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REVIEW

Functionalization of gold surfaces: recent developments and applications

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Abstract Gold surface chemistry is an important field of nanotechnology. The multiple uses provided by gold surfaces expand the repertoire of possible applications and highlight the need for new strategies to strengthen current research in this field. In this article, we present a brief summary of the advances and applications in the use of gold surfaces reported in 2010. Far from writing a standard review, this manuscript intends to underline some outstanding articles that mark new tendencies in this field.

Introduction

Several decades ago, "surface science" was defined as the study of physical and chemical phenomena that occur at the interface of two phases, including solid–liquid, solid–gas, solid–vacuum, and liquid–gas interfaces [1]. Specifically, surface chemistry could be defined as the study of chemical reactions at these interfaces.

Initially, the term "surface chemistry" was directly related to heterogeneous catalysis, chemisorptions, and physisorptions [2, 3]. The concept of this field has now broadened to include some aspects of nanotechnology.

Surfaces have a long and documented history but it was not until the 1970s that the term "nanotechnology" appeared as such [4], being developed mainly in the late 1980s [5]. Nanotechnology encompasses a broad field that involves the derivatization of a variety of surfaces with a range of molecules that bear distinct reactive groups. These molecules are amenable to being attached to other molecules and are highly informative to researchers. Many types of surfaces, differing in properties, are used in derivatization studies, with glass, silicon, and gold being the most versatile ones. This article focuses on gold surfaces.

The Scifinder® database gives 7316 entries for "gold surface". Analysis of these results by year of publication shows that the number of articles related to this subject increased from 297 papers in 2001 to 555 papers in 2010. Thus, in less than 10 years the number of studies relating to gold surfaces doubled, reflecting the increasing relevance of this field (Fig. 1).

Analysis of the papers published in 2010 indicates the striking broadness of this term. Gold surfaces are not used for only one purpose, but have multiple and varied applications. New uses combining various aspects of gold surfaces are developed every year. Innovative strategies for pre-existing assays as well as for novel applications, or even combinations of two uses reported in one new assay, can be found in the literature.

Comparison of the ten subjects on gold surfaces with the highest number of publications allows appreciation of the amplitude to the topics covered. However, self-assembled monolayers (SAMs) are, by far, the most commonly discussed topic (Fig. 2). Of note, recent studies on gold surface chemistry fall into two or more fields, thereby

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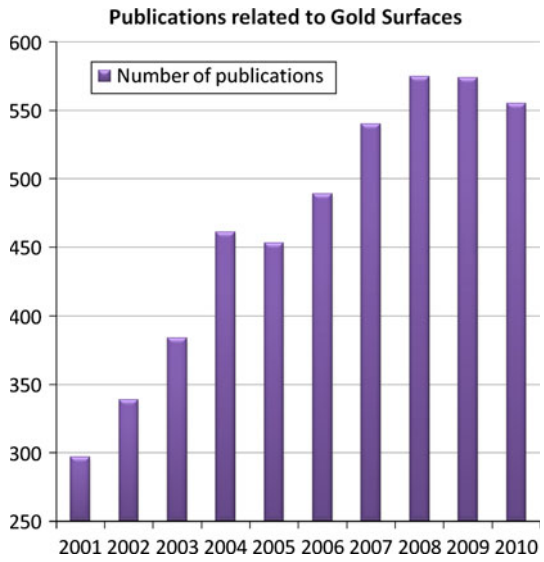

Fig. 1 Publications related to gold surfaces classified by years

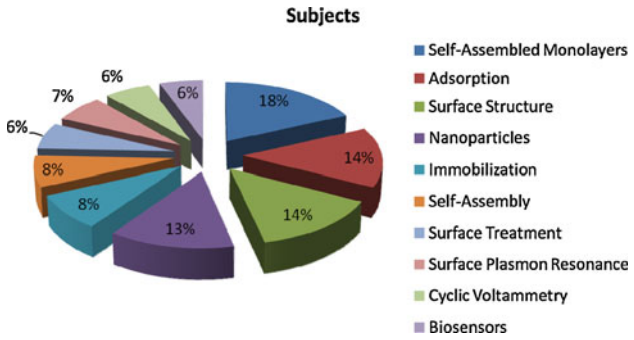

Fig. 2 Relative percentages of the ten most published subjects related to gold surfaces

demonstrating that this chemistry is a widely applied tool in modern science.

SAMs on gold surfaces and gold nanoparticles (AuNps) will be the two main topics discussed in this paper.

From conventional to non-standard SAMs

The use of SAMs [6] is the most widely used strategy for studying gold surface modification. New synthetic strategies and applications for SAM immobilization are being developed, thus making these monolayers a hot topic. The capacity to construct tailored surfaces with a range of functionalities for diverse purposes is envisaged in many studies. As an example, Zhang et al. [7] designed new strategies to functionalize gold surfaces with maleimide groups using aminophenyl to form SAMs. This approach is crucial to immobilize biomolecules onto the surfaces. Furthermore, non-standard SAMs, created by the functionalization of hyaluronic acid on a thiosemicarbazide–gold surface, have been used to study quartz crystal balance and XPS. This research illustrates the use of the bifunctional scaffold for cell culture applications [8]. In this regard, studies on cell migration in patterned gold surfaces [9] continue to be one of the most recurrent subjects, with new variations appearing regularly in the application. With the aim to observe epithelial cell migration, surfaces dynamically designed to switch from adhesive to non-adhesive properties have been developed [9].

Various molecules differing in their properties have been attached to gold surfaces, thereby resulting in more sophisticated and more efficient immobilization processes. Kengne-Momo et al. [10] used an electrochemical process to functionalize a gold surface with sulfanilic acid and subsequently modified it to sulfonyl chloride to attach antibodies through the nucleophilic nitrogen atoms of the protein to form the final sulfonamide bonds.

The interests of materials science are driven towards hybrid materials. In this regard, the immobilization of polymers on gold surfaces has been reported by Dubacheva et al. [11]. The creation of multilayer polymer film systems on these surfaces has many applications in materials science, such as the coating of biological material and self-supporting membranes to enhance mechanical properties.

The direct immobilization of biomolecules onto gold surfaces has also been the focus of many recent studies. To better understand the absorption of biomolecules, Hoefling et al. [12] used computational methods to study direct amino acid absorption on gold surfaces, and the preferential position they adopted once immobilized. This study has greatly paved the way to improve these systems through removal of intermediate steps or linkers. Similarly, Wolny et al. [13] described the immobilization of biotin-binding proteins, such as avidin, neutravidin, or streptavidin, directly on the gold surface. They assayed adsorption on silica and on gold, succeeding only on the latter. Nevertheless, the optimal orientation of the biotin-binding proteins is still unresolved. However, as previously explained, the difficulty to find a proper linker leads to the need for trials aimed at optimizing and discovering new applications in this field.

Many other examples of SAM formation are explained by González et al. [14] and Scheppokat et al. [15]. The former describes the use of fluorophores (Fig. 3) as macromolecules that can be organized as SAMs on gold surfaces for the development of new organic materials. In the second publication, force AFM studies show that glycosurfaces previously coated with mercapto-alkyl-PEG simulate, at single molecule level, sugar-binding affinities.

Chandekar et al. [16] report the thermal stability of thiol and silane monolayers. Almost all SAM applications focus on the biological field, thus, making sterilization necessary or advisable in some cases. In this regard, the results they

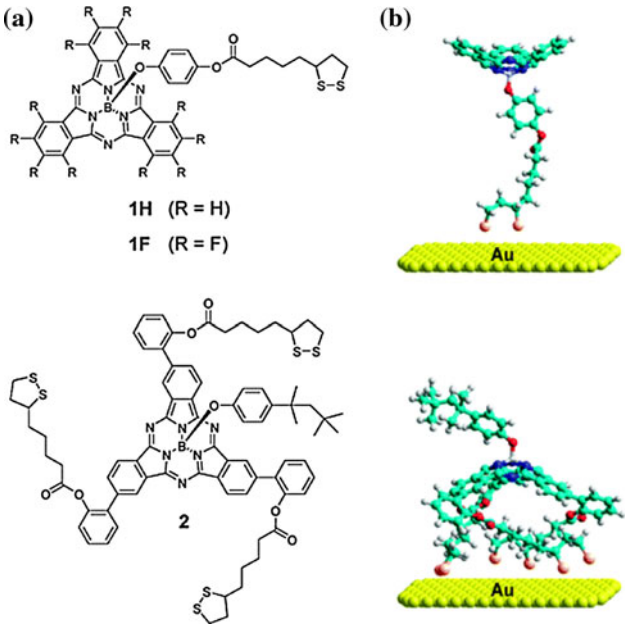

Fig. 3 **a** Structure of the corresponding fluorophores (Subphthalocyanines) **1H**, **1F** and **2**. **b** Molecular models of their respective monolayers on a gold surface. Reprinted with permission from Ref. 14. Copyright© 2010 American Chemical Society

obtained suggest that silicon-based SAMs are more stable when subjected to high temperatures while thiol monolayers, in general, prefer moderate temperature conditions. Furthermore, the authors show the dependence of the thermal stability on the specific thiol attached on the surface. While 1-octadecanethiol degrades at 110 °C, the mercaptohexadecanoic acid does it at 145 °C. This can suggest that are still within the limit for use in autoclaves, which rise the temperature until 134 °C.

AuNPs in combination with flat gold surfaces

Although it may appear that AuNPs [17]–[19] cannot be treated as gold surfaces due to their shape and their colloidal nature, strictly speaking these particles can be approached in a similar way to flat gold surfaces, such as the case of chips. Consequently, the inclusion of AuNPs as gold surfaces extends the number of subjects in surface chemistry.

AuNPs have been used for many applications [20], among these the following: (i) drug delivery, where AuNPs are functionalized by an active compound [21] able to bind to receptors [22] that are overexpressed in some types of cancer; (ii) tumor imaging, in which AuNPs are labeled with molecules that recognize specific proteins from tumoral cells; [23] (iii) thermal cell destruction, a method used to treat cancer; in addition these particles can be used as a heat source [24] for the manipulation of tissues; and (iv) sensors, to measure the concentration of DNA sequences [25]. These are just a few illustrative examples of the many applications of AuNPs.

However, the most promising aspect is the new avenues opening up as a result of the multiple uses derived from combining flat gold surfaces with AuNPs. In 2010, many publications reported this combination.

Cheng et al. [26] immobilized AuNPs on gold surfaces using SAMs for the detection of bacteria biomarkers. The technique used for measurement was Raman Scattering [27], which is enhanced for this hybrid system, in particular, resulting in an improvement in the optical properties of the technique. In this regard, other articles [28] show the optimization of this kind of immobilization between AuNPs and the surfaces using alkyldithiols to build 3D biosensors for XPS [29] (X-Ray Photoelectron Spectroscopy), a technique that characterizes the elemental composition of the surfaces. Such as the case of Snow et al. [30] that study the self assembly conditions to increase the packing density and the number of free thiols with the aim of enlarging the number of AuNps on the planar surface. Gehan et al. [31] also used this hybrid system; however, in this case, the formation of SAMs was performed via electroreduction [32] and the attachment to the AuNP was accomplished through click chemistry [33] (Fig. 4). The aim of this system, once again, is to enhance the optical properties of the surface to perform Surface Enhanced Raman Scattering (SERS).

The publications analyzed also included applications without using the combination of gold surfaces and AuNPs, such as the study by Boronat et al. [34], in which the catalytical activity of several nanoparticles is examined by measuring the adsorption and dissociation of molecular O_2 on them.

Interestingly, all these new applications are fueling the discovery of more basic applications for AuNPs. Hence, these particles can improve surfactants (a crucial step to stabilize colloidal solution), particularly, when they are functionalized with peptide nucleic acids [35].

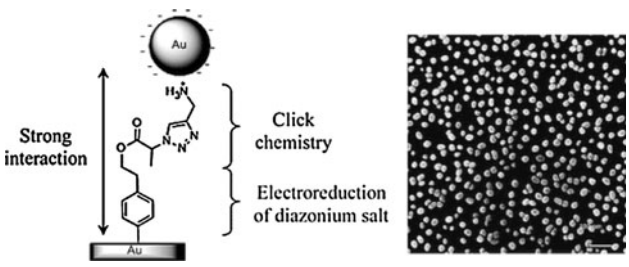

Fig. 4 Surface modification of gold electrodes by click chemistry. Reprinted with permission from Ref. 31. Copyright© 2010 American Chemical Society

Insertion of the gold surface in applications and techniques

Another application of gold surfaces is their integration into devices, such as sensors, for the quantification of a range of parameters.

Once again, the variety of devices or applications is as wide as the imagination of the researchers involved. The main classification in sensors is caused by the source of detection, which can be electrochemical or optical, among others. The study of biosensors is crucial since these devices are intended to facilitate life in general, and are widely used in industrial processes as well as in diagnostic medicine, among other applications. Considerable attention has been devoted to the design of biosensors based on impedance measurements. One example of this use has been applied to cheese production [36]. In that case a SAM on a gold surface was designed to study the coagulation of milk micelles (Fig. 5).

Sensors to carry out studies on carbohydrate–protein interactions, which are crucial for many cell processes, are also reported in the literature. A specific type of photo-coupling chemistry for the construction of carbohydrate microarrays that can be analyzed by SPR [37, 38] imaging has been developed. In this case, SAMs are based on perfluorophenyl azides, onto which the carbohydrates are attached. Once again, a great variety of linkers to promote the immobilization of non-derivatized biomolecules have been examined.

Studies to improve the design of a gold surface biosensor are also described by Lee and Han [39]. They designed a polydimethylsiloxane (PDMS) nanofluidic preconcentrator of the sample to decrease the amount of sample required in the detections where a low concentration of the biomarkers is present.

Micro-electromechanical systems (MEMS) are also an interesting field. There is an increasing need for hybrid devices made of biocompatible material. With this aim, Ouellet et al. [40] described a methodology to bind carboxy-coated gold surfaces to aminated PDMS, thus forming an irreversible amide bond that confers the hybrid structure.

Gold surfaces are also present in the development of single-walled carbon nanotubes [41, 42]. Metal surfaces are designed to accommodate the carbon nanotubes. Sakashita et al. [43] described the suitability of rough gold for the formation of nanotubes.

Due to the extraordinary properties of carbon nanotubes, their possible derivatization with a thiol linker (Fig. 6), which would allow their attachment onto a gold surface, as described by Minati et al. [44], opens up the way for the future enhancement of their sensing properties.

Many techniques use gold surfaces as a support. This is the case of the SAM desorption ionization [45, 46]

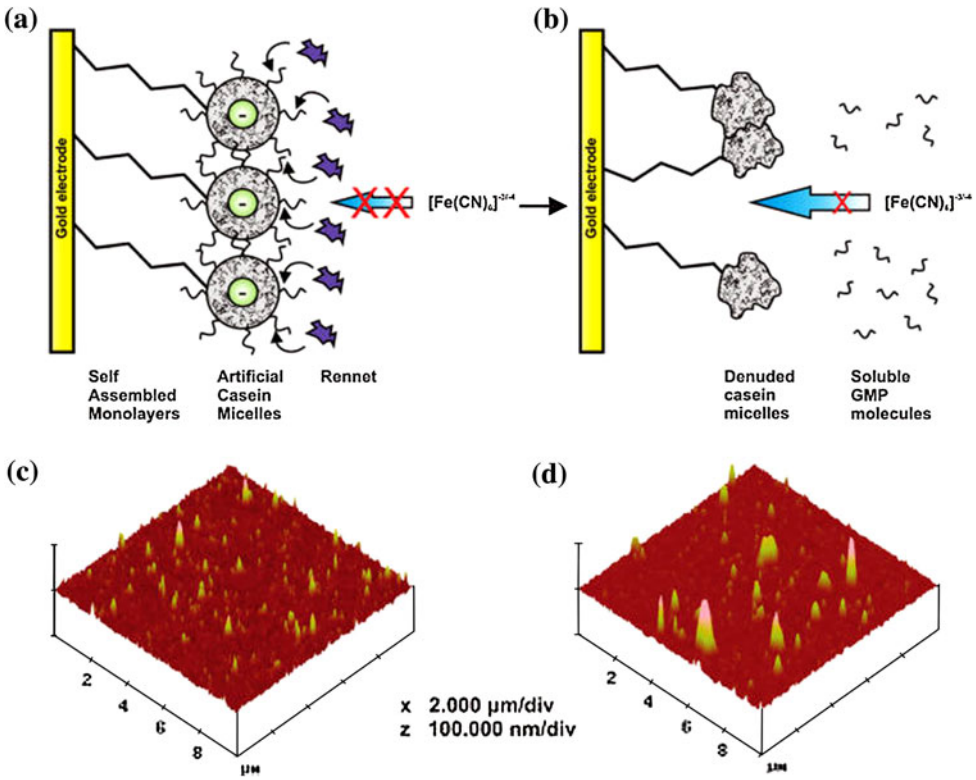

Fig. 5 Idealized view of Au/SAM/ACM electrodes (**a**) before and (**b**) after their interaction with rennet (Natural complex of enzymes that cause milk coagulation) AFM micrographs obtained from Au/DTSP/ACM surfaces (**c**) before and (**d**) after incubation in a rennet solution. Drawings **a** and **b** are not true scale. Reprinted with permission from Ref. 36. Copyright© 2010 American Chemical Society

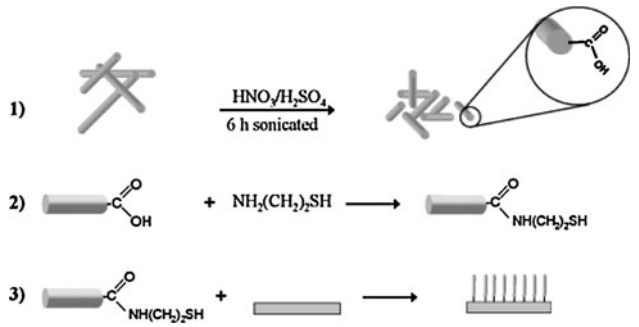

Fig. 6 Scheme of functionalization processes and reactions. *1*) Cutting of the MWCNT by means of the HNO_3/H_2SO_4 mixture and *2*) condensation reaction between thiol and carbon nanotubes. *3*) Representation of the chemical adsorption of the thiol-functionalized carbon nanotubes on the gold plate. Reprinted with permission from Ref. 44. Copyright© 2010 Elsevier

(SAMDI), which allows the study of molecular interactions or reactions on gold surfaces by attaching the substrate of interest to a thiol maleimide linker, and then performing a MALDI assay on the gold surface to obtain the mass of the molecules adsorbed. Developed by Mrksich and co-workers, this powerful technique allows the identification of substrates for specific enzymes, as described in Gurard-Levin et al. [47]. (Fig. 7), as well as the study of a cell adhesion receptor inhibitor that promotes cell migration [48].

Regarding the mass detection of SAMDI, this technique is mainly an improvement of TOF–SIMS [49] in some aspects, a very similar technique that also requires gold surfaces but with some limitations regarding the characterization of bioreactions. However, Johnson et al. [50] described new equipment to measure the mass-selected ions on surfaces. This advance extends the potential applications of this technique to include catalysis studies.

Dip-Pen nanolithography [51, 52] is another technique that could be defined as the smart functionalization of the surface. In the same way as a pen deposits ink on a paper, Dip-Pen nanolithography deposits molecules on the gold surface through an AFM tip. Due to the versatility and precision of this method, which can work at nanoscale, it has a wide variety of applications. One of these was described by Curran et al. [18]. They patterned the gold surface with nanodots that differed in terminal functionalities, with the aim to detect whether these differences affected the behavior of stem cells. This study was principally aimed to a future use in regenerative medicine.

Outlook

Here, we have provided a brief summary of the papers published in 2010 on research related to gold surfaces. On

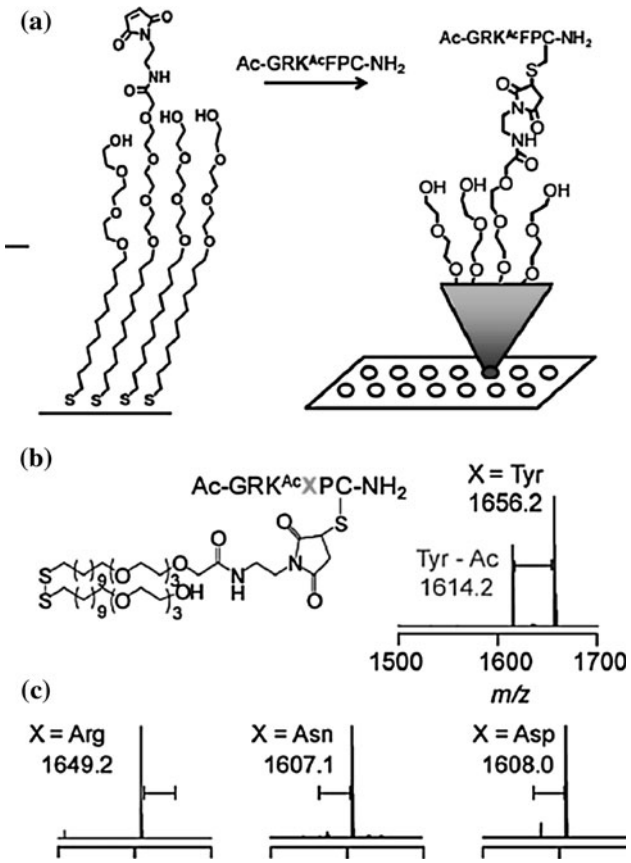

Fig. 7 SAMDI follows the deacetylation of peptides immobilized to maleimide-terminated self-assembled monolayers. **a** An array of self-assembled monolayers presenting maleimide groups allows the specific immobilization of cysteine-terminated peptides in an even orientation and density. **b** The structure of the monolayer and immobilized peptide and the corresponding SAMDI spectrum after treatment with the enzyme. **c** A series of representative SAMDI spectra where a shift of 42 *m/z* corresponds to a deacetylation reaction. *Gray* spectra indicate reactions where the enzyme showed high activity for the substrate. Reprinted with permission from Ref. 47. Copyright© 2010 American Chemical Society

the basis of our bibliographical analysis, we conclude that current uses of gold surfaces demonstrate the diversity and consolidation of this scientific field, and although some cases still require further improvement, the studies suggest the open way to success. The future of gold surface chemistry passes through the combination of various applications and uses to enhance the properties of each approach, what reflect that new applications are still very much in demand. Thus, synergies of the combined approaches are expected to contribute to the development of this highly promising field of research.

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References

1. Prutton M (1994) Introduction to Surface Physics. Oxford University Press, Oxford
2. Christmann K, Schober O, Ertl G, Neumann MJ (1974) Chem Phys 60:4528
3. Conrad H, Ertl G, Latta EE (1974) Surf Sci 41:435
4. Taniguchi N (1974) Proc Int Conf Prod Eng Tokyo 18–23
5. Drexler EK (1986) The coming era of nanotechnology. Anchor Books, New York
6. Love JC, Estroff LA, Kriebel JK, Nuzzo RG, Whitesides GM (2005) Chem Rev 105:1103
7. Zhang X, Sun G, Hovestädt M, Syritski V, Esser N, Volkmer R, Janietz S, Rappich J, Hinrichs K (2010) Electrochem Commun 12:1403
8. Tanaka N, Yoshiike Y, Yoshiyama C, Kitaoka T (2010) Carbohydr Polym 82:100
9. Raghavan S, Desai RA, Kwon Y, Mrksich M, Chen CS (2010) Langmuir 26:17733
10. Kengne-Momo R, Jeyachandran Y, Assaf A, Esnault C, Daniel P, Pilard J, Durand M, Lagarde F, Dongo E, Thouand G (2010) Anal Bioanal Chem 398:1249
11. Dubacheva GV, Dumy P, Auzely R, Schaaf P, Boulmedais F, Jierry L, Coche-Guerente L, Labbe P (2010) Soft Matter 6:3747
12. Hoefling M, Iori F, Corni S, Gottschalk K-E (2010) ChemPhysChem 11:1763
13. Wolny PM, Spatz JP, Richter RP (2009) Langmuir 26:1029
14. González-Rodríguez D, Martínez-Díaz MV, Abel J, Perl A, Huskens J, Echegoyen L, Torres T (2010) Org Lett 12:2970
15. Scheppokat AM, Gerber A, Schroven A, Meinke S, Kopitzki S, Beketow E, Thimm J, Thiem J (2010) Eur J Cell Biol 89:39
16. Chandekar A, Sengupta SK, Whitten JE (2010) Appl Surf Sci 256:2742
17. Giljohann DA, Seferos DS, Daniel WL, Massich MD, Patel PC, Mirkin CA (2010) Angew Chem Int Ed 49:3280
18. Curran JM, Stokes R, Irvine E, Graham D, Amro NA, Sanedrin RG, Jamil H, Hunt JA (2010) Lab Chip 10:1662
19. Sardar R, Funston AM, Mulvaney P, Murray RW (2009) Langmuir 25:13840
20. Sperling RA, Rivera Gil P, Zhang F, Zanella M, Parak WJ (2008) Chem Soc Rev 37:1896
21. Gibson JD, Khanal BP, Zubarev ERJ (2007) Am Chem Soc 129:11653
22. Jain PK, El-Sayed IH, El-Sayed MA (2007) Nano Today 2:18
23. Qian X, Peng X-H, Ansari DO, Yin-Goen Q, Chen GZ, Shin DM, Yang L, Young AN, Wang MD, Nie S (2008) Nat Biotechnol 26:83
24. Pissuwan D, Valenzuela SM, Cortie MB (2006) Trends Biotechnol 24:62
25. Nam J-M, Stoeva SI, Mirkin CA (2004) J Am Chem Soc 126:5932
26. Cheng H-W, Luo W-Q, Wen G-L, Huan S-Y, Shen G-L, Yu R-Q (2010) Analyst 135:2993
27. Graham D (2010) Angew Chem Int Ed 49:9325
28. Morel A-L, Volmant R-M, Méthivier C, Krafft J-M, Boujday S, Pradier C-M (2010) Colloid Surf B 81:304
29. Surman DJ, Blomfield C, Roberts A, Moffitt C (2010) Microscopy Microanal 16:358
30. Snow AW, Foos EE, Coble MM, Jernigan GG, Ancona MG (2009) Analyst 134:1790
31. Gehan H, Fillaud L, Felidj N, Aubard J, Lang P, Chehimi MM, Mangeney C (2009) Langmuir 26:3975
32. Evrard D, Lambert F, Policar C, Balland V, Limoges B (2008) Chem Eur J 14:9286
33. Kolb HC, Finn MG, Sharpless KB (2001) Angew Chem Int Ed 40:2004
34. Boronat M, Corma A (2010) Dalton Trans 39:8538
35. Duy J, Connell L, Eck W, Collins S, Smith R (2010) J Nanopart Res 12:2363
36. Panagopoulou MA, Stergiou DV, Roussis IG, Prodromidis MI (2010) Anal Chem 82:8629
37. Smith EA, Corn RM (2003) Appl Spectrosc 57:320A
38. Hutter E, Fendler JH (2004) Adv Mater 16:1685
39. Lee J, Han J (2010) Microfluid Nanofluid 9:973
40. Ouellet E, Yang CWT, Lin T, Yang LL, Lagally ET (2010) Langmuir 26:11609
41. Kiang C-H, Goddard WA, Beyers R, Bethune DS (1995) Carbon 33:903
42. Wang X, Li Q, Xie J, Jin Z, Wang J, Li Y, Jiang K, Fan S (2009) Nano Lett 9:3137
43. Sakashita T, Miyauchi Y, Matsuda K, Kanemitsu Y (2010) Appl Phys Lett 97:063110
44. Minati L, Speranza G, Torrengo S, Toniutti L, Migliaresi C, Maniglio D, Ferrari M, Chiasera A (2010) Surf Sci 604:1414
45. Mrksich M (2008) ACS Nano 2:7
46. Mrksich M (2008) Mater Matters 3:67
47. Gurard-Levin ZA, Kilian KA, Kim J, Bähr K, Mrksich M (2010) ACS Chem Biol 5:863
48. Shabbir SH, Eisenberg JL, Mrksich M (2010) Angew Chem Int Ed 49:7706
49. Benninghoven A (1994) Angew Chem Int Ed 33:1023
50. Johnson GE, Lysonski M, Laskin J (2010) Anal Chem 82:5718
51. Braunschweig AB, Huo F, Mirkin CA (2009) Nat Chem 1:353
52. Salaita K, Wang Y, Mirkin CA (2007) Nat Nano 2:145