3D Bioprinting of a Living Aortic Valve

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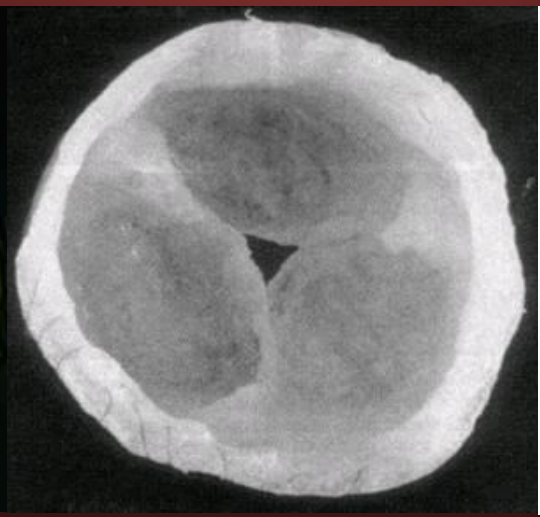
Clinical Need and State of the Art

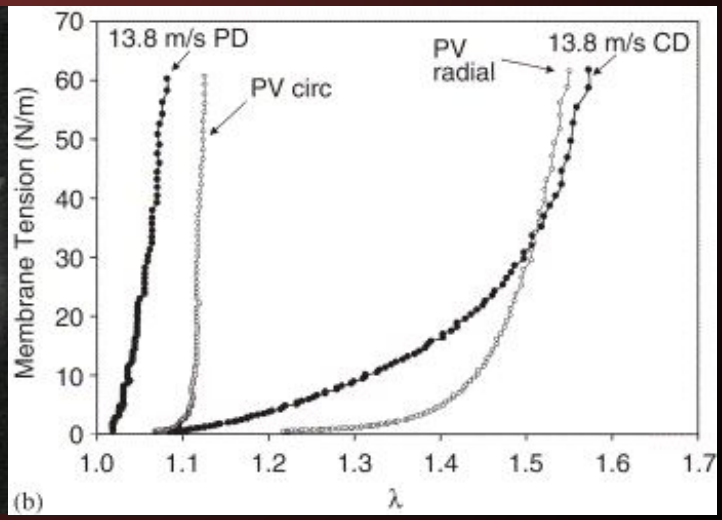
- Nearly 100,000 valve replacements annually in US
- Prosthetic valves poor choice for young/active
- Tissue engineering has potential but limited by inability to mimic 3D anatomy and heterogeneous material properties

Native Aortic Valve

TE Aortic Valve



Mechanical Properties



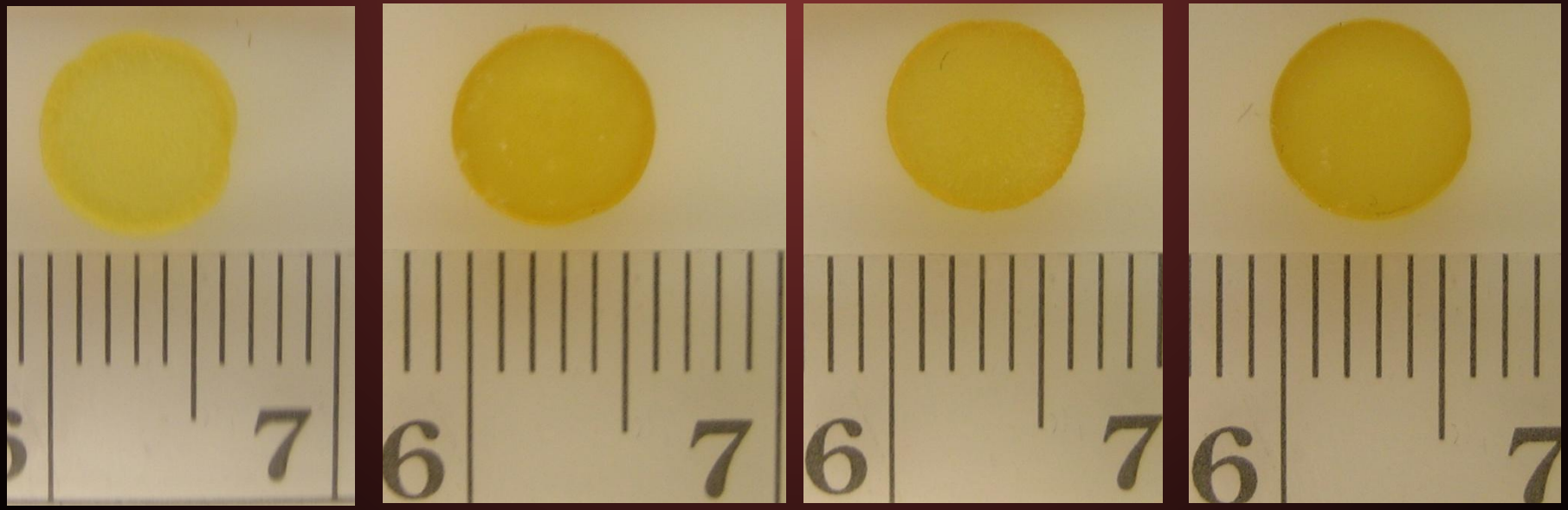
Ideal Biomaterial Characteristics for Engineered Heart Valves

- Enzymatically bioadsorbable
  - Cell mediated, non-toxic end products
- Aqueous based hydrogel
  - Can fabricate with cells distributed within matrix
- Non-thrombogenic/non-immunogenic
- Tunable material properties: crosslinking
- Bio-functionality
  - Charge, hydrophobicity, hydroxyl/amine groups

Arginine Based PEA Hydrogels (A-PEA)

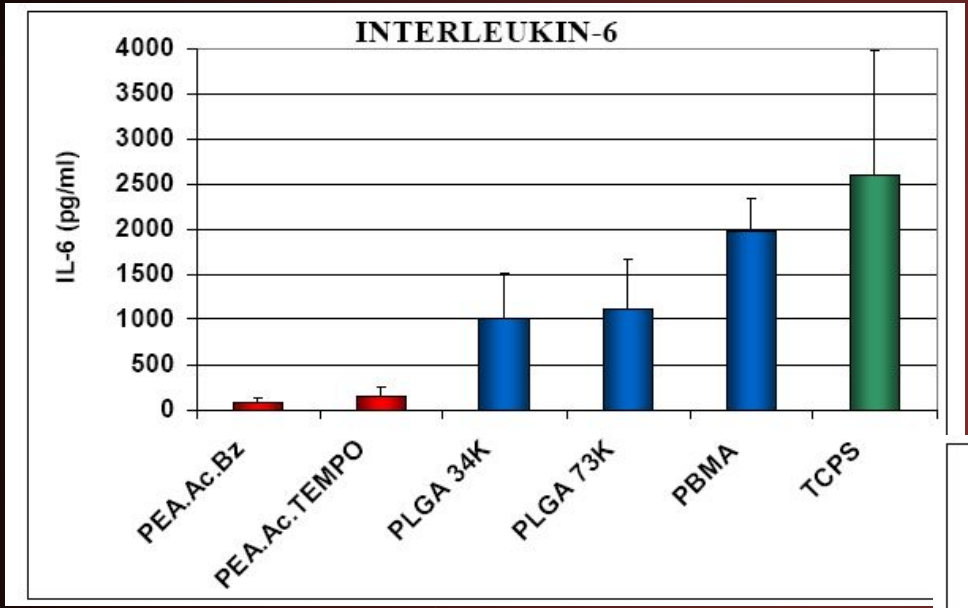
- Precursors are water soluble
- Can be photo-crosslinked by UV light
- Degraded by a variety of cellular enzymes
- Numerous accessible functional groups

WF68DA WF68DA/A2 WF68DA/A3 WF68DA/A4



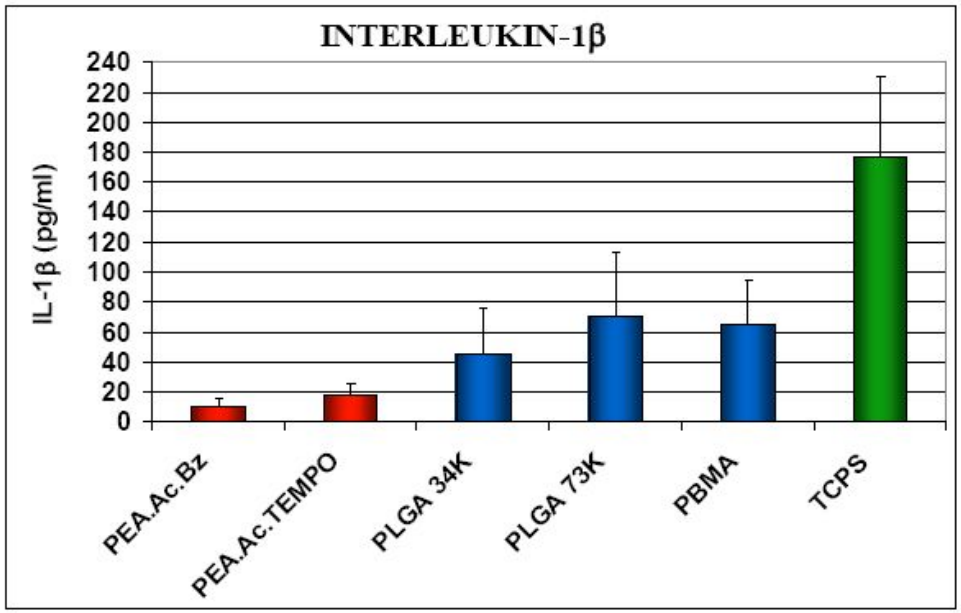
A-PEA is Minimally Immunogenic/Thrombogenic

IL-6 : proinflammatory cytokine, ↑ macrophage cytotoxic activity



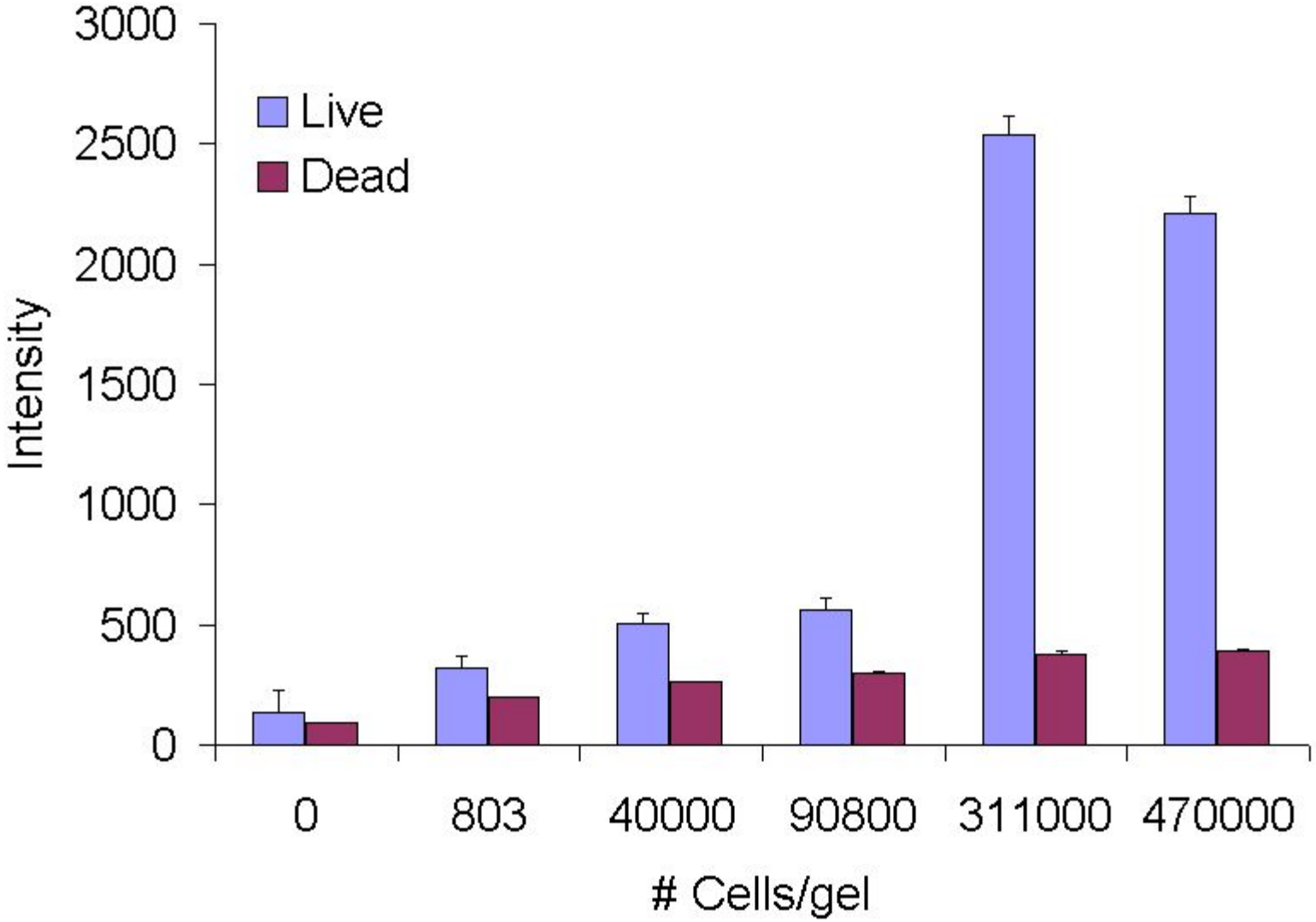
Monocytes secreted over 5-fold less IL-6 on PEAs than on other polymers, 24 hrs

Monocytes on PEAs secreted less IL-1β, a potent pro-inflammatory cytokine, that can increase the surface thrombogenicity of the endothelium, 24 hrs

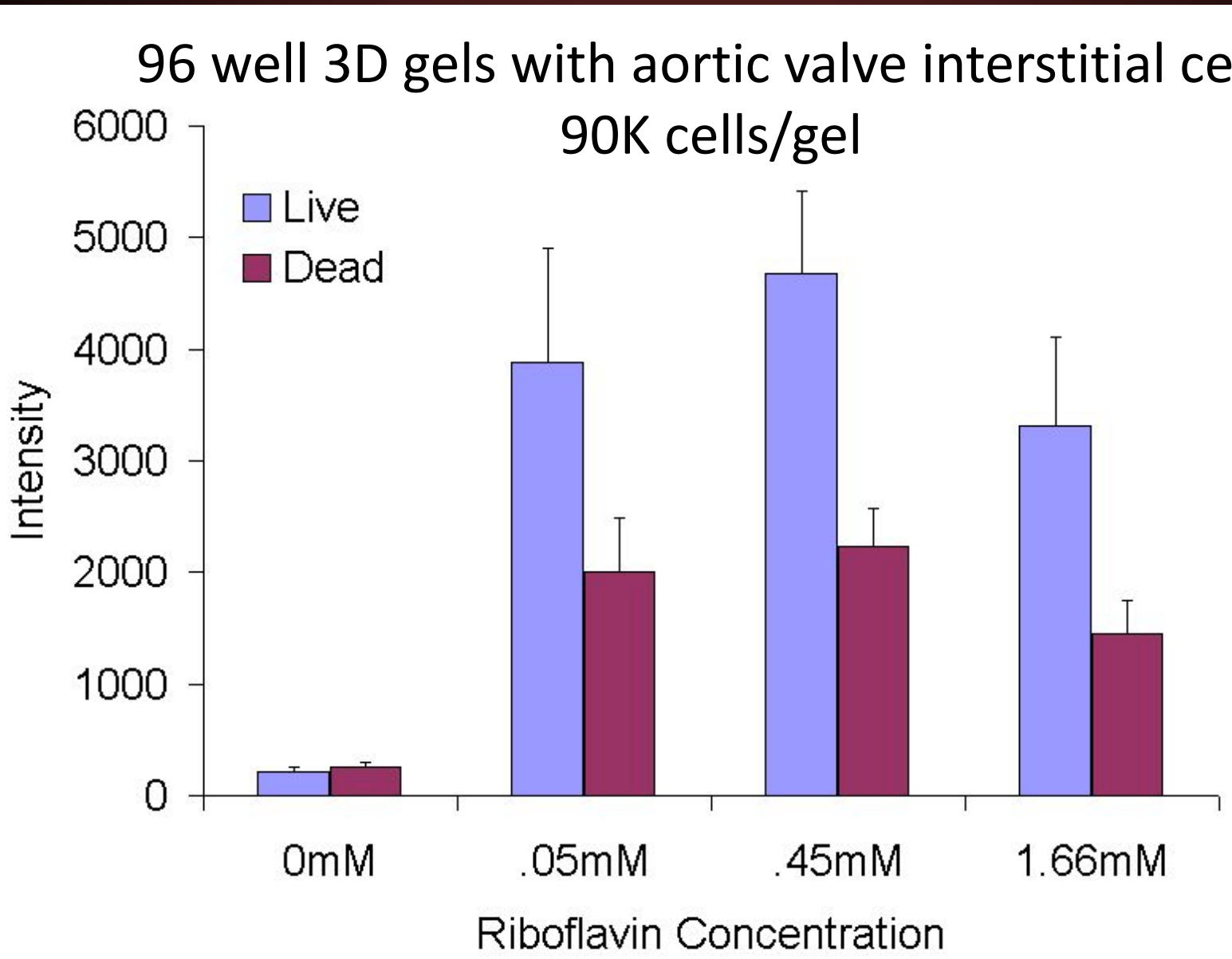


3D Hydrogel Cytotoxicity Assay

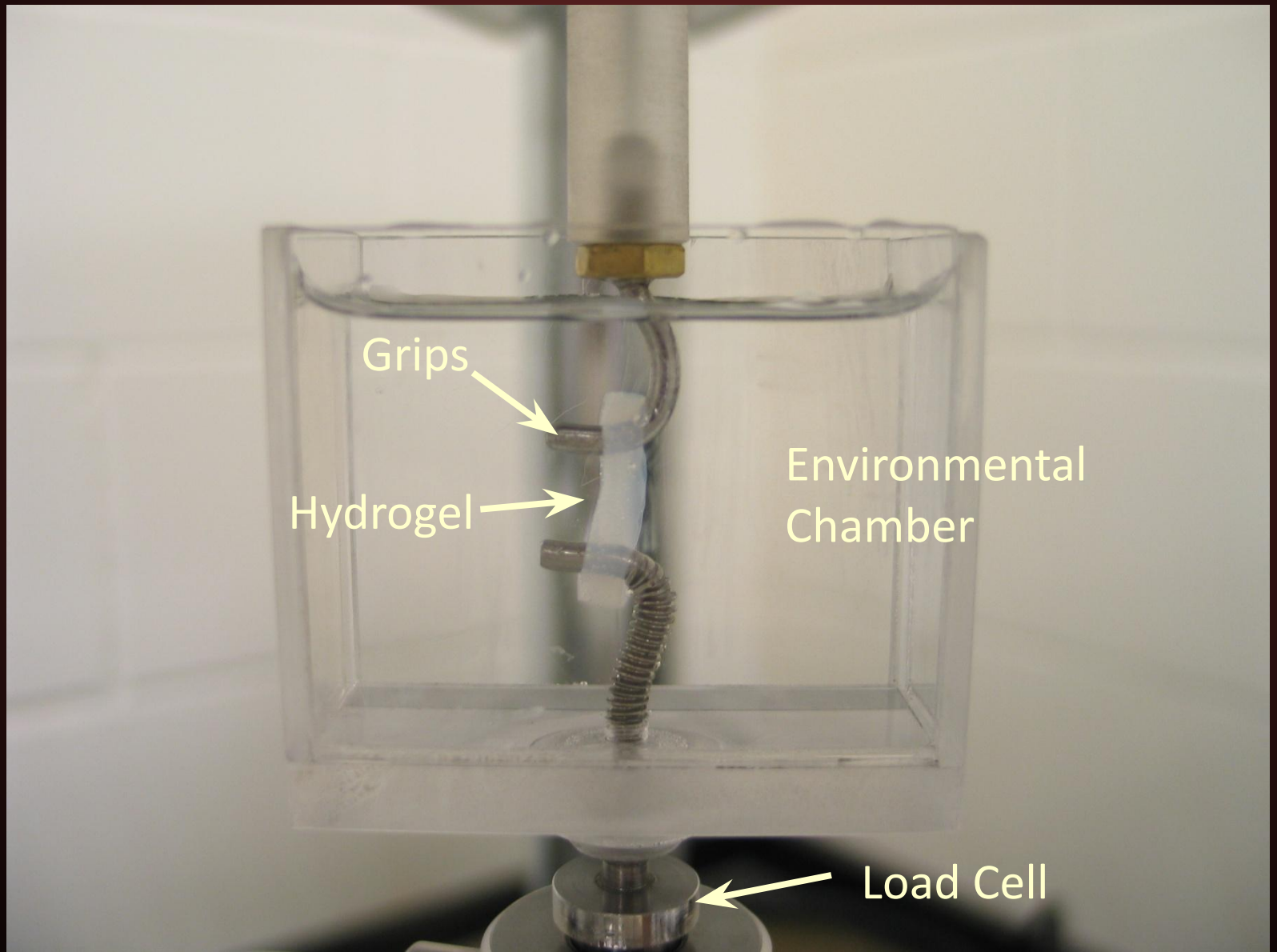
96 well 3D gels with aortic valve interstitial cells



3D Cyotoxicity with Photo-Crosslinking

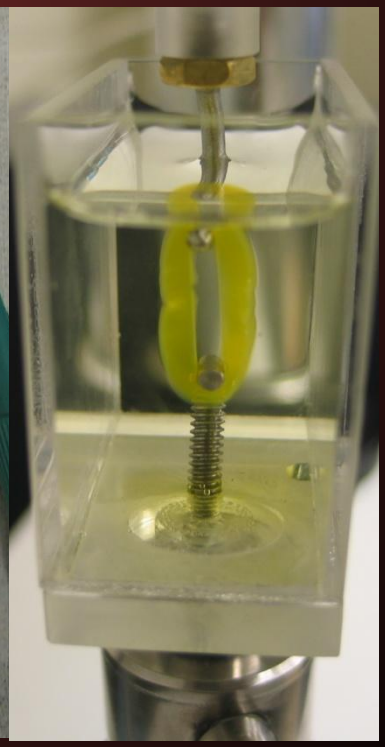


Mechanical Testing of Hydrogels

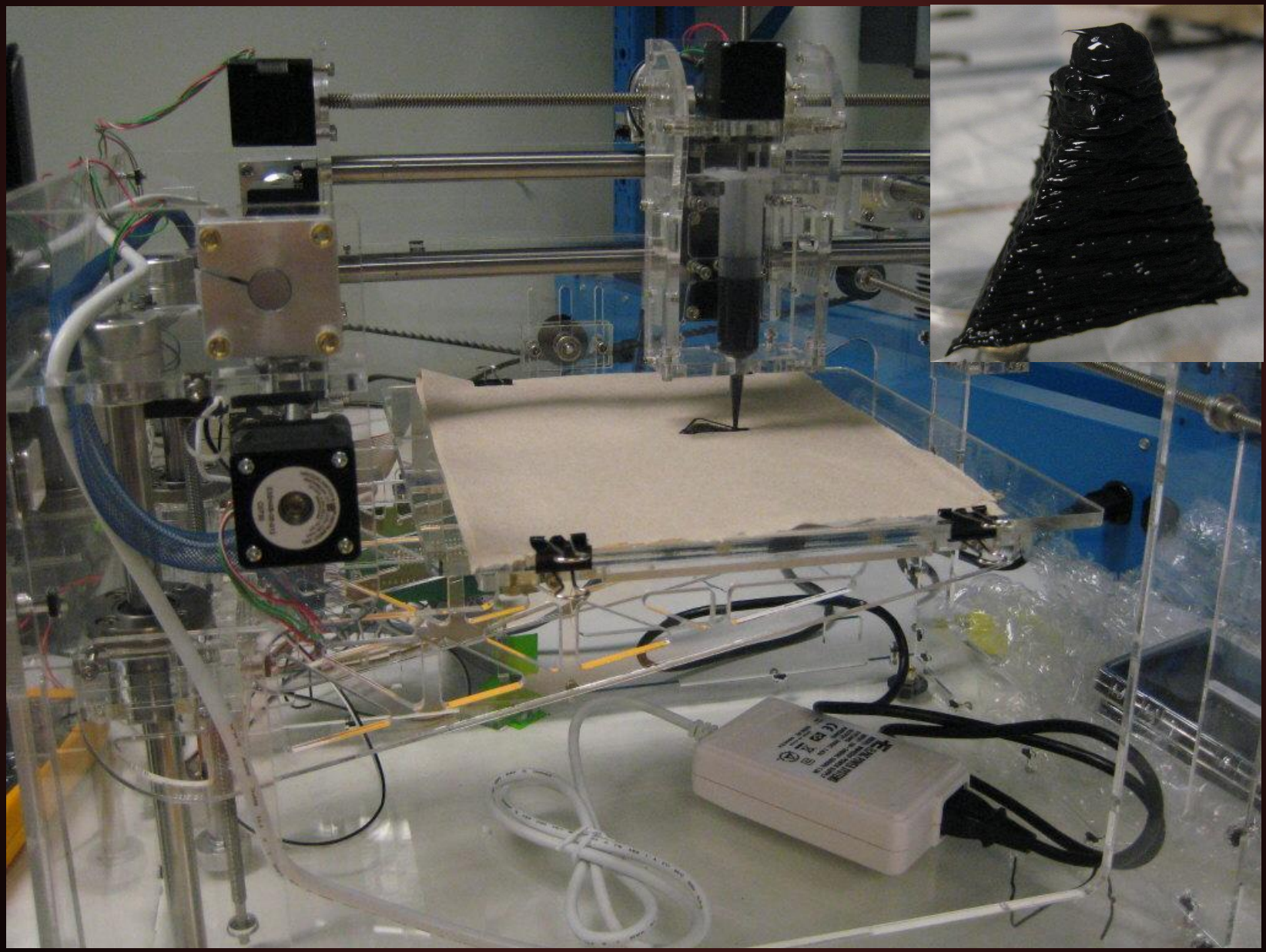


High Throughput Measurement of Photo-Crosslinking Effects

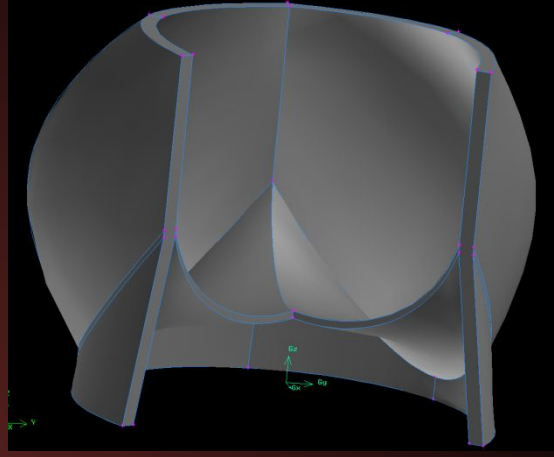
- Riboflavin induced crosslinking of collagen I
- Central disk punched out via well guide
- Dose dependent effects



3D Bioprinting Technology



Next Steps



- Switch to A-PEA based hydrogels
  - Cytotoxicity of crosslinking dose
  - Mechanical testing of crosslinking effects
- Incorporate a second syringe in the printer
  - Print a temporary “scaffold” to support structure
- Print 3D anatomical models of heart valves
  - Axisymmetric aortic valve geometry
  - Anatomical models via MRI: Yi Wang, Weill Med
- Incorporate a tuned UV laser to the print head
  - Spot specific engineered tissue material properties