ABSTRACT
Titanium has been widely used as a biomedical material in orthopedics, dentistry, cardiology, and cardiovascular surgery due to the excellent biostability and biocompatibility that results from its spontaneous formation of a highly passivating oxide layer in air and blood. However, little research has been done on the development of titanium for bioMEMS applications. This is likely due to the immaturity of titanium bulk micromachining technology to date. Here we report the application of new high-aspect-ratio bulk titanium micromachining techniques recently developed within our group towards the fabrication of a titanium-based multi-frequency traveling wave dielectrophoresis (DEP) device targeted for the separation of bioparticles. The device serves to illustrate the potential of these techniques for enabling the realization of novel bioMEMS devices with enhanced functionality and capability.

INTRODUCTION
Interest in the application of MEMS technology towards the biological and biomedical fields has increased significantly in recent years. Much of this interest has focused on the utilization of silicon micromachining, although various glass and polymeric material systems have been explored as well. Nevertheless, materials selection is still rather limited in this area. Consequently, there exists a need for microfabrication techniques that provide greater materials selection capability for bioMEMS applications.

Here we present the capabilities and advantages of using titanium as a micromechanical material for bioMEMS applications. Titanium is chosen mainly for its excellent biocompatibility and mechanical properties, which might allow for future use in in vitro and in vivo bioMEMS applications [1]. On the macroscale, titanium’s biocompatibility has been well exploited in the biomedical field for dental implants, hip and knee prostheses, prosthetic heart valves, etc. Titanium has also been clinically proven to be bio-stable and biologically safe inside the human body due to its exceptional corrosion resistance in the physiological environment.

Although there have been multiple investigations into the interactions of proteins, cells and tissues on titanium surfaces, little work has been done toward the miniaturization of titanium biomedical devices. This is likely due to the lack of micromachining technology that enables realization of complex, high-aspect-ratio structural features in bulk titanium at the MEMS length scale. Electrochemical micromachining [2], wet etching [3], and surface micromachining [4,5] of titanium have been previously reported in the literature, however our group is the first to report high-aspect-ratio dry etching of bulk titanium. The recent development of the Metal Anisotropic Reactive Ion etching and Oxidation (MARIO) and Titanium Inductively coupled plasma Deep etch (TIDE) processes has enabled the fabrication of arbitrarily complex, high-aspect-ratio titanium structures on various thickness substrates ranging from 500 micrometers thick sheets down to 10 micrometer thick free-standing foils [6,7].

In this paper, a detailed process flow for the fabrication of an all titanium (titanium substrate, titanium electrodes, titanium channel and reservoirs) DEP device is presented. The device serves as a platform for the demonstration of the utility of our bulk titanium micromachining technology for bioMEMS applications and highlights issues such as polishing, anisotropic dry etching, and multilayered assembly of thin titanium foils.

APPLICATION OF TITANIUM FOR BIOMEMS DEVICES: DEP DEVICE DEMO
Titanium is well known for its biocompatibility and robustness and therefore has many potential applications for bioMEMS devices. Our research is based on the application of titanium micromachining technology towards the creation of devices for biological and harsh environment applications. Here we propose a multi-frequency traveling wave DEP device which is targeted for the separation of bioparticles as a demonstration of titanium-based bioMEMS device processing capability.
Device Design

Particle separation has numerous biological and biomedical applications and is often the first step of bio-analysis. When compared to mature molecule sorting technology such as electrophoresis and centrifugation, dielectrophoresis has the advantages of lower electrical field, independence from particle charge, and wider sorting ability due to dependence on the dielectric properties of the molecules. The device fabrication undertaken here serves to experimentally validate the use of multi-frequency traveling wave dielectrophoresis to separate bioparticles, as proposed theoretically by Chang et al [8].

Device Fabrication

Comparing with previous DEP devices [9-11], the electrodes in our device are manufactured on a 1 mm thick titanium substrate, and the channel is fabricated by novel high aspect ratio bulk titanium etching.

Substrate preparation

While atomically smooth silicon or glass substrates are commonplace, the titanium substrates used in this study did not have sufficiently low surface roughness for photolithography-based micromachining. As a result, polishing is needed. The 2-inch square, 1 mm thick titanium substrates (99.6% commercially pure Ti, annealed, Goodfellow Corp) used for the Electrode substrate were commercially polished (Valley Design Corp) to 10 nm RMS surface roughness, as measured by optical profilometry (Wyko NT1100, Veeco Instrument, Inc.). After polishing, a 4 micrometer thick PECVD SiO$_2$ layer is deposited to enable electrical isolation of the electrodes from the titanium substrate below (Versalock VLR, Unaxis, 100ºC, 10 mT, SiH$_4$/Ar 250/20 sccm, ICP power 800 W, and RIE power 16 W).

Electrode Substrate Fabrication

Electrodes structures were formed using a lift-off process based on negative tone photoresist (AZ 5214 photoresist, Shipley) with image reversal. It is worth mentioning that a 3 min, 120 ºC post-development bake is then needed to prevent possible stripping of the photoresist during the subsequent metallization. Metal deposition is carried out by electron-beam evaporation of a 400 nm titanium thin film (CHA SEC600 Multi-Wafer Evaporator). After the Ti electrode deposition, lift-off is achieved by soaking the sample in photoresist stripper (AZ300T or PC X 127) for 12 hrs or more, followed by ultrasonic agitation in acetone for 20 min. Between the two electrode layers, a 300 nm thick silicon dioxide isolation layer is deposited and patterned on the area shown in Fig.1 using the same lift-off process.

Channel Die Fabrication

The titanium Channel Die, consisting of the two reservoirs connected by a 200-micrometer wide 6 mm long channel, is fabricated using either the MARIO or TIDE processes. Both processes begin with Chemical Mechanical Polishing (CMP) of 1 in square Ti foils (99.6% commercially pure Ti, annealed, Goodfellow Corp) with thickness ranging from 10 to 75 micrometers. A 1.3 micrometer thick TiOx etch mask is then deposited on the polished titanium surface by DC reactive sputtering (Endeavor 3000 Cluster Sputter Tool, Sputtered Films, Inc., 2300 W, 3.7 mT, Ar/O$_2$ 20/10 sccm, 4500 s). Once the titania film is deposited, the reservoirs and channel are patterned using positive tone photolithography (SPR 220-3.0, Shipley) and CHF$_3$-based dry etching (E640 ICP, Panasonic, pressure of 1 Pa, 500 W ICP power, 400 W bias power, 40 sccm CHF$_3$, 10 min).

Once the mask oxide is etched, the pattern is transferred into the titanium substrate below using either the MARIO or TIDE dry etch processes. The MARIO process cycles repetitively between a Cl/Ar-based slightly isotropic etch step and an oxygen plasma-based passivation step using a parallel...
plate RIE etch tool (Plasmatherm SLR 770, Unaxis, etching at pressure of 23mTorr, 220 RIE power, Cl₂/Ar 45/15 sccm). The scallops on the channel sidewall shown in the Fig. 3, Top result from the cyclic etch nature of the process. Currently, the MARIO process yields an etch rate of 0.3-0.4 µm/min, with selectivity of TiOₓ mask to titanium etching of approximately 1:35. In contrast to the MARIO process, the TIDE process consists of a single, highly anisotropic Cl/Ar-based etch step performed on a high density ICP-based etch tool (E640 ICP, Panasonic, pressure of 2 Pa, 400 W ICP power, 100 W bias power, Cl₂/Ar 100/5 sccm). This process yields etch rates as high as 2 µm/min and vertical, scallop-free sidewalls, as seen Fig. 3, Bottom and Fig. 4.

Assembly of the Channel Die and Electrode Substrate

Gold-gold thermocompression bonding was performed to achieve sealing of the channel to the electrode substrate. Since both the Channel Die and the Electrode Substrate are titanium, a lift-off process was used to pattern 300 nm silicon dioxide layer deposited by PECVD followed by a 50/500 nm Ti/Au bonding layer deposited by e-beam evaporation. A complementary 500nm thick gold film was deposited directly on the backside of the titanium surface by the e-beam evaporation.

After alignment under an optical microscope, the Channel Die and Electrode Substrate are bonded together (SB6E substrate bonder, Suss Microtec, 300 °C, 5e-3 mbar chamber pressure, 234 N bond force, 5 min). Bonding temperature is a key issue. Silicon dioxide spallation was observed at temperatures above 350 °C due to the huge thermal mismatch between silicon dioxide ($\alpha_{\text{SiO}_2} = 0.5e-6 \, \text{K}^{-1}$, $\alpha_{\text{SiO}_2} = 8.6e-6 \, \text{K}^{-1}$).

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**Fig. 3 Top:** Non-through-etched 25 micrometer thick titanium foil etched by MARIO process. The scallops on the channel sidewall are the result of the cyclic etch-passivation nature of the MARIO process. **Bottom:** Through-etched 25 µm Ti foil by the TIDE process that produces straight, scallop-free sidewalls.

**Fig. 4** Completed bulk titanium-based DEP device. **Top:** Low magnification view of the reservoir and channel with 24 electrodes located at the bottom of the channel (before macromachining of the reservoir to form vertical fluidic interconnect to the fluid supply stage below). **Bottom:** Detail featuring the channel wall and the interdigitated electrodes.
TITANIUM DEP DEVICE CHARACTERIZATION

After the thermal compression bonding step, the DEP device was coated with a 7-micron thick photoresist layer (SPR 220-7.0, Shipley), and the fluid inlet and outlet reservoir features were lithographically patterned. Afterwards, the two reservoirs were macromachined through the thickness of the Electrode Die using a conventional drill press, with the photoresist serving as a protective layer. The ability to combine both micromachining and conventional macro machining demonstrates one of the advantages of titanium as a bioMEMS material over silicon, especially with regards to the time and costs savings in fabricating large fluid reservoirs.

A plain PDMS lid was utilized to cover the channel and reservoirs for the purpose of optical detection and prevention of evaporation. The sealing is not permanent therefore enabling convenient cleaning for multiple uses. The completed device and the Fluid Supply Stage are clamped together with O-ring seals. The assembled device is shown in Fig. 5.

Preliminary testing shows that the electrodes are electrically isolated and there is no leakage at the Channel Die/ Electrode Substrate interface. Characterization of the particle separation efficacy of the device is currently underway.

CONCLUSIONS

Titanium has been widely used in the biomedical field as a structural material. With the aid of our new titanium high-aspect-ratio dry etching technology, we can now explore the fabrication and characterization of titanium bioMEMS devices for potential in vivo and in vitro applications. In this paper, a detailed process flow for the fabrication of an all titanium (titanium substrate, titanium electrodes, titanium channel and reservoirs) dielectrophoresis device has been presented as a demonstration of titanium bioMEMS processing capability. Issues such as titanium polishing, bulk dry etching and device assembly have been addressed and successfully applied in the device fabrication. The device serves to illustrate the capabilities of titanium bulk micromachining such as: the ability to create arbitrary complex 3-D microstructures with varying cross-sections through the sequential layering of titanium foils; the uniqueness of combining macro- and micro-machining of titanium to enable process simplification; and the potential in vivo and harsh environment applications with titanium, all of which may inspire the creation of innovative bioMEMS devices.

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REFERENCES