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Malaria detection using custom Semantic Segmentation Neural Network Architecture

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Summary

Malaria is a significant disease that affects both animals and humans. The four main Plasmodium species that cause human malaria are *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae*, and *Plasmodium ovale*. *Plasmodium knowlesi*, a parasite typically infecting forest macaque monkeys, was recently revealed to be able to be transmitted by anophelines and provoke malaria in humans. This provides an increasing risk of spreading the disease to areas previously unaffected with it and infecting people during the increasingly popular travels abroad. Microscopic examination remains one of the most often used methods for its laboratory confirmation. These tests, however, should be performed immediately after receiving samples from a first-contact doctor to allow immediate therapy. This research presents a novel, semantic segmentation neural network architecture designed to quickly create a classification mask, giving the doctor information about the position, shape, and possible affiliation of detected elements. The evaluation method is based on a light microscope imagery and was created to overcome problems resulting from the human diagnosis specifics. There are 3 abstract classes containing healthy cells, cells with malaria and background. The outputted mask can be later mapped to a more readable form with the inclusion of contrasting colors, next to an original image for quick validation. Such an approach allows for semi-automatic recognition of possible disease, nevertheless still giving the final verdict to the specialist. The developed solution has achieved a high recognition accuracy of 96.65%, while the computer power requirements are kept at a minimum. The proposed solution can help reduce misclassification rates by providing additional data for the doctor and speed up the entire process with the early diagnosis made by a deep learning model.

Keywords: Malaria, diagnostic method, artificial intelligence, veterinary medicine, infectious diseases

Malaria is a disease induced by pathogenic factors of the genus *Plasmodium*. These protozoan parasites occur globally and represent a threat for both humans and animals. Until recently, this disease has been categorized as a tropical illness, eradicated from Europe before the 20th century, but according to numerous researchers, an increasing number of cases are recorded in Europe. The non-characteristic course of the infection is often a challenge for the correct diagnosis. Unfortunately, many doctors and veterinarians are still unaware of the increasing significance of this disease. The lack of pathognomic symptoms and the need for multi-steps diagnosis may easily lead to misdiagnoses, as the clinical course often involves a febrile condition similar, to the flu (1, 2, 15).

The climate is one of the most important factors determining the health of living organisms, as it has an extreme impact on fluctuations in the numbers of both pathogens and their vectors, the host's immune defence and habitat availability. Such changes can constrain the spreading of infectious diseases or lead to outbreaks and greater intensity of illness (8). Currently, global warming favours the expansion and redistribution of many important diseases, such as malaria (4, 11, 20).

The increasing importance of malaria also reflects social changes – its transmission is favoured by an increasing number of sightseers and both human and pet migrations between areas affected and unaffected. The pathogen can then spread to new regions

offering a suitable microclimate for its survival because of global warming.

Anopheles mosquitoes as a natural malaria vector gain a lot due to the currently warmer climate in Europe. It significantly increases their survival rate and enhances reproduction through longer breeding seasons and feeding periods. Currently, it is known that about 50% of the world's human population is at risk of encountering this disease and this number will increase. Such dependency is also present among both wild and domestic animals. The transmission occurs through the bite of an infected female *Annopheles* mosquito. An important fact is that this disease is much more dangerous for naive, European endemic animal species than for individuals who have been exposed to it for generations. The reason can be semi-immunity developed by long co-existence history (27).

In Europe a typical representative of the parasite that transmits malaria is *Plasmodium falciparum*, which originates from Sub-Saharan regions. Its maturation inside the vector takes 26 days at 20°C, but only 13 days at 25°C (10, 21, 26). Those single-cell blood protozoa affect various animal species. It undergoes a complex life cycle. After the mosquito's blood meal, there is an inoculation of an anti-coagulant with a sporozoite into the animal's bloodstream. The sporozoites penetrate the hepatocytes and mature into schizonts, then replicate asexually and releasing of merozoites occurs. During erythrocytic schizogony, merozoites infect the red blood cells and multiply asexually, where they also develop into trophozoites. Finally, the trophozoites differentiate into schizonts, which rupture and release other merozoites or gametocytes. Merozoites produce and release surface proteins which recognize the erythrocytes. Antibodies against them can be potentially used in new therapies and diagnostic processes (5). The intraerythrocytic cycle can be recognized clinically as it manifests by a repetitive exacerbation of symptoms and pyrexia. The content of damaged erythrocytes stimulates the production of inflammatory mediators responsible for the disease's clinical course. Those cells will be then ingested by another mosquito during its blood meal. In the vector, the parasite undergoes a sexual phase of reproduction. Motile ookinetes invade the wall of the midgut and develop into oocysts from which another generation of sporozoites will be produced and wait in the salivary gland for inoculation (41).

In recent years, among wild animals a particularly large number of reports of malaria cases in previously unaffected areas have been recorded in birds.

Avian malaria is induced by protozoan parasites of *Plasmodium* and *Haemoproteus* genera e.g., *Plasmodium relictum*, *Plasmodium anasum* and *Plasmodium gallinaceum*.

The reports indicate that it does not produce significant mortality among the natural hosts often, however, it may sorely decrease the number of naive birds (25). The example of the deadly impact of those newly introduced pathogens on non-endemic species can be exemplified by the Hawaiian and New Zealand Islands. Malaria there has brought many endemic species to the brink of extinction (3).

In Europe, an increasing number of asymptomatic infections produced by hematozoa have been reported among songbirds. This trend can also be noticed in countries considered in the past as unsuitable for vector survival, such as Germany or Switzerland. As a response to unexplained deaths of European parrots, the researchers performed numerous tests on the avian population. The results included malaria-positive, yellow-crowned parakeets (*Cyanoramphus auriceps*), barred parakeets (*Bolborhynchus lineola*) and budgerigars (2, 29, 38). Such statements indicate that avian malaria should therefore be considered a threat to exotic parrots in Europe. The problem however also concerns native birds, like the sparrow (*Passer domesticus*). The reason for their visible decline is multi-factorial. The increasing urbanisation, free-ranging cats and loss of their habitats play the main role, but also an increasing number of new infections is of great importance here. Research in London showed the prevalence of *Plasmodium relictum* in birds at 74%. These numbers were unexpected as previous reports did not notice such diseases in North Europe's wild bird population (6).

There were also numerous research studies made for malaria prevalence screening among both captive and wild mammals worldwide. The outcomes showed an increasing number of cases demonstrating parasitaemia in collected blood. The first malaria parasites among mammals were observed in Europe in 1898. As for now, the *Apicomplexa* species associated with malaria were discovered in primates, rodents, ungulates, bats, elephant shrews, and pangolins. Among apes, extensive investigation started in 2009 and to date, there are many papers showing parasitaemia in gorillas, chimpanzees, and bonobos. The *Plasmodium vivax*-like parasite was discovered in chimpanzees and whole new lineages of the *Laverania* subgenus of *Plasmodium*, *Plasmodium reichenowi* and *Plasmodium gaboni* discovery have drastically changed the view of malaria's thread (9, 16-18, 31, 32).

With regards to ungulate species, research can be found about *Plasmodium cephalophi* infection from African duikers, *Plasmodium bubalis* in domestic buffalo, *Plasmodium ofocoilei* in white-tailed deer. Malaria has also been observed in water buffalo and domestic goats.

The history of malaria in bats is well documented. Investigations in this field started at the end of the 19th century and are continued till now. It is currently claimed that among bats there can be nine haemosporidian genera, of which seven are distinctive only for these hosts. The hepatocyte parasites exhibit a high prevalence in fruit bats. The breaking point in those studies was the rediscovery of two *Plasmodium* species

in bats due to their very close phylogenic association with rodent species, pointing to some host switches in different mammalian orders.

There was *Plasmodium cyclopsi* from an insectivorous bat and *Plasmodium voltaicum* detected in an African fruit. Those taxa are sister taxa that are used as experimental models for human malaria disorder for many years (7, 12-14, 19, 24, 35, 36, 39).

Diagnosis of malaria is mainly based on the finding of the parasitaemia in a blood sample made by the thick drop method (Giemsa stain). It is possible to differentiate *Plasmodium* species from peripheral blood by light microscopy based on differences in the amount and structure of intracellular forms in erythrocytes, as well as changes in the shape of infected red blood cells.

Most components seen during microscopy of the blood smears are quite nonspecific and only when considering their general picture can a diagnostic clue be obtained. This can be easily omitted by a doctor. Among parameters characteristic of malaria infection there can mostly be seen normocytic and normochromic anaemia, marked thrombocytopenia, haemolysis, and free haemoglobin breakdown products. There can also be seen variations in leucocyte count, usually combined with monocytosis and lymphopenia. The microscopic examination of Giemsa-stained blood smears in case of parasitaemia is considered one of the most often used methods of detection. The sensitivity of this method is currently considered as five parasites per microlitre (30).

The recognition of the parasitaemia severity plays an important role in treatment plans as depending on that parameter, different courses of therapy are chosen. In future work, such classification could be implemented as an extension of the current recognition model, but some additional information to the present dataset would have to be prepared.

Other accessible methods of malaria detection include the composition of radiography, urine, blood and biochemistry parameters findings and PCR methods (0.01 parasites per microlitre after lysis; 1 parasite per microlitre without lysis) (23). However, such methods are expensive, and their availability is limited; in the case of microscopy detection, there is a need for qualified microscopists employment, which also can be difficult to obtain even in larger medical centres.

The research aimed to develop and train an innovative semantic segmentation neural network architecture supporting the detection of the presence of malaria parasite in erythrocytes. This method accelerates the identification of suspicious elements and analyses the entire smear image in a short time, thus minimizing human error.

Material and methods

The presented method attempts to deal with both monetary and time factors, as it needs only microscopic images for detection, and because the main classification is made by an Artificial Intelligence (AI) model there is no need for constant, fully qualified human supervision, making it more accessible for smaller clinics.

Dataset. The dataset, found on kaggle.com and called „Malaria Bounding Boxes", consists of 3 sets of images (1364 in total) with description of around 80,000 cells where different researchers have prepared their own subset: from Brazil (Stefanie Lopes), from Southeast Asia (Benoit Malleret), and time course (Gabriel Rangel). Blood smears were stained with Giemsa reagent.

Labels. There are two classes of uninfected cells (RBCs and leukocytes) and four classes of infected cells (gametocytes, rings, trophozoites, and schizonts). Annotators were allowed to mark some cells as difficult if they were not clearly in one of the cell classes. The data had a heavy imbalance towards uninfected RBCs versus uninfected leukocytes and infected cells, making up over 95% of all cells. For this research above labels were simplified to two classes: healthy cells and infected cells.

A class label and set of bounding box coordinates were given for each cell. For all data sets, infected cells were given a class label by Stefanie Lopes, malaria researcher at the Dr. Heitor Vieira Dourado Tropical Medicine Foundation hospital, indicating stage of development or marked as difficult.

Preprocessing. As the labels are in rectangle form, which is highly inaccurate with overlapping objects and background noise, in this research the conversion to semantic segmentation mask has been made using a custom algorithm for better accuracy. To achieve this, the clustering threshold has been manually set to distinguish a darker cell from a light background. Later 3 passes of denoising based on heuristics has been evaluated to further enhance the accuracy by removing unwanted artefacts. And finally, an appropriate label was attached based on the rectangle mask.

Normalization. As all images were in 8 bits, the normalization after integer to floating point number conversion has been made by dividing all values by 255.0.

Proposed Deep Learning Solution. Malaria detection can be approached using various techniques, from which some of the most accurate methods include visual classification. Currently most of such examinations are performed by a human specialist and contains manual classification of thousands of objects within previously selected frames per patient. This process is extremely slow and requires full focus of the doctor for the whole time to avoid misclassification and oversight, especially considering very small differences between healthy and infected cells.

As such examinations are defined by high repeatability and small amount of additional stimulus, it can be very difficult for doctors to maintain the peak detection performance and accuracy during the whole process, especially considering some external factors like tiredness, small amount of time or lack of special interest in the field.

Many common convolutional neural network (CNN) techniques contain rectangular masking, such as in (42) and (43), however in this research for better accuracy the semantic segmentation method has been used.

Such a network provides additional data in the form of a two-dimensional mask with elements classification to the doctor next to the original image for easy and fast

verification. Such an approach can highly reduce error rate by providing an initial diagnosis made by the system and pointing out suspicious elements, as well as speeding up the entire diagnosis process by reducing the time needed to analyse the image.

Additionally, by choosing segmentation architecture over the classical rectangle masking one, the classification is made with per-pixel accuracy and thus there is more clarity and accuracy improvement on images with higher number of overlapping objects.

In this research a novel deep neural network solution is presented. The proposed model is based on semantic segmentation neural network idea with custom architecture and layers layout. The finally developed model can be seen in Figure 1. The input of the network consists of a 256 × 256 pixel image taken with a light microscope. Later, the encoder section down samples the image 4 times using max pooling layers with a factor of 2. During that process the signal is additionally enhanced by skipped connections combined using added layers and a small amount of dropout is used after pooling to deal with overfitting. The bottleneck section is minimal with only 3 layers as experiments showed no visible gains with more complications. Finally, the decoder section consists of a mirrored encoder with skipped connections inspired by the U-Net shaped architecture with the total number of parameters of 61,879,874. The entire model used Rectified Linear Unit (ReLU) eq. 1 as a main activation function and the final layer used Softmax eq. 2. The training has been optimized with NAdam algorithm Alg.1.

Equation 1.

$$\mathrm{Relu}(z) = \max(0, z),$$

Equation 2.

$$\sigma(z_i) = \frac{e^{z_i}}{\sum_{j=1}^{K} e^{z_j}} \qquad \text{for } i = 1, 2, \ldots, K.$$

NAdam algorithm. To improve training performance in terms of validation accuracy and training times the NAdam training algorithm has been used. The formula can be described as follows:

Equation 3.

$$z_s = \gamma_1 z_{s-1} + (1 - \gamma_1) g_s,$$

Equation 4.

$$k_s = \gamma_2 k_{s-1} + (1 - \gamma_2) g_s^2,$$

where: γ parameters are constant hyper-parameters and g is the current gradient value of an error function. Values z_s and k_s are used later for computing the correlations marked as $\hat{z}_s$ and $\hat{k}_s$ according to the following equations:

Equation 5.

$$\hat{z}_s = (1 - \gamma_1) g_s + \gamma_{1_{s+1}} z_s$$

Equation 6.

$$\hat{k}_s = \frac{k_s}{1 - \gamma_2^s}$$

Finally, using previously calculated variables, the final formula can be defined as:

Equation 7.

$$w_s = w_{s-1} - \mathrm{LR} \frac{\hat{z}_s}{\sqrt{\gamma_{2_s}} + \varepsilon}$$

where ε is a small, constant value and LR is a learning rate.

Algorithm 1 NAdam training algorithm

Generate random weights,
while *global error value* $\varepsilon < error\_value$ **do**
  Shuffle the training data,
  for each batch inside training data **do**
    Compute gradient vector g on the batch,
    Update vector z eq. (3),
    Update vector k eq. (4),
    Rescale vector $\hat{z}$ eq. (5),
    Rescale vector $\hat{k}$ eq. (6),
    Update variable $\hat{w}_s$ eq. (7).
    Step = Step + 1,
  end for
  Calculate *global error* ε,
end while

Fig. 1. NAdam training algorhitm

Used hardware. During this research all computations were made on a PC with the following specification:
– CPU: AMD Ryzen Threadripper 2950X 16c/32t,
– RAM: 128 GB,
– GPU: NVidia RTX 3090 24 GB.

Results and discussion

The training has been performed for 1000 epochs and resulted in 96.65% per pixel validation accuracy, while the overall detection rate was much higher due to small inaccuracies on the borders of cells. Training plots can be seen in Figure 2.

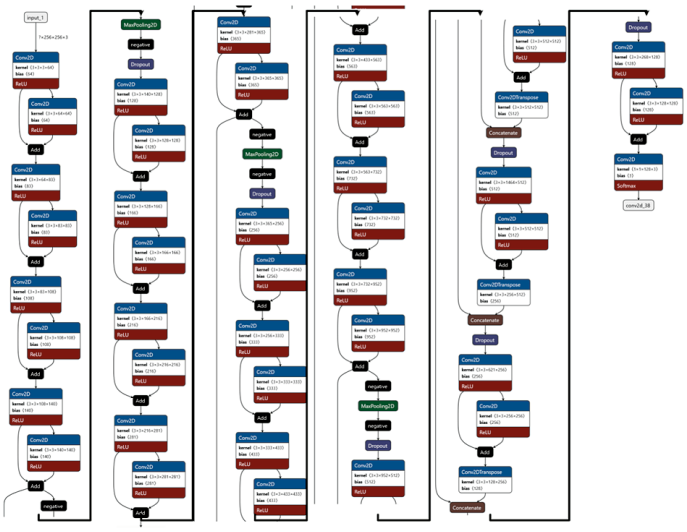
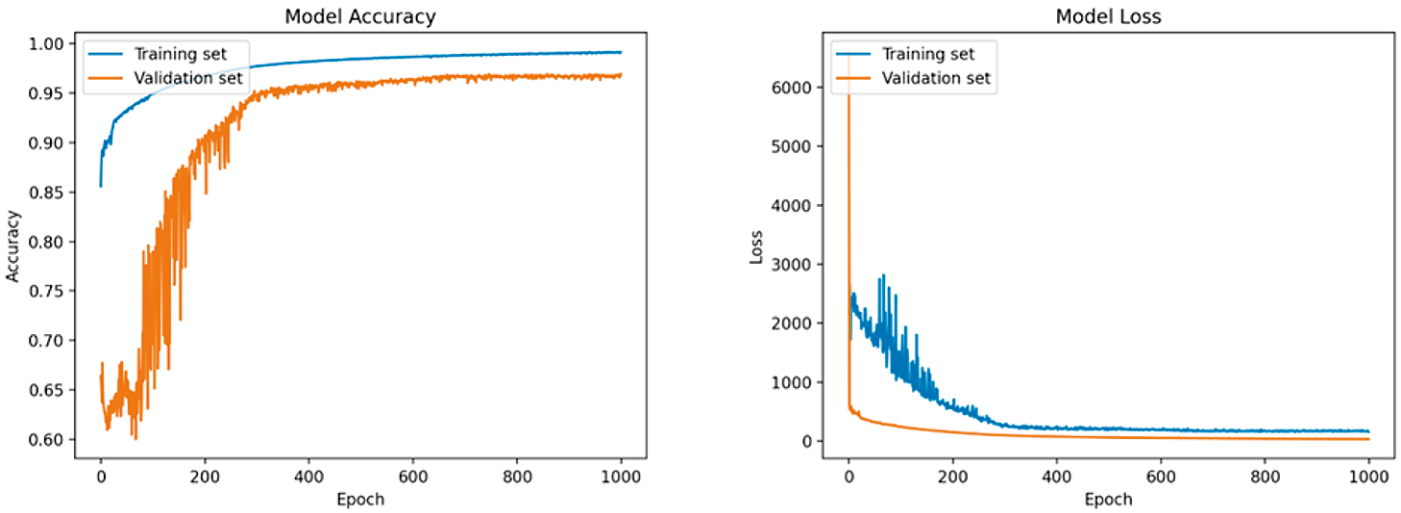


Fig. 2. Network's Architecture Model

Sample predictions made by the network can be seen in Figure 3. These images were previously unseen by the network during training for better validation of the model's performance. As shown, the presented solution correctly classifies all cells with some detection errors near borders, where in some cases pixels labelled as background are added to the cell's mask and vice versa. Such inaccuracy is nevertheless only important numerically as in a real-world scenario it is negligible. Using the clustering algorithm with labels taken from



(a) Accuracy plot during training.

(b) Loss plot during training.

Fig. 3. Network's Training Plots

rectangle masks there is a possibility to easily check the real performance of the AI architecture. During that test the overall detection accuracy is around 99.66% for the validation dataset. Comparison between our results and other state-of-the-art articles can be seen in table below (Tab. 1).

Tab. 1. Chosen available diagnostic methods

Article	Type	Year	Accuracy
Nicastri et al. (28)	Microscopy	2009	93.5%
Nicastri et al. (28)	ParaHIT test	2009	97.6%
Saglam et al. (34)	FPGA CNN	2019	94.70%
Shekar et al. (37)	Fine-Tuned CNN	2020	95.99%
Loh et al. (22)	Mask R-CNN	2021	94.57%
Turuk et al. (40)	Integrated CNN	2022	93.89%
Razin et al. (33)	YOLOv5 CNN	2022	96.21%
Ours	Semantic Segmentation CNN	2023	99.66%

Comparison. As shown in the comparison table, our model shows high potential in the malaria detection field when compared to previous state-of-the-art papers from recent years. Due to increased complexity of the architecture itself it can detect infected cells with higher accuracy on the given validation dataset than other Computer Vision models and can be a direct competitor for other cheap classical methods like light microscopy or rapid tests in terms of speed, money required and precision.

Performance. The final training on the described computer needed around 18 hours to finish. On the same hardware the evaluation time is around 15 ms for a single image and on a more standard machine, computing on Intel i5 3rd generation CPU, the evaluation time is below 1 second for a single image.

Visualization. The network originally outputs the data in the form of a two-dimensional matrix with sparse representation of classes using integer values. Such data are optimal for being stored and analysed by the computer; however, it presents no useful value for the non-technical user and requires further processing to create an informative image. That is why, to make it readable, the matrix has been expanded by 3 additional colour channels and integer values from the [0.2] range has been mapped to brown, green and blue channels, where green is the background, brown are healthy cells and blue are infected cells (Fig. 4). Such a prepared mask is subsequently presented next to the original image for fast and easy validation by the user.

Potential usage. As the system is based on the Artificial Intelligence architecture, there is a need of having a computer equipped with a microscope camera and running at least Windows 10 or a mid-tier smartphone from at least 2016 that could run such a program, however newer equipment is recommended, as the evaluation times will be much quicker, allowing for better usage experience.

Conclusion. This paper presents a novel solution for fast malaria detection using a custom Semantic Segmentation Neural Network. The system's output is later presented in an easy to understand and clear way, which allows for quick diagnosis and validation. Although the training has been performed on a top tier GPU, the evaluation can be made on equipment far more affordable reducing cost and making the system more accessible. The presented solution can improve the detection time by providing additional information to the microscopy image, helping the doctor performing the evaluation spot and analyse potential threats. Such solution can not only allow for testing more animals at the same time, but also massively reduce the cost of a such diagnosis.

Future possibilities. In future works there are many ways to improve such a system. One of them is to expand the dataset by additional images, which can improve the accuracy of the model in difficult

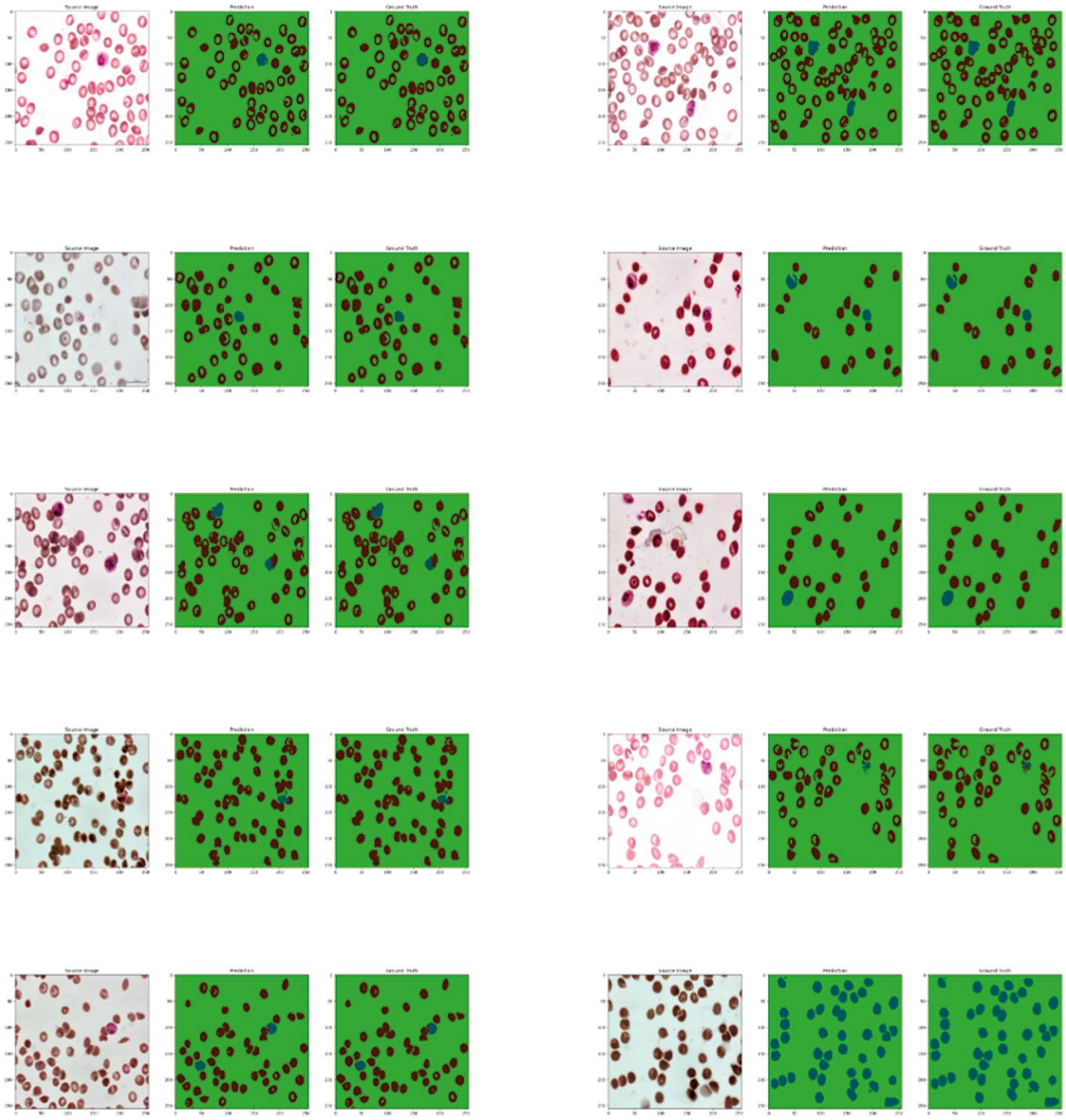


Fig. 4. Network's output visualization

situations, as well as extend the network's knowledge about the exact shape of infected cells regardless the conditions. Another option is to further fine tune the model's architecture for better optimization in terms of time and detection performance. There could also be a possibility to detect more abstract classes and distinguish the infected cells by the malaria development phase. Finally experiments with image augmentation can be performed to artificially enlarge the amount of data and possibly reduce classes imbalance for better detection of infected cells.

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