ASSAY SONICATION APPARATUS AND METHODOLOGY

REFERENCE TO PUBLICATIONS AND CORRESPONDING APPLICATIONS

[0001] The following published PCT Applications are hereby incorporated in their entirety by reference: U.S. No. 92/00982 (WO 92/14138); U.S. No. 92/00992 (WO 92/14139); and U.S. No. 96/03190 (WO 96/28538).

[0002] The following commonly owned and copending U.S. and PCT Applications, filed on even date herewith are incorporated in their entirety by reference: U.S. patent application Ser. No. ______ filed Sep. 17, 1997 entitled MULTI-ARRAY, MULTISPECIFIC ELECTROCHEMILUMINESCENCE TESTING and PCT Application No. ______ filed Sep. 17, 1997 entitled MULTI-ARRAY, MULTISPECIFIC ELECTROCHEMILUMINESCENCE TESTING (WO ______).

BACKGROUND OF THE INVENTION

[0003] Diagnostic tests upon liquid samples and diagnostic tests utilizing liquids are in widespread use in medical technology, environmental monitoring devices, and commercial applications. A significant impediment to the utilization of many diagnostic testing processes has been the impractical delay required for chemical reactions in such processes to proceed to a meaningful completion. It is not uncommon for diagnostic chemical reactions occurring in a liquid system to proceed for extended periods of time, e.g., in excess of thirty minutes. Such delay may make certain diagnostic tests entirely unsuitable for situations in which timely results are needed.

[0004] In an emergency room, delay in obtaining results from a diagnostic test may delay accurate evaluation of a patient's condition, to the extreme detriment of the patient. Even under less critical circumstances, such as a routine visit to a doctor's office, an hour delay in obtaining results from a diagnostic test may hinder a doctor's diagnosis and treatment of a patient during a single consultation. Any delay in treatment could result in harm to the patient. At the least, an extended delay in obtaining test results may necessitate an additional follow-up consultation and office visit, thereby increasing the overall cost of treatment to the patient. In the laboratory, the slow chemical reaction time of a diagnostic test may significantly reduce the efficiency of research efforts and burden researchers. Further, time-consuming diagnostic testing in industrial chemical processes may dramatically increase manufacturing costs and reduce production volume.

[0005] To avoid the above-described consequences, apparatus and methodology for increasing the speed of diagnostic testing processes are greatly desired, especially in connection with assays that incorporate a binding reaction, e.g., immunoassays, nucleic acid hybridization assays, and receptor-ligand binding assays. It would be particularly useful to increase the reaction rate in assays utilizing binding reactions that involve the binding of components of a solution to reagents located at a solid-phase support. Such assays should provide precise, quantitative results and be highly sensitive. In addition, it is also desirable that apparatus for conducting diagnostic test assays be small, portable, low cost, robust, and easy to operate. The above considerations are especially important in the field of Point-of-Care (POC) medical diagnostic testing (e.g., testing done at home, at a hospital bedside, in an emergency room, or in a doctor's office).

[0006] It is believed that the rate of a binding reaction depends upon the mass transport rate of the reagents involved. For binding reactions that occur at a solid-phase support, the rate at which molecules in solution bind to reagents located at a solid-phase surface may be limited by the rate of mass transport of the molecules to the surface. When such systems are not subject to active mixing, molecules in solution reach the solid-phase surface primarily by diffusion through the solution. It has been found that diffusion rates are generally too slow to allow binding reactions to approach completion with a 30 minute period. In addition, the presence of small convection currents in the solution, e.g., due to temperature gradients, can cause the rates of a binding reaction to vary considerably and thus be difficult to predict and control.

[0007] There have been numerous prior attempts to improve the mass transport of molecules to a solid phase support in a binding reaction system. Considerable efforts have been directed to increasing mass transport rates through the introduction of controlled convection currents, e.g., by vortexing, by using stirring devices, or by passing a solution over a solid-phase surface in a flow cell arrangement. Such approaches commonly utilize relatively expensive and complex mechanical devices, such as solution stirrers or pumps, and, consequently, are not suited for use in an assay device that is small in size, robust, inexpensive to manufacture, and easy to use.

[0008] Also, a liquid ultrasonication bath to promote mixing has been described in U.S. Pat. No. 4,575,485 (Sizto et al.). Sizto et al. mention a container, holding a volume of assay medium and a "dip-stick" immersed in the medium, submersed in the bath of a conventional liquid-bath ultrasonic cleaning device. Ultrasonic vibrations from the shell of the cleaner bath are liquid-coupled to the container. The vibrations traveling through the liquid of the cleaner bath dissipate in the volume of the bath and reflect off of the container material and off of the shell of the bath. Such liquid-coupling is clearly inefficient and can dissipate considerable amounts of ultra sonic energy.

[0009] The exact nature of the ultrasonic vibrations being transmitted to the assay medium and to the dip-stick will significantly depend upon apparatus design and usage conditions. For example, the shape of the container for the assay medium, the shape of the shell of the bath, the position of the container in the bath, the position of the dip-stick in the container, the position of the source of vibrations, the amount of dissolved gas in the liquid in the bath, and the volume of liquid in the bath will each affect the transmission of ultrasonic vibrations. In use, the volume of liquid could easily change due to evaporation, splashing or release of gasses dissolved in the liquid in the bath. All of these may affect the vibration transmission characteristics of the bath.

[0010] Since small variations in structure and operational conditions will considerably affect the transmission of ultrasonic energy in a device according to Sizto et al., it can be expected that precise reproduction of particular ultrasonic bath conditions throughout the duration of a particular reaction will be extremely difficult, if not impossible, to