAGING

Validation of the technique was confirmed by the ability to visualize both the calibration beads and cells as well as the ability to measure not only the aggregates but it's individual cells as well.

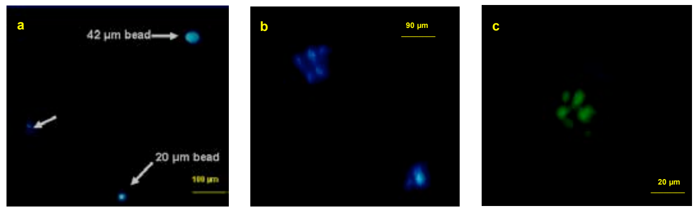


Figure 1. A.) Perceiving size differences between calibration beads. **B.)** Imaging of calibration bead aggregates. **C.)** Visualization of PC12 cell aggregate. Notice the ability to differentiate the number of cells comprising the aggregate.

PHASE II: COST REDUCTION, MINIATURIZATION & PACKAGING

- Replaced blue laser with smaller, less costly green laser
- Updated biological agents to acquire cheaper cell dyes and calibration beads
- Updated laser optics to reduce both use of mirrors and device's area

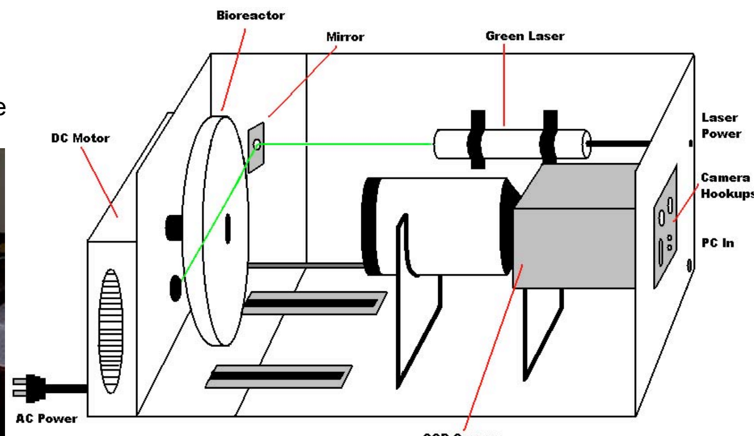


Figure 2. Schematic of current device modifications

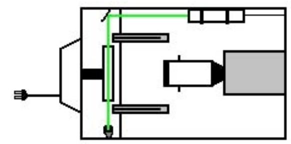


Figure 3.
Overhead schematic

- Reduced cost of system from $22,000 to $1500
- Miniaturized system from 3' X 5' to 1' X 2'
- Packaged system for easy PC connectivity and condensed power supply

INTELLIGENT FEEDBACK SOFTWARE DESIGN

1. In-house software developed to append CCD camera film files and extract images
2. Images are analyzed by the software package for size of aggregates as well as the number of cells that it comprises
3. Based upon an intelligent feedback mechanism, the package controls the bioreactor motor, thus increasing or decreasing the growth of the forming tissue

BIOMEDICAL USES

Pharmacological: Therapeutic cancer modeling in a 3-D environment to assist in the creation of high throughput drug manufacturing

Clinical: Analysis of a patient's specific cancer cell response to ongoing therapy

Regenerative Medicine: Creation of specific types of tissues. Possibilities include cardiology, neurology, wound healing, bone replacement, organ repair.

PHASE III: FUTURE WORK

Next steps require funding for:
- Upgrading and updating the intelligent feedback software
- Increasing the efficiency and resolution of the imaging analysis
- Commercializing the miniaturization and packaging
- Product testing trials upon numerous cell types