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A flexible polyimide cable for implantable neural probe arrays

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Abstract A flexible polyimide cable developed for implantable neural probe array application is presented. The flexible cable is used to connect two implantable platforms—one in direct touch with the brain containing a neural probe array and its interface IC, and the other on the skull including a wireless link IC, a coil and an antenna for power and data transfer through the transcutaneous link. The cable needs to be highly flexible to minimize post-insertion injury caused by the probe array in the presence of brain micro-motion. Polyimide is used to form a flexible substrate and an insulator layer of the cable. For the advanced neural recording system, a large amount of neural recording data has to be communicated between the two platforms through the flexible cable. High-rate data transmission performance of the fabricated flexible cable is characterized and discussed. The measured insertion loss (IL) of the flexible cable is less than 3 dB and the isolation between two adjacent interconnects is better than 17 dB up to 2 GHz. The data transmission through the flexible cable is verified to be highly reliable at 100 Mbps. For surgical

manipulation and long term implantation of the neural probe microsystem, the flexible cable needs to have excellent mechanical strength and resistance to fatigue. The mechanical characteristics and fatigue strength of the flexible cable are also measured and discussed. The measured maximum tensile stress and strain of the flexible cable before failure are 251.2 ± 7.1 MPa (14.35 ± 0.3 N) and 4.16 ± 0.11 %, respectively. The Young's modulus of the fabricated flexible cable is 8.21 GPa. From the fatigue strength testing, the measured resistance change of the flexible cable's interconnect is less than 4.8 % after 250,000 cycles of cyclic mechanical stretch.

1 Introduction

Millions of people worldwide are unable to move due to paralysis, a debilitating disease of the neuromuscular system identified by partial or complete loss of motor functions. A potential treatment for paralysis is to route control signals from the brain around the injury by artificial connections. Such signals could control electrical stimulation of muscles, thereby restoring volitional movement to paralyzed limbs. Recent studies have shown that quadriplegic patients can consciously control the activity of nerve cells or neurons in the motor cortex responsible for upper limb movements, even after several years of paralysis. Velliste et al. (2008) presented a monkey's motor cortical activity to control a robotic hand replica in a self-feeding task by using implantable neural interface device. The demonstration can fully simulate the prosthesis for real-time interaction with the physical environment. For implantation in human's brain (Hochberg et al. 2006), a paralytic human successfully controlled a computer cursor through an intracortical neural probe array, which inserted into the region of motor cortex.

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A high density interconnect cable is one of key components in the wireless implantable neural probe microsystem, which is composed of two implantable platforms—one in direct touch with the brain and the other on the skull. The cable is used to transmit a large amount of neural recording data between these two platforms. Furthermore, in order to minimize post-insertion injury caused by the probe array in the presence of brain micro-motion, high flexibility of the cable is required (Goldstein and Salzman, 1973). In the previous studies, silicon ribbon cables have been used for implantable microelectrode arrays (Hetke et al. 1994; Bai et al. 2000). The silicon ribbon cable can be realized by a shallow boron diffusion technique and integrated with the silicon probe. However, the silicon substrate of the cable is not flexible enough to tolerate surgical manipulation. Therefore, various biocompatible polymer-based materials, such as parylene and polyimide, were proposed as the substrates for flexible cables or probe arrays (Pang et al. 2005; Yao et al. 2007; Wise et al. 2008; Rubehn and Stieglitz 2010; Rousche et al. 2001; Takeuchi et al. 2004; Norlin et al. 2002; Herwik et al. 2009; Lee et al. 2010).

For polymer-based flexible cables, parylene and polyimide are frequently used for the flexible substrate and the insulator layer. The parylene polymer has excellent biocompatibility and can be monolithically integrated with Micro-Electro-Mechanical Systems (MEMS) devices. In (Pang et al. 2005), the parylene flexible cable was monolithically integrated with a probe array for the implantable neural recording. Yao et al. (2007) proposed a parylene cable that can be integrated with silicon microprobes by using tetraethyl ammonium hydroxide (TMAH) released from the wafer. Wise et al. (2008) proposed a high density cochlear electrode array with on board circuitry for neural stimulation and recording. An eight-lead parylene ribbon cable was used to connect the microprocessor and the electrode array. In their work, it was demonstrated that the parylene-based cable could provide sufficient biocompatibility and flexibility characteristics. However, these approaches usually require relatively complex micromachining processes.

The flexible cable for neural implants can also be realized using polyimide as a flexible substrate and a dielectric layer. Polyimide is a well-known polymer material for various biomedical applications. Its long-term stability was also proven for neural implants (Rubehn and Stieglitz 2010). A polyimide-based probe array and a cable have been micromachined with multilayer metallization (Rousche et al. 2001). Takeuchi et al. (2004) proposed a 3D neural probe array, which was fabricated with polyimide-based interconnects using magnetic force to fold the planar probe. Since the material exhibits low stiffness, the polyimide probe array is susceptible to buckling during the

insertion procedure. As a result, silicon-based microprobe arrays integrated with flexible polyimide cables are frequently used for neural recording application (Norlin et al. 2002; Herwik et al. 2009; Lee et al. 2010). But none of these works reported detailed evaluation result of the mechanical and fatigue strength characteristics and high data rate transmission performance of the flexible cables.

In this paper, design, fabrication and characterization of a flexible cable for the wireless implantable neural probe microsystem are presented. The fabricated flexible cable is used to make an electrical connection between two implantable platforms. Polyimide is used as a flexible substrate and an insulator layer of the cable. The high-rate data transmission performance of the cable is evaluated as it is important to process comprehensive neural signals in real-time. Mechanical tensile tests of the cable are performed to examine mechanical strength required to tolerate surgical manipulation of neural probe arrays. The fatigue strength is also considered to be critical for chronic implantation. The mechanical characteristics and fatigue strength of the cable are measured and discussed. This paper is organized as follows: the design and fabrication of the flexible cable are described in Sects. 2 and 3, respectively. Measured results are presented in Sect. 4 with discussion. Finally, Sect. 5 draws conclusions.

2 Design

The wireless implantable neural probe microsystem can provide high resolution neural signal information for prosthesis and neuroscience study. Figure 1 shows the schematic of a wireless implantable neural probe microsystem, which is implanted in the human brain to extract neural signals. Various components of the whole microsystem and how the components are placed in different layers of a human head are described. The microsystem consists of three main parts, which are a neural probe array with a neural interface IC, a wireless IC for power and data link, and a flexible cable. The neural probe array is inserted into the region of motor cortex and is used for recording the neural signal from a large number of neurons. The wireless power and data link IC is mounted subcutaneously above the skull. The target of the wireless link IC is to transmit the extracted neural signal to a receiver of physical environment. The neural probe array with its interface IC and the wireless link IC are connected by the flexible cable. High density interconnects are embedded in the cable. The cable is used to transmit the neural signal acquired by the probe array and the interface IC to the wireless link IC, as well as to deliver the power received by the wireless link IC to the interface IC as well as recording and stimulation purposes.

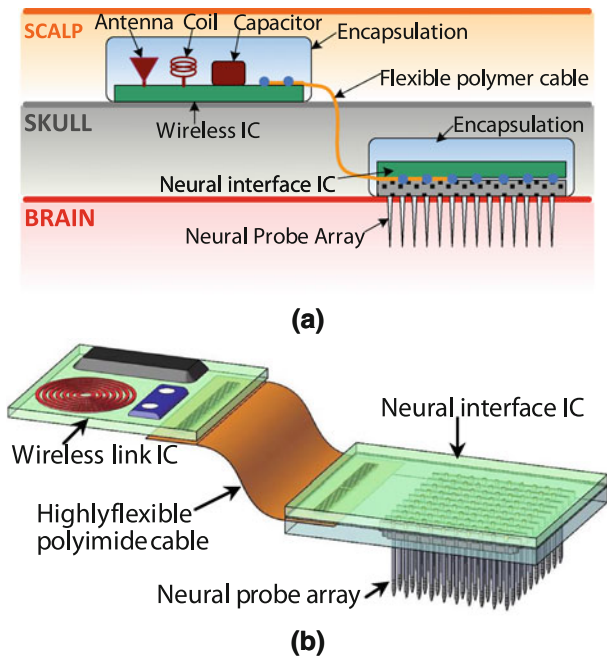


Fig. 1 **a** Schematic of implantable neural probe system. **b** The highly flexible polyimide cable connects the wireless link IC and the neural interface IC

Table 1 The specifications of the proposed flexible polymer cable

Data transmission rate of cable	100 Mbps
Data transmission rate per interconnect	10 Mbps
Thickness of cable	9 μm
Number of interconnects	30
Pitch of interconnects	150 μm
Width of interconnects	100 μm
Thickness of interconnects	1 μm
Length of interconnects	20 mm
Metal of interconnects	Gold
Flexible substrate	Polyimide PI 2611

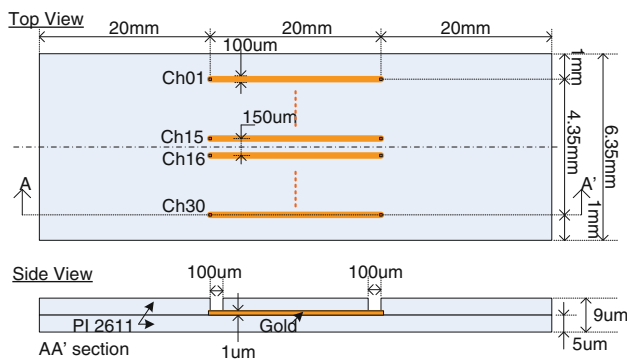


Fig. 2 The detailed illustration and dimensions of the proposed flexible polyimide cable. This figure is not drawn to scale

The polyimide Pyralin PI 2611 (from HD Microsystems Inc.) is chosen as a flexible substrate and an insulation layer of the cable. This is because the PI 2611 exhibits excellent mechanical strength (8.5 GPa Young’s modulus), good insulation characteristics and high material flexibility. Also, it has relatively low water uptake (0.5 %) and low thermal expansion coefficient ($3 \times 10^{-6}/\text{K}$). Therefore, PI 2611 is well suited for chronic biomedical implants and has been proven to be nontoxic in biomedical applications, e.g. retina stimulator devices (Stieglitz et al. 2000; Meyer et al. 2001). For fabrication process, the polyimide can be patterned using standard microfabrication processes such as photolithography and reactive ion etching.

Table 1 shows the specifications of the proposed cable. In order to transmit large amount of neural signal information, the cable is designed to transmit at a data rate of 100 Mbps. Thirty interconnects are sandwiched between a polyimide substrate and an insulator layer of the cable. There are ten interconnects for data transmission, fourteen interconnects for shielding or ground, two interconnects for power supply and four interconnects for serial peripheral interface (SPI) control. Each interconnect can transmit at a data rate of 10 Mbps. In order to obtain high flexibility and high density interconnects, the thickness and pitch of interconnects are designed to be 9 and 150 μm , respectively. Figure 2 shows the detailed illustration and dimensions of the proposed polyimide cable.

3 Fabrication and integration

3.1 Fabrication of flexible cable

Fabrication process of the flexible polyimide cable is shown in Fig. 3. As the first step depicted in Figs. 3a, b, a thin layer of titanium (3,000 Å) is deposited on an 8-inch silicon wafer through physical vapor deposition process, which forms an adhesion layer. The titanium layer will help in the stripping of the cable from the wafer substrate at the end of the fabrication. After titanium layer sputtering, a 5 μm thick layer of polyimide resin is spin-coated onto the wafer, and the polyimide is cured on a hot plate with the temperature of 325 °C for 45 min, as shown in Fig. 3c. In order to increase adhesion of metal to polyimide substrate, oxygen plasma cleaning treatment of the polyimide film is performed. Then, a 7 μm thick negative photoresist (Microresist Tech Man-1440) is spin-coated onto the silicon wafer for patterning, as shown in Fig. 3d.

In Fig. 3e, a thin metallization layer (20 nm chromium, 1,000 nm gold and 20 nm chromium) is deposited by thermal evaporation process. Then, the interconnects and bonding pads are patterned by applying a lift-off method, as shown in Fig. 3f. The second polyimide layer with 4 μm

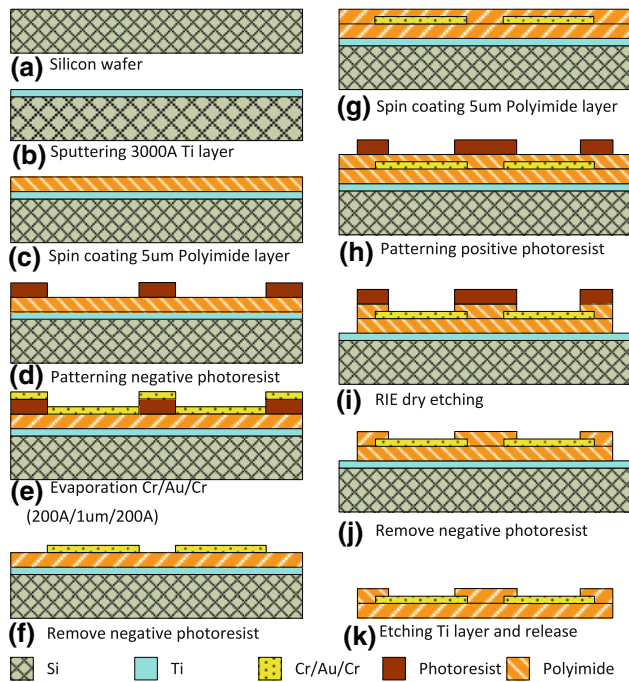


Fig. 3 Fabrication process of the flexible cable

thickness, for insulation purpose, is spin-coated onto the wafer, as shown in Fig. 3g. Similarly, the second layer is cured on the hot plate with the temperature of 325 °C for 45 min. Subsequently, a 10 µm thick positive photoresist (SPR220, Rohm and Haas) is spin-coated onto the wafer, as shown in Fig. 3h. As shown in Fig. 3i, reactive-ion etching (RIE) is used to open up the bonding pads of the cable. The RIE parameters for etching through polyimide layer are as follows: 10-sccm O₂, 10-sccm CF₄, 300 W, and 100 mTorr. The etch rate of the polyimide layer with the parameters is 150 nm/min. Finally, after removing the photoresist, the cable embedded with the metallization interconnects is separated manually from the wafer with the use of tweezers, as shown in Figs. 3j, k. The total thickness of the polyimide cable is 9 µm.

3.2 Integration of flexible cable

For integration with the neural probe array, ne and wireless link IC, an assembly technique of the flexible cable is proposed in Fig. 4. Firstly, the cable is placed on the bonding stage shown in Fig. 4a. In order to integrate the flexible cable with the neural probe array, via holes are designed at both ends of interconnects representing the center of contact pads. With the contact pads facing up, the solder bumps of dummy chip 1, i.e. the neural interface IC, are aligned with the contact pads of the cable, as shown in Fig. 4b. The solder bumps are bonded to the contact pad of the cable at 260 °C, with 2 MPa bonding pressure using Suss and Microtech FC 150 Flip Chip bonding machine, as

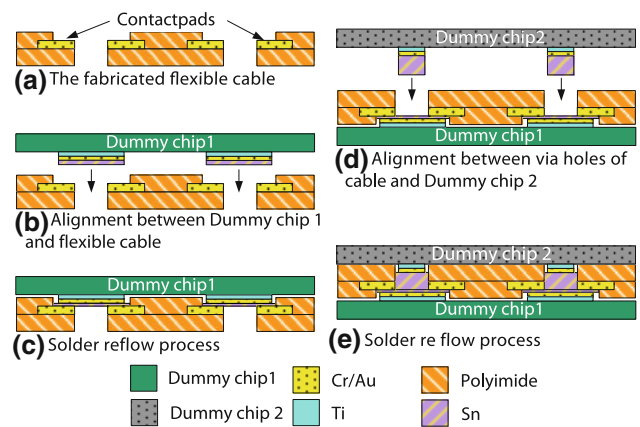


Fig. 4 Integration scheme of the flexible cable, the neural interface IC and the probe array

shown in Fig. 4c. After flipping dummy chip 1 and the cable, dummy chip 2, i.e. the neural probe array with the solder bumps, is aligned with the bumps of the dummy chip 1 and inserted through the via holes of the cable, as shown in Fig. 4d. Then the device is heated up to soldering temperature of 260 °C with bonding pressure of 2 MPa. Finally, the assembly device is shown in Fig. 4e.

4 Measurement results and discussions

4.1 Fabricated device

The fabricated flexible polyimide cable is presented in Fig. 5a, b. It is demonstrated that thirty gold interconnects are well-positioned in between two thin polyimide layers with its flexible bending deformation. Optical microscope images of the interconnect and contact pads are shown in Fig. 5c, d, respectively. Figure 6a shows the assembly device including the cable, dummy chip 1, and dummy chip 2. The interconnect microstructure by Cu/Sn bump soldering is shown in Fig. 6b. The proposed assembly method is specifically suitable for integration with silicon-based neural probe arrays since small bonding force is required during the soldering process. In addition, high density interconnect of the flexible cable can be obtained by this approach. Furthermore, the footprint of the device can be miniaturized since the structure allows stacking of the chips.

4.2 Electrical characteristics

In order to realize comprehensive neural signal processing, 100-Mbps data rate is required for digital baseband transmission through the flexible polyimide cable in our design. Accordingly, each signal interconnect of the cable is aimed at 10-Mbps data rate in the system configuration.

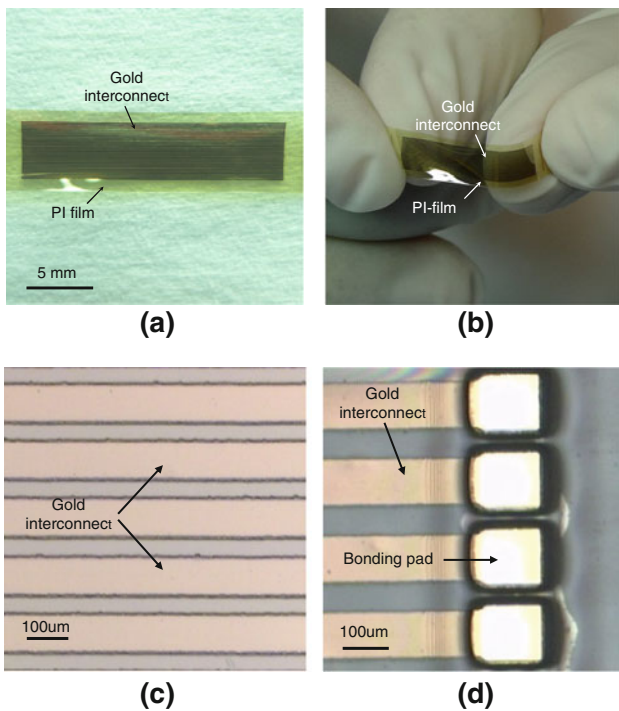


Fig. 5 **a** and **b** Fabricated flexible polyimide cable; **c** and **d** Optical microscope images of interconnects and bonding pads

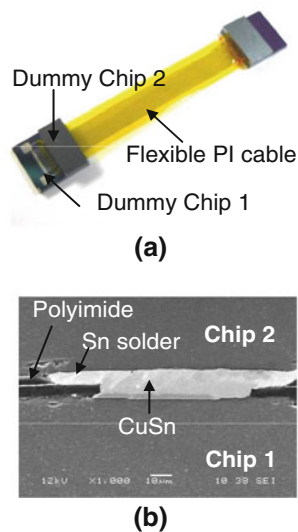


Fig. 6 **a** Assembly device composed of the flexible polyimide cable and bonded chips; **b** Interconnect microstructure using Cu/Sn solder bump

Moreover, isolation between any two signal interconnects should be high enough to avoid crosstalk. To characterize the electrical performance of the flexible cable, a method based on S-parameter measurement in the frequency domain has been demonstrated using the vector network analyzer (VNA) and the probe station.

As shown in Fig. 7, the fabricated flexible cable is fixed on the probe station. Test signals are applied and the transmitted and reflected signals are measured through the ACP40-GSG probes (Cascade Microtech, Inc.) which are

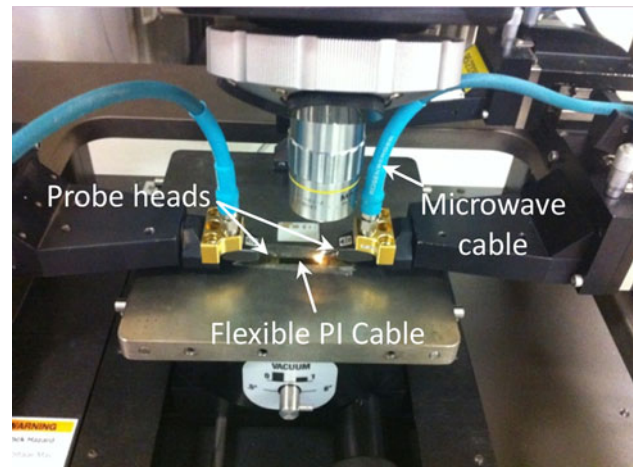


Fig. 7 Experimental setup of data transmission analysis

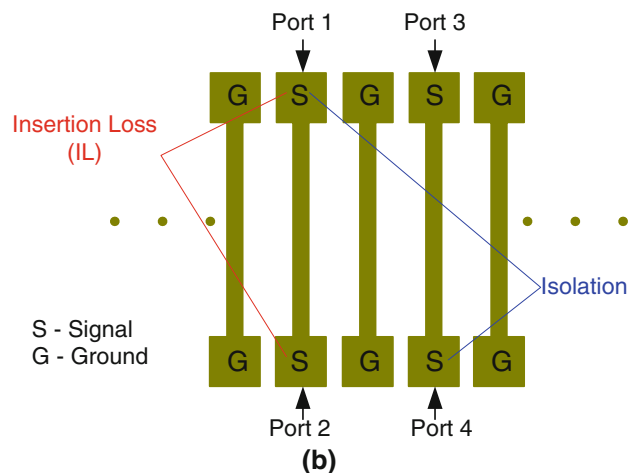
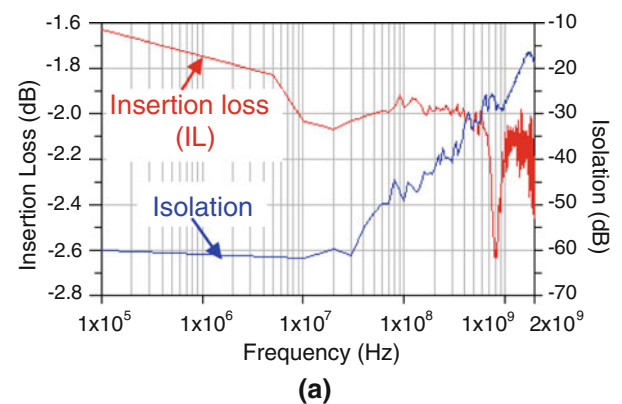


Fig. 8 **a** The measured insertion loss (IL) and isolation of the flexible cable. **b** Schematics of measurement configuration of two signal interconnects

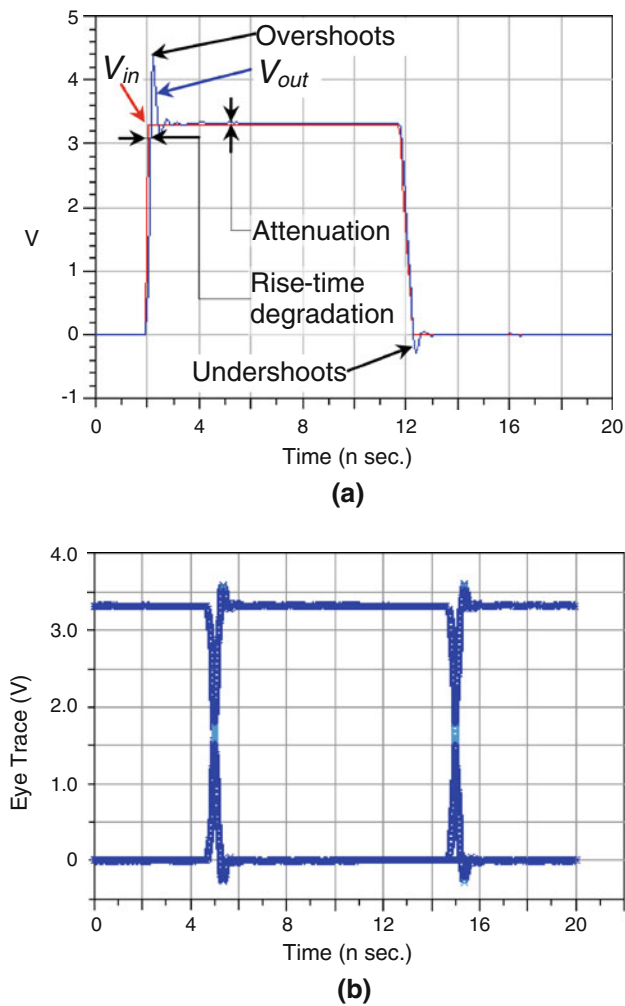


Fig. 9 **a** Time response of the flexible cable under high-rate data transmission. **b** Eye diagram of data transmission through the flexible cable

connected to the Agilent 8753 VNA via microwave cables. Parasitic effects due to the probes and microwave cables are de-embedded through calibration. The S-parameter measurement is conducted over the frequency range of 100 kHz to 2 GHz. Figure 8a shows the measured insertion loss and isolation of the flexible cable. The measured insertion loss of the flexible cable is less than 3 dB and the isolation between two adjacent interconnects is better than 17 dB up to 2 GHz. The measurement configuration of two signal interconnects is shown in Fig. 8b. For the isolation performance characterization, the measurement is performed between ports 1 and 4, while being measured between ports 1 and 2 for insertion loss characterization.

To assess the high data transmission capability of the cable, the measured S-parameters are used to extract the equivalent transmission line parameters, and the transmission characteristics in the time domain are obtained

(Eisenstadt and Eo 1992). As an example, given 100-Mbps digital signal at one end of the interconnect, the time domain response and eye diagram at the other end of the interconnect are shown in Fig. 9. It is concluded that each signal interconnect is reliable enough even at 100-Mbps data transmission, which is considerably higher than the system requirement of 10 Mbps.

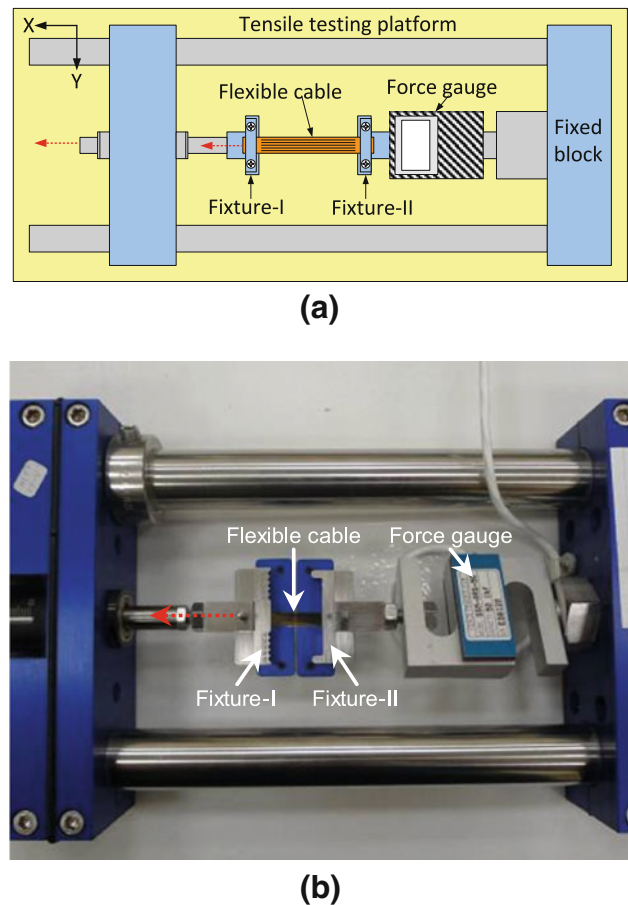


Fig. 10 **a** Schematic and **b** actual experimental setup for measuring mechanical characteristics of the flexible cable

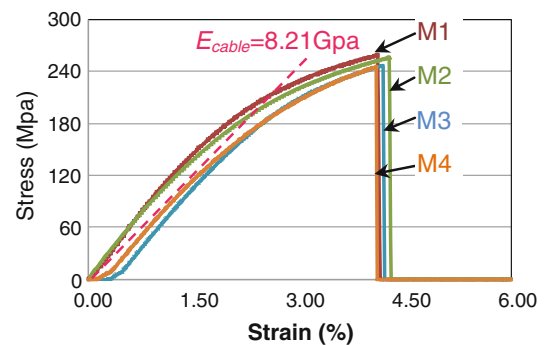
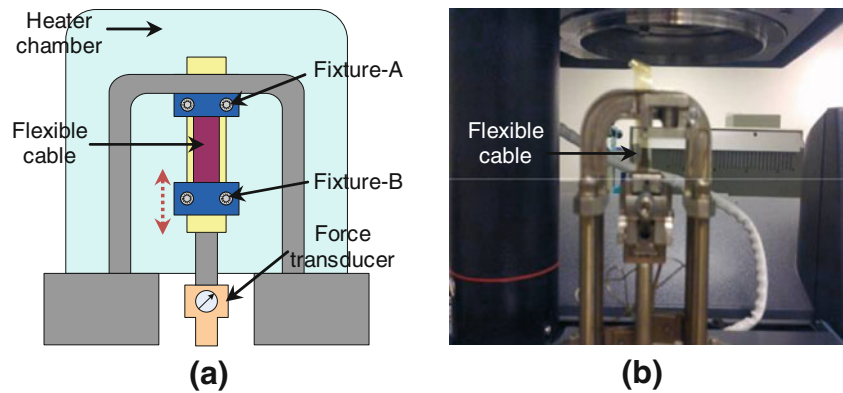


Fig. 11 Measured stress–strain curves of the flexible cable

Fig. 12 **a** Schematic and **b** actual DMA experimental setup for measuring fatigue strength of the flexible cable



4.3 Mechanical characteristics

The flexible cable is subjected to tensile testing for mechanical characterization. Figure 10 shows the experimental setup for mechanical property measurement. A force gauge with the maximum resolution of 10 mN is used to measure the applied force. The force gauge is attached to the fixed block. The cable is clamped between the force gauge and a horizontally translational stage whose displacement resolution is 10 μm . Cable strains can be measured by moving distance of the translational stage. Also, cable stresses can be calculated from the applied force by the force gauge. The measured stress–strain data of the cables are presented in Fig. 11. The curves from four cables (M1–M4) show good repeatability. The measured maximum stress and strain of the cable are $251.2 \pm 7.1 \text{ MPa}$ ($14.35 \pm 0.3 \text{ N}$) and $4.16 \pm 0.11 \%$, respectively. The strain at cable break is measured at 4.3 % stretch. Young's modulus of the cable is calculated by linear curve fitting of each stress–strain data before the break point, and the average modulus is obtained by using these results (Rubehn and Stieglitz 2010). In Fig. 11, the dotted line represents the average Young's modulus of the cable, which is 8.21 GPa, and this value is similar to Young's modulus of PI-2611 (8.5 GPa). As mentioned in the design section, PI-2611 provides excellent mechanical strength for implantable neural devices as the flexible substrate and insulator layer.

4.4 Fatigue testing

The cable of the neural probe microsystem has to sustain cyclic stretching or bending deformation due to micro-motions of the brain after implantation. Fatigue strength of the cable is critical for long-term implantation, and fatigue testing is conducted to check cable durability. The dynamic mechanical analyzer (DMA Q800, TA Instruments co., Ltd.) has been used in the tests. Figure 12 shows the schematic and actual image of the experimental setup for measuring fatigue strength of the cable. The cable is clamped between fixture-A and fixture-B. Then, the cable

is stretched periodically by the fixture-B connected to a force transducer. The applied force of the cable is measured by the force transducer. Table 2 shows the test parameters and the result of the fatigue testing with a number of selected stretch cycles. The fatigue strength measurement is conducted within 20,000–250,000 cycles of cyclic mechanical stretch. The temperature in the fatigue testing is set to $37 \pm 3 \text{ }^\circ\text{C}$, which is similar to the human body temperature. The force applied to the cable is 0.2 N during the tests. After 250,000 cycles of cyclic stretching, the resistance change of the cable is less than 4.8 % without any noticeable increase in the resistance of interconnects. Another set of fatigue tests is performed with

Table 2 The parameters of fatigue strength testing and the interconnect resistance change after different number of cyclic mechanical stretches

Cycles	Applied force (N)	Testing frequency (Hz)	Temperature ($^\circ\text{C}$)	Resistance change (%)
20,000	0.2	50	37 ± 3	1.92 ± 0.36
40,000	0.2	50	37 ± 3	1.56 ± 0.25
60,000	0.2	50	37 ± 3	3.07 ± 0.51
80,000	0.2	50	37 ± 3	3.37 ± 0.26
100,000	0.2	50	37 ± 3	4.42 ± 0.31
250,000	0.2	50	37 ± 3	4.77 ± 0.24

Table 3 The parameters of fatigue testing with different applied forces and the corresponding interconnect resistance changes after 100,000 cycles of mechanical stretches

Cycles	Applied force (N)	Testing frequency (Hz)	Temperature ($^\circ\text{C}$)	Resistance change (%)
100,000	0.1	50	37 ± 3	3.49 ± 0.33
100,000	0.2	50	37 ± 3	4.42 ± 0.31
100,000	0.4	50	37 ± 3	6.10 ± 0.25
100,000	0.7	50	37 ± 3	6.65 ± 0.51
100,000	1.0	50	37 ± 3	7.67 ± 0.27

different force levels, which is summarized in Table 3. The applied stretching forces are in the range from 0.1 to 1.0 N with 1,000, 000 cycles. At 1.0 N applied force, the resistance change of the cable is less than 7.7 %, which provides an indication of the life-time of the flexible cable.

5 Conclusions

The development of the flexible polyimide cable for implantable neural probe array application has been presented. For neural recording applications, high-rate transmission of neural recording data through the flexible cable is important to provide comprehensive neural signal information in real time. The measured insertion loss of the flexible cable is less than 3 dB and the measured isolation between the two signal interconnects is better than 17 dB up to 2 GHz. The measured results show that the developed flexible cable can support the data transmission at the rate much higher than 100 Mbps. Also, the mechanical characteristics and fatigue strength of the flexible cable have been measured and discussed. The measured maximum stress and measured maximum strain of the cable are 251.2 ± 7.1 MPa and 4.16 ± 0.11 %, respectively. The average Young's modulus of the cable is about 8.21 GPa, which is similar to Young's modulus of PI-2611. The PI-2611 as the flexible substrate and insulator layer of the cable provides excellent mechanical strength for implantable neural device. In the fatigue strength testing, the resistance change of the cable is less than 4.8 % after 250,000 cycle times of cyclic stretching.

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