CELL-MET ERC:

Vision & Strategic Planning

Thomas Bifano
Professor, Mechanical Engineering
- Americans suffer one million heart attacks every year
- Heart disease is the leading cause of death in the US
- 2,000 people in the US die daily from heart disease, ~600k/year
- 1 in 4 Americans will die from heart disease
- World-wide, 17 million people per year die from heart disease
• By 2030, the cost to the US of heart disease will exceed $1T/year*
• Bringing a single drug to market costs ~$2.6B** and these costs are rising ~10%/year
• 40% of all drugs fail in clinical trials due to adverse cardiac effects
• Drug clinical trials in 2013 cost ~$10B, There were 6200 trials in 2013

*CDC: >$818B direct medical costs, lost productivity >$275B
** Tufts Center for the Study of Drug Development
The Economic Costs to Society

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Our Vision

Use scalable nanomanufacturing technologies to produce clinically transformative cardiac tissues
We will design, build, and test integrated 3D tissue patches that can be used for cardiac repair.
The Engineering Genealogy of Our Vision

- **Nano-Mechanics**
- **Cell Engineering**
- **Atomic Calligraphy**
- **Optical Sensing/Actuation**
- **Lab on a Chip**
- **Organic Vapor Jet Printing**
The Engineering Genealogy of Our Vision

**Nanomechanics**
Build dynamic functional scaffolds using nanofabrication tools

**Atomic Calligraphy**

**Optical Sensing/Actuation**
Use advanced microscopy and optogenetics tools to image and control cells in tissue

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**Cell Engineering**
Exploit cardiac cell biology, stem cell techniques, and cell mechanics in 3D tissue platforms

**Organic Vapor Jet Printing**
Develop cellular “glues” for focal cell attachments on scaffolds

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**Lab on a Chip**
Create functional tissue patches with increasing complexity, to be used as enablers for a heart-repair industry.
Three Plane Diagram

TECHNOLOGY INTEGRATION
- CELL-MET TEST BED
  - Optics
  - Scaffolds
  - Cellular Glue
  - Cell Assembly

WORKFORCE DEVELOPMENT
- Technology Base
  - Dynamic 3D Scaffolds
  - Optical Tools
  - Cellular Glue
  - Nanoscale Actuators & Sensors
  - Tissue Architectures
  - Multiscale Structures

BARRIERS
- Cell Adhesion
- Cell Lifetimes
- Tissue Growth

TECHNOLOGY BASE
- Nano Patterning 2D/3D
- Optogenetic Actuation
- Dynamic 2D/3D Meta-Materials
- Optical Sensing & Imaging
- Cellular Assembly
- Atomic & Molecular Glues

WORKFORCE DEVELOPMENT
- Knowledge Base
  - New Materials
  - Biocompatibility
  - Imaging tissue
  - Nano-mechanics

INNOVATION ECOSYSTEM
- Nano Assembly
- Optical Systems
- 3D Meta Materials
- Tissues
Our Ten Year Vision

<table>
<thead>
<tr>
<th>Year 1</th>
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<tbody>
<tr>
<td>Imaging</td>
<td>Microscope development</td>
<td>Imaging and optogenetically controlling cardiac tissues</td>
<td>Increase throughput and depth penetration of imaging/optogenetic techniques and develop embedded optical sensor networks</td>
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<td>Cell Eng.</td>
<td>2D cardiac bundles</td>
<td>3D cardiac tissue without vasculature “Patches”</td>
<td>3D cardiac tissues with vasculature</td>
<td>3D macro assembled vascularized cardiac tissues</td>
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<tr>
<td>Scaffolds</td>
<td>2D scaffolds</td>
<td>3D scaffolds with embedded sensors and actuators</td>
<td>3D scaffolds with complex functionality such as vessel trees, valves and conduction system</td>
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<tr>
<td>Nano Manuf.</td>
<td>2D printing</td>
<td>3D printing development</td>
<td>Direct printing of all structures needed for cardiac tissue with complex functionality</td>
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<tr>
<td>Products</td>
<td>2D Cardiac Tissues on a Chip for Drug Development</td>
<td>Cardiac Tissues with implanted Sensors for Monitoring Cardiac Function</td>
<td>Muscle Tissues that can Assist Cardiac Function</td>
<td>Cardiac Tissues Beyond Muscles</td>
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Centimeter scale cardiac tissue with complex functionality including heart chambers, large vessel trees, cardiac valves and conduction system.
## Our Workplan

### MATERIALS
- **YEAR 1**
  - Q1: Build catalog of bio-comp glues
  - Q3: Cell material interactions
- **YEAR 2**
  - Q5: Improve tissue maturation
  - Q7: Selecting/testing scaffold materials
- **YEAR 3**
  - Q11: Image Ca2+
  - Q13: Sensing/actuating cell interface

### TEST BEDS
- **Atomic Calligraphy/OVJP Test Bed**
- **Sensors and Actuators Test Bed**
- **Stem Cell Engineering Test Bed**
- **Multi-Photon Microscope Test Bed**

### TECHNOLOGIES
- **YEAR 4**
  - Q14: Assembling cardiac patches
  - Q16: Integrating sensors/actuators
  - Q18: In vitro/in vivo application
- **YEAR 5**
  - Q20: Assembling cardiac bundles
  - Q20: Embed channels for vasc.
  - Q20: AC/OVJP-2D
  - Q20: Atomic calligraphy/organic vapor jet printing-3D
  - Q20: Iterating on 2D/3D scaffold designs
  - Q20: Develop 3D assembly scheme

### CELL-MET Test Bed
- **YEAR 1**
  - Q1: Assembling vascularized 3D tissue units
- **YEAR 2**
  - Q3: Develop optogenetic tools to sense/activate/inhibit cellular tissue
  - Q5: Assembling vessels
  - Q7: Develop AO and coherent control systems
  - Q9: Volume manufacturing of glued scaffolds
- **YEAR 3**
  - Q11: Measure blood flow/tissue oxygen

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## Our Workplan

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### Interrelated Tasks

28 Interrelated Tasks
Three Plane Diagram

Techology Integration
- Optics
- Scaffolds
- Cellular Glue
- Cell Assembly

Workforce Development
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- Optical Tools
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- Nanoscale Actuators & Sensors
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Knowledge Base
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Innovation Ecosystem
- Nano Assembly
- Optical Systems
- 3D Meta-Materials
- Tissues

Cell-MET System
- Metrology
- Multiscale System
- Cellular Differentiation
- Cell Adhesion
- Cell Lifetimes
- Tissue Growth
- New Materials
- Biocompatibility
- Imaging tissue
**Strategic goal:**

Develop 3D tissue platforms and cardiac patches using enabling new science and engineering tools in cell biology, nanofabrication tools, and optical engineering.

**Work plan:**

Pursue coordinated projects that aim to produce progressively more complex 3D tissue structures involving interdisciplinary collaboration among Thrust Areas.
Listening to the Demand Signals
Inputs From:

- CELL-MET faculty who are world-class scientific leaders
- Scientific Advisory Board
- Industrial Practitioners Advisory Board
- Workforce Development Advisory Board
- Academic Policy Board
- Council of Deans
- Annual NSF review process and their referees
- Workshops and conferences hosted by CELL-MET
- Inputs from other funding agencies
The CELL-MET Annual Planning Cycle

- Annual Meeting (March)
- Progress Report (February)
- Annual Retreat (May)
- Planning/Budgeting (Summer)
- Program Year Begins (October)
The CELL-MET Annual Planning Cycle

- **Annual Meeting (March)**
  - Potential mid-year corrections
  - NSF, SAB, NSF Review Panel, IPAB, WDAB feedback

- **Planning/Budgeting (Summer)**
  - Analysis and input from CELL-MET Team
  - Review and funding decisions on ongoing programs and seeds

- **Progress Report (February)**
- **Annual Retreat (May)**
- **Program Year Begins (October)**
Thank You