FINAL REPORT

AI-Enhanced MEMS Drug Delivery Catheter

SATHWIK CHOWDARY MERLA
TIRTH PATEL
YASHWANTH RAGHAVENDRA MUPPANENI

College of Engineering

Northeastern University

Microelectromechanical Systems

Professor Marco Colangelo

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Abstract:

This Final report highlights the current progress in developing an AI-enhanced MEMS catheter for controlled drug delivery. This bellows-based microfluidic pump with real-time sensing and AI sensor fusion is integrated for precise flow control. Preliminary simulations demonstrate the catheter's ability to deliver target flows under dynamic physiological pressures while compensating for sensor noise and environmental variability.

Introduction:

The capability for direct and accurate delivery of drugs to the target site can, in fact, reduce side effects to a very low level and enhance treatment effectiveness. MEMS-based actuators open the possibility of integrating tiny pumps into catheters for use in minimally invasive procedures. Our work is centered around the idea of uniting a bellows-driven microfluidic pump with AI-powered sensor readings for exact flow control in changing physiological conditions.

Objectives:

- Model and simulate bellows-based MEMS actuator behavior.
- Develop corrective AI algorithms for sensor measurements.
- Implement adaptive PID control to maintain target flow rates.
- Visualize device operation and performance through plots and dashboards.
- Analyze preliminary results to guide design improvements.

Methods/Approach:

1. Device Design

Bellows Actuator

- Parylene C material (10 μm thickness) with 2 convolutions and 50–100 μL volume capacity providing electrolysis-driven expansion for drug pumping

Electrodes

- Platinum/Titanium bilayer (200/50 nm) in interdigitated pattern serving as water electrolysis catalyst for gas generation

Membrane

- Parylene C substrate (5 μm thickness) with 50 mm² surface area providing stable electrode foundation

Reservoir

- Silicone rubber construction with 100–300 μL capacity for secure drug storage and biocompatibility

Check Valve

- MEMS/Spring-loaded mechanism with <10 kPa cracking pressure preventing backflow and ensuring unidirectional delivery

Catheter

- Silicone tubing with 0.3–0.5 mm inner diameter and 10–30 mm length enabling targeted drug delivery directly to tumor site

2. Fabrication Process

The complete device fabrication involves three sequential process flows: (1) electrode base fabrication, (2) Parylene bellows fabrication, and (3) assembly and integration. All processes use standard MEMS cleanroom techniques and employ biocompatible materials. The total time for fabrication per batch is 8-12 days.

Process flow 1: Fabrication of electrode base

Step 1: Preparation of Silicon Wafer:

- Four-inch <100> Si wafers (500 μm thickness) are first cleaned by the RCA standard protocol: RCA-1 solution ($NH_4OH:H_2O_2:H_2O$ = 1:1:5) at 75°C for 10 min, DI water rinse, followed by RCA-2 solution ($HCl:H_2O_2:H_2O$ = 1:1:6) at 75°C for 10 min, finishing with dehydration bake at 150°C for 30 min.

Step 2: Sacrificial Layer Deposition:

- Copper, 50-100 nm, is deposited by an electron beam evaporator at a base pressure of 1×10^{-6} Torr, with a deposition rate of 2-5 Å/s at room temperature. This is a sacrificial layer that enables release from the silicon substrate later.

Step 3: Parylene C membrane deposition (5 μm)

- Parylene C is deposited by chemical vapor deposition, SCS Labcoter. Parameters include: chamber pressure 20-30 mTorr, vaporisation temperature 150°C, pyrolysis temperature 690°C, dimer charge 5-10 g, deposition rate ~0.5 μm/hr and total time 2-3 hours. The CVD process yields conformal, pinhole-free coating.

Step 4: Depositing the Metal Electrode

- A Ti/Pt bilayer is deposited by DC magnetron sputtering without vacuum break. For the Ti layer: base pressure 5×10^{-7} Torr, Ar pressure 3 mTorr, 150 W DC power, rate 2 Å/s. The thickness of the Ti layer is 50 nm, and the Pt layer is 200 nm at the same conditions, with a rate of 1-2 Å/s. The function of the Ti is adhesion, while Pt acts as the catalyst for electrolysis.

Step 5: Photolithography and Lift-Off

- Dual-layer liftoff process: LOR 3A underlayer (300 nm, 3000 rpm, 180°C/5 min) and SPR 220-3.0 imaging layer (3 μm, 3000 rpm, 115°C/90 sec). UV exposure at 365 nm: 200-250 mJ/cm^2 through chrome photomask defining the pattern of interdigitated electrodes (width and spacing of fingers are 50-100 μm, 10 pairs). Development in MF-319 for 60-90 sec. Liftoff in Remover PG at 80°C for 2-4 hours with gentle agitation. Rinse in acetone, IPA, and DI water.

Step 6: Transfer to PEEK Substrate

- Flexible PEEK film (100-500 μm thickness) is prepared by O_2 plasma treatment at 100 W for 1 min to enhance adhesion. Parylene membrane with patterned electrodes is bonded to PEEK using medical-grade adhesive transfer tape by applying 50-100 kPa pressure for 30 s, followed by curing in a 60°C oven for 1 hour. Silicon wafer is then released by etching the Cu sacrificial layer in the $FeCl_3$ or APS solution for 5-30 min, resulting in a flexible electrode assembly on rigid PEEK support. Silicon wafer is cleaned and reused.

Process Flow 2: Parylene Bellows Fabrication

Step 1: Master Mold Fabrication

- Profile of the bellow: diameter 5-8 mm, height 3-5 mm, 2 convolution(s) CNC machined, or 3D printed with surface finish <1 μm Ra.

Step 2: Silicone Rubber Mold Casting

- To fabricate a negative mold cavity, PDMS (addition-cure silicone) is mixed in a 1A:1B ratio, degassed for 5 min at 0.1 Torr, poured over a master, and cured at 60°C for 4 hours.

Step 3: PEG Bellows Form Creation

- Polyethylene glycol will be heated at 70-80°C until molten, poured into a silicone mold, cooled slowly to room temperature in 1-2 hours, and demolded to obtain the solid PEG bellows form. The molecular weight of polyethylene glycol is 6000-10,000 Da.

Step 4 - Parylene C Deposition on PEG: 10 μm

- PEG form is coated with Parylene C via CVD (parameters same as Step 3 of Process Flow 1 but dimer charge at 10-15 g, deposition time at 4-5 hours). All PEG surfaces are covered with this thin and conformal coating.

Step 5: PEG Dissolution

- Parylene-coated PEG is soaked in hot DI water at 85°C for 30-60 min with gentle agitation. Changes of water multiple times (3-4×) are performed to fully remove PEG, yielding an empty hollow Parylene bellows structure. Critical point drying or careful N_2 drying prevents collapse.

Step 6: Bellows Filling

- Hollow bellows is filled with degassed DI water 50-100 μL via syringe with 25-30 G needle. Remove air bubbles and seal the fill port with UV-curable adhesive - cure 2 min at 365 nm.

Process Flow 3: Assembly and Integration

Step 1: Adhesive Film Application

- Double-sided pressure-sensitive adhesive (3M 9502, 50-100 μm thickness) is laser-cut into ring pattern (OD 8 mm, ID 4 mm) and applied to Parylene membrane over electrodes.

Step 2: Bellows-to-Base Bonding

- Water-filled bellows are aligned to electrode base using a fixture or microscope. Uniform pressure (50 kPa) is applied for 30 sec. Cure the assembly at 60°C for 30 min.

Step 3: Epoxy Reinforcement

- Seal perimeter is then covered with biocompatible epoxy (EPO-TEK 301), which after curing at a temperature of 60°C for 2-4 hours develops a hermetic seal with less than 1 kPa/min leak rate as verified by the pressure decay test.

Step 4: Electrical Connections

- Fine wires (30-36 AWG) are bonded to the contact pads using conductive epoxy (EPO-TEK H20E), cured at 150°C for 30 min. Strain relief was added with non-conductive epoxy.

Step 5: Reservoir Integration

- Medical-grade silicone reservoir (NuSil MED-6015, 100-300 μL capacity); cast with rounded contours. Insert actuator assembly into reservoir opening and seal with PDMS, cure at 60°C for 1 hour. Step 6: Valve and Catheter Attachment A MEMS or spring-loaded check valve with a cracking pressure below 10 kPa is fitted at the reservoir outlet. Silicone catheter tubing (ID: 0.3-0.5 mm, L: 10-30 mm) is attached using medical adhesive to secure. The complete assembly is pressure-tested to verify leak-free operation.

3. Operating Principal

Electrolysis-based actuation mechanism:
The MEMS drug delivery device is electrochemically actuated by the electrolysis of water. The entire actuation cycle consists of six sequential steps to allow for controlled, repeatable drug delivery.

- Step 1: Current Application
  A constant DC current of 1.0 mA is applied across Pt/Ti interdigitated electrodes (10 pairs, 50-100 μm width/spacing), which are immersed in DI water within the sealed bellows chamber. Operating voltage: 3-5 V DC; power consumption: ~3 mW.

- Step 2: Electrolysis of Water
  Electrochemical decomposition at the electrode surfaces:
  Overall Reaction: $2H_2O(l) \rightarrow 2H_2(g) + O_2(g)$
  Anode: $2H_2O(l) \rightarrow O_2(g) + 4H^+ + 4e^-$ ($E° = +1.23$ V)
  Cathode: $4H^+ + 4e^- \rightarrow 2H_2(g)$ ($E° = 0.00$ V)
  The generation rate of gas fulfills Faraday's law: $dn/dt = I/(zF)$, where $z = 2.67$ electrons/molecule, $F = 96\,485$ C/mol.

- Step 3: Development of Pressure
  According to the ideal gas law, gas accumulation increases internal pressure:
  $P = nRT / V$
  where n = moles of gas, R = 8.314 J/(mol·K), T = 310 K (body temperature), V = bellows volume (m^3). Pressure finally overcomes elastic resistance of the bellows and back pressure of tissues.

- Step 4: Bellows Expansion
  Internal pressure forces the Parylene bellow (10 μm walls, 2 convolutions) to expand vertically from 4 mm -relaxed-to 8 mm -expanded-, corresponding to ~100% height increase.

- Step 5: Drug Elimination
  Bellows expansion displaces the drug solution from the reservoir through a check valve-a device that prevents backflow-through a catheter (ID 0.3-0.5 mm) to the tumor site. The flow rate follows Poiseuille's law: $Q = \pi r^4 \Delta P/(8\eta L)$, where ΔP = bellows pressure - tissue backpressure.

- Step 6: Gas Recombination & Reset
  When the current is turned off, H_2 and O_2 spontaneously recombine on the surface of the Pt catalyst:
  Recombination: $2H_2(g) + O_2(g) \rightarrow 2H_2O(l)$ In a case where the pressure is decreased, the bellows will relax to 4 mm and therefore prepare for the next cycle.

4. Physics and Flow Modeling

- Gas generation by electrolysis is used to drive bellows expansion.
- Pressure-volume behavior modeled using the ideal gas law.
- Fluid flow modeled with Poiseuille approximation:

$$Q = \frac{P_{net}}{R_{hydro}}$$

5. Sensor and AI Modeling

- Sensors used: hot-film for flow, RTD for temperature, glucose sensor for concentration.
- AI Model: Random Forest regressor trained to correct sensor noise and estimate true flow.
- Control: Adaptive PID adjusts pump input to maintain target flow under changing backpressure.

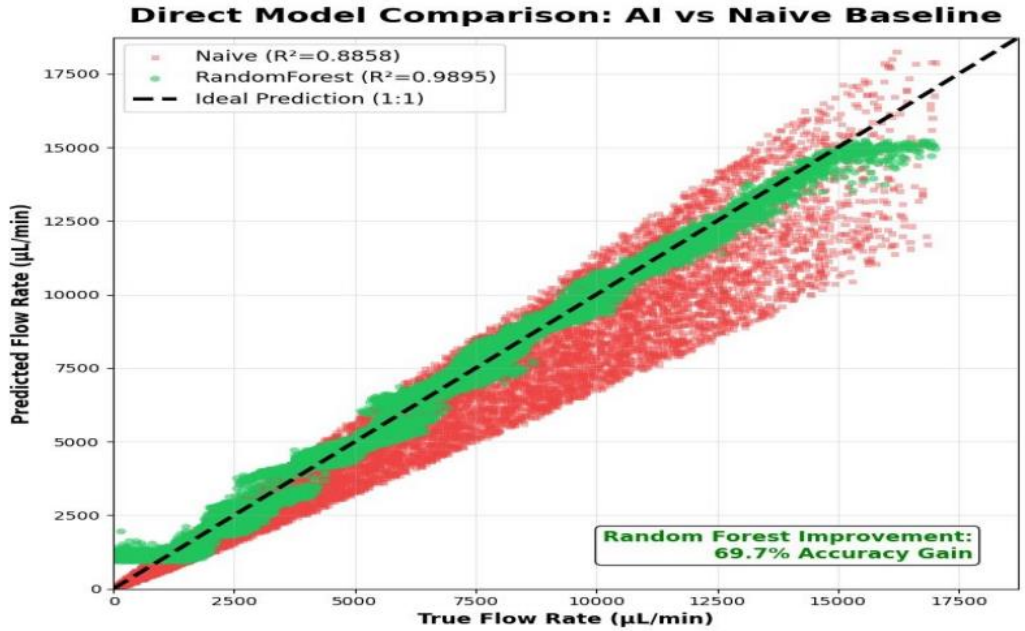
6. Simulation

- Environment: Python with 0.05 s time steps over 80 s duration.
- Scenarios: Static and dynamic pressures, different target flows.
- Outputs: Flow rate, bellows pressure, reservoir volume, sensor readings, and glucose concentration.

Preliminary Results:

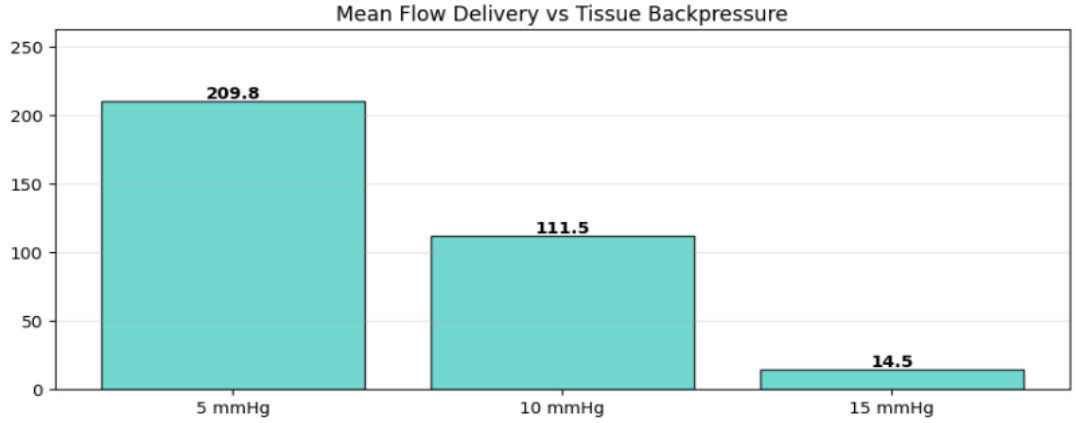
6.1. Sensor Fusion Calibration Accuracy (Scatter Plot)

- The scatter plot compares the "Standard Sensor" (red, uncorrected) with the "AI Sensor Fusion" (green, corrected) against the true flow. The AI sensor fusion significantly reduces measurement errors and shows much closer alignment with the true flow values.



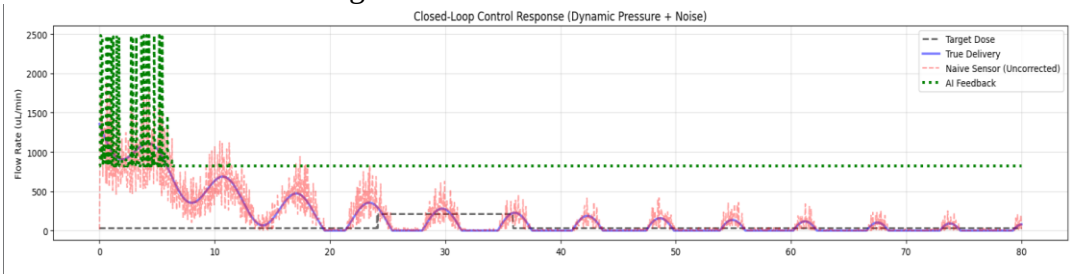
6.2. Mean Flow Delivery vs. Tissue Backpressure (Bar Chart)

- The bar chart displays, for the same pump, its performance under tissue backpressures of 5, 10, and 15 mmHg. The device maintains near-target delivery even as backpressure increases, demonstrating consistent performance.



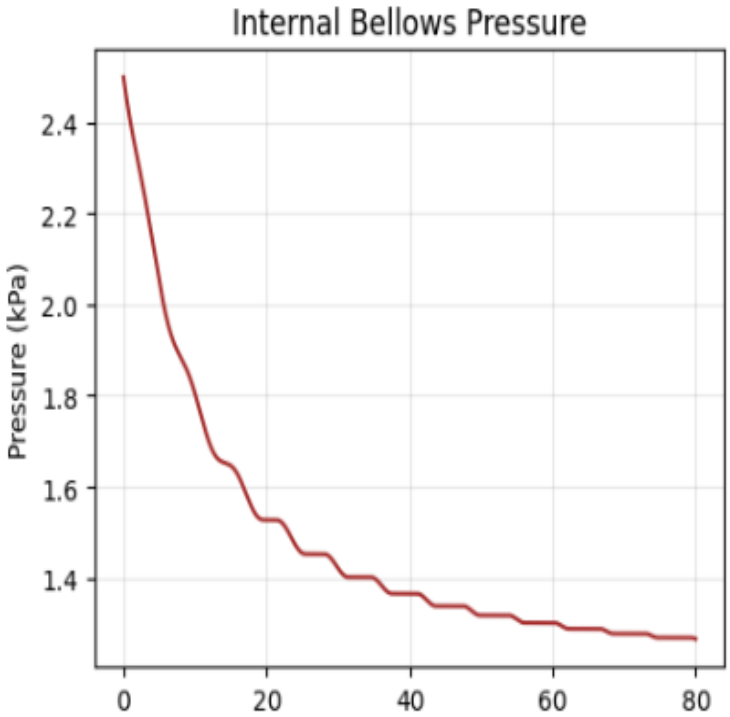
6.3 Closed-Loop Control Response (Time Series)
The graph below summarizes the main performance of:

- Target Dose (black dashed line)
- True Delivery (blue solid line)
- Naive Sensor Reading
- AI Feedback Corrected Reading

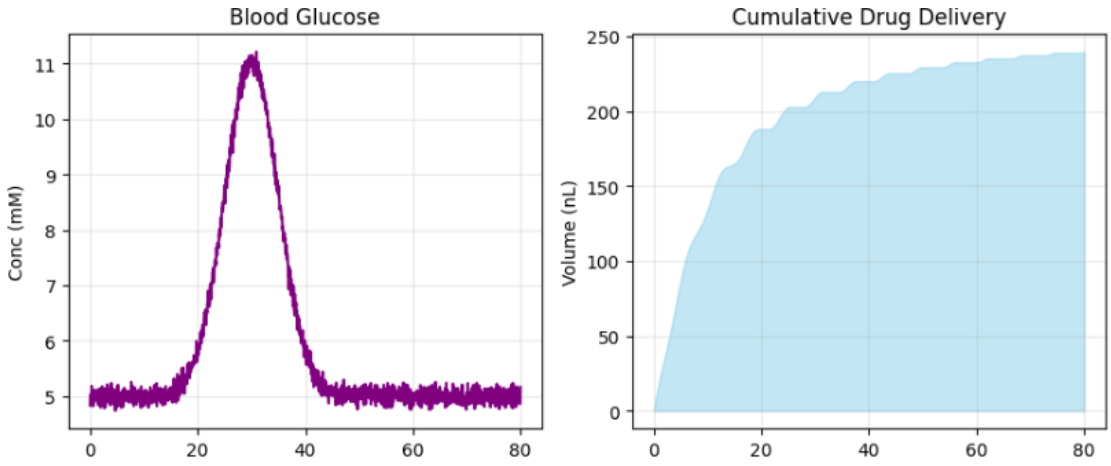


The bottom row shows system diagnostics, including:

- Internal Bellows Pressure (kPa)



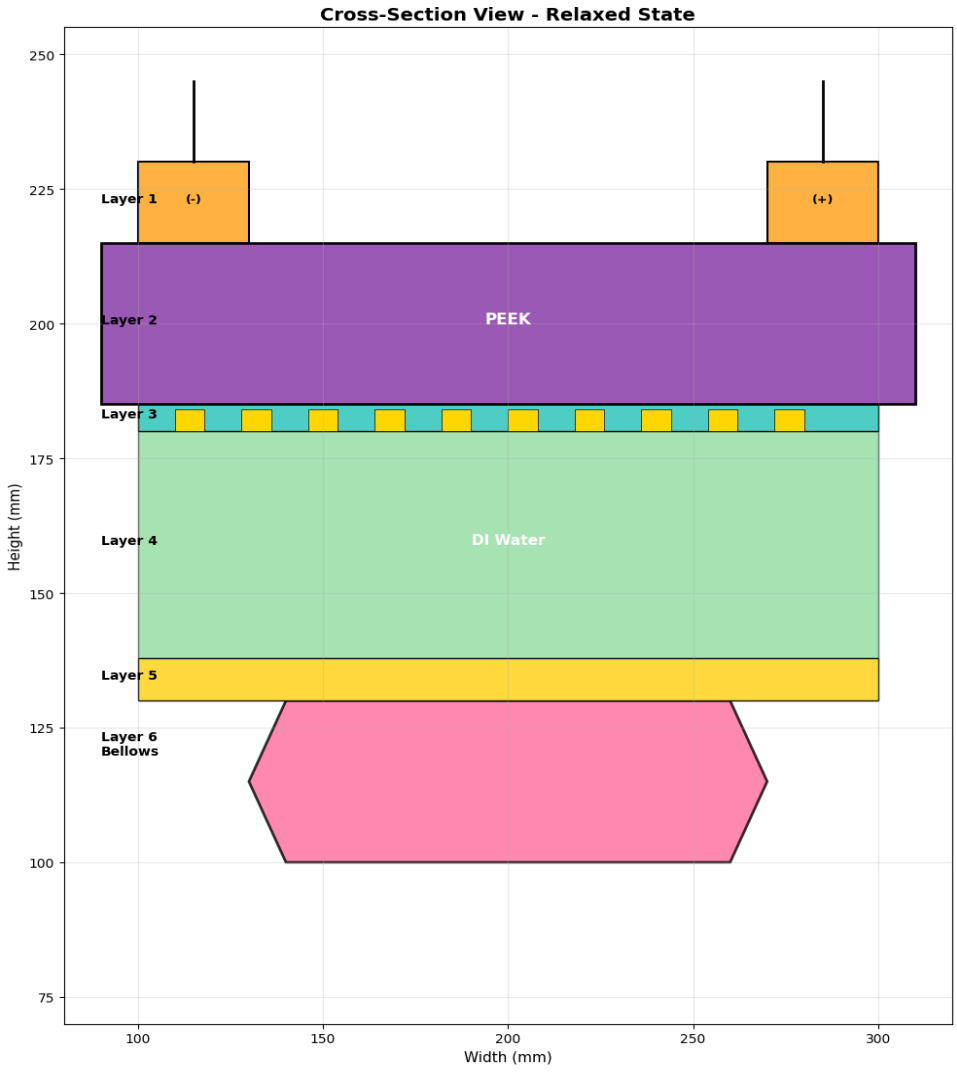
- Blood Glucose Concentration (mM)
- Cumulative Drug Delivery (nL)



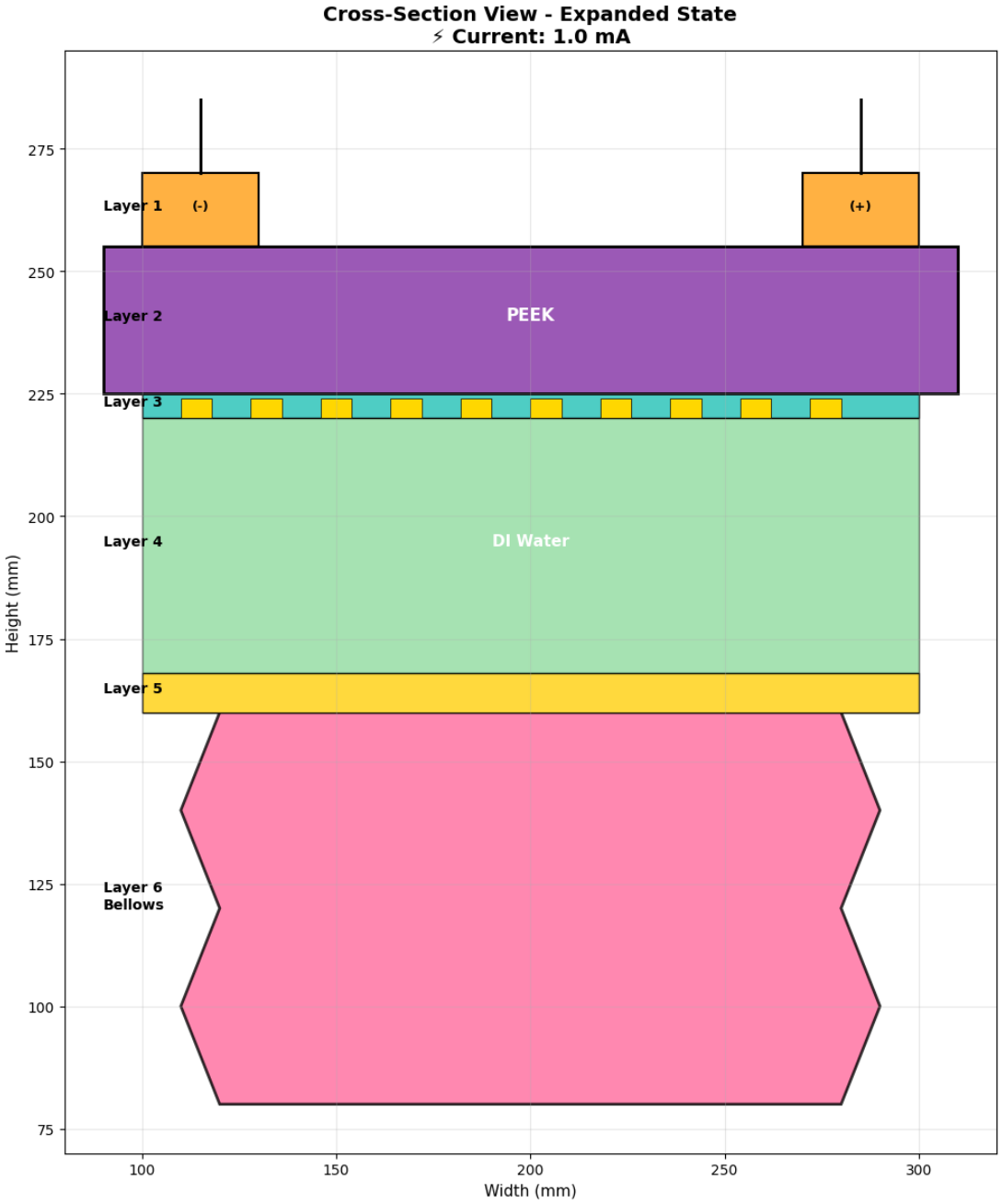
This demonstrates how the closed-loop system corrects errors and maintains precise drug delivery.

6.4 Device Cross-Section Views

- Relaxed State: Shows internal layers (contacts, PEEK, membrane, DI water, bellows) when the pump is off.

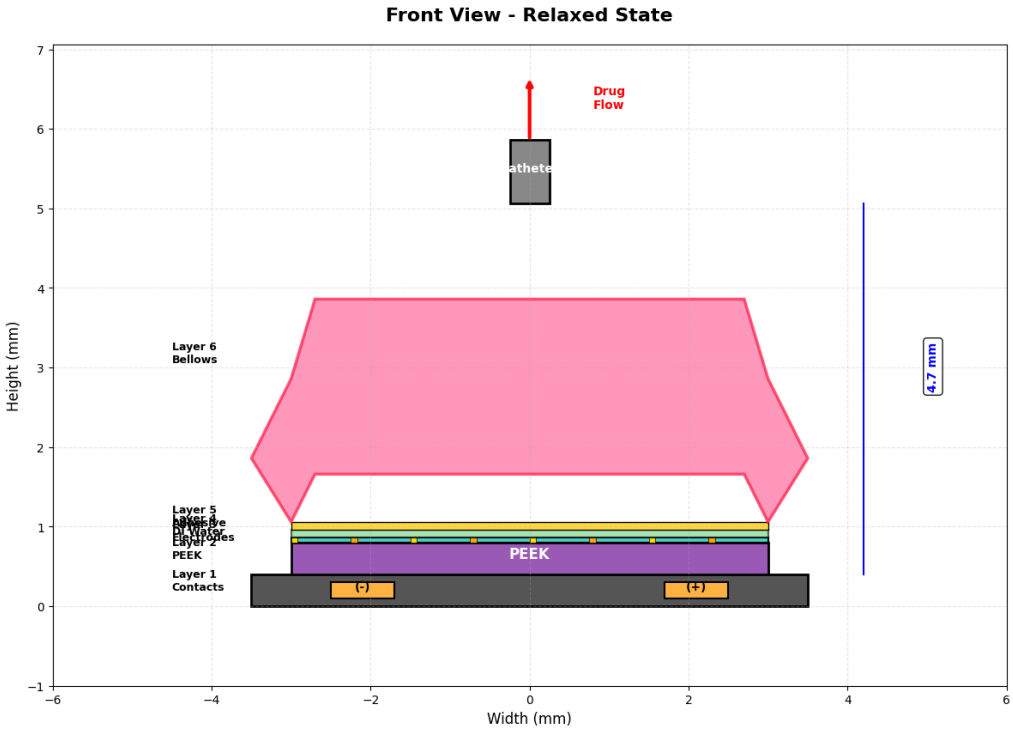


- Expanded State: The bellows extend vertically at 1.0 mA, increasing the volume of the water chamber, and demonstrating actuation of the device.

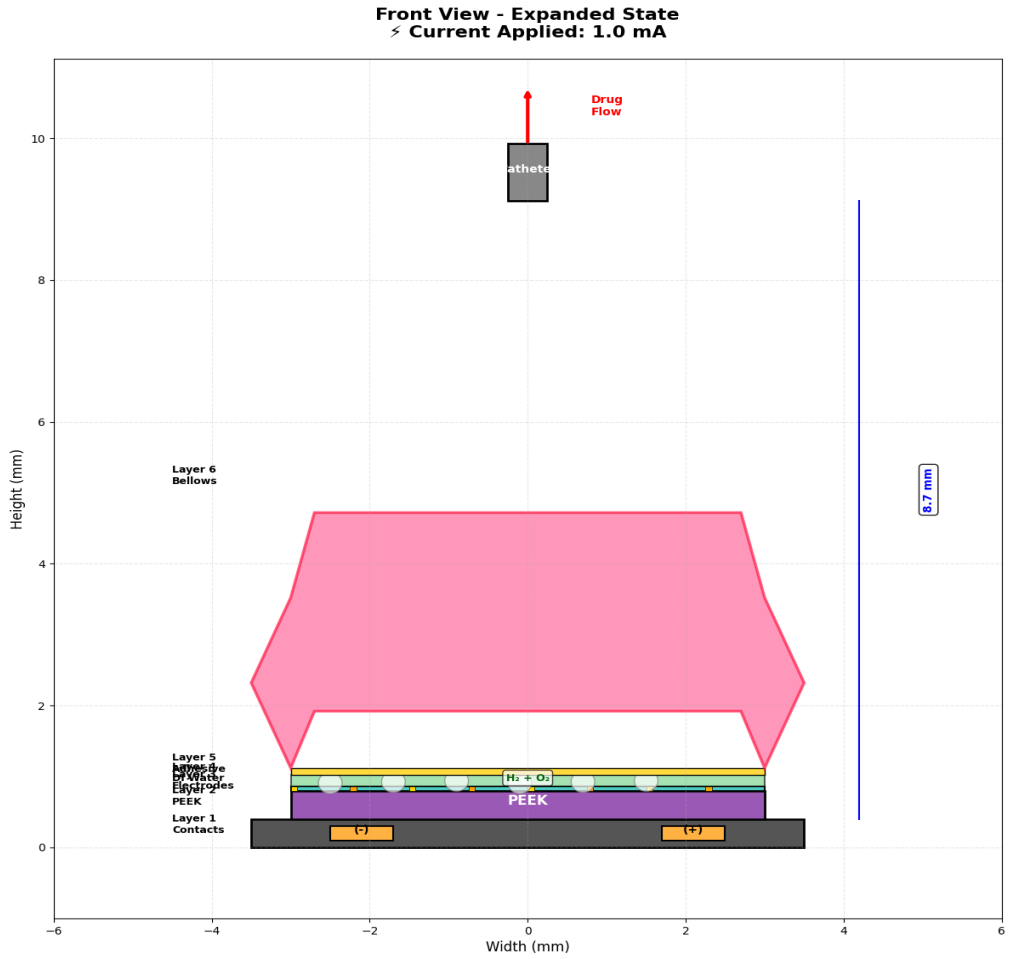


6.5 Device Front Views

- Relaxed State: Exterior stack layers and catheter outlet are shown.

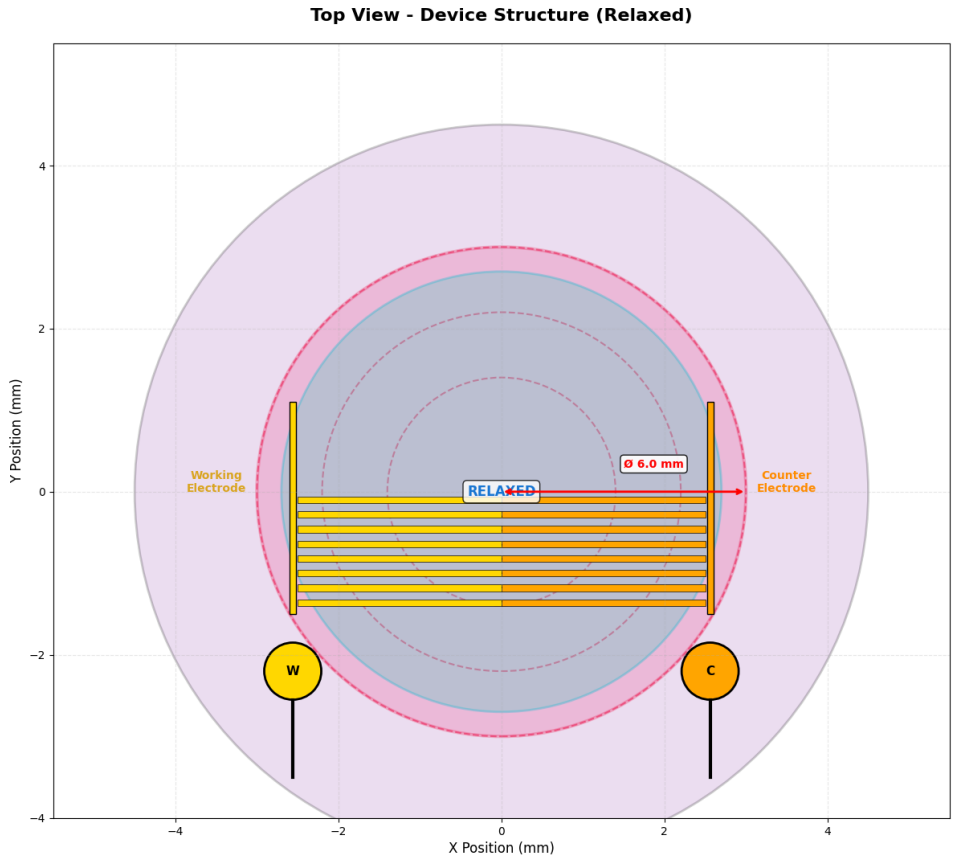


- Expanded State: The vertical expansion of the bellows and the formation of electrolysis gas bubbles ($H_2 + O_2$).

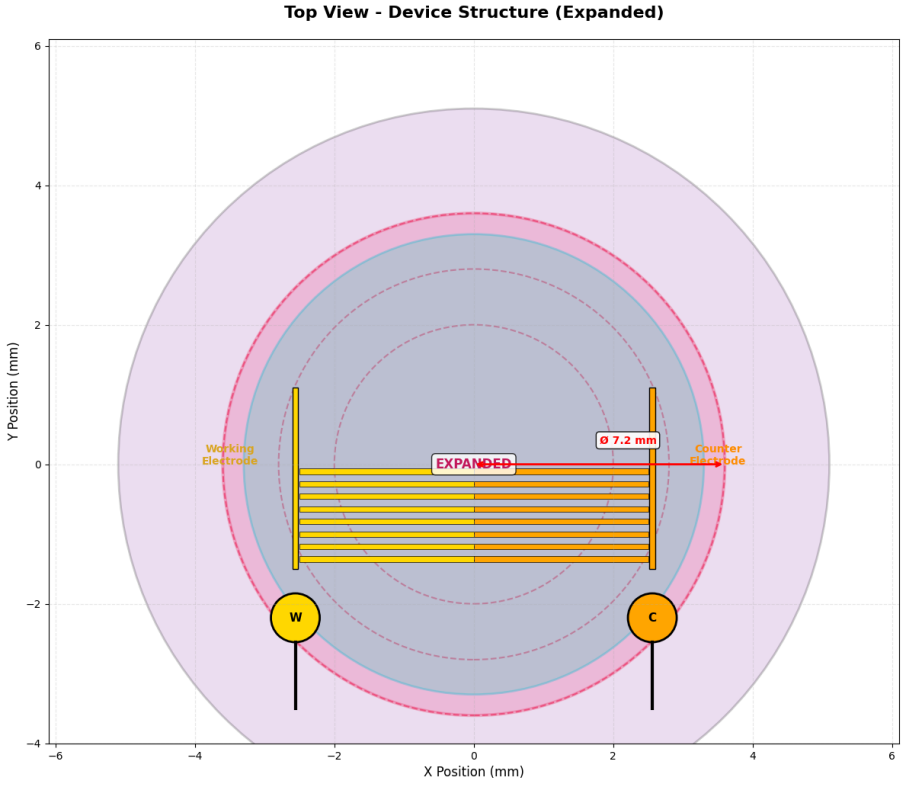


6.6 Device Top Views

- Relaxed State: Top-down view of the circular bellows, PEEK substrate, and interdigitated electrode pattern.

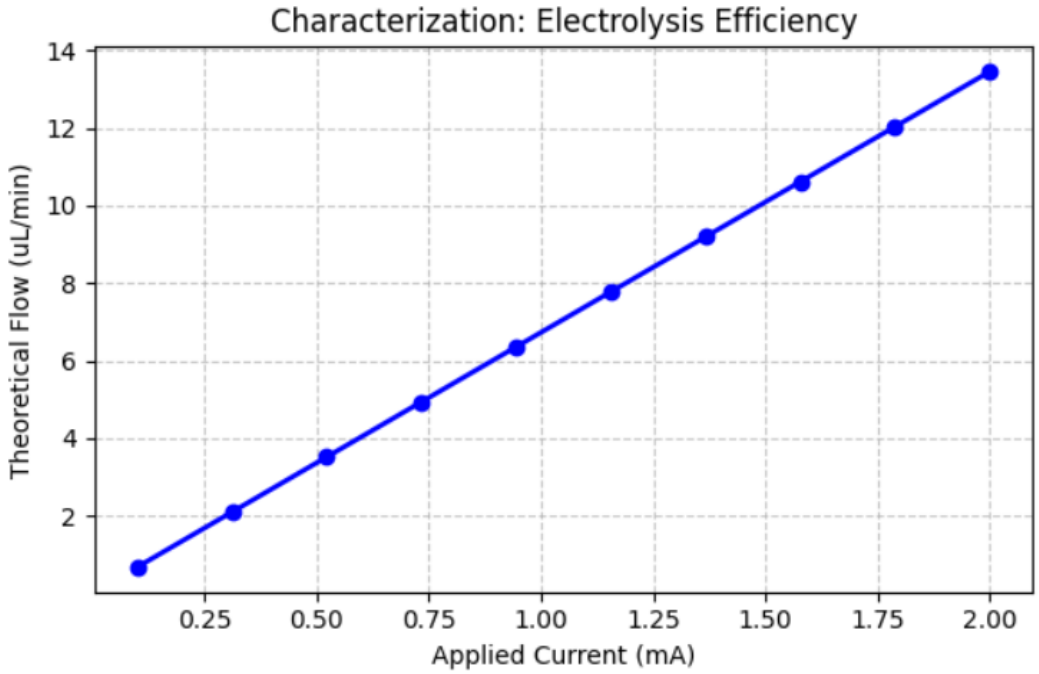


- Expanded State: The internal pressure increases the diameter of the bellows slightly, which reflects expansion dynamics.



6.7 Characterization Curve: Electrolysis Efficiency

- A line graph plots applied current (mA) versus theoretical flow (µL/min). It shows a linear relationship that points toward predictable electrochemical actuator performance.



Packaging Process

The packaging process turns the assembled actuator-reservoir system into a completely biocompatible, hermetically encapsulated implantable device. Such a multi-layer encapsulation strategy protects against moisture; provides electrical insulation, mechanical robustness, and a smooth biocompatible outer surface suitable for chronic subcutaneous implantation. Packaging also integrates the wireless power reception system and ensures that all the external surfaces are compatible with ISO 10993 requirements.

Step 1-Parylene C Conformal Coating (Primary Encapsulation)

- Provide electrical insulation and moisture barrier for all electronic components and wire connections.Mask selectively to protect areas that need to stay exposed (refill port, catheter outlet). Place assembled device in Parylene CVD coater.Deposit Parylene C conformally over all electronics to 5-10 µm thickness.

  Deposition Parameters:
  Chamber pressure: 20-30 mTorr
  Pyrolysis temperature: 690°C
  Dimer charge: 8-12 g
  Deposition time: 2-4 hours
  Coverage: All exposed electronics and connections

- This conformal Parylene layer offers pinhole-free electrical insulation, with a breakdown voltage of >200 V/µm; moisture barrier, with <0.1% water absorption; and provides the primary biocompatible interface. Coating follows all surface contours uniformly, ensuring complete wire bond and solder joint coverage.

Step 2: Wireless Power Coil Integration

- Planar spiral coil with 15-20mm in diameter is fabricated using AWG 38-42 copper wire with the number of turns 15-20. The coil is positioned concentrically around the device body and embedded into the packaging layers.
- Assemble the rectifier circuit (Schottky diode bridge), filter capacitor (10-100 μF), and voltage regulator (LDO, 3-5 V output) on a flexible PCB or discrete components. Connect this to the bellows actuator electrodes using the wires that have been attached in advance.
- The receiver coil and electronics are encapsulated in 1-2 mm of medical-grade silicone to protect the components while maintaining inductive coupling efficiency.

Wireless Link Specifications:
Operating frequency 1-13 MHz (typically 6.78 MHz ISM band)
Link efficiency: ~ 82% for aligned coils (separation 5-15 mm)
Transmitted power: 4-12 mW - suffices for 0.5-2.0 mA operation
Tolerance for coil misalignment: ±10 mm lateral offset

Step 3: Silicone Rubber Overmolding (Secondary Encapsulation)

- A two-part overmold is fabricated with a cavity geometry matching the device profile plus 1-2 mm clearance for silicone thickness. The mold has provisions for the refill port and catheter exit. Material: medical-grade silicone rubber (NuSil MED-6015 or Dow Corning MDX4-4210)
- Position device in lower mold half with catheter and refill port aligned to mold features. Mix the silicone components (1A:1B by weight) and degas for 5 min at 0.1 Torr. Pour in silicone into mold cavity to cover it completely.
- Close mold and apply pressure (10-20 kPa) to remove air. Cure at 150°C for 1 hr or at room temperature for 24 hrs. Demold carefully and excess flash off.

Design Features
Wall thickness: 1-2 mm - for mechanical protection
Outer contours: smooth, rounded surfaces (radius >2 mm), which will prevent tissue erosion.
General dimensions: 12-18 mm diameter, 10-15 mm height
Weight: <2 g total (implant + silicone packaging)

Step 4: Refill Port Integration
Septum Design

- Integrated into the top surface of the overmolded package, a self-sealing silicone septum (2-3 mm diameter, 0.5-1 mm thickness) provides immediate access to the drug reservoir.

Integration Method

- The septum can be either molded-in-place during overmolding or bonded post-molding with PDMS adhesive. The septum material will be selected for high tear resistance and self-sealing capability after repeated punctures.

Performance Specifications
Needle compatibility: 25–30-gauge hypodermic needles
Puncture cycles: >100 refills without leak development
Seal integrity - Immediate resealing after needle withdrawal
Access volume: Full reservoir capacity accessible (100-300 μL)

Step 5: Final Inspection and Testing

Dimensional Verification

- Calipers or optical profilometry used to verify overall dimensions-diameter, height-within tolerances ±0.5 mm.

Electrical Testing

- Continuity test: Check electrical path from outside contacts to electrodes (<100 Ω)

Insulation test: Check no shorts between electrodes or to ground (>10 MΩ)

- Wireless power test: Confirming that the receiver coil is functioning, and its output voltage is between 3 to 5 volts.

Leak Testing

- Method 1 - Pressure Decay: Seal all ports except refill port, apply 10 kPa of air pressure via septum, monitor for 10 min. Acceptance: pressure decay <1 kPa/min.

- Method 2 - Immersion Test: Fill reservoir with colored dye solution, seal refill port, submerge in clear water bath 1-hour. Acceptance: no visible leakage of dye.

Conclusion:

This research has shown very promising results in developing a MEMS catheter that can achieve accurate, AI-assisted drug delivery. Simulations validated the operation of an actuator and sensor system, and prototype validation and optimization were identified as the next steps in the process.

Reference:

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- Cobo, R. Sheybani, H. Tu, and E. Meng, "A wireless implantable micropump for chronic drug infusion against cancer," *Sens. Actuators A, Phys.*, vol. 239, pp. 18–25, Mar. 2016, doi: 10.1016/j.sna.2015.12.025.