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...and the Iodine Clock

goes round...

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PAPER

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Stable and transient self-propagating supramolecular gelation†

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The ability to program sol–gel transition in time is key for living organisms to maintain their vital functions and to grow complex materials. Replicating this behavior with synthetic chemical networks is challenging, but highly rewarding for the design of intelligent biomimetic materials. Thanks to a combination of autocatalysis and supramolecular complexation, the iodate–hydroxymethanesulfinate–poly(vinyl alcohol) system features the emergence of self-propagating gelation fronts, stable or transient depending on the fine-tuning of the system.

Design, System, Application

Artificial systems that enable the programming in time of sol–gel transitions are of great interest for the development of biomimetic dynamic materials. However, most state-of-art systems rely on externally provided triggers, such as temperature and light. Clock reactions are versatile *in situ* time-controlled chemical triggers with great potential for advanced materials applications. Here we describe the application of the iodate–hydroxymethanesulfinate (iodate–HMS) reaction, an autocatalytic “iodine clock”, to program the autonomous formation and dissolution of a supramolecular poly(vinyl alcohol) (PVA)–iodine gel. Based on the chosen clock parameters, the resulting gel can be stable or transient. Because of autocatalysis the sol–gel transition is extremely fast, yet measurable with conventional rheometry thanks to a tunable induction time. Other complex phenomena, such as chemical patterns, can also emerge from the iodate–HMS reaction, providing fertile ground for future investigations.

Introduction

Developing autonomous chemical systems that could imitate the properties of living matter is a challenge at the meeting point of materials science and systems chemistry.^{1–5} The time-programming of sol–gel transition has gained increasing attention in recent years, an interest being fueled both by its possible technological applications⁶ and its relevance for understanding living systems' biology.^{7–10}

For our research on materials programming by reaction networks¹¹ we are exploring new ways to control gelation in time. Clock reactions are chemical networks in which the desired product(s) can be observed only after an initial, usually tailorable, induction time.¹² Their usefulness for programming the autonomous generation of chemical stimuli, such as pH changes, in self-assembly systems has been clearly demonstrated.^{11,13–16} Previous reports on controlled gelation mostly focused on pH-driven systems, using enzymatic reactions (e.g. between urease and urea,^{17–20}

or glucose oxidase and glucose²¹), slow acid generators (e.g. δ -gluconolactone^{22,23}), or pH-clocks²⁴ to trigger sol–gel transitions. We recently described an alternative approach to program gelation in time by means of supramolecular complex formation.²⁵ “Iodine clocks”, such as the iodide–persulfate–thiosulfate (IPT) system, generate iodine‡ as a product after an initial lagtime. By adding poly(vinyl alcohol) (PVA) to the IPT system, we could control both the time of formation and the mechanical properties of the resulting PVA–iodine gel simply by adjusting the parameters of the iodine clock as well as by introducing competitive iodine-complexing agents. However, due to internal constraints, this system would not allow us to program the gel to be transient *i.e.* to autonomously dissolve.

We then turned our attention to the oxidation of hydroxymethanesulfinate $\text{HOCH}_2\text{SO}_2^-$ (HMS) by iodate IO_3^- , a reaction which has been investigated in detail by the group of R. H. Simoyi.²⁶ Under certain conditions, the iodate–HMS system behaves as an iodine clock thanks to interconnected reactions. First, iodide I^- is generated through the reduction of iodate with hydroxymethanesulfonic acid (Fig. 1A, eqn (1)),

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‡ Iodine I_2 has a limited solubility in water (around 0.29 g L^{-1} at 20°C)³⁵ but it quickly reacts with iodide I^- forming water-soluble triiodide I_3^- and possibly also other poly(iodide)s. For the sake of simplicity, throughout the manuscript we refer to iodine I_2 , triiodide I_3^- and poly(iodide) species collectively as “iodine”.



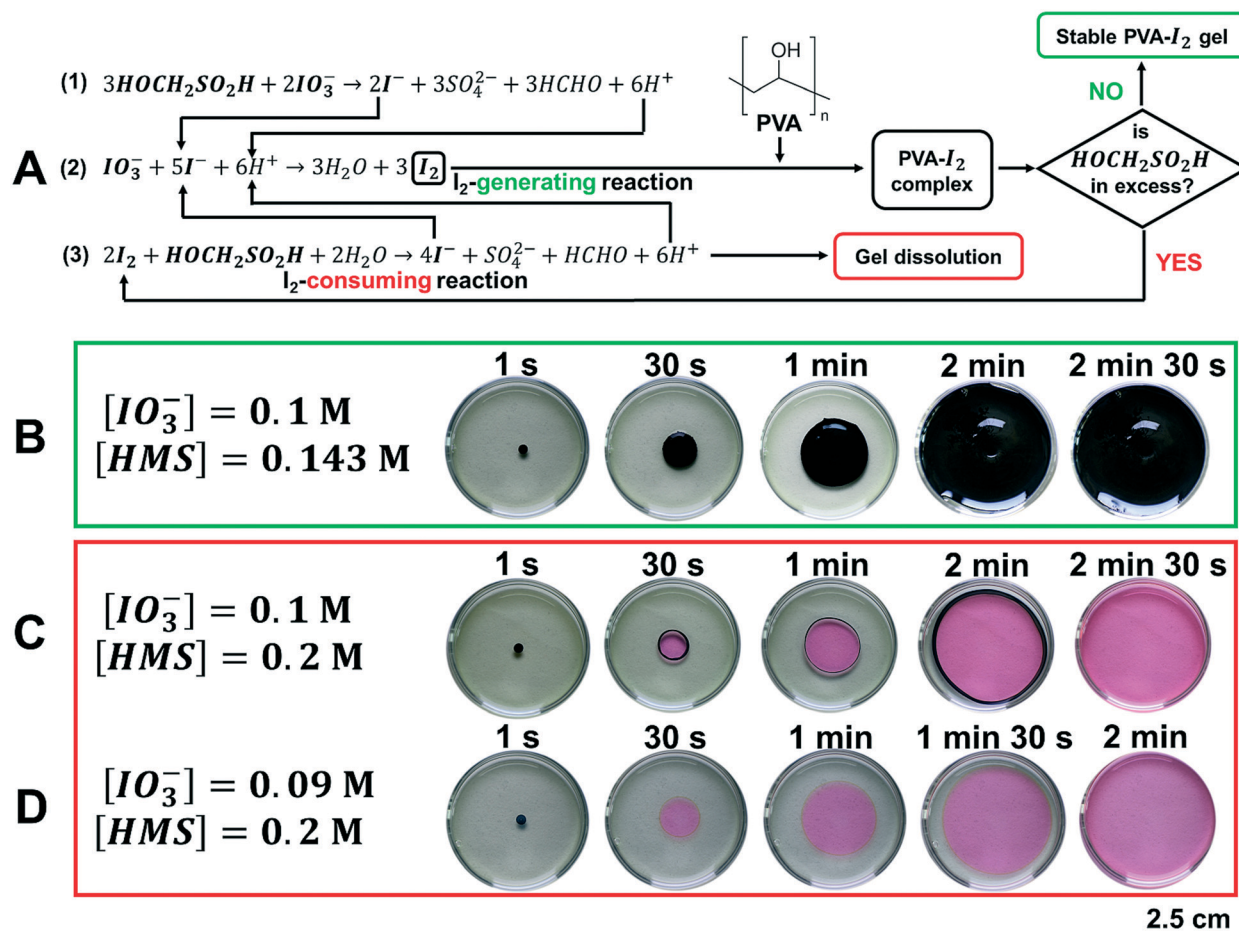


Fig. 1 (A) Simplified reaction mechanism of the iodate-HMS-PVA system. (B-D) Self-propagating reaction fronts in the iodate-HMS-PVA system, showing the dramatic effect that the relative concentrations of iodate and hydroxymethanesulfonate have on their evolution. The green and red frames symbolize the predominant reaction pathway. Each reaction mixture contains 5% of PVA 130 kDa, and two pH indicators (methyl yellow MY and bromocresol green BG). The reaction is started by pipetting 7 μL of 50 mM sodium bisulfate. The moment the acid drop touches the mixture is set as time $t = 0$. The liquid layer thickness is ca. 2.5 mm. The images in (B-D) are snapshots taken from Movies S1-S3.†

then iodine I₂ is formed thanks to the reaction between iodate and iodide (Dushman reaction,²⁷ Fig. 1A, eqn (2), “I₂-generating reaction”), but is quickly transformed back to iodide if HMS is in excess (Fig. 1A, eqn (3), “I₂-consuming reaction”). The formaldehyde HCHO generated in these reactions seems to have no or negligible contribution to the overall mechanism.

According to Simoyi and coworkers,²⁶ the iodine clock behaviour manifests only when iodate is in excess *i.e.* for a 2:3 iodate:hydroxymethanesulfonate equivalent ratio. The length of the induction time is directly proportional to the initial hydroxymethanesulfonate concentration [HMS] and inversely proportional to the initial iodate concentration [IO₃⁻]. A minimum acid concentration [H⁺] = 4.0×10^{-4} M (corresponding to pH \approx 3.4) is needed to initiate the formation of iodine and the induction time is shortened by increasing the initial [H⁺]. An earlier report²⁸ stated that the iodate-iodide reaction (eqn (2)) becomes fast enough only below pH 4.5. Both acid and iodide have a strong catalytic effect on the whole reaction network, and their concentration

builds up autocatalytically. The oxidation of iodine by hydroxymethanesulfonate (eqn (3)) is very fast, thus the appearance of iodine is delayed until all HMS has reacted. This is a typical feature of substrate-depletive chemical clocks,¹² like the previously mentioned IPT system. However, thanks to autocatalysis, much more complex dynamics (such as self-propagating and transient reaction fronts) can emerge in the iodate-HMS system. We are the first to describe these phenomena and their use to control sol-gel transition in time through the formation of supramolecular PVA-I₂ complexes.

Results and discussion

We started our investigation of the iodate-HMS-PVA system by triggering the reaction with a drop of acid (50 mM sodium bisulfate NaHSO₄). The addition of methyl yellow (MY) and bromocresol green (BG) allowed to visualize changes in pH during the reaction course.²⁹ Full experimental details are available in the ESI.†



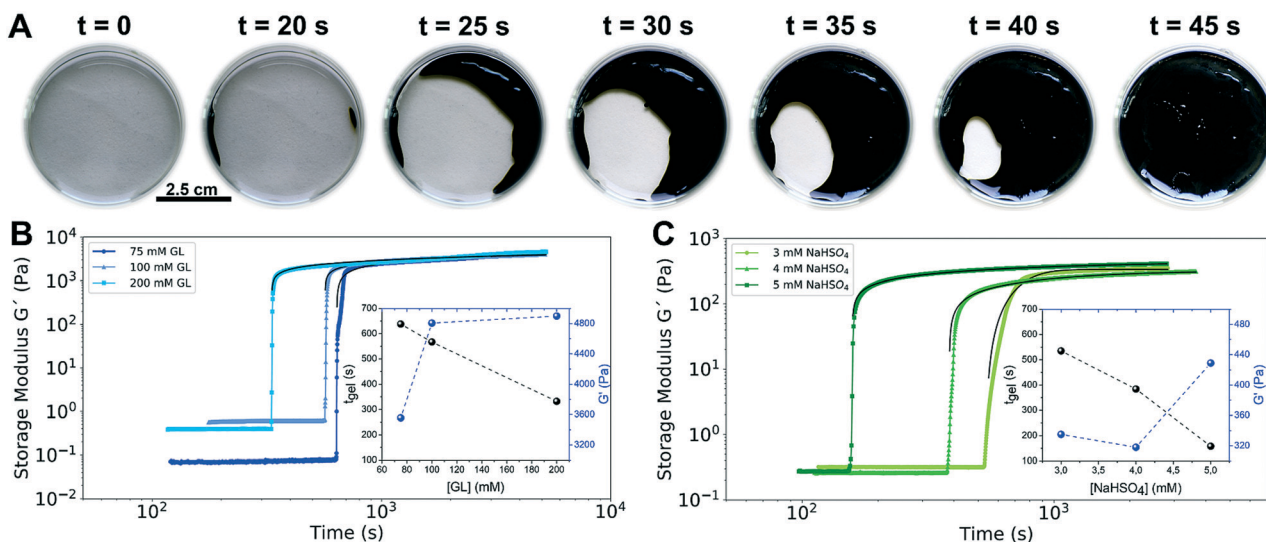


Fig. 2 (A) Photographic sequence showing the formation of a stable PVA- I_2 gel with excess iodate and δ -gluconolactone GL as *in situ* slow acid generator (iodate 100 mM, HMSNa 143 mM, GL 100 mM, 5% PVA 130 kDa, MY-BG mixture). The moment immediately before the first appearance of the PVA- I_2 complex is set as time $t = 0$. The snapshots were taken from Movie S6.† (B and C) Rheology plots of the iodate-HMS-PVA system triggered by different concentrations of (B) GL, (C) sodium bisulfate. For the sake of clarity, we show only the evolution of G' , together with the Cao fit³⁰ used to determine its final value. The insets show the dependence of gelation time t_{gel} and storage modulus G' on the concentration of bisulfate or GL. The lines are a guide for the eye. The complete rheology plots are shown in Fig. S3.†

As shown in Fig. 1B–D, a black spot of PVA- I_2 complex forms immediately after the addition of the acid droplet to the iodate-HMS-PVA system. The dramatic influence of the relative concentrations of iodate and HMSNa on the evolution of the system over time is also evident. For all systems, the I_2 -generating reaction (Fig. 1A, eqn (2)) develops as a self-propagating circular front (“ring”). However, a stable PVA- I_2 supramolecular gel forms only when iodate is in excess (Fig. 1B, Movie S1†). If HMSNa is in excess, the gel is either transient (Fig. 1C, Movie S2†) or does not even form (Fig. 1D and Movie S3,† the outer ring is light brown because of uncomplexed iodine). In these two latter cases, the I_2 -generating ring is followed by an I_2 -consuming one (eqn (3)). In the case shown in Fig. 1D, the decomposition of iodine is so fast that the complex with PVA cannot form.

While the I_2 -producing reaction is activated by acid, the I_2 -consuming reaction produces acid. This behavior is confirmed by the color change from light green (pH \approx 10) to pink (pH $<$ 2) that accompanies the I_2 -consuming reaction front.‡ We estimated the propagation speed of the PVA- I_2 front to be around 0.1 mm s^{-1} (Movie S4a†). The speed of the front did not seem to be affected by the average molecular weight of PVA. Without PVA, the iodine front propagated faster, up to 0.2 mm s^{-1} (Movie S4b†). Other phenomena worthy of future investigation emerge from the interplay between I_2 -generating and I_2 -consuming reactions, such as a

seemingly periodic thickness change of the PVA- I_2 ring (Fig. 1C, Movie S2†) and complex spatiotemporal patterns (Fig. S1, Movie S5†).

It is noteworthy that the iodate-hydroxymethanesulfonate reaction has some elements of similarity with another autocatalytic iodine clock, the iodate-sulfite-thiosulfate (IST) system.^{31,32} Both are autocatalytic in acid and iodide, and can generate complex nonlinear phenomena such as reaction-diffusion acid and iodine fronts, instabilities and patterns. However, in the IST system the iodine front follows the acid one, while in the iodate-HMS system the behavior is exactly the opposite.

As mentioned before, a certain pH value is needed for the iodate-HMS reaction to occur at an appreciable rate, and in the experiments described so far this was achieved by the direct addition of acid. However, our main interest is to program chemical systems to perform their tasks autonomously, without external control. We already showed that slow acid generators such as cyclic esters can be used to control the dynamics of clock reactions.^{14,15,33,34} Here we demonstrate the same approach for programming autonomous sol-gel transitions in the iodate-HMS-PVA system with δ -gluconolactone (GL). The gradual hydrolysis of GL yields gluconic acid ($pK_a = 3.86$), which lowers the pH allowing reactions (1) and (2) to take place. Keeping $[IO_3^-]$ and $[HMS]$ constant, respectively 100 mM and 143 mM, the lagtime before iodine formation and the consequent gelation of the PVA- I_2 complex (t_{gel}) is a direct function of the acid concentration *i.e.* of $[GL]$. Lagtimes ranged from \sim 11 min with 75 mM GL to \sim 6 min with 200 mM GL.

Once started, the gel formation is very fast (Fig. 2A and S2†). We further investigated this behavior by means of

‡ The actual pH values were measured with a glass electrode. The initial pH of the iodate-HMSNa mixture (before the addition of acid) is around 10 due to the basic hydrolysis of HMSNa, while after the I_2 -consuming reaction the pH can be as low as 1.3.



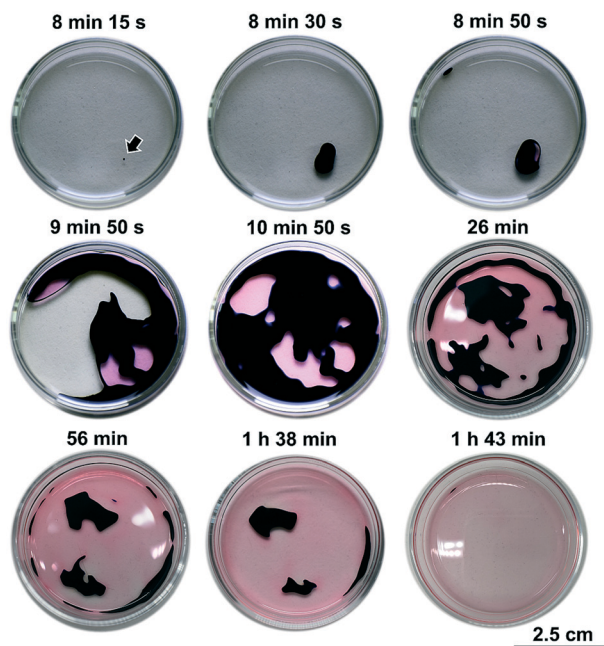


Fig. 3 Photographic sequence showing autonomous sol-gel-sol transition in the iodate-HMS-PVA system (iodate 100 mM, HMSNa 200 mM, 10 mM bisulfate, 5% PVA 130 kDa, mixture of MY and BG). The recording of time is started from the addition of HMSNa. The first appearance of the PVA-I₂ complex is indicated with an arrow. It is noteworthy that, while the gel formation is very fast, its dissolution is much slower and happens by gradual surface erosion.† The snapshots were taken from Movie S7.†

rheometry. As can be seen from Fig. 2B, the storage modulus G' suddenly increases when the iodine clock strikes, and quickly reaches its maximum value. How sudden this sol-gel transition is can be best appreciated by comparing it with the one observed for the IPT-PVA system²⁵ (Fig. S4†). In both systems the storage modulus G' increased about four orders of magnitude after the iodine clock struck, but in the iodate-HMS-PVA system this change happened much faster compared to the IPT-PVA one.

Substituting GL with bisulfate in the iodate-HMS-PVA system, the same fundamental rheological behavior is observed (Fig. 2C) but the lagtimes are consistently shorter (Fig. S5†), from ~9 min to ~3 min for 3 mM and 5 mM bisulfate, respectively, and the resulting gels less stiff, with G' values about one order of magnitude lower. More importantly, bisulfate allows to obtain autonomous sol-gel-sol transitions. With 10 mM bisulfate in a mixture of 100 mM iodate, 200 mM HMSNa and 5% PVA 130 kDa, islands of dark blue PVA-I₂ complex form over time and subsequently start to degrade (Fig. 3). Due to its very fast and complex dynamics, we could not obtain proper rheological data for this transient gel system.

† We observed the same kind of behavior for the gel obtained with the IPT-PVA system.²⁵

Conclusions

We showed that self-propagating supramolecular sol-gel transition can be achieved and programmed in time using an autocatalytic iodine clock, the iodate-HMS system, and that stable or transient PVA-I₂ gels can be obtained depending on the chosen reaction conditions. We were able to program gelation in time and thus to quantify the almost instantaneous gel formation induced by the autocatalytic iodine buildup. In the course of this investigation we noticed that the iodate-HMS system can give rise to other complex phenomena, such as the generation of chemical patterns, which also deserve further investigation.

Our results further demonstrate the power of complex chemical networks, such as clock reactions, for the programming of soft materials. Our approach will inform and inspire the design of future programmable and transient hydrogels. Furthermore, the sharp pH change that accompanies the dissolution of the transient gel could be exploited for example to trigger the self-assembly of a different building block, or even another set of reactions. Thanks to its excitable behavior, the iodate-HMS system could be applied also for the development of transient chemomechanical actuators and for chemistry-based computing.

Conflicts of interest

There are no conflicts to declare.

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