

such as ELISA and RIA. Unexpectedly, we found that sonication of reagents reduced the time required for completion of these binding reactions to a matter of minutes. The apparatus and methodology of the present invention is not limited to immunoassays and will be useful for a wide variety of binding interactions (e.g., nucleic acid hybridization, antigen-antibody, receptor-ligand, enzyme-substrate, etc.). The invention is advantageously employed in ECL assays using binding domains located on a working electrode (i.e., said working electrode also functioning as a solid-phase support), for example, as described in copending U.S. application Ser. No. \_\_\_\_\_ filed on even date herewith, and PCT Application No. \_\_\_\_\_ (WO \_\_\_\_\_) filed on even date herewith, both of which are incorporated by reference above.

[0040] Sonication is also advantageously employed in systems where the solid-phase support has a plurality of binding domains, wherein two or more of said binding domains reside on a different location on the solid phase support. In this case obtaining accurate and reproducible results requires that the sample be mixed sufficiently so that all portions of the sample are exposed to all binding domains. Sonication, by increasing mass transport not only increases the rate of the reaction but can also make the reactions between sample, reagents, and binding domains more uniform.

[0041] Sonication is also advantageously employed in systems where the solid-phase support has a plurality of binding domains, some or all of said binding domains being specific for different analytes. Obtaining accurate and reproducible results requires that the sample be uniformly exposed to the binding domains on the support.

[0042] Sonication can have beneficial effects besides increasing the rate of the binding reaction. For example, the rate of color development in an ELISA assay may be limited by the rate at which the enzyme substrate travels to the solid surface and the rate of which the enzyme product travels away from the solid surface. Similarly, many chemiluminescent reactions used in assays are initiated by the reaction of chemiluminescent labels, bound to a solid-phase support, with co-reagents present in solution and, thus are accelerated by sonication. Also subject to improvement are assays utilizing electrochemical detection methods that require the mass transport of electroactive species to an electrode surface. Apparatus according to the present invention demonstrate a more-than threefold increase in the ECL signal produced by a solution containing TAG1 and the ECL coreactant tripropylamine (TPA) when the experimental cell is sonicated during the excitation of ECL. The present invention can, therefore, be applied to the more sensitive ECL detection of ECL labels and ECL coreactants.

[0043] Sonication will not only increase the rate of mass transport of reagents to a surface of a solid but will also increase the rate of mass transport of reagents, products, byproducts, contaminants, and the like away from the surface. Sonication can be used to increase the rate of displacement reactions, e.g., the displacement by an unlabeled analyte present in a sample of a labeled analyte bound to a binding reagent. Sonication may also be used to increase the rate of desorption of undesired contaminants on a solid-phase support, thus, reducing the amount of interference and non-specific binding produced in a particular assay. Further,

sonication may increase the rate of adsorption of desired materials, such as assay reagents or a protective coating, or the like, and increase the rate of desorption of expended or otherwise undesirable materials, such as a protective coating, non-specifically bound reagents, or the like. Sonication may be used to re-suspend particulate contamination, e.g., cell membranes or particulate reagents, that has settled on a surface.

[0044] Sonication may also be used in a sample preparation step. For example, sonication may be used to disrupt materials such as biological tissue cells, microorganisms, virus particles and the like, to release components of the materials into the reaction media. Preferably, said sample preparation occurs, in situ, in a measurement cell, e.g., an ECL cell.

[0045] Still further, sonication may be used to decrease the time needed to mix two or more solutions to homogeneity, the time needed to dissolve a solid in a solution, and the time needed to rehydrate a dried material. Sonication is also useful in increasing the rate of fluid flow through thin capillaries.

[0046] The slow rate of chemical reactions can also be a limiting constraint in conducting assays that incorporate chemical reactions between reagents in solution and/or between reagents in solution and reagents on a solid. Sonication improves the mixing of reagents in solution and the mass transport of reagents in solution to reagents located on or near the surface of a solid. The increased mixing afforded by sonication can dramatically decrease the time required to conduct an assay that utilizes chemical reactions between reagents in solution and chemical reactions between reagents in solution and reagents located on or near a solid support.

[0047] The slow rate of binding kinetics can also be a limiting constraint in conducting assays that incorporate binding reactions between reagents in solution. Sonication improves the mixing of reagents in solution and can dramatically decrease the time required to conduct a binding assay in solution.

[0048] Sonication may be used for assays that incorporate chemical reactions between reagents in solution and/or between reagents in solution and reagents located on a solid. Sonication may also be used for assays that incorporate binding reactions between reagents in solution.

[0049] Sonication may be created by a variety of mechanical and electromechanical devices. Such devices include electric motors with an eccentrically mounted cam, electromagnetic actuators, such as, speakers, crystal oscillators, pendulum devices, solenoids and the like. A preferred device for creating sonication at a frequency and amplitude particularly suitable for the present invention incorporates a piezoelectric material. Piezoelectric materials are generally inexpensive, commonly available, lightweight, and can be induced to sonicate over a wide range of frequencies and amplitudes. Conveniently, piezoelectric sonication devices are usually rather small in size, making them especially useful in desktop and portable devices. Most advantageously, piezoelectric devices may be operated with very small amounts of electrical power. Piezoelectric devices are, therefore, compatible with small, portable, power sources such as batteries. Sonication apparatus according to the