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New Trends in Photobiology (Invited Review)

Time-resolved detection of lanthanide luminescence for ultrasensitive bioanalytical assays

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Abstract

The principles and practice of the application of time-resolved lanthanide chelate luminescence (or fluorescence) as a detection method for ultrasensitive bioanalytical assays such as immunoassays and nucleic acid hybridization assays are reviewed. The various lanthanide chelate-based detection systems which have been developed for use in heterogeneous and homogeneous assay formats are described, including reagents, assay methods, and instrumentation, along with recent improvements in these methods. Detection systems described include those based on dissociative enhancement of lanthanide ions, direct labeling with luminescent chelates, enzyme-amplified lanthanide luminescence, lanthanide luminescence quenching, and energy transfer.

Keywords: Time-resolved fluorescence; Time-resolved luminescence; Lanthanide chelate; Europium; Terbium; Samarium; Immunoassay; Nucleic acid hybridization assay; DNA probing assay

1. Introduction

1.1. Ultrasensitive bioanalytical assays

Ultrasensitive bioanalytical assays involve the detection of the presence or concentration of a specific material (the analyte), by utilizing a biologically derived reagent which specifically binds or reacts with the analyte. The analyte is usually contained at low concentration in a complex biological aqueous-based sample containing a large excess of extraneous material, and thus detection sensitivity and specificity are both required. Detection limits required for the analyte are on the order of μg to pg/ml, with sample sizes often a few hundred microliters or less. Bioanalytical assays can be used for detection of man-made or naturally occurring analytes in such diverse fields as medicine, forensics and environmental sciences, amongst others. The potential provided for sensitive, reliable, rapid and simple detection of specific analytes has been realized in the well-known example of the home pregnancy test kit.

Given the range and number of possible applications for ultrasensitive bioanalytical assays, there has been room for the development of many different types of assay formats and detection systems [1,2]. Assay design variables include the nature of the assay reagents and solid supports, and the necessity for instrumentation to provide, as needed, automation, quantification, or increased sensitivity [3]. All these design variables, dictated by the analyte of interest, the type of user, and the choice of detection system, can affect assay sensitivity, specificity, simplicity and cost.

The nature of the analyte to be detected dictates the possible types of specific binding or chemical reaction which can be used. The ultrasensitive bioassay types covered in this review are: the immunoassay, in which an antibody is used as the specific binding reagent (SBR), and the analyte is any species to which a specific antibody can be raised [2,4,5]; the nucleic acid hybridization assay, in which the SBR is a nucleic acid fragment complementary to the analyte nucleic acid fragment [1,4,6]; and the enzyme assay, in which the analyte is the enzyme, or alternately an enzyme substrate

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