removal rates for mammalian cell cultures. This is accomplished in stainless steel microbial fermentors through a number of means, including, e.g., very vigorous agitation by multiple impellers to disperse air bubbles and increase absorption of oxygen by the cells; very high flow rates of air to supply more oxygen; extra cooling surfaces such as cooling coils to remove from the culture fluid the large amount of heat that is generated by the metabolism of the microbial cells and by the frictional heat generated by the vigorous agitation. However, in single-use bioprocessing bags, heat removal is an ongoing problem, especially for microbial bioreactors.

[0005] As is well known by those of skill in the field of polymeric or plastic materials such as films and flexible bags, polymeric or plastic films are relatively very poor conductors of heat. Therefore, cooling a fluid inside a vessel containing a replaceable container, e.g., a flexible plastic bag, may require specific modification of the cooling surfaces of the flexible bag and/or the vessel. There is an ongoing need for systems and methods to improve the removal of the large amount of heat generated by microbial cell cultures.

SUMMARY ~~OF THE INVENTION~~

[0006] Methods and apparatus are disclosed for use in a chemical, pharmaceutical or biological reactor system for temperature control. In one ~~aspect~~embodiment, the ~~invention~~ disclosure includes a heat exchange module that can be disposed in a reactor system having an inner replaceable reactant container such as, for example, a flexible bag or a semi-rigid container.

[0007] ~~One embodiment~~In a first aspect of the ~~invention is~~disclosure, there is provided a heat exchange module for use in a chemical, pharmaceutical or biological reactor system having a single use flexible container, the module comprising: a body having a central chamber configured for

receiving the single use flexible container and configured to be disposed in a reactor vessel, the body comprising: an outer surface configured to conform to a shape of the reactor vessel; at least one thermally conductive surface adapted to contact the single use reactant container to facilitate heat transfer; and at least one integral strong baffle forming a protrusion into the central chamber; wherein the body is an elongate body having a top end and a bottom end and is adapted to be inserted into the reactor vessel such that the body extends at least a substantial portion of the distance between a top and a bottom of the reactor vessel, and a heat exchanger disposed at the outer surface of the body, the heat exchanger comprising a fluid circulation path through which a heat exchange fluid can be circulated around the circumference of the body and into and out of a channel in the at least one strong baffle, such that when the flexible container is inserted into the chamber, a fluid within the flexible container is heated or cooled by the heat exchange fluid and baffled by the at least one strong baffle.

[0008] In one embodiment of the ~~invention~~disclosure, the heat exchange module body is configured to extend to a position opposite an impeller positioned at or near the bottom of the single use flexible container, and the at least one integral strong baffle is configured to baffle a shear field produced by the impeller.

[0009] ~~Another~~ In a second aspect of the ~~invention is~~disclosure, there is provided a container chosen from a flexible bioreactor bag, a flexible mixer bag, and a flexible tubing, the container comprising at least one double wall portion comprising an inner and an outer wall and a heat conductive material attached to or embedded in a portion of at least one of the inner wall and the outer wall.

[0010] ~~Yet another~~In a third aspect of the ~~invention~~ disclosure, there is provided is a flexible polymeric wall chosen from a bioreactor wall, a mixer wall, and a tubing wall, the flexible wall comprising a

heat conductive material attached to or embedded in a portion of the flexible wall.

[0011] ~~Yet another embodiment~~In a fourth aspect of the ~~invention is~~ disclosure, there is provided a jacketed, tiered baffle, bioreactor tank comprising: an outer cylindrical-shaped jacket; and a cylindrical tank having an inner tank surface defining a chamber configured for supporting a flexible bag disposed within the chamber, and an outer tank surface having tiered baffles configured for routing a heat exchange fluid around the entirety of the outer tank surface, the cylindrical tank disposed axially within the outer cylindrical-shaped jacket, wherein the outer cylindrical-shaped jacket is sealed to the cylindrical tank in a manner sufficient to prevent or minimize loss of the heat exchange fluid.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] The foregoing and other non-limiting objects, features and advantages of the invention will be apparent from the following more particular description of illustrative embodiments of the invention, as illustrated in the accompanying drawings in which like reference characters refer to the same parts throughout the different views. The drawings are schematic and not intended to be drawn to scale, emphasis instead being placed upon illustrating the principles of the invention. The drawings are schematic and not intended to be drawn to scale, emphasis instead being placed upon illustrating the principles of the invention. The features illustrated or described in connection with one exemplary embodiment can be combined with the features of other embodiments. Such modifications and variations are intended to be included within the scope of the present invention.

[0013] FIG. 1A is a perspective view of a schematic representation of an exemplary heat exchange module having a serpentine flow path for a heat exchange liquid, and a partial cut-away view of an outer support structure or outer vessel wall.