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Colorimetric Nanofibers as Optical Sensors

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Sensors play a major role in many application areas today, ranging from biomedicine to safety equipment, where they detect changes in the environment and warn us about these alterations. Nanofibers, characterized by high porosity, flexibility and a large specific surface area, are the ideal material for ultrasensitive, fast-responding and user-friendly sensor design. Indeed, a large specific surface area increases the sensitivity and response time of the sensor as the contact area with the analyte is enlarged. Thanks to the flexibility of the membranes, nanofibrous sensors cannot only be applied in high-end analyte detection, but also in personal, daily use. Many different nanofibrous sensors have already been designed, albeit the most straightforward and easiest-to-interpret sensor response is a visual change in color, which is of particular interest in the case of warning signals. Recently, many researchers have focused on the design of these so-called colorimetric nanofibers, which typically involves the incorporation of a colorimetric functionality into the nanofibrous matrix. Many different strategies have been used and explored for colorimetric nanofibrous sensor design, which is outlined in this feature article. The many examples and applications demonstrate the value of the use of colorimetric nanofibers for advanced optical sensor design and could provide directions for future research in this area.

1

1. Introduction

According to Frost&Sullivan's market research, the global sensors market revenue generated $106.86 billion in 2015 and is estimated to increase to $162.36 billion by 2019, resulting in a compound annual growth rate of 11.6% over a period of four years.[1] This enormous growth reflects the increasing interest and importance of sensors today, as they become smaller, smarter, faster, more sensitive, easier to use, more reliable and moreover, personal and wearable. Sensors are used in almost all end-user markets with industrial process control, food and beverages, life sciences and safety being among the key markets.[1] One of the main types of sensors are chemical sensors, which detect the presence of a chemical substance, called analyte, in a gas, liquid or solid phase.[1–3]

As sensors monitor and respond to changes in our environment, we rely on them to warn us whenever necessary. This imposes some strict requirements on sensors, such as reliability, fast response time and ultra-sensitivity. Many efforts have been made to fulfill these requirements and further enhance the sensor properties.[1,2,4–12] Among these efforts, nanofibers are a hot topic in recent advanced sensor design.[7,13–26] Many production techniques exist for the fabrication of nanofibers, including self-assembly and phase separation.[27–34] However, solvent-electrospinning is the most commonly used production technique today as it is the only scalable process combined with high flexibility and versatility, already being applied in industry.[32,35,36] In solvent-electrospinning the applied polymer is dissolved in an appropriate solvent system resulting in the electrospinning solution, which is then pumped through an electrically charged needle. Due to this electrical field the droplet at the tip of the needle is drawn into a jet towards the collector while the solvent evaporates. Under the correct process conditions, *e.g.* suitable viscosity, tip-to-collector distance, voltage, flow rate, ambient parameters, a stable process, *i.e.* stable Taylor cone, is achieved wherein a combination of bending and splitting of the jet results into long, uniform, bead-free nanofibers with a diameter typically below 500 nm (**Figure 1**). As a result of their sub-micron dimensions, nanofibers possess unique properties including a

high volume of small pores and a good inter-pore connectivity, resulting in a remarkably high specific surface area.[28,33,34] These properties are interesting for many application areas and particularly sensors, as a large specific surface area results in fast response times and ultra-sensitivity.[7,22,24,37–42] Compared to bulk materials, films and coatings, nanofibers are reported to enhance the sensitivity and responsivity of sensors.[7,13,16,18,22,24,43–48] They are widely applicable as they can be produced on a very small scale, *e.g.* porous coatings, but also as large scale, *i.e.* several square meters, light-weight stand alone membranes. These membranes are flexible and drapable, increasing the contact surface with the skin or machine parts, which is specifically interesting for advanced sensor design. Additionally, solvent-electrospinning allows for the production of many different nanofiber morphologies, *e.g.* hollow fibers, porous fibers, ribbon-like fibers, nanowebs, which may enhance the nanofibrous properties in specific applications.[7,24,26,31,34,40,49] Nanofibers are, thus, highly promising materials for high-end sensor applications.

A (nanofibrous) sensor generally executes two functions, *i.e.* recognition and transduction (**Figure 1**).[3] For this, the sensor consists of a detection system (Functionality in **Figure 1**) that is able to (selectively) interact with, and therefore recognize, the analyte.[3] Secondly, a suitable translation system, *i.e.* transducer, is present, which converts the interaction between the analyte and the detector into a readable output signal.[3] Signals that are easily interpreted by the user are mainly based on electrical or optical changes.[3] Other literature studies and reviews have discussed and summarized the use of nanofibers to produce sensors based on acoustic wave, resistive, photoelectric and amperometric signals and are only briefly reported here.[7,13,16,17,19,21,23,24,26,38–40,42,44,50–56] Acoustic wave sensors are mainly gas sensing devices that detect a change in electrical conductivity or mass on an electrode, which disturbs the velocity of acoustic waves resulting in an interpretable frequency shift.[7,16,24,40,44,50] Nanofibers have been deposited on the electrode to improve the sensitivity of the sensor towards various analytes, such as formaldehyde, moisture and NH_3.[7,16,24,40,44,50] In the case of resistive sensors,

conductive nanofibers are applied to the electrodes, which respond to the analyte by a measurable change in conductivity or resistivity.[7,16,17,19,20,24,26,39,44,50,52,55,56] Mainly metal-oxide semiconductors, *e.g.* TiO_2 and ZnO, and conducting polymers, *e.g.* polyaniline and polypyrrole, have been used to detect gaseous compounds, such as CO, NO_2, amines, alcohols and other volatile organic vapors. In photoelectric sensors the conductivity or current response upon illumination is largely increased if nanofibers are applied.[7,13,19,24,42,44,50,57,58] The use of GaN or Au-embedded silica nanofibers led to promising photodetectors or photo-switches. Electrochemical sensors based on amperometric signals are typically applied as biosensors to detect biological compounds such as glucose and urea. Such biosensors are based on conducting nanofibers that are deposited on the electrodes being either enzymatic or enzyme-free. This improves the amount of adsorption sites for the analyte and enhances the signal transfer.[7,19–21,23,24,26,38,45,51,53,54,59,60] All of the aforementioned examples prove the high potential of nanofibers within advanced sensor applications. However, many of them require conductive nanofibers to enhance the sensitivity of the electrodes, restricting the amount of applicable polymers. Moreover, advanced analytical read-out equipment and an experienced user are needed to interpret the achieved data, leaving a broad public of non-experts unanswered.
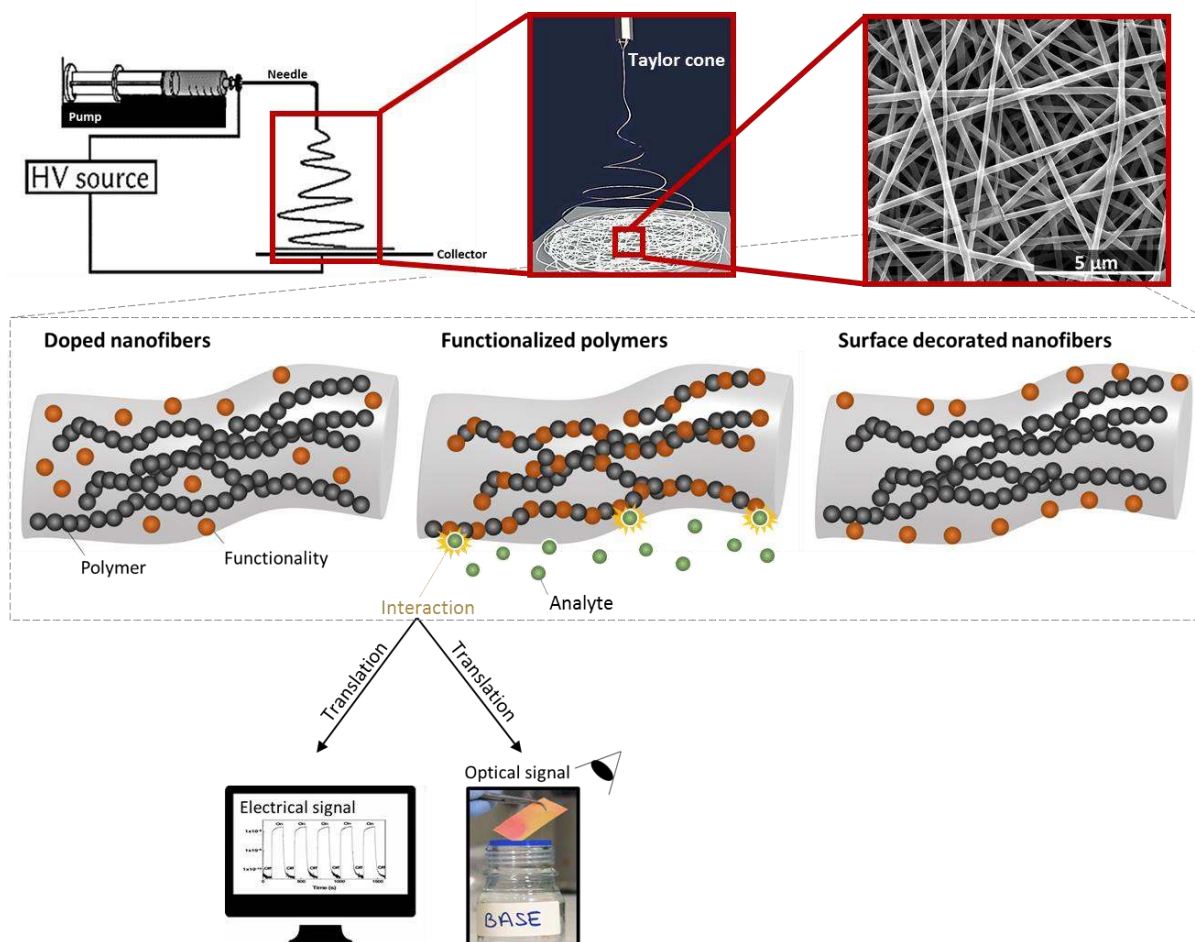
Figure 1. Nanofibrous sensors are fabricated by the solvent electrospinning process, in which a polymer solution is drawn into sub-micron fibers by the application of an electrical field. In order to introduce a sensing function, different functionalities can be incorporated in the nanofibers by three different techniques: doping of the electrospinning solution with the functionality, functionalizing the polymers itself with functionalities or modifying the surface of the produced nanofibers. In all cases, the functionalities are the detection system of the sensor and are able to interact with the analyte. This interaction is subsequently translated into a readable signal, which can be electrical or optical.

In contrast to electrical signals, optical signals are more straightforward and easier to interpret, especially in the case of warning signals. Additionally, optical sensors do not show electromagnetic interference, neither do they need electric contacts.[7,14,18,22,50,60–63] As there is no need for electrodes or sophisticated equipment, optical nanofibrous sensors are easily

portable or wearable and enable the production of large-scale sensors that are capable of monitoring large areas, yet resulting in local signaling if desired. In summary, they are more user-friendly and show more geometrical versatility than their electrical counterparts, which makes them more suitable for field-analysis and personal use.

Optical nanofibrous sensors mainly focus on Fourier transform infrared (FTIR), fluorescence and currently also colorimetric output signals. For example, Hahn *et al.* fabricated a sensor based on polyacrylonitrile nanofibers loaded with metal oxide semiconductors (Fe_2O_3, Ab-SnO_2 and ZnO) to detect CO_2, which was visualized and quantified by FTIR spectroscopy.[61] Optical nanofibrous sensors based on fluorescence involve quenching/regaining the fluorescence of the detection system due to the interaction with the analyte.[7,13,14,18,19,22,24,37,41,56,60,64] This phenomenon is generally measured by Stern-Volmer plots and visualized by fluorescent microscopy. Many optical nanofibrous sensors for electron-deficient compounds such as explosives and heavy metal ions have been designed based on this technique by either doping fluorescent compounds into the electrospinning solution[22,37,41,65–85], chemically modifying nanofibers [22,37,41,86–95] or "decorating" the surface of the nanofibers[96–103]. Very often, these changes in fluorescence intensity can be seen with the naked eye or with the help of relatively simple equipment such as LED light sources, CCD cameras or compact inexpensive spetrometers.[22,64] Thus, although FTIR- and fluorescence-based optical sensors already provide a visual translation system, these techniques still require additional equipment, *e.g.* spectrometer (FTIR), illuminating source for excitation (fluorescence). In contrast, the recently explored colorimetric nanofibrous sensors provide a visual color change, interpretable by the naked eye, upon interaction with the analyte without any other technological requirement.[13,14,22,60,104] In addition to the naked eye qualitative analysis, ideally suited for warning signaling, a quantification is also possible by means of simple spectrophotometric measurements. Although these sensors are still in their infancy, they are of increasing interest and believed to show enormous potential not only in high-end applications, but particularly in

personal care and daily use, wherever fast, visual warning signals are of crucial importance, due to their user-friendly, flexible and portable nature. Therefore, this paper will summarize the developments within this field as to encourage further exploration and research. First, the principles of colorimetric sensors will be outlined, followed by the various techniques used for colorimetric sensor design. These techniques are explained and illustrated based on several literature examples and our own research.

2. Colorimetric nanofibers

Colors have been used since the very beginning of humanity and have always been a powerful tool of communication. For example, red and green are universal indicators for respectively stop/danger and go/safety. Since colors are so easily and intuitively interpreted, they represent the ideal output signal for monitoring systems such as sensors. Many types of colorimetric sensors have already been developed and there is a continuous evolution to more advanced and smarter sensors. For instance, Suslick *et al.* reported the first colorimetric sensor array system, providing for a sensor that does not ontly detect the analyte, but is also capable of differentiating between different compounds.[105] Among these high-end colorimetric sensors, nanofibers are receiving a lot of interest today. Colorimetric nanofibers can be defined as nanofibers that possess a specific functionality capable of changing color, visible by the naked eye, upon a change in the environment, such as pH, O_2, CO_2, volatile organic compounds (VOC's) and metal ions. This straightforward and easy-to-interpret function gave rise to the recent emergence of colorimetric nanofibers as novel advanced optical sensor materials with enormous potential, particularly in applications that demand fast warning signals. For the latter, ultra-sensitivity and fast response times are extremely important, which justifies the use of nanofibers as matrix material. Indeed, in our work, it was clearly shown for conventional textiles that a decrease in fabric density, results in higher sensitivity and lower response times, *i.e.* reduction from hours to minutes.[47,106] It is, thus, not surprising that nanofibers, having diameters below 500 nm arranged in a very porous, open structure, reduce the response time

potentially to seconds and enhance the sensor sensitivity. Also in other literature studies, nanofibers proved to enhance sensor sensitivity mainly thanks to their large surface area to volume ratio, which provides an increased number of sites for analyte interaction and/or signal transduction.[7,16,18,22,24,45,47,48] Of course, at this small scale, sensitivity and response time will also be influenced by other factors, such as the intrinsic properties of the applied polymer, interactions between the polymer and the added functionality and diffusion processes, as will be shown in this feature article.

The functionality responsible for the interaction with and, therefore, the recognition of the analyte, also induces the visible color change of the entire material. Therefore, the functionalities are typically molecules which are capable of absorbing energy in the visual part of the electromagnetic spectrum, such as complexes with Fe, Cu, Zn, and molecules characterized by a linear or cyclic system of conjugated double bonds, such as dyes and conjugated polymers.[3,22,107,108] Every stimulus, *e.g.* analyte, causing significant changes to the energy levels of these functionalities will result in a color change, since the absorbed energy and, thus, the corresponding wavelength will be altered. Color change phenomena are classified according to the trigger that causes the change, *e.g.* photochromism (light), electrochromism (oxidation/reduction), thermochromism (heat), solvatochromism (solvent polarity), ionochromism (ions) and halochromism (pH). To introduce the color changing function into the nanofibrous material three different techniques are typically applied: doping of nanofibers, functionalizing polymers or altering the nanofibers' surface, as discussed in the following sections (**Figure 1**). The main goal of the design of colorimetric nanofibrous sensors is to provide for a fast and naked-eye visual warning signal. In addition the use of colorimeters can further enhance color quantification and detection for a more detailed information analysis.

3. Colorimetric sensors based on doped nanofibers

The best known method to incorporate the functionality into the nanofibers as to produce colorimetric nanofibrous sensors is called doping. Many researchers have used and are still

investigating this technique. Doping is a fast and easy procedure as it simply involves the addition of the sensing functionality to the polymer solution prior to electrospinning. Typically, dyes or metal-based nanoparticles are added to produce doped colorimetric nanofibers. The main drawback of this technique is the fact that the functionality is only physically entrapped within the nanofibrous polymer network. This means that the functionality is able to leach from or migrate through the nanofibrous structure. This not only affects the long-term sensitivity and stability of the sensor, but the potential contamination of the environment, *e.g.* toxicity of the leaching compound, is of significant concern. Many colorimetric nanofibrous sensors have been designed via doping techniques, mainly for environmental applications, *e.g.* pH and heavy metals, as well as biomedical applications, *e.g.* glucose and dopamine, as listed in **Table 1**.

Table 1. List of colorimetric nanofibrous sensors based on doping techniques.

Type of doping	Polymer matrix	Functionality	Analyte	Response time	Detection limit	Ref.
Dye-doped	PA 6.6	Ethyl Orange Cresol Red p-Rosolic Acid Bromothymol Blue Bromocresol Purple Brilliant Yellow Neutral Red Alizarine Red Chlorophenol Red Xylenol Blue Nitrazine Yellow	pH	< 10 min	-	[109]
	PA 6	Nitrazine Yellow	pH	< 5 min	-	[48,110]
	PCL	Nitrazine Yellow	pH	< 5 min	-	[48,110]
	PCL/Chitosan	Nitrazine Yellow	pH	< 5 min	-	[48,110]
	Polyacrylonitrile	Pyran-derivative	pH	-	-	[111]
	PA 6	Combination of Phenol Red, Methyl Red, Bromothymol Blue, Phenolphthalein and Bromocresol Green	pH	3 s	-	[112]
	Poly(ether sulfone)	Rhodamine	Cu^{2+}	< 10 min	$1.1 \cdot 10^{-9}$ M	[113]
	Cellulose acetate	Curcumin	Pb^{2+}	-	$20 \cdot 10^{-6}$ M	[114]
	Zein	Curcumin	$Fe3+$	< 90 min	0.4 mg/L	[115]
	PCL	Dimethylglyoxime	$Ni2+$	-	1 ppm	[116]
	Polycaprolactam/PVA	Dimethylglyoxime	$Ni2+$	-	5 µg/mL	[117]
	Cellulose acetate	Br-PADAP	Uranyl	< 80 min	50 ppb	[118]
	PEO	*o*-phenylenediamine derivatives containing rhodamine, 1,8-naphtalimide and 4-chloro-7-nitrobenzo [c] [1,2,5] oxadiazole	Phosgene	< 2 min	0.7 ppb	[119]
	PAA	Hydrazone-tricyanofuran	NH_3	-	0-750 nM	[120]
	PLA	Tetraphenylporphyrin	HCl	< 5 s	34 ppb	[121]
	Silica	Methyl Red Methyl Yellow	HCl, NH_3, biogenic amines	< 1s	20 ppm	[122]
	PU	ABTS o-dianisidine	Glucose	< 5 min	0.05 µM	[123]
NP-doped	PA 6	Au/Cu	Ascorbic acid	< 3 min	0.018 mg/L	[124]
	PA 6	Au	Dopamine	< 5 min	$5 \cdot 10^{-7}$ M	[125]
	PVA	Cu	Glyphosate	< 3 s	0.1 µg/mL	[126]
	PEO	Au	TNT	< 1 s	1 ppb	[127]

3.1 Colorimetric sensors based on dye-doping

Dye-doped nanofibers are produced by addition of stimuli-sensitive dyes to the polymer solution before electrospinning and was applied for the first time by Costa *et al.*[128] Indicator dyes are well-known stimuli-sensitive dyes that are able to sense the analyte by hydrogen bonding, Coulomb, Van der Waals and/or hydrophobic interactions.[22] In addition, many research has been focusing and is still ongoing to develop new and improved dye molecules for sensor applications. For instance, Mohr has reviewed the developments in the use of (reversible)

covalent bonding to detect neutral and ionic analytes such as cyanide, formaldehyde, amino acids, peptides and proteins.[129] This extensive knowledge on stimuli-sensitive dyes can easily be combined with the advantageous properties of nanofibers by dye-doping leading to novel, improved colorimetric sensors. Costa *et al.* showed for the first time that the addition of dyes (powder form) to the polymer solutions does not significantly affect the electrospinning process nor the final nanofiber morphology as long as the dyes are well soluble in the applied solvent system.[128] It was found that this solubility, prior to electrospinning, is an important requirement for the stability of the process as the use of poorly soluble pigments and dyes led to great alterations in electrospinnability and nanofiber uniformity. We made similar observations in our work.[109] Dye-doping is, thus, a relatively easy and versatile production technique for a wide range of colorimetric nanofibrous sensors.

An important part of the research on colorimetric nanofibers is focused on developing halochromic sensors, as pH plays an important role in many applications such as protective equipment and clothing, food and biomedicine.[47,130,106,131] Additionally, many halochromic dyes are widely available. We have explored several commercial pH-indicator dyes for dye-doping of polyamide 6.6 nanofibers, which resulted in a wide range of nanofibrous membranes showing halochromic behavior (**Table 1**, top).[109] It was observed that the incorporation of the dye in the nanofibrous matrix could influence the halochromic behavior of the dye with respect to its behavior in solution. Depending on the strength and mode of the polymer-dye interaction, the pH-range of the color change of the dye shifted and/or broadened upon incorporation in the nanofibers; even the color itself could be influenced. In order to further investigate these phenomena in more detail, Nitrazine Yellow was incorporated in three different polymer matrices, *i.e.* polyamide 6, poly(ε-caprolactone) and poly(ε-caprolactone)/chitosan.[48,110] This revealed that the change in microenvironment of the dye, due to the incorporation of the dye in the nanofibrous matrix, can have a significant influence on the colorimetric and response behavior of the dye. Three levels of alteration can be distinguished: (i) changes in the

absorbance spectrum, *i.e.* color, (ii) alterations in the dynamic pH-range such as broadening or a shift in pK_a, (iii) differences in response time. For example, doping of polyamide 6 and polyamide 6.6 nanofibers with Nitrazine Yellow resulted in a shift of the wavelength maxima accompanied with a shift and broadening of the dynamic pH-range. If Nitrazine Yellow is doped in a poly(ε-caprolactone) matrix, the dye's halochromic behavior was even completely suppressed. Addition of chitosan to this polymer system regains the halochromic behavior and effectively lowers the response time from 3 hours to 5 minutes, due to the increased hydrophilicity of the nanofibers which increases the dye's accessibility. These results clearly indicate that the choice of the nanofibrous matrix is crucial as interactions between the polymer and the dye may have a significant influence on sensitivity and responsivity of the colorimetric sensor. Molecular modelling was used to further underpin the dye-polymer interactions and understand the experimental sensing observations. Based on a combination of molecular dynamic simulations and time-dependent density functional theory, we developed a theoretical procedure, which can be used to predict the behavior of (azo) dyes in aqueous environment.[132] It is, thus, possible to understand at the molecular level the structural differences that are at the origin of halochromism. Additionally, our research demonstrated that a computational study can provide crucial information on the effects of substituents of a chromophore on its halochromic behavior.[133] This makes it possible to predict the behavior of hypothetical dyes with the same chromophore and of existing dyes in a different environment, such as a polymer nanofibrous matrix. In this way, molecular modelling was used to explain the difference in halochromic behavior of Nitrazine Yellow in aqueous solution and the three nanofibrous polymer matrices described above.[48,110] Ab initio calculations of the neutral and deprotonated dye molecules confirmed that changes at the azo group (N=N) induce the color change of the dye. Model systems for the three polymer matrices, *i.e.* polyamide, poly(ε-caprolactone) and chitosan, were designed and allowed the evaluation of the interactions of Nitrazine Yellow with the polymer matrices. The simulations revealed that the azo group of Nitrazine Yellow is

shielded from the water molecules by the long-range interactions of the ester groups of poly(ε-caprolactone) with the chromophore (**Figure 2**, left). This explains the suppressed halochromic behavior. In comparison, chitosan shows very different behavior and shielding does not occur (**Figure 2**, right). Hydrogen bonding and electrostatic interactions between the sulphate groups of Nitrazine Yellow and the amino groups of chitosan enable deprotonation in an alkaline environment.
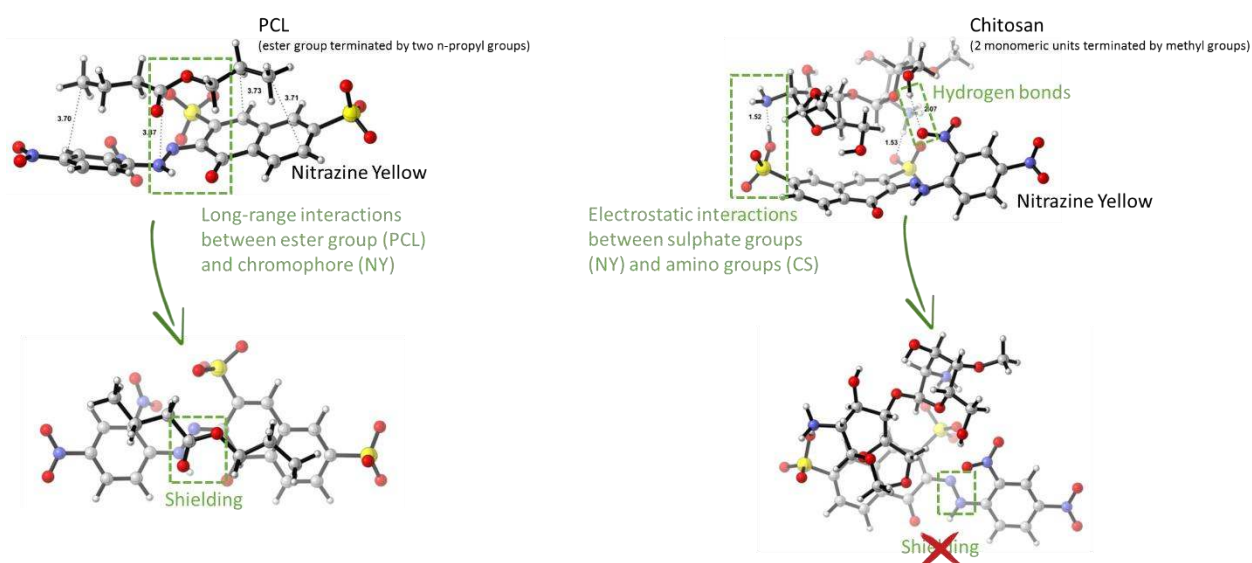

Figure 2. Molecular modelling supports and enhances the understanding of experimental results. Here, for instance, the strong interactions between poly(ε-caprolactone) (PCL) and the chromophore of Nitrazine Yellow (NY) are simulated, which supports the hypothesis of shielding of the dye, hindering a visual color change. Chitosan (CS), on the contrary, clearly shows different interactions, which do not lead to shielding, leaving the halochromic behavior of Nitrazine Yellow intact. Reproduced and adjusted with permission.[110] 2012, Elsevier.

Additionally, the Gibbs free energy of the interactions was estimated by the theoretical model, which gave a value of -35.6 kJ/mol for PCL and -132.3 kJ/mol for chitosan. These values explain the preferential interaction of Nitrazine Yellow with chitosan, resulting in a restored halochromic behavior after addition of chitosan to the poly(ε-caprolactone) matrix. These findings clearly show the power of molecular modelling to support experimental results as to

gain better understanding of sensing mechanisms and predict the behavior of future dye-doped nanofibers. Eventually, this paves the way for the design of tailor-made dyes for specific applications. Recently, also several other researchers reported colorimetric nanofibers based on tailor-made dyes as to improve the sensing function according to the anticipated application. For instance, Bae *et al.* synthesized a pyran-based halochromic dye to produce colorimetric polyacrylonitrile nanofibers which changed color from yellow to red by changing from acidic to basic conditions.[111] Typically, an indicator dye changes its color within a specific pH-range, meaning that different colorimetric sensors should be used for the detection of specific pH-values. In order to broaden the functionality and applicability of the halochromic nanofibers, multiple dyes with different pH-ranges and color changes can be doped into the polymer solution altogether. Chandra *et al.* applied this technique to produce an effective and universal pH-sensor indicating each pH by a unique color.[112] For this, five indicator dyes (Phenol Red, Methyl Red, Bromothymol Blue, Phenolphthalein and Bromocresol Green) were doped in polyamide 6 nanofibers in a specific ratio.

Next to pH-sensors, which have many applications in biomedicine and safety, also colorimetric sensors for the detection of (toxic) heavy metals are a hot topic in recent research, as environmental monitoring becomes more important. Singh *et al.* have reviewed different dye-classes and their mechanisms to detect metal ions.[134] For instance, rhodamines are a class of dyes widely used for sensing applications. The probe is colorless in the closed spirolactam form. However, upon interaction with a suitable analyte, the ring opens via a reversible coordination or an irreversible chemical reaction, which results in a detectable pink color. Wang *et al.* have used rhodamine-doped poly(ether sulfone) nanofibers for the reversible detection of Cu^{2+} in aqueous medium.[113] The sensor was tested in the presence of alkali, alkaline earth and other transition metal ions, but proved to be selective towards copper. Selectivity is another important issue in sensor design as to decrease false positives. Shankaran *et al.* designed a selective colorimetric sensor for Pb^{2+} based on curcumin-doped cellulose acetate nanofibers.[114] The

colorimetric nanofibers appeared yellow, but turned brown upon detection of lead, even in the presence of other metal ions (**Figure 3**).
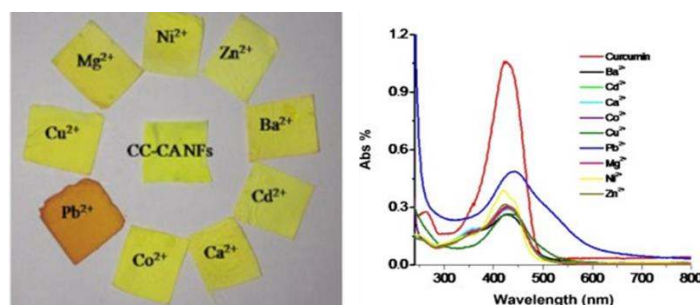

Figure 3. Unambiguous selectivity of curcumin-doped cellulose acetate nanofibers for Pb^{2+} in the presence of other metal ions. Reproduced and adjusted with permission.[114] 2015, Elsevier

Imyim *et al.* also used curcumin to produce an Fe^{3+} colorimetric sensor, but used the natural polymer zein as polymer matrix.[115] The produced sensor was tested in different water samples, *i.e.* drinking water, tap water and pond water, showing a clear color change upon the detection of iron above the maximum acceptable concentration set by regulations. Although the produced Fe^{3+} sensor showed a response time of 90 minutes for the lowest concentration detectable by the naked eye, which is much slower compared to a hydrogel detection system based on a rhodamine derivative (response time of 20 minutes, detection limit of 0.1 mg/L), this sensor had the advantage of being environmental friendly. However, further optimization of the sensitivity is definitely necessary in order to be competitive with other sensors based on other support materials. Also sensors for Ni^{2+} have been produced by Dubas *et al.*[116] and Sereshti *et al.*[117] by doping of dimethylglyoxime in respectively poly(ε-caprolactone) and polycaprolactam/polyvinylalcohol nanofibers. The resulting red color is due to the formation of a complex between two dimethylglyoxime molecules and nickel.

Next to heavy metals, also other toxic compounds either present as trace elements in aqueous media or in gaseous form can be detected by colorimetric nanofibrous sensors for environmental monitoring. A colorimetric nanofibrous strip was designed by Shan *et al.* to detect uranyl, which is the soluble form of the toxic and radioactive compound uranium used

in nuclear industry.[118] The sensor was fabricated by doping a cellulose acetate solution with 2-(5-bromo-2-pyridylazo)-5-(diethylamino)phenol (Br-PADAP) prior to electrospinning. The nanofibrous membranes doped with Br-PADAP showed a yellow color due to absorption at 450 nm (**Figure 4**).
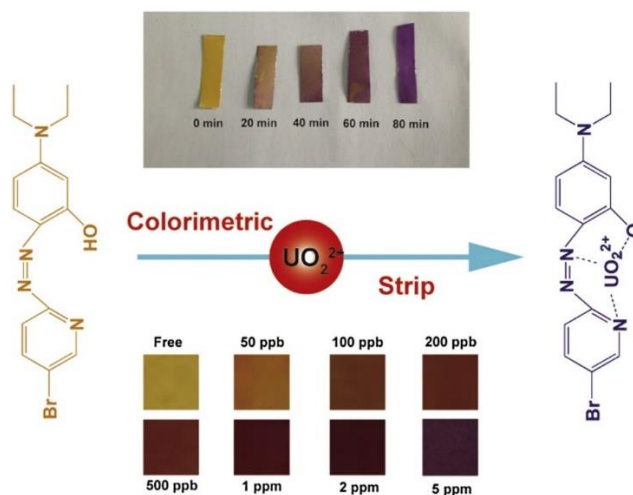

Figure 4. Br-PADAP-doped cellulose acetate nanofibers provide a clear color change upon detection of uranyl with a detection limit of 50 ppb. Although the change in color could be visualized after 20 minutes, only after 80 minutes the membrane had reached its final color. Reproduced with permission.[118] 2017, Elsevier.

Upon uranyl presence, Br-PADAP is capable of forming a complex with uranyl, resulting in an extra peak in the absorbance spectrum at 550 nm, which leads to a purple color. Under optimal conditions, the sensor showed a detection limit of 50 ppb. It should be noted, however, that this low detection limit was accompanied with a response time of 80 minutes before the membranes had fully changed their color. This low response time is probably due to the diffusion process necessary for the color change to occur. As the authors found that Br-PADAP is located inside the nanofibers, the analyte, *i.e.* uranyl, first had to diffuse through the nanofibers before complexation with Br-PADAP could take place. Due to electrostatic repulsion with the cellulose acetate polymers, the formed complex diffuses back to the surface as shown with X-ray photoelectron spectroscopy. This finally results in the visual color change of the membrane,

however only after the specific time needed for the diffusion processes. Further optimization of the sensor could include an investigation of the influence of the position of the functionality in the nanofibers on the sensor sensitivity and response time. It would probably be advantageous if the functionality could be positioned at the surface of the nanofibers. Nevertheless, the authors also successfully applied their sensor to seawater samples, proving the applicability of the colorimetric nanofibers. Much faster response times (1 to 2 minutes) combined with low detection limits (0.7 to 2.8 ppb) were achieved by Yoon *et al.* for the detection of phosgene vapors by doping polyethylene oxide nanofibers with three different *o*-phenylendiamine derivatives containing 4-chloro-7-nitrobenzo[c][1,2,5]oxadiazole (NBD-OPD), rhodamine (RB-OPD) and 1,8-naphtalimide (NAP-OPD).[119] Only NBD-OPD and RB-OPD showed a clear visual color change respectively from orange to pale yellow and from colorless to pink due to the formation of the benzimidazolene derivatives upon detection of triphosgene gas. Other gasses that gain a lot of attention in sensor design lately are HCl and NH_3 vapors. The detection of NH_3 is of particular interest since, although the alkaline gas is highly toxic at low concentrations (25 ppm), huge amounts of ammonia are used in industry for the production of artificial fertilizers, polymers, textiles and explosives.[120] Many ammonia-sensors have been developed based on thin films, however their sensitivity is limited and should be improved. Moreover, colorimetric sensors enable fast and easy-to-interpret warning signals. Therefore, Klapötke *et al.* have designed a colorimetric detector for ammonia gas based on electrospun nanofibers doped with a hydrazone-tricyanofuran compound.[120] In the presence of ammonia, deprotonation occurs at the hydrazone NH-group which reversibly converts it into a hydrazone anion. This increases the electron-donating character of the hydrazone moiety, which changes the electron delocalization within the chromophore, leading to a yellow to purple color shift. At the other side of the pH spectrum, acidic gases such as HCl vapors are also widely used, yet extremely toxic. Also in this case, colorimetric sensors acting as instant warning signals upon leakages or exposure are of crucial importance in protective clothing or safety equipment. Kang

et al. used poly(lactic acid) nanofibers doped with tetraphenylporphyrin for the design of HCl gas sensors showing a detection limit of 34 ppb.[121] Within only 5 seconds the nanofibrous membrane had changed its color from pink to green upon exposure to HCl. Compared to recently reported film-based methods for HCl detection, *e.g.* porphyrinated polyimide honeycomb film or TMPyP/TiO$_2$ composite thin film, the detection limit is decreased from around 100 ppb to 34 ppb and the response times are two to four times faster, clearly indicating the advantage of using nanofibers over thin films.[121,135,136] In such applications where detection of strong acids and/or bases is important, the sensors should often be able to withstand harsh chemical conditions, for example in industrial plants. Also at high temperatures, the aforementioned polymeric nanofibers will not survive. Therefore, it is beneficial to not restrict colorimetric sensor design to organic polymers, but broaden their applicability by producing sensors from ceramic nanofibers. By combining stimuli-sensitive dyes, the advantageous properties of nanofibers and the high temperature and chemical resistance of ceramic sol-gel based materials, we designed an advanced colorimetric sensor with a unique combination of properties based on dye-doping of silica nanofibers.[122] In contrast to the usually non-flexible bulk glass or thin film sensors, our designed large-area ceramic nanofibrous sensors were flexible. The produced sensors were sensitive not only towards HCl and NH$_3$ vapors but also to bioligcally relevant concentrations of biogenic amines (**Figure 5**).
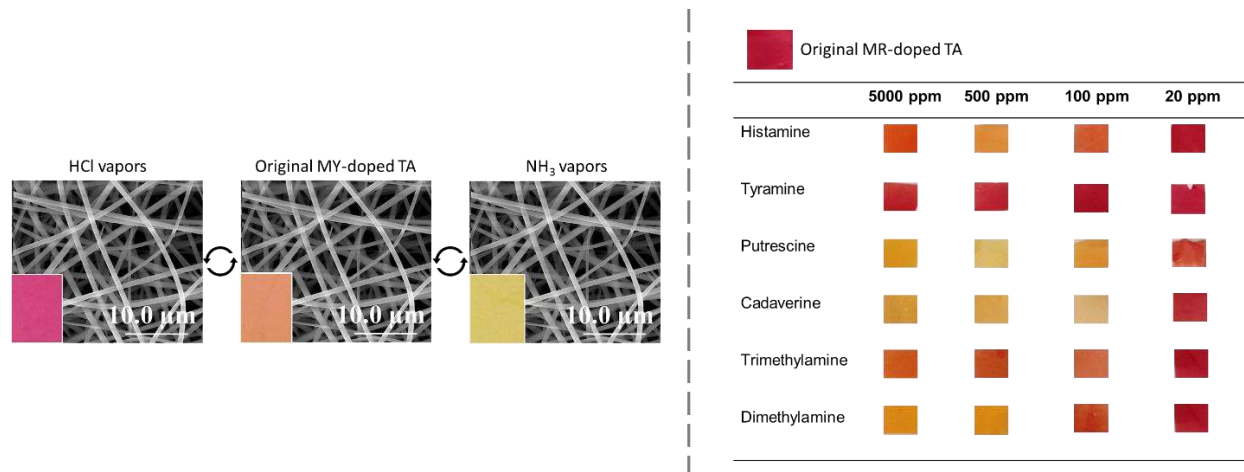
Figure 5. TEOS-APTES (TA) ceramic nanofibers doped with the dye Methyl Yellow show a clear and reversible visual response upon detection of HCl and NH₃ vapors (left). TEOS-APTES ceramic nanofibers doped with the dye Methyl Red show visual responsivity towards biogenic amines (right). Reproduced and adjusted with permission[122] 2016, WILEY-VCH Verlag GmbH & Co.

By optimization of viscosity, amount of solvent and control of the condensation degree, sol-gel technology could be combined with stable electrospinning without the need for additional organic polymers and the additional calcination step.[122,137,138] Although the electrospinning of pure triethylorthosilicate (TEOS) is more challenging, the post-heat-treatment is avoided which would be deleterious to the nanofibrous structure and the introduced sensing functionality. Prior to electrospinning, the sols were doped with the indicator dyes Methyl Red or Methyl Yellow in order to produce dye-doped ceramic nanofibers. The colorimetric nanofibers showed reversible color changes from pink to yellow to pink when exposed to respectively HCl, NH₃ and again HCl vapors. These ceramic nanofibrous sensors with high sensitivity and reversibility could be of great interest for application in protective clothing or safety equipment to be used in harsh environments. In order to prove the versatility of the produced sensors, the colorimetric nanofibers were exposed to different biogenic amines which are released during the decomposition of fish and meat. A clear color change upon detection of the biogenic amines

was observed and a detection limit down to 20 ppm was achieved for putrescine, indicating the potential of these sensors within the food industry.

Another important class of sensors are those that detect biological compounds such as glucose. Since most of the analytical tests are time-consuming and need sophisticated equipment and professional operators, the accurate, rapid and easy detection of glucose remains a crucial issue in clinical diagnostics, food industry and biotechnology.[60] Zhang *et al.* reported the production of glucose testing strips composed of polyurethane nanofibers by co-electrospinning.[123] The core-phase solution included the bi-enzymatic system composed of glucose oxidase and horseradish peroxidase, whereas the shell-phase solution included polyurethane. The colorimetric function was either added to the core-phase (in which case 2,2'-azinobis-(3-ethylbenzthiazoline-6-sulphonate) was applied) or the shell-phase (in which case *o*-dianisidine was applied). As soon as the colorimetric sensor was immersed in the glucose solution, the coupled reaction by glucose oxidase and horseradish peroxidase is initiated and the colorless reduced chromogenic agent is converted into its oxidized form, resulting in a brown or green color, depending on the used chromogenic agent. It was observed that the activity of the sensor was much higher if the colorimetric function was added to the shell-phase instead of the core-phase, which was attributed to the fact that in the last case the oxidized products first have to diffuse across the fiber wall in order to color the solution. Leaching of the chromogenic functionality is here, thus, a positive aspect of the dye-doped colorimetric sensor.

3.2 Colorimetric sensors based on doping with nanoparticles

Nanoparticles (NP's) can also be doped into the polymer solution prior to the electrospinning process. Nanoparticles are defined as particles with sizes ranging from 1 to 100 nm and are composed of a number of atoms or molecules that are bonded together.[139,140] As they are smaller than bulk materials, yet larger than individual atoms or molecules, their behavior is in between that of a macroscopic and an atomic or molecular system. For instance, metallic

nanoparticles such as gold or copper, show unique optical properties which are different from their individual atoms or their bulk material.[140] Due to their surface plasmon resonance, these noble metal nanoparticles possess a strong absorption band in the visible region of the electromagnetic spectrum, which may be of great interest to sensor applications.[140] The incorporation of these nanoparticles in nanofibrous structures could lead to colorimetric sensors with unique optical sensing properties.

Direct fabrication of electrospun nanofibers doped with nanoparticles is possible if the nanoparticles form a uniform dispersion in the applied solvent system combined with a suitable support polymer that is well soluble in that solvent system.[141] Many different types of nanoparticles, *i.e.* zero-dimensional NP's such as metals, metal oxides, quantum dots and microgels, one-dimensional NP's such as nanochains and nanorods, and two-dimensional NP's such as nanosheets, graphene and graphene oxide, have been doped into polymer solutions and successfully electrospun into NP-doped nanofibers. The advances and future prospects of the electrospinning of nanoparticles has recently been reviewed by Yu *et al.*[141] In case of colorimetric nanofibrous sensors, mainly zero-dimensional spherical nanoparticles with chromogenic properties have been applied, such as the noble metallic nanoparticles mentioned above. Electrospinning of these materials generally leads to a random dispersion of the nanoparticles within the polymer nanofibers.

A popular class of nanoparticles known for their extremely high extinction coefficient compared to traditional chromophores are gold nanoparticles. Gold nanoparticles typically show red to purple and blue color transitions upon aggregation, due to the surface plasmon resonance effect.[140,142] Chigome and Torto reported the opportunity to incorporate gold nanoparticles in electrospun nanofibers and their possible sensing mechanism relying on the variable proximity phenomena of the gold nanoparticles in a review on electrospun nanofibers in analytical chemistry.[104] Based on this mechanism, Mudabuka *et al.* designed a colorimetric probe for ascorbic acid.[124] Ascorbic acid is an essential vitamin in various biochemical

processes and is found in multiple sources ranging from biological fluids to pharmaceuticals. Gold and copper nanoparticles were doped in a polyamide 6 polymer solution, leading to colorimetric nanofibers that change color from white to blue/black. In presence of ascorbic acid, residual Au^+ and Cu^{2+} ions present in the nanofibers were reduced, leading to growth of the Au/Cu nanoparticles. This phenomenon results in a bathochromic shift of the surface plasmon resonance band, represented by the blue color. Since no sample preparation is required for the detection of ascorbic acid with colorimetric nanofibers, the time and cost of analysis can be significantly reduced compared to other analytical methods such as HPLC, spectrophotometry or methods based on enzymes, which proves the viability of colorimetric nanofibrous sensors.[124] Gold nanoparticles were also applied in another polyamide 6 nanofibrous matrix to detect dopamine as reported by Krause *et al*.[125] As dopamine concentrations are linked to various neurological diseases, such as Parkinson and Schizophrenia, colorimetric detection of dopamine could be of great value to personal medical care. Most detection systems for dopamine are solution based, which means that a solid nanofibrous detector would enhance transportability and in-field use. To produce their dopamine detection system, Krause *et al*. doped a polyamide 6 solution with $HAuCl_4 \cdot xH_2O$. After addition of a reducing agent, a purple solution was obtained, which resulted in uniform nanofibers containing well dispersed, spherical gold nanoparticles. Upon presence of dopamine, which has a strong affinity for gold nanoparticles, the nanoparticles interact with the dopamine proposedly leading to the diffusion and aggregation of the nanoparticles near the surface of the nanofibers, resulting in a colorimetric sensor changing color from purple to navy blue/black.

Colorimetric NP-doped nanofibers have also been used for environmental monitoring. For example, Pletschke *et al*. proposed a two-step method to detect glyphosate with the help of copper-doped poly(vinyl)alcohol nanofibers.[126] Glyphosate is the most widely applied herbicide, but its use is restricted due to potential environmental impact and health hazards. Additionally, the glyphosate detection systems today are very labor-intensive and require

specialized equipment. The two-step method of Pletscke *et al.* includes first the reaction of glyphosate with carbon disulfide, resulting in a dithiocarbamic acid intermediate which is then subsequently detected by copper, leading to a color change from blue to yellow. This color shift, however, could only been visualized at alkaline conditions (pH > 11) because at lower pH-values the deprotonation of glyphosate does not occur. This hinders the formation of the dithiocarbamic acid intermediate and, thus, the formation of a metal complex with copper. Moreover, the sensing system showed to be very sensitive to ions and other compounds commonly found in environmental water samples, meaning that a pretreatment of the samples is crucial to avoid interfering effects. Although this first-generation nanofibrous colorimetric sensor for glyphosate needs further optimization, a low detection limit (0.1 µg/ml) and fast response time (1-3 seconds) were obtained as a consequence of the nanofibrous structure. Also sensors for explosive compounds, such as sensors for trinitrotoluene (TNT), have been designed based on NP-doped nanofibers. Uyar *et al.* incorporated highly red fluorescent bovine serum albumin (BSA) capped gold nanoparticles in polyethylene oxide nanofibers.[127] Although the detection system was mainly based on the decrease of fluorescence upon the presence of TNT, a clear color change from white to deep red or blue, depending on the analyte concentration, could be observed by the naked eye. This visual phenomenon is subscribed to the formation of so-called Meisenheimer complexes between TNT and BSA as an electron is transferred from the amino groups in BSA to the aromatic rings of the electron-deficient TNT. These TNT-amine complexes not only suppress fluorescence, but also strongly absorb the green part of visible light, resulting in the deep red color of the nanofibrous sensor. This visible response showed a sensitivity of 1 ppb, which is lower than the tolerable TNT-level in drinking water.

It can be concluded from the examples above that doping is a well-known, popular and commonly applied technique within colorimetric nanofibrous sensor design as it is relatively easy to perform and it leads to well-functioning sensors with low detection limits and fast response times. An important lesson to learn in the design of colorimetric nanofibrous sensors,

however, is that many factors, other than the high specific surface area, might play a crucial role in sensor sensitivity and response times. As was shown by the example of Nitrazine Yellow, polymer-functionality interactions and the intrinsic properties of the applied polymer can significantly alter the final sensor properties. As simple the technique of dye-doping may be, there is one poorly emphasized, major drawback of doped nanofibers. As the doped compounds, either dyes or nanoparticles, are only physically entrapped within the nanofibrous structure, they are able to leach from or migrate through the membrane.[48,109,112] This not only affects the long-term stability and sensitivity of the sensor, it also raises questions about the toxicity of the leaching compounds as they are now able to contaminate the environment wherein the sensor is used. In the case of dye-doping, we showed that the use of a polycationic complexing agent can efficiently suppress leaching of the dye.[109,110] However, leaching can never completely be eliminated and complexation is not possible for all kinds of dyes.

4. Colorimetric nanofibers by electrospinning of functionalized polymers

In order to solve the problem of leaching or migration of the functionality from the sensor, covalent linkage of the functionality to the polymer matrix is an efficient immobilization strategy. Specifically for dyes, a lot of research is carried out to develop new dyes suitable for covalent bonding, as leaching is not a problem specific for nanofibers, but also for other matrices commonly used in sensor design, *e.g.* films.[143–149] It is a major challenge today to apply the knowledge on dye-immobilization to nanofibrous matrices, without compromising the electrospinnability or resulting nanofiber morphology. Additionally, as was also the case for dye-doping, covalently linking the functionality to the nanofibers may induce significant alterations in the sensing behavior of the functionality compared to its behavior in free form. Indeed, the molecular composition and microenvironment of the functionality are significantly changed. Even though the sensor design based on covalent modification is more complex, it provides important advantages over doping and research towards colorimetric nanofibrous sensors based on functionalized polymers is on the rise. In general, two types of functionalized

polymers are applied for the design of colorimetric nanofibers.[22] First, conjugated polymers will be reviewed, which possess inherent colorimetric properties due to their conjugated backbone. Secondly, functionalized (co)polymers will be discussed, for which the colorimetric response is due to a covalently build-in functionality. These functionalized colorimetric nanofibers have mainly been used for the production of sensors applicable in environmental monitoring and are summarized in **Table 2**.

Table 2. List of colorimetric nanofibers sensors based on functionalized polymers.

Type of functionalization	Polymer matrix	Functionality	Analyte	Response time	Detection limit	Ref.
Conjugated polymers	PEO/TEOS	PDA	VOC's	-	-	[150]
	PEO/TEOS	PDA	Organic solvents	< 1 s	-	[151]
	PEO	PDA tethered with alkylamine	CO_2	< 30 min	400 ppm	[152]
	PS PAA	PDA	Adulterated gasoline	< 3 s	10 % methanol/toluene composition	[153]
	PA 6	PANI-EB	Cu^{2+}	< 10 min	1 ppb	[154]
	PA 6	PANI-EB	Hg^{2+}	< 1 min	5 nM	[155]
	PA 6.6	PANI-ES	Ascorbic acid	< 30 min	50 ppb	[156]
Functionalized (co)polymers	PA 6	Disperse Red 1-acrylate monomer copolymerized with 2-hydroxyethyl acrylate	pH HCl	< 3 s	-	[157]
	-	Porphyrinated polyimide	HCl	< 10 s	5 ppm	[158]
	PCL	Rose Bengal-chitosan Methyl Red-chitosan	pH HCl NH_3	< 3 s	-	[159]
	-	Pyrene-polystyrene copolymer	TNT	< 5 s	$5\cdot10^{-5}$ M	[160]
	TEOS	Methyl Red-APTES	pH HCl NH_3 Biogenic amines	< 1 s	100 ppm	[122]

4.1 Colorimetric nanofibers by electrospinning of conjugated polymers

Conjugated polymers possess interesting properties such as (semi)conductivity, optoelectronic behavior and optical characteristics, due to the large conjugated system in their backbone.[22,62,161] Due to the fast energy transfer of excitons along the delocalized π-system, sensors based on conjugated polymers show increased sensitivity (amplification) to minor interactions with the analyte, providing an important advantage over sensors based on small

molecules, such as dyes.[22,62,161] Many research has been done and is still ongoing to produce different types of sensors based on several classes of conjugated polymers, such as polythiophenes, polyphenylenes, polyfluorenes, polypyrroles, polyanilines and polyacetylenes. [161–165] Lately, these conjugated polymers are being used to produce nanofibrous structures, although electrospinning of these polymers is quite challenging. Indeed, conjugated polymers are generally characterized by relatively low molecular weights (10^3-10^4), high chain rigidity and limited solubility.[14] These problems are typically solved by blending the conjugated polymer with a well-electrospinnable polymer, *e.g.* polyethylene oxide and polyvinyl alcohol. In this case, however, the solvent choice is of crucial importance to avoid phase separation. The latter, though, can be solved by the recently explored coaxial electrospinning process, which increases the popularity of these polymers even more.

In colorimetric nanofibrous sensor design, polydiacetylenes (PDA's) are, by far, the most commonly applied class of conjugated polymers. The DA-monomers are blended with a suitable support polymer and subsequently electrospun. During electrospinning and solvent evaporation, self-assemby of the monomers takes place, since the DA-monomers are more attracted towards one another than to the support polymer (**Figure 6**).[150] After the nanofiber formation, the fibers are irradiated with light to induce photopolymerization, which creates PDA within the nanofibers through the 1,4-addition of the aligned DA-monomers.[15,22,62]
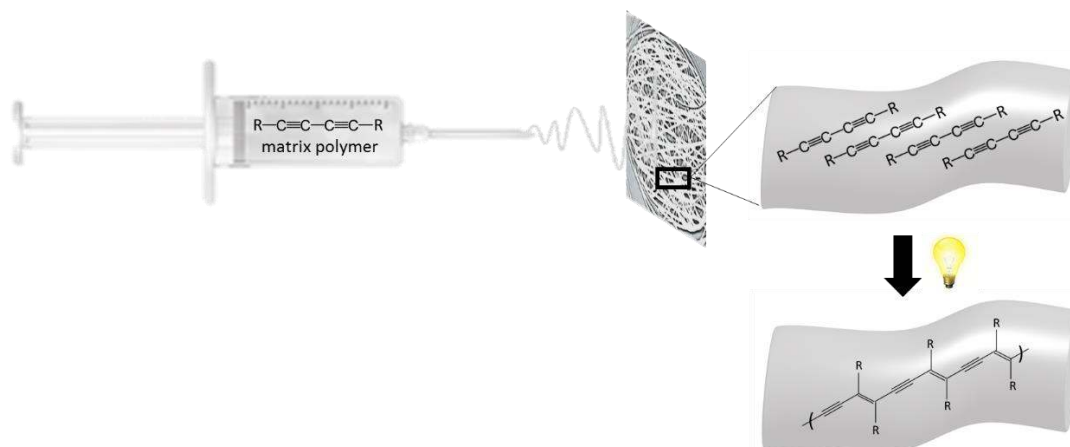
Figure 6. Nanofibers functionalized with the conjugated polymer PDA are produced from a solution containing diacetylene (DA) monomers and a support polymer. During electrospinning the DA monomers self-assemble after which PDA is created upon irradiation with light.

Nanostructured PDA's typically show a blue color due to the electron delocalization within the conjugated system.[15,62] Interestingly, the polymer is able to change its blue color to red in response to different stimuli, *e.g.* heat, mechanical stress, ligand-receptor interactions, but also organic solvents, which is related to an irreversible stress-induced structural transition of the polymer backbone.[15,62,151,166] Kim *et al.* have used this principle to detect common volatile organic compounds, such as methanol, hexane, acetone, tetrahydrofuran and chloroform, in both the liquid and gaseous phase.[150] By blending different types of DA-monomers with a poly(ethylene oxide)/tetraethyl orthosilicate matrix, chemically inert colorimetric nanofibers were produced that changed from blue to red upon detection of a whole range of different volatile organic compounds. Kim *et al*. improved their sensors by combining two different DA-monomers within one nanofibrous matrix in different ratios, displaying different colorimetric responses to specific organic solvents.[151] This provides a strategy for the differentiation of organic solvents based on a color pattern procedure. Yoon *et al.* used a PDA-based colorimetric nanofibrous sensor for the detection of CO_2.[152] The DA-monomers were functionalized with imidazolium and amine groups and subsequently electrospun with poly(ethylene oxide) as support polymer, after which an alkylamine-tethered PDA was created by photopolymerization.

The tethered amines are able to interact with CO_2 to form carbamoate salts. By addition of a base, the nascent carbamoate salt is deprotonated, leaving the amines reactive towards CO_2. This process influences the solvation of the polymer side chains, which alters the backbone conformation, resulting in the typical blue to red color change. The covalent linkage of the sensing mechanism, *i.e.* tethered amines, is necessary to prevent diffusion of the formed carbamoates, which maximizes the signal. This working principle is in strong contrast with the commonly reported optical sensors for the detection of CO_2, which typically rely on the pH-change induced by the hydration of CO_2 to carbonic acid and are characterized by a low selectivity. Among environmental monitoring applications, also the detection of fake and adulterated gasoline, characterized by the presence of toluene and methanol, has been reported. Kim *et al.* embedded PDA in two matrices, *i.e.* polystyrene and polyacrylic acid nanofibers.[153] Here, the matrix polymer is of crucial importance as it provides a so-called protective layer for the PDA. Only upon immersion of the nanofibers in fake and adulterated gasoline, which contain toluene and methanol, the matrix polymers are dissolved. Consequently, the PDA-polymers are released and the toluene is detected by the solvatochromism of PDA, which results in the blue to red color shift.

Polyanilines (PANI) are another class of conjugated polymers that are being reported for colorimetric nanofibrous sensor design. The existence of the nitrogen atom in between the phenyl rings enables the polymer to transform to several conformations with different degrees of oxidation and protonation, giving rise to remarkable changes in electrical and optical properties.[154] The oxidation state can be varied continuously from fully reduced (leucoemeraldine base) over half oxidized (emeraldine base) to fully oxidized (pernigraniline base).[154,167,168] Additionally, emeraldine base can be completely or partially converted into emeraldine salts upon protonation of the imine nitrogen atoms.[154,168,169] However, as was also the case for PDA, PANI typically lacks mechanical flexibility, stability and solubility, leading to the need for blend electrospinning by the addition of a support polymer.[154] Ding *et al.* used

a combination of PANI-EB (emeraldine base) and polyamide 6 to produce colorimetric nanofibers for the detection of copper (II) ions in water.[154] After electrospinning, the PANI-EB was converted into PANI-LB (leucoemeraldine base), which is responsible for the sensitivity towards copper. In presence of copper, PANI-LB is oxidized by Cu^{2+}, leading to the transformation of the polymer to PANI-EB. Subsequently, two different doping mechanisms, *i.e.* a pseudo-protonation mechanism and a two-step redox process, lead to copper complexation. Depending on the amount of H^+ in the solution, *i.e.* pH of the solution, the colorimetric nanofibers changed from white to green (low pH) or blue (high pH). A detection limit of 1 ppb was achieved. The same mechanism was applied by Ding *et al.* to produce a colorimetric nanofibrous sensor for mercury (II) ions.[155] The nanofibers changed from white over green to blue, depending on the concentration of mercury. Both sensors need a hydrazine treatment to regenerate the nanofibrous sensors.

Conjugated polymers, particularly PANI, can also be designed as potential sensors for biomedical applications. Ding *et al.* recently reported blending of PANI with polyamide 6.6 for the production of colorimetric nanofibers sensitive to the neurochemical ascorbic acid.[156] For the production of the nanofibers, PANI-ES was synthesized to blend with polyamide 6.6. After electrospinning, the nanofibers were treated with $KMnO_4$ to convert PANI-ES to PANI-PB (pernigraniline base), which enables the redox reaction with ascorbic acid, creating dehydroascorbic acid and converting PANI-PB into PANI-EB. This is followed by a doping process wherein both PANI-ES and PANI-LB (leucoemeraldine base) are produced, resulting in different colors (brown-purple-blue-green) for different detected ascorbic acid concentrations (**Figure 7**). To prove the applicability of the produced sensor, Ding *et al.* constructed a color-difference map to provide an assay and quantification of ascorbic acid concentrations in food samples, such as juices.
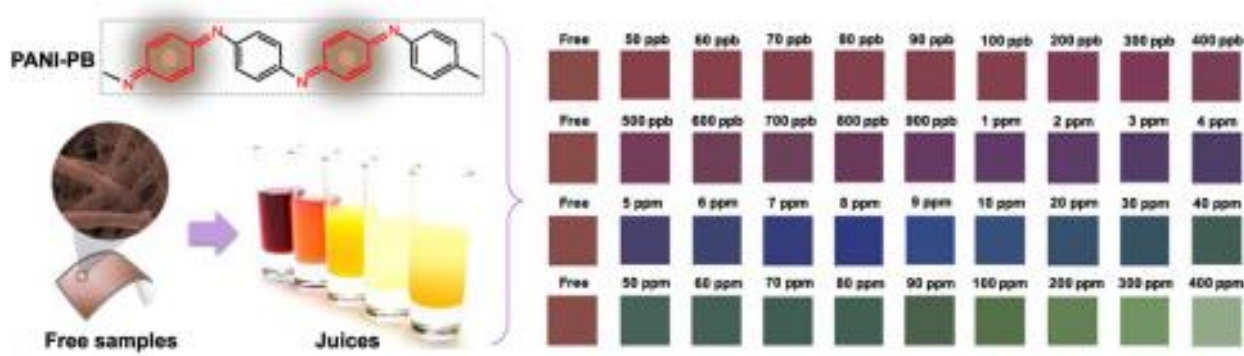
Figure 7. PA 66 is blended with PANI-PB for the production of colorimetric nanofibers that detect L-ascorbic acid in juices. A color differentiation map was constructed to link color to analyte concentration. Reproduced with permission.[156] 2015, Elsevier.

The previous examples nicely show that conjugated polymers provide interesting opportunities for sensor materials. However, synthesis and production as well as processing is rather complex as a consequence of their low molecular weight and poor solubility. Moreover, the versatility of the strategy is limited due to the limited availability of conjugated polymers.

4.2 Colorimetric nanofibers by electrospinning of dye-functionalized (co)polymers

Since many different dyes, *i.e.* different colors and sensitivities to different stimuli, already exist and continue being developed, covalent modification of polymers with these dyes provides for a broad range of possible colorimetric sensors. Compared to the few conjugated polymers, which are limited in sensitivity and colors, this dye-functionalization strategy provides much more possibilities and opportunities for colorimetric nanofibrous sensor design. This widens the range of applications and provides high versatility. In contrast to conjugated polymers, which exhibit an inherent colorimetric function, this technique functionalizes polymers that lack such a colorimetric function, by incorporation of a colorimetric functionality, *e.g.* dye, in the polymer backbone or in the side chains. This strategy of covalent modification leads to stable colorimetric sensors as the dyes are covalently linked to the nanofibrous matrix, which efficiently immobilizes the dye within the sensor. It should, however, be noted that the covalent

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modification of chromogenic agents, particularly dyes, might significantly influence the colorimetric properties of the compounds, as not only the microenvironment but also the molecular structure of the dyes is altered by the introduction of a covalent bond with the polymer matrix. Mainly two strategies are followed to introduce the dye covalently into the nanofibers, *i.e.* dye-functionalization of the monomer followed by polymerization or dye-functionalization of an existing polymer.

In our work, the first strategy was first applied for the production of halochromic nanofibers applicable as pH-sensors.[157] Efficient dye-immobilization was achieved by covalently linking Disperse Red 1 to an acrylate monomer, which was subsequently copolymerized with 2-hydroxyethyl acrylate. In order to produce nanofibers, the dye-functionalized copolymer was blended with polyamide 6 and electrospun from a 50/50 acetic acid/formic acid solvent system. The obtained, uniform nanofibers showed, within a few seconds, a clearly visible and reversible color change form bright pink to orange with increasing pH in aqueous solutions, but also when exposed to hydrochloric acid vapors, which proves the viability of the produced nanofibers as pH-sensors. As mentioned above and which was also the case for dye-doping, the alteration in the environment of Disperse Red 1 affected the halochromic behavior of the dye. Comparison of the behavior of the dye-functionalized polymer in aqueous solution and in the blended nanofibers allowed to evaluate the influence of the polyamide 6 nanofibrous environment. The results showed that the colorimetric response was similar, yet the pH-range in which the color change takes place, was shifted to lower pH-values. This is possibly due to specific interactions, such as hydrogen bonding and ionic interactions, between the dye and the polyamide 6 nanofibrous matrix. On the contrary, the visible colors of the dye are not influenced by the covalent modification as the monomer is coupled to a functional group of Disperse Red 1 that is isolated from the chromophore. As this functional group is not a crucial part of the chromophore, the effect of the covalent modification on the colors of the chromogenic compound is limited. This conclusion is an important requirement within colorimetric

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nanofibrous sensor design based on dye-functionalized polymers. As soon as the covalent modification disrupts or even destroys the chromophore of the dye, the inherent property of showing color, and consequently the stimuli-responsive behavior, can be lost. We also proved the value of covalent modification as an efficient dye-immobilization technique by comparing dye-migration of the dye-modified nanofibers with dye-doped nanofibers (**Figure 8**). For this, dye-release was analyzed by the transfer of Disperse Red 1 from the dye-containing nanofibrous samples to standardized reference fabrics under normalized conditions. By subsequently comparing the colors of the reference fabrics to their blank counterparts, the amount of dye-release could be quantified.
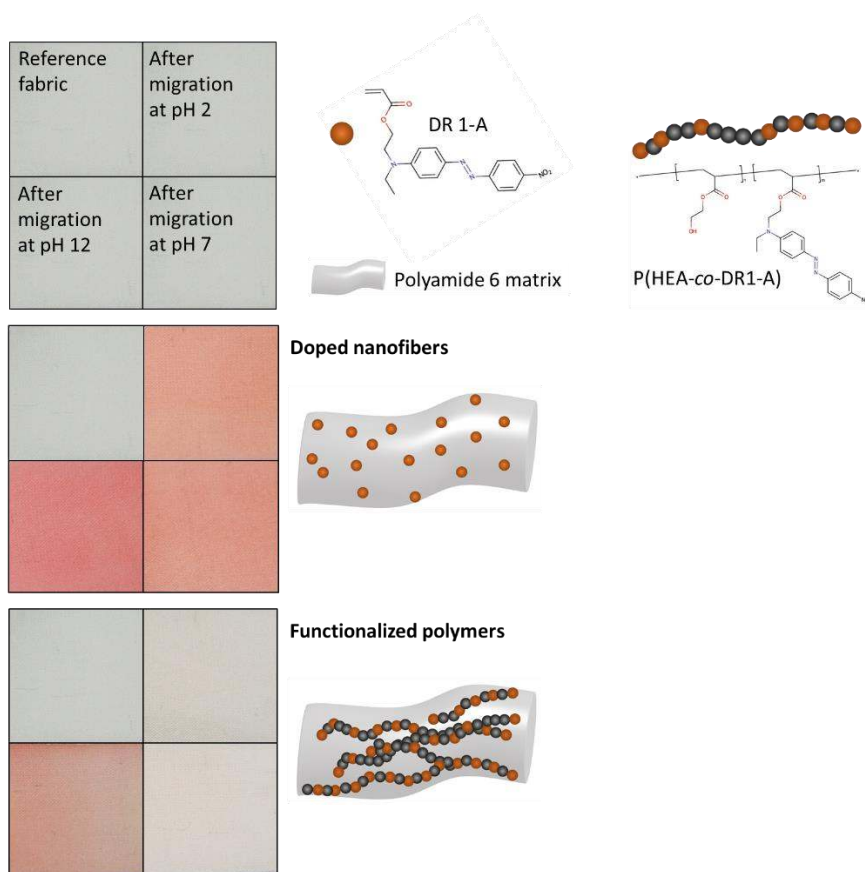

Figure 8. Dye-migration as measured by staining of reference fabrics in contact with dye-containing nanofibers clearly illustrates that reference fabrics in contact with doped nanofibers are much more stained due to dye-leaching at all pH-values than reference fabrics in contact with covalently modified nanofibers. These results clearly prove the potential of covalent

modification as a dye-immobilization technique. Note that at pH 12, more dye-leaching appears for the covalently modified nanofibers due to partial hydrolysis of the polymer in alkaline conditions. Reproduced and adjusted with permission.[157] 2015, The Royal Society of Chemistry.

As illustrated in **Figure 8**, the dye-doped nanofibers showed significantly higher dye-release at all pH-values compared to the nanofibrous samples in which the dye was covalently linked to the polymer. The higher staining of the reference fabrics at pH 12 could be explained by the hydrolysis of the dye-functionalized copolymer under these alkaline conditions. This phenomenon may be minimized by replacing the acrylate monomer with the more stable methacrylate or acrylamide monomers. In this work, the dye-functionalized copolymer was blended with a support polymer for the production of nanofibers. This blend electrospinning is an emerging technique for the production of functional nanofibers as it provides some advantages, *i.e.* the support polymer can be chosen according to the foreseen application, the amount of functionalized polymer can be minimized for economic reasons and the electrospinnability of the pure functionalized polymer is less crucial as this will be mainly provided by the support polymer. However, pure functionalized polymers can also be electrospun to create colorimetric nanofibers, as is demonstrated by the work of Xu *et al.*[158] Here, a porphyrin-dye, *i.e.* 5,10-*bis*(4-aminophenyl)-15,20-diphenylporphyrin, was synthesized and reacted with 4,4'-hexafluoroiso-propylidenediphtalic anhydride and oxydianiline to form a polyimide in which the porphyrin-derivative is incorporated in the backbone of the polymer. The porphyrinated polyimide was subsequently electrospun from *N,N'*-dimethyl acetamide to form colorimetric nanofibers. Thanks to the covalent coupling between the dye and the polymer, not only dye-release, but also the aggregation of the porphyrin compounds was prevented. Upon the presence of hydrochloric acid vapor the porphyrin ring changes from the planar free base form into the saddle conformation as the central nitrogen atoms are protonated by the acidic gas

(**Figure 9**). This distortion of the ring structure results within 10 seconds in a clear red to green color change with increasing intensity of the green color with increasing HCl concentration. The colorimetric nanofibrous sensors could be reused after puffing with nitrogen.
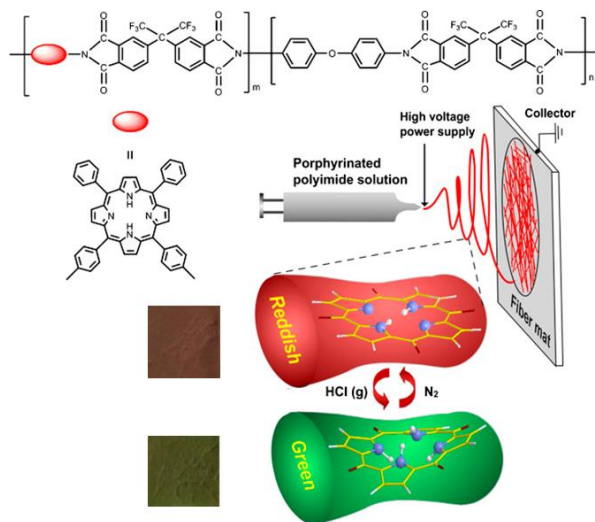

Figure 9. Polyimide modified with porphyrin was electrospun to produce colorimetric nanofibrous sensors which respond to the presence of HCl by a red to green color shift. Reproduced and adjusted with permission.[158] 2010, Elsevier.

Next to the functionalization of monomers or the incorporation of the dye in the polymer backbone, the dyes can also be introduced in the side chains of an existing polymer before electrospinning. This is an interesting approach particularly for natural biomolecules, which combines high natural abundance with degradability. Moreover, this technique is less labor intensive as only a non-polymerizable dye should be synthesized and purified. We used this strategy to produce colorimetric nanofibrous sensors from chitosan functionalized with Rose Bengal (RB) and Methyl Red (MR) in the side chain *via* an amide linkage.[159] Both dyes possess a functional carboxyl group that can be used for the covalent modification with the amino-groups of chitosan while it is not crucially involved in the color-changing mechanism of the dye. The covalent modification, therefore, does not disrupt the chromophore and leaves the halochromism intact (**Figure 10**). Again, blend electrospinning was applied with poly(ε-caprolactone) as support polymer, since a biocompatible pH-sensor was aimed for. In contrast

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to the aforementioned examples, this covalent modification showed a major impact on the electrospinnability of the polymer. An increased amount of MR-occupied amino-groups of chitosan compromises the solubility of the functionalized polymer in the applied formic acid/acetic acid solvent system. This is possibly due to the double protonation of the dye and leads to poor electrospinnability. Nevertheless, nanofibers functionalized with low MR-concentrations led to effective pH-sensors which immediately changed color from pink to yellow with increasing pH (**Figure 10**). On the contrast, the modification of chitosan with Rose Bengal increased the solubility of the polymer in the applied solvent system, leading to lower viscosities, excellent electrospinnability and small nanofiber diameters. This was subscribed to the decrease in polymer charge and/or the bulkiness of the dye, which suppresses interpolymer interactions. The produced RB-functionalized nanofibrous sensors showed a clear and direct color change from white to pink with increasing pH (**Figure 10**). In addition, both produced nanofibrous sensors were also instantaneously responsive to hydrochloric acid and ammonia vapors.
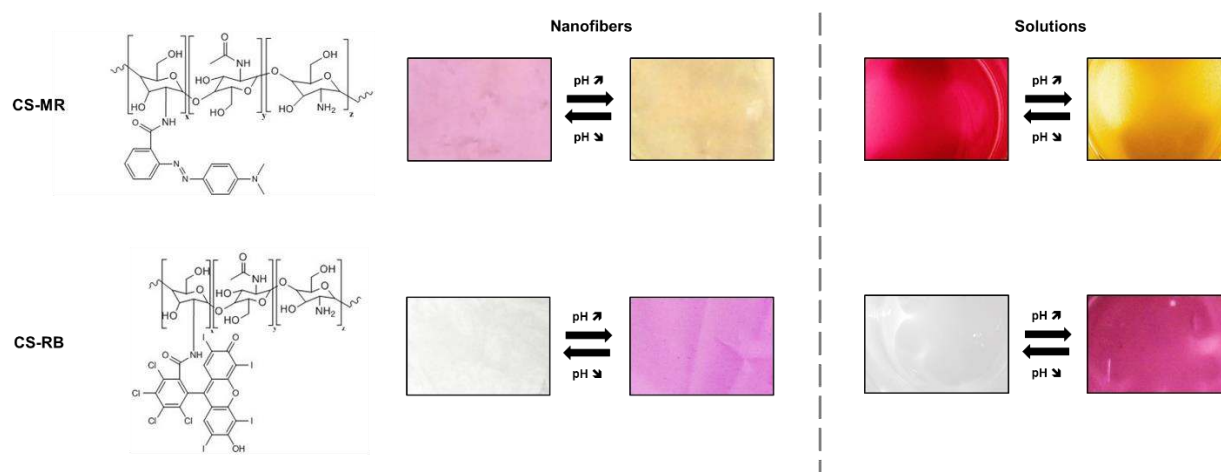

Figure 10. If the chromophore remains intact upon covalent functionalization, the produced nanofibers show similar colorimetric behavior as the original dyes in solution. Reproduced and adjusted with permission.[159] 2016, The Royal Society of Chemistry.

Although the visible colors remained intact with respect to the colors of the dyes in free form, a small bathochromic shift was observed for the RB-containing nanofibers in comparison with RB in solution, due to the presence of the polymer matrix. Additionally, as was the case for the nanofibers functionalized with Disperse Red 1, the dynamic pH-range of both dye-doped and covalently modified nanofibers was affected by the change in microenvironment as it shifted towards lower pH-values for both MR- and RB-containing nanofibers. This can be subscribed to dye-matrix interactions such as hydrogen bonding and ionic interactions. For the nanofibers containing covalently modified chitosan with MR, the dynamic pH-range was even further decreased compared to the MR-doped nanofibers, due to the transformation of the carboxylic acid group into an amide, which changes interactions with the azo-group. Dye-migration and dye-leaching tests proved the long-term stability of the nanofibrous sensors. The dyes were efficiently immobilized at all physiologically relevant pH-values, being a result of the covalent link between the dye and the polymer. This work, thus, provided well-functioning pH-sensitive nanofibers, but clearly showed the possible consequences of the covalent modification of dyes on both processing and final sensor behavior.

Another interesting work on covalently linking dyes to the side chain of a polymer is provided by Uyar et al.[160] A TNT sensor was prepared via a 1,3-dipolar cycloaddition reaction between an azide-functional styrene copolymer and 1-ethynylpyrene followed by electrospinning. Due to the covalent modification, no leaching nor aggregation of the dye was observed. Besides a strong fluorescent response, the pyrene-functionalized nanofibers showed an instantaneous visual color change from light yellow to dark yellow. In the presence of several metal ions, the sensor proved to be selective towards TNT.

As was the case for dye-doping, we also covalently modified ceramic nanofibers with dyes to provide for chemically and thermally inert nanofibrous sensors. Our previous work on dye-doping of ceramic nanofibers led to colorimetric sensors to be used in gaseous media. By covalently modifying the ceramic nanofibers with the dyes, we expanded the applicability of

the colorimetric sensors to aqueous media. We used our knowledge and expertise on electrospinning based on sol-gel technology, described above (see section 3.1), to produce flexible pH-sensitive silica nanofibers without the need for additional organic polymers. Thereby, we avoid the calcination step which is typically involved in the production of ceramic nanofibers.[122] The pH-indicator dye Methyl Red (MR) was immobilized in the nanofibrous silica structure by covalently linking the carboxylic acid functional group of the dye to the amino group of (3-aminopropyl)triethoxysilane (APTES) through a carbodiimide-assisted amide coupling (**Figure 11**). MR-functionalized APTES was combined with the silica precursor tetraethylorthosilicate (TEOS) in a 0.0024:1 ratio resulting in an appropriate viscosity for stable electrospinning, yielding orange-colored nanofibrous membranes in which the dye is trapped in its alkaline form. The dye-functionalized nanofibers showed a clear and instantaneous color response from orange to pink with decreasing pH and vice versa. Also with these ceramic silica nanofibrous matrices, an effect of the change in environment of the dye on the dynamic pH-range could be observed. The pH-range in which the color change is located, is shifted towards more acidic pH-values for the MR-functionalized APTES in solution compared to free MR in solution. This clearly indicates an important effect of the covalent modification on the sensitivity of the dye. When the MR-functionalized APTES is incorporated in a nanofibrous silica matrix, the dynamic pH-range is further shifted downwards due to the influence of the covalent bond formation of the MR-APTES with the silica matrix and the interaction of the dye with the surrounding silica matrix. These results are, thus, in line with the observations for covalent dye-modification of organic polymers described above. Apart from pH-sensitivity, the produced ceramic nanofibers also showed high sensitivity and reversibility towards hydrochloric acid and ammonia vapors (**Figure 11**). When exposed to HCl vapors, the nanofibers immediately changed color from orange to pink. When exposed to NH_3 vapors, the nanofibers immediately changed from orange to yellow.
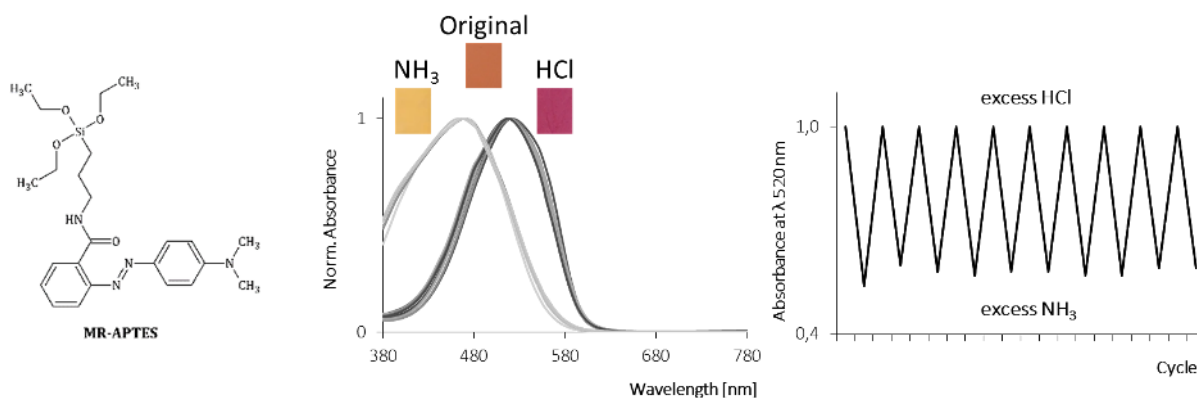
Figure 11. Ceramic nanofibrous sensors can be produced by covalently linking the dye, here Methyl Red, to a silica precursor. MR-APTES functionalized nanofibers show a clear and reversible color change upon detection of hydrochloric acid and ammonia vapors. Reproduced and adjusted with permission.[122] 2016, WILEY-VCH Verlag GmbH & Co.

Also the sensitivity of the covalently modified ceramic nanofibers towards biogenic amines, *e.g.* histamine, putrescine, released during decomposition of meat and fish, was tested. Complementary to the dye-doped nanofibers, the dye-modified nanofibers can, thus, be applied for food quality applications in both gaseous and aqueous media, without the risk of dye-leaching. Moreover, after detection, the nanofibers were able to maintain their color for 20 minutes before going back to their original color. This provides a valuable memory function which could be very interesting for real-life sensors.

The research examples above prove that the use of polymers with an inherent chromogenic function, either due to a conjugated backbone or the covalent modification with a dye, is a valuable approach to immobilize the sensing functionality in nanofibers. In this way, a robust sensor is created that is not only stable over time, but also prevents leakage of toxic compounds into the environment. Moreover, the covalent modification technique shows remarkable versatility as many novel chromogenic agents, *e.g.* dyes, are being discovered and synthesized. Although the synthesis step in this strategy is less straightforward than doping, in many cases the covalent modification can be easily achieved by known chemical processes. Especially

compared to the strategy of conjugated polymers, the combination of straightforward covalent modification and convenient processability by either blending or electrospinning the pure polymer, makes covalent modification a valuable sensor designing strategy. Future challenges for this approach include the selection of a proper dye, as it was shown that not only the sensing properties of the dye are decisive, but also its availability for functionalization. Indeed, the dyes used for covalent modification should possess a functional group that is suitable for functionalization, but that is not crucially involved in the chromophore to leave the colorimetric sensing function intact. It was shown that the effects of the covalent modification on the polymer solubility, electrospinnability and colorimetric behavior are important parameters and they should, thus, be taken into account. This implies that knowledge on the influence of the microenvironment on the dye is crucial and should be investigated in detail. Shielding of the dye remains a main factor in decreasing sensor sensitivity, although it was shown that this can be influenced by applying a proper blend during the electrospinning process. Another technique for achieving more control on the microenvironment, and thus positioning of the dye, is applying the dye at the nanofibrous surface. This strategy is described in the next section.

5. Colorimetric nanofibers based on surface functionalization

The main issue with the previously described strategies for the design of colorimetric nanofibrous sensors is the ignorance on the exact position of the functionality within the nanofibrous membrane. Indeed, both in case of doping and covalent modification, it is possible that the functionalities are positioned within the nanofibers, at the surface of the nanofibers or as a combination of both. If the functionalities are positioned in the bulk of the nanofibers, they risk to be shielded from the environment by the surrounding polymer chains.[48,110] Thus, intuitively, it seems better for the functionalities to be positioned at the surface of the nanofibers to exploit the large specific surface area for ultrasensitivity of the sensors. A possible route is the decoration of the surface of the nanofibers with chromogenic functionalities after the

electrospinning process. This decoration can be achieved by either physical interactions or chemical reactions. It is most important for the interactions between the dye and the polymers to be strong enough to withstand the application conditions. If not, the functionalities will definitely leach from the sensor, compromising the sensor's stability and contaminating the environment, as was the case for doping. Where, in the case of doping, leaching of the functionalities may be hindered by interactions with the surrounding polymers, this is not the case if the functionalities are only positioned at the surface. It is, thus, of utmost importance to provide for a strong physical/chemical linkage between the nanofibrous surface and the applied functionality. As coatings are already widely studied and largely applied in industry, a lot of possibilities may exist for the surface decoration of nanofibers. However, this research topic is only poorly explored so far. A limited amount of examples can be found in literature and are listed in **Table 3**. They mainly include environmental monitoring applications, such as detection of volatile organic compounds and metal ions. In the following sections, both the physical and chemical interaction-based functionalization of nanofibers after the electrospinning process are illustrated.

Table 3. List of colorimetric nanofibrous sensors produced by techniques that involve the decoration of the nanofiber surface.

Type of surface decoration	Polymer	Functionality	Analyte	Response time	Detection limit	Ref.
Dye-coating	Cellulose acetate	Pararosaniline/ sodium sulfite	Formaldehyde	< 15 min	0.06 mg/m³	[170]
	PAN	Fluoral-p	Formaldehyde	-	40 ppb	[171]
	PA 6	Methyl Yellow/ hydroxylamine sulfate	Formaldehyde	< 5 min	50 ppb	[172]
	PAN	Bromocresol Green	NH₃ Methylamine Ethylenediamine	< 1 min	1 ppm	[173]
NP-coating	PA 6/ nitrocellulose	Bovin serum albumin-Au	Pb²⁺	< 10 min	0.2 µM	[174]
	PA 6/ polyvinylidene fluoride	L-glutathione-Au	Pb²⁺	< 10 min	10 µg/dL	[175]
Host-guest	Adamantane-functionalized PMMA	Rhodamine-β cyclodextrin	Hg²⁺	< 1 min	6·10⁻⁵ mol/L	[176]
Grafting	PVBC	Imidazole derivative	Fe²⁺	-	2 µg/mL	[177]
	Poly (MMA-*co*-AHPA)	Rhodamine B	Cu²⁺	-	5·10⁻⁶ mol/L	[178]
	Deacetylated cellulose acetate	Pyromellitic dianhydride	Pb²⁺	< 30 min	0.048 µM	[179]
	PA 6/PANI	Phenolphthalein	pH	< 100 s	-	[180]
	PVBC	Pyridylimidazole-iron complex	Dopamine Ascorbic acid	-	18.4 mg/L 17.6 mg/L	[181]
Plasma	PA 6 Cellulose PP Teflon HDPE LDPE	Disperse Red 1 Bromothymol Blue Brommocresol Purple Rose Bengal 4-Bromo-1,8-naphthalic anhydride	pH	-	-	[182]

5.1 Nanofiber surface functionalization based on physical interactions

Three different types of surface decoration based on physical interactions have been reported in literature, *i.e.* coating of nanofibers with dyes, coating of nanofibers with nanoparticles and coatings based on host-guest interactions. If the nanofiber surface is coated with dyes, mainly gas sensors are aimed for. Although not reported, this may very probably be due to dye-leaching in moist environments. For example, Ding *et al.* have designed a colorimetric nanofibrous sensor for the detection of formaldehyde by dipping hydrolyzed cellulose acetate nanofibrous membranes in a pararosaniline and sodium sulfite solution (**Figure 12**).[170]
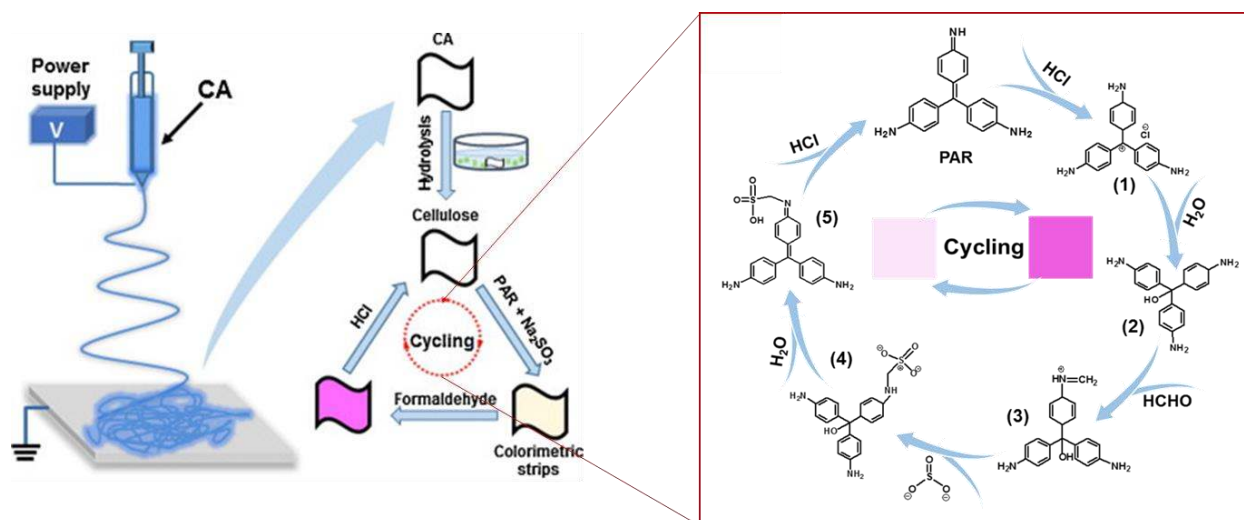
Figure 12. Cellulose acetate nanofibers coated with pararosaniline show a visual color change upon detection of formaldehyde. Reproduced and adjusted with permission.[170] 2014 Elsevier.

Under protic conditions, a series of interactions eventually leads to a color change from light pink to purple (**Figure 12**). The sensor could be reused several times after flushing with HCl. Due to the specific interaction between formaldehyde and pararosaniline-sodium sulfite, the sensor showed good selectivity in presence of other volatile organic compounds. The superiority of the nanofibers as substrate material was indicated by a comparison of the formaldehyde-detection by nanofibrous membranes and equally-functionalized filter paper. The nanofibrous membranes showed a sensitivity which was 5 times higher than for the filter paper, resulting in a more clear visual color change. This was supported by analysis of the BET surface area and pore volume, respectively being 8 and 6 times higher for the nanofibrous sensor. In addition, the N_2 adsorption-desorption isotherms indicated mesoporous characteristics for the nanofibers, yet macroporous or nonporous characteristics for the filter paper. The increased sensitivity can, thus, be subscribed to the high specific surface area of the nanofibers as a result of their low nanofiber diameter and high pore volume, thereby providing many sites for analyte interaction and detection. The same author also designed another sensor for selective formaldehyde detection based on polyacrylonitrile (PAN) nanofibers dip-coated with fluoral-p.[171] The color of the nanofibrous sensor changed from white to yellow upon detection of

formaldehyde due to the Hantzch reaction between fluoral-p and the gas. The authors indicated also here the superior sensing properties of a nanofibrous sensor by comparing their PAN/fluoral-p nanofibrous membranes with commercial filter paper-based strips. When exposed to 60 ppb formaldehyde under optimized conditions, the colorimetric response of the nanofibers was significantly higher than for the filter paper-based strips, resulting in a better visual signal. The authors attributed this result again to the higher specific surface area characteristic for nanofibers. Yet another formaldehyde-sensor was designed by Ding et al.[172] Here, polyamide 6 was electrospun into nanofibers and subsequently immersed in a water/hydroxylamine sulfate/Methyl Yellow/glycerin/methanol solution, which led to nanofibers impregnated with Methyl Yellow and hydroxylamine sulfate. Upon exposure to formaldehyde, the release of sulfuric acid decreases the pH, which is detected by Methyl Yellow, giving result to a clear yellow to red color change. Next to formaldehyde, also sensors for the detection of ammonia vapors have been produced by coating nanofibers with dyes. Kim et al., for instance, dispensed a bromocresol green/oxalic acid solution on polyacrylonitrile nanofibers, which changed color from yellow to green and eventually blue upon increasing presence of ammonia vapors and other alkaline gaseous analytes such as methylamine and ethylenediamine.[173]

Coating of nanofiber surfaces with nanoparticles has been reported by Ding et al.[174,175] Two colorimetric nanofibrous sensors were prepared for the detection of lead ions. A first sensor was designed by spotting polyamide 6/nitrocellulose nanofibers, fabricated by so-called dual-component alternate distribution multi-jet electrospinning, with bovine serum albumin decorated gold nanoparticles.[174] Here, leaching of the gold nanoparticles from the nanofiber surface is essential for the deep pink to white color change. Upon comparison with functionalized films, the nanofibrous membranes showed substantially higher colorimetric responses. A second sensor was also based on the mobilization of gold nanoparticles at the surface of the nanofibers, however the gold nanoparticles are now modified with L-glutathione

(GSH).[175] The GSH-gold nanoparticles were spotted on the surface of polyamide 6/polyvinylidene fluoride nanofibers, produced by multi-jet electrospinning. Upon the presence of lead ions, GSH, positioned as a layer around the nanoparticles, forms a chelating complex with Pb^{2+}, which induces the aggregation of the gold nanoparticles (**Figure 13**). This decreased distance between the gold nanoparticles leads to a combined surface plasmon resonance accompanied by a pink to purple color change.
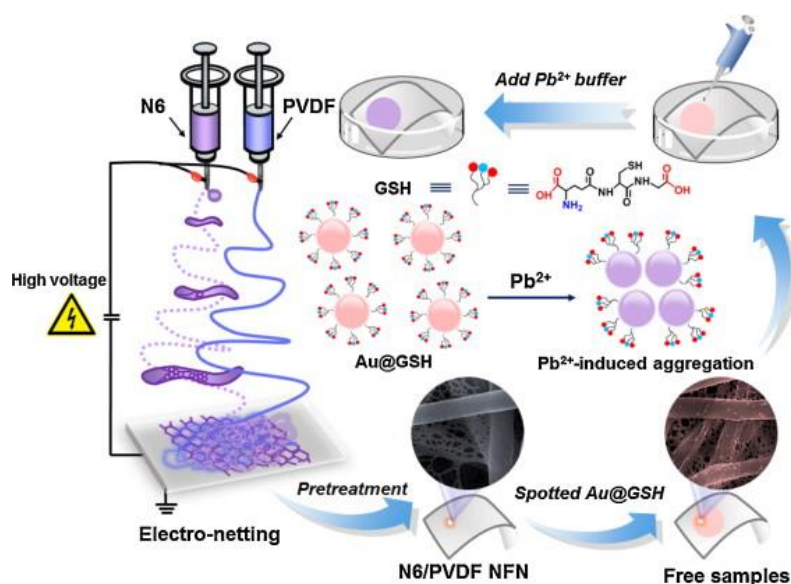

Figure 13. Multi-jet electrospinning of PVDF/PA 6 nanofibers followed by spotting of L-glutathione-conjugated gold nanoparticles results in a colorimetric sensor for lead ions, which induce the aggregation of the gold nanoparticles. Reproduced with permission.[175] 2014, Elsevier.

A third and interesting approach on physically decorating the surface of nanofibers with colorimetric functionalities is proposed by Yang *et al.*[176] As an alternative to physical adsorption strategies, supramolecular host-guest interactions are put forward as an easily tunable technique *via* the appropriate selection of β-cyclodextrin as a geometrically complementary host and adamantane as guest. Adamantane-functionalized nanofibers were produced by electrospinning of poly(methyl methacrylate-co-adamantylmethyl acrylate). Via

host-guest interactions between the adamantane and Rhodamine B-functionalized β-cyclodextrin compounds after electrospinning, the colorimetric functionality is introduced at the surface of the nanofibers (**Figure 14**). Upon detection of mercury ions in solution, the spirolactam configuration is opened, which visually leads to a selective color change from white to pink-red.
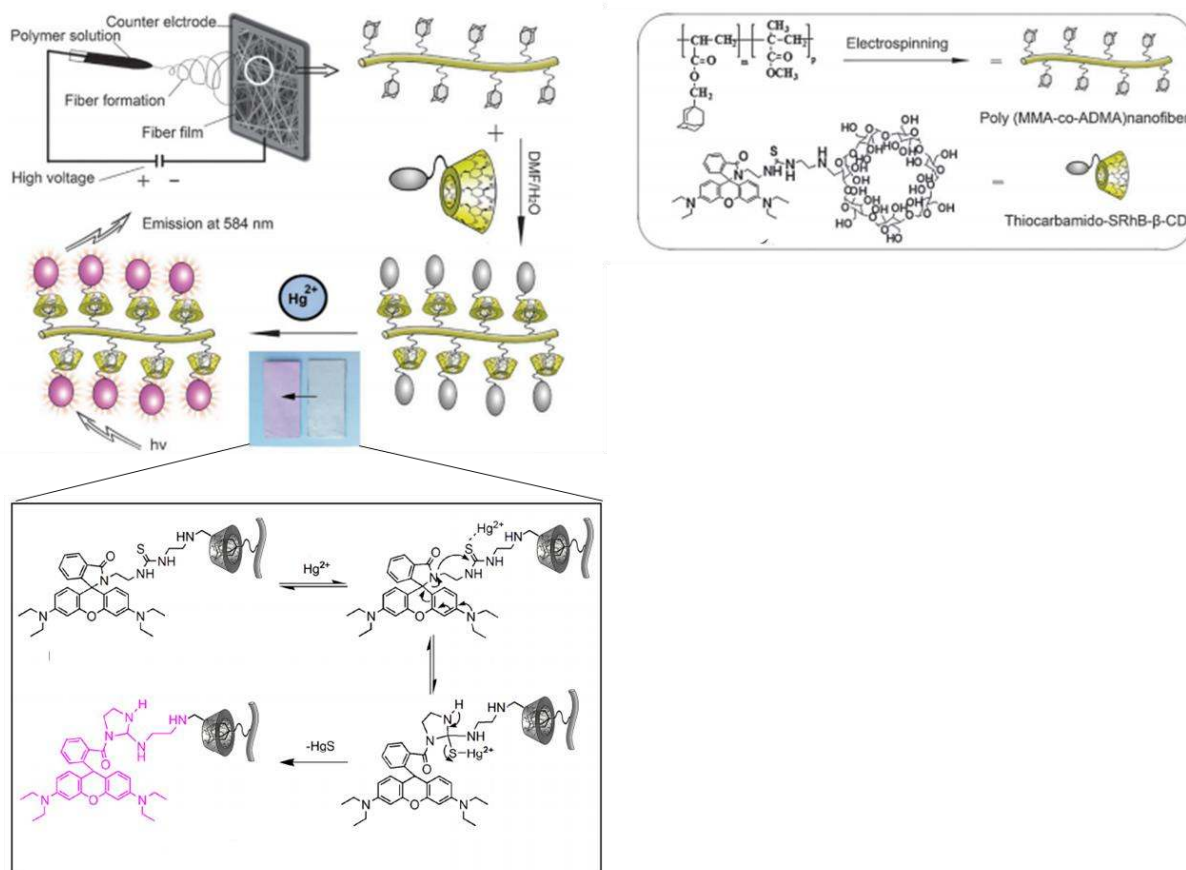

Figure 14. The surface of the nanofibers is decorated with rhodamine-cyclodextrin via host-guest interactions, resulting in a colorimetric sensor for mercury ions. Reproduced and adjusted with permission.[176] 2012, The Royal Society of Chemistry.

5.2 Nanofiber surface functionalization based on chemical reactions

Compared to physical surface functionalization, chemically bonding the functionality onto the polymers at the surface of the nanofibers after electrospinning, is probably a more complex, yet more efficient strategy to immobilize the functionality onto the nanofibers. In this way, the stability of the sensor is secured, which is of particular interest for detection in moist

environments. Two techniques, *i.e.* covalent grafting and plasma coating, are recently being explored to introduce colorimetric functionalities onto nanofiber surfaces.

Covalent grafting is a convenient and efficient approach to permanently introduce the functionalities onto the colorimetric sensor, as the functionality is simply coupled to a functional group already present/introduced on the polymer chain. Sensors for environmental monitoring have been designed according to this technique. Torto *et al.* post-functionalized poly(vinylbenzyl chloride) nanofibers with an imidazole derivative, *i.e.* 2-(2'-pyridyl)imidazole (PIMH), to achieve an Fe^{2+} colorimetric sensor.[177] The nanofibrous sensors showed a visual color change from yellow to red-orange upon detection of iron, resulting from the spin crossover from high spin Fe^{2+} to low spin Fe^{2+} upon interaction with the PIMH-ligand, as illustrated in **Figure 15**. In presence of other metal ions (Zn^{2+}, Mg^{2+}, Cd^{2+}, Co^{2+}, Ni^{2+}, Cr^{3+}, Cu^{2+}, Fe^{3+}) the sensor proved to be selective towards Fe^{2+}. However, after the post-functionalization procedure the nanofibers showed some swelling and breakage. Although the authors mention that the inherent nanofibrous structure remained, the post-functionalization step possibly influences the dimensional stability of the produced sensor material.
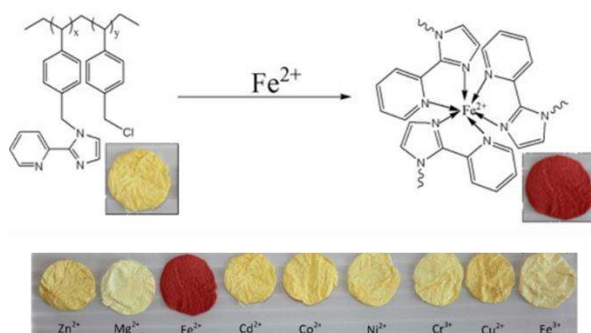

Figure 15. PVBC nanofibers were post-functionalized with an imidazole derivative PIMH, which is able to form a complex with iron ions. This complexations results in a color shift from yellow to red, providing a selective colorimetric sensor for iron. Reproduced and adjusted with permission.[177] 2013, Elsevier.

A similar detection system based on complexation of metal ions was applied for the detection of copper ions by Song *et al.*[178] Methyl methacrylate and 4-aldehyde-3-hydroxy phenyl acrylate were copolymerized, electrospun and easily functionalized by the reaction of the amino groups of Rhodamine B-hydrazine with the aldehyde functional groups at the surface of the nanofibers. As was also observed by Torto *et al.* the post-functionalization step increased the nanofiber diameters slightly. Upon exposure to Cu^{2+} in aqueous solution, the metal ions form a chelating complex with Rhodamine B, resulting in the opening of the spirolactam ring, which leads to a clearly visible white to pink color change. Ding *et al.* developed colorimetric nanofiber strips that could be used simultaneously for sensing and removal of metal ions.[179] Deacetylated cellulose acetate nanofibers were covalently grafted with pyromellitic dianhydride, for which Pb^{2+} has a good affinity. However, only after the addition of an aqueous Na_2S solution, a white to yellow-brown color change is observed due to the deposition of PbS. This sensor, thus, needs an extra step to activate the colorimetric function.

An efficient colorimetric pH-sensor was designed by Yang *et al.*[180] Polyaniline and polyamide 6.6 were simultaneously electrospun via a two-nozzle electrospinning technique. Polyamide 6.6 was added as to increase the mechanical strength of the sensor, whereas the polyaniline inside the nanofibrous sensor was aminated and subsequently grafted with phenolphthalein. The colorimetric sensors showed a color change from yellow to pink upon increasing the pH from 7 to 14.

Covalent grafting has also been applied for the design of robust colorimetric nanofibrous sensors for biomedical applications. Mudabuka *et al.* immobilized a tris-(2,2'-pyridylimidazole) iron(III) complex on poly(vinylbenzyl chloride) nanofibers for the detection of ascorbic acid and dopamine, both important biomedical compounds in the human metabolism and the central nervous system.[181] Upon the appropriate pH-conditions and the presence of ascorbic acid and dopamine, Fe^{3+} is reduced to low spin Fe^{2+} (red color) and high

spin Fe^{2+} (blue color) respectively. However, at pH 4 the nanofibrous sensor showed the same response to glutathione as to ascorbic acid, which could lead to false positives.

Although covalent grafting is an efficient immobilization technique for colorimetric nanofibrous sensor design, further optimization and research is necessary. In addition, most of the examples given above suffer from swelling of the nanofibers due to the post-functionalization step. For example, Torto *et al.* report an increase in nanofiber diameter from 340 nm to 860 nm.[177] These increased nanofiber diameters decrease the Brunauer-Emmett-Teller (BET) surface, which reduces the specific surface area of the nanofibrous sensor. Moreover, the increased thickness of the nanofibers might not only compromise the advantageous ultrasensitive nature of nanofibers, but also the dimensional stability of the nanofibrous membrane. The latter, however, has not been discussed in literature.

Another emerging technique for the efficient immobilization of colorimetric functionalities on nanofibrous sensor surfaces is plasma coating. Plasma coating is a recent and promising strategy based on the generation of surface radicals upon a short plasma treatment. The technique was first described by Hansen and Schonhorn in 1966 as "cross-linking by activated species of inert gases" (CASING)[183]. In our work, we further developed this technique to permanently link chromogenic agents onto nanofibrous surfaces for the design of colorimetric sensors[182]. Typically, stimuli-sensitive dyes are functionalized with polymerizable groups and pre-adsorbed on the nanofibrous sensor surface (**Figure 16**). During the short plasma treatment, activated species of inert gases create surface radicals which are used to link the polymerizable groups of the pre-adsorbed layer to the surface of the nanofibers.
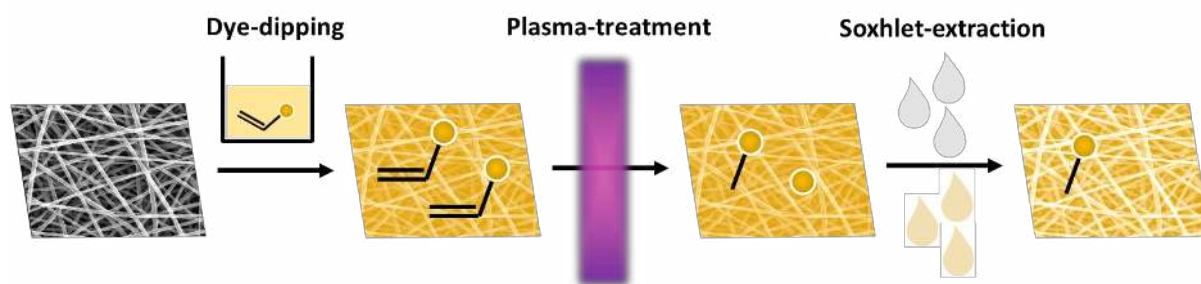
Figure 16. During plasma dye-coating the nanofibers are dipped in the dye-solution after which the membrane is treated with a non-thermal plasma to allow for covalent immobilization of the dye. The last step of the procedure consists of removing all residual dye from the nanofibrous membrane.[182]

We applied this procedure to covalently link five different dyes, *i.e.* Disperse Red 1, Bromothymol Blue, Bromocresol Purple, Rose Bengal and 4-Bromo-1,8-naphthalic anhydride, to electrospun polyamide 6 nanofibers as well as to cellulose filterpaper and flat sheets of polypropylene, polytetrafluoroethylene, high-density polyethylene and low-density polyethylene.[182] Four critical process parameters were identified and optimized, which led to the successful immobilization of the dyes on the different surfaces, *i.e.* dipping time, dye-concentration in the dipping solution, time of plasma treatment and identity of the radical sensitive group. The results indicated that these process parameters are both dye- and polymer-specific, which means the procedure should be optimized for each dye-polymer combination. Nonetheless, all polymer surfaces could be modified with all different dyes and all resulting samples showed an instantaneous and reversible color change upon detection of the analytes. Since this technique does not require a specific combination of reactive functional groups, it expands the range of applicable dyes and polymers. This provides for great versatility in colorimetric sensor design. Moreover, the dye-consumption and production times are relatively low, which makes the technique economically interesting. Combined with the fact that continuous plasma dye-coating is possible, industrial upscaling of the process is made feasible. It should be noted, however, that also the highly energetic plasma can influence the properties

of the applied dyes, since partial degradation of the dyes might occur. This could result in mixed optical properties due to the appearance of multiple immobilized derivatives or colored degradation products. On the contrast, the highly energetic plasma treatment did not significantly influence the inherent nanofibrous structure.

6. Conclusions and future outlook

It can be stated without doubt that nanofibers find their way in many application areas, including the optical sensor market. Solvent electrospinning is a straightforward and upscalable technique for the fabrication of uniform nanofibers, both on a small and large scale, as proved by the increasing amount of industrial companies producing electrospinning machines and nanofibrous materials. Because of their inherent structure, nanofibers provide a large specific sensing area, which has triggered research to explore and design colorimetric nanofibrous sensors. These color-changing materials provide for a fast, easy-to-understand, visual warning signal without power consumption, making these nanofibrous sensors applicable for not only high-end analyte-detection, but also for personal, daily use. Many current research is focusing on different strategies to introduce the colorimetric functionalities into the nanofibrous matrix, which were highlighted in this feature article. Based on a thorough analysis of the literature and the authors' expertise and experience, a few general insights on colorimetric nanofibrous sensor design can be concluded. First of all, by the application of nanofibers, the sensors are characterized by ultra-sensitivity and fast response times. However, this sensitivity and response times may be influenced by other factors than the nanofiber diameter only, *e.g.* diffusion processes, polymer properties, polymer-functonality interactions. Furthermore, it may intuitively be expected that the sensing functionalities are best located at the surface of the nanofibers. However, in order to produce sensors that are stable in time, the functionalities should be covalently linked to the nanofiber surface to provide efficient immobilization of the functionalities. Here, it is important that process conditions, including the steps taken for

efficient immobilization, do not influence the sensing behavior of the functionality, *e.g.* dye-chromophore, nor the inherent nanofiber morphology. On the other hand, also the choice of a specific functionality-matrix combination and its linking processes are crucial as they might alter the electrospinnability of the system. Whereas the relatively easy doping and coating techniques, based on physical interactions, have already proven to be valuable for optical sensor design by showing ultrasensitivity and fast response times, they lack sensor stability. Researchers have now found other, more robust ways to incorporate the chromogenic agents in the nanofibrous sensor. By covalently linking the colorimetric functionality to the polymer, before or after the electrospinning process, the functionalities are efficiently immobilized. However, the examples given in this article illustrate the increase in complexity accompanied with the switch from physical to chemical linkage. Microenvironmental and microstructural changes due to the covalent modification often influence processing parameters and final colorimetric properties, which leads to unpredicted results that are not always completely understood. There is, thus, still a lack of fundamental knowledge on the different and specific interactions between the colorimetric functionalities, *e.g.* dyes, and the polymer nanofibrous matrix, before, during and after the electrospinning process. However, more experimental work combined with molecular modelling will give more and more insight in the fascinating world of colorimetric nanofibrous sensor design. There is no doubt that many challenges still have to be faced as the techniques mentioned in this article still have to be further exploited and new techniques have to be explored. In parallel with these different strategies for the incorporation of functionalities into nanofibers, also structural properties of the produced sensors should be studied thoroughly and optimized. For example, the correlation between sensor sensitivity or response time and nanofiber microstructure, *i.e.* diameter, porosity, specific surface area, could be investigated in depth. Also a study on functionalization degree in relation to sensitivity and response time would reveal important insights for design of next generation nanofibrous sensors. Only with an optimal combination of structural properties and production technique,

colorimetric nanofibrous sensors with optimal sensitivity can be achieved. As proven by the demanding market and the increasing amount of research within this field, many researchers recognize the potential of colorimetric nanofibers as advanced, ultrasensitive optical sensors leading to continuous progress in the design of colorimetric nanofibrous sensors for environmental monitoring, biomedical diagnostics, agriculture and food monitoring. It seems to be only a matter of time before the first colorimetric nanofiborus sensor systems will reach the market.

7. Acknowledgments

References

[1]   Frost&Sullivan, *Global Sensor Outlook 2016*; 2016.

[2]   NATIONAL RESEARCH COUNCIL, *Expanding the Vision of Sensor Materials*; National Academies Press: Washington, D.C., 1995.

[3]   F. G. Bănică, In *Chemical Sensors and Biosensors: Fundamentals and Applications*; John Wiley & Sons, Ltd: Chichester, UK, 2012; pp. 1–20.

[4]   F. Arduini, S. Cinti, V. Scognamiglio, D. Moscone, G. Palleschi, *Anal. Chim. Acta* **2017**, *959*, 15.

[5]   R. Byrne, F. Benito-Lopez, D. Diamond, *Mater. Today* **2010**, *13*, 16.

[6]   G. T. Chandran, X. Li, A. Ogata, R. M. Penner, *Anal. Chem.* **2016**, *89*, acs. analchem.6b04687.

[7]   B. Ding, M. Wang, X. Wang, J. Yu, G. Sun, *Mater. Today* **2010**, *13*, 16.

[8]   P. Kumari, L. Mathew, P. Syal, *Biosens. Bioelectron.* **2017**, *90*, 298.

[9] E. Priyadarshini, N. Pradhan, *Sensors Actuators, B Chem.* **2017**, *238*, 888.

[10] L. Wang, W. Ma, L. Xu, W. Chen, Y. Zhu, C. Xu, N. A. Kotov, *Mater. Sci. Eng. R Reports* **2010**, *70*, 265.

[11] S. A. Wilson, R. P. J. Jourdain, Q. Zhang, R. A. Dorey, C. R. Bowen, M. Willander, Q. U. Wahab, M. Willander, S. M. Al-hilli, O. Nur, E. Quandt, C. Johansson, E. Pagounis, M. Kohl, J. Matovic, B. Samel, W. van der Wijngaart, E. W. H. Jager, D. Carlsson, Z. Djinovic, M. Wegener, C. Moldovan, E. Abad, M. Wendlandt, C. Rusu, K. Persson, *Mater. Sci. Eng. R Reports* **2007**, *56*, 1.

[12] L. Zhang, M. Fang, *Nano Today* **2010**, *5*, 128.

[13] S. Agarwal, A. Greiner, J. H. Wendorff, *Prog. Polym. Sci.* **2013**, *38*, 963.

[14] A. Camposeo, L. Persano, D. Pisignano, *Macromol. Mater. Eng.* **2013**, *298*, 487.

[15] S. Chigome, N. Torto, *Anal. Chim. Acta* **2011**, *706*, 25.

[16] L. I. Dan, J. Huang, R. B. Kaner, *Acc. Chem. Res.* **2009**, *42*, 135.

[17] L. Feng, N. Xie, J. Zhong, *Materials (Basel).* **2014**, *7*, 3919.

[18] W. Guan, W. Zhou, J. Lu, C. Lu, *Chem. Soc. Rev.* **2015**, *44*, 6981.

[19] C. Huang, S. J. Soenen, J. Rejman, B. Lucas, K. Braeckmans, J. Demeester, S. C. De Smedt, *Chem. Soc. Rev.* **2011**, *40*, 2417.

[20] Y.-Z. Long, M.-M. Li, C. Gu, M. Wan, J.-L. Duvail, Z. Liu, Z. Fan, *Prog. Polym. Sci.* **2011**, *36*, 1415.

[21] L. Matlock-Colangelo, A. J. Baeumner, *Lab Chip* **2012**, *12*, 2612.

[22] I. Steyaert, H. Rahier, K. D. De Clerck, *Nanosci. Technol.* **2015**, *96*, 157.

[23] J. Wang, Y. Lin, *TrAC - Trends Anal. Chem.* **2008**, *27*, 619.

[24] X. F. Wang, B. Ding, J. Y. Yu, In *Functional Nanofibers and their Applications*; Elsevier, 2012; pp. 209–235.

[25] C. Yang, M. E. Denno, P. Pyakurel, B. J. Venton, *Anal. Chim. Acta* **2015**, *887*, 17.

[26] C.-L. Zhang, S.-H. Yu, *Chem. Soc. Rev.* **2014**, *43*, 4423.

[27] S. Agarwal, M. Burgard, A. Greiner, J. Wendorff, *Electrospinning: A Practical Guide to Nanofibers*; De Gruyter Textbook; De Gruyter, 2016.

[28] L. A. Andrady, *Science and Technology of Polymer Nanofibers*; 2008.

[29] N. Bhardwaj, S. C. Kundu, *Biotechnol. Adv.* **2010**, *28*, 325.

[30] S. De Vrieze, T. Van Camp, A. Nelvig, B. Hagström, P. Westbroek, K. De Clerck, *J. Mater. Sci.* **2009**, *44*, 1357.

[31] D. Pisignano, *Polymer Nanofibers: Building Blocks for Nanotechnology*; 2013; Vol. 8.

[32] S. Ramakrishna, *An Introduction to Electrospinning And Nanofibers (Google eBook)*; World Scientific, 2005.

[33] S. Ramakrishna, K. Fujihara, W. E. Teo, T. Yong, Z. Ma, R. Ramaseshan, *Mater. Today* **2006**, *9*, 40.

[34] J. H. Wendorff, S. Agarwal, A. Greiner, *Electrospinning: Materials, Processing, and Applications*; John Wiley & Sons, 2012.

[35] T. R. Hayes, I. C. Hosie, *Nanosci. Technol.* **2015**, *96*, 305.

[36] L. Persano, A. Camposeo, C. Tekmen, D. Pisignano, *Macromol. Mater. Eng.* **2013**, *298*, 504.

[37] A. Camposeo, M. Moffa, L. Persano, *Nanosci. Technol.* **2015**, 129.

[38] F. De Cesare, A. Macagnano, *Nanosci. Technol.* **2015**, *96*, 225.

[39] I.-D. Kim, S.-J. Choi, H.-J. Cho, *Nanosci. Technol.* **2015**, *96*, 65.

[40] Y. Li, J. Yu, B. Ding, *Nanosci. Technol.* **2015**, *96*, 1.

[41] A. Senthamizhan, T. Uyar, *Nanosci. Technol.* **2015**, *96*, 179.

[42] E. Zampetti, A. Macagnano, A. Bearzotti, *Nanosci. Technol.* **2015**, *96*, 115.

[43] S.-J. Choi, L. Persano, A. Camposeo, J.-S. Jang, W.-T. Koo, S.-J. Kim, H.-J. Cho, I.-D. Kim, D. Pisignano, *Macromol. Mater. Eng.* **2017**, 1600569.

[44] B. Ding, M. Wang, J. Yu, G. Sun, *Sensors* **2009**, *9*, 1609.

[45] C. Kriegel, A. Arrechi, K. Kit, D. J. McClements, J. Weiss, J. Weiss, *Crit. Rev. Food*

Sci. Nutr. **2008**, *48*, 775.

[46]   *Electrospinning for High Performance Sensors*; Macagnano, A.; Zampetti, E.; Kny, E.,

Eds.; NanoScience and Technology; Springer International Publishing: Cham, 2015.

[47]   L. Van der Schueren, K. De Clerck, *Color. Technol.* **2012**, *128*, 82.

[48]   L. Van Der Schueren, K. Hemelsoet, V. Van Speybroeck, K. De Clerck, *Dye. Pigment.*

2012, *94*, 443.

[49]   F.-L. Zhou, P. L. Hubbard Cristinacce, S. J. Eichhorn, G. J. M. Parker, *Nanosci.*

Technol. **2015**, *96*, 289.

[50]   S. X. Wang, C. C. Yap, J. He, C. Chen, S. Y. Wong, X. Li, *Nanotechnol. Rev.* **2016**, *5*,

51.

[51]   K. Mondal, A. Sharma, *RSC Adv.* **2016**, *6*, 94595.

[52]   N. J. Pinto, *Nanosci. Technol.* **2015**, *96*, 103.

[53]   M. Scampicchio, A. Bulbarello, A. Arecchi, M. S. Cosio, S. Benedetti, S. Mannino,

Electroanalysis **2012**, *24*, 719.

[54]   M. Espinoza-Castañeda, A. de la Escosura-Muñiz, A. Merkoçi, *Nanosci. Technol.*

2015, *96*, 205.

[55]   Z. Li, H. Zhang, W. Zheng, W. Wang, H. Huang, C. Wang, A. G. MacDiarmid, Y.

Wei, *J. Am. Chem. Soc.* **2008**, *130*, 5036.

[56]   F. S. Kim, G. Ren, S. A. Jenekhe, *Chem. Mater.* **2011**, *23*, 682.

[57]   H. Wu, W. Pan, D. Lin, H. Li, *J. Adv. Ceram.* **2012**, *1*, 2.

[58]   L. Zang, *Acc. Chem. Res.* **2015**, *48*, 2705.

[59]   M. M. Rahman, A. J. S. Ahammad, J.-H. Jin, S. J. Ahn, J.-J. Lee, *Sensors (Basel).*

2010, *10*, 4855.

[60]   A. Senthamizhan, B. Balusamy, T. Uyar, *Anal. Bioanal. Chem.* **2015**, *408*, 1285.

[61]   R. Luoh, H. T. Hahn, *Compos. Sci. Technol.* **2006**, *66*, 2436.

[62]   Y. Song, W. Wei, X. Qu, *Adv. Mater.* **2011**, *23*, 4215.

[63] K. M. Tripathi, T. Kim, D. Losic, T. T. Tung, *Carbon N. Y.* **2016**, *110*, 97.

[64] M. Schäferling, *Angew. Chemie Int. Ed.* **2012**, *51*, 3532.

[65] M. K. Balaconis, Y. Luo, H. A. Clark, *Analyst* **2015**, *140*, 716.

[66] B. W. Davis, N. Niamnont, R. Dillon, C. J. Bardeen, M. Sukwattanasinitt, Q. Cheng, *Langmuir* **2011**, *27*, 6401.

[67] B. W. Davis, N. Niamnont, C. D. Hare, M. Sukwattanasinitt, Q. Cheng, *ACS Appl. Mater. Interfaces* **2010**, *2*, 1798.

[68] S. Kacmaz, K. Ertekin, A. Suslu, M. Ozdemir, Y. Ergun, E. Celik, U. Cocen, *Sensors Actuators, B Chem.* **2011**, *153*, 205.

[69] X. He, L. Tan, X. Wu, C. Yan, D. Chen, X. Meng, F. Tang, Q. Wang, P. K. Chu, M. T. McMahon, J. W. Bulte, P. C. van Zijl, A. A. Gilad, *J. Mater. Chem.* **2012**, *22*, 18471.

[70] R. Kai, W. Jun, J. Huali, *Sensors Actuators B Chem.* **2017**, *240*, 697.

[71] M. Li, J. Zhang, H. Zhang, Y. Liu, C. Wang, X. Xu, Y. Tang, B. Yang, *Adv. Funct. Mater.* **2007**, *17*, 3650.

[72] C. Liu, C. Shi, H. Li, W. Du, Z. Li, L. Wei, M. Yu, *Sensors Actuators B Chem.* **2015**, *219*, 185.

[73] C. Meng, Y. Xiao, P. Wang, L. Zhang, Y. Liu, L. Tong, *Adv. Mater.* **2011**, *23*, n/a.

[74] M. Z. Ongun, K. Ertekin, C. G. Hizliates, O. Oter, Y. Ergun, E. Celik, *Sensors Actuators B Chem.* **2013**, *181*, 244.

[75] M. Z. Ongun, O. Oter, G. Sabancı, K. Ertekin, E. Celik, *Sensors Actuators B Chem.* **2013**, *183*, 11.

[76] A. Senthamizhan, A. Celebioglu, T. Uyar, K. Chen, J. Wang, J. Yu, H. Wang, B. Ding, S. Carregal-Romero, W. J. Parak, *J. Mater. Chem. A* **2014**, *2*, 12717.

[77] X. Sun, Y. Liu, G. Shaw, A. Carrier, S. Dey, J. Zhao, Y. Lei, *ACS Appl. Mater. Interfaces* **2015**, *7*, 13189.

[78] J.-H. Syu, Y.-K. Cheng, W.-Y. Hong, H.-P. Wang, Y.-C. Lin, H.-F. Meng, H.-W. Zan,

S.-F. Horng, G.-F. Chang, C.-H. Hung, Y.-C. Chiu, W.-C. Chen, M.-J. Tsai, H. Cheng, *Adv. Funct. Mater.* **2013**, *23*, 1566.

[79] L.-Y. Wang, Y. Xu, Z. Lin, N. Zhao, Y. Xu, *J. Lumin.* **2011**, *131*, 1277.

[80] M. Wang, G. Meng, Q. Huang, Y. Qian, *Environ. Sci. Technol.* **2012**, *46*, 367.

[81] Y. Wang, A. La, Y. Ding, Y. Liu, Y. Lei, *Adv. Funct. Mater.* **2012**, *22*, 3547.

[82] W. Xue, Y. Zhang, J. Duan, D. Liu, Y. Ma, N. Shi, S. Chen, L. Xie, Y. Qian, W. Huang, A. Xia, *J. Mater. Chem. C* **2015**, *3*, 8193.

[83] Y. Yang, X. Fan, Y. Long, K. Su, D. Zou, N. Li, J. Zhou, K. Li, F. Liu, *J. Mater. Chem.* **2009**, *19*, 7290.

[84] Y. Yang, H. Wang, K. Su, Y. Long, Z. Peng, N. Li, F. Liu, J. Pei, F. Liu, *J. Mater. Chem.* **2011**, *21*, 11895.

[85] C. Zhou, Y. Shi, X. Ding, M. Li, J. Luo, Z. Lu, D. Xiao, *Anal. Chem.* **2013**, *85*, 1171.

[86] S. K. Chae, H. Park, J. Yoon, C. H. Lee, D. J. Ahn, J.-M. Kim, *Adv. Mater.* **2007**, *19*, 521.

[87] Y.-C. Chiu, Y. Chen, C.-C. Kuo, S.-H. Tung, T. Kakuchi, W.-C. Chen, *ACS Appl. Mater. Interfaces* **2012**, *4*, 3387.

[88] Y.-C. Chiu, C.-C. Kuo, J.-C. Hsu, W.-C. Chen, *ACS Appl. Mater. Interfaces* **2010**, *2*, 3340.

[89] C.-C. Kuo, Y.-C. Tung, W.-C. Chen, *Macromol. Rapid Commun.* **2010**, *31*, 65.

[90] C.-C. Kuo, C.-T. Wang, W.-C. Chen, *Macromol. Mater. Eng.* **2008**, *293*, 999.

[91] Y. Long, H. Chen, Y. Yang, H. Wang, Y. Yang, N. Li, K. Li, J. Pei, F. Liu, *Macromolecules* **2009**, *42*, 6501.

[92] A. L. Medina-Castillo, J. F. Fernandez-Sanchez, A. Segura-Carretero, A. Fernandez-Gutierrez, Y. B. He, A. Zankel, P. Polt, I. Klimant, *J. Mater. Chem.* **2011**, *21*, 6742.

[93] W. Wang, Q. Yang, L. Sun, H. Wang, C. Zhang, X. Fei, M. Sun, Y. Li, *J. Hazard. Mater.* **2011**, *194*, 185.

[94]   X. Wang, C. Drew, S. H. Lee, K. J. Senecal, J. Kumar, L. A. Samuelson, *Nano Lett.* **2002**, *2*, 1273.

[95]   H. Zhou, Q. Ye, W. T. Neo, J. Song, H. Yan, Y. Zong, B. Z. Tang, T. S. A. Hor, J. Xu, *Chem. Commun.* **2014**, *50*, 13785.

[96]   Y. Cai, L. Yan, G. Liu, H. Yuan, D. Xiao, *Biosens. Bioelectron.* **2013**, *41*, 875.

[97]   C.-J. Cho, S.-T. Lu, C.-C. Kuo, F.-C. Liang, B.-Y. Chen, C.-C. Chu, *React. Funct. Polym.* **2016**, *108*, 137.

[98]   S. Jo, J. Kim, J. Noh, D. Kim, G. Jang, N. Lee, E. Lee, T. S. Lee, *ACS Appl. Mater. Interfaces* **2014**, *6*, 22884.

[99]   L. Ma, K. Liu, M. Yin, J. Chang, Y. Geng, K. Pan, *Sensors Actuators B Chem.* **2017**, *238*, 120.

[100]   A. Senthamizhan, B. Balusamy, Z. Aytac, T. Uyar, *Anal. Bioanal. Chem.* **2016**, *408*, 1347.

[101]   A. Senthamizhan, A. Celebioglu, T. Uyar, *Sci. Rep.* **2015**, *5*, 10403.

[102]   X. Wang, Y. G. Kim, C. Drew, B. C. Ku, J. Kumar, L. A. Samuelson, *Nano Lett.* **2004**, *4*, 331.

[103]   L. Zhao, S. Xie, X. Song, J. Wei, Z. Zhang, X. Li, *Biosens. Bioelectron.* **2017**, *91*, 217.

[104]   S. Chigome, N. Torto, *Anal. Chim. Acta* **2011**, *706*, 25.

[105]   N. A. Rakow, K. S. Suslick, *Nature* **2000**, *406*, 710.

[106]   L. Van der Schueren, K. De Clerck, *Text. Res. J.* **2009**, *80*, 590.

[107]   P. Bamfield, M. G. Hutchings, *Chromic Phenomena: Technological applications of colour chemistry*; Royal Society of Chemistry, 2010.

[108]   H. Zollinger, *Color chemistry : syntheses, properties, and applications of organic dyes and pigments*; Verl. Helvetica Chimica Acta, 2003.

[109]   L. Van Der Schueren, T. Mollet, Ö. Ceylan, K. De Clerck, *Eur. Polym. J.* **2010**, *46*, 2229.

[110] L. Van Der Schueren, T. De Meyer, I. Steyaert, Ö. Ceylan, K. Hemelsoet, V. Van Speybroeck, K. De Clerck, *Carbohydr. Polym.* **2013**, *91*, 284.

[111] S. H. Kim, J. S. Bae, *Fibers Polym.* **2013**, *14*, 1981.

[112] A. Agarwal, A. Raheja, T. S. Natarajan, T. S. Chandra, *Sensors Actuators, B Chem.* **2012**, *161*, 1097.

[113] M. Min, X. Wang, Y. Chen, L. Wang, H. Huang, J. Shi, *Sensors Actuators, B Chem.* **2013**, *188*, 360.

[114] S. Raj, D. R. Shankaran, *Sensors Actuators, B Chem.* **2016**, *226*, 318.

[115] A. Saithongdee, N. Praphairaksit, A. Imyim, *Sensors Actuators, B Chem.* **2014**, *202*, 935.

[116] T. Poltue, R. Rangkupan, S. T. Dubas, L. Dubas, *Mater. Lett.* **2011**, *65*, 2231.

[117] H. Najarzadekan, H. Sereshti, *J. Mater. Sci.* **2016**, *51*, 8645.

[118] L. Hu, X.-W. Yan, Q. Li, X.-J. Zhang, D. Shan, *J. Hazard. Mater.* **2017**, *329*, 205.

[119] Y. Hu, L. Chen, H. Jung, Y. Zeng, S. Lee, K. M. K. Swamy, X. Zhou, M. H. Kim, J. Yoon, *ACS Appl. Mater. Interfaces* **2016**, *8*, 22246.

[120] T. A. Khattab, S. Abdelmoez, T. M. Klapötke, *Chem. - A Eur. J.* **2016**, *22*, 4157.

[121] M. Hu, W. Kang, B. Cheng, Z. Li, Y. Zhao, L. Li, *Microchim. Acta* **2016**, *183*, 1713.

[122] J. Geltmeyer, G. Vancoillie, I. Steyaert, B. Breyne, G. Cousins, K. Lava, R. Hoogenboom, K. De Buysser, K. De Clerck, *Adv. Funct. Mater.* **2016**, *26*, 5987.

[123] X. Ji, Z. Su, P. Wang, G. Ma, S. Zhang, *Analyst* **2014**, *139*, 6467.

[124] B. Mudabuka, D. Ondigo, S. Degni, S. Vilakazi, N. Torto, *Microchim. Acta* **2014**, *181*, 395.

[125] N. Ngomane, N. Torto, R. Krause, S. Vilakazi, In *Materials Today: Proceedings*; 2015; Vol. 2, pp. 4060–4069.

[126] L. K. S. De Almeida, S. Chigome, N. Torto, C. L. Frost, B. I. Pletschke, *Sensors Actuators, B Chem.* **2015**, *206*, 357.

[127] A. Senthamizhan, A. Celebioglu, T. Uyar, *Chem. Commun.* **2015**, *51*, 5590.

[128] D. Fantini, L. Costa, *Polym. Adv. Technol.* **2009**, *20*, 111.

[129] G. J. Mohr, *Anal. Bioanal. Chem.* **2006**, *386*, 1201.

[130] T. R. Dargaville, B. L. Farrugia, J. a. Broadbent, S. Pace, Z. Upton, N. H. Voelcker, *Biosens. Bioelectron.* **2013**, *41*, 30.

[131] L. Van der Schueren, K. De Clerck, In *Handbook of Medical Textiles*; Bartels, V., Ed.; 2011; pp. 547–566.

[132] T. De Meyer, K. Hemelsoet, L. Van Der Schueren, E. Pauwels, K. De Clerck, V. Van Speybroeck, *Chem. - A Eur. J.* **2012**, *18*, 8120.

[133] T. De Meyer, K. Hemelsoet, V. Van Speybroeck, K. De Clerck, *Dye. Pigment.* **2014**, *102*, 241.

[134] D. Sareen, P. Kaur, K. Singh, *Coord. Chem. Rev.* **2014**, *265*, 125.

[135] M. Cano, P. Castillero, J. Roales, J. M. Pedrosa, S. Brittle, T. Richardson, A. R. González-Elipe, A. Barranco, *Sensors Actuators, B Chem.* **2010**, *150*, 764.

[136] F.-W. Lin, X.-L. Xu, L.-S. Wan, J. Wu, Z.-K. Xu, *RSC Adv.* **2015**, *5*, 30472.

[137] J. Geltmeyer, J. De Roo, F. Van den Broeck, J. C. Martins, K. De Buysser, K. De Clerck, *J. Sol-Gel Sci. Technol.* **2016**, *77*, 453.

[138] J. Geltmeyer, L. Van Der Schueren, F. Goethals, K. De Buysser, K. De Clerck, *J. Sol-Gel Sci. Technol.* **2013**, *67*, 188.

[139] G. Schmid, *Clusters and Colloids: From Theory to Applications*; Schmid, G., Ed.; Wiley-VCH Verlag GmbH: Weinheim, Germany, 2007.

[140] S. K. Ghosh, T. Pal, *Chem. Rev.* **2007**, *107*, 4797.

[141] C.-L. Zhang, S.-H. Yu, *Chem. Soc. Rev.* **2014**, *43*, 4423.

[142] W. Zhao, M. M. Ali, S. D. Aguirre, M. A. Brook, Y. Li, *Anal. Chem.* **2008**, *80*, 8431.

[143] C. Munkholm, *Talanta* **1988**, *35*, 109.

[144] T. Carofiglio, C. Fregonese, G. J. Mohr, F. Rastrelli, U. Tonellato, *Tetrahedron* **2006**,

62, 1502.

[145] C. McDonagh, C. S. Burke, B. D. MacCraith, *Chem. Rev.* **2008**, *108*, 400.

[146] P. Makedonski, M. Brandes, W. Grahn, W. Kowalsky, J. Wichern, S. Wiese, H.-H. Johannes, *Dye. Pigment.* **2004**, *61*, 109.

[147] S. Trupp, M. Alberti, T. Carofiglio, E. Lubian, H. Lehmann, R. Heuermann, E. Yacoub-George, K. Bock, G. J. Mohr, *Sensors Actuators B Chem.* **2010**, *150*, 206.

[148] T. H. Nguyen, T. Venugopala, S. Chen, T. Sun, K. T. V. Grattan, S. E. Taylor, P. A. M. Basheer, A. E. Long, *Sensors Actuators B Chem.* **2014**, *191*, 498.

[149] G. J. Mohr, H. Müller, B. Bussemer, A. Stark, T. Carofiglio, S. Trupp, R. Heuermann, T. Henkel, D. Escudero, L. González, *Anal. Bioanal. Chem.* **2008**, *392*, 1411.

[150] J. Yoon, S. K. Chae, J. M. Kim, *J. Am. Chem. Soc.* **2007**, *129*, 3038.

[151] J. Yoon, Y. S. Jung, J. M. Kim, *Adv. Funct. Mater.* **2009**, *19*, 209.

[152] Q. Xu, S. Lee, Y. Cho, M. H. Kim, J. Bouffard, J. Yoon, *J. Am. Chem. Soc.* **2013**, *135*, 17751.

[153] J. Lee, S. Balakrishnan, J. Cho, S.-H. Jeon, J. Kim, *J. Mater. Chem.* **2011**, *21*, 2648.

[154] B. Ding, Y. Si, X. Wang, J. Yu, L. Feng, G. Sun, *J. Mater. Chem.* **2011**, *21*, 13345.

[155] Y. Si, X. Wang, ab K. C. Yan Li, J. Wang, J. Yu, H. Wang, B. Ding, *J. Mater. Chem. A* **2014**, *2*, 645.

[156] Y. Wen, Y. Li, Y. Si, X. Wang, F. Li, J. Yu, B. Ding, *Talanta* **2015**, *144*, 1146.

[157] I. Steyaert, G. Vancoillie, R. Hoogenboom, K. De Clerck, *Polym. Chem.* **2015**, *6*, 2685.

[158] Y. Y. Lv, J. Wu, Z. K. Xu, *Sensors Actuators, B Chem.* **2010**, *148*, 233.

[159] E. Schoolaert, I. Steyaert, G. Vancoillie, J. Geltmeyer, K. Lava, R. Hoogenboom, K. De Clerck, *J. Mater. Chem. B* **2016**, *4*, 4507.

[160] A. Senthamizhan, A. Celebioglu, S. Bayir, M. Gorur, E. Doganci, F. Yilmaz, T. Uyar, *ACS Appl. Mater. Interfaces* **2015**, *7*, 21038.

[161] S. W. Thomas, G. D. Joly, T. M. Swager, *Chem. Rev.* **2007**, *107*, 1339.

[162] M. Leclerc, In *Encyclopedia of Materials: Science and Technology*; Elsevier, 2001; pp. 6120–6124.

[163] J. Bai, S. Beyer, D. Trau, *Conjugated Polymers for Biosensor Devices*; Elsevier, 2011.

[164] *Conjugated Polymers: A Practical Guide to Synthesis*; Müllen, K.; Reynolds, J. R.; Masuda, T., Eds.; RSC Polymer Chemistry Series; Royal Society of Chemistry: Cambridge, 2013.

[165] D. Tyler McQuade, A. E. Pullen, T. M. Swager, *Chem. Rev.* **2000**, *100*, 2537.

[166] A. Alam, J. Yapor, M. Reynolds, Y. Li, *Materials (Basel).* **2016**, *9*, 202.

[167] Celly M. S. Izumi, Ana Maria D. C. Ferreira, and Vera R. L. Constantino, M. L. A. Temperini*, **2007**.

[168] A. G. MacDiarmid, A. J. Epstein, *Faraday Discuss. Chem. Soc.* **1989**, *88*, 317.

[169] A. Varela-Álvarez, J. A. Sordo, G. E. Scuseria, *J. Am. Chem. Soc.* **2005**, *127*, 11318.

[170] X. Wang, Y. Li, X. Li, J. Yu, S. S. Al-Deyab, B. Ding, *Sensors Actuators, B Chem.* **2014**, *203*, 333.

[171] X. Wang, Y. Si, X. Mao, Y. Li, J. Yu, H. Wang, B. Ding, *Analyst* **2013**, *138*, 5129.

[172] X. Wang, Y. Si, J. Wang, B. Ding, J. Yu, S. S. Al-Deyab, *Sensors Actuators, B Chem.* **2012**, *163*, 186.

[173] A. T. Hoang, Y. B. Cho, J. S. Park, Y. Yang, Y. S. Kim, *Sensors Actuators, B Chem.* **2016**, *230*, 250.

[174] Y. Li, Y. Si, X. Wang, B. Ding, G. Sun, G. Zheng, W. Luo, J. Yu, *Biosens. Bioelectron.* **2013**, *48*, 244.

[175] Y. Li, B. Ding, G. Sun, T. Ke, J. Chen, S. S. Al-Deyab, J. Yu, *Sensors Actuators, B Chem.* **2014**, *204*, 673.

[176] W. Wang, Y. Li, M. Sun, C. Zhou, Y. Zhang, Y. Li, Q. Yang, *Chem. Commun.* **2012**, *48*, 6040.

[177] D. A. Ondigo, Z. R. Tshentu, N. Torto, *Anal. Chim. Acta* **2013**, *804*, 228.

[178] W. Wang, X. Wang, Q. Yang, X. Fei, M. Sun, Y. Song, *Chem. Commun. (Camb).* **2013**, *49*, 4833.

[179] Y. Li, Y. Wen, L. Wang, J. He, S. S. Al-Deyab, M. El-Newehy, J. Yu, B. Ding, *J. Mater. Chem. A* **2015**, *3*, 18180.

[180] C. Zhang, Y. Li, W. Wang, N. Zhan, N. Xiao, S. Wang, Y. Li, Q. Yang, *Eur. Polym. J.* **2011**, *47*, 2228.

[181] B. Mudabuka, A. S. Ogunlaja, Z. R. Tshentu, N. Torto, *Sensors Actuators, B Chem.* **2016**, *222*, 598.

[182] G. Vancoillie, L. De Smet, P. Minshall, K. Lava, I. Steyaert, E. Schoolaert, E. Van De Walle, P. Dubruel, K. De Clerck, R. Hoogenboom, *Prep.*

[183] R. H. Hansen, H. Schonhorn, *J. Polym. Sci. Part B Polym. Lett.* **1966**, *4*, 203.

List of Tables and Figures

Figure 1. Nanofibrous sensors are fabricated by the solvent electrospinning process, in which a polymer solution is drawn into sub-micron fibers by the application of an electrical field. In order to introduce a sensing function, different functionalities can be incorporated in the nanofibers by three different techniques: doping of the electrospinning solution with the functionality, functionalizing the polymers itself with functionalities or modifying the surface of the produced nanofibers. In all cases, the functionalities are the detection system of the sensor and are able to interact with the analyte. This interaction is subsequently translated into a readable signal, which can be electrical or optical.

Table 1. List of colorimetric nanofibrous sensors based on doping techniques.

Figure 2. Molecular modelling supports and enhances the understanding of experimental results. Here, for instance, the strong interactions between poly(ε-caprolactone) (PCL) and the chromophore of Nitrazine Yellow (NY) are simulated, which supports the hypothesis of shielding of the dye, hindering a visual color change. Chitosan (CS), on the contrary, clearly

shows different interactions, which do not lead to shielding, leaving the halochromic behavior of Nitrazine Yellow intact. Reproduced and adjusted with permission.[106] 2012, Elsevier.

Figure 3. Unambiguous selectivity of curcumin-doped cellulose acetate nanofibers for Pb^{2+} in the presence of other metal ions. Reproduced and adjusted with permission.[110] 2015, Elsevier

Figure 4. Br-PADAP-doped cellulose acetate nanofibers provide a clear color change upon detection of uranyl with a detection limit of 50 ppb. Although the change in color could be visualized after 20 minutes, only after 80 minutes the membrane had reached its final color. Reproduced with permission.[114] 2017, Elsevier.

Figure 5. TEOS-APTES (TA) ceramic nanofibers doped with the dye Methyl Yellow show a clear and reversible visual response upon detection of HCl and NH_3 vapors (left). TEOS-APTES ceramic nanofibers doped with the dye Methyl Red show visual responsivity towards biogenic amines (right). Reproduced and adjusted with permission[118] 2016, WILEY-VCH Verlag GmbH & Co.

Table 2. List of colorimetric nanofibers sensors based on functionalized polymers.

Figure 6. Nanofibers functionalized with the conjugated polymer PDA are produced from a solution containing diacetylene (DA) monomers and a support polymer. During electrospinning the DA monomers self-assemble after which PDA is created upon irradiation with light.

Figure 7. PA 66 is blended with PANI-PB for the production of colorimetric nanofibers that detect L-ascorbic acid in juices. A color differentiation map was constructed to link color to analyte concentration. Reproduced with permission.[151] 2015, Elsevier.

Figure 8. Dye-migration as measured by staining of reference fabrics in contact with dye-containing nanofibers clearly illustrates that reference fabrics in contact with doped nanofibers are much more stained due to dye-leaching at all pH-values than reference fabrics in contact with covalently modified nanofibers. These results clearly prove the potential of

covalent modification as a dye-immobilization technique. Note that at pH 12, more dye-leaching appears for the covalently modified nanofibers due to partial hydrolysis of the polymer in alkaline conditions. Reproduced and adjusted with permission.[152] 2015, The Royal Society of Chemistry.

Figure 9. Polyimide modified with porphyrin was electrospun to produce colorimetric nanofibrous sensors which respond to the presence of HCl by a red to green color shift. Reproduced and adjusted with permission.[153] 2010, Elsevier.

Figure 10. If the chromophore remains intact upon covalent functionalization, the produced nanofibers show similar colorimetric behavior as the original dyes in solution. Reproduced and adjusted with permission.[154] 2016, The Royal Society of Chemistry.

Figure 11. Ceramic nanofibrous sensors can be produced by covalently linking the dye, here Methyl Red, to a silica precursor. MR-APTES functionalized nanofibers show a clear and reversible color change upon detection of hydrochloric acid and ammonia vapors. Reproduced and adjusted with permission.[118] 2016, WILEY-VCH Verlag GmbH & Co.

Table 3. List of colorimetric nanofibrous sensors produced by techniques that involve the decoration of the nanofiber surface.

Figure 12. Cellulose acetate nanofibers coated with pararosaniline show a visual color change upon detection of formaldehyde. Reproduced and adjusted with permission.[165] 2014 Elsevier.

Figure 13. Multi-jet electrospinning of PVDF/PA 6 nanofibers followed by spotting of L-glutathione-conjugated gold nanoparticles results in a colorimetric sensor for lead ions, which induce the aggregation of the gold nanoparticles. Reproduced with permission.[170] 2014, Elsevier.

Figure 14. The surface of the nanofibers is decorated with rhodamine-cyclodextrin via host-guest interactions, resulting in a colorimetric sensor for mercury ions. Reproduced and adjusted with permission.[171] 2012, The Royal Society of Chemistry.

Figure 15. PVBC nanofibers were post-functionalized with an imidazole derivative PIMH, which is able to form a complex with iron ions. This complexations results in a color shift from yellow to red, providing a selective colorimetric sensor for iron. Reproduced and adjusted with permission.[172] 2013, Elsevier.

Figure 16. During plasma dye-coating the nanofibers are dipped in the dye-solution after which the membrane is treated with a non-thermal plasma to allow for covalent immobilization of the dye. The last step of the procedure consists of removing all residual dye from the nanofibrous membrane.[177]

Author Summary

Karen De Clerck (1970) studied textile materials engineering at Ghent University (Belgium) and textile technology at UMIST-Manchester University (UK). In 2002, she obtained her PhD at Ghent University for which she obtained the 'De Meulemeester-Piot' prize. She was appointed as associate professor at Ghent University in 2007. Her research interests include fiber technology and textile chemistry, with an important focus during the last decade towards the production and functionalization of nanofiber based materials. The group of Prof. De Clerck developed expertise on several in-house designed electrospinning set-ups and the spinning of many (functionalized) polymer systems for a range of advanced applications. She has published > 100 scientific articles. Prof. De Clerck received The Society of Dyers and Colourists Centenary Medal 2013.

Richard Hoogenboom (1978) studied chemical engineering at the Eindhoven University of Technology (the Netherlands). In 2005, he obtained his Ph.D. under the supervision of Ulrich S. Schubert and continued working as a project leader for the Dutch Polymer Institute. After postdoctoral training with Martin Moeller and Roeland Nolte, he was appointed as associate professor at Ghent University in 2010 and in October 2014 he was promoted to full professor. His research interests include stimuli-responsive polymers, supramolecular polymers, and poly(2-oxazoline)s. He has published > 330 scientific articles and is currently associate editor for European Polymer Journal and Australian Journal of Chemistry. Prof. Hoogenboom is the recipient of the inaugural Polymer Chemistry Lectureship (2015), the fifth PI IUPAC award (2016) and the ACS Macromolecules/Biomacromolecules young investigator award (2017).

Ella Schoolaert (1992) graduated from the Faculty of Engineering and Architecture at the Ghent University (Belgium) in 2015 as a Master of Science in Sustainable Materials Engineering with a major in Polymers and Fiber Structures. She started her Ph.D. under the supervision of Prof. Karen De Clerck and Prof. Richard Hoogenboom and obtained an FWO Strategic Basic Research grant in 2016. Her research project is about the functionalization and processing of poly(2-oxazoline)s for the production of nanofibrous sensors suitable for many application areas. During the first year of her Ph.D. she received several awards on poster and shotgun presentations and she published her first article about biocompatible pH-sensors.

Table of Contents Entry

The design of colorimetric nanofibrous materials for advanced, ultrasensitive and user-friendly optical sensors is a hot topic recently. By combining electrospinning and a chromogenic agent, color-changing nanofibers responsive to specific analytes are designed, which are applied in many application areas. This feature article gives an overview of the several techniques used for the production of colorimetric nanofibrous sensors.

Colorimetric nanofibers

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Colorimetric Nanofibers as Optical Sensors