

The silica hypothesis for homeopathy: physical chemistry

David J Anick^{1,*} and John A Ives²

¹Harvard Medical School, McLean Hospital, Belmont, MA, USA

²Samueli Institute for Information Biology, 1700 Diagonal Road, Alexandria, VA, USA

The 'silica hypothesis' is one of several frameworks that have been put forward to explain how homeopathic remedies, which often are diluted beyond the point where any of the original substance remains, might still be clinically effective. We describe here what the silica hypothesis says. From a physical chemistry viewpoint, we explore three challenges that the hypothesis would have to meet in order to explain homeopathy: thermodynamic stability of a large number of distinct structures, pattern initiation at low potencies, and pattern maintenance or gradual evolution at higher potencies. We juxtapose current knowledge about silicates with some of the conventional wisdom about homeopathic remedies, to see how well the latter might be a consequence of the former. We explore variants of the hypothesis including some speculations about mechanisms. We outline laboratory experiments that could help to decide it. *Homeopathy* (2007) 96, 189–195.

Keywords: homeopathy; mechanism; silica; silicate; physical chemistry

Introduction

Homeopathy has been called the third-most commonly used system of healing on the planet, and for that reason alone it deserves serious attention from the modern scientific community. As the reader of this article undoubtedly knows, many conventional scientists and doctors dismiss homeopathy as physically impossible because of the high dilutions that are commonly used. If a mother tincture (MT) contains a 1 M solution of starting substance (typically the concentration will be considerably smaller, eg sodium chloride in sea water is only 0.5 M), then a 20 ml bottle of its 12c potency has only a 1% chance of containing even a single solute molecule from that MT. For higher potencies like 30c, figures like 10^{-60} have been given but it is meaningless to call the concentration anything other than 'zero'. Within conventional chemistry, a solution at concentration zero must be identical with the unprepared solvent (water or ethanol-water). The

challenge is to explain or justify how one sample of concentration zero can be different from another sample of concentration zero.

The challenge is greater than scientists working on the physics or chemistry of homeopathy usually admit. There are three physical chemistry puzzles that will have to be solved before homeopathy can be considered to be 'explained', and this does not even include explaining how remedies influence biological systems. Generally researchers have focused on finding some measurement or test according to which remedies and controls can be told apart. As significant as a consistent finding of this kind would be, it would not be enough for homeopathy. According to homeopathic theory, the 'vibration' of each living thing is different, and remedies of different potencies made from the same MT are subtly different too. Helios pharmacy [<http://www.helios.co.uk>] sells 2320 different remedies, each at three to eight (or more) different potencies. It would not be enough to demonstrate that liquid water can exist in a few distinct thermodynamically stable (or meta-stable) forms. Theoretically there should be a nearly infinite variety of 'waters,' each one constant over a time scale of at least several minutes. In one minute the H-bond network of liquid water will

*Corresponding author. DJ Anick, Harvard Medical School, McLean Hospital, Centre Bldg 11, Belmont, MA 02478, USA.
E-mail: david.anick@rcn.com

Received 22 February 2007; accepted 27 July 2007

undergo literally trillions of rearrangements, yet something about the sample has to be recognizably the same at the end as at the start of that minute, and yet different from 'other remedy' and from 'control.' This is the first challenge: to describe thermodynamically stable parameter(s) that not only show how remedies might differ from controls, but also how thousands of remedies can all be different from each other.

Consider two vials of pure water (in practice doubly deionized distilled water is used) each containing 198 drops (about 4 ml). To the first, two drops of pure water (from the same source) are added, making 200 drops. To the second, two drops of Sepia 29c are added. Each vial is covered and succussed. At the end, one is Sepia 30c, and the other is succussed water. To a homeopath, Sepia 30c and shaken water are as different as night and day. From a scientist's perspective, the only difference between these samples is the 2-drop 'seed' added just before succussion. Other than the seed representing 1% by volume, 99% of the two samples (before succussion) were identical. If Sepia 30c is different from succussed water, then something in that seed causes the whole sample, once succussed, to come out different from what we get if the seed is not first added. And the seed is Sepia 29c, which means it too contains nothing of the starting material, and its only difference from pure water is whatever arose from succussing a seed of Sepia 28c placed in 99 parts pure water.

So this is the second challenge: whatever pattern or information is in a remedy, it must somehow 'survive' being mixed into 99 parts of water, and then 'convert' the whole sample to that same pattern (or a slightly different pattern) when the whole is succussed. The 198 drops of unprocessed fresh water must never 'convert' the two added drops to its 'ordinary' pattern.

Finally let us describe the third challenge: generation of the pattern in the first place. The first few dilutions and succussions of the MT may consist principally of diluting and mixing, since these samples would still differ from controls (and each other) by virtue of their solutes. At some stage, however, the solute must act as a seed that initiates a 'pattern' in the diluent to which it has been added. Perhaps this starts just as the last molecules are disappearing, around 11c, or perhaps it starts much earlier in the sequence. If it starts earlier, then some low potencies will contain both low-concentration solute and 'patterned solvent'. It is conceivable that low-concentration solute and 'incipient pattern' work together to establish the 'mature pattern' during succussion.

Hahnemann made his remedies using glass vials, and the practice of always using glass has continued. Small amounts of silicon dioxide and ions dissolve from the glass walls into aqueous solution, during succussion. The quantities dissolved are larger for soda glass, and smaller for borosilicate glass, but there is always some. The silicates and minerals have usually been ignored as unavoidable contaminants, as something to be minimized. However Milgrom¹ demonstrated that differences

in T1 relaxation times between remedies and controls could be explained by different levels of dissolved silicates. Demangeat *et al*² found higher than expected silica content in remedies prepared in glass vials, and more silica in certain remedies than in succussed controls.

Could vial-derived silicates be the long-sought active ingredients in remedies?

This idea, the silica hypothesis, is the subject of this article. Others have noted a possible role for silica³⁻⁵ in homeopathy, but it has not previously been examined at the level of detail given here. After a brief discussion of silicate structures, we will state the hypothesis and explore how well it can meet the three challenges listed above. Consideration of how biological systems might 'read' the information in structured silicates is beyond the scope of this article.

Brief overview of silicates

Silicon dioxide SiO_2 , the principal ingredient in glass, dissolves in water by combining with two H_2O molecules to form a molecule of silicic acid, $\text{Si}(\text{OH})_4$ (Figure 1a). The solubility of silica depends on many factors. Alexander *et al.* demonstrated a strong temperature dependence for solubility of amorphous silica and gave a figure of around 0.010% (or 47 ppm Si) at 20 C.⁶ Quartz exhibits a much lower solubility than amorphous, and the addition of small amounts of Na_2O or other alkali can dramatically increase solubility.⁷ Two molecules of $\text{Si}(\text{OH})_4$ can link up, forming the dimer $\text{H}_6\text{Si}_2\text{O}_7$ (Fig. 1b) by expelling a single H_2O and forming a Si-O-Si bond. The Si-O-Si bond is called a siloxane bond. This reaction is called condensation or polymerization, and its reverse reaction (the splitting of a siloxane bond by H_2O to make Si-OH and HO-Si) is called hydrolysis or depolymerization. The dimer can

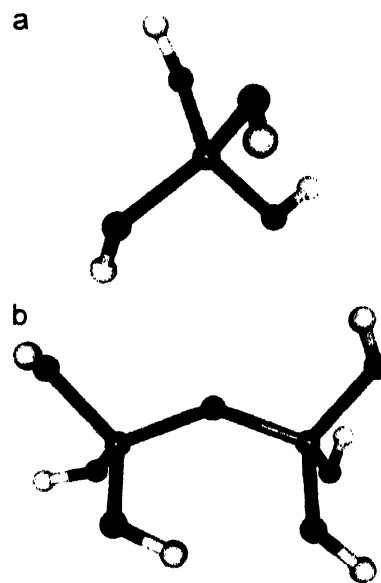


Fig. 1 (a) $\text{Si}(\text{OH})_4$ monomer, optimized at B3LYP/6-311++G(3d,3p) level. (b) $\text{Si}(\text{OH})_3\text{-O-Si}(\text{OH})_3$ dimer, optimized at B3LYP/6-311++G(3d,3p) level.

join another $\text{Si}(\text{OH})_4$ unit to make a trimer, and so on. The minimum-energy configuration for the gas-phase dimer has the siloxane bond bent at about 140° , but the strain is not great for angles anywhere from 130° to 150° . As a result, chains of polymerized $\text{Si}(\text{OH})_4$ can close, making rings, and can branch by allowing up to four siloxane bonds at each Si, creating a virtually infinite variety of polymeric species. Quartz and cristabolite are crystalline forms of $(\text{SiO}_2)_x$, and glass is an amorphous form that incorporates small quantities of other materials such as sodium or borate. 'Silica' is a general term for any bulk material consisting of polymerized, condensed, or crystallized SiO_2 . Removing one H^+ from $\text{Si}(\text{OH})_4$ produces the H_3SiO_4^- anion; likewise the dimer can dissociate to H^+ and $\text{H}_5\text{Si}_2\text{O}_7^-$, and so on for the more complex forms. A 'silicate' is any of these anionic forms, generally combined with one or more cations, or a crystalline or amorphous material composed of cations and $\text{H}_2\text{Si}_x\text{O}_y^-$ anions. (Obviously we cannot pretend to do justice in a few sentences to the complexity of silica and silicate chemistry, which accounts for most of the variety of minerals in Earth's crust.) We will refer to any $\text{H}_x\text{Si}_y\text{O}_z$ (charge would be $4x-2y+z$) that is held together entirely by Si-O and O-H covalent bonds as a 'silicate', regardless of its dissociation state, charge, hydration, or extent of association with cations. Our interest is in the behavior of silicates in aqueous solution, or in ethanol-water solution.

A notation that has been used to characterize the connectivity of a Si in a silicate is Q^n , with the superscript indicating the number of siloxane bonds.⁸ Thus Q^0 is the monomer, Q^1Q^1 is a notation for the dimer (since each of the Si atoms is involved in a single siloxane bond), and the linear trimer would be $Q^1Q^2Q^1$. The cyclic trimer is Q_3^2 ; branched polymers would contain Q^3 's or Q^4 's. Q^0 through Q^4 have distinct signatures when a sample is examined with ^{29}Si -NMR. The cyclic trimer is also denoted 3R for '3-membered ring', and the 4R, 5R, 6R, and 8R structures are also often seen. Commonly two rings combine into a prism ('double ring'), for which the notation would be D3R, D4R, etc. The D4R motif or cube is shown in Figure 2a.

Silicate patterns that occur in natural minerals include: monomer (nesosilicates), dimer (sorosilicates), single and double chains (inosilicates including rings of 3-8 SiO_2 units, the cyclosilicates), sheet (honeycomb pattern of hexagonal rings, or phyllosilicates), and framework silicate (complex 3D or tectosilicates). The last category includes the quartz group (minerals that are just $(\text{SiO}_2)_x$) and zeolites (crystals containing large pores that are typically occupied by cations). Figure 2b shows how the cube is a subunit in one zeolite structure called ACO.⁹

Condensation of aqueous silicic acid is slow under conditions of 20°C , 1 atm, and neutral pH. In a system with only silica and water, equilibrium of dissolved monomers with a condensed (amorphous) silica phase can take months to establish. A low-concentration system without a condensed phase produces few

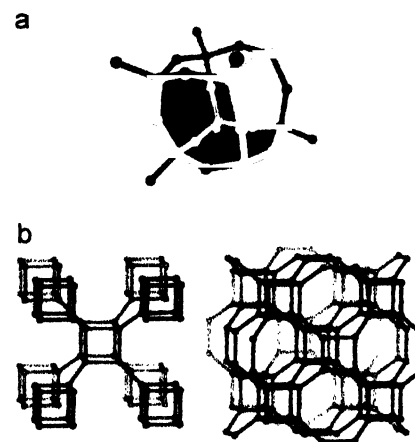


Fig. 2 (a) D4R cube (H's omitted). (b) Two representations of ACO zeolite showing how the cube of Fig. 2a occurs in a repeating 3-D structure. Siloxane bonds are shown as straight rods even though they actually include an angle. One O atom is implied on each siloxane bond.

dimers,¹⁰ and the amount of dimer increases with pressure.^{11,12} In a concentrated potassium silicate solution, Harris *et al* found 11 distinct oligomers via ^{29}Si -NMR analysis,⁸ and oligomers containing up to 12 Si atoms have been identified.¹³ Polymerization is favored by low temperatures, high Si concentration, and low alkalinity.^{14,15} Catalysis of polymerization by other solutes can be dramatic and will be addressed in the next section. Depolymerization and interconversion of silicate species occurs slowly at 20°C , so for practical purposes most silicate polymers can be considered to be 'stable' over a time frame of hours or longer.

When a sample is succussed, it is subjected to a series of brief intense shocks during which the pressure jumps for perhaps a millisecond to hundreds and probably thousands of atmospheres. Our premise is as follows. The first few succussion strokes agitate the glass walls by mechanical action and generate a saturated or super-saturated solution of silicic acid. During later succussion strokes, the momentary high-pressure shifts the equilibrium for silicic acid in favor of condensation, and polymers form. (Demangeat *et al*² reported a mean Si concentration of 6 ppm for their remedies, near the solubility limit for quartz,⁷ with certain remedies showing consistently higher concentrations than others. Our laboratory obtained Si concentrations of 1.3 to 4.0 ppm in succussed solutions [unpublished data]. These measurements are obtained after a remedy has had some time to "settle" in its glass vial so there could be higher concentrations during and immediately after the succussion strokes.) We will later discuss how, in remedies, specific condensation patterns might be catalyzed. As the high-pressure abates, the polymers remain as polymers.

(There is also some evidence that succussion may cause larger silica units as well as $\text{Si}(\text{OH})_4$ to enter solution.¹⁶ We have unpublished light-microscopy and EM observations from our laboratory that indicate relatively large particles in succussed solutions. Although these are possibly due to condensation of

silica units during the sample preparations, it is also likely that some large particles exist immediately after succussion.)

The 'silica hypothesis' for homeopathy states that remedies differ from succussed water controls and from each other, in the structure (not primarily in the quantity) of their dissolved silicates. At this point we lack experimental evidence to be more specific, but the differences could include the distribution of polymer sizes, the degree of arborization (Q^3 and Q^4 vs Q^2), the frequency of specific motifs like 6R or D5R, or quite specific long-range patterns in larger units such as particular crystalline or zeolite forms. Characteristics such as these would be stable enough to last for at least a few minutes at ambient temperature and pressure while a remedy was being transferred to begin the next potency, or while being transferred onto lactose pellets (which would absorb the water and cease any further hydrolysis or condensation) for clinical use. In a glass bottle that would provide a baseline $Si(OH)_4$ concentration, these 'identifying characteristics' of a remedy could quite possibly last for days or months, though we would expect it eventually to degrade.

Interestingly, the fact that liquid remedies are normally kept for long-term storage in 87% ethanol rather than plain water might help their stability. Hydrolysis consumes H_2O , so hydrolysis incurs a higher free energy cost in hygroscopic ethanol than in water. Ethanol should slow the degradation of the 'information' in dissolved silicate structures, though the formation of some ethoxysilicates might be expected instead.¹⁷

Generation and perpetuation of remedy-specific silicates

Having seen how the silica hypothesis could address the first challenge, viz. the thermodynamic stability of a remedy's 'information' encoded in its silicate structures, let us turn to the third challenge: generation of remedy-specific information. How feasible is it that components in the original MT could direct or catalyze remedy-specific silicate structures?

This turns out to be extremely feasible. An extensive literature already documents the capacity for both organic and inorganic solutes to direct the condensation of silicic acid into solute-specific patterns.¹⁸ Indeed, this capacity is the basis for numerous natural and commercial processes to generate specific silicate and organosilicate structures. We will review only a small part of this literature, emphasizing its relevance to pattern initiation in low-potency remedies.

For inorganic solutes, Kinradet and Pole¹⁹ observed effects of metal cations on silicate condensation. Paired cations facilitated the approach of the negatively charged silicates so that condensation could occur. Alkali metals from Na^+ to Cs^+ stabilized different oligomers, with Li^+ - H_2O interactions further enhan-

cing polymerization in the case of Li^+ . Tossell²⁰ has explained the role of fluoride ion F^- in promoting the formation of D4R cubes. A comparative study of substituted ammonium, NA_4^+ , shows markedly different results depending on whether the alkyl group A is methyl, ethyl, or propyl.^{13,21} If A is methyl the preference is for D4R, whereas ethyl makes D3R and propyl guides the formation of the zeolite ZSM-5²²⁻²⁴ but does not make double rings.

Organic solutes can choreograph the production of highly specific crystalline (repetitive) silicates. Diatoms, single-celled plants that live inside a silicate coat called a frustule, 'produce an enormous variety of biosilica structures'.²⁵ The number of known species exceeds 20,000. The silica-condensing molecules are long-chain poly-amines (LCPAs) and modified proteins called silaffins, which generate the same species-specific structures from silicic acid solutions when used *in vitro*.^{25,26} Working with LCPAs including spermine and spermidine, Belton *et al*²⁷ determined that 'chain length, intramolecular N-N spacing and C:N ratio of the additives' was responsible for 'the combination of unique catalytic effects and aggregation behaviours' that determined the materials' properties. Working with amino acid silicate solutions, Belton and coworkers found that 11 of the 20 amino acid residues 'affect the kinetics of small oligomer formation, the growth of aggregate structures and the morphology and surface properties of the silicas produced'.²⁸

Given this information, it is tempting to imagine that almost any inorganic or organic material could guide the formation of specific silicates. Focusing on plants, which are the source of the majority of remedies in clinical use, could the particular proteins or N-containing alkaloids in a plant account for plant-specific silicates appearing in remedies made from that plant? Obviously some compounds will be more effective than others at condensing silica, eg silaffins evolved specifically for that purpose. In a low-potency remedy like a diluted 3c being succussed to make a 4c, perhaps silicic acid 'ignores' most plant components while allowing particular 'active ingredients' to catalyze the relevant structures. It would be interesting if the silica-condensing ingredients were the same as the pharmacologically active ingredients. If so, it could explain why, say, the atropine in *Belladonna* plays the key role in determining the properties of potentized *Bell*, and it would suggest that remedy made from whole plant should be essentially identical to remedy made by starting with purified atropine. It is widely believed that the homeopathic remedies *Bell* and *Atropinum* have very similar clinical activity.

We should also express some notes of caution. While it is true that inorganic and organic solutes guide silicate formation, in many cases these solutes are incorporated into the final product, eg the cations occupy the pores in a zeolite, or organic matter remains embedded in the final silicate. Or, the concentration of 'catalyst' is comparable to that of silicate, eg, Belton *et al*²⁸

used a 2:1 molar ratio of Si to amino acid. This poses a problem for the silica hypotheses. As the remedy becomes progressively more dilute, there is less and less catalytic material available. To our knowledge, the question of how low the solute concentrations can get, and still generate significant quantities of solute-specific silica structures, has never been studied. Nor is it known how a pulse of high pressure, as in succussion, would affect the process. For the silica hypothesis to work, it would be essential that some components of the MT act as true catalysts, yielding many structured silicates per molecule, and not become trapped in individual silicate complexes. Questions can also be raised about how far the specificity of the catalysts can extend. For example atropine and hyoscyamine are enantiomers, differing solely in their orientation at a single C locus, yet *Bell* and *Hyos* are considered to be rather different remedies. Most silicates that have been studied are achiral, but some, like trigonal quartz, can be chiral.

Let us turn now to the second challenge: perpetuation of the pattern after all of the MT has been diluted away. Let us assume that a 12c remedy sample contains a measurable population of remedy-specific silicates. What happens when that remedy is diluted 1:100 and succussed? The process can begin the same way: the early succussion strokes release silicic acid from the vial walls. However there is no catalyst to condense the silicic acid—or is there? Clearly we would require that the remedy-specific silicate polymers from the prior potency serve as the catalyst. Suppose the relevant structure in the 12c were nanocrystals of a particular zeolite. We would be saying that diluting this zeolite solution 1:100, adding silicic acid, and succussing, should generate more zeolite. Indeed, we would need to have about 100 times as much zeolite nanocrystal at the end of the succussion cycle, as we had just after the 1:100 dilution. If we do not amplify the active ingredient by a factor of 100 each time, then with subsequent dilutions the amount of structured silicate will soon diminish to zero.

How feasible is it to generate particular silicates from silicic acid, by using only a seed containing already-structured silicate, and then succussing? We admit this is the weakest point of the silica hypothesis, but it is not impossible. We propose four ways it could happen. First, some silica motifs may be inherently amenable to self-replication. Perhaps a double ring like D5R has a tendency to split (hydrolyze) into two single 5R rings when vigorously shaken, and perhaps the two resulting single rings have a tendency to attract a second layer of condensation, re-creating the double ring. If so, a single succussion stroke could double the amount of D5R, and repeated succussion strokes could amplify the amount of D5R as much as 100 times. This hypothetical process would be comparable to the polymerase chain reaction for DNA. Building on the DNA analogy, in addition to double rings we could imagine a double form of any flat linear or branched silicate polymer. As noted above, single and double chains are among the naturally occurring forms of silicate in minerals. (Some cycles

could be allowed too but joined rings and highly branched topologies cannot be 'doubled' without introducing a lot of bond angle strain.) If the double form were to 'unzip' like DNA, and if each half were then to act as a template to re-create the double form, we would have a mechanism for preserving the structure from one potency to the next.

This idea also permits us to see a way that remedies might change gradually with potency. For instance, if the 'replication' described above were not 100% perfect, but instead there was a tendency for small but predictable changes to occur, then the 13c might be subtly different from the 12c, the 14c might be slightly changed from the 13c, and so on. By 'small but predictable changes' we mean things like lengthening a chain by one or two units or adding a short side-branch. Small changes could function like point mutations in DNA: alterations that leave the structure mostly unchanged, and do not interfere with the capacity for replication, but which would be inherited and maintained by subsequent dilution/succussion cycles. Small changes might occur with low probability but might accumulate over many cycles, like DNA mutations, to result in a noticeably different structure with different clinical benefits. This would fit with the conventional wisdom of homeopaths that a 12c and a 13c and a 14c are not much different, but with passage of enough cycles, the 200c and the 12c can be quite different.

Second, we have alluded to silica nanocrystals as the information-carrying component. Crystals are well known for acting as seeds that can extend their pattern as other molecular units crystallize onto them. Once a particular silica crystal pattern got started, could it grow more of its own pattern when added to a silicic acid solution and succussed? We would be saying that of the 200+ known zeolite structures, if tiny nanocrystals of one zeolite are added to silicic acid and succussed, the result would be 100 times as much of that very same zeolite. This strikes us as *a priori* unlikely, yet it might work for at least some zeolite or other crystalline forms. We doubt the question has ever been studied.

Third, an intriguing mechanism could involve transfer of information from the silicates to structure the water during succussion, and transfer of information back from the structured water onto silicate particles, which then 'hold' the information when the succussion pressure abates. Zeng and coworkers²⁹ proposed such a mechanism when they studied the well known 'memory effect' of water. The 'memory effect' does not involve homeopathy: it says that a water sample that has been crystallized under pressure into a gas hydrate, and then melted, will more quickly re-form the clathrate hydrate structure when mixed with gas and re-pressurized, compared to a water sample that did not previously experience the hydrate state. Analysis of water samples with neutron scattering could not find any structural basis for a 'memory effect'.³⁰ When Zeng and coworkers discovered that low concentrations of certain ice nucleation inhibitors could destroy the memory effect,

they inferred that the effect was due to small impurity particles that received the 'imprint' of the clathrate state and, by holding that imprint long after melting and degassing, supplied a template for rapid nucleation back to the clathrate state.

Quoting Zeng *et al.*, the memory effect 'must be ascribed to an alteration of the surface states of the impurity particles that amplifies their nucleating action. This could occur because of an imprinting of the surface of the impurities by the growth of a hydrate crystal on the particle surfaces. For instance, if the impurities are hydrated or *hydroxylated silicon* or *iron oxides*, a hydrate crystal may well alter the surface geometry so that when the hydrate melts, the surface is now a better nucleator of hydrate than it was during the first nucleation cycle' (emphasis added). They are explicitly postulating that silicate particles could be the information carriers that cause water, when pressurized, to form a particular pattern, and that the pattern could imprint other silicate particles. We are not proposing that water forms a momentary clathrate hydrate during succussion, but there could be other structural alterations. These alterations could start at (be nucleated by) silicate particles, could spread throughout the sample, and then imprint other silicate particles throughout the sample. The result would be an amplification, conceivably by the needed factor of 100, of the specific surface pattern on silica particles. Although the structural change in the water would be lost when the pressure returns to 1 atm, the information would persist in the silica surface changes. This explanation works best if silica is released into solution as nanoparticles, rather than as monomeric silicic acid, when agitated during succussion.

Fourth, if we postulate that silica surface carries the information, could the glass vial wall itself be that carrier? Some commercial remedies are prepared by the Korsakoff method. In this method, a single vial is used, and dilution is achieved by decanting most of the liquid and then refilling. Then the vial is succussed. A thin layer of water that wets the inside vial walls stays there when most of the liquid is decanted. This layer is estimated to be about 1% of the vial volume; so subsequent refilling accomplishes the 1:100 dilution. Asay and Kim³¹ found that water adsorbing onto glass at 20°C forms a three-molecule thick layer of ice. The pattern of the water adjacent to the glass will certainly be affected by alterations in the glass surface. Once a pattern is established on the vial walls, subsequent Korsakoff cycles might do nothing or might slowly alter the pattern. In order to transmit this information after the final potency is removed, however, it would have to contain some imprinted silica particles as well.

Experiments to test the silica hypothesis

The silica hypothesis and its variants are amenable to experiment and measurement to verify or negate them.

Its challenges are the low concentrations at which silicates occur, and the difficulty of teasing apart chemically similar oligomers or surface features. A starting point will be to measure the amount of monomeric and polymeric silicates in remedies, in succussed water, and in diluted remedies after 0, 2, 8, 20, and 40 succussion strokes (or any similar sampling sequence). Alexander *et al.*⁶ successfully used a molybdic acid assay to measure the amount of monomeric silicate, while mass spectroscopy can provide the total Si content of a sample. Obviously we would want to repeat these measurements for several different types of glass vials, and for ethanol-water vs water for the solvent.

Raman spectroscopy and ²⁹Si-NMR provide insight into the degree of polymerization of silicates. ²⁹Si-NMR will tell us ratios among Q' loci. Assuming we see some consistent differences among remedies or between remedies and controls, we can use these methods to ask how well homeopathically relevant substances such as atropine can serve as silicate polymerizers, and whether their condensed silicate products have consistent and substance-specific properties. The protocol would be to add a known concentration of atropine to a silicic acid solution of known concentration (in plastic vial) and succuss. Electron microscopy of frozen and cracked samples or very thin frozen layers is one way to look for suspended silica nanoparticles and to examine their surface. If surface features seem to be the information-carrying aspect, we will ultimately need to develop assays that detect particular features. Such an assay might measure adsorption of particular molecules, or enhancement or stabilization of a particular enzyme.

If early experiments lead us to suspect that remedy-specific oligomers are the information-carrying ingredient, we will ultimately need to make remedies enriched in ²⁹Si in order to identify them via ²⁹Si-NMR. To make a vial out of ²⁹SiO₂ would be prohibitively expensive, but here is an alternative. Remedies could be made by succussing them in polypropylene vials, and silica could be added in the form of small (~1 mm diameter) recoverable beads. The total surface of the beads could be calculated to equal that of the vial (typically an 8-, 12-, or 20-ml vial). Beads would be strained away after the last succussion stroke. It would be an open question whether such beads can be immediately reused for another remedy or potency, or whether they would be 'imprinted' in some way that would carry information that could affect the next remedy made with them. If remedies made via 'succuss with silica beads in plastic' appear via ²⁹Si-NMR to yield similar results to 'succuss in glass,' the idea would be to replace the beads with ²⁹Si-enriched beads. Now, even that would get expensive when 95% ²⁹SiO₂ runs \$3 to \$5 per mg. But one could coat ceramic beads with melted ²⁹SiO₂ making a layer perhaps 10–30 μm thick. This would not require too much ²⁹SiO₂ and would allow us to

simulate exposure to a $^{29}\text{SiO}_2$ vial. All of the resulting silicate structures would then be $^{29}\text{SiO}_2$ -enriched. Note that only the potencies we intend to study would have to be made with the $^{29}\text{SiO}_2$ beads.

Conclusion

The clichéd scientific objection to homeopathy is that it cannot work because 'remedies have nothing in them chemically,' besides water. The silica hypothesis turns this objection on its head. It declares that remedies made in glass do have something else in them chemically, namely silicates, and that the silicates are not irrelevant contaminants but meaningfully structured active ingredients. According to the hypothesis, succussion releases silicic acid monomers into the solution, which are then polymerized into remedy-specific patterns by catalytic action of MT components. For potencies above 12c, structured silicates themselves act as the catalysts or templates for perpetuation of the remedy-specific patterns. In a variant on the hypothesis, silica delaminates from the glass walls in the form of nanoparticles rather than $\text{Si}(\text{OH})_4$ monomers, and the information is carried via silica surface alterations.

In this brief overview of the silica hypothesis we have begun to ask how the hypothesis might be able to meet three physical chemistry challenges that any explanation for homeopathy will have to overcome. Silicates can indeed form a huge variety of distinct and thermodynamically stable (for minutes or longer) structures in aqueous solution. Organic and inorganic MT components can guide selective silicate pattern formation. Structured silica seeds may be able to direct the formation of more copies of themselves, and may be capable of slowly changing or 'evolving' over the course of repeated dilution-succussion cycles. Gradual 'evolution' of silicate properties would explain the widely believed-in gradual change in clinical properties of remedies as the potency is increased.

Our overview contains many ideas that are speculations and extrapolations, and where this is the case we have admitted it. Rather than argue these points, it seems wisest to begin to collect experimental evidence that will support or negate various claims and versions of the hypothesis.

References

- Milgrom LR, King KR, Lee J, Pinkus AS. On the investigation of homeopathic potencies using low resolution NMR T2 relaxation times: an experimental and critical survey of the work of Roland Conte *et al.* *Br Hom J* 2001; **90**(1): 5-13.
- Demangeat J-L, Gries P, Poitevin B, *et al.* Low-field NMR water proton longitudinal relaxation in ultrahighly diluted aqueous solutions of silica-lactose prepared in glass material for pharmaceutical use. *Appl Magn Reson* 2004; **26**: 465-481.
- Walach H, Jonas WB, Ives J, *et al.* Research on homeopathy: state of the art. *J Altern Comp Med* 2005; **11**(5): 813-829.
- Witt CM, Ludtke R, Weisshuhn TE, *et al.* The role of trace elements in homeopathic preparations and the influence of container material, storage duration, and potentiation. *Forsch Komplementarmed* 2006; **13**: 15-21.
- Roy R, Tiller WA, Bell I, Hoover MR. The structure of liquid water: novel insights from materials research; potential relevance to homeopathy. *Mat Res Innovat* 2005; **9-4**: 93-124.
- Alexander GB, Heston WM, Iler RK. The solubility of amorphous silica in water. *J Phys Chem* 1954; **58**: 453.
- Iler RK, ed., *The Chemistry of Silica*, ch. 1 & 2 (pp. 3-171). Wiley, New York (1979).
- Harris RK, Knight CTG, Hull WE. Nature of species present in an aqueous solution of potassium silicate. *J Amer Chem Soc* 1981; **103**: 1577-1578.
- Source: <http://www.iza-structure.org/databases/>
- Bussey RH, Mesmer RE. Ionization equilibria of silicic acid and polysilicate formation in aqueous sodium chloride solutions to 300 °C. *Inorg Chem* 1977; **16**(10): 2444.
- Manning CE. Polymeric silicate complexing in aqueous fluids at high pressure and temperature. In: Wany RB, (ed.). *Water Rock Interaction I*. Taylor & Francis, 2004; pp. 45-52.
- Zotov N, Keppler H. Silica speciation in aqueous fluids at high pressures and high temperatures. *Chem Geol* 2002; **184**: 71-82.
- Hendricks WM, Bell AT, Radke CJ. Effects of organic and alkali metal cations on the distribution of silicate anions in aqueous solutions. *J Phys Chem* 1991; **95**: 9513-9518.
- Kinradet SD, Swaddle TW. Silicon-29 NMR studies of aqueous silicate solutions. 1. Chemical shifts and equilibria. *Inorg Chem* 1988; **27**: 4253-4259.
- Xue X, Stebbins JE, Kanzaki M, McMillan PF, Poe B. Pressure-induced silicon coordination and tetrahedral structural changes in alkali oxide-silica melts up to 12 GPa: NMR, Raman, and infrared spectroscopy. *Amer Mineral* 1991; **76**: 8-26.
- Ennis RD, Pritchard R, Nakamura C, *et al.* Glass vials for small volume parenterals: influence of drug and manufacturing processes on glass delamination. *Pharm Dev Technol* 2001; **6**(3): 393-405.
- Jal PK, Sudarshan M, Saha A, *et al.* Synthesis and characterization of nanosilica prepared by precipitation method. *Colloids Surf A: Physicochem Eng Aspects* 2004; **240**: 173-178.
- Corma A, Davis ME. Issues in the synthesis of crystalline molecular sieves: towards the crystallization of low framework-density structures. *Chemphyschem* 2004; **5**(3): 305-313.
- Kinradet SD, Pole DL. Effect of alkali-metal cations on the chemistry of aqueous silicate solutions. *Inorg Chem* 1992; **31**: 4558-4563.
- Tossell JA. Calculation of ^{19}F and ^{29}Si NMR shifts and stabilities of F-encapsulating silsesquioxanes, preprint.
- Mortlock RF, Bell AT, Radke CJ. Incorporation of aluminum into silicate anions in aqueous and methanolic solutions of TMA silicates. *J Phys Chem* 1991; **95**: 7847-7851.
- Burkett SL, Davis ME. Mechanism of structure direction in the synthesis of Si-ZSM-5, an investigation by intermolecular ^1H - ^{29}Si CP MAS NMR. *J Phys Chem B* 1994; **98**: 4647.
- Burkett SL, Davis ME. Mechanisms of structure direction in the synthesis of pure-silica zeolites. 1. Synthesis of TPNSJ-ZSM-5. 2. hydrophobic hydration and structural specificity. *Chem Mater* 1995; **7**: 920-928, 1453-1463.
- Houssin CJY, Kirschhock CEA, Maguin PCMM, *et al.* Combined *in situ* ^{29}Si NMR and small-angle X-ray scattering study of precursors in MFI zeolite formation from silicic acid in TPAOH solutions. *Phys Chem Chem Phys* 2003; **5**: 3518-3524.
- Poulsen N, Sumper M, Kröger N. Biosilica formation in diatoms: characterization of native silaffin-2 and its role in silica morphogenesis. *Proc Nat Acad Sci* 2003; **100**: 12075-12080.
- Poulsen N, Kröger N. Silica morphogenesis by alternative processing of silaffins in the diatom *Thalassiosira pseudonana*. *J Biol Chem* 2004; **279**(41): 42993-42999.
- Belton DJ, Patwardhan SV, Perry CC. Spermine, spermidine and their analogues generate tailored silicas. *J Mater Chem* 2005; **15**: 4629-4638.
- Belton DJ, Paine G, Patwardhan SV, Perry CC. Towards an understanding of (bio)silicification: the role of amino acids and lysine oligomers in silicification. *J Mater Chem* 2004; **14**: 2231-2241.
- Zeng H, Wilson LD, Walker VK, Ripmeester JA. Effect of antifreeze proteins on the nucleation, growth, and the memory effect during tetrahydrofuran clathrate hydrate formation. *J Am Chem Soc* 2006; **128**: 2844-2850.
- Buchanan P, Soper AK, Thompson J, *et al.* Search for memory effects in methane hydrate: Structure of water before hydrate formation and after hydrate decomposition. *J Chem Phys* 2005; **123**: 164507.
- Asay DB, Kim SH. Evolution of the adsorbed water layer structure on silicon oxide at room temperature. *J Phys Chem B* 2005; **109**: 16760-16763.