

Team Results Document

BrainSense Glasgow



SensUs 23 Traumatic Brain Injury

University: University of Glasgow

Team members:

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Coaches:

N/A

Supervisor:

Julien Reboud

1. Abstract

We are happy to introduce BrainSense Glasgow's revolutionary biosensor technology, redefining the safety and performance paradigm in contact sports. Our biosensor employs a modified localised surface plasmon resonance (LSPR) mechanism, ensuring rapid and precise detection of specific biomarkers associated with traumatic brain injuries (TBIs). Uniquely, our approach combines a competitive assay with artificially-expressed sensing elements to amplify the signal from our sensor. Secondly, our sensor makes use of a minimal measurement strategy to significantly reduce costs and simplify implementation, thus leading to easy-to-use devices.

By seamlessly integrating into existing healthcare settings, our user-friendly biosensor enables contact sport teams to monitor their athletes' health regularly. Our biosensor focuses on athlete well-being and performance optimisation, therefore minimising the risk of injuries and ensuring peak athletic performance within teams.

2. Biosensor system and assay

Surface Preparation and Antibody Immobilisation

A gold surface onto which the antibodies can be placed is one of the core components of our sensor. The first step to create this surface is treating a glass slide with an APTES solution in order to provide a layer of amines that allow the gold nanoparticles to bind to the glass surface (Lyu et al., 2023; Sypabekova et al., 2023). Following treatment, a layer of gold nanoparticles must be put on the slide in order to obtain the desired wavelength of 520-535 nm (He et al., 2005; Ljungblad, 2009).

Following the layer of gold, anti-GFAP needs to be anchored to the surface of the gold in order to provide a baseline for the sensor. The anti-GFAP layer would be created by applying an even layer of the anti-GFAP to the gold, followed by a wash and dry step. Figure 1 shows the general mechanism of how the GFAP will bind to the anti-GFAP.

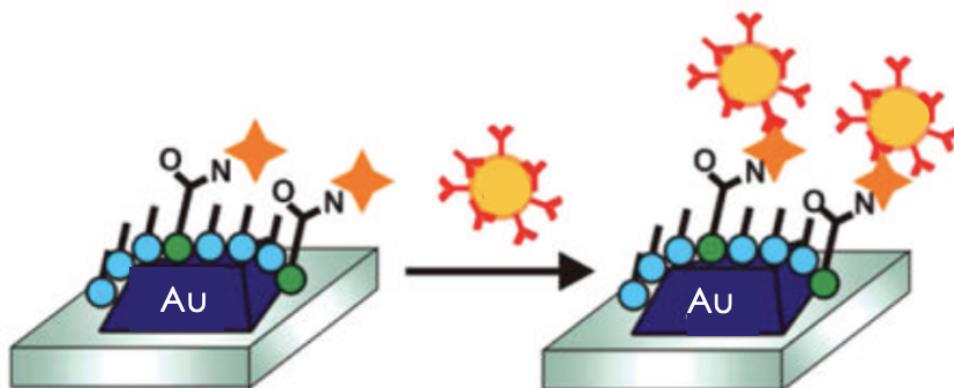


Figure 1. A schematic of antigens binding to antibodies on a gold surface. (Hall et al., 2011)

The anti-GFAP (represented by the green and blue circular units) are bound to the gold nanoparticles on the slide. The addition of the GFAP (yellow circle with red appendages) will bind to the anti-GFAP, increasing the mass on the surface, therefore resulting in an LSPR shift (Hall et al., 2011; Ljungblad, 2009). Upon confirmation that the slide is providing the correct initial wavelength, the slide is complete and ready for use within the sensor.

Reader Instrument: Compact LSPR Detector

A compact LSPR detector was made using LEDs of select dominant wavelengths (465,525 and 630 nm), And the transmittance at those wavelengths was detected by the use of a singular photodiode. By precomputing and storing an approximation of the spectrum we then match the relative shifts in amplitudes at the measured wavelengths to the change in the values of the pre-computed approximation transmittance spectra and shifting the spectra to match the expected value the shift required for the matching process is the peak-to-peak shift detected in LSPR.

3. Technological feasibility

Results of Surface Preparation

When creating the surface, the goal is to have a distinct absorption peak at the 520-535 nm mark. Figure 2 shows a microspectrophotometer graph indicating the beginnings of a peak at the desired wavelength, but nothing particularly strong.

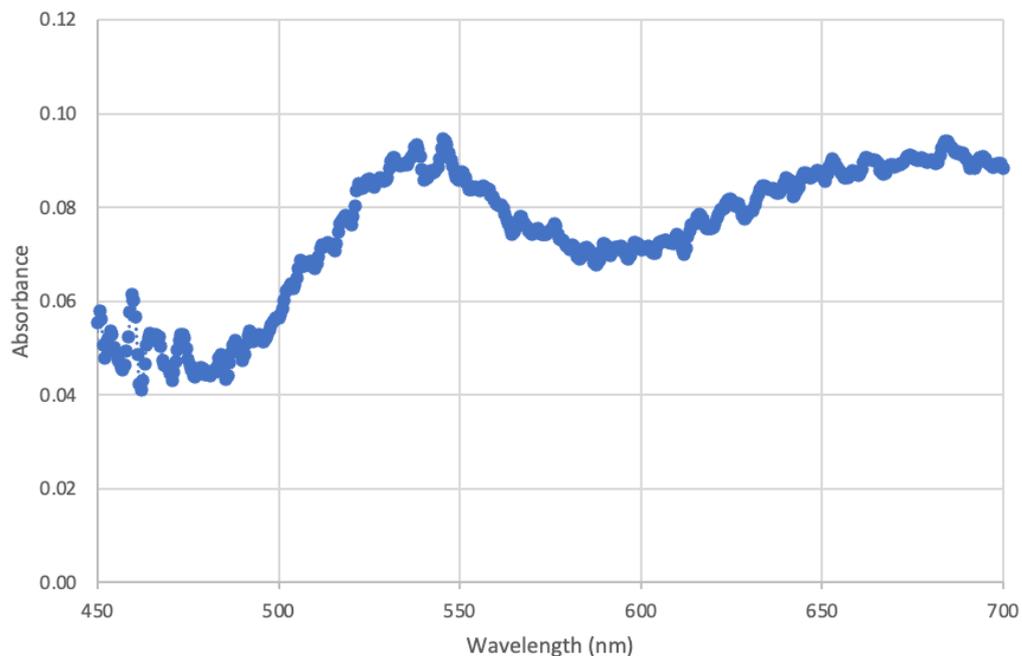


Figure 2. The microspectrophotometry graph shows a peak around 530 nm with an absorbance around 0.095.

A higher absorbance is needed for the LSPR to be successful. Therefore, the amount of

gold nanoparticles and their concentrations will need to be altered before the final product is complete.

Results of Antibody Attachment to the Surface

The current results of antibody attachment to the slides is promising. By attaching rabbit antibodies to one gold slide and leaving the other slide clear of the antibodies, we were able to apply anti-rabbit antibodies that were fluorescently tagged to both slides to determine if the antibody-gold binding was successful. Figure 3 shows that there was no binding on the slide lacking the rabbit antibodies (left), but the white dots on the slide containing the rabbit antibodies (right) indicate fluorescence expected with successful binding.

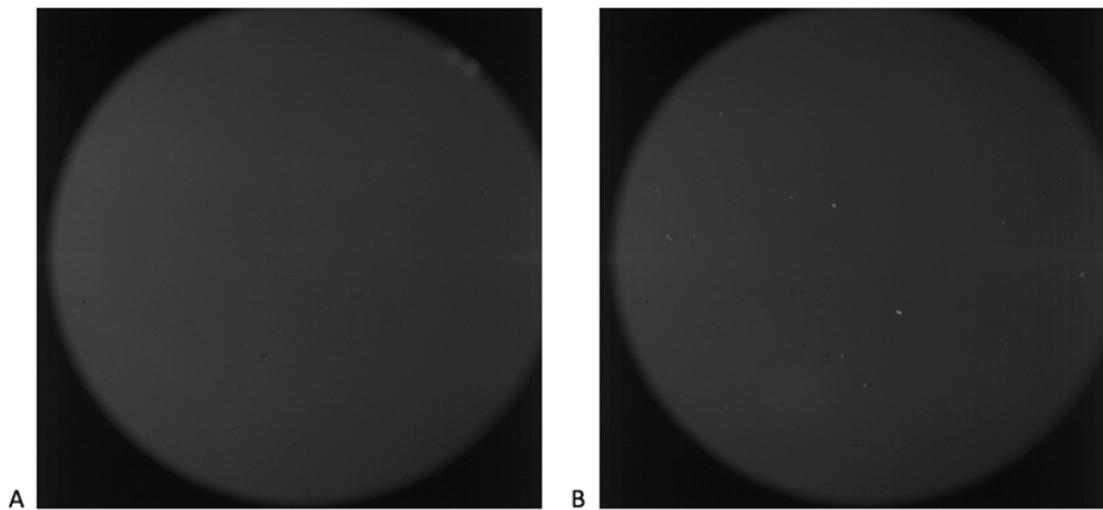


Figure 3. A comparison of glass slides shows that primary antibodies were successfully bound to gold nanoparticles as shown by the white dots indicating fluorescence (B). The negative control lacks any sort of fluorescence (A).

Results of detecting the peak shift and comparing them with the true spectrum.

The tests were conducted using Gold nanoparticles. In this context, we compare two prepared solutions: one in which the particles are highly aggregated, and another in which the particles are not, resulting in a very slight shift, as depicted in **Figure 4a**. This shift measures about 5nm.

The approximation for the subsequent wave is more intricate, involving the implementation of a Taylor series of order 500 to approximate the spectrum. Using the relative values from the sensor data, the shift was calculated to be 10nm.

This discrepancy can be elucidated by considering the true transmittance of the solutions, as presented in **Figure 4b**. Instead of relying solely on normalised values, a marked distinction in true values is evident. Unfortunately, this information becomes obscured during the preprocessing stage, as the detection method places a higher emphasis on the shift in peak compared to other factors. Nevertheless, the sensor data retains this information, and

the calculations reflect this discrepancy through an increase in the shift magnitude.

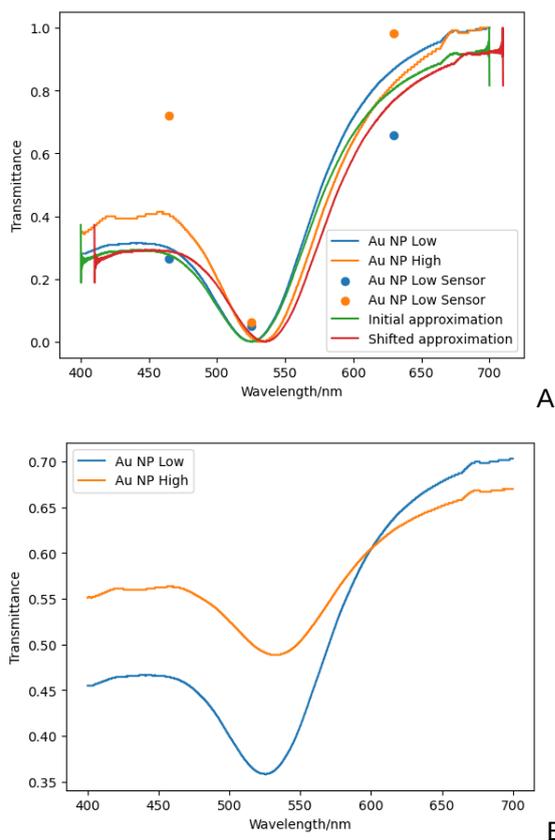


Figure 4: (A) Comparison showing the initial and final positions of the approximations and how they compare to the true shift. (B) Displaying the difference in true transmittance values of the samples.

4. Originality (max. 1 A4)

(1) Statement by the Team Captain

As the team captain of BrainSense Glasgow and on behalf of the whole team, I am excited to share the journey and innovations behind our biosensor project. Our biosensor represents a significant step forward in enhancing the safety and performance of contact sport athletes.

Novelties of the Biosensor:

Our biosensor incorporates a modified version of the LSPR mechanism, the approach makes it viable to detect shifts within a predetermined range and a known initial condition with very little realtime information enabling us to make a compact system than what the traditional instruments of the same technique offer. This sensor takes a direct sandwich assay approach on a fabricated gold surface to allow the detection to occur quickly.

Team's Contribution:

We collaborated closely to conceive the biosensor concept, acknowledging its potential to significantly impact athlete well-being. During the selection phase, we meticulously assessed various approaches proposed by team members and ultimately settled on a mechanism that was not only appropriate for development but also harmonised with each team member's unique specialisation and strengths. Throughout the development cycle, team members with diverse specialisations effectively communicated, ensuring the seamless functioning of individual sections. This open communication provided ample information for team members to adjust their development strategies in response to

advancements in other sections.

Sincerely,

Tasneem Khodair

Team Captain, BrainSense Glasgow

(2) Statement by the Supervisor

I can confirm that the team has developed their idea **completely independently**.

Some of the team members took a course on Biosensors as part of their curriculum, that I teach in. The course covers the basics of biosensing and provides examples of different sensor systems and strategies. Members of the team were thus exposed to optical sensors and sandwich assays, along with concepts of microfluidics. However I should stress that they started their work from scratch, through literature searches of possible strategies.

They realised that optical sensing is often easier/faster to implement, which guided their choices. They also realised that simplicity of implementation was extremely important to arrive at a sensor that is robust and yet easy-to-use. Given the costs and complexity associated with using antibodies in sandwich assays (which the team members coming from life sciences were very familiar with), they also decided to minimise the use of labels (which eventually could lead to a wash-free device, although this is not yet in their aims). This led them to devise the competitive assay scheme that they have presented and worked on, where the target is mimicked with an artificially-expressed fusion construct to amplify signals. This is not a scheme that I had encountered before or that the wider research group had researched.

My role was kept at an advisory level (outlining potential challenges in their strategies), as well as to guide access to existing equipment in the wider campus. The second innovation, on using partial coverage to obtain simpler measurements of spectral shift, was inspired by previous research (Reboud & Nezil, 2018 - doi: 10.1021/ac800335q) and by discussions with PhD students in co-located groups. However, I must stress that no active research is taking place in the group at the moment on these topics. All in all, I am very proud of how the team focussed on a difficult challenge and provides a workable solution.

Sincerely



Julien Reboud

5. Translation potential

Business Model Canvas

In this section, we present a comprehensive view of our business strategy through the Business Canvas Model. It serves as a dynamic framework that outlines how we intend to create, deliver, and capture value while addressing the needs of both our customers and stakeholders.

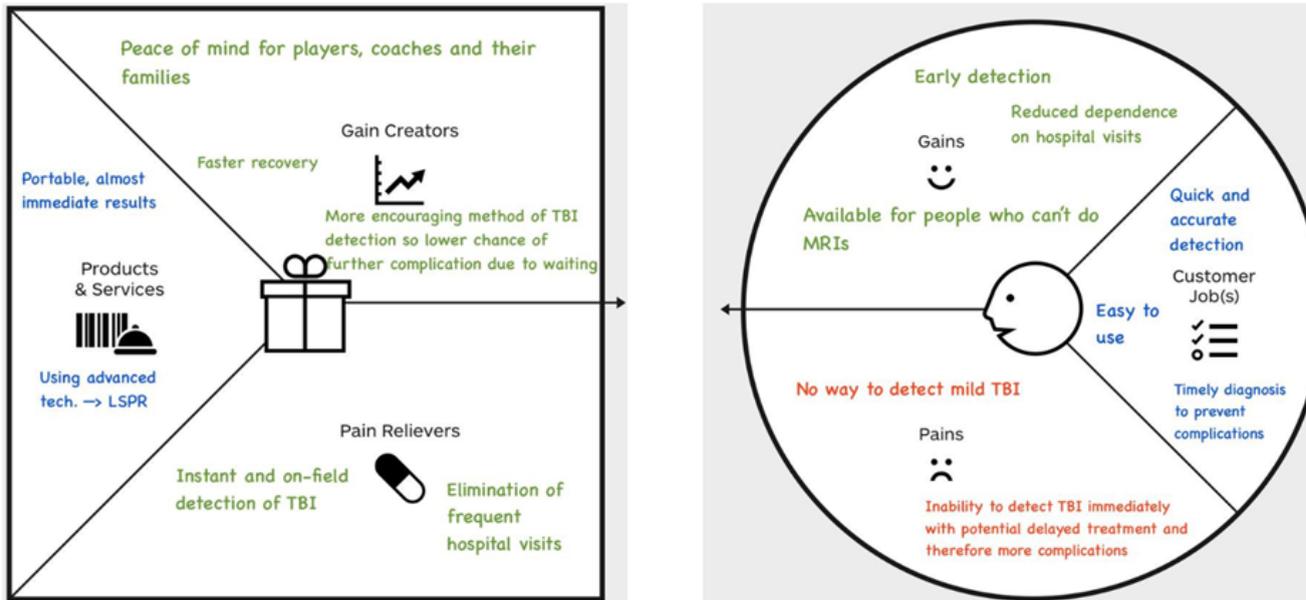


Figure 5: The Business Canvas Model of the biosensor

Overview of Validation

Interviews with the coach of the University of Glasgow rugby team and various martial art coaches outlined that:

- People playing contact sports are unaware of the detrimental effect of cumulative mild TBIs (concussions).
- Long waiting times and underestimation of the problem are the main cause for undetected TBIs of different severities.
- There is a high demand on training schedules, based on the vulnerability of the individual players.

Financial Viability

Made from readily available components:

As the components are made from readily available components it will be easier to mass produce the sensor and cost can be significantly reduced.

Easy to Adapt:

The detection mechanism is relatively easy to re-calibrate and can be used to detect other biomarkers. The relative simplicity of recalibrating the detection mechanism positions us to explore opportunities beyond our initial focus. By detecting a range of biomarkers, we enhance the versatility of our biosensor, broadening its potential market and revenue streams.

Finally, by utilising cost-efficient components and creating a flexible detection mechanism, we anticipate a positive financial trajectory. The reduced manufacturing costs and the potential expansion of applications both contribute to a promising outlook for revenue generation and overall financial sustainability.

Business Feasibility

The robust market demand for our advanced biosensor technology, as highlighted by the compelling reasons to buy – reduced hospital visits and efficient diagnosis – underscores our business's feasibility. The significant number of individuals engaged in contact sports, including players from various levels

and sport organisations, offers a substantial market volume. This wide-reaching audience forms a strong foundation for our business's sustainability and growth.

Additionally, our economic viability is supported by the potential cost savings our biosensor offers when compared to the cumulative expenses of private MRIs and medical treatments for TBIs. This cost-effectiveness not only aligns with customer preferences but also enhances our potential profitability.

Our strategic marketing approach, targeting environmentally-conscious institutions open to technological innovation, further boosts our business feasibility. By catering to sports organisations and training facilities, as well as healthcare facilities and emergency rooms, we tap into existing distribution channels, ensuring efficient product access and utilisation.

Overall, our business feasibility is grounded in the alignment of market demand, economic viability, and strategic marketing. Stakeholder desirability highlights the value our biosensor brings to athletes, sports organisations, healthcare facilities, and potential investors.

Stakeholder Desirability

Athletes and Teams: The prospect of regular health monitoring and optimised performance resonates strongly with athletes and teams, aligning with their goals of achieving peak performance while minimising health risks.

Sports Organisations and Training Facilities: These stakeholders desire tools that enhance player welfare, improve performance, and minimise the impact of injuries. Our biosensor directly addresses these desires, making it an appealing solution.

Healthcare Facilities and Emergency Rooms: The efficiency and accuracy of our biosensor align with the needs of healthcare providers. The potential to streamline diagnosis and early intervention for TBIs makes our technology desirable in medical settings.

Investors: The significant market volume, economic viability, and strategic marketing approach offer a compelling case for investors seeking promising opportunities in both technology and healthcare sectors.

6. Team and support

- **Team Supervisor:**
 - Julien Reboud: Our esteemed team supervisor, whose invaluable guidance and support have been crucial in driving our project's success.
- **Team Members:**
 - Tasneem Khodair:
 - Xinyi Shi
 - Elizabeth Wybren: Focused on chemistry needed to create the sensor surface
 - Adit Chauhan: Focused on the algorithm for detection mechanism
 - Vito Margaritondo
- **Auxiliary Support**
 - Yana Li: Provided insight and expertise in antibody behaviour in the presence of gold nanoparticles
 - Chandresh Sindal: Assisted with acquiring microscope-based data

- Andrew Philips: Supplied us with the necessary components and tools.
- Andrew Glidle: Supplied us with the necessary components and tools.
- Tao Xu: Demonstrated surface preparation techniques and provided surface chemistry knowledge.

7. Final Remarks (max. ½ A4)

We are deeply grateful for the contributions and assistance of all the individuals mentioned above, as well as any other individuals or organisations who supported our journey. Their dedication and expertise have been pivotal in our journey at SensUs 2023.

8. References (no page limitation)

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