Long term *in vitro* stability of fully integrated wireless neural interfaces based on Utah slant electrode array

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We herein report *in vitro* functional stability and recording longevity of a fully integrated wireless neural interface (INI). The INI uses biocompatible Parylene-C as an encapsulation layer, and was immersed in phosphate buffered saline (PBS) for a period of over 150 days. The full functionality (wireless radio-frequency power, command, and signal transmission) and the ability of INI to record artificial action potentials even after 150 days of PBS soaking without any change in signal/noise amplitude constitutes a major milestone in long term stability, and evaluate the encapsulation reliability, functional stability, and potential usefulness for future chronic implants. © *2010 American Institute of Physics*. [doi:10.1063/1.3318251]

There has been a growing interest to develop biomedical implants for use, e.g., in neuroprosthetics that can provide an electrical interface to the human nervous system and to allow treatment of patients with neurodegenerative diseases, sensory, or movement dysfunctions.[1–3] One example of such a device is the 100-electrode neural interface based on the Utah slant electrode array (USEA), designed to record/stimulate signals from peripheral nerves.[4,5] The device is a modification of the Utah electrode array, the only penetrating multichannel array today available in the Food and Drug Administration approved version for use with human patients. One of the most significant challenges for implanted neural interfaces is the percutaneous connector, which is likely to cause infections during chronic use. To eliminate the wired connections significant research efforts have been put into the development of fully integrated wireless neural interfaces (INI).[6–8] These implantable INI must be designed to eventually function *in vivo* for years. The failure of chronic neural implants can occur due to both physiological reasons as well as failure of the encapsulation, leading short circuits, delamination of films, or corrosion of contacts and interconnects, rendering the active and passive electronic components in the device nonfunctional or destroying them permanently. The challenges have lead to the development/investigation of various encapsulation materials: polyimide, parylenes, Si_3N_4, *a*-SiC, diamondlike carbon, and historically known silicones.[9–14] The hermiticity verifications are based on electrical leakage, impedance, transport rates for H_2O and ionic species, dissolution rates from IR spectra.[11,13,14] However, a single material that can satisfy biocompatibility and all the aforementioned criteria, and can protect the electronic circuitry of INI from the harsh *in vivo* environment is difficult to find. Parylene-C is a biologically inert polymer capable of being deposited in conformal nanoscale layers and is easily patternable to expose the electrode tips for sensing, making it a viable material for the implant encapsulation.[11,14–16] The impedance and leakage on the interdigitated electrodes (IDEs) in phosphate buffered saline (PBS) have shown that encapsulation and insulation properties of Parylene-C are stable for more than one year.[11] However, in a fully integrated device the variation in the geometry (topography due to capacitor, inductive coil, etc.), and several additional processing steps (flip chip bonding, interconnects, and tip deinsulation) that are not involved in IDEs can alter the diffusion rates of PBS and invalidate the failure prediction for a chronic implant.

Here, we report the long term *in vitro* functional stability and recording longevity of fully integrated and encapsulated USEA/INI-R5 (integrated neural interface-recording version 5) systems (will be designated as U5 throughout). *In vivo* wireless recording of neuronal data using U5 has been recently demonstrated in an acute experiment.[17] The U5 employed Parylene-C as an encapsulation layer and was immersed in PBS for a period of over 150 days. The U5, while being soaked was powered and configured wirelessly through 2.765 MHz inductive link and the transmitted frequency shift keying (FSK) modulated radio-frequency (RF) (900 MHz Industrial, scientific, medical-ISM band) signal was also recorded wirelessly as a function of soak time. The full functionality together with the ability to track artificial neural signals for >150 days of PBS soak provides a measure of the encapsulation reliability, and the functional stability in the INI that has not been reported previously in wireless implantable devices.

For the fully integrated system, the INI-R5 integrated circuit capable of amplifying, digitizing, and transmitting neural signals out wirelessly was flip-chip bonded to the USEA. The details of the system integration are described elsewhere.[8,18,19] Silquest A-174 silane (GE silicones) was vaporized on the U5 as an adhesion promoter prior to Parylene-C coating. Parylene-C film (6 μm) was chemically vapor deposited using Paratech 3000 labtop deposition system (Paratech Coating, Inc.).[11] The electrode tips for sensing were de-insulated by exposing the tips (30–50 μm) with an aluminum foil mask followed by a dc pulsed oxygen plasma. Custom made transmit coil that uses a class E power ampli-

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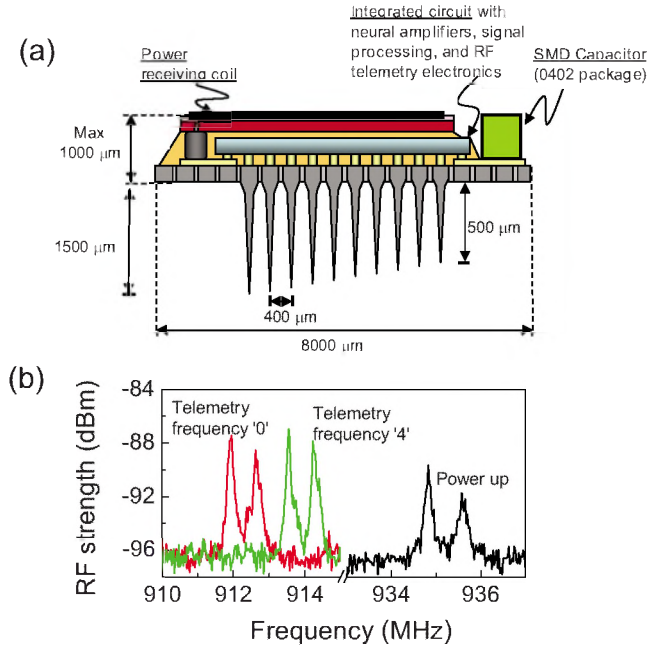

FIG. 1. (Color online) (a) Schematic of the fully integrated U5 device. (b) FSK modulated RF spectra transmitted wirelessly from U5 in PBS upon power up, and command telemetry frequency "0" and telemetry frequency "4".

fier to create a 2.765 MHz waveform of up to 80 V_{rms} from a 10 V supply was used to deliver the power. The resulting ac magnetic field was inductively coupled to the receiving coil present in the U5 and was supplied to the chip in the INI. The transmitted RF spectra were measured on spectrum analyzer (Agilent E4402B). PBS (1% NaCl) in a covered glass Petri dish with 11 mm depth was used for long term soak testing (PBS depth was maintained at constant level). For generating the artificial neural signals, Grass SD-9 pulse stimulator was used.

Figure 1(a) shows the schematic of U5 device used for the long term stability in PBS. First, the initial bench-top testing was performed to check the wireless power/command reception and responsiveness to change the telemetry frequency in PBS. Figure 1(b) shows the RF spectra transmitted wirelessly from the U5 device in PBS that was measured using the monopole antenna connected to the spectrum analyzer. Upon reception of the wireless inductive power, the RF signature appeared with peak at 934.8 MHz and signal strength of −89 dBm was measured at 8 cm distance from the device. The chip in the INI contains an 8-bit register that can take a value between "0" and "255" and sets the command transmitter frequency in the range of 902–928 MHz (ISM band).[8] The responsiveness of the INI to the commands for two different telemetry frequencies ("0" and "4") are depicted in Fig. 1(b) to show the full functionality of the INI in PBS. The strengths of the transmitted RF signal for the two telemetry frequencies are close to −87 dBm. The FSK modulated RF signal was also analyzed on a custom-developed wireless receiver board which displays the frequency and signal strength, and decodes the real time information in the MATLAB to a personal computer through the universal serial bus interface. Table I shows the wireless FSK signal characteristics measured using the receiver board (corresponding measurements from spectrum analyzer are also shown for comparison). The wireless receiver measured the

TABLE I. FSK modulated wireless RF signal characteristics of U5 measured in PBS using a custom-developed wireless receiver and the spectrum analyzer, when antenna was placed at 8 cm from the device.

Soak time	Telemetry frequency	RF signal using wireless receiver (MHz, dBm)	RF signal using spectrum analyzer (MHz, dBm)
$t=0$	"0"	911.2, −57	911.9, −87.4
	"4"	912.5, −59	913.5, −86.9
$t=150$ days	"0"	910.6, −57	910.8, −80
	"4"	912.5, −57	912.6, −81

RF signal for the telemetry frequency "0" at 911.2 MHz with strength of −57 dBm at 8 cm from the device. The discrepancies between the signal strengths measured by receiver board and the spectrum analyzer can be expected because of two different antenna-receiver systems.

In order to study the long term functionality of the INI in PBS, the FSK modulated RF signal for telemetry frequency "0" that corresponds to 911.2 MHz was monitored as a function of soak time. Figure 2(a) shows the peak RF signal strength and the respective frequency as a function of soak time that were extracted from the spectra measured on the spectrum analyzer. For clarity, the extracted values are presented for every after 1 h, although the RF spectra were measured every after 20 min. (as depicted in the inset for few consecutive intervals). Corresponding measurements using the wireless receiver board are shown in Fig. 2(b). It can be seen from Figs. 2(a) and 2(b) that the RF functionality of the INI is maintained in PBS even after 150 days. The variation in the RF strength and the frequency lies within 12% and 0.2% of the initial values, respectively. The RF signal strength and the corresponding frequency for PBS soak time $t=0$ and 150 days for two telemetry frequencies ("0" and "4") are compared in Table I. The INI device continued to receive power and commands, and transmitted RF signature even after 150 days of soaking in PBS at RT.

In order to test the long term recording ability of the electrodes in U5 that was soak tested, *in vitro* wireless recording was performed in agarose for few channels at time $t=0$, 108, and 150 days of PBS soaking. The INI was inserted into agarose gel in a petri dish and the artificial neural

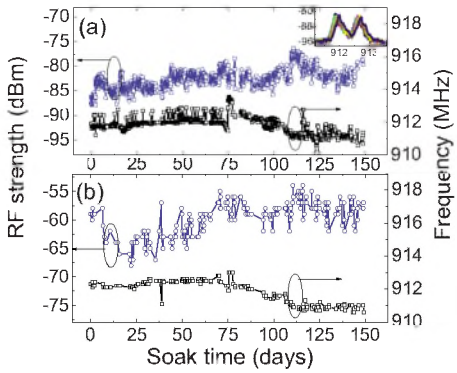

FIG. 2. (Color online) Transmitted wireless RF signal monitored for the telemetry frequency "0" as a function of soak time in PBS. (a) Peak RF signal strengths and the respective frequencies as extracted from the spectra measured using the spectrum analyzer (inset shows few consecutive RF spectra at 20 min intervals). (b) RF signal strengths and the respective frequencies as monitored on custom-developed wireless receiver board.

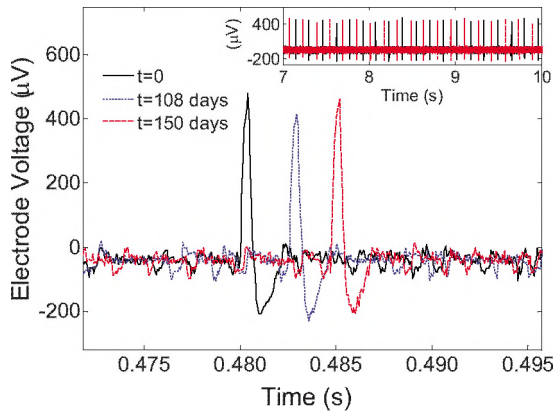

FIG. 3. (Color online) *In vitro* wirelessly recorded artificial action potentials from one channel at time $t=0$ (continuous line), at soak time $t=108$ days (dotted line), and at soak time $t=150$ days (dashed line). Inset shows the recording of the artificial action potentials at $t=0$, and at soak time $t=150$ days at different time scale.

signals were introduced into the agarose. The input signal consisted of a biphasic cyclic pulse of 2 V peak-to-peak (V_{pp}) with a frequency of 6 pulses/s (0.4 ms duration). The agarose impedance measured between the testing probe and the reference Pt electrode separated at 8 cm distance was 5 kΩ at 1 kHz frequency (10 nA current signal). During recordings, the probes for injecting the signal into agarose were also separated by 8 cm for maintaining the similar impedance and consistence voltage drop (for micrometer lengths, the voltage will be dropped to a few millivolt). Figure 3 shows the real time wirelessly recorded artificial action potentials from one channel at $t=0$ and after soaking the device in PBS for $t=108$ and 150 days. The inset compares the recording of the artificial action potentials (for soak time $t=0$ and 150 days) at different time scale. The V_{pp} of the action potential waveform that was wirelessly recorded at $t=0$, soak time $t=108$ days, and soak time $t=150$ days is 684, 646, and 670 μV, respectively. The variance in the recorded V_{pp} within 5% (with similar noise levels) indicates that the long term soaking did not influence the tip deinsulated areas of the electrodes. Similar long term recoding ability was observed for few other channels (not shown here). These *in vitro* recordings indicate that for a given channel the ability to track the artificial action potential is maintained even after 150 days of PBS soak.

In conclusion, *in vitro* functional stability and recording longevity of fully integrated and encapsulated wireless neural interface device was investigated. The device was fully functional together with the ability to track artificial action potentials even after 150 days soaking without significant change in the transmitted RF signal strength and the recorded signal/noise amplitude. These *in vitro* results provide a measure of the encapsulation reliability, functional stability, and the recording longevity in the INI. The stability of the INI in PBS over five months potentially evaluates the stability in real physiological environment, and the usefulness of wireless neural interface for future chronic implants.

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