Local *vs.* Global: Achieving Better Raman Glucose Detection with Simplified Models

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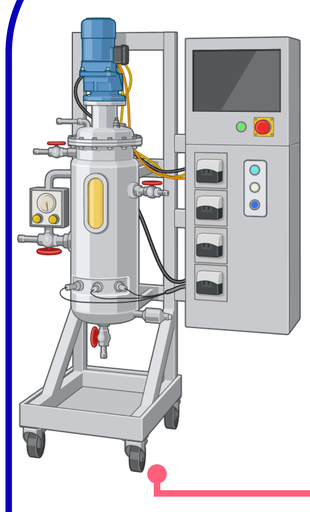
Introduction

Online glucose monitoring using **Raman spectroscopy** requires calibration models to translate spectra into concentrations[1]. Conventional **global** models assume that a **single calibration** can capture all process conditions, but this assumption **is invalid** in real fermentations due to **variability between batches** and **temporal drift**[2]. Consequently, **model accuracy deteriorates over time**, resulting in reduced robustness and the need of frequent **recalibration**.

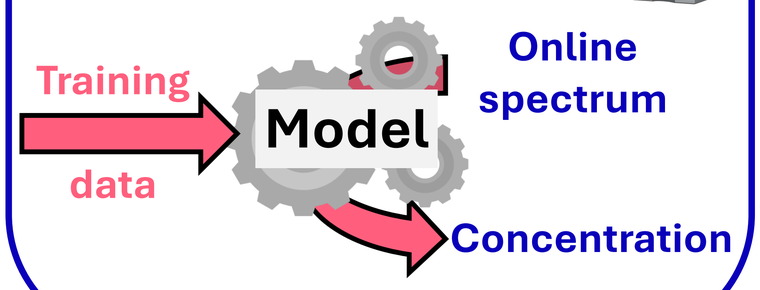
In this work, a **local calibration**[3] approach is investigated, where only the **most relevant spectra** are **selected** for each prediction to build a **context-specific model**. This strategy aims to capture process variability more effectively and **improve prediction reliability** under industrial conditions.

Set Up



A **Raman** spectrometer is plugged to a fermenter through **optical fibers** and acquires spectra **24/7**.

Off-line **reference concentrations** are acquired. These references, along with **their corresponding spectra** are used to **train** the models.



Local model

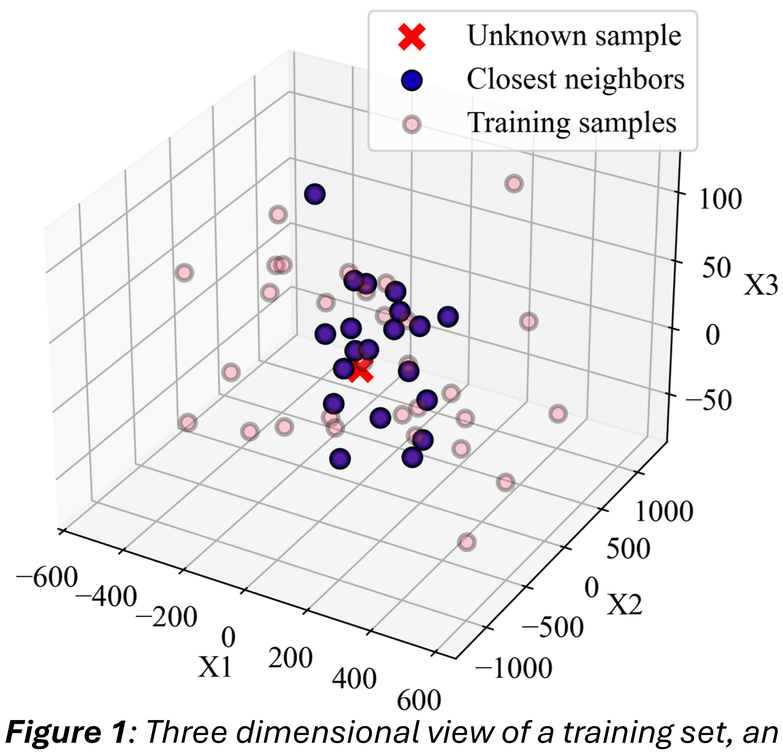


***Figure 1**: Three dimensional view of a training set, an unknown spectrum and its closest neighbors in the set.*

Unlike the **Global** model, which uses **all the training data** to build **one model**, the **Local** approach uses only a **few data** points to build a model adapted to **each new sample**. Only the **20** spectra **closest to the new sample** are selected (**Figure 1**).

Local vs Global

First evaluation: predictions *versus* reference measurements (**Figure 2**). A perfect model would produce a perfect line, with a R^2 of 1.

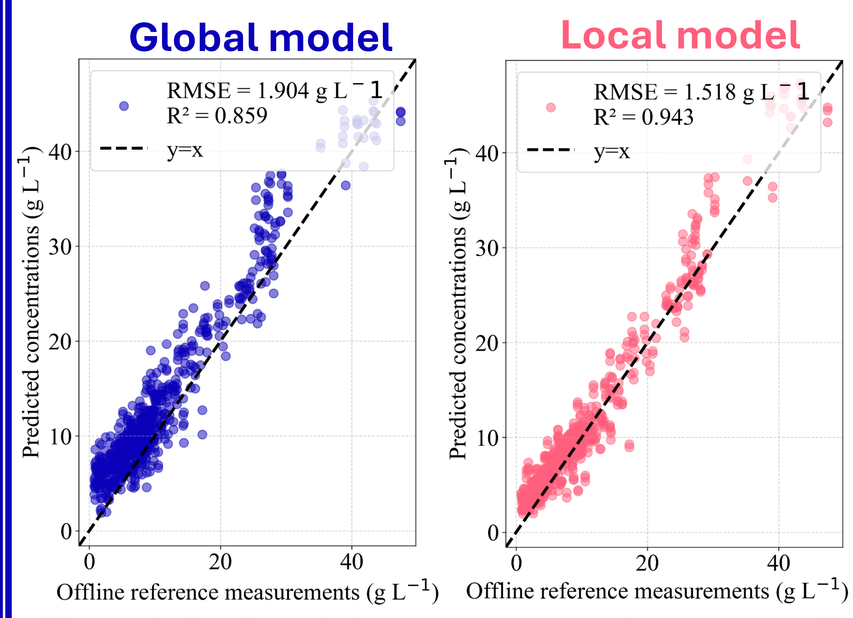


***Figure 2**: Predicted glucose concentrations versus off-line acquired reference concentrations, using a Global model (blue – left) and Local models (pink – right).*

300 **training** points & 700 **validation** points
Local models decreased the error by **20%**

Time Robusteness

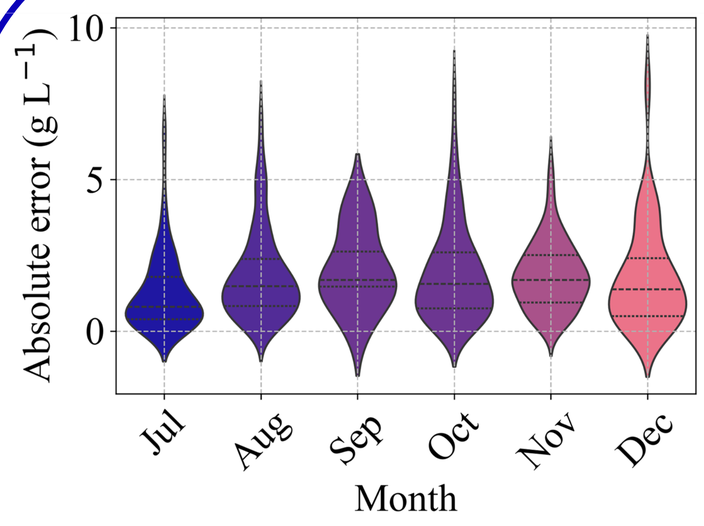


***Figure 3**: Evolution of the model errors over 6 months*

When applying the Local model to the monitoring of fermentations **subsequent** to its **training**, **no significant drift** in accuracy is observed (**Figure 3**).

In a similar fashion, along a **complete fermentation**, through **multiple metabolic phases**, **no drift** can be detected (**Figure 4**).

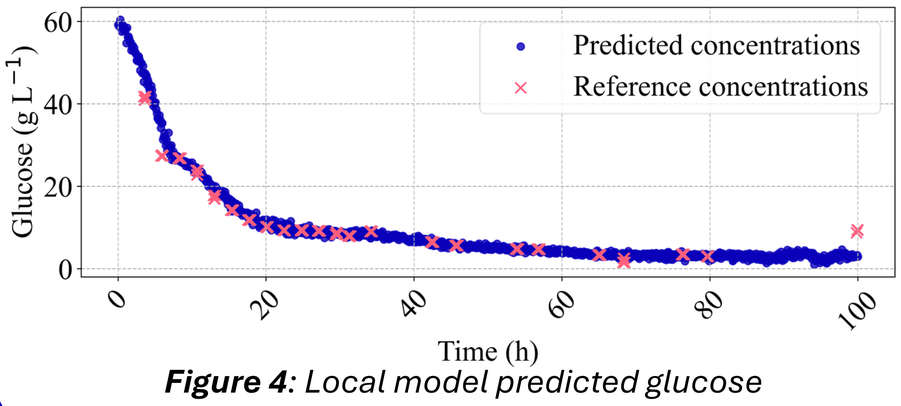


***Figure 4**: Local model predicted glucose concentrations during a complete fermentation batch*

No shift over **6 months**,
No shift over a **full fermentation**

Conclusion

Local calibration consistently **improved** glucose prediction accuracy compared to Global models, reducing errors and maintaining stable performance over six months of operation.

By selecting **context-relevant spectra**, the approach adapts to process variability and mitigates the impact of drift.

These results demonstrate that **Local modelling** provides a **more robust framework** for Raman-based monitoring in industrial fermentation, supporting **more reliable control** strategies and future integration into advanced **data-driven bioprocessing systems**.

References

[1]Borg, A. *et al.*, *Biotechnol. Bioeng.*, **2026**, *123* (3), 544–563.
[2]Guo, S. *et al.*, *Nat. Protoc.* **2021**, *16* (12), 5426–5459.
[3]Shenk, J. S. *et al.*, *J. Near Infrared Spectrosc.*, **1997**, *5* (4), 223–232.