

METHOD AND DEVICE FOR THAWING BIOLOGICAL MATERIAL

Field of the Technology

[001] The present disclosure relates to a heating device and, more particularly, to systems and methods for thawing biological material.

Background

[002] Various biological materials are typically stored below freezing. For long term storage, cells, peptides, or nucleic acids can be stored at -80°C, -20°C, or at liquid nitrogen at -195°C. Short term storage can include temperatures at or greater than 0°C.

[003] Many biological experiments are typically conducted at temperatures greater than these storage temperatures. For example, eukaryotic cells are often grown at 37°C, while prokaryotic cells often prefer different temperatures.

[004] Traditionally, biological materials are aliquoted in vials and frozen for storage. To heat these vials, a person would usually take each vial and place it in a hot water bath. The person would carefully stir the vial in the bath to ensure uniform heating of the vials contents and to swirl the biological material within the vial. After some time, the person would remove the vial from the water bath and determine if the contents had sufficiently thawed. Once properly thawed, the biological material would be ready for use.

[005] Several problems exist with traditional heating protocols. Firstly, the chance of contamination is high as multiple vials are usually placed in the same water bath. To ensure sterility, the vial is typically wiped with an ethanol solution following removal from the water bath. However, the wipe may not be complete and contaminants may remain on the vial or cap surface.

[006] Secondly, the heating process may not be repeatable from vial to vial as operators introduce human variability. Heating times, swirling duration, swirling speed, etc. may all vary significantly. Because some biological materials are sensitive to

differing thermal gradients, shear forces, or agitation levels, experimental outcomes can be affected.

[07] Thirdly, tracking vials using traditional water baths can be difficult. Labels can be removed by the warm water and markings on the vials can be inadvertently removed by the ethanol wipe.

[08] Finally, thawing may not include uniform heat dispersion. If a portion of material thaws and is not mixed correctly, refreezing may occur. Refreezing can cause re-crystallization and damage cells. An improved thawing device should be optimized to reduce non-uniform thawing and re-crystallization. Accordingly, there is a need for systems and methods to better thaw biological materials.

SUMMARY OF THE DISCLOSURE

[09] One embodiment consistent with the principles of this disclosure is a method for thawing a frozen biological material. The steps can include setting a target temperature for the biological material and applying heat to the biological material via a heating device. The method can also include controllably moving the heating device for a specific time period, wherein the time period is determined based on the target temperature, the vial content material and the content volume.

[010] Another embodiment of this disclosure is directed to a system for heating a biological material in a vessel. The system can include a heating device configured to transmit energy to the vessel and a base moveably coupled to the heating device. The system can also include a processor configured to receive an input associated with a target temperature, and transmit a signal to controllably move the heating device relative to the base for a time period, wherein the time period is determined based on the target temperature and the content volume.

[011] Additional embodiments consistent with principles of the disclosure are set forth in the detailed description which follows or may be learned by practice of methods or use of systems or articles of manufacture disclosed herein. It is understood that both the foregoing general description and the following detailed description are exemplary and explanatory only, and are not restrictive of the disclosure as claimed. Additionally, it is to be understood that other embodiments may be utilized and that

electrical, logical, and structural changes may be made without departing from the spirit and scope of the present disclosure.

BRIEF DESCRIPTION OF THE DRAWINGS

[012] The accompanying drawings, which are incorporated in and constitute a part of this specification, illustrate several embodiments of the disclosure and together with the description, serve to explain the principles of the disclosure. In the drawings:

[013] Fig. 1 illustrates a thawing system, according to an exemplary embodiment of the present disclosure.

[014] Fig. 2 illustrates a thawing system with an open lid, according to an exemplary embodiment of the present disclosure.

[015] Fig. 3 illustrates a thawing system with an open water tray, according to an exemplary embodiment of the present disclosure.

[016] Fig. 4 illustrates an exploded view of a thawing system, according to an exemplary embodiment of the present disclosure.

[017] Fig. 5 illustrates a view of an upper section of a thawing system, according to an exemplary embodiment of the present disclosure.

[018] Fig. 6 illustrates a view of a base of a thawing system, according to an exemplary embodiment of the present disclosure.

[019] Fig. 7 illustrates a view of a heating device of a thawing system, according to an exemplary embodiment of the present disclosure.

[020] Fig. 8 illustrates a chart showing cellular vitality from use of a thawing device, according to an exemplary embodiment of the present disclosure.

DESCRIPTION OF THE EMBODIMENTS

[021] Reference will now be made in detail to the present embodiments of the disclosure, examples of which are illustrated in the accompanying drawings. Wherever possible, the same reference numbers will be used throughout the drawings to refer to the same or like parts.

[022] Fig. 1 illustrates a thawing system, according to an exemplary embodiment of the present disclosure. System can include a base and a lid. Base can

include one or more interfaces configured to receive operator input. For example, base can include one or more buttons, such as, an activation button, a pause button, a first target temperature button, a second target temperature button, and an ejector switch. A vial eject button can aid extraction of a vial from the thawing chamber.

[023] As explained below, lid may move to allow one or more vessels to be loaded into system. In some embodiments, system can be configured to receive a vial containing biological or chemical material.

[024] Biological material can include material derived from a biological source. For example, biological material can include cells, peptides, nucleic acid, lipids, and carbohydrates. Various cells can be engineered to produce various natural and non-natural biological products. Cells can include eukaryotic and prokaryotic cells, including for example, stem cells, bacterial cells, yeast cells, and various cell lines derived from biological sources.

[025] System can be configured to receive one or more vials of various shape and size. For example, system can be configured to receive an Eppendorf vial having a 1.6 ml capacity. Various other vials may be thawed using system.

[026] Fig. 2 illustrates a thawing system with an open lid, according to an exemplary embodiment of the present disclosure. The lid may be lightweight, such as plastic. Various other materials are contemplated. Lid can maintain a generally closed environment and protect the user from moving parts. Lid may be moveably coupled to base to permit an operator to load one or more vials into system.

[027] Fig. 3 illustrates a thawing system with an open water tray, according to an exemplary embodiment of the present disclosure. Water tray can include a liquid collection drawer configured to receive liquid collected by system. A drawer, or liquid catch tray, can collect condensation water or leakage, enabling clean work as needed for aseptic environment such as clean room operation and surgery room. In some embodiments, drawer may be slidably coupled to base to allow drawer to be opened and emptied. In other embodiments, system can include a conduit to a sink or other receptacle to receive unwanted liquid collected by system.

[028] Fig. 4 illustrates an exploded view of a thawing system, according to an exemplary embodiment of the present disclosure. System is shown with lid, base,

collection drawer, and heating device. In other embodiments, one or more components may be not included, combined with other components, or additional components added to system.

[029] Fig. 5 illustrates a view of an upper section of a thawing system, according to an exemplary embodiment of the present disclosure. Upper section can include lid and one or more components configured to receive user input. While several buttons are shown, lid can include other user interfaces, such as, for example, a touch sensitive screen, a keyboard, or an interface to a remote device. Lid may also be moveably coupled to upper section using various mechanical linkages. Upper section may also include one or more electrical components of system. For example, a processor, memory, user interface, power source, communications, module may be included in upper section. In other embodiments, one or more electrical components could be included in base or another part of system.

[030] Fig. 6 illustrates a view of a base of a thawing system, according to an exemplary embodiment of the present disclosure. The base can include a controller board, processor, collection drawer, and various other components of system. Power can be supplied from mains power. Low voltage demand can allow activation using a battery or portable power source. Base can also be moveably coupled to heating device, as described below.

[031] Fig. 7 illustrates a view of a heating device of a thawing system, according to an exemplary embodiment of the present disclosure. Heating device can be rotatably coupled to base or other part of system. The heating device may be configured to controllably move vial or other vessel containing a biological or a chemical material.

[032] Fig. 8 illustrates a chart showing cellular vitality from use of a thawing device, according to an exemplary embodiment of the present disclosure. Placenta derived adherent stromal cells (PLX-PAD) were thawed in a thawing device following long term cryopreservation in liquid nitrogen (-195°C). The data demonstrates higher viability using thawing device at, for example, either 180 or 400 RPM agitation rates. Other cell types, storage conditions, heating temperatures, and agitation rates may also provide improved cellular vitality compared with typical use of water bath by an average

operator. The system thus reduces operator error and variability in thawing multiple samples, enhancing the reproducibility of thawing for batch processing.

[033] Various heating mechanisms can be used to transmit heat to biological material. For example, electro-resistive heating, microwave, ultrasound, and other heating modalities can be used. In some embodiments, the system can include a water heater configured to operate at one or more specific temperatures.

[034] For example, the heating device can include a heating block configured to receive one or more vials of different size and shape. Heating device can have one or more sensors configured to detect a temperature. For example, heating device can include two heat sensing probes. Multiple heating probes can be used to reduce or eliminate over-heating of biological or chemical material.

[035] In other embodiments, an IR thermometer can be added to system to measure a temperature associated with the vial or solution contained within the vial. Various other types of thermometer could be used with system.

[036] The heating device can also include one or more cooling devices to assist temperature regulation. For example, heating device could include two fans located on opposite sides of heating device.

[037] The heating device may be configured to move. Various movement devices may be used with system. For example, the heating device may be equipped with one or more motors configured to rotate. Such a motor could operate between 0-500 RPM. Various other motors could be changed to provide various speeds or speed profiles. For example, the motor could be configured to operate at constant speed or variable speed.

[038] In some embodiments, the motor can have one reference point for each round. The reference point can be set to HOME. The controller can calculate the rotation speed of the motor by the time that passes between the reference point transitions. The speed control can be essentially recursion speeds of previous rounds. For example, the next round velocity can be half the speed of the previous round, a quarter of the speed of rotation before, and so on. That is, as the speed gets closer to the target, the amendments made to it can get smaller.

[039] System may also be equipped with a barcode reader that can identify a serial number of one or more vials and store data associated with the one or more vials. Other functions based on barcode information can include allowing activation, inhibiting use if the vial has passed an expiration date, inhibiting double thawing of the same vial, warm up the device, or provide calibration information. An alert could be generated based on such information. For example, an operator may be alerted that a vial is out of date, has previously been thawed, has remained within the device for too long, or has overheated. It is also contemplated that a barcode may set one or more heating programs. This could allow running of different programs for different products set by the manufacture. Various other types of devices configured to identify biological materials are also contemplated.

Operation of Thawing System

[040] System can be configured to operate with various biological or chemical materials. For example, system can include a first target temperature of 4°C and a second target temperature of 25°C.

[041] The thawing procedure of system can be based on automatically shaking the vial at a generally constant temperature. For example, a temperature controlled chamber can be made of aluminum. Heating can occur for a predetermined time period. The device temperature and shaking speed, as well as the thawing time, can be adjusted in order to fit the thawing conditions for different volumes and solutions.

[042] In some embodiments, system can include a processor or controller. The controller can be configured to receive information from one or more sources. For example, the controller can be configured to operate with one or more heat sensors, a time counter, a speed monitor and a barcode reader. Using the controller, system can be programmed to follow various thawing protocols. These protocols can be set by an operator. One exemplary embodiment is outlined below, and other protocols are also contemplated.

[043] Initially, a thawing cycle may active only after heating device has reached an initial temperature. This may reduce the affect of room and/or device temperature on the thawing procedure.

[044] During a thawing protocol, a controller may be configured to control a shaking speed of a vial. The controller may also adjust vial movement speed when the operation exceeds the thawing speed boundaries.

[045] The controller may also control a temperature of the heating device during a run. For example, the controller may adjust the temperature when the operation exceeds the thawing temperature boundaries. System can include a sensor specifically configured to monitor conditions within the vial.

[046] System can be equipped with two temperature sensors localized in the two sides of heating device or thawing chamber. Further, the controller can activate two heating elements separately based on the temperature measured by each sensor. If the measured temperature is lower than the target temperature (e.g., 38°C), the heating force can increase. If the target is approaching the target temperature, the heating force can decrease. When one of the temperature probes reaches the target temperature, the heating may be stopped in both heating blocks. If one of the sensors indicates a temperature higher than 39°C, the device can start cooling until the higher temperature of the two measured falls below 39°C.

[047] When system operates in the range of 38°C to 39°C degrees, there may be no heating or cooling in order to save electricity.

[048] System may be configured to produce a warning when the operation exceeds the thawing temperature parameters or the thawing speed parameters. A thawing cycle may be stopped based on a temperature associated with vial, biological material, heating device, or other metric. For example, if an IR sensor is present, the run may be terminated based on vial temperature. In other embodiments, a cycle time may be used to reach a more precise thawing temperature.

[049] System may also be configured to keep the vial in a controlled temperature at various stages throughout a run. For example, temperature may be maintained at higher or lower than the thawing temperature at the end of a thawing procedure until the vial is extracted for use.

[050] System may be further configured to activate the thawing cycle upon detecting a unique structure of barcode. System could, for example, compare the detected vial barcode against the device database in order to prevent a vial return. Other

actions may be based on various identifier information, such as, for example, information obtained using an ID tag reader.

[051] In some embodiments, a display may be included. For example, an HMI display can be added in order to display the thawing process parameters or error indications. System could be configured to store information on up to 100 runs including, for example, vial ID number, duration, date, time, and error indications.

[052] As indicated above, system can be configured to receive, store, and transmit various data associated with the biological material. For example, data can be extracted and imported from system by a network connection. System can also be programmed to extract a report summarizing the thawing process data.

[053] In some embodiments, system can be operated using the following steps:

- [054] 1. Open the device by switching the rear electrical switch to the on mode;
- [055] 2. Press on the activation switch or swipe barcode;
- [056] 3. Wait 30 sec in order to let the chamber pre-warm to 37°C wait for signal;
- [057] 4. Press on the cover eject switch and open the lid;
- [058] 5. Assure that the thawing chamber is centered;
- [059] 6. Insert a vial in to the chamber by pressing the vial down;
- [060] 7. Close the lid;
- [061] 8. Press on the "25°C" button or start (automatic program set by identifying the barcode);
- [062] 9. The thawing chamber will start to shake in a predetermined speed (RPM) for the predetermined thawing time;
- [063] 10. At the end of the thawing time the system will alert and immediately will pass to standby mode;
- [064] 11. To open the lid press on the cover eject switch;
- [065] 12. Push the vial extraction button down until the vial can be handled and extract the vial;
- [066] 13. Close the lid; and
- [067] 14. Repeat steps 4 to 12 for additional vial to be thawed.

[068] By way of example, Fig. 8 illustrates a chart showing cellular vitality from use of a thawing device, according to an exemplary embodiment of the present disclosure. Using system can lead to better post-thaw cells vitality compared to the water bath. Using different thawing speeds (RPM) may have an effect on the cells post-thaw vitality. Data shown here were obtained from 6m1 Crystal vials (Aseptic Technologies) filled with 5.5 cell suspension, 3 vials in each group.

[069] Other embodiments of the disclosure will be apparent to those skilled in the art from consideration of the specification and practice of the present disclosure. It is intended that the specification and examples be considered as exemplary only, with a true scope and spirit of the disclosure being indicated by the following claims.

WHAT IS CLAIMED IS:

1. A method for thawing a frozen biological therapeutic, comprising:
reading information contained on a code or tag associated with the
frozen biological therapeutic;
setting a target temperature for the frozen biological therapeutic;
applying heat to the frozen biological therapeutic via a heating device,
wherein said reading information contained on a code or tag is performed by a reader
operably connected with said heating device; and
controllably moving the biological therapeutic for a time period to allow
generally uniform heat dispersion, wherein the time period is determined based on at least one
of the target temperature and a content volume of the biological therapeutic, wherein said
controllably moving is directed by a processor configured to (a) receive an input associated
with said target temperature, wherein said input is received from one or more sources,
including said code or tag, and (b) transmit a signal to controllably move the biological
therapeutic for said time period,
and wherein said code or tag determines a program of said step of applying
heat.
2. The method of claim 1, wherein the frozen biological therapeutic
includes a suspension of a population of cells.
3. The method of claim 1 or claim 2, wherein the frozen biological therapeutic
is located within a vial, and the heating device is configured for receiving said vial.
4. The method of any one of the preceding claims, further comprising halting
movement of the biological therapeutic after the time period has elapsed.
5. The method of any one of the preceding claims, further comprising the
step of halting said step of applying heat after the time period has elapsed.
6. The method of any one of the preceding claims, further comprising
recording an identifier associated with the frozen biological therapeutic.
7. The method of any one of the preceding claims, further comprising

recording information associated with at least one of a temperature of the heating device, a speed of movement of the heating device, and the time period of said step of applying heat.

8. The method of any one of the preceding claims, further comprising terminating said applying heat after a target temperature is reached.

9. The method of any one of the preceding claims, wherein the heating device is movably coupled with the base such that it rotates relative to the base.

10. The method of any one of the preceding claims, wherein the processor is configured to controllably rotate the heating device relative to the base at a variable speed.