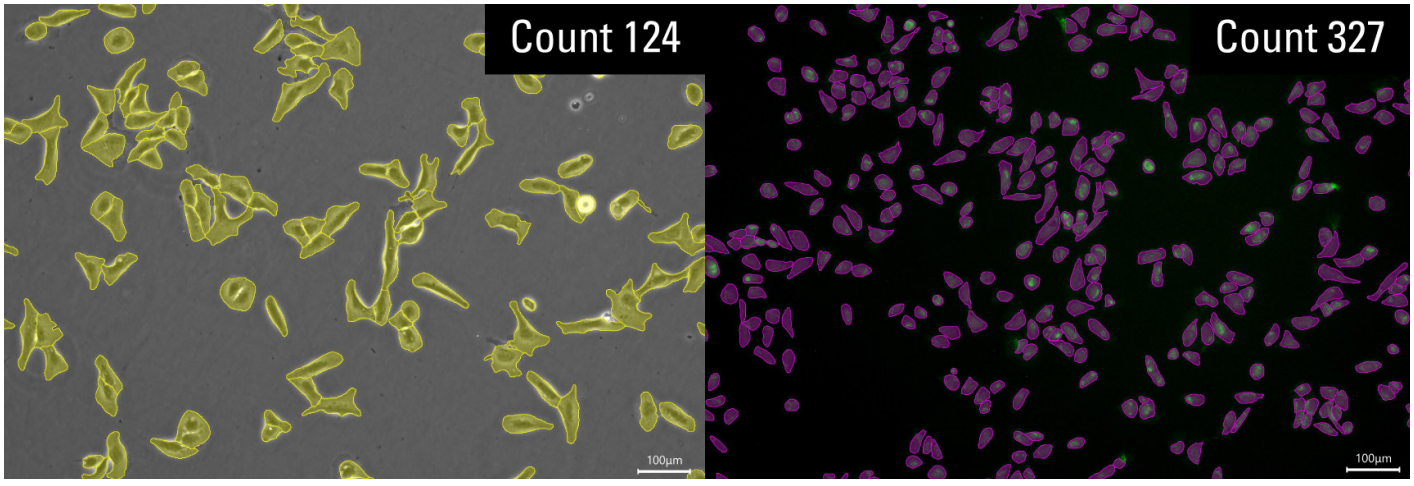
From Eye to Insight

Leica MICROSYSTEMS

PRECISION AND EFFICIENCY WITH AI-ENHANCED CELL COUNTING

Leverage AI to get an accurate cell count in just a few seconds



AI-based cell counting performed with a phase-contrast and fluorescence image using the Mateo FL microscope.

Authors

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Introduction

Accurate cell counting is very important for research with 2D cell cultures, playing a pivotal role in understanding cellular dynamics, drug discovery, and disease modeling [1-3]. In 2D cell cultures, where cells adhere to flat surfaces such as petri dishes (refer to Fig.1), precision in cell counting is indispensable for determining cell viability, proliferation rates, and evaluating the effects of experimental conditions. Reliable cell counts are essential in maintaining experimental reproducibility and ensuring the robustness of results, forming the cornerstone of advancements in fields ranging from cancer research to regenerative medicine.

This application note delves into the transformative integration of artificial intelligence (AI) in the domain of 2D cell culture, specifically focusing on the paramount importance of precision and efficiency in cell counting. Our objective is to explore and showcase how AI technologies can significantly enhance the accuracy and speed of cell counting processes, reshaping the landscape of cellular research.

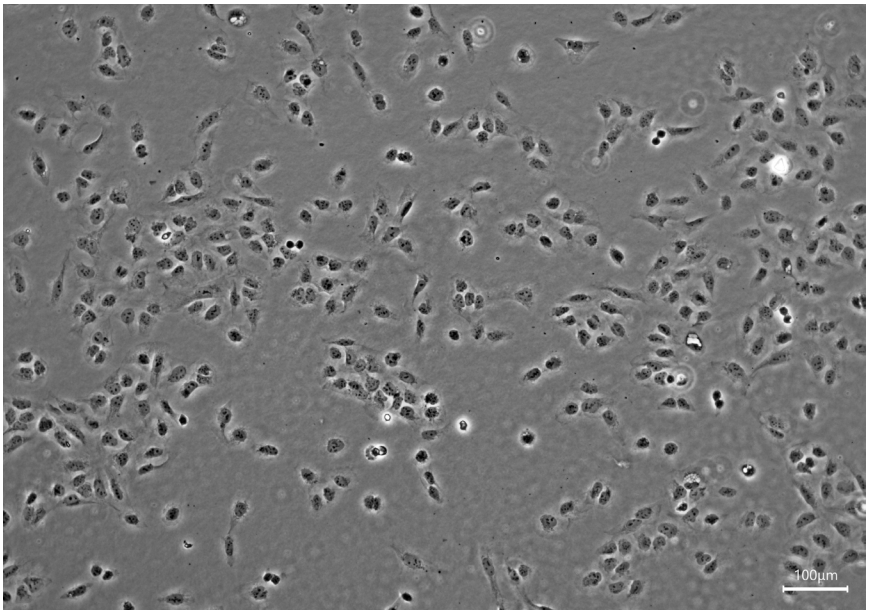


Fig. 1: Microscope image of a cell culture which is used for manually counting the number of cells.

Challenges with Manual Counting Methods

Despite the critical nature of accurate cell counting, conventional manual counting methods pose several challenges that hinder the progress of research endeavors. Manual counting is labor-intensive, time-consuming, and prone to human error, leading to inconsistencies and variations in results. The subjectivity inherent in manual counting further complicates data interpretation and can introduce biases. As the demand for high-throughput and reproducibility intensifies, there is an urgent need for technological advancements to overcome the limitations of traditional cell counting approaches.

In response to the limitations of manual counting, researchers are increasingly turning to technology-driven solutions to enhance the precision and efficiency of cell counting in 2D cell cultures. The rise of artificial intelligence presents a paradigm shift in this regard, offering the potential to streamline the cell counting process, reduce human error, and provide a level of accuracy and efficiency unattainable through manual methods alone.

Methodology

> AI-based Cell Counting Approach:
The foundation of our AI methodology lies in an advanced cell-counting approach, leveraging state-of-the-art image analysis algorithms. They go beyond conventional methods, incorporating deep learning techniques to continually enhance accuracy.

> Image Analysis Algorithms:
Central to our methodology are specialized image analysis algorithms designed for efficient cell segmentation and counting (refer to Fig. 2). These algorithms play a pivotal role in overcoming challenges inherent in traditional counting methods, offering more accuracy and reliability

> Data Preprocessing:
A crucial step in our AI methodology is meticulous data preprocessing to ensure optimal input for the AI model. It involves employing techniques for noise reduction and data enhancement, refining the raw data into a format conducive to accurate cell counting.

> Deep Learning Integration:
Our methodology integrates deep learning models for cell recognition, utilizing pretrained models as a foundation. This approach enables the AI system to swiftly adapt to diverse cell types, demonstrating flexibility and responsiveness.

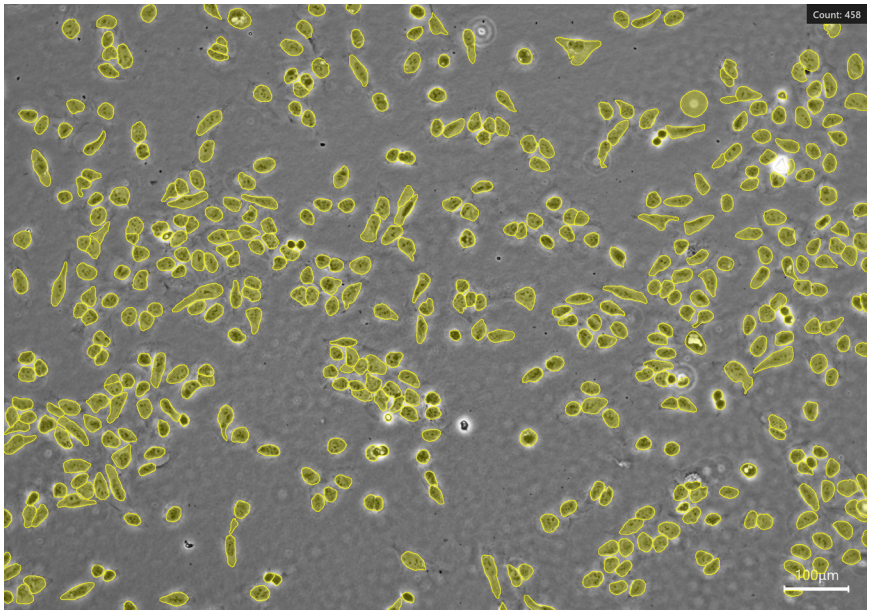


Fig. 2: Microscope image of a cell culture specimen where AI was used to count the number of cells. A cell count of 458 was obtained.

Comparative Analysis Manual vs. AI cell counting

> Accuracy, Precision, and Time Saving
Manual cell counting, while a longstanding practice, is susceptible to human error, variability, and subjectivity. In contrast, the AI-based approach consistently demonstrated heightened accuracy and precision, reducing counting discrepancies significantly, especially with complex cell cultures. Importantly, the time-saving aspect of AI-based counting was quantified through experiments, revealing a remarkable reduction in processing time compared to manual methods.

> Efficiency and Throughput
The efficiency gained with AI-based counting led to significantly reduced processing time compared to manual methods. With automated image analysis and rapid data interpretation, the AI approach substantially increased throughput, allowing researchers to focus on higher-level tasks rather than labor-intensive counting processes.

> Adaptability to Varied Conditions
The adaptability of AI models to diverse experimental conditions and cell types emerged as a standout feature. While manual counting methods may struggle with consistency across different samples, the AI system showcased remarkable versatility and robust performance.

> Consistency and Reproducibility
The comparative analysis highlighted the inherent consistency and reproducibility of AI-based counting. Manual counting, influenced by human subjectivity and fatigue, often exhibits variability between different individuals and sessions. This advantage of AI-based counting is critical for reliable research results.

Results from cell-counting experiments

Cell counting with Mateo FL is as much as 180x faster when compared to manual cell counting (refer to Fig. 3)

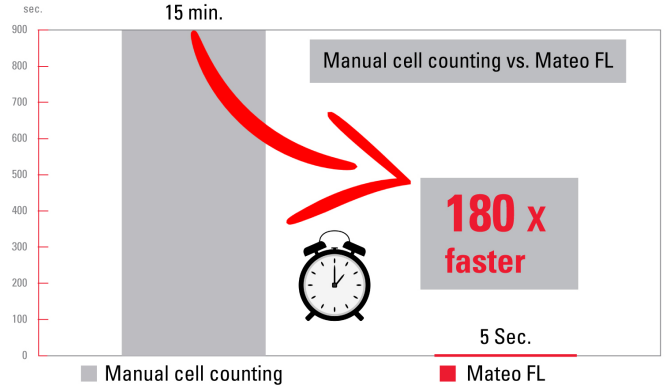


Fig. 3: Cell counting with Mateo FL is completed in 5 secs versus 15 mins for manual counting, thus counting with Mateo FL is 180x faster than by hand.

Comparison of cell counting data with t-test analysis

The cell-count values obtained with Mateo FL using AI and then compared with the ground-truth value are shown in Table 1 below. The comparison was done with percent difference.

Cell count case	Mateo FL	Ground truth	% Difference Mateo FL & ground truth
1	255	259	1.54
2	458	459	0.22
3	302	323	6.5
4	278	291	4.47
5	266	277	3.97

Table 1: Comparison of cell-count values obtained with Mateo FL and ground truth in terms of % difference.

The cell-count value for case 1 obtained with manual counting and then compared with the ground-truth value are shown in Table 2 below. The comparison was done via statistical analysis using a t-test. There is a significant difference between the values for cell counting by hand and ground truth.

Cell count case 1 Tester	Manual	Ground truth	t-test comparison manual & ground truth
A	190	259	t value = -4.53
B	211		Degrees of freedom (df) = 3
C	202		p value = 0.0202
D	240		$p < 0.05$
Average	211		**Significant difference**
Standard error of mean (SEM)	11		

Table 2: t-test comparison of cell-count values obtained manually and ground truth.

All cases for manual cell counting are shown in Table 3 below.

Manual cell counting vs Mateo FL

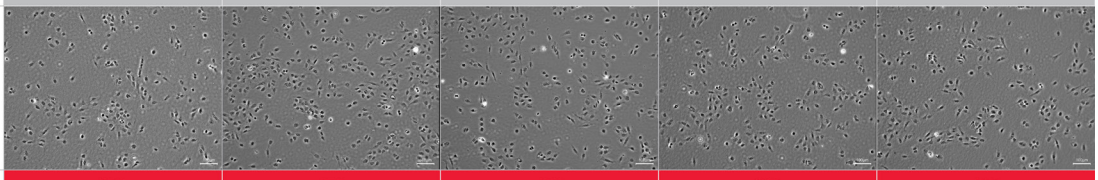
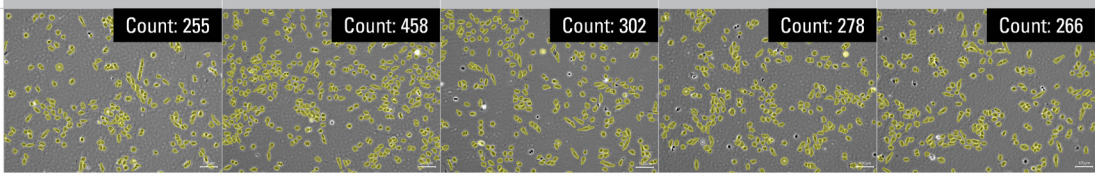
Test round	1	2	3	4	5
Test image					
Ground Truth	**259**	**459**	**323**	**291**	**277**
Tester A	190	230	170	180	170
Tester B	211	308	197	188	200
Tester C	202	300	290	250	220
Tester D	240	416	297	267	278
AI result	**255**	**458**	**302**	**278**	**266**
Gap Tester A vs. AI result (%pt.)	25%	50%	44%	35%	36%
Gap Tester B vs. AI result (%pt.)	17%	33%	35%	32%	25%
Gap Tester C vs. AI result (%pt.)	21%	34%	4%	10%	17%
Gap Tester D vs. AI result (%pt.)	6%	9%	2%	4%	-5%
AI image					

Table 3: Summary of results from manual and AI cell counting which are compared to ground truth values.

Conclusion

For 2D-cell-culture research, the integration of artificial intelligence (AI) for cell counting is a transformative leap forward. The AI-based approach, with its advanced image analysis algorithms and deep learning integration, offers heightened accuracy, precision, and significant time savings compared to manual counting methods. This innovation not only addresses the limitations of traditional approaches, but also enhances efficiency, adaptability, and consistency in cell quantification. The AI methodology's impact extends beyond mere technological advancement - it reshapes the very fabric of cellular research by providing researchers with a reliable, reproducible, and efficient tool. As AI-powered cell counting becomes a cornerstone in 2D cell culture studies, its broader implications promise to propel advancements in drug discovery, disease modeling, and various biotechnological applications, accelerating the pace of scientific discovery in these critical domains.

References

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