Scanning Electrochemical Microscopy: A New Technique for the Characterization and Modification of Surfaces

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Introduction and Basic Concepts

Microscopes are devices that allow one to image structures that are too small to see with the naked eye. Conventional microscopes are based upon the interaction of electromagnetic radiation, in the form of light or electron beams, with the sample. In these, resolution is determined by the wavelength of the radiation used. More recently other kinds of microscopes have been devised that form images by moving a small tip on or near a surface and sensing the changes in tip position or some other tip variable. Here the size of the tip and its distance from the substrate limit the available resolution. For example, in scanning tunneling microscopy (STM)[1] the tunneling current that flows between an atomically sharp metal tip and a conductive or semiconductive substrate as the tip is scanned within about 1 nm of the surface can show the surface topography and sometimes provide data about surface electronic energy levels. While STM can image with astounding resolution, and in favorable cases atoms can be "seen", it cannot be used with insulating substrates, and it does not yield information about the chemical nature of a surface. While other scanning microscopes, such as the atomic force and the ion-conductance microscopes,[1e] can image insulators, they are not "chemically sensitive". Our research group has constructed a new type of scanning-tip-type microscope in which the imaging process depends on the interaction of the substrate with a species electrogenerated at the tip. As discussed below, the response of such a device is firmly grounded on well-established electrochemical principles and it can be used to probe the conductivity of the sample (even when it is an insulator) and its chemical properties as well.

In scanning electrochemical microscopy (SECM)[2] (this abbreviation is also used for the device), the substrate and the tip are part of an electrochemical cell that also contains reference and auxiliary electrodes (Figure 1). The current at the tip of the electrode is a function of the solution composition, the distance between the tip and the substrate, and the nature of the substrate itself. Images can be obtained by monitoring the tip current as the tip is scanned in a rastered pattern across the substrate surface. These images contain information about chemical and electrochemical activity at the substrate surface as well as the substrate topography.

The imaging signal in SECM arises because the faradaic current flow resulting from the electron-transfer reaction at the tip is perturbed by the substrate surface. This is shown schematically in Figure 2. The solution in which tip and substrate are immersed contains an electroactive species, O (for example, $Fe(CN)_6^{3-}$), and usually some supporting electrolyte to minimize solution resistance. If the potential at the SECM tip is sufficient to reduce O to a species R at a diffusion-limited rate, the current will rapidly assume a steady-state value, which is proportional to the concentration of species O.[3,4] Far from the substrate, the diffusion layer near the tip electrode is roughly hemispherical (Figure 2A); however, this diffusion layer will be changed as the tip is brought closer to the substrate. If the substrate is an insulator, part of the diffusion layer will be blocked and the tip current decreases (Figure 2C). If the substrate is a conductor and is at a potential where species R can be oxidized back to O, the current at the tip will increase due to the recycling of species O (Figure 2B). This "feedback" process is an important feature of the SECM method. The direction of the current feedback indicates the nature of the surface (i.e., electrically conducting or insulating), while the magnitude of the signal gives an indication of the distance of the tip from the substrate, or alternatively, an indication of the rate of species turnover at the substrate.

Other workers have also described electrochemical techniques for investigating substrate electrodes. A scanning reference-electrode tip has been used to provide potential distributions over a substrate, such as corroding stainless steel.[5,6] This scanning potentiometry was carried out at lower resolution than that of the SECM. Another mode of operation of the SECM is to

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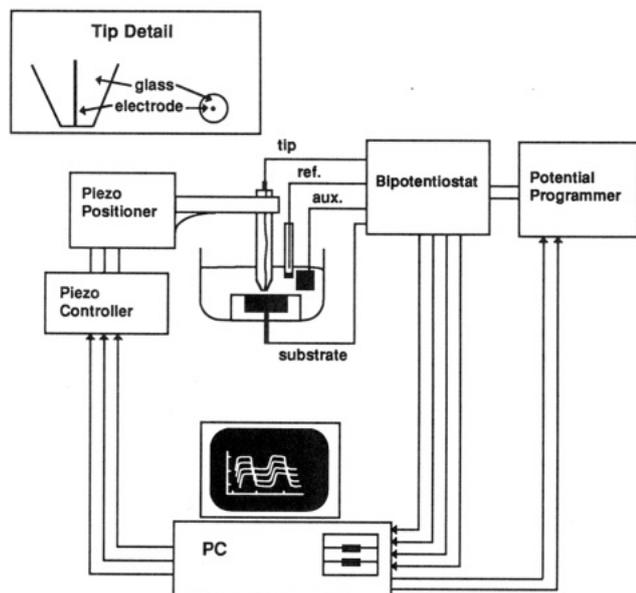
Figure 1. Block diagram of the SECM apparatus.
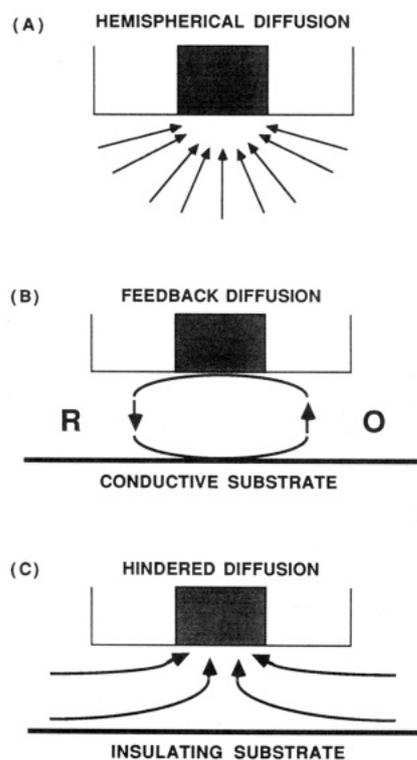
Figure 2. Basic principles of scanning electrochemical microscopy (SECM): (A) far from the substrate, diffusion leads to a steady-state current, $i_{T,\infty}$; (B) near a conductive substrate, feedback diffusion leads to $i_T > i_{T,\infty}$; (C) near an insulating substrate, hindered diffusion leads to $i_T < i_{T,\infty}$.

use the tip to monitor a substance generated at the substrate. This generation/collection mode has also been used in a nonimaging mode by other workers.[7,8]

In addition to its use as an imaging tool, the SECM can also be used for fabrication of very small structures on a substrate. In this mode the electrochemical reaction at the tip is used to etch various materials or to deposit metals, semiconductors, and polymers.

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Apparatus

The apparatus for performing SECM experiments is shown schematically in Figure 1. The tip electrode is mounted in a micropositioner that is driven by piezoelectric elements to provide submicron tip movement in the *x*, *y*, and *z* directions. The tip and substrate are immersed in the electrochemical cell. A bipotentiostat can be used to control the potential (bias) of the tip and substrate. As described in the next section, in many cases the substrate, either insulating or conducting, need not be connected to a potentiostat (termed an unbiased substrate). A personal computer is used to control the speed and direction of the tip movement via the piezoelectric controller. The computer is also used to provide potential biases for the tip and substrate electrodes or to provide a trigger for more sophisticated potential programmers. Finally, the computer also digitizes and stores the current at the tip (and the substrate) as a function of tip position or potential of the tip or substrate. The SECM tip can be prepared in different ways. Currently, the most useful tips are Pt or C microwires or fibers (0.2 – 50 μm in diameter) sealed in glass. The end of the glass is polished to expose a disk-shaped electrode. The sides of the glass insulating sheath are then carefully ground down with emery paper and diamond abrasive to form a truncated cone. This step is essential to the success of the experiment, because the inevitable small angular deviations of the tip surface from parallel will allow the sheath to contact the substrate first, and thus prevent a close tip–substrate spacing.

Theory

A quantitative treatment of SECM for both insulating and conductive substrates is available.[9] This is based on the usual models of electrochemical systems.[10] When the tip is far (i.e., more than 5–10 tip electrode diameters), the steady-state current attained at the tip, $i_{T,\infty}$ is given by[2-4]

$$i_{T,\infty} = 4nFCDa \tag{1}$$

where *n* is the number of electrons in the electrode reaction at the tip ($O + ne^- \rightarrow R$), *F* is the Faraday constant, *a* is the tip radius, and *C* and *D* are the concentration and diffusion coefficients of species O in solution. When the tip is moved close to an insulating substrate, diffusion of O to the tip is hindered and the tip current i_T is smaller than $i_{T,\infty}$. The magnitude of i_T can be computed from a computer simulation based on a finite element method.[9] This value of i_T depends upon the tip–substrate distance, *d*; i_T decreases as *d* decreases (Figure 3). It also depends upon the radius of the insulating sheath, which also blocks diffusion to the electrode.

When the substrate is an electrical conductor, oxidation of R back to O can occur at the substrate, and the flux of O to the tip is increased, because it includes both this positive feedback component and continued diffusion of O from bulk solution. In this case $i_T > i_{T,\infty}$ (Figure 3) and is essentially independent of the size of the insulating sheath.[9] In an approximate way, one can think of the tip–substrate pair as forming a "leaky" thin-layer electrochemical cell of variable width, d.[11]

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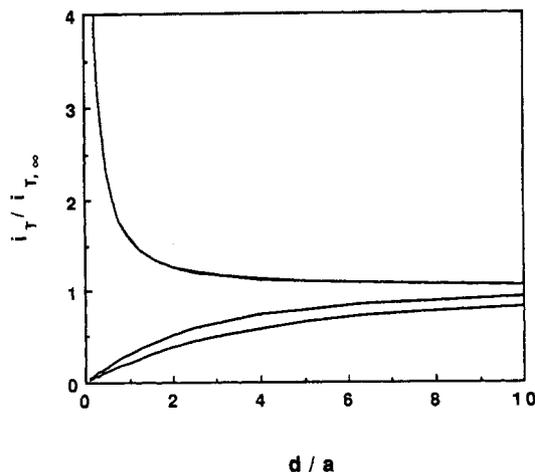
Figure 3. Plot of i_T normalized with respect to $i_{T,\infty}$ as a function of the tip-substrate distance normalized with respect to the radius a of the tip. Above a conducting substrate (top curve), different sheath sizes exhibit no difference in tip current. Above an insulating substrate (bottom curves), different sheath sizes lead to different tip currents (the larger the sheath, the smaller the tip current).

Note that while it is possible to drive the reaction R → O + ne^- at the substrate by controlling its potential via a connection to an external potentiostat, this reaction can also often occur at an unbiased conductive substrate as well. Since the substrate is usually much larger than the tip electrode, most of it will be bathed in solution containing only species O. In this case the potential of the substrate will be established well positive of the E° of the O,R couple. R striking the substrate beneath the tip is oxidized, while O at the substrate surface at locations away from the tip is reduced. This ability to study unbiased substrates simplifies the instrumentation and allows study of substrates that would be inconvenient to connect as electrodes.

A number of operating modes are possible. The tip current, a measure of d, can be monitored as the tip is rastered above the substrate to yield topographic images, after the tip is brought to a distance where i_T is sensitive to changes in d. The tip current can also be monitored as a function of substrate potential (tip-substrate voltammetry) to probe the products of reactions occurring at the substrate. It is also possible to measure the alternating current response of the tip electrode,[2] although this mode has not yet been used in SECM studies.

Characterization by SECM

SECM has been used with a number of different types of samples, including electrodes (e.g., minigrids and interdigitated electrode arrays),[12,13] polymer films on electrodes,[13,14] and biological materials.[15] Several examples will be described below. SECM scans of several test samples, such as a 50-μm Pt wire on glass, a 50-μm glass fiber on glass, a gold minigrid (25-μm periodicity), a Pt foil, and a KCl crystal in both aqueous and MeCN solutions with Pt and C tip electrodes (5-μm radius) have been reported.[12]

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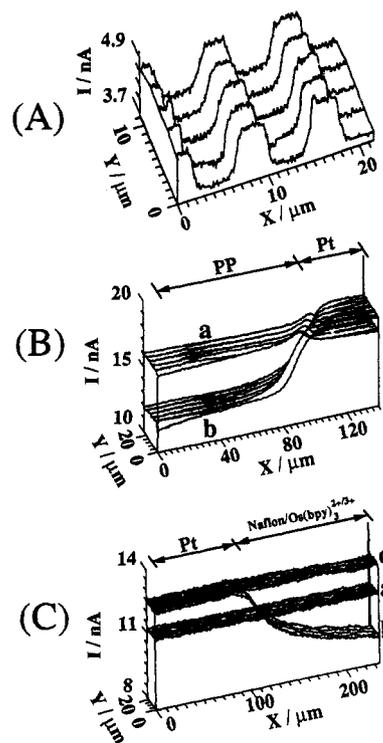
Figure 4. (A) Scan of an IDA: tip, 0.1-μm-radius Pt microdisk electrode; E_T = -0.78 V vs SCE; solution, 0.2 M MVCl$_2$ and 2 M KCl; $|i_{T,\infty}|$ = 3.7 nA. (B) Scans of the boundary between PP and Pt (d = 6 μm): tip, 5.5-μm-radius C microdisk electrode; E_T = -0.4 V vs SCE; solution, aqueous 10 mM Ru(NH$_3$)$_6$Cl$_3$ and 0.1 M K$_2$SO$_4$; $|i_{T,\infty}|$ = 12.5 and 13.5 nA for planes a and b, respectively. Plane a, at E_S = 0.7 V (PP: conductor); plane b, at E_S = -0.1 V (PP: insulator). (C) Scans of the boundary between Pt and a Nafion film containing Os(pby)$_3^{2+}$ in a 10 mM K$_3$Fe(CN)$_6$ and 0.1 M Na$_2$SO$_4$ solution; tip, 5.5-μm-radius C; E_T = -0.4 V vs SCE. (a) $i_{T,\infty}$ plane at d = 98 μm; (b) at E_S = 0.42 V [Os(bpy)$_3^{2+}$ form] and d = 10 μm; (c) at E_S = 0.8 V [Os(bpy)$_3^{3+}$ form] and d = 10 μm.

Figure 4A shows an SECM scan of an interdigitated array (IDA) immersed in an aqueous solution of methylviologen (MV) dichloride and KCl using a Pt microdisk electrode tip ($a \approx 0.1$ μm).[16] The scan in Figure 4A is an electroactive-site image of the magnitude of the tip current, which can provide information about the spatial composition of the substrate. These data can also be plotted as contour plots or gray-scale images, where the current level is converted to a color intensity. The average periodicity of Pt bands in the IDA is 7.9 μm, which is in good agreement with the manufacturer's specification (3-μm Pt band, 0.1 μm thick, and 5-μm SiO$_2$ gap, with an overall 8-μm periodicity).[17] In this example, the SECM response depicts surface conductivity, e.g., $i_T > i_{T,\infty}$ (positive feedback) over the Pt bands.

The potential dependence of the conductivity of the electronically conductive polymer polypyrrole (PP) was studied by SECM in a similar way.[14] A reduced PP film is insulating, while an oxidized one conducts.[18] The topography and the conductive nature of the substrate can be probed by SECM x-y scans above the region where the boundary between the Pt and the PP lies (Figure 4B). One sees positive feedback on both the Pt

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and PP zones at a substrate potential, E_S, of 0.7 V, where PP is a conductor (curve a). On the other hand, a negative feedback response is seen on the PP side at $E_S = -0.1$ V, where PP is an insulator (curve b). In an alternative approach the tip can be held fixed above a given position on the PP film and held at a potential (E_T) where the reduced form of the solution redox couple, $Ru(NH_3)_6^{2+}$, was generated. By scanning E_S and recording i_T vs E_S one can study the region of potentials where the transition between insulating and conducting PP occurs, as well as the kinetics of this transition.[14]

SECM can also be used to study the distribution of electroactive sites on a substrate. For example, if the substrate is a film of polymer with electroactive sites on a conductive electrode, and the tip-generated species can react with those sites, i_T will be greater than $i_{T,\infty}$. Thus the SECM can probe the chemical nature of the substrate. An example of this type of SECM study is shown in Figure 4C. The substrate was a Pt electrode partially coated with the ionomeric polymer Nafion, containing $Os(bpy)_3^{2+}$, and the boundary between these zones was scanned with a Pt tip in an $Fe(CN)_6^{3-}$ solution held at $E_T = -0.4$ V vs SCE where $Fe(CN)_6^{4-}$ is generated at the tip. Plane *a* results when *d* is large and represents $i_{T,\infty}$. Plane *b* is obtained at $E_S = 0.42$ V [$Os(bpy)_3^{2+}$ form], where the film behaves as an insulator, since this form cannot react with tip-generated $Fe(CN)_6^{4-}$. Plane *c* is found with $E_S = 0.8$ V [$Os(bpy)_3^{3+}$ form], where the film shows positive feedback since the reaction at the interface,

$$Fe(CN)_6^{4-} + Os(bpy)_3^{3+} \rightarrow Fe(CN)_6^{3-} + Os(bpy)_3^{2+}$$
(2)
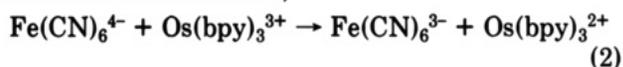
regenerates $Fe(CN)_6^{3-}$. In studies of this type, the i_T response depends on the nature of the polymer, the substrate electrode potential, the identity of the solution redox species, and the tip potential. Other polymer films on electrode surfaces investigated by this approach[13] included poly(vinylferrocene) (PVF) and *N*,-*N*′-bis[3-(trimethoxysilyl)propyl]-4,4′-bipyridinium (PQ^{2+}) dibromide. In a similar way, the effect of a thin oxide film on a metal surface can be studied. This approach was used to distinguish different metal substrates, gold and oxide-covered chromium in an IDA, by employing a solution containing two different redox couples.[13] These examples show how the SECM can be used to obtain information about the spatial distribution of chemically distinct sites on a surface. Note that in these examples the tip current response indicates chemical, rather than topographic, information about the surface.

SECM can also be used to obtain topographic information about biological samples immersed in an electrolyte solution either by using the feedback mode or by detecting a substrate-generated electroactive species (e.g., oxygen) at the tip.[15] For example, the upper surface of a blade of grass that was immersed in an aqueous solution of $Fe(CN)_6^{4-}$ could be imaged by SECM (Figure 5A). At $E_T = 0.7$ V, the tip reaction produces an anodic current via the production of $Fe(CN)_6^{3-}$. Since the surface is an electronic insulator, $i_T < i_{T,\infty}$. The variation of i_T can be converted to a color intensity to produce the gray-scale presentation. Here the dark shades represent maximum i_T and larger *d*, and light shades, minimum i_T and smaller *d*. The image, taken over an area of 188 × 142 μm, shows the
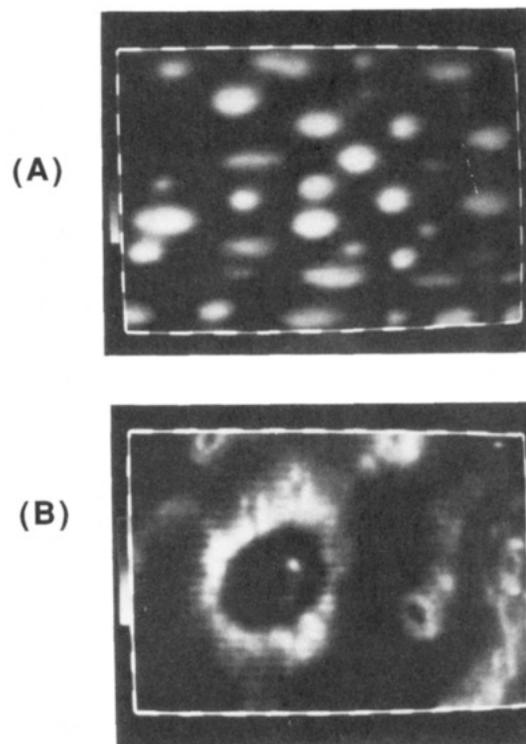
Figure 5. Gray-scaled image of biological substrates in a 20 mM $K_4Fe(CN)_6$ and 0.1 M KCl solution scanned with 1-μm-radius Pt tip: scan area, 188 × 142 μm (white lines around edge: 10 μm). (A) Top surface of grass. (B) Bottom surface of *L. sinense* leaf.

parallel venation pattern characteristic of monocot leaves. An SECM scan over the bottom surface of a *Ligustrum sinense* leaf is shown in Figure 5B. Several open stomata structures are shown in the gray-scale image, since the guard cells (pairs of specialized epidermal cells surrounding each stoma) are swollen and protrude above the surrounding epidermal cells. The scanning tip can also be used to detect electrochemical products generated at a biological substrate. Preliminary studies of the detection of oxygen during illumination of an elodea leaf were carried out in a 10 mM KCl solution saturated with CO_2. Changes in local concentration of substrate-generated oxygen under illumination were detected with a carbon microdisk electrode (radius, 5.5 μm).[15] Chemical identification of zones on a substrate appears to be a potentially important application of SECM. For example, generation of a species at the tip that could react at appropriate sites on the substrate (e.g., those containing an enzyme) or detection at the tip of species generated at the substrate by a suitable perturbation (e.g., a neurotransmitter, under electric or chemical excitation of a nerve) would provide information about site distribution, size, and shape.

The ultimate resolution attainable in SECM characterization is mainly determined by the tip size. The application of mathematical approaches (e.g., a two-dimensional spatial deconvolution) might also be useful in improving resolution. Smaller metal tips surrounded by insulators, such as those described for use in STM for samples immersed in liquids,[19,20] might be useful in SECM. Our best resolution at this time, as shown in

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B

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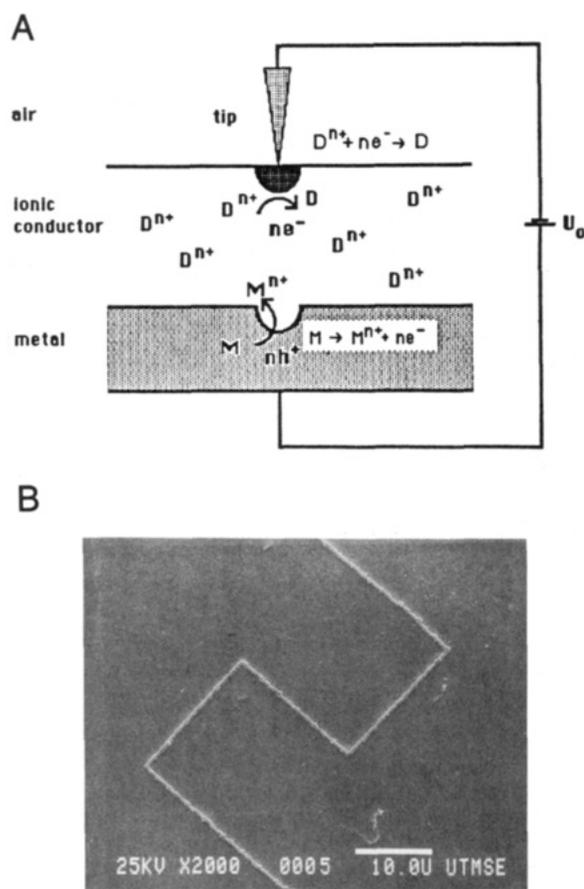
Figure 6. (A) Schematic representation of the SECM operating in the direct mode. (B) Scanning electron micrograph of silver lines deposited in a Nafion film by using the SECM in the direct mode. Tip material, tungsten; bias, 5 V; tip current, 0.5 nA; and scan rate, 900 Å/s.[23] Reprinted with permission form ref 23. Copyright 1989 The Electrochemical Society, Inc.

Figure 4A, is obtained with tips with a 0.1-μm radius.[16] For higher resolution scans it will be necessary to use a constant i_T mode, as is frequently used in STM, where topographic information is obtained from the voltage applied to the z-axis piezoelectric device to maintain a given value of i_T. This mode would only be useful, however, for substrates that do not have both conductive and insulation regions. While it is very unlikely that SECM will ever attain the atomic resolution found with the STM, 100-Å levels should eventually be possible.

Applications of the SECM to Fabrication

The SECM has been used to fabricate microstructures by deposition or etching via two different approaches, i.e., a direct mode and a feedback mode. The direct mode approach is illustrated in Figure 6A. Faradaic current is passed between a tip ultramicroelectrode and a metal substrate electrode. The two electrodes are separated by a thin film made of an ionically conductive polymer such as Nafion or protonated poly(vinylpyridine) (PVP). The current that flows through the film is mainly a function of the area of the tip that touches the film. Since the tip is not insulated, the degree of penetration into the film strongly affects the current and resolution. Thus, the distance between the tip and the substrate electrode, i.e., the extent of penetration into the film, can be maintained constant by monitoring the current. This

is accomplished by using a conventional electronic STM feedback control that controls the magnitude of the current and adjusts the interelectrode spacing accordingly. When a relatively low current (on the order of nanoamperes) is applied, the tip penetrates the film only slightly. When a negative potential is applied to the tip, a reduction reaction takes place at the tip/polymer interface and a complementary process occurs on the substrate, while a positive potential at the tip leads to an electrochemical oxidation at the tip and a reduction process on the substrate.

By this approach, metal deposition, metal etching, and electropolymerization with high resolution have been accomplished.[21-24] Silver, gold, and palladium were electrodeposited at the tip when their ions were present in the ionically conductive polymer and a negative potential was applied to the tip. Silver ions were incorporated into Nafion while gold and palladium ions, i.e., $AuCl_4^-$ or $PdCl_4^{2-}$, were incorporated into protonated PVP. Metal lines were formed on the film by moving the tip electrode in a given pattern across the surface while maintaining a constant current (Figure 6B). Lines as narrow as 0.3 μm were produced by this approach. Changing the polarity of the electrode, i.e., making the tip electrode positive, in the presence of metal ions incorporated in the polymer, resulted in metal deposition on the conductive substrate.

Metal etching, e.g., of copper, was observed when a copper substrate was biased at a positive potential while the tip, which carried out a reduction process, e.g., MV^{2+} reduction, was scanned over the polymer. Because of the electric-field distribution inside of the polymer the electrochemical reactions, such as copper etching and metal deposition, carried out on the substrate were of lower resolution than the corresponding metal deposits at the air/polymer interface. Electropolymerization of protonated aniline with high resolution was accomplished by applying the same approach. Namely, a conductive substrate was spin-coated with Nafion followed by soaking of the sample in protonated aniline solution. Polyaniline was electrodeposited on the substrate/Nafion interface, with hydrogen evolved at the tip/Nafion interface.

The resolution of the microstructures obtained by this approach is determined by several parameters. The most dominant factor is the size and the shape of the tip. The best results obtained so far have been achieved with uninsulated, very sharp, needle-like tips. The current also affects the resolution, because it determines how deeply the tip penetrates into the film and thus the area of contact between tip and film. The resolution is also a function of the speed at which the tip scans across the polymer, since it determines the amount of charge passed per unit area traveled. The maximum speeds were about 0.5 μm/s. The thickness of the film is also important, as the electric-field distribution depends on the distance between the tip and the substrate. Instrument parameters, such as vibrational and thermal stability and the response speed of the feed-

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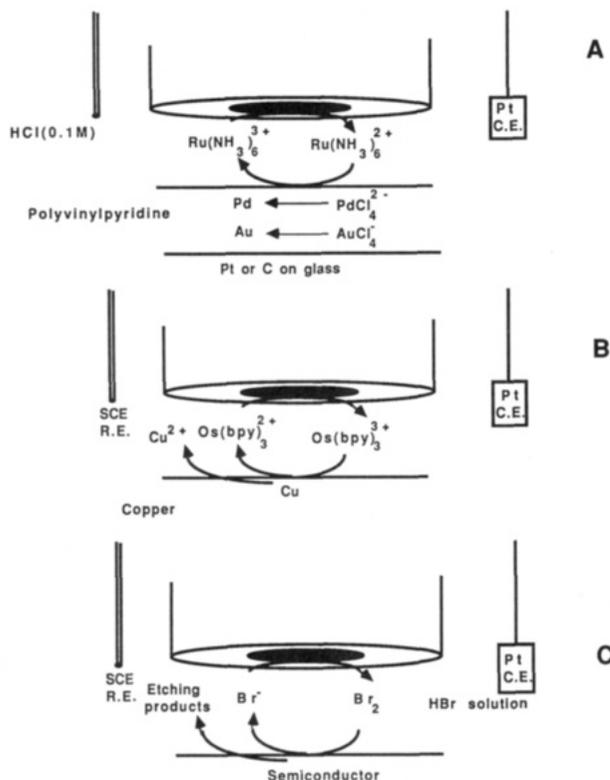
Figure 7. Schematic representation of the SECM applied in the feedback mode for (A) metal deposition, (B) copper etching, and (C) semiconductor etching.

Figure 8. Scanning electron micrograph and the profile of GaAs (Cr doped) etched in three places for 5, 6, and 20 min in a 0.02 M HBr and 0.1 M HCl solution with a 25-μm Pt ultramicroelectrode.[25] Reprinted with permission from ref 25c. Copyright 1990 The Electrochemical Society, Inc.

back device, also affect the resolution. Finally, the electrode reaction chemistry at tip and substrate (e.g., whether gas evolution occurs at the tip) is important.

The feedback mode is schematically illustrated in Figure 7. In this case the substrate is a reactive surface which can irreversibly react with the tip-generated species. The electron transfer that takes place on this surface can drive an electrochemical reaction on the surface, if the net reaction is thermodynamically and kinetically feasible. However, since the electron transfer is localized and is limited by the diffusion of the tip-generated species, high-resolution electrochemical reactions can be carried out. Note that in this approach the generated mediator feedback current serves to control the distance between the tip and the substrate and, in addition, drives the electrochemical processes on the surface.

The feedback mode has been used to deposit metals as well as etch metals and semiconductors.[25] In addition, the SECM was used as an analytical tool to study semiconductor–electrolyte surface processes, such as hole injection.[26] For example, gold and palladium were electrodeposited[25a] in polymer films by reducing $Ru(NH_3)_6^{3+}$ at the tip and allowing the +2 species to diffuse to a protonated PVP in which $AuCl_4^-$ and $PdCl_4^{2-}$ were incorporated (Figure 7A). For high-resolution copper etching, the Cu surface itself was reactive and no polymer coating was needed. A strong oxidant, such as $Os(bpy)_3^{3+}$, was generated at a Pt tip, diffused to the surface, and etched the Cu (Figure 7B). The subsequent dissolution of copper was confirmed by SEM and profilometry measurements.[25b] This feedback

mode of etching has a number of advantages over the direct mode: The etching profile depends upon the diffusion of the tip-generated species rather than the electric field and current distribution between the tip and the substrate. Operating in the feedback mode allows straightforward control of the distance between the ultramicroelectrode and the substrate. Since the tip is held at a positive potential, dissolved copper will not be deposited on it. The substrate surface is not biased directly, but its potential is controlled by the solution species. Therefore, it will not corrode except where the oxidant is produced.

The feedback mode was also successfully applied to the etching of III–V (e.g., GaAs) and II–VI semiconductors.[25c] Bromine electrogenerated at the tip was the etchant (Figure 7C). Etched spots were detected when the electrode was left biased for several minutes above the surface (Figure 8). The nature of the etching process was also studied by using different electrogenerated oxidants, varying the pH, and changing the type of semiconductor, i.e., n-type, p-type, and undoped GaAs.[26] A study of the behavior of the feedback current allowed assignment of the primary process as a hole injection from the oxidized form of the redox couple into the valence band. The energy of the valence band edge in the semiconductor could also be estimated. Moreover, selective etching was found: n-GaAs and undoped GaAs were etched, while p-GaAs was not. This difference can be explained by difference in the field distributions at the solution interface with n-type and p-type material.

Future Prospects

A number of new applications of SECM are under development. The characterization of conductive and

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insulating substrates by measurement of the feedback current really represent two limiting cases where the heterogeneous electron transfer (et) to tip-generated species is either very fast or very slow. However, measurements at finite et rates at the substrate are also possible and lead to steady-state i_T vs d curves that span the region between the limiting cases. Similarly it should be possible to measure the porosity of a nonconductive film coating a conductive substrate. If the tip radius, a, is small compared to the pore size, the actual pore distribution can be determined. Even for pores that are small compared to a, information about the porosity should be obtainable from the i_T vs d curve. SECM studies of polymer films or other types of modified electrode surfaces have been described earlier. It should also be possible to modify the tip electrode, e.g., with an organized monolayer or polymer film, and study et reactions between it and a suitable substrate. Such studies would be related to those carried out in the ultrathin-layer cell[27] but, with proper tip electrode construction, may be somewhat easier to execute.

While most SECM studies involved steady-state currents and studies of substrate properties, measurements of current transients should also be informative, e.g., in determination of diffusion coefficients and rate

constants. Measurement of steady-state and transient currents might also be used to characterize homogeneous reactions of the tip-generated species that occur in the solution gap between the tip and substrate, in a manner analogous to measurements made with the rotating ring-disk electrode.[10,28] These applications await the development of suitable models, probably digital simulation ones.

Finally, many applications to the characterization and modification of insulating and conducting substrates are possible. The ultimate resolution possible with the SECM depends upon our ability to construct scanning tips of a small size of the proper shape. While it is unlikely that the resolution will ever approach that of the STM, improvements to bring SECM to the levels of several tens of nanometers, by reduction in tip size and by employing deconvolution or tomographic-type techniques, should be possible.

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Structure and Mechanism of Action of a Multifunctional Enzyme: Fatty Acid Synthase

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The synthesis of fatty acids is a ubiquitous process in nature. However, a variety of different enzymes catalyze the synthesis, and their structures display considerable variation. In this account, we will be concerned with the fatty acid synthase from chicken liver which primarily produces palmitic acid. In most procaryotes, the synthesis of palmitic acid is carried out

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by seven different and separable monofunctional enzymes and an acyl carrier protein (cf. refs 1 and 2). However, in eucaryotes a multifunctional enzyme is involved that contains the seven enzyme activities. In yeast and other fungi, a multifunctional enzyme of two different types of polypeptides is found $(\alpha_6\beta_6)$,[3] whereas in animals, the enzyme consists of two identical polypeptides (α_2).[1,2] The multifunctional enzymes in animals catalyze a reaction sequence that leads to palmitic acid according to the overall reaction

$$\text{acetyl-CoA} + 7\text{malonyl-CoA} + 14\text{NADPH} + 14\text{H}^+ \rightarrow$$
$$\text{palmitic acid} + 8\text{CoA} + 14\text{NADP}^+ + 6\text{H}_2\text{O} + 7\text{CO}_2 \tag{1}$$
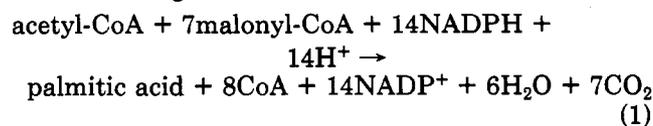
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