

A Microfluidic chip

Technical field

[0001] The present invention relates to the field of in vitro diagnostic techniques, and more particularly to a microfluidic chip.

Background technique

[0002] The microfluidic chip is the main platform for microfluidic technology, which can be integrated into a small chip on a small chip. Automatic analysis through microchannels is used to achieve various functions of conventional chemical or biological laboratory. The microfluidic chip has a light volume, the use of samples and the amount of reducing, and the reaction speed is fast, and a large amount of parallel can be treated and can be used in the advantages of discard, in the fields of biological, chemical, medical, have been developed in recent years. Become a new research area with a creature, chemistry, medicine, fluid, electronics, materials, machinery and other disciplines.

[0003] The current microfluidic chip generally uses the cover sheet and the substrate bonding to form the corresponding flow zone and reaction zone, which is extremely high for the sealing technique. Once the sealing effect of the bond is not good, there will be liquid sample leakage. Question, at the same time, the microfluidic chip involves the detection of different disease markers. According to the requirements of different samples, different reaction time may be required, and the existing microfluidic chip is in the microchannels due to its inherent structural characteristics. The reaction time is limited, which exists when detecting certain disease markers, the detection range is narrow.

Inventive content

[0004] It is an object of the present invention to provide a microfluidic chip for solving the technical problems raised in the above background techniques for the shortcomings of the prior art.

[0005] In order to achieve the above object, the technical solution of the present invention is to be realized, a microfluidic chip comprising a microchannel formed from a substrate and a cover sheet, and the microchannel is injected into a sample fluid by a sample pore, the micro The top wall height of the passage is lower than the height of the substrate and the cover sheet contact surface, and the sample fluid flows down the exit of the microchannels.

[0006] Specifically, the microchannel is connected to the extended hole through an upward connection channel.

[0007] Specifically, the microchannel is connected to the extended hole through a connection channel of the inclined upward.

[0008] Specifically, a groove is provided in the longitudinal direction of the substrate, and the lower surface of the cover is protruded as the top wall of the microchannel, and the microchannel is formed with the bottom wall of the groove.

[0009] Specifically, the extended hole extends in a longitudinal direction parallel to the microchannel; or the extended hole is disposed in a direction parallel to the direction of the microchannel length.

[0010] Specifically, the extended well is arranged on one side of the microchannel side, or while it is located on both sides of the microchannel.

[0011] Specifically, the microfluidic chip includes injective regions and waste liquids that communicate with both ends of the microchannel, and induced sample fluid and buffer, respectively.

[0012] Specifically, the sample drawn hole is located between the buffer coefficient hole and the microchannel.

[0013] Specifically, the exit of the microchannel is connected to the waste liquid region, the waste liquid region communicates with the outside, and the sample outlet is inserted with a water absorbent material that can slide in the sample outlet, and the sample outlet has at least two ends. , One end is close to the microchannel outlet, and the other end is far from the microchannel outlet.

[0014] Specifically, the extended hole is formed by a groove and substrate that is opened on a cover sheet; or a groove and a cover sheet on the substrate, or the expanded hole is formed on a cover sheet. The grooves opened on the substrate are cohered together.

[0015] A micro-fluore chip obtained by the above technical solution, which is beneficial to:

[0016] 1. Effectively prevent microchannel side leakage liquid situation, making the test results more accurate, reduce invalid detection rate and scrap rate.

[0017] 2, tilted connecting channels and expansion holes are advantageous for exhaust, avoid bubbles to block microchannels, so that liquid flow is smoother.

[0018] 3, through the double hole arrangement of the sample plus sample hole and the buffer, after the reaction is completed in the microchannel, the buffer will promote the rapid flow of the reaction waste to the waste liquid region, and the reaction time of the entire microfluidic chip is reduced. At the same time, the fluorescent solution remaining in the microchannel can be rinsed, and the residual liquid can be disturbed to detect the test results.

[0019] 4, in the sample outlet, the movable water absorbent material is provided. When the fluid sample reacts in the microchannel, the water-absorbent material is disconnected from the microchannel, and the sample flow is retained in the microchannel, forming a liquid phase reaction pool, not only can increase The reaction time, but also caused the dry fluorescent reaction to liquid phase fluorescence reaction, which greatly increases the sufficiency of the reaction, and improves precision of the detection

result. When the reaction is completed, the water absorbing material is moved, so that the water absorbing material and the microchannel exit Connect, the waste liquid will absorb the water absorbing material to the waste liquid region, to avoid the detection result of the waste liquid, the movement of the water absorbing material can be controlled according to the reaction in the microchannel, which is controllable method, Further improve the flexibility of the reaction time of different products, and at the same time can accelerate the quick flow to the waste liquid region and shorten the detection time.

Drawings

[0020] figure 1 It is a cross-sectional view of one of the embodiments of the microfluidic chip of the present invention.

[0021] figure 2 It is a plan view of the microfluidic chip of the present invention.

[0022] image 3 It is a cross-sectional view of another embodiment of the microfluidic chip of the present invention.

[0023] Figure 4 It is a cross-sectional view showing another embodiment of the microfluidic chip of the present invention.

[0024] In the figure, the substrate 1; the cover sheet 2; microchannel 3; connection channel 4; expansion hole 5; injection region 6; waste liquid region 7; sample outlet 8; water absorbing material 9; sample plus sample hole 10; buffer Plus the sample hole 11; the fluorescent label region 3a; the quality control region 3b; the detection zone 3c.

Detailed description

[0025] It should be noted that the features of the present invention in the present invention may be combined with each other in the case of an unable conflict.

[0026] In the description of the present invention, it is to be understood that the terms "center", "longitudinal", "horizontal", "upper", "lower", "front", "post", "left", "right", "The orientation relationship between the orientation of the indicated by the vertical ", " horizontal ", " top ", " bottom ", " inside ", " outer ", etc. is based on the orientation or positional relationship shown in the drawings, is merely described in the present invention and Simplify the description, rather than indicating or implying that the device or element must have a specific orientation, constructed and operated in a particular direction, and thus is not to be construed as limiting the invention. Moreover, the terms "first", "second", etc. are only used to describe purposes, and cannot be understood as an indication or implies relative importance or implicitting the number of techniques indicated. Thus, features with "first", "second", and the like may be indicated or implicitly including one or more of this feature. In the description of the invention, the meaning of "multiple" is two or more than one otherwise indicated.

[0027] In the description of the invention, it is to be described in that, unless otherwise specified and defined, the term "installation", "connected", "connected", "set" should be used to understand, for example, may be a fixed connection, It can be a detachable connection, or integrally connected; may be a mechanical connection, or an electrical connection; may be a direct connection, or by an intermediate medium can be connected inside the two elements. For those skilled in the art, the specific meaning of the above terms can be understood in the art.

[0028] The present invention provides a microfluidic chip comprising a microchannel 3 having a defined height and width formed by the substrate 1 and the cover sheet 2, and the sample fluid can lower the microchannel 3 on the capillary force of the microchannel 3. The exit flow is flow, the top wall height of the microchannel 3 is lower than the height of the substrate 1 and the contact surface of the cover sheet 2.

[0029] The present invention will be described in detail below with reference to the examples and drawings.

[0030] figure 1 As shown in the microfluidic chip cross-sectional view of the first embodiment of the present invention, the microchannel 3 is embodied by the lower surface of the cover sheet 2 and the substrate 1, the substrate 1 along the substrate 1 length direction The groove is provided, and the lower surface of the cover sheet 2 protrudes as the top wall of the microchannel 3, and forms a microchannel 3 that flows from the bottom wall of the groove to flow through and the reaction occurs.

[0031] like figure 2 As shown, the fluid flow direction in the microchannel 3 may be provided with a fluorescent labeling region 3a, a detection zone 3c, and a heat regions 3b in the direction of the fluid direction.

[0032] After the sample liquid is injected from the injection hole, after the capillary force of the microchannel 3, the microchannel 3 is in the mouth of the microchannel 3, since the height of the top wall of the microchannel 3 is lower than the height of the substrate 1 and the cover sheet 2, as long as the guarantee The amount of injection of the sample liquid can effectively prevent the microchannel 3 side leakage, making the detection result more accurate, reduce invalid detection rate and scrap rate, and reduces the process requirements for microfluidic chip bonding.

[0033] image 3 As shown, the microfluidic chip also includes an expansion hole 5, which is in communication with the extended hole 5, and the height of the expansion hole 5 is higher than the height of the microchannel 3, the expansion hole 5. 5 Based on the groove and substrate 1 of the cover sheet 2, or be formed by the groove and cover sheet 2 on the substrate 1; or the groove and base from the cover sheet 2 The grooves opened on the sheet 1 are coincided with.

[0034] The setting of the expansion hole 5 can reduce the bubble during the flow of the sample fluid flow, the expansion hole 5 may be separately disposed on one side of the microchannel 3 side, or may

be located on both sides of the microchannel 3; it can be along the microchannel 3 The length direction interval is set or set up.

[0035] Figure 4 As shown, another preferred embodiment of the present invention, image 3 Different, the convex portion of the groove on the substrate 1 forming the microchannel 3 is a trapezoid, i.e., the expansion hole 5 is connected to the extended hole 5 by an upwardly inclined connecting passage 4, which can be connected. Better discharge of bubbles generated during sample fluid flow.

[0036] like figure 2 As shown, the chip in the above-described embodiment also includes injectable regions 6 and waste liquid region 7, injectable region 6, and the height of the waste liquid region, respectively, and the microchannel 3, respectively, and the microchannel 3 at the same, respectively. The sample portion 6 is injected into the sample fluid and buffer by the sample pore hole 10 and the buffer drawing hole 11 provided by the top surface of the cover sheet 2, wherein the sample pore 10 is located between the buffer and the sample hole 11 and the microchannel 3. The width of the inflow region 6 is greater than the width of the microchannel 3, and the injection region 6 and the microchannel 3 are connected by a curved connection portion that is gradually tightened by the width.

[0037] After the sample fluid reacture, the buffer is added to the hole, and the buffer pushes the reaction waste liquid to quickly flow to the waste liquid region 7, and the residual fluorescent solution after the reaction in the microchannel 3 can avoid the residue within the microchannel 3. The liquid causes interference to the test results while reducing the overall time of the entire chip detection operation, meeting the instant detection of POCT, and the fast-moving market demand.

[0038]The waste liquid region 7 communicates with the outside from the sample outlet 8 provided on the substrate 1, and the sample outlet 8 is inserted with a water absorbing material 9 that can slide in the sample outlet 8, and the sample outlet 8 has at least two ends, one The end is close to the microchannel 3 outlet, and the other end is away from the microchannel 3 outlet, respectively, and the water absorbing material 9 is connected to the microchannel 3 outlet and away from the microchannel 3 outlet.

[0039] The water absorbing material 9 can use a polyester fiber, a water absorbent resin, a water absorbent gelatin, a papermaking wood pulp or other material having a water absorbing character, and the specifications of the water absorbing material 9 can be carried out according to the addition of the chip. Adjusting, the water absorbing capacity of the water absorbing material 9 is maintained in whole is 2-4 times the amount of sample injection of the sample to avoid the water absorbing material 9, resulting in leakage from the sample outlet 8 caused by the sample outlet 8.

[0040] Before the sample, it was confirmed that the water absorbing material 9 was located at one end of the sample outlet 8 away from the microchannel 3, and after adding a quantified sample fluid to the sample drawing hole 10, the sample fluid flows into the microchannel 3 by the sample area, and under capillary One end is moved to the microchannel 3, at which time the connection of the water absorbing material 9 is lacking, the sample fluid is reinforced in the microchannel 3, and the water absorbing

material 9 is manually slide to the microchannel 3 outlet, The water absorbent material 9 is in contact with the sample, and the sample fluid flowing into the waste liquid region 7 is fully absorbed, and the optical analyzer is detected.

[0041] D-Dimer is mainly used for the detection of thrombotic diseases, below to quantify plasma, the D dimer content in whole blood is an example of microfluidic chips and existing in the second embodiment of the present invention. The microfluidic chip performs comparative experiments.

[0042] 1, material preparation

[0043] Improved D-Dimer microfluidic chip A and Improved D-Dimer microfluidic chip B (in the water absorbing material relative to microfluidic chip B) In the middle fixed, the waste liquid zone of the microfluidic chip A is connected by the sample outlet and the external boundary, and the water-absorbent material can be smoothly produced by Shandong Mai Microbiotechnology Co., Ltd.;

[0044] D-Dimer clinical samples S1, S2, obtained by related hospitals;

[0045] The fluorescent immunoassay, timer (such as stopwatch) and pipette produced by Shandong Mai Microbiotechnology Co., Ltd.

[0046] 2, package is site

[0047] The package is located in the detection zone 3c, and the package is known as a D-Dimer antibody.

[0048] The package was located in the heat rodification area 3b, and the package was secondary;

[0049] The fluorescent label region 3a is fixed to a dry D-Dimer fluorescence comparative antibody.

[0050] 3, detection method

[0051] 3.1 Improved D-Dimer microfluidic chip

[0052] After improved D-Dimer microfluidic chip A is flat on the experiment, the sample preparation water absorbing material 9 and the microchannel 3 are broken, and the sample is added to the microfluidic chip sample. In the hole 10, after 2min, the anti-direction moving water absorbing material 9 is connected to the microchannel 3, and 15 μ l of buffer is added to the buffer plus sample hole 11, after 3min, the chip is judged by the fluorescent immunoassay, record D- The detection result of the Dimer sample. Parallel assay S1, S2, each sample repeatedly detected 5 times, calculating the relative deviation of each sample detection result value and the original concentration value, and calculating the variation coefficient (CV) of each sample detection result.

[0053] 3.2 Improvement of the former D-Dimer microfluidic chip

[0054] Improve the pre-D-Dimer microfluidic chip B is flat on the experiment, add the sample to the microfluidic chip, after 5min, the chip is judged by the fluorescent immunoassay, record D-Dimer samples Detection results. Parallel assay S1, S2, each sample repeatedly detected 5 times, calculating the relative deviation of each sample detection result value and the original concentration value, and calculating the variation coefficient (CV) of each sample detection result.

[0055] 4, result

[0056] As shown in Table 1, the relative deviation of the detection result of the D-Dimer microfluidic chip does not exceed $\pm 5\%$, and the CV is less than 5%, and the detection of the former D-Dimer microfluidic chip is improved. The relative deviation of the result and the original concentration value did not exceed $\pm 10\%$, and the CV was less than 10%, and the improved deviation and CV were less than improved. It indicated that the chip detection result was more accurate and more uniform. As can be seen from the detection point signal value, the improved fluorescence signal value is higher than the highly improved fluorescence signal value, indicating that the reaction is more sufficient;

[0057] Table 1 Sample test results before and after microfluidic chip improvement

[0058]

Sample	Concentration (ng/mL)	Microfluidic Chip1 （After improved）				
		Fluorescence value	Concentration (ng/mL)	Average (ng/mL)	relative deviation	CV
S1	500.1	24229	484.6	515.1	3.01%	3.52%
		26650	532.7			
		25954	518.9			
		25853	516.9			
		26146	522.7			
S2	2012.5	102466	2039.6	2094.4	4.07%	3.27%
		103314	2056.5			
		108172	2153.1			
		102472	2039.8			
		109681	2183.1			
Sample	Concentration (ng/mL)	Microfluidic Chip2 （Before improved）				
		Fluorescence value	Concentration (ng/mL)	Average (ng/mL)	relative deviation	CV
S1	500.1	13990	522.1	456.2	-8.78%	9.63%

		11988	447.8			
		12398	463.0			
		10689	399.6			
		12008	448.5			
S2	2012.5	44626	1658.7	1812.4	-9.94%	9.07%
		45804	1702.4			
		53249	1978.7			
		53892	2002.5			
		46262	1719.4			

[0059] The above technical solution reflects only the preferred technical solutions of the technical solutions of the present invention.

Claims

1. A microfluidic chip comprising a microchannel formed by a substrate and a cover sheet, and the microchannel is injected into the sample fluid by a sample drawing hole. It is characterized by it. The height of the microchannel is lower than the height of the substrate and the cover sheet contact surface, and the sample fluid flows downwardly on the capillary force of the microchannel.
2. The microfluidic chip according to claim 1, It is characterized by it. The microchannel is connected to the extended hole through an upward connection channel.
3. The microfluidic chip according to claim 1, It is characterized by it. The microchannel is connected to the extended hole through an inclined upward connection passage.
4. The microfluidic chip according to any one of claims 1 to 3, It is characterized by it. A groove is provided along the length direction of the substrate, and the lower surface of the cover is protruded from the top wall of the microchannel, and the microchannel is formed with the bottom wall of the groove.
5. A microfluidic chip according to claim 2 or 3, It is characterized by it. The extended hole extends in a longitudinal direction parallel to the microchannel; or the extended hole is disposed in a direction parallel to the length of the microchannel length.
6. A microfluidic chip according to claim 2 or 3, It is characterized by it. The extended wells are individually disposed on one side of the microchannel side, or simultaneously located on both sides of the microchannel.
7. The microfluidic chip according to any of claims 1-3, It is characterized by it. The microfluidic chip includes a sample region and a waste liquid region communicating with both ends of the microchannel, which are injected into the sample fluid and buffer by sample drawing holes and buffer plus sample holes.
8. The microfluidic chip according to claim 6, It is characterized by it. The sample drawn hole is located between the buffer coefficient hole and the microchannel.
9. The microfluidic chip according to claim 1, It is characterized by it. The exit connection of the microchannels is connected to the waste liquid region, the waste zone communicates with the outside, and the sample outlet is embedded with a water absorbent material that can slide in the sample outlet, and the sample outlet has at least two ends, one end The

ministry is close to the microchannel exit, and the other end is far from the microchannel outlet.

10. The microfluidic chip according to claim 2 or 3, It is characterized by it. The expanded hole is formed by the groove and substrate where the cover sheet is formed; or the groove and cover of the substrate are embodied; or the extended hole is formed on the groove and substrate on the cover sheet. The open grooves are coincided with.