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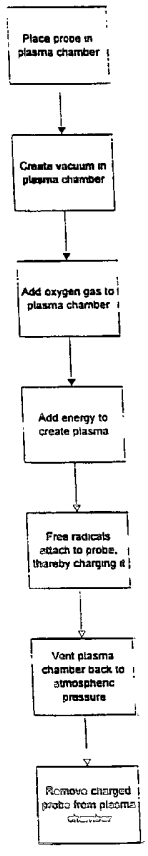
(54) Title: METHOD FOR PLASMA CHARGING A PROBE



(57) Abstract: A method for electrically charging a probe/spray head/pin tool by plasma technology for use in pipetting compounds in small volumes includes the steps of placing the probe to be charges in a plasma chamber; creating a vacuum within the plasma chamber and then introducing a stable gas into the plasma chamber; applying electromagnetic energy to the plasma chamber with an electrode or by using the probe as the electrode, thereby molecularly disassociating the gas, thus creating charged ions, free electrons, and free radicals, charging the probe by the free radicals attaching to the probe; venting the plasma chamber to back to atmospheric pressure; and removing the charged probe from the plasma chamber, whereby the charged probe can pipette compounds is small volumes. The method is applicable to pipetting both liquid and solid compounds.

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METHOD FOR PLASMA CHARGING A PROBE

Claim of Priority

This application claims the priority of U.S. Serial No. 60/176,201 filed January 14, 2000.

Field of the Invention

The present invention relates to a method for charging a probe to pipette compounds in small volumes, and, more particularly, to a method utilizing a plasma-generating process to modify the surface properties by applying a charge to the probe.

Background of the Invention

In biotechnology research, scientists often work with liquid compounds in volumes between a drop (about 50 microliters) and a few nanoliters. There a number of standard methods presently employed to transfer the compounds from a source station where a specimen or other compound is aspirated into the probe to the delivery station where the specimen or other compound is dispensed. Four common techniques are (1) a scheme using a metal probe, that may or may not be coated with a non-metallic layer, which is attached to a pumping device, (2) a scheme using a disposable pipet instead of the metal probe but otherwise similar, (3) a scheme using a spray head and pumping system that propels multiple precisely metered microdroplets, and (4) a scheme using metal shafts with precisely machined hollowed out spaces that hold fluid by surface tension (commonly referred to a "pin tool"). However, it is often difficult to pick up and deliver with a high degree of accuracy and precision these very small quantities of fluids, due to the various effects that the properties of a liquid have on droplet formation (e.g., surface tension, viscosity, and polarity) and interactions between the liquid and

the probe/spray head/pin tool. It would be desirable to use plasma technology in such a way so as to place a charge on the probe/spray head/pin tool, in order to use the properties of the liquid compounds to attract or repel the compound to or from the probe/spray head/pin tool. By controlling the charge, the optimum conditions for fluid transfer can be reached depending on the application, liquid, the compound dissolved in the liquid and the type of probe or delivery mechanism used. Charge on the probe/spray head/pin tool will alter the shape of droplet formation, the force required to release the droplet from the probe/spray head/pin tool, the surface tension interaction between the liquid and the probe/spray head/pin tool, and the formation of microdroplets during dispensing. Some pump and probe/spray head/pin tool configurations allow the plasma to be pulled into the probe/spray head/pin tool internal spaces thereby adding an additional variable to the affect of the plasma charge on the liquid.

Plasma technology is known in the art and is presently primarily used in connection with semiconductor manufacturing and in the sterilization of medical devices. In semiconductor manufacturing, plasma technology is used, via plasma deposition and plasma etching, to create the circuit lines on the wafer. These two techniques are used to deposit material on a surface, as opposed to imparting an electrical charge to the surface.

To sterilize medical devices, a technique known as glow discharge is often used, in which the items are sterilized in air, as opposed to a gas-filled evacuated chamber. For example, U.S. Patent No. 5,633,424 relates to a method of sterilizing items using a water vapor-based plasma. The items to be sterilized are placed in a chamber, which is then evacuated. Water vapor is introduced into the chamber and is allowed to uniformly

disperse throughout the chamber. Electromagnetic radiation energy is then applied to the chamber, fractionating the water molecules into reactive radicals. These radicals then combine with the microorganisms on the items, effectively vaporizing the microorganisms. The by-product gases are exhausted from the chamber, and the now-sterilized items can be removed from the chamber.

U.S. Patent No. 5,700,327 recites a method for removing organic compounds from hollow containers, thereby cleaning the containers. The container is placed into a vacuum chamber, and an oxidizing gas is introduced into the chamber. An electric field is then applied to the chamber, converting the oxidizing gas into a low temperature plasma, which then oxidizes substantially all of the organic compounds within the container.

U.S. Patent No. 6,059,935 discloses two methods and corresponding electrode designs for the generation of a plasma, for example, at or about one atmosphere. Using the disclosed methods, various webs, films and three-dimensional objects are beneficially treated in a reduced amount of time. A first method utilizes a repetitive, asymmetric voltage pulse to generate a plasma discharge between two electrodes. An asymmetric voltage pulse is used to generate a discharge in which a substrate can be exposed predominately to either positive or negative plasma species depending on the voltage polarity used. A second method uses the gap capacitance of an electrode pair and an external inductor in shunt to form a resonant LC circuit. The circuit is driven by a high power radio frequency source operating at 1 to 30 MHz to generate a uniform discharge between the electrode pair. Both methods have temperature controlled discharge surfaces with supply gas temperature, humidity and flow rate control. The gas

flow is typically sufficient to cause a turbulent flow field in the discharge region where materials are treated. Electrode pairs implement these methods and include a metal faced electrode and a dielectric covered electrode, one or both of which have a series of holes extending through the electrode face for supply gas flow. The second of the above-described methods will also operate with paired, metal faced electrodes, but under more restricted operating conditions.

U.S. Patent No. 6,132,813 discloses a method for modifying a substrate surface, including the step of applying a high density plasma to the substrate surface in the presence of a hydrofluorocarbon gas and a carrier gas to form an antiwetting layer on the substrate surface. Optionally, the method includes a cleaning step of contacting the slider surface with a carrier gas for a period of time effective to clean the surface.

U.S. Patent No. 6,105,589 is directed to an improved method and apparatus are provided for cleaning the specimen and interior specimen chamber of electron microscopes, and similar electron beam instruments. The apparatus consists of a glow-discharge, oxygen-radical generator placed on a specimen chamber port with an excitation source to create a low-power glow-discharge plasma inside the generator. Air or other oxygen and nitrogen mixture is admitted to the generator at a pressure between 0.3 Torr and 5 Torr. The low power glow discharge is used to disassociate oxygen preferentially over nitrogen to create the oxygen radicals. The oxygen radicals then disperse by convection throughout the chamber to clean hydrocarbons from the surfaces of the chamber, stage and specimen by oxidation to CO and H2O gases. The excitation power of the plasma is limited to limit the nitrogen ion production that destroys the oxygen radicals and to limit the projection of the electrically active plasma into the

specimen chamber. The optical emission or color of the plasma is observed for the selection of the correct power level for maximum oxygen radical production.

While the foregoing uses of plasma technology employ similar basic methods (i.e., placing an article in a sealed chamber and applying energy to the chamber to create a plasma), they are mainly designed for coating a substrate or removing a layer of material such as in plasma etching and they do not lead to the desired result, which is the controlled charging of a probe. There is therefore a need in the art for a method for using plasma technology to charge a probe such that it can attract or repel compounds in small volumes.

Summary of the Invention

It is an object of the present invention to apply an electrostatic charge to a metal probe, a TEFLON-coated probe (or other similar coated probe) or a spray head or pin tool, such that the probe/spray head/pin tool can attract or repel liquid compounds in volumes of less than a drop, i.e., 50 microliters or less. Using this method, it is possible to "tune" any type of probe assembly with a charge so it is able to attract or repel certain compounds for more optimal pipetting accuracy and precision, since the compounds themselves also have a charge and other physical properties affected by the electrostatic charge on the surface of the probe assembly.

To perform this method, a probe (hereafter "probe" refers to either any embodiment of "probe or spray head or pin tool") to be charged is placed within a plasma chamber or the body of the probe forms part of the chamber and thereby completes the chamber assembly when the probe is placed. A vacuum is created in the chamber, and a gas mixture of oxygen and argon (the latter as a carrier gas) or other

plasma gas mixture containing oxygen is introduced into the chamber. After the gas mixture has filled the chamber, electromagnetic energy is applied to the gas with the probe being either passively exposed to the gas within the chamber or with the probe being an electrode and thereby a source of the electromagnetic energy. The electromagnetic energy within the chamber causing a breakdown of the O_2 molecules into O‡ ions, free electrons, and free radicals (i.e., the plasma). When the probe is placed into the chamber, there is virtually no organic material for the free radicals to bond with, causing the free radicals to attack the probe, thereby imparting a charge to the probe. This process is performed like a "tip wash" process, as is known in the art. A tip wash might proceed this process to reduce the amount of organic materials present on the probe. The process is fully-automated once the probe is within or completes the chamber. The process is to create a plasma is initiated, takes one or two seconds to complete, and does not require human intervention to be performed as probe, chamber and support hardware and gas are part of or an accessory component of the automated instrumentation. The probe or head would be the negative electrode and placed in a small vacuum chamber, which is evacuated and an appropriate gas or gas mixture discharged into. The rF energy would be applied to the chamber with the probe or head acting as the negative electrode. The gas plasma would then be intensified and generated on the probe itself thus creating the charged probe. The vacuum chamber would be an integral part of the instrument itself as a stage or an accessory to an instrument that integrates into the normal operation of the instrument.

A method for electrically charging a probe by plasma technology for use in pipetting compounds in small volumes includes the steps of placing the probe to be charged in a plasma chamber; creating a vacuum within the plasma chamber and then introducing a stable gas into the plasma chamber; applying electromagnetic energy to the plasma chamber, thereby molecularly disassociating the gas, thus creating charged ions, free electrons, and free radicals; charging the probe by the free radicals attaching to the probe; venting or opening the plasma chamber back to atmospheric pressure; and removing the charged probe from the plasma chamber, whereby the charged probe can pipette compounds in small volumes. This method is applicable to pipetting both liquid and solid compounds.

Brief Description of the Drawings

For a better understanding of the present invention, reference is made to the following detailed description of an exemplary embodiment considered in conjunction with the accompanying drawing, in which:

Figure 1 is a flowchart illustrating the steps of the method according to the present invention.

Detailed Description of the Invention

Figure 1 outlines the steps of the method of the present invention. First, a probe, preferably TEFLON-coated (but the method applies to metal probes with or without a TEFLON coating or other coating) is placed into a plasma chamber and the chamber is sealed. Next, a vacuum is crated in the sealed plasma chamber, and oxygen gas, along with an argon carrier gas (or other plasma gas mixture with oxygen gas as a component), is introduced into the chamber and dissipates throughout the chamber.

Sufficient electromagnetic energy is added to the chamber using electrodes or the probe assembly as an electrode to ionize the oxygen gas within the carrier gas mixture, creating mainly O^+ ions, free electrons, and free radicals. Because the probe is virtually clean (i.e., virtually free of organic material) when it is placed in the plasma chamber, the free radicals have no other substance to attach to, and cling to the TEFLON-coated probe, thereby imparting a charge to the probe. The vacuum chamber is the vented or opened, returning it to atmospheric pressure, and the now-charged probe is removed from the chamber.

This method is performed by a machine that does not require human contact with the probe, which could dissipate the charge and possibly "contaminate" the probe. Under these conditions, the method is performed in a manner similar to a "tip wash" as is commonly performed in many applications including those in biomedical research, clinical applications and numerous other standard laboratory techniques. This method can for many applications be used as a replacement for a conventional tip wash, as any small amounts of organic material remaining on the probe from the prior pipetting step will be vaporized by the plasma, and the probe will also be charged by the plasma.

After the probe has been plasma-charged according to the method, it can be used to pipette liquid compounds. The compounds and solvents being pipetted with the probe can be quite variable in consistency and physical properties. The major variables affecting the consistency of a liquid compound are surface charge characteristics (ranging widely from hydrophilic to hydrophobic), viscosity (runnier than water to approaching honey), polarity (the electric charges of the molecules themselves, which

can be different than the polarity of the compound, which with greater concentration become more significant), pH, ionic strength, and vapor pressure.

By using the plasma-charging method, the surface characteristics of a probe can be modified and controlled to optimally attract or repel the different types of compounds used or altered for a desired result. Typically, coated probes such as those coated with TEFLON are hydrophobic, but even the surface of the TEFLON can be made to carry an electric charge that makes the material act uniquely different than untreated TEFLON coated probes. In other words, the TEFLON surface can be "tuned" to the optimum requirements for the precise transfer of a certain type of compound. By modifying the surface characteristics of the TEFLON in this manner, the pipetting system can work in a more optimal manner with a broad range of compounds and solvents. Other surfaces can be similarly modified to optimally improve the precision and accuracy of the pipet assembly over a broader ranges of compounds and solvents.

Applications in numerous scientific specialties use many types of solvents and very unusual compounds, such as novel combinatorial compounds common in pharmaceutical drug discovery and a number of industrial applications using combinatorial type processes. This approach controls a critical set of variables when working with small volumes that improve precision and accuracy of the pipetting process. At low volumes, compound characteristics will cause a liquid to cling to the surface it is attached to and remain attached to the column of fluid from which it is being metered, thus making the accurate and reproducible metering of small volumes difficult. Applying a charge to the probe can overcome a liquid's tendency to cling to other surfaces and allow better control of other surface and physical properties.

It will be understood that the embodiment described herein is merely exemplary and that a person skilled in the art may make many variations and modifications without departing from the spirit and scope of the present invention. For example, the method can also be applied to charging a probe for use in connection with solid (i.e., dry powder) compounds. All such variations and modifications are intended to be included within the scope of the invention as defined in the appended claims.

Claims

1. A method for electrically charging a probe by plasma technology for use in pipetting compounds in small volumes comprising the following steps:

placing a probe to be charged in a plasma chamber or using the probe assembly to complete the chamber;

creating a vacuum within the plasma chamber and then introducing a stable gas into the plasma chamber;

applying electromagnetic energy to the plasma chamber with an electrode or by using the probe as the electrode, thereby molecularly disassociating the gas, thus creating charged ions, free electrons, and free radicals, and charging the probe by the free radicals attaching to the probe;

venting the plasma chamber to back to atmospheric pressure; and

removing the charged probe from the plasma chamber, whereby the charged probe can pipette compounds in small volumes.

2. A method for electrically charging a probe by plasma technology for use in pipetting compounds in small volumes comprising the following steps:

placing a probe to be charged in a plasma chamber or using the probe assembly to complete the chamber;

creating a vacuum in the chamber, and introducing a gas mixture of oxygen and a carrier gas into the chamber; and

applying electromagnetic energy with an electrode or by using the probe as the electrode to the gas mixture, thereby causing a breakdown of the O_2 molecules into O‡

Ions, free electrons, and free radicals; (i.e., the plasma), thereby causing the free radicals to attack the probe, thereby imparting a charge to the probe.

3. The method of claim 2 wherein the carrier gas is argon.

4. A method for electrically charging a probe by plasma technology for use in pipetting compounds in small volumes comprising the following steps:

placing a Teflon coated probe to be charged in a plasma chamber;

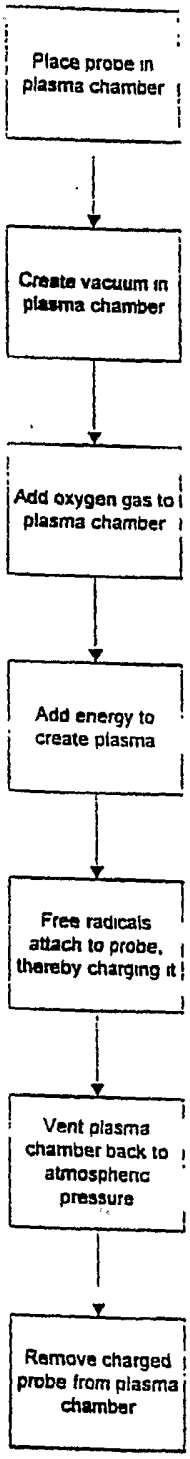
creating a vacuum within the plasma chamber and then introducing a gas mixture of oxygen and argon into the plasma chamber;

applying electromagnetic energy to the plasma chamber with an electrode or by using the probe as the electrode, thereby molecularly disassociating the gas, thus creating charged ions, free electrons, and free radicals, and charging the probe by the free radicals attaching to the probe;

venting the plasma chamber to back to atmospheric pressure; and

removing the charged probe from the plasma chamber, whereby the charged probe can pipette compounds in small volumes.

Fig. 1


Place probe in plasma chamber
Create vacuum in plasma chamber
Add oxygen gas to plasma chamber
Add energy to create plasma
Free radicals attach to probe, thereby charging it
Vent plasma chamber back to atmospheric pressure
Remove charged probe from plasma chamber

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/00931

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C23C 14/00,16/00; H05F 3/00; H01H 47/32; H01T 23/00
US CL : 118/723R, 723CB, 50.1, 621, 622; 361/227, 229, 230, 231, 234

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 118/723R, 723CB, 50.1, 621, 622; 361/227, 229, 230, 231, 234

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
none

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
none

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,700,327 A (Babacz et al.) 23 December 1997 (23.12.1997) See whole document.	1-4
A	US 5,468,453 A (Holt et al.) 21 November 1995 (21.11.1995) See whole document.	1-4
A	US 6,342,187 B1 (Jacob et al. 29 January 2002 (29.01.2002) See whole document.	1-4
A	US 5,633,424 A (Graves et al.) 27 May 1997 (27.05.1997) See whole document.	1-4

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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