precise location on the test field. Thus, in most cases, either blank values in different locations than the location of the sample application on the test field will have to be used, leading to a high uncertainty of the blank value, or, a large number of images of the test field before and after sample application will have to be stored and evaluated, leading to high need for data storage and calculation resources. The latter, however, is specifically disadvantageous for hand-held test devices which typically provide rather limited hardware capabilities.

Further, specifically with regard to the determination of the blank value, mechanical tolerances and tolerances of optical image acquisition have to be considered, specifically in systems having sophisticated transfer mechanisms for transferring the sample onto the test fields. Thus, in systems using micro-samplers, such as in WO 2010/094426 A1, a sample transfer from the micro-samplers onto the test fields takes place by pressing the capillaries of the micro-samplers onto the test fields. This method of sample transfer or other types of sample transfer may lead to a highly structured sample application, requiring a high optical resolution of image acquisition and image evaluation. This type of sample transfer, however, typically implies dynamic processes involving moving parts, which may lead to a displacement of the test fields or parts thereof. Thus, pressing the micro-samplers onto the test fields may lead to a distortion and/or displacement of the test fields. Further, the test fields often are accommodated in a housing of the test elements in a rather loose fashion, such as by simply inserting annular test chemistries into the housing without actually mounting the test fields in a shock-proof fashion. Thus, during use and handling of the test devices, specifically during measurements, the test fields may move, thereby creating inaccuracies regarding acquisition of the blank values and regarding the determination of the actual area of the test fields to be evaluated for analyte determination.

Problem to be solved

It is therefore an objection of the ~~present invention~~ embodiments disclosed herein to provide methods and devices which at least partly overcome the above-mentioned shortcomings of known methods and devices. Specifically, methods and devices for detecting at least one analyte in at least one sample of a body fluid shall be disclosed, which are capable of evaluating even very small sample volumes at a high precision, by widely avoiding artifacts and inaccuracies generated by mechanical disturbances and by sample application in a structured fashion.

In a first aspect, there is provided a method for detecting at least one analyte in at least one sample of a body fluid, wherein at least one test element with at least one test field is used, the at least one test field having at least one test chemistry, wherein the test chemistry is adapted to perform at least one optically detectable detection reaction in the presence of the analyte, wherein the method comprises acquiring an image sequence of images of the test field by using at least one image detector, wherein each image comprises a plurality of pixels, wherein the method fur-

ther comprises detecting at least one characteristic feature of the test field in the images of the image sequence, wherein the method further comprises correcting a relative position change between the image detector and the test field in the image sequence by using the characteristic feature, thereby obtaining a sequence of corrected images, wherein the sequence of corrected images is adapted for observing a time-dependent change of at least one optically detectable property of the test field due to the detection reaction of the test chemistry with the analyte to be detected.

In a second aspect, there is provided device for detecting at least one analyte in at least one sample of a body fluid, wherein the device comprises at least one test element receptacle for receiving at least one test element having at least one test field with at least one test chemistry, wherein the device further comprises at least one image detector for acquiring an image sequence of images of the test field, wherein the device further comprises at least one control unit, wherein the control unit is adapted to perform the method as defined herein.

In a third aspect, there is provided a test system for detecting at least one analyte in at least one sample of a body fluid, the test system comprising at least one device as defined herein, the test system further comprising at least one test element having at least one test field with at least one test chemistry, wherein the test chemistry is adapted to perform at least one optically detectable detection reaction in the presence of the analyte

Detailed description of the invention

This problem is solved by a method and a device for detecting at least one analyte in at least one sample of a body fluid having the features of the independent claims. The problem is further solved by a computer program, a computer system, a storage medium and a test system having the features of the further independent claims.

Claims

1. A method for detecting at least one analyte in at least one sample of a body fluid, wherein at least one test element ~~(124)~~ with at least one test field ~~(162)~~ is used, the at least one test field ~~(162)~~ having at least one test chemistry ~~(154)~~, wherein the test chemistry ~~(154)~~ is adapted to perform at least one optically detectable detection reaction in the presence of the analyte, wherein the method comprises acquiring an image sequence of images of the test field ~~(162)~~ by using at least one image detector ~~(178)~~, wherein each image comprises a plurality of pixels, wherein the method further comprises detecting at least one characteristic feature of the test field ~~(162)~~ in the images of the image sequence, wherein the method further comprises correcting a relative position change between the image detector ~~(178)~~ and the test field ~~(162)~~ in the image sequence by using the characteristic feature, thereby obtaining a sequence of corrected images, wherein the sequence of corrected images is adapted for observing a time-dependent change of at least one optically detectable property of the test field ~~(162)~~ due to the detection reaction of the test chemistry ~~(154)~~ with the analyte to be detected.

2. The method according to the preceding claim, wherein the detecting of the characteristic feature comprises selecting at least one specific part of one or more images of the image sequence, denoting the information contained in this part as the characteristic feature, wherein other images of the image sequence are scanned or searched for this information or similar types of information.

3. The method according to any one of the preceding claims, wherein the correction is individually adapted for each image of the image sequence, according to the characteristic feature detected in the specific image.

4. The method according to any one of the preceding claims, wherein the correction of the relative position change comprises using at least one image of the image sequence as a reference image, wherein the reference image is kept unchanged, wherein the remaining images of the image sequence are corrected by using at least one calculational correction of the position of the pixels, wherein the calculational correction is chosen such that a correlation between the reference image and the corrected remaining images of the image sequence is maximized.

5. The method according to the preceding claim, wherein the calculational correction comprises at least one of the following:

- a shifting of the pixels of the remaining images of the image sequence in at least one spatial direction, wherein the shifting is chosen such that the correlation between the reference image and the corrected remaining images is maximized.
- at least one rotation of the remaining images of the image sequence about at least one rotational axis by at least one rotation angle, wherein the rotational axis and/or the rotation angle are chosen such that the correlation between the reference image and the corrected remaining images is maximized.

6. The method according to one of the preceding claims, wherein the characteristic feature comprises at least one feature selected from the group consisting of: a roughness of the test field ~~(162)~~ detectable in the images of the image sequence; a granularity of the test chemistry ~~(154)~~ of the test field ~~(162)~~ detectable in the images of the image sequence; faults of the test field ~~(162)~~ detectable in the images of the image sequence; at least one, preferably at least two, fiducial marks comprised in the test field ~~(162)~~ and detectable in the images of the image sequence.

7. The method according to one of the preceding embodiments, wherein the sample of the body fluid is applied to the test field ~~(162)~~ during acquisition of the image sequence, wherein at least one touchdown image is detected in the image sequence, wherein the touchdown image is an image of the image sequence acquired at a point in time closest to the moment of application of the sample of the body fluid onto the test field ~~(162)~~.

8. The method according to one of the preceding claims, wherein the sample of the body fluid is applied to the test field ~~(162)~~ during acquisition of the image sequence, wherein the image sequence comprises a blank image sequence, wherein the blank image sequence comprises a plurality of blank images acquired before applying the sample of the body fluid to the test field ~~(162)~~, wherein at least one averaged blank image is derived from the blank images of the blank image sequence after performing the correction of the relative position change of the blank images of the blank image sequence.

9. The method according to the preceding claim, wherein the averaged blank image is derived in a continuous process during acquiring the images of the image sequence, wherein a preliminary averaged blank image is derived from the corrected blank images acquired so far, wherein new acquired blank images are used for revising the preliminary averaged blank image.

10. The method according to one of the two preceding claims, wherein the analyte is detected by comparing the images of the sequence of corrected images with a touchdown image

and/or the blank image sequence, wherein the comparison is performed on a pixel-by-pixel basis.

11. The method according to the preceding claim, wherein at least one averaged normalized value is created over at least part of the sequence of corrected relative images, wherein the averaged normalized value is monitored as a function of time after application of the sample of the body fluid to the test field ~~(162)~~.

12. The method according to one of the preceding claims, wherein boundaries ~~(212)~~ of the test field ~~(162)~~ and/or boundaries ~~(212)~~ of a visible window of the test field ~~(162)~~ are detected in the sequence of corrected images.

13. The method according to one of the preceding claims, wherein a moment of application of the sample of the body fluid onto the test field ~~(162)~~ is detected in the image sequence.

14. The method according to one of the preceding claims, wherein after application of the sample of the body fluid onto the test field ~~(162)~~ at least one region of interest is determined in the image sequence.

15. The method according to the preceding claim, wherein at least one corrected image acquired before or during application of the sample of the body fluid onto the test field ~~(162)~~ is compared to at least one corrected image acquired after application of the sample of the body fluid onto the test field ~~(162)~~ on a pixel-by-pixel basis, thereby generating a difference value for each pixel, wherein the difference value denotes a difference of the information contained in corresponding pixels of the corrected images acquired before or during and after application of the sample of the body fluid onto the test field ~~(162)~~, wherein the pixels are classified as pixels belonging to the region of interest or as pixels not belonging to the region of interest based on the difference values.

16. The method according to one of the two preceding claims, wherein an image mask is generated denoting the pixels belonging to the region of interest.

17. A device ~~(112)~~ for detecting at least one analyte in at least one sample of a body fluid, wherein the device ~~(112)~~ comprises at least one test element receptacle ~~(116)~~ for receiving at least one test element ~~(124)~~ having at least one test field ~~(162)~~ with at least one test chemistry ~~(154)~~, wherein the device ~~(112)~~ further comprises at least one image detector ~~(178)~~ for acquiring an image sequence of images of the test field ~~(162)~~, wherein the device ~~(112)~~ further comprises at least one control unit ~~(118)~~, wherein the control unit ~~(118)~~ is adapted to perform the method according to one of the preceding method claims.

18. A test system ~~(110)~~ for detecting at least one analyte in at least one sample of a body fluid, the test system comprising at least one device ~~(112)~~ according to the preceding claim, the test system ~~(110)~~ further comprising at least one test element ~~(124)~~ having at least one test field ~~(162)~~ with at least one test chemistry ~~(154)~~, wherein the test chemistry ~~(154)~~ is adapted to perform at least one optically detectable detection reaction in the presence of the analyte.

19. The test system ~~(110)~~ according to the preceding claim, wherein the test system ~~(110)~~ further comprises at least one puncture element ~~(140)~~, wherein the test system ~~(110)~~ is adapted to puncture at least one skin portion of a user by using the puncture element ~~(140)~~, thereby creating the sample of the body fluid, wherein the test system ~~(110)~~ is further adapted to transfer the sample of the body fluid onto the test field ~~(162)~~ of the test element ~~(124)~~.