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Fachhochschulen – Hautes Ecoles Spécialisées

Materials Science at Swiss Universities of Applied Sciences

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Abstract: In the Swiss Universities of Applied Sciences, several research institutes are involved in Materials Science, with different approaches and applications fields. A few examples of recent projects from different groups of 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) are given.

Keywords: Biocatalysis · Biomaterials · Biomineralization · Heterogeneous catalysis · Materials Science · Photografting · Polymers · Porous Materials · Processing · Self-Assembly · Synthetic fuels · Tissue engineering · Zirconia coatings

1. Introduction

Materials science plays a major economic and social role. For instance, because of acute environmental concerns, more efficient use of material and energy resources is urgently required. Materials science is helping to develop new energy technologies, more energy efficient devices, and easily recyclable and less toxic materials. Overcoming disease is another topic where materials science, in conjunction with biotechnology, can play a role, *e.g.* by developing artificial bones and organ implants, or for safe drug delivery systems. Materials science can improve not only the performance of the products but also the ways they are produced and handled considering their full life cycle (*e.g.* packaging).

The ability to control, manipulate, and design materials on the nanometer scale (10^{-9} m) will be one of the major technology drivers of the 21st Century. The potential of these materials for generating new functionalities, minimizing waste and pollution, and optimizing properties and performance is huge. Nanomaterials are being developed from almost every type of material, including polymers, metals, ceramics, composites, and biomaterials. In a number of cases, it is now possible to predict materials properties before they have even been manufactured, thus greatly reducing the time spent on testing and development. The objective of modern materials science is to tailor a material in order to obtain a desired set of properties suitable for a given application. One area of research that will revolutionize our concept of synthetic materials, as well as how we interact with our surroundings, are 'smart' materials. Unlike normal, inert materials, smart materials are designed to respond to external stimuli, adapting to their environment in order to boost performance, extend their useful lifetimes, save energy, or simply adjust conditions to be more comfortable for human beings. The rapidly emerging field of biomimetic materials forms another very important technology today. Biomimetic materials seek to replicate or mimic biological processes and materials, both inorganic and organic. To develop these materials, we need new chemical strategies that combine self-assembly with the ability to form hierarchically structured materials. Finally, materials scientists constantly require new and more powerful analytical techniques, so that they can continue the discovery of new phenomena and develop improved materials for the future.

This article is intended to highlight the current research on Materials Science in the Swiss Universities of Applied Sciences, and more specifically projects that strongly involve chemistry in the general sense.

2. HEIA-FR – Haute Ecole d'Ingénierie et d'Architecture de Fribourg

Several examples of research activities dealing with materials at the Institute of Chemical Technology of the HEIA-FR are presented, namely on polymers and plasma-sprayed zirconia coatings.

2.1 *Polymers*

The institute ChemTech has various activities in development, synthesis and scale-up of novel and innovative polymeric materials (Profs. Dr. Roger Marti & Ennio Vanoli). A recent successful example is the development of novel dental polymers. Current dental polymers suffer from limited stability by enzymatic attack in the saliva. Beside the mechanical degradation of the filling, it liberates small molecules, which cause allergic reactions. In a project financed by Innosuisse, together with the industrial partner Saremco AG and HES-SO Valais, the institute ChemTech worked on the optimization of the polymer structure. Novel, more stable pre-polymers based on classical dental monomers were prepared and formulated into novel dental composites. The best new dental composites produced around 10 times less degradation products than current materials. A safe and reproducible scale-up of the synthesis of the pre-polymer on a multi-kg scale was performed, which allows marketing the new dental material with improved biocompatibility under the name 'SAREMCO APT – Advanced Polymer Technology' (Fig. 1, left).

Another activity is hydrogels – these are three-dimensional network structures, which can absorb and retain significant amounts of water. They can be obtained from synthetic and/or natural polymers and we developed in collaboration with the research group of Prof. Stoppini at HES-SO Geneva (HEPIA) a toolbox to support applications in tissue engineering and bioprinting. A variety of building blocks for the synthesis of hydrogels were prepared (thiol, allyl and hydrazone modified hyaluronic acid and gelatin with various degree of functionalization; allyl PEG derivatives for thiol-ene cross-linking) that allow the synthesis of hydrogels by UV or thermal cross-linking. These new hydrogels were successfully used in bio-printing (in col-

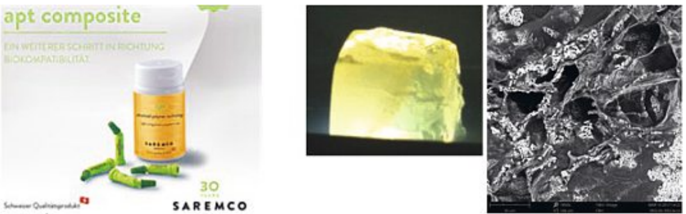

Fig. 1. The novel dental material 'SAREMCO APT – Advanced Polymer Technology' with improved biocompatibility (left) and hydrogel materials (right).

laboration with institute iPRINT of HEIA-FR), drug delivery and tissue engineering application (Fig. 1, right).

The ChemTech Institute, in collaboration with the Plastic Innovation Competence Center PICC in Fribourg, participates in the European project BIOSMART for the development of novel bio-based packaging applications (*biosmart-project.eu*). In our labs, we are working on polyester amide block polymers, which are fully bio-sourced and biodegradable. By varying the chemical structure – the hard and soft segment – we can fine-tune and adjust the physico-chemical, mechanical and barrier properties. Scale-up studies with kneader reactors by LIST Technology AG are under way to prepare larger quantities and evaluate the industrialization of these biopolymers. Beside these polyester amides, the institute ChemTech works on polylactic acid (PLA), especially in the synthesis of the lactide monomer and its reactive extrusion *via* ring opening polymerization (ROP) as a sustainable process.

The ChemTech Institute is also active in material recycling projects, some of which are carried out in collaboration with developing countries. In a recent project involving partners in sub-Saharan Africa, the group developed and optimized an innovative method of recycling used vehicle tires into versatile rubber tiles. The technique consists of grinding the tires into rubber particles, separating out the tissue and metal components, and conditioning the particles to form tiles that can be used for flooring or insulation purposes. The novelty of the approach is that no glue or binder is needed in the process, making the technique cheaper, safer and more widely accessible.

One of the biggest challenge of plastics industries is to predict how the material will age. Indeed, extremely various applications expose the base polymers to strong temperatures variations, sunlight, air, aggressive chemicals *etc.*, all contributing to their degradation. Base material suppliers provide indications of ageing based on standardized tests, but application industries are producing final objects exposed to non-constant environmental stresses, often for much longer times than advised by the base material suppliers. In order to help these companies producing final polymer-based products, several public–private research projects have been carried out at HEIA-FR/ChemTech. In collaboration with major industrial partners of the Fribourg region, producing polymer goods ranging from water tubes to automotive components and electric connectors, the research team led by Prof. Dr. Pierre Brodard selected the most appropriate characterization methods.[1]

In 2014–2015, the POLYAGE project focused on chemical ageing of polyethylene- and polyamide-based plastics (PE and PA).[2,3] New samples were first fully characterized by differential scanning calorimetry, thermogravimetric analysis, infrared and Raman spectroscopy, and scanning electron microscopy. Then the samples were exposed to various temperature programs to force their degradation, and compared to aged products provided by our industrial partners. As expected, PE-based materials are chemically decomposed by oxidation, which was easily confirmed by spectroscopy, and we were able to quantify the kinetics of oxidation by chemiluminescence, thus allowing an exact prediction of the lifetime of the samples at any temperature. On the other hand, PA-based materials did not seem to change their chemical composition: even though their mechanical integrity was strongly fading during ageing, their infrared and Raman spectra were almost unaffected. Indeed, the fracture toughness measured by tensile tests was reduced by 40% in the hardest conditions (20 days at 200 °C), but the composition remained the same. We then found out that the structure of the material had changed: SEM images revealed a highly inhomogeneous dispersal of the glass fibers in the reinforced PA-based samples after thermal ageing, which probably accounts for their apparent fragility (Fig. 2).

As a logical next step, we decided to concentrate on physical ageing in the follow-up project POLYLIFE, in 2015–2016.[4] By physical ageing, we mean no change in the chemical composition but a modification of the structure, like the above-mentioned alteration of the glass fibers distribution in the PA matrix. For this purpose, and with the strong support of our mechanical engineering department, a new method based on ultrasound was developed: a piezoelectric transducer generates ultrasonic waves in the sample, and an interferometric laser head is used for detection. Two implementations have been devised: ultrasonic Lamb waves propagating in the plane of a thin flat sample and mapped by the scanning laser head, allowing determination of the elastic modulus of the material in different directions, and resonance of ultrasonic frequencies through the sample, enabling to measure more complicated, non-flat objects (Fig. 3).

These two non-destructive techniques are sensitive to any modification of the physical structure, even on final industrial products. Both approaches are in excellent correlation with mechanical properties obtained by macroscopic (tensile test) and microscopic (nanoindentation) methods. For the PA-based samples exposed to several temperature programs (160 °C to 270 °C, 30 h to 3000 h), we found out a temperature-dependent exponential decay of the fracture toughness with time. Based on these results, we were able to calculate the kinetics parameters and predict their lifetimes.

Recently, we investigated the recycling process of a high-performance engineering polymer. Small parts produced with this material generate a significant quantity of offcuts (~60%) that must be reprocessed (Fig. 4) to be re-useable for further production, an operation inducing a large thermal load on the polymer.[5]

We found out that the chemical stability is proved up to 3 cycles of re-extrusion under inert atmosphere, but that the Young's modulus slightly decreases due to a decrease in the length of the reinforcing glass fibers, observed during the recycling process by micro CT-scan. However, the decisive element to assert whether the recycled material is suitable or not is to test it on parts in production at the industrial level, a process now in progress in the companies.

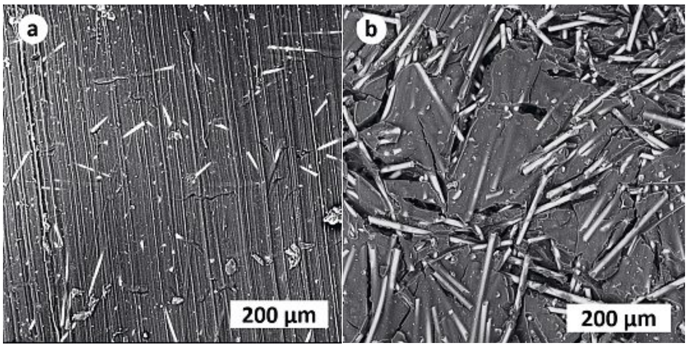

Fig. 2. SEM images of PA before (a) and after (b) thermal ageing at 200 °C for 20 days.

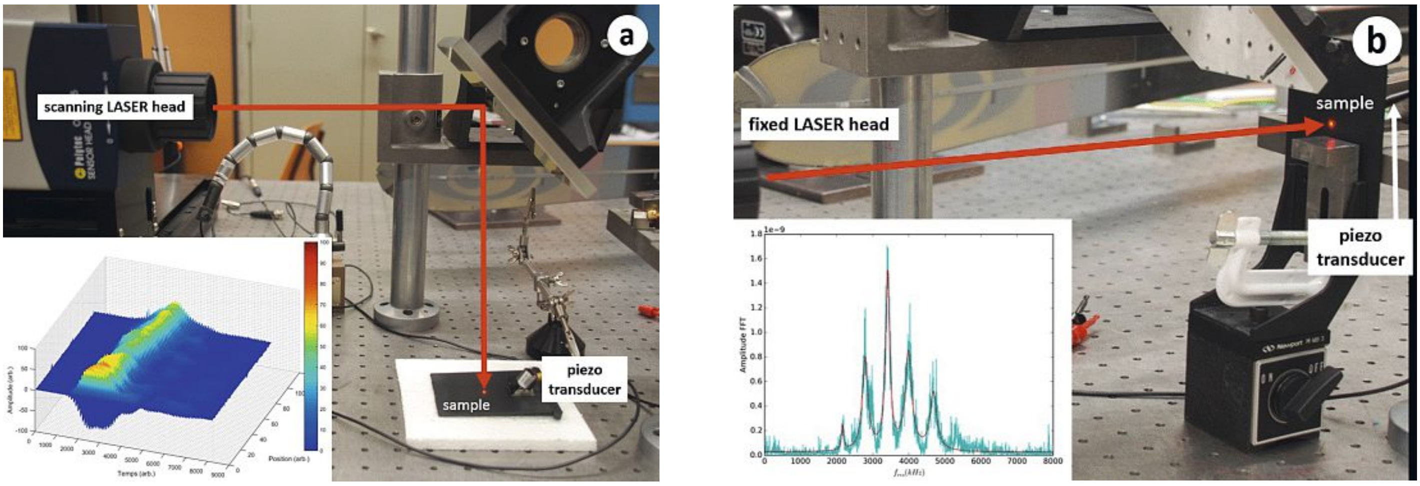

Fig. 3. Ultrasonic characterization method, with a) waves propagating in the plane, or b) through the sample.

Fig. 4. Twin screw extruder for offcuts reprocessing.

2.2 *Zirconia Coatings*

Another example is plasma spraying. In this process, material in the form of powder is injected into a very high temperature plasma flame, where it is rapidly heated and accelerated to a high velocity. The individual molten particles impact on a substrate kept in front of the plasma gun and stick to the substrate. These deformed particles are known as splats, with layers of splats building up a coating.[6] The first layer of splats determines the adhesion of the coating to the substrate: during freezing, the coefficients of thermal expansion of the splat and the substrate materials being different, the splat experiences residual stress. A stressed splat, depending on the magnitude of the stress, can either crack significantly or peel off completely from the substrate, and thus initiate coating failure at either the splat–splat or splat–substrate interfaces. Hence, residual stress is a very important factor in determining coating cohesion and adhesion. As-sprayed coatings are porous, but it is possible to reduce the porosity to a great extent and improve the coating properties by remelting the coating using a laser. For example, zirconia thermal barrier coatings can be laser-remelted to seal the coating and prevent ingress of corrosive gases to the metallic bond coat. However, laser remelting modifies the nature of residual stress of the coating. Raman spectroscopy can be effectively used for strain determination for materials like zirconia which has a Raman active tetragonal phase, and the relation between the applied stress in zirconia coating and Raman shift is linear. Micro-Raman spectroscopy focuses an exciting laser beam with a microscope objective down to a few µm, and hence is suitable for detecting residual stress in splats (typical diameters 40–100 µm). The strain is measured from the difference in Raman peak position of a stressed sample relative to a stress-free sample (as-received powders).

Splats and coating deposition were carried out by Professor Partha P. Bandyopadhyay at the Indian Institute of Technology of Kharagpur, West Bengal, India. Prior to deposition, steel samples were grit blasted and a layer of NiCrAlY bond coat was deposited on this roughened surface. The bond coat layer was polished, and zirconia splats were then deposited on the polished substrates. Raman spectroscopy was undertaken at HEIA-FR. First, as-received powders, assumed to be stress-free, were measured, and the tetragonal peak found at 638.35 cm^{-1} was selected as a reference: a peak shift above this wavenumber is attributed to a compressive residual stress, and a peak shift below means tensile residual stress (a shift of 1 cm^{-1} corresponds to a residual stress of 220 MPa).

Fig. 5 shows the variation of splat residual stress with particle velocity and temperature, calculated by averaging the data obtained from 1000 particles. The melting point of zirconia is around 2715 °C and hence, this temperature was chosen for spraying. In all cases, the stress was tensile: this is attributed to rapid quenching of the splats when it hits the substrate. During quenching, the splat shrinks, and this shrinkage is retarded by the substrate, hence a tensile stress develops in the splat. It also appears that splat residual stress does not have any direct correlation with either particle speed or temperature. The average stress in remelted splats is much less than that of as-sprayed splats. A laser-remelted splat forms a large molten pool that cools slowly as compared to an as-sprayed splat. Hence, the residual stress keeps low. Laser remelting also produces an annealing effect on the metal surrounding the splat.

Fig. 6 shows the residual stress profiles of the as-sprayed and laser-remelted samples. The as-sprayed coating sample shows a moderate tensile stress through the entire cross-section. However, in the laser remelted coating, a transition to compressive stress occurs in the remelted layer. In both cases, the stresses were moderate as compared to single splats. A highly tensile splat is compressed by the splat deposited above it. In addition, in ceramic coatings, stress relief occurs due to cracking. As a result, the stress in coatings kept lower. Raman spectroscopy appears

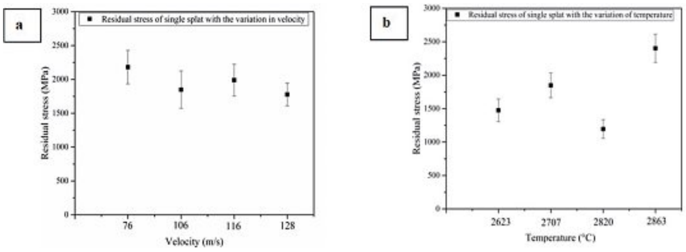

Fig. 5. Variation of splat residual stress with a) particle velocity and b) temperature.

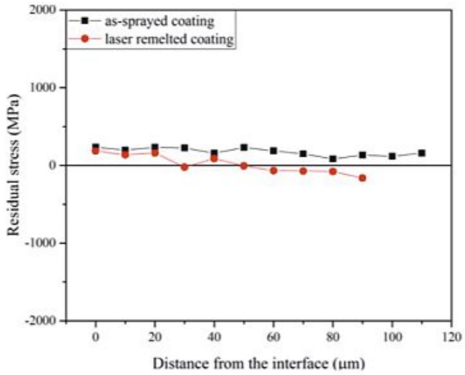

Fig. 6. Residual stress profile of as-sprayed and remelted samples.

to be a potent tool for experimental stress analysis of thermally sprayed coatings, and we proved that it is possible to analyze small features like splats, as well as to perform stress depth profiling of bulk coatings.[7]

3. HES-SO Valais-Wallis – Haute école spécialisée de Suisse occidentale, Sion

3.1 *Polymeric Biomaterials*

The biosynthesis, chemical modification, purification and application of biopolymers for industrial and medical purposes is one of the main foci of the research group Biotechnology and Sustainable Chemistry (BioSusChem) at the Institute of Life Technologies of HES-SO Valais-Wallis. Besides the biopolyesters polyhydroxyalkanoate (PHA), polylactate (PLA), and poly(lactate-*co*-glycolate) (PLGA), also proteins (*e.g.* collagen) and polysaccharides (*e.g.* pullulan and microbial cellulose) are investigated with respect to their medical or industrial applications (Fig. 7).

A particular expertise of BioSusChem is the biosynthesis of PHA in bacteria using fed-batch and continuous cultivation. Typically, the cells deposit PHA intracellularly as a carbon and energy storage compound when a nutrient (nitrogen, phosphorus, sulfur, *etc.*) is limiting growth and the carbon source is available in ample amounts. In order to fine-tune the biosynthesis of PHA, much effort has been put on the design of the culture medium to establish multiple nutrient-limited (MNL) growth conditions.[8] Under such a growth regime, wild-type and recombinant microorganisms accumulate large amounts of polymers and, most importantly, the flux of carbon substrates into the cell can be controlled resulting in a tailored monomeric unit composition that finally determines also the chemo-physical properties of the PHA produced. This had been exemplified by the tailored biosynthesis of the PHA poly(3-hydroxybutyrate-*co*-3-hydroxyvalerate) (PHBV) in *Cupriavidus necator* enabling the control of the melting temperature between 80–180 °C.[9] A similar approach was used for tailoring the functionality of the side chains in *Pseudomonas putida* GPo1 by the feed of functional fatty acids during chemostat cultivation. Double bonds in the ω-position of the side chains are of particular interest, because they are very reactive to chemical modifications using mild chemistry. Thus, the first organic–inorganic PHA hybrid copolymer could be produced with the free radical addition of the nano-cage polyhedral oligomeric silsesquioxane containing seven isobutyl groups and one mercaptopropyl group (POSS-SH) to the olefinic PHA side-chain. The melting temperature (Tm) increased from 48–120 °C due to this modification.[10] Other reactions such as epoxidation or the synthesis of comb-polymers showed a significant influence on the material properties, too.

Genetic engineering of metabolic pathways using traditional or modern CRISPR-CAS9 techniques,[11] or the engineering of key enzymes (*e.g.* PHA polymerase) are elaborated tools to extend the material properties of PHAs. In general, PHAs have an excellent biocompatibility making them also interesting candidates for medical applications. Recently, the biosynthesis of poly(4-hydroxybutyrate) (P4HB) could be optimized to enable a cheaper production with a recombinant *Escherichia coli* strain.[12] To date, P4HB is routinely produced at HES-SO Valais for research purposes or during contract fermentations for companies that are interested in testing this FDA-approved polymer for specific medical applications.

In an ongoing collaboration with Prof. K. Matsumoto at the University of Hokkaido (Japan) the growth of an engineered *E. coli* strain was assessed that contained a lactate polymerizing enzyme (LPE) to enable the polymerization of unusual monomeric units such as lactic acid into PHA.[13] This strain is able to biosynthesize the copolymer poly(3-hydroxybutyrate-*co*-2-hydroxypropionate) (P(HB-co-LA)) even at higher cell densities.[14]

The synthesis of block-copolymeric PHAs, either produced *in vivo* by bacteria or by (bio-) chemical modification after biosynthesis *in vitro* is currently being investigated in a project supported by the Swiss Higher Education Council. The first results demonstrated that blocky PHAs have extended material properties because of the combination of the chemophysical properties of their blocks. The goal of this research is to design a PHA-based bioplastic that does not need any addition of typical additives such as softeners, UV stabilizers or crystallization agents.

Another important topic of the BioSusChem group is the design of sustainable PHA production to avoid the conflict 'food to material'. In a first approach, it could be shown that the pomaces of fruit wastes (cherry, apple, and apricots) could be used as carbon sources for the biosynthesis of PHAs.[15] In the wine region Valais, larger amounts of grape pomace end up as waste during wine production. A simple washing procedure yielded in a glucose content of more than 150 g L^{-1} that was successfully used for the production of olefinic PHAs.[16]

Alternative interesting waste streams are gases. Syngas, a typical waste gas in the steel industry that can also be produced from organic waste materials by pyrolysis, was used for the biosynthesis of poly(3-hydroxybutyrate) (PHB) in *Rhodospirillum rubrum*.[17] Different anaerobic, multiple nutrient-limited fed-batch cultivations were assessed that were based on CO as energy and acetate as PHB source. Interestingly, a limitation by phosphate in the culture medium yielded in doubled amounts of PHB in the biomass (30% w/w) in comparison to the traditionally used nitrogen limitation.[18] Along with PHB also H_2 was produced that could be eventually applied for energy gain by fuel cells.

In an ongoing HES-SO project, this gained knowhow in gas fermentations is applied to the aerobic fermentation of *Cupriavidus necator* in presence of CO_2, H_2. This CO_2 negative fermentation process worked very well at the lab scale and will be scaled-up to a 300 L bioreactor at Martigny (VS) within 2019.

3.2 *Particular Processing of Biomaterials*

In a joint project with Prof. E. Carreño (HES-SO Valais), PHA was tested whether it could be used in metal powder injection molding (MIM) as a binder molecule.[19] Best performance was found for PHBV with nickel-free stainless steel powder when it was blended with paraffin wax and stearic acid.[20] This metal–organic blend was further processed by injection molding at 120 °C to form green parts that were subsequently debinded, firstly in organic solvent and secondly by heat, and finally sintered at 1260 °C with the complete removal of PHBV. The resulting stainless steel part had suitable properties and displayed a surface structure appropriate for medical applications, *e.g.* as bone implant.

A flexible electrode for transcutaneous electrical nerve stimulation (TENS) and electrocardiography applications was devel-

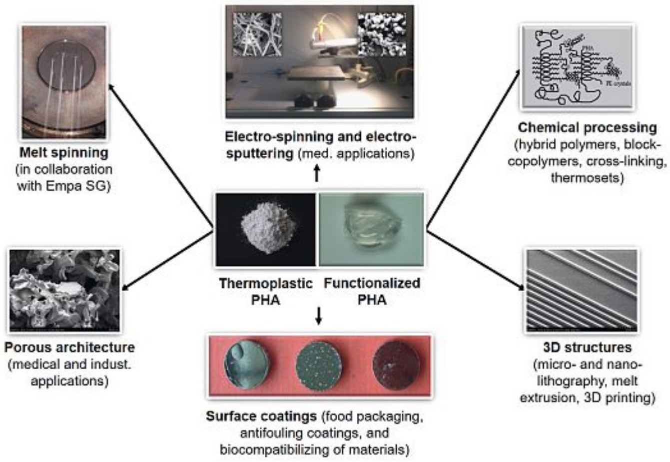

Fig. 7. Processing options for thermoplastic and functionalized polyhydroxyalkanoate (PHA).

oped in collaboration with Prof. S. Schintke at HEIG. PHAs were blended with silver nanowires (AgNW) to obtain different conductivities. A prototype with a film thickness of 150 µm with PHB and a AgNW content of 3 wt% with an average conductivity of 253 S m^{-1} was manufactured and found to be suitable for TENS[21] (see also video: *https://www.hes-so.ch/de/bioflex-4668.html*).

The Innosuisse project 'Polymeric NanoBioMaterials for drug delivery: developing and implementation of safe-by-design concept enabling safe healthcare solutions' investigates the toxicity and implementation of polymeric nanobiomaterials such as chitosan, PLA and PHA within an international consortium. Within this project an electrospinning and electrosputtering unit was constructed that also allows the integration of drugs in the PHA or other biopolymeric matrices. Currently, guidelines how to use and process the materials are in preparation (*http://gonanobiomat.eu/*).

In 2020 HES-SO Valais will organize the 17th International Symposium on Biopolymers (*www.isbp2020.com*) in Crans-Montana with about 200 participants, where also one day will be dedicated to industrial processing and applications. It is anticipated that this conference should also represent the Swiss activities in the field of polymeric biomaterials.

4. ZHAW – Zürcher Hochschule für Angewandte Wissenschaften, Wädenswil

The research of materials science at ZHAW is cultivated in the Institute of Materials and Process Engineering as well as in the Institute of Chemistry and Biotechnology. Topics range from biomaterials for drug testing, coatings that will speed up Swiss skiers, catalysts, to fundamentals in nano scale self-assembly and different types of porous materials that are used as specific nano containers or for environmental remediation.

4.1 *Biomaterials*

Today, preclinical drug discovery still relies on tissue cultures from sacrificed animals, since 2D cell cultures do not reflect the *in vivo* situation. Therefore, we have developed a concept of a 3D drug screening platform for the automated production of 3D musculoskeletal-tendon-like tissues that may be used to develop therapies against degenerative muscle and tendon diseases.[22] The platform is compatible with multiwell plates and comprised of a postholder where cells are bioprinted to be differentiated into the corresponding tissues afterwards. Bioprinting was achieved using a gelatine methacryloyl-polyethylenglycol dimethacrylate (GelMA-PEGDMA)-based bioink, that was photo-polymerizable at 365 nm. We demonstrated the printing capabilities (Fig. 8) for mono- and co-cultures of primary rat tail tenocytes (printed around the posts) and primary human skeletal muscle-derived myoblasts (printed in the interstice). After differentiation for 7 days formation of tendon-and muscle-like tissue was demonstrated, which showed auto contractions, as well as electrical pulse stimulated contractions of single myofibers.

4.2 *Photografting*

Durability and hydrophobicity are the key elements of an efficient ski wax coating. To render polyethylene surfaces strongly and permanently hydrophobic, photocatalytically generated nitrenes were used as reactive groups to insert into the carbon–hydrogen bonds of polyethylene (Fig. 9). The effect of photocatalytically linked fluorocarbons was demonstrated by an up to 2.5 fold increase in abrasion resistances as compared with polyethylene surfaces conventionally coated with long-chain perfluoroalkanes.[23] Spectroscopic evidence for the grafted monolayer was found using UV and XPS.[24] The efficiency of such equipped cross country skies was improved by 1.5 %.

4.3 *Catalysts for Synthetic fuels*

To enable the energy transition, efficient and stable catalysts for the conversion of CO$_2$ with regenerative H$_2$ into energy sources such as methane (CH$_4$) have to be developed. Catalysts based on Co/Al$_2$O$_3$ undergo deactivation by the formation of a secondary CoAl$_2$O$_4$ phase. This was avoided by substituting the Al-based support with Mn. The CoAl$_{2x}$Mn$_x$O$_4$ supported catalyst showed a drastically increased reducibility. Starting from the spinel a significantly improved methanation catalyst was obtained, which was able to convert 80% CO$_2$ at a selectivity of over 97% to methane at 350 °C.

In addition, the activation energy for the methanation decreases from 94 to 56 kJ mol^{-1} due to the modification of the spinel.[25]

4.4 *Self-Assembly*

A promising way of developing reconfigurable materials is self-assembly of micro/nanoparticles into suprastructures. Shape and amphiphilicity play a vital role in the self-assembly of colloidal particles. Therefore, as compared to spherical building blocks, anisotropic colloidal particles may yield a significantly larger variety of self-assembled structures.[26] The decisive functional roles of self-assembled proteins in nature depend on the anisotropy of their building blocks. Snowman-shaped Janus nanoparticles (JNPs) consisting of two different lobes were systematically studied to understand the relationship between the shape of the colloidal building blocks and the assembled suprastructure (Fig. 10). Geometrically different JNPs were synthesized from poly(tert-butyl acrylate) nanoparticles (NPs) using seeded emulsion polymerization. Phase separation of 3-(triethoxysilyl)propyl methacrylate from the PtBA seed NPs allowed to the formation of JNPs. These JNPs differed in the geometric aspects lobe size, separation degree, and overall size.[26] Depending on the geo-

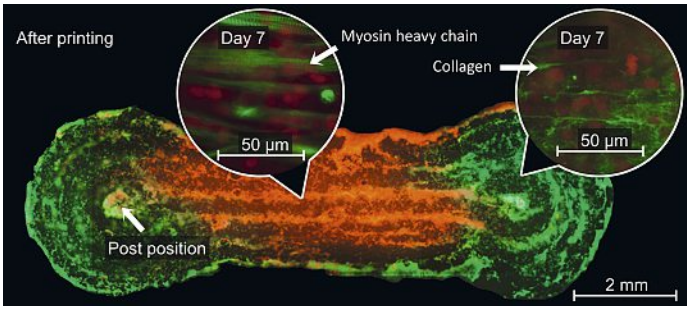

Fig. 8. Three-dimensional printed co-culture with tenocytes (green) around the posts and myoblasts (red) in the middle part of the dumbbell-shaped structure. Adapted with permission from ref. [22].

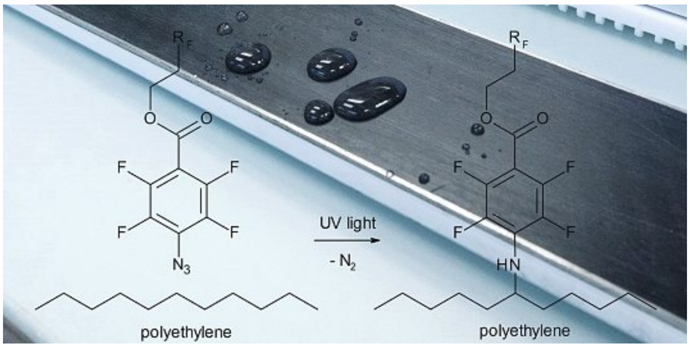

Fig. 9. Fluorocarbon coated ski surface by photografting.

metrical parameters of the JNPs, different self-assembled supra-structures were obtained from spherical micelles, mono-walled capsules, planar mono-/bilayers to capsules with randomly oriented JNPs (Fig. 10). Such correlations between geometry and self-assembled structure have been well studied for surfactants and an equivalent Janus critical packing parameter (JCpp) was suggested to describe the self-assembly of JNPs depending on their shape.[26]

In addition to geometry, the amphiphilicity of JNPs can be switched on or off, which in turn affects their ability to self-assemble at interfaces.[27] At high ($pH > 7.0$) pH values, the amphiphilicity of JNPs containing amine groups on one lobe is switched off and their interfacial behavior was similar to that of homogeneous nanoparticles, but a low ($pH < 6.0$) pH, the interfacial activity was enhanced and JNP stabilized Pickering emulsions underwent reversible water-in-oil to oil-in-water phase inversion when the aqueous phase changed from basic to acidic (Fig. 10). Similarly, foam formation of such JNP Pickering emulsions was strongly influenced by the pH.[28]

4.5 *Porous Materials*

Porous materials with defined pores in the microporous (< 2 nm) and mesoporous (2–50 nm) range are of particular interest for host–guest systems. Guest molecules can be released from the nanoporous hosts in a controlled manner or stabilized against degradation. Based on this concept, a new type of colorant (True Color Pigments, TCP) was developed.[29] Conventional pigments are colorants that are insoluble in the application medium. Their hue, however, not only depends on the light absorption properties of the chromophores, but also to a large extent on the particle size and crystallinity. Chemical properties are defined by the surface functional groups, which have to be accounted for during their application. The extraordinarily stable ancient Maya Blue pigment relies on the host–guest concept of indigo incorporated into inorganic palygorskite, but the variable presence of oxidized indigo (dehydroindigo) gives rise to a peculiar hue. Intercalation of indigo into zeolite L crystals followed by reductive washing and sealing of the indigo-filled nanochannels led to a colorant, for which the colorimetric properties were only determined by the isolated guest molecules and were – in contrary to Maya Blue – identical with the absorption spectrum of dissolved indigo molecules. The chemical properties, on the other hand, were defined by the zeolite L host. As a consequence, the formulation and application of such TCP is color-independent and the particle size is determined by the size of the zeolite crystals (0.4 µm in this case).

Post-condensed arrays of silica nanochannels (ASNCs) represent functional mesoporous materials, which are characterized by a one-dimensional channel system with three inherently different surface regions: pore entrances (hexagonal faces), external surfaces (rectangular faces), and internal surfaces (cylindrical pores).[30] Pore entrances and internal surfaces were selectively functionalized in a one-pot reaction using different driving forces such as steric hindrance and mobility supported by an end-on particle growth (Fig. 11). The materials provide a platform for the development of drug delivery systems and sensors.

Nanofiber aerogels (NFAs) or sponges are a recent class of ultralight highly porous materials containing a 3D fibrous network of pre-formed nanofibers.[31] They lack the microporous properties of classical aerogels, but they allow a fine control of the nature and architecture of the 3D fibrous network (Fig. 12). This is exploited in applications where controlled mass transport is combined with interfacial interactions, such as for separation, or heat insulation.[32] We prepared such nanofiber aerogels by electrospinning the biopolymer pullulan together with PVA, followed by cutting, freeze drying and thermal cross-linking. Such obtained materials are amphiphilic with large absorption capacities of > 100 m^3 m^{-3} for both, water and non-polar solvents. However, upon silylation, the fibrous surface became water repellent allowing their application in environmental remediation as demonstrated for the purification of water from chlorinated hydrocarbons (Fig. 12).[33] The OH groups

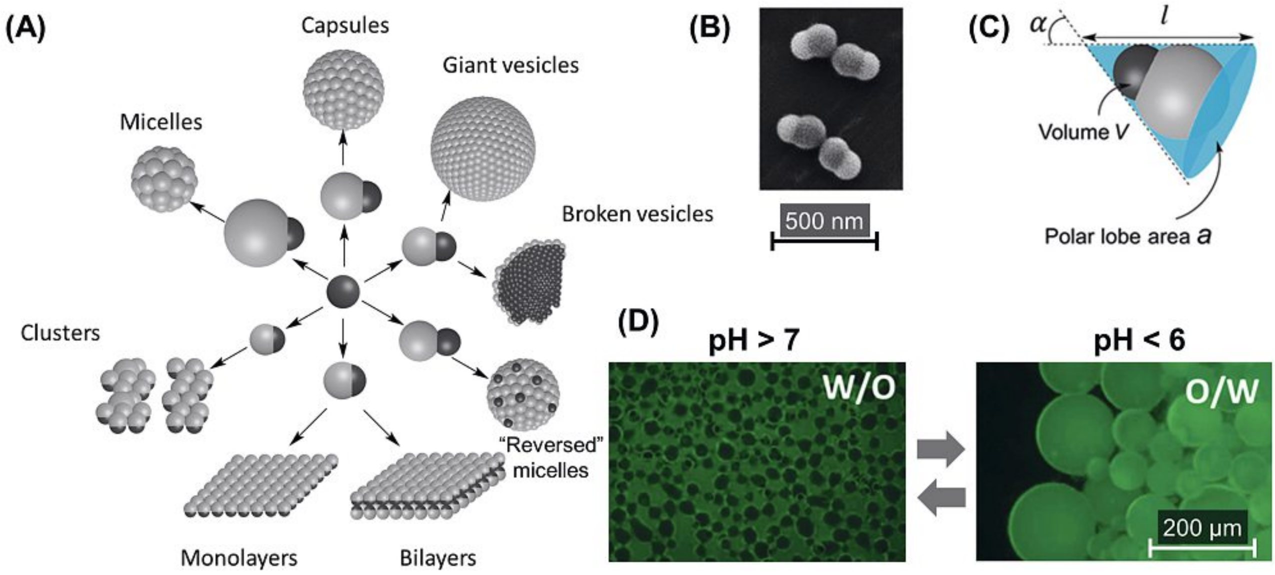

Fig. 10. (A) Self-assembled supracolloidal structures obtained from JNPs with different geometries. (B) SEM image of snowman shaped JNPs. (C) Representation of the Janus critical packing parameters $JCpp = \frac{V}{l\,a}$ (D) w/o Pickering emulsion (toluene:water = 4:5 ratio, pH > 7) changing reversibly to o/w at pH < 6 after addition of HCl. Adapted with permission from ref. [26], copyright © 2018 American Chemical Society.

of pullulan provide also favorable interactions with dissolved impurities such as organic dyes. This was demonstrated in a continuous process for the purification of water from the cationic dye methylene blue. The adsorption capacity was approx. 0.4 g dye/g NFA and twenty recycling cycles were achieved by simply switching the pH.[34]

Nanofiber-based materials are mostly applied in aerosol filtration since these thin fibers allow the separation of small particles in the 100 nm range at decent differential pressure. However, there are given physical limits between high separation efficiency and a low differential pressure asking for an increased filter area. Technically, this is solved by pleating the filters like an accordion. NFAs, however, intrinsically contain such a pleated structure where the major pores represent the interstice while the cell walls are the effective filter. Using NFAs, we were able to achieve > 99.998% filtration efficiency at considerably low differential pressure of 550 Pa (Fig. 12).[35]

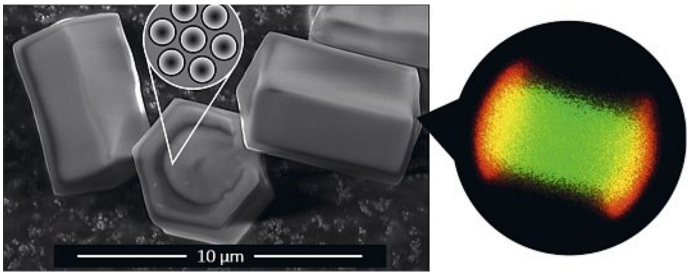

Fig. 11. SEM image of functionalized ASNCs. Each of the particles contains roughly 500'000 parallel nanochannels (*ca.* 4 nm in diameter) with the entrances located at the base surfaces of the hexagonal prisms. The confocal laser scanning microscopy image shows an optical slice through the center of a particle, revealing fluorescence-labeled amino groups at the pore entrances (red) and thiol groups (green) at the internal surfaces. The bifunctionalized region near the pore entrances appears yellow.[30]

5. School of Life Sciences, University of Applied Sciences and Arts Northwestern Switzerland (FHNW)

The School of Life Sciences, FHNW holds extended and multidisciplinary expertise in many areas of modern material sciences, ranging from medicinal implant development to the 3D printing of cells and bacteria for numerous applications. In the following paragraphs, we highlight some of those activities.

The material science and nanotechnology research group of Prof. Dr. U. Pieles at the University of Applied Sciences and Arts, Northwestern Switzerland (FHNW), performs material science on nanoscale level with focus on surface chemistry technology. The group works on a broad range of materials *e.g.* biomaterials, nanoparticles & colloids, ceramics, polymers, textiles, paper, construction material and so on. The group's core-expertise includes state-of-the-art instruments & techniques to perform synthetic manipulations and characterization of structures and materials. The laboratory is equipped with chemical & BSL2 cabinets, electron microscopes (TEM, SEM), energy dispersive X-ray (EDX), atomic force microscopy (AFM), X-ray photoelectron spectroscopy (XPS), quartz crystal microbalance (QCM-D), infrared- and Raman imaging microscopes and spectrometer, laser confocal scanning microscope (LEXT), ellipsometer, micro computed tomography (µCT) and nanoindenter to determine viscoelastic properties. This comprehensive collection of techniques allows the determination of important material parameters and a deep understanding of surface-related processes.

The groups expertise and instrumentation is highly attractive for small & medium enterprises, who benefit in highly productive collaborations with the School of Life Sciences, FHNW. Such collaborations address unmet challenges, lead to new and innovative products or in-depth understanding of processes or products. Thus many of the activities of the materials science and nanotechnology group, are performed in collaboration with industrial and/or academic partners in direct-funded or governmental supported projects. An extract of such projects is given below:

5.1 *Biomaterials for Dental Therapy*

Self-assembling peptide (SAP) hydrogels have been used for several years in the area of tissue engineering and regenerative medicine.[36] Together with the Swiss company Credentis AG, hydrogel forming P11-SAPs have been developed for the therapy of dental diseases, such as the treatment of early caries lesions. We have investigated the therapeutic effect of a P11-SAP formulation applied on affected tooth-lesions and its capability to

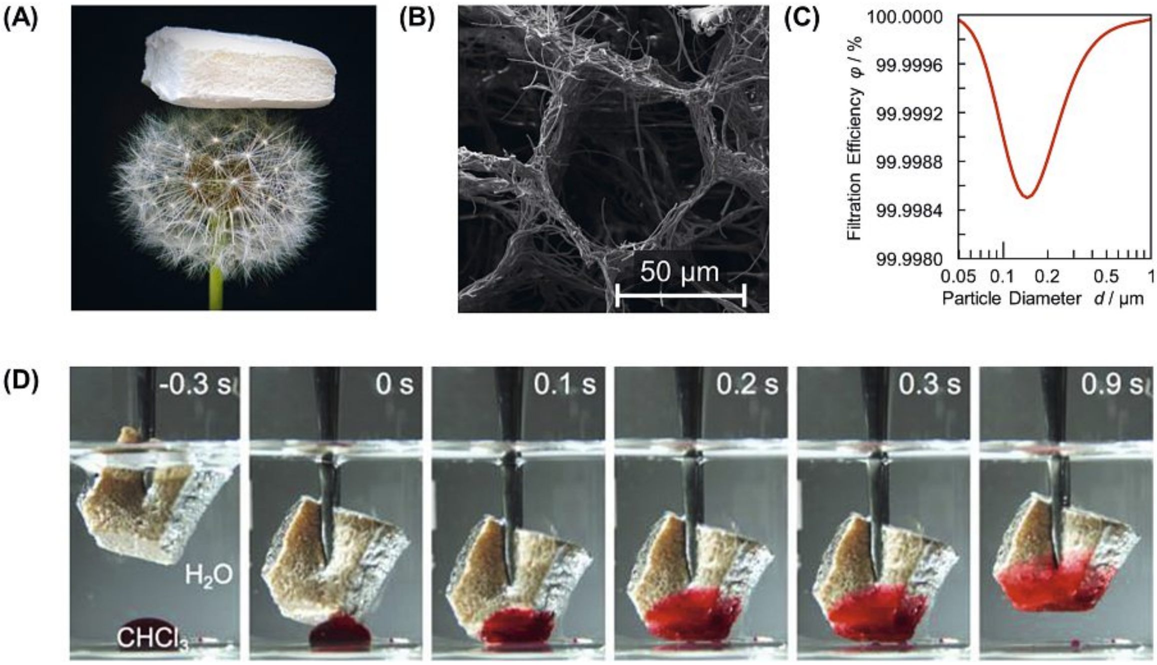

Fig. 12. (A) Ultralight NFA sitting on a dandelion. (B) Hierarchical cellular architecture of an NFA. (C) Aerosol filtration efficiency of NFAs. (D) Water remediation using NFAs. Adapted with permission from refs [31,33,35].

induce biomineralization and regeneration of the tooth.[37] The regeneration capacity of the P11-SAP formulation was evaluated by measuring the interaction of P11-SAP with dentin surfaces (Fig. 13) and by determining the degree of remineralization (Fig. 14). Micro computed tomography (µ-CT) measurements after 40 days showed an increase of 68% in mineralization with P11 SAP formulation treatment compared to 20% mineralization of untreated lesion.[36]

Beside the regenerative potential for dental hard tissue (dentin), P11-SAPs promote additionally the formation of dental soft tissue. Periodontitis, another major dental disease, is characterized by the destruction of tooth supporting structures (*e.g.* periodontal ligament). We are currently investigating if the properties of P11-hydrogels – the fast and tunable self-assembling process, the fibrillar architecture and its variable viscoelastic properties (Fig. 15A–C) – can be exploited to promote cell adhesion, migration, proliferation and differentiation and thereby eventually support restoration of damaged soft tissue.[38–40] Human Periodontal Ligament Fibroblasts (HPDLF) expressed a stretched cell phenotype with actin stress fiber formation, after 24 h of culture on P11 hydrogels (Fig. 15D). The metabolic activity rates of human dental follicle stem cells (DFSC) on P11-4 hydrogels were comparable to cells cultured on tissue culture polystyrene (TCPS) after 14 days. Noticeably, P11-4 hydrogels strengthen the osteogenic differentiation of DFSCs compared with TCPS.[39]

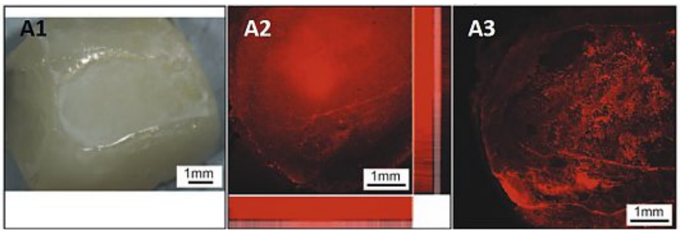

Fig. 13. Interaction of fluorescent labeled P11-4 with human dentin surface. (A1) Artificial caries lesion of human dentin surfaces. (A2) Confocal microscopy picture of artificial enamel lesions treated with fluorescence-labeled P11-4 (ATTO647-P11-4) after 1 day and 14 days (A3).

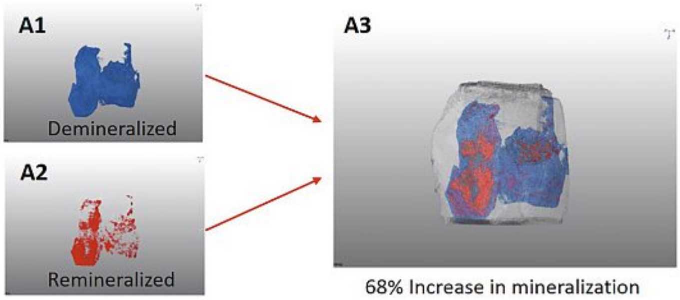

Fig. 14. Remineralization of an artificial caries lesion after application with a P11-4 formulation. µ-CT Measurements were performed before (A1) and after application of P11-4 (A2, A3).

5.2 *Nano-structured Mixed Mode Metal Catalyst Immobilized on Self-supporting Carrier*

Together with the Swiss Company SKAN AG a new efficient, cost effective, nano-structured mixed mode catalyst made ofmetal or metal oxides immobilized on a stable inorganic carrier was developed for the production of new and improved design concept of SKAN isolator systems. Those isolators are sterilized through the usage of hydrogen peroxide. However, following a cleaning cycle it is mandatory to effectively remove and destroy remaining hydrogen peroxide. Traditionally, this is done by time-consuming flushing of the system with large amounts of air which is then released directly into the environment. More modern methods use catalysts which decompose and destroy the hydrogen peroxide, and such processes allow to recirculate the air into the building, saving time and energy consumption. Previously such catalysts were applied to a compact carrier material.

Scientists in the Pieles group at the School of Life Sciences, FHNW developed a new process to coat a porous ceramic substrate in a batch process with metallic nano particles (Fig. 16). This increased the available surface area tremendously and thus multiplied the efficacy of the catalyst. SKAN has successfully commercialized this technology worldwide.

5.3 *SERS-based Imaging for the Detection of Glioblastoma Tumor Cells during Surgery*

A sharp delineation between tumor and healthy brain tissue, followed by a complete tumor resection, remains an unmet challenge in high grade brain tumor as Glioblastoma (GBM). Imaging technologies are essential for preoperative planning and intraoperative surgical removal of tumors, nevertheless they do not allow for visualization of residual tumor layers in the infiltration zone.[41,42] To overcome this limit, we use surface enhanced Raman spectroscopy (SERS) in combination with the injection of tumor specific functionalized gold nanoparticles (GNPs).[40,43,44] Since about 50% of GBM over express the epidermal growth factor receptor (EGFR), anti-EGFR functionalized Raman active GNPs were developed. The optical properties were further optimized by modify GNPs with enhancing agents, in combination with anti-EGFR functionalization this allows then a sensitive targeting of tumor cells (Fig. 17, top). Hence the two functionalities on the GNP surface both strongly influence the method sensitivity either in terms of the amount of GNP on cells or the SERS signal intensity. Unfortunately they are competitive, thus the appropriate ratio for high amount of cell binding GNPs and highest SERS signal had to be elaborated. Moreover a polyethylene glycol shell had

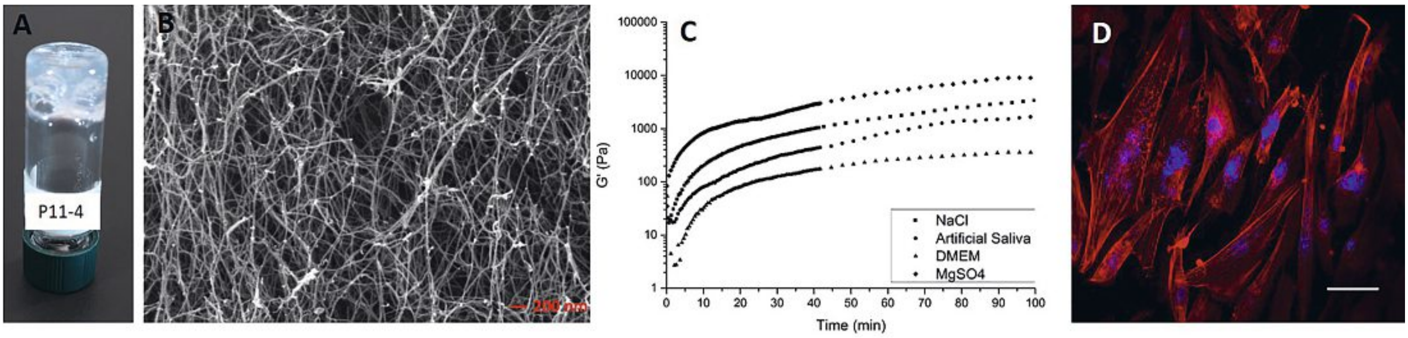

Fig. 15. (A) P11-4-hydrogel prepared in a Tris-NaCl buffer (140 mM NaCl, pH 7.2) after 2 hours of self-assembling. (B) Nanofibrillar architecture of a P11-4 hydrogel, prepared for Scanning Electron Microscopy. (C) Oscillatory rheology measurements of P11-4 hydrogels, prepared in different buffers. Storage modulus (G') has been used as parameter for stiffness. (D) HPDLF after 24 h culture on P11-4 hydrogels. Actin cytoskeleton has been stained with rhodamine-conjugated phalloidin (red), cell nuclei were stained with DAPI (blue). Scale bar 100 µm.

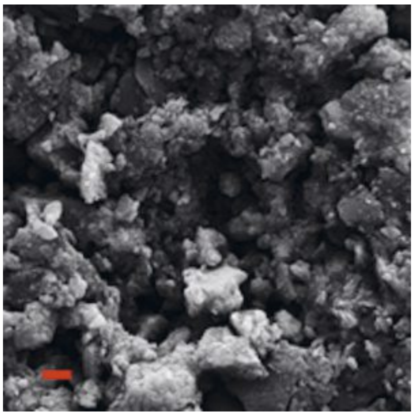

Fig. 16. Scanning electron microscope picture of the catalyst coated support material. Measured by Zeiss Supra SEM, gold coated, scale bar equals 10 µm.

to be introduced to prevent unspecific interaction with other cells. The specificity of GNPs binding was investigated *in vitro* with human GBM cells expressing high to low EGFR levels: BS153 and U87MG, respectively, while mouse astrocytes, IMA2.1, were used as EGFR-negative cells. Raman-active GNPs with no anti-EGFR were used as further control. An in depth characterization was performed to find the best parameters to ensure a distinct Raman detection of GBM cells while minimizing non-specific binding.

Raman analysis showed that anti-EGFR GNPs bound specifically to the surface of the GBM cells with high affinity allowing for discrimination of tumor cells from the control cells. Furthermore, a comparable high Raman signal intensity was detected among the different GBM cell lines depending on the expression level of EGFR (Fig. 17, bottom).

This work demonstrates *in vitro* that GNPs, visualized with Raman imaging, may be implemented intra operatively for immediate GBM-specific cell visualization improving the dismal outcomes of patients.

The research focus of the Laboratory of Nanochemistry of the School of Life Sciences of the FHNW, led by Prof. Dr. Patrick Shahgaldian, is on the development of nanomaterials capable of molecular recognition and biocatalysis for a variety of applications ranging from environmental bioremediation, biotechnology and biocatalysis to bio-analytics and nanomedicine; representative research results are highlighted hereinafter.

5.4 *Nanoparticles Supporting Bacteria Combating Oil Spill Disasters*

The Kill·Spill EU-supported project (Integrated biotechnological solution for combating marine oil spills) focused on the development of highly efficient, economically and environmentally viable biotechnological solutions for the clean-up of oil spills caused by maritime transport or offshore oil exploration and related processes. Oil spills in marine environments cause massive damage to marine ecosystems. Besides possible technological solutions to recover spilled hydrocarbons, scientists have also explored the potential of bacteria, ubiquitously present in marine environments, capable of degrading oil hydrocarbons (e.g. Alcanivorax, Marinobacter, Pseudomonas, Acinetobacter). It is established that the main limitation for the efficient biodegradation of fuel-borne hydrocarbons is the limited amount of necessary nutrients (mainly nitrogen and phosphorus) in seawater. In order to tackle this limitation, we have developed a new class of porous nanomaterials capable to carry nutrients (N & P) in seawater and to release their content when in contact with an oil phase. Based on mesoporous silica nanoparticles, the nanomaterial developed allows retaining the encapsulated nutrients in aqueous media, which in turn is released in contact with an oil phase thus supporting bacterial degradation of hydrocarbons.[45]

5.5 *In silica Protein Engineering: From Molecular Recognition to Biocatalysis*

In our efforts to develop recognition nanomaterials for large protein assemblies such as viruses, we established a method to

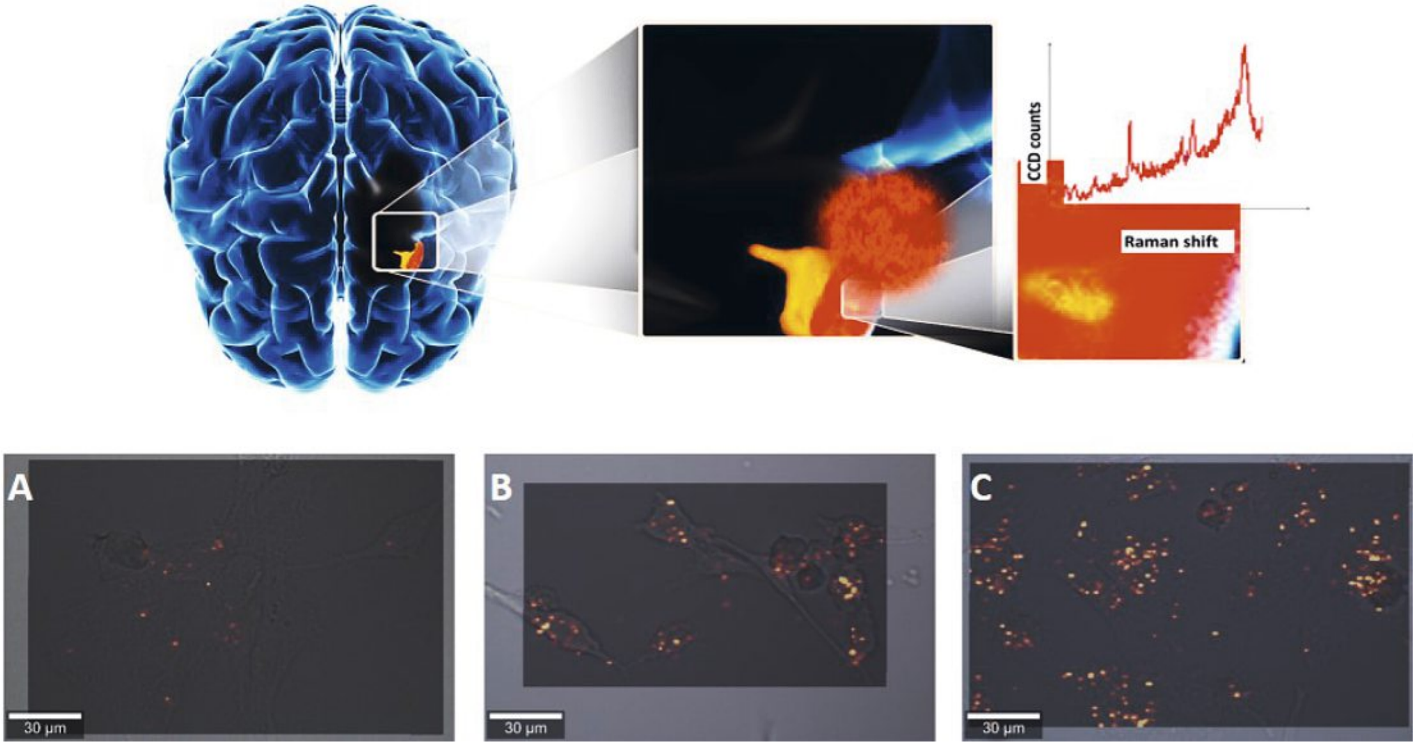

Fig. 17. Top : Schematic representation of Raman-guided surgery to differentiate brain tumor cells at the border of the cavity resection. Bottom: Overlay images of brightfield, and Raman mapping of anti-EGFR GNPs incubated with EGFR negative (A) and EGFR positive cells with low (B) and high (C) EGFR expression level respectively. The brighter the color, the higher the number of GNPs attached to the cells.

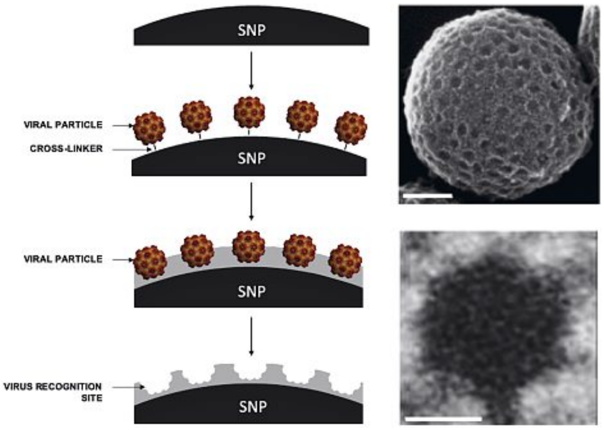

Fig. 18. Schematic representation of the virus imprinting method (left) and representative scanning electron micrographs of the nanosystems produced. Scale bars represent 100 (top) and 20 (bottom) nm.

create molecular recognition imprints of non-enveloped icosahedral viruses at the surface of silica nanoparticles; cf. Fig. 18.[46] This method is based on surface imprinting using silica nanoparticles as carrier material and organosilanes serving as building blocks to produce a virus recognition layer. Following this proof of concept, we adapted this chemical strategy to virus-like particles[47] and implemented an internal enzyme-based detection system allowing for label-free virus detection.[48]

Enzyme immobilization and encapsulation represent established strategies to retain enzymatic activity while improving their stability against physicochemical stress conditions. Building upon our findings on virus imprinting, we have developed the concept of supramolecular enzyme engineering which, in contrast to enzyme engineering, does not require genetic manipulation or covalent modification of the enzyme. We have demonstrated that enzymes, when immobilized at the surface of silica and shielded in a soft organosilica shell, retain their enzymatic activity with a drastic improvement of their stability against external stress conditions.[49] In the same context, we also demonstrated that enzyme–polymer conjugates can be attached in a stable yet reversible fashion on polymeric filtration membranes exploiting surface supramolecular interactions.[50] The commercial implementation of the enzyme protection technology developed is now carried out by INOFEA AG, a biotech company that spun-off from the activities of our laboratory.

5.6 Two-dimensional Metal–Organic or Supramolecular Networks

Self-assembled networks featuring nanometer-sized pores and long-range crystallinity provide configurable templates for host–guest recognition and site-specific chemistry and may impact several technological applications, provided that the resulting material is of sufficient stability. We have recently demonstrated that calixarene-based amphiphiles, when bearing suitable chemical moieties, can self-assemble as stable and crystalline 2D networks. For example, working on the self-assembly of a carboxylate-modified calix[4]arene at the air–water interface, we demonstrated that the presence of Cu^{2+} transition metal ions in the water phase causes the formation of crystalline and stable 2D metal organic network, which can be further transferred on solid surfaces using the Langmuir-Schaeffer method.[51] An analogue of this amphiphile, bearing cyano functions at the *para* rim was shown to form 2D crystalline layers; the self-assembly has been shown to be driven by the formation of a network of concerted dipole–dipole interactions (Fig. 19). We demonstrated that, in spite of the limited energy of dipole–dipole interactions, the stability of the layer was sufficient to allow producing free-standing layers.[52] This opens up new perspectives in the use of such self-assembled films as support surfaces for advanced electron microscopy methods and single particle X-ray analyses.

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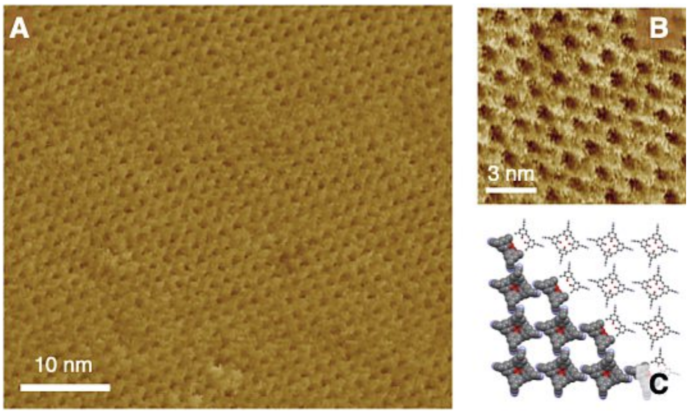

Fig. 19. Molecular resolution atomic force micrographs of a supramolecular organic network of p-cyano-calix[4]arene produced at the air-water interface and transferred on a silicon dioxide substrate using the Langmuir-Schaeffer method (A & B) and molecular model of this supramolecular network (C).

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