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An OCTA - Advancements in Retinal Microvascular Imaging: A Comprehensive Review of Diagnostic Applications

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ABSTRACT: This comprehensive review explores the evolving landscape of Optical Coherence Tomography Angiography (OCTA) in the realm of retinal microvascular imaging. In the field of retinal microvascular imaging, it has become a useful instrument that provides non-invasive understanding of a range of ocular disorders. This advanced imaging technique provides high-resolution, three-dimensional visualization of retinal vasculature, allowing for the identification and monitoring of microvascular abnormalities. In the context of retinal diseases, OCTA aids in the assessment of conditions such as diabetic retinopathy by detecting microaneurysms, capillary non-perfusion, and neovascularization. In Age-Related Macular Degeneration (AMD), OCTA enables the visualization of choroidal neovascularization and helps in assessing disease severity. Additionally, OCTA has proven effective in studying retinal vascular changes in conditions like retinal vein and artery occlusions, providing valuable information for diagnosis and management. The technology's non-invasive nature and ability to produce detailed, depth-resolved images make it a preferred method for studying retinal microvasculature, offering clinicians a powerful diagnostic and monitoring tool for various retinal disorders. Despite its advantages, ongoing research and refinement of OCTA techniques are essential to further enhance its capabilities and address potential limitations in specific clinical scenarios

KEYWORDS: Artifact, optical coherence tomography, angiography, retinal vessels, structure and flow information

I.INTRODUCTION

Since the 1990s, the most crucial imaging modalities that can be used for the analysis of different retinal diseases is optical coherence tomography (OCT) [1]. Low coherence interferometry is the foundation of the imaging method. The capacity to visualize and measure intraocular blood flow is crucial to the worldwide ophthalmology community because the majority of eye diseases are linked to vascular abnormalities [2]. Variety of invasive and non-invasive imaging techniques can be utilized. For a thorough clinical analysis and evaluation of blood flow procedures in retina and blood circulation in Choroid, procedures such as fluorescein angiography (FA) and indocyanine green angiography (ICGA) are used, but they are possessed to be invasive method Moreover they are time consuming and has significant side effects such as redness in eye and painful [3,4]. Color Doppler ultrasound [5] and functional magnetic resonance imaging [6] are non-invasive and studied methods, but their low resolution and poor performance make them clinically unacceptable in ophthalmology. Other prominent imaging techniques, such as laser Doppler flow measurement and blood velocimetry, laser spot estimation, and water field entropy have been employed to research and analyze the physiology of the retinal arteries, but their practical use declines from measurement complexity and reproducibility.

Doppler OCT (DOCT) was developed as an OCT intensifier to image retinal vessels and measure blood flow, while retinal microvasculature is perpendicular to OCT. Therefore, this method is suitable for microanalysis of retinal blood vessels. Blood flow which acts as parallel to the OCT laser can be detected using DOCT. The effective methodology of studying and analysing the retinal microvasculature is Optical Coherence Tomography Angiography (OCTA) that has emerged as a new development in retinal image flow analysis [11]. This is a non-invasive technique of imaging that uses backscattering of light waves to create high-resolution sections. Analysing retinal microstructures, this method is based on repetitive changes in the same OCT B scan over a period of time to determine blood flow. Therefore, as shown in Figure 1, OCTA uses motion inversion to determine the flow of Oct data. OCTA uses repetitive scans of the same location to detect motion at high scan speeds. It was initially characterized as an 18.7 kHz SD-OCT system [12]. Improvements in technology and imaging equipment may result in better OCT angiography. For

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improvising the accuracy of evaluation of retinal and choroidal vessels, accurate structural segmentation of images is crucial. but anatomical features of the patient's eye are often distorted, and segmentation algorithm failures require manual correction.

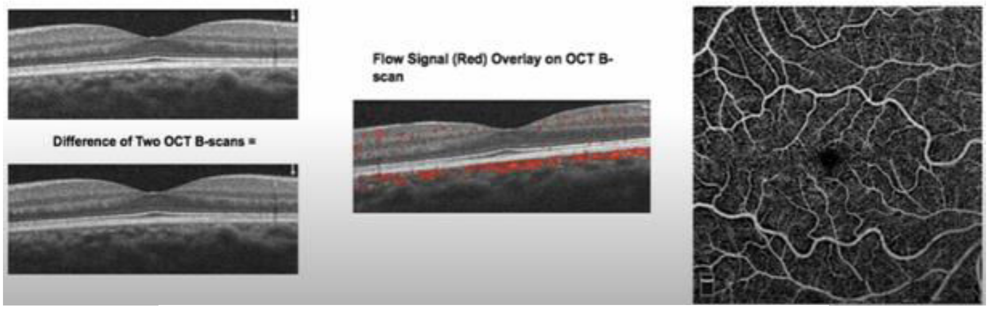

Figure 1. OCTA flow signal from difference of two B-Scans

Therefore, advanced image processing techniques have been developed to analyze retinopathy [13]. The OCTA count is an important measure of retinal problems. The measurements vascular density and flow index, which can be derived from frontal angiography [14,15,16,17,18,19,20], are frequently used measurements. The percentage of an area that is taken up by vessels is known as vessel density, and the average flow signal in the study area is used to compute flow index [2]. The evaluation of the most prevalent eye conditions, such as DR, AMD, and retinal vein blockage, by OCTA is promising.

Diabetes mellitus, scientifically known as diabetes mellitus (DM), is most prevailing in India and is expected to affect 422 million people worldwide by 2020. Basically, two types of DM can occur; Type1 and Type2. Type 1 diabetes can be found when enough insulin is not generated in human body to control blood sugar, and type 2 diabetes occurs to women during her pregnancy when develops insulin resistance [21, 22]. Diabetes affects the tissues of eye during the early stages of the disease. Although the main manifestations of vascular degeneration are nephropathy and retinopathy [23], DR is the most commonly affected disease and major cause of blindness in working-age adults [24]. It is usually asymptomatic in its early stages of the disease and the retinal microvascular changes are difficult to detect. However, if not recognized earlier and treated properly, it leads to serious vision loss and blindness. Therefore, it is important to identify methods to detect small lesions in diabetic retinopathy [25].

Retinal vascular density compares uncorrelated signals (differences in background signal intensity or amplitude) taken at precise diameters to produce a blood flow map [19]. Since the movement of the axial mass caused by the movement of the patient is removed, the motion plot between the density of the retinal vessels repeated scans accurately reflects the red blood cells movement in the retina vessels [26]. Assessment of retinal vascular density requires faster imaging speeds than existing OCT systems to achieve dense sample volumes. The scan speed of conventional retinal vascular density devices results in reduced field of view, reduced quality in image, and significant increase in scan time. Retinal vascular density, a new parameter to be visualized in retinal and choroidal microvasculature can be done without dye injection using OCTA. This is done by scanning the same site several times and detecting changes in the OCT signal reflected through the blood vessels [28, 29]. Increase in DR, diabetic maculopathy, and anterior segment involvement in DR the other issues to addressed in early stages, if not may cause serious vision related issues [31–33]. Existing models include techniques for combining sets of two-dimensional images over time which allows imaging of blood flow over large areas dynamically. Therefore, dye leaching, aggregation, and staining are highly valued and well documented in the literature [34]. There are few problems with the existing models available.

Problems with related models:

- Retinal pathology is masked by macular leakage that causes hemorrhage
- central aperture is the location and depth of corneal darkness.
- Imaging techniques are not deeply resolved, making it difficult to determine the extent of neovascularization due to contrast leakage.

One retinal illness that affects the eye is called choroidal neovascularization (CNV), particularly the one that causes AMD. The development of new blood cells visible in the retinal vasculature is what clearly defines the diabetic eye's vascular zone (FAZ), displays minute microvascular anomalies in the diabetic eye, and indicates vascular occlusion. OCTA can also show optic disc degeneration in glaucomatous eyes. Therefore, in order to identify the pathology's central site, it is vital to know the type of obstruction and leakage. The review study of OCTA imaging is organized as follows: The current paradigm for diagnosing DR based on blood flow analysis is described in Part 2 of

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this article. Section 3 describes the problems with the existing model. Chapter 5 describes future goals. Section 4 provides a comparative analysis and Section 5 summarizes future work.

II. TAXONOMY FOR DR DETECTION BASED ON BLOOD FLOW ANALYSIS

A various approaches of DR detection based on blood flow analysis is shown in Figure 2. The figure gives an idea of possible ways to detect DR. Structural methods such as detection of retinal microvascular lesions and segmentation of diabetic macular edema are used as diagnostic methods for DR. Another approach is based on the analysis of perfusion index using local retinal vessels and retinal blood flow. Nabila Eladawi and Mohammed Elmoghi [35] examined the use of optical coherence tomography angiography (OCTA) images for local retinal vascular investigation in the early detection of diabetic retinopathy.

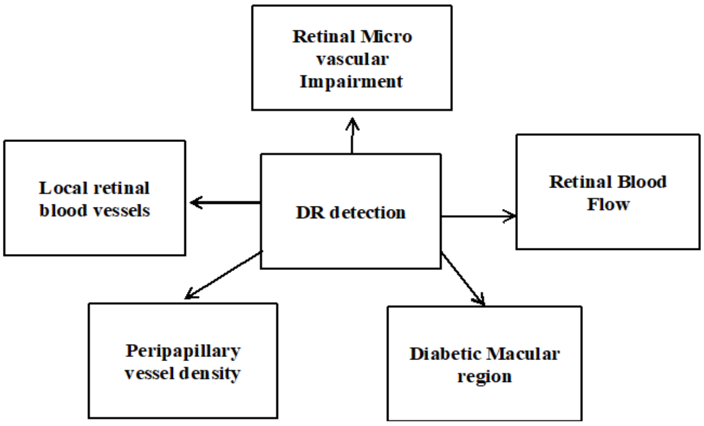

Figure 2. Approaches of DR detection

Nabila Eladawi and Mohammed Elmoghi [35] examined the use of optical coherence tomography angiography (OCTA) images for local retinal vascular investigation in the early detection of diabetic retinopathy. The Markov-Gibbs random field model, which combines a first-order body shape model with a three-dimensional spatial statistical model, is what gives the segmentation approach its outstanding performance. Following the segmentation procedure, the segmented vessel and FAZ are used to calculate three new local properties: vessel density, vessel caliber, and FAZ breadth. The goal of future research will be to find more features that can enhance CAD systems' capacity for diagnostics. This technique can also be applied to the analysis of other retinal disorders. Jorge Gonzalez-Zamora et al. [36] diagnosed bilateral COVID-19 pneumonia with retinal microvascular damage based on optical coherence CT angiography. The assessment of vascular density (VD) and vascular zone (FAZ) was conducted in the shallow deep capillary system (SCP, DCP) and the choriocapillaris. (CC). Each patient had only one eye chosen for them based on the exclusion criteria, and a total of 50 eyes—25 patients and 25 controls—were used in the study. In the end, this research shows that VD and FAZ expansion are lower in patients with bilateral pneumonia and COVID-19 when compared to controls of similar ages and sexes. Furthermore, GCL thickness was lower in COVID-19 patients relative to controls, while RNFL thickness was larger in patients without CWS than in controls. The danger of contamination in personal care is minimal if the suggested safety measures are followed, therefore OCTA should be used to assess the patient's microvascular condition and choose the best course of systemic medication. We think patients may find it to be a helpful test.

Omer Aharony et al. [37] developed an automatic classification of retinal blood flow using angiography. The method provides quantitative information extracted from angiograms, including total vascular density, fractal dimension, and FAZ area, and automatically classifies images into one of four groups (healthy, DR, AMD, or RVO). The classification results were compared with the diagnosis made by retinal specialists. The quantitative results were contrasted with those found in the literature and on OCTA machines. It's also less expensive than what the OCTA machine charges. However, the blood vessel density in healthy persons is higher than the majority of current values,

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which can be considered the standard. (based on the layers of the retina). The vessel density numbers that our method computes are substantially less than the values that the OCTA instrument and the literature indicate.

Sahar Hojjati and others. [38] used the MATLAB software package to automatically extract flow indices from Oct-A image scans using automated vessel manipulation technique. They created a basic piece of software in this paper to take off artificial shadows and extract digital information from Oct-A images. For this purpose, deep optic nerve data using blood flow data in the form of vascular density (DV) map (lift) from a 4.5 x 4.5 mm rectangular scanner focused on the optic nerve head has been acquired, measured the raw image and small vessel data from the image, those being peripapillary region (PP) and the superior and inferior regions. This characteristic was crucial to the understanding and diagnosis of hematological diseases. Since compression was only observed in a small percentage of scans, it is thought to be artifact rather than vascular tissue. Although the current study does not exclude this area from the calculation of VD, this can be considered in future work.

A hybrid computer-aided diagnostic design for detection of retinopathy was created by Mohammed Ramzi Ibrahim et al. [39] by fusing optical coherence tomographic scans with machine learning, and localization methods. The central chorioretinopathy (CC) identifiable through spectral domain optical coherence tomography (SD-OCT) images serve as the foundation for the HyCAD hybrid learning system, which blends deep learning architecture with region of interest (RoI) segmentation. The suggested system combines a number of techniques, such as feature extraction, classification, and detection, as well as ROI localization. An efficient feature fusion step is presented to merge these features that were extracted from the ROI segmentation step with the OCT image by deep convolutional neural network (CNN). Finally, a novel robust diagnostic method is presented to support ophthalmologists in their decision-making about various retinal illnesses, providing automated ROI segmentation. Moreover, HyCAD is a generic design that lacks fundamental presumptions that hinder generalization, making it easy to learn and apply to related issues..

Anne-Sofie Wessel Lindberg and others[40], proposed a technique to visualize retina vessel density This process generates a vessel density heat map that shows the area of vessel density. In a case study, this technique was applied to show its applicability and promise for researching how local conditions affect vessel density. This method has been used to show its value and promise for researching how local conditions affect vessel density in small-scale environments. Further study is necessary, and given how quickly OCTA quality is improving, high-density studies can aid in the investigation of this problem. To get around this issue, we only took into account OCTA scans with SSI that were bigger than 50. In the image from October, Joaquim de Moura et al. [41] devised a methodology for segmentation and characterization of diabetic macular edema(DME). This article introduced a system which is completely automated for the recognition, classification, and segmentation of three types of ME in this context utilizing. OCT images. For the precise discovery and identification of SRD and CME swelling, a variety of techniques are used to match active shape segments and contours. For, DRT edema, a thorough analysis using learning methods for intensity, structure, and clinical data is recommended because of the condition's hazy localization, which necessitates a difficult extraction procedure. They intend to greatly increase the size of their database for Convolutional Neural Network (CNN) applications as part of their ongoing research. The work can be expanded to use the suggested technique to automatically identify other retina related diseases like AMD, Central serous retinopathy, and peripheral retinal holes after taking the potential of other structures into consideration.

Deep learning techniques were used by Yukukun Guo et al. [42] to create an automated segmentation of retinal fluid from OCT and OCTA. For the identification and segmentation of retinal fluid, CNN and U-Net architecture was designed. To train and evaluate ReF-Net, cross-sectional Oct scans and angiography frames are used. In this research, they looked into, how segmenting retinal fluid was affected by OCTA data. The volumetric amount of retinal fluid could be constructed using the ReF-Net result. This deep learning method can accurately used to segment the volumetric content of retinal fluid in OCT/OCTA images and is robust against shadowing artifacts. OCTA scans can improve retinal fluid segmentation. The volumetric representation of the retinal fluid is superior than the two-dimensional projection. Nonetheless, differences are easy to identify in the later stages of retinal detachment. Another limitation is the decision-making procedures.

In order to create reliable multimodal captures of fluorescence in optical coherence tomography and angiographic images, Javier Martnez-Rio et al. [43] used evolutionary algorithms. However, FA and OCTA pairs must be pre-registered so that their shared areas overlap and the image is focused on the area of interest in order to make this analysis easier. In this article, they suggested a three-step process for reliable multimodal registration of surface tissue in an OCTA picture. To minimize the noise and separation of the main vessels in both kinds of images, a special pre-processing step is performed first. The preprocessed data is used in the second step to make a rough match based on matching patterns. To get the best registration, an evolutionary algorithm which is based on differential evolution was used in third stage to filter the prior registration. Nonetheless, research in the relevant literature suggests that this process is complex. On the one hand, the requirement for two OCTA and FA picture blocks offers a great opportunity for the advancement of alternative deep learning-based computing methods for more less retinal analysis. Because these methods yield more precise results, they may handle more complex problems, such as spotting early pathology indications.

III. PROBLEMS WITH EXISTING MODELS

Problems with the current models include:
• Corneal opacities, dark iris pigment, and large blood vessels in anterior OCTA may not indicate an iris tumor.
• Low flow density of small-diameter red blood vessels may create the detection limit, resulting in low detection effectiveness for the vessels with the lowest flow rate.
• current models are mainly optimized for posterior vessels with continuous blood flow and fail to identify anterior vessels with axial flow.
• Artifacts from eye movements degrade image quality, drag artifacts, and damage blood vessels.
• High resistance movement reduces the effect of movement, but must be offset by blood flow. A quick search can miss a slow moving ship.
• Small eye movement and lack of commercially available high-speed equipment, optimal motion artifact correction algorithms, projection artifacts that reduce depth estimation and reliability, small area of commercially available OCTA equipment, and equipment variability. The difference between the measurements taken
• Ocular pathology-affected eyes exhibit high levels of tilt, movement, and segmentation abnormalities. While automatic segmentation frequently separates irregular layers wrongly, manual segmentation takes a lot of time.
Future Goals
Our future goals are as follows.
• Automatic Registration and Selective Merging (RSM) algorithms improve image quality and remove minor artifacts after registration.
• Eye tracking system will significantly reduce dynamic artifacts. The use of OCTA is very limited due to the narrow image area.
• Wavelength-sensitive adaptive optics improve imaging of the peripheral retina and produce sharp wide-angle mosaic images.
• OCTA's advanced technology will be an important advance in increasing the use of OCTA by physicians.
• Comprehensive standardized data on vascular indices in normal and diseased eyes measured by each instrument should be collected and used as future reference values.

IV. COMPARATIVE ANALYSIS

Table 1 provides a comparison of existing models using OCTA for state-of-the-art blood flow analysis.

Authors	**Method**	**Advantage**	**Limitation**	**Performance measure**
Nabila Eladawi and Mohammed Elmogy [35]	support vector machine (SVM) classifier with the radial basis function (RBF)	The segmentation step, three new local features are estimated from the segmented vessels and the foveal avascular zone and test a SVM classifier with the radial basis function (RBF)	In our future work, we will investigate this point by adding more features to the 3D segmentation model and study their impact on the diagnostic accuracy	Accuracy of 94.3%, a sensitivity of 97.9%, a specificity of 87.0%, the area under the curve (AUC) of 92.4%, and a Dice similarity coefficient (DSC) of 95.8%.
Mohamed M. Abdelsalam [44]	Multi fractal Geometry Analysis	Analyzing the macular OCTA images for diagnosing early Non-Proliferative Diabetic Retinopathy (NPDR)	In case of the large number of features,an over-fitting problem was occurred and Long training time was consumed for large datasets	Accuracy = 98.5 Precision = 96.8 Sensitivity= 100 Specificity=97.3

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	Support Vector Machine (SVM)	analyzed the multi fractal geometry . Using SVM algorithm automate the diagnosis process and improving the resultant accuracy.	was by SVM	
Mohamed M.Abdelsalam [45]	Artificial Neural Network	Blood vessel reconstruction, enhancement, and re-continuity using written custom programs, and Artificial Neural Network (ANN) as an automatic classifier between the diabetic without diabetic retinopathy (DR) and the Mild to Moderate NPDR subjects.	The study aims at detecting the early stages, which may be confused at times based on the quality of the images or multiple diagnoses to make the appropriate decision.	Accuracy=97%. sensitivity =97.5% , Specificity 96.67%, and precision of 95.2%
Toshihiko Nagasawa [46]	Deep Convolutional Neural Network	The combination of Optos and OCTA imaging with DCNN could detect DR at desirable levels of accuracy and may be useful in clinical practice and retinal screening. accurate results.	Deep learning generally requires more than a million samples to train without over fitting	AUC of 0.981, 0.928, and 0.964; sensitivity rates of 90.2%, 74.5%, and 80.4%; and specificity rates of 97%, 97%, and 96.4%,

VI.CONCLUSION

The future of retinal blood flow analysis methods for DR imaging is promising. Qualitative imaging of vascular

Table 1: comparison of existing models of advanced techniques for blood flow analysis using OCTA

changes at different stages of DR will improve our understanding of the pathophysiology of DR. Quantitative measurement of retinal blood flow provides an objective assessment of chronic vascular changes in the retina, choroid, and optic nerve, demonstrating its potential as an objective tool to monitor DR progression. This study has limitations. First, it is not possible to explain how deep learning improves retinal blood flow for image quality analysis because deep learning algorithms automatically extract parameters from training. Second, a small patient sample can mask small differences between groups. Third, because the training data set is based on the average retinal perfusion analysis images, we did not evaluate spatial images larger than 3x3 in this study. Fourth, only superficial vascular plaques were evaluated in this study. This is due to the implementation of the same strategy for deep vessels until the exhibition. FUTURE, a new deep learning technique, provides high-quality retinal blood flow analysis compared to multi-image averaging and single-cycle acquisition time. This learning-based denoising technique has the potential to facilitate research on retinal microvasculature. Wide retinal blood flow analysis techniques can provide a wider area of the peripheral retina and improve the detection of peripheral retinal perfusion and neovascularization.

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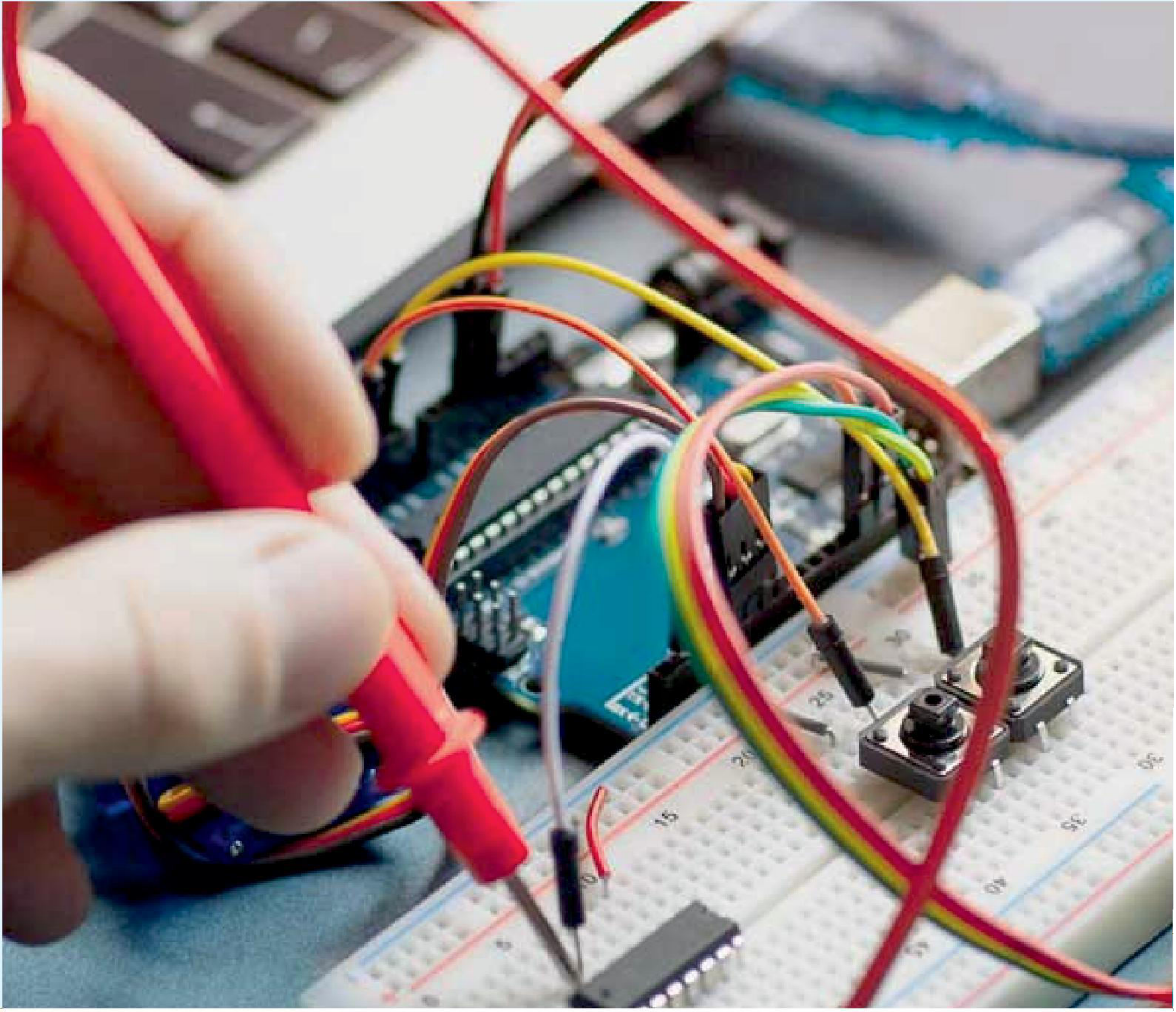

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