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Electrochemically Controlled Release of Drug Ions from Conducting Polymers

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The binding and release of organic ions from conducting polymer films can be controlled electrochemically.

The redox properties of conducting heterocyclic polymers like polypyrrole are central to many applications of these materials. For this reason the electrochemistry of thin films of these polymers has received a lot of attention. We became interested in these materials for use in electrically controlled ion binding and delivery. The general idea is that the heterocyclic conducting polymers have cationic backbones and will incorporate counter anions. Upon reduction of the backbone, the anions will be flushed out. Thus, in principle one can develop devices to absorb anions of interest or to release them in response to an electric current. Our work has been spurred by the possibility of delivering drugs with a completely controlled rate.

New methods of drug delivery are of intense interest and transdermal controlled release of drugs is a field of importance.[1] Controlled release typically aims for and achieves a zero-order release rate. This ensures that the drug concentrations in vivo remain in an appropriate range over a long period of time. Our interest is in a more sophisticated system where the release could be turned on and off, and varied in some appropriate way. It might, for example, be used to respond to metabolical or diabolical changes. One approach to this problem is to use electrochemistry to drive ionic drugs through the skin. The stratum corneum prevents transport of most materials through the skin, especially ions, but an electrochemical potential

can be used to force ions through. This method is called transdermal iontophoresis.[2]

A conducting polymer would be used in such a device as the reservoir for drug ions. The ions would be metered out by controlling the number of coulombs passed through the electrical circuit which involves (at least) an electrode coated with polymer, the skin, the body fluid, the skin, and a second electrode placed on the skin nearby the first. Drug ions are forced out of the polymer and through the skin. Other ions (Na^+, Cl^-) carry the current in the body and back through the skin.

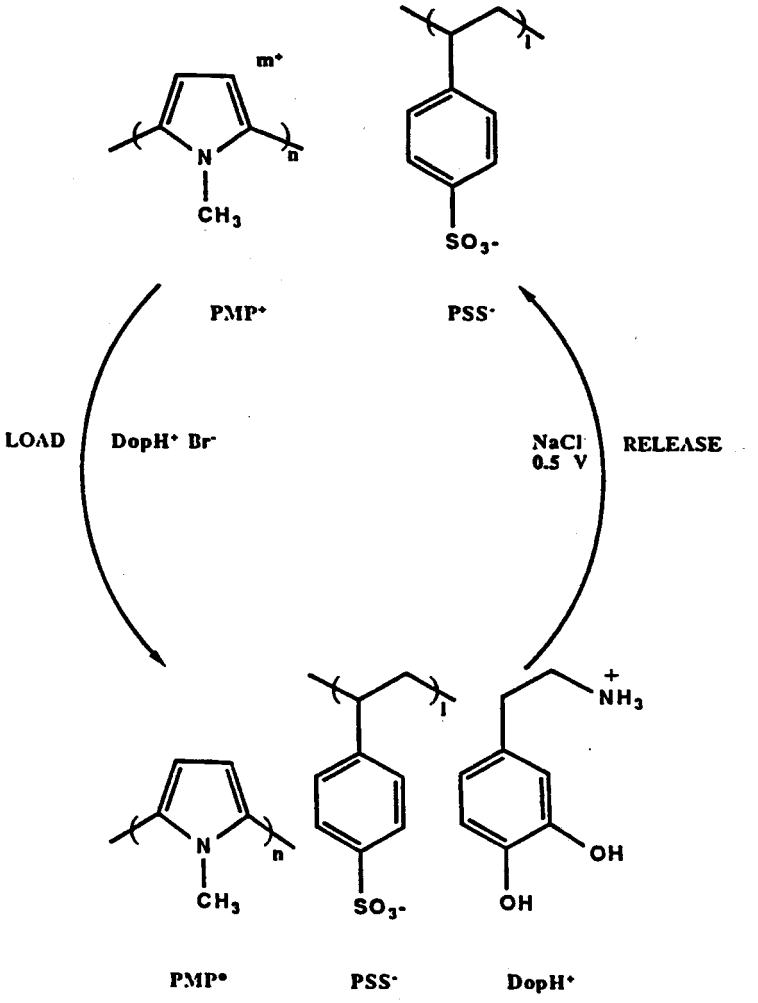
Beyond introducing the concept of iontophoresis, this paper provides references to work in this field and describes one recent example that we have worked on where electrochemically controlled dopamine release rate and thermodynamics were monitored spectroscopically.

The general idea of release from heterocyclic conducting polymers has been reduced to practice for the binding and release of anions from polypyrrole[3] and oligomeric 3-methoxythiophene.[4] Organic anions that have been bound and released include glutamate, salicylate and $TCNQ^-$. As an example,[3] a polymer film has been anodically synthesized which is composed of oxidized, cationic polypyrrole that contains $Fe(CN)_6^{3-}$ to balance the charge. When this film (on a carbon electrode) is placed in aqueous NaCl solution, the $Fe(CN)_6^{3-/4-}$ species remain strongly bound in the film unless the potential of the film is made as negative as -0.5 V. At -0.5 V $Fe(CN)_6^{4-}$ is flushed out. If the electrode potential is sequentially pulsed to -0.4 V for short times, each pulse gives release, providing increasing amounts of ferrocyanide. Thus, release can be controlled in time.

Cation binding was achieved by preparing a conducting, composite polymer, poly(N-methylpyrrole) poly(styrenesulfonate)(PMP^+PSS^-).[5] Each component of this material was attractive for our purpose. The poly(styrenesulfonate) was expected to be strongly bound in the film and chemically inert. On the basis of literature reports of poly(N-methylpyrrolylium) "doped" with small anions, this polymer's electrochemical properties were appropriate, and considering the redox potentials, we expected reduced poly(N-methylpyrrole) to be somewhat more stable than polypyrrole in air.

For our drug delivery experiments, protonated dopamine was the cation of choice. Because it is a protonated amine, the binding and release of dopamine serves as a model for an extremely large class of pharmaceutically important amine and alkaloid compounds. Dopamine is neurotransmitter and is itself of biological and medicinal interest.

Initial electrochemical studies showed that PMP^+PSS^- could be formed and the composite films behaved as expected when studied electrochemically. Cathodic reduction of the film in aqueous dopamine hydrobromide at -0.6 V gave dopammonium incorporation.



The dopammonium$^+$, PMP°, PSS^- electrode was then placed in aqueous NaCl. The electrode potential was stepped to 0.5 V (SCE) for 1 min. Dopamine was released and identified electrochemically in the solution. It was only slowly released by ion exchange if the electrode potential was not stepped positively.

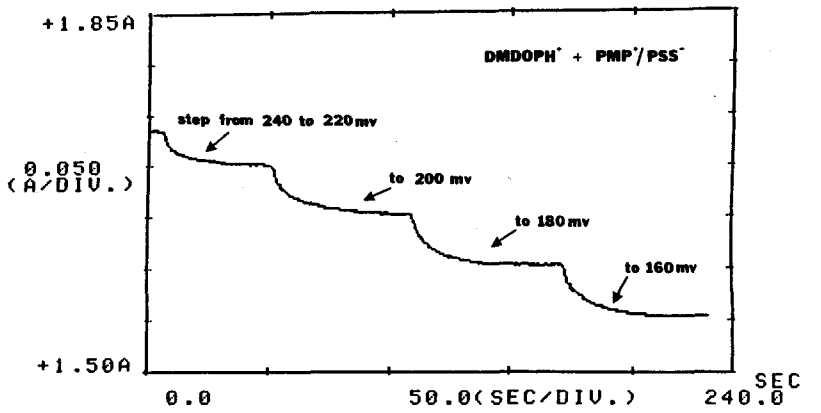


FIGURE 1 Absorbance at 277 nm from a solution of aqueous dopamine hydrobromide in contact with PMP^+PSS^- at various potentials (SCE).

Spectroscopic experiments used a thin layer cell in which a pair of Pt electrodes were fit into a standard UV cell with a gap of 2 mm between them. An aqueous solution of dopamine or dimethyldopamine ($DMDOPH^+$) (which is more stable under these conditions) filled the gap, and a SCE reference with a micro-salt-bridge tip was

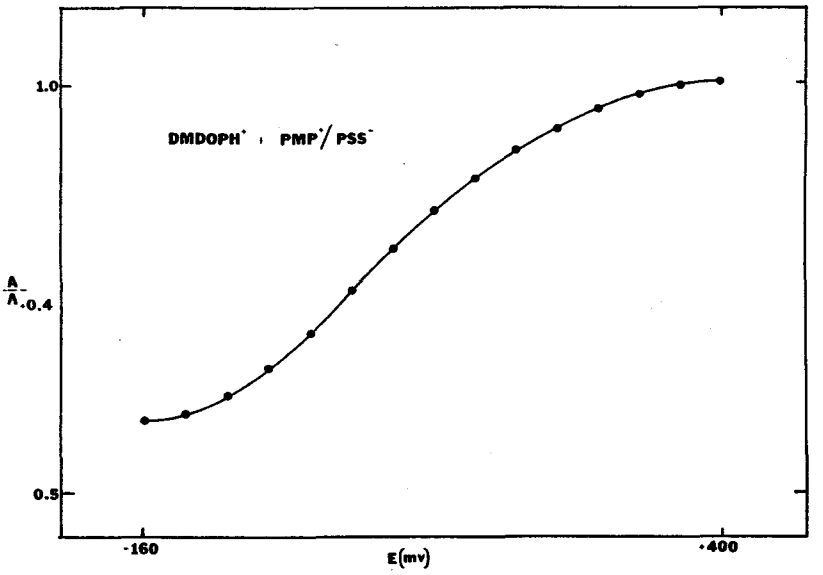


FIGURE 2 Absorbance at 277 nm measured at equilibrium as E varied for an aqueous ($DMDOPH^+$) solution in contact with PMP^+PSS^-.

inserted in the gap. The solution concentration was measured by UV through the gap. One electrode was coated with PMP^+PSS^-.

Figure 1 shows how the solution concentration responds to a change in the filmed electrode potential. The kinetics conform to a diffusion controlled process. The equilibrium between solution and a 2 coulomb film was established in a few minutes and the thermodynamics could be investigated over the range −160 to 400 mV (SCE) (Figure 2). Taking the amount of dimethyldopamine in the film as a measure of the number of reduced sites in the film, it was possible to make Nernst plots. These linear plots have slopes of 220 mV independent of film thickness. They cannot be used to get an accurate E° value because complete conversion to a stable oxidized film could not be obtained. The formal potential is estimated, however, for the binding reaction in 0.75 mM dimethyldopamine to be 170 mV.

These experiments demonstrate how electrode potential controls ion binding. The utility for drug delivery is limited by the polymer instability and remains to be evaluated fully. Such experiments are in progress using hairless mouse skin as an in vitro model.

References

1. A. F. Kydonieus and B. Berner, ed. "Transdermal Delivery of Drugs," Vols. I, II, III, CRC Press, Boca Raton, Florida 1987.
2. See for example, K. Okabe, H. Yamaguchi and Y. Kawai, *J. Controlled Release*, **4**, 79–85, (1986); W. Warwick *et al. Clinical Chem.*, **32**, 850–853 (1985).
3. B. Zinger and L. L. Miller, *J. Am. Chem. Soc.*, **106**, 6861 (1984); L. L. Miller, B. Zinger and Q. X. Zhou, *J. Am. Chem. Soc.*, **109**, 2267–2272 (1987).
4. R. Blankespoor and L. L. Miller, *Chem. Commun.*, **90**, (1985); A. C. Chang and L. L. Miller, *J. Electroanal. Chem.*, in press.
5. L. L. Miller and Q. X. Zhou, *Macromolecules*, **20**, 1594 (1987).