



US 20150024152A1

(19) **United States**

(12) **Patent Application Publication**

Carr et al.

(10) **Pub. No.: US 2015/0024152 A1**

(43) **Pub. Date: Jan. 22, 2015**

(54) **METAL COMPONENTS WITH INERT VAPOR PHASE COATING ON INTERNAL SURFACES**

(71) Applicant: **Agilent Technologies, Inc.**, Loveland, CO (US)

(72) Inventors: **Elizabeth Carr**, Santa Clara, CA (US); **Karen L Seaward**, Santa Clara, CA (US); **Kevin P Killeen**, Santa Clara, CA (US)

(21) Appl. No.: **13/946,942**

(22) Filed: **Jul. 19, 2013**

Publication Classification

(51) **Int. Cl.**

C23C 16/24 (2006.01)
C23C 16/40 (2006.01)
B01D 15/22 (2006.01)
C23C 16/44 (2006.01)

(52) **U.S. Cl.**

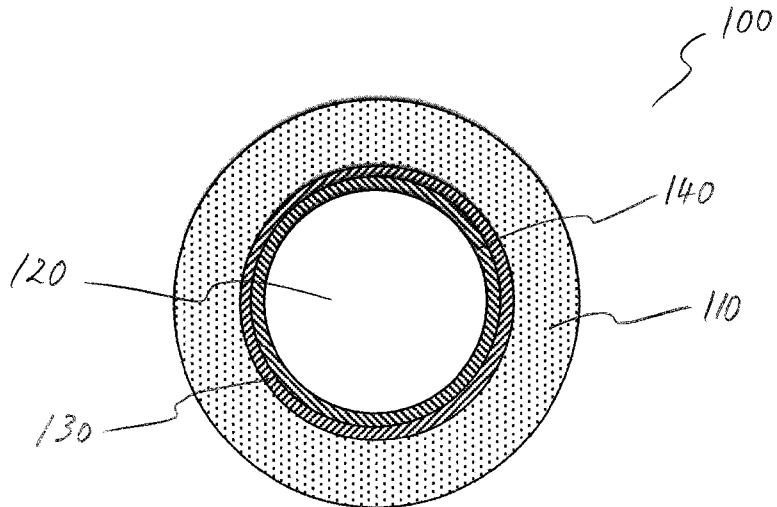
CPC **C23C 16/24** (2013.01); **C23C 16/44** (2013.01); **C23C 16/405** (2013.01); **C23C 16/403** (2013.01); **B01D 15/22** (2013.01)

USPC **428/34.1**; 427/237

(57)

ABSTRACT

The invention provides metal liquid chromatography components with uniformly coated internal surfaces and methods for achieving the same. The invention addresses the problem of corrosion or interference of metal components in the flow path for LC analyses in which the sample interacts with metal ions or surfaces. The invention also alleviates the difficulties in coating very long metal tubes and very small metal channels with an inert, continuous coating that adheres well to metal surfaces. The metal flow path is rendered inert by the coating, and thus compatible with bioanalytical separations, for example, by using a vapor phase deposition process to coat the inner surfaces with a coating that continuously covers all metal surfaces in the flow path.



Schematic illustration of an exemplary embodiment of the invention with dual layers of coatings

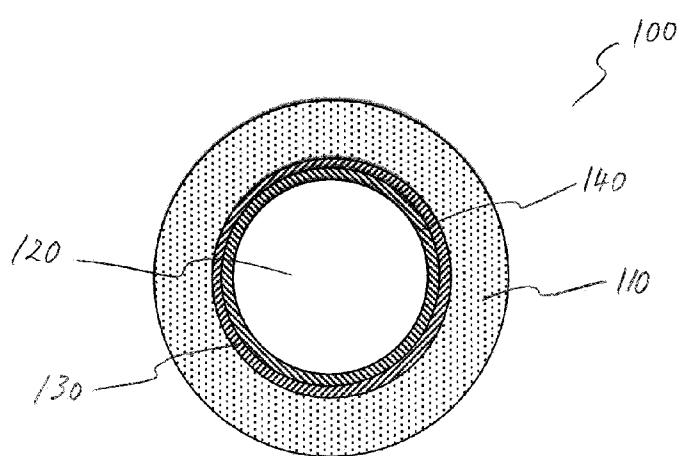


FIG. 1. Schematic illustration of an exemplary embodiment of the invention with dual layers of coatings

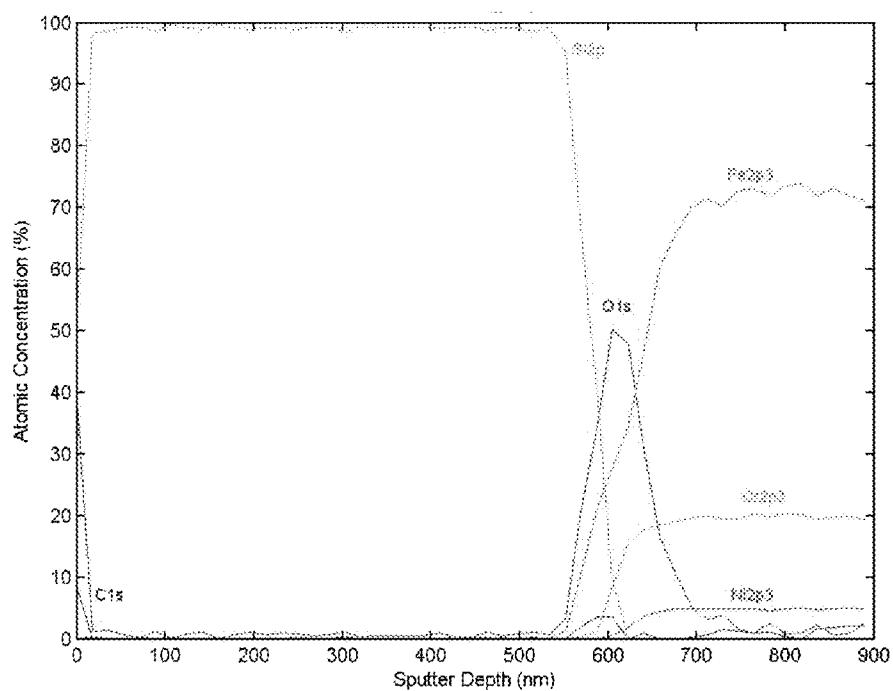


FIG. 2. X-ray Photoelectron Spectroscopy compositional depth profile of a-Si coating on stainless steel.

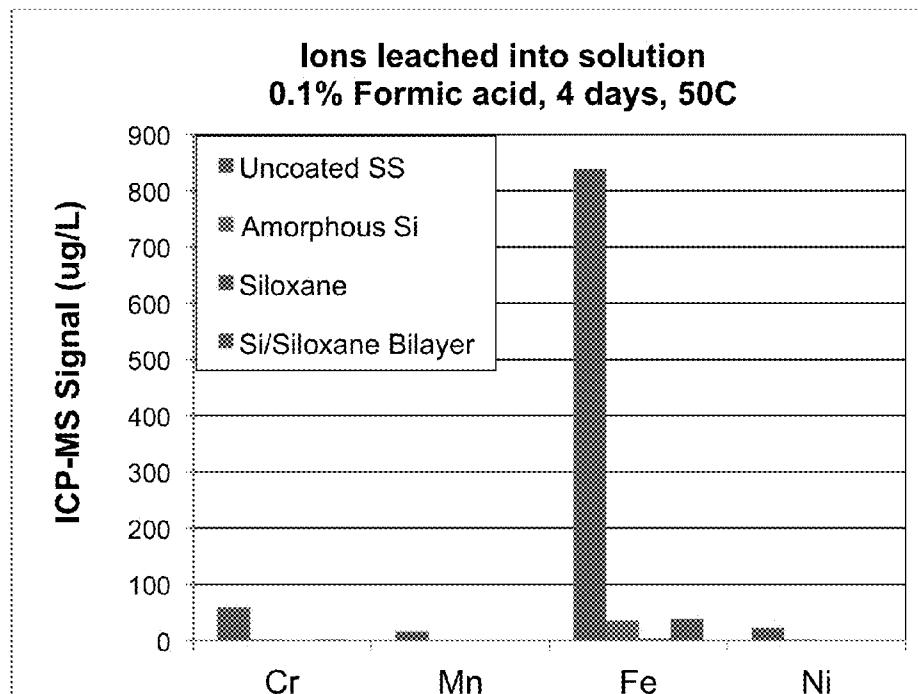


FIG. 3. Comparison of ions leached into solution from 2x3 cm stainless steel coupons coated with a-Si, siloxane, and Si/Siloxane bilayer compared to ions leached from uncoated stainless steel. Coupons were soaked in 0.1% formic acid at 50C for four days. Metal ion concentration in solution measured by Inductively Coupled Plasma-Mass Spectrometry.

METAL COMPONENTS WITH INERT VAPOR PHASE COATING ON INTERNAL SURFACES

FIELD OF THE INVENTION

[0001] The invention generally relates to coated metal components and related methods. More particularly, the invention relates to metal liquid chromatography components with uniformly coated internal surfaces and methods for achieving the same.

BACKGROUND OF THE INVENTION

[0002] Liquid chromatography (LC) is a chromatographic technique used to separate a mixture of compounds with the purpose of identifying, quantifying or purifying the individual components of the mixture. This separation occurs based on the interactions of the sample with the mobile and stationary phases. There are many stationary/mobile phase combinations that can be employed when separating a mixture. Liquid-solid column chromatography, the most popular chromatography technique, features a liquid mobile phase that slowly filters down through the solid stationary phase, bringing the separated components with it.

[0003] LC uses many metal components for transport of liquid. Examples include pump components, autosampler needles, and separation columns. Many samples analyzed by LC have no interaction with metal, but some samples, particularly those in bio-analytical applications, are sensitive to leached metal ions and/or are prone to interaction with metal surfaces giving rise to interference with the analytical process or impurities in the isolated components.

[0004] A conventional solution has been to use inert materials, such as polyether ether ketone (PEEK), for the flow path for these applications. In addition to being expensive, PEEK is difficult to form into many required shapes and sizes of LC components, and not readily available in all forms that are desired. Additionally, PEEK is not as strong as metal mechanically and is therefore unable to withstand the pressures (typically above about 400 bar) that are used for ultra-high pressure LC (UHPLC). Other existing approaches include inserting a biocompatible, polymeric inner tube inside a metallic outer tube and coating the metal tubing with liquid-phase organic layers. (U.S. Pat. Nos. 5,482,628; 5,651,885; 5,736,036; U.S. Patent Application Nos. 20050255579; 20110259089.) Another approach is to use a glass tube inserted into a jacket made of metal or plastic, which has limited applications to LC components. (U.S. Pat. No. 4,968,421.)

[0005] Conventional approaches and existing alternative designs have exhibited the disadvantages of not adhering well to the metal surfaces being protected, not being able to coat uniformly down long lengths of small tubing, and not being able to coat small channels (e.g., 5-10 μm diameter).

[0006] Thus, there remains an unmet need for metal liquid chromatography components with continuous and uniformly coated internal surfaces and efficient methods for achieving the same.

SUMMARY OF THE INVENTION

[0007] The invention is based in part on the unique method for controlled and uniform coating of metal components having lengthy, narrow and/or constricted interior surfaces. The invention effectively addresses the problem of corrosion or interference of metal components in the flow path for LC

analyses in which the sample interacts with metal ions or surfaces. The invention also alleviates the difficulties in coating very long metal tubes and very small metal channels with an inert, continuous coating that adheres well to metal surfaces. The metal flow path is rendered inert by the coating, and thus compatible with bioanalytical separations, for example, by using a vapor phase deposition process to coat the inner surfaces with a coating that continuously covers all metal surfaces in the flow path.

[0008] In one aspect, the invention generally relates to a metallic component having a lumen, passageway or cavity having an interior surface continuously covered with a protective coating having a substantially uniform thickness. The protective coating is formed via a vapor phase process that includes: providing one or more molecular precursors in the gas phase; exposing an interior surface of the lumen, passageway or cavity to the one or more molecular precursors in the gas phase; allowing the one or more molecular precursors to react, decompose, condense or otherwise change at or near the exposed interior surface and subsequently depositing thereon; and flushing with an inert gas or creating a vacuum thus removing unreacted one or more molecular precursors and reaction byproducts, if any.

[0009] In another aspect, the invention generally relates to a method for coating an interior surface of a metallic object having a lumen, passageway or cavity. The method includes forming a continuous protective coating having a substantially uniform thickness by a vapor-phase process.

[0010] In yet another aspect, the invention generally relates to a metallic object having an interior surface coated with a protective coating according to a method disclosed herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] FIG. 1 shows a schematic illustration of an embodiment of the invention.

[0012] FIG. 2 shows exemplary data of X-ray Photoelectron Spectroscopy compositional depth profile of a-Si coating on stainless steel.

[0013] FIG. 3 shows exemplary data on comparison of ions leached into solution from 2x3 cm stainless steel coupons coated with a-Si, siloxane, and Si/Siloxane bilayer compared to ions leached from uncoated stainless steel.

DEFINITIONS

[0014] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs.

[0015] As used herein, the term "coating" and "coated" refer to a separate and distinct layer of material from an underlying material. A coated material exhibits an identifiable boundary, e.g. diffuse or abrupt, between the coating material and the underlying material, e.g. support material.

[0016] As used herein, the term "substantially uniform thickness" refers to a coating over a substrate that has a thickness across the entire coating area that is greater than a minimum thickness. As used herein, the minimum thickness refers to a coating having about 1 nm, about 5 nm, about 10 nm, about 50 nm, about 100 nm or more thickness.

[0017] As used herein, the term "fluid" refers to a liquid capable of flowing (e.g., through a flow channel) having at

least one cross-sectional dimension less than 1 mm. For purposes of this disclosure, the term "fluid" does not encompass gasses.

[0018] As used herein, the term "microfluidic device" refers to a single unit that has a microfluidic reactor, microfluidic flow channels, and/or valves. Microfluidic devices may also have other microfluidic components, such as pumps, columns, mixers, and the like.

[0019] As used herein, the term "chemical vapor deposition" refers to a chemical process used to produce thin films or coatings. In a typical chemical vapor deposition (CVD) process, the substrate is exposed to one or more volatile precursors, which react, decompose, condense or otherwise change on or near the substrate surface to produce the desired deposit. Frequently, volatile by-products are also produced, which are removed by gas flow or vacuum through the reaction chamber. The materials to be deposited may take in various forms, including: monocrystalline, polycrystalline, amorphous, and epitaxial. In a typical CVD process, the substrate is heated to an elevated temperature, which can be important in allowing the precursors to react on the surface. In certain CVD processes, however, the deposition may be performed at room temperature. For example, certain atomic layer deposition (ALD) processes can be performed at ambient temperature.

[0020] CVD techniques include: atmospheric pressure CVD (APCVD)—CVD process at atmospheric pressure; low-pressure CVD (LPCVD)—CVD process at sub-atmospheric pressures (reduced pressures tend to reduce unwanted gas-phase reactions and improve film uniformity across the substrate); Ultrahigh vacuum CVD (UHVCVD)—CVD process at very low pressure, for example, below 10^{-6} Pa ($\sim 10^{-8}$ torr).

[0021] As used herein, the term "molecular precursor" refers to molecules in the gas phase that include one or more of the elements desired to be in the coating. These precursors can undergo a chemical or physical change such that the desired elements can be deposited on the surface and be incorporated in the coating. The molecular precursors can be inorganic or organic compounds. For example, the inorganic molecular precursors can include metal-based materials that would result in protective coating on the surface wherein the protective coating is selected from Si-based, Ti-based, Zr-based or Al-based inorganic compounds (e.g., oxides, nitrides or oxynitrides). The inorganic molecular precursors could also include, for example, H_2O for producing oxides, or NH_3 for producing nitrides. For example, the organic molecular precursors can include polymeric materials that can result in Si-based polymeric materials as protective coating on the surface. The molecular precursors can also include metallo-organic materials, for example, tri-methyl aluminum, to provide means for including a metal, in this example, aluminum, into the coating. Many other possibilities for precursors exist and are evident in the literature, and precursors yet to be developed could also fall under the scope of this invention.

[0022] As used herein, the term "atomic layer deposition" or "ALD" refers to a type of thermal CVD in which layer-by-layer control of deposition of thin films is achieved using sequential, self-limiting surface reactions. The two half-reactions associated with a two precursor deposition are separated in time, and the reactor is purged with inert gas or evacuated to ensure physical separation of the precursors. Each half-reaction is self-limiting, leading to highly conformal and controllable deposition on structures of complex topography and high aspect ratio.

DETAILED DESCRIPTION OF THE INVENTION

[0023] The invention provides a unique method for achieving continuous and uniform interior coating of metal components with lengthy, narrow and constricted interior surfaces. Very long metal tubes with small metal channels can be coated with a continuous and uniform coating, such as an inert or protective coating. These components can be current parts, such as the metal tubes and fittings for separation columns, needles autosamplers, pumps, or microfluidic parts. The invention provides metal components that do not corrode or interfere with LC analyses and can be effectively used in the flow path for LC systems.

[0024] Vapor phase coating (e.g., CVD) of metal LC components for the flow path of LC system has several advantages over previous techniques that utilize non-metal components or non-coated metal parts. The coated metal is inert and does not interfere with LC analyses yet is strong enough to withstand pressures over 1,000 bar, making it compatible with conditions required in UHPLC analyses. Fabrication of parts is done in metal, rather than substrate such as PEEK-based materials, so a much greater variety of components are available for fabrication, including metal microfluidic parts and porous sintered metal fits. Vapor phase coating is preferable to liquid-phase coating because it is better able to coat long, narrow channels (e.g., less than 10 μm in diameter) and provide strong adhesion to metal.

[0025] The LC components may be fabricated from various metals as required (e.g., stainless steel, titanium or other metals or alloys). Although amorphous Si is effective in protecting metal surfaces exposed to gases or vacuum (U.S. Pat. Nos. 6,444,326; 6,511,760; 7,070,833), amorphous Si is subject to attack at high pH in liquid. Amorphous Si is thus not ideal to provide inertness in LC applications requiring high pH. As disclosed herein, thermal CVD for the deposition of inert coatings is now successfully extended to materials that are stable in both high and low pH solutions, high salt solutions, and a large variety of solvents. In addition, the coating is resistant to adhesion of biomolecules to the coating surface. The coating method according to the disclosed invention is able to coat long columns of metal LC components with small inner diameters with a coating that is continuous and adheres well to the metal column.

[0026] In one aspect, the invention generally relates to a metallic component having a lumen, passageway or cavity having an interior surface continuously covered with a protective coating having a substantially uniform thickness. The protective coating is formed via a vapor phase process that includes: providing one or more molecular precursors in the gas phase; exposing an interior surface of the lumen, passageway or cavity to the one or more molecular precursors in the gas phase; allowing the one or more molecular precursors to react, decompose, condense or otherwise change at or near the exposed interior surface and subsequently depositing thereon; and flushing with an inert gas or creating a vacuum thus removing unreacted one or more molecular precursors and reaction byproducts, if any.

[0027] In certain embodiments, the vapor phase process further includes: repeating one or more of the above steps as necessary to arrive at a desired film thickness and/or composition.

[0028] In another aspect, the invention generally relates to a method for coating an interior surface of a metallic object having a lumen, passageway or cavity. The method includes

forming a continuous protective coating having a substantially uniform thickness by a vapor-phase process.

[0029] In certain preferred embodiments, the vapor phase process comprises a chemical vapor deposition process.

[0030] In certain preferred embodiments, the vapor phase process includes an atomic layer deposition process.

[0031] In certain embodiments, the lumen, passageway or cavity is characterized by at least one dimension of less than about 10 mm and one dimension longer than about 20 mm. In certain embodiments, the metallic component is a chromatographic column characterized by an inner diameter of less than about 10 mm (e.g., less than about 5 mm, 3 mm, 1 mm, 500 μ m, 300 μ m, 100 μ m, 50 μ m, 30 μ m, 10 μ m, 5 μ m) and a length greater than about 20 mm (e.g., greater than about 30 mm, 50 mm, 100 mm, 500 mm, 1,000 mm, 5,000 mm).

[0032] In certain embodiments, the protective coating has a substantially uniform thickness in the range of about 10 nm to about 5 μ m (e.g., about 10 nm to about 500 nm, about 10 nm to about 300 nm, about 10 nm to about 200 nm, about 10 nm to about 100 nm, about 10 nm to about 80 nm, about 10 nm to about 50 nm, about 20 nm to about 800 nm, about 50 nm to about 800 nm, about 100 nm to about 800 nm, about 200 nm to about 800 nm, about 300 nm to about 800 nm, about 100 nm to about 500 nm, about 100 nm to about 300 nm, about 200 nm to about 500 nm).

[0033] In certain embodiments, the metallic component is a microfluidic device or a component thereof having at least one interior dimension less than about 1 mm (e.g., less than about 500 μ m, 300 μ m, 100 μ m, 50 μ m, 30 μ m, 10 μ m, 5 μ m).

[0034] In certain embodiments, the metallic component is a porous metal frit such as the kind used to hold in place the silica particles that are the solid stationary phase in a liquid chromatographic column. The coating covers surfaces that will be in contact with the liquid mobile phase and includes interior surfaces and/or exterior surfaces of the frit.

[0035] The protective coating may be any suitable material, for example, a material selected from Si-based, Ti-based, Zr-based or Al-based inorganic compounds (e.g., oxides, nitrides or oxynitrides). In certain embodiments for metal parts used in LC applications, the protective coating includes a material selected from SiO_2 , SiC , Si_3N_4 , SiO_xC_y , SiO_xN_y , SiC_xH_y , Al_2O_3 , TiO_2 , ZrO_2 , Y_2O_3 and mixtures thereof.

[0036] The coating can also be multilayered (2, 3, 4 or more layers each comprising a different protective material). For example, an initial coating may be a Si coating layer for good adhesion to the metal, followed by a coating of SiC for chemical inertness. FIG. 1 is a schematic illustration of a cross-section of a column 100 with a metallic tubing 110, a passageway 120, and two coated layers on the inside surface, 130 and 140.

[0037] The metallic component may be made of any suitable material, for example, stainless steel, titanium, or titanium alloy.

[0038] In yet another aspect, the invention generally relates to a metallic object having an interior surface coated with a protective coating according to a method disclosed herein.

EXAMPLES

[0039] Four bio-inert coatings were formed and tested on stainless steel and titanium parts.

Example 1

Amorphous Si Coating

[0040] The first coating, an amorphous Si coating, was deposited on stainless steel coupons, frits and HPLC columns, and on titanium coupons. Deposition was done by thermal chemical vapor deposition in a closed reactor using SiH_4 gas as a molecular precursor. Temperature for deposition was between 350° C. and 450° C. and partial pressure of SiH_4 in the reactor was between 50-1000 mbar in dry nitrogen gas. Two depositions were done in succession to achieve a coating thickness of 550 nm on coupons and 100 nm in the interior of the HPLC column. Coating thickness on the coupons was measured using spectral reflectance and verified by X-ray Photoelectron Spectroscopy. Coating thickness on the column interior was estimated from the relative intensities of the

[0041] Fe K series and Si K series lines from Energy Dispersive X-ray Spectroscopy, compared to relative intensities on flat surfaces with known a-Si thickness. Thickness of the coating on titanium coupons, deposited in a separate run, was 200 nm.

[0042] Effectiveness of the coatings for providing bio-inertness was evaluated by soaking the parts in 0.1% formic acid for a period of days and measuring the metal ions released into solution using Inductively Coupled Plasma-Mass Spectrometry. Both coated stainless steel coupons and coated stainless steel frits provided greater than 10 \times reduction in metal ion concentration compared to similar uncoated parts.

[0043] FIG. 2 shows X-ray Photoelectron Spectroscopy compositional depth profile of a-Si coating on stainless steel.

Example 2

Polymeric Siloxane Coating

[0044] The second coating, a polymeric siloxane coating, was deposited using chemical vapor deposition at a temperature between 350° C. and 450° C. Coating thicknesses of 100 nm to 300 nm were achieved on stainless steel coupons, stainless steel frits, and on the interior surface of HPLC columns. All parts demonstrated greater than 10 \times reduction in metal ion concentration released into solution when soaked in 0.1% formic acid. In addition, a siloxane coated HPLC column was packed with silica beads held in place by two siloxane-coated frits. This column showed superior performance to a stainless steel column with stainless steel frits in a liquid chromatography separation of Cytochrome C, an enzyme known to be sensitive to metal ions.

Example 3

Bilayer Coating (Si/Siloxane)

[0045] The third coating was a bilayer consisting of 200 nm of a-Si directly on the stainless steel, covered by 150 nm of siloxane coating on the a-Si. This coating was deposited by the above described chemical vapor deposition processes on stainless steel coupons. These coupons demonstrated 10X reduction in metal ion concentration after soaking in 0.1% formic acid. A similar bilayer was also deposited on the interior surface of an HPLC column and demonstrated a superior liquid chromatography separation of Cytochrome C compared to a stainless steel column.

[0046] FIG. 3 shows comparison of ions leached into solution from 2×3 cm stainless steel coupons coated with a-Si, siloxane, and Si/Siloxane bilayer compared to ions leached from uncoated stainless steel. Coupons were soaked in 0.1% formic acid at 50C for four days. Metal ion concentration in solution measured by Inductively Coupled Plasma-Mass Spectrometry.

Example 4

Bilayer Coating (Al₂O₃/TiO₂)

[0047] The fourth coating was a bilayer of Al₂O₃ underneath TiO₂, deposited by atomic layer deposition. This Al₂O₃/TiO₂ bilayer was deposited on stainless steel coupons and fits, and on the interior and exterior surfaces of 100 mm long capillaries with inner diameters of 100 µm and 250 µm. The coating was deposited with 100 cycles of alternating exposures of trimethyl aluminum and water at 200C, followed by 827 cycles of alternating exposure of Tetrakis(dimethylamido)titanium(IV) and water at 200° C. Final thickness of the layers were approximately 7 nm of Al₂O₃ and 40 nm of TiO₂.

INCORPORATION BY REFERENCE

[0048] References and citations to other documents, such as patents, patent applications, patent publications, journals, books, papers, web contents, have been made in this disclosure. All such documents are hereby incorporated herein by reference in their entirety for all purposes. Any material, or portion thereof, that is said to be incorporated by reference herein, but which conflicts with existing definitions, statements, or other disclosure material explicitly set forth herein is only incorporated to the extent that no conflict arises between that incorporated material and the present disclosure material. In the event of a conflict, the conflict is to be resolved in favor of the present disclosure as the preferred disclosure.

EQUIVALENTS

[0049] The representative examples disclosed herein are intended to help illustrate the invention, and are not intended to, nor should they be construed to, limit the scope of the invention. Indeed, various modifications of the invention and many further embodiments thereof, in addition to those shown and described herein, will become apparent to those skilled in the art from the full contents of this document, including the examples which follow and the references to the scientific and patent literature cited herein. The following examples contain important additional information, exemplification and guidance that can be adapted to the practice of this invention in its various embodiments and equivalents thereof.

What is claimed is:

1. A metallic component having a lumen, passageway or cavity having an interior surface continuously covered with a protective coating having a substantially uniform thickness, wherein the protective coating is formed via a vapor phase process comprising:

providing one or more molecular precursors in the gas phase;

exposing an interior surface of the lumen, passageway or cavity to the one or more molecular precursors in the gas phase;

allowing the one or more molecular precursors to react, decompose or otherwise change at or near the exposed interior surface and subsequently depositing thereon; and

flushing with an inert gas thus removing unreacted one or more molecular precursors and reaction byproducts, if any.

2. The metallic component of claim 1, wherein the vapor phase process further comprises:

repeating one of more of the above steps as necessary to arrive at an desired film thickness and/or composition.

3. The metallic component of claim 1, wherein the lumen, passageway or cavity is characterized by at least one dimension of less than about 10 mm and one dimension longer than about 20 mm.

4. The metallic component of claim 3, being a chromatographic column characterized by an inner diameter of less than about 10 mm and a length greater than about 20 mm.

5. The metallic component of claim 4, wherein the protective coating has a substantially uniform thickness of about 10 nm to about 5 µm.

6. The metallic component of claim 1, being a microfluidic device or a component thereof having at least one interior dimension less than about 1 mm.

7. The metallic component of claim 1, wherein the protective coating comprises a material selected from Si-based, Ti-based, Zr-based or Al-based inorganic compounds.

8. The metallic component of claim 7, wherein the protective coating comprises a material selected from SiO₂, SiC, Si₃N₄, SiO_xC_y (wherein 2x+4y=4), SiO_mN_n, (wherein 2m+3n=4), SiC_xH_y (wherein 4x+y=4), TiO₂, ZrO₂, Al₂O₃ and mixtures thereof

9. The metallic component of claim 1, wherein the protective coating comprises two or more layers each comprising a different protective material.

10. The metallic component of claim 1, wherein the metallic component is made of stainless steel, titanium, or titanium alloy.

11. A method for coating an interior surface of a metallic object having a lumen, passageway or cavity, comprising forming a continuous protective coating having a substantially uniform thickness by a vapor-phase process.

12. The method of claim 11, wherein the vapor-phase process comprises chemical vapor deposition.

13. The method of claim 11, wherein the vapor-phase process comprises atomic layer deposition.

14. The method of claim 11, being a chromatographic column characterized by an inner diameter of less than about 10 and a length greater than about 20 mm.

15. The method of claim 13, wherein the protective coating has a substantially uniform thickness of about 10 nm to about 5 µm.

16. The method of claim 11, being a microfluidic device or a component thereof having at least one interior dimension less than about 1 mm.

17. The method of claim 11, wherein the protective coating comprises a material selected from Si-based, Ti-based, Zr-based or Al-based inorganic compounds.

18. The method of claim 17, wherein the protective coating comprises a material selected from SiO₂, SiC, SiC_xH_y, Si₃N₄, TiO₂, ZrO₂ or Al₂O₃ and mixtures thereof.

19. The method of claim 17, wherein the protective coating comprises two or more layers each comprising a different protective material.

20. The method of claim 11, wherein the metallic component is made of stainless steel, titanium, or titanium alloy.