

WATERJET MICROMACHINED MICROSPOTTING PINS

Field of the Invention

[0001] The present invention generally relates to printing tools for microarrays of different biological samples, and more particularly to microspotting pins with low cost and methods for the production of microspotting pins by waterjet micromachining.

Background of the Invention

[0002] Microarray technology provides an extremely useful tool to conduct biological or chemical experiments in a massively parallel fashion because of the large number of different probes that can be fabricated onto the microarray. Usually, a microarray is an array of spots of biological or chemical samples ("probes") immobilized at predefined positions on a substrate. The spots are deposited onto the substrate by microspotting pins (also printing tools and spotting pins, all of them will be used interchangeably hereinafter). The microspotting pins at their tips have channels, narrow openings or slits that act as miniature reservoirs so that a very small and precise quantity of liquid samples can be transferred onto the substrate therefrom.

[0003] Microspotting pins are usually made of metal including stainless steel. Currently, the cost of spotting pins is extremely high and the spotting pins are very vulnerable to damages if extremely careful handling is not adhered. Moreover, the presently available production techniques including EDM, ECM and laser machining induce residual thermal stresses and inherent surface roughness on the narrow slit of a microspotting pin. The slit is critically important for determining the efficiency of capillary action, and the quality and quantity of biological fluids such as DNA deposited on a substrate during the fabrication of a microarray.

[0004] Therefore, there is an imperative need to have a microspotting pin of high quality that could be produced at a reduced cost with short production time. This invention satisfies this need by disclosing a microspotting pin with a smooth surfaced slit and a method for producing the microspotting pin, wherein the method is thermal-stress free, low

cost, and high speed. Other advantages of this invention will be apparent with reference to the detailed description hereinafter.

Summary of the Invention

[0005] The present invention provides a microspotting pin to be used in a microspotting device for depositing a small controlled precise quantity of a liquid sample onto a substrate. The microspotting pin comprises a head portion, a tip portion opposite to the head portion, and a shank portion connecting the head portion and the tip portion; wherein the tip portion is tapered from the shank portion to a point at the end of the tip portion; and wherein the tip portion has a diametrical slit formed by a waterjet cutting system, thereby the slit holds the liquid sample to be deposited onto the substrate. The present invention also provides a waterjet micromachining method for producing the microspotting pin by locating, locking and securing the microspotting pin in the waterjet cutting system, and diametrically cutting the tip portion to form the slit with predetermined configurations and dimensions.

[0006] Accordingly, one objective of the present invention is to provide a microspotting pin with high quality.

[0007] Another objective of the present invention is to provide a method for manufacturing a microspotting pin with reduced cost and shortened production time.

[0008] The objectives and advantages of the invention will become apparent from the following detailed description of preferred embodiments thereof in connection with the accompanying drawings

Brief Description of the Drawings

[0009] Preferred embodiments according to the present invention will now be described with reference to the Figures, in which like reference numerals denote like elements.

[0010] FIG 1 shows an exemplary microspotting pin.

[0011] FIGS 2A –2D are cross-section views of the tip portions in different configurations.

[0012] FIG 3 is a schematic view of the waterjet cutting device.

[0013] FIG 4 shows a portion of a DNA array fabricated by microspotting pins in accordance with the present invention.

Detailed Description of the Invention

[0014] The present invention may be understood more readily by reference to the following detailed description of certain embodiments of the invention.

[0015] Throughout this application, where publications are referenced, the disclosures of these publications are hereby incorporated by reference, in their entireties, into this application in order to more fully describe the state of art to which this invention pertains.

[0016] Referring now to FIG 1, the present invention provides a microspotting pin **10** that has a head portion **11**, a tip portion **13** opposite to the head portion, and a shank portion **12** connecting the head **11** and tip portions **13**. The head portion **11** may have variable shapes and dimensions for being adaptively mounted in various microspotting systems. For example, the head portion may have a cylindrical shape but with one or more planar surfaces so that the possible rotation of the pin **10** in any pin holder may be prevented. The shank portion **12** may also have variable shapes and dimensions. While FIG 1 depicts the shank portion **12** that is different from the head portion **11**, a shank portion may have the same shape and dimensions as the head portion. In addition, the head portion may be an integral extension from the shank portion or a separable entity that can be appropriately attached to the shank portion after the pin is assembled. The tip portion **13** is typically conically shaped. It is appreciated that other shapes may also be adopted. Furthermore, any specific length and diameter of a microspotting pin may be determined by one skilled in the art when a particular microspotting system is identified.

[0017] It is known that the tip portion **13** is critical for any microspotting pin to produce uniform spots with predetermined sizes and volumes. The inventors of the present invention have discovered that certain configurations of the microspotting pins produce good quality spots on microarrays. FIGS 2A-2D illustrates microspotting pins with unique geometrical designs that enable good deposition of biological samples onto substrates. In addition, the effective use life of the microspotting pins is substantially prolonged. The slit

14 is formed by cutting diametrically through the tip portion **13**. In preferred embodiments, the slit is a straight channel extending from the tip point for a predetermined length. The width and length of the slit **14** are functions of the diameter of the microspotting pins. As shown in FIGS 2A-2D, the microspotting pins have a diameter of 1.55 mm, and the slits are about 3.0 mm long and 100 μm wide.

[0018] Furthermore, the tip portion **13** in FIG 2A is shaped by four planar surfaces, of which two planar surfaces are opposite to each other and form a 38 - 42° angle at the tip point, and the other two planar surfaces are also opposite to each other and form a 22- 25° angle at the tip point. The slit is formed by through the planar surfaces forming the 38 - 42° angle at the tip point. FIG 2B shows a tip portion **13** with a conical shape. The angle of the tip point viewed from a center-cross section of the tip portion is 22- 25°. FIG 2C shows a tip portion that is identical to the one shown in FIG 2A except that the slit is formed by through the planar surfaces forming the 22- 25° angle at the tip point. FIG 2D shows a tip portion with a conical shape, but the tip portion is cut by two planar surfaces opposite to each other. The angle formed by the round surfaces is 28 - 32 °, and the angle formed by the two planar surfaces is 22- 25°.

[0019] In preferred embodiments, the microspotting pin **10** is made of stainless steel. It should be appreciated that the microspotting pin **10** can be fabricated from a variety of materials with efficacy such as metals, alloys, ceramics, plastics and semiconductor materials, as required or desired, giving due consideration to the goals of providing chemical inertness and robustness. In addition, the tip portion **13** may be coated with a thin film or coating that is not only chemically inert and mechanically robust but is also hydrophobic to most fluids such as aqueous reagents, DMSO, and other common solvents. Suitable coatings are silicon nitride, silicon carbide, titanium nitride, among others.

[0020] The present invention provides a waterjet micromachining method for producing microspotting pins. More specifically, the waterjet cutting technique is employed to machine the slit **14** of a spotting pin because it is highly efficient in the removal of resultant materials from the slit with speed, accuracy and cost effectiveness. The waterjet micromachining method provides extremely accurate dimensional control of the precision slit that maintains the geometrical tolerance and stability of the microspotting pins. In addition, the water-jet micromachining method does not generate any heat during

the production so that the integrity of material being machined is maintained throughout its thickness during the whole process. Moreover, unlike the laser cutting, the water-jet micromachining method does not change the microstructures of microspotting pins or sacrifice their original mechanical properties at all.

[0021] Abrasive waterjet cutting systems have been known and used for many years. Typically water is pressurized and released through an abrasive waterjet cutting nozzle. The great speed of the pressurized water entrained with abrasive particulates provides the energy required to abrade the target material. While the specifications of a waterjet cutting system particularly suitable for the present invention will be described hereinafter, a detailed description of the waterjet cutting system will be dispensed with herein for the sake of brevity.

[0022] It will be appreciated that any commercial waterjet cutting system may be employed so long as that the cutting system satisfies the specifications required for microfabricating a microspotting pin in accordance with the present invention. See, U.S. Pat. Pub. No. US2002/0173220. With respect to the cutting nozzle, it may be formed to a variety of geometric configurations, but is typically conical, with the smaller diameter near its outlet to effectuate an accurate, precise and controlled fine abrasive stream. Abrasive particulate materials contemplated for use in the present invention are known in the art. For example, the abrasive particulate material may include, but is not limited to, garnet, silica, aluminum oxide, and the like. In addition, it should be understood that the term “water” is intended to include not only water, but also various other liquids that may be used as an appropriate medium for displacing abrasive particulate materials to the nozzle of the waterjet cutting device. Similarly, as used herein, the term “waterjet cutting system” should be construed to include any type of cutting system that utilizes liquid in combination with an abrasive material to cut or abrade target objects made of various materials.

[0023] The fabrication of a microspotting pin in accordance with the present invention is described herein with reference to FIG 3.

[0024] The blank of a typical microspotting pin or any other similar pin shaped component can be precisely fabricated by conventional manufacturing process including, but not limited to, lathe, milling and any other new emerging micromachining techniques.

[0025] Referring now to FIG 3, the waterjet cutting device comprises a fixture/jig **21**, a datum block **20**, a cover plate **22** and a waterjet nozzle **30** emitting a waterjet stream, wherein the waterjet system is omitted. Before cutting, the blank of a microspotting pin **10** is placed, located and secured in the unique jig and/or fixture **21**. The purpose of which is to precisely lock the blank rigidly in a position against critically predefined and predetermined datum faces/reference planes of the datum block **20** in the three-dimensional space. In certain embodiments, such devices may incorporate loaded spring or other anti-backlash mechanisms to prevent the blank from all possible movements in all directions.

[0026] The jig and/or fixture **21** with the blank secured therein is mounted directly below the cover plate **22** which has an opening or a slot through which the waterjet stream from the nozzle **30** can work on the blank **10**. The waterjet nozzle is located directly above the pointed tip of the pin at a desired effective distance depending on the pin diameter, its controlled slit dimensions and tolerances. The waterjet stream with its fine abrasive mixture is ejected through the nozzle at predetermined velocities at the pin tip so that the stream cuts through the pin diametrically. The nozzle is then translated in a desired linear fashion along the lateral axis of the pin parallel to the axis of the pin, starting from the tip of the pin towards the pin body until the intended or designed length of cut is achieved or vice versa while maintaining a constant cutting rate. Upon attaining the required length of the cut or slit, the waterjet stream is terminated and the nozzle is returned to a safe position. This entire cutting sequence and parameters including positional data, velocities and acceleration and other relevant process parameters are stored in the waterjet machine control system. The pin is released from the jig and/or fixture and appropriate dimensional and/or geometrical inspections are performed to ensure the pin in conformance to the intended design specifications.

[0027] In preferred embodiments, the waterjet processing parameters include water pressure at about 900 – 1200 bar, abrasive size about 0.005- 0.02 mm, feed rate at about 45 – 55 mm/min, and diamond nozzle diameter about 0.05 – 0.15 mm.

[0028] The microspotting pins fabricated in accordance with the present invention were tested for their functionality by producing an array of DNA samples. These spots were observed via a light microscope. For such visual inspections, the spots are expected to possess similar shape and size. As shown in FIG 4, the waterjet micromachined

microspotting pins showed excellent functionality by producing the array with similar spots.

[0029] While the application of the microspotting pins in accordance with the present invention has been illustrated by producing DNA microarrays, it shall be appreciated that the microspotting pins described herein can also be used to produce microarrays of a wide range of biological and chemical probe materials which include but not limited to ribonucleic acids (RNA), synthetic oligonucleotides, antibodies, cells, tissues, proteins, peptides, lectins, modified polysaccharides, synthetic composite macromolecules, functionalized nanostructures, synthetic polymers, modified/blocked nucleotides/nucleosides, modified/blocked amino acids, fluorophores, chromophores, ligands, chelates, haptens, drug compounds, and chemical compounds that have associated substance which binds, associates, or interacts with the probe material.

[0030] While the present invention has been described with reference to particular embodiments, it will be understood that the embodiments are illustrative and that the invention scope is not so limited. Alternative embodiments of the present invention will become apparent to those having ordinary skill in the art to which the present invention pertains. Such alternate embodiments are considered to be encompassed within the spirit and scope of the present invention. Accordingly, the scope of the present invention is described by the appended claims and is supported by the foregoing description.

Claims

What is claimed is:

1. A microspotting pin to be used in a microspotting device for depositing a small quantity of a liquid sample onto a substrate, comprising:
 - a head portion;
 - a tip portion opposite to the head portion; and
 - a shank portion connecting the head portion and the tip portion;wherein the tip portion is tapered from the shank portion to a point at the end of the tip portion; and wherein the tip portion has a diametrical slit formed by a waterjet cutting system, thereby the slit holds the liquid sample to be deposited onto the substrate.
2. The microspotting pin of claim 1, wherein the liquid sample is composed of any material selected from the group consisting of DNA, RNA, synthetic oligonucleotides, antibodies, cells, tissues, proteins, peptides, polysaccharides, synthetic composite macromolecules, functionalized nanostructures, synthetic polymers, modified/blocked nucleotides/nucleosides, modified/blocked amino acids, fluorophores, chromophores, ligands, chelates, haptens, and drug compounds.
3. The microspotting pin of claim 1, wherein the tip portion is shaped by four planar surfaces, of which two planar surfaces are opposite to each other and form a 38 - 42° angle at the tip point, and the other two planar surfaces are also opposite to each other and form a 22- 25° angle at the tip point, and wherein the slit is formed by through the planar surfaces forming the 38 - 42° angle at the tip point.
4. The microspotting pin of claim 1, wherein the tip portion is shaped by four planar surfaces, of which two planar surfaces are opposite to each other and form a 38 - 42° angle at the tip point, and the other two planar surfaces are also opposite to each other and form a 22- 25° angle at the tip point, and wherein the slit is formed by through the planar surfaces forming the 22- 25° angle at the tip point.

5. The microspotting pin of claim 1, wherein the tip portion has a conical shape, and wherein the angle of the tip point viewed from a center-cross section of the tip portion is 22- 25°.
6. The microspotting pin of claim 1, wherein the tip portion has a conical shape but is cut by two planar surfaces opposite to each other, and wherein the angle formed by the round surfaces is 28 - 32 °, and the angle formed by the two planar surfaces is 22- 25°.
7. The microspotting pin of claim 1, wherein the microspotting pin is made of stainless steel or any other ferrous and non-ferrous materials.
8. The microspotting pin of claim 1, wherein the waterjet cutting system has a water pressure about 900 – 1200 bar, an abrasive size about 0.005 – 0.02 mm, a feed rate about 45 – 55 mm/min, and a nozzle diameter about 0.05 – 0.15 mm.
9. A waterjet micromachining method for producing a microspotting pin to be used in a microspotting device for depositing a small quantity of a liquid sample onto a substrate, wherein the microspotting pin comprises a tip portion where a diametrical slit is formed by a waterjet cutting system, said method comprising:
 - locating, locking and securing the microspotting pin in the waterjet cutting system;
 - and
 - diametrically cutting the tip portion to form the slit with predetermined configurations and dimensions.
10. The waterjet micromachining method of claim 9, wherein the waterjet cutting system has a water pressure about 900 – 1200 bar, an abrasive size about 0.005 – 0.02 mm, a feed rate about 45 – 55 mm/min, and a nozzle diameter about 0.05 – 0.15 mm.
11. The waterjet micromachining method of claim 9, wherein the microspotting pin is made of stainless steel or any other ferrous and non-ferrous materials.