TEAM RESULTS DOCUMENT

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1. Summary

The VanGow team has developed a highly innovative, sensitive and robust magnetic biosensor for detecting vancomycin's concentration in plasma for SensUs 2018. We have utilised the latest technology in the field of magnetic sensing, TMR (Tunnelling Magneto-Resistance). TMR detects the magnetic field created by the magnetised beads to identify the sandwich arrangement between two antibodies and a vancomycin molecule. The biosensor is concise, durable and made up of biocompatible and commonly available materials. A 2-model approach has been followed; keeping the applicability of the device in mind for both personalised and commercial healthcare. While the personalised model includes features like an app (usable in all iOS) for cloud storage and update of sensor's readings; the commercial model facilitates the uploading of the readings to the patients' electronic file and/or readout printing. Moreover, the biosensor has a multifunctional approach and is not restricted to vancomycin detection. By replacing the antibody, the antigen (vancomycin in this case) of any other disease, drug or essential biomolecule can be analysed. All these features along with a greatly attractive and non-invasive design resembling a miniaturized MRI-scan device makes our biosensor unique and proficient.

2. Biosensor system and assay

2.1. The Device

The device comprises of 4 main parts: the cartridge (and holder), the reader, the display (or readout mechanism) and the disposal system. The details of the features of each of these parts are as follows:

2.1.1. The Cartridge

- Uses widely available cling film as the surface material which is attached to laser-cut wells made of acrylic with double-sided tapes.
- Accommodates a sample volume of approximately 15-20 µL.
- Contains immobilised antibodies (capture antibodies) on the surface.
- Sample for detection is added to the wells after mixing with detection antibodies with magnetic beads attached.
- Sandwich immunoassay development carried out here.
- Is placed on a holder for ease of handling and accurate detection.
- Rack within the sensor system for convenient and safe storage of cartridges before usage.

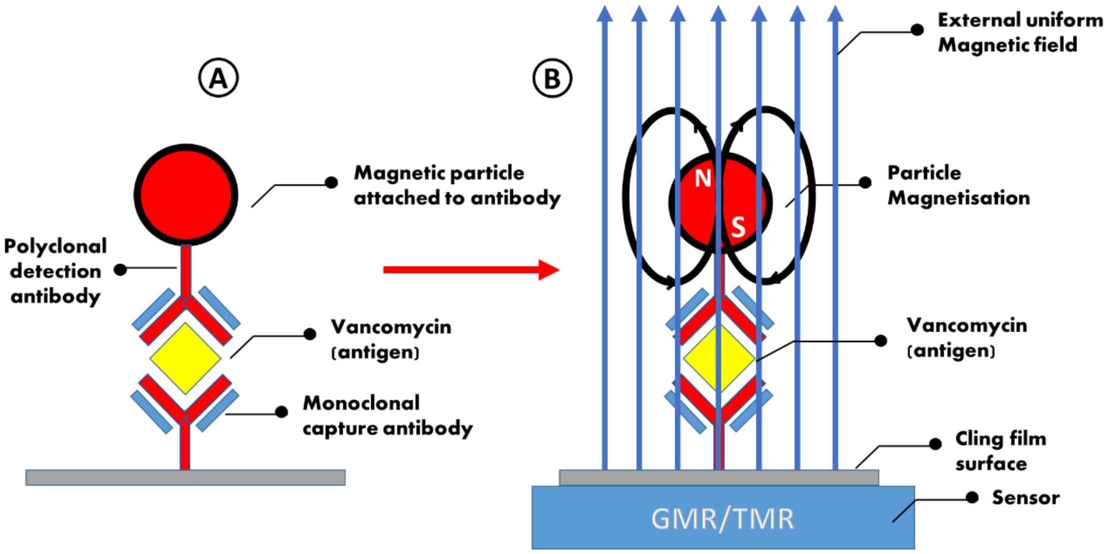

Figure 1. Bead detection methods

A. *Vancomycin immobilisation by "antibody sandwich". Polyclonal detection antibody is attached to a magnetic bead.* ***B.*** *Magnetisation of the bead and analysis of the magnetic field with a TMR sensor.*

2.1.2. The Reader

- Resembles a miniaturized MRI-scan equipment.
- Contains 1 cc magnets arranged in various directions within a circular frame to create a focused perpendicular magnetic field.
- Fabricated by 3-D printing using PLA (poly-lactic acid) polymer.
- The TMR sensor array is placed at the centre with a frame to fix the position for the cartridge placement.
- The magnetic field of the magnetic beads is enhanced in the magnetic field of the surrounding magnets which is detected by the sensor.

2.1.3. The Display

- LCD screen used for displaying results.
- The magnetic field change is converted into electrical voltage (in mV).
- Uses multi-coloured LEDs to inform user about the stage of detection being carried out.
- In-built printer for printing out results (for the commercial model).
- Results can be uploaded to patient’s electronic file (for the commercial model).
- Mobile application to obtain readout (for the personal model).

2.1.4. *The Disposal System*

- System to discard used cartridges to avoid contamination.
- Direct disposal mechanism using the cartridge holder to ensure no-touch system at all stages to prevent contamination.
- Bin capacity monitored by the sensor; auto-sealing once the fill-up limit is reached.

2.2. The Assay

The biological detection system involves a sandwich assay developed on the cartridge surface. The steps followed are:

- The monoclonal vancomycin antibody (capture antibody) is added to carbonate-bicarbonate buffer (pH 9.6) in a dilution of 1:100 and added to the to the cartridge well (15 µL) and incubated for 2 hours for optimum immobilization.
- Vancomycin polyclonal antibody (detection antibody) is biotinylated using Biotin-NHS for 2 hours followed by addition of ethanolamine and storing for 30 minutes.
- Magnetic beads (Dynal M-280) are added at a dilution of 1:20 to the biotinylated antibodies.
- Vancomycin in plasma is added to the detection antibody attached to the beads (1:1).
- The sandwich system is formed as shown in **Figure 1A**.
- The beads create a magnetic field which is amplified and detected by the reader (**Figure 1B**).

3. Analytical performance

TMR sensors change their resistance with the change of the magnetic field. Interestingly, they are only sensitive to the magnetic field changes in one axis which means that the sensor will not pick up magnetic fields that are in another axis. For example, in **Figure 2**, the direction of the Halbach magnetic field is in the z-axis while the sensor is sensitive to changes in the x-axis. Therefore, this will enable the uniform magnetic field to magnetize the magnetic beads inside the sample but not affect the sensor's detection. This setup needs to be very accurately positioned so that the sensor is in the middle of the generated Halbach field and that the field is perpendicular to the sensitivity axis.

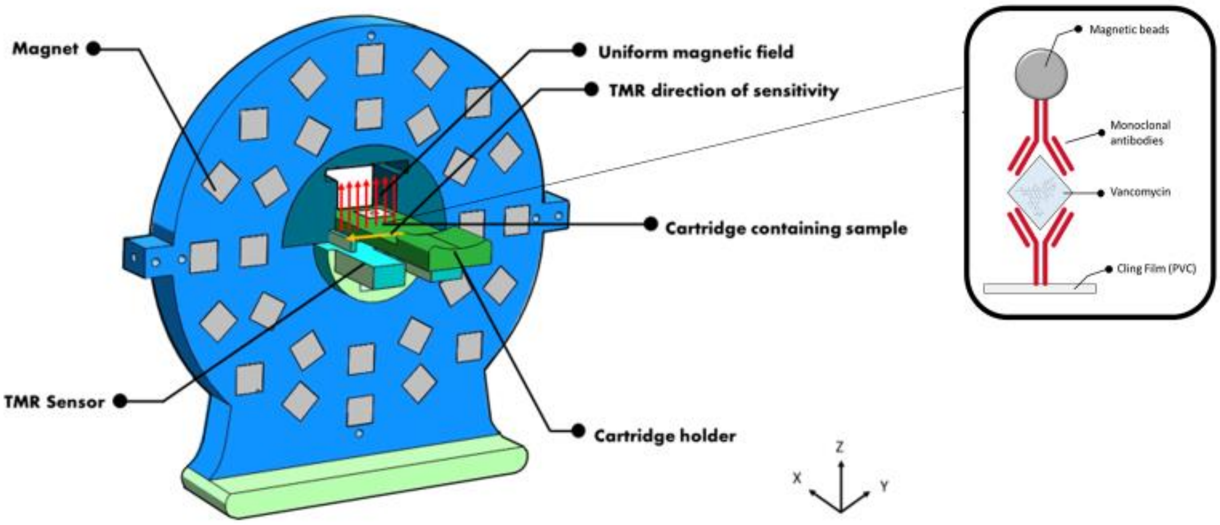

Figure 2. Biosensor structure

Functional layout of the biosensor device. The analyte-bound-immuno-beads are magnetised. The bead's magnetic field signal is read by the TMR sensor and sent for analysis.

3.1. Experimental setup

Halbach array provides the external magnetic field needed to initiate the beads magnetisation. The TMR sensor detects the fringing magnetic field of the beads and the cartridge delivers the sample with beads onto the surface of the sensor. The Arduino-PCB-LCD complex receives the data from the sensor and displays the results on the LCD screen. Finally, the battery provides the power supply required.

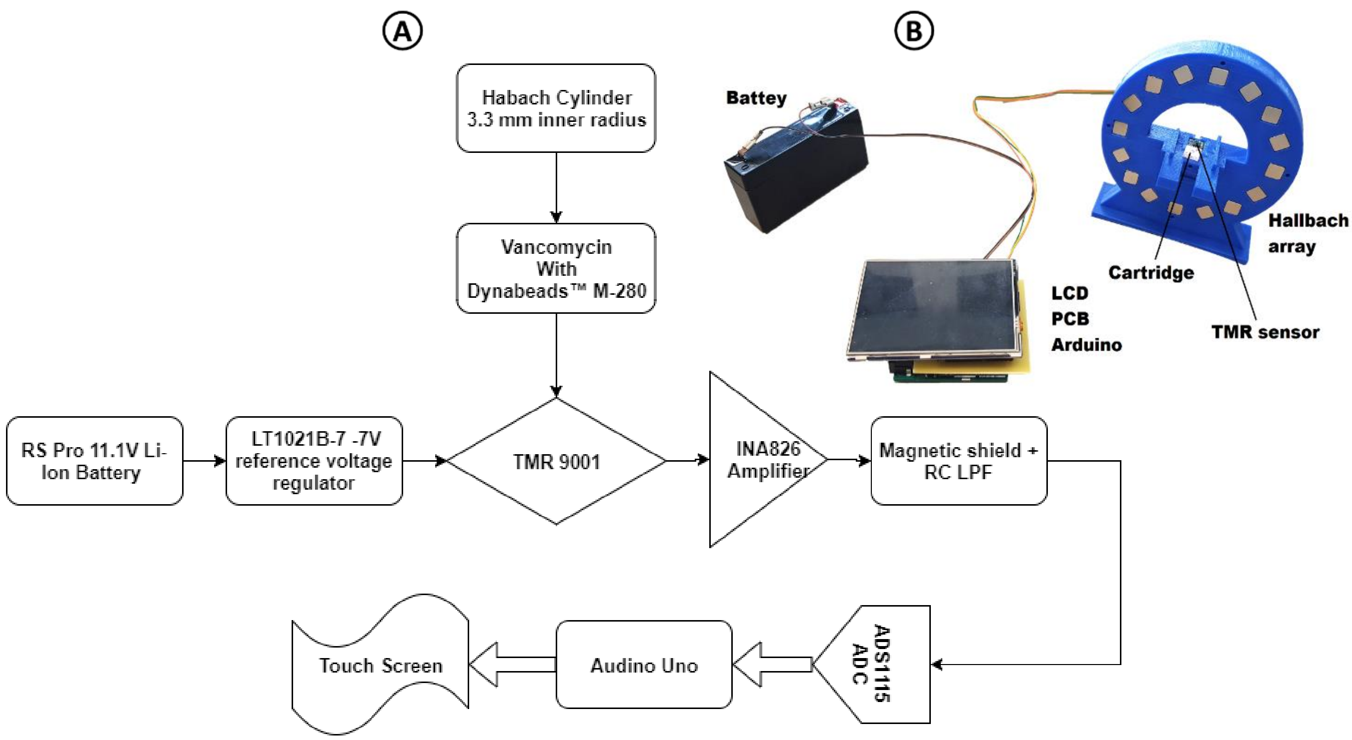

Figure 3. System structural layout

A. *Sensor mechanism flowchart.* ***B.*** *Visualisation of the flowchart components.*

3.2. Sensor signal analytical model

$$V_{out} = 0.3589 * S * V_{supply} * N * \frac{3.488 * ln(H + 4.461) - (0.01503 * H + 5.483)}{\left(1 + \frac{P + CT}{a}\right)^3}$$

An analytical model was created to calculate the output voltage of the sensor to validate the results according to the calculation.

3.3. Results

The output voltage of the sensor for different beads dilutions based on the analytical results and the experimental results. The output voltage of the sensor is linear below 20:1000 dilution of the beads and it begins to saturate after that.

The sensor output voltage for the different concentrations of vancomycin based on the experimental results. The result shows a gradual and almost linear sensor output voltage with the vancomycin concentration range. The results demonstrate that our device is a viable and reliable method for vancomycin detection and monitoring.

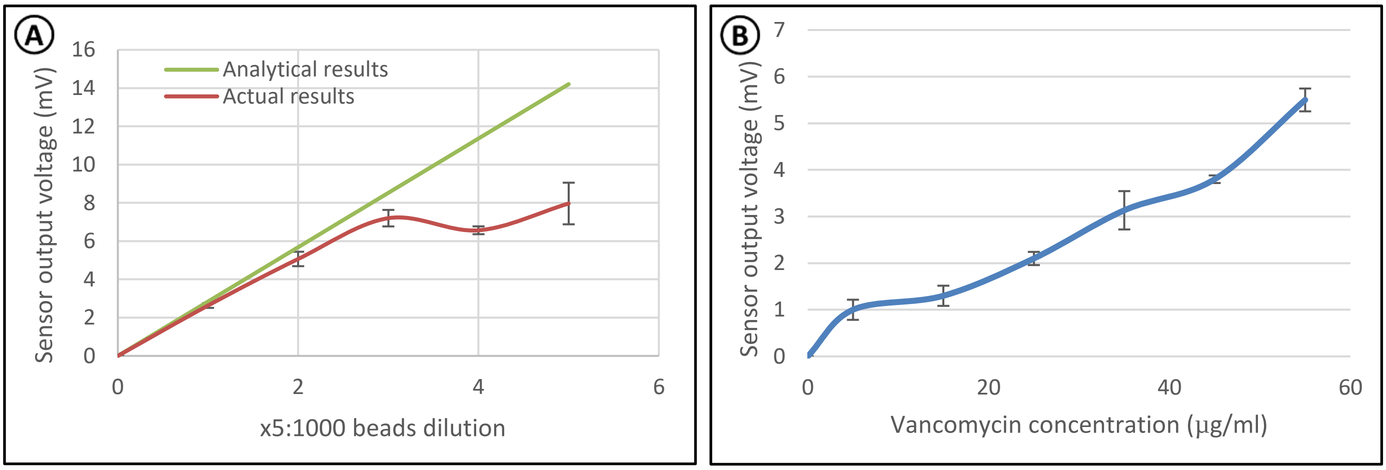

Figure 4. Biosensor performance
***A**. Device detection for varying dilutions. **B**. Device vancomycin detection.*

3.4. System specifications

Figure 5 illustrated the final device and the progress so far.

Accuracy: 89%	**Sensitivity:** 0.5 µg/ml	**Time to result:** 3 min
Precision: 97.6%	**Range of detection:** [5-55] µg/ml	**Sample volume:** 15 µl

Table 1. Device specifications results

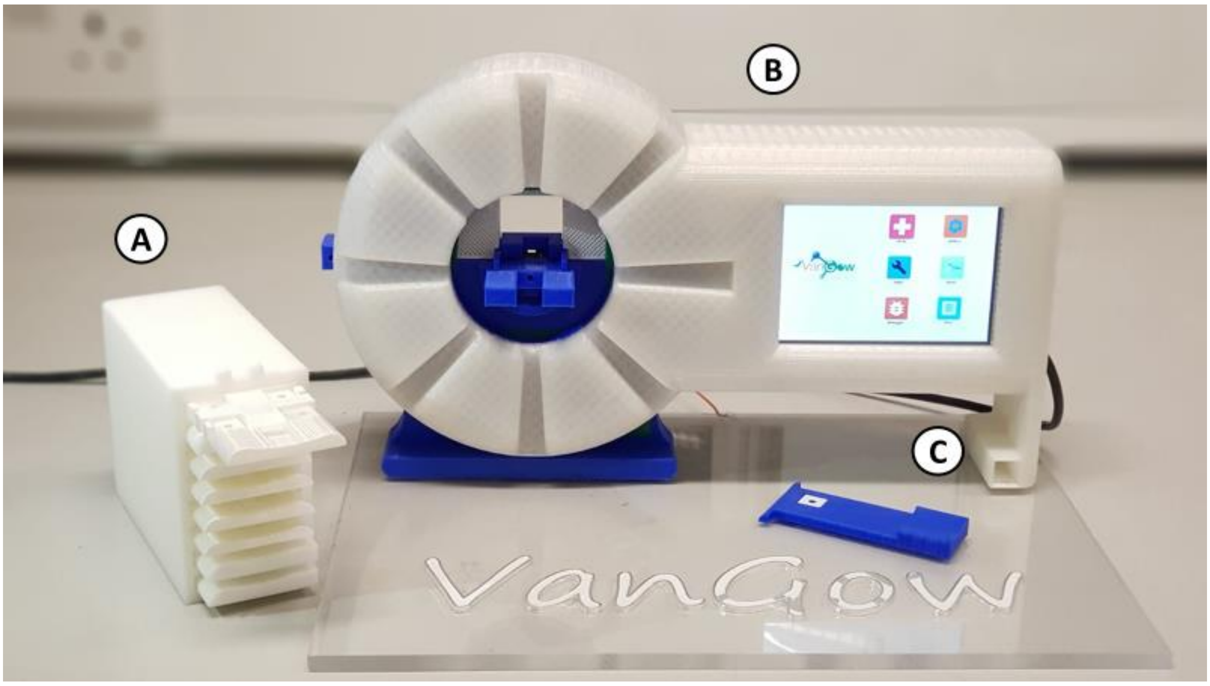

Figure 5. Final prototype built.

A. *Cartridge storage box (capacity 80 units).* ***B.*** *Main body* ***C.*** *Cartridge holder and the cartridge*

4. Novelty and creativity

4.1. Already available

We have based our design on TMR (Tunnelling magnetoresistance)-based biosensors which are the state-of-the-art technologies in the field of magnetic sensing boasting the highest sensitivity so far. TMR sensors are built from two ferromagnetic and one conductive layer. One of the ferromagnetic layers has a permeant pole direction and the other can align itself with the external field. This changes the measured resistance of the sensor (Fermon, 2013) which is six times more sensitive than the previously developed GMR (Giant magnetoresistance)-based technology and 20 times higher than AMR (Anisotropic magnetoresistance)-based biosensors (Brzeska, 2004; Tsukakoshi, 2017). Multi Dimension Technologies (MDT), a leading supplier of TMR and GMR sensors worldwide, kindly provided us five TMR sensors with a market value of 6,000$. Unlike some fluorescent and chromogenic labels magnetic beads are cheaper and can be used as labels for a wide variety of substances due to their non-selective nature (Schotter et al., 2004; Zhan et al., 2017). The beads help analyse a sandwich immunoassay-based system which involves the use of two antibodies: a capture antibody immobilized on the surface and a detection antibody to which the label is attached. Immunoassays have been used for detecting vancomycin levels in protein-rich samples previously. (Odekerken et al., 2015).

4.2. New developments

4.2.1. Cartridge innovation

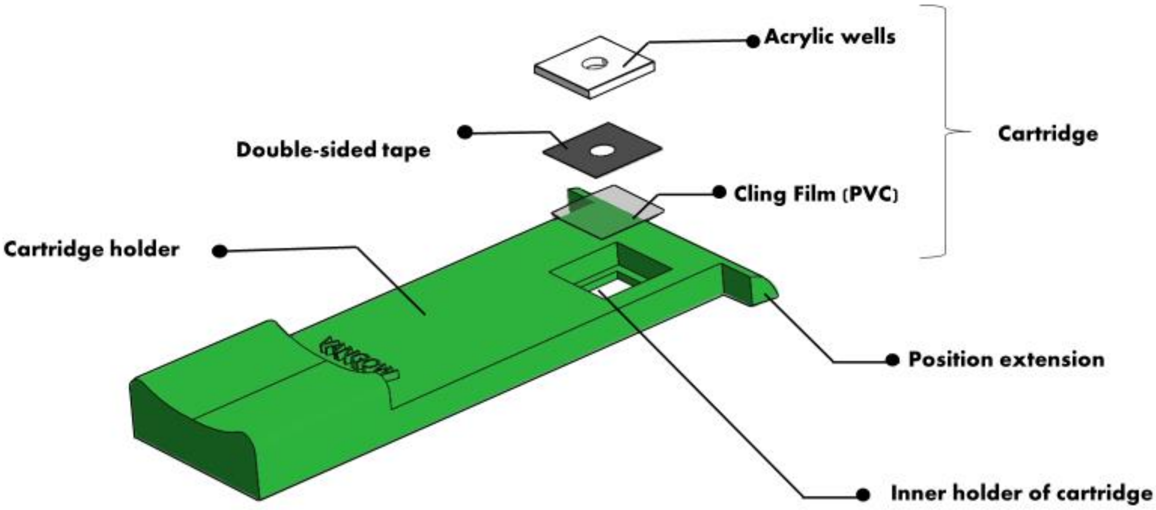

Figure 6. Cartridge and holder.
Structural components and innovation in cartridge and holder design.

- **Facilitating reusability -** Previous magnetic biosensors were coated with immobilised antibodies for detection. The usage of a cartridge coated with the stated antibodies ensures that the sensor can be used for a multiple number of tests.
- **Enabling sample variety -** Due to the sensor's surface not being coated, the sensor can be used to detect multiple analytes by using a variety of cartridges coated with other antibodies.
- **Cling film surface -** Commercially available cling film is used as the surface of the cartridge which ensures a cheap and easy method of fabrication. This material contains PVC (polyvinyl chloride) which has been used for other biotest equipment like ELISA plates.
- **Acyclic wells -** High-precision laser-cut wells, costumed designed for enabling micro-volume testing.
- **Double-sided tape -** Easily available; strong and durable attachment, makes the manufacture process

4.2.2. Storage and handling

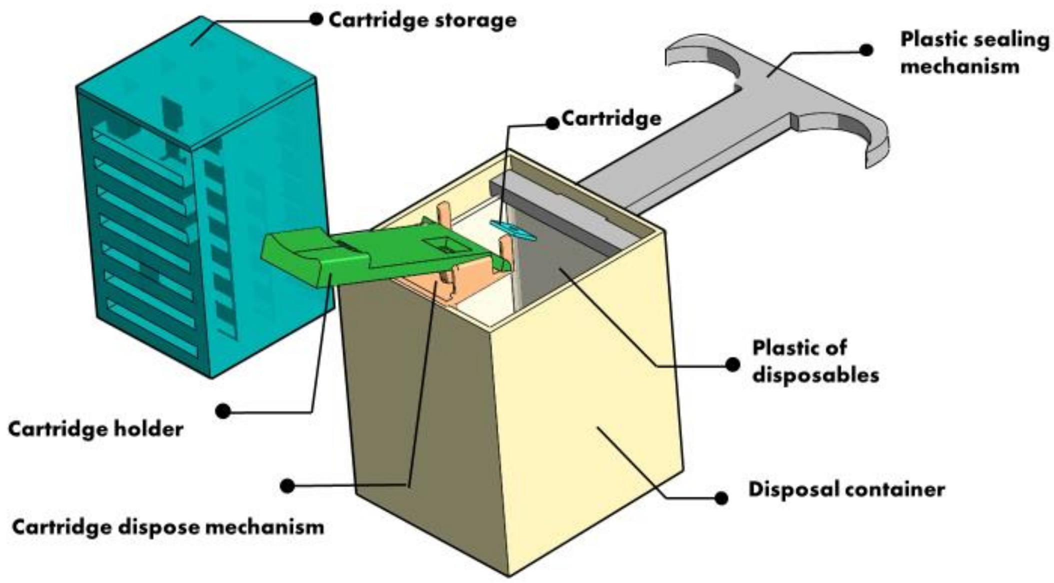

Figure 7. Storage and disposal

Cartridge storage and disposal system for minimal contamination and safety improvement

- **Cartridge storage safety -** The cartridge storage system prevents the samples from getting contaminated by placing them in a sheltered environment.
- **Cartridge storage capacity -** The cartridge storage system can store up to 80 samples in one cartridge box. While one box may be used to store to-be-processed samples, another box can be used to keep tested samples for future measurements.
- **Easy handling -** The cartridge holder enables an easy handling of small cartridges; preventing spillage, interference by contaminants and accurate positioning of the cartridge for precise and repeatable sensor-detection in the device.
- **Safe disposal -** Non-contact disposal system which uses a needle-like mechanism to drop the cartridge into the bin after being tested. The bin uses an auto-sealed mechanism using plastic bags, preventing the user to have any contact with the inner parts of the bin. IR sensors imbedded in the system will detect the capacity of the bin. If the bin has over-reached its capacity, a signal will be sent preventing the device from accepting new samples to be tested.

4.2.3. Sensing device

- **Calibration -** The cartridge allows the sensor to be reused. As such, there is no need to keep a regular calibration between samples. Although regular calibration is not required, 10 calibration samples are provided for higher accuracy and ease of troubleshooting.

- **Robust system -** The device contains a second sensor which will check if all components are functioning correctly and self-calibrate the device if needed.
- **Nivel sensor -** First time use of a TMR sensor in a healthcare diagnostics application.
- **Diversity -** The magnetic sensor system detects the magnetics beads and not the analyte directly. Therefore, the usage of the device is not limited to vancomycin only.
- **Auto-washing system -** The magnetic field inside the halbach array has an overall magnetic field in an upward direction which pulls non-specifically bound beads away from the sensor enabling the detection of only analyte-bound beads. The magnetic field is not too strong to overcome the biological binding of the analyte-bound beads, hence only non-bound beads would be removed without the need of additional washing.

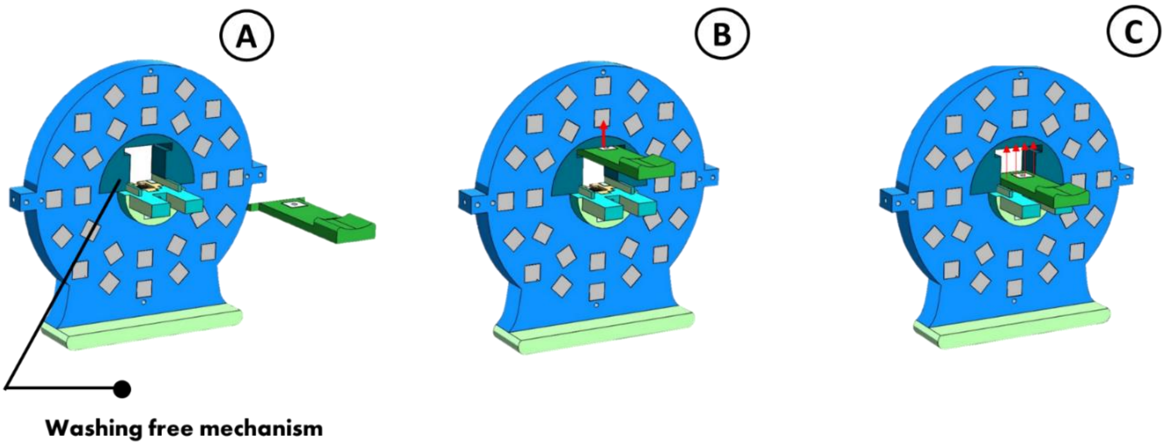

Figure 8. Magnetic wash mechanism.

A. *Cartridge holder insertion.* ***B.*** *Non-specific bead-analyte binding is removed.* ***C.*** *Bound bead's magnetic field signal is sensed by TMR.*

5. Translation potential

5.1. Stakeholder desirability

Despite the availability of clinical practice guidelines (CPGs) for therapeutic drug monitoring (TDM) of vancomycin, vancomycin serum concentrations still do not fall under the therapeutic concentration threshold in many patients (Zhi-kang, 2014). This is due to the narrow therapeutic margin of vancomycin and the inter-individual variability threating the patient's health and increasing the antibiotic resistance.

5.1.1 Patients:

Our biosensor grants safety and efficiency for vancomycin-treated patients allowing full monitoring during the administration process. It is a point-of-care testing device that gives a new perspective on vancomycin blood measurements with a cheaper, faster and easy method. Currently, vancomycin blood levels are measured using big analysers available in large healthcare institutions, hospitals or private laboratories. Small healthcare institutions cannot afford the cost related to this equipment. Therefore, it increases the risk of ineffective treatment, antibiotic resistance and the development of side effects.

5.1.2 Medical practitioners:

Clinical practice in small and mid-size hospitals are required to ship the patients' samples to specialized laboratories. This leads to a high cost and time wait. Hence, clinicians (especially in the developing world) are unable to access those practices and switch to other drug prescriptions (Gastli, 2018). Furthermore, in large hospitals in developed countries, clinicians need a “real-time monitoring system" to measure vancomycin blood concentrations (Manjunath, 2014), as currently, biologists perform tests in clusters causing considerable delays for the patients' diagnostics (Gargouri, 2018). These analysers are also unable to detect higher concentration (over 50ug/L) and push biologists to perform dilutions rising the cost and time waste.

- Gain creators

  ↑ The device ensures accurate and quick measurements

  ↑ The device is handheld, easy to use and individual measurement available in the bedside of the patient

  ↑ Device includes option of uploading the results to the patient's electronic file or printed and attached to reports

- Pains and pain relievers

  ↓ Small and single use cartridges can lead to complexity and confusion, to counter this issue we have the cartridge holder which makes handling and storage of the cartridges very easy.

5.1.3 Hospital management:

Monitoring serum concentrations requires a lengthy process starting with the authorized orders, collecting and processing of blood samples, reporting and analysing results, and finally document recommendations. The use of time for these purposes is associated with opportunity costs (Meghan, 2017). Many issues arise during this process from the conservation and blood transport to time consumption and high related costs. Hospital and laboratory regulations should also be considered (how and when they receive the samples).

- Gain creators

  ↑ One sample measured at a time so no need to wait for batches and patient-focus can be increased

↑ Compact and can be easily moved around. Can be taken to patient's bedside and measurements done

↑ Multi-utility device so it can be used for detecting more than one type of analyte by replacing with different antibodies

- Pains and pain relievers

  ↓ Does not allow multi-testing simultaneously which can be time consuming, but each analysis takes less time as the cartridge holder fixes the cartridge exactly on top of the sensor to show immediate results

  ↓ Too many samples can create confusion due to small size, for this we have the storage box which has different racks and samples can be arranged accordingly and then tested one after the other. (Vicky, 2018)

5.1.4 Insurance companies:

- By effectively monitoring the vancomycin administration, insurances companies will significantly decrease the side effect incidence. Many authors have shown an incremental risk of neph-rotoxicity associated with higher VCM doses, ranging from 12 to 42.7 % of patients (cataldo,2012).
- Decrease the length of hospital stay (Jeffres, 2017)

Our biosensor overcomes most of the challenges presented by ensuring a quick and accurate measurement. The device has an 89% accuracy with a 3-minute response time, speeding up the process. Instant measurement of vancomycin blood levels will enable the healthcare practitioners to monitor and adjust the posology in real-time, if needed. This flexibility will give more patient security with an emphasis in early stages of treatment when the organism response to vancomycin is still unpredictable.

5.2. Technical feasibility

In the prototype development phase, feedback form researchers, specialists and companies were taken into consideration for further improvement of the product. Some key points that were mentioned are as follows:

- Cartridge safety and contamination prevention needed
- Sample storage and Disposal system necessary
- Device robustness is required. In hospitals medical equipment are displaced constantly and therefore, can be damaged in the process. For a biosensor that is

portable like the one in this research the device should be strong enough not to be damaged easily.

- Biology robustness: the biological components should not be affected by the environment. E.g. temperature or fluid PH.
- The device should have minimum noise. E.g. the biosensor can be used in a room close to an MRI machine. The coils used in the MRI machine can affect the Halbach array therefore, adding noise to the signal or even disrupting all readings.
- The components should have a minimum number of sharp edges and should be easy to wipe with a cloth for cleaning purposes.
- The color of the components should be such that any contamination is easily detectable for this reason white and light green are usually preferred e.g. red is not a good color as blood contamination is difficult to spot
- The device should be user friendly.
- Mobile apps are currently not an option for usage in hospitals but can be an option for the device to be implemented in homes. (personalized care)
- System calibration should be dealt with.
- Device components should be easy and cheap to mass produce.

The current prototype is very close to the final version of the product, several parameter optimisations have been made to achieve best setup for the prototype. Due to the accessibility of all components in the market and the use of mass manufacture techniques like molding, the production process is straight forward. Furthermore, many challenges to reach mass production have been addressed e.g. heat and pressure implantation on the cartridge surface for bubble reduction and folding issues. The current prototype developed has been able to overcome many technical aspects and is the 5th prototype built with constant improvement, therefore the current prototype is very close to becoming a commercial product. Our unique selling point lies on the use of materials which are commonly available and simple to manufacture, design and assemble. For example, the cling film in the cartridge surface which is widely used for food packaging. Moreover, we have developed an easy to manufacture biocompatible cartridge. Once used, the cartridge is disposed of in an innovative disposal system using a sample holder. Furthermore, a unique and user-friendly user interface has been built. The interface can store, display and send data. It can also be used for calibration and troubleshooting of the device. Due to different requirement from costumers around the world, we have developed three modular read out systems, LCD/Touch screen, mobile app and paper printouts, which can be add according to the need of the customers. The main market for different readout devices has been mentioned below:
Paper printing: Developing countries
LCD/Touch screen: Developed countries
Mobile app: for personalized healthcare/home care in developed countries

➢ The route to market diagram has been shown below

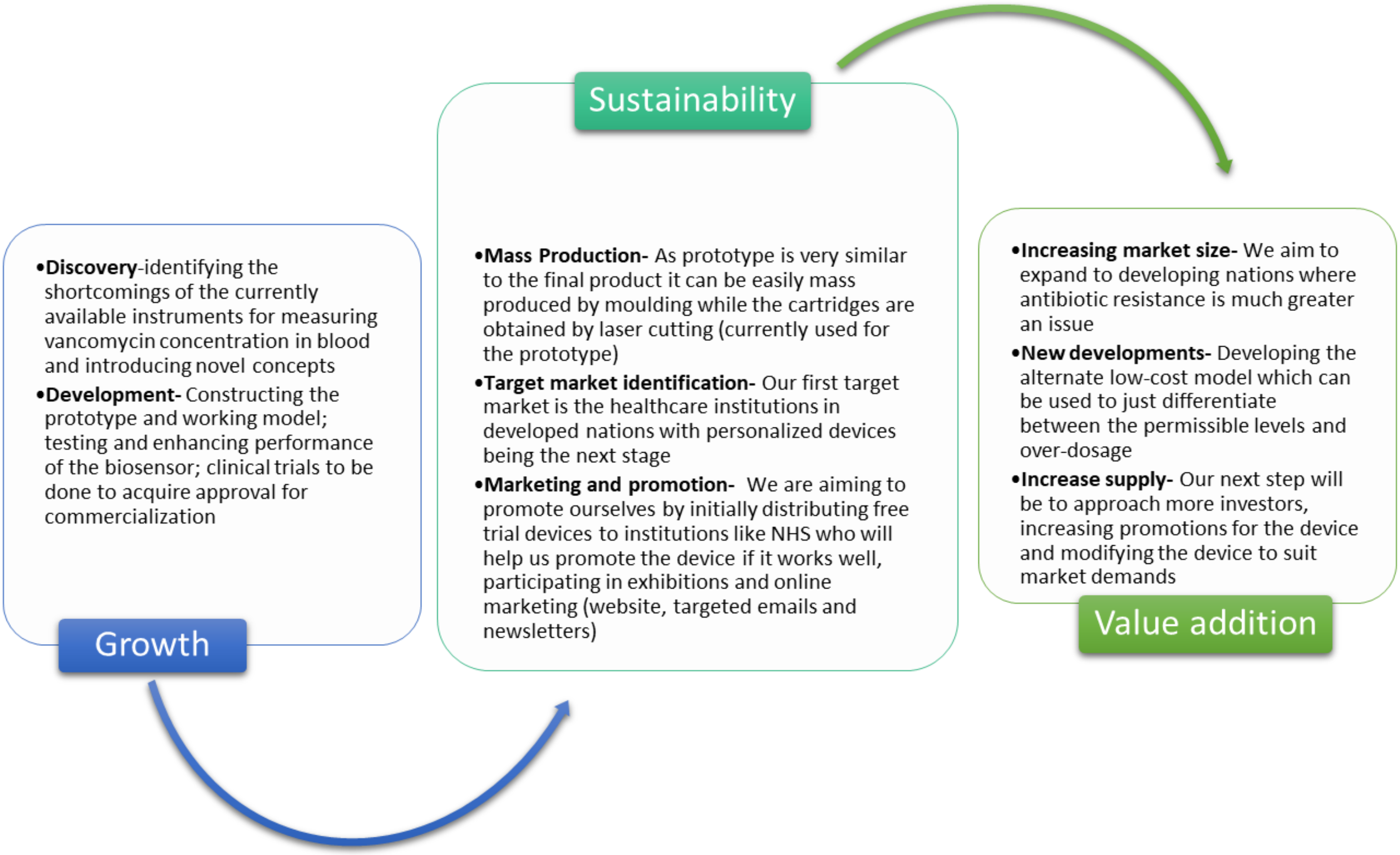

Figure 9. Route to market diagram

5.3. Business Viability

The initial cost of our first analyser prototype is 1300 $. This is mainly due to the high cost of the TMR sensor which was specifically designed for this purpose (appendix 7). The cartridge cost is about 0.1 $ per unit. However, after consulting our sponsors we estimated the total production cost of the device for 2000 units to be around 350$. After analysing the market and consulting some experts in the medical device industry, we have decided to sell our analyser instrument slightly higher than the produced cost at 500$. This will generate additional revenues besides the main income of the company obtained from the cartridges sales. The cartridge price will be fixed at 1$ per test. Details of the expected costs and revenues are described in the appendix 8.

Vancomycin therapeutic drug monitoring costs $109 which was estimated by including the cost of phlebotomy ($40 per draw) and cost of vancomycin trough measurement $69 per concentration measurement (Suryadevara, 2012). Our main competitors (Abott, Roche and

Siemens) price range of the kit (cartridge) is between 1.5 $ and 2 $ per test. Hence, we truly believe that our product can compete in this market bringing added value with a cheaper price.

The last published statistics about the use of vancomycin reported a yearly usage of 13000 injectable vancomycin units in 1998 in the US and major European countries (Herbert, 1998). Following the slow increase of usage of vancomycin in the last years we aim to achieve a target sale of 2000 device by the third year. Our business model will be based on medical device distributors and we already start negotiations with some partners to test and promote our product (e.g. MACE: Medical Auto Control Equipment).

We also supposed that the vancomycin monitoring market trends will follow the overall antibiotic drug monitoring market with a growth of 2.5%.

6. Team and support

6.1. Contributions of the team members

- Engineering team: Amin Rigi, Abdul Wadood Tadbier and Nuha Irshad.
- Business and marketing: Debjita Mukherjee, Amin Rigi, Marc Vives Enrich, Anouar Chamakhi.
- Biology and chemistry: Debjita Mukherjee and Oluwasegun Aro
- Outreach and biomedical advisor: Marc Vives Enrich

6.2. People who have given support

- We would like to thank the following people for their support, advice and mentorship.
  - ✓ Abdul Hadi Chibli, University of Glasgow – PCB and additional help to team members.
  - ✓ Huckleberry hopper University of Glasgow- for his supporting the business financial part
  - ✓ Dr. Gargouri Mahmoud, Resident biologist from the hospital René Debret, Paris
  - ✓ Dr. Gastli Mondher, Private practice specialist in infectious diseases
  - ✓ Dr. Chouchene Farhat Clinical pharmacist in Hospital Farhat Hached-Tunisia-Sousse.
  - ✓ Dr. Oluwasegun, General practitioner from Nigeria
  - ✓ Vicky Copper, Nurse in the NHS Scotland

- ✓ Salah Zied Business consultant specialist from Alira health
- ✓ Dr Ahmed Rigi, General practitioner, provided clinical information and consultancy.
- ✓ Madame Ghalloussi Monia, CEO of MACE (Medical Auto Control Equipment), medical device distributor company
- ✓ Brian Robb, University of Glasgow, for technical support and access to equipment and facilities at the university.
- ✓ Jesper Svenning Kristensen, Principal R&D Engineer, Medtronic ltd.
- ✓ Carolien Oppeneer, Business Manager, Cbusinez ltd.

6.3. Sponsors

- **MultiDimension Technology (MDT):** http://multidimensiontech.com/
  A leading supplier of GMR and TMR sensors, provided us with several TMR sensors and are willing to support us to take our product to the market. MDT provided $6000 of products to our team along with advice on how to best use their products.

- **Vivomotion:** https://www.vivomotion.co.uk/
  Consultancy on how to produce animated videos.

- **EM Works:** https://www.emworks.com/
  They have provided us with free software for electromagnetic simulation of our system

- **University of Glasgow:** https://www.gla.ac.uk/
  Support facilities and feedback, leading to the improvement of the device and the project overall.

- **SMedical:** http://www.smedical.com/en/home-2/
  Consultancy on medical device market research information and marketing design strategy.

- **Medtronic:** http://www.medtronic.com/uk-en/index.html
  Consultancy on product development.

- **CbusineZ:** http://www.cbusinez.nl/
  Consultancy on how to develop our concept into a business and get it into the market.

- **EIT Health:** https://www.eithealth.eu/
  Provided with funding for the development of the device.

- **Sirotics:** http://sirotics.com/
  Provided 3d printing service and product consultancy.

- **Micronit:** https://www.micronit.com/
  Consultancy on magnetic beads and biological detection systems.

- **Said Foundation:** https://www.saidfoundation.org/
  Promotion of our team.

- **IIE:** https://www.iie.org/
  Promotion of our team.

- **MACE (Medical Auto Control Equipement):** http://www.autocontrol.com/
  Commercialization of the product

- **Alira Health:** https://www.alirahealth.com/
  Business consulting

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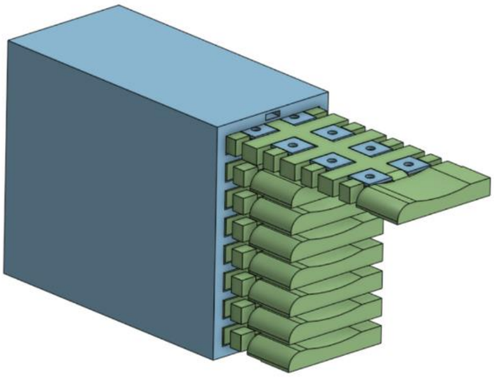
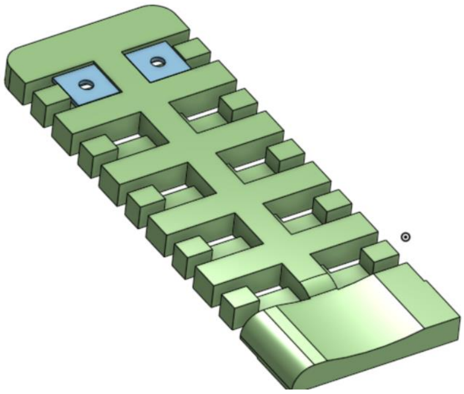
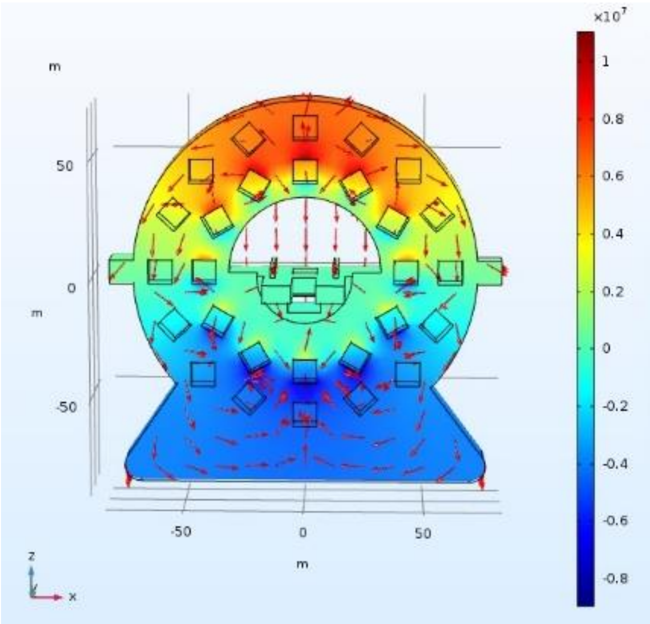
8. Appendix

8.1.Appendix1



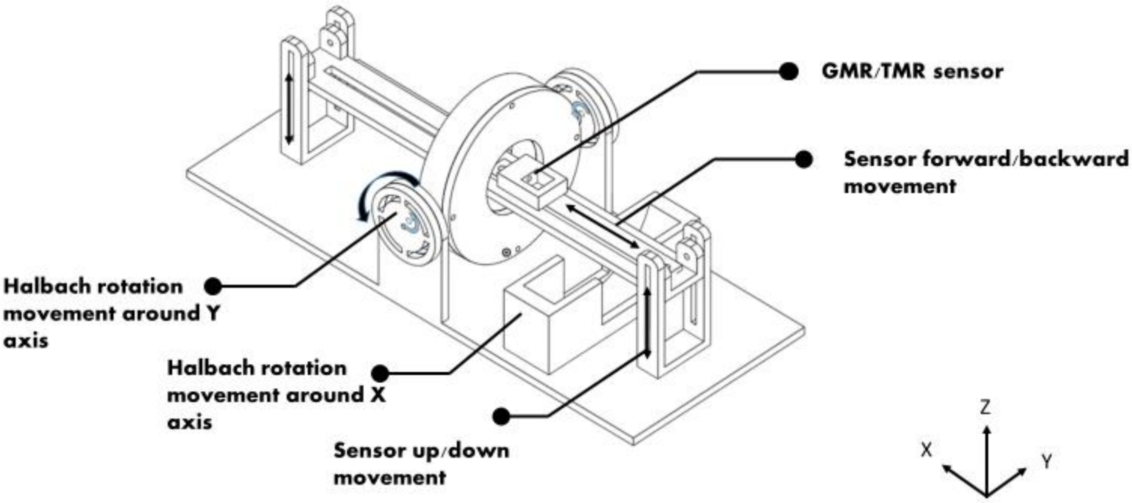


8.2 Appendix2



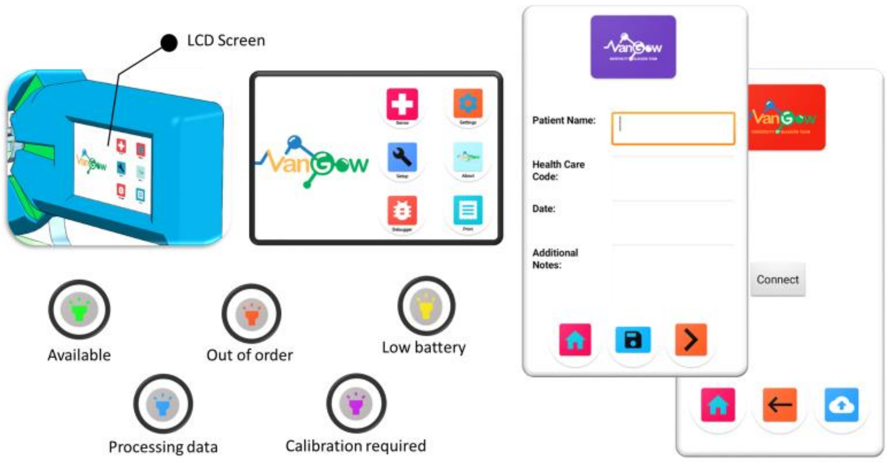
Magnetic field simulation for Halbach uniform field generation in COMSOL

8.3 Appendix3



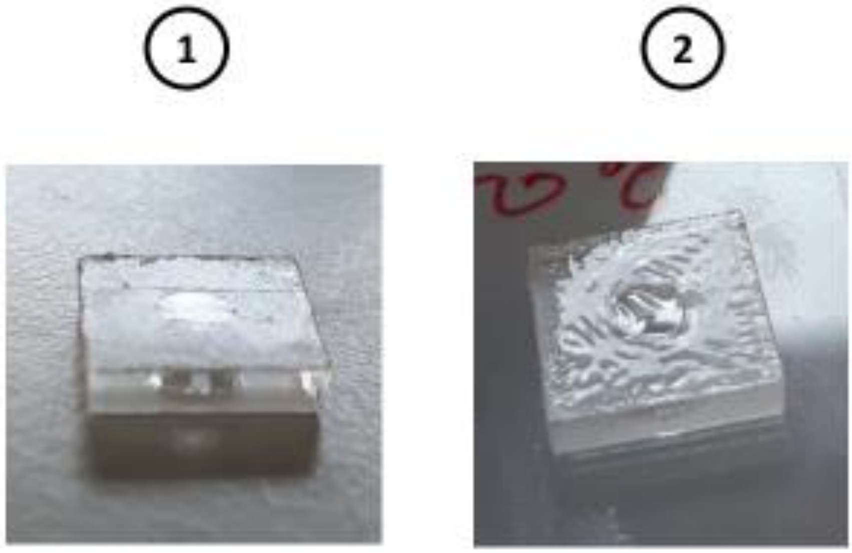
Test structure for accurate positioning of sensors and Halbach array

8.4 Appendix4

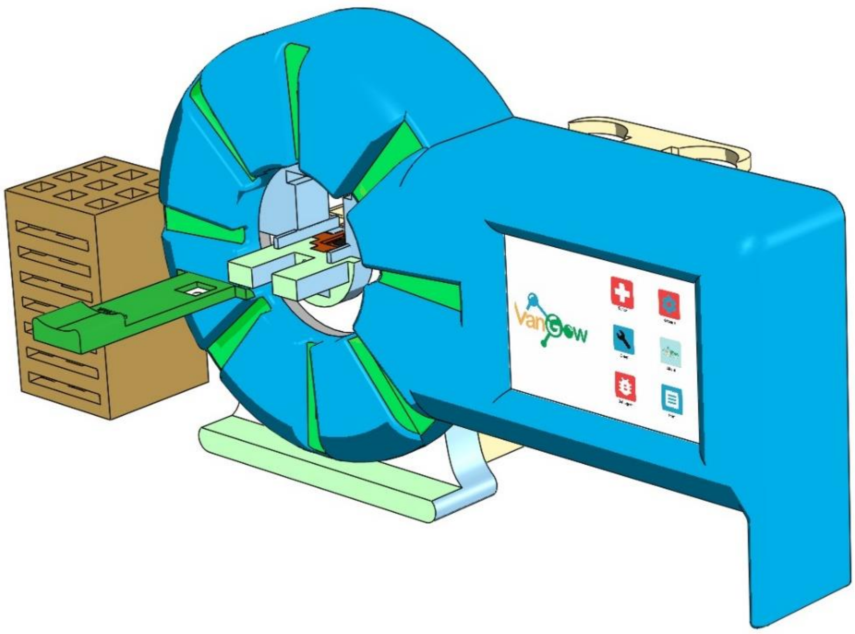


User interface for LCD and app

8.5 Appendix 5



8.6 Appendix 6



8.7 Appendix 7

VANGOW COST BENEFIT ANALYSIS

COMPANY NAME	VANGOW	DATE CONDUCTE	
PROPOSED PRODUCT/INITIA	Biosensor for detection of Vancomyin concentration in hum	COMPLETED BY	

QUANTITATIVE ANALYSIS	YEAR 1	YEAR 2	YEAR 3	YEAR 4	YEAR 5	TOTAL
Research and Development						
Prototype development (3D printin	$ 45,000.00	$ 50,000.00	$ 10,000.00	$ 10,000.00	$ 10,000.00	$ 125,000.00
Magnetic sensing (Halbach array,	$ 9,000.00	$ 15,000.00	$ 16,000.00	$ 18,000.00	$ 18,000.00	$ 76,000.00
Cartridge (Cling film, Acrylic)	$ 2,000.00	$ 4,000.00	$ 5,000.00	$ 5,500.00	$ 6,500.00	$ 23,000.00
Biological Assay (antibodies, buffe	$ 4,500.00	$ 6,000.00	$ 8,000.00	$ 9,500.00	$ 11,000.00	$ 39,000.00
Reading system (LCD, Printer, blue	$ 200.00	$ 2,000.00	$ 2,500.00	$ 2,500.00	$ 2,500.00	$ 9,700.00
Storage/Disposal system	$ 1,000.00	$ 100.00	$ 200.00	$ 250.00	$ 250.00	$ 1,800.00
Additional equipment/ costs (meas	$ 45,000.00	$ 25,000.00	$ 1,200.00	$ 1,200.00	$ 1,200.00	$ 73,600.00
Software (CAD design e.g. Solidwo	$ 8,000.00	$ 1,500.00	$ 1,500.00	$ 1,500.00	$ 1,500.00	$ 14,000.00
Production	**UNITS**	**20**	**2000**	**5000**	**9000**	**13000**
Mold build (cartridge holder, main c	$ -	$ 35,000.00	$ 45,000.00	$ 25,000.00	$ 25,000.00	$ 130,000.00
Clinical trials and health care appro	$ -	$ 50,000.00	$ -	$ -	$ 50,000.00	$ 100,000.00
Biological Assay (antibodies, buffe	$ -	$ 1,000.00	$ 10,000.00	$ 40,000.00	$ 50,000.00	$ 101,000.00
Cartridge build	$ -	$ 150.00	$ 2,000.00	$ 8,000.00	$ 8,000.00	$ 18,150.00
Product build (sensors, circuits, dis	$ -	$ 30,000.00	$ 70,000.00	$ 280,000.00	$ 300,000.00	$ 680,000.00
3D printing	$ -	$ -	$ 1,000.00	$ 5,000.00	$ 8,000.00	$ 14,000.00
Additional costs (travel, equipment	$ -	$ 5,000.00	$ 10,000.00	$ 10,000.00	$ 10,000.00	$ 35,000.00
Other costs						
Legal fees	$ 5,000.00	$ 20,000.00	$ 30,000.00	$ 40,000.00	$ 40,000.00	$ 135,000.00
Labor	$ 140,000.00	$ 336,000.00	$ 560,000.00	$ 1,230,000.00	$ 1,230,000.00	$ 3,496,000.00
Infrastructure	$ 5,000.00	$ 25,000.00	$ 80,000.00	$ -	$ -	$ 110,000.00
Office space and equipmet	$ 1,000.00	$ 3,000.00	$ 6,000.00	$ 6,000.00	$ 6,000.00	$ 22,000.00
Marketing						
Digital marketing budget	$ 650.00	$ 3,500.00	$ 6,500.00	$ 6,500.00	$ 6,500.00	$ 23,650.00
Print	$ 250.00	$ 450.00	$ 450.00	$ 450.00	$ 450.00	$ 2,050.00
Exhibitions	$ 5,000.00	$ 10,000.00	$ 25,000.00	$ 25,000.00	$ 25,000.00	$ 90,000.00
PR and Press	$ 1,000.00	$ 1,000.00	$ 1,000.00	$ 1,000.00	$ 1,000.00	$ 5,000.00
Travel & Subsistence	$ 8,000.00	$ 8,000.00	$ 12,000.00	$ 20,000.00	$ 30,000.00	$ 78,000.00
Promotioal material (Video produtio	$ 3,000.00	$ 3,000.00	$ 3,000.00	$ 5,000.00	$ 5,000.00	$ 19,000.00
TOTAL COSTS	$ 283,600.00	$ 623,720.00	$ 893,350.00	$ 1,730,400.00	$ 1,819,900.00	$ 5,336,950.00
Company Recurring Costs						
Hardware/Software	$ 2,000.00	$ 2,000.00	$ 2,000.00	$ 2,000.00	$ 2,000.00	$ 10,000.00
Software Maintenance and Upgrad	$ 1,500.00	$ 1,500.00	$ 1,500.00	$ 1,500.00	$ 1,500.00	$ 7,500.00
Machinary (Cnc machine, 3D printe	$ 1,000.00	$ 3,000.00	$ 5,000.00	$ 5,000.00	$ 5,000.00	$ 19,000.00
Product support, maintenance & re	$ -	$ 1,000.00	$ 5,000.00	$ 14,000.00	$ 20,000.00	$ 40,000.00
Ongoing Additional Labor costs	$ 7,000.00	$ 16,800.00	$ 28,000.00	$ 61,500.00	$ 61,500.00	$ 174,800.00
IT Costs	$ 250.00	$ 1,250.00	$ 4,000.00	$ 4,000.00	$ 4,000.00	$ 13,500.00
User Training	$ -	$ 40,000.00	$ 200,000.00	$ 200,000.00	$ 200,000.00	$ 640,000.00
TOTAL RECURRING COSTS	$ 11,750.00	$ 65,550.00	$ 245,500.00	$ 288,000.00	$ 294,000.00	$ 904,800.00
TOTAL COSTS	$ 295,350.00	$ 689,270.00	$ 1,138,850.00	$ 2,018,400.00	$ 2,113,900.00	$ 6,241,750.00
QUANTITATIVE BENEFITS	**YEAR 1**	**YEAR 2**	**YEAR 3**	**YEAR 4**	**YEAR 5**	**TOTAL**
REVENUES FROM PRODUCT SALES						
UK	$ -	$ 12,000.00	$ 150,000.00	$ 1,000,000.00	$ 1,800,000.00	$ 2,600,000.00
Eurpoe	$ -	$ -	$ 12,000.00	$ 666,666.67	$ 1,200,000.00	$ 1,733,333.33
Africa	$ -	$ -	$ 6,000.00	$ 833,333.33	$ 600,000.00	$ 2,166,666.67
America	$ -	$ -	$ 12,000.00	$ 1,000,000.00	$ 1,800,000.00	$ 2,600,000.00
Others	$ -	$ -	$ -	$ 4,800.00	$ 480,000.00	$ 1,200,000.00
TOTAL REVENUES	$ -	$ 12,000.00	$ 168,000.00	$ 2,500,000.00	$ 3,600,000.00	$ 6,500,000.00
OTHER BENEFITS						
Sale of cartrdige	$ -	$ 32,850.00	$ 3,285,000.00	$ 8,212,500.00	$ 14,782,500.00	$ 21,352,500.00
Grants and government funds	$ -	$ 200,000.00	$ 200,000.00	$ -	$ -	$ 400,000.00
Sponsers and product support	$ 10,000.00	$ 20,000.00	$ 20,000.00	$ 20,000.00	$ 20,000.00	$ 90,000.00
TOTAL OTHER BENEFITS	$ 10,000.00	$ 252,850.00	$ 3,505,000.00	$ 8,232,500.00	$ 14,802,500.00	$ 21,842,500.00
TOTAL BENEFITS	$ 10,000.00	$ 264,850.00	$ 3,673,000.00	$ 10,732,500.00	$ 18,402,500.00	$ 28,342,500.00
TOTAL PROFIT/LOSS	$ (285,350.00)	$ (424,420.00)	$ 2,534,150.00	$ 8,714,100.00	$ 16,288,600.00	$ 22,100,750.00

8.8 Appendix 8

8.9 Appendix 9