In their system, the chemistry is initiated after photoexcitation of the catalyst precursor (see the figure). This liberates CO from the coordination sphere of one of the Rh centers, providing the necessary vacancy for the proton source (present as a hydrohalic acid, HX) to bind to the catalyst and leading to the formation of half an equivalent of H_2 in what is likely a thermal process. At this stage, the photochemical cycle begins, with photon absorption producing another vacancy and yielding another 0.5 equivalents of H_2. The absorption of the next photon activates the Rh-X moiety to reform the same species as is produced after the initial loss of CO [see Scheme 2 in (*2*)]. This completes the catalytic cycle.

Heyduk and Nocera provide evidence for catalysis by documenting the production of more than 100 μmol of H_2 from a solution containing less than 1 μmol of the catalyst precursor. The two-electron mixed valency likely plays an important role in facilitating catalytic turnover by helping to maintain the integrity of the catalyst after the Rh-X elimination step. This is the truly novel feature of their system.

To be fair, their success is tempered by certain problems not unlike those faced by Gray and co-workers. As the authors themselves point out, a complete catalytic system would have to be able to handle the other half of the reaction, the halogen (X) from the hydrohalic acid. In the present case, a trap removes X from the cycle, eventually leading to the buildup of an unwanted side product. In addition, the conversion efficiency is very low and the catalyst degrades too readily for long-term practicality.

However, the importance of this work does not lie in the specifics of the catalyst's performance, but rather in the new opportunities it offers. Heyduk and Nocera have taken fundamental ideas of photochemistry and harnessed them to achieve a long sought-after but elusive goal, the molecular-based photocatalytic production of a usable fuel. What the scientific community does along this exciting new path remains to be seen.

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PERSPECTIVES: SURFACE SCIENCE

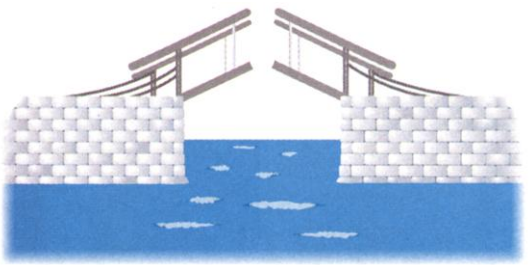
Bridging Gaps and Opening Windows

Nils I. Jaeger

On page 1635 of this issue, Sachs *et al.* (*1*) demonstrate how advanced surface science tools allow a catalyzed chemical reaction to be monitored in situ on the atomic scale while spatiotemporal patterns such as reaction fronts crossing the surface of a catalyst are observed under the same conditions on the micrometer scale. A gap between length scales several orders of magnitude apart is thus bridged. Systems of increasing complexity may be studied by adapting this approach.

The paper is a milestone in the ongoing efforts to observe, analyze, and simulate spatiotemporal patterns that evolve on surfaces in nonlinear chemical reaction systems far from equilibrium. Such patterns play a crucial role in catalytic processes but are difficult to understand in detail because of their complexity.

Because of technical constraints, catalytic phenomena on surfaces were long studied with model reactions on single-crystal surfaces of metals under ultrahigh vacuum conditions. However, application of the acquired knowledge in the rational design of catalysts and the control of catalyst performance under realistic conditions was hampered by the fact that up to 80% of chemical production depends on catalysis at ambient or elevated pressure. Furthermore, "real" catalysts are highly complex systems such as dispersed metals on oxidic supports.



Lowering the bridge. New techniques allow the characterization of spatiotemporal reaction patterns across a range of pressures and length scales, thus bridging the previous gap between operating conditions of real catalysts and model systems accessible to direct observation.

These problems are gradually being overcome as techniques are developed that can operate from ultrahigh vacuum to millibar pressures on complex materials. For example, infrared-visible sum frequency generation (SFG) surface vibrational spectroscopy is capable of operating at elevated pressures. In this method, vibrations in reactant molecules adsorbed on the surface of a catalyst are excited by absorbing energy from overlapping pulses of visible and of tunable infrared light. The generated signal provides almost exclusive information on the state of adsorbed molecules and hence their reactivity across a wide range of pressures (*2*, *3*). The power of the method was recently demonstrated by Dellwig *et al.* (*4*), who studied the dynamics of carbon monoxide adsorbed on palladium clusters deposited on an alumina support at pressures of up to 200 mbar. Structural information was obtained in parallel under ultrahigh vacuum conditions from scanning tunneling microscopy at atomic resolution (*4*).

However, such studies do not provide information on dynamic changes in the structure of the nanometer-sized metal particles, which often play an important role in the activity of real catalysts. In situ structural information on the operating catalyst is therefore needed. Efforts to build the bridge on the high-pressure side of the gap are in progress, for example, with the use of in situ x-ray absorption spectroscopy on the working catalyst (*5*). In situ high-resolution electron microscopy under millibar pressures may be available in the near future.

A detailed understanding of surface reactions and the mechanisms leading to spatiotemporal structures has emerged from such studies (*1*, *4*), opening a window toward rational catalyst design. Ingenious strategies are emerging, such as the microchemical engineering of catalytic reactions (*6*). With microlithograpic techniques, the size and geometry of catalytically active surfaces can be tuned to optimize the interaction of

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materials of different activities. Knowledge of reaction mechanisms including self-organization processes on catalytic surfaces can be exploited through joining sets of microreactors coupled by diffusive transport of adsorbed molecules. Moreover, the role of promoters, a central topic in catalysis, is now accessible to detailed investigations.

The study of model catalytic and electrochemical systems also contributes to the general understanding of nonlinear dynamics. Major issues are the control of spatiotemporal chaos and the study and the control of the catalytic and electrochemical reaction dynamics. The suppression of chemical turbulence in the catalytic oxidation of carbon monoxide on a platinum single-crystal surface by global delayed feedback via the carbon monoxide partial pressure is an impressive example (*7*). Another is the synchronization and cluster formation in large sets of chaotic electrochemical oscillators consisting of nickel electrodes in sulfuric acid via global coupling through external resistors (*8*).

The analysis, simulation, and control of complex nonlinear processes benefit many areas of science and engineering. For example, interest in the dynamics of electrochemical systems has been revived because of progress in the analysis and simulation of spatiotemporal patterns, such as the inhomogeneous distribution of reaction currents (*9*). Spatiotemporal patterns form on electrode surfaces during electrochemical reactions because of a subtle interplay between electrode kinetics, the conductivity and composition of the electrolyte, the geometry of the electrochemical cell, and the external electric circuit. The nature of the patterns is determined by long-range coupling between reacting sites through the electric field. This coupling can be easily fine tuned, opening a whole new window toward the understanding of pattern formation. Recently, the adjustment of long-range inhibition by migration currents has led to the appearance of structures on the surface of an electrode that could be identified as Turing patterns (*10*). Such findings may even help to understand structure formation in biological systems with gradients in electrical potential.

A rich harvest of basic knowledge will continue to result from studies of the self-organization of surface reactions, as exemplified by the report by Sachs *et al.* (*1*). I expect to see practical applications within the first decade of the 21st century in many areas, including electrocatalysis in fuel cells, corrosion control, electrochemical machining of metals, and—most importantly—industrial and environmental catalysis.

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PERSPECTIVES: BIOMEDICINE

Clotting Factors Build Blood Vessels

Peter Carmeliet

For blood vessels to deliver oxygen to distant tissues, they must remain intact. When the vessel is injured, bleeding is stopped by clotting (coagulation) factors that form a thrombus (clot) of fibrin threads that trap platelet aggregates. The protease thrombin is essential for fibrin formation and platelet activation. Platelets become activated when thrombin binds to several protease-activated G protein-coupled receptors (PARs) expressed on their surface (*1*). One member of the PAR family, PAR1, is not expressed by mouse platelets—yet, mouse embryos lacking this receptor die of fatal bleeding. The question is why? Emerging evidence implicates the clotting system in the building and stabilization of new blood vessels (angiogenesis) during embryonic development. On page 1666 of this issue, Griffin *et al.* report that expression of PAR1 by endothelial cells rescues the fatal vessel fragility and bleeding of mouse embryos engineered to lack PAR1 (*2*). These findings emphasize the importance of thrombin and its receptors in angiogenesis, not only in the embryo but also in the adult, where angiogenesis has been implicated in numerous disorders including cancer and ischemic heart disease (*3*).

The primary task of the clotting system is to form blood clots composed of fibrin and platelet aggregates. Tissue factor, the initiator of blood coagulation, usually remains separate from blood and circulating clotting factors. It is expressed by smooth muscle cells in and surrounding blood vessels, and at low levels by blood cells or activated endothelial cells that line blood vessels. At sites of vascular injury, plasma coagulation factor VIIa (FVIIa) contacts extravascular tissue factor, thereby triggering the coagulation cascade (see the figure). Tissue factor is a cofactor for activation of factor X (FX) by FVIIa. Activated factor X (FXa) with the assistance of cofactor Va (FVa) then converts prothrombin to active thrombin, which converts circulating fibrinogen to fibrin. Not surprisingly, therefore, the absence of any of these clotting factors (TF, FVIIa, FVa, FXa, prothrombin, fibrinogen) predisposes animals to severe, often life-threatening, bleeding disorders (*4*, *5*).

Thrombin further enhances blood clot formation by activating circulating platelets, which then aggregate (see the figure). This clotting enzyme promotes activation of human platelets by cleaving the amino-terminal extracellular domain of PAR1 or PAR4, cleavage of either being sufficient to trigger platelet aggregation (*1*, *6*). PAR3 and PAR4 are expressed by mouse platelets but, curiously, PAR3 is an accessory cofactor for PAR4 activation at low thrombin concentrations (*7*). In contrast to the residual thrombin response in PAR3-deficient platelets, PAR4-deficient platelets lose all thrombin signaling, and PAR4-deficient mice, although viable, suffer prolonged bleeding. Remarkably, however, despite severe platelet defects, PAR4-deficient embryos develop normally, indicating that platelets are not essential for blood clotting (hemostasis) in the embryo. Moreover, genetic studies suggest that fibrinogen is also not required for embryonic hemostasis. As expected, loss of PAR2, which is not expressed by platelets, does not affect hemostasis (*6*). Surprisingly, as Griffin *et al.* report, loss of PAR1 (which is not expressed by mouse platelets) leads to fatal bleeding defects in a fraction of early mouse embryos (*2*). Yet,

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