

CLAIMS

What is claimed is:

1. A system for determining an impact of a therapeutic agent on diseased cells, comprising:
 - one or more processors;
 - a memory; and
 - one or more programs, wherein the one or more programs are stored in the memory and configured to be executed by the one or more processors, the one or more programs including instructions for:
 - obtaining a first plurality of images captured at a first plurality of time points of one or more untreated diseased live biological cells expressing a disease phenotype;
 - obtaining a second plurality of images captured at a second plurality of time points of one or more treated diseased live biological cells expressing the disease phenotype that has been treated with the therapeutic agent;
 - inputting the first plurality of images into a trained machine-learning model to obtain a first plurality of embedding vectors representing positional and morphological changes over time in particular cellular substructures of the one or more untreated diseased live biological cells;
 - inputting the second plurality of images into the trained machine-learning model to obtain a second plurality of embedding vectors representing positional and morphological changes over time in particular cellular substructures of the one or more treated diseased live biological cells; and
 - determining, from at least a subset of the first plurality of embedding vectors and the second plurality of embedding vectors, the impact of the therapeutic agent on a reversion of the one or more treated diseased live biological cells from a diseased state.
2. The system of claim 1, further comprising:
 - obtaining a third plurality of images captured at a third plurality of time points of one or more healthy live biological cells;
 - inputting the third plurality of images into the trained machine-learning model to obtain a third plurality of embedding vectors representing positional and morphological changes over time in particular cellular substructures of the one or more healthy live biological cells; and

determining, from at least a subset of the first plurality of embedding vectors, the second plurality of embedding vectors, and the third plurality of embedding vectors, the impact of the therapeutic agent on the reversion of the one or more treated diseased live biological cells from the diseased state to a healthy state.

3. The system of claim 2, wherein the one or more treated diseased live biological cells are a first set of treated diseased live biological cells and are treated with a first dosage of the therapeutic agent, the method further comprising:

obtaining a fourth plurality of images captured at a fourth plurality of time points of a second set of treated diseased live biological cells expressing the disease phenotype that has been treated with a second dosage of the therapeutic agent;

inputting the fourth plurality of images into the trained machine-learning model to obtain a fourth plurality of embedding vectors representing positional and morphological changes over time in particular cellular substructures of the second set of treated diseased live biological cells; and

comparing the impact of the first dosage and the second dosage based on at least a subset of the first plurality of embedding vectors, the second plurality of embedding vectors, and the fourth plurality of embedding vectors.

4. The system of claim 3, wherein the one or more treated diseased live biological cells are a first set of treated diseased live biological cells and wherein the therapeutic agent is a first therapeutic agent, the method further comprising:

obtaining a fifth plurality of images captured at a fifth plurality of time points of a third set of treated diseased cells expressing the disease phenotype that has been treated with a second therapeutic agent;

inputting the fifth plurality of images into the trained machine-learning model to obtain a fifth plurality of embedding vectors representing positional and morphological changes over time in particular cellular substructures of the third set of treated diseased live biological cells; and

comparing the impact of the first therapeutic agent and the second therapeutic agent based on at least a subset of the first plurality of embedding vectors, the second plurality of embedding vectors, and the fifth plurality of embedding vectors.

5. The system of any one of claims 1-4, wherein the first plurality of time points are the same as the second plurality of time points, or wherein the first plurality of time points are different from the second plurality of time points.
6. The system of any one of claims 1-5, wherein the therapeutic agent is a chemical treatment, a genetic treatment, or any combination thereof.
7. The system of any one of claims 1-6, further comprising:
determining one or more dose administration intervals for administering the therapeutic agent based on the second plurality of embedding vectors.
8. The system of any one of claims 1-7, further comprising:
providing a medical recommendation or administering the therapeutic agent to a patient.
9. The system of any one of claims 1-8, wherein the first plurality of images and the second plurality of images comprise phase images.
10. The system of any one of claims 1-8, wherein the first plurality of images and the second plurality of images are generated from fluorescence images or autofluorescence images.
11. The system of any one of claims 1-10, wherein the trained machine-learning model is a self-supervised machine-learning model.
12. The system of any one of claims 1-11, wherein the trained machine-learning model is trained using unlabeled data.
13. The system of claim 12, wherein the trained machine-learning model is pre-trained using unlabeled images that do not depict biological samples.
14. The system of claim 13, wherein the trained machine-learning model is retrained using unlabeled images of biological samples.
15. The system of any one of claims 1-14, wherein evaluating the impact of the therapeutic agent comprises:
inputting the first plurality of embedding vectors into a trained classifier to obtain a first plurality of disease scores, wherein the trained classifier is a model configured to receive

an input embedding and output a corresponding disease score; and
inputting the second plurality of embedding vectors into the classifier to obtain a second plurality of disease scores.

16. The system of claim 15, further comprising:
generating a first time trend based on the first plurality of disease scores;
generating a second time trend based on the second plurality of disease scores; and
comparing the first time trend and the second time trend.
17. The system of claim 15 or 16, further comprising:
generating a first plurality of distributions based on the first plurality of disease scores;
generating a second plurality of distributions based on the second plurality of disease scores; and
comparing the first plurality of distributions and the second plurality of distributions.
18. The system of any one of claims 15-17, wherein the classifier is a logistic regression classifier.
19. The system of claim 1, wherein determining the impact of the therapeutic agent on the reversion of the one or more treated diseased live biological cells from the diseased state comprises:

identifying a first plurality of positions in a latent space corresponding to the first plurality of embedding vectors;

identifying a second plurality of positions in the latent space corresponding to the second plurality of embedding vectors; and

determining the impact of the therapeutic agent by comparing the first plurality of positions in the latent space and the second plurality of positions in the latent space.
20. The system of claim 19, wherein determining the impact of the therapeutic agent comprises determining a movement in the latent space based on the first plurality of positions in the latent space and the second plurality of positions in the latent space.