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(54) **METHOD AND APPARATUS FOR AC ELECTROSPRAY**

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**A61M 31/00** (2006.01)

(52) **U.S. Cl.** ..... **604/500**; 604/20; 604/173; 128/200.14

(58) **Field of Classification Search** ..... 604/46, 604/65, 67, 68, 890.1, 892.1, 20, 173, 500; 128/200.14, 200.16; 222/645

See application file for complete search history.

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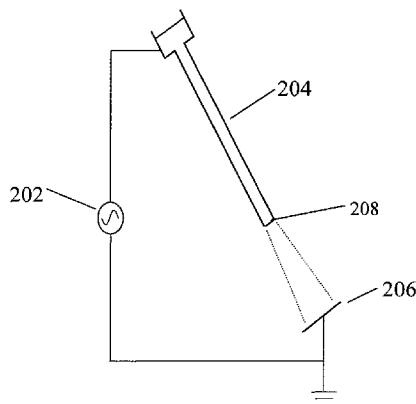
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(57) **ABSTRACT**

The present invention provides an electrospray device using a high frequency alternating current (AC) above 10 kHz to generate fine micron sized drops. The apparatus generally functions by applying a high frequency alternating current electric field across one or more micro-needles and one or more conducting elements. The present invention may be used to generate aerosol drops for respiratory drug delivery or as a microencapsulation technique for the encapsulation of drugs, DNA, protein, osteogenic or dermatological growth factors, bacteria, viruses, immobilized enzyme receptors and fluorescent particles for controlled release drug delivery, tissue or bone engineering, clinical or environmental field testing and as biosensors for clinical or drug monitoring. In addition, the present invention may be used to synthesize biodegradable fibers as bioscaffolds for tissue engineering, surgical sutures or medical gauze that enhance blood coagulation, and further may be encapsulated by other agents.

**41 Claims, 9 Drawing Sheets**



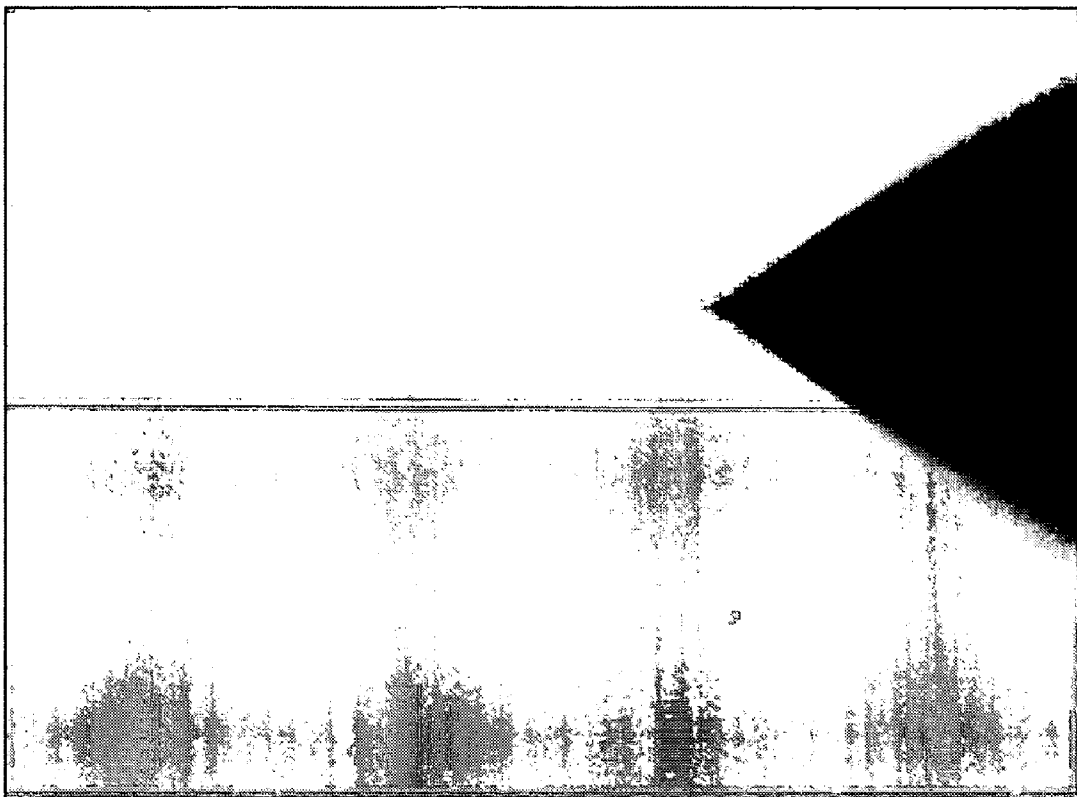
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**FIG. 1**



**Prior Art**

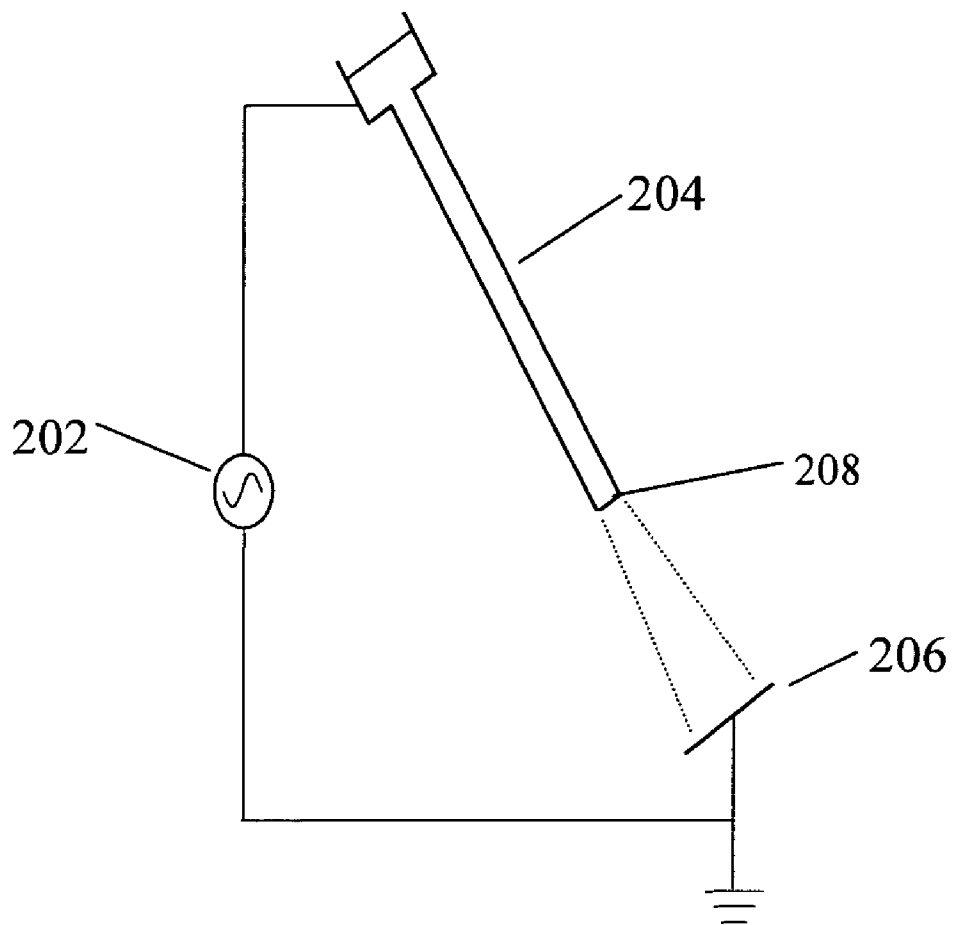
**FIG. 2**

FIG. 3A

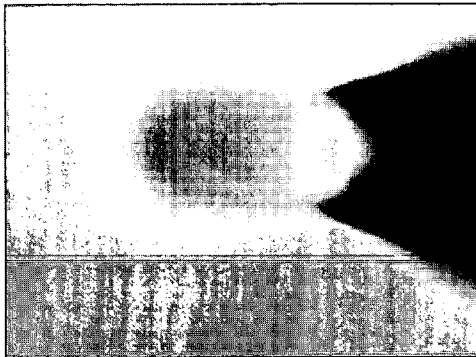


FIG. 3B

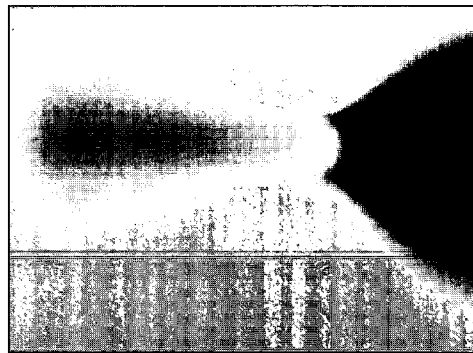


FIG. 3C

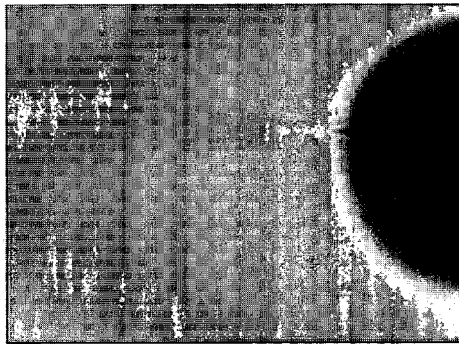


FIG. 3D

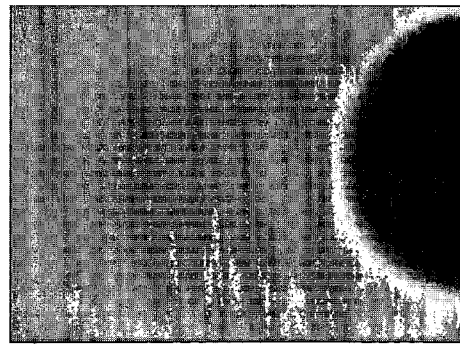
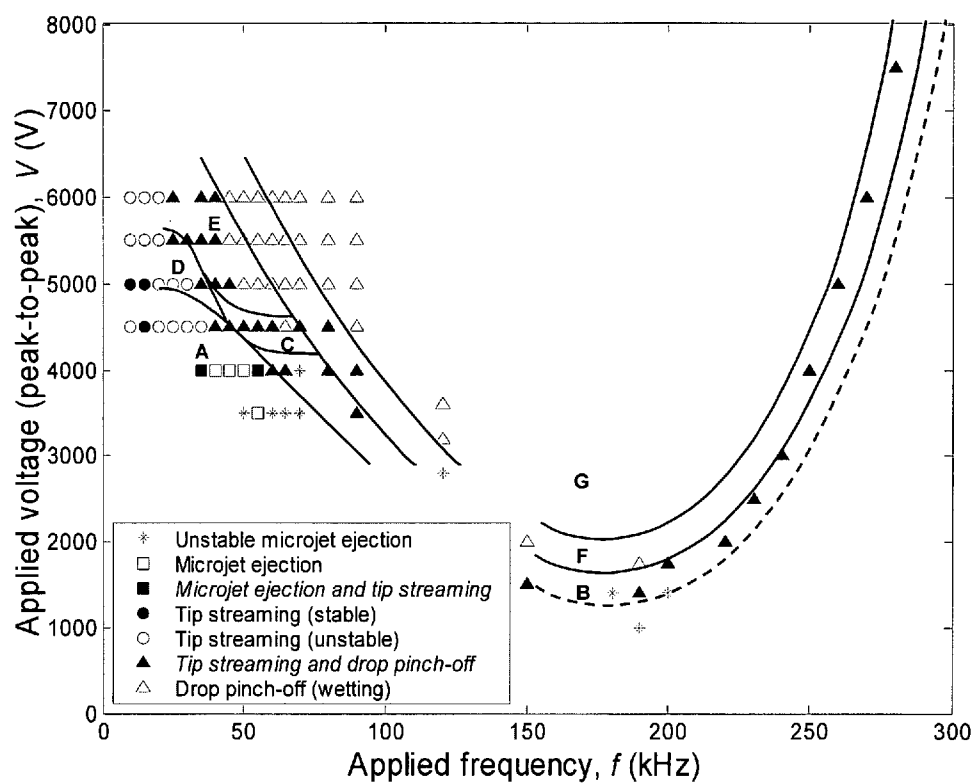
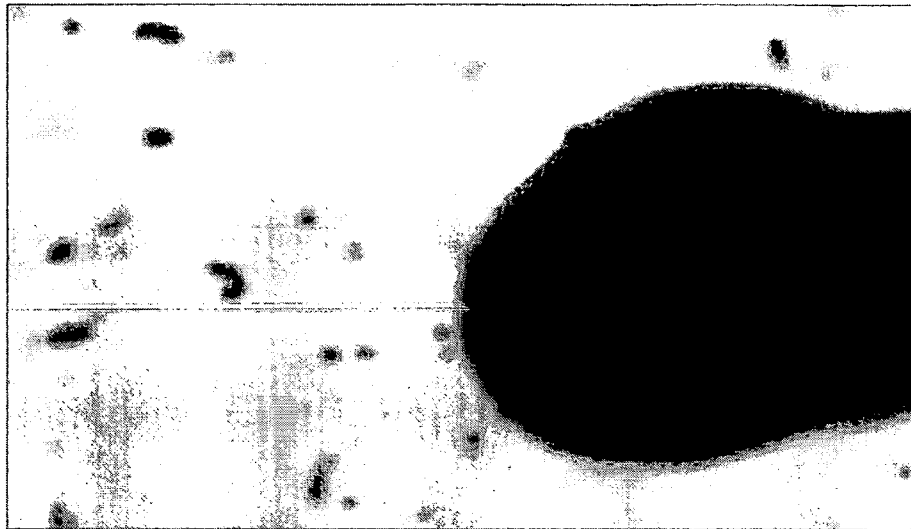


FIG. 4



**FIG. 5**





**FIG. 6**

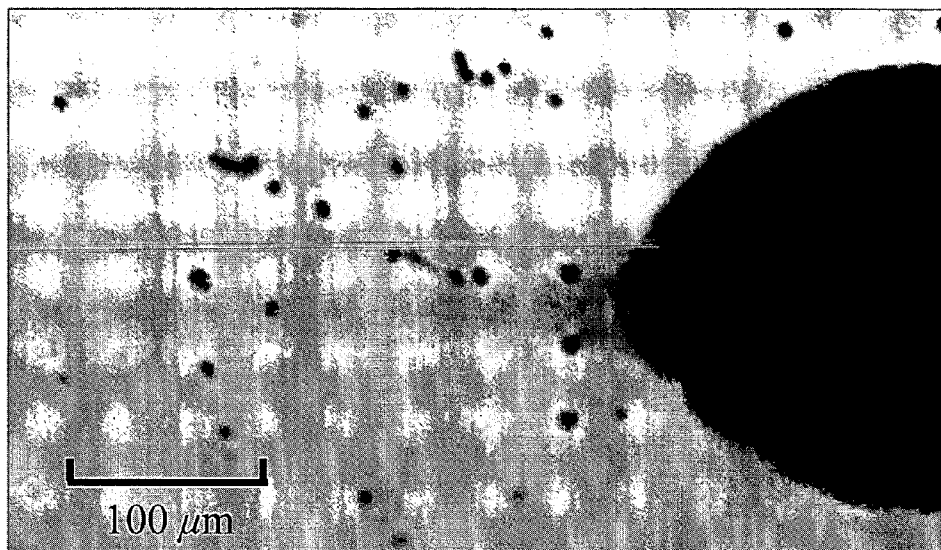


FIG. 7

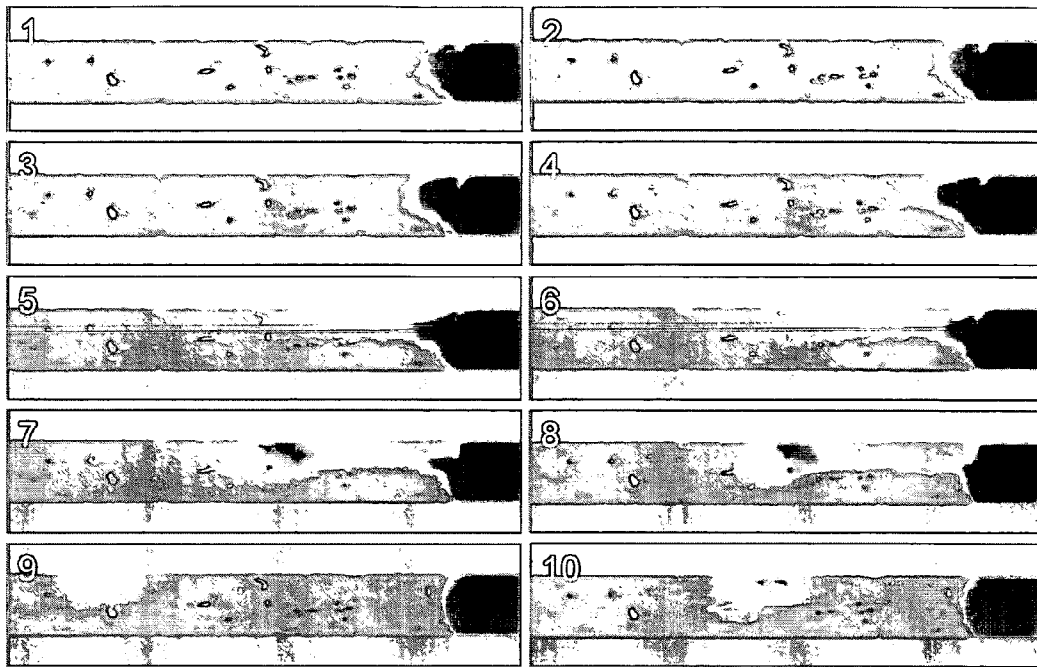
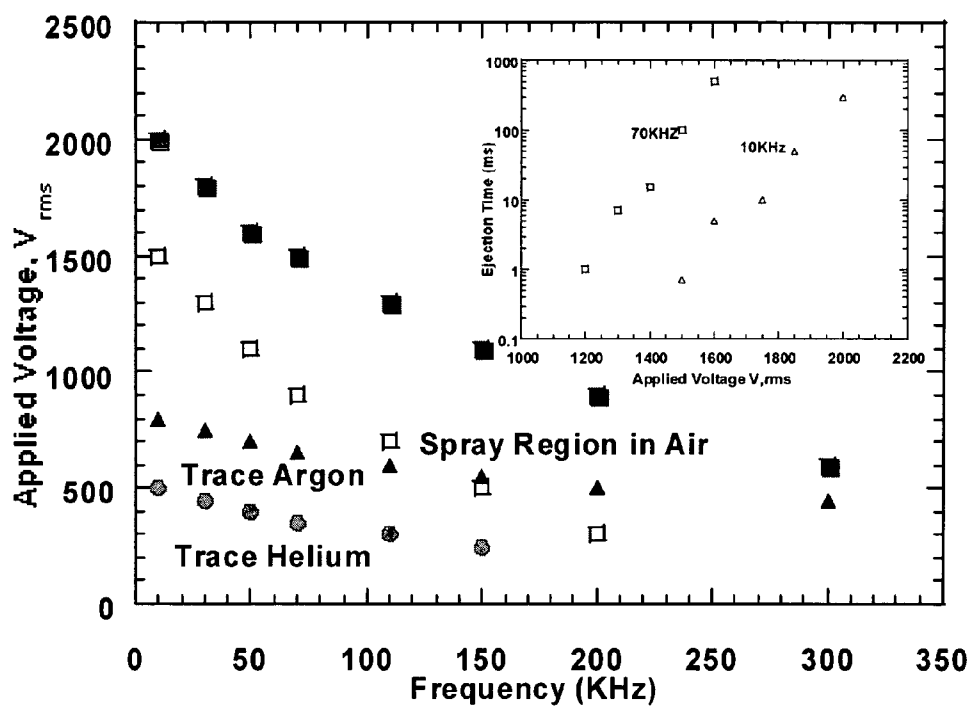
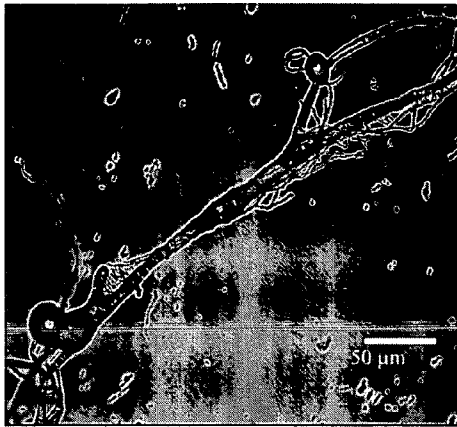


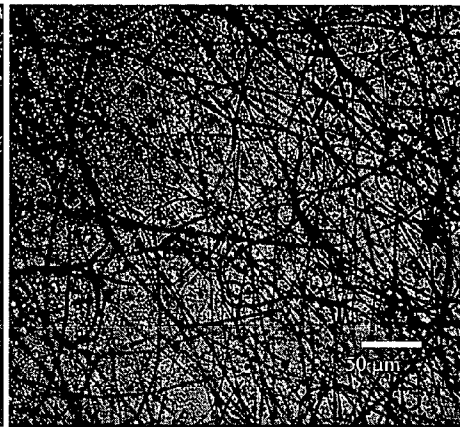
FIG. 8



**FIG. 9A**



**FIG. 9B**



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## METHOD AND APPARATUS FOR AC ELECTROSPRAY

### CROSS-REFERENCE TO RELATED APPLICATIONS

This application makes reference to and claims priority to U.S. Provisional Patent Application No. 60/511,365, entitled "High-Frequency AC Electro-sprays," filed Oct. 16, 2003, the entire contents and disclosure of which is hereby incorporated by reference.

### BACKGROUND

#### 1. Field of the Invention

The present invention relates generally to electrospray devices, and more particularly, to methods and apparatus for an alternating current (AC) electrospray operating in a vacuum or gaseous ambient medium with frequencies above 10 kHz.

#### 2. Related Art

The application of a direct current (DC) electric field to generate charged liquid droplets from Taylor cones in DC electrospray is widely used in pharmaceutical mass-spectrometry because of its ability to produce a beam of relatively mono-dispersed and small (<100 nm) charged droplets that can contain individual protein molecules, see J. B. Fenn, M. Mann, C. K. Meng, S. F. Wong, and C. M. Whitehouse, *Science* 246, 64, 1989, the entire contents and disclosure of which is hereby incorporated by reference. Other areas of application include electrostatic printing, nano-particle technology, micro-encapsulation, fiber electrospinning, etc., see G. Castano, and V. Hruby, *J. Fluid Mech.* 459, 245, 2001, G. Loscertales, A. Barrero, I. Guerrero, R. Cortijo, M. Marquez, and A. M. Ganan-Calvo, *Science* 295, 1695, 2002, the entire contents and disclosures of which are hereby incorporated by reference. The DC field and interfacial charges combine to produce a Maxwell force that stretches the drop into a conic shape (known as a Taylor cone) and ejects streams of small charged droplets from the tip at large frequencies (>1 kHz).

The Taylor cone is formed due to a static balance between the azimuthal capillary stress and the Maxwell normal stress exerted by the predominantly tangential and singular electric field in the liquid. For electrolyte spraying from a DC Taylor cone, surface ions from the bulk electrolyte are transported and concentrated at the tip to drive a Rayleigh fission process. Spraying of dielectric liquid via DC Taylor cones is also possible, but it requires significantly higher voltages and is believed to be driven by the momentum and mass flux of an ion evaporation process at the cone tip, see M. Gamero-Castano and J. Fernandez de la Mora, *J. of Mass Spectrom.*, 35, 790-803, 2000, the entire contents and disclosure of which is hereby incorporated by reference.

In DC electrospinning, a steady, continuous beam of sub-micron charged droplets (typically 0.2-0.3 microns) stream out in a Taylor cone. A typical image of a DC Taylor cone obtained by spraying ethanol into air using DC electric fields is shown in FIG. 1. The Taylor cone and the spray initiation for ethanol depends on several experimental conditions, but is typically observed beyond 2-3 kilovolts.

There has been little investigation into using an AC field for electrosprays. In earlier AC electrospray work it was expected that, at high frequency, the net Maxwell stress would vanish and drop ejection would be impossible. The few reported studies concentrated on low frequencies and superimposing a small AC bias onto a large DC field, see S. B. Sample, and R. Bollini, *J. Colloid Interface Sci.*, 41, 185, 1972; and M. Sato,

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*J. Electrostatics*, 15, 237, 1984, the entire contents and disclosures of which are hereby incorporated by reference. Both of the studies described above, however, do not report spraying dynamics that are fundamentally different from DC electrosprays. One other reported work consisted of using a high frequency AC electric field with 30 kHz and 45 kHz frequencies, see G. Gneist and H. J. Bart, *Chem. Eng. Technol.*, 25, 129-133, 2002, the entire contents and disclosure of which is hereby incorporated by reference. However, this work involved dispersing drops into an ambient liquid medium purely with the intention of generating emulsion drops in liquid/liquid systems.

### SUMMARY

The present invention relates to an electrospray device using a high frequency alternating current above 10 kHz that provides a means for generating micron sized drops. The first broad aspect of the invention relates to the electrospray device. The second broad aspect of the invention relates to a method for producing liquid aerosol drops. The third broad aspect of the invention provides a method for microsphere encapsulation using biodegradable materials, whereas the last broad aspect of the invention provides a method of fiber synthesis using biodegradable materials.

According to the first broad aspect of the present invention, an electrospray device is provided comprising one or more micro-needles providing a passageway for transmission of a fluid; one or more conducting elements in electrical communication with the one or more micro-needles; and a source for generating an alternating current electric field with a frequency above 10 kHz across the one or more micro-needles and the one or more conducting elements.

According to the second broad aspect of the present invention, there is provided a method of producing liquid aerosol drops, the method comprising providing one or more micro-needles; introducing a fluid into the one or more micro-needles; providing one or more conducting elements in electrical communication with the one or more micro-needles; introducing an alternating current electric field with a frequency greater than approximately 10 kHz across the one or more micro-needles and the one or more conducting elements to induce the ejection of liquid aerosol drops from the one or more micro-needles.

According to the third broad aspect of the present invention, there is provided a method of microsphere encapsulation, comprising providing one or more micro-needles; introducing a fluid into the one or more micro-needles, wherein the fluid comprises a biodegradable material, a solvent and a material to be encapsulated; providing one or more conducting elements in electrical communication with the one or more micro-needles; and introducing an alternating current electric field with a frequency greater than approximately 10 kHz across the one or more micro-needles and the one or more conducting elements to induce the ejection of microspheres from the one or more micro-needles, wherein the microspheres contain the encapsulated material and the microspheres are encapsulated with the biodegradable material.

According to the fourth broad aspect of the present invention, there is provided a method of fiber synthesis, comprising providing one or more micro-needles; introducing a fluid into the one or more micro-needles, wherein the fluid comprises a biodegradable material and a solvent; providing one or more conducting elements in electrical communication with the one or more micro-needles; and introducing an alternating current electric field with a frequency greater than approxi-

mately 10 kHz across the one or more micro-needles and the one or more conducting elements to induce the ejection of fibers from the one or more micro-needles, wherein the fibers comprise the ejected biodegradable material.

### BRIEF DESCRIPTION OF THE DRAWINGS

The invention will be described in conjunction with the accompanying drawings, in which:

FIG. 1 is a depiction of the DC electro spray liquid meniscus which forms a steady Taylor cone. A jet emanates from the tip of the cone due to coulombic fission and subsequently breaks up to form a continuous stream of drops;

FIG. 2 is a schematic of an AC electro spray apparatus according to an embodiment of the present invention;

FIGS. 3A, 3B, 3C, and 3D show four consecutive images of AC electro spray of ethanol in air at a frequency of 70 kHz and a root mean squared voltage of 1750 V in accordance with an embodiment of the present invention. The frames are about 0.2 milliseconds apart and the captured event represents one drop ejection in a rapid sequence. Note that unlike the conic tips of DC and low-frequency AC sprays, the high-frequency AC electro spray has a rounded tip. Before ejection, the tip region elongates and expands as the neck shrinks until a micron-sized drop is ejected when the neck pinches;

FIG. 4 maps out various AC electro spray regimes in accordance with embodiments of the present invention as a function of the applied voltage and the applied frequency: A—Capillary dominant regime (no drop ejection), B—Unstable microjet ejection, C—Microjet ejection with/without tip streaming, D—Stable tip streaming, E—Unstable tip streaming, F—Tip streaming with drop pinch-off (onset of wetting), and G—Drop pinch-off and wetting;

FIG. 5 shows the suppression of drop ejection due to an apparent electrowetting effect at a micro-needle tip at an applied frequency of 45 kHz and a root mean squared voltage of 4500 V in accordance with an embodiment of the present invention;

FIG. 6 shows drop ejection by a tip streaming mechanism at a frequency of 10 kHz and a root mean square voltage of 4500 V in accordance with an embodiment of the present invention;

FIG. 7 shows image sequences at 6000 fps taken 300  $\mu$ s apart illustrating microjet formation and subsequent drop detachment at a frequency of 15 kHz and a root mean square voltage of 4000 V in accordance with an embodiment of the present invention;

FIG. 8 illustrates the drop ejection window for ethanol in air in the voltage-frequency space represented by the closed and open squares in accordance with an embodiment of the present invention. The upper boundaries of the drop ejection window when trace amounts of argon and helium flow over the meniscus are in closed triangles and circles, respectively. The insert depicts the time interval between two successive drop ejection events for ethanol in air in the spray window as a function of applied voltage and frequency. At the lower voltages, the drops are ejected periodically at about a 0.1 ms interval from a stable meniscus. At larger voltages, each ejection event produces a rapid succession of 5-10 drops but there is a longer interval between the events. The meniscus tends to oscillate at the high voltage end of the window; and

FIG. 9A shows a 10  $\mu$ m composite fiber that consists of an entanglement of sub-micron fiber strands, and FIG. 9B shows a mesh network of single strand fibers, both of which are

synthesized using AC electro spray in accordance with an embodiment of the present invention.

### DETAILED DESCRIPTION

It is advantageous to define several terms before describing the invention. It should be appreciated that the following definitions are used throughout this application.

### DEFINITIONS

Where the definition of terms departs from the commonly used meaning of the term, applicant intends to utilize the definitions provided below, unless specifically indicated.

For the purposes of the present invention, the term “AC electro spray” refers to a high frequency alternating current device.

For the purposes of the present invention, the term “drop ejection window” refers to the range of voltage and frequency that yields ejection of drops from an electro spray.

For the purposes of the present invention, the term “microencapsulation” refers to the technique of capturing small volumes of liquid, particles or molecules within a micron sized shell consisting of another material.

For the purposes of the present invention, the term “micro-emulsion” refers to two immiscible liquid phases in a state in which one phase assumes a dispersed medium comprising drops with dimensions on the order of  $\mu$ m and below and the other phase assumes a continuous phase surrounding the drops.

For the purposes of the present invention, the term “micro-needle” refers to a syringe with capillary dimensions on the order of approximately 100  $\mu$ m and below.

For the purposes of the present invention, the term “micro-jet” refers to a long slender column of liquid extending out from the tip of a liquid meniscus located at the exit end of a micro-needle.

For the purposes of the present invention, the term “electrical communication” refers to a direct or indirect electrical connection formed between two or more elements.

For the purposes of the present invention, the term “intermittent” refers to an action or operation that is not continuous across a measured time period, but has time periods of no or differing action or operation

### DESCRIPTION

The use of high frequencies, approximately 10 kHz to approximately 280 kHz, or, in some embodiments, as much as approximately 10 MHz, for the AC electric field leads to new electro spray phenomena in which micron-sized electro-neutral drops are generated, see also L. Y. Yeo, D. Lastochkin, S. C. Wang and H. C. Chang, Phys. Rev. Lett., 92, 133902, 2004, the entire contents and disclosure of which is hereby incorporated by reference. The spray modes observed, as well as the electro-neutrality and dimensions of the drops produced, are distinct from that in DC electro spraying. Thus, the use of electro sprays is immediately extended to a wider area of possible applications by the teachings of the present invention.

The experimental setup of an embodiment of an AC electro spray in accordance with the present invention is schematically shown in FIG. 2. A high frequency AC electric field source 202 is connected to a micro-needle 204 and a conducting element 206 that exists as a ground electrode. Liquid is passed through micro-needle 204 by means of a gravitational head (not shown) or a syringe pump (not shown), or other

suitable pumps or transmission mechanisms. The electric field acts to pull out a liquid meniscus at micro-needle tip 208 of micro-needle 204. Thus, according to an embodiment of the present invention, there is provided an electrospray device comprising one or more micro-needles providing a passage-way for transmission of a fluid; one or more conducting elements in electrical communication with the one or more micro-needles; and a source for generating an alternating current electric field with a frequency above 10 kHz across the one or more micro-needles and the one or more conducting elements. A micro-needle of the present invention may be placed approximately 1 mm to approximately 25 mm away from the conducting elements. In operation, an electrospray device of the present invention may be placed in a vacuum or a gaseous ambient medium. Suitable ambient media include air, vacuum, trace gas, argon, helium, neon, etc. To accommodate the use of various ambient media, the entire electrospray apparatus may be housed in a sealed chamber connected to a vacuum pump or to inlet/outlet gas ports.

Suitable alternating current sources for use in embodiments of the present invention include all possible waveform signals such as sine waves, sawtooth waves, square waves, trapezoidal waves and triangle waves, amongst others.

Micro-needles of the present invention may be any suitable micro-needle now known or later developed including, metal hub micro-needles, metal hub syringe tip micro-needles, hypodermic stainless steel micro-needles, metallic spray heads, nozzles or tubes pierced with a hole, metallic conical tips, glass or plastic capillaries with electrode connections, etc. Micro-needles of the present invention may be exposed, insulated, or partially insulated. They may be mounted in various configurations, including horizontal, vertical, or any desired angle with respect to the horizontal plane. Micro-needles of the present invention may have channel diameters of between approximately 100 nm and approximately 1 cm.

Conducting elements of the present invention may be constructed of any suitable material such as a metallic (e.g., copper, brass, etc.) tape strip. A conducting element of the present invention may be a flat strip or a ring, or any other suitable shape.

According to an embodiment of the present invention, an alternating current electric field may be provided at a frequency of between approximately 10 kHz and approximately 10 MHz. According to an embodiment of the present invention, an alternating current electric field may be provided at a voltage of between approximately 100 V and 50,000 V. According to embodiments of the present invention, there are preferable operating window ranges between approximately 10 kHz and approximately 400 kHz and between approximately 500 V and approximately 5000 V. According to embodiments of the present invention, alternating current electric fields may be approximately greater than 500 V/cm.

In sharp contrast to the steady DC Taylor cone shown in FIG. 1, a conic geometry does not develop at the meniscus according to an embodiment of the present invention, as seen in FIGS. 3A, 3B, 3C, and 3D. Instead, the meniscus is pulled forward and a neck develops similarly to drops from a faucet. The drop beyond the neck elongates and expands considerably before the neck pinches off to eject the entire drop. Once the drop is ejected, the meniscus shrinks from its elongated state and the above cycle of events is repeated. The meniscus in AC electrosprays is thus observed to resonate whilst intermittently ejecting drops, in contrast to DC electrospraying in which the meniscus forms a steady Taylor cone from which drop ejection occurs in a continuous fashion. The AC electrospray behavior associated with the present invention, which is attributed to the interfacial polarization resulting from atmo-

spheric ionization or interfacial liquid reaction, is not observed in the experiments of Gneist and Bart; their use of a liquid ambient medium suppresses the AC electrospray behavior that is provided by the present invention.

The entire pinch-off event lasts several milliseconds, much slower than the streaming pinch-off of DC sprays at the tip of the Taylor cone. The ejected drops are electro-neutral due to the large difference in the inverse AC frequency and the ejection time—the number of cations and anions, if they exist in the liquid, that have migrated into the drop due to the AC field should be roughly the same over the relatively long interval for drop pinch-off that contains hundreds or thousands of AC periods. The ejected drops, on the order of approximately 1  $\mu\text{m}$  to approximately 10  $\mu\text{m}$  in diameter, are also comparable or larger than the meniscus dimension and are much larger than the nm sized DC electrospray-created drops. Unlike DC drops, where coulombic fission that arises from charge repulsion within the drop leads to a relatively small size, AC electrospray-created drops may be larger because of their electro-neutrality.

Drops ejected in accordance with embodiments of the present invention may have diameters from approximately 1 nm to approximately 1000  $\mu\text{m}$ .

The drop ejection window, characterized by the V-shaped curve in FIG. 4 is a strong function of the applied frequency. The critical onset voltage for drop ejection with typical solvents is approximately 0.5-1 kV, depending on the ambient medium used, compared to the higher critical onset voltage of 2-3 kV required for drop ejection in DC electrospraying.

In FIG. 4, the two boundaries of the drop ejection window and their separation both decrease with increasing applied frequency to a minimum at approximately 180 kHz before increasing again; drop ejection ceases entirely beyond approximately 400 kHz. Below the lower boundary of the voltage window, drops are not ejected as there is insufficient electrical stress to overcome the capillary stress in the micro-needle. The upper boundary is signified by a dramatic corona discharge that releases all charges from the meniscus such that it equilibrates into a spherical capillary shape, resulting in the cessation of further drop ejection. Also, at high frequencies and high voltages, an apparent electrowetting effect is observed that pushes liquid in the opposite direction up the micro-needle wall, thus suppressing further drop ejection, as depicted in FIG. 5.

In accordance with embodiments of the present invention, a meniscus is stable at low voltages and drops are ejected in a periodic manner. At the higher voltages of the operating window, the drops tend to eject in sequences with a long interval between ejection sequences. The meniscus oscillates between the ejection sequences at the capillary-viscous resonance frequency. At low applied frequencies, drop ejection occurs due to viscous pinch-off by a tip streaming mechanism, as illustrated in FIG. 6. As the applied frequency is increased beyond a frequency associated with the viscous-capillary pinch-off frequency of the drop, inertial effects dominate to pull out a long slender microjet, at the tip of which the drop detaches, as shown in FIG. 7.

Several experiments have been conducted with a number of liquids with different relative dielectric constants. Suitable liquids include dielectric liquids, electrolytes, methanol, ethanol, dichloromethane, acetone or mixtures thereof. The operating voltage window for methanol is lower than that of ethanol by a factor of 2 while there is an insignificant difference among the operating windows of ethanol, dichloromethane and acetone. An ethanol-water mixture of up to 50 percent by weight ethanol produces approximately the same voltage window as pure ethanol. Moreover, changing the

ethanol electrolyte composition and conductivity by six orders of magnitude via addition of hydrochloric acid does not significantly change the voltage window or the ejection frequencies. Furthermore, when the water/dielectric liquid volume ratio exceeds about one, the spraying ceases, or at least diminishes to an insignificant amount. This may be attributed to the high ionization potential of water, which does not allow a gas phase ionization reaction to occur. Low volatility of the aqueous solution and high surface tension may also play a role.

As depicted in FIG. 8, the drop ejection window is shifted downward thereby lowering the critical onset voltage for drop ejection when air is replaced by inert gases such as argon, helium or neon as the ambient medium. These gases catalyze the ionization of gas which, in turn, results in greater polarization at the meniscus interface for a given voltage, thus enabling drops to be pulled out from the meniscus and pinched-off with greater force.

The production of micron-sized electro-neutral drops using embodiments of the present invention provides a design for a portable respiratory drug delivery device that may be administered directly by electrospraying of drug compounds such as asthmatic steroids (beclomethasone dipropionate), insulin or exogenous lung surfactant (Surfactant Replacement Therapy) to treat asthmatic and diabetic patients, and, neonates suffering from Respiratory Distress Syndrome (RDS). When conventional inhalation devices are used, only small fractions of the drug reach the lower airways; most of the drug is deposited in the mouth or throat, and subsequently absorbed in the gastrointestinal tract. Direct local administration to target organs such as a lung provides an immediate effect, thus requiring lower drug quantities compared to oral delivery.

The present invention has several advantages over DC electrosprays. The electro-neutral drops of the present invention do not have to be neutralized before administration to the patient. Moreover, prior research has indicated that uniform distributions of droplets 2.8  $\mu\text{m}$  in size results in optimum dose efficiency, see J. C. Ijsebaert, K. B. Geerse, J. C. M. Marijnissen, J. W. J. Lammers and P. Zanen, *J. Appl. Physiol.*, 91, 2735, 2001; and A. Gomez, *Resp. Care*, 47, 1419, 2002, the entire contents and disclosures of which are hereby incorporated by reference. The micron-sized drops obtained using the AC electrosprays in accordance with the present invention therefore present a distinct advantage to the nanodrops obtained using DC electrosprays. One other distinct advantage of the electro-neutral drops obtained using AC electrospraying in accordance with the present invention is that the low power requirement reduces power consumption, increases safety, and presents potential for the device to be miniaturized to dimensions commensurate with portability.

Thus, according to an embodiment of the present invention, there is provided a method of producing liquid aerosol drops, the method comprising providing one or more micro-needles; introducing a fluid into the one or more micro-needles; providing one or more conducting elements in electrical communication with the one or more micro-needles; introducing an alternating current electric field with a frequency greater than approximately 10 kHz across the one or more micro-needles and the one or more conducting elements to induce the ejection of liquid aerosol drops from the one or more micro-needles.

The present invention may also be used as a microencapsulation technique to encapsulate drugs, DNA, proteins, osteogenic or dermatological growth factors, bacteria, viruses, fluorescent particles and immobilized enzyme receptors for controlled release drug delivery, bone or tissue engi-

neering, storage of positive controls in clinical or environmental field tests or biosensors for clinical diagnostics and environmental, water or illicit drug monitoring.

A microencapsulation technique of the present invention involves spraying a microemulsion consisting of a material to be encapsulated dissolved in water within a continuous phase of organic solvent (e.g., dichloromethane, a dichloromethane/ethanol mixture, a dichloromethane/butanol mixture, etc.) in which a biocompatible and biodegradable polymeric excipient (e.g., poly-glycolic-acid, poly-lactic-acid, poly-L-lactic-acid and poly-lactic-acid-glycolic-acid) is dissolved. The solvent evaporates as the spray drops release into the atmosphere, leaving a polymer shell in which the drug is encapsulated.

Thus, according to an embodiment of the present invention, there is provided a method of microsphere encapsulation, comprising providing one or more micro-needles; introducing a fluid into the one or more micro-needles, wherein the fluid comprises a biodegradable material, a solvent and a material to be encapsulated; providing one or more conducting elements in electrical communication with the one or more micro-needles; and introducing an alternating current electric field with a frequency greater than approximately 10 kHz across the one or more micro-needles and the one or more conducting elements to induce the ejection of microspheres from the one or more micro-needles, wherein the microspheres contain the encapsulated material and the microspheres are encapsulated with the biodegradable material.

A similar technique used for microencapsulation may be used to synthesize bio-fibers for tissue and bone engineering. Composite fibers with diameters between approximately 100 nm and approximately 100  $\mu\text{m}$ , as shown in FIG. 9A, or a mesh network of single strand fibers with diameters between approximately 1 nm and approximately 100  $\mu\text{m}$  with adjustable pore sizes between approximately 10 nm and approximately 1 cm, as shown in FIG. 9B, may be produced. These may be used as surgical threads, medical gauze or bioscaffolds for bone or tissue engineering.

The synthesis of fibers described above with the microencapsulation techniques of the present invention allows the encapsulation of dermatological or osteogenic growth factors for bone or tissue engineering as well as antibodies or coloring agents for clothing to be encapsulated within the fiber.

Thus, according to an embodiment of the present invention, there is provided a method of fiber synthesis comprising providing one or more micro-needles; introducing a fluid into the one or more micro-needles, wherein the fluid comprises a biodegradable material and a solvent; providing one or more conducting elements in electrical communication with the one or more micro-needles; and introducing an alternating current electric field with a frequency greater than approximately 10 kHz across the one or more micro-needles and the one or more conducting elements to induce the ejection of fibers from the one or more micro-needles, wherein the fibers comprise the ejected biodegradable material.

All documents, patents, journal articles and other materials cited in the present application are hereby incorporated by reference. Although the present invention has been fully described in conjunction with several embodiments thereof with reference to the accompanying drawings, it is to be understood that various changes and modifications may be apparent to those skilled in the art. Such changes and modifications are to be understood as included within the scope of the present invention as defined by the appended claims, unless they depart therefrom.



What is claimed is:

1. An electrospray device comprising:  
one or more micro-needles providing a passageway for transmission of a fluid, each of said micro-needles having a micro-needle tip;  
one or more conducting elements in electrical communication with said one or more micro-needles; and  
a source for generating an alternating current electric field with a frequency above 10 kHz across said one or more micro-needles and said one or more conducting elements, wherein the electric field pulls out a liquid meniscus at each micro-needle tip to thereby form liquid aerosol drops from said one or more micro-needles.
2. The electrospray device of claim 1, further comprising an external pump connected to said one or more micro-needles, wherein, when in operation, the fluid flows through said one or more micro-needles by a pressure-gradient imposed by said external pump.
3. The electrospray device of claim 1, wherein said one or more micro-needles has a channel diameter of between approximately 100 nm and approximately 1 cm.
4. The electrospray device of claim 1, wherein said one or more micro-needles comprises a metal hub syringe.
5. The electrospray device of claim 1, wherein said one or more micro-needles comprises a metal hub syringe tip.
6. The electrospray device of claim 1, wherein said one or more micro-needles is exposed.
7. The electrospray device of claim 1, wherein said one or more micro-needles is insulated.
8. The electrospray device of claim 1, wherein said one or more micro-needles is partially insulated.
9. The electrospray device of claim 1, wherein said one or more micro-needles is mounted horizontally, vertically, or at any angle with respect to the horizontal plane.
10. The electrospray device of claim 1, wherein said one or more conducting elements is located between approximately 1 mm and approximately 25 mm from each said micro-needle tip.
11. The electrospray device of claim 1, wherein said one or more conducting elements comprises a flat strip or a ring.
12. The electrospray device of claim 1, wherein said alternating current electric field source is capable of operating at frequencies between 10 kHz and 10 MHz.
13. The electrospray device of claim 1, wherein said alternating current electric field is capable of operating at voltages between 100 V and 50,000 V.
14. A method of producing liquid aerosol drops, said method comprising:  
providing one or more micro-needles;  
introducing a fluid into said one or more micro-needles;  
providing one or more conducting elements in electrical communication with said one or more micro-needles;  
introducing an alternating current electric field with a frequency greater than approximately 10 kHz across said one or more micro-needles and said one or more conducting elements to induce the ejection of liquid aerosol drops from said one or more micro-needles.
15. The method of claim 14, wherein said liquid aerosol drops are electro-neutral.

16. The method of claim 14, wherein said liquid aerosol drops are between approximately 1 nm and approximately 1000  $\mu$ m in diameter.
17. The method of claim 14, wherein said fluid comprises a dielectric liquid or a mixture of dielectric liquids.
18. The method of claim 17, wherein said dielectric liquid comprises methanol.
19. The method of claim 17, wherein said dielectric liquid comprises ethanol.
20. The method of claim 17, wherein said dielectric liquid comprises ethanol and water.
21. The method of claim 17, wherein said dielectric liquid comprises dichloromethane.
22. The method of claim 17, wherein said dielectric liquid comprises acetone.
23. The method of claim 14, wherein said fluid comprises an electrolyte or a mixture of electrolytes.
24. The method of claim 14, wherein said fluid comprises a mixture of dielectric liquids and electrolytes.
25. The method of claim 14, wherein said fluid comprises a drug.
26. The method of claim 14, wherein said fluid comprises an asthmatic steroid.
27. The method of claim 14, wherein said fluid comprises insulin.
28. The method of claim 14, wherein said fluid comprises an exogenous lung surfactant.
29. The method of claim 14, wherein said method is conducted in a vacuum or a gaseous ambient medium.
30. The method of claim 29, wherein said ambient medium of operation comprises air.
31. The method of claim 29, wherein said ambient medium of operation comprises a vacuum.
32. The method of claim 29, wherein said ambient medium of operation comprises a trace gas.
33. The method of claim 29, wherein said ambient medium of operation comprises argon.
34. The method of claim 29, wherein said ambient medium of operation comprises helium.
35. The method of claim 29, wherein said ambient medium of operation comprises neon.
36. The method of claim 14, wherein said alternating current electric field is at a frequency of between approximately 10 kHz and approximately 10 MHz.
37. The method of claim 14, wherein said alternating current electric field is at a voltage of between approximately 100 V and approximately 25,000 V.
38. The method of claim 14, wherein each of said one or more micro-needles comprises a tip and said one or more conducting elements is placed between approximately 1 mm and approximately 25 mm from each said micro-needle tip.
39. The method of claim 14, wherein said fluid is moved through said one or more micro-needles by operation of gravity.
40. The method of claim 14, wherein said fluid is moved through said one or more micro-needles by operation of an external pump connected to said one or more micro-needles.
41. The method of claim 14, wherein said liquid aerosol drops are ejected intermittently.