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Chapter 15

Silicon Carbide: A Biocompatible Semiconductor Used in Advanced Biosensors and BioMEMS/NEMS

Mahboobeh Mahmoodi and Lida Ghazanfari

Additional information is available at the end of the chapter

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1. Introduction

In the last decade, there has been a tremendous development in the field of miniaturization of chemical and biochemical sensor devices. Microelectromechanical systems (MEMS) refer to microscopic devices that have a characteristic length of less than 1 mm but more than 100 nm and combine electrical and mechanical components. Nanoelectromechanical systems (NEMS) refer to nanoscopic devices that have a characteristic length of less than 100 nm and combine electrical and mechanical components. In mesoscale devices, if the functional components are on micro- or nanoscale, they may be referred to as MEMS or NEMS, respectively. These are referred to as an intelligent miniaturized system comprising sensing, processing, and/or actuating functions and combine electrical and mechanical components. The acronym MEMS originated in the USA. The term commonly used in Europe is micro system technology (MST) and in Japan, the term is micromachines. Another term generally used is micro/nanodevices.

MEMS/NEMS terms are also now used in a broad sense and include electrical, mechanical, fluidic, optical, and/or biological functions. MEMS/NEMS for optical applications are referred to as micro/nano optoelectromechanical systems (MOEMS/NOEMS). MEMS/NEMS for electronic applications are referred to as radio-frequency-MEMS/NEMS or RF-MEMS/RF-NEMS. MEMS/NEMS for biological applications are referred to as BioMEMS/BioNEMS. MEMS and emerging NEMS are expected to have a major impact on our lives, comparable to that of semiconductor technology, information technology, or cellular and molecular biology. MEMS/NEMS are used in electromechanical, electronics, information/communication, chemical, and biological applications [1]. To put the dimensions of MEMS and NEMS in perspective refer to Fig.1.

MEMS/NEMS need to be designed to perform expected functions in short durations, typically in the millisecond to picosecond range. Through MEMS it is possible to incorporate micro-scale types of devices such as motors, pumps, fluidic channels, sample preparation (including mixing or vaporization) chambers, and various types of sensors (including optical sensors) that will perform assorted tasks, such as monitoring. Again, one can do both monitoring in the physical sense and the chemical sense. SiC has been known for its outstanding mechanical and chemical properties making it equally attractive for MEMS and NEMS.

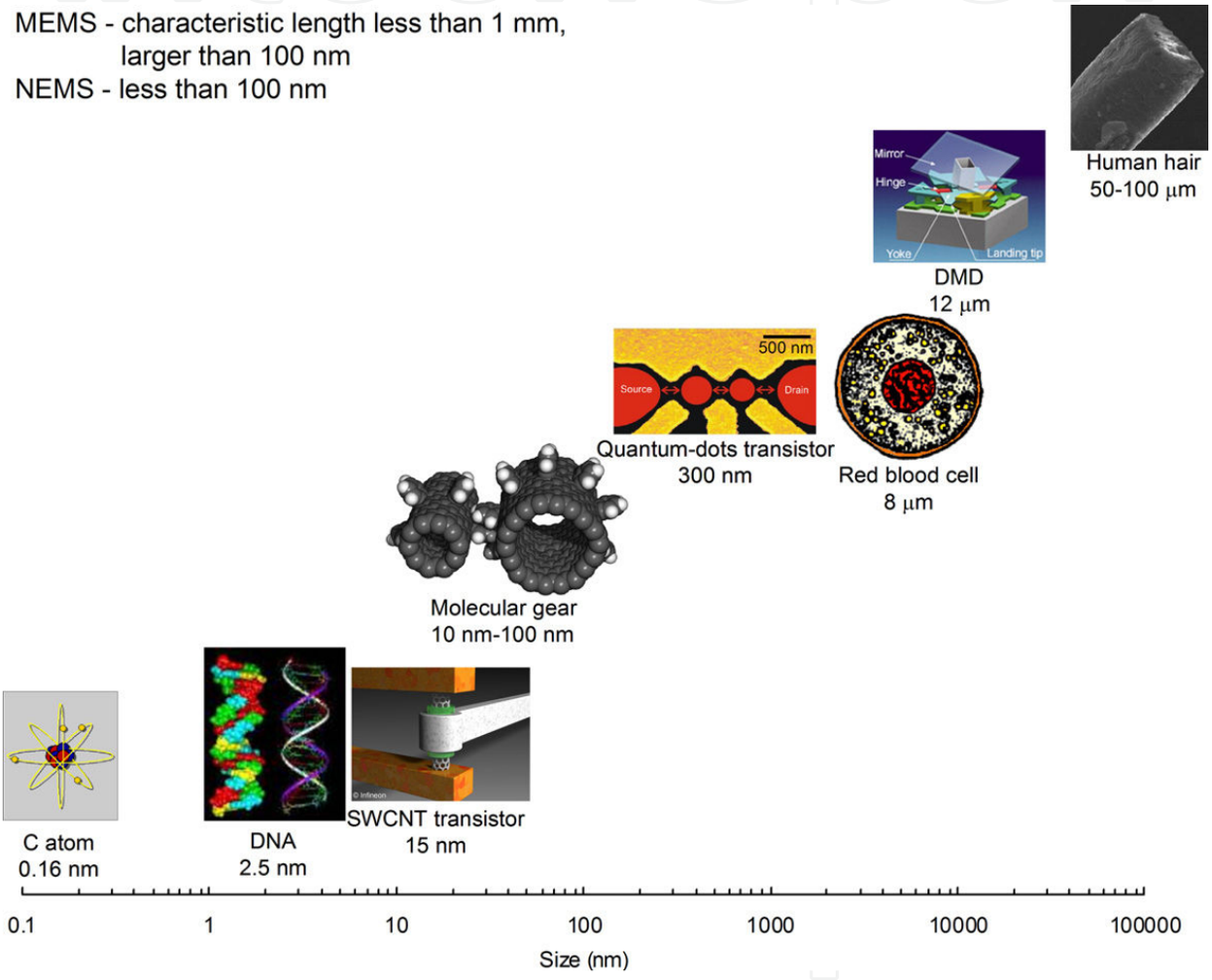

Figure 1. Dimensions of MEMS and NEMS in perspective. MEMS/NEMS examples shown are of a vertical single walled carbon nanotube (SWCNT) transistor (5 nm wide and 15 nm high), of molecular dynamic simulations of a carbon-nanotube based gear, quantum-dot transistor obtained from van der Wiel et al., and DMD obtained from www.dlp.com.

An ever-increasing demand for biomedical devices provides motivation for the development of advanced semiconducting materials for challenging applications ranging from disease detection to organ function restoration. The superior bioelectrical properties of silicon carbide (SiC) make it an ideal substrate for bioelectrodes thus allowing for an all-biocompat-

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ible, non-metalic biomedical system. Most of the studies conducted in the past on single-crystal SiC provide evidence of the attractive bio-potentialities of this material and hence suggest similar properties for crystalline SiC.

Recent interest has risen in employing these materials, tools and technologies for the fabrication of miniature sensors and actuators and their integration with electronic circuits to produce smart devices and systems. This effort offers the promise of: (1) increasing the performance and manufacturability of both sensors and actuators by exploiting new batch fabrication processes developed including micro stereo lithographic and micro molding techniques; (2) developing novel classes of materials and mechanical structures not possible previously, such as diamond-like carbon, silicon carbide and carbon nanotubes, micro-turbines and micro-engines; (3) development of technologies for the system level and wafer level integration of micro components at the nanometer precision, such as self-assembly techniques and robotic manipulation; (4) development of control and communication systems for MEMS, such as optical and wireless radio frequency, and power delivery systems, etc. The integration of MEMS, NEMS, interdigital transducers and required microelectronics and conformal antenna in the multifunctional smart materials and composites results in a smart system suitable for sending and control of a variety of functions in automobile, aerospace, marine and civil strutures and food and medical industries. The principle aim of this chapter is to present an overview of bioMEMS and bioNEMS technologies that utilize SiC as a key component in the structure. Therefore, this chapter focuses on reviewing examples where SiC is used in the mechanical components of micro /nanofabricated devices and biosensors for biomedical applications that can be used to further develop the technology.

2. SiC MEMS and NEMS

SiC is an excellent structural material for MEMS and NEMS applications due to its outstanding mechanical, chemical, and electrical properties combined with its compatibility with Si micromachining techniques. Nowhere is the limitation to silicon-based MEMS more apparent than in applications characterized by high temperature environments. The electronic properties of silicon place an upper limit on the operating temperature of electronic devices at roughly 250 °C for devices fabricated on conventional bulk silicon substrates and around 300 °C for devices built on silicon-on-insulator substrates. As for the mechanical properties, the upper limit for silicon-based micromechanical structures is around 500 °C, as seen in the plastic deformation of Si membranes subjected to deflecting loads at that temperature. The silicon surface is chemically active and will appreciably oxidize at temperatures above 800 °C. These material limitations require that silicon-based MEMS structures be enclosed in protective packaging to make them suitable for use in these conditions. In many cases, the packaging is so extensive that the benefits of using a silicon based MEMS device (i.e., low cost and small device size) are completely negated by the package. The desire to capitalize on MEMS technology for applications where the use of silicon is impractical has motivated the development of alternative semiconductors whose material properties are better suited for such applications [2].

Mostly, efforts to develop SiC for MEMS have focused on developing device technologies for harsh environment applications where Si, the dominant material in MEMS, is not well suited. Such environments include high temperature (>600 °C), high mechanical wear, high radiation, high oxidation, and harsh chemicals. Properties that make SiC particularly well suited for harsh environments include a wide electronic bandgap (ranging from 2.9 eV for 3C-SiC to 3.2 eV for 4H-SiC), high hardness (2,480 kg/mm^2), high resistance to chemical etching in acids and bases, slow oxidation rates, and very strong covalent Si–C bonds. SiC is of particular interest for use in MEMS-based microactuators, where its inert surface resists the deleterious effects of stiction and its high Young's modulus (~400 GPa) enables fabrication of mechanical resonators that can operate over a very wide frequency range, including the GHz range. Its chemical inertness, favorable mechanical properties, and biocompatibility make SiC particularly attractive for bioMEMS applications. Several comprehensive reviews of SiC MEMS technology, including material properties, processing techniques, and device examples have recently been published [2, 3].

The fabrication of bulk micromachined SiC MEMS structures using conventional Si bulk micromachining techniques is enabled by the ability of 3C-SiC films to be epitaxially grown on bulk Si substrates. These processes benefit tremendously from the chemical inertness of SiC with respect to Si etchants [2]. In applications where SiC surfaces are desired but bulk SiC substrates could be technically or economically constraining, 3C-SiC films grown on Si substrates provide a convenient and low-cost alternative to 6H- and 4H-SiC wafers. One of the earliest 3C-SiC MEMS structures to be fabricated was the freestanding membrane [4].

In general, the material properties of poly-SiC that are of importance to MEMS closely resemble its single crystalline counterpart. The poly-SiC films are not generally viewed as desirable for electronic devices for largely the same reasons as polysilicon. In terms of chemical inertness, fully crystallized poly-SiC is essentially as inert as 3C-SiC. Poly-SiC oxidizes slightly faster than 3C-SiC due to grain boundary diffusion of oxidants. The Young's modulus is typically reported to be around 400 GPa.

SiC, owing to its chemical inertness, is of interest as a structural material for biomedical microsystems. A recent study that investigated a wide range of MEMS materials (including Ti, Si, SiO2 and Si3N4) has shown that single crystal SiC is both biocompatible (to the extent of the tests performed) and sterilizable [2].

3. Biocompatibility

Biocompatibility is related to the behavior of biomaterials in various contexts. The term may refer to specific properties of a material without specifying where or how the material is used, or to more empirical clinical success of a whole device in which the material or materials are featured. The ambiguity of the term reflects the ongoing development of insights into how biomaterials interact with the human body and eventually how those interactions determine the clinical success of a medical device (such as pacemaker, hip replacement or stent). Modern medical devices and prostheses are often composed of more than one materi-

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al so it might not always be sufficient to talk about the biocompatibility of a specific material. Cell-semiconductor hybrid systems represent an emerging topic of research in the biotechnological area with intriguing possible applications. A comprehensive understanding of the interactions governing such systems is the basis of present and future development of biologically interfaced device performance. To date, very little is known about the main processes that govern the communication between cells and the surfaces they adhere to. When cells adhere to an external surface an eterophilic binding is generated between the cell adhesion proteins and the surface molecules. After they adhere, the interface between them and the substrate becomes a dynamic environment where surface chemistry, topology, and electronic properties have been shown to play important roles. The biocompatibility single-crystal SiC was determined by culturing mammalian cells directly on SiC substrates and by evaluating the resulting cell adhesion quality and proliferation. The crystalline SiC is indeed a very promising material for bio-applications, with better bio-performance than crystalline Si. 3C-SiC, which can be directly grown on Si substrates, appears to be an especially promising bio-material: the Si substrate used for the epi-growth would in fact allow for cost-effective and straightforward electronic integration, while the SiC surface would constitute a more biocompatible and versatile interface between the electronic and biological world. The main factors that have been shown to define SiC biocompatibility are its hydrophilicity and surface chemistry. SiC surface morphology is shown to influence cell adhesion only when macropatterned, while SiC polytypism and doping concentration seem to have no influence on cell proliferation. The identification of the organic chemical groups that bind to the SiC surface, together with the calculation of SiC zeta potential in media, could be used to better understand the electronic interaction between cell and SiC surfaces. Using an appropriate cleaning procedure for the SiC samples before their use as substrates for cell cultures is also important. The cleaning chemistry may affect cell proliferation and emphasize the importance of the selection of an appropriate cleaning procedure for biosubstrates. SiC has been shown to be significantly better than Si as a substrate for cell culture, with a noticeably reduced toxic effect and enhanced cell proliferation. One of the possible drawbacks that may be associated with the use of SiC in vivo is related to the unclear and highly debated cytotoxic level of SiC particles. Nonetheless, the potential cytotoxicity of SiC particles does not represent a dramatic issue as much as it does for Si, since the great tribological properties of SiC make it less likely to generate debris.

Several papers have discussed testing silicon SiC in vitro. In one study the researchers tested SiC deposited from radiofrequency sputtering using alveolar bone osteoblasts and gingival fibroblasts for 27 days. The investigators reported that ''Silicon carbide looks cytocompatible both on basal and specific cytocompatibility levels. However, fibroblast and osteoblast attachment is not highly satisfactory, and during the second phase of osteoblast growth, osteoblast proliferation is very significantly reduced by 30%''. According to another paper, in a 48 h study using human monocytes, SiC had a stimulatory effect comparable to polymethacrylate. Cytotoxicity and mutagenicity has been performed on SiC-coated tantalum stents. Amorphous SiC did not show any cytotoxic reaction using mice fibroblasts L929 cell cultures when incubated for 24 h or mutagenic potential when investigated using Salmonella

typhimurium mutants TA98, TA100, TA1535, and TA1537. An earlier study by the same authors of a SiC-coated tantalum stent reported similar results [5].

Kotzar et al. [6] evaluated materials used in microelectromechanical devices for biocompatibility. These included single crystal silicon, polysilicon (coating, chemical vapor deposition, CVD), single crystal cubic SiC (3C SiC or β-SiC, CVD), and titanium (physical vapor deposition). They concluded that the tested Si, SiC and titanium were biocompatible. Even though crystalline SiC biocompatibility has not been investigated in the past, information exists concerning the biocompatibility of the amorphous phase of this material (a-SiC). Materials commonly used in the fabrication and packaging of standard MEMS devices were recently evaluated for cytotoxicity using the ISO 10993 biocompatibility testing standards [7]. The material set comprised of: silicon (Si, 500 μm-thick), silicon dioxide (SiO_2, 0.5 μm-thick), silicon nitride (Si_3N_4, 0.2 μm-thick), polycrystalline silicon (polysilicon, 0.5 μm-thick), silicon carbide (SiC, 0.5 μm-thick), titanium (Ti, 0.5 μm-thick), and SU-8 (50 μm-thick) (Table 1).

The biocompatibility of the materials used in silicon-based devices, such as single crystalline silicon, polysilicon, silicon dioxide, silicone nitride and silicon carbide, were evaluated according to ISO 10993 standards by Kotzar et al. [6]. Using mouse fibroblasts in the tests, none of the materials were found to be cytotoxic. An in vivo tests based on implantation in rabbit muscle showed no sign of irritation. Only silicone nitride and SU-8 showed detectable nonvolatile residues. Furthermore, in vivo studies using Stainless Steel cages and Teflon cages reveal that silicon, silicon nitride, silicon dioxide, gold, and SU-8 are biocompatible. However, silicon and SU-8 have shown increased biofouling.

Material	Reactivity (0-4)
Positive Control (tin stabilized polyvinylchloride)	4
Negative Control (high density polyethylene)	0
Si (monocrystalline silicon)	0
Sio_2 (silicon dioxide)	0
Polysilicon (polycrystalline silicon)	0
Si_3N_4 (silicon nitride)	0
SiC (monocrystalline 3C silicon carbide)	0
Ti (sputtered titanium)	0
SU-8 (epoxy photoresist)	0

Table 1. In vitro cytotoxicity of MEMS materials [7]

4. Hemocompatibility

The interaction between blood proteins and the material is regarded as an important source of thrombogenesis. The adsorption of proteins is explained, from the thermodynamic point

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of view, in terms of the systems free energy or surface energy. However, adsorption itself does not induce thrombosis. Theories regarding correlations between thrombogenicity of a material and its surface charge or its binding properties proved not to be useful.

Thrombus formation on implant materials is one of the first reactions after deployment and may lead to acute failure due to occlusion and serve as a trigger for neointimal formation. Next to the direct activation by the intrinsic or extrinsic coagulation cascade, thrombus formation can also be initiated directly by an electron transfer process while fibrinogen is close to the surface. The electronic nature of a molecule can be defined as semiconductor or insulator. Contact activation is possible in the case of a metal since electrons in the fibrinogen molecule are able to occupy empty electronic states with the same energy. Therefore, the obvious way to avoid this transfer is to use a material with a significantly reduced density of empty electronic states within the range of the valence band of the fibrinogen. This is the case for the used silicon carbide coating.

Hemocompatibility leads to the following physical requirements: (1) to prevent the electron transfer, the solid must have no empty electronic states at the transfer level, i.e., deeper than 0.9 eV below Fermi's level. This requirements met by a semiconductor with a sufficiently large band gap (its valence band edge must be deeper than 1.4 eV below Fermi´s level) and a low density of states inside the band gap. (2) To prevent electrostatic charging of the interface (which may interfere with requirement 1) the electric conductivity must be higher than 10-3 S/cm. A material that meets these electronic requirements is silicon carbide in an amorphous, heavily n-doped, hydrogen-rich modification (a-SiC:H). The amorphous structure is required in order to avoid any point of increased density of electronic states, especially at grain boundaries.

At present, a-SiC:H is known for its high thromboresistance induced by the optimal barrier that this material presents for protein adhesion. These properties may translate into less protein biofouling and better compatibility for intravascular applications rather than Si. SiC has a relatively low level of fibrinogen and fibrin deposition when contacting blood. These proteins promote local clot formation; thus, the tendency not to adsorb them will resist blood clotting. It is now well established that SiC coatings are resistant to platelet adhesion and clotting both in vitro and in vivo [5]. In the Bolz et al. [8] study, a-SiC:H films were deposited using the glow discharge technique or plasma-enhanced chemical vapour deposition (PECVD). The technique provides the most suitable coating process due to its high inherent hydrogen concentration which satisfies the electronically active defects in the amorphous layers. They used fibrinogen as an example model for thrombogenesis in implants, although most haemoproteins are organic semiconductors. a-SiC:H coatings showed no time-dependent increase in the remaining protein concentration, confirming that no fibrinogen activation and polymerisation had taken place. These results support the electrochemical model for thrombogenesis at artificial surfaces and prove that a proper tailoring of the electronic properties leads to a material with superior hemocompatibility. The in vitro test showed that the morphology of the cells was regular. The a-SiC:H samples showed the same behaviour as

the control samples. Blood and membrane proteins have similar band-gaps, because the electronic properties depend mainly on the periodicity of the amino acids, and the proteins differ only in the acid sequence, not in their structural periodicity. Apparently, similar reactions inducing a modification of proteins are responsible for the cell culture results.

A-SiC: H has superior hemocompatibility; its clotting time is 200 percent longer than to that of titanium and pyrolytic carbon. Furthermore, it has been shown that small variations in the preparation conditions cause a significant change in hemocompatibility. Therefore, it is of paramount importance to know the exact physical properties of the material in use. Amorphous silicon carbide can be deposited on any substrate material which is resistant to temperatures of approximately 250 °C. This property makes amorphous silicon carbide a suitable coating material for all hybrid designs of biomedical devices. The substrate material can be fitted to the mechanical needs, disregarding its hemocompatibility, whereas the coating ensures the hemocompatibility of the device. Possible applications are catheters or sensors in blood contact and implants, especially artificial heart valves.

Bolz and Schaldach [8] evaluated PECVD amorphous SiC for use on prosthetic heart valves. They showed decreased thrombogenicity of an amorphous layer of SiC compared to titanium. Several other studies showed that a hydrogen-rich amorphous SiC coating on coronary artery stents is anti-thrombogenic. Three studies showed a benefit that was attributed to the SiC-coated stent. In a direct comparison of the blood compatibility silicon wafers and SiC-coated (PECVD) silicon wafers, both appeared to provoke clot formation to a greater extent than diamond-like coated silicon wafers; silicon was worse than SiC-coated silicon. In conclusion, the hemocompatibility of SiC was demonstrated [5].

5. Microfabrication techniques

5.1. Material selection

MEMS or microelectromechanical systems, is the integration of mechanical elements, sensors, actuators, and electronics on a substrate, in which micro-fabrication technologies are used. The first step when designing a process flow for fabrication of a micromachined device is to choose the structural and other materials which are to be used in the process flow. Some of the properties of materials that are commonly used in MEMS fabrication are listed in Table 2. Traditionally, silicon and polysilicon have been used most often as the structural materials for MEMS. This was initially due to the wealth of existing knowledge on processing of silicon samples from microelectronic fabrication. Luckily for the micromachining engineers, silicon has several favourable mechanical properties in addition to its superb electrical specifications that have made it the material of choice for microelectronics. Nevertheless, there are numerous cases where other materials offer significant advantages over silicon. Examples include applications where a piezoelectric material is needed or when the devices are designed to work in harsh environments.

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Materials	T_m (°C)	E (GPa)	σ_y (GPa)	ν	ρ (Kg/m ^{3})	H (GPa)
Bulk silicon	1,415	160-200	-	0.22	2,330	5-13
Polysilicon	1,415	181-203	-	-	-	10-13
Silicon dioxide	1,700	70-75	8.4	0.17	2,200	15-18
Pyrex glass	-	64	-	0.2	2,230	8
Silicon nitride	1,800	210-380	14	0.25	3,100	24-27
Silicon carbide	-	300-400	21	0.19	3,210	-
CVD-diamond	661	800-1,100	0.2	0.07	3,530	-
Aluminum	1,772	70	0.137-0.170	0.33	2,700	-
Platinum	1,065	170	0.120	0.38	21,440	-
Gold	-	80	2.1	0.38-0.42	19,280	6.5
Stainless steal	-	200	0.045-0.345	0.3	7,900	-
Polyimide	410	7.5-15	0.042	0.35-0.45	1,420	-
Parylene-N	290	2.4	0.055	-	1,100	-
Parylene-C	380	2.7	0.062	-	1,290	-
Parylene-D	-	2.6	0.034	-	1,418	-
Hard backed SU-8		4-5		0.22	-	

Table 2. Mechanical Properties of Typical Functional Materials (Tm: Melting Temperature, E: Young's Modulus, σy: Yield Strength, ν: Poisson's Ratio, ρ: Density, H: Knoop Hardness) [9]

SiC has also been used for the coating of other MEMS devices for increased wear resistance. On the other hand, the same advantages of SiC over silicon bring up challenges in deposition and etching of SiC films. The fabrication technologies differ depending on what needs to be accomplished. The aim is to incorporate electronics; they are normally fabricated using standard integrated circuit processes or sequences, such as Complementary Metal-Oxide Semiconductor (CMOS) technology or bipolar technology. On the mechanical side, the micromechanical components are fabricated using compatible micromachining processes that in essence selectively etch away parts of the silicon wafer or add new structural layers to form a mechanical device, or an electromechanical device if it has additional integrated electronics.

There are several types of methods used for micromechanical fabrications. Two of the common techniques are MUMPS, which applies to a poly-silicon and stands for Multi-User MEMS Processing System. A similar process called MUSIC is used for silicon carbide, another common substrate material used in MEMS. Through MEMS, it is possible to incorporate micro-scale types of devices such as motors, pumps, fluidic channels, sample preparation (including mixing or vaporization) chambers, and various types of sensors (including optical sensors) that will perform assorted tasks, such as monitoring. Monitoring can be performed in both the physical and chemical sense.

Therefore, MEMS can be thought of as an enabling technology that allows for the development of what we commonly call smart or intelligent systems, which operate without the need for external computing resources. This integrated microelectronics can process the information derived from the sensors and through some decision-making process direct actuators to respond by moving, positioning, regulating, pumping, and/or filtering, thereby

controlling the environment for some desired outcome or purpose. Because MEMS devices are manufactured using batch fabrication techniques similar to those used over multiple decades in the integrated circuit industry, we see unprecedented levels of functionality, reliability, and sophistication being placed on small silicon chips at a relatively low cost. Therefore, there is significant potential for MEMS technologies.

Although crystalline SiC is a polymorphic material that exists in well over 100 distinct polytypes, only the cubic 3C-SiC, and the hexagonal 4H-SiC and 6H-SiC polytypes are technologically relevant for MEMS applications since they are the only configurations that can be produced as high-quality substrates and/or thin epitaxial films. At present, 6H-SiC and 4H-SiC are the only polytypes that are commercially available in large-area, integrated circuit (IC)-grade wafer form suitable for epitaxial growth of single crystalline films. In contrast, 3C-SiC is not widely available as bulk substrates, but single crystalline films can be epitaxially grown directly on Si wafers despite a significant mismatch in both lattice constant and thermal coefficient of expansion.

Single crystalline 3C-SiC piezoresistive pressure sensors have been fabricated using bulk micromachining for high temperature gas turbine applications. Bare silicon exhibits inadequate tribological performance. It needs to be coated with a solid and/or liquid overcoat or be surface treated (e.g., oxidation and ion implantation, commonly used in semiconductor manufacturing), which exhibits lower friction and wear. SiC films exhibit good tribological performance. Studies have been conducted on undoped polysilicon film, heavily doped (n+-type) polysilicon film, heavily doped (p+-type) single-crystal Si (100) and 3C-SiC (cubic or b-SiC) film [10].

5.2. Surface micromachining

Surface micromachining involves the monolithic fabrication of suspended microscale structures by selective removal of underlying thin film sacrificial layers. Surface micromachining is inherently an additive process utilizing thin film deposition techniques to produce both structural and sacrificial layers. As such, the primary function of the substrate is to provide mechanical support for the resulting device. Patterning of the thin film layers involves wet and dry etching techniques that are sensitive only to the chemical properties of the materials, and not their microstructure or crystallinity, thereby enabling a high degree of flexibility with respect to planar designs. In concept, there is no restriction on the structural and sacrificial materials to be used in the fabrication of a particular device as long as the materials are compatible with each other during the fabrication process. As such, surface micromachining is not constrained by the properties of the substrate and, thus, can accommodate an extremely wide range of materials, including SiC.

Like silicon, SiC thin films can be deposited by chemical vapor deposition (CVD), making it particularly well adapted as a “plug-and-play” substitute for polysilicon in surface micromachining. SiC films can be deposited by low pressure chemical vapor deposition (LPCVD), atmospheric pressure chemical vapor deposition (APCVD), and plasma-enhanced chemical vapor deposition (PECVD). Even for non- MEMS applications, CVD is the by far most common method to deposit SiC due at least in part to the availability of precursor gases as well

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as numerous process and equipment similarities to silicon CVD. The silicon carbide analog to polysilicon is polycrystalline 3C-SiC, hereafter referred to simply as poly-SiC. Poly-SiC is actually more versatile than polysilicon in that it can be deposited directly on SiO_2 and polysilicon. In essence, the process of fabricating MEMS structures in poly-SiC by surface micromachining mirrors that of polysilicon. The main differences are process used to deposit the SiC films, the selection of sacrificial layer material, and the etch recipes used to pattern the structural films. A significant breakthrough in the advancement of SiC surface micromachining was the development of reactive ion etching techniques that are highly selective to SiC, which when combined with MEMS-friendly SiC deposition techniques, allow SiC surface micromachining to follow directly from polysilicon micromachining.

A wide range of micromachined structures, such as lateral resonators, flow sensors, capacitive pressure sensors, micromotors, and microbridge resonators can be fabricated using the deposition, patterning, etching, and sacrificial release techniques commonly used in polysilicon surface micromachining [11]. Several groups have demonstrated surface micromachining using a-SiC films as structural layers. Examples include RF switches and accelerometers [12]. Amorphous-SiC films deposited by PECVD generally exhibit a very wide range of residual stress (typically compressive in as-deposited films) that exhibit a strong dependence on deposition conditions [13].

5.3. Bulk micromachining

Bulk micromachining can generally be defined as a process to fabricate suspended structures by selective bulk removal of the supporting substrate. Bulk micromachined structures can be comprised of the substrate material itself or thin films that are deposited directly onto the substrate. Unlike surface micromachining, the substrate in bulk micromachined devices is not merely a solid mechanical support, but rather forms a key component of the device structure.

In Si MEMS, direct wafer bonding has proven to be a key enabling process in the production of silicon-on-insulator (SOI) wafers for the realization of single crystalline Si MEMS devices. To create a SiC-on-insulator substrate, the Si wafer that was originally used as the substrate for SiC growth is removed by etching. The principal factor affecting yield is wafer bowing due to high tensile residual stress in the 3C-SiC films. The techniques developed for Si bulk micromachining, including photoelectrochemical etching, DRIE, and laser micromachining, have been successfully adapted for SiC albeit typically with much lower etch rates [13]. Among the first SiC MEMS structures to be routinely fabricated were diaphragms, cantilever beams, and related structures fabricated out of single crystalline 3C-SiC films by silicon anisotropic etching. Although conventional wet chemical techniques are not effective in etching structures into SiC substrates, several electrochemical etch processes have been demonstrated and used in the fabrication of bulk micromachined SiC MEMS devices from 6H- and 4H-SiC substrates. Examples of such structures include pressure sensors [14], accelerometers [15], and more recently, biosensors [16]. It is worth mentioning that, the good biocompatibility of devices made with common micromachining technologies allows the exploration of these technologies.

5.4. Encapsulation and protection

In addition to using capsules or shells for providing a hermetic or vacuum package for MEMS, it is increasingly attractive to use thin films to provide the necessary protection or encapsulation [17-19] (Fig.2). Thin films are attractive because they occupy a very small area, can be formed using a variety of techniques, and are compatible with wafer-level processing. In addition, they can take any shape or form. However, most thin film materials are either not hermetic, or are so thin that they can be compromised easily when exposed to the environmental conditions MEMS typically experience. Two categories of thin film materials can be identified: organic and inorganic materials. Organic materials include such films as epoxies, silicones, a variety of polymers including polyimides, polyurethanes, Parylene-C, etc. The majority of these films can be deposited at low temperatures, are quite conformal and their characteristics can be modified for different applications. However, most of these films are not hermetic and most are prone to moisture penetration, or can be attacked in harsh environments. In spite of this, these materials have found widespread use because they can be selectively used in applications which may not require very long-term operation, or where the conditions are controlled, or where the performance specifications are not highly restrictive. In fact, polymers are perhaps the most widely used material for packaging, albeit not hermetic or vacuum packaging. The second category of materials used for packaging and protection is in-organic materials. These materials include films such as silicon nitride, silicon carbide, polycrystalline diamond, metal thin films, tantalum oxide, or thin films of other materials that are resistant to environmental parameters. Semiconductor materials such as silicon or silicon carbide are quite attractive because they can be deposited readily and are resistant to many corrosive environments. The main challenge in using these materials is that they typically require a high temperature to achieve a reasonable deposition rate, and in some instances the films are not quite as conformal as required by some applications. Therefore, they have not been widely used for hermetic packaging, especially where hybrid components are involved. The discussion is limited to inorganic thin films since it is not possible to discuss the broad category of organic materials that are used nowadays in the encapsulation and packaging of microdevices [20].

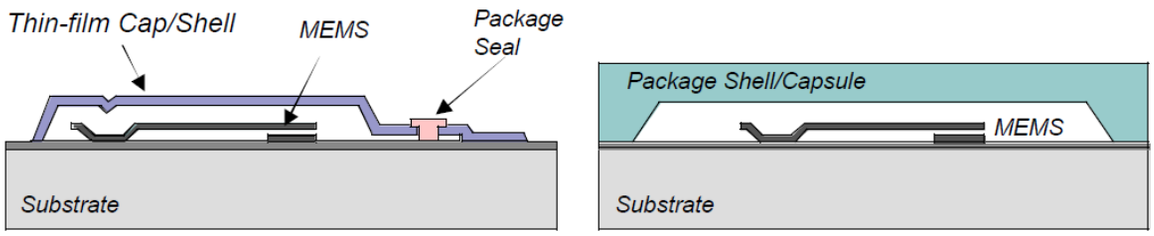

Figure 2. Structure of a MEMS package formed using a thin film capsule or shell, compared with a package formed using a bonded capsule or shell [20].

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6. Implantable BioMEMS

To date, the majority of the development efforts in the MEMS field have focused on sophisticated devices to meet the requirements of industrial applications. However, MEMS devices for medical applications represent a potential multi-billion dollar market, primarily consisting of micro miniature devices with high functionality that are suitable for implantation. These implanted systems could revolutionize medical diagnostics and treatment modalities. Implantable muscle microstimulators for disabled individuals have already been developed. Precision sensors combined with integrated processing and telemetry circuitry can remotely monitor any number of physical or chemical parameters within the human body and thereby allow evaluation of an individual's medical condition.

MEMS processing technology is also being used to fashion functionally simple passive microdevices like retinal implants [21, 22]. In the future, in order to improve functionality and reduce size, ever increasing numbers of MEMS devices will have direct patient contact thus requiring that biocompatibility testing be performed on MEMS materials of construction. Kotzar et al. selected the following materials as MEMS materials of construction for implantable medical devices: (1) single crystal silicon (Si), (2) polycrystalline silicon (polysilicon), (3) silicon oxide (SiO_2), (4) silicon nitride (Si_3N_4), (5) single crystal cubic silicon carbide (3C-SiC or b-SiC), (6) titanium (Ti), and (7) SU-8 epoxy photoresist. Of these, polysilicon, Si_3N_4, and 3C-SiC were deposited by chemical vapor deposition (CVD), SiO_2 by thermal oxidation of Si, Ti by physical vapor deposition (PVD), and SU-8 by spin coating [23]. Many of the earlier studies examining the biocompatibility of SiC employed materials generated by fabrication methods suited to other implantable applications, such as RF sputtering. The results of the biocompatibility tests for these fabrication methods may not apply to materials fabricated using MEMS technology.

The Kotzar et al. study [6] results for SiC show that when the material is generated using MEMS fabrication techniques, it elicited no significant non-biocompatible responses to the test battery employed in this series. The biocompatibility testing discussed by Kotzar et al. did not uncover any MEMS material that was not biocompatible when subject to the processing, packaging, and sterilization methods. Amorphous-SiC (a-SiC) has the longest and most diverse track record of any SiC microstructure used in biomedical microdevices. Early work using a-SiC for medical applications focused on developing a-SiC films as corrosion-resistant coatings for macroscale structures, such as Ti alloy-based orthopedic implants and metallic coronary stents [24], thus setting the stage for its use in biomedical microsystems.

7. Biosensing

7.1. Biosensors

Most of the studies conducted in the past on Single-crystal SiC provide evidence of the attractive bio potentialities of this material and hence suggest similar properties for crystalline

SiC. The properties that make this material particularly promising for biosensing applications are: 1) the wide bandgap that, as mentioned before, increases the sensing capabilities of a semiconductor; 2) the chemical inertness that suggests the material's resistance to corrosion in harsh environments such as body fluids (e.g. SiC does not react with any known material at room temperature, the only efficient etch being molten KOH at 400-600 ºC); 3) the high hardness (5.8 GPa), high elastic modulus (424 GPa), and low friction coefficient (0.17) that make it an ideal material for smart-implants and in-vivo biosensors. Studies report the significant finding that SiC surfaces are better substrates for mammalian cell culture than Si in terms of both cell adhesion and proliferation. In the past, the fact that cells could be directly cultured on Si crystalline substrates led to a widespread use of these materials for biosensing applications [25-27].

Singh and Buchanan [28] studied silicon carbide carbon (SiC-C) composite fiber as an electrode material for neuronal activity sensing and for biochemical detection of electroactive neurotransmitters. The SiC-C electrode surface has nanosized pores which significantly increase the real surface area for higher charge densities for a given geometrical area. Neurotransmitters including dopamine and vitamin C were successfully detected using SiC-C composite electrodes. Researchers fabricated impedance and temperature sensors on bulk SiC for a biomedical needle that can be used for open heart surgery monitoring or graft monitoring of organs during transportation and transplantation. According to Godignon [29], other applications can be foreseen, such as DNA polymerase chain reaction (PCR), electrophoresis chips and cell culture micro-arrays. In DNA electrophoresis devices, the high critical electric field and high resistivity of semi-insulating SiC would be beneficial. In DNA PCR, it is the high thermal conductivity which could improve the device's behaviour. In addition, in most of these cases, the transparency of semi-insulating SiC can be used for optical monitoring of biological processes, such as the DNA reaction or the cell culture activity. Ghavami et al. used Field emission scanning electron microscopy (FE-SEM) and transmission electron microscopy (TEM) techniques to examine the structure of the SiCNP/GC modified electrode. The modified electrode shows excellent electrocatalytic activity toward guanine, adenine, thymine and cytosine. Differential pulse voltammetry (DPV) was proposed for simultaneous determination of four DNA bases. The effects of different parameters such as the thickness of the SiC layer, pulse amplitude, scan rate, supporting electrolyte composition and pH were optimized to obtain the best peak potential separation and higher sensitivity. The modified electrode can be used for simultaneous detection of purine and pyrimidine bases without any separation or pretreatment processes and may be used as a DNA biosensor in real samples [30].Caputo et al. [31] reported on biomolecule detection based on a two-color amorphous silicon photosensor. The device design has been optimized in order to maximize the spectral match between the sensor responses and the emission spectra of the fluorochromes. This optimization process has been carried out by means of a numerical device simulator, taking into account the optical and the electrical properties of the amorphous silicon materials. The development of minimally invasive and short-term implantable devices for on-line tissue monitoring is a field of increasing clinical and industrial interest, with applications in areas such as open-heart surgery or insulin control. Multisensory micro-needles have been developed to measure physiologically relevant intra-

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tissular parameters during cold transportation of transplantation organs. Si-based minimally invasive probes have already gone beyond the proof-of-concept stage and are currently undergoing Phase-I clinical trials [32]. Gabriel et al. [33] examine the feasibility of using SiC as a substrate for the development of minimally invasive multi-sensor micro-probes in the context of organ monitoring during transplantation. In particular, they make a thorough comparison of Si and SiC material mechanical and electrical properties. As illustrated in Figure 3, Si and semi-insulating SiC micro-needles for impedance and temperature measurement were fabricated using remarkably similar methods.

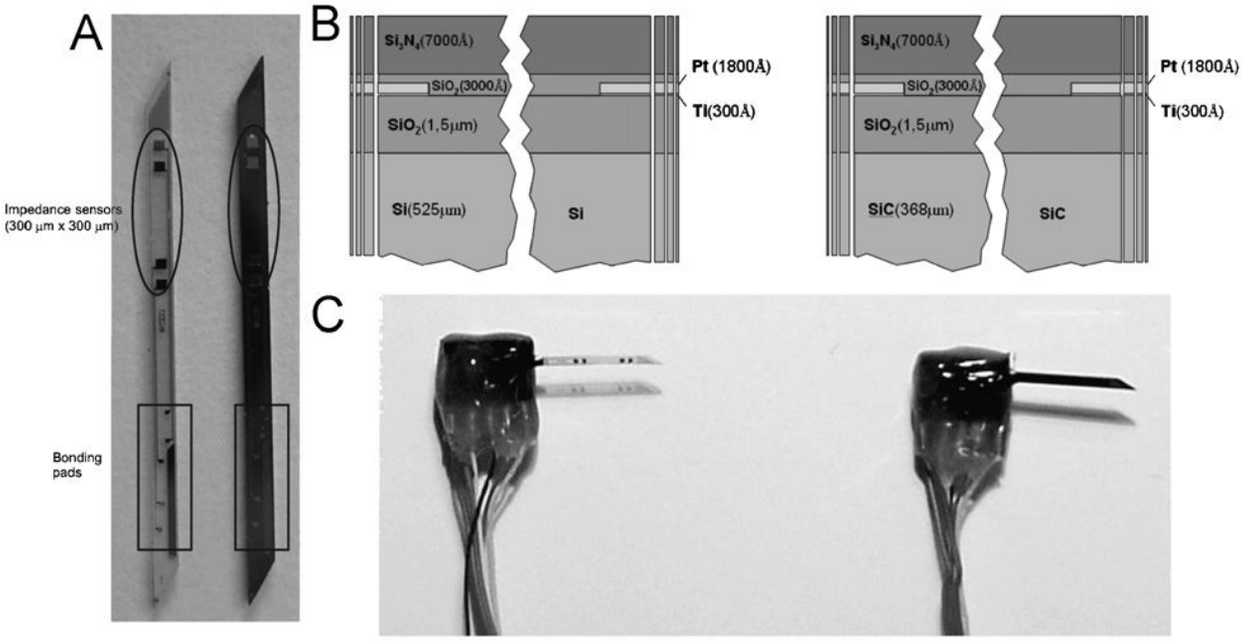

Figure 3. A) Needle-shaped Si (left) and SiC (right) probes for impedance and temperature monitoring. (B) Schematic drawing of the technological process for Si (left) and SiC (right) probe production. (C) Encapsulated SiC (left) and Si (right) devices [33].

Their results show that SiC outperforms Si in all respects, with a four times higher modulus of rupture for SiC devices and a 10-fold increase in the frequency range for electrical measurements in SiC-based probes. These results suggest that SiC should be preferably used over Si in all biomedical applications in which device breakage must be avoided or very precise electrical measurements are required [33]. 3C-SiC has a distinct advantage over the other SiC polytypes in that simple micromachining technique can be used to fabricate nanoscale 3C-SiC structures. In fact, the first SiC NEMS were demonstrated in 3C-SiC due to the ability to grow ultrathin 3C-SiC films on Si substrates combined with selective reactive ion etching processes that enable patterning and release of the nanostructures with essentially the same plasma [34]. Other groups have used similar techniques to create 3C-SiC and AlN NEMS structures [35]. Figure 4 shows SEM images of 3C-SiC NEMS microbridges. Naik et al. extended this work toward biosensing applications by demonstrating that 3C-SiC NEMS resonators were able to detect individual protein adsorption events by observing frequency

shifts for each exposure event when the resonators were selectively exposed to bovine serum albumin (BSA) and β-amylase (200 kDa) [36].

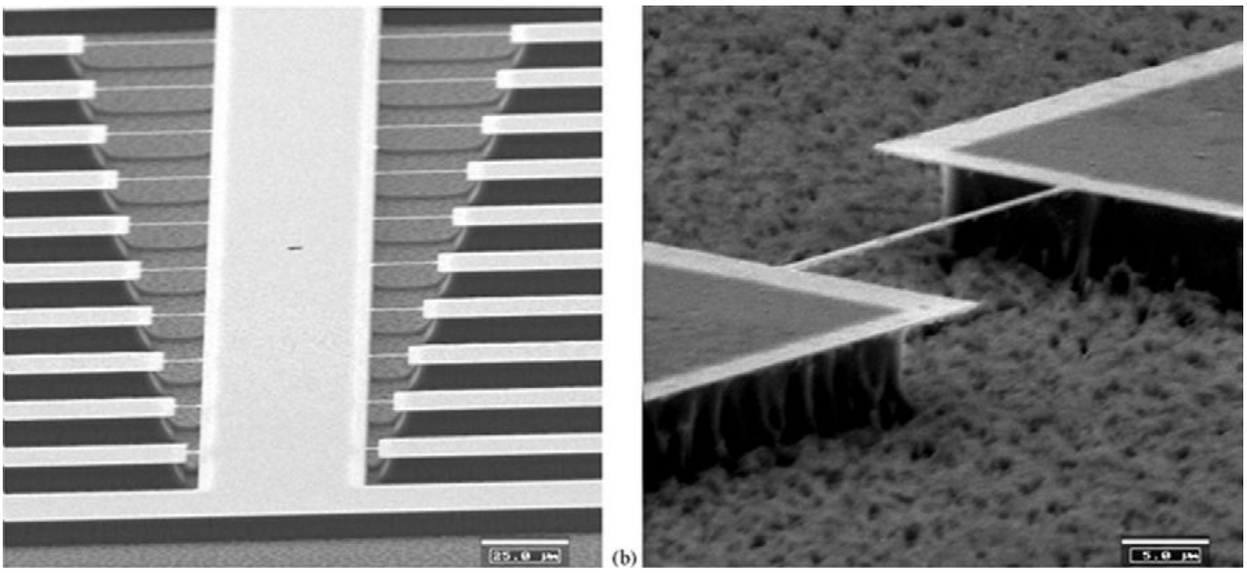

Figure 4. Scanning electron micrographs of 3C-SiC NEMS microbridges [35].

Silicon carbide for chemical sensing devices has been demonstrated to be the best candidate for high temperature chemical gas sensors. The wide bandgap, combined with chemical inertness, result in SiC being the best material for gas sensing in harsh environments or at high temperatures. Thin film silicon carbide exhibits thermal conductivity on the same order of single crystalline silicon and has a fast thermal response [13]. MEMS-based microprobes for neural interfacing and biosensing applications are currently the subject of intense research due to the promise of achieving high functionality in a minimally invasive form-factor. A typical planar neural probe, for example, consists of a thin shank that supports multiple, thin film metallic electrodes. A common material for the shank is Si; however, concerns over the electrical performance, mechanical robustness and biological interactions of these structures currently limit their applicability in long-term deployment situations.

For neurostimulation applications, the electrode material must provide charge transfer under low interface impedance to avoid tissue trauma. Surface morphology plays an important role in the electrode's charge carrying capabilities. The real surface area of an electrode can be significantly different from its geometrical area. Higher real surface areas can deliver higher charge densities for a smaller electrode. For a microelectrode, size is a limiting factor, so there should be ways to increase real surface area. Real surface areas can be modified by treating the electrodes electrolytically. The SiC-C electrode surface as seen in the SEM images (Fig. 5) has nanosized pores which significantly increase the real surface area for higher charge densities for a given geometrical area. Thus high real surface area electrodes are highly desirable and were observed in electrolytically modified SiC-C electrode surfaces. Neurotransmitters including dopamine and vitamin C were successfully detected using SiC-C composite electrodes [37].

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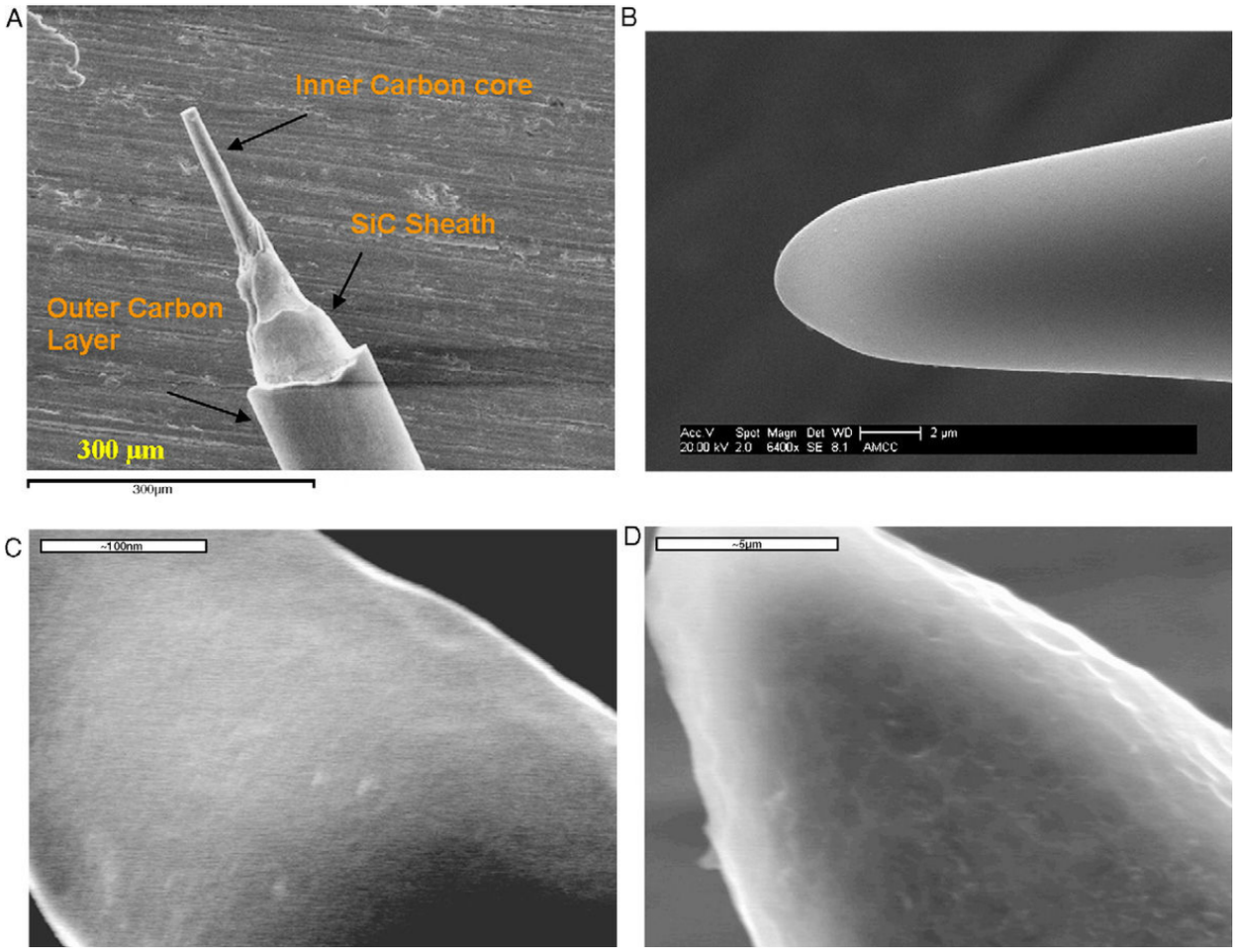

Figure 5. SEM pictures of (A) silicon carbide carbon composite fiber's etched section, (B) carbon recording tip, (C) low voltage etch (smooth surface), and (D) high voltage etch (high surface area surface) [37]

In many clinical settings, a decrease of the blood supply to body organs or tissues can have fatal consequences if it is not properly addressed promptly (e.g. mesenteric or myocardial ischemia). Sustained ischemia leads to hypoxia, a stressful condition for cells that can induce cell lysis (necrosis) and trigger programmed cell death (apoptosis) and, consequently, lead to organ failure. Aside from ischemic diseases, ischemia underlies other natural and clinically induced conditions, such as tumor growth, cold-preservation of grafts for transplantation or induced heart-arrest during open heart surgery. Therefore, the ability to monitor ischemia in clinical and experimental settings is becoming increasingly necessary in order to predict its irreversibility (e.g. in the transplantation setting), to develop drugs to prevent and revert its effects, and to develop vascular-targeting drugs for the treatment of growing tumors. To address these issues and to extend the utility of MEMS-based probe technology, a minimally invasive system for the continuous and simultaneous monitoring of tissue impedance has been developed, and experimental results have shown its reliability for early ischemia detection and accurate measurement of ischemic effects. This minimally invasive system consists of a small micro-machined silicon needle with deposited platinum electrodes for impedance measurement that can be inserted in biological tissues with minimal

damage. High frequency impedance monitoring, based on both the phase and modulus components of impedance, has been correlated to the combined dielectric properties of the extracellular and intracellular compartments and insulating cell membranes, and can give complementary information on other effects of sustained ischemia. Moreover, multi-frequency monitoring of impedance has the advantage of yielding to more comprehensive empirical mathematical characterizations (i.e. the Cole model) that can provide additional information through the analysis of derived parameters and improve the reproducibility of results [5]. Gomez et al. [38] examined the feasibility of producing SiC-based needle-shaped impedance probes for continuous monitoring of impedance and temperature in living tissues. SiC needle-shaped impedance probes (Fig.6) were produced in standard clean room conditions.

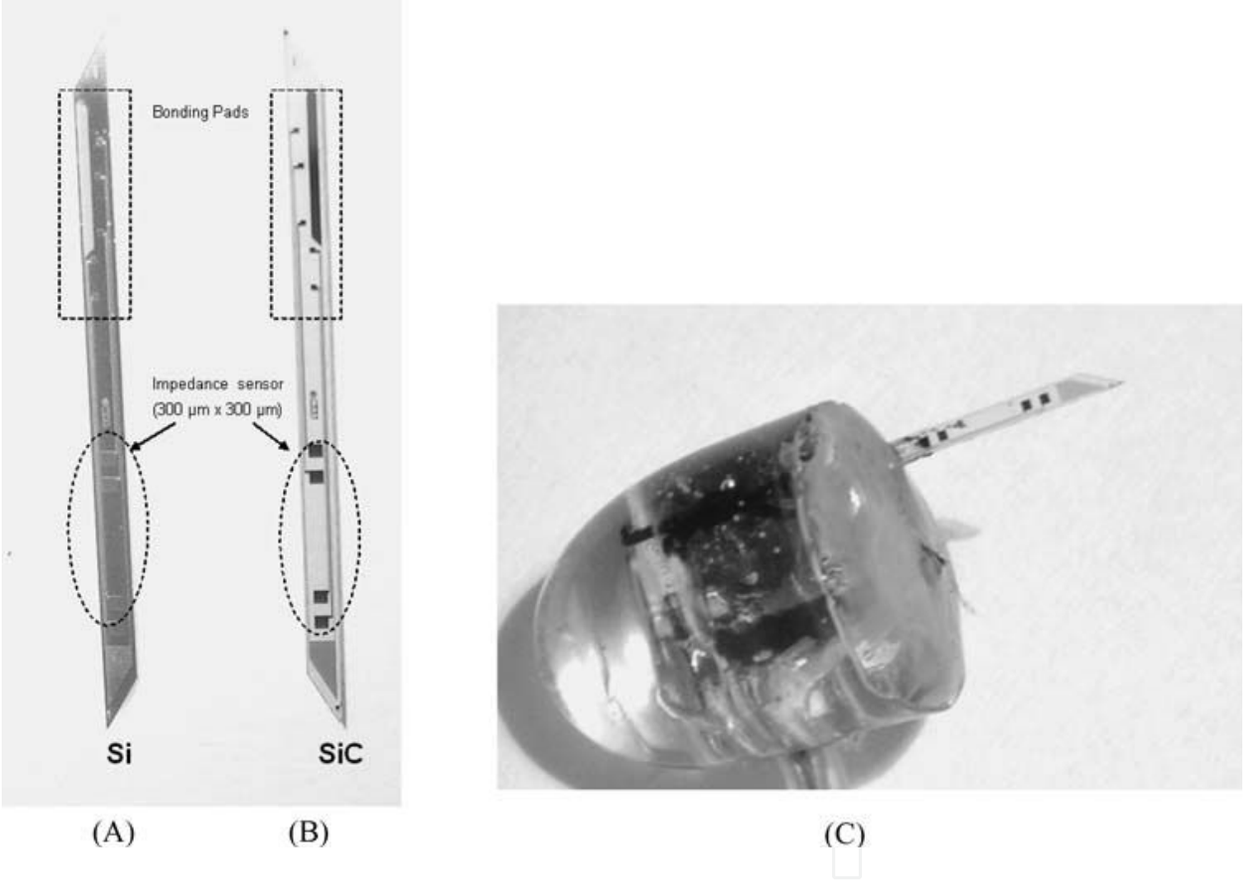

Figure 6. A) Needle-shaped Si probe for impedance; (B) Needle-shaped SiC probe for impedance; (C) Needle-shaped with packaging [38]

In vitro results obtained with SiC based impedance probes were compared with those obtained with Si-based probes, and they demonstrated that the use of SiC substrates was mandatory to extend the effective operation range of impedance probes beyond the 1 kHz range. In-vivo evaluation of SiC-based impedance probes was conducted on rat kidneys undergoing warm ischemia by dissecting and clamping the renal pedicles. A substantial rise in impedance modulus was shown throughout the ischemic period (5 to 50 min); this increase can

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be attributed to the occurrence of hypoxic edema as the result of cell swelling, which leads to a reduction of extracellular space, an increase in extracellular resistance, and cell-to-cell uncoupling. Upon unclamping of the renal artery (50 min), impedance modulus can be seen to return to its basal value, a fact that can be attributed in this experimental setting to a reversion from a short period of ischemia without substantial structural damage to the tissue. A fall in impedance modulus at low frequencies, however, has also been reported as a consequence of membrane breakdown and cell lysis due to sustained ischemia. It is in this respect that the multifrequency analysis of the phase component of impedance made possible by the use of SiC-based probes conveys useful complementary information [5]. Therefore, according to this set of materials, one can conclude that SiC would be considered a good candidate for biosensing applications.

7.2. Microelectrode arrays

The emerging field of monitoring biological signals generated during nerve excitation, synaptic transmission, quantal release of molecules and cell-to-cell communication, stimulates the development of new methodologies and materials for novel applications of bio-devices in basic science, laboratory analysis and therapeutic treatments. The electrochemical gradient results in a membrane potential that can be measured directly with an intracellular electrode. Extracellular signals are smaller than transmembrane potentials, depending on the distance of the signal source to the electrode. Over the last 30 years, non-invasive extracellular recording from multiple electrodes has developed into a widely-used standard method. A microelectrode array is an arrangement of several (typically more than 60) electrodes allowing the targeting of several sites for stimulation and extracellular recording at once. One can plan the realisation of four activities with the following tasks:

Task 1. Development of new biocompatible substrates favouring neuronal growth along specific pathways.

Task 2. Monitoring of electrical activity from neuronal networks.

Task 3. Resolution of cellular excitability over membrane micro areas.

Task 4. Detection of quantal released molecules by means of newly designed biosensors.

Task number 1 can be realized by means of SiC substrates, by plating the cells directly on the substrate or eventually with an additional proteic layer. For this aim, 3C-SiC films with controlled stoichiometry, different thickness and crystalline quality can be grown directly on silicon substrates or on silicon substrates previously 'carbonised'. The main objective of task number 2 is the realization of SiC microelectrode arrays whose dimensions will be compatible with the cellular soma (10-20 μm). In this structure, every element of the array is constituted by a doped 3C-SiC region, with metallic interconnections coated with amorphous silicon carbide, so that silicon carbide represents the only material interfaced to the biological environment. For the realization of Task number 3, the SiC array will be improved by constructing microelectrodes in the submicrometric range, in order to reveal electrical signals from different areas of the same cell. The objective of task number 4 is the construction of a prototype of SiC-electrodes array as a chemical detector for oxidizable molecules re-

leased during cell activities triggered by chemical substances (KCl or acetylcholine) on chromaffin cells of the adrenal gland. With respect to classical electrochemical methods requiring polarized carbon fibers with rough dimensions of 10 micrometers in diameter, the SiC multielectrode array should greatly improve the monitoring of secretory vesicle fusion to the plasma-membrane, allowing the spatial localization and temporal resolution of the event [5].

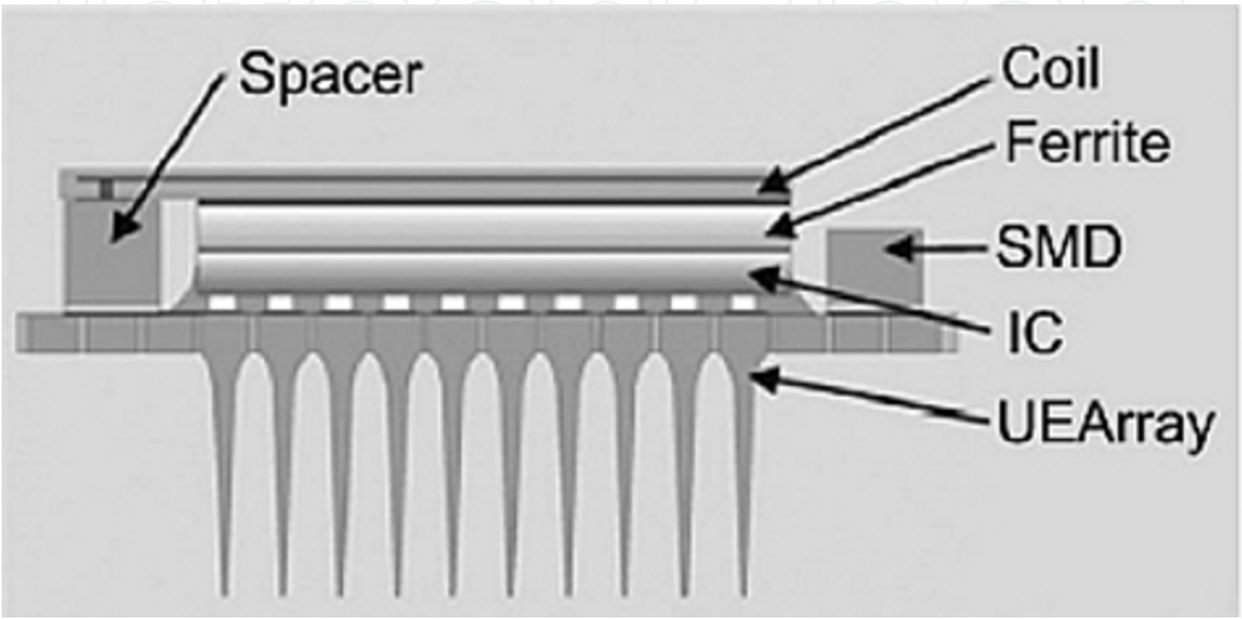

Figure 7. Schematic diagram of the Utah Electrode Array [41]

To demonstrate the feasibility of developing SiC-based devices on large-area SiC substrates, Godignon et al. recently reported the development of 4H-SiC-based microelectrode arrays on semi-insulating 4-in. diameter hexagonal substrates [39]. The microelectrode arrays consisted of a SiO_2/Si_3N_4 passivation layer sandwiched between microfabricated Pt electrodes and the SiC substrate. Carbon nanotubes (CNTs) were easily grown by rapid thermal chemical vapor deposition on the Pt electrodes using CH4 and H2 at 800 °C, conditions for which the SiC substrate is well suited. The detection of biological species using microarrays and lab on-a-chip systems is a powerful diagnostic tool that enables the acquisition of genetic, proteomic, and cellular information. Such approaches allow rapid analysis of disease diagnostics, drug discovery, or food and environmental analysis. In microarray applications, each pixel in the array is functionalised with well-defined probe molecules and a molecular recognition reaction occurs between the probe and the target molecules to be detected [40]. Hsu et al. [41] has recently developed a-SiC as a protective coating for MEMS-based Si penetrating microelectrodes. The technology driver for this research is an integrated, Si-based microneedle electrode array known as the Utah Electrode Array (UEA). Shown schematically in Figure 7, the UEA is a three-dimensional structure consisting of a 10 × 10 array of tapered silicon shanks that are bulk micromachined into a Si substrate. Each shank supports Ti/Pt/Ir electrodes that provide the electrical interface to nerve tissue. The array is integrated

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with Si-based IC's and packaged using a variety of conventional approaches that are adapted for this particular device. Hsu et al. have developed PECVD-based a-SiC:H coatings to encapsulate components of the UEA.

8. Biofiltration

Absorption filters based on hydrogenated amorphous silicon–carbon alloys are developed for application as fluorescence filters in microarray and lab-on-a-chip systems. Fluorescence is one of the most commonly used methods for the detection of proteins, cells and DNA in microarrays [42, 43]. The method uses an external light source, which excites the fluorophores that label the entities of interest. The integration of a fluorophore sensor at each pixel of a microarray would allow for a rapid and real-time detection of the biological recognition event, while potentially increasing sensitivity and portability, and reducing costs. Fluorescence detection, however, requires the development of efficient light management to prevent the excitation light from reaching the detector and at the same time allow the emission light to be transmitted to the detector. Lipovesk et al. [40] proposed a layer of hydrogenated amorphous silicon carbide (a-SiC:H) as a suitable optical filter which can be easily integrated with a-Si:H photosensors for on-chip detection of biomolecules labelled with Alexa Fluor 430 or PyMPO. Simple fabrication of absorbing a-SiC:H filters (single-layer, low cost, with low dependence on the incidence angle) presents an important advantage compared to other filtering solutions, such as interference filters [44] where a large number of layers need to be tuned accurately during deposition. The challenge is to optimise the filtering characteristics of the a-SiC:H filter in order to match the excitation/emission wavelength fingerprint of any selected fluorophore. Therefore, a-SiC:H filters of different carbon content resulting in appropriate optical properties have to be designed. The relation between the carbon content in the a-SiC:H film and its optical filtering characteristics must be determined to enable the fabrication of the optimal filter for detection of a selected fluorophore.

The filtering characteristics of all filters are compared to the excitation/emission properties of numerous biologically relevant natural fluorophores. For each fluorophore, the most suitable a- SiC:H filter is necessary in order to ensure the highest rejection ratio between the transmitted emission/excitation light, thus achieving the optimal sensitivity of the fluorescence measuring system. As a proof-of-concept, one of the filters is tested to demonstrate the detection of the reduced form of nicotinamide adenine dinucleotide (NADH), an enzyme cofactor and an important marker for cell metabolic activity [45]. MEMS devices fabricated from bulk 6H-SiC wafers leverage heavily on the outstanding mechanical durability of the substrate, the chemical inertness of the 6H-SiC surface, the commercial availability of high-quality wafer substrates and the versatile micromachining techniques available to render devices from them. As such, bulk SiC substrates offer nearly all the advantages of bulk Si substrates but with more robust properties. Like Si, porous SiC structures can be formed from 6H-SiC wafers by electrochemical etching. Under the proper conditions, the pore size and porosity of the resulting structures offer the potential to use porous SiC in biofiltration applications. For biofilteration applications, the porous material was formed by bulk electro-

chemical etching of p-type and n-type, 6H-SiCsubstrates [13]. Rosenbloom et al. reported the development of porous SiC membranes for use as protein filters [46]. The performance of the porous SiC membranes was evaluated using protein-containing solutions with proteins ranging in molecular weight from 17,000 to 80,000 Daltons (Da). It was found that the membranes were able to pass proteins with molecular weights of up to 29 kDa and were able to exclude proteins in excess of 45 kDa. Moreover, the porous SiC membranes exhibited lower protein absorption as compared to commercially available polymer-based membranes specifically designed for protein absorption, indicating the potential for SiC membranes in biofilteration applications [13].

Micromachined 3C-SiC membranes also provide excellent specimens to study the mechanical durability of 3C-SiC films since the adhesion of the film to the micromachined substrate is extremely high, due in part to the carbonization based growth process. Suspended 3C-SiC membranes have proven to be an attractive mechanical structure for micromachined pressure sensors owing to their chemical inertness, mechanical durability and high temperature stability. In comparison with Si membranes, SiC membranes are much easier to fabricate [2].

9. Biomedical imaging

In addition to its outstanding mechanical properties, 3C-SiC thin films have unique electro-optic properties that can be exploited for biomedical imaging. In conventional optical microscopy, diffraction effects limit the spatial resolution to one-half of the illuminating wavelength. A technique known as near-field scanning optical microscopy (NSOM) has recently emerged as a means to resolve images below the diffraction limit. NSOM utilizes a detector that is placed in very close proximity to a sample in order to detect evanescent fields associated with the surface of the specimen. Such characteristics make NSOM a potentially powerful tool for biological imaging. However, a drawback of NSOM is that the AFM-based probe significantly limits the ability to image biological specimens in fluidic environments [13, 47].

10. Microfluidics/Lab-on-a-Chip

An example of a wristwatch type biosensor based on microfluidics referred to as lab-on-a-chip system is shown in Fig. 8. The advantages of these systems are incorporating sample handling, separation, detection, and data analysis onto one platform. The chip relies on microfluidics and involves manipulation of tiny amounts of fluids in microchannels using microvalves. The test fluid is injected into the chip generally using an external pump or syringe. Some chips have been designed with an integrated electrostatically-actuated diaphragm type micropump. The sample, which can have volume measured in nanoliters, flows through microfluidic channels via an electric potential and capillary action using microvalves (having various designs including membrane type) for various analyses. The fluid is preprocessed and then analyzed using a biosensor.

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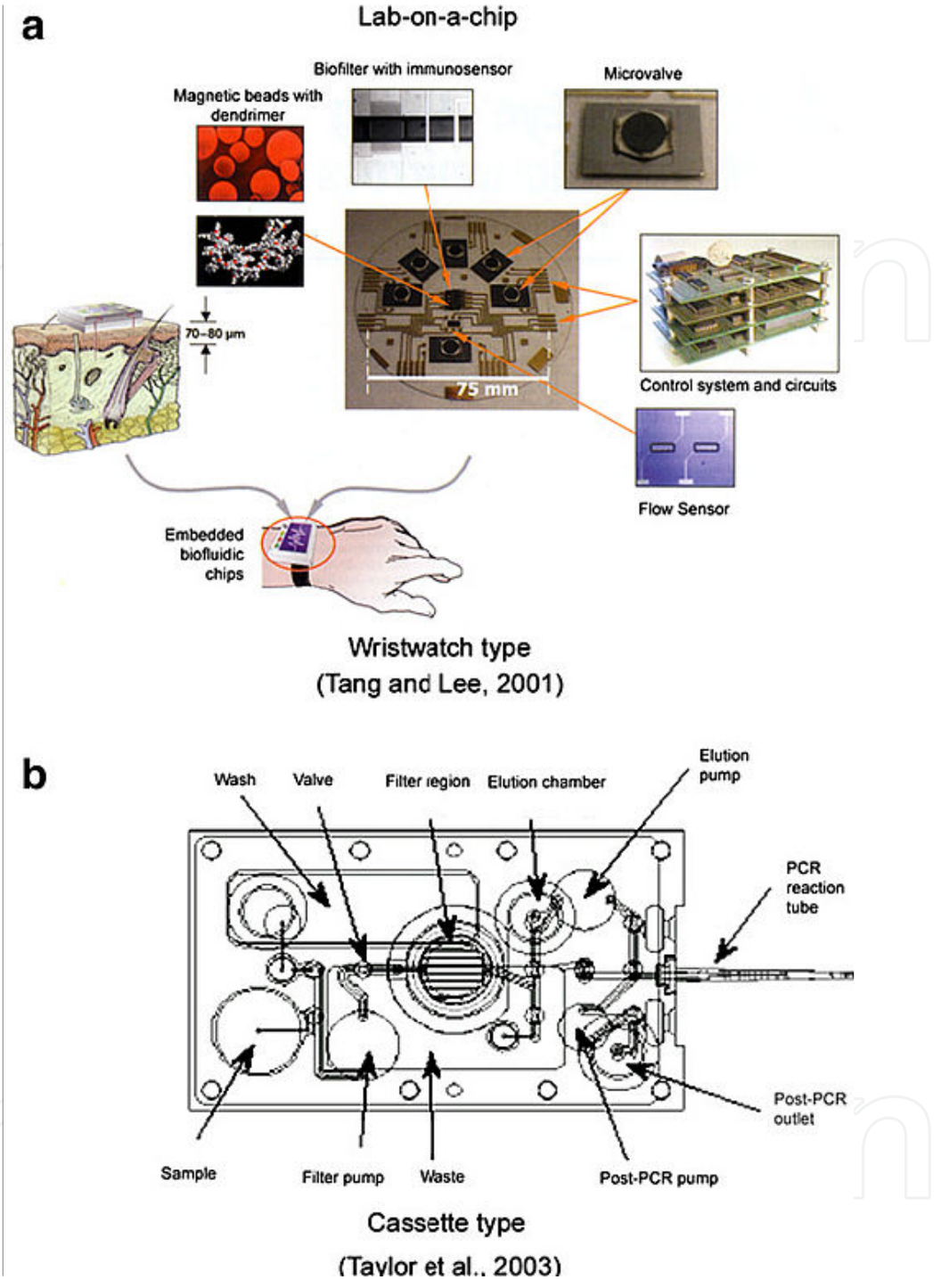

Figure 8. MEMS based biofluidic chip, commonly known as a lab-on-a chip that can be worn like a wristwatch [1].

The implementation of micropumps and microvalves allows for fluid manipulation and multiple sample processing steps in a single cassette. The three basic components of a mechanic valve are the actuator, the valve spring and the valve seat. The spring force keeps the valve shut in normally closed valves. In the case of normally open valves, the spring keeps the valve open and works against the actuator. A small spring constant can be realized with a soft mate-

rial such as rubber. The solution with soft materials offers a further advantage of excellent sealing characteristics. The leakage ratio can be improved from three to four orders of magnitude compared to those made of hard material such as silicon, glass, or silicon nitride. If the valve is designed for bistable operation, there is no need for a valve spring because the two valve states are controlled actively. Since the non-powered state is undefined, a valve spring can still be considered for the initial, nonpowered state to assure safe operation. A bistable valve spring allows the valve seat to snap into its working position. In this case, the actuator needs to be powered in a short period to have enough force to trigger the position change. The force generated by the spring is then high enough to seal the valve inlet [48].

Valve seats represent a large challenge to microvalve design and fabrication. The valve seat should satisfy two requirements: low leakage and high resistance against particulate contamination. For a minimum leakage rate, the valve should be designed with a large sealing area, which must be extremely flat. Softer materials such as rubber or other elastomers are recommended for the valve seat. Resistance against particles can be realized in many ways. First, a hard valve seat can simply crush the particles. For this purpose, the valve requires actuators with large force such as piezostacks and hard coating layer for the valve seat. Second, the particles can be surrounded and sealed by a soft coating on the valve seat. Third, small particle traps such as holes or trenches can be fabricated on the valve seat or on the opposite valve base. A combination of the third measure with the first and second measures is recommended, so that tiny particles can be trapped and buried after being crushed by the large actuation force. For the first and third measures, the valve seat needs to be coated with hard, wear-resistant material such as silicon nitride, silicon carbide, or diamond [9].

Blood or other aqueous solutions can be pumped into the system where various processes are performed. If the adhesion between the microchannel surface and the biofluid is high, the biomolecules will stick to the microchannel surface and restrict flow. In order to facilitate flow, the microchannel surfaces with low bioadhesion are required. Fluid flow in polymer channels can produce triboelectric surface potential which may affect the flow. Polymers are known to generate surface potential and the magnitude of the potential varies from one polymer to another [1]. Conductive surface layers such as SiC can be deposited on the polymer channels to reduce triboelectric effects. Compared with its crystalline counterparts, amorphous-SiC is particularly attractive for microfluidics and related lab-on-a-chip applications because it can be deposited on a much wider range of substrate materials while retaining a high level of chemical inertness.

These features are the way for on-line monitoring of several processes in many application fields. A large new area is that of micrototal analysis systems (μTAS) or lab-on-a chip, where attempts are made to completely integrate biochemical systems on one silicon or glass chip. A currently emerging development is that of miniaturized integrated physical chemosensors and biosensors. Rather than applying a chemical interface to determine the biochemical properties of fluids, physical properties or phenomena in the fluid are used. Persisting problems with such a chemically sensitive interface layer, such as poor reproducibility, drift, ageing and contamination, are circumvented in this approach. All these devices require new technological approaches for the fabrication of small channels, novel integrated microdetec-

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tors, and other components. Most compounds used for biochemical analysis do not possess a fluorescent functionality, and thus labeling with a fluorescent marker is required. Recently, the on-chip integration of electrochemical and conductivity detection has been reported [49]. A schematical drawing of the chip is shown in Fig. 9.

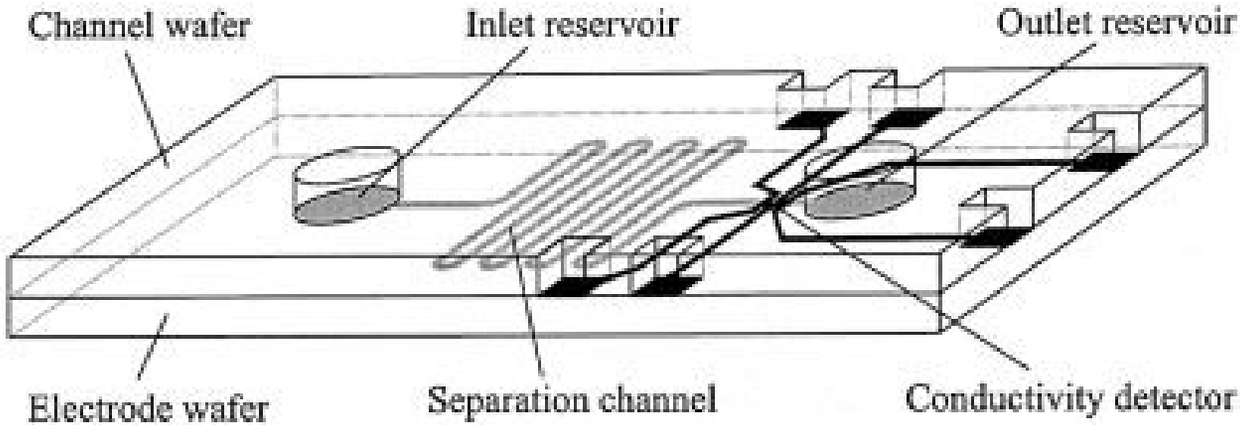

Figure 9. Drawing of a microchemical detector containing electrophoresis separation and conductivity detection [49]

Conductivity detection can be used for on-chip measurements. To avoid electrolysis and electrode fouling when the solution was in contact with the measurement electrodes, contactless conductivity detection was proposed. A four-electrode capacitively coupled (contactless) detector has been integrated on a Pyrex glass chip for detection of peptides (1 mM) and cations (5 mM K+, Na+, Li+). The Al electrode (500 nm Al/100 nm Ti) was deposited in a 600- nm-deep trench and was covered with a thin dielectric layer (30-nm SiC). The other parts of the channel were covered and insulated with Si_3N_4 (160 nm). This four-electrode configuration allows for sensitive detection at different background conductivities without the need for adjustment of measurement frequency. In contactless mode, the dielectric thickness should be small [50]. Iliescu et al. [51] recently explored the use of a-SiC membranes as structures for chip-based cell culturing. The optical properties of the SiC film supported the use of classical fluorescence microscopy and thus were ideal for cell culturing studies. NH_4F was used to reduce the native oxide on the SiC surfaces. The NH_4F surface treatment resulted in greater cell density on the a-SiC samples as compared with untreated surfaces. Collectively, these achievements show the potential for SiC in highly functional lab-on-a-chip devices.

11. Conclusions

Silicon Carbide is a wide-band-gap semiconductor biocompatible material that has the potential to improve biomedical applications. SiC devices offer higher power densities and lower energy losses, enabling lighter, more compact and more efficient products for biocompatible and long-term in vivo applications such as sensors. The main problem facing the

medical community today is the lack of biocompatible materials that are also capable of electronic operation. Silicon carbide has gained favor in the biomedical microdevice community for its potential as a structural and packaging material. Currently, bioMEMS devices that utilize SiC are relatively simple in design. Continued development of processing techniques that make SiC compatible with polymeric and other temperature-sensitive substrates is critical if SiC is to play a significant role in next-generation implantable biomedical microdevices. Therefore, SiC will have matured to the point where it can take its place with Si and its derivatives (SiO_2 and Si_3N_4) in the toolbox of commonly used MEMS and NEMS materials. In the near future it is expected that the semiconductor structures will have a profound effect on the capabilities of BioMEMS. Not only will the quantum dots and quantum planar structures be a major player in this area, but it is also expected that nanoporous and especially nanorods and nanocolumn arrays will provide new directions for the development of chemical sensors and biosensors capable of tackling the modern challenges of direct chemical analysis.

Author details

Mahboobeh Mahmoodi[1*] and Lida Ghazanfari[2]

*Address all correspondence to: m.mahmoodi@aut.ac.ir

1 Department of Materials science and Engineering, Yazd Branch, Islamic Azad university, Yazd, Iran

2 Biomateials Group, Faculty of Biomedical Engineering, Amirkabir University of Technology, Tehran, Iran

References

[1] Bhushan B. Nanotribology and Nanomechanics of MEMS/NEMS and BioMEMS/BioNEMS Materials and Devices, Microelectronic Engineering 2007; 84, 387–412.

[2] Zorman C. A., Parro R. J. Micro- and Nanomechanical Structures for Silicon Carbide MEMS and NEMS, Phys. Stat. Sol. B 2008; 245(7) 1404–1424.

[3] Cimalla V., Pezoldt J., Ambacher O. Group III Nitride and SiC Based MEMS and NEMS: Materials Properties, Technology and Applications J. Phy. D 2007; 40, 6386–434.

[4] Coletti C., Jaroszeski M. J., Pallaoro A., Hoff A. M., Iannotta S., Saddow S. E. Biocompatibility and Wettability of Crystalline SiC and Si Surfaces. In: Proceedings of 29th Annual International Conference of the IEEE EBMS, Lyon, France, August 23–26, 2007; p. 5849–52.

[5] Mahmoodi M., Ghazanfari L. Fundamentals of Biomedical Applications of Biomorphic SiC. In: Gerhardt R. (ed.) Properties and App lications of Silicon Carbide. InTech;2011. p 297-345. Avaliable from http://www.intechopen.com/books.

[6] Kotzara G., Freasa M., Abelb P., Fleischmanc A., Royc S., Zormand C., Morane J. M., Melzak J. Evaluation of MEMS Materials of Construction for Implantable Medical Devices, Biomat.

[7] Ferrari M. BioMEMS and Biomedical Nanotechnology, Volume III, Therapeutic Micro /Nano Technology, Springer 2006.

[8] Bolz A., Schaldach M. Biomaterials Haemocompatibility Optimization of Implants by Hybrid Structuring. Med. Biol. Eng. Comput. 1993; 31, 123-130.

[9] Nguyen N. T., Wereley S. T. Fundamentals and Applications of Microfluidics Artech House, 2002; 471.

[10] Bhushan B., S. Sundararajan, Li X., Zorman C.A., Mehregany M. Tribology Issues and Opportunities in MEMS, Kluwer Academic, Dordrecht, Netherlands 1998; 407-430.

[11] Mehregany M., Zorman C. A. SiC MEMS: Opportunities and Challenges for Applications in Harsh environments. Thin Solid Films 1999; 355–356:518–24.

[12] Parro R. J., Scardelletti M. C., Varaljay N. C., Zimmerman S., Zorman C. A. Amorphous SiC as a Structural Layer in Microbridge Based RF MEMS Switches for Use in Software Defined Radio. Solid-State Electron 2008;52, 1647–51.

[13] Zorman C. A., Barnes A. C. Silicon Carbide BioMEMS, Elsevier Inc. Chapter 10, 2012.

[14] Okojie R. S., Ned A. A., Kurtz A. D. Operation of a 6H-SiC Pressure Sensor at 500 °C. Sens Actuators A 1998; 66, 200–4.

[15] Atwell A. R., Okojie R. S., Kornegay K. T., Roberson S. L., Beliveau A. Simulation, Fabrication and Testing of Bulk Micromachined 6H-SiC High-g Piezoresistive Accelerometers. Sens Actuators A 2003;104, 11–18.

[16] Zhao F., Islam M. M. Fabrication of Single Crystal Silicon Carbide MEMS/NEMS for Bio Sensing and Harsh Environments. In: Proceedings of MEMS 2011. Cancun, Mexico, January 23, 2011; p. 261–3.

[17] Kageyama, et al. Resonating Microstructures in Microshells with HF Permeable Polycrystalline Silicon and Vacuum Sealing Thin Films, Digest, The 10th IEEE Int. Conf. On Solid-State Sensors and Actuators (Transducers '01), Sendai, Japan, June 1999; 340-343.

[18] Stark B.H., Najafi K. An Ultra-Thin Hermetic Package Utilizing Electroplated Gold, Technical Digest, 11th IEEE Int. Conf. Solid-State Sensors and Actuators (Transducers '01), Munich, Germany June 2001; 194-197.

[19] Stark B. H., Najafi K. A Wafer-Level Vacuum Packaging Technology Utilizing Electroplate Nickel, ASME Congress, MEMS And Nanotechnology Symposium, New Orleans, USA, Nove. 17-22, 2002.

[20] Najafi K. Micropackaging Technologies for Integrated Microsystems: Applications to MEMS and MOEMS, Micromachining and Microfabrication Process Technology VIII, Proceedings of SPIE 2003; 4979.

[21] Miller S., Rizzo J. F., Wyatt J. L. Development of a Silicon Retinal Implant: Long-Term Biocompatibility of Materials, Invest Ophthalmol Visual Sci. 1995; 36(4) S746.

[22] Zrenner E., Kohler K., Haemmerle H., Nisch W., Stelzle M. Biocompatibility and Long Term Stability of Silicon Photodiode Arrays Implanted in the Subretinal Space, Soc. Neurosci. Abstr. 1999; 25(1–2) 219.

[23] Peachey N. S., Chow A.Y. Subretinal Implantation of Semiconductor-Based Photodiodes: Progress and Challenges, J. Rehab. Res. Dev. 1999; 36(4) 371–6.

[24] Amon M., Bolz A., Schaldach M. Improvement of Stenting Therapy with a Silicon Carbide Coated Tantalum Stent. J. Mater. Sci. Mater. Med. 1996; 7, 273–8.

[25] Thewes R., Paulus C., et al. Integrated Circuits for the Biology-to-Silicon Interface, ESSDERC Proceedings 2004; 19-28.

[26] Rizzo J. F., Wyatt J., Kelly S., Shire D. Perpetual Efficacy of Electrical Stimulation of Human Retina with a Microelectrode Array During Short-Term Surgical Trials, Invest.Ophtalm. Vis. Sci. 2003; 44, 5362-9.

[27] Humayun M. S., et al. Visual Perception in a Blind Subject with a Chronic Microelectr. Retinal Prosthesis, Vis. Res. 2003; 43, 2537-81.

[28] Singh S. h., Buchanan R. C. SiC-C Fiber Electrode for Biological Sensing. Mater. Sci. and Eng. C 2007; 27, 551–557.

[29] Godignon P. New Generation of SiC Based Biodevices Implemented on 4 Wafers. Mater. Sci. Forum 2005; 483–485. 1097-1100.

[30] Ghavami R., Salimi A., Navaee A. SiC Nanoparticles-Modified Glassy Carbon Electrodes for Simultaneous Determination of Purine and Pyrimidine DNA Bases, Biosensors and Bioelectro. 2011; 26, 3864–3869.

[31] Caputo D., De Cesare G., Nascetti A. Scipinotti R. Two-Color Sensor for Biomolecule Detection. Sensor Letters, 2008; 6, 4, 542-547.

[32] Mai Y., Atkins A.G. Further Comments on J-Shaped Stress-Strain Curves and the Crack Resistance of Biological Materials, J. Phys. D: Appl. Phys. 1989; 22, 48–54.

[33] Gabriela G., Erilla I., Carob J., Gomeza R., Rierab D., Villaa R., Godignon P. Manufacturing and Full Characterization of Silicon Carbide-Based Multi-Sensor Micro-Probes for Biomedical Applications, Microelectronics Journal 2007; 38, 406–415.

[34] Yang Y. T., Ekinci K. L., Huang X. M. H., Schiavone L. M., Zorman C. A., Mehregany M., et al. Monocrystalline Silicon Carbide NEMS. Appl Phys Lett 2001; 78, 162–4.

[35] Cimalla V., Neibelschutz F., Tonish K., Foerster C. h., Brueckner K., Cimalla I., et al. Nanoelectromechanical Devices for Sensing Applications. Sens Actuators B 2007;126, 24–34.

[36] Naik A. K., Hanay M. S., Hiebert W. K., Feng X. L., Roukes M. L.. Towards Single-Molecule Nanomechanical Mass Spectroscopy. Nat Nanotechnol 2009; 4, 445–50.

[37] Singh S., Buchanan R. C. SiC-C Fiber Electrode for Biological Sensing, Materials Science and Engineering C 2007; 27, 551–557.

[38] Gomez R , Ivorra A., Villa R., Godignon P., Mill´an J., Erill I.,Sola A., Hotter G., Palacios L. A SiC Microdevice for the Minimally Invasive Monitoring of Ischemia in Living Tissues, Biomed Microdevices 2006; 8, 43–49.

[39] Godigon P., Martin I., Gabriel G., Gomez R., Placidi M., Villa R. New Generation of SiC Based Biodevices Implemented on 4 wafers. Mater. Sci. Forum. 2010;645–648:1097–100.

[40] Lipovsek B., Joskowiak A., Krc J., Topic M., Prazeres D. M. F., Chu V., Conde J. P. Characterisation of Hydrogenated Silicon–Carbon Alloy Filters with Different Carbon Composition for On-Chip Fluorescence Detection of Biomolecules, Sensors and Actuators A 2010; 163, 96–100.

[41] Hsu J. M., Tathireddy P., Rieth L., Norman A. R., Soltzbacher F. Characterization of a-SiC:H Thin Films as an Encapsulation material for Integrated Silicon Based Neural Interface Devices. Thin Solid Films 2007;516, 34–41.

[42] Salitermann S. S. Fundamentals of BioMEMS and Medical Microdevices, SPIE, Bellingham, WA, USA, 2006.

[43] Pennathur S., Fygenson D. K. Improving Fluorescence Detection in Lab on Chip Devices, Lab on a Chip 2008; 8, 649–652.

[44] Born M., Wolf E. Principles of Optics, Cambridge University Press, Cambridge 1999.

[45] Fixe F., Prazeres D. M. F., Chu V., Conde J. P. An on-Chip Thin Film Photodetector for the Quantification of DNA Probes and Targets in Microarrays, Nucleic Acids Research 2004; 32 e70.

[46] Rosenbloom A. J., Sipe D. M., Shishkin Y., Ke Y., Devaty R. P., Choyke W. J. Nanoporous SiC: a Candidate Semi-Permeable Material for Biomedical Applications. Biomed. Microdevices 2004; 6, 261–7.

[47] Taubner T., Korobkin D., Urzhumov Y., Shvets G., Hillenbrand R. Near-Field Microscopy Through a SiC Superlens. Science 2006; 313, 1595.

[48] Zahn J. D. Methods in Bioengineering, Biomicrofabrication and Biomicrofluidics, Artech House 2010.

[49] Berthold A., Laugere F., Schellevis H., de Boer C. R., Laros M., Guijt R. M., Sarro P. M., Vellekoop M. J. Fabrication of a Glass-Implemented Microcapillary Electrophoresis Device with Integrated Contactless Conductivity Detection, Electrophoresis 2002; 23, 3511–3519. 2002; 23, 2737–2750.

[50] Li P. C. H. Microfluidic Lab-on-a-Chip for Chemical and Biological Analysis and Discovery, Taylor & Francis 2005; 94.

[51] Iliescu C., Chen B., Poenar D. P., Lee Y. Y. PECVD Amorphous Silicon Carbide Membranes for Cell Culturing. Sens. Actuators B 2008; 129, 404–11.