based actuation, (2) **miniaturized form factor** for subcutaneous implantation in mice, (3) **refillability** for chronic studies (> [redacted] refills), (4) **on-demand, automated electronic control** of dosing and drug profile (e.g. zero-order or sustained), and (5) completely **wireless operation from a remote user interface**. The pump's electrolysis mechanism is the first to combine microfluidic pumping capability with wireless power transfer to enable safe, on-demand, high-accuracy dosing suitable for reliable chronic infusions in rodents. Our system can deliver a diverse assortment of drugs at the right dose, to the right tissue, and at the right time over the entire course of treatment. The technique has low heat dissipation and a wide dynamic range (1000:1[1,2]). Miniaturization is achieved through the ***innovative integration of microfabricated components with a precision 3D-printed housing*** that incorporates all components into a tiny form factor. The housing materials are coated in a thin protective Parylene C film to reduce moisture absorption, improve mechanical rigidity, and provide biocompatibility. The pump is scalable allowing larger reservoirs for veterinary and clinical applications. The reservoir is refillable by percutaneous injection through the resealable refill port[3,4] (> [redacted] punctures with non-coring 30G needle[3,4,5]). Pump refill capability is considered essential by [redacted] of potential users however there is no refillable pump on the market for use in animals as small as mice. The software interface conveniently automates operation of multiple pumps from a single workstation. Wireless operation by inductive power transfer eliminates the need for transcutaneous wires or batteries, achieves a small form factor, and enable ambulatory infusion in freely-behaving animals. Our feature set facilitates market entry by providing new opportunities to evaluate existing drugs and screen new drugs.

B. Approach

The objective of this proposal is translation of prototypes developed at the University [redacted] into manufacturable, multi-component, implantable, and wireless micro infusion pump systems suitable for accurate, safe, and humane chronic dosing studies in small animals. The FlatSync[TM] micropump consists of (1) electrolysis-based microactuator (bellows, electrodes, and electrolyte), (2) drug reservoir, (3) refill port, (4) flow control valve, (5) catheter attachment port, (6) wireless power module (receiving coil and circuitry), and (7) molded, rigid housing (Fig. 1). The pump is based on the original design developed by [redacted] for molding [redacted] drug volumes in rat and rabbit eyes and for ~1 volumes into tumor xenografts in mice[1, 2, 3, 4]. A bellows membrane separates the drug reservoir from the electrolysis reaction. Electrical current applied to the actuator electrodes results in electrolysis, the generation of hydrogen and oxygen gases[1, 2, 3, 4] and a pressure increase that deflects the bellows and expels drug through a pressure-responsive valve[3,4]. This reaction is reversible, allowing the pump to be cycled ON and OFF repeatedly. The volume delivered and dosing scheme are precisely controlled (e.g. ~0.~1 nL/min selectable flow rates) by the magnitude and duration of current (typically µA-mA) applied which is linearly correlated to flow rate[1, 2, 3, 4, 5, 6]. No electrode degradation was observed in pumps that were powered daily (> [redacted] months). Successful and reversible electrolysis within the bellows actuator was demonstrated over similar periods.

Figure 1. FlatSync[TM] micropump in cross-section. (1) electrolysis-based microactuator, (2) drug reservoir, (3) refill port, (4) flow control valve, (5) catheter attachment port, (6) wireless power module, and (7) molded, rigid housing.

This SBIR Phase I proposal addresses (1) the significant engineering challenges in enabling a collection of miniaturized pumps (up to 8) to operate within a single cage and (2) initial in vivo validation of the full multi-pump system which will significantly de-risk this technology in preparation for a Phase II proposal. Our approach targets the necessary user-derived milestones to make this innovation available for research, veterinary, and preclinical applications.

B.1 Specific Aim 1: Develop robust inductive power transfer system for orientation-independent wireless activation of multiple pumps per cage.

Rationale: Consistent and repeatable dosing performance of the battery-less pump is contingent upon reliable power transfer regardless of orientation. This must extend to each and every pump within a single cage. Therefore, we will develop an inductive powering system that enables complete pump orientation independence within an electromagnetic field and provide the ability to power multiple pumps within this field (allowing for multiple implanted animals). Pumps must be able to achieve a flow rate range of [redacted] µL/hr.

Figure 2. 3D-printed pump prototype components: pump actuator, outlet assembly, mini flex circuit, and coil.

Preliminary Results: In our NSF Phase I SBIR, we evaluated several designs through rapid prototyping by stereolithography to produce compact packaging of the microactuator, drug reservoir, and pump housing (Figs. 1 &