

NANOSTRUCTURED COATINGS BY CLUSTER BEAM DEPOSITION: METHOD AND APPLICATIONS

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ABSTRACT

One of the key issues to be addressed in order to exploit nanomaterial peculiar properties is the way devices, and surfaces in general, can be functionalized by nanomaterials. To allow the jump beyond lab-scale, deposition techniques are asked to fulfill requirements such as reliability and repeatability, batch deposition, scalability, compatibility with micromachining techniques.

Here we show how supersonic cluster beam deposition, based on pulsed microplasma cluster source, may answer these requests, while offering at the same time a wide library of available nanomaterials, including carbon, oxides, and noble metals. The growth of nanostructured functional coating takes place directly onto whatever surface exposed in front of the cluster beam. Cluster soft-assembling generates nanoporosity and, as a consequence, coatings with large specific surface, which are particularly suited for applications where interaction with liquid solutions or gas-phase atmospheres has to be favored.

Results on the integration of nanostructured coatings into devices with applicative purposes in sensing field and in biotech field, will be reported. They include gas sensing, stretch sensing, protein adsorption, cell adhesion, and selective capture of peptides, as examples of functions that may be added to devices by cluster beam deposition of nanomaterials.

INTRODUCTION

One of the most important ways to exploit the peculiar properties of nanomaterials is their integration into devices or generally onto surfaces, in form of functional coatings. For example, devices with applications in the field of energy storage/production, such as supercapacitors, fuel cells, or electrochemical photovoltaic cells, may enhance their performances by using high specific surface nanostructured coatings deposited onto their electrodes, in order to favor the interaction with the liquid or gas phases.¹⁻⁴ Usually, the synthesis of the precursors of the nanostructured coatings and the integration in devices are two well-separated production steps, whose characteristics may frequently limit the range of the applications of the nanomaterials from a given synthesis route. For example, the use of nanomaterials from wet-chemistry synthesis routes as active sensing layer into micromachined gas sensing platforms, is hampered on one side by the mechanical delicacy of micromachined parts, and on the other side by the presence of solvents in precursor material.⁵⁻⁶ Moreover, nanomaterials from synthesis routes that require high temperature calcination step are incompatible with thermolabile substrates, such as polymers. Finally, the functionalization of devices in batch requires patterned deposition with suitable lateral resolution, in order to deposit nanomaterials onto the proper functional area, within each single device. Although photolithography is the common approach to fulfill this task, it raises non-trivial issues in the case of micromachined devices.⁶ Hence, a demand does exist of alternative methods for the production of nano-enhanced systems, where nanoparticle synthesis, manipulation, and integration steps are synergic parts of a unique process, overcoming most of the limitations of current approaches.

Here we describe a gas-phase method, based on supersonic cluster beams, for the functionalization of surfaces and devices with nanomaterials that may offer interesting opportunities with respect to nanomaterial integration issue. The first part of the paper will report on the deposition technique, with particular emphasis on cluster source. Results of morphological and structural characterization of cluster-assembled materials by means of electron microscopy and scanning probe

techniques will be also reported. The second part of the paper will show some relevant examples of applications of nanostructured materials by supersonic cluster beam deposition within various applicative fields in sensing and biotech, such as chemical and mechanical sensing, protein adsorption, cell adhesion, and peptide selective capture.

EXPERIMENTAL

Supersonic Cluster Beam Deposition (SCBD)

As shown in figure 1, SCBD apparatus basically consists of two vacuum chambers, each having its own pumping system. The cluster source is connected to the first chamber, which is named expansion chamber. Driven by pressure difference between source inner and expansion chamber, a supersonic expansion of a inert gas (typically Argon), takes place through the source nozzle, carrying clusters out from production region (source inner), towards deposition region. At odd with respect to effusive sources, supersonic expansion causes the cluster beam to concentrate within a divergence of few degrees, ensuring that a large fraction of the material produced into the source is directed towards deposition region.

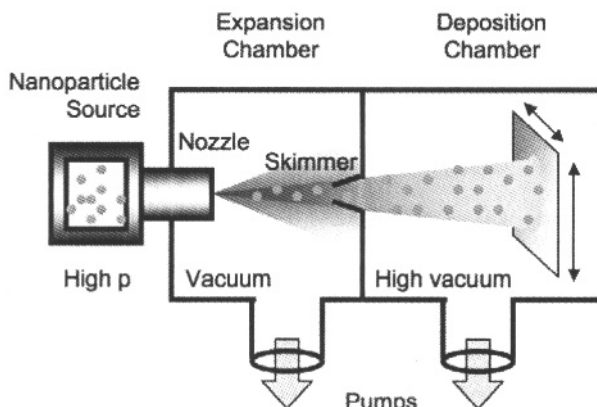


Figure 1. Scheme of the apparatus for supersonic cluster beam deposition. Arrows in deposition chamber indicate substrate rastering for large area depositions.

The second chamber is separated from the expansion chamber by means of a collimator with aerodynamic shape (skimmer), which removes most of the gas load due to cluster carrier, allowing only the central portion of the cluster beam to reach deposition region. In the case that the growth of cluster-assembled material should be performed in ultra-high-vacuum (UHV) conditions, as in Surface Science experiments, the number of vacuum chambers may be increased (according to the so-called differential vacuum approach) since beam collimation anyway provides for an adequate material collection.

If the coverage of areas exceeding the size of the cluster beam spot, which is typically few cm^2 , is needed, substrate rastering may be adopted: exploiting motorized sample holder, substrate scanning in front of the cluster beam is operated, so that areas extending up to few hundreds of cm^2 can be processed.

Pulsed Microplasma Cluster Source (PMCS)

Although various cluster sources adopt supersonic expansion for the production of their cluster beam, such as Laser Vaporization Sources or Pulsed Arc Sources⁷, we will focus here on Pulsed Microplasma Cluster Source (PMCS). PMCS is a rather recent system that we engineered and scaled-up in the last decade, and used to explore various applications of nanostructured coatings, as described in Sensing and Biotech Results section.

As first described in⁸ and successively in^{7,9}, PMCS consists of a cylindrical ceramic element, hosting a suitable reaction cavity. A solenoid pulsed valve for the injection of the inert carrier gas closes the back side of the cavity, while a nozzle closes the front side. The solenoid valve is typically backed with a 50 bar gas line, and operates at an opening time of about two hundreds of microseconds. A channel perpendicular to cavity axis holds the metal rod-shaped target, which is used for clusters production. In presence of the inert gas pulse from solenoid valve, the metal target is negatively pulsed by means of a high-voltage, high-current dedicated power supply. An electric discharge from grounded nozzle to negatively-pulsed target takes place, generating a plasma of the inert gas. Plasma jet impinges on target surface and vaporizes part of it. Then, ablated atoms thermalize and condense to form clusters.

The pressure difference between the source cavity and the vacuum chamber where the source is faced (expansion chamber) causes the expansion across the source nozzle of the clusters-inert gas mixture, generating the supersonic clusters beam. The supersonic expansion accelerates clusters at a kinetic energy of few tenths of eV per atom, thus promoting an adequate adhesion of the resulting cluster-assembled coating while preserving the cluster original structure and avoiding any significant damage or heating of the substrate.

If supersonic expansion is forced through aerodynamic lenses¹⁰, it is possible to obtain a highly collimated (divergence <1 deg) and intense cluster beam (aerodynamic focusing). By exploiting this property, patterned deposition of nanostructured coatings with sub-micrometric lateral resolution can be produced by non-contact stencil mask.¹¹ This feature marks a fundamental difference with respect to other gas-phase deposition techniques, since it allows for the easy integration of nanomaterials in functional areas of micro electro mechanical systems (MEMS) and micromachined platforms in general, avoiding photolithographic approach (see Gas sensing section below).

COATING CHARACTERIZATION

Atomic Force Microscopy

Surface morphology of cluster-assembled coatings has been studied by atomic force microscopy (AFM). Four examples are reported in figure 2, where the surface morphology of Ti, Hf, Zr, Fe nanostructured oxides is shown. Similar morphological features are observed in almost every nanostructured coating obtained by SCBD-PMCS. Therefore, we suppose that they can be ascribed to the deposition process in itself, and in particular to the low kinetic energy and limited diffusion of nanoparticles at the impact with the substrate, determining ballistic regime growth^{7,12}, which is characterized by nanoscale porosity, poorly-connected and non-compact structures with lower density respect to bulk and a surface roughness increasing with thickness.

AFM has been also adopted to evaluate the size distribution of coating precursors. To this purpose, very low coverage samples, with isolated nanoparticles, were deposited. Careful substrate preparation before deposition, as well as reference samples not exposed to the cluster beam, were adopted to favor artifacts identification/elimination in AFM images. Statistic of in-plane diameters was compared with statistic of heights, in order to identify the nanoparticle subset characterized by the height-diameter relation of spheroidal objects, and rule out non-spheroidal ones. In addition, size over-estimation due to AFM tip radius was avoided by limiting the counts of final size distribution to the heights of spheroidal objects subset. Size distributions were found to be lognormal, as expected for

nanoparticles growth by gas-phase monomer aggregation into PMCS, as reported in¹³ in the case of gold nanoparticles.

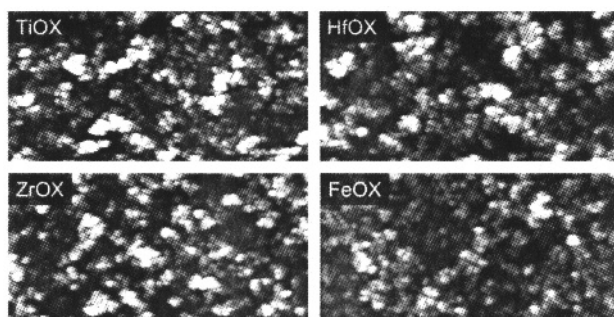


Figure 2. AFM images showing the surface morphology of four nanostructured oxides, with thicknesses around 200 nm. Each image has a size of $1 \times 2 \mu\text{m}^2$. It clearly appears that surface morphologies are very similar among the different oxides, a feature that is ascribable to growth dynamics of deposition process in itself.

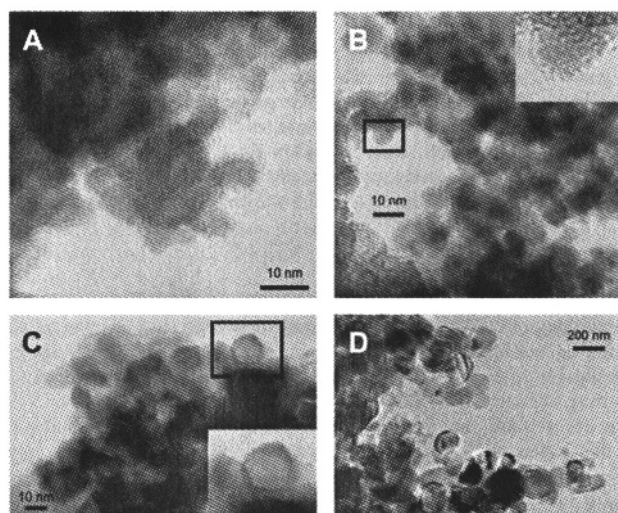


Figure 3. TEM images showing the nanostructure of as-deposited WO_3 film (A) and its evolution after thermal treatments at 200, 400, and 800 °C (B, C, D, respectively). Absence of lattice fringes inside nanoparticles of as-deposited film (A) indicates an amorphous structure. Annealing causes the evolution of nanoparticle structure toward crystalline order, which is almost completely reached after 400 °C. A progressive increase of crystal size is also observed, however nanoporous structure is preserved up to 800 °C. Reprinted with permission from¹⁴.

Transmission Electron Microscopy

The as-deposited coatings have generally an amorphous and porous structure at the nanoscales, independently on the material. As in the case of surface morphology by AFM, this result may be attributed to the deposition process in itself.

In order to investigate the stability of the film nanostructure with respect to temperature, post-deposition annealing in pure air has been carried out. Annealing causes the amorphous grains to rearrange into a crystalline structure, while the nanoporosity is preserved up to temperature of several hundreds of °C. Figure 3 shows transmission electron microscopy (TEM) images of as-deposited, 200, 400, and 800 °C annealed tungsten oxide coating, chosen as a paradigmatic example.¹⁴ Absence of lattice fringes inside nanoparticles of as-deposited film indicates for them an amorphous structure; size is about 10 nm. After 200 °C annealing, crystalline seeds nucleate within the amorphous aggregates and lattice fringes start becoming visible. After 400 °C, nanocrystals increase their size to about 20–30 nm, while a fraction of the material maintain its amorphous characteristic. After 800 °C, the average grain size increases to approximately 150 nm, while at higher temperatures (1000 °C, not shown) the cluster-assembled material loses its nanocrystalline feature and transforms to a polycrystalline continuous film.

It is worth to highlight that grain growth is minimal after annealing up to at least 400 °C, and that the nanoporous structure is preserved even at higher temperatures (800 °C). This is a fundamental feature for the use of cluster-assembled nanoporous materials as active layer in metal-oxide gas sensors, whose operation temperature is in the range 300–400 °C.

Spectro-ellipsometry

Beside microscopic techniques, SCBD-PMCS coatings have been studied with optical techniques, such as spectro-ellipsometry, as reported in¹³. Here, the optical response of cluster-assembled gold was modeled by explicitly introducing film porosity and finite-size effects due to nanoparticle size. Indications on clusters size as obtained by the optical model matched extremely well the size distribution obtained by AFM on isolated clusters. Since clusters are in contact each other into the coating, this result demonstrates that they retain their crystallographic individuality when assembled in three-dimensional structures.

The same kind of measurements were subsequently adopted to investigate the interaction between cluster-assembled nanoporous coatings and the liquid phase, at increasing degree of complexity of liquid compound/mixture: ethanol, octadecanethiol (C18), yeast cytochrome *c* (YCC).¹⁵⁻¹⁷ A clear correlation between the density of the material and the fraction of pores that could be filled by ethanol molecules was observed. In the presence of abundant open pores, C18 molecules were observed to diffuse within the coating interior and bind to the pore walls, while in presence of porous coatings with less abundant open pores the tendency of the molecules to remain confined to the surface region, adopting a self-assembled monolayer (SAM) configuration.

YCC has been chosen as molecular system model to probe optical methods in detecting conformational changes upon adsorption at surfaces. Well-defined features related to molecular optical absorptions typical of the YCC heme group appear in the same position found for molecules in solution. This suggests that YCC native conformation is maintained upon adsorption onto nanostructured-nanoporous gold substrate.

SENSING AND BIOTECH RESULTS

Gas sensing

Since few decades, metal-oxide-based gas sensors are attracting considerable interest due to large potential impact on several applicative areas such as air quality monitoring, control of industrial processes, detection of harmful emissions, etc.¹⁸⁻²⁰ Metal-oxide gas sensors operate according to the

change of the resistance of an oxide layer, occurring at high temperature in the presence of reactive compounds.²¹⁻²³ Due to their large specific surface area favouring the interaction with the atmosphere, nanoporous oxides can be successfully exploited as gas sensing active layers. With respect to other techniques, SCBD-PMCS method has the advantage of allowing direct integration of nanoporous metal-oxide layer onto platforms for sensing, at room temperature, with sub-micrometric lateral resolution, and avoiding any pre- or post-deposition treatment. Being a gas-phase deposition method, it provides the delicacy needed for functionalization of micromachined platforms, such as those based on the extremely delicate microhotplates.²⁴⁻²⁶

As reported in^{27,28}, we used SCBD-PMCS to integrate nanostructured oxide layer into microhotplate-based platforms for gas sensing (figure 4). Exploiting the high collimation of supersonic cluster beams, the deposition of nanomaterials was patterned with high lateral resolution by non-contact hard mask. This allows skipping photolithographic step, whose use may result as very difficult in the case of micromachined substrates. Gas sensing performances were characterized respect to various oxidizing and reducing species diluted in air, such as IO_2 , ethanol vapors, and hydrogen. The measurements (not shown) suggest a detection limit in the 10-100 ppb range, linearity up to several tens of ppm, and fast response and recovery times. The microsensors were operated at temperatures in the range 200-300 °C spending as low as few tens mW of heating power.

As a perspective, the wide library of materials available by PMCS; the possibility to produce them with very similar morphological features, as shown in Coating Characterization section; and the capability to pattern the deposition, may together play a key role in advanced chemical sensing based on array approach. Beyond gas sensing, the overall features of SCBD-PMCS method may disclose new opportunities within the general issue of parallel integration of nanomaterials in MEMS.

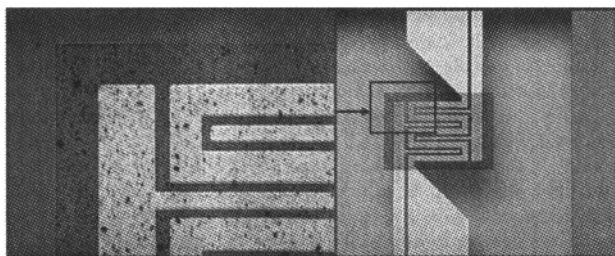


Figure 4. Optical microscope images showing a microhotplate-based platform for gas sensing after the deposition of nanostructured WO_3 coating (the darker rectangle in the centre of right image, enlarged in left image). The interdigitized electrodes pair and the serpentine-like heater, typical of metal-oxide gas sensors, are visible in right image. This platform is part of a batch of one hundred devices, which have been simultaneously deposited. Reprinted with permission from²⁷.

Mechanical stretch sensing

As reported in²⁹, nanocomposites with peculiar electrical properties can be produced by exposing a stretchable polymer, such as poly-dimethyl-siloxane (PDMS), to supersonic cluster beam by PMCS. The kinetic energy of clusters, gained during supersonic expansion, is enough to induce a certain degree of penetration into the soft substrates, according to the so-called supersonic cluster beam implantation (SCBI) phenomenon, the authors report. A nanocomposite layer extending few tens of nanometers below the surface of the soft polymer is then generated, where clusters are embedded into polymer. Nanocomposite surface layer provides the polymer the capability of conducting an electrical

current, whose intensity depends on the amount of percolating paths available for electron transport, among embedded nanoparticles.

As the polymer is stretched, the relative distance between embedded clusters increases, reducing the number of percolating paths, that in turns decreases electrical conduction. Once the polymer is released, original conduction is recovered. Proof of concept experiment exploiting a motorized uniaxial stretcher was reported in²⁹, where the reversibility of the phenomenon was demonstrated over 50,000 cycles of 40% applied strain. This result marks a dramatic difference with respect to the behavior of evaporated metallic films onto polymers, whose performances typically degenerate soon, mainly for the formation of cracks and for delamination.³⁰

From a general point of view, results reported in²⁹ disclose the possibility to use supersonic cluster beam to easily create thin conductive patterns onto flexible substrates: a step ahead towards flexible electronics. Although the perspective of the research in²⁹ regards the production of flexible electrodes for biomedicine and smart prosthetics, nanocomposites by SCBI may offer the base transducing element for sensors of mechanical stretch.

Protein absorption

Within the technological trend reshaping biological analysis and assays towards high-content/high-throughput tools and methods, the development of novel miniaturized devices, such as biochips and microarrays, plays a key role. The first issue to be addressed in such devices, is the way how biological entities (DNA, proteins, cells) can be fixed in suitable positions, in stable and reliable configuration. This in turn depends on the optimization of the complex interactions that occur between biological entities and the immobilizing surface. In this framework, nanostructured oxides may be an interesting alternative to standard approaches to adhesion, in force of a nanostructure-mediated adhesion mechanism, which co-exists with other useful properties of the oxides, such as for example, the transparency at visible wavelength and the absence of auto-fluorescence.

As reported in³¹, we have characterized nanostructured TiO₂ deposited on standard glass slides by SCBD-PMCS, as protein binding surface, in comparison with mostly diffused commercial substrates for protein and antibody microarrays. Nanostructured TiO₂ showed remarkable properties, in terms of protein adsorption, optical transparency at visible wavelengths (due to optical gap larger than 3 eV³²), absence of auto-fluorescence background, and signal-to-noise ratio, suggesting its possible use in different protein microarray applications. The compatibility of SCBD-PMCS deposition method with several substrates (glass, quartz, silicon, polymers), as well as with microfabrication techniques, as shown in the section on gas sensing, suggests that cluster-assembled nanostructured materials may represent a new family of functional coatings for immunodetection on miniaturized biochips and biosensors.

Cell adhesion

In the framework of the studies on the interaction between cluster-assembled nanostructured coatings and biological entities, we extended the research on cell adhesion in³³ to other materials and cell lines. We observed, as a general result, that nanostructured oxides by SCBD-PMCS, such as for example TiO₂, ZrO₂, WO₃, favor the adhesion of cell. This holds even in the case of living hematopoietic (circulating) cells, which are non-adhering cells by definition.

Nanostructured coatings with 50 nm thickness have been deposited on standard glass slides and annealed overnight at 250 °C, in clean and dry air atmosphere. After growing under standard conditions, living hematopoietic U937 model cells have been collected by centrifugation. Cellular pellets have been subsequently resuspended in Phosphate Buffer Saline (PBS) at 10⁷ cells/ml.

To check cell adhesion in conditions of shear stress induced by moving flow, as those encountered in microfluidic systems, glass slides with straight, 300 µm wide and 50 µm depth, microfabricated channels have been clamped onto nanostructured oxide coated glass slides. The same

setup has been used with standard Poly-D-Lysine coated slides (a common substrate for cell adhesion) and uncoated slides, as reference. 1.5 μ l of cell suspension (total amount of about 15.000 cells) has been loaded into each channel and incubated for 2 minutes at 37 °C. After cell fixation with common fixative agents (paraformaldehyde 4% or methanol/acetic acid 1:1) and extensive PBS washing, we have performed DAPI staining to visualize the nuclei. Then microfluidic slides have been disassembled and stained cells on coated and uncoated slides have been analyzed through fluorescence microscopy.

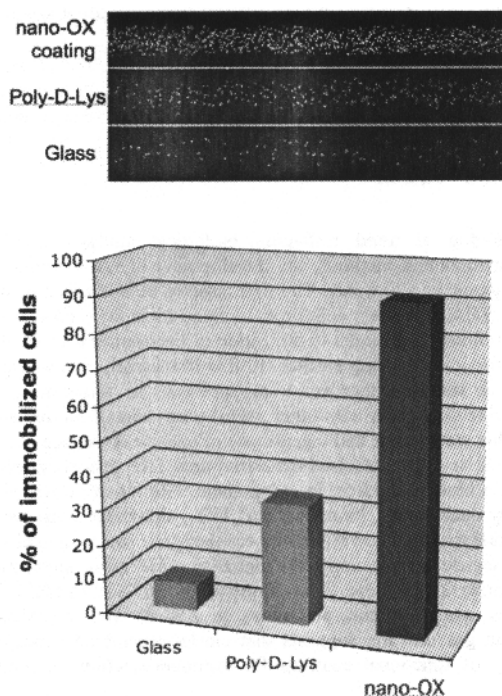


Figure 5. Results of cell adhesion experiments, in condition of microfluidic shear stress. In this case, nano-OX is TiO_2 . Upper image shows cells (white dots) along microchannel at the end of one adhesion experiment. With respect to the total amount of cells injected into microchannel, at the end of the adhesion experiment we observed around 80% on nanostructured oxide coated slide, while less than 10% on bare glass slide (histogram graph).

Figure 5 shows an example of adhesion result after microfluidic experiment. Cells appear as a stable and homogeneous layer on nanostructured oxide coated slides, while on the control uncoated glass slides fewer cells are present. Poly-D-Lysine performance stays in between. We carried out several independent experiments to statistically evaluate the amount of cells surviving microfluidic shear stress test. We found that around 80% of cells are recovered at the end of the experimental protocol on nanostructured oxide coated slide, while less than 10% are present on the uncoated glass slide.

Optical transparency and good adhesive properties, even in the case of haematopoietic cells, make nanostructured oxides by SCBD-PMCS an interesting class of materials, which may be successfully adopted to solve the open issue of cell adhesion into microdevices for cytological applications with optical readout, as fluorescence-based analytical assays, and generally for lab-on-a-chip applications.³⁴

Peptide selective capture

In the framework of biomarkers research, whose main applicative purpose is the identification of compounds helping in early diagnosis of diseases, Proteomics investigates the complex relationships between pathologies and the "Proteome", which is the huge ensemble of proteins within the organism. Among the biochemical processes occurring on Proteome, phosphorylation is a fundamental and reversible reaction modulated by kinase and phosphatase enzymes, whose action is frequently associated to pathological condition. In real clinical samples the identification and quantification of phosphorylated proteins is made particularly challenging, since it deals with the targeting of specific compounds dispersed at low concentration into high complexity samples. This task is usually addressed by Matrix-Assisted-Laser-Desorption-Ionization (MALDI) Mass Spectrometry, a powerful analytical technique providing high-sensitivity for detection of low concentration peptides.

Before undergoing MALDI analysis, a sample preparation step is required, where phosphorylated peptides are separated from complex samples, according to a standard enrichment method. This is a rather elaborated protocol, based on chromatographic approach, which exploits the affinity between phospho-peptides and metal-oxides, in form of small-size beads, pre-packed into a suitable chromatographic column.

Enrichment protocol can be largely simplified and shortened by performing phospho-peptide selective capture directly on MALDI plate, which has been previously functionalized with an oxide coating to this purpose. Although many techniques do exist to prepare an oxide-functionalized MALDI plate, the characteristics of SCBD-PMCS make it particularly suited for this purpose. In particular, the nanoporous nature of the coatings offers a large specific surface area for efficient interaction with liquid samples containing peptide mixtures, while the wide library of different oxides available allows to exploit the different level of specific affinity of various materials towards the variety of phospho-peptides.³⁵

As reported in³⁶, we deposited Ti, Zr, Hf and Fe nanostructured oxides on MALDI plates and used them within experiment of phospho-peptide enrichment, in collaboration with MS Proteomics Unit at IFOM-IEO Campus. Figure 6 shows the comparison between two mass spectra, one collected from untreated MALDI plate and one from nanostructured TiO₂ coated plate, where selective capture of phospho-peptide is demonstrated through the signal of the singly phosphorylated 2061 peptide. Exploiting various concentrations of betacasein, a limit-of-detection of about 100 fmol was observed, which is quite similar to that of standard approach based on TiO₂ beads. Phospho-peptide selective capture was also observed in the case of complex samples, such as protein mixture (betacasein, fetuin, BSA, ovalbumin, ribonuclease A, cytochrome C) and real biological samples (Idc80-Spc25 protein complex).

Exploiting the large library of nanostructured oxides by SCBD-PMCS, we envisage the possibility to adopt a combinatorial approach in the characterization of complex peptide samples in one single MALDI analysis session. This may be done by processing the same sample on an array-like MALDI plate, hosting various nanostructured oxides, and exploiting affinity differences between functionalized peptides and different oxides. In perspective, array-like MALDI plates by SCBD-PMCS could then become a novel tool for proteomic base research, as well as for clinical analysis of real samples.

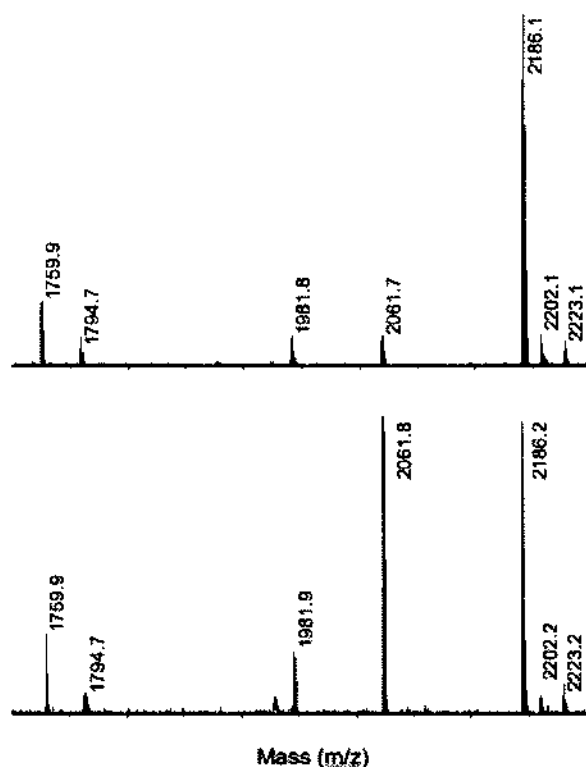


Figure 6. MALDI-TOF mass spectra showing selective capture of phosphorilated peptides. The phenomenon has been observed through the comparison of the peak height of reference phosphorilated peptide ($m/z = 2061$) with peak height of reference non-phosphorilated peptide ($m/z = 2186$), whose intensity has been used for spectra normalization. Top spectrum has been obtained by processing a reference peptide mixture on standard MALDI plate without any functionalization; bottom spectrum has been obtained by processing the same peptide sample on nanostructured TiO_2 coated plate. Phosphorilated / non-phosphorilated peaks heights ratio of reference 2061-2186 peptides greatly increases if peptides sample is processed onto functionalized plate.

CONCLUSION

Supersonic Cluster Beam Deposition based on Pulsed Microplasma Cluster Source allows the direct integration of nanomaterials in devices, in form of a nanostructured and nanoporous coating. The characteristics of the method include room temperature processing, compatibility with any substrate (micromachined platforms and thermolabile materials included), hard mask patterning at sub-micrometric lateral resolution, as well as a wide library of nanomaterials available. Cluster soft-assembling generates nanoporous materials with large specific surface area, particularly suited for

application where the interaction with liquid-phase or gas-phase environment has to be favored, such as in gas sensing, as well as in liquid-mediated biotech applications.

Peculiar properties of nanostructured coatings by SCBD-PMCS have been investigated in various applicative fields: gas sensing, stretch sensing, protein adsorption, cell adhesion, and peptide selective capture. In particular, the method allows for parallel and safe functionalization of hundreds of microfluidic-based platforms for gas sensing; while nanoparticle penetration and embedding into soft polymers allows for the production of nanocomposites with superior stability with respect to mechanical deformation. Regarding biotech area, although the study of the interaction between nanostructured coatings and biological entities (cells, proteins, viruses, DNA, etc.) is still in its infancy, solid results are already available, such as those regarding the improvement of cell adhesion by nanostructured oxides.

On the bases of the research outcomes reported in the present paper, the direct integration of nanomaterials in micromachined platforms for advanced physical and chemical sensing, as well as in microfluidic systems for the miniaturization of biological assay and for biosensing, may be the key technological issue addressed and solved by SCBD-PMCS, for innovative nano-enhanced systems.

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