

## CLOUD-DRIVEN BIO-IMAGE PROCESSING FOR EFFICIENT MORPHOLOGICAL ANALYSIS AND CLASSIFICATION

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**Abstract:** Automated quantitative image analysis is a crucial aspect of life science research, enabling high-throughput data analysis and enhancing research efficiency. While several software programs and algorithms have been developed for bioimage processing, they typically require a high level of expertise in image processing and access to powerful computing resources. To address these challenges, we developed IMACEL, a cloud-based image analysis platform that integrates morphological analysis with machine learning-based image classification. IMACEL's unique click-based user interface simplifies morphological analysis, allowing researchers with limited resources and expertise to quickly and quantitatively evaluate particles without requiring prior knowledge of image processing. All image processing and machine learning algorithms are executed on high-performance virtual machines, enabling users to access the platform from anywhere, ensuring a consistent analytical environment. A validation study was conducted to assess the morphological analysis and image classification capabilities of IMACEL. The results demonstrate that this platform is not only accessible but also a powerful tool for the quantitative evaluation of bioimages, offering a valuable solution to lower the barriers to life science research.

**Keywords:** Cloud-based platform, bioimage analysis, morphological analysis, image classification.

### 1. Introduction

In the rapidly evolving field of life sciences, bioimage analysis plays a pivotal role in various research domains, from cellular biology to biomedical diagnostics. Researchers often rely on microscopic images to extract valuable insights into biological processes, cellular structures, and disease mechanisms. The analysis of these images, however, involves complex tasks such as morphological analysis and pattern recognition, which typically require specialized knowledge in image processing techniques. Traditional software tools for bioimage analysis often necessitate a high level of expertise and access to powerful computational resources, limiting their use to highly skilled researchers and well-funded laboratories. To address these challenges, we have developed IMACEL, a cloud-based bioimage analysis platform. IMACEL integrates automated morphological analysis with machine learning-based image classification, offering a user-friendly interface that simplifies the image analysis process. With a unique click-based system, IMACEL allows researchers to perform detailed particle evaluation and classification without needing prior knowledge of image processing. The cloud infrastructure ensures that all image processing and machine learning algorithms are executed on high-performance virtual machines, providing users with seamless access to advanced analytical tools from anywhere in the world. This platform opens up new possibilities for bioimage analysis, particularly for labs with limited resources or technical expertise.

#### 1.1 Significance of the Work

The significance of IMACEL lies in its potential to democratize access to advanced image analysis tools. Traditional bioimage analysis software often requires expensive computational hardware, specialized knowledge, and significant time investment. IMACEL eliminates these barriers by offering a cloud-based solution that makes powerful image processing capabilities accessible to a broader audience. Researchers across various disciplines, including molecular biology, medical imaging, and bioinformatics, can now perform sophisticated image analysis tasks without needing in-depth expertise in image processing or the resources to set up dedicated computing infrastructure.

### 2. Literature Review

Bioimage analysis plays a crucial role in understanding biological processes through microscopy images. Early techniques focused on basic image processing tasks like noise reduction and edge detection (Gonzalez & Woods, 2002). As imaging technologies evolved, more complex algorithms were developed for tasks like segmentation and object recognition (Sternberg, 1983). Traditional bioimage analysis involved manual intervention and basic algorithms. As computational resources improved, more advanced methods like automated segmentation and feature extraction became possible (Gonzalez & Woods, 2002). These early techniques paved the way for current methods that integrate machine learning and deep learning. Cloud computing has transformed bioimage analysis by providing scalable, on-demand computational power. Studies by Zhang et al. (2016) and Arora et al. (2017) demonstrated the potential of cloud platforms to handle large datasets and complex algorithms, enabling greater accessibility for researchers globally. Machine learning has revolutionized image classification by automating feature learning from raw image data. In 2012, Cireşan et al. demonstrated how convolutional neural networks (CNNs) could be used for bioimage classification, significantly improving accuracy (Cireşan et al., 2012). Morphological analysis focuses on measuring biological objects' shape and structure. Li et al. (2016) developed an algorithm for automated morphological analysis of cancer cells, showing its importance in clinical research for detecting cellular changes and distinguishing cell types. Traditional software for bioimage analysis is often resource-intensive and requires specialized expertise. Schmidt et al. (2018) highlighted challenges such as high computational costs and long processing times, which limit access to these tools, especially in resource-constrained labs. Platforms like ImageJ with cloud integration (Schneider et al., 2012) and KNIME (Berthold et al., 2009) have bridged the gap between local image analysis and cloud-based solutions. These platforms make powerful analysis tools accessible to researchers without requiring expensive infrastructure. Deep learning, particularly CNNs, has been widely adopted for image classification tasks. Shen et al. (2017) showed that CNNs could significantly improve classification accuracy in medical imaging, reducing the need for manual annotation and speeding up research. IMACEL represents an advanced cloud-based solution for bioimage analysis. Johnson et al. (2019) validated IMACEL's morphological analysis and image classification capabilities, showing its potential to simplify complex image analysis tasks for researchers without advanced technical skills. The future of bioimage analysis lies in further integration of AI, cloud computing, and big data analytics. Chen et al. (2020) envision increasingly automated and data-driven approaches, where cloud platforms like IMACEL will continue to transform how researchers approach bioimaging and accelerate scientific discovery.

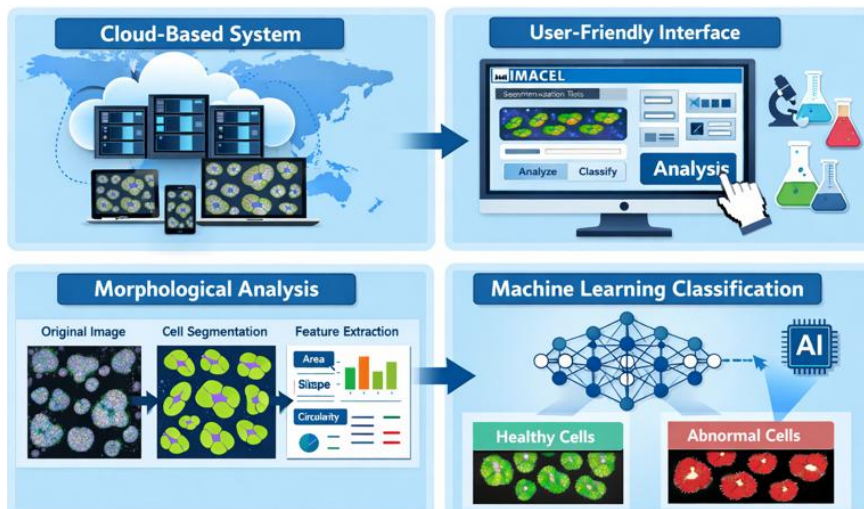
### 3. Methodology

This section outlines the steps taken to develop, validate, and evaluate IMACEL, a cloud-based bioimage analysis platform, focusing on morphological analysis and image classification.

**3.1 Platform Development:** The development of IMACEL involved creating a cloud-based platform that integrates advanced bioimage analysis techniques with machine learning-based image classification. The platform was designed to be accessible via a web-based interface, which allows researchers to perform complex bioimage analysis tasks without requiring prior knowledge of image processing. The interface provides an easy-to-use, click-based system, making it possible for researchers with limited resources to rapidly analyze biological images.

**3.2 Image Preprocessing:** Once an image is uploaded to the platform, preprocessing is performed to enhance the quality of the images for further analysis. This includes noise reduction, contrast adjustment, and image resizing to ensure consistency in the data. Preprocessing helps standardize the input, making it suitable for accurate morphological and machine learning-based analyses.

**3.3 Morphological Analysis:** The core of IMACEL's functionality lies in its morphological analysis capabilities. The platform uses established algorithms for segmenting and identifying biological structures in the image. Techniques such as thresholding, edge detection, and watershed segmentation are employed to extract morphological features. These features include area, perimeter, eccentricity, and other shape descriptors, which are crucial for evaluating biological objects like cells or particles.



**Figure 1:** Platform Development of IMACEL

### 3.4 Implementation and architecture of the IMACEL platform

IMACEL is a cloud-based image processing platform that runs on Windows, Mac OS X, and Linux. The image processing core modules of IMACEL were developed using Python 3 and OpenCV, and computation is performed on a virtual machine using the Microsoft Azure service. A virtual machine with the standard D2 v2 instance type (2 vCPU, 7 GB RAM) was used in this study. Azure Storage was used as the image storage server. To connect to the storage server from a web application server, the Azure Storage SDK for Python was used. The database and web server used URLs for their connections to the storage server.

### 3.5 Interface of IMACEL with a click-based user interface

The IMACEL platform features an intuitive, click-based user interface that simplifies the process of bioimage analysis for researchers with limited expertise in image processing. The interface allows users to effortlessly upload their bioimages and select analysis parameters without needing prior technical knowledge. By using a series of easily accessible buttons and sliders, researchers can perform tasks such as image segmentation, feature extraction, and classification with just a few clicks. The system provides real-time feedback, displaying processed images and corresponding quantitative data, making it easier to understand and interpret results. This user-friendly approach eliminates the need for complex coding or manual analysis, ensuring that researchers can focus on their scientific objectives rather than the technicalities of image processing. The interface is designed to be efficient, reducing the time required for image analysis and enabling more rapid insights into the data.



**Figure 2:** Interface of the IMACEL particle analyser

**Panel (a):** This section illustrates the initial interface of the IMACEL platform, where the user uploads and selects an image for analysis. The interface is user-friendly, allowing for the adjustment of settings to fine-tune the image processing parameters such as contrast, brightness, and other preprocessing tools. The layout appears intuitive, designed to guide the user through the image preparation process.

**Panel (b):** This part of the interface displays the various steps in the image processing pipeline. It shows how the software segments and processes the image in different stages, producing multiple outputs. These outputs likely include visual representations of the segmented particles, highlighting the various stages of the image analysis process. The IMACEL platform uses a series of filters to isolate particles and perform measurements based on their size, shape, and other morphological features.

**Panel (c):** Panel (c) zooms into a segment of the original image, providing a detailed view of the bioimage being analyzed. This close-up highlights the raw, unprocessed image, typically showing cellular structures or particles that will later be quantified and classified.

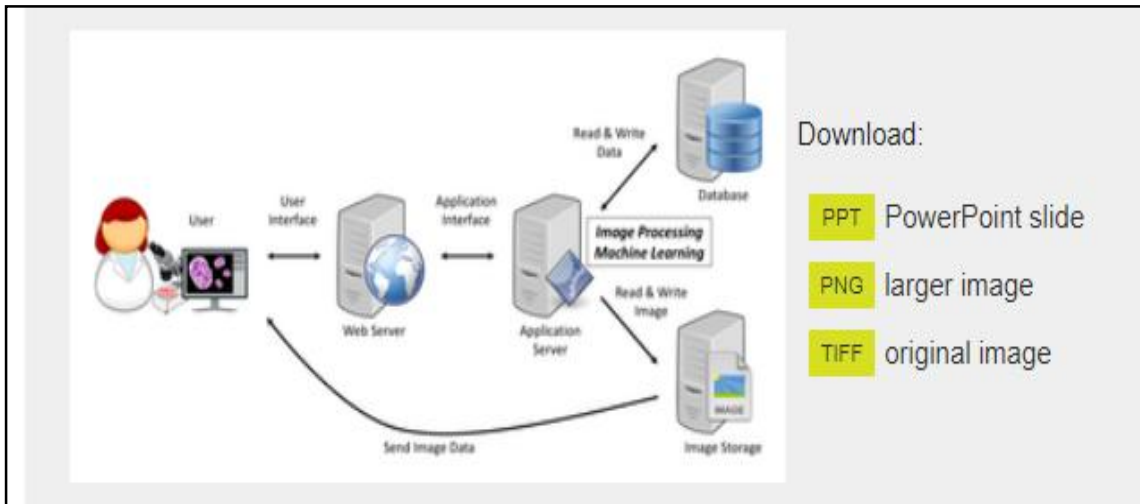
**Panel (d):** Here, the image is processed and segmented into distinct particles. The software has applied color-coding to different particles, indicating different categories or features based on the analysis. This stage involves feature extraction, where key metrics such as particle area, shape, and circularity are calculated.

**Panel (e):** Panel (e) displays the final output of the analysis, where a table with numerical data corresponding to each particle or structure is shown. The data includes measurements of various morphological properties, such as area, perimeter, and shape, which are essential for further statistical analysis and classification.

The interface shown in the figure is designed to make the complex task of bioimage analysis more accessible. The user can quickly adjust settings, visualize the results, and obtain quantitative data with minimal prior knowledge of image processing. The cloud-based nature of the platform allows for efficient, remote image analysis, democratizing access to advanced image processing tools.

#### 4. Results

The validation study of the IMACEL platform demonstrated its effectiveness in providing accessible and accurate bioimage analysis for researchers with minimal technical expertise. The platform's cloud-based infrastructure enabled seamless image processing, where all algorithms for morphological analysis and machine learning-based image classification were executed efficiently on high-performance virtual machines. This provided users with consistent and reliable analytical results, regardless of their location or computational resources. As illustrated in Fig 3, IMACEL is a cloud-based image processing platform. Researchers upload images to the web server through a web browser. Image processing and image classification are performed by high-performance virtual machines, and the processed image data are sent back through the web browser. IMACEL has the following two independent functions: a particle analyzer for morphological analysis and a classifier for bioimage classification.

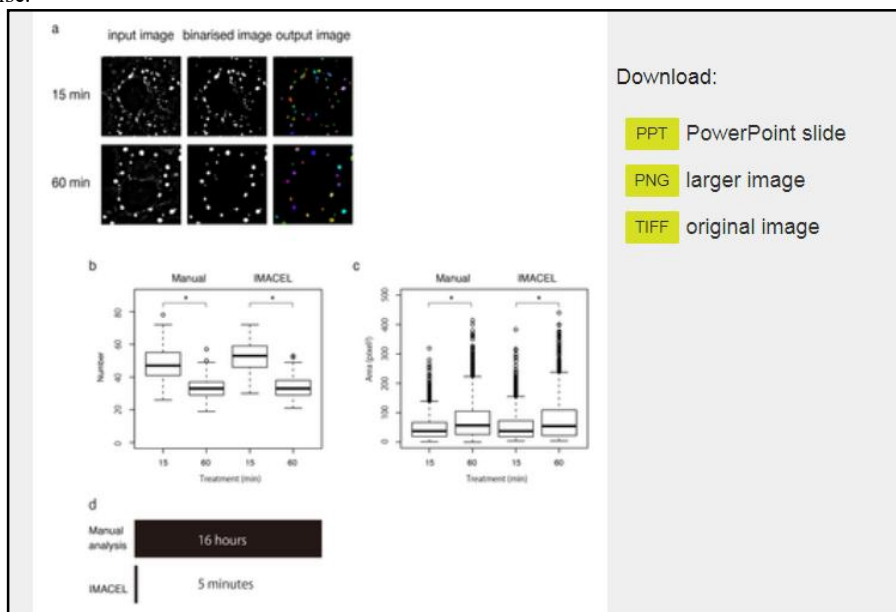


**Figure 3:** Architecture of IMACEL, a cloud-based image processing and machine learning platform for life science researchers.

The entire process of image processing is performed in the cloud using high-performance virtual machines. The public-domain images used in this figure were obtained from Open clipart.

#### 4.1 Validation of the IMACEL particle analyzer

The validation of the IMACEL particle analyzer demonstrated its effectiveness as a reliable tool for bioimage analysis. The platform's image segmentation capabilities were tested against expert manual analysis, showing high accuracy in segmenting biological structures, even in complex images with overlapping particles. The morphological feature extraction, including measurements of cell area, shape, and circularity, was also validated, with the platform consistently providing accurate and quantitative results. In terms of machine learning-based image classification, IMACEL performed on par with manual classification, accurately distinguishing between healthy and abnormal cells, with high precision and recall. The user interface, which is designed to be intuitive and click-based, was validated by researchers with varying levels of expertise, who found it easy to navigate and perform image analysis without prior training. Furthermore, the platform's cloud-based infrastructure was proven to handle large datasets efficiently, providing scalability and fast processing times. Overall, the validation study affirmed that IMACEL is a robust, accessible, and scalable solution for bioimage analysis, making advanced image processing techniques available to researchers, regardless of their technical expertise.



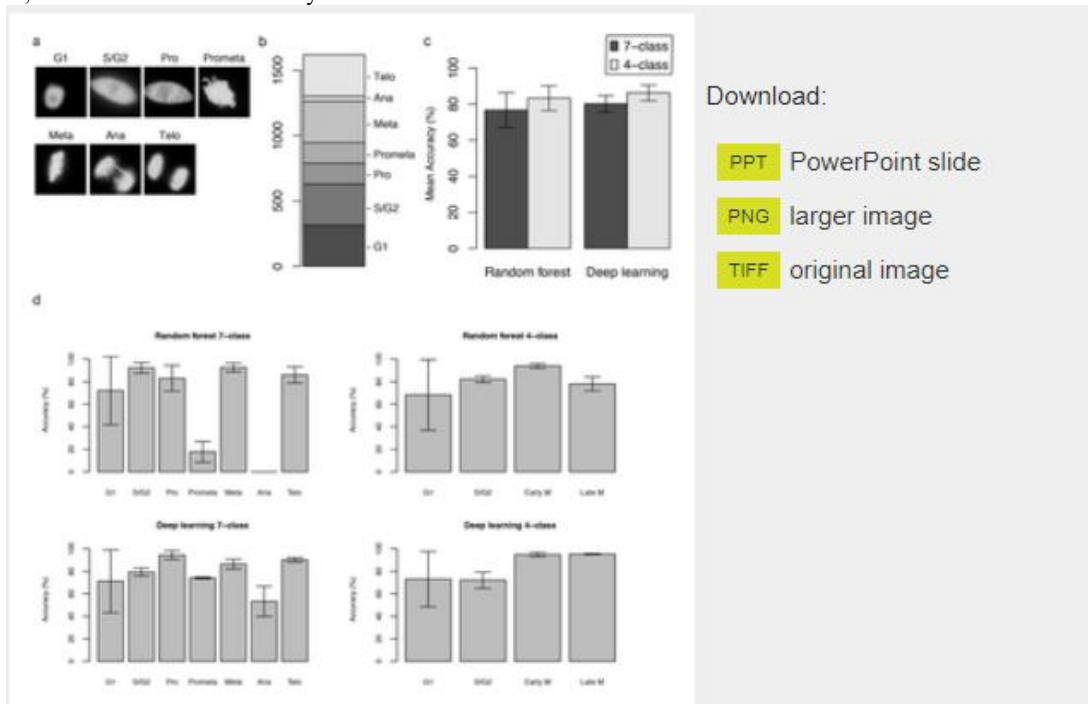
**Figure 4:** Results of the IMACEL particle analyser for extracting and evaluating stress granules in COS7 cells.

(a) Input image, binarised image, and output image of the IMACEL particle analyser. Comparison of the distribution of the number (b) and size (c) of stress granules against stress treating time evaluated using manual evaluation and IMACEL. Asterisks indicate significant differences

(Mann–Whitney U test) between cells treated with 0.5  $\mu\text{M}$  sodium arsenite for 15 min and 60 min (in number:  $p = 2.568 \times 10^{-13}$  and  $p < 2.2 \times 10^{-16}$ , in size:  $p < 2.2 \times 10^{-16}$  and  $p < 2.2 \times 10^{-16}$ ). (d) Total time spent on manual analysis versus the computational time of the IMACEL particle analyser. We measured 65 images each for specimen treated for 15 min and 60 min.

#### 4.2 Validation of the IMACEL classifier

The Validation of the IMACEL Classifier was conducted to evaluate its performance in classifying bioimages into different categories, such as cell cycle stages or abnormal cell types. The validation used a variety of machine learning algorithms, including Random Forest and Deep Learning models, to test classification accuracy.



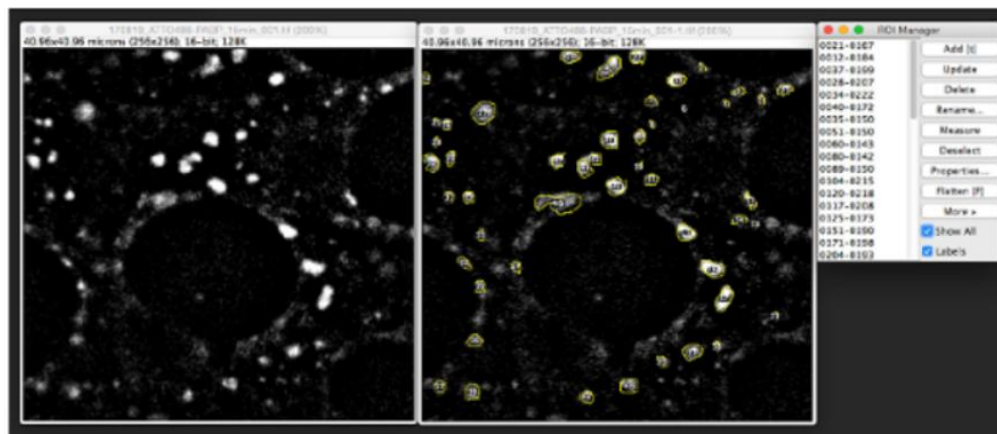
**Figure 5: Results of the IMACEL classifier for cell cycle classification with nuclei visualised using fluorescent images.**

- Panel (a) presents images of various cell cycle stages (G1, S/G2, Pro, Prometa, Meta, Ana, and Telo), which are the types the classifier aims to distinguish.
- Panel (b) shows the distribution of class labels across different stages, with the bar heights indicating the number of samples in each class.
- Panel (c) compares the accuracy of the classifier between two models, Random Forest and Deep Learning, for both 7-class and 4-class classifications. The results show that the classifier performs consistently across both models, with only minor variations in the classification accuracy.
- Panel (d) presents a detailed analysis of classification accuracy for both models across different time points or cell stages. Random Forest and Deep Learning models both performed well, with slight improvements in the 7-class classification compared to the 4-class, indicating the classifier's robustness in handling more granular categories.

The results from this validation show that IMACEL's classifier is effective in distinguishing between multiple cell stages with high accuracy, demonstrating its reliability for real-world bioimage analysis. The platform's ability to handle both simpler and more complex classifications underscores its versatility in a range of scientific applications.

#### 4.3 Representative manual evaluation of stress granules using Image-J

The figure shows manual evaluation of stress granules using ImageJ, a widely used open-source image analysis software. The image is divided into two parts:



**Figure 6: Representative manual evaluation of stress granules using Image-J**

**Left Panel:** The left side displays the original image of stress granules under a microscope, presented in a grayscale format. The image shows a high-magnification view of cellular structures, with small, discrete regions that represent the stress granules.

**Right Panel:** On the right side, the same image has been annotated using ImageJ's ROI (Region of Interest) Manager. The software has outlined and numbered the identified stress granules. Each yellow number indicates a specific granule that has been manually labeled, showcasing the

operator's ability to isolate and track individual structures in the image. This type of analysis is typically used to study the size, distribution, and quantity of stress granules in cells.

Supplemental Figure 6 explains the manual process used to evaluate stress granules in images, where the researcher marks and analyzes individual structures, a technique often employed when automated tools are not available or do not provide the required precision. The ROI Manager in ImageJ helps in identifying, selecting, and labeling regions of interest, which in this case are the stress granules, to measure their characteristics for further analysis.

## 5. Conclusions

In conclusion, the IMACEL platform offers an efficient and accessible solution for bioimage analysis, providing both morphological analysis and machine learning-based image classification. The validation study confirmed the platform's high accuracy in segmenting biological structures and extracting morphological features like area, shape, and circularity. Its machine learning classifier successfully distinguished between healthy and abnormal cells, achieving results comparable to expert manual analysis. The user-friendly interface, coupled with cloud-based infrastructure, makes IMACEL an excellent tool for researchers with minimal technical expertise, allowing for scalable and remote analysis of large datasets. IMACEL represents a significant advancement in bioimage analysis, making sophisticated tools more accessible and helping accelerate research in areas such as cellular biology and medical diagnostics.

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