INNOVATIVE IMPLANTABLE NEUROTECHNOLOGIES TO RESTORE THE BIOMIMETIC CONTROL OF THE LOWER URINARY TRACT

A. Giannotti[1]*, M. Ceradini[1], S. Musco[2], F. Bernini[3], G. Del Popolo[2], S. Micera[1,4,5]

[1] BioRobotics Institute, Department of Excellence in Robotics & AI, Scuola Superiore Sant'Anna, Pisa, Italy; [2] Careggi University Hospital, Florence, Italy; [3] Life Science Institute, Scuola Superiore Sant'Anna, Pisa, Italy; [4] Modular implantable neurotechnologies (MINE) Laboratory, Università Vita-Salute San Raffaele & Scuola Superiore Sant'Anna, Milan, Italy; [5] Bertarelli Foundation Chair in Translational NeuroEngineering, Centre for Neuroprosthetics and Institute of Bioengineering, École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland.

THE BIOROBOTICS INSTITUTE

Sant'Anna School of Advanced Studies – Pisa

INTRODUCTION and OBJECTIVE

Restoring normal urinary function is a highly desired outcome for patients suffering from neurological disorders due to the profound disruptions in daily life;

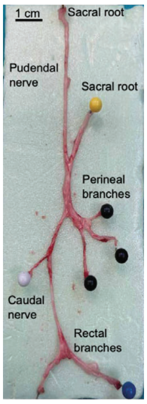
Bioelectronic medicine offers a promising alternative to conventional therapies for urinary dysfunction;

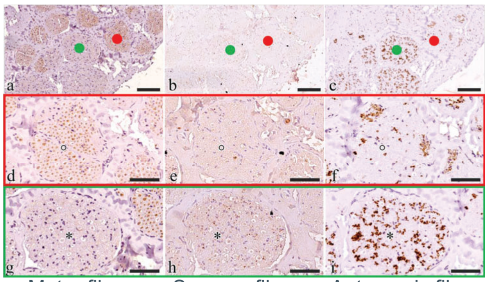
Current neuromodulation devices are limited by continuous or intermittent stimulation paradigms, **lacking real-time adaptability** to changes in bladder fullness.

Closed-loop stimulation paradigms demonstrated increased bladder capacity and micturition efficiency compared to continuous stimulation, but real-time decoding strategies of bladder fullness are still required.

We explored the swine pudendal nerve as a model for developing innovative neurotechnologies to restore lower urinary tract dysfunction with a biomimetic approach.

SWINE PUDENDAL NERVE



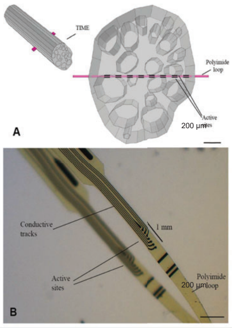


Motor fibers (ChAT) | Sensory fibers (P-Substance) | Autonomic fibers (TH)

Giannotti et al., IJMS, 2024

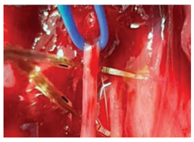
EXPERIMENTAL SET-UP

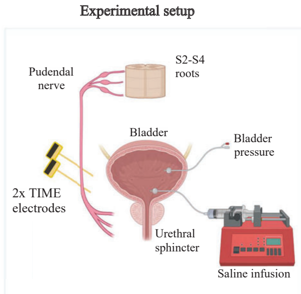
Intraneural electrode adapted to swine pudendal nerve



Anesthetized female farm pig (30-32kg, 3-4 months old)

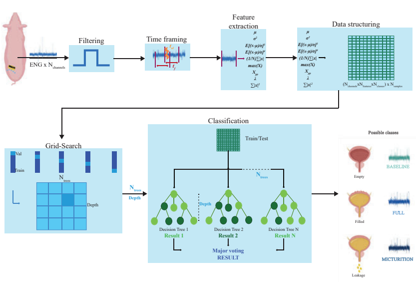
16-channel intraneural electrodes implantation



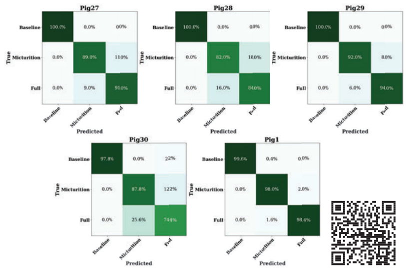


BLADDER FILLING STATE

- ENG signals categorized into three states: empty, full, and micturition;
- Preprocessing: 4th order Butterworth band-pass filter within 1–6 kHz;
- Nine handcrafted features extraction from the ENG signal;
- Random forest (RF) chosen due to balance between high accuracy and computational efficiency;
- Nested cross-validation tuned hyperparameters for optimal model performance.



- RF classifier achieved a mean balanced accuracy of over 86.67% across all five pigs when decoding the three bladder states;
- Average prediction successes: Baseline 97,8%, Full 88.36%, Micturition 89.76%.
- Feature importance evaluated using the Gini index (variance, power, mean absolute value, and skewness most informative features).



Giannotti et al.,2023 APL Bioengineering

DETRUSOR PRESSURE ESTIMATION

ENG and detrusor pressure signals processing:

- Transurethral 6-Fr dual-lumen catheter: bladder filling (50 ml/min) and intravesical pressure measurement;
- 10-Fr catheter placed in the rectum to measure abdominal pressure;
- Detrusor pressure was estimated as the difference between intravesical and abdominal pressure.

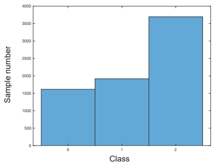
Raw ENG signal → Band pass filtering (3000-6000Hz) *Butterworth 4th order* → Downsampling 12000Hz → SBP calculation

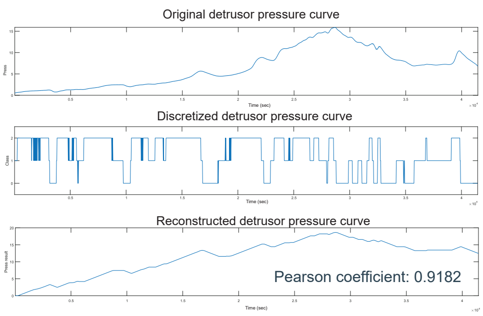
SBP = Spike Band Power = mean(|signal_bin|) / signal_bin length sbp_bin_length = 40ms

Raw pressure signal → Moving average over bins of 5s

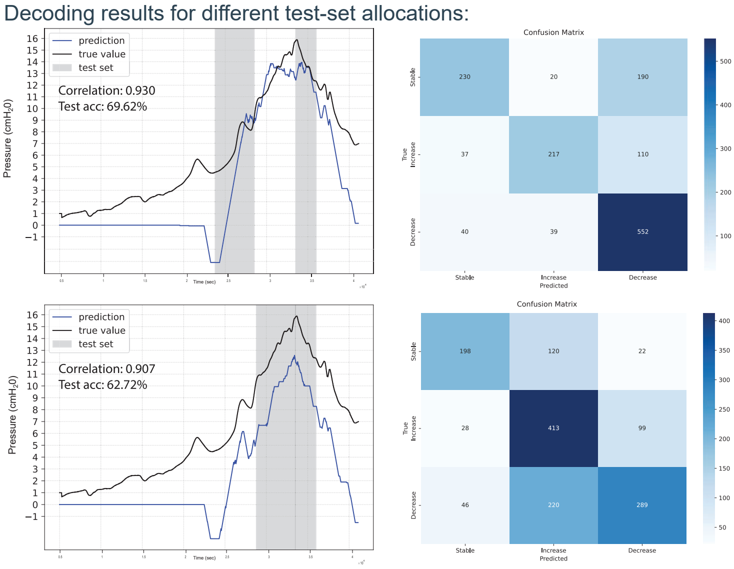
Dataset - detrusor pressure discretization:

1. Current pressure (average pressure over 500ms);
2. Historical pressure (average pressure over previous 5 sec);
3. Relative pressure change (normalized difference between the current and historical pressures);
4. Output classification into three categories: pressure decrease (0), constant pressure (1), or pressure increase (2).

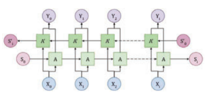




Decoding results for different test-set allocations:



Model - Bidirectional LSTM (Long Short-Term Memory)



LSTM processes input data in both forward and backward directions, capturing dependencies from past and future states.

Useful for neural signals as it enhances the model's ability to capture temporal patterns in both directions, improving prediction accuracy.

Training

The network receives as input 1 second of neural data (i.e. 10 SPB samples) across 32 ENG channels.
The label associated with each SPB sample is the corresponding discretized pressure value.
For each input, the network outputs a classification in one of three categories: [0, 1, 2].

The dataset consisted of a single cystometric curve, thus we allocated 80% of the data for training and 20% for testing to ensure a reliable evaluation of the model performance.

RESULTS and FUTURE STEPS

- The here proposed custom-developed deep-learning-based algorithm showed promising results in predicting detrusor pressure from intraneural swine pudendal nerve signals;
- The algorithm considered approximately 1s of neural data preceding the instant under consideration, making this algorithm potentially suitable for real-time applications;
- Our findings pave the way towards implementing a real-time adaptive closed-loop stimulation protocol for pudendal nerve modulation;
- Limitation of the present study is the use of a single cystometric curves; thus, testing of the proposed algorithm using multiple cystometric curve and multiple animal datasets may be needed;
- Future studies may explore the use of different filtering approaches and feature extraction from the ENG signals (e.g., frequency domain features).

CONTACT: alice.giannotti@santannapisa.it

FUNDING: Bidirectional multimodal bionic interfaces “BioInterNect” (PR23-PAS-P2) project, INAIL Prosthesis Center