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Surface Chemistry at Swiss Universities of Applied Sciences

Pierre Brodard[a], Marc E. Pfeifer[b], Christian Adlhart[c], Uwe Pieles[d], and Patrick Shahgaldian*[d]

*Correspondence: Prof. P. Shahgaldian[d], E-mail: patrick.shahgaldian@fhnw.ch
[a]School of Engineering and Architecture of Fribourg and [b]Institute of Life Technologies of Sion, University of Applied Sciences and Arts Western Switzerland; [c]Institute of Chemistry and Biological Chemistry, Zurich University of Applied Sciences; [d]University of Applied Sciences and Arts Northwestern Switzerland; Gründenstrasse 40, CH-4132 Muttenz

Abstract: In the Swiss Universities of Applied Sciences, a number of research groups are involved in surface science, with different methodological approaches and a broad range of sophisticated characterization techniques. A snapshot of the current research going on in different groups from the University of Applied Sciences and Arts Western Switzerland (HES-SO), the Zurich University of Applied Sciences (ZHAW) and the University of Applied Sciences and Arts Northwestern Switzerland (FHNW) is given.

Keywords: Bio-compatible surface · FHNW · HES-SO · Nanoparticle · Sensor · Surface functionalization · ZHAW

Introduction

Surfaces have been described as the '*fourth state of matter*' as a large majority of their constituents is at the outer interface experiencing, with respect to the bulk, different environments in terms of structural and thermodynamic parameters.[1] A surface can be defined as a phase boundary between a material and its surrounding environment. Consequently, the physical and chemical properties of materials' surfaces may strongly influence their ability to interact with their environment and may thus impact their overall behavior. Examples to substantiate this statement are countless, ranging from the exquisite surface structure of a lotus leaf to the wettability of concrete materials. As a matter of fact, surface sciences have implications in every industrial fields ranging from the pharmaceutical and diagnostic industries, all the way to construction and automotive industries, to name but a few.

When it comes to nanomaterials for which the surface-to-volume ratio is substantially greater, the influence of the surface is even more pronounced. As a matter of fact, surface chemistry and nanotechnology largely overlap.

In the Swiss Universities of Applied Sciences, a number of research groups are involved in surface science, with different methodological approaches and a broad range of sophisticated characterization techniques. This article intends to give a snapshot of the current research going on in different groups from the University of Applied Sciences and Arts Western Switzerland (HES-SO), the Zurich University of Applied Sciences (ZHAW) and the University of Applied Sciences and Arts Northwestern Switzerland (FHNW).

University of Applied Sciences and Arts Western Switzerland (HES-SO)

Research activities dealing with surfaces at the Institute of Chemical Technology (ChemTech) in Fribourg are mainly focused on our research axis *Characterization Technology*, the other two axes being *Chemical Process Development* and *Flow Chemistry*. Within this framework, we specialize in chemical imaging of solid surfaces by Raman mapping. In Raman spectroscopy, a visible-light laser is focused onto the surface of a sample through a microscope objective, and the backscattered radiation, frequency-shifted by the vibrations of the atoms or molecules in the sample, is collected through the same objective to yield a Raman spectrum. This spectral response is specific for each material, and allows an unambiguous chemical identification. This technique is non-destructive, preparation-free, and can measure millimeter- to centimeter-sized solid samples in ambient conditions in a matter of seconds. In addition, the sample is installed on a motorized table, allowing the generation of a grid of spectra over a portion of the sample surface, effectively creating a chemical image with micrometer spatial resolution (Fig. 1).

One example of application of this technique is the monitoring of active pharmaceutical ingredients (APIs) inside the excipient matrix of drug tablets. The uniform distribution of the API is crucial for the final formulation. Firstly, owing to different pharmacokinetic profiles, the bioavailability of an agglomerated active ingredient, localized in only one position of the tablet, is not the same as for a well-distributed API. Secondly, for a tablet to be divided, which is convenient for patients, the APIs have to be well distributed. By mapping the Raman response of the surface or a section of a tablet, we can image the distribution of the API within the excipient and quantify the size and numbers of API islands.[2] Another benefit of Raman spectroscopy is illustrated in the scope of a cooperative project between ChemTech and HES-SO Sion. In this project, a polyhydroxyalkanoate (PHA), which is a biodegradable polyester possessing interesting adhesive properties, is synthesized bacteriologically from agricultural wine production waste streams. In this context, we implemented Raman spectroscopy to allow an efficient monitoring of the production of PHA during the fermentation process, directly within the biomass.[3] A third field of application is on the characterization of cultural heritage objects (*cf.* Fig. 1). Pieces of art like paintings, statues, or any other historic artifacts often require a detailed chemical analysis to allow their correct chronological/archeological assignation, or even to identify fake modern copies. However, such samples obviously should not be altered and only non-destructive methods able to analyze directly *in situ*, on the entire object, can be employed. A careful Raman

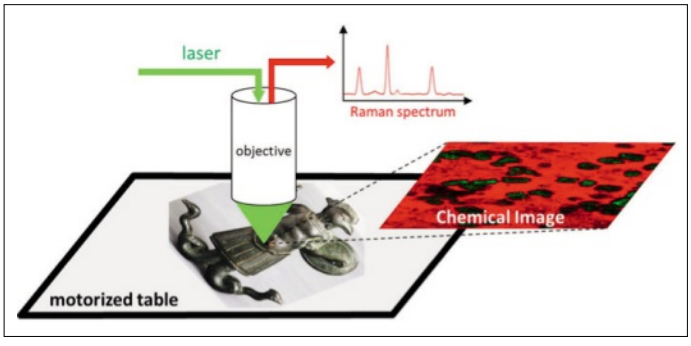

Fig. 1. Principle of chemical imaging using a confocal Raman microscope.

spectroscopy investigation is particularly well suited for such problems, providing information on the chemical composition of various areas of the object, without any sample damage if the experimental parameters have been cautiously selected.

Functionalization and characterization of surfaces are also in the focus of several ongoing projects at the Institute of Life Technologies of the HES-SO in Sion. In the development of medical devices, unfavorable surface properties may lead to serious biocompatibility and drug stability issues. Using an existing and approved biocompatible polymer to develop a new type of insulin delivery device for diabetes patients may seem straightforward. However, changes to container size, fill volume and particularly surface chemistry, roughness, morphology and porosity have been reported to cause medicament stability issues and foreign body reactions.[4]

Heterogeneous immunoassays, by contrast, are challenged with non-specific binding of molecules present in complex sample matrices to the solid surface and thus can result in poor performance characteristics due to elevated background signals. When studying this behavior with peptide microarrays developed to detect tumor auto-antibodies (TAA) in serum samples (*cf.* Fig. 2), we demonstrated that immobilized dextran and bovine serum albumin (BSA) efficiently blocked a fluorophor-labeled immunoglobulin from binding to the array surface.[5]

In another ambitious project named *SupraDiag*, we are developing a supramolecular biosensor to be directly inserted into a vein *via* a catheter in order to continuously monitor drug concentrations in blood. Aside of potential risks to patients, device longevity and functionality may be strongly impacted by non-specific adsorption of blood and tissue fluid proteins as well as cellular components onto the surface of the implanted sensor device. Employing natural materials such as collagen, hyaluronan and dextran or synthetic ones like poly(lactic-co-glycolic acid) (PLGA) and poly(ethylene glycol) (PEG) as biocompatible scaffolds of miniaturized sensors may be a good approach to reduce possible device usability and lifetime limitations. In fact these hydrogel-forming polymers, with their significant water content and flexibility, provide properties close to those of the surrounding tissue environment.

Functionalization of surfaces with living cells as smart recognition elements in portable diagnostic devices is currently being investigated within a new interdisciplinary HES-SO project named *MOVABLE*. Sample collection and immobilization within a smartphone-like device and subsequent counting of CD4+ white blood cells is thought to be useful in remote areas of developing countries for monitoring and medical treatment of individuals that have acquired AIDS. The surface chemistry inside the device has to meet ideally two requirements: i) even distribution and immobilization of the cells to be examined and prepared for an optical read-out, and ii) preservation of cell viability.

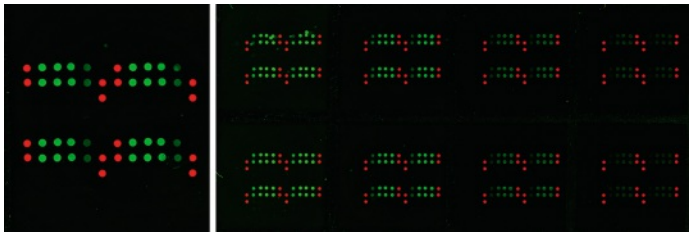

Fig. 2. Azide-derivatized peptides covalently attached *via* click chemistry to azadibenzocyclooctyne (ADIBO)-activated glass slide surfaces. In a titration experiment a specific peptide sequence immobilized at different concentrations was assayed with a mouse anti-BRCA1-associated RING domain protein 1 (BARD1) antibody and a Cy3-labeled goat anti-mouse IgG (green spots). Control features (red spots) are an azide-derivative of Cy5 co-ejected during the microarray manufacturing process.

Zurich University of Applied Sciences

Surfaces and interfaces are central research topics at ZHAW. Our research interests cover different aspects from materials with large surface area to the formation of molecular monolayers on surfaces. Understanding phenomena taking place at surfaces and interfaces is essential towards developing new functional materials such as nanofibers, medical implants, self-cleaning surfaces and super-adsorbent fibers. We use bottom-up approaches to design functional surfaces, such as electrospinning. Using electrospinning methods,[6] we produce fibers with diameters down to 50 nm that exhibit large specific surface areas. Bundles of nanofibers can be deposited as a thin layer on a supporting material and significantly change its surface properties. This is of particular interest for wound dressing applications, where the nanofiber layer serves as a non-adherent superabsorbent contact surface between the wound and the dressing's backing material. Antimicrobial properties can be incorporated by addition of drugs to the fibers, *e.g.* as complexes with molecular imprinted polymer (MIP) beads, that can physically be bound to the nanofibers.[7] Low wettability or surfaces with super-hydrophobic self-cleaning properties are of interest in textile applications. Rough surfaces exhibit such properties as described by Cassie's law.[8] By tuning the electrospinning conditions we are able to obtain rough super-hydrophobic surfaces without addition of fluorinated or silicon-containing compounds.

Deposition of protein thin-layers on the surfaces of medical implants is yet another approach towards surface functionalization. For medical surfaces, their interaction with cells and biological systems is crucial. Surface modifications may provoke increased or decreased cell adhesion and tissue remodeling, depending upon the dedication of the material. Soft tissue cells are next to osteoblasts of special interest for evaluation of dental implant materials as proper integration of the soft tissue will prohibit the invasion of microorganisms and establishment of biofilms that will finally result in peri-implantitis. As cell adhesion is mediated by a protein layer on the surface of the material, cell attachment can be directly modulated by the ability to bind endogenous proteins.[9] Surface polarity, hydrophobicity and topography are the main factors triggering the strength of the association of the biological system to the implant material.[10]

Another bottom-up approach to surface functionalization is to use Langmuir-Blodgett (LB) methods to generate molecular and nanoparticle monolayers at air–water interfaces, which can be transferred on various substrates. Well-defined molecular monolayers from amphiphilic molecules are obtained with this method. For example, oriented LB lipid monolayers at air–water interfaces are typically used as model systems to study for instance the interaction of drugs, proteins, pollutants and nanoparticles with cellular membranes (Fig. 3).

Currently we are exploiting the LB technique to deposit monolayers of amphiphilic nanoparticles on surfaces and explore their fundamental properties and potential application in microelectronics, sensors or drug-delivery systems. Top–down approaches can also be used to modify surface properties. For example we can also produce two-dimensionally surface polarity gradients by photo-patterning.[11] These polarity gradients can be mapped using hydrophobic interaction fluorescence microscopy. Furthermore, we take advantage of polarity gradients to harness the kinetic energy of Brownian motion and convert it into directed motion at solid–liquid interfaces, this is important for the future development of nanomotors and nano-propulsion systems.

University of Applied Sciences and Arts Northwestern Switzerland

The research carried out in the group of Nanotechnology of the School of Life Sciences of FHNW focuses on micro- and nanotechnology and is oriented towards applied science. It is

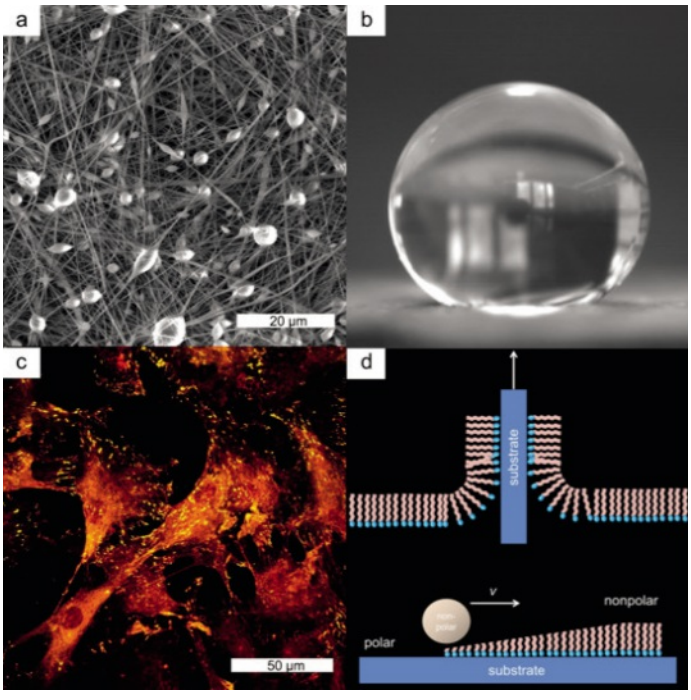

Fig. 3. a) Structural domains on nanofibers; b) hydrocarbon-based superhydrophobic surface; c) human normal primary osteoblasts growing on a titanium oxide surface; d) surfaces with polarity gradients through Langmuir-Blodgett technique.

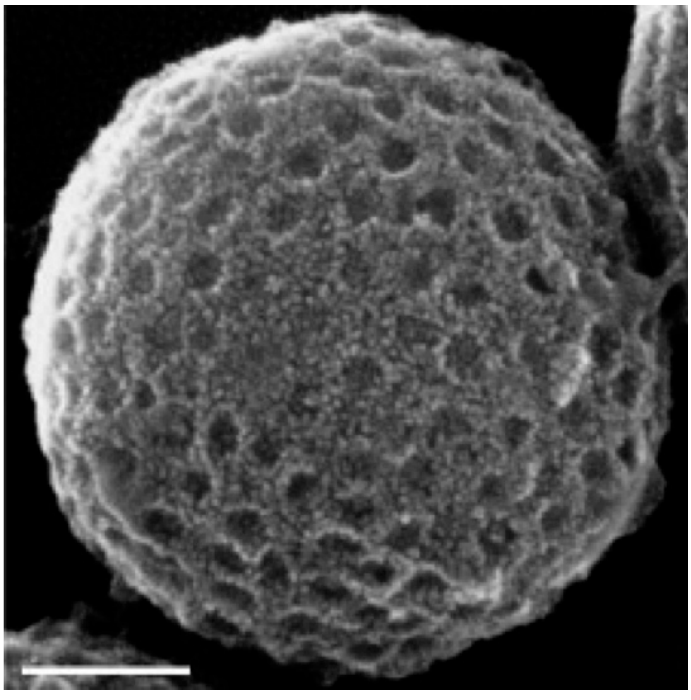

Fig. 4. Scanning electron micrograph of a virus-imprinted particle [scale bar 100 nm].

dedicated to support companies through innovative applied research, technical development, and problem solving. The group runs several CTI and other funded projects in the area of nanotechnology. In order to gain more detailed information about the chemistry of the outermost surface layer of materials, the HLS recently acquired an X-ray photoelectron spectroscopy (XPS) instrument. This technique is highly surface-specific as it allows the analysis of only the top layer of a material (5–10 nm), allowing not only the determination of chemical elements at the surface but also their chemical binding states, thus giving essential information about chemical alterations of surface-bound molecules. Furthermore, by applying an ion sputtering process, deeper layers of the materials can be accessed in order to investigate layer composition or the bulk material underneath the outermost layer. Since the XPS technique has been set-up in our laboratory, it has become indispensable being applied in a variety of projects where surface properties play a significant role, *e.g.* surfaces exhibiting antimicrobial activity, anti-adhesion properties or implant surfaces in general. The XPS instrument complements the surface analysis techniques available at the School of Life Sciences ranging from electron microscopes, energy dispersive X-ray, atomic force microscopy, IR and Raman imaging microscopy to surface ellipsometry. This comprehensive collection of techniques allows the determination of important surface parameters and a deep understanding of surface-related processes.

In the group of Nanochemistry of the FHNW, research is focused on the design of nanomaterials with enhanced molecular recognition and catalytic properties. Several of our projects are focusing on the design of functional surfaces. For instance, since more than a decade, we are working on the design of calixarene macrocycles, able to self-assemble as well defined monomolecular Langmuir monolayers. We have recently demonstrated that those surfaces can be used to template the crystallization of API from water.[12] Besides a clear effect on the crystallization kinetics,[12a,b] we have also demonstrated that controlling the monolayer density achieving a control over the polymorphic form of the produced crystalline API.[12c] In order to enable the stable transfer of Langmuir monolayers on solids, we have recently developed a novel strategy, based on the use of supramolecular clips, that allow 'clipping' together the amphiphiles to allow their transfer on solids using the Langmuir-Blodgett technique.[13] In our efforts to develop biomolecular recognition nanomaterials, we have recently developed a novel class of surface-imprinted nanoparticles, which possess enhanced recognition properties for a virus that was used to produce this nanomaterial (*cf.* Fig. 4).[14] The work is underway to develop a virus diagnostic kit for environmental monitoring.

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[1] J. C. Love, L. A. Estroff, J. K. Kriebel, R. G. Nuzzo, G. M. Whitesides, *Chem. Rev*. **2005**, *105*, 1103.
[2] P. Brodard, S. Roth, O. Vorlet, *Chimia* **2013**, *67*, 923.
[3] P. Brodard, E. Kilcher, M. Yerly, M. Zinn, 2nd Annual Conference on Applied Raman Spectroscopy, **2013**.
[4] Y. Onuki, U. Bhardwaj, F. Papadimitrakopoulos, D. J. Burgess, *J. Diabetes Sci. Technol.* **2008**, *2*, 1003.
[5] D. Prim, F. Rebeaud, V. Cosandey, R. Marti, P. Passeraub, M. E. Pfeifer, *Molecules* **2013**, *18*, 9833.
[6] J. Doshi, D. H. Reneker, *J. Electrostat.* **1995**, *35*, 151.
[7] R. Buttiker, J. Ebert, C. Hinderling, C. Adlhart, *Chimia* **2011**, *65*, 182.
[8] A. B. D. Cassie, S. Baxter, *Trans. Faraday Soc.* **1944**, *40*, 0546.
[9] E. Bono, S. H. Mathes, N. Franscini, U. Graf-Hausner, *Chimia* **2010**, *64*, 808.
[10] a) W. Holand, V. Rheinberger, E. Apel, C. van 't Hoen, M. Holand, A. Dommann, M. Obrecht, C. Mauth, U. Graf-Hausner, *J. Mater. Sci. Mater. Med.* **2006**, *17*, 1037; b) U. Muller, T. Imwinkelried, M. Horst, M. Sievers, U. Graf-Hausner, *Eur. Cell Mater.* **2006**, *11*, 8.
[11] R. Walder, A. Honciuc, D. K. Schwartz, *Langmuir* **2010**, *26*, 1501.
[12] a) N. Moridi, D. Elend, O. Danylyuk, K. Suwinska, P. Shahgaldian, *Langmuir* **2011**, *27*, 9116; b) N. Moridi, O. Danylyuk, K. Suwinska, P. Shahgaldian, *J. Colloid. Interface Sci.* **2012**, *377*, 450; c) L. G. Tulli, N. Moridi, W. J. Wang, K. Helttunen, M. Neuburger, D. Vaknin, W. Meier, P. Shahgaldian, *Chem. Commun.* **2014**, *50*, 3938.
[13] N. Moridi, C. Wackerlin, V. Rullaud, R. Schelldorfer, T. A. Jung, P. Shahgaldian, *Chem. Commun.* **2013**, *49*, 367.
[14] A. Cumbo, B. Lorber, P. F. Corvini, W. Meier, P. Shahgaldian, *Nat. Commun.* **2013**, *4*, 1503.