or reduced permeation is required, an impermeable thin-film metal coating can be applied via sputter deposition while still preserving the desired mechanical compliance.

Electrodes will be arranged in an already optimized interdigitated layout to reduce the resistive path through the electrolyte. This improves pumping efficiency and reduces heat generation. In our previous work, Nafion coating of electrodes dramatically increased efficiency (~90% compared to ~50% for uncoated), linearity, and reproducibility of gas generation over time. Nafion is a polymer electrolyte with high gas solubility to allow rapid diffusion of generated bubbles away from the Pt catalyst surface and improves achievable current density by 20%. **(Reviewer response)** The electrodes are only exposed to water (electrolyte) so no electrode fouling occurs. Pt is a highly stable and inert metal that is neither reduced nor oxidized during electrolysis therefore guaranteeing electrode stability.

Robust and repeatable actuator activation with wide dynamic range: When electrical current (DC) is applied to the actuator's interdigitated electrodes, electrolysis commences and produces gas in a manner that is linearly dependent on current magnitude (Fig. 1). The resultant pressure increase deflects the bellows, coupling the pressure increase to the drug reservoir. This opens the normally-closed check valve (once the critical cracking pressure is reached) and allows drug to flow through the catheter to the site of delivery (tip surgically placed at the site of treatment). When current is removed, hydrogen and oxygen gases recombine in the presence of the platinum catalyst and the bellows returns to its starting position. The volume dosed is determined by the magnitude and duration of current application; current magnitude is linearly correlated to flow rate. The timing of delivery is controlled by the timing of current application. By combining electrolysis control of drug delivery with wireless operation, bolus, continuous, and combination dosing as well as on-demand control of dosing are possible. Precise flow rate control in the pL/min to μL/min range is achieved using current in the μA to mA range in long term studies (Fig. 1). **This wide delivery range is not possible with any existing implantable pump.**

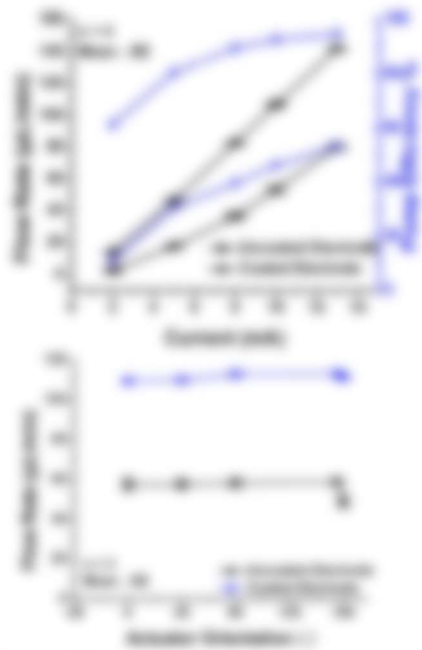

Figure 1: (top) Precise constant current control of flow rate in the μL/min range using an electrochemical bellows actuator having uncoated or Nafion coated electrodes (100 μm wide and 100 μm gap electrodes). Lower flow rates are possible at lower driving currents (data not shown). (bottom) Flow rate is independent of actuator actuation with Nafion coating.

<u>**Objective 2B: Integrate multi-component pump that is wirelessly powered and controlled**</u>

Packaging, assembly and construction requirement: Actuator configuration and supporting components are illustrated in the schematic cross-sectional view in Fig. 2. One strategy is to minimize the number of separate components and to achieve all critical requirements through a combination of off-the-shelf components and custom elements that can be produced at low cost after their initial tooling. The final assembly of components within the pump package must also be made compatible with standard sterilization techniques. EtO gas sterilization is the preferred method as minimal thermal excursions are encountered. The components include (1) electrolysis microactuator (bellows and electrodes), (2) receiving coil and electronic circuitry, (3) a molded, rigid housing, (4) a refill port, and (5) check valve. A description of these components and associated requirements follows below.

Biocompatibility requirement: The micropump must be constructed of biocompatible materials to limit undesirable immunological responses. All pump materials are medical grade including platinum,