resource intensive. Thus, fluorescence images can be difficult to obtain at scale and in a low-cost manner.

[0004] Transforming bright-field images of biological samples into enhanced, high-quality images can be difficult for a number of reasons. First, the bright-field images suffer from the inherent class imbalance problem (i.e., abundant low frequency signals but fewer high frequency signals). Further, the overall geometry of the bright-field images needs to be extracted and maintained through the transformation. Furthermore, many factors such as the illumination pattern under which the bright-field images are taken can impact the effectiveness of the transformation. Further still, the robustness of the transformation in supporting downstream analyses needs to be quantified and validated.

SUMMARY

[0005] Described are systems and methods for training machine-learning models to generate images of biological samples. Also described are systems and methods for generating enhanced images of biological samples. The systems and methods can be used, for example to obtain images of a first type, for example, a bright-field image type. The obtained images of the first image type can then be used by the systems and methods to generate a synthetic image of a second type, for example, a fluorescence image.

[0005a] In an aspect, the present disclosure refers to a method for generating enhanced images of biological samples, comprising: obtaining, using a microscope, an image of a biological sample; and generating, based on the image, an enhanced image of the biological sample using a machine-learning model, wherein the machine-learning model has been trained by: obtaining a plurality of training images comprising a training image of a first type, and a training image of a second type; generating, based on the training image of the first type, a plurality of wavelet coefficients using the machine-learning model; generating, based on the plurality of wavelet coefficients, a synthetic image of the second type; comparing the synthetic

image of the second type with the training image of the second type; and updating the machine-learning model based on the comparison.

[0005b] In an aspect, the present disclosure refers to a method for training a machine-learning model to generate images of biological samples, comprising: obtaining a plurality of training images comprising: a microscopic training image of a first type, and a microscopic training image of a second type; generating, based on the training microscopic image of the first type, a plurality of wavelet coefficients using the machine-learning model; generating, based on the plurality of wavelet coefficients, a synthetic image of the second type; comparing the synthetic image of the second type with the microscopic training image of the second type; and updating the machine-learning model based on the comparison.

[0006] In some examples, a method for training a machine-learning model to generate images of biological samples, comprises obtaining a plurality of training images. The plurality of images comprises a training image of a first type, and a training image of a second type. The method also comprises generating, based on the training image of the first type, a plurality of wavelet coefficients using the machine-learning model; generating, based on the plurality of wavelet coefficients, a synthetic image of the second type; comparing the synthetic image of the second type with the training image of the second type; and updating the machine-learning model based on the comparison.

[0007] In some example, a method for generating enhanced images of biological samples, comprises obtaining, using a microscope, an image of a biological sample; and generating, based on the image, an enhanced image of the biological sample using a machine-

learning model. The machine-learning model may be trained by: obtaining a plurality of training images comprising a training image of a first type, and a training image of a second type; generating, based on the training image of the first type, a plurality of wavelet coefficients using the machine-learning model; generating, based on the plurality of wavelet coefficients, a synthetic image of the second type; comparing the synthetic image of the second type with the training image of the second type; and updating the machine-learning model based on the comparison.

[0008] In some examples, a system for training a machine-learning model to generate images of biological samples, comprises: a computing system comprising one or more processors, and one or more memories storing a machine-learning model, wherein the computing system is configured to receive a plurality of training images of a first type and one a training image of a second type. The computing system may be configured to: generate, based on the training images of the first type, a plurality of wavelet coefficients using the machine-learning model; generate, based on the plurality of wavelet coefficients, a synthetic image of the second type; compare the synthetic image of the second type with the training image of the second type; and update the machine-learning model based on the comparison.

[0009] In some examples, a system for generating enhanced images of biological samples, comprises: a computing system comprising one or more processors, and one or more memories storing a machine-learning model. The computing system may be configured to receive an image of a biological sample obtained from a microscope and generate, based on the image, an enhanced image of the biological sample using a machine-learning model. The machine-learning model may be been trained by: obtaining a plurality of training images comprising a training image of a first type, and a training image of a second type; generating, based on the training image of the first type, a plurality of wavelet coefficients using the machine-learning model; generating, based on the plurality of wavelet coefficients, a synthetic image of the second type; comparing the synthetic image of the second type with the training image of the second type; and updating the machine-learning model based on the comparison.

[0010] An exemplary method for training a machine-learning model to generate images of biological samples comprises: obtaining a plurality of training images comprising: a training

image of a first type, and a training image of a second type; generating, based on the training image of the first type, a plurality of wavelet coefficients using the machine-learning model; generating, based on the plurality of wavelet coefficients, a synthetic image of the second type; comparing the synthetic image of the second type with the training image of the second type; and updating the machine-learning model based on the comparison.

[0011] In some examples, the training image of the first type is a bright-field image of a biological sample.

[0012] In some examples, the training image of the second type is a fluorescence image of the biological sample.

[0013] In some examples, the machine-learning model comprises a generator and a discriminator.

[0014] In some examples, the machine-learning model comprises a conditional GAN model.

[0015] In some examples, the generator comprises a plurality of neural networks corresponding to a plurality of frequency groups.

[0016] In some examples, each neural network of the plurality of neural networks is configured to generate wavelet coefficients for a respective frequency group.

[0017] In some examples, the plurality of neural networks comprises a plurality of U-Net neural networks.

[0018] In some examples, the discriminator is a PatchGAN neural network.

[0019] In some examples, the method further comprises: generating, based on the training image of the first type, an image of a third type.

[0020] In some examples, the image of the third type is a phase shift image.

[0021] In some examples, the method further comprises: generating, based on the training image of the first type, an image of a fourth type.

[0022] In some examples, the image of the fourth type comprises segmentation data.

[0023] In some examples, the training image of the first type is captured using a microscope according to a first illumination scheme.

[0024] In some examples, the first illumination scheme comprises one or more illumination patterns.

[0025] In some examples, the training image of the first type is part of a bright-field image array.

[0026] In some examples, the plurality of training images is a first plurality of training images, the method further comprising: based on the comparison, identifying a second illumination scheme; obtaining a second plurality of training images comprising one or more images of the first type, wherein the one or more images of the first type are obtained based on the second illumination scheme; training the machine-learning model based on the second plurality of training images.

[0027] In some examples, the method further comprises obtaining, using a microscope, a plurality of images of the first type; and generating, based on the obtained plurality of images, a plurality of synthetic images of the second type using the machine-learning model.

[0028] In some examples, the method further comprises training a classifier based on the plurality of synthetic images of the second type.

[0029] In some examples, the microscope is a first microscope, wherein the classifier is a first classifier, further comprising: obtaining, using a second microscope, a plurality of images of the second type; training a second classifier based on the plurality of images of the second type; comparing performance of the first classifier and the second classifier.

[0030] In some examples, the second microscope is a fluorescence microscope.

[0031] An exemplary method for generating enhanced images of biological samples comprises: obtaining, using a microscope, an image of a biological sample; and generating, based on the image, an enhanced image of the biological sample using a machine-learning model, wherein the machine-learning model has been trained by: obtaining a plurality of training images comprising a training image of a first type, and a training image of a second type; generating, based on the training image of the first type, a plurality of wavelet coefficients using the machine-learning model; generating, based on the plurality of wavelet coefficients, a synthetic image of the second type; comparing the synthetic image of the second type with the training image of the second type; and updating the machine-learning model based on the comparison.

[0032] In some examples, the training image of the first type is a bright-field image of a biological sample.

[0033] In some examples, the training image of the second type is a fluorescence image of the biological sample.

[0034] In some examples, the machine-learning model comprises a generator and a discriminator.

[0035] In some examples, the machine-learning model comprises a conditional GAN model.

[0036] In some examples, the generator comprises a plurality of neural networks corresponding to a plurality of frequency groups.

[0037] In some examples, each neural network of the plurality of neural networks is configured to generate wavelet coefficients for a respective frequency group.

[0038] In some examples, the plurality of neural networks comprises a plurality of U-Net neural networks.

[0039] In some examples, the discriminator is a PatchGAN neural network.

[0040] In some examples, the method further comprises: generating, based on the training image of the first type, an image of a third type.

[0041] In some examples, the image of the third type is a phase shift image.

[0042] In some examples, the method further comprises: generating, based on the training image of the first type, an image of a fourth type.

[0043] In some examples, the image of the fourth type comprises segmentation data.

[0044] In some examples, the training image of the first type is captured using a microscope according to a first illumination scheme.

[0045] In some examples, the first illumination scheme comprises one or more illumination patterns.

[0046] In some examples, the training image of the first type is part of a bright-field image array.

[0047] In some examples, the plurality of training images is a first plurality of training images, the method further comprising: based on the comparison, identifying a second illumination scheme; obtaining a second plurality of training images comprising one or more images of the first type, wherein the one or more images of the first type are obtained based on the second illumination scheme; training the machine-learning model based on the second plurality of training images.

[0048] In some examples, the method further comprises obtaining, using a microscope, a plurality of images of the first type; and generating, based on the obtained plurality of images, a plurality of synthetic images of the second type using the machine-learning model.

[0049] In some examples, the method further comprises: training a classifier based on the plurality of synthetic images of the second type.

[0050] In some examples, the microscope is a first microscope, wherein the classifier is a first classifier, further comprising: obtaining, using a second microscope, a plurality of images of the second type; training a second classifier based on the plurality of images of the second type; comparing performance of the first classifier and the second classifier.

[0051] In some examples, the second microscope is a fluorescence microscope.

[0052] An exemplary system for training a machine-learning model to generate images of biological samples comprises: a computing system comprising one or more processors, and one or more memories storing a machine-learning model, wherein the computing system is configured to receive a plurality of training images of a first type and one a training image of a second type, and wherein the computing system is configured to generate, based on the training images of the first type, a plurality of wavelet coefficients using the machine-learning model; generate, based on the plurality of wavelet coefficients, a synthetic image of the second type; compare the synthetic image of the second type with the training image of the second type; and update the machine-learning model based on the comparison.

[0053] In some examples, the training image of the first type is a bright-field image of a biological sample.

[0054] In some examples, the training image of the second type is a fluorescence image of the biological sample.

[0055] In some examples, the machine-learning model comprises a generator and a discriminator.

[0056] In some examples, the machine-learning model comprises a conditional GAN model.

[0057] In some examples, the generator comprises a plurality of neural networks corresponding to a plurality of frequency groups.

[0058] In some examples, each neural network of the plurality of neural networks is configured to generate wavelet coefficients for a respective frequency group.

[0059] In some examples, the plurality of neural networks comprises a plurality of U-Net neural networks.

[0060] In some examples, the discriminator is a PatchGAN neural network.

[0061] In some examples, the computing system is further configured to: generate, based on the training image of the first type, an image of a third type.

[0062] In some examples, the image of the third type is a phase shift image.

[0063] In some examples, the computing system is further configured to: generate, based on the training image of the first type, an image of a fourth type.

[0064] In some examples, the image of the fourth type comprises segmentation data.

[0065] In some examples, the training image of the first type is captured using a microscope according to a first illumination scheme.

[0066] In some examples, the first illumination scheme comprises one or more illumination patterns.

[0067] In some examples, the training image of the first type is part of a bright-field image array.

[0068] In some examples, the plurality of training images is a first plurality of training images, and wherein the computing system is further configured to: based on the comparison, identify a second illumination scheme; obtain a second plurality of training images comprising one or more images of the first type, wherein the one or more images of the first type are obtained based on the second illumination scheme; train the machine-learning model based on the second plurality of training images.

[0069] In some examples, the computing system is further configured to: obtain, using a microscope, a plurality of images of the first type; and generate, based on the obtained plurality of images, a plurality of synthetic images of the second type using the machine-learning model.

[0070] In some examples, the computing system is further configured to: train a classifier based on the plurality of synthetic images of the second type.

[0071] In some examples, the microscope is a first microscope, wherein the classifier is a first classifier, wherein the computing system is further configured to: obtain, using a second

microscope, a plurality of images of the second type; train a second classifier based on the plurality of images of the second type; compare performance of the first classifier and the second classifier.

[0072] In some examples, the second microscope is a fluorescence microscope.

[0073] An exemplary system for generating enhanced images of biological samples comprises: a computing system comprising one or more processors, and one or more memories storing a machine-learning model, wherein the computing system is configured to receive an image of a biological sample obtained from a microscope and generate, based on the image, an enhanced image of the biological sample using a machine-learning model, wherein the machine-learning model has been trained by: obtaining a plurality of training images comprising a training image of a first type, and a training image of a second type; generating, based on the training image of the first type, a plurality of wavelet coefficients using the machine-learning model; generating, based on the plurality of wavelet coefficients, a synthetic image of the second type; comparing the synthetic image of the second type with the training image of the second type; and updating the machine-learning model based on the comparison.

[0074] In some examples, the training image of the first type is a bright-field image of a biological sample.

[0075] In some examples, the training image of the second type is a fluorescence image of the biological sample.

[0076] In some examples, the machine-learning model comprises a generator and a discriminator.

[0077] In some examples, the machine-learning model comprises a conditional GAN model.

[0078] In some examples, the generator comprises a plurality of neural networks corresponding to a plurality of frequency groups.

[0079] In some examples, each neural network of the plurality of neural networks is configured to generate wavelet coefficients for a respective frequency group.

[0080] In some examples, the plurality of neural networks comprises a plurality of U-Net neural networks.

[0081] In some examples, the discriminator is a PatchGAN neural network.

[0082] In some examples, the machine learning model is further trained by generating, based on the training image of the first type, an image of a third type.

[0083] In some examples, the image of the third type is a phase shift image.

[0084] In some examples, the machine-learning model has been trained by: generating, based on the training image of the first type, an image of a fourth type.

[0085] In some examples, the image of the fourth type comprises segmentation data.

[0086] In some examples, the training image of the first type is captured using a microscope according to a first illumination scheme.

[0087] In some examples, the first illumination scheme comprises one or more illumination patterns.

[0088] In some examples, the training image of the first type is part of a bright-field image array.

[0089] In some examples, the plurality of training images is a first plurality of training images, wherein the machine-learning model has been trained by: based on the comparison, identifying a second illumination scheme; obtaining a second plurality of training images comprising one or more images of the first type, wherein the one or more images of the first type are obtained based on the second illumination scheme; training the machine-learning model based on the second plurality of training images.

[0090] In some examples, the machine-learning model has been trained by: obtaining, using a microscope, a plurality of images of the first type; and generating, based on the obtained plurality of images, a plurality of synthetic images of the second type using the machine-learning model.

[0091] In some examples, the machine-learning model has been trained by: training a classifier based on the plurality of synthetic images of the second type.

[0092] In some examples, the microscope is a first microscope, wherein the classifier is a first classifier, wherein the machine-learning model has been trained by: obtaining, using a second microscope, a plurality of images of the second type; training a second classifier based on the plurality of images of the second type; comparing performance of the first classifier and the second classifier.

[0093] In some examples, the second microscope is a fluorescence microscope.

[0094] An exemplary method of processing images of a biological sample to obtain one or more output images comprises: obtaining a plurality of images of the biological sample using a plurality of configurations of a SLM of an optical system, wherein the SLM is located in an optical path between the biological sample and an image recording device; and inputting the plurality of images of the biological sample into a trained machine-learning model to obtain the one or more outputs images.

[0095] In some examples, at least one configuration of the plurality of configurations of the SLM is to generate one or more optical aberrations.

[0096] In some examples, generating one or more optical aberrations comprises a spherical aberration, astigmatism, defocus, distortion, tilt, or any combination thereof.

[0097] In some examples, at least one configuration of the plurality of configurations of the SLM is to enhance one or more features.

[0098] In some examples, the one or more features comprise a cell border, an actin filament, nuclear shape, cytoplasm segmentation, or any combination thereof.

[0099] In some examples, at least one configuration of the plurality of configurations of the SLM is to reduce optical aberrations.

[0100] In some examples, the plurality of SLM configurations is to obtain images of the biological sample at different depths.

[0101] In some examples, the machine-learning model is configured to generate, based on an image of a first type, an image of a second type.

[0102] In some examples, the first type of images are bright-field images.

[0103] In some examples, the second type of images are fluorescence images.

[0104] In some examples, the second type of images are enhanced versions of the first type of images.

[0105] In some examples, the machine-learning model is a GAN model or a self-supervised model.

[0106] In some examples, the plurality of images are obtained using a plurality of configurations of a light source of the optical system.

[0107] In some examples, the light source is a LED array of the optical system.

[0108] In some examples, at least one configuration of the plurality of SLM configurations is obtained by: training the machine-learning model; evaluating the trained machine-learning model; and identifying the at least one configuration based on the evaluation.

[0109] In some examples, the trained machine-learning model is configured to receive an input image and output an enhanced version of the input image.

[0110] In some examples, the enhanced version of the input image comprises one or more enhanced cellular phenotypes.

[0111] An exemplary electronic device for processing images of a biological sample to obtain one or more output images comprises: 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 plurality of images of the biological sample using a plurality of configurations of a SLM of an optical system, wherein the SLM is located in an optical path between the biological sample and an image recording device; and inputting the plurality of images of the biological sample into a trained machine-learning model to obtain the one or more output images.

[0112] An exemplary non-transitory computer-readable storage medium stores one or more programs for processing images of a biological sample to obtain one or more output images, the one or more programs comprising instructions, which when executed by one or more processors of an electronic device, cause the electronic device to: obtain a plurality of images of the biological sample using a plurality of configurations of a SLM of an optical system, wherein the SLM is located in an optical path between the biological sample and an image recording

device; and input the plurality of images of the biological sample into a trained machine-learning model to obtain the one or more output images.

[0113] An exemplary method of classifying images of a biological sample comprises: obtaining a plurality of images of the biological sample using a plurality of configurations of an SLM of an optical system, wherein the SLM is located in an optical path between the biological sample and an image recording device; and inputting the plurality of images of the biological sample into a trained machine-learning model to obtain one or more classification outputs.

[0114] In some examples, at least one configuration of the plurality of configurations of the SLM is to generate one or more optical aberrations.

[0115] In some examples, generating one or more optical aberrations comprises a spherical aberration, astigmatism, defocus, distortion, tilt, or any combination thereof.

[0116] In some examples, at least one configuration of the plurality of configurations of the SLM is to enhance one or more features.

[0117] In some examples, the one or more features comprise a cell border, an actin filament, nuclear shape, cytoplasm segmentation, or any combination thereof.

[0118] In some examples, at least one configuration of the plurality of configurations of the SLM is to reduce optical aberrations.

[0119] In some examples, the plurality of SLM configurations is to obtain images of the biological sample at different depths.

[0120] In some examples, the plurality of images are obtained using a plurality of configurations of a light source of the optical system.

[0121] In some examples, the light source is a LED array of the optical system.

[0122] In some examples, at least one configuration of the plurality of SLM configurations is obtained by: training the machine-learning model; evaluating the trained machine-learning model; and identifying the at least one configuration based on the evaluation.

[0123] In some examples, the trained machine-learning model is configured to receive an input image and detect one or more pre-defined objects in the input image.

[0124] In some examples, the pre-defined objects include a diseased tissue.

[0125] An exemplary electronic device for classifying images of a biological sample comprises: 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 plurality of images of the biological sample using a plurality of configurations of an SLM of an optical system, wherein the SLM is located in an optical path between the biological sample and an image recording device; and inputting the plurality of images of the biological sample into a trained machine-learning model to obtain one or more classification outputs.

[0126] An exemplary non-transitory computer-readable storage medium stores one or more programs for classifying images of a biological sample, the one or more programs comprising instructions, which when executed by one or more processors of an electronic device, cause the electronic device to: obtain a plurality of images of the biological sample using a plurality of configurations of an SLM of an optical system, wherein the SLM is located in an optical path between the biological sample and an image recording device; and input the plurality of images of the biological sample into a trained machine-learning model to obtain one or more classification outputs.

[0127] An exemplary method for training a machine-learning model comprises: obtaining a plurality of images of a biological sample using a plurality of configurations of an SLM of an optical system, wherein the SLM is located in an optical path between the biological sample and an image recording device; and training the machine-learning model using the plurality of images.

[0128] In some examples, at least one configuration of the plurality of configurations of the SLM is to generate one or more optical aberrations.

[0129] In some examples, generating one or more optical aberrations comprises a spherical aberration, astigmatism, defocus, distortion, tilt, or any combination thereof.

[0130] In some examples, at least one configuration of the plurality of configurations of the SLM is to enhance one or more features.

[0131] In some examples, the one or more features comprise a cell border, an actin filament, nuclear shape, cytoplasm segmentation, or any combination thereof.

[0132] In some examples, at least one configuration of the plurality of configurations of the SLM is to reduce optical aberrations.

[0133] In some examples, at least one configuration of the plurality of configurations of the SLM is to obtain images of the biological sample at different depths.

[0134] In some examples, the machine-learning model is configured to generate, based on an image of a first type, an image of a second type.

[0135] In some examples, the first type of images are bright-field images.

[0136] In some examples, the second type of images are fluorescence images.

[0137] In some examples, the machine-learning model is a GAN model or a self-supervised model.

[0138] In some examples, the machine-learning model is a classification model.

[0139] In some examples, the plurality of images are obtained using a plurality of configurations of a light source of the optical system.

[0140] In some examples, the light source is a LED array of the optical system.

[0141] In some examples, training the machine-learning model comprises: (a) training the machine-learning model using a first image, wherein the first image is obtained using a first configuration of the SLM of the optical system; (b) evaluating the trained machine-learning model; (c) based on the evaluation, identifying a second configuration of the SLM; and (d) training the machine-learning model using a second image, wherein the second image is obtained using the second configuration of the SLM of the optical system.

[0142] In some examples, the evaluation is based on a loss function of the machine-learning model.

[0143] In some examples, the method further comprises: repeating steps (a)-(d) until a threshold is met.

[0144] In some examples, the threshold is indicative of convergence of the training.

[0145] In some examples, the trained machine-learning model is configured to receive an input image and output an enhanced version of the input image.

[0146] In some examples, the enhanced version of the input image comprises one or more enhanced cellular phenotypes.

[0147] In some examples, the trained machine-learning model is configured to receive an input image and detect one or more pre-defined objects in the input image.

[0148] In some examples, the pre-defined objects include a diseased tissue.

[0149] An exemplary electronic device for training a machine-learning model comprises: 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 plurality of images of a biological sample using a plurality of configurations of an SLM of an optical system, wherein the SLM is located in an optical path between the biological sample and an image recording device; and training the machine-learning model using the plurality of images.

[0150] An exemplary non-transitory computer-readable storage medium stores one or more programs for training a machine-learning model, the one or more programs comprising instructions, which when executed by one or more processors of an electronic device, cause the electronic device to: obtain a plurality of images of a biological sample using a plurality of configurations of an SLM of an optical system, wherein the SLM is located in an optical path between the biological sample and an image recording device; and train the machine-learning model using the plurality of images.

[0151] An exemplary method of generating enhanced images of biological samples comprises: obtaining, using a microscope, an image of a biological sample illuminated using an illumination pattern of an illumination source, wherein the illumination pattern is determined by: training a classification model configured to receive an input image and output a classification result, training, using the trained classification model, a machine-learning model having an plurality of weights corresponding to a plurality of illumination settings, and identifying the illumination pattern based on the plurality of weights of the trained machine-learning model; and generating an enhanced image of the biological sample by inputting the obtained image of the biological sample into the trained machine-learning model.

[0152] In some examples, the obtained image is a bright-field image.

[0153] In some examples, the enhanced image is a fluorescence image, a phase image, or a combination thereof.

[0154] In some examples, the illumination source comprises an array of illumination emitters.

[0155] In some examples, the illumination source is a LED array.

[0156] In some examples, the illumination pattern indicates whether each illumination emitter is turned on or off and the intensity of each illumination emitter.

[0157] In some examples, each illumination setting of the plurality of illumination settings corresponds to a respective illumination emitter of the illumination source; and wherein each weight corresponds to an intensity of the respective illumination emitter.

[0158] In some examples, the classification model is configured to receive an input phase image or an input fluorescence image and output a classification result indicative of one class out of a plurality of pre-defined classes.

[0159] In some examples, the plurality of pre-defined classes comprises a healthy class and a diseased class.

[0160] In some examples, the machine-learning model is a GAN model comprising an attention layer comprising the plurality of weights, a discriminator, and a generator.

[0161] In some examples, the machine-learning model is a conditional GAN model.

[0162] In some examples, the generator comprises a plurality of neural networks corresponding to a plurality of frequency groups.

[0163] In some examples, each neural network of the plurality of neural networks is configured to generate wavelet coefficients for a respective frequency group.

[0164] In some examples, the plurality of neural networks comprises a plurality of U-Net neural networks.

[0165] In some examples, the discriminator is a PatchGAN neural network.

[0166] In some examples, training, using the trained classification model, the machine-learning model comprises: applying the plurality of weights to a plurality of bright-field training images; aggregating the plurality of weighted bright-field training images into an aggregated bright-field image; inputting the aggregated bright-field training image into the machine-learning model to obtain an enhanced training image and a generator loss; inputting the enhanced training image into the trained classifier to obtain a classifier loss; augmenting the generator loss based on the classifier loss; and updating the plurality of weights based on the augmented generator loss.

[0167] In some examples, the method further comprises: classifying the enhanced image using the trained classifier.

[0168] In some examples, the method further comprises: displaying the enhanced image.

[0169] An exemplary system for generating enhanced images of biological samples comprises: 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, using a microscope,

the second plurality of enhanced images, and the third plurality of enhanced images to evaluate the treatment.

[0172] In some examples, the first plurality of images, the second plurality of images, and the third plurality of images are bright-field images.

[0173] In some examples, the first plurality of enhanced images, the second plurality of enhanced images, and the third plurality of enhanced images are fluorescence images.

[0174] In some examples, the first plurality of enhanced images, the second plurality of enhanced images, and the third plurality of enhanced images are phase images.

[0175] In some examples, comparing the first plurality of enhanced images, the second plurality of enhanced images, and the third plurality of enhanced images to evaluate the treatment comprises: identifying, in each image, a signal associated with a biomarker.

[0176] In some examples, comparing the first plurality of enhanced images, the second plurality of enhanced images, and the third plurality of enhanced images to evaluate the treatment further comprises: determining a first distribution based on signals of the biomarker in the first plurality of enhanced images; determining a second distribution based on signals of the biomarker in the second plurality of enhanced images; and determining a third distribution based on signals of the biomarker in the third plurality of enhanced images.

[0177] In some examples, comparing the first plurality of enhanced images, the second plurality of enhanced images, and the third plurality of enhanced images to evaluate the treatment further comprises: comparing the first distribution, the second distribution, and the third distribution to evaluate the treatment.

[0178] In some examples, comparing the first plurality of enhanced images, the second plurality of enhanced images, and the third plurality of enhanced images to evaluate the treatment comprises: determining, for each image, a score indicative of the statement of the disease of interest.

[0179] In some examples, comparing the first plurality of enhanced images, the second plurality of enhanced images, and the third plurality of enhanced images to evaluate the treatment further comprises: determining a first distribution based on scores of the first plurality of enhanced images; determining a second distribution based on scores of the second plurality of enhanced images; and determining a third distribution based on scores of the third plurality of enhanced images.

[0180] In some examples, comparing the first plurality of enhanced images, the second plurality of enhanced images, and the third plurality of enhanced images to evaluate the treatment further comprises: comparing the first distribution, the second distribution, and the third distribution to evaluate the treatment.

[0181] In some examples, the treatment is a first treatment, the method further comprising: receiving a fourth plurality of images depicting a fourth set of treated biological samples affected by the disease of interest and treated by a second treatment; inputting the fourth plurality of images into the trained machine-learning model to obtain a fourth plurality of enhanced images; comparing the first plurality of enhanced images, the second plurality of enhanced images, the third plurality of enhanced images, and the fourth plurality of enhanced images to compare the first treatment and the second treatment.

[0182] In some examples, the method further comprises: selecting a treatment out of the first treatment and the second treatment based on the comparison.

[0183] In some examples, the method further comprises: administering the selected treatment.

[0184] In some examples, the method further comprises: providing a medical recommendation based on the selected treatment.

[0185] In some examples, the trained machine-learning model is is a GAN model comprising a discriminator and a generator.

[0186] In some examples, the machine-learning model is a conditional GAN model.

[0187] In some examples, the generator comprises a plurality of neural networks corresponding to a plurality of frequency groups.

[0188] In some examples, each neural network of the plurality of neural networks is configured to generate wavelet coefficients for a respective frequency group.

[0189] In some examples, the discriminator is a PatchGAN neural network.

[0190] An exemplary system for evaluating a treatment with respect to a disease of interest comprises: 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: receiving a first plurality of images depicting a first set of healthy biological samples not affected by the disease of interest; receiving a second plurality of images depicting a second set of untreated biological samples affected by the disease of interest; receiving a third plurality of images depicting a third set of treated biological samples affected by the disease of interest and treated by the treatment; inputting the first plurality of images into a trained machine-learning model to obtain a first plurality of enhanced images; inputting the second plurality of images into the trained machine-learning model to obtain a second plurality of enhanced images; inputting the third plurality of images into the trained machine-learning model to obtain a third plurality of enhanced images; comparing the first plurality of enhanced images, the second plurality of enhanced images, and the third plurality of enhanced images to evaluate the treatment.

[0191] An exemplary non-transitory computer-readable storage medium stores one or more programs for evaluating a treatment with respect to a disease of interest, the one or more programs comprising instructions, which when executed by one or more processors of an electronic device, cause the electronic device to: receiving a first plurality of images depicting a first set of healthy biological samples not affected by the disease of interest; receiving a second plurality of images depicting a second set of untreated biological samples affected by the disease of interest; receiving a third plurality of images depicting a third set of treated biological samples affected by the disease of interest and treated by the treatment; inputting the first plurality of images into a trained machine-learning model to obtain a first plurality of enhanced images; inputting the second plurality of images into the trained machine-learning model to obtain a