Simulating the First Breath: Design of the Respiratory Reflex in a Fetal Manikin

Tamara Hoveling
Industrial Design, Eindhoven University of Technology

Juliette S. Van Haren
Industrial Design, Eindhoven University of Technology
j.s.v.haren@tue.nl

Frank L.M. Delbressine
Industrial Design, Eindhoven University of Technology
FDelbres@tue.nl

ABSTRACT

Extremely premature babies (24 to 28 weeks) have underdeveloped bodies, resulting in a survival rate of only 50-70%. To increase this rate, researchers around the globe are developing an artificial womb (AW), a safe environment that mimics the natural uterus, allowing the fetus to develop further. To successfully transfer the fetus from the natural uterus to the AW - while avoiding the respiratory reflex and thus neonatal transition - it is important that no air enters the lungs. To improve safety and minimize animal testing, the transfer procedure is first tested and trained using a fetal manikin simulation. To this end, the intent of this study was to perform a literature analysis to understand how the breathing reflex of a premature infant can be simulated in a fetal manikin. This study resulted in an overview of triggers known to initiate the respiration at birth and ways to detect these triggers, leading to a proposal for an electromechanical system. This proposal was incorporated into a realistic-looking prototype, which was subsequently evaluated with medical end users.

CCS CONCEPTS

• **Sensors and Actuators**; • **Design**; • **Life and Medical Sciences**;

KEYWORDS

Artificial Womb, Fetal Manikin, Gasp Reflex, Medical Simulation, Perinatal Life Support System

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1 INTRODUCTION

Due to underdeveloped body functions, the survival rate of extremely premature infants is only 50-70% [14, 18]. Since a 24-week fetus is not fully mature, it is unable to breathe properly on its own. This leads to morbidity in 20-50% of the surviving neonates [6]. To improve the survival rate and quality of life for premature babies, the European Perinatal Life Support (PLS) project has been initiated for the development of a liquid based Perinatal Life Support system. The PLS system is a fluid-filled environment that mimics the function of the natural uterus, allowing the fetus to safely develop further, before taking the first breath. While transferring the underdeveloped fetus from the natural uterus into such an AW, the respiratory reflex has to be avoided [22, 25, 47].

As soon as the premature lungs come into contact with air, the respiratory reflex is initiated due to the transition to neonatal life. It is therefore important that the function of the PLS system and its transfer procedure are thoroughly and safely tested and sequentially trained with the medical staff. As high-fidelity manikins in the medical setting have already been proven effective for training purposes [21, 36, 54], and since manikins allow to minimize animal testing, a realistic 24-week-old fetal manikin is currently being developed.

Prevention of the respiratory reflex is one of the most important aspects when transporting a fetus to the AW [22, 25, 47]. Yet, realistic simulations of the breathing reflex have not been investigated before. Therefore, the following question was proposed during this study: *How might we successfully incorporate an actuator that mimics the gasp/breathing reflex in the fetal manikin?*

First, a design space analysis was conducted to investigate the real-life respiration triggers at birth. Based on the in-depth processes that take place before, during and directly after the first breath, a visual synthesis was created, illustrating the prior knowledge about possible initiators of respiration at birth. Some of the found respiratory triggers could be embedded in future manikins. Yet, within this paper focus lies on the actuation of the breathing reflex.

In the scenario in which one or multiple respiratory triggers occur in the manikin, a sensor should sent a signal that actuates the simulation of the breathing reflex. This concerns an opening of the mouth and movement of the chest during inhalation. The way how and with which actuators this movement should be realized has been analyzed by comparing various options based on predefined design criteria.

2 RELATED WORK

2.1 High-Fidelity Manikin-Based Simulation

Simulation provides the possibility of experiential learning and to train in a risk-free setting [2, 54]. Realistic, high-fidelity simulation using manikins was proven to enhance the quality of medical training [21, 36, 54], due to the 'suspension of disbelief': the ability of the medical user to believe in that the simulation is 'real' [36]. In fetal and neonatal resuscitation training, it was previously proven that by providing important visual, aural and tactile cues, a high level

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of physical, biological and psychological loyalty to the real-world setting can be reached [21]. Due to the experience-based learning possibilities of high-fidelity medical simulation, positive influences can be reached for both the medical learners as well as for the patients that they serve [54]. Apart from that, the use of medical simulations can potentially be an effective alternative to animal testing [32]. For these reasons, a high-fidelity medical simulation of the breathing reflex of a 24-weeks-old fetus is being created. This fetal manikin will be used to validate the product and procedures of the concept of Artificial Womb, with as a future aim to serve as a training aid in the AW procedures.

2.2 Initiation of the First Breath

The exact bodily processes that are directly responsible for the first breath are still unknown [1, 12, 23, 42, 44]. Yet, multiple studies have been conducted on preterm and full-term infants, adults and animals, from which conclusions can be derived about the functioning of the respiration reflex.

There are different views on how the young lungs get rid of fluid to then fill with air. A combination of various related works has shown that at least the temperature of the baby's skin [6, 19, 33, 42, 50], the pressure on the baby from the birth canal [3, 24, 35, 46, 48, 50] and the entry of air bubbles into the respiratory tract [11] play a major role. In the *design space analysis* of this paper, a more thorough synthesis of the design space (and thus initiation of breathing) is described using several relevant related works.

2.3 Breathing Reflex Simulation

At present, no manikin exists harboring the components to simulate a breathing reflex. A 27-week-old manikin, developed by SimCharacters, showcases the function of spontaneous breathing [48], but no studies or design processes were found related to the simulation of a fetal respiratory reflex.

Of added value could be the integration of thermal functionality, since the onset of the neonatal respiratory reflex is hugely dependent on the amount of cutaneous cooling [6, 9, 19, 33, 50]. In the past, a thermal manikin was developed [45], which proved to provide accurate methods for the assessment of thermal conditions in the neonatal intensive care unit (NICU).

3 DESIGN SPACE ANALYSIS

To be able to simulate the breathing reflex, all factors that may play a role in triggering the respiration reflex in a newborn neonate were mapped. This analysis led to a visual synthesis of prior knowledge about possible triggers of the initiation of the breathing reflex. When determining which triggers might unintentionally trigger the breathing reflex during the PLS procedures, the target groups that were used during the evaluation were taken into account (full term, preterm, adult and animal subjects). Thereafter, it was determined which of the numerous triggers found could be measured in the fetal manikin during the AW procedure. In the following two paragraphs, the design space of the respiratory reflex simulation is discussed.

3.1 Initiation of the First Breath

Although the exact cause of the initiation of the breathing reflex is still unknown [1, 12, 23, 42, 44], possible processes could be derived from various sources. An extremely simplified version of the schematic overview of the found respiration triggers is shown in Figure 1. This overview represents the most relevant respiration triggers without the connections needed to initiate those triggers.

The process that leads to the initiation of the respiratory reflex starts before or with the onset of labor [23]. Due to cervix contractions, three different processes are initiated. Firstly, the contractions cause limited intrauterine space for the body of the fetus [24, 42]. Due to the limited space, the fetal posture changes [51], because of which transpulmonary pressure is increased and the chest wall configuration is altered [50]. If the pressure of the thorax, and thus the *birth canal squeeze (BCS)*, is larger than 145.4 cm H_2O measured from the esophagus, the lungs will be 'squeezed' and cleared from liquid [46, 50]. Once this pressure is released [35], the first breath is initiated.

Secondly, in case of full term babies, the limited intrauterine space caused by the birth canal contractions may lead to a stimulation of the sciatic nerve [6]. Since this stimulation triggers the receptors of pain, temperature, touch, etc. [6], it makes the fetal body increasingly sensitive for contiguity [35], light changes and sound [28]. Also, it has previously been proven that even mild tactile stimulation triggers the respiratory drive of premature babies [26, 34]. Because of this, the perinate can more easily detect its own body temperature [1], and therefore respond to the cutaneous cooling that occurs once its wet skin comes into contact with air directly after birth [1, 42]. Once cutaneous cooling of approximately 2°C [33] occurs within approximately 10.8 seconds after birth [50], the first breath is initiated [15, 19, 42].

Simultaneously, the perception of the senses that is stimulated by the sciatic nerve, impacts the state of arousal of the premature baby. Directly after birth, the newborn can likely be considered to be 'awake' [39], which makes it more sensitive to blood gas changes [12]. An O_2 decrease of 5 mmHg, CO2 increase of 10 mmHg and an increase in pH have been linked to the initiation of breath [4, 43]. This might be due to the chemoreceptors of the aorta and carotids, which are stimulated by changing blood gasses [1] and the aforementioned clearance of the lungs [42]. Those chemoreceptors have namely been proven to have a reflective influence on the respiratory center [1, 34, 40].

Changes in hormone levels were also connected to the initiation of breathing [1]. Due to the cervix contractions, fetal stress is induced [29, 48]. Because of this, the levels of vasopressin [31], angiotensin [8] and (nor)epinephrine [16] increase, while prostaglandin and progesterone levels decrease due to the loss of the placenta [27, 30, 37].

Furthermore, occlusion or clamping of the umbilical cord may also be involved in the initiation of the first breath. Once the umbilical cord is (temporarily) occluded, activity from the pulmonary stretch receptors first increases and then falls down to zero, after which the respiration reflex is initiated [1, 41, 42].

As a popular way to support newborns that are not breathing, the vagus nerve is blocked using electric pulses [42]. Blocking the vagus nerve can lead the initiation of the first breath as well [41].

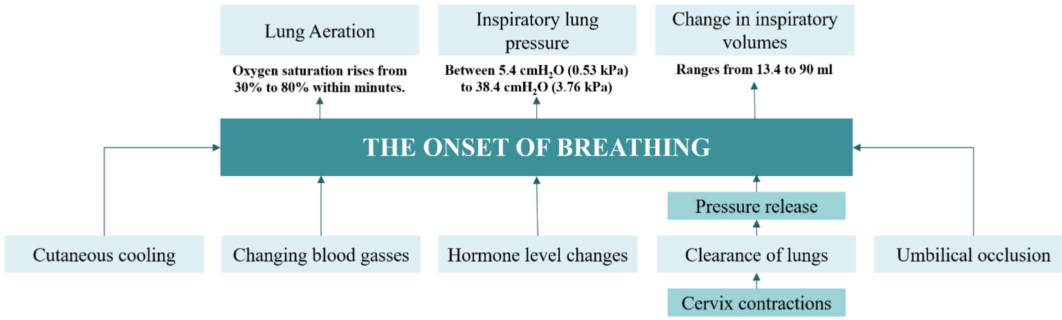

Figure 1: Simplified schematic overview of relevant triggers that may lead to the initiation of the breathing reflex.

Table 1: Measurement of Respiration Triggers Suggestions

Respiratory trigger	Measurable data	Output
Cutaneous cooling [13, 33]	Cooling of 2°C within 10.8 seconds	Breathing reflex
Thorax pressure release [46, 50]	Pressure decrease after 145.4 cm H_2O BCS	Breathing reflex
Lung aeration (under development)	Air bubble detection in airway increased to 80%.	Breathing reflex
Umbilical cord occlusion [13]	Decrease in liquid flow	Cyanosis

Table 2: Design Criteria Respiration Simulation

Size	The solution fits within 221 cm3 (head) or 230 cm3 (torso), including the manikin 'skin', based on the fetal manikin anatomy, which was calculated using Materialise Mimics (Materialise NV, Leuven, Belgium).
Weight	The weight of the components does not exceed 536 grams, which is 80 percent of the average weight of a 24 weeks old fetus (670 grams) [20].
Location	The jaw movement is located close to the jaw (in the head of the manikin) and the chest movement is located close the chest (upper-torso).
Movement	The chest moment should simulate the average initial inspiratory volume change of a 24 weeks old fetus, which ranges from 13.4 to 90 ml [35].
Sound	The sound of the integrated actuators should be kept below 25 dBA, based on the WHO recommendation to keep the average noise in hospitals at 35 dB [4, 52].
Realism	The skin of the manikin should feel and look like realistic. Therefore, the actuators must be soft and mimic anatomy.
Actuation time	The actuation should be operative for a least 30 minutes after which energy sources can be replaced if needed.

3.2 Measurement of Respiratory Triggers

Ideally, the following respiratory triggers could be measured in the fetal manikin: *umbilical cord occlusion, cutaneous cooling* and *thorax pressure release (after clearance of the lungs).* Those three triggers are relevant to the PLS procedure, as errors could occur with the maintenance of the temperature of the artificial amniotic fluid (AAF) and the pressure applied on the thorax and umbilical cord. Furthermore, it was found that during the first breath, *lung aeration* can be measured to determine the initiation of the simulated breathing reflex. Once blood oxygen saturation rises from 30% to 80% within minutes after birth, respiration would have already been initiated [11]. Table 1 describes the measurable data per trigger. The measurement method would be based on the source from which the data was derived.

As an occlusion of the umbilical cord leads to oxygen deficiency, but not often to the initiation of breathing [5, 10, 49], the output of this trigger should therefore be cyanosis [38]. In this study, we focused on the realistic movement of the mouth and chest of the manikin. Cyanosis simulation was therefore disregarded.

4 DESIGN REQUIREMENTS

The analysis of the design space for the simulation of the onset of breathing, has led to several design requirements. Based on videos of breathing neonates, an estimation was made of what the breathing reflex in the manikin should look like. This led to two different movements: an opening of the mouth and a lifting of the chest during inhalation. For a realistic simulation, design criteria (Table 2) were created based on found prior research and pre-established norms.

Due to often large volumes of actuators [3, 17], size was the limiting factor. Since linear electromagnetic actuators [55], such as solenoids and electric linear motors [13] are harder to locate in the limited anatomical space, the search was focused on rotating actuators (micro servo motors) and pneumatic artificial muscles. A

Table 3: Comparison of Micro Servo Motors and Pneumatic Artificial Muscles

	Micro servo motors	Pneumatic artificial muscles [7, 53]
Size	Approx. 22 * 12 * 31 mm	Can be adjusted to surroundings
Weight	Example small version: 9 grams	Extremely lightweight
Noise	clearly perceptible sound	Air pump noise placed outside the manikin
Movement direction	Unlimited rotation	Nonlinear behavior

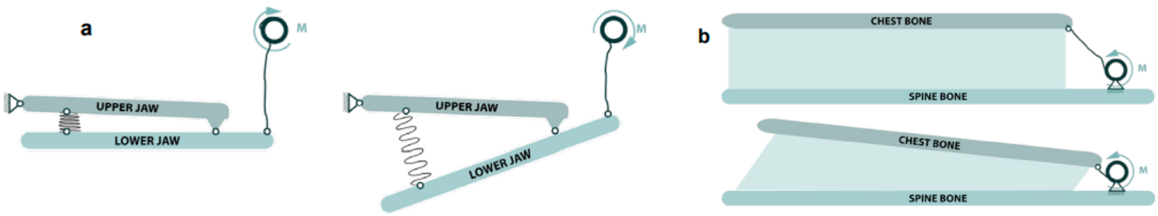

Figure 2: a) CAM mechanism operating the movement of the jaw (mouth-opening respiration reflex) and b) Crack connecting rod mechanism operating the movement of the torso (chest-lifting respiration reflex).

comparison analysis showed that micro servo motors would be the best choice (Table 3). For this study we used two micro servos, as this type of actuator does not require external air compressors, and in this way, the entire movement can be controlled from within the manikin. However, as servo motors produce an undesirable amount of noise, and thereby decrease the simulation realism, noise reduction was tested by encapsulating the actuator in a prototype made of sound absorbing material; silicone rubber. The jaw movement was created by a CAM (transforming rotary motion into linear motion), and the movement of the chest was created using a crank connecting rod mechanism, as is described in the next section.

5 PROPOSAL AND EVALUATION

Based on the aforementioned research outcomes and the suggested design criteria, a first prototype iteration was developed. This prototype has led to several conclusions, upon which recommendations and suggestions were made for possible future iterations (as described in the discussion).

5.1 First Iteration and Prototype

In the jaw movement mechanism (Figure 2a), the rear end of the lower jaw is pulled upwards by twisting a wire around a pulley on the micro servo motor. A spring ensures a default closed jaw position. The crank connecting rod mechanism used for the chest is similar to this CAM mechanism, while holding it in the default upwards position by using a spring. As the material of an all flexible rib cage automatically reforms to its original shape, the need for a spring was later eliminated (see Figure 2b).

For a realistic movement simulation, MRI scan models of a 24-week-old fetus were used. The front of the skull with a loose lower jaw were 3D printed using PLA filament. The parts were adjusted in such way that an elastic band could be added as a spring. The servo was glued into the skull (Figure 3). For the chest movement, multiple material options were tested. A rib cage was printed with a solid sternum and backbone (Vero White, Stratasys, Rehovot, Israël) and

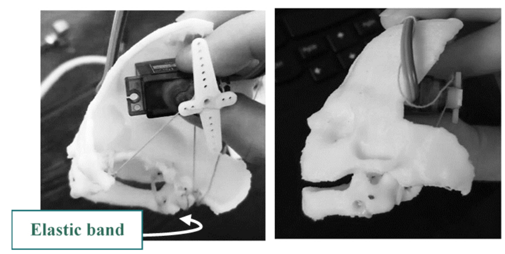

Figure 3: Initial prototype of the movement of the jaw.

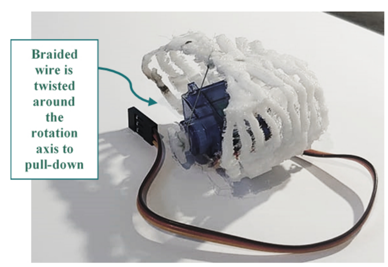

Figure 4: Final placement of micro servo in ribcage.

flexible ribs (S40, Stratasys), to offer stability and prevent bending. This prototype turned-out to be too flexible and break at frequent bending. Another rib cage was created in flexible material (S95, Stratasys) with a rigid spine, and another fully flexible rib cage in TPU (Ultimaker). In Table 4, the different tests of rib cages are evaluated. In Figure 4, the final placement of the servo in the rib cage is illustrated. Based on the created jaw and chest mechanisms, a final research prototype was created (Figure 5).

5.2 Prototype Evaluations

The first iteration was both evaluated based on the design criteria (weight, size, location, movement, actuation time) and by medical

Table 4: Comparison of Rib Cage Prints

All flexible TPU***Ultimaker***	3 pieces TB S40***Stratasys***	2 pieces soft TB S40***Stratasys***	2 pieces rigid TV S95***Stratasys***
Advantages: Cheap and easy to print **Disadvantage:** Unrealistic bending	**Advantages:** No bending, controlled motion **Disadvantages:** Too flexible, breaking ribs	**Advantage:** Less pressure needed **Disadvantages:** Too flexible, too soft	**Advantages:** Strong, realistic movement **Disadvantage:** Danger of breaking

Figure 5: Final research prototype of 24 weeks old metal manikin with respiratory reflex

expert feedback on video recordings of the prototype performing breathing movements. The most pressing issue of this first iteration is the noise exerted by the servo (Table 5). By changing Arduino programming settings, using new servo motors and closing-up the silicone skin, noise was minimized.

Secondly, evaluations on realism were conducted by medical staff from the NICU and gynecology department at the Maxima Medical Centre, Veldhoven, The Netherlands. The additional medical evaluations have shown that the movement of the simulated breathing reflex was considered to be "impressively realistic" by at least 3 medical doctors of the Máxima Medical Center (MMC, Veldhoven, the Netherlands). Yet, additional recommendations by two medical professionals entail that during the neonatal inhalation, not only the thorax, but also the abdomen should lift. While the torso retracts, the abdomen stretches. According to another neonatologist, it is advisable to rethink the breathing patterns and timing of both movements in relation to each other.

5.3 Possible Future Iterations

As the most promising recommendation of this study is to implement the abdominal expansion into a future prototype, there are two possible future iterations that deserve to be discussed. One possible suggestion (iteration 2), is easily implementable, as it concerns the same concept with a different placement of the servo. This requires the use of a spring to allow the abdomen to move effectively. This spring can be fixed in the silicone skin, possibly at the location of the umbilical cord. Iteration 2 is illustrated at Figure 6a.

Other options for this concept would be to use servo motors that are less noisy. Additionally, the concept leaves enough room in the abdominal and thorax area to implement additional components for other manikin functions. Additionally, in case of malfunction, the servo motor in this suggestion would be hard to replace.

Based on the evaluations from medical experts as well as to wish to minimize noise, another option would be to use a pneumatic artificial muscle to simulate both the thorax and abdominal movement of the manikin. A rough sketch of this idea is shown in Figure 6b. For this solution, less and lighter components are needed, which are likely leading to a more realistic abdominal expansion. This concept also provides possibilities for simultaneous control of the thorax, abdominal and jaw movement with only one actuator. As mentioned in Table 3, downsides of pneumatics include the need for a CO_2 cartridge and associated noise. To overcome this, the

Table 5: Comparison of Micro Servo Motors and Pneumatic Artificial Muscles

Weight	+ +	436 grams including silicone skin; fits within the average 670 grams of a 24 weeks old fetus [20].
Size	+	Fits well within 221 cm^3 (head) and 230 cm^3 (Torso), but the skin is too thick.
Location	+ +	Actuations are located close to their intended respiration movements.
Movement	+ / -	The chest movement of approx. 5 mm could be enhanced by implementing an abdominal movement
Sound	- -	The servo motors are easily hearable in this initial prototype.

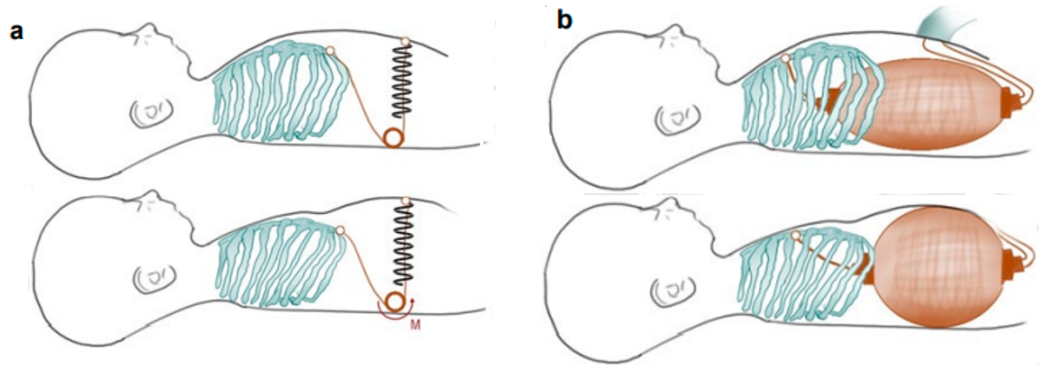

Figure 6: a) Suggestion for iteration 2 (with servo) and b) Suggestion for iteration 3 (with pneumatics).

external air supply can be placed outside of the manikin and linked via the artificial umbilical cord.

Additional testing is needed to verify whether this concept can be molded in silicone, to create a realistic abdominal softness.

6 DISCUSSION

The found indications can be of added value within medical healthcare, further research into the very first stages of life and future design in the field of the PLS system. It is important to note that the triggers were partly based on studies with animals and full term infants, rather than merely premature infants. This could potentially have affected the parameters.

Furthermore, a recommendation was given for the measurement of these triggers and simulating the breathing reflex in a 24 week old high-fidelity manikin, which can be of added value for simulating procedures during medical training. Of particular interest is the development of a PLS system, through which this project contributes to the enhanced testing and training.

7 CONCLUSION

This study demonstrates a method to simulate the breathing reflex of premature born infants in a high-fidelity medical manikin for testing and training purposes of the Perinatal Life Support system. A literature analysis showed a wide variety of bodily processes that trigger the onset of breathing. For simulating the respiratory initiation in the manikin, occlusion of the umbilical cord, cooling of the skin, lung aeration and thorax pressure release that clears the lungs from fluid are especially relevant. Subsequently, ways to simulate breathing in a fetal manikin were explored. The breathing reflex involves the opening of the mouth and inhale/exhale-movement of the chest, which can be simulated in response to the aforementioned triggers, using 3D-printed bone structures of the skull and torso, which are controlled by micro servo motors. Pneumatic artificial muscles are considered as a possible alternative to servo motors to enhance the realism of the breathing movements. This study can be useful input for the development of a high-fidelity preterm infant manikin to be used for PLS procedures, and in addition be of added value for innovations in perinatology.

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