CONTROLLED ENVIRONMENT INCUBATOR FOR LIGHT MICROSCOPY

This invention relates to biological incubators for light microscopes, and more particularly to biological incubators suitable for continuous microscopic observation of living cell cultures under environmentally controlled conditions.

BACKGROUND AND PRIOR ART

It is frequently desirable to observe biological cells, for a variety of purposes, for extended periods of time. This is generally accomplished by locating cells to be observed, in a suitable medium such as liquid medium or semi-solid medium. Since biological cells require a habitable environment in which to live, microscopic observation of living cell cultures is generally restricted to very short observation periods unless a habitable environment is provided around the cell culture as it rests on a microscope stage, or the microscope is moved into an incubator containing a habitable environment, as is sometimes done in the case of time lapse photography.

Prior art devices have striven to provide a biologically habitable environment around the cell culture as it rests on a microscope stage but have exhibited numerous disadvantages, limiting their usefulness for continuous observation. These prior art devices are usually in the form of plastic boxes that are large and cumbersome, ranging from boxes which enclose the entire microscope to boxes which enclose only the microscope stage. Common for all is that they are difficult to use, requiring large doors on the boxes to allow access, as well as holes to accommodate microscope parts protruding to the outside, such as eyepieces, and mechanical interfaces which enable the microscope to be operated from outside the box. The large size of these prior art devices necessitates a considerable period of time for the restoration of the preselected environment after opening the chamber, for instance to exchange cultures, due to the fact that the preconditioned atmosphere in the chamber is rapidly lost during such an exchange and requires a considerable amount of new prepared atmosphere to restore the environment in the chamber to the proper conditions, the time period required often being too long for the cells to survive.

Another important consideration for observation of cell cultures during extended observation periods, is the need for high humidity to prevent dehydration of the cell culture during such extended observation periods. The prior art devices presently available have the disadvantage that they are unable to maintain high humidity during extended observation periods, since the outside walls of these devices are below the operating temperature required to maintain habitable conditins for the cells in the cell culture, due to the fact that no insulation is provided in such prior art devices. This results in continuous condensation on the entire inside surface of these prior art devices and on the microscope, due to heat loss from parts projecting out from the chamber, such condensation seriously compromising the ability of these devices to maintain high internal humidity and tending in addition to corrode the equipment. Since such condensation also occurs on lenses and the like, cleaning of such surfaces is required before suitable observation may be carried out.

A special gaseous environment, habitable for the culture, is often required and may be maintained by purging the incubator, but since prior art devices are poorly sealed and have a comparatively large internal volume, a high rate of purge is necessary to maintain a desired gaseous environment. Purge gases need to be highly humidified, necessitating the use of accessory humidifying equipment external to the incubator since none of the prior art incubators of this type offer internal humidifying means. Sufficiently thorough sterilization of the prior art devices has also been shown to be extremely difficult.

The present invention overcomes all the aforementioned problems by providing an incubator having a miniature environment chamber that is able to continuously maintain a gaseous environment of high humidity and controlled temperature around a tissue culture dish situated, for example, on a microscope stage.

It is an object of the present invention to provide a miniature incubator that allows continuous observation of cell cultures in a tissue culture dish contained in the incubator, at low or medium objective lens power, using either an upright or inverted microscope, and observation at high objective lens power using an inverted microscope.

It is another object of this invention to provide a miniature incubator that permits continuous observation of a cell culture with video equipment for the purpose of computerized image analysis and cell tracking.

It is still another object of this invention to provide a miniature incubator that allows continuous microscopic observation of living cell cultures, located in disposable tissue culture dishes, by providing a miniature biologically habitable environment around the tissue culture dish, the environment being controlled to maintain a suitable constant temperature, high humidity and ability to be purged with gases suitable for survival of the type of cells being cultured, while the incubator is situated on a microscope stage and attached to the motion controls of the stage.

It is another object of this invention to provide a miniature incubator containing means for effectively humidifying purging gases entering the incubator, in order to maintain a high humidity therein.

It is still another object of this invention to provide a miniature incubator supplied with a plurality of covers to suit various methods of microscopic observation.

These and other objects and features of the present invention will be apparent from the following detailed description and accompanying drawings in which: FIG. 1 is a perspective view of a miniature incubator, illustrating a preferred form of this invention. FIG. 2 is a perspective view of a transparent cover for the miniature incubator shown in FIG. 1. FIG. 3 is an enlarged fractional, sectional elevation of the miniature incubator shown in FIG. 4 taken on line A–B, a culture dish, shown in phantom, being located therein. FIG. 4 is a plan view of the miniature incubator shown in FIG. 1, illustrating thermal means for maintaining controlled temperature environment within the incubator, and hollow fiber tube, located in the miniature incubator for purging the internal incubator chamber with humidified gases. FIG. 5 is a mid-vertical, cross-sectional view of the transparent cover shown in FIG. 1. FIG. 6 is a mid-vertical, cross-sectional view of the miniature incubator shown in FIG. 4, taken on line A–C, having an alternate cover located thereon, illustrating a preferred method for maintaining a sealed, preselected environmental atmosphere in a closed chamber surrounding the culture dish while permitting a substantially high-power