

METHODS FOR IN VIVO AND IN VITRO USE OF GRAPHENE AND OTHER TWO-DIMENSIONAL MATERIALS

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. provisional application 61/951,926 filed March
5 12, 2014 which is incorporated by reference herein in its entirety.

BACKGROUND OF THE INVENTION

The present disclosure generally relates to transportation and delivery of substances in a biological environment, and, more specifically, to methods and devices for transportation and delivery of substances using a carbon nanomaterial.

10 Drug and cell delivery in both immune competent and immune incompetent organisms is a real and current problem in medical research and practice today. Present studies use polymeric devices and hydrogels as a delivery vehicle. Some examples include polytetrafluoroethylene with a backing of unwoven polyester mesh, silicon, hydrogels, alginate, cellulose sulfate, collagen, gelatin, agarose, chitosan and
15 the like. Current delivery vehicles and devices are challenged by biofouling, biocompatibility issues, and delayed response. The thickness of current state devices can limit efficacy as limited diffusion of nutrients can kill cells contained within, or delay bi-directional transport of drugs or molecules that are being sensed. Low permeability, at least in part, due to thickness and mechanical stability in view of
20 physical stress and osmotic stress can also be problematic.

In view of the foregoing, improved techniques for transportation and delivery of substances under a variety of conditions, particularly in a biological environment, would be of considerable benefit in the art. The present disclosure satisfies this need and provides related advantages as well.

SUMMARY OF THE INVENTION

In one aspect, there is provided an enclosure comprising (1) a perforated two-dimensional material comprising graphene or a graphene-based material encapsulating a substance, and (2) a porous substrate providing support to the perforated two-dimensional material, encapsulating at least one substance, such that the substance is released to an environment external to the enclosure by passage through the holes in the perforated two-dimensional material.

The present disclosure describes enclosures formed from perforated graphene or other perforated two-dimensional materials. The enclosures can house various substances therein allowing bi-directional movement of selected substances to and from the interior of the

enclosure, retaining other selected substances therein and preventing entry of yet other selected substances into the enclosure. The enclosure of the disclosure can be employed to release one or more selected substances into an environment external to the enclosure, to allow entry into the enclosure of one or more selected substances from an environment external to the enclosure, to inhibit and preferably prevent entry of one or more selected substances from the external environment into the enclosure, to retain (inhibit or preferably prevent exit) one or more selected substances within the enclosure or a combination of these applications. The hole or aperture size or range of sizes is selected based on the specific application of the enclosure. The term enclosure refer to a space for receiving one or more substances formed at least in part by perforated two-dimensional material, such as a graphene-based material, where one or more substances in the enclosure can exit the enclosure by passage through the perforated two-dimensional material. Similarly, in certain embodiments, one or more substances from the external environment can enter the enclosure by passage through the perforated two-dimensional material. In specific embodiments the external environment is a biological environment, which may be an in vivo biological environment or an in vitro biological environment.

In embodiments, an enclosure comprises one or more than one sub-compartments each sub-compartment comprising perforated two-dimensional material such that at least a portion of the walls or sides forming the sub-compartment are perforated two-dimensional material. Fluid communication is achieved by selective passage of one or more substance in and/or out of the enclosure or sub-compartment thereof. The fluid may be liquid or gas and includes fluids having entrained gases. Substances may be dissolved or suspended or otherwise carried in a fluid. The fluid can be aqueous. A sub-compartment can be in direct fluid communication with adjacent sub-compartments or the external environment (where adjacent sub-compartments share at least one wall or side). In an embodiment one or more sub-compartments can be in direct fluid communication with adjacent sub-compartments, but not in direct fluid communication with the external environment. At least one sub-compartment in an enclosure is in direct fluid communication with an external environment. An enclosure can have various configurations of sub-compartments. A sub-compartment can have any shape. A sub-compartment may, for example, be spherical, cylindrical or rectilinear In an embodiment, sub-compartments can be nested. In an embodiment, the enclosure can have a central sub-compartment which shares a wall or side with a plurality of surrounding sub-compartments. In an embodiment, sub-compartments may be linearly aligned within the

In another aspect, the disclosure provides a method comprising: introducing an enclosure comprising perforated two-dimensional material to a an environment, the enclosure containing at least one substance; and releasing at least a portion of at least one substance through the holes of the two-dimensional material to the environment external to the enclosure. Any enclosure herein can be employed in this method.

In a further aspect, the disclosure provides a method comprising: introducing an enclosure as disclosed herein into an environment, the enclosure containing at least one substance; and releasing at least a portion of at least one substance through the holes of the two-dimensional material to the environment external to the enclosure.

Another aspect relates to a device for delivering a substance to an environment comprising: an enclosure comprising (A) a perforated two-dimensional material comprising graphene or a graphene-based material and (B) a porous substrate providing support to the perforated two-dimensional material, encapsulating a substance, such that the substance is released to an environment external to the enclosure by passage through holes in the perforated two-dimensional material.

The foregoing has outlined rather broadly the features of the present disclosure in order that the detailed description that follows can be better understood. Additional features and advantages of the disclosure will be described hereinafter. These and other advantages and features will become more apparent from the following description.

BRIEF DESCRIPTION OF THE DRAWINGS

For a more complete understanding of the present disclosure, and the advantages thereof, reference is now made to the following descriptions to be taken in conjunction

with the accompanying drawings describing specific embodiments of the disclosure, wherein:

FIG. 1 shows an illustrative schematic demonstrating the thickness of graphene-based material in comparison to conventional drug delivery vehicles and devices. This figure
5 also illustrates an embodiment of the invention in a biological environment in contact with biological tissue in which enclosure is provided with one or more support materials which are external to the perforated two-dimensional material and indicates possible capillary vascularization into such support materials.

FIGs. 2A-D shows illustrative schematics of various configurations of enclosure
10 configurations prepared from two-dimensional material useful according to various embodiments of the present disclosure.

CLAIMS

1. An enclosure comprising (1) a perforated two-dimensional material comprising graphene or a graphene-based material encapsulating a substance, and (2) a porous substrate providing support to the perforated two-dimensional material, encapsulating at least one substance, such that the substance is released to an environment external to the enclosure by passage through the holes in the perforated two-dimensional material.
2. The enclosure of claim 1 encapsulating more than one different substance, wherein not all of the different substances are released to an environment external to the enclosure.
3. The enclosure of claim 2, wherein different substances are released into an environment external to the enclosure at different rates and/or at different relative concentrations
4. The enclosure of claim 1 encapsulating more than one different substance, wherein all of the different substances are released into an environment external to the enclosure.
5. The enclosure of claim 4, wherein different substances are released at different rates and/or at different relative concentrations.
6. The enclosure of claim 1, wherein the enclosure comprises two or more sub-compartments, wherein at least one sub-compartment is in direct fluid communication with an environment external to the enclosure through holes in a two-dimensional material of the sub-compartment.
7. The enclosure of claim 6, wherein each sub-compartment comprises a perforated two-dimensional material and each sub-compartment is in direct fluid communication with an environment external to the enclosure, through holes in the two-dimensional material of each sub-compartment.
8. The enclosure of claim 1, wherein the enclosure is subdivided into two sub-compartments separated from each other at least in part by perforated two-dimensional material, such that the two-sub-compartments are in direct fluid communication with each other through holes in two-dimensional material.

15. The enclosure of any one of claims 1-13, wherein at least one substance within the enclosure that is released to an environment external to the enclosure through holes in two-dimensional material is a drug and wherein the holes in the two-dimensional material range in size from 1-50 nm.
16. The enclosure of any one of claims 1-13, wherein at least one substance within the enclosure that is released to an environment external to the enclosure through holes in two-dimensional material is a drug and wherein the holes in the two-dimensional material range in size from 1-10 nm.

17. The enclosure of any one of claims 1-13, wherein the size of the holes in the two-dimensional material ranges from 3-10 nm.
18. The enclosure of any one of claim s 1-13, wherein the size of the holes in the two-dimensional material ranges from 3-5 nm.
19. The enclosure of any one of claims 1-13, wherein at least a portion of the holes in the two-dimensional material are functionalized.
20. The enclosure of any one of claims 1-13, wherein at least a portion of the two-dimensional material is conductive and a voltage is applied to at least a portion of the conductive two-dimensional material.
21. A method comprising:

introducing an enclosure comprising perforated two-dimensional material to a an environment, the enclosure containing at least one substance; and

releasing at least a portion of at least one substance through the holes of the two-dimensional material to the environment external to the enclosure.
22. The method of claim 21, wherein the environment is a biological environment.
23. The method of claim 21 or 22, wherein the at least one substance a portion of which is released in a drug.

24. A method comprising:

introducing an enclosure of any one of claims 1-13 into an environment, the enclosure containing at least one substance; and

releasing at least a portion of at least one substance through the holes of the two-dimensional material to the environment external to the enclosure.

25. A device for delivering a substance to an environment comprising: an enclosure comprising (A) a perforated two-dimensional material comprising graphene or a graphene-based material and (B) a porous substrate providing support to the perforated two-dimensional material, encapsulating a substance, such that the substance is released to an environment external to the enclosure by passage through holes in the perforated two-dimensional material.

26. The enclosure of claim 1, wherein the perforated two-dimensional material comprises chemical vapor deposition graphene.
27. The enclosure of claim 26, wherein the perforated two-dimensional material comprises two to five layers of chemical vapor deposition graphene.
28. The enclosure of claim 1, wherein the perforated two-dimensional material has been subjected to ion bombardment.
29. The device of claim 25, wherein the porous substrate comprises a track-etched polymer.
30. The device of claim 25, wherein the perforated two-dimensional material comprises chemical vapor deposition graphene.
31. The device of claim 30, wherein the perforated two-dimensional material comprises two to five layers of chemical vapor deposition graphene.
32. The device of claim 25, wherein the perforated two-dimensional material has been subjected to ion bombardment.
33. The device of claim 25, wherein the perforated two-dimensional material comprises one or more graphene domain having a domain size greater than 100 nm to 1 micron.
34. The device of claim 25, wherein the perforated two-dimensional material comprises perforations limited to a 1-10% deviation in size.