

METASTABLE ZONE IDENTIFICATION IN PHARMACEUTICAL CRYSTALLISATION USING BULK VIDEO MONITORING

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This work describes the proof of concept of the newly introduced bulk video imaging (BVI) and presents the comparison with existing process analytical technologies (PAT) such as focused beam reflectance measurement (FBRM), attenuated total reflectance (ATR) ultra violet/visible (UV/Vis), IR spectroscopy and calorimetry. While these methods sample the system in small volumes closely to the probe, the BVI approach monitors the entire or large parts of the crystallizer volume.

A. The BVI methodology

A1. BVI experimental equipment

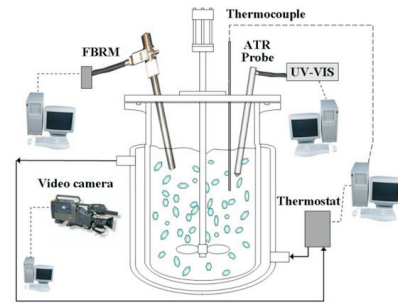


Fig. 1 External bulk video monitoring (eBVI)

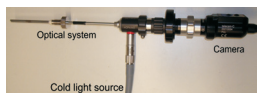


Fig. 2 Endoscope

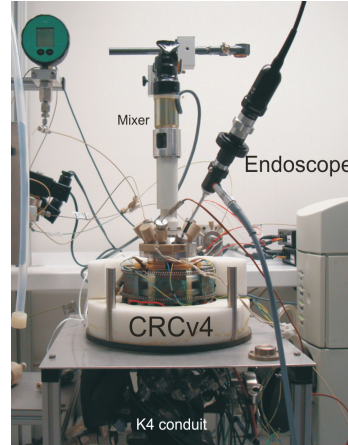


Fig. 3 In-situ bulk video monitoring (iBVI)

B. BVI monitoring results for pharmaceuticals and food crystallization processes

B1. External monitoring (eBVI) of caffeine crystallization

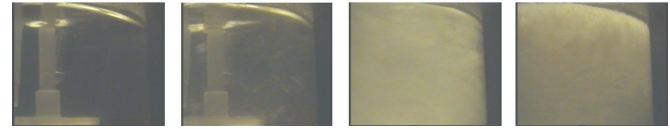


Fig. 6 Liquid state evolution.

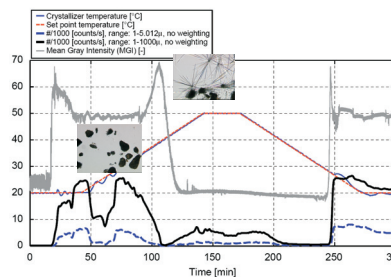


Fig. 7 Mean Gray Intensity BVI and FBRM signal comparison

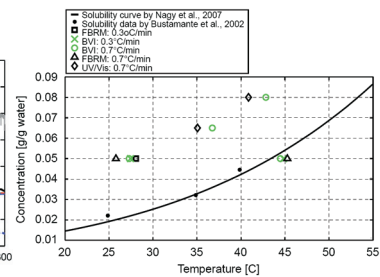


Fig. 8 Caffeine metastable zone identification

A2. Image processing strategies

Mean Gray Intensity Trend

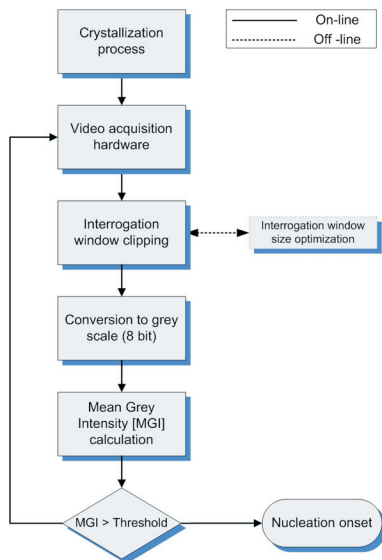


Fig. 4 Calculation of mean gray intensity trend.

Image analysis for crystal detection

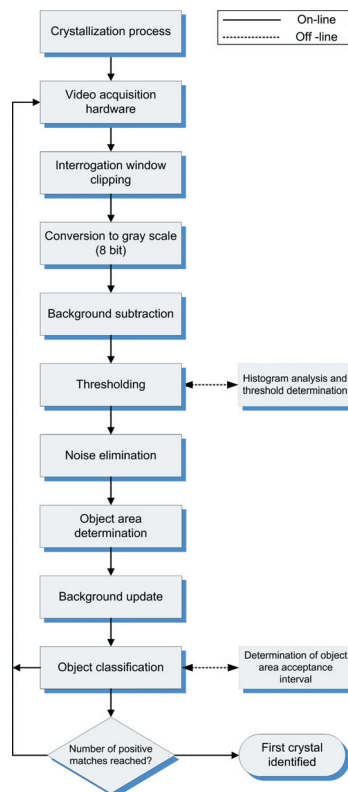


Fig. 5 The crystal detection algorithm.

B2. External monitoring (eBVI) of palm-oil crystallization

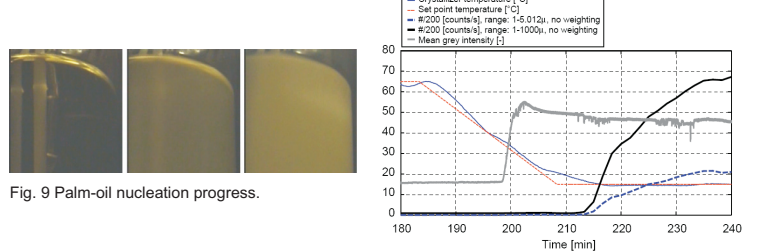


Fig. 10 Mean Gray Intensity BVI and FBRM signal comparison.

B3. In-situ monitoring (iBVI)

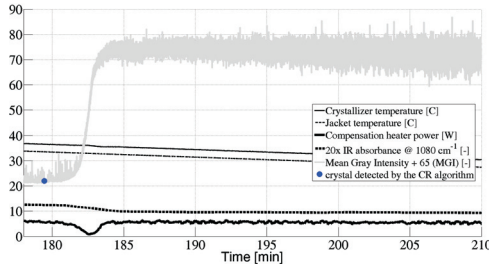


Fig. 11 Crystal recognition, Mean Gray Intensity iBVI, IR-spectroscopy and calorimetric signal comparison.

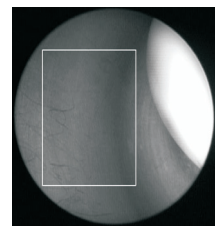


Fig. 12 Endoscopy image.

C. Conclusions

The proof of concept of the bulk video imaging (BVI) was introduced in this work. It was shown that BVI has comparable performance in detecting the nucleation onset to the FBRM, IR, UV/Vis and calorimetric signals. BVI is proposed as a complementary approach to the existing PAT tools and it provides significantly lower sensitivity to mixing conditions than other probes based on local measurements. The endoscopy based monitoring provides an in-situ, low-cost, robust, probe based method which can be easily integrated and automated with existing laboratory hardware and software.

D. References

Simon, L. L., Nagy Z. K., Hungerbühler K
Comparison of external bulk video imaging with focused beam reflectance and ultra violet-visible spectroscopy for metastable zone identification in food and pharmaceutical crystallization processes
Chemical Engineering Science, Volume 64, 14, 2009, p. 3344

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Endoscopy based in-situ bulk video imaging of crystallization processes
Organic Chemistry Research & Development, Special Issue on Crystallization and Polymorphism, In press