BIOMASS AND ACETATE CONCENTRATION ESTIMATION FROM IMPEDANCE RADIOFRECUENCY (IRF) SENSOR, REAL TIME (RT) MEASUREMENTS OF CAPACITANCE AND CONDUCTIVITY

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Introduction. Unique behavior of viable cells exposed to electrical fields, has made capacitance measurement a robust method for biomass estimation (1). IRF sensors are gaining terrain as process analytical technology tools for on-line bioprocess monitoring (2). They provide real time measurements of capacitance ($\Delta\varepsilon_i$) and conductivity (κ). However, their dual capability has not been extensively exploited yet. κ depends on ionic species concentration. Hence, mineral substrates consumption and organic acids excretion can be followed by conductivity changes in the broth (3). The aim of this work was to develop estimators for biomass (*X*) and acetate (*A*) concentration from on-line $\Delta\varepsilon_i$ and κ RT measurements.

Methods. A small fraction of $\Delta\varepsilon_i$ and κ RT data from an Aber IRF (Aber Instruments Ltd, Averystwyth, UK) sensor installed in bioreactors, was correlated with off-line *X* and *A* measurements, respectively, from twelve *E. coli* DH5α thermo-induced pDNA production cultivations. The resulting models and parameters were verified in the remaining data of the same cultivations to adjust parameter for the best fit to experimental data. Additionally, specific growth rate (μ) was estimated from *X* estimates and working volume computations.

Results. A non-parametric smoothig algorithm was applied to noisy data (Fig1a-b) before applying estimators to clarify trends. *X* and *A* estimations indicate process critical steps such as loss of viability (by the difference between experimental and predicted *X*) and acetate accumulation (Fig1 c-d), as well as perturbations on fed-batch operation. The validated models and parameters are shown in table 1.

Conclusions. The estimators developed take advantage of the dual capability of IRF sensor and had predictive potential for on-line bioprocess monitoring and control.

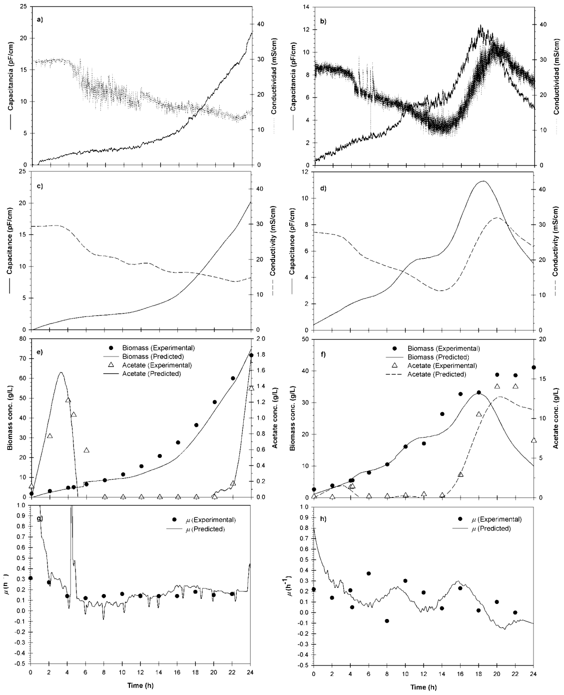

Fig1. Raw (a-b) and filtered $\Delta\varepsilon_i$ and κ measurements (c-d) and comparison between experimental and predicted *X*, *A* (e-f) and μ (g-h).

Table 1. Parameters and models for X and A from $\Delta\varepsilon_i$ and κ measurements. *t* is time.

	Units	35 °C	42 °C
a	g cm pF^{-1} L^{-1}	2.63 ± 0.00	2.63 ± 0.00
b	g cm pF^{-1} L^{-1}	3.7 ± 0.0	3.39 ± 0.14
c	pF L g^{-1} cm^{-1}	0.4 ± 0.2	0.3 ± 0.0
δ	g cm mS^{-1} L^{-1}	0.65 ± 0.00	0.45 ± 0.00
dk/dt	mS cm^{-1} h^{-1}	0.71 ± 0.07	1.1 ± 0.2
k_o	mS cm^{-1}	30.1 ± 2.9	31.3 ± 2.9
$\hat{X}_i = a \cdot \Delta\varepsilon_i$ (Batch)		$\hat{A}_i = \delta \cdot (k - \frac{d\kappa}{dt} \cdot t_i + k_o)$	
$\hat{X}_i = b \cdot (\Delta\varepsilon_i - c \cdot \hat{A}_i)$ (Fed-batch)			

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