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(54) FLOW CELL ARRAY AND THE UTILIZATION THEREOF FOR MULTIANALYTE DETERMINATION

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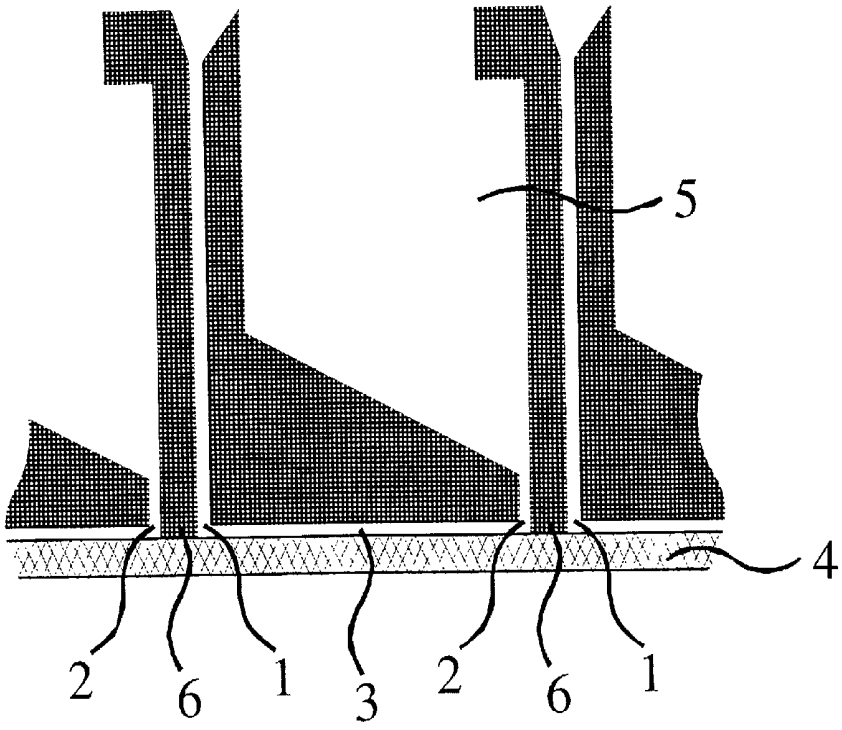
(57) **ABSTRACT**

The invention is related to a one- or two-dimensional arrangement of flow cells, as part of an array of sample compartments, with at least one in- and outlet for each sample compartment, formed by a base plate and a body, with an arrangement of spatial recesses corresponding to the (geometrical) arrangement of the sample compartments, combined with said base plate. The arrangement allows for supplying to or removing from the sample compartments, which can be arranged at a high quantity on a small base area, even very small amounts of samples or reagents. Subject of the invention is an arrangement of one or more sample compartments, comprising a base plate and and a body combined with said base plate in such a way, that one or more recesses for generation of one or more flow cells fluidically sealed against one another, each with at least one inlet and one outlet, are formed between said base plate and said body, wherein at least one outlet of each flow cell is joined with a reservoir fluidically connected with said flow cell, the reservoir being operable to receive liquid exiting the flow cell, besides methods for its manufacturing and their use.



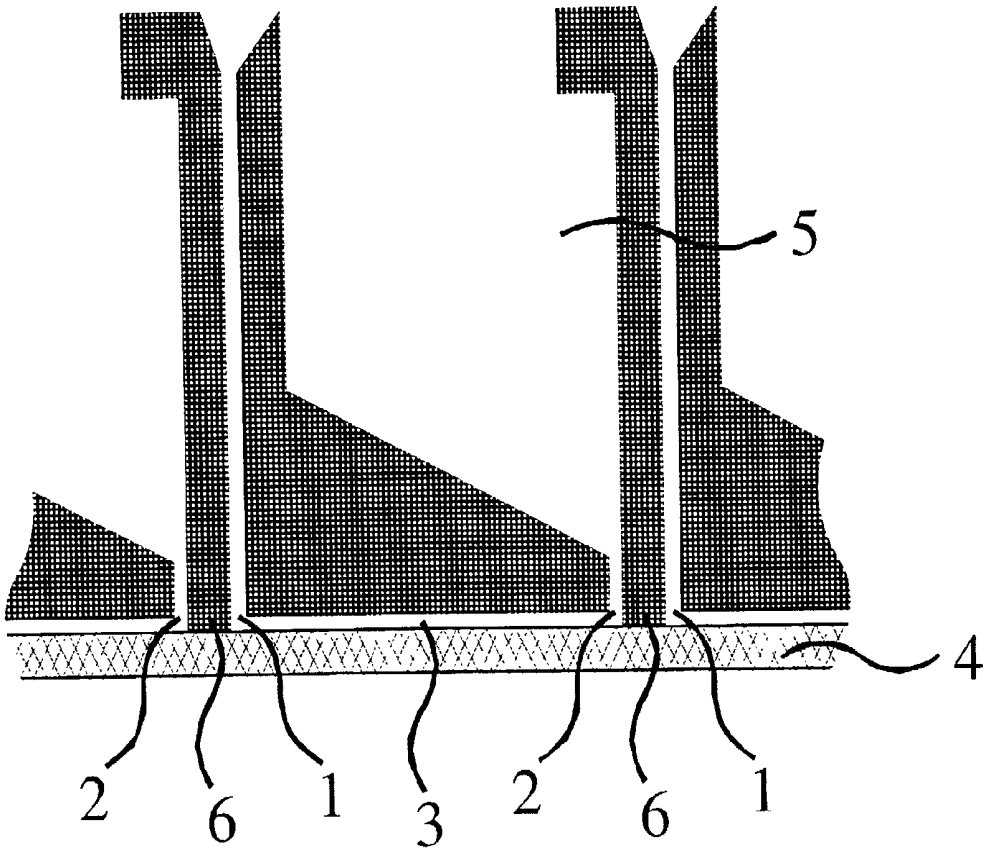


Fig 1

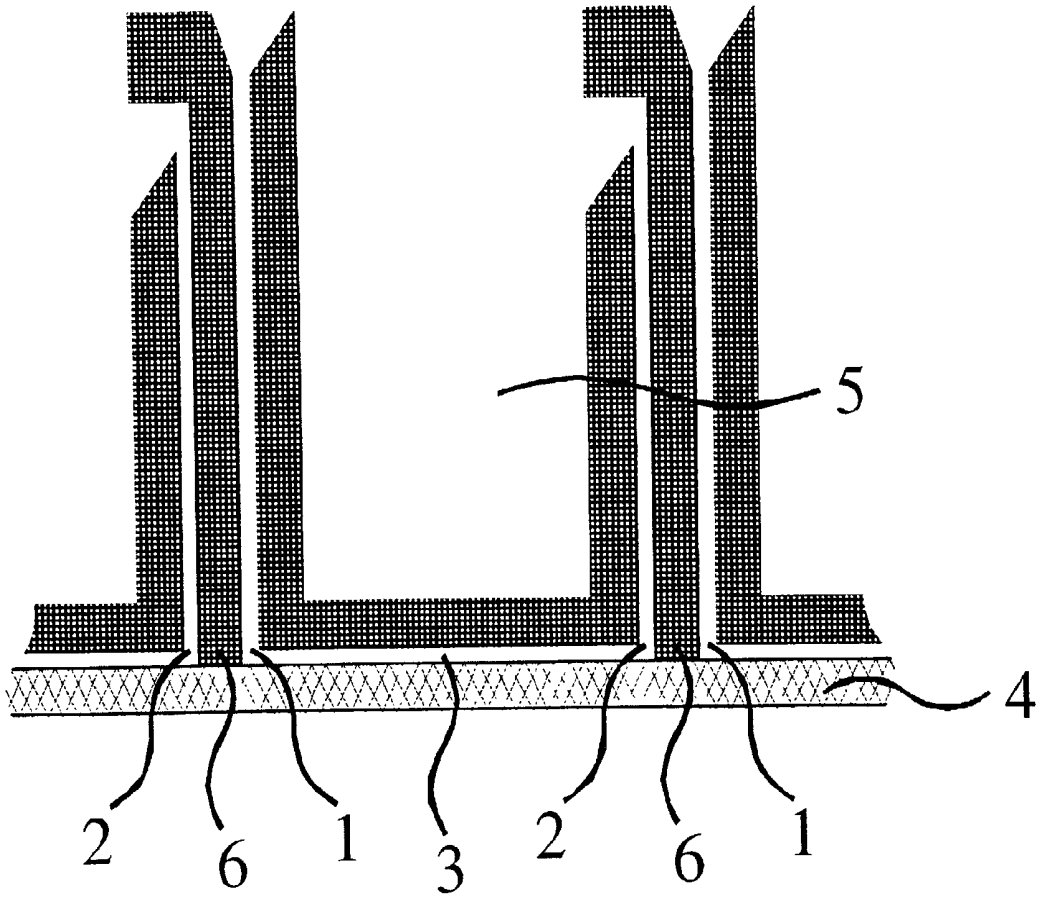


Fig 2

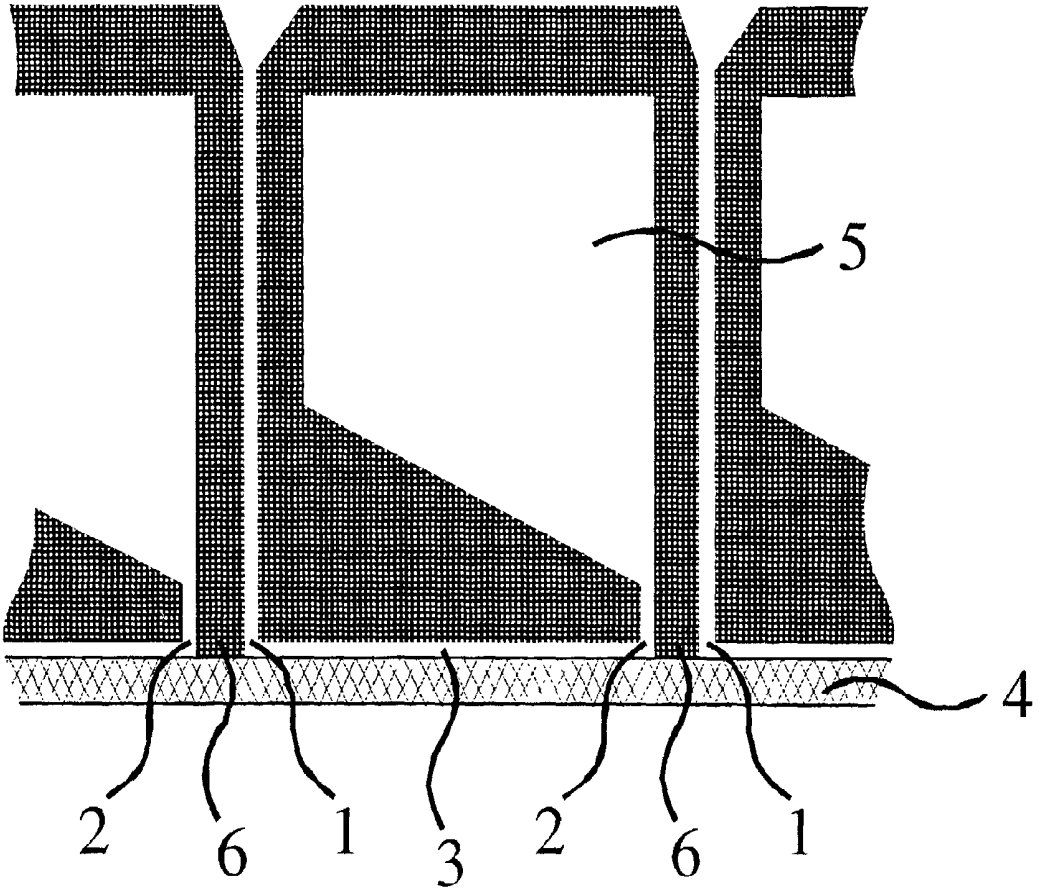


Fig 3

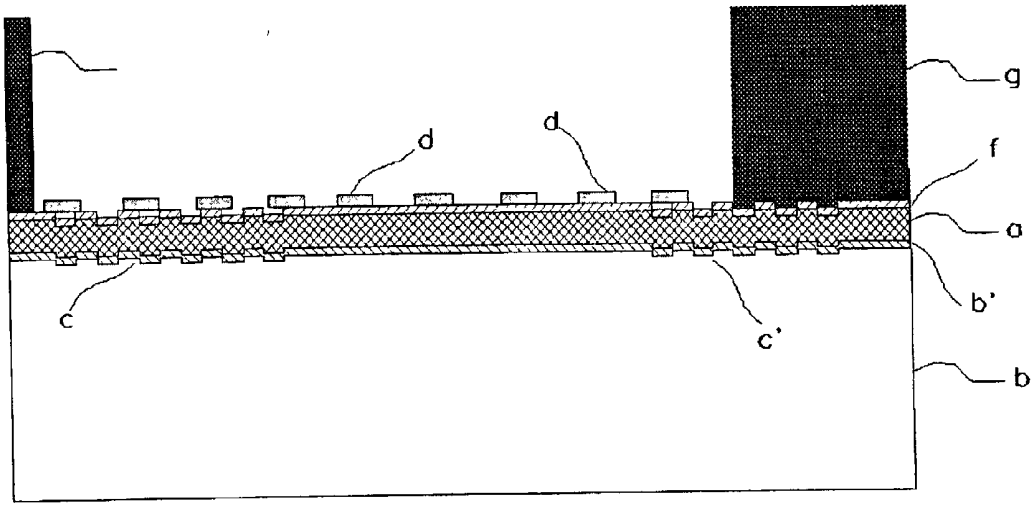


Fig 4

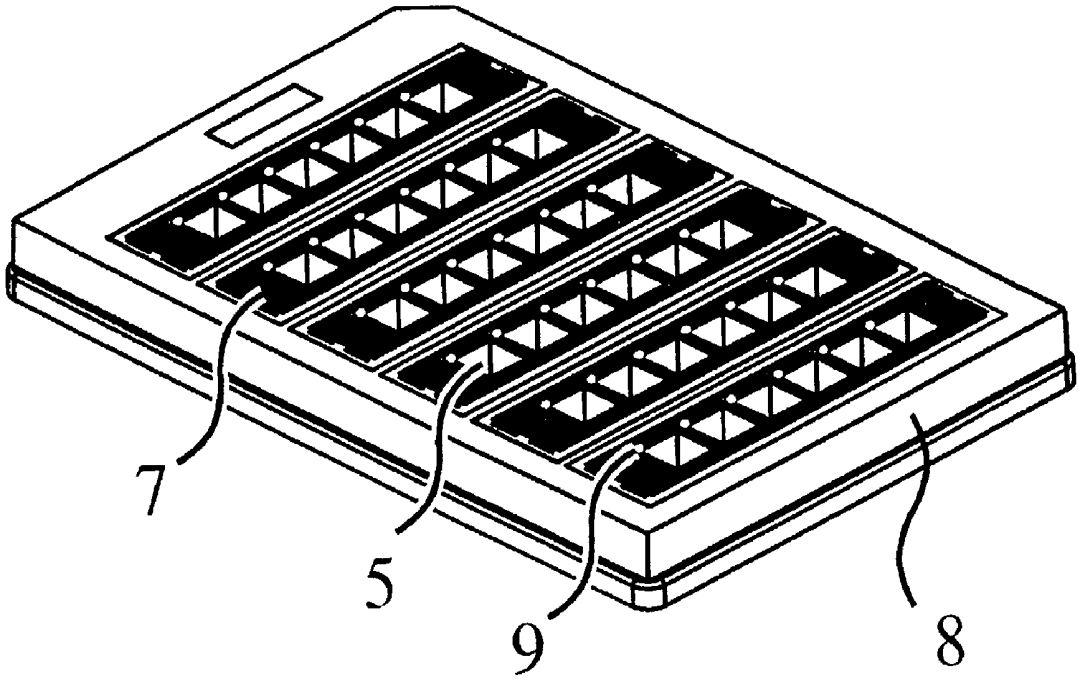


Fig 5

FLOW CELL ARRAY AND THE UTILIZATION THEREOF FOR MULTIANALYTE DETERMINATION

[0001] The invention is related to a one- or two-dimensional arrangement of flow cells, as part of an array of sample compartments, with at least one in- and outlet for each sample compartment, formed by a base plate and a body, with an arrangement of spatial recesses corresponding to the (geometrical) arrangement of the sample compartments, combined with said base plate. The arrangement allows for supplying to or removing from the sample compartments, which can be arranged at a high quantity on a small base area, even very small amounts of samples or reagents. For each sample compartment at least one reservoir for receiving liquids to be removed from the respective sample compartment being integrated in the arrangement, the peripheral manifold of liquid supply and removal means can be simplified significantly in comparison to conventional technical solutions.

[0002] For the determination of a single analyte in a sample, especially for diagnostics, numerous arrangements have become known, wherein the transport of samples or reagents is performed using capillary forces. Thus the use of pumps for fluidic transport can often be avoided. In U.S. Pat. No. 5,019,351 a special embodiment of such a device is described, wherein a reaction capillary with an inlet end and an outlet end is arranged between a base plate and a cover plate, the inlet end being fluidically connected with a region dedicated for receiving a sample and mixing the sample with reagents, and wherein the reaction capillary is divided into an upstrem region and a downstream region, with increasing thickness of the reaction capillary from the upstream region towards the downstream region. With this arrangement constant, reproducible flow condititions shall be achieved within the reaction capillary. Additionally, embodiments are described in that patent disclosure, wherein the outlet end of the reaction capillary is connected with a region for collecting exiting liquid. Thereby, all components of the structure, except for the inlet region, are provided in a continuous channel or capillary system, respectively, between the common base plate and a common cover plate. The essential technical background of the patent disclosure is based on liquid transport by the capillary effect.

[0003] However, especially because of the necessary large space requirements, such an arrangement pf capillary-type flow cells is hardly suited for an application in combination with a multitude of measurement areas, for the determination of different analytes or the analysis of different samples, on a common support. Accordingly, there not any hints towards array-type arrangements of several flow cells of this type in U.S. Pat. No. 5,019,351. Additionally, a removal of liquid having entered the collection region is not possible.

[0004] For the determination of a multitude of analytes, currently mainly such methods are used, wherein the determination of different analytes is performed in discrete sample compartments or "wells" of so-called microtiter plates. The most common are plates with a pitch (geometrical arrangements in rows and columns) of 8×12 wells on a footprint of typically about 8 cm×12 cm (see, for example, Coming Costar catalogue No. 3370, 1999), wherein a volume of some hundred microliters is required for filling a single well. It would be desirable for many applications, however, to reduce the sample volume considerably, not only for a reduction of necessary amounts of samples and reagents, which might be available only at small amounts, but especially for a reduction of the diffusion pathways and thus of the assay times, for assays wherein biological or biochemical or synthetic recognition elements for the recognition of one or more analytes in a sample are immobilized on the inner wall of a sample compartment.

[0005] In case of open sample compartments arranged in an array, derived from the classical microtiter plate, a well-known technical solution for a reduction of the volumes of the individual sample compartments was provided by arrangeing a larger number of wells on the same base area (foot print), for example 384 (see, for example, Coming Costar catalogue No. 3702, 1999) or 1536 instead of classically 96 wells. This approach has the advantage that the instruments and laboratory robots, established as the industrial standard, can be further used at least for a part of the necessary steps of sample manipulation, such as sample supply and removal. Other known technical solutions were provided by abandoning the classical plate foot print and adapting the size of the individual wells to the sample volumes required for a certain application, exclusively. Such arrangements became known under the name "nanotiter plates", the volumes of the individual sample compartments partially being only some nanoliters. However, this technical solution requires the abandonment of the currently widespread laboratory robots designed for the classical microtiter plate standard.

[0006] Along with the reduction of the size of the individual, open sample compartments and/or with the reduction of the thickness of the liquid layer on the base surface, desired for a reduction of the diffusion pathways, however, the increasing effect of liquid evaporation during the time of an assay becomes a more and more severe problem that has to be taken care of.

[0007] Said problem of evaporation can be avoided by using sample compartments that are closed, except for openings for sample inlet and outlet.

[0008] Such through-flow cells, operable for receiving a liquid sample and or reagents in a single flush or continuously, are known since long time for the case of a single measurement area in contact with a sample compartment.

[0009] In U.S. Pat. No. 5,747,274, measurement arrangements and methods for the early recognition of a cardiac infarction, upon determination of several from at least three infarction markers, are described, wherein the determination of these markers can be performed in individual sample compartments or in a common sample compartment, a single (common) sample compartment being provided, according to the disclosure for the latter case, as a continuous flow channel, one demarcation of which being formed, for example, by a membrane, whereon antibodies for the three different markers are immobilized. However, there are no hints for an arrangement of several sample compartments or flow channels of this type on a common support. Additionally, there are no geometrical informations concerning the size of the measurement areas.

[0010] Optical methods, for example based on the determination of the change of an absorbance or of a luminescence, have been developed for analyte determination in one

or more samples to an increasing extent in the past, as such methods can be performed without contact and without sigificant effect on the sample itself. The classical measurement methods, such as absorption or fluorescence measurements, are generally based on the direct illumination of a sample volume in a sample compartment or of a measurement area on the inner wall of the compartment of a liquid sample. As a disadvantage of these configurations, in general a significant part of the surroundings, besides the excitation volume or excitation area where a signal for analyte determination shall be generated, is illuminated by excitation light, which can lead to disadvantageous generation of disturbing background signals.

[0011] For achieving lower detection limits, numerous measurement arrangements have been developed, wherein the determination of an analyte is based on its interaction with the evanescent field, which is associated with light guiding in an optical waveguide, wherein biochemical or biological recognition elements for the specific recognition and binding of the analyte molecules are immobilized on the surface of the waveguide. When a light wave is coupled into an optical waveguide surrounded by optically rarer media, i.e. media of lower refractive index, the light wave is guided by total reflection at the interfaces of the waveguiding layer. In that arrangement, a fraction of the electromagnetic energy penetrates the media of lower refractive index. This portion is termed the evanescent (=decaying) field. The strength of the evanescent field depends to a very great extent on the thickness of the waveguiding layer itself and on the ratio of the refractive indices of the waveguiding layer and of the media surrounding it. In the case of thin waveguides, i.e. layer thicknesses that are the same as or smaller than the wavelength of the light to be guided, discrete modes of the guided light can be distinguished. As an advantage of such methods, the interaction with the analyte is limited to the penetration depth of the evanescent field into the adjacent medium, being of the order of some hundred nanometers, and interfering signals from the depth of the (bulk) medium can be mainly avoided. The first proposed measurement arrangements of this type were based on highly multi-modal, self-supporting single-layer waveguides, such as fibers or plates of transparent plastics or glass, with thicknesses from some hundred micrometers up to several millimeters.

[0012] In U.S. Pat. No. 4,978,503, a measurement arrangement is disclosed, wherein a liquid sample is drawn into a cavity by capillary forces, wherein an optically transparent side wall is provided as a self-supporting multimode waveguide, wherein at least on a part of the surface of that side wall ("patch"), facing the cavity, a biochemical recognition element for the recognition and binding of an analyte from a sample is immobilized. As a disadvantage of this arrangement, an exchange of the liquid drawn into the capillary is not provided for, such an exhange being for example desirable for a multi-step assay.

[0013] In WO 94/27137, measurement arrangements are disclosed, wherein "patches" with different recognition elements, for the determination of different analytes, are immobilized on a self-supporting optical substrate waveguide (single-layer waveguide), excitation light being incoupled at the distal surfaces ("front face" or "distal end" coupling), wherein laterally selective immobilization is performed using photo-activatable cross-linkers. According to the disclosure, several patches can be arranged row-wise in common, parallel flow channels or sample compartments, wherein the parallel flow channels or sample compartments extend over the whole length of the range on the waveguide used as a sensor, in order to avoid an impairment of light guiding in the waveguide. However, there are no hints to a two-dimensional integration of multiple patches and sample compartments. In a similar arrangement disclosed in WO 97/35203, several embodiments of an arrangement are described, wherein different recognition elements for the determination of different analytes are immobilized in separate, parallel flow channels or sample compartments for the sample and for calibration solutions of low and, optionally in addition, of high analyte concentration. Again, no hint to two-dimensional arrangements is given.

[0014] For an improvement of the sensitivity and simultaneously for an easier manufacturing in mass production, planar thin-film waveguides have been proposed. In the simplest case, a planar thin-film waveguide consists of a three-layer system: support material (substrate), waveguiding layer, superstrate (respectively the sample to be analyzed), wherein the waveguiding layer has the highest refractive index. Additional intermediate layers can further improve the action of the planar waveguide.

[0015] Several methods for the incoupling of excitation light into a planar waveguide are known. The methods used earliest were based on front face coupling or prism coupling, wherein generally a liquid is introduced between the prism and the waveguide, in order to reduce reflections due to air gaps. These two methods are mainly suited with respect to waveguides of relatively large layer thickness, i.e. especially self-supporting waveguides, and with respect to waveguides with a refractive index significantly below 2. For incoupling of excitation light into very thin waveguiding layers of high refractive index, however, the use of coupling gratings is a significantly more elegant method.

[0016] Different methods of analyte determination in the evanescent field of lightwaves guided in optical film waveguides can be distinguished. Based on the applied measurement principle, for example, it can be distinguished between fluorescence, or more general luminescence methods, on one side and refractive methods on the other side. In this context methods for generation of surface plasmon renonance in a thin metal layer on a dielectric layer of lower refractive index can be included in the group of refractive methods, if the resonance angle of the launched excitation light for generation of the surface plasmon resonance is taken as the quantity to be measured. Surface plasmon resonance can also be used for the amplification of a luminescence or the improvement of the signal-to-background ratios in a luminescence measurement. The conditions for generation of a surface plasmon resonance and the combination with luminescence measurements, as well as with waveguiding structures, are described in the literature, for example in U.S. Pat. Nos. 5,478,755, 5,841,143, 5,006,716, and 4,649,280.

[0017] In this application, the term "luminescence" means the spontaneous emission of photons in the range from ultraviolet to infrared, after optical or other than optical excitation, such as electrical or chemical or biochemical or thermal excitation. For example, chemiluminescence, bioluminescence, electroluminescence, and especially fluorescence and phosphorescence are included under the term "luminescence".

[0018] In case of the refractive measurement methods, the change of the effective refractive index resulting from molecular adsorption to or desorption from the waveguide is used for analyte detection. This change of the effective refractive index is determined, in case of grating coupler sensors, from changes of the coupling angle for the in- or out-coupling of light into or out of the grating coupler sensor, in case of interferometric sensors from changes of the phase difference between measurement light guided in a sensing branch and a referencing branch of the interferometer.

[0019] The aforesaid refractive methods have the advantage, that they can be applied without using additional marker molecules, so-called molecular labels. The disadvantage of these label-free methods, however, is, that the achievable detection limits are limited to pico- to nanomolar concentration ranges, dependent on the molecular weight of the analyte, due to lower selectivity of the measurement principle, which is not sufficient for many applications of modern trace analysis, for example for diagnostic applications.

[0020] For achieving lower detection limits, luminescence-based methods appear as more adequate, because of higher selectivity of signal generation. In this arrangement, luminescence excitation is limited to the penetration depth of the evanescent field into the medium of lower refractive index, i.e to the immediate proximity of the waveguiding area, with a penetration depth of the order of some hundred nanometers into the medium. This principle is called evanescent luminescence excitation.

[0021] By means of higly refractive thin-film waveguides, based on an only some hundred nanometers thin waveguiding film on a transparent support material, the sensitivity could be increased considerably during the last years. In WO 95/33197, for example, a method is described, wherein the excitation light is coupled into the waveguiding film by a relief grating as a diffractive optical element. The isotropically emitted luminescence from substances capable of luminescence, that are located within the penetration depth of the evanescent field, is measured by adequate measurement devices, such as photodiodes, photomultipliers or CCD cameras. The portion of evanescently excited radiation, that has back-coupled into the waveguide, can also be out-coupled by a diffractive optical element, like a grating, and be measured. This method is described, for example, in WO 95/33198.

[0022] For performing, simultaneously or sequentially, exclusively luminescence-based, multiple measurements with essentially monomodal, planar anorganic waveguides, for example in the specification WO 96/35940, arrangements (arrays) have been proposed, wherein at least two discrete waveguiding areas are provided on one sensor platform, such that the excitation light guided in one waveguiding area is separated from other waveguiding areas.

[0023] In the spirit of this invention, spatially separated measurement areas (d) (according to Fig. IV) shall be defined by the area that is occupied by biological or biochemical or synthetic recognition elements immobilized thereon, for recognition of one or multiple analytes in a liquid sample. These areas can have any geometry, for example the form of dots, circles, rectangles, triangles, ellipses or lines.

[0024] In WO 98/22799, arrangements of sample compartments for measurement configurations for the determination of luminescence excited in the evanescent field of a planar waveguide are proposed, wherein the gratings used for incoupling of the excitation light are covered by the material forming the side walls of the sample compartments. Thus, any change of the incoupling conditions can be avoided. This is, however, associated with very high requirements on the transparency, freedom of fluorescence and a refractive index of the side wall material as low as possible, which combination of requirements can hardly be satisfied simultaneously.

[0025] As a disadvantage, all devices described in the known technical state of the art do either not allow for an exchange of sample or reagent liquids or require relatively complex arrangements for such an exchange, namely the interfacing to fluidically sealing supplies and tube connections, for the supply and removal of liquid samples and reagents, especially impeding an automated operation and exchange of combinations of base plates, used as sensor platforms, with bodies placed thereon, for providing flow cells, for single use operation, or requiring complex technical solutions.

[0026] Therefore, there is a need for a simple arrangement of flow cells, especially in form of one- or two-dimensional arrays, wherein the supply of sample solutions and reagents and the removal of exiting sample and reagent fluids can be simplified significantly, without impairing the measurement accuracy in a negative way.

[0027] Surprisingly, it now has been found, that a multitude of sample compartments can be provided on a small base area, without the requirement of a complex system of peripheral supply and removal lines for an automated supply and removal of samples and reagents, thanks to the design of sample compartments according to the invention, the sample compartments being each provided with a reservoir, for example in form of a recess in an exterior sample compartment wall, for receiving liquids exiting the sample compartments. Simultaneously, the volume capacities of the individual sample compartments can be kept low, even when relatively large base areas of the sample compartments on a base plate are required for generation of a sufficiently high measurement signal, because the sample compartments are closed except for inlet and outlet openings for sample and reagent supply and removal, and because the height of a sample compartment, i.e. the distance between a base plate and the opposite demarcation of a recess in a body combined with the base plate, can be kept very small, i.e. even below 100 μm.

[0028] Due to this arrangement, even very low sample volumes can be administered and kept constant. Due to the possible small volumes, the flow cells provided by the arrangement according to the invention can be cleaned very efficiently by displacement washing. If biological or biochemical or synthetic recognition elements for the determination of an analyte are immobilized on the base plate, as described below for some embodiments of an arrangement according to the invention, the endpoint of diffusion-controlled analyte binding is reached fast, due to only short diffusion pathways towards the analyzing surface, which is another advantage. It is also favorable, that a signal caused by the analyte binding is essentially independent of the total

volume of a supplied sample, as long as at least the flow cell, as part of an arrangement according to the invention, is filled completely. The flow cells being closed except for inlets and outlets, an evaporation of liquid can mainly be avoided, allowing for operation of the arrangement also at temperatures significantly above room temperature. In summary, the present invention thus provides significant advantages in comparison to the known state of the art.

[0029] Subject of the invention is an arrangement of one or more sample compartments in a one- or two-dimensional array, comprising a base plate and and a body combined with said base plate in such a way, that an array of recesses for generation of an array of flow cells fluidically sealed against one another, each with at least one inlet and one outlet, are formed between said base plate and said body, wherein at least one outlet of each flow cell is joined with a reservoir fluidically connected with said flow cell, the reservoir being operable to receive liquid exiting the flow cell.

[0030] Thereby, the reservoir for receiving liquid exiting the flow cell is formed as a recess in the exterior wall of the body combined with the base plate.

[0031] The arrangement according to the invention allows for supplying simultaneously, locally addressed, numerous different sample and reagent solutions to different sample compartments, without the necessity of removing liquids that may have been supplied in advance. This does not require fixed tubing connections, but can be performed, for example using the squirt of a dispenser, which can be directed to the inlet of a flow cell of the arrangement according to the invention. The reservoirs for receiving liquids exiting from the flow cells being integrated in the arrangement, exit tubes and their connections, which would be required otherwise, are not needed. Thus, a multitude of flow cells for analysis of different samples can be integrated on a minimum base area.

[0032] For the simultaneous supply of samples or reagents to a multitude of sample compartments, multi-channel pipettors for manual or automated reagent administration can be used, wherein the individual pipettes are arranged in one- or two-dimensional arrays, provided that the inlets of the arrangement of sample compartments according to the invention are arranged in the same pitch (geometrical arrangement in rows and/or columns). Preferably, therefore, the pitch of the arrangement does correspond to the pitch of the wells of a standard microtiter plate. Thereby, an arrangement of 8×12 wells at a (center-to-center) distance of about 9 mm is established as the industrial standard. Smaller arrays with, for example, 3, 6, 12, 24 and 48 wells, arranged at the same distance, are compatible with this standard. Several arrangements of sample compartments, according to the invention, provided as smaller arrays of flow cells, can also be combined in such a way, that the individual inlets of said flow cells are located at a whole-numbered multiple of the distance of about 9 mm.

[0033] Recently, also plates with 384 and 1536 wells, as a whole-numbered multiple of 96 wells on the same foot print at a correspondingly reduced well-to-well distance, are used, which shall also be called standard microtiter plates. By adaptation of the pitch of the sample compartments in the arrangement according to the invention, including the in- and outlets of each flow cells, to these standards, numerous commercially established and available laboratory pipettors and robots can be used for sample supply.

[0034] It is preferred, that the exterior dimensions of the arrangement according to the invention do correspond to the foot print of these standard microtiter plates.

[0035] Whereas the sample supply is performed in the center of the open sample compartments in case of commercially availabe microtiter plates, it is advantageous for the arrangement according to the invention, due to physical reasons, if the in- and outlets and the corresponding inlet and outlet openings are arranged at the border of the corresponding flow cells, for example at corner points opposite to each other, preferably, however, at the diagonally opposite corner points, as it is shown in one of the examples of break-down-to-praxis. Therefore, the position of the whole array, of e.g. 8×12 cells in case of an arrangement of 96 flow cells, is preferably slightly displaced from the position of the cells of a classical microtiter plate with respect to its foot print, thus allowing to address the inlets and/or reservoirs using standard laboratory robots, without the requirement for re-programming. This is achieved with a displacement of 4.5 mm with respect to the two main borders (axes) in case of the 96-well pitch, and, correspondingly, of 2.25 mm, in case of the 384-well pitch, and of 1.125 mm, in case of the 1536-well pitch. Due to technical reasons (available wall thickness of the arrangament) a displacement of 2.25 mm is preferred, such that the arrangement according to the invention can be addressed by robots provided for the 384-standard, without a modification of their programming.

[0036] A further subject of the invention is an arrangement with, for example, 2 to 8 sample compartments in a column, with the properties as described above, or, for example, 2 to 12 sample compartments in a row, which themselves are combined with a carrier ("meta-carrier") with the dimensions of standard microtiter plates in such a way, that the pitch (geometrical arrangement in rows and/or columns) of the inlets of the flow cells does correspond to the pitch (geometrical arrangement) of the wells of a standard microtiter plate.

[0037] The adjoining of the arrangement of sample compartments with the meta-carrier can, for example, be performed by glueing or by exact fitting without glueing, if it is intended for single-use, or, for example by latching or inserting, if it is intended for multiple use. The material of the meta-carrier can, for example, be selected from the group comprising formable, moldable or millable plastics, metals, silicates, such as glass, quartz or ceramics.

[0038] Several rows or columns of such sample compartments can also be combined with a single meta-carrier in such a way, that the pitch (geometrical arrangement in rows and/or columns) of the inlets of the flow cells does correspond to the pitch (geometrical arrangement) of the wells of a standard microtiter plate, i.e., to a whole-numbered multiple of 9 mm (corresponding to a 96-well plate) or of 4.5 mm (corresponding to a 384-well plate, see above) or of 2.25 mm (corresponding to a 1536-well plate, see above).

[0039] Of course, the arrangement of sample compartments according to the invention can also be arranged in another pitch (geometry). Liquid exiting a flow cell, for example after sequential addition of different reagents, can be collected in the reservoir fluidically connected with the corresponding flow cell or also be removed by exhausting at the position of the inlet or of the reservoir.

[0040] There are several technical solutions for the generation of the spatial recesses between the base plate and the

body combined therewith. In one possible arrangement, three-dimensional structures, with the pitch (geometrical arrangement in rows and/or columns) of the arrays of flow cells to be generated, are formed on the base plate. These structures on the base plate can, for example, form the walls or parts of the walls, such as sockets, between flow cells adjacent to each other, which flow cells are formed by combination of the base plate with an adequately formed body. For generation of the array of flow cells, that, for generation of the spatial recesses between the base plate and the body combined therewith, these recesses are formed in the base plate.

[0041] Characteristic for another embodiment is, that, for generation of the recesses between the base plate and the body combined therewith, recesses are formed in said body. For this embodiment it is preferred, that the base plate is essentially planar.

[0042] The body to be combined with the base plate for the generation of the array of flow cells can consist of a single workpiece. In another embodiment, the body combined with the base plate is formed from several parts, wherein the combined parts of said body preferably form an irreversibly combined unit.

[0043] It is preferred, that the body combined with the base plate comprises auxiliary means facilitating the combination of said body and the base plate.

[0044] It is further preferred that the arrangement comprises a multitude, i.e., 2-2000, preferably 2-400, most preferably 2-100 flow cells.

[0045] Preferably the pitch (geometrical arrangement in rows and/or columns) of the inlets of the flow cells does correspond to the pitch (geometrical arrangement) of the wells of a standard microtiter plate.

[0046] Characteristic for another embodiment of the arrangement is, that it is closed by a covering top, such as a foil, membrane or cover plate.

[0047] The capacity of the flow cells can be varied within a large range upon variation of the size of the base areas and of the depth of the trecesses, so that the inner volume of each flow cell is typically 0.1 μl-1000 μl, preferably 1 μl-20 μl. Thereby, the inner volumes of different flow cells can be similar or different.

[0048] If different sample or reagent solutions are filled sequentially into a flow cell, typically a multiple liquid volume of the cell volume is applied, in order to displace as completely as possible the liquid and components dissolved therein, which had been added before. Therefore it is preferred, that the capacity of the reservoir fluidically connected to the flow cell is larger, preferably at least 5 times larger than the inner volume of the flow cell.

[0049] It is preferred, that the depth of the recesses between the base plate and the body combined with said base plate is 1-1000 μm, preferably 20-200 μm. The size of the recesses of an array can be uniform or diverse and the base areas can have any geometry, preferably rectangular or polygonal or also other geometry. The lateral dimensions of the base areas can be varied within a large range as well, wherein typically the base areas of the recesses between the base plate and the body combined with said base plate are 0.1 mm^2-200 mm^2, preferably 1 mm^2-100 mm^2. It is preferred, that the corners of the base areas are rounded. Rounded corners affect the flow profile in a favorable way and facilitate the removal of gas bubbles that might be formed, respectively prevent their formation.

[0050] The materials for the baseplate, the body combined therewith, and the optional additional covering top have to satisfy the requirements of the actually intended application. Dependent on the specific application, these requirements are related to chemical and physical stability, for example upon exposure to acidic or basic media, salts, alcohols or detergents as parts of aqueous solutions, or to formamide, to stability upon temperature variations (e.g. between −30° C. and 100° C.), to thermal expansion coefficients of the base plate and of the body combined therewith as similar as possible, to optical properties (such as non-fluorescence, reflectivity), to mechanical workability, etc. It is preferred, that the material of the body combined with the base plate is selected from the group formed by formable, moldable or millable plastics, metals, silicates, such as glass, quartz or ceramics. Also the material of the additional, contiguous covering top can be selected from the group formed by formable, moldable or millable plastics, metals, silicates, such as glass, quartz or ceramics. Concerning the base plate, it is also preferred, that its material comprises materials from the group formed by formable, moldable or millable plastics, metals, silicates, such as glass, quartz or ceramics. Thereby, the aforementioned components (base plate, body combined therewith, covering top) can be composed of a uniform material or can comprise a mixture or a composition. adjoined in layers or laterally of different materials, wherein the materials can substitute each other.

[0051] Characteristic for a preferred embodiment is, that biological or biochemical or synthetic recognition elements for the determination of one or more analytes are immobilized on the base plate.

[0052] The simplest method of immobilization consists in physical adsorption, for example due to hydrophobic interaction between the recognition elements and the base plate. However, the extent of these interactions can be affected strongly by the composition of the medium and its physical-chemical properties, such as polarity and ionic strength. Especially in case of sequential addition of different reagents in a multi-step assay, the adhesion of the recognition elements on the surface, after only adsorptive immobilization, is often insufficient. In an advanced embodiment of the arrangement, the adhesion is improved by deposition of an adhesion-promoting layer (f) (according to Fig. IV) on the base plate for the immobilization of the biological or biochemical or synthetic recognition elements. It is preferred, that the adhesion-promoting layer (f) has a thickness of less than 200 nm, preferably of less than 20 nm. For the generation of the adhesion-promoting layer, many materials can be used. Without any restriction, it is preferred, that the adhesion-promoting layer (f) comprises chemical compounds from the groups of silanes, epoxides, "self-organized functionalized monolayers", functionalized polymers and polymer gels.

[0053] In case of the simultaneous determination of different analytes, preferably upon their binding to different, selective recognition elements, it is of advantage, if the registration of these binding events can be performed by detection of laterally resolved signals. Characteristic of an

advanced embodiment of the arrangement according to the invention is, that the biological or biochemical or synthetic recognition elements are immobilized in discrete (laterally separated) measurement areas (d). These discrete measurement areas can be formed by spatially selective deposition of the biological or biochemical or synthetic recognition elements on said base plate. Numerous methods can be used for the deposition. It is preferred without any restriction of generality, that the biological or biochemical or synthetic recognition elements are deposited on the base plate by one or more methods from the group of methods comprising "ink jet spotting, mechanical spotting by means of pin, pen or capillary, "micro contact printing", fluidically contacting the measurement areas with the biological or biochemical or synthetic recognition elements upon their supply in parallel or crossed micro channels, upon exposure to pressure differences or to electric or electromagnetic potentials.

[0054] As said biological od biochemical or synthetic recognition elements, components from the groups formed by nucleic acids (DNA, RNA) or nucleic acid analogues (for example peptide nucleic acids PNA), antibodies, aptamers, membrane-bound and isolated receptors, their ligands, antigens for antibodies, cavities generated by chemical synthesis to host molecular imprints, and "histidin-tag components", are deposited. Also whole cells and cell fragments can be deposited as biological or biochemical or synthetic recognition elements.

[0055] The arrangement according to the invention is intended for numerous applications, wherein not only a single, but two or more analytes in a sample shall be determined. Therefore it is preferred, that arrays of two or more discrete measurement areas (d) each are arranged in the regions of the recesses between the base plate and the body combined with said base plate, in which measurement areas similar or different biological or biochemical or synthetic recognition elements are immobilized.

[0056] In general, the immobilized recognition elements are selected in such a way, that they recognize and bind the analyte to be determined with a specificity as high as possible. Typically however, it must be expected that also a nonspecific adsorption of analyte molecules on the surface of the base plate does occur, especially if there are still empty sites between the recognition elements immobilized in the measurement areas. Therefore it is preferred, that compounds which are "chemically neutral" towards the analyte are deposited between the discrete measurement areas (d), in order to reduce nonspecific binding or adsorption. As "chemically neutral" compounds such components are meant, which do not show a recognition or binding of the analyte, such that no or only minimum nonspecific binding does occur. The choice of these compounds is dependent on the properties of the analyte. Without any restriction it is preferred, that said "chemically neutral" compounds are selected from the groups comprising, for example, albumins, especially bovine and human serum albumin, herring sparm or also polyethylen glycols.

[0057] The arrangement according to the invention can be used for the determination of numerous different parameters (measurands), wherein the specific embodiment, especially of the baseplate, is dependent on the actually applied measurement method. One subject of the invention is an arrangement, wherein the base plate with the biological or biochemical or synthetic recognition elements immobilized thereon is operable for the determination of a change of optical, electrical, electrochemical or thermal parameters, or for the determination of radioactive radiation. It is preferred, that the base plate with the biological or biochemical or synthetic recognition elements immobilized thereon is operable for the determination of a change of optical parameters, and that said base plate is transparent in at least one region of wavelengths in the visible or near-infrared spectral region. It is especially preferred, that the base plate comprises a supporting substrate of glass or of a thermoplastic or moldable plastic, which is transparent in at least one region of wavelengths in the visible or near-infrared spectral region.

[0058] Within the optical detection methods, the methods based on analyte detection within the evanescent field of a waveguide are characterized by improved sensitivity and by restriction of the detection volume to the layer penetrated by the ecvanescent field, in proximity to the waveguide. Therefore it is preferred, that the base plate comprises an optical waveguide, which is continuous or partitioned into discrete areas. Thereby, especially preferred is an arrangement, wherein the optical waveguide is an optical film waveguide with a first optically transparent layer (a), facing the recesses, on a second optically transparent layer (b) with lower refractive index than layer (a) (according to Fig. IV). Thereby, the terminus "optical transparency" does mean (here and in the following) transparency at one or more excitation wavelengths in the visible or near-infrared spectral range.

[0059] The optically transparent layer (b) should be characterized by low absorption and fluorescence, in the ideal case free of absorption and fluorescence. Addionally, the surface roughness should be low, because the surface roughness of the layer (b) does affect, dependent on the deposition process to a more or less large extent, the surface roughness of an additional layer (a) of higher refractive index, when it is deposited on layer (a) as a waveguiding layer. An increased surface roughness at the boundary (interface) layers of layer (a) leads to increased scattering losses of the guided light, which, however, is undesired. These requirements are fulfilled by numerous materials. It is preferred that the material of the second optically transparent layer (b) comprises silicates, auch as glass or quartz, or a transparent thermoplastic or moldable plastic, preferably of the group comprising polycarbonate, polyimide, or polymethylmethacrylate, or polystyrene.

[0060] For a given layer thickness of the optically transparent layer (a), the sensitivity of an arrangement according to the invention increases along with an increase of the difference between the refractive index of layer (a) and the refractive indices of the adjacent media, i.e., along with an increase of the refractive index of layer (a). It is preferred, that the refractive index of the first optically transparent layer (a) is higher than 1.8.

[0061] Another important requirement on the properties of layer (a) is, that the propagation losses of the light guided in layer (a) should be as low as possible. It is preferred, that the first optically transparent layer (a) comprises TiO_2, ZnO, Nb_2O_5, Ta_2O_5, HfO_2, or ZrO_2, preferably TiO_2, Ta_2O_5 or Nb_2O_5. Combinations of several such materials can also be used.

[0062] For a given material of layer (a) and given refractive index, the sensitivity does increase with decreasing layer thickness, up to a certain lower limiting value of the layer thickness. The lower limiting value is determined by the cut-off of light guiding, if the layer thickness falls below a threshold value determined by the wavelength of the light to be guided, and by an observable increase of the propagation losses in very thin layers, with further decrease of their thickness. It is preferred, that the thickness of the first optically transparent layer (a) is between 40 and 300 nm, preferably between 100 and 200 nm.

[0063] If an autofluorescence of layer (b) cannot be excluded, especially if it comprises a plastic such as polycarbonate, or for reducing the effect of the surface roughness of layer (b) on the light guiding in layer (a), it can be advantageous, if an intermediate layer is deposited between layers (a) and (b). Therefore, it is characteristic for another embodiment of the arrangement according to the invention, that an additional optically transparent layer (b') (according to Fig. IV) with lower refractive index than and in contact with layer (a), and with a thickness of 5 nm-10 000 nm, preferably of 10 nm-1000 nm, is located between the optically transparent layers (a) and (b).

[0064] Many methods are known for the in-coupling of excitation light into an optical waveguide. In case of relatively thick waveguiding layers, up to self-supporting waveguides, the light can be focused into a front end (distal end) of the waveguide, using lenses of adequate numerical aperture, in such a way, that it is guided by internal total reflection. In case of waveguides with larger width of the front face than thickness, then preferably cylindrical lenses are used. Thereby, the lenses can be arranged remote from the waveguide or can also be directly connected to it. This method of front face coupling is less suited in case of lower thicknesses of the waveguiding layer. A more adequate method is then the coupling by prisms, which are preferably connected to the waveguide without any intermediate spacing or mediated by an index-matching fluid. It is also possible to supply the excitation light to the optical waveguide of the arrangement according to the invention by means of an optical fiber, or to couple light that has been in-coupled into another waveguide into the waveguide of said arrangement, upon bringing both waveguides in such a proximity to each other, that their evanescent fields overlap, thus enabling the energy transfer. Therefore, a part of the arrangement according to the invention is, that the in-coupling of excitation light into the optically transparent layer (a), to the measurement areas (d), is performed using one or more optical in-coupling elements from the group comprising prism couplers, evanescent couplers comprising joined optical waveguides with overlapping evanescent fields, front face (distal end) couplers with focusing lenses arranged in front of a front face (distal end) of the waveguiding layer, and grating couplers.

[0065] It is preferred, that the in-coupling of excitation light into the optically transparent layer (a), to the measurement areas (d), is performed using one or more grating structures (c) (according to Fig. IV), that are formed in the optically transparent layer (a).

[0066] A further part of the invention is, that the out-coupling of light guided in the optically transparent layer (a) is performed using grating structures (c') (according to Fig. IV), that are formed in the optically transparent layer (a).

[0067] Thereby, grating structures (c) and (c') formed in the optically transparent layer (a) can have the same or different periodicity and can be arranged in parallel or not in parallel to one another.

[0068] The arrangement can be provided in such a way, that grating structures (c) and (c') can interchangeably be used as in-coupling and/or out-coupling gratings.

[0069] It is preferred, that the grating structures (c) and optional additional grating structures (c') have a period of 200 nm-1000 nm and a grating modulation depth of 3 nm-100 nm, preferably of 10 nm-30 nmn.

[0070] Thereby it is preferred, that the ratio of the modulation depth to the thickness of the first optically transparent layer (a) is equal or smaller than 0.2.

[0071] The grating structure can be provided in different forms (geometry). It is preferred, that the grating structure (c) is a relief grating with any profile, such as rectangular, triangular or semi-circular profile, or a phase or volume grating with a periodic modulation of the refractive index in the essentially planar optically transparent layer (a).

[0072] Characteristic for an advanced embodiment of the arrangement is, that a thin metal layer, preferably of gold or silver, optionally on an additional dielectric layer of lower refractive index than layer (a), for example of silica or magnesium fluoride, is deposited between the optically transparent layer (a) and the immobilized biological or biochemical recognition elements, wherein the thickness of the metal layer and the optional, additional intermediate layer is selected in such a way, that a surface plasmon at the excitation wavelength and/or at the luminescence wavelength can be excited.

[0073] For one embodiment of the arrangement it is preferred, that the grating structure (c) is a diffractive grating with a uniform period.

[0074] For specific applications however, for example for in-coupling simultaneously excitation light of different wavelengths, it can be of advantage, if the grating structure (c) is a multi-diffractive grating.

[0075] Usually it is preferred, that grating structures (c) and optional additional grating structures (c') are located within the region of the sample compartments.

[0076] If however, for example, very small sample volumes shall be applied on a very small base area, it can be advantageous if grating structures (c) and optional additional grating structures (c') are located outside the region of the sample compartments.

[0077] For applications, wherein a number as high as possible, of sample compartments within one sample compartment, shall be provided, and wherein simultaneously a propagation of the guided excitation light to adjacent sample compartments, in the direction of propagation of the guided excitation light, shall be prevented by means of its controlled outcoupling, it is preferred, that the grating structures (c) are located within the region of the sample compartments, and that optional additional grating structures (c') are located outside of the sample compartment, within which the incoupling of the excitation light is performed.

[0078] Especially in case of sequential execution of measurements in different sample compartments, the gratings

structures can be arranged in such a way, that the excitation light is in-coupled by a grating structure (c) within one sample compartment, propagates through the sample compartment (guided in the waveguiding layer), and enters the waveguiding layer under an adjacent sample compartment, located in direction of propagation of the guided excitation light, where it is out-coupled by means of a grating structure (c') provided therein. After lateral displacement of the arrangement, the last-mentioned grating structure (c') can be used as in-coupling grating itself for a subsequent measurement.

[0079] Also additional embodiments of the arrangement according to the invention are provided, wherein grating structures (c) and optional additional grating structures (c') extend over the range of multiple or all sample compartments.

[0080] Multiple grating structures (c) and (c') can also be located within one sample compartment, for sequential measurements within a single sample compartment.

[0081] For most applications of the arrangement it is preferred, that the material of the body combined with the baseplate, in the incumbent surface area on the base plate, is optically transparent, both for the excitation radiation and for one or more optionally excited luminescence radiations, at least within the penetration depth of the evanescent field.

[0082] In an advanced embodiment, the material of the body combined with the base plate is provided in form of a two-layer system, the first layer of which, to be brought into contact with the surface of the base plate, being transparent both for the excitation radiation and optionally for one or more excited luminescence radiations, whereas the adjacent layer, being located more remote from the base plate, is absorbent in the spectral range of the excitation radiation and of the optionally excited luminescence radiations.

[0083] If an optical cross-talk of excitation light between adjacent sample compartments shall be minimized, it is advantageous to interrupt or minimize (as far as possible) the waveguiding upon contacting the waveguide in the intermediate regions between the sample compartments with an absorbent material. This is especially advantageous, if light in- and outcoupling by grating structures (c), respectively (c'), is performed within the sample compartments, or if a large-area grating structure extends over a multitude of sample compartments and a large area is illuminated with excitation light. It is characteristic for such an advanced embodiment, that the material of the layer in contact with the base plate is absorbent in the spectral range of the excitation radiation and of the optionally excited luminescence radiations.

[0084] It is of advantage, if the material of the layer in contact with the base plate is selfadhesive and tightly sealing. Thereby it is preferred, that the material of the layer in contact with the base plate comprises a polysiloxane.

[0085] The arrangement according to the invention is operable to determine simultaneously a multitude of analytes in one sample. Therefore it is advantageous, if 5-1000, preferably 10-400 measurement areas are located in one sample compartment.

[0086] For an advanced embodiment it is preferred, that optically or mechanically recognizable marks are provided on the base plate, in order to facilitate the adjustment in an optical system and/or to facilitate the combination of the base plate with the body comprising the recesses for the sample compartments.

[0087] A further subject of the invention is an analytical system for the determination of one or more analytes, comprising

[0088] an arrangement according to any of the aforementioned embodiments

[0089] means for the locally addressed supply of samples or reagents to the sample compartments of said arrangement, and

[0090] at least one detector for the detection of a change of a parameter (measurand) due to the presence of the one or more analytes, which parameter (measurand) preferably is an optical, electrical, electrochemical or thermal parameter (measurand) or a signal from radioactive radiation.

[0091] Subject of the invention is also an analytical system for the determination of one or more luminescences comprising

[0092] an arrangement according to any of the aforementioned embodiments

[0093] means for the locally addressed supply of samples or reagents to the sample compartments of said arrangement

[0094] at least one excitation light source, and

[0095] at least one detector for the detection of the light emanating from the at least one or more measurement areas (d) on the base plate.

[0096] Preferred is an analytical system for the determination of one or more analytes, comprising

[0097] an arrangement according to any of the aforementioned embodiments

[0098] means for the locally addressed supply of samples or reagents to the sample compartments of said arrangement

[0099] at least one excitation light source, and

[0100] at least one detector for the detection of a change of an optical parameter (measurand), which is preferably a change of the refractive index and/or of one or more luminescences in the vicinity of the one or more analytes.

[0101] Characteristic of a possible embodiment of the analytical system is, that the launching of the excitation light to the measurement areas (d) is performed in a surface or transmissive illumination configuration.

[0102] For specific applications it is of advantage, if the launching of the excitation light to the measurement areas (d) and the detection of the measurement light from the measurement areas (d) is performed at opposite sides of the base plate

[0103] For a larger number of applications it is preferred, that the launching of the excitation light to the measurement areas (d) and the detection of the measurement light from the measurement areas (d) is performed at the same side of the base plate.

[0104] Characteristic of a special embodiment is, that the launching of the excitation light to the measurement areas (d) and the detection of the measurement light from the measurement areas (d) is performed in a confocal arrangement.

[0105] For another embodiment of the analytical system according to the invention, with an arrangement of sample compartments according to the invention, comprising an optical film waveguide, it is preferred, that the excitation light rays of one (common) wavelength are located in a common plane, which is defined by the resonance angle for in-coupling the excitation light of said excitation wavelength into the optically transparent layer (a) by an optical coupling element.

[0106] For the simultaneous detection of signals from a multitude of measurement areas it is preferred, that at least one laterally resolving detector is used for signal detection, which is preferably selected from the group formed by CCD cameras, CCD chips, photodiode arrays, Avalanche diode arrays, multi-channel plates, and multi-channel photomultipliers.

[0107] The invention encompasses analytical systems, the characteristics of which is, that optical components of the group comprising lenses or lens systems for the shaping of the transmitted light bundles, planar or curved mirrors for the deviation and optionally additional shaping of the light bundles, prisms for the deviation and optionally spectral separation of the light bundles, dichroic mirrors for the spectrally selective deviation of parts of the light bundles, neutral density filters for the regulation of the transmitted light intensity, optical filters or monochromators for the spectrally selective transmission of parts of the light bundles, or polarization selective elements for the selection of discrete polarization directions of the excitation or luminescence light are located between the one or more excitation light sources and the base plate, as part of an arrangement according to any of the aforementioned embodiments, and/or between said base plate and the one or more detectors.

[0108] The light excitation can be performed continuously. It is preferred, however, that the excitation light is launched in pulses with duration of 1 fsec to 10 min.

[0109] Characteristic of an advanced embodiment of the analytical system is, that the emission light from the measurement areas is measured time-resolved.

[0110] It is preferred, that for referencing the available excitation light, light signals of the group comprising excitation light at the location of the light sources or after expansion of the excitation light or after its multiplexing into individual beams, scattered light at the excitation wavelength from the location of the one or more discrete measurement areas, and light of the excitation wavelength outcoupled by the grating structures (c) or (c') are measured.

[0111] It is especially preferred, that the measurement areas for determination of the emission light and of the reference signal are identical.

[0112] In one embodiment of the analytical system according to the invention, launching and detection of the emission light is performed simultaneously for all measurement areas. Characteristic of another embodiment is, that launching of the excitation light and detection of the emission light from the one or more measurement areas is performed sequentially for one or more sample compartments. It is also possible, that sequential launching of the excitation light and detection of the emission light from one or more measurement areas is performed several times within a single sample compartment.

[0113] Thereby it is preferred, that sequential excitation and detection is performed using movable optical components of the group comprising mirrors, deviating prisms, and dichroic mirrors.

[0114] It is preferred in especial, that sequential excitation and detection is performed using an essentially focus and angle preserving scanner.

[0115] Characteristic of another embodiment of an analytical system with sequential excitation and detection is, that the arrangement, according to any of the aforementioned embodiments, is moved between steps of sequential excitation and detection.

[0116] A further subject of the invention is a method for manufacturing an arrangement of sample compartments in a one- or two-dimensional array, comprising a base plate and and a body combined with said base plate in such a way, that an array of (spatial) recesses for generation of an array of flow cells, each with at least one inlet and one outlet, are formed between said base plate and said body, wherein at least one outlet of each flow cell is joined with a reservoir fluidically connected with said flow cell, the reservoir being operable to receive liquid exiting the flow cell, wherein said base plate and said body are combined in such a way, that different ones of said (spatial) recesses are fluidically sealed against one another.

[0117] As a possible embodiment of this method, the base plate and the body combined with that base plate can be joined irreversibly. Thereby it is preferred, that the base plate and the body combined with the base plate are glued together.

[0118] Thereby a glue is preferred, which is characterized by transparency as high as possible, at least at the excitation wavelength, and is fluorescent as weak as possible under the excitation conditions, in the ideal case free of fluorescence. For applications, wherein the excitation light shall be restricted to a single sample compartment, however, it can also be advantageous, if the glue is absorbent at the excitation wavelength, for example black, but again fluorescent as low as possible, in the ideal case free of fluorescence. Furtheron, similar material requirements hold for the glue as for the material of the body combined with the base plate, i.e. chemical and physical stability, for example upon exposure to acidic or basic media, salts, alcohols, or detergents as parts of aqueus solutions, or formamide, and temperature stability. Of course, the glue has to be adapted simultaneously to the chemical surface properties of the materials to be joined. Chemical reactions with analytes and/or the immobilized recognition elements shall also not occur.

[0119] If the biological or biochemical or synthetic recognition elements for the analyte determination are deposited on the base plate before the combination with said body, also the compatibility of the necessary glue curing method with the stability of said recognition elements has to be taken into account. This, in general, excludes those glues, which

require for curing the application of very short-wavelength UV-radiation (e.g. shorter than 280 nm), of high temperatures (e.g. above 100° C.), especially when required for longer periods (e.g. longer than 2 hours). Thereby, the requirements are generally stricter, when proteins, such as antibodies, are used as recogntion elements, than in combination with nucleic acids as recognition elements.

[0120] The base plate and the body combined therewith can also be joined reversibly, for example by latching, enabled by adequate means provided to that body, such as barbed hooks, or by inserting into provided guideways. An essential criterium for the choice of the method for the joining of the base plate with said body is, that, after its accomplishment, adjacent sample compartments are fluidically sealed against one another. The fluidic sealing can optionally be supported by using formable sealing materials. For example, said body can be provided as two- or more-component (layer) system, the layer facing the base plate being formed by an elastic material, or gaskets ("O-rings") can be used for sealing. Also the application of a diffusion barrier, in form of a recess in the separation wall between adjacent sample compartments, the separation wall being brought into contact with the base plate, can be intended for this purpose.

[0121] Part of the invention is a method for the determination of one or more analytes in one or more liquid samples with an arrangement according to any of the aforementioned embodiments and an analytical system according to any of the aforementioned embodiments, wherein sample and optionally additional reagent solutions are supplied to the sample compartments, and wherein these liquids can exit into a reservoir fluidically connected with the flow cell, as part of said sample compartments.

[0122] Characteristic of an advanced embodiment of the method is, that biological or biochemical or synthetic recognition elements for the determination of one or more analytes are immobilized on the base plate of said arrangement, excitation light is directed to the measurement areas on said base plate, and the light emanating from said measurement areas is detected by at least one detector.

[0123] Thereby a method is preferred, wherein the base plate comprises an optical waveguide, which is continuous or partitioned into discrete areas, excitation light is launched into said waveguide using an optical coupling element, and measurement light from the meassurement areas, which are in optical interaction with said optical waveguide, is detected by one or more detectors.

[0124] Especially preferred is a method, wherein said optical waveguide is provided as an optical film waveguide, with a first optically transparent layer (a) on a second optically transparent layer (b) with lower refractive index than layer (a), wherein furthermore excitation light is in-coupled into the optically transparent layer (a), by one or more grating structures formed in the optically transparent layer (a), and directed, as a guided wave, to the measurement areas located thereon, and wherein furthermore the luminescence from molecules capable to luminesce, which is generated in the evanescent field of said guided wave, is detected by one or more detectors, and wherein the concentration of one or more analytes is determined from the intensity of these luminescence signals.

[0125] In case of arrangements with grating structures (c) for the in-coupling of excitation light and additionally provided grating structures (c') for the out-coupling of light guided in the waveguiding layer, the in-coupling can be optimized by directing the excitation light out-coupled by a grating structure (c'), directly or after ray deviation, by means of mirrors or prisms, and optionally after focusing by means of an adequate lens, onto a detector, such as a photodiode connected to an amplifier. Thereby it is preferred, that the excitation light is out-coupled along the whole width (dimension normal to the direction of propagation of the guided excitation light in the plane of the waveguiding layer) and is focused onto the light-sensitive area of the detector. An optimum in-coupling is achieved, when the signal of the out-coupled light generated by this detector reaches its maximum.

[0126] It is especially preferred, that (1) the isotropically emitted luminescence or (2) luminescence that is in-coupled into the optically transparent layer (a) and out-coupled by a grating structure (c) or luminescence comprising both parts (1) and (2) is measured simultaneously.

[0127] Part of the method according to the invention is, that for the generation of said luminescence, a luminescent dye or a luminescent nano-particle is used as a luminescence label, which can be excited and emits at a wavelength between 300 nm and 1100 nm.

[0128] It is preferred, that the luminescence label is bound to the analyte or, in a competitive assay, to an analyte analogue or, in a multi-step assay, to one of the binding partners of the immobilized biological or biochemical or synthetic recognition elements or to the biological or biochemical or synthetic recognition elements.

[0129] Characteristic of another emobodiment of the method is, that a second or more luminescence labels of similar or different excitation wavelength as the first luminescence label and similar or different emission wavelength are used.

[0130] Thereby, it is preferred, that the second or more luminescence labels can be excited at the same wavelength as the first luminescence label, but emit at other wavelengths.

[0131] It is especially advantageous, if the excitation and emission spectra of the applied luminescent dyes do not overlap or overlap only partially.

[0132] Characteristic of another embodiment of the method is, that charge or optical energy transfer from a first luminescent dye, acting as a donor, to a second luminescent dye, acting as an acceptor, is used for the detection of the analyte.

[0133] Characteristic of still another embodiment of the method is, that, besides determination of one or more luminescences, changes of the effective refractive index on the measurement areas are determined.

[0134] In an advanced embodiment of the method, the one or more determinations of luminescences and/or determinations of light signals at the excitation wavelength are performed polarization-selective.

[0135] It is preferred, that the one or more luminescences are measured at a polarization that is different from the one of the excitation light.

[0136] Part of the invention is a method according to any of the aforementioned embodiments for the simultaneous or sequential, quantitative or qualitative determination of one or more analytes of the group comprising antibodies or antigens, receptors or ligands, chelators or "histidin-tag components", oligonucleotides, DNA or RNA strands, DNA or RNA analogues, enzymes, enzyme cofactors or inhibitors, lectins and carbohydrates.

[0137] Characteristic of possible embodiments of the method is, that the samples to be examined are naturally occurring body fluids, such as blood, serum, plasma, lymphe or urine or tissue fluids, or egg yolk.

[0138] Characteristic of other embodiments is, that the samples to be examined are optically turbid liquids or surface water or soil or plant extracts or bio- or process broths.

[0139] The samples to be examined can also be taken from biological tissue.

[0140] A further subject of the invention is the use of a method according to any of the aforementioned embodiments for the quantitative or qualitative determination of chemical, biochemical or biological analytes in screening methods in pharmaceutical research, combinatorial chemistry, clinical and preclinical development, for real-time binding studies and the determination of kinetic parameters in affinity screening and in research, for qualitative and quantitative analyte determinations, especially for DNA- and RNA analytics and for the determination of genomic or proteomic differences in the genome, such as single nucleotide polymorphisms, for the measurement of protein-DNA interactions, for the determination of control mechanisms for mRNA expression and for the protein (bio)synthesis, for the generation of toxicity studies and the determination of expression profiles, especially for the determination of biological and chemical marker compounds, such as mRNA, proteins, peptides or small-molecular organic (messenger) compounds, and for the determination of antibodies, antigens, pathogens or bacteria in pharmaceutical product development and research, human and veterinary diagnostics, agrochemical product development and research, for symptomatic and pre-symptomatic plant diagnostics, for patient stratification in pharmaceutical product development and for the therapeutic drug selection, for the determination of pathogens, nocuous agents and germs, especially of salmonella, prions and bacteria, in food and environmental analytics.

EXAMPLES

[0141] The arrangement according to the invention is exemplified in the following figures, without restriction of the subject of the invention.

[0142] Fig. I shows a cross-sectional partial view, comprising the inlet and outlet of a single flow cell and parts of the adjacent flow cell.

[0143] Fig. II shows a cross-sectional partial view corresponding to Fig. I, for another embodiment of the arrangement according to the invention.

[0144] Fig. III depicts shows a cross-sectional partial view corresponding to Fig. I, for still another embodiment of the arrangement according to the invention.

[0145] Fig. IV depicts a cross-sectional partial view, restricted to the base plate, for an embodiment with an optical film waveguide as the base plate. Fig. V shows an arrangement, wherein column-like arrangements of base plates and the bodies combined therewith (according to the arrangement of Fig. II), for generation of, for example, 6 colums with 6 flow cells each, are themselves then inserted into a common carrier ("meta-carrier").

EXAMPLE 1

[0146] It is of advantage, if the arrangements of sample compartments according to the invention are stackable, and if they comprise means for avoiding a contamination of the base plates **4**, upon contact with the environment.

[0147] The arrangement according to Fig. I comprises a base plate **4** and a body **6** combined therewith. The body has a recess **3**, which forms a spatial (three-dimensional) recess for generation of a flow cell, with an inlet **1** and an outlet **2**, after combination of the body with the base plate. The recess **3** can have any geometrical base area; for example, it can be rectangular. It is preferred, that the corners are rounded (not shown in the figures). The diameters and cross-sectional areas of inlets **1** and outlets **2** can be identical or different, and can remain constant or changing between the inlet opening for the liquid addition and the entrance into the three-dimensional recess **3**, respectively between the exit from the spatial (three-dimensional) recess **3** and the entrance into the reservoir **5** fluidically connected to this flow cell.

[0148] For a reduction of sample and reagent volumes required for filling the flow cells, it can be advantageous, if the inlet section **1** is broadened in such a way, that also pipet tips of larger diameter can be inserted into the inlet, and if the inlet section is closed again at its lower end, except for a narrow opening for the entrance into the recess **3**. The later entrance opening can additionally be surrounded by a low surrounding wall, within the inlet section **1** (not shown). An additional sealing of the inlet **1** against adjacent reservoirs **5** can be achieved, for example, if a conically shaped (tapered) pipet tip of a soft, elastic material is pressed against a harder wall material of the body **6** (especially concerning the walls of the inlet **1**), thus providing a sealing function.

[0149] For enabling the use of larger pipet tips for the filling step, it can be further advantageous, if the pitch (geometrical arrangement in rows and columns) of the reservoirs **5** is displaced with respect to the pitch of the flow cells, including their recesses **3** and the related inlet openings of the inlets **1**, in such a way, that the entrance openings are always located at the edge or at a corner of a recess **3** (as shown in Fig. I), but that the walls (as part of the body **6**) towards the reservoir **5** are displaced in direction towards the next flow cell. This configuration can be helpful for avoiding, within the recesses **3**, dead volumes without flow, and for simultaneously keeping low the required liquid volumes.

[0150] For facilitating the filling step, the inlet **1** can, for example, be shaped conically (tapered), such that a tip inserted into this inlet is guided towards the entrance opening of the recess **3**. The insertion can further be facilitated by additional, mechanically structured aids, such as grooves or ripples in a (conical) entrance opening, towards said entrance opening in direction of the recess **3**. Furtheron,

concentrical ring structures in the wall of the inlet can be provided as aids for centering.

[0151] Furtheron, the addition of components, such as detergents, reducing the surface tension of the supplied liquids and thus reducing the contact angle with the walls of the flow cells, to the supplied sample and to reagent solutions can facilitate the filling process and avoid the formation of air bubbles during the filling step. For the same purpose it can be helpful, if the walls of the body **6** are themselves modified by chemical or physical surface treatment, such as plasm treatment, in such a way, that the contact angle is reduced and the wettability thus improved.

[0152] Also shown is the inlet **2** respectively the outlet **1** of the adjacent flow cells (in this cross-sectional view). It is preferred that the inlet and the outlet of a flow cell are always located at opposite corner points of the base area of the recess, in case of an essentially rectangular base area for example at the endpoints of the diagonal.

[0153] In order to allow for a more constant filling and fill velocity respectively surface wetting of the base plate **4** (for avoiding a parabolic flow profile in the cross-sectional plane normal to Fig. I), it can be of advantage, if the recesses **3** have an increased depth in direction normal to the figure plane, i.e. if the flow cross section is not rectangular or elliptic, but expanded towards the edges. Thus, a more even flow velocity within the cross-sectional distribution can be achieved, and the formation of dead volumes in the border regions can again be reduced.

EXAMPLE 2

[0154] Fig. II shows another embodiment of the arrangement according to the invention, wherein the reservoir **5** is provided as a recess in the exterior wall of the body combined with the base plate **4**. Thanks to this embodiment, liquid exiting the flow cell can enter the reservoir **5**, but cannot flow back into the flow cell, as long as the reservoir is not filled up to the upper edge of the side wall at the site of the liquid exit.

EXAMPLE 3

[0155] Fig. III shows a modified version of an arrangement according to Fig. I, wherein the reservoir **5** is closed on top. As a consequence, liquid cannot escape, by evaporation, from the reservoir as well. This variant is associated with the additional advantage, that such an arrangement according to the invention can be fluidically sealed completely, especially safe, upon using an additional covering top, such as a foil, a septum or a cover plate. This is of special importance and advantageous, if, for example, an escape of biologically or chemically hazardous molecules or liquids from the arrangement according to the invention shall be prevented after the use. With respect to all described examples, the body **6** can consist of a single or also of several pieces, which are preferably combined to a unit irreversibly.

EXAMPLE 4

[0156] Fig. IV exemplifies an arrangement according to the invention, wherein the base plate is provided as an optical film waveguide with biological or biochemical recognition elements immobilized thereon. Here, with "g" are denoted the bordering walls of a flow cell, which is generated upon combination of the base plate with a body **6**, according to the examples described before. Therefore, "g" corresponds to the denoting label "6" in Fig. I-III.

[0157] On a layer (b), which is transparent at least in a part of the visible or near-infrared spectral region, first a thin intermediate layer (b') and then a layer (a) is deposited, the refractive index of which is larger than the refractive indices of layers (b) and (b'). The layers (a) and (b') are also optically transparent at least in a part of the visible and near-infrared spectral range. Grating structures (c) and (c') are provided in form of relief gratings in layer (b), which gratings are transferred into the layers located above upon their deposition. Then an adhesion-promoting layer (f) is deposited on layer (a), which can improve the adhesion of biological or biochemical or synthetic recognition elements to be immobilized. In the provided example, the recognition elements are immobilized in discrete (laterally separated) measurement areas (d), which can be arranged, according to this embodiment, both on and between the grating structures (c) and (c'). In this example, the base plate is finally combined with the body (g) (corresponding to "6" according to the denotation for Fig. I-III).

EXAMPLE 5

[0158] Fig. V shows an arrangement, wherein column-like arrangements of base plates and the bodies combined therewith (according to the arrangement of Example 2), for generation of totally 6 colums with 6 flow cells each, are themselves then inserted into a common carrier ("meta-carrier"). The column-like base plates **4** and bodies **6** combined therewith together form insertion modules **7**, which are inserted into the meta-carrier **8**.

[0159] In the shown example, the meta-carrier has the foot print of a microtiter plate. The inlet openings **9** towards the inlets **1** (not resolved in this figure) are positioned in such a way, that they are compatible with the pitch (geometrical arrangements in rows and columns) of a 96-well standard microtiter plate, i.e., they are always positioned at intervals of a whole-numbered multiple of 9 mm (in this example: interval of the inlets within a column: 9 mm; interval of the inlets between adjacent columns: 18 mm). Upon an adequate displacement of the meta-carrier, together with the insertion modules, the geometrical arrangement of the reservoirs **5** is compatible with the pitch of a standard 96-well microtiter plate correspondingly.

[0160] In the shown example, the meta-carrier is provided in such an embodiment, that it can receive up to 6 insertion modules. However, sites for insertion modules can also remain vacant.

[0161] The insertion of the insertion modules into the meta-carrier, optionally also in an automated way, can be facilitated by mechanical aids, such as mechanical limit points or walls, aids for centering, such as mechanical guides or optical marks.

[0162] The adjoining of the arrangement of sample compartments with the meta-carrier can, for example, be performed by glueing or by exact fitting without glueing, if it is intended for single-use, or, for example by latching or inserting into an adequately formed mounting, if it is intended for multiple use.

[0163] The shown example illustrates an embodiment of a reusable meta-carrier, into which the insertion modules **7** are

introduced by means of an attachment mechanism and from where they can be removed again, after execution of a measurement.

[0164] Preferably, the insertion modules **7** with rows or columns of flow cells and the corresponding receiving sites of the meta-carrier are provided in such a form, that only a single orientation of the insertion modules is possible upon their insertion.

1. An arrangement of sample compartments in a one- or two-dimensional array, comprising a base plate **(4)** and a body **(6)** combined with said base plate in such a way, that an array of recesses **(3)** for generation of an array of flow cells fluidically sealed against one another, each with at least one inlet **(1)** and one outlet **(2)**, are formed between said base plate and said body, wherein at least one outlet **(2)** of each flow cell is joined with a reservoir **(5)** fluidically connected with said flow cell, the reservoir being operable to receive liquid exiting the flow cell, and wherein said reservoir is formed as a recess in the exterior wall of the body combined with the base plate.

2. An arrangement according to claim 1, wherein three-dimensional structures, with the pitch (geometrical arrangement in rows and/or columns) of the arrays of flow cells to be generated, are formed on the base plate **(4)**.

3. An arrangement according to any of claims **1-2**, wherein, for generation of the recesses **(3)** between the base plate **4)** and the body **(6)** combined therewith, recesses **(3)** are formed in the base plate **(4)**.

4. An arrangement according to any of claims **1-3**, wherein, for generation of the recesses **(3)** between the base plate **(4)** and the body **(6)** combined therewith, recesses **(3)** are formed in said body.

5. An arrangement according to any of claims **1-4**, wherein the body **(6)** combined with the base plate **(4)** is formed from several parts, wherein the combined parts of said body preferably form an irreversibly combined unit.

6. An arrangement according to any of claims **1-5**, wherein the arrangement comprises 2-2000, preferably 2-400, most preferably 2-100 flow cells.

7. An arrangement according to any of claims **1-6**, wherein the pitch (geometrical arrangement in rows and/or columns) of the inlets **(1, 9)** of the flow cells does correspond to the pitch (geometrical arrangement) of the wells of a standard microtiter plate.

8. An arrangement according to any of claims **1-7**, with, for example, 2 to 8 sample compartments in a column or, for example, 2 to 12 sample compartments in a row, which themselves are combined with a carrier **(8)** ("meta-carrier") with the dimensions of standard microtiter plates in such a way, that the pitch (geometrical arrangement in rows and/or columns) of the inlets **(1, 9)** of the flow cells does correspond to the pitch (geometrical arrangement) of the wells of a standard microtiter plate.

9. An arrangement according to any of claims **1-8**, wherein said arrangement of sample compartments is closed with an additional covering top, for example a film, a membrane or a cover plate.

10. An arrangement according to any of claims **1-9**, wherein the inner volume of each flow cell is 0.1 μl-1000 μl, preferably 1 μl-20 μl.

11. An arrangement according to any of claims **1-10**, wherein the capacity of the reservoir **(5)** fluidically connected to the flow cell is larger, preferably at least 5 times larger than the inner volume of the flow cell.

12. An arrangement according to any of claims **1-11**, wherein the depth of the recesses **(3)** between the base plate **(4)** and the body **(6)** combined with said base plate is 1-1000 μm, preferably 20-200 μm.

13. An arrangement according to any of claims **1-12**, wherein the base areas of the recesses **(3)** between the base plate **(4)** and the body **(6)** combined with said base plate are 0.1 mm^2-200 mm^2, preferably 1 mm^2-100 mm^2 each, wherein the size of the recesses **(3)** of an array can be uniform or diverse, and wherein the base areas can have any geometry, preferably rectangular or polygonal or also other geometry.

14. An arrangement according to any of claims **1-13**, wherein the materials of the base plate **(4)**, of the body **(6)** combined with said base plate and of an additional covering top according to claim 9 are selected from the group of formable, moldable or millable plastics, metals, silicates, such as glass, quartz or ceramics.

15. An arrangement according to any of claims **1-14**, wherein biological or biochemical or synthetic recognition elements for the determination of one or more analytes are immobilized on the base plate.

16. An arrangement according to any of claims **1-15**, wherein an adhesion-promoting layer (f) (according to Fig. IV) is deposited on the base plate for the immobilization of the biological or biochemical or synthetic recognition elements.

17. An arrangement according to claim 16, wherein the adhesion-promoting layer (f) has a thickness of less than 200 nm, preferably of less than 20 nm.

18. An arrangement according to any of claims **16-17**, wherein the adhesion-promoting layer (f) comprises chemical compounds from the groups of silanes, epoxides, "self-organized functionalized monolayers", functionalized polymers and polymer gels.

19. An arrangement according to any of claims **1-18**, wherein biological or biochemical or synthetic recognition elements are immobilized in discrete measurement areas (d), which are formed by spatially selective deposition of said biological or biochemical or synthetic recognition elements on the base plate **(4)**.

20. An arrangement according to claim 19, wherein the biological or biochemical or synthetic recognition elements are deposited on the base plate by **(4)** one or more methods from the group of methods comprising "ink jet spotting", mechanical spotting by means of pin, pen or capillary, "micro contact printing", fluidically contacting the measurement areas with the biological or biochemical or synthetic recognition elements upon their supply in parallel or crossed micro channels, upon exposure to pressure differences or to electric or electromagnetic potentials.

21. An arrangement according to claim 19, wherein, as said biological or biochemical or synthetic recognition elements, components from the groups formed by nucleic acids (DNA, RNA) or nucleic acid analogues (for example peptide nucleic acids PNA), antibodies, aptamers, membrane-bound and isolated receptors, their ligands, antigens for antibodies, cavities generated by chemical synthesis to host molecular imprints, and "histidin-tag components", are deposited.

22. An arrangement according to claim 19, wherein, as said biological or biochemical or synthetic recognition elements, whole cells or cell fragments are deposited.

23. An arrangement according to any of claims **1-22**, wherein arrays of two or more discrete measurement areas (d) each are arranged in the regions of the recesses **(3)** between the base plate **(4)** and the body **(6)** combined with said base plate **(4)**, in which measurement areas similar or different biological or biochemical or synthetic recognition elements are immobilized.

24. An arrangement according to any of claims **19-22**, wherein compounds which are "chemically neutral" towards the analyte are deposited between the discrete measurement areas (d).

25. An arrangement according to claim 24, wherein said "chemically neutral" compounds are selected from the groups comprising, for example, albumins, especially bovine and human serum albumin, herring sparm or also polyethylen glycols.

26. An arrangement according to any of claims **1-25**, wherein the base plate with the biological or biochemical or synthetic recognition elements immobilized thereon is operable for the determination of a change of optical, electrical, electrochemical or thermal parameters, or for the determination of radioactive radiation.

27. An arrangement according to claim 31, wherein the base plate **(4)** with the biological or biochemical or synthetic recognition elements immobilized thereon is operable for the determination of a change of optical parameters, and wherein said base plate is transparent in at least one region of wavelengths in the visible or near-infrared spectral region.

28. An arrangement according to any of claims **1-27**, wherein the base plate **(4)** comprises a supporting substrate of glass or of a thermoplastic or moldable plastic, which is transparent in at least one region of wavelengths in the visible or near-infrared spectral region.

29. An arrangement according to any of claims **1-28**, wherein the base plate **(4)** comprises an optical waveguide, which is continuous or partitioned into discrete areas.

30. An arrangement according to claim 29, wherein the optical waveguide is an optical film waveguide with a first optically transparent layer (a), facing the recesses **(3)**, on a second optically transparent layer (b) with lower refractive index than layer (a).

31. An arrangement according to claim 30, wherein the material of the second optically transparent layer (b) comprises silicates, auch as glass or quartz, or a transparent thermoplastic or moldable plastic, preferably of the group comprising polycarbonate, polyimide, or polymethylmethacrylate, or polystyrene.

32. An arrangement according to any of claims **30-31**, wherein the refractive index of the first optically transparent layer (a) is higher than 1.8.

33. An arrangement according to any of claims **30-32**, wherein the first optically transparent layer (a) comprises TiO_2, ZnO, Nb_2O_5, Ta_2O_5, HfO_2, or ZrO_2, preferably TiO_2, Ta_2O_5 or Nb_2O_5.

34. An arrangement according to any of claims **30-33**, wherein the thickness of the first optically transparent layer (a) is between 40 and 300 nm, preferably between 100 and 200 nm.

35. An arrangement according to any of claims **30-33**, wherein an additional optically transparent layer (b') with lower refractive index than and in contact with layer (a), and with a thickness of 5 nm-10 000 nm, preferably of 10 nm-1000 nm, is located between the optically transparent layers (a) and (b).

36. An arrangement according to any of claims **30-35**, wherein the in-coupling of excitation light into the optically transparent layer (a), to the measurement areas (d), is performed using one or more optical in-coupling elements from the group comprising prism couplers, evanescent couplers comprising joined optical waveguides with overlapping evanescent fields, front face (distal end) couplers with focusing lenses arranged in front of a front face (distal end) of the waveguiding layer, and grating couplers.

37. An arrangement according to any of claims **30-35**, wherein the in-coupling of excitation light into the optically transparent layer (a), to the measurement areas (d), is performed using one or more grating structures (c), that are formed in the optically transparent layer (a).

38. An arrangement according to any of claims **30-37**, wherein the out-coupling of light guided in the optically transparent layer (a) is performed using grating structures (c'), that are formed in the optically transparent layer (a).

39. An arrangement according to claim 37 and claim 38, wherein grating structures (c) and (c') formed in the optically transparent layer (a) have the same or different periodicity and are arranged in parallel or not in parallel to one another.

40. An arrangement according to claim 39, wherein grating structures (c) and (c') can interchangeably be used as in-coupling and/or out-coupling gratings.

41. An arrangement according to any of claims **37-40**, wherein the grating structures (c) and optional additional grating structures (c') have a period of 200 m 1000 nm and a grating modulation depth of 3 nm-100 nm, preferably of 10 nm-30 nm.

42. An arrangement according to claim 41, wherein the ratio of the modulation depth to the thickness of the first optically transparent layer (a) is equal or smaller than 0.2.

43. An arrangement according to any of claims **37-42**, wherein the grating structure (c) is a relief grating with any profile, such as rectangular, triangular or semi-circular profile, or a phase or volume grating with a periodic modulation of the refractive index in the essentially planar optically transparent layer (a).

44. An arrangement according to any of claims **30-43**, wherein a thin metal layer, preferably of gold or silver, optionally on an additional dielectric layer of lower refractive index than layer (a), for example of silica or magnesium fluoride, is deposited between the optically transparent layer (a) and the immobilized biological or biochemical recognition elements, wherein the thickness of the metal layer and the optional, additional intermediate layer is selected in such a way, that a surface plasmon at the excitation wavelength and/or at the luminescence wavelength can be excited.

45. An arrangement according to any of claims **37-44**, wherein the grating structure (c) is a diffractive grating with a uniform period.

46. An arrangement according to any of claims **37-44**, wherein the grating structure (c) is a multi-diffractive grating.

47. An arrangement according to any of claims **37-46**, wherein grating structures (c) and optional additional grating structures (c') are located within the region of the sample compartments.

48. An arrangement according to any of claims **37-46**, wherein grating structures (c) and optional additional grating structures (c') are located outside the region of the sample compartments.

49. An arrangement according to any of claims **37-46**, wherein grating structures (c) and optional additional grating structures (c') extend over the range of multiple or all sample compartments.

50. An arrangement according to any of claims **37-46**, wherein grating structures (c) are located within the region of the sample compartments, and wherein optional additional grating structures (c') are located outside of the sample compartment, within which the incoupling of the excitation light is performed.

51. An arrangement according to any of claims **1-50**, wherein the material of the body (**6**) combined with the baseplate (**4**), in the incumbant surface area (g) on the base plate, is optically transparent, both for the excitation radiation and for one or more optionally excited luminescence radiations, at least within the penetration depth of the evanescent field.

52. An arrangement according to claim 51, wherein the material of the body (**6**) combined with the base plate (**4**) is provided in form of a two-layer system, the first layer (g) of which, to be brought into contact with the surface of the base plate, being transparent both for the excitation radiation and for one or more optionally excited luminescence radiations, whereas the adjacent layer, being located more remote from the base plate (**4**), is absorbent in the spectral range of the excitation radiation and of the optionally excited luminescence radiations.

53. An arrangement according to claim 47 or claim 49, wherein the material of the layer in contact with the base plate is absorbent in the spectral range of the excitation radiation and of the optionally excited luminescence radiations.

54. An arrangement according to any of claims **1-53**, wherein the material of the layer (**6**) in contact with the base plate (**4**) is self-adhesive and tightly sealing.

55. An arrangement according to any of claims **1-54**, wherein the material of the layer (**6**) in contact with the base plate (**4**) comprises a polysiloxane.

56. An arrangement according to any of claims **1-55**, wherein 5-1000, preferably 10-400 measurement areas are located in one sample compartment.

57. An arrangement according to any of claims **1-56**, wherein optically or mechanically recognizable marks are provided on the base plate (**4**), in order to facilitate the adjustment in an optical system and/or to facilitate the combination of the base plate (**6**) with the body comprising the recesses for the sample compartments.

58. An analytical system for the determination of one or more analytes, comprising

an arrangement according to any of claims **1-57**

means for the locally addressed supply of samples or reagents to the sample compartments of said arrangement, and

at least one detector for the detection of a change of a parameter (measurand) due to the presence of the one or more analytes, which parameter (measurand) preferably is an optical, electrical, electrochemical or thermal parameter (measurand) or a signal from radioactive radiation.

59. An analytical system for the determination of one or more luminescences comprising

an arrangement according to any of claims **1-57**

means for the locally addressed supply of samples or reagents to the sample compartments of said arrangement

at least one excitation light source, and

at least one detector for the detection of the light emanating from the at least one or more measurement areas (d) on the base plate.

60. An analytical system for the determination of one or more analytes, comprising

an arrangement according to any of claims **1-57**

means for the locally addressed supply of samples or reagents to the sample compartments of said arrangement

at least one excitation light source, and

at least one detector for the detection of a change of an optical parameter (measurand), which is preferably a change of the refractive index and/or of one or more luminescences in the vicinity of the one or more analytes.

61. An analytical system according to any of claims **59-60**, wherein the launching of the excitation light to the measurement areas (d) is performed in a surface or transmissive illumination configuration.

62. An analytical system according to any of claims **59-61**, wherein the launching of the excitation light to the measurement areas (d) and the detection of the measurement light from the measurement areas (d) is performed at opposite sides of the base plate.

63. An analytical system according to any of claims **59-61**, wherein the launching of the excitation light to the measurement areas (d) and the detection of the measurement light from the measurement areas (d) is performed at the same side of the base plate.

64. An analytical system according to any of claims **59-63**, wherein the launching of the excitation light to the measurement areas (d) and the detection of the measurement light from the measurement areas (d) is performed in a confocal arrangement.

65. An analytical system according to any of claims **59-63** with an arrangement according to any of claims **30-57**, wherein the excitation light rays of one (common) wavelength are located in a common plane, which is defined by the resonance angle for in-coupling the excitation light of said excitation wavelength into the optically transparent layer (a) by an optical coupling element.

66. An analytical system according to any of claims **58-65**, wherein at least one laterally resolving detector is used for signal detection, which is preferably selected from the group formed by CCD cameras, CCD chips, photodiode arrays, Avalanche diode arrays, multi-channel plates, and multi-channel photomultipliers.

67. An analytical system according to any of claims **59-66**, wherein optical components of the group comprising lenses or lens systems for the shaping of the transmitted light bundles, planar or curved mirrors for the deviation and optionally additional shaping of the light bundles, prisms for the deviation and optionally spectral separation of the light

bundles, dichroic mirrors for the spectrally selective deviation of parts of the light bundles, neutral density filters for the regulation of the transmitted light intensity, optical filters or monochromators for the spectrally selective transmission of parts of the light bundles, or polarization-selective elements for the selection of discrete polarization directions of the excitation or luminescence light are located between the one or more excitation light sources and the base plate **(4)**, as part of an arrangement according to any of claims **1-57**, and/or between said base plate and the one or more detectors.

68. An analytical system according to any of claims **59-67**, wherein the excitation light is launched in pulses with duration of 1 fsec to 10 min.

69. An analytical system according to any of claims **59-68**, wherein the emission light from the measurement areas is measured time-resolved.

70. An analytical system according to any of claims **59-69**, wherein, for referencing the available excitation light, light signals of the group comprising excitation light at the location of the light sources or after expansion of the excitation light or after its multiplexing into individual beams, scattered light at the excitation wavelength from the location of the one or more discrete measurement areas, and light of the excitation wavelength out-coupled by the grating structures (c) or (c') are measured.

71. An analytical system according to claim 70, wherein the measurement areas for determination of the emission light and of the reference signal are identical.

72. An analytical system according to any of claims **59-71**, wherein launching of the excitation light and detection of the emission light from the one or more measurement areas is performed sequentially for one or more sample compartments.

73. An analytical system according to claim 72, wherein sequential excitation and detection is performed using movable optical components of the group comprising mirrors, deviating prisms, and dichroic mirrors.

74. An analytical system according to claim 73, wherein sequential excitation and detection is performed using an essentially focus and angle preserving scanner.

75. An analytical system according to any of claims **72-74**, wherein the arrangement, according to any of claims **1-57**, is moved between steps of sequential excitation and detection.

76. A method for manufacturing an arrangement of sample compartments in a one- or two-dimensional array, according to any of claims **1-57**, comprising a base plate **(4)** and and a body **(6)** combined with said base plate in such a way, that an array of (spatial) recesses **(3)** for generation of an array of flow cells, each with at least one inlet **(1)** and one outlet **(2)**, are formed between said base plate **(4)** and said body **(6)**, wherein at least one outlet **(2)** of each flow cell is joined with a reservoir **(5)** fluidically connected with said flow cell, the reservoir being operable to receive liquid exiting the flow cell and being formed in the exterior wall of the body **(6)** combined with the baseplate **(4)**, wherein said base plate **(4)** and said body **(6)** are combined in such a way, that different of said (spatial) recesses **(3)** are fluically sealed against one another.

77. A method according to claim 76, wherein the base plate **(4)** and the body **(6)** combined with that base plate are joined irreversibly.

78. A method according to claim 77, wherein the base plate **(4)** and the body **(6)** combined with the base plate are glued together.

79. A method according to claim 76, wherein the base plate **(4)** and the body **(6)** combined with that base plate are joined reversibly.

80. A method for the determination of one or more analytes in one or more liquid samples with an arrangement according to any of claims **1-57** and an analytical system according to any of claims **58-75**, wherein sample and optionally additional reagent solutions are supplied to the sample compartments, and wherein these liquids can exit into a reservoir **(5)** fluidically connected with the flow cell, as part of said sample compartments.

81. A method according to claim 80, wherein biological or biochemical or synthetic recognition elements for the determination of one or more analytes are immobilized on the base plate **(4)** of said arrangement, excitation light is directed to the measurement areas on said base plate **(4)**, and the light emanating from said measurement areas is detected by at least one detector.

82. A method according to claim 81, wherein the base plate **(4)** comprises an optical waveguide, which is continuous or partitioned into discrete areas, excitation light is launched into said waveguide using an optical coupling element, and measurement light from the meassurement areas (d), which are in optical interaction with said optical waveguide, is detected by one or more detectors.

83. A method according to claim 82, wherein said optical waveguide is provided as an optical film waveguide, with a first optically transparent layer (a) on a second optically transparent layer (b) with lower refractive index than layer (a), wherein furthermore excitation light is in-coupled into the optically transparent layer (a), by one or more gratings structures formed in the optically transparent layer (a), and directed, as a guided wave, to the measurement areas (d) located thereon, and wherein furthermore the luminescence from molecules capable to luminesce, which is generated in the evanescent field of said guided wave, is detected by one or more detectors, and wherein the concentration of one or more analytes is determined from the intensity of these luminescence signals.

84. A method according to claim 83 with an arrangement according to any of claims **37-57**, wherein (firstly) the isotropically emitted luminescence or (secondly) luminescence that is in-coupled into the optically transparent layer (a) and out-coupled by a grating structure (c) or luminescence comprising both parts (firstly and secondly) is measured simultaneously.

85. A method according to any of claims **83-84**, wherein, for the generation of said luminescence, a luminescent dye or a luminescent nano-particle is used as a luminescence label, which can be excited and emits at a wavelength between 300 nm and 1100 nm.

86. A method according to claim 85, wherein the luminescence label is bound to the analyte or, in a competitive assay, to an analyte analogue or, in a multi-step assay, to one of the binding partners of the immobilized biological or biochemical or synthetic recognition elements or to the biological or biochemical or synthetic recognition elements.

87. A method according to any of claims **85-86**, wherein a second or more luminescence labels of similar or different excitation wavelength as the first luminescence label and similar or different emission wavelength are used.

88. A method according to claim 87, wherein the second or more luminescence labels can be excited at the same wavelength as the first luminescence label, but emit at other wavelengths.

89. A method according to claim 87, wherein the excitation and emission spectra of the applied luminescent dyes do not overlap or overlap only partially.

90. A method according to claim 87, wherein charge or optical energy transfer from a first luminescent dye, acting as a donor, to a second luminescent dye, acting as an acceptor, is used for the detection of the analyte.

91. A method according to any of claims **83-90**, wherein, besides determination of one or more luminescences, changes of the effective refractive index on the measurement areas are determined.

92. A method according to any of claims **83-91**, wherein the one or more determinations of luminescences and/or determinations of light signals at the excitation wavelengths are performed polarization-selective.

93. A method according to any of claims **83-92**,wherein the one or more luminescences are measured at a polarization that is different from the one of the excitation light.

94. A method according to any of claims **83-93** for the simultaneous or sequential, quantitative or qualitative determination of one or more analytes of the group comprising antibodies or antigens, receptors or ligands, chelators or "histidintag components", oligonucleotides, DNA or RNA strands, DNA or RNA analogues, enzymes, enzyme cofactors or inhibitors, lectins and carbohydrates.

95. A method according to any of claims **83-94**, wherein the samples to be examined are naturally occurring body fluids, such as blood, serum, plasma, lymphe or urine or tissue fluids, or egg yolk.

96. A method according to any of claims **83-94**, wherein the samples to be examined are optically turbid liquids or surface water or soil or plant extracts or bioor process broths.

97. A method according to any of claims **83-96**, wherein the samples to be examined are taken from biological tissue.

98. The use of an arrangement according to any of claims **1-57** for the quantitative or qualitative determination of chemical, biochemical or biological analytes in screening methods in pharmaceutical research, combinatorial chemistry, clinical and preclinical development, for real-time binding studies and the determination of kinetic parameters in affinity screening and in research, for qualitative and quantitative analyte determinations, especially for DNA- and RNA analytics and for the determination of genomic or proteomic differences in the genome, such as single nucleotide polymorphisms, for the measurment of proteinDNA interactions, for the determination of control mechanisms for mRNA expression and for the protein (bio)synthesis, for the generation of toxicity studies and the determination of expression profiles, especially for the determination of biological and chemical marker compounds, such as mRNA, proteins, peptides or small-molecular organic (messenger) compounds, and for the determination of antibodies, antigens, pathogens or bacteria in pharmaceutical product development and research, human and veterinary diagnostics, agrochemical product development and research, for symptomatic and pre-symptomatic plant diagnostics, for patient stratification in pharmaceutical product development and for the therapeutic drug selection, for the determination of pathogens, nocuous agents and germs, especially of salmonella, prions and bacteria, in food and environmental analytics.

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专利名称(译)	流动池阵列及其用于多分析物测定的用途		
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摘要(译)

本发明涉及流动池的一维或二维布置，作为样品隔室阵列的一部分，每个样品隔室具有至少一个入口和出口，由基板和主体形成，具有空间凹槽的布置对应于样品室的（几何）布置，与所述底板结合。该布置允许向样品隔室供应或从样品隔室移除，所述样品隔室可以在小的基础区域上以大量布置，甚至非常少量的样品或试剂。本发明的主题是一个或多个样品隔室的布置，包括基板和与所述基板结合的主体，使得一个或多个凹槽用于产生彼此流体密封的一个或多个流通池。每个都具有至少一个入口和一个出口，形成在所述基板和所述主体之间，其中每个流动池的至少一个出口与与所述流动池流体连接的储存器连接，所述储存器可操作以接收液体离开流动池，除了制造和使用它们的方法。