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Using Thermochromism to Simulate Blood Oxygenation in Extracorporeal Membrane Oxygenation

Abstract

Introduction: Extracorporeal membrane oxygenation (ECMO) training programs employ real ECMO components, causing them to be extremely expensive while offering little realism in terms of blood oxygenation and pressure. To overcome those limitations, we are developing a standalone modular ECMO simulator that reproduces ECMO's visual, audio, and haptic cues using affordable mechanisms. We present a central component of this simulator capable of visually reproducing blood oxygenation color change using thermochromism.

Methods: Our simulated ECMO circuit consists of two physically distant modules responsible for adding and withdrawing heat from a thermochromic fluid. This manipulation of heat creates a temperature difference between the fluid in the drainage line and the fluid in the return line of the circuit, and hence a color difference.

Results: Thermochromic ink mixed with concentrated dyes was used to create a recipe for a realistic and affordable blood-colored fluid. The implemented "ECMO circuit" reproduced blood's oxygenation and deoxygenation color difference or lack thereof. The heat control circuit costs 300 USD to build and the thermochromic fluid costs 40 USD/L. During a ten-hour in-situ demonstration, nineteen ECMO specialists rated the fidelity of the oxygenated and deoxygenated "blood" and the color contrast between them as highly realistic.

Conclusions: Using low-cost yet high-fidelity simulation mechanisms, we implemented the central subsystem of our modular ECMO simulator which creates the look and feel of an ECMO circuit without using an actual one.

Keywords

Simulation-based training (SBT), extracorporeal membrane oxygenation (ECMO), blood oxygenation, thermochromism, high-fidelity simulation.

Introduction

Among the many sophisticated pieces of technology found in the intensive care unit (ICU), the extracorporeal membrane oxygenation (ECMO) machine is arguably the most complex.[1] It is used as an invasive life-sustaining device that provides cardiopulmonary support for patients during recovery of their diseased lung or heart or while awaiting for a transplant.[2] Patients' vital dependence on ECMO makes its uninterrupted and smooth operation of paramount importance. Unfortunately, ECMO is burdened with many complications caused by the patient's pathology, mechanical failures of the equipment, or clinical error and inexperience of the clinical care team.[3,4] ECMO's vulnerability to human errors and its technically challenging nature requires ECMO practitioners to come equipped with adequate technical, behavioral, and crisis resource management skills.[5] Since ECMO is a relatively low-volume and high-risk procedure that permits no room for learning from errors, training novice practitioners and maintaining competencies without compromising patients' safety must preferably be done through simulation-based training (SBT).[6–9]

Most ECMO centers offering SBT use different variations of the simulation model described by Anderson and her colleagues in 2006.[10,11] The model consists of an ECMO circuit filled with red-colored saline and connected to itself through a reservoir (e.g. bladder) featuring a hidden connection to a syringe which facilitates circuit volume adjustment and injection of air.[11] Emergency scenarios are simulated by discreet manual adjustments made to the circuit as the simulation session begins.[11,12] For example, hypovolemia can be simulated by withdrawing fluid from the circuit while a confederate nurse sways a thread attached to the tubing to create shatters in the drainage line.[11,12]

Although realistic from an equipment point of view, using an ECMO circuit and machine for simulation purposes has major drawbacks. First, many simulated emergency scenarios are detached from reality or require trainees to imagine and

pretend. In an oxygenator failure scenario, for example, it is not possible to increase the delta-pressure across the oxygenator, produce deoxygenated blood color in the return line, or manipulate blood gas saturations displayed on modern ECMO consoles or in-line monitors without complex circuit modifications or using real blood. Many other scenarios suffer from the same issue, which is mainly caused by the simulator's inability to control circuit and blood parameters, or reproduce relevant visual/audio cues. Some commercial ECMO simulators address some of those issues by providing instructors with a wirelessly controlled screen to display relevant parameters.[13,14] Still, there remains a disconnect between the parameters that are displayed on the real ECMO system and the ones displayed on the emulated screens. Second, disposable ECMO circuit components such as the oxygenation membrane, are expensive, making continuous replacement for training purposes limiting or prohibitive.[15]

Motivated by the aforementioned drawbacks, we are developing a standalone ECMO simulator that does not require the presence of a real ECMO machine or its expensive circuit components. The core principle is to recreate an ICU ECMO environment which instructors can fully and remotely control and learners can interact with. This is done by designing affordable but high-fidelity modules capable of reproducing ECMO visual, audio, and tactile cues (e.g. blood color, air entry pump noise, and line-shattering) without their physical or physiological requirements.[16,17] These modules are then enclosed within 3D printed cases that resemble real ICU or ECMO components. Naturally, our initial development efforts were drawn to simulating the most observable and indicative ECMO visual cue: blood oxygenation color change. Blood color transitions from dark-red to red as it gains oxygen (O_2) and loses carbon dioxide (CO_2). It is a critical diagnostic tool that indicates normal operation, successful ECMO initiation, low-oxygen saturation in the return line, and recirculation. This article describes the use of thermochromism in the development of the oxygenation and deoxygenation modules used in our ECMO simulator with the objective of reproducing a realistic oxygenated-deoxygenated blood color difference and building a standalone "ECMO circuit".

Methods

Thermochromism is a property of a substance that allows reversible color change with temperature. Thermochromic inks and powders are products designed to transition between two distinct states (colors) above and below a fixed transition temperature (T_t).[18] Our simulated ECMO circuit exploits this property by circulating a thermochromic fluid (diluted thermochormic ink mixed with other dyes) through two physically-distant modules responsible for adding or withdrawing thermic energy (heat). Heat manipulations drive temperature change in the fluid, triggering it to change state. The circuit design is presented in Figure 1. Besides the "patient"

location sits a reservoir containing the thermochromic fluid that is pumped through a heat exchanger (HE), cooling it below its T_t. On the opposite side of the circuit, a 3D printed "oxygenator" conceals the bypassing of the fluid to another HE, which heats it above its T_t. The continuous change of the fluid temperature—in two separate locations—creates a noticeable color difference pre-and-post oxygenator (and pre-and-post patient), hence simulating observable blood oxygenation color difference.

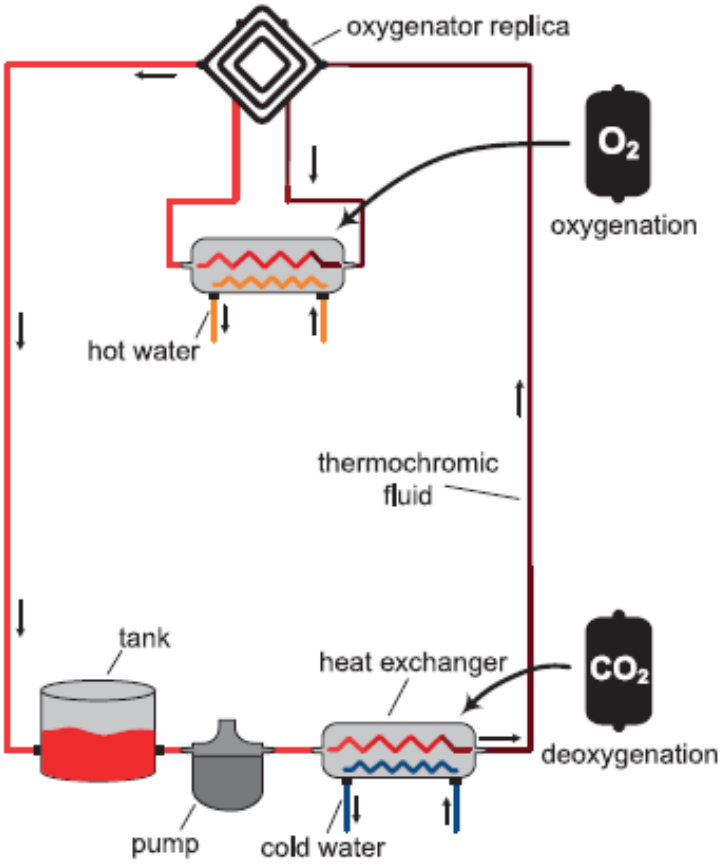

Figure 1: Simulated ECMO circuit design.

Thermochromic Fluid

Many fluid colors can be achieved by mixing thermochromic inks with other variants or coloring products. Our aim was to find an affordable, yet optimal mixture that visually resembles blood. Initially, red and black thermochromic inks (SFXC, East Sussex, UK) were mixed and diluted in distilled water. Considering that the black thermochromic ink becomes invisible when heated to $31°$C, the premise was

for the black thermochrome to be cooled to introduce a dark tint onto the red and heated to eliminate itself, creating a dark-red to red color difference. Unfortunately, diluting the inks in water caused a subtle gray-shift in their colors (black → gray, and red → pink) resulting in a purple to pink thermochromic fluid. An attempt to color-correct the purple into red was pursued by mixing in yellow and red concentrated dyes (Mayhems Solutions, Darlington, UK). However, it proved impractical as it was necessary to add large amounts of dye to make a noticeable difference, raising the overall cost of the simulated blood. This was addressed by eliminating the red thermochromic ink from the mixture, allowing lower amounts of dye to produce a more potent effect. Diluting the ink in water was also observed to cause the black ink to change state between 27°C to 32°C rather than the advertised $31\ ^{\circ}\mathrm{C}$. This temperature transition region was kept in mind during the design process of the circuit. The final fluid recipe is presented in Results.

Heat Exchange

Each of the two modules contains a plate heat exchanger (PHE) chosen on the virtue of its compactness and efficiency. PHEs take two liquid streams (primary and secondary) and facilitate heat transfer from the hot stream to the colder one through thermal conductive plates. In both modules, the primary stream is the thermochromic fluid and the secondary stream is hot or cold water supplied by a heater-cooler machine. The aim of this section is to describe the selection of a flow rate for the primary stream and flow rates and temperatures for the secondary streams which will result in a sufficient (thermochromic state-altering), balanced (between the two modules), and bounded (by the capacity of the heater-cooler machine) heat exchange process.

The relationship between the heat exchanged between the two streams, their input temperatures, and their flow rates is summarized in (1).[19] Where Q is the heat transferred between the two streams (in W), T_{in} and T_{out} are, respectively, the fluid's temperature into and out of the HE (in °C), F is the fluid's flow rate (in L/min), U is the heat exchange coefficient (in $\mathrm{W} \times\ \mathrm{m}^{-2}\ \times {}^{\circ}\mathrm{C}$), and A is the heat exchange area (in m^2). The subscripts h and c are used to refer to the warmer or colder streams with respect to the other as seen at the input of the HE (i.e. the thermochromic fluid is considered a hot stream when compared to cold water and a cold stream when compared to hot water).

$$\Delta T_{in} = T_{h,in} - T_{c,in}$$
$$T_{out} = T_{in} + \frac{60\ Q}{4180\ F} \quad (1)$$

$$Q = UA\frac{\Delta T_{in} - [\left(T_{h,in} + \frac{60\ (-Q)}{4180\ F_h}\right) - \left(T_{c,in} + \frac{60\ \mathrm{Q}}{4180\ F_c}\right)]}{\ln(\Delta T_{in}) - \ln([\left(T_{h,in} + \frac{60\ (-Q)}{4180\ F_h}\right) - \left(T_{c,in} + \frac{60\ \mathrm{Q}}{4180\ F_c}\right)])}$$

Since the final equation in (1) is non-linear and has many variables, an iterative empirical approach is used to determine the appropriate temperature and flow rate values. The procedure is applied per module and is as follows:

1. Select a PHE and find the constant UA using its physical properties and properties of distilled water.[20]
2. Select an operational temperature range for the thermochromic fluid. Estimate the initial temperature values allowed into the tank before the system startup (common to both modules).
3. Assume a flow rate for the thermochromic fluid (common to both modules).
4. Assume a temperature and flow rate for the secondary stream (hot or cold water depending on the module). This is typically found in the heater-cooler machine specifications.
5. Find Q using a non-linear solver such as MATLAB's *fsolve()* function.
6. Check if Q causes sufficient temperature change to output the desired thermochromic state (in this case $T_{out} < 27$ when cooling and $T_{out} > 32$ when heating).
7. Check if the maximum Q transferred is within the heating/cooling capacity of the heater cooler-machine.
8. Repeat steps 3, 4, and 5 until 6 and 7 are met.

Circulation and Flow Control

This section aids in the pump selection process by describing the estimation method of the required pump head. Head is the positive pressure, exerted on a liquid, required to overcome the flow resistance caused by circuit components (tube and HEs, in-line sensors, etc.).

The tube-generated head is described in (2), where H_t is the tube's head (in m), λ is the tube's friction coefficient, L is the tube's length (in m), and d is the tube inner diameter (in m).[21] The friction coefficient depends on the tube's wall material and (3) provides an estimation based on the use of polyvinyl chloride (PVC) tubes, where Re is the circuit Reynolds number. The additional head generated by other components (HEs, in-line sensors, etc.) can be found in the corresponding component's specifications sheet.

$$H_t \approx \frac{2.2975\,\lambda\,F^2 L}{10^{11}\,d^5} \tag{2}$$

$$\lambda \approx \begin{cases} \dfrac{64}{Re}, & \text{if } Re < 2000 \\ [-2\log_{10}\left(\dfrac{2.51}{Re\sqrt{\lambda}} + \dfrac{0.0015}{3700\,d}\right)]^{-2}, & \text{if } Re \geq 2000 \end{cases} \tag{3}$$

$$Re \approx \frac{F}{0.037605\,d}$$

Running any pump at a constant rotation per minute (RPM) will produce a flow rate proportional to the flow resistance of the circuit it is connected to. In ECMO, the circuit flow resistance changes significantly based on the patient's size, age group, and the health condition of the veins and arteries. Hence to maintain the flow rate required for sufficient heat exchange, the pump's RPM requires continuous adjustment. Fortunately, brushless direct-current (BLDC) motor pumps are easy to control, readily available, and inexpensive. A metal-oxide-semiconductor field-effect transistor (MOSFET) can act as a variable electric current "valve" when placed in series with the pump's power source. In this implementation, a microcontroller reads the flow rate from a flowmeter and subsequently controls the current that goes through the MOSFET. This results in more or less electric current reaching the pump, hence, varying its power and RPM to maintain the circuit's flow rate.

Thermochromic Circuit Design

Following the design procedure outlined in the previous section, the HXP-193 (Koolance, Auburn, WA) was the selected PHE used to heat and cool the thermochromic fluid above and below the aforementioned transition region. The PHE's UA constant was calculated as $(433\ \frac{\mathrm{W}}{^\circ\mathrm{C}})$ and the thermochromic fluid operational temperature range was set from $21\ ^\circ$C to $40\ ^\circ$C and the secondary streams values (temperature and flow rate) were bound by the Sorin 3T (LivaNova, London, England) heater-cooler available in our partner hospital. The resultant configuration is as follows:

- Thermochromic flow rate: ≤ 1.6 L/min
- Cold water: $25\ ^\circ$C at 15 L/min (Sorin 3T patient circuit)

- Hot water: 35 °C at 9 L/min (Sorin 3T cardioplegia circuit)

Using the maximum thermochromic fluid flow rate (1.6 L L/min) and the 3/8" polyvinyl chloride (PVC) tube used in our circuit, λ was estimated to be 0.0388. Consequently, the total circuit head considering a 10 m tube, two heat-exchangers, and a flow sensor is 0.5 m. Koolance's PMP-300 (Koolance, Auburn, WA) BLDC pump was selected since it offers head up to 2.6 m. It was controlled by a Teensy 3.2 microcontroller (PJRC, Sherwood, OR) with feedback from an INS-FM14 (Koolance, Auburn, WA) flow meter.

Assessment

The thermochromic fluid color-temperature characteristics were quantified using a digital camera (Canon EOS 600D, Canon, Tokyo, Japan). Cold thermochromic fluid was filled in a beaker and placed on top of a hot plate to vary its temperature. A camera was fixed 50 cm away looking down into the beaker ($\approx 10° - 20°$ clockwise) to minimize reflection. Pictures were taken under cool-white fluorescent lighting (≈ 4100 K) and the camera's exposure was fixed with the help of a luminance histogram. To reproduce colors correctly, the photos were digitally white balanced using an objective technique.[22] Then, ten-pixel points were sampled from the fluid's surface and the average of the pixels' standard Red-Green-Blue (sRBG) components was considered the quantified color.

The circuit was implemented and tested with a convenience sample of ECMO clinicians from Hamad Medical Corporation (HMC), our partner hospital. Nineteen participants from different professions (physicians, perfusionists, nurses, and respiratory therapists) evaluated the thermochromic effect. They, on average, had 4.73 $(0.5 - 12)$ years of ECMO experience and had cared for an average of 75 $(3 - 150)$ ECMO patients each. The demographics are summarized in Table 1. Participants were introduced to the circuit and were asked to fill in a questionnaire that included a set of statements about the realism of the "blood" color in its oxygenated and deoxygenated states along with the contrast between the two states using a 5-point Likert scale (1=not realistic at all; 5=very realistic).

To assess the thermochromic fluid consumability, samples were taken from the circuit's reservoir every two hours of the circuit's operation as the fluid was continuously circulating through the cooling and heating system. Samples' ink concentration was estimated using a calibrated $400nm$ absorbance versus concentration plot.

Table 1: Demographic characteristics of evaluation participants.

	$n(\%)$
Gender	
Male	$14\ (73.6\%)$
Female	$5\ (26.4\%)$
Age (years)	
25 – 34	$4\ (21\%)$
35 – 44	$9\ (47\%)$
45 – 54	$4\ (21\%)$
55 – 64	$2\ (11\%)$
Profession	
Physician	$5\ (26.4\%)$
Perfusionist	$5\ (26.4\%)$
Nurse	$8\ (42.1\%)$
Respiratory therapist	$1\ (5.1\%)$
	Mean ($\pm$std)
ECMO experience (years)	$4.7\ (\pm 3.2)$
Number of patients cared for	$75\ (\pm 52)$

Ethics

The clinicians' evaluation aspect of this research project was approved by HMC's Medical Research Center (#17231/17) and classified as "exempt" from full ethical review.

Results

Thermochromic Fluid

As outlined in Methods, thermochromic ink enables achieving a variety of possible color variants. Our final recipe consisted of black thermochromic ink with red and yellow concentrate dyes. The ink was first diluted in distilled water to obtain the desired concentration. Afterwards, the volume of dyes is determined proportional to the ink's weight. Figures 2A and 2B show, respectively, how fluid temperature and ink concentration affect the color of the mixture. The ink's concentration was kept constant during temperature variations and vice-versa with the dyes' concentration always proportional to the ink's weight.

sRGB components of the quantified color bars in Figures 2A and 2B are plotted in Figure 3 where the ink temperature transition region can be clearly

observed. Moreover, we found that concentrations lower than 13 mg/mL were too translucent, and hence a black thermochromic ink of that concentration or higher was considered visually acceptable.

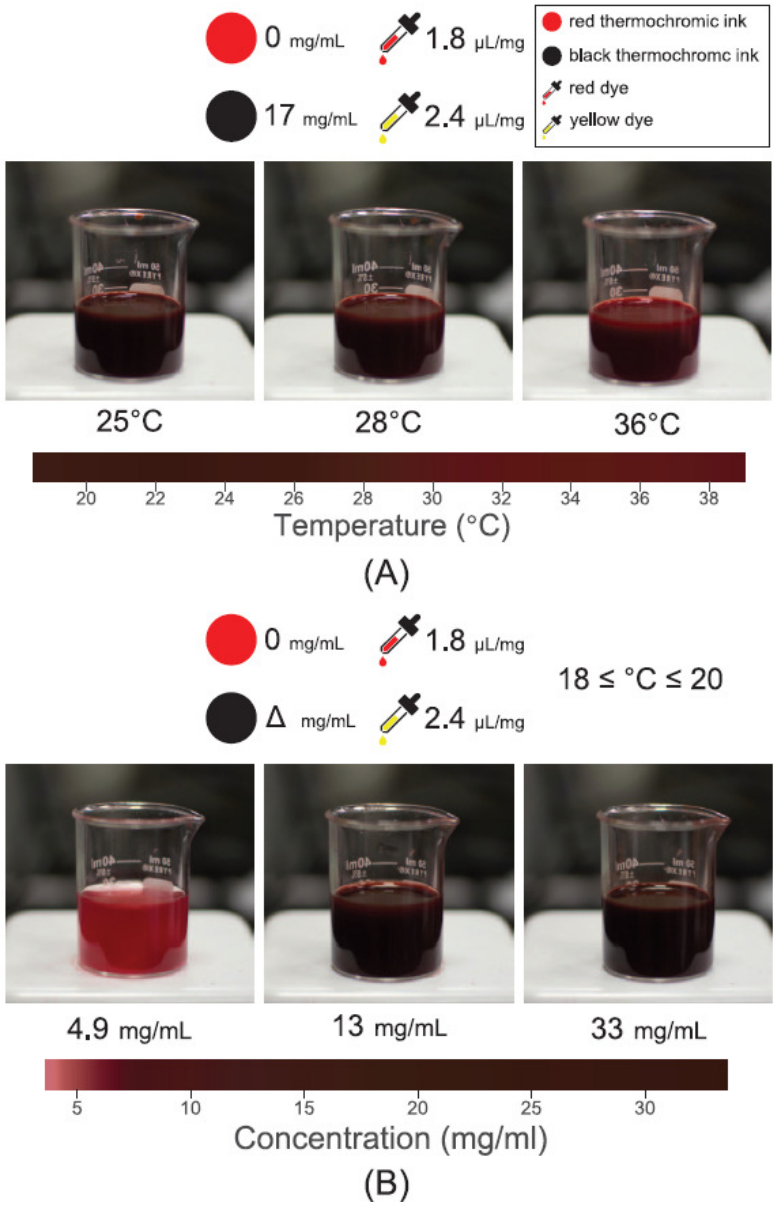

Figure 2: Thermochromic fluid final recipe. (A) The fluid recipe varied over the selected operational temperature range at a fixed concentration (B) The fluid recipe varied over thermochromic ink concentrations.

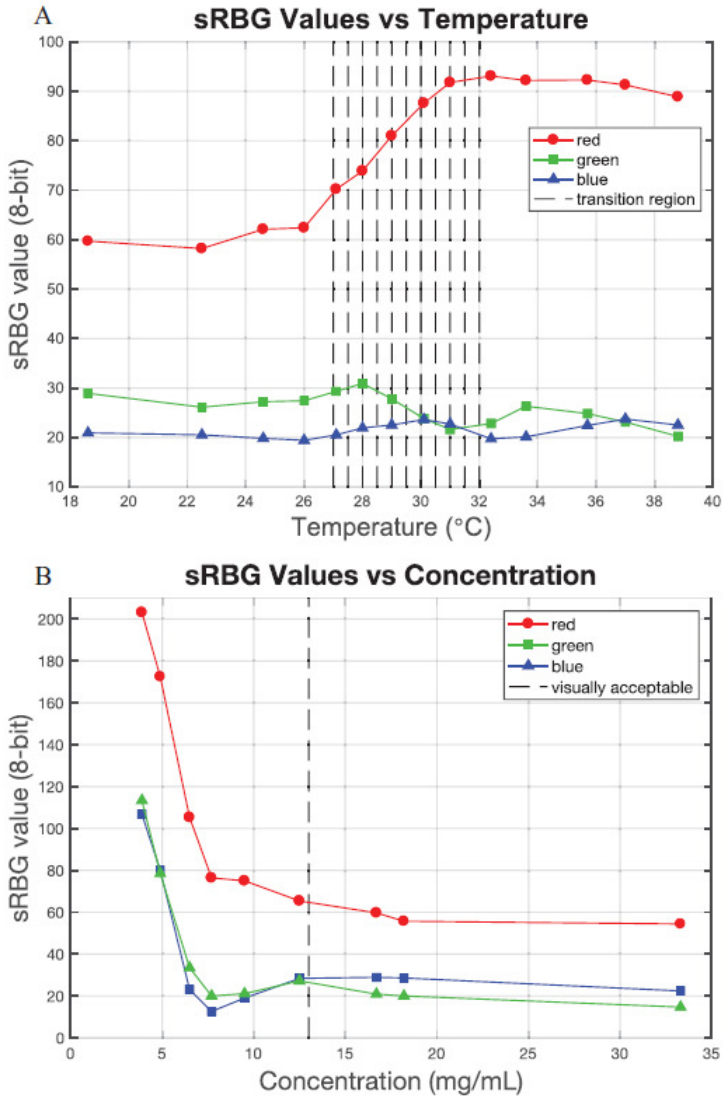

Figure 3: Quantified standard red green blue (sRGB) components. (A) sRGB against temperature variation. (B) sRGB against concentration.

Circuit Implementation

The circuit described in Methods was setup in an intensive care unit at HMC as seen in Figure 4. A prototype mock-up of Maquet's HLS oxygenator (Maquet, Rastatt, Germany) was 3D printed and used to discreetly bypass the liquid to the oxygenation module (heating unit) and receive it after heating via an opaque PVC tube. The circuit produced three distinct color visual effects as seen in Figure 5:

blood oxygenation and deoxygenation, low-oxygen saturation in the return line, and high-oxygen saturation in the drainage line.

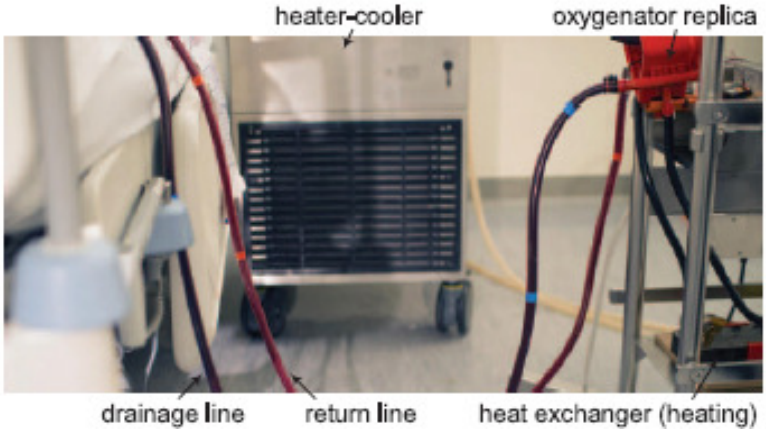

Figure 4: Simulated “ECMO circuit" setup in an ICU.

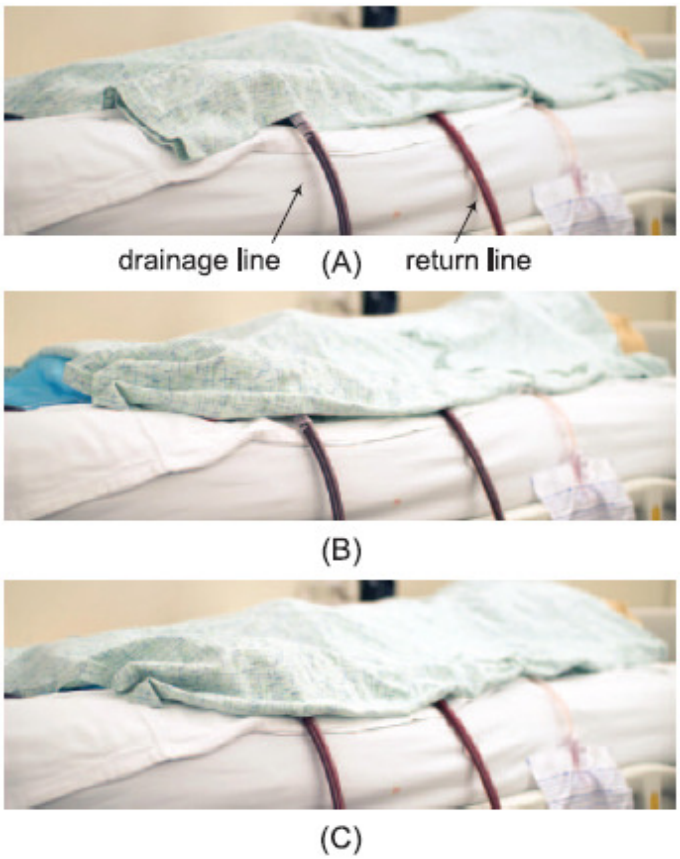

Figure 5: Simulated “ECMO circuit" in its three states. (A) Blood oxygenation and deoxygenation. (B) Low oxygen saturation in return line. (C) High oxygen saturation in the drainage line.

The mean rating (out of 5) for oxygenated and deoxygenated blood color realism, and realism of their contrast were 4.63, 4.79, and 4.53 respectively. Table 2 summarizes the results. Over the period of ten hours, five samples of the thermochromic fluid were taken from the reservoir and their concentration was measured. Using a linear fit, we found that the fluid degrades by a 0.38 mg/mL ($R^2 = 0.84$) per hour. Between the tenth and eleventh hours of operation, the thermochromic fluid failed whereby the black thermochromic ink stopped transitioning when heated. None of the participants witnessed the thermochromic fluid in its non-functioning state.

Table 2: Results descriptive statistics

Sample size n = 19	
Oxygenated "Blood" Color Realism	Mean = 4.63 (± 0.482) Min = 4.00 Max = 5.00 Mode = 5.00 Median = 5.00
Deoxygenated "Blood" Color Realism	Mean = 4.79 (± 0.408) Min = 5.00 Max = 4.00 Mode = 5.00 Median = 5.00
"Blood" Color Contrast Realism	Mean = 4.53 (± 0.595) Min = 3.00 Max = 5.00 Mode = 5.00 Median = 5.00

Discussion

High-fidelity simulation sessions aid in achieving suspension of disbelief in trainees and prevent negative learning, a key to successful SBT.[24,25] However, high-fidelity systems and environments are costly and require a significant financial commitment.[26] This is exacerbated with the currently used ECMO SBT

approaches. On top of simulation equipment, ECMO centers that offer SBT also rely on a functioning ECMO machine alongside expensive consumable circuit components which offer little in terms of context because the visual/audio cues they produce and parameters they display are generally inconsistent or uncontrollable in relation to enacted scenarios.

We sought to address the limitations of the ECMO simulation paradigm by developing a standalone and modular ECMO simulator. In this article, we demonstrated the design and implementation of a patented simulated "ECMO circuit" featuring a unique thermochromic effect that resembles blood oxygenation color change in real ECMO circuits[27]. The circuit operates on a balanced and continuous heat exchange process, producing a temperature difference between the drainage and return lines, and hence a color difference due to thermochromism. It can create visual cues relevant to many emergency scenarios including oxygenator failure, disconnected gas supply, increased oxygen consumption, decreased lung function, inadequate circuit flow, and recirculation. Nineteen clinicians specializing in ECMO at HMC with varying degrees of experience evaluated the fidelity of the thermochromic effect. On average, the participant rated the effect as highly realistic. The common criticism received was that the oxygenated and deoxygenated "blood" colors were too dark and should be slightly brighter and redder, which can be corrected by changing the concentration of dyes and ink in the fluid mixture.

Advantages of an ECMO independent simulator with a modular design approach are the reduced deployment and maintenance cost, customizability and expandability, and full system control. The simulated blood color change circuit components (excluding the heater-cooler) costs 300 USD to build and can be used indefinitely (or until a component is damaged) since components are non-consumable. Our thermochromic recipe costs 40 USD/L with a low (0.38 mg/mL) concentration degradation over time and an operational lifetime of ten hours. It is up to the user to determine whether circuit component costs and the fluid's realism, cost, and lifetime is acceptable as every component used in the circuit can be substituted by other brands and there are many possible recipes due to the broad selection of thermochromes and dyes in the market. Moreover, our in-house design facilitates ease of use and control since the system electronics are programmable to the user's preference and can be wirelessly enabled to receive remote commands to perform simulation actions. Overall, many of the existing ECMO related SBT programs could greatly benefit from this innovation to further enhance their participants' learning.[24]

This study has several limitations. First, we had no access to quantitative color-measuring tools, limiting the color quantification to a digital camera, where it can vary based on the illuminance and the camera exposure settings. We

attempted to mitigate this weakness by (i) presenting photos of the fluid in two different environments and illuminants (in-lab and in-situ); (ii) using the camera's luminance histogram to make sure the exposure is set in the middle (not too dark or too bright); and (iii) surveying ECMO specialists about the realism of the color. Second, our assessment of the circuit's efficacy is limited by the prototypic nature of the implementation. Thus, our design can only be truly assessed when the system is complete with a "product level" quality and is compared head to head with the traditional simulation method. Finally, the realism of the simulator is highly dependent on the fidelity of our 3D printed components and casings and how well we can integrate the modules into the ICU environment. Future work includes obtaining a thermochromic fluid with longer operational time and establishing a dynamic relationship between simulated blood color and various ECMO parameters such as hemoglobin and oxygen saturation.

Conclusions

A novel system consisting of modules that work together to reproduce ECMO's visual, audio, and haptic cues is proposed. In this article, we presented the use of a low-cost but high-fidelity technology in the design of two modules responsible of creating a simulated ECMO circuit with the ability to reproduce ECMO's blood oxygenation visual cue (or the lack thereof) using the thermochromism properties of a fluid mixture. The two modules work together to create a temperature difference between the drainage and return lines of the "ECMO circuit", resulting in a color difference. ECMO practitioners found the circuit highly realistic and they could easily distinguish the two colors of the simulated blood.

We envision that, after completion, our modular ECMO simulator will feature more simulated ECMO cues including drainage line vibrations (line-shattering), patient bleeding, air noise in the pump head, blood oxygenator clotting, and others. Those modules will be wirelessly connected to a tablet application, giving instructors full control of the ECMO environment and facilitating the creation of high-fidelity and immersive simulation scenarios.

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Declaration of Conflicting Interests

The Authors declare that there is no conflict of interest.