Eat, Test, Digest: Towards Diagnostic Food for Next-Generation Gastrointestinal Tract Monitoring

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***Abstract* - The development of edible electronics and robotics represents a novel opportunity in several application scenarios, from food monitoring and healthcare to search and rescue. In this context, the EU-funded ROBOFOOD project aims to merge food science, robotics, and engineering to study the possible application of food-derived materials in traditional electronic and robotic components. Besides the possible out-of-body applications, the use of food-derived materials holds great potential for gastrointestinal (GI) monitoring. Avoiding the use of toxic materials, digestible sensors – i.e. diagnostic food - can reduce the risk of poisoning and retention in case of device malfunctioning, limiting the need for surgical extractions.**

Here we present an edible pressure-induced contact-resistance pressure sensor made of a gelatin-based body, an activated carbon conductive coating, printed gold electrodes and an ethyl cellulose substrate. Preliminary results show that the sensor is successful in detecting pressure changes above a certain threshold depending on the diaphragm height. For a device with a height of 500 µm, the pressure threshold was between 20.3 and 25.3 g/cm^2. While further developments are required to enable the use of the sensor in real-case scenarios, this work represents a first proof-of-concept of diagnostic food.

Keywords— Edible electronics, green electronics, green sensors, pressure sensor, diagnostic food

I. INTRODUCTION

ROBOFOOD is a highly interdisciplinary project funded by the European Union's "Horizon 2020 Research and Innovation" program aiming at delivering edible materials, methods, and components for integration into edible robots and robotic food [1]. The project is coordinated by the EPFL (École Polytechnique Fédérale de Lausanne) and involves food scientists, roboticists, and engineers from other European institutions. One of the key activities within the project concerns the development of edible electronics for edible robots and robotic food. In particular, the research focuses on the delivery of edible sensors, control circuits and power sources for later integration in more complex systems. Delivering these systems represents a technological revolution aiming at employing materials which are biodegradable, biocompatible, ecologically friendly and – above all – safe and even digestible in case of ingestion (accidental or voluntary). The use of food-like components opens novel application scenarios. In the future, rescue drones could integrate edible components, effectively increasing the food payload of the mission [2]. Also, robotic food could be employed as a vector for drug delivery to wild animals. Ultimately, miniaturised edible robots could enable novel diagnostic tools that can be digested by the body after performing a specific task. ROBOFOOD works toward the development of similar revolutionary demonstrators.

Implementing electronics and sensors using food-derived materials represents a major technological challenge. Food is inherently unstable, inhomogeneous, evolves over time and is heavily affected by environmental factors such as temperature, humidity, oxygen, and light exposure. On the contrary, stability, reliability, robustness, reproducibility are all highly desirable qualities of electronic circuits. As such, the challenge lies in identifying, optimising, and adopting material formulations, fabrication techniques and design solutions adequate for implementing edible electronic components and circuits. The use of food-derived materials to deliver electronics has several interesting implications [3 - 8]. Edible systems can take advantage of the minimal toxicity levels of the material involved. Thus, edible electronics hold strong potential in biomedical applications [6, 9, 10] with the vision of delivering diagnostic food for gastrointestinal (GI) tract monitoring.

The first system for GI tract monitoring was introduced in 1957 [11]. The device was about 8 cm long with a 1 cm diameter therefore hardly swallowable. Thereafter, commercial ingestible devices measuring physiological parameters gradually emerged, facilitated by extensive advancements in integration and miniaturization [12, 13]. Currently, ingestible devices are commercially available at an ever-growing rate (CAGR 18.1 %) and an estimated business of $1495 billion by 2027 [14, 15]. So far, many ingestible [16-23] and miniaturised [13, 24-29] diagnostic platforms have been demonstrated, including systems capable of measuring temperature [21], pH [22], pressure [17-19], bleeding [23] or imaging [16, 29]. Nevertheless, the material selection remains one of the main limitations of ingestible technology [30]. In fact, when assessing a medical device, the Food and Drug Administration (FDA) evaluates the device in its entirety rather than evaluating single materials [31]. Thus, potentially toxic materials are used in ingestible systems with proper encapsulation. However, in cases of device malfunctioning, the toxic non-degradable material can leak, and, in case of device retention, surgical extraction might be necessary. It has been estimated that the occurrence of device retention within the GI tract is 2.6%. Also, 58.7% of these retention events require surgical extraction as retention can last up to four years [30]. Furthermore, the use of non-degradable devices also poses concerns about the accumulation of electronic waste in wastewater and the environment. As the ingestible industry rapidly advances, these concerns about toxicity, medical complications, and sustainability demand a paradigm change toward the usage of innovative materials.

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Several materials with electronic properties have been identified as safe-to-eat with respective “no observed adverse effect level” (NOAEL) by the European Food Safety Agency (EFSA) [7, 32, 33]. For instance, activated carbon – a highly porous form of processed carbon with a large surface area - is an electronic conductor and is approved as food additive and food supplement [4]. Edible electronic components have also been documented, such as conductors, resistors [4], transistors [34], power sources [35, 36], and sensors [3–10].

In this work, we present a first proof-of-principle edible pressure sensor implemented using edible materials. The novelty of this work lies in the use of food-derived materials to deliver technology. As such, our sensor is composed of inherently safe materials and can be swallowed by the human body with no associated electronic waste. Preliminary data shows that the sensor can potentially trigger a new approach to non-invasive peristaltic movement monitoring (Fig. 1a). The sensor can be metabolised by the body therefore the retention risk is potentially removed.

II. Edible Pressure Sensor

Hydrogels have already been widely exploited in soft robotics [37-39]. Notably, they have also been used for pressure sensing, typically leveraging a capacitive [40, 41] or resistive [42] transduction mechanism. Among the large variety of pressure sensors [43], a certain class is typically known as pressure-induced contact-resistance pressure sensors [44-46]. This class of sensors is typically composed of a conductive diaphragm and multiple electrical contacts (switch array). In the presence of pressure, the diaphragm creates an electrical path between one or more electrical contacts. Since the contact area increases with pressure, the resistance of the electrical path is reduced when increasing pressure. These sensors can benefit from being resistive therefore they can use simple readout circuits, very low voltage, and can be used as a load to modulate a radiofrequency carrier. Differently from capacitive or ionic pressure sensors which are typically operated in an alternated current regime [43], resistive sensors can be operated in direct current. As such, this class of sensors is suitable to be included in edible circuits, which currently have a low complexity level. On the other hand, this class of sensors has a small dynamic range compared to other classes and is typically non-linear. However, these drawbacks can be mitigated by forcing the device to work in a bistable configuration (pressure switch) [47].

Starting from similar resistive pressure sensors [44-46], we substituted each material with edible equivalents. To fabricate the interdigitated contacts, we used inkjet printing of gold onto an ethyl cellulose substrate. The diaphragm was obtained by moulding a gelatin/glycerol hydrogel while the conductive coating was obtained using activated carbon. The sheet resistance of the coating was modulated to be in the hundreds of kΩ/sq range. As such, the pressure-induced contact between the interdigitated electrodes and the diaphragm is transduced as a resistance change between the two electrodes. The resistance between the two electrodes is reduced as the pressure is increased due to increased contact area.

A schematic illustration of the fabrication method is shown in Fig. 1c. The fabrication starts with the design and the fabrication of a mould. The mould is designed using CAD software (KLayout in our case) and can be fabricated using a variety of techniques, including photolithography, laser engraving and micromachining. In this work, the mould was fabricated by 3D printing Polylactic acid (PLA) using a commercial printer (Ultimaker 5S).

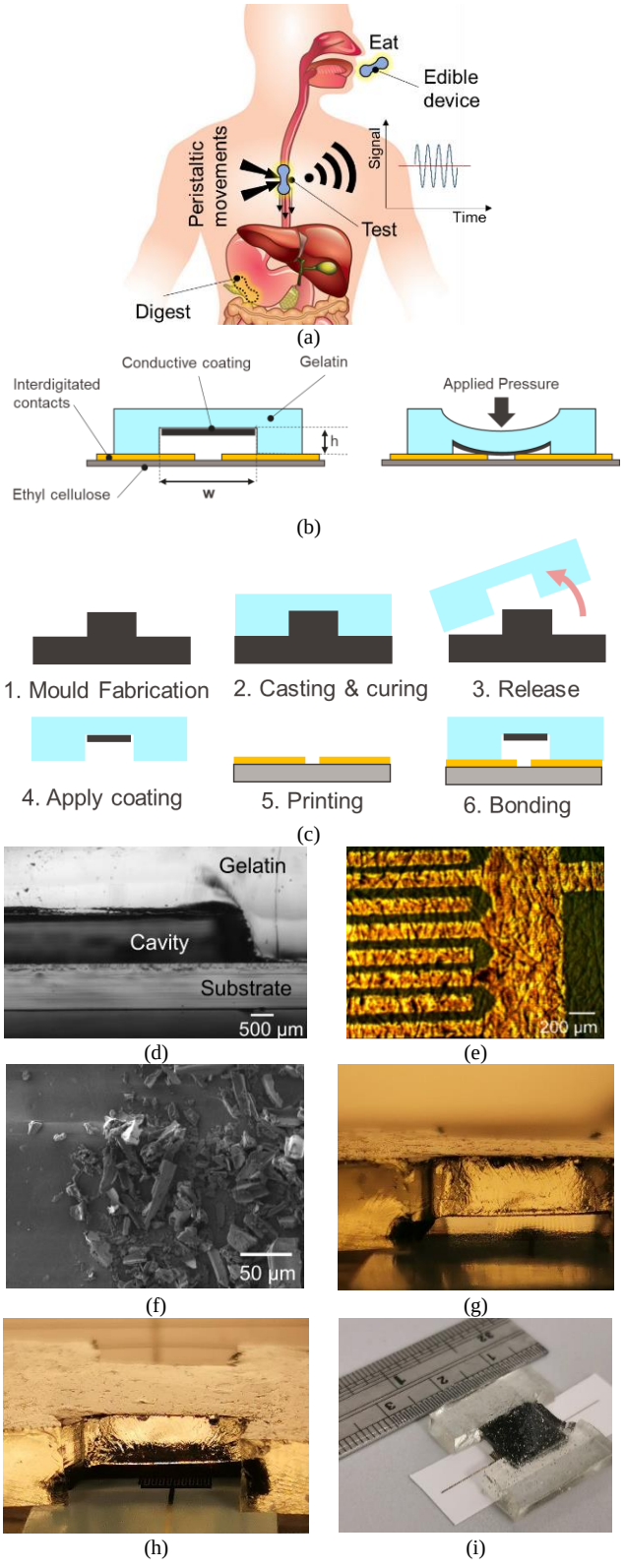

Fig. 1. (a) Application scenario. (b) Working principle of the edible resistive pressure sensor. (c) Fabrication method of the sensor. (d) Section of the gelatin/glycerol microscture (h = 1 mm). (e) Micrograph of the interdigitated printed gold electrodes. (f) SEM micrograph of activated carbon flakes. (g-i) Demonstrative picture of the elements of the components.

The mould was used to cast the hydrogel prior to gelatinisation. The hydrogel was prepared using gelatin, deionised (DI) water, and glycerol [48]. Gelatin (from porcine skin) and glycerol (ACS reagent ≥ 99.5%) were purchased from Sigma Aldrich. The resulting patterned hydrogel was then cut with a sharp knife and peeled off the mould yielding to the desired gelatin/glycerol microstructure. The cavity of the microstructure was coated with an edible electrically conductive ink based on activated carbon. The gelatin/glycerol structure was then cut with a sharp knife to achieve an H-shaped structure.

The interdigitated electrical contacts were produced separately using inkjet printing (Dimatix Materials Printer DMP-2850 by Fujifilm). The pattern to be printed was first designed using KLayout and then printed using a commercial water-based gold ink onto an ethyl cellulose substrate. The interdigitated was designed to have 20 fingers, with width of 0.94 mm and distance between two fingers of 75 µm. The substrate was first exposed to plasma (100 W for 1 min) to improve its wettability. The printing was then carried out by heating the substrate at 60°C using a drop spacing of 20 dpi. After printing, the printed pattern was sintered for 30 min at 100°C. Finally, the gelatin/glycerol microstructure was bonded onto the electrical contacts. The diaphragm was designed with a width (w) and length (l) of 1 cm. Diaphragms were fabricated with different heights of 0.5 mm and 1 mm.

III. Preliminary Results and Discussion

The impedance spectra of the sensor (with and without applied pressure) and of its constituting elements were first analyzed (see Fig. 2a, 2b). Without any applied pressure, the behavior of the sensor is comparable to the impedance of the electrodes. When pressure is applied, the sensor switches to a resistive behavior. This creates a large variation of the impedance modulus of more than four orders of magnitude. The resistance of the sensor was then quantified in direct current (Fig. 2c, 2d, 2e). Data suggests that changing the height of the gelatin/glycerol structure affects the pressure threshold. In particular, for a structure with a height of 500 µm and 1 mm, the pressure threshold was in the range 20.3 – 25.3 g/cm^2 and 50.3 – 57.9 g/cm^2, respectively. Once over the threshold, the sensor is still sensitive to slight pressure variations. In a dynamic range of 25.3 – 30.3 g/cm^2, the device with h = 500 µm shows a sensitivity of -544.3 Ω·cm^2/g. The device with an increased height of 1 mm showed a slightly larger dynamic range from 57.9 g/cm^2 to 106.0 g/cm^2 with a lower estimated sensitivity of -59.01 Ω·cm^2/g. To provide an initial proof-of-concept that the sensor can detect repeated pressure changes, cyclic testing was performed (Fig. 2f and 2g). Repeated pressure stimuli were applied to the sensor (h = 500 µm). The pressure stimuli – even with an added hold time (Fig. 2g) - were clearly detected by the sensor in a reliable and repeatable way.

Primary peristaltic contractions are progressive and generate an estimated intraluminal pressure between 54.4 and 108.8 g/cm^2 (40 to 80 mm Hg) [49]. A preliminary characterisation of the sensor output versus pressure level comparable to those observed during peristaltic movements has been reported herein. A more systematic characterisation involving a larger number of devices is needed to fully demonstrate its suitability for peristaltic movement monitoring. However, data suggests there is merit in developing such a device. The materials herein involved are all potentially edible and are processed using simple and straightforward methods. The resistive nature of the device is particularly advantageous as the read-out circuit can be as easy as a voltage divider.

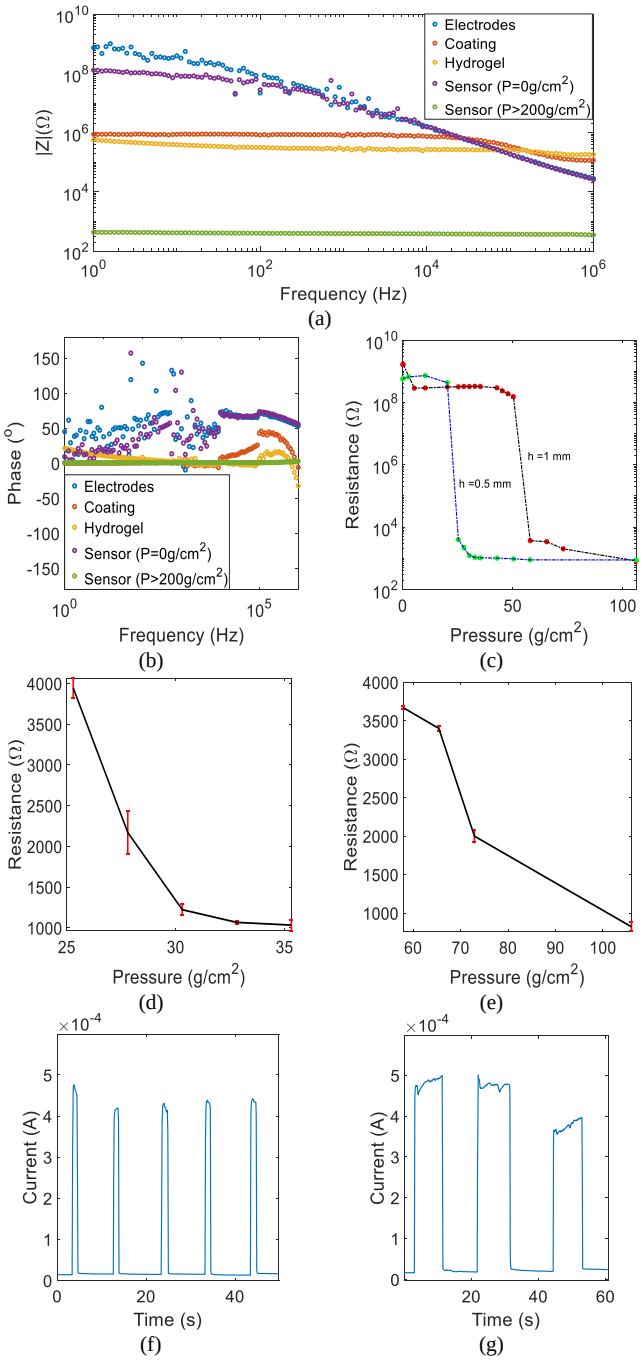

Fig. 2. (a) Bode diagram (modulus) for the impedance of the electrodes, the complete sensor (h = 500 µm) and the sensor with applied pressure levels. (b) Bode diagram (phase) for the impedance of the electrodes, the complete sensor (h = 500 µm) and the sensor with applied pressure levels. (c) Sensor resistance (DC measurement) with different levels of applied pressure for two devices with diaphragm heights of 0.5 mm and 1 mm. (d) Sensor resistance (DC measurement) above the threshold for evaluating the dynamic range with diaphragm height of 0.5 mm. (e) Sensor resistance (DC measurement) above the threshold for evaluating the dynamic range with diaphragm height of 1 mm. (f) Pressure sensor used in a bistable mode with cyclic stimulus (h = 500 µm, P > 200 g/cm^2) (g) Pressure sensor used in a bistable mode with cyclic stimulus and hold time (h = 500 µm, P > 200 g/cm^2).

We also expect that the device has very low (virtually zero) power consumption when no pressure is applied and can be operated at very low voltages.

Data also suggests that the pressure threshold, dynamic range, and sensitivity of the device can be tuned by modifying the geometric parameter of the gelatin-based structure. Future works will also include a systematic characterisation of the structure by quantifying the main metrics depending on the size and geometry of the diaphragm and the use of patterned edible gold foils instead of commercial ink.

IV. Conclusions

Here we report a proof-of-concept diagnostic food, i.e. edible swallowable devices that can provide diagnostically relevant information before being metabolized by the human body. We describe the fabrication process of a resistive pressure sensor made of potentially edible materials for possible applications in healthcare. Preliminary data shows that the device is indeed sensitive to pressure with repeatable output. Next steps include a full characterisation of the sensor, as well as size reduction and integration into a pressure-sensitive array. Future implementations of the sensor will also be integrated with other edible technologies developed in our group – such as edible power sources [35], edible readout circuitry [7], and edible communication module [50] - aiming at delivering a fully edible swallowable system. We believe our findings can trigger a paradigm shift where greener and more sustainable materials are considered in lieu of traditional alternatives for a wide range of applications, including food monitoring and healthcare.

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