Calibration free fluorescence pH fiber optic microsensor

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Abstract:

This work is part of the development of a fiber optic fluorescence pH sensor for *in vivo* measurements. The sensor uses pH dependent molecules grafted at the cleaved-end of an optical fiber. Fluorescent indicators like SNARF® allow measuring pH by calculating the ratio of the emitted fluorescence at two distinct wavelengths. This ratiometric technique is however not calibration free and molecule manufacturers advise users to perform a pre-calibration using the acidic and basic endpoints of titration respectively. This calibration procedure requires controlling very accurately the experimental conditions and is time consuming for clinical applications.

Among different reasons, calibration is required to account for degradation of the sensor probe due to aging or repetitive use. In fact, pH sensing is based on the monitoring of the acid-base reaction which occurs in the indicator layer grafted at the end of the optical fiber. Calibration is required because the pKa of the acid-base reaction cannot be considered constant. pKa variations are due to several factors like temperature and/or ionic strength of the solution to be measured, structure and thickness of the indicator layer at the end of the fiber. Indeed, pKa can differ from almost 2 units between the value in a low concentration solution and the value in a dense layer close to a solid surface which is the case in fiber optic pH sensors [1]. Furthermore, it is extremely difficult to fabricate pH sensitive fibers with a reproducibility high enough to control the pKa of the acid-base reaction in the sensing volume. In fact, even if an ideal fabrication method was discovered, variations of the pKa due to aging would make calibration a priori unavoidable.

In this conference, we show that modeling the fluorescence properties of ratiometric indicators existing in their 2 acidic and basic forms cannot be used to access calibration free pH sensing. We then explain how pH indicators exhibiting more complex prototropic equilibria can be used to not only compute the pH value but also the value of the pKa at the moment when measurements are performed. We present the complete mathematical modeling of the fluorescence properties of a pH indicator exhibiting a very high quantum efficiency and we explain how, from any fluorescence spectrum, it is possible to fit the values of both pH and pKa.

This is, to the best of our knowledge, the first example of calibration free micro pH sensor which: 1) can be used for measurements in the human body where body fluids exhibit extremely varying ionic strengths and 2) avoid any calibration procedure thanks to the automatic pKa adjustment included in the mathematical description of the fluorescence spectra.

Reference:

[1] C. Rottman, M. Ottolenghi, R. Zusman, O. Lev, M. Smith, G. Gong, M.L. Kagan, D. Avnir, Doped sol-gel glasses as pH sensors, Materials Letters, Volume 13, Issue 6, 1992, Pages 293-298, doi.org/10.1016/0167-577X(92)90055-O.

Acknowledgement:

This work was partially supported by the European Commission [grant number H2020-SC1-2017, operation 754907].