

Article

Localized Spatial Decomposition for Convolutional Classification of Heterogeneous Dried Droplet Patterns

Carlos A. Martínez-Miwa ¹, Rocío M. Sánchez-Albores ², Yojana J. P. Carreón ^{2,3},
Jorge González-Gutiérrez ^{2,*} and Mario Castelan ^{1,*}

¹ Robotics and Advanced Manufacturing, Center for Research and Advanced Studies of the National Polytechnic Institute, Ramos Arizpe 25900, Coahuila, Mexico; carlos.miwa@cinvestav.mx

² Faculty of Physics and Mathematics Sciences, Autonomous University of Chiapas, Tuxtla Gutierrez 29050, Chiapas, Mexico; magdalena.sanchez@unach.mx (R.M.S.-A.); yojana.carreon@unach.mx (Y.J.P.C.)

³ Ministry of Science, Humanities, Technology and Innovation, Mexico City 03940, Mexico

* Correspondence: jorge.gutierrez@unach.mx (J.G.-G.); mario.castelan@cinvestav.mx (M.C.)

Abstract

Dried droplet imaging has become an established approach for analyzing complex fluid systems as evaporation patterns preserve physicochemical and structural information. However, spatial variability of these patterns limits the effectiveness of conventional texture descriptors. This work presents a region-aware deep learning algorithm for the classification of dried droplets through spatial decomposition and convolutional learning. Dried droplet images were geometrically standardized prior to patch extraction. The Hough transform supported consistent crown–core localization and patch extraction across the dataset. Each image was divided into twenty localized regions. Twelve represented peripheral patches sampled at 30° intervals. The remaining eight patches were extracted from four central regions using two complementary angular orientations (30° and 90°) per region. This process allowed dataset augmentation and evaluation of regional contributions. Patches were processed using the VGG16 convolutional neural network, following repeated patch-level and droplet-level partitioning strategies designed to prevent data leakage. The proposed algorithm was evaluated on Methotrexate (MTX) droplets prepared with 40%, 60%, and 80% water dilution levels relative to a reference solution. Results show that the proposed strategy increases classification accuracy, outperforming traditional descriptors. These findings demonstrate that spatial decomposition combined with convolutional learning constitutes an effective approach for heterogeneous evaporative pattern classification.

Keywords: spatial decomposition; convolutional neural networks; evaporated droplets; pattern recognition; image classification; region-aware learning; feature extraction



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1. Introduction

The morphology of evaporative residues formed by drying droplets can preserve physicochemical and structural information associated with complex fluid systems. During evaporation, solvent transport, interfacial instabilities, and solute redistribution generate structured deposition patterns that emerge from confined self organization processes. Such phenomena have been widely studied in soft matter systems and are relevant to applications including additive manufacturing of pharmaceutical formulations [1–3] and aerosol jet printing [4]. From an image analysis perspective, dried droplets provide naturally

structured patterns whose morphology can encode information related to composition, transport dynamics, and internal phase organization [5].

The deposition patterns in drying droplets are governed by multiple interacting mechanisms, including solute composition, substrate properties, and thermal gradients. Capillary transport associated with contact line pinning promotes the redistribution of outward material, producing peripheral accumulation commonly described as the coffee ring effect [6]. Surface tension gradients may simultaneously induce Marangoni flows that alter or compete with this redistribution process [7]. Additional phenomena such as crystalline aggregation, shell formation, and phase separation can emerge within the droplet interior, generating heterogeneous textures distributed in peripheral and central regions [7,8]. As a result, evaporative deposits often exhibit strong spatial heterogeneity characterized by localized structural domains with distinct morphological organization.

Such heterogeneity presents a major challenge for computational analysis and pattern recognition. Variations in ambient conditions, surface energy, and internal flow dynamics can produce a wide spectrum of morphologies ranging from sharply defined rings to amorphous or dendritic structures [9]. Even within the same experimental condition, droplets may exhibit substantial class variability, while gradual transitions between the crown and core regions can produce partial overlap between the compositional states. Mechanisms including heterogeneous nucleation, colloidal jamming, and solute crystallization further amplify local structural fluctuations under nominally identical preparation conditions. Conventional global texture descriptors, including gray level co-occurrence matrix (GLCM) features, can capture average structural properties but frequently lose discriminative capability when spatial organization becomes heterogeneous or noisy [5,10]. Whole image classification approaches may similarly obscure localized morphological information by collapsing region dependent structures into global representations. Computational frameworks capable of preserving spatial organization while analyzing localized morphological domains are therefore needed to improve discrimination performance in heterogeneous evaporative systems.

Methotrexate (MTX) provides a relevant model system for evaluating computational strategies aimed at analyzing heterogeneous evaporative patterns. As a widely used therapeutic agent in the management of oncology and autoimmune diseases [11,12], MTX formulations require reliable monitoring of compositional integrity during preparation and handling. Aqueous MTX solutions generate drying morphologies that are sensitive to solvent concentration, making them suitable for investigating how controlled dilution modifies spatial organization within evaporative deposits. Droplet imaging approaches are particularly attractive in this context because they operate with minimal sample volumes and avoid chemical derivatization, enabling morphology analysis directly from the resulting deposition patterns.

Interpreting morphological variability as an intrinsic feature of evaporation self organization rather than as experimental noise requires computational frameworks that accommodate spatial heterogeneity. In evaporating droplets, peripheral and central regions respond differently to compositional perturbations due to combined effects [13]. Analytical strategies that preserve the crown-core organization while quantifying structural changes across dilution levels are therefore particularly suited to discriminate formulation states. Convolutional neural networks provide an approach to extract multiscale features from complex droplet images. By learning spatially structured representations directly from image data, such models can overcome limitations associated with handcrafted descriptors and capture the heterogeneous organization of phase-separated deposits. Previous studies have demonstrated CNN-based classification and clustering of dried droplet patterns across diverse chemical and biological matrices, highlighting the capacity of neural models

to handle substantial class variability. Supervised and unsupervised pipelines have been applied to analyze self assembled deposits from evaporated droplets [14], protein–sugar mixtures exhibiting composition-dependent textures [15], and tap water residues where coffee ring morphologies correlate with chemical composition [16]. Related applications include histone DNA droplets imaged under polarized light [17], evaporative milk residues used for adulteration detection [18,19], and clinical biofluids [20], all of which report reliable discrimination despite complex morphological diversity. A practical constraint in droplet analysis is the limited availability of large image datasets. Preparing and imaging thousands of deposits under reproducible conditions is often impractical in laboratory settings. Although convolutional neural networks typically benefit from extensive training examples, standard data augmentation techniques such as rotations or noise injection do not necessarily reflect the physics variability of evaporative systems. Strategies that incorporate intrinsic spatial information about the morphology of droplets are therefore desirable. Recent work on the quantification of chemical compounds from drying droplet patterns, such as cyanuric acid analysis, demonstrates that evaporation structures encode relevant information for quantitative tasks. These findings highlight the effectiveness of using meaningful morphological features of droplets for predictive purposes [21]. Previous approaches have analyzed whole droplet images or imposed radial or polar transformations, for example, through logarithmic power spectra in polar representations [22]. Patch extraction from droplet regions with rich texture has also been explored to support classification tasks [14]. However, systematic ROI (region of interest) sampling that explicitly distinguishes crown and center domains remains less common.

Despite recent advances in droplet image analysis, computational frameworks capable of preserving localized spatial organization while operating under limited dataset availability remain comparatively underexplored. Most existing approaches either analyze complete droplets as globally homogeneous structures or apply transformations that partially obscure region-dependent morphology. Systematic decomposition strategies that explicitly preserve the organization of the crown and the core during feature extraction and classification are less common. In this study, a localized spatial decomposition framework is introduced for convolutional classification of heterogeneous dried droplet patterns. Each droplet image is decomposed into localized peripheral and central patches that preserve radial morphological organization while expanding the effective number of analytical instances available for training and evaluation. The proposed strategy is evaluated using methotrexate (MTX) droplets prepared under controlled dilution conditions. The classification performance obtained through localized convolutional analysis is compared with conventional global texture descriptors to assess the contribution of spatially resolved feature extraction.

Existing computational approaches therefore face two fundamental challenges: preserving the spatial heterogeneity generated during evaporation while remaining effective under the limited availability of experimentally acquired droplet images. These challenges motivate the localized spatial decomposition framework proposed in this work.

Our contribution is then twofold. First, a region-aware computational framework is proposed to preserve localized spatial organization during the convolutional classification of heterogeneous evaporative patterns under limited dataset availability. Second, a curated dataset of spatially localized MTX droplet patches generated specifically for this study is introduced as a structured resource for future machine learning and pattern recognition studies involving evaporation morphologies.

2. Materials and Methods

2.1. Droplet Dataset Generation

Experimental procedures were designed to evaluate whether spatially resolved image analysis of drying methotrexate (MTX; Ulmextral, Ulsa Tech, Guadalajara, Mexico) droplets enables discrimination between controlled dilution states. The dried droplets were obtained from a commercial injectable MTX stock solution and from water diluted formulations prepared under controlled laboratory conditions, as illustrated in Figure 1.

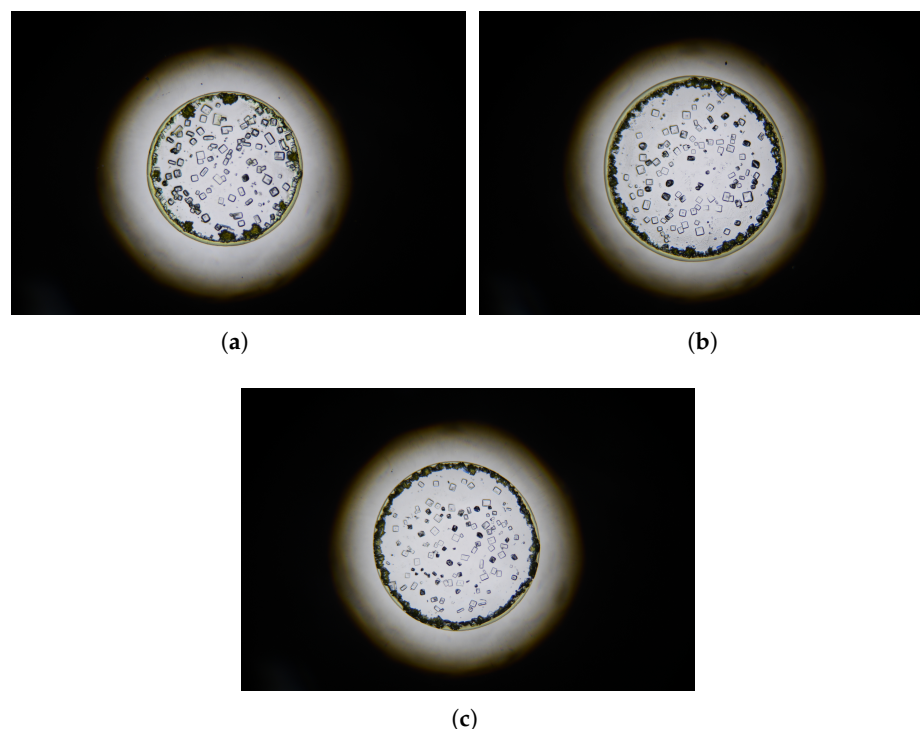


Figure 1. Examples of methotrexate (MTX) dried droplets analyzed in the present study. Images illustrate: (a) 60% purity sample (40% W.C.); (b) 40% purity sample (60% W.C.); (c) 20% purity sample (80% W.C.).

A reference formulation was defined as the analytical control and used for image analysis calibration. This solution was prepared by mixing 10% of the commercial MTX stock solution with 10% of a 10% (*w/w*) NaCl stock solution and 80% distilled water. The formulation was considered equivalent to 100% relative purity. All experimental formulations were designed to preserve ionic strength while systematically modulating solvent composition, thereby inducing controlled perturbations in evaporation pattern formation.

The diluted MTX formulations were prepared by partially replacing the MTX stock fraction with distilled water. The term water content (W.C.) denotes the fraction of distilled water added relative to the reference solution. Three levels of dilution were investigated, corresponding to relative purities of 60%, 40% and 20%, equivalent to water contents of 40%, 60% and 80%, respectively. For example, the 60% purity formulation (40% W.C.) was obtained by mixing a 6% MTX stock solution with 10% of the 10% (*w/w*) NaCl stock solution and 84% distilled water. The remaining dilution levels were prepared analogously by progressively reducing the MTX fraction while maintaining a constant saline contribution. These formulations defined the experimental classes evaluated in the image discrimination task.

All solutions were prepared under standard laboratory conditions. Droplets of (3 μ L) were deposited onto pristine polymethyl methacrylate (PMMA) substrates. The PMMA substrates were used in the untreated/as-received condition, without mechanical sanding,

polishing, plasma activation, chemical functionalization, or additional coating. Therefore, surface treatment was not introduced as an experimental variable, and the same substrate condition was used for all water content groups to minimize substrate-induced differences in contact-line pinning and evaporation-driven deposition. Each deposition area was used only once to avoid cross-contamination or modification of the surface by previous drying events.

Quantitative roughness characterization of the pristine PMMA surface was not performed in the present study. However, representative untreated PMMA areas were inspected optically, including observation with a ($60\times$) objective, and no optically resolvable roughening marks, scratches, or micrometric topographic defects associated with mechanical surface treatment were detected. This inspection was used only as a qualitative verification of surface uniformity. Because the optical microscopy system used for droplet imaging does not provide calibrated vertical profilometry, numerical roughness parameters such as (R_a) or (S_a) were not assigned. Accurate quantification of the nanoscale or submicrometric roughness of pristine PMMA would require atomic force microscopy, optical profilometry, or confocal profilometry.

Droplet evaporation was carried out under monitored laboratory conditions. Temperature and relative humidity were recorded near the deposition area using a Xiaomi NUN4126GL sensor during the experimental session. Depositions were performed within an operational window of (20–25 °C) and (25–30%) relative humidity. The fixed droplet volume, identical substrate condition, single-use deposition areas, and constant imaging configuration were used to maintain comparable confinement geometry, contact-line behavior, and evaporation conditions across all samples.

After complete evaporation, high resolution images (5568×3712 pixels) were acquired using a VLab-M5 microscope coupled to a Nikon D7500 camera (ISO 100, exposure time 1/40 s).

2.2. Algorithm Design

Each droplet image was decomposed into twenty localized patches in order to preserve spatial organization during feature extraction and classification. Twelve patches were sampled from the peripheral crown region at regular angular intervals of 30° , while eight additional patches were extracted from central regions using complementary angular orientations.

The selected spatial sampling scheme was designed to preserve the crown–core organization generated by evaporation while maintaining manageable dataset size and computational complexity. The angular spacing of 30° was adopted as a compromise between spatial coverage and redundancy. Smaller angular intervals would produce highly correlated neighboring patches, whereas larger intervals could fail to capture localized morphological variations distributed along the droplet perimeter. Under this configuration, twelve peripheral patches provide complete circumferential coverage of the crown region. Eight additional patches were extracted from the central domain to represent the greater morphological heterogeneity typically observed within the droplet core and to provide complementary spatial information.

The relationship between independent droplets and localized patches generated through crown–core spatial decomposition is summarized in Table 1.

Unlike conventional image augmentation, we propose a strategy in which physically meaningful localized instances associated with distinct evaporation domains can be used. The peripheral patches captured the ridge structures produced by outward capillary transport, while the central patches represented regions dominated by aggregation and phase redistribution. Before decomposition, the Hough transform was used to identify droplet

geometry and standardize crown–core patch extraction. All extracted patches were resized to 224×224 pixels before convolutional analysis.

Table 1. Dataset composition after crown–core spatial decomposition. Each droplet was decomposed into 12 crown patches and 8 central patches, resulting in 20 localized patches per droplet.

Condition	Droplets	Patches per Droplet	Total Patches per Class
Control	48	20	960
40% W.C.	48	20	960
60% W.C.	48	20	960
80% W.C.	48	20	960

Algorithm 1 describes the localized spatial decomposition procedure used to preserve the radial morphological organization within each droplet image. The algorithm receives as input a standardized droplet image I , previously standardized to ensure a consistent radial geometry throughout the data set.

Algorithm 1 Localized crown–core patch extraction

Require: Standardized droplet image I

- 1: **for** $\theta = 0^\circ$ to 330° step 30° **do**
- 2: Extract peripheral patch P_θ
- 3: **end for**
- 4: **for** central orientations **do**
- 5: Extract central patches C_k
- 6: **end for**
- 7: Construct:

$$D = \{P_1, P_2, \dots, P_{12}, C_1, C_2, \dots, C_8\}$$

- 8: **return** D
-

Peripheral patches are extracted along the crown region of the droplet at regular angular intervals of 30° . The angular variable θ therefore takes values from 0° to 330° , generating a total of twelve peripheral patches. Each extracted peripheral patch is denoted as P_θ , where P_1 to P_{12} correspond to the ordered peripheral regions sampled around the droplet perimeter.

Additional patches are extracted from the central region of the droplet using complementary orientations designed to capture localized aggregation and internal texture variability. These central patches are represented as C_k , where k indexes the central regions extracted. In the present implementation, eight central patches were generated, denoted as C_1 to C_8 . The complete localized patch representation of a droplet is defined as

$$D = \{P_1, P_2, \dots, P_{12}, C_1, C_2, \dots, C_8\}$$

where D represents the structured patch dataset associated with a single droplet image. The resulting decomposition preserves crown–core spatial organization while generating localized image instances suitable for convolutional training and region resolved classification analysis.

Two dataset partitioning strategies were evaluated. The first configuration (Experiment 1) employed patch-level partitioning, in which extracted patches were randomly assigned to training, validation, and testing subsets. For the second configuration (Experiment 2), partitioning was performed at droplet level, ensuring that all patches extracted from a given droplet were assigned exclusively to a single subset. As a result, no patches originating from the same physical droplet could simultaneously appear in training, validation, and testing datasets, preventing information leakage between subsets.

Experiment 1 was intended as a patch-level consistency assessment of the present study, whereas Experiment 2 provides the primary evaluation of model generalization because complete droplets remain unseen during training and validation.

The proposed localized decomposition strategy was partly motivated by the limited availability of independent droplet images. This limitation is common in dried droplet datasets, where experiments are often labor-intensive, require controlled preparation conditions, and produce relatively small numbers of samples per experimental condition. The transformation of each droplet into multiple physically meaningful localized samples substantially increases the effective number of training instances while preserving regional morphological information. Nevertheless, the diversity of the dataset ultimately remains constrained by the number of independent droplets available. In this sense, additional droplet acquisitions may further improve model robustness and generalization under broader experimental variability.

The overall workflow implemented in the present study is summarized in Figure 2.

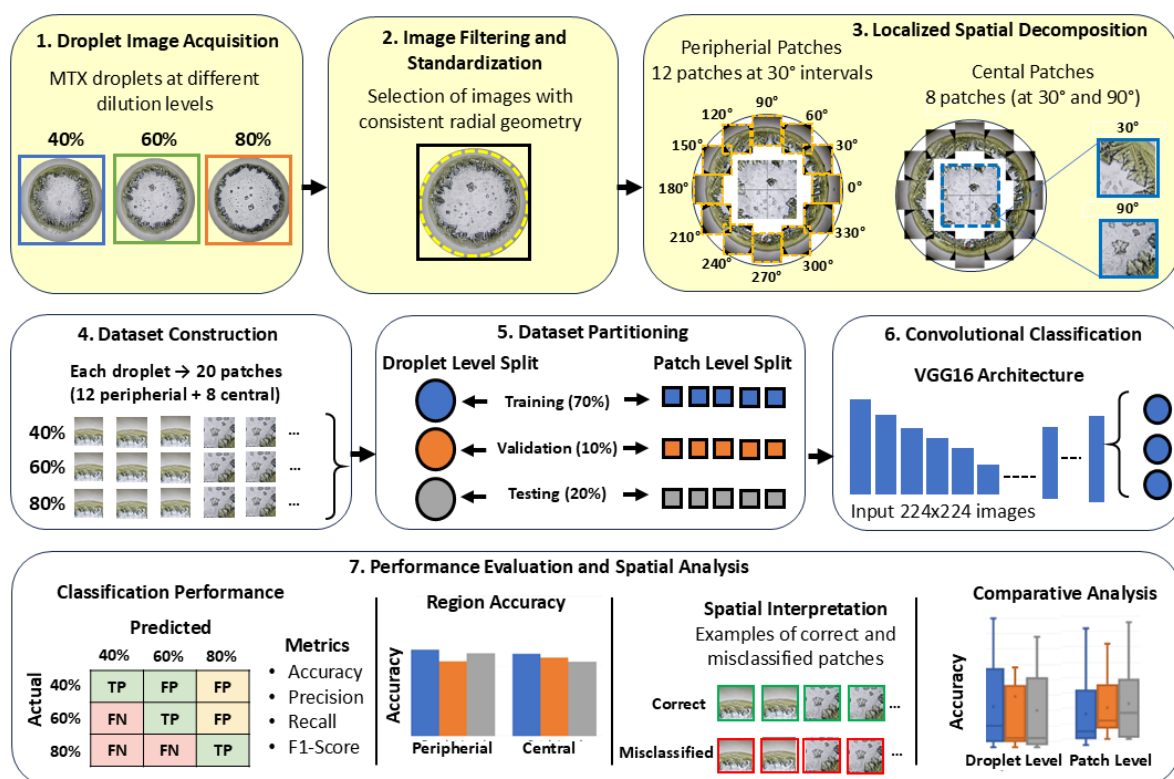


Figure 2. Localized spatial decomposition and convolutional classification workflow for heterogeneous dried droplet analysis, including geometric standardization, crown–core patch extraction, dataset partitioning, convolutional training, and region resolved performance evaluation.

2.3. Convolutional Classification Pipeline

Region resolved patch datasets were analyzed using a convolutional neural network based on the VGG16 architecture. VGG16 was selected because its well-established design facilitates methodological evaluation while reducing the number of architectural variables that may influence performance. The network was implemented using transfer learning with weights pretrained on ImageNet, enabling the use of robust visual representations learned from a large-scale image corpus. This strategy is particularly advantageous in experimentally acquired datasets, where sample availability is often limited. The objective of the present study is not to optimize the neural network architecture itself, but rather to evaluate the effectiveness of the localized spatial decomposition framework. Consequently,

VGG16 serves as a representative convolutional classifier that allows the contribution of the spatial decomposition strategy to be assessed independently of more recent architectural developments.

The implemented network consisted of convolutional blocks with 3×3 kernels and ReLU activation functions, followed by max pooling operations for spatial downsampling and fully connected layers for feature representation. The final dense layer employed Softmax activation with two output units corresponding to binary classification between control and diluted droplet conditions.

Training was performed using the Adam optimizer with a learning rate of 0.001, 0.5 dropout and categorical cross entropy loss. The batch size was set to 32 and all models were trained for 30 epochs. Computations were conducted on a workstation equipped with an AMD Ryzen 7 processor, 16 GB RAM, 1 TB solid state storage, and an NVIDIA GeForce RTX 3050 GPU (4 GB VRAM).

In Experiment 1, localized patches were randomly assigned to training, validation, and testing subsets. For each binary classification task, 70% of the patches (672 patches per class) were allocated to training, 10% (96 patches per class) to validation, and 20% (192 patches per class) to testing. In Experiment 2, partitioning was performed at droplet level rather than patch level. Each experimental condition contained 48 independent droplets, which were assigned to the training, validation, and testing subsets following the same target proportions used in Experiment 1. Because complete droplets were preserved during partitioning, the final allocation consisted of 34 training droplets, 5 validation droplets, and 9 testing droplets per class. Since each droplet generated 20 localized patches, the resulting subsets contained 680, 100, and 180 patches per class, respectively. This strategy ensured that all patches originating from a given droplet remained within the same subset, thereby preventing information leakage between training, validation, and testing datasets. The resulting droplet-level partitioning is summarized in Table 2.

Table 2. Summary of dataset partitioning strategies used for model evaluation. Values are reported per class for each binary classification task.

Dataset Split	Experiment 1 Patch-Level	Experiment 2 Droplet-Level
Training (70%)	672 patches	34 droplets (680 patches)
Validation (10%)	96 patches	5 droplets (100 patches)
Testing (20%)	192 patches	9 droplets (180 patches)
Total 960 patches	48 droplets (960 patches)	

The proposed framework was specifically developed to address two characteristics commonly encountered in dried-droplet analysis: pronounced spatial heterogeneity and limited availability of independent experimental samples. The representation of each droplet as a structured collection of localized analytical instances simultaneously preserves region-dependent morphological information while increasing the number of physically meaningful samples available for learning. In this sense, a direct comparison with a conventional whole-image classifier would involve not only a different classification strategy but also a fundamentally different data representation, where each droplet is treated as a single sample instead of a collection of localized regions. Such a comparison would therefore reflect both differences in representation and differences in the amount of analytical information available for learning.

Model performance during training was quantified using mean Average Precision (mAP)

$$mAP = \frac{1}{N} \sum_{i=1}^N AP_i,$$

where AP_i represents the average precision for class i , and N corresponds to the total number of classes.

2.4. Performance Evaluation Metrics

Classification performance was evaluated using the accuracy, precision, recall and F1-score metrics derived from the confusion matrix. The global classification accuracy was computed as

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN},$$

where TP , TN , FP , and FN correspond to true positives, true negatives, false positives, and false negatives, respectively.

To quantify spatial contributions, classification accuracy was additionally computed independently for peripheral crown regions and central regions

$$Accuracy_r = \frac{\text{Correct predictions in region } r}{\text{Total predictions in region } r},$$

where r corresponds to crown or center patches extracted from each droplet image.

Precision and recall were computed as

$$Precision = \frac{TP}{TP + FP}$$

$$Recall = \frac{TP}{TP + FN},$$

while F1-score was calculated as

$$F1 = 2 \times \frac{Precision \times Recall}{Precision + Recall}.$$

These metrics provide complementary information on classification reliability, sensitivity, and discriminative stability under conditions of high morphological heterogeneity.

3. Results

The analytical performance of the proposed approach was examined through complementary quantitative and qualitative analyses. Quantitative results first evaluate the entropy derived from gray level co-occurrence matrices (GLCM) as a global texture descriptor. This is followed by the performance of convolutional models trained on spatially resolved image patches. Here, the aim was to enable assessment of the extent to which global descriptors capture evaporation morphological variability and provide a rationale for region resolved analysis. The qualitative observations presented afterwards illustrate representative morphological features in the crown and center of the drop that contribute to the classification results.

3.1. Limitations of Global Texture Descriptors

Within the quantitative evaluation, entropy was first investigated as a global descriptor. The discriminative capacity of CLP was then compared with that of convolutional models designed to exploit spatial heterogeneity across the droplet surface.

For the global texture-descriptor analysis, GLCM-derived entropy was computed for each complete droplet image and summarized for each W.C. group as mean $\pm$ standard

deviation using $n = 48$ independent deposits per group. ROC analysis was performed by comparing each diluted group (40%, 60%, and 80% W.C.) against the 0% W.C. reference group. AUC values, standard errors, 95% confidence intervals, and p -values for the null hypothesis $AUC = 0.5$ were reported to quantify the discriminative capacity of entropy.

Figure 3 presents the entropy values obtained from the GLCM analysis as a function of the water content (W.C.) for four groups of methotrexate deposits (MTX). Each data point corresponds to the mean entropy for a given dilution level, while vertical bars indicate the associated error range. For the control condition (0% W.C.), the mean entropy slightly exceeds 8.0 a.u., with a relatively narrow dispersion, suggesting stable structural characteristics under reference conditions. At 40% W.C., the mean entropy decreases to just below 8.0 a.u., accompanied by a substantially broader error range, indicating increased variability in the resulting drying patterns.

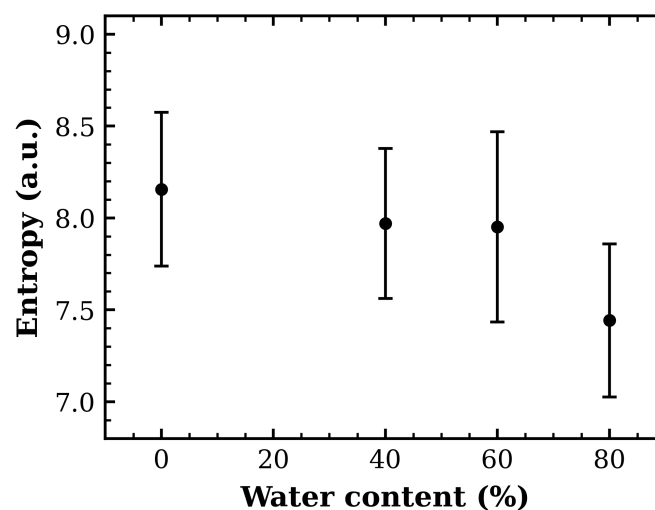


Figure 3. Entropy as a function of water content in MTX deposits. Symbols represent the mean entropy value for each water content condition, and error bars indicate ± 1 standard deviation (SD) across $n = 48$ independent deposits per group. The error bars quantify deposit-to-deposit variability in spatial disorder/texture heterogeneity, rather than the standard error of the mean or a confidence interval.

At 60% W.C., entropy values remain comparable to those observed at 40% W.C., with similarly wide uncertainty intervals. This overlap reduces the interpretability of changes across intermediate dilution levels. In contrast, at 80% W.C., the mean entropy decreases further to approximately 7.5 a.u., while the error range becomes narrower than at 40% and 60% W.C., indicating improved measurement consistency under higher solvent fractions. Considerable overlap of confidence intervals is observed across the control, 40%, and 60% W.C. conditions.

To further evaluate discriminative capacity, receiver operating characteristic (ROC) curves were computed and the corresponding areas under the curve (AUC) were determined. Table 3 summarizes the AUC values obtained for the classification of entropy at each dilution level. For W.C. = 40%, the AUC is 0.68123 with a standard error of 0.06847 and an asymptotic significance value of $p = 0.01018$, indicating a statistically significant separation from the reference threshold of 0.5. Although this result reflects moderate discriminative performance, the relatively wide confidence interval (0.54702–0.81543) limits the precision of the estimate.

At W.C. = 60%, the AUC decreases to 0.62284 with a similar standard error (0.06837). The higher asymptotic probability ($p = 0.08156$) indicates that the separation from the reference value is not statistically significant, suggesting reduced discriminative performance at this dilution level. In contrast, at W.C. = 80%, the AUC increases markedly to 0.89879 with a

lower standard error (0.03797), resulting in a more precise estimate. The associated asymptotic probability ($p = 1.56 \times 10^{-8}$) demonstrates strong statistical significance, supported by a narrower confidence interval (0.82437–0.97321), consistent with robust discriminative performance under high dilution.

Overall, entropy discrimination improves with increasing water content. However, at intermediate dilution levels (40% and 60% W.C.), substantial overlap with the control condition leads to broad uncertainty ranges and limited statistical separation. These findings indicate that global entropy does not fully capture the radial redistribution of material occurring during evaporation. In particular, peripheral and central structural domains remain partially coupled at moderate dilution states, limiting the effectiveness of global texture descriptors. Reliable discrimination is only achieved at 80% W.C., where increased solvent fraction appears to enhance radial morphological contrast and reduce ambiguity between spatial regions.

Table 3. AUC values for entropy-based classification at different water content (W.C.) levels in methotrexate (MTX) deposits. Each ROC analysis compared the entropy distribution of the indicated W.C. group against the 0% W.C. reference group, using $n = 48$ independent deposits per group. The 95% confidence intervals quantify the uncertainty of the AUC estimates, and p -values test the null hypothesis $AUC = 0.5$.

W.C.	AUC	Std. Error	p -Value	95% LCL	95% UCL
40%	0.66732	0.05819	0.00478	0.55326	0.78137
60%	0.62326	0.05757	0.03776	0.51042	0.73611
80%	0.88194	0.03496	1.16×10^{-10}	0.81342	0.95047

3.2. Convolutional Classification Under Localized Spatial Decomposition

A convolutional classification pipeline was implemented to evaluate whether spatially localized morphological domains retain discriminative information under controlled dilution. The workflow comprised two stages: network training and validation using specific region patches extracted from each water content (W.C.) dataset versus the control condition, followed by classification of unseen test patches to determine their assignment to control or diluted samples.

As stated in Section 2.3, two data partitioning strategies were examined. Experiment 1 was designed as a patch-level consistency assessment in which image patches were randomly divided into training, validation, and testing subsets. Although all test patches were excluded from model optimization, some could originate from droplets partially represented in the training data. Experiment 2 constituted the primary generalization evaluation. In this configuration, partitioning was constrained at droplet level, with the test subset containing complete droplets that were not represented in the training or validation sets. This design ensured full independence between training and evaluation data and enabled assessment of model performance on previously unseen deposits.

Figure 4 presents the confusion matrices accumulated across the ten repetitions for both experimental settings. Values correspond to the counts of correctly identified experimental patches (true positives), correctly identified control patches (true negatives), control patches misclassified as experimental (false positives), and experimental patches misclassified as control (false negatives).

Under the patch-level partitioning scheme (Figure 4a), the network achieves consistent discrimination at intermediate dilution states (40% and 60% W.C.), with high numbers of correct classifications for both experimental and control patches. Residual overlap between classes remains detectable at these levels, indicating partial morphological similarity between deposits. Classification performance improves further at 80% W.C., where

misclassification events become minimal. The progressive reduction of overlap at higher solvent fractions is consistent with enhanced radial contrast between peripheral and central structural domains.

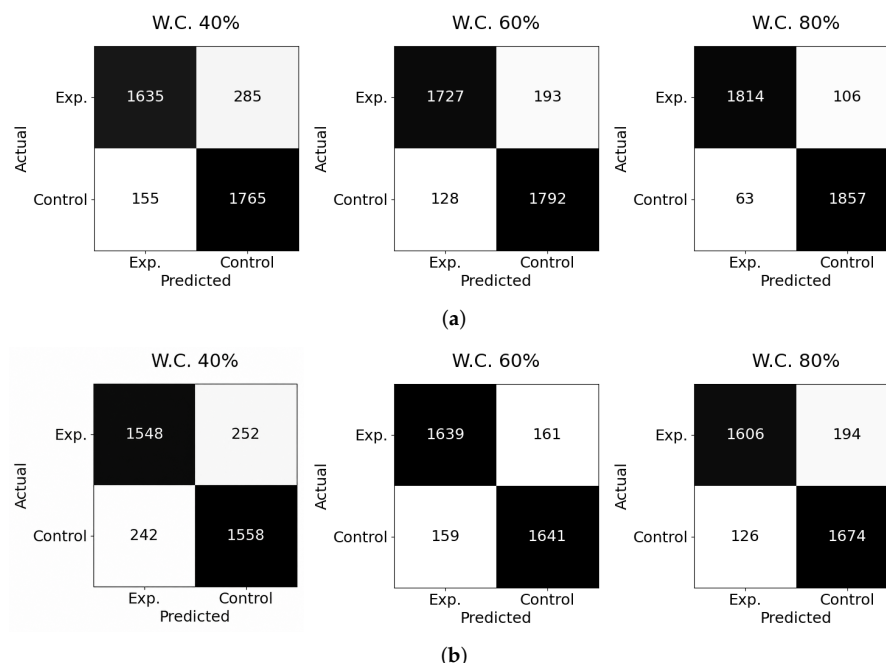


Figure 4. Confusion matrices of accumulated TP, TN, FP and FN across ten runs, per W. C. for Experiment 1 (a) Confusion matrices for Experiment 1. Number of patches per class: 1920, corresponding to 192 test patches $\times$ 10 runs and Experiment 2 (b) Confusion matrices for Experiment 2. Number of patches per class: 1800, corresponding to 180 test patches $\times$ 10 runs.

When evaluated under droplet-level partitioning (Figure 4b), overall performance decreases slightly due to the more stringent separation between training and test data. Classification accuracy improves substantially from 40% W.C. to the higher dilution conditions, indicating enhanced separability relative to the lowest dilution level. However, the results obtained at 60% and 80% W.C. are comparable, suggesting that the principal improvement occurs between 40% W.C. and the higher water content conditions rather than as a strictly monotonic progression across all dilution levels.

The persistence of the observed classification trends under droplet-level partitioning indicates that the extracted spatial representations remain informative when evaluated on previously unseen droplets. This stricter evaluation protocol complements the patch-level analysis as it reduces potential dependencies arising from localized image similarity within individual droplets.

Average performance metrics across both configurations are summarized in Table 4. In the patch-level experiment, classification accuracy increases from approximately 0.89 at 40% W.C. to about 0.96 at 80% W.C., accompanied by corresponding improvements in precision, sensitivity, and F1-score for both experimental and control classes. In the droplet-level experiment, overall accuracy is slightly lower, ranging from approximately 0.86 at 40% W.C. to around 0.91 at 60–80% W.C., while showing improved performance relative to the 40% W.C. condition and comparable performance between the 60% and 80% W.C. datasets. Across both evaluation strategies, discriminative performance scales with solvent fraction, indicating that controlled dilution modulates the spatial separability of morphological domains within the deposits.

Additional analysis comparing peripheral (ring) and central patches supports this interpretation. Peripheral patches consistently exhibit higher correct classification rates,

typically exceeding 0.94, whereas central patches display greater variability, particularly at intermediate dilution levels. Such asymmetry suggests that the crown region contains more robust structural features linked to evaporation transport mechanisms. Contact line pinning and outward capillary flow promote persistent ridge formation at the droplet edge, while the central region remains more sensitive to aggregation heterogeneity and transitional texture development.

To further assess droplet classification performance, the predictions of the 20 localized patches associated with each droplet were aggregated using majority-vote criteria with voting thresholds ranging from 50% to 90%. A droplet was considered correctly classified when the number of correctly classified localized patches satisfied the selected threshold. The droplet-level performance metrics are summarized in Table 5. High classification accuracy was observed across all experimental conditions, ranging from 84.8% to 91.4%. Thus, the classifier decisions remained highly consistent across multiple spatial regions within the same droplet and demonstrated the ability of the presented framework to correctly classify previously unseen droplets.

Table 4. Average performance metrics across 10 runs for water content (W.C.) conditions: 80%, 60%, and 40%. Confusion matrix values correspond to the accumulated counts shown in Figure 4. Mean values are presented in the last row of each experiment.

(a) Experiment 1 *															
W.C.	Acc.	Experimental			Control			Conf. Matrix				Central		Ring	
		Prec.	Sens.	F1	Prec.	Spec.	F1	TP	FP	TN	FN	EC	CC	ER	CR
40%	0.89	0.92	0.85	0.88	0.86	0.92	0.89	1635	155	1765	285	0.87	0.82	0.95	0.89
60%	0.92	0.93	0.90	0.92	0.90	0.93	0.92	1727	128	1792	193	0.86	0.83	0.98	0.96
80%	0.96	0.97	0.94	0.96	0.95	0.97	0.96	1814	63	1857	106	0.93	0.90	0.99	0.98
μ	0.92	0.94	0.90	0.92	0.90	0.94	0.92	1725	115	1805	195	0.89	0.85	0.97	0.94
(b) Experiment 2 *															
W.C.	Acc.	Experimental			Control			Conf. Matrix				Central		Ring	
		Prec.	Sens.	F1	Prec.	Spec.	F1	TP	FP	TN	FN	EC	CC	ER	CR
40%	0.86	0.88	0.86	0.86	0.87	0.87	0.86	1548	242	1558	252	0.84	0.85	0.90	0.89
60%	0.91	0.92	0.91	0.91	0.92	0.91	0.91	1639	159	1641	161	0.88	0.84	0.94	0.98
80%	0.91	0.94	0.89	0.91	0.91	0.93	0.91	1606	126	1674	194	0.90	0.87	0.96	0.94
μ	0.90	0.91	0.89	0.89	0.90	0.90	0.89	1598	176	1624	202	0.87	0.85	0.93	0.93

*Abbreviations: Acc. (accuracy); Prec. (precision); Sens. (sensitivity); Spec. (specificity); F1 (F1-score); TP (true positives); FP (false positives); TN (true negatives); FN (false negatives); EC (experimental class—center); CC (control class—center); ER (experimental class—ring); CR (control class—ring).

Table 5. Average classification performance across 10 runs for the majority-vote analysis using voting thresholds of 50%, 60%, 70%, 80%, and 90%. Predictions from the 20 localized patches associated with each droplet were combined into a single droplet classification. The evaluated thresholds define the minimum level of agreement required among localized patch predictions. TP, FP, TN, and FN are the average numbers of complete droplets in each confusion matrix category after the 10 runs.

W.C.	Acc.	Experimental			Control			Conf. Matrix			
		Prec.	Sens.	F1	Prec.	Spec.	F1	TP	FP	TN	FN
40%	0.848	0.841	0.853	0.847	0.856	0.842	0.849	76.8	14.2	75.8	13.2
60%	0.902	0.898	0.908	0.903	0.907	0.895	0.901	81.8	9.4	80.6	8.2
80%	0.914	0.921	0.903	0.912	0.907	0.924	0.915	80.4	7.8	83.2	8.6
μ	0.889	0.887	0.889	0.887	0.89	0.887	0.888	79.6	10.4	79.8	10

Detailed numerical results for each of the ten runs used to compute the averaged metrics in Tables 4 and 5 and Figure 4 are provided in Appendix A.

3.3. Regional Discriminative Behavior and Spatial Sensitivity

Qualitative inspection was conducted to examine how classification outcomes relate to spatial organization within complete droplets across dilution levels. Figure 5 presents representative results obtained from the droplet-level evaluation for the three water content conditions, selecting the run with median accuracy in each case. In every panel, rows correspond to individual test droplets. Upper rows show experimental patches, while lower rows display the corresponding control patches. Misclassified regions are indicated by red bounding boxes. This layout enables direct visual comparison of radial pattern reorganization as solvent fraction increases.

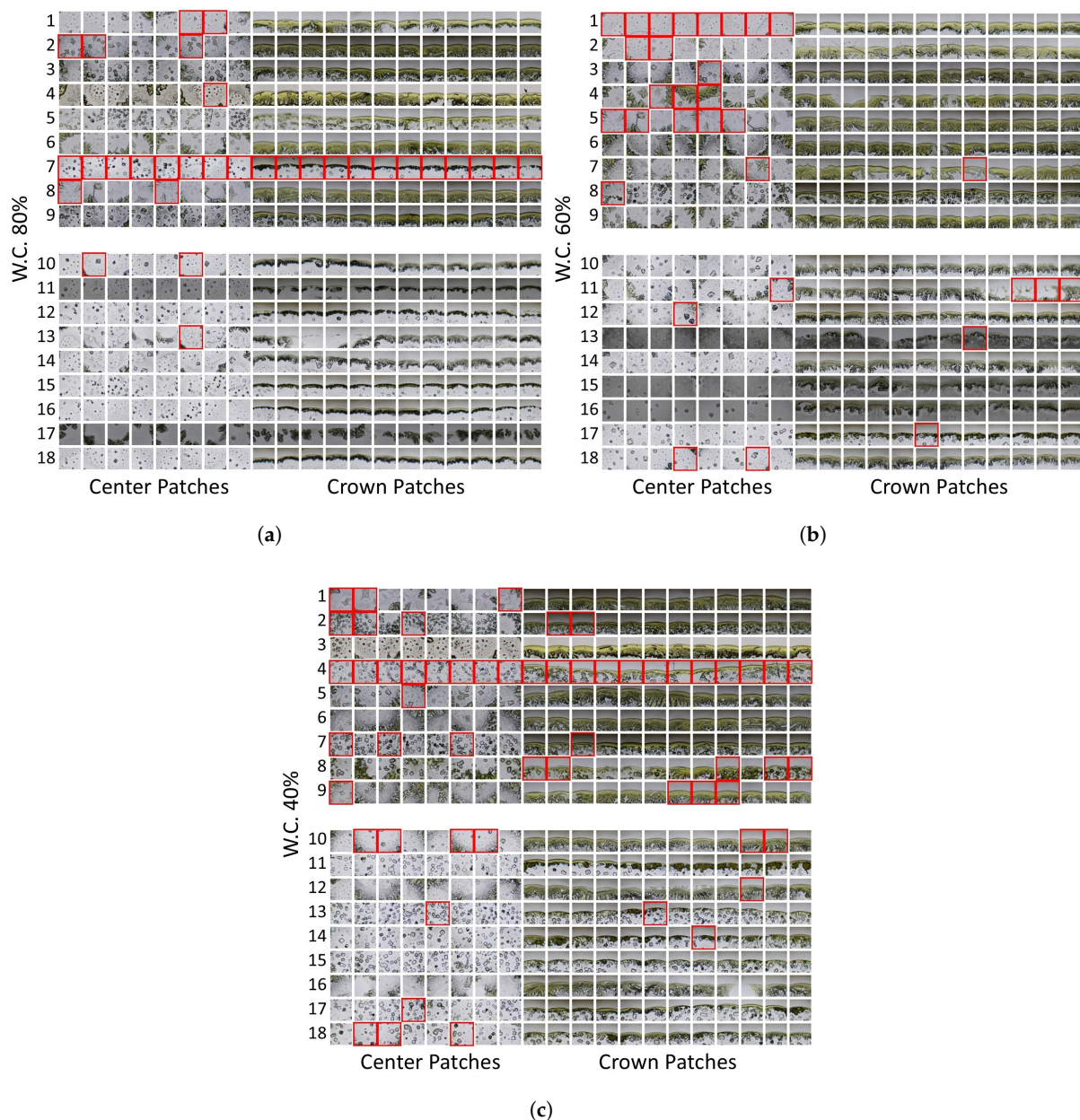


Figure 5. Classification results for each W. C. test set in run 1 of 10, under the partitioning strategy of Experiment 2. Rows 1–9 correspond to experimental droplets, while rows 10–18 correspond to control droplets. Misclassified patches are highlighted in red.

At 80% W.C., experimental droplets exhibit pronounced peripheral ridges forming banded crown structures with marked textural anisotropy and fine striations along the ring. Central regions typically contain heterogeneous aggregates and porous textures with elevated local contrast. In contrast, control droplets display smoother crowns characterized by thinner peripheral rings and reduced high frequency texture. Their centers appear more uniform, with sparse deposits and extended homogeneous zones. These morphological differences account for the strong separation observed at this dilution level. Peripheral patches supply stable structural cues, whereas experimental centers present a richer microstructure than controls. The formation of pronounced ridges is consistent with intensified outward capillary transport at high solvent content, while the heterogeneous core suggests localized aggregation and phase redistribution within the confined droplet interior.

Misclassification events remain limited and are predominantly associated with central patches. One experimental droplet (row 7) shows a higher error concentration affecting several crown patches. In this case, the peripheral ridge appears attenuated, with reduced relief and partial blending with transitional textures between crown and center. This qualitative assessment does not allow us to determine which specific image attributes were used by the network for its predictions. Minor focus or illumination variations and local discontinuities along the peripheral ring may also have contributed to the increased ambiguity of these patches. Thus, these observations should be regarded as qualitative descriptions of the image appearance rather than evidence of the internal decision-making process of the model.

Despite these isolated cases, the general trend remains stable. Crown morphology at 80% W.C. provides the most reliable discriminative features, whereas central domains retain greater variability and account for most residual confusion. The stronger contrast observed at the droplet periphery supports the interpretation that evaporation stabilizes structural organization in this region, while the interior evolves through more dynamic aggregation processes.

At 60% W.C., classification results reveal a higher number of errors relative to the 80% condition. Misclassifications occur mainly within central patches of experimental droplets, particularly in the first rows. Grainy aggregates interspersed with smoother voids generate textures resembling those of control centers. Such morphological convergence explains the concentration of errors at this dilution level. Solvent redistribution appears insufficient to produce a clear separation between peripheral ridge formation and central aggregation regimes, leading to partial overlap in structural characteristics.

Peripheral regions in experimental droplets still display identifiable ridged patterns, although classification errors are occasionally observed where the crown shows local flattening or reduced contrast. Control droplets are generally classified correctly at the crown, with sporadic errors occurring in areas where small fractures or debris introduce high frequency texture similar to experimental rings. Central regions in controls may also contribute to confusion when sparse crystalline deposits mimic the denser aggregates found in diluted samples.

The qualitative evidence at 60% W.C. indicates that the crown continues to act as a stronger source of discriminative information than the center. However, transitional morphologies persist across both regions, consistent with the moderate quantitative performance observed at this dilution level. These observations suggest that intermediate solvent fractions maintain partially coupled radial domains that have not yet undergone full structural differentiation. At 40% W.C., classification becomes more challenging, with errors distributed across both central and peripheral domains. In experimental droplets (rows 1–9), center patches frequently display dispersed deposits and irregular voids that resemble the smoother textures observed in control centers. Such similarities lead to re-

current misclassifications, particularly in rows 1, 4 and 7. Peripheral regions also show notable variability. Although several ridged structures are correctly identified, some peripheral patches exhibit flattened or discontinuous rings (rows 4, 6 and 8), which reduce morphological contrast and make them visually closer to control crowns.

In control droplets (rows 10–18), misclassifications again occur mainly in the central regions. Sparse aggregates may appear denser under local illumination or focus variations, promoting confusion with experimental textures, as observed in rows 10 and 13. Peripheral patches in controls remain generally consistent, yet local disruptions such as broken rings or isolated high contrast deposits (rows 10 and 14) can resemble the more textured crowns of diluted samples. The convergence of morphological traits between experimental and control droplets at this dilution level explains the higher error frequency compared with the 60% and 80% conditions. Class separation at 40% W.C. is less robust. Structural features in both crown and center domains show partial overlap across experimental and control droplets. This reduced contrast accounts for the lower classification reliability and reflects the increased difficulty of distinguishing groups when solvent-driven morphological differentiation remains limited. Under these conditions, evaporation transport and aggregation appear to generate partially overlapping structural regimes throughout the droplet radius.

A broader qualitative observation concerns the internal variability of the control group. Three distinct sets of control droplets were available for inspection, revealing considerable diversity in both central and peripheral morphologies. Centers range from nearly clean regions with sparse deposits to denser crystalline clusters. Peripheral rings vary from smooth and continuous structures to irregular edges with localized relief. Such heterogeneity is less evident in the experimental sets, which contain fewer droplets per dilution level. This variability contributes to misclassification events, since some control patches locally reproduce features typically associated with diluted samples. From a methodological perspective, these findings support the use of deep learning approaches capable of extracting subtle, spatially consistent cues despite substantial class diversity.

Comparative inspection across dilution levels reveals a progressive increase in classification reliability. At 40% W.C., both radial domains display frequent confusion due to morphological overlap. At 60% W.C., separation improves, although central regions remain susceptible to misinterpretation, while crowns offer more stable discriminative information. At 80% W.C., morphological contrast becomes most pronounced. Peripheral ridges show clear structural persistence, central textures diverge markedly between conditions, and classification performance reaches its highest level. This progression indicates that increasing water content enhances radial differentiation within the droplet. The gradual sharpening of crown structures and the evolving heterogeneity of core textures suggest that solvent composition modulates the balance between contact line pinning, capillary transport, and interior aggregation during evaporation.

4. Conclusions

Controlled dilution produced systematic morphological differences between peripheral crown regions and central domains of drying methotrexate droplets. These spatial differences motivated the proposed localized decomposition framework, which enables convolutional classification under limited dataset availability.

Consistent discrimination performance was observed on both patch-level and droplet-level partitioning strategies. Particular emphasis, however, should be placed on the droplet-level evaluation, which provides a stricter assessment of model generalization by ensuring complete separation between training, validation, and testing droplets. The persistence of robust classification performance under these conditions demonstrates that the localized

spatial decomposition framework captures reproducible morphological signatures that generalize across previously unseen droplets.

The proposed framework should be viewed as a methodology for spatial representation rather than as a specific classification model. Its primary contribution resides in the transformation of a single droplet image into a structured collection of spatially localized analytical instances that preserve crown–core organization. It was shown that this representation enables localized morphological information to be analyzed independently while maintaining direct correspondence with the underlying evaporation dynamics. As demonstrated by the experimental results, such region-aware decomposition provides a more informative basis for classification than global texture descriptors alone.

A direct comparison with a whole-image CNN would require a substantially larger number of independent droplets than those available in the present dataset. After droplet-level partitioning, only 34 independent droplets per class remain for training. The proposed localized spatial decomposition was specifically designed to address this limitation by generating physically meaningful localized training instances while preserving the crown–core organization of the evaporation process. Accordingly, the proposed framework should be interpreted as a methodological strategy for learning under limited sample availability rather than as a direct alternative to whole-image classification.

From an engineering perspective, the ability to automatically distinguish between MTX dilution states provides a foundation for the development of image-based quality assessment and process monitoring tools in evaporation-driven systems. More broadly, the proposed methodology may support automated analysis workflows in applications where compositional changes are reflected through complex spatial morphologies and where conventional global descriptors fail to provide sufficient discrimination.

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Data Availability Statement: The data described in this paper are available at figshare at <https://doi.org/10.6084/m9.figshare.30442889.v1>. The source code used for localized spatial decomposition, dataset construction, and convolutional classification can be found at <https://github.com/cmtzmiwa/Localized-Spatial-Decomposition-for-CNN-Classification-of-Heterogeneous-Dried-Droplet-Patterns>, accessed on 8 July 2026.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

The following abbreviations are used in this manuscript:

MTX	Methotrexate
W.C.	Water content
PMMA	Polymethyl methacrylate
GLCM	Grey-level co-occurrence matrix
ROC	Receiver operating characteristic
AUC	Area under the curve
mAP	Mean Average Precision
Acc.	Accuracy

Prec.	Precision
Sens.	Sensitivity
Spec.	Specificity
F1	F1-score
TP	True positives
FP	False positives
TN	True negatives
FN	False negatives
EC	Experimental class—center
CC	Control class—center
ER	Experimental class—ring
CR	Control class—ring

Appendix A. Performance Metrics

Table A1. Performance metrics across 10 runs for water content (W.C.) conditions in Experiment 1: 80% (MTX at 2%), 60% (MTX at 4%), and 40% (MTX at 6%). Metrics include: Acc. (accuracy), Prec. (precision), Sens. (sensitivity), F1 (F1-score), Spec. (specificity), TP (true positives), FP (false positives), TN (true negatives), FN (false negatives), EC. (experimental class in the center), CC (control class in the center), ER (experimental class in the ring), and CR (control class in the ring). For the center and ring areas the metric shown is precision. Mean values are shown in the last row of each subtable.

(a) Performance metrics for Experimental class: W.C. at 40%															
Run	Acc.	Experimental			Control			Conf. Matrix				Center		Ring	
		Prec.	Sens.	F1	Prec.	Spec.	F1	TP	FP	TN	FN	EC	CC	ER	CR
1	0.93	0.98	0.89	0.93	0.90	0.98	0.94	170	3	189	22	0.97	0.82	0.99	0.94
2	0.84	0.86	0.81	0.83	0.82	0.86	0.84	156	26	166	36	0.79	0.85	0.92	0.81
3	0.88	0.94	0.80	0.87	0.83	0.95	0.88	154	10	182	38	0.87	0.75	0.97	0.88
4	0.92	0.98	0.87	0.92	0.88	0.98	0.93	167	4	188	25	0.98	0.84	0.97	0.91
5	0.87	0.91	0.81	0.86	0.83	0.92	0.87	156	15	177	36	0.92	0.84	0.91	0.82
6	0.91	0.93	0.89	0.91	0.89	0.93	0.91	170	13	179	22	0.83	0.85	0.99	0.92
7	0.83	0.84	0.82	0.83	0.83	0.84	0.83	158	31	161	34	0.76	0.76	0.89	0.88
8	0.89	0.87	0.90	0.89	0.90	0.87	0.88	173	25	167	19	0.84	0.86	0.89	0.93
9	0.88	0.96	0.80	0.87	0.83	0.97	0.89	153	6	186	39	0.95	0.77	0.97	0.87
10	0.91	0.89	0.93	0.91	0.92	0.89	0.90	178	22	170	14	0.77	0.88	0.97	0.94
μ	0.89	0.92	0.85	0.88	0.86	0.92	0.89	164	16	177	29	0.87	0.82	0.95	0.89
σ	0.03	0.05	0.05	0.04	0.04	0.05	0.03	8.61	9.48	9.48	8.61	0.08	0.05	0.04	0.05

(b) Performance metrics for Experimental class: W.C. at 60%															
Run	Acc.	Experimental			Control			Conf. Matrix				Center		Ring	
		Prec.	Sens.	F1	Prec.	Spec.	F1	TP	FP	TN	FN	EC	CC	ER	CR
1	0.92	0.95	0.88	0.92	0.89	0.96	0.92	169	8	184	23	0.91	0.77	0.98	0.99
2	0.92	0.94	0.90	0.92	0.90	0.94	0.92	173	12	180	19	0.86	0.83	0.98	0.97
3	0.91	0.91	0.92	0.92	0.92	0.91	0.92	176	17	175	16	0.81	0.86	0.98	0.95
4	0.91	0.95	0.86	0.92	0.87	0.95	0.92	165	9	183	27	0.88	0.82	1.00	0.91
5	0.93	0.97	0.89	0.92	0.89	0.97	0.92	170	6	186	22	0.97	0.82	0.96	0.96
6	0.93	0.93	0.92	0.92	0.92	0.93	0.92	177	13	179	15	0.89	0.82	0.96	0.97
7	0.92	0.93	0.91	0.92	0.91	0.93	0.92	174	13	179	18	0.86	0.85	0.97	0.95
8	0.90	0.88	0.93	0.90	0.92	0.88	0.90	178	24	168	14	0.76	0.89	0.96	0.94
9	0.93	0.96	0.89	0.92	0.90	0.96	0.92	171	7	185	21	0.90	0.81	0.99	0.97
10	0.90	0.90	0.91	0.92	0.91	0.90	0.92	174	19	173	18	0.78	0.81	1.00	0.96
μ	0.92	0.93	0.90	0.92	0.90	0.93	0.92	173	13	180	19	0.86	0.83	0.98	0.96
σ	0.01	0.03	0.02	0.01	0.02	0.03	0.01	4.00	5.77	5.77	4.00	0.06	0.03	0.01	0.02

Table A1. *Cont.*

(c) Performance metrics for Experimental class: W.C. at 80%															
Run	Acc.	Experimental			Control			TP	Conf. Matrix			Center		Ring	
		Prec.	Sens.	F1	Prec.	Spec.	F1		FP	TN	FN	EC	CC	ER	CR
1	0.97	1.00	0.94	0.97	0.95	1.00	0.97	181	0	192	11	1.00	0.92	1.00	0.96
2	0.95	0.95	0.94	0.94	0.94	0.95	0.95	180	9	183	12	0.89	0.91	1.00	0.96
3	0.97	0.96	0.98	0.97	0.98	0.96	0.97	188	8	184	4	0.90	0.98	1.00	0.98
4	0.97	0.99	0.95	0.97	0.95	0.99	0.97	183	2	190	9	0.97	0.91	1.00	0.98
5	0.94	0.97	0.91	0.94	0.92	0.97	0.94	175	5	187	17	0.94	0.84	0.99	0.97
6	0.94	0.92	0.96	0.94	0.96	0.92	0.94	185	16	176	7	0.81	0.93	1.00	0.98
7	0.96	0.99	0.92	0.95	0.92	0.99	0.96	176	1	191	16	0.99	0.87	1.00	0.98
8	0.95	0.98	0.93	0.95	0.93	0.98	0.95	178	4	188	14	0.99	0.86	0.97	0.98
9	0.95	0.94	0.95	0.95	0.95	0.94	0.95	183	11	181	9	0.89	0.88	0.99	1.00
10	0.96	0.96	0.96	0.96	0.96	0.96	0.96	185	7	185	7	0.94	0.94	0.98	0.98
μ	0.96	0.97	0.94	0.96	0.95	0.97	0.96	181	6	186	11	0.93	0.90	0.99	0.98
σ	0.01	0.02	0.02	0.01	0.02	0.03	0.01	3.98	4.69	4.69	3.98	0.06	0.04	0.01	0.01

Table A2. Performance metrics across 10 runs for water content (W.C.) conditions in Experiment 2: 80% (MTX at 2%), 60% (MTX at 4%), and 40% (MTX at 6%). Metrics include: Acc. (accuracy), Prec. (precision), Sens. (sensitivity), F1 (F1-score), Spec. (specificity), TP (true positives), FP (false positives), TN (true negatives), FN (false negatives), EC. (experimental class in the center), CC (control class in the center), ER (experimental class in the ring), and CR (control class in the ring). For the center and ring areas the metric shown is precision. Mean values are shown in the last row of each subtable.

(a) Performance metrics for Experimental class: W.C. at 40%															
Run	Acc.	Experimental			Control			TP	Conf. Matrix			Center		Ring	
		Prec.	Sens.	F1	Prec.	Spec.	F1		FP	TN	FN	EC	CC	ER	CR
1	0.84	0.91	0.77	0.83	0.80	0.92	0.86	138	14	166	42	0.85	0.77	0.94	0.82
2	0.76	0.70	0.91	0.79	0.87	0.62	0.72	163	69	111	17	0.63	0.86	0.77	0.87
3	0.89	0.96	0.83	0.89	0.85	0.96	0.90	149	7	173	31	0.95	0.78	0.96	0.90
4	0.81	0.86	0.74	0.80	0.77	0.88	0.82	133	21	159	47	0.87	0.73	0.86	0.80
5	0.93	0.93	0.93	0.93	0.93	0.93	0.93	167	12	168	13	0.86	0.94	0.99	0.92
6	0.91	0.92	0.91	0.91	0.91	0.92	0.91	164	15	165	16	0.85	0.91	0.97	0.91
7	0.89	0.93	0.84	0.88	0.85	0.93	0.89	151	12	168	29	0.93	0.80	0.92	0.89
8	0.93	0.88	0.99	0.93	0.99	0.86	0.92	179	25	155	1	0.79	0.98	0.95	1.00
9	0.83	0.75	0.98	0.85	0.97	0.67	0.79	176	59	121	4	0.76	0.94	0.74	0.99
10	0.83	0.94	0.71	0.81	0.77	0.96	0.85	128	8	172	52	0.94	0.75	0.94	0.78
μ	0.86	0.88	0.86	0.86	0.87	0.87	0.86	155	24	156	25	0.84	0.85	0.90	0.89
σ	0.05	0.08	0.09	0.05	0.07	0.11	0.06	16.91	20.67	20.67	16.91	0.09	0.09	0.08	0.07

(b) Performance metrics for Experimental class: W.C. at 60%															
Run	Acc.	Experimental			Control			TP	Conf. Matrix			Center		Ring	
		Prec.	Sens.	F1	Prec.	Spec.	F1		FP	TN	FN	EC	CC	ER	CR
1	0.91	0.95	0.88	0.91	0.89	0.95	0.92	158	9	171	22	0.93	0.76	0.96	0.99
2	0.86	0.84	0.89	0.87	0.89	0.83	0.86	161	31	149	19	0.77	0.77	0.88	0.97
3	0.97	0.96	0.98	0.97	0.98	0.96	0.97	177	8	172	3	0.91	0.96	0.99	1.00
4	0.96	0.94	0.97	0.96	0.97	0.94	0.95	175	11	169	5	0.92	0.93	0.96	1.00
5	0.86	0.96	0.74	0.84	0.79	0.97	0.87	134	6	174	46	0.88	0.69	1.00	0.86
6	0.88	0.83	0.96	0.89	0.95	0.81	0.87	172	35	145	8	0.76	0.87	0.88	1.00
7	0.86	0.87	0.86	0.86	0.86	0.87	0.87	154	23	157	26	0.94	0.73	0.84	1.00
8	0.93	0.97	0.89	0.93	0.90	0.97	0.93	160	5	175	20	0.93	0.77	0.99	1.00
9	0.93	0.88	0.99	0.93	0.99	0.86	0.92	178	25	155	2	0.86	0.97	0.89	1.00
10	0.96	0.97	0.94	0.96	0.95	0.97	0.96	170	6	174	10	0.94	0.91	0.98	0.97
μ	0.91	0.92	0.91	0.91	0.92	0.91	0.91	164	16	164	16	0.88	0.84	0.94	0.98
σ	0.04	0.05	0.07	0.04	0.06	0.06	0.04	12.83	10.84	10.84	12.83	0.06	0.10	0.05	0.04

Table A2. Cont.

(c) Performance metrics for Experimental class: W.C. at 80%															
Run	Acc.	Experimental			Control			Conf. Matrix				Center		Ring	
		Prec.	Sens.	F1	Prec.	Spec.	F1	TP	FP	TN	FN	EC	CC	ER	CR
1	0.91	0.98	0.84	0.91	0.86	0.98	0.92	152	3	177	28	0.95	0.81	1.00	0.90
2	0.96	0.93	0.98	0.96	0.98	0.93	0.95	177	13	167	3	0.84	0.95	1.00	1.00
3	0.82	0.74	0.99	0.85	0.99	0.64	0.78	179	64	116	1	0.72	0.98	0.74	1.00
4	0.98	0.97	0.99	0.98	0.99	0.97	0.98	178	5	175	2	0.93	0.97	1.00	1.00
5	0.83	0.98	0.68	0.80	0.75	0.98	0.85	122	3	177	58	0.93	0.66	1.00	0.82
6	0.94	0.93	0.95	0.94	0.95	0.93	0.94	171	13	167	9	0.88	0.91	0.96	0.97
7	0.91	0.96	0.85	0.90	0.87	0.97	0.91	153	6	174	27	0.92	0.82	0.99	0.90
8	0.98	0.97	0.99	0.98	0.99	0.97	0.98	179	5	175	1	0.97	0.99	0.97	1.00
9	0.88	0.93	0.83	0.88	0.85	0.94	0.89	149	11	169	31	0.88	0.77	0.96	0.90
10	0.90	0.98	0.81	0.89	0.84	0.98	0.91	146	3	177	34	0.95	0.78	1.00	0.88
μ	0.91	0.94	0.89	0.91	0.91	0.93	0.91	161	13	167	19	0.90	0.87	0.96	0.94
σ	0.05	0.07	0.10	0.06	0.08	0.10	0.06	18.24	17.55	17.55	18.24	0.07	0.10	0.07	0.06

Table A3. Detailed classification results for the majority-vote analysis. The table reports the results obtained with a 70% voting threshold (14 of 20 localized patches) as an illustrative example. Complete droplet classification was obtained by combining the predictions of the 20 localized patches associated with each droplet. Performance metrics are reported for each of the 10 independent runs. TP, FP, TN, and FN correspond to the numbers of complete droplets classified as true positives, false positives, true negatives, and false negatives, respectively.

(a) Majority-vote analysis for Experimental class: W.C. at 40%												
Run	Acc.	Experimental			Control			Conf. Matrix				
		Prec.	Sens.	F1	Prec.	Spec.	F1	TP	FP	TN	FN	
1	0.944	0.900	1.000	0.947	1.000	0.889	0.941	9	1	8	0	
2	0.722	0.833	0.556	0.667	0.667	0.889	0.762	5	1	8	4	
3	0.889	0.818	1.000	0.900	1.000	0.778	0.875	9	2	7	0	
4	0.889	0.818	1.000	0.900	1.000	0.778	0.875	9	2	7	0	
5	1.000	1.000	1.000	1.000	1.000	1.000	1.000	9	0	9	0	
6	0.944	0.900	1.000	0.947	1.000	0.889	0.941	9	1	8	0	
7	0.944	0.900	1.000	0.947	1.000	0.889	0.941	9	1	8	0	
8	1.000	1.000	1.000	1.000	1.000	1.000	1.000	9	0	9	0	
9	0.833	1.000	0.667	0.800	0.750	1.000	0.857	6	0	9	3	
10	0.833	0.750	1.000	0.857	1.000	0.667	0.800	9	3	6	0	
μ	0.900	0.892	0.922	0.897	0.942	0.878	0.899	8.3	1.1	7.9	0.7	
σ	0.086	0.088	0.166	0.102	0.125	0.110	0.080	1.494	0.994	0.994	1.494	

(b) Majority-vote analysis for Experimental class: W.C. at 60%												
Run	Acc.	Experimental			Control			Conf. Matrix				
		Prec.	Sens.	F1	Prec.	Spec.	F1	TP	FP	TN	FN	
1	0.944	0.900	1.000	0.947	1.000	0.889	0.941	9	1	8	0	
2	0.778	0.857	0.667	0.750	0.727	0.889	0.800	6	1	8	3	
3	1.000	1.000	1.000	1.000	1.000	1.000	1.000	9	0	9	0	
4	1.000	1.000	1.000	1.000	1.000	1.000	1.000	9	0	9	0	
5	0.833	0.750	1.000	0.857	1.000	0.667	0.800	9	3	6	0	
6	0.889	1.000	0.778	0.875	0.818	1.000	0.900	7	0	9	2	
7	0.778	0.727	0.889	0.800	0.857	0.667	0.750	8	3	6	1	
8	0.944	0.900	1.000	0.947	1.000	0.889	0.941	9	1	8	0	
9	0.944	1.000	0.889	0.941	0.900	1.000	0.947	8	0	9	1	
10	1.000	1.000	1.000	1.000	1.000	1.000	1.000	9	0	9	0	
μ	0.911	0.913	0.922	0.912	0.930	0.900	0.908	8.3	0.9	8.1	0.7	
σ	0.088	0.107	0.118	0.088	0.100	0.133	0.093	1.059	1.197	1.197	1.059	

Table A3. Cont.

(c) Majority-vote analysis for Experimental class: W.C. at 80%											
Run	Acc.	Prec.	Experimental Sens.	F1	Prec.	Control Spec.	F1	TP	Conf. Matrix FP	TN	FN
1	0.944	0.900	1.000	0.947	1.000	0.889	0.941	9	1	8	0
2	1.000	1.000	1.000	1.000	1.000	1.000	1.000	9	0	9	0
3	0.722	1.000	0.444	0.615	0.643	1.000	0.783	4	0	9	5
4	1.000	1.000	1.000	1.000	1.000	1.000	1.000	9	0	9	0
5	0.833	0.750	1.000	0.857	1.000	0.667	0.800	9	3	6	0
6	1.000	1.000	1.000	1.000	1.000	1.000	1.000	9	0	9	0
7	0.944	1.000	0.889	0.941	0.900	1.000	0.947	8	0	9	1
8	1.000	1.000	1.000	1.000	1.000	1.000	1.000	9	0	9	0
9	0.941	0.889	1.000	0.941	1.000	0.889	0.941	8	1	8	0
10	0.889	0.889	0.889	0.889	0.889	0.889	0.889	8	1	8	1
μ	0.927	0.943	0.922	0.919	0.943	0.933	0.930	8.2	0.6	8.4	0.7
σ	0.091	0.085	0.174	0.118	0.114	0.107	0.082	1.549	0.966	0.966	1.567

References

- Carou-Senra, P.; Rodríguez-Pombo, L.; Awad, A.; Basit, A.W.; Alvarez-Lorenzo, C.; Goyanes, A. Inkjet Printing of Pharmaceuticals. *Adv. Mater.* **2024**, *36*, 2309164.
- Mau, R.; Seitz, H. Influence of the volatility of solvent on the reproducibility of droplet formation in pharmaceutical inkjet printing. *Pharmaceutics* **2023**, *15*, 367. [\[CrossRef\]](#) [\[PubMed\]](#)
- Daly, R.; Harrington, T.S.; Martin, G.D.; Hutchings, I.M. Inkjet printing for pharmaceuticals—a review of research and manufacturing. *Int. J. Pharm.* **2015**, *494*, 554–567. [\[CrossRef\]](#) [\[PubMed\]](#)
- Guyll, B.I.; Sanford, B.L.; Pint, C.L.; Secor, E.B. Controlling droplet evaporation in aerosol jet printing to understand and mitigate overspray. *Small Sci.* **2025**, *5*, 2500069. [\[CrossRef\]](#) [\[PubMed\]](#)
- Carreón, Y.J.; Díaz-Hernández, O.; Santos, G.J.E.; Cipriano-Urbano, I.; Solorio-Ordaz, F.J.; González-Gutiérrez, J.; Zenit, R. Texture analysis of dried droplets for the quality control of medicines. *Sensors* **2021**, *21*, 4048. [\[CrossRef\]](#) [\[PubMed\]](#)
- Deegan, R.; Bakajin, O.; Dupont, T.; Huber, G.; Nagel, S.; Witten, T. Capillary flow as the cause of ring stains from dried liquid drops. *Nature* **1997**, *389*, 827–829. [\[CrossRef\]](#)
- Sefiane, K. Patterns from drying drops. *Adv. Colloid Interface Sci.* **2014**, *206*, 372–381. [\[CrossRef\]](#) [\[PubMed\]](#)
- Parsa, M.; Harmand, S.; Sefiane, K. Mechanisms of pattern formation from dried sessile drops. *Adv. Colloid Interface Sci.* **2018**, *254*, 22–47. [\[CrossRef\]](#) [\[PubMed\]](#)
- Sadek, C.; Schuck, P.; Fallourd, Y.; Pradeau, N.; Floch-Fouere, C.L.; Jeantet, R. Drying of a single droplet to investigate process–structure–function relationships: A review. *Dairy Sci. Technol.* **2015**, *95*, 771–794.
- Pal, A.; Gope, A. Texture identification in liquid crystal-protein droplets using evaporative drying, generalized additive modeling, and K-means Clustering. *Eur. Phys. J. E* **2024**, *47*, 35. [\[CrossRef\]](#) [\[PubMed\]](#)
- Cronstein, B.N. The mechanism of action of methotrexate. *Rheum. Dis. Clin. N. Am.* **1997**, *23*, 739–755. [\[CrossRef\]](#)
- Friedman, B.; Cronstein, B. Methotrexate mechanism in treatment of rheumatoid arthritis. *Jt. Bone Spine* **2019**, *86*, 301–307. [\[CrossRef\]](#)
- Molina-Courtois, J.N.; Hidalgo, R.B.P.; Carreón, Y.J.P.; Martínez-Miwa, C.A.; Jiménez, L.D.; Castelán, M.; González-Gutiérrez, J. Stabilization of drug droplet contact line via Bovine Serum Albumin Solution-Phase Additive. *Eur. J. Mech./B Fluids* **2025**, *115*, 204385. [\[CrossRef\]](#)
- Acuña, C.; Kokornaczyk, M.O.; Baumgartner, S.; Castelán, M. Unsupervised Deep Learning Approach for Characterizing Fractality in Dried Drop Patterns of Differently Mixed Viscum album Preparations. *Fractal Fract.* **2023**, *7*, 733. [\[CrossRef\]](#)
- Pal, A.; Yanagisawa, M. Pattern recognition of drying lysozyme–glucose droplets using machine learning classifiers. *Phys. A Stat. Mech. Its Appl.* **2024**, *654*, 130141. [\[CrossRef\]](#)
- Li, X.; Sanderson, A.R.; Allen, S.S.; Lahr, R.H. Tap water fingerprinting using a convolutional neural network built from images of the coffee-ring effect. *Analyst* **2020**, *145*, 1511–1523. [\[CrossRef\]](#) [\[PubMed\]](#)
- Vaez, S.; Dadfar, B.; Koenig, M.; Franzreb, M.; Lahann, J. Deep Learning-Based Classification of Histone–DNA Interactions Using Drying Droplet Patterns. *Small Sci.* **2024**, *4*, 2400252. [\[CrossRef\]](#) [\[PubMed\]](#)
- Mamgain, A.; Kumar, V.; Dash, S. Image-based detection of adulterants in milk using convolutional neural network. *ACS Omega* **2024**, *9*, 27158–27168. [\[CrossRef\]](#) [\[PubMed\]](#)

19. Molina-Courtois, J.N.; Morales, Y.J.A.; Escalante-Zarate, L.; Castelán, M.; Carreón, Y.J.P.; González-Gutiérrez, J. Pattern Recognition in Dried Milk Droplets Using Lacunarity and Deep Learning. *Appl. Sci.* **2025**, *15*, 5676. [[CrossRef](#)]
20. Demir, R.; Koc, S.; Ozturk, D.G.; Bilir, S.; Ozata, H.; Williams, R.; Christy, J.R.E.; Akkoc, Y.; Tinay, İ.; Gunduz-Demir, C.; et al. Artificial intelligence assisted patient blood and urine droplet pattern analysis for non-invasive and accurate diagnosis of bladder cancer. *Sci. Rep.* **2024**, *14*, 2488. [[CrossRef](#)] [[PubMed](#)]
21. Caspin, N.; Mindlina, O.; Sharon, U.H.; Sharpe, G.R.; Gridin, V.V.; Manevich, M.; Schechter, I. A new method for quantitation of cyanuric acid in water based on image analysis of drying patterns using computer vision. *Anal. Methods* **2026**, *18*, 2078. [[CrossRef](#)] [[PubMed](#)]
22. Hamadeh, L.; Imran, S.; Bencsik, M.; Sharpe, G.R.; Johnson, M.A.; Fairhurst, D.J. Machine learning analysis for quantitative discrimination of dried blood droplets. *Sci. Rep.* **2020**, *10*, 3313. [[CrossRef](#)] [[PubMed](#)]

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