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ScienceDirect
Organic Electronics 9 (2008) 303–309
Organic Electronics
www.elsevier.com/locate/orgel

Electronically controlled pH gradients and proton oscillations

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Received 31 July 2007; received in revised form 21 November 2007; accepted 28 November 2007
Available online 15 December 2007

Abstract

An organic electronic ion pump, including poly(3,4-ethylenedioxythiophene) as the active material has been used to electronically control the transport of protons between two electrolytes and to change the pH of the target solution from 7 to 3 in a few minutes. The number of transported protons equals the time-integrated current between the two addressing electrodes. If no voltage is applied the leakage due to diffusion is not detectable, which indicates an overall proton delivery on/off ratio exceeding 1000. Locally, the pH drop can be even larger and the relationship between the proton delivery rate of the pump and proton diffusion in the electrolyte forms pH gradients. If the device is instead addressed with short pulses, local pH oscillations are created. The transport of protons presented here can be extended to other small sized ions, which in combination with the biocompatibility of the delivery surface make the device promising for cell communication studies and lab-on-a-chip applications.

PACS: 81; 82.35Cd; 82.45−h; 87

Keywords: Electronic ion pump; Conjugated polymer; pH; Ion oscillations

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1. Introduction

In biology, intra- and intercellular communication depend to a large extent on spatially as well as temporally regulated ion fluxes and gradients [1,2]. Such ionic signals often have an oscillatory character, thus creating specificity for diverse cellular mechanisms. This is exemplified by neurotransmitter exocytosis, which is triggered within microseconds and, at the other end of the scale, cell proliferation and fertilization with periodicities of several hours [3].

Living organisms are critically dependent on the physiological proton concentration. The intracellular pH levels of the cytosol and different organelles are crucial for the function of most macromolecules in our body and membrane gradients, created by proton pumps [4], are necessary for the cellular metabolism via the respiratory chain. The pH is typically close to 7 [5,6] but can vary depending on specific functions of intracellular compartments.

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doi:10.1016/j.orgel.2007.11.011

In e.g. the phagosomes of immune cells, the pH can be as low as 5.5 to create a lethal environment for pathogenic microorganisms [7,8]. Also, as studied by e.g. Wolf and coworkers [6,9], the pH in the extracellular microenvironment is an important regulator of many cellular functions and interactions and can decrease to five close to tumor cells. The most acidic extracellular environment in the body is the stomach, where the very high proton concentration (pH 2) helps in the digestion of food [10].

Apart from actuating cellular responses, induced gradients and fluctuations in pH have many other potential applications regarding e.g. peptide organization [11], interfacial properties [12] and isoelectric separation [13].

Similarly to biological systems, electrochemical organic electronic devices utilize ions as information carriers [14,15]. Conjugated polymer–polyelectrolyte systems, which can work as both ionic conductors and electron-to-ion transducers are therefore well-suited materials for electronic control of biological systems. In addition, the inherent biocompatibility [16,17] of many such polymers in combination with the ease (ultimately low cost) of manufacturing on flexible and transparent substrates, make them promising candidates for single-use bioelectronic applications. Conjugated polymer electrodes have therefore been explored extensively in the delivery devices to offer electronic control of the release of charged species [18–21]. Particular interest has been devoted to electrically trigger the delivery of bio-relevant ions to regulate various physiological mechanisms and overall signaling in biological systems. These electrodes typically operate according to the principle that the charged (bio-)molecule is to a varying extent imprisoned inside the polymer bulk, as predicted by the oxidation state of the conjugated polymer [21–23]. When the electrode is electrochemically switched, its volume, water content and charging character changes, and the coupling to the source molecule is altered. So, in one oxidation state the molecule can more freely diffuse out from the polymer and induce desired effects in the adjacent biological system. However, such electrodes typically suffer from a number of limitations. First, the spontaneous ion exchange in between the electrode and the target fluid is high independently of the oxidation state of the polymer. This reduces the on/off ratio. Also, the electrodes can in general store a rather low overall concentration of the charged source species. This limits these electrodes to applications, in which the source species has strong therapeutic effect already at very low concentrations. Third, there is little correlation between the electronic signal (current or voltage) applied to the electrode and the amount of ions emitted out from the polymer surface, which makes it difficult to deliver an exact dose. The ultimate drug delivery electrode must fulfill several requisites, the most important ones are: perfect match between the addressing signal and the release rate over time and the possibility to entirely shut off the release of charged species during desired moments [19]. With such characteristics, the electronic delivery device can produce oscillations of the source species at high enough concentrations matching the signaling levels of biology.

We have in earlier work [24] developed an organic electronic ion pump to, as a first step, gain electronic control of ion homeostasis of individual neuronal cells. Here, we utilize the organic electronic ion pump to create electronically controlled pH gradients and local oscillations on single plastic chips, without the need for mechanical valves and pumps that create convection at the point of delivery. The ion pump includes a delivery electrode that can be regenerated via electrophoretic transport of protons from an acidic source. In this configuration, we obtain improved delivery rates as well as on/off ratios as compared to prior work.

2. The ion pump

The basis of the organic electronic ion pump is a plastic foil covered with a 200 nm thin film of the conjugated polymer poly(3,4-ethylenedioxythiophene) (PEDOT) doped with polystyrene sulfonate (PSS). This polymer–polyelectrolyte system is a very common material for use in electrochemical devices since it is stable in the oxidized state and has a relatively high ionic and electronic conductivity [25,26]. Examples of such devices made from PEDOT:PSS or similar materials include displays and smart windows [27–29], transistors and logic circuits [30], surface wettability switches [31,32] and sensors [33,34], all of which could potentially be integrated on the same plastic sheet.

In the case of the ion pump used here, the film of PEDOT:PSS was patterned into four electrodes, labelled A–D, as shown in Fig. 1a. The region between electrode B and C has been chemically over-oxidized and is therefore ionically but no longer electronically conducting [35]. On top of the polymer film, a hydrophobic layer of SU-8