2.2 Specific Aim 2: Demonstration of consistent wireless performance of single and multiple pumps

Rationale: Accurate and reproducible flow rate across micropumps must be established using the wireless hardware and software interface in preparation for *in vivo* demonstration in Aim 3. Wireless inductive power transfer to implanted pumps is achieved using a base station placed below the animal cage. This approach eliminates the need for wires or batteries, achieves a small form factor implant, and enables ambulatory infusion in freely-behaving animals. LabVIEW-based software will automate operation of multiple implanted pumps from a single workstation (Fig. 2).

Table 1: End user requirements and performance-based success criteria

[redacted]	[redacted]	[redacted]
[redacted]		
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]		
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Preliminary Results: Physical and functional pump requirements were determined through primary interviews of animal researchers and technicians in academia and industry familiar with current implantable infusion pumps and mouse physiology (Table 1). Specifically, the pump must be [redacted] of the body weight (~ 1ml of an adult mouse (~ 30g)) and sized for minimally invasive subcutaneous implantation (drug payload of [redacted]). We also determined that the pumps must operate within [redacted] cm of the cage floor in order to fully cover the rodent living space. Successful delivery of [redacted] from a wireless pump prototype was demonstrated (data not shown) with the flow regulation capability of the integrated valve verified. This demonstration was based on a single pump/base station approach.

Approach: Pre-calibrated pump performance will be used to validate delivery under the following methodology. Flow rate will be calculated from measurements of pumped volume through a calibrated micropipette. a 1 μL air bubble will be introduced into the pipette and tracked at preset time intervals (1-30 minutes) by an automated image capture apparatus. Operation under backpressure (11 mmHg is the venous pressure of the mouse) will be evaluated (1-20 mmHg). For each flow experiment, a minimum of 5 pumps will be used and each in at least four trials for each test condition. For all experiments, averages and standard errors are calculated and statistical differences evaluated by student t-test and ANOVA with control data obtained using wired pumps in Aim 1 ($p < 0.05$).

Once the stability of the wireless power link is established, benchtop characterization of pump performance (using 1 pumps powered by a single base station) will be performed as outlined in Table 2 to meet the system requirements and success criteria detailed in Table 1.

Expected outcomes, potential problems, and solutions: Any fluctuations in primary coil current are nullified through the pump's receiving circuitry, we expect at least [redacted] flow rate accuracy over the entire volume range for up to 1 pumps powered by a single base station. Stiction of the valve, if present, will be avoided with anti-stiction coatings, surface treatments, and by keeping the valve hydrated. It may be necessary to implement a set of calibration curves linking dosing parameters to flow rate. These curves can be easily embedded and modified within the LABVIew software.

We expect this system will be compatible with a variety of testing environments. With the low power requirements of electrolysis-based actuation and our previous experiences, we expect the inductive link will provide sufficient power under all cases (coil orientation and distance from primary). In the event of interference between adjacent base stations, the magnetic flux output will be tuned so as to limit significant coupling within a calibrated volume above the base station. However, interference is not anticipated based on previous experience. Future configurations of the system may also be made compatible with rack-style animal housing systems for large-scale automation. Modifications will focus on increased space-efficiency of the powering system and ease of integration with existing housing systems.

Table 2: Pump system verification

[redacted]	[redacted]
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[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

2.3 Specific Aim 3: *In vivo* demonstration of group wireless dosing and bioluminescence imaging

Rationale: Field deployment is proposed to verify *in vivo* performance, biocompatibility, and reliability of the the FluidSync™ micro infusion system. Transgenic mice in which the testes express the firefly luciferase gene will be implanted with micropumps, group housed into a single