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REVIEW

General Super-Resolution Techniques: A Literature Review

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ABSTRACT

Super-resolution (SR) is a technique aimed at improving the resolution of images. In blood cell imaging, it aids in the accurate identification and classification of cells. Improving the analysis process of microscopic images is necessary to achieve better disease diagnoses, especially the image quality, so that health professionals can reach a diagnosis closer to the ideal. For those aiming to implement SR algorithms to analyze microscopic blood cell images, it is crucial to determine which algorithms are in use, their intended purposes, future trends, and current gaps. No review of SR techniques focusing on blood cells was found in the literature. Therefore, this paper presents various techniques to improve the resolution of blood images. Data screening and inclusion followed the PRISMA method. Articles were grouped into four subtopics: generic (25.0%), vascular imaging (28.1%), cell imaging (9.4%), and blood cell imaging techniques (37.5%). Results revealed that more research efforts on cell imaging techniques would be required to achieve a more balanced distribution. This study contributes to knowledge by reviewing the most used techniques, their purposes, and applications, helping researchers find the best technique for their studies, especially for pathological researchers involved in image enhancement.

KEYWORDS

super-resolution (SR), machine learning, neural networks, deep learning, blood cells

1 INTRODUCTION

The scientific literature addresses various needs in the health sector, particularly in the analysis of blood cells using advanced equipment to achieve highly accurate diagnoses. Blood is composed of four main components: red cells, white cells, platelets, and plasma. Red cells, or erythrocytes, are responsible for oxygen transport in the body. White cells, or leukocytes, are essential for the body's defense. The platelets are responsible for acting on blood clotting. Finally, the plasma is the liquid in which the cells are immersed [1–3].

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The correct functioning of blood cells is essential for overall health, making blood testing crucial for diagnosing diseases [2]. However, identifying and classifying cells is an arduous and laborious task. It requires a skilled health professional and several hours of analysis (involving the study, preparation, and observation) by a pathologist, a physician specialized in the study of the human body's fluids.

Specifically, for blood cell analysis, a hematopathologist identifies and classifies each cell, noting any abnormalities that could indicate diseases that may occur [4]. However, a major challenge in this process is the suboptimal image resolution, which complicates the identification and classification of cells [5] (see Figure 1).

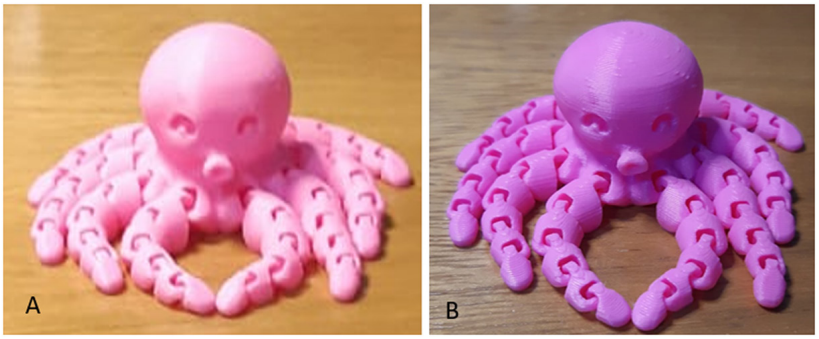

Fig. 1. Images with different resolutions (A has a lower resolution than B)

In this context, laboratories, startups, and other health-related area companies are searching for technologies to develop state-of-the-art systems and equipment (both hardware and software) to improve image resolution and classification, thus enabling more accurate and faster diagnosis. However, the ideal system should offer good value for money, being highly technological yet affordable in terms of acquisition and maintenance [6], [7].

The search for artificial intelligence increased, offering automated work with high precision and short computational time compared to the health professional, therefore lowering costs [8–10]. Therefore, several techniques focus on improving the resolution of microscopic images, known as super-resolution (SR) methods (see Figure 2). For instance, there are generic techniques, such as those using Fourier equations [11], [12]. Other methods stand out for micro vessel images [13] or blood flow [14] and, mainly, methodologies for cells [15], especially in blood cells [16–18].

Fig. 2. Super-resolution generic operation

The most used techniques are convolutional neural networks (CNN) (6), structured illumination microscopy (SIM) (3), and stimulated emission depletion (STED) (3), which will be explained in the section "Literature Analysis and Review" with different applications, however, aimed at improving the image. Microscopic image quality is critical for an accurate diagnosis, making SR techniques essential for enhancement.

The process of developing computer applications will at some point involve learning techniques whose knowledge needs to be acquired. Systematic literature reviews are important for synthesizing available research in a given field. Searches

carried out on the main search engines did not return a comprehensive review of SR techniques applied to the area of blood cells. Therefore, a novice developer may have to lengthen their learning curve. Helping the beginner developer to shorten his/her learning time by focusing on the most promising SR techniques is therefore the motivation behind this work. Therefore, the primary purpose is to help other researchers determine the most appropriate SR technique in blood cell analysis.

This study reviewed SR techniques applied in blood cell imaging, categorizing and comparing them. Articles considered for inclusion must either explain the SR methods or cite their use. The focus is on blood and blood cells, but this work also discusses possible future applications of SR techniques to recent studies.

2 METHODS

The review's theoretical foundation was the PRISMA methodology (see Figure 3), which aimed to address SR techniques in health, especially blood cell analysis.

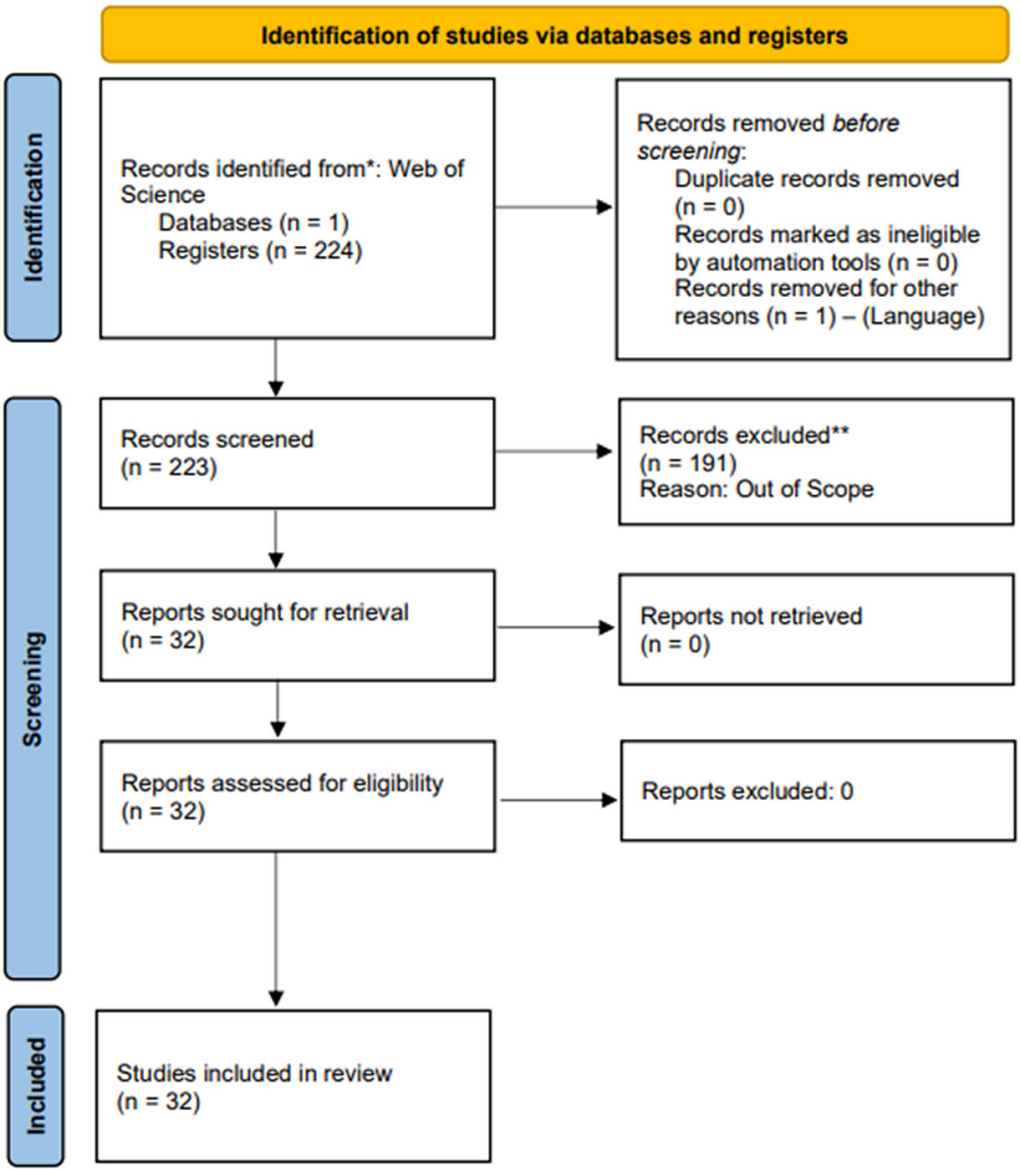

Fig. 3. PRISMA flowchart

Before determining the query terms for the review, the most appropriate, frequent terms for this subject were investigated. Thus, in the Web of Science database, the following query was used: "((“Super Resolu*”) AND (“Blood” OR “Hemo*” OR “Blood*”))". This query yielded a total of 224 records, with one result excluded because it was not in English and there were no duplicates. After reading the titles and abstracts of the remaining 223 articles, 191 were excluded for being out of scope. Thus, 32 articles that were tangent (27) or within the scope (5) remained. After a thorough reading, they were analyzed, summarized, and later grouped by similar techniques to extract the main features.

2.1 Literature analysis and review

Table 1 summarizes the techniques used in all the articles. The initial column starts by identifying the article, followed by the application theme or category, then the name of the method and whether it is used in microscopic applications for blood cells.

The 32 articles were divided into four categories: generic techniques, which are different from each other and do not fit into a single specific group; vascular imaging techniques, which focus on the micro-vessel part without actually focusing on the blood cells; cell imaging techniques, which highlight methods for imaging cells, not necessarily blood cells, and blood cell imaging techniques, which focus on SR techniques to improve blood cell imaging.

Some articles provide better descriptions and details regarding SR algorithms, such as presentations of tables, pseudocodes, images, formulas, equations, or graphs. These articles received extra emphasis on information presentation, leading to a better understanding of the techniques and procedures.

2.2 Generic techniques

In this category, eight articles were presented that used generic microscopy methods. For example, some works [6], [7] used holographic techniques, while others [11], [12] used approaches with Fourier equations. In addition, three other articles used different methods to apply in abnormal cells [19], spherical shape for the retina [20], and 3D imaging for hemodynamics [21]. Furthermore, another used binary masking for images in general [22]. All these studies had the same objective of improving the resolution of the images regardless of their application, being in different circumstances without having a specific area, presenting different techniques with their purposes, and helping the researcher to choose depending on the application area.

Li et al. [11] developed an SR-based method that measures the elasticity of the red blood cell (RBC) membrane in real time. In this way, the resolution is defined by the noise of the image (being independent of the optical resolution of the light microscope), which uses a maximum adaptive weighted averaging (MAWA) filter to minimize the noise standard deviation and, together with an SR algorithm, to convert a single low-resolution image to a high-resolution image. Furthermore, the authors stated that the method allowed the measurement of RBC parameters under different conditions. In their article, the authors compared the proposed method with the restoration method of using only a single frame. The proposed technique can obtain complementary information from a set of different images beyond that obtained from a single one, thereby improving the performance of the restoration.

Table 1. Article overview regarding microscopic application for blood cells

Article	Theme	Technique	Aplies?
[11]	Fourier	MAWA	Yes
[12]	Fourier	FPM	–
[6]	Holographic	–	Yes
[7]	Holographic	–	–
[19]	3D	SIM & STED	–
[20]	Abnormal cell	STED	–
[21]	Spheres	WSSA	–
[22]	General SR	–	–
[23]	General vascular	–	–
[13]	Vascular	MRA	–
[24]	Vascular/ultrasound	SUSHI	–
[25]	Animal vascular	OMAG	–
[26]	Vascular	–	–
[27]	Vascular	ULM	–
[28]	Vascular	PAM	–
[14]	Vascular	mULM	–
[29]	Vascular	–	–
[15]	Platelets	SIM & STORM	–
[30]	Non-blood cells	STED	–
[31]	Blood	SIM	Yes
[32]	Blood	PAM	–
[33]	Blood	–	Yes
[17]	Blood		Yes
[34]	Blood	–	Yes
[18]	Blood	CNN	Yes
[35]	Blood	–	Yes
[16]	Blood	SROFM	Yes
[36]	Blood	CNN & SISR	Yes
[37]	Blood	CNNSR & ELMSR	Yes
[38]	Blood	–	Yes
[39]	Blood	CSRNet & FSRCNN	Yes
[40]	Blood	SISR & CNN	Yes

Sun et al. [12] used the Fourier ptychographic microscopy (FPM) method to improve the resolution based on the illumination of the top of numerical apertures (NA), known as enhanced resolution Fourier ptychographic microscopy (REFPM). This technique uses low-resolution images to produce high-resolution images that

are the space bandwidth product. Their investigation proves that REFPM improves resolution by demonstrating images (not blood) with the highest resolution.

The studies of Li et al. [11] and Sun et al. [12] used techniques applying Fourier equations. However, they are very complex and require different equations for better results. Nevertheless, their solutions confirmed the better quality of the images.

Mudanyali et al. [6] developed a technique based on super-pixel resolution in microscopy that does not use lenses and a portable system. The method is performed using an iterative pixel SR algorithm based on the acquisition of several spatially obtained frames, which recover in high resolution the holograms of the objects. These holograms, captured without lenses, are sequentially digitally placed together, retrieving a hologram of the highest resolution object. In addition to the technique, the authors discussed the use of a wetting film to help improve experimental results concerning signal-to-noise (SNR) up to four times, verifying that the wetting film allowed stability and repeatability to enhance the ability of holographic methods (lens less and portable) in the microscopic area, as it preserved the specimens' characteristics. As a final remark, the article could verify high-resolution images, and red blood and other types of cells could be detected.

Greenbaum et al. [7] developed a device for on-chip microscopy that does not have lenses based on holography. The device records the object's shadow, or "hologram" to be reconstructed. It uses the SR per pixel method to generate a high-resolution image based on sets of low-resolution images combined with different computational techniques. The article details the SR method used, even though it focuses on Pap smears, not blood tests. It illustrates the device development process through flowcharts and demonstrates the improvement of images with SR techniques.

Mudanyali et al. [6] and Greenbaum et al. [7] present how holographic methods can improve image quality. However, both articles showed shadows or holograms of cells, not typical images obtained from microscopes, as microscopes and their lenses are costly. So, the authors point out that the systems are made without the need for lenses, making the equipment cheaper and easier to produce. The system is used for highlighting both RBCs and Pap smear images, respectively.

York et al. [21] explained the diversities between STED and SIM, claiming that the latter could achieve better results faster. The article made the analog application of the SIM technique, which achieved twice the spatial resolution (with more details to be observed) of a fluorescent microscope without affecting speed (to show results), phototoxicity (change the image), or field of view (the angular extent of an environment that is seen at any given time). The paper focused only on hardware, using multiple lenses, which resulted in better resolution with the technique without employing algorithms. Additionally, there was no emphasis on blood cell microscopy, only on 3D images (fast and non-invasive) and hemodynamics.

Becatti et al. [19] highlighted the biological area, using an SR technique to find similar parameters in abnormal cells. They used the STED method, which could identify changes in fiber diameter and clot porosity. The technique was only stated without introducing the codes, and no images of blood cells were investigated.

Cai et al. [20] detailed the wavelet-based spherical segmentation algorithm (WSSA) for spherical images, intended to be a segmentation method for identifying spherical patterns. The technique performs the segmentation differently, as it does not require training, which is a highlight. The authors state that, to succeed in learning deep learning algorithms, it is necessary to study the characteristics of data over the network and have quality in the data groups for training. The authors stated the main contribution as the framework's use of an iterative strategy with the flexibility to adapt according to the data types and resources (e.g., Earth or retina

images), with different kinds of "ripples" tested and implemented in the framework. The article demonstrates that spherical images (like the globe) were used for testing, and then the eyeball test recreated the micro vessels observed in the retina. This way, the equations, graphs, and pseudocodes demonstrate the WSSA algorithm's steps. However, the algorithm focused on spherical shapes rather than blood cells, which is the focus of this review.

Zalevsky et al. [22] prepared the article emphasizing the geometric SR technique, which uses matrices and binary masks to achieve better image resolution. This method adds a random binary mask (because it reduces the dependence on manufacturing tolerances) with the low-resolution image. This mask aims to overcome the geometric resolution reduction resulting from the non-ideal sampling of pixels, using equations as adjustments to generate a "super-resolved" reconstruction after matrix inversion. The article has equations and images demonstrating that it achieved the expected results. However, blood cell images are not used.

The last four articles showed various techniques, from algorithms focusing on spherical structures (analysis and identification) [20] and abnormal cells [19] to the detection and categorization of (2D) images in general [22] and even 3D images [21]. Thus, the focus was only on improving the resolution of images in general.

Even though all eight articles used SR methods, most codes were applied to images that did not focus on blood cells. Some articles employed qualitative parameters for image analysis, whereas others used different parameters (e.g., noise variance or SR factor) to verify an improvement in image resolution. This difference compromises the comparison of the articles, as they do not use the same qualitative parameters. Nevertheless, all of the results showed improvements in the desired image quality.

2.3 Techniques for vascular imaging

The articles introduced in this section deal with the vascular part of the blood (not focusing on the cells). They are methods for analyzing hemodynamics or micro vessels. Most techniques fall under the ultrasound theme [23–25], not examining the blood slide. Others focus more on the biological part [26], such as the reconstruction of blood vessels [13], [27], and some also emphasize the physical area, verifying the speed and volume of blood passing through the vessels [14], [28], [29].

In the article by Lavina and Gaengel [26], different techniques were explained to analyze the vascular part of humans and animals (the article was used to better understand this area), not the microscopy of blood cells. This work reviews different techniques, but all are for the vascular part and are aimed at the biological part without having many parameters to compare with other articles.

Cai et al. [13] showed the segmentation "framelet" technique to automatically gain as much detail as possible and appropriately for tubular structures in real time. The results exhibit the method's efficacy in segmenting tubular structures, presenting speed, and extracting exact and smooth limits or surfaces. Furthermore, the article exposes formulas, images, and pseudocode to achieve accurate, smooth boundaries or surfaces of tubular structures such as blood vessels. However, despite the detailed explanations, their work does not aim at blood cells, which is the focus of this review.

Piepenbrock et al. [25] used ultrasonic localization microscopy (ULM) with microbubbles (MB). This method depends on the location of the subwavelength of individual MB for microvasculature reconstruction to occur (at least one MB must cross the micro vessel). Thus, the article discussed scarcity-based SR ultrasound hemodynamic imaging (SUSHI), which is being used in fluorescence-activated photo

localization microscopy (fPALM) in combination with contrast-enhanced ultrasound (CEUS) to achieve high-resolution (vascular) images. This method was combined with algorithms (Gauss, depth-dependent point scattering functions (PSFs)) to verify the accuracy. In conclusion, techniques that use high levels of MB and simulated PSFs that depend on depth should be preferred to the ideal Gauss kernel because it is more appropriate to use such techniques to achieve greater efficiency in computational capacity when using algorithms that take advantage of deep learning. The article discussed the algorithm and the method used in detail. However, the technique is applied to ultrasound images, not blood cell microscopy.

Yousefi et al. [28] used the technique known as optical microangiography (OMAG), based on optical coherence tomography (OCT), to generate an SR spectral estimate to enable the observation of microvascular hemodynamics. The article used OMAG and OCT techniques to accelerate and enhance the observation of micro vessels and their hemodynamics. Equations and images (both black/white and color) that demonstrate the results are presented in the article, showing the blood dynamics in mouse ears and indicating the temperature and how it affects the velocity of micro vessels. Although the article includes all these details, the technique used in the article is used in CT scans and hemodynamics, not in blood cell microscopy.

Ackermann et al. [23] explained a method that uses the positions of individual MBs on ultrasound in micro vessels to achieve SR, estimates the blood flow velocity, and reconstructs the vessels (from the images). The article demonstrates how equations and functions identify MBs. The algorithm estimates simple MBs velocities and, afterward, the reconstruction of the vessel tree, giving the flow velocity in SR. However, the technique is used for micro vessels and hemodynamics, not blood cells.

Dencks et al. [24] described the ULM SR method, which uses MBs to estimate the relative blood volume and reconstruct the micro vessels more accurately and quickly than other methods. The technique also allows for acquiring information about blood speed and flow direction. However, ULM focuses on ultrasound images, which is inappropriate for blood cell microscopy.

Kim et al. [29] presented the localization photoacoustic microscopy (L-PAM) method based on "ultrasonic waves that are generated by the transient thermal expansion of molecules absorbing optical light." Therefore, waves are used to recreate images of blood (from animals and humans) in vivo, making it possible to analyze the microvasculature and hemodynamics and discover the positions of endogenous contrasts to reconstruct the localized images. However, this technique aims to recreate blood (microvasculature) images and not detect blood cells.

Opacic et al. [14] exhibited the ultrasound localization microscopy model (mULM), an advanced screening method suitable for clinical settings, as an alternative SR technique distinct from CEUS. The mULM method can achieve SR images and obtain new parameters quickly and efficiently, making it easy to differentiate tumors with different vascular phenotypes precisely. In addition to informing the varied vascular textures of various tumors, this technique can determine the blood flow velocity through the vessels corresponding to arteries or veins. The technique discussed in the article uses MB for ULM, a method used for the ultrasound area, so it needed to be highlighted for microscopy, focusing on blood vessels and not on blood cells.

Kohler et al. [27] described the SR multi-frame technique that reconstructs a high-resolution image with enhanced SNR from low-resolution multi-frame videos to observe the retinal fundus. The technique's main contributions are (i) the insertion of lighting correction for the photometric record to compensate for heterogeneous spatial and temporal lighting, (ii) the evaluation of unreferenced quality to provide image quality scores, and (iii) the selection of parameters that perform the reconstruction automatically. Experimental verification occurs with the last contribution, revealing

the importance of diagnostic assistance using fundus video cameras. The article details equations, flowcharts, and tables that display performance percentage values along with images that confirm the resolution improvement at the bottom of the retina, highlighting the quality of the micro vessels. Once again, there is no focus on blood cells.

In summary, some articles highlighted the image textures, while others emphasized the speed and direction of blood flow. All nine articles focused on improving the image resolution of the structures of micro blood vessels, with results verifying the improvement as an essential area in medicine. However, none focused on blood cells.

2.4 Techniques for cellular imaging

This section presents three articles focusing on SR methods in cell imaging, not necessarily blood cells. Westmoreland et al. [15] observed platelets, looking for any abnormal form. Pennanen et al. [30] described osteoclast structures (what they look like and how to recognize them), and Jiang et al. [31] clarified how to use high frequency to improve blood sample images.

Westmoreland et al. [15] demonstrated SR microscopy (SRM), aiming to reliably and practically diagnose the structural shape of platelets. The article uses the SIM technique to identify platelets from healthy individuals and abnormal platelets. Images and graphs verify the improved resolution, highlighting the results. However, it is preferable to use an algorithm that can identify all types of blood cells (RBCs, white blood cells, and platelets), not only one.

Pennanen et al. [30] used the STED technique to examine human osteoclasts cultured in vitro. The results showed a better image resolution of the curves and ramifications of osteoclasts compared to the images obtained by the microscope. According to the authors, STED provided new features of the variety of structures and dynamics of osteoclasts, and the SR results confirmed the greater precision achieved by the STED method for microscopy. In addition, the images show an improvement in resolution, although the focus is on osteoclasts, not blood cells.

Jiang et al. [31] discussed the frequency domain diagonal extension (FDDE) microscopy technique, which uses a "high-frequency component in the diagonal direction" to achieve better resolution. The FDDE microscopy technique records the image with a 2D sensor with pixels in a grid format. The article highlights the theory involved, the algorithm used, and the results achieved, revealing an improvement in the resolution of a blood sample, but once again, not the cells.

In short, all the articles explained the theory in depth, using different methods and results to prove the improvement. However, Westmoreland et al. [15] focused on only one type of blood cell, indicating a need to add or change the algorithm to identify the other blood cell types. Pennanen et al. [30] focused on osteoclasts, which are not one of the main blood cells (platelets, red, or white blood cells), requiring changes to the algorithm or the addition of a new one. Moreover, in Jiang et al. [31], a blood sample was improved but in its macro- and non-microscopic form with the primary blood cells highlighted.

2.5 Techniques for blood cell imaging

This section displays articles that demonstrate SR techniques in blood cell microscopy. The articles described by Luo et al. [32], Bhandari et al. [17], and Kim et al. [33] show techniques that cannot be used with images obtained from a database, as they

are acquired differently or not by looking at the microscope slide to analyze the blood cells. In addition to developing new software and hardware, others [16], [18], [34], [35] showed that using complementary metal oxide semiconductor (CMOS) or on-chip imaging, moving shadows of the cells were observed, generating different images from those made by the microscopes that analyze the blood slide. Maiseli et al. [36], Huang et al. [37], and Ayas and Ekinci [38] focused on software, emphasizing the possibility of implementing CMOS or other components in hardware devices. Ma et al. [39] and Tom et al. [40] compared different CNNs, presenting SR algorithms that recognize and classify blood cells. They provided demonstrations to verify the algorithms' accuracy.

Kim et al. [33] demonstrated a method known as photoacoustic imaging (PAI), which uses the ultrasonic waves generated by the transient thermal expansion of molecules that absorb optical light. The localization technique does not show limitations when using hardware components. However, it is necessary to use exogenous contrast agents (microspheres or MB) that are undesirable in clinical settings. The article is focused on a new localization photoacoustic microscopy (PAM) free of contrast agents and equipped with a galvanometer scanner (L-PAM-GS), which improves temporal and spatial resolution through the localization process. Images and results demonstrate the analyses performed on the microvessels of small animals and humans in vivo as well as the hemodynamics of the mouse ear.

Luo et al. [32] detailed the super-pixel resolution technique, which is based on sweeping technical wavelength and uses low raw measurements captured at different wavelengths (in a narrow spectral range). Hence it is possible to reconstruct high-resolution images. The method is grounded (in the physical part) because of the "intense wavelength dependence of subsampled interference patterns in coherent or partially coherent diffraction imaging systems such as lensless or blurred holographic microscopy of lens-based imaging systems." This technique makes image acquisition quicker and requires fewer measurements to achieve high resolution. Moreover, one can recreate color images without code changes. With such benefits, minimizing data storage and transmission costs is feasible, aiding telemedicine and remote reconstructions using the server. The article highlights images exhibiting the functions and results achieved in the on-chip hardware (and the built-in software).

Bhandari et al. [17] described the SR technique that uses photoacoustic waves to recognize and classify blood cells. The method uses the spectral characteristic in the Fourier domain (which uses frequencies for differentiation), as the photoacoustic waves effect converts electromagnetic energy to acoustic energy with information about dimensions and densities (depending on how it propagates), highlighting a differentiated acquisition mode that does not use the microscope.

Huang et al. [34] used single-frame SR CNN to generate high-resolution images from low-resolution cell shadow images, thus identifying, classifying, and performing blood cell counts. According to the authors, CNNs are used in deep learning to serve large image bases, and the CNN-based SR method (CNNSR) is fast and (computationally) efficient using minimal pre-processing or post-processing optimization (achieving improved usage). The device and process are explained through images, showing the functioning of a CMOS that does not need lenses to observe the cells. The device requires light and efficient software because it is developed in hardware with limited memory. The algorithm is the focus, presenting figures that verify the improvement in blood cell resolution.

Liu et al. [18] demonstrated the single-frame (SF) method with CNNSR, which processes cell shadows to identify, classify, and count. In addition to this method, a source-follower CNN (SF-CNN) algorithm was used to enhance images from low

to high resolution, mainly focusing on nuclei and edges of membranes performed in real-time, requiring less processing and done in a fast and practical way. Finally, schematics and figures with the acquired results are presented, highlighting the development of CMOS with the help of the CNN algorithm to classify and count different blood cells.

Li et al. [35] explained the development of an SR-based algorithm to recognize the oval shape of blood cells. The device is made with a CMOS image sensor (CIS) that does not contain lenses. It works by comparing diffraction and elliptocyte patterns automatically, without professionals needing to recognize the cells. The algorithm is divided and clarified into four parts: image segmentation, image pre-processing, SR, and judgment base for elliptocytes. This method must overcome specific difficulties, such as the diffraction effect and low resolution. The process is explained with functions, images, and flowcharts to demonstrate each solution step.

Zheng et al. [16] developed on-chip hardware without lenses using a subpixel resolution optofluidic microscope (SROFM) based on an SR algorithm. Schematics, images, and graphics demonstrate the development process of hardware and software, highlighting methods to avoid the "aliasing" effect and how to improve image resolution quality. The developed equipment was able to identify healthy and infected blood cells (with the malaria virus), and the authors say that it is possible to mass-produce the portable microscope for commercialization, which focuses on recognizing diseases that cover diseases that affect the format of blood cells and water-borne parasites.

Ayas and Ekinci [38] detailed the single-image SR (SISR) method, using multi-scale deep CNNs on low-resolution (microscopic) images to achieve high-resolution images. SISR recreates a high-resolution image from a low-resolution image by adding all the missing high frequencies. Soon after, the three-layer CNN processes the data and trains to achieve greater accuracy in recognizing the correct images and connecting to achieve a higher resolution. The results prove the improvement in the resolution of the blood samples, but they did not go further with the classification and identification of the cells.

Huang et al. [37] explained the development of a low-cost and practical CMOS device, which uses SR algorithms known as extreme learning machine-based SR (ELMSR) and CNNSR, which are machine learning algorithms based on SR single-frame. The algorithms are trained with an extensive database. Both are not computationally heavy and can be implemented on a chip. "Feed-forward" neural networks were used as this mode is more efficient and has little pre-processing or post-processing optimization, using low-resolution images to reconstruct a high-resolution image. With the device, it is possible to recognize and classify, from the shadow (without lenses), whether the cell is blood or a tumor cell. The article details both algorithms used and their advantages (e.g., extracting and aggregating patches of CNNSR are done as convolutional layers). Therefore, non-linear mapping and averaging, among others, are involved in filter optimization to obtain a higher quality of restoration and also to streamline the training process; ELMSR is more suitable) and disadvantages (ELMSR has more noise and blur compared with CNNSR). The process verifies that CNNSR obtained less noise than ELMSR, and the edges were not blurred, with a 9.5% improvement in quality over the other method.

Maiseli et al. [36] developed an algorithm that uses SR (though with an unrevealed method) to improve resolution, aiming to recognize normal and abnormal cells affected by malaria, enabling automated diagnosis. Flowcharts and procedures are explained to understand each step of resolution improvement and to compare low- and high-resolution images to detect malaria disease, verifying (with images)

that the algorithm managed to capture the infected cells better with the resolution improvement. Additionally, graphs and correlations demonstrate the algorithm's accuracy level. In short, the article focuses on developing the SR algorithm and recognizing healthy and unhealthy RBCs.

Ma et al. [39] compared different algorithms for single-frame SR reconstruction based on CNNs. The article shows the equations, flowcharts with the steps, tables and images with the results, and how the CMOS was built (not highlighted). The cell SR network (CSRNet) method can transform low-resolution images (collected by a lensless detection device) into detailed, high-resolution images compared to other techniques. The article highlights techniques to compare the results of different algorithms to analyze which one achieves the best resolution in RBCs, verifying the results with the final images.

Tom et al. [40] allied SISR with CNN to obtain a SR network (SRNet) trained to reduce the loss of detail in the recreation between the actual images and the SR images. They also used relativistic visual Turing test (rVTT) networks to distinguish between real and SR images with a pair of real and SR spots selected from the region of interest to increase the accuracy of the nuclei and cytoplasm recognition algorithm, as well as to recover the texture of the cell parts. Images, equations, and tables detail the steps implemented in this algorithm for blood cell microscopy.

In summary, the 12 articles in this section used methods that addressed SR algorithms for blood cells. Some articles focused on hardware, others on software, but all detailed the ongoing processes. Emphasis was given to articles that compared the performance of algorithms and devices with the results of other authors to verify the differences and improvements made. All articles aimed to improve the resolution of blood cell images, and some stand out for recognizing and classifying cells accurately.

3 DISCUSSION

The search performed in this review discussed SR techniques in the blood area. It is assumed that the aforementioned search terms and the inclusive criteria did not introduce bias into the results. A broad range of works was considered, including those that only mentioned SR and blood. Thus, after reading the titles and abstracts, only articles that clearly stated to cover SR in the blood area were included in the review. Articles that did not emphasize or include these terms were discarded. Despite our efforts, we were unable to find a review of SR techniques in the literature. Therefore, this study makes a significant contribution to the knowledge base of a developer starting out in the application of SR techniques to blood cell images.

The results section highlighted aspects of particular interest, and discussion was held regarding the results available in the literature. However, this review has limitations. The search was conducted only on the Web of Science, one of the largest article databases [41]. Additionally, the study focused on papers discussing SR algorithms only in the blood area. Therefore, SR techniques that might perform better but were not applied to blood or mentioned were excluded from the review.

However, in order to avoid biasing and help identify areas of application for the technique under review, considerations regarding SR in areas other than blood cells can be discussed, highlighting some aspects of studies that can benefit from incorporating SR in their solutions. Gharaibeh et al. [2023], Al-hazaimeh et al. [2023], and Al-Nawashi et al. [2024] demonstrate solutions that use images to classify different types of diseases, such as magnetic resonance images for detecting

Alzheimer's disease, fundus images to identify the causes of diabetic retinopathy, and digital mammography images to confirm breast cancer, respectively [42–44]. These studies can jointly use SR techniques to obtain even better results, improve metric values, and further help healthcare professionals in making more accurate and correct diagnoses.

Gharaibeh et al. (2023) implemented a deep learning algorithm to identify and classify Alzheimer's disease in MRI images [42]. The solution proposed by these authors consists of three parts. The first one is pre-processing, which has three levels inside: removing noise, removing uninteresting parts (non-brain tissues), and improving image quality to detect the disease. The second part, which implemented the technique of Swin transformer-based segmentation using Modified U-Net and Generative Adversarial Network (ST-MUNet) to extract the main features, aims to improve classification accuracy and reduce complexity. The last part, which does the disease detection based on a multiscale feature pyramid fusion module (MSFP-VGG16) with the aim of increasing classification accuracy, can be classified into three stages: normal, Alzheimer's disease, and mild cognitive impairment. For evaluation, the authors selected the metrics of accuracy, specificity, sensitivity, confusion matrix, and positive predictive value, as well as presented pseudocodes for parts of the algorithm for greater understanding. Finally, the authors demonstrated that the proposed solution achieved better performance metrics than the previously mentioned approaches. The article uses deep learning algorithms; however, it does not focus on blood cell microscopy but on MRI.

Al-hazaimeh et al. (2023) applied image processing and artificial intelligence to detect diabetic retinopathy in fundus images [43]. The authors explain that diabetic retinopathy diseases such as exudates, retinal hemorrhage, and microaneurysms need to be identified and studied to detect the initial stage in order to have treatment as soon as possible, as diabetic retinopathy has 4 levels of severity. To identify these diseases, the authors created an architecture that ranged from pre-processing to extraction of disease characteristics and classification, using (in the last part) deep CNNs. To evaluate the performance of the solution, performance measures such as accuracy, specificity, and sensitivity were used. The authors also highlighted that the dataset size is a crucial factor in determining model performance, as larger datasets typically improve classification performance, whereas smaller datasets can result in overfitting. Finally, to ensure the accuracy of the results, the authors stated that ophthalmologists compared the results of the MATLAB simulation with those of experts. Thus, the test results demonstrate that the sensitivity, specificity, and precision are greater than 99.20%, 96.40%, and 98.80, respectively, demonstrating excellent results compared to other approaches. The article uses deep learning algorithms; however, it focuses on fundus imaging rather than blood cell microscopy.

Al-Nawashi et al. (2024) employed CNNs to automatically classify digital mammography images to detect breast cancer, as well as using preprocessing techniques on the images and choosing accuracy and precision metrics to evaluate model performance [44]. Furthermore, the authors compared five algorithms (Random Forest, SVM, KNN, Naïve Bayes classifier, and logistic regression) to observe and analyze the results compared to the proposed solution. In the theoretical part, the authors state that detecting breast cancer at an early stage is crucial to receiving treatment as soon as possible, with different techniques, equipment, and algorithms available to identify it, each with its advantages and disadvantages. Finally, the authors compared the results of the proposed solution to those of different authors, obtaining greater accuracy than those of the existing methods. The article uses machine and deep learning algorithms, not focusing on blood cell microscopy but on digital mammography images.

These three articles used different methods to make the necessary classification of each disease different from each article; however, all of them can benefit from the application of SR, as they further increase the possibilities of detecting and identifying each specific characteristic, improving analysis values, and facilitating the work of health professionals.

This review has the potential to help other researchers select the technique they would like to use. It was conducted as a feature of descriptive analysis, taking a closer look at the explanation and techniques without intending to influence the reader but helping them choose the best method depending on the application area. Even the features of techniques not discussed with blood cells were explained, detailing their pros and cons.

4 CONCLUSION

The review discussed different techniques to improve image resolution, with 32 articles reviewed using the PRISMA methodology. The articles were grouped into four main subtopics: generic techniques, with 25% of the total, with Fourier and holographic techniques, among others; vascular imaging techniques, with 28.1% of the set, with most methods used for ultrasound; cell imaging techniques, with 9.4% of the group, with the majority using the SIM technique; and blood cell imaging techniques, with 37.5% of the whole, using mainly CNNs to achieve the best results. The division between categories was uneven, as few results were found on cell imaging techniques that do not focus on blood cells. This indicates that more research investigations on cell imaging techniques focusing on blood cells can help balance the distribution and provide more information on SR applications. The differential aspect of this study was to identify the most used techniques, their purposes, and applications aiding researchers find the best technique for their work, particularly benefiting pathological researchers and professionals involved in image enhancement.

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6 REFERENCES

[1] D. D. Zhang, P. F. Zhang, and L. S. Wang, "Cell counting algorithm based on YOLOv3 and image density estimation," in *IEEE 4th International Conference on Signal and Image Processing (ICSIP)*, 2019, pp. 920–924. https://doi.org/10.1109/SIPROCESS.2019.8868603

[2] N. M. Deshpande, S. Gite, and R. Aluvalu, "A review of microscopic analysis of blood cells for disease detection with AI perspective," *Peerj Computer Science*, vol. 7, p. e460, 2021. https://doi.org/10.7717/peerj-cs.460

[3] A. W. Tessema, M. A. Mohammed, G. L. Simegn, and T. C. Kwa, "Quantitative analysis of blood cells from microscopic images using convolutional neural network," *Medical & Biological Engineering & Computing*, vol. 59, pp. 143–152, 2021. https://doi.org/10.1007/s11517-020-02291-w

[4] M. M. Alam and M. T. Islam, "Machine learning approach of automatic identification and counting of blood cells," *Healthcare Technology Letters*, vol. 6, no. 4, pp. 103–108, 2019. https://doi.org/10.1049/htl.2018.5098

[5] Z. H. Wang, J. Chen, and S. C. H. Hoi, "Deep learning for image super-resolution: A survey," *IEEE Transactions on Pattern Analysis and Machine Intelligence*, vol. 43, no. 10, pp. 3365–3387, 2021. https://doi.org/10.1109/TPAMI.2020.2982166

[6] O. Mudanyali, W. Bishara, and A. Ozcan, "Lensfree super-resolution holographic microscopy using wetting films on a chip," *Optics Express*, vol. 19, no. 18, pp. 17378–17389, 2011. https://doi.org/10.1364/OE.19.017378

[7] A. Greenbaum, N. Akbari, A. Feizi, and A. Ozcan, "Field-portable lensfree holographic color microscope for telemedicine applications," in *3rd IEEE Global Humanitarian Technology Conference (GHTC)*, 2013, pp. 215–220. https://doi.org/10.1109/GHTC.2013.6713683

[8] A. Khashman, "Investigation of different neural models for blood cell type identification," *Neural Computing & Applications*, vol. 21, pp. 1177–1183, 2012. https://doi.org/10.1007/s00521-010-0476-3

[9] N. Kasamsumran, P. Chanchaithong, N. Wattanamongkhol, W. Pora, and S. Pumrin, "Applying faster R-CNN for hematocytes detection on compound microscope with image sensor device and multiple GPU computation," in *8th International Electrical Engineering Congress (iEECON)*, 2020, pp. 1–4. https://doi.org/10.1109/iEECON48109.2020.229490

[10] F. Long, J. J. Peng, W. T. Song, X. B. Xia, and J. Sang, "BloodCaps: A capsule network-based model for the multiclassification of human peripheral blood cells," *Computer Methods and Programs in Biomedicine*, vol. 202, 2021. https://doi.org/10.1016/j.cmpb.2021.105972

[11] J. Li, Y. X. Huang, H. Y. Zhao, M. Tu, and W. X. Chen, "Superresolution measurement on the minute fluctuation of cell membrane," *Chinese Science Bulletin*, vol. 51, pp. 143–147, 2006. https://doi.org/10.1007/s11434-004-0573-8

[12] J. S. Sun, Q. Chen, C. Zuo, and L. Zhang, "Resolution-improved Fourier ptychographic microscopy using high-numerical-aperture condenser," in *Annual Conference of the Chinese-Society-for-Optical-Engineering (CSOE) on Applied Optics and Photonics China (AOPC) – Optical Sensing and Imaging Technology and Applications*, Beijing, China, 2017. https://doi.org/10.1117/12.2284458

[13] X. H. Cai, R. H. Chan, S. Morigi, and F. Sgallari, "Framelet-based algorithm for segmentation of tubular structures," in *Scale Space and Variational Methods in Computer Vision, SSVM 2011,* in Lecture Notes in Computer Science, A. M. Bruckstein, B. M. ter Haar Romeny, A. M. Bronstein, and M. M. Bronstein, Eds., vol. 6667, Springer, Berlin, Heidelberg, 2012, pp. 411–422. https://doi.org/10.1007/978-3-642-24785-9_35

[14] T. Opacic *et al.*, "Motion model ultrasound localization microscopy for preclinical and clinical multiparametric tumor characterization," *Nature Communications*, vol. 9, 2018. https://doi.org/10.1038/s41467-018-03973-8

[15] D. Westmoreland *et al.*, "Super-resolution microscopy as a potential approach to diagnosis of platelet granule disorders," *Journal of Thrombosis and Haemostasis*, vol. 14, no. 4, pp. 839–849, 2016. https://doi.org/10.1111/jth.13269

[16] G. A. Zheng, S. A. Lee, S. Yang, and C. H. Yang, "Subpixel resolving optofluidic microscope based on super resolution algorithm," in *8th IEEE International Symposium on Biomedical Imaging (ISBI) – From Nano to Macro*, 2011, pp. 1362–1365. https://doi.org/10.1109/ISBI.2011.5872653

[17] A. Bhandari, E. M. Strohm, M. C. Kolios, and R. Raskar, "Photoacoustic ToF tomography of blood cells: From mathematical approximation to super-resolution," in *12th International Conference on Sampling Theory and Applications (SAMPTA)*, 2017, pp. 475–479. https://doi.org/10.1109/SAMPTA.2017.8024437

[18] X. Liu *et al.*, "A microfluidic cytometer for complete blood count with a 3.2-megapixel, 1.1-mu m-pitch super-resolution image sensor in 65-nm BSI CMOS," *IEEE Transactions on Biomedical Circuits and Systems*, vol. 11, no. 4, pp. 794–803, 2017. https://doi.org/10.1109/TBCAS.2017.2697451

[19] M. Becatti *et al.*, "Super-resolution microscopy reveals an altered fibrin network in cirrhosis: The key role of oxidative stress in fibrinogen structural modifications," *Antioxidants*, vol. 9, no. 8, p. 737, 2020. https://doi.org/10.3390/antiox9080737

[20] X. H. Cai, C. G. R. Wallis, J. Y. H. Chan, and J. D. McEwen, "Wavelet-based segmentation on the sphere," *Pattern Recognition*, vol. 100, 2020. https://doi.org/10.1016/j.patcog.2019.107081

[21] A. G. York *et al.*, "Instant super-resolution imaging in live cells and embryos via analog image processing," *Nature Methods*, vol. 10, pp. 1122–1126, 2013. https://doi.org/10.1038/nmeth.2687

[22] Z. Zalevsky *et al.*, "Recent advances in the field of super-resolved imaging and sensing," in *Optical Measurement Systems for Industrial Inspection VII*, vol. 8082, 2011. https://doi.org/10.1117/12.895001

[23] D. Ackermann and G. Schmitz, "Super-resolution velocity estimation in microvessels using multiple hypothesis tracking," in *IEEE International Ultrasonics Symposium (IUS)*, 2015, pp. 1–4. https://doi.org/10.1109/ULTSYM.2015.0219

[24] S. Dencks *et al.*, "Relative blood volume estimation from clinical super-resolution US imaging in breast cancer," in *IEEE International Ultrasonics Symposium (IUS)*, 2018, pp. 1–4. https://doi.org/10.1109/ULTSYM.2018.8580013

[25] M. Piepenbrock, A. Brieden, S. Dencks, and G. Schmitz, "Advancing the feasible microbubble concentration in super-resolution," in *IEEE International Ultrasonics Symposium (IUS)*, 2019, pp. 388–391. https://doi.org/10.1109/ULTSYM.2019.8925761

[26] B. Lavina and K. Gaengel, "New imaging methods and tools to study vascular biology," *Current Opinion in Hematology*, vol. 22, no. 3, pp. 258–266, 2015. https://doi.org/10.1097/MOH.0000000000000141

[27] T. Kohler *et al.*, "Multi-frame super-resolution with quality self-assessment for retinal fundus videos," in *Medical Image Computing and Computer-Assisted Intervention – MICCAI 2014, MICCAI 2014,* in Lecture Notes in Computer Science, P. Golland, N. Hata, C. Barillot, J. Hornegger, and R. Howe, Eds., vol. 8673, Springer, Cham, MA, 2014, pp. 650–657. https://doi.org/10.1007/978-3-319-10404-1_81

[28] S. Yousefi, J. Qin, and R. K. Wang, "Super-resolution spectral estimation of optical micro-angiography for quantifying blood flow within microcirculatory tissue beds in vivo," *Biomedical Optics Express*, vol. 4, no. 7, pp. 1214–1228, 2013. https://doi.org/10.1364/BOE.4.001214

[29] J. Kim, J. K. Kim, S. Jeon, J. W. Baik, S. H. Cho, and C. Kim, "Agent-free high speed localization photoacoustic microscopy," in *Conference on Photons Plus Ultrasound – Imaging and Sensing*, 2019, vol. 10878. https://doi.org/10.1117/12.2510841

[30] P. Pennanen *et al.*, "Diversity of actin architecture in human osteoclasts: Network of curved and branched actin supporting cell shape and intercellular micrometer-level tubes," *Molecular and Cellular Biochemistry*, vol. 432, pp. 131–139, 2017. https://doi.org/10.1007/s11010-017-3004-2

[31] S. Jiang *et al.*, "Frequency-domain diagonal extension imaging," *Advanced Photonics*, vol. 2, no. 3, 2020. https://doi.org/10.1117/1.AP.2.3.036005

[32] W. Luo, Y. Zhang, A. Feizi, Z. Gorocs, and A. Ozcan, "Pixel super-resolution using wavelength scanning," *Light-Science & Applications*, vol. 5, 2016. https://doi.org/10.1038/lsa.2016.60

[33] J. Kim, J. Y. Kim, S. Jeon, J. W. Baik, S. H. Cho, and C. Kim, "Super-resolution localization photoacoustic microscopy using intrinsic red blood cells as contrast absorbers," *Light-Science & Applications*, vol. 8, 2019. https://doi.org/10.1038/s41377-019-0220-4

[34] X. W. Huang *et al.*, "A convolutional neural network based single-frame super-resolution for lensless blood cell counting," in *12th IEEE Biomedical Circuits and Systems Conference (BioCAS)*, 2016, pp. 168–171. https://doi.org/10.1109/BioCAS.2016.7833758

[35] J. W. Li, L. Dai, N. M. Yu, Z. P. Li, and S. J. Li, "Elliptocyte detection technology based on super-resolution algorithms for a lensless imaging system," *Measurement Science and Technology*, vol. 32, no. 2, 2021. https://doi.org/10.1088/1361-6501/abbb65

[36] B. Maiseli, J. Y. Mei, H. J. Gao, and S. Yin, "An automatic and cost-effective parasitemia identification framework for low-end microscopy imaging devices," in *International Conference on Mechatronics and Control (ICMC)*, 2014, pp. 2048–2053. https://doi.org/10.1109/ICMC.2014.7231926

[37] X. W. Huang *et al.*, "Machine learning based single-frame super-resolution processing for lensless blood cell counting," *Sensors*, vol. 16, no. 11, p. 1836, 2016. https://doi.org/10.3390/s16111836

[38] S. Ayas and M. Ekinci, "Microscopic image super resolution using deep convolutional neural networks," *Multimedia Tools and Applications*, vol. 79, pp. 15397–15415, 2020. https://doi.org/10.1007/s11042-019-7397-7

[39] X. Ma, N. M. Yu, Y. Fang, and D. F. Wang, "Research on single-frame super-resolution reconstruction algorithm for low resolution cell images based on convolutional neural network," in *3rd IEEE International Conference on Image, Vision and Computing (ICIVC)*, 2018, pp. 369–373. https://doi.org/10.1109/ICIVC.2018.8492913

[40] F. Tom, H. Sharma, D. Mundhra, T. R. Dastidar, and D. Sheet, "Learning a deep convolution network with Turing test adversaries for microscopy image super resolution," in *16th IEEE International Symposium on Biomedical Imaging (ISBI)*, 2019, pp. 1391–1394. https://doi.org/10.1109/ISBI.2019.8759443

[41] G. D. G. Carvalho *et al.*, "Bibliometrics and systematic reviews: A comparison between the Proknow-C and the Methodi Ordinatio," *Journal of Informetrics*, vol. 14, no. 3, 2020. https://doi.org/10.1016/j.joi.2020.101043

[42] N. Gharaibeh *et al.*, "Swin transformer-based segmentation and multi-scale feature pyramid fusion module for alzheimer's disease with machine learning," *International Journal of Online & Biomedical Engineering*, vol. 19, no. 4, pp. 22–50, 2023. https://doi.org/10.3991/ijoe.v19i04.37677

[43] O. M. Al-Hazaimeh *et al.*, "Combining artificial intelligence and image processing for diagnosing diabetic retinopathy in retinal fundus images," *International Journal of Online & Biomedical Engineering (iJOE)*, vol. 18, no. 13, pp. 131–151, 2022. https://doi.org/10.3991/ijoe.v18i13.33985

[44] M. M. Al-Nawashi, O. M. Al-Hazaimeh, and M. Kh. Khazaaleh, "A new approach for breast cancer detection-based machine learning technique," *Applied Computer Science*, vol. 20, no. 1, pp. 1–16, 2024. https://doi.org/10.35784/acs-2024-01

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