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Review

Implantable and Ingestible Medical Devices With Wireless Telemetry Functionalities: A Review of Current Status and Challenges

Asimina Kiourti,* Konstantinos A. Psathas, and Konstantina S. Nikita

School of Electrical and Computer Engineering, National Technical University of Athens, Athens, Greece

Wireless medical telemetry permits the measurement of physiological signals at a distance through wireless technologies. One of the latest applications is in the field of implantable and ingestible medical devices (IIMDs) with integrated antennas for wireless radiofrequency (RF) communication (telemetry) with exterior monitoring/control equipment. Implantable medical devices (MDs) perform an expanding variety of diagnostic and therapeutic functions, while ingestible MDs receive significant attention in gastrointestinal endoscopy. Design of such wireless IIMD telemetry systems is highly intriguing and deals with issues related to: operation frequency selection, electronics and powering, antenna design and performance, and modeling of the wireless channel. In this paper, we attempt to comparatively review the current status and challenges of IIMDs with wireless telemetry functionalities. Full solutions of commercial IIMDs are also recorded. The objective is to provide a comprehensive reference for scientists and developers in the field, while indicating directions for future research. Bioelectromagnetics 35:1–15, 2014. © 2013 Wiley Periodicals, Inc.

Key words: implantable antenna; ingestible antenna; implantable and ingestible medical devices; medical telemetry

INTRODUCTION

Medical telemetry permits the measurement of physiological signals at a distance, through either wired or wireless communication technologies. Physiological signals are obtained by means of appropriate transducers, post processed and eventually transmitted to an exterior monitoring/control device. One of the latest applications of medical telemetry is in the field of implantable and ingestible medical devices (IIMDs). Implantable medical devices (MDs) may be used as sensors [Kawoos et al., 2008], nerve stimulators [Guillory and Normann, 1999] or drug delivery devices [Yasukawa et al., 2005] to perform an expanding variety of diagnostic and therapeutic functions (Fig. 1a). Ingestible MDs receive significant attention in gastrointestinal (GI) endoscopy (physiological data and image retrieval from within the GI tract through a swallowable smart capsule) for timely detection of early stage, and, thus, curable cancers of the GI tract (Fig. 1b) [Pan and Wang, 2012]. As technology continues to evolve, use of IIMDs is expected to rapidly increase.

Historically, low-frequency (tens to hundreds kHz) inductive links [Tang et al., 1995] and invasive endoscopy techniques have been the most prevalent methods of medical telemetry for IIMDs, respectively. However, in order to overcome the weaknesses of inductive telemetry related to low data rate (1–30 kbps), restricted communication range (less than

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*Correspondence to: A. Kiourti, BIOSIM Laboratory, Faculty of Electrical and Computer Engineering, National Technical University of Athens, 9 Iroon Polytechniou Str., 15780 Zografos, Athens, Greece. E-mail: akiourti@biosim.ntua.gr

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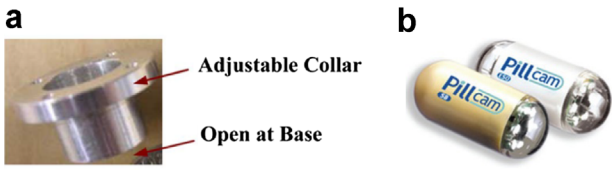

Fig. 1. Example IIMDs: (**a**) intracranial pressure implant [Kawoos et al., 2008], and (**b**) PillCam ingestible devices [Pan and Wang, 2012].

10 cm), and sensitivity to coils' positioning, as well as the limitations of invasive endoscopy regarding patient discomfort and inability to examine the whole GI tract, research is nowadays further oriented towards antenna-enabled IIMDs [Karargyris and Bourbakis, 2010; Kiourti and Nikita, 2012a]. Design of such radio-frequency (RF) IIMD telemetry systems is facilitated by the rapid advances in wireless communications and electronics, and attracts high scientific interest to deal with: (1) operation frequency selection; (2) electronics and powering considerations; (3) antenna design and performance (antenna type, antenna size, biocompatibility, influence of the human body, and patient safety); and (4) modeling of the wireless channel.

In this paper, we attempt to comparatively review the current status and challenges of IIMDs with wireless telemetry functionalities. Contributions from researchers of various disciplines build a rich pool of background information, while highlighting future prospects. In the literature, there exist two recent review studies on IIMDs [Yuke and Dissanayake, 2012; Kiourti and Nikita, 2012b]. However, the first is limited to antenna design and performance for implantable MDs [Kiourti and Nikita, 2012b], while the second mainly addresses operation frequency selection and electronics and powering considerations for ingestible MDs [Yuke and Dissanayake, 2012]. This paper deals with both IIMDs, by extending the scope to all four aforementioned research areas (operation frequency selection, electronics, and powering considerations, antenna design and performance, and modeling of the wireless channel), and comparing the differences in requirements between IIMDs, where possible. The current status and challenges raised are discussed, while full solutions of commercial IIMDs are also recorded. The objective is to provide a comprehensive reference for scientists in the field, while indicating directions for future research.

OPERATION FREQUENCY SELECTION

Selection of the operation frequency for IIMDs is receiving considerable attention from the scientific community, as attributed to a number of competing events. The most recent contribution in the field is the Institute of Electrical and Electronics Engineers (IEEE) 802.15.6 standard [IEEE, 2012] which was released by the IEEE in 2012 to deal with short-range, wireless communications in the vicinity of, or inside, the human body. The standard refers to existing industrial, scientific, medical (ISM) bands as well as frequency bands approved by national medical and/or regulatory authorities. According to the standard, an MD shall be able to support transmission and reception in at least one of the following frequency bands: 402.0–405.0, 420.0–450.0, 863.0–870.0, 902.0–928.0, 950.0–958.0, 2360.0–2400.0, and 2400.0–2483.5 MHz. Ultra wide band (UWB) MDs which implement low band (3494.4–4492.8 MHz) or high band (6489.6–9984.0 MHz) channels are also supported.

Table 1 summarizes recent research studies on antenna design for IIMDs operating at various frequencies. It can be seen that the 433.1–434.8, 868.0–868.6, 902.8–928.0 and 2400.0–2500.0 MHz ISM bands are commonly utilized for medical telemetry of IIMDs [ITU-R, 2008], while the global positioning system (GPS) and the wireless medical telemetry service (WMTS) bands have also been reported for implantable and ingestible MDs, respectively. The ISM band of 2400.0–2500.0 MHz is appearing as one of the most promising solutions because of being well-developed in terms of technology (Bluetooth, Wi-Fi, and WLAN), antennas, integrated circuits, and embedded systems. Furthermore, higher operation frequencies allow the use of smaller-sized antennas and components. It is for this purpose that implantable antennas operating at much higher frequencies have also been proposed in the literature, as indicated in Table 1 (5.85 and 31.5 GHz). However, interference issues in the aforementioned bands, which are attributed to the high number of co-located operating services, constitute a limiting factor. Interference may cause harmful effects in terms of false IIMD activation, link-unavailability, and data corruption. To deal with interference issues, focus for implantable MDs is mainly on the 402.0–405.0 MHz band, which has been exclusively allocated for medical implant communications systems (MICS), and is regulated by the European Radiocommunications Committee (Tromso, Norway) [ERC, 1997]. The MICS band is internationally available and feasible with low power circuits, falls within a relatively low noise portion of the spectrum, and allows for acceptable propagation through human tissue. Despite the fact that the MICS recommendation emphasizes on interference mitigation, no signif-

TABLE 1. Operation Frequencies of Designed Antennas for IIMDs

Frequency	References for implantable MDs	References for ingestible MDs
402 MHz	Kim and Rahmat-Samii [2004], Soontornpipit et al. [2004, 2005], Abadia et al. [2009], Chen et al. [2009], Sani et al. [2009], Karacolak et al. [2009], Sanchez-Fernandez et al. [2010], Gemio et al. [2010], Huang et al. [2011], Vidal et al. [2012], Kiourti and Nikita [2012c]	Alomainy and Hao [2009]
433 MHz	Weiss et al. [2009], Gemio et al. [2010], Huang et al. [2011], Kiourti and Nikita [2012c]	Xu et al. [2009a,b, 2010]
500 MHz	—	Yun et al. [2010], Lee et al. [2011]
650 MHz	—	Izdebski et al. [2009]
800 MHz	—	Xu et al. [2009b, 2010]
868 MHz	Sani et al. [2009, 2010], Kiourti and Nikita [2012c]	Alomainy and Hao [2009]
915 MHz	Scanlon et al. [2000], Gemio et al. [2010], Kiourti and Nikita [2012c]	—
1200 MHz	—	Xu et al. [2009b, 2010]
1400 MHz	—	Izdebski et al. [2009], Rajagopalan and Rahmat-Samii [2010]
1575 MHz	Azad and Ali [2009]	—
2400 MHz	Kawoos et al. [2008], Karacolak et al. [2009], Xia et al. [2009], Sánchez-Fernández et al., [2010], Gemio et al. [2010], Huang et al. [2011], Scarpello et al. [2011]	Xu et al. [2009b], Alomainy and Hao [2009], Cheng et al. [2011]
5.85 GHz	Ahmed [2010]	—
31.5 GHz	Ahmed et al. [2008], Ahmed [2010]	—

icant research has appeared so far in the field. Ways of enhancing interference tolerance, which have the potential for further investigation, include: (a) automatic repeat request (ARQ) and forward error correction (FEC) techniques to mitigate the effects of impulsive noise (noise which is very short in duration and often of greater amplitude than the IIMD signal levels), and (b) the use of frequency agility and channelization as a means of avoiding narrow-band interferers (sources with bandwidths comparable to the IIMD signal waveform).

The effect of operation frequency on the performance of IIMDs has additionally been addressed. Single-cell excitation used to simulate vagina [Scanlon et al., 2000] and gastric/bladder/cardiac [Sani et al., 2009] implants has been shown to exhibit increased power absorption, higher net body losses, and reduced penetration depths with increasing frequency. Recently, implantable antennas at higher frequencies were found to achieve enhanced gains (a 10.7% increase in the maximum far-field gain at 915 MHz, compared to the gain at 402 MHz); increased maximum allowable net-input-power levels (10.1% and 1.3% increases imposed by the IEEE C95.1-1999 [IEEE, 1999] and IEEE C95.1-2005 [IEEE, 2005] safety standards, respectively); and more expanded specific absorption rate (SAR) distributions [Kiourti and Nikita, 2012c]. Results were attributed to the authors' choice of keeping the antennas' physical dimensions identical, and modifying their effective size. Studies for ingestible MDs have demonstrated adequate communication to take place between 600 and 1000 MHz [Chirwa et al., 2003a], with maximum radiation occurring between 450 and 900 MHz [Chirwa et al., 2003b], and a peak in the transmitted power being identified at approximately 650 MHz [Chirwa et al., 2003a]. Furthermore, selection of operation frequency is directly related to bit rate: higher operation frequencies allow for an increase in bandwidth and enable higher bit rates, which are favorable for high data rate applications, such as the real-time video transmission of ingestible MDs. For example, the maximum channel capacity for a band-limited additive white Gaussian noise (AWGN) channel is given by:

$$C = BW\, log_2\left(1 + \frac{S}{N}\right), \tag{1}$$

where BW is the channel bandwidth, S is the mean signal power, and N is the mean noise power. Therefore, the MICS band ($BW \leq 300$ kHz) enables low bit rates, the WMTS ($BW = 8.5$ kHz to 6 MHz) and ISM (selectable BW) bands enable medium bit rates, whereas the UWB ($BW > 500$ MHz) is appearing as the most promising solution for high data rates. It is worth noting that according to the recent IEEE 802.15.6 standard [IEEE, 2012], data rates of typically

up to 10 Mbps are required to satisfy evolutionary healthcare services. As for the future, more complex body area networks need to be designed in order to provide the computational functionalities required for high data rate applications.

ELECTRONICS AND POWERING CONSIDERATIONS

Advances in biological, chemical, electrical, and mechanical sensor technologies as well as in micro-electro-mechanical systems (MEMS) have led to a wide range of IIMDs. In principle, picked-up physiological signals need to be further amplified, digitized, and fed to a transceiver which will code and modulate the data, and, finally lead them to the antenna. Example components of implantable and ingestible MDs are shown in Figures 2 and 3, respectively. Size constraints leading to the coexistence of electronic components introduce significant challenges related to the optimal selection and placement of the components so as to enhance isolation and reduce noise. Significant research focus is also on the design of: (a) novel amplifiers which amplify the signal to a usable level and scale it to the operating range of the transceiver while introducing minimum noise, and (b) novel transceivers with advanced data mining and compression techniques that provide high data bit rates at increased distances.

All aforementioned components require power. Integrated power supplies, such as batteries, are suitable for applications where the IIMD lifespan is short. This proves to be an adequate solution for MDs which are intended to be implanted for months or few years (depending on the duty cycle), as well as for ingestible MDs which are designed to be swallowed, move through the intestine, and, finally, be naturally excreted from the human body within a short period of time (up to 32 h) [Wang et al., 2005]. To elongate the battery life of implantable MDs, external power transmission has been proposed for recharging purposes [Kendir et al., 2005]. The technique is based on electromagnetic (EM) induction between an exterior-transmitting and an implantable-receiving coil, which are placed in close distance, and are often wound around a dielectric or ferrite core to improve the efficiency. Furthermore, power scavenging sources including motion, vibration, air flow, temperature difference, light and infra-red radiation have been suggested. For example, a vibration-based generator for implantable MDs, capable of delivering 2 μJ/cycle, has been designed while ambient EM energy harnessing has recently been investigated [Mitcheson et al., 2004]. Such solutions are solicited for implantable MDs which are intended for an implantation period of several years or even a lifetime (cochlear implants for the deaf or retina implants for the blind).

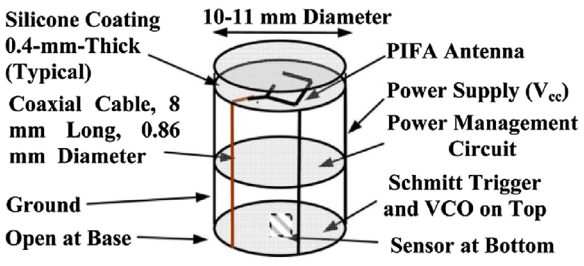

Fig. 2. Example components of an implantable MD for intra-cranial pressure monitoring [Kawoos et al., 2008].

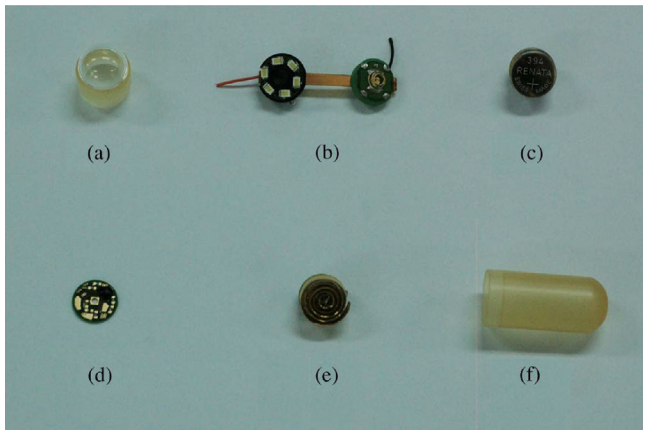

Fig. 3. Example components of an ingestible MD: (**a**) transparent cap, (**b**) LEDs and camera, (**c**) battery, (**d**) RF transmitter, (**e**) antenna, and (**f**) dielectric container [Lee et al., 2011].

To meet potential longevity requirements of the IIMDs and guarantee their on demand availability, power conservation techniques can additionally be applied. Suggested ideas include pre-configured on-off function of the IIMD [Furse, 2009], and transmission/detection of a "wake-up" alarm signal [Karacolak et al., 2008]. In the first case, devices spend most of their time in an ultra-efficient sleep mode followed by short bursts of data transmission. Data mining or compression techniques may be used to reduce the actual bits of data to be transmitted. In the second case, the system uses two frequency bands, one for "wake-up" and one for transmission. The transceiver stays in "sleep mode" with low power consumption until a "wake-up" signal is sensed in one frequency band. In "normal mode," the IIMD is fully powered and exchanges data in the other frequency band. Following the data transfer, the IIMD transceiver returns back to the "sleep mode."

ANTENNA DESIGN AND PERFORMANCE

Antenna Type

Relative position and orientation between an implantable MD and its exterior monitoring/control equipment counterpart is known a priori. As a result, patch designs are most commonly chosen for implantable antennas because they exhibit directive radiation patterns, lend themselves easily to a number of miniaturization techniques and are highly flexible in design, conformability and shape (Fig. 4a). In a realistic scenario, the implantable patch antenna will be mounted on the existing hardware of the implantable MD, which will also serve as its ground plane. Dipole [Kim and Rahmat-Samii, 2004], loop [Chen et al., 2009], monopole [Weiss et al., 2009], modified dipole [Scarpello et al., 2011], and 3D spiral [Abadia et al., 2009] antennas have also been reported for implantation purposes.

In the case of ingestible MDs, wireless transmission is performed while the capsule is traveling along the gastrointestinal (GI) tract. Therefore, ingestible antennas need to be omni-directional and exhibit circular polarization in order to transmit signals independent of their position and orientation which are, in principle, unknown. Given these requirements, normal mode helical antennas (Fig. 4b) are most commonly employed for such applications [Xu et al., 2009a,b, 2010]. Difficulties in modeling miniature helical structures in the presence of anatomical tissue models have been assessed in Koulouridis and Nikita [2004]. Recently, a wideband spiral antenna was presented for ingestible capsule endoscope systems at 500 MHz [Lee et al., 2011]. A thick-arm spiral structure was applied in the design to achieve an isotropic radiation pattern. Outer-wall loop [Yun et al., 2010], conformal chandelier meandered dipole [Izdebski et al., 2009] and patch with complementary split ring resonator loading [Cheng et al., 2011] antennas have also been implemented and reported in the literature.

Since implantable and ingestible antennas are intended for operation inside the tissue of various individuals, it becomes crucial to take into account their sensitivity to (1) the structure of the surrounding tissue environment (anatomical features of the individual) [Sani et al., 2009; Vidal et al., 2012]; and (2) the uncertainties and inter-subject variability of the tissue's dielectric parameters (permittivity and conductivity) [Schmid et al., 2003; Gabriel, 2005]. For example, a numerical study has recently been carried out to quantify such uncertainties for a scalp-implantable MICS antenna to variations in head properties (anatomy and dielectric parameters) [Kiourti and Nikita, 2013]. Five head models (three- and five-layer spherical, 6-, 10-, and 13-tissue anatomical models) and seven dielectric-parameter scenarios (variations by $\pm 20\%$ in the reference permittivity and conductivity values) were considered. Compared with the reference dielectric-parameter scenario within the three-layer spherical-head model, maximum variations of -19.9% and $+3.7\%$ were computed for the maximum allowable net input-power levels imposed by the IEEE C95.1-1999 [IEEE, 1999] and IEEE C95.1-2005 [IEEE, 2005] safety standards, respectively, with maximum variations of -55.1% for the return loss and -39.2% for the maximum far-field gain. Therefore, in both implantable and ingestible antennas, wide impedance bandwidths should be targeted in order to guarantee adequate resonance performance, regardless of such inter-subject variability and uncertainties.

Antenna Size

Dimensions of the traditional half-wavelength ($\lambda/2$) or quarter-wavelength ($\lambda/4$) antennas at the

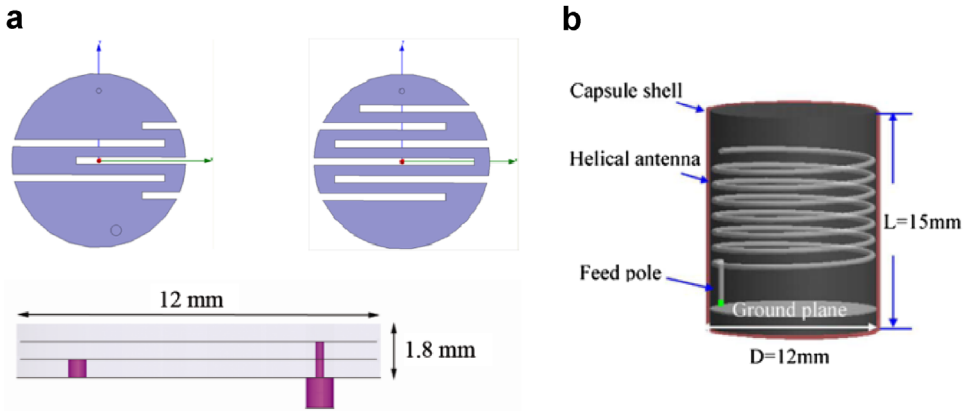

Fig. 4. Example antennas for IIMDs: (**a**) patch implantable antenna [Kiourti and Nikita, 2012c], and (**b**) helical ingestible antenna [Xu et al., 2009a].

frequency bands allocated for IIMDs, and especially at the low-frequency bands, make them useless for implantable and ingestible applications. An implantable or ingestible antenna should be as small as possible so that it can fit inside the IIMD case. For example, an implantable intra-cranial pressure monitor should be small enough to fit in standard 12 mm burr holes in the skull [Warty et al., 2008], whereas the size of a typical ingestible capsule does not exceed the size of a large vitamin (usually less than 11 mm × 30 mm). On the other hand, there are no restrictions about the size of the exterior receiving antennas, unless they are intended to be worn by the patient, in which case patient comfort issues need to be taken into account. Therefore, miniaturization becomes one of the greatest challenges in antenna design for IIMDs.

Recent studies mainly emphasize on the furthest possible miniaturization for implantable antennas. Use of patch designs for implantable antennas allows for several additional miniaturization techniques such as: (a) use of high-permittivity dielectric materials; (b) lengthening of the current flow path on the radiating patch surface (e.g., meandering/spiraling of the conductive patch); (c) addition of shorting pins, or, equivalently, conversion to planar inverted-F antennas (PIFAs); and (d) patch stacking [Kiourti and Nikita, 2012a]. For example, the skin-implantable antenna of Figure 4a adopts a stacked PIFA structure of meandered patches built on Rogers RO 3210 (Rogers, Rogers, CT) substrate to achieve a miniaturized structure (a volume of 214.9 mm^3), resonating in the MICS band [Kiourti and Nikita, 2012c]. A comparison of the volume occupied by skin-implantable patch antennas reported in the literature for medical telemetry in the MICS band with respect to the applied miniaturization techniques is shown in Table 2. Occupied volumes are found to range between 10240 mm^3 (spiral-shaped patch antenna for skin-tissue implantation) [Kim and Rahmat-Samii, 2004] and 121.6 mm^3 (hook-slotted patch antenna with shorting pin for skin-tissue implantation) [Liu et al., 2009].

On the other hand, an ingestible MD needs only to be swallowed, so the size of an easy-to-swallow pill would be adequate. Helical antennas with a radius of 3.5–5 mm and a height of 6–9 mm [Chirwa et al., 2003b; Xu et al., 2009b], as well as on-capsule printed antennas with dimensions depending on the capsule size have been proposed [Izdebski et al., 2009]. Sizes of ingestible antennas reported in the literature are shown in Table 3, along with a brief description of the applied design techniques.

However, it is important to highlight that design of IIMD antennas is considered as highly critical and intriguing owing to the simultaneous requirements for miniaturization, gain increase, and patient safety. Equivalently, the designed antenna must be small enough to be implanted or swallowed, exhibit high gain to allow the transmitted signal to be picked up by the exterior receiver, and conform to international safety standards for the SAR. Therefore, designers of IIMD antennas need to deal with the fact that antenna miniaturization generally comes in expense of its radiation and safety performance. For example, generic results for a skin-implantable antenna placed inside a tissue-simulating cube have indicated degraded gain and SAR performance with a reduction in size. Miniaturization by 32% and 65% has been found to reduce the maximum far-field gain values by 5% and 19%, respectively, and the maximum allowable input powers imposed by the IEEE C95.1-1999 safety standard [IEEE, 1999] by 21% and 44%, respectively. Antenna implantation inside an anatomical head model has qualitatively validated the results, although quantitative deviations were observed, which can be attributed to the difference in antenna loading by the surrounding tissues and exterior air. The significance of application-specific rather than miniaturization-oriented IIMD antenna design is, thus, emphasized.

TABLE 2. Volume and Applied Miniaturization Techniques for Skin-Implantable MICS Patch Antennas Reported in the Literature

		Miniaturization techniques			
Refs	Volume (mm^3)	Permittivity of dielectric material	Patch shape	Shorting pin	Patch stacking
Kim and Rahmat-Samii [2004]	6144.0	10.2	Spiral	Yes	—
Kim and Rahmat-Samii [2004]	10240.0	10.2	Spiral	—	—
Liu et al. [2008a]	190.0	10.2	Spiral	Yes	Yes
Liu et al. [2008b]	149.2	10.2	Hook-slotted	Yes	Yes
Liu et al. [2009]	121.6	10.2	Hook-slotted	Yes	Yes
Sánchez-Fernández et al. [2010]	1375.4	6.1	Spiral	Yes	—
Kiourti and Nikita [2012c]	203.6	10.2	Meandered	Yes	Yes

TABLE 3. Design Techniques and Size for Ingestible Antennas Reported in the Literature

Refs	Frequency (MHz)	Volume (mm^3)	Design	
			Antenna type	Brief description
Chirwa et al. [2003b]	150, 300, 434, 600, 800, 1000, 1200	201.1	Helical	4 turns, radius of 4 mm, pitch of 1 mm
Izdebski et al. [2009]	1400	—	Conformal	Conformal capsule antenna attached to the external capsule cell (freq.: 1.4 GHz)
Xu et al. [2009b]	430	471.2	Helical	6 turns, radius of 5 mm, pitch of 1 mm
	800	169.6	Helical	6 turns, radius of 3 mm, pitch of 1 mm
	1200	351.9	Helical	7 turns, radius of 4 mm, pitch of 1 mm
	2400	346.4	Helical	9 turns, radius of 3.5 mm, pitch of 1 mm
Yun et al. [2010]	500	—	Printed	Full-wavelength meandered loop with symmetric pattern with respect to capsule center
Lee et al. [2011]	500	392.7	Thick-arm spiral	Spiral arm with a thickness of 0.5 mm
Cheng et al. [2011]	2400	—	Folded patch	Folded patch with complementary split-ring resonator (CSRR) loading

Biocompatibility

IIMDs (antennas and electronics) must be biocompatible so that they do not harm the patient and cause rejection of the implant. Furthermore, human tissues are conductive, and would short-circuit the implantable or ingestible antenna if they were allowed to be in direct contact with its metallization.

In the case of implantable antennas, the requirement for biocompatibility entails encapsulation inside a thin layer of low-loss biocompatible coating, and/or, in the case of patch antennas, use of biocompatible substrates and addition of a biocompatible superstrate dielectric layer to cover the metal patch on top. Commonly used materials for biocompatible encapsulation include zirconia ($\varepsilon_r = 29$, $\tan\delta = 0.05$), polyetheretherketone (PEEK) ($\varepsilon_r = 3.2$, $\tan\delta = 0.01$), polydimethylsiloxane (PDMS) ($\varepsilon_r = 3$, $\tan\delta = 0.005$), Silastic MDX-4210 Biomedical Grade Base Elastomer (Dow Corning, Midland, MI) ($\varepsilon_r = 3$, $\tan\delta = 0.001$), and parylene ($\varepsilon_r = 2.95$, $\tan\delta = 0.005$) [Kiourti and Nikita, 2012a], while biocompatible substrate/superstrate materials include macor, teflon, and ceramic alumina [Soontornpipit et al., 2004]. Because of its electrical properties, zirconia is a better candidate material for biocompatible insulation from an electromagnetic point of view. High permittivity and low loss-tangent values allow the near fields of the antenna to concentrate inside the low-loss encapsulation layer, thus mitigating power loss. However, easiness of preparation and handling must also be taken into account. Furthermore, thickness of the biocompatible insulation layer is an important factor in antenna design. Computation of its optimum thickness is, thus, considered to be highly significant for lowering power loss without aimlessly increasing antenna size. Addition of an insulation coating or superstrate layer significantly affects the performance of the antenna, and, thus, needs to be taken into account within the design. Furthermore, a biocompatible hermetic package is necessary for housing the electronics, which may be made of low temperature co-fired ceramic (LTCC), parylene, liquid crystal polymer (LCP), silicon, or alumina [Chow et al., 2010].

Biocompatibility for ingestible helical antennas is most commonly accomplished by packaging the antennas inside a biocompatible shell [Wang et al., 2005; Xu et al., 2009a,b]. Capsule casings have been found to have a negligible effect on the performance of the ingestible antenna [Chirwa et al., 2003b]. Therefore, taking the effects of casing into account while modeling the antenna is not required.

Influence of the Human Body

The fact that antennas for IIMDs are intended to operate inside biological tissue rather than in free space affects their design and performance in a number of ways. So far, research interest in this area has mainly been oriented towards: (a) development of fast and accurate methodologies for implantable antenna design, and (b) studies on the effect of position and orientation of ingestible antennas within the body.

Given the presence of the human body, design of implantable antennas should be performed either inside free space and further refined for tissue implantation, or directly inside an environment surrounded by human tissue. Suggested techniques include: (a) antenna design in free space, and further

refinement inside an anatomical model of the intended implantation site by means of a tunable varactor diode [Rucker et al., 2007]; (b) antenna design in free space targeting at high gain values, and further refinement inside a single-layer tissue model simulating the intended tissue properties [Abadia et al., 2009]; (c) antenna design directly inside a single-layer tissue model (cubical, rectangular parallelepiped or cylindrical) of the intended implantation tissue [Kiourti and Nikita, 2012b]; (d) approximate antenna design inside a cube filled with the intended tissue material, and further Quasi-Newton optimization inside a canonical model of the intended implantation site [Kiourti and Nikita, 2012c]; and (e) antenna design inside a small-sized single- or multi-layer tissue box [Kiourti and Nikita, 2012d]. Numerical results inside small-sized tissue boxes have been found to be almost identical to those inside canonical models of the intended implantation site, thus, rendering design directly into the latter unnecessary and inadequately slow. As already demonstrated by the authors, canonical tissue models are equally suitable to anatomical ones for assessing the performance of implantable antennas. Therefore, effectiveness can be assessed within canonical models of the intended implantation site, in an attempt to simplify and speed-up simulations. The aim is to minimize the use of required computational resources, or, equivalently, the required simulation time, towards designing implantable antennas optimized for specific medical implantation scenarios. Incorporation of the dielectric loading of the surrounding tissues and exterior air in the design, and use of canonical, small-sized tissue models have been found to form the optimum solution for design purposes. On the other hand, design of ingestible antennas is generally performed directly inside the capsule shell in which they are intended to operate [Izdebski et al., 2009; Xu et al., 2009a,b].

Unlike implantable antennas, position and orientation of ingestible antennas within the human body is variable. Such issues have been investigated by carrying out simulations for several antenna positions and orientations within the human body, as summarized in Table 4. Results show that antenna performance varies greatly with position and orientation, with position affecting the results more compared to orientation. Anatomy around the gut region highly affects the exhibited EM field, while radiation characteristics differ significantly according to the distance between the ingestible antenna and the outer surface of the body [Chirwa et al., 2003b]. For example, antenna positioning at the front-most and back-most locations of the small intestine has shown to exhibit maximum and minimum electric intensities outside the human body, respectively. For the majority of positions, vertically polarized radiation has been found to attenuate more than horizontal radiation [Chirwa et al., 2003b], and intensity of the electric field in the anterior of the human body has been shown to be, generally, higher than that in the posterior [Xu et al., 2009b]. In Chirwa et al. [2003a], the radiated field was found to be predominantly strongest in the same horizontal transverse plane as the source, and in the direction that was on the line from the source to the nearest body surface. Therefore, the optimum location for a receiver antenna would be an anterior location slightly to the left of the abdomen (as the small intestine does not extend so much to the right due to the presence of the colon). Overall, it has been demonstrated that if the motion of the ingestible antenna inside the GI tract could be controlled, then the quality of communication would be improved by, at least, 3 dB [Xu et al., 2009b].

Patient Safety

It was not until recently that research on the biological effects of IIMDs started being carried out. The SAR (rate of energy deposited per unit mass of tissue) is generally accepted as the most appropriate dosimetric measure, and compliance with the ICNIRP [1998] and IEEE [1999, 2005] standards is assessed [Lin, 2003a,b; Lin, 2006]. The ICNIRP [1998] basic restrictions limit the SAR averaged over 10 g of contiguous tissue to less than 2 W/kg. The IEEE C95.1-1999 standard [IEEE, 1999] restricts the SAR averaged over any 1 g of tissue in the shape of a cube to <1.6 W/kg. To harmonize with the ICNIRP guidelines, the IEEE C95.1-2005 standard [IEEE, 2005] restricts the SAR averaged over any 10 g of tissue in the shape of a cube to less than 2 W/kg.

Contrary to exterior or on-body antennas, high local SAR values are achieved for implantable and

TABLE 4. Studies on the Effect of Position and Orientation of Ingestible MDs

		Antenna		
Refs	Anatomical tissue model/tissue types	Type	Positions	Orientations
Chirwa et al. [2003b]	Male/25	Helical	5 (small intestine)	3 (X, Y, Z)
Xu et al. [2009b]	Female/34, male/23	Helical	7 (GI tract)	3 (X, Y, Z)

ingestible antennas, which need to be considered carefully due to higher local energy depositions. A number of safety evaluation studies have been performed for implantable and ingestible antennas. The IEEE C95.1-1999 standard has been found to be much stricter than the recent IEEE C95.1-2005 standard [Kiourti and Nikita, 2012c], whereas the latter has shown to be almost insensitive to changes in the tissue model properties (anatomical features and dielectric parameters) [Kiourti and Nikita, 2013]. Example maximum allowable input power levels reported in the literature are shown in Table 5.

The power absorbed by the human body from an incident EM field is given by:

$$P_{\text{abs}} = \frac{1}{2}\int \sigma |E|^2 \mathrm{d}V, \tag{2}$$

where σ is the conductivity of the human tissues, and $|E|$ is the intensity of the electric field inside the body. Absorbed power is, thus, related to the electric field, so that maximum SAR values are recorded in the areas where maximum electric field intensities occur. Based on this deduction, novel antennas can be designed aiming at lower electric field intensities. Such an attempt has already been performed in the field of implantable antennas, where replacement of a uniform-width spiral radiator with a non-uniform width radiator has shown to decrease the electric field intensity and, in turn, SAR. Similar techniques may also appear as promising in the field of ingestible antenna design.

Finally, it is important to highlight that, in the case of ingestible antennas, temperature rise in human tissues induced by the radiated EM fields has also received considerable attention. Numerical calculations are based on the bio-heat equation [Pennes, 1948] which incorporates parameters such as thermal conduction, metabolic heat generation, EM energy deposition, heat exchange through blood flow into various tissues, and heat dissipation at the surface of the numerical model. Results have shown high values of temperature rise to be localized at the area near the ingestible MD. However, even in the cases of maximum SAR values, temperature rise maxima remain adequately low [Xu et al., 2009b]. Only preliminary investigations have been performed in assessing the temperature increase induced by implantable antennas. Temperature elevations for a generic active implant have indicated that compliance with the basic safety restrictions might not be sufficient for patients with implants, and that special considerations might be required [Kyriakou et al., 2012].

WIRELESS CHANNEL MODELING

Modeling the medical telemetry channel between IIMDs and exterior monitoring control equipment is a highly challenging task. Unlike free-space propagation, the various tissues and organs within the body have their own unique electrical characteristics, the lossy medium absorbs EM energy, and the presence of objects causes EM field refraction, diffraction, reflection and absorption. So far, limited research has been reported in the area of developing propagation models inside the human body, and channel modeling has mostly been conducted for particular scenarios with specific antennas and orientation. A summary of reported studies is presented in Table 6. Studies for implantable MDs may be summarized as follows. When far-field conditions are fulfilled inside a free-space environment, then a free-space propagation model can be assumed to calculate the link-budget, or, equivalently, the power received by the exterior

TABLE 5. Maximum Power Levels for Compliance with Safety Standards (ICNIRP [1998], IEEE C95.1-1999 [1999], and IEEE C95.1-2005 [IEEE, 2005])

IIMD	Refs	Frequency (MHz)	Safety standard	Power level (mW)
Implantable	Kim and Rahmat-Samii [2004]	402	IEEE C95.1-1999	8.791
	Huang et al. [2011]	402	IEEE C95.1-1999	4.692
	Kiourti and Nikita [2012c]	402	IEEE C95.1-1999	4.927
			IEEE C95.1-2005	30.02
		433	IEEE C95.1-1999	5.166
			IEEE C95.1-2005	3.13
		868	IEEE C95.1-1999	5.388
			IEEE C95.1-2005	30.28
		915	IEEE C95.1-1999	5.426
			IEEE C95.1-2005	30.41
Ingestible	Xu et al. [2009a]	430	ICNIRP	56.05
			IEEE C95.1-2005	12.66
	Xu et al. [2009b]	430	ICNIRP	36.00
			IEEE C95.1-2005	11.00

TABLE 6. Reported Studies for Modeling the Wireless Channel of IIMDs

IIMD	Refs.	Antenna	Environment	Channel modeling
Implantable	Gupta et al. [2003]	Hertzian dipole	Near-field, in-body	$P_r = \frac{16\delta(P_t - P_{NF})}{\pi L^2} A_e$ (P_{NF} is given in Gupta et al. [2003])
	Gupta et al. [2003]	Hertzian dipole	Far-field, in-body	$P_r = \frac{(P_t - P_{NF} - P_{FF})\lambda^2}{(4\pi d)^2} G_t G_r$ (P_{NF}, P_{FF} are given in Gupta et al. [2003])
	Sani et al. [2009, 2010], Gemio et al. [2010]	Point source simple dipole RFID	Far-field, free-space	$P_r = P_t \cdot (1-\lvert S_{11}\rvert^2) G_t \left(\frac{\lambda}{4\pi d}\right)^2 G_r (1-\lvert S_{22}\rvert^2)$
	Sani et al. [2009, 2010]	Point source RFID	Far-field, indoor	$P_r = (P_t G_t G_r)/PL$, where $\mathrm{PL}(d)[\mathrm{dB}] = 10n \log\left(\frac{d}{d_{ref}}\right) + \mathrm{PL}(d_{ref})[\mathrm{dB}]$
Ingestible	Alomainy and Hao [2009]	Monopole	In-body	$P_r = (P_t \cdot G_t \cdot G_r)/PL$, where $\mathrm{PL}(d)[\mathrm{dB}] = 10n \log\left(\frac{d}{d_{ref}}\right) + \mathrm{PL}(d_{ref})[\mathrm{dB}] X_{\sigma_s}$
	Rajagopalan and Rahmat-Samii [2010]	Dipole/capsule	Free-space, in-body	$P_r = P_t \cdot G_t \left(\frac{\lambda}{4\pi d}\right)^2 G_r$
	Lee et al. [2011]	Spiral	In-body	$P_r = P_t G_t \left(\frac{\lambda}{4\pi d}\right)^2 G_r (e^{-\alpha R})^2$ where $\alpha = \mathrm{Re}(\gamma) = \mathrm{Re}\left(j\omega\sqrt{\mu\varepsilon_r}\sqrt{1-j\frac{\sigma}{\omega\varepsilon_r}}\right)$

$|S_{11}|/|S_{22}|$, reflection coefficient of the transmitting/receiving antennas; P_t/P_r, transmitted/received power; G_t/G_r, gain of the transmitting/receiving antenna; d, distance between transmitter and receiver; PL, path loss; d_{ref}, reference distance; n, factor indicating the degree of power decay with distance; P_{NF}/P_{FF}, loss in the near/far field, $\delta = A_e/A$ with A_e the effective aperture and A the physical aperture of the antenna; L, largest dimension of the antenna; ε_r/σ, permittivity/conductivity values of the medium; and X_σ: zero—mean Gaussian distributed random variable with standard deviation σ_ε.

equipment can be calculated using the Friis formula [Sani et al., 2009, 2010; Gemio et al., 2010]. In an indoor environment, where the transmitted signal reaches the receiver via more than one path due to reflections, diffraction, and scattering of the EM waves, the log-distance model has been suggested instead [Sani et al., 2009, 2010]. However, in estimating the propagation loss for wireless transmission inside the human body, changing the loss coefficient of the free-space formula, will only change the rate of decrease in power, and will not help in estimating the total loss in the form of absorption. A propagation loss model (PMBA) for homogeneous tissue bodies has been reported in Gupta et al. [2003], which calculates the received power as being decreased more rapidly than free-space loss. For example, the PMBA calculates an additional 30–35 dB of attenuation at small distances in the far-field, compared to free space. It is important to highlight that even though the PMBA applies only in the case of small dipole implantable antennas, power loss formulas for similar applications with other antennas could be derived in a similar way.

Channel modeling of ingestible MDs differs in two senses: the ingestible MD is placed deeper inside the body so that surrounding tissues and organs affect its performance in a more substantial way, while position and orientation of the MD, and, thus, the wireless channel, change with time. In the literature, there have been performed only limited research studies, which can be summarized as follows. In [Rajagopalan and Rahmat-Samii, 2010], the antenna along with the body have been assumed to act as a transmitter, and the signal to noise ratio has been calculated by using the free-space Friis formula. Emphasis has been given on quantifying the link for different orientations, given the random movement of the capsule system inside the body. The Friis transmission equation inside a lossy medium has been used in [Lee et al., 2011] to calculate the link-budget for ingestible antennas. Finally, in [Alomainy and Hao, 2009], the average path loss has been expressed as proportional to the inter-antenna distance raised to the path loss exponent value (calculated as 1.90–2.80). The path loss observed at any given point has been considered to deviate from this average value due to variations in the environment, according to a log-normal distribution.

FULL-SOLUTIONS OF COMMERCIAL IIMDs

A number of commercial IIMDs have recently been reported, as shown in Table 7. Defibrillators and pacemakers are the most common examples of implantable MDs. Biotronik has recently proposed a

TABLE 7. Example Full—Solutions of Commercial IIMDs

IIMD	Commercial IIMD	Function of the IIMD
implantable	Biotronik Lumax	Defibrillator
	Medtronik Adapta with MVP	Pacing system
	Medtronik Revo MRI SureScan	Pacing system for magnetic resonance imaging
	VeriChip/Positive ID	Identity verification
	Nucleus Freedom Cochlear	cochlear implant
	Medtronik SynchroMed Pump	Drug infusion system
	Second Sight Argus II	Retinal prosthesis
	Medtronik Guardian REAL-Time	Glucose monitor
	Abott Free Style Navigator	Glucose monitor
	DexCom SEVEN Plus	Glucose monitor
	Medtronik MiniMed Paradigm Neo	Glucose monitor
Ingestible	Given Imaging PillCam	Small bowel endoscope
	Olympus EndoCapsule	Small bowel endoscope
	Intromedic MiroCam	Small bowel endoscope
	Chongqing OMOM	Gastrointestinal disease diagnosis
	RF System Lab Sayaka	Image capturing of the digestive tract
	Awaiba Nan Eye	Endoscope imaging
	Medtronik Bravo pH	pH sensing of the esophagus
	Given Imaging SmartPill	pH, pressure and temperature sensing of the gastrointestinal tract
	Philips Intellicap	Drug delivery to the gastrointestinal tract

small battery-powered electrical impulse generator to be implanted in patients who are at risk of sudden cardiac death due to ventricular fibrillation and ventricular tachycardia (Lumax 540 DR-T) [Biotronik, 2012]. The Medtronik Adapta with MVP pacing system offers managed ventricular pacing, atrial therapy, ventricular capture, and remote cardiac telemetry [Medtronik, 2010a], whereas the Medtronik Revo MRI SureScan pacing system is magnetic resonance (MR) conditional designed to allow patients to undergo magnetic resonance imaging (MRI) under the specified conditions of use [Medtronik, 2011a]. VeriChip (renamed to PositiveID in 2010) was the only human-implantable microchip to receive approval by the Food and Drug Administration (FDA) in 2004 [PositiveID, 2004]. The device was typically implanted between the shoulder and elbow of the individual, and, once scanned, it replied with a unique 16-digit number, which could be used to retrieve personalized information, for example, identity verification, medical records, etc. However, privacy concerns generated controversy and debate, and marketing was discontinued in 2010. The Nucleus Freedom cochlear implant includes a sound processor which is worn behind the ear, and a cochlear implant which is placed under the skin, behind the ear [Nucleus Freedom, 2010]. The sound processor captures sounds, digitizes them, and sends the digital code to the implant. The implant converts the digitally coded sound to electrical impulses and sends them along an electrode array to further stimulate the cochlea's hearing nerve. The Medtronik SynchroMed Pump is a drug infusion system, which provides precise drug delivery for chronic therapy of severe spasticity [Medtronik, 2012]. In addition to the implanted pump, the system uses a catheter to deliver programmed amounts of intrathecal baclofen to the intrathecal space and cerebrospinal fluid. The Argus II retinal implant was approved by FDA's Ophthalmic Devices Advisor Panel in 2012 [Second Sight, 2012]. It includes a video camera, a transmitter mounted on a pair of eyeglasses, a video processing unit and a 60-electrode implanted retinal prosthesis that replaces the function of degenerated cells in the retina. Although it does not fully restore vision, this setup can improve a patient's ability to perceive images and movement. Finally, implantable glucose monitoring systems appear as a promising treatment for diabetes on a continuous basis (e.g., Medtronik Guardian REAL-Time [Medtronik, 2010b], Medtronik MiniMed Paradigm Veo [Medtronik, 2011b], Dexcom SEVEN Plus [Dexcom, 2008], Abbott FreeStyle Navigator [Abbott, 2011]). A tiny sensor is inserted under the skin to measure glucose levels, and further transmits this information to an exterior monitor via radio waves.

Commercial ingestible MDs are used for capsule endoscopy, which allows for direct, noninvasive visual examination of the gastrointestinal (GI) tract. Images are transmitted from a disposable, ingestible wireless video capsule and are further downloaded for review. In 2000, the introduction of low-power, complementary metal oxide semiconductor-based (CMOS-based) image sensors and application-specific integrated

TABLE 8. Comparison of Selected Commercial Ingestible MDs

Model	Given Imaging PillCam	Olympus EndoCapsule	Intromedic MiroCam	RF System Lab Sayaka	Philips IntelliCap
Size	11 mm × 26 mm	11 mm × 26 mm	11 mm × 24 mm	9 mm × 22 mm	11 mm × 26 mm
Weight	3.45 g	3.8 g	3.25 g	—	?
Operative region	Small intestine	Small intestine	Small intestine	Entire gastrointestinal tract	Low gastrointestinal tract
Operating frequency	433 MHz	433 MHz	Body transmission	—	?
Camera	CMOS	CCD	—	CCD	No
Resolution	256 × 256 pixels	320 × 320 pixels	320 × 320 pixels	—	—
Frame rate	2 frames/s	2 frames/s	3 frames/s	30 frames/s	—
Illumination	4–6 white LEDs	6 white LEDs	6 white LEDs	4 LEDs	No
Field/depth of view	156°/–	145°/0–20 mm	170°/0–30 mm	—	—
Motion	Peristalsis	Peristalsis	Peristalsis	Peristalsis	Peristalsis
Sensors	No	No	No	Fluorescent LEDs	pH, temperature
Actuators	No	No	No	Rotating system	Fluid pump, drug reservoir
Power source	Battery (8 h)	Battery (8 h)	Battery (12 h)	—	Battery (—)

CMOS, complementary metal oxide semiconductor; CCD, charge coupled device.

circuits (ASICs) made the video capsule possible. Capsules are mainly composed of a CMOS image sensor, light emission diodes (LEDs) for illumination, a miniature video transceiver of sufficient output power, a microcontroller unit (MCU), a cell battery, and optional sensors. They travel through the small intestine via normal muscle contractions, with pictures and data being wirelessly transmitted to a patient-worn receiving device. Up until 2007, wireless endoscopic capsules were only developed by Given Imaging [2012a]. However, after 2007, other companies, such as Olympus [2012] and Intromedic [2012] made significant improvements in their own endoscopic capsules. Most of the capsules are intended for visualization, monitoring, and diagnosis of small bowel abnormalities, such as obscure GI bleeding, iron deficiency anemia and Crohn's disease [RF System Lab, 2001; Li et al., 2008; Awaiba, 2012]. However, there exist capsules with integrated sensor technology which are able to measure pH, temperature and pressure parameters from within the entire GI tract [Medtronik, 2010c; Given Imaging, 2012b]. Recently, Philips marketed the Intellicap ingestible device which performs targeted delivery of pharmaceutical drugs and biological to the GI tract [Philips, 2008]. A comparison of selected commercial ingestible MDs is provided in Table 8, in terms of technical specifications.

CONCLUSION

IIMDs with wireless telemetry functionalities appear as a highly promising option towards improving the patients' quality of life and providing medical systems with constant availability, context-awareness, reconfigurability and unobtrusiveness. Significant scientific efforts have been carried out to deal with issues for IIMDs related to operation frequency selection, electronics and powering, antenna design and performance, and modeling of the wireless channel, with a number of challenges being highlighted for future research. With rising healthcare costs, an aging population, a growing acceptance of home-based medical monitoring and advances in supporting technology, IIMDs are gaining a continually increasing interest in both academia and industry.

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