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**FILTERS WITH PICOMETER-LEVEL SENSITIVITY INCORPORATING
COAXIALLY STACKED MACROCYCLES EMBEDDED IN SOLID FILLER
MATERIAL, AND METHODS OF MANUFACTURE OF SAME**

RELATED APPLICATIONS

This application claims priority to U. S. Provisional Patent Application No. 63/592,646, filed October 24, 2023, entitled "Methods for Modifying Surface Properties
5 and for Constructing Membranous Materials," the contents of which are hereby incorporated by reference as if fully set forth herein.

TECHNOLOGICAL FIELD

The present disclosure relates to the fields of supramolecular chemistry,
10 composite materials, and filtration, and more specifically, but not exclusively, to the construction of highly sensitive filters through the formation of a substantially perpendicular array of channels formed of tubular structures comprising coaxial stacks of macrocycles, embedded within a solid material deposited between such tubular structures on a porous substrate.

15 **BACKGROUND OF THE INVENTION**

The energy, transportation, food, agriculture, semiconductor, plastics and other industrial sectors are crucially dependent on small molecules. The production of some small molecules, O₂ from the air for example, is solely a separation process. The production of other small molecules requires a chemical reaction plus a separation process
20 in most of the cases. Small molecules could generally be separated utilizing only three methodologies: distillation, sorption and membrane-based filtration.

Distillation separates mixtures to their components utilizing temperature changes, where some of the components of the mixture change their state of matter. It is energy intensive. Some important mixtures such as the air are still distilled to obtain high purities
25 of the air's components (by first liquefying the air to -200°C).

Using chemical sorption for separating mixtures in high purities requires forming chemical bonds between a sorbent and a component, and breaking that bond later for regenerating the sorbent. This process is thus energy-intensive as well.

Filtration is the technique of separating two or more substances in a mixture by passing the mixture through a medium that permits some of the substances therethrough while preventing passage of other substances. Filtration theoretically possesses the ability to perform separations under low energy consumption and simple equipment to obtain high purities of the components. Filtration is a common and well-understood process for relatively large molecules. However, filtration of extremely small molecules, such as those with diameter three nanometers or smaller, poses unique challenges.

One common technology for filtration of very small molecules is reverse osmosis. Reverse osmosis utilizes industrial membranes that are composed from a continuous polymeric layer on top of an intermediate layer of a polymer that is on top of a fabric used as mechanical support. *See* [1]. Familiar examples include layers of polyamides and polycellulose-acetates, on top of an intermediate polysulfone, on top of polyester fabric. The selectivity of these membranes is due to the different miscibility of the materials. For illustration, even if one material is 20 times more permeable than another material through a membrane, such a difference is utilized to pass a mixture of these materials through a series of such membranes to obtain purer material.

A porous material may serve as another type of filter. Generally, the passage of a material through a layer with precise pores requires less energy than passage through a polymeric layer, because the passage is not performed via miscibility and dissolution but rather by passage through voids. For filtration of extremely small molecules, a membrane may be designed, in theory, having a pore size which is small enough to distinguish between different pico-scale and angstrom-scale molecules. For example, methane has a kinetic diameter of 3.8 Angstroms, and carbon dioxide has a kinetic diameter of 3.3 Angstroms. Filtration of these two gases from each other would proceed if they were exposed to a membrane having a pore size that precisely tailored within the 0.5 Angstrom size difference between them.

Various attempts have been made to manufacture such filtering membranes, but they all have been hindered by the technical limitations. Typically, periodic three-dimensional materials such as Zeolites, Metal-Organic Frameworks (MOF) and Covalent Organic Frameworks (COF) have been considered as porous membranes. However, fabricating continuous thin uniform membranes from the mentioned 3D materials in industrial scale is challenging.

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Some current research focuses on incorporating nanocrystals of such 3D materials inside a thin polymeric membrane as Mixed Matrix Membranes (MMM), also referred to as Thin Film Nanocomposites (TFN). An example is disclosed in [2], in which the researchers utilized a MOF membrane of ZIF-8, which has an outstanding permeability but low selectivity due to pores of 3.4 Angstroms that is exactly between the diameters of methane and carbon dioxide. However, even this membrane had a major drawback, due to the presence of two kinds of pores in ZIF-8 – the mentioned 3.4 Angstroms and another one that is over a nanometer. Most 3D periodic porous materials contain pores that are too large to exclude on the basis of size, as typical pore diameters are 5 Angstroms. Even if a 3D material contains pores in a diameter that could exclude by size, a mixture of the 3D material may have larger pores in other orientations of its crystal structure, and controlling the orientation of nanocrystals within a polymer layer is difficult.

An alternative to 3D periodic materials as membranes are 2D periodic materials. [3] discloses a DFT simulation, which showed that a periodic 2D 'Graphene like' membrane of 2D polyphenylene freestanding sheet could possess unprecedented selectivity. The simulation showed that the 2D sheet could be 10^{23} more selective to H_2 over CO_2 , CO , and CH_4 compared to traditional silica and carbon membranes. However, this was just a simulation; there is still no known method to fabricate such a membrane or any other 2D freestanding sheet with precise pores without defects.

Due to the extreme difficulty of manufacturing a freestanding periodic 2D sheet, some current research focuses on freestanding porous graphene/graphene-oxide, which are 2D materials, but are not periodic, and moreover do not have precise uniform pores. One of the best publications in the field is [4] which is claimed to be the first fabrication of defect-free porous graphene on top of porous tungsten as the mechanical support. However, a population of pores was obtained with diameters ranging from 0.6 to 1.2 nanometers. Their membrane was 25 more times permeable to H_2 than to CH_4 , which is not even near the selectivity of the 2D polyphenylene materials discussed above.

Recently, [5] disclosed a system and method of molecular sieving using aligned macrocycle pores. Macrocycles were selectively functionalized and aligned at liquid-liquid interfaces to create well-defined, ordered pores across an ultrathin nanofilm. The size of the pores was tailored to about an angstrom precision by varying the macrocycle identity, and the narrowest pore diameter obtained was 4 Angstroms, which is still larger

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than many important small molecules. The macrocycles were used to filter between cannabidiol oil (width 0.65 nm) and chlorophyll (width 1.17 nm). However, these films are produced in a liquid-liquid interface – they performed cross-linking and obtained a covalent organic framework (COF)-like material. The liquid-liquid interface may limit the ability to create high surface area versions. [6] disclosed formation of pore channels consisting of alpha-cyclodextrin housed within nanochannels of a covalent organic framework (COF), in a host-guest inclusion complex. The pore channels were capable of separating hydrogen from carbon dioxide and methane only to a low selectivity, since both gases could pass through the center of the cyclodextrin. Unlike [5], [6] could not provide passage only via the macrocycles.

A rotaxane is a supramolecular structure comprised of a template molecule threaded within an internal cavity of a macrocycle. A polyrotaxane is a rotaxane in which more than one macrocycle is threaded around a template molecule. Extensive research has been performed regarding formation of rotaxanes and polyrotaxanes of cyclodextrin. Examples may be found in [7] and [8].

References

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SUMMARY OF THE INVENTION

The present disclosure introduces solid, 3D apparatuses for filtration of molecules ranging from a few angstroms to a few nanometers in diameter, in which the deltas between diameters of the molecules being separated may be sub-angstrom or even picometer level in resolution. The apparatuses consist of the following components: a porous substrate; aligned tubular structures formed within the substrate, wherein each tubular structure comprises a coaxial stack of macrocycles arranged cylindrically, and has an opening that is sized according to the desired size and composition of the pore; and a filler material deposited between the tubular structures and configured to embed at least a portion of the sides of the tubular structures.

In preferred embodiments, the tubular structures are asymmetric over their heights. At a base portion of the tubular structures, the structures may be comparatively wider. At a tip portion of the tubular structures, the structures are comparatively narrower, to thereby permit only select molecules to enter the structures.

The apparatuses described herein have various advantages over known filters. First, the size of the opening of each pore may be tailored, as desired, to be larger than the size of the molecule/s that is/are desired to be filtered while narrower than the molecule/s that is/are desired to be excluded. The opening may comprise a tip molecule that is bonded to the top of the stack of macrocycles.

Second, because the macrocycle is embedded in a skin that is attached to a porous substrate, and because the macrocycles are arranged in three-dimensional stacks, the apparatuses are solid. The apparatuses are stable in response to movement, heat, and chemical stimuli.

The manufacture of the apparatuses described herein requires overcoming numerous technical challenges. These include:

- Preparing a Substrate for Attachment of Tubular Structures. In preferred embodiments, the tubular structures are built directly on a solid substrate. This solid

substrate is typically not capable of direct attachment of organic material thereto. Accordingly, it is necessary to prepare the substrate by filling its pores with a sacrificial material, such as gold, and associating the tubular structures to the sacrificial material. Optionally, a template molecule may be attached to the sacrificial material, around which the tubular structures are arranged. The gaps between the tubular structures are then filled. The sacrificial material is then removed to complete the apparatuses, to thereby generate a pore.

- Building the Tubular Structures. The tubular structures may be formed at least partially in solution, and then are subsequently associated to the substrate. The macrocycle stacks may be built in different ways, depending on where in the tubular structures they are to be situated. The macrocycle stacks may also be formed entirely on the substrate.
- Filling in Gaps Between Tubular Structures in the Array to Thereby Form a Tight Seal. Using techniques such as Atomic Layer Deposition (ALD) and molecular layer deposition (MLD), the gaps between macrocycle stacks are filled sufficiently to ensure that no space remains large enough for a larger molecule to enter via the side of the macrocycle stack, and/or via the ALD layer itself. It is necessary to perform this process while ensuring, on the one hand, that no gaps remain between the tubular structures and the filler material, and, on the other hand, that the filler material does not bury the tubular structures.
- Filling in Spaces Between Adjacent Macrocycles Within a Stack. Inevitably, the macrocycle stacks include vertical gaps, which may exceed the desired sensitivity of the filter. At lower portions of the stacks, these gaps are covered by the filler material, and thus do not hinder the performance of the filters. The macrocycles at the top of the stack are bonded together at multiple locations, optionally before they are placed on the stack, thereby reducing the size of the gap to below the required tolerance.
- Forming the Opening at the Top of the Macrocycle Stack. Typically, the macrocycles themselves have internal cavities that are too wide for effective filtration. Thus, it is necessary to narrow the gaps of the opening. This may be accomplished by bonding a tip or “endcap” molecule to the top of the macrocycle stack. Methods of bonding such endcap molecules will be described herein. Alternatively, a bulky stopper may be associated with the opening which allows

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only narrow molecules to access the gap between the bulky stopper and macrocycle tubular structure.

In total, the present disclosure incorporates numerous novel techniques, which, when combined, achieve the desired outcome of a solid, stable, filter array with picometer-level
5 sensitivity.

According to a first aspect, a filter configured to allow communication of substances from one side to another side, and configured to separate substances passing therethrough, is disclosed. The filter includes a mechanically stable porous substrate; and a solid material in contact with the porous substrate, the solid material defining a skin
10 having at least one channel, each channel having at least one entrance at a surface of the skin and at least one exit at a pore of the porous substrate. The entrance of each channel has a diameter which is 3 nm or less. The terms “entrance” and “exit” are to be understood as referring to

Optionally, the at least one channel is comprised of the solid material, without any
15 additional material encased therein. In such embodiments, macrocycles that had been used to build the channels are removed from the final product.

Optionally, the at least one channel is comprised of the solid material, with one or more tubular structures comprised of macrocycles overlaid on the solid material. In these embodiments, the tubular structures are attached to the tops of the solid material, but are
20 not necessarily

Optionally, the at least one channel is comprised of one or more tubular structures comprised of macrocycles that are at least partially embedded within the solid material. In this embodiment, the tubular structures that are used in the construction of the channel are preserved in the final product. Each tubular structure may include a stack of
25 macrocycles having a first internal diameter which are coaxially associated. The macrocycles may be comprised of cyclodextrins, calixarenes, pillararenes, porphyrins, crown ethers, helical molecules, cubril[n]s, cucubriturils, aspherands, kekulenes, cage molecules, metallic macrocycles, carbon nanotubes, or any combination thereof. In particularly advantageous embodiments, the macrocycles may be alpha-, beta-, or
30 gamma-cyclodextrins.

The macrocycles may have a substantially frustum-like shape, as is typical for cyclodextrins and other macrocycles described above. A molecular orientation of

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adjacent macrocycles may include one or more of: wide-wide associations, narrow-narrow associations, and wide-narrow associations.

Each macrocycle in the stack may be bound to one or more adjacent macrocycles in the stack with the filler material.

5 Each macrocycle in the stack may be linked to adjacent macrocycles in the stack with one or more molecular bridges.

Optionally, a top portion of each channel comprises an asymmetric tubular structure. The asymmetric tubular structure includes at least one molecule having a second internal diameter which is narrower than the first internal diameter. The molecule
10 having a second internal diameter is at a tip of the asymmetric tubular structure, such that the tip comprises an entrance of the channel. In some such embodiments, the skin extends to above a height of the tip molecule but does not encase the entrance of the channel. Alternatively, the at least one molecule having a second internal diameter is within the asymmetric tubular structure but not at a tip thereof, such that the asymmetric tubular
15 structure has an hourglass-like configuration. One example of the molecule having a second molecular diameter is a crown ether.

Optionally, the filter includes at least one stopper molecule and elongated molecule attached to the at least one stopper and inserted within a top of an uppermost tubular structure in the channel. A gap between the stopper molecule, elongated molecule,
20 and the top of the uppermost tubular structure is a second internal diameter, wherein the second internal diameter is narrower than the first internal diameter and comprises an entrance to the channel.

In another embodiment, the filter includes a stopper molecule and elongated molecule attached to the at least one stopper and inserted within a top of an uppermost
25 tubular structure in the channel. A passage between adjacent macrocycles at an outer shell of the at least one tubular structure defines a second internal diameter. The second internal diameter is narrower than the first internal diameter and comprises an entrance to the channel.

In another embodiment, the entrance of at least one channel is blocked due to at
30 least one of the following: a stopper molecule and elongated molecule attached to the at least one stopper and inserted within a top of an uppermost tubular structure in the channel; an elongated molecule attached to the solid material and inserted within a top of an uppermost tubular structure in the channel; and deposition of solid material in a manner

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that buries the top of an uppermost tubular structure in the channel. A passage between adjacent macrocycles at an outer shell of the at least one tubular structure defines a second internal diameter, wherein the second internal diameter is narrower than the first internal diameter and comprises an entrance to the channel. In this embodiment, the entrance to the channel is from the side of the channel rather than from the top of the channel.

Optionally, the filter includes at least one elongated molecule inserted with a top of an uppermost tubular structure in the channel and chemically associated to the uppermost tubular structure in the channel or to the solid material, such that the uppermost tubular structure and at least one elongated molecule define a second internal diameter, wherein the second internal diameter is narrower than the first internal diameter and comprises an entrance to the channel.

Optionally, the skin encases a lower portion of the at least one tubular structure and does not encase an upper portion of the at least one tubular structure. The lower portion of the at least one tubular structure comprises macrocycles that are associated with each other in a manner that preserves gaps that are greater than a size of an entrance to the channel. The upper portion of each tubular structure comprises macrocycles that are associated with each other in a manner that reduces gaps between adjacent macrocycles to below the size of the entrance to the channel. Advantageously, the associations with more chemical bonds, which are more challenging to form, are required only for those portions of the channels which are not embedded in the solid material and are thus exposed.

Optionally, the solid material embeds the at least one tubular structure without being adhered thereto in a chemical link. Optionally, the solid material is adhered to the at least one tubular structure with at least one chemical link. This choice is determined, *inter alia*, by the materials from which the tubular structures are formed, and the manner in which the solid material is deposited (e.g., ALD or MLD).

The at least one tubular structure may further comprise one or more anti-sticking functional groups on an exterior face thereof. The anti-sticking functional groups may help prevent sticking of the tubular structures to the surface of the substrate during the patterning process.

In some embodiments, the at least one channel extends from the entrance thereof to the exit thereof at a pore of the porous substrate, in a substantially uniform width. In some embodiments, the at least one channel comprises a narrower portion adjacent to the

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pore of the porous substrate. For example, the channel may be built over a narrow “pit” that had been previously been formed with the solid material on the porous substrate.

The substrate may be an anodic aluminum oxide (AAO).

At least a portion of the solid material may be deposited via atomic layer deposition. In such embodiments, the material deposited via atomic layer deposition is one or more of titanium dioxide, silicon dioxide, aluminum oxide, or silicon nitride. At least a portion of the solid material may also, or alternatively, be deposited via molecular layer deposition.

A diameter of the entrance may be between 2.5 and 4.5 angstroms. Advantageously, 4.5 angstroms is the internal diameter of alpha-cyclodextrin. The internal diameter may be calibrated to even narrower than that based on the use of the tip molecules, template molecules, and/or bulky stoppers in the entrance, as discussed. The 2.5 - 4.5 angstrom minimum diameter is sufficient to filter gases and other small molecules which have diameters in that range.

According to a second aspect, a method of manufacturing a filter is disclosed. The method includes: building at least one tubular structure over at least one pore of a porous substrate that is filled with a sacrificial pore-filling material, each tubular structure comprised of a coaxial stack of associated macrocycles; filling gaps between tubular structures with a solid gap-filling material; and removing the sacrificial pore-filling material from the pores of the porous substrate; to thereby generate at least one channel in which the solid material defines a skin, an entrance of each channel is at a surface of the skin and an exit of each channel is at a pore of the porous substrate. The entrance of each channel has a diameter which is 3 nanometers or less.

Optionally, the method may include, prior to the building step, filling the pores of the porous substrate with the pore-filling sacrificial material. Prior to the step of filling the pores, the method may include layering a sacrificial layering material over the porous substrate, wherein the sacrificial layering material is configured to form associations with both the sacrificial pore-filling material and with the porous substrate. In such embodiments, the step of filling pores comprises adhering the pore-filling material to the sacrificial layering material. The method further includes, following the step of filling pores, selectively etching the sacrificial layering material to thereby leave the porous substrate with pores filled with the pore-filling material. These steps are used to render

the porous substrate capable of forming chemical associations with the organic material of the tubular structures.

Optionally, the porous substrate is a high surface area ceramic material. Optionally, the porous substrate is anodized aluminum oxide, the sacrificial pore-filling material is gold, and the sacrificial layering material is silver.

In alternative embodiments, the method includes, prior to the building step, selecting a substrate of a sacrificial material; depositing a porous layer on the sacrificial substrate; and filling pores of the porous layer with the pore-filling sacrificial material, to thereby adhere the pore-filling material to the sacrificial layering material, and selectively etching the sacrificial substrate. The porous substrate may be a high surface area material, or a ceramic.

Optionally, each tubular structure comprises a stack of macrocycles having a first internal diameter which are coaxially associated. Without limitation, the macrocycles may be comprised of cyclodextrins, calixarenes, pillararenes, porphyrins, crown ethers, helical molecules, cubril[n]s, cucubriturils, aspherands, kekulenes, cage molecules, metallic macrocycles, carbon nanotubes, or any combination thereof.

The macrocycles may have a substantially frustum-like shape. A molecular orientation of adjacent macrocycles comprises one or more of: wide-wide associations, narrow-narrow associations, and wide-narrow associations.

The building step may include: patterning a template molecule on the sacrificial pore-filling material; and threading at least a portion of at least one tubular structure around the template molecule. The step of patterning a template molecule may include: attaching a precursor molecule to the sacrificial pore-filling material, the precursor molecule formed of an X-Y-Z structure, wherein the Z functional group is configured to bond with the pore-filling material, and the X-Y bond is cleavable; and cleaving the X-Y bond. The template molecule may be itself the remaining Z-Y structure. Alternatively, the following cleaving of the X-Y bond, the template molecule may be bonded to the Y group. Optionally, X is any type of branched polymer. The branched polymer may be useful, at this early stage of the patterning process, to help ensure that the template molecules are patterned with sufficient separation, so that there is proper spacing between adjacent tubular structures.

The method may further include forming at least one molecular bridge between coaxial and vicinal tubular structures while the tubular structures are threaded on the

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template molecule. Optionally, this molecular bridge is performed by attaching a bulky stopper to the template molecule, to thereby form a rotaxane or polyrotaxane; forming the at least one molecular bridge when the bulky stopper is attached to the template molecule; and removing the bulky stopper and template molecule. The threading step may be performed when the tubular structures and porous substrates are immersed in solution, and optionally by ultrasonication or heating the solution. In advantageous embodiments, the solution is a dilute solution, as this leads to a higher yield, although a saturated solution may also be used.

When a template molecule is used, following the step of filling gaps, the template molecule may be removed.

Optionally, following the step of filling gaps, the template molecule may be lengthened. The method then includes threading at least one additional macrocycle or tubular structure onto the lengthened template molecule, to thereby lengthen the channel. The step of lengthening the template molecule may be performed with click chemistry.

Optionally, a template molecule attached to a bulky stopper may be threaded into an entrance of each channel, to thereby define a passage into each channel based on dimensions of the entrance, of the bulky stopper, and of a portion of the template molecule near the entrance of each channel.

Optionally, the method may include forming the tubular structures prior to the building step by forming molecular bridges between macrocycles in solution. Advantageously, the available chemical methods available for building molecular bridges in solution may be more varied and versatile than those available for building on the porous substrates. In such embodiments, the step of building the tubular structures comprises introducing macrocycles into a solution containing template molecules, to thereby thread the macrocycles around the template molecules. The method may further include ultrasonication of the solution. The solution is advantageously a saturated solution, which generates higher yields, but may also be a dilute solution.

In embodiments in which the associations are formed in solution, the step of forming molecular bridges may include: modifying at least one functional group of each macrocycle; and forming one molecular bridge between adjacent macrocycles by associating the macrocycles at the modified functional groups, to thereby generate a train of macrocycles. The train is a versatile structure that may form the basis for additional chemical reactions. For example, the method may further include: threading the train of

macrocycles on a template molecule having a bulky stopper removably attached at one end; attaching a bulky stopper to a second end of the template molecule; forming at least a second molecular bridge between adjacent macrocycles, to thereby generate a ladder of macrocycles; cleaving the removable bulky stopper from the template molecule; and removing the template molecule from the ladder of macrocycles.

The bridges may be formed in sequential reactions, in which each sequential reaction increases a proximity of different portions of the macrocycles to each other, thereby enabling the subsequent reactions. This may be analogized to closing of a zipper, in which initiating the closing process makes the rest of the closing easier.

The method may further include forming the bridges with at least one branched bridge using a linker molecule that forms connections between adjacent macrocycles at two or more locations. Additional functional groups may be added onto the linker molecule, following attachment of the linker molecule to the adjacent macrocycles, and additional bridges may be added between the adjacent macrocycles with the additional functional groups. In this manner, the branched bridge may grow, potentially indefinitely, to form more bridges between the adjacent macrocycles.

Optionally, the tubular structures formed in solution are asymmetric tubular structures, said asymmetric tubular structures comprising of a coaxial stack of associated macrocycles having a substantially identical internal diameter, and a molecule having a second internal diameter, said second internal diameter being narrower than the first internal diameter of the macrocycles of the coaxial stack. In such embodiments, the bridges between macrocycles that are adjacent to the tip molecule reduce a gap between said macrocycles to less than the second internal diameter. The second internal diameter may be between 2.5 and 4.5 angstroms.

The method may further include lengthening an asymmetric tubular structure in solution by associating the asymmetric tubular structure with a symmetric tubular structure. Optionally, the lengthening step comprises forming a semirotaxane including a template molecule inserted into both the symmetric tubular structure and the asymmetric tubular structure, associating the asymmetric and symmetric tubular structures, and removing the template molecule.

The method may further include, prior to the building step, modifying the tubular structures with anti-sticking functional groups on an outer shell thereof.

The method may further include, prior to the building step, modifying the tubular structures with branched polymers, to thereby promote spacing and perpendicularity of the tubular structures in relation to the substrate, and, prior to the filling step, if said branched polymers do not form chemical connections with the filler material, removing
5 said branched polymers.

The building step comprises may include patterning the at least one tubular structure directly onto the at least one pore, without first patterning a template molecule onto the pore and without patterning the tubular structures on the template molecule. In such scenarios, the patterning step may include patterning tubular structures having
10 contained therein at least one template molecule that is associated to at least one bulky stopper. The template molecule may thus be included without being bonded to the pores, and may be utilized for lengthening the channel, or for narrowing the channel, for example. Optionally, the at least one bulky stopper is chemically linked to the at least one tubular structure.

15 In some embodiments, the filling step comprises performing atomic layer deposition (ALD). In some such embodiments, the solid gap-filling material is one or more of titanium dioxide, silicon dioxide, aluminum oxide or silicon nitride. The method may further include, prior to the ALD, attaching precursor molecules to the tubular structures, such that the gap-filling material is directly linked to the tubular structures.
20 The method may further include, prior to the ALD, attaching protecting groups to the tubular structures, such that the gap-filling material does not adhere to at least some parts of the tubular structures. Optionally, the method may include, during the ALD process, using scavengers or etchants to regenerate functionalities found at the outer shell of the tubular structures in a super cycle process. In addition or in alternative to ALD, the filling
25 step may comprise performing molecular layer deposition.

The method may further include sequentially lengthening the tubular structures after the filling step, and repeating the filling step with respect to the lengthened tubular structures. Advantageously, this repetitive process may be used to lengthen the tubular structures to a sufficient height, in the nanometer range, without requiring all of the
30 deposition of the solid material to be performed at once.

Optionally, after the step of filling gaps, the method includes decomposing the tubular structures, to thereby, following the step of removing the sacrificial pore-filling material, obtain channels having a skin formed solely of the solid material.

According to a third aspect, a method of manufacturing a filter is disclosed. The method includes: selecting a sacrificial substrate, said sacrificial substrate capable of attachment to organic compounds; attaching a template molecule to the sacrificial substrate; building at least one channel onto the sacrificial substrate, each channel
5 comprised of one or more tubular structures comprised of a coaxial stack of associated macrocycles; filling gaps between the tubular structures by adhering a solid gap-filling material to the sacrificial substrate; attaching a porous substrate to one of the open ends of the tubular structures or the filler material; and removing the sacrificial substrate and template molecule. Optionally, the method further includes lengthening the channels by
10 attaching additional tubular structures to the ends of the channels that had previously been associated with the sacrificial substrate.

According to a fourth aspect, a method of forming a tubular structure comprised of macrocycles connected by molecular bridges in solution is disclosed. The method includes modifying at least one functional group of two or more macrocycles; and forming
15 one molecular bridge between said macrocycles by associating the macrocycles at the modified functional groups, to thereby generate a train of macrocycles. Optionally, the method further includes threading the train of macrocycles on a template molecule having a bulky stopper removably attached at one end; attaching a bulky stopper to a second end of the template molecule; forming at least a second molecular bridge between adjacent
20 macrocycles, to thereby generate a ladder of macrocycles; cleaving the removable bulky stopper from the template molecule; and removing the template molecule from the ladder of macrocycles. The bridges may be formed in sequential reactions, in which each sequential reaction increases a proximity of different portions of the macrocycles to each other, thereby enabling the subsequent reactions. The bridges may be formed with at least
25 one branched bridge using a linker molecule that forms connections between adjacent macrocycles at two or more locations. Optionally, the tubular structures formed in solution are asymmetric tubular structures, said asymmetric tubular structures comprising of a coaxial stack of associated macrocycles having a substantially identical internal diameter, and a molecule having a second internal diameter, said second internal diameter
30 being narrower than the first internal diameter of the macrocycles of the coaxial stack. In such embodiments, the asymmetric tubular structures may be lengthened in solution by associating the asymmetric tubular structure with a symmetric tubular structure. The lengthening step may include forming a semirotaxane including a template molecule

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inserted into both the symmetric tubular structure and the asymmetric tubular structure, associating the asymmetric and symmetric tubular structures, and removing the template molecule.

According to a sixth aspect, a method of filtering a mixture of two or more substances is disclosed. The method includes: exposing the mixture of substances through any filter described above, wherein at least one of the substances is smaller sized, such that it is configured to pass through the channel, and at least a second of the substances is larger sized, such that it is unable to pass through the channel; and passing at least one molecule of the at least one smaller sized substance through the filter. The substances may be, for example, two liquids or two gases, or a liquid undergoing desalination.

Optionally, the mixture is under a chemical equilibrium. Filtering one of the substances thereby shifts the equilibrium, causing a reaction to proceed.

Optionally, the mixture is in contact with a catalyst. Filtering one of the substances towards the catalyst causes a chemical reaction to proceed.

BRIEF DESCRIPTION OF THE DRAWINGS

In order to better understand the subject matter that is disclosed herein and to exemplify how it may be carried out in practice, embodiments will now be described, by way of non-limiting example only, with reference to the accompanying drawings, in which:

FIGS. 1A-1H illustrate a process of building tubular structures on a substrate, according to embodiments of the present disclosure;

FIGS. 2A-2D illustrate a process of building tubular structures and attaching the tubular structures to a substrate, according to embodiments of the present disclosure;

FIGS. 3A and 3B illustrate schematically the processes of FIGS. 1A-1H and 2A-2D, respectively;

FIG. 4A illustrates a cross section of a channel including tubular structure having a tip molecule chemically bonded to the opening of the tubular structure, according to embodiments of the present disclosure;

FIG. 4B illustrates a variant of the channel of FIG. 4A, in which the channel includes a pattern of repeating tubular structures;

FIG. 4C illustrates a cross-section of a tubular structure having a bulky stopper filling the opening of the tubular structure;

FIG. 4D illustrates a cross-section of a tubular structure in which the solid material rises above the tip molecule;

FIGS. 4E-4J illustrate small macrocyclic molecules that illustrate picometer-level sensitivity between derivatives of the same macrocycle;

5 FIGS. 5A-5S illustrate processes of building tubular structures in solution;

FIGS. 6A-6E illustrate a process of building a tubular structure on a substrate and forming cross-links between adjacent tubular structures;

FIGS. 7A-7B illustrates schematically a process of directly attaching a tubular structure to a surface of a substrate;

10 FIGS. 8A-8I illustrate processes for lengthening tubular structures while the tubular structures are attached to the porous substrates;

FIGS. 9A-9L illustrate experimental results of a gap-filling process, according to embodiments of the present disclosure.

15 FIGS. 10A-10E illustrate steps in manufacturing, sealing, and filling pits, according to embodiments of the present disclosure;

FIGS. 10F-10I illustrate steps in building structures on pitted substrates, according to embodiments of the present disclosure; and

FIG. 11 depicts local gap filling, according to embodiments of the present disclosure.

20 **DETAILED DESCRIPTION OF EMBODIMENTS**

The present disclosure relates to the fields of supramolecular chemistry, composite materials, and filtration, and more specifically, but not exclusively, to the construction of highly sensitive filters through the formation of a substantially perpendicular array of tubular structures comprising macrocycles, embedded within a solid material deposited between such tubular structures on a porous substrate.

25 Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not necessarily limited in its application to the details of construction and the arrangement of the components and/or methods set forth in the following description and/or illustrated in the drawings and/or the Examples. The invention is capable of other embodiments or of being practiced or carried out in various ways.

As described in the present disclosure, the term “rotaxane” refers to a supramolecular structure in which a cyclic molecule is threaded onto an “axle” molecule and end-capped by bulky groups at the terminal of the “axle” molecule. The term “end-cap” is to be understood in its broadest sense, to cover any type of material that retains the threaded molecules in place, such as a molecular material or a surface. The term “poly-rotaxane” refers to a structure in which multiple cyclic molecules are threaded onto the axle molecule in a chain. The terms “pseudo-rotaxane” and “pseudo-poly-rotaxane” refer to a situation in which the axle is not end-capped, but the cyclic molecules remain on the axle in a thermodynamically preferred position. A semi-rotaxane is a supermolecular structure similar to a rotaxane, but in which only one end is capped. Likewise, a semi-poly-rotaxane is a tubular structure similar to a poly-rotaxane, but in which only one end is capped. An “inclusion complex” is a supramolecular complex in which at least one chemical compound (the “host” or “hosts”) has a cavity or cavities into which one or more guest compounds is accommodated, and in which the interactions between the hosts and the guests involves purely weak interactions.

As used in the present disclosure, the term “bulky stopper” refers to a molecule that is bonded to, or otherwise situated in, a rotaxane or inclusion complex, in a manner that prevents unthreading of the rotaxane or inclusion complex. The bulky stopper prevents macrocycles and multimers thereof that form the tubular structure from separating from the template molecule of the inclusion complex. The bulky stopper may also prevent any materials from entering the inclusion complex, depending on the dimensions of the macrocycle at the tip of the inclusion complex and the bulky stopper. One exemplary bulky stopper used in embodiments of the present disclosure is DNBS. The bulky stoppers may also include branched polymers, such as dendrons or dendrimers, appended thereto.

In general, the present disclosure uses three terms to refer to cylindrical structures – macrocycles, tubular structures, and channels. A “macrocycle” is a molecule including three or more atoms arranged in a ring structure. Examples of macrocycles include cyclodextrins, calixarenes, pillararenes, porphyrins, crown ethers, helical molecules, cubril[n]s, cucubriturils, aspherands, kekulenes, cage molecules, metallic macrocycles, and carbon nanotubes. A “tubular structure” is a molecule comprised of individual macrocycles arranged in a coaxial stack, in which adjacent macrocycles are bonded together with at least one molecular bridge. The term “tubular structure” may also be

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used, in certain examples herein, to describe individual macrocycles, or dimers or multimers thereof, that are associated in place in a fixed manner, for example by being embedded within a solid gap-filling material. A tubular structure may be “symmetric,” meaning that it has the same cross-section throughout its entire length, or “asymmetric,” meaning that it has at least one macrocycle which is narrower than the other macrocycles in the tubular structure. This narrower macrocycle may be a “tip” molecule of the tubular structure, or it may be internal to the tubular structure. The term “channel” refers to a complete passageway having an entrance and an exit. The channels may be formed of coaxial stacks of macrocycles or tubular structures passing from the entrance to a pore of a porous substrate, which serves as the exit. The channels may also be formed partly or exclusively of solid material, with the macrocycles or tubular structures around which they were constructed having been removed. The “channels” may be comprised of multiple tubular structures coaxially stacked one on top of the other, of which, in some embodiments, at least one is an asymmetric tubular structure.

Other relevant terms will be defined subsequently in the specification.

I. Overview

The present disclosure introduces novel membranes for filtration, with the ability to design the membranes with picometer-level sensitivity. In some embodiments, the membranes consist of channels made of tubular structures in which the tip of the uppermost tubular structure is modified, so that an opening is obtained with a particular diameter, subject to normal variations due to atomic vibrations. The gaps between the tubular structures are filled with solid material.

In addition, the present disclosure discloses methods of modification of surfaces in order to build up such channels on a substrate. The methods permit bottom-up construction of nanometric or sub-nanometric structures, with ordered pores, having sub-Angstrom-level precision.

The filters described herein are configured to allow communication of substances from one side to another side, and are configured to separate substances passing therethrough.

The filters are formed of channels, which are substantially perpendicularly oriented structures arranged, within a skin of solid material, on a surface. Typically, the surface is a porous substrate. The channels define an entrance at a surface of the skin and

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an exit at a pore of the porous substrate. The entrance has a diameter which is 3 nm or less, and, in particularly advantageous embodiments, between 2.5 and 4.5 angstroms.

Generally, the channels are formed by co-axially stacking macrocycles or tubular structures, and optionally adding an endcap, or a series of endcaps, to the top of the stack of macrocycles, or to the uppermost tubular structure. Each endcap, also described herein as a “tip” molecule, has an inner cavity of a diameter defining the diameter of the pore or feature and the ability of a material to be contained within the pores or permeate therethrough. Other manners of controlling the diameter of the tip will be described further herein.

Since different macrocycles and different endcap molecules have different inner cavity ‘textures’, an efficient size-dependent or functionality-dependent separation is enabled. Various molecules that otherwise would not have been separable, due to a great similarity in size or chemical or physical characteristics, are potentially separable.

Stacks of macrocycles, such as nanotubes, rotaxanes, poly-rotaxanes, helical molecules and others, and/or tubular structures formed of such macrocycles, provide elongated channels or features that are substantially parallel to each other and substantially perpendicularly oriented within the skin on a substrate surface region. These channels serve as means for patterning the substrate’s surface. Such channels can also be used as templates or structural precursors for constructing organic or inorganic or hybrid (organic/inorganic) membranes. The substrate may be further modified by various means, e.g., Atomic Layer Deposition (“ALD”), Molecular Layer Deposition (“MLD”) and other techniques and their combinations, to fill in gaps between the channels, to thereby incorporate/embed the channels in a bulk material (a “filler” material).

In subsequent steps, the membrane may be further modified to permit gaseous and/or liquid communication between its two ends. In one scenario, the initial substrate could be a composite material, e.g., a porous substrate, wherein its pores are filled with another sacrificial material to cause association with the tubular structures. The sacrificial material may be removed at a later stage. Alternatively, the deposition may take place on a sacrificial substrate. Following the formation of the membrane, porous layer(s) could be deposited on top of the active layer, to increase its mechanical stability, after which deposition the initial substrate may be removed.

A. Direct Manufacture on a Mechanically Stable Substrate

FIGS. 1A-1H illustrate a high-level overview of a first method of manufacture of a filter.

In FIG. 1A, a substrate 10 is provided. The substrate 10 is a generally porous, mechanically stable, solid material, such as a nanoporous anodized aluminum oxide (AAO), or a porous ceramic material. The substrate 10 has multiple pores 12.

At FIG. 1B, a layer 13, such as silver, is deposited onto the surface of the porous substrate 10. Layer 13 is also referred to herein as a “sacrificial layering material.” At FIG. 1C, a second pore-filling material 14, such as gold, is adhered to the sacrificial layering material 13, to thereby fill the pores 12 of the porous substrate. Material 14 is also referred to herein as a “sacrificial pore filling material.” The second material 14 is capable of forming associations with both the covering layer 13 and organic compounds. The organic compounds include, in particular, those that are incorporated in the tubular structures and channels. At FIG. 1D, the layering material 13 is removed, leaving the gold layer 14 in place within the pores 12.

At FIG. 1E, optionally, template molecules are attached to the gold layers within the pores 12. In alternative embodiments, template molecules are not used.

At FIG. 1F, coaxial stacks 16 of individual macrocycles or tubular structures containing such coaxial stacks are built on the substrate 10 through overlaying onto the template molecules. The uppermost tubular structures may have tip molecules 18 attached thereto.

At FIG. 1G, the gaps between the coaxial stacks 16 are filled with a solid material 19. Solid material 19 may also be referred to herein as a “gap filling material,” “gap filling layer,” or simply “filler.” The solid material 19 may be added, for example, with atomic layer deposition (ALD) or molecular layer deposition (MLD) or combinations thereof.

At FIG. 1H, the sacrificial pore-filling material 14 and template molecules 15 are removed, leaving the pores 12. The coaxial stacks are maintained in place. A through channel 20 is thus established, with a narrow opening at tip 18, constituting the entrance, and a wide outlet at pore 12, constituting the exit.

FIG. 3A is another schematic illustration of the process of FIGS. 1A-1H. Tubular structures 31 are built on a substrate, and gap-filing layer 32 is filled in between the tubular structures. The initial substrate includes porous layer 33 and secondary pore-filling material 30 that is removed selectively at the end of the process.

B. Manufacture of Tubular Structures on Temporary Substrates

FIGS. 2A-2D depict a high-level overview of a second method of manufacture of the filter array. In this method, instead of building the channels on the composite substrate, the channels are first built separately, and only afterwards the skin comprising the channels is attached to the substrate. At FIG. 2A, a sacrificial substrate 24 is provided. The substrate is made of a material capable of attachment to organic materials, such as gold. The substrate is sacrificial, to be used only during manufacture. Channels 22 made of tubular structures are constructed on the substrate. The channels 22 may be poly-rotaxanes, with an internal thread molecule 21 around which the tubular structures are threaded, and a bulky stopper 26 for keeping the tubular structures in place. At FIG. 2B, the gaps between the channels 22 are filled in with solid layer 25, such as with ALD or MLD. At FIG. 2C, the gold substrate layer 24 is removed. The device is flipped over. At FIG. 2D, a porous permanent substrate (such as an AAO or a porous ceramic) is attached to the filler material, thereby generating the channels. Variations in the order of these steps may be implemented, such as removing the gold layer as the final step.

FIG. 3B is another schematic representation of the process of FIGS. 2A-2D. In FIG. 3B, tubular structures 31 are added to sacrificial substrates 30. The gaps between the tubular structures are filled in with gap-filling layer 32. Then, porous layer 33 is deposited, followed by selective removal of the sacrificial substrate 30 (the device is flipped).

In this embodiment, the gap-filling layer, arranged as a skin, is attached to the porous support after being formed. In certain embodiments, the porous support is added by depositing or placing the porous layer on top of the device. The porous support layer could be chemically attached to the gap-filling-layer and/or the tubular structures. The porous support layer could be held by the accumulation of weak interactions (hydrogen bonds for example) to the gap filling layer. The gap-filling-layer could be trapped between two porous layers (with or without chemical bonds, with or without the accumulation weak interactions).

CVD and sol-gel techniques may be implemented in the deposition of the porous support. Another technique could be taking a powder of nanoparticles or nanoparticles immersed in a solution of an oxide and creating a porous layer from them on top of the gap-filling-layer (under moisture-free conditions). Transforming the powder or solution of nanoparticles into a porous support could be done by applying the following and/or

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their combinations: 1) Heat (can condense two M-OH into M-O-M); 2) Pressure; 3) Water steam; 4) ALD (this is done carefully in order to not bury the tubular structures).

In an alternative method, in order to create a porous support under destructive conditions for the tubular structures (high temperatures, for example) the following may take place: After the deposition of the gap-filling-layer (TiO₂ for example) immediately
5 in a following batch, or afterwards, another extra-sacrificial material (ZnO for example) could be deposited to cover the tubular structures. Afterwards the porous support could be deposited (porous TiO₂ or SiO₂ for example). Etchant/s (acid or base) could be used to remove selectively the extra-sacrificial material (ZnO), and if a very diluted (acid or
10 base) or small quantities of acid gases are used to remove the extra-sacrificial material (ZnO) then some of it may stay as an adhesive between the gap-filling-layer and the porous support.

C. Cross-Sectional Views of Embodiments of the Filters

15 FIG. 4A illustrates a cross-section of a filter 40 that may be manufactured according to the methods of the present disclosure. Filter 40 includes a mechanically stable solid, porous substrate 41. For example, the substrate 41 may be AAO. For purposes of illustration, only the top portion of the substrate 41 is illustrated, so that the substrate appears as being relatively thinner than the tubular structures and skin; in
20 actuality, the substrate is substantially thicker than the tubular structures and skin. This substrate has one or more pores 42. Channels 43 are located above pores 42. The channels 43 have a height of approximately a few nanometers to several tens of nanometers. Each channel 43 has an entrance at the top of the channel, and an exit at the pore. The channel 43 includes a series of macrocycles 44. Functionally, the "macrocycles" described herein
25 may also be tubular structures. At lower layers, the macrocycles are connected with a minimal number of bonds or bridges 45 sufficient to maintain structural integrity of the structure, e.g., one or two bonds. At these lower layers, the channels are surrounded by a filler material 48, such as a metal oxide (ceramic) deposited through ALD or an organic material deposited through MLD, and combinations thereof. At upper portions of the
30 channels 43, portions of the tubular structures are not embedded in filler material 48. In these locations, a denser ligature 46 made of multiple molecular bridges (e.g., more than two) is formed between adjacent macrocycles, to thereby block passage between said macrocycles. At the top of filter 40, a tip molecule 47 is attached to the tubular structure

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43. The tip molecule 47 has a diameter (a “second internal diameter”) which is narrower than the internal diameter of the rest of the macrocycles comprising the structure (the “first internal diameter”). The tip molecule may be selected to have a specific diameter, configured to permit the passage of selected molecules while excluding other molecules.

5 The second internal diameter may be 3 nm or less, or even as low as 2.5 to 4.5 angstroms.

The tip molecule may be attached to the uppermost tubular structure when said tubular structure is already built onto the channel. Alternatively, the uppermost tubular structure may be pre-formed with the tip molecule in solution.

In the illustrated embodiment, the tip molecule is at the entrance of the channel.

10 In alternative embodiments, the molecule with the second internal diameter may be located within the channel, so that the channel (and specifically the tubular structure that has the molecule with the second internal diameter) is shaped like an hourglass.

FIG. 4B illustrates a cross-section of a second embodiment of a filter 40. The filter 40 is constructed similarly to the filter of FIG. 4A, except that, in this case, the channel is constructed of a pattern of tubular structures that have different types of bridges between them. Specifically, some of the macrocycles 44 that are embedded within the filler material have the denser ligature 46 connecting between them. This configuration may be preferred if the tubular structures are formed in this manner in solution prior to building the channels on the substrate, as will be discussed further herein.

20 FIG. 4C illustrates a cross-section of a third embodiment of a structure that may be manufactured according to the teachings of the present disclosure. In this embodiment, a bulky stopper 49 with a long template molecule 50 fills the opening, permitting only molecules of certain sizes to penetrate the opening. In this embodiment, instead of a passage via the opening being formed at the top of the tubular structure, the passage is via the outer shell of the tubular structure.

In order to manufacture such a configuration, a polymeric template molecule that is bonded to a bulky stopper on one end may be associated to an open end of a channel. The bulky group may then be bonded to the top of the channel at certain locations thereon, while leaving an opening at the entrance of a desired size. Optionally, the bulky stopper 30 49 is anchored to the tubular structure with one or more bridges 51; these need not be present in all embodiments.

The formation of such a complex between a bulky stopper and a channel may be controlled through various mechanisms. In one example, the channels may be built with

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reactive functional groups (such as alcohols) at their tips. The channels may then be exposed to a surfactant molecule that contains a bulky stopper with functional groups (such as primary alkyl bromides) associated to a template molecule. The surfactants assemble into the openings of the channels. With or without drying, the alcohol or other
5 functional groups may be activated (for example, with a base) to chemically bond the bulky stopper to the opening of the channels. The process may be repeated in order to increase the yield of the reaction. The bulky stopper-template molecule combination may be selected to fill only a small portion of the volume of the channel.

Theoretically, a similar effect may be accomplished through the use of a surfactant
10 molecule containing a bulky stopper, which blocks the opening of the channel without being bonded thereto. In still another embodiment, the template molecule may be chemically associated with the channel in a manner that narrows the entrance of the channel, even without the bulky stopper.

Generally, a blockage may be placed at an entrance of each channel through one
15 of three manners: a bulky stopper and elongated molecule, as discussed; an elongated molecule attached to the solid material of the skin, and inserted within a top of an uppermost tubular structure in the channel, or deposition of solid material in a manner that buries the top of the uppermost tubular structure in the channel, followed by etching of the solid material to expose the outer shell of the tubular structure.

20 In still another embodiment (not illustrated), regardless of whether an end-cap or bulky stopper is utilized, the bottom of the channel may be filled with a valve. The valve is oriented between the porous support and lower part of the skin. The valve may block the flux from the side of the membrane with higher pressure, so the flux could form only through the outer shell of the tubular structures.

25 FIG. 4D illustrates still another embodiment, in which ALD or MLD may be used to block the opening of the channels. The ALD or MLD may be used in place of surfactants. In such embodiments, the ALD or MLD may even intentionally be laid to “bury” or embed the openings of the channels, and then selectively etched in order to expose an opening to the channel of a desired size.

30 In each of the depicted embodiments, the channels include tubular structures that are at least partially embedded therein. In other embodiments, this configuration is only an intermediate step, and, prior to completion of the channels, the tubular structures are

removed, thereby leaving channels of the solid material, without any additional material encased or embedded therein.

The filler material surrounding the tubular structure may be laid in different layers, each made of a different material. For example, one of the layers may be titanium dioxide (TiO₂) and a second layer may be silicon nitride (Si₃N₄). One of these layers may
5 be selectively etched with an etching solution, to expose tiny pores at the exterior of the shell of the tubular structures.

FIGS. 4E-4J illustrate examples of crown ethers, which illustrate how similar macrocycles may have very slight, even picometer-level, variation in their internal
10 diameters. These will be discussed further herein.

II. Selection and Preparation of the Substrate

A. The Substrates

In some embodiments according to the approach of FIGS. 1A-1H, and specifically
15 1A-1D, the substrate 83 is defined by arrays of pores, which may be presented at any density, may be random or ordered, may be uniform in their pore diameter or not. The substrate may have asymmetric pores or not. Notwithstanding any particular material or processing conditions, the pores may be of diameters as low as 1-5 nanometers or smaller and as high as 200 microns, or more.

The selection of the porous substrate depends, *inter alia*, on its ability to react
20 with precursors used in the process of filling the gaps between the tubular structures, on its mechanical stability, chemical stability, thermal stability and other considerations. Generally, the substrate must have suitable physical characteristics both to support the construction of the filters (the channels and the skin formed of the gap-filling layer) and
25 to provide mechanical support of the completed filters.

One particular example of a porous substrate is anodic aluminum oxide (AAO), whose pores are filled with material, for example gold or gold alloy. A porous substrate whose pores are filled may be referred to herein as a "composite substrate," and the gold alloy may be referred to as the "sacrificial pore-filling material." Other examples include
30 oxides and other ceramics, which had pores pierced inside of them using electron beams, ion beams, or other kinds of beams or techniques. Other such porous materials could be fabricated using sol-gel, plasma processes, CVD, PVD, plastic extrusion and others or any other method known in the art.

Innovative techniques for tuning parameters and characteristics of the composite layer will be described further herein. In some embodiments, depending on how the composite layer is generated, polishing and/or other means are utilized to expose the composite layer.

5 In some embodiments, the porous substrate is a plastic or polymer filled with gold or gold alloy. In some embodiments, gold or gold alloy nanoparticles are integrally embedded on the topmost surface of a porous material while the gaps between them are filled.

10 In some embodiments, the porous substrate is a layered material of two or more porous layers on top of each other, with no chemical bonds between them. In some embodiments the substrates have a high surface area, such as hollow fibers, stacked sheets and others.

15 In some embodiments a “linker” molecule or molecules could be associated to the surface of the porous substrate. The molecule is associated to the substrate using one of its parts while another part of such molecule will react with precursors used in the process of filling the gaps between the tubular structures, as will be discussed further herein. One example of a linker molecule is tri-ethoxy-silicon amine $(\text{CH}_3\text{CH}_2\text{O})_3\text{Si}-(\text{CH}_2)_3-\text{NH}_2$. The silicon-tri-ethoxy group could bind ceramic surfaces, while the amine could react with silver nanoparticles. In some embodiments, the porous layer is, eventually, chemically
20 associated with the gap-filling-layer and/or the tubular structures and/or surrounds it and/or is associated to by an accumulation of weak interactions. In another alternative, the diameter of the pores could be filled by gold, in cases of defects, where a void was not filled properly with gold, filling the gaps could also cover/block such pores if they are narrow enough.

25 The selection between the two main approaches of creating a membrane depends, *inter alia*, on the desired porous layer for mechanical support, which may be industrially available, and the ability to deposit such in the presence of tubular structures that may contain an organic material.

30 In devices constructed according to the present disclosure, a silicon wafer coated with a 100 nm film of gold (with a few nanometers of chromium as adhesion layer between the gold and the oxide layer present at the surface of the silicon wafer) was used as a substrate.

B. Attaching Sacrificial Materials to Form Composite Substrates

In this section, reference is made to a “primary sacrificial material” and a “secondary sacrificial material.” A “secondary sacrificial material,” also referred to herein as a “sacrificial layering material,” is a material that is deposited directly on the substrate, and which may serve as a precursor for deposition of another sacrificial material, the “primary sacrificial material.” A “primary sacrificial material,” also referred to herein as a “sacrificial pore-filling material,” is a material that is deposited onto the secondary sacrificial material while filling the pores of the porous substrate to at least some extent and which is used in order to form a base for attachment of other materials, such as template polymers and/or tubular structures.

In some embodiments, a dense layer of the secondary sacrificial material is deposited on the surface of the porous substrate. Then, the inside of the pores of the substrate are deposited with the primary sacrificial material, de novo, in order to fill the pores of the substrate. The dense layer of the secondary sacrificial material is then etched, leaving the pores filled with the primary sacrificial material. On this material, the tubular structures are deposited.

In one example, the substrate is an AAO (Anodic Aluminum Oxide) membrane. The secondary sacrificial material is silver. The silver is deposited on the exterior surface of the AAO substrate (as shown in FIG. 1B) by CVD and PVD methods, such as thermal deposition, sputtering, and e-beam. Then, electroplating (electro-deposition) of a gold (Au) as a primary sacrificial layer is carried out, filling the pores, as shown in FIG. 1C. Selective etching may then be performed, such as with nitric acid, to remove the silver layer.

Other materials may be used as substrates, with different materials requiring different types of deposition techniques, including ones having a high surface area configuration/s, possibly hollow fibers. The substrate may be formed of titanium dioxide (TiO₂), silicon dioxide (SiO₂), or silicon nitride (Si₃N₄). When the porous substrate is titanium dioxide, silver may be deposited directly with electroless deposition (ELD). ELD may then be used to deposit gold in the pores. Note that ELD processes will not deposit gold directly on titanium dioxide. This is advantageous, as it is desired to insert the gold within the pores, but not to cover the surface of the substrate with gold.

A similar two-step process may be used to deposit gold in the pores of a porous Al₂O₃.

When the porous substrate is silicon dioxide (SiO_2), additional preparatory steps are required. For example, a self-assembling monolayer (SAM) may be formed at the surface of the silicon dioxide. Then, silver is deposited at the exterior, and the rest of the SAM from inside the pores is removed. The SAM may be an amine-type of SAM having the structure $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{Si}-(\text{X})_3$ (X is a leaving group), which can be associated to the SiO_2 and afterwards can be associated with an Ag^+ ions, following ELD of Ag. After the ELD, remaining Ag^+ ions could be removed by adding ligands and/or adding an acid, then the remaining SAM-amine could be removed by immersing in H_2O . Finally, if present, electric currents could remove ligands from the metallic Ag film.

10 In some embodiments, a SAM is first formed on the surface of the porous substrate, and then all or some of the SAM at its exterior is temporarily protected, and the rest of the SAM is removed from the inside of the pores. The protection of the SAM from the exterior is then removed. The remains of the SAM at the exterior are then used, with or without further modification/s, to deposit a secondary sacrificial film. For example, if 15 the porous substrate is SiO_2 , an amine SAM could be protected specifically at the exterior by depositing nanoparticles, too large to pass via the pores of the SiO_2 . Such nanoparticles could protect the removal of the SAM from the exterior. The nanoparticles could then be removed, either by selectively etching them (Au and Ag nano-particles could be selectively etched by cyanide and/or iodine solutions) or detaching them by 20 using weak acid. In some embodiments, the unprotected SAM is not removed but reacted to become inert/nonreactive (for example, an amine SAM could be reacted to form an amide, oxidized to nitro and more). The remains of the SAM at the exterior could be used to initiate the deposition of the secondary sacrificial material, by CVD, PVD, ELD or any other means, such as nano-particles deposition and their combinations.

25 In some embodiments nanoparticles that are too large to pass via the pores of the porous substrate are deposited on the exterior of the porous substrate to initiate the deposition of secondary sacrificial material. Such nanoparticles may contain in their composition one or more secondary sacrificial material/s. In some embodiment, the nanoparticles are liganded, and the ligands could be utilized for their surface association 30 at the exterior of the porous substrate.

Depositing functional groups may be performed at the exterior of a porous substrate. For example, molecules of the type $(\text{X})_3-\text{Si}-\text{Y}-\text{Z}$ may be used, where X is a leaving group, Z is a branched polymer, of any type, too large to pass via the pores of the

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porous substrate. Y is a selectively cleavable link which yields a functional group after its cleaving, where $-NH_2$, $-SH$, $-S^-$, $-COO^-$ and $-COOH$ are of special interest.

Another approach involves creating a porous layer, for example, SiO_2 and/or Al_2O_3 , around a non-porous, dense fiber (possibly hollow), for example of Cu/Ag/Cu-Ag alloy. Then filling the pores is performed with Au, and finally etching selectively using nitric acid the Cu/Ag/Cu-Ag.

In some embodiments, the porous substrate has relatively uniform pores. After its pores are filled with a primary sacrificial material, it could be drilled/polished/grinded/patterned to obtain high surface area configurations, such as an array of wires, stacked sheets, an array of pores, or even detached fibers or other shapes. The secondary sacrificial material may or may not be selectively etched before or after the drilling/polishing/grinding steps.

In some embodiments, the surface of a dense wire, hollow or not, polymeric (PEI for example) or not, is deposited, possibly sparsely, with nanoparticles made of or containing a primary sacrificial material. The surface is further deposited by a porous layer for mechanical support, having pores, at least at the layer close to the dense wire and the nanoparticles of the primary sacrificial material, that is narrow enough that will be covered and closed during advanced steps of fabrication. Last is the removal of the dense wire.

In some embodiments, a thin composite film may be used, for example on top of a porous substrate, using known methods for creating such thin composite film having metal nanoparticles embedded within a cross-linked polymer for reverse osmosis. The nanoparticles could be made from a primary sacrificial material.

FIGS. 2A-2D show the fabrication steps of a layered, non-composite substrate. This methodology could be used for high surface area configurations as well, for example by surface associating tubular structures on the exterior of a dense fiber substrate, depositing a gap-filling-layer between the tubular structure, followed by depositing a porous layer and finally by etching selectively the initial substrate. The initial substrate may be a hollow fiber of gold alloy with a little silver, which can be mechanically stable.

Variations on the above-described mechanisms are disclosed in the literature. These variations include alternative methods of using SAMs during the deposition process, alternative methods of selective etching of the secondary sacrificial material, the use of ligands to initiate deposition of the secondary sacrificial material, use of a water-

oil interface to layer a film containing the secondary sacrificial material, activating the porous substrate prior to deposition of the secondary sacrificial material, and others.

C. Etching of the Gold Layer

5 In some embodiments, whether the first or the second main approach for creating membranes is used, the selective removal of gold, or a gold alloy such as gold-silver alloy, is required at the end of the process. In particular, gold could be used as a material that could fill the pores of a substrate and on top of it the construction of the tubular structures could take place, and after the gaps between the tubular structures are filled, then the gold
10 could be removed selectively in an etching process in order to empty the pores. Gold could be selectively etched using sodium or potassium cyanide in the presence of an oxide, silicon dioxide for example. That process could also selectively etch silver. Another process for selectively etching gold is by using iodine. In other embodiments, silicon oxide is selectively removed, which could be done selectively by hydro fluoric
15 acid and its buffers in wet conditions, or dry etching in the presence of titanium dioxide or aluminum oxide.

 In some embodiments, a protective coating is first used as a molecular adhesive between the sacrificial surface and the gap-filling-layer. Such coatings could also protect the porous substrate. Such protective coatings could also be used if the materials are not
20 the same. In some embodiments, the tubular structures could allow the passage of the etchant to the other side of the membrane, which is not desired, so they may be blocked temporarily, by adding a cap or by forming an inclusion complex with template molecules associated to a bulky group at one of its ends. In some embodiments a second porous layer is coated/deposited/placed from the other side of the membrane.

25 In some embodiments, before the etching, a temporary layer is coated, such as wax, in order to increase the mechanical stability and allow more aggressive stirring to be performed during the etching. Another reason is in cases where an entire layer of a continuous substrate is etched and the porous support is desired to be on the side where the continuous substrate layer was. Another reason is to hold the tubular structures intact
30 with the gap filling layer and after the etching to thicken the outer layer of the tubular structures at the side where etching had occurred.

III. Template Molecules and Methods of Attachment Thereof to the Substrates

In many embodiments of the present disclosure, and as seen in FIG. 1E, the channels are formed on template molecules. The template molecules are attached to the substrate, e.g., to the primary sacrificial material which is overlaid onto the substrate. Following attachment of the template molecules, monomers or tubular structures of the
5 macrocycles are overlaid onto the template molecules.

Referring to FIG. 6A, a template molecule 61, such as a polymer, is attached to a surface region of a substrate 60. A functional group, depicted as an asterisk, is positioned at the end of the template molecule 61. Although, in the illustrated Figure, only one polymer is attached to the substrate, it is understood that a network of polymers is attached
10 to the substrate.

The template molecule is patterned on a surface position within the surface region and enables direct placement of the tubular structures at these surface positions. The template molecules are molecules that may be selected amongst any elongated molecules that have a linear backbone and at least one terminal functionality that can surface-
15 associate to a surface region of the substrate. The template molecules may be similarly selected amongst such linear molecules which are mono-functional or optionally bi-functional meaning that they have two or more terminal groups, at least two of which functionalized or substituted or positions at the different termini of the linear molecule (one or more terminal groups at one end and one or more same or different groups at
20 another end). Where both termini are substituted with a functional group, one end may be selected for surface binding while the other for association with a functional group that acts as, e.g., a capping group or a stopper group once the macrocycles and/or tubular structures are threaded on the template molecule.

The selection of the functionalities depends, *inter alia*, on the template molecule
25 used, the surface material to which the template molecules are to be associated, and on other processing parameters. The functionalities may be selected to comprise at least one heteroatom or an atom having an affinity to the surface material or an ability to associate to a capping material. Such functionalities may comprise a sulfur atom, a selenium atom, a carboxylic acid group, an ester, an activated ester, an amine group (or a nitrogen
30 containing group including cyclic and aromatic amines), an hydroxy group (including phenols and other –OH containing molecules), an azide, aryl halides, alkyl halides, aryl pseudo-halides, alkyl pseudo-halides, and pseudo stable functionalities such as acyl halides and others.

The template molecules may be selected amongst aliphatic molecules having a number of carbon atoms defining the molecule length. The template molecules may be further selected amongst polymers or mixed polymers and oligomers. The elongated molecules are selected from such compounds having between a number of atoms in their
5 linear backbone, a measurable length or an effective length permitting efficient construction of the tubular structures.

The template molecules are associated to a surface region of a substrate material to achieve a patterned surface. Thus, in some embodiments, the template molecules are a plurality of such molecules, same or different, each associated to the surface region to
10 provide a pattern having a pre-selected or random surface density and surface profile. The plurality of template molecules may be a population of such materials, e.g., polymers, wherein the population is homogenous, i.e., each template polymer is the same as another, or heterogeneous, i.e., the population comprises different template molecules, wherein the difference is in at least one of material composition, length, molecular weight,
15 presence of functionalities, and others; or in the material chemical, physical or mechanical properties.

Generally speaking, the surface region may be any region of a surface of a substrate material onto which patterning is desired, or which surface properties are to be modified. The surface region may be of a single material or may comprise two or more
20 surface regions, each of a different surface material. In such cases, patterning with the template molecules may be directed to one or both of the different surface materials.

As discussed above, the substrate and its surface may be of the same material, or the substrate may be coated with a film of a different material. The material of the substrate and/or the surface may be selected amongst metallic materials, polymeric
25 materials, glass, paper materials, ceramic materials, oxide materials, nitride materials, phosphates, sulfides, carbides and others. In some embodiments, the surface is a metallic substrate, such as gold. In some embodiments, the substrate is a substrate surface (such as silicon) coated with a metallic material such as gold.

Patterning of the template molecules on the surface of the substrate may be
30 achieved to provide an ordered pattern or a random pattern or a mixed pattern, wherein a region of the surface is ordered while a second region is not. Hierarchical patterning is also possible, i.e., surface regions may be orderly patterned and within each ordered region template molecules will be associated randomly. Ordered patterns may be formed

by any means known in the art. These include lithography, optical lithography, soft lithography, dip-pen nanolithography, masking methods, photoresist-based methods, focused ion beam, electron beam, reactive ion etching, plasma reactive etching, and others. Random patterning may be achieved, for example, by contacting the surface region with a solution comprising the template molecules and permitting association of the molecules onto the surface region. Patterning of the template materials could be performed in one step or multiple steps, such as associating a molecule to a surface, which could be homogenous or patterned by itself, cleaving selectively at least one of its chemical bonds with or without further association of another molecule, or, sequentially, multiple molecules, to the resultant residue on the surface to obtain a surface associated with template molecules.

In some embodiments, contacting the surface with a solution would yield an ordered patterning. Particular examples of interest are using polymers with a dendron/dendrimer/branched polymers and combination of them, whose surface spacing has been investigated. For illustration, dendrons that have a selectively cleavable chemical bond near their stems, where the tip of the stem has a functionality for surface association could be used for ordered patterning of residues on a surface (there are even commercial examples for such dendrons). The entire spectrum between dendrons and dendrimers could be utilized for such surface spacing of patterned template molecules/residues that will be associated with template molecules. In some embodiments, such polymers are also degradable under certain conditions and not just one of the links between its atoms is selectively cleavable. A molecule used for patterning residues on a surface may have more than one functionality, such that after removing the molecule, there will be more than one residue per such molecule. The spacing between residues originating from the same molecule could be controlled due to shape, flexibility and other characteristics of such molecule. Residues originating from the same molecule could have the same or different functionalities. The means used for surface association depends, *inter alia*, on the surface used, the functionality present on the template molecules which is purposed for achieving surface association, the pattern structured required, the desired density of association and others.

Attaching a molecule to a surface is a process having several kinds of possible deposition kinetics, such as island formation, especially for small and linear molecules. Important parameters and conditions that determine the kinetics include: the phase/state

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of the deposited molecule, solvent (mixture of solvents, buffers), the concentration of the template polymer in the solution, temperature, immersion time, stirring, shaking, ultrasonication (during immersion), suction (to evaporate the solvent), and atmosphere.

5 Addition of other materials before or during the immersion, that cannot react chemically with the surface but only to physically adsorb into it could gain some control over the process. Physically adsorbed materials, whether the previous or another method was used, could be removed later by stirring and/or ultrasonication.

The following methods describe conditions and processes for attaching template molecules to surfaces while controlling the surface density of the template molecules, 10 their spacing and other parameters.

As discussed above, in preferred embodiments, the substrate is a metal substrate, such as gold, or a gold layer overlaid onto another substrate. Advantageously, gold reacts with groups that may be functionalized onto polymers, such as thiols, selenols, and disulfides. The template molecule has such a group on one end, such as a thiol group. The 15 template molecule may be functionalized on its other end with an amine or a protected amine. One example of a suitable polymer is polyethylene glycol (PEG), and more specifically one which is functionalized with a thiol group on one end and an amine on the other end.

If the template molecule does not tend to form islands on the surface, then the 20 attachment may be performed by immersing the substrate in a diluted solution containing the polymer.

If the template molecule tends to form islands on the surface (and the distance between each molecule chain is too close in such an island and interferes with threading of the macrocycles or tubular structures then attaching a template polymer may be 25 performed by immersing the substrate in an extremely diluted solution of thiols while heating, ultrasonication, and/or vacuum pumping. This yields a polymer-grafted surface in which individual polymer chains are attached apart from each other, not forming islands. Oxidation of the thiols may be avoided by working under inert gas. The template polymer may be functionalized at its other end with an amine or protected amine.

30 In the foregoing example, the template molecule is attached to the surface in a single step. In alternative embodiments, this process may be further split into two or more steps. First, a molecule having the structure X-Y-Z-SH is attached, where: X denotes a sacrificial polymer or other functional group, optionally with a bulky group (e.g., dendron

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or dendrimer) on one end. Y denotes a cleavable link between X and Z, such that after cleaving Z will be end-functioned. Z denotes a short molecule. SH denotes a thiol group. After immersing the substrate in such a dilute solution with such a thiol, thereby causing the thiol to attach to the substrate, the Y link is cleaved. Afterwards, the template polymer
5 is added by reacting with the end-function of Z. Instead of the thiol group, a disulfide group may also be used.

For example, a solution of a molecule $\text{HS-CH}_2\text{-COO-PEG}_{10\text{k}}\text{-OCH}_3$ may be prepared. In this scenario, the “X” group is PEG with OCH_3 as the long group, and the “Z” group is $\text{CH}_2\text{-COO}$. A gold surface is immersed in a vial containing the solution.
10 After cleaning (washing, rinsing, ultrasonication with various solvents) the surface is immersed in a basic solution (NaOH), yielding a surface of: $\text{Au-S-CH}_2\text{-COO}^-\text{Na}^+$. This group could be functionalized with a template polymer, for example $\text{H}_2\text{N-PEG}_{2\text{k}}\text{-NH-trityl}$, via EDC-NHS coupling of carboxylic acid and the amine (or through other ester activating procedures). After cleaning (washing, rinsing, ultrasonication with various
15 solvents) the protection of the amine (trityl amine) could be removed under mild acidic conditions or reduction. A bulky stopper could be attached to the amine after forming an inclusion complex with a tubular structure.

Various other examples for the “X,” “Y,” and “Z” groups may be utilized, without departing from the scope of the present disclosure. For example, instead of the thiol group,
20 a disulfide group may also be used.

In some embodiments, after the cleavage step, the remaining molecule on the surface is not short but is a template molecule that sometimes does not even require further modification/activation so it could thread and react with a bulky stopper to yield rotaxane/poly-rotaxane. In such embodiments, the “Z” component becomes the template
25 molecule.

The methodology described herein may be used for attaching to surfaces other than gold.

In addition, the previous discussion related to the use of template molecules that are appended to the surface of the substrate. In alternative embodiments, the template
30 molecules may be utilized in solution, during a process of forming tubular structures. These embodiments will be discussed in the next section.

IV. Macrocycles, Tubular Structures, and Methods of Preparation of Same

A. Macrocycles

Macrocycles are the backbones of the channels described in the present disclosure.

A “macrocycle” is a cyclic macromolecule containing a multiple number of ring structures (e.g., three or more) or atoms that are connected to form a cyclic molecule. The cyclic molecule, as defined, does not have terminal ends and is defined by an inner cavity that is formed by the atoms or bonds or rings forming the macrocycle. The cyclic macromolecule may be any such structure known in the art. The macrocycle may be synthetically produced, may be derived from nature or may be chemically modified to provide derivatives, substituted forms, or modified forms or analogue forms thereof.

The macrocycle may be used as such, namely used as a cyclic molecule as defined, or manufactured during any of the process steps disclosed herein. For example, a macrocycle may be constructed from linear fragments and formed into a cyclic molecule or a tubular structure, as defined herein, around a central template molecule. Notwithstanding whether the macrocycle is pre-made and used as such, or formed during the construction of the tubular structure, the macrocycle should be understood in its broadest known definition.

Non-limiting examples of such macrocycles, either used as such or constructed around the template molecule, or during the preparation of a tubular structure, as defined, are known in the art, and thus may be envisaged as any such cyclic molecule that once threaded on a template molecule can be pictured as a rotaxane or a poly-rotaxane. Such cyclic molecules may be, for example, calixarenes, porphyrins, cyclodextrins, pillararenes, crown ethers, helical molecules (which may, for example, be constructed around the template molecule), Cubril[n], cucubrituril, spherands, cyclophanes, carcerands, cavitand, cyclohexa-m-phenylene macrocycle, azamacrocycles, thiamacrocycles, glycophanes, oxacalixarenes, pyrogallol[n]arenes, resorcin[n]arenes, kekulene, cage molecules, inorganic macrocycles, metallic macrocycles, organic-inorganic hybrid macrocycles, organo-silicon macrocycles, organo-bor macrocycles, carbon nanotubes, and others. In processes of the invention, the macrocycles are stacked, typically in a coaxial manner, to provide an elongated channel which may comprise any number of macrocycles. The channel may thus be formed as an elongated assembly of a plurality of macrocycles that are coaxially stacked, and which are associated to each other, namely each two neighboring macrocycles are chemically or physically associated to each other. In the channels, each macrocycle may be the same or different and may be

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selected based on the macrocycle size, presence of functionalities, stability, structure of the macrocycle inner cavity, size of the inner cavity, functionalities present at the inner cavity and others. The channels may thus be the same or different and may differ from each other in the macrocycle used, the sequence of macrocycles used, the length of the channels, the average core diameters and others.

The channels may be selected amongst homogenous structures constructed of identical macrocycles and heterogeneous structures constructed of a plurality of macrocycles that may be different in at least one of chemical and physical properties. Such properties may be selected, without limitation, from macrocycle size, presence of functionalities, stability, structure of the macrocycle inner cavity, size of the inner cavity, functionalities present at the inner cavity and others.

One exemplary suitable macrocycle is α -cyclodextrin. Nanotubes composed of α -cyclodextrin cross-linked together using supramolecular chemistry have already been made. Moreover, the internal diameter of α -cyclodextrin is only 4.5 angstroms. As a result, it is feasible to attach an endcap to α -cyclodextrin to create membranes in the sub 4.4 angstrom domain, and specifically between 2.5 and 4.5 angstroms, as discussed. There are many known and possible modifications for α -cyclodextrins. Such modifications could alter the selectivity and permeability of membranes composed from tubular structures of the α -cyclodextrins.

Another exemplary material is γ -cyclodextrin. γ -cyclodextrin has an internal diameter of 8.5 Å, and also presents a platform to create membranes, in the sub 8.5 Å size, poly-rotaxanes, and pseudo-poly-rotaxanes with modifications.

B. Associating Macrocycles in Solution to Form Tubular Structures

The tubular structures according to the present disclosure are formed of macrocycles that are associated together in a linear manner to thereby form a tube.

Various techniques are known in the art for associating adjacent macrocycles. Macrocycles could be associated by using any method/s known in the art and their combinations, with or without utilizing supramolecular chemistry.

Macrocycles, their opening/s and/or other parts, could be modified and/or converted and/or decorated and/or patterned and/or deactivated and/or protected by using any method/s known in the art and their combinations, with or without utilizing

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supramolecular chemistry for the purpose of associating macrocycles into elongated tubular structures.

FIGS. 5A-5F illustrate exemplary schematic models for associating adjacent macrocycles in solution. FIGS. 5A-5C illustrate schematically two cyclodextrins 51 aligned opposite each other. Cyclodextrins are asymmetric compounds with a cross section similar to a frustum of a cone, and exhibit a “wide” side 52 and a “narrow” side 53. Prior art has demonstrated that it is possible to form dimers of cyclodextrins through forming narrow-narrow connections (FIG. 5A), wide-narrow connections (FIG. 5B), and wide-wide connections (FIG. 5C). Each of these types of associations may be present in the tubular structures according to the present disclosure. In each case, the connection is one or more bridges 54 between possibly opposite sides or positions of two cyclodextrins through reactions such as condensation reactions. Each of the carbons of the macrocycle has terminal groups (such as alcohols), at both the “wide” end and “narrow” end of the macrocycle. These terminal groups may be functionalized in order to enable formation of a bond between the cyclodextrins. The functionalization may enable associating two opposite groups at the wide side of the cyclodextrin or at the narrow side. Prior to association, it may be necessary to deactivate other groups, such as by methylation.

FIGS. 5D-5F illustrate, schematically, how bridges may be used to form chains of α -cyclodextrin. In FIG. 5D, multiple α -cyclodextrins 51 are threaded together along a template molecule 56 and sealed in place by bulky stoppers 55, to thereby form a poly-rotaxane. The α -cyclodextrins 51 are arranged so that the wide ends of one cyclodextrin are opposite the narrow ends of a second cyclodextrin. In FIG. 5E, bridges 54 are formed to connect adjacent cyclodextrins. In FIG. 5F, the bulky stoppers 55 and template molecule 56 are removed, leaving a multimer 57 of cyclodextrins that may serve as a building block for a tubular structure.

Threading

Macrocycles may be threaded together to form inclusion complexes. The term “threading” refers to insertion of the template molecules into the inner cavity of each macrocycle, or of macrocycle dimers, trimers, etc., to thereby achieve the inclusion complexes. Threading of a plurality (one or more) of macromolecules may be achieved by mixing macrocycles and template polymers in a solvent. The solution may be selected for particular properties, and may be saturated with macrocycles, or diluted with

macrocycles. Optionally, ultrasonic treatment and/or temperature control may also be utilized.

Threading of macrocycles or elongated tubular structures, for example nanotubes composed of two or more macrocycles already bonded to each other, onto a template molecule, to form an inclusion complex between them, sometimes denoted as a poly-pseudo-rotaxane or pseudo-rotaxane, is a process that depends on various factors. The factors include: functionalities and other characteristics of the template molecule, including polarity or a-polarity of the template molecule and the cavity of macrocycles, the cavity of the tubular structures, the outer shell of the tubular structures, the solvent/mixture of solvents, temperature, the flexibility/rigidity of the template molecules, the lengths of the template molecules, the macrocycles/tubular structures, and others. Often ultrasonication is used to initiate the process of threading. In some cases, threading is achieved in a saturated solution of macrocycles or tubular structures, and in other cases in diluted solutions. Some inclusion complexes are formed in water also due to hydrophobic interactions between the cavity of the tubular structures and the template molecule. After their formation, some inclusion complexes can be sustained for some time without unthreading in a solvent that could not have promoted their initial formation. For example, some inclusion complexes formed in water could be sustained for some time in a polar aprotic solvent. Some nanotubes composed of macrocycles could be threaded by template molecules in polar aprotic solvents. In some cases, even though hydrophobic interactions play a role in the formation of an inclusion complex formation, the hydrophobic cavities of the tubular structures could be threaded by template molecules having polar groups.

In some cases, a plurality of macrocycles may be associated to each other prior to surface association. In some embodiments, the outer shells of the tubular structures or a portion of them are sacrificial to some degree, i.e., could be removed selectively, for example in order to increase solubility in solutions that promote the inclusion complex, and also to generally increase the solubility of the tubular structure. In some embodiments, surfactants could be used to increase such solubility of tubular structures or a part of them. Surfactants that do not compete with the template molecules to form inclusion complexes with the tubular structures are of special interest. Such surfactants could be for example ones that all their ends are associated with bulky groups preventing threading.

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The addition of the bulky stopper 55 may be achieved through various mechanisms. Generally, the bulky stopper may be added to the solution containing the pseudo-poly-rotaxane in one or more of the following manners: as a powder; or dissolved in a separate solution. A base may be added to promote the attachment of the bulky stopper to the template polymer.

Exemplary mechanisms for adding bulky stoppers to template molecules in liquid are described in the art. In one example, the polymer template molecule ended in a primary amine, and the bulky stopper was 2,4,6-tri-nitro-benzene sulfonic acid sodium salt or sodium 2,4-dinitrobenzenesulfonate. In this instance, the poly-rotaxane was created on a surface. Other mechanisms for attaching bulky stoppers to template molecules in liquid are described in the art as well.

In another mechanism, the surface with the threading template polymer and macrocycles/tubular structures is dried, and a volatile bulky stopper is evaporated onto the surface. Another gas may function as a base. In another mechanism, the bulky stopper is added as a solid powder. Various bulky stoppers may be used, and various methods of applying the bulky stopper may be employed, in a manner known to those of skill in the art.

Forming Molecular Bridges

The formation of molecular bridges between adjacent (vicinal) macrocycles creates a tubular backbone. The association may be via any chemical association or binding, such as ionic bonding, covalent bonding, hydrogen bonding and others. In some embodiments, association is achievable by covalent bonding, e.g., by forming a covalent bond between a functionality on one macrocycle and another or a neighboring macrocycle. Typically, the functionalities permitting association are present on the outer circumference of the macrocycle and not in their inner cavities. However, association may be achieved via any functionality present on the macrocycles, either on their circumference or in their inner cavities.

Association may be achievable by chemically reacting functionalities present on the macrocycles, e.g., reacting a carboxylic acid on one macrocycle and an amine present on another macrocycle, or by associating the macrocycles by a linker moiety (a linker molecule) that comprises two or more functionalities that can associate to a functionality present on each of the macrocycles.

In some embodiments, association is achievable by crosslinking. Crosslinking, in this context, refers to addition of an external molecule that links two different macrocycles or tubular structures. In some embodiments, association is achieved by condensation reactions between vicinal macrocycles. In some embodiments association is achieved by a combination of methods, i.e., for example by condensation reactions followed by crosslinking. Condensation reactions may require conversion/s of some group/s.

For crosslinking to be efficient, the macrocycles/tubular structures may be threaded densely on the template molecule or at least on a portion of it. Crosslinking could be performed in solution or in vapor or solid phases after drying the surface. The rate of exposure of the crosslinking agent and its shape, among other parameters, could control the rate of associations.

Various methods for vicinally linking adjacent macrocycles have been disclosed in the art. Generally, there are two basic approaches: using chemical linkages directly, and using supramolecular chemistry to achieve chemical linkages.

With respect to forming chemical linkages directly, one approach took the macrocycle Calix[4]arene and added two external opposite bridges to each of the sides of this macrocycle. Using the two bridges, a bifunctional chemical association was performed to another such macrocycle. The process could be repeated to create nanotubes of Calix[4]arenes. In some embodiments, groups at required positions are reacted more than once with a single molecule (sometimes known as a "looper"). The looper may be removed, as needed, to yield a specifically modified side of a macrocycle, following formation of different interconnections.

In some embodiments, aftermodifying one or both side/s of a macrocycle (by converting and/or protecting and/or deactivating groups), the side or sides could be associated with molecules functioning as "arms" that will form later bridges with other macrocycles or tubular structures containing them. One side of a cyclodextrin could be associated with two or more "full" arms, or "half" arms, or any partition, such as a single "full" arm. As used herein, a "full" arm is an arm that extends all the way from one cyclodextrin to the other in the tubular structure, while a "half" arm meets another "half" arm in the middle. The tip of any arm may be protected.

Associating cyclodextrins and tubular structures containing them may also be done utilizing supramolecular chemistry. In these embodiments, the cyclodextrins are

threaded around a template molecule to form a pseudo-polyrotaxane, a bulky stopper is appended to the template molecule to hold the cyclodextrins in place (optionally, bulky stoppers are appended on both ends of the template molecule) and thereby form a poly-rotaxane/rotaxane, bridges are formed between adjacent cyclodextrins, and then the
5 template molecule is removed. Optionally, following removal of a bulky stopper, a template molecule may be elongated, so that more macrocycles may be joined to the chain.

Supramolecular chemistry has been used in order to create nanotubes of α -cyclodextrins, using a polymer penetrating a plurality of such macrocycles at once. The
10 tips of the penetrating polymer were reacted with bulky groups to prevent unthreading of the macrocycles from the penetrating polymer, yielding a dense poly-rotaxane. Then external bridges were added to chemically associate vicinal macrocycles. Finally, the links between the tips of the penetrating polymer and the bulky groups were selectively cleaved and the penetrating polymer was released, yielding nanotubes of α -cyclodextrins.

15 In certain embodiments, a slow addition of the bridge molecule may be performed. The reaction could take place in the solid state, gas state, or in a solution.

When the multimers are formed in solution, the type of links between adjacent macrocycles may vary. For macrocycles that are on the lower part of the tubular structure, and which will anyway be buried by the gap filling layer (see FIG. 4A), it is sufficient to
20 connect the macrocycles with one or two bridges. This type of connection is illustrated in FIGS. 5A-5F. By contrast, for macrocycles which are on the upper part of the tubular structure, which will not be buried by the gap filling layer, the macrocycles are linked at more than two locations. The additional links ensure that no molecules may enter the tubular structure in the area that is not buried by the gap-filling layer.

25

Specific Strategies for Formation of Bridges, including Initial Formation of “Trains” and “Ladders”

FIG. 5G illustrates a general strategy for forming a tubular structure. In FIG. 5G, a macrocycle 501 (such as a cyclodextrin) with functional groups X, Y, may be bonded
30 to a second macrocycle 502 with functional groups X, Y, and additionally functional groups Z and W (which may be an alcohol, for example). Functional group “X” includes an arm that will subsequently be used to form a bridge between adjacent macrocycles, and also may include a protecting group to render the arm non-reactive. Functional group

“Z” also includes an “arm”, which may include a protecting group. The functional group “Z” from macrocycle 502 reacts with group “Y” from macrocycle 501, to thereby form a dimer 503. This process is repeated to form a multimer 504. Although, in the illustrated embodiment, only a single pair of “X” and “W” is illustrated for each pair of adjacent
5 macrocycles, more than one such pair may be included.

Tubular structure 504 is referred to herein as a “train” configuration, because it resembles a train with multiple cars connected with only a single link. In general, for tubular structures having a “train” design, the tubular structure is comprised of at least two macrocycles, where vicinal macrocycles are associated to one another by at least one
10 association, where at least two vicinal macrocycles are associated to each other by exactly one association. Thus, some trains are comprised of “units” where within each unit the macrocycles are associated to their adjacent macrocycles by at least two associations, and the units are associated to one another by exactly one association. This design is of special interest also due to its relatively simpler production. The lengths of the units of a tubular
15 structure having a train design may not be uniform.

At FIG. 5H, a template molecule 506, having a bulky stopper 507 on one end thereof, is mixed with multimer 504 in solution, to thereby form a complex. The length of the template molecule 506 is selected so that the end 508 of the template molecule extends just beyond the terminal macrocycle in the multimer 504.

20 The presence of the bulky stopper 507 is valuable for ensuring that end 508 of the template molecule 506 remains exposed. In the absence of a bulky stopper, chains such as those depicted in FIG. 5I may form, which would bury the ends 508 of the template molecules, without enabling further reaction at those ends. The connection between the bulky stopper 507 and the template molecule 506 is selectively cleavable, as will be
25 discussed further herein.

Next, at FIG. 5J, a second bulky stopper 509 is introduced, and is reacted with the end 508 of the template molecule. This reaction does not necessarily form a selectively cleavable link.

At FIG. 5K, the “X” protecting groups are removed and/or activated. Specific
30 examples are discussed further herein. The “X” functional groups at the terminal end of the tubular structure may also be replaced, and/or may be selectively protected after the formation of bridges. This reactive group reacts with the opposite W groups, to thereby form a second bridge between adjacent macrocycles in the tubular structure.

At FIG. 5L, the first bulky stopper 507 is cleaved from the template molecule 506. This allows, at FIG. 5M, removal of the second bulky stopper and template molecule, to thereby leave the tubular structure with two links between each macrocycle.

The resulting tubular structure may be analogized to a "ladder," insofar as each of the macrocycles is connected with two connections, like rungs of a ladder. In general, for tubular structures having a "ladder" design, the tubular structure is comprised of at least two macrocycles, where vicinal macrocycles are associated to one another by at least two associations, possibly substantially opposite to each other. Thus, some ladders are comprised of "units" where within each unit the macrocycles are associated to their adjacent macrocycles by at least three associations, and the units are associated to one another by exactly two associations, possibly substantially opposite to each other. The lengths of the units of a tubular structure having a ladder design may not be uniform.

Optionally, in this method of construction, the first macrocycle (the one which is closest to the first bulky stopper may have specific functional groups. These functional groups may be used to bond to a tip or endcap molecule.

In the event that not all of the reactions proceeded to completion, the tubular structures that did proceed to completion may be separated from the partially-formed tubular structures using any known separation technique.

Optionally, the bridges between adjacent macrocycles may be selectively cleavable. For example, when both bulky stoppers are attached to the template molecule, one or more bridges may be cleaved.

An advantage of arranging the macrocycles in a "train" or "ladder" orientation and then removing the bridges between the respective macrocycles is that, after the bridges are removed, the macrocycles remain in a specific orientation. For example, the orientation may be a pattern in which pairs of wide ends are opposite each other, or pairs of narrow ends are opposite each other, or there are repeating patterns of wide-narrow. As a result, following the removal of the bridges, certain types of associations may be implemented that would not have been possible without the prior orientation of the macrocycles. Some of these associations are described in the following examples.

FIG. 5N illustrates two functional groups S and T, present at the openings of two adjacent macrocycles within the same supramolecular structure, where a bridge between them is to be formed. Even though FIG 5N illustrates just one S and one T, more such groups may be present in some embodiments, to form more than one bridge between the

two adjacent macrocycles. Also, one or more bridges may have already been formed before forming the bridge between S and T. In some embodiments, S and T are both primary alcohol. The primary alcohols are converted to primary alkyl bromides, for example, by reacting them with NBS/PPh₃. Following addition of a catalyst, a carbon-carbon bond is formed. The process may be performed to generate one bridge or more between adjacent macrocycles.

In some embodiments, a second type of bridge between adjacent macrocycles is formed, this one being an ether bridge. The process begins with each macrocycle having a primary alcohol (S=T=primary alcohol). Next, only one of the primary alcohols is converted to an alkyl bromide, while the other remains a primary alcohol. A strong base, which is not a nucleophile, is added. The base removes the hydrogen from the unreacted alcohol, thereby activating the primary alcohol to perform a nucleophilic reaction. As a result, an ether connection is formed. The bromide salt that is formed as a byproduct may be removed and discarded. Again, the process may be performed to generate more than one bridge between adjacent macrocycles.

If during this process, initially, both of the primary alcohols are converted to primary alkyl bromides, then the two alkyl bromides cannot react to form an ether bridge. Accordingly, the bromination must be reversed. NaOH base is added in order to convert one or both of the bromides back to an alcohol. At this point, the process may be performed again, in order to form the molecular ether bridges, as discussed.

In alternative configurations, one of the alcohols may be converted into a different leaving group. One exemplary is by reacting with a molecule of the type Cl-S-O₂-R.

Converting two vicinal primary alcohols into an ether bridge may be done by acid catalysis. The catalysis may be performed with any acid. A Lewis acid may also be used to perform the catalysis.

This process may be performed in order to generate a high number of links, such as up to 6 narrow-narrow links for alpha-cyclodextrin, or 8 narrow-narrow links for gamma-cyclodextrin if, for example, reacting the native primary alcohols of the narrow sides.

In certain embodiments, the formation of different bridges between different adjacent macrocycles may proceed in sequential reactions, instead of all at once, which may require to reverse certain conversions before repeating the process/processes for forming the bridge/s. Each sequential reaction increases a proximity of different portions

of the macrocycles to each other, thereby enabling the subsequent reactions. This may be advantageous because the formation of one bridge may cause other opposite functional groups to come closer together to each other, thereby enabling a reaction which was not possible when the macrocycles were merely complexed together on a template molecule.

5 In this manner, the macrocycles may be “ratcheted” shut gradually, until a sealed structure is obtained.

In some embodiments, one of the macrocycles includes arms of the form $R-CH_2-OH$ ($=S$), ending in a primary alcohol, or alternatively, S is a native primary alcohol of the opening of a macrocycle. The other macrocycle just has a non-primary alcohol/s ($=T$,
10 secondary alcohol/s and/or phenol/s). The primary alcohol/s may be selectively converted into primary alkyl bromide/s, using NBS/ PPh_3 or Br_2/PPh_3 or other leaving groups. The bromination may not be done on all of the primary alcohols at once, in a case in which more than one bridge is being formed. A non-nucleophilic base is added, to remove the hydrogen/s of the non-primary alcohol/s. The activated alcohol/s attack/s the bromide/s,
15 and the result is formation of two ether links. It is possible to form in this process two bridges at substantially opposite positions. This process may be performed in order to generate a high number of links, such as up to 6 narrow-wide links for α -cyclodextrin, or 8 narrow-wide links for γ -cyclodextrin if, for example, reacting the native primary alcohols of the narrow side with the native secondary alcohols of the wider side.

20 In some similar embodiments, in the two vicinal macrocycles, each one is equipped with one arm or more (of the form $R-CH_2-OH$) and one non-primary alcohol at 2 substantially opposite positions. The reactions proceed as described before in order to make two bridges.

Referring to FIG. 5O, in still another embodiment, a branched bridge is formed.

25 In this embodiment, two macrocycles (and/or openings of tubular structures) are arranged vicinal to each other within the same supramolecular structure, each could be with the same functional group ($S=T$). The macrocycles are reacted with a group having the form $X1-R1-X2-R2$, and which is also referred to herein as a type of “linker.” $X1$ is a group that is capable of reacting with S or T but not with both of them. $R1$ is a bridge, or part of
30 it. $R2$ is a long molecule, a dendron, or a dendrimer. The volume of $R2$ enables the molecule to react only with one molecule S or T . The bond between $X2$ and $R1$ may be selectively cleaved, such that $X2$ may be reacted with a further branched molecule having at least 3 functionalities, some may be protected. After the linkage to $X2$, the other

functionalities of the branched molecule may be used to form a link with the non-reacted functional group (S or T). This intermediate state is illustrated in FIG. 5O. Having more than one functional group increases the chances to react with this functional group (S or T). Alternatively, after attempting to link between the branched molecule and S or T, the remaining functionalities of the branched molecule may be reacted with other branched molecules iteratively, where from time to time, attempt/s to react with remaining functional groups S or T is/are executed. As a result, the bridge may be constructed with any degree of branching, as desired. Also, as a result, the branched bridge may connect more than two groups, i.e., also groups at the same opening in addition to two vicinal groups. This method could also be used for adding more associations to a train structure.

Processes that will be described *infra* for creating a gap-filling layer that is also chemically associated to the outer shell of the tubular structures may be used for forming a branched bridge as well.

FIG. 5P illustrates, schematically, a process of adding associations to an asymmetric tubular structure, such as a train structure. A train structure is formed with only one link between adjacent macrocycles or units. Then, a template molecule with only one tip associated to a bulky stopper is inserted into the asymmetric train structure (forming a semi-rotaxane), to thereby bring the two openings of the two macrocycles that are linked by exactly one bridge closer together. More associations occur, using any of the reactions described above, and the template molecule is removed.

FIG. 5Q illustrates another process of forming a train or ladder structure. Initially, a tubular structure is mixed in solution with a template molecule that is attached to a bulky stopper. Another template molecule is added and bonded to the first template molecule, and a second tubular structure (here, illustrated with a tip molecule) is threaded over the lengthened template molecule. The two tubular structures are then bonded to each other in two (or more) connections, and the elongated template molecule is removed.

FIG. 5R illustrates still another embodiment. In this embodiment, following association of the template molecule within the tubular structure, the bulky stopper of the template molecule is bonded to the tubular structure. The template molecule could afterwards be lengthened (not shown in FIG. 5R), and an association with another tubular structure (possibly asymmetric), similarly, to as described in FIG. 5Q could occur. Finally, the bulky stopper is removed from the tubular structure and the template molecule is removed. The advantages of using a bulky stopper that is associated to the tip of the

template molecule and is also associated to the opening of the tubular structure in order to add/form more associations within the tubular structure, include that the used solution may not promote the threading and/or enable application of ultrasonication.

One advantage of the processes described in connection with FIGS. 5P, 5Q, and 5R is that these processes may be used to lengthen asymmetric tubular structures in solution. It is then possible to include such lengthened asymmetric tubular structures during the building of the channels.

FIG. 5S illustrates an alternative process of forming “ladders.” The process begins by taking two cyclodextrins, functionalizing two opposite groups on their wide side, and deactivating and/or protecting the rest of the groups on the wide side (for example, via methylation). As part of this process, all except one of the functional groups on the narrow side may be temporarily protected. Then, a bond is formed between the two narrow ends of the cyclodextrins. This bond is selectively cleavable. Next, a rotaxane is formed including the cyclodextrin dimer, in which at least one of the bonds between the template molecule and a bulky stopper is cleavable. Finally, the bond between the two cyclodextrins is broken. The resulting structure is a poly-rotaxane in which the narrow ends are pointing toward the center and the wide ends are pointing toward the bulky stoppers.

Next, one of the processes described above is implemented, to form at least two ether connections between the primary alcohols. The primary alcohols are sufficiently distant from each other around the perimeters of the cyclodextrins that they will react with the alcohols or other functional groups at the adjacent macrocycle, and not with each other within the same macrocycle.

Next, at least one bulky stopper is selectively removed to yield a dimer.

The resulting dimer has its wide ends open on both sides. These wide ends may be further functionalized, for example with two arms, each being associated to a different wide end, by reacting one such functionalized dimer with two non-functionalized dimers, to thereby enable formation of a train. This train could be used as a precursor to a supramolecular structure, by methods mentioned above, in order to add associations and to form a ladder.

C. Preparation on a Substrate

FIGS. 6A-6H illustrate a different process, in which a tubular structure is formed on a substrate. In the illustrated example, the tubular structure is formed of monomers of the macrocycle that are bonded together. In alternative embodiments, the tubular structure is formed of multimers that had previously been prepared in solution.

5 In FIG. 6A, a template molecule 61 is attached to a substrate 60. In FIG. 6B, macrocycles 62 are threaded onto the template molecule 61, using a saturated or diluted solution. As a result, a poly-pseudo-rotaxane is formed, with the macrocycles 62 stacked around the template molecule 61 on the substrate 60.

Referring to FIG. 6C, in a third step, a bulky stopper 63 is attached to the template
10 molecule 61. This causes formation of a poly-rotaxane.

In FIG. 6D, external bridges 64 are added to the spaces between adjacent macrocycles 62. As a result, rigid structures are formed on the surface, consisting of the macrocycles 62 linked via the bridges 64. The external bridges 64 are also referred to herein as crosslinks.

15 Optionally, in FIG. 6D, connectors 66 are added, for adhering the macrocycles directly to the surface 60. Connectors 66 may be the same molecules as bridges 64 or different molecules, and they may be adhered during the same reaction as bridges 64 or a different reaction.

In some embodiments, as discussed, the bridges between the macrocycles are
20 formed prior to threading of the macrocycles on the template molecule (i.e., the step of FIG. 6D is performed before the step of FIG. 6C). The macrocycles are thus threaded in a tube form. For example, the tubular structures may be dimers or trimers prior to their threading on the template molecules. The dimers or trimers are then connected with bridges following threading.

25 In still other embodiments, the cross-linking is performed even without addition of a bulky stopper. That is, an array of tubular structures composed of poly-pseudo-rotaxanes could be cross-linked without forming a poly-rotaxane at first, i.e., without reacting the tip of the template polymer with a bulky stopper after the threading of tubular structures. Such a process has been described, in the liquid phase. This may also be done
30 in the gas phase. Still another approach is to graft the surface with a template polymer or a molecule that contains a template polymer, thread tubular structures around the polymer, and linking chemically the tip of the tubular structure to the surface, with or without special activation after threading.

D. Asymmetric Tubular Structures

As discussed above, the present disclosure teaches formation of macrocycle tubes with narrow openings at their tips, which are capable of filtering between small
5 molecules. The macrocycle α -cyclodextrin, has an inner rim diameter of 4.5 Å. This diameter is still greater than the diameters of many molecules that are desirable to filter, such as carbon dioxide and methane. Thus, in order for the macrocycle tubes to serve as filters, it is necessary to append an even narrower opening to one entrance of the tubular structure.

10 In one exemplary embodiment, a narrower macrocycle (a “tip” or “endcap”) is associated to the tip of a tubular structure made of wider macrocycles (i.e., macrocycles with a larger internal cavity. The tip is attached to the tubular structure with at least two external bridges on substantially opposite / relatively opposite positions of its mouth or opening. The shell between the associated narrower macrocycle and the tubular structure
15 is less permeable than the opening in the endcap, thus ensuring that materials to be filtered enter the tube via the endcap. One or more intermediate-sized macrocycles could be used as a bridge between a smaller endcap and larger macrocycles. More than one endcap may also be applied, in a progression from larger to smaller internal diameters. A given endcap may be associated to the same tip of a tubular structure by different types of connections,
20 where different bridges, their number and the different sites of bridging could each yield a tip with different parameters.

The modified tip presents a unique cavity whose shape and atom composition, as well as its internal cavity diameter, influence its selectivity and permeability toward different materials. The flexibility of the tubular structure also plays a role in restricting
25 or forcing the conformations of the macrocycle. An extra layer at the surface of the membrane could also contribute to this effect.

The modifications to the tips of tubular structures may be performed when the tubular structures are already embedded into a membrane, or during/between different steps of its fabrication. The modifications may alternatively be performed on a tubular
30 structure and even a single macrocycle before its incorporation to a membrane, where the opposite tip of the tubular structure/ macrocycle could potentially be elongated, as previously described. Such one-tip-modified tubular structures could by themselves be

incorporated to a membrane device or to surfaces that are precursors to a membrane at different stages of manufacturing.

FIGS. 4E-4J illustrate macrocyclic molecules, with similar structures, but with different internal diameters.

5 FIG. 4E depicts 15-crown-5, a crown ether with an internal diameter of 1.7 – 2.2 Å. This diameter is too small to be penetrated by the gases which are desired to be filtered in the present embodiments. FIGS. 4F and 4G depict variations of the 15-crown-5 ether, in which a furan ring (FIG. 4F) and a pyran ring (FIG. 4G) is drawn around an oxygen atom. FIGS. 4H-4J depict variations of 15-crown-ether with additional groups attached
10 to a carbon-carbon bond, such as alkyl carbons (FIG. 4H), an aromatic ring (FIG. 4I) or a functionalized aromatic ring (FIG. 4J).

The modifications of the crown ether introduce minor variations in flexibility and length. For example, the bond between two aryl carbons (FIGS. 4I, 4J) is about 14 picometers, or 0.014 nm, shorter than the bond between two alkyl carbons (FIG. 4H).
15 This 14 picometers difference at the perimeter is translated to less than 5 picometers in difference in internal diameter. Further functionalization of the benzene itself, adding a nitro group for example, may cause even more delicate differences in the diameters.

Another crown ether, 18-crown-6 (a crown ether with 6 oxygens) has an internal diameter of between 2.6 to 3.2 Å. The pores of a membrane composed of its derivatives
20 at the tips of their tubular structures, possess the ability to separate gases like hydrogen whose kinetic diameter is 2.89 Å, from gases like methane, and carbon-dioxide that have diameters above 3.2 Å. Such pores also may be able to separate gases with diameters within the 2.6-3.2 angstrom range due to different selectivity.

In order to generate a separation in the range of 3.3 to 3.8 Å, another endcap
25 molecule, including but not limited to a larger crown ether, may be employed. The macrocycles may have specific functional groups or compositions, similar to those of the crown ethers described herein, in order to generate a “second internal diameter” with picometer-level sensitivity.

Furthermore, optionally, and referring back to FIG. 4A and FIGS. 5P-5R, various
30 types of tubular structures may be prepared in solution. These include: “lower” parts of the tubular structures, made of identical macrocycles, with only minimal connections therebetween; “upper” parts of the tubular structures, made of identical macrocycles, with substantial connections therebetween, and a “tip” tubular structure, including at least one

tip molecule having a narrower diameter than the lower parts of the tubular structure. More generally, any combination of macrocycles of different widths may be included in the tubular structures.

In the illustrated embodiment, the tip molecules are at an end of the tubular structure. As discussed, the narrower molecules may also be at intermediate points of the tubular structures.

In the illustrated embodiment, there is a single “tip” molecule. In alternative embodiments, there may be a sequence of multiple “tip” molecules, each with a gradually narrowing diameter.

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E. Removal of the Bulky Stopper and Template Molecule

In FIG. 6E, the bulky stopper and the template molecule are removed. A stacked tube of macrocycles remains on the substrate, with an internal pore. Often, this process is performed only after completion of the gap-filling layer, and, as a result, specific methods for removal of the template molecule are discussed further herein, after discussion of the gap filling.

15

F. Direct Attachment of the Closest Macrocycle to the Surface

Referring to FIG. 7A, the closest macrocycle to the surface 72 (the “first macrocycle”) may form an association, via links 71, with the surface region 70. This may occur during the crosslinking process of FIG. 6D, or in a separate process.

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In order to achieve this attachment, the first macrocycle may have one or more protected functionalities that could be activated to form such surface associations, after one or more such associations using unprotected functionalities occurred with such residues. In addition, the patterning of a surface with such tubular structures, or even single macrocycles, could be space controlled by bulky protecting groups present at different positions of the outer shell of the tubular structures. These protecting-groups serve a similar function to the dendrons of the template polymers, as discussed above. The protecting groups may be removed after the surface association. The bulky protecting groups at the outer shell or a portion of them, should be understood in its broadest context, such as oligomers, polymers, dendrons, dendrimers, branched polymers, oligomers/polymers that are too thick to be threaded by the tubular structures, or alternatively their other tip/s are associated to a bulky group to prevent threading and

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others that their association to the outer shell of the tubular structures is selectively cleavable without damaging the tubular structures, the surface and the surface association. In some embodiments, such polymers at the outer shell are degradable under certain conditions and not just their association to the outer shell is selectively cleavable. In some
5 embodiments, after the removal of such protecting groups, the obtained functional/groups could be utilized for different utilities regarding lengthening of the tubular structures, reacting, and/or with precursors of the gap-filling process/processes, and/or others.

FIG. 7B schematically illustrates an archetypical tubular structure that could be used directly to pattern the surface, without prior patterning of the surface by a template
10 molecule. In such instances, it is desirable to form the outer shell of the tubular structure with functional groups 73 that may bond to the surface.

Not all the options presented in FIG. 7B are necessarily executed in a single embodiment. For example, the groups of 74, 75, and 76 all denote sites for containing bulky protecting group/s as described above, and typically only one type would be
15 employed in a certain part of the tubular structure in an embodiment – near its groups for surface association (74), at its opening that will be far from the surface substrate (75) or at its cap (76). The number of such groups may be different than illustrated in this figure.

In some embodiments there is no threading template molecule. In some embodiments there are no links 78 that are selectively removable between the opening of
20 the tubular structures and the cap 77.

If there is a threading template molecule then there must also be a cap 77, which in such a case also functions as a bulky stopper.

In some embodiments there is no cap 77 at all.

25 **G. Lengthening Channels**

As discussed above, the channels may be formed of tubular structures with different, small building blocks of macrocycles. The channels could be further lengthened by associating them with more tubular structures to form lengthened tubular structures associated to the surface. The lengthening process may utilize supramolecular chemistry,
30 such as a threading template molecule. In some embodiments a surface associated tubular structure is threaded by a surface associated template molecule extending out of it, and could potentially thread another tubular structure, so the two tubular structures will become vicinal. The vicinity could be utilized to associate the two tubular structures.

The lengthening process may occur once, for example if one of the openings/tips of the added tubular structure is permanently blocked or narrow, so that a threading template molecule could not penetrate through such an opening/tip. In such cases, the length of the part of the template molecule extending out of the surface associated tubular structure should be less than that of the added tubular structure. Alternatively, the lengthening process could be iterative, either by adding and associating tubular structures one after the other on the same template molecule (that extended from a surface associated tubular structure), optionally with repeatedly lengthening the template molecule by associating it with another template molecule before associating one or more tubular structures.

Instead of direct chemical anchoring of the tip of the tubular structures to the surface, a gap-filling-layer, or another layer deposited on the surface surrounding the tubular structures could also be used to supply further association of the tubular structures to the surface (methods of creating such a layer will be described later). Moreover, it is possible to thicken iteratively the gap-filling-layer in order to associate an added tubular structure.

In some cases it is possible to chemically associate vicinal tubular structures without forming a poly-rotaxane, for example if the formed inclusion complex could be sustained for enough time in a solvent that is suitable for a chemical reaction to occur between the tips of the surface associated tubular structure and the added one (it is possible to form the inclusion complex in one solvent, dry the surface and to form the reaction in another solvent). Another option is to form an inclusion complex on the surface, to dry the surface by evaporating the solvent (by heating and/or using suction and/or purging an inert gas on the surface), and expose the surface to vapors of a gas that will promote the reaction (non-nucleophile nitrogen base gases for example), or to add a powder of a material. If it is impossible to do so, then a poly-rotaxane should be formed, and more group compatibilities should be considered.

Another advantage of forming a surface associated poly-rotaxane is the ability to use ultrasonication in order to remove physically adsorbed tubular structures (if such exist). However, avoiding scenarios where any of the tubular structures threaded by the surface-associated template molecule could be associated to the physically adsorbed tubular structures is possible by selecting parameters in advance – for example by selecting the length and flexibility of the tubular structure that is associated via its tip to

the surface (and not only by the threading surface associated template molecule) so its other tip will be far enough from any possible shorter added tubular structure that could also physically adsorb to the surface. This consideration is also relevant if the tubular structure that is wished to be added is 'long' – but adsorbing to the surface means they are
5 lying horizontally – thus shorter than their 'full extent.' After the lengthening due to the association between the tubular structures, ultrasonication could remove physically adsorbed tubular structures.

In some cases, even if an inclusion complex is formed, or could be sustained for enough time in a solvent that enables the intended chemical reactions, a poly-rotaxane
10 should still be formed so heating and/or stirring and/or ultrasonication could be performed so groups found at vicinal tubular structures could get closer and react in order to associate the vicinal tubular structures.

The methods that will be described in this section are also compatible with tubular structures comprising cyclodextrins that are associated to each other by ether and other
15 linkages.

Referring to FIG. 8A, a surface associated template molecule 81a is threading to provide a tubular structure 88a associated via means 89 to the surface 80. First, if a bulky group 83a had been associated to the top end of the template molecule 81a then it is removed, yielding a functional group FG1.

20 Second, FG1 is reacted with functionality FG2 present in an introduced template molecule 81b. A lengthened surface associated template molecule 81c is obtained. The lengthening of the template molecule may be performed through any known mechanism, including click chemistry. The lengthened template molecule could now thread one or more tubular structures. This is illustrated in FIG. 8B, in which a tubular structure 88b is
25 threaded onto template molecule 81c, and a bulky stopper 83b is associated to the end of the template molecule 81c.

For example, if a rotaxane/poly-rotaxane was formed by creating a bulky amide (bulky group 83a) at the tip of the template molecule, then the amide may be selectively cleaved under extreme basic conditions, or LiAlH_4 , or addition of an amine (by carbonyl
30 addition-elimination), or other processes. It should be noted that some bulky amides such as Fmoc could be cleaved under milder conditions, such as tertiary amines. 2,4-di-nitro-benzene-amine could be selectively cleaved under extreme basic conditions. After the cleaving, the amine could be further reacted, to form a non bulky amide for example, to

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lengthen the template molecule. The other tip of the added template molecule may be functional (potentially protected) or not.

FIG. 8C depicts another manner of linking two tubular structures. A template molecule is depicted as associated to a bulky group assisting further association between two tubular structures which are already partially linked (not specifically shown) and coaxial. FIGS. 8D and 8E introduce further alternatives. In FIG. 8D, a threading template molecule is associated to a bulky group associated by itself to the opening of a tubular structure. The threading template molecule is threaded into a surface associated tubular structure. In FIG. 8E, associating tubular structures is achieved by associating the ends of the template molecules penetrating them, by forming a reaction between two functional groups, FG1 and FG2.

One exemplary two-step method could be used to lengthen tubular structures that are anchored chemically to the surface (or by a gap-filling/another layer), and that their threading surface associated template molecule also extends out of them. The added tubular structures have at least two functionalities at each of their tips, and are the same in both tips, for example primary alkyl halides/pseudo-halides, while the surface associated tubular structures have groups that could attack the alkyl halides, with or without more materials to promote the reaction, such as alcohols with the addition of a non-nucleophile base.

This method assumes that it is possible to form the reaction after the formation of the inclusion complex with or without drying and changing the solvent, or otherwise, drying and exposing to vapors of another material, for example vapors of non-nucleophile base such as DIPEA or DBU in order to activate alcohols, or adding powder of a non-nucleophile base such as sodium hydride (NaH).

If several added tubular structures are stacked on each other in the formed poly-pseudo-rotaxane, they could not react with each other, and reaction could occur only between the surface associated tubular structure and the first added tubular structure to be threaded by the template molecule, since vicinal alkyl halides will not react with each other in the presence of a non-nucleophile base.

After lengthening, ultrasonication could remove the rest of the tubular structures. In the next iteration a tubular structure having only functionalities that can attack alkyl halides is added (alcohols for example). This "AB cycle" could be repeated as needed.

It is possible to use in advance a long enough template molecule in order to form several iterations. However, since some inclusion complexes are formed within a certain range of molecular weights of the template molecules, it may be necessary to lengthen the template molecule itself from time to time. For example, aryl bromide will not react under conditions suitable for the reaction between an alcohol/phenol and an alkyl halide. It is possible to lengthen such an aryl bromide terminated template molecule, when it threads tubular structures that contain alcohols/phenols, and not alkyl halide, with a template molecule whose tip includes a derivative of aryl boronic acid and whose other tip is aryl bromide, using a Suzuki reaction (certain protocols of this reaction could occur under the presence of alcohols). It should be noted that due to the process of this reaction it is possible that the aryl bromide that is in the same molecule with the derivative of the boronic acid will not react during the coupling with the surface associated aryl bromide, thus the presented process could be repeated. Alternatively, it is possible to perform here an "AB cycle" as well, with template molecules terminated by 2 aryl boronic acids and another template molecule terminated by 2 aryl bromides.

If the template polymer was first lengthened after cleaving a bulky group protecting an amine, and the amine was reacted to lengthen the template molecule by forming amide functionality, then conditions should be selected such that the amide will not attack the alkyl halides. First the amide may be hindered inside a tubular structure and could not react. Second, only extremely strong bases could activate an amide, while some alcohols could be activated by much weaker bases, especially some carbohydrate alcohols.

The surface may contain Si-OH or M-OH (where M is a metal) groups. Such groups, especially in the presence of a base, may attack primary alkyl halides. However, the formed bond is labile, and could be cleaved easily using water or little acidic/basic water, without cleaving ethers for example formed during the association between tubular structures. Forming a protective monolayer on top of the oxide layer in advance could also be used to avoid this scenario. The protective monolayer may contain protected functional groups that may be activated in a future process.

Still another method may be employed to lengthen tubular structures in cases where a poly-rotaxane must be formed. The tubular structures are surface-associated, as in FIG. 7A, not only via the template molecule. The functional groups at both the surface associated tubular structures and the added tubular structures are primary alcohols. The

tip of the surface associated template molecule is an amine, and after forming an inclusion complex, a poly-rotaxane is formed by reacting the amine with an activated ester associated to a bulky group in order to form an amide. Now acid catalysis is used to condense vicinal primary alcohols into ether bond (as is performed in ethanol dehydration to ether, by diluted sulfuric acid under 140°C, while avoiding heating to 180°C where elimination occurs). The process could repeat itself. Primary alcohols at the same tip of a tubular structure should be far enough from each other to avoid reactions within the same molecule.

FIGS. 8F-8I illustrate processes for lengthening of a tubular structure that is associated to a surface. A second tubular structure, containing a template molecule, is adhered to the existing tubular structure, as shown in FIG. 8F. Then, a connection is formed between the added tubular structure and the tubular structure that was already associated to the surface.

In FIG. 8G, a portion of the tubular structure is cleaved from the rest of the tubular structure while the rest of the tubular structure is in place. For this to work, the tubular structure (or the portion thereof) must be constructed with selectively removable bridges. The bulky stopper is removed as well, possibly with removing a portion of the template molecule.

In FIG. 8H, the bulky stopper is removed, and subsequently the tubular structure/s that are not trapped within the gap-filling layer are released, leaving a small tubular structure, with a threading surface associated template molecule extending significantly from it. A new tubular structure may then be appended to the template molecule.

In FIG. 8I, the bulky stopper and template molecule are removed from the surface, leaving tubular structure/s that is/are trapped within the gap-filling layer. A new longer template molecule could be used to thread it and extend out of it after its surface association. Alternatively, it could be lengthened as shown in prior Figures.

The foregoing examples for lengthening the tubes represent exemplary embodiments, and other mechanisms may be employed, without departing from the scope of the present disclosure. Also, in general, strategies for lengthening tubular structures that may be performed in solution (described above) may be performed on the surface of the porous substrate, and vice versa, although some methods may be more effective in one context of the other, depending on the circumstances.

H. Methods of Enhancing Perpendicularity of the Channels

First, selecting a smooth substrate surface promotes perpendicularity.

Second, the surface density of the tubular structures may be tuned, such that they will encounter each other and could not 'stick' parallel to the surface.

5 Third, functional groups at the outer shell of the tubular structures may be reacted with groups, such as bulky/rigid/robust groups, to help ensure that they remain upright. This could be done multiple times. Such groups may also be attached to the bulky stopper. In addition, it is possible to react the groups that have not reacted with a molecule before depositing the gap-filling-layer.

10 In another approach, the surface of the substrate may be protected, so that the tubular structures cannot 'stick' parallel to the surface. This could be done multiple times. That could be done after there is an array of tubular structures on the surface and/or after there is only a template polymer attached to the surface.

15 In still another approach, the tubular structures may be attached to the surface through the use of protected functional groups (that can react with the surface) near the tip or tips of the tubular structures. For example, if the surface is gold, then thiol protected groups at the tip could be cleaved and reaction with the surface will occur immediately. Further deactivation of thiol groups that were deprotected but did not react with the surface may be necessary, especially if such groups are present not only at the tips of the
20 tubular structures. Another example is if the surface (has nucleophilic groups / groups that can become nucleophilic once activated) and the tubular structures have leaving groups near their tip or tips (or vice versa). Adding an activator, for example a base (gas or liquid phase) will promote the reaction between the surface and the leaving groups on the tubular structures.

25 Finally, it is possible to use a less flexible template polymer. For example, there are macrocycles that can form inclusion complexes with PEG but also with polyphenylene and other molecules which are less flexible.

V. Gap Filling

A. Theory

30 The gap filling may be performed using any known deposition process. In exemplary embodiments, the gap filling process is atomic layer deposition (ALD). Other suitable processes include: Molecular Layer Deposition (MLD), MVD, CVD, PVD,

thermal deposition of a metal, sputtering, application of titanium and letting it oxidize afterwards, metal deposition of gold, spin coating, and dip coating, including of dilute solutions of nano-particles (metal or ceramic) that after the coating and the evaporation of the solvent are melted. In a similar dip or spin coating process, polymer chains may be dissolved in a mixture. Combinations of different processes are possible too.

In some embodiments, the gaps between the tubular structures are filled in a chemical process creating a layer originating and iteratively growing from the substrate and/or via a molecule, optionally an adhesive, associated to the substrate between the tubular structures. In some embodiments the gap-filling originates via a portion of the 'bottom part' – the part closer to the surface of the outer shell of the tubular structures, where the tubular structures are in proximity to each other and cover the entire substrate. In some embodiments, a combination of the former two approaches is performed.

In some embodiments, the gaps between the tubular structures are filled with an inorganic material, titanium dioxide for example, by using atomic layer deposition (ALD). In some embodiments the gaps between the tubular structures are filled with an organic material, cross-linked polyamide for example by using molecular layer deposition (MLD). Alternatively, a hybrid organic-inorganic material is used to fill the gaps between tubular structures. In some embodiments, the material filling the gaps is also chemically associated to the tubular structures (as opposed to just the substrates). The selection of a gap-filling-layer and its creation process depends, *inter alia*, on its mechanical properties, density/impermeability, chemical stability, thermal stability, its ability to entrap the tubular structures without covering them from above and without blocking their cavities.

The gap-filling process requires various functional results. Obviously, in order to form a membrane for picometer-sized pores, it is essential to adhere the gap-filling layer to the sides of the tubular structures, in a manner that is sealed, virtually hermetically. The degree of the seal depends on the type of molecules that are to be filtered. In addition, the gap-filling process needs to be tuned so as to ensure that the gap-filling layer does not bury the openings of the tubular structures.

There are various strategies for tuning the interface between the tubular structures and the gap-filling layer, in order to achieve these and other goals.

In one example, the tubular structures are formed with an outer shell which may improve entrapment during the gap-filling process. The outer shell may include bulky

molecules associated to the shell with thinner linking molecules. These bulky molecules may be used as anchors inside the gap-filling-layers.

The template molecules inside the tubular structures (when present) could also be used to determine the properties of the tubular structures-gap-filling-layer interface. Specifically, the template molecules cause a reduction in flexibility, and physically form a barrier from within the tubular structures, so that the gap filling structure will not have any voids to penetrate and grow within.

The properties of the interface could be tuned by the selection of the shape of the ligands of an atom used in an ALD process. An ALD process could use different ligands to the same atom, and/or change from time to time during the process the selection of the ligands, to control the properties of the tubular structures-gap-filling-layer interface.

In some embodiments, an atom or a molecule or mixtures of such are first associated to the surface, to initiate the gap-filling-process while having more functionalities that can react with ALD/MLD precursors. In some embodiments, such molecules are dendrons associated to the surface by their stems, while their 'leaves' could react with ALD precursors. Such embodiments could reduce enveloping of the bottom part of the tubular structures during the gap-filling.

In some embodiments, functionalities at the outer shell of the tubular structures and/or a bulky stopper group and/or the template molecule are protected before the gap-filling-process. The cavity of the tubular structures could be protected by a template molecule optionally associated to the surface, optionally associated at one of its ends to a bulky group. In some cases, if a bulky group at the end of the threading template molecule reacts with ALD precursors, opened pores could still be obtained once the template molecule is released with a portion of the tubular structures.

Even though ALD is sometimes considered to be a particular case of Chemical Vapor Deposition ("CVD"), the term ALD should be understood in its broadest known definition, and to include processes that achieve ALD growth even in wet conditions and a combination of wet and dry conditions, and catalytic ALD.

Between and during ALD/MLD cycles, scavengers or etchants could be used to regenerate functionalities found at the outer shell of the tubular structures, to reduce the potential for burying the tubular structures during the gap filling process. This process may also be referred to as a "super cycle." For example, suppose that, prior to the gap-filling process, each tubular structure includes one or more exposed alcohols at an outer

perimeter thereof. The surface of the substrate (e.g., Al_2O_3) includes Al-OH groups. During a first stage of the ALD, $\text{Al}(\text{O}-\text{CH}_2-\text{CH}_3)_3$ is added. These molecules react with the alcohol groups, both on the tubular structures and on the aluminum hydroxides, to produce, both on the tubular structures and on the surface of the substrate, groups of $\text{Al}(\text{O}-\text{CH}_2-\text{CH}_3)_2$, with ethanol as a byproduct. A phenol or an ethanol is then added, as a scavenger. The phenol or ethanol performs ligand exchange, thereby cleaving the aluminum groups from the tubular structures, thereby restoring the alcohols on the tubular structures. The phenol may also substitute the ethanol in the Al-O complexes at the surface of the structure. These phenol groups may be subsequently replaced with aluminum oxide by mixing with water, prior to the next step of ALD.

In some embodiments, after filling the gaps between the tubular structures, the outer shell of the tubular structure is associated with groups, once or in a repeated process, to thicken the shell. In some embodiments, with or without thickening the shell at first, the shell could be associated to the surface of the gap-filling-layer. The former could be done by activating groups at the outer shell and/or removing protection from groups at the outer shell and other means such as reacting the surface of the gap-filling-layer with a molecule that could later be associated to the 'bottom' of the outer shell of the tubular structures. In some cases, the former molecule could be detached selectively from the surface of the gap-filling-layer while keeping the association to the bottom part of the outer shell of the tubular structures. The residual functionality could be used for thickening the outer shell. In some embodiments more gap-filling could be done afterwards.

In some embodiments, an extra layer is deposited on top of the gap-filling-layer to protect against chemical attacks and limit sticking.

In some embodiments, the gap-filling-layer could be accessed from the inside of the pores of the final device and could influence the flux through these pores.

The gap filling process could be used to intentionally cover some of the tubular structures, when appropriate. If a surface is associated with tubular structures that do not have a uniform length, for example because some of them were lengthened successfully while others were not, the gap-filling-process could cover ("bury") the shorter of such tubular structures, while only filling the gaps between the longer tubular structures. This process depends, *inter alia*, on the differences between the lengths of the tubular

structures, their perpendicularity, flexibility, distinguished presence of functionalities at their openings and other characteristics.

The gap-filling-layer could also cause surface association to the tubular structures, for example by entrapping some or all of their structures and/or by chemical association
5 between the gap-filling-layer and the tubular structures. This could be exploited if, for example (and unlike in the example of FIG. 7A), before the gap-filling-process, the tubular structures had no direct association to the surface, and they were associated to it only via rotaxane/poly-rotaxane association.

Moreover, the gap filling process could supply co-axial association between
10 vicinal tubular structures, with or without forming chemical bonds between such gap-filling layers and tubular structure/s, for example by forming chemical bonds between the part of the tubular structure/s that is closer to the surface and/or with the bridges used to associate vicinal tubular structures if such are present, and/or between openings of vicinal tubular structures. Thus, a process whereby, first the tubular structures are lengthened,
15 and second, the gaps are filled, could be repeated. After each instance in which a tubular structure is added, a gap filling process is performed, in order to fix the new tubular structure in place. This gap filling process may build up the existing solid material to at least partially encase the new tubular structure. Alternatively, the gap filling process may form a new solid layer which is not connected to the existing solid material, but which
20 itself serves as a connection between the original tubular structure and the new tubular structure, in a manner similar to the "local gap filling" process described below.

The following examples explicate specific methods that may be used for the gap filling process.

25 **1. Precursors**

If the substrate is a metal that can react with thiols, gold for example, a prior deposition to assist the ALD initiation could be deposited (by solution or vapor). An example of a molecule that could be used for such a deposition is a molecular adhesive, such as $\text{HS}(\text{CH}_2)_3\text{Si}(\text{OMe})_3$, with or without further conversion of the methoxy silicon
30 groups to silanols. Such deposition could be done in a set of several reactions – forming a multilayer and not just monolayer. Such deposition does not destroy completely the array of tubular structures. Another way to create a site for ALD initiation is wetting the surface with water, then drying the water from the tubular structures (this can work with

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a surface that has stronger affinity to water than the tubular structures). Some ALD precursors such as TDMAT could be deposited directly on certain metal surfaces such as gold.

The precursors used for the deposition of the gap-filling-layer ideally do not have kinetic energy that could damage the tubular structures during the surface reaction.

A water-oil interface could also be utilized for forming a gap-filling layer. If one part of the outer shell of the tubular structures is more hydrophobic than the other it could assist such gap-filling-processes, for example if the part closer to the surface is hydrophilic and the part more distant than the surface is hydrophobic (and the water and oil are formed correspondingly). Ceramics such as oxides and also cross-linked organic polymers could be formed in the interface between the water and oil.

For some tubular structures the gap-filling-layer could have a synergetic effect (especially ones in which the outer shell is not sealed tightly, for example if there is a long distance between adjacent macrocycles), and could influence the flux through the pores of the final device.

2. Area Selective ALD for Embedding the Tubular Structures Without Forming Bonds

Where the tubular structures do not contain groups that can react with the ALD precursors and their corresponding leaving groups/ligands and do not contain groups that can form adducts with them (Lewis acid-base bond), then area selective ALD could take place. Key parameters for controlling the results include: mobility of the tubular structures, their length, their perpendicularity, their density, their outer shell permeability, their flexibility, and all the regular ALD parameters. Precursors that did not react chemically must be removed from the surface by heating, vacuum pumping, or carrier gas purging, if the process is performed at the gas phase.

The deposition could be done at once or in sequences. The temperature may be changed from one sequence to another. Heating and cooling could be performed drastically or gradually. Different materials could be grown simultaneously. Layers of different materials could be grown on the other/s.

For TiO₂ as an example, generally its ALD precursors could be classified from more to less reactive: TiCl₄, Ti-nitrogen ligands (such as TDMAT) and Ti-oxygen ligands (such as Ti(isopropoxide)₄, Ti-(OMe)₄, Ti-(OEt)₄, Ti-(OBu)₄). In experimental

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results, an area selective ALD was performed using TDMAT under the presence of a THP ether and other groups comprising the tubular structures.

By such deposition, the gap-filling-layer has no chemical bonds to the tubular structures, but they are nevertheless integrally trapped within it.

5 If the tubular structures are poly-rotaxanes (of macrocycles, dimers of macrocycles and/or trimers of macrocycles and so on), and only the bulky stopper contains a group that could react with ALD precursors, then ALD could still be used, since the template molecule will eventually be removed alongside the bulky stopper and optionally the top portion of the tubular structures well.

10

3. Functional Groups on Tubular Structures for ALD for Forming Bonds at the Surface

15 If there are functional groups for ALD at the part of the tubular structures that is near the surface, then creating the gap-filling-layer could be done with no blocking from above and with chemical bonds between the gap-filling-layer and the tubular structures. That method also enhances the tightness of the gap-filling-layer around the tubular structures.

20 One way to perform this is as follows: After there is an array of tubular structures (that have functional groups for ALD at their outer shell) on a surface, the surface could be deposited to form a layer with molecules that contain a protected group that could react with ALD once activated by a small, possibly nucleophile base (such a layer may be a multilayer formed in more than a single process). Then, by activating with a large base, possibly a non-nucleophile, and for an example an alkylating agent, the functional groups of the tubular structures that are higher than the surface and are not masked by the
25 previously formed layer could become inert to ALD (the yield may not be 100% but high so few tubular structures will be covered from above). Then a small base could break the protecting group and expose functional groups to ALD at the surface and also unmask functional groups at the tubular structures near the surface.

30 In some embodiments, the tubular structures have a temporary thicker outer shell at the region near the part of surface association, for controlling their surface patterning. Specifically, the thicker outer shells may be shaped like dendrons (dendrimers?) (you probably meant dendrimers if that is the name of the ones with the accessible stem that have the shape of a tree), to help ensure minimum spacing between adjacent tubular

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structures when they are patterned onto the surfaces. After the surface patterning had occurred, this temporary outer shell could be selectively removed, leaving residues (such as alcohols) that could form bond/s with the ALD layer.

Another option is similar to the former but in which such thicker outer shell near
5 the part of surface association is not temporary, and it has groups that could form bond/s with the ALD layer.

Also, obviously, the tubular structures may have such groups near the surface 'naturally', due to design.

Another way to obtain a similar result is by using molecular layer deposition as
10 follows. The illustration supposes that the surface is gold and the tubular structures have alcohols at their outer shell as functional groups. The steps include: A) Reacting the gold surface to create a monolayer with $\text{HS}-(\text{CH}_2)_n-\text{NH}_3\text{Cl}^-$ (and adding base to activate the amine). B) Adding a molecule with at least three alkyl halides. There are conditions where the alcohols of the tubular structures will not attack such alkyl halides, but amines at the
15 surface will attack, for example by under a weak base. Non-reacted species are then removed. C) Adding a strong base, NaH for example, so that now alcohols will attack remaining groups of alkyl halide close to them (this will occur only near the surface if the tubular structures are sufficiently perpendicular). The base is then neutralized. D) Adding a molecule with at least two amines. E) Repeating steps B, C and D until desired.

20 There are many variations to this method. For example, oxide surface initiation could be performed using $\text{H}_2\text{N}(\text{CH}_2)_3\text{Si}(\text{OMe})_3$. Thiols and phenols could be used instead of amines. Instead of forming "AB" cycles with leaving and attacking groups, 1 molecule having at least 3 functional groups may be used, where at least 1 functional group is a leaving group and at least 1 functional group is a protected attacking group. Protection is
25 removed from the attacking groups after or during the conditions where the alcohols react with the leaving groups.

Another option is to use phenols and/or secondary alcohols on the outer shell of the tubular structures, while using a molecule with at least 3 primary alcohols to create the gap-filling-layer. After the molecule with 3 alcohols reacts with the surface the
30 remaining primary alcohols could be selectively converted to primary alkyl halides and react with the phenols/alcohols of the outer shell of the tubular structures.

Another version is to use tubular structures having a minor random percentage of functional groups at their outer shell, then after gap filling some will be covered from

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above, some will not be covered from above and will have chemical bonds with the gap-filling-layer and some will be integrally trapped with no chemical bonds with the gap-filling-layer.

Another version is to use tubular structures in which only one of their sides has functional groups that can react during the gap filling. If the creation of the array does not discriminate which of their sides is closer to the surface, then after ALD is performed, some will be covered from above while others will not.

These two versions may require some minimal distance between adjacent tubular structures.

Another option is to create on the surface tubular structures that are a [3]rotaxane/pseudo-rotaxane of two tubular structures, when one of their tips contains groups that could react during the gap filling, and the two such tips are facing each other in the middle of the [3]rotaxane/pseudo-rotaxane. Gap filling will cross-link the tubular structures and also create a gap-filling-layer. If the original tubular structure is a poly-rotaxane/poly-pseudo-rotaxane that contains more than two such tubular structures, then after the gap filling only the two tubular structures closest to the surface will remain part of the final device after removing the template polymer.

In all of the above-described embodiments, protecting groups may be present at the openings of the tubular structures. The protecting groups protect the openings of the tubular structures from reacting during the gap filling, and are removed afterwards, to enable lengthening of the tubular structure. After this lengthening, the gap-filling process could be executed again, possibly forming also chemical bond/s between one or two of the opening with of the tubular structures that were associated during the lengthening. This could happen more than once.

If the tubular structures have protected functional groups as discussed, then creating the gap-filling-layer could be done with no blocking from above the tubular structures and with chemical bonds between the gap-filling-layer and the tubular structures. After some deposition of the gap-filling-layer, the deposition could be stopped, the protection could be removed and then the deposition could be continued. This can occur at least once, when utilizing different protected groups found at different locations of the outer shell of the tubular structures.

Creating bonds between the tubular structures and the gap-filling-layer could also be performed after and not during the deposition of the gap-filling-layer, by several

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means. One example is to react a bi-functional group, of which one of its functional groups could react with the tubular structures and another with the surface of the gap-filling-layer (this could be done by one step or more with protected groups).

One way to do this is if the deposition of the gap-filling-layer is carried out while
5 there are still functional groups at the outer shell of the tubular structures that will not react with the ALD precursors, and to perform one last (or a few last) ALD cycle with another precursor that will react with the functional groups of the outer shell.

Another way is to convert functional groups at the outer shell of the tubular structures in advance to a protected group. After finishing the deposition of the gap-
10 filling-layer the protection could be removed and linking chemically the tubular structures and the gap-filling-layer could be done.

Still another method involves creating the gap-filling-layer on an array of tubular structures of the types: rotaxane/poly-rotaxane/pseudo-rotaxane/pseudo-poly-rotaxane, where the threaded structures are not threaded on a significant part of the template
15 polymer:

- A) Without further considerations.
- B) Converting and deactivating groups of the tubular structures so they will not react with precursors of ALD, before and/or after cross-linking.
- C) Applying cross-linking between macrocycles, which could also link the
20 macrocycles to the surface.
- D) Applying cross-linking between the tips of the tubular structures and the surface (anchoring see above methods).
- E) ALD with alternating heating and cooling between exposures of precursors (heating is done to remove excesses of precursors – if heating gets to a
25 temperature that causes unthreading – then working with rotaxanes and poly-rotaxanes is better).
- F) Depositing the surface with a molecule (vapor or solution) that could react with ALD precursor and trap at least a portion of the tubular structures versus the surface (with or without forming a self condensation between adjacent such
30 molecules). This could be done by multiple steps with or without protecting groups.
- G) Creating the gap-filling-layer under low temperatures, for example macrocycles that have alcohols that stabilize the tubular structure of their poly-pseudo-

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rotaxane by hydrogen bonds. ALD of TiO_2 could be performed below 80°C with precursors such as $\text{Ti}(\text{OR})_4$. At those temperatures, growth is indeed slow.

Another option is to use the same precursors but performing ALD-like growth in a combination of vapor and solution. If the substrate is an oxide, then vapor of
5 the titanium precursor to the device, then removing residues under a nitrogen stream, then immersing the device in liquid water (if water indeed promotes the complex between the tubular structure and the template polymer), then removing residues under nitrogen stream and repeating the process.

In yet another possible method, creating the gap-filling-layer is performed on an
10 array of tubular structures that contain a template polymer and are not rotaxanes. The template polymer is shorter than the cavity of the tubular structures. The ALD may be performed using conditions that promote threading. For example, wet ALD may be performed using solvents that promote threading or vapor phase ALD under temperatures that maintain threading or a combination of wet and vapor ALD. Another option is to first
15 associate the tips of the tubular structures by more means than the threading surface associate template molecule.

In yet another possible method, if the tubular structures do contain groups that can react with the ALD precursors to form adducts (by forming coordinative/additive/Lewis acid-base bonds), then area selective ALD could be done if adding to the AB cycles of
20 the ALD deposition an exposure of a competing agent/scavenger/etchant to form super cycles. For example, ether on the tubular structures could form an adduct with tri-methyl-aluminum (TMA). Exposure of phenol after exposures of TMA could form tri-phenyl-aluminum and methane. The ligand exchange of the aluminum from CH_3^- to phenoxide transforms the aluminum to be less acidic (in terms of Lewis acidity). In the next exposure
25 of water alumina will form area selective deposition. This method is advantageous in cases that require heating that will damage the tubular structures and/or rest of the device in order to break the adduct, and also to widen the range of functionalities present at the tubular structures.

There are cases in which the tubular structures contain groups that can react with
30 the ALD precursors to form covalent bonds (that are not coordinative/additive/Lewis acid-base bonds) or ionic bonds/static interactions. For example, alkyl alcohol on the tubular structures could form a bond with TMA (metal alkoxide bond). Again, exposure of phenol after exposures of TMA could form tri-phenyl-aluminum and convert back the

metal alkoxide to alkyl alcohol. The ligand exchange of the aluminum from RO^- to (where R is an alkyl) phenoxide transforms the aluminum to be less acidic (in terms of Lewis acidity). In addition to that, it is possible to add molecules with a similar affinity to the ones forming the undesired interactions, but in a large excess of the introduced molecules to cause ligand exchanges and/or to compete with the undesired interactions in order to release deposition of the ALD from the tubular structures themselves.

If the ligand exchange creates a metal-ligands complex that could not be evaporated from the surface, then this method could be applied to wet-ALD.

Although this method can derive the ALD to be area selective, it could potentially form bonds between the tubular structures and the ALD layer (because the metal may be less accessible during the gap filling). That way the gap-filling-layer could be deposited with no blocking from above of the tubular structures, and with bonds between the tubular structure and the gap-filling-layer.

4. Specific Strategies for Controlling the Interface Between the Gap Filling Layer and the Tubular Structures

It may be beneficial to retain the template molecule within the tubular structure during the gap filling, since the template molecule blocks the ALD precursors from penetrating into within certain tubular structures. Moreover, the choice of which template molecule is important, since thicker template molecules could prevent the penetration better than thinner template molecules.

As discussed, groups at the outer shell of the tubular structures (as well as the actual design of the outer shell) may prevent the gap filling layer from coming too close to the tubular structures. These groups may be protecting groups that could be removed later (some will be buried inside the gap-filling-layer and will not be accessible).

If creating the gap-filling layer is done by ALD, then the deposition of the same material could be done by more than one metal organic precursor. For example, if the required material is Al_2O_3 then $\text{Al}(\text{CH}_3)_3$ is not the only option, bulkier ligands could be used for example $\text{Al}(\text{CH}_2\text{CH}_3)_3$. That methodology keeps the metal atoms at a greater distance from the tubular structures. Once water is exposed to create the oxide they also will keep greater distance from the tubular structures. Combinations are possible as well, i.e., exposing a mixture of metal organic precursors at the same time and/or exposing pure $\text{Al}(\text{CH}_3)_3$ in one ALD cycle and exposing pure $\text{Al}(\text{CH}_2\text{CH}_3)_3$ in other cycles. Another

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important factor is the condition and the state of the ALD precursor under these conditions - some are monomers under certain temperatures while others form dimers and even tetramers. These states can also influence the distance from the tubular structures.

Decreasing the flexibility of the tubular structures assists the deposition of the gap-filling-layer to better surround the tubular structures. This could be done by using one or more methods mentioned above.

Another method that could influence the interface is if the tubular structures have groups that could react with ALD precursors. Working with small ALD precursors could also increase the tightness of the gap filling.

The interface between the gap-filling layer and the tubular structures may not be uniform. At some areas the interface may be more or less tight than in others.

B. Experimental Results

FIGS. 9A-9M illustrate experimental results of preparation of tubular structures and gap filling with ALD on surfaces coated with tubular structures.

The substrates that were used to demonstrate the next examples were 100 nm of gold coated on silicon wafers (prime degree) using a few nanometers of chromium as an adhesion layer between the gold and the oxide layer present at the surface of the silicon wafer Si-Cr-Au. The deposition method was thermal deposition or sputtering. After the gold coating, the wafers were spin coated with photo-resist to protect the coated gold. The wafers were diced into 1cm x 1cm films. The films were kept in a Teflon sealed box. Before experiments, the photo-resist layer was removed by immersing the films in a beaker of acetone for about 3 minutes under ultrasonication cleaning. Afterwards, the films were washed with acetone, followed by washing with isopropanol. The films were dried with purges of 0.3 micron filtered N₂. The films were then cleaned under O₂ plasma or a combination of O₂ and inert gas (N₂ or Argon) plasma for 5-10 minutes. After the plasma cleaning and until the experiments began, the films were kept in sealed vials containing de-ionized H₂O that covered the films. During sealing, the vials were purged with 0.3 micron filtered N₂. The vials were further sealed with parafilm.

FIG. 9A shows an Atomic Force Microscope (AFM) characterization of a plasma cleaned Si-Cr-Au film. All AFM characterizations were under air. The bottom of the Figure is a chart illustrating the line profile of the layer across the length of the film. For purposes of evaluating the height, the peaks should be considered from the lowest

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measured height – that is, the “zero” height is the lowest height on the chart, rather than the height marked “0” on the scale.

Beakers including their mouths and glass plates were carefully cleaned by washing with isopropanol and then H₂O. The beakers were dried by purges of 0.3 micron
5 filtered N₂, or heated and then left at ambient conditions to cool.

Except for immersions that were done under heating, in all other cases the beakers were sealed from above using parafilm and the parafilm was sealed using a Teflon tape around the mouth of the beakers. In some of the experiments the parafilm sealing was done under purging of 0.3 micron filtered N₂.

10 H₂O was de-ionized and filtered from micron particles. Organic solvents were of HPLC/MOS/CMOS degrees.

Depositing the template polymer H₂N-PEG_{1.25k}-NH₂ to the Si-Cr-Au surface to create Si-Cr-Au-S-CH₂-CONH-PEG_{1.25k}-NH₂ was done in four steps:

In step one, a cleaned gold film was immersed in a diluted solution of HS-CH₂-
15 COO-PEG_{10k}-OCH₃ (COO denoting an ester), about 1-2 milligrams in 5 ml of H₂O. The diluted solution was ultrasonicated for few minutes prior to the immersion. The immersion took place for about 10 minutes. After the immersion the film was washed with H₂O and then was cleaned under ultrasonication for several minutes (the solvent was H₂O) followed by more washing with H₂O.

20 In step two, the gold film was immersed for 10 minutes under aqueous 0.1M NaOH in order to cleave the ester. After the immersion, the film and the control film were washed with H₂O and then were cleaned under ultrasonication for several minutes (the solvent was H₂O) followed by more washing with H₂O. The vial was sealed and extra sealed with parafilm.

25 In step 3, a beaker that was cleaned from residues (was heated and then left at ambient conditions) was filled with about 5 ml of acetone and 20-30 milligrams of 2-Chloro-4,6-dimethoxy-1,3,5-triazine. This compound was added in order to convert the sodium salt of the carboxylic acid into an activated ester. The gold film was immersed in this beaker for about 15 minutes (optionally, cleaning with acetone may be performed
30 prior to this). The gold film was then washed with acetone and afterwards with H₂O, and was cleaned under ultrasonication for several minutes (the solvent was H₂O) followed by more washing with H₂O. The beaker that was used for the ultrasonication cleaning was similarly cleaned from residues prior to placing the gold film inside of it.

In the final step, the gold film was then immersed for 15 minutes under 5 ml of H₂O and 1-3 milligrams of H₂N-PEG_{1.25k}-NH₂ (C₅₆H₁₁₆N₂O₂₇). The activated ester could react with an amine in order to form an amide. The beaker that was used was similarly cleaned from residues prior to placing the gold film inside of it. After the immersion the film was washed with H₂O and then was cleaned under ultrasonication for several minutes (the solvent was H₂O) followed by more washing with H₂O.

The polymer-coated surface was then immersed in a solution of macrocycles to create a poly-pseudo-rotaxane on the surface. A gold surface containing Si-Cr-Au-S-CH₂-CONH-PEG_{1.25k}-NH₂ was immersed in a diluted solution of macrocycles (few milligrams per few milliliters, to immerse the surface. The surface in the diluted solution was 10 minutes under ultrasonication and then left untouched for at least 1 hour before the AFM characterization. Before the characterization the film was washed with H₂O and then extensively purged with 0.3 micron filtered N₂.

FIG. 9B depicts an AFM characterization under air of gold films containing poly-pseudo-rotaxane of α -CD, using Si-Cr-Au-S-CH₂-CONH-PEG_{1.25k}-NH₂ as the template polymer on the surface. The bottom of the Figure is a line profile, showing the presence of a long tubular structure.

Next, the tip of the template polymer was reacted with a bulky stopper to create poly-rotaxane on the surface. In a beaker containing a few milliliters of a diluted solution of a macrocycle, about 25 milligrams of DNBS (Sodium 2,4-dinitrobenzenesulfonate) were added. A few minutes of ultrasonication were used to homogenize the solution. This mixed solution was added slowly and carefully to the beaker containing the film (after it was left untouched for one hour in the diluted solution of a macrocycles). This beaker was left untouched overnight. In the morning it was stirred gently from time to time during a period of a few hours. The immersion was stopped, and the film was washed with H₂O and then was cleaned under ultrasonication for several minutes (the solvent was H₂O) followed by more washing with H₂O.

FIG. 9C depicts XHR-SEM (extra high resolution scanning electron microscope) characterization under air of gold films with poly-rotaxane of methylated α -CD. DNBS was used as the bulky stopper. The sample is shown at 200,000 degree magnification. The sample is tilted 45° in order to enhance the contrast between the tubular structures (the small bumps on the surface, with electron shadows beneath them) and the surface

itself. As can be seen, the surface is covered with numerous perpendicular tubular structures.

FIG. 9D depicts, at the top, an overhead view of the tubular structures with higher magnification. The overhead view does not provide as much contrast; however, the widths of the tubular structures are indicated. At the bottom of FIG. 9D, a view of another sample made by the same procedure is provided with AFM.

FIGS. 9E show AFM and XHR-SEM characterization under air of gold films with poly-rotaxane of α -CD-OCH₃. That is, all 18 of the alcohols in each α -CD were O-methoxy converted. The height of some of them is parallel to the length of the template polymer (PEG_{1.25k}). DNBS was used as the bulky stopper (it looks like the version after ALD of 3 nm TiO₂....).

Out of eleven poly-rotaxanes in the area shown in the AFM figure, nine were measured, combined with another area of this sample in which 11 poly-rotaxanes were measured, the average height of the 20 poly-rotaxanes was 11.1 nanometers. Note that the length of the stretched template polymer plus the bulky group associated to its tip should indeed be close to 11 nanometers.

Following formation of the tubular structures, ALD was performed.

Table 1 summarizes the ALD procedures that were performed.

Table 1 – ALD Procedures

Procedure number	Oxygen source	Metal source	Temperature (C)	Vacuum (Torr)	Carrier gas (was also used for purges between cycles)	Number of cycles	Ellipsometry characterization of a control sample on silicon film
1: TiO ₂ – 3nm	H ₂ O	Ti-(N(CH ₃) ₂) ₄ (TDMAT)	130	10 ⁻⁵	Argon	100	2.9 nm
2: TiO ₂ – 6nm	H ₂ O	TDMAT	130	2X10 ⁻²	N ₂	110	6.1 nm

20

The films were in the chamber of the ALD (Atomic Layer Deposition) reactor under the final temperature and final vacuum for several minutes in order to clean them.

The differences in the growth rate using the same metal sources are most probably due to conditions where they were kept, since different systems were used for different depositions.

Before the ALD the films were dipped shortly in a moderately basic aqueous solution (NaOH was the used base), to neutralize any possible acidic leaving groups on the poly-rotaxanes.

Procedure 1 was carried in a Fiji ALD system. Procedure 2 was carried in a Savannah ALD system.

FIG. 9E shows an AFM characterization of a gold film deposited with poly-rotaxanes (of α -CD-OCH₃ using the template polymer PEG_{1.25k}. DNBS was used as the bulky stopper, followed by ALD of 3 nm of TiO₂. The ten poly-rotaxanes shown in the AFM were measured, and combined with two more poly-rotaxanes measured in another area of the sample, the average height of the 12 poly-rotaxanes was 7.8 nanometers. Note that the difference in the averages of the heights between these and poly-rotaxanes that were not deposited by ALD is 3.3 nanometers, which is approximately corresponding to the 2.9 nanometers growth characterized in the control. FIGS. 9F and 9G depict views of the same sample with XHR-SEM.

FIG. 9H shows an AFM characterization of a gold film deposited with poly-rotaxanes (of α -CD-OCH₃ using the template polymer PEG_{1.25k}. DNBS was used as the bulky stopper) followed by ALD of 6 nm of TiO₂. The ALD procedure was number 2, within Table 1. The average height of 11 poly-rotaxanes measured in the AFM area was 4.7 nanometers. Note that the difference in the averages of the heights between these and poly-rotaxanes that were not deposited by ALD is 6.4 nanometers, which is approximately corresponding to the 6.1 nanometers growth characterized in the control. FIGS. 9I and 9J depict views of the same sample with XHR-SEM.

It is particularly instructive to compare the XHR-SEM views of the surface with tubular structures alone (FIG. 9D), the surface with the tubular structures deposited by 3 nm ALD (FIGS. 9F and 9G), and the surface with the tubular structures deposited by 6 nm ALD (FIGS. 9I and 9J). The comparison illustrates a reduction in contrast between the tubular structures and the surface, reflecting the rise in the surface, reflecting the filled gaps, caused by the ALD.

Fig. 9K and 9L show an XHR-SEM characterization of a gold film deposited with poly-rotaxanes of α -CD using the template polymer PEG_{1.25k}. DNBS was used as the

bulky stopper. The alcohols of the α -CD were not methylated, enabling reaction of the ALD with the tubular structures. ALD of 6 nm of TiO_2 was then performed. The ALD procedure was number 2, from within Table 1. The images clearly show that the ALD reacted with the entire surface, including covering the poly-rotaxanes from above, unlike
5 the growth mechanism for poly-rotaxanes comprising α -CD- OCH_3 , where the ALD only filled the gaps between the poly-rotaxanes.

Thus, the experiments demonstrated, first, that it is possible to build the tubular structures on the substrates in the manner described. In addition, the experiments demonstrated, that it is possible to perform ALD to thereby fill the gaps, while
10 maintaining the tubular structures intact, provided that the tubular structures are not reacting during the ALD process.

VI. Additional Processes

A. Extraction of the Template Molecule

In most of the embodiments discussed above, the tubular structures are formed
15 around a template molecule. In order for the tubular structures to permit passage of materials therethrough, it is necessary to remove the template molecule.

Removal of the template molecules may be achieved by treating the patterned surface region with a material capable of selectively detaching, dissociating or removing the template material without affecting the stability or integrity of the tubular structures.
20 Alternatively, the template molecules may be decomposed or dissolved without affecting the stability or integrity of the tubular structure. Chemical or physical methods or conditions enabling decomposition, dissolution or unthreading/releasing of the template molecules include thermal treatments, use of solvents or etching solutions, sonication/ultrasonication and others such as a flux of a material through the membrane.

25 The template molecule serves a function of associating tubular structures, to ensure that they are co-axially stacked. With its removal, the gap filling layer is used for that purpose. In some embodiments, a portion of the tubular structures is also released along with the template molecule. In order to completely release the template molecule, it should not have even a single functionality that could bind an internally accessible
30 functionality of the tubular structures. In some embodiments, only some of the template molecules are completely released while others are not due to the former or any other issue. In some cases, due to the etching of the substrate or a portion of it, the part of the

template molecule that was used for such association may be further modified in order to release the template molecule.

In some embodiments the template molecule is released without the etching of the substrate or a portion of it.

- 5 In some embodiments it is also required to remove a cap from the tubular structures or to remove a bulky stopper from the template molecule/tubular structures if such were used for surface association of the tubular structures.

B. Etching of the Sacrificial Layer or Attachment to the Permanent Substrate

- 10 In embodiments in which the tubular structures are formed on pores filled with a sacrificial material of a permanent substrate (FIGS. 1A-1H), the sacrificial material is etched, to thereby leave an open hole. The final etching is selective. For example, when the sacrificial material is gold or a gold alloy, iodine can etch the gold/gold-alloy without etching the porous metal/silicon oxide, tubular structures and the layer that filled the gaps
15 between the tubular structures. Alternative etching processes are discussed above, in connection with the description of the substrate.

- In embodiments in which the tubular structures are formed on a substrate which is not the permanent substrate (FIGS. 2A-2D), the layer embedding (skin) tubular structures are attached to the permanent substrate or the permanent substrate is deposited
20 on the embedded layer.

C. Etching of the Gap Filling Layer

- Optionally, etching to some degree the gap-filling-layer (selective or non-selective), from the side that was closer to the initial substrate, is performed. This is
25 possible by using extremely diluted HF buffer solution if the gap-filling-layer is made of an oxide (TiO₂ as an example). This potentially exposes better the tubular structures and increases accessibility. This can also increase the distance between the gap-filling layer and the mouths of the tubular structures, which may decrease sticking of molecules to it. This could also be achieved not just by slow non-selective etching, but by depositing two
30 layers as the gap-filling-layer (Si₃N₄ first and then TiO₂), and after the fabrication of the device to remove by selective etching the first layer or a portion of it (in the example Si₃N₄ is less stable towards vapors of HF than TiO₂). Another option if the initial substrate is a metal like gold, is to evaporate gold before the deposition of the gap-filling-layer

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(gold attaches quite selectively to gold). This gold will be etched with the gold of the initial substrate.

If a monolayer was deposited in order to initiate the ALD for creating the gap-filling-layer, and there is a cleavable link within the molecule of the monolayer, then
5 cleaving the cleavable link could also increase the distance between the gap-filling-layer and the mouths of the tubular structures.

D. Miscellaneous Modifications

Protecting groups at the outer shell and/or mouths of the tubular structures could
10 be removed and further modified. Reasons for protecting/removing of protection/modifications after the removing of the protection may include promoting selective formation of molecular bridges, which is no longer needed following completion of the tubular structures, as well as introduction of anti-sticking groups to promote patterning of the tubular structures, as will be discussed further herein.

15 Burning/plasma/acid/etching could be used to destroy the tubular structures, to leave the channels formed solely of the skin. In such instances, the channels may be completely inorganic. Such pores could further be modified with Atomic Layer Deposition ("ALD") for example. Before modifying the diameter by methods like ALD that shorten the diameter, a mild etching could be performed to achieve later a specific
20 diameter.

Enveloping the sides of the membrane may be performed so that fluxes will not leak from the sides.

E. Modification of the Tubular Structures

25 When the tubular structures were reacted with protecting groups prior to initiation of the ALD, those protecting groups may be removed.

For example, teflonization (protecting with an anti-sticking layer) may be performed prior to the ALD. The teflonization involves reacting with fluoro/per-fluoro compounds to prevent fouling/sticking and increasing chemical stability of the tubular
30 structures. Such modifications could occur at the outer shell of the tubular structure/their mouths, the surface of the gap-filling-layer and at combinations of all of the above. Such a modification can be reacting with a compound that has a Teflon part near the part that will react with the outer shell/mouths of the tubular structures and/or the surface of the

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gap filling layer and possibly that a more distant part will be water soluble. Such teflonization could also prevent forming of ice on the surface of the membrane.

As discussed, the outer shell could be reacted with protecting groups before the ALD, which are afterward cleaved. Cleaving may be desirable because if bulky groups
5 are reacted with the reformed groups, or if the reformed groups are reacted sequentially, they could influence the diameter of the tubular structures (reducing the diameter for an example) and/or affect the flux through them. Also, they could influence the interface between the tubular structures and the gap-filling layer.

Alternatively, some groups do not require protection before the ALD/gap-filling,
10 and could be reacted afterwards.

VII. Building Tubular Structures after Initial Deposition of the Solid Material

A. Pits

In the foregoing discussion, the methods described herein were used for
15 generating tubular structures with through holes. In alternative embodiments, the structures that are created are pits, with solid bottoms.

FIG. 10A schematically illustrates a process in which a pit is created. The process is performed with a substrate 100, to which a template polymer 104 had been attached, and on which a tubular structure 102 had been built with a bulky stopper 103 at the top thereof. Then, gap filling was performed, as discussed. The tubular structure and bulky
20 stopper are then removed, thereby leaving the template molecule associated to the bottom of an open pit.

In cases where all the tubular structure is selectively removed, with or without selectively removing a bulky group if such was present, only a surface associated template
25 molecule is left inside a pit/pore. Note that non-flexible/rigid template molecules will not necessarily coil into the pit obtained after the removal of the tubular structure and bulky stopper. The end of the template molecule could be associated with another molecule.

Subsequently, in some embodiments, a portion of the template molecule 104 is selectively removed, leaving a residue, long or short, a single residue per pit. The obtained
30 residue could be associated with another molecule, which could be very rigid. Some molecules may be harder to associate than others, so an "AB cycle" could be performed, i.e., associating only portions at a time. Uniformity in the lengths could be increased if reacting with a bulky terminal group that could not enter the pit between the "AB cycles",

so association is possible once the lengthened molecule is long enough to extend out of the pit. Such bulky terminal group may be removed before the last required association.

In some embodiments the entire template molecule is removed, by heating and/or oxidizing the surface, leaving a surface with empty pits. The bottom of the pits may be of
5 another material than the material that was used to fill the gaps between the tubular structures, thus obtaining a surface patterned with pits.

In some embodiments before creating the pits, a deposition of an extra layer on top of the gap-filling-layer could be performed. Such a layer could be utilized for different processes, as will be described later. In some cases, the layer has protected functionalities.

10 The former methods could be utilized not just for creating a surface with empty pits, but also for creating surfaces with pits containing a single molecule per pit. This could be obtained, for example, by using rod like branched polymers/dendronized polymers where the links between the main backbone chain and the branches/dendrons are selectively cleavable, as illustrated in FIG. 10B. In FIG. 10B, a rod like dendronized
15 polymer is associated with a bulky group. The gaps between such polymers were filled, and the dendrons 105, could be selectively removed from the main backbone chain. In some cases, the branches/dendrons are also degradable under certain conditions, and their links to the main backbone chain are selectively cleavable. If the obtained main backbone chain is suspected to coil into the pit, and it is desired to prevent this scenario, then
20 association with a bulky group could prevent this. It is required that this bulky group will be larger than the obtained pit.

In some embodiments a surface is patterned by uniform dendrons via a functionality at its stem. The gaps are filled and afterwards the dendrons are selectively etched to leave a residue per pit. Alternatively, the dendrons are removed completely to
25 leave empty pits. Tubular structures which comprise even a single macrocycle (modified at both of its openings) could be used for such patterning with or without the usage of a template molecule.

A surface patterned with empty pits could be used to associate tubular structures to the bottom of the pits via single or plural functionalities at the opening of the tubular
30 structure. In some cases, the dimensions of the pit could allow only a single tubular structure association per pit. Substantial perpendicularity of the tubular structure could be contributed due to the dimensions of the pit. The surface association of a tubular structure could also be performed with a template molecule associated to the bottom of the pit.

In some embodiments, before the creation of the pits, a layer may be deposited. Such a layer could have a non-sticking character, reducing the physical adsorption of tubular structures to the surface between the pits, thus enhancing accessibility to the pits. In some cases, even a non-sticking coating could have protected functionalities. The unprotected functionalities could be used after the surface association of the tubular structures, for example in order to fill the gaps between the tubular structures. In some embodiments a loosely packed non-sticking layer could leave access to enough surface sites for initiating the gap filling. The two methodologies could be combined. In some cases, only the local gaps between a tubular structure and the pit to which it was associated are filled. Depositing a monolayer on the bottom of the pits could enhance this gap filling and also enhance covering pits to which no tubular structures were associated. There are other possible embodiments where a local gap-filling could be used as will be described later.

FIG. 10C depicts a step of local gap filling between a tubular structure and the pit to which the tubular structure was associated. In the scheme, the tubular structure was associated to the bottom of the pit using a single link between the opening of the tubular structure and the bottom of the pit. Diagonal lines 106 denote a layer that blocks growth. Local gap filling material 107 is added around the top of the pit.

Associating a single molecule, which could be a template molecule of a tubular structure or another kind of molecule, rigid for example, into an empty pit, could be done by associating a single residue per pit and associating that residue with another molecule later. Dendrons that have a selectively cleavable chemical bond near their stems, where the tip of the stem has a single functionality for surface association, could be used for associating a single residue per empty pit, if the dimensions of the dendron and the pit could not allow more than one dendron to be associated inside a pit. The dimensions of the dendron and the pit could direct the association to some degree to the center of the pit. In some cases, the dendrons are also degradable under certain conditions and not just one of the links between its atoms is selectively cleavable. Another method to direct the association of a single template molecule relative to the center of the pit is by growing a sacrificial layer around the pit. This may require forming another sacrificial layer in the bottom of the pit before creating the sacrificial layer around the pit. In any case, after creating the sacrificial layer around the pit, the bottom of the pit should be empty. A

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template molecule could be associated to the pit, and the sacrificial layer around the pit could be selectively removed.

A surface with a single molecule in each of its pits, rigid or flexible with associated bulky group at its end could be further modified in order to enhance the entrapment around such molecule. This could be performed by another step of ALD. In some embodiments, especially where such molecule is flexible, ALD could be performed in solution conditions, coupled with stirring and/or sonication/ultrasonication to stretch the molecule. In some cases, an end associated bulky group is also magnetic, and by applying magnetic fields the molecule could be stretched. In some cases, a layer was deposited before the creation of the pits. Such a layer could block the growth of more ALD, thus could direct the gap filling to be more around such molecule without covering it. Note that in some cases it is possible to obtain such entrapment around a molecule that is not a tubular structure, simply by performing the gap-filling process without covering the top of such molecule to a surface associated with tubular structures threaded by a molecule associated to another molecule or alternatively surface associated structural analogues of tubular structures associated at their 'top' end to such another molecule. It is possible to perform more steps with such surfaces as if they were embedding tubular structures in order to form a membrane.

FIG. 10D illustrates a step of enhancing entrapment around a molecule is shown. The diagonal lines denote a layer that blocks growth.

A surface with a single template molecule in each of its pits could be associated with tubular structures, by forming an inclusion complex. In some cases, the opening of the tubular structure can reach the bottom of the pit, while in other cases it cannot. In some cases, the pit is narrower closer to the bottom, for example, because the tubular structure or its structural analogue that was used to create the pit was wider in its upper part, thus the inclusion complex between the introduced tubular structure could be until some point inside the pit. Another case that would lead to the former is where some of the outer shell of the tubular structure is wider.

Fig. 10E illustrates different degrees of hosting tubular structures inside a pit.

Note that different scenarios could lead to a tubular structure wider in some parts (rightmost sketch in FIG. 10E). It is possible that the tubular structure is wider in some parts and the cavity in that part is also wider. In that case, threading with a template

molecule may not be possible due to different abilities of the cavities to form an inclusion complex. In another scenario it is possible that all the parts of the tubular structures will be able to form an inclusion complex with a template molecules because the cavities are the same, and some part is wider due to differences at the outer shell.

5 As discussed, the pits may be utilized for formation of different tubular structures. Certain additional mechanisms for such are disclosed in FIG. 10F and onward.

FIG. 10F illustrates a basic schematic cross section of a structure that is left following removal of the tubular structure, or another material that was used to form the pits. Composite substrate 801 has gold 802 filling a pore that is within. The top of the
10 substrate is covered with gap filling layer 803, which may be of titanium dioxide. A pit 804 is located where the tubular structure had previously been built.

FIG. 10G discloses a second possibility for creation of a pit. In this possibility, the tubular structure is removed from the pit, but the template molecule 805 remains present.

15 What is common to both FIG. 10F and FIG. 10G is that the pit has a significantly narrower diameter than the pore of the composite substrate on which it is arranged. The diameter of the pit may be, for example, in the vicinity of 2 nanometers, or even less. Indeed, sometimes, two pits 804 may fit within the area of a single pore. It is significantly easier to surface associate tubular structures including asymmetric tubular structures to
20 pits of this size as compared to the original pores of the composite substrate. As can be seen already in FIG. 10H, the tubular structure 806 (with bulky stopper 807) may be selected to be wider than the tubular structure or the other material that is used to create the pit 804. As a result, the tubular structure 806 could be bonded with the gap filling layer rather than the base of the pit 804.

25 FIG. 10I illustrates adhering an asymmetric tubular structure 809 to a pitted structure, and in particular illustrates the benefits of protecting the deposited gap filling layer when doing so. On the top left side of the Figure, a tubular structure with a template molecule in a pit is illustrated, as in FIG. 10G. On the top right side, the same structure is illustrated with a monolayer 808 adhered thereto. The monolayer may be
30 polytetrafluoroethylene (PTFE) or any other fluorine-containing molecule. The monolayer may also be of the form surface-Si-CH₂-CH₂-X, in which the X is a leaving group, to which the tubular structure may be bonded. The monolayer helps assure that the

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tubular structure adheres only to the template molecule, as on the right side of the Figure, as opposed to adhering to the surface, as on the left side of the Figure.

B. Local Gap Filling

5 Local gap filling may alternatively be used, independent of the structure of the layers (i.e., tubular structures as in most of the present disclosure, or pits as in the immediately preceding section).

 If a surface with defined and uniform pores was filled selectively with another material inside its pores, then a local gap filling could be used as well. Tubular structures
10 could be associated to the surface of the filled pores. Then, on the outer shell of the 'bottom' part of the tubular structure a layer could be grown. This layer is then associated to the surface between the pores that were filled. Finally, the material that filled the initial pores is selectively removed. Note that the filled pores that were not associated with a tubular structure could be associated with some layer in order to cover such future pores
15 so they will be blocked once the material that filled them is selectively removed.

 In FIG. 11, another embodiment is exemplified where a local gap-filling could be used. Original porous materials 110 had defined pores were filled by another material 111. A tubular structure 112 was associated to the surface of the filled pores, including bulky stopper 113 and template molecule 114, followed by a layer 115 that was grown
20 around the outer shell of the tubular structure. That layer is then associated to the original surface 110, followed by selective removal of the material 111 that filled the pores. Possible removal of a template molecule and/or bulky stopper may be performed, if such were present. This could work also for asymmetric tubular structures.

VIII. Applications

25 While, as discussed above, the materials described herein may be utilized primarily for filtration (extracting the smaller substance/s out of a mixture), other uses are possible as well.

 The structures formed according to the processes described herein modify surface
30 properties of a substrate. The surface property that may be modified by constructing the channels on the surface region may be any one or more of surface roughness, increasing the area of the surface, hydrophobicity, hyperphobicity, hydrophilicity, wetting, surface

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area, electrostatic screening, anti-stick properties, antifouling properties, anti ice-forming properties, self cleaning, and others.

While, typically, passage of materials is from the “entrance” to the “exit” of the channel, where the entrance is at the tip and the exit is at the pore of the substrate, a
5 reverse flow may also occur, such as in a process known as “backwashing.”

Without limitation, the conditions at the different sides of the membranes that influence the passage through the membrane include: pressure differences, partial pressure differences, applying suction from one side and/or applying pressure from the other side, presence of sorbent/s at a side – chemical and/or physical, chemical reaction/s,
10 including flare/s, temperature difference including a temperature low enough to liquefy/solidify a gas, and combinations thereof.

Without limitation, the devices of the present disclosure may be utilized for one or more of the following applications:

Sorption and Extraction. Some macrocycles have known abilities to sorb certain
15 materials. Thus, membranes composed of them, using primarily suction from one side of the membrane, could potentially increase the content of the sorbed material in that side of the membrane. Examples include: cyclodextrins and noble gases, carcerand and argon, pillararene and carbon dioxide, and nanotubes of Calix[4]arenes and NO_x gases.

Sometimes if two materials are smaller than a pore, the larger material will
20 permeate superiorly through the membrane, given a mixture of the two materials.

Catalysis. If at least one product is smaller than all the reactants, its removal, possibly continuously, could shift the equilibrium of such catalysis. Examples include:
 $0.5\text{N}_2 + 1.5\text{H}_2 \rightleftharpoons \text{NH}_3$, $4\text{H}_2 + \text{CO}_2 \rightleftharpoons \text{CH}_4 + 2\text{H}_2\text{O}$, $3\text{H}_2 + \text{CO}_2 \rightleftharpoons \text{CH}_3\text{OH} + \text{H}_2\text{O}$ and
others. In other reactions, hydrogen is released from its carrier/s (possibly organic and
25 liquid) or produced from reacting CO with steam. Exploiting that known phenomenon (the Le Chatelier Principle), it is possible to couple a membrane with suction from one side and/or applying pressure from the other side to a reactor, using catalysis for example, to separate/extract products from reactants in real time and to influence the equilibrium. This could save energy by enabling to form the catalysis at more moderate conditions and
30 thus preserve better the catalyst/s. This could also simplify the separation required for the production.

It is possible to associate a catalyst to the opening of the tubular structures, and by suction/applying pressure/both to couple catalysis and separation.

Passage through the outer shell of tubular structures incorporated in a membrane: It is possible to block the entrance to the pores found at the tips of the tubular structures of a membrane so passage could be performed only through the shell of the tubular structures. It is possible to block them temporarily or permanently by several means. One means is to react groups present only at the tips of the tubular structures with groups to block their entrance (may require sequential reactions). If the groups are protective then the blocking could be temporary. Another means which could be used, especially if the groups found on the tips of the tubular structures are also found on other sites is to form an inclusion complex between the tubular structures and a template molecule that to one of its sides there was attached a bulky group. Such an inclusion complex could be temporary, and it may be necessary to form it from time to time. If the bulky group has a functional group reacting it with groups of the tips of the pores, this blocking could be permanent. However, if the link between the bulky group and the tips is selectively cleavable then this blocking could be temporary. Passage through the outer shell of the tubular structures could be of interest, if for example vicinal macrocycles are associated by bridges that are themselves macrocycles, or form a pore of interest.

A unique example of 'conditioned blocking' is by using a 'molecular valve' in one side of the membrane so passage could be performed only from one side to the other. This could be done by attaching a template polymer to one side of the membrane.

Note that one of the functions of the outer shell of the tubular structures is to block the deposition of the gap-filling-layer within the tubular structures. Thus, tubular structures containing outer shells of interest could be associated to tubular structures already incorporated within a gap-filling-layer.

Sensors/recognition. Surfaces that are precursors to membranes, such as surfaces associated with tubular structures, could be used as a platform for sensors. A tubular structure, even if possessing some flexibility, is substantially perpendicular to the surface and thus is remote from the surface and its possible contaminations. In some embodiments the surface is modified to have anti-stick/antifouling/anti ice-forming properties, for illustration by association with hydrophobic/super-hydrophobic/hyper-hydrophobic compounds (hydrocarbon/fluorocarbon/perfluorocompounds) while the outer shells of the tubular structures are associated with antibodies/macrocycles/single stranded DNA or RNA. In some embodiments antibodies/macrocycles are associated to the bulky stopper, while the surface and/or the outer shell of the tubular structures are modified to have anti-

stick/antifouling/anti ice-forming properties. In some embodiments some of the upper part of the tubular structures is associated with antibodies/macrocycles while the surface and/or some of the bottom part of the outer shell of the tubular structures were modified to have anti-stick/antifouling/anti ice-forming properties.

5 Tuning the density and flexibility/rigidity of the tubular structures with or without association with hydrophobic/super-hydrophobic/hyper-hydrophobic compounds could influence the anti-stick/antifouling/anti ice-forming properties. The presence of a gap-filling-layer could be one of the means used for such tuning. The gap-filling-layer can be used for other reasons, such as protection of the underlying surface, entrapping the tubular
10 structures and more.

 One particular example of interest is where a macrocycle is associated to the tip of a tubular structure with at least two external bridges on opposite or almost opposite sites. Such association could alter the macrocycle's selectivity comparing to other associations. In another example a macrocycle is used as a bridge between vicinal
15 macrocycles of the tubular structures.

 In some embodiments, sensors could be regenerated by cleaning with solvents, with or without heating/ultrasonication.

 A membrane could be utilized to become a sensor, by using pumps and pressure sensors. When keeping one side of the membrane in sub-pressure (once or continuously
20 or from time to time), exposure to a material or materials that can permeate the membrane will increase the pressure on the other side, which could be detected by the pressure sensor. Regeneration of such a sensor could be done via suction and tuning the pressure to the initial sub-pressure. Further cleaning with solvents with or without heating/ultrasonication may be necessary.

25 Where a macrocycle is associated to the tip of a tubular structure with at least two external bridges on opposite/almost opposite sites, whether if the device is a sensor, a membrane or both, the ability to 'doubly protect' the rest of the device – its surface or gap-filling-layer and the outer shell of the tubular structures to have anti-stick/antifouling/anti ice-forming properties by modifications – presents unprecedented
30 protection.

 In some embodiments, a partially formed device, made according to the methods of the present disclosure, may serve as a sensor. Such a partially formed device may

include the tubular structures attached to the porous substrate, without a gap filling layer in between. Such devices may also be used to modify surface properties of the substrate.

Decomposing the embedded tubular structures or other kinds of molecules to create derived membranes.

A prepared membrane with embedded tubular structures and the previously described 'membrane-like' devices where a molecule is integrally entrapped, could be transformed into a new kind of membrane by selectively removing the tubular structures/entrapped molecules within the gap-filling-layer. In some embodiments the tubular structures/entrapped molecules are organic and the gap-filling-layer is a metal/silicon oxide or another ceramic material. It is possible to remove selectively the organic part without harming the ceramic part by several means such as strong acids, burning by high temperature under oxygen environment, oxidizing by strong oxidizing agents, plasma processes, Piranha solution and more. The obtained membrane is completely ceramic. The obtained membrane could be further modified by ALD for example. Note that according to ceramic membranes for nanofiltration (pores of one nanometer and below) are commercially available by only one company, although about 7,000 companies use them. Within the presented methodologies, it is possible to create such ceramic membranes, for example by using tubular structures of α -Cyclodextrin, which have an external diameter of about 1.5 nanometers, and which after their selective removal the derived ceramic pores could easily be tuned further to be one nanometer or below.

It is also possible to etch under extremely diluted conditions of an etching factor the ceramic membranes, for example so later more space of the pore will be available to different combinations of modifications, or for other possible modifications such as the next. It is also possible to coat the ceramic surface of the membrane with hydrophobic/hyper-hydrophobic/super-hydrophobic molecules such as hydrocarbons/fluorocarbon/perfluoro compounds, by forming a monolayer or sequentially by forming a multilayer. These modifications could be used to control the slipperiness of the pores of the membranes. It is recommended to clean the ceramic surface by Piranha or plasma before such coating. Potential applications will be described in the next section.

Water Desalination. The ability of ceramic nanofiltration membranes to desalinate water is discussed in the art. That art also discusses the ability of hydrophobic slippery pores about 1 nanometer in diameter to desalinate water. The previously

described methods, where the organic part was removed and their further hydrophilic or hydrophobic/superhydrophobic/hyperhydrophobic modifications could be used to fabricate both types of such membranes.

Moreover, membranes composed of tubular structures could have pores below 1
5 nanometer, and thus could possibly desalinate water. Macrocycles with either hydrophobic or hydrophilic internal cavities could be associated to other macrocycles with either hydrophobic or hydrophilic internal cavities (finally all the cavities of the resultant tubular structure could be all hydrophobic, or all hydrophilic or mixtures). The association between the macrocycles itself could be performed with either hydrophobic
10 or hydrophilic or mixtures of bridges between the macrocycles (the internal side of the bridges is the important side of the bridge to this manner) and/or hydrophobic or hydrophilic or a mixture of a gap-filling-layer.

Hydrogen transport using existing natural gas pipelines. Separating hydrogen from natural gas is important. Pure hydrogen cracks steel, which comprises natural gas
15 distribution pipelines. However, a mixture of hydrogen and natural gas does not crack steel. Using membranes, enabling the passage of hydrogen while blocking the natural gas could be used to transport Hydrogen via those pipelines while substantially keeping the natural gas trapped inside such pipelines.

Hydrogen Storage. Separating hydrogen from its carrier/s (which are larger than
20 hydrogen) using a membrane could keep such carrier/s, possibly volatile, trapped inside the storage system. The discharge of hydrogen uses catalysis, thus a membrane can enable to perform the discharge at more moderate condition/s and/or better preserve the catalyst and/or the carrier and its derivative/s.

If hydrogen is stored in CH_3OH then it could be released in two manners. In the
25 first, CH_3OH is exposed to catalyst following the equilibrium $\text{CH}_3\text{OH} \rightleftharpoons 2\text{H}_2 + \text{CO}$. The smaller H_2 could be selectively removed/extracted using a membrane. The remaining CO could be reacted with H_2O (possibly steam) to produce more H_2 . The second option is to add water to the CH_3OH and to use a membrane for extracting the formed H_2 .

When extracting H_2 from a carrier in the presence of H_2O , which are smaller than
30 H_2 , more membrane/s may be used, for example to first extract H_2O from the mixture, and/or extra water may be added to the carrier/s to release more H_2 once or from time to time. If H_2O is added to be reacted with H_2 carrier/s, then they could be added in advance at precise quantities, once or more times.

The released H₂ may be consumed using flame/internal combustion engine, or alternatively fuel cells. Even if using fuel cells, the usage of membranes prohibits the need that O₂ and the carrier will be mixed, thus the membrane could keep the carrier/s and its/their derivative/s locked within the storage system.

- 5 If NH₃ is the H₂ carrier, then despite NH₃ being smaller than H₂, a catalyst could be used to release the H₂ (and N₂) from the NH₃, and after this catalyst is removed from the system, a membrane, possibly combined with a flare/sorbent could be used to selectively remove remains of NH₃.

- 10 Membrane/s may be used not just for H₂ removal from its carrier/s, but also for other required purification/s before and/or after and/or during the releasing of H₂ from its carrier/s and its/their derivative/s, and/or other required purification/s before and/or after and/or during reacting H₂ with the discharged form/s of its carrier/s.

Gas Diffusion. Membranes could be used as a selective gas diffusion layers, when their skin is towards a solution.

- 15 When extracting substances out of a mixture, it is possible to place the pulling (and pushing) piston/s in a chamber under sub pressure or vacuum, in order to use less energy.

CLAIMS:

1. A filter configured to allow communication of substances from one side to another side, and configured to separate substances passing therethrough, comprising:
 - a mechanically stable porous substrate;
 - 5 a solid material in contact with the porous substrate, the solid material defining a skin having at least one channel, each channel having at least one entrance at a surface of the skin and at least one exit at a pore of the porous substrate;
 - wherein the entrance of each channel has a diameter which is 3 nm or less.
2. The filter of claim 1, wherein the at least one channel is comprised of the solid
- 10 material, without any additional material encased therein.
3. The filter of claim 1, wherein the at least one channel is comprised of the solid material, with one or more tubular structures comprised of macrocycles overlaid on the solid material.
4. The filter of claim 1, wherein the at least one channel is comprised of one or
- 15 more tubular structures comprised of macrocycles that are at least partially embedded within the solid material.
5. The filter of claim 4, wherein each tubular structure comprises a stack of macrocycles having a first internal diameter which are coaxially associated.
6. The filter of claim 5, wherein the macrocycles are comprised of cyclodextrins,
- 20 calixarenes, pillararenes, porphyrins, crown ethers, helical molecules, cubril[n]s, cucubriturils, aspherands, kekulenes, cage molecules, metallic macrocycles, carbon nanotubes, or any combination thereof.
7. The filter of claim 4, wherein the macrocycles have a substantially frustum-like shape.
- 25 8. The filter of claim 7, wherein a molecular orientation of adjacent macrocycles comprises one or more of: wide-wide associations, narrow-narrow associations, and wide-narrow associations.
9. The filter of claim 4, wherein each macrocycle or tubular structure in the stack is bound to one or more adjacent macrocycles or tubular structures in the stack with the
- 30 filler material.
10. The filter of claim 4, wherein each macrocycle or tubular structure in the stack is linked to adjacent macrocycles or tubular structures in the stack with one or more molecular bridges.

11. The filter of claim 4, wherein a top portion of each channel comprises an asymmetric tubular structure, wherein the asymmetric tubular structure includes at least one macrocycle having a second internal diameter which is narrower than the first internal diameter.

5 12. The filter of claim 11, wherein the at least one macrocycle having a second internal diameter is at a tip of the asymmetric tubular structure, such that the tip comprises an entrance of the channel.

13. The filter of claim 12, wherein the skin extends to above a height of the tip molecule but does not encase the entrance of the channel.

10 14. The filter of claim 11, wherein the at least one molecule having a second internal diameter is within the asymmetric tubular structure but not at a tip thereof, such that the asymmetric tubular structure has an hourglass-like configuration.

15 15. The filter of claim 11, wherein the at least one molecule having a second molecular diameter is a crown ether.

16. The filter of claim 4, further comprising at least one stopper molecule and elongated molecule attached to the at least one stopper and inserted within a top of an uppermost tubular structure in the channel, such that a gap between the stopper molecule, elongated molecule, and the top of the uppermost tubular structure is a second internal diameter, wherein the second internal diameter is narrower than the first internal diameter
20 and comprises an entrance to the channel.

17. The filter of claim 4, wherein the entrance of at least one channel is blocked due to at least one of the following:

- 25 a) a stopper molecule and elongated molecule attached to the at least one stopper and inserted within a top of an uppermost tubular structure in the channel;
- b) an elongated molecule attached to the solid material and inserted within a top of an uppermost tubular structure in the channel; and
- c) deposition of solid material in a manner that buries the top of an uppermost tubular structure in the channel;

30 and wherein a passage between adjacent macrocycles at an outer shell of the at least one tubular structure defines a second internal diameter, wherein the second internal

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diameter is narrower than the first internal diameter and comprises an entrance to the channel.

18. The filter of claim 4, further comprising at least one elongated molecule inserted with a top of an uppermost tubular structure in the channel and chemically
5 associated to the uppermost tubular structure in the channel or to the solid material, such that the uppermost tubular structure and at least one elongated molecule define a second internal diameter, wherein the second internal diameter is narrower than the first internal diameter and comprises an entrance to the channel.

19. The filter of claim 4, wherein the skin encases a lower portion of the at least
10 one tubular structure and does not encase an upper portion of the at least one tubular structure; wherein the lower portion of the at least one tubular structure comprises macrocycles that are associated with each other in a manner that preserves gaps that are greater than a size of an entrance to the channel; and wherein the upper portion of each tubular structure comprises macrocycles that are associated with each other in a manner
15 that reduces gaps between adjacent macrocycles to below the size of the entrance to the channel.

20. The filter of claim 4, wherein the solid material embeds the at least one tubular structure without being adhered thereto in a chemical link.

21. The filter of claim 4, wherein the solid material is adhered to the at least one
20 tubular structure with at least one chemical link.

22. The filter of claim 4, wherein the at least one tubular structure further comprises one or more anti-sticking functional groups on an exterior face thereof.

23. The filter of claim 1, wherein the at least one channel extends from the entrance thereof to the exit thereof at a pore of the porous substrate, in a substantially
25 uniform width.

24. The filter of claim 1, wherein the at least one channel comprises a narrower portion adjacent to the pore of the porous substrate.

25. The filter of claim 1, wherein the substrate comprises an anodic aluminum oxide (AAO).

30 26. The filter of claim 1, wherein at least a portion of the solid material is deposited via atomic layer deposition.

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27. The filter of claim 26, wherein the solid material deposited via atomic layer deposition is one or more of titanium dioxide, silicon dioxide, aluminum oxide, or silicon nitride.

28. The filter of claim 1, wherein at least a portion of the solid material is deposited via molecular layer deposition.

29. The filter of claim 1, wherein a diameter of the entrance is between 2.5 and 4.5 angstroms.

30. A method of manufacturing a filter, comprising:

building at least one tubular structure over at least one pore of a porous substrate that is filled with a sacrificial pore-filling material, each tubular structure comprised of a coaxial stack of associated macrocycles;

filling gaps between tubular structures with a solid gap-filling material;

and removing the sacrificial pore-filling material from the pores of the porous substrate;

to thereby generate at least one channel in which the solid material defines a skin, an entrance of each channel is at a surface of the skin and an exit of each channel is at a pore of the porous substrate;

wherein the entrance of each channel has a diameter which is 3 nanometers or less.

31. The method of claim 30, further comprising, prior to the building step, filling the pores of the porous substrate with the pore-filling sacrificial material.

32. The method of claim 31, further comprising, prior to the step of filling the pores, layering a sacrificial layering material over the porous substrate, wherein the sacrificial layering material is configured to form associations with both the sacrificial pore-filling material and with the porous substrate, wherein the step of filling pores comprises adhering the pore-filling material to the sacrificial layering material, and further comprising, following the step of filling pores, selectively etching the sacrificial layering material to thereby leave the porous substrate with pores filled with the pore-filling material.

33. The method of claim 32, wherein the porous substrate is a high surface area ceramic material.

34. The method of claim 32, wherein the porous substrate is anodized aluminum oxide, the sacrificial pore-filling material is gold, and the sacrificial layering material is silver.

35. The method of claim 30, further comprising, prior to the building step,
5 selecting a substrate comprised of a sacrificial layering material; depositing a porous layer on the sacrificial substrate; and filling pores of the porous layer with the pore-filling sacrificial material, to thereby adhere the pore-filling material to the sacrificial layering material, and selectively etching the sacrificial substrate.

36. The method of claim 35, wherein the porous substrate is a high surface area
10 material.

37. The method of claim 35, wherein the porous substrate is a ceramic.

38. The method of claim 30, wherein each tubular structure comprises a stack of macrocycles having a first internal diameter which are coaxially associated.

39. The method of claim 38, wherein the macrocycles are comprised of
15 cyclodextrins, calixarenes, pillararenes, porphyrins, crown ethers, helical molecules, cubril[n]s, cucubriturils, aspherands, kekulenes, cage molecules, metallic macrocycles, carbon nanotubes, or any combination thereof.

40. The method of claim 30, wherein the macrocycles have a substantially frustum-like shape.

20 41. The method of claim 30, wherein a molecular orientation of adjacent macrocycles comprises one or more of: wide-wide associations, narrow-narrow associations, and wide-narrow associations.

42. The method of claim 30, wherein the building step comprises:

25 patterning a template molecule on the sacrificial pore-filling material;
and threading at least a portion of at least one tubular structure around the template molecule.

43. The method of claim 42, wherein the step of patterning a template molecule comprises:

30 attaching a precursor molecule to the sacrificial pore-filling material, the precursor molecule formed of an X-Y-Z structure, wherein the Z functional group is configured to bond with the pore-filling material, and the X-Y bond is cleavable; and
cleaving the X-Y bond.

44. The method of claim 43, further comprising, following cleaving of the X-Y bond, bonding the template molecule to the Y group.

45. The method of claim 43, wherein X is any type of branched polymer.

46. The method of claim 42, further comprising forming at least one molecular
5 bridge between coaxial and vicinal tubular structures while the tubular structures are threaded on the template molecule.

47. The method of claim 42, further comprising:

attaching a bulky stopper to the template molecule, to thereby form a rotaxane or polyrotaxane;

10 forming the at least one molecular bridge when the bulky stopper is attached to the template molecule; and

removing the bulky stopper and template molecule.

48. The method of claim 42, wherein the threading step is performed when the tubular structures and porous substrates are immersed in solution.

15 49. The method of claim 48, further comprising one or more of ultrasonication or heating the solution.

50. The method of claim 48, wherein the solution is a dilute solution.

51. The method of claim 42, further comprising, following the step of filling gaps, removing the template molecule.

20 52. The method of claim 38, further comprising, following the step of filling gaps, lengthening the template molecule, and threading at least one additional macrocycle or tubular structure onto the lengthened template molecule.

53. The method of claim 52, wherein the step of lengthening the template molecule is performed with click chemistry.

25 54. The method of claim 30, further comprising: threading a template molecule attached to a bulky stopper into an entrance of each channel, to thereby define a passage into each channel based on dimensions of the entrance, of the bulky stopper, and of a portion of the template molecule near the entrance of each channel.

30 55. The method of claim 30, further comprising forming the tubular structures prior to the building step by forming molecular bridges between macrocycles in solution.

56. The method of claim 55, wherein the step of building the tubular structures comprises introducing macrocycles into a solution containing template molecules, to thereby thread the macrocycles around the template molecules.

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57. The method of claim 56, further comprising ultrasonicated the solution.

58. The method of claim 56, wherein the solution is a saturated solution.

59. The method of claim 55, wherein the step of forming molecular bridges comprises:

5 modifying at least one functional group of each macrocycle; and
 forming one molecular bridge between adjacent macrocycles by associating the
macrocycles at the modified functional groups, to thereby generate a train of macrocycles.

60. The method of claim 59, further comprising:

 threading the train of macrocycles on a template molecule having a bulky stopper
10 removably attached at one end;
 attaching a bulky stopper to a second end of the template molecule;
 forming at least a second molecular bridge between adjacent macrocycles, to
thereby generate a ladder of macrocycles;
 cleaving the removable bulky stopper from the template molecule; and
15 removing the template molecule from the ladder of macrocycles.

61. The method of claim 55, further comprising forming the bridges in sequential reactions, in which each sequential reaction increases a proximity of different portions of the macrocycles to each other, thereby enabling the subsequent reactions.

62. The method of claim 55, further comprising forming the bridges with at least
20 one branched bridge using a linker molecule that forms connections between adjacent macrocycles at two or more locations.

63. The method of claim 62, further comprising adding additional functional groups onto the linker molecule, following attachment of the linker molecule to the adjacent macrocycles, and adding one or more additional bridges between the adjacent
25 macrocycles with the additional functional groups.

64. The method of claim 55, wherein the tubular structures formed in solution are asymmetric tubular structures, said asymmetric tubular structures comprising of a coaxial stack of associated macrocycles having a substantially identical internal diameter, and a macrocycle having a second internal diameter, said second internal diameter being
30 narrower than the first internal diameter of the macrocycles of the coaxial stack.

65. The method of claim 64, wherein the bridges between macrocycles that are adjacent to the tip molecule reduce a gap between said macrocycles to less than the second internal diameter.

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66. The method of claim 64, wherein the second internal diameter between 2.5 and 4.5 angstroms.

67. The method of claim 64, further comprising lengthening an asymmetric tubular structure in solution by associating the asymmetric tubular structure with a symmetric tubular structure.

68. The method of claim 67, wherein the lengthening step comprises forming a semi-rotaxane including a template molecule inserted into both the symmetric tubular structure and the asymmetric tubular structure, associating the asymmetric and symmetric tubular structures, and removing the template molecule.

69. The method of claim 55, further comprising, prior to the building step, modifying the tubular structures with anti-sticking functional groups on an outer shell thereof.

70. The method of claim 55, further comprising, prior to the building step, modifying the tubular structures with branched polymers, to thereby promote spacing and perpendicularity of the tubular structures in relation to the substrate, and, prior to the filling step, if said branched polymers do not form chemical connections with the filler material, removing said branched polymers.

71. The method of claim 30, wherein the building step comprises patterning the at least one tubular structure directly onto the at least one pore.

72. The method of claim 71, wherein the patterning step comprises patterning tubular structures having contained therein at least one template molecule that is associated to at least one bulky stopper.

73. The method of claim 72, wherein the at least one bulky stopper is chemically linked to the at least one tubular structure.

74. The method of claim 30, wherein the filling step comprises performing atomic layer deposition (ALD).

75. The method of claim 74, wherein the solid gap-filling material is one or more of titanium dioxide, silicon dioxide, aluminum oxide or silicon nitride.

76. The method of claim 75, further comprising, prior to the ALD, attaching precursor molecules to the tubular structures, such that the gap-filling material is directly linked to the tubular structures.

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77. The method of claim 74, further comprising, prior to the ALD, attaching protecting groups to the tubular structures, such that the gap-filling material does not adhere to at least some parts of the tubular structures.

78. The method of claim 74, further comprising, during the ALD process, using
5 scavengers or etchants to regenerate functionalities found at the outer shell of the tubular structures in a super cycle process.

79. The method of claim 30, wherein the filling step comprises performing molecular layer deposition.

80. The method of claim 30, further comprising sequentially lengthening the
10 tubular structures after the filling step, and repeating the filling step with respect to the lengthened tubular structures.

81. The method of claim 30, further comprising, after the step of filling gaps, decomposing the tubular structures, to thereby, following the step of removing the sacrificial pore-filling material, obtain channels having a skin formed solely of the solid
15 material.

82. A method of manufacturing a filter, comprising:

selecting a sacrificial substrate, said sacrificial substrate capable of attachment to organic compounds;

attaching a template molecule to the sacrificial substrate;

20 building at least one channel onto the sacrificial substrate, each channel comprised of one or more tubular structures comprised of a coaxial stack of associated macrocycles; filling gaps between the tubular structures by adhering a solid gap-filling material to the sacrificial substrate;

25 attaching a porous substrate to one of the open ends of the tubular structures or the filler material; and

removing the sacrificial substrate and template molecule.

83. The method of claim 82, further comprising lengthening the channels by attaching additional tubular structures to the ends of the channels that had previously been associated with the sacrificial substrate.

30 84. A method of forming a tubular structure comprised of macrocycles connected by molecular bridges in solution, comprising:

modifying at least one functional group of two or more macrocycles; and

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forming one molecular bridge between said macrocycles by associating the macrocycles at the modified functional groups, to thereby generate a train of macrocycles.

85. The method of claim 84, further comprising:

- threading the train of macrocycles on a template molecule having a bulky stopper
- 5 removably attached at one end;
- attaching a bulky stopper to a second end of the template molecule;
- forming at least a second molecular bridge between adjacent macrocycles, to thereby generate a ladder of macrocycles;
- cleaving the removable bulky stopper from the template molecule; and
- 10 removing the template molecule from the ladder of macrocycles.

86. The method of claim 84, further comprising forming the bridges in sequential reactions, in which each sequential reaction increases a proximity of different portions of the macrocycles to each other, thereby enabling the subsequent reactions.

87. The method of claim 84, further comprising forming the bridges with at least
- 15 one branched bridge using a linker molecule that forms connections between adjacent macrocycles at two or more locations.

88. The method of claim 84, wherein the tubular structures formed in solution are asymmetric tubular structures, said asymmetric tubular structures comprising of a coaxial stack of associated macrocycles having a substantially identical internal diameter, and a
- 20 molecule having a second internal diameter, said second internal diameter being narrower than the first internal diameter of the macrocycles of the coaxial stack.

89. The method of claim 88, further comprising lengthening an asymmetric tubular structure in solution by associating the asymmetric tubular structure with a symmetric tubular structure.

- 25 90. The method of claim 88, wherein the lengthening step comprises forming a semirotaxane including a template molecule inserted into both the symmetric tubular structure and the asymmetric tubular structure, associating the asymmetric and symmetric tubular structures, and removing the template molecule.

91. A method of filtering a mixture of two or more substances, comprising:

- 30 exposing the mixture of substances through a filter of any of claims 1-29, wherein at least one of the substances is smaller sized, such that it is configured to pass through the channel, and at least a second of the substances is larger sized, such that it is unable to pass through the channel; and

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passing at least one molecule of the at least one smaller sized substance through the filter.

92. The method of claim 91, wherein the mixture is under a chemical equilibrium.

93. The method of claim 91, wherein the mixture is in contact with a catalyst.