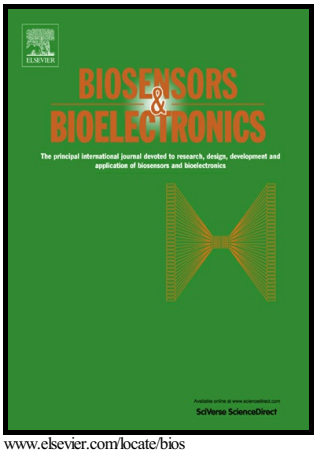

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Detection of BCG bacteria using a magnetoresistive biosensor: a step towards a fully electronic platform for tuberculosis point-of-care detection

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Abstract

Tuberculosis is one of the major public health concerns. This highly contagious disease affects more than 10.4 million people, being a leading cause of morbidity by infection. Tuberculosis is diagnosed at the point-of-care by the Ziehl-Nielsen sputum smear microscopy test. Ziehl-Nielsen is laborious, prone to human error and infection risk, with a limit of detection of 10^4 cells/mL. In resource-poor nations, a more practical test, with lower detection limit, is paramount. This work uses a magnetoresistive biosensor to detect BCG bacteria for tuberculosis diagnosis. Herein we report: i) nanoparticle assembly method and specificity for tuberculosis detection; ii) demonstration of proportionality between BCG cell concentration and magnetoresistive voltage signal; iii) application of multiplicative signal correction for systematic effects removal; iv) investigation of calibration effectiveness using chemometrics methods; and v) comparison with state-of-the-art point-of-care tuberculosis biosensors.

Results show a clear correspondence between voltage signal and cell concentration. Multiplicative signal correction removes baseline shifts within and between biochip sensors, allowing accurate and precise voltage signal between different biochips. The corrected signal was used for multivariate regression models, which significantly decreased the calibration standard error from 0.50 to 0.03 $\log_{10}$ (cells/mL). Results show that Ziehl-Nielsen detection limits and below are achievable with the magnetoresistive biochip, when pre-processing and chemometrics are used.

Keywords: Tuberculosis, nanotechnology, magnetic nanoparticles, magnetoresistive biosensor, chemometrics.