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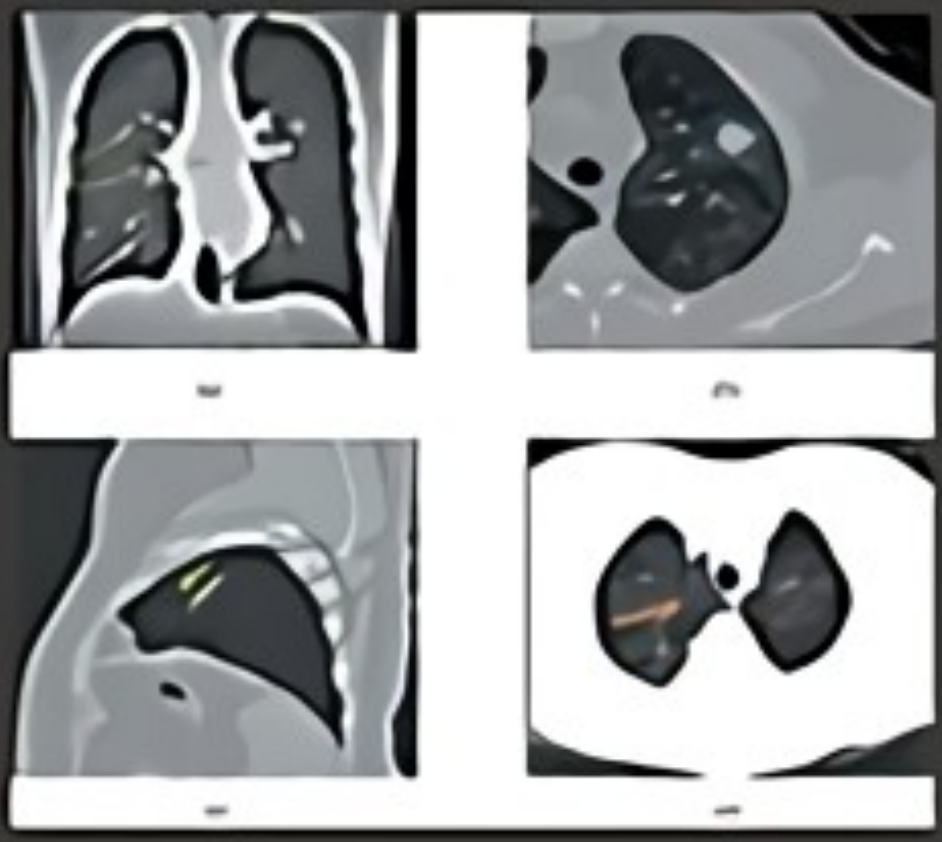

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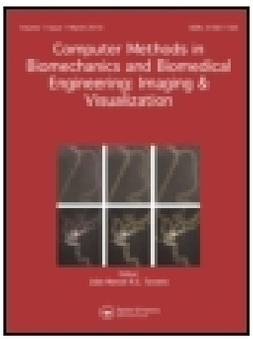

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COMPUTER METHODS IN BIOMECHANICS AND BIOMEDICAL ENGINEERING: IMAGING & VISUALIZATION
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Classification of adeno carcinoma, high squamous intraephithelial lesion, and squamous cell carcinoma in Pap smear images based on extreme learning machine

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ABSTRACT

Cervical cancer is a malignant tumour that attacks the female genital area originating from epithelial metaplasia in the squamous protocol junction area. One method of diagnosis of cervical cancer is to do a Pap smear examination by taking a cervical cell smear from the woman's cervix and observing its cell development. However, examination of cervical cancer from Pap smear results usually takes a long time. This is because medical practitioners still rely on visual observations in the analysis of the results of Pap smear so that the results are subjective. Therefore, we need a programme that can help the classification process in establishing a diagnosis of cervical cancer with high accuracy results. In this study, a cervical cancer classification program was developed using a combination of the Grey Level Co-occurrence Matrix (GLCM) and Extreme Learning Machine (ELM) methods. There are three classes of cervical cell images classified, namely adenocarcinoma, High Squamous Intraepithelial Lesion (HSIL) and Squamous Cell Carcinoma (SCC). From the results of the training program obtained an accuracy 100% and from the testing program obtained an accuracy of 80%.

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Cervical cancer; extreme learning machine; GLCM

Introduction

Cancer is one of the leading causes of death worldwide. In 2018, the death rate caused by cervical cancer in Indonesia is 18,279 people. This amount resulted in an average value of death from cervical cancer of 13.8%. The average death rate in Indonesia is higher than in Southeast Asia with 10.90% (ICO, 2018). The high number of deaths from cervical cancer in Indonesia is caused by delays in the examination and treatment of the disease. The examination is usually done when the symptoms caused by cervical cancer are obvious or the condition of the cancer is severe.

Pap smear is generally performed as an early detection of cervical cancer. Through the Pap smear image, abnormal cell growth can be identified which is the forerunner to cancer. This is what makes the importance of early examination of Pap smear where it can prevent the occurrence of more severe cancers. Examination of cervical cancer from Pap smear results usually takes a long time. This is because medical practitioners still rely on visual observations in the analysis of the results of Pap smear so that the results are subjective. Therefore, we need a program that can help the classification process in establishing a diagnosis of cervical cancer with high accuracy results.

One of the most important changes in cells when they are precancerous is the change in chromatin texture. Texture analysis of the cell nucleus provides information about the spatial distribution of grey levels of pixels in the cell nucleus through digital microscopic images (Liang 2012). Medical image classification using texture analysis has been developed for various types of medical images, such as breast cancer, liver cancer, lung disease and cervical cancer. Initially, cell textures were analysed based on first-order statistical textures and second-order statistical textures. Feature extraction using a cohesion matrix was first performed by Haralick (1973). Then, Weszka (1976) compared texture feature extraction using Fourier Power Spectrum, second-order grey level statistics, Grey Level Co-Occurrence Matrix (GLCM) and Grey Level Run Length Matrix (GLRLM). Based on his research, obtained feature extraction from cell images using GLCM gives the best results. This method measures the appearance of pixels with a certain paired grey intensity at certain relative positions.

Junita (2017) conducted a study using mammogram images to identify breast cancer by extracting the Grey Level Co-Occurrence Matrix (GLCM) feature and the Support Vector Machine (SVM) classification method. In this study, GLCM feature extraction was performed to obtain the value of the Contrast, Correlation, Energy and Homogeneity features as input in the SVM classification process. The implementation of the GLCM feature extraction method and the SVM classification method on mammogram images produces an accuracy value of 60% with testing data used 10 combined images (5 benign and 5 malignant) and learning data used 10 benign data and 10 malignant data.

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There are many computational methods that can be used in the classification process with a good degree of accuracy. To improve the performance of cervical cancer identification in previous researches, this study used Extreme Learning Method (ELM) to classify the value of features obtained from the Grey Level Co-occurrence Matrix (GLCM) method, where the method extracts five texture features, namely, Contrast, Correlation, Energy, Entropy and Homogeneity. The advantage of ELM algorithm is the level of generalisation that is better than gradient-based learning so that it can handle minimal local problems (Huang, Zhu, & Siew, 2006). Another advantage of the ELM method is that it can work optimally on complex functions with both linear and non-linear data (Toprak, 2018). ELM is also able to do learning well so as to produce a classification with accurate results.

Materials and methods

Datasets

The data used in this research were collected from microscopy cervical cell slides, based on the results of Pap smear examination at Dr. Soetomo General Hospital Surabaya Indonesia. Observations were made using a microscope Olympus BX 41 with a magnification of 400x. This microscope is equipped with a digital camera connected to a PC to capture an image of each FoV (Field of View) with the data stored in a .jpg format. The dimensions of the Pap smear images are 1440 x 1024 pixels. The number of the data is 76 images data of squamous cell, Adenocarcinoma, HSIL (as shown in Figure 1) based on the condition the patients who come to the doctor mostly are already in the high risk of cervical cancer cases. The obtained image data are 2560 × 1920 and saved in .bmp format.

Feature extraction

Grey Level Co-occurrence Matrix (GLCM) is a feature extraction method by analysing texture features from dataset images. Each dataset image is composed of several pixels of a certain grey intensity. Texture analysis performs feature extraction by comparing the value of grey intensity between two neighbouring pixels in a certain distance and direction in an image (Mullangi et al. 2017). The tabulation of the relationship between the two neighbouring pixels is then stated in a Grey Level Co-occurrence Matrix. GLCM is a matrix of size m × n, where m is equal to n, which is the maximum grey intensity value of an image, with the matrix element p (i, j). Each element p (i, j) states the frequency of occurrence of a pixel related to a particular pixel in the distance r and the direction θ (Cherian et al. 2017).

There are 5 different features that are calculated from a cohesion matrix, namely contrast, correlation, homogeneity, entropy and energy features. Each feature is calculated using the following equation.

Contrast

The contrast feature states the variation in the difference in intensity of a pixel with neighbouring pixels.

$$Contrast = \sum_{i=1}^{L}\sum_{j=1}^{L} |i-j|^2 P_{r,\theta}(i,j) \tag{1}$$

Correlation

The correlation feature expresses linearly the grey level of pixels of a neighbouring pixel.

$$Correlation = \sum_{i=1}^{L}\sum_{j=1}^{L} \frac{(i-\mu_i)(j-\mu_j)P_{r,\theta}(i,j)}{\sigma_i\sigma_j} \tag{2}$$

Where,

$$\mu_i = \sum_{i=1}^{L}\sum_{j=1}^{L} i\left(P_{r,\theta}(i,j)\right) \tag{3}$$

$$\mu_j = \sum_{i=1}^{L}\sum_{j=1}^{L} j\left(P_{r,\theta}(i,j)\right) \tag{4}$$

$$\sigma_i = \sqrt{\sum_{i=1}^{L}\sum_{j=1}^{L} P_{r,\theta}(i,j)(i-\mu_i)^2} \tag{5}$$

$$\sigma_j = \sqrt{\sum_{i=1}^{L}\sum_{j=1}^{L} P_{r,\theta}(i,j)(j-\mu_j)^2} \tag{6}$$

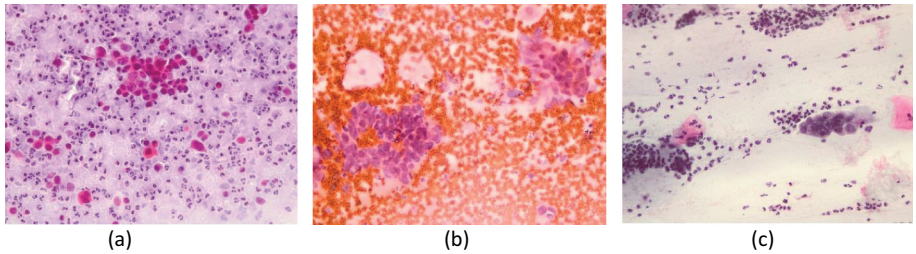
Homogeneity

Homogeneity features show the homogeneity of variations in pixel intensity in an image.

$$Homogeneity = \sum_{i=1}^{L}\sum_{j=1}^{L} \frac{P_{r,\theta}(i,j)^2}{1+(i-j)^2} \tag{7}$$

Entropy

The entropy feature calculates the irregularity in the grey intensity distribution of an image.



(a) (b) (c)

Figure 1. Cervical cancer cell (a) Squamous cell (b) Adeno carcinoma (c) HSIL.

$$Entropy = \sum_{i=1}^{L}\sum_{j=1}^{L} P_{r,\theta}(i,j)\left(logP_{r,\theta}(i,j)\right) \quad (8)$$

Energy

The energy feature calculates the uniformity of pixels in an image. Energy is a reverse form of entropy.

$$Energy = \sum_{i=1}^{L}\sum_{j=1}^{L} P_{r,\theta}(i,j)^2 \quad (9)$$

ELM classification

The Extreme Learning Machine (ELM) method is a Single-Hidden-Layer Feed-forward Networks (SLFNs) method with the main function of generalising a pattern. The selection of input weights and input refractive values is done randomly so that SLFNs can be considered a linear system and output weights can be analysed using simple generalised inverse operations. In addition, ELM also has the ability to generalise with a smaller error value of training (training error) and the determination of the value of a lower training weight so that it has a better generalisation ability (Huang et al, 2006).

Figure 1. ELM structure

The structure of ELM has similarities with feed-forward artificial neural networks in general, but ELM has a different mathematical model. N different number of input and output pairs (Xi, Xt), with:

$$Xi = [Xi_1, Xi_2, \ldots, Xi_n]^T \in R^n \quad (10)$$

$$Xt = [Xt_1, Xt_2, \ldots, Xt_n]^T \in R^m \quad (11)$$

The following is a mathematical model of SLFNs with the number of hidden nodes as $\tilde{N}$ and the activation function g(x):

$$\sum_{i=1}^{\tilde{N}} \beta_i g_i(x_j) = \sum_{i=1}^{\tilde{N}} \beta_i g_i(w_i.x_j + b_i) = o_j, j = 1, 2, \ldots, N \quad (12)$$

Where:

$wi = (w_{i1}, w_{i2}, \ldots, w_{in})^T$: vector of weights connecting all components to i of hidden nodes and input nodes

$\beta_i = (\beta_{i1}, \beta_{i2}, \ldots, \beta_{in})^T$: vector of weights that connect all components to i of hidden nodes and output nodes

b_i = threshold from data to i hidden nodes

$w_i x_j$ = inner product from *Wi* and *Xj*

SLFNs with N hidden nodes and activation function g(x) are assumed to be approximate with an error rate of 0 or have the meaning $\sum_{j=1}^{N} oj - tj = 0$, so that there are *βi, wi* and *bi* such that:

$$\sum_{i=1}^{\tilde{N}} \beta_i g_i(w_i.x_j + b_i) = t_j, j = 1, 2, \ldots, N \quad (13)$$

Equation (13) can be written as follows:

$$\widehat{\beta} = H^{+}T \;\; where \;\; T = [t_1, t_2, \ldots, t_N]^T \quad (14)$$

Where:

$$H = \begin{matrix} g(w_1.x_1 + b_1) & \ldots & g(w_1.x_1 + b_1) \\ \vdots & \vdots & \vdots \\ g(w_1.x_N + b_1) & \ldots & g(w_1.x_1 + b_1) \end{matrix} \quad (15)$$

H^{+} is a matrix of H that has been changed by the Moore – Penrose Pseudo Generalised Inverse method to force matrix multiplications of inputs that have different matrix dimensions to the matrix dimensions of the hidden layer. Equation 14 has the following conditions:

$$\beta = \begin{matrix} \beta_1^T \\ \vdots \\ \beta_N^T \end{matrix} \quad (16)$$

$$T = \begin{matrix} t_1^T \\ \vdots \\ t_N^T \end{matrix} \quad (17)$$

Where,

H in Equation (15) = matrix of hidden layer output

$g(wi.xj+bi)$ = the output of hidden neurons related to input xi

β = matrix of output weights

T = matrix of target or output

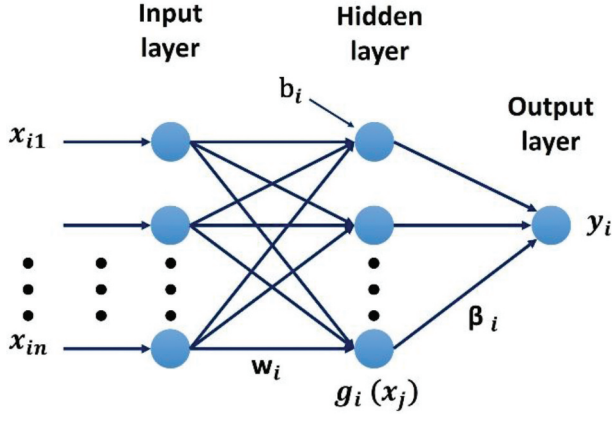


Figure 2. Struktur ELM (Agustina et al., 2005)

As previously stated, ELM has randomly determined input weight and hidden bias values, so the value of the output weights associated with hidden layers can be determined from Equation (14).

Results and discussion

The results of the average value of the GLCM feature in each data are used as an input for the ELM classification system. The ELM training and testing process using 5 GLCM texture features produces an accuracy value of 100% and 80%.

Feature value

In this study, the formation of a cohesion matrix was performed with a pixel spacing of 1 and 4 orientation angles, namely, 0°, 45°, 90° and 135°. The use of 4 orientation angles causes the formation of 4 cohesion matrices for 1 data so that 4 values are generated for 1 type of feature based on the cohesion matrix. Calculation of averages is used to simplify this condition. Each feature value is an average of 4 feature values based on its cohesiveness matrix.

In this study, the introduction of the condition of cervical cancer has not been able to achieve maximum results at the testing stage that is 100%. This is caused by the existence of overlapping feature values in different classes. This overlapping condition can be overcome by doing pre-processing to improve image quality so that important information is obtained from images with minimum noise.

Classification result

The classification stage using the Extreme Learning Machine method is divided into two processes, namely the training process and the testing process. Based on 76 overall data, each class is divided into 80% (61 data) used as training data and 20% (15 data) as test data. The ELM method has an architecture consisting of three types of layers, namely the input layer, hidden layer and output layer (Sun et al., 2008). The input used is obtained from the feature extraction in the previous process, while the output or target of this study is to classify each data into three classes; namely Adenocarcinoma, Squamous Cell and HSIL. The value of the hidden layer, especially the input weight value and the hidden layer input bias value is randomly determined, and 55 hidden nodes are used because they produce maximum accuracy values.

The classification results from the system are then validated by comparing these results with the target value, where the results of the validation of the training process and the testing process are shown in Tables 1 and 2, respectively.

Accuracy values for the training process are calculated as follows:

Accuracy = (33 + 20 + 8)/61 x 100% = 100%

In the training process, the accuracy value for each class classification is 100%, which means that the system is able to predict the results of the classification output based on the specific pattern that has been trained. Value input weight, input bias and output weight obtained from the training process are then used to carry out the testing process. In this process, 20% of the dataset is used or as many as 15 other data are tested for system performance in generalising patterns from new data.

Accuracy values for the training process are calculated as follows:

$$\text{Accuracy} = \frac{7+4+1}{15}\text{x}100\% = 80\%$$

System performance in the testing process produces an accuracy value of 80% which is caused by several things, including overlapping parameter values on some data, so the system is less able to generalise patterns. In addition, the amount of data in this study is not balanced for each class, and the lack of overall data used is also a limitation that can reduce system performance.

To be able to show the advantages of the method proposed in this study, table 5 will show the results of comparisons with other journals using ELM method for pap smear image. Where it can be seen that the accuracy value obtained from the method proposed in this study is higher than the other methods and has more class divisions of 3 classes. In this study has better performance indicator with the accuracy value 100% than other studies (in Table 5). This study has excess result by using the original own data from Dr. Soetomo Hospital, Surabaya, Indonesia with the whole slide of Pap smear images compared with other

Table 1. Confusion Matrix.

		System's classification (*Prediction*)		
		1	2	3
Doctor's diagnosis (*Actual*)	**1**	AC-AC(A)	AC-SC(B)	AC-HSIL(C)
	2	SC-AD(D)	SC-SC(E)	SC-HSL(F)
	3	HSIL-AC(G)	HSIL-SC(H)	HSIL-HSIL(I)

where 1 = *Adeno Carcinoma (AC)*, 2 = *Squamous Cell Carcinoma (SC)*, 3 = HSIL

Table 2. Testing process validation results.

		System's classification (*Prediction*)		
		1	2	3
Doctor's diagnosis (*Actual*)	**1**	33	0	0
	2	0	20	0
	3	0	0	8

Where 1 = *Adenocarcinoma*, 2 = *Squamous Cell Carcinoma*, 3 = HSIL

Table 3. Testing process validation results.

		System's classification (*Prediction*)		
		1	2	3
Doctor's diagnosis (*Actual*)	**1**	7	1	0
	2	0	4	1
	3	1	0	1

where 1 = *Adeno Carcinoma*, 2 = *Squamous Cell Carcinoma*, 3 = HSIL

Table 4. The resume of ELM performance.

	Training			Testing		
Indicator	*Adeno Carcinoma*	*Squamous Cell Carcinoma*	*HSIL*	*Adeno Carcinoma*	*Squamous Cell Carcinoma*	*HSIL*
Accuracy	100%	100%	100%	80%	80%	80%
Sensitivity	100%	100%	100%	87.5%	80%	50%
Specificity	100%	100%	100%	85.71%	90%	92.31%

Table 5. Comparison with similar journals.

No	Author	Paper Title	Datasets	Features Extraction	Classification	Result
1	Khamparia, Aditya (2020)	Internet of Health Things-Driven Deep Learning System for Detection and Classifcation of Cervical Cells Using Transfer Learning	1168 of Pap smear images of diferent types from Herlev dataset.	CNN encorder with diferent types of pre-trained transfer learning models like InceptionV3, SqueezeNet, VGG19 and ResNET5	K-NN, naïve Bayes, RF and SVM	The highest accuracy obtained by ResNet50 with random forest classifer is 97.89% for normal and abnormal.
2	Siqi, Li (2018).	Structure Convolutional Extreme Learning Machine and Case-Based Shape Template for HCC Nucleus Segmentation	Experimental data containing 127 liver pathology images (76 patients)	Lasso, PCA and mRMR	random forest (RF), support vector machine (SVM) and ELM	The highest average ACC obtained by mRMR with SVM classifer is 96.47%, and the lowest average ACC obtained by PCA with ELM classifier is 87.43%.
3	Ahmed, Ghoneim (2019)	Cervical Cancer Classification Using Convolutional Neural Networks And Extreme Learning Machines	There are total 917 cells and seven classes from Herlev University Hospital (Denmark), There are 242 images for normal and 675 images for abnormal.	Convolutional Neural Networks (CNNs) with architecture of Shallow, VGG-16 Net, CaffeNet	ELM	The proposed CNN-ELM-based system achieved 99.5% accuracy in the detection problem (2-class) and 91.2% in the classification problem (7-class).
4	Lili, Zhao (2017)	An Efficient Abnormal Cervical Cell Detection System Based on Multi-instance Extreme Learning Machine	The dataset contains 917 single-cell images in which there are 675 dysplastic cells and 242 normal cells from Herlev datasets.		Multi-instance extreme learning machine (MI-ELM) as main method, KNN, mi-SVM and MI-SVM	The highest accuracy shown by MI-ELM is 97.45%
5	Authors proposed method	Classification of Adeno Carcinoma, High Squamous Intraepithelial Lesion and Squamous Cell Carcinoma in Pap Smear Image Based on Extreme Learning Machine	The dataset contains 76 pap smear images in which there are 33 data for Adeno Carcinoma, 20 data for Squamous Cell Carcinoma and 8 data for HSIL	Grey Level Co-occurrence Matrix (GLCM)	Extreme Learning Machine (ELM) method	The authors proposed GLCM-ELM-based system achieved 100% accuracy for Adeno Carcinoma, Squamous Cell Carcinoma and HSIL

studies which used one single cervical cell cropping images form Herlev dataset.

Conclusion

In this study, a classification system for cervical cancer was developed which automatically recognises the Pap smear image and classifies it into adenocarcinoma, High Squamous Intraepithelial Lesion (HSIL) or Squamous Cell Carcinoma (SCC). The benefit of this research is that it can help doctors to enforce decisions in classifying cervical cell image classes. The method used to develop the system is a combination of the Grey Level Co-Occurrence Matrix (GLCM) method and Extreme Learning Machine (ELM). The 5 feature extraction results from GLCM then become input values at the classification stage using ELM. From the research it was found that the combination of GLCM and ELM was able to extract features of cervical cells well, that is 100% from the training process accuracy and 80% from the testing process accuracy.

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Disclosure statement

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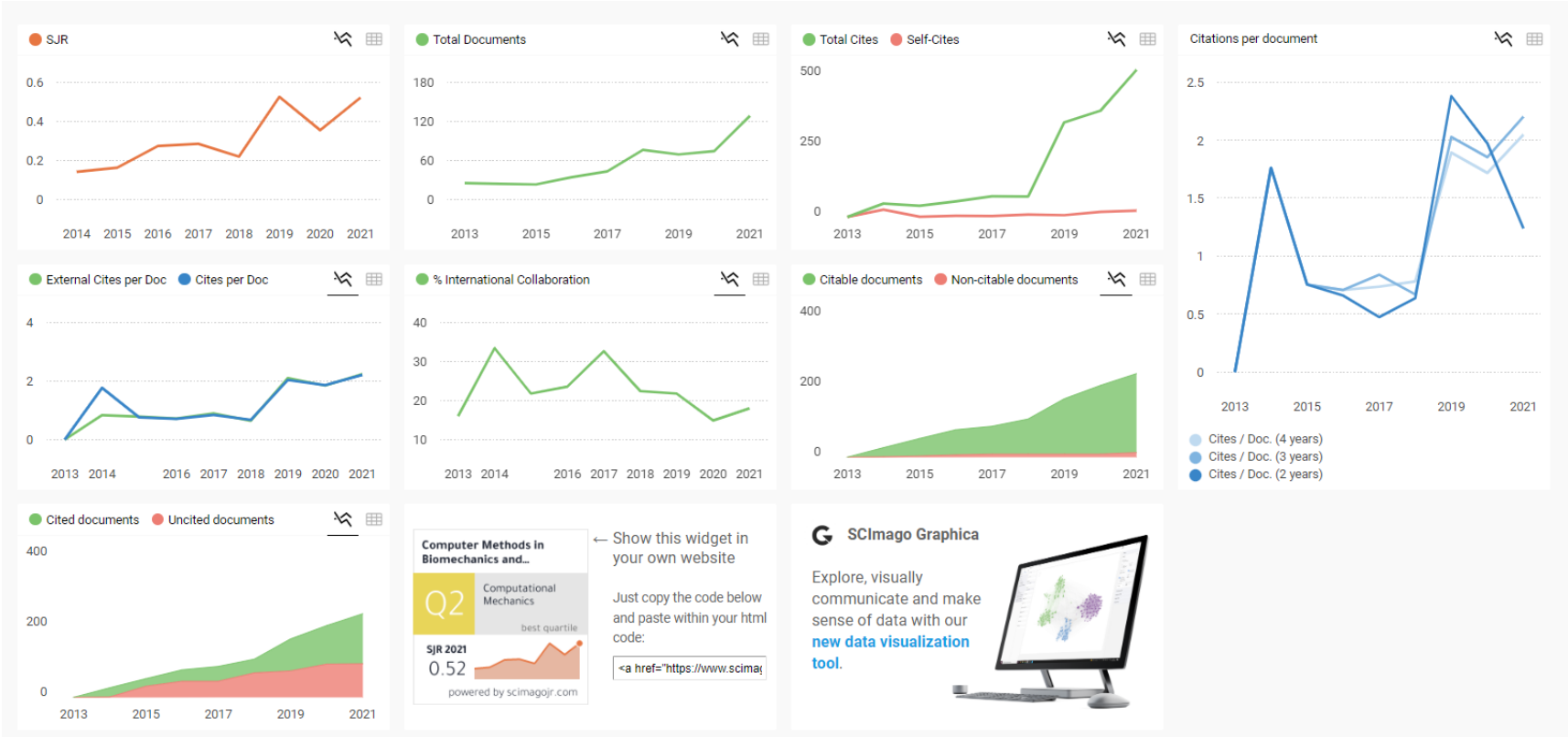

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1	Skrining Kanker Serviks dengan Pemeriksaan Pap Smear di Puskesmas Tanah Kali Kedinding Surabaya dan RS Mawadah Mojokerto	2015	Data Penelitian didapatkan dari data Pengabdian Masyarakat
2	Histopathology Grading Identification of Breast Cancer Based on Texture Classification Using GLCM and Neural Network Method	2018	Penelitian Menggunakan file foto mikroskopis HistoPA
3	Problem diagnostic of Krukenberg tumor Penulis : Reza Wangsanagara, Pungky	2019	Penelitian merupakan laporan kasus
4	Aplikasi Microscope Image Stitcher	2019	Haki (Program computer)
5	Cervical single cell of squamous intraepithelial lesion classification using shape features and extreme learning machine	2021	Penelitian Menggunakan file foto mikroskopis HistoPA
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