Analysis of Anomaly Detection Techniques for In-line Permittivity Sensors in Bioprocesses

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BACKGROUND

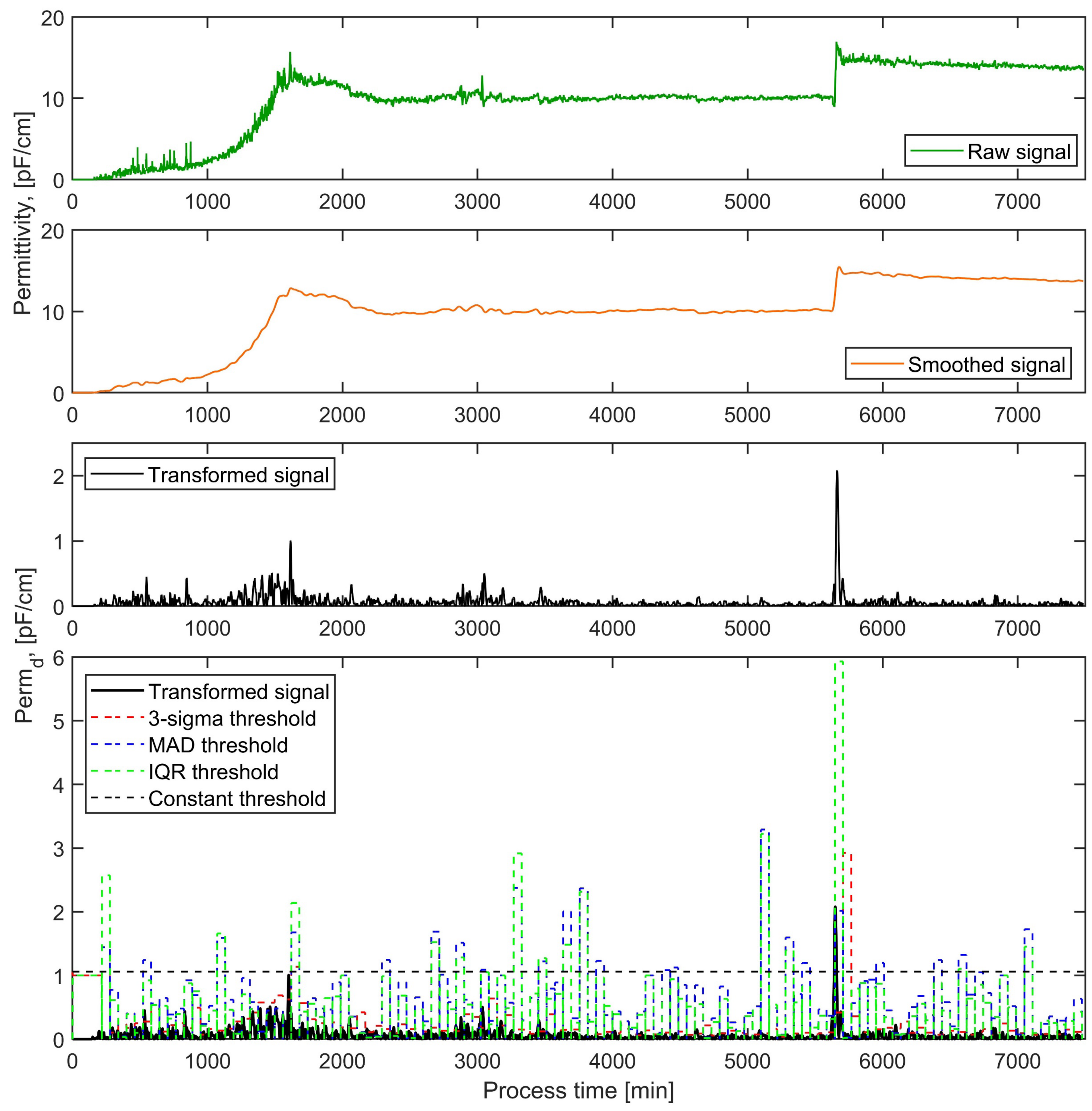
In-line sensors enable real-time monitoring and control of bioprocesses. Among these, permittivity probes are widely used to estimate viable cell density. However, signal anomalies, such as spikes and shifts, can occur due to changes in agitator speed, antifoam addition, or bubble interference [1]. Timely detection and correction of these anomalies are crucial to ensure reliable and effective control.

MOTIVATION

Bioprocess signals are dynamic and non-stationary, requiring specialized preprocessing techniques [2]. Simple filters, such as moving averages, are insufficient to capture the complexity of these signals. Both traditional manual anomaly detection approaches and modern machine learning methods share the drawback of rarely operating in real time.

METHODOLOGY & RESULTS

Permittivity measurements from eight recombinant *Pichia pastoris* fermentations were used to investigate different anomaly detection techniques.



Signal processing workflow shown for an exemplary *Pichia pastoris* fermentation.

Reduction of noise

- 'Noiseless' reference via offline local quadratic regression (smoothing factor: 0.03).
- Evaluation of smoothing methods using NRMSE (reference vs. real-time smoothed signals).

Signal transformation

- Transformation of the smoothed signal by double rolling aggregate (DRA) (mean as aggregation function; overlapping windows; window sizes 1 – 20).

Anomaly detection

1. Manual annotation of signal anomalies.
2. Application of threshold methods (varying window sizes) to the transformed signal Perm$_d$:
   - manually selected static threshold
   - dynamic thresholds based on:
     - 3-sigma rule
     - Median of Absolute Deviation (MAD) scale estimate
     - Interquartile Range (IQR) scale estimate
3. Analysis of true positives (TP), false positives (FP), and false negatives (FN).
4. Calculation of precision, recall, and F1-score for method evaluation.

Static threshold

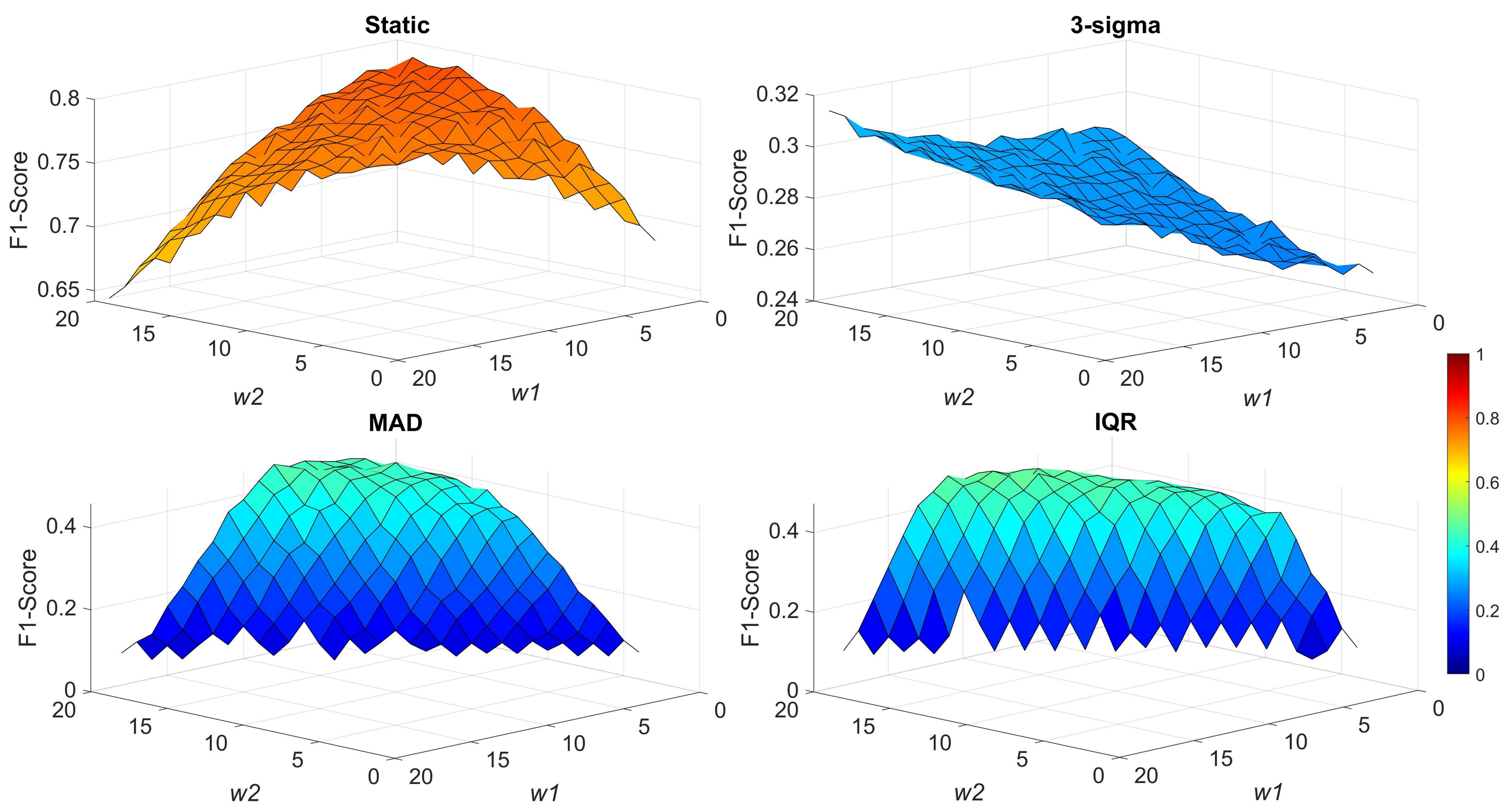
- Achieved best anomaly detection performance with an F1-score of 0.79 (threshold of 1.06 pF/cm).

3-sigma threshold

- Similar true positive and false negative rates as the static threshold approach.
- High false positive rate, impacting the overall F1-score.

MAD & IQR threshold

- Similar results, as the methods are conceptually similar.
- F1-score was significantly affected by false positive and false negative anomalies.



Highest F-scores achieved for respective thresholds at selected DRA transformer window sizes *w1* and *w2* with optimized threshold values (for static threshold) and window sizes *w3* (for dynamic thresholds).

CONCLUSION

The anomaly detection achieved a high performance, with an F1-score of 0.79, using a static threshold of 1.06 and DRA window sizes of *w1* = 1 and *w2* = 15.

The static method offers low computational cost, is easy to implement, and is well-suited for real-time applications. In contrast, dynamic thresholds respond slowly to sudden increases in signal volatility, resulting in poor real-time detection performance due to delayed threshold adjustment.

[1] Grigs, O., Bolmanis, E., & Galvanauskas, V. (2021). Application of *In-Situ* and Soft-Sensors for Estimation of Recombinant *P. pastoris* GS115 Biomass Concentration: A Case Analysis of HBcAg (Mut+) and HBsAg (MutS) Production Processes under Varying Conditions. *Sensors, 21*(4), 1268.

[2] Ramm, S., Rodríguez, T. H., Frahm, B., & Pein-Hackelbusch, M. (2023). Systematic Preprocessing of Dielectric Spectroscopy Data and Estimating Viable Cell Densities. In *2023 IEEE 21st International Conference on Industrial Informatics (INDIN).*

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