TOWARDS AN IMPLANTABLE PULSED MODE ELECTROLYTIC DRUG DELIVERY SYSTEM
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ABSTRACT
This work presents a prototype of an implantable drug delivery system that delivers pulsed doses of a low solubility drug by pulling bodily fluid into a reservoir with the drug in solid form, allowing the drug to dissolve to its maximum concentration, and then ejecting the drug laced fluid back into the tissue. The cyclical actuation of the drug delivery system is performed using an electrolytic pump. By periodical pulsed pumping a stable and constant drug release can be accomplished, so that the effect of the delivered drug is controllable.

KEYWORDS: Electrolytic pump, Drug delivery, Platinum electrode, Displacement rate.

INTRODUCTION
Previous electrolytic pumps for drug delivery [1-2] have been operated using a liquid drug reservoir (LDR) approach, which means the drug dosing must be controlled by accurate delivery of extremely small fluid volumes. For electrolytic pumps this is complicated by the recombination of the gases back into water making long-term stable dosing difficult. The solid drug in reservoir (SDR) approach was recently developed using magnetic actuation to pump fluid in and out of a reservoir that is filled with a low solubility drug in solid form. This solves the stable dosing issue by allowing the drug to saturate the solution in the reservoir, which is then ejected to provide a single dose [3]. The reservoir can then refill and dissolve the next dose, which simplifies the delivery system's control to stable discrete doses. However, magnetic actuation complicates the system, being orientation specific, and short range, the location of the magnetic delivery system is limited.

Our drug delivery system combines a SDR systems’ simple control with the lower power and flexibility of electrolytic pump systems. The aim of this work is to produce a consistent drug release, during periodical actuation.

Figure 1: a) A cross-section view of the electrolytic pump with major system components. b) Micrograph of 400nm thick Pt electrode layout showing element width and spacing of both 100µm.

THEORY
Figure 1 (a) illustrates a general working principle of our initial prototype system. The critical component of the system is a platinum (Pt) electrode array, which were fabricated by a sputtering technique and then patterned on a silicon wafer. The corresponding design is shown in Figure 1 (b). The dimensional parameters are 100 µm in width with 100µm spacing’s and a 400 nm height. Pt electrodes are immersed in a deionized (DI) water filled pumping chamber before assembling the other components. The pumping chamber is separated from the drug reservoir by a 60µm thick membrane to avoid electrochemical interaction with body fluids. When voltage is applied to the electrodes, bubbles are generated, pressurizing the bottom chamber and pushing the membrane upwards, so that the dissolved drug can be delivered into the human body. When the power is turned off, the generated gas (H₂ and O₂) in the electrolytic reservoir recombine into water, assisted by the catalytic properties of the Pt electrodes. The recombination reduces the pressure in the pumping...
chamber and the membrane moves downward drawing body fluids into the top reservoir to dissolve more of the remaining solid drug. By repeatedly turning on and off the power, fresh drug can be dissolved and delivered periodically. For easy prototype testing a cannula is replaced by an inlet and outlet tube, which can be mechanically clamped, as shown in Figure 2.

![Figure 2: Photograph of the experimental setup and structure of electrolytic pump.](image)

**EXPERIMENTAL**

The assembled pump was mounted and evaluated using the test fixture as shown in Figure 2. The size of the holder is 2 cm : 2cm : 2 cm (length : width : height). In prospective drug delivery applications, the pump could be permanently bonded allowing the size of the structure to be significantly reduced. DC voltage is applied to the pump through two probes contacting the electrodes. A digital camera is placed in front of the setup to record the displacement rate of the pump.

**RESULTS AND DISCUSSION**

In the experiment, Nafion was uniformly spin-coated onto electrodes to form a 235 nm thin film. Figure 3 represents the flow rates of Nafion-coated electrodes compared to untreated electrodes over different applied powers ranges. We can observe that Nafion coating of the electrode to significantly improve the electrolysis efficiency, which had been previously reported by Meng’s group [4] as well.

![Figure 3: Electrolytic pump flow rate vs. applied power for both Nafion coated and uncoated electrodes.](image)

Because our system requires cyclical pumping to operate, we tested the reverse flow rate during gas recombination, as well as the pump’s cyclical operation, as shown in Figure 4. The bottom plot of Figure 4 also gives a periodic stable pumping pulse, with relatively low power consumption of 1 mW that definitely can be obtained via a wireless power transfer technique [5].

We used Solvent Blue 38 (SIGMA) as a low solubility proxy for our solid drug and measured the dose delivered per pulse by extracting the pumped fluid using a pipette and allowing the reservoir to refill with fresh water. The extracted doses were then quantified using a Picodrop Pico200 spectrophotometer and show a stable value of 2µg/dose over 7 doses as shown in Figure 5.

![528](image)
CONCLUSION

Our prototype drug delivery system can provide consistent doses from a solid drug stored in a reservoir and together with the integration of our previously developed resonant power transfer system [5] will form a drug delivery system that can be flexibly placed within the body and simply controlled without the need for any transdermal wiring. Moreover adjusting the applied power can precisely control the pumping of the liquid drug through cyclical bubble generation and recombination.

REFERENCES


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