SENSORS ARE TOOLS – BUT HOW DO YOU MAKE THEM SMART?

In this article, Gaël Senée, Research and Development Engineer, and Arnaud Guillet, Business Development Director, both of Biocorp, explore the benefits of Mallya – a smart sensor that turns conventional injection pens into connected devices. They also discuss the crucial role Biocorp's connected prefilled syringe, Injay, could play in future COVID-19 vaccination programmes.

The digital revolution in progress over the last few years has had an impact on various aspects of everyday life, including in the medical field. One of the reasons is the increasing ageing of the population and the rise in the number of chronic disease cases, such as diabetes. According to the World Health Organisation, 425 million people were affected in 2017 – and this number may reach 629 million in 2045.

With the development of the Internet of Things and telemedicine, both doctors and patients are becoming increasingly digital. From the preventive stage to the onset of the disease, patients want better control of their disease and to live as normally as possible. This process may include more personalised follow-up, which can help avoid complications and emergency hospitalisations.

Several forecasts predict a global e-health market representing hundreds of billions of dollars by 2022–2023. As a result, connected healthcare is a booming market. It attracts more and more healthcare players who want to take advantage of it. Few people anticipated the potential of this phenomenon.

ANTICIPATION OF NEEDS

Biocorp was a pioneer. Since 2013, our teams have been working on the development of connected devices. Step by step, Biocorp developed a range of products that addressed unmet needs. These devices are intended to help patients to optimise the treatment of various pathologies. Examples include asthma, diabetes or the development of connected syringes for easy monitoring of injections.

> "Mallya is an add-on device – a smart sensor that turns conventional injection pens into connected devices."

The market for diabetes apps has exploded. Many patient-friendly smartphone apps have been created, allowing automatic data transfer from a blood glucose monitoring device or an insulin pump to a mobile phone via near-field communication (NFC) or Bluetooth. Despite this, one piece of the puzzle was still missing: the one allowing the automatic collection of insulin injection data from pen injectors. The Biocorp Mallya device fills this gap and is available for diabetes patients using disposable insulin pens for their daily treatment.

Mallya is an add-on device – a smart sensor that turns conventional injection pens into connected devices. It automatically records treatment information (selected dose, date and time of injection). Data is sent in real time to a mobile app thanks to Bluetooth technology. Mallya is currently the only device in its category that has been classified as a class IIb CE medical (CE0469).

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"The patient selects a dose by rotating the dose knob, then the pen is placed where the injection needs to be made, and finally the knob is pushed down until it reaches the end, in order to deliver the selected amount of drug."

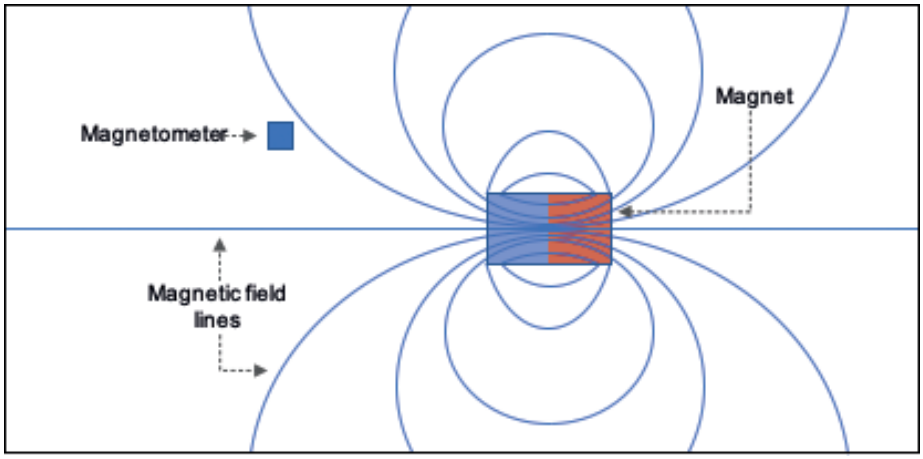

Figure 1: Several simulations and studies of the magnet positioning are made.

The use of such devices involves the processing and exploitation of health data. It must be shared, stored and secured – and be as accurate as possible, since it is the basis for medical monitoring. The stakes are high. Thanks to its technology, Mallya is able to record accurate information, which gives it a strong advantage in the field. The purpose of the Mallya device is to record and log any dose dialled by the patient. The accuracy of the dose determination and the reliability of the detection need to be ensured.

A MAGNETIC APPROACH

The device is made of two parts: a body, containing an electronic board that is clipped to the pen; and a plastic cap, with a magnet inside, which covers the dose knob of the pen. Mallya can be used on several pen platforms. Its usage generally consists of the same procedure – the patient selects a dose by rotating the dose knob, then the pen is placed where the injection needs to be made, and finally, the knob is pushed down until it reaches the end, in order to deliver the selected amount of drug. The knob proceeds through two phases: a rotation and a thrust. The magnet encased in the knob cap allows the device to follow these movements by acquiring magnetic field data. Processing this data will lead to the reconstruction of the magnet's track, and the determination of the dialled dose.

RAW DATA ACQUISITION

The Mallya device is designed with a custom-made electronic board, the choice of components for which is essential. Several magnetic sensors have been tested to find one complying with specific features (e.g. measurement accuracy, range of use, measurement noise, etc.). Magnets are obviously the key element when it comes to studying magnetism. Selecting the type of magnet, its direction of magnetisation, its dimensions and its grade are all different factors to understand and to take account of. According to the shapes and sizes of the platform pens, several simulations and studies of the magnet positioning have been conducted (Figure 1).

Each criterion noted above plays a role. The goal is to define a reference magnet, for which the magnetic field data acquired will be adequate over the entirety of the injection process. For example, under-dimensioned magnets will have a low field intensity, not fitting with the sensors' range of use, and sensitive to external interferences. An in-depth study is therefore needed. The magnets that are selected undergo several tests to check their conformity, both individually and regarding the batch they come from.

Processing magnetic field data requires handling of all the sources generating a signal in the area of the sensors. The magnet in the knob is the sole part we want the magnetometers to react to. However, external sources like the earth's magnetic field or any interference caused by a nearby device or object containing magnetic elements (such as a phone, a ring, a metallic part inside the pen, etc.) can impact the signal. Using two magnetic sensors simultaneously enables this issue to be tackled. By combining the signals, it is possible to ignore the disturbances of the external sources. However, this requires a more complex analysis and processing of the final data.

CREATING A MODEL AND AN ALGORITHM

During the manipulation of the pen, the knob's position will evolve in relation to the body of the Mallya device. This specific movement will help determine the dialled dose. In order to get enough data and measurements for this task, a magnetic test bench was conceived, on which a Mallya electronic board and a magnet can be placed. This allows reproduction of the magnet movements, without the pen obstructing the manipulation.

With measurements made at key positions, a model is developed. Note that this model depends on the platform pen. For each pen, the model needs to be adapted to fit its characteristic. The dose calculation algorithm revolves around two sets of data – one for each magnetometer. Associating these two sets results in a pseudo-field, which is averaged and smoothed for eliminating the measurement noise. This newly computed data consists of tri-axis co-ordinates (x, y, z), from which an angle and a norm can be calculated.

First of all, it is essential to determine the origin of the magnetic field measurement with precision – the overall offset due to several intrinsic deviations. In fact, when the knob is the furthest from the Mallya body, the intensity (i.e. the norm) of the magnetic field is the lowest. This is when the sensor is the most sensitive to these zero deviations. The accuracy of the angle calculation is greatly impacted by the intensity of the magnetic field. Determining the offset and negating it to each computed field increases this accuracy (Figure 2).

The idea is to roughly follow the magnet as it moves and revolves during the injection cycle. During the dial of the dose, the knob will rotate, thus the angle will change. Moreover, the knob is moving further and further away from the body, thus the norm

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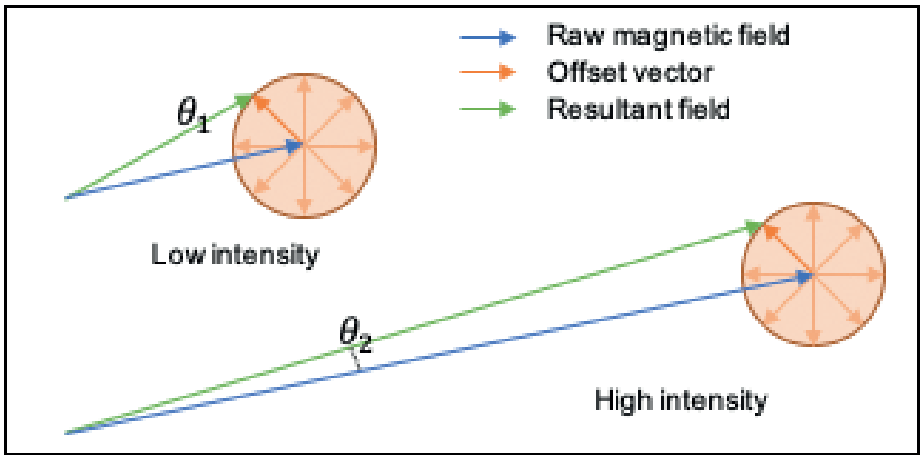

Figure 2: The impact of the overall offset on the magnetic field.

will decrease. When it is time to deliver the dose, the knob is pushed, without being rotated: the angle stays the same and the norm increases.

In short, analysing this couple of parameters allows us to track the positioning of the knob, count the number of full revolutions of the magnet and then determine which dose has been dialled by the patient.

CHECKING MODEL ACCURACY

Validating the accuracy of the model and the reliability of the algorithm relies entirely on testing. With the help of another custom-made testing bench, injections can be made over and over again. From these injections, several measurements are used to obtain training data. Retrieving them with a mechanical bench ensures that the process is repeatable and is not affected by the user's handling. The acquired signal is as neutral as possible. With specific tools, developed in-house, measurement constants and criteria are determined, analysed, learned and verified by the training data set – and used to complete the model. More injections are made, and a set of testing data validates the consistency of the overall model.

Controlling the reliability of the model on the test bench is not enough to validate the whole algorithm. Indeed, the device needs to be tested by users and patients doing real case injections. As previously mentioned, the pen and device being held by hand can lead to some interference and slightly distorted data, compared with the clean measurements made with the repeatable and straight-to-the-point test bench. The implementation of a few validation parameters, such as intensity and norm stability – or the detection of a rotation occurring during an injection – ensures that the device will not give the patient an incorrect piece of information. In which case, the user will be warned that an unexpected manipulation occurred.

THE RACE FOR A COVID-19 VACCINE

At the time of writing, a novel coronavirus (COVID-19) pandemic is unfolding across the world causing hundreds of thousands of deaths and hospitalisations and severe social and economic disruption. In this context, the remainder of our article will discuss the significant role connected injection devices can play in the global roll-out of a SARS-COV-2 vaccine.

The publication of the complete genome sequence of the SARS-COV-2 coronavirus in the Chinese Medical Journal on February 25, 2020 started a fierce race for the release of a vaccine, with nearly 150 projects involving pharma, biotech and institutional players, including J&J, GSK, Moderna Therapeutics and Inovio Pharmaceuticals. This wave has raised the expectation of a vaccine available for healthcare professionals (HCPs) and citizens within 12 to 18 months, maybe even before.

Given the unprecedented scale and stakes of this work, and the uncertainties related to the emergency context in which such a vaccine is being developed, it is absolutely paramount to run the vaccination campaign in the most secure and effective way. This means trace vaccines from the industrial filling line to the final administration, accurately identify patients and hold records, guarantee proper administration of the product, record vaccine information, run effective pharmacovigilance afterwards and manage any potential follow-ups if needed.

On the patient identity (ID) side, electronic health records (EHR) solutions have reached a mature stage in the US and can be leveraged if needed, even though

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"In the context of a nationwide COVID vaccination campaign, Injay can provide extensive benefits."

there are no centralised federal database or standardised solutions at this stage. In Europe, patient ID can be supported in many countries by EHR national initiatives – e.g. the National Patient Summary in Finland, the NHS Care Records Service in the UK or the Shared Medical Record (DMP) in France – and the European Union has launched some initiatives to centralise patient information, including the European Health Data and Evidence Network (EHDEN) project involving 22 states, which aims to standardise around 200 million patient records across Europe in the coming years.

In the rest of the world, countries such as Australia, New Zealand and Singapore already propose advanced EHR solutions that can support a nationwide patient ID and vaccination tracking campaign. The patient ID options will have to be fully accessible by all stakeholders involved in the vaccination and patient monitoring (GPs, hospitals and clinics, vaccination centres, public health authorities, etc.), while guaranteeing authentication of every access to the system and complying with the highest standards of data security.

Beyond patient ID, Biocorp's Injay device can provide a reliable solution to guarantee full traceability, safe delivery and optimal pharmacovigilance for a successful COVID-19 vaccination campaign.

Injay is a standard prefilled syringe (PFS) featuring an NFC tag on the piston rod and a customised finger flange. The NFC tag contains key product information such as type of drug, concentration, batch number and expiry date – previously encoded by the drug manufacturer during assembly of the syringe. Once Injay detects a complete injection, the product information, stamped with a specific time and date, can be transferred to any device via an NFC reader. This solution is available for various PFS formats, including 1 mL short – the standard format for vaccines.

In the context of a nationwide or international COVID-19 vaccination campaign, Injay can provide extensive benefits:

- Optimal traceability of vaccine from the industrial filling line – product information and vaccine ID are encoded by the drug manufacturer or contract manufacturing organisation in the NFC tag of the piston rod directly on the assembly line.
- Patient identification – at point of care, HCPs can verify patient ID and check physiological data, treatment history and declared symptoms prior to injection, through the selected EHR solution.
- Easy treatment identification – HCPs can read the piston rod of the syringe to check the product reference and expiry date before injection.
- Simple and proper administration – Injay is seamless from a user perspective as it does not interfere with the traditional use of the syringe and injection process. Plus, the system detects that the piston rod is pushed down until the stopping point, which guarantees complete injection of the product. A mechanical feature also locks the piston rod in its final position, avoiding any reuse of an empty syringe.
- Simple and accurate reporting – after injection, the data (product reference, batch number, expiry date and successful injection) can be easily scanned and time stamped using standard NFC readers, and directly fed into the selected EHR solution. It avoids the need for manual entry by healthcare professionals, which saves significant time and guarantees exhaustivity and accuracy of reporting.
- Effective pharmacovigilance – with this new set of data available and a proper EHR solution enabling patients to report incidents, this solution can significantly improve pharmacovigilance.
- Thanks to the data provided by Injay, any incident reported by a patient can be linked to a specific product, batch number and administration date, helping authorities and healthcare companies to trace the issue easily and provide the appropriate response.

The introduction of Injay in connection with an EHR solution will not happen all at once on a global scale. It is expected to be a progressive process. The objective is to start this initiative in a few pilot countries and progressively expand to other geographies – eventually making it a worldwide standard for vaccination.

This initiative can play a role in a broader objective to accelerate the digital revolution in healthcare for the benefit of patients, HCPs, public health institutions and payers. The need to record, protect, access and share digital health data is more intense than ever at a time when a global pandemic of a novel virus makes physical access to doctors challenging, and decision making by public authorities is hampered by a shortage of meaningful information.

ABOUT THE COMPANY

Recognised for its expertise in the development and manufacture of medical devices and delivery systems, Biocorp has acquired a strong position in the connected medical device market, thanks to Mallya. This intelligent sensor for insulin injection pens allows reliable monitoring of injected doses and thus offers better compliance in the treatment of diabetes. Available for sale from 2020, Mallya spearheads Biocorp's product portfolio of innovative connected solutions.

ABOUT THE AUTHORS

Gaël Senée is a Research and Development Engineer at Biocorp. He first joined the team as an intern, and now works on connected devices. His main tasks are focused on data analysis, signal processing and technical studies around several projects. He studied at the École Nationale Supérieure d'Ingénieurs (ENSIM) engineering school in Le Mans (France), which specialises in acoustics, vibrations and sensors.

Arnaud Guillet is Business Development Director at Biocorp, in charge of finding partnerships and licence opportunities for Biocorp's range of connected devices. Previously, Mr Guillet worked for a healthcare consulting firm with a strong focus on connected health strategies for pharma and insurance companies and has additional past experience in the pharmaceutical industry (with Sanofi) and the insurance industry (with AXA). He graduated from HEC Paris, a major European business school.

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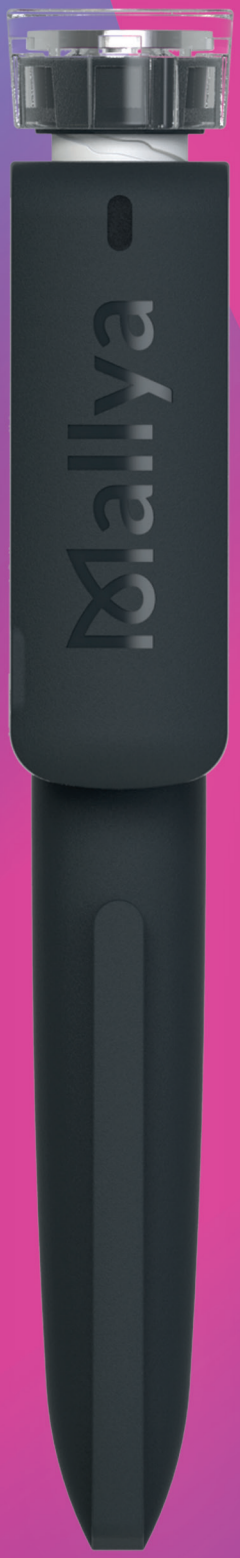
Mallya

Connected diabetes *



* Mallya automatically captures injection data (dose, date and time) and sends the information in real time to a companion software thanks to Bluetooth technology.

Mallya is CE-marked - medical device class II-b. Mallya is compatible with Solostar®, Kwikpen® and Flexpen®. Further information on www.biocorp.fr

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