Chapter 1

Introduction and Background

The heart is a robust pump capable of beating rhythmically for over 2 ½ billion times in a lifetime. At very early stages of development, the embryonic heart is basically a thick-walled tube. It is during later stages that it will take its four chambers shape. The tubular heart is a remarkable pump that achieves unidirectional pumping even before valve formation.[25] A periodic contractile wave down the embryonic heart flexible walls drive the red blood cells through it.

There are two ways to achieve pumping in valveless elastic tubes: by peristalsis or by the use of impedance mismatch (figure 1). In a peristaltic pump successive sections of the elastic tube are compressed pushing fluid from one end of the tube to the other by positive displacement. In an impedance pump (IP) however, a single actuation location is sufficient to produce a net unidirectional flow. The driving mechanism is the result of the interaction of elastic waves created by local periodic excitations of the tube at an off-center longitudinal position, and their reflection at the tube's extremities where a mismatch of impedance is present.[5]

Recent experimental investigations have revealed that the embryonic heart was an impedance and not a peristaltic pump as commonly thought.[25] The embryonic heart possesses an interesting multilayered wall structure. We use it as an inspiration point for the design of an innovative valveless impedance pump: the multilayer impedance pump.

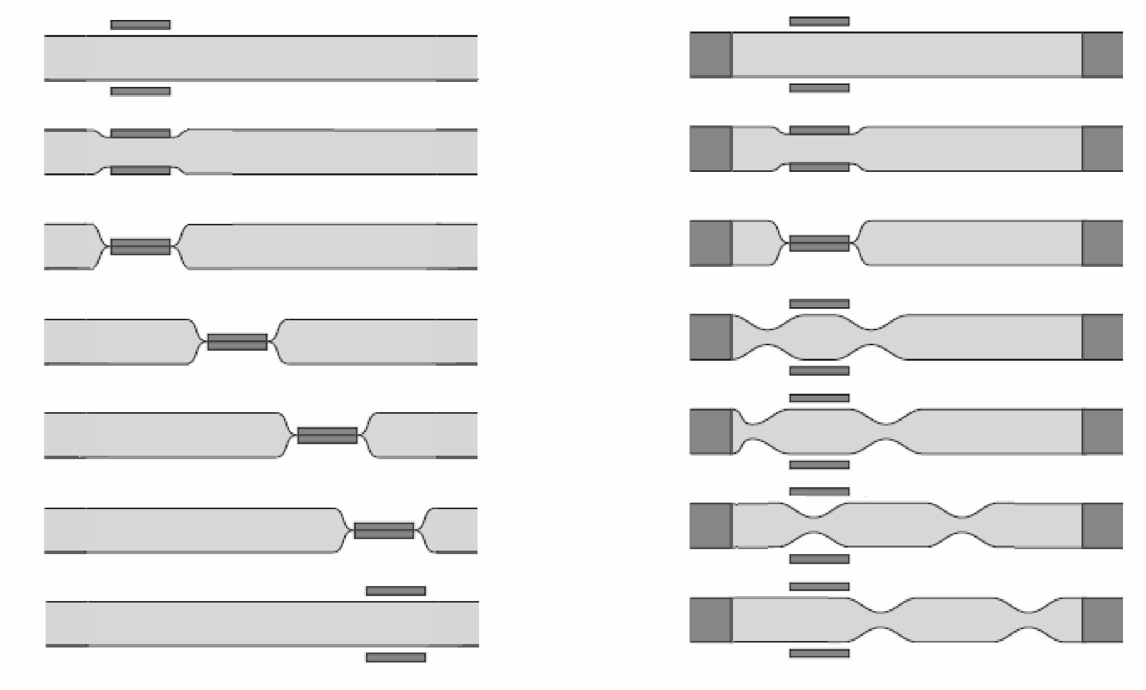

Figure 1. (Left) Schematic of a peristaltic pump. The pump functions by positive displacement, a propagating compression zone pushes the fluid along the tube. (Right) Schematic of an impedance pump. The pump functions by elastic wave propagation and reflection. The dark colored edges of the pump represent a mismatch of impedance. (adapted from Hickerson[27])

1.1 The embryonic heart

1.1.1 Formation and structure

An adult vertebrate heart is formed out of four chambers, but at early stages the primitive heart is a simple tube. The heart morphogenesis is done by first the looping of the primitive heart tube on itself. Later, cell differentiation ensures the shaping of the ventricules.[41]

More specifically, the very first stages of the heart development begin with a pair of epithelial tubes formed on opposite sides of the embryo (figure 2.A). Fusions of those tubes along the ventral midline lead to the formation of the cardiac tube (figure 2.B). In the chick, contractions begin soon after the tube forms (Hamburger and Hamilton[26] stage 9 (HH-9)), but before effective blood flow occurs (HH-12, figure 2.D). Flow is driven by a wave propagating along the length of the tube, and becomes pulsatile at HH-stage 17. [23]

The heart tube is composed of three layers: myocardium, cardiac jelly and endocardium (figure 3)[56]. The myocardium is a highly organized tissue composed of smooth muscle cells, fibroblasts and cardiac myocites. This two- to three-cell-thick layer is the only layer of the tube containing contractile elements, the myofibrils, which slide toward each other upon contraction. The second layer is the cardiac jelly, accounting for the bulk of the tube walls. It is a gelatinous acellular connective tissue matrix playing a central role in septation of the heart and formation of the atrioventricular canals. As the heart differentiates, the cardiac jelly disappears to the profit of the myocardium. Finally, the endocardium is a single layer of cells lining the wall of the heart and is directly in contact with the blood.

1.1.2 The embryonic beating heart as a pump

Of particular interest is the heart tube before valve formation (HH-9 &10). It is mainly straight tube composed of three layers –endocardium, cardiac jelly and myocardium-. This primitive pump produces a net unidirectional flow. A wave propagates along the tube driving flow through it. Long thought to be a peristaltic wave[21, 52], Forouhar et al.[25] were able to contradict this hypothesis and proposed instead that the embryonic heart functions as an impedance pump.

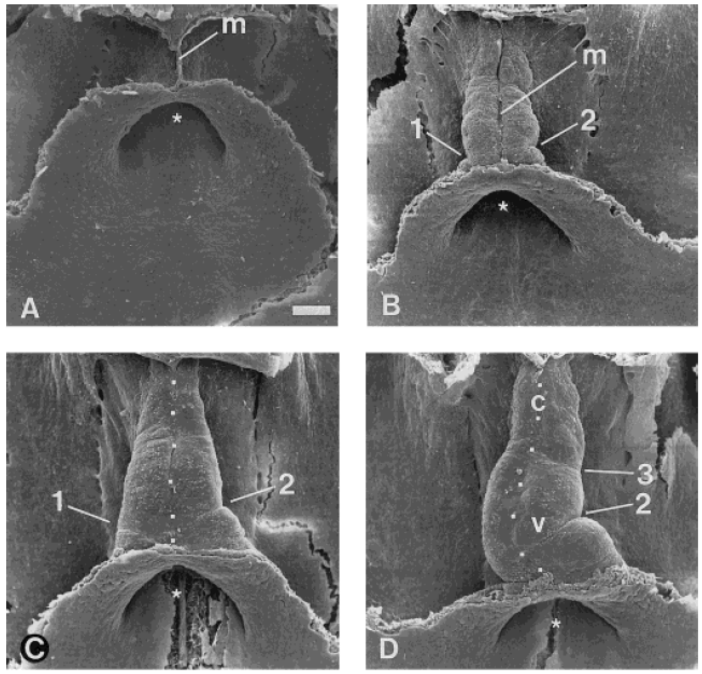

Figure 2. Ventral views of the embryonic heart tube formation in the chick (reproduction of Manner[41]). HH-9 &10. Scale bar = 100 µm.

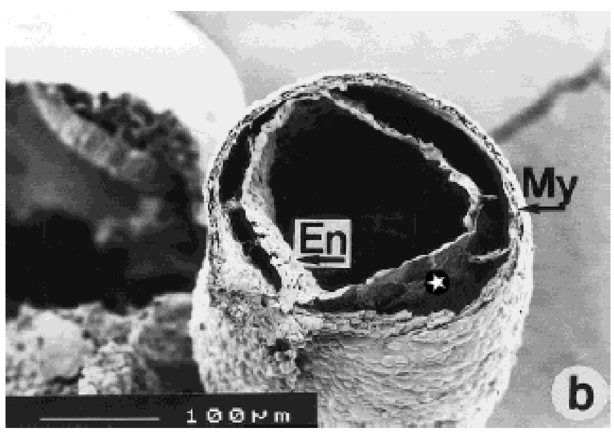

Figure 3. Cross section of the embryonic heart tube in the chick (reproduction of Sedmera[56]). My=myocardial mantle, *=cardiac jelly, En= endocardium. Scale bar = 100 µm

To understand the pumping mechanism they used confocal microscopy and 4D reconstruction protocols on zebrafish, a canonical model for vertebrate development.[22] Forouhar et al. identified three mechanical properties of embryonic heart tube contractions that contradict the peristaltic hypothesis:

(i) a bidirectional, as opposed to unidirectional, wave traversing the endocardial layer

(ii) blood cell trajectories that do not follow local endocardial wave trajectories and that exhibit velocities greater than those of the traveling wave

(iii) a nonlinear frequency-flow relationship that exceeds the maximum flow rate a peristaltic pump would produce.[a]

In addition to having contradicted the peristaltic hypothesis, they found several elements suggest that the embryonic heart may function as a hydroelastic impedance pump instead:

(i) resonance peaks in the frequency-flow relationship;

(ii) mismatched impedance at inflow and outflow tracts and visible wave reflections at the heart tube boundaries

(iii) a pressure-flow relationship that exhibits a phase difference between the maximum acceleration of blood and the maximum local pressure gradient.

In conclusion, the embryonic heart can be seen as a valveless impedance pump that uses elastic wave propagation and reflection to drive the flow unidirectionaly.

[a] In a peristaltic pump the flow rate is linearly dependant with the frequency of excitation.

1.2 Properties of an impedance pump

1.2.1 The concept of impedance

Impedance represents the measure of opposition to flow presented by a system. Conventionally impedance is resistance in the case of oscillatory systems. The term impedance is used in the electric current theory (electrical impedance), vibrating solid systems (mechanical impedance) or gas-filled systems (acoustic impedance). We are here referring impedance as the hindrance to flow, which is expressed as the ratio of the instantaneous pressure over the instantaneous flow rate at the section considered (input impedance).[47,50] In the case of a fluid-filled elastic tube IP, mismatch of impedance can be practically achieved by connecting the system to tubes of different stiffnesses or different radii. The mismatch of impedance creates a wave reflection site, a necessary condition to achieve pumping.

1.2.2 The impedance pump function

The first demonstration of valveless pumping, known as Liebau effect, has been done by Gerhart Liebau in 1954.[37] Using an elastic tube connected to reservoirs at different heights, he was able to pump against the pressure head by periodically compressing the elastic tube at a unique location. He suggested that elasticity, viscosity, and inertia affected the performance of the device, but he was not able to explain how these parameters contributed to the pumping.

Since these first observations, mathematical[4,34,51,59], experimental[13,28,29,51,53] and lately numerical[5,12,32,42] models have been proposed. These models consist of fluid-filled elastic tubes in open and closed loops excited by a periodic total or partial compression of the tube. Their limited assumptions (1D, inviscid, linear) and the lack of description of the physics of fluids failed to completely explain this fascinating phenomenon. Although flow dependence on excitation frequency has been observed since Bredow's experiment[13] in 1968, it is only recently that the resonant behavior of the system had been characterized.[5,29,42] Hickerson's experiment[27] was a fluid-filled elastic tube in a closed loop that was connected to reservoirs at the extremities of the tube. These reservoirs were filled with water and allowed to adjust the pressure head. By varying the parameters defining the pump, she was able to show some interesting features of the impedance pump:

(i) Exit flow rate (flow rate at the distant extremity to pinching) is pulsatile

(ii) Mean exit flow is:

- non linear with respect to the frequency of excitation;
- maximum when the pump is excited at resonant frequency or at harmonics of the resonant frequency;
- linearly dependant to the amplitude of pinching (up to 90% radial compression);
- increased with the asymmetry in pincher location;
- linearly increasing with the shortening of the duty cycle;
- linearly decreasing with resistance (increase of pressure head).

The latest numerical work done by Avrahami and Gharib[5] based on the experiment of Hickerson[27], allowed to understand for the first time the interplay of pressure flow and elasticity in an impedance pump. Pumping is the result of a constructive wave interaction located at the extremity of the elastic tube distant to the pincher, the *pumping region*.

This interaction location is very sensitive to the timing, and therefore to the frequency of excitation. The wave interaction mechanism can be decomposed in three fundamental factors that participate in driving the flow: volume suction, pressure gradient and inertia. In addition, a velocity node is present toward the extremity of the tube. The energy used to compress the tube is transmitted as elastic energy to deform the tube and kinetic energy to push the fluid. Considering the energy exchanged in the system *pump*, they concluded that the velocity node was the point where the elastic energy of the tube starts to be converted into kinetic energy in the fluid. Only at resonance is that energy exchange the most efficient. Their open-looped fluid-filled elastic tube model demonstrated that pumping is not driven by inertia[59] or asymmetry in losses[42] as proposed in closed loop systems, but rather by a resonant wave interaction.

1.3 Concept of multilayer impedance pump

This work proposes a new kind of IP that features a multilayered wall similar to the geometry of the embryonic heart. The main advantage of a multilayer pump over a single-layer impedance pump is that it requires only small excitations to produce significant flow.

The Multilayer Impedance Pump (MIP) is modeled as a valveless composite fluid-filled elastic tube of circular cross section that is periodically excited at a unique location following the impedance pumping mechanism. The tube walls are made of a thick gelatin-like layer modeling the cardiac jelly, and a thin stiffer external layer modeling the myocardium layer. They form together an efficient wave propagation system (figure 4). Elastic waves are generated by periodic compressions of the elastic tube at a single offcentered location on the external surface of the tube. The elastic waves emitted by the excitation location reach maximum amplitude at the fluid-gelatin interface. They are propagated along the length of the pump and are reflected at the two reflection sites. Because the flexible stiffer layer is compressible but not distensible, all large wave motion is confined inside the pump. The tube's extremities are fixed, creating an impedance mismatch, to allow full reflection of the traveling longitudinal elastic waves. Their interaction results in the driving of the net flow in a preferential direction. Numerical and experimental studies on SLIP[5,27,42] have shown that, in order to achieve significant flow, an IP must typically be compressed at relatively high amplitudes (about 70% of the tube's external radius). This strong compression can strain the tube walls, create large outward radial motion of the tube that would make the pump not compatible with confined environments, or also occlude the flow that would make the device not suitable to many biomedical applications. The proposed MIP addresses these difficulties with the combined use of gelatin and the stiffer layer. The presence of the stiffer layer forbids large radial outward motion, while the softness and thickness of the gelatin are used to amplify and efficiently propagate elastic waves.

Therefore, in a MIP only small excitations are needed to generate elastic waves that last longer and are of greater amplitude than the ones in a SLIP. In addition to its special design, the pumping is based on resonance, meaning that the pump performance is frequency dependant and maximizes at resonance. One of the features of resonant pumping is that the pump requires minimal input energy to operate when exited at resonance.[5]

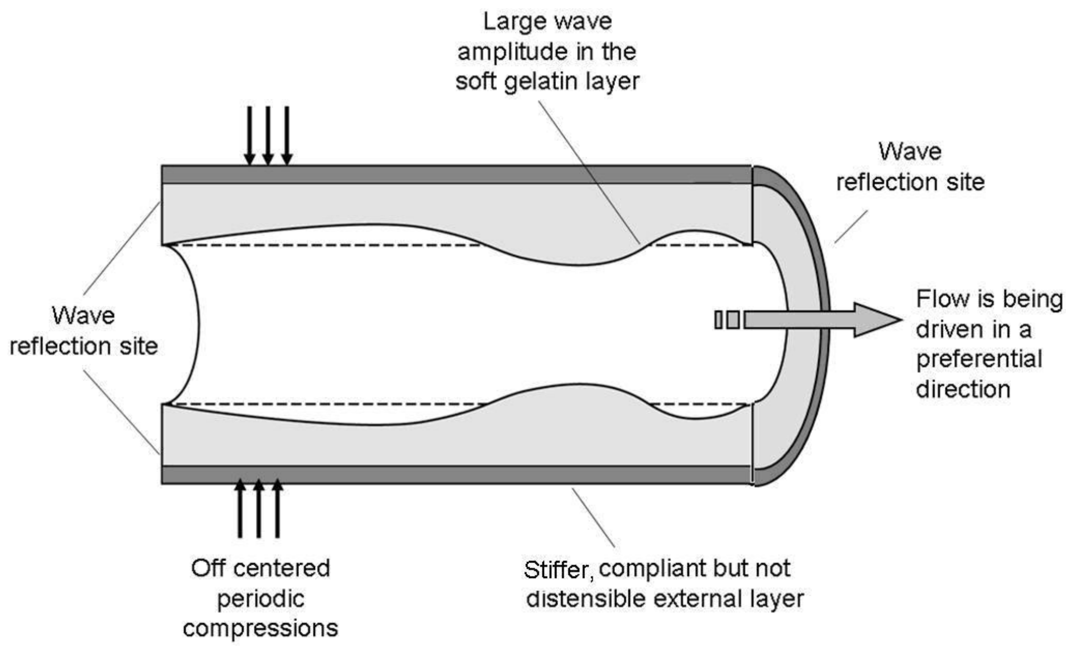

Figure 4. Illustration of the function of the Multilayer Impedance Pump (MIP).

1.4 Overview

We propose to investigate the potential of a Multilayer IP using numerical simulations. The novelty of the design requires a large design optimization as well as characterization of the pump under dynamical conditions. The choice of numerical simulations is motivated by the possibility of extensive use in design optimization and by the fact that one can isolate factors which in many cases cannot be separated experimentally. In addition, they provide detailed description of the unsteady flow field and the solving of structural behavior at any point in the elastic tube.

This thesis presents the innovative MIP design in Chapter 2. In Chapter 3 flow and structure response to periodic excitation is explored, with an emphasis on the system's behavior at resonance conditions. The energy exchange between the elastic tube and the fluid that leads to resonance pumping is especially investigated. Chapter 4 is a discussion on the MIP model, its strength and its limitations. In Chapter 5, using an impedance and a peristaltic multilayer pump model, we bring an additional proof that the embryonic heart is a multilayer impedance pump. The role of the gelatin layer in pumping is assessed through the comparison the multilayer pump performances with the exact same pump without gelatin in Chapter 6. Several biomedical applications of the MIP are given in Chapter 7. A physiologically correct model of an adult descending aorta is used to test the pump as a fully implantable intra-aortic pump. Chapter 8 contains concluding remarks over the previous chapters.