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Virtual Experiments of Extracellular Matrix-Cell Interactions of Heart Valve Tissues

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Introduction and Background

- Objective: Develop an automated finite element analysis to study extracellular matrix-cell interactions in heart valves.
- The interactive content is made possible through the use of BioTester (Figure 1), photomicrographs (Figure 2), and an open source finite element software-OOF2, developed by National Institute of Standards and Technology[1].
- OOF2 wasn't designed to handle heart valve tissue unique microstructures

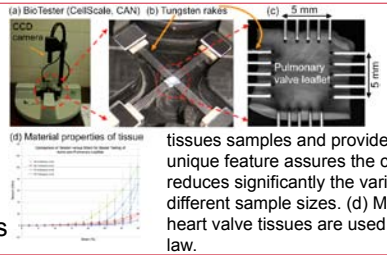


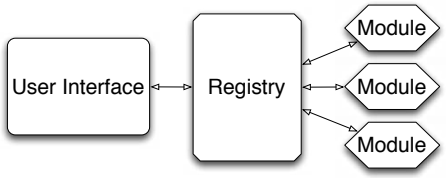
Figure 1: (a) The BioTester is capable of applying physiologically plausible biaxial loading states on tissue samples. (b)-(c) The tungsten rakes pierce through heart valve tissues samples and provide evenly distributed loading. This unique feature assures the control of loading conditions and reduces significantly the variability associated with testing different sample sizes. (d) Measured material properties of heart valve tissues are used to develop a matrix-constitutive law.

Figure 2, The microstructure of pulmonary valve tissue. Collagen fibers and extracellular matrix are shown in pink and the cell nuclei are in black (400x).

- Extension OOF2 for automated analysis of heart valve tissue is required.

Design and Implementation

OOF2 Architecture



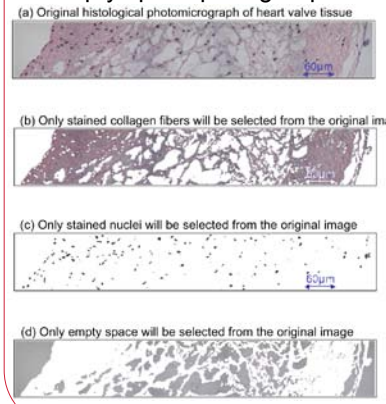
- Framework provides the UI and a Registry and is written in Python.
- Modules provide each individual feature. Some are written in Python while others are written in C++.
- Loaded modules are accounted for in the Registry. The UI uses registry information to pass user input to the modules for processing.
- The modules compute some output and pass it back to the user interface.

Extensions:

- Extensions were developed to better differentiate and describe photomicrographs of cells and collagen fibers in heart valve tissues.

1. Pixel Selection Extension

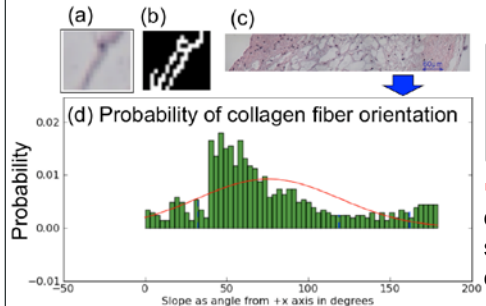
- Objective: Use image properties to differentiate between the collagen, nuclei, and space.
- Method: Based on hue, saturation, intensity color space from (a) an original image, the developed pixel selection extension are able to filter (b) only stained collagen fibers to a collagen fiber pixel group, (c) only stained nuclei to a nuclei pixel group, and (d) only empty space to an empty space pixel group.



- Outcome: Quickly assign material properties to all pixels in the image for more accurate simulation.

2. Materials Property Extension

- Objective: User-defined stiffness matrices for collagen fibers in the radial and the circumferential directions.



- Method: Hough Transform detects the slope of the strongest line displayed in each element.
- It is observed that most of the collagen fibers in are alignment with ~55 degrees from +x axis.
- The slope is used to calculate how much of each stiffness matrix contributes to the net stiffness for that element.

Discussion

- The automated finite element model captures heterogeneous cell and collagen fiber microstructures from heart valve tissue histological photomicrographs.
- Finite element analysis is performed on an image to conduct virtual experiments.

[1] OOF: Finite Element Analysis of Microstructures, Applied and Computational Mathematics Division National Institute of Standard and Technology, U.S. Department of Commerce.

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