

Automated Image Analysis for Gastrointestinal Polyp and Ulcer Identification towards Sustainable Health Diagnostics

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Abstract

Wireless capsule endoscopy (WCE) is an advanced imaging technology for the diagnosis of patients remotely during gastrointestinal (GI) procedures, thereby improving patient comfort and data resolution. The WCE procedure involves a swallowable miniature camera device equipped with light emitting diodes (LEDs) to record images of the GI tract. These images are then transmitted to gastroenterologists to examine the images to identify clinical conditions or abnormalities such as polyps, lesions, or bleeding, thereby facilitating diagnostic evaluations. The recorded images have a significant amount of redundancy, along with low-resolution or unclear features which need to be removed to extract useful information from the recorded images. A number of deep learning models have been developed for automated detection of polyps and ulcers, each having their benefits and drawbacks. Colorectal polyps exhibit diverse shape, texture, and color features even within a single patient's video, complicating the task of recognizing polyps and ulcers. Here we review the deep learning models for the detection and segmentation of polyps and ulcers from WCE recorded videos, the challenges involved in data segmentation and image processing, and future outlook in automated polyp and ulcer detection.

Introduction

Video capsule endoscopy (VCE) is an advanced imaging method employed for visualizing the gastrointestinal (GI) tract and associated clinical conditions [1-5]. Compared to tethered endoscopy, VCE offers portability and ease of use, making it particularly valuable for remote monitoring healthcare services. It involves the use of a swallowable miniature camera device equipped with light emitting diodes (LEDs) to capture digital photographs of the GI tract [5-7]. These images are then transmitted to a portable recording device for post-analysis. Gastroenterologists examine the images to identify abnormalities such as polyps, lesions, or bleeding, thereby facilitating diagnostic evaluations. A typical VCE recording session generates over 50,000 images over a duration of eight to ten hours, making the manual analysis process very time consuming [1-3]. Therefore, the development of an efficient and accurate automatic detection method would alleviate the workload for medical experts. The processing of the vast amount of video data generated during VCE procedures requires substantial computational resources for analysis and retrieval of pertinent video frames. To manage the extensive video data produced by

VCE, it is essential to leverage the techniques deployed in image processing, computer vision, and machine learning [6-16].

Wireless capsule endoscopy

Wireless capsule endoscopy (WCE) facilitates the diagnosis of patients remotely, thereby improving their healthcare accessibility and patient comfort during the procedure. This swallowable technology is primarily designed to offer diagnostic imaging of the entire digestive tract. Within WCE, patients ingest a pill-sized capsule containing a miniature camera, light source, RF transmitter, and batteries. As the capsule traverses the gastrointestinal (GI) tract propelled by normal peristalsis, it records visual footage. These captured frames are transmitted via a small wireless sensor device to a portable receiver positioned outside the body. Presently, wireless capsule batteries typically endure around eight hours, generally sufficient for comprehensive GI imaging. Although most capsules are naturally expelled within 72 hours, the initial eight-hour period is crucial for capturing GI visuals. Consequently, a standard WCE procedure lasts approximately eight hours, yielding an average of 50,000 image frames at a rate of two frames per second. The visualization of the GI tract empowers physicians to identify diseases in their early stages. Moreover, the data gathered from remote patient monitoring using body sensors equips doctors to promptly address any anomalies and implement suitable interventions.

Wireless capsule endoscopy serves as a valuable complement to colonoscopy in non-invasively diagnostics of the digestive system. WCE can either complement incomplete colonoscopies or serve as an investigative tool to assess the necessity for therapeutic colonoscopies or surgery [10-21]. The invasive nature of traditional colonoscopy may lead to discomfort and undesired side effects, potentially impacting acceptability and causing diagnostic delays; initiating with a capsule study could mitigate some of these concerns. While severe complications following colonoscopies are rare in screening programs, the relatively significant number of investigations with relatively few positive findings raises concerns. Colon capsule endoscopy (CCE) proves particularly beneficial for patients with prior incomplete colonoscopy attempts. CCE may complement an unfinished colonoscopy investigation by capturing the furthest point reached in the previous attempt. As the capsule traverses the intestine, it captures frames transmitted wirelessly to a mobile receiver. The portability of these CCE systems allows patients to maintain their regular daily activities without being confined to medical facilities. Studies demonstrate that capsule-based endoscopy aids in detecting several clinically relevant features in the GI tract, including intestinal bleeding, ulcers, vascular lesions, inflammatory diseases, polyps, tumors, and cancers [16-22].

Wireless capsule endoscopy (WCE) videos contain substantial redundant data, with only a fraction being diagnostically useful or informative [1-4]. The capsule's camera captures mucosal images across various scales and orientations, leading to redundancy in the data. Non-informative image frames can arise from exposure to turbid fluids and food particles. Consequently, extraction of key information from the recorded videos (i.e., video summarization) becomes crucial in WCE to address the challenges of storage and efficient browsing posed by the large, unrefined dataset. Video summarization offers a practical solution, saving transmission costs and reducing the time required for doctors to review patient information. However, implementing high-level signal

processing solutions like video summarization directly on wireless WCE is impractical due to its limited memory, energy, and computational capabilities. Additionally, transmitting extensive video data before processing is unfeasible due to its high energy consumption [23-30]. Analyzing WCE videos on local servers, such as smartphones, is a viable alternative. Smartphones, with their advanced hardware and operating systems, serve as excellent platforms for performing low-level computer vision tasks and acting as WCE-coordinators. Their portability enables patients wearing wireless sensors to engage in outdoor activities, making them ideal for remote monitoring solutions. A visual attention-based WCE video summarization scheme has been proposed, leveraging the integral-image concept for efficient computation of visual saliency, suitable for smartphones. However, smartphones' limitations in computing power, energy supply, and storage hinder their ability to support long-duration remote monitoring applications. Mobile-cloud computing emerges as a solution to overcome these constraints, enabling the generation of video summaries and deploying cost-effective pervasive healthcare systems [29-35].

Convolutional Neural Networks (CNNs)

Medical image analysis benefits greatly from the application of deep learning tools. Deep learning has proven its efficacy in automating disease diagnosis, thereby enhancing medical image examination. This advancement in medical image analysis helps clinicians and healthcare professionals with improved capabilities for early disease detection, potentially helping with prognosis and formulation of effective treatment strategies. In the realm of medical imaging, several deep learning models have been developed and deployed. Among these, convolutional neural networks (CNNs) are capable of automatically extracting high-level features from multi-dimensional data with remarkable accuracy. CNNs possess the versatility to process data in diverse forms, including signals, images, and videos, thereby offering comprehensive solutions in medical image applications [24-33].

Typically, a Convolutional Neural Network (CNN) architecture comprises three types of layers: convolutional, pooling, and fully connected layers [6, 34-42]. CNN layers organize neurons in three dimensions—width, height, and depth. Each layer in a CNN transforms a 3D input volume into a 3D output volume of neuron activations. Notably, not all neurons in one layer need to be connected to all neurons in the next layer. The input data undergoes sequences of convolutions and pooling operations using filters to generate feature maps, which are then combined to produce the final output of the convolutional layer. This layer is regarded as the fundamental building block of a CNN and consequently contributes to the time-consuming training process. Within these layers, a convolution operation is applied to compute neuron outputs, with the parameters of convolutional layers sharing sets of weights. The pooling layers utilize nonlinear down-sampling techniques, with max pooling being a popular choice. In max pooling, the input is divided into non-overlapping groups, and the maximum value within each group becomes the output [6]. Max-pooling layers effectively reduce the number of parameters, mitigate the risk of overfitting, and lessen the computational complexity of the network. Hence, a max-pooling layer is commonly inserted between convolutional layers.

Several pretrained CNN models are available in the literature, such as AlexNet, VGGNet, GoogleNet, and ResNet. Among these, GoogleNet and AlexNet are frequently employed for

feature extraction and classification, delivering excellent results. Pretrained networks are fine-tuned by freezing the weights of the initial layers during system training, while the fully connected layers, responsible for mapping the feature representations into class label information, undergo fine-tuning [33-40].

Automatic Polyp Detection Techniques

Various automatic polyp detection algorithms have been proposed, each with its level of success and model accuracy [10-21]. While the field of polyp detection in colonoscopy and traditional endoscopy images is advancing, detecting polyps automatically in Video Capsule Endoscopy (VCE) presents unique challenges due to its distinct imaging characteristics. Here, we examine the different approaches to polyp detection in VCE imagery and highlight the challenges faced by conventional image processing and computer vision methods. Detecting polyps in VCE imagery stands as a key challenge in developing automated computer-aided detection and diagnosis systems [5-9]. Physicians typically characterize polyps based on their distinctive shapes, colors, and textures, which can often resemble shades of red or rose and exhibit textures akin to the human brain. In colonoscopy imagery, polyp detection approaches encompass utilizing features such as elliptical shapes, texture, color, and position features.

Polyp detection techniques employed in colonoscopy and Computed Tomography (CT) colonography predominantly rely on geometry-based methods [21-38]. However, the unique imaging modality of Video Capsule Endoscopy (VCE) necessitates distinct approaches for efficient polyp detection across its various frames. While several shape-based schemes have been proposed for virtual colonoscopy or CT colonography, most rely on reconstructed surfaces representing the colon's interior or specific imaging techniques. In contrast, VCE employs an unaided photographic device that moves autonomously, prone to illumination saturation from near-field lighting. VCE images markedly differ from those obtained via traditional colonoscopy. For instance, liquid content in the lumen section is less in colonoscopy, resulting in more specular images. Conversely, VCE images exhibit diffusive mucosa tissue due to the presence of liquid, with trash and turbidity hindering mucosal surface visibility. The unaided movement of the capsule camera introduces blurring effects, reducing image sharpness, while mucosal tissue color under VCE presents peculiar characteristics. Consequently, VCE's sensitivity for detecting colonic lesions is lower compared to optical colonoscopy. Although capsule endoscopy effectively detects colorectal polyps, especially in the colon, challenges persist in small-bowel and esophageal examinations. Advances in sensor and camera technology have improved sensitivity and specificity for detecting colorectal polyps, yet increased imaging complexity and higher frame rates place a greater burden on gastroenterologists. Thus, the development of efficient, robust automatic computer-aided detection and segmentation methods for colorectal polyps is crucial.

The variable lighting and sporadic occurrence of polyps in VCE videos pose challenges in devising reliable detection and segmentation methods [3-12]. Polyp detection/segmentation methods can be classified into two categories: (a) polyp detection—identifying frames containing polyps, without necessarily pinpointing their exact locations within the frame; and (b) polyp segmentation—segmenting the mucosal area in frames containing polyps. Polyp detection is more challenging due to the rarity of polyp-containing frames, necessitating machine learning-based

approaches. Colorectal polyps exhibit diverse shape, texture, and color features even within a single patient's video, complicating the task. Despite these challenges, efforts have been made in automatic data-driven algorithms for identifying polyp frames. Polyp segmentation is comparatively simpler, as algorithms need only analyze individual polyp-containing frames to locate and localize polyps [17-21].

Automatic polyp detection and segmentation is an emerging field that necessitates the application of advanced computer vision methodologies, including geometrical primitives, color spaces, texture descriptors, feature matching, and robust machine learning components [8-20]. Traditional polyp detection methods in colonoscopy imagery often rely on the assumption that polyps exhibit high geometrical features, such as well-defined shapes or protrusions from mucosal surfaces. Consequently, curvature measures are commonly employed for polyp detection, albeit with limited success when applied to Video Capsule Endoscopy (VCE) imagery. Additionally, in video sequences, neighboring frames may only provide a partial view of the polyp, with mucosa folds presenting similar textures, further complicating detection. Similarly, the color of polyps varies within a patient's video and significantly across different patient examinations.

A comprehensive learning framework may incorporate both local and global texture features, vascularization, and color information to distinguish polyps [33-45]. However, existing approaches encounter challenges such as the presence of debris and bubbles, as VCE exams do not require colon cleaning. Robust polyp detection methods must integrate efficient trash and bubble detectors to mitigate false positives. An integrated approach that combines motion, geometry, color, and texture with a robust machine learning paradigm holds promise for achieving reliable and efficient automatic polyp detection in VCE imagery.

Future Outlook of Automatic Polyp Detection

Drawing insights from current polyp detection and segmentation methods provides valuable perspectives for the future trajectory of this technology. The recent surge of interest in deep learning presents a promising avenue, as neural network-based classifiers trained on vast datasets show potential for distinguishing polyp frames from normal frames more effectively [27-33]. However, deep learning networks typically require extensive training data, particularly labeled samples of positive (polyp frames) and negative (normal frames). One potential solution to address data imbalance is data augmentation, wherein polyp frames are artificially augmented through perturbation.

In the past two years, significant strides have been made in endoscopy image analysis using deep learning, alongside other approaches such as deep sparse feature selection [10-23]. Establishing a well-defined database with polyp regions marked by expert gastroenterologists is crucial for benchmarking and standardizing different methodologies for automatic polyp detection and segmentation. Improvements in sensor technology, including novel capsule systems with enhanced image resolution, standardized illumination/contrast, controlled capsule speed, and variable image capturing mechanisms, hold promise for facilitating automatic image analysis. Embedding image analysis within capsule endoscopy imaging systems is an exciting research avenue, enabling real-time decision-making by gastroenterologists [1-5].

Despite these advancements, some challenges need to be addressed to provide realistic value to patients and medical practitioners [40-47]. In recent years, deep learning has emerged as a leading force in automated analysis and recognition, demonstrating significant advancements over traditional machine learning algorithms. Deep learning methods are widely regarded as credible solutions for automated detection and diagnosis of abnormalities in medical images. Future applications of this research will focus on evaluating its clinical feasibility, particularly in aiding the localization of significant findings like colorectal polyps, in conjunction with polyp detection algorithms, and estimating the completeness of investigations [6, 29-33].

Future research will also address challenges such as validation and error propagation in localization, along with exploring extensions to reconstructing the small intestine using visual-based processing techniques [9-19]. As neural networks continue to advance in image processing, smart image processing holds promise for future applications. Deep learning and smart image processing in capsule endoscopy have garnered attention for texture classification, polyp and abnormality detection and segmentation, and localization [3-12]. Notable innovation lies in the utilization of pretrained CNN models for identifying ulcer regions in Wireless Capsule Endoscopy (WCE) images. Models like GoogleNet and AlexNet, pretrained on a subset of the ImageNet database, have demonstrated zero classification error and 100% accuracy in detecting ulcers under specific network parameter settings, despite limited data availability.

References

- [1]. Iddan, G.; Meron, G.; Glukhovsky, A.; Swain, F. Wireless capsule endoscopy. *Nature*, 405, 417, 2000.
- [2]. Dylan Miley, et al., "Video Capsule Endoscopy and Ingestible Electronics: Emerging Trends in Sensors, Circuits, Materials, Telemetry, Optics, and Rapid Reading Software", *Advanced Devices & Instrumentation*, Volume 2021, Article ID 9854040, 2021.
- [3]. Iakovidis, D.K.; Maroulis, D.E.; Karkanis, S.A. An intelligent system for automatic detection of gastrointestinal adenomas in video endoscopy. *Comput. Biol. Med.* 36, 1084–1103, 2006.
- [4]. Paik, D.S.; Beaulieu, C.F.; Rubin, G.D.; Acar, B.; Jeffrey, R.B., Jr.; Yee, J.; Dey, J.; Napel, S. Surface normal overlap: A computer-aided detection algorithm with application to colonic polyps and lung nodules in helical CT. *IEEE Trans. Med. Imaging*, 23, 661–675, 2004.
- [5]. Li, B.; Meng, M.Q.H. Automatic polyp detection for wireless capsule endoscopy images. *Expert Syst. Appl.* 39, 10952–10958, 2012.
- [6]. U. Kalwa, et al., "Skin Cancer Diagnostics with an All-Inclusive Smartphone Application." *MDPI Symmetry*, 11, 790-809, 2019.
- [7]. Yuan, Y.; Li, B.; Meng, M.Q.H. Improved bag of feature for automatic polyp detection in wireless capsule endoscopy images. *IEEE Trans. Autom. Sci. Eng.* 13, 529–535, 2016.
- [8]. Yuan, Y.; Li, B.; Meng, M.Q.H. WCE abnormality detection based on saliency and adaptive locality-constrained linear coding. *IEEE Trans. Autom. Sci. Eng.* 1–1, 2016..
- [9]. Xianting Ding, et al., "Effective drug combination for *Caenorhabditis elegans* nematodes discovered by output-driven feedback system control technique", *Science advances*, 3 (10), eaa01254, 2017.
- [10]. Cong, Y.; Wang, S.; Liu, J.; Cao, J.; Yang, Y.; Luo, J. Deep sparse feature selection for computer aided endoscopy diagnosis. *Pattern Recognit.* 48, 907–917, 2015.

- [11]. Iakovidis, D.K.; Koulaouzidis, A. Software for enhanced video capsule endoscopy: Challenges for essential progress. *Nat. Rev. Gastroenterol. Hepatol.* 12, 172–186, 2015.
- [12]. Van Wijk, C.; Van Ravesteijn, V.F.; Vos, F.M.; Van Vliet, L.J. Detection and segmentation of colonic polyps on implicit isosurfaces by second principal curvature flow. *IEEE Trans. Med. Imaging*, 29, 688–698, 2010.
- [13]. Deutmeyer, P. Murphy, R. Raman, et al., “Effect of magnetic field on the fermentation kinetics of *Saccharomyces cerevisiae*”, *Advances in Bioscience and Biotechnology*, 2(4), 207-213, 2011.
- [14]. S. Pandey, “Analytical Modeling of the Ion Number Fluctuations in Biological Ion Channels”, *Journal of Nanoscience and Nanotechnology*, 12(3), 2489-2495, 2012.
- [15]. Spada, C.; Hassan, C.; Munoz-Navas, M.; Neuhaus, H.; Deviere, J.; Fockens, P.; Coron, E.; Gay, G.; Toth, E.; Riccioni, M.E.; et al. Second-generation colon capsule endoscopy compared with colonoscopy. *Gastrointest. Endosc.* 74, 581–589, 2011.
- [16]. Nawarathna, R.; Oh, J.; Muthukudage, J.; Tavanapong, W.; Wong, J.; De Groen, P.C.; Tang, S.J. Abnormal image detection in endoscopy videos using a filter bank and local binary patterns. *Neurocomputing* 144, 70–91, 2014.
- [17]. K. Kalantar-Zadeh, N. Ha, J. Z. Ou, and K. J. Berean, “Ingestible sensors,” *ACS Sensors*, vol. 2, no. 4, pp. 468–483, 2017.
- [18]. A.-M. Singeap, “Capsule endoscopy: the road ahead,” *World Journal of Gastroenterology*, vol. 22, no. 1, pp. 369–378, 2016.
- [19]. Axon, “Fifty years of digestive endoscopy: successes, setbacks, solutions and the future,” *Digestive Endoscopy*, vol. 32, no. 3, pp. 290–297, 2020.
- [20]. S. C. Payne, J. B. Furness, and M. J. Stebbing, “Bioelectric neuromodulation for gastrointestinal disorders: effectiveness and mechanisms,” *Nature Reviews Gastroenterology and Hepatology*, vol. 16, no. 2, pp. 89–105, 2019.
- [21]. Vishal Patel, Austin Chesmore, Christopher M. Legner, Santosh Pandey, “Trends in Workplace Wearable Technologies and Connected-Worker Solutions for Next-Generation Occupational Safety, Health, and Productivity”, *Advanced Intelligent Systems*, Article ID 2100099, 2021.
- [22]. B. Chen, et al., “Folded floating-gate CMOS biosensor for the detection of charged biochemical molecules”, *IEEE Sensors*, 2011.
- [23]. M.-M. Pan, Y.-F. Wang, L. Wang, X. Yu, and L. Xu, “Recent advances in visual detection for cancer biomarkers and infectious pathogens,” *Journal of Materials Chemistry B*, vol. 9, no. 1, pp. 35–52, 2021.
- [24]. S. Pandey, A. Bortei-Doku, and M. White, “Simulation of biological ion channels with technology computer-aided design”, *Computer Methods and Programs in Biomedicine*, 85, 1-7, 2007.
- [25]. N. van Helleputte, A. J. G. Even, F. Leonardi et al., “Miniaturized electronic circuit design challenges for ingestible devices,” *Journal of Microelectromechanical Systems*, vol. 29, no. 5, pp. 645–652, 2020.
- [26]. Zach Njus, et al., “Flexible and disposable paper-and plastic-based gel micropads for nematode handling, imaging, and chemical testing”, *APL Bioengineering*, 1 (1), 016102, 2017.
- [27]. F. Munoz, G. Alici, and W. Li, “A review of drug delivery systems for capsule endoscopy,” *Advanced Drug Delivery Reviews*, vol. 71, pp. 77–85, 2014.

- [28]. P. J. Turnbaugh, R. E. Ley, M. Hamady, C. M. Fraser-Liggett, R. Knight, and J. I. Gordon, "The human microbiome project," *Nature*, vol. 449, no. 7164, pp. 804–810, 2007.
- [29]. Upender Kalwa, Taejoon Kong, Baoqing Guo, Phillip C. Gauger, David Peters, Kyoung-Jin Yoon, Behavioral Monitoring Tool for Pig Farmers: Ear Tag Sensors, Machine Intelligence, and Technology Adoption Roadmap, *Animals*, Vol. 11, Issue 9, pages 2665, 2021.
- [30]. L. Wang, A. Mannalithara, G. Singh, and U. Ladabaum, "Low rates of gastrointestinal and non-gastrointestinal complications for screening or surveillance colonoscopies in a population-based study," *Gastroenterology*, vol. 154, no. 3, pp. 540–555.e8, 2018.
- [31]. D. Becker, J. Zhang, T. Heimbach et al., "Novel orally swallowable IntelliCap® device to quantify regional drug absorption in human GI tract using diltiazem as model drug," *Ageing International*, vol. 15, pp. 1490–1497, 2014.
- [32]. K. Kalantar-Zadeh, K. J. Berean, R. E. Burgell, J. G. Muir, and P. R. Gibson, "Intestinal gases: influence on gut disorders and the role of dietary manipulations," *Nature Reviews Gastroenterology & Hepatology*, vol. 16, no. 12, pp. 733–747, 2019.
- [33]. S. N. Adler, "The history of time for capsule endoscopy," *Annals of Translational Medicine*, vol. 5, no. 9, p. 194, 2017.
- [34]. Taejoon Kong, Nicholas Backes, Upender Kalwa, Christopher M. Legner, Gregory J. Phillips, "Adhesive Tape Microfluidics with an Autofocusing Module That Incorporates CRISPR Interference: Applications to Long-Term Bacterial Antibiotic Studies", *ACS Sensors*, 4, 10, 2638-2645, 2019.
- [35]. Christopher Legner, Upender Kalwa, Austin Chesmore, Vishal Patel, "Sweat sensing in the smart wearables era: Towards integrative, multifunctional and body-compliant perspiration analysis", *Sensors and Actuators A*, 296, 200-221, 2019.
- [36]. P. Swain, "Wireless capsule endoscopy," *Gut*, vol. 52, no. 90004, pp. iv48–iv50, 2003.
- [37]. G. Iddan, G. Meron, A. Glukhovsky, and P. Swain, "Wireless capsule endoscopy," *Nature*, vol. 405, no. 6785, p. 417, 2000.
- [38]. S. Pandey and M. White, "Parameter-Extraction of a Two-Compartment Model for Whole-Cell Data Analysis", *Journal of Neuroscience Methods*, 120, 131-143, 2002.
- [39]. L. A. Beardslee, G. E. Banis, S. Chu et al., "Ingestible sensors and sensing systems for minimally invasive diagnosis and monitoring: the next frontier in minimally invasive screening," *ACS Sensors*, vol. 5, no. 4, pp. 891–910, 2020.
- [40]. C. Spada, D. McNamara, E. J. Despott et al., "Performance measures for small-bowel endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) quality improvement initiative," *United European Gastroenterology Journal*, vol. 7, no. 5, pp. 614–641, 2019.
- [41]. D. L. Donoho, "Compressed sensing," *IEEE Transactions on Information Theory*, vol. 52, no. 4, pp. 1289–1306, 2006.
- [42]. Kiourti, K. A. Psathas, and K. S. Nikita, "Implantable and ingestible medical devices with wireless telemetry functionalities: a review of current status and challenges," *Bioelectromagnetics*, vol. 35, no. 1, pp. 1–15, 2014.
- [43]. T. Kong, et al., "A fast, reconfigurable flow switch for paper microfluidics based on selective wetting of folded paper actuator strips", *Lab on a Chip*, 17 (21), 3621-3633, 2017.
- [44]. T. Kong, R. Brien, Z. Njus, U. Kalwa, et al., "Motorized actuation system to perform droplet operations on printed plastic sheets", *Lab Chip*, 16, 1861-1872 (2016).

- [45]. M. J. Christoe, J. Han, and K. Kalantar-Zadeh, "Telecommunications and data processing in flexible electronic systems," *Advanced Materials Technologies*, vol. 5, no. 1, article 1900733, 2020.
- [46]. J. Carr, A. Parashar, R. Gibson, A. Robertson, R. J. Martin, S. Pandey S. A microfluidic platform for high-sensitivity, real-time drug screening on *C. elegans* and parasitic nematodes. *Lab on Chip*, 11(14), 2385-2396, 2011.
- [47]. Kiourti and K. S. Nikita, "A review of in-body biotelemetry devices: implantables, ingestibles, and injectables," *IEEE Transactions on Biomedical Engineering*, vol. 64, no. 7, pp. 1422–1430, 2017.