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# Control of an air pressure actuated disposable bioreactor for cultivating heart valves

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ABSTRACT

A disposable injection molded bioreactor for growing tissue-engineered heart valves is controlled to mimic the physiological heart cycle. Tissue-engineered heart valves, cultured from human stem cells, are a possible alternative for replacing failing aortic heart valves, where nowadays biological and mechanical heart valves are used. Growing and conditioning is done by mechanically stimulating the tissue in a bioreactor. The disposable injection molded bioreactor uses flexible membranes and steering valves to mimic a physiological heart cycle. In this work, an air pressure actuation control system for this bioreactor is designed. One membrane is position controlled to achieve a desired flow through the heart valve, while another membrane controls the aortic pressure. A third actuator controls a steering valve used to impose a resistance on the flow back to the first membrane, in order to control the heart valve closing pressure. Due to the repetitive character of the setpoints, repetitive controllers are designed and implemented. A high position tracking performance is achieved and pressure setpoints are mimicked successfully, while preventing large pressure oscillations and suppressing disturbances that could be damaging for the tissue heart valve. The control system allows full adjustability of operating conditions needed for the growing, conditioning and testing phases of tissue engineered heart valves.
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## 1. Introduction

The human aortic heart valve [18], lying between the aorta and the left ventricle, prevents blood to flow back between strokes. Annually, 6000 children are born in Europe with aortic heart valve conditions, needing a heart valve replacement. Nowadays, patients are treated by surgically replacing the aortic valve by an artificial one, which can be a biological or a mechanical valve. Biological valves are valves from animals, most often from a pig. There are risks associated with implanting a biological valve, such as the human body's tendency to reject foreign tissue. Also, the biological heart valve has a limited lifetime. Mechanical valves can last multiple life times, but current mechanical heart valves all require lifelong treatments with blood thinners, to prevent blood clothing. Another drawback of both valve replacements is that they are unable to grow with the patient.

An alternative for biological and mechanical heart valves are cultivated, tissue-engineered heart valves [2,3,7,8,15,18], see Fig. 1.1. An attractive promise of these 'living' tissue replacements is their potential for repair, adaptation and growth. Human stem cells are seeded into a biodegradable artificial structure (scaffold). Culturing the tissue (growing and conditioning) is done by mechanically stimulating it in a bioreactor.

Recently much research has been done on the subject of Tissue Engineering by various research groups. From their experience with cultivating heart valves, the need for a new kind of bioreactor arose, since existing bioreactors have drawbacks. Therefore, a new bioreactor [20,21] has been developed by Neerincx and Meijer, which is novel compared to existing bioreactors since it meets five key requirements: (1) It is fabricated using injection molding, a technique well suited for mass production. It allows the bioreactor to be sterilizable and disposable, which is convenient for medical applications. (2) Some bioreactors [14] aim at controlling either the flow through or the pressure over the heart valve, while this design controls both simultaneously. (3) All setpoints are tracked by means of active control, while other bioreactors [9,24] use mock circulatory systems, where the elements of the human circulatory system are represented by mechanical imitations in order to mimic the physiological response. These bioreactors are large and consist of a large number of parts. (4) This bioreactor is small enough to fit inside an incubator. (5) The bioreactor is capable of handling both the growing and the testing phase of the cultivated valve. Other devices [10,11,22] are developed for only testing heart valves using pulsating air pressure to deform an elastic tube or membrane.

The contribution of this paper is the design and realization of a control system for the disposable bioreactor, achieving all necessary functionality for cultivating tissue into well constructed heart valves, by means of mimicking the physiological cardiac cycle. In [16], the author designed a feedback system for a prototype of this

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