In-line recognition of agglomerated pharmaceutical pellets

with density-based clustering and convolutional neural network

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INTRODUCTION

Pharmaceutical pellets are small spherical particles, which are enclosed in capsules or compressed into tablets and contain the active pharmaceutical ingredient.

Coating is employed to layer active pharmaceutical ingredient, mask odor and taste, achieve controlled release and/or enhance chemical and physical stability. Pellets are most commonly coated using a fluidized bed coating method (Fig. 1).

Agglomeration occurs when the pellets adhere to each other due to an excess of the applied coating dispersion. It affects the coating process yield (agglomerates are discarded) and the coating integrity/ uniformity.

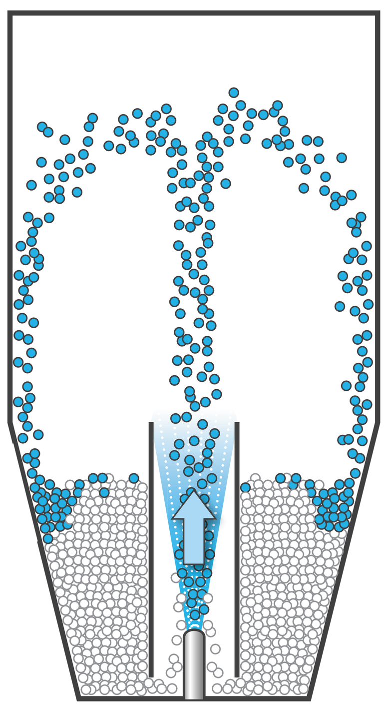


Fig. 1: Fluidized bed coating process

GOALS

Develop an in-line machine vision system that could be mounted to the observation window of a coater and would enable real-time:

— acquisition and monitoring of pellet images,
— detection of pellets,
— recognition of agglomerates, and
— estimation of agglomerate fraction.

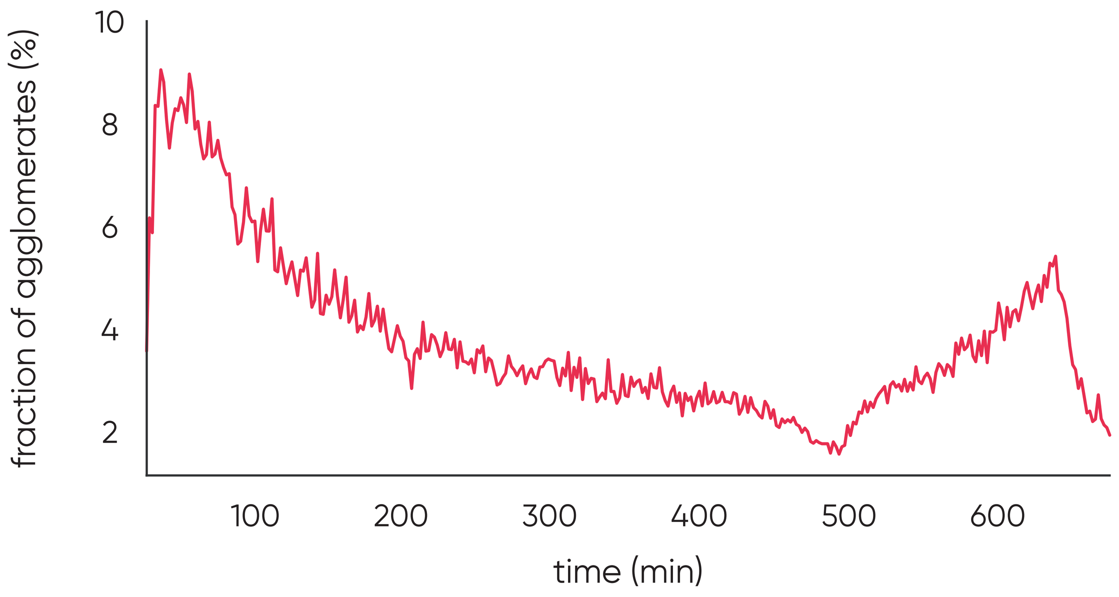


Fig. 2: Estimated fraction of agglomerates during the coating process.

CHALLENGES

Differentiate between groups of pellets that are only visually in contact (i.e. they are occluded or overlapped from the point of view of a camera) and actual physical agglomerates.

Obstacles:
— occlusions,
— random group of pellets,
— pellets are not perfectly dispersed.

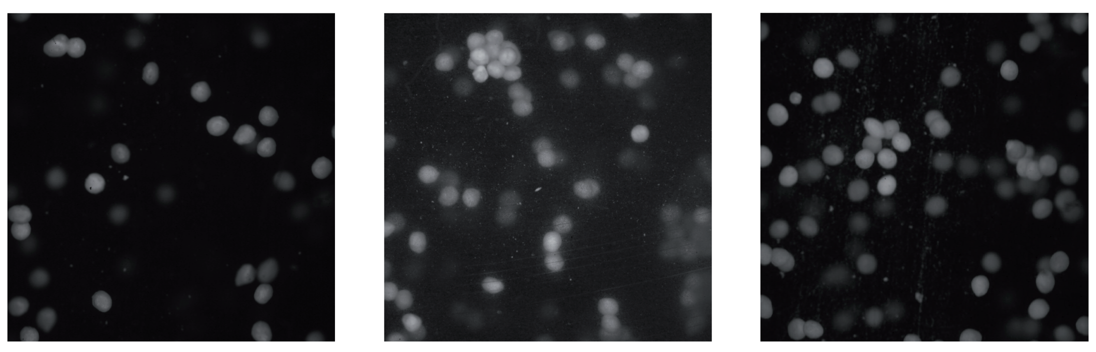
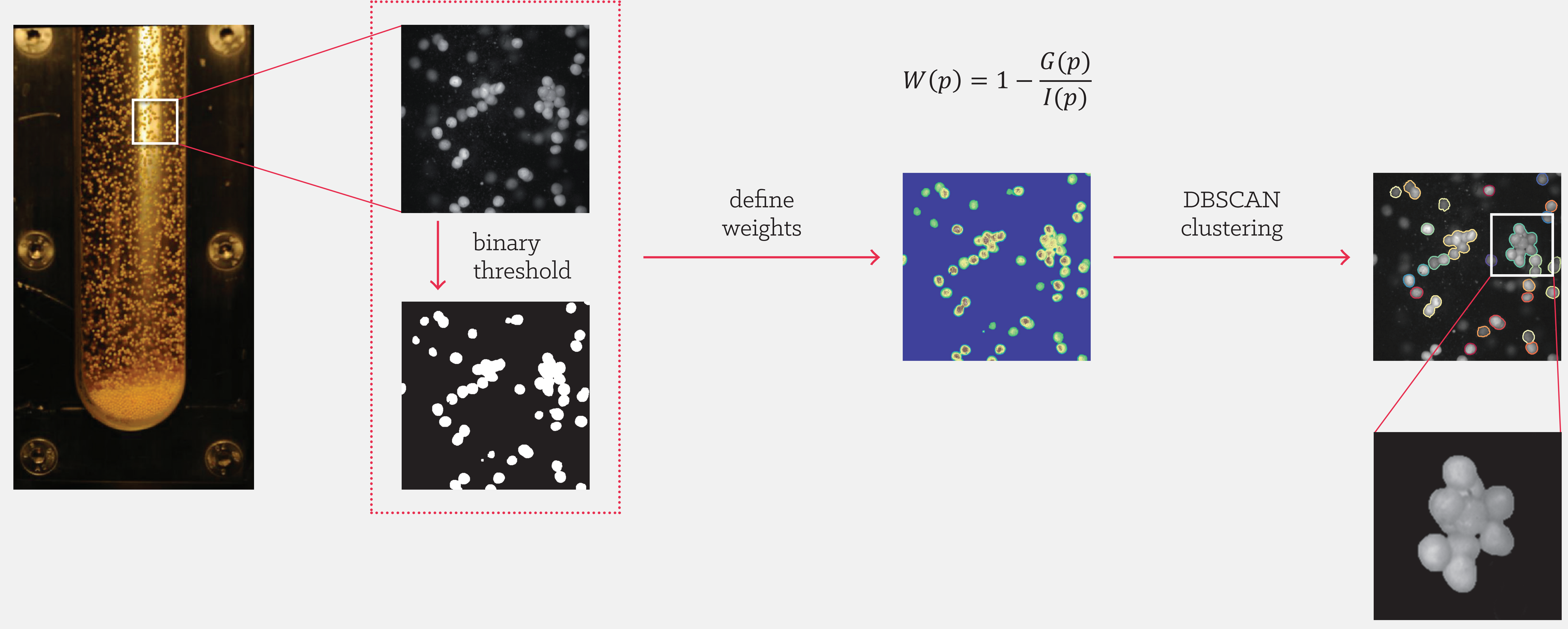


Fig. 3: Samples of the acquired images

Fig. 4: A primary particle (left), a group of primary particles (middle), an agglomerate (right).

METHOD

CANDIDATE REGION DETECTION with DBSCAN image segmentation



CLASSIFICATION with convolutional neural network

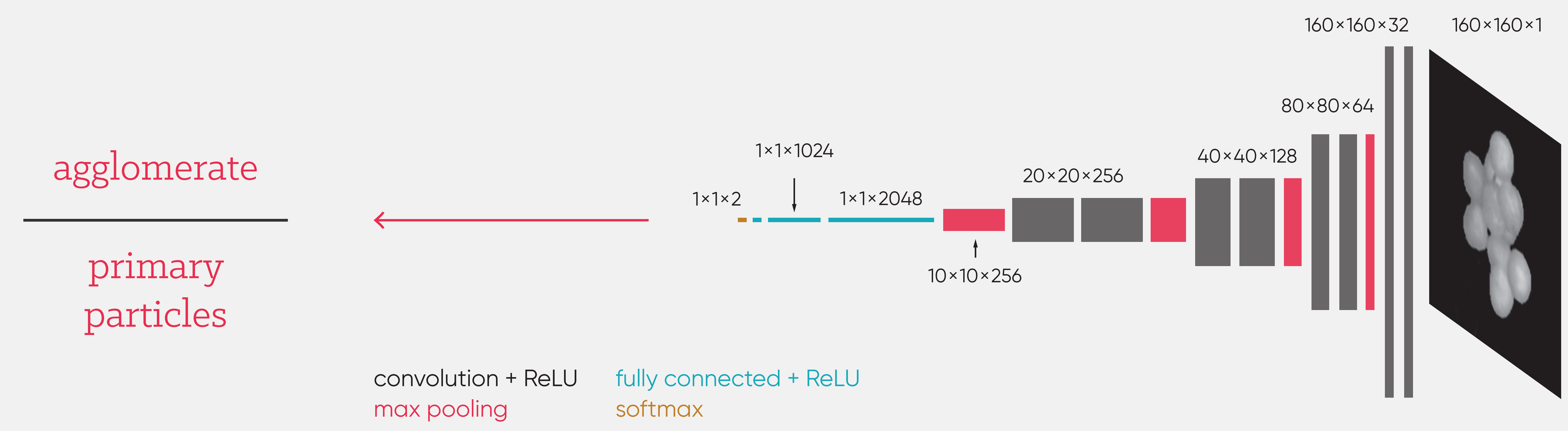


Fig. 5: After canditate regions are detected by DBSCAN clustering, each region is calssified by a convolitional neural network; G - image gradient, I - pixel intensity.

EXPERIMENTS

Image acquisition
We executed a coating process of pellets in a pilot-scale fluidized bed coater. The process parameters were deliberately set to induce substantial particle agglomeration. Pellet images were acquired by an in-line visual inspection system PATVIS APA (Sensum, Slovenia - *www.sensum.eu*) through the observation window of the fluidized bed coater.

Trainig of the CNN
The ground truth was obtained by manually classifying 2000 candidate images. With regard to the ground truth, 1100 images included single particles and 900 images included agglomerates.

Learning procedure:
— image augmentation (random noise, rotation),
— in batches of 50 images.

The performance was compared to the classification based on the area of candidate regions (i.e., an estimate of particle size).

Fig. 6: Imaging setup.

RESULTS AND CONCLUSION

The trained CNN model achieved 93 % classification accuracy on the test set.

Pros of the CNN classifier:
— good performance independent of the candidate region area; it was able to correctly recognize 92 % of agglomerates while falsely recognizing 5 % of primary particles as agglomerates,
— outperforms area-based classification,
— discriminative features are learned automatically.

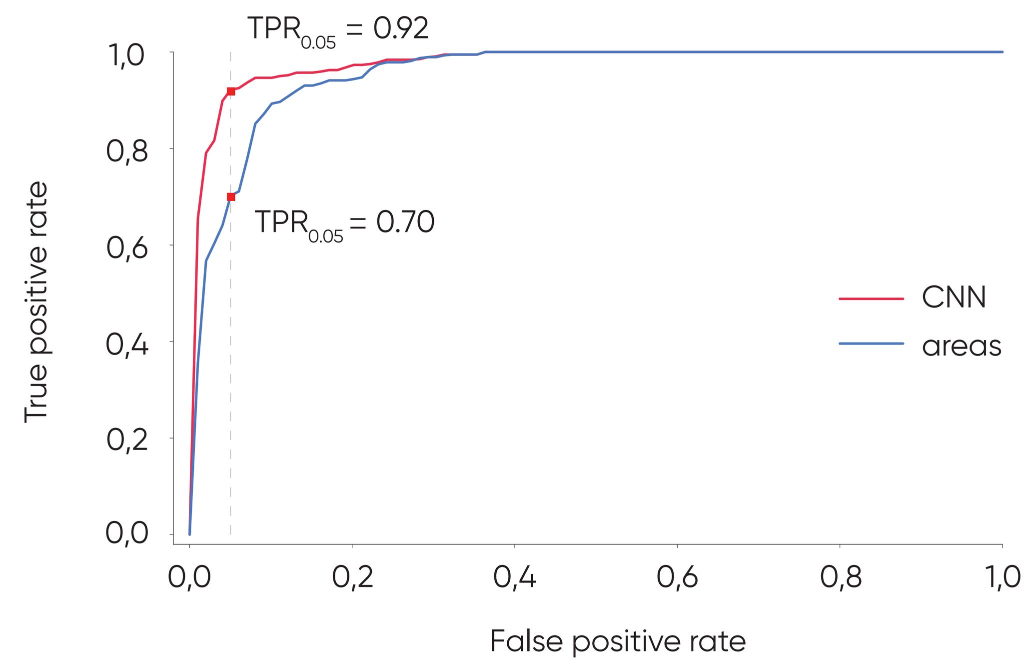


Fig. 7: Receiver operating curve for classification with CNN and classifaction based on pellet areas.

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