Team Results Document

SensETH

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SensUs

1. Abstract: Summary for the SensUs website

The wearable biosensor of SensETH introduces an innovative approach to continuous creatinine monitoring through its aptamer-based double-chamber system, building on the work by Nagarkatti et al. (2012). This design precisely eliminates background noise after each measurement, enhancing the accuracy. The biosensor features a modular design with two key components: a disposable patch and a reusable electronic module.

At the heart of the disposable system is a microneedle array that continuously extracts Interstitial Skin Fluid (ISF) at a consistent rate of $2\mu L/min$, delivering it to a microfluidic system designed by us. This innovative flow cell incorporates a Polyethersulphone (PES) membrane that filters out larger molecules, while allowing creatinine to diffuse through to the sensing chamber. Here, aptamers immobilized on the electrode surface specifically detect creatinine binding (anti-creatinine chamber), or are used for common-mode rejection (non-specific chamber).

Designed for everyday use, the biosensor includes a spring-loaded applicator and stays comfortably in place with a medical-grade hydrogel adhesive patch. By combining cutting-edge microfluidic, materials science, and molecular recognition technology, SensETH's biosensor delivers continuous creatinine monitoring in a compact, wearable product, offering new possibilities for patient care.

2. AP award: Biosensor developed for the Eindhoven Testing Event

2.1. Molecular recognition

The biosensor employs redox-labeled aptamers with the following sequence:

`5-CGACGGTGGCCTATTAAATAGCTTTAGTTTAAGAAAAGTAATAGGGGGTGTCG-3 (Ganguly et al., 2024)`

The 3′ end is functionalized with methylene blue as a redox label to enable electrochemical detection. The signal is generated by conformational changes of the aptamer reversibly and reagentlessly binding to creatinine. This brings the covalently attached label closer to the electrode surface, allowing for more redox reactions to occur. For immobilization to a gold electrode, the 5′ end includes a six-carbon spacer and a thiol group at the end (Schoukroun-Barnes et al. (2016)).

As an alternative sensing approach, Molecularly Imprinted Polymers (MIPs) were synthesized for creatinine detection. Following the methodology of Li et al. (2022), dopamine hydrochloride was polymerized in the presence of creatinine templates on graphene nanoplatelets. After template removal, the MIPs retained specific three-dimensional binding sites for creatinine when drop-cast onto glassy carbon electrodes (Li et al. (2022)).

2.2. Physical transduction

The detection of creatinine in our aptamer-based biosensor is achieved through an electrochemical transduction mechanism using Cyclic Voltammetry (CV). This approach converts the molecular recognition of creatinine into a measurable electrical signal via the following components and processes:

- **Sensor Surface**: The system uses a three-electrode configuration: the reference electrode is composed of silver (Ag), and both the working electrode and the counter electrode are made of gold (Au).
- **Transduction Mechanism**: Upon exposure to a sample, creatinine molecules specifically bind to the redox-labeled aptamers immobilized on the sensor surface. This binding induces a conformational change in the aptamer, which directly affects the position and electron transfer characteristics of the redox label relative to the electrode. As a result, the efficiency of electron transfer between the redox label and the electrode is altered, leading to measurable changes in the electrochemical signal (Mirceski et al., 2018). While most aptamers in a sensor get closer to the surface, preliminary results have indicated that in our case it operates the other way around (*See Section 2.4*).
- **Signal Generation via Cyclic Voltammetry**: CV is used to probe these changes by applying a linearly swept potential to the electrode while monitoring the resulting current. The creatinine-aptamer interaction leads to measurable variations in redox current peaks or potential shifts observed in the voltammogram. The magnitude of these changes is proportional to the concentration of creatinine present in the sample.

2.3. Cartridge technology

The microfluidic system underwent several design iterations using Polydimethylsiloxane (PDMS)-based flow cells molded from Stereolithography (SLA)-printed resin molds (Poskus et al., 2023) before achieving the final configuration (*See Appendix for detailed Evolution of the Flow Cell Design*). The objective was to develop a flow cell with an internal volume of less than 100 μL.

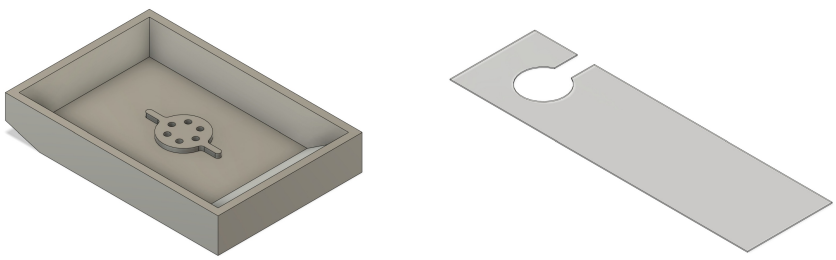


Figure 1: Final flow cell design: (a) Top layer mold, (b) Bottom layer

The final design incorporates a PES membrane with a 500 Da Molecular Weight Cut-Off (MWCO) for cross-flow filtration, enabling the removal of larger molecules like proteins from artificial ISF. This cartridge employs a layered structure in which the membrane is sandwiched between PDMS layers using oxygen plasma bonding (Aran et al., 2010). The top PDMS layer *Figure 1 (a)* serves as the flow cell, where the sample flows through, while the membrane is positioned beneath the flow cell and bonded to the double-sided tape layer *Figure 1 (b)* that is placed on top of the electrodes. The bottom layer contains the internal fluid necessary for diffusion. To ensure precise flow control, sample introduction is managed by two peristaltic micropumps (CPP1-180-ZM, Jobst Technologies). The two outlets are connected to a shared waste reservoir. Due to the system's overall internal volume (<100 μL), each new sample completely displaces the previous one, ensuring minimal carryover between measurements.

2.4. Reader instrument and user interaction

To measure the current produced by the redox reaction, we utilized the Army Corps of Engineering Potentiostat (ACEstat). This compact, low-power device leverages the functionalities of the Analog Devices ADuCM355 integrated circuit, incorporating a potentiostat amplifier, data converters (DAC/ADC), microprocessor, Trans-Impedance Amplifier (TIA), and signal processing hardware in a single package (Brown et al., 2022). A critical feature of the ACEstat is its dual-channel measurement capability, which enables simultaneous recording of both the specific aptamer signal and the reference signal from the scrambled aptamers (*See Section 3.2.1*). The system is controlled through an open-source Graphical User Interface (GUI) that allows precise configuration of CV parameters. During operation, the working electrode potential is swept linearly in both forward and backward directions while measuring the oxidation and reduction currents, respectively.

Figure 2: ACEstat PCB

The acquired signals are then processed using a moving average filter to reduce noise, followed by an algorithm that identifies the forward and backward peak currents. Calibration experiments revealed that as creatinine concentration increases, the distance between the redox label and the electrode surface was further increased, resulting in a decrease in the forward peak current while the backward peak current increased (*See calibration curves in the Appendix*).

3. IN award: Biosensor innovation

3.1. Wearable sensor

Our wearable creatinine biosensor and its applicator introduce several innovations compared to existing glucose monitoring devices (e.g., CGMs like Dexcom G7 or Abott FreeStyle Libre (Rodbard, 2017)): a modular two-part design, enhanced ISF extraction via microneedle array, and continuous bidirectional creatinine tracking. As shown in *Figure 3*, the biosensor consists of two main components: a disposable patch and a reusable electronic module. The disposable patch includes a microneedle array, an integrated microfluidic flow cell, and an adhesive hydrogel layer for secure skin attachment over extended periods (Hong et al., 2024). For individuals prone to adhesive allergies, alternative attachment methods may be employed to minimize skin irritation. The reusable module contains a flexible Lithium-Polymer (LiPo) battery rechargeable via inductive charging (Perez et al., 2022), and a Printed Circuit Board (PCB) that processes the electrochemical signals. The PCB integrates a low-power microcontroller for real-time signal analysis similar to the architectures used in wearable biosensors by Brown et al. (2022).

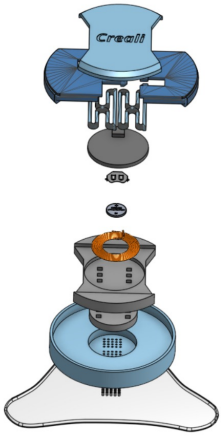


Figure 3: Wearable creatinine biosensor: the reusable upper module contains the rechargeable battery and PCB, while the disposable lower patch integrates the flow cell with immobilized aptamers, adhesive layer, and (not visible) microneedle array.

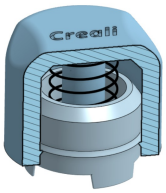


Figure 4: Applicator mechanism for precise biosensor deployment

The spring-loaded applicator, depicted in *Figure 4*, ensures reliable deployment of the biosensor onto the skin surface. Following application, the microneedle array facilitates continuous ISF extraction through passive capillary action (Parrilla et al., 2022), drawing fluid into the microfluidic flow cell. The microneedles, fabricated from medical-grade polycarbonate (Donnelly et al., 2012), extract ISF at a steady rate of about 2 $\mu L/min$, in compliance with SensUs competition specifications. This flow rate ensures sufficient sample volume for continuous creatinine monitoring. The flow cell operates as described in *Section 2.3*, with a PES membrane separating the upper flow channel from the lower sensing chamber. As new ISF enters, creatinine

molecules diffuse bidirectionally across this membrane (500 Da MWCO) moving from the flow channel to the measurement chamber when the incoming concentration is higher, and in the opposite direction when it is lower (Wijmans and Baker, 1995). The creatinine level of the measurement chamber is a weighted average of previous and real-time measurements, enabling continuous tracking of concentration changes. The electrochemical aptamer-based sensor detects creatinine binding events through CV, which we have selected over Square Wave Voltammetry (SWV) since the latter can speed up the desorption of the aptamer layer (Aller Pellitero et al., 2021). The PCB converts these analog signals into digital creatinine concentration values using this back-calculation algorithm (*detailed in Section 3.1.2*).

3.1.1. Technological novelty of wearable sensor

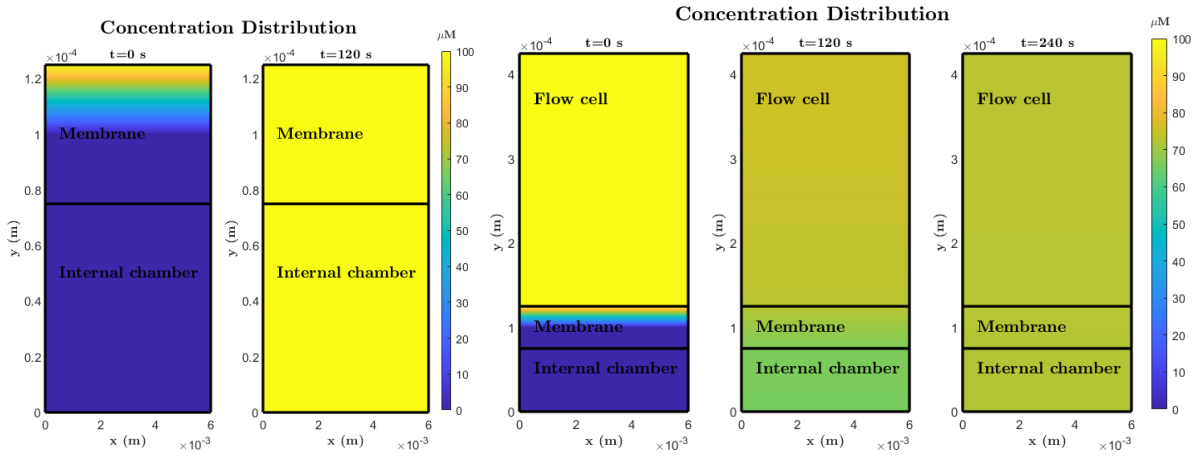
The technological innovation of the biosensor lies in the integration of different components. A distinctive feature of our biosensor is its modular composition, consisting of a disposable part and a reusable part. The disposable part of a future wearable sensor should include a microfluidic system fabricated from SU-8 photoresist instead of PDMS, since it offers better performance for wearable use. The two-compartment design of the microfluidic system, which we have developed, incorporates the concentration tracking mechanism described in *Section 3.1.2*. Together with the application of SWV for the release of the creatinine-aptamer bond (*described in Section 3.2.1*), this system enables continuous monitoring of creatinine.

Our microneedle array design represents an alternative to the single flexible electrodes used in current CGMs (Tehrani et al., 2022), offering several advantages: enhanced ISF extraction efficiency through multiple access points, reduced patient discomfort due to limited ($50 - 500\ \mu m$) penetration depth (Strambini et al., 2015), and continuous capillary-driven ISF transport into the microfluidic sensing system without active pumping mechanisms (Parrilla et al., 2022). This approach enables real-time, wireless monitoring of creatinine while maintaining minimal invasiveness (Tehrani et al., 2022).

3.1.2. Technical feasibility of wearable sensor

To validate the diffusion-based creatinine measurement approach, a Partial Differential Equation (PDE) model was set up in the MATLAB environment. The governing equation was based on Fick's Second Law of Diffusion, with distinct diffusion coefficients assigned to each region (Snyder et al., 2011) (*detailed in the Appendix*).

Two main approaches were established for validation, focusing on the corner cases (best-case and worst-case scenarios). In the case of continuous sample flow within the flow cell, a Dirichlet boundary condition was applied at the top of the membrane, with a constant cre-



(a) (b)

Figure 5: Numerical simulation of creatinine diffusion. The sample continuously flow in the flow cell, thus Dirichlet boundary condition is applied (left). The internal concentration is settled after two minutes (right) (a). The sample is quickly introduced to the flow cell and left there undisturbed (left). After two minutes, the concentration of the different regions is approximately the average of their initial concentrations, weighted by their volume (middle). After four minutes, the concentration of the different regions equalized (right) (b).

atinine concentration equal to that of the introduced sample. In the case of a sample that remained static in the flow cell after introduction, the area of the flow cell was also taken into consideration with an initial concentration equal to the sample concentration, and a Neumann boundary condition was applied with the no-flow condition across the boundaries. In this case, the final concentration can be calculated as

$$c_{final} = \frac{c_{int,prev} \cdot V_{int} + c_{memb,prev} \cdot V_{memb} + c_{sample} \cdot V_{flowcell}}{V_{int} + V_{memb} + V_{flowcell}}, \tag{1}$$

where c is the concentration, V is the volume, indices int, $memb$, $sample$, $flowcell$ refer to the internal chamber, membrane, sample and flow cell, index $prev$ refer to the steady state value before the introduction of the new sample and c_{final} is the new steady state concentration. The results of the corner cases are illustrated in *Figure 5*.

3.2. Reliability of sensor output

The biosensor's measurement variability primarily originates from three sources: electronic drift, biofouling effects, and surface instability (Leung et al., 2021). Initial testing revealed an offset drift in the potentiostat circuitry when using dummy cells, which can potentially affect baseline accuracy. Second, as reported by Leung et al. (2021), biofouling causes exponential signal drift, particularly during early stages of sensing, which can significantly distort the signal. Third, aptamer desorption may further contribute to signal degradation over time (Leung et al., 2021).

To address these challenges, we have implemented a combination of hardware and surface engineering strategies. The potentiostat undergoes pre-measurement calibration using a dummy cell to identify and compensate for baseline offsets. This ensures that the initial signal is accurately zeroed, minimizing measurement bias. Additionally, the microfluidic system incorporates a PES membrane to reduce biofouling. For the sensing surface, we intend to utilize commonly used methods such as thiolated Polyethylene Glycol (PEG) or Bovine Serum Albumin (BSA) to minimize nonspecific binding and improve monolayer stability (Shaver and Arroyo-Currás, 2022) (Watkins et al., 2023).

These combined modifications are expected to significantly enhance both the reliability and reproducibility of concentration measurements in real-world wearable applications.

3.2.1. Technological novelty of reliability concept

Our biosensing approach introduces two important innovations for improved performance. First, we reduce background noise using a scrambled aptamer sequence that does not bind to our target molecule, creatinine. This sequence serves as a reference channel to help distinguish specific signals from nonspecific interactions or system noise. The scrambled aptamer sequence was randomised from the original sequence using the program by Stothard (2000) and the likelihood of it folding in a hairpin shape was validated with AlphaFold 3 to maintain structural stability. The selected sequence is:

5'-CGACGTAAATGAGGTGTCTGGGTGTAAATAAGAAAATTGTATCGTTGACGTCG-3'

To preserve the aptamer's ability to fold into a stable structure, the first and last four bases - being complementary - were intentionally left unchanged.

A second novel feature of our sensing method involves the regeneration of the aptamer by actively releasing the bounded creatinine. This was achieved using SWV in the range of 0.0 to 0.3 V at 100 Hz, applied to the working electrode. This technique, building on the work by Zargartalebi et al. (2024), demonstrates that such voltage oscillations can accelerate the dissociation of protein-aptamer complexes. Unlike negative potentials, which were shown to have a negligible effect, the application of positive potentials is believed to maintain aptamer attachment on the surface due to their negatively charged backbone. According to Zargartalebi et al. (2024), these oscillations likely induce mechanical forces - such as drag, inertia, and increased water molecule collisions- that weaken the aptamer-analyte binding and promote release.

Together, these innovations enhance measurement accuracy by distinguishing specific signals from background interference while enabling repeated sensor use through controlled regeneration.

3.2.2. Technical feasibility of reliability concept

Critical Sensor Components

The sensor's performance relies on two critical components: the aptamer-redox probe and the ACEstat potentiostat. The aptamer-redox probe enables specific creatinine recognition while simultaneously facilitating signal transduction through redox activity. The ACEstat potentiostat serves as the compact, open-source electrochemical reader that plays a crucial role in the measurement acquisition, though its operation requires precise offset calibration to ensure reliable and accurate readings.

Initial testing with a laboratory-grade Autolab potentiostat revealed several key trends through CV measurements while using the same material for all electrodes in PBS (*See Appendix for results*). The data showed a slight positive shift in the redox peak potential as creatinine concentration increased, indicating a concentration-dependent electrochemical response. Additionally, there was a noticeable decrease in peak current, which we attribute to binding-induced conformational changes in the aptamer structure upon creatinine interaction. Variability in the shape of the peaks was also present, likely resulting from aptamer structural transitions during the sensing process. While these results suggest that the system responds to changes in creatinine levels, additional calibration work is needed to quantify the response more accurately and improve reproducibility. To create a calibration curve that links the signal from our ACEstat potentiostat to creatinine concentration, we're focusing on accurately detecting the signal peaks, calculating the area under each curve, and analyzing the difference in the potentials where these peaks occur .

Feasibility Discussion

Our approach has shown promising early results, indicating its potential for effective creatinine detection. However, demonstrating feasibility will depend on several critical factors. Foremost among these is ensuring signal reproducibility across multiple measurements, which is essential for reliable sensor performance. Equally important is maintaining surface stability over time, achieved through the implementation of anti-fouling layers that prevent degradation and non-specific interactions. Furthermore, it will be crucial to confirm that the ACEstat potentiostat is compatible with low-current detection, as this will directly impact the sensitivity and practical deployment of the biosensor in real-world settings.

With further testing and calibration, our sensor concept holds strong potential for reliable, real-time creatinine monitoring in wearable applications.

3.3. Original contributions

From SensETH team:

Participating as ETH Zurich's first-ever SensUs team presented significant challenges,

but we have gained invaluable skills throughout this journey. Our Biosensing Subgroup explored two parallel approaches - aptamers and MIPs - with primary focus on aptamer-based sensing. A key innovation in our biosensor design is the dual-chamber system featuring one chamber with anti-creatinine aptamers for specific detection, and another chamber with non-specific scrambled aptamers as reference. This configuration enables real-time background subtraction, building on established methods from other fields (Nagarkatti et al., 2012). The scrambled aptamer sequence was carefully designed using specialized software by Stothard (2000) to maintain structural similarity while eliminating creatinine binding.

The Flow Cell Subgroup developed a revolutionary microfluidic design, both innovatively developed and manufactured, to fulfill the dimensional and technical requirements stipulated by the other subgroups. A measurement chamber was developed, which is filled with a steady internal liquid and is enclosed by a membrane that prevents proteins and large molecules from entering the internal chamber. The continuous flow of the samples on the opposite side of the membrane ensures undisturbed diffusion of creatinine into the internal measurement chamber. In order to accommodate the dual-chamber system, two independent flow cells were manufactured for the nonspecific and specific anti-creatinine aptamers.

From Prof. Morteza Aramesh, SensETH supervisor:

In designing the sensor, ETH team (first time participant) explored multiple options for selecting a suitable biorecognition element and finally turned their focus on aptamer-based sensors and electrochemical transduction. They designed a microfluidic system to meet the competition criteria in an innovative way, making a balance between sensitivity and specificity for real-time measurements.

Their key innovation is a real-time strategy to minimize and correct for nonspecific binding, achieved by combining a filtration system with a scrambled-sequence reference electrode. They also customized an open-source potentiostat for multi-electrode sensing and automated the data analysis pipeline. Despite challenges like analyte unbinding, their work represents a creative and practical approach for sample handling.

I supported with lab access, but the success was entirely driven by the teams effort. Their achievement was especially notable given ETHs exam-period constraints, lack of prior resources, and missing the 2024 competition experience that may have helped other teams select a suitable biorecognition element for creatinine. The team demonstrated independence and excellence by securing funding and promoting awareness about kidney diseases among the local and international stakeholders.

Signatures:

Prof. Morteza Aramesh	Sabine Schär	Flavia Pirotta
SensETH supervisor	*Team Captain*	*Team Captain*

4. TP award: Translation potential

4.1. Customer interviews

As part of our research, we interviewed key stakeholders involved in the management of kidney failure, primarily nephrologists and patients. These conversations provided us with valuable insights into the real-world challenges and needs surrounding kidney disease detection and monitoring.

Our initial focus was on the doctors, both nephrologists and general practitioners, as they play a central role in diagnosing the condition and determining the stage of kidney failure. They are also responsible for designing personalized treatment plans for each patient, which includes the recommendation of treatment or monitoring options. From our discussions, it became clear that doctors see a strong need for faster and more accurate testing methods. They emphasized the importance of reducing false positives and minimizing the reliance on frequent blood draws, which can be especially challenging for patients with Chronic Kidney Disease (CKD).

Interestingly, the nephrologists told us that creatinine is not the most useful biomarker for detecting Acute Kidney Injury (AKI). In fact, they typically need to monitor other biomarkers such as sodium, potassium and urea alongside creatinine to get an idea of kidney health.

A key takeaway from these interviews was that creatinine plays a more relevant role in managing CKD or monitoring post-transplant patients, rather than in the early detection of acute conditions. When it comes to prevention, doctors acknowledged that it remains difficult - most patients begin to feel symptoms only in the later stages of CKD, typically stage 3 or 4.

Doctors closely monitor their patients and are deeply involved in tracking disease progression. They expressed a strong need for technologies that can ease the burden on both patients and caregivers. However, they also noted that in ICU settings, where most cases of AKI happen (Kellum et al., 2021), such wearable or non-invasive sensor technologies would be less relevant, as hospitals already employ more advanced and precise monitoring systems. Furthermore, patients already undergo different tests and blood draws for other analytes. Therefore, a continuous observation of creatinine in the ISF is highly unlikely to result in a reduction of blood draws or general discomfort. Additionally, intensivists mentioned that ISF is not considered an ideal matrix for assessing kidney function or disease progression

in such critical care environments, among other things due to the delay in concentrations between blood and the ISF.

Our second group of stakeholders were patients living with CKD, including those who have undergone kidney transplants. Many of them suffer from genetic conditions such as ADPKD (Autosomal Dominant Polycystic Kidney Disease), which causes a progressive decline in kidney function. By around the age of 50, these patients typically face the need for renal replacement therapy - either dialysis or a transplant.

Patients often find themselves in a passive role when it comes to managing their disease. They cannot control its progression and must rely on nephrologists for treatment and decision-making. Several patients expressed feelings of powerlessness and lack of information, saying that they do not always understand the full extent of their condition. In some cases, they feel that doctors withhold certain details, leaving them uncertain about their own health status.

One patient described how their life - once focused on work and family - became increasingly dictated by the disease. After undergoing a transplant, they now deal with frequent follow-up visits, a strict medication regimen, and regular blood draws to monitor creatinine and other critical parameters. Although they have received a new kidney, the burden of ongoing monitoring and immunosuppressive treatment remains significant.

Importantly, patients do not currently have access to any continuous sensors for monitoring kidney function - unlike diabetic patients, who benefit from CGMs. They clearly voiced a need for more patient-centered monitoring tools that would allow them to better understand and manage their condition at home.

The hereditary nature of ADPKD means that many patients have close relatives - siblings, parents, or children - who are also affected. This adds an emotional layer, as patients often witness their loved ones go through the same struggles. Family members and friends are often willing to become living donors, and many transplants occur through this route. However, patients are acutely aware of the risks and sacrifices involved for the donor, including long and painful recoveries.

Patients also highlighted the indirect impact of their disease on those around them. Loved ones often feel helpless watching their health decline and are eager to support in any way they can. Some patients find comfort and community through national and regional kidney associations, where they can attend awareness events, connect with others in similar situations, and speak with specialists.

Despite the many hardships, patients were remarkably resilient and hopeful. They shared a strong will to continue fighting and to make the best of their situation. In our interviews, they were genuinely enthusiastic about our work, excited that young researchers are work-

ing toward solutions that could improve their quality of life.

The openness and support we received - often from individuals still recovering from surgery - was incredibly moving. Their stories provided a deep understanding of the lived experience of kidney disease and reinforced the urgency and impact of developing better, continuous monitoring technologies.

4.2. Design of validation study

Our interviews with clinicians highlighted the limitations of conventional creatinine monitoring in diagnosing AKI, especially in a hospital setting with more advanced diagnostic tools available. Therefore, our first step is to focus on an application away from the acute hospital setting. Since creatinine is a clinical biomarker to monitor organ rejection in kidney transplants (Sharaby et al., 2023; Naik and Shawar, 2023) - and interviewed patients revealed needs to lessen the emotional burden - we prioritized supporting patients who had undergone a kidney transplant due to CKD. Kidneys are the most transplanted organ worldwide (on Donation and Transplantation, 2024), with over 350 transplants performed in Switzerland in 2023, and numbers projected to rise (Fed, 2024). Our main goal is to guarantee that patients feel more in control and informed about their current health status, enabling them to advocate for their needs without having to constantly worry about their condition. The proposed product is intended to be used in the time span after the surgery, when patients are required to go to the hospital for regular check-ups. While continuous creatinine sensing might already alleviate anxieties in patients, we want to go one step further and offer a three-part solution.

Our creatinine sensor is offered with an accompanying phone app for the patients as well as a browser application for the responsible healthcare team. The app is designed to enable the supervision of the patient condition. As shown in Figure 11, the app's home page displays the current measurements and includes a daily overview, for example medication reminders. Another asset is the symptoms tab, where patients can log their day-to-day symptoms. This, together with the measurement history, allows doctors to get an insight into how the patient's status progresses from day to day. This might allow the doctor to tailor the treatment more patient-specifically. The ultimate goal is that the doctor can schedule appointments with their patients based on the measured history and not just based on a standardized regimen, potentially reducing the time patients spend in the hospital. The measurement data is automatically transmitted via Bluetooth from the sensor to the patient's phone. The patient will be automatically warned by a notification if the measured values cross a certain threshold established by the clinician. Other app functionalities include a calendar with upcoming doctor's appointments and previously logged symptoms, as well as a page with general resources and more patient-specific recommendations for an

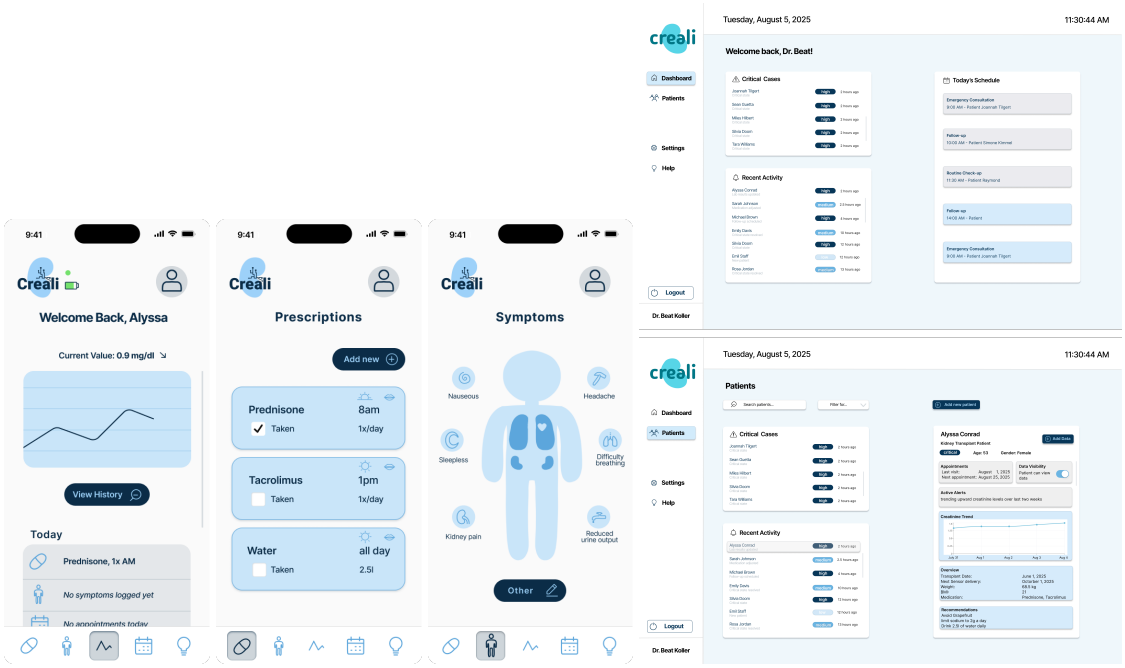


Figure 6: Part of the user interface of the two applications

optimal regeneration, as can be seen in *Section 8.6* in the Appendix.

Part of the application for doctors and other healthcare personnel can be seen in Figure 11, the rest can be found in *Section 8.6* in the Appendix. It provides a general overview over patient cases, while highlighting patients with more critical status. Further, all the necessary patient information as well as upcoming appointments are displayed. is also available.

A validation study would primarily need to test whether the use of the sensor with the corresponding application a) reduces anxiety b) enables doctors to provide more personalized care and c) reduce time patients spend in the hospital.

The study will be held in some of the six transplantation centers in Switzerland; the University Hospital Zurich, the University Hospital Bern, the Centre hospitalier universitaire Vaudois, the University Hospital Basel, the HOCH Health Ostschweiz and the Hôpitaux Universitaires de Genève. The protocol will be established as a randomized controlled trial where one cohort of the transplant patients receives only the sensor, another subgroup receives the sensor set including the applications, and a third unit receives the current standard care regimen without any sensor component. All patients receive the same evaluations. The first two goals will be addressed using a specific questionnaire. The one for patients will include questions about their current worry-levels and a subjective estimation on how frequently they think about the transplanted organ. The doctors' questionnaire will include how well they manage to personalize their treatment after using the app. The last question can be investigated by comparing the three groups' frequency of appointment and comparing them

to the standardized care regimen. This should reveal whether the data from the sensor and the app allows for less frequent appointments or if the scheduling is more dynamic.

5. Team and support

5.1. Contributions of the team members

Biosensing Subgroup: Co-design of experimental protocols. Lab work. Validation experiments. Research

- **Jamie Balfour:** Lab work. UX design. Presentations Manager. Interviews
- **Charlotte Kalbermatten:** Chemistry and lab safety. Sponsor Newsletter. TRD
- **Flavia Pirotta:** Team captain. UI/UX design. Presentations Manager. Merch
- **Sabine Schär:** Team captain. Funding Manager. Presentations Manager

Flow Cell Subgroup: Flow Cell design, manufacturing and validation. Research. Filtering

- **Vince Facskó:** 3D design. Simulation. Excel sheet
- **Marta Gidoff Lorén:** Social Media Manager. TRD. Treasurer. Interviews

Readout Subgroup: Potentiostat selection and setup. Validation experiments. Research

- **Antonio Bacchin:** Prototype model design. Interviews. ACEstat calibration
- **Lovisa Joos:** TP Manager. Social Media Manager. UI/UX design. Interviews. Research Collaborations
- **Shakambari Saxena:** TRD. Interviews. ACEstat calibration
- **Benedikt Wahl:** Funding and treasury. Sponsor Newsletter. Research Collaborations

5.2. People who have given support

- **Laboratory of Biosensors and Bioelectronics (LBB):** Provided laboratory access, including materials and consumables
- **Prof. Dr. Morteza Aramesh:** Supervisor. Supportive regular meetings
- **Annina Stuber:** Guidance in aptamer related questions
- **Julian Hengsteler:** Guidance in flow cell design and validation
- **Léo Sifringer:** Provided preliminary electrode material and fabrication know-how
- **Justin Cronk:** SensETH website Manager

- **Isabel Schär:** Assistance and advice in filming and editing of Social Media videos. Provision of professional filming equipment. Logo design assistance
- **Oleksii Ustinov:** Provided guidance in membrane related questions

5.3. Sponsors and partners

6. Final remarks

In 2023, over 111.135 kidney transplantation surgeries were performed world-wide(org, 2024). Projections by Astrazeneca Switzerland (Campbell-James et al., 2024) suggest that by 2030, over one million people will be affected by CKD. Of the available treatment options, kidney transplants have the best 10-year outcome (Shi et al., 2023). This further escalates the demand for transplants.

Our creatinine biosensor aims to improve post-transplant patient care by enabling continuous monitoring. Based on doctor feedback, future iterations will prioritize multiplexing capabilities to detect additional CKD-relevant biomarkers, like potassium or immunosuppressant levels, building on the foundational work of Jarczewska et al. (2016) and Mansouri et al. (2020).

To ensure compliance with European Union Medical Device Classification (EU MDR) standards and pursue approvals from Swissmedic and potential Food and Drug Administration (FDA) clearance, we have established a rigorous development pathway. The process begins with six to twelve months of in vitro and animal testing to validate the biosensor's core functionality and safety profile. Following successful proof-of-concept results, we will implement a comprehensive quality management system within six months to meet all regulatory requirements. The clinical evaluation phase will then be conducted in collaboration with Switzerland's leading transplantation centers (*Section 4.2*), focusing on three critical aspects: manufacturing process validation, sensor performance characterization, and data reliability assessment. Only after completing these stages will we proceed with final regulatory submissions and certifications required for market launch.

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8. Appendix

8.1. Abbreviations

- **ACEstat:** Army Corps of Engineering Potentiostat
- **AKI:** Acute Kidney Injury
- **ADC:** Analog-to-Digital Converter

- **ADPKD:** Autosomal Dominant Polycystic Kidney Disease
- **BSA:** Bovine Serum Albumin
- **CKD:** Chronic Kidney Disease
- **CGM:** Continuous Glucose Monitor
- **CV:** Cyclic Voltammetry
- **DAC:** Digital-to-Analog Converter
- **EIS:** Electrochemical Impedance Spectroscopy
- **EU MDR:** European Union Medical Device Classification
- **FDA:** Food and Drug Administration
- **GUI:** Graphical User Interface
- **ISF:** Interstitial Skin Fluid
- **LiPo:** Lithium-Polymer
- **MIPs:** Molecularly Imprinted Polymers
- **MWCO:** Molecular Weight Cut-Off
- **PCB:** Printed Circuit Board
- **PDE:** Partial Differential Equation
- **PDMS:** Polydimethylsiloxane
- **PEG:** Polyethylene Glycol
- **PES:** Polyethersulfone
- **QCM:** Quart Crystal Microbalance
- **SLA:** Stereolithography
- **SWV:** Square Wave Voltammetry
- **TIA:** Trans-Impedance Amplifier

8.2. Cartridge technology

The first prototype featured a single inlet that split into two circular chambers before reconnecting at the outlet (*Figure 1, Appendix*). However, this design exhibited two major issues: asymmetric filling between the chambers and fluid shock upon entry into the large circular spaces. These challenges were addressed in the subsequent iteration (*Figure 2, Appendix*) by introducing a teardrop-shaped geometry to smooth flow transitions and implementing two independent flow cells to eliminate asymmetry. Despite these improvements, incomplete filling at the chamber edges persisted. To resolve this, the chamber height was optimized, significantly enhancing filling efficiency and overall flow dynamics (*Figure 3, Appendix*).

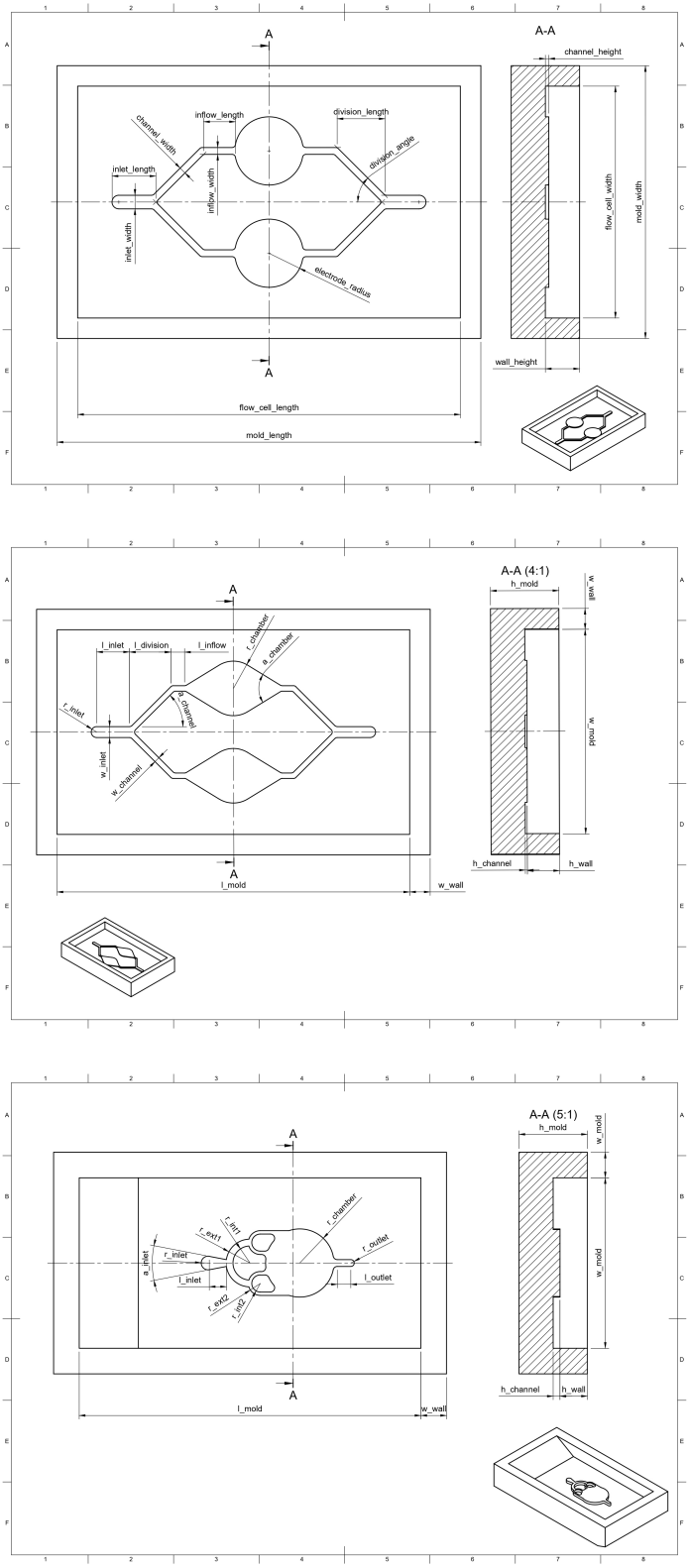


Figure 7: (a) Initial dual-chamber configuration with shared inlet and outlet, (b) Refined teardrop-shaped chamber for improved flow uniformity, (c) Optimized chamber height to enhance flow dynamics

8.3. Reader instrument and user interaction

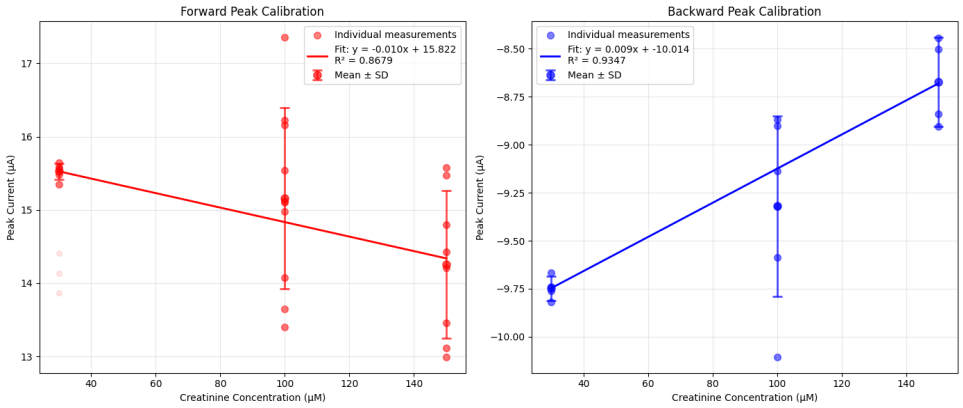


Figure 8: Calibration using 30, 100, and 150 μM creatinine for forward and backward peak currents in CV measurements.

8.4. Wearable sensor

Creatinine diffusion

The time-dependent diffusion process is described by Fick's Second Law:

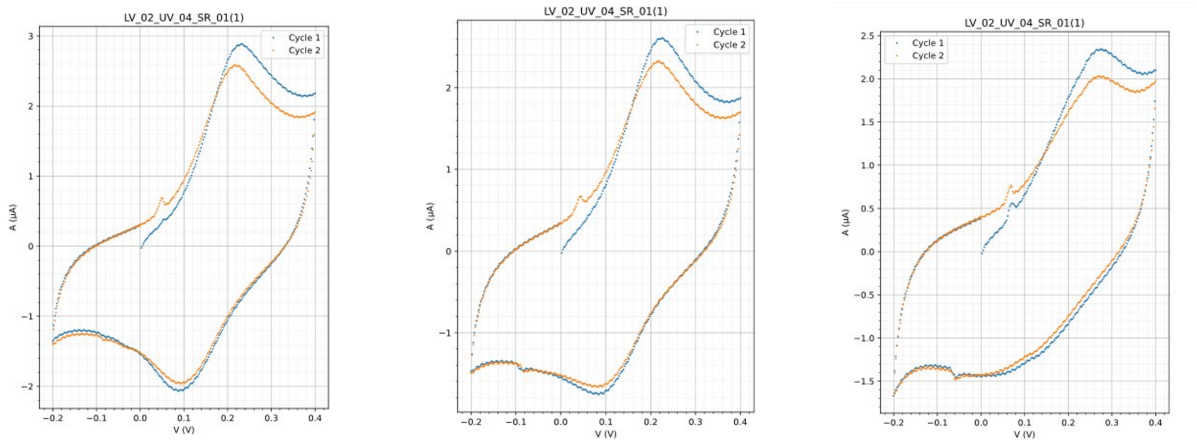
Fick's Second Law

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} \tag{2}$$

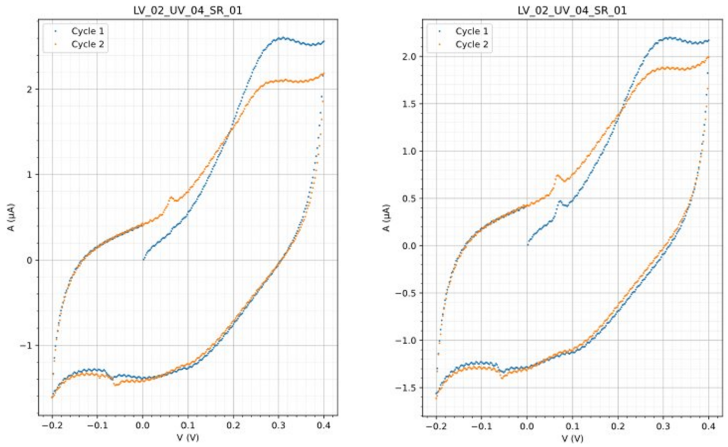
where:

- c = creatinine concentration (mol/m^3),
- t = time (s),
- D = diffusion coefficient (m^2/s),
- x = spatial coordinate (m).

8.5. Result of Cyclic Voltammetry from Autolab



(a) 0 μM (b) 30 μM (c) 100 μM



(d) 150 μM (e) 300 μM

Figure 9: CV curves for varying concentration from 0 μM to 300 μM

8.6. User Interface of Patient and Doctor App

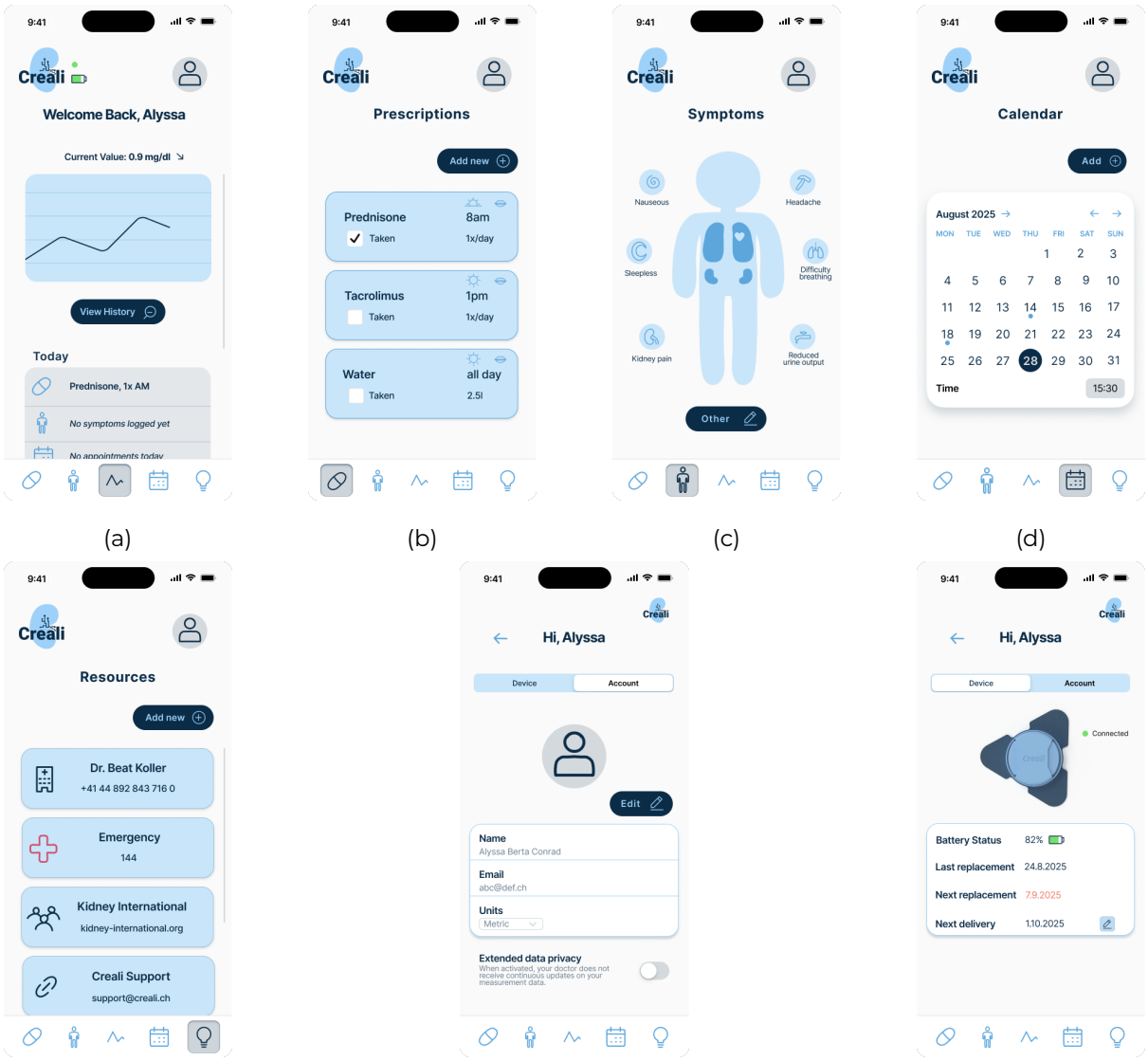
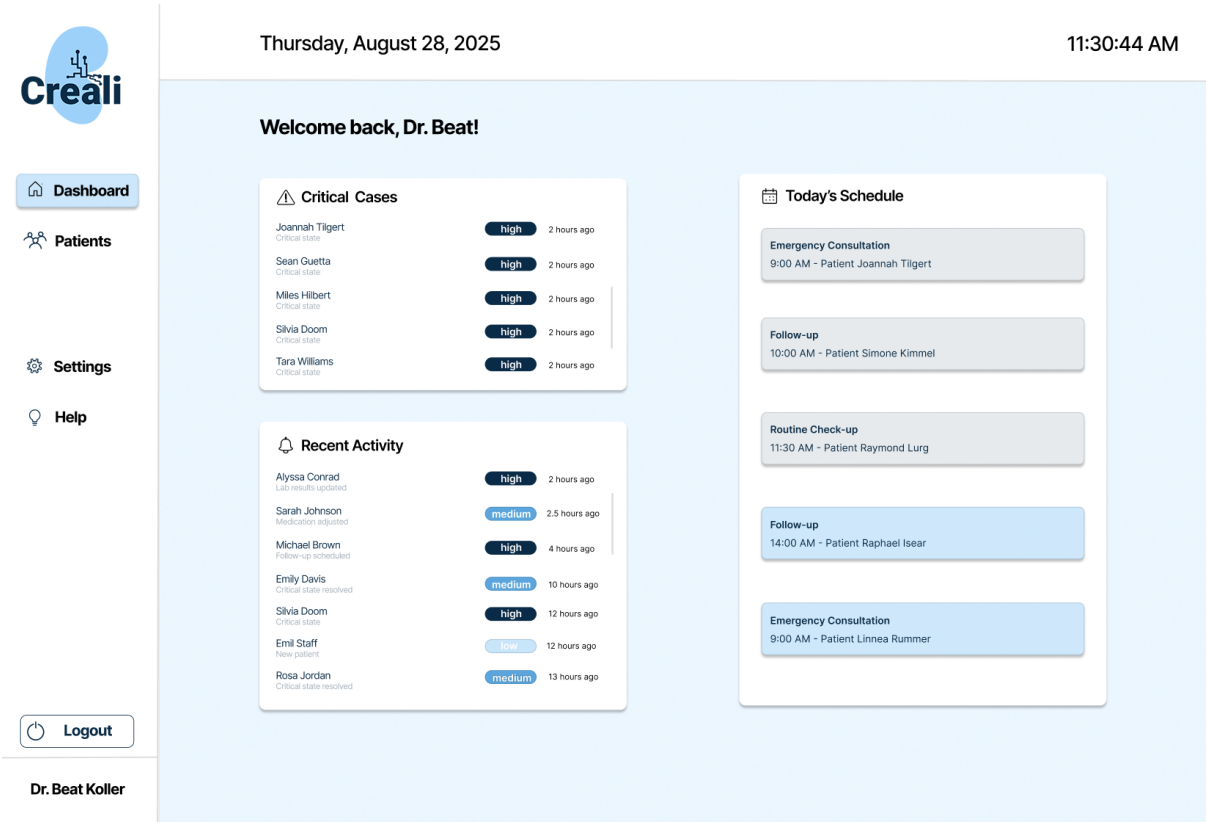
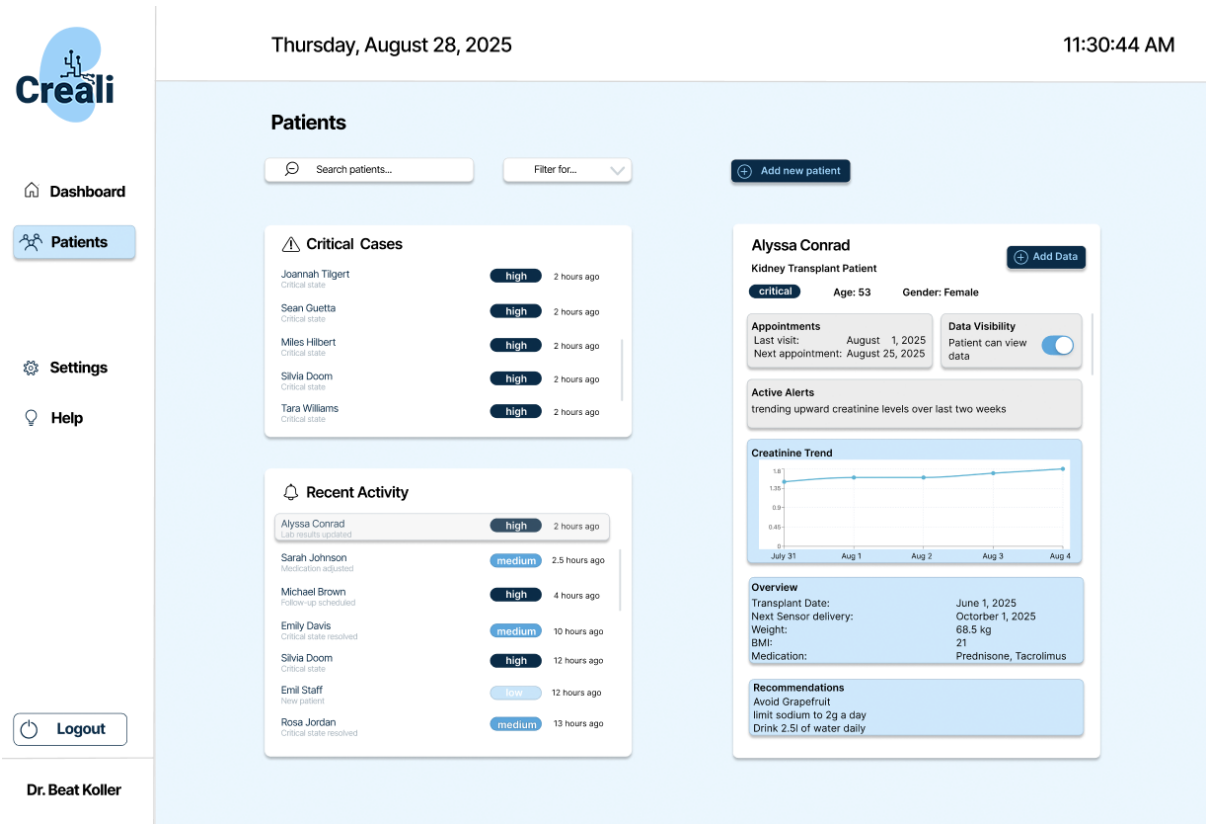


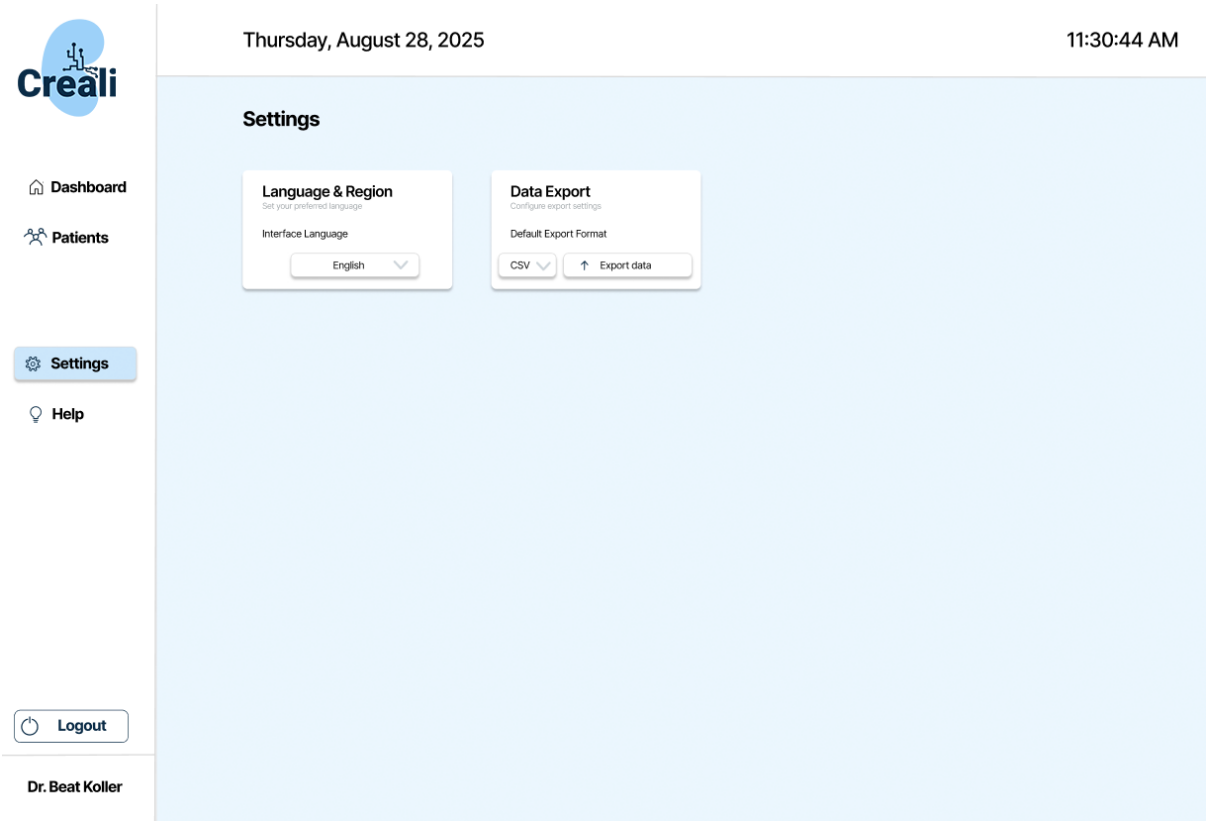
Figure 10: User interface of the patient app. a) Home screen, b) Medication reminders, c) Symptoms logger, d) Calendar, e) Resources for the patient, f) Personal information of the patient as well as privacy options, g) Device overview for the creali sensor


Creali
Thursday, August 28, 2025
11:30:44 AM
Welcome back, Dr. Beat!
Dashboard
Patients
Settings
Help
Logout
Dr. Beat Koller
Critical Cases
Joannah Tilgert
Critical state
high
2 hours ago
Sean Guetta
Critical state
high
2 hours ago
Miles Hilbert
Critical state
high
2 hours ago
Silvia Doom
Critical state
high
2 hours ago
Tara Williams
Critical state
high
2 hours ago
Recent Activity
Alyssa Conrad
Lab results updated
high
2 hours ago
Sarah Johnson
Medication adjusted
medium
2.5 hours ago
Michael Brown
Follow-up scheduled
high
4 hours ago
Emily Davis
Critical state resolved
medium
10 hours ago
Silvia Doom
Critical state
high
12 hours ago
Emil Staff
New patient
low
12 hours ago
Rosa Jordan
Critical state resolved
medium
13 hours ago
Today's Schedule
Emergency Consultation
9:00 AM - Patient Joannah Tilgert
Follow-up
10:00 AM - Patient Simone Kimmel
Routine Check-up
11:30 AM - Patient Raymond Lurg
Follow-up
14:00 AM - Patient Raphael Isear
Emergency Consultation
9:00 AM - Patient Linnea Rummer

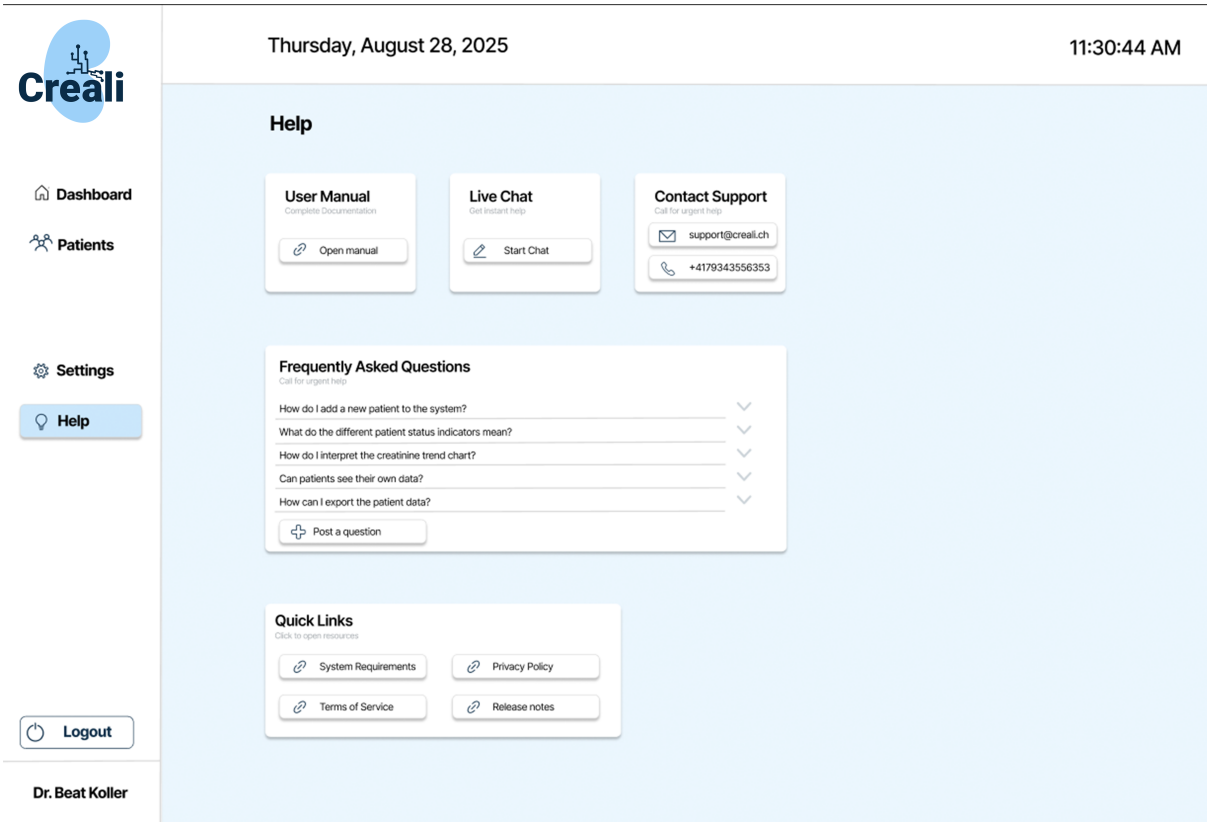
(a)


Creali
Thursday, August 28, 2025
11:30:44 AM
Patients
Dashboard
Patients
Settings
Help
Logout
Dr. Beat Koller
Search patients...
Filter for...
Add new patient
Critical Cases
Joannah Tilgert
Critical state
high
2 hours ago
Sean Guetta
Critical state
high
2 hours ago
Miles Hilbert
Critical state
high
2 hours ago
Silvia Doom
Critical state
high
2 hours ago
Tara Williams
Critical state
high
2 hours ago
Recent Activity
Alyssa Conrad
Lab results updated
high
2 hours ago
Sarah Johnson
Medication adjusted
medium
2.5 hours ago
Michael Brown
Follow-up scheduled
high
4 hours ago
Emily Davis
Critical state resolved
medium
10 hours ago
Silvia Doom
Critical state
high
12 hours ago
Emil Staff
New patient
low
12 hours ago
Rosa Jordan
Critical state resolved
medium
13 hours ago
Alyssa Conrad
Kidney Transplant Patient
Add Data
critical
Age: 53
Gender: Female
Appointments
Last visit: August 1, 2025
Next appointment: August 25, 2025
Data Visibility
Patient can view data
Active Alerts
trending upward creatinine levels over last two weeks
Creatinine Trend
July 31
Aug 1
Aug 2
Aug 3
Aug 4
Overview
Transplant Date: June 1, 2025
Next Sensor delivery: Octorber 1, 2025
Weight: 68.5 kg
BMI: 21
Medication: Prednisone, Tacrolimus
Recommendations
Avoid Grapefruit
limit sodium to 2g a day
Drink 2.5l of water daily

(b)



(c)



(d)

Figure 11: Doctor interface of the doctor's app. a) Dashboard screen, b) Patient screen, c) Settings, d) Help screen