Team Results Document

TU Eindhoven Sensing Team

(T.E.S.T.)

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SensUs

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1. Abstract

Managing heart failure requires a delicate balance between cardiac treatment and renal function. High-dose heart medications can decrease kidney function, making close monitoring essential. Current practices rely on subjective signs of deterioration. Creatinine is typically measured only once, a week after medication changes. This delay can cause renal decline to go undetected for days. As a result, readmissions are frequent, medications are often stopped prematurely, and treatment adjustments require trial an error

Team T.E.S.T. has developed a wearable biosensor for creatinine detection, utilizing Biosensing by Particle Motion (BPM) in a competitive assay format. The sensor's molecular recognition is driven by an anti-creatinine aptamer that selectively binds creatinine. Upon binding, the aptamer undergoes a conformational shift that acts as a molecular trigger, initiating the BPM signal. BPM operates by tracking the Brownian motion of biofunctionalized particles as they interact with a specially prepared sensing surface. These particles exhibit random movement, and subtle changes in their motion patterns reveal the presence and concentration of creatinine in the sample. This wearable biosensor will be able to continuously monitor creatinine levels from patients' homes, enabling earlier intervention and reducing the risk of acute kidney injury (AKI).

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

T.E.S.T. has developed a biosensor for the detection of creatinine, based on *Biosensing by Particle Motion* (BPM) in a competitive assay format [1] [2]. BPM uses biofunctionalized particles that interact with functionalized sensing surface, while continuously monitoring the particles' Brownian motion characteristics, which reflect their random movement [3].

2.1. Molecular recognition

Molecular recognition relies on an anti-creatinine aptamer: a synthetic single-stranded DNA oligonucleotide that folds into specific three-dimensional conformations that selectively binds to creatinine [4] [5]. Upon target binding, the aptamer undergoes a conformational change that serves as a molecular trigger, which is detected by BPM [6].

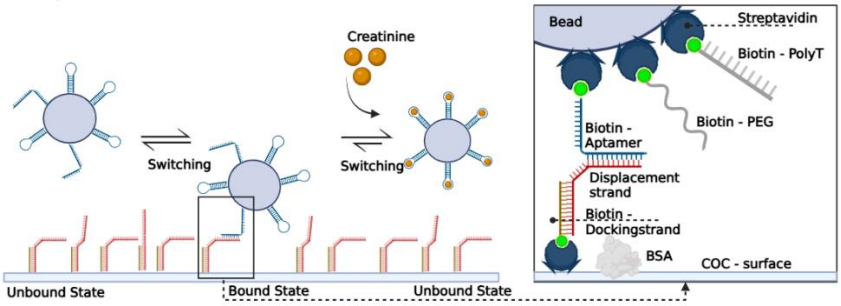

Figure 1: Schematic of BPM assay: particles switch between unbound (free movement) and bound (restricted movement) states via the displacement strand – aptamer interaction. Creatinine competes with the DS for aptamer binding, shifting the equilibrium toward the unbound state.

The sensor particles used are paramagnetic streptavidin-coated particles, functionalized with the biotinylated aptamer. The biotinylated single-stranded DNA 'docking strand' is immobilized on the cartridge surface via binding to pre-deposited neutravidin. The single-stranded DNA 'displacement strand' (DS) can then partially hybridize to the docking strand (Fig. 1). The DS contains three functional domains: a 26 nucleotide region complementary to the docking strand, a 7 nucleotide central flexible spacer, and a 9 nucleotide terminal sequence complementary to part of the aptamer, found in Appendix A. Non-specific binding to the surface and particles is prevented using coats of biotin–PEG, biotin–polyT, and BSA. In the absence of creatinine, the DS hybridizes with the aptamer, restricting particle motion. When creatinine is present, it competes with the DS, resulting in increased particle mobility. This configuration is referred to as free BPM (f-BPM). In tethered BPM (t-BPM), particles are anchored to the surface via a DNA tether, which increases the effective binding rate and enables rapid sample exchange, as tethered particles are not washed away.

2.2. Physical transduction

Video microscopy is used to record particle trajectories in the xy-plane. These trajectories are used to calculate diffusivity, Bound Fraction (BF), and activity. BF is defined as the

population of bound states over the total population of states. A threshold is used to distinguish between bound and unbound states. Activity reflects the switching dynamics between bound and unbound states and is reported as the average number of switching events per particle per unit time (typically in millihertz).

2.3. Cartridge technology

The cartridge is made of cyclic olefin copolymer (COC) and has a 20 µL internal volume. Sample exchange is performed via a syringe pump with multiple ports for pushing or pulling fluids or air. Samples are separated by air gaps, to prevent sample cross-contamination, which are removed just before entering the flow cell using a Y-junction (Fig. 2). Air is pulled into a waste channel, after which the sample flows into the cell. The initial part of the sample is used to rinse the cartridge.

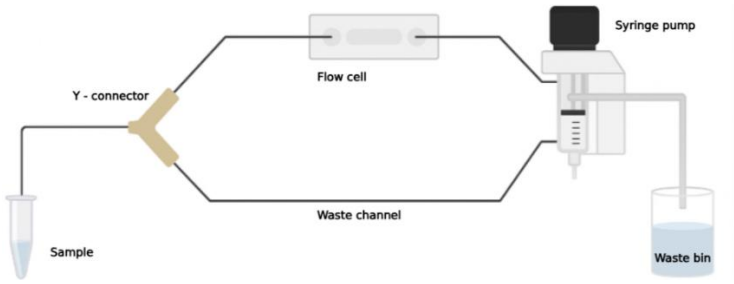

Figure 22: Schematic of the cartridge flow system. Samples are separated by air gaps and moved by a syringe pump. At the Y-junction, the air gap and some sample are sent to the waste channel to prevent cross-contamination. Then, 74 µL of the sample is pulled through the flow cell to flush the system; the final 20 µL in the flow cell is measured and then expelled into the waste.

2.4. Reader instrument and user interaction

Particles are tracked in real time via brightfield video microscopy (Fig. 3), using a FLIR camera, a green LED, and a microscope objective. Control software—developed in Python and MATLAB—integrates pump control, live imaging feedback, particle tracking, and data analysis for creatinine quantification. From the particle trajectories, diffusivity is extracted by analysing the mean squared displacement over time. Based on this diffusivity, particles are classified as either bound or unbound using a controllable threshold. The fraction of bound particles is a quantitative readout that can be directly related to creatinine concentration. Thanks to this integrated interface, user interaction is minimal: the only manual step is connecting the sample tube; all other operations are automated.

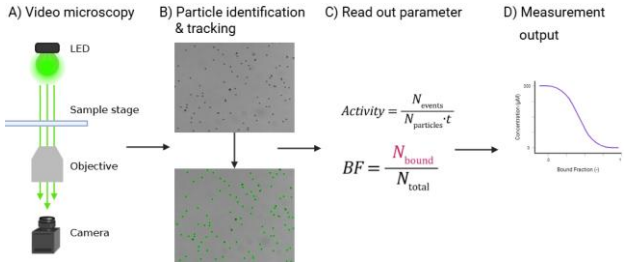

Figure 33: A) Brightfield microscopy setup with LED illumination. The cartridge is positioned above the objective and camera. B) Particle trajectories are recorded over time. C) Software classifies particles' activity and bound fraction. D) The bound fraction is linked to creatinine concentration.

3. IN award: Biosensor innovation

3.1. Wearable sensor

To enable continuous creatinine monitoring, we aim to develop a biosensor that combines microdialysis-based sampling with a miniaturized optical detection system (Fig. 4). A microdialysis probe, implanted subcutaneously, allows small molecules like creatinine to diffuse into the circulating perfusate [7]. An extra filter is implemented to prevent clogging of the probe. Another filter is used to prevent the outflow of particles implemented in the assay cartridge. The microdialysis probe, implanted subcutaneously, allows small molecules like creatinine to diffuse into the circulating perfusate. A compact peristaltic pump ensures flow through the sensor unit to maintain a continuous flow of ISF toward the assay [8]. A compact peristaltic pump ensures flow through the sensor unit to maintain a continuous flow of ISF toward the assay [8]. Although capable of high-frequency measurements, the system samples every 2 hours to reduce power consumption and this gives enough data to support the decisions from the clinicians for the chosen use case mentioned in section 4. Collected data are transmitted to an online platform for further analysis.

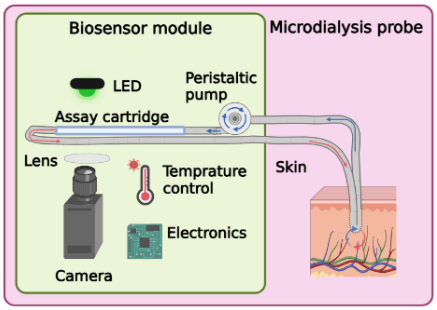

Figure 4: Closed-loop microdialysis biosensing system. ISF is sampled via a skin-implanted microdialysis probe, allowing bidirectional diffusion of small molecules like creatinine. The dialysate circulates through a biosensor module via peristaltic pumping, where optical detection is performed using green LED illumination and camera capture. The sample is then recirculated, completing the loop. Integrated electronics regulate flow and temperature for optimal assay performance

3.1.1. Technological novelty of wearable sensor

Transforming the biosensor into a wearable device required substantial miniaturization of the BPM setup. The sensor unit, is worn near the microdialysis probe using a soft strap. The peristaltic pump draws ISF via the probe in the skin into the sensor unit. Final placement of both elements will be determined through validation studies. For imaging, the NanEyeC camera–was selected [9], an ultra-compact camera optimized for close-range detection. With dimensions of 2.77 × 1.05 × 1.05 mm and a weight under 100 mg, the camera ensures comfort and compactness. Its short working distance (~2 mm) and flat optical front allow easy lens integration, making it suitable for wearable use. A 10x magnification lens is added to visualize particles, for example the Thorlabs A390TM-A [10].

Illumination is provided by a green LED, chosen for its optimal scattering-properties and minimal interference. During measurement, data is captured by a processor linked to the camera and transmitted via Bluetooth to the user's app. The BPM software processes the data, and results are displayed directly in the app. By integrating these components, BPM

is used to enable continuous, non-invasive tracking of creatinine levels in interstitial fluid, a novel approach that enhances both precision and real-time responsiveness.

3.1.2. Technical feasibility of wearable sensor

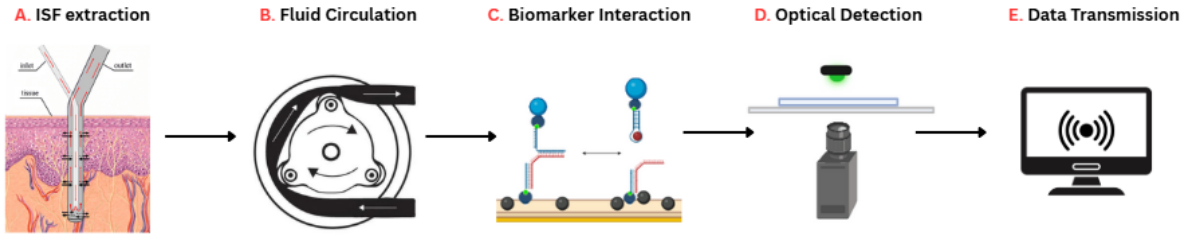

Figure 55: Workflow of the creatinine biosensor. (A) ISF extraction and directing to biosensor. (B) Microfluidic flow enables circulation across sensing surface. (C) Creatinine binds to aptamer probes for target recognition. (D) Optical detection is perform

For continuous and reliable biomarker monitoring, the sensor combines microfluidics, optical detection, and wireless communication in a compact, skin-friendly design. Figure 5 illustrates the integrated wearable sensor system, highlighting the key components and processes that enable the functionality. A miniaturized camera with a compatible lens system eliminates bulky optics, allowing smooth integration into the housing made from Polydimethylsiloxane (PDMS). Both the LED and camera operate at low power, making the system suitable for extended battery use. Every two hours, everything switches on for 8 minutes to measure the sample, except for the processor, which is on all the time, to switch the system on and off based on the time. This enables extended battery use of the sensor to one use based on a 3400 mAh battery.

Sample flow is maintained by a peristaltic micropump, for example the Takasago BCP [11], which transport perfusate from the microdialysis probe to the sensor chamber. The probe's semipermeable membrane selectively allows small molecules like creatinine to pass [12]

One challenge is the temperature drop as sample moves from the body (~37 °C) to the ambient sensor unit, which can affect particle behavior and binding kinetics. To address this, a temperature controller is added to stabilize assay conditions to ~25 °C for optimal performance. For example a temperature controller developed by the City University of Hong Kong, which is approximately 1.3 grams and is less than a millimeter thick [13]. All these small components make the sensor unit is lightweight (~80 g), compact box (±5x7x2 cm), and secured with a soft strap to minimize discomfort and motion artefacts. Patient movement has minimal impact because all imaging components are enclosed within a rigid housing, eliminating relative motion between the different components. Data is transmitted via Bluetooth to a secure online platform for continuous monitoring. Compared to a commonly used insulin pump worn similarly, our proposed sensor falls within the same size and weight range, supporting its feasibility as a wearable device [14].

3.2. Reliability of sensor output

The core reliability of the proposed biosensor lies in its ability to generate accurate and reproducible data, while maintaining robustness during long-term monitoring. Building on the proven long-term stability of BPM design leverages aptamer-based molecular recognition to achieve high specificity and tunability [15]. The addition of novel binding constructs, such as the use of a docking- and displacement strand complex in combination with a DNA sensor makes the sensor inherently modular. To anticipate performance with varying creatinine concentrations, a computational model was developed to predict the reliability of the sensor, further explained in Section 3.2.2.. Together, they form a sensing framework that matches the accuracy of clinical gold standards while remaining flexible and suited for wearable, real-world applications.

3.2.1. Technological novelty of reliability concept

The conceptual novelty comes from the integration of aptamer-based molecular recognition into a BPM biosensor. Before this, the BPM biosensors have primarily used antibodies or aptamers with a DNA strand as target [15]. Our aptamer selectively binds to creatinine, while BPM enables label-free detection with high precision (97.9%) [16]. The design is also inherently modular; the aptamer and complementary DS can be swapped out for a new target, while the docking strand and surface chemistry remains unchanged. The combination of aptamer recognition and BPM transduction represents a novel, reliable and flexible sensing platform.

3.2.2. Technical feasibility of reliability concept

To assess feasibility, two aptamer constructs were tested, differing in the position of the biotin modification (5' or 3' end). Each were immobilized on either particles or the surface, with the DS complex presented on the opposing platform. The BF of the 5'-biotinylated aptamer on particles with the DS, showed a concentration-dependent gradient, indicating effective binding behavior (Fig. 6)

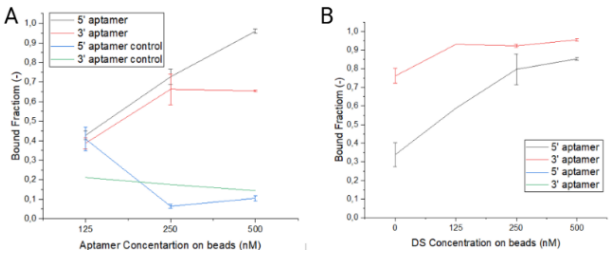

Figure 6: Binding efficiency of 5′ and 3′ aptamers and their respective controls to beads. (A) Bound fraction of aptamers and controls at varying aptamer concentrations. (B) Bound fraction of aptamers and controls at varying DS concentrations. Error bars represent measurement variability.

Single-particle–tracking confirmed the reversibility of the DS–aptamer complex. A clear difference in the diffusion coefficient of a population of individual particles was seen in Figure 7A, with a threshold of 0.15 μm/s^2 [1]. This difference indicates binding and unbinding of particles, consistent with BPM principles, and s essential for ensuring the availability of the aptamer for creatinine binding. Population level switching can be seen in Figure 7B.

Not all particles undergo switching, but this is consistent with the heterogeneity of particles described by Vu et al. (2024) [17]. To further validate the reversible binding of the DS to the aptamer, an experiment was performed in which different concentrations of aptamer were used across the particles, (25nM–500nM) to generate a gradient in binding affinity. Four DS variants were evaluated, all targeting a different region in the aptamer, as shown in Appendix A, to identify which produced the most consistent concentration dependent response BF was clearly linked with increasing aptamer concentration, as seen in Figure 8, DS 2 showed the most well-defined gradient and was selected.

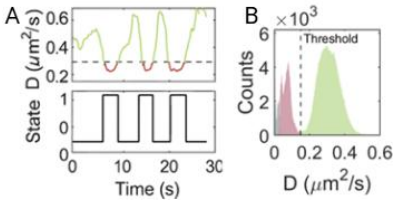

Figure 7: (A) Temporal profile of the diffusion coefficient (D) for a single particle over 30 seconds, with a threshold of 0.15 μm/s² used to distinguish bound (red) and unbound (green) states. The lower panel indicates the binary state assignment over time. (B) Histogram of diffusion coefficient values across all particles, showing a bimodal distribution with a separation at the threshold of 0.15 μm/s², enabling identification of binding and unbinding events

A Simulink model was developed to simulate the creatinine and the DS competing for the aptamer–binding sites. The full Simulink model and associated script can be seen in Appendix B. The specific k_{on} and k_{off} rates are based on previous research done on other small molecule-aptamer interactions and were respectively $k_{on\_CreaApt}$=1.4*10^6 M^{-1} s^{-1}, $k_{off\_CreaApt}$ = 50 s^{-1}, k_{on_DSApt}= 2.1*10^6 M^{-1} s^{-1} and k_{off_DSApt}= 0.024 s^{-1} [18] [19] [5].

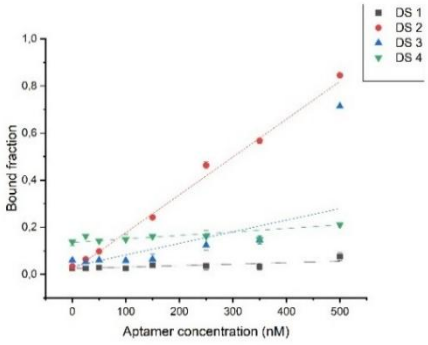

Figure 8: Bound fraction of four displacement strands (DS 1–4) plotted against increasing aptamer concentration. DS 2 demonstrates the strongest concentration-dependent binding, indicating its enhanced responsiveness and affinity compared to the other strands.

As the aptamer is present on the particles in solution, the simulation corrects for the effective aptamer concentration that is accessible for DS binding on the surface. This is corrected using a spherical cap approximation based on the bead's radius and the height of the DS-Aptamer complex, which is derived from the complex's radius of gyration. The simulation is first run under zero creatinine concentration to establish the initial steady-state binding between the aptamer and DS. When creatinine is added, the simulation shows a progressive displacement of DS by creatinine from aptamer binding sites in Figure 9. The fractional occupancy from the computational model can be related to the BF captured by the BPM sensor. An increase in fractional occupancy of the DS, leads to an increase in BF observed in BPM. This suggests a direct relation between fractional occupancy of the model and the BF of the BPM biosensor allowing for direct comparison between the model predictions and experimental data. This competition occurs within a concentration range of 10^{-6} to 10^{-3}, which includes physiologically relevant creatinine levels in ISF [20].

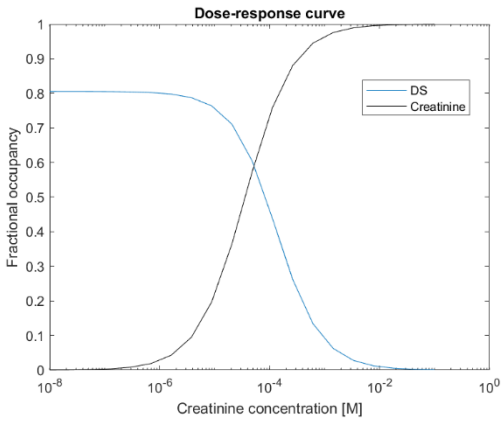

Figure 9: Dose-response curve illustrating the fractional occupancy of DS (blue) and creatinine (black) as a function of increasing creatinine concentration. As creatinine levels rise from 10^{-8} to 10^{0} M, DS occupancy decreases while creatinine occupancy increases, indicating competitive binding dynamics.

3.3. Original contributions

Team captains:

After elaborate research done by the team, the team decided to explore a new sensing concept using Förster Resonance Energy Transfer (FRET) in combination with an anti-creatinine aptamer [6]. This idea was adapted by the team using the anti-creatinine aptamer found on Creative Biolabs and in other research [4] [21]. The design process of the displacement strand and other molecular parts from the assay setup were all done by the team itself.

After several months of lab testing in collaboration with the Molecular Biosensing group (MBx) from the Eindhoven University of Technology, the experimental outcomes were inconsistent and irreproducible. In response to this, the team decided to switch from the FRET idea to BPM, in consultation with their supervisors. The team chose to preserve the anti-creatinine aptamer and displacement strand mechanism allowing for reversible and highly specific detection of creatinine while simplifying the optical readout. This optical readout was inspired by the already existing setups from the university's MBx group. For the sample stage the team used a custom design, 3D printed by the Innovation Space facilities at the TU/e. The core functionality of the team's software was based on already existing code provided by Max Bergkamp, a former team T.E.S.T. member, providing a foundation for the team's software which has been developed using Python in VS Code as well as MATLAB.

Team's supervisor:

After an extensive literature review, the team decided to follow a challenging route by selecting a FRET-based competitive assay principle based on publications for Tom Soh's group. They started with a creatinine-DNA construct to test the interaction with the anti-creatinine aptamer. They decided to use the construct synthesized by last year's team, however after many tests this appeared not to be functional, and the quality of the product was doubted. The assay was based on the competitive binding of a DNA displacement strand to the anti-creatinine aptamer. Fluorescence polarization based experiments gave no indication of creatinine interaction with the aptamer. At that point the choice was made to use BPM experiments to study the interactions of creatinine and displacement strands to the aptamer and finally the decision was made to continue with BPM as sensor platform.

Signatures

dr. ir. Arthur de Jong (Supervisor T.E.S.T.)	Alain Dresen (Co-captain T.E.S.T.)	Tiago Fernandez-Nespral (Co-captain T.E.S.T.)
		

4. TP award: Translation potential

4.1. Customer interviews

To ensure a structured and ethically sound approach, all interviews were conducted using tailored question sets designed to match the expertise and role of each stakeholder. Each interview followed a semi-structured format, allowing for consistent data collection while leaving room for individual insights. The technical direction of our solution, continuous creatinine monitoring via a wearable device, was already defined. The interviews were designed to explore which patient group would benefit most from such a device and to uncover pain points in their diagnosis and treatment pathways. This method enabled a reproducible comparison across specialties and helped identify the most clinically relevant use-case. Full interview guides can be found in Appendix C and tables consisting of the most important quotes form interviews ordered by topic, can be found in Appendix F.

Determining the Most Suitable Use-Case

We began by interviewing nephrologists and patients with chronic kidney disease (CKD) to explore whether continuous creatinine monitoring could support early intervention and improve treatment planning. However, since creatinine levels in CKD progress slowly, more frequent measurements offered limited clinical benefit. Even in late-stage CKD, where we hypothesized it might help with dialysis scheduling, patients and clinicians indicated that once a routine is established, scheduling becomes predictable and is not a major burden.

We also considered using our biosensor in clinical trials that deal with nephrotoxic medications to save time and increase safety. However, through conversations with two people in research and development in the companies Johnson & Johnson and La Roche it became clear that a single biomarker monitoring system was insufficient, and they avoided technologies not first implemented in regular clinical systems. Use in monitoring artificial kidney prototypes was considered during an interview with Two PhD researchers from the NxtGen Hightech Biomed 04 “Artificial Organs” consortium but was deemed insufficient without an ability to track membrane flow.

We then shifted our focus to patients with more rapidly changing kidney function, interviewing ICU physicians, oncologists, and cardiologists. We found that whilst ICU and cancer patients are at high risk for Acute Kidney Injury (AKI), they are already closely monitored through frequent blood tests covering a wide biomarker range. Introducing a wearable device in these settings would only be valuable if it could replace this routine entirely, which is currently not feasible.

With heart failure patients, however, cardiologists indicated a need for more frequent testing to monitor nephrotoxic medication dosing. With creatinine being measured only

once per week, AKI in these patients is often detected relatively late, leading to heart failure treatment interruptions and hospital readmissions. AKI frequently arises in the context of heart failure due to the close interplay between cardiac output and renal perfusion, and even modest drops in kidney function can trigger fluid overload and worsen cardiac stress, making this cohort particularly reliant on timely renal monitoring [22]. Continuous tracking could bridge this gap and integrate easily into existing home-monitoring systems already used by these patients. With fewer required biomarkers and an established digital workflow, heart failure emerged as the most fitting and practical focus for our target group.

In-Depth Interviews: Heart Failure Focus

The timeline in Figure 10 illustrates the standard 3-week medication titration pathway for heart failure patients, during which kidney function is closely monitored. Three out of these four medications affect kidney function.

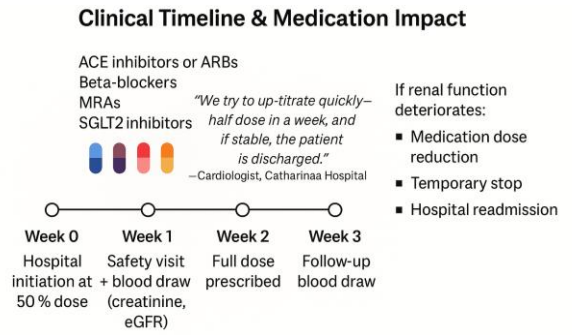

Figure 10: Clinical Timeline & Medication Impact. Cardiologists aim to reach target doses quickly: patients typically begin at 50% target dose during hospital stay. If stable, full dosing is prescribed by Week 2.

Even though rapid up-titration improves the chance of patient recovery, it can trigger AKI, forcing clinicians to pause or reduce therapy before target doses can be achieved [23]. Following discharge, most heart failure patients are enrolled in home monitoring programs coordinated by specialized heart failure nurses. Patients are expected to measure and report key health parameters daily through digital platforms that connect directly to the hospital. These parameters typically include body weight, blood pressure, and subjective symptoms such as breathlessness or fatigue. The monitoring nurse reviews the data and, if necessary, consults with a cardiologist to determine whether intervention is required. Although this system helps manage fluid balance and blood pressure remotely, it does not currently include kidney function. Creatinine levels are measured only during scheduled in-clinic blood draws. As a result, critical deterioration in kidney function may go unnoticed for several days. This delay can lead to missed opportunities for early intervention, potentially resulting in avoidable complications or hospital readmissions. Due to frequent hospital (re)admissions and the extensive use of medication, heart failure accounts for one of the highest burdens on healthcare expenditure in the Netherlands [24]. Nurses and cardiologists consistently noted that if deterioration had been visible earlier, interventions could have been more timely and better targeted.

4.2. Design of validation study

Solution and Critical Aspects from Interviews

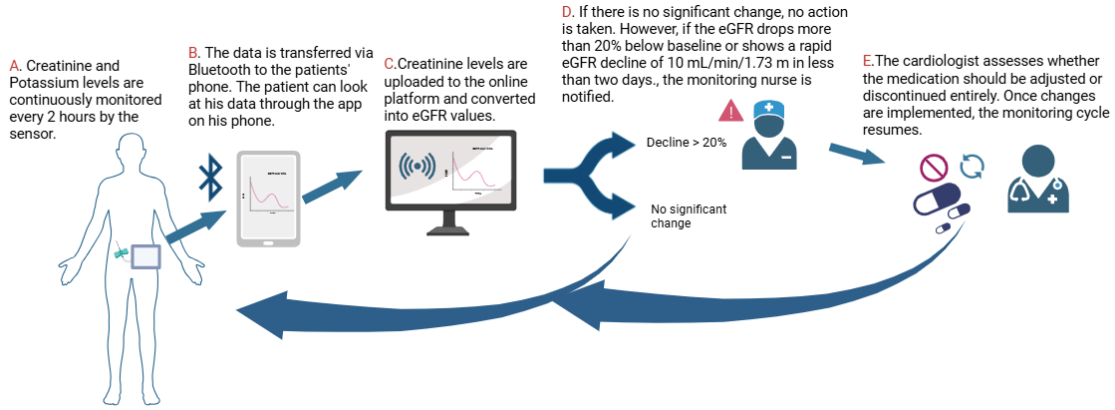

Figure 11: Workflow of the biosensor implementation. The patient is asked to submit their body weight, blood pressure and well-being on a daily basis via the app, this is also integrated in the current practices. The estimated Glomerular Filtration Rate (eGFR) is calculated using a formula that considers creatinine level, age, sex and body size *[25]*

Current monitoring of heart failure patients tolerance to medications relies on subjective signs of deterioration, and weekly in-clinic blood tests. Renal decline frequently goes undetected for days, leading to premature medication stoppage and hospital readmissions. To address this gap, we propose a wearable biosensor that continuously monitors creatinine levels from patients' homes, enabling earlier intervention and reducing the risk of AKI. The implementation of this biosensor in the healthcare system can be seen in Figure 11. Clinicians agreed that creatinine-only monitoring would improve detection of AKI in heart failure patients. However, to make home monitoring fully autonomous and eliminate blood draws during the unstable phase, at home potassium measurement is also needed. An additional chamber could be added to our biosensor in the future to measure potassium.

Clinician Validation Study

To test our core assumption that frequent creatinine monitoring improves renal assessment, we conducted a structured survey with a specialized nurse, a monitoring nurse, and a cardiologist. Using visual scenarios of two heart failure patients, respondents compared daily versus weekly eGFR data collection. Clinicians evaluated when they would adjust medication, their confidence in the data, and the likelihood of missing important changes. They also assessed their ability to distinguish temporary variation from true decline, and identified alert thresholds and acceptable response times. The full questionnaire and supporting quotes are provided in Appendix D.

Survey results showed that daily creatinine data led to earlier clinical action and clearer trend interpretation. On average, clinicians intervened three days earlier in the daily data scenario (day 9–13) compared to the weekly scenario (day 14). Confidence scores were

higher for daily monitoring (average 3.3) than for weekly (2.7), and perceived risk of missing important changes was lower (1.3 for daily vs. 3.3 for weekly, on a 1–5 scale). Despite these advantages, distinguishing between temporary fluctuations and meaningful decline remained challenging, indicating that frequency alone may not resolve diagnostic ambiguity. Clinicians identified a 20–33% baseline drop in eGFR as the appropriate alert threshold, with urgency influenced by the rate of decline. Acceptable delays before intervention ranged from one to three days, depending on clinical context.

Regarding workflow integration, clinicians raised concerns about the potential for data overload and emphasized the need for personalized filtering based on individual patient trajectories. There was also strong interest in expanding biosensor capabilities to include potassium as an additional biomarker.

In conclusion, the survey responses confirm the clinical value of frequent creatinine monitoring, particularly when combined with contextual data interpretation and broader biomarker support. For deeper validation of this critical aspect, more specialists should conduct the survey. Also a broader range of patient groups should be implemented in the survey, to better investigate which patient groups need to be continuously monitored. A summary of the answers of the clinicians can be found in Appendix E.

Additional validation studies will be conducted to assess user experience with our biosensor. To evaluate the digital environment and communication dynamics, we will conduct mock-up interface trials and usability walkthroughs. These sessions will assess how clearly information is conveyed and how useful it feels to both patients and clinicians. Given concerns about patients misinterpreting data or becoming anxious, we will test multiple interface versions with varying levels of detail: a simplified color-coded indicator, a daily trend graph without numerical data, a full graph with detailed values, and a hybrid version with optional expanded views. Participants will interact with all versions in randomized order and rank them based on their ability to interpret the data, emotional responses such as anxiety or reassurance, and UI preferences. Optional think-aloud protocols may be included to capture real-time reactions. This evaluation will help determine which interface offers the best balance of clarity, emotional comfort, and user empowerment across different age groups and health literacy levels.

To evaluate the comfort of wearing the biosensor and the ease of replacing cartridges, participants will wear a mock device of a similar size, shape, and weight for three weeks, replacing cartridges daily. Participants will rate the wearable on a scale of 1-5 for comfort, ease, and practicality. These ratings can be qualitatively compared to their opinions on current practices. Installation will be tested using instructional mock-ups, with outcomes measured by task completion time, clarity, accessibility, and error rates.

5. Team and support

5.1. Contributions of the team members

The team was divided into two main subgroups, team assay and team detection. Team assay focused on developing the assay, while team detection focused on developing the physical transduction, the reader instrument and software. To tackle the business case, a separate subgroup, Translational potential was created. As well as that, every team member had an organizational function.

Team Member	Function within the team
Luuk Brouwer	Member of team detection, head of Translational potential
Alain Dresen	Member of team assay, co-captain
Tiago Fernández-Nespral	Head of team detection, member of Translational potential, co-captain
Austėja Štaraitė	Member of team assay, member of Translational potential, Public relations
Megan van Meurs	Member of team assay, member of Translational potential, Public relations
Senne van Osch	Head of team assay, External relations
Sjoerd Wels	Member of team assay, Treasurer, External relations
Charlotte de Witte	Member of team detection, member of Translational potential, secretary, External relations

5.2. People who have given support

The team received great support from many people throughout the project. First of all, we would like to thank our general supervisor dr. ir. **Arthur de Jong**, who guided us throughout the whole process also during our (bi-)weekly meetings. Alongside him, we would like to thank ir. **Selina Janssen**, and ir. **Koen Valk** who were always ready to provide the team with advice and support where needed during the weekly meetings, but also outside of these hours. **Selina Janssen** was the main point of contact for team assay providing help, lab protocols and other assay related questions. **Koen Valk** was the main point of contact for team detection, providing help and giving advice when problems arose. We would also like to thank **Bart van Grevenhof** who guided us throughout the business case. He was the main contact point for the translational potential team and was always ready to schedule a meeting and provide the team with advice and support where needed. As well as that, we would like to thank all members of the **MBx group** for their guidance and always willing to help us when problems arose and providing us with the materials needed for the project.

5.3. Sponsors and partners

T.E.S.T. 2025 would also like to thank all sponsors and partners that supported us this year. We would like to thank TU/e Innovation space, Chroma, Merck, Forbion, Thorlabs, Antibodies Online and Onera for sponsoring with financial support, resources/ hardware and knowledge.

6. Final remarks

This project has been an amazing opportunity for us to explore a wide variety of innovative biosensing strategies during our pursuit for a method of creatinine detection in interstitial fluid. We began with a FRET-based design, which ultimately proved unfeasible within the competition's scope. Although this was disappointing, the process was highly instructive and led us to develop the aptamer-displacement strand system that became central to our final sensor.

Building on that foundation, we implemented a novel approach by combining the displacement system with BPM, a relatively new technique. To our knowledge, this is the first time BPM has been applied in this way, and it allowed us to explore a flexible and modular biosensing platform with promising potential.

In the coming months, we aim to further improve the accuracy and precision of the sensor, focusing on extensive testing and iterative refinement.

We would once again like to express our gratitude to our supervisors Arthur de Jong, Selina Janssen, and Koen Valk for their continued guidance throughout the project. We would also like to express our gratitude to Siebe van den Elzen and Wim Nijskens for their input during the assay development process, Bart van Grevenhof for his guidance in the business case and Max Bergkamp for providing software parts for us to work on. Finally, we thank our sponsors for making this project possible.

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8. Appendix

Appendix A: DNA sequences

The aptamer sequence

- 5'-CGACGGTGGCCTATTAAATAGCTTTAGTTTAAGAAAAGTAATAGGGGGTGTCG-3'

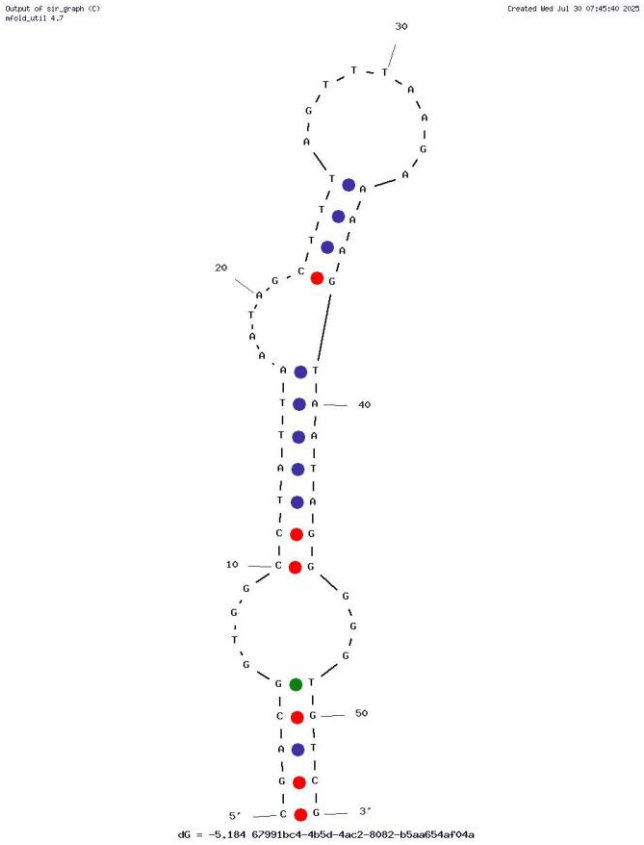
The docking strand sequence:

- 5'- TTTTTACTACTACTGACTGACACTGAATCAA -3'

The displacement strand sequence:

- 5'-AAACACCCCCT GGTCACT TTGATTCAGTGTCAGTCAGTAGTAGT-3'

Aptamer folding (IDT)



Binding of docking strand to the displacement strand

Delta G: -39.4 kcal/mol **Base Pairs:** 26

```
5' TTTTTACTACTACTGACTGACACTGAATCAA
       ||||||||||||||||||||||||||||
3'     TGATGATGACTGACTGTGACTTAGTTTCACTGGTCCCCCACAAA
```

Overlap DS 1 (secondary sequence) with anti-creatinine aptamer (primary sequence)

Primary Sequence: 5'- CGACGGTGGCCTATTAAATAGCTTTAGTTTAAGAAAAGTAATAGGGGGTGTCG -3'
Secondary Sequence: 5'- TCTAAAGCTAAAGTCACTTTGATTCAGTGTCAGTCAGTAGTAGT -3'

Maximum Delta G: -100.96 kcal/mol

Delta G: -13.75 kcal/mol **Base Pairs:** 9

```
5'                  CGACGGTGGCCTATTAAATAGCTTTAGTTTAAGAAAAGTAATAGGGGGTGTCG
                          :           |||||||||
3' TGATGATGACTGACTGTGACTTAGTTTCACTGAAATCGAAATCT
```

Overlap DS 2 (secondary sequence) with anti-creatinine aptamer (primary sequence)

Primary Sequence: 5'- CGACGGTGGCCTATTAAATAGCTTTAGTTTAAGAAAAGTAATAGGGGGTGTCG -3'
Secondary Sequence: 5'- AAACACCCCCTGGTCACTTTGATTCAGTGTCAGTCAGTAGTAGT -3'

Maximum Delta G: -100.96 kcal/mol

Delta G: -18.51 kcal/mol **Base Pairs:** 9

```
5' CGACGGTGGCCTATTAAATAGCTTTAGTTTAAGAAAAGTAATAGGGGGTGTCG
             ::: ::   :     : :  :  :::   :  |||||||||
3'          TGATGATGACTGACTGTGACTTAGTTTCACTGGTCCCCCACAAA
```

Overlap DS 3 (secondary sequence) with anti-creatinine aptamer (primary sequence)

Primary Sequence: 5'- CGACGGTGGCCTATTAAATAGCTTTAGTTTAAGAAAAGTAATAGGGGGTGTCG -3'
Secondary Sequence: 5'- TTCTTAAACTAGGTCACTTTGATTCAGTGTCAGTCAGTAGTAGT -3'

Maximum Delta G: -100.96 kcal/mol

Delta G: -15.81 kcal/mol **Base Pairs:** 11

```
5'          CGACGGTGGCCTATTAAATAGCTTTAGTTTAAGAAAAGTAATAGGGGGTGTCG
                :       :: :::  :   ||||||||||
3' TGATGATGACTGACTGTGACTTAGTTTCACTGGATCAAATTCTT
```

Overlap DS 4 (secondary sequence) with anti-creatinine aptamer (primary sequence)

Primary Sequence: 5'- CGACGGTGGCCTATTAAATAGCTTTAGTTTAAGAAAAGTAATAGGGGGTGTCG -3'
Secondary Sequence: 5'- GGGCTATTTAAAGTCACTTTGATTCAGTGTCAGTCAGTAGTAGT -3'

Maximum Delta G: -100.96 kcal/mol

Delta G: -13.97 kcal/mol **Base Pairs:** 9

```
5'                     CGACGGTGGCCTATTAAATAGCTTTAGTTTAAGAAAAGTAATAGGGGGTGTCG
                          :   :     |||||||||
3' TGATGATGACTGACTGTGACTTAGTTTCACTGAAATTTATCGGG
```

Appendix B: Simulink model

Appendix B.1 : MATLAB script

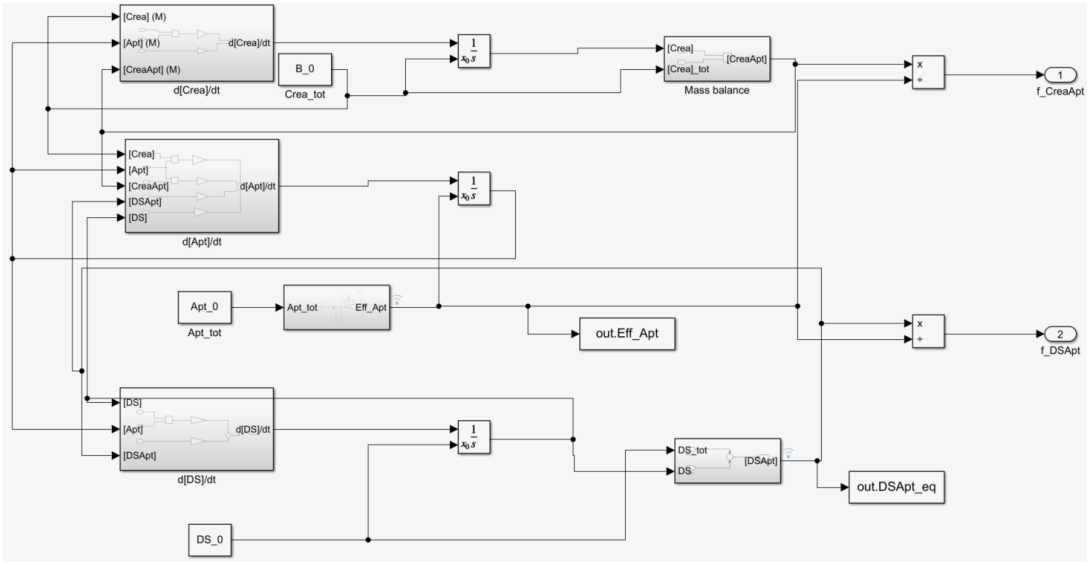
```
clear
clc

%% 1. Parameters
k_on = 1.4e6;%Creatinine-Aptamer
k_off = 50; %Creatinine-Aptamer
k_d = k_off/k_on;
k_on_1 = 2.1e6; %DS-Aptamer
k_off_1 = 0.024; %DS-Aptamer
k_d_1 = k_off_1/k_on_1;

%Effective Apt calculations
r_beads = 0.5e-6; %radius of Dynabeads 1 ?m
R_beads = 4*(r_beads)^2; %radius for total area of Dynabeads 1 µm

BP_ssDNA = 23; %Amount of nucleotides ssDNA in Docking-DS-Aptamer complex
BP_dsDNA = 37; %Amount of nucleotides dsDNA in Docking-DS-Aptamer complex
Biotin_streptavidin = 2; %Amount of biotin-streptavidin complexes in system
length_ssDNA = 0.59e-9 * BP_ssDNA; %length of ssDNA part
length_dsDNA = 0,34e-9 * BP_dsDNA; %length of dsDNA part

pers_length_ssDNA = 1.98e-9; %persistence length of one nucleotide ssDNA
pers_length_dsDNA = 50e-9; %persistence length of one nucleotide dsDNA
length_Bio_strep = 12e-9; %estimation of length of biotin-streptavidin
complexcons

%% Run function Radius of Gyration
Rg = calcRg(length_dsDNA, length_ssDNA, pers_length_ssDNA,
pers_length_dsDNA);


%% First plotting
%Concentrations
Apt_tot = 500e-9; %Aptamer concentration on the beads
DS_tot = 50e-9; %DS concentration on the surface

% Plotting range (concentratie creatinine)
DataPoints = 1;
Range = logspace(-8, -1, DataPoints);

f_CreaApt = zeros(1, DataPoints);
f_DSApt = zeros(1, DataPoints);
index = 1;

% Model openen
open_system('Model_Creatinine_final');

B_0 = 0;  % No creatinine
DS_0 = DS_tot;
Apt_0 = Apt_tot;
SimOut = sim("Model_Creatinine_final", "SimulationMode", "normal",
"StopTime", "0.01");

% Extract Eff_Apt uit logsout
logs = SimOut.logsout;
Eff_Apt = SimOut.get('Eff_Apt').Data(end);
DSApt_eq = SimOut.get('DSApt_eq').Data(end);
```

```
fprintf("Eff_Apt = %.2e M\n", Eff_Apt);
fprintf("DSApt_eq = %.2e M\n", DSApt_eq);
% Bereken de bijbehorende DS_0 (vrije DS bij evenwicht)
DS_0 = DS_tot - DSApt_eq;
Apt_0 = DS_tot - DSApt_eq;

% Zet in workspace
 assignin('base', 'DS_0', DS_0);
 assignin('base', 'DSApt_eq', DSApt_eq);
 assignin('base', 'Apt_0', Apt_0);

 fprintf("DSApt_eq = %.2e M (%.1f%% van Eff_Apt)\n", DSApt_eq, 100 *
DSApt_eq / Eff_Apt);
 fprintf("DS_0 = %.2e M\n", DS_0);

%% 3. Range voor creatinine
DataPoints = 15;
Range = logspace(-8,-1,DataPoints);

f_DSApt = [];
f_CreaApt = [];
index = 1;

%% 4. Simuleer voor elk B_0
for B_0 = Range
    SimOut = sim("Model_Creatinine_final", "SimulationMode", "normal");

    % Extract output signalen
    y_crea = SimOut.yout{1}.Values.Data;
    y_ds   = SimOut.yout{2}.Values.Data;

    f_CreaApt(index) = max(y_crea);
    f_DSApt(index)   = max(y_ds);
    index = index + 1;
end

%% 5. Plot Tijdscurves Creatinine
figure
for i = 1:DataPoints
    B_0 = Range(i);
    SimOut = sim("Model_Creatinine_final", "SimulationMode", "normal");
    plot(SimOut.yout{1}.Values.Time, SimOut.yout{1}.Values.Data)
    hold on
end
title('Fractional occupancy Creatinine')
xlabel('Time (s)')
ylabel('Fractional occupancy Creatinine')
legend(compose('[B]_0 = %.1e M', Range), 'Location', 'best')
hold off

%% 6. Plot Tijdscurves DS
figure
for i = 1:DataPoints
    B_0 = Range(i);
    SimOut = sim("Model_Creatinine_final", "SimulationMode", "normal");
    plot(SimOut.yout{2}.Values.Time, SimOut.yout{2}.Values.Data)
    hold on
end
title('Fractional occupancy Displacement strand')
xlabel('Time (s)')
```

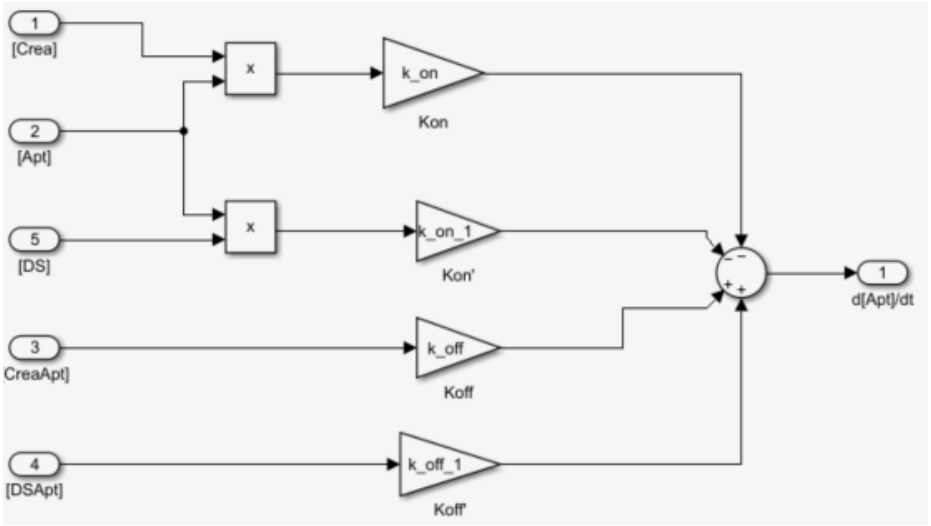
```
ylabel('Fractional occupancy Displacement strand')
legend(compose('[B]_0 = %.1e M', Range), 'Location', 'best')
hold off

%% 7. Dosis-response curve
figure
semilogx(Range, f_DSApt, '-')
hold on
semilogx(Range, f_CreaApt, '-k')
hold off
title('Dose-response curve')
xlabel('Creatinine concentration [M]')
ylabel('Fractional occupancy')
legend('Displacement Strand', 'Creatinine', 'Location', 'best')

 %% Radius of gyration
 function Rg = calcRg(length_dsDNA, length_ssDNA, pers_length_ssDNA,
pers_length_dsDNA)
     length_ds = 2 * pers_length_dsDNA;
     length_ss = 2 * pers_length_ssDNA;

     % Number of segments
     N_ds = length_dsDNA / length_ds;
     N_ss = length_ssDNA / length_ss;

     % Individual Rg values
     Rg_ds = sqrt(N_ds) * length_ds / sqrt(6);
     Rg_ss = sqrt(N_ss) * length_ss / sqrt(6);

     % Total Rg
     Rg = sqrt(Rg_ds^2 + Rg_ss^2);
 end
```

Appendix B.2 : Simulink model

Full model Visualization



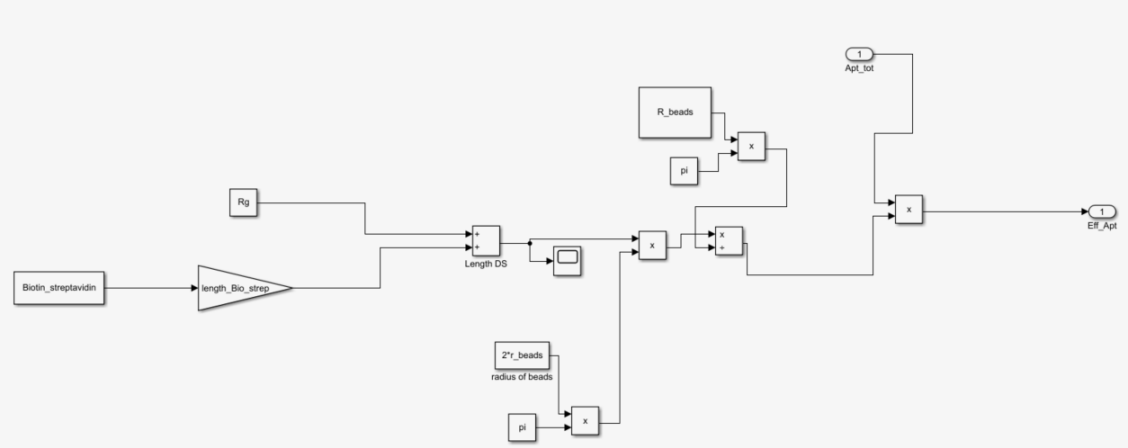
Visualization of mass-action kinetics rate equation of aptamer concentration



Formulas net rate

- $\frac{d[Crea]}{dt} = k_{off}[CreaApt] - k_{on}[Crea][Apt]$.
- $\frac{d[Apt]}{dt} = k_{off}[CreaApt] + k_{off\_1}[DSApt] - k_{on}[Crea][Apt] - k_{on\_1}[DS][Apt]$.
- $\frac{d[DS]}{dt} = k_{off\_1}[DSApt] - k_{on\_1}[DS][Apt]$.

Visualization of Effective aptamer calculation



Formulas used for effective aptamer calculation

- Spherical cap: $A = 2 * \pi * r * h$
- Height h: $R_g = \sqrt{\frac{1}{3}(length_{dsDNA} \cdot persis.length_{dsDNA} + length_{ssDNA} \cdot persis.length_{ssDNA}}$
- Spherical volume: $V = 4 * \pi * r^2$
- Correction factor:-$f = \frac{Spherical\ cap}{Spherical\ volume}$

Appendix C: Full Interview Guides

This appendix presents the comprehensive, semi-structured question guides used for each stakeholder group. Not all questions were asked in every interview; these guides served as master templates to ensure thematic depth and consistency.

1. Chronic Kidney Disease (CKD) Patients

A. Diagnostic Process

- When and how did you first discover that your kidneys were not functioning properly?
- What symptoms or complaints did you experience before the diagnosis?
- Can you walk us through the steps of your diagnostic journey? Which healthcare professionals were involved?
- How long did it take before a definitive diagnosis of kidney failure was made?
- Were there misunderstandings or delays during that process?

B. Monitoring and Follow-Up

- Which tests (blood, urine, imaging) do you regularly undergo to monitor your kidney function?
- How often do you receive test results, and how are they explained to you?
- Do you understand your creatinine and GFR values? If not, what would help make them clearer?

C. Dialysis Experience

- Which dialysis modality (hemodialysis or peritoneal dialysis) did you choose, and why?
- Describe a typical dialysis day: scheduling, session length, and recovery.
- What physical or emotional challenges do you face during or after dialysis?
- Have you been offered home dialysis? If so, what appealed to you or held you back?

D. Transplantation (if applicable)

- How did your journey before and after kidney transplantation unfold?
- How did you feel when you learned a donor kidney was available?
- What changes have you noticed in your daily life since the transplant?
- How often do you now attend follow-up appointments, and what do those visits involve?

E. Impact on Daily Life and Support

- What adjustments have you made in work, education, or leisure due to your kidney disease?

- What emotional or social support (family, patient groups, social workers) have you received?
- In your view, what are the biggest pain points in current CKD care?
- Do you have suggestions for improving the patient experience?

F. Wearable Creatinine Monitoring

- At which point in your treatment journey would a wearable creatinine sensor be most valuable, and why?
- How important is continuous access to your creatinine levels for your peace of mind and treatment decisions?
- What concerns or reservations would you have about using such a device?

2. Heart-Failure Patients

A. Diagnostic and Treatment Process

- How did you first learn that you had heart failure?
    - When was your medication regimen established, and which drugs were prescribed?
    - How often do you attend follow-up appointments, and which tests are performed?
    - Did you notice any impact of your heart-failure medications on your kidney function?
    - What challenges or delays did you encounter during this phase?
- If you underwent a transplant, did you need to adjust your heart-failure medication afterwards?
- How often do you currently go for follow-ups?
    - What parameters are measured during these visits?
    - Do you receive direct feedback on your results, including creatinine values? Would you like to?
    - Are these check-ups done in the hospital or could they be managed by your general practitioner?

B. Cardiorenal Interaction

- How does your cardiologist explain the interaction between heart function and kidney function?
- Have you experienced any kidney issues or side effects from your heart-failure medications?
- How is your kidney function monitored alongside your heart treatment?

C. Monitoring and Home Management

- How frequently do you attend routine check-ups, and what measurements are included?
- How are your creatinine values interpreted alongside cardiac biomarkers (e.g., NT-proBNP)?
- Do you use any home-monitoring tools (blood pressure monitor, scales, app)?
    - If yes, how do you incorporate that data into your daily care?

D. Impact on Daily Life and Quality of Life

- How has heart failure affected your work, study, or social activities?
- What physical or emotional challenges arise from the combined strain on your heart and kidneys?
- Since your medication was established or after any transplant, has your quality of life returned to previous levels?
    - Has this remained consistent, or have there been setbacks?

E. Care Experience and Support

- How would you describe communication among your cardiologist, nephrologist, and other care providers?
- Do you feel you receive clear explanations about your combined heart-kidney treatment?
- What are the main frustrations or pain points in your care journey?
- What changes would you suggest to improve collaboration between cardiology and nephrology teams?

F. Wearable Creatinine Monitoring

- At what stage in your treatment process would a wearable creatinine sensor be most beneficial, and why?
    - How often would you expect it to take measurements to be useful?
    - Which features or interface elements would you consider essential for effective use?

3. Nephrologists

A. General

- Which tests do you order after a GP referral to confirm and stage kidney disease?
- What does a standard treatment plan for kidney failure look like?
- Which treatment options are available, and how often do you measure creatinine throughout the plan?
- Why isn't creatinine measured more frequently, and what barriers exist?

- Which additional biomarkers or measurements do you rely on to monitor kidney function?
- If a patient feels unwell but isn't due back for a week, how do you respond?
- How do you reassure patients that more frequent monitoring may not improve outcomes?
- Which external factors (exercise, diet, hydration) influence creatinine levels, and how do you account for them?

B. Dialysis

- When do you initiate dialysis, and how do you choose the modality (hemodialysis vs. peritoneal dialysis)?
- What are the pros and cons of each approach, and how do you determine session duration?
- Is creatinine a reliable indicator of dialysis adequacy?
- How do comorbidities factor into your dialysis modality decision?
- Do you offer home dialysis? If so, how is it monitored and why?

C. Transplantation and Follow-Up

- Do you see advantages in continuous creatinine monitoring for post-transplant patients?
- How would you integrate a non-invasive continuous sensor into your clinical workflow?
- Could you connect us with post-transplant patients for follow-up interviews?

4. Drug Trial Experts

A. General Trial Design

- What is your role in clinical trials regarding measurement protocols and data quality?
- How does the regulatory approval process for a new drug incorporate biomarker data?
- Have you observed trials fail due to poor measurement quality?
- How are long-term patient outcomes monitored, especially in high-risk populations?
- Which trends have you seen in measurement reliability and regulatory acceptance of novel devices?

B. Measurements and Monitoring

- How are new measurement devices validated and approved for trial use?
- What challenges arise when integrating wearable sensor technologies?

- What benefits would you expect from more accurate and frequent biomarker measurements?
- Can you provide a rough estimate of the costs and timelines for device validation?
- How do you manage data variability across trial sites and delayed data delivery?

C. Acute Kidney Injury (AKI)

- What obstacles do you face when approving nephrotoxic compounds?
- How is AKI currently monitored in trials, and which biomarkers are lacking for early detection?
- Are there emerging technologies or biomarkers you find promising for AKI monitoring?

5. Cardiologists

A. Cardiorenal Interaction

- Can you explain at a high level how heart and kidney functions influence each other?
- How does kidney function affect your heart-failure treatment and medication dosing?
- What factors determine length of stay and timing of discharge for heart-failure patients?
- To what extent does kidney dysfunction prolong hospitalizations?

B. Monitoring and Biomarkers

- Which blood and urine tests do you routinely perform, and what roles do NT-proBNP, creatinine, Cys-C, or KIM-1 play?
- How often do you measure these biomarkers, and how do you interpret fluctuations in GFR?
- If you could detect medication-induced kidney stress earlier, how would it alter your treatment plan?

C. Wearable Technology

- How do you envision using wearable devices within cardiology—both in-hospital and at home?
- What benefits and limitations do you foresee?
- Could continuous creatinine monitoring affect discharge planning for heart-failure patients?
- What interface information would you need, and can you refer us to colleagues or nurses experienced with wearables?

6. Nurses

A. Outpatient Clinic (Polyclinic)

- Which heart-failure patients visit your clinic, and what is their typical clinical status?
- Can you walk us through a patient's clinic visit: measurements performed, turnaround times, and result interpretation?
- How many times per year do these patients visit, and how much time do you spend per patient?
- How often do you encounter patients whose kidney function deteriorates during treatment, and how do you respond?
- When a creatinine result is borderline, what actions do you take?

B. Home Monitoring

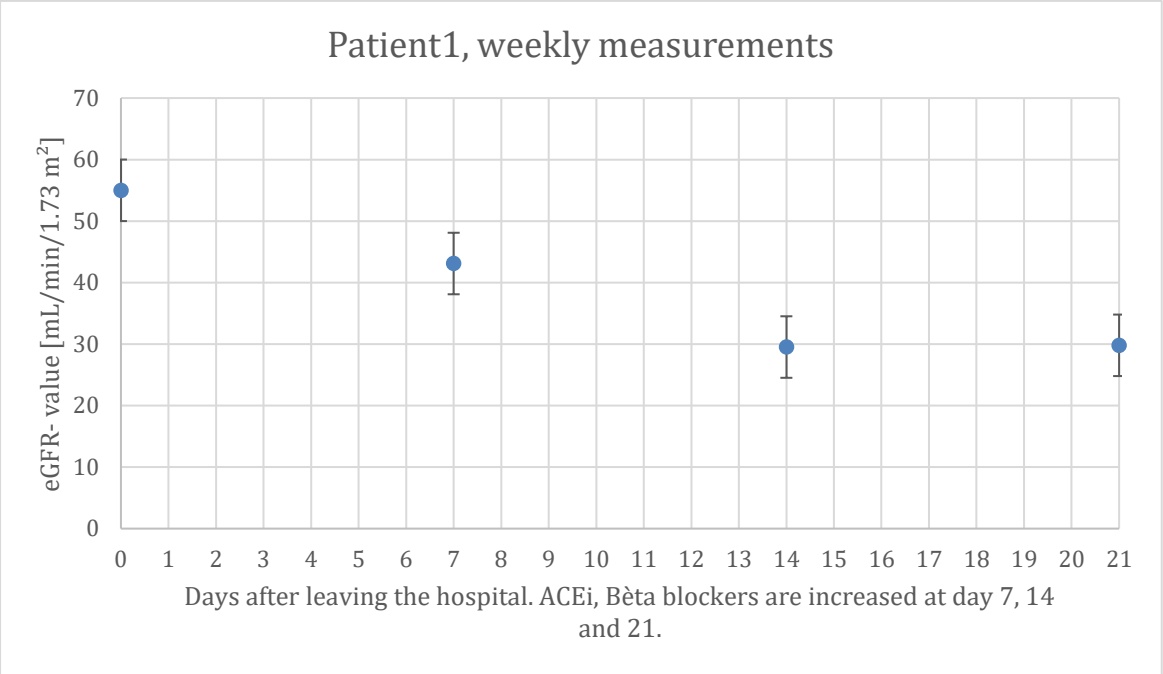
- Are you involved in patients' home-monitoring programs? How often do you review incoming data, and how much time does that require?
- Which patient groups engage with the associated app, and which do

Appendix D: Questionnaire Clinicians

Enquête: Visualisation of kidney function for heart failure patients

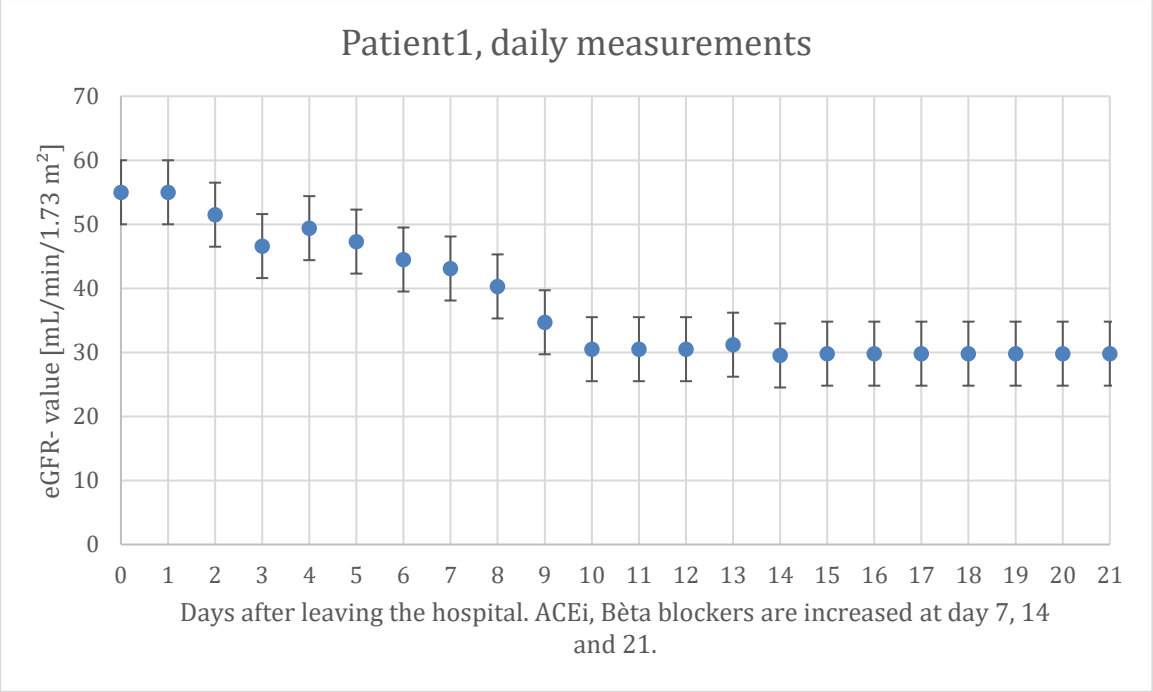
In this questionnaire, you will be asked several questions about graphs displaying measurements of creatinine/eGFR values for two different patients. Both patients have heart failure with reduced ejection fraction and are being treated with diuretics, RAAS inhibitors, and beta blockers. The same questions are asked for each patient, and they are repeated for daily and weekly measurements. You may assume that the patients show no risk based on potassium (K^+) and weight measurements, and they report no new symptoms. Completing this questionnaire takes approximately 15 minutes.

Patiënt 1



Questions for weekly measurements

1. Would you have taken action if you saw these data? If yes, at what point would you have intervened to modify the treatment, and what would you have done?
2. To what extent do these data help you take timely action? (1 = not at all, 5 = very well)
3. How risky is it to measure at this frequency and potentially miss an unexpected change? (1 = not at all risky, 5 = very risky)
4. How well can you distinguish, based on these data, between a temporary expected decline in kidney function and an intrinsic decline? (1 = not at all, 5 = very well)
5. Suppose you could set an alarm that triggers when a certain eGFR threshold is crossed for this patient under weekly measurement. At what value would you set this alarm? (You may also answer as a percentage of the baseline of 55 if that's easier.)
6. How many days can you wait before intervention is truly necessary after this alarm goes off, in order to prevent patient risk?
7. Day 14 may be a tricky point to determine whether this patient can tolerate another dose increase. How difficult is it to estimate the best treatment plan at this time? (1 = not at all difficult, 5 = very difficult)
8. What would you do in this situation?



Questions for Daily Measurements

9. Would you have taken action if you saw these data? If yes, at what point would you have intervened to modify the treatment, and what would you have done?

10. To what extent do these data help you take timely action? (1 = not at all, 5 = very well)

11. How risky is it to measure at this frequency and potentially miss an unexpected change? (1 = not at all risky, 5 = very risky)

12. How well can you distinguish, based on these data, between a temporary expected decline in kidney function and an intrinsic decline? (1 = not at all, 5 = very well)

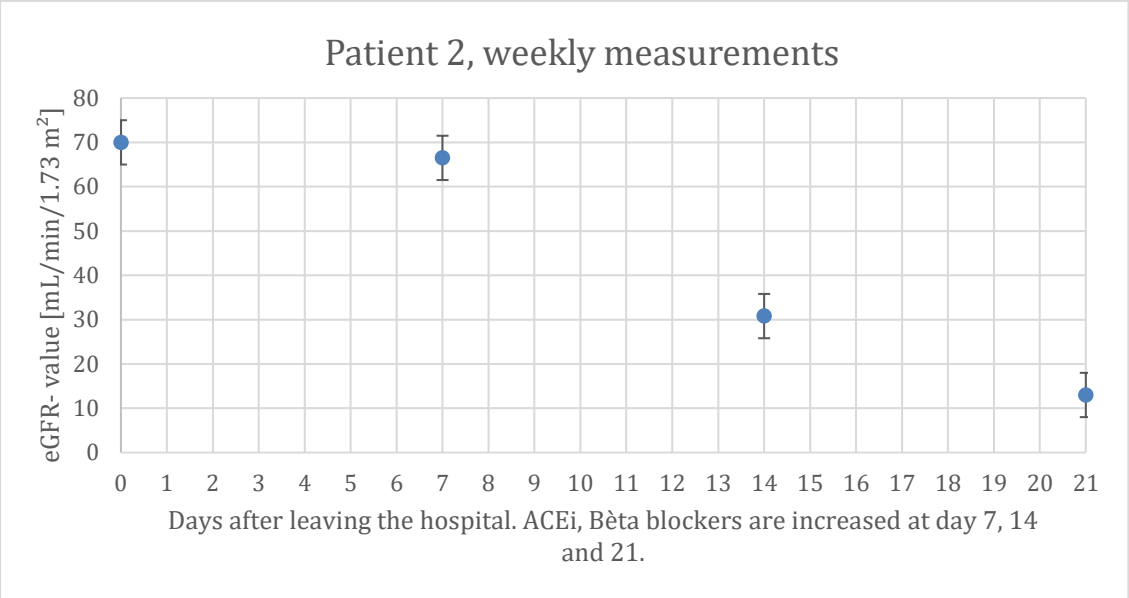
13. Suppose you could set an alarm that triggers when a certain eGFR threshold is crossed for this patient if measured daily. At what value would you set this alarm? (You may also answer as a percentage of the baseline of 55 if that's easier.)

14. How many days can you wait before intervention is truly necessary after this alarm goes off, in order to prevent risk to the patient?

15. Day 14 may be a tricky point to determine whether this patient can still tolerate a dose increase. How difficult is it now to estimate the best treatment plan? (1 = not at all difficult, 5 = very difficult)

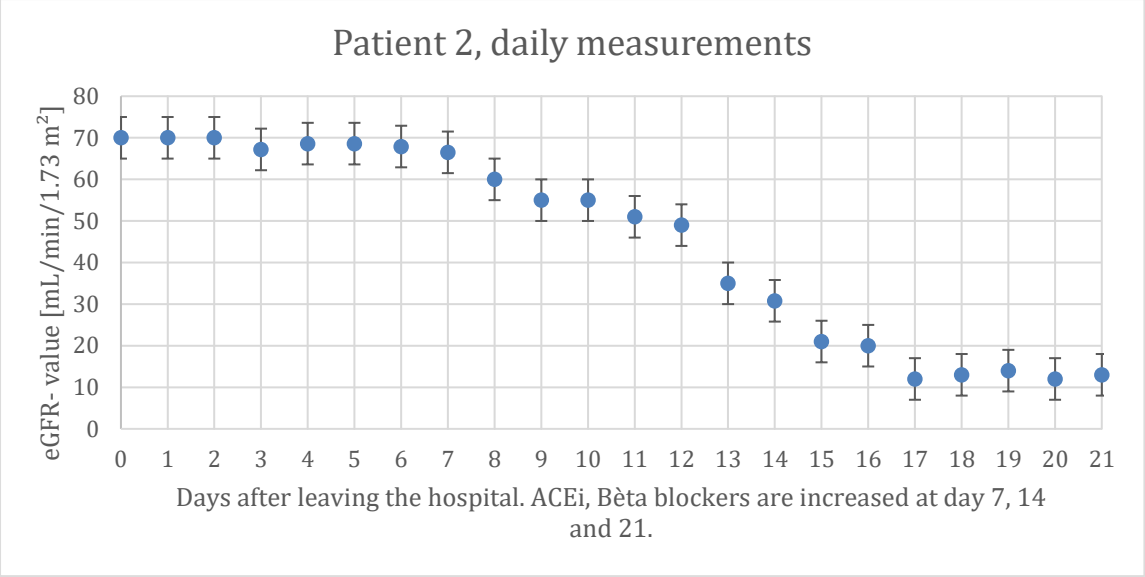
16. What would you do in this situation?

Patiënt 2



Questions for Weekly Measurements

1. Would you have taken action if you saw these data? If yes, at what point would you have intervened to modify the treatment, and what would you have done?
2. To what extent do these data help you take timely action? (1 = not at all, 5 = very well)
3. How risky is it to measure at this frequency and potentially miss an unexpected change? (1 = not at all risky, 5 = very risky)
4. How well can you distinguish, based on these data, between a temporary expected decline in kidney function and an intrinsic decline? (1 = not at all, 5 = very well)
5. Suppose you could set an alarm that triggers when a certain eGFR threshold is crossed for this patient under weekly measurement. At what value would you set this alarm? (You may also answer as a percentage of the baseline of 70 if that's easier.)
6. How many days can you wait before intervention is truly necessary after this alarm goes off, in order to prevent risk to the patient?
7. Day 14 may be a tricky point to determine whether this patient can tolerate another dose increase. How difficult is it to estimate the best treatment plan at this time? (1 = not at all difficult, 5 = very difficult)
8. What would you do in this situation?



Questions for Daily Measurements

8. Would you have taken action if you saw these data? If yes, at what point would you have intervened to modify the treatment, and what would you have done?

9. To what extent do these data help you take timely action? (1 = not at all, 5 = very well)

10. How risky is it to measure at this frequency and potentially miss an unexpected change? (1 = not at all risky, 5 = very risky)

11. How well can you distinguish, based on these data, between a temporary expected decline in kidney function and an intrinsic decline? (1 = not at all, 5 = very well)

12. Suppose you could set an alarm that triggers when a certain eGFR threshold is crossed for this patient under daily measurement. At what value would you set this alarm? (You may also answer as a percentage of the baseline of 70 if that's easier.)

13. How many days can you wait before intervention becomes truly necessary after this alarm goes off, in order to prevent risk to the patient?

14. Day 14 may be a tricky point to determine whether this patient can still tolerate a dose increase. How difficult is it now to estimate the best treatment plan? (1 = not at all difficult, 5 = very difficult)

15. What would you do in this situation?

Final Questions

1. What is the maximum interval between measurements before useful information starts to be lost?

2. How realistic do you find the data presented for these patients? (1 = unrealistic, 5 = very realistic)

3. Which parameters are essential in a decision-support system for heart failure patients?

Potassium (K^+), Sodium (Na^+), Change in creatinine concentration relative to baseline, eGFR, Weight, Patient status, Blood pressure, Heart rate; Other, namely: _____

4. Would you use a wearable sensor that measures creatinine daily to determine eGFR in a clinical setting?

5. Would you use a wearable sensor that measures creatinine daily to determine eGFR for home monitoring?

6. What would be a barrier to integrating this type of monitoring into your workflow?

7. Do you have any suggestions to improve or expand this questionnaire? Any other comments?

Appendix E: Summary of clinicians' responses to the questionnaire

Metric	Weekly Monitoring	Daily Monitoring
Median day of intervention	Day 14	Days 9–13
Confidence in timely action (mean score, 1–5)	4.0	4.3
Perceived risk of missing important changes (1–5)	3.0	1.5
Ability to distinguish temporary vs. true decline (1–5)	3.5	4.5
Alert threshold (eGFR drop from baseline)	20–50 %	20–33 %
Acceptable response time after alarm (days)	0–3	1–3
Max interval before losing critical information	7–14 days	1 day
Wearable sensor use in clinic	2 of 3 clinicians yes	3 of 3 clinicians yes
Wearable sensor use for home monitoring	3 of 3 clinicians yes	2 of 3 clinicians yes
Workflow integration concerns	Data overload; need patient-specific filtering	Data overload; need patient-specific filtering
Interest in expanded biomarkers	Potassium (K^+), others	Potassium (K^+), others

Appendix F: Combined quotes from interviews, organized by topic

1. Monitoring Frequency and Timing

Specialty	Quote
Cardiologist	"We always have those patients come back after a week to check kidney function again, because we know that medication can lower kidney function."
Cardiologist	"Every outpatient we see has kidney function…checked at least twice a year. That's only twice yearly, so we sometimes lag behind the facts."
Cardiologist	"During admission with IV diuretics, kidney function is measured every day."
Cardiologist	"If you're in the unstable protocol…you measure once a week…once you're stable it's once a month to once a year."
Cardiologist	"When a patient gets medication, you check kidney function seven to ten days later. And further it's periodically checked at follow-up…once every six months to once a year."
Cardiologist	"When we admit people and give IV medication, we basically measure every day."
Cardiologist	"Stable heart failure patients we sometimes send to the GP…we ask them to check kidney function once a year."
Cardiologist	"If you're in the unstable protocol, kidney function is checked weekly, and if you're stable it's only monthly to yearly."
Cardiologist	"When a patient gets medication, you check kidney function seven to ten days later. And further it's periodically checked…once every six months to once a year."
Cardiologist	"We adjust a pill and about two to three weeks later we draw blood to see what happens to kidney function."
Cardiologist	"Two weeks later it's 60 or 55. That's still my best 'okay' value, but you don't know if it's stable or still decreasing."
Cardiologist	"After every medication change, kidney function should be checked within 1–2 weeks; a maximum of 10% GFR loss per adjustment."
Cardiologist	"We titrate heart failure medication to target dose in two to four weeks based on survival benefit, but that can lead to acute kidney dysfunction."
Health Technology Specialist	"Vital signs…are entered by about half of the population, so we can already monitor vital signs remotely."
Health Technology Specialist	"Then we'd really like to add a kidney function test…so patients currently still have to travel to a lab…"
Nurse	"In the unstable phase…the next kidney function test often isn't for another week…so you don't have the accurate kidney function yet."

2. Biomarkers and Lab Markers Beyond Creatinine

Specialty	Quote

Cardiologist	“We do not just check creatinine and urea, but especially also the potassium level.”
Cardiologist	“Urea is an earlier sign (of dehydration). Often urea goes up first and then creatinine.”
Cardiologist	“Below a certain value, under 30, you have to adjust medication.”
Cardiologist	“If you have more than a 10–20% drop in kidney function, that’s a problem.”
Nurse	“Potassium can lead to arrhythmias…so you want potassium to stay between 3.5 and 5 mmol/L.”
Cardiologist	“For good monitoring, multiple biomarkers are essential: creatinine, potassium, sodium, phosphate, total CO_2, calcium, albumin, hemoglobin, and iron status.”
Cardiologist	“If you have more than 20% GFR-loss for your kidney function, then as a doctor you have to think if more is going on than just medication.”
Cardiologist	“If you’re in the hospital on IV meds, we measure kidney function every day.”
Cardiologist	“Three out of the four medications you prescribe affect kidney function.”
Cardiologist	“Heart failure patients now report daily weight, blood pressure, and kidney function via the Lucy app; a biosensor could automate creatinine measurements.”
Cardiologist	“There are three phases with different measurement frequencies: initiation, chronic, and acute, each with its own interval.”
Health Technology Specialist	“We’d really like to add a kidney function test…so patients now still have to go to lab.”
Cardiologist	“As long as you take those medications you have lower kidney values. But if you stop them, two or three days later values return. So it’s not damage.”

3. Medication Impact and Dose Adjustments

Specialty	Quote
Cardiologist	“Then you’re quicker to lower the dose so you can anticipate that a bit.”
Cardiologist	“We titrate to target dose in two to four weeks…but that can lead to acute kidney dysfunction.”
Cardiologist	“If you measure that continuously, you no longer need the blood draw…a continuous value is much nicer…”
Cardiologist	“If you have more than 20% drop in kidney function, then you have to consider something else beyond medication.”
Cardiologist	“If you’re in the unstable protocol, kidney function is checked weekly…if stable it’s monthly to yearly.”
Cardiologist	“Three of the four meds you give affect kidney function.”
Cardiologist	“You must use a percent deterioration of your function to create an alert.”

Health Technology Specialist	“And if people can’t discover symptoms themselves…then you still need the numbers to confirm.”
Cardiologist	“We adjust a pill then two to three weeks later draw blood to see what happens.”
Cardiologist	“Depending on how many meds the patient has…sometimes you see in two or three days a big drop in kidney function.”
Cardiologist	“Below a value under 30, you have to adjust medication.”
Cardiologist	“If you have more than a 10–20% drop in kidney function, that’s a problem.”
Cardiologist	“After every medication change, kidney function should be checked within 1–2 weeks; maximum 10% GFR loss per adjustment.”
Nurse	“In the unstable phase… they sometimes draw blood after three days though they used it only for one day…so you don’t get accurate function.”
Nurse	“Too high potassium can lead to arrhythmias…so you want potassium between 3.5 and 5 mmol/L.”
Cardiologist	“Lab draws are once a week or biweekly, so no frequent control.”

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4. Reversibility & Dynamic Nature of Changes

Specialty	Quote
Cardiologist	“As long as you take those meds you have lower kidney values. Stop them, two or three days later values return. So it’s not damage.”
Cardiologist	“As long as you take those medications you have lower kidney values. Stop them, two or three days later values return. So it’s not damage.”
Cardiologist	“If you measure that continuously, you no longer need the blood draw…a continuous value is much nicer…especially with temperature changes….”
Cardiologist	“We titrate to target dose in two to four weeks…that can lead to acute kidney dysfunction.”
Cardiologist	“Urea is an earlier sign (of dehydration). Often urea goes up first then creatinine.”

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5. Phases of Care & Protocols

Specialty	Quote
Cardiologist	“There are three phases with different measurement frequencies: initiation, chronic, and acute intercurrent problems, each with its own control interval.”
Cardiologist	“If you’re in the unstable protocol, kidney function is checked weekly…if stable it’s monthly to yearly.”
Cardiologist	“Often the cardiologist does the follow-up themselves…nefrology checks are outsourced…we titrate to target in two to four weeks….”
Cardiologist	“Stable heart failure patients…we ask the GP to check kidney function once a year.”
Cardiologist	“Two weeks later it’s 60 or 55…you don’t know if it’s stable or still decreasing.”
Nurse	“In the unstable phase…you still haven’t used that med long enough for a change to manifest, then the blood draw may be inaccurate.”

Cardiologist	“Depending on how many meds…sometimes you see a big drop over two or three days.”

6. Remote Monitoring & Telehealth

Specialty	Quote
Health Technology Specialist	“Vital signs…are entered by about half of the population…we can already monitor remotely.”
Health Technology Specialist	“…we’d really like to add kidney function…patients must still go to a draw site.”
Cardiologist	“If you measure that continuously, you no longer need the blood draw…”
Cardiologist	“Home monitoring based only on weight fails…no reliable volume estimate.”
Nurse	“Home monitoring…we pick up alerts if weight changes by 1.5 kg, but we have no clinical examination…you miss context.”
Cardiologist	“Patients report daily weight, BP, kidney function via Lucy app; a biosensor could automate creatinine.”
Cardiologist	“Remote monitoring makes care more efficient…nurses manage stable patients; cardiologists focus on acute.”
Cardiologist	“…a wearable sensor would be quite useful in hospital and at home.”
Cardiologist	“When admitted with IV meds, we measure daily…then switching to oral meds…weekly home safety visit.”

7. Workflow Impact & Staff Roles

Specialty	Quote
Cardiologist	“Often cardiologists do follow-up themselves…nefrology checks are outsourced.”
Cardiologist	“Home telemetry frees doctors to focus on acute cases; nurses cover stable patients, but it increases nurse workload.”
Cardiologist	“You need intelligent filtering…you can’t have ten thousand alarms a day.”
Nurse	“We interpret labs weekly and discuss with doctors. We don’t make decisions ourselves.”
Cardiologist	“Stable patients are sent to GP…we rely on outside lab draws which can be delayed by region.”
Cardiologist	“We monitor daily in hospital but can’t stay daily on outpatient.”
Cardiologist	“A biosensor could offload hospital visits and allow patients to self-manage some diuretic adjustments.”