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Technological Development of Biospeckle Laser: a Systematic Review

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Abstract: Over the last few decades, the known as biospeckle laser (BSL) has been presented by academics as a non-invasive technique alternative of biological materials analysis. Despite the advances observed in it's use, the researches that have been carried out in the universities/institutes have led to modest development of innovative products, or of commercial equipment. Based on this context, the following questions are asked: How can the BSL technique be evaluated in recent decades? What are the determining factors that connect technology to the market? To help answer these questions a systematic review of the literature was carried out with the aim to describe and identify the state-of-art of BSL to know the reasons for the scarcity of a commercial equipment. The results showed a positive and continuous increase of the research involving the BSL during the years, presenting some particular characteristics that can be used to answer the elected questions.

Keywords: Biospeckle Laser (BSL), Systematic Review, Experimental Configuration, Image Analysis Methods

1 INTRODUCTION

Since the '70s, researches have been carried out involving the optical phenomenon known as biospeckle laser (BSL). The first to demonstrate the feasibility of this technique were J. Briers (1975), followed by Asakura (1988) and by Fujii et al (1985) monitoring of blood flow [1], [2], [3]. In the following decades, the technique was applied in many other biological phenomena such as seed analysis [4] and fruits [5], parasite activities [6] among others.

The biospeckle laser (BSL) or dynamic laser speckle (DLS) is an option of non-destructive and non-invasive analysis of biological materials [7]. The phenomenon is observed when a sample of biological material is illuminated by a coherent light source such as the laser. As a result, light scattering occurs forming an interference phenomenon represented by a granular image known as speckle pattern [8]. This phenomenon becomes dynamic when light scatterers change position due to the most diverse physical, chemical and biological phenomena present in the illuminated tissue.

BSL images are captured by a camera [9] and used to analyze biological activities. The activities present in the dynamic laser images require particular conditions to generate useful information through graphical or numerical methods. The graphic output is summarized in the processing of digital images returning maps of the activities, whereas the numerical outputs return unidimensional values that represent the biological activities [10].

Although BSL has been researched for over four decades, there are limited registrations of products based on the use of BSL. Based on this context, the following questions are asked: How can the BSL technique be evaluated in recent decades? What are the determining factors that connect technology to the market?

Thus, the objective of this work was to describe and to identify through a systematic review of the literature the state-of-art of BSL and its particular characteristics to know the reasons for the lack of commercial equipment.

This article is divided in four sections. In the introduction, we explain the purpose and scope of this study. The second section discusses the methodology used to select and evaluate papers that meet the inclusion criteria. In the third section, the results and discussion are presented. Finally, in the fourth section, the conclusions are presented.

2 METHODOLOGY

Research and technological development on biospeckle laser are influenced by innumerable variables, and in this work, these variables will be grouped into two types: I) Experimental set-up, devices, and samples; and II) Methods of image analysis. In type I, the devices used in the experimental configuration of the biospeckle technique vary in relation to the laser type, lenses, camera and the positioning of these in relation to the sample [11]. In addition, the environment where the experiments are performed may contain noise as vibrations that interfere with the results [12].

Regarding type II, many methods can be seen in the literature, but there is no standardization of methods for BSL imaging [10]. Since the samples are diverse, there are many sources of activity observed that can be from the multiple sources of biological phenomena [13], as well from chemical effects [14] and from a variation of pigments [15] which enhance the difficulty to choose a standard method [16] to all applications.

All papers in this systematic review were divided into two categories as shown in Fig. 1 They are AB (Biospeckle Application Papers) and IB (Biospeckle Improvement Papers). In addition, category IB was divided into 2 groups: 1) evolution of experimental configuration, devices, and samples and 2) evolution of image analysis methods.

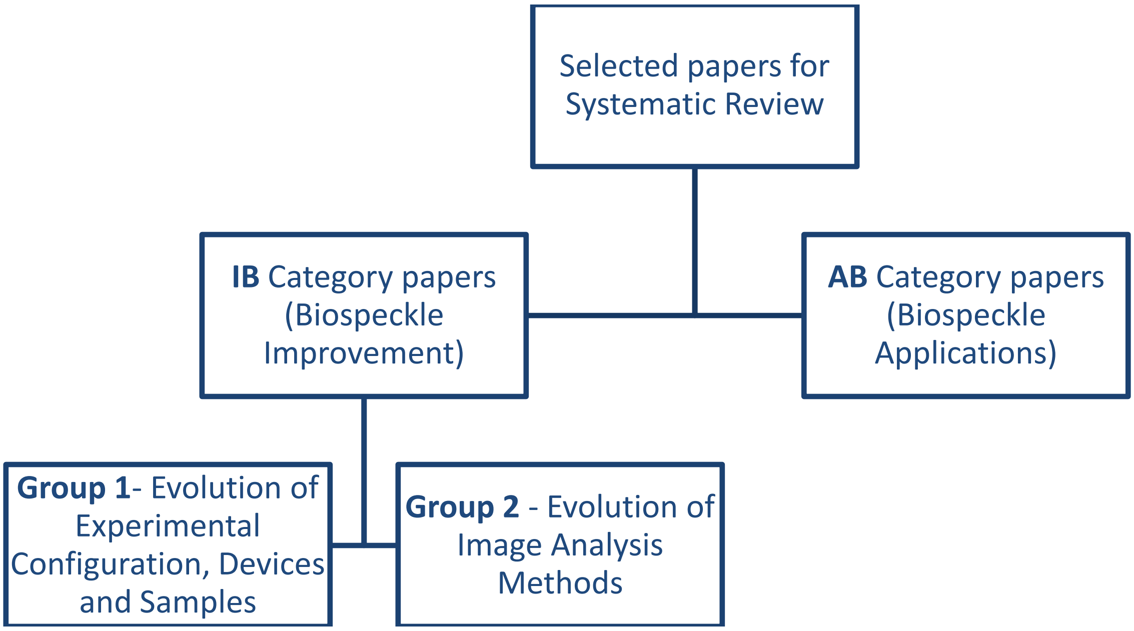

Figure 1: Division of papers into two categories and two groups.

In the IB papers, we found data linked to the evolution of the experimental setup, devices and methods of image analysis in BSL. In other words, these papers presented new methodologies of image analysis or experimental configuration. On the other hand, AB papers are dedicated to the use of BSL in new applications.

2.1 Inclusion Criteria

Five criteria were used to select scientific paper with potential to meet the objective:

1. Papers that address only the application of biospeckle (AB);
2. Papers that report improvements or new methodologies of image analysis or experimental setup of biospeckle (IB) analysis;
3. The Biospeckle should be the main theme technique;
4. Only scientific papers published in internationally recognized journals between 1996 and 2016. Books, conference proceedings and other types of papers will not be considered;
5. There are no restrictions on where the experiments took place. Industry or academic environment.

2.2 Selections of Papers and Research Sources

This part was divided into five steps. The first was the selection of the bases: Science Direct, Scopus and Web of Science as primary sources of research. The second step was the choice of the keywords that selected the largest number of papers. The key words "dynamic speckle" and "biospeckle" were tested, and the biospeckle has resulted in the greatest number of papers. During the search, the word biospeckle should be present in the title of the article "and" in the abstract "or" in keywords. The total number of papers found using only biospeckle was 245.

In the third step, 38 duplicate papers were removed. After reading all the abstracts, in step four, 50 papers were excluded because they did not meet the inclusion criteria. In the fifth step, 157 papers were read completely and another 66 papers were excluded for not meet all the inclusion criteria. The number of papers that met the criteria of inclusion was 91. Fig. 2 shows the selection process of the papers.

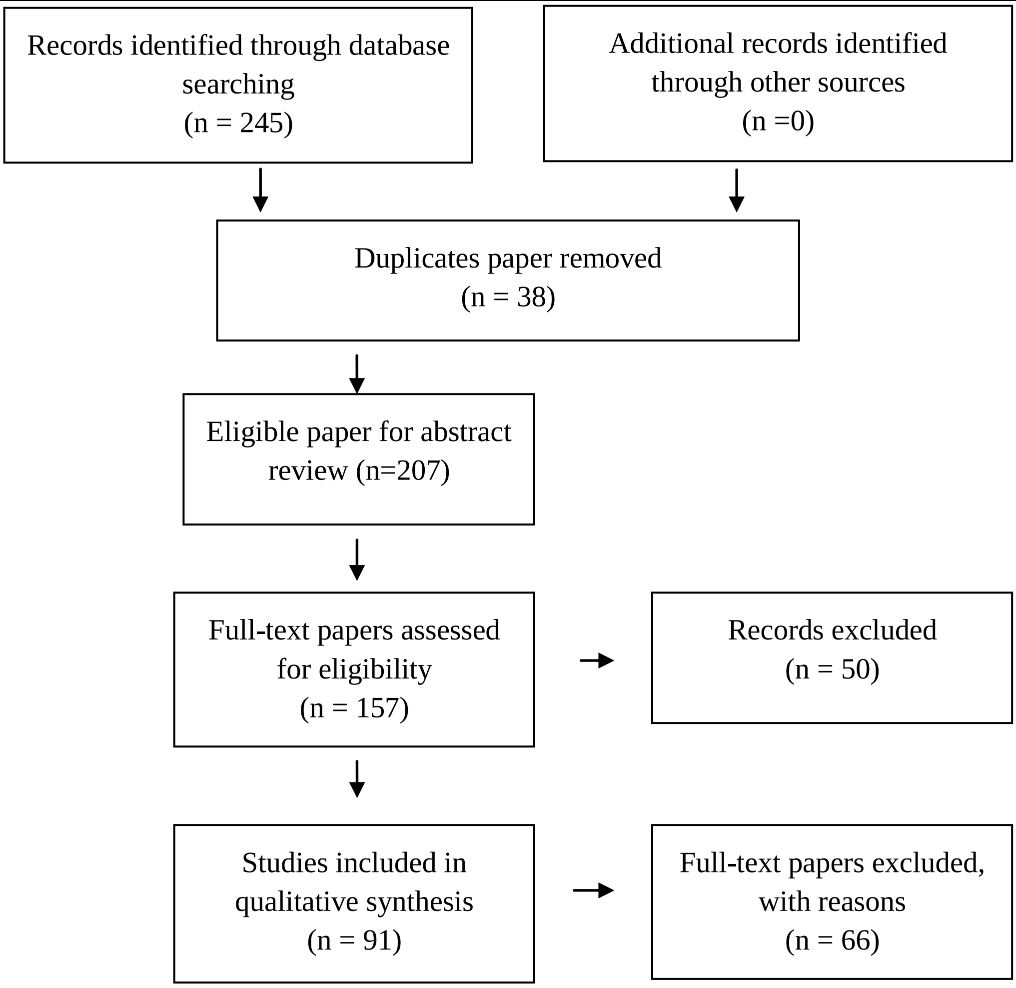

Figure 2: Literature search and selection.

2.3 Data Collections

All 91 papers that met the inclusion criteria were inserted into a spreadsheet to organize and to classify the data, such as into categories AB and IB. Additional information was collected such as methods of image analysis, information about devices used in setup, types of samples, place of the experiment (laboratory or field), year of publication, country, journal, recommendations, and key conclusions.

After data mining, it was possible to use descriptive statistics as averages, standard deviation, and frequency for better visualization, summary, and interpretation of the data. The selection and data collection were performed by two independent researchers with experience in biospeckle and then the results were confronted and adjusted.

3 RESULTS AND DISCUSSION

3.1 General Characteristics Of The Included Studies

The rate of repeated papers between the bases proves the efficiency of the selection. This saturation occurred with 16% of the total papers. As shown in Fig. 1, the 91 papers were divided into two main categories: IB and AB, where in the first category, 33 papers were found, corresponding to 36% of the studies included in the review, and in the second category, 58 papers were selected, or 64%.

In Fig. 3, it is possible to notice that from 1997 to 2002 and in 2010 not one article of IB was published. The papers of AB had publications in all the analyzed years with a peak of growth between the years 2012 and 2014. The standard deviation of the papers of AB is 2.90 with an average of 3 publications per year. The IB papers presented a standard deviation of 1.65 and an average of 1.80 per year.

There is a trend of growth in this field of research throughout the analyzed period. The relevant growth rate from 2010 may indicates a continuous and greater recent interest in this topic.

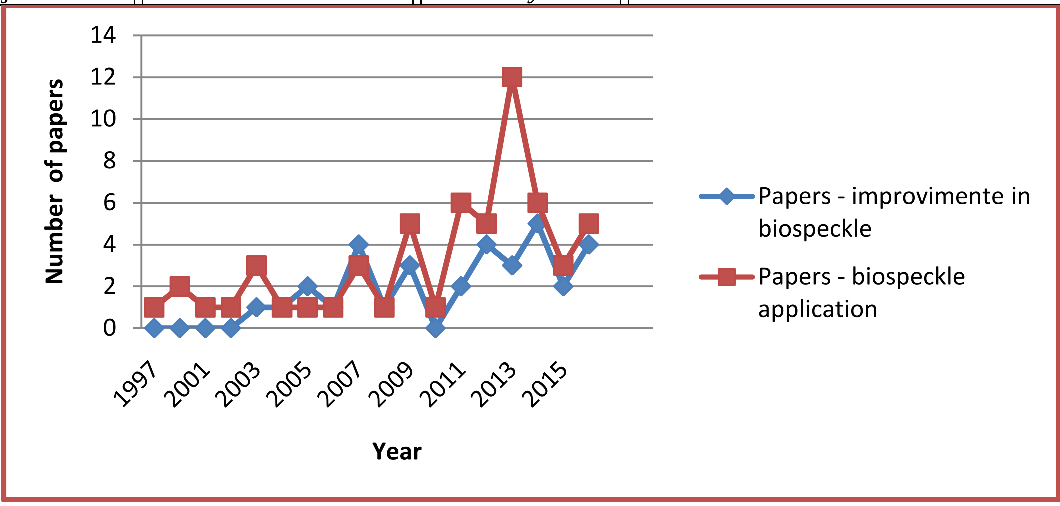

Figure 3: Distribution of IB and AB papers during the period from 1997 to 2016.

The 91 selected papers were published in 46 scientific journals as can be seen in Table 1, where 7 journals published between 4% and 9% of the papers. Fifteen journals published only 1% of the papers.

The journals that published research with BSL are in the fields of engineering, medicine, optics, and agriculture. The higher concentration of research in engineering and optics is indicative of possible areas of concentration of efforts in new researches.

Table 1: Percentage of Publication of paper by journal and subject área.

Jornal and subject area	**%**
Agriculture	
Annals of botany	1,1
Ciência e Agrotecnologia	1,1
Computers and electronics in agriculture	1,1
Food biophysics	1,1
Food Research International	1,1
International Agrophysics	1,1
Journal of Environmental Sciences	1,1
Journal of Food Engineering	1,1
Physiological measurement	1,1
Plant Cell, Tissue and Organ Culture	1,1
Postharvest Biology and Technology	5,5
Revista Brasileira de Engenharia Agricola e Ambiental	1,1
Scientia Horticulturae	1,1
Engineering	
Biosystems Engineering	5,5
Flow Measurement and Instrumentation	1,1
Journal of Engineering Physics and Thermophysics	1,1
Measurement: Journal of the International Measurement Confederation	1,1
Sensors	4,4
Signal Processing	1,1
Medicine	
Acta cirurgica brasileira	1,1
Journal of biomedical optics	4,4

Journal of Medical Imaging and Health Informatics	1,1
Lasers Med Sci	1,1
Optics	
Applied optics	3,3
Biofizika	1,1
EPJ Applied Physics	1,1
European biophysics journal	1,1
Fractals	1,1
Journal of Optics A: Pure and Applied Optics (From 2010 Journal of Optics A: Pure and Applied Optics has become Journal of Optics)	1,1
Journal of Optoelectronics and Advanced Materials	2,2
Journal of Physics: Conference Series	1,1
Journal of the European Optical Society	1,1
Journal of the Optical Society of America A: Optics and Image Science, and Vision	2,2
Laser Physics	2,2
Optica Applicata	1,1
Optical Engineering	1,1
Optics & Laser Technology	3,3
Optics and Lasers in Engineering	9,9
Optics and Spectroscopy (English translation of Optika i Spektroskopiya)	1,1
Optics Communications	9,9
Optics Express	1,1
Optics letters	2,2
Optik - International Journal for Light and Electron Optics	7,7
Physica Scripta	1,1
Proceedings of SPIE-The International Society for Optical Engineering	2,2
Romanian Journal of Physics	1,1

In Table 2, you can see the countries of the authors who contributed the most to the development of the theme, avoiding duplication of contributions if there are more authors from the same country in a specific article. As can be seen, the countries where the biospeckle research was most performed are Brazil, Argentina, and India.

The fact that the researchers are mostly from developing countries can be explained by the following hypotheses: low cost of applying the biospeckle technique and the strong agricultural activity practiced in these countries. The predominance of biospeckle application in agriculture, Table 6, reinforces these hypotheses.

Table 2: Countries leading research with biospeckle.

Country where the searches were made	% (Number of Scientific Journals)
Brazil	32%
Argentina	28%
India	12%
Poland	10%
UK	7%
Japan	4%
Ukraine, China, Romania	3%
Lebanon, France, Bulgária, Germany	2%
Peru, Ireland, Singapore, Belarus, Iran, Venezuela, Italy, Russia, South Korea, Spain	1%

3.2 Experimental Configurations, Devices and Samples

The experimental configuration is the way that devices like lasers, cameras, and lenses are positioned to the biological sample as can be seen in Fig. 4. Additionally, Table 3 lists the information about the experimental configuration, including the details of the spatial arrangement of the equipment.

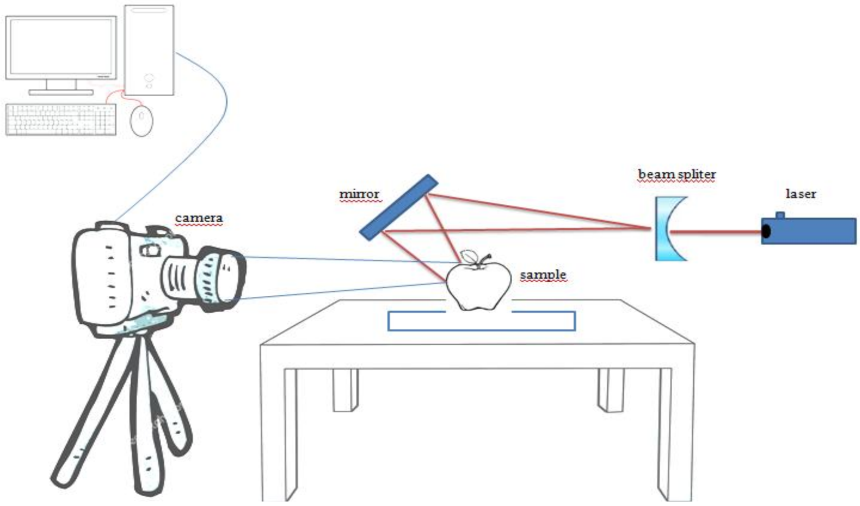

Figure 4: Experimental setup most used in Universities/institutes in research with BSL.

It was observed that in case 2, "Does not describe and has an image", that in 43% of the papers, the sole image was not enough to reproduce the experiment with the same angles and distances.

Table 3: Description of the setup and the existence of explanatory images of the analyzed papers.

Does it describe setup in detail? (angles, distances and explanatory images)	% Papers
1 Does not describe and has no image	17
2 Does not describe and has an image	43
3 Describe and have an image	30
4 Describe and have no image	3
5 Does not use setup (mathematical models, database images)	7

The correct arrangement of the experimental configuration is determinant for the reliability of the biospeckle usage and for the standardization of the results [14]. The lack of standardization of devices and protocols may invalidate the quality of the experiments and the application of techniques as demonstrated by [17] where the lack of standardization in a routine known as Shear Force (SF) compromised the tests.

In this sense, the devices used in the experiments as well as their adjustments and the way the data were analyzed influence directly in the results of the research creating some barriers to compare applications obtained in different laboratories.

In BSL, the camera is of extreme importance to ensure the quality of the image, however, only 35% of the authors describe the model and manufacturer, while others have insufficient or absent data on the camera, Table 4. Reports of camera adjustments were not expressive, such as describing magnification, if the white balance and the ISO were fixed or it the câmera had automatic adjustments.

Regarding the types of cameras used in image capture, 88,75% are Charge Coupled Device (CCD), 10% were CMOS type and 1.25% are not specified.

Table 4: Camera model and manufacturer description

Camera Description	%
Describe model and manufacturer	35
Describes only the pixels	13
Does not describe model and manufacturer	42
Analysis of previous images	3
Uses only mathematical model	3
Does not quote which camera uses	3

In Table 5, it is possible to see that HeNe lasers are still widely used in BSL technique, though there are papers that did not quote the laser used. The restrictions of the BSL usage to optical labs can be the main reason for that predominance of HeNe laser, the tendency can change the figure in some years since solid-state lasers are cheaper and smaller than the HeNe ones, as well as presenting stable outcomes [11] .

Almost all of the lasers used in more recent work were of the He Ne type that came to replace the laser diode. This occurs due to the restricted use of BSL to optical labs and a lack of information about the stability of diode lasers.

Table 5: Laser Types used in experimental setup.

Laser Type	%
He-Ne	73
Laser Diode	15,9
Do not quotes	5,7
Do not use (only theoretical researches)	5,4

Table 6 shows the applications and it was verified the highest concentration of research in apple 20%, seeds 17%, and human blood flow 12%. The great variety of samples used is a positive point, as it demonstrates the broad range of potential applications. Despite many applications in different biological samples, we observed that all were based in optical laboratory conditions, this without the use of a commercial equipment.

Table 6: Types and percentages of samples found in the research

Types of Samples	**%**
Bacterium	3
Potato	2
Beef	1
Animal cancer cells	1
Human Red Cells	1
Carrot	2
Human Teeth	1
Water flux	1
Blood flow in animal tissues	2
Blood flow in human tissues	12
Leaves of different plants	3
Milk	1
Apple	20
Strawberry	1
Human Eye (live)	2
Parasites	1
Pear	2
Bovine Protein (Albumin)	1
Root of different plants	5
Sperm of different animals	3
Seeds	17
Ice cream	1
Human Biological Tissue	2
Animal Biological Tissue	2
Paints (water-based or synthetic)	9
Tomato	4
Human Urine	2

In addition to the camera, to the laser and to the type of samples, there are other devices that play a key role in BSL such as beam splitter, mirrors, and software. Laser Beam Expander 20x was specified in only four papers though were known its use in the setup. In one article the computer configuration was described and anyone specified the mirror in the papers. Regarding image analysis software, one could see Matlab R2010A (Math Wors USA), ImageJ (NHI, USA) and C ++ mentioned. However, in 83% of the papers, the type of software was not specified.

Regarding the place where the surveys took place, none of them were carried out in the field. All experiments occurred in controlled environments of university laboratories. One of the justifications is that the setup of the BSL is very sensitive to noise as mechanical vibrations [11].

3.3 Image Analysis Methods

The methods of analysis of the BSL can be divided into two large groups, the first being the graphical methods and the second the numerical methods. The most used methods of each group can be seen in Table 7. Despite the difference between graphical and numerical methods, it was found that in 10% of the papers the two types were used together [18], [6]. The purpose of this practice is complementarity. That is, a graphical method is used to cover the shortcomings of a numerical method and vice versa.

Table 7: Conventional methods of biospeckle analysis and examples of works found.

Method Type	Conventional Methods	References
Graphic Method	GD,Fujji, LASCA, WGD,	[19],[20],[21], [22], [23], [24]
Numerical method	IM, AVD, Spatial time speckle (STS) signals, Method of Aizu and Azakura, Modified Spatial-Temporal Speckle Correlation Technique	[14], [25],[26]],[27],[28] ,[29] ,[5], [30],[31],[32],[12],[33],[34],[35],[36]

Is there any relationship between the type of image analysis and the sample used? No relationship of this nature was found in this study. However, numerical methods predominated in about 80% of the studies. As shown in Table 8, both the graphical and numerical methods can be used in a wide variety of samples. Despite the absence of a defined method to analyze a sample, we know that numerical methods are used in homogeneous samples, or in homogeneous areas of a sample, while the graphical approaches is likely used to create maps of activity of a sample.

Table 8: Percentage of application of numerical and graphical methods in biospeckle.

Method Type	%	Sample
Graphical Method	20	Seeds, Apple, Ink, Root Plants, Plant Leaves, Mobility of Parasites, Pear, Flow of Water and Blood
Numerical Method	80	Human and animal biological tissues, Bacteria, parasites, potato, animal semen, beef, seeds, ink, apple, human eye, animal and vegetable biological tissue, ice cream, cancer cells, animal blood and human blood, bovine protein, strawberry, pear, Human Eye, Human Teeth, Apple

In addition to conventional methods, proposals for other alternative methods have been identified, Table 9, which are indispensable for the advancement of image analysis, since conventional methods would not yet provide a definitive or standard assessment.

Another interesting observation was the presence of many methods that were proposed but not used in other works. Thus, it may be observed that, apart from the usefulness of the proposed new methods, it seems that they are intended to justify a publication rather than pave the way to the accessibility of BSL technology.

Table 9: Non-conventional methods of biospeckle analysis and examples of researches found.

Method Type	Unconventional methods	References
Graphic Method	Alternative algorithm for Fujii (Alternative Fujji) e WGD,SMR, PTD, TZ Teste, Konishis's algorithms,MHI	[37],[23],[38]

Numerical method	Empirical mode decomposition (EMD), Assimetria, DYNAMIC MODEL,Gravimetric measurements, LM, Mathematical morphology and Fuzzy mathematical morphology, MTCF and MITCF, Normalized autocorrelation function, Descritor de biospeckle whith a wavelet-based Husts, SC, Others	[39], [40],[41], [42],[26],[43], [44], [45],[46],[13], [23],[47],[48],[49],[15],[50], [51],[36]

4 CONCLUSIONS AND IMPLICATIONS FOR FUTURE RESEARCH

The objective of this work was to describe and identify through a systematic review the state- of- art of BSL and its particular characteristics to know the reasons for the lack of commercial equipment. The results showed a positive and continuous increase of the research involving the BSL during the years.

BSL has presented many application possibilities, but the current state-of-art does not yet allow research that has been carried out in the universities/institutes a commercial application of BSL. As there is no research carried out outside the laboratories, it is believed that the major challenge is to enable the application of BSL in the field.

Equipment such as cameras, lasers, and computers used in the experimental configuration of BSL showed considerable technological evolution in the analyzed period, however, the setup configurations were not satisfactorily detailed. The image analysis methods did not show the same evolution, which can be seen in the absence of patterns in the use of graphical and numerical methods.

BSL is most commonly used in agriculture for seed and fruit analysis. The most common image analysis methods are numerical methods, with an emphasis on IM and AVD.

Further research is recommended to improve image analysis methods and field application of BSL. This research is useful for researchers and entrepreneurs wishing to study and improve BSL.

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