

OPTICAL POLARIMETRIC IMAGING

BACKGROUND

1. Technical Field

The present invention is related to probing morphology of tissue, such as in vivo skin
5 tissue in vivo.

2. Description of Related Art

The phenomena of changing polarization state of back scattered light from a turbid medium are well known. In 1988, Philip et al.[2] studied these phenomena in skin tissue and followed by Anderson et al.[3] in 1991. In 1998-2002 Jacques used a side
10 illumination apparatuses.[4,5,6] In 2003, Anderson used his method for skin lesion boundary detection for Mohs micrographic surgery. [7] An enhanced view of vasculature and pigmented lesions was obtained. In 1999, Bueno et al.[8] showed an imaging of the eye retina by extracting the 16 parameters of Mueller matrix. The degree of polarization (DOP) was extracted from those images for the retinal plane. In 2004, Boulesteix et al.[9]
15 used the method for stained hepatic biopsy, extracting the degree of polarization from Mueller matrices at the visible and near infrared spectral realms, and anomalous structure of the collagen was emphasized at different wavelengths. In the same year Ramella et al. [10] simplified the readout of two polarization (parallel and crossed polarizations compared with the light source polarization) from a tissue by using two cameras and
20 calculated the normalized contrast between them simultaneously (S1 parameter of Stokes vector). Weber et al.[11] manipulated the cross and parallel polarizations separately so a tiny vein in the eye could be recognized. Liu et al.[12] measured the back-scattering Mueller matrix of a rat-skin sample almost in real-time using side illumination and the diattenuation, retardance and the depolarization parameters were deduced from the
25 Mueller matrices. In 2005 Ramella et al.[13] described a better way to illuminate the tissue by skewed illumination for back scattered imaging and even a handy tool. [14] This allowed them to eliminate the glare with no need for oil or water as matching refractive index. Polarization contrast symbolized by Stokes parameters $Pol = S1/S0$ carry only few

percentages of the light source. Thus in 2006 Zhao et al.[15] removed the noise by using adaptive wavelet transform method that can be easily applied to tissue imaging. Bruno et al.[16] constructed hemispherical spectro-polarimetric scattering instrument to manipulate series of Stokes parameters. In 2009 Zhao et al.[17] harnessed the principal component analysis (PCA) and image fusion[18,19] to the analysis of tissue characteristics and proposed a visual enhancement method to fuse the acquired spectral and polarimetric information by using false color mapping.

US patent 7289211 [1] discloses methods for calculating Stokes parameters on reflection from skin tissue.

10 Zhang *et al.* [20] performed research on an Asian male with a dark red skin and a Caucasian male with a light-pink skin. As a rule of thumb, these types of skin are the typical among all kinds of skin and surely suitable for spectral decision of preferable wavelengths.

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5 spectrophotometric measurements based on optimization by genetic algorithms," J. Biomed. Opt. 10(2), 024030 (2005).

BRIEF SUMMARY

According to features of the present invention, there is provided a method for probing
10 morphology of a tissue surface using a system which may include a light source, a polarizer, an analyzer, and a camera with multiple picture elements. The method illuminates the tissue surface with incident light through the polarizer. The illumination may be performed for incident light of different spectral content. The camera may capture through the analyzer, scattered light from the tissue surface in a continuous sequence of
15 image frames. Variation of polarization state may be of at least one of (1) the incident light from the light source by varying the polarizer or (2) the scattered light from the tissue surface by varying the analyzer. During the capture, for a picture element of the camera, a varying intensity signal of the scattered light is detected responsive to the varying polarization state. The varying intensity signal may be a periodic intensity signal.
20 The varying intensity signal may be analyzed for at least one of the picture elements throughout the image frames to probe the morphology of the tissue surface. The analysis may include determination of light intensity contrast between peaks and troughs of the varying intensity signal. The analysis may include determination of an intensity differential of the varying intensity signal between image frames. The analysis may
25 include the determination of an intensity differential of the varying intensity signal between consecutive image frames. The analysis may include the determination of a second or higher derivative of the varying intensity signal between the image frames. The varying intensity signal may be a function of time and the analysis may include performing a transform of the varying intensity signal to a transformed intensity signal in

frequency domain. The analysis may include the determination of an average of contrasts between frames of the varying intensity signal. The analysis may include determination of a variance of the varying intensity signal.

According to features of the present invention, there is provided a system including a light
5 source, a variable polarizer, a second polarizer, and a camera including an image sensor with a plurality of picture elements. The system may be operable to illuminate the tissue surface with incident light through the polarizer. Scattered light is captured by the camera through the analyzer from the tissue surface in a continuous sequence of image frames. Polarization state is varied of at least one of (1) the incident light from the light source (2)
10 the scattered light from the tissue surface. A varying intensity signal of the scattered light is detected responsive to the varying polarization state. The varying intensity signal may be a periodic intensity signal. The varying intensity signal may be a periodic intensity signal. An analysis of the varying intensity signal is performed for at least one of the picture elements throughout the image frames to probe the morphology of the tissue
15 surface. The analysis of the varying intensity signal may include a light intensity contrast between peaks and troughs of the varying intensity signal. The analysis of the varying intensity signal may include an intensity differential of the varying signal between image frames. The analysis of the varying intensity signal may include a second derivative of the varying intensity signal between the image frames. The analysis of the varying intensity
20 signal may include an average intensity of contrasts between frames of the varying intensity signal. The analysis of the varying intensity signal may include a variance of the varying intensity signal. The varying intensity signal may be a function of time and the analysis of the varying intensity signal may perform a transform of the varying intensity signal to a transformed intensity signal in frequency domain. The system may further
25 include a mechanism for varying spectral content of the incident light.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention is herein described, by way of example only, with reference to the accompanying drawings, wherein:

Figure 1a shows a system diagram for probing morphology of a tissue surface, according to a feature of the present invention.

Figures 1b and 1c show a cross section view and a plan view respectively of an implementation of system components found in the system shown in Figure 1a, according to an exemplary feature.

Figure 1d shows a cross section view of an implementation of system components found in the system shown in Figure 1a, according to another exemplary feature.

Figure 1e shows a cross section view of an implementation of system components found in the system shown in Figure 1a, according to yet another exemplary feature.

10 Figure 2a shows a series of captured image frames according to an feature of the present invention.

Figure 2b shows two examples of I_s and I_d of basal cell carcinoma.

Figure 3 shows an example of such an SD image using the image frames I_s and I_d shown in Figure 2b, illustrating a well defined boundary of the basal cell carcinoma.

15 Figures 4a and 4b show the sampled signal on one of the camera's pixels.

Figure 5 shows an image of a lesion type - compound nevus (CN), with imaging of compound nevu.

Figure 6 illustrates a second example of very hard cutaneous malignant melanoma (CMM).

20 Figure 7 which shows a method, according to a feature of the present invention.

Figure 8a and 8b show respective time and frequency domains of a varying light intensity signal.

DETAILED DESCRIPTION

25 Reference will now be made in detail to features of the present invention, examples of which are illustrated in the accompanying drawings, wherein like reference numerals refer to the like elements throughout. The features are described below to explain the present invention by referring to the figures.

By way of introduction aspects of the present invention are directed to novel methods for probing tissue such as skin tissue. In the methods disclosed herein, Stokes parameters or Mueller matrix parameters are not explicitly determined. The polarization state of the light incident on the surface being probed is varied for instance periodically. The scattered light is viewed by a camera through an analyzer. A sequence of image frames are obtained of the scattered light while the incident or scattered light polarization is being varied. Varying, (typically periodic) intensity signals of scattered light are produced for one or more picture elements of the camera. Processing of the image frames and the intensity signals may be performed in several ways according to different aspects of the present invention. For instance, the sequence of image frames may be used to extract the average contrast between adjacent image frames. The sequence of the image frames may be used to extract the scattered light intensity differential at one or more nearby picture elements from image frame to image frame. Similar, higher order derivatives of the intensity variation may be determined for one or more pixels from image frame to image frame.

The methods as disclosed herein may be applied to diagnose skin lesions.

The terms "polarizer" and "analyzer" are used herein to refer to one or more polarizing optical elements which operate by refraction, reflection, absorption and/or diffraction including one or more birefringent waveplates and/or electro-optic devices.

The term "average" or "mean" as used herein refers to an average value of a set of light intensity values. The average is calculated by combining the light intensity values from the list in a specific way, *e.g.* adding, and computing a single number as being the average of the list *e.g.*, by dividing by the number of light intensity values in list.

The term “variance” as used herein refers to a measure of how far a set of light intensity values are spread out. Variance is one of several descriptors of a probability distribution describing how far the set of light intensity values are from the average light intensity value. In particular, the variance may be one of the moments of the probability
5 distribution. Variance may be the expected value of the squared difference between measured light intensity and the average of the light intensity.

Reference is now made to Figure 1a which shows a system diagram **10** for probing morphology of a tissue surface, according to a feature of the present invention. System **10** includes a light source **12** with optics to direct, *e.g.* collimate, light emitted from light
10 source **12** onto a surface **8**, *e.g.* skin lesion, being probed. The light emitted from light source **12** passes through a polarizer **18** which may continuously and/or periodically changes the polarization state of the light emitted from light source **12** to transmit variable polarized incident light **9** onto surface **8**. Light scattered from surface **8** passes through an analyzer **4** and is received by an image sensor or camera **2**. Alternatively, or in addition to
15 the incident light, the polarization of scattered light may be varied continuously and/or periodically by for instance rotating analyzer **4**. Camera **2** may be a charge coupled device (CCD) or complimentary metal oxide semiconductor CMOS type etc. Camera **2** is connected to processor **14** which receives captured image frames **16** from camera **2**. A transparent window **11** may be used to contact tissue surface **8** and incident and scattered
20 light are transmitted through window **11**.

Variable polarization of incident light **9** or scattered light **6** may be achieved in any way known in the arts of optics and electro-optics. Polarization may be varied by rotating a birefringent wave plate. Other devices used to vary incident or scattered light polarization may include use of spatial modulation, *e.g.* liquid crystal polarization
25 modulator. The polarization of incident light **9** may be varied from linear to circular or circular to linear. The angle of linearly polarized light or elliptically polarized light may be varied. One state of elliptical polarization may be varied to any other state of polarization. Any change in the Stokes parameters or Mueller parameters may be represented in incident light **9**.

Varying polarization state may be performed by varying polarization state for instance by rotation, of polarizer **18** and/or of analyzer **4**. Polarization of incident light **9** may be changing while analyzer **4** in front of camera **2** is fixed. Polarizer **18** of incident light **9** may be fixed and analyzer **4** in front of camera **2** may be changing, *e.g.* rotating.

5 Polarizer **18** and analyzer **4** may both be changing, *e.g.* rotating at the same time.

In all cases, camera **2** captures a sequence of image frames **16** during the varying polarization.

If surface **8** has monotonic optical morphology, scattered light **6** may not experience significant change while polarization is varied. Boundaries and high scattering zones may

10 be more sensitive to changes in the polarization of incident light **9** and may produce different images for different incident polarization states.

Reference is now made to Figures 1b and 1c which show a cross section view **10a** and a plan view **100** respectively of an implementation of system components found in system **10** shown in Figure 1a, according to an exemplary feature. Camera **2** is shown with image

15 sensor **2a** and lens **2b**. With sensor **2a** and lens **2b** perpendicular to the **Z** axis are analyzer **4**, polarizer **18** and window **11**. A motor **5a** with drive shaft **5b** is connected to cog wheel **5c**. Cog wheel when rotated by motor **5a** rotates polarizer **18** in a direction at right angles to the **Z** axis. Light source **12** may include a lamp **12a** and lens **12b**. The focused light emitted from light source **12** goes through polarizer **18** to transmit variable

20 polarized incident light **9** onto window **11** and/or surface **8** by virtue of the rotation of polarizer **18**. Scattered light from window **11** and/or surface **8** goes through stationary analyzer **4**, through lens **2b** and onto image sensor **2a**.

Reference is now made to Figure 1d which shows a cross section view **10b** and of an implementation of system components found in system **10** shown in Figure 1a, according

25 to another exemplary feature. Cog wheel **5c** when rotated by motor **5a** rotates polarizer **18** and analyzer **4** by virtue of angular components **18a** and **4a** attached to polarizer **18** and analyzer **4** respectively. Analyzer **4** rotates in a plane which is at right angles to the **Z** axis and polarizer **18** rotates in a plane at an angle **B** relative to the **Z** axis. Angle **B** may be greater than zero degrees

and less than ninety degrees. The focused light emitted from light source **12** goes through polarizer **18** to transmit variable polarized incident light **9** onto window **11** and/ or surface **8** by virtue of the rotation of polarizer **18**. Scattered light from window **11** and/ or surface **8** goes through analyzer **4** which is also rotating, through lens **2b** and onto image sensor **2a**.

Reference is now made to Figure 1e which shows a cross section view **10c** and of an implementation of system components found in system **10** shown in Figure 1a, according to yet another exemplary feature. Figure 1e and 1d are similar except two motors **5a** and **5d** respectively, which rotate polarizer **18** and analyzer **4** independently from each other. cog wheel **5c** attached to drive shaft **5b** and motor **5a**, connects with angular component **18a** of polarizer **18** so as to rotate polarizer **18**. Similarly cog wheel **5f** attached to drive shaft **5e** and motor **5d**, connects with analyzer **4** so as to rotate polarizer **4**.

Pre-processing of the captured video sequence

A skin lesion is a good example due to scattering in its epidermal layers. The captured sequence can be processed as separate files of image frames **16**, or the sequence may also optionally be processed as a video sequence in a single file. System **10** may be applied to image skin lesions, while the angle of linearly polarized light is changed by rotating polarizer **18**. Scattered light scatters upward toward camera **2**. Camera **2** captures frames **16** as shown schematically in Figure 2a. Image frames **16** have indices $k=1$ to N , I_k is the k^{th} frame among N frames. Polarizer **18** may be rotated multiple times to improve signal to noise in algorithms. Each frame I_k of e.g. 640 X 480 picture elements (pixels) in current examples corresponds substantially to a single state of polarization angle- α_k produced by polarizer **18**.

Reference is now made to Figure 2 which illustrates schematically a sequence of image frames **16** captured at different incident polarization states of a skin lesion. N frames are taken during continuous change in polarization state α_k . I_s is shown as the image frame **16** when a prominent specular-like image appears. I_d is shown when the image appears

diffuse and non-specular. The images labelled "specular" and "diffused" are for a basal cell carcinoma (BCC).

Methods disclosed herein using skin lesion surface **8** as a non-limiting example of tissue or scattering material; however the method may optionally be applied to any other
5 semitransparent surface.

During variations in polarizer **18**, the scattered light **6** from the lesion is also change due to scattering from hetro-structures inside the skin. Areas which have no variation in their structure will not produce significant differences in the scattered light **6**, hence, the captured image frames **16** may show minimal change from frame to frame. More
10 significant differences are expected between image frames **16** when material boundaries or scattering sites are present. In this case, scattered light **6** may change its polarization and intensity for each state of polarization of the incident light. To uncover these structural variations in the material index of refraction or in general – optical morphology, different algorithms are optionally used to emphasize boundaries and degree of scattered
15 light **6** over the surface being probed.

- 1) Specular-Diffuse Algorithm, ***SD algorithm***.
- 2) Average Frame Contrast, named ***AFC algorithm***.
- 3) Averaged Differential algorithm, named ***AD2 algorithm***, when applied for the 2nd order of differentiation.

20 NOTE: ***AD3, AD4 ... ADn*** (n=integer), may be applied for higher orders of differentiation.

SD Algorithm: Specular-Diffused

Among the whole sequence of image frames **16** a specular-like reflection may be seen clearly from the superficial layer of the inspected surface. In skin, it would be the stratum
25 corneum. Specular-like image frames **16** are marked as I_s in Figure 2., where s stands for specular-like signatures (bright surface) usually happen when the incident polarization is at the same polarization as analyzer **4**. Between the I_s image frames **16** there are the

diffusive image frames I_d which usually happen when the polarization of the surface reflection and analyzer **4** are orthogonal. Figure 2b shows two examples of I_s and I_d of basal cell carcinoma. It can be seen that I_s image frame **16** has more glare on its surface and I_d is lack of this glare. In a similar manner to the definition of the normalized second Stokes parameter one may define the following SD image designating the contrast between the specular-like I_s image frame **16** and diffusive I_d image frames **16**:

$$SD = (I_s - I_d) / (I_s + I_d) \quad (1)$$

SD image is different than the second Stokes parameter when the polarizer at camera **2** is fixed and the glare in I_s can be from arbitrary reflection angle. Eq. 1 enables to emphasize boundaries of different scattering zones.

Figure 3 shows an example of such an SD image using the image frames **16** I_s and I_d shown in Figure 2b, illustrating a well defined boundary of the basal cell carcinoma.

AFC Algorithm: Average Frame Contrast

The optical morphology of surface such as skin lesion has arbitrary optical characteristics of absorption, transmission, scattering and will always be different from lesion to lesion, different areas in the body or for different people. Thus, *AFC algorithm* takes the average of all contrasts of two adjacent image frames **16** I_{k+m} and I_k . m is an integer number, to be chosen by the user, here $m=2$. Equation (2) demonstrates the contrast between two adjacent states. High spatial change in morphology like scattering areas will produce larger values in C_k images. Recalling the random optical morphology, C_k 's will be averaged in the final post process as *AFC* image, defined in Eq. 3.

$$C_k = \frac{|I_{k+2} - I_k|}{I_{k+2} + I_k} \quad (2)$$

$$AFC = \frac{1}{N-1} \sum_{k=1}^N C_k \quad (3)$$

AFC algorithm emphasizes the spatial inner changes of high scattering areas over the inspected surface. In skin lesions it can indicate about abnormalities, for instance dysplasia emergence, which can lead to malignancy.

5 *AD2 Algorithm: Averaged Differential of the 2nd degree*

Assuming that a surface has high optical scattering, changing the polarization will seldom produce linear change in the recorded intensity of camera 12. Intensity (or image frame 16) recorded by camera 12 will generate a curvature at each pixel during the change in the polarization state. The degree of this curvature is represented by *AD2* algorithm in Eq. 4, averaging the differential of the 2nd degree for each pixel on camera 2 detector. The higher the curvature the higher the value of *AD2*.

$$AD2 = \frac{1}{2(N-1)} \sum_{k=1}^N |I_{k+2} - I_k| \times |I_{k+2} + I_k - 2I_{k+1}| \quad (4)$$

$|I_{k+2} + I_k - 2I_{k+1}|$ is related to the numerical second derivation and indicates about the degree of curvature of the change in intensity I_k .

In order to avoid cases where the change between two points I_{k+2} and I_k is not prominent or originating from noise, $|I_{k+2} + I_k - 2I_{k+1}|$ is multiplied by the difference $|I_{k+2} - I_k|$. Eq. 4 can also be written using normalizations by dividing with sum of subtracted elements at the denominator, Eq. 5-7, or just averaging the second derivation as in Eq. 8. Then the image color map will have to be modified. The brackets $(AD2)_1.. (AD2)_4$ indicates the several options to define *AD2*.

$$(AD2)_1 = \frac{1}{2(N-1)} \sum_{k=1}^N \frac{|I_{k+2} - I_k| \times |I_{k+2} + I_k - 2I_{k+1}|}{|I_{k+2} + I_k| \times |I_{k+2} + I_k + 2I_{k+1}|} \quad (5)$$

$$(AD2)_2 = \frac{1}{2(N-1)} \sum_{k=1}^N \frac{|I_{k+2} - I_k| \times |I_{k+2} + I_k - 2I_{k+1}|}{|I_{k+2} + I_k + 2I_{k+1}|} \quad (6)$$

$$(AD2)_3 = \frac{1}{2(N-1)} \sum_{k=1}^N \frac{|I_{k+2} - I_k| \times |I_{k+2} + I_k - 2I_{k+1}|}{|I_{k+2} + I_k|} \quad (7)$$

$$(AD2)_4 = \frac{1}{2(N-1)} \sum_{k=1}^N |I_{k+2} + I_k - 2I_{k+1}| \quad (8)$$

5 To understand the meaning of $AD2$ let us follow the sampled signal on one of the camera's pixels, as shown in Figure 4a and 4b, where the axes are the intensity on a particular pixel versus the discrete polarization angle α_k of the incident light on a skin lesion. Numerical curvature measuring can expressed as the magnitude of distance between sampled intensity of the measurement at point $\{\alpha_{k+1}, I_{k+1}\}$, and average value
 10 between two adjacent points I_k and I_{k+2} , $\{\alpha_{k+1}, (I_{k+2} + I_k)/2\}$. Distance between these two points would be $|(I_{k+2} + I_k)/2 - I_{k+1}|$. Note, in Eq.4-8 the division by 2 was taken out of the summary sign.

During the scan the angle of the incident polarization on the lesion changes continuously – hence we expect a continuous change on camera 2 as well, so if I_{k+2} image frame
 15 does not change much compared to I_k , we interpret the jump in I_{k+1} as a noise and can be ignored and $AD2$ should be close to the dark level means I_{k+2} and I_k are close to each other.

Reference is now also made to Figures 4(a) and 4(b). Figure 4(a) shows a change in intensity of an arbitrary pixel in camera 2 while α changes. The solid line is the analog
 20 intensity, the black circles are its numerical samples. Figure (b) shows a case where there

is practically no prominent change between I_k and I_{k+2} where I_{k+1} doesn't lay on the dashed line. In this case I_{k+1} can be considered as a noise.

The graph of Figure 4b takes into account the multiplication of $|I_{k+2} - I_k|$ in Eq. 4. In other words, Eq. 4 collects cases similar to Figure 4a when there is a prominent difference between I_k , and I_{k+2} which is enforced with the magnitude of the intensity difference between points I_k , and I_{k+2}). The differential polarization scanning method may consider the fact that deep layers will cause the incident polarized light to lose its polarization and emerge as a non-polarized background light. So equations 3-8 mainly emphasize the changes of the superficial layer of the lesion, while still some degree of polarization is preserved.

Examples: using methods as disclosed herein in a clinic

Clinical *in vivo* images were obtained in Soroka Hospital, Beer-Sheva Israel. Images of skin lesions have been captured before the patients entered into the operation room for their surgery. The following section presents post processing images of *AFC* and *AD2* algorithms using two wavelength 520nm and 700nm. Different wavelengths may be applied for different penetration, based on properties that can be inferred from the work of Zhang *et al.*[20]:

- (1) large difference between the transmittance at 520nm and 700nm and
- (2) the spectral dependence around each of these wavelengths is nearly flat.

Reference is now also made to Figure 5 which shows an image of a lesion type - compound nevus (CN), with imaging of compound nevus. As shown in Figure 5, patterns concealed from the naked eye (Figure 5-Normal image frame) can be seen very clearly using algorithms *AFC* and *AD2*. *AFC* refers to areas with higher scattering characteristics than the surrounding of the lesion and *AD2* indicates on the curvature of the change in the back-scattering. Both cases reveal the tendency of the lesion to become neoplastic.

Reference is now made to Figure 6 which illustrates a second example of very hard cutaneous malignant melanoma (CMM). In this example, the collagen and elastin structures are already damaged and therefore generate random areas of high scattering regions, shaped as islands.

5 Algorithms, *SD*, *AFC* and *AD2* enable to distinguish between different degrees of scattered light 6 light from a surface. *SD* algorithm is mainly used for recognizing lesion's boundary. Monotonic surface appears in *AFC* and *AD2* images as hazy or smeared images, in which variations in surface optical properties appear with patterns alluding to inner structure of the first surface layers, depending on the wavelength. The penetration
10 depth governed by the incident wavelength is a debate of light and matter interaction, in most of the turbid media deep layers will cause the impinged polarized light to lose its polarization and emerges from the surface as background light.

Algorithms may be applied not just for skin lesions but also to any other scattering or turbid medium. The change in captured image frames 16 by camera 2 can be generated in
15 several ways: (1) variations in polarization at the light source or in front of camera 2 (2) changing wavelengths (3) changing light intensity (4) changing apparatus geometry (5) changing light path (6) or any other system parameter resulting change in the captured image frame 16 by camera 2.

Reference is now made to Figure 7 which shows a method 701, according to a feature of
20 the present invention. With window 11 placed on a tissue surface 8, and in step 703, the tissue surface 8 is illuminated through window 11 with polarized incident light 9. Polarized incident light 9 comes from light source 12 through polarizer 18. The scattered light from tissue surface 8 in step 705, transmits through analyzer 4 and into camera 2, through lens 2b and onto image sensor 2a. Camera 2 is operatively attached to processor
25 14 and multiple image frames 16 are captured and processed by processor 14. As discussed previously, polarizer 18 may be fixed, move together with analyzer 4 or move independently of analyzer 4. Similarly, analyzer 4 may be fixed, move together with polarizer 18 or move independently of polarizer 18. Therefore in step 707, the polarization state may be varied for at least one case of the incident light 9 by varying

polarizer **18** or in another case where the scattered light from surface **8** is varied by varying analyzer **4**. In step **709** a picture element of camera **2** may be detected which gives a varying intensity signal which is responsive to the polarization state being varied (step **707**). In step **711** the varying intensity signal may be analyzed for at least one of the
5 picture elements throughout the image frames **16**.

Analysis step **711** may include the determination of an intensity differential or a second differential of the varying intensity signal between image frames **16** or between consecutive image frames **16**. Analysis step **711** may further include determination of an average of contrasts between frames of the varying intensity signal and / or a variance of
10 the varying intensity signal. If the varying intensity signal is a function of time, the analyzing step **711** may include a transform of the varying intensity signal to a transformed intensity signal in frequency domain. The transform form may be a fast Fourier transform, Laplace transform or any transform known in the art of signal processing.

15 Making reference now to Figures 8a and 8b which show respective time **80a** and frequency **80b** domains of a varying light intensity signal. In Figure 8a, a dotted line shows a sine wave of time period **T** and the actual measured amplitude time varying light intensity signal. The frequency domain **80b** shows a peak amplitude at a frequency of 1 divided by time period **T**. Analyzing step **711** in this case may include a determination of
20 light intensity contrast between peaks and troughs of the varying intensity signal shown in time domain **80a**. The frequency domain **80b** shows that the varying intensity signal is a periodic intensity signal with a fundamental peak as shown by the peak at a frequency of 1 divided by time period **T**. The fundamental peak may be indicative of analyzer **4** being in a fixed position and polarizer **18** rotating periodically or vice versa. Two fundamental
25 peaks at two different frequencies may be indicative of both polarizer **18** and analyzer **4** rotating at two different constant velocities. The frequency domain **80b** shows as well, other frequency components which may be indicative of a particular condition of the tissue surface **8**.

The indefinite articles "a", "an" is used herein, such as "a polarizer ", "a light source" have the meaning of "one or more" that is "one or more polarizers" or "one or more light sources".

CLAIMS

1. A method for probing morphology of a tissue surface using a system including a light source, a polarizer, an analyzer, and a camera with a plurality of picture elements, the method comprising:

illuminating the tissue surface with incident light through the polarizer;

capturing by the camera, through the analyzer, scattered light from the tissue surface in a continuous sequence of image frames;

changing at the same time respective polarization states of said incident light from the light source by varying the polarizer and of said scattered light from the tissue surface by varying the analyzer;

during said capturing, detecting a plurality of picture elements of the camera a varying intensity signal of the scattered light responsive to the varying polarization state;

analyzing the varying intensity signal for the picture elements throughout the image frames, thereby probing the morphology of the tissue surface, wherein said analyzing includes determining an average of contrasts between frames of the varying intensity signal.

2. The method according to claim 1, wherein said illuminating is performed for incident light of different spectral content.

3. The method according to claim 1, wherein said analyzing includes determining light intensity contrast between peaks and troughs of the varying intensity signal.

4. The method according to claim 1, wherein said analyzing includes determining an intensity differential of the varying intensity signal between image frames.

5. The method according to claim 1, wherein said analyzing includes determining an intensity differential of the varying intensity signal between consecutive image frames.

6. The method according to claim 1, wherein said analyzing includes determining a second derivative of the varying intensity signal between the image frames.

7. The method according to claim 1, wherein said analyzing includes determining a variance of the varying intensity signal.

8. The method according to claim 1, wherein the varying intensity signal is a function of time, wherein said analyzing includes performing a transform of the varying intensity signal to a transformed intensity signal in frequency domain.

9. The method according to any of the preceding claims wherein the varying intensity signal is a periodic intensity signal.

10. A system including a light source, a variable polarizer, an analyzer, and a camera including an image sensor with a plurality of picture elements, the system operable to:

illuminate a tissue surface with incident light through the polarizer;

capture by the camera through the analyzer, scattered light from the tissue surface in a continuous sequence of image frames;

change at the same time respective polarization states of said incident light from the light source and of said scattered light from the tissue surface;

detect for a plurality of picture elements of the camera a varying intensity signal of the scattered light responsive to the varying polarization state;

perform an analysis of the varying intensity signal for the picture elements throughout the image frames to probe the morphology of the tissue surface, wherein the analysis of the varying intensity signal includes an average of contrasts between frames of the varying intensity signal.

11. The system according to claim 10, wherein the analysis of the varying intensity signal includes a light intensity contrast between peaks and troughs of the varying intensity signal.

12. The system according to claim 10, wherein the analysis of the varying intensity signal includes an intensity differential of the varying signal between image frames.

13. The system according to claim 10, wherein the analysis of the varying intensity signal includes a second derivative of the varying intensity signal between the image frames.

14. The system according to claim 10, wherein the analysis of the varying intensity signal includes a variance of the varying intensity signal.

15. The system according to claim 10, wherein the varying intensity signal is a function of time, wherein the analysis of the varying intensity signal performs a transform of the varying

intensity signal to a transformed intensity signal in frequency domain.

16. The system according to claim 10, further comprising;

a mechanism for varying spectral content of the incident light,

17. The system of claim 10, further comprising a coupling between the polarizer and the analyzer configured to rotate the polarizer and the analyzer at the same time to change the respective polarization states at the same time.