Microelectronic Engineering 175 (2017) 7–11

Contents lists available at ScienceDirect

Microelectronic Engineering

journal homepage: www.elsevier.com/locate/mee

Research paper

Metal enhanced fluorescence on super-hydrophobic clusters of gold nanoparticles

Edmondo Battista [a,b,*], Maria Laura Coluccio [c], Alessandro Alabastri [d], Marianna Barberio [e], Filippo Causa [a,b], Paolo Antonio Netti [a,b], Enzo Di Fabrizio [c,f], Francesco Gentile [g]

[a] Interdisciplinary Research Center on Biomaterials and DICMAPI, University Federico II, P.le Tecchio 80, Naples, Italy
[b] Center for Advanced Biomaterials for HealthCare @CRIB, Istituto Italiano di Tecnologia, Largo Barsanti e Matteucci 53, Naples, Italy
[c] Department of Experimental and Clinical Medicine, University of Magna Graecia, 88100 Catanzaro, Italy
[d] Physics and Astronomy Department, Rice University, Houston, TX, USA
[e] Ipat-lab, INRS-EMT, 1650 Boul Lionel Boulet, Varennes, Qb, Canada
[f] PSE Division, King Abdullah University of Science and Technology, Thuwal 23955 — 6900, Saudi Arabia
[g] Department of Electrical Engineering and Information Technology, University Federico II, Naples, Italy

ARTICLE INFO

Article history:
Received 13 October 2016
Received in revised form 12 December 2016
Accepted 14 December 2016
Available online 15 December 2016

Keywords:
Metal enhanced fluorescence (MEF)
Super-hydrophobic surfaces
Gold nanoparticles
Electroless deposition
Gold-binding peptides
Fluorescence lifetime microscopy (FLIM)

ABSTRACT

We used optical lithography, electroless deposition and deep reactive ion etching techniques to realize arrays of super-hydrophobic gold nanoparticles arranged in a hierarchical structure. At the micro-scale, silicon-micro pillars in the chip permit to manipulate and concentrate biological solutions, at the nano-scale, gold nanoparticles enable metal enhanced fluorescence (MEF) effects, whereby fluorescence signal of fluorophores in close proximity to a rough metal surface is amplified by orders of magnitude. Here, we demonstrated the device in the analysis of fluorescein derived gold-binding peptides (GBP-FITC). While super-hydrophobic schemes and MEF effects have been heretofore used in isolation, their integration in a platform may advance the current state of fluorescence-based sensing technology in medical diagnostics and biotechnology. This scheme may be employed in protein microarrays where the increased sensitivity of the device may enable the early detection of cancer biomarkers or other proteins of biomedical interest.

1. Introduction

The new paradigm of Materials Science is realizing materials in which the structure of the material itself is controlled at a molecular level [1]. Similar nano-scale materials display enhanced properties with respect to their macro-scale counterparts. Excellent properties associated with nanostructures of controlled geometry has opened up exciting opportunities for new materials design and will potentially revolutionize current practice in biology and medicine. Metal enhanced fluorescence (MEF) is a physical effect that occurs when fluorophores are located in close proximity to a rough metal surface [2–5]. In MEF, silver or gold nanoparticles with a regular rather than periodic motif interact with an electromagnetic field to yield site specific increments of that field. This in turn allows to obtain the fluorescence signature of biological molecules with unprecedented sensitivity and thus to diagnose a disease at the very early stages of its progression. Compared to conventional fluorescence, MEF benefits of increased spontaneous emission rate, quantum yield and photo-stability, decreased fluorescent lifetime of fluorophores, directional emission [3]. In MEF, fluorescence amplification depends on three separate mechanisms, that are, (i) energy transfer from the fluorophore to the metal; (ii) enhancement of the local electromagnetic field; (iii) modification of the radiative decay rate of the fluorophore through the local modification of the photon density of states [3]. Mechanisms from (i) to (iii) are driven by the geometry of the metal/fluorophore interface. Designing and fabricating such interface at the submicron or nanoscale dimension, and controlling its nano-topography, may lead to MEF devices with enhanced sensitivity, reliability, signal to noise ratio.

Here, we used optical lithography, Reactive Ion Etching and electroless deposition [6,7] techniques to obtain super-hydrophobic silicon micro-pillars (Fig. 1a), where the surface of the pillars is decorated with gold nanoparticle clusters (Fig. 1b–c). The device incorporates multiple functionalities that arise because of the multiscale/hierarchical structure of the material. At the micro-meter dimension, silicon micro-pillars manipulate and concentrate diluted solutions as precedently described in [8,9], at the nano-meter dimension, gold nano-grains modify locally the electromagnetic field (Fig. 2) to generate enhanced MEF signals. To demonstrate the device, we selectively adsorbed a fluorescein derived GBP-FITC peptide onto the gold nanoparticles; then we verified peptide/metal binding and resulting enhancement of fluorescence

* Corresponding author at: Center for Advanced Biomaterials for HealthCare @CRIB, Istituto Italiano di Tecnologia, Largo Barsanti e Matteucci 53, Naples, Italy.
E-mail address: edmondo.battista@unina.it (E. Battista).

http://dx.doi.org/10.1016/j.mee.2016.12.013
0167-9317/

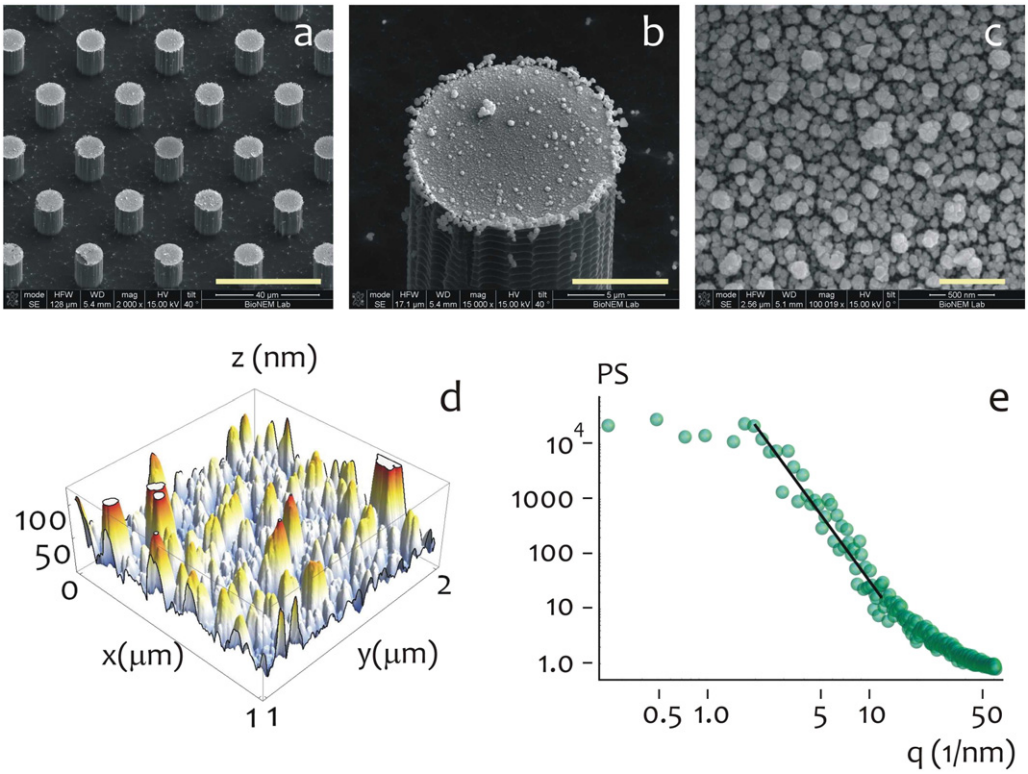

Fig. 1. Super-hydrophobic silicon micro-pillars are arranged in in a hexagonal lattice in the plane over extended regions of the substrate (a); high magnification SEM micro-graphs of the upper surface of the pillars reveal the morphology of the gold nanoparticles clusters, where the average diameter of the particles is 60 nm (b, c). AFM profile of the gold nanoparticles clusters was acquired (d) and analyzed to extract the information content of the image over different scales (e), from this, the fractal dimension of the structures is derived as $D_f = 2.4$, that is strictly larger than the Euclidean dimension of surface $D = 2$.

through fluorescence microscopy and fluorescence lifetime microscopy (Fig. 3). This technology may be employed in protein microarrays where the increased sensitivity of the device may enable the detection of cancer biomarkers or other proteins of biomedical interest in heretofore unattainable detection ranges.

2. Methods

2.1. Fabrication of the device

We used P type (100) Silicon wafers as substrates. After cleaning with acetone, substrates were spin-coated with a S1813 positive tone resist (from Rohm and Haas). Standard optical lithography techniques (Karl Suss Mask Aligner MA 45, Suss MicroTec GA, Garching, Germany) were used to generate patterns of holes in the resist, with an average diameter $d = 10$ μm and pattern to pattern distance $\delta = 20$ μm. The diameter to gap 1:2 ratio guaranties the best compromise between non-wettability and long evaporation times of a solution in a non-wetting/Cassie state [10]. Gold nanoparticles were deposited in the holes using electroless deposition techniques as described in references [6,7] and recapitulated below. The residual resist was removed with acetone and the sample was processed with Bosch Reactive Ion Etching (MESC Multiplex ICP, STS, Imperial Park, Newport, UK) to generate patterns of cylindrical pillars where the height of the pillars is $h = 15$ μm. Electroless grown Au particles served as a mask during the reactive ion etching (RIE) process. The samples were finally covered with a thin (few nm) film of a Teflon-like (C4F8) polymer to assure hydrophobicity. The masks for optical lithography were fabricated using Electron Beam Lithography (Crestec CABL-9000C electron beam lithography system). The Bosch DRIE process is a pulsed, time-multiplexed etching that alternated repeatedly between three modes, namely (i) a deposition of a chemically inert passivation layer of C_4F_8; (ii) an isotropic plasma etch of SF_6; and (iii) a phase for sample/chamber cleaning. Based on this alternate process, the pillars were fabricated with nano-threads at the

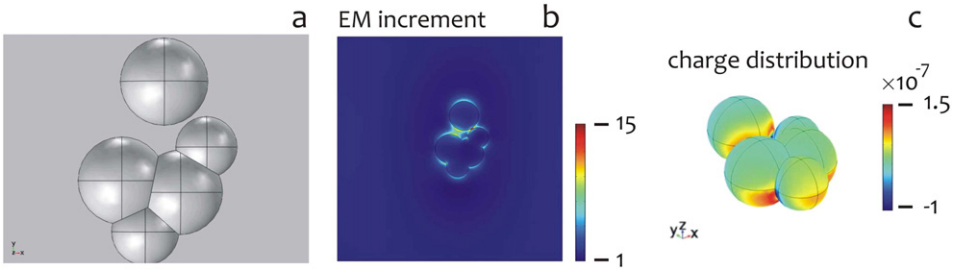

Fig. 2. Simulations of the electromagnetic (EM) field around Au nanoparticles clusters were performed using a finite element method (FEM). Nanoparticles are represented as partially overlapping spheres (a), where the diameter of the spheres ranges from 50 to 60 nm. EM amplifications and charge density reach a maximum at the particle-particle interfaces (b, c). For this configuration, the maximum EM increment is $Q \sim 15$, and thus the MEF amplification is $Q^2 \sim 225$.