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Harnessing Aryldiazonium Salts Reduction for Tailored Bi-Functionalized Surface Engineering

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Keywords

mixed films, diazonium reduction, simultaneous immobilization, successive graftings, post-functionalization

Abstract

The functionalization of various substrates through the reduction of diazonium salts is a widely used and expanding method, leading to the formation of highly robust functional surfaces, which is essential for specific applications. To further broaden the applications of functional surfaces, it is relevant to control the bi-functionalization with two independent and simple molecules. Some strategies, which differ according to the objectives sought, have been proposed to lead to the formation of such surfaces.

The main objective of this review is to compare the strengths and weaknesses of the methods already described, with a specific focus on their ability to control the layer composition.

Introduction

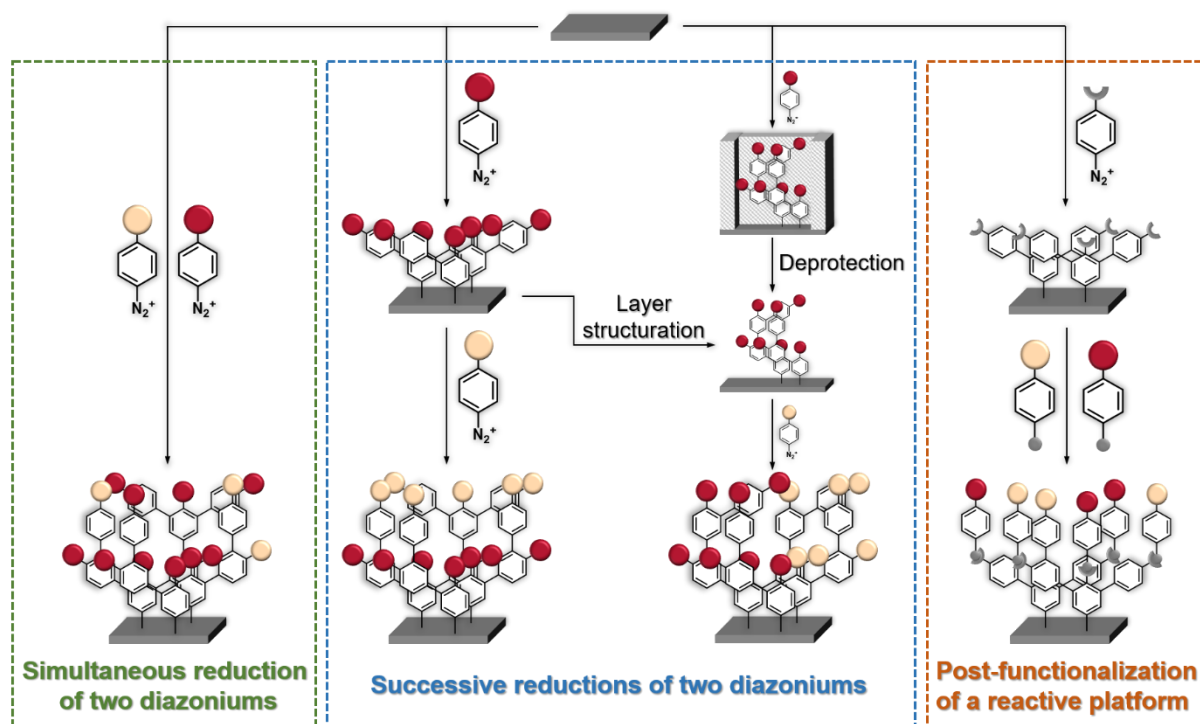
The vast majority of works involving the modification of surfaces by two different entities is based on the development of self-assembled monolayers (SAMs).^{1,2} The popularity of such molecular buildings is primarily driven by the advantages they offer, with the synthetic tunability of their precursors, their organized 2D dimensionality (a single molecular layer) and ease of implementation playing pivotal roles in their development.³ Indeed, they can be easily and

spontaneously obtained by simply immersing a gold substrate in a mixture of organosulphide precursors⁴ or by successively immersing it in two distinct solutions.^{5,6} The proportions of immobilized species may not necessarily mirror the organosulfide proportions of the initial solution, but this parameter is typically controllable either by adjusting the ratio of the two species in the precursor mixture or by manipulating the immersion time in the second precursor solution. As for the distribution of species on the surface, its control is considerably more challenging and often difficult to master, resulting in mixed self-assembled monolayers (SAMs) that are usually disordered and exhibit phase segregation.^{1,7-11} Several alternatives, based either on modifying the design of the engaged molecules or on the protocol used to form the organic layer, have been proposed to address these limitations. Among these, one can mention: i) the use of organosulfur compounds with one anchor and two backbones,¹²⁻¹⁴ ii) the homogenization of the chain lengths of the two precursors,¹⁵ or iii) the use of exchange reactions.¹⁶⁻¹⁹

However, a certain fragility in the molecular structures formed has been demonstrated, particularly under exposure to air,²⁰ heat,²¹ or electrochemical stresses.²² These limitations, problematic for applications requiring exposure to ambient conditions,²³ likely account for the increasing interest in the more robust thin layers achieved through the reduction of aryldiazonium cations. This reduction, whether spontaneous or electrogenerated, gives rise to the formation of highly reactive radicals. When generated in close proximity to a substrate, these radicals lead to the functionalization of the substrate through the deposition of an organic layer. The formation of nitrogen-substrate bonds and azo bridges (-N=N-) within the layer is usually observed,^{24,25} without knowing yet the mechanism involved, whether it comes from a coupling between grafted rings and diazoniums²⁶ or from the direct grafting of aryl diazenyl radicals.²⁷ Conventionally, a direct carbon contact with the substrate is established, which represents a definite advantage in terms of stability.²⁸⁻³⁵

Three different pathways leading to bi-functional surfaces through the reduction of diazonium salts have been described in the literature (Scheme 1):

- the simultaneous reduction of a diazonium mixture,
- the successive graftings of two diazoniums,
- the chemical modification, with two different entities, of a pre-grafted reactive platform.



Scheme 1. Scheme representing the different approaches allowing the elaboration of bi-functional surfaces from aryl diazonium salts.

The objective of this review is to describe the three aforementioned approaches and, above all, to compare them in order to determine their strengths and weaknesses. Before delving into the core of the matter, the first paragraph aims to justify the interest in developing such bi-functional surfaces, to better understand the underlying issues.

What is the interest in developing bi-functional surfaces from two different molecules?

One strategy for developing bi-functional surfaces involves immobilizing sophisticated molecules that bear several constituents, each having a specific property.^{36,37} However, this approach can involve significant upstream synthetic work. Therefore, controlling the bi-

functionalization with several simple molecules is relevant, as the two functional units can be introduced from two independent and, consequently, easier-to-synthesize molecules.

The bi-functionalization of a surface from two different molecules, resulting in organic layers called "mixed layers," also offers other advantages related to the flexibility of this approach. Indeed, mixed systems can show new property that cannot be accessed by pure system of each component.³⁸ With this strategy, if mastered, multiple situations can be envisaged, ranging from diluting active species to improve their reactivity,^{39,40} to exploiting the cooperative nature of complementary properties carried by neighboring species.^{41,42} Unlike the scenario involving a single molecule incorporating both functionalities, mixed layers, wherein the groups of interest are hosted by two distinct molecular entities, enable the coexistence of molecules with diverse lengths^{11,43} and functionalities⁴⁴ on the same surface. This approach can allow for the adjustment of their respective surface coverage and affords more precise control over the layer properties. This is why bi-component layers are gaining increasing attention across various domains, including molecular electronics,¹ sensing,^{45,46} and catalysis.^{47,48} In this context, it seems obvious that controlling the proportions of two different immobilized molecules plays a major role in the development of high-performance bi-functional systems. The challenge lies in adapting a surface engineering strategy to strike control, stability and reproducibility of bi-functional surfaces.

Simultaneous reduction of two diazonium salts

The most intuitive and commonly used approach to develop mixed surfaces through the reduction of aryldiazonium salts is to mix the molecules to be immobilized in a solution and applying a potential able to reduce all these species.

Numerous articles focus on the reduction of diazonium salts mixtures on various substrates such as gold (flat electrode⁴⁹⁻⁵⁶ or nanoparticles^{45,57,58}), chromium,⁵² copper,⁵⁵ iron,⁵⁵ indium tin oxide (ITO),⁵⁹⁻⁶¹ graphene,⁶²⁻⁶⁴ glassy carbon,^{49,50,53,55,62,65-79,47,80} carbon black^{42,55} or carbon nanotubes (CNTs).^{47,81}

Some of these studies explore fundamental aspects and report interesting data regarding the impact of the two diazotized structures on the control of the immobilized species proportions. These results highlight some trends and help identifying the relevant parameter(s) that can be adjusted to achieve a mixed organic layer of controlled composition from the reduction of a binary mixture of diazonium cations. From these studies, it clearly appears that the reduction potentials of the two considered salts play a key role in this control.

When the reduction potentials of the two species to be reduced are very close (within a few tens of mV) and the two molecules are comparable in size, the proportion of the two immobilized entities is very similar to that of the starting mixture. This was highlighted in a study published by Downard et coll., in which two diazoniums - one carrying a protected TIPS-ethynyl group ($E_{\text{red}} = 0.2 \text{ V vs. SCE, 1 M LiCl}$), and the other a protected Fmoc-amine group ($E_{\text{red}} = 0.15 \text{ V vs. SCE, 1 M LiCl}$) - were reduced. After deprotection of the layers obtained and post-functionalization of these reactive platforms, respectively with azidomethylferrocene and 4-nitrobenzoic acid, voltammetric analyzes revealed that a 1:1 ratio of the two diazoniums in solution led to a 1:1 ratio (Fc:Ph-NO₂) on the electrode.⁷⁸ It should be noted that this quantification does not solely depend on the first functionalization resulting from the diazoniums reduction, but also on the respective yield of the post-functionalization reactions (1,3-dipolar cycloaddition and amide bond formation). However, the close ratios of species in the deposition solution and the immobilized state seems to indicate that it is possible to control the composition of the layer - in this particular case - by modulating the composition of the diazoniums mixture.

A slight difference between the reduction potentials of the two species to be immobilized ($\Delta E \leq 200 \text{ mV}$) does not necessarily jeopardize the control of the layer composition. In this case, although the proportion of the immobilized species may slightly differ from that of the constituents in the diazonium mixture, adjusting the concentrations of the two species in the solution allows for the modulation of their respective surface concentrations.^{47,77}

When ΔE is higher ($\Delta E \geq 300 \text{ mV}$), controlling the respective quantities of the two immobilized species becomes less achievable, or even impossible.

A sequential approach, similar to that described by Downard et coll., was reported by M. Etienne et coll involving, as a first step, the preparation of a reactive azide-alkene bifunctionalized anchoring layer.⁴⁷ Ferrocene and Cobaltocenium derivatives were then respectively attached by thiol-ene and CuAAC (Copper (I) assisted Azide Alkyne 1,3 dipolar Cycloaddition) coupling. Electrochemical analysis and X-ray Photoelectron Spectroscopy (XPS) results consistently showed that a fine modulation of the redox probe surface concentrations can be obtained by varying the azide/alkene diazonium derivative ratio used for the anchoring layer preparation. An equimolar surface ratio of ferrocene and cobaltocenium was reached for a 30:70 azide:alkene ratio in the grafting solution, indicating that the azide diazonium derivative is preferentially grafted and/or that the coupling yield of the CuAAC reaction is slightly higher than that of the thiol-ene reaction.

J. Gooding et coll., in turn,⁶⁰ and G. Liu et coll. 2 years later,⁸² encountered difficulties in controlling the stoichiometry of mixed carboxyphenyl (CP) / phenylphosphorylcholine (PPC) layers formed by co-reduction of the corresponding diazonium salts (Figure 1).

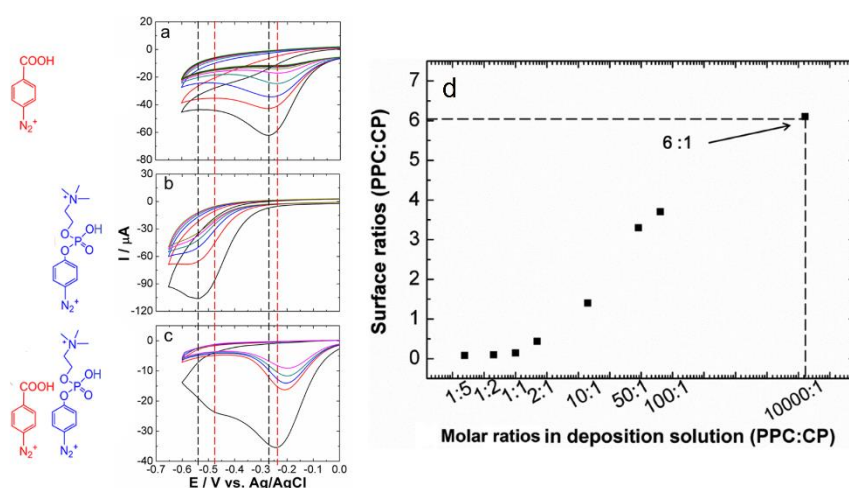


Figure 1. Cyclic voltammograms recorded in a solution containing (a) 1 mM 4-aminobenzoic acid (CP) in 0.1 M HCl, (b) 1 mM 4-aminophenylphosphorylcholine in 0.1 M HCl and (c) 1 mM mixture of 4-aminobenzoic acid (CP) and 4-aminophenylphosphorylcholine (PPC) with 1:1 molar ratio in 0.1 M HCl, with 1 mM NaNO₂ at a scan rate of 0.1 V/s. (d) Comparison of molar ratios obtained by X-ray photoelectron spectroscopy analysis of the surfaces as a function of the molar ratio in the functionalization solution. Adapted from reference 60. Copyright 2016 American Chemical Society.

Not only are the surface ratios significantly different from the ratios in the diazonium solution, but the results also show that obtaining a mixed layer predominantly composed of the PPC derivative - which is more difficult to reduce than its CP equivalent - is not accessible by this route. Indeed, a PPC:CP ratio in solution of 10 000:1 led to only a 6:1 surface ratio.⁶⁰ To overcome this difficulty and homogenize the reduction potentials, the PPC derivative was then co-reduced with a 4-(4-aminophenyl)butyric acid (PBA) derivative.⁶¹ The structural modification of the CP derivative, which involves the incorporation of a n-propyl bridge between the phenyl ring and the acid function to lead to the PBA derivative, proved to be effective since the reduction potential of the latter was shifted from -0.26 V to -0.58 V (both vs. Ag/AgCl), thus reducing ΔE to 30 mV. Thanks to this structural modification, a PPC:PBA surface ratio of 8.1:1 could be obtained from a 9:1 molar ratio in the deposition solution. The key point of this elegant study lies in the removal of the -COOH group (which is electron withdrawing) from the aryldiazonium function, allowing for the screening of its electronic effect on the potential of the reducible species. Using the same idea, B. A. Messerle et coll. varied the structure of aryldiazonium cations substituted with rhodium and iridium complexes. Carbon materials (carbon black and reduced graphene oxide) were functionalized by equimolar mixtures of these two diazonium salts and then analyzed by XPS to determine the proportions of each grafted compound. In this study, which is based on spontaneous grafting and not electrogenerated grafting, the reduction potentials of these two diazonium cations are not mentioned, but one can note that the addition of methylene groups between the functional group and the aromatic ring improves the control of the proportions on the surface. The Ir:Rh ratio determined on the mixed surfaces obtained from an equimolar mixture in the grafting solution thus changed from 1:9 to 3:7 after addition of the methylene spacer in the diazonium structure.⁴²

If the last two aforementioned articles do not extend the studies towards obtaining similar molar ratios between grafted species and those in solution, they nevertheless highlight the beneficial impact of increasing the distance between the functional group and the diazonium function through the introduction of methylene bridges. A recently described method has taken a further

step by introducing a 12-carbon alkyl chain between the aromatic ring and the functional group, thereby canceling out its electronic effect.^{22,83} Such homogenization of the considered diazonium structures has i) standardized the reduction potentials regardless of the end-group ($\Delta E = 50$ mV), ii) enabled equalization of radicals reactivity and iii) uniformized the steric hindrance of the molecules involved, thereby allowing a precise stoichiometric control of immobilized species.⁸⁴ Consistent electrochemical, spectroscopic and XPS results showed that mixed layers with controlled composition closely resembling that of the original diazonium mixture were obtained via this approach.

The impact of the homogenization of structures on the control of the immobilized species proportion has also been clearly demonstrated in the work undertaken by C. Lagrost et coll. on the electrografting of calix[4]arenes. The use of four diazonium cations having a common skeleton and, therefore, close reduction potentials ($\Delta E \leq 120$ mV) led to on-surface molecular ratios close to those of the starting diazonium mixtures.⁵⁴ When the reduction of the two calix[4]arene-tetradiazoniums is chemically ensured (by the addition of a reducing agent such as NaBH_4),^{45,57} the reduction potential is no longer a key parameter since all species are a priori reduced under these conditions. The nearly identical structure of the two species involved remains crucial for controlling the proportions of immobilized species. This ensures both similar reactivities and comparable steric hindrances of the formed radicals, so that the deposition of one is not favored over the other, thus leading to a ratio of immobilized species close to that of the initial diazonium mixture.

Thus, when the structure of the two involved species does not allow the necessary control for the intended application, an alternative can be based on the successive graftings of the considered diazoniums.⁶⁰

Successive graftings of two diazoniums

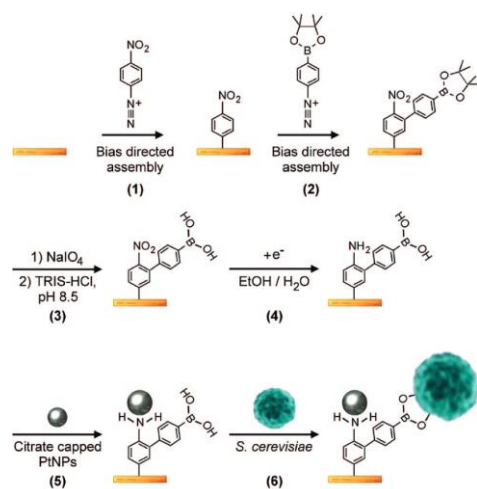
The successive graftings of two diazoniums can offer a much more flexible approach as different deposition protocols can be applied for each diazotized precursor. Playing on the

deposition conditions and set up can thus lead to molecularly mixed layers, physically patterned films or stratified stacks. In the literature, some fundamental works compile information on the modifier ratio that can be expected on the surface depending on the fixed experimental parameters.^{85–88} Additionally, several works have exploited successive graftings to prepare patterned substrates,^{89–92} multifunctional sensing surfaces,^{60,79,93–95} imaging probes for cancer cells⁹⁶ or structured layers that exhibit interesting properties for molecular electronics.^{97–101}

One of the pioneering work reported by Downard et coll. validated the possibility of grafting successive layers using diazonium electroreduction.⁸⁵ This multilayer preparation is made possible by the radical polymerization nature of the reactive species obtained from the diazonium precursors. A first 2-nanometer layer of nitroazobenzene (NAB) was deposited, followed right above by the grafting of a second layer of methylbenzene (MB). Due to the increasing resistance of the film with increasing thickness, the driving force applied for the generation of the top layer was larger than that used for the initial NAB sub-layer (i.e. -600 mV (Ag/Ag⁺) versus -155 mV (Ag/Ag⁺)). Atomic force microscopy (AFM) scratching results unambiguously demonstrated a continuous increase of the top layer up to 3 nm. Interestingly, the electroactivity of the NAB moieties was not significantly perturbed by the presence of the MB covering layer, indicating that the underlying layer can behave as an active material. These results align with an extensive study reported by Daasbjerg et coll. that focused on the electrochemical response of bilayers with various thicknesses, incorporating both electroactive and electro-inactive modifiers.⁸⁶ In the case of a nitrophenyl film covered by a phenyl layer, it was found that, even if thick films always incorporate non-responsive electroactive nitrophenyl groups in their inner part, the presence of a thick nonpolar top layer slows down the electrolyte permeation in the inner sublayer, but without affecting the overall coverage determined. For the reverse case (i.e. phenyl inner film covered by a nitrophenyl layer), kinetic data tend to show that electroactive groups can be treated as a single entity, independent of the nature of the intermediate layer, as long as they are confined to similar conditions and environments in the outer layer. The NAB/MB binary system was also exploited by the Downard's group to

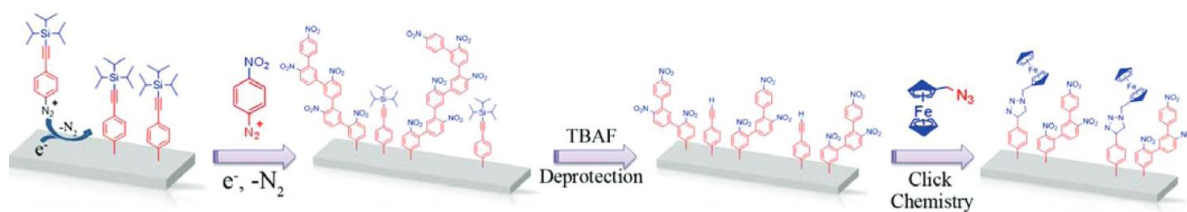
prepare patterned surfaces using an AFM tip.⁸⁹ After a first MB layer grafting, a film section was removed by the AFM tip and the freshly exposed carbon surface was modified by a NAB layer. It was shown that, by generating a first layer with a thickness of at least 2 nm and applying a moderate reduction potential to immobilize the second modifier (typically -0.2 to -0.3 V (Ag)), the latter can be overwhelmingly grafted in the designed pattern. These two studies illustrate the major role played by the driving force in limiting and/or controlling the film thickness thanks to the self-limited electron transfer for increasing film thickness. By mainly manipulating the grafting potential and the number of repetitive voltammetric cycles, relatively controlled bilayers can be obtained, with a thickness ranging from 5 to 20 nm. This convenient approach has been particularly well implemented for the preparation of molecular junctions by the groups of Lacroix^{98,99,101} and McCreery.^{97,99,100}

The limitation of the consecutive electrochemical grafting protocol lies in the poor accessibility of the functional moieties constituting of the inner layer. To ensure true bi-functionality of the film, the outer layer must be limited to a monolayer or a sub-monolayer. Brozik et coll.⁹³ reported a successful example of bi-functional ultrathin layer preparation. In this study, nitrophenyl and phenylboronic pinacol ester were sequentially grafted on a gold substrate, followed by the electrochemical conversion of the nitrophenyl functions into their amine analogous. Aminophenyl groups were exploited to immobilize platinum nanoparticles through electrostatic interaction, while yeast cells were captured by the phenylboronic acid functions (Scheme 2). Increasing the aminophenyl surface concentration from 0.9×10^{-11} to 1.1×10^{-10} mol.cm⁻² had a great impact on the number of immobilized platinum nanoparticles and their activity, but was detrimental to their stability. Having a precise control over the second diazonium's grafting was mandatory to obtain the right compromise and consider a possible application.



Scheme 2. Assembly of a multifunctional thin film electrode surface by a sequential electrografting of 4-nitrobenzene diazonium and phenylboronic pinacol ester diazonium. Reproduced from reference 93. Copyright 2009 American Chemical Society.

An alternative to avoid the tedious control of grafting conditions for each diazonium was developed by Hapiot et coll. by exploiting the protection-deprotection strategy previously reported.¹⁰² In this work, the first layer was prepared by reduction of a silyl-protected alkyne group on a carbon substrate (Scheme 3).⁸⁷ The presence of the bulky triisopropylsilyl-ethynyl group prevents multilayer formation, as confirmed by AFM scratching measurements (i.e. thickness of 0.92 ± 0.17 nm). The subsequent grafting of nitrobenzene diazonium on the loosely packed silyl-protected layer led to a nitrophenyl surface concentration of 8.8×10^{-10} mol.cm⁻², a much lower value than that obtained by directly electrografting nitrobenzene diazonium on bare carbon (i.e. 30×10^{-10} mol.cm⁻²). Finally, the deprotection of the alkyne groups resulted in a loss of one-half of the electroactive nitrophenyl groups, and the film showed a thickness of 2.79 ± 0.16 nm. The CuAAC “click” reaction was tested using azido-methylferrocene on this binary layer, leading to a ferrocene surface concentration of 2.9×10^{-10} mol.cm⁻². By obtaining a well-defined and thin layer with a nitrophenyl/ferrocene ratio of 3/1, this work demonstrated that an effective bi-functional layer can be obtained using the sequential electrografting.



Scheme 3. Principle of the different modification steps using the trisopropylsilyl-ethynyl protected azide group as the starting layer. Adapted from reference 87. Copyright 2011 American Chemical Society.

A further study by Downard et coll. starting with the same diazonium binary evidenced that the critical point for this approach was determined by the final balance between the surface concentration of the two functional groups, which was dictated by the compactness of the first grafted layer.⁸⁸ By first preparing an alkyne-tethered surface, subsequently post-functionalized by ferrocene groups, and then filled using 4-nitrobenzene diazonium, a mixed monolayer characterized by a nitrophenyl/ferrocene ratio of 1/1 was obtained. The authors, however, stated that the presence of nitrophenyl groups coupled to the first grafted layer cannot be excluded.

Post-functionalization of a reactive platform

The post-functionalization method, similar to sequential electroreduction, involves multiple steps. Firstly, a reactive platform is formed on the electrode by reducing a diazonium cation. Secondly, this platform is functionalized by reacting with a mixture of molecules. This approach has proven to be an efficient way to covalently link entities that cannot be directly grafted onto the surface through an electrochemical procedure, replacing the immobilization of organic moieties in a purely chemical framework, where the reaction of the molecules with the platform determines the surface proportions.

Post-functionalization has demonstrated its effectiveness in immobilizing mixtures of entities on vitreous carbon,^{48,103–106} exfoliated molybdenum sulfide,¹⁰⁷ CNTs^{108,109} and carbon nano-ions¹¹⁰). These mixed layers are typically built using peptide coupling^{80,103,106,110} or click chemistry reactions (copper-assisted azide-alkyne cycloaddition - CuAAC^{48,104,105,107,108} or thiol-

ene¹¹⁰). The chemistry used in these coupling reactions has the advantage of simplifying synthetic and purification efforts for attaching functional moieties to the surface, and it is mild and non-destructive for sensitive biological entities such as DNA strands.¹¹⁰

In the case of peptide coupling, platforms made from 4-(carboxymethyl)benzene diazonium have been shown to be effective in the development of biological sensors by co-immobilizing an organic analyte sensor moiety with chains limiting the non-specific adsorption of proteins.¹⁰³

Two sequences can theoretically be employed in such surface modification way: attaching an amine derivative on a carboxy-tethered surface or linking a carboxyl derivative on an aminated surface. However, the two examples reported in the literature both involved, as a first step, the formation of a carboxylic acid anchoring layer, after reduction of the corresponding diazonium salt. E. Creager et coll. were the first to use this approach to develop a sensing surface on a reticulated glassy carbon electrode (RVC).¹⁰³ The carboxy-tethered surface was sequentially coupled to two PolyEthylène Glycol (PEG) amine derivatives, one non-functional and one linking a neutravidin-alkalin phosphatase (NA-ALP), used as an enzyme for the detection of hydroquinone diphosphate. Compared to unmixed layers (i.e. NA-ALP film), the catalytic response obtained showed that the presence of non-functional PEG mixed with the phosphatase efficiently suppressed the non-specific binding on enzymes but the resulting ratio of the two components on the surface was not investigated.

The post-functionalization approach was also applied to modify carbon nano-onion (CNO) with the DNA recognition sequence of Papillomavirus Oncogene and aliphatic alcohol groups.¹¹⁰

Two reactive platforms consisting of carboxyphenyl or 4-maleimide phenyl units were first attached to the CNO via the diazonium chemistry.¹¹⁰ Then an amine derivative and a thiolated derivative of the DNA sequence were respectively coupled to the carboxy-tethered and the maleimide platform in the presence of ethanolamine or mercaptohexanol. The co-immobilization of the DNA and the alcohol group at a 1:100 ratio led to enhanced sensitivities and detection limits compared to the successive coupling protocol involving the backfilling of the surface by ethanolamine after the DNA coupling. These two examples illustrate that the interfacial reactivity of a sensing interface can be improved by the incorporation of a diluting

moiety but systematic characterizations of the ratio of the two immobilized species from the carboxylic reactive platform are needed for a better understanding of the activity enhancement. Surface composition studies were more reported in the case of post-functionalization through click chemistry. The CuAAC, the most common reaction in this field, involves a reaction between azide and alkyne functions, forming a triazole link. The post-functionalization sequence can involve the preparation of an azide-tethered surface followed by a coupling with an alkyne-terminated functional target^{48,105,107–109} or the reverse scheme.¹⁰⁴ The choice of one or the other route is mainly guided by synthetic limitations, and the most straightforward one is preferred.

G. Giambastiani et coll reported two fundamental studies based on the post-functionalization of an azide-tethered platform prepared from exfoliated molybdenum disulfide (MoS₂)¹⁰⁷ and CNTs¹⁰⁸ and in-situ generated 4-azidobenzene diazonium. An equimolar mixture of two different alkynes was involved in a simultaneous post-functionalization of the reactive layer. Characterizations have shown that the ratio of the two coupled alkynes on the surface is different from the ratio in the starting solution in both studies. Notably, the surface ratio was successfully modulated by simply varying the proportions of the reactive mixture. These two studies pointed to the efficiency of the mixed post-functionalization but did not focus on the control of the surface composition.

C. Gautier, T. Breton et coll. reported the preparation of reactive platforms constructed from electroreduced 4-azidobenzene diazonium on carbon (Figure 2).

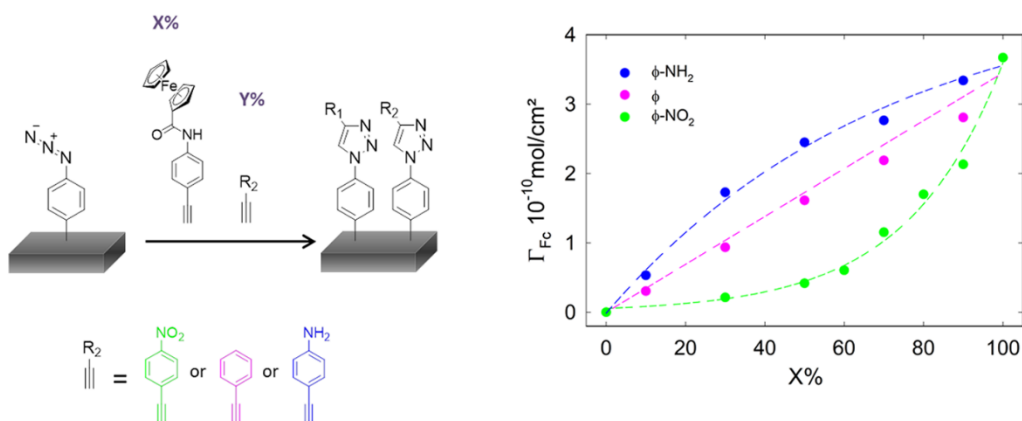


Figure 2. Left: Co-immobilisation of ferrocene and various diluents. Right: Evolution of ferrocene surface concentration as function of the considered diluent and the molar fraction of ferrocene in the co-immobilisation solution. Reproduced from reference 105. Copyright 2018 American Chemical Society.

It was demonstrated that, for a given phenylethynyl derivatives binary, inductive and mesomeric electronic effects of the group in para position of the ethynyl strongly influence the surface proportions obtained. For example, the co-immobilization of a phenyl/phenyl ferrocene binary led to a direct transposition of the solution ratio onto the surface (i.e. linear relationship between the percentage of ferrocene in solution and its surface concentration once immobilized).¹⁰⁵ In contrast, replacing the phenyl by an aminophenyl (donor mesomeric effect) favored the phenyl ferrocene coupling and conversely, replacing the phenyl by a nitrophenyl (withdrawing inductive and mesomeric effect) led to a preferential coupling of the nitrophenyl group. This work provides a general procedure allowing the control of the surface concentration ratio for a given binary.^{107,108} This functionalization sequence was further exploited to prepare TEMPO-tethered surfaces starting from a mixture of TEMPO- and phenyl-ethynyl derivatives. By precisely controlling the surface concentration ratio of the catalytic moiety (TEMPO) and the diluent (phenyl), it was demonstrated that the interfacial activity of the TEMPO can be controlled and enhanced by a dilution effect on the surface.⁴⁸

Since the triple bond of ethynyl platforms can be involved in various coupling reactions, S. Kume et coll. have exploited the reverse scheme of post-functionalization through click chemistry in an elegant biomimetic approach. It was demonstrated that it is possible to selectively trigger two different coupling reactions.¹⁰⁴ As CuAAC and oxidative Glaser-Hay

coupling reactions exploit the reactivity of copper complexes, respectively at the +I degree and +II degree, one reaction or the other can be promoted by applying the appropriate potential. Electrodes functionalized by an ethynyl platform were immersed in a solution containing copper and two redox probes, each sensitive to one of the reactions: ethynylferrocene (Glaser-Hay) and 4-azidodimethylaniline (CuAAC) (Figure 3).

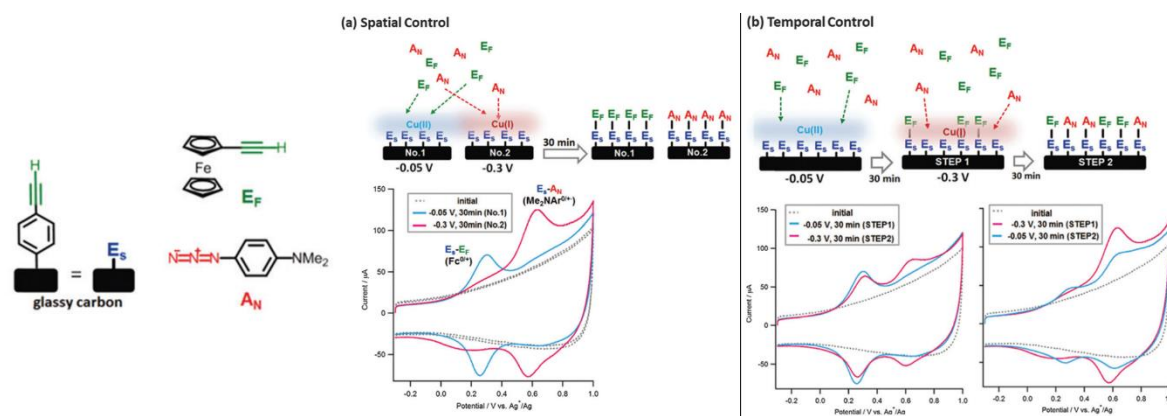


Figure 3. Spatial or time-controlled reaction of a terminal alkyne immobilized on a vitreous carbon electrode. **a)** Simultaneous application of a -0.05 V and -0.3 V potentials to adjacent electrodes. **b)** Sequential application of these potentials on the same electrode. Adapted with permission from reference 104. Copyright 2016 RSC.

The results showed that the Glaser-Hay coupling is favored at low driving force (i.e. -0.05 V), for which copper is under its Cu²⁺ form, whereas CuAAC is favored in the presence of Cu⁺, at higher driving force (i.e. -0.3 V). The success of the sequential post-functionalization demonstrated that starting with the Glaser-Hay coupling does not prevent subsequent CuAAC reactions, but the reverse scheme is much less efficient, likely because a large proportion of the ethynyl platform is already functionalized. Such a difference in reactivity in favor of the CuAAC reaction had already been detailed in the literature.¹⁰⁴

These studies demonstrate that post-functionalization methodologies can lead to high-performance multifunctional layers. However, they require the implementation of multi-step protocols that can affect reproducibility. In addition, couplings usually require long reaction times, often several hours. Depending on the reactivity of the molecule/platform pair, low coupling yields are observed, especially when bulky structures are involved. Additionally, when the reactive layer is made of a multilayered film, species in solution cannot have access to the

inner part of the film and only react with the outer part. Such incomplete functionalization leads to an inherent chemical inhomogeneity in the formed layer.

Conclusion

Surface functionalization through diazonium salt reduction provides a powerful and flexible toolkit for creating robust bi-functional layers. The selection of the method for their formation hinges on the desired surface composition and the complexity of the immobilized molecules.

In this review, we have delved into three main approaches described in the literature: simultaneous reduction of a diazonium mixture, successive graftings of two diazoniums, and post-functionalization of a reactive platform. Each method offers distinct advantages and challenges in controlling the layer composition.

Simultaneous reductions allow precise control when reduction potentials and molecular structures closely match. Conversely, successive graftings offer flexibility and the formation of patterned films, although the immobilized entities may not be intimately mixed. Post-functionalization, while enabling covalent linkage of complex entities, suffers from significant drawbacks inherent to multi-step processes, such as extensive reaction times and incomplete coupling yields, leading to chemically heterogeneous surfaces.

Research on bi-component organic layers obtained through the reduction of diazonium salts is considerably less abundant than mixed SAMs studies. While structural defects causing, for example, low breakdown voltages in traditional mixed SAMs are documented,^{17,111–113} a gap exists in detailed structural analysis of diazonium-derived layers and the impact of their structure on properties. A substantial effort is therefore required to better comprehend the potential of these bi-component surfaces. Future research should concentrate on optimizing the methods discussed in this review to engineer controlled surfaces with enhanced structural integrity and electrical properties.

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