Deep Learning-Based Machine Vision System for Use in High-Shear Granulation

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Aim

Develop a prototype machine vision system and evaluate feasibility of a deep learning-based image analysis approach for estimation of the state of granulation on the acquired granule bulk surface images.

1 **Acquisition** of granule bulk images

2 **Deep learning** image analysis

3 **Estimation** of the state of granulation

Introduction

Despite many decades of research in granulation technology, the high-shear granulation process is still poorly understood. Practical knowledge of technologists suggests that **granule appearance largely indicates the process state**.
As an alternative to subjective visual examination, **machine vision could provide a more reliable and continuous solution**, which was already demonstrated on the lab scale [1].

Figure 1: Granule appearance at various states of granulation.

Materials and methods

Granules

- Commercially produced via high-shear granulation on production-scale.
- Bulk composition – 55 %w/w API (BCS class II), lactose monohydrate, low substituted hydroxypropyl cellulose, hydroxypropyl cellulose, sodium lauryl sulfate.
- Granulation liquid – purified water.
- Sifted in order to obtain 12 size classes: 40 µm, 102.5 µm, 152.5 µm, 215.0 µm, 302.5 µm, 377.5 µm, 450.0 µm, 550.0 µm, 655.0 µm, 780.0 µm, 925.0 µm, 1200.0 µm.

Imaging setup

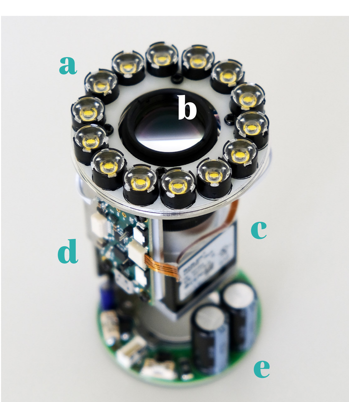

Figure 2: The prototype machine vision system.

- The prototype machine vision system is designed for installation on granulator sight glasses and acquisition of the granule bulk surface images at varying bulk levels during granulation.
- The vision system comprises of a high density illumination unit (a), a variable focus liquid lens optical system (b), a high-speed camera (c), and a liquid lens and an illumination unit controller (d, e).
- In a laboratory setup, granule samples were subjected to rigorous mixing while being imaged at various distances, simulating the conditions in granulators.
- 800 images of size 2048 px x 2048 px were acquired at a frame rate of 80 fps at each distance and for each granule size class.

Image analysis

- Images of one size class (655.0 µm) were selected to represent optimally granulated particles. Optimal size class was determined based on the measured average particle size of the final product.
- A convolutional neural network TriNet [2] was trained to recognize the visual appearance of the optimally granulated size class. The reference value for training was set to 1 for the optimally granulated size class and 0 for all the other size classes (binary classification).
- On each test image, the optimally granulated regions were recognized: each output pixel of the prediction image is proportional to the probability of it representing an optimally granulated region.
- The final prediction value is calculated as the mean of all prediction image values.

Evaluation

- For each size class, the mean and the standard deviation of prediction values.
- MAE from the reference values (the reference value is 1 for the optimally granulated size class and 0 for all the other classes).

Results and discussion

The results show that the **trained neural network can recognize the specified optimally granulated size class, i.e., 655 µm, with high confidence.** With a mean prediction value of the positive size class 0.99 (MAE 0.013) and a maximum mean prediction value 0.02 (MAE 0.020) within all negative size classes, **the model achieved 100 % classification accuracy at threshold 0.5.**
It is worth noting that the sole neighboring size classes, i.e., 550 µm and 780 µm, have a non-zero mean prediction value. Some regions in these images are detected as optimally granulated, which is expected.

In addition to providing a prediction value, the output of the neural net has the added benefit of a visual feedback displaying specific regions on the acquired images, where prediction values are high.

Conclusion

The results confirmed the feasibility of the deep learning-based approach for determination of the state of granulation within a controlled laboratory setup.

Our final goal is the application of the presented approach for the in-line and real-time determination of the optimal granulation endpoint, facilitating process development, scale-up and transfer, and increasing the product consistency during production in pharma.

References
[1] G. Podrekar, D. Kitak, U. Urnaut, A. Mehle, S. Vidovič, P. Usenik, et al., “In-line monitoring of a high-shear granulation process using digital imaging,” 11th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology, Mar. 2018, doi: 10.13140/RG.2.2.15212.21129, available from: https://search.datacite.org/works/10.13140/RG.2.2.15212.21129
[2] D. Rački, D. Tomaževič, and D. Skočaj, “Detection of surface defects on pharmaceutical solid oral dosage forms with convolutional neural networks,” Neural Comput & Applic, vol. 34, no. 1, pp. 631–650, Jan. 2022, doi: 10.1007/s00521-021-06397-6.

Figure 3: The major stages of the proposed approach.

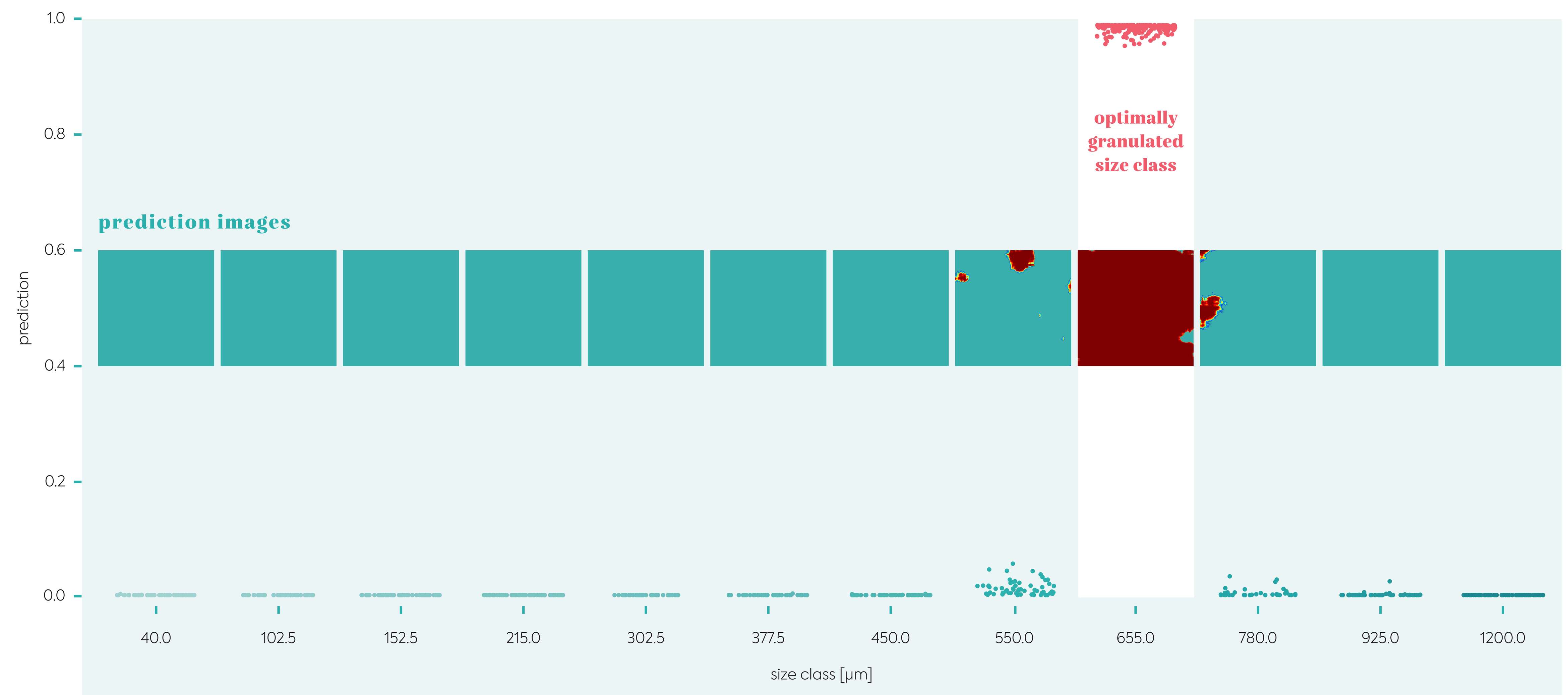

Figure 4: The prediction values for all images from each size class and the representative prediction images.

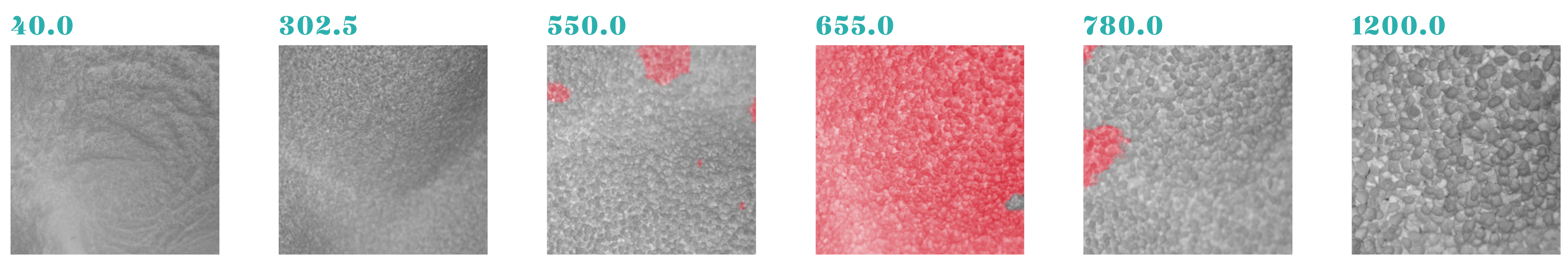

Figure 5: The predictions overlayed over the input images for selected size classes.

Table 1: The results on the test images for each size class.

size class (µm)	40	102.5	152.5	215	302.5	377.5	450	550	655	780	925	1200
# of samples	60	48	63	63	33	45	60	60	240	36	63	69
reference	0	0	0	0	0	0	0	0	1	0	0	0
mean prediction	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.99	0.01	0.00	0.00
MAE	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.01	0.01	0.00	0.00