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Diffusion of dissolved ions from wet silica sol–gel monoliths: Implications for biological encapsulation

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ABSTRACT

Divalent nickel (Ni^{2+}), Cu(II)EDTA, methyl orange, and dichromate were used to investigate diffusion from hydrated silica sol–gel monoliths. The objective was to examine diffusion of compounds on a size regime relevant to supporting biological components encapsulated within silica gel prepared in a biologically compatible process space with no post-gelation treatments. With an initial sample set, gels prepared from tetraethoxysilane were explored in a factorial design with Ni^{2+} as the tracer, varying water content during hydrolysis, acid catalyst present during hydrolysis, and the final concentration of silica. A second sample set explored diffusion of all four tracers in gels prepared with aqueous silica precursors and a variety of organically modified siloxanes. Excluding six outliers which displayed significant syneresis, the mean diffusion constant (D_{gel}) across the entire process space of sample set 1 was 2.42×10^{-10} m^2 s^{-1}; approximately 24% of the diffusion coefficient of Ni^{2+} in unconfined aqueous solution. In sample set 2, the tracer size and not gel hydrophobicity was the primary determinant of changes in diffusion rates. A strong linear inverse correlation was found between tracer size and the magnitude of D_{gel}. Based on correlation with the tracers used in this investigation, the characteristic 1-h diffusion distance for carbonate species relevant to supporting active phototrophic organisms was approximately 1.5 mm. These results support the notion that silica sol–gel formulations may be optimized for a given biological entity of interest with manageable impact to the diffusion of small ions and molecules.

1. Introduction

Sol–gel derived silica is gaining interest as an attractive material for the encapsulation of biological components. The broad variety of applications, from bioreactors to biosensors to tissue therapy and drug delivery systems, has been the subject of many recent reviews [1–8]. Silica gel offers the ability to effectively encapsulate functional proteins and viable cells. The material is inert and stable compared to organic polymer alternatives, creating a stabilize platform for enzymatic or biological conversion of substrates, biosensing, or biomedical applications.

In many potential biological applications the transport of dissolved materials can be critically important for optimal performance of the encapsulated component. Once gelation has occurred, diffusion is the dominant transport mechanism. The structural features and surface chemistry of the gel can have a strong influence on diffusion, especially as the size of the diffusing species approaches the size of the pores in the gel [9,10]. The precursor composition and processing parameters can control the size distribution of the gel porosity to some degree [11–14], so therefore should provide the ability to exercise some control over diffusion rates of dissolved species within the gel.

Diffusion in condensed gels that have undergone post-gelation processing (aging, drying, solvent exchange and/or heat treatments) has been extensively studied [9,10,15,16], as have structural features [11]. However, these investigations have generally been performed in the context of separations, such as membrane filtration or chromatography [8,17], and frequently the post-gelation treatments are incompatible with biological components. Characterization of diffusion in wet gels that have received no post-gelation treatment has received comparatively less attention. This is due to both a lack of relevant applications until recently and the dearth of experimental techniques that allow direct examination of the structure of the gel at high resolution without supercritical drying or chemical modification, both of which fundamentally alter the gel structure.

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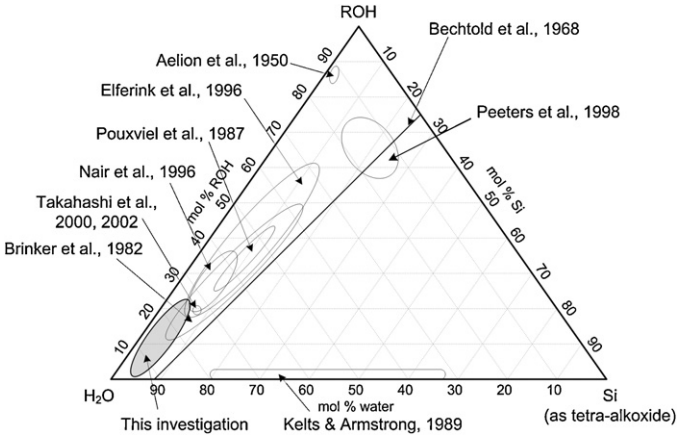

Fig. 1. Ternary phase diagram illustrating the process space for numerous investigations of sol–gel processed silica, including the present study.
Adapted from Brinker et al. [21].

In this study, we report the diffusion of dissolved ions from impregnated silica gels prepared via silicon alkoxide and sodium silicate (aqueous) sol–gel synthesis. Our interest lies in optimizing gels for the encapsulation of viable cyanobacteria as a platform for photobiological hydrogen production [18,19]. Although it has been claimed that virtually any microorganism that can be cultured can be encapsulated [2], it remains clear that the encapsulation process must be uniquely tailored to the organism of interest [4]. Therefore, the current investigation focuses on the effects that manipulating parameters in a processing space relevant to biological encapsulation (low silica, low alcohol, high water, and no cytotoxic post-gelation treatments) have on the diffusion of small molecules from bulk gel monoliths. The goal was to determine the processing space that allowed for maximum diffusion rates while maintaining adequate integrity and stability of the silica gel. The approximate process space selected for this investigation is shown graphically in the ternary phase diagram in Fig. 1. The parameters of previous investigations shown in Fig. 1 helped define the process space of the current work and provided fundamental descriptions of acid-catalyzed hydrolysis, base-catalyzed condensation, and polymerization prior to and during gelation [11,12,20–25]. However, prior investigations generally used supplemental alcohol as a co-solvent to prepare gels with relatively high silica content and performed post-gelation treatments (e.g. solvent exchange, annealing, etc.), reducing the relevance for biological encapsulation.

This investigation was conducted in two phases. First, divalent nickel, Ni^{2+}, was used as a tracer to probe diffusion from gel monoliths synthesized across a broad range of processing space. The parameters varied included the amount of water present during hydrolysis, the amount of acid catalyst present during hydrolysis, and the amount of silica present in the final gel (see Section 2). Ni^{2+} was selected because it is easy to measure the concentration with UV–Vis spectroscopy and it is similar in size to other dissolved ions and molecules that are of biological significance (e.g. CO_2 and bicarbonate) but not easily measured with UV–Vis spectroscopy.

Second, ions of differing size and charge were used to explore diffusion in a smaller process space, presumably most relevant to biological encapsulation. The selected ions included Ni^{2+}, methyl orange, ethylenediaminetetraacetic acid copper(II) disodium salt (Cu(II)EDTA), and potassium dichromate. These probes were selected for both their range of charge and size as well as ease of measurement with UV–Vis spectroscopy. Also included in this second phase was the incorporation of organically modified siloxanes (ORMOSILs) into the gels, including methyltriethoxysilane (MTES), dimethyldiethoxysilane (DMDES), trimethylethoxysilane (TMES), ethyltriethoxysilane (ETES), and propyltriethoxysilane (PTES). To varying degrees, these compounds introduce hydrophobicity to an otherwise hydrophilic gel, potentially altering the interaction with, and diffusion of the selected tracer molecules. It was the intent of the current study to determine how process space and the use of ORMOSILs may impact the bulk diffusion rates of molecules in a size regime comparable to compounds requisite for viable cyanobacterial cells.

2. Experimental methods

2.1. Materials

Gel precursors, including tetraethoxysilane (TEOS), ethyltriethoxysilane (ETES) (Alfa Aesar, Ward Hill, MA, or Gelest, Morrisville, PA), methyltriethoxysilane (MTES), dimethyldiethoxysilane (DMDES) (Sigma Aldrich, St. Louis, MO, or Gelest, Morrisville, PA), trimethylethoxysilane (TMES) (Tokyo Chemical Industry Co., Tokyo, Japan; and Gelest, Morrisville, PA), propyltriethoxysilane (PTES) (Gelest, Morrisville, PA), 40% sodium silicate (Na_2SiO_3) solution (aqueous precursor), nickel chloride hexahydrate (Fisher Scientific, Fair Lawn, NJ), ethylenediaminetetraacetic acid copper(II) disodium salt (Cu(II)EDTA), powdered methyl orange, and potassium dichromate (Sigma Aldrich, St. Louis, MO) were used as received. Additional reagents included potassium hydroxide (J.T. Baker, Phillipsburg, NJ) and nitric acid (Fisher Scientific, Pittsburgh, PA), both used as received to prepare 1.0 M stock solutions. Deionized water with a resistivity of 18.2 MΩ-cm was produced in house by reverse osmosis (Millipore Corp., Danvers, MA) and used for all gel solutions, stock solutions, and the preparation of buffered BG-11 medium [26] with 35 mM HEPES buffer (4-(2-Hydroxyethyl)piperazine-1-ethanesulfonic acid, N-(2-hydroxyethyl) piperazine-N′-(2-ethanesulfonic acid), an organic buffer used as received (Sigma Aldrich, St. Louis, MO).

2.2. Gel preparation

All of the alkoxide-derived gel samples were prepared with a two step process beginning with acid-catalyzed hydrolysis of the precursor to prepare a 'sol,' followed by base-catalyzed condensation. Base-catalyzed condensation was selected for two reasons: (1) for biological encapsulation, neutral pH is generally preferred, so using a base to neutralize the acidic sol served this purpose; and (2) base-catalyzed condensation yields a more highly condensed particulate structure, as opposed to acid-catalyzed condensation which tends to yield a network of linear polymers [33]. Firstly, a mixture of silicon alkoxide was hydrolyzed with varying amounts of nitric acid and deionized water. Secondly, buffered BG-11 medium [26] was added to catalyze gelation, containing a suitable concentration of potassium hydroxide to neutralize the acid catalyst and a tracer. All gels were prepared in 35 mm Petri dishes at a volume of 8.0 mL, filling the Petri dish and creating nearly ideal one-dimensional diffusion geometry. BG-11 was used over deionized water in sample preparation because it is typically used to grow cultures of the cyanobacterium *Synechocystis* sp. PCC 6803 (*Synechocystis*) for encapsulation studies [18,19]. Since BG-11 contains a variety of trace minerals and nutrients which may alter gelation kinetics, it was used in order to ensure the current investigation was directly applicable to on-going encapsulation studies. The amounts of water and acid used were determined based on gel formulation and the concentration of tracer was consistent for all samples prepared.

For the first phase of the investigation (sample set 1, using N^{2+} as a tracer), three parameters were varied over the following ranges: