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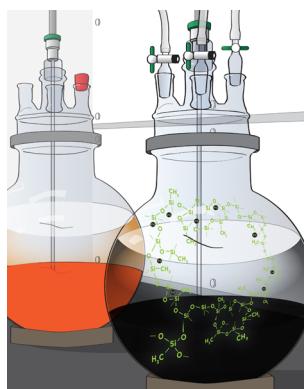
The Sol–Gel Route to Advanced Silica-Based Materials and Recent Applications

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1. INTRODUCTION

1.1. Historic Perspective

Silica and doped silica materials obtained via the solution–gelation (“sol–gel”) inorganic polymerization process are functional materials with an impressive range of applications, including the two pillars of the chemistry practice, synthesis and analysis, but also controlled release, protective coatings, adsorption, chromatography, separation, biotechnology, energy conservation, cultural heritage restoration, environmental remediation, and many other fields of contemporary technology.¹ Moreover, sol–gel glasses are highly transparent and have a variety of optical applications.²

The term “sol–gel” was coined by Graham in 1864 during his work on silica sols.³ In 1640, van Helmont had discovered “water glass” by dissolving silicate materials in alkali and then precipitating silica gel upon acidification.⁴ In 1846, Ebelmen observed the formation of a transparent glass following exposure to the atmosphere of a silane obtained from SiCl_4 and ethanol.⁵ In 1866, Nobel discovered that explosive nitroglycerine adsorbed on kieselguhr, a diatomite silica mined in Germany, was chemically stabilized, allowing much safer transport and handling than nitroglycerin in its raw form. He patented this mixture as “dynamite”, and this, still today, is the most important commercial product of an entrapped organic substance (oil) within silica.⁶

Early sol–gel technology is based on patents from the first 1900s.⁷ Patrick, during his doctoral studies at the University of Goettingen in 1912–1915, devised an economically viable and rapid sol–gel method to make silica gel from sodium silicate (Na_2SiO_3) in large quantities.⁸ Besides being an excellent desiccant (dehumidifying agent), silica gel was found highly effective in adsorbing the infamous “mustard gas” [$\text{S}(\text{CH}_2\text{CH}_2\text{Cl})_2$] from the air, and found immediate use in soldier’s gas masks during World War I. He patented his method in 1919 and established a company to manufacture silica gel in Baltimore, MD.⁹

Kistler, in 1931, described the first synthesis of a highly porous silica (SiO_2) form, which he dubbed “aerogel”, by supercritically drying the gel obtained by hydrolytic polycondensation of silicic acid $[\text{Si}(\text{OH})_4]$.¹⁰

This first example of practical use of SiO_2 gel evidences how, historically, silica gels have been used as functional, rather than

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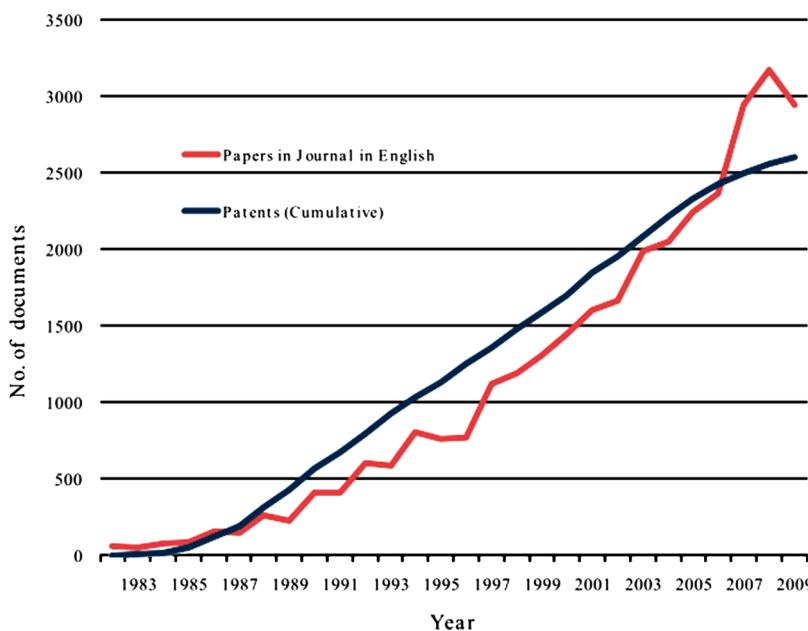
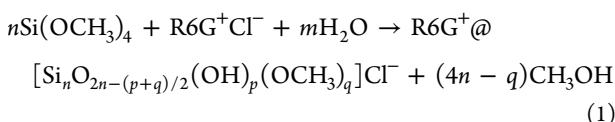


Figure 1. Publications in the sol–gel materials field, 1982–2010. Reprinted with permission from Dr. C. J. Barbé. Copyright 2013 Dr. C. J. Barbé.

structural, materials ever since their very first inception. This aspect was also emphasized in Iler's seminal book on silica,¹¹ in the late 1970s, wherein a variety of functional applications of silica gels were described. These structure-driven properties were, at that time, mostly based on the surface chemistry of SiO₂, as well as on its very large and tunable porosity. "Sooner or later", Iler was somehow prophetically writing in 1978, "in such diverse fields as industrial chemistry, electronics, agriculture...and even biochemistry and medicine, problems arise involving this common element oxide."

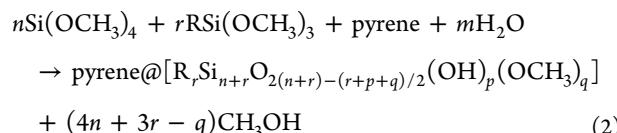
In 1949, Dickey entrapped organic dyes in a silica matrix prepared at room temperature starting from an aqueous solution of sodium silicate.¹² Aiming at preparing the first silica template material capable of selectively adsorbing molecules with structure resembling that of the template, he further removed the dyes by extraction with methanol and assessed selective adsorption by UV spectroscopy.

The radical chemical innovation, however, occurred in 1984, when Avnir and co-workers reported the sol–gel entrapment of a dye, rhodamine 6G, in a silica matrix obtained by basic hydrolysis of a silicon alkoxide, tetramethoxysilane [TMOS, Si(OCH₃)₄], followed by room-temperature condensation (eq 1, where $m = 2n + (q - p)/2$):¹³



The sol–gel polycondensation was simply carried out in the presence of the dye in solution. The resulting transparent doped silica glass was nonleachable in water and in methanol and did not show any aggregation up to a 1.6×10^{-4} M concentration in the glass, smoothly fluorescing as the result of excitation of non aggregated dye molecules homogeneously entrapped in the inner porosity of the gel. Moreover, the authors recognized that encapsulation resulted in enhanced photostability and thermal stability. The chemistry of doped silica glasses or, better said, "for obtaining chemical interactions",¹⁴ was born.

Shortly afterward, the same researchers in Israel entrapped another dye precursor, pyrene, in what they called "reversed-phase organic silica gel",¹⁵ starting from a mixture of an organically modified silane (phenyl or ethyl trimethoxysilanes, RSi(OCH₃)₃) along with Si(OCH₃)₄. Now, the organic modification of the SiO₂ matrix allowed room-temperature phosphorescence and photochromism in the resulting inorganic–organic, or "hybrid", sol–gel materials (eq 2, where $m = 2n + (3r + p - q)/2$):



In 1990, Avnir and co-workers reported that the approach to utilize molecules via structural organization in the solid-state framework of porous silica could surprisingly (alcohol released in the sol–gel process is a denaturing agent) be extended to enzymes,¹⁶ opening the route to practical applications of biotechnology (such as biocatalysis, biosensing, bioremediation, and biomedical materials)¹⁷ that had remained unfulfilled due to lack of stability of most entrapping matrixes.

Environmental and clean energy concerns were responsible for another impetus on the search for new sol–gel materials. For example, recent results with doped sol–gels of long-lasting photobioreactors and biofuel cells, which can advantageously exploit solar radiation to convert polluting carbon dioxide into useful biofuels and electricity,¹⁸ constitute a significant advance toward the practical chemical exploitation of solar energy. By the same token, the huge development that followed from the introduction of the term "nanocomposite"¹⁹ in 1986 resulted from a combined effort of academic and industrial research inspired by the growing demand for novel ecofriendly materials (biodegradable and nontoxic), produced with lower energy consumption and possibly from renewable resources.

Since the late 1980s, the sol–gel method has evolved into an advanced chemical technology, affording countless functionalized materials capable of satisfying the "insatiable"²⁰ society's

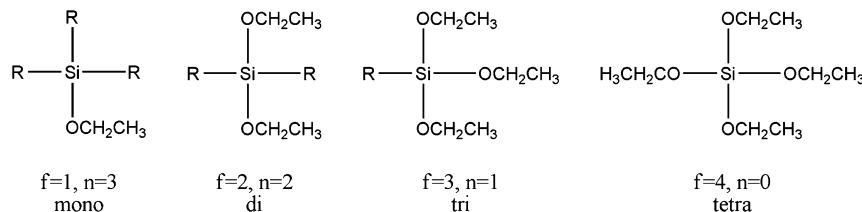


Figure 2. ORMSIL functionalities. A tetra-functional silicon alkoxide ($n = 0$) acts as a “network forming” structure, a trifunctional silicon alkoxide ($n = 1$) behaves as a “cross-linker”, a difunctional silicon alkoxide ($n = 2$) behaves as a “bridging” agent, and a monofunctional silicon alkoxide ($n = 4$) can be used as a “terminating” agent.

demand for new and purposeful materials, as testified by a continuous increase in published papers, conferences, and patents (Figure 1).²¹

The first major account on the sol–gel process published by Hench²² in 1990 was followed, in 1995, by the first report²³ dealing with organic chemistry within doped silica materials. Numerous comprehensive reviews were published afterward, including recent accounts on sol–gel sensors,²⁴ coatings with optical activity,²⁵ and electrochemistry within doped sol–gel.²⁶ The field is currently so broad that journal thematic issues are frequently devoted to sol–gel chemistry and materials.²⁷ In this context, an overview on the state of the art and the perspectives of sol–gel silica-based materials is timely for two main reasons.

First, there is a need for a perspective and unified view on the actual development of the science and technology behind these advanced materials, especially in light of the fast growth in scientific publications addressing disparate new applications in fields as diverse as catalysis for fine chemicals and healthcare. Second, there is a strong contemporary research interest in clean energy and environmental issues. However, there are more than 2000 studies devoted to silica-based sol–gel nanocomposites alone. Hence, there are two options to review this activity: either to systematically review the different studies, an approach that is almost impossible in this field (unless the review covers only a limited period), or to summarize the main achievements and draw some useful conclusions that offer a perspective view on contemporary sol–gel science and technology.

Following the latter approach, this account focuses on a selection of recent advances to identify emerging trends. In the conclusions, we emphasize that the widespread emergence of sol–gel-derived products and technologies implies also important educational consequences for the undergraduate and graduate chemistry curricula. Overall, this approach will hopefully help the readers to make decisions that may open new trends in their own projects or even start new research projects.

1.2. Achievements in Sol–Gel Technology

Following Patrick’s findings, in 1939 Geffcken and Berger of Schott Glaswerke, in Germany, developed a sol–gel method for preparing single oxide coatings,²⁸ whose large-scale production for coating automotive rear-view mirrors started in 1959. In 1969, Dislich and Hinz, at the same company, reported that any type of multicomponent oxide (amorphous and crystalline substances) could be synthesized via sol–gel from the alkoxides of the different elements.²⁹ The resulting ceramic materials were termed either “xerogels”, when drying was carried out by a mild desiccation step, or “aerogels”, when drying was achieved under supercritical conditions.

In 1942, Monsanto began production of the first commercial aerogel, trade named Santocel, using Kistler’s high pressure

Na_2SiO_3 polycondensation induced by sulfuric acid and slow salt elimination.³⁰ These aerogels were used as additives or thixotropic agents in cosmetics and toothpastes, and also as insulators for freezers and oxygen-producing plants.

Aiming to use SiO_2 aerogel as a medium to store oxygen and liquid rocket fuel, in 1968, Nicolaon, then a student at Lyon’s University, discovered that by replacing aqueous Na_2SiO_3 by TMOS, an “alcogel” was rapidly produced in one step by hydrolysis of the alkoxide in a solution of methanol.³¹ The alcogel was easily dried under supercritical alcohol conditions, affording an excellent silica aerogel. This process successfully eliminated two major drawbacks of Kistler’s method, by avoiding the water-to-alcohol transfer prior to drying the “aquagel”, because the gel was produced directly immersed in alcohol, and simultaneously preventing the formation of residual sodium salts.

In general, due to the price of silicon alkoxides, the production of glass via the sol–gel process will cost 100 times that of glass obtained by conventional silica melting and cast. As a consequence, the production of glass via the sol–gel process only makes economically sense when addressing high value-added products.³² For example, in 2000 the inventor of the bioactive (bone binding) melt–cast glass Bioglass 45S5 (an eutectic formulation of SiO_2 , Na_2O , CaO , and P_2O_5 manufactured since 1985, whose derived medical and dental products are sold in over 35 countries) reported that sol–gel processing of bioactive gel-glasses allowed one to reduce the composition to just two components (CaO and SiO_2) and that the $70\text{SiO}_2/30\text{CaO}$ (in mol %) system was as bioactive as the melt-derived 45S5 Bioglass.³³ This $\text{CaO}–\text{SiO}_2$ system is now the basis for many of the third generation tissue regeneration materials presently under development.³⁴

In 1985, Schmidt disclosed basic findings emerging from years of applied research in the field of organically modified silicates (ORMOSILs) carried out at the Fraunhofer’s Institut für Silicatforschung.³⁵ These are the “reverse phase” silicas, derived from silicon alkoxides in which one of the hydrolyzable groups is replaced by an organic moiety connected to the silicon atom, thus reducing the functionality, f , or number of possible achievable siloxane ($\text{Si}–\text{O}–\text{Si}$) bridges, of the ORMSIL (Figure 2).³⁶

Ten years later, Reetz reported the first sol–gel entrapped biocatalysts made of lipase enzymes encapsulated in ORMSIL matrixes, with up to 100-fold increase in catalytic performance as compared to the free enzymes.³⁷ The materials were readily commercialized and, to the best of our knowledge, were the first example of doped sol–gel materials to reach the market.

In 1989, Carturan reported the pioneering immobilization of living microorganisms within a sol–gel matrix of SiO_2 (inclusion of whole cells of yeast *Saccharomyces cerevisiae*),^{38a} followed, in 1996, by the three-step Biosil technology to

immobilize whole cells in a sol–gel silica layer, by treating SiO_2 supported plant cells with a gas flow of tetraethoxysilane [TEOS, $\text{Si}(\text{OCH}_2\text{CH}_3)_4$] and diethoxymethylsilane (DEDMS).^{38b} The silanes react with the water adsorbed on the plant cell wall and toxic alcohol rapidly evaporates, preventing cell damage.³⁹

The first massive application of sol–gel silica-based materials took place in Germany, in 1985, with the production of antireflective Amiran glasses by Schott AG (closely connected with the inventor H. Dislich^{29b}).⁵² This was followed in 1998 by Toshiba, with the commercialization of TV screens with enhanced contrast thanks to coating with silica/zirconia thin films doped with indigo dye.⁴⁰

In 1999, Ozin reported the discovery of a new class of organic–inorganic nanocomposite materials called periodic mesoporous organosilicas (PMOs), starting from bridged silanes (Figure 3) whose organic moiety eventually gets integrated into the pore walls.⁴¹

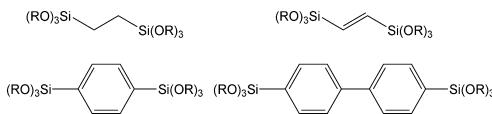


Figure 3. Typical bis-silylated organosilanes used to synthesize periodic mesoporous organosilicas (PMOs).

In the subsequent decade, PMOs including organic aliphatics and aromatics, dendrimers, fullerenes, and oligomeric silsesquioxanes were reported, delivering properties that are currently finding widespread interest in microelectronic packaging, chromatography stationary phases, catalysis, and drug delivery.⁴²

Year 2001 saw commercialization of silica-microencapsulated UV absorbing avobenzone for sunscreen lotions, providing sunscreen formulators photostabilization, flexibility in formulation, and excellent sensory properties, due to the formation of stable transparent colloids in water.⁴³ In 2003, Cabot Corp., in Germany, began producing ORMOSIL aerogels under ambient conditions, using a continuous manufacturing process, bypassing the high-cost (and safety risks) of traditional supercritical drying.⁴⁴ The process used was first reported in 1994 by Brinker and co-workers at the University of New Mexico, who discovered the basis of this alternative drying technique, namely how to control gel shrinkage via silylation of organogels (containing an organic solvent, not necessarily an alcohol, as the dispersing medium).⁴⁵

In 2007, likely pointing to the maturity stage of the field, the IUPAC published a document providing definitions of the terms most commonly used in relation to sol–gel processing.⁴⁶ Since then, accelerated innovation has resulted in a number of striking achievements: from SiO_2 aerogels ready for massive commercialization,⁴⁷ to the first commercial entrapped organocatalyst for fine chemicals manufacturing;⁴⁸ from nanocomposites that combine a wide range of biological functionalities and metals,⁴⁹ to sol–gel hybrid membranes for organic solvent or hydrogen purification.⁵⁰ In the following section, we provide an overview of the synthetic chemistry and methods that made these advances possible.

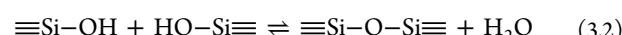
Table 1 lists a selection of important achievements in sol–gel technology. The framework attempts to give a useful overview, but, like the entire account, it cannot be comprehensive.

Table 1. Selected Achievements in Sol–Gel Technology

year	inventor/company	discovery
1640	van Helmont	“water glass”, sodium silicate, by melting sand with excess alkali; on acidification silica gel is obtained ⁴
1845	Ebelmen	transparent glass following atmospheric exposure of a silane obtained from SiCl_4 and ethanol ⁵
1913	Patrick	quick and cheap method of making silica gel in large quantities ^{8,9}
1931	Kistler	aerogel by supercritical drying ¹⁰
1939	Geffcken and Berger	sol–gel method for preparing single oxide coatings ²⁸
1942	Monsanto	production of Santocel starts ³⁰
1949	Dickey	preparation of specific silica adsorbents ¹²
1968	Nicolaon and Teichner	alkoxide route to aerogels ³¹
1968	Stöber	silica nanosols ⁵¹
1984	Avnir	doped sol–gel materials ¹³
1985	Schott	antireflective Amiran glasses ⁵²
1985	Schmidt	organically modified silicates (ORMOSILs) ³⁵
1989	Carturan	immobilization of living microorganisms within silica ³⁸
1990	Avnir	immobilization of enzymes within silica ¹⁶
1994	Brinker	ORMOSIL aerogels bypassing supercritical drying ⁴⁵
1995	Reetz/Fluka	commercialization of ORMOSIL-entrapped lipase ³⁷
1998	Boeing	sol–gel coatings replacing chromates ⁵³
1998	Bright	first low-cost O_2 optical sensor based on Ru-doped luminescent material ⁵⁴
1998	Toshiba	sol–gel optical coatings for TV screens ⁴⁰
1999	Böttcher	embedding of liquids by nanosols ⁵⁵
1999	Ozin	periodic mesoporous organosilicas (PMOs) ⁴¹
1999	de Vos and Verweij	long-lasting ORMOSIL-based membranes ⁵⁶
2000	Hench	sol–gel-derived Bioglass as third generation tissue regeneration materials ³³
2001	Sol–Gel Technologies/Merck	manufacturing of sol–gel microencapsulated avobenzone ⁵³
2003	Cabot Corp.	production of silica aerogels under ambient conditions ⁴⁴
2007	SiliCycle	commercialization of multipotent sol–gel catalysts for synthetic organic chemistry ⁴⁸
2008	Su	photosynthetic bioreactors based on silica-entrapped cyanobacteria ⁵⁷
2012	Warren and Wiesner	silica gels doped with high amounts of metal nanoparticles of unprecedented conductivity ⁴⁹

2. SOL–GEL CHEMISTRY AND METHODS FOR FUNCTIONAL MATERIALS

Functional sol–gel materials are generally synthesized via the hydrolytic polycondensation, at room temperature, of liquid precursors such as silicon alkoxides, under controlled conditions. The synthesis is generally carried out in an organic cosolvent (alkoxysilanes are not water-soluble), through simultaneous or sequential reactions of hydrolysis (eq 3.1) and polycondensation, releasing water (eq 3.2) and/or alcohol (eq 3.3).



The overall gelation process is slow due to the low polarity of the Si–O bond in silicon alkoxides (the Si atoms bear a δ^+ =

0.32 low positive charge in TEOS). Therefore, catalysis is essential. This is a key advantage because, in practice, the relative hydrolysis and condensation rates are very sensitive to the medium, which allows a relatively independent control through acid or base catalysis. One- or two-step processes can be used. The structure of a sol–gel material indeed evolves sequentially as the product of successive and/or simultaneous hydrolysis, condensation, and their reverse reactions (esterification and depolymerization, respectively).⁵⁸

Overall, silica gels with a texture closer to that of polymeric gels derived from organic chemistry are obtained if the hydrolysis rate is larger than that of condensation. This is usually the case under acidic catalysis. On the other hand, bases accelerate the condensation above the hydrolysis reactions, which then favors the formation of denser colloidal silica particles and colloidal gels.

The fundamental structural units of silica gel are similar to those of vitreous silica (long accepted as a continuous random network of nearly perfect SiO_4 tetrahedral units).⁵⁹ It was proposed that the tetrahedral units are mostly arranged in cyclic siloxane structures, 4-rings [$(\text{SiO})_4$], which are thermodynamically favored, plus less tensioned 6-rings [$(\text{SiO})_6$], which are kinetically favored (Figure 4). Broken siloxane bridges and rings of different dimensions were considered structural defects.⁶⁰

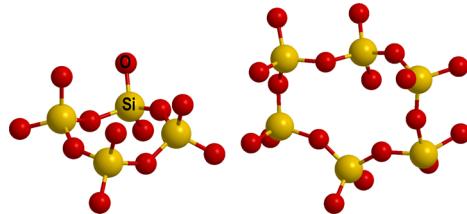


Figure 4. Schematic diagrams of the more common types of primary cyclic arrangements of the SiO_4 structural units in silica gels.

The relative proportions of these structural units depend on the synthesis conditions. The 6-rings may even predominate when the precursor is an alkyl alkoxide (in ORMSILS). A beautiful example was obtained using mixtures of TMOS and methyltrimethoxysilane [MeTMOS, $\text{CH}_3\text{Si}(\text{OCH}_3)_3$] in different proportions: the silica structure ranged from 15% to 97% of [$(\text{SiO})_6$] as the precursor changed from pure TMOS to pure MeTMOS.⁶¹

Thus, by chemical control of the mechanisms and kinetics of the sol–gel reactions, by thoughtful choice of the sol–gel process parameters (such as the nature of the precursors, the use of surfactants, acid or base catalysis, water/precursor and cosolvent/precursor ratios, aging, washing and drying conditions), it is possible to tailor the structure of the resulting gels over a wide range, affording materials with the desired functional properties.⁶²

As mentioned above, when drying of the alcogel is carried out by a mild thermal treatment, a micro- or mesoporous xerogel is obtained. Supercritical drying avoids shrinkage of the alcogel matrix and affords an aerogel. In both cases, the process is highly reproducible and can be scaled up to manufacture amorphous functional oxides in a wide range of compositions and shapes, including monoliths, coatings, disks, rods, powders, fibers, and porous membranes.

Governing the sol–gel process at molecular level implies the ability to control the monomer → oligomer → sol → gel →

xerogel (or aerogel) transition affording a porous silicon oxide material with the desired textural, surface chemical, and morphological properties. This is what Mann has called “a chemistry of form”⁶³ in the laboratory, or the ability to control the shape of porous materials⁶⁴ by using void space, that is, nothing,⁶⁵ as a fundamental factor affecting the chemistry of the resulting nanostructured (sol–gel) material. It is indeed the inner porosity of the resulting silica-based material that ensures accessibility, dispersion, and effective confinement of the entrapped molecules.²³

Hence, the first message conveyed by this approach is to look at doped silica-based sol–gels as porous solids filled with nanometer voids where all sorts of molecules can be entrapped, affording materials of large potential utility in widely different areas of application. The encapsulation of doping molecules is homogeneous and the dispersion is very high, as is nicely shown by the linear Stern–Volmer plot of ORMSIL-entrapped dyes (Figure 5), a class of materials nowadays widely exploited to manufacture optical oxygen sensors.⁶⁶

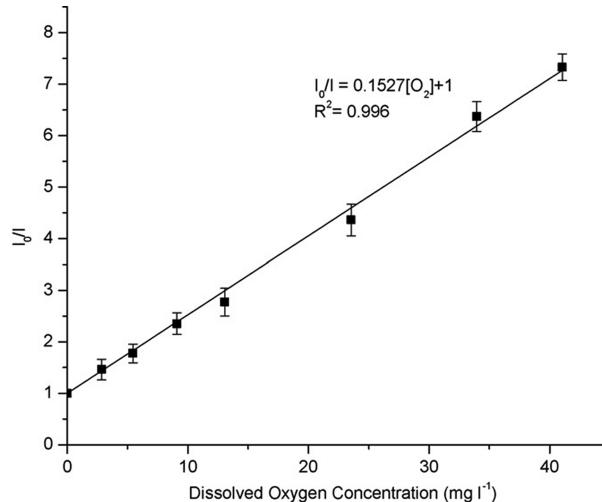


Figure 5. Linear plot of $[\text{Ru}(\text{dpp})_3]^{2+}$ -doped octyltriethoxysilane/TEOS composites is a measure of the homogeneous environment sensed by the Ru complex in the sol–gel cages. Reprinted with permission from ref 66. Copyright 2003 American Chemical Society.

From the structural point of view, ORMSILs are generally heterogeneous systems, given that the hydrolysis rates of alkoxy silanes and alkylalkoxy silanes are normally different: for instance, in acid medium the hydrolysis rate is much higher for MeTEOS than for TEOS, while the opposite is observed in alkaline medium. Therefore, depending on the medium, large quantities of self-condensates may be obtained in addition to the co-condensates. A convincing example is the system TEOS–vinyltriethoxysilane–ethanol–water–HCl,⁶⁷ in which self-condensation of VTEOS is dominant in the initial condensation stage, because the hydrolysis of VTEOS is faster than that of TEOS, while co-condensation and self-condensation of TEOS become the dominant mechanisms as the reaction proceeds. However, from an optical viewpoint, copolymerization of the silicon monomers in ORMSILs is homogeneous at all ratios, as shown by the linear correlation between the cage polarity and the molar amount of the methyl-modified monomer in a TMOS/MeTMOS-derived ORMSIL (Figure 6).⁶⁸

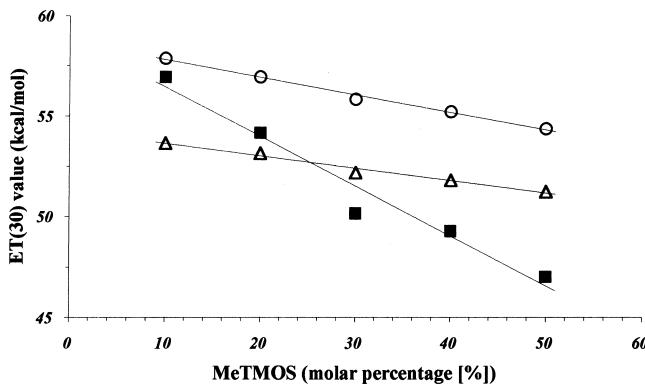


Figure 6. Cage polarity as a function of the molar % of MeTMOS: ■, dried ORMOSILS; ○, methanol at the interface; △, ethanol at the interface. Reprinted with permission from ref 68. Copyright 1996 American Chemical Society.

The different plots in Figure 6 show that external solvent molecules easily access the sol–gel cages where they solvate the entrapped dye, which in turn becomes more sensitive to the solvent in its surrounding than to the polarity of the dried cage. Furthermore, early XRD structural studies of ORMOSILs pointed out that the hydrocarbon moiety was at the pore surface, where the electron density varied evenly, affording a smooth, rather than fractal, surface.⁶⁹ Today we know that the fractal dimension in nature is limited to a few (1–2) orders of magnitude.⁷⁰ Yet its chemical utility in the field of sol–gel materials has not been lost. For example, it has been extensively used by researchers to screen ORMOSIL particles with the optimal size and surface geometry in ceramic membranes (see section 3.5).

Our second tenet is thus that the progress in sol–gel science and technology can be regarded as the development of synthesis methods to produce the required functional materials, by assembling the appropriate precursor building blocks, and the dopant species, with the required geometry for optimal performance.

From this perspective, one can clearly identify the historic development of the two main methodologies for the synthesis of silica-based doped sol–gel materials: (i) the direct physical or chemical entrapment of organics in disordered silica and organosilica porous matrix particles (Figure 7a), assembled into monoliths, thin films, capillaries, disks, and powders; and (ii) the use of templates to induce ordered silica structures (Figure 7b) with the adequate functionality to encapsulate the desired molecules.

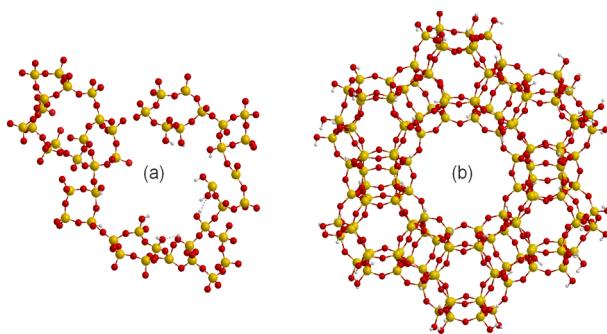
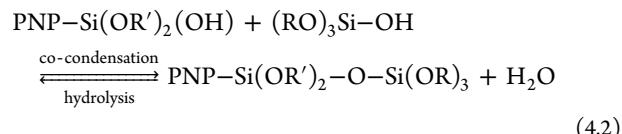
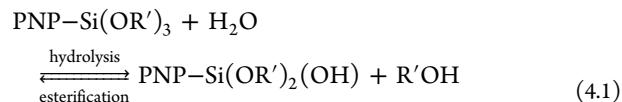


Figure 7. Examples of (a) disordered and (b) ordered mesoporous structures for silica-based doped sol–gel materials.

The direct entrapment approach was pioneered by Avnir and co-workers Levy, Reisfeld, Blum, and Lev in Israel since 1984,¹³ and was rapidly followed by researchers worldwide, as it was soon realized how the parameters of the sol–gel hydrolytic polycondensation rule the nanostructure of the resulting gel (primary particles size, pores size distribution, fractality, tortuosity, density, etc.).

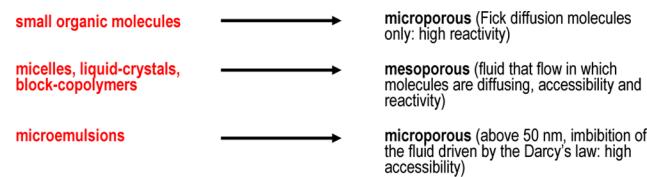
Further methods were devised to better control nanostructuration, such as the two-step processes, which can effectively separate the hydrolysis and condensation reactions by controlling the amount and type of catalyst used in each step.⁷¹ For example, a nanohybrid aerogel with superior insulating properties and good mechanical behavior is easily obtained by copolymerization of functionalized core–shell colloidal polymer nanoparticles (PNP) that participate in the two-step sol–gel process (eqs 4.1, 4.2, where R' stands for H or CH₃ and R stands for H or C₂H₅):⁷²



Sol–gel silica-based materials are indeed an eminent example of nanocomposites, multiphase materials in which a bulk matrix incorporates one or more nanosized phase(s), generally with one dimension smaller than 100 nm, differing in properties due to dissimilarities in structure and chemistry.⁷³ In detail, they possess unique scalable property combinations due to remarkable surface-to-volume ratio of the nanofiller and/or its large specific surface area, which lead to an exceptionally high interfacial area when good dispersion is achieved.

The template-induced approach was triggered by different inputs, from Kresge's discovery of MCM-41⁷⁴ to Ozin's PMOs,⁴¹ on to Brinker's evaporation-induced self-assembly (EISA)⁷⁵ and to chiral organosilica helices of Moreau and Wong-Chi-Man.⁷⁶ The field was further advanced by the use of soft matter (lyotropic mesophases, foams, emulsions, and beyond), to afford mesostructured materials via self-organization of nanoparticles in three-dimensional structures with all sorts of shapes (Scheme 1).⁷⁷

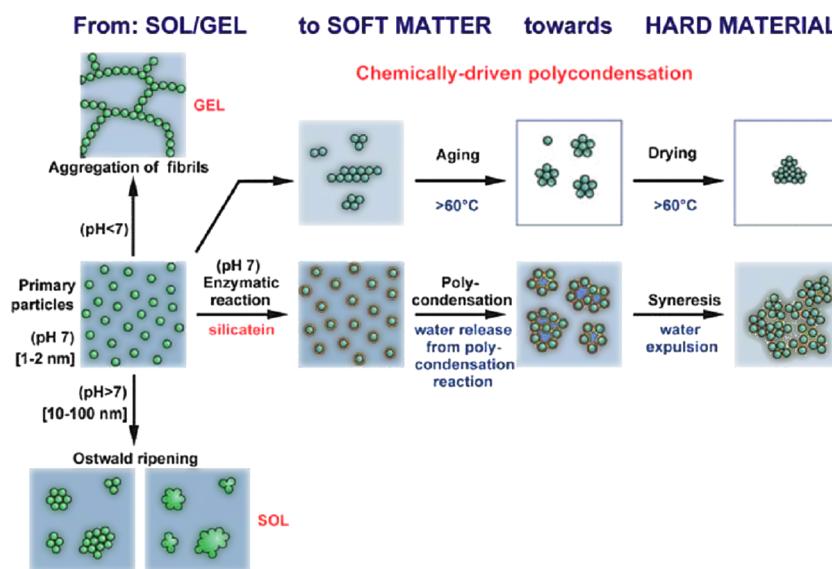
Scheme 1. How Organic Templates Control Porosity of Materials, and Consequences from a Functional Viewpoint



Therefore, the relevant factors affecting the performance of doped sol–gel materials, their chemical and physical properties, are:

- (i) the chemistry of the entrapped dopant;
- (ii) the geometry of the sol–gel cages on the nano or on the meso scale; and

Scheme 2. Chemically Driven versus Biochemically Driven Polycondensation of Silica: Under Acidic Reaction Conditions ($\text{pH} < 7$), the Silica Units Form Fibrillar Aggregates Embedded in an Aqueous Environment (Gel Formation)^a



^aAt a more alkaline milieu ($\text{pH} > 7$), the number of particles decreases under formation of larger silica particles (10–100 nm) (Ostwald ripening process; sol formation). The chemically driven polycondensation passes over an aging and drying process (at temperatures of $>60^\circ\text{C}$) and reaches the phase of stabilization prior to the formation of glass. The silicate biochemically driven polycondensation proceeds under physiological conditions, at $\text{pH} 7$, and undergoes water expulsion before reaching the stage of hard biosilica material. Reprinted with permission from ref 78. Copyright 2012 Royal Society of Chemistry.

- (iii) the surface chemical properties of the encapsulating cages.

Looking at the synthesis methodologies mentioned above, it is remarkable to recognize that the relevance of the geometry and morphological aspects of silica-based materials emerged well before the introduction of the soft matter templating agents. For example, the tendency of Si(OH)_4 to assemble in spheres was discovered by Stöber as early as 1968,⁵¹ when he reported that monodispersed SiO_2 microspheres were easily obtained in the ammonia-catalyzed hydrolysis of TEOS in the presence of a low molar-mass alcohol, such as ethanol (Scheme 2). Manufacturing of silica sols in industry is widely based on the Stöber process.

In general, widely different particle structures are formed at the polycondensation of silicic acid in acid, neutral (bio-silification in nature), or alkaline medium, as beautifully illustrated in Scheme 2.⁷⁸ The coating and immobilization properties will obviously be different.

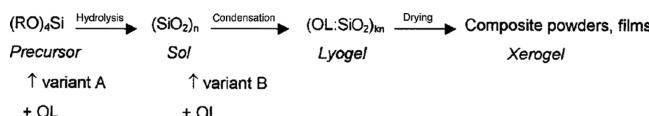
Today, sols of monodisperse SiO_2 particles with diameters between 50 and 2000 nm, depending on the type of silicate ester, alcohol, and volume ratios employed, are manufactured in industry, generally from Na_2SiO_3 by ion-exchange or cation-exchange membranes. The resulting sols are commercially available as aqueous dispersions of colloidal polysilicic acid (resulting from the condensation of two or more molecules of Si(OH)_4) with typical loads up to 50 wt % of solid material to ensure stability for at least 6 months (Table 2).

These sols are widely and increasingly employed for functionalizing surfaces with functional silica layers for disparate applications that range from protective to optical coatings. In 1999, indeed, Böttcher and co-workers were the first to use silica nanosols to form silica powders and thin films (Scheme 3), entrapping high amounts (up to 30% in weight with respect to silica) of organic liquids, including oils.⁵⁵

Table 2. Selected Commercially Available Silica Dispersions

trademark	producer
Ludox	Grace
Nyacol/Bindzil	Eka Chemicals (Akzo Nobel)
Levasil	Bayer
Köstrosol	Chemiewerke Bad Köstritz
Silicadol	Nippon Chemical Industrial

Scheme 3. Sol–Gel Route to Silica Xerogel Films and Coatings Doped with Organic Liquids^a



^aReprinted with permission from ref 55. Copyright 1999 Wiley-VCH.

Almost concomitantly, the microencapsulation of organic substances inside spherical silica and organosilica microcapsules, by simply carrying out the sol–gel process in the micellar core of microemulsions, was reported by Avnir and co-workers,⁷⁹ and, for hydrophilic substances, by Barbé.⁸⁰

In the following, therefore, the advantages and limitations of some of the above-mentioned methods to afford silica-based functional materials are critically assessed with reference to selected recent achievements, to show how these materials offer a solution to relevant problems currently faced in green chemical synthesis, purification, clean energy, effective delivery of organic molecules, and protection of surfaces.

3. EMERGING APPLICATIONS OF SILICA-BASED MATERIALS

3.1. Materials for Controlled Release

An ever increasing number of industrial applications, from the development of long-lasting fragrances to the protection of materials surfaces against bacterial attack, or the targeting of diseases, require the production of delivery systems in particulate or film form. The use of porous and surface-modified silicas for controlled drug delivery, as well as a means of stabilizing drugs, was published as early as in 1983,⁸¹ and in 1998 Böttcher could already review the status of sol–gel carrier systems for controlled drug delivery.⁸²

Basic patents of controlled releasing systems based on sol–gel irregular silica and ORMOSIL xerogels were also filed by Feinchemie Sebnitz AG between 1993 and 1995,⁸³ when the company started manufacturing silica sols for wood protection by controlled release of boric acid (trade named Sebosil HB). It also provided silica sols for the immobilization and controlled release of volatile corrosion inhibitors (VCIs), used as coatings in anticorrosion packaging paper (trade named Abrigo) by the German company Excor.⁸⁴

In year 2000, researchers in Finland reported the evaluation of drug distribution and tissue effects after implantation of a silica xerogel disc as a drug carrier in mice.⁸⁵ The SiO₂ discs showed a sustained release of toremifene citrate over 42 days, and no tissue irritation at the site of the implantation.

The sol–gel microencapsulation technology and its broad application potential are now well-known.⁸⁶ Relevant here is that silica can be used for encapsulation and controlled release of both hydrophilic and hydrophobic molecules, ensuring considerable chemical and physical protection of the valued entrapped dopants.

The first industrial applications of sol–gel silica particles for controlled release took place in 2001, and consisted of sol–gel microcapsules obtained by emulsion chemistry (“second generation”) rather than granular particles (“first generation”), in which the UV filter avobenzone was encapsulated (Eusolex UV Pearls).^{1,43} Silica microspheres (with monodisperse dimensions typically between 10 and 100 μm) share the same basic advantages of SiO₂ matrix particles, enhanced mechanical strength, chemical and physical stability, biocompatibility, and an environmentally benign nature. Yet, in comparison to fast, short-term release of the entrapped molecules by diffusion through the matrix pores, the release from the microspheres is slower and of longer duration.⁸⁷ In addition, the degradation rate of microspheres is significantly slower than that of the granules, enabling the use of sol–gel microcapsules for controlled long-term release.

Whatever the sol–gel technology chosen, granular particles or microspheres, the release profiles will be determined by the internal structure of the particles (pore volume, pore size, tortuosity, and surface chemistry). Hence, the release rate of the encapsulated species will be controlled by adapting the structure of the internal pore network to the release requirements in a certain application. Below, referring to practical applications, we discuss and compare the main encapsulation methodologies as they emerged through the actual development of the sol–gel encapsulation technology.

3.1.1. Controlled Release of Fragrances and Aromas.

The flavor and fragrance industry is a global and large (20 billion \$ sales in 2010)⁸⁸ sector of the chemical industry. Fragrance chemicals are added to consumer products such as

personal care products, perfumes, laundry detergents, fabric softeners, soaps, detergents, as well as to numerous other products. Encapsulation techniques are increasingly used by this industry for improving the efficiency of odorant and aroma chemicals.⁸⁹

In cosmetic and personal care products, new encapsulation technologies are required (i) for longer life and improved delivery of fragrance materials,⁹⁰ and (ii) to enable usage of unstable biodegradable fragrance molecules in place of the typical nonbiodegradable odorant molecules that industry is forced to employ to avoid oxidative degradation.⁹¹ Most of the synthetic nitro- and polycyclic musks used as additives in many consumer products, including perfumes, deodorants, and detergents, are toxic and are severely contaminating the environment,⁹² as well as human milk (via dermal absorption and inhalation),⁹³ because they are not biodegradable.

Industry, however, demands a versatile technology that effectively controls the way active compounds are released.⁹⁴ In this sense, the potential of sol–gel technology is unsurpassed as shown, for example, by the release mechanism of benzoyl peroxide encapsulated in silica microcapsules due to the sebo action, in therapeutic formulations for treating acne that are now commercial.⁹⁵

Following early attempts of the Japanese industry dating back to 1987,⁹⁶ numerous different liquids encapsulated in SiO₂ xerogel matrix particles were investigated by Böttcher and co-workers, aiming to functionalize textiles with mixtures of volatile natural agents such as eucalyptol,⁹⁷ camphor, and menthol for the therapeutic treatment of the diseased respiratory tract.⁹⁸

In general, the release of the embedded liquid from both xerogel and coating systems occurs in a two-step process (Figure 8). A fast initial liberation process from open pores near the bulk surface is followed by a much slower process

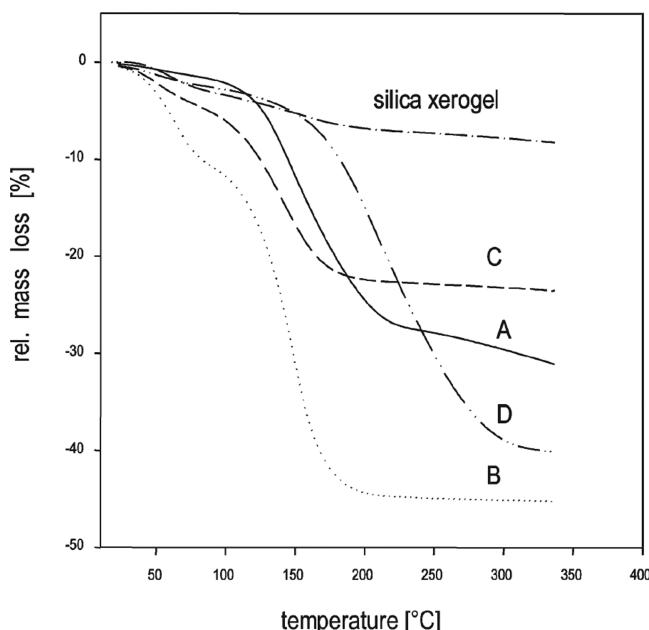


Figure 8. Thermogravimetric analysis of silica xerogels with embedded liquids (A = nitrobenzene; B = formamide; C = citronella; D = dimethylphthalate). Reprinted with permission from ref 97. Copyright 2005 Royal Society of Chemistry.

reflecting the strong activated diffusion of the remaining liquid from inside the sol–gel cages.

The relevance of the sol–gel approach to fragrance encapsulation was clearly confirmed by Pratsinis and co-workers, from the food industry, who studied fragrance⁹⁹ and flavor¹⁰⁰ retention in SiO₂ matrix particles made by sol–gel processing of TEOS, using aroma molecules from different chemical classes (alcohols, esters, aldehydes, and terpenes).

Sol–gel silica matrixes showed a unique release behavior. Molecules that do not interact, or interact only physically with the silica surface, will be released first, followed by chemically adsorbed ones. Denser matrixes behave like carbohydrate matrixes (starch), showing a reduced retention with increasing load. Particles with a more open porosity tend to show an increase in retention with an increased total load. In other words, and unique to sol–gel materials, the fragrance load and release kinetics are coupled.

For example, Figure 9 shows that the average aldehyde retention of a mixture of aldehydes (hexanal, octanal, and

interact less with the silica surface. Aldehydes are better retained than esters because of their ability to form hemiacetals, and alcohols are best retained because they can easily hydrogen bond to the Si–OH groups.

In brief, encapsulating a fragrance mixture containing different molecular species, such as a perfume, in sol–gel–made SiO₂ particles, will result in a pronounced shift of the fragrance profile. In general, a perfume consists of three different liquids with very different optimized volatility. Upon adsorption and sol–gel immobilization, the release profile is altered and therefore the original scent is changed. Indeed, Böttcher entrapped many of the most common essential (ethereal) oils (lavender, eucalyptus, thyme, balm, rosemary, sage, peppermint, basil, and ginger) within silica coatings aiming to prepare prolonged fragrant paper, flavor-releasing home textiles, or garments with well-being or healing effects. Invariably, an exponential decay of the flavor concentration over a period of 85 days was observed, in which the two-step course of release mentioned above blurs because of the mixture of different volatile components present in natural perfumes.

Rather than entrapment in the inner surface of SiO₂ matrix particles, encapsulation within the core of core–shell micro-particles allows the fragrance to be released with enhanced precision and effectiveness of action. Indeed, a recent patent application¹⁰¹ claims that sol–gel microcapsules doped with fragrances are ideally suited for applications ranging from personal care to cleaning products. The fragrance capsules retain their odor far better than does the neat fragrance, as shown, for example, once applied through an antiperspirant (AP) roll-on base.

The product containing the capsules (100 μL) in AP roll-on based was thus applied to the forearm of six panelists, and the fragrance intensity was evaluated by 20 intensity judges immediately after and 5 h after application upon rubbing the applied product. Rated in a scale ranging from 0 to 30, the numerical values of fragrance intensity suggest whether the fabric only produces very weak intensity (value of 5) or generates a strong smell (a value of 30). After the product containing the capsules was rubbed, the intensity was almost unvaried, whereas that of the product containing neat fragrance was almost halved. Finally, the long-term stability of the capsules is shown by the modest leaching after simultaneous storage tests, indicating that only 10% fragrance leaches out of the capsule after 5 weeks at 37 °C.¹⁰¹

3.1.2. Controlled Release of APIs. An increasing amount of new drugs developed consist of active pharmaceutical ingredients (APIs) that are chemically very unstable and cannot be administered orally. Furthermore, there is an increasing need for nonoral advanced delivery technologies that can maintain the viability of therapeutic agents, and expand applications from small molecular drugs to a host of different therapeutics.

Silica is a biocompatible natural component of the body, which does not affect the pH of the surrounding tissues, reducing the risk of inflammation. As such, it is widely approved for oral, mucosal, and topical administration. ORMSILs, in their turn, are not approved. However, a recent study has shown that after feeding ORMSIL nanoparticles in the fruit fly (*Drosophila*) larvae, no toxic effects on the whole organism or the neuronal cells are observed.¹⁰² We recall here that the *Drosophila* genome is highly conserved when compared to higher organisms and that many human neuronal disease models have also been developed in the fly.

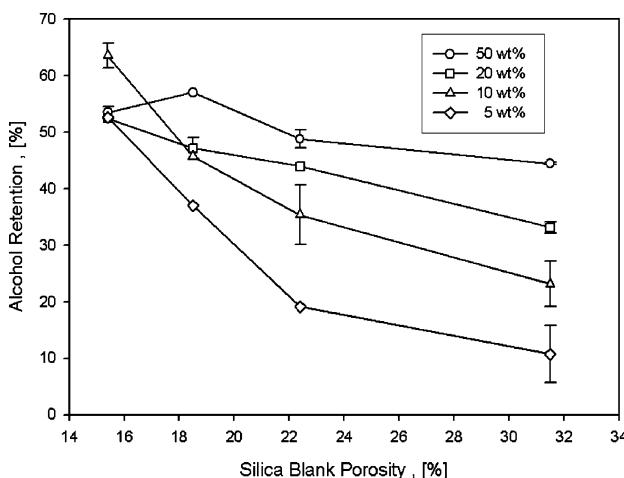


Figure 9. Average aldehyde retention (hexanal, octanal, and decanal) in SiO₂ xerogels as a function of porosity for total initial aroma loadings of 5, 10, and 20 wt %. Reprinted with permission from ref 99. Copyright 2004 American Chemical Society.

decanal) entrapped in silicas at initial loadings of 5, 10, and 20 wt % increases with decreasing porosity, especially in the sample with an initial load of 5 wt %. In practice, the initial aroma load, affecting the size of the sol–gel cages where the dopant molecules are entrapped, largely affects the release kinetics. As a result, higher loadings induce larger pore structures from which the aroma is lost much faster as compared to smaller cages at low loadings. Large molecules of low volatility and lower diffusion coefficients are retained better than smaller ones.

The silica matrix is highly polar due to the numerous silanol groups at the cages surfaces. Hence, the retention performance decreases in the order alcohols > aldehydes ≥ esters > terpenes, due to the different van der Waals interactions and also to the hydrogen bonds that may be established between the dopant and the silanol groups (both as charge donors, due to the electron pairs of oxygen, and acceptors, due to the charge-deficient hydrogen). For alcohols, esters, and aldehydes, the retention performance of the different chemicals in a porous sample is nearly linear with molecular weight. Nonpolar compounds like terpenes are poorly retained because they

For any material to be useful as a therapeutic delivery system, it must meet three basic requirements: (i) be nontoxic to the organism, (ii) effectively incorporate into the specific tissue type that the treatment targets, and (iii) not interfere with the normal functions of that tissue type. When tested in the fruit fly, the ORMSIL nanoparticles made of aminopropylsilica with covalently incorporated fluorophores (rhodamine-silane precursor, conjugated to aminopropyltriethoxy silane), obtained by an oil-in-water microemulsion, successfully passed all three tests (Figure 10).¹⁰²

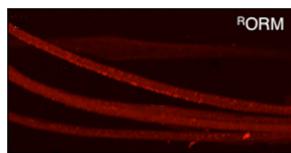


Figure 10. Confocal microscopy image of clusters of ORMSIL particles in axons of fruit fly neurons. Reprinted with permission from ref 102. Copyright 2012 Public Library of Science.

For a given drug, the release rates can be designed to range from very slow to very fast, as porosity, and thus diffusion through different porous structures, can be easily controlled in any sol–gel silicate.

In one encapsulation approach for the controlled delivery of a wide range of active ingredients, suitable for synthetic small molecular compounds, the technology is based on doped SiO₂ matrix particles.¹⁰³ Release is due to dissolution of the doped xerogel in contact with body's fluids, and the liberation rate is governed by the relationship between the rates of dissolution and diffusion through solvent-filled capillary channels.

As a representative example, heparin incorporated into a biodegradable silica xerogel matrix is subsequently released over a prolonged time period, retaining its biological activity, with the degradation of xerogel being linear and independent of the heparin concentration.¹⁰⁴

The release mechanism is governed by a modified power law (eq 5), which takes into account an initial release period that differs from the main release phase:¹⁰⁵

$$\frac{M_t - M_2}{M_\infty} = k(t - t_2)^{n_B} \quad (5)$$

where M_t is the cumulative release at time t , M_2 is the amount released within the initial release phase (that differs from the main release phase), M_∞ is the cumulative drug release at infinite time, k is a constant that depends on the structural and geometrical characteristics of the device, t_2 is the final instant of the initial release, and n_B is the release exponent characteristic of the mechanism of drug release after the initial burst. The values of n_B are characteristic for the drug release mechanism.

Longer delivery times can be attained by changing the parameters of the sol–gel synthesis. For example, in the in vitro delivery of phenytoin sodium (an antiepileptic active principle) to artificial cerebrospinal fluid (ACSF), silica matrixes with lower total porosity and smaller average pore size proved to be better for a long-term release. Renovation of ACSF around the delivery device (simulating what happens in the real cerebral medium) proved relevant to ensure a constant concentration of phenytoin in the vicinity of the device (Figure 11).¹⁰⁶

The silica matrix can be designed to degrade at the required rate to ensure a tightly controlled release of the active substance, providing a better therapeutic effect *in situ*, and

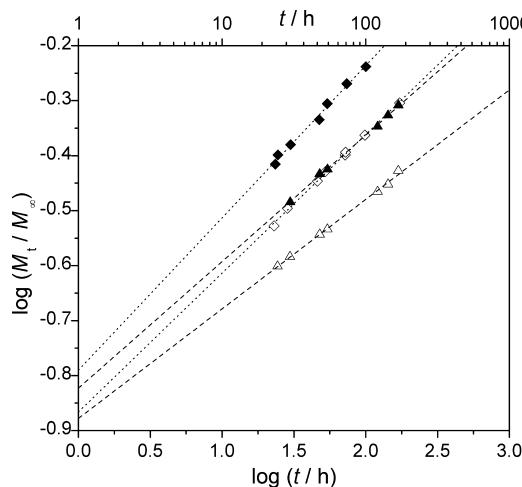


Figure 11. Logarithmic variation of the fraction of drug release with time: dotted, fitted lines. ◆, NaPhe/matrix A/H₂O; ◇, NaPhe/matrix B/H₂O; ▲, NaPhe/matrix A/ACSF; △, NaPhe/matrix B/ACSF. Matrix A is more porous and with larger average pore size than B. Reprinted with permission from ref 106. Copyright 2009 Springer.

causing lower systemic toxicological side-effects than alternative delivery systems. For example, it was recently reported that a slow and tonic drug release occurs in rats implanted with silica-entrapped dopamine.¹⁰⁷ The *in vitro* dopamine delivery profiles indicate two regimes: a fast and sustained release observed up to 24 h, the rate of delivery becoming constant from then on. Rats showed no signs of dyskinesias at any time, which contrasts with the effect of intermittent systemic L-dopa administration, that causes orofacial dyskinesias. The authors concluded that the route is now open to its use as a release system for dopamine administration in patients with Parkinson's disease.

In another encapsulation approach, more suitable for biopharmaceuticals,⁸⁰ the encapsulation of APIs takes place into spherical microparticles using room-temperature sol–gel polymerization in reverse emulsions. The surface of the particles can be functionalized to minimize protein interaction and enhance blood circulation, for active targeting. *In vitro*, and now also *in vivo* experiments, show that the particles degrade relatively rapidly (from hours to weeks) in physiological media. In addition, they show good biocompatibility, interfering with cellular processes only at very high doses (20 mg/mL). In both cases, the advantages of sol–gel SiO₂-based drug delivery technology are evident in terms of safety and enhanced performance (the resulting solid matrix biodegrades, can be shaped in variable forms, and yields delivery times that can be adjusted from days to several months).^{80,82}

Pioneered by academic researchers, the Biomaterial Research Group in Turku, Finland, the nanotechnology based on silica gels has been developed to afford the first injectable therapeutics delivery technology for implants (DelSiTech): subcutaneous and intramuscular administration is suitable for the controlled delivery of a wide range of active ingredients, providing a better therapeutic effect *in situ* and causing lower toxicological side-effects than many alternative delivery systems.⁸⁰

Another field in which silica sol–gels may soon produce a large impact in healthcare is in healing wounds, especially large-area wounds currently treated with poor success rate with conventional bioabsorbable materials, which degrade too

Table 3. Relevant Achievements in Controlled Release from Sol–Gel Silica-Based Materials^a

year	author/company	matrix form	dopant	ref
1987	Yamamoto/Nakato Laboratory	silica monoliths	aromatic substances	96
1994	Feinchemie Sebnitz	silica monoliths	oils	83
1997	Carturan et al.	silica monoliths	flavors	122
1999	Böttcher et al.	powders and thin films from silica nanosols	organic liquids, including oils	55
2004–05	Pratsinis et al.	silica particles	aromas and flavors	99, 100
2005–08	Böttcher et al.	xerogel silica particles	eucalyptol, camphor, and menthol	97, 98
2010	Popplewell et al.	core–shell silica microcapsules	fragrances	101
1983	Kirchner et al.	porous and surface modified silica	different drugs	81
1993–95	Feinchemie Sebnitz AG	silica monoliths	different APIs	83
1996	Sieminska and Zerda	silica	steroids	123
1997	Ducheyne et al.		growth factor beta-1	124
1998	Böttcher et al.	ORMOSILs	nifedipine	82
2000	Kortesuo et al.	silica discs	toremifene citrate	85
2001	Sol–Gel Technologies/Merck	silica microcapsules (Eusolex UV Pearls)	avobenzone	43
2001	Kortesuo et al./Orionpharma	ORMOSIL	API (sedative)	125
2001	Radin, Ducheyne et al.	silica xerogel disks	antibiotics (vancomicin)	126
2002	Lindén et al.	silica fibers	drugs	109
2003–2012	Barbé/CeramiSphere	silica spherical particles	biomolecules, APIs (insulin, wound healing, improved vaccines, and gene therapy)	80
2005	Lindén et al.	spray dried sol–gel silica particles	API (biphosphonate)	127
2008	Probst et al./Bayer Innovation	silica fibers	antibiotics, growth factors, and analgesic	110
2008–12	Sol–Gel Technologies	silica microcapsules	dermatological (acne and rosacea) substances	128
2009	Ducheyne et al.	silica emulsified microspheres	vancomycin (antibiotic) or bupivacaine (analgesic)	87
2012	Fraunhofer ISC/Bayer Innovation	silica fibers	antibiotics, growth factors, and analgesic	111
2013	DelSiTech	injectable	different drugs	108
1993	Feinchemie Sebnitz	silica monoliths	biocides	83
1997	Böttcher et al.	silica	biocidal substances	129
1999	Böttcher et al./Feinchemie Sebnitz AG	silica or ORMOSIL coatings	VCIs	84

^aChronological order for each type of dopant.

rapidly. The technology is based on biodegradable silica fibers, originally conceived in 2002,¹⁰⁹ which may act also as drug deliverers.

In 2008, researchers at the Fraunhofer Institute for Silicate Research in co-operation with Bayer patented a new type of biocompatible dressing made of silica gel fibers (SGF) suitable as enhanced wound-healing agents.¹¹⁰ The fibers are produced by sol–gel processing TEOS in ethanol and water in a multistage, acid-catalyzed synthesis. The resulting honey-like hydrogel is processed in a spinning tower and then pressed through fine nozzles at constant temperature and humidity levels, to afford fine SiO₂ threads that are collected and spun to produce a large multilayered textile web. Unlike collagen, the sol–gel fiber (SGF) scaffold remains in the wound for 1–2 weeks before being resorbed and replaced by new tissue during the healing process. The fibers provide the healthy cells around the edges of the wound with a new three-dimensional structure for fresh cell growth. In other words, SGF acts as a physical scaffold to aid the growth of new cells and the collagen structure that supports them. Unlike collagen, the SGF scaffold stays in the wound for 1–2 weeks, while it is progressively resorbed and replaced by new tissue during the healing process. Bioactive substances such as antibiotics, growth factors, and analgesics can be incorporated into the fibers during the manufacturing process to further promote wound healing.

The industrial partner built a pilot plant in Germany to produce sterile silica fibers according to good manufacturing

practices (GMP) standards. In 2012, following successful clinical trials, the first SGF-based product was commercialized in the European Union.¹¹¹

3.1.3. Controlled Release of Biocides. There is an obvious prolonged interest in the research of low-cost antibacterial highly efficient surface treatments and coatings to avoid the proliferation of microbes and bacteria for hygienic and medicinal purposes in textiles, devices, laboratories, operating rooms, and surgical instruments.¹¹² Similar great interest exists for new antifouling and anticorrosive paints devoid of harmful effects. Whether as doped or undoped ORMOSILs and silica/polymer composites, organosilica coatings obtained by the sol–gel process are eventually finding remarkable applications affording coated surfaces with multifunctional, highly desirable chemical and physical properties.¹¹³

For example, silica nanosols doped with immobilized biocides show excellent antimicrobial efficacy as they act as biocide source slowly released onto the surface of textiles, surgical instruments, and other surfaces. In particular, SiO₂ nanosols doped with inorganic (silver) or organic (quaternary ammonium salts, octenidine) biocidals are well suited as simple antimicrobial postproduction coating of any common fiber.¹¹⁴ Silica layers coated on textiles show an excellent long-term inhibition of fungi growth. Because of the low degree of leaching of octenidine, the fungicidal effect of coating embedded with octenidine is stable even after 18 h of leaching.¹¹⁵

Especially efficient Ag nanoparticles with large surface-to-volume ratio have been successfully immobilized on silica thin films,¹¹⁶ affording antibacterial materials whose high and durable antibacterial activity makes them an excellent candidate for practical applications. Recently, researchers in Spain developed a facile method to produce organic-inorganic biocide films in a fast and simple way by using the dip-coating technique onto glass substrates.¹¹⁷ The material is actually a nanocomposite between TEOS and polyelectrolyte PAA (poly(acrylic acid sodium salt) doped with Ag ions.

Like silver, the entrapped species should combine high toxicity for bacteria with a low toxicity for humans; hence, it is expected that the entrapment of ecofriendly antimicrobial natural products¹¹⁸ to afford finishing textiles using bioactive agents will emerge in the near future.

In 2005, Bright and Detty reported new antifouling ORMOSIL coatings simply based on surface energy minimization to prevent adhesion from freshwater and marine organisms. Reduced zoospore settlement, increased removal of zoospores, and fouling release of biomass were achieved with xerogel surfaces of low wettability and low critical surface tension.¹¹⁹ The product ("AquaFast") is commercialized as a water-based sol-gel painting for boats to be used in fresh or in salty water, while even better results with respect to algae, diatoms, and zebra mussels are obtained with formulations containing low amounts of expensive fluorinated alkoxysilane precursors¹²⁰ such as TDF (tridecafluoro-1,1,2,2-tetrahydrooctyltriethoxysilane) in combination with TEOS and two other alkyl-modified silanes affording optically transparent coatings that are uniquely well suited as antifouling coatings where optical transparency is important (marine sensors, underwater cameras, submersible solar panels).

Similar good results are obtained encapsulating a biocide such as zinc pyrithione (ZnP) to develop yacht paints with a reduction of 70% of biocide, relative to presently commercial antifouling products for yachts, but without zinc- or copper-based pigments (cuprous oxide and zinc oxide) that cause long-term adverse effects in the aquatic environment.¹²¹ The doped silica gel is dispersed together with pigments and fillers in the paint. When the xerogel is exposed to marine water, the silica absorbs water and swells, thus boosting the biocidal effect due to slow and sustained release of the biocide, affording an antifouling product considerably more efficient in comparison with non encapsulated, free ZnP.

As an overview of section 3.1, Table 3 lists a selection of important achievements in sol-gel silica-based materials for controlled release.

3.2. Inks and Coatings

Silica-based nanostructured coatings are one of the more mature areas of nanotechnology.¹¹³ There are already business reports listing the different types of coatings that have been commercialized in the past decade, and their applications as antimicrobial, antifingerprinting, easy-to-clean, self-cleaning,抗scratches, antifog, antiadhesive, and anticorrosion coatings.¹³⁰ In 2000, about 5% of the world's TEOS production was already consumed by the semiconductor industry for the so-called "spin-on-glass" (SOG) technique, for spin-coating silicon chips with organosilica low-k thin films, with dielectric constants as low as 2.5.¹³¹

In the following, we review selected recent achievements, to show that sol-gel surface functionalization with silica-based nanosols is a key technology for a variety of applications in inks

and coatings industries. For example, a sol-gel ink made of aqueous silica sol doped with different dyes for decorating glass with flatbed printers has been recently commercialized by Durst Phototechnik.¹³² Decoration of glass using digital technology and organic inks is currently of great interest to architects and interior designers for kitchens and bathrooms, where moisture levels have thus far prevented the use of decorated glass.

Unlike standard inkjet UV inks, which, if exposed to moisture or solvent, result in strong delaminating from glass unless primers are applied, the sol-gel ink actually forms a chemical bond with the glass to provide unique resistance characteristics. In practice, the organically doped silica-based ink binds to the glass silanol groups upon a brief heat treatment at 200 °C. Furthermore, the sol-gel ink does not require a primer coat.

Another example is the new series of stable sols with high (ca. 30 wt %) solid concentrations in diethylene glycol, supplied under the trade name iSys.¹³³ The precursor sols, whose detailed preparation may be found elsewhere,¹³⁴ are obtained starting from monomer compounds of silicon, titanium, aluminum, or zirconium, and are supplied as thin, colorless liquids that can be either applied pure or diluted with water, leading to an aqueous sol with low content of organic solvent. As a result, these sols do not contain any volatile or flammable organic solvents that were necessary in the past for the sol-gel process (VOC load much lower as compared to conventional sols). Finally, because of the high activity of the sols, only small application amounts are needed to achieve functional layers.

After application, the layer is cured by a thermal treatment at temperatures $100 < T < 200$ °C, depending on the sol formulation. These coatings are versatile and can be used to functionalize surfaces with which we all interact on a daily basis, for example, to protect the surfaces of house fronts, walls, or concrete buildings sprayed with colorful graffiti. A preventive treatment of the wall with the organic-inorganic coating agent iSys PRO for the hydrophobic impregnation of building material minimizes the cleaning and repair efforts that are required to remove the paint from untreated surfaces.

The "easy to clean effect" of this coating is based on the formation of a special functional layer on the surface to be treated that prevents the deep penetration of the graffiti paint into the surface structure. Moreover, treated surfaces are long-term protected against water, due to the hydrophobic effect of the ORMOSIL coating.

The worldwide costs of metallic corrosion are estimated at over \$500 billion per annum. For example, to prevent the oxidation of aluminum alloyed with copper or zinc, hexavalent chromium is widely used by the aviation industry. It is introduced in coating compositions, especially in the form of strontium chromate (SrCrO_4) or zinc chromate ($\text{H}_2\text{CrO}_4\text{Zn}$) pigments, which are soluble in water, allowing Cr^{6+} ions to diffuse quickly to active corrosion sites. The strong oxidizing power of Cr^{6+} allows its rapid reduction to Cr^{3+} and the corresponding precipitation of an insoluble passivating oxohydroxide layer. However, the same oxidizing properties of Cr^{6+} make it severely toxic and carcinogenic. Sol-gel coatings are an effective solution to overcome the serious environmental and health drawbacks of using chromium in solution. In 1998, researchers at a leading aviation company patented a chromate-free sol-gel coating,¹³⁵ later to be widely used as a promoter for adhesive bonding and painting applications in the aerospace industry (both aircrafts and hangars).

Now, a sol-gel formulation is used that, after application, forms a high performance hybrid coating, which enhances the

adhesion of paint systems on metals and alloys such as aluminum, titanium, and stainless steel.

In detail, Boegel-EPII is a specific formulation derived from an acid-catalyzed aqueous solution of organofunctional silane and zirconium alkoxide precursors. The mixed Zr/Si oxide system is an aqueous solution (3–30 wt % in solid),¹³⁶ and the silane component is chosen to match to primer, sealant, or adhesive.

In each case, the sol–gel formulation is designed for spray/flood applications onto elements of different sizes, enabling zero-waste. Once again, the employment of hybrid organic/inorganic ORMSIL coatings allows a greater range of properties than previously used polymeric systems, as it ensures the robustness of glass with the possibility to adapt to different resin/paint organic chemistries. In a typical average size aircraft, the use of Boegel results in the elimination of ~400 gallons of chromated pretreatment and wastewater material. The technology was licensed to a paint company, and is now also used with the trademark Socogel for the preparation of fuselage and wings of aircrafts prior to painting, to increase the paint adhesion and therefore improve the durability of the paint systems.¹³⁷

The two main classes of materials (matrix and microcapsule particles) are being used to develop such coatings. The homogeneous ORMSIL nanosol coating shows good adhesion on substrates, giving place to high density and uniform morphology, with outstanding barrier properties, corrosion protection, high resistance against scratch, and erosion protection. The use of sol–gel microcapsules, in turn, offers the advantage of being able to encapsulate far larger amounts of corrosion inhibitors, up to 70% in weight of each capsule. Moreover, the size and surface chemistry of the silica particles can be made similar to that of the pigment particles used in paint, and thus made compatible with most coating formulations.

Barbé and co-workers have developed a series of micro-particles doped with corrosion-inhibiting additives (trademarked Inhibispheres) to be incorporated into coating paints.¹³⁸ Inorganic (for example, Ce(NO₃)₃, Na₂MoO₄), organic (for example, benzotriazole or 10-methylphenothiazine), or organometallic (such as cerium(III) salicylate) corrosion inhibitors are entrapped in SiO₂ microcapsules to be released to the metal surface, triggered by the presence of moisture (hence, when required), to prevent corrosion. Trial formulations of different anticorrosion coatings produce positive results in a number of field tests.¹³⁹

A range of doped coatings based on a silica organic/inorganic platform have been developed since 2005 by Akid and co-workers in the UK, which are hydrophobic, low in VOC content, curing at low-temperature, with curing times as short as 30 s, thus being highly effective in corrosion and wear resistance.¹⁴⁰ Furthermore, a single thick (15 μm) coating system eliminates the need to apply separate pretreatments, so that a sol–gel corrosion-resistant coating can be applied directly as a primer over a range of substrates, including aluminum alloys and stainless steel, combining environmental benefits and simple application.

This unique coating is made of an organically modified hybrid silica–alumina sol doped with cerium nitrate, prepared by mixing organosilica (TEOS, methyltriethoxysilane and ethanol in molar ratios of 5:4:1) and alumina sols, with corrosion inhibitor cerium nitrate, an ideal inhibitor due to low

cost, compatibility with the sol–gel process, and environmentally benign nature, at final 0.5 wt % concentration.

The performance of the resulting sol–gel coating, deposited over a polyester topcoat sample after 600 h neutral salt spray testing, is fully comparable (Figure 12a) with that of a

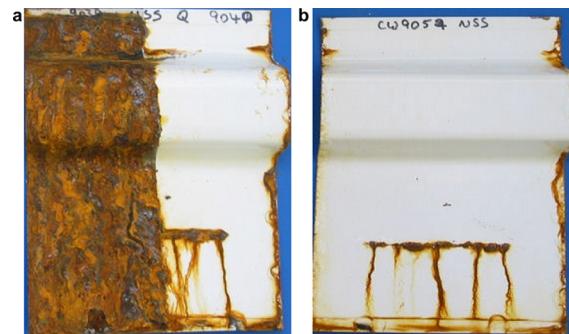


Figure 12. Salt spray test results. (a) Sol–gel coat plus half polyester top coat; (b) commercial coating consisting of Cr⁶⁺ pretreatment and primer and polyester top coat. Part (b) presents a comparison sample at the same time after 576 h neutral salt spray test. Reprinted with permission from ref 140a. Copyright 2008 Elsevier.

commercial product coating system consisting of a Cr⁶⁺ pretreatment, Cr⁶⁺ primer coating, and polyester topcoat (Figure 12b). Since the original report in 2008, a range of doped coatings based on a silica organic/inorganic platform have been developed by the team, and are currently undergoing the last trials aimed at commercialization.

3.3. Catalysis for Fine and Specialty Chemicals

Silica-based sol–gel catalysts (made of entrapped organic molecules, metal complexes, as well as metal nanoparticles) for the synthesis of fine and specialty chemicals have been intensively researched since the late 1980s. Comprehensive reviews including hydrolytic¹⁴¹ and nonhydrolytic¹⁴² sol–gel routes have been lately published, and the reader is referred to them for a detailed treatment of this relevant topic. Here, we assess the performance of selected recent sol–gel catalysts relative to catalytic materials based on traditional carriers (polymeric, charcoal, or metal oxides).

The first example is the new sol–gel entrapped ORMSIL catalyst for the selective hydrogenation of edible fats and vegetable oils.¹⁴³ The method enables one to carry out the selective and complete hydrogenation (hardening) of an ample variety of vegetable oils under hydrogen balloon conditions, over an ultrasmall catalyst amount (0.1 mol %), affording only healthy cis fatty acids.

Natural oils and fats are always found in cis configuration. For example, vegetable oleic acid is the cis isomer of an 18-carbon fatty acid with the double bond in the ninth carbon atom. Its trans isomer, elaidic acid, has a straighter acid chain (Figure 13). To increase their shelf life and enable more stable flavor, edible oils are often subjected to partial hydrogenation over supported nickel catalysts. Unfortunately, the reaction is not selective, and vegetable oils are converted into a mixture of cis and trans unsaturated fats.

In detail, hydrogenation over traditional Ni catalysts is typically carried out under 20 bar H₂ pressure and at 200 °C. Even under such relatively harsh conditions, however, hydrogenation of double bonds is only partial. The double bond in the cis fatty acid undergoing hydrogenation breaks, due both to heat and to incomplete interaction with the catalyst, and

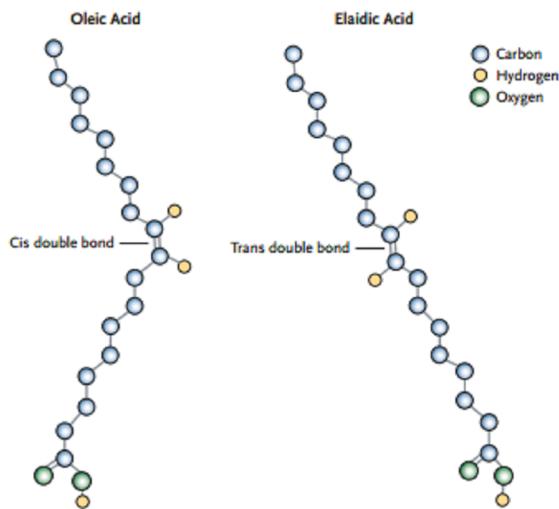


Figure 13. The trans bond imparts a structure more similar to that of saturated fats, altering the physiological properties and effects of the fatty acid. In elaidic acid, the double bond occurs at the ninth carbon atom (*trans*-18:1n-9). Reprinted with permission from ref 143. Copyright 2012 American Chemical Society.

subsequently reforms mainly in trans geometry, which is strongly favored over the natural cis for both thermodynamic and steric reasons.¹⁴⁴

In the case of partially hydrogenated oleic acid, for example, the final mixture will contain isomers in which the trans bond may occur anywhere between the fourth and the 10th carbon, while smaller amounts of isomers with a second trans double bond (*trans,trans*-18:2) are also present. These trans fats accumulate in the brain and in the retina and have been linked to heart disease and increased cholesterol levels.¹⁴⁵ The trans fat content of vegetable oils and spreadable margarines, for example, should not exceed 2% percent of the total fat content, whereas margarine and shortening stocks produced commercially from vegetable oils can have trans fat concentration as high as 40%.¹⁴⁶ Mandatory labeling of trans fat has been lately introduced in many countries, including Canada and the U.S.

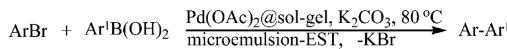
With nanostructured immobilized-Pd catalyst SiliaCat Pd(0), the hydrogenation process can be run at full efficiency at atmospheric pressure and room temperature.¹⁴³ No cis/trans isomerization takes place, whereas the catalyst is truly recyclable with low leached amounts of valued palladium, thereby providing the fat and oleochemicals industry with a suitable replacement for silica-supported Ni catalysts. When, for comparison, Pd is traditionally supported by impregnation of various oxide supports, hydrogenation of sunflower oil led to 30–40% C18:1 cis-trans isomerization, while requiring considerably higher reaction temperature and pressure (40 °C and 10 bar H₂) for optimal reactivity.¹⁴⁷

Replacement of nickel with palladium has been investigated since the early 1960s.¹⁴⁸ Yet, results of pure margarines production over Pd catalysts thus far have been uneconomical, as the amount of costly palladium needs to be significantly reduced and the catalyst recycled. Otherwise, Ni will continue to be used, even though it shows lower activity than Pd.

In another achievement, the high-yield and selective Heck, Stille, and Suzuki coupling reactions of numerous hydrophobic substrates are attained by carrying out the reactions in aqueous microemulsion over a 27% octyl-modified silica sol-gel matrix doped with Pd⁰ nanoparticles, under three-phase emulsion/

sol-gel transport (EST) conditions.¹⁴⁹ For example, the Suzuki cross-coupling of hydrophobic bromoarenes with different arylboronic acids in water under the EST conditions (Scheme 4) is highly selective, and no homocoupling (a common situation in many cases of the Suzuki coupling under conventional conditions) takes place.

Scheme 4. Suzuki Cross-Coupling of Hydrophobic Bromoarenes with Different Arylboronic Acids in Sodium Dodecyl Sulfate Emulsified in Water^a



^aReprinted with permission from ref 149. Copyright 2008 Wiley-VCH.

The method is an improved version of the EST technique first devised by Avnir and Blum in 2002.¹⁵⁰ Substrates are initially transformed into a microemulsion (an emulsion brought to clarity by titration of regular emulsion with an alcoholic cosurfactant), which consists of nearly 90% water, with the aid of a surfactant and a cosurfactant, such as PrOH or BuOH. The surfactant carries the molecules of the substrates to Pd⁰ nanoparticles entrapped within a hydrophobized silica sol-gel matrix, where the coupling between the substrates takes place. The products are then returned by the surfactant into the microemulsion, from which it can be released. What is further remarkable is that a general formula for the composition of stable microemulsions, suitable for different various hydrophobic substrates, was identified. A typical composition of such a microemulsion is 89.3 wt % of water, 3.3 wt % of the surfactant sodium dodecyl sulfate (SDS), 6.6 wt % of the cosurfactant (usually n-BuOH or n-PrOH), and 0.8 wt % of the hydrophobic substrates.

The immobilized palladium catalyst may be used in various coupling processes, at least six times, without loss of activity. Catalysis is truly heterogeneous and is due to Pd⁰ nanoparticles entrapped within the sol-gel matrix, resulting from the Pd²⁺ reduction induced by the methanol released during the preparation of the sol-gel matrix, as well as from the alcoholic cosurfactant.¹⁵¹ The amount of leached palladium in the reaction solution after removal of the sol-gel material is less than 1 ppm, and the filtrate has no catalytic activity (even after concentration).

Another recent report showing the superior performance of sol-gel silica-based materials in heterogeneous catalysis is the continuous synthesis of benzaldehyde via organocatalyst TEMPO-mediated oxidation of benzyl alcohol.¹⁵² This is an important synthetic methodology, nowadays widely employed in the laboratory and by pharma or fine chemicals companies to manufacture valued synthons and chemical products.

Under flow conditions (Figure 14) over the hydrophobized ORmosil-entrapped TEMPO, the reaction is complete in 1.5 min, leading to full conversion to pure benzaldehyde using NaOCl as unique oxidant at room temperature.

For comparison, under batch conditions, it takes 1 h to achieve maximum 97% conversion, while both low reaction temperature (0 °C) and KBr (a corrodant agent) are required to maximize yield and selectivity. For further comparison, the same reaction over polystyrene-supported TEMPO, even under flow, still requires cooling at 0 °C and the use of KBr as cocatalyst.¹⁵³

An overview of relevant achievements in sol-gel silica-based entrapped catalysts is given in Table 4.

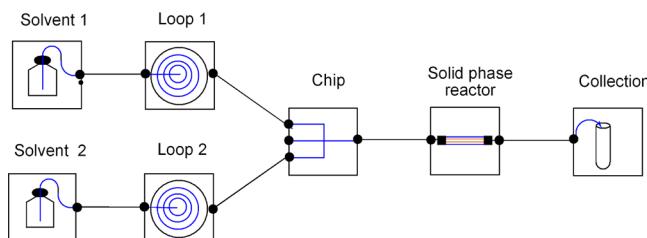


Figure 14. Fluidic setup for the heterogeneous oxidation of benzyl alcohol in flow over SiliaCat TEMPO. The reactants mixtures, a solution of benzyl alcohol in DCM (solvent 1) and a buffered 0.5 M NaOCl (solvent 2) solution, are premixed at room temperature prior to injection in the solid-phase reactor. Reprinted with permission from ref 152. Copyright 2013 Elsevier.

3.4. Nanocomposites

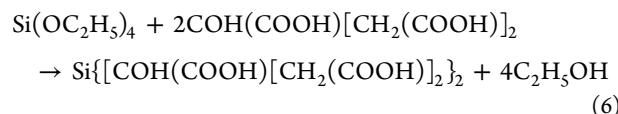
As was briefly referred to in section 2, nanocomposites are multiphase materials built up from a bulk matrix and one or more nanodimensional (1–100 nm) phases, the intent of which is to achieve, through synergistic interactions between the components at their interfaces, enhanced properties (e.g., mechanical, electrical, thermal, optical, electrochemical, and catalytic) relative to either of the single homogeneous constituents.¹⁶⁴ They are common materials in nature, for example, in the structure of bones, teeth, and seashells.¹⁶⁵ Nanocomposite inks were already used almost 3000 years ago, while nanoscale organo-clays have been used as thickening agents of polymer solutions (e.g., as paint viscosifiers) or emulsions (e.g., as homogenizers in cosmetics) for more than 50 years.¹⁶⁶ Polymer/clay composites were already the theme of textbooks by the late 1970s.¹⁶⁷

Depending on the phases involved, nanocomposites can be classified as inorganic, organic, or hybrid organic/inorganic materials. A narrower classification uses the chemical nature of the bulk matrix and of the nanodimensional phase(s): ceramic-matrix nanocomposites (CMnC) consist of a bulk ceramic with finely dispersed inorganic or organic nanofiller(s), to achieve improved mechanical, optical, electrical, and/or magnetic properties, as well as corrosion-resistance and other protective capacities;¹⁴⁸ polymer-matrix nanocomposites (PMnC) have their enhanced performance due to an organic polymer matrix (responsible for flexibility, ductility, processability, and electric properties) and to metallic or other inorganic or nanofillers (for

rigidity, thermal stability), even in extremely low concentrations;^{168,169} finally, metal-matrix nanocomposites (MMnC) have a metal matrix reinforced either with a ceramic nanofiller, carbon nanotubes or fibers, silicon carbide, or boron/carbon nitride.^{170–172}

The sol–gel technology marked a decisive point in the development of nanocomposites: (i) in the synthesis of ceramic matrixes, because it allows tailoring the inorganic final properties on account of its versatility, extending the range of organic nanofillers due to the mild conditions involved, and finally achieving a good dispersion of the nanophase; and (ii) in the synthesis of inorganic nanofiller(s), because it allows obtaining highly reproducible nanoparticles, with controlled size, structure, composition, and surface properties.¹⁷³

3.4.1. Silica Matrix Nanocomposites. Since the 1990s, sol–gel processes proved to be efficient for dispersing iron, nickel, copper, cobalt, silver, and gold¹⁷⁴ nanoparticles within silica-matrixes, with excellent potential for biomedical and catalytic applications, and, as silica is an insulator, for achieving improved electrical conductivity.¹⁷⁵ An interesting example is the single-step process developed by Leite and co-workers in Brazil to produce well-dispersed Ni particles (in the range of 3–41 nm) in a mesoporous silica material, for catalytic purposes, soon generalized with success to other transition metal nanoparticles.¹⁷⁶ The simple nonhydrolytic sol–gel process makes use of citric acid first reacting with TEOS (eq 6), followed by calcination.



The CO/CO₂ atmosphere resulting from the pyrolysis of the organic material promotes the reduction of the metal cations producing an amorphous SiO₂ matrix with metal nanoparticles well-dispersed and embedded within this matrix (Figure 15).

Hollow silica/Ag nanocomposite spheres with excellent antibacterial properties were recently produced by a relatively simple sol–gel method. In this approach, the Ag⁺ ions were adsorbed onto the surfaces of functionalized, monodisperse hollow silica nanoparticles (prepared by a combined dispersion polymerization and sol–gel process), and then in situ reduced by the deprotonated silanol groups, with no need for extra reducing agents or catalysts.¹⁷⁷

Table 4. Selected Relevant Achievements in Sol–Gel Silica-Based Entrapped Catalysts^a

year	author/company	catalyst	ref
1990	Avnir et al.	silica-entrapped enzymes	16
1992	Gonzalez et al.	sinter-resistant silica-entrapped Pt nanocatalysts	154
1993	Blum and Avnir	silica-entrapped organometallic catalysts	155
1995	Reetz/Fluka	ORMOSIL-entrapped lipases	83
1999	Blum and Avnir	enantioselective catalysis in water with silica-entrapped unsoluble organometallic complex	156
2000	Davis and Katz	bulk imprinted silica	157
2000	Wong Chi Man and Moreau	asymmetric syntheses with enhanced enantioselectivity with chiral silica-entrapped organometallic catalysts	158
2001	C.-M. Che et al.	asymmetric epoxidation of alkenes with silica-entrapped porphyrin	159
2002	Blum and Avnir	organometallic catalysis in water with ORMOSIL-entrapped catalysts (EST, three-phase emulsion–solution–transfer)	150
2003	Ciriminna et al.	aerobic oxidation with ORMOSIL-entrapped TPAP, more efficiently as compared to TPAP in solution	160
2007	Sullivan/Phosphonics	silica-entrapped Pd complex for cross-coupling reactions	161
2010	Pandarus and Béland/SiliCycle	ORMOSIL-entrapped Pd complex for cross-coupling reactions	162
2011	Pagliaro et al./SiliCycle	ORMOSIL-entrapped metal nanoparticles	163

^aChronological order.

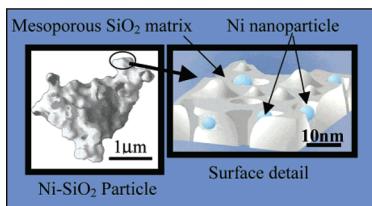


Figure 15. A schematic representation of well-dispersed Ni nanoparticles in a mesoporous silica support. Reprinted with permission from ref 176. Copyright 2002 American Chemical Society.

A versatile sol–gel strategy was recently designed by Warren, Wiesner, and co-workers for obtaining silica nanocomposites with electrical conductivity improved by 3 orders of magnitude over existing silica nanocomposites.⁴⁹

The process is general and starts by linking the silicon alkoxide to the amino acid, and then using the resulting ligand to complex the metal ions in solution. For example, organosilane 3-isocyanatopropyltriethoxysilane (ICPTS) is first linked to an amino acid by reductive amination, which in turn coordinates the metal ion M^{n+} .

Chemical bonding of the metal ions to the silica sol–gel precursor prevents the phase separation that was disrupting in the previously reported self-assembly process for producing porous silica/metal nanocomposites. Now the metal content in the final glass is high, and the resulting porous silica/metal/carbon nanocomposites show electrical conductivities as high as those of pure metals (over 1000 S cm⁻¹).

Traditional doped sol–gel silica glasses have a rich and varied electrochemistry,²⁶ but they are not suitable for high-current-density devices. Thus, while sol–gel encapsulation remains ideally suited to stabilize and even increase the catalytic performance of entrapped bioentities, providing an inert host material (silica), the use of better conductive silica is required to enhance the current density of sol–gel biofuel cells, because it improves the diffusion of the fuel or oxidant to the active sites.¹⁷⁸ Now, this new process will allow building a library of materials that will be advantageously used in fuel cells and as electrodes in batteries, as alternative to porous metal films of large surface area.

Another example of silica nanocomposites with a metal nanophase are the “energetic nanocomposites”. They are metastable intermolecular composites, also called superthermites, formed by a silica matrix, nanoscale aluminum powder, and metal oxides (usually iron, molybdenum, or copper oxide).¹⁷⁹

The silica-based magnetic nanocomposites, formed by magnetic nanoparticles (either Fe_3O_4 or $\gamma-Fe_2O_3$) dispersed in a silica matrix, are of relevant technological and scientific interest. Here, encapsulation in silica prevents interactions between the magnetite particles, and consequently assures a uniform dispersion, essential for an efficient performance in most applications, including diagnostic and therapeutic, where they must display high magnetization, be stable against oxidation, and, most important, remain nonaggregated. The main approaches for the synthesis of $SiO_2-Fe_2O_3$ nanocomposites were recently and thoroughly reviewed.⁷³ Sol–gel methods play here an important role, allowing the efficient dispersion and stabilization of Fe_2O_3 particles with 2–10 nm diameter.^{180–183} Mesoporous silica matrixes are the most successful for this purpose, because the magnetic particles can be effectively confined to the channels of the silica structure.¹⁸⁴

Metal nitride (e.g., Cu_3N , GaN) nanoparticles confined in a silica host matrix are well-known for applications in superhard coatings, spintronic devices, optics, or catalysis.¹⁸⁵ An ingenious method for preparing metal nitride@ SiO_2 nanocomposites (gallium and copper nitride, Figure 16) was recently developed



Figure 16. Copper nitride@ SiO_2 nanocomposite with a highly dispersed nanophase. Reprinted with permission from ref 186. Copyright 2011 Royal Society of Chemistry.

by Schubert’s group, via nitridation of the corresponding metal oxide nanoparticles obtained through sol–gel processing of organotrialkoxysilane-substituted metal complexes.¹⁸⁶ They simply used N -[3-trimethoxysilyl]propyl]ethylenediamine complexing Cu^{2+} or Ga^{3+} and sol–gel processed the complex with TEOS. Anhydrous ammonia gas was used for the nitridation at high temperature, eventually obtaining a homogeneous distribution of the nanoparticles in the host matrix and a good control over of the average particle size.

Silicon carbide fibers, carbon fibers, or nanotubes are also used as nanofillers to silica-based nanocomposites with remarkably high strength and stiffness.¹⁸⁷ A recent example consists of a new strategy for the *in situ* incorporation of multiwalled carbon nanotubes into a silica matrix for electrochemical sensing, using a biofriendly sol–gel route, based on the preparation of a water-soluble carboxymethylchitosan derivative having pendant pyrene moieties.¹⁸⁸ These groups act as stabilizing agents for preparing the colloidal dispersions of the nanotubes, and also as catalysts for the sol–gel reactions of the silica precursor (tetrakis(2-hydroxyethyl)orthosilicate, THEOS). These nanocomposites may be used to fabricate amperometric biosensors for hydrogen peroxide with improved response, by entrapping horseradish peroxidase during the sol–gel process.

The silica-matrix nanocomposites with an organic or polymeric nanophase have the range of applications extended to fields as diverse as biomedical, aerospace, and automotive industries.¹⁸⁹ Those with a mesoporous silica framework and a polymer nanophase (e.g., polyacrylate or polymer sulfonate) exhibit relevant catalytic properties.¹⁹⁰ For example, a unique catalyst for α -methylstyrene dimerization was developed in 2000 by Fujiwara and co-workers, consisting of Nafion resin incorporated in the framework of M41S type of mesoporous silica.¹⁹¹ A simple preparation method was more recently proposed, in which a polymer sulfonate (Nafion and poly-(sodium-styrenesulfonate)), silica precursor, and surfactants are mixed in an alkaline aqueous solution to generate polymer sulfonate/mesoporous silica nanocomposites (Figure 17).¹⁹²

Nanocomposite silica-based aerogels form a class of CMnCs with appealing properties and foreseen applications in fields

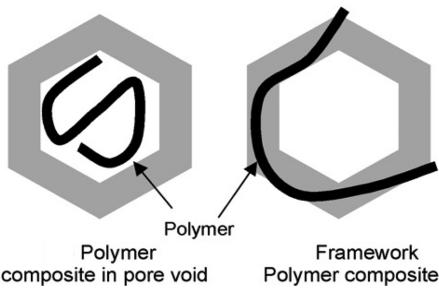


Figure 17. Conceptual schemes of composite materials of mesoporous silica with a polymer nanophase. Reprinted with permission from ref 192. Copyright 2007 Elsevier.

where high-performance thermal and acoustic insulators are needed. They are extremely light (envelope densities below 500 kg m⁻³), have excellent thermal and acoustic insulating properties (thermal conductivity in the range 0.01–0.02 W m⁻¹ K⁻¹ and acoustic impedance 103–106 kg m⁻² s⁻¹), are nonflammable due to the inorganic aerogel matrix, and gain stability toward atmospheric moisture and mechanical resistance due to the organic nanophase.¹⁹³ They are already commercialized in Europe and in the U.S. using supercritical and also subcritical drying of the wet gels.¹⁹⁴ A recent EU-

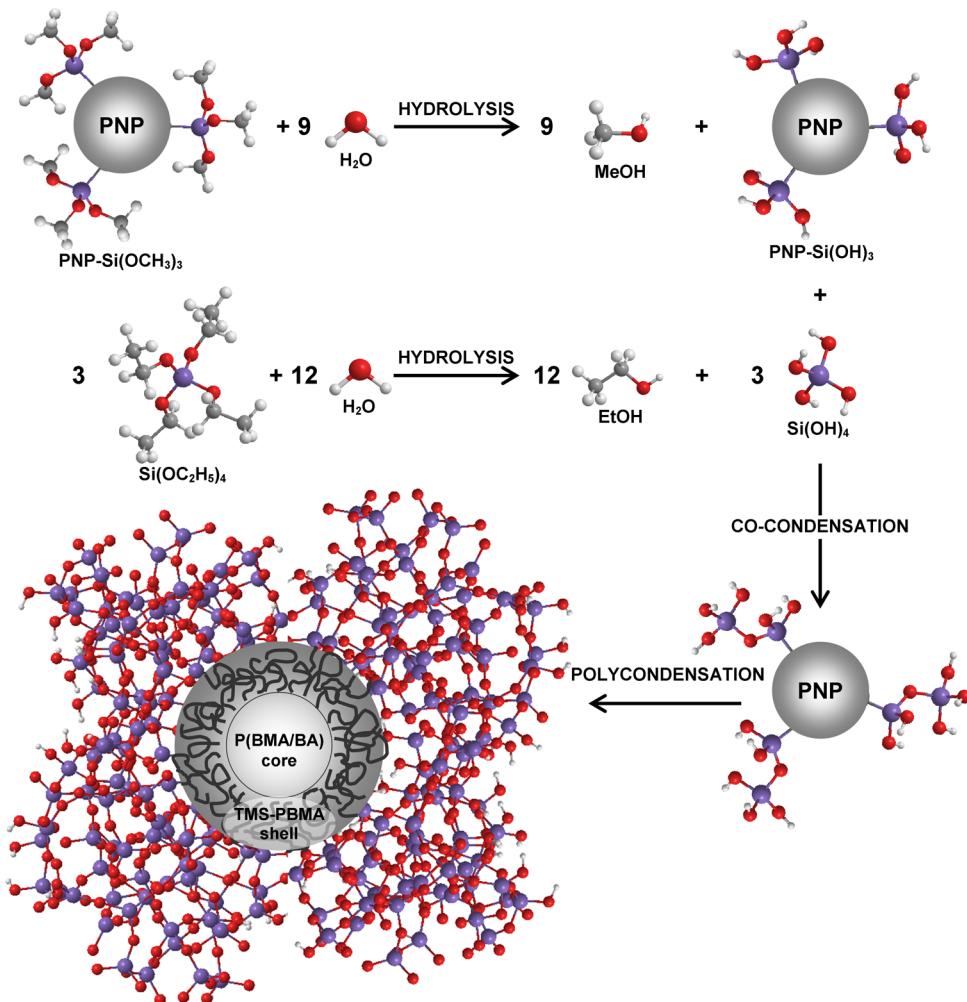
funded project¹⁹⁵ aims to optimize nanohybrid aerogel building components for insulating purposes, via silylation of the silica network and thus avoiding supercritical drying.

Another most promising material in this context is Airsiltex^{72,196,197} obtained via desiccation of the precursor alcogel under subcritical conditions, affording a nanohybrid aerogel with superior insulating properties and good mechanical behavior.

Scheme 5 shows that the nanofiller here is formed by functionalized core–shell colloidal polymer nanoparticles (PNP), synthesized by a two-stage emulsion polymerization technique, containing a trimethoxysilyl-modified poly(butyl metacrylate) shell and a poly(butyl metacrylate-*co*-butyl acrylate) core. Cross-linking stabilizes the PNPs to be dispersed in the sol–gel organic medium. The functional groups (hydrolyzable trimethoxysilyl) allow binding the nanoparticles to the growing silica network. The production of Airsiltex is environmentally benign, with no significant hazardous by-products, because the reactions and drying take place in mild conditions (low temperature, atmospheric pressure, and aqueous environment, without silylation of the silica).

Because the polymers in both the core and the shell of the nanoparticles have low T_g , they contribute to improve the mechanical properties of the nanohybrid aerogel and act as

Scheme 5. Sequence of the Typical Sol–Gel Hydrolytic Polycondensation Reactions To Produce Airsiltex^a



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impact modifiers. As an example, the nanocomposite with 3 wt % PNP has an envelope density of 357 kg m^{-3} , a total porosity of 83% with average mesopore diameter of 11.5 nm, mechanical resistance to compression of 4.24 MPa, and maximum deformation of 14.4%. Besides, comparing the stress–strain (σ – ϵ) curve obtained from unidirectional compression tests with that of a pure silica aerogel (Figure 18), it is clear that,

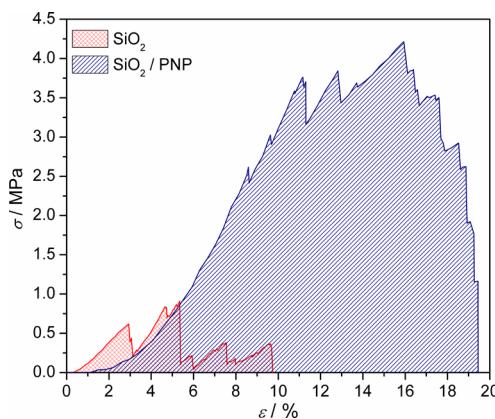


Figure 18. Stress–strain curves obtained from unidirectional compression tests of pure silica and a hybrid aerogel containing 3 wt % PNP. Reprinted with permission from ref 72. Copyright 2007 American Chemical Society.

although the brittle behavior of a cellular material is kept, the energy absorbed by the nanocomposite to the maximum compression strength (~area under the σ – ϵ curve) is much higher.

Carbon nanofibers also proved to significantly improve the mechanical properties of silica aerogels, keeping densities below 100 kg m^{-3} . This is important for increasing mechanical integrity when a specific application requires lower density, or higher porosity.¹⁹⁸ Most recently, a notable advance in nanocomposite aerogels in terms of mechanical properties without loss of performance as thermal insulators below 300°C was reported.¹⁹⁹ Regenerated cellulose gel (fibrils less than 10 nm wide) prepared from an aqueous alkali–urea solution was used as template to prepare cellulose–silica composite aerogels by an *in situ* sol–gel process from organic silicate, followed by drying with supercritical CO_2 . The resulting composite aerogels have the mechanical strength and flexibility, and low thermal conductivity of the cellulose aerogels.

3.4.2. Polymer Matrix Nanocomposites. Among the inorganic nanofillers for polymer matrix nanocomposites, the nanoparticles have attracted much attention,^{200,201} due to the synergistical improvement of properties achieved. Other important inorganic nanofillers of relevance to this Review are the mesoporous silicas, due to their ordered structure, high surface area, and easiness for functionalization of the mesopores,²⁰² and the layered silicates (e.g., montmorillonite, hectorite, saponite).^{203,204} Herein, we will focus only on the cases where the nanofiller is sol–gel silica, in different forms.

The sol–gel routes to reinforce polymer matrixes are mostly used in the bottom-up methods, a chemical approach, which consists of synthesizing the ceramic nanophase followed by incorporation.²⁰⁵ Obtaining a high degree of dispersion of nanoparticles in the polymer matrix remains a challenge.

A variety of synthesis procedures have been proposed, among which heterophase polymerization (which generally implies a premodification of the surface of the inorganic particles to increase their compatibility with the polymer), emulsion or miniemulsion polymerization (suitable for the synthesis of nanocomposite particles with a controlled morphology), and catalytic emulsion polymerization in the presence of a modified inorganic nanophase.²⁰⁶ An important parameter for the final properties of the nanocomposite is the number of reactive functional groups available on the nanoparticle surface: the higher is the functionality, the more cross-linked structures are obtained (Figure 19).

The mechanical, thermal, and electric properties of the nanocomposite depend on the dispersion of the nanoparticles, on the adhesion at the polymer–nanofiller interface, on concentration, and size. Table 5 lists examples of PMnCs whose properties were modified relative to the matrix, as a function of the polymer, the silica form, content, and size, when applicable. The growing academic and industrial interest on polymer/layered silicate (PLS) nanocomposites relies on the remarkable improvement in properties that may be achieved: high moduli, increased strength and heat resistance, decreased gas permeability and flammability, and increased biodegradability of biodegradable polymers.²⁰⁴ Responsible for triggering this interest was the Nylon-6 (N6)/montmorillonite (MMT) nanocomposite reported in 1989,²⁰⁷ in which very small amounts of sol–gel layered silicate loadings resulted in pronounced improvements of thermal and mechanical properties.

Since then, PMnCs have been made with a large variety of polymers, such as polypropylene, polyethylene, polystyrene,

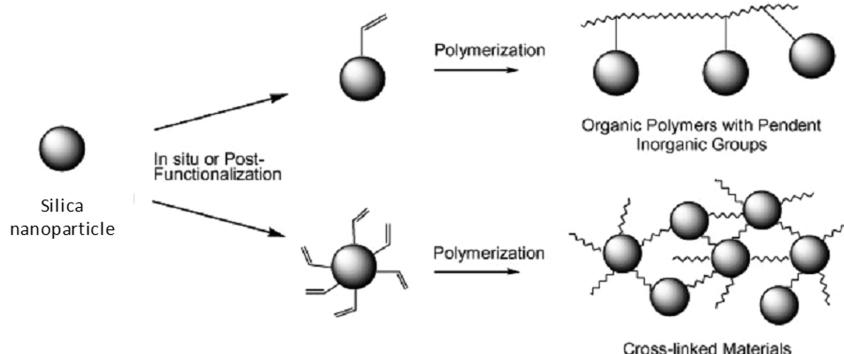


Figure 19. Influence of the functionality of a silica nanoparticle on the final structure of the nanocomposite. Reprinted with permission from ref 206. Copyright 2006 American Chemical Society.

Table 5. Examples of PMnCs Whose Properties Were Modified Relative to the Matrix, as a Function of the Polymer, the Silica Form, Content, and Size^a

polymer matrix	nanofiller			modified properties
	form	size (nm)	content	
epoxy (commercial)	silica nanoparticles	25	1–14 vol %	increased microhardness, fracture toughness, and modulus; decreased T_g and increased T_β ²⁰⁸
epoxy (DGEBA)	silica nanoparticles	400	50–70 wt %	increased T_g and brittleness, decreased coefficient of thermal expansion ²⁰⁹
epoxy (DGEBA)	silica nanoparticles	240, 1560	30 vol %	increased storage and loss modulus; decreased T_g for 1560 nm particles ²¹⁰
epoxy (DGEBA)	silica nanoparticles	75, 330	1–5 wt %	increased elastic modulus (modeled) and aggregation level ²¹¹
epoxy (DGEBA)	silica nanoparticles	10–20	10–70 wt %	increased thermal stability; decreased T_g ²¹²
epoxy (DGEBF)	silica nanoparticles	90	1–7 wt %	increased fracture toughness; larger deformation resistance (up to 3 wt %) ²¹³
epoxy (TGDDM)	silica nanoparticles	12.5	5, 10 wt %	increased elastic and yield modulus, and brittle fracture; decreased T_g constant T_β ²¹⁴
epoxy (PBA)	silica nanoparticles	9	2.17 vol %	decreased frictional coefficient and specific wear rate; modified silica nanoparticles promote cure reaction of epoxy ²¹⁵
epoxy	silica nanoparticles	4000	14–39 vol %	increased Young's modulus; monotonic variation in the yield strength and yield stress ²¹⁶
epoxy	silica nanoparticles +short C fibers	12–14	0.5–5 vol %	enhanced the modulus, strength, and fracture toughness ²¹⁷
PCL	silica nanoparticles	100–200	1–2.5 wt %	Young's modulus ²¹⁸
PU	silica nanoparticles	14–260	1–4 wt %	increased T_g with particle size up to 66 nm; decreased surface and interface free energies by incorporation of silica ²¹⁹
PU	silica nanoparticles	30	5	improved silica dispersion ²²⁰
PU	silica nanoparticles	175, 395, 730	1–10 wt %	constant T_g at different particle size and concentrations ²²¹
PU (thermoplastic)	silica nanoparticles	7	10 wt %	increased shear and storage modulus, tensile and peel strength, decreased T_g ²²²
polyimide	silica nanoparticles	20	10–50 wt %	increased dielectric constant; enhanced thermal stability ²²³
PS	silica nanoparticles	25–200	5–10 wt %	increased DTA peaks; strong interaction between silanes group and polymer chains ²²⁴
PP	silica nanoparticles	50–110	1–5 wt %	increased thermal degradation stabilization; increased elastic modulus ²²⁵
PP	silica nanoparticles	80–100	2 wt %	very good dispersion due to in situ polymerization ²²⁶
PTMSPMA	silica nanoparticles	15–20	10–50 wt %	increased thermal stability; enhanced hardness; excellent optical transparency ²²⁷
PTMSPMA	mesoporous silica/PMA		8.4–28.2 wt %	tensile strength, modulus toughness, with little sacrifice on the strain at break ²²⁸
P(MMA- <i>b</i> -BA)	silica nanoparticles	20	0–12 wt %	enhanced mechanical properties and improved fire-retardant behavior ²²⁹
PMMA	AEROSIL, R812; R805; R972	7, 12, 16	0–4 wt %	increased T_g ; increased degradation temperature; increased degradation activation energy; higher storage and loss moduli ²³⁰

^a T_g , glass transition temperature; DGEBA, diglycidylether of bisphenol A; DGEFB, diglycidylether of bisphenol F; TGDDM, tetraglycidyl 4,4-diaminodiphenylmethane; PBA, polybutyl acrylate; PS, polystyrene; PEO, polyethylene oxide; PP, polypropylene; PU, polyurethane; PCL, polycaprolactone; PTMSPMA, poly (3-trimethoxysilyl)propyl methacrylate; PMMA, polymethylmethacrylate.

polycarbonate, polyethylene oxide, polyacrylate, polyethylene terephthalate, unsaturated polyester, polyurethane, epoxy resins, and nylon, among others. The most commonly used layered silicates for the preparation of nanocomposites are smectite-type: hectorite [$\text{Na}_{0.3}(\text{Mg},\text{Li})_3\text{Si}_4\text{O}_{10}(\text{OH})_2$] and montmorillonite [$(\text{Na},\text{Ca})_{0.33}(\text{Al},\text{Mg})_2(\text{Si}_4\text{O}_{10})(\text{OH})_2 \cdot n\text{H}_2\text{O}$], because of their high cation exchange capacities, surface area, surface reactivity, adsorptive properties, and, in the case of hectorite, high viscosity and transparency in solution.²⁰⁴

3.5. Ceramic Membranes

Polymeric membranes are widely used in the pharmaceutical industry and in water treatment plants, but not in the chemical industry, due to the low stability of the polymers under the typical harsh conditions needed for many chemical reactions.

Stable ceramic membranes are currently mainly employed in gas separations, but their application in liquid-phase separations of chemical reactions is of obvious interest. For example, dewatering of organics is of high relevance in the chemical industry. Hence, the molecular separation of water and organic solvents via membranes could replace distillation by membrane pervaporation processes, thus leading to considerable energy

savings. Ceramic membranes, however, should be more stable than traditional polymeric membranes.

Sol-gel microporous SiO_2 applied as thin film as membrane material shows high gas separation selectivities, but its well-known poor hydrothermal stability, silica is soluble, fragile, and densifies changing the required porosity, prevents any practical application. ORMSILs, however, show enhanced hydrothermal stability due to the nonhydrolyzable bonds and lower surface diffusion coefficient. Moreover, they are less prone to crack propagation.

Hence, following the original efforts of Schmidt,²³¹ Okui,²³² Noble,²³³ and Zhang,²³⁴ who had already observed enhanced performance of different ORMSIL-based membranes in gas separation (O_2/N_2 , CO_2/N_2 , and CO_2/O_2 mixtures), a breakthrough occurred in 2004, when researchers at Energy Research Centre of The Netherlands (ECN) reported that 30%-methyl-modified silica membranes afforded constant performance for >18 months in the dehydration of a butanol-water mixture at 95 °C (Figure 20).²³⁵

Shortly after that breakthrough, Dubois reported that the fracture energy values of dense organic/inorganic thin films prepared from bridged silicon precursors were larger than those of dense SiO_2 (15–17 versus 10 J m⁻²) (Figure 21).²³⁶

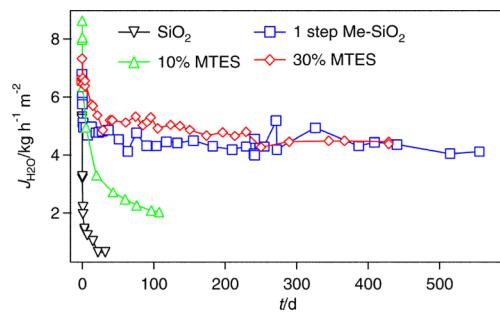


Figure 20. SiO_2 and methylsilicas pervaporation results of a 5 wt % H_2O in butanol (BuOH) mixture. Addition of MeTEOS affords stable performance, whereas the silica membrane lasts a few days only. “1 step Me-SiO_2 ” refers to methylsilica prepared in a single-step sol–gel polycondensation, whereas the other organosilicas are obtained via a two-step synthesis starting from a prehydrolyzed sol. Reprinted with permission from ref 235. Copyright 2004 Royal Society of Chemistry.

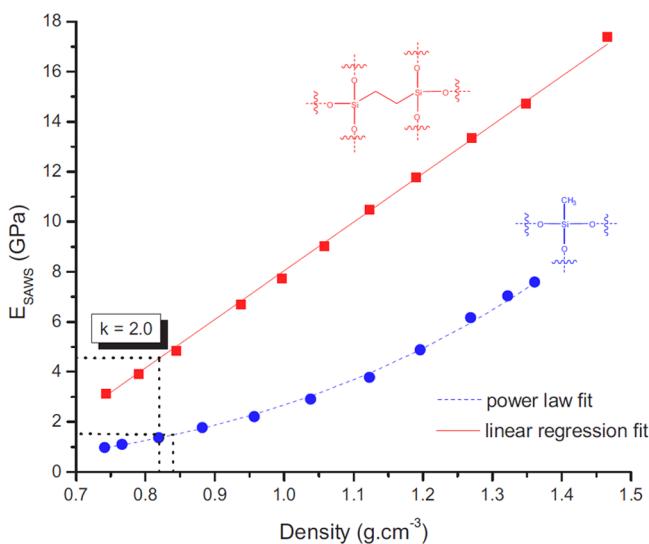


Figure 21. Young's modulus follows a linear decay when porosity is introduced, a unique observation as compared to traditional organosilicates. Reprinted with permission from ref 236. Copyright 2007 Wiley-VCH.

Soon, ceramic sol–gel microporous membranes from bridged silica precursors of unprecedented long-term stability, even compared to state-of-the-art methylated silica, were reported by Castricum and co-workers.²³⁷ Because these polymeric systems are prepared under acid-catalyzed conditions, they are expected to yield small fractal dimensions, contrarily to base-catalyzed systems that generally show fractal dimensions >3 .²³⁸ Thus, base-catalyzed systems usually result in mesoporous materials (with pores in the order of the size of the colloidal particles), with hard-sphere-type packing, while acid catalysis produces microporous materials, whose pore sizes are not related to the dimensions of the polymeric colloids.

The particle size of the colloids and their fractal dimension can be used to determine the stage of development of a polymeric sol. These can be measured via dynamic light scattering (DLS) and SAXS, respectively.²³⁹

The degree of branching of a polymer can be expressed in terms of the fractal dimension, D_f , which relates the mass, m , contained within a radius of gyration, R_g , of a polymer, via eq 7:²⁴⁰

$$m \approx R_g^{D_f} \quad (7)$$

Usually, D_f varies between 1 for linear nonbranched polymers and 3 for dense spherical particles. Branched polymers have a fractal dimension between these two extreme values.²⁴¹

According to Mandelbrot's demonstration, fractal like structures can interpenetrate one another only if their fractal dimensions are smaller than 1.5.²⁴² Thus, it is not surprising that, for pervaporation and gas separation membrane production, the optimal stage of development corresponds to particle sizes in the 5–10 nm range and fractal dimensions $1 < D_f < 1.5$. Larger values lead to mesoporous systems, because the fractal-like structures behave as semisolid objects and cannot interpenetrate each other, while smaller values lead to no structure buildup.²⁴³

Recent assessment of the structure for a set of membranes prepared from different organosilica precursors (varying the organic bridge) allowed concluding once more that the differences in membrane properties must be related to the structure of the organic bridge, rather than to differences in preparation conditions.⁵⁰

Overall, this powerful sol–gel technology allows the purification of various industrial solvents at a reduced cost and at an enhanced efficiency. The capital cost of installation is higher than that of polymeric membranes, but the operational costs are lower, because ceramic membranes are much more stable and robust. The sol–gel process was readily scaled up and reproduced, and these membranes are now commercialized with the HybSi trademark having been licensed from ECN.²⁴⁴

Another important green technology enabled by ORMSIL-based glassy membranes is related to high energy density direct methanol fuel cells (DMFCs). Low methanol crossover is critical to achieving high energy efficiency and long life, because fuel loss through the membrane is the dominant loss mechanism in long lifetime devices. Minimizing the fuel loss due to methanol crossover is the most important issue for creating long-life, low-power (μW to mW) DMFC sources. In closer detail, Kohl and co-workers synthesized sulfonic acid-functionalized glass membranes via sol–gel polycondensation of 3-glycidoxypropyltrimethoxysilane (GPTMS), 3-mercaptopropyl trimethoxysilane (3MPS, Figure 22), and TEOS.²⁴⁵

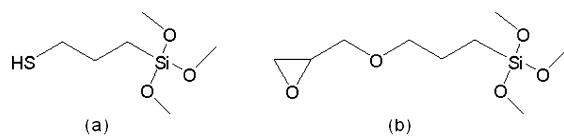


Figure 22. Molecular structure of (a) 3MPS and (b) GPTMS.

The optimum glass membrane was obtained from a mixture containing 90:7:3 molar ratios of 3MPS:GPTMS:TEOS and a $\text{H}_2\text{O}:\text{Si}$ ratio of 2. The sol–gel mixture was condensed and dried, after which the thiol groups were oxidized to sulfonic acid groups with 10% hydrogen peroxide for 3 h at 60 °C. The epoxy content of the GPTMS improved the mechanical properties of the electrode by cross-linking with the ORMSIL matrix. The resulting membrane had a conductivity of 3.71 mS cm^{-1} , and methanol permeability of 2.17×10^{-9} mol $\text{cm} \text{ cm}^{-2}$ day $^{-1}$ Pa $^{-1}$, which is significantly better than Nafion or other previously reported membranes for this application. In brief, the hydrophobized ORMSIL glassy matrix prevents methanol permeation, while closer packing of the sulfonic acid groups provides low activation energy for proton transport in the glass

membrane. As a result, the conductivity increases and the permeability decreases, resulting in a high selectivity membrane. The PtRu/C catalyst nanoparticles for methanol oxidation are sol–gel entrapped into the glassy silica-based matrix, affording a $236 \mu\text{A cm}^{-2}$ at 0.4 V methanol fuel cell performance that was stable for more than 10 days.²⁴⁶

4. AN INSIGHT INTO CONTEMPORARY RESEARCH IN SOL–GEL SCIENCE

It is useful to gain a perspective view on this relevant field of contemporary chemical research, both from a scientific and from an economic viewpoint, as the industrial emergence of sol–gel technology has, in our view, profound educational consequences for the chemistry curriculum. The International Sol–Gel Society (ISGS), whose international workshop is attended every 2 years by some 600 researchers, recently carried out a revealing investigation aimed at sketching a picture of contemporary sol–gel science and technology.

Figure 1 demonstrates the dramatic growth in interest for sol–gel technology in academia, through the large progression of the number of publications in the last 20 years, from less than 100/year in 1987 to about 3000 papers in 2009.²⁴⁷ Not all of these papers deal with silica-based materials, because the field of sol–gel materials exceeds the subdomain of functional silica gels. Nonetheless, the figures are enlightening and relevant to this account. Out of the 12 top publishing institutions listed in Table 6, apart from the Kyoto University and the Russian

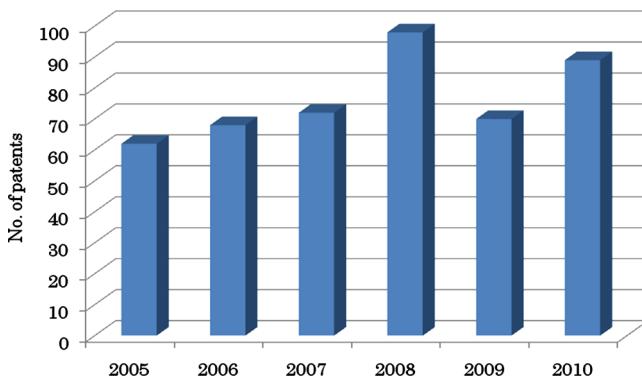


Figure 23. Trend in PCT patents in sol–gel technology in the period between 2005 and 2010. Reprinted with permission from Dr. C. J. Barbé. Copyright 2013 Dr. C. J. Barbé.

(projected to grow to \$2.2 billion by 2017).²⁴⁸ Most, but not all, of these products are silica-based materials or liquid formulations. However, along with leading practitioners of the sol–gel technology, we argue that the sol–gel market is greater than what is generally assumed. A first argument supporting this claim is that a variety of commercial aqueous silica (and titania) nanosols are available (Table 2). Why should companies produce hundreds of tons of these sols if there were not manifold applications?

For example, as mentioned above, Schott has produced the Amiran glass in a large amount since 1985.²⁴⁹ This is pure sol–gel technique based on triple dip-coating glass with SiO_2 – TiO_2 – SiO_2 sols. As a result, the boundaries between the outside and inside disappear so that canopies or other constructive measures designed to avoid reflections are no longer necessary. In fact, a lot of silica-based optical products with antireflective and NLO properties, microelectronic coatings, and interlayers are produced using sol–gel processes. However, such industrial know-how is only published in the patent literature, while market data remain undisclosed. In brief, statements about the industrial application of sol–gel technique should be taken cautiously, because many applications remain unrevealed.

Another rapidly growing market is that encompassing organosilica applications. In the sole field of silica-based nanocoatings, we witnessed the launch of many innovative products by large and medium-sized chemical companies in the last 5 years, with applications ranging from textiles to construction industries. Even higher growth rates have been observed for the application of sol–gel functionalized products based on silica-entrapped organics in the healthcare and cosmetic business segments. For example, the sol–gel micro-encapsulated drug for treating Rosacea (the DER45-EV Gel, currently undergoing a phase II clinical stage study in the U.S.) recently led to a \$27 million contract.²⁵⁰ Another argument supporting our claim is that in the U.S., the leading market for sol–gel-derived products, the main silane provider²⁵¹ has expanded twice its original size in the past few years, pointing to a fast growth of practical applications of sol–gel techniques.

5. OUTLOOK AND PERSPECTIVES

In perspective, functionalized silicas will have a profound impact on a number of chemical domains. Looking at the near future, for example, we believe that the route is now open to transform the industrial practice of synthetic organic chemistry, by using silica-entrapped catalysts and reactants. This is so

Table 6. Top 12 Institutions for Sol–Gel Publications in the Last 5 Years^a

rank	institution	no. of publications
1	Chinese Academy of Sciences, China	412
2	Tsinghua University, China	206
3	Zhejiang University, China	123
4	Kyoto University, Japan	106
5	Tongji University, China	97
6	Shandong University, China	95
7	Jilin University, China	92
8	Fudan University, China	83
9	Tianjin University, China	82
10	University of Science and Technology, China	82
11	Russian Academy of Sciences, Russia	80
12	Nanjing University, China	76

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Academy of Science, all are Chinese institutions, in line with the increasing China's contribution to the world's scientific research, especially applied research aiming at industrial applications.

Figure 23, in turn, shows that on average 80 international patents are granted every year, with a peak of 98 patents granted in 2008, the year before the global financial crisis.

Table 7 clearly shows that Japan leads the global patent ranking, with the majority of patents having been granted to large industrial corporations, confirming the prolonged interest of the Japanese industry in sol–gel technologies, many of which historically commercialized by Japanese companies.²⁴⁸ Table 7 also evidences a strong progress of China and Korea in patenting sol–gel related technologies.

The overall global market for sol–gel products, however, remains relatively small, having reached \$1.4 billion in 2011

Table 7. Patent Repartition by Language during the Last 5 Years^a

no. of patents	language								
	Japanese	English	Chinese	German	French	Spanish	Portuguese	Korean	others
332	140	182	50	13	6	4	39	8	

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because the sol–gel heterogenization allows drastic cuts in manufacturing costs of the fine chemicals and pharmaceutical products, as it eliminates waste (spent solvents and reactants), affords pure products, and allows catalyst recycle. In the past decade, many synthetic chemists in wealthy countries have lost their jobs in those industries, following the production transfer to India and China, where the labor and overhead costs are low.²⁵² Laird aptly points out²⁵³ that the profession needs to expand its knowledge base, for instance, to provide low-cost and highly efficient solutions for molecules' manufacturing in countries where the labor and overhead costs are high.

For example, a considerable proportion of APIs for generic drugs are still made in western countries by companies with competitive cost of goods. This can only be the case if the synthetic route to the API uses low-cost raw materials and an innovative synthesis, using highly efficient manufacturing processes with good space-time-yield and few isolated intermediates, by using heterogeneous catalysis, and preferably in low-volume continuous processes. Let us suppose that one such efficient process employs the valued oxidation catalyst TEMPO, a radical species that is widely employed in industry, dissolved in an organic solvent in the presence of bleach, to selectively oxidize alcohols into carbonyl compounds at low temperature.²⁵⁴ Once dissolved, the radical cannot be recovered after reaction, thus incurring higher cost due to additional separation steps and waste byproduct (solvent).

Conversely, once entrapped in an ORMOSIL matrix, the radical selectively mediates the formation of high yields of valued carbonyl compounds, while at the end of the reaction it is easily recovered and reused.⁴⁸ Clearly, molecular sol–gel encapsulation adds economic value to the non entrapped TEMPO because, once entrapped in a sol–gel matrix, it retains the basic physical and chemical properties that define its chemical functional value, further expanding them and imparting a new set of desirable properties, such as enhanced stability and the possibility to recover and recycle the catalyst. In this exact sense, the sol–gel entrapment in a silica-based matrix adds significant economic value to organic molecules, affording a new functional material capable to meet numerous different requirements in a single good. This large value accretion process in doped sol–gel materials is what eventually determines their utilization in disparate fields such as optics, coatings, catalysis, sensors, medicine, and biotechnology. The same logic indeed holds for entrapped bioentities such as plant cells.

Biocatalysis over higher plants cells has become the method for the industrial synthesis of bulk chemicals, pharmaceuticals and agrochemicals, active pharmaceuticals, and food ingredients.²⁵⁵ Plant cells are very sensitive to their environment, and we owe to Carturan the powerful idea that combining inert materials with biological entities is an ideal way to create stable "living materials", capable of affording plenty of valued substances from sugars and other simple nutrients. For example, *Ajuga reptans* cells are cultivated and used for the production of invertase, an enzyme widely used by industry for the hydrolysis of sucrose into fructose and glucose.

These plant cells are immobilized by a sol–gel SiO₂ membrane, which is built up directly on the cell surface by exposure to a gaseous flow of silicon alkoxide precursors. The immobilization enhances the metabolic activity of cells, resulting in a 40-fold increase in invertase production with respect to free cells.²⁵⁶ Today, Italy's IRB company efficiently manufactures extracts from plant cell cultures for cosmetic and nutritional companies over plant cell cultures. As an example, for the production of one kilogram of echinacoside, a natural phenol, by the sol–gel entrapped cells technology, only 3 m² of surface and 1 t of water are required, as compared to the more than 1000 m² of land and 1300 t of water required by the traditional technology.²⁵⁷

So, will the fine chemicals and pharmaceutical industries eventually start using these newly developed sol–gel catalysts and green processes at large scale?

Industry is reluctant to change any process for which they have invested in, whether for fear of needing to change equipment or that the new change (say new catalyst) leads to changes in quality that their customers may not want. Soon, however, companies in India and China, where processes are far from green, will need new catalysts and new processes to remain competitive, because their costs are increasing much faster than in Europe or in the U.S.²⁵⁸

Therefore, to succeed in the marketplace again, chemists trained in traditional synthetic or analytical chemistry will need to expand their curriculum, because the boundaries that separated traditional chemistry disciplines, inorganic, organic, organometallic, bio-, and materials chemistry, have eventually merged with the emergence of a multidisciplinary community of researchers with a keen scientific and technological interest in "all" aspects of chemistry. The intrinsically interdisciplinary science of doped sol–gel materials is an eminent example of this evolution, as it is the outcome of the integration of the once isolated domains of organic, inorganic, and biochemistry. To paraphrase Ozin, a student asking why he should risk his/her career "in a field that might not make it"²⁵⁹ should better ask himself what will be the risk if he does not get involved.

On the other hand, companies using sol–gel manufacturing technologies to be successful need to deliver standardized products with reproducible performance, and thus will need to develop a manufacturing process under quality control conditions, offering commercial availability in bulk to customers wanting to scale up. Getting back to the industrial catalysis example used above, one of the reasons why industrial chemists do not suggest using the sol–gel technology is that they need large amounts of commercially available catalysts, in the same way as heterogeneous and homogeneous hydrogenation catalysts are commercially available in commercial catalogues.

Increasing applications of sol–gel materials in the future will certainly be in areas that require a combination of mechanically stable, but porous solids, which can be loaded in a simple way with any functional species (e.g., catalysts, biocatalysts, fragrances, biocides, flavours, dyes, waxes, sensing species, etc.), as well making use of their excellent coating behavior (e.g., functional layers for soft materials like polymers, textiles,

wood, skin). The resulting advanced functional materials will find widespread use in the chemical, biotechnological, optical, construction, transportation, pharmaceutical, cosmetic, analytical, and medical industries. Moreover, they will do so in an environmentally benign way, as silica and ORMOSIL gels are generally nontoxic, while a sustainability approach to silica sol-gels manufacturing is already emerging.²⁶⁰

In 2009, Babonneau and co-workers reported²⁶⁰ that the price of TEOS had dropped to \$2–6 per kg (depending on grade and amount). Today, the price of TEOS ranges is below \$1.4 per kg (and continues to decrease), as its overall production (today being mainly based in China)²⁶¹ dramatically grew with the increasing number of sol–gel silica-based products and devices. This, along with the typical mild conditions under which TEOS (or organosilanes) are sol–gel processed, has lowered the manufacturing cost up to the point that silica-based materials and formulations can be used as coatings, cosmetics, catalysts, scavengers, reactants, sensors, adsorbents, and drugs, now accessible to an increasingly larger customers base.

Researchers willing to take their sol–gel silica-based technology to the marketplace, and therefore needing to raise finance by convincing investors, have now a wide range of successful companies that have established their commercial credibility, by placing numerous functionalized silica materials or precursors in the market.²⁶² This has been instrumental in projecting the commercial value of the technology and thereby in providing a powerful boost to investor's confidence by reducing the perceived technical risk.

Another lesson from two decades of attempts at commercializing different sol–gel technologies is that the biggest markets are not always the best. In other words, niche market opportunities can be more attractive because they may be less competitive, generate bigger profit margins, and offer fewer barriers to entry. To quote a leading industry practitioner, “market pull” is always easier to address than “technology push”, and because there are numerous problems in industry and society that can be solved through the use of sol–gel technologies, it is realistic to look forward to a number of successful sol–gel products capable to fit the above-mentioned needs.

This growth in number and applications of sol–gel silicas will continue until sol–gel nanochemistry will impact the most important applications of scientific and technological expertise, tackling the energy and environmental crises due to massive consumption of fossil fuels, by sunlight-powered recycling of carbon dioxide and water into energy-rich fuels or to generate electricity in biofuel cells. This route, opened by the research of Carturan mentioned above, has been pursued by Su and co-workers since 2008 via immobilization of photosynthetically active biological entities (cyanobacteria,⁵⁷ thylakoids,²⁶³ and red microalgae²⁶⁴) within porous and transparent silica frameworks affording photosynthetic, leaf-like materials that hold large promise in the development of new chemical processes using atmospheric CO₂ as a source of carbon to produce valuable compounds or biofuels.²⁶⁵

Chemistry practitioners at all levels will increasingly need more education on sol–gel hybrid silicas, and this Review will hopefully contribute to this end.

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Notes

The authors declare no competing financial interest.

Biographies



Rosaria Ciriminna graduated in Chemistry from the University of Palermo in 1995 with a thesis on the chemistry of terpenes after having joined the staff of then CNR's Institute of Chemistry and Technologies of Natural Products as a chemistry technician during her undergraduate studies. Her research is primarily developed at Palermo's Institute of Nanostructured Materials in cooperation with several leading Laboratories abroad. She has worked with Joël Moreau and Michel Wong Chi Man at Montpellier's ENSCM and, more recently, at Québec's Laval University. In early 2001 she became a full-time research chemist at Italy's CNR where she has worked ever since on research of broad scope that encompasses green chemistry methods for fine chemistry applications, fundamental studies on sol–gel materials, and nanochemistry. Her work was instrumental in advancing the field of sol–gel entrapped catalysts from basic knowledge to commercial products. She is a highly cited researcher, having coauthored more than 80 research papers and 4 books on these and related topics.



Alexandra Fidalgo graduated in Chemical Engineering from Instituto Superior Técnico (IST) of the Universidade Técnica de Lisboa in 1994, obtained a M.Sc. degree in Science and Engineering of Surfaces and Interfaces from Faculdade de Ciências da Universidade de Lisboa in 1999, and a Ph.D. degree in Chemistry (Synthesis of controlled porosity silica by the sol–gel process: from xerogels to aerogels) from IST in 2003. She was a postdoctoral research fellow at Centro de

Química-Física Molecular (CQFM) of IST from 2004 to 2008. Currently she is an assistant professor of statistics at Instituto Superior de Línguas e Administração de Lisboa - Laureate International Universities, and a research assistant at CQFM and the Institute of Nanoscience and Nanotechnology. Her research interests focus on the synthesis and characterization of advanced functionalized silica-based sol-gel materials for thermal insulation, catalysis, and drug encapsulation.



Valerica Pandarus was born in Romania where she studied chemistry at the University of Bucharest. In 2007 she obtained her Masters Degree in Organometallic Chemistry and Catalysis from the Université de Montréal under the supervision of Professor Davit Zargarian. She then joined the research group of Dr. François Béland at SiliCycle Inc. where she began to carry out research on the SiliaCat sol-gel heterogeneous catalysts family for fine-chemicals synthesis. Her research interests include the preparation of heterogeneous catalysts for fine chemicals green manufacturing, and she has been instrumental in the development of the SiliaCat S-Pd and SiliaCat DPP-Pd palladium(II) solid catalysts for cross-coupling reactions.



François Béland obtained his Ph.D. in 1999 from Laval University in Quebec City, Canada, where he studied silica-based catalysts by different spectroscopy methods. After getting his Ph.D. he moved to Montpellier for postdoctoral studies at the ENSCM. There, he studied different reactions in organic chemistry catalyzed by silica-based heterogeneous catalysts. He started working at SiliCycle as a researcher after his postdoc. A year later he was promoted to R&D Director, and his focus was to develop the SiliaBond (functionalized silica gels) product line. Recently he has been promoted to Vice-president of R&D. Dr. Béland has 15 years of experience with silica-based products for different applications in chromatography and for organic chemistry.



Laura Ilharco received her Ph.D. degree in Chemical Engineering from the Technical University of Lisboa, Portugal, and did her postdoctoral studies on surface science with Professor Michael Chesters, at the School of Chemical Sciences, University of East Anglia, UK. She earned the habilitation degree in Chemistry from Instituto Superior Técnico, Lisboa, in 2005, where she is an assistant professor of Physical Chemistry and Spectroscopy. She lectures regular post-graduate courses on sol-gel at Portuguese and Mexican universities. Her research is developed at Centro de Química-Física Molecular and Institute of Nanoscience and Nanotechnology, Lisboa. Her primary research interests include surface and interface chemistry, model catalytic surfaces under ultrahigh vacuum, and also the design and characterization of novel materials by sol-gel processes. She is currently interested in silica-based nanomaterials tailored for specific purposes, ranging from encapsulation of biologically relevant molecules and drug delivery, to thermal and acoustic insulation for building and transportation industries. She contributed to more than 80 international scientific publications, to several patents, and was awarded the Solvay Ideas Challenge 2003 prize.



Mario Pagliaro is chemistry and energy scholar based in Palermo, at Italy's CNR. In 1998 he received a doctorate in chemistry from the University of Palermo, following work carried out with David Avnir at the Hebrew University of Jerusalem and Arjan de Nooy at the TNO Food Research Institute in Zeist. In late 2000 he joined the staff of the CNR Institute of Chemistry of Natural Products. In 2002 he worked with Carsten Bolm at Aachen's RWTH. In 2005 he was appointed "Maître de conférences associé" at Montpellier's Ecole Nationale Supérieure de Chimie, and in 2008 he established the Sicily's PV Research Pole, a lively joint educational and research center on solar energy. He currently works yearly also in Québec where he is engaged in spreading solar energy and new green chemistry technologies. His research interests are in nanochemistry, sustainability and management. Mario has often been cited for his excellence in teaching and

writing. He has co-authored a large body of publications, including renowned volumes on glycerol, silica-based materials and flexible solar cells. Dr. Pagliaro regularly organizes conferences, and gives courses and tutorials on the topics of his research. In 2009 he chaired the 10th edition of the FIGIPAS Meeting in Inorganic Chemistry. In 2011 his research Group established the SuNEC international Conference on solar energy followed, in 2012, by the FineCat Symposium on catalysis for fine chemicals. Both meetings are held annually in Sicily.

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