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OPTICAL ENZYMATIC SENSORS FOR CONTINUOUS MONITORING OF BIOREACTORS

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Continuous monitoring of biotechnological processes is important for control and optimization of quality and productivity. Typically, samples must be removed from the cultivation and analyzed in a laboratory to determine the concentrations of substrates and products. These time-delayed data cannot be used for real-time process control. The Process Analytical Technology initiative of the FDA supports the use of on-line measurement techniques for process development, production, and quality. An overview of sensors will be presented, focusing on in-situ sensors that contact the biological medium, and external sensors that contact the medium either optically (ex situ) or via a sterile (and disposable) sample removal system (on line). A specific example will then be presented: a new optical enzymatic sensor system for the continuous, direct, quantitative measurement of sugars and other organic molecules in aqueous media. This sensor system has three parts: a replaceable sensor tip, an opto-electronic hardware unit, and an optical fiber with a length appropriate for the application. The sensor tip includes a two-layer detection element – one layer containing a detection enzyme affixed to another fluorophore-containing layer. The change in fluorescence characteristics depends on the analyte concentration, and these sensors can be designed to provide quantitative output over different concentration ranges. These sensors can be sterilized with gamma irradiation. Performance metrics including the limit of detection have been determined for glucose, lactose, and other analytes.