SYSTEMS AND METHODS FOR SEED TRAIN OPTIMIZATION

RELATED APPLICATIONS

[0001] This application claims the benefit of priority under 35 U.S.C. § 119(e) to U.S. Application Serial No. 63/489,958, filed March 13, 2023, entitled "SYSTEMS AND METHODS FOR SEED TRAIN OPTIMIZATION", the entire contents of which is incorporated by reference herein.

BACKGROUND

[0002] Biological products are used to treat, prevent, and diagnose various medical conditions and diseases. Biological products may be produced by cells specifically engineered for their production. Some biological products include polypeptides (e.g., therapeutic proteins, monoclonal antibodies, vaccines, etc.), nucleic acids (e.g., messenger RNA (mRNA), small interfering RNA (siRNA), microRNA, etc.), or viral vectors (e.g., lentiviral vectors, adenoviral vectors, recombinant adeno-associated virus (rAAv) vectors, etc.).

[0003] Growing a cell culture that is used to produce biological products helps to increase their production. Such a culture is typically grown using a "seed train process," which refers to the process used to progressively scale a culture from a small volume of cells to a larger volume of cells. A seed train process typically includes multiple stages, each of which corresponds to a cultivation system used to expand the culture to a volume larger than that achieved during the preceding stage.

SUMMARY

[0004] In one aspect, the present disclosure provides a method for determining seed train process parameters for a seed train process for growing a culture of cells, the method performed using at least one software application program comprising a common interface module, a parameter optimization module, and a simulation module, the method comprising: using at least one computer hardware processor to perform: obtaining, using the common interface module, a specification of seed train process constraints for multiple stages of the seed train process; determining the seed train process parameters using the parameter optimization module and the seed train process constraints, the seed train process parameters comprising a respective set of parameters for each particular stage of the multiple stages of the seed train process, the determining comprising: determining the seed train process parameters using the parameter optimization module and the seed train process constraints, the seed train process parameters

comprising a respective set of parameters for each particular stage of the multiple stages of the seed train process, the determining comprising: determining, for each particular stage of the multiple stages and using the parameter optimization module and the seed train process constraints, the respective set of parameters for growing the culture during the particular stage; determining, using the simulation module, historical cell growth data, and the determined seed train process parameters, a likelihood indicative of whether performing the seed train process using the determined seed train process parameters will satisfy seed train process success criteria; and outputting the respective set of seed train process parameters determined for each stage of the multiple stages of the seed train process and the likelihood indicative of whether performing the seed train process using the determined seed train process parameters will satisfy the seed train process success criteria.

[0004a] Some examples provide for a method for determining seed train process parameters for a seed train process for growing a culture of cells, the seed train process having multiple stages, the method performed using at least one software application program comprising a common interface module, a parameter optimization module, and a simulation module. In some examples, the method includes using at least one computer hardware processor to perform: obtaining, using the common interface module, a specification of seed train process constraints for the multiple stages of the seed train process; determining the seed train process parameters using the parameter optimization module and the seed train process constraints, the seed train process parameters comprising a respective set of parameters for each particular stage of the multiple stages of the seed train process, the determining comprising: determining, for each particular stage of the multiple stages and using the

parameter optimization module and the seed train process constraints, the respective set of parameters for growing the culture during the particular stage; determining, using the simulation module, historical cell growth data, and the determined seed train process parameters, a likelihood indicative of whether performing the seed train process using the determined seed train process parameters will satisfy seed train process success criteria; and outputting the respective set of seed train process parameters determined for each stage of the multiple stages of the seed train process and the likelihood indicative of whether performing the seed train process using the determined seed train process parameters will satisfy the seed train process success criteria.

[0005] In another aspect, the present disclosure provides for a system, comprising: at least one computer hardware processor; and at least one non-transitory computer-readable storage medium storing processor-executable instructions that, when executed by the at least one computer hardware processor, cause the at least one computer hardware processor to perform the method as disclosed herein. Some examples provide for a system comprising: at least one computer hardware processor; and at least one non-transitory computer-readable storage medium storing processor-executable instructions that, when executed by the at least one computer hardware processor, cause the at least one computer hardware processor to perform a method for determining seed train process parameters for a seed train process for growing a culture of cells, the seed train process having multiple stages, the method performed using at least one software application program comprising a common interface module, a parameter optimization module, and a simulation module. In some examples, the method includes using at least one computer hardware processor to perform: obtaining, using the common interface module, a specification of seed train process constraints for the multiple stages of the seed train process; determining the seed train process parameters using the parameter optimization module and the seed train process constraints, the seed train process parameters comprising a respective set of parameters for each particular stage of the multiple stages of the seed train process, the determining comprising: determining, for each particular stage of the multiple stages and using the parameter optimization module and the seed train process constraints, the respective set of parameters for growing the culture during the particular stage; determining, using the simulation module, historical cell growth data, and the determined seed train process parameters, a likelihood indicative of whether performing the seed train process using the determined seed train process parameters will satisfy seed train process

success criteria; and outputting the respective set of seed train process parameters determined for each stage of the multiple stages of the seed train process and the likelihood indicative of whether performing the seed train process using the determined seed train process parameters will satisfy the seed train process success criteria.

[0006] In another aspect, the present disclosure provides for at least one non-transitory computer-readable storage medium storing processor-executable instructions that, when executed by at least one computer hardware processor, cause the at least one computer hardware processor to perform the method as disclosed herein. Some examples provide for at least one non-transitory computer-readable storage

medium storing processor-executable instructions that, when executed by at least one computer hardware processor, cause the at least one computer hardware processor to perform a method for determining seed train process parameters for a seed train process for growing a culture of cells, the method performed using at least one software application program comprising a common interface module, a parameter optimization module, and a simulation module. In some examples, the method includes using at least one computer hardware processor to perform: obtaining, using the common interface module, a specification of seed train process constraints for the multiple stages of the seed train process; determining the seed train process parameters using the parameter optimization module and the seed train process constraints, the seed train process parameters comprising a respective set of parameters for each particular stage of the multiple stages of the seed train process, the determining comprising: determining, for each particular stage of the multiple stages and using the parameter optimization module and the seed train process constraints, the respective set of parameters for growing the culture during the particular stage; determining, using the simulation module, historical cell growth data, and the determined seed train process parameters, a likelihood indicative of whether performing the seed train process using the determined seed train process parameters will satisfy seed train process success criteria; and outputting the respective set of seed train process parameters determined for each stage of the multiple stages of the seed train process and the likelihood indicative of whether performing the seed train process using the determined seed train process parameters will satisfy the seed train process success criteria.

[0007] In some examples, determining, for each particular stage of the multiple stages, the respective set of parameters for growing the culture during the particular stage comprises: determining at least one seed train process parameter selected from the group consisting of: a viable cell density, an indication of whether the particular stage is included in the seed train process, a targeted duration of the seed train process, a batch medium volume, a working volume per vessel, and a number of vessels.

[0008] In some examples, obtaining the specification of the seed train process constraints comprises: obtaining a specification of at least one seed train process constraint selected from the group consisting of: a target viable cell density range, a target working volume range, a split ratio culture growth process constraint, and a batch media volume range.

[0009] In some examples, the historical cell growth data comprises data indicative of a doubling time associated with the growth of one or more cultures of cells.

[0010] In some examples, determining the seed train process parameters using the parameter optimization module comprises determining the seed train process parameters using a genetic algorithm.

[0011] In some examples, determining the likelihood indicative of whether performing the seed train process using the determined seed train process parameters will satisfy the seed train process success criteria comprises performing Monte Carlo simulations using the historical cell growth data.

[0012] In some examples, the seed train process success criteria comprise, for each stage of the multiple stages of the seed train process: a first criterion that an expected duration needed to grow the culture during the particular stage does not exceed a threshold duration for growing the culture during the particular stage; and a second criterion that an expected viable cell density resulting from growing the culture during the particular stage does not exceed a threshold viable cell density resulting from growing the culture during the particular stage.

[0013] In some examples, determining the respective set of parameters for each particular stage of the multiple stages comprises: determining, using the respective set of parameters, the expected duration needed to grow the culture of cells during the particular stage; and determining whether the expected duration exceeds the respective threshold duration for the particular stage.

[0014] In some examples, determining the respective set of parameters for each particular stage of the multiple stages comprises: determining, using the respective set of parameters, the expected viable cell density resulting from growing the culture of cells during the particular stage; and determining whether the expected viable cell density exceeds the respective threshold viable cell density for the particular stage.

[0015] In some examples, outputting the set of seed train process parameters for each stage of the multiple stages of the seed train process and the likelihood indicative of whether performing the seed train process will satisfy the seed train process success criteria comprises: generating a graphical user interface (GUI) using the common interface module; and displaying the set of seed train process parameters and/or the likelihood through the generated GUI.

[0016] In some examples, displaying the set of seed train process parameters through the common interface module comprises: displaying a visual indication of whether a seed train process parameter of the set of seed train process parameters violates a seed train process

constraint of the seed train process constraints.

[0017] In some examples, determining the seed train process parameters comprises: determining the seed train process parameters based on a set of estimate culture doubling times included in the seed train process constraints, the set of estimate culture doubling times including an estimate culture doubling time for each of the multiple stages of the seed train process; and determining whether performing the seed train process using the determined seed train process parameters will satisfy the seed train process success criteria. Some examples further comprise displaying, through a graphical user interface (GUI) generated by the common interface module, a visual indication of a result of determining whether performing the seed train process using the seed train process parameters will satisfy the seed train process success criteria.

[0018] Some examples further comprise: comparing the determined likelihood to a likelihood threshold, wherein outputting the set of seed train process parameters for each stage of the multiple stages of the seed train process comprises outputting determined the seed train process parameters upon determining that the likelihood exceeds the likelihood threshold.

[0019] In some examples, outputting the set of seed train process parameters for each stage of the multiple stages of the seed train process comprises: when the likelihood indicative of whether performing the seed train process using the determined seed train process parameters will satisfy the seed train process success criteria satisfies a likelihood threshold, outputting a recommendation to perform the seed train process using the set of seed train process parameters for each stage of the multiple stages of the seed train process.

[0020] In some examples, the at least one software application program further comprises a seed train process automation module, and outputting the set of seed train process parameters for each stage of the multiple stages of the seed train process and the likelihood indicative of whether performing the seed train process will satisfy the seed train process success criteria comprises: transmitting the set of seed train process parameters and/or the likelihood to the seed train process automation module; and using the seed train process automation module to cause a seed train process automation system to perform a particular stage of the multiple stages of the seed train process according to the respective set of seed train process parameters.

[0021] Some examples further comprise: obtaining, using the common interface module, input indicative of a result of growing the culture of cells during a first stage of the multiple

stages of the seed train process; determining, using the parameter optimization module, the input, and the seed train process constraints, updated seed train process parameters for subsequent stages of the seed train process; and outputting the updated seed train process parameters.

[0022] Some examples further comprise: obtaining, using the common interface module, a specification of second seed train process constraints for multiple stages of a second seed train process; determining, using the parameter optimization module and the second seed train process constraints, second seed train process parameters for the second seed train process; determining, using the simulation module, the historical cell growth data, and the second seed train process parameters, a second likelihood indicative of whether performing the second seed train process, using the second seed train process parameters, will satisfy second seed train process criteria; and outputting the second seed train process parameters and the second likelihood indicative of whether performing the second seed train process, using the second seed train process parameters, will satisfy the second seed train process criteria.

[0023] In some examples, determining the seed train process parameters using the parameter optimization module comprises: determining, using an objective function, a first score for first candidate seed train process parameters; determining, using the objective function, a second score for second candidate seed train process parameters; comparing the first score and the second score; and selecting, based on the result of the comparing, the seed train process parameters from among the first candidate seed train process parameters and the second candidate seed train process parameters.

[0024] In some examples, the seed train process parameters comprise a first set of seed train process parameters for a first stage of the multiple stages of the seed train process, and determining the likelihood indicative of whether performing the seed train process using the seed train process parameters will satisfy the seed train process success criteria comprises: determining, for the first stage of the seed train process, a first likelihood indicative of whether growing the culture of cells during the first stage, using the first set of seed train parameters for the first stage, will satisfy first criteria of the seed train process success criteria.

[0025] In some examples, determining the likelihood indicative of whether performing the seed train process using the seed train process parameters will satisfy the seed train process success criteria comprises: simulating a first set of cell growth values using the

historical cell growth data, the first set of cell growth values including a first historical cell growth value for each of the multiple stages of the seed train process; predicting, using the seed train process parameters and the first set of cell growth values, a first outcome of performing the seed train process, wherein the first outcome is indicative of whether performing the seed train process using the determined seed train process parameters will satisfy the seed train process success criteria; simulating a second set of cell growth values using the historical cell growth data, the second set of cell growth values including a second historical cell growth value for each of the multiple stages of the seed train process; predicting, using the seed train process parameters and the second set of cell growth values, a second outcome of performing the seed train process, wherein the second outcome is indicative of whether performing the seed train process using the seed train process parameters will satisfy the seed train process success criteria; and determining the likelihood based on the predicted first and second outcomes.

[0026] In some examples, determining the likelihood based on the predicted first and second outcomes comprises: determining a number of predicted outcomes that indicate that performing the seed train process using the seed train process parameters and respective historical cell growth data will satisfy the seed train process success criteria; and determining a ratio of the number of predicted outcomes to a total number of predicted outcomes.

[0027] In some examples, the seed train process success criteria comprise, for each stage of the multiple stages of the seed train process: a first criterion that an expected duration needed to grow the culture during the particular stage does not exceed a threshold duration for growing the culture during the particular stage, predicting the first outcome comprises, for each particular stage of the multiple stages: determining, using the respective set of seed train process parameters for the particular stage and a historical cell growth value of the first set of historical cell growth values, a first expected duration needed to grow the culture of cells during the particular stage of the seed train process; and comparing the first expected duration to the threshold duration, and predicting the second outcome comprises, for each particular stage of the multiple stages: determining, using the respective set of seed train process parameters for the particular stage and a historical cell growth value of the second set of historical cell growth values, a second expected duration needed to grow the culture of cells during the particular stage of the seed train process; and comparing the second expected duration to the threshold duration.

[0028] In some examples, the seed train process success criteria comprise, for each stage