for a subcutaneous placement in the back of the animal (personal communication). Drug reservoir volume requirements are dictated by typically flow rates utilized in mice experiments (0.1-1 μL/hr). Reservoir volume of 200 μL is suitable for both acute and chronic experiments. The size and volume requirements for rodents validated by multiple customer interviews are summarized below (Table 1). The complete pump system will be researched and developed to meet these customer-derived specifications.

Table 1. Volume and size requirements

Weight (g)	Volume (μL)	Length (mm)	Width (mm)	Height (mm)
< 3	200	18	15	6

Refillability requirement: The ability to refill the pump is a key design requirement and is considered to be essential by 90% of all potential users. There is no refillable pump on the market for use in animals as small as mice. Currently customers are forced to perform **multiple surgical procedures** per animal for experiments exceeding 10-15 days. This makes the most high-value experiments cumbersome, expensive, and risky to run due to the repeated risk of infection. To address this unmet need, the FluidSync pump will integrate a re-sealable silicone-based refill port that allows percutaneous needle access to refill the reservoir. This port design was demonstrated to withstand multiple refill injections (> 20) with non-coring 30G needles while maintaining a liquid-tight seal[illegible]. The port is integrated directly into the pump housing and can be easily detected by the animal handler through palpation.

Low power, space-efficient actuator requirement: The size and form of the micropump must be compatible with subcutaneous implantation. The pump mechanism and associated powering scheme are the single most important factors impacting implant size. Achieving actively controlled dosing in a small package necessitates low power (ultimately battery-less) operation; the design specifications of our pumping system are based our extensive experience in the design of implantable mini- and micropumps[illegible]. The core microactuator technology has been de-risked through previous research and development efforts performed at the University of Southern California.

The FluidSync pump features an electronically activated actuator that operates based on electrolysis. While many other actuation mechanisms are possible (e.g. shape memory alloy[illegible], piezoelectric[illegible], electrostatic[illegible], and thermopneumatic[illegible]), electrolysis was selected as the pumping actuation mechanism for its compelling advantages. Electrolysis, the oldest example of direct conversion of electrical energy to pressure-volume changes[illegible], is also the only form of actuation to combine the following features: low power consumption, low heat dissipation, large displacement (>1000% volume expansion), and reversibility (position of actuated element can be repeated returned to initial starting position)[illegible]. Electrolysis-based actuators possess simple structure (only one moving part - a bellows) and small footprint. The actuator consists of an interdigitated microelectrode pair (platinum) immersed in an electrolyte (water) and contained in a flexible bellows diaphragm (Parylene C). Construction is straightforward. Together, these characteristics make high performance MEMS electrolysis actuators ideal for precision pumping applications such as drug delivery[illegible].

Bellows were selected over other diaphragms (flat, dome, and corrugated membranes[illegible]) for their superior deflection with minimal driving force, low intrinsic stress, and mechanical stability[illegible]; this maximizes drug volume that can be displaced from the reservoir. Bellows offer optimal mechanical performance for drug pumping with minimal increase in dimension. Furthermore, the increased deflection capability allows significantly greater volume displacement and thus permits greater access of the drug volume which is necessary to minimize the frequency of refills. Our **key enabling innovation** is a patent-pending process to create **high expansion microscale Parylene C bellows.** Due to the inherent flexibility of the polymer (Young's modulus of Parylene is 4 GPa vs 110 GPa for Ti) our bellows are capable of far greater displacement (stroke volume) than a metal bellows of the same size. When additional mechanical rigidity