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(54) Title: BULK FREEZING OF BIOPHARMACEUTICALS

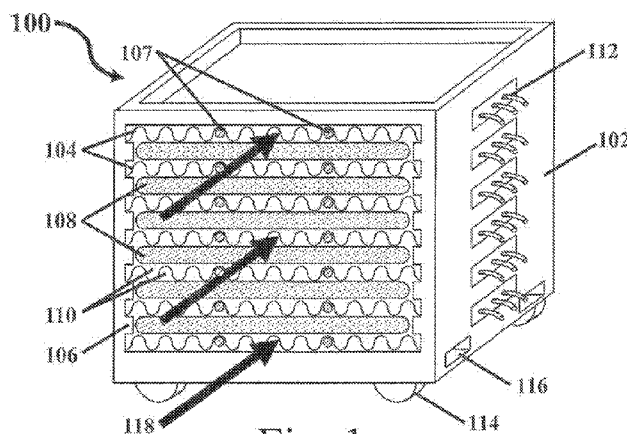


Fig. 1

(57) Abstract: A system and method for bulk freezing is provided. In one embodiment, the system and method for bulk freezing includes a bulk freezing container adapted to hold at least one and preferably a plurality of bags holding a biopharmaceutical liquid. The bulk freezing container includes at least a first and second shelf having corrugations wherein the second shelf is vertically arranged above the first shelf with the bags disposed between the shelves. The bags and the corrugations of the first and second shelves define a plurality of substantially parallel flow channels through which a cryogenic cold fluid or a warming fluid is passed to freeze and/or thaw the biopharmaceutical fluid. In another embodiment, the bulk freezing system and method includes a bulk freezing container with a plurality of adjacent elongated chambers adapted for holding the biopharmaceutical fluid. The adjacent elongated chambers have side walls defining a plurality of substantially parallel flow channels between the plurality of adjacent elongated chambers through which a heat transfer medium is passed for heat exchange through the side walls of the elongated chambers to the fluid within the elongated chambers.



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BULK FREEZING OF BIOPHARMACEUTICALS

FIELD OF THE INVENTION

(0001) This invention relates to systems and methods for bulk freezing/thawing of biopharmaceuticals materials, and more particularly, to systems and methods of bulk freezing that employ a bulk freezing container having a plurality of shelves defining a plurality of parallel flow channels adapted to carry a heat exchange medium through said plurality of flow channels to freeze/thaw bags or containers of the biopharmaceutical materials disposed on the shelves.

BACKGROUND

(0002) Biopharmaceuticals are often times frozen in bulk form to stabilize the product and build up inventory. When the biopharmaceutical is needed, the frozen product is transferred to a fill and finish operation for subsequent thawing and distribution.

(0003) Current bulk freezing systems provide freezing of material in various ways. In a one approach, bottles or containers are simply filled and placed in a freezer. Such an approach is labor intensive and offers little scalability and control over the freezing and thawing processes. In another method, disposable bags are vertically hung in a freezer. The vertically hung bags may sag into a pear shape under the weight of the contained liquid. The resulting uneven cross section down the length of the bag results in differences in the freezing of the material in different sections of the bag. Furthermore, each bag must be manually handled during filling, hanging in a freezer, removal from a freezer, storage, and subsequent thawing. During each handling stage, the bags are subject to possible damage and/or tearing. Another method utilizes a vessel with internal jacketed slots that are each arranged to receive multiple bags and to cool the bags placed into the slots. However, bags in contact with the jacketed slots offer the potential for non-uniform heat transfer due to imperfect and/or non-uniform contact between the bags and the jacketed slots. In addition, the disposable bags used in the jacketed slots require similar handling as described above for the vertically hung bags.

(0004) Each of the above systems is labor intensive and/or prone to damage of filled bags or containers during multiple required handling steps. Due to non-uniform shapes and thermal contact, the above systems do not facilitate controlled freezing of a material. This lack of control may result in yield losses of biopharmaceuticals on the order of approximately 5% to 50%. Furthermore, the above described systems are not easily scaled for larger volumes and do not provide adequate handling controls for the product during freezing, storage, and

delivery. A system and method is needed that is easily scalable and provides uniform, controllable, and repeatable freezing of bulk biopharmaceuticals while minimizing possible damage to the product due to handling.

SUMMARY OF THE INVENTION

(0005) The inventor has recognized and appreciated a need for providing a system that offers ease of handling, scalability of volumes, and greater uniformity and control of a freezing and/or thawing process with minimal handling by personnel. More generally, the inventor has recognized the advantages of providing a device and method capable of freezing or thawing a fluid using a plurality of flow channels capable of exchanging heat with multiple separate or interconnected volumes.

(0006) In one exemplary embodiment, a bulk freezing system includes at least first and second shelves having corrugations. The second shelf is located vertically above the first shelf. The system includes at least one bag, adapted for holding a fluid, which is horizontally disposed between the first and second shelf. The bag and the corrugations of the first and second shelves define a plurality of substantially parallel flow channels through which fluid or other medium may flow.

(0007) In a further exemplary embodiment, a method includes: providing first and second shelves having corrugations; providing at least one bag, adapted for holding a fluid, which is horizontally disposed between the first and second shelf, wherein the at least one bag and the corrugations of the first and second shelves define a plurality of substantially parallel flow channels; filling the at least one bag with a fluid; and flowing a heat exchange fluid or medium through the plurality of flow channels while the bag is disposed between the first and second shelves to transfer heat with respect to the liquid in the at least one bag.

(0008) In yet another exemplary embodiment, a system includes an upper structure with at least two adjacent elongated chambers adapted for holding a fluid. The elongated chambers have side walls. A lower support platform supports the upper structure. At least one flow channel is located between the at least two adjacent elongated chambers for heat exchange through the side walls of the at least two adjacent elongated chambers.

(0009) In a further exemplary embodiment, a method includes: providing an upper structure comprising at least two elongated chambers adapted for holding a liquid, wherein the at least two elongated chambers have side walls; providing at least one flow channel located between the at least two adjacent elongated chambers; supporting the upper structure with a support

platform; filling the at least two elongated chambers with a fluid ; flowing a heat exchange medium through the at least one flow channel; and freezing or thawing the fluid .

(00010) In another exemplary embodiment, a shipping and/or storage container includes an outer shell. The outer shell has a front and back surface with a front window located on the front surface and a back window located on the back surface. The front and back windows are adapted and arranged to permit a flow of cooling medium or other heat exchange medium to pass through the shipping container and a plurality of flow channels of a parallel flow container enclosed therein. A parallel flow container includes exemplary systems such as those described above.

(00011) In a further exemplary embodiment, a method includes: providing at least one shipping and/or storage container comprising an outer shell having a front and back surface, wherein a front window is located on the front surface and a back window is located on the back surface, wherein the front and back windows are adapted and arranged to permit a flow of cooling medium to pass through the shipping container and a plurality of flow channels of a parallel flow container enclosed therein; enclosing at least one parallel flow container in the at least one shipping container; and flowing a heat exchange medium through the at least one shipping container and the at least one parallel flow container. A parallel flow container includes exemplary systems such as those described above.

(00012) It should be appreciated that all combinations of the foregoing concepts and additional concepts discussed in greater detail below (provided such concepts are not mutually inconsistent) are contemplated as being part of the inventive subject matter disclosed herein. In particular, all combinations of claimed subject matter appearing at the end of this disclosure are contemplated as being part of the inventive subject matter disclosed herein.

(00013) The foregoing and other aspects, embodiments, and features of the present teachings can be more fully understood from the following description in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

(00014) The accompanying drawings are not intended to be drawn to scale. In the drawings, each identical or nearly identical component that is illustrated in various figures is represented by a like numeral. For purposes of clarity, not every component may be labeled in every drawing. Various embodiments of the invention will now be described, by way of example, with reference to the accompanying drawings, in which:

- (00015) Fig. 1 is a schematic perspective view of a parallel flow container including corrugated shelves and fluid filled bags;
- (00016) Fig. 2 is a schematic front view of a parallel flow container including corrugated shelves and fluid filled bags;
- (00017) Fig. 3a is a schematic perspective view of a parallel flow container including elongated chambers;
- (00018) Fig. 3b is a schematic perspective view of an elongated chamber;
- (00019) Fig. 4 is a schematic front view of a parallel flow container including elongated chambers;
- (00020) Fig. 5 is a schematic perspective view of a support platform;
- (00021) Fig. 6 is a schematic perspective view of a parallel flow container including removable elongated chambers;
- (00022) Fig. 7 is a schematic side view of a parallel flow container and a flow of cooling or warming medium;
- (00023) Fig. 8 is a schematic perspective view of a parallel flow container being placed in a freezing or thawing system;
- (00024) Fig. 9 is a schematic perspective view of a shipping container used with a parallel flow container; and
- (00025) Fig. 10 is a schematic perspective view of a shipping container connected to a flow of cooling or warming medium through a connection to the front window.

DETAILED DESCRIPTION

(00026) It should be understood that aspects of the invention are described herein with reference to the figures, which show illustrative embodiments in accordance with aspects of the invention. The illustrative embodiments described herein are not necessarily intended to show all aspects of the invention, but rather are used to describe a few illustrative embodiments. Thus, aspects of the invention are not intended to be construed narrowly in view of the illustrative embodiments. It should be appreciated, then, that the various concepts and embodiments introduced above and those discussed in greater detail below may be implemented in any of numerous ways, as the disclosed concepts and embodiments are not limited to any particular manner of implementation. In addition, it should be understood that aspects of the invention may be used alone or in any suitable combination with other aspects of the invention.

(00027) In one possible embodiment a parallel flow container includes a vertical arrangement of shelves, which may each include smooth regularly spaced corrugations. The spacing between each shelf may be sufficient to accommodate a fluid filled bag. The bags may have an elongated configuration and may be horizontally arranged on the shelves. The spacing between the corrugations may be selected to prevent excessive sag in the bags when horizontally disposed on the shelves and/or the bags themselves may be arranged to help resist excessive sagging. By preventing sagging in the bags, the bags may retain a substantially uniform cross section across the length (or other dimension) of the bag in contrast with the non-uniform pear shape that vertically hung bags may assume. When the bags are filled, each bag, and the adjacent corrugations of the shelves above and below each bag, may define a plurality of substantially parallel flow channels. In one embodiment, each fluid filled bag may contact both the shelf it is disposed on and the shelf above it. Contact between a bag and the shelf disposed above it may help to further define the flow channels located above each bag. In some embodiments, the bags may be filled to a desired size or pressure to establish a desired contact pressure with the shelves the bags are disposed between. The contact pressure may be selected to secure the bags in the parallel flow container for freezing and/or shipping.

(00028) During respective freezing and thawing processes, a cooling or warming medium (generally, a heat transfer medium) may be passed through the flow channels to cool or warm the material in the bags. Since flow channels are defined on both the upper and lower surface of each bag, heat may be transferred from both the upper and lower surface of each bag. Furthermore, the cooling or warming medium may be in direct contact with the bags mitigating non-uniform contact issues. In some embodiments, the temperature of the cooling or warming medium may be varied during a freezing or thawing process to actively control the temperature profile of the material contained in the bags.

(00029) While some embodiments of the system may use uniform bag sizes and each bag may contain the same material, the current invention is not limited in this regard. In some embodiments, the system may be adapted to accept different size bags and may be used to freeze or thaw multiple products and materials at once. In other embodiments, the system may include multiple and different sized bags. In another embodiment, the bags may be disposable. In still further embodiments the bags may be filled and/or emptied while disposed between the shelves. In addition, the parallel flow container may be intended to act as a storage unit for the bags during filling, freezing, storage, shipping, and thawing. In such an arrangement, personnel would only need to insert and remove empty bags from the system substantially

minimizing the risk of damaging or tearing a bag while it is filled, frozen, transported, thawed and/or emptied. In addition, the bags may be filled and/or emptied sequentially or at the same time through connections provided to each bag. In one embodiment, the parallel flow container may use bags ranging in volume from 1 liter to 200 liters each. The combined total volume of each bag included on a parallel flow container could range from 10 liters to 5,000 liters or more. A production sized bioreactor could include volumes ranging from 15,000 to 20,000 liters.

(00030) In another embodiment, a parallel flow container includes an upper structure and a lower support platform. The upper structure includes at least two adjacent elongated chambers incorporated into the upper structure. The elongated chambers may be vertically oriented or otherwise arranged to hold a fluid and in some embodiments may contain a combined volume of fluid of at least 10 liters, 100 liters, 200 liters, or more. The individual elongated chambers may either be filled individually, or they may be linked to a single fluid inlet, or fluid source, to permit simultaneous filling of each elongated chamber. A heat exchange medium flow channel may be located between adjacent elongated chambers, so that each flow channel guides a flow of cooling or warming medium between adjacent elongated chambers. In some embodiments the flow of heat exchange medium may be substantially unidirectional, uniform in temperature, uniform in flow rate, and/or laminar with respect to each flow channel. Heat may be transferred between the material in the elongated chambers through the side walls of the adjacent elongated chambers to the flow of cooling or warming medium. The elongated chambers may have a thickness substantially smaller than their width and depth to increase the effective heat transfer area available for the transfer of heat between the flow of cooling or warming medium and the material contained in the elongated chambers. The temperature of the cooling or warming medium may be varied during a freezing or thawing process to actively control the temperature profile of the material contained in the elongated chambers.

(00031) In some embodiments the elongated chambers may be integrally formed with the upper structure. In other embodiments, the elongated chambers may be individually formed and are selectively removable from the upper structure. The elongated chambers may be retained in the upper structure using any appropriate means. In some embodiments, the elongated chambers are retained in the upper structure using: slots, guide rails, locking mechanisms, magnets, or any other appropriate structure or combination of structures. In other

embodiments, a plurality of removable elongated chambers may be used to provide an adjustable total storage volume or may be used as part of a modular container design.

(00032) The lower support platform may be operatively joined to the upper structure using any number of methods. In one possible embodiment, the support platform includes grooves that interlock with the elongated chambers extending from the upper structure. Such an arrangement not only provides stability for the overall structure, but may also provide support for each elongated chamber, helping to mitigate possible buckling and/or displacement of individual elongated chambers. In other embodiments, the support platform may be operatively joined to the upper structure using any appropriate joining method including, but not limited to, ultrasonic welds, bolts, rivets, and adhesives. In still other embodiments, it is possible that the upper structure and lower support platform are integrally formed with one another, or that the upper structure simply rests on the support platform without any attachment.

(00033) In some embodiments, the above described parallel flow containers may be used in conjunction with a shipping container. The shipping container may include an outer shell and front and back windows. The front and back windows may be arranged to permit a flow of cooling or warming medium to pass through the shipping container and the flow channels of a parallel flow container contained therein. The shipping container may be located in a flow of cooling or warming medium, or the flow of cooling or warming medium may be provided through a connection to the windows of the shipping container. In one embodiment a parallel flow container may be preassembled into a shipping container incorporating the above disclosed features. Consequently, the parallel flow container may be filled, frozen, stored, shipped, thawed, and emptied with a minimal amount of direct handling since it is the outer shipping container that is directly handled. In other embodiments, a parallel flow container may be filled and/or frozen prior to enclosing the parallel flow container in a shipping container.

(00034) The shipping container may also include front and back window covers to seal and/or insulate the container during storage and shipment. In some embodiments, the shipping container includes temperature monitoring and logging equipment as well as space to hold a cold material, such as dry ice, to maintain a cold temperature during shipment.

(00035) While the above systems have been described for use with flows of cooling or warming medium as might be observed in forced convection systems, the invention is not limited in this regard. The systems may also be used with conventional freezing or thawing

systems without the need for a forced flow of cooling or warming medium. In some embodiments, the above disclosed systems may be used in cryogenic freezers. When used in a cryogenic freezer, the cooling medium could include cryogenic liquid, cryogenic cold gas, and/or mixtures of the two. The systems may also be used with bulk freezing or thawing systems. When used in such a manner, the parallel flow containers may simply be rolled into a chamber for exposure to the heat exchange medium. Alternatively, the parallel flow containers may be operatively connected with a freezing or thawing system that is adapted to provide a flow of heat exchange medium to a single parallel flow container at a time.

(00036) The above disclosed systems may be used with any number of materials to facilitate bulk freezing and preservation of material. Such materials include, but are not limited to, biopharmaceuticals, microorganisms, live cells, stem cells, primary cells, cell lines, small multicellular organisms, complex cellular structures, live or attenuated viruses, nucleic acids, monoclonal antibodies, polyclonal antibodies, biomolecules, nonpeptide analogues, peptides, proteins, RNA, DNA, oligonucleotides, and/or viral particles.

(00037) Turning now to the figures, several possible embodiments are described in further detail. Figs. 1 and 2 present a schematic perspective view and a front view of one embodiment of a parallel flow container 100. The parallel flow container 100 may be used to either freeze or thaw a solution. Parallel flow container 100 includes a support structure 102. Corrugated shelves 104 are incorporated into support structure 102. Corrugated shelves 104 support bags 108 adapted for holding a liquid. In some embodiments, bags 108 are disposable. In the depicted embodiment, corrugated shelves 104 are supported by ledges 106. While ledges 106 are depicted for supporting corrugated shelves 104, any appropriate method for supporting shelves 104 may be used including, but not limited to, peg and slot structures, welds, bolts, rivets, and interlocking tabs. In some embodiments, horizontal supporting rods 107 may be used to prevent the corrugated shelves 104 from sagging under the weight of filled bags 108. In one embodiment, at least one substantially horizontal supporting rod 107 may be arranged in at least one flow channel of each corrugated shelf 104. While a horizontal support has been shown, other arrangements and types of supports may be used to prevent the corrugated shelves 104 from sagging.

(00038) Bags 108 are horizontally arranged on the corrugated shelves 104. The spacing between the corrugations may be selected to prevent excessive sag in the bags when horizontally disposed on the shelves. By preventing sagging in the bags and arranging them in a horizontal orientation, the bags may retain a substantially uniform cross section across the

length of the bag for exposure to a flow of cooling or warming medium. When filled, bags 108 and the corresponding corrugations of the shelves above and below each bag define a plurality of substantially parallel flow channels 110. In some embodiments, bags 108 may be filled to a pressure and/or volume so as to contact the shelf above each bag. Contact between the bags and the shelves above each bag may further define the flow channels above each bag and may help to retain the bags in the parallel flow containers. A flow of cooling or warming medium 118 (direction of flow is indicated by the arrows) may be supplied to flow channels 110. The direction of the flow 118 is preferably substantially parallel to the flow channels 110. To ensure adequate cooling or warming medium can flow through flow channels 110, the corrugations of each shelf may be adapted to adequately support the bags 108 with minimal sag into the space between adjacent corrugations. In some embodiments, the corrugations may be smooth and regularly spaced.

(00039) In some embodiments bags 108 may include tubes 112. Support structure 102 and tubes 112 may be arranged and adapted to permit bags 108 to be filled and/or emptied while disposed between shelves 104. If the parallel flow container was used to freeze, store, ship and subsequently thaw a solution, personnel would only need to insert and remove empty bags from the parallel flow container 100 substantially minimizing the risk of damaging or tearing a bag due to manual handling. In another embodiment tubes 112 associated with each of the plurality of bags 108 may be used to fill/empty each bag at the same time to improve overall throughput of the system.

(00040) To facilitate the transport of the parallel flow container 100, support structure 102 may incorporate one or several transportation systems. In one embodiment, the parallel flow container 100 includes rollers or wheels 114. In another embodiment, the parallel flow container 100 includes fork lift holes 116. It is also possible for a system to incorporate both of the above features or any other appropriate transportation aid including, but not limited to, handles, tethers, hooks, air platform support, and skids. By incorporating transportation systems, the parallel flow container may easily be moved between filling, freezing, storage, packaging, and shipment areas.

(00041) Figs. 3a and 4 present a schematic perspective view and a front view of another embodiment of a parallel flow container 300. The parallel flow container 300 may be used to either freeze or thaw a solution. The parallel flow container 300 includes an upper structure 302 and a lower support platform 304. At least two elongated chambers 306 adapted to hold liquid are incorporated with upper structure 302. In one embodiment, the elongated chambers

306 are integrally formed with the upper structure 302. Adjacent elongated chambers 306 are separated by flow channels 308 defined by the side walls of adjacent elongated chambers 306. In some embodiments all adjacent elongated chambers are separated by flow channels 308. Fig. 4 depicts flow channels 308 as the shaded regions between elongated chambers 306. A fluid inlet 310 may be in fluid communication with all of the elongated chambers 306 to provide simultaneous filling of all elongated chambers 306 at once. Alternatively, each elongated chamber 306 may include a separate fluid inlet 310 permitting different volumes and/or materials to be contained in each elongated chamber 306.

(00042) In some embodiments, flow channels 308 are a plurality of substantially parallel flow channels that direct a flow of cooling or warming medium 318 (direction of flow is indicated by the arrows). In a preferred embodiment, flow 318 is substantially unidirectional and parallel to the flow channels defined by gaps 308. Flow 318 may also be laminar and uniform in temperature and flow rate with respect to each flow channel 308. Heat may be exchanged between a material contained in the elongated chambers and flow 318 through the side walls of adjacent elongated chambers 306 that define flow channels 308.

(00043) Fig. 3b is a schematic perspective view of an elongated chamber 306 from parallel flow container 300. Each elongated chamber 306 has a thickness t , a width w , and a depth d extending in a direction substantially parallel to the flow of cooling or warming medium through the system. In some embodiments, the elongated chambers may have a thickness substantially smaller than their width and depth to increase the available surface area for heat transfer between the flow of cooling or warming medium and the material contained in the elongated chambers. Furthermore, each elongated chamber 306 may have the same thickness, or, alternatively, some elongated chambers 306 may have different thicknesses. In another possible embodiment, the thickness of each blade (elongated chamber) is selected to reduce concentration gradients in a frozen solution and/or temperature gradients present across the thickness of the elongated chambers 306 during a freezing or thawing process. Elongated chambers 306 may be used to subdivide a larger volume of solution into smaller discrete volumes to facilitate faster and/or more uniform freezing of the solution. In other embodiments, elongated chambers 306 have uniform cross sections for exposure to the flow of cooling or warming medium extending along the path of flow channels 308.

(00044) Fig. 5 presents a schematic perspective view of a lower support platform 304 incorporated into the parallel flow container 300 of Figs. 3a-4. Support platform 304 may optionally include grooves 304a that interlock with the elongated chambers 306 of Figs. 3a-4.

Such an arrangement not only provides stability for the overall structure, but may also provide support for each elongated chamber helping to mitigate possible buckling or displacement of individual elongated chambers. In other embodiments, the support platform 304 may be operatively joined to the upper structure using any appropriate joining method including, but not limited to, ultrasonic welds, bolts, rivets, and adhesives. In another embodiment, it is possible that the upper structure and lower support platform are integrally formed with one another, or the upper structure may simply rest on the support platform without being physically joined to the platform.

(00045) Fig. 6 is a schematic perspective view of another embodiment of a parallel flow container 600 that includes individual removable elongated chambers 606. Upper structure 602 may be constructed to enable each elongated chamber 606 to be selectively inserted and removed from the system. Alternatively, only some of the elongated chambers 606 may be adapted for removal from the upper structure. Similar to the embodiments described above, a plurality of substantially parallel flow channels 608 are located between adjacent elongated chambers 606. Each elongated chamber 606 may include a separate fluid inlet 610. The elongated chambers may be retained in the upper structure using any appropriate means. In some embodiments, the elongated chambers are selectively retained in the upper structure using: slots, guide rails, locking mechanisms, magnets, or any other appropriate structure or combination of structures. In one embodiment, a plurality of removable elongated chambers may be used to construct a modular parallel flow container to accommodate a variable total volume of fluid.

(00046) Fig. 7 is a schematic side view of a parallel flow container 700 and a flow of cooling or warming medium 718. The flow entering the parallel flow container 700 is labeled as flow 718a. The flow exiting the parallel flow container 700 is labeled as flow 718b. In one embodiment, flow 718 proceeds through the parallel flow container 700 with minimal recirculation of medium within the system. In another embodiment, flow 718a may be substantially uniform in temperature and flow rate across the front surface of parallel flow container 700. In a further embodiment, flow 718a is substantially parallel to the flow channels through parallel flow container 700 and/or substantially laminar.

(00047) Fig. 8 is a schematic perspective view of a filled parallel flow container 802 being placed in a freezing or thawing system 800. In some embodiments, parallel flow container 802 may simply be rolled, or similarly transported, into and out of the system 800. System 800 may either be sized for a single parallel flow container 802, or may be a bulk

freezing or thawing system sized for a plurality of parallel flow containers 802. In one embodiment, system 800 is a bulk freezing or thawing system capable of delivering forced convective flows substantially uniform in temperature and flow rate through a parallel flow container 802. Such a system may actively adjust the temperature profile of the flow of cooling or warming medium provided to the parallel flow container 802 during a freezing or thawing process. In one embodiment, freezing or thawing system 800 is a bulk cryogenic freezer. The bulk cryogenic freezer could provide a source of liquid cryogen, cold cryogenic gas, or suitable mixtures of the two to one or more parallel flow containers 802. In other embodiments, a system 800 may be a freezer that includes nucleation controls including, but not limited to, temperature spike nucleation, pressure change induced nucleation, ice fog nucleation, low pressure induced nucleation, crystal seeding, etching, or additives. A system incorporating nucleation controls may be used to implement more consistent temperature profiles for each batch of material, container-to-container. The system may provide more consistent temperature profiles by controlling not only the temperature of heat exchange medium supplied to the parallel flow containers, but also the amount of sub-cooling a solution may experience prior to nucleation of freezing. In another embodiment, freezing or thawing system 800 is a conventional freezing or thawing system which may be used with parallel flow container 802 without the need for a forced convective flow, nucleation control, or cryogenic temperatures.

(00048) Fig. 9 is a schematic perspective view of an insulated shipping container 900 that may be used with a parallel flow container 902. Filled parallel flow container 902 may either be placed in shipping container 900 prior to or after a freezing process, as the invention is not limited in this regard. Shipping container 900 includes an insulated outer enclosure 904 and insulated top cover 908 that encloses parallel flow container 902. Shipping container 900 may also include front and back surfaces with front and back windows 910. Front and back windows 910 are adapted and arranged to permit a flow of cooling or warming medium 912 to pass through shipping container 900 and the associated flow channels of parallel flow container 902 enclosed therein. Shipping container 900 may further include insulated front and back window covers 914 for covering front and back windows 910 to seal and insulate the container during storage and shipment. When filled parallel flow container 902 is enclosed in shipping container 900, the entire combined system may be placed in a flow of cooling or warming medium similar to that provided by a bulk freezing or thawing system as described above in reference to Fig. 8.

(00049) Alternatively, a flow of cooling or warming medium may be applied directly to the front window 910 through a connection 918 as depicted in Fig. 10. In one embodiment, a parallel flow container 902 is placed into shipping container 900. The combined system may then be used during subsequent filling, freezing, storing, shipping, thawing, and draining processes without the need to remove the inner parallel flow container 902. Such a use minimizes the required direct manual handling of the product and inner container and/or bags. Alternatively, parallel flow container 902 may be filled and frozen prior to being placed in shipping container 900, the current system is not limited in this regard. The combined system may then be used for either all or only some of the subsequent storage, shipping, thawing, and draining processes.

(00050) In some embodiments, insulated shipping container 900 may include temperature monitoring and logging systems 916 to monitor the temperature of the material throughout the freezing, storage, shipping, and thawing processes. Temperature monitoring of the container may be conducted throughout the product cycle to ensure the product has been maintained at an appropriate temperature during preservation, storage, and shipping. Shipping container 900 may also include a space 906 to hold a cold material, such as dry ice or cryogenic liquid, to maintain the frozen product at an appropriate cold temperature during shipment.

(00051) While the present teachings have been described in conjunction with various embodiments and examples, it is not intended that the present teachings be limited to such embodiments or examples. On the contrary, the present teachings encompass various alternatives, modifications, and equivalents, as will be appreciated by those of skill in the art. Accordingly, the foregoing description and drawings are by way of example only.

CLAIMS

1. A bulk freezing system comprising:
 - a bulk freezing container having a first shelf and a second shelf each shelf having corrugations, wherein said second shelf is arranged above said first shelf;
 - a support platform arranged to support said bulk freezing container; and
 - at least one bag adapted for holding a fluid and disposed between said first shelf and said second shelf, wherein said bag and said corrugations of said first and second shelf define a plurality of substantially parallel flow channels.

2. A bulk freezing system comprising:
 - a bulk freezing container having an upper structure comprising at least two adjacent elongated chambers adapted for holding a fluid, wherein said at least two adjacent elongated chambers have side walls, and a plurality of substantially parallel flow channels located between said at least two adjacent elongated chambers for heat exchange through said side walls of said at least two adjacent elongated chambers; and
 - a support platform adapted to support said bulk freezing container.

3. The system of claims 1 or 2, further comprising a source of cryogenic cold fluid arranged to provide cryogenic cold fluid to said plurality of said flow channels within said bulk freezing container.

4. The system of claim 3, wherein said source of cryogenic cold fluid provides a substantially uniform temperature and flow of cryogenic cold fluid to each bag or to said side walls of said elongated chambers within said bulk freezing container.

5. The system of claim 3, wherein said bulk freezing container is moveably disposed in a bulk freezing chamber and said source of cryogenic cold fluid is delivered to said bulk freezing container within said bulk freezing chamber.

6. The system of claims 1 or 2, further comprising a source of warming fluid arranged to provide warming fluid to said plurality of said flow channels within said bulk freezing

container and wherein said source of warming fluid provides a substantially uniform temperature and flow of warming fluid to each bag or to said side walls of said elongated chambers within said bulk freezing container.

7. The system of claims 1 or 2 wherein said fluid is a liquid and comprises biopharmaceuticals, microorganisms, live cells, stem cells, primary cells, cell lines, small multicellular organisms, complex cellular structures, live or attenuated viruses, nucleic acids, monoclonal antibodies, polyclonal antibodies, biomolecules, nonpeptide analogues, peptides, proteins, RNA, DNA, oligonucleotides, and/or viral particles.

8. The system of claims 1 or 2 wherein said support platform includes rollers arranged to moveably dispose said bulk freezing container to one or more prescribed locations including a bulk freezing chamber, a cold storage location, a fluid filling station, or a shipment location.

9. The system of claim 1, wherein said bulk freezing container further comprises a plurality of support rods arranged to support a set (no antecedent basis for set) of said first and second shelf and wherein said plurality of support rods are substantially horizontally arranged in said plurality of substantially parallel flow channels.

10. The system of claim 1, wherein said at least one bag is configured to be filled or emptied while disposed between said first and second shelf.

11. The system of claim 1, further comprising a plurality of bags disposed between said first and second shelf and wherein said bags are arranged to be simultaneously filled or emptied.

12. The system of claim 1, wherein said corrugations of said first and second shelf define flow channels for a plurality of bags disposed above and below each of a set of said first and second shelf.

13. A method for freezing and/or thawing a fluid in a bag comprising the steps of:

providing a bulk freezing container comprising a first shelf and a second shelf each having corrugations;

providing a support platform arranged to support said first and second shelf

providing at least one bag adapted for holding a fluid horizontally disposed between said first and second shelf, wherein at least one bag and said corrugations of said first and second shelf define a plurality of substantially parallel flow channels;

filling said at least one bag with said fluid; and

flowing a heat exchange medium through said plurality of flow channels to transfer heat with respect to said fluid in said at least one bag to freeze or thaw said fluid in said at least one bag.

14. A method for freezing and/or thawing a fluid comprising the steps of:

providing a bulk freezing container comprising a plurality of elongated chambers adapted for holding a fluid, wherein said plurality of elongated chambers have side walls;

providing a plurality of substantially parallel flow channels located between said plurality of adjacent elongated chambers;

providing a support platform to support said bulk freezing container;

filling said plurality of elongated chambers with said fluid;

flowing a heat exchange medium through said plurality of flow channels; and

freezing or thawing said fluid.

15. The method of claims 13 or 14, wherein said method is a method for freezing said fluid and wherein said heat exchange medium is a cryogenic cold fluid.

16. The method of claims 13 or 14, wherein said method is a method for warming said fluid and wherein said heat exchange medium is water.

17. The method of claims 13 or 14, wherein the step of flowing the heat exchange medium through said flow channel(s) further comprises providing a substantially uniform temperature and flow of heat exchange medium via said flow channel(s) to each bag or side wall of said elongated chambers.

18. The method of claims 13 or 14, wherein said fluid is a liquid and comprises biopharmaceuticals, microorganisms, live cells, stem cells, primary cells, cell lines, small multicellular organisms, complex cellular structures, live or attenuated viruses, nucleic acids, monoclonal antibodies, polyclonal antibodies, biomolecules, nonpeptide analogues, peptides, proteins, RNA, DNA, oligonucleotides, and/or viral particles.
19. The method of claims 13 or 14, wherein said support platform includes rollers arranged to moveably dispose the bulk freezing container to one or more prescribed locations including a bulk freezing chamber, a cold storage location, a fluid filling station, or a shipment location.
20. The method of claim 14, wherein said plurality of adjacent elongated chambers are removable from said bulk freezing chamber.

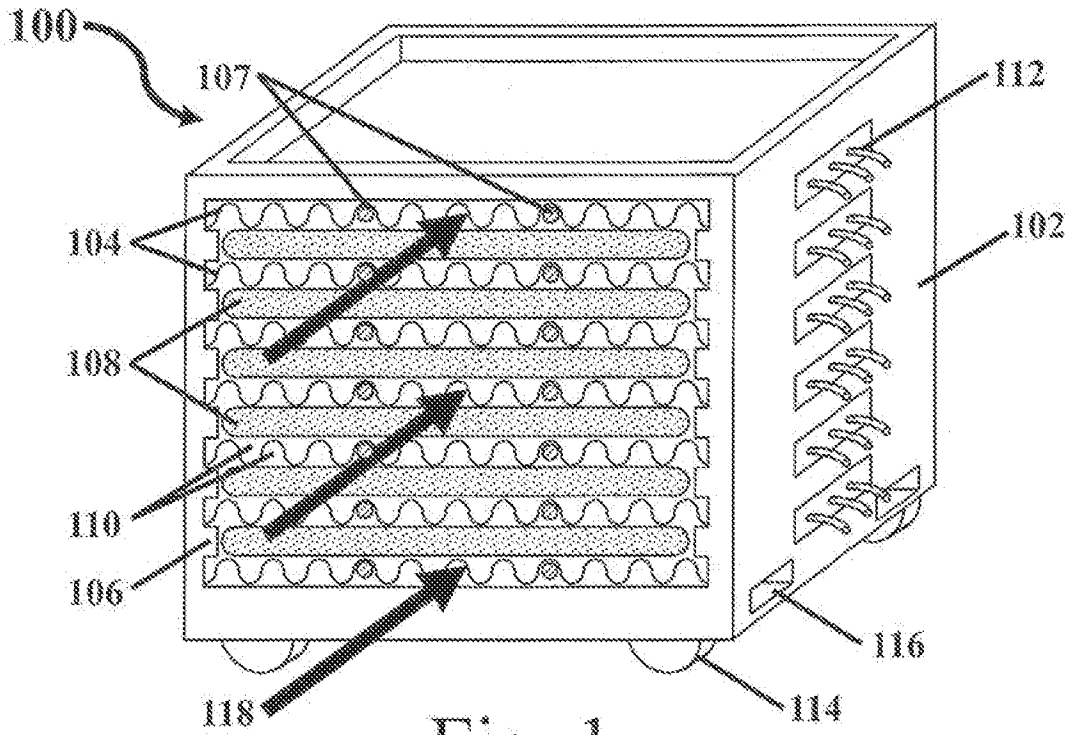


Fig. 1

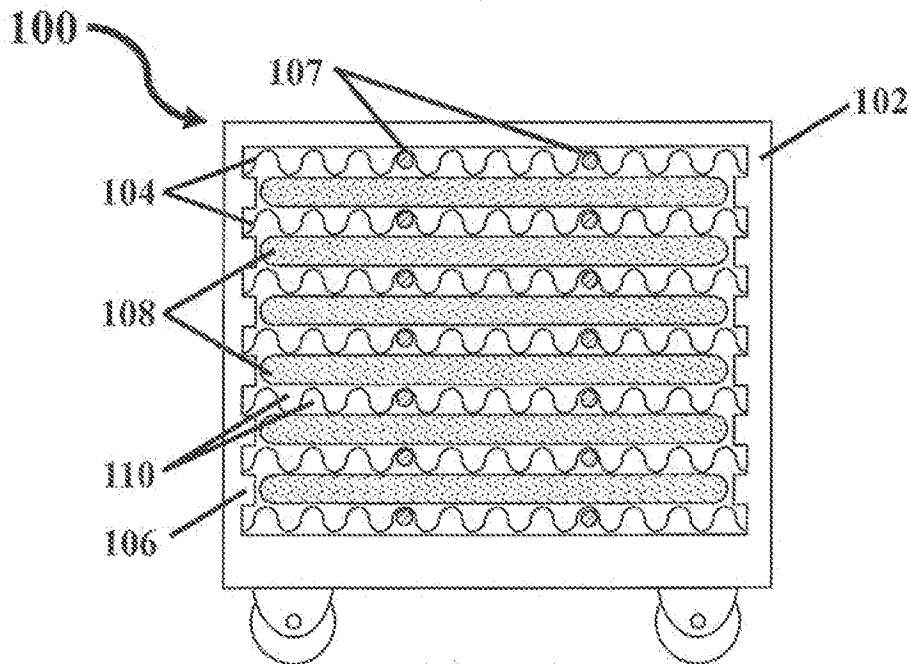


Fig. 2

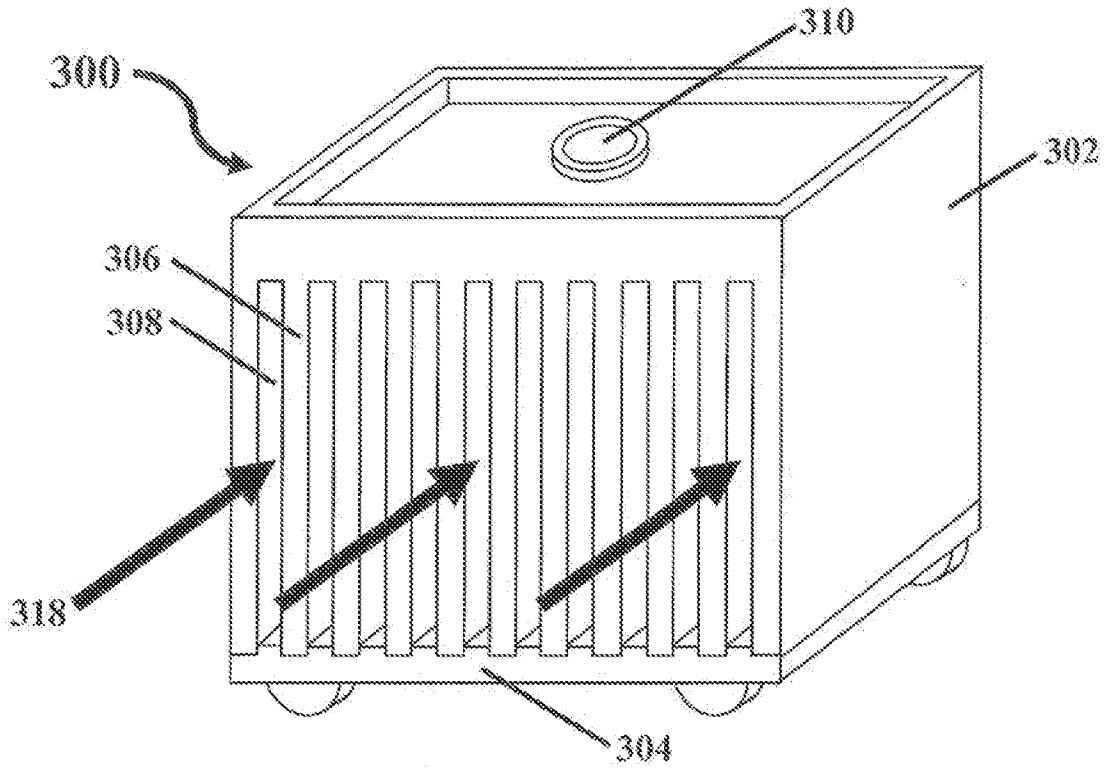


Fig. 3a

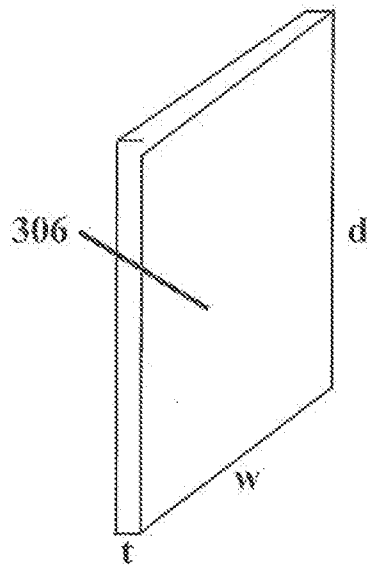


Fig. 3b

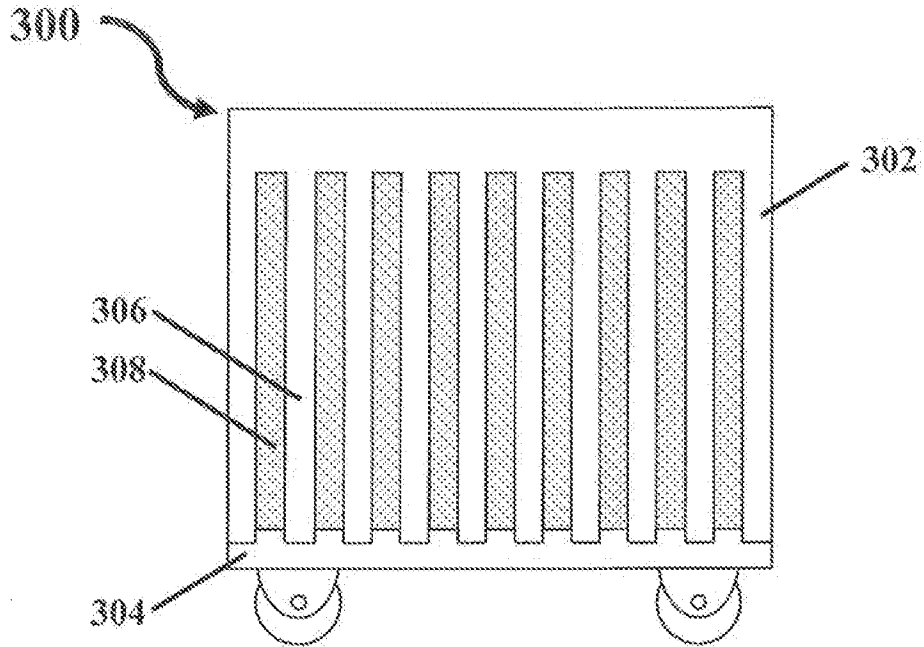


Fig. 4

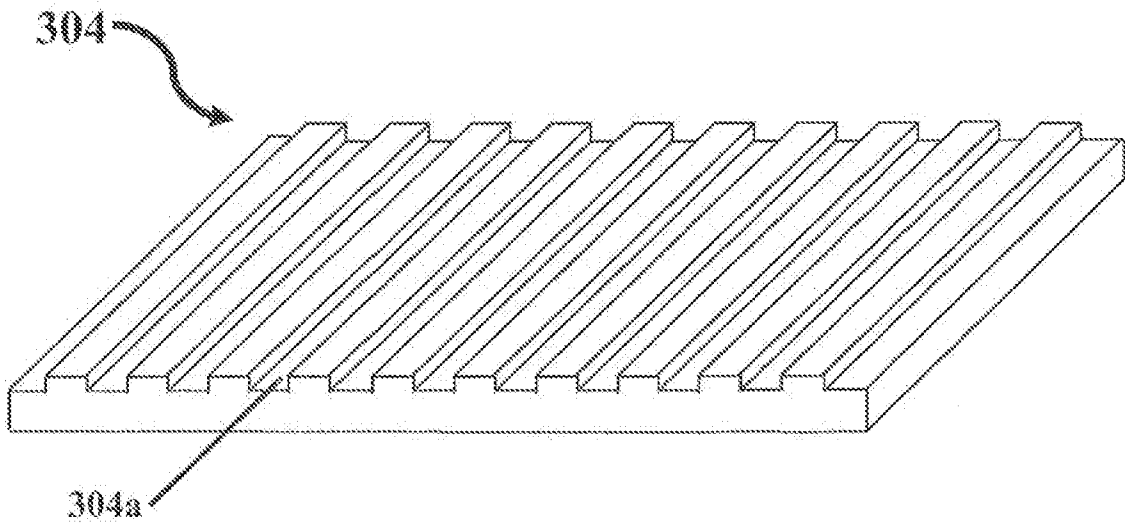


Fig. 5

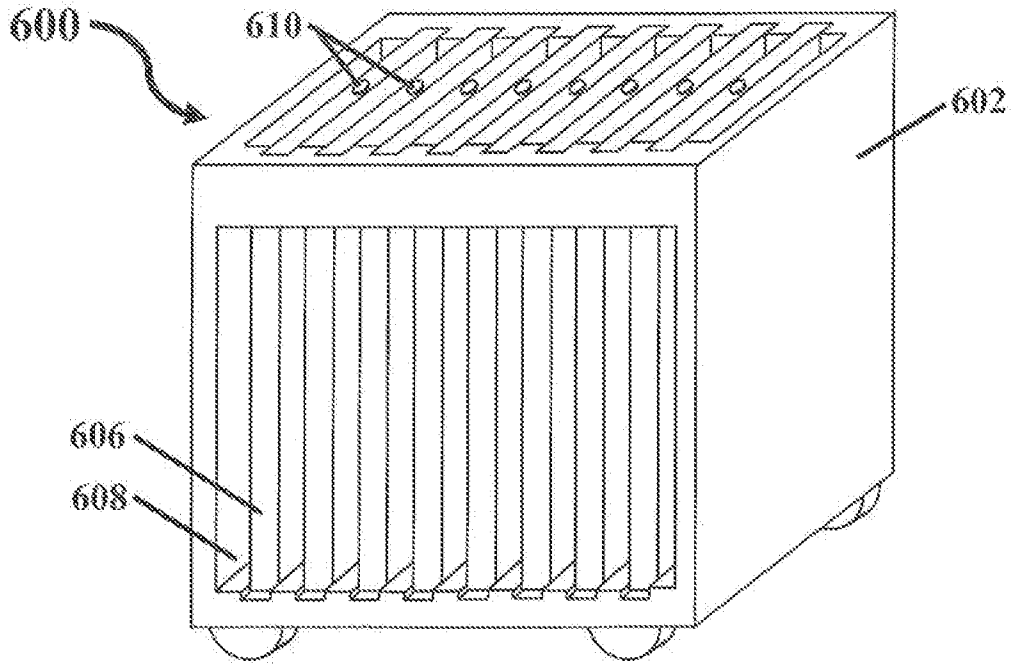


Fig. 6

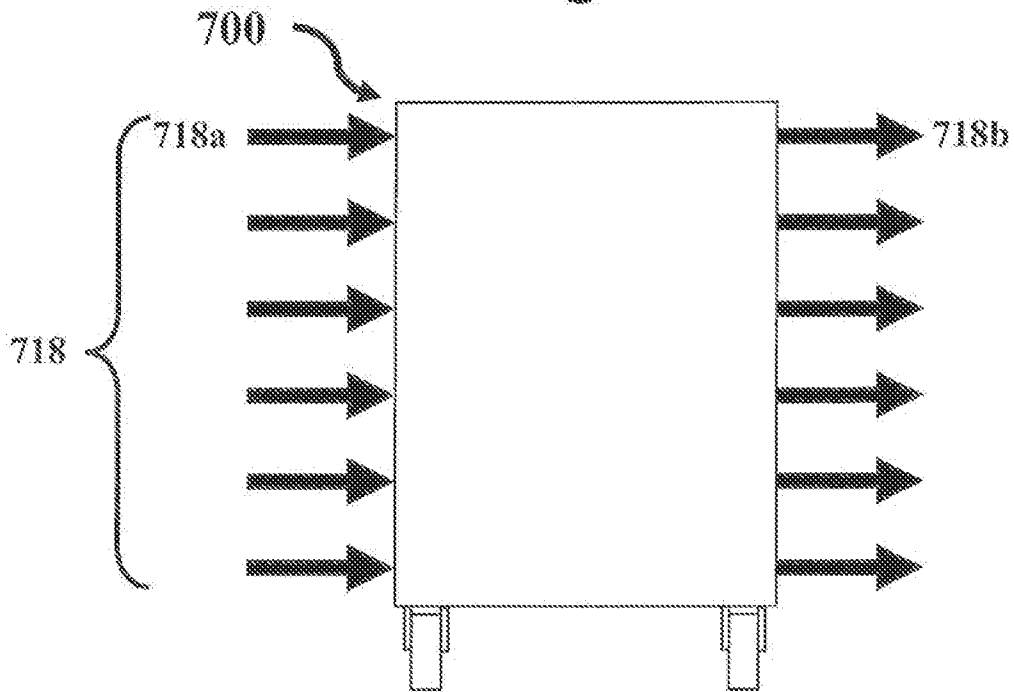


Fig. 7

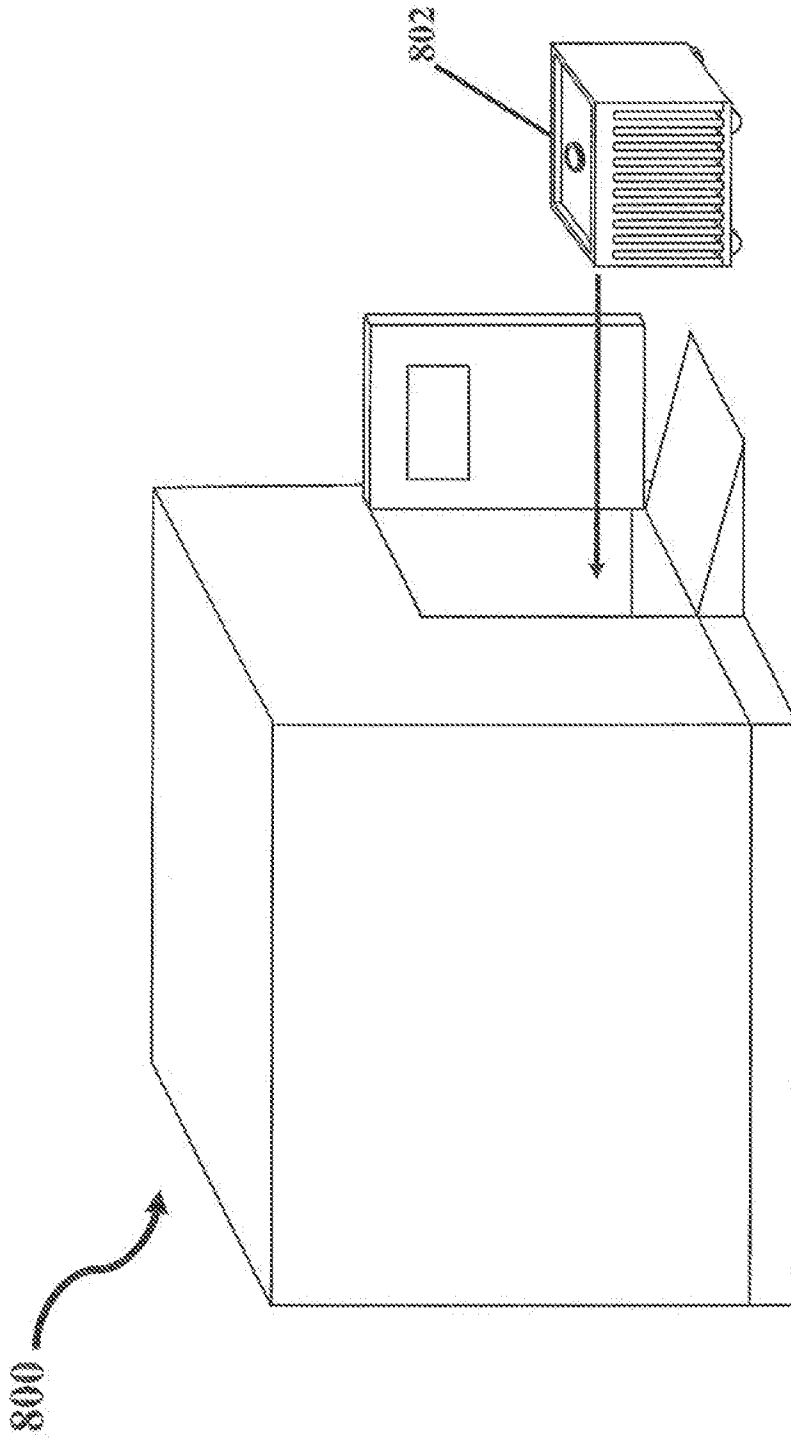


Fig. 8

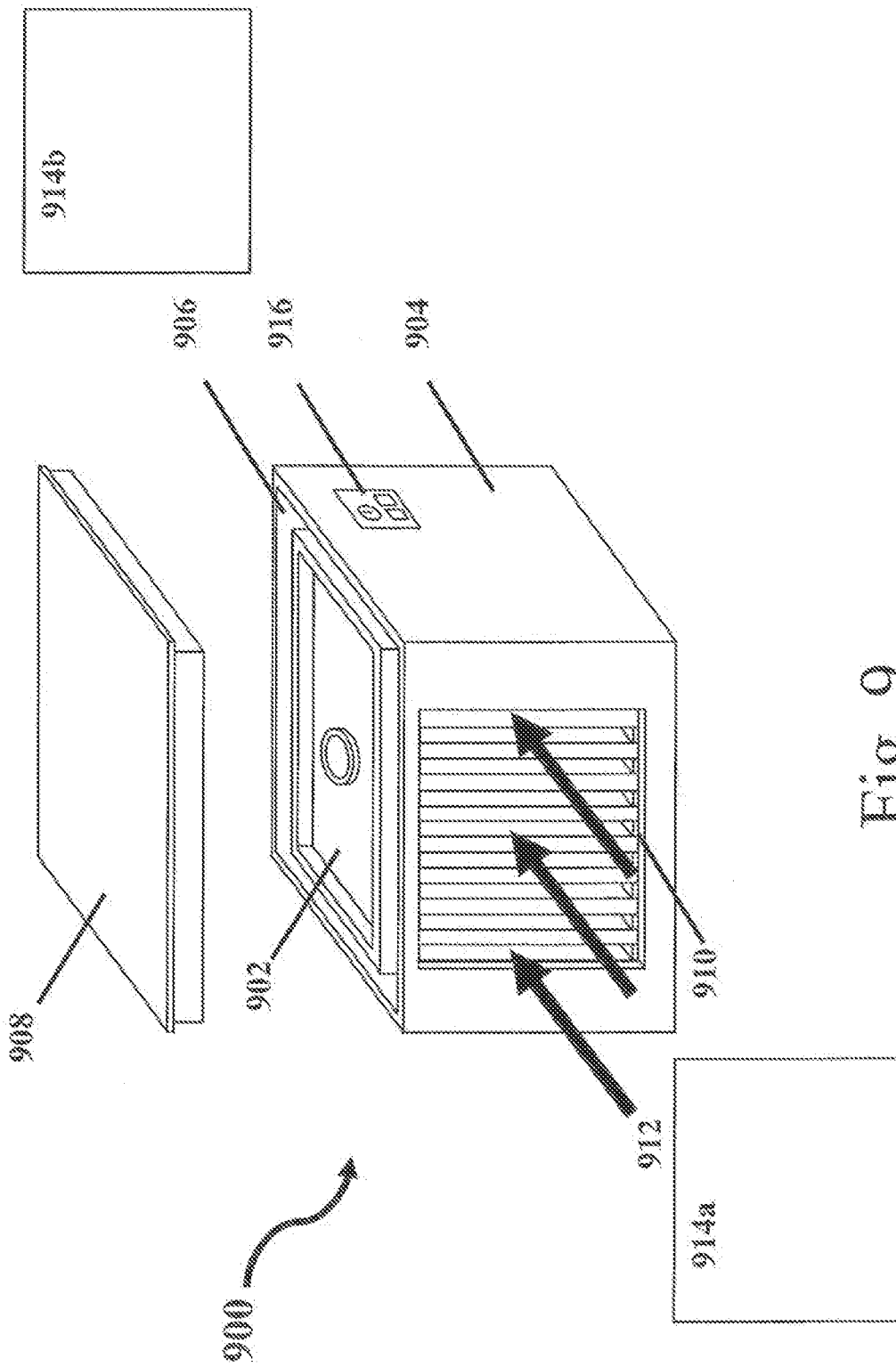


Fig. 9

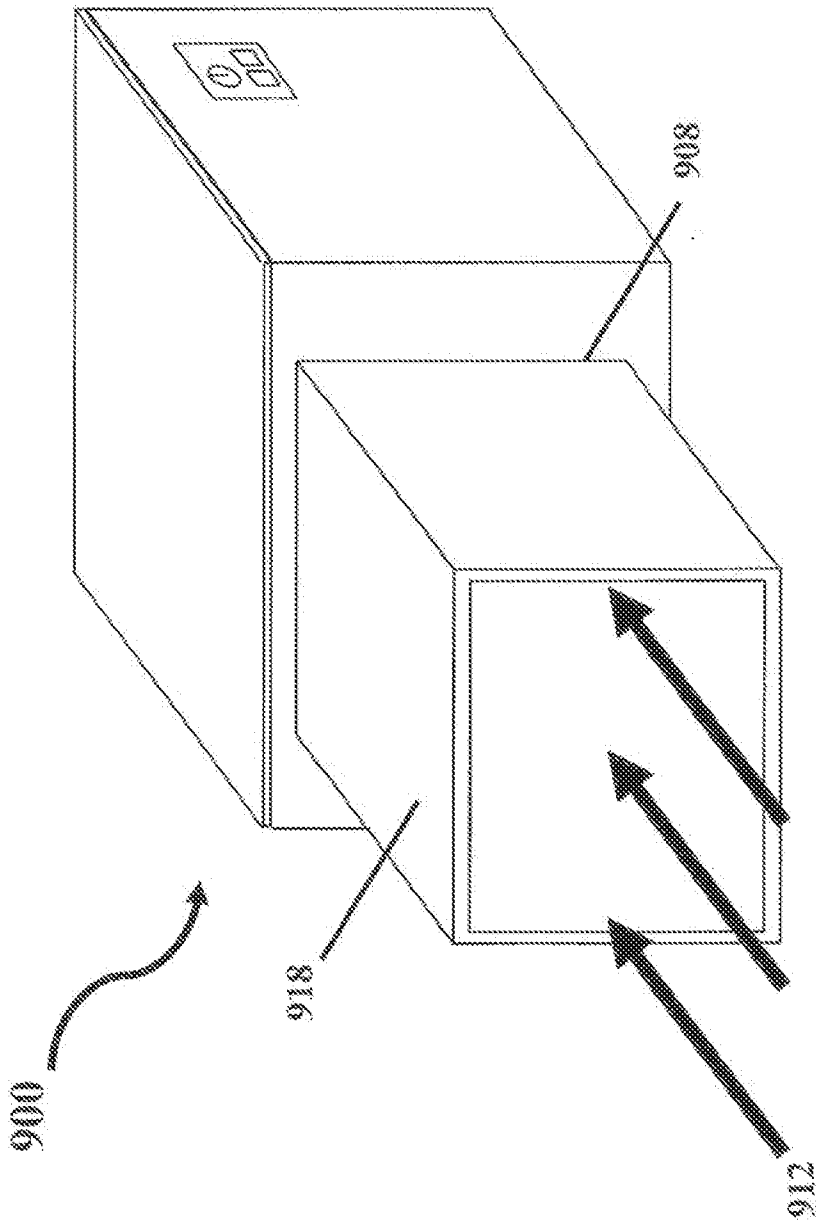


Fig. 10