CLAIMS:

[Claim 1]. A method for quantifying a biomarker of a tissue, the method comprising:

acquiring light reflectance data from the tissue at discrete wavelengths within a main wavelength interval using an imaging sensor;

determining, using a processor, at least two spectral sub-intervals in a manner such that a combination of the light reflectance data in the at least two spectral sub-intervals is correlated with a clinical variable of interest; and

calculating a measure of the biomarker of the tissue using only the light reflectance data in the at least two spectral sub-intervals using the processor;

wherein the main wavelength interval is broader than each of the at least two spectral sub-intervals and at least one spectral confounder causing a spectral variability of the acquired data is present in the tissue.

[Claim 2]. A method for quantifying a biomarker of a tissue, the method comprising:

determining, using a processor, at least two spectral sub-intervals from light reflectance data of the tissue acquired at discrete wavelengths within a main wavelength interval using an imaging sensor in a manner such that the combination of the reflectance data in the at least two spectral sub-intervals is correlated with a clinical variable of interest;

illuminating the tissue using one or more light sources with wavelengths within the at least two spectral sub-intervals;

acquiring a measurement of the light reflected by the tissue using an imaging sensor; and

calculating a measure of the biomarker of the tissue using only the acquired measurement;

wherein the main wavelength interval is broader than each of the at least two spectral sub-intervals and at least one spectral confounder causing a spectral variability of the acquired light reflectance data is present in the tissue.

[Claim 3]. The method of claim 1 or 2, wherein the clinical variable of interest comprises any one or a combination of a disease, a severity or subtype of disease, a known biomarker or a physiological state.

[Claim 4]. The method of any of claims 1 to 3 wherein the main wavelength interval is such that the acquired data represents a hyperspectral or multispectral representation of the tissue.

[Claim 5]. The method of any one of claims 1 to 4, wherein acquiring light reflectance data comprises using one or more cameras operating at different wavelengths.

[Claim 6]. The method of any of claims 1 to 5 comprising extracting a spectral parameter for each of the at least two spectral sub-intervals to form a multispectral representation of the tissue.

[Claim 7]. The method of any of claims 1 to 6 comprising identifying at least one spectral confounder causing a spectral variability in the acquired light reflectance data.

[Claim 8]. The method of any one of claims 1 to 7, wherein determining at least two spectral sub-intervals is performed in a manner such that the spectral information of the combination of the at least two spectral sub-intervals and the spectral confounder are orthogonal, uncorrelated or independent.

[Claim 9]. The method of any one of claims 1 to 8, wherein determining at least two spectral sub-intervals is performed by applying a band selection method, a machine learning algorithm or an artificial intelligence engine.

[Claim 10]. The method of any one of claims 1 to 10, wherein the variable of interest comprises the amount or distribution of amyloid beta measured in a brain using positron emission tomography (PET), or measured in cerebrospinal fluid (CSF).

[Claim 11]. The method of any one of claims 1 to 10, wherein determining at least two spectral sub-intervals comprises using a multivariate statistics, machine learning or artificial intelligence

techniques.

[Claim 12]. The method of any one of claims 1 to 11, wherein calculating a measure of the biomarker uses multivariate statistics, machine learning or artificial intelligence techniques.

[Claim 13]. The method of claim 12, wherein the multivariate statistics include regression, logistic regression or discrimination.

[Claim 14]. The method of claim 11 or 12, wherein the machine learning or artificial intelligence techniques account for demographic information, clinical information, other variables of interest or multiple regions of interest in the light reflectance data.

[Claim 15]. The method of any one of claims 1 to 14, wherein determining at least two spectral sub-intervals is performed by a machine learning algorithm that transforms multispectral data into a score that represents the biomarker.

[Claim 16]. The method of any one of claims 2 to 16, further comprising applying an optical filter to the one or more light sources.

[Claim 17]. The method of claim 16, wherein further comprising applying an optical filter along a light path of the light generated by the one or more light sources.

~~18. The method of claims 16 or 17, wherein the tissue is the retina of a person and the optical filter is embedded within a contact lens applied on an eye of the person.~~

[Claim 18~~9~~]. A system for quantifying a biomarker of a tissue, the system comprising:

a biomarker selection assembly arranged to select ~~the~~ at least two light spectral intervals based on a user selected biomarker of a tissue;

an optical assembly comprising one or more light sources arranged to illuminate a portion of the tissue at wavelengths within at least two selected spectral intervals;

an imaging assembly comprising an imaging sensor arranged to receive light reflected from the portion of the tissue and translate the light to digital data; and

a processing module arranged to receive data from the imaging sensor and being configured to:

combine and process the data received from the imaging sensor to extract spectral information and form a multispectral representation of the tissue; and

process the multispectral representation of the tissue to quantify the biomarker;

wherein the at least two ~~predetermined~~ selected spectral ~~sub-~~intervals are specific to a known variable of interest.

[Claim 19~~20~~]. The system of any of claims ~~19~~18, wherein the tissue is a portion of the retina and the biomarker is a measure of amyloid beta (AB) for predicting/stratifying risk, screening or diagnosing Alzheimer's disease and the at least two spectral intervals consist of three wavebands located within about 100 nm of 475 nm, within about 100 nm of 545 nm, and within about 100 nm of 725 nm, and each with a bandwidth under about 200 nm.

[Claim 20~~1~~]. The system of any of claims ~~19~~ 18 or ~~20~~19, wherein the optical assembly is arranged to generate light with a spectrum within the at least two spectral intervals.

[Claim 21~~2~~]. The system of any of claims ~~19~~ 18 to ~~21~~20, wherein the illumination assembly comprises optical filters arranged to filter the generated light path or the reflected light path within the at least two sub-spectral intervals.

[Claim 22~~3~~]. The system of any one of claims ~~19~~ 18 to ~~22~~21, wherein the tissue is a portion of the retina and the variable of interest is brain or cerebrospinal fluid amyloid beta level related to Alzheimer's disease and the at least two spectral intervals consist of three wavebands located within about 100 nm of 475 nm, within about 100 nm of 545 nm, and within about 100 nm of 725 nm, and each with a bandwidth under about 200 nm.

[Claim 23~~4~~]. A method for quantifying a biomarker of a tissue, the method comprising:

acquiring hyperspectral light reflectance data of the tissue using an imaging sensor within a contiguous wavelength interval;

identifying at least one spectral confounder causing a spectral variability of the hyperspectral light reflectance data;

deriving a spectral model of the tissue in a manner such that the correlation of the spectral model and the identified spectral confounder is minimized; and

calculating a measure of the biomarker of the tissue using the derived spectral model;

wherein the spectral model of the tissue is derived to be orthogonal, uncorrelated or independent to the identified spectral confounder.

[Claim 245]. The method of claim 2423, wherein the spectral model is derived from the main spectral difference between two groups, each group having a distinct amount of the variable of interest.

[Claim 256]. The method of any of claims 24 23 or 2524, wherein deriving a spectral model of the tissue comprises deriving a clean hyperspectral representation of the tissue by processing the hyperspectral representation of the tissue and a spectral signature of the at least one spectral confounder in a manner such that the clean hyperspectral representation of the tissue has reduced variability caused by the spectral signature of the at least one spectral confounder.

[Claim 267]. The method of any one of claims 24 23 to 2625, wherein acquiring an hyperspectral light reflectance data of the tissue comprises sequentially illuminating the tissue, using one or more light sources, with monochromatic or narrow bandwidth light within a contiguous predetermined range of wavelengths and, for each wavelength, using the imaging sensor to acquire a measurement of the light reflected by the tissue.

[Claim 278]. The method of any of claims 24 23 to 2726, wherein identifying at least one spectral confounder comprises reading from a spectral database one or more spectral profiles of spectral confounders and processing the spectral information from the hyperspectral light reflectance data and the one or more spectral profile.

[Claim 289]. The method of any of claims 24 23 to 2827, wherein deriving a clean hyperspectral representation comprises removing, from the spectral information, a spectral

variability caused by the spectral profile of the at least one spectral confounder.

[Claim 2930]. The method of any one of claims ~~24~~ 23 to ~~29~~ 28 wherein identifying at least one spectral confounder comprises using a specific spectral confounder as a reference cofounder and calculating a delta hyperspectral light reflectance data which represents a pixel-by-pixel and wavelength-by-wavelength difference between two hyperspectral light reflectance data.

[Claim 301]. The method of any one of claims ~~24~~ 23 to ~~30~~29, wherein the spectral information is processed in accordance with the following steps:

computing the inter-class spectral variability between groups that differ with respect to the variable of interest;

extracting a first set of principal eigenvectors of the intra-class spectral database; and

removing one or more eigenvectors using an orthogonal projection to produce an intermediate dataset in which the intra-class variability is substantially removed;

wherein the biomarker is quantified using a spectral dimension reduction based on the clean spectral representation of the tissue.

[Claim 312]. The method of any one of claims ~~24~~ 23 to ~~31~~30, wherein the spectral information is processed in accordance with the following steps:

computing the inter-class spectral variability between distinct groups of the spectral database;

extracting a first set of principal eigenvectors of the inter-class variability between the distinct groups;

removing the inter-class variability using an orthogonal projection based on the first set of principal eigenvectors from a combination of the distinct groups to produce an intermediate dataset in which the inter-class variability is substantially removed;

computing intra-class variability within the intermediate dataset; extracting a second set of principal eigenvectors of the intra-class variability of the intermediate dataset; and

extracting a third set of principal eigenvectors of a plurality of clean spectral presentations in the statistical database;

wherein removing, from the interim spectral information, the spectral variability caused by the at least one non-specific confounder comprises removing, from the interim spectral information, the intra-class variability using an orthogonal projection based on the second set of principal eigenvectors to create the clean spectral representation of the tissue; and

wherein the biomarker is quantified using a projection based on the third set of principal eigenvectors on the clean spectral representation of the tissue.

[Claim 32~~3~~]. The method of claim ~~32~~31, wherein the at least one spectral confounder comprises at least one ocular confounder and the quantified biomarker indicates the presence or absence of a variable of interest in the retina of the person.

[Claim 33~~4~~]. The method of claim 33, wherein the at least one ocular spectral confounder is comprised of variations in melanin content, cataract, discolouration of ~~the~~ a lens, hemoglobin content, retinopathy, retinal pigment epithelial thickness or density, RNFL thickness, choroidal thickness, macular pigment content and/or a combination thereof.

[Claim 34~~5~~]. A system for quantifying a biomarker of a tissue, the system comprising:

an illumination assembly arranged to successively illuminate a portion of a tissue with monochromatic light within a contiguous range of wavelengths;

an imaging assembly comprising an imaging sensor arranged to receive light reflected by the portion of the tissue and translate the light to digital data; and

a processing module and a memory module arranged to receive data from the imaging sensor and being configured to execute instructions to perform a method in accordance with anyone of claims ~~24~~ 23 to ~~34~~33.