this continuous feeding strategy for mammalian cell cultures relies on equipment feedback control, which can introduce variability into a feeding process.

Summarily, a drawback common to all of these methods is the fact that they all rely on some sort of instrument-obtained feedback in order to manage the process. What is needed, therefore, is a method of feeding a cell culture that can be tailored to the specific needs of a given cell culture, can be automated and does not rely on instrument-mediated feedback to control the nutrients delivered to the cell culture.

SUMMARY

In one aspect, there is provided a method of continuously feeding a mammalian cell culture that does not employ feedback control, comprising:

(a) providing a vessel comprising a mammalian cell culture comprising mammalian cells and media;

(b) determining K_1 which is a preferred value for the consumption rate of a nutrient, K_{21} which is a preferred value for the growth rate and K_{22} which is a preferred value for the growth rate of the cell culture;

(c) providing an apparatus adapted to impart a continuous feed stream to the cell culture, wherein the apparatus comprises a controller module adapted to continuously feed the culture at a flow rate F, wherein

F is defined as $K_1\exp(K_{21}t^2 + K_{22}t)$;

t is the duration of time from the time the feed stream is added to the bioreactor to the time when the feed stream is stopped; and

K_1, K_{21} and K_{22} are the values determined in (b); and

(d) activating the controller module to initiate continuous feeding of the cell culture.

A method of continuously feeding a mammalian cell culture that does not employ feedback control is provided. In one example the method comprises (a) providing a vessel comprising a mammalian cell culture comprising mammalian cells and media; (b)

Claims

What is claimed is:

1. A method of continuously feeding a mammalian cell culture that does not employ feedback control, comprising:

(a) providing a vessel comprising a mammalian cell culture comprising mammalian cells and media;

(b) determining K_1 which is a preferred value for the consumption rate of a nutrient, K_{21} which is a preferred value for the growth rate, and K_{22} which is a preferred value for the growth rate of the cell culture;

(c) providing an apparatus adapted to impart a continuous feed stream to the cell culture, wherein the apparatus comprises a controller module adapted to continuously feed the culture at a flow rate F, wherein

F is defined as $K_1\exp(K_{21}t^2 + K_{22}t)$;

t is the duration of time from the time the feed stream is added to the bioreactor to the time when the feed stream is stopped; and

K_1, K_{21} and K_{22} are the values determined in (b); and

(d) activating the controller module to initiate continuous feeding of the cell culture.

2. The method of claim 1, wherein K_1, K_{21} and K_{22} are empirically determined.

3. The method of claim 1, wherein K_1, K_{21} and K_{22} are modeled.

4. The method of claim 1, wherein the controller module comprises a computer.

5. The method of claim 1, wherein the osmolality of the cell culture remains constant throughout the method.

6. The method of claim 1, wherein the nutrient is glucose.

7. The method of claim 1, wherein the mammalian cell culture is a CHO cell culture.

8. The method of claim 1, wherein the controller module is activated in response to a preselected lactate level in the cell culture.

9. The method of claim 1, wherein the controller module is activated in response to a preselected glucose level in the cell culture.

10. The method of claim 1, wherein the controller module is activated in response to a preselected level of an amino acid.

11. The method of claim 10, wherein the amino acid is asparagine.

12. The method of claim 10, wherein the amino acid is glutamine.

13. The method of claim 1, wherein the feed stream comprises two or more nutrients.