15th IAPR International Conference on Machine Vision Applications (MVA)
Nagoya University, Nagoya, Japan, May 8-12, 2017.

Model based visual inspection of pharmaceutical tablets with photometric stereo

Gregor Podrekar[1], Dejan Tomaževič[1,2], Boštjan Likar[1,2], Peter Usenik[1,2]
[1]Sensum, Computer Vision Systems, Tehnološki park 21, 1000 Ljubljana, Slovenia
[2]University of Ljubljana, Faculty of Electrical Engineering, Tržaška 25, 1000 Ljubljana Slovenia
gregor.podrekar@sensum.eu

Abstract

A model based visual inspection of pharmaceutical tablets is proposed for the detection of surface defects that occur during the tableting process. A novel RB-BR photometric stereo configuration is used to obtain four images for every tablet at different lighting orientations. During the inspection, reconstructed 3D depth maps derived from acquired images are compared to the tablet model, obtained during the training phase. Inspected tablets are classified as defective if the difference exceeds a predefined threshold. The approach was tested on two sets of tablets and compared to the current state of the art methods. The results yield 89 % and 87 % successful defect detection rate for tablets without and with embossing, respectively.

1 Introduction

Tablets are the most common pharmaceutical solid dosage form being produced by well established pharmaceutical manufacturing processes. Tablet formation is performed by dedicated tablet presses where a mixture of one or more active substance and excipients in the form of a powder, granules or pellets is filled into a die, followed by the combined pressing action of two punches turning the powder into a tablet of a uniform size and weight. Modern tablet press machines have production rates of more than 250.000 tablets per hour, depending on the tablet size, shape, material and press configuration.

High rate production often results in high number of tablet defects in the batch. For example, the compressed material sometimes adheres to the surface of a tablet punch and consequently affects the form of the tablets being compressed afterwards. Defective tablets enter the following production stages, such as tablet coating and packaging which can compromise whole batches of tablets. This can lead to great financial losses, wasted production time, and delays in deliveries.

In 2004, the Food and Drug Administration introduced a Process Analytical Technology (PAT) initiative, which encourages the pharmaceutical industry to employ new in-line and on-line quality measure techniques in order to measure critical process parameters with the purpose of quality assurance and better process understanding. Since then, many PAT techniques have been developed and applied to the pharmaceutical industry. For example, digital imaging techniques have been successfully used for measuring coating thickness of the pellets during the coating process [1] and for the automated visual inspection of tablets during the tablet coating process [2].

Following the PAT initiative, same principles could be used for monitoring the visual appearance of the pharmaceutical tablets during the tableting process. In this way, the defects could be detected immediately after the tablet compression production stage and removed from the following processes. Additionally, the immediate feedback to the tablet press operator could prevent further defects. For that reason, automated visual inspection of pharmaceutical tablets should be integrated into the tablet press machines and should perform inspection of the tablets on-line, while the tablets are being produced.

Most commonly, tableting defects occur on one of the two faces of the tablet. They can be divided into appearance defects and surface defects. In general, appearance defect detection is an easier and already explored topic, providing many effective developed algorithms [3, 4]. On the other hand, surface defect detection and its reliability is a much more difficult task as these defect are sometimes hardly visible. In particular, the defect detection must take into account the imprints or embosses that might appear on one or both tablet faces, which introduces additional challenges.

Existing methods [3, 4] simultaneously detect both types of defects from the same image, which often yields poor results for the surface defects. We propose a novel method, which employs a photometric stereo technique in order to separate the appearance and the surface geometry information of the tablet. We show that the detection of the surface defects can be improved that way.

2 Methods

Model based visual inspection requires a model definition for the samples without defects. During inspection, each sample is compared to this model. If the difference exceeds a predefined threshold, the sample is regarded as a defective. Our tablet analysis is divided into a training phase and an inspection phase. In the training phase, a model of an ideal tablet is created. Inspected samples are then compared to this model during the inspection phase. Layout of the training and inspection phase is illustrated in Figure 1 and further explained in the next sections.

2.1 Image acquisition

The standard photometric stereo technique utilizes three or more image snapshots of the observed object under different lighting conditions [5]. By assuming the Lambertian reflectance model the surface normal and the albedo can be estimated. Furthermore, from the estimated surface normals, 3D information of the object can be obtained using an appropriate surface reconstruction method [6].

The acquisition of three or more consequent images could be problematic, when the observed object is mov-

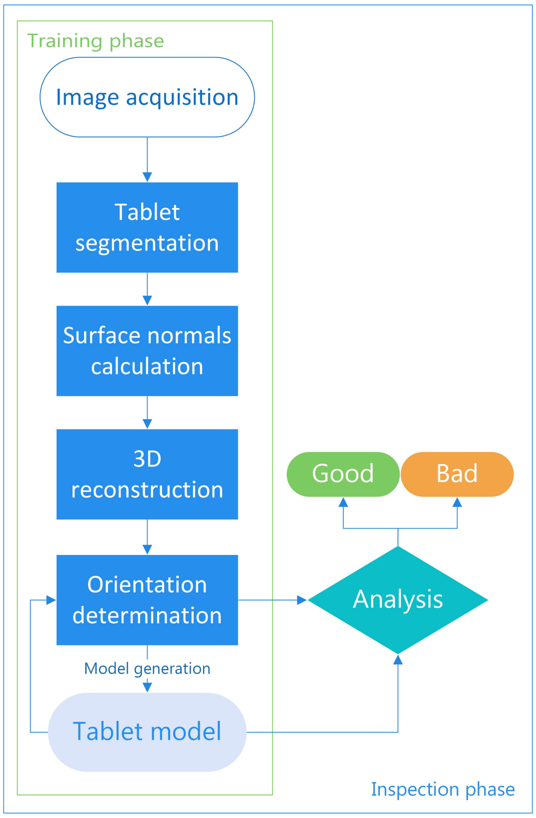


Figure 1: Main processing steps required by the proposed approach. The tablet analysis procedure is divided into a training phase and an inspection phase. During the inspection phase, inspected samples are compared to the ideal model of the tablet, created in advance during the training phase.

ing. This problem can be overcome by photometric stereo with colored light sources [7]. In this way, the red, green and blue light sources and a standard color camera with three independent color channels can provide information on the three illumination scenes in a single snapshot. The drawback of this approach is the need for calibration with a reference surface material, whose color needs to exactly match the color of the imaged objects and is limited to uniformly colored surfaces.

We propose a photometric stereo configuration based on two temporally separated pairs of red-blue lights (RB-BR) (Figure 2). Such configuration represents a good compromise between the standard and the color photometric stereo as it allows acquisition of moving objects of different color, with the exception of colors that would yield no response to the red or blue illumination sources.

The RB-BR photometric stereo configuration comprises two pairs of red and blue illumination sources. Compared to classical color photometric stereo, there is no green light source, because in practice, the green light source yields a response on both the blue and the red camera channel, which is one of the reasons for the aforementioned limitations of the color photometric stereo. The RB-BR light sources have to be positioned in a way, so that the blue light in the first sequence is opposite to the blue light in the second sequence and that the red light in the first sequence is opposite to the red light in the second sequence. Ideally, the lights are aligned with the camera axes.

The RB-BR photometric stereo configuration requires two sequential color image acquisitions in order to obtain four images of the same scene illuminated from four different orientations. During the first acquisition, only the first RB pair is turned on and during the second acquisition, only the second RB pair is turned on. Therefore, in order to be able to use this configuration with dynamic scenes, the consecutive images should be acquired within a narrow time interval. Many of the modern CMOS cameras allow such acquisitions in less than 200 μs by using the overlapping shutter mode. Acquiring more than two sequential images in contrast is currently limited to only high end super speed cameras which are relatively big and too expensive for most of the machine vision applications.

2.2 Tablet segmentation

The tablet segmentation starts with an estimation of the tablet center using a simple thresholding scheme. According to the tablet center, a border tracking algorithm is used to segment the region of the imaged tablet, providing a contour and mask of the imaged tablet [8]. High contrast between the tablet and the background is required for this step. All further analysis is performed only on segmented tablet regions.

2.3 Surface normals calculation

When light sources are aligned with camera axes, for example blue lights with the horizontal camera axis and red lights with the vertical axis, the horizontal and vertical components of the surface normals (N_x, N_y) are calculated separately by solving two light photometric stereo equations (1) for both pairs of light sources, whose directions (L) are determined in advance during the photometric calibration.

$$\begin{aligned} \left[I_{blue_1} \quad I_{blue_2}\right] &= a_{blue} N_x \left[L_{x_{blue_1}} \quad L_{x_{blue_2}}\right] \\ \left[I_{red_1} \quad I_{red_2}\right] &= a_{red} N_y \left[L_{y_{red_1}} \quad L_{y_{red_2}}\right] \end{aligned} \tag{1}$$

Additionally, blue and red surface albedo components (a_{blue}, a_{red}) are obtained.

2.4 3D reconstruction

Many methods for 3D reconstruction based on surface normals have already been introduced. Proposed approach employs the path integration procedure, which satisfies the speed requirements of our application. This method integrates horizontal and vertical normals, row by row and line by line, respectively. If the tablets are imaged in defined face position, the height of tablet border is known and the integrated line paths are shifted and rotated in order to fit the border points. In this way, two depth maps are obtained. The average of the two depth maps reduces the reconstruction error.

2.5 Orientation determination

Modeling of the embossing information requires tablet orientation determination in terms of face position and rotation. The circular profile matching was used for rotation determination [9]. The side position determination was simply performed by rotation estimation for both sides of the model, where higher matching score indicated the face position.

2.6 Model generation

The 3D tablet model consists of two separate depth maps, one for each face. Model is generated during the training phase by averaging the registered depth maps of the tablets from the training set.

2.7 Analysis

The final analysis is performed by subtracting each reconstructed depth map of the inspected tablet from the registered depth map of the model. The maximal difference is used as a similarity measure between the inspected sample and the model. Sample deviation from the model above predefined threshold classifies the sample as defective.

3 Experiment

3.1 Experimental setup

A rotary bowl feeder was used for sorting the mass of tablets into an ordered row, which simulates the output of the tablet press machine. An imaging system, based on the described RB-BR photometric stereo configuration, was built and positioned at the output of the bowl feeder (Figure 2) in order to image every tablet). Red and blue illumination sources, composed of high power LEDs, were connected to a LED driver. A microcontroller (ATmega32u4) was used for the synchronization of the illumination sources with a camera (acA2040-25gc) running in the overlapping shutter mode. Additionally, linear polarizers (Edmund optics) were placed in front of the illumination sources and the camera for specular reflection suppressions, which is essential for the correct estimation of the surface normals. Image analysis was implemented partly in python and partly in C++ programming language.

3.2 Calibration

Calibration of the photometric system was performed as follows. Illumination directions were first calculated from the locations of light spots on a metal sphere. Linear polarizers on the illumination sources were than rotated until all the spots disappeared. Next, a white plane was imaged in order to determine the gains of individual light sources. Finally, the pixel size (0.03 mm) was determined by measuring the distance between the corners on an imaged chessboard calibration pattern.

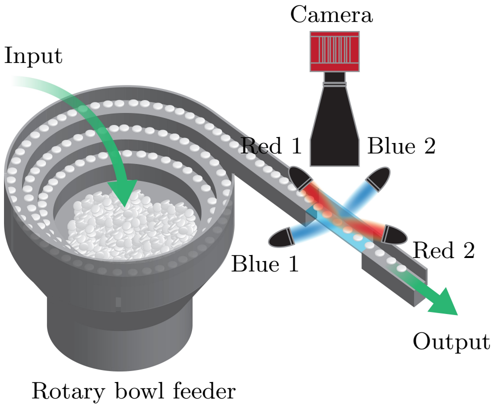
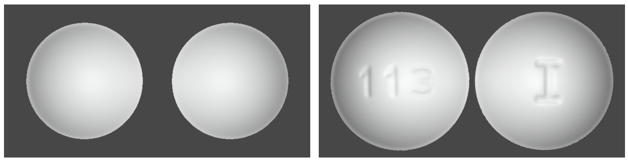


Figure 2: Output of the tablet press was simulated by a rotary bowl feeder. RB-BR photometric stereo configuration was used for the acquisition of two color images of each tablet, from which a 3D depth map was reconstructed and compared to the model.

3.3 Tablets

Two samples of tablets were used in the experiment (Figure 3). The first sample consisted of 191 white tablets without embossing (154 without defects and 37 with surface defects). The second sample consisted of 382 white tablets (185 without defects and 197 with surface defects). Surface defects were created manually, and were similar to those that can occur during the tableting process.



(a) (b)

Figure 3: Rendered 3D models of both tablet samples used for the experiment. The first sample consisted of tablets without embossing and the second sample consisted of tablets with embossing. The 3D models were generated during the training phase.

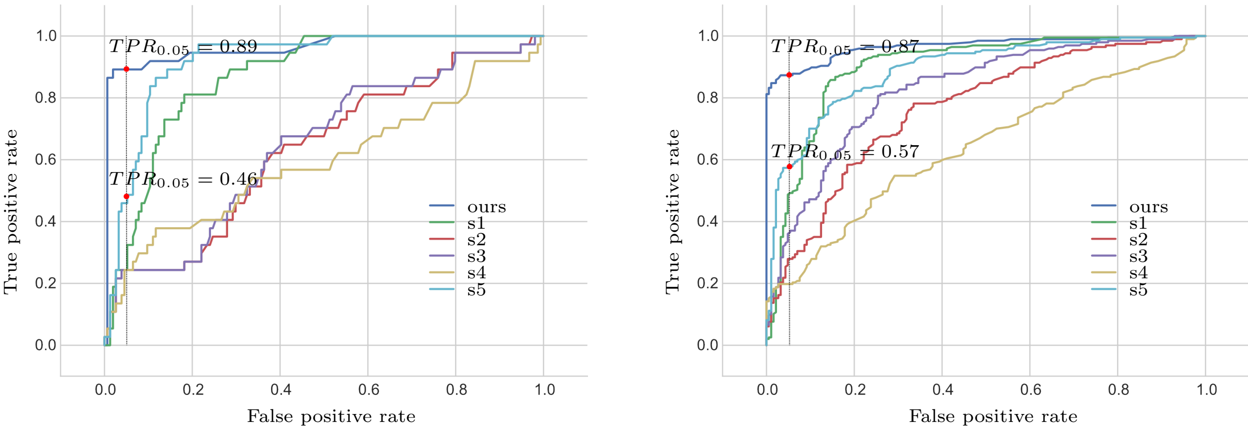
3.4 Validation

Tablets of both samples were divided into training sets and inspection sets. Training sets were composed of only good tablets and were used for the training phase to build tablet models. The training sets of tablets without and with embossing consisted of 20 and 40 tablets (20 per each face) respectively. Rest of the tablets were used for the inspection where all tablets were first manually inspected and classified as good or bad ones. For the comparison, the tablets were also imaged while being illuminated with all four lights at once and the resulting intensity images were analyzed with the reference approach [3]. Orientation of the tablets was determined on depth maps for both the proposed method and the reference method.

4 Results and discussion

Receiver operating curves (ROC) were used for presenting the results obtained by the proposed method based on photometric stereo and the reference method based on features ($s_1 - s_5$) derived from a single intensity image (Figure 4). The proposed method, compared to the reference method, yields increase of true positive rate from 0.46 to 0.89 at 0.05 false positive rate for the tablets without embossing and increase from 0.57 to 0.87 for the tablets with embossing. In order to achieve such results, detection thresholds have to be set to 0.048 mm and 0.063 mm for the tablets without and with the embossing, respectively. In other words, we were able to correctly detect 89 % and 87 % of all surface defects deeper than 0.048 mm and 0.063 mm while wrongly detecting 5 % of good tablets as defective ones. The presented results show, that the proposed method outperforms the reference method, which does not use the 3D image information and relies solely on image intensity information. Examples of correctly detected defective tablets are showed in Figure 5.

Note that the imaging setup used for the acquisition



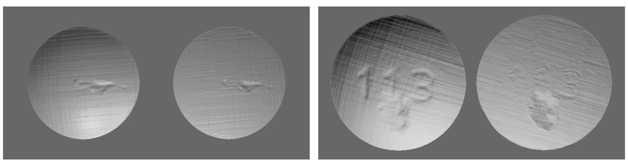
(a) (b)

Figure 4: ROC curves, showing the detection performance of the proposed method based on 3D information in comparison to the approach based on features ($s_1 - s_5$) derived from the intensity image [3]. Tablets without the embossing (a) and tablets with the embossing (b). True positive rates at 0.05 false positive rates are also showed for the proposed method and the best performing features of the reference method.

of the intensity images that were analyzed with the reference method differed from the one used in [3] and might have affected the obtained results. Additional evaluations will therefore be performed in the future. The proposed method will also be compared to the method presented in [4].

A shortcoming of the presented photometric stereo configuration is a limitation to objects of colors that yield at least some response toward red and blue lights and whose surface exhibits Lambertian or quasi-Lambertian properties. This is rarely an issue for pharmaceutical tablet production applications as the tablet press input material is generally diffuse and white shade colored.

Various technical issues, that we didn't address in this work, also need to be solved before implementing the proposed inspection approach, such as finding a solution that will enable acquisition of both tablet faces and designing an appropriate tablet sorting mechanism for example.



(a) (b)

Figure 5: Rendered depth map of an inspected tablet with a defect together with rendered error depth map, obtained as a difference between the depth map of a tablet model and the inspected tablet. Tablet without the embossing (a) and tablet with the embossing (b).

5 Conclusion

This work presents a model based automated visual inspection of pharmaceutical tablets with surface defects that occur during the tableting process using a novel RB-BR photometric stereo technique. Although the method was originally designed for pharmaceutical tablets, it can be applied to similar objects in other industries.

The method can be further extended for the detection of appearance defects by separately analyzing the albedo components, already obtained by the photometric stereo technique. Advances in rapid image acquisition of three or more sequential images in very short time are needed, allowing the use of standard photometric stereo techniques with white illumination sources enabling the object inspection regardless of its color.

References

[1] K. Knop and P. Kleinebudde, "PAT-tools for process control in pharmaceutical film coating applications," *International Journal of Pharmaceutics*, vol. 457, no. 2, pp. 527–536, 2013.

[2] G. Podrekar, B. Bratanic, B. Likar, F. Pernus, and D. Tomazevic, "Automated visual inspection of pharmaceutical tablets in heavily cluttered dynamic environments," in *2015 14th IAPR International Conference on Machine Vision Applications (MVA)*, pp. 206–209, May 2015.

[3] M. Bukovec, i. Špiclin, F. Pernuš, and B. Likar, "Automated visual inspection of imprinted pharmaceutical tablets," *Measurement Science and Technology*, vol. 18, pp. 2921–2930, Sept. 2007.

[4] M. Možina, D. Tomaževič, F. Pernuš, and B. Likar, "Automated visual inspection of imprint quality of pharmaceutical tablets," *Machine Vision and Applications*, Sept. 2011.

[5] R. J. Woodham, "Photometric Method For Determining Surface Orientation From Multiple Images," *Optical Engineering*, vol. 19, no. 1, pp. 191139–191139–, 1980.

[6] S. Herbort and C. Wöhler, "An introduction to image-based 3d surface reconstruction and a survey of photometric stereo methods," *3D Research*, vol. 2, p. 4, Dec. 2011.

[7] G. J. Brostow, C. Hernandez, G. Vogiatzis, B. Stenger, and R. Cipolla, "Video Normals from Colored Lights," *IEEE Transactions on Pattern Analysis and Machine Intelligence*, vol. 33, pp. 2104–2114, Oct. 2011.

[8] M. Možina, D. Tomaževič, F. Pernuš, and B. Likar, "Real-time image segmentation for visual inspection of pharmaceutical tablets," *Machine Vision and Applications*, vol. 22, pp. 145–156, Aug. 2009.

[9] Z. Špiclin, M. Bukovec, F. Pernuš, and B. Likar, "Image registration for visual inspection of imprinted pharmaceutical tablets," *Mach. Vision Appl.*, vol. 22, pp. 197–206, Jan. 2011.