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**ELECTROCHEMICAL MODULATION OF THE SAMPLE STREAM
IN MASS SPECTROMETRY**

DISSERTATION

Presented in Partial Fulfillment of the Requirements for
the
Degree Doctor of Philosophy in the Graduate School of The
Ohio State University

By

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1995

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To my parents and brother

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GLOSSARY OF TERMS

A_e	Area
A	Amplitude of steady-state response
C^*	Initial concentration
C	Concentration
D^s	Solution diffusion coefficient
D^m	Membrane diffusion coefficient
E	Potential
F	Faraday
FT	Fourier transfer
f	Fundamental frequency
$i.d$	Inner diameter
i_e	Electrochemical current
$i(s)$	Transformed electrochemical current
I	Flux of species through membrane
K	Partition coefficient
l	Thickness of membrane

-m	Distance between electrode and membrane
MoMS	Modulation mass spectrometry
MS	Mass spectral
n	Number of electrons
O	Electrochemical reactant
o.d.	Outer diameter
PERMS	PERmeable membrane Mass Spectrometry
R	Electrochemical product
s	Laplace variable
t	Time
$t_{1/2}$	Time to reach $I_{m/z} = 1/2 (I_{m/z, \max})$
t_0	Transport time of species
$\underline{U}$	Real part of FT
$\underline{V}$	Imaginary part of FT
ϕ	Phase angle
δ	Thickness of diffusion layer
δ_{ss}	Thickness of diffusion layer at steady-state
τ	Intervals of electrochemical excitation

CHAPTER I

INTRODUCTION

Electrochemistry is a sensitive technique and has proved its value as an analytical method. It is capable of quantitative measurement of analytes in the range from 10^{-2} to 10^{-6} M and can easily be performed on less than ten milliliters of solution. However, electrochemistry provides little information about the structure of products formed in electrochemical reactions. Therefore, electrochemical methods frequently require the support of other techniques. For example, electrochemical measurements have combined with UV-Vis, IR, Raman, NMR, ESR and x-ray techniques to provide chemical information on electrochemical reactions.¹⁻³

UV-Vis offers quantitation in the concentration range from 10^{-8} to 10^{-2} M, but little structural information. IR and Raman provide structural information, but sensitivity and absolute quantitation are poor. ESR detects only species containing unpaired electrons, and NMR is limited to samples with relatively high concentrations ($> 10^{-3}$ M). None of these techniques offers the combination of structural

identification, high sensitivity, and real-time measurement of electroactive species in electrochemical reactions.

Mass spectrometry offers a sensitive and specific method to identify and determine the structure of molecular species participating in electrochemical reactions.⁴⁻¹⁷ The on-line combination of electrochemistry and mass spectrometry (known as EC/MS) offers the capability to directly monitor and detect electrochemical species in complex mixtures. The inherent selectivity and sensitivity of MS allow monitoring and identification of individual species in mixtures that may be too complex for analysis by other on-line methods. However, a problem is often encountered before mass spectral analysis can be carried out on an electrochemical solution: the analyte molecules must be separated from each other and from the solvent matrix, and introduced into the moderate vacuum of the MS source.

Gas and liquid chromatography have been used successfully for the separation of electrochemical species. Gas chromatography/mass spectrometry combined can achieve separation and detection of millimolar quantities of analyte, and they have been used in combination with modern electrochemistry to study many electrochemical reactions.¹⁵⁻¹⁸

Willetts et al. have used GC/MS with polarography to study the electrochemical reduction of 6-iodo-1-phenyl-hexyne and 6-bromo-1-phenyl-hexyne.¹⁸ Brajter-Toth et al. have studied the electrochemical reactions of biologically active compounds, and the electrochemical products were identified by GC/MS.¹⁵⁻¹⁷ However, the sampling required for application of gas chromatography to an electrochemical solution during active electrolysis is extremely difficult. Only a few picomoles of analyte are contained in several nanoliters of solution, which are confined to a layer a few microns thick adjacent to the surface of the electrode.

LC is also well suited for separating the electrochemically active molecules and has been used extensively in the detection of electrochemical species in solution.^{15,17,19-24} Since Blackley and Vestal²⁵ invented a thermospray ionization technique, it has been possible to use mass spectrometry for the direct study of species dissolved in bulk solution. The total LC effluent is vaporized into the ion source of a mass spectrometer with flow rates of several mL/min.

Hambitzer and Heitbaum²⁶ were the first to successfully use a thermospray interface to combine the mass spectrometer

with an on-line electrochemical cell. The experimental setup is illustrated in Figure 1. An appropriate electrochemical cell is directly connected to the thermospray device. The electrolyte is forced by pressure from the working electrode into the heated capillary tube of a thermospray ion source. A Pt wire of 0.05 mm diameter and 600 mm long in the form of a helix is used as a working electrode. Electrooxidation of N,N-dimethylaniline in an aqueous solution was studied by this method.

Brajter-Toth¹³ has also used the thermospray technique to study bioactivation reactions in which the large molecular weight products were nonvolatile. In order to remove solvent, sophisticated pumping systems, the use of high voltages, and heating or nebulization of the sample stream are necessary for injection of LC effluent into the MS source. However loss of analytes is often incurred, and the very small quantities of analyte are near the limit of detection, due to the modest signal-to-background of an MS interfaced to an LC system.

Bartmess et al.²⁷ have described the electrolysis of analytes directly within an MS source vacuum to study the effect of applied potential on the efficiency of formation of

Figure 1. Schematic diagram of the experimental setup for electrochemical thermospray mass spectrometry (Adapted from Hambitzer and Heitbaum, see reference 26).

Figure 1.

gas phase ions for mass analysis. A thin layer of a sample was placed on the probe tip to contact both the ring and disk electrodes, using glycerol as solvent. But this research addressed neither controlled potential/current electrolysis nor quantitation of electrochemical products.

Mass spectral analysis of electrochemical products generated directly with the MS source vacuum has also been described by House et al.⁶. In that study, they addressed the mass spectral identification and quantitative measurement of volatile electrochemical products generated at the rate of a few picomoles per second, and those products were detected in real time. Identification of the products was based on analysis of the resulting mass spectra and quantitation was achieved by measurement of the MS ion-current at a target mass.

House calibrated the mass spectral intensity to moles of product using a calibration factor, $\Theta_{A,B}$, where $Q_A / Q_B =$ moles A. Q_{MS} is the integrated ion current in coulombs; A is the product, and B is the target mass. This calibration method was applied to determine the current efficiency of the production of benzene by the oxidation of benzoate ion at a platinum electrode in poly(ethylene glycol) (PEG).

Generation of electrochemical products within the ion source allows collection of all volatile products, and offers an increased signal-to-noise ratio due to the minimum loss of products. However, the selection of a suitable solvent is difficult. The solvent must possess adequate dielectric constant, analyte solubility and diffusion. The vapor pressure must be low enough to allow electrolysis to occur before evaporation of the solvents, and to prevent interference from solvent ion-currents in some regions of the mass spectrum.

An ideal mass spectrometer introduction system would be simple, rapid, highly selective to analyte, and independent of instrument design. It should also be adaptable to automation for convenient on-line analysis or monitoring. Permeable membrane systems, composed of a thin semi-permeable silicone membrane or micro-porous Teflon membrane, have several of these characteristics.

Membranes have been used as separators in a variety of analytical determinations.²⁸⁻³⁵ The selective nature of membranes has made them particularly suitable for rapid analytical determination or continuous on-line monitoring. The incorporation of membranes into process sampling

analytical instrumentation is gradually becoming more common. Membranes have been used as molecular separators in GC/MS to reduce the amount of helium carrier gas flowing into the analyzer. Llewellyn and Littlejohn³⁶ have used a flat silicone membrane that is selectively permeable to organic molecules over helium.

The use of semi-permeable membranes for sample introduction in mass spectrometry was first described by Hoch and Kok³⁷ in 1963 to study reaction kinetics in aqueous solution during photosynthesis. Since then, a significant amount of research has been conducted using membrane systems to interface environmental air and aqueous samples directly to the MS high-vacuum source. The membrane used in the experiment acts as a selective barrier to polar and ionic species and allows nonpolar volatile compounds and dissolved gases to pass into the mass spectrometer. This method has been given the acronym, MIMS, Membrane Introduction Mass Spectrometer.³⁸ Usually the extraction, concentration, desorption, and analysis of species from a solution matrix can be accomplished in a single step by using a membrane sampling device, providing continuous sample introduction and rapid analysis of solution reactions.

In 1974, Westover et al.³⁹ designed and evaluated hollow fiber probes constructed of different permeable materials for a mass-spectrometric sampling device. The membrane was the direct interface between the sample and analyzer, with the inside of the hollow fiber exposed to the MS vacuum and the outer surface exposed to the sample. Among probes made of different materials, the silicone rubber probe was the most useful because of its unique property to reject water and most atmospheric gases, and its very high permeability to a wide range of volatile organic compounds.

The membrane selective introduction of volatile organic compounds has made MIMS with silicone membranes a popular technique for the on-line monitoring of biological and environmental samples. Application to the monitoring of bioprocess solutions^{30,40,41} and environmental samples⁴²⁻⁴⁴ have been pursued vigorously. The most important advantage of MIMS for identification and quantitation of organic compounds from aqueous solution is that the analytes can be measured directly at parts-per-billion levels without any preconcentration or derivatization steps.⁴⁴ It also offers the capability for multicomponent analysis, typically shows rapid response times, and requires minimal operator intervention. MIMS has also been applied for analysis of

photochemical systems,⁴⁵ physiological studies,^{46,47} industrial fermentation monitoring and controlling,⁴⁸⁻⁵⁰ and monitoring reaction kinetics.⁵¹⁻⁵³

MIMS is a valuable technique to directly study electrochemical reactions since it allows continuous fluid introduction, makes rapid analysis of solution reactions possible in real time, and also allows directly monitoring of electrochemical species as a function of electrode potential with high selectivity for individual components.

Bruckenstein et al.⁵⁴⁻⁵⁶ first described direct couplings of electrochemistry and mass spectrometry by using a porous platinum electrode contacting a porous Teflon membrane (Figure 2a). Volatile electrochemical products effuse through the Teflon membrane and enter the ion source. This method allows *in situ* qualitative and quantitative analysis of volatile intermediates and products formed during electrochemical reactions. They studied several electrochemical reactions involving gaseous products/reactants in aqueous solution. For example, reduction of NO_2^- in HClO_4 , oxidation of methoxyphenols and hydrazines, and electrochemical behaviors of adsorbed carbon monoxide have been studied. The calibration was achieved by

injection of known amounts of products into the source vacuum. This method required additional experiments to account for the inefficiencies of diffusional capture of the electrolysis products by the membrane.

A semi-permeable silicone rubber membrane, as a mass spectrometer sampling device, was used by Pinnick *et al.*⁵⁷ to study the reduction of dibromocyclohexene to cyclohexane in HMPA. In this study, a thin silicone rubber membrane, in intimate contact with a gold-minigrid electrode, extracted electroactive species from within the diffusion layer (Figure 2b). The silicone membrane allows apolar electroactive species to partition into it and diffuse through, and enter the source vacuum of the mass spectrometer.

Partition into the membrane is controlled by the products of the vapor pressure of the analyte and their solubility in the membrane phase. This method is called PERmeable membrane Mass Spectrometry (PERMS).

Brockman⁵⁸ used PERMS to study carboxylate oxidation in water and dimethylsulfoxide solvents. Deconvolution of the mass spectral data was achieved by factor analysis, and current efficiencies of product formation were estimated. However, the PERMS method was applied to analysis of

Figure 2. (a) Schematic diagram of a Teflon porous electrode (see reference 54); (b) Schematic diagram of a silicone membrane probe (see reference 57).

Figure 2.

electrochemical species under conditions where product analysis has been reported in literature.

By using the same technique, Szpylka⁵⁹ studied the products of the oxidation of the acetate ion and the anions derived from 4-oxopentanoic and 2-oxopentanoic acids. In his study, he described $\pm 0.5\%$ quantitation by comparison of the MS ion-current at m/z 32 and 44 to constant current electrolysis of water in 0.1 M NaHCO_3 /0.1 M KNO_3 solution, producing O_2 and CO_2 . Quantitation of CO_2 and O_2 produced from aqueous Kolbe reactions were reported.

Szpylka also developed a new technique to improve signal-to-background of the PERMS experiment particularly at low analyte concentrations. Using Modulation Mass Spectrometry (MoMS), he identified electrochemically coupled species which were not observed by the PERMS experiment alone.⁵⁹ In the MoMS technique, a periodically changing electrochemical current is applied to an electrode attached to a silicone rubber membrane, thus periodically changing the concentration of permeable species in the solution adjacent to the sampling membrane. The flux of molecules released into the MS source is thus modulated at the frequency of the electrochemical current applied. The electrochemically

modulated ion-currents can be distinguished from background by Fourier Transformation (FT) and separated from the ion-currents produced by constant levels of solvent or electrolyte. However, Szpylka did not describe the theory behind the MoMS process or the methods necessary to separate mixed-mass-spectra obtained from a mixture of membrane permeable analytes.

Since molecules which permeate the membrane are detected as parent and fragment ions in a mass spectrometer, chemical analysis of a mixture presents many problems. Therefore, our major goal of this study was to develop a general method to separate and identify a mixture of apolar molecules in polar media using modulation of the flow of molecules through a membrane sampling device.

Because different molecules diffuse through a silicone membrane at different rates, based on their molecular size, a measurement of the time required for diffusion through the membrane has many of the analytical properties of the retention time in chromatography. Delay times can be measured as a function of the phase shift observed experimentally between the periodic variation of the MS response and the modulating event at the external surface of

the semipermeable membrane. Thus, the second goal of this research was to study effects of periodic changes induced in the concentration of analytes bathing the outside surface of the membrane. The flux of each molecule through the membrane was modulated at the frequency of change in concentration induced at the membrane surface. Diffusional delay induced by the membrane uniquely shifts the phase of each particular analyte, unequivocally identifying it and its impact fragments in the mixed-mass-spectrum. FT correlation between the modulated flux and a periodic excitation recovers the amplitude and phase for each analyte signal.

The third goal of this investigation was to obtain a theoretical solution for mass transport through membrane. There are three steps for the permeation of a substance through a membrane: (1) partitioning of the substance into the membrane at its external surface, (2) diffusion of the substance through the membrane, and (3) transport of the substance from the interior surface of the membrane into the MS vacuum. Quantitative solution of the boundary value problem describing frequency dependent steady-state diffusion through the membrane was solved using Fick's laws and the Laplace transform. The method was tested against model

analytes whose concentrations were modulated electrochemically. Finally, we verified that as a result of the coupling of electrochemistry with mass spectrometry, an interpretation of mass spectra of Kolbe reactions is possible.

CHAPTER II

THEORY

Permeable Membrane Mass Spectrometry (PERMS)

Permeable membrane mass spectrometry, PERMS, employs a thin silicon-rubber membrane in intimate contact with a gold-minigrid electrode as a means to separate volatile species directly from the electrochemical solution matrix, and the membrane-permeable species are introduced into the source vacuum of the mass spectrometer (Figure 3).^{57,58} Under steady-state conditions, mass spectral ion-currents are directly proportional to the concentrations of the corresponding species in the solution contacting the membrane surface. The mass transport process of electroactive species into the solution and membrane involves the series of steps illustrated in Figure 4.

A complete solution of the mathematical problem describing mass transport of analyte to the electrode, from the electrode to the membrane, and through the membrane to the MS source has not been attempted. But semi-quantitative description of this complex mass transport system is

Figure 3. Schematic diagram of the geometry of the electrode/solution/membrane interfaces during generation of product, R.

Figure 3.

Figure 4. Mass transport steps for PERMS experiment
(see reference 58).

Figure 4.

possible by invoking several plausible assumptions.^{60,61}

In this research, we used these assumptions with some modification to derive a time-dependent relationship between the MS ion-current and the electrochemical current for a PERMS experiment. This new methodology has been given the acronym, MoMS, for Modulation Mass Spectrometry.

Mass Transport Problems in EC/MS

1. Mass transport to the solution

For an electrochemical oxidation,

the electrode surface concentration of each product, O_k , $[O_k]_{e,s}$ is related to the electrochemical current, i_e , as predicted by Nernst diffusion theory:

$$i_e = \frac{nFA_e D_{k,s}}{\delta(t)} \left(\frac{[O_k]_{e,s}}{a_k} \right) \quad (2)$$

Where n is the membrane of electrons transferred, F is

Faraday constant, A_e is the electrode surface area (cm^2), $D_{k,s}$ is the solution diffusion coefficient (cm^2/s) of species k , and $\delta(t)$ is the thickness of the diffusion layer (cm).

The electrochemical species at the minigrid electrode surface are transported by diffusion into the solution, into the holes between the wires of the minigrid, and enter the vacuum of MS source.

The gold minigrid electrode shown in Figure 11 is not a strictly planar surface. Instead it consists of a fine gold foil in which a highly regular pattern of square holes has been etched (1000 lines/in). The problem of mass transport at this kind of surface has been addressed by Murray^{60,61} and Brockman.⁵⁸ They have discussed that the linear diffusion theory is suitable if the diffusion layer thickness of the analyte in the solution phase, δ_{ss} , is large compare to the hole dimension of the minigrid electrode. Therefore, the aqueous solution bathing the membrane at $x = 0$ becomes virtually homogeneous in the y - and z -directions. In this study, the physical dimension of the minigrid mesh (9.92 μm wire width and 23.98 μm hole size) used in experiments is met this condition for electrolysis time longer than about 0.2 s.

Figure 5. Schematic diagram of electrolysis shown in a one-dimensional, equivalent geometry; and mass transport in a membrane/electrode system situated between the solution and the MS-source vacuum. (a) Species O undergoing reduction; (b) Species R, produced by the electrolysis.

Figure 5.

So it is possible to transform the two dimensional geometry in Figure 3 to an equivalent, one-dimensional form shown in Figure 5, where the electrode grid is positioned a short distance, $-m$, away from the membrane surface. Mass transport is sufficiently rapid in the region $-m < x < 0$ and the concentrations are virtually constant throughout.

2. Mass transport to the membrane

The permeation process of species includes several steps: (1) selective partition of the species into the membrane, (2) selective diffusion of the species through the thickness (ℓ) of the membrane, and (3) transport from the inner surface of the membrane into the MS vacuum source. Each step depends on the molecular properties of the analyte and the membrane material.

At the solution/membrane interface, $x = 0$, partition processes are at equilibrium and the equilibrium is assumed to be established quickly relative to mass transport of the species through the membrane. This assumption is analogous to rapid equilibrium assumed in chromatographic systems. The partition coefficient at $x = 0$ is:

$$K = \frac{C^s(0,t)}{C^m(0,t)} \quad (3)$$

where $C^s(0,t)$ is concentration of the analyte at the surface on the solution side and $C^m(0,t)$ is concentration on the membrane side.

Mass transport through the membrane is assumed to be the rate determining process. Transport in the solution ($x < 0$) and in the source vacuum ($x > l$) are sufficiently rapid, and concentrations at the outside surfaces of the membrane are at virtual steady-state. Partitioning at the outer surface and desorption from the inner surface of the membrane are also considered instantaneous.^{58,59}

If diffusion through the solution adjacent to the membrane meets the assumption of Murray et al. (a pseudo-planar condition),^{60,61} then mass transport within the membrane also can be treated as a one dimensional diffusion process.

Using above assumption, Fick's second law that describes mass transport through the membrane can be solved exactly for several useful boundary-value problems. We assume here a simple electrochemical reaction:

in which both oxidizing species (O) and reducing species (R) are soluble in the solution phase. Only O is present initially at a concentration C_o^* . Figure 5 shows a steady-state initial condition where O and R bathe the outside surface of the membrane, create linear concentration gradients through the membrane itself, and are swept into the source for continuous MS analysis. At time $t = 0$, a current, $i(t)$, is applied to the minigrid electrode, depleting the concentration of O and enhancing the concentration of R at the surface. This perturbation propagates a change in flux of O and R into the source of the mass spectrometer. Diffusional mass transport of O and R through the membrane is described by the following equations.

(1) In the solution: ($x < -m$)

$$\frac{\partial C_R(x, t)}{\partial t} = D_R^s \left(\frac{\partial^2 C_R(x, t)}{\partial x^2} \right) \quad (5a)$$

$$C_R^s(x, 0) = 0 \quad (6a)$$

$$D_R^s \left(\frac{\partial C_R(x, t)}{\partial x} \right)_{x=-m} = \frac{i(t)}{nFA} \quad (7a)$$

$$\frac{\partial C_O(x, t)}{\partial t} = D_O^s \left(\frac{\partial^2 C_O(x, t)}{\partial x^2} \right) \quad (5b)$$

$$C_O^s(x, 0) = C_o^* \quad (6b)$$

$$D_O^s \left(\frac{\partial C_O(x, t)}{\partial x} \right)_{x=-m} = - \left(\frac{i(t)}{nFA} - \frac{D_O^m C_o^* K}{l} \right) \quad (7b)$$

where $\underline{D}_R^s$ and $\underline{D}_O^s$ are diffusion coefficients of R and O respectively in the solution phase. ℓ is thickness of membrane.

(2) At the solution/membrane interface: ($-\underline{m} < x < 0$)

There are two equilibria. The first one is partition process of O and R in the solution and membrane, and the second one is flux equilibrium at outer and inner membrane.

$$K_R = \frac{C_R^m(+0, t)}{C_R^s(-0, t)} \quad (8a)$$

$$K_O = \frac{C_O^m(+0, t)}{C_O^s(-0, t)} \quad (8b)$$

$$-D_R^s \left(\frac{\partial C_R(x, t)}{\partial x} \right)_{x=0} = D_R^m \left(\frac{\partial C_R(x, t)}{\partial x} \right)_{x=0} \quad (9a)$$

$$D_O^s \left(\frac{\partial C_O(x, t)}{\partial x} \right)_{x=0} = -D_O^m \left(\frac{\partial C_O(x, t)}{\partial x} \right)_{x=0} \quad (9b)$$

where $\underline{D}_R^m$ and $\underline{D}_O^m$ are diffusion coefficients of R and O respectively in the membrane. $x = \pm 0$ means species are on the membrane and solution sides of interface respectively.

(3) In the membrane: ($0 < x < \ell$)

In a membrane of thickness ℓ , surface concentrations of species, $\underline{C}^m(0, t)$ and $\underline{C}^m(\ell, t)$, at $x = 0$ and $x = \ell$ remain constant. The steady-state concentration at each point

within the membrane is also a constant.

$$\frac{\partial C_R(x,t)}{\partial t} = D_R^m \left(\frac{\partial^2 C_R(x,t)}{\partial x^2} \right) \quad (10a)$$

$$C_R^m(x,t) = 0 \quad (11a)$$

$$C_R^m(l,t) = 0 \quad (12a)$$

$$\frac{\partial C_O(x,t)}{\partial t} = D_O^m \left(\frac{\partial^2 C_O(x,t)}{\partial x^2} \right) \quad (10b)$$

$$C_O^m(x,t) = (1-x/l)KC_O^* \quad (11b)$$

$$C_O^m(l,t) = 0 \quad (12b)$$

These boundary value problems in $C_R(x,t)$ and $C_O(x,t)$ can be solved by Laplace transform methods. Analytically, the fluxes of the species O and R at $x = l$, the interior (evacuated) surface of the membrane, are proportional to the MS ion-current for the parent and fragment ions of these species. The expressions of flux of O and R inside Laplace transforms are following:

$$\bar{I}_R = D_R^m \left[\frac{d\bar{C}_R(x,s)}{dx} \right]_{x=l} = \frac{2\bar{i}(s)}{nFA \left[\exp\left(\frac{sl^2}{D_R^m}\right)^{\frac{1}{2}} + \exp\left(\frac{sl^2}{D_R^m}\right)^{\frac{1}{2}} \right]} \quad (13)$$

$$\bar{I}_O = D_O^m \left[\frac{d\bar{C}_O(x,s)}{dx} \right]_{x=l} = \frac{2\bar{i}(s)}{nFA \left[\exp\left(\frac{sl^2}{D_O^m}\right)^{\frac{1}{2}} + \exp\left(\frac{sl^2}{D_O^m}\right)^{\frac{1}{2}} \right]} \quad (14)$$

$$\text{where } \Delta \bar{C}_0(x, s) = \bar{C}_0(x, s) - \left[\frac{(1-x/l) KC_0^*}{s} \right],$$

In eqs 13 and 14, I_R and I_0 are the Laplace transform mass spectral ion-currents for reduced and oxidized species respectively. The Laplace variable, s , indicates that the expression is inside the Laplace transforms. We also assumed the diffusion coefficient constants in membrane are much greater than in solution for both R and O. In eqs 13 and 14, $i(s)$ is the transformed electrochemical excitation current that may be any function of time, such as a potential step or a sinusoid. In the cases discussed here, $i(t)$ results either from a potential or a current step. Once the function of $i(s)$ has been decided, the relationship between the surface concentration of analyte species and the electrochemical excitation function $i(t)$ can be found by taking inverse Laplace transform.

A particularly useful current function for this study is the periodic square wave, shown in Figure 6, because it can be experimentally achieved by simply turning a current on and off. In the first half the square wave excitation cycle, reductive electrolysis decreases the concentration of O at

Figure 6. Schematic of periodic current excitation function and an MS ion-current response of product.

Figure 6.

the membrane surface and simultaneously increases the concentration of R. In the second half of the cycle, the current is turned off (not reversed, but simply brought to zero), O is replenished at the membrane surface by diffusion from the bulk solution, and R is depleted by diffusion into the solution and into the membrane. After several cycles, the MS response reaches a virtual steady-state, with a dominant signal at the frequency of the electrochemical excitation (Figure 6).

The mathematical expression of this excitation function can be represented by Fourier expansion as an infinite sum of harmonic sinusoids of the fundamental frequency, $f = 1/\tau$, where τ is intervals of square-wave.⁶²

$$i(t) = \frac{1}{2} + \frac{4}{\pi} \sum_{n=1,3,\dots} \left[\frac{1}{n} \sin\left(\frac{2n\pi t}{\tau}\right) \right] \quad (15)$$

The expression of eq 15 inside Laplace transforms is:

$$i(s) = \frac{1}{2s} + \frac{4}{\pi} \sum_{n=1,3,\dots} \left[\frac{1}{n} \left(\frac{f}{s^2 + (2n\pi f)^2} \right) \right] \quad (16)$$

The final ion-current response, eqs. 13 and 14, will be a constant background plus a sum of sinusoidal currents containing all the harmonics of the driving square-wave frequency. Because the intervening membrane has a system function that attenuates the responses at higher frequencies, the time-varying portion of the measured ion-current will be dominated by the fundamental (Figure 7). If the fundamental is chosen, so that $f = 1/(\ell^2/D^m)$, the time constant for analyte transport through the membrane (about 10 to 20 s), then the magnitude of the response signal will be relatively large.

Modulation Mass Spectrometry (MoMS)

During a MoMS experiment, a periodic square-wave current/potential is imposed at the electrode attached to a permeable membrane. The concentrations of both reactants and products of the electrode reaction thus vary with the same periodicity as the applied electrochemical excitation at fundamental frequency. Apolar molecules, coupled to the electrochemical current, permeate through the membrane, and enter the mass spectrometer. The corresponding ion-currents attenuate into a sinusoidal signal with fundamental

Figure 7. Schematic diagram of Fourier expansion of square wave and response after passing through the membrane. Diagram shows attenuation of higher frequencies and little change at lower frequencies.

Figure 7.

frequency. So I_0 and I_R will be modulated at the square-wave frequency by the electrochemical process (see Figure 16).

A modulated MS ion-current, measured at a particular m/z ratio in the mass spectrum, indicates that the electrochemical process modifies the concentration of that species. That species may be a parent or fragment ion at that m/z ratio. Quantitative evaluation of the modulated MS ion-currents can differentiate electrochemical reactants from products.

Fourier transform of the total ion current can separate the signals of reactants and product ions from high frequency white noise and from high background.⁵⁹ The phase and amplitude of the modulated steady-state MS response can be calculated by the real and imaginary parts of the FT signals.

Phase Shift and Transport Time

For a time-domain function:

$$B(t) = \cos(2\pi ft) = \cos(\omega t) \quad (17)$$

where f is fundamental frequency, t is time. If the time-domain signal is delayed by t_0 (Figure 6), the function will

be:⁶³

$$B(t-t_0) = \cos[2\pi f(t-t_0)] = \cos(\omega t - \phi) \quad (18)$$

the corresponding phase shift, $\phi(\omega t_0)$, would be determined by:

$$\phi(\omega) = \omega t_0 + \arctan \left(\frac{\text{Im}[F(\omega)]}{\text{Re}[F(\omega)]} \right) \quad (19)$$

The amplitude of the FT signal at $\underline{f}$ and a particular $\underline{m/z}$ is:

$$A_{m/e} = \sqrt{(\text{Im}[F(\omega)])^2 + (\text{Re}[F(\omega)])^2} \quad (20)$$

where $\text{Re}[F(\omega)]$ and $\text{Im}[F(\omega)]$ are the amplitudes of the real and imaginary parts of the complex FT of a time delayed sinusoid of frequency, $\underline{f}$. (see Figure 17).

In general, the observed phase angle, ϕ_{tot} , between the MS ion-current and electrochemical excitation is composed of two parts:

$$\phi_{\text{tot}} = \phi_{\text{fund}} + \phi_{\text{diff}} \quad (21)$$

The ion-current response leads or lags the electrochemical excitation for two principle reasons. First, it depends on whether the molecule detected by the mass spectrometer is a reactant or a product of the electrochemical excitation. The phase difference (ϕ_{fund}) of MS ion-currents between a reactant and a product should be 180° in the simple cases (Figure 8). If the molecule detected by the mass spectrometer is a reactant, ϕ_{fund} equals 0° (in phase with the excitation). If it is a product, ϕ_{fund} equals 180° (out-of-phase with the electrochemical excitation).

Second, slow mass transport of species through the membrane also contributes to the phase difference (ϕ_{diff}) (Figure 9). Different species have different transport rates through the silicone permeable membrane, depending on differences in molecules size, volatility, polarity, and solubility. So ϕ_{diff} is characteristic of species and describes how the response is affected by the rate of transport of the analyte through the membrane. Its value is

Figure 8. Schematic of MS responses to an electrolysis process. The reactant and product of the electrochemical reaction are 180° out of phase with each other.

Figure 8.

Figure 9. Schematic diagram of diffusional mass transport through membrane delays responses by t_0 . Fast (dot line) and slow (solid line) mass transport through the membrane.

Figure 9.

a measure of the identity of the diffusing species responsible for that particular MS ion-current. There are also other factors which may cause phase different, such as a nonlinear process. In this study, we assume that they are insignificant.

Phase angles of the MS ion-current responses for a reactant and a product would be calculated by equation 19. It is very difficult to obtain the inverse transform from eqs 13 and 14 at the first few ion-current response cycles (the transient region)(see Figure 6). But after the signal reaches steady-state, it is particularly simple to derive the amplitude and phase expressions of the ion-current response from the solution inside the Laplace transform.

If a sinusoid is used as an excitation function to a linear system, the steady-state response is also a sinusoid with a frequency equal to the frequency of the excitation. The steady-state amplitude and phase of the response can be found directly from the Laplace transformed system function by replacing the Laplace parameter, s , with $j\omega$ in the transformed systems function (eqs 13 and 14) where $j=(-1)^{1/2}$, and $\omega = 2\pi f$ which is the angular frequency of the sinusoidal excitation.⁶⁴

Since a square-wave consists of a simple sum of harmonic sinusoids, steady-state MS ion-current responses are also simple sums of the response at each frequency. For simplicity, the following derivation is done for the fundamental frequency only. But the derivation is generally applicable to each of the harmonic components of a Fourier expansion of any driving function.

When s is replaced by $j\omega$ in a systems function, the resulting function of ω may be rearranged into a complex variable of the form, $U + jV$. The phase and amplitude of the steady-state response can be calculated by:

$$\tan(\phi) = \tan \frac{V}{U} \quad (22)$$

$$Amplitude = \sqrt{V^2 + U^2} \quad (23)$$

In general, when a linear system is excited by an external source, the resulting response will be:

(Response transform) = (Excitation transform) $\times$ (System transform)

where the excitation and system transform are mutually independent. According to equation 13 and 14, the $\underline{i}(\underline{s})$ is the excitation transform and the system transform functions of R and O are:

$$\text{System transform}(R) = \frac{2}{nFA \left[\exp\left(\frac{st^2}{D_R^m}\right)^{\frac{1}{2}} + \exp\left(-\frac{st^2}{D_R^m}\right)^{\frac{1}{2}} \right]} \quad (24)$$

$$\text{System transform}(O) = \frac{2}{nFA \left[\exp\left(\frac{st^2}{D_o^m}\right)^{\frac{1}{2}} + \exp\left(-\frac{st^2}{D_o^m}\right)^{\frac{1}{2}} \right]} \quad (25)$$

The final steady-state solutions for the fluxes of O and R (eq 4) from the inside surface of the membrane are:

$$I_R = \left[\frac{\cos\left(\frac{\pi f t^2}{D_R^m}\right)^{\frac{1}{2}} \cosh\left(\frac{\pi f t^2}{D_R^m}\right)^{\frac{1}{2}}}{nFAG} \right] - j \left[\frac{\sin\left(\frac{\pi f t^2}{D_R^m}\right)^{\frac{1}{2}} \sinh\left(\frac{\pi f t^2}{D_R^m}\right)^{\frac{1}{2}}}{nFAG} \right] \quad (26)$$

$$I_o = \left[\frac{\cos\left(\frac{\pi f t^2}{D_o^m}\right)^{\frac{1}{2}} \cosh\left(\frac{\pi f t^2}{D_o^m}\right)^{\frac{1}{2}}}{nFAG} \right] + j \left[\frac{\sin\left(\frac{\pi f t^2}{D_o^m}\right)^{\frac{1}{2}} \sinh\left(\frac{\pi f t^2}{D_o^m}\right)^{\frac{1}{2}}}{nFAG} \right] \quad (27)$$

$$\text{Where } G = \left[\cos\left(\frac{\pi f \ell^2}{D^m}\right)^{\frac{1}{2}} \cosh\left(\frac{\pi f \ell^2}{D^m}\right)^{\frac{1}{2}} \right]^2 + \left[\sin\left(\frac{\pi f \ell^2}{D^m}\right)^{\frac{1}{2}} \sinh\left(\frac{\pi f \ell^2}{D^m}\right)^{\frac{1}{2}} \right]^2.$$

Eqs 26 and 27 indicate that the expressions for the fluxes of species O and R are identical, except that the sign of $\underline{U}$ is positive for R (product) and negative for O (reactant); whereas the sign of $\underline{V}$ is negative for R and positive for O. Because the processes of taking the ratio in eq 22 and of squaring in eq 23 both remove any distinctions of sign in $\underline{U}$ and $\underline{V}$, the phase and amplitude expressions are ambiguous between reactant and product.

The phase of the MS ion-current for the oxidized species (proportional to the flux of O escaping from the inside surface of the membrane) is:

$$\tan(\phi) = \tan\left(\left(\frac{\pi f \ell^2}{D_o^m}\right)^{\frac{1}{2}}\right) \tanh\left(\left(\frac{\pi f \ell^2}{D_o^m}\right)^{\frac{1}{2}}\right) \quad (28)$$

and its amplitude is:

$$A = \left(\frac{\left[\cos\left(\frac{\pi f \ell^2}{D_o^m}\right)^{\frac{1}{2}} \cosh\left(\frac{\pi f \ell^2}{D_o^m}\right)^{\frac{1}{2}} \right]^2 + \left[\sin\left(\frac{\pi f \ell^2}{D_o^m}\right)^{\frac{1}{2}} \sinh\left(\frac{\pi f \ell^2}{D_o^m}\right)^{\frac{1}{2}} \right]^2}{nFAG^2} \right)^{\frac{1}{2}} \quad (29)$$

Figure 10 shows a plot of eq 28 for arbitrary values of $\ell = 150 \text{ }\mu\text{m}$, and $D = 1 \times 10^{-5} \text{ cm}^2/\text{s}$. As ϕ approaches $\pi D/4\ell^2$, the phase angle approaches $\pi/2$ radians or 90° , and $\tan(\phi)$ approaches infinity. Thus eq 28 predicts periodic singularities in $\tan(\phi)$ as the experimental square-wave frequency is varied from zero to infinity.

If a reactant and a product (such as O and R) have identical diffusion coefficients and are transmitted through a membrane of the same thickness, ℓ , then their phase angles will differ by π -radians (180°). A phase angle spectrum, like the one in Figure 10, will be identical whether the angle is in the first quadrant (species O) or the third quadrant (species R). But the quadrant can be determined unequivocally from the signs of the real and imaginary parts of eq 26 and 27.

On the other hand, if two species are known to be products of the electrochemical reaction (such as an alkane and carbon dioxide in the Kolbe oxidation of carboxylate ions), and they are transmitted through the same membrane (identical ℓ -values), then the frequency at which a singularity in $\tan(\phi)$ occurs will be determined by the D -

Figure 10. Tangent of the phase angle vs. frequency at an arbitrary value $\ell^2/D = 22.5$ s.

Figure 10.

value alone. Products with different D -values are separated on the 150 μm long silicone rubber column, and each is identified by its singularity in the $\tan(\phi)$ spectrum.

Further, if the modulated ion-currents at several values of m/z are analyzed for their $\tan(\phi)$ singularities, those values of m/z attributable to the same diffusing species (say an MS parent, R^+ and its fragment ions) will show identical phase-angle spectra, thus identifying them as derived from the same membrane-diffusing species, R .

Of course noise, background, phase angle ambiguities and other problems may complicate analysis of real data by this scheme.

Anyhow, routine mathematical formalisms are available for calculation of $\tan(\phi)$ and A from data such as that in Figure 16.^{63,65} We describe here, how Fourier transformation of such data can recover the signal from the noise and background, measure the amplitude and phase of the recovered signal, and distinguish phase shifts due to mass transport from those due to the mechanism of the electrochemical reaction. The data demonstrate the feasibility of this new method to deconvolute mixed-mass-spectra from PERMS experiments.

CHAPTER III

EXPERIMENTAL

Membrane/Electrode Construction

In this research, a membrane/electrode probe forms the interface between an electrochemical cell and the mass spectrometer. It was designed using the following criteria:

(1) The probe must provide the desired intimated contact between the gold minigrid electrode and the semipermeable silicone rubber membrane to analyze species present in the solution.

(2) The electrode must be porous and thin enough to admit products and reactants to the membrane surface.

(3) The membrane must be sufficiently strong to support a one atmosphere pressure difference between the electrochemical solution and the source vacuum of the mass spectrometer.

(4) The probe must connect directly to the source vacuum of the mass spectrometer and be easily replaceable.

(5) The tip of the probe must be immersible in various solvents.

The membrane/electrode probe, shown in Figure 11, was a modification of previous designs.^{57,58} The probe body consisted of a 20 cm piece of Pyrex tubing (5 mm o.d./3.0 mm i.d.) which was ring sealed to a $\frac{1}{4}$ " 14/35 Pyrex male joint. The tip of the probe was bent 180° to allow bubbles formed during electrolysis to escape easily. A fine gold wire (Materials Research Corporation, Orangeburg, N.J.) was fed through two small holes as shown, and secured with Torr Seal epoxy (Varian, Lexington, MA). The 5 cm stainless-steel tubing (3 mm o.d./2 mm i.d.) was silver-soldered into a copper cylinder, drilled to the specifications required. This stainless-steel tube allows attachment of the probe, with standard fittings, to the inlet of the mass spectrometer. The proximal end of the glass probe was inserted into the copper cylinder, sealed with Torr Seal epoxy, and cured overnight.

The electrode/membrane was assembled on the previously prepared probe body. A small piece of stainless-steel screen (75 wires/in.) was placed over the open end of the glass tube to support the membrane. A 7 mm² section of silicone rubber membrane (100 μ m thick, nominal, Membrane Products, Troy, NY) was soaked in a 50/50 (v/v) solution of toluene and silicone

Figure 11. Silicone membrane probe used to sample solution for mass spectral studies of electrochemical reactants and products. (a) Silicone rubber membrane; (b) Gold minigrid electrode; (c) Stainless steel mesh support; (d) Gold contact wire; (e) Stainless tubing; (f) Copper cylinder; (g) Glass tubing.

Figure 11.

rubber cement (Borden, Columbus, OH) for 5 min, and then placed flat on the surface of a clean Teflon block. Excess cement/toluene was squeezed off with the side of a disposable Pasteur pipette. The tacky membrane was lifted from the Teflon surface and placed onto the stainless-steel screen covering the probe tip. Any portion of membrane protruding over the edge of the glass tube was carefully pulled down around the probe with a glass rod.

The electrode consisted of gold minigrid (1000 line/in, Buckbee-Mears, Minneapolis, MN). A 5 mm² section of this gold minigrid electrode was carefully placed on the tacky membrane and a slight vacuum was applied for 10 s, to draw the gold minigrid firmly into contact with the membrane. The gold wire was attached to a corner of the minigrid with a small amount of silver epoxy (Tra-Con Inc, Medford, MA) and allowed to set overnight.

The completed probe tip was vacuum sealed at the membrane edges with additional silicone rubber cement, being careful not to coat the active electrode surface. Then a rough vacuum was applied to the inside the probe to draw the membrane firmly onto the supporting screen. After 20 min, if the pump noise did not cease, more silicone rubber cement was

applied. When the seal was satisfied, the silicone cement was allowed to cure overnight before use. Electrical contact of the wire to the minigrid was checked with an ohmmeter, and the resistance should be less than 1 ohm.

Before the probe was attached to the mass spectrometer, it was tested for leakage by immersing the tip of the probe into distilled water and applying a rough vacuum to the inside of the probe. If water was observed entering the probe, the probe tip was dried with a tissue, another layer of silicone rubber cement was applied, allowed to cure overnight, and the probe checked again for leakage as described above. If leaks were still present, the probe was disassembled completely.

A further check of probe suitability was made by attaching the probe to the mass spectrometer by a detachable fitting⁵⁹ as shown in Figure 12. A pressure, measured at the mass spectrometer's ion gauge, in range of 10^{-7} to 10^{-6} Pa suggested a well-sealed probe. If the pressure was higher than 10^{-6} Pa, the probe was dismantled. Intimate physical contact between the minigrid electrode and the membrane was tested in follows. The probe was attached to the mass spectrometer, oxygen and carbon dioxide were generated

Figure 12. Schematic drawing of the probe/mass spectrometer connection assemble. (a) EC/MoMS probe; (b) Fitting cap; (c) Stainless-steel ferrule; (d) Rubber O-ring; (e) Stainless-steel tube; (f) Thermometer; (g) Heating tape; (h) On-off valve; (i) Copper gasket.

Figure 12.

electrochemically by applying a 15 μA anodic current to the gold electrode immersed in 0.1 M NaHCO_3 /0.1 M KNO_3 solution. The reactions that occur are:

Before electrolysis, the solution was degassed for several minutes with argon to reduce the background of atmospheric oxygen and carbon dioxide, and an argon blanket was maintained over the solution during the electrolysis. For a properly constructed probe, as soon as the current was turned on, the MS ion-current rose quickly and a virtual steady-state was achieved within 10 s for both oxygen and carbon dioxide (Figure 13a.1&b.1). Figure 13 shows typical ion-current responses at m/z 32 and 44 on current application after recording of the background ion-currents for oxygen and carbon dioxide for 10 s. If the ion-current responses were slow, as shown in Figure 13a.2&b.2, when steady-state was not achieved quickly, the minigrid was not in intimate contact

Figure 13. Ion current responses at (a) m/z 32 and (b) m/z 44 to a $15\ \mu\text{A}$ anodic current step applied to the gold grid electrode immersed aqueous solution containing $0.1\ \text{M}\ \text{NaHCO}_3/0.1\ \text{M}\ \text{KNO}_3$. Arrow indicates time of current application.

Figure 13.

with the membrane and the probe was dismantled.

Chemicals

Sodium bicarbonate, potassium nitrate, sodium hypophosphate (Mallinckrodt Inc., Paris, KY) and phosphoric acid (Ashland Chemical Company, Easton, PA) were ACS reagent grade and used as received.

The solutions utilized in the MoMS experiments comprised the following compounds; acetic acid (Mallinckrodt Inc., Paris, KY), sodium acetate (MCB Manufacturing Chemists, Inc. Cincinnati, OH), hydroquinone, quinone (Eastman Organic Chemicals, Rochester, N.Y), and sodium benzoate (Aldrich, Milwaukee, WI) all were used as received.

Methanol, used as solvent, was purchased from Corco Chemical Corporation (Fairless Hills, PA) and used as received.

Apparatus

Electrochemical Instrumentation: Electrochemical experiments were conducted using a PAR Model 173 potentiostat/galvanostat (Princeton Applied Research, Princeton, NJ) equipped with a Model 276 IEEE-GPIB interface.

Princeton, NJ) equipped with a Model 276 IEEE-GPIB interface. Computer control was achieved through IEEE-488 programming via Asystant GPIB software (Kiethley Instruments, Inc., Cleveland, OH).

Mass Spectrometer: Mass spectra were acquired by using a Balzers Model QMG 511 quadrupole mass spectrometer equipped with a secondary electron multiplier (Balzers, Hudson, NH). The QMG 511 front panel controls were used to set MS instrument parameters, and to select mass range, scan mode and scan rate. The resolution of the mass spectrometer was 54 and acceleration voltage was 1100 V.

Data Acquisition: The mass spectrometer was interfaced to the IEEE-488 bus through a Model 199 multimeter (Kiethley Instruments, Inc., Cleveland, OH) to achieve computer monitoring of the detector voltages. The multimeter acted as an A/D converter and was capable of storing upto 500 readings of the mass spectrometer's signal port before downloading to the computer. This voltage was proportional to the mass spectral ion-current.

A Hewlett-Packard Model Vectra ES/12 PC, equipped with a HPIB card, allowed computer control of the potentiostat and monitoring of the mass spectral ion-current. A schematic of

Figure 14. Block diagram of EC/MS instrument modified from the figure presented by House (see reference 6).

Figure 14.

the apparatus used in these studies is shown in Figure 14. Appendix I&II give a listing of the routines written with Asystant GPIB to control and acquire data from EC/MS experiments.

Electrochemical PERMS Experiments

The electrochemical cell for all experiments was a 10 mL glass vial. A gold minigrid electrode was used as the working electrode. A platinum-flag electrode (5 cm²) was used both as an auxiliary electrode and as a pseudo-reference. Precise potential control was not attempted unless specified in the text. The cell was cleaned daily by rinsing of distilled water, 5 M nitric acid, acetone and distilled water.

The PERMS probe was attached to the inlet of the mass spectrometer by a Swageloc fitting, and the interior of the probe was opened to the 1×10^{-7} Pa pressure of the MS source. The volatile electrochemical products diffused through the membrane, entered the mass spectrometer and were measured (Figure 15). In order to increase sensitivity, the stainless-steel tube and adjoining areas were heated to 100 °C with heating tape, wrapped over the tubing (Figure 12).

Figure 15. Cross-sectional schematic of PERMS probe
(modified from a figure presented by Szpylka, see ref. 59).

Figure 15.

Mass spectral analysis of electrochemical species was performed using one of the following two methods: selected ion monitoring (SIM), in which the mass spectral ion-current was recorded as a function of time at a single m/z value; entire spectrum monitoring (ES), in which MS ion-currents in a selected mass range were recorded as a function of time.

The procedure used to monitor and identify the electrochemical species in the Kolbe reactions using PERMS was performed in the following manner. After attachment of the probe to the MS inlet, the probe was rinsed with distilled water and its interior was evacuated until the pressure was less than 1.0×10^{-7} Pa. The probe was immersed in the prepared solutions along with the platinum flag electrode for 10 min. The galvanostat was set to zero current and the ion current(s) were monitored at the selected mass-to-charge ratio(s) to determine background. Then the electrochemical current was stepped to the desired value.

Mixed-mass-spectral ion-currents of all membrane permeable reactants and products were obtained by applying the desired current and recording the spectrum after the transport process had reached virtual steady-state using the ES method. Because of possible accumulation of organics on

minigrid gold surface during electrolysis, the electrode was cleaned periodically by passage of a 15 μ A reductive current for 30 s and the surface rinsed with distilled water.

Modulation Mass Spectrometry Measurements

In a MoMS experiment, the mass spectrometer was set to continuously monitor the ion-current at a single preselected m/z value and the MS ion-current was measured as a function of time. The solution to be studied was degassed with argon for 10 min prior to initiation of electrolysis.

A background mass spectrum was determined by setting the electrochemical current equal to zero and monitoring the ion-current at a preselected m/z value. Then a periodically changing electrochemical current square wave, such as that shown in Figure 16, (frequencies in the range from 0.005 to 0.5 Hz) was applied to the gold grid by computer control of the galvanostat, and the MS ion-current at the desired m/z value was monitored as a function of time.

After the response had achieved steady-state (from 3 to 4 electrochemical cycles), approximately ten additional cycles were recorded for Fourier transform analysis. In this study, each response was recorded for 15 cycles and 100

Figure 16. Periodic current excitation and MS ion-current response of the product, oxygen ($m/z=32$), during electrolysis of water at a fundamental frequency, 0.05 Hz.

Figure 16.

points were collected in each electrochemical cycle. Figure 16 shows a 15 μA periodic current excitation at a frequency of 0.05 Hz and the MS ion-current response of oxygen at m/z 32 during oxidation of water. For different preselected m/z values, the procedure above was repeated at different frequencies in order to establish the reactants, products and their fragments for the reaction studied.

In some cases, MoMS was also performed by applying a square wave potential (see, for example, Figure 20), the resulting current is not a pure square wave described by eq 15, but, since the membrane greatly attenuates higher frequency components, the fundamental still dominates. The ion-current is therefore dominated by sinusoidal response at the fundamental frequency of the potential square wave.

Computational Method

The phase of a preselected m/z value was calculated from the ratio of the imaginary to the real part of the Fourier transform of the MS ion-current (see eq 21). Fourier transform analysis used 2^{10} points of each steady-state MS ion-current response. The software FT package was Asystant GPIB.

Since the MS ion-current takes three to four electrochemical cycles to reach steady-state and each electrochemical cycle was recorded as 100 points, the starting points of Fourier analysis of the steady-state response are at $400 + n$ (taken after four pre-steady-state cycles had elapsed). The value of n ($n = 1, 2, 3, \dots$) is a correction for the time delay caused by the IEEE-488 protocol between the computer and the potentiostat/galvanostat. The time delay is in the range of two to three seconds, so the n -value is different at various frequencies.

The amplitudes of the imaginary and real parts were obtained from the FT of an MS signal at the fundamental frequency of electrochemical excitation. Calculation of a MoMS spectrum is demonstrated by the following example. Figure 17 shows FT of the MS ion-current response modulated at 0.05 Hz in Figure 16, where the value of real part is -4.85 and imaginary part is -49.23 at 0.05 Hz. The value of the $\tan(\phi_{32})$ between the electrochemical current excitation and the ion-current response is then calculated from the ratio, $A_{\text{imag}}/A_{\text{real}}$ ($\tan(\phi_{32}) = -49.23/-4.85 = 12.34$), and the result plotted as the single point at 0.05 Hz in the oxygen phase angle spectrum (Figure 28b). This process, repeated at

Figure 17. Real and imaginary components of the Fourier transform of the MS response of oxygen ($m/z=32$) in Figure 16. (a) Imaginary part; (b) Real part.

Figure 17.

various square wave frequencies from 0.005 to 0.17 Hz, produced the complete spectrum in Figure 28b (dotted line).

The transport time ($t_0 = \ell^2/D$) for oxygen was determined by fitting the $\tan(\phi_{32})$ experimental data obtained at different frequencies to eq 28 with a non-linear curve-fitting process (TableCurve). Using an initial estimate of t_0 , equation was fit by an iterative process. Then the correlation coefficient (R^2) of determination was calculated. The best-fit curve was obtained when the correlation coefficient was unchanged within one part in 10^6 for five successive iterations.

An example of a best-fit of data to eq 28 for oxygen is shown as the solid line in Figure 28b and the best-fit value of t_0 was 19.01 s for oxygen. The curve-fit program used in this research was Jandel Scientific TableCurve (Version 3.11, AISN software, 1992).

CHAPTER IV

RESULTS AND DISCUSSION

Mass spectrometry is a highly sensitive technique that provides unequivocal structural information on many molecular species. Two general problems are often encountered when using mass spectrometry to analyze condensed phase solutions for trace analytes. The analyte must be separated from a large excess of solvent, and it must be vaporized into the moderate vacuum of the MS source.

As described in the introduction, a semi-permeable silicone rubber membrane has been used as an effective sampling device to separate apolar volatile compounds from the solution matrix. Membrane sampling is particularly effective for aqueous solutions because silicone rubber discriminates against the polar solvent and allows continuous introduction of apolar solutes.

Part I. Membrane Isolation Mass Spectrometry

Separation of Apolar Volatile Compounds from the Solution

In order to separate apolar volatile compounds from the solution matrix and introduce them into the MS source using a membrane, the first requirement for the PERMS probe is that it must be tightly sealed against adventitious leaks. Partition into the membrane and permeation through the membrane should be the only significant route for molecules to enter the MS source from the solution phase being sampled. In addition, the PERMS probe must provide intimate contact between the electrode and the membrane to assure a rapid response time. This property was checked by monitoring the ion-currents at m/z 32 and 44.

Figure 13 (see chapter III) shows the ion-current responses of O_2 (I_{32}) and CO_2 (I_{44}) during electrolysis of 0.1 M $NaHCO_3$ /0.1 M KNO_3 solution using different probes. In Figure 13a.1&b.1, rapid and relative large ion-current responses are observed, and virtual steady-state ion-currents are reached within 10 s. The results show that membrane can effectively separate O_2 and CO_2 from the solvent and the electrolyte matrix. Diffusion through the membrane is the

predominant path for O_2 and CO_2 transport. The responses shown in Figure 13a.2&b2 are much slower and virtual steady-state is not observed within the time-scale of the experiment. This delay is due to the presence of a water layer between the electrode and membrane (incomplete attachment) that must be traversed by the O_2 and CO_2 . Such a probe is unacceptable.

Second, diffusion through the membrane should be the slowest step in the mass transport process as we described in the Theory section. This was tested by measuring the diffusion coefficient of known species in the membrane. The rise time for O_2 and CO_2 responses also was used to determine the diffusion coefficients of O_2 and CO_2 .

Parks⁶⁶ has shown that the time ($t_{1/2}$) necessary for the flux to reach one-half of the steady-state value depends only on the thickness of the membrane and on the diffusion coefficient of the species within the membrane,

$$t_{1/2} = (\ell^2 / 7.199 \times D_{\text{mem}}) \quad (32)$$

Since MS ion-current responses are directly proportional to the flux of species entering the mass spectrometer, we can

use the equation above to calculate D_{mem} of each species. The value of $t_{1/2}$ can be estimated from Figure 13 to be 2.6 s for O_2 , and 3.3 s for CO_2 . If we assume $l = 180 \text{ } \mu\text{m}$ (see discussion Part II, p133), the calculated value of $D_{O_2, \text{mem}}$ is $1.7 \times 10^{-5} \text{ cm}^2/\text{sec}$ and $D_{CO_2, \text{mem}}$ is $1.4 \times 10^{-5} \text{ cm}^2/\text{sec}$. The literature values^{67,68} for D_{O_2} and D_{CO_2} in silicone rubber are 1.7×10^{-5} and $1.1 \times 10^{-5} \text{ cm}^2/\text{sec}$ respectively. This agreement confirms that diffusion through the membrane is the rate determining step in this PERMS experiment.

We have examined the apparent signal-to-background (S/B) ratio for the PERMS method. Examples are illustrated in Figure 18. Figure 18a shows that the background is relatively low and the signal-to-background ratio is 9:2 where the I_{32} response was monitored during electrolysis of water to form oxygen. Figure 18b shows that the background is relatively high and the signal-to-background ratio is 2:3 where the I_{32} response was monitored during reduction of oxygen to water in oxygen-saturated solution. In both cases, mass spectral signals can be discerned from background, but we will describe correlation methods (MoMS) below, which can greatly enhance the S/B ratio.

Figure 18. (a) Controlled current oxidation of water to form oxygen. Response of the MS ion-current at m/z 32, to the current steps between 0 and -1.0 mA/cm^2 ; (b) Controlled current reduction of oxygen to water. Response of the MS ion-current at m/z 32, to the current steps between 0 and $+1.0 \text{ mA/cm}^2$.

Figure 18.

Effect of Solvent on Sensitivity

Because the ion-current of the mass spectrometer responds to the partial pressure of each chemical component in the source, and the partial pressure of a compound is governed by the ratio of the permeation rates of all compounds present,⁵⁸

$$\frac{P_i}{\sum P_i} = \frac{Flux_i}{\sum Flux_i}, \quad (33)$$

the sensitivity of the method depends strongly on the permeability of the membrane to the solvent. Solvent suitable for PERMS experiments should have low permeation rates through the membrane.

We have studied both water and methanol using the PERMS method. Figure 19 shows the MS ion-current response of CO₂ at m/z 44, I_{44} , during oxidation of acetate ion in water and in methanol containing 0.2 M CH₃COOH/0.2 M CH₃COONa (pH = 4.75). The background is much higher in methanol (0.974) than in water (0.198), so $\sum p_i$ is higher in MS source when methanol is present.

Figure 19 also shows a higher sensitivity for CO₂, I_{44} , in water (S/B 3:4) than in methanol (S/B 1:4). However both

Figure 19. Controlled current oxidation of acetate ion to form carbon dioxide in 0.2 M CH_3COOH /0.2 M CH_3COONa (pH = 4.75) solution at a gold-grid electrode. Response of the MS ion-current at m/z 44 to current steps between 0 and -10.0 mA/cm². (a) in water; (b) in methanol.

Figure 19.

methanol and water are suitable solvents for PERMS experiments.

MS Identification of Apolar Species

In order to use electrolysis of hydroquinone, quinone and oxygen as model systems to test the MoMS method, the mass spectra of O_2 , quinone ($C_6H_4O_2$) and hydroquinone ($C_6H_4O_2H_2$) were studied using the PERMS method. MS ion-current responses were monitored at the selected m/z where the peak has maximum intensity. We have found that apolar species (O_2 and $C_6H_4O_2$) diffused through the membrane and were detected by the mass spectrometer. The polar species ($C_6H_4O_2H_2$) could not be detected when the probe was immersed in a solution containing $\sim 10^{-2}$ M hydroquinone. Table 1 lists spectra of some molecular species and intensity of their peaks.⁶⁹

The results above indicated that the ability of a semi-permeable silicone rubber membrane to separate apolar volatile compounds from the solution matrix makes it a suitable sampling device for electrochemical mass spectrometry and allows continuous introduction of apolar solutes into the MS source.

Table 1. Mass Spectra of Species and Intensity.

Molecules	<u>m/z</u> and intensity							
O ₂	32 ^a	16						
	100 ^b	9						
CO ₂	44	16	28	12				
	100	9	8	7				
C ₆ H ₄ O ₂	108	52	80	51	50	109	54	38
	100	96	68	34	28	9	6	6
C ₆ H ₅ O ₂ H ₂	110	55	81	53	39	27	111	54
	100	17	14	10	8	8	7	5
C ₆ H ₆	78	52	51	77	50	39	79	76
	100	18	17	15	14	11	7	5
C ₆ H ₅ COOH	105	77	122	51	50	39	38	74
	100	96	68	34	28	9	6	6

^a m/z values; ^b intensity of peaks.

Part II. Study of Electrochemically Induced Periodic
Changes in Concentration of Species Outside the Membrane

Modulation of Molecular Flow into the MS Source

Based on an earlier discussion (Theory, Chapter II), a periodic excitation function may be used to modulate the flux of membrane-permeable species (reactant or product) into the MS source. When a periodically changing electrochemical excitation function is imposed at the membrane/electrode probe in a PERMS experiment, the concentrations of permeable species at the electrode surface are varied at the frequency of the electrochemical excitation. The flux of species released into the MS source are modulated also. We have used both controlled potential and controlled current to effect modulation of this molecular flux.

Modulation of oxygen flux into the MS source: Oxygen was chosen to serve as a model system because oxygen concentrations in the solution may be modulated, by electrochemical reaction, either as a reactant or as a product of electrolysis.

(1) **Oxygen as a product:** Oxidation of water is a four-electron, four-proton process, and oxygen is produced with

nearly 100% current efficiency.⁷⁰

Square-wave potential steps (Figure 20b) from 0 to +1.4 V vs. a Pt electrode were applied to a gold minigrid/membrane electrode immersed in a solution containing 0.2 M CH₃COOH/0.2 M CH₃COONa (pH = 4.75). The ion-current was monitored at m/z 32. Figure 20c shows the ion-current response to a periodic, 0.025 Hz, potential excitation. This excitation produces periodic changes in the MS ion-current response at m/z = 32.

Figure 20c shows that the magnitude of oxygen response (I_{32}) was modulated by electrochemical excitation. When the potential turns on (the first half of the square wave cycle), oxygen is generated at the surface of gold electrode. The concentration of oxygen increases, permeates the membrane, and causes I_{32} to increase. When the potential returns to zero (the second half of the cycle), the electrode stops generating oxygen. The concentration of oxygen is depleted by diffusion into the solution and into the membrane, so I_{32} decreases. Since the value of I_{32} increased shortly following each positive E-step, O₂ is obviously the product of the

Figure 20. Controlled potential oxidation of water to form oxygen. (a) Response of the electrochemical current to the potential steps shown in b. below; (b) Periodic potential steps between zero and +1.4 V vs. Pt, applied to the gold-grid electrode at frequency of 0.025 Hz; (c) Response of the MS ion-current at m/z 32, to the potential steps shown in b. above.

Figure 20.

electrode reaction.

The electrochemically driven alternating I_{32} response was superimposed on an approximately constant background, caused by dissolved oxygen and adventitious leaks into the MS inlet system. Figure 20 also shows that the I_{32} response is more sinusoidal than the square wave excitation. Because the system function, eqs 23 and 24, attenuates higher frequency response, I_{32} is dominated by the fundamental frequency (see Figure 7).

Oxygen was also produced by electrochemically generated square-wave current steps between 0 and -1.0 mA/cm^2 in a solution containing $0.2 \text{ M CH}_3\text{COOH}/0.2 \text{ M CH}_3\text{COONa}$. The I_{32} response at a frequency of 0.025 Hz is shown in Figure 18a. The fact that the signal (I_{32}), shows that oxygen is a product of electrolysis at the gold-minigrid electrode. The results suggest that the flux of oxygen as a electrochemical product into the MS source can be modulated by both controlled potential and controlled currents.

(2) Oxygen as a reactant: Oxygen may also be reduced at the gold-grid electrode in an oxygen-saturated solution, producing a complementary deficiency of oxygen at the membrane surface. The I_{32} response decreases when the

reductive electrochemical excitation turns on, because O_2 is a reactant in the electrochemical reaction.

Oxygen undergoes a four-electron reduction to water at a standard potential of +1.23 V vs. the standard hydrogen electrode.⁷⁰

Figure 21 shows that, when a periodic negative potential is applied between 0 and -1.4 V vs. a Pt electrode, the I_{32} response decreases from the level shown by the oxygen-saturated solution. Figure 18b shows that a similar I_{32} response may be achieved by applying a square-wave current steps between 0 and +1.0 mA/cm².

When the potential/current is applied, oxygen is consumed by reduction, and I_{32} decreases. When the potential/current excitation is relaxed, oxygen is replenished by diffusion from the bulk solution, and I_{32} increases.

Modulation of other apolar volatile molecules: We have studied modulation of the flux of oxygen in a PERMS experiment previously. In order to study further the

Figure 21. Controlled potential reduction of oxygen to water. (a) Response of the electrochemical current to the potential steps shown in b. below; (b) Periodic potential steps between -1.4 and 0 V vs. Pt, applied to the gold-grid electrode at frequency of 0.025 Hz; (c) Response of the MS ion-current at m/z 32, to the potential steps shown in b. above.

Figure 21.

modulation of molecular flow into the mass spectrometer, we investigated quinone as a product and as a reactant in electrochemical reactions, under both controlled potential and controlled current conditions.

(1) **Quinone as a product:** Oxidation of hydroquinone proceeds by two-electron, two-proton transfer to form quinone:⁷¹

Figure 22a shows the MS ion-current response of quinone at $m/z = 108$, I_{108} , during oxidation of 0.04 M hydroquinone/0.1 M phosphate buffer, pH = 5.5, solution under controlled potential steps between 0 and +1.4 V. Since oxidation of hydroquinone in aqueous solution competes with oxidation of water, generation of quinone does not achieve 100% current efficiency. The value of I_{108} was modulated by each electrochemical excitation step. Modulation of I_{108} under controlled current is similar to that obtained under controlled potential.

Quinone as a reactant: Benzoquinone can be reduced to form hydroquinone,⁷¹ and the reaction is:

Figure 22. Response of the MS ion-current at m/z 108, I_{108} , at a fundamental frequency of 0.005 Hz. (a) Oxidation of hydroquinone to form quinone in 0.04 M hydroquinone/0.1 M phosphate buffer solution (pH = 5.5) under controlled potential between 0 and +1.4 V vs. Pt; (b) Reduction of quinone to form hydroquinone in 0.018 M quinone/0.1 M phosphate buffer (pH = 5.5) solution under controlled potential between -1.4 and 0 V vs. Pt. At 0 V, no current flows between electrodes.

Figure 22.

Quinone was reduced by applying either a square-wave potential or current in a solution containing 0.018 M quinone/0.1 M phosphate buffer, PH=5.5. The results in Figure 22b show the MS ion-current response, I_{108} , to a periodic negative potential excitation at a frequency of 0.005 Hz. The value of I_{108} decreases with each potential step, indicating quinone is a reactant of the electrode reaction. Analysis of quinone data will be discussed in later sections.

In this work, we have chosen an electrochemical excitation function to modulate molecular flow through the membrane because of its experimental convenience. But, other possible methods could be used to produce periodic oscillation of the solution concentration at the membrane surface, such as variation, pulsed pumping of chromatographic eluant, photochemical stimulation or chemical kinetics.

Fourier Transform of the Modulated MS Ion Current

In order to apply quantitatively eqs 21 through 26 to modulated experimental data, it is necessary to separate the periodic signal(s) from the background and from each other, and to isolate the portions of the I_{ms} signal that are in-phase and out-of-phase with respect to i_e . Fourier transform of the ion-current response has been used for this purpose.

Figures 23a and 23b show the in-phase and out-of-phase portion of the Fourier transform of the I_{s2} response in Figure 20c, after it has reached a virtual steady-state (from 140 s to 400 s). The process of Fourier transformation greatly enhances the S/B ratio (see Figure 20c and Figure 23). Eqs 25 and 26 predict (and we observe) that the amplitude reaches a maximum at the fundamental frequency of the square-wave excitation, 0.025 Hz, and progressively smaller maxima are seen at the higher harmonics of this fundamental frequency (0.05, 0.075, etc). These data are analyzed more completely in the section on identification of pure materials.

The results indicate that FT can effectively separate the signal from background noise and from higher odd harmonics, and it greatly increases the sensitivity of the ion-current response in PERMS experiments.

Figure 23. Real and imaginary components of the Fourier transform of the MS response in Figure 20c. (a) Imaginary part, out of phase with the electrochemical current in Figure 20a; (b) Real part, in phase with the electrochemical current.

Figure 23.

Quantitation of FT Signal Amplitude

The amplitudes of the Fourier transform of the periodic MS ion-current is a measure of the amount of the chemical species generated, and it can be calculated as the amplitude of the FT signal, $A_{m/e}$ (eq 23). At steady-state, the number of moles of a species diffusing through the membrane per unit time is constant and it should be proportional to the current density.

For example, Figure 24a is an FT of the I_{108} response for hydroquinone oxidation at current steps between 0 and -7.0 mA/cm² in 0.04 M hydroquinone/0.1 M phosphate buffer solution (pH = 5.5). From Figure 24a, we estimate that the amplitudes of real part (A_{real}) and imaginary part (A_{imag}) at 0.0125 Hz are 289 pA and 596 pA. Therefore current of quinone generated during electrolysis of hydroquinone is 638 pA. A plot of A_{108} vs. current density at 0.0125 Hz is shown in Figure 25, indicating the linear relationship between the FT amplitude and current density.

Identification of Pure Materials Permeating the Membrane

As we described in Chapter II of the Theory section, the

Figure 24. Real and imaginary components of the Fourier transform of the MS response of I_{108} at a frequency of 0.0125 Hz. (a) Electrolysis of hydroquinone in 0.04 M quinone/0.1 M phosphate buffer solution (pH = 5.5) at current steps between 0 and -7.0 mA/cm²; (b) Electrolysis of quinone in 0.018 M quinone/0.1 M phosphate buffer solution (pH = 5.5) at current steps between 0 and +10.0 mA/cm².

Figure 24.

Figure 25. A_{108} as a function of current density at 0.0125 Hz during electrolysis of hydroquinone in a solution containing 0.04 M hydroquinone/0.1 M phosphate buffer (pH = 5.5) .

Figure 25.

transport time of species and the phase angle are characteristic of a molecular species sampled by the silicone membrane, which are qualitative indicators of molecular identity. The observed phase angle, ϕ_{tot} , between the MS ion-current and electrochemical excitation is composed of ϕ_{fund} and ϕ_{diff} . The value of ϕ_{fund} indicates whether the species is a reactant or a product of the electrode reaction in the simplest case, and ϕ_{diff} describes the rate of mass transport of the analyte through the membrane.

Reactants and products: Identification of reactants and products may be achieved using ϕ_{fund} . The difference between ϕ_{fund} -values for MS ion-currents between a reactant and a product should be 180° . Figure 18 shows that the I_{32} response of oxygen as a reactant (Figure 18b) and a product (Figure 18a) differ by $\sim 190^\circ$. The value of ϕ_{fund} for quinone (m/z 108) when it participates as a reactant or as a product (Figure 22) shows a similar result ($\phi_{\text{fund}} \approx 185^\circ$), indicating that ϕ_{fund} is a reliable indicator of whether the material detected participates as a reactant or as a product in a simple electrochemical reaction.

Reactants and products can be also identified by the signs of imaginary and real parts of FT. The Fourier

Figure 26. (a) Real and imaginary components of the Fourier transform of the periodic response at m/z 44 shown in Figure 19a; (b) Phase angle spectrum for the correlation between MS response at m/z 44 and EC excitation when acetate ion is oxidized to form CO_2 at a gold minigrid electrode under controlled potential.

transformed data shown in Figure 23 can be interpreted in the following way. At the fundamental frequency, the sign of imaginary part, $\underline{V}$ (Figure 23a), is negative and the sign of real part, $\underline{U}$ (Figure 23b), is positive. By comparing eq 28, we can conclude that O_2 is a product of the electrochemical reaction. Fourier transform of the $\underline{I}_{44}$ response (see Figure 19) shows that the signs of $\underline{U}$ and $\underline{V}$ are negative and positive respectively at low frequencies (Figure 26), which are the same as those for $\underline{I}_{32}$ as product in Figure 23. This identifies CO_2 as a product of the electrochemical reaction.

Figure 27 is the FT of $\underline{I}_{32}$ response during oxidation of oxygen (shown in Figure 21). Analysis of Figure 27 also shows that for $\underline{I}_{32}$ resulting from eq 33, ϕ is 180° out-of-phase with respect to $\underline{I}_{32}$ produced by the water oxidation reaction eq 32 (the sign of $\underline{V}$ is positive and the sign of $\underline{U}$ is negative in Figure 27).

An FT of the $\underline{I}_{108}$ response produced by hydroquinone oxidation shows that the signs of $\underline{V}$ and $\underline{U}$ are positive (Figure 24a). Eq 28 indicates that the signs of imaginary part ($\underline{V}$) and real part ($\underline{U}$) for products should be positive when ϕ -value is greater than 90° (in second quadrant, see discussion on p130), indicating quinone is a product of the

Figure 27. In-phase (a) and out-of-phase (b) components of the Fourier transform of the periodic response at m/z 32 shown in Figure 21c.

Figure 27.

electrochemical reaction. According eq 28, the signs of $\underline{U}$ and $\underline{V}$ are negative for reactant when a phase angle (ϕ) is in second quadrant. Figure 24b is an FT of the $\underline{I}_{108}$ response for quinone reduction, where signs of $\underline{U}$ and $\underline{V}$ are negative, indicating quinone is a reactant of this reaction. Above results are consistent with the discussion in the Theory section (Chapter II).

Phase shift and transport time: Since different species pass through the membrane with different transport rates, the transport time of a species is an identifying characteristic of that species. The portion, ϕ_{diff} , of the phase shift between the MS ion-current response and the periodic electrochemical excitation can be calculated from the amplitudes of imaginary and real parts of the FT corrected for the independently determined value of ϕ_{fund} . This ϕ_{diff} -value is frequency-dependent (eq 19) and allows us to measure mass transport rates of species through the membrane. We have studied ϕ_{diff} -values of several species including O_2 as a product and a reactant.

A phase angle spectrum of oxygen is shown in Figure 28, when oxygen is a product during the oxidation of water under both controlled potential and controlled current. While

Figure 28. Phase angle spectra for the correlation between the MS response and the EC excitation when oxygen is a product of oxidation of water at a gold-grid electrode. (a) Controlled potential; (b) Controlled current.

Figure 28.

Figure 20b indicates that the current generated during potential excitation is not strictly the square wave described by eq 15, we have applied the sinusoidal analysis from eq 21 onward at the fundamental frequency without modification. The $\tan(\phi_{32})$ -value of I_{32} (in Figure 20c) calculated (using eq 24) from A_{real} and A_{imag} , (shown in Figure 23), has been plotted as the single point at 0.025 Hz in Figure 28a. This MoMS process, repeated at several square-wave frequencies from 0.005 to 0.17 Hz, produces the complete $\tan(\phi)$ spectrum in Figure 28a (dots) which allows estimation of the transport time (t_0) of oxygen through the membrane by the following process.

The t_0 -value of oxygen was calculated by using a curve-fitting procedure. The experimental data were fitted to eq 28 with a nonlinear least-squares algorithm and the best-fit curve is shown as the solid line in Figure 28a with a correlation coefficient, R^2 , 0.90. As eq 28 shows, $\tan(\phi)$ approaches infinity when the phase shift approaches $\pi/2$. Figure 28a shows a singularity at approximately 0.042 s^{-1} and the transport time of oxygen through the membrane, $t_0 = \ell^2/D$, is 19.1 s. Figure 28b shows the $\tan(\phi)$ spectrum of oxygen produced under controlled current, the value of the

Figure 29. Phase angle spectra for the correlation between MS response and EC excitation during reduction of oxygen to water in an oxygen-saturated solution. (a) Controlled potential; (b) Controlled current.

Figure 29.

singularity is near 0.043 Hz and t_0 is 19.1 s.

The $\tan(\phi)$ spectrum shown in Figure 29 is the case of oxygen as a reactant during reduction of oxygen under both controlled potential and controlled current. The $\tan(\phi)$ spectrum and transport time (19.0 s, in Figure 29a) of oxygen as a reactant and a product under controlled potential are virtually identical.

The results indicate that a reactant and a product with identical diffusion coefficients and diffusion through the same membrane thickness have identical $\tan(\phi)$ spectra and t_0 -values. However, they can be identified from the signs of real and imaginary parts of their FT spectra at same frequency.

Changes in mechanism: The electrochemical behavior of oxygen reduction is more complex than water oxidation under controlled current conditions. When a value of 180° is assumed for ϕ_{fund} under controlled current reduction of oxygen, the measured phase shift yields an estimate of 59 s (in Figure 29b) for t_0 . This is much larger than the value of 19 s measured for controlled potential reduction of the same species. The most likely explanation is that ϕ_{fund} is determined in part by the electrode mechanism and may vary

with current density. The following discussion is highly speculative, and only serves here to point out where further studies by new methods such as MoMS, may be useful in studying one of the most complex of electrochemical reactions.

Apparently, the rate of reduction of oxygen is potential dependent, so rapid electrolysis occurs only at large overpotentials. At a smaller overpotential value, the reduction of oxygen produces (at least in part) hydrogen peroxide instead of direct four-electron reduction to water. Therefore, the observed ϕ -value depends on current density.

The two general pathways for reduction of oxygen in acid solution are:⁷²

1. Direct 4-electron pathway

2. Peroxide Pathway

followed by either the reduction of peroxide

plus the decomposition of peroxide,

There are many steps involved in the direct 4-electron pathway in which oxygen is reduced to water. The reduction steps may involve an adsorbed peroxide intermediate, but this species does not lead to peroxide in the solution. The peroxide pathway involves peroxide species present in solution. If peroxide decomposes in solution, the resulting oxygen is recycled via reaction 36, and the over all reaction is the 4-electron pathway.

It has been found that H_2O_2 is a stable intermediate of oxygen reduction at a gold electrode in acid solutions.⁷³ With gold cathodes, the steady-state concentration of H_2O_2 is about 10^{-4} M , suggesting that gold is a poorer catalyst for the decomposition of H_2O_2 .

At controlled current, oxygen reduction at a gold electrode involves both pathways 1 and 2, but pathway 2 may be predominant at low current density. Since gold is a poorer catalyst for the decomposition of H_2O_2 , H_2O_2 is a stable intermediate and may be present in solution during oxygen reduction. Thus H_2O_2 may diffuse through the membrane and be detected by the mass spectrometer as a fragment at m/z

32.

If this analysis is correct, oxygen is detected by MS not only as a reactant but also as a fragment of H_2O_2 (product), making the phase angle (ϕ) between excitation and MS response more complex. Thus, the phase angle observed, ϕ_{diff} , is not only comprised of ϕ_{diff1} due to O but also ϕ_{diff2} due to formation of H_2O_2 . When the reductive current is on, the depletion rate of oxygen is decreased by formation of H_2O_2 measured at I_{32} . Thus the phase angle between excitation and I_{32} response increased and t_0 -value also increased.

The t_0 -values of oxygen were measured at several current densities and Table 2 lists the value of t_0 at each current density. It appears that pathway 1 may predominate at high current density, and pathway 2 may predominate at low current density. Apparently, pathway 1 predominates at controlled potential.

Further work must be done on the theory of MoMS for complex electrochemical processes, before a more quantitative evaluation of oxygen reduction should be attempted.

Carbon dioxide: The potential shown in Figure 20a oxidizes water, but a small fraction of the current also causes a second electron transfer reaction, oxidation of

Table 2. The t_0 -Values of Oxygen at Different Current Densities during Electrolysis of Oxygen.

Reductive Current density (mA/cm ²)	t_0 (s)
0.5	59
1.0	59
1.3	59
1.5	40
2.0	36
2.5	32
5.0	30

acetate ion in solution containing 0.2 M CH_3COOH /0.2 M CH_3COONa . CO_2 diffuses through the silicone membrane, enters the MS vacuum and is detected. Since the molecular weight of CO_2 is greater than that of O_2 , CO_2 should take longer time to diffuse through the membrane. A t_0 -value of 22.4 s for CO_2 is calculated from the singularity in the $\tan(\phi)$ spectrum (Figure 26b), which is greater than the 19 s calculated for O_2 . Acetate oxidation at a gold minigrid electrode was also studied at controlled current. The value, 22.1 s, is the same as measured under controlled potential conditions.

Quinone: We have also studied ϕ_{diff} -values of quinone. The t_0 -value of quinone as a reactant and a product was studied at both controlled potential and controlled current.

The phase angle spectra of quinone as a product and as a reactant under controlled current is shown in Figure 30. The t_0 -values are same under both conditions, 204 s. Analysis of Figure 30 shows that the $\tan(\phi)$ spectra of quinone are different from those $\tan(\phi)$ spectra discussed previously, we can only see phase angle (ϕ) is greater 90° (in second quadrant, third quadrant...). Because quinone diffuses slowly through the membrane, it was not possible to experimentally determine a reliable value for ϕ_{108} at very low

Figure 30. Phase angle spectra for the correlation between I_{108} response and EC excitation. (a) Oxidation of hydroquinone in a solution containing 0.04 M hydroquinone/0.1 M phosphate buffer, pH = 5.5 at current steps between 0 and -10.0 mA/cm²; (b) Reduction of quinone to hydroquinone in a solution containing 0.018 M quinone/0.1 M phosphate buffer (pH = 5.5) at current steps between 0 and +10.0 mA/cm².

Figure 30.

frequency.

The $\tan(\phi)$ spectra and t_0 -values of quinone as a product and as a reactant under controlled potential are virtually identical from those at controlled current, where t_0 -value is 204 s.

A more precise estimate of the t_0 -value of quinone would be obtained by measuring the $\tan(\phi)$ -values in the first quadrant of the quinone phase angle spectrum. This could be achieved by reducing the membrane thickness to near 25 μm , but such a membrane free of holes was not available to us.

From the values of t_0 , we have also estimated the diffusion coefficient of oxygen through the silicone rubber membrane. If the membrane is assumed to be 100 μm thick (the nominal value), then a t_0 -value of 19 s is calculated, which corresponds to a diffusion coefficient of approximately $5 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$ for oxygen in the separator membrane. The literature value⁶⁷ for D_{O_2} in silicone rubber is $1.7 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$. If, on the other hand, the literature value of D_{O_2} is assumed, the effective membrane thickness is estimated to be 180 μm . Then the estimated diffusion coefficient, D_{CO_2} , is calculated from t_0 (l^2/D_{CO_2}) to be $1.4 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$ using the effective membrane thickness (180 μm) calculated from the t_0 -

value of O_2 . The diffusion coefficient of CO_2 was also estimated from the Stokes-Einstein relation to be $1.5 \times 10^{-5} \text{ cm}^2\text{s}^{-1}$ using O_2 as the standard.

The diffusion coefficient for quinone calculated from t_0 -value is $1.6 \times 10^{-6} \text{ cm}^2\text{s}^{-1}$, which is much smaller than estimated from the Stokes-Einstein equation ($1.1 \times 10^{-5} \text{ cm}^2\text{s}^{-1}$ using O_2 as a standard). One possible explanation is that electrolysis of hydroquinone is not 100% current efficient.

If the large diffusion coefficient of quinone relates to current efficient, the observed ϕ_{diff} for quinone should vary with current density. The value of phase angle (ϕ) was measured at several current densities at a constant frequency, 0.016 Hz, and Table 3 lists the value of $\tan(\phi)$ at each current density. The Table 3 shows that the value of $\tan(\phi)$ decreases with increasing current density, indicating large diffusion coefficient of quinone does relate current efficient.

Summary. We conclude that the MoMS method is suitable for study of electrochemical reactions under both controlled current and controlled potential. The transport time (t_0) is a parameter characteristic of each individual molecular species. So it is possible to identify chemical species

Table 3. The $\tan(\phi)$ -Values of Quinone as a Function of Current Density during Electrolysis of Hydroquinone at a Frequency of 0.016 Hz.

Current Density (mA/cm ²)	$\tan(\phi)$
0.5	-1.18
1.0	-1.07
1.5	-0.89
2.0	-0.71
2.5	-0.64
3.0	-0.53
3.5	-0.47
4.0	-0.45
4.5	-0.44
5.0	-0.45

using t_0 -values. The diffusion coefficient of CO_2 through the membrane estimated to be $1.4 \times 10^{-5} \text{ cm}^2\text{s}^{-1}$ is close to the literature value. There is evidence to suggest that oxygen reduction undergoes a very complex pathway at controlled current. The MoMS method also demonstrated the ability to distinguish between reactants and products of an electrochemical reaction using the signs of real and imaginary parts of their FT spectra.

Part III. Deconvolution of Mixed Mass Spectra from a PERMS Experiment

The previous section showed the primary phase shift, ϕ_{fund} , has been used to identify whether a particular molecular species is a product or a reactant in an electrochemical reactions. It also showed that the transport time (t_0) is characteristic of each molecular species.

The diffusion-induced portion of the phase shift, ϕ_{diff} represents an elution (lag) time (t_0) for each molecule from the 180 μm long chromatographic system (the silicone rubber membrane). Parent and fragment ions formed from the same molecule in the E.I. source are expected to produce the same phase shift. All ion-currents with the same ϕ_{diff} -value are tagged as originating from the one molecular species experiencing that delay as it permeates the membrane. The utility of this latter property of the MoMS experiment to identify molecular species during electrolysis of carboxylate ions is further illustrated in the following example.

Oxidation of carboxylate ions, commonly called the Kolbe reaction, is an important method for electrochemical synthesis in organic chemistry. When a radical mechanism

occurs, the overall reaction may be represented by:^{74,75}

Several separate steps and many possible intermediates are involved in this reaction. The different mixtures of products of the Kolbe reaction may be used to determine the mechanisms of the reaction, whether it is a radical mechanism or an alternative carbocation mechanism.

The radical mechanism, a one-electron oxidation, often leads to form alkanes, alkenes, and dimers.

The carbocation mechanism is a two-electron transfer. Most of these products are alcohols, ethers, and esters, depending on the solvent.

The mechanistic pathways are controlled by several factors, such as anode material, pH, current density, solvent and the concentration of the carboxylic acid. The optimum conditions for the radical pathway are high concentration of carboxylate ion, low pH, and a high current density at a Pt electrode. On the other hand, the carbocation pathway is favored in aqueous solution at high pH and at a gold electrode.⁷⁶

In general, the characterization of reaction products is carried out by GC of the volatile species released after bulk electrolysis of the carboxylate solution.⁷⁷ It is usually very time-consuming and requires a series of extraction/separation steps prior to analysis. This method does not offer the capability to monitor reactants and products generated during an electrochemical reaction in real time. PERMS has been used to identify hydrocarbons, alcohols, acids and other products.^{58,59} We report here the direct identification and determination of electrochemically generated species by the MoMS method. Using the MoMS technique, we studied the oxidation of benzoate ion at a gold electrode. The identification of products was achieved by using transport times (t_0) of species through the membrane.

Oxidation of Sodium Benzoate in Methanol

Kolbe electrolysis of benzoate ion has been studied previously.^{6,78-80} Oxidation of benzoic acid at a Pt electrode in both methanol⁷⁸ and pyridine⁷⁹ has been studied. The results showed that benzoic acid gave benzene rather than biphenyl under the usual Kolbe conditions. Only a trace of biphenyl, along with 4-phenylpyridine and 4-phenylbenzoic acid has been observed during electrolysis in pyridine.

Matsuda *et al.*⁸⁰ studied anodic oxidation of benzoic acid at a Pt electrode in acetonitrile and propionitrile. In acetonitrile, benzoic acid loses one electron to form the benzoyloxy radical. The resulting radical then reacted with the solvent to give *N*-acetylanthranilic acid at constant potential. In propionitrile, *N*-propionyl-anthranilic acid, *N*-propionylbenzamide, and dipropionylamine were detected. No dimer (biphenyl) was observed.

House⁶ reported the anodic electrolysis of sodium benzoate in PEG at platinum at a constant current density of 2.0 mA/cm² with product detection performed directly inside the mass spectrometer ion source. Detectable ion-current increases at m/z -values of 44, 51, 52, 77, 78, 106 and 122

were reported to occur during the constant-current electrolysis. By comparison with literature spectra, the ion at 44 was assigned to CO_2 , 51, 52, and 78 assigned (in part) to benzene, and 51, 77, 106, and 122 assigned to benzoic acid, but uncertainty remained as to some of these assignments. Neither biphenyl nor any carbocation-derived products were observed.

In this research, we study anodic electrolysis of sodium benzoate at a gold electrode in methanol using the MoMS technique. Methanol is commonly used as a solvent in Kolbe electrolysis and the experimental conditions for optimum yield of dimer are often less critical than in aqueous media.

Direct mass spectral analysis of species evolved during sodium benzoate oxidation was performed. When the anodic current of 10.0 mA/cm^2 was applied at a gold-grid/membrane electrode in neat methanol containing 0.15 M sodium benzoate, the spectrum in Figure 31 was recorded from m/z 35 to 235 after electrolysis for 300 s. The background spectrum taken before electrolysis showed peaks at m/z 40 and 44, assigned Ar and CO_2 . After stepping the current, the peak at m/z 44 increased and a series of new peaks appeared at m/z 122, 105, 92, 78, 74, and 52. This spectrum is obviously the result of

Figure 31. Mixed mass spectrum of the membrane-permeable electrochemical reactants and products present near the gold-grid electrode/membrane surface during Kolbe oxidation of benzoic acid in methanol.

Figure 31.

more than one molecular species sampled by the membrane and ionized in the electron impact source, and ion currents are observed at many values of m/z in the spectrum.

Deconvolution of this mixed-mass-spectrum may be accomplished using MoMS. All fragment peaks derived from the same diffusing species will show the same values of t_n , which identifies them as being derived from the same electrochemical species. The value of t_0 was estimated for each of the major peaks in Figure 31 on the basis of the correlation spectra, and the results are summarized in Table 3.

The peak at m/z 122 is the parent ion for benzoic acid, whose formation can be explained as follows. Benzoic acid can be formed by protonation of benzoate ion, and protons are formed in abundance by the coincident oxidation of water (a principal contamination of methanol).

The peak at m/z 105 (base peak) results from loss of an oxygen-atom from benzoic acid, which is a fragment of the benzoic acid. The peak at m/z 74 is assigned as a fragment ion of the benzoic acid, because its t_0 -value is the same as the species of m/z at 105.

The peak at m/z 78, with a t_0 -value of 57 s, is assigned as the benzene parent ion, the product of electrochemical

oxidation of benzoate ion. Since the peak at m/z 52 also has a t_0 -value of 57 s, it may be identified as $\dot{C}H^+$ species derived from fragmentation of molecular benzene. The formation of benzene indicates that phenyl radical may be an intermediate formed by hydrogen abstraction from the solvent after Kolbe decarboxylation of benzoate ion:

Phenyl radical may also dimerize to form biphenyl and we found no evidence for biphenyl at m/z 152 in this study.

Finally, the peak at m/z 92 had a measured t_0 -value of 90 s, significantly different from either of the diffusing molecular species so far identified. We have been unable to identify this molecule. Of course, the peak at m/z 44 is carbon dioxide, which has been previously identified to have a t -value of 22 s.

Table 4. Values of $\ell^2/\underline{D}$ for Various Peaks Found in Mixed Mass Spectrum Shown in Figure 31, Recorded during Electrolysis of Benzoate Ion

mass/charge ratio	singularity in $\tan(\phi)$ (Hz)	$\ell^2/\underline{D}$ ^a (s)	$\underline{D}, \times 10^5$ ^b (cm^2s^{-1})	$\underline{M}$ -value, relative ^c	identity of fragment
44	0.037	21.1	1.4 ^d	44 ^d	CO_2^+
52	0.0139	57.2	4.2	79	C_4H_4^+
74	0.0118	66.2	3.5	121	C_6H_2^+
78	0.0137	57.0	4.1	78	C_6H_6^+
92	0.0084	88.5	-	299(?)	-
105	0.0116	66.1	3.5	122	$\text{C}_6\text{H}_5\text{CO}^+$
122	-	-	-	122	$\text{C}_6\text{H}_5\text{COOH}$

^a From singular frequency and eq 21. ^b Assuming, $\ell = 180 \mu\text{m}$, and taking $\underline{D}$ - and $\underline{M}$ -values of benzoic acid as reference, except CO_2 . ^c $\underline{M}$ -value is the apparent mass of the molecule, calculated from eq 46, which diffused through the membrane and was responsible for this peak in the mass spectrum. ^d $\underline{D}$ - and $\underline{M}$ -values of O_2 taken as reference, see text.

These assignments may be checked for internal consistency by using the Stokes-Einstein relationship⁸¹ relating diffusion coefficient and molecular weight and the diffusion coefficients estimated from the observed phase shifts:

$$\frac{D_1}{D_2} = \sqrt[3]{\frac{M_2}{M_1}} \quad (46)$$

The next to last column in Table 4 summarizes these results.

The phenyl radical also can be further oxidized to carbocation and form carbocation-derived products.

In this study, carbocation products (such as phenol at m/z 94 and ester at m/z 198) have not been observed or identified. The results are consistent with previous studies.⁶ We can conclude that Kolbe electrolysis of

benzoate ion at a gold electrode in methanol occurs predominantly by a radical pathway. However, if the radical pathway (eq 24) is active, biphenyl (m/z 154) should be detected. It is not clear why biphenyl was not produced in detectable amount.

Summary. The EC/MoMS study of oxidation of acetate and benzoate ions shows that MoMS is a powerful method to interpret mixed-mass-spectra from PERMS experiments. In benzoate oxidation, molecular products and their electron impact fragments have been identified. Electrochemical modulation of the sample stream allows deconvolution of the mixed-mass-spectrum produced by single-stage extraction of volatile species in a polar solvent adjacent to a silicone rubber membrane sampling device.

CONCLUSION

Modulation mass spectrometry (MoMS) has proven to be a useful technique for the identification of electrochemical species in solutions. MoMS demonstrates several advantages, such as rapid response, on-line detection, higher sensitivity over PERMS method.

In this study, sub-millimolar concentrations of oxygen, carbon dioxide, and carboxylic acids and their electrolysis products were sampled using a silicone membrane during electrolysis and identified within a second of the time they were electrolyzed. The electrolysis process modulates solution concentrations near a ~150 μm thick silicone rubber membrane sampling device. The phase between the mass-spectral response and the electrochemical excitation can be determined by Fourier analysis. Reactants and products of an electrochemical reaction are identified using signs of real and imaginary of FT. The transport time of various species for diffusion through the membrane is characteristic of the molecule and is derived from these FT correlation spectra.

In benzoate oxidation, molecular products and their electron impact fragments have been identified using MoMS

method. Electrolysis of benzoic ion at a gold electrode produces radical-derived products such as benzene, CO_2 , and benzoic acid. Neither diphenyl nor carbocation-derived products were identified.

In short, we have used the silicone membrane as an ultra-short (25-100 micron long), rapid response (1-20 second elution time) chromatographic column, to separate and inject apolar electrochemical products into the mass spectrometer. While the application described here is electrochemical in nature, the principle of modulation of the ion-current is quite general. When the MS ion-current varies at the modulation frequency, that signal is tagged; it has originated in the excitation applied to the external system. The elution time and the phase shift are characteristic of a molecular species sampled by the silicone membrane, and are qualitative indicators of molecular identity.

APPENDICES

GPIB (IEEE) routines written to control the acquisition of mass spectral data by Keithley model 199 multimeter (interface to the Balzers QMG 511 mass spectrometer), and control the Par model 173/276

Routine I. MS- monitor mass spectrum as a function of time

Initialize

Set Device: Meter

Reset T&L Index: R

Talk:

Literal: F0R3X

Literal: S0B2G1X

Literal: M0X

Literal: T6Q60I500M2X

Message: Awaiting Mass Spectra: Trigger

Wait: SRQ

Listen:

Variable R

Setup: [F] Auto y(x)

Draw: [F] R Indexed

End Routine

Routine II. EC/MoMS method monitor single m/z prior to and upon electrochemical excitation step as a function of time.

Reset T&L Index: Z

Exec Rout #7: MS Backgro

Exec Rout #6: Control I

Set Device: PAR

Talk:

Literal: Cell 0

A: data: Append Z

C: data: Append Z

End-routine

(1) Rout #7: MS Backgro

Initialize

Set Device: Meter

Talk:

Literal: FOR3S0B2G1X

Literal: MOX

Literal: T4Q1000I50M2X

Wait: SRQ

Listen:

Variable Z

(2) Rout #6: Control I

Exec Rout #4: MS/EC(1)

Exec Rout #5: MS/EC(2)

(3) Rout #5: MS/EC(1)

Set Device: PAR

Talk:

Literal: DCL

Wait: Delay

Talk:

Literal: SETI 30,-6; TMB 1000; LP 999; I/E -3

Wait: Delay

Talk:

Literal: NC; Cell 1; TC; WCD

Set Device: Meter

Talk:

Literal: FOR3S0B2G1X

Literal: M0T4Q100I50M2X

```
Wait: SRQ

Listen:

    Variable Z

End-Routine

Rout #4: MS/EC(2)

Set Device: PAR

Talk:

    Literal: DCL

Wait: Delay

Talk:

    Literal: SETI 0,-6; TMB 1000; LP 999; I/E -3

Wait: Delay

Talk:

    Literal: NC; Cell 1; TC; WCD

Set Device: Meter

Talk:

    Literal: F0R3S0B2G1X

    Literal: M0T4Q100I50M2X

Wait: SRQ

Listen:

    Variable Z

End-Routine
```

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