Towards biodegradable wireless implants

BY CLÉMENTINE M. BOUTRY1,* HENGY CHANDRAHALIM1, PATRICK STREIT1, MICHAEL SCHINHAMMER2, ANJA C. HÄNZI2 AND CHRISTOFER HIEROLD1

1Micro and Nanosystems, Department of Mechanical and Process Engineering, ETH Zurich, 8092 Zurich, Switzerland
2Laboratory of Metal Physics and Technology, Department of Materials, ETH Zurich, 8093 Zurich, Switzerland

A new generation of partially or even fully biodegradable implants is emerging. The idea of using temporary devices is to avoid a second surgery to remove the implant after its period of use, thereby improving considerably the patient’s comfort and safety. This paper provides a state-of-the-art overview and an experimental section that describes the key technological challenges for making biodegradable devices. The general considerations for the design and synthesis of biodegradable components are illustrated with radiofrequency-driven resistor–inductor–capacitor (RLC) resonators made of biodegradable metals (Mg, Mg alloy, Fe, Fe alloys) and biodegradable conductive polymer composites (polycaprolactone–polypyrrole, polylactide–polypyrrole). Two concepts for partially/fully biodegradable wireless implants are discussed, the ultimate goal being to obtain a fully biodegradable sensor for in vivo sensing.

Keywords: biodegradable polymer; biodegradable metal; conductive polymer; resistor–inductor–capacitor (RLC) resonator; wireless implant

1. Introduction

Wireless operation of implantable devices is required for many emerging biomedical applications, in order to reduce the risk of infection resulting from transcutaneous wires breaching the skin [1,2]. However, this requirement adds to the complexity of the system and increases the overall size of the implant. The first objective of this paper is to identify the elements of a biomedical implant that could be made biodegradable. The resulting device would be partially or even fully biodegradable, including the antennas/coils used for wireless communication. The idea is to avoid a second surgery to remove the implant after its period of use, thereby improving considerably the patient’s comfort and safety [3–5].

The second objective of this paper is the development of radiofrequency-driven resistor–inductor–capacitor resonators (RF-driven RLC resonators) made of biodegradable materials. RLC resonators are commonly used for wireless power and data transmission in short-range telemetry (inductive link); the successful fabrication of biodegradable RLC resonators is a first step towards the ultimate

*Author for correspondence (clementine.boutry@micro.mavt.ethz.ch).

One contribution of 10 to a Theme Issue ‘Biosensors: surface structures and materials’.
Towards biodegradable wireless implants

goal of making a fully biodegradable implant for \textit{in vivo} operation. Section 2 provides a state-of-the-art overview, describes the challenges and constraints currently encountered when developing implantable devices, and gives possible design rules for fabricating partially/fully biodegradable implants. Section 3 focuses in particular on the key technological challenges for making biodegradable devices, illustrated with RF-driven \textit{RLC} resonators made of biodegradable metals [6–9] and biodegradable conductive polymers [4, 5, 10, 11].

2. A new generation of wireless implants including biodegradable parts

(a) Wireless implantable devices, challenges and constraints

(i) Applications

A large variety of medical problems are addressed by specific implantable systems. Among the few applications that have widely penetrated the medical market, the oldest and probably the most famous example is the fully implantable pacemaker, which was developed in 1958 by Greatbatch & Chardack [12]. Each year, physicians implant approximately 600,000 pacemakers worldwide [13], corresponding to a market for cardiac surgery devices of over $2 billion in 2010 just for the USA [14]. Closely related, there is a high demand for implants dedicated to \textit{in vivo} electrocardiography [15]. Another successful field of application concerns electrically stimulating implants that are used to treat brain disorders such as epilepsy [13]. \textit{In vivo} electroencephalography implants [16] are used to perform chronic or longer-term measurements of brain activity, correlated to specific physiological phenomena such as sleep, excitation and epilepsy [17]. Other implants perform \textit{in vivo} electromyography [18, 19], with the long-term objectives to acquire muscle signals and to control an artificial prosthesis. The \textit{in vivo} measurement of intracranial pressure by means of wireless implants is also an active research field [20], because a number of brain diseases are related to this parameter. Moreover, considerable efforts have been made to develop implantable devices dedicated to glucose level detection in the blood, given the large number of diabetic patients worldwide [21]. The idea is to create an artificial pancreas, controlling the glucose level and administering insulin inside the body [22]. Other biosensors are dedicated to the measurement of tissue bio-impedance [23], finding a clinical use associated with pacemakers [17]. These devices follow the functionality of transplanted organs by evaluating the physiological performance of living tissues, and warn the surgeon in case of tissue decease. Other advanced biomedical implants are dedicated to the restoration of vision for patients having incurable diseases (e.g. degeneration of retinal photoreceptors) [24]. Again, another application field is the development of ‘brain–computer interfaces’ to re-establish motor function for the limbs of patients with severe motor disabilities [25]. Last, but not least, video capsule endoscopy (VCE) ingestible devices are already approved for clinical practice [26].

(ii) Data and power telemetry

The vast majority of the biomedical implants have common characteristics in their organization. They are composed of an implantable (\textit{in vivo}) device,
and one or more external (ex vivo) hosts that are used to control and/or collect the data provided by the internal part. The implant either (i) telemeters data externally, (ii) receives and executes commands from an external host or (iii) performs both operations [17]. The choice of design for data and power transfer between the implant and the external host depends on many factors, including the implant size, its location in the body and the desired data rate.

**Short-range telemetry, inductive link.** For short-range links (tens of centimetres), low-frequency inductive links are often preferred [1]. The primary coil (external host) is coupled to the secondary coil (on the implant). The coupling strength depends strongly on the coils’ geometry, their relative position and excitation frequency. Both power and data can be transmitted via the RF inductive link to the implant. The external transmitter emits a carrier signal that is received by the implanted device. On the implant side, the secondary coil is integrated in a passive $RLC$ resonator and the voltage received in the coil is amplified. A fraction of this signal is used to generate a constant DC supply using an AC/DC converter, thus powering the implant. The forward data transfer (from the external host to the implant) is realized by modulating the envelope of the power carrier, usually via amplitude modulation [17]. For an inductive link, the backward data transfer (from the implant to the external host) is generally realized using a load modulation technique known as load shift keying (LSK) [1,17,27]; the implant measures, for example, a physiological signal corresponding to a variation of the secondary coil impedance, which is ‘reflected’ in the primary coil over the existing RF link (no need for an active transmitter on the implant) [1,17]. Telemetry by inductive coupling is used only for short distances, because the magnetic field strength along the coil axis decreases as the third power of distance [1]. Inductive links are generally applied at frequencies below 10 MHz, with output power in the range of 10–250 mW and data rates of 1–2 Mbs$^{-1}$ [1]. Another commonly used approach for short-range telemetry consists of using several coils/antennas for the power and data links, with the objective to optimize them independently [2,28–31]. The frequency, location and geometry are adapted to have high bandwidth for data telemetry and high quality factor $Q$ for power transfer [1]. A careful design is required to minimize the cross-coupling between the different signals (e.g. power carrier interference in the received data carrier) [2]. Frequently employed modulation techniques are amplitude modulation (analogue amplitude modulation; amplitude shift keying; on–off keying), frequency modulation (analogue frequency modulation; frequency shift keying, FSK; binary FSK) and phase modulation (phase-shift keying, PSK; differential PSK) [1,17].

**Long-range telemetry.** For long-range links (more than 2 m), present devices usually include batteries to provide energy to the implant, and antennas for the data transfer. These applications require transmitters with a high output power, and receivers with a high sensitivity, resulting in high power dissipation [1], which is strictly regulated by standards. A clinical example is the VCE ingestible device mentioned earlier. The operation frequency is typically chosen in the authorized bands—such as the Federal Communication Commission (FCC)-approved Medical Implant Communication Service (MICS) band, 402–405 MHz, and the Industrial, Scientific and Medical (ISM) bands, 902–928 MHz, 2.4–2.483 GHz and 5.725–5.875 GHz [1,26].
(iii) Challenges and constraints

When developing implants with given functionalities (data transmission rates, channel resolution, number of sensors/ peripherals), the main constraints are the size and the power consumption/losses. The design is always a compromise between these factors [1].

**Size.** Currently, the main limiting factors for miniaturizing wireless implants are the size of the battery, and the size of the coils/antennas [2,28,29,32]. Certain sophisticated designs take advantage of a particular geometry associated with a specific application, e.g. the stent developed by Chow *et al.* [31], where the antenna used for power transfer is the stent itself. However, in most cases, the size of the antenna cannot be reduced because it depends on the transmission frequency, which in turn depends on the implant’s location inside the body. The RF losses in biological tissues are smaller for low operating frequencies, corresponding to higher magnetic field penetrability [33]. But a lower operation frequency implies a larger antenna (to keep enough radiation efficiency), resulting in the earlier-mentioned trade-off. For coils used in inductive telemetry, the appropriate size of the secondary coil depends again on the operating frequency and implant location. Moreover, efforts have been made to reduce the size of the electronics. Most often, the central processing/controlling core, dedicated to supporting the functionality of the implant, has a fully customized design (not component-based) incorporating mixed-signal circuitry (not only analogue), the objective being to reduce the size as much as possible [17]. Another strategy to minimize the circuit size (and power consumption) consists of performing complex data processing outside the body, transmitting the data back and forth between the implant and the external host, thus forming a closed-loop system [34].

**Power.** The power consumption (to ensure proper operation of the implant) and power radiating losses (in the tissues surrounding the implant) must both be minimized. In the future, medical sensors might be able to take the power they need from the heat of the human body or other *in situ* energy sources [35]. However, this is not yet the case, and the available power sources are either implantable batteries or RF links as described earlier. The favoured powering method depends strongly on the application, size constraints and implant lifetime [1]. Implanted batteries display interesting new features, such as onboard rechargeable batteries with wireless charger; the drawback, however, remains their overall size [32]. The implant power consumption can be reduced by using sleep/low-power and duty-cycle modes [1,17]. Moreover, for inductive coupling links, closed-loop power control mechanisms can be implemented. The implant maintains the power delivered to the external host at a constant level even when the distance and/or alignment between the primary and secondary coils change. This also has the advantage of minimizing the power dissipation in the tissue surrounding the implant [28,30]. The two main sources of power dissipation are (i) the temperature rise due to thermal losses by conduction in the implant (risk of damage to the surrounding tissues) and (ii) the electromagnetic power dissipated into the tissues when forming the RF inductive link between the implant and the external host [17]. The maximum authorized specific absorption rate (SAR; in watts per kilogram) is strictly defined by the standards for given frequency ranges (e.g. in the range 100 kHz–10 GHz, the whole-body SAR should not exceed 0.4 W kg\(^{-1}\); the localized SAR in limbs and in the trunk/head should not exceed 20 W kg\(^{-1}\) and 10 W kg\(^{-1}\), respectively) [36,37].

Phil. Trans. R. Soc. A
Towards partially/fully biodegradable implants

After discussing the challenges and constraints currently encountered when developing wireless biomedical implants, the next step consists of identifying which elements could advantageously be made of biodegradable materials. The available materials are (i) conventional biodegradable polymers, (ii) biodegradable metals and (iii) biodegradable conductive polymer composites. The well-known and widely used biodegradable polymers poly(l-lactide) (PLLA) and polycaprolactone (PCL) can be used as substrate and packaging material because they combine high strength and long-term mechanical stability [38,39]. Metals known to be biodegradable (Mg, Fe and their alloys) [6–9] can be used for electrical circuits (biodegradable stents made from Mg alloys are already being used in clinical trials [8]). The same applies for the biodegradable conductive polymer composites PLLA–polypyrrole (PPy) and PCL–PPy [4,5], where the conductivity is ensured by the biocompatible PPy nanoparticles. Based on these materials, two concepts for partially/fully biodegradable wireless implants are proposed in figures 1 and 2. The idea in figure 1 is the following. The main limiting factor for miniaturizing the implant is the size of the coil and/or antenna used for telemetry (§2a(iii)). In contrast, the data-processing block and sensors are generally small compared with the coil. The concept proposed in figure 1 consists of making the coil/antenna fully biodegradable, while the rest of the system remains ‘conventional’. By making the large coil/antenna from a biodegradable material, this part can be left in the body to degrade, while the small electronics/sensors part can be removed with a syringe. Therefore, a second intervention to remove the implant after its period of use can be avoided. Figure 2 gives the concept for a fully biodegradable sensor, using wireless telemetry with an inductive link. The implant is made of an RLC resonator (biodegradable) with a sensing layer (biodegradable), which is sensitive to a...
stimulus (e.g. the permittivity varying with glucose level [40]). The secondary coil (inductor of RLC resonator, on the implant) is inductively coupled to a primary coil (external host, not shown). The stimulus causes a shift and a damping of the resonant frequency of the RLC resonator, which is detected by the external host (reflected impedance in the primary coil) [1,17,41]. The substrate and packaging are also made of biodegradable materials. For the partially biodegradable implant (figure 1), the backward data transfer (from the implant to the external host) can be realized by LSK, i.e. the load is ‘reflected’ in the primary (external) coil through the inductive link. The transmitted signal is modulated in the electrical block by one of the modulation techniques mentioned in §2a(ii). For the fully biodegradable implant (figure 2), there is no data-processing block to modulate the signal measured by the sensor. Instead, and as described earlier, the reflected impedance corresponding to the sensor signal is measured by monitoring the overall impedance of the external coil [41]. When performing such inductive coupling measurements, the measured data are the loaded resonant frequency $f_{\text{loaded}}$ and the loaded quality factor $Q_{\text{loaded}}$, which depend strongly on the coupling between the primary and secondary coils (i.e. the relative position between the measurement coil and the RLC resonator, and the tissues in between). Then, further data processing is required to derive the unloaded parameters $f_{\text{unloaded}}$ and $Q_{\text{unloaded}}$, which contain the ‘useful’ sensor signal.

3. Key technological challenges for making biodegradable devices

In this section, the primary challenges for making biodegradable devices are discussed. The key technological challenges concern (i) the development of new biodegradable materials with adequate conductivity, (ii) the implementation of high-precision fabrication processes with low impact on material properties, (iii) the development of characterization procedures adapted to these particular
components, and (iv) the evaluation of the DC and RF material properties for circuit design. These considerations are illustrated with RF-driven RLC resonators made of biodegradable materials.

**RLC resonators made of biodegradable materials.** Figure 3 shows RLC resonators made of biodegradable materials. RLC resonators are typically used for wireless telemetry using an inductive link. Resonators made of biodegradable polymer composites are based on (i) a biodegradable matrix (PLLA or PCL), and (ii) conductive polymer nanoparticles, made of PPy (40% of the total weight). The chemical polymerization process is described elsewhere [5]. The resonators are fabricated by compression moulding, and the capacitor gap is laser cut. Resonators made of biodegradable metals are fabricated from six different metals known to be biodegradable [6–9]. The materials used are (i) pure magnesium (Mg 99.9%, Goodfellow Ltd, UK), (ii) pure iron (Fe 99.5%, Goodfellow Ltd, UK), (iii) a magnesium alloy (‘Mg alloy 1’, Mg–2Y–1Zn–0.25Ca–0.15Mn in wt%, [6]) and (iv) three different iron alloys (‘Fe alloy 1, 2, 3’, Fe–21Mn–0.7C, Fe–21Mn–0.7C–0.5Pd and Fe–21Mn–0.7C–1Pd in wt%, [7]). The metal resonators are fabricated by electric discharge machining (EDM).

(a) Development of new biodegradable conducting materials

One of the main key technological challenges for the design and synthesis of biodegradable components is the development of appropriate materials. The conductivity of these biodegradable materials should be high enough in order to have (i) high quality factors $Q$ and (ii) low power dissipation in the implant and in the surrounding tissues (see §2a(iii)). Figure 4 shows the $Q$ factors and resonant frequencies of the RLC resonators presented in figure 3. As expected, the resonators made of biodegradable metals have higher $Q$ factors than the resonators made of biodegradable conducting polymers. The highest $Q$ factors are obtained for resonators made of Mg (conductivity $2.24 \times 10^7$ S m$^{-1}$, $Q > 400$) [42]. The remarkably low $Q$ factors measured for the resonators made of Fe (conductivity $1.07 \times 10^7$ S m$^{-1}$) are explained by the high relative
Towards biodegradable wireless implants

Figure 4. Quality factors $Q$ and resonant frequencies of the $RLC$ resonators shown in figure 3. The $RLC$ resonators are characterized by capacitive coupling (biodegradable metals Mg, Mg alloy, Fe, Fe alloys) and inductive coupling (biodegradable conducting polymers PLLA–PPy, PCL–PPy). Here the unloaded $Q$ factor and unloaded resonant frequency are given. The unloaded parameters, which describe the resonators’ performances independent of the measurement set-up, are derived from the measured loaded parameters. Adapted from Boutry et al. [42]. (Online version in colour.)

permeability of pure iron, having a negative impact on $Q$. In comparison, the Fe alloys show higher $Q$ factors (around 100) compared with pure iron. The resonators made of polymer composites have $Q$ factors no higher than 18, their conductivity being about four orders of magnitude lower than for metals [42]. Moreover, particular constraints are associated with the development of biodegradable polymer composites with high conductivity. In the present study, the widely used semicrystalline biodegradable polymers PLLA and PCL were chosen for their good mechanical properties and biocompatibility upon degradation [38]. PPy was selected because of its long-term ambient stability in air and water, easy synthesis and excellent biocompatibility in vivo [43]. PPy has already previously been combined with biodegradable polymers by other groups [10,11,44,45] in order to get biodegradable conducting composites. But all faced the same issue, which is that PPy is regarded as non-degradable. Even though the biodegradation behaviour and in vivo biocompatibility of poly(D,L-lactide) (PDLLA)–PPy composites (similar to the composites used in the present study) have been evaluated by Wang et al. [46,47], with the conclusion that the tissue reaction was not affected by the presence of PPy, the challenge remains to keep a sufficient conductivity at the lowest possible PPy concentration [11]. In parallel, research is being carried out on the synthesis of PPy–based polymers that would be inherently conductive and fully biodegradable, the difficulty being
to maintain a conductivity that allows electronic applications [48]. Finally, for the biodegradable metals, the main challenge consists of tailoring alloys with the desired degradation rate. The pure metals are easier to obtain, while the alloys exhibit improved mechanical and electrochemical properties, fulfilling the requirements for temporary implant solutions such as cardiovascular stents—an application for which they were developed [6,7]. Owing to their superior properties, the alloys allow enhanced freedom for device design. The three Fe alloys selected in this study exhibit different degradation rates based on their Pd content. Pure iron degrades rather slowly in the body, while the Fe alloys exhibit enhanced corrosion rates and are therefore more suitable for temporary implant applications [7].

(b) Fabrication processes

The fabrication processes have to be adapted to the newly developed biodegradable conducting materials. As illustrated in figure 3, selecting biodegradable metals to fabricate the resonators is advantageous because it allows the use of conventional fabrication techniques with high precision. In particular, the EDM technique provides a precision better than 50 μm. However, this is a serial and time-consuming fabrication process, which might be disadvantageous for large-scale production. For the polymer resonators, the fabrication process has to be carefully selected in order to reduce its impact on material conductivity. The compression moulding step offers high precision and reproducibility, in particular when custom-made cylindrical moulds are used. In contrast, the laser-cutting step used to obtain the capacitor gap has a precision no better than 0.5 mm (for a cutting thickness of 3 mm), and it might potentially damage the polymer composite locally by heat. Developing moulds that take into account the overall geometry (including the capacitor gap) and that allow the fabrication of the RLC resonator in one step might be a future step to completely avoid laser cutting in the fabrication process. Finally, other fabrication techniques might be better suited to fabricate complex structures such as those presented in figure 2. An approach would be to cast the polymer composite in a mould made of a photoresist previously structured by conventional photolithography. Moreover, metal sputtering might be used to deposit biodegradable metals on polymer substrates.

(c) Characterization procedures

Another key parameter to successfully fabricate wireless biodegradable devices is the development of characterization procedures adapted to the particular material properties. As an illustration, the RLC resonators shown in figure 3 are characterized by capacitive and inductive coupling measurements. However, because of their low conductivity compared with metals (approx. four orders of magnitude), the polymer resonators display low Q factors, and they cannot be characterized using the same procedure as used for the metal resonators. For the metal resonators (figure 5a), the unloaded quality factor $Q_{\text{unloaded}}$ and the unloaded resonant frequency $f_{\text{unloaded}}$ are directly measured from the capacitive coupling measurements. Simulations are performed with the electromagnetic fields simulation software HFSS (Ansoft, Inc., USA), which allows us to extract the RF relative permeability and RF conductivity of the biodegradable metals.
The RLC resonators made of metal are also characterized by inductive coupling. For the polymer resonators (figure 5b), \( f_{\text{unloaded}} \) and \( Q_{\text{unloaded}} \) cannot be extracted from the capacitive coupling measurements because the resonance is too weak to be detected by this method. Instead, \( f_{\text{loaded}} \) and \( Q_{\text{unloaded}} \) are obtained from the inductive coupling measurements. The capacitive coupling measurements, combined together with the HFSS simulations, allow extraction of the RF conductivity of the polymer composites.

(d) Evaluation of the DC and radiofrequency electrical properties of the biodegradable materials

A good understanding of the DC and RF electrical properties of the biodegradable materials is required to successfully design and fabricate wireless implants. For the biodegradable metals, no difference is measured between the
Figure 6. Conductivity of the polymer composite (here PCL–PPy) as a function of frequency [56], modelled according to Papathanassiou’s and Jonscher’s models [54,55]. (Online version in colour.)

DC and AC conductivities of the investigated materials. For magnetic materials (Fe and Fe alloys), relative permeability falls off with frequency [49–51], which has a direct impact on the $Q$ factor and has to be taken into account in circuit design. For the polymer composites, it is known that the RF conductivity of conducting and semiconducting polymers (including PPy) is larger than the DC conductivity and can be different by several orders of magnitude [52,53]. A qualitative explanation consists of considering the polymer structure as a network of conduction paths of various lengths, which are accessible to electric charge carriers. At higher frequencies, shorter paths also contribute to the overall conduction [54]. Modelling the conductivity of polymer composites as a function of frequency is required for the design of electrical circuits, in particular when changing the operation frequency of the device depending on the implant’s location in the body. Papathanassiou’s and Jonscher’s models [54,55] describe the conductivity as a function of frequency, as illustrated in figure 6.

4. Conclusions

This paper provides a state-of-the-art overview and an experimental section that describes the key technological challenges for making biodegradable devices. After discussing the constraints currently encountered when developing biomedical implants, two concepts for partially/fully biodegradable devices were proposed. The general considerations for the design and synthesis of biodegradable components were illustrated with RF-driven $RLC$ resonators made of biodegradable metals (Mg, Mg alloy, Fe, Fe alloys) and biodegradable conductive polymer composites (PCL–PPy, PLLA–PPy). The measured resonant frequencies were in the range of 500 MHz to 1 GHz for the metal resonators, and 2–3.3 GHz for the polymer resonators. Future design will focus on the technically relevant frequencies of (i) 2.4–2.483 GHz (ISM frequency band), (ii) 402–405 MHz (FCC-approved MICS band) and (iii) 2–10 MHz (typical operation frequency used for short-distance telemetry with inductive link). The highest unloaded $Q$ factors were obtained for the resonators made of Mg ($Q \approx 300–400$) and Mg alloy 1.
The polymer resonators had unloaded $Q$ factors in the range of 5–18. These results show that magnesium is presently the most promising candidate to fabricate RLC resonators. Future research will consist of developing materials with high conductivity (high $Q$), biodegradable features and higher flexibility in the fabrication process (for example, photolithography-based process). Light weight, compatibility with magnetic resonance imaging and transparency to X-rays are also highly desirable for in vivo application, which emphasize the interest in developing highly conductive biodegradable polymers.

Many thanks to Dr Jan Hesselbarth for his kind help with the capacitive coupling measurements and HFSS simulations, Hans-Rudolf Benedikter for his advice on the measurements, Prof. Dr Bradley Nelson for access to the laser cutting equipment, and the Materials Research Center (MRC)—a platform for all materials-related research at ETH Zurich.

References


Towards biodegradable wireless implants


