

MAGNETIC IN SITU DILUTION

RELATED APPLICATIONS

[0001] This non-provisional application claims the benefit under Title 35, U.S.C. §119(e) of co-pending U.S. provisional application no. 60/237,427, filed Oct. 3, 2000 and U.S. provisional application no. 60/272,727, filed Mar. 1, 2001, each of which is incorporated by reference herein..

FIELD OF THE INVENTION

[0002] This invention relates to methods, assays, and components for the detection and analysis of binding between biological or chemical species, and can be used specifically for drug discovery.

BACKGROUND OF THE INVENTION

[0003] In certain areas of chemistry and biology the determination of binding interactions between molecules is of utmost importance. This is especially true in connection with studies involving physiology. A myriad of chemical and biochemical interactions associated with physiological processes, or with the interaction of chemicals with physiological processes, involve recognition of one molecular entity by another. One class of such interactions involves the physiological activity of pharmaceuticals (drugs). Precise understanding of the interaction of drugs with physiological entities, and the design of and/or discovery of drugs that can interact physiologically is, of course, of huge interest to society.

[0004] Drug discovery typically is facilitated by screening large numbers of candidate drugs for interaction with physiological targets such as target receptors or proteins. Known techniques for drug screening include studying candidate drugs individually for their pharmaceutical potential, often in parallel with tens, hundreds, or thousands of other drug candidates. In a typical process thousands of drug candidates (a library), each known to have at least some potential for some type of pharmaceutical use, are studied, in parallel, for their activity in connection with a specific physiological target. While this and other techniques for screening drugs, and studying other chemical or biological binding interactions are known, some are time-consuming and laborious. A need exists for improved, varied, and in some cases more rapid techniques for studying such interactions.

SUMMARY OF THE INVENTION

[0005] The present invention provides, generally, techniques for separating interacting components from a mixture of putative binding partners, determining the identity of an unknown analyte, determining which of a number of species binds to a known species, determining whether a species exists in a mixture that binds to another species, and/or a combination these and other techniques.

[0006] In one embodiment, the invention involves magnetically drawing a first article and a first chemical or biological agent immobilized relative to the first article to a first location, and drawing a second article to a second location. The first or second article is selectively released from its location while the other is held at its location.

[0007] In a further embodiment, a decision whether to release the first or second article can be made based upon

whether the first or second article has captured a binding partner or analyte. Repeated magnetic drawing and releasing steps can result in isolation, from a series of putative binding partners, a single binding partner of an analyte.

[0008] Other advantages, novel features, and objects of the invention will become apparent from the following detailed description of the invention when considered in conjunction with the accompanying drawings, which are schematic and which are not intended to be drawn to scale. In the figures, each identical or nearly identical component that is illustrated in various figures is represented by a single numeral. For purposes of clarity, not every component is labeled in every figure, nor is every component of each embodiment of the invention shown where illustration is not necessary to allow those of ordinary skill in the art to understand the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] FIG. 1 illustrates schematically (as do the remaining figures) binding between colloid-immobilized proteins and a first magnetic-bead-immobilized drug candidate but not a second magnetic-bead-immobilized drug candidate;

[0010] FIG. 2 illustrates a first drug candidate, immobilized relative to a magnetic bead and bound to colloid-immobilized proteins, and a second drug candidate, also immobilized to magnetic beads but not bound to colloid-immobilized proteins, in a mixture in the vicinity of magnetically-equipped electrodes;

[0011] FIG. 3 illustrates the magnetic beads of FIG. 2, and components immobilized thereto, drawn to the surfaces of magnetically-equipped electrodes;

[0012] FIG. 4 illustrates the arrangement of FIG. 3 after selective deactivation of magnetic force associated with one electrode; and

[0013] FIG. 5 illustrates the arrangement of FIG. 4 following deactivation of magnetic force associated with the remaining electrode and reactivation of magnetic force associated with both electrodes.

[0014] FIG. 6 illustrates a multiplexing apparatus for applying and releasing a magnetic force at multiple locations on a continuous surface.

DETAILED DESCRIPTION OF THE INVENTION

[0015] International patent application serial number PCT/US00/01997, filed Jan. 25, 2000 by Bamdad et al., entitled "Rapid and Sensitive Detection of Aberrant Protein Aggregation in Neurodegenerative Diseases" (published as WO 00/43791 on Jul. 27, 2000, International patent application serial number PCT/US00/01504, filed Jan. 21, 2000 by Bamdad, et al, entitled "Interaction of Colloid-Immobilized Species with Species on Non-Colloidal Structures" (published as WO 00/34783 on Jul. 27, 2000), commonly-owned, copending U.S. patent application Ser. No. 09/602,778, filed Jun. 23, 2000 by Bamdad et al., entitled "Interaction of Colloid-Immobilized Species with Species on Non-Colloidal Structures"; and commonly-owned, copending U.S. patent application Ser. No. 09/631,818, filed Aug. 03, 2000 by Bamdad et al., entitled "Rapid and Sensitive Detection of Protein Aggregation" all are incorporated herein by reference.