Inorganic Chemical Cells

Modular Redox-Active Inorganic Chemical Cells: iCHELLs**

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Compartments are vital for the partitioning of biological and chemical systems, allowing the controlled[1] passage of energy, materials, and ions between different environments.[2] To achieve function, the barrier should be able to act as a membrane with controlled porosity,[2] and materials with this capability are being widely used in processes ranging from gas separation to molecular recognition.[3] However, the manufacture of such compartments is normally restricted to using high-molecular weight polymeric materials.[4] Therefore, the assembly of flexible membranes that can form compartments with functionality reflecting the choice of the molecular building blocks is a challenge, in which success will give insight into the design of materials with many applications, for example, as sensors,[5] in soft materials,[6] medicine,[7] and for the confinement of chemical reactions.[8] Traditional methods by which flexible membranes are produced include surface deposition, doping of a pre-existing material and using macromolecular amphiphilic molecules or polymers.[4,9] In all these cases the membrane is formed at a phase boundary; membrane formation at an aqueous–aqueous interface and the formation of hybrid organic–inorganic membranes from low-molecular weight building blocks are rare.[10]

Herein, we present the fabrication of hybrid inorganic chemical cells (iCHELLs) at the liquid–liquid interface between aqueous solutions of simple polyoxometalate clusters (POMs)[11] and organic/coordination-complex cations, and demonstrate that this process is general for a wide variety of starting materials. The use of POM building blocks is interesting since these can impart enhanced functionality including redox, catalytic, photochemical, and magnetic properties.[11,12] Using this method we can controllably produce robust, spontaneously repairing membranous iCHELLs with diameters that range from 50 μm to cell-like compartments of several millimeters (see Figure 1). The membranous pouches display intrinsic physical properties that reflect their molecular building blocks, such as redox activity or chiral structure, while also being able to partition chemical components within a system. As such, the inorganic "cells" can be manufactured in bulk or can be "nested" within one another to produce clearly separated domains within a single structure. The membrane is formed by simply extruding an aqueous solution of one component through a nozzle into an aqueous solution of the other, forming a closed compartment. This approach allows iCHELLs with radically different functionality to be produced simply by changing either of the reagents that are mixed together.
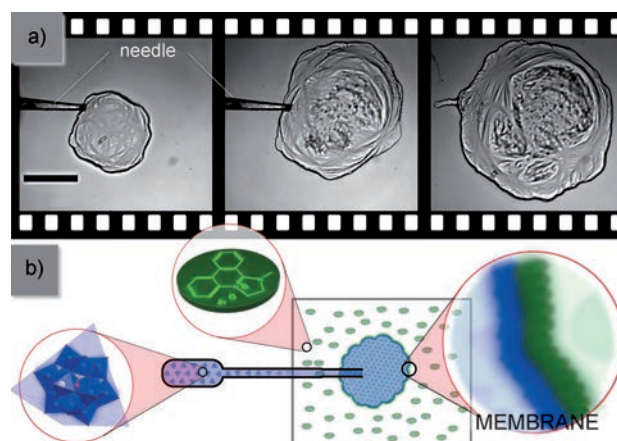

Figure 1. a) A sequence of images showing the formation of a 1.2 mm diameter cell as the POM solution (phosphotungstic acid) is injected into the solution of the organic cation (methyl dihydroimidazophenanthridinium, DIP-Me).[14] Needle aperture: ca. 20 μm. b) Schematic illustration of the "extrusion-exchange" mechanism of membrane formation. One component is injected into a solution of the other, in which cation exchange occurs on the POM, hence leading to aggregation.

The key to our approach is the ion-exchange reactions that occur at the interface between the solution extruded from the nozzle, and the bulk solution, allowing highly controlled fabrication of the membrane.[13] The formation is achieved through an "extrusion-exchange" mechanism, in which the small cations (such as H^+ or Na^+ ions) associated with the large POM anions are exchanged for the larger organic cations (previously accompanied by small anions, e.g. Br^-), thus leading to the formation of an insoluble aggregate at the

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solution boundary (see Figure 1 and supplementary video SV1). In the general case, an aqueous solution of the POM, phosphotungstic acid ($H_3PW_{12}O_{40}$, $\{PW_{12}\}$), is injected into a droplet of aqueous cation (in this case a phenanthridinium-based heterocycle)[14] using a micromanipulator needle and results in the immediate formation of a membrane that partitions the two solutions (see the Experimental Section). The reverse scenario, in which the cation is injected into the POM solution also causes membrane formation. These structures can be deflated and re-inflated several times by drawing the contents back into the micromanipulator and then re-injecting. Several such architectures can coexist with one another, with no coalescence upon contact. Ruptures in the membrane are repaired as the two solution components come into contact at the interface.

The structure of the membranes produced using the "extrusion-exchange" process has been studied using scanning electron microscopy (SEM) of dried samples, and shows that variation of the POM starting material results in large differences in the morphology (see Figure 2 and the Supporting Information). For a given cation concentration, membranes produced from large highly charged clusters are thicker. For example, the small 1.2 nm $\{PW_{12}\}^{3-}$ POM anion produces a thinner (1–2 μm), more wrinkled membrane surface, while a larger 1.8 nm sized POM cluster ($[P_8W_{48}O_{184}]^{40-}$, $\{W_{48}\}^{40-}$)[15] gives a much thicker, more featureless membrane. Elemental analysis (for C, H, and N) of the membranes shows that the composition of the individual components is retained and that the cations and anions aggregate in the ratio required to balance their charge.
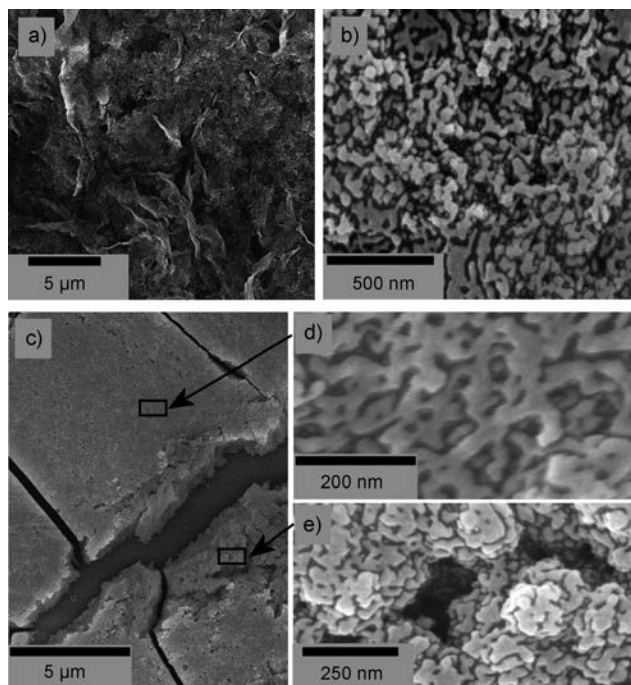
To demonstrate the modular approach that can be taken in the fabrication of the iCHELLs, we produced membranes using a range of organic cations (e.g. from heterocylic derivatives of phenanthridiniums (DIPs) to the highly fluorescent [Ru^{II}(bipy)$_3$](BF$_4$)$_2$ (bipy = 2,2′-bipyridyl) and a range of POM clusters such as $\{PW_{12}\}$ and phosphomolybdic acid ($H_3PMo_{12}O_{40}$, $\{PMo_{12}\}$) through to more complex materials including a very large 3.6 nm wheel-shaped cluster ($[Mo_{154}(NO)_{14}O_{420}(OH)_{28}(H_2O)_{70}]^{(25\pm5)-}$, $\{Mo_{154}\}$).[16] It is even possible to produce chiral membranes, as evidenced by circular dichroism (CD) spectroscopy, using enantiomerically pure [Ru^{II}(bipy)$_3$]$^{2+}$ cations, thus opening the way to utilize inherently chiral membranes for chiral catalysis, sensing or separation technologies (see the Supporting Information). The mechanical strength of $\{PW_{12}\}$-based membranes was investigated by using an AFM cantilever to tear the membrane and by observing the deflection of the tip as tearing occured. Initial results indicate that a force of approximately 110 μN is exerted before the tip tears the membrane when it is derived from DIP-Me cations. This value is around 100 × less than the force required to rupture a biological vesicle wall.[17] However, we also observed that the strength of membranes can be enhanced by approximately 15 % by using a larger, more highly charged cation in place of DIP-Me (see the Supporting Information), thus providing a route to significantly strengthen the membranes.

Since selective permeability is an essential feature in synthetic hybrid membranes, we examined the permeability of $\{PW_{12}\}$-based cells (in DIP-Me solution) to a flow of ammonium hydroxide solution and solutions of tetraalkylammonium hydroxides of varying chain lengths (see Figure 3 and supplementary video SV2). Upon contact with any of these ammonium species, $\{PW_{12}\}$ immediately precipitates so we were able to easily observe the time taken between addition of the ammonium salt outside of the cell and the precipitation of $\{PW_{12}\}$ inside. Treatment with ammonium hydroxide and tetramethylammonium hydroxide resulted in very rapid
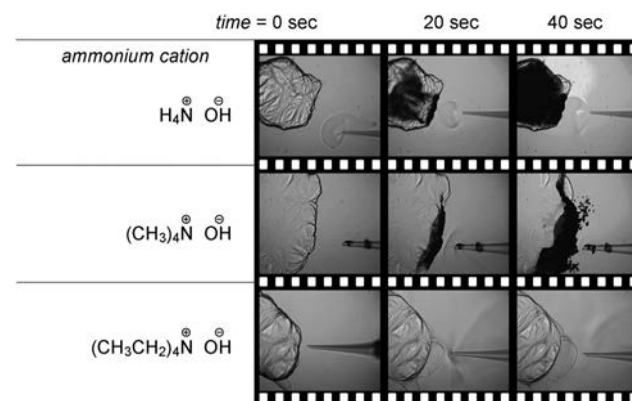
Figure 2. SEM images a) $\{PW_{12}\}$-DIP-Me membrane 3000× magnification. b) $\{PW_{12}\}$-DIP-Me membrane 45 000× magnification. c) $\{W_{48}\}$-DIP-Me membrane 5000× magnification. d) $\{W_{48}\}$-DIP-Me membrane 80 000× magnification. e) $\{W_{48}\}$-DIP-Me membrane 130 000× magnification.

Figure 3. Photographs showing the effect of injecting ammonium ions next to the $\{PW_{12}\}$-DIP-Me iCHELL as a function of time. The top sequence shows the passage of ammonium ions into the iCHELL and the resulting precipitation inside. The middle sequence, with tetramethylammonium ions, only shows slight precipiatation at the membrane, and the bottom sequence appears to show that tetraethylammonium ions cannot traverse the membrane on the timescale shown.

precipitation inside the cell. However, when larger tetraethyl- or tetrapropylammonium hydroxide was used, there was a significant time-lag before precipitation was observed and when tetrabutylammonium was added, no precipitation was observed, thus demonstrating that our membranes are more permeable to smaller molecules. It is also possible to use the iCHELLs to form membrane barriers and set up a pH or redox gradient by separating a reducing agent or acid from a redox or acid indicator (methylene blue or bromocresol purple, see the Supporting Information).

As injection of either component into the other produces a membranous pouch, the construction of a cell within another cell is possible. These "nested" systems can be used to compartmentalize chemical reactions. As a simple demonstration of this principle, a DIP-Me solution was injected into a solution of $\{PMo_{12}\}$ and the resulting cell was then further injected with a solution that contains $\{PW_{12}\}$ with a small amount of potassium permanganate added, thus producing a smaller dyed "cell" inside the first (see Figure 4 and supplementary video SV3). Both cells remained stable for a period of several hours without merging or leakage, unless physically pushed together. Addition of hydrogen peroxide to the outer $\{PMo_{12}\}$ solution caused discoloration of the potassium permanganate after a short diffusion time, showing that the "nested" system can be used to compartmentalize chemical reactions since the H_2O_2 is able to pass over both
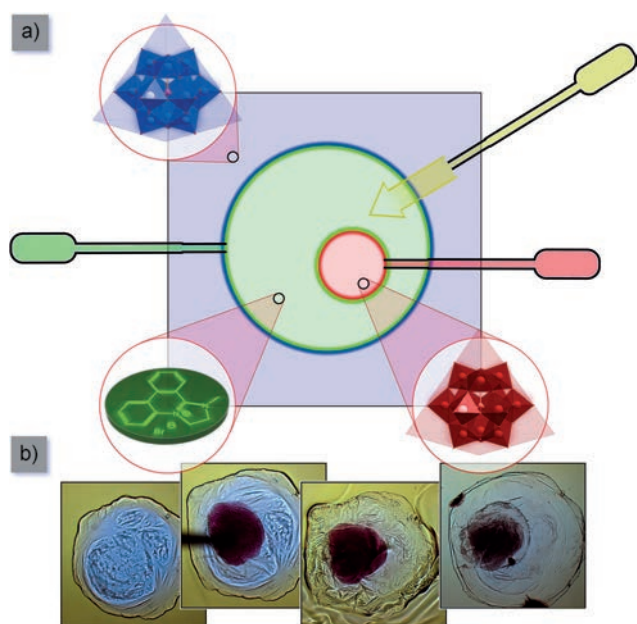

Figure 4. a) A schematic representation of one cell being grown inside another. A salt containing a large organocation (green) is injected into a salt solution containing a large POM anion (blue) forming a membrane. A second POM that contains another POM reagent (red) is injected into the first cell, producing a second membrane. Adding an external reagent (yellow) can then cause a reaction in the inner cell after a diffusion time. b) Time-lapse images are shown below with the growth of a DIP-Me cell in $\{PMo_{12}\}$, followed by the construction of a $\{PW_{12}\}$ cell inside the encapsulated DIP-Me droplet. The $\{PW_{12}\}$ cell contains potassium permanganate and when hydrogen peroxide solution is added to the outer $\{PMo_{12}\}$ solution, discoloration of the $\{PW_{12}\}$ cell is observed after a few minutes.

membranes and through the DIP solution. We hypothesize that compartmentalized cell-to-cell reaction systems would also be possible, in which the cells containing different reagents (able to cross the membrane at different rates) are brought into proximity with one another, thus allowing sequences of chemical transformations to occur with a good degree of control.

Once formed, the cells can be successfully transferred out of their mother liquor, as long as they remain in a sufficiently high ionic-strength environment. The construction of membranes on polymer supports allows a number of further applications to be investigated, as the membrane-coated matrix can be easily removed from the initial solution and can be washed several times without losing its structural integrity. In this respect we are also able to show that the iCHELL membranes can be grown on a supporting hydrogel matrix by sorbing the cationic membrane-forming component into an anionic hydrogel material, such as partially deprotonated polyacrylic acid. The cation-soaked hydrogel material was then immersed in a solution containing the POM component, thus forming membranous material on the surface of the hydrogel. This material was confirmed to be similar in appearance to the free membrane material by SEM analysis and the hydrogel-supported membranes respond identically to external stimuli such as oxidizing/reducing agents as their unsupported counterparts (see the Supporting Information).

Finally, to demonstrate that these membranes could be mass-produced with a reliable size and shape, a microfluidic device was used to generate water-in-oil emulsions, in which the inner aqueous phase contained the cation solution and the oil phase consisted of oleic acid with 2% (w/w) Span80 non-ionic surfactants. These droplets, with diameters that varied between 100 and 400 μm, were then injected into the POM solution ($\{PW_{12}\}$). Loss of the oil phase to the sample surface resulted in the controlled formation of membrane cells with diameters of 100–400 μm, much smaller than those produced by manual injection (see Figure 5).

In summary we have shown it is possible to fabricate inorganic chemical cells (iCHELLs) at the liquid–liquid interface by combining large polyoxometalate anions with large organic/coordination-complex cations. This ion-exchange process allows the design of redox-active, chiral, and nested cells simply by choosing the reagents, and the ability to "mass produce" the cells in a microfluidic system means that it will be interesting to use these systems as "capsule" catalysts that can selectively import reagents and
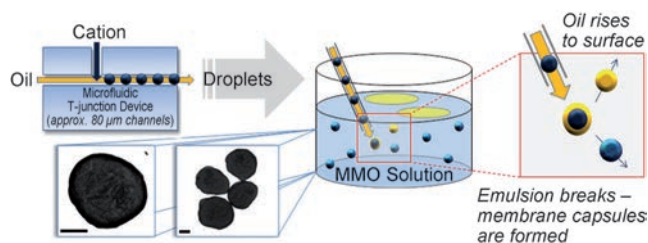

Figure 5. Mass-production of membrane cells ranging from 100–400 μm using a microfluidic device to generate water-in-oil emulsions. Scale bar in inset micrographs is 50 μm.

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sense the exterior environment. In future work, we will investigate the use of iCHELLs as carriers for complex dynamic chemistry that can give the inorganic chemical cells individual chemical characteristics, and to engineer these iCHELLs to undergo fission into daughter iCHELLs. The grand aim is to construct complex chemical cells with life-like properties, because the development of non-biotic inorganic chemical cells could be one route to probe how life emerged from the "inorganic world" around 4.3 billion years ago and how new synthetic[18] or inorganic biology outside of the current "organic" toolbox could be achieved in the laboratory today.

Experimental Section

The general methodology employed in the formation of membranous cells for optical microscopy and micromanipulation was as follows: A droplet of cation solution was placed on a 0.1 mm thickness glass coverslip (for DIP-Me, a concentration of 38.70 mM was used). A solution of the POM (0.4–0.7 M for {PW$_{12}$}) was loaded into an Eppendorf "femtotip" needle and was injected into the droplet of cation solution. The solutions were reversed when fabricating "cation-in-POM" materials and for larger cells, a glass Pasteur pipette was used for injection. Further details of specific experiments are available in the Supporting Information.

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