Team Results Document
SensingBarcelona

University: UB & UPC

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SensUs

SensUs 2024
Acute Kidney Injury

1. Abstract (max. 200 words)

Our biosensor offers an affordable and accessible solution for monitoring creatinine levels, which is crucial for assessing kidney function. It uses a simple chemical reaction to produce a color change in the presence of creatinine. This color change is detected by a camera and analyzed by a Raspberry Pi, providing accurate results with minimal cost. The system's simplicity and low-cost components make it an ideal choice for widespread use, even in areas with limited resources. This easy-to-use, low-investment biosensor is designed to be practical and effective anywhere in the world, enabling routine health monitoring and early detection of kidney issues without requiring significant financial investment.

2. Biosensor (max. 2 A4)

Molecular recognition

The sensor that is intended to be designed employs a detection method based on the Jaffé reaction. In this method, creatinine is mixed with picric acid in an alkaline sodium hydroxide solution [1]. This reaction results in the formation of the Janovsky complex, an orange-red chromophore. The amount of precipitate formed, or the colour change produced, is directly proportional to creatinine's concentration.

To facilitate the reaction, the sensor includes a designated area for this process. On one side, simulated interstitial fluid containing creatinine is introduced using a microfluidic pipette, while on the other side, the two reaction reagents (working solution) are delivered via injection. These reagents (picric acid and sodium hydroxide) are mixed in equal volumes and stored in the sensor's reservoir.

Cartridge Technology

A microfluidic chip is intended to:

a. Transport the sample from the inlet (inserted by microfluidic pipette) to the detection site.
b. Ensure the proper mixing (reagents and sample) and optimal reaction time.
c. Store and dispense reagents in the peak amounts determined theoretically and adjusted through trial and error in the laboratory.
d. Act as the detection zone of the creatinine concentration.

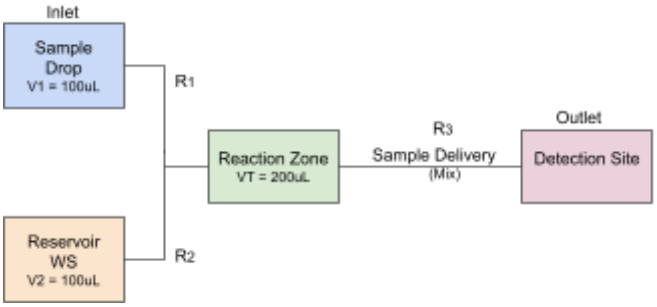

Figure 1. Sketch of the microfluidics chip's function.

Table I summarizes the design parameters selected for each section, ensuring a reaction time of 247 seconds (~4 min) for a flow rate of 50 uL/min.

TABLE I. Theoretical results for each section of the channel.

Section	$R_{H,c}$ [Pa.s/m3]	Flow velocity [mm/s]	Volume [uL]	Pressure [mbar]
R1 (inlet)	3.43E+8	1.6	2.51	0.19
R2 (reservoir)	3.43E+8	1.6	2.51	0.19
R3 (mix)	4.29E+8	0.41	201.06	0.19

These measurements served as a reference for purchase of Microfluidic Starter Kit.

Physical Transdcution: Image Processing

The detection zone is the canal itself, since the camera operates directly above it. Colour intensity manifestation is directly proportional to the concentration of creatinine. Therefore, to ascertain the concentration of creatinine, an image of the detection area is captured and image processing techniques are applied. Lighting is controlled with non-coloured LEDs and closed casing for consistent results.

Firstly, a Region of Interest (ROI) is defined in the microfluidic channel and applied to each of the captured images. Subsequently, the three channels are extracted from the RGB colour space, and the weighted intensity is obtained. This weighted intensity is computed with the following formula, which is a modification of the *Luminance* formula but adding more weight to the red and green channel as they are the ones that change the most at different concentrations:

$$Luminance = 0.6 \cdot \frac{R}{R+G} + 0.3 \cdot \frac{G}{R+G} + 0.1 \cdot \frac{B}{R+G}$$

Following this, experimental data is utilized to calibrate the relationship between color intensity and creatinine concentration. Afterwards, this calibration is applied to establish the mathematical relationship for creatinine concentration, which will serve as the basis for future sensing and display of results.

Similar techniques have been demonstrated [2] via a smartphone application.

Reader Instrument

The overall system consists on a closed box where all the components are stored inside, this box has different attachments to fix the RaspBerry Camera and the RaspBerry Microcontroller as well as the bomb which pumps the Jaffe's Reactives and the microfluidic channel, the illumination of the system is done by a LED near the camera and illuminating the microfluidic chamber. The overall images of the 3D design of the box is added to the Appendix of the document.

User Interaction

Since the display screen is non-tactile, interaction is achieved using a keyboard and mouse, also attached to the microcontroller. This could be easily changed in the future.

3. Technological feasibility (max. 2 A4)

The results obtained using the RaspBerry Camera over time from the sample at specific conditions showed specific evolution of the color distribution over time common in all of the concentrations as shown in the following figure:

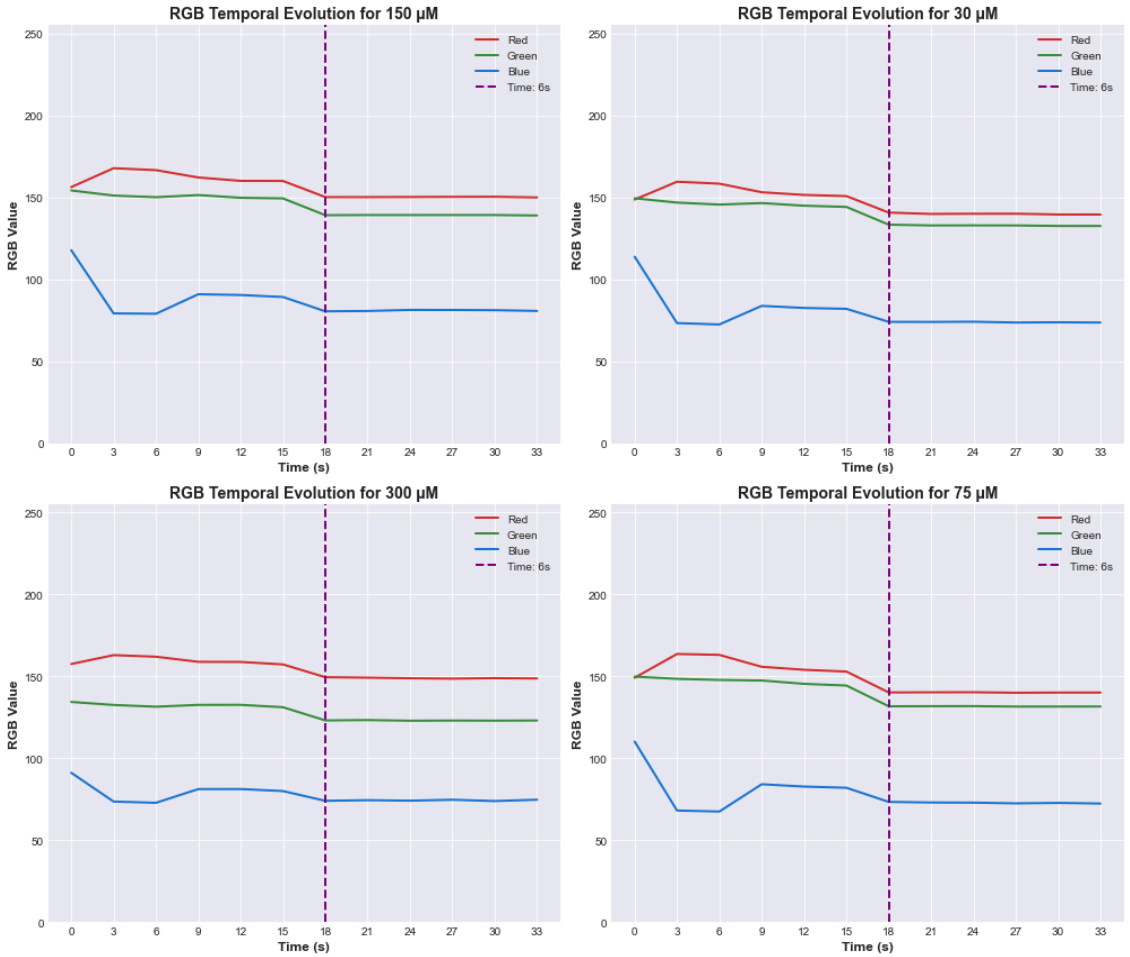

Figure 2. Temporal Evolution of RGB images acquired with the RaspBerry Camera at different concentrations.

Due to this noise from the beginning of capture of images, those obtained before the 18th second were discarded. Then, the luminance values of the RGB of the predefined ROI in each of the images were calculated and saved to a csv file which the mean was computed to do the calibration of the luminance to concentration.

With an initial view of the data it was obvious that the model used for the calibration was an exponential model approach. Using the *curve_fit* function from the *scipy* package the final function of calibration was computed. It changes depending on the data used but the final one was obtained using the mean luminance value of different samples at different concentrations. The final calibration curve used is the following one:

$$Concentration = 0.00210119 \cdot e^{0.00614206 \cdot Luminance} + 0.47833411$$

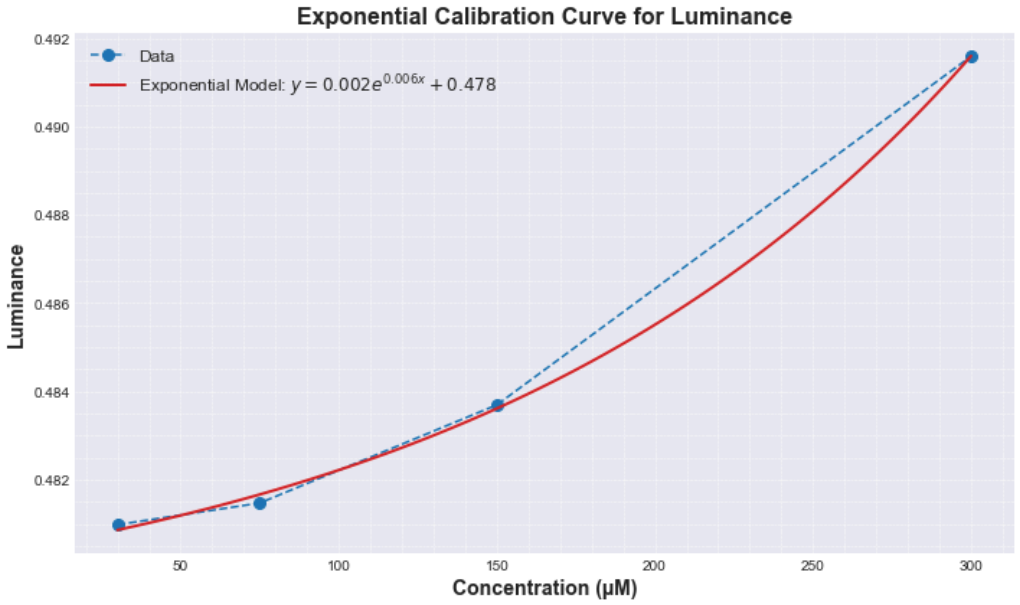

Figure 3. Calibration Curve that relates the Luminance Computation of the image with the actual creatinine concentration of the sample.

This calibration formula demonstrates that our sensor is able to successfully detect creatinine concentration changes accurately. The main factor that could potentially affect the result is the stability of lighting conditions. However, this is solved by encapsulating the system and providing stable light. Another possible problem lies in the Jaffé reaction, since it is unknown for us if other variables in human ISF can affect the resulting colour.

4. Originality (max. 1 A4)

(1) We strongly believe our sensor's most significant innovation lies in its affordability and easily replication, since it only requires basic reagents which serve as consumable materials and a camera-microcontroller. This simplicity reduces costs as well as makes it accessible to a diverse group of users. We have made it possible for this technology to be implemented anywhere in the world with minimal investment. All the work has been done collaboratively by the team members through meetings, where we developed strategies. We then asked for feedback from our supervisors and coaches, who provided valuable insights on the viability of our approach and helped us gain access to the resources needed. This same dynamic has ruled our lab and confection sessions.

(2) The sensor designed by the Sensing Barcelona team is based on the Jaffé reaction and a microfluidic flow cell. This reaction, first reported in 1886 by Max Jaffé, has been used in clinical diagnostics for over a century. It involves the interaction of creatinine with picric acid in an alkaline medium, resulting in a color change that can be quantitatively measured. While the reaction itself is well-established, the innovation introduced by the Catalan team lies in the application of this chemistry to a microfluidic environment with optical detection for continuous monitoring of creatinine levels. The team has developed image acquisition and analysis software, coupled with custom-designed hardware, to ensure accurate and continuous measurement of creatinine concentrations. These components are designed in-house under strict budgetary constraints, which demonstrate the ability to implement it in low-resource settings.

The simplicity of this method exemplifies the principle of Occam's razor, as it achieves fast, reliable, and cost-effective detection of creatinine. The microfluidic nature of the systems also allows for further development, for example for multiplexing, or increasing specificity by enzyme selection. Despite the challenges posed by limited resources, the Sensing Barcelona team has succeeded in creating a sensitive biosensor that operates efficiently within a short time frame. The originality of their work is subtly embedded in their ability to engineer low-cost, self-fabricated components, while still maintaining a simple yet robust optical detection system. This balance between simplicity and functionality underscores the innovative nature of their contribution to sensing technology.

5. Translation potential (max. 5 A4)

Business model canvas

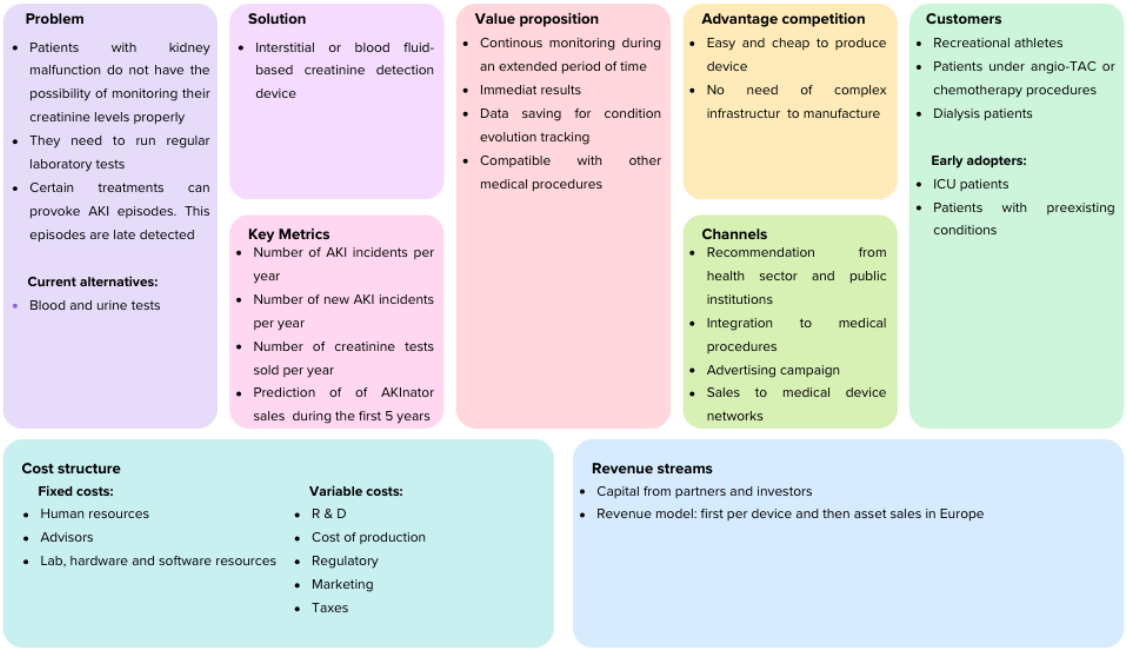

Figure 4. Business Model Canvas of the Project.

Market description

The incidence of acute kidney injury (AKI) among hospitalized patients presents a significant clinical challenge, affecting a broad range of individuals, particularly those in critical care settings. AKI, characterized by a sudden decline in kidney function, is associated with increased mortality, prolonged hospital stays, and higher healthcare costs. This condition can result from various factors, including sepsis, major surgery, and exposure to nephrotoxic drugs. Early detection and monitoring are crucial for improving outcomes, yet current methods, primarily reliant on intermittent creatinine measurements, are insufficient for timely diagnosis and intervention [3].

In the context of endurance athletes, AKI also emerges as a significant concern. Intense physical exertion, particularly in prolonged endurance events, can lead to a condition known as exercise-induced acute kidney injury (EIAKI). This condition, though often transient, can have severe implications if not properly managed. The risk is heightened by factors such as dehydration, heat stress, and the use of nonsteroidal anti-inflammatory drugs (NSAIDs), which are common in endurance sports. The potential for EIAKI in this population underscores a substantial market opportunity for continuous creatinine monitoring [4].

Continuous creatinine monitoring could revolutionize the management of AKI by enabling real-time detection and early intervention, which is especially critical in settings where patients are at high risk, such as intensive care units or during endurance events. For endurance athletes, this technology could provide valuable insights into kidney function during and after extreme physical exertion, allowing for timely interventions that could prevent long-term kidney damage as well as help them maintain optimal hydration levels and show them their hydration status [5]. The ability to continuously monitor kidney function represents a significant advancement over traditional methods, offering a proactive approach to AKI management and potentially reducing the incidence of severe outcomes. An integration of this creatinine monitoring to the Dialysis Machines is also one of the main improvements that can be done, as nowadays the only follow up of the creatinine levels of the patient are done before and after the procedure, a continuous monitoring would show the creatinine clearance during the session, ensuring the removal of the waste before finishing the session [6].

Stakeholder Desirability

The methods available to test creatinine for diagnosing Acute Kidney Injury (AKI) have two principal problems: they are expensive and can make just one measure. To diagnose and monitor AKI, it's necessary to measure the changes on creatinine or other indictors concentration in different human body fluids (blood or urine) [7]. The most accurate methods are done in a laboratory, where all the variables can be successfully controlled (glucose levels, certain medications, bilirubine, etc.). Therefore, AKI patients are constantly required to stay at the hospital to provide several urine or blood samples, which can be inconvenient and painful to obtain. Although the majority of AKI patients tend to be ICU patients [8], it has been proved that this condition is also commonly acquired by patients under certain treatments such as angio-TAC or chemotherapy, as well as by endurance athletes [9,10,11]. For them, having regular visits to the hospital can negatively impact their daily lives. Laboratory methods, although having the biggest accuracy, can't reflect the current kidney health given that they don't use instant data. Instant data devices are single use blood or urine biosensors, which can't give continuous data of creatinine levels. The prices of these devices can vary between 200 and 500€ [12,13], making them particularly difficult to afford.

Our biosensor based on a colorimetric imaging technology gives a real-time, in situ and continuous monitoring of creatinine levels in body fluids such as blood or interstitial fluid. Results are obtained in no more than 5 min per sample and easily shown in an LCD monitor for instant feedback. All the results are saved in the device for tracking proposes. It can work up to 2 hours without needing a change in the reactives deposit. This device gives the customers the ability to check their creatinine levels in any place or after procedures with high AKI risk (see Figure 5 at the Appendix for our value proposition).

Moreover, our device can be adaptable to be used alongside certain procedures such as dialysis. Dialysis is a common procedure endured to patients with Acute Kidney Injury [14]. The same blood filtered by the device can be used to evaluate the functionality of the kidney's patient and consider stopping dialysis for the patient in the near future.

Business feasibility

Our biosensor's production and manufacturing process is designed to be highly scalable. The simplicity of our design, which includes widely available components such as the Raspberry Pi, microfluidic chips, and basic reagents like picric acid and sodium hydroxide, ensures that it can be produced at scale without requiring complex or expensive manufacturing processes. We plan to partner with manufacturers experienced in microfluidic technology to facilitate large-scale production. The global availability of these materials also provides a stable supply chain, minimizing the risk of production delays or cost fluctuations. To ensure consistent quality, we will implement rigorous quality control processes at each stage of production, including calibration checks for the image processing unit and thorough testing of the Jaffé reaction in each batch of reagents.

As we prepare to enter the market, regulatory approval will be a key focus. Given the healthcare application of our biosensor, obtaining approvals such as the CE marking in Europe and FDA approval in the United States is essential. We will initiate these processes early to ensure compliance with medical device regulations. Our market entry strategy will initially target low-resource settings where affordability and ease of use are critical. By providing a cost-effective and simple solution, we aim to fill a significant gap in these regions. Once established, we will expand into developed markets, focusing on home healthcare and outpatient monitoring, where continuous creatinine monitoring can provide early warnings for kidney issues. To reach our target customers, we will establish partnerships with healthcare providers, NGOs, and telemedicine platforms in developing regions, while in developed markets, we will utilize e-commerce platforms, pharmacy chains, and direct sales to healthcare institutions.

In terms of competition, our biosensor stands out due to its affordability and ease of use. Current solutions, such as laboratory-based blood tests or expensive wearable sensors, either require significant infrastructure or are prohibitively expensive for widespread use. Our sensor offers a low-cost, portable, and user-friendly alternative. While the simplicity of our design could potentially be replicated by competitors, we believe that our expertise in optimizing the Jaffé reaction within a microfluidic environment and our proprietary image processing algorithms will provide a competitive edge.

Financial viability

Our cost structure is designed to ensure that the production of our biosensor remains affordable while allowing for profitability. The initial development costs, including research and development, prototyping, and securing intellectual property rights, have been substantial but manageable, thanks

to funding from our universities and external grants. As we move into production, the unit cost of manufacturing the biosensor is expected to be low, thanks to the use of readily available materials and efficient production processes. We anticipate that economies of scale will further reduce these costs as production volumes increase. Operational costs, including facility rent, salaries, marketing, distribution, and customer support, will be carefully managed to maintain a healthy profit margin.

Our primary revenue stream will come from the direct sale of biosensors to healthcare providers, NGOs, and end-users. We plan to price the sensor competitively, ensuring it remains accessible while generating a high margin. In addition to direct sales, we are exploring the potential for a subscription model that would offer users cloud-based data storage and analysis services for a monthly fee. This model could provide a steady stream of recurring revenue and add value for our customers by enabling them to access historical data, advanced analytics, and telemedicine services. We also plan to pursue government grants and subsidies, particularly for deployment in low-resource settings, which could help offset initial production and distribution costs.

Our financial projections indicate that we will reach the break-even point after selling a certain number of units, which we expect to achieve within a few months of market launch. Given the low production costs and high demand for affordable healthcare solutions, we anticipate a strong return on investment within the first year of operation. We are confident in the long-term viability of our biosensor, especially as its design allows for incremental improvements and the potential to add new features, such as detecting additional biomarkers. This will help ensure that our product remains relevant and profitable as market needs evolve.

To bring our biosensor to market, we estimate that we will need additional funding to scale up production, marketing, and regulatory compliance. We plan to seek this funding through a combination of venture capital, angel investors, and crowdfunding. As our company grows, we may require further investment to expand into new markets, diversify our product line, and increase production capacity. We will take a staged approach to fundraising, setting clear milestones for each round of investment.

The components of our sensor are listed in the a below (Table 2.) Taking into account the costs of our sensor (see Table 2 at the Appendix) we have a fixed cost of 189,39€ of the overall machine and a variable cost of 32,18€ for 2L of reactants. If only 0.1 mL of reactant is used per measure, a total of 20.000 measures can be done with one Reactant’s Kit. Taking into account that a measure is done each 30 seconds, the system can work for 10.000 hours. With this information the unitary prize of each measure is of **0,006€**.

6. Team and support (max. 1 A4)

All team members have contributed to our sensor's development, many on different stages and parts but overall contributing to the final product. Janet has been with us in every meeting, providing constant support and insightful guidance throughout the whole process. Jordi and Jasmina have been invaluable, offering feedback on their respective fields and helping us secure necessary resources. Lexa has provided critical feedback on the sensor itself and has guided us on how to effectively and confidently present it to the medical market.

Funding for our presence in the competition has been provided by our universities, University of Barcelona (UB) and Polytechnic University of Catalonia (UPC), covering our inscription fees and flights to Eindhoven.

IBEC's participation has been crucial in acquiring specialized materials and a lab to conduct molecular recognition experiments, under supervision of our coach, Janet.

Additionally, we want to thank Dr.Francisco José Parrilla for his invaluable insights in determining the clinical applications of our sensor in the field of nephrology.

All their contributions have been essential to our project's success.

7. Final Remarks (max. ½ A4)

Our new sensor is the result of an exciting collaboration between students from different universities. This project brought us together from different fields, creating a sensor that represents the power of teamwork and student-driven innovation.

8. References (no page limitation)

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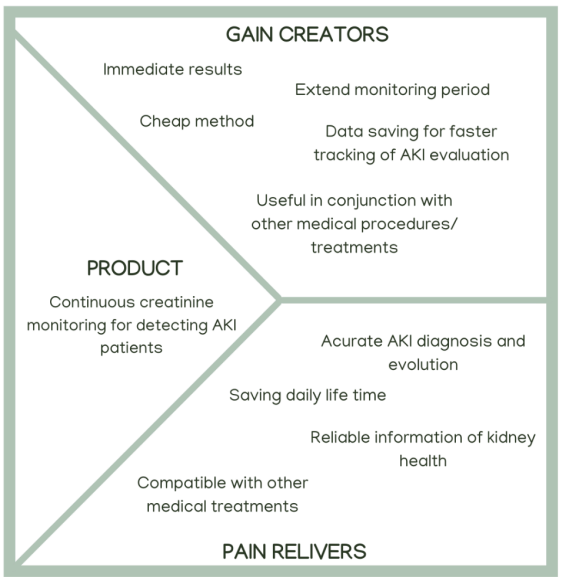
9. (Optional) Appendix (no page limitation)

Table 2. Table of prizes of the machine and project.

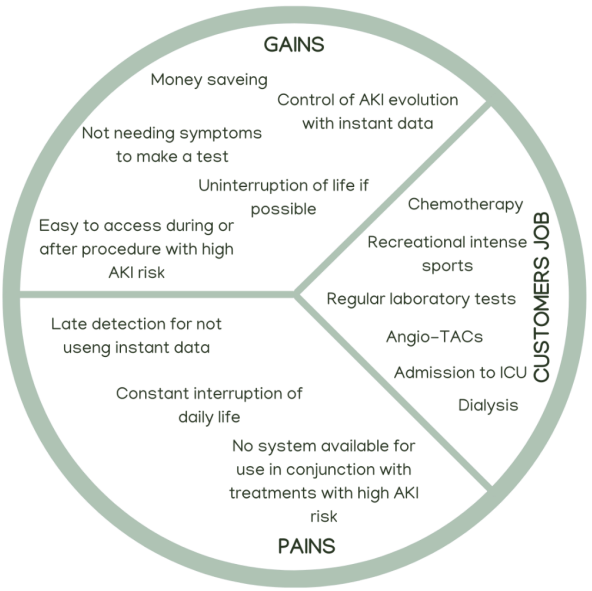
Description	Distributor	Manufacturer	Unitary Price	Nº of Units	Link
Microfluidic Pipette 20-200 uL	Labotienda	Digipette	47,00€	1	https://www.labotienda.com/es/productos-laboratorio/pipeta-autoclavable-vol-variable-20-200-ul/
Microfluidic Pipette Tips	Labotienda	Digipette	5,18€	2	https://www.labotienda.com/es/productos-laboratorio/puntas-para-micropipetas-200-l-baja-retencion-high-quality-rack-esteril-96-uds/
RaspBerry Display	RS Amidata	RaspBerry Pi	35,55€	1	https://es.rs-online.com/web/p/kits-de-desarrollo-de-pantallas/2539306?gb=s
RaspBerry Pi	RS Amidata	RaspBerry Pi	38,81€	1	https://es.rs-online.com/web/p/raspberry-pi/811

					1284?gb=s
RaspBerry Pi Camera	RS Amidata	RaspBerry Pi	47,68€	1	https://es.rs-online.com/web/p/camaras-para-raspberry-pi/2012852?gb=s
Stepper Motor	Amazon	AX Electronic	9,99€	1	https://www.amazon.es/gp/product/B00U744GJU/ref=ox_sc_act_title_1?smid=ACVR5JKB028QH&psc=1
Jaffe's Reactants	CormaKit	CromaKit	32,18€	1	https://cromakit.es/tienda/bioquimica-clinica/sustratos/creatinina-jaffe-2x1000-ml/
TOTAL PRICE:					**221,57€**

Value Proposition Canvas



Value proposition



Customer segments

Figure 5. Value Proposition Canvas of the Project.

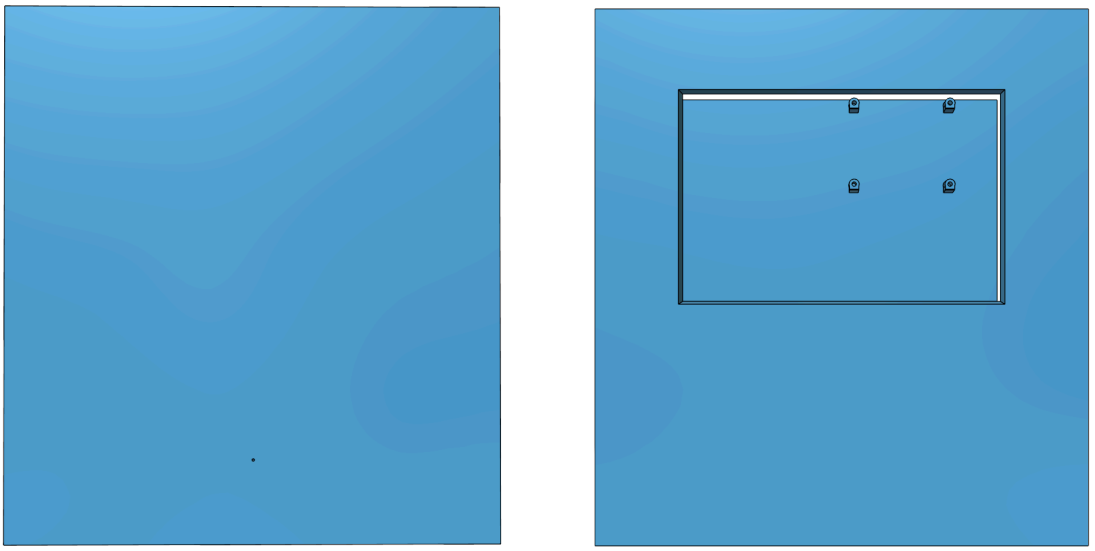


Figure 6. Back (Left) and Front (Right) View of the box.

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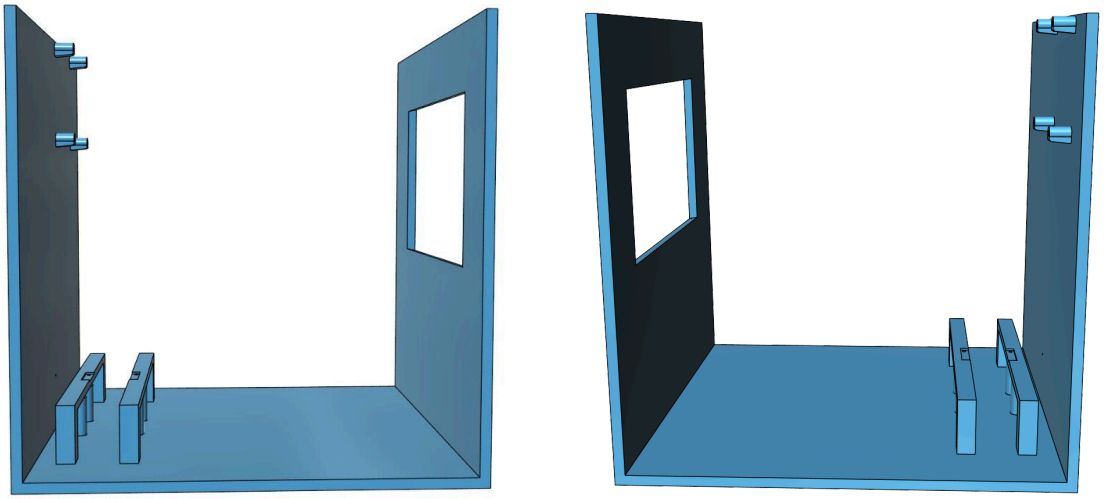

Figure 7. Left (Left) and Right (Right) View of the box.

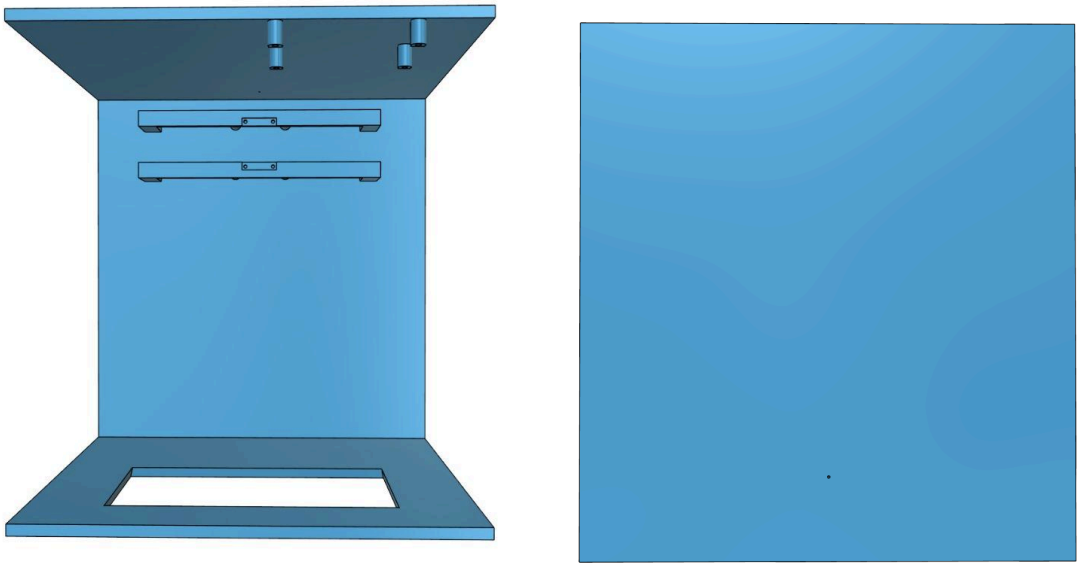

Figure 8. Top (Left) and Bottom (Right) View of the box.

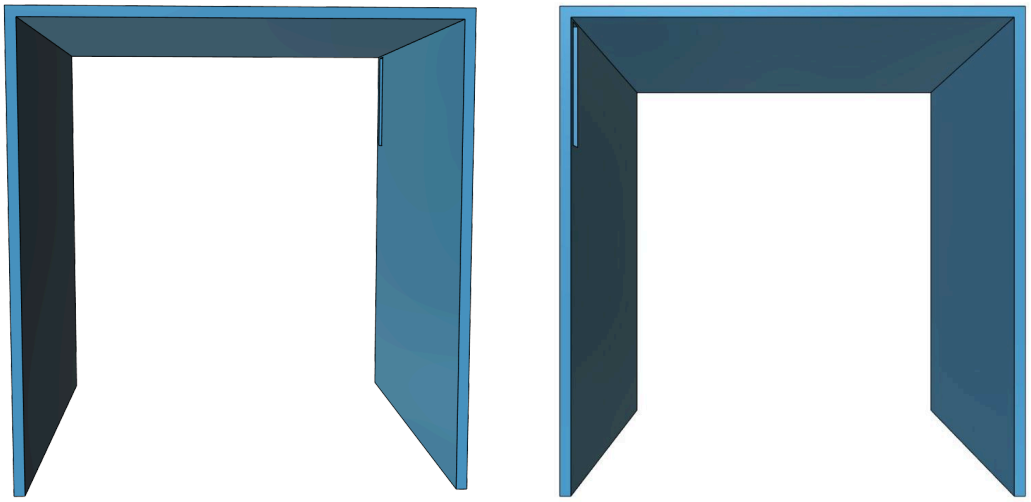

Figure 9. Front (Left) and Back (Right) View of the box.

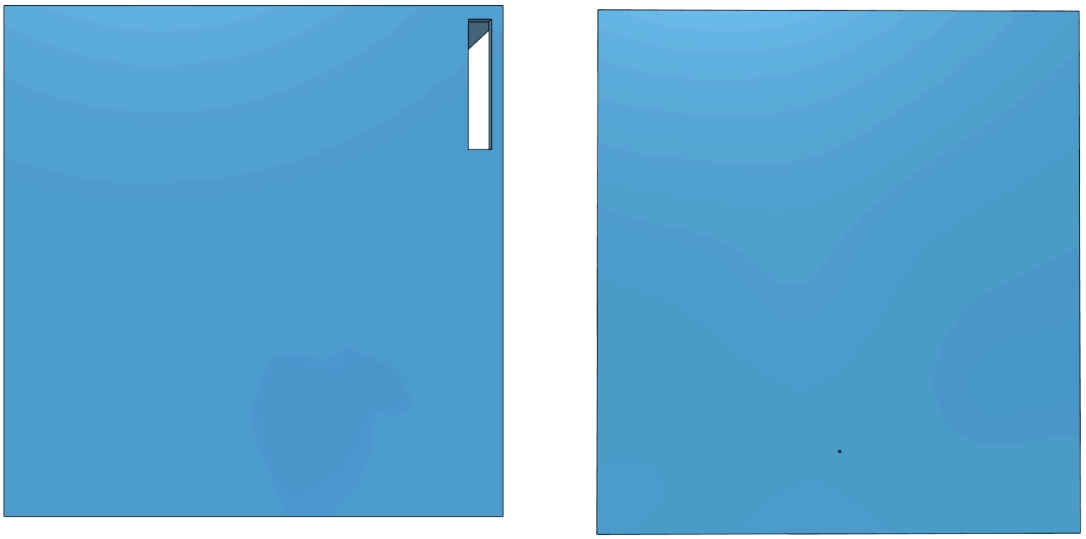

Figure 10. Right (Left) and Left (Right) View of the box.

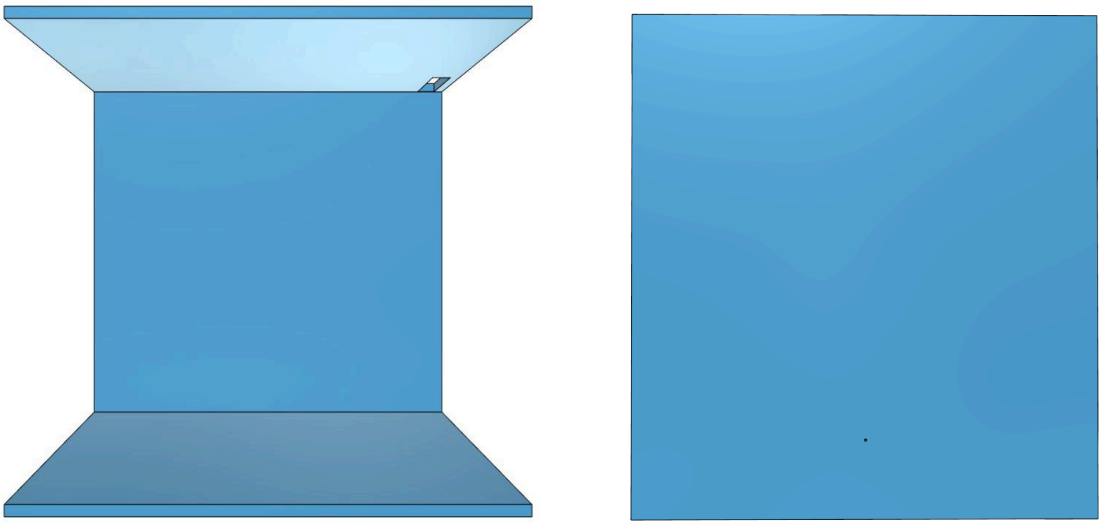

Figure 11. Top (Left) and Bottom (Right) View of the box.

Janet van der Graaf Mas, August 12th (Team Coach)	Aitana Carceller, August 12th (Team Captain)	Vicent Roig Roig, August 12th (Team Captain)