

Documenting and predicting topic changes in Computers in Biology and Medicine: A bibliometric keyword analysis from 1990 to 2017



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ABSTRACT

The Computers in Biology and Medicine (CBM) journal promotes the use of computing machinery in the fields of bioscience and medicine. Since the first volume in 1970, the importance of computers in these fields has grown dramatically, this is evident in the diversification of topics and an increase in the publication rate. In this study, we quantify both change and diversification of topics covered in. This is done by analysing the author supplied keywords, since they were electronically captured in 1990. The analysis starts by selecting 40 keywords, related to Medical (M) (7), Data (D) (10), Feature (F) (17) and (AI) (6) methods. Automated keyword clustering shows the statistical connection between the selected keywords. We found that the three most popular topics in CBM are: Support Vector Machine (SVM), Electroencephalography (EEG) and IMAGE PROCESSING. In a separate analysis step, we bagged the selected keywords into sequential one year time slices and calculated the normalized appearance. The results were visualised with graphs that indicate the CBM topic changes. These graphs show that there was a transition from Artificial Neural Network (ANN) to SVM. In 2006 SVM replaced ANN as the most important AI algorithm. Our investigation helps the editorial board to manage and embrace topic change. Furthermore, our analysis is interesting for the general reader, as the results can help them to adjust their research directions.

1. Introduction

Documenting the use of computers in bioscience and medicine is a very dynamic endeavour. Therefore, Computers in Biology and Medicine (CBM) is a journal which was set-up as a forum to publish scientific articles and reviews.¹ The content areas include medical disease diagnosis [1–4], medical data [5], information processing [6–8] and dissemination [9]. Medical disease creates the need to build physical problem solutions and computer methods realize the required functionality [10,11]. The problem solutions can take the form of biochemical [12], biocontrol [13], neural simulation [14] and automatic computer analysis systems [15–17]. Keeping track of topic changes in that scientific area is important for steering the use of computing machinery in medicine and biology towards novel and forward thinking applications. However, the diverse and dynamic nature of the forum makes it difficult to track and analyse topics over time.

Bibliographic research aims to provide an overview of trends and issues encountered in dynamic literature [18–20]. As such, it is a meta-analysis method which is applied to a substantial body of research literature [21,22]. Not only the topics and the writing style evolve, also the bibliographic features of the documents change over time. For

example, the author supplied keywords in CBM are only captured since 1990. Before that, Topic Detection and Tracking (TDT) [23] was difficult and error prone, because a third party had to extract the topic from the paper text. The ability to conduct TDT studies is significant for meta research on science, technology and policy [24,25]. TDT tools can be used to profile research [26,27], document trends and topics [28–30] as well as analyse research impact [31,32]. Linear models can be used to predict incremental change, but they underperform when it comes to predicting disruptive and revolutionary events [33]. Unfortunately, traditional methods use linear models on static data [34]. For example, keyword cluster analysis is static, because the clusters do not reflect change over time. Therefore, these methods cannot be used to document and predict topic changes [33].

To address the issues raised above, we have analysed the topics covered in CBM with static and dynamic keyword analysis methods. We have applied static frequency and cluster analysis to author supplied keywords from all papers published in CBM since 1990. The frequency analysis shows that Support Vector Machine (SVM), Electroencephalography (EEG), and IMAGE PROCESSING are the most widely used keywords in CBM publications. The cluster analysis reveals the structure within the keyword co-occurrence matrix. With a second analysis step,

¹ URL (01.09.2017): <https://www.journals.elsevier.com/computers-in-biology-and-medicine/>.

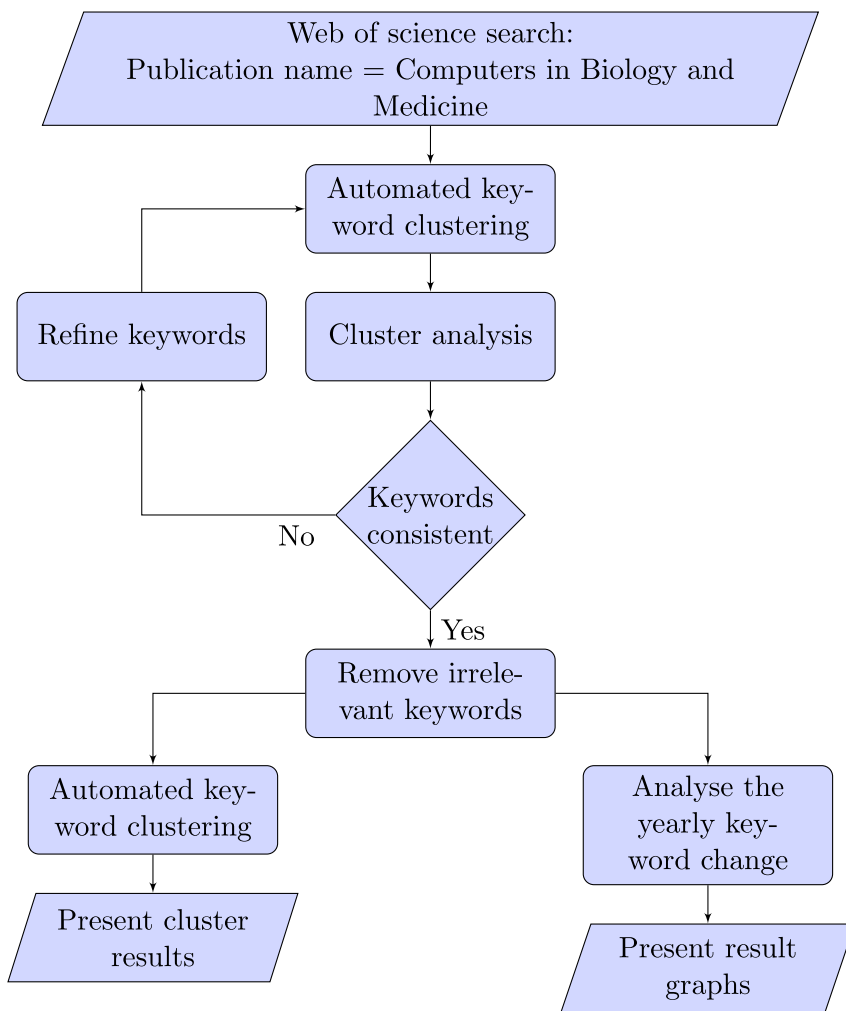


Fig. 1. Flowchart of the keyword analysis.

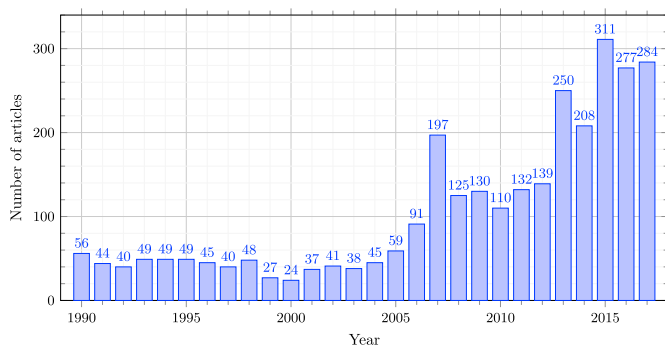


Fig. 2. Number of articles published in from 1990 (Volume 20) to 2017 (Volume 87).

we found the normalized appearance of the most important keywords in yearly intervals from 1990 to 2017. Analysing the normalized keyword appearance reveals the topic change dynamics. In order to interpret these dynamics, we put forward that future topics in CBM will be influenced by Medical (M) needs and advances in Artificial Intelligence (AI), Feature (F) extraction and medical Data (D) acquisition. Based on these four categories, we found that the most striking topic change happened in AI, namely the transition from Artificial Neural Network (ANN) to SVM. The static and dynamic bibliographic analysis results can serve as a basis for the editorial board to keep CBM relevant for the advancement of science

Table 1

Corrections done to the original author keywords.

Keyword	Correction
ALGORITHMS	→ ALGORITHM
SUPPORT VECTOR MACHINE	→ SVM
SUPPORT VECTOR MACHINE (SVM)	→ SVM
SVMS	→ SVM
NUERAL NETWORKS	→ NN
NUERAL NETWORK	→ NN
FINITE ELEMENT METHOD	→ FEM
FINITE ELEMENT ANALYSIS	→ FEM
ELECTROCARDIOGRAM	→ ECG
ELECTROCARDIOGRAM (ECG)	→ ECG
ELECTROENCEPHALOGRAM	→ EEG
ELECTROENCEPHALOGRAM (EEG)	→ EEG
MAGNETIC RESONANCE IMAGING	→ MRI
COMPUTED TOMOGRAPHY	→ CT
ARTIFICIAL NEURAL NETWORK	→ ANN
ARTIFICIAL INTELLIGENCE	→ AI
VIRTUAL REALITY	→ VR
MODELING	→ MODELLING
HEART RATE VARIABILITY	→ HRV
AUTONOMOUS NERVOUS SYSTEM	→ ANS
GENETIC ALGORITHM	→ GA

and technology. The bibliometric research results are interesting for the general reader as well, because they reveal both statistical connections between keywords and trending topics. That information is useful when it comes to deciding on what technology to focus.

Table 2

SVM.csv file content, where ‘na’ stands for ‘Normalized appearance in %’.

year	na	year	na
1990	0	2004	2.2222
1991	0	2005	0
1992	0	2006	1.0989
1993	0	2007	2.0305
1994	0	2008	0.8
1995	0	2009	1.5385
1996	0	2010	2.7273
1997	0	2011	3.0303
1998	0	2012	3.5971
1999	0	2013	2.8
2000	0	2014	2.4038
2001	2.7027	2015	3.537
2002	0	2016	3.2491
2003	0	2017	0.7874

The paper text refers to the bold part in Table 2: "The time slice 2015 (high-lighted) links the example, shown in Equation (2), with the content of the SVM.csv file, shown in Table 2.

To substantiate our claim of supporting both editorial management and readers of CBM, we have organized the rest of this paper as follows. The next section introduces the materials used for the bibliographical research. Section 3 presents the research results. These results are discussed in Section 4. The discussion centres on interpreting and relating our findings to the wider research community. The study concludes with Section 5.

2. Materials

We had two distinct ideas for analysing the author supplied keywords in CBM papers. The first idea was keyword cluster analysis. There is good tool support for that method and the algorithms are well established. Cluster analysis reveals the statistical connections between individual topics [35]. However, cluster analysis does not document topic changes. With the second idea we address that shortcoming by incorporating the time, when the keywords were used, into the analysis process [30,36,37]. We plot the normalized appearance of the keyword over time, together with a trend-line, which indicates whether a topic is a) trending, b) static, or c) in decline.

The flowchart, shown in Fig. 1, documents the mechanics of our analysis process. It starts with keyword data acquisition. The next step sequence refines the keywords, such that they are relevant and consistent. The stable set of keywords was subjected to both cluster and yearly keyword change analysis. The next sections introduce the individual steps in greater detail.

2.1. Data acquisition

Data acquisition started with a straight forward publication search in the web of science [38]. The search term ‘Computers in Biology and Medicine’ resulted in a data set with 3406 entries. Each entry represents a paper that was published in the time period from 1970 to 2017. However, careful analysis reveals that the web of science captured author supplied keywords only from Volume 20 Issue 1 in 1990 onward. Restricting the publication years to the timespan from 1990 (Volume 20 Issue 1) to 2017 (Volume 91,² published 1 December 2017) yielded 2946 entries. Fig. 2 shows the distribution of these entries. For example, the graph in Fig. 2 indicates that there were 311 articles published in 2015. The keywords of these papers became the raw data for the refinement process which is discussed in the next section.

Table 3

Keywords mapped to the analysis results. C indicates the cluster number and m is the gradient value. The list is ordered in accordance with the cluster number. The individual cluster entries are ordered by the keyword occurrence.

Keyword	Area	C	Occurrence	m
IMAGE PROCESSING	F	1	58	$1.50 \cdot 10^{-2}$
SEGMENTATION	F	1	55	$9.14 \cdot 10^{-2}$
Magnetic Resonance Imaging (MRI)	D	1	47	$-4.70 \cdot 10^{-2}$
Computed Tomography (CT)	D	1	37	$6.81 \cdot 10^{-2}$
IMAGE SEGMENTATION	F	1	32	$3.24 \cdot 10^{-2}$
IMAGE ANALYSIS	F	1	20	$-3.67 \cdot 10^{-2}$
ULTRASOUND	D	1	19	$0.335 \cdot 10^{-2}$
MEDICAL IMAGING	D	1	18	$-1.73 \cdot 10^{-2}$
IMAGE REGISTRATION	F	1	14	$1.49 \cdot 10^{-2}$
MYOCARDIAL INFARCTION	M	1	12	$0.905 \cdot 10^{-2}$
<hr/>				
Electrocardiogram (ECG)	D	2	50	$9.02 \cdot 10^{-2}$
Heart Rate Variability (HRV)	D	2	38	$5.42 \cdot 10^{-2}$
ATRIAL FIBRILLATION	M	2	26	$6.09 \cdot 10^{-2}$
WAVELET TRANSFORM	F	2	26	$1.96 \cdot 10^{-2}$
SPECTRAL ANALYSIS	F	2	19	$-1.96 \cdot 10^{-2}$
Principal Component Analysis (PCA)	F	2	18	$2.86 \cdot 10^{-2}$
ENTROPY	F	2	15	$4.06 \cdot 10^{-2}$
FRactal DIMENSION	F	2	12	$-3.18 \cdot 10^{-2}$
Autonomic Nervous System (ANS)	M	2	12	$-0.61 \cdot 10^{-2}$
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SVM	AI	3	111	$13.27 \cdot 10^{-2}$
GENETIC ALGORITHM	AI	3	31	$5.46 \cdot 10^{-2}$
ANN	AI	3	20	$-9.62 \cdot 10^{-2}$
Discrete Wavelet Transform (DWT)	F	3	17	$2.7 \cdot 10^{-2}$
CANCER	M	3	16	$5.60 \cdot 10^{-2}$
PHARMACOKINETICS	F	3	15	$-5.41 \cdot 10^{-2}$
GENE EXPRESSION DATA	D	4	15	$2.62 \cdot 10^{-2}$
FUZZY LOGIC	AI	3	14	$1.07 \cdot 10^{-2}$
<hr/>				
Neural Network (NN)	AI	4	48	$-6 \cdot 10^{-2}$
BREAST CANCER	M	4	31	$5.2 \cdot 10^{-2}$
CLUSTERING	AI	4	25	$4.83 \cdot 10^{-2}$
GENE EXPRESSION	F	4	14	$3.92 \cdot 10^{-2}$
MAMMOGRAPHY	D	4	14	$1.89 \cdot 10^{-2}$
MICROARRAY DATA	D	4	11	$2.69 \cdot 10^{-2}$
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Finite Element Method (FEM)	F	5	48	$0.364 \cdot 10^{-2}$
FLUID DYNAMICS	F	5	22	$3.18 \cdot 10^{-2}$
ATHEROSCLEROSIS	M	5	18	$3.42 \cdot 10^{-2}$
WALL SHEAR STRESS	F	5	17	$2.51 \cdot 10^{-2}$
BLOOD FLOW	F	5	13	$-2.2 \cdot 10^{-2}$
<hr/>				
EEG	D	6	71	$2.80 \cdot 10^{-2}$
EPILEPSY	M	6	21	$3.66 \cdot 10^{-2}$
<hr/>				
Total			1117	78.93×10^{-2}

2.2. Keyword refinement

The refinement process aims to extract the most relevant keywords. The process follows the flowchart shown in Fig. 1. It starts with an initial analysis, which revealed that the documents contained 15707 keywords and 10016 of these keywords were unique. Furthermore, the analysis indicated that the unique keywords were inconsistent. These inconsistencies arise from singular and plural forms of the same word as well as spelling differences. In order to correct the inconsistencies, we entered into an iterative refinement process. Table 1 documents the changes made during the refinement process. Most of these changes are self-evident. For example, the first entry in Table 1 documents a change from the plural form of the keyword ALGORITHM(S) to its singular form. The information loss, with respect to our meta-analysis, for doing this change is minimal. The acronyms were introduced to make the result diagrams more readable.

Once the keywords were consistent, we progressed to a second refinement step. This step removed irrelevant keywords. To facilitate this irrelevance reduction, we specified that each keyword must appear 15 or more times in the 2946 papers. 57 keywords met this criteria. However,

² Since Volume 44, discontinued Issues – only volumes are used.

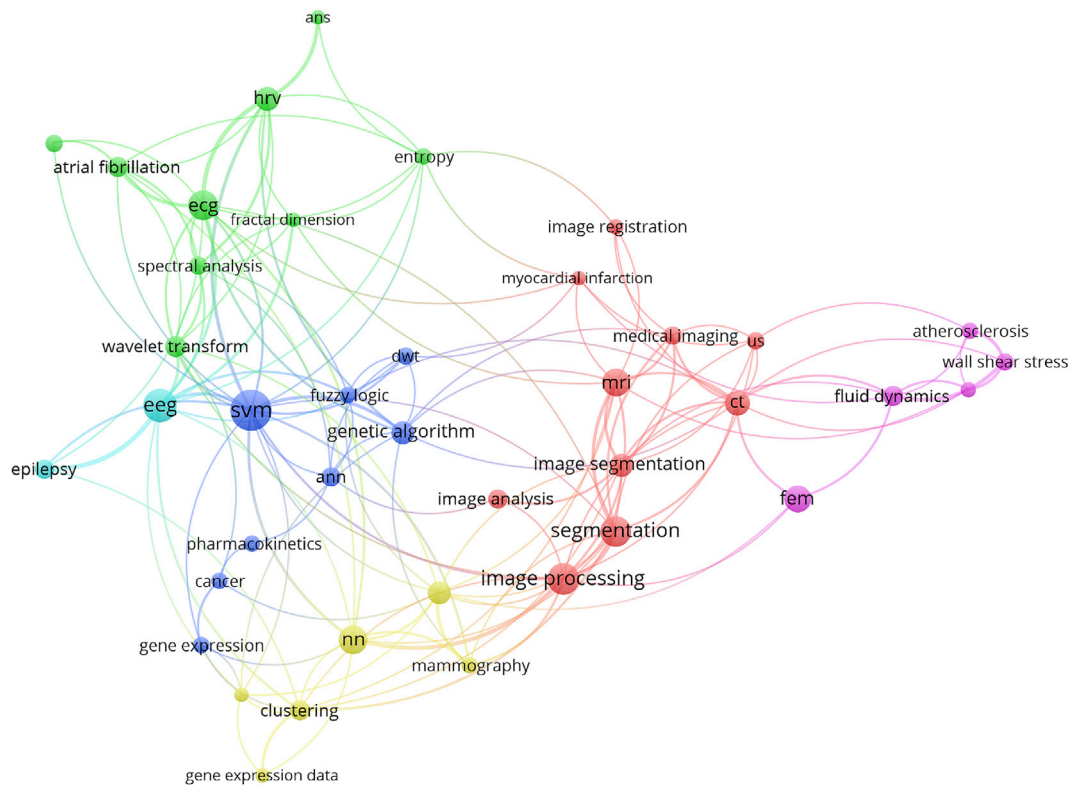


Fig. 3. Visualization of keyword clusters, as listed in Table 3.

17 of these keywords were not relevant for documenting and predicting topic changes. The following list details the removed keywords and provides the rationale as to why they were deemed to be irrelevant.

- CLASSIFICATION, COMPUTER SIMULATION, BIOINFORMATICS, MODELING, MODEL, ALGORITHM and SOFTWARE – These keywords are not focused enough to shed light on potential future trends in CBM.
- EXPERT SYSTEM, COMPUTER-AIDED DIAGNOSIS, DECISION SUPPORT, MACHINE LEARNING and DIAGNOSIS – These are important keyword categories. However, the importance of these categories for topic changes comes from the underlying methods.
- DATA MINING, SIGNAL PROCESSING and DATA ANALYSIS – The keywords are too broad. Most studies in CBM involve some sort of data analysis and signal processing. Data mining is a more recent term, however it is the underlying method which makes the topic important.
- PREDICTION – The term is covered by the AI methods.
- VISUALIZATION – Most of the CBM studies involve some sort of visualization. Therefore, this term is not a good indicator of future trends.
- OPTIMIZATION – As such, the keyword is a poor predictor of future trends, because it is too broad. The specific methods, which execute the optimization or the area where optimization is used, are better predictors.

After that irrelevance reduction, we selected 40 keywords which occurred most often in the papers. These keywords represent the main topics covered in CBM.

For the dynamic keyword change analysis, we have split the 40 selected keywords into four subsets according to the keyword area. These four areas are roughly aligned with concepts and methods for computers in biology and medicine. The following list details the keyword areas:

1. M – This subset includes medical terms as well as diseases. Fighting diseases and improving medical processes provides a powerful justification for computers in biology and medicine.
2. D – Includes both medical data and data acquisition methods. That data constitutes the input for the computer algorithms.
3. F – Includes both features and feature extraction methods. Feature extraction algorithms extract relevant information from medical data.
4. AI – Includes methods for automated decision making. Computer based decision making is important for diagnosis support.

2.3. Keyword clustering

There are two map types commonly used in bibliometric research [39]. These types are referred to as distance-based maps and graph-based maps. Distance-based maps establish the distance between two items. To be specific, the distance reflects the strength of the relation between the items [40]. We used the VOSviewer software to carry out distance based keyword clustering [41–43]. The distance between the selected keywords is established by counting the number of papers that contain both keywords. A large number of co-occurrences indicates a short distance between the selected keywords. That distance is reflected in the co-occurrence map which is used to visualize the clusters [44,45].

2.4. Keyword change analysis

Keyword change analysis was conducted with three different tools. In the first step, the bibliographics [46] package for R [47] was used to extract the keywords together with the year of publication information. The R code implements an algorithm which counts how often a specific keyword appears in a year. In effect that created a quantisation where all 15707 keywords were mapped into 28 sequential time slices.

Over time, the number of publications, and hence the number of keywords fluctuates. For CBM, there is a clear trend towards more publications in recent years, as shown in Fig. 2. That creates a problem if we take the number of keywords, within a year, as a measure of keyword

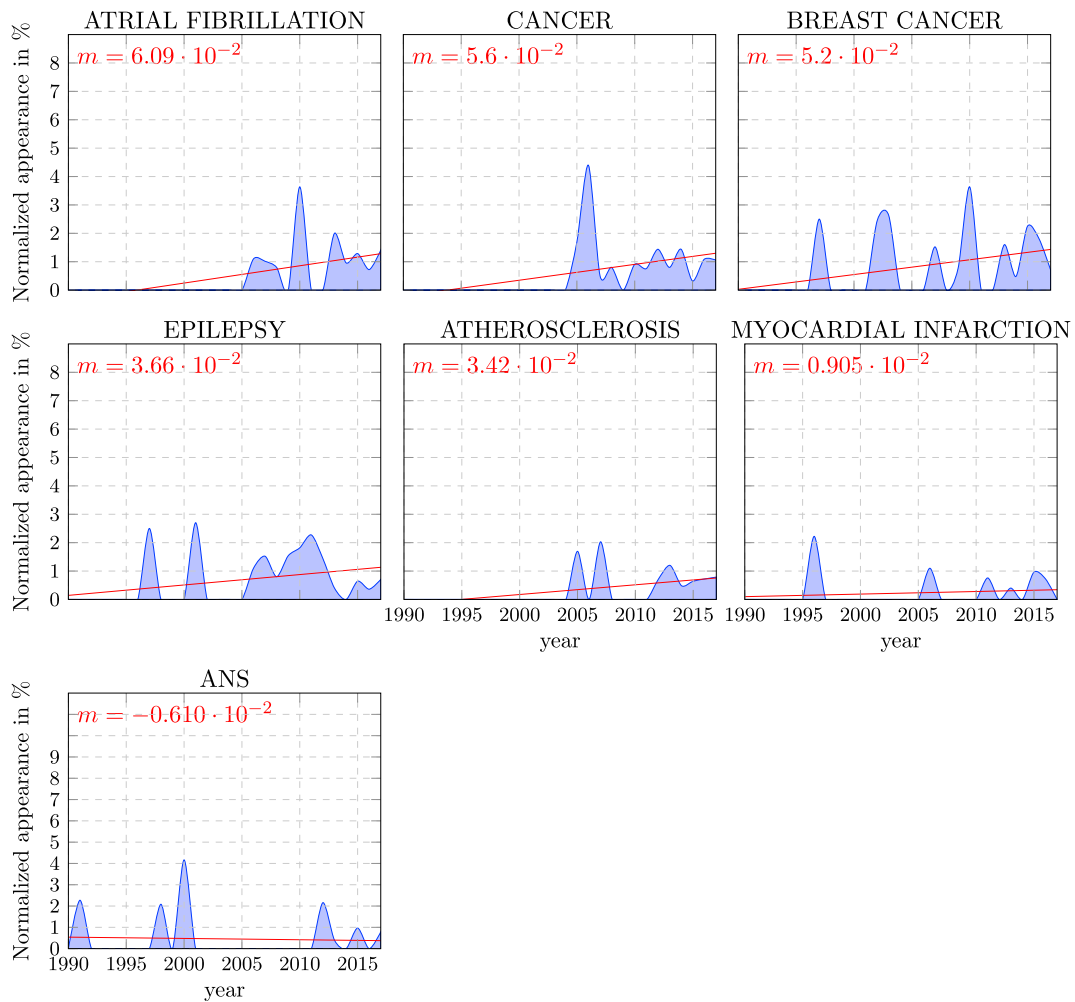


Fig. 4. Normalized appearance in % of keywords in the area of Medical (M).

importance. To be specific, it makes a difference if a keyword appears once in 24 publications or once in 311 publications. Clearly, the keyword appearing once in 24 publications is more important than the keyword that appears once in 311 publications.

To address the fluctuation problem, we have normalized the number of appearances for a specific keyword within a year ($S_{Y,K}$) by the number of appearances for all the keywords within a year (N_Y). The following equation defines the normalization:

$$\text{Normalized appearance in } \%_{Y,K} = \frac{S_{Y,K}}{N_Y} \times 100 \quad (1)$$

where Y is the year and K is the keyword. For example, the keyword SVM appeared in 2015 48 times and the number of appearances for all keywords was 1357. Plugging these values into Equation (1):

$$\begin{aligned} \text{Normalized appearance in } \%_{2015,SVM} &= \frac{S_{2015,SVM}}{N_{2015}} \times 100 = \frac{48}{1357} \times 100 \\ &= 3.537\% \end{aligned} \quad (2)$$

The results were saved as CBM_all.csv. That file was loaded into the Matlab environment.³ The Matlab script extracted a time-line for each topic. The function result = timeline (...) plugs the gaps within a time-line. To be specific, when there was no keyword detected, within a specific year, the function inserted a 0 in the time-line. A separate .csv file

is saved, with the time-line data for each of the selected keywords. For example, Table 2 shows the SVM.csv file content. Column 1 lists the 28 time-slices, labelled as the year of publication. Column 2 states the normalized appearance in %. In 1990, SVM did not appear in any CBM paper, therefore a 0 was inserted. The time slice 2015 (highlighted) links the example, shown in Equation (2), with the content of the SVM.csv file, shown in Table 2.

In a final step, 40.csv files, with the analysis results for the selected keywords, were loaded into the text processing system LaTeX [48]. The data is displayed with the pgplots package [49]. The package was also used generate a trend-line for each graph. Mathematically, that trend-line is a linear approximation [50], which takes the form:

$$\text{trend} - \text{line}(Y) = b + mY \quad (3)$$

where Y is the year, b is an offset and m is the trend-line gradient. The following section presents a plot of the normalized yearly appearance for each selected keyword as well as the static analysis results.

3. Results

The result presentation starts by listing the selected keywords. That is done in Column 1 of Table 3. This column states the acronym and, if not done so in the text before, the acronym is introduced. Column 2 provides the keyword area. We found: 7 keywords for Medical (M), 10 keywords for Data (D), 17 keywords for Feature (F) = 17, and 6 keywords for Artificial Intelligence (AI). The header C in Column 3 indicates the cluster

³ MATLAB 6.1, The MathWorks Inc., Natick, MA, 2000.

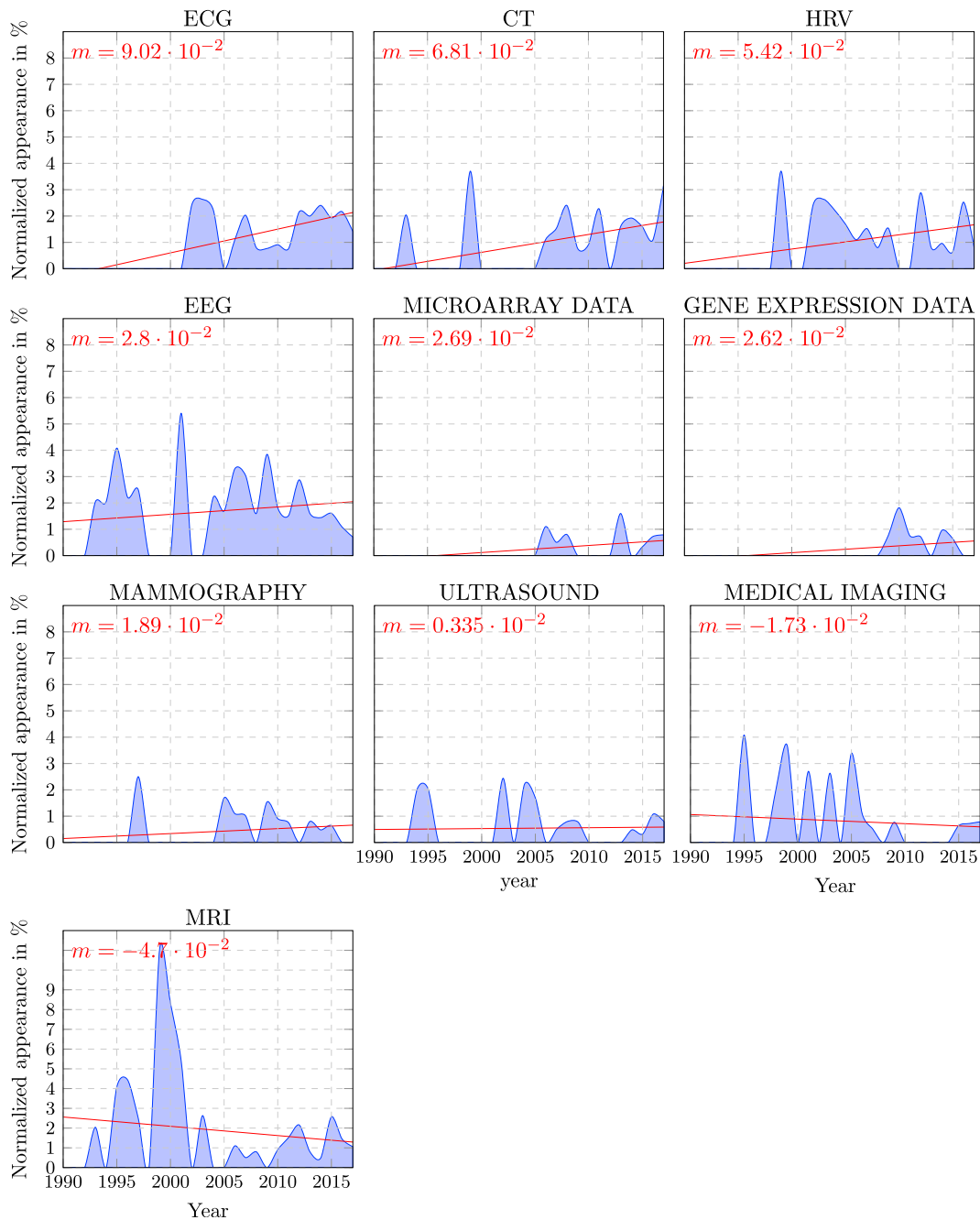


Fig. 5. Normalized appearance in % of keywords from the area of Data (D).

to which a particular keyword belongs. The occurrence, reported in Column 4, indicates how often the keyword appeared in the 2946 papers. In total the 40 selected keywords appeared 1117 times. Column 5 reports the trend-line gradient, which is a result of the topic change analysis. The sum of the 40 gradient values is $78.93 \cdot 10^{-2}$. Compared to the individual m values, this is a large positive number. Being large and positive indicates that the keyword diversity increases over time.

The network graph, shown in Fig. 3, visualizes the distance based clustering result. The node colour was assigned as follows: Blue to cluster 3, light blue to cluster 6, green to cluster 2, red to cluster 1, purple to cluster 4. We discuss the clustering result in Section 4.

Fig. 4 shows the 7 graphs for the keyword change analysis in the area M, for diseases and medical terms. The graphs are ordered in terms of their trend-line gradient m . A positive gradient shows that the keyword gained importance in the CBM journal over the observed period.

Conversely, a negative gradient indicates that the topic lost importance. In the upper left corner of Fig. 4, we start with ATRIAL FIBRILLATION, because its trend-line has the steepest ascent, i.e. the highest m value. The subsequent plots have a decreasing trend-line gradient value. In effect that orders the keywords in terms of their importance for CBM. The arithmetic mean of all trend-line gradients for the area M is $3.47 \cdot 10^{-2}$. That means, the keyword change dynamics in CBM are such that the keywords for get more important.

Fig. 5 shows the 10 graphs for the keyword change analysis in the area D, for data and data acquisition methods. The graphs are ordered in terms of the trend-line gradient m . We start in the upper left corner with plotting normalized appearance of ECG over the publication years, because this keyword has the highest trend-line gradient in the area., shown in the lower left corner, has the trend-line with the steepest decent. The arithmetic mean of all trend-line gradients for that area is

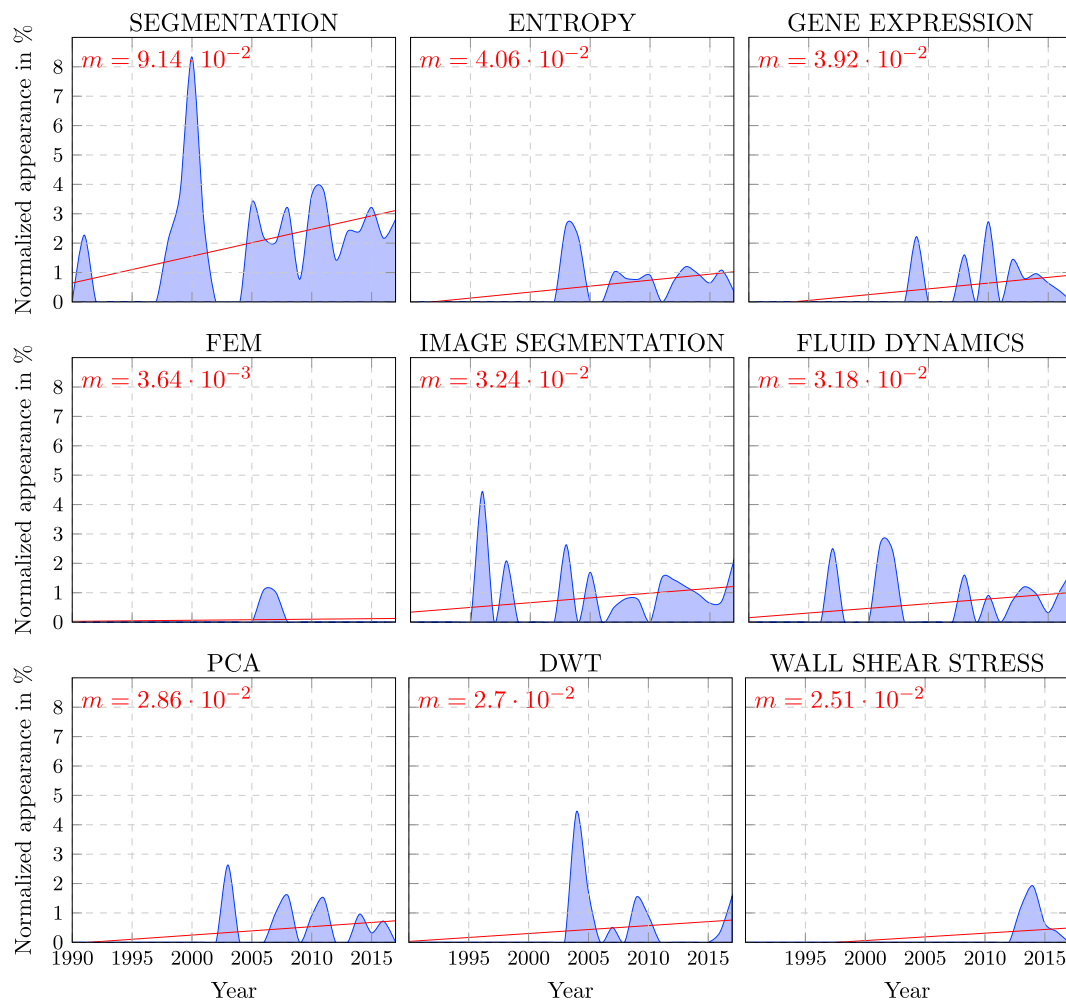


Fig. 6. Normalized appearance in % of keywords from area of Feature (F), part 1.

$2.52 \cdot 10^{-2}$.

Figs. 6 and 7 show the 17 graphs for the keyword change analysis in the area F, for features and feature extraction methods. The graphs are ordered in terms of the trend-line gradient m . We start from the steepest ascent, for SEGMENTATION, and progress to the steepest descent, for PHARMACOKINETICS. The arithmetic mean of all trend-line gradients for that area is $1.21 \cdot 10^{-2}$.

Fig. 8 shows the 6 result graphs for the keyword change analysis in the area AI, for soft computing methods and decision support. The graphs are ordered in terms of the trend-line gradient m . We start from the steepest ascent, for SVM, and progress to the steepest descent, for SVM. The arithmetic mean of all trend-line gradients for that area is $1.50 \cdot 10^{-2}$.

4. Discussion

We start this section by discussing the distance based clustering results. The results were presented in Column 3 of Table 3 and the diagram in Fig. 3 visualizes the clusters. The following paragraphs highlight the main properties of each cluster.

Cluster 1 is centred on IMAGE PROCESSING [51–54]. These images can come from MRI [55,56], ULTRASOUND [57,58] or [59,60]. As such, MYOCARDIAL INFARCTION can be diagnosed using on ultrasound images [61,62], therefore this topic is included in cluster 1.

Cluster 2 is centred on ECG [63] signals. HRV is extracted from ECG signals [64] and as such it is a good predictor for ANS [65,66]. The cluster reveals that FRACTAL DIMENSION [67,68], PCA [69,70], SPECTRAL ANALYSIS [71,72], and WAVELET TRANSFORM [73–75] are used

to extract features from these biomedical signals. These features can be used to detect heart diseases, such as ATRIAL FIBRILLATION [76,77].

Cluster 3 is centred on the AI methods, such as SVM [78,79], ANN [80], GENETIC ALGORITHM [81], and FUZZY LOGIC [82]. These methods are often used in CANCER [83,84] diagnosis support systems. They can incorporate GENE EXPRESSION [85,86] and PHARMACOKINETICS [87,88] methods for gene analysis. These systems can also incorporate DWT, usually for feature extraction from images and signals [89–93].

Cluster 4 centres on BREAST CANCER and MAMMOGRAPHY [94, 95]. For automated diagnosis support NN can be used [96]. GENE EXPRESSION DATA can be analysed with CLUSTERING [97,98].

Cluster 5 is centred on ATHEROSCLEROSIS and the feature extraction methods associated with that disease. To be specific, the feature extraction methods are BLOOD FLOW [99,100], FLUID DYNAMICS [101], FEM [102], WALL SHEAR STRESS [103].

Cluster 6 is centred EEG signals [104,105]. These signals can be used to diagnose EPILEPSY [106,107].

The yearly keyword change result graphs, shown in Figs. 4–8, reveal the dynamic topic changes in CBM. We found that the topic area of AI moves fast. The graphs and trend-lines, shown in Fig. 9, document that ANN was superseded by SVM. The trend-line for ANN has the steepest descent for all the analysed keywords. In contrast, the trend-line for SVM has the steepest ascent for all analysed keywords. Both methods are in the same area, namely AI, hence they are in direct competition. According to the trend-lines, SVM superseded ANN around 2006. That paradigm shift indicates that AI is a very active area with research being conducted far

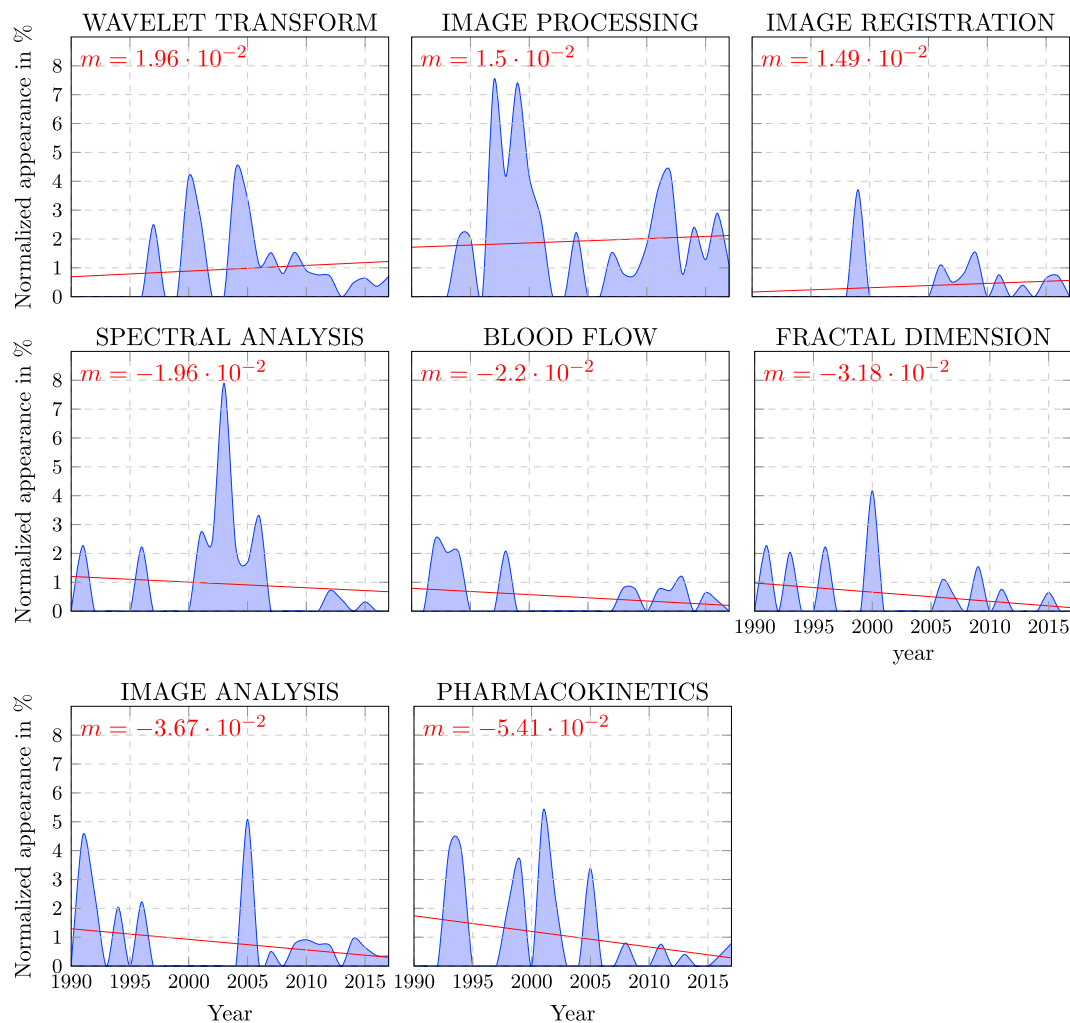


Fig. 7. Normalized appearance in % of keywords from area of Feature (F), part 2.

beyond medicine and biology. Therefore, we expect further topic changes in that area. For example, deep learning has the potential to supersede SVM as the predominant method [108–110].

The yearly keyword distribution reveals that GENETIC ALGORITHM is a new topic in CBM. It started trending in 2005 and it has the second largest trend-line gradient of all AI methods [111,112]. SEGMENTATION [113] has the highest trend-line gradient within F. That feature extraction method is important for computer aided diagnosis of retinopathy [114–116] and cancer [117–119]. ATRIAL FIBRILLATION is associated with significant morbidity and mortality [120]. That cardiac arrhythmia is a risk factor for ischemic stroke [121]. Therefore, it is not supersizing that ATRIAL FIBRILLATION has the highest trend-line gradient of group M. Similarly, ECG has the highest trend-line gradient for group D. That is hardly supersizing, because that physiological signal is used to diagnose a wide range of heart diseases [122]. One particular interest for ECG processing is QRS detection, which is used for HRV analysis [123–125]. Furthermore, ECG is the signal of choice for arrhythmia detection [126–128]. That versatility explains the growing levels of interest in ECG.

The declining trend-lines for IMAGE ANALYSIS and MEDICAL IMAGING indicate that these methods don't find their way into CBM any longer. Similarly, MRI shows also a declining trend-line. IMAGE ANALYSIS and MEDICAL IMAGING are used to extract features from medical images, such as MRI [129–131]. Outside the scope of CBM, all three topics are important, because these methods have a significant role to play in the diagnosis of soft tissue cancer [132–134] and other dangerous

diseases [135,136]. Furthermore, the trend for imaging data goes towards more images and higher resolution [137]. Computer assisted feature extraction can be used to avoid data overloading of the reading radiographer [138]. The mediocre success of CBM to attract publications in these areas can be attributed to the competition from specialized journals. We suspect that these journals take the majority of papers about IMAGE ANALYSIS, MEDICAL IMAGING and MRI.

Diseases create the need for computer based problem solutions. Therefore, we were surprised that diabetes [139] did not feature in the selected keywords; neither did diseases related to ageing, like Alzheimer and dementia. We can only speculate on the reasons why CBM could not attract more papers on these topics. There are other journals that may take these papers. Real-time is another topic that did not feature in the 40 selected keywords, despite the fact that real-time is mentioned twice in the journal aims. One reason for that lack of real-time related papers might be that modern computing machinery is fast enough for most applications [140]. Furthermore, this topic is very specialized, hard real-time is only needed for control applications, such as smart prosthesis and brain stimulation [141]. Therefore, we suspect that papers, which address real time issues, go to journals with a narrow focus on that area. Another point is that none of the selected keywords is related to safety and reliability of computer systems for biology and medicine. This is a big and growing problem, because most scientists are working on creating ever more complex problem solutions and only a minority reflects on how to ensure safety and reliability [142,143]. To be specific, CBM does not publish research work that indicates whether these complex systems

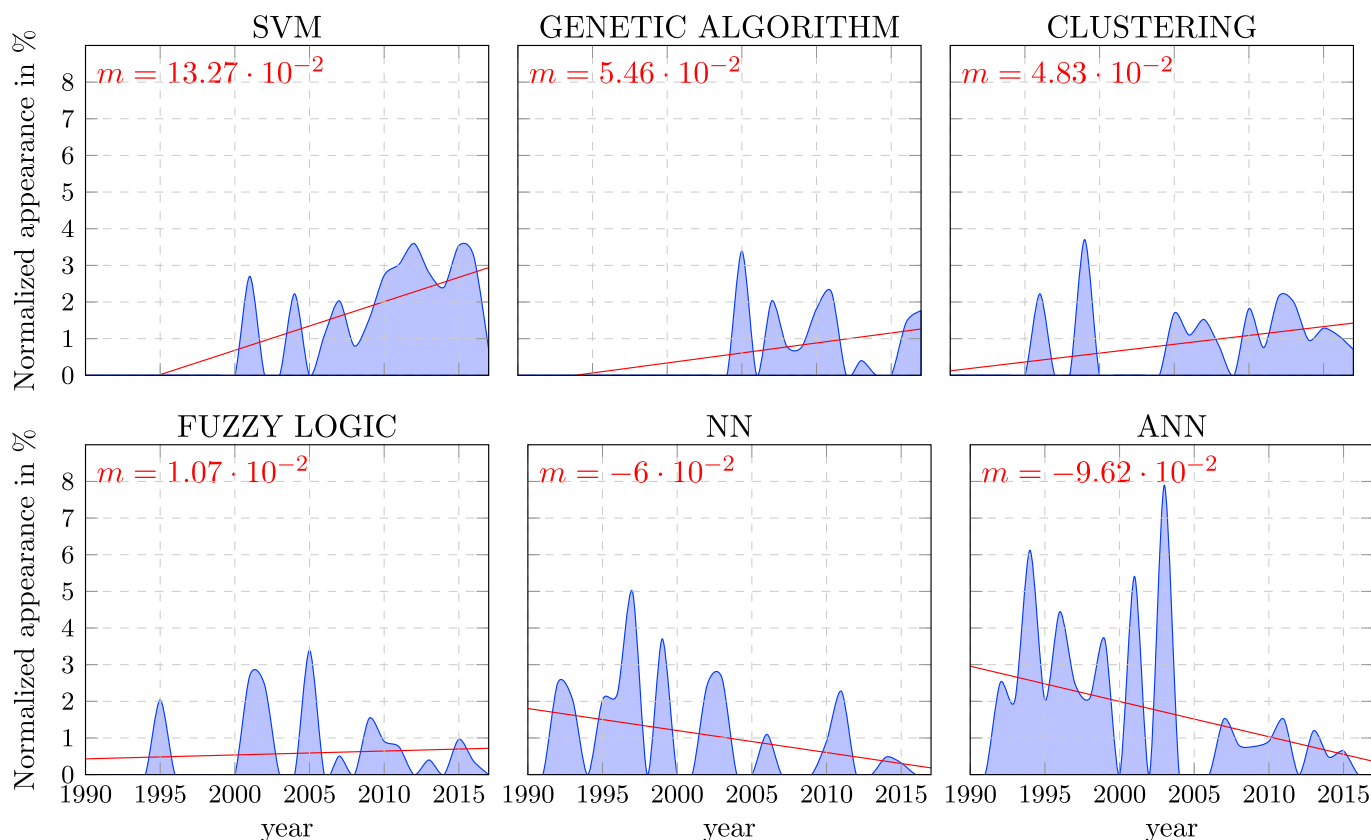


Fig. 8. Normalized appearance in % of keywords in the area of Artificial Intelligence (AI).

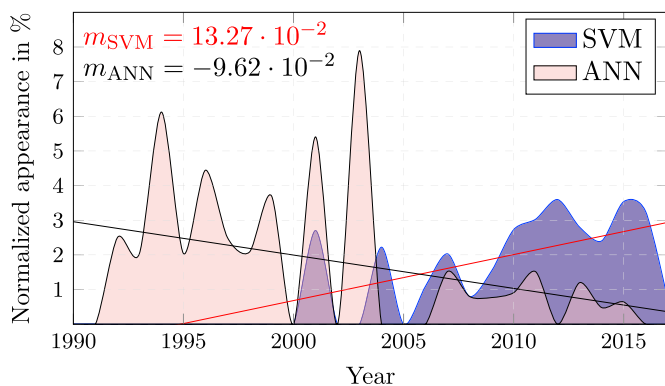


Fig. 9. Normalized importance of ANN and SVM.

have dangerous side effects. The lack of research in that area has far reaching consequences, because safety and reliability concerns are a big hurdle when it comes to large scale deployment of computer executed algorithms for medicine and biology [144].

Having discussed our analysis results, we move on to present some insights into the processes which influence topic change. There are technical aspects which cause one topic to be superseded by another. For example, ANN is in decline because SVM delivers better classification results [145]. However, there are topic changes which cannot be explained by technical aspects alone. For example, the normalized appearance graph for IMAGE REGISTRATION, shown in Fig. 7, peaked in 1999. Subsequently, the keyword did not appear in any paper for 6 consecutive years before it picked up again. Similar gaps exist for BLOOD FLOW and CT. We suspect that these gaps indicate a problem in the CBM management. Fig. 2 shows that CBM did not attract many papers during the period from 2000 to 2004. That means the gaps in the normalized

appearance of keywords plots coincide with a period of low article output. Since 2005, the number of articles published in CBM increased significantly. A lack of focus and effort from the editorial board is likely to have caused that downturn.

The editorial board and the editor in chief in particular play a crucial role in the journal success. CBM has a broad scope, hence good quality control is needed to attract and publish outstanding papers from a wide range of biomedical research fields. Reviews with a high standard should be provided to authors as fast as possible. That will encourage authors to submit their good papers and this in turn will improve the reputation of the journal. Another way to increase the topic diversity, while maintaining quality control, is to incorporate special issues. The guest editors need to be pioneers in the special issue areas, in order to attract good quality submissions. For example, Fig. 2 shows that the year 2007 had 197 articles, considerably higher than all the previous years and the following 5 years. Closer inspection shows that there were 12 issues⁴ in 2007, the same number as in 2006 and 2008. However, there were 3 special issues during 2007. In 2008 there was no special issue published and in 2006 there were 2 special issues. The special issue on medical ontologies was published in July and August 2006, i.e. as issues 7 and 8. That means, there were only 11 content issues in 2006.

This study depends on the web of science database. There are other sources, such as EMBASE⁵ and MEDLINE,⁶ available. However, the alternative sources provide the data in a different format. Therefore, using them was impracticable. Furthermore, the CBM publications are listed in the web of science database – that was sufficient for the current study. The main limitation of this study is the subjective selection of 40

⁴ The number refers to the sum of regular and special issues.

⁵ URL (01.09.2017): <https://www.elsevier.com/solutions/embase-biomedical-research>.

⁶ URL (01.09.2017): <https://www.nlm.nih.gov/bsd/pmresources.html>.

keywords. Using more keywords might reveal further trends and topic changes. Another limitation is that we have used linear models to predict future topics from past observations. We recognise that computers and related topics are the engine of change. That change is rather predictable and, according to Moore's law, it is almost linear [146]. However, a new medical data acquisition method or a new widespread disease may become a game changer. Unfortunately, these game changers are hard to predict, especially with linear models.

5. Conclusion

In this study, we documented and predicted topic changes in CBM. On a technical level, that was done by analysing author supplied keywords in all CBM publications from 1990 to 2017. The analysis was structured into two distinct parts. The first part was cluster analysis and the second part focused on tracking the keywords over time. The cluster analysis revealed the depth and breadth of topics covered in CBM. Tracking keywords over time resulted in 40 graphs that document the normalized yearly keyword appearance in percent. A large value of the accumulated gradients provides strong evidence for the diversity of CBM topics.

Our bibliometric analysis can help the CBM readership and the wider research community to plan their research. We found that SVM, EEG and IMAGE PROCESSING are very well established topics in. In the discussion section, we put forward some research gaps and highlight deep learning as an up and coming decision making algorithm. We recognise that computers in biology and medicine will continue to be an engine for progress and indeed change. That change will be gradual and linear, similar to the gradual demise of ANN and the steady rise of SVM. We do not anticipate any sudden and unexpected events from using mature computing machinery. Such sudden and unexpected events can occur as a reaction to new wide spread diseases and, to a lesser extent, in reaction to new data acquisition methods. The outcomes of our analysis can help the CBM editors to maintain the journal as a relevant forum to exchange ideas on the latest trends for computing machinery in biology and medicine. We recommend embracing new ideas and not shying away from complex methods, because they are the agents of change. Fast and sound reviews will improve the reputation with authors. Frequent guest editions can also help to explore new topics or vitalize dormant areas.

Acronyms

ANS	Autonomic Nervous System
ANN	Artificial Neural Network
AI	Artificial Intelligence
CBM	Computers in Biology and Medicine
CT	Computed Tomography
D	Data
DWT	Discrete Wavelet Transform
ECG	Electrocardiogram
EEG	Electroencephalography
F	Feature
FEM	Finite Element Method
HRV	Heart Rate Variability
M	Medical
MRI	Magnetic Resonance Imaging
NN	Neural Network
PCA	Principal Component Analysis
SVM	Support Vector Machine
TDT	Topic Detection and Tracking

References

- [1] Usman Akram M, Khalid Shehzad, Tariq Anam, Khan Shoab A, Azam Farooque. Detection and classification of retinal lesions for grading of diabetic retinopathy. *Comput Biol Med* 2014;45:161–71.
- [2] Subasi Abdulhamit. Medical decision support system for diagnosis of neuromuscular disorders using dwt and fuzzy support vector machines. *Comput Biol Med* 2012;42(8):806–15.
- [3] Rajendra Acharya U, Faust Oliver, Adib Kadri Nahrizul, Suri Jasjit S, Yu Wenwei. Automated identification of normal and diabetes heart rate signals using nonlinear measures. *Comput Biol Med* 2013;43(10):1523–9.
- [4] Mookiah Muthu Rama Krishnan, Rajendra Acharya U, Koh Joel EW, Chandran Vinod, Kuang Chua Chua, Hong Tan Jen, Min Lim Choo, Ng EYK, Noronha Kevin, Tong Louis, et al. Automated diagnosis of age-related macular degeneration using greyscale features from digital fundus images. *Comput Biol Med* 2014;53:55–64.
- [5] Farhadi Ghalati Pejman, Keshavarzian Erfan, Abouali Omid, Faramarzi Abolhassan, Tu Jiyuan, Shakibafard Alireza. Numerical analysis of micro-and nano-particle deposition in a realistic human upper airway. *Comput Biol Med* 2012;42(1):39–49.
- [6] Rajendra Acharya U, Bhat Shreya, Koh Joel EW, Bhandary Sulatha V, Adeli Hojjat. A novel algorithm to detect glaucoma risk using texture and local configuration pattern features extracted from fundus images. *Comput Biol Med* 2017;88:72–83.
- [7] Maheshwari Shishir, Bilas Pachori Ram, Kanhangad Vivek, Bhandary Sulatha V, Rajendra Acharya U. Iterative variational mode decomposition based automated detection of glaucoma using fundus images. *Comput Biol Med* 2017;88:142–9.
- [8] Mookiah Muthu Rama Krishnan, Rajendra Acharya U, Fujita Hamido, Koh Joel EW, Tan Jen Hong, Noronha Kevin, Bhandary Sulatha V, Kuang Chua Chua, Lim Choo Min, Laude Augustinus, et al. Local configuration pattern features for age-related macular degeneration characterization and classification. *Comput Biol Med* 2015;63:208–18.
- [9] Zou Quan, Mao Yaozong, Hu Lingling, Wu Yunfeng, Ji Zhiliang. mirclassify: an advanced web server for mirna family classification and annotation. *Comput Biol Med* 2014;45:157–60.
- [10] Faust Oliver, Acharya Rajendra, Krishnan SM, Min Lim Choo. Analysis of cardiac signals using spatial filling index and time-frequency domain. *Biomed Eng Online* 2004;3(1):30.
- [11] Rajendra Acharya U, Sudarshan Vidya K, Rong Soon Qing, Tan Zechariah, Lim Choo Min, Koh Joel EW, Nayak Sujatha, Bhandary Sulatha V. Automated detection of premature delivery using empirical mode and wavelet packet decomposition techniques with uterine electromyogram signals. *Comput Biol Med* 2017;85:33–42.
- [12] Basiri Parsa A, Rashidi MM, Anwar Bég O, Sadri SM. Semi-computational simulation of magneto-hemodynamic flow in a semi-porous channel using optimal homotopy and differential transform methods. *Comput Biol Med* 2013;43(9):1142–53.
- [13] Porta Alberto, Bassani Tito, Bari Vlasta, Tobaldini Eleonora, Takahashi Anielle CM, Catai Aparecida M, Montano Nicola. Model-based assessment of baroreflex and cardiopulmonary couplings during graded head-up tilt. *Comput Biol Med* 2012;42(3):298–305.
- [14] Arthur Campfield L, Blocker David C. Simulation of the autonomic neural control of insulin secretion. *Comput Biol Med* 1979;9(3):191–203.
- [15] Lemaître Guillaume, Marti Robert, Freixenet Jordi, Vilanova Joan C, Walker Paul M, Meriaudeau Fabrice. Computer-aided detection and diagnosis for prostate cancer based on mono and multi-parametric mri: a review. *Comput Biol Med* 2015;60:8–31.
- [16] Mookiah Muthu Rama Krishnan, Rajendra Acharya U, Chua Chua Kuang, Lim Choo Min, Ng EYK, Laude Augustinus. Computer-aided diagnosis of diabetic retinopathy: a review. *Comput Biol Med* 2013;43(12):2136–55.
- [17] Rajendra Acharya U, Mookiah Muthu Rama Krishnan, Koh Joel EW, Tan Jen Hong, Noronha Kevin, Bhandary Sulatha V, Krishna Rao A, Hagiwara Yuki, Kuang Chua Chua, Laude Augustinus. Novel risk index for the identification of age-related macular degeneration using radon transform and dwt features. *Comput Biol Med* 2016;73:131–40.
- [18] Yu Dejian, Shi Shunshun. Researching the development of atanassov intuitionistic fuzzy set: using a citation network analysis. *Appl Soft Comput* 2015;32:189–98.
- [19] Wan Kevin, Anyi Utap, Anuar NB, Zainab AN. Bibliometric studies on single journals: a review. *Malays J Libr Inf Sci* 2009;14(1).
- [20] Wang Chong-Chen, Ho Yuh-Shan. Research trend of metal-organic frameworks: a bibliometric analysis. *Scientometrics* 2016;109(1):481–513.
- [21] Louis Heck J, Bremser Wayne G. Six decades of the accounting review: a summary of author and institutional contributors. *Account Rev* 1986;735–44.
- [22] Roy Sanku Bilas, Basak Moutusi. Journal of documentation: a bibliometric study. *Libr Philos Pract* 2013:1.
- [23] Allan James. Topic detection and tracking: event-based information organization, vol. 12. Springer Science & Business Media; 2012.
- [24] Yu HONG, Zhang Yu, Ting LIU, Sheng LI. Topic detection and tracking review. *J Chin Inf Process* 2007;6(21):77–9.
- [25] Lavrenko Victor, Allan James, DeGuzman Edward, LaFlamme Daniel, Pollard Veera, Thomas Stephen. Relevance models for topic detection and tracking. In: Proceedings of the second international conference on human language technology research. Morgan Kaufmann Publishers Inc.; 2002. p. 115–21.
- [26] Cobo Manolo J, Martínez MA, Gutiérrez-Salcedo M, Fujita Hamido, Herrera-Viedma Enrique. 25years at knowledge-based systems: a bibliometric analysis. *Knowl Base Syst* 2015;80:3–13.
- [27] Goodall Amanda H. Highly cited leaders and the performance of research universities. *Res Pol* 2009;38(7):1079–92.
- [28] Small Henry, Boyack Kevin W, Klavans Richard. Identifying emerging topics in science and technology. *Res Pol* 2014;43(8):1450–67.

- [29] Suominen Arho, Toivanen Hannes. Map of science with topic modeling: comparison of unsupervised learning and human-assigned subject classification. *J Assoc Inf Sci Technol* 2016;67(10):2464–76.
- [30] Xie Shaodong, Zhang Jing, Ho Yuh-Shan. Assessment of world aerosol research trends by bibliometric analysis. *Scientometrics* 2008;77(1):113–30.
- [31] Li Zhi, Ho Yuh-Shan. Use of citation per publication as an indicator to evaluate contingent valuation research. *Scientometrics* 2008;75(1):97–110.
- [32] Mao Ning, Wang Ming-Hung, Ho Yuh-Shan. A bibliometric study of the trend in articles related to risk assessment published in science citation index. *Hum Ecol Risk Assess* 2010;16(4):801–24.
- [33] Zhang Yi, Zhang Guangquan, Chen Hongshu, Porter Alan L, Zhu Donghua, Lu Jie. Topic analysis and forecasting for science, technology and innovation: methodology with a case study focusing on big data research. *Technol Forecast Soc Change* 2016;105:179–91.
- [34] Zhang Yi, Chen Hongshu, Lu Jie, Zhang Guangquan. Detecting and predicting the topic change of knowledge-based systems: a topic-based bibliometric analysis from 1991 to 2016. *Knowledge-Based Systems*; 2017.
- [35] Fu Hui-Zhen, Wang Ming-Huang, Ho Yuh-Shan. Mapping of drinking water research: a bibliometric analysis of research output during 1992–2011. *Sci Total Environ* 2013;443:757–65.
- [36] Zhang Gangfeng, Xie Shaodong, Ho Yuh-Shan. A bibliometric analysis of world volatile organic compounds research trends. *Scientometrics* 2010;83(2):477–92.
- [37] Ho Yuh-Shan, Satoh Hiroaki, Lin Shih-Yuan. Japanese lung cancer research trends and performance in science citation index. *Intern Med* 2010;49(20):2219–28.
- [38] Garfield Eugene. The web of knowledge: a Festschrift in honor of Eugene Garfield. *Information Today, Inc.*; 2000.
- [39] Garfield Eugene. From the science of science to scientometrics visualizing the history of science with histcite software. *Journal of Informetrics* 2009;3(3):173–9.
- [40] Van Eck Nees Jan, Waltman Ludo. Software survey: vosviewer, a computer program for bibliometric mapping. *Scientometrics* 2010;84(2):523–38.
- [41] van Eck Nees Jan, Waltman Ludo. Visualizing bibliometric networks. In: *Measuring scholarly impact*. Springer; 2014. p. 285–320.
- [42] Van Eck Nees Jan, Waltman Ludo. Text mining and visualization using vosviewer. *arXiv preprint arXiv:1109.2058*. 2011.
- [43] Waltman Ludo, Van Eck Nees Jan, Noyons Ed CM. A unified approach to mapping and clustering of bibliometric networks. *Journal of Informetrics* 2010;4(4):629–35.
- [44] Flis Ivan, van Eck Nees Jan. A large-scale term co-occurrence analysis of scientific literature in psychology. *Framing psychology as a discipline Hist Psychol* 1950–1999:1–54. Online; 2017.
- [45] Su Hsin-Ning, Lee Pei-Chun. Mapping knowledge structure by keyword co-occurrence: a first look at journal papers in technology foresight. *Scientometrics* 2010;85(1):65–79.
- [46] Cuccurullo Corrado, Aria Massima, Sarto Fabrizia. Foundations and trends in performance management: a twenty-five years bibliometric analysis in business and public administration domains. *Scientometrics* 2016;108(2):595–611.
- [47] Ihaka Ross. R: past and future history. *Computing science and statistics*. 1998. 392396.
- [48] Lamport Leslie. LATEX: a document preparation system: user's guide and reference manual. *Addison-wesley*; 1994.
- [49] Feuersänger Christian. *Manual for package pgfplots*. 2011. p. 17. URL, <http://www.ctan.org/tex-archive/help/Catalogue/entries/pgfplots.html>. [Probablement installé dans vos systèmes sous le nom pgfplots.pdf](http://www.ctan.org/tex-archive/help/Catalogue/entries/pgfplots.html).
- [50] Anton Howard, Bivens Irl, Davis Stephen. *Calculus, volume 2*. Wiley Hoboken; 2002.
- [51] Minerbo Gerald. Maximum entropy reconstruction from cone-beam projection data. *Comput Biol Med* 1979;9(1):29–37.
- [52] Ong SH, Jin XC, Sinniah R, et al. Image analysis of tissue sections. *Comput Biol Med* 1996;26(3):269–79.
- [53] Adelman Holger G. An edge-sensitive noise reduction algorithm for image processing. *Comput Biol Med* 1999;29(2):137–45.
- [54] Uenohara Michihiro, Kanade Takeo. Vision-based object registration for real-time image overlay. *Comput Biol Med* 1995;25(2):249–60.
- [55] Lynch Michael, Ghita Ovidiu, Whelan Paul F. Automatic segmentation of the left ventricle cavity and myocardium in mri data. *Comput Biol Med* 2006;36(4):389–407.
- [56] Chiverton John, Wells Kevin, Lewis Emma, Chen Chao, Podda Barbara, Johnson Declan. Statistical morphological skull stripping of adult and infant mri data. *Comput Biol Med* 2007;37(3):342–57.
- [57] Zhang Ying, Sankar Ravi, Qian Wei. Boundary delineation in transrectal ultrasound image for prostate cancer. *Comput Biol Med* 2007;37(11):1591–9.
- [58] Hosseini Seyed Morteza, Naghs-Nilchi Ahmad-Reza. Medical ultrasound image compression using contextual vector quantization. *Comput Biol Med* 2012;42(7):743–50.
- [59] Reticco Alessandra, Delogu Pasquale, Evelina Fantacci Maria, Gori Ilaria, Preite Martinez A. Lung nodule detection in low-dose and thin-slice computed tomography. *Comput Biol Med* 2008;38(4):525–34.
- [60] Kerr JP, Bartlett EB. Medical image processing utilizing neural networks trained on a massively parallel computer. *Comput Biol Med* 1995;25(4):393–403.
- [61] Sudarshan Vidya K, Ng EYK, Rajendra Acharya U, Meng Chou Siaw, San Tan Ru, Ghista Dhanjoo N. Computer-aided diagnosis of myocardial infarction using ultrasound images with dwt, glcm and hos methods: a comparative study. *Comput Biol Med* 2015;62:86–93.
- [62] Sudarshan Vidya K, Rajendra Acharya U, Ng EYK, San Tan Ru, Meng Chou Siaw, Ghista Dhanjoo N. Data mining framework for identification of myocardial infarction stages in ultrasound: a hybrid feature extraction paradigm (part 2). *Comput Biol Med* 2016;71:241–51.
- [63] Martis Roshan Joy, Rajendra Acharya U, Adeli Hojjat. Current methods in electrocardiogram characterization. *Comput Biol Med* 2014;48:133–49.
- [64] İşler Yalçın, Kuntalp Mehmet. Combining classical hrv indices with wavelet entropy measures improves to performance in diagnosing congestive heart failure. *Comput Biol Med* 2007;37(10):1502–10.
- [65] Faust Oliver, Rajendra Acharya U, Molinari Filippo, Chattopadhyay Subhagata, Tamura Toshiyo. Linear and non-linear analysis of cardiac health in diabetic subjects. *Biomed Signal Process Contr* 2012;7(3):295–302.
- [66] Faust Oliver, Ramanan Prasad V, Swapna G, Chattopadhyay Subhagata, Lim Teik-Cheng. Comprehensive analysis of normal and diabetic heart rate signals: a review. *J Mech Med Biol* 2012;12(05):1240033.
- [67] Katz Michael J. Fractals and the analysis of waveforms. *Comput Biol Med* 1988;18(3):145–56.
- [68] Pradhan N, Narayana Dutt D. Use of running fractal dimension for the analysis of changing patterns in electroencephalograms. *Comput Biol Med* 1993;23(5):381–8.
- [69] Ince Nuri F, Tewfik Ahmed H, Arica Sami. Extraction subject-specific motor imagery time-frequency patterns for single trial eeg classification. *Comput Biol Med* 2007;37(4):499–508.
- [70] Singh Anurag, Sharma LN, Dandapat Samarendra. Multi-channel eeg data compression using compressed sensing in eigenspace. *Comput Biol Med* 2016;73:24–37.
- [71] Abboud Shimon, Sadeh Dror. Spectral analysis of the fetal electrocardiogram. *Comput Biol Med* 1989;19(6):409–15.
- [72] Güler Inan, Kemal Kiyimik M, Akin Mehmet, Alkan Ahmet. Ar spectral analysis of eeg signals by using maximum likelihood estimation. *Comput Biol Med* 2001;31(6):441–50.
- [73] Kemal Kiyimik M, Güler Inan, Dizibüyük Alper, Akin Mehmet. Comparison of stft and wavelet transform methods in determining epileptic seizure activity in eeg signals for real-time application. *Comput Biol Med* 2005;35(7):603–16.
- [74] Tohumoglu Gülay, Erbil Sezgin K. Ecg signal compression by multi-iteration ezw coding for different wavelets and thresholds. *Comput Biol Med* 2007;37(2):173–82.
- [75] Koh Joel EW, Rajendra Acharya U, Hagiwara Yuki, Raghavendra U, Hong Tan Jen, Vinita Sree S, Bhandary Sulatha V, Krishna Rao A, Sivaprasad Sobha, Chua Chua Kuang, et al. Diagnosis of retinal health in digital fundus images using continuous wavelet transform (cwt) and entropies. *Comput Biol Med* 2017;84:89–97.
- [76] Özbay Yüksel, Ceylan Rahime, Karlik Bekir. A fuzzy clustering neural network architecture for classification of eeg arrhythmias. *Comput Biol Med* 2006;36(4):376–88.
- [77] Ros Eduardo, Mota Sonia, Fernández FJ, Toro FJ, Bernier José Luis. Ecg characterization of paroxysmal atrial fibrillation: parameter extraction and automatic diagnosis algorithm. *Comput Biol Med* 2004;34(8):679–96.
- [78] Rajendra Acharya U, Mookiah Muthu Rama Krishnan, Koh Joel EW, Tan Jen Hong, Bhandary Sulatha V, Krishna Rao A, Fujita Hamido, Hagiwara Yuki, Kuang Chua Chua, Laude Augustinus. Automated screening system for retinal health using bi-dimensional empirical mode decomposition and integrated index. *Comput Biol Med* 2016;75:54–62.
- [79] Rajendra Acharya U, Raghavendra U, Fujita Hamido, Hagiwara Yuki, Koh Joel EW, Hong Tan Jen, Sudarshan Vidya K, Vijayanathan Anushya, Yeong Chai Hong, Gudigar Anjan, et al. Automated characterization of fatty liver disease and cirrhosis using curvelet transform and entropy features extracted from ultrasound images. *Comput Biol Med* 2016;79:250–8.
- [80] Kara Sadik, Dirgenali Fatma, Okkesim Şükürü. Detection of gastric dysrhythmia using wt and ann in diabetic gastroparesis patients. *Comput Biol Med* 2006;36(3):276–90.
- [81] Marinakis Yannis, Dounias Georgios, Jantzen Jan. Pap smear diagnosis using a hybrid intelligent scheme focusing on genetic algorithm based feature selection and nearest neighbor classification. *Comput Biol Med* 2009;39(1):69–78.
- [82] Barboni Miranda Gisele Helena, Felipe Joaquim Cezar. Computer-aided diagnosis system based on fuzzy logic for breast cancer categorization. *Comput Biol Med* 2015;64:334–46.
- [83] Moayed Fatemeh, Azimifar Zohreh, Boostani Reza, Katebi Serajodin. Contourlet-based mammography mass classification using the svm family. *Comput Biol Med* 2010;40(4):373–83.
- [84] Chen Yen-Chen, Ke Wan-Chi, Chiu Hung-Wen. Risk classification of cancer survival using ann with gene expression data from multiple laboratories. *Comput Biol Med* 2014;48:1–7.
- [85] Shah Shital, Kusiak Andrew. Cancer gene search with data-mining and genetic algorithms. *Comput Biol Med* 2007;37(2):251–61.
- [86] Shen Qi, Mei Zhen, Ye Bao-Xian. Simultaneous genes and training samples selection by modified particle swarm optimization for gene expression data classification. *Comput Biol Med* 2009;39(7):646–9.
- [87] Zhong Lei, Ma Chang-Ying, Zhang Hui, Yang Li-Jun, Wan Hua-Lin, Xie Qing-Qing, Li Lin-Li, Yang Sheng-Yong. A prediction model of substrates and non-substrates of breast cancer resistance protein (bcrp) developed by ga-cg-svm method. *Comput Biol Med* 2011;41(11):1006–13.
- [88] Proost Johannes H, Meijer Dirk KF. Mw/pharm, an integrated software package for drug dosage regimen calculation and therapeutic drug monitoring. *Comput Biol Med* 1992;22(3):155–63.
- [89] Subasi Abdulhamit. Application of adaptive neuro-fuzzy inference system for epileptic seizure detection using wavelet feature extraction. *Comput Biol Med* 2007;37(2):227–44.

- [90] Fonseca Everthon Silva, Guido Rodrigo Capobianco, Scalassara Paulo Rogério, Maciel Carlos Dias, Pereira José Carlos. Wavelet time-frequency analysis and least squares support vector machines for the identification of voice disorders. *Comput Biol Med* 2007;37(4):571–8.
- [91] Mookiah Muthu Rama Krishnan, Rajendra Acharya U, Koh Joel EW, Chua Chua Kuang, Tan Jen Hong, Chandran Vinod, Lim Choo Min, Noronha Kevin, Laude Augustinus, Tong Louis. Decision support system for age-related macular degeneration using discrete wavelet transform. *Med Biol Eng Comput* 2014;52(9):781–96.
- [92] Rajendra Acharya U, Mookiah Muthu Rama Krishnan, Koh Joel EW, Tan Jen Hong, Bhandary Sulatha V, Krishna Rao A, Hagiwara Yuki, Kuang Chua Chua, Laude Augustinus. Automated diabetic macular edema (dme) grading system using dwt, dct features and maculopathy index. *Comput Biol Med* 2017;84:59–68.
- [93] Rajendra Acharya U, Mookiah Muthu Rama Krishnan, Koh Joel EW, Tan Jen Hong, Noronha Kevin, Bhandary Sulatha V, Krishna Rao A, Hagiwara Yuki, Kuang Chua Chua, Laude Augustinus. Novel risk index for the identification of age-related macular degeneration using radon transform and dwt features. *Comput Biol Med* 2016;73:131–40.
- [94] Eltoukhy Mohamed Meselhy, Faye Ibrahim, Samir Brahim Belhaouari. A statistical based feature extraction method for breast cancer diagnosis in digital mammogram using multiresolution representation. *Comput Biol Med* 2012;42(1):123–8.
- [95] Eltoukhy Mohamed Meselhy, Faye Ibrahim, Samir Brahim Belhaouari. A comparison of wavelet and curvelet for breast cancer diagnosis in digital mammogram. *Comput Biol Med* 2010;40(4):384–91.
- [96] Kahn Charles E, Roberts Linda M, Shaffer Katherine A, Haddawy Peter. Construction of a bayesian network for mammographic diagnosis of breast cancer. *Comput Biol Med* 1997;27(1):19–29.
- [97] Kerr Grainne, Ruskin Heather J, Crane Martin, Doolan Pdraig. Techniques for clustering gene expression data. *Comput Biol Med* 2008;38(3):283–93.
- [98] Fernandez Elmer A, Balzarini Monica. Improving cluster visualization in self-organizing maps: application in gene expression data analysis. *Comput Biol Med* 2007;37(12):1677–89.
- [99] Piskin Senol, Serdar Celebi M. Analysis of the effects of different pulsatile inlet profiles on the hemodynamical properties of blood flow in patient specific carotid artery with stenosis. *Comput Biol Med* 2013;43(6):717–28.
- [100] Tian Fang-Bao, Zhu Luoding, Fok Pak-Wing, Lu Xi-Yun. Simulation of a pulsatile non-Newtonian flow past a stenosed 2d artery with atherosclerosis. *Comput Biol Med* 2013;43(9):1098–113.
- [101] Murphy Jonathan, Boyle Fergal. Predicting neointimal hyperplasia in stented arteries using time-dependant computational fluid dynamics: a review. *Comput Biol Med* 2010;40(4):408–18.
- [102] Creane Arthur, Maher Eoghan, Sultan Sherif, Hynes Niamh, Kelly Daniel J, Lally Caitriona. Finite element modelling of diseased carotid bifurcations generated from in vivo computerised tomographic angiography. *Comput Biol Med* 2010;40(4):419–29.
- [103] Van Wyk Stevin, Prahil Wittberg Lisa, Fuchs Laszlo. Wall shear stress variations and unsteadiness of pulsatile blood-like flows in 90-degree bifurcations. *Comput Biol Med* 2013;43(8):1025–36.
- [104] Lee Jong-Min, Kim Dae-Jin, Kim In-Young, Park Kwang-Suk, Kim Sun I. Detrended fluctuation analysis of eeg in sleep apnea using mit/bih polysomnography data. *Comput Biol Med* 2002;32(1):37–47.
- [105] Sridhar Chaitra, Bhat Shreya, Rajendra Acharya U, Adeli Hojjat, Muralidhar Bairy G. Diagnosis of attention deficit hyperactivity disorder using imaging and signal processing techniques. *Comput Biol Med* 2017;88:93–9.
- [106] Sargolzaei Saman, Cabrerizo Mercedes, Goryawala Mohammed, Salah Eddin Anas, Adjouadi Malek. Scalp eeg brain functional connectivity networks in pediatric epilepsy. *Comput Biol Med* 2015;56:158–66.
- [107] Benlamri R, Batouche M, Rami S, Bouanaka C. An automated system for analysis and interpretation of epileptiform activity in the eeg. *Comput Biol Med* 1997;27(2):129–39.
- [108] Burlina Philippe, Pacheco Katia D, Joshi Neil, Freund David E, Bressler Neil M. Comparing humans and deep learning performance for grading amd: a study in using universal deep features and transfer learning for automated amd analysis. *Comput Biol Med* 2017;82:80–6.
- [109] Zhou Teng, Han Guoqiang, Nan Li Bing, Lin Zhizhe, Ciaccio Edward J, Green Peter H, Qin Jing. Quantitative analysis of patients with celiac disease by video capsule endoscopy: a deep learning method. *Comput Biol Med* 2017;85:1–6.
- [110] Rajendra Acharya U, Lih Oh Shu, Hagiwara Yuki, Hong Tan Jen, Adam Muhammad, Gertych Arkadiusz, San Tan Ru. A deep convolutional neural network model to classify heartbeats. *Comput Biol Med* 2017;89:389–96.
- [111] Morbiducci Umberto, Tura Andrea, Grigioni Mauro. Genetic algorithms for parameter estimation in mathematical modeling of glucose metabolism. *Comput Biol Med* 2005;35(10):862–74.
- [112] Qian Wei, Sankar Ravi, Song Xiaoshan, Sun Xuejun, Clark Robert. Standardization for image characteristics in telemammography using genetic and nonlinear algorithms. *Comput Biol Med* 2005;35(3):183–96.
- [113] Nan Li Bing, Kong Chui Chee, Chang Stephen, Ong Sim Heng. Integrating spatial fuzzy clustering with level set methods for automated medical image segmentation. *Comput Biol Med* 2011;41(1):1–10.
- [114] Zhang Bob, Zhang Lin, Zhang Lei, Karray Fakhri. Retinal vessel extraction by matched filter with first-order derivative of Gaussian. *Comput Biol Med* 2010;40(4):438–45.
- [115] Al-Rawi Mohammed, Qutaishat Munib, Arrar Mohammed. An improved matched filter for blood vessel detection of digital retinal images. *Comput Biol Med* 2007;37(2):262–7.
- [116] Vermeer Koen A, Vos Frans M, Lemij Hans G, Vossepoel Albert M. A model based method for retinal blood vessel detection. *Comput Biol Med* 2004;34(3):209–19.
- [117] Yu Yanyan, Xiao Yang, Cheng Jieyu, Chiu Bernard. Breast lesion classification based on supersonic shear-wave elastography and automated lesion segmentation from b-mode ultrasound images. *Comput Biol Med* 2018;93:31–46.
- [118] Liu Jun, Li Ling, Wang Lei. Acetowhite region segmentation in uterine cervix images using a registered ratio image. *Comput Biol Med* 2018;93:47–55.
- [119] Ilunga-Mbuyamba Elisee, Gabriel Avina-Cervantes Juan, Cepeda-Negrete Jonathan, Alberto Ibarra-Manzano Mario, Chalopin Claire. Automatic selection of localized region-based active contour models using image content analysis applied to brain tumor segmentation. *Comput Biol Med* 2017;91:69–79.
- [120] Asgari Shadnaz, Mehri Alireza, Moussavi Maryam. Automatic detection of atrial fibrillation using stationary wavelet transform and support vector machine. *Comput Biol Med* 2015;60:132–42.
- [121] Petrés Andrius, Marozas Vaidotas, Sörmö Leif. Low-complexity detection of atrial fibrillation in continuous long-term monitoring. *Comput Biol Med* 2015;65:184–91.
- [122] Blanco-Velasco Manuel, Weng Binwei, Barner Kenneth E. Ecg signal denoising and baseline wander correction based on the empirical mode decomposition. *Comput Biol Med* 2008;38(1):1–13.
- [123] Benitez D, Gaydecki PA, Zaidi A, Fitzpatrick AP. The use of the hilbert transform in ecg signal analysis. *Comput Biol Med* 2001;31(5):399–406.
- [124] Pal Saurabh, Mitra Madhuchhanda. Empirical mode decomposition based ecg enhancement and qrs detection. *Comput Biol Med* 2012;42(1):83–92.
- [125] Karimipour Atiyeh, Homaeinezhad Mohammad Reza. Real-time electrocardiogram p-qrs-t detection-delineation algorithm based on quality-supported analysis of characteristic templates. *Comput Biol Med* 2014;52:153–65.
- [126] Dai Huhe, Jiang Shouda, Li Ye. Atrial activity extraction from single lead ecg recordings: evaluation of two novel methods. *Comput Biol Med* 2013;43(3):176–83.
- [127] Alcaraz Raúl, Rieta José Joaquín. Surface ecg organization analysis to predict paroxysmal atrial fibrillation termination. *Comput Biol Med* 2009;39(8):697–706.
- [128] Yuri Di Marco Luigi, Raine Daniel, Bourke John P, Langley Philip. Recurring patterns of atrial fibrillation in surface ecg predict restoration of sinus rhythm by catheter ablation. *Comput Biol Med* 2014;54:172–9.
- [129] Aggarwal Priya, Gupta Anubha. Double temporal sparsity based accelerated reconstruction of compressively sensed resting-state fmri. *Comput Biol Med* 2017;91:255–66.
- [130] Li Yuqian, Liu Xin, Wei Feng, Sima Diana M, Van Cauter Sofie, Himmelreich Uwe, Pi Yiming, Hu Guang, Yao Yi, Van Huffel Sabine. An advanced mri and mrsi data fusion scheme for enhancing unsupervised brain tumor differentiation. *Comput Biol Med* 2017;81:121–9.
- [131] Cao Peng, Liu Xiaoli, Yang Jinzhu, Zhao Dazhe, Huang Min, Zhang Jian, Zaiane Osmar. Nonlinearity-aware based dimensionality reduction and over-sampling for ad/mci classification from mri measures. *Comput Biol Med* 2017;91:21–37.
- [132] Vinita Sree Subbhuraam, Yin-Kwee Ng Eddie, Acharya Rajendra U, Faust Oliver. Breast imaging: a survey. *World J Clin Oncol* 2011;2(4):171.
- [133] Rajendra Acharya U, Faust Oliver, Vinita Sree S, Molinari Filippo, Suri Jasjit S. Thyroscreen system: high resolution ultrasound thyroid image characterization into benign and malignant classes using novel combination of texture and discrete wavelet transform. *Comput Meth Progr Biomed* 2012;107(2):233–41.
- [134] Shan Lee Hoi, Faust Oliver, Yu Wenwei. Data mining framework for breast cancer detection in mammograms: a hybrid feature extraction paradigm. *Journal of Medical Imaging and Health Informatics* 2014;4(5):756–65.
- [135] Rajendra Acharya U, Faust Oliver, Molinari Filippo, Vinita Sree S, Junnarkar Sameer P, Sudarshan Vidya. Ultrasound-based tissue characterization and classification of fatty liver disease: a screening and diagnostic paradigm. *Knowl Base Syst* 2015;75:66–77.
- [136] Faust Oliver, Rajendra Acharya U, Ng EYK, Jen Hong Tan, Yu Wenwei. Application of infrared thermography in computer aided diagnosis. *Infrared Phys Technol* 2014;66:160–75.
- [137] Egan Gary F, Liu Zhi-Qiang. Computers and networks in medical and healthcare systems. *Comput Biol Med* 1995;25(3):355–65.
- [138] Ng KH, Faust Oliver, Sudarshan Vidya, Chattopadhyay Subhagata. Data overloading in medical imaging: emerging issues, challenges and opportunities in efficient data management. *Journal of medical imaging and health informatics* 2015;5(4):755–64.
- [139] Adam Muhammad, Ng Eddie YK, Hong Tan Jen, Heng Marabelle L, Tong Jasper WK, Rajendra Acharya U. Computer aided diagnosis of diabetic foot using infrared thermography: a review. *Comput Biol Med* 2017;91:326–36.
- [140] Faust Oliver, Yu Wenwei, Rajendra Acharya U. The role of real-time in biomedical science: a meta-analysis on computational complexity, delay and speedup. *Comput Biol Med* 2015;58:73–84.
- [141] Ozgoren Murat, Erdogan Ugras, Bayazit Onur, Taslica Serhat, Oniz Adile. Brain asymmetry measurement using emis (embedded interactive stimulation unit) in applied brain biophysics. *Comput Biol Med* 2009;39(10):879–88.
- [142] Faust Oliver, Acharya Rajendra, Spath Bernhard HC, Min Lim Choo. Systems engineering principles for the design of biomedical signal processing systems. *Comput Meth Progr Biomed* 2011;102(3):267–76.
- [143] Faust Oliver, Rajendra Acharya U, Sudarshan Vidya K, Tan Ru San, Hong Yeong Chai, Molinari Filippo, Ng Kwan Hoong. Computer aided diagnosis of coronary artery disease, myocardial infarction and carotid atherosclerosis using ultrasound images: a review. *Phys Med* 2017;33:1–15.

- [144] Faust Oliver, Shetty Ravindra, Vinitha Sree S, Acharya Sripathi, Acharya Rajendra, Ng EYK, Kok Poo Chua, Suri Jasjit. Towards the systematic development of medical networking technology. *J Med Syst* 2011;35(6):1431–45.
- [145] Faust Oliver, Rajendra Acharya U, Choo Min Lim, Spath Bernhard HC. Automatic identification of epileptic and background eeg signals using frequency domain parameters. *Int J Neural Syst* 2010;20(02):159–76.
- [146] Schaller Robert R. Moore's law: past, present and future. *IEEE Spectrum* 1997; 34(6):52–9.